

5. simpozij studenata doktorskih studija PMF-a : knjiga sažetaka

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KNJIGA SAŽETAKA
BOOK OF ABSTRACTS



April 24–25, 2021
24.–25. travnja 2021. g.

5. Simpozij
Studentata
PhD doktorskih
Student Symposium Studija

PMF

2021



Prirodoslovno-matematički fakultet | Zagreb
Faculty of Science | Zagreb
& ONLINE

**Simpozij studenata doktorskih studija PMF-a
PhD Student Symposium 2021**

**Knjiga sažetaka
Book of Abstracts**

Prirodoslovno-matematički fakultet, Sveučilište u Zagrebu
Faculty of Science, University of Zagreb

24.-25. travnja 2021. g.
April 24–25, 2021

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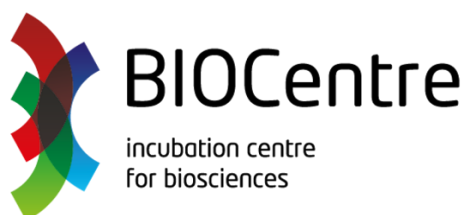
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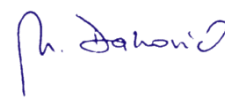
Drage studentice i dragi studenti doktorskih studija,

veliko mi je zadovoljstvo pozdraviti vas na petom jubilarnom Simpoziju doktoranda PMF-a. Izrazito me veseli da smo, unatoč svim izazovima koje je zadnja godina pred nas stavila, uspjeli se okupiti i organizirati još jedan u nizu simpozija doktorskih studenata.

Kako to priliči obljetnicama, i ovo smo peto izdanje Simpozij nadogradili te po prvi puta Simpozij održavamo tijekom dva dana. Osim toga, ove smo godine pozvali i doktorske studente ne samo izvan PMF-a već i izvan naše države da vam se pridruže i podijele s vama zadovoljstvo izlaganja svojih znanstvenih rezultata te čari istraživanja i bavljenja znanosti. Kako bismo omogućili što većem broju studenata doktorskih studija da se pridruže Simpoziju, ali i svima vama još malo podigli letvicu u vašoj doktorskoj izobrazbi te vas tako što bolje pripremili za sve izazove koji vas čekaju na vašem istraživačkom i znanstvenom putu, omogućili smo prezentaciju vaših rezultata i na engleskom jeziku, koju izrazito preporučujemo.

No, svakako, ovoga Simpozija sa svim njegovim proširenjima i nadgradnjama ne bi bilo da nema vas i vaše želje za istraživanjem, vašeg entuzijazma i znanstvene radoznalosti koja je iznjedrila brojne kvalitetne rezultate, a radi kojih ste ovaj vikend ovdje i koje ćete, vjerujem, s ponosom predstaviti svojim kolegama, mentorima i nastavnicima iz svojih ali i srodnih znanstvenih područja. Koliko vama studentima doktorskih studija ovaj Simpozij znači govore i brojke vas koji ste se prijavili kako biste svoje uspjehe u znanstvenom istraživanju podijelili s drugima, ali i vas koji ste se prijavili kako biste poslušali rezultate drugih i time pružili podršku jedni drugima na zajedničkom znanstvenom putu. A kakav taj put obično biva, da je pun uspona i padova, velikog broja uličica i slijepih ulica, s tek možda po kojom brzom cestom ili prečicom, u potpunosti razumijemo i mi seniorniji koji smo tim istim putem prošli prije vas. I zato vam možemo poručiti, hodajte tim putem široko otvornih očiju i nemojte nikada izgubiti mladenačku zaigranost i znatiželju, ne odustajete prerano, vjerujte svojim idejama i idealima, ali i poslušajte savjete onih koji su putem kročili prije vas. Iskoristite svaku mogućnost da prikupite znanje i iskustvo i ponesete ga sa sobom, jer put je dug i izazovan, a znanje i iskustvo bit će vaši najvjerniji suputnici na tom putu. No, isto tako, ne zaboravite, ovaj put donosi brojne nagrade i ispunjenja, a svaki sljedeći uspjeh vas osnažuje, izgrađuje i budi želju za osvajanjem novih vrhunaca!

A samo jedan od takvih vrhunaca osvojile su danas i vaše kolegice iz Organizacijskog odbora. Nakon više mjeseci neumornog rada i svih izazova koje su na tom putu morale svladati, dovele su ovaj Simpozij do njegove realizacije, na čemu im od srca čestitam i zahvaljujem! A svima vama koji ste se okupili, u ime Znanstvenog i Organizacijskog odbora Simpozija želim uspješan i ugodan znanstveni vikend na PMF-u.



Izv. prof. dr. sc. Marijana Đaković
prodekanica za znanost i doktorske studije

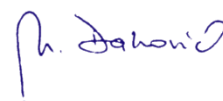
Dear PhD Students,

It is my great pleasure to welcome you to the fifth Faculty of Science PhD Student Symposium. I am extremely happy that, despite all the challenges that the last year has put before us, we managed to gather and organize another edition of Symposium and celebrate its fifth anniversary.

As it usually goes with anniversaries, we have here as well introduced some novelties and upgraded Symposium to a two-day meeting. Besides, we are inviting PhD students from and outside Croatia to join you in sharing the excitement of doing science and presenting research findings. To be in a position to invite a larger number of PhD students to the Symposium, but also to raise the standards of your PhD training and prepare you for all the challenges that await you on your scientific path, we have made this Symposium bilingual, and warmly welcome your presentations in English.

But despite all the novelties and upgrades, it is certainly you who make this Symposium possible! You and your desire, enthusiasm and scientific curiosity that has yielded loads of high-quality results, which you are here this weekend for, and which, I believe, you will be proudly presenting to your colleagues, mentors, and teachers from your own and related scientific fields. And what this Symposium means to you is clearly visible in the overall attendees' numbers, the number of those of you who will present, but also those of you who applied just to attend Symposium and supporting your colleagues on the scientific path you all just stepped on. But how this path looks like? It is certainly not the straight one, but rather full of ups and downs, full of smaller and larger dead-end streets, with maybe only a few fast roads or shortcuts. Although it mostly seems to you that we (seniors) are not aware of a large number of downs and dead-end streets, we ensure you, we walked the same path before you. Any suggestions? Certainly, yes! Walk this path with eyes wide open, and never, never lose your youthful playfulness and curiosity, do not give up too early, believe in your ideas and ideals, but also listen to advice of those who walked the path before you, and you will soon find out how enjoyable this path is. Moreover, take every opportunity to gain knowledge and experience, as the journey is challenging, and the knowledge and experience proved to be the most helpful and faithful companions on this trip. Once in such good company, surrounded with helpful and faithful friends, this journey brings plenty rewards and fulfillments, with each success empowering you, and awakening your desire to climb higher and conquer new heights!

And only one of those heights was conquered today by your colleagues from the Organizing Committee. After several months of tireless and dedicated work, and all the challenges that had to be overcome along the way, they brought this Symposium to its realization, for all of you to gather and have wonderful and enjoyable time together. I sincerely congratulate them! And to all of you who have gathered to make this Symposium happen, on behalf of the Scientific and Organizing Committee of the Symposium, I wish you a successful and pleasant scientific weekend at the Faculty of Science.



Assoc. Prof. Marijana Đaković
Vice-Dean for Science and Doctoral Studies



Subota Saturday

8:30----	Registracija <i>Registration</i>
9:00-9:15	Otvaranje <i>Opening</i>
9:15-9:45	PL 1
9:45-11:10	Sekcija 1: Usmena i mikro-izlaganja <i>Section 1: Oral and Flash Presentations</i>
11:10-11:30	
11:30-11:50	Embassy of France, EuChemS
11:50-13:20	Sekcija 2: Usmena i mikro-izlaganja <i>Section 2: Oral and Flash Presentations</i>
13:20-14:30	Pauza za ručak <i>Lunch Break</i>
14:30-15:00	PL 2
15:00-16:00	Sekcija 3: Usmena izlaganja <i>Section 3: Oral Presentations</i>
16:00-16:15	
16:15-17:15	Sekcija 4: Usmena izlaganja <i>Section 4: Oral Presentations</i>
17:15-17:30	
17:30-19:30	Posterska sekcija <i>Poster Section</i>

Nedjelja Sunday



9:00----	Registracija <i>Registration</i>
9:30-10:00	PL 3
10:00-11:00	Sekcija 5: Usmena izlaganja <i>Section 5: Oral Presentations</i>
11:00-11:15	
11:15-11:45	PL 4
11:45-12:45	Sekcija 6: Usmena izlaganja <i>Section 6: Oral Presentations</i>
12:45-13:45	Pauza za ručak <i>Lunch Break</i>
13:45-15:45	Radionica <i>Workshop</i>
15:45-16:00	
16:00-16:10	U.S. Embassy
16:10-17:35	Sekcija 7: Usmena izlaganja <i>Section 7: Oral Presentations</i>
17:35-17:55	Sponzori <i>Sponsors</i>
17:55-18:00	Zatvaranje <i>Closure</i>

Kratka pauza
Short break

PL - predavanja pozvanih predavača
Invited Lecturers



Detaljni program Simpozija

Detailed Symposium Program

SUBOTA 24. travnja 2021. g.
SATURDAY April 24, 2021


8:30–	Registracija – <i>Registration</i>
9:00–9:15	Svečano otvaranje Simpozija – <i>Symposium Opening</i>

9:15–9:45	<p>Pozvano predavanje 1 – <i>Invited Lecture 1</i></p> <p>prof. dr. sc. MARIJAN HERAK SEIZMOLOGIJA KAO MULTIDISCIPLINARNA ZNANOST – RECENTNI PRIMJERI ISTRAŽIVANJA POTRESA KOD ZAGREBA I PETRINJE 2020./2021. GODINE – <i>SEISMOLOGY AS A MULTIDISCIPLINARY SCIENCE – RECENT EXAMPLES OF STUDIES OF EARTHQUAKES NEAR ZAGREB AND PETRINJA IN 2020/2021</i></p> <p>Moderatorica – <i>Moderator</i>: doc. dr. sc. Kristina Pikelj</p>
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9:45–11:15	<p>Sekcija 1: Usmena i mikro-izlaganja <i>Section 1: Oral and Flash Presentations</i></p> <p>Moderatorica – <i>Moderator</i>: Valerija Butorac</p>
9:45–9:55	<p> TENA ČADEŽ: BUTIRILKOLINESTERAZA – BIJEG IZ ACETILKOLINESTERAZINE SJENE KAO PSEUDOKATALITIČKO BIOČISTILO ŽIVČANIH OTROVA – <i>BUTYRYLCHOLINESTERASE- STEPING OUT OF ACETYLCHOLINESTERASE'S SHADOW AS PSEUDOCATALYTIC BIOSCAVENGER OF NERVE AGENTS (O-K1)</i></p>
9:55–10:00	<p> IVA KOKOTOVIĆ: UČINAK VIŠESTRUKIH STRESORA NA VODENE KUKCE: ŠTO MOŽEMO NAUČITI IZ LABORATORIJSKOG POKUSA? – <i>MULTIPLE STRESSOR EFFECTS ON STREAM AQUATIC INSECTS: INSIGHTS FROM A MICROCOSM EXPERIMENT (M-B1)</i></p>


10:00–10:05	 VALERIJA BEGIĆ: EKSPRESIJA GENA CIRKADIJANOG RITMA KOD NEMODELNIH KUKACA – <i>CIRCADIAN GENE EXPRESSION IN NON-MODEL INSECTS (M-B2)</i>
10:05–10:15	 MIRNA ŠVOB: JEDNODIMENZIONALNI MODEL RASPODJELE VODE U TLU KRŠKOG PODRUČJA – <i>ONE-DIMENSIONAL HYDROLOGICAL MODEL OF WATER CONTENT IN KARST SOIL (O-GL1)</i>
10:15–10:20	 ANA MATOŠEVIĆ: DIZAJN, SINTEZA I BIOLOŠKA EVALUACIJA SPOJEVA KAO LIJEKOVA AKTIVNIH U CENTRALNOM I PERIFERNOM ŽIVČANOM SUSTAVU – <i>DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF COMPOUNDS AS ACTIVE DRUGS IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM (M-K1)</i>
10:20–10:30	 PAULA DRAGIČEVIĆ: PROMJENE U MIKROBIOMU USPJEŠNE INVAZIVNE STRANE VRSTE, SIGNALNOGA RAKA, DUŽ NJENOG INVAZIVNOG AREALA – <i>CHANGES IN THE MICROBIOME OF A SUCCESSFUL INVADER, THE SIGNAL CRAYFISH, ALONG ITS INVASION RANGE (O-B1)</i>
10:30–10:35	 ENA PRITIŠANAC: DIVERZITET EPIFITSKIH BAKTERIJSKIH ZAJEDNICA PRONAĐENIH NA SMEĐIM ALGAMA SJEVERNOG JADRANA – <i>DIVERSITY OF EPIPHYTIC BACTERIAL COMMUNITIES FOUND ON NORTHERN ADRIATIC FUCACEN SPECIES (M-O1)</i>
10:35–10:40	 MATEJ PERANIĆ: KVANTNA KOMUNIKACIJA POMOĆU PAROVA KVANTNO PREPLETENIH FOTONA – <i>QUANTUM COMMUNICATION WITH ENTANGLED PHOTON PAIRS (M-F1)</i>
10:40–10:50	 ANA RADOŠEVIĆ: REZULTATI JEDINSTVENOSTI I REGULARNOSTI ZA PROBLEME INTERAKCIJE FLUIDA I KRUTOG TIJELA – <i>UNIQUENESS AND REGULARITY RESULTS FOR FLUID-RIGID BODY INTERACTION (O-M1)</i>
10:50–10:55	 NIKA GAZDEK: NASTAJANJE INKLUZIJSKIH KOMPLEKSA DERIVATA FEROCENA S β -CIKLODEKSTRINOM – <i>BINDING ABILITY OF FERROCENE DERIVATIVES WITH β-CYCLODEXTRINS AS INCLUSION COMPLEXES (M-K2)</i>
10:55–11:00	 MATKO BIŠČAN: VAŽNOST ČUVARA PRIRODE JAVNIH USTANOVA ZAŠTIĆENIH PODRUČJA PRIRODE U MONITORINGU BIORAZNOLIKOSTI: NA PRIMJERU ISTRAŽIVANJA SISAVACA POMOĆU FOTO ZAMKI NA PODRUČJU NACIONALNOG PARKA PAKLENICA (HRVATSKA) – <i>THE VALUE OF PROTECTED AREAS RANGER SERVICE PERSONNEL FOR BIODIVERSITY MONITORING: CASE STUDY - CAMERA TRAPPING SURVEY OF MAMMALS IN PAKLENICA NATIONAL PARK (CROATIA) (M-B3)</i>
11:00–11:10	 ROBERT KEREP: ISPITIVANJE UTJECAJA GLIKOZILACIJSKOGA OBRASCA ALFA-KISELOG GLIKOPROTEINA NA VEZANJE LIJEKOVA DIPIRIDAMOLA I IMATINIBA – <i>ALPHA-ACID GLYCOPROTEIN GLYCOSYLATION PATTERN EFFECT ON THE BINDING OF DRUGS DIPYRIDAMOLE AND IMATINIB (O-K2)</i>






11:10–11:30	Pauza <i>Short Break</i>
11:30–11:50	Predstavljanje Francuskog veleposlanstva u Zagrebu i EuChemS Sekcije mladih kemičara Hrvatskog kemijskog društva <i>Presentations of Embassy of France and EuChemS – European Young Chemists' Network</i>
11:50–13:20	Sekcija 2: Usmena i mikro-izlaganja <i>Section 2: Oral and Flash Presentations</i> Moderatorica – <i>Moderator: Marija Čuić</i>
11:50–12:00	 DAMJAN IVEKOVIĆ: STVARANJE DEFEKATA U GRAFENU S BRZIM TEŠKIM IONIMA – MD PRISTUP – <i>DEFECT CREATION IN GRAPHENE WITH SWIFT HEAVY ION IRRADIATION – MD APPROACH (O-F1)</i>
12:00–12:05	 VALENTINA MARTINEZ: EFIKASNO I KONTROLIRANO UKLAPANJE BUCKMINSTERFULLERENA U ZIF-8 SODALITNE TOPOLOGIJE MEHANOKEMIJSKIM PUTEM – <i>EFFICIENT AND CONTROLLABLE ENTRAPMENT OF BUCKMINSTERFULLERENE INTO ZIF-8 OF SODALITE TOPOLOGY BY MECHANOCHEMISTRY (M-K3)</i>
12:05–12:10	 NATAŠA BURIĆ: SINTEZA DIAMANTOIDNIH ESTERA ZA SUPRAMOLEKULSKO SAMOUDRUŽIVANJE – <i>SYNTHESIS OF DIAMONDOID ESTERS FOR SUPRAMOLECULAR SELF-ASSEMBLY (M-K4)</i>
12:10–12:20	 MAGDALENA KRALJ: UČINKOVITA MEHANOKEMIJSKA SINTEZA GRAFENSKIH KVANTNIH TOČAKA – <i>EFFICIENT MECHANOCHEMICAL SYNTHESIS OF GRAPHENE QUANTUM DOTS (O-K3)</i>
12:20–12:25	 DARKO KUČAN: ZDRUŽENO DJELOVANJE CISPLATINE I RESVERATROLA NA METALOPROTEINAZNU AKTIVNOST U EHRlichOVOM ASCITESNOM SOLIDNOM TUMORU MIŠA – <i>COMBINED EFFECT OF CISPLATIN AND RESVERATROL ON METALLOPROTEINASE ACTIVITY IN EHRlich ASCITES SOLID MOUSE TUMOR (M-B4)</i>
12:25–12:30	 ZUZANA REDŽOVIĆ: ENERGIJSKI STATUS U POPULACIJAMA <i>Synurella ambulans</i> IZ HIPOREIČKE ZONE RIJEKE SAVE I IZVORA MALA BRŠLJANICA, HRVATSKA – <i>ENERGY STATUS IN Synurella ambulans POPULATIONS FROM HYPORHEIC ZONE OF SAVA RIVER AND MALA BRŠLJANICA SPRING, CROATIA (M-B5)</i>
12:30–12:40	 MARIJA ZELJKOVIĆ: PERCEPCIJA LOKALNIH STANOVNIKA O TURISTIČKIM POTENCIJALIMA ZAŠTIĆENIH PRIRODNIH PODRUČJA I RAZVOJU EKOTURIZMA U REGIJI JUŽNI BANAT – <i>LOCAL RESIDENTS' PERCEPTION TOWARDS TOURISM POTENTIALS AND ECOTOURISM DEVELOPMENT IN PROTECTED NATURAL AREAS IN THE SOUTH BANAT REGION (O-GG1)</i>

12:40–12:45	 ARIAN IVEC: MOTORNI PROTEINI SU ZASLUŽNI ZA ZAKRIVLJNE OBLIKE MIKROTUBULA U DIOBENOM VRETENU – <i>MOTOR PROTEINS GENERATE THE CURVED SHAPE OF THE MITOTIC SPINDLE (M-F2)</i>
12:45–12:50	 IVA ZONJIĆ: INTERAKCIJE DERIVATA BENZOTIAZOLSKIH AMIDINA S DNA – <i>INTERACTIONS OF BENZOTHAZOLE AMIDINE DERIVATIVES WITH DNA (M-K5)</i>
12:50–13:00	 JELENA MARTINČIĆ: OSVJETLJAVANJE STANIČNE DIOBE KORIŠTENJEM OPTOGENETIKE – <i>SHINING A LIGHT ON CELL DIVISION USING OPTOGENETICS (O-B2)</i>
13:00–13:05	 TAMARA VUK: ULOGA PROTEINA BPM1 U KONTROLI METILACIJSKIH OBRAZACA GENA CML41 I FWA PUTEM MEHANIZMA RDDM U VRSTI <i>Arabidopsis thaliana</i> L. – <i>ROLE OF BPM1 PROTEIN IN A CONTROL OF METHYLATION PATTERNS OF CML41 AND FWA GENES THROUGH RDDM PATHWAY IN Arabidopsis thaliana L (M-B6)</i>
13:05–13:10	 ARBEN BERIŠA: ORGANOKATALITIČKA STEREOSELEKTIVNA SINTEZA α -TRIARILMETANAMINA FORMALNOM BETTIJEVOM REAKCIJOM – <i>STEREOSELECTIVE ORGANOCATALYTIC SYNTHESIS OF α-TRIARYLMETHANAMINES VIA FORMAL BETTI REACTION (M-K6)</i>
13:10–13:20	 IVAN ANTIČEVIĆ: ULOGA TIROZILSKE DNA-FOSFODIESTERAZE 1 U POPRAVKU KRIŽNO VEZANIH PROTEINA NA OKOSNICI DNA <i>IN VIVO</i> – <i>ROLE OF TYROSYL DNA-PHOSPHODIESTERASE 1 IN THE REPAIR OF THE DNA-PROTEIN CROSSLINKS IN VIVO</i>





13:20–14:30	Pauza za ručak <i>Lunch Break</i>
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14:30–15:00	Pozvano predavanje 2 – <i>Invited Lecture 2</i> dr. sc. IVA TOLIĆ MEHANOBIOLOGIJA DIOBENOG VRETENA – <i>MECHANOBIOLOGY OF THE MITOTIC SPINDLE</i> Moderatorica – <i>Moderator:</i> izv. prof. dr. sc. Petra Korać
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15:00–16:00	Sekcija 3: Usmena izlaganja <i>Section 3: Oral Presentations</i> Moderatorica – <i>Moderator:</i> Zuzana Redžović
15:00–15:10	 TIJANA RADENKOVIĆ: 3-GRUPE I KATEGORIJSKA UNIFIKACIJA INTERAKCIJA – <i>3-GROUPS AND HIGHER GAUGE THEORY UNIFICATION OF ALL INTERACTIONS (O-F2)</i>

15:10–15:20	 MARSEJ MARKOVSKI: DINAMIKA MIKROBNIH ZAJEDNICA SEDIMENTA U PROPADAJUĆOJ LIVADI VRSTE <i>Cymodocea nodosa</i> – <i>DYNAMICS OF SEDIMENT MICROBIAL COMMUNITIES IN A DECLINING Cymodocea nodosa MEADOW (O-O1)</i>
15:20–15:30	 GORAN POJE: ANTIPLAZMODIJSKO DJELOVANJE HARMICINA TRIAZOLSKOG TIPA NOVE GENERACIJE – <i>ANTIPLASMODIAL ACTIVITY OF NOVEL GENERATION OF TRIAZOLE-TYPE HARMICINES (O-K4)</i>
15:30–15:40	 DOMAGOJ HACKENBERGER KUTUZOVIĆ: PROSTORNO MODELIRANJE POPULACIJA KOMARACA (<i>Culicidae</i>) POMOĆU MATRIČNIH POPULACIJSKIH MODELA – <i>SPATIAL MODELING OF MOSQUITOES (Culicidae) POPULATIONS USING MATRIX POPULATION MODELS (O-B4)</i>
15:40–15:50	 MARINA MARINOVIĆ: ANTIMALARIJSKO DJELOVANJE HARMICINA AMIDNOG TIPA – <i>ANTIMALARIAL ACTIVITY OF NOVEL AMIDE-TYPE HARMICINES (O-K5)</i>
15:50–16:00	 NINA ČORAK: TRANSKRIPCIJSKE ZNAČAJKE PLEOMORFNIH VARIJANTI BAKTERIJE <i>Borrelia burgdorferi</i> – <i>TRANSCRIPTOME PROFILING OF Borrelia burgdorferi PLEOMORPHIC VARIANTS (O-B5)</i>

16:00–16:15	Pauza <i>Short Break</i>
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16:15–17:15	Sekcija 4: Usmena izlaganja <i>Section 4: Oral Presentations</i> Moderatorica – <i>Moderator: Dajana Barišić</i>
16:15–16:25	 MARKO VISKIĆ: STRATEGIJE ANALIZE SORTNIH TIOLA U VINU: DERIVATIZACIJA I IZOTOPNO RAZRJEĐENJE – <i>STRATEGIES FOR ANALYSIS OF VARIETAL THIOLS IN WINE: DERIVATIZATION AND STABLE ISOTOPE DILUTION ANALYSIS (O-K6)</i>
16:25–16:35	 BARBARA BOŠNJAK: TEORIJA REPREZENTACIJA p -ADSKIH GRUPA – LANGLANDSOV PROGRAM – <i>REPRESENTATION THEORY OF p-ADIC GROUPS – LANGLANDS PROGRAM (O-M2)</i>
16:35–16:45	 ANDREA USENIK: OD LEDENJAKA DO GEJZIRA: PRIČA O HIDROFOBNOG EFEKTU – <i>FROM ICEBERGS TO GEYSERS: THE STORY BEHIND HYDROPHOBIC EFFECT (O-K7)</i>
16:45–16:55	 MARIJA KOVAČEVIĆ: UČINCI STROBILURINSKIH FUNGICIDA NA REPRODUKCIJU, PREŽIVLJAVANJE I IZLJEVANJE VRSTE <i>Enchytraeus crypticus</i> – <i>EFFECTS OF STROBILURIN FUNGICIDES ON SURVIVAL REPRODUCTION AND HATCHING SUCCESS OF Enchytraeus crypticus (O-B6)</i>

16:55–17:05	 NIKOLA GIZDAVEC: PRIMJENA DALJINSKIH ISTRAŽIVANJA U ISTRAŽIVANJU MINERALNIH SIROVINA – <i>APPLICATION OF REMOTE SENSING IN MINERAL RESOURCES EXPLORATION (O-GL2)</i>
17:05–17:15	 EMA SVETLIČIĆ: BIOTIPIZACIJA I IDENTIFIKACIJA PROTEINA POMOĆU SPEKTROMETRIJE MASA I <i>de novo</i> SEKVENCIRANJA PEPTIDA – <i>BIOTIPIZATION AND PROTEIN IDENTIFICATION BY MASS SPECTROMETRY ANALYSIS AND PEPTIDE de novo SEQUENCING (O-B7)</i>

17:15–17:30	Pauza <i>Short Break</i>
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17:30–19:30	Posterska sekcija <i>Poster Section</i> Popis izlagača na stranicama 11–19. <i>Presenters listed on pages 11–19.</i> <p style="text-align: right;">Moderatorice – <i>Moderators:</i> Marija Čuić, Katarina Kajan</p>
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NEDJELJA 25. travnja 2021. g.

SUNDAY April 25, 2021

9:00–	Registracija – <i>Registration</i>
9:30–10:00	<p>Pozvano predavanje 3 – <i>Invited Lecture 3</i></p> <p>prof. dr. sc. JOSIP TAMBAČA MATEMATIČKO MODELIRANJE STENTOVA – <i>MATHEMATICAL MODELING OF STENTS</i></p> <p>Moderator – <i>Moderator</i>: prof. dr. sc. Eduard Marušić-Paloka</p>
10:00–11:00	<p>Sekcija 5: Usmena izlaganja <i>Section 5: Oral Presentations</i></p> <p>Moderatorica – <i>Moderator</i>: Marija Čuić</p>
10:00–10:10	 <p>NATALIJA PANTALON JURAJ: STEREOKEMIJA KOMPLEKSA TRIDENTATNIH LIGANADA S BAKROM(II) I CINKOM(II) – <i>STEREOCHEMISTRY OF TRIDENTATE LIGAND COMPLEXES WITH COPPER(II) AND ZINC(II)</i> (O-K8)</p>
10:10–10:20	 <p>TATJANA MIJOŠEK: DUGOROČNI TRENDOVI KONCENTRACIJA METALA I KAKVOĆE VODE RIJEKE KRKE U DIJELU TOKA POD UTJECajem OTPADNIH VODA – <i>LONG-TERM TRENDS OF METAL CONCENTRATIONS AND WATER QUALITY OF THE WASTEWATER IMPACTED KRKA RIVER COURSE</i> (O-B8)</p>
10:20–10:30	 <p>JADRANKA PELIKAN: FIZIKALNO-KEMIJSKA I EKOTOKSIKOLOŠKA ANALIZA MORSKOG SEDIMENTA U SJEVERNOM JADRANU – <i>PHYSICO-CHEMICAL AND ECOTOXICOLOGICAL ANALYSIS OF MARINE SEDIMENT IN THE NORTHERN ADRIATIC</i> (O-O2)</p>
10:30–10:40	 <p>MATEJA MATIŠIĆ: STEREOSELEKTIVNA PRIPRAVA β, β-DIARIL-KETONA S β-KVATERNIM STEREOGENIM CENTROM – <i>STEREOSELECTIVE SYNTHESIS OF β, β-DIARYL KETONES WITH β-QUATERNARY STEREOGENIC CENTER</i> (O-K9)</p>
10:40–10:50	 <p>LUKA TURIĆ: MULTIFREKVENCIJSKA ANALIZA RAVNIH DEPOLARIZIRANIH KANALA U OKOLINI POLJA 3C196 – <i>MULTI-FREQUENCY STUDY OF THE STRAIGHT DEPOLARIZATION CANALS IN A SURROUNDING OF THE 3C196 FIELD</i> (O-F3)</p>
10:50–11:00	 <p>IVANA COLIĆ: PRIPRAVA C-GLIKOZIL AMINOKISELINA POST-KONDENZACIJSKOM MODIFIKACIJOM PASSERINIJEVIH PRODUKATA – <i>SYNTHESIS OF C-GLYCOSYL AMINO ACIDS BY POST-CONDENSATION MODIFICATION OF PASSERINI PRODUCTS</i> (O-K10)</p>

11:00–11:15	Pauza <i>Short Break</i>
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11:15–11:45	<p>Pozvano predavanje 4 – <i>Invited Lecture 4</i></p> <p>prof. dr. sc. VERNESA SMOLČIĆ</p> <p>RAZVOJ GALAKSIJA KROZ SVEMIRSKO VRIJEME – <i>EVOLUTION OF GALAXIES THROUGH COSMIC TIME</i></p> <p>Moderator – <i>Moderator</i>: izv. prof. dr. sc. Aleksandar Lukić</p>
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11:45–12:45	<p>Sekcija 6: Usmena izlaganja <i>Section 6: Oral Presentations</i></p> <p>Moderatorica – <i>Moderator</i>: Petra Schneider</p>
11:45–11:55	<p> IVANA MIKULANDRA: PRIPRAVA I KARAKTERIZACIJA MAKROZONA, NOVIH BIOAKTIVNIH DERIVATA AZITROMICINA – <i>SYNTHESIS AND CHARACTERIZATION OF MACROZONES, NOVEL BIOACTIVE DERIVATIVES OF AZITHROMYCIN (O-K11)</i></p>
11:55–12:05	<p> DANIELA ANČIĆ: ANTIPROLIFERATIVNI I ANTIANGIOGENI UČINAK NANOKRISTALA RESVERATROLA NA EHRlichov ASCITESNI TUMOR U MIŠA – <i>ANTI-PROLIFERATIVE AND ANGIO-SUPPRESSIVE EFFECT OF RESVERATROL NANOCRYSTALS ON EHRlich ASCITES TUMOR IN MOUSE (O-B9)</i></p>
12:05–12:15	<p> ALOJZIJE BRKIĆ: NOVI POGLED NA STRUKTURNE OSNOVE ANTIBIOTSKE OTPORNOSTI IZOLEUCIL-TRNA SINTETAZA TIPA 2 – <i>NOVEL INSIGHTS INTO STRUCTURAL BASIS OF ANTIBIOTIC RESISTANCE IN TYPE II ISOLEUCYL-tRNA SYNTHETASES (O-K12)</i></p>
12:15–12:25	<p> IVAN BIOČIĆ: SEMILINEARNE JEDNADŽBE ZA NELOKALNE OPERATORE: VIŠE OD FRAKCIONALNOG LAPLACEOVOG OPERATORA – <i>SEMILINEAR EQUATIONS FOR NON-LOCAL OPERATORS: BEYOND THE FRACTIONAL LAPLACIAN (O-M3)</i></p>
12:25–12:35	<p> SARAH MATEŠA: ULOGA ELEMENTARNOG SUMPORA (S^0) BIOLOŠKOG PORIJEKLA U STVARANJU POLISULFIDA U MORSKOM EUKSINSKOM OKOLIŠU (ROGOZNIČKO JEZERO) – <i>THE ROLE OF BIOLOGICALLY PRODUCED ELEMENTARY SULFUR (S^0) ON POLYSULPHIDE FORMATION IN THE MARINE EUXINIC ENVIRONMENT (ROGOZNICA LAKE) (O-O3)</i></p>
12:35–12:45	<p> NIKOLA LESAR: NEURODEGENERATIVNE PROMJENE U MOZGU ŠTAKORA IZAZVANE SEVOFLURANOM I ŽELJEZO-DEKSTRANOM – <i>NEURODEGENERATIVE CHANGES IN THE RAT BRAIN INDUCED BY SEVOFLURANE AND IRON-DEXTRAN (O-B10)</i></p>

12:45–13:45	Pauza za ručak <i>Lunch Break</i>
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13:45–15:45	<p>Radionica – <i>Workshop</i></p> <p>dr. sc. DEJAN VINKOVIĆ LIFE IS LIKE A BOX OF CHOCOLATES: OD ASTROFIZIKE DO ZNANSTVENOG PODUZETNIŠTVA</p> <p>dr. sc. PAULA DOBRINIĆ <i>CAREERS BEYOND ACADEMIA: EXPERIENCE FROM THE UNIVERSITY OF OXFORD</i></p> <p>dr. sc. JELENA ČULIĆ VISKOTA <i>CAREER IN INDUSTRY- KEY SKILLS AND MINDSET FOR SUCCESS</i></p> <p>Moderatorica – <i>Moderator: prof. dr. sc. Vernesa Smolčić</i></p>
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15:45–16:00	Pauza <i>Short Break</i>
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16:00–16:10	Predstavljanje Veleposlanstva Sjedinjenih Američkih Država u Hrvatskoj <i>Presentation of U.S. Embassy in Croatia</i>
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16:10–17:30	<p>Sekcija 7: Usmena izlaganja <i>Section 7: Oral Presentations</i></p> <p>Moderatorica – <i>Moderator: Valerija Butorac</i></p>
16:10–16:20	<p> MARIN MIĆUNOVIĆ: MORFOLOŠKE PROMJENE ŽALA OTOKA HVARA OD 1834. DO DANAS – <i>MORPHOLOGICAL CHANGES OF THE ISLAND OF HVAR BEACHES FROM 1834 TO PRESENT DAY (O-GG2)</i></p>
16:20–16:30	<p> PETRA PRANIĆ: EVALUACIJA KLIMATSKE SIMULACIJE „ADRIATIC SEA AND COAST“: MORE – <i>PERFORMANCE OF THE ADRIATIC SEA AND COAST CLIMATE SIMULATION: OCEAN (O-O4)</i></p>
16:30–16:40	<p> PAULA GRŠKOVIĆ: UTJECAJ POMOĆNIČKIH LIMFOCITA T NA PREŽIVLJENJE PACIJENATA S DIJAGNOZOM FOLIKULARNOG LIMFOMA – <i>THE INFLUENCE OF HELPER T LYMPHOCYTES ON THE SURVIVAL OF PATIENTS DIAGNOSED WITH FOLLICULAR LYMPHOMA (O-B11)</i></p>

16:40–16:50	 TIN KLAČIĆ: PRIPRAVA I KARAKTERIZACIJA POLIELEKTROLITNIH NANOFILMOVA – <i>PREPARATION AND CHARACTERIZATION OF POLYELECTROLYTE NANOFILMS (O-K13)</i>
16:50–17:00	 SILVESTAR BELJAN: IDENTIFIKACIJA, FUNKCIJA I UNUTARSTANIČNA LOKALIZACIJA SPUŽVINOG HOMOLOGA LJUDSKOG SUPRESORA METASTAZIRANJA DRG1 – <i>IDENTIFICATION, FUNCTION AND INTRACELLULAR LOCALIZATION OF SPONGE HOMOLOG OF HUMAN METASTASIS SUPPRESSOR DRG1 (O-B12)</i>
17:00–17:10	 VANJA MARIĆ: SPINSKI LANCI FRUSTRIRANI TOPOLOGIJOM – <i>TOPOLOGICALLY FRUSTRATED SPIN CHAINS (O-F4)</i>
17:10–17:20	 JURICA SABOL: PRIMJENA FORAMINIFERSKIH ZAJEDNICA U ISTRAŽIVANJU MIOCENSKIH NASLAGA ODABRANIH LOKALITETA HRVATSKOG ZAGORJA – <i>APPLICATION OF FORAMINIFERAL ASSEMBLAGES IN RESEARCH OF MIOCENE DEPOSITS FROM HRVATSKO ZAGORJE (O-GL3)</i>
17:20–17:30	 SUZANA HARABAJSKA: LJUDSKI PAPILOMA VIRUS KOD KARCINOMA PLUĆA NEMALIH STANICA S MUTACIJAMA GENA EGFR – <i>HUMAN PAPILLOMAVIRUS IN NON-SMALL CELL LUNG CANCER WITH EGFR GENE MUTATIONS (O-B13)</i>
17:30–17:35	 KARLA JAGIĆ: PRELIMINARNI REZULTATI O ONEČIŠĆENJU ZAGREBAČKIH KUĆNIH PRAŠINA POLIBROMIRANIM DIFENIL ETERIMA – <i>PRELIMINARY RESULTS ON POLYBROMINATED DIPHENYL ETHER CONTAMINATION STATUS IN ZAGREB HOUSE DUSTS (M-K7)</i>

17:35–17:55	Predstavljanje zlatnih sponzora <i>Golden Sponsors Promotion</i>
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17:55–18:00	Zatvaranje Simpozija <i>Closure of the Symposium</i>
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POSTER SEKCIJA - LISTA IZLAGAČA

SUBOTA 24. TRAVNJA 2021. G., 17:30–19:30

POSTER SECTION - PRESENTERS LIST

SATURDAY, APRIL 24, 2021, 17:30–19:30

Moderatorice – Moderators:
Marija Čuić, Katarina Kajan









BIOLOGIJA – BIOLOGY

-  **MARTA BAKŠIĆ:** AKUTNA, OBOSTRANA ISHEMIJA NOGU NAKON SARS-CoV-2 INFEKCIJE I COVID-19: PRIKAZ SLUČAJA – ACUTE, BILATERAL LOWER LIMB ISCHEMIA AFTER SARS-CoV-2 INFECTION AND COVID-19: A CASE REPORT (P-B1)
-  **VALERIJA BEGIĆ:** EKSPRESIJA GENA CIRKADIJANOG RITMA KOD NEMODELNIH KUKACA – CIRCADIAN GENE EXPRESSION IN NON-MODEL INSECTS (M-B2)
-  **MATKO BIŠĆAN:** VAŽNOST ČUVARA PRIRODE JAVNIH USTANOVA ZAŠTIĆENIH PODRUČJA PRIRODE U MONITORINGU BIORAZNOLIKOSTI: NA PRIMJERU ISTRAŽIVANJA SISAVACA POMOĆU FOTO ZAMKI NA PODRUČJU NACIONALNOG PARKA PAKLENICA (HRVATSKA) – THE VALUE OF PROTECTED AREAS RANGER SERVICE PERSONNEL FOR BIODIVERSITY MONITORING: CASE STUDY - CAMERA TRAPPING SURVEY OF MAMMALS IN PAKLENICA NATIONAL PARK (CROATIA) (M-B3)
-  **DORA BJEDOV:** ANALIZA BIOMARKERA UČINKA I OKSIDATIVNOG STRESA U KRVI PTIĆA BIJELE RODE (*Ciconia ciconia*) S PODRUČJA HRVATSKE – BIOMARKERS OF EFFECT AND OXIDATIVE STRESS ANALYSIS IN BLOOD OF WHITE STORK (*Ciconia ciconia*) NESTLINGS FROM CROATIA (P-B2)
-  **ANDRIJANA BOGOJE RASPOPOVIĆ:** MEĐUODNOS EKSPRESIJE BDNF, IL-6 I POKAZATELJA OKSIDACIJSKOG STRESA PRI DEMIJELINIZACIJSKIM OŠTEĆENJIMA – CORRELATION OF BDNF, IL-6 EXPRESSION AND OXIDATIVE STRESS MARKERS IN DEMYELINATING DAMAGE (P-B3)
-  **ANA BORIĆ BILUŠIĆ:** POLIMORFIZAM GENA ZA METABOLIČKE ENZIME I TRANSPORTNE PROTEINE KOD BOLESNIKA S TRANSPLANTIRANIM BUBREGOM – GENETIC POLYMORPHISM OF METABOLIC ENZYMES AND TRANSPORTERS IN RENAL TRANSPLANT RECIPIENTS (P-B4)
-  **TAMARA ĐERĐ:** UTJECAJ TRIAZOLNIH FUNGICIDA NA PONAŠANJE I FIZIOLOŠKU AKTIVNOST *Daphnia magna* – THE EFFECTS OF TRIAZOLE FUNGICIDES ON BEHAVIOUR AND PHYSIOLOGY OF *Daphnia magna* (P-B5)
-  **EVELIN DESPOT-SLADE:** EPIGENOMIKA HOLOCENTROMERA – EPIGENOMICS OF HOLOCENTROMERE (P-B6)
-  **MARKO DOBOŠ:** VELIČINE GENOMA VRSTE *Festuca bosniaca* (Poaceae) NA BALKANSKOM POLUOTOKU – GENOME SIZE OF *Festuca bosniaca* (Poaceae) ON THE BALKAN PENINSULA (P-B7)
-  **ANA DOBROVIĆ:** MODELI DINAMIČKIH ENERGIJSKIH BUDŽETA ZA UGROŽENE AUTOHTONE I INVAZIVNE VRSTE RAKOVA – DYNAMIC ENERGY BUDGET MODELS FOR ENDANGERED NATIVE AND INVASIVE CRAYFISH SPECIES (P-B8)
-  **MIA DŽELALIJA:** MOLEKULARNA OSNOVA VIRULENCIJE I ANTIBIOTSKE REZISTENCIJE VANKOMICIN-REZISTENTNIH *Enterococcus faecium* IZOLATA IZ OTPADNE I MORSKE VODE SA JAVNE PLAŽE – MOLECULAR BASIS OF VIRULENCE AND ANTIBIOTIC RESISTANCE IN VANCOMYCIN-RESISTANT *Enterococcus faecium* FROM WASTEWATER AND RECEIVING BEACH WATER (P-B9)
-  **KLARA FILEK:** KOKULTIVACIJA DIJATOMEJA: BLISKI SUSRETI *Achnanthes elongata* I *Psammodyction* sp. – DIATOM CO-CULTURES: CLOSE ENCOUNTERS OF *Achnanthes elongata* AND *Psammodyction* sp. (P-B10)





-  **JASENKA GRGURIĆ:** ANALIZA EKSPRESIJE LNCRNA ANRIL I PVT1 U PERIFERNOJ CIRKULACIJI PACIJENATA SA KALCIFICIRAJUĆOM STENOZOM AORTNIH ZALISTAKA SRCA – *ANALYSIS OF EXPRESSION OF LNCRNA ANRIL AND PVT1 IN PERIPHERAL CIRCULATION OF PATIENTS WITH CALCIFYING AORTIC VALVE STENOSIS (P-B11)*
-  **DORA HLEBEC:** PRIMJENA INTEGRATIVNE TAKSONOMIJE U OPISU DVIJU NOVIH STENOENDEMSKIH VRSTA OBALČARA (PLECOPTERA) U HRVATSKOJ – *USE OF INTEGRATIVE TAXONOMY IN DESCRIPTION OF TWO NEW STENOENDEMIC STONEFLY SPECIES (PLECOPTERA) FROM CROATIA (P-B12)*
-  **LADA JOVOVIĆ:** OMOKROMI – BIOLOŠKI PIGMENTI VANJSKIH SRODNICA ŠPILJSKIH JEDNAKONOŽNIH RAKOVA (ISOPODA, CRUSTACEA) – *OMMOCHROMES – BIOLOGICAL PIGMENTS IN SURFACE RELATIVES OF CAVE-DWELLING ISOPODS (CRUSTACEA) (P-B13)*
-  **LUCIJA KANJER:** CIJANOBAKTERIJE NA MORSKIM KORNJAČAMA: ISTRAŽIVANJE RAZNOLIKOSTI METODOM METABARKODINGA – *CYANOBACTERIA ASSOCIATED WITH SEA TURTLES: A DIVERSITY STUDY USING METABARCODING APPROACH (P-B14)*
-  **MIRNES KARIĆ:** HIGIJENSKO-SANITARNI UVJETI U ŠKOLI SA OSVRTOM NA COVID-19 – *HYGIENIC AND SANITARY CONDITIONS IN SCHOOL WITH REFERENCE TO COVID-19 (P-B15)*
-  **IVA KOKOTOVIĆ:** UČINAK VIŠESTRUKIH STRESORA NA VODENE KUKCE: ŠTO MOŽEMO NAUČITI IZ LABORATORIJSKOG POKUSA? – *MULTIPLE STRESSOR EFFECTS ON STREAM AQUATIC INSECTS: INSIGHTS FROM A MICROCOSM EXPERIMENT (M-B1)*
-  **BRUNO KOMAZEC:** UTJECAJ NANOČESTICA I IONA SREBRA NA ALGU *Chlorella vulgaris* – *THE EFFECTS OF SILVER NANOPARTICLES AND IONS ON Chlorella vulgaris (P-B17)*
-  **ISABELLA KOPRIVEC:** AUGMIN REGULIRA SILU NAPETOSTI IZMEĐU SESTRINSKIH KINETOHORA I PROSTORNI RASPORED MIKROTUBULA NUKLEACIJOM PREMOŠĆUJUĆIH VLAKANA – *AUGMIN REGULATES KINETOCHORE TENSION AND SPATIAL ARRANGEMENT OF SPINDLE MICROTUBULES BY NUCLEATING BRIDGING FIBERS (P-B18)*
-  **SARA KOSKA:** KORELACIJA FILOGENIJE I ONTOGENIJE TIJEKOM STANIČNE DIFERENCIJACIJE – *PHYLOGENY-ONTOGENY CORRELATION DURING CELL DIFFERENTIATION (P-B19)*
-  **KARLA KOŠPIĆ:** PROMJENE U AKTIVNOSTI I OBRASCU IZOFORMI ANTIOKSIDACIJSKIH ENZIMA U BILJKAMA DUHANA NAKON IZLAGANJA NANOČESTICAMA SREBRA I IONSKOM SREBRU – *CHANGES IN ACTIVITIES AND ISOFORM PATTERNS OF ANTIOXIDANT ENZYMES IN TOBACCO PLANTS UPON EXPOSURE TO SILVER NANOPARTICLES AND SILVER NITRATE (P-B20)*
-  **DARKO KUČAN:** ZDRUŽENO DJELOVANJE CISPLATINE I RESVERATROLA NA METALOPROTEINAZNU AKTIVNOST U EHRlichOVOM ASCITESNOM SOLIDNOM TUMORU MIŠA – *COMBINED EFFECT OF CISPLATIN AND RESVERATROL ON METALLOPROTEINASE ACTIVITY IN EHRlich ASCITES SOLID MOUSE TUMOR (M-B4)*
-  **MAJA LEDINSKI:** UPOTREBA ČVRSTIH LIPIDNIH NANOČESTICA S UGRAĐENIM ASKORBATOM ZA TRETMAN TUMORSKIH MATIČNIH STANICA – *APPLICATION OF ASCORBATE-INCORPORATED SOLID LIPID NANOPARTICLES FOR TREATMENT OF CANCER STEM CELLS (P-B21)*
-  **LEONA LOVRENČIĆ:** GENETSKA RAZNOLIKOST I POPULACIJSKA STRUKTURA PLEMENITOG RAKA U HRVATSKOJ – *GENETIC DIVERSITY AND POPULATION STRUCTURE OF THE NOBLE CRAYFISH IN CROATIA (P-B22)*
-  **LUCIJA LULIĆ:** UTJECAJ ONKOPROTEINA E6 PAPILOMAVIRUSA ČOVJEKA TIPA 16 (HPV16) NA REGULATORE STANIČNE POLARNOSTI U TUMORIMA GLAVE I VRATA – *EFFECTS OF HUMAN PAPILOMAVIRUS 16 (HPV16) E6 ONCOPROTEIN ON CELL POLARITY REGULATORS IN HEAD AND NECK CANCERS (P-B23)*
-  **LUCIJA MIJANOVIĆ:** ULOGA PROTEINA IQGC PORODICE RASGAP U STANIČNOJ ADHEZIJI – *A NOVEL FUNCTION OF THE RASGAP PROTEIN IQGC IN CELL ADHESION (P-B24)*

-  **RAFAELA MRDJEN-HODŽIĆ:** POVEZANOST GLAZBENIH AKTIVNOSTI I RAZINE KORTIZOLA KOD TRUDNICA – ASSOCIATIONS OF MUSICAL ACTIVITIES ON CORTISOL LEVELS IN PREGNANT WOMEN (P-B25)
-  **MARIJA NAZLIĆ:** USPOREDBA ANTIOKSIDATIVNOG DJELOVANJA I SASTAVA ETERIČNOG ULJA I HIDROLATA IZOLIRANIH IZ VRSTA *Veronica austriaca* ssp. *jacquinii* (BAUMG.) EB. FISCH. I *Veronica saturejoides* VIS. ssp. *Saturejoides* – COMPARISON OF THE ANTIOXIDANT ACTIVITY AND COMPOSITION OF THE ESSENTIAL OIL AND HYDROLATE ISOLATED FROM *Veronica austriaca* ssp. *jacquinii* (BAUMG.) EB. FISCH. AND *Veronica saturejoides* VIS. ssp. *Saturejoides* (P-B26)
-  **DOROTEA PALI:** REKOMBINANTNA CJEPIVA ZA RSV I HCV TEMELJENA NA VIRUSU MUMPSA – RECOMBINANT RSV AND HCV VACCINES BASED ON MUMPS VIRUS (P-B27)
-  **IVANA PAVIČIĆ:** S-ADENOZIL HOMOCISTEIN HIDROLAZNA DEFICIJENCIJA – S-ADENOSYL HOMOCYSTEIN HYDROLASE DEFICIENCY (P-B28)
-  **ENA PEŠUT:** U POTRAZI ZA NOVIM BIOMARKERIMA RAKA VRATA MATERNICE – SEARCHING FOR NEW CERVICAL CANCER BIOMARKERS (P-B29)
-  **GORAN PIPALOVIĆ:** REGULATORNI MEHANIZMI KONTROLE SEGREGACIJE KROMOSOMA U *Streptomyces coelicolor* – REGULATORY MECHANISMS THAT CONTROL CHROMOSOME SEGREGATION IN *Streptomyces coelicolor* (P-B30)
-  **DARIJA PUTAR:** MEHANIZMI REGRUTACIJE RASGAP PROTEINA IQGC NA MAKROPINOSOME U AMEBI *Dictyostelium discoideum* – RECRUITMENT MECHANISMS OF RASGAP PROTEIN IQGC TO MACROPINOSOMES IN AMOEBIA *Dictyostelium discoideum* (P-B31)
-  **BARBARA RADOVANI:** PROMJENE U N-GLIKOZILACIJI IMUNOGLOBULINA G I UKUPNIH PROTEINA PLAZME KOD PACIJENATA S FIBRILACIJOM ATRIJA – ALTERED N – GLYCOSYLATION OF IMMUNOGLOBULIN G AND TOTAL PLASMA PROTEINS IN PATIENTS WITH ATRIAL FIBRILLATION (P-B32)
-  **ZUZANA REDŽOVIĆ:** ENERGIJSKI STATUS U POPULACIJAMA *Synurella ambulans* IZ HIPOREIČKE ZONE RIJEKE SAVE I IZVORA MALA BRŠLIJANICA, HRVATSKA – ENERGY STATUS IN *Synurella ambulans* POPULATIONS FROM HYPORHEIC ZONE OF SAVA RIVER AND MALA BRŠLIJANICA SPRING, CROATIA (M-B5)
-  **RAJKO ROLJIĆ:** MORFOMETRIJSKE ZNAČAJKE I KONDICIJSKI INDEKSI RIJEČNOG RAKA *Astacus astacus* L. IZ RIJEKE PLIVE – MORPHOMETRIC CHARACTERISTICS AND CONDITION INDICES OF NOBLE CRAYFISH *Astacus astacus* L. FROM THE PLIVA RIVER (P-B33)
-  **IVA SOŠIĆ:** GREŠKE U RAZDVAJANJU KROMOSOMA U STANICAMA S RAZLIČITIM RAZINAMA MEĐUSTANIČNOG KONTAKTA – CHROMOSOME SEGREGATION ERRORS IN CELLS WITH VARYING CELL-TO-CELL CONTACT LEVELS (P-B34)
-  **ANITA STOJANOVIĆ MARKOVIĆ:** FILOGEOGRAFSKA DISTRIBUCIJA HAPLOTIPOVA GENA *CYP2D6* – PHYLOGEOGRAPHIC DISTRIBUTION OF *CYP2D6* HAPLOTYPES (P-B35)
-  **MAJA ŠETINC:** DULJINA TELOMERA I DOB SMRTI KOD OSOBA DUBOKE STAROSTI – TELOMERE LENGTH AND AGE AT DEATH IN VERY OLD INDIVIDUALS (P-B36)
-  **ENA ŠIMUNIĆ:** ANALIZA FIBROBLASTA PACIJENTA S NEDOSTATNOM AKTIVNOSTI S-ADENOZILHOMOCISTEIN-HIDROLAZE METODOM RNA-Seq – RNA-Seq ANALYSIS OF FIBROBLASTS FROM PATIENT WITH S-ADENOSYLHOMOCYSTEINE HYDROLASE DEFICIENCY (P-B37)
-  **PAULA ŠTANCL:** UTJECAJ MUTACIJSKOG POTPISA PROTEINA APOBEC NA PREDVIĐANJE ISHODIŠNE STANICE RAZLIČITIH MOLEKULARNIH SKUPINA RAKA DOJKE – APOBEC MUTATIONAL SIGNATURE AFFECTS PREDICTION OF CELL OF ORIGIN IN DIFFERENT MOLECULAR GROUPS OF BREAST CANCER (P-B38)
-  **VALENTINA ŠTIMAC:** PIVOTIRANJE KAO MEHANIZAM DOLASKA POLARNIH KROMOSOMA NA DIOBENO VRETENO – POLAR CHROMOSOMES PIVOT THEIR WAY TOWARDS THE SPINDLE BODY (P-B39)
-  **ANTEA TALAJIĆ:** IDENTIFIKACIJA, BIOKEMIJSKA KARAKTERIZACIJA I UNUTARSTANIČNA LOKALIZACIJA SPUŽVINOG HOMOLOGA LJUDSKOG PROTEINA *RRAS2* – IDENTIFICATION, BIOCHEMICAL

CHARACTERIZATION AND INTRACELLULAR LOCALIZATION OF SPONGE HOMOLOG OF HUMAN RRAS2 (P-B40)



-  **ANA TERLEVIĆ:** MORFOLOŠKA VARIJABILNOST *Dianthus sylvestris* Wulfen s. l. NA BALKANSKOM POLUOTOKU – MORPHOLOGICAL VARIABILITY IN *Dianthus sylvestris* Wulfen s. l. ON THE BALKAN PENINSULA (P-B41)
-  **MIRTA TOKIĆ:** UTJECAJ POVIŠENE TEMPERATURE NA KLIJANCE VRSTA *Arabidopsis thaliana*, *Brassica rapa* I *Solanum lycopersicum* – EFFECT OF INCREASED TEMPERATURE ON *Arabidopsis thaliana*, *Brassica rapa* AND *Solanum lycopersicum* (P-B42)
-  **MONIKA TUNJIĆ CVITANIĆ:** IDENTIFIKACIJA, KARAKTERIZACIJA I LOKALIZACIJA SATELITNIH SEKVENCIJA DNA GENOMA PACIFIČKE KAMENICE *Crassostrea gigas* (Thunberg, 1793) – IDENTIFICATION, CHARACTERIZATION AND LOCALIZATION OF SATELLITE DNA SEQUENCES OF THE PACIFIC OYSTER *Crassostrea gigas* (Thunberg, 1793) (P-B43)
-  **MARINA VESELI:** MAKROFITI KAO SPREMNICI ZA ONEČIŠĆUJUĆE TVARI – MACROPHYTES AS STORAGE UNITS FOR EMERGINIG CONTAMINANTS (P-B44)
-  **DAMIRA VESELJAK:** ANALIZA SATELITOMA KUKCA BRAŠNARA *Tribolium freemani* VISOKOPROTOČNIM SEKVENCIJANJEM – ANALYSIS OF THE SATELLITOME OF THE FLOUR BEETLE *Tribolium freemani* BY HIGH-THROUGHPUT SEQUENCING (P-B45)
-  **SANDRA VITKO:** UČINAK STRESNIH UVJETA NA FOTOSINTETSKU UČINKOVITOST KLIJANACA UROČNJAKA (*Arabidopsis thaliana*) S PROMIJENJENOM EKSPRESIJOM GENA *BPM1* – EFFECT OF STRESS CONDITIONS ON PHOTOSYNTHETIC EFFICIENCY OF *Arabidopsis thaliana* SEEDLINGS WITH MODIFIED *BPM1* GENE EXPRESSION (P-B46)
-  **MARIN VOLARIĆ:** ORGANIZACIJA HOLOCENTROMERE U DUGIM POTEZIMA – LONG-RANGE ORGANISATION OF HOLOCENTROMERES (P-B47)
-  **BARBARA VUIĆ:** TERAPIJSKI POTENCIJAL NEUROSTEROIDA I NEUROTROFINA U DEMENCIJI – THERAPEUTIC POTENTIAL OF NEUROSTEROIDS AND NEUROTROPHINS IN DEMENTIA (P-B48)
-  **TAMARA VUK:** ULOGA PROTEINA *BPM1* U KONTROLI METILACIJSKIH OBRAZACA GENA *CML41* I *FWA* PUTEM MEHANIZMA RDDM U VRSTI *Arabidopsis thaliana* L. – ROLE OF *BPM1* PROTEIN IN A CONTROL OF METHYLATION PATTERNS OF *CML41* AND *FWA* GENES THROUGH RDDM PATHWAY IN *Arabidopsis thaliana* L (M-B6)
-  **BARBARA NIKOLIĆ:** POVEĆAN BROJ PROPINJANJA I POVEĆANA RAZINA DOPAMINA U MOŽDANOM DEBLU KOD ŠTAKORSKOG MODELA BLAGE NEONATALNE NORMOBARIČNE HIPOKSIJE – INCREASED REARING AND BRAINSTEM DOPAMINE LEVELS IN A RAT MODEL OF MILD NEONATAL NORMOBARIC HYPOXIA (P-B49)

FIZIKA – PHYSICS





-  **DOMJAN BARIĆ:** RAZUMIJEVANJE SLOŽENIH INTERAKCIJA VREMENSKIH SERIJA KROZ LEĆU DUBOKOG UČENJA – UNDERSTANDING COMPLEX TIME SERIES INTERACTIONS THROUGH THE LENS OF DEEP LEARNING (P-F1)
-  **JOSIPA DIKLIĆ:** PRIJENOS KORELIRANIH PAROVA NUKLEONA U TEŠKO-IONSKE REAKCIJE – PAIRING CORRELATIONS IN THE HEAVY-ION TRANSFER REACTION (P-F2)
-  **MARTA FATOVIĆ:** POTRAGA ZA PROMJENJIVIM IZVORIMA S MALIM AMPLITUDAMA I DUGIM PERIODIMA – SEARCH FOR SMALL-AMPLITUDE LONG-PERIOD VARIABILITY (P-F3)
-  **SAFER GRBIĆ:** BLUMENBERGOVA GENEZA DVOSMISLENOSTI NEBA – BLUMENTBERG'S GENESIS OF THE AMBIGUITY OF HEAVEN (P-F4)

-  **SARA IVASIĆ:** NEDAVNO SLABLJENJE DALJINSKE VEZE EL NIÑO-JUŽNE OSCILACIJE ZIMI NAD PODRUČJEM SJEVERNOG ATLANTIKA I EUROPE – *RECENT WEAKENING IN THE WINTER ENSO TELECONNECTION OVER THE NORTH ATLANTIC-EUROPEAN REGION (P-F5)*
-  **ARIAN IVEC:** MOTORNI PROTEINI SU ZASLUŽNI ZA ZAKRIVLJINE OBLIKE MIKROTUBULA U DIOBENOM VRETENU – *MOTOR PROTEINS GENERATE THE CURVED SHAPE OF THE MITOTIC SPINDLE (M-F2)*
-  **ANA MARIJA KOŽULJEVIĆ:** ISPITIVANJE GAGG:CE SCINTILATORA ZA PRIMJENE U SUSTAVIMA ZA OPAŽANJE GAMA ZRAČENJA – *INVESTIGATION OF GAGG:CE SCINTILLATORS FOR APPLICATIONS IN GAMMA IMAGING SYSTEMS (P-F6)*
-  **MATEO KRULJAC:** LASERSKO HLAĐENJE ATOMA UNUTAR OPTIČKOG REZONATORA POMOĆU FREKVENTNOG ČEŠLJA – *LASER COOLING OF ATOMS INSIDE AN OPTICAL RESONATOR USING A FREQUENCY COMB (P-F7)*
-  **HELENA LATEČKI:** SIMULACIJA POTRESNE TREŠNJE ZA GRAD ZAGREB, HRVATSKA – *SEISMIC SHAKING SCENARIOS FOR CITY OF ZAGREB, CROATIA (P-F8)*
-  **MATEJ PERANIĆ:** KVANTNA KOMUNIKACIJA POMOĆU PAROVA KVANTNO PREPLETENIH FOTONA – *QUANTUM COMMUNICATION WITH ENTANGLED PHOTON PAIRS (M-F1)*
-  **KREŠIMIR RUIĆ:** PROCJENA DOPRINOSA VISOKOFREKVENTNIH OSCILACIJA RAZINE MORA EKSTREMNIM RAZINAMA U JADRANSKOM MORU – *ESTIMATING CONTRIBUTION OF HIGH-FREQUENCY SEA-LEVEL OSCILLATIONS TO THE EXTREME SEA LEVELS IN THE ADRIATIC SEA (P-F9)*
-  **BRUNO ŠLAUS:** FUNKCIJE LUMINOZITETA AKTIVNIH GALAKTIČKIH JEZGRI I NJIHOVA EVOLUCIJA – *AGN LUMINOSITY FUNCTIONS AND THEIR EVOLUTION (P-F10)*
-  **MARIJA TKALČEVIĆ:** DEPOZICIJA TANKIH FILMOVA SA UREĐENOM 3D MREŽOM NANOPORA NA RAZLIČITE SUPSTRATE – *DEPOSITION OF THIN ALUMINA FILMS CONTAINING 3D ORDERED NETWORK OF NANOPORES ON DIFFERENT SUBSTRATES (P-F11)*
-  **NIKOLA VUKMAN:** ISTRAŽIVANJE KLASTERSKE GRAĐE NEUTRONSKI BOGATIH IZOTOPA BERILIJA REAKCIJAMA SNOPA ⁹LI NA LIF METI – *EXPLORING CLUSTERING IN NEUTRON RICH BERYLLIUM ISOTOPES BY REACTIONS OF ⁹LI BEAM ON LIF TARGET (P-F12)*

GEOGRAFIJA – GEOGRAPHY

-  **MILENA SEKULIĆ:** UTJECAJ POPULACIJSKE POLITIKE NA VELIČINU OBITELJI U SRBIJI U 21. STOLJEĆU – *THE IMPACT OF POPULATION POLICIES ON FAMILY SIZE IN SERBIA IN THE 21st CENTURY (P-GG1)*
-  **STEFAN STAJIĆ:** ADAPTATION OF FOREIGN STUDENTS TOWARD THE SERBIAN SYLLABUS (P-GG2)

GEOLOGIJA – GEOLOGY

-  **ANJA JARIĆ:** KASNOMIOCENSKI PROCVAT SLATKOVODNIH SRČANKI (BIVALVIA: CARDIIDAE) U PANONSKOM JEZERU – *LATE MIOCENE FLOURISHING OF FRESHWATER COCKLES (BIVALVIA: CARDIIDAE) IN THE PANNONIAN LAKE (P-GL1)*
-  **MARIJA PETROVIĆ:** MOBILNOST OKSIANIONA IZ OSTARJELOG INDUSTRIJSKOG ODLAGALIŠTA U HRVATSKOJ (ŠTRMAC, ISTRA) – *MOBILITY OF OXYANIONS FROM AN AGED INDUSTRIAL WASTE IN CROATIA (ŠTRMAC, ISTRIA) (P-GL2)*
-  **NATALIA ŠENOLT:** POTOPLJENI KRAJOLIK PROKLJANSKOG JEZERA – *SUBMERGED LANDSCAPE OF THE PROKLJAN LAKE (P-GL3)*
-  **NINA TRINAJSTIĆ:** VULKANOKLASTIČNI ZAPISI DONJEG I SREDNJEG MIOCENA NA KALNIKU I POŽEŠKOJ GORI – *EARLY AND MIDDLE MIOCENE VOLCANICLASTIC RECORD ON MTS. KALNIK AND POŽEŠKA GORA (P-GL4)*



MARINA TRPČIĆ: METODOLOŠKI PRISTUP ISTRAŽIVANJU UTJECAJA NA SEDROTVORNI OKOLIŠ U SLIVU SLUNJČICE – *METHODOLOGICAL APPROACH TO THE RESEARCH OF IMPACTS ON THE TUFA ENVIRONMENT IN THE SLUNJČICA RIVER BASIN (P-GL5)*

KEMIJA – CHEMISTRY



MARIJA BAKIJA: “ONE POT” PRISTUP SINTEZI MONODENTATNIH OKSAZOLINA S AROMATSKOM JEZGROM-ASIMETRIČNA SUPSTITUCIJA PREKURSORA U JEDNOM KORAKU – „ONE POT“ APPROACH TO SYNTHESIZING MONODENTATE OXAZOLINES WITH AN AROMATIC CORE-ASYMMETRIC SUBSTITUTION OF PRECURSORS IN ONE STEP (P-K1)



MATEJA BELOVARI: BIS(TRIAZOLILPIRENSKI)-DERIVATI PSEUDOPEPTIDA KAO FLUORESCENTNI SENZORI: PRIMJENA U VIZUALIZACIJI STANICA – BIS(TRIAZOLYLPYRENE)-DERIVED PSEUDOPEPTIDES AS POTENTIAL FLUORESCENT SENSORS: APPLICATION IN CELL IMAGING (P-K2)



ARBEN BERIŠA: ORGANOKATALITIČKA STEREOSELEKTIVNA SINTEZA α -TRIARILMETANAMINA FORMALNOM BETTIJEVOM REAKCIJOM – STEREOSELECTIVE ORGANOCATALYTIC SYNTHESIS OF α -TRIARYLMETHANAMINES VIA FORMAL BETTI REACTION (M-K6)



EDVIN BRUSAČ: PROCJENA KAKVOĆE DODATAKA PREHRANI I PREHRAMBENIH PROIZVODA NA BAZI KURKUME – QUALITY ASSESSMENT OF TURMERIC DIETARY SUPPLEMENTS AND FOOD SAMPLES (P-K3)



ANĐELINA BUBALO: MIKROVALNO SUŠENJE MULJA S UPOVA I SVOJSTVA MIKROVALNO OSUŠENOG MULJA – MICROWAVE DRYING OF SEWAGE SLUDGE (P-K4)



MATEJ BUBAŠ: DFT PRISTUP PODEŠAVANJU PLAZMONIČKIH SVOJSTAVA LEGIRANJEM – A DFT APPROACH TO PLASMONIC PROPERTIES TUNING BY ALLOYING (P-K5)



KRISTINA BULE: STARENJE MIKROPLASTIKE POLISTIRENA NAPREDNIM OKSIDACIJSKIM PROCESIMA – AGING OF POLYSTYRENE MICROPLASTIC BY ADVANCED OXIDATION PROCESSES (P-K6)



NATAŠA BURIĆ: SINTEZA DIAMANTOIDNIH ESTERA ZA SUPRAMOLEKULSKO SAMOUDRUŽIVANJE – SYNTHESIS OF DIAMANTOID ESTERS FOR SUPRAMOLECULAR SELF-ASSEMBLY (M-K4)



LUCIJA DONČEVIĆ: AGITACIJOM POTAKNUTO REVERZIBILNO POVEZIVANJE PROTEINA rHu-G-SCF – AGITATION INDUCED REVERSIBLE SELF-ASSOCIATION OF PROTEIN rHu-G-SCF (P-K7)



MORANA DRUŠKOVIĆ: PROČIŠĆAVANJE ZAULJENIH OTPADNIH VODA ELEKTROKEMIJSKIM POSTUPCIMA – ELECTROCHEMICAL PROCESSES IN OILY WASTERWATER TREATMENT (P-K8)



VALENTINA EVIĆ: DJELOVANJE MISTRANSLACIJE I OKSIDACIJSKOG STRESA NA RAST I VIJABILNOST BAKTERIJE *Escherichia coli* – EFFECT OF MISTRANSLATION AND OXIDATIVE STRESS ON GROWTH AND VIABILITY OF BACTERIA *Escherichia coli* (P-K9)



NIKA GAZDEK: NASTAJANJE INKLUZIJSKIH KOMPLEKSA DERIVATA FEROCENA S β -CIKLODEKSTRINOM – BINDING ABILITY OF FERROCENE DERIVATIVES WITH β -CYCLODEXTRINS AS INCLUSION COMPLEXES (M-K2)



MIA GOTOVUŠA: UTJECAJ REAKCIJSKIH PARAMETARA NA SINTEZU OKTILNIH ESTERA MASNIH KISELINA – INFLUENCE OF REACTION PARAMETERS ON THE SYNTHESIS OF OCTYL ESTERS OF FATTY ACIDS (P-K10)








LUCIJA HOK: UTJECAJ DEUTERACIJE NA AFINITET HISTAMINA PREMA H₂ RECEPTORU: RAČUNALNA STUDIJA – DEUTERATION AFFECTS HISTAMINE AFFINITY FOR ITS H₂ RECEPTOR: A COMPUTATIONAL STUDY (P-K11)














KARLA JAGIĆ: PRELIMINARNI REZULTATI O ONEČIŠĆENJU ZAGREBAČKIH KUĆNIH PRAŠINA POLIBROMIRANIM DIFENIL ETERIMA – PRELIMINARY RESULTS ON POLYBROMINATED DIPHENYL ETHER CONTAMINATION STATUS IN ZAGREB HOUSE DUSTS (M-K7)








ZOE JELIĆ MATOŠEVIĆ: RAČUNALNE SIMULACIJE TRANSKRIPCIJSKOG FAKTORA MntR IZ BAKTERIJE *Bacillus subtilis* – COMPUTATIONAL SIMULATIONS OF THE TRANSCRIPTIONAL REGULATOR MntR FROM THE BACTERIUM *Bacillus subtilis* (P-K12)

-  **NIKOLINA KALČEC:** ISTRAŽIVANJE INTERAKCIJA RAZLIČITO FUNKCIONALIZIRANIH ZLATNIH NANOČESTICA S DOPAMINOM I L-DOPOM PRIMJENOM FLUORESCENCIJSKE SPEKTROSKOPIJE – *FLUORESCENCE SPECTROSCOPIC STUDY OF THE INTERACTION OF DIFFERENTLY COATED GOLD NANOPARTICLES WITH DOPAMINE AND L-DOPA (P-K13)*
-  **MATEJ KERN:** MODELIRANJE ADSORPCIJE FARMACEUTSKI AKTIVNIH TVARI NA UGLJIKOVE NANOMATERIJALE – *MODELLING OF THE ADSORPTION OF PHARMACEUTICALLY ACTIVE COMPOUNDS ON CARBON-BASED NANOMATERIALS (P-K14)*
-  **DAVID KLARIĆ:** INKLUZIJSKI KOMPLEKSI NABUMETONA S β -CIKLODEKSTRINOM I NJEGOVIM ODABRANIM DERIVATIMA – *INCLUSION COMPLEXES OF NABUMETONE WITH β -CYCLODEXTRIN AND ITS SELECTED DERIVATIVES (P-K15)*
-  **ROBERT JUNIOR KOLMAN:** PRIPRAVA PROPARGILNIH EPOKSIDA – *SYNTHESIS OF PROPARGYLIC EPOXIDES (P-K16)*
-  **MILENKO KORICA:** STRUKTURNA KARAKTERIZACIJA MAKROCIKLIČKE SCHIFFOVE BAZE S INKLUDIRANIM AMONIJAKOM, SUMPOROVIM DIOKSIDOM I KLOROM – *STRUCTURAL CHARACTERISATION OF MACROCYCLIC SCHIFF BASE WITH INCLUDED AMMONIA, SULPHUR DIOXIDE AND CHLORINE (P-K17)*
-  **JOSIPA KOSIĆ-VUKŠIĆ:** ODREĐIVANJE FOSFODIESTERAZA TIP 5 INHIBITORA U DODACIMA PREHRANI PRIMJENOM LC-TOF METODE – *DETERMINATION OF PHOSPHODIESTERASE TYPE 5 INHIBITORS IN DIETARY SUPPLEMENTS USING LC-TOF METHOD (P-K18)*
-  **MARTA KOŠČAK:** FLUORIMETRIJSKO PREPOZNAVANJE DNA I BSA OVISI O POVEZANOSTI KONJUGATA TRIARILBORANSKOG KATIONA S FLUORESCENTNOM SUPSTITUENTOM ILI SEKVENCOM PEPTIDA – *FLUORIMETRIC RECOGNITION BETWEEN DNA AND BSA DEPENDS ON TRIARYLBORONE CATIONE CONNECTIVITY TO FLUORESCENT SUPSTITUENT OR PEPTIDE SEQUENCE (P-K19)*
-  **IVONA KROŠL:** KARAKTERIZACIJA NOVOSINTETIZIRANIH DERIVATA 7-HIDROKSIKUMARINA – *CHARACTERISATION OF NEWLY SYNTHESIZED 7-HYDROXYCOUMARIN DERIVATIVES (P-K20)*
-  **DINO KUZMAN:** UTJECAJ REAKCIJSKIH UVJETA NA DOBIVANJE POLIOKSALATOMOLIBDATA RAZLIČITE NUKLEARNOSTI – *THE INFLUENCE OF REACTION CONDITIONS ON OBTAINING POLYOXSALATOMOLYBDATES OF VARIOUS NUCLEARITY (P-K21)*
-  **ANA LOZANČIĆ:** HOMO- I HETEROPOLINUKLEARNI SPOJEVI DOBIVENI KORIŠTENJEM GRAĐEVNIH BLOKOVA $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ ILI Fe) I ALKIL SUPSTITUIRANIH AMINA – *HOMO- AND HETEROPOLYNUCLEAR COMPOUNDS OBTAINED USING $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ OR Fe) AS BUILDING BLOCKS AND ALKYL-SUBSTITUTED AMINES (P-K22)*
-  **MIRNA MANDARIĆ:** POLIOKSOMOLIBDATI RAZLIČITIH NUKLEARNOSTI FUNKCIONALIZIRANI HIDRAZONSKIM KOMPLEKSIMA $Mo(VI)$ – *POLYOXOMOLYBDATES OF VARIOUS NUCLEARITIES FUNCTIONALIZED WITH $Mo(VI)$ HYDRAZONE COMPLEXES (P-K23)*
-  **VALENTINA MARTINEZ:** EFIKASNO I KONTROLIRANO UKLAPANJE BUCKMINSTERFULLERENA U ZIF-8 SODALITNE TOPOLOGIJE MEHANOKEMIJSKIM PUTEM – *EFFICIENT AND CONTROLLABLE ENTRAPMENT OF BUCKMINSTERFULLERENE INTO ZIF-8 OF SODALITE TOPOLOGY BY MECHANOCHEMISTRY (M-K3)*
-  **ANA MATOŠEVIĆ:** DIZAJN, SINTEZA I BIOLOŠKA EVALUACIJA SPOJEVA KAO LIJEKOVA AKTIVNIH U CENTRALNOM I PERIFERNOM ŽIVČANOM SUSTAVU – *DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF COMPOUNDS AS ACTIVE DRUGS IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM (M-K1)*
-  **MIHOVIL MEDIĆ:** UTJECAJ PROPILNIH ESTERA MASNIH KISELINA NA NAPETOST POVRŠINE, VISKOZNOST I GUSTOĆU MJEŠAVINA S DIZELOM – *EFFECT OF FATTY ACID PROPYL ESTERS ON SURFACE TENSION, VISCOSITY AND DENSITY OF BLENDS WITH DIESEL FUEL (P-K24)*
-  **DANIJELA MIHELEC:** PRIPRAVA LIPOFILNIH PREKURSORA ZA SINTEZU NOVIH DESMURAMIL-DIPEPTIDNIH DERIVATA – *PREPARATION OF LIPOPHILIC PRECURSORS FOR SYNTHESIS OF NEW DESMURAMYL DIPEPTIDE DERIVATIVES (P-K25)*







-  **ANA MIKELIĆ:** ODREĐIVANJE VIŠECILJNE ANTIMIKROBNE AKTIVNOSTI PRIMJENOM STROJNOG UČENJA – *MACHINE LEARNING-BASED PREDICTION OF MULTI-TARGET ANTIMICROBIAL ACTIVITY (P-K26)*
-  **MARTINA MILOLOŽA:** BIORAZGRADNJA MIKROPLASTIKE PRIMJENOM GRAM NEGATIVNIH BAKTERIJA RODA *Pseudomonas* I *Delftia* – *BIODEGRADATION OF MICROPLASTICS BY GRAM NEGATIVE BACTERIA FROM GENERA OF Pseudomonas AND Delftia (P-K27)*
-  **OZANA MIŠURA:** UGAĐANJE SAVITLJIVOSTI KRISTALA KOORDINACIJSKOG POLIMERA KADMIJA(II) KOKRISTALIZACIJOM – *MODULATING MECHANICAL FLEXIBILITY OF CADMIUM(II) COORDINATION COMPOUND VIA CO-CRYSTALLIZATION (P-K28)*
-  **ANTONIJA OŽGOVIĆ:** FENIL 3-HIDROKSIPROPIONSKA KISELINA KAO GRAĐEVNI BLOK ZA KIRALNE TEKUĆE KRISTALE SVINUTE GEOMETRIJE – *A NOVEL PHENYL-3-HYDROXY PROPIONIC ACID BUILDING BLOCK FOR BENT-SHAPED LIQUID CRYSTALLINE DIMERS (P-K29)*
-  **BARBARA PANIĆ:** UTJECAJ STRUKTURNIH I EKSPERIMENTALNIH PARAMETARA NA SAMOUDRUŽIVANJE DERIVATA NITROZOBENZENA NA POVRŠINI ZLATA – *INFLUENCE OF STRUCTURAL AND EXPERIMENTAL PARAMETERS ON SELF-ASSEMBLY OF NITROSOBENZENE DERIVATIVES ON GOLD SURFACE (P-K30)*
-  **ANTONIO PELESK:** KOROZIJSKA ZAŠTITA UGLJIČNOG ČELIKA HLAPLJIVIM INHIBITORIMA KOROZIJE – *CORROSION PROTECTION OF CARBON STEEL BY VOLATILE CORROSION INHIBITORS (P-K31)*
-  **MARIJANA POCRNIĆ:** ANALIZA INKLUZIJSKIH KOMPLEKSA MELOKSIKAMA I CIKLODEKSTRINA SPEKTROMETRIJOM MASA VISOKOG RAZLUČIVANJA – *HIGH RESOLUTION MASS SPECTROMETRIC ANALYSIS OF MELOXICAM – CYCLODEXTRINS INCLUSION COMPLEXES (P-K32)*
-  **IVAN PUCKO:** UTJECAJ UDJELA METIL METAKRILATA U POLIMERNOM ADITIVU NA NISKOTEMPERATURNI SVOJSTVA MINERALNOG DIZELSKOG GORIVA – *INFLUENCE OF POLYMER ADDITIVE WITH DIFFERENT AMOUNTS OF METHYL METHACRYLATE ON LOW TEMPERATURE PROPERTIES OF MINERAL DIESEL FUEL (P-K33)*
-  **MARTA RAZUM:** UTJECAJ STRUKTURE NA PRIENOS KALIJEVIH IONA U NIOBIJEVIM FOSFATNIM STAKLIMA – *INFLUENCE OF STRUCTURE ON THE TRANSPORT OF POTASSIUM IONS IN NIOBIUM PHOSPHATE GLASSES (P-K34)*
-  **LUCIJA REBROVIĆ:** UTJECAJ VIŠESTJENČANIH UGLJIKOVIH NANOCIJEVI RAZLIČITIH DIMENZIJA NA SVOJSTVA NANOFLUIDA POLIETILEN GLIKOLA – *INFLUENCE OF DIFFERENT SIZE MULTI-WALLED CARBON NANOTUBES ON POLYETHYLENE GLYCOL BASED NANOFLUID PROPERTIES (P-K35)*
-  **MARKO ROBIĆ:** UBRZANA HIDROLIZA OTOPINA $FeCl_3$ U PRISUTNOSTI IONA Cr^{3+} U KISELOM MEDIJU – *FORCED HYDROLYSIS OF $FeCl_3$ SOLUTIONS IN THE PRESENCE OF Cr^{3+} IONS IN ACIDIC MEDIUM (P-K36)*
-  **IVANA RUBIĆ:** NECILJANI METABOLOMSKI PROFIL SERUMA PASA INFICIRANIH S *Babesia canis* POMOĆU GC-MS – *UNTARGETED METABOLOMICS PROFILE OF SERUM IN DOGS INFECTED WITH *Babesia canis* BY GC-MS (P-K37)*
-  **IVANA ŠARIĆ:** JEZGRA/LJUSKA Ge/AI KVANTNE TOČKE U AMORFNOJ Al_2O_3 MATRICI DOBIVENE MAGNETRONSKIM RASPRAŠENJEM – *MAGNETRON SPUTTERING DEPOSITION OF CORE/SHELL Ge/AI QUANTUM DOT LATTICES IN AMORPHOUS Al_2O_3 MATRIX (P-K38)*
-  **JAKOV SLADE:** DIFUZIJA RADIKALA U PROPILEN KARBONATU I DMF-U – *RADICAL DIFFUSION IN PROPYLENE CARBONATE AND DMF (P-K39)*
-  **KARLO SOVIĆ:** KONFORMACIJSKA ANALIZA DERIVATA KINUKLIDINSKIH KARBAMATA – *CONFORMATIONAL ANALYSIS OF QUINUCLIDINE CARBAMATE DERIVATIVES (P-K40)*
-  **ZLATAN SPAHIĆ:** SINTEZA I KARAKTERIZACIJA NOVIH OKSIMSKIH ANTIDOTA PRI OTROVANJU ORGANOFOSFORNIM SPOJEVIMA – *SYNTHESIS AND CHARACTERIZATION OF NOVEL OXIME ANTIDOTES FOR ORGANOPHOSPHORUS POISONING (P-K41)*




-  **KRISTINA SUŠAC:** UTJECAJ SLOJEVITIH SILIKATA ISTIH VELIČINA ČESTICA NA TOPLINSKU VODLJIVOST U NEZASIĆENOJ POLIESTERSKOJ IMIDNOJ SMOLI – *INFLUENCE OF SAME PARTICLE SIZE LAYERED SILICATES ON THERMAL CONDUCTIVITY OF UNSATURATED POLYESTER IMIDE RESIN (P-K42)*
-  **PETAR ŠUTALO:** FEROCENSKI KROMOFOR KAO POTENCIJALNI SENZOR ZA ODREĐIVANJE ZAVIJENOSTI PEPTIDA – *FERROCENE CHROMOPHORE AS A POTENTIAL PROBE FOR THE ASSESSMENT OF HELICITY IN TRIPEPTIDES (P-K43)*
-  **LU TURKOVIĆ:** OPTIMIZACIJA UVJETA ZA ISTOVREMENU EKSTRAKCIJU RIBOCIKLIBA, ANASTROZOLA I LETROZOLA IZ LJUDSKE PLAZME – *PARAMETER OPTIMISATION FOR SIMULTANEOUS EXTRACTION OF RIBOCICLIB, ANASTROZOLE AND LETROZOLE FROM HUMAN PLASMA (P-K44)*
-  **IVA ZONJIĆ:** INTERAKCIJE DERIVATA BENZOTIAZOLSKIH AMIDINA S DNA – *INTERACTIONS OF BENZOTHIAZOLE AMIDINE DERIVATIVES WITH DNA (M-K5)*

MATEMATIKA – MATHEMATICS

-  **ANGELA BAŠIĆ-ŠIŠKO:** JEDNODIMENZIONALNI MODEL TOKA VISKOZNOG REALNOG MIKROPOLARNOG PLINA KOJI PROVODI TOPLINU – *ONE-DIMENSIONAL MODEL OF VISCOUS AND HEAT-CONDUCTING REAL MICROPOLAR GAS FLOW (P-M1)*
-  **DUBRAVKA BOŽIĆ:** RASPODJELA OPTEREĆENJA BESPILOTNIH LETJELICA PRILIKOM KOOPERATIVNOG PRENOŠENJA TERETA – *DISTRIBUTION OF LOAD DURING COOPERATIVE CARGO TRANSFER BY UNMANNED AERIAL VEHICLES (P-M2)*
-  **LUKA MIKEC:** INTERPRETABILNOST – *INTERPRETABILITY (P-M3)*
-  **DAMIR MIKOČ:** GENERALIZIRANI WRONSKIANI I MODULARNE KRIVULJE – *GENERALIZED WRONSKIANI AND MODULAR CURVES (P-M4)*
-  **IVANA VUKOREP:** O TEORIJI REPREZENTACIJA ALGEBRE $L_{-5/2}(SL(4))$ – *ON THE REPRESENTATION THEORY OF $L_{-5/2}(SL(4))$ (P-M5)*

OCEANOLOGIJA – OCEANOLOGY

-  **ANĐELA BAČINIĆ:** STVARANJE Co(II)-LIPIDNOG MIJEŠANOG KOMPLEKSA NA HIDROFOBNOJ POVRŠINI ŽIVINE KAPI – *FORMATION OF Co(II)-LIPID MIXED LIGAND COMPLEX AT THE MODEL SURFACE OF MERCURY ELECTRODE (P-O1)*
-  **TONKO BOGOVAC:** PREGLED DOHRANJIVANJA PLAŽA U HRVATSKOJ – *AN OVERVIEW OF BEACH NOURISHMENT IN CROATIA (P-O2)*
-  **NADIA DUNATO PEJNOVIĆ:** OLUJNI BLOKOV I DUŽ ISTOČNE OBALE JADRANA I NJIHOVO DATIRANJE METODOM ^{14}C – *STORM BOULDERS ALONG THE EASTERN COAST OF THE ADRIATIC AND THEIR DATING BY THE ^{14}C METHOD (P-O3)*
-  **IVANA HAZDOVAC:** UTJECAJ NANOČESTICA SREBRA, BAKRA I PLASTIKE NA RAST MORSKE MIKROALGE *Chlorella salina* – *INFLUENCE OF SILVER, COPPER AND NANOPLASTIC NANOPARTICLES ON THE GROWTH OF THE MARINE MICROALGA *Chlorella salina* (P-O4)*
-  **NINA MAJNARIĆ:** IZLAGANJE PLAŠTENJAKA *Clavelina oblonga* MORSKOJ VODI RAZLIČITIH SALINITETA, KAO MOGUĆI PRIRODAN NAČIN SUZBIJANJA OVE AKTUALNE INVAZIVNE VRSTE – *EXPERIMENTAL EXPOSURE OF TUNICATE *Clavelina oblonga* TO REDUCED SALINITIES AS A POSSIBLE ERADICATION MEASURE OF INVASION IN MUSSEL MARICULTURE (P-O5)*
-  **ANDREA MILINKOVIĆ:** SEZONSKE PROMJENE ATMOSFERSKOG TALOŽENJA DUŠIKA I FOSFORA NA PODRUČJU SREDNJEG JADRANA I BIOGEOKEMIJSKE POSLJEDICE – *SEASONAL VARIABILITIES OF NITROGEN AND PHOSPHORUS ATMOSPHERIC DEPOSITION TO THE CENTRAL ADRIATIC AREA AND BIOGEOCHEMICAL IMPLICATIONS (P-O6)*

-  **ENA PRITIŠANAC:** DIVERZITET EPIFITSKIH BAKTERIJSKIH ZAJEDNICA PRONAĐENIH NA SMEĐIM ALGAMA SJEVERNOG JADRANA – *DIVERSITY OF EPIPHYTIC BACTERIAL COMMUNITIES FOUND ON NORTHERN ADRIATIC FUCACEN SPECIES (M-01)*
-  **LORENA SELAK:** RANJIVOST OBALNIH SLATKOVODNIH SUSTAVA NA PODRUČJU MEDITERANA – MIKROBIOLOŠKO ISTRAŽIVANJE NA VRANSKOM JEZERU – *THE FRAGILITY OF COASTAL FRESHWATER RESOURCES IN THE MEDITERRANEAN AREA – A MICROBIAL-BASED CASE STUDY OF LAKE VRANA (P-07)*
-  **NIKI SIMONVIĆ:** ORGANSKI UGLJIK KAO INDIKATOR PROMJENA U MORSKOM STRATIFICIRANOM VODENOM OKOLIŠU – *ORGANIC CARBON AS AN INDICATOR OF CHANGES IN THE MARINE STRATIFIED AQUATIC ENVIRONMENT (P-08)*

Sadržaj

Pozvana predavanja/Invited Lectures

Marijan Herak

SEIZMOLOGIJA KAO MULTIDISCIPLINARNA ZNANOST – RECENTNI PRIMJERI ISTRAŽIVANJA POTRESA KOD ZAGREBA I PETRINJE 2020./2021. GODINE – *SEISMOLOGY AS A MULTIDISCIPLINARY SCIENCE – RECENT EXAMPLES OF STUDIES OF EARTHQUAKES NEAR ZAGREB AND PETRINJA IN 2020/2021* 48

Iva Tolić

MEHANOBIOLOGIJA DIOBENOG VRETENA – *MECHANOBIOLOGY OF THE MITOTIC SPINDLE* 50

Josip Tambača

MATEMATIČKO MODELIRANJE STENTOVA – *MATHEMATICAL MODELING OF STENTS* 52

Vernesa Smolčić

RAZVOJ GALAKSIJA KROZ SVEMIRSKO VRIJEME – *EVOLUTION OF GALAXIES THROUGH COSMIC TIME* 54

Usmena izlaganja/Oral presentations

Tena Čadež

BUTIRILKOLINESTERAZA – BIJEG IZ ACETILKOLINESTERAZINE SJENE KAO PSEUDOKATALITIČKO BIOČISTILO ŽIVČANIH OTROVA – *BUTYRYLCHOLINESTERASE- STEPING OUT OF ACETYLCHOLINESTERASE'S SHADOW AS PSEUDOCATALYTIC BIOSCAVENGER OF NERVE AGENTS* 57

Mirna Švob

JEDNODIMENZIONALNI MODEL RASPODJELE VODE U TLU KRŠKOG PODRUČJA – *ONE-DIMENSIONAL HYDROLOGICAL MODEL OF WATER CONTENT IN KARST SOIL* 59

Paula Dragičević

PROMJENE U MIKROBIOMU USPJEŠNE INVAZIVNE STRANE VRSTE, SIGNALNOGA RAKA, DUŽ NJENOG INVAZIVNOG AREALA – *CHANGES IN THE MICROBIOME OF A SUCCESSFUL INVADER, THE SIGNAL CRAYFISH, ALONG ITS INVASION RANGE* 61

Ana Radošević

REZULTATI JEDINSTVENOSTI I REGULARNOSTI ZA PROBLEME INTERAKCIJE FLUIDA I KRUTOG TIJELA – *UNIQUENESS AND REGULARITY RESULTS FOR FLUID-RIGID BODY INTERACTION* 63

Robert Kerep

ISPITIVANJE UTJECAJA GLIKOZILACIJSKOGA OBRASCA ALFA-KISELOG GLIKOPROTEINA NA VEZANJE LIJEKOVA DIPYRIDAMOLA I IMATINIBA – *ALPHA-ACID GLYCOPROTEIN GLYCOSYLATION PATTERN EFFECT ON THE BINDING OF DRUGS DIPYRIDAMOLE AND IMATINIB* 65

Damjan Iveković

STVARANJE DEFEKATA U GRAFENU S BRZIM TEŠKIM IONIMA – MD PRISTUP – *DEFECT CREATION IN GRAPHENE WITH SWIFT HEAVY ION IRRADIATION – MD APPROACH* 67

Magdalena Kralj

UČINKOVITA MEHANOKEMIJSKA SINTEZA GRAFENSKIH KVANTNIH TOČAKA – *EFFICIENT MECHANOCHEMICAL SYNTHESIS OF GRAPHENE QUANTUM DOTS* 69

Marija Zeljković PERCEPCIJA LOKALNIH STANOVNIKA O TURISTIČKIM POTENCIJALIMA ZAŠTIĆENIH PRIRODNIH PODRUČJA I RAZVOJU EKOTURIZMA U REGIJI JUŽNI BANAT – <i>LOCAL RESIDENTS' PERCEPTION TOWARDS TOURISM POTENTIALS AND ECOTOURISM DEVELOPMENT IN PROTECTED NATURAL AREAS IN THE SOUTH BANAT REGION</i>	71
Jelena Martinčić OSVJETLJAVANJE STANIČNE DIOBE KORIŠTENJEM OPTOGENETIKE – <i>SHINING A LIGHT ON CELL DIVISION USING OPTOGENETICS</i>	73
Ivan Antičević ULOGA TIROZILSKE DNA-FOSFODIESTERAZE 1 U POPRAVKU KRIŽNO VEZANIH PROTEINA NA OKOSNICI DNA <i>IN VIVO</i> – <i>ROLE OF TYROSYL DNA-PHOSPHODIESTERASE 1 IN THE REPAIR OF THE DNA-PROTEIN CROSSLINKS IN VIVO</i>	75
Tijana Radenković 3-GRUPE I KATEGORIJSKA UNIFIKACIJA INTERAKCIJA – <i>3-GROUPS AND HIGHER GAUGE THEORY UNIFICATION OF ALL INTERACTIONS</i>	77
Marsej Markovski DINAMIKA MIKROBNIH ZAJEDNICA SEDIMENTA U PROPADAJUĆOJ LIVADI VRSTE <i>Cymodocea nodosa</i> – <i>DYNAMICS OF SEDIMENT MICROBIAL COMMUNITIES IN A DECLINING Cymodocea nodosa MEADOW</i>	79
Goran Poje ANTIPLAZMODIJSKO DJELOVANJE HARMICINA TRIAZOLSKOG TIPA NOVE GENERACIJE – <i>ANTIPLASMODIAL ACTIVITY OF NOVEL GENERATION OF TRIAZOLE-TYPE HARMICINES</i>	81
Domagoj Hackenberger Kutuzović PROSTORNO MODELIRANJE POPULACIJA KOMARACA (<i>Culicidae</i>) POMOĆU MATRIČNIH POPULACIJSKIH MODELA – <i>SPATIAL MODELING OF MOSQUITOES (Culicidae) POPULATIONS USING MATRIX POPULATION MODELS</i>	83
Marina Marinović ANTIMLARIJSKO DJELOVANJE HARMICINA AMIDNOG TIPA – <i>ANTIMALARIAL ACTIVITY OF NOVEL AMIDE-TYPE HARMICINES</i>	85
Nina Čorak TRANSKRIPCIJSKE ZNAČAJKE PLEOMORFNIH VARIJANTI BAKTERIJE <i>Borrelia burgdorferi</i> – <i>TRANSCRIPTOME PROFILING OF Borrelia burgdorferi PLEOMORPHIC VARIANTS</i>	87
Marko Viskić STRATEGIJE ANALIZE SORTNIH TIOLA U VINU: DERIVATIZACIJA I IZOTOPNO RAZRJEĐENJE – <i>STRATEGIES FOR ANALYSIS OF VARIETAL THIOLS IN WINE: DERIVATIZATION AND STABLE ISOTOPE DILUTION ANALYSIS</i>	89
Barbara Bošnjak TEORIJA REPREZENTACIJA <i>p</i> -ADSKIH GRUPA – LANGLANDSOV PROGRAM – <i>REPRESENTATION THEORY OF p-ADIC GROUPS – LANGLANDS PROGRAM</i>	91
Andrea Usenik OD LEDENJAKA DO GEJZIRA: PRIČA O HIDROFOBNOG EFEKTU – <i>FROM ICEBERGS TO GEYSERS: THE STORY BEHIND HYDROPHOBIC EFFECT</i>	93

Marija Kovačević UČINCI STROBILURINSKIH FUNGICIDA NA REPRODUKCIJU, PREŽIVLJAVANJE I IZLJEKANJE VRSTE <i>Enchytraeus crypticus</i> – EFFECTS OF STROBILURIN FUNGICIDES ON SURVIVAL REPRODUCTION AND HATCHING SUCESS OF <i>Enchytraeus crypticus</i>	95
Nikola Gizdavec PRIMJENA DALJINSKIH ISTRAŽIVANJA U ISTRAŽIVANJU MINERALNIH SIROVINA – APPLICATION OF REMOTE SENSING IN MINERAL RESOURCES EXPLORATION	97
Emma Svetličić BIOTIPIZACIJA I IDENTIFIKACIJA PROTEINA POMOĆU SPEKTROMETRIJE MASA I <i>de novo</i> SEKVENCIRANJA PEPTIDA – BIOTIPIZATION AND PROTEIN IDENTIFICATION BY MASS SPECTROMETRY ANALYSIS AND PEPTIDE <i>de novo</i> SEQUENCING	99
Natalija Pantalon Juraj STEREOKEMIJA KOMPLEKSA TRIDENTATNIH LIGANADA S BAKROM(II) I CINKOM(II) – STEREOCHEMISTRY OF TRIDENTATE LIGAND COMPLEXES WITH COPPER(II) AND ZINC(II)	101
Tatjana Mijošek DUGOROČNI TRENDOVI KONCENTRACIJA METALA I KAKVOĆE VODE RIJEKE KRKE U DIJELU TOKA POD UTJECAJEM OTPADNIH VODA – LONG-TERM TRENDS OF METAL CONCENTRATIONS AND WATER QUALITY OF THE WASTEWATER IMPACTED KRKA RIVER COURSE.....	103
Jadranka Pelikan FIZIKALNO-KEMIJSKA I EKOTOKSIKOLOŠKA ANALIZA MORSKOG SEDIMENTA U SJEVERNOM JADRANU – PHYSICO-CHEMICAL AND ECOTOXICOLOGICAL ANALYSIS OF MARINE SEDIMENT IN THE NORTHERN ADRIATIC	105
Mateja Matišić STEREOSELEKTIVNA PRIPRAVA β , β -DIARIL-KETONA S β -KVATERNIM STEREOGENIM CENTROM – STEREOSELECTIVE SYNTHESIS OF β , β -DIARYL KETONES WITH β -QUATERNARY STEREOGENIC CENTER	107
Luka Turić MULTIFREKVENCIJSKA ANALIZA RAVNIH DEPOLARIZIRANIH KANALA U OKOLINI POLJA 3C196 – MULTI-FREQUENCY STUDY OF THE STRAIGHT DEPolarIZATION CANALS IN A SURROUNDING OF THE 3C196 FIELD	109
Ivana Colić PRIPRAVA C-GLIKOZIL AMINOKISELINA POST-KONDENZACIJSKOM MODIFIKACIJOM PASSERINIJEVIH PRODUKATA – SYNTHESIS OF C-GLYCOSYL AMINO ACIDS BY POST- CONDENSATION MODIFICATION OF PASSERINI PRODUCTS	111
Ivana Mikulandra PRIPRAVA I KARAKTERIZACIJA MAKROZONA, NOVIH BIOAKTIVNIH DERIVATA AZITROMICINA – SYNTHESIS AND CHARACTERIZATION OF MACROZONES, NOVEL BIOACTIVE DERIVATIVES OF AZITHROMYCIN	113
Daniela Ančić ANTIPROLIFERATIVNI I ANTIANGIOGENI UČINAK NANOKRISTALA RESVERATROLA NA EHRlichOV ASCITESNI TUMOR U MIŠA – ANTI-PROLIFERATIVE AND ANGIO-SUPPRESSIVE EFFECT OF RESVERATROL NANOCRYSTALS ON EHRlich ASCITES TUMOR IN MOUSE	115

Alojzije Brkić	
NOVI POGLED NA STRUKTURNE OSNOVE ANTIBIOTSKE OTPORNOSTI IZOLEUCIL-TRNA SINTETAZA TIPA 2 – <i>NOVEL INSIGHTS INTO STRUCTURAL BASIS OF ANTIBIOTIC RESISTANCE IN TYPE II ISOLEUCYL-tRNA SYNTHETASES</i>	117
Ivan Biočić	
SEMILINEARNE JEDNADŽBE ZA NELOKALNE OPERATORE: VIŠE OD FRAKCIONALNOG LAPLACEOVOG OPERATORA – <i>SEMILINEAR EQUATIONS FOR NON-LOCAL OPERATORS: BEYOND THE FRACTIONAL LAPLACIAN</i>	119
Sarah Mateša	
ULOGA ELEMENTARNOG SUMPORA (S^0) BIOLOŠKOG PORIJEKLA U STVARANJU POLISULFIDA U MORSKOM EUKSINSKOM OKOLIŠU (ROGOZNIČKO JEZERO) – <i>THE ROLE OF BIOLOGICALLY PRODUCED ELEMENTARY SULFUR (S^0) ON POLYSULPHIDE FORMATION IN THE MARINE EUXINIC ENVIRONMENT (ROGOZNICA LAKE)</i>	121
Nikola Lesar	
NEURODEGENERATIVNE PROMJENE U MOZGU ŠTAKORA IZAZVANE SEVOFLURANOM I ŽELJEZO-DEKSTRANOM – <i>NEURODEGENERATIVE CHANGES IN THE RAT BRAIN INDUCED BY SEVOFLURANE AND IRON-DEXTRAN</i>	123
Marin Mićunović	
MORFOLOŠKE PROMJENE ŽALA OTOKA HVARA OD 1834. DO DANAS – <i>MORPHOLOGICAL CHANGES OF THE ISLAND OF HVAR BEACHES FROM 1834 TO PRESENT DAY</i>	125
Petra Pranić	
EVALUACIJA KLIMATSKE SIMULACIJE „ADRIATIC SEA AND COAST“: MORE – <i>PERFORMANCE OF THE ADRIATIC SEA AND COAST CLIMATE SIMULATION: OCEAN</i>	127
Paula Gršković	
UTJECAJ POMOĆNIČKIH LIMFOCITA T NA PREŽIVLJENJE PACIJENATA S DIJAGNOZOM FOLIKULARNOG LIMFOMA – <i>THE INFLUENCE OF HELPER T LYMPHOCYTES ON THE SURVIVAL OF PATIENTS DIAGNOSED WITH FOLLICULAR LYMPHOMA</i>	129
Tin Klačić	
PRIPRAVA I KARAKTERIZACIJA POLIELEKTROLITNIH NANOFILMOVA – <i>PREPARATION AND CHARACTERIZATION OF POLYELECTROLYTE NANOFILMS</i>	131
Silvestar Beljan	
IDENTIFIKACIJA, FUNKCIJA I UNUTARSTANIČNA LOKALIZACIJA SPUŽVINOG HOMOLOGA LJUDSKOG SUPRESORA METASTAZIRANJA DRG1 – <i>IDENTIFICATION, FUNCTION AND INTRACELLULAR LOCALIZATION OF SPONGE HOMOLOG OF HUMAN METASTASIS SUPPRESSOR DRG1</i>	133
Vanja Marić	
SPINSKI LANCI FRUSTRIRANI TOPOLOGIJOM – <i>TOPOLOGICALLY FRUSTRATED SPIN CHAINS</i>	135
Jurica Sabol	
PRIMJENA FORAMINIFERSKIH ZAJEDNICA U ISTRAŽIVANJU MIOCENSKIH NASLAGA ODABRANIH LOKALITETA HRVATSKOG ZAGORJA - <i>APPLICATION OF FORAMINIFERAL ASSEMBLAGES IN RESEARCH OF MIOCENE DEPOSITS FROM HRVATSKO ZAGORJE</i>	137
Suzana Harabajsa	
LJUDSKI PAPILOMA VIRUS KOD KARCINOMA PLUĆA NEMALIH STANICA S MUTACIJAMA GENA EGFR – <i>HUMAN PAPILOMAVIRUS IN NON-SMALL CELL LUNG CANCER WITH EGFR GENE MUTATIONS</i>	139

Mikro-izlaganja i poster/Flash presentations and posters

Iva Kokotović

UČINAK VIŠESTRUKIH STRESORA NA VODENE KUKCE: ŠTO MOŽEMO NAUČITI IZ LABORATORIJSKOG POKUSA? – *MULTIPLE STRESSOR EFFECTS ON STREAM AQUATIC INSECTS: INSIGHTS FROM A MICROCOSM EXPERIMENT* 142

Valerija Begić

EKSPRESIJA GENA CIRKADIJANOG RITMA KOD NEMODELNIH KUKACA – *CIRCADIAN GENE EXPRESSION IN NON-MODEL INSECTS* 144

Ana Matošević

DIZAJN, SINTEZA I BIOLOŠKA EVALUACIJA SPOJEVA KAO LIJEKOVA AKTIVNIH U CENTRALNOM I PERIFERNOM ŽIVČANOM SUSTAVU – *DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF COMPOUNDS AS ACTIVE DRUGS IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM* 146

Ena Pritišanec

DIVERZITET EPIFITSKIH BAKTERIJSKIH ZAJEDNICA PRONAĐENIH NA SMEĐIM ALGAMA SJEVERNOG JADRANA – *DIVERSITY OF EPIPHYTIC BACTERIAL COMMUNITIES FOUND ON NORTHERN ADRIATIC FUCACEN SPECIES* 148

Matej Peranić

KVANTNA KOMUNIKACIJA POMOĆU PAROVA KVANTNO PREPLETENIH FOTONA – *QUANTUM COMMUNICATION WITH ENTANGLED PHOTON PAIRS* 150

Nika Gazdek

NASTAJANJE INKLUZIJSKIH KOMPLEKSA DERIVATA FEROCENA S β -CIKLODEKSTRINOM – *BINDING ABILITY OF FERROCENE DERIVATIVES WITH β -CYCLODEXTRINS AS INCLUSION COMPLEXES* 152

Matko Bišćan

VAŽNOST ČUVARA PRIRODE JAVNIH USTANOVA ZAŠTIĆENIH PODRUČJA PRIRODE U MONITORINGU BIORAZNOLIKOSTI: NA PRIMJERU ISTRAŽIVANJA SISAVACA POMOĆU FOTO ZAMKI NA PODRUČJU NACIONALNOG PARKA PAKLENICA (HRVATSKA) – *THE VALUE OF PROTECTED AREAS RANGER SERVICE PERSONNEL FOR BIODIVERSITY MONITORING: CASE STUDY - CAMERA TRAPPING SURVEY OF MAMMALS IN PAKLENICA NATIONAL PARK (CROATIA)* 154

Valentina Martinez

EFIKASNO I KONTROLIRANO UKLAPANJE BUCKMINSTERFULLERENA U ZIF-8 SODALITNE TOPOLOGIJE MEHANOKEMIJSKIM PUTEM – *EFFICIENT AND CONTROLLABLE ENTRAPMENT OF BUCKMINSTERFULLERENE INTO ZIF-8 OF SODALITE TOPOLOGY BY MECHANOCHEMISTRY* 156

Nataša Burić

SINTEZA DIAMANTOIDNIH ESTERA ZA SUPRAMOLEKULSKO SAMOUDRUŽIVANJE – *SYNTHESIS OF DIAMANTOID ESTERS FOR SUPRAMOLECULAR SELF-ASSEMBLY* 158

Darko Kučan

ZDRUŽENO DJELOVANJE CISPLATINE I RESVERATROLA NA METALOPROTEINAZNU AKTIVNOST U EHRLICHOVOM ASCITESNOM SOLIDNOM TUMORU MIŠA – *COMBINED EFFECT OF CISPLATIN AND RESVERATROL ON METALLOPROTEINASE ACTIVITY IN EHRlich ASCITES SOLID MOUSE TUMOR* 160

Zuzana Redžović

ENERGIJSKI STATUS U POPULACIJAMA *Synurella ambulans* IZ HIPOREIČKE ZONE RIJEKE SAVE I IZVORA MALA BRŠLJANICA, HRVATSKA – *ENERGY STATUS IN *Synurella ambulans* POPULATIONS FROM HYPORHEIC ZONE OF SAVA RIVER AND MALA BRŠLJANICA SPRING, CROATIA*..... 162

Arian Ivec MOTORNI PROTEINI SU ZASLUŽNI ZA ZAKRIVLJNE OBLIKE MIKROTUBULA U DIOBENOM VRETENU – <i>MOTOR PROTEINS GENERATE THE CURVED SHAPE OF THE MITOTIC SPINDLE</i>	164
Iva Zonjić INTERAKCIJE DERIVATA BENZOTIAZOLSKIH AMIDINA S DNA – <i>INTERACTIONS OF BENZOTHAZOLE AMIDINE DERIVATIVES WITH DNA</i>	166
Tamara Vuk ULOGA PROTEINA BPM1 U KONTROLI METILACIJSKIH OBRAZACA GENA CML41 I FWA PUTEM MEHANIZMA RDDM U VRSTI <i>Arabidopsis thaliana</i> L. – <i>ROLE OF BPM1 PROTEIN IN A CONTROL OF METHYLATION PATTERNS OF CML41 AND FWA GENES THROUGH RDDM PATHWAY IN Arabidopsis thaliana L</i>	168
Arben Beriša ORGANOKATALITIČKA STEREOSELEKTIVNA SINTEZA α -TRIARILMETANAMINA FORMALNOM BETTIJEVOM REAKCIJOM – <i>STEREOSELECTIVE ORGANOCATALYTIC SYNTHESIS OF α- TRIARYLMETHANAMINES VIA FORMAL BETTI REACTION</i>	170
Karla Jagić PRELIMINARNI REZULTATI O ONEČIŠĆENJU ZAGREBAČKIH KUĆNIH PRAŠINA POLIBROMIRANIM DIFENIL ETERIMA – <i>PRELIMINARY RESULTS ON POLYBROMINATED DIPHENYL ETHER CONTAMINATION STATUS IN ZAGREB HOUSE DUSTS</i>	172

Posterska priopćenja/Poster presentations

Biologija/Biology

Marta Bakšić AKUTNA, OBOSTRANA ISHEMIJA NOGU NAKON SARS-CoV-2 INFEKCIJE I COVID-19: PRIKAZ SLUČAJA – <i>ACUTE, BILATERAL LOWER LIMB ISCHEMIA AFTER SARS-CoV-2 INFECTION AND COVID -19: A CASE REPORT</i>	175
Dora Bjedov ANALIZA BIOMARKERA UČINKA I OKSIDATIVNOG STRESA U KRVI PTIĆA BIJELE RODE (<i>Ciconia ciconia</i>) S PODRUČJA HRVATSKE – <i>BIOMARKERS OF EFFECT AND OXIDATIVE STRESS ANALYSIS IN BLOOD OF WHITE STORK (Ciconia ciconia) NESTLINGS FROM CROATIA</i>	177
Andrijana Bogoje Raspopović MEĐUODNOS EKSPRESIJE BDNF, IL-6 I POKAZATELJA OKSIDACIJSKOG STRESA PRI DEMIJELINIZACIJSKIM OŠTEĆENJIMA – <i>CORRELATION OF BDNF, IL-6 EXPRESSION AND OXIDATIVE STRESS MARKERS IN DEMYELINATING DAMAGE</i>	179
Ana Borić Bilušić POLIMORFIZAM GENA ZA METABOLIČKE ENZIME I TRANSPORTNE PROTEINE KOD BOLESNIKA S TRANSPLANTIRANIM BUBREGOM – <i>GENETIC POLYMORPHISM OF METABOLIC ENZYMES AND TRANSPORTERS IN RENAL TRANSPLANT RECIPIENTS</i>	181
Tamara Đerđ UTJECAJ TRIAZOLNIH FUNGICIDA NA PONAŠANJE I FIZIOLOŠKU AKTIVNOST <i>Daphnia magna</i> – <i>THE EFFECTS OF TRIAZOLE FUNGICIDES ON BEHAVIOUR AND PHYSIOLOGY OF Daphnia magna</i>	183

Evelin Despot-SladeEPIGENOMIKA HOLOCENTROMERA – *EPIGENOMICS OF HOLOCENTROMERE* 185**Marko Doboš**VELIČINE GENOMA VRSTE *Festuca bosniaca* (Poaceae) NA BALKANSKOM POLUOTOKU – *GENOME SIZE OF Festuca bosniaca* (Poaceae) ON THE BALKAN PENINSULA 187**Ana Dobrović**MODELI DINAMIČKIH ENERGIJSKIH BUDŽETA ZA UGROŽENE AUTOHTONE I INVAZIVNE VRSTE RAKOVA – *DYNAMIC ENERGY BUDGET MODELS FOR ENDANGERED NATIVE AND INVASIVE CRAYFISH SPECIES* 189**Mia Dželalija**MOLEKULARNA OSNOVA VIRULENCIJE I ANTIBIOTSKE REZISTENCIJE VANKOMICIN-REZISTENTNIH *Enterococcus faecium* IZOLATA IZ OTPADNE I MORSKE VODE SA JAVNE PLAŽE – *MOLECULAR BASIS OF VIRULENCE AND ANTIBIOTIC RESISTANCE IN VANCOMYCIN-RESISTANT Enterococcus faecium FROM WASTEWATER AND RECEIVING BEACH WATER* 191**Klara Filek**KOKULTIVACIJA DIJATOMEJA: BLISKI SUSRETI *Achnanthes elongata* I *Psammodyction* sp. – *DIATOM CO-CULTURES: CLOSE ENCOUNTERS OF Achnanthes elongata AND Psammodyction* sp. ... 193**Jasenka Grgurić**ANALIZA EKSPRESIJE LNCRNA ANRIL I PVT1 U PERIFERNOJ CIRKULACIJI PACIJENATA SA KALCIFICIRAJUĆOM STENOZOM AORTNIH ZALISTAKA SRCA – *ANALYSIS OF EXPRESSION OF LNCRNA ANRIL AND PVT1 IN PERIPHERAL CIRCULATION OF PATIENTS WITH CALCIFYING AORTIC VALVE STENOSIS* 195**Dora Hlebec**PRIMJENA INTEGRATIVNE TAKSONOMIJE U OPISU DVIJU NOVIH STENOENDEMSKIH VRSTA OBALČARA (PLECOPTERA) U HRVATSKOJ – *USE OF INTEGRATIVE TAXONOMY IN DESCRIPTION OF TWO NEW STENOENDEMIC STONEFLY SPECIES (PLECOPTERA) FROM CROATIA* 197**Lada Jovović**OMOKROMI – BIOLOŠKI PIGMENTI VANJSKIH SRODNICA ŠPILJSKIH JEDNAKONOŽNIH RAKOVA (ISOPODA, CRUSTACEA) – *OMMOCHROMES – BIOLOGICAL PIGMENTS IN SURFACE RELATIVES OF CAVE-DWELLING ISOPODS (CRUSTACEA)* 199**Lucija Kanjer**CIJANOBAKTERIJE NA MORSKIM KORNJAČAMA: ISTRAŽIVANJE RAZNOLIKOSTI METODOM METABARKODINGA – *CYANOBACTERIA ASSOCIATED WITH SEA TURTLES: A DIVERSITY STUDY USING METABARCODING APPROACH* 201**Mirnes Karić**HIGIJENSKO-SANITARNI UVJETI U ŠKOLI SA OSVRTOM NA COVID-19 – *HYGIENIC AND SANITARY CONDITIONS IN SCHOOL WITH REFERENCE TO COVID-19* 203**Bruno Komazec**UTJECAJ NANOČESTICA I IONA SREBRA NA ALGU *Chlorella vulgaris* – *THE EFFECTS OF SILVER NANOPARTICLES AND IONS ON Chlorella vulgaris* 205

Isabella Koprivec

AUGMIN REGULIRA SILU NAPETOSTI IZMEĐU SESTRINSKIH KINETOHORA I PROSTORNI RASPORED MIKROTUBULA NUKLEACIJOM PREMOŠĆUJUĆIH VLAKANA – *AUGMIN REGULATES KINETOCHORE TENSION AND SPATIAL ARRANGEMENT OF SPINDLE MICROTUBULES BY NUCLEATING BRIDGING FIBERS* 207

Sara Koska

KORELACIJA FILOGENIJE I ONTOGENIJE TIJEKOM STANIČNE DIFERENCIJACIJE – *PHYLOGENY-ONTOGENY CORRELATION DURING CELL DIFFERENTIATION* 209

Karla Košpić

PROMJENE U AKTIVNOSTI I OBRASCU IZOFORMI ANTIOKSIDACIJSKIH ENZIMA U BILJKAMA DUHANA NAKON IZLAGANJA NANOČESTICAMA SREBRA I IONSKOM SREBRU – *CHANGES IN ACTIVITIES AND ISOFORM PATTERNS OF ANTIOXIDANT ENZYMES IN TOBACCO PLANTS UPON EXPOSURE TO SILVER NANOPARTICLES AND SILVER NITRATE* 211

Maja Ledinski

UPOTREBA ČVRSTIH LIPIDNIH NANOČESTICA S UGRAĐENIM ASKORBATOM ZA TRETMAN TUMORSKIH MATIČNIH STANICA – *APPLICATION OF ASCORBATE-INCORPORATED SOLID LIPID NANOPARTICLES FOR TREATMENT OF CANCER STEM CELLS* 213

Leona Lovrenčić

GENETSKA RAZNOLIKOST I POPULACIJSKA STRUKTURA PLEMENITOG RAKA U HRVATSKOJ – *GENETIC DIVERSITY AND POPULATION STRUCTURE OF THE NOBLE CRAYFISH IN CROATIA* 215

Lucija Lulić

UTJECAJ ONKOPROTEINA E6 PAPILOMAVIRUSA ČOVJEKA TIP 16 (HPV16) NA REGULATORE STANIČNE POLARNOSTI U TUMORIMA GLAVE I VRATA – *EFFECTS OF HUMAN PAPILLOMAVIRUS 16 (HPV16) E6 ONCOPROTEIN ON CELL POLARITY REGULATORS IN HEAD AND NECK CANCERS* 217

Lucija Mijanović

ULOGA PROTEINA IQGC PORODICE RASGAP U STANIČNOJ ADHEZIJI – *A NOVEL FUNCTION OF THE RASGAP PROTEIN IQGC IN CELL ADHESION* 219

Rafaela Mrdjen-Hodžić

POVEZANOST GLAZBENIH AKTIVNOSTI I RAZINE KORTIZOLA KOD TRUDNICA – *ASSOCIATIONS OF MUSICAL ACTIVITIES ON CORTISOL LEVELS IN PREGNANT WOMEN* 221

Marija Nazlić

USPOREDBA ANTIOKSIDATIVNOG DJELOVANJA I SASTAVA ETERIČNOG ULJA I HIDROLATA IZOLIRANIH IZ VRSTA *Veronica austriaca ssp. jacquinii* (BAUMG.) EB. FISCH. I *Veronica saturejoides* VIS. ssp. *Saturejoides* – *COMPARISON OF THE ANTIOXIDANT ACTIVITY AND COMPOSITION OF THE ESSENTIAL OIL AND HYDROLATE ISOLATED FROM Veronica austriaca ssp. jacquinii (BAUMG.) EB. FISH. AND Veronica saturejoides VIS. ssp. Saturejoide*..... 223

Barbara Nikolić

POVEĆAN BROJ PROPINJANJA I POVEĆANA RAZINA DOPAMINA U MOŽDANOM DEBLU KOD ŠTAKORSKOG MODELA BLAGE NEONATALNE NORMOBARIČNE HIPOKSIJE – *INCREASED REARING AND BRAINSTEM DOPAMINE LEVELS IN A RAT MODEL OF MILD NEONATAL NORMOBARIC HYPOXIA* 225

Dorotea Pali

REKOMBINANTNA CJEPIVA ZA RSV I HCV TEMELJENA NA VIRUSU MUMPSA – *RECOMBINANT RSV AND HCV VACCINES BASED ON MUMPS VIRUS* 227

Ivana Pavičić	
S-ADENOZIL HOMOCISTEIN HIDROLAZNA DEFICIJENCIJA – <i>S-ADENOSYL HOMOCYSTEIN HYDROLASE DEFICIENCY</i>	229
Ena Pešut	
U POTRAZI ZA NOVIM BIOMARKERIMA RAKA VRATA MATERNICE – <i>SEARCHING FOR NEW CERVICAL CANCER BIOMARKERS</i>	231
Goran Pipalović	
REGULATORNI MEHANIZMI KONTROLE SEGREGACIJE KROMOSOMA U <i>Streptomyces coelicolor</i> – <i>REGULATORY MECHANISMS THAT CONTROL CHROMOSOME SEGREGATION IN Streptomyces coelicolor</i>	233
Darija Putar	
MEHANIZMI REGRUTACIJE RASGAP PROTEINA IQGC NA MAKROPINOSOME U AMEBI <i>Dictyostelium discoideum</i> – <i>RECRUITMENT MECHANISMS OF RASGAP PROTEIN IQGC TO MACROPINOSOMES IN AMOEBA Dictyostelium discoideum</i>	235
Barbara Radovani	
PROMJENE U N–GLIKOZILACIJI IMUNOGLOBULINA G I UKUPNIH PROTEINA PLAZME KOD PACIJENATA S FIBRILACIJOM ATRIJA – <i>ALTERED N – GLYCOSYLATION OF IMMUNOGLOBULIN G AND TOTAL PLASMA PROTEINS IN PATIENTS WITH ATRIAL FIBRILLATION</i>	237
Rajko Roljić	
MORFOMETRIJSKE ZNAČAJKE I KONDICIJSKI INDEKSI RIJEČNOG RAKA <i>Astacus astacus</i> L. IZ RIJEKE PLIVE – <i>MORPHOMETRIC CHARACTERISTICS AND CONDITION INDICES OF NOBLE CRAYFISH Astacus astacus L. FROM THE PLIVA RIVER</i>	239
Iva Sošić	
GREŠKE U RAZDVAJANJU KROMOSOMA U STANICAMA S RAZLIČITIM RAZINAMA MEĐUSTANIČNOG KONTAKTA – <i>CHROMOSOME SEGREGATION ERRORS IN CELLS WITH VARYING CELL-TO-CELL CONTACT LEVELS</i>	241
Anita Stojanović Marković	
FILOGEOGRAFSKA DISTRIBUCIJA HAPLOTIPOVA GENA <i>CYP2D6</i> – <i>PHYLOGEOGRAPHIC DISTRIBUTION OF CYP2D6 HAPLOTYPES</i>	243
Maja Šetinc	
DULJINA TELOMERA I DOB SMRTI KOD OSOBA DUBOKE STAROSTI – <i>TELOMERE LENGTH AND AGE AT DEATH IN VERY OLD INDIVIDUALS</i>	245
Ena Šimunić	
ANALIZA FIBROBLASTA PACIJENTA S NEDOSTATNOM AKTIVNOSTI S-ADENOZILHOMOCISTEIN-HIDROLAZE METODOM RNA-Seq – <i>RNA-Seq ANALYSIS OF FIBROBLASTS FROM PATIENT WITH S-ADENOSYLHOMOCYSTEINE HYDROLASE DEFICIENCY</i>	247
Paula Štanc	
UTJECAJ MUTACIJSKOG POTPISA PROTEINA APOBEC NA PREDVIĐANJE ISHODIŠNE STANICE RAZLIČITIH MOLEKULARNIH SKUPINA RAKA DOJKE – <i>APOBEC MUTATIONAL SIGNATURE AFFECTS PREDICTION OF CELL OF ORIGIN IN DIFFERENT MOLECULAR GROUPS OF BREAST CANCER</i>	249
Valentina Štimac	
PIVOTIRANJE KAO MEHANIZAM DOLASKA POLARNIH KROMOSOMA NA DIOBENO VRETENO – <i>POLAR CHROMOSOMES PIVOT THEIR WAY TOWARDS THE SPINDLE BODY</i>	251

Antea Talajić

IDENTIFIKACIJA, BIOKEMIJSKA KARAKTERIZACIJA I UNUTARSTANIČNA LOKALIZACIJA SPUŽVINOG
HOMOLOGA LJUDSKOG PROTEINA RAS2 – IDENTIFICATION, BIOCHEMICAL CHARACTERIZATION AND
INTRACELLULAR LOCALIZATION OF SPONGE HOMOLOG OF HUMAN RAS2 253

Ana Terlević

MORFOLOŠKA VARIJABILNOST *Dianthus sylvestris* Wulfen s. l. NA BALKANSKOM POLUOTOKU –
MORPHOLOGICAL VARIABILITY IN *Dianthus sylvestris* Wulfen s. l. ON THE BALKAN PENINSULA 255

Mirta Tokić

UTJECAJ POVIŠENE TEMPERATURE NA KLIJANCE VRSTA *Arabidopsis thaliana*, *Brassica rapa* I *Solanum
lycopersicum* – EFFECT OF INCREASED TEMPERATURE ON *Arabidopsis thaliana*, *Brassica rapa* AND
Solanum lycopersicum 257

Monika Tunjić Cvitanić

IDENTIFIKACIJA, KARAKTERIZACIJA I LOKALIZACIJA SATELITNIH SEKVENCIJA DNA GENOMA PACIFIČKE
KAMENICE *Crassostrea gigas* (Thunberg, 1793) – IDENTIFICATION, CHARACTERIZATION AND
LOCALIZATION OF SATELLITE DNA SEQUENCES OF THE PACIFIC OYSTER *Crassostrea gigas* (Thunberg,
1793)..... 259

Marina Veseli

MAKROFITI KAO SPREMNICI ZA ONEČIŠĆUJUĆE TVARI – MACROPHYTES AS STORAGE UNITS FOR
EMERGINIG CONTAMINANTS 261

Damira Veseljak

ANALIZA SATELITOMA KUKCA BRAŠNARA *Tribolium freemani* VISOKOPROTOČNIM SEKVENCIRANJEM
– ANALYSIS OF THE SATELLITOME OF THE FLOUR BEETLE *Tribolium freemani* BY HIGH-THROUGHPUT
SEQUENCING 263

Sandra Vitko

UČINAK STRESNIH UVJETA NA FOTOSINTETSKU UČINKOVITOST KLIJANACA UROČNJAKA (*Arabidopsis
thaliana*) S PROMIJENJENOM EKSPRESIJOM GENA *BPM1* – EFFECT OF STRESS CONDITIONS ON
PHOTOSYNTHETIC EFFICIENCY OF *Arabidopsis thaliana* SEEDLINGS WITH MODIFIED *BPM1* GENE
EXPRESSION 265

Marin Volarić

ORGANIZACIJA HOLOCENTROMERE U DUGIM POTEZIMA – LONG-RANGE ORGANISATION OF
HOLOCENTROMERES 267

Barbara Vuić

TERAPIJSKI POTENCIJAL NEUROSTEROIDA I NEUROTROFINA U DEMENCIJI – THERAPEUTIC POTENTIAL
OF NEUROSTEROIDS AND NEUROTROPHINS IN DEMENTIA 269

Fizika/Physics**Domjan Barić**

RAZUMIJEVANJE SLOŽENIH INTERAKCIJA VREMENSKIH SERIJA KROZ LEĆU DUBOKOG UČENJA –
UNDERSTANDING COMPLEX TIME SERIES INTERACTIONS THROUGH THE LENS OF DEEP LEARNING 271

Josipa Diklić

PRIENOS KORELIRANIH PAROVA NUKLEONA U TEŠKO-IONSKE REAKCIJAMA – PAIRING
CORRELATIONS IN THE HEAVY-ION TRANSFER REACTION 273

Marta Fatović

POTRAGA ZA PROMJENJIVIM IZVORIMA S MALIM AMPLITUDAMA I DUGIM PERIODIMA – *SEARCH FOR SMALL-AMPLITUDE LONG-PERIOD VARIABILITY* 275

Safer Grbić

BLUMENBERGOVA GENEZA DVOSMISLENOSTI NEBA – *BLUMENTBERG'S GENESIS OF THE AMBIGUITY OF HEAVEN* 277

Sara Ivasić

NEDAVNO SLABLJENJE DALJINSKE VEZE EL NIÑO-JUŽNE OSCILACIJE ZIMI NAD PODRUČJEM SJEVERNOG ATLANTIKA I EUROPE – *RECENT WEAKENING IN THE WINTER ENSO TELECONNECTION OVER THE NORTH ATLANTIC-EUROPEAN REGION* 279

Ana Marija Kožuljević

ISPITIVANJE GAGG:CE SCINTILATORA ZA PRIMJENE U SUSTAVIMA ZA OPAŽANJE GAMA ZRAČENJA – *INVESTIGATION OF GAGG:CE SCINTILLATORS FOR APPLICATIONS IN GAMMA IMAGING SYSTEMS* 281

Mateo Kruljac

LASERSKO HLAĐENJE ATOMA UNUTAR OPTIČKOG REZONATORA POMOĆU FREKVENTNOG ČEŠLJA – *LASER COOLING OF ATOMS INSIDE AN OPTICAL RESONATOR USING A FREQUENCY COMB* 283

Helena Latečki

SIMULACIJA POTRESNE TREŠNJE ZA GRAD ZAGREB, HRVATSKA – *SEISMIC SHAKING SCENARIOS FOR CITY OF ZAGREB, CROATIA* 285

Krešimir Ruić

PROCJENA DOPRINOSA VISOKOFREKVENTNIH OSCILACIJA RAZINE MORA EKSTREMNIM RAZINAMA U JADRANSKOM MORU – *ESTIMATING CONTRIBUTION OF HIGH-FREQUENCY SEA-LEVEL OSCILLATIONS TO THE EXTREME SEA LEVELS IN THE ADRIATIC SEA* 287

Bruno Šlaus

FUNKCIJE LUMINOZITETA AKTIVNIH GALAKTIČKIH JEZGRI I NJIHOVA EVOLUCIJA – *AGN LUMINOSITY FUNCTIONS AND THEIR EVOLUTION* 289

Marija Tkalčević

DEPOZICIJA TANKIH FILMOVA SA UREĐENOM 3D MREŽOM NANOPORA NA RAZLIČITE SUPSTRATE – *DEPOSITION OF THIN ALUMINA FILMS CONTAINING 3D ORDERED NETWORK OF NANOPORES ON DIFFERENT SUBSTRATES* 291

Nikola Vukman

ISTRAŽIVANJE KLASTERSKE GRAĐE NEUTRONSKI BOGATIH IZOTOPA BERILIJA REAKCIJAMA SNOPI ^9Li NA LIF METI – *EXPLORING CLUSTERING IN NEUTRON RICH BERYLLIUM ISOTOPES BY REACTIONS OF ^9Li BEAM ON LIF TARGET* 293

Geografija/Geography**Milena Sekulić**

UTJECAJ POPULACIJSKE POLITIKE NA VELIČINU OBITELJI U SRBIJI U 21. STOLJEĆU – *THE IMPACT OF POPULATION POLICIES ON FAMILY SIZE IN SERBIA IN THE 21st CENTURY* 295

Stefan Stajić

ADAPTATION OF FOREIGN STUDENTS TOWARD THE SERBIAN SYLLABUS 297

Geologija/Geology

Anja Jarić

KASNOMIOCENSKI PROCVAT SLATKOVODNIH SRČANKI (BIVALVIA: CARDIIDAE) U PANONSKOM JEZERU – LATE MIOCENE FLOURISHING OF FRESHWATER COCKLES (BIVALVIA: CARDIIDAE) IN THE PANNONIAN LAKE 298

Marija Petrović

MOBILNOST OKSIANIONA IZ OSTARJELOG INDUSTRIJSKOG ODLAGALIŠTA U HRVATSKOJ (ŠTRMAC, ISTRJA) – MOBILITY OF OXYANIONS FROM AN AGED INDUSTRIAL WASTE IN CROATIA (ŠTRMAC, ISTRIA) 300

Natalia Šenolt

POTOPLJENI KRAJOLIK PROKLJANSKOG JEZERA – SUBMERGED LANDSCAPE OF THE PROKLJAN LAKE 302

Nina Trinajstić

VULKANOKLASTIČNI ZAPISI DONJEG I SREDNJEG MIOCENA NA KALNIKU I POŽEŠKOJ GORI – EARLY AND MIDDLE MIOCENE VOLCANICLASTIC RECORD ON MTS. KALNIK AND POŽEŠKA GORA 304

Marina Trpčić

METODOLOŠKI PRISTUP ISTRAŽIVANJU UTJECAJA NA SEDROTVORNI OKOLIŠ U SLIVU SLUNJČICE – METHODOLOGICAL APPROACH TO THE RESEARCH OF IMPACTS ON THE TUFA ENVIRONMENT IN THE SLUNJČICA RIVER BASIN 306

Kemija/Chemistry

Marija Bakija

“ONE POT” PRISTUP SINTEZI MONODENTATNIH OKSAZOLINA S AROMATSKOM JEZGROM- ASIMETRIČNA SUPSTITUCIJA PREKURSORA U JEDNOM KORAKU – „ONE POT“ APPROACH TO SYNTHESIZING MONODENTATE OXAZOLINES WITH AN AROMATIC CORE- ASYMMETRIC SUBSTITUTION OF PRECURSORS IN ONE STEP 308

Mateja Belovari

BIS(TRIAZOLILPIRENSKI)-DERIVATI PSEUDOPEPTIDA KAO FLUORESCENTNI SENZORI: PRIMJENA U VIZUALIZACIJI STANICA – BIS(TRIAZOLYLPIRENE)-DERIVED PSEUDOPEPTIDES AS POTENTIAL FLUORESCENT SENSORS: APPLICATION IN CELL IMAGING 310

Edvin Brusač

PROCJENA KAKVOĆE DODATAKA PREHRANI I PREHRAMBENIH PROIZVODA NA BAZI KURKUME – QUALITY ASSESSMENT OF TURMERIC DIETARY SUPPLEMENTS AND FOOD SAMPLES 312

Anđelina Bubalo

MIKROVALNO SUŠENJE MULJA S UPOVA I SVOJSTVA MIKROVALNO OSUŠENOG MULJA – MICROWAVE DRYING OF SEWAGE SLUDGE 314

Matej Bubaš

DFT PRISTUP PODEŠAVANJU PLAZMONIČKIH SVOJSTAVA LEGIRANJEM – A DFT APPROACH TO PLASMONIC PROPERTIES TUNING BY ALLOYING 316

Kristina Bule

STARENJE MIKROPLASTIKE POLISTIRENA NAPREDNIM OKSIDACIJSKIM PROCESIMA – AGING OF POLYSTYRENE MICROPLASTIC BY ADVANCED OXIDATION PROCESSES 318

Lucija Dončević

AGITACIJOM POTAKNUTO REVERZIBILNO POVEZIVANJE PROTEINA rHu-G-SCF – *AGITATION INDUCED REVERSIBLE SELF-ASSOCIATION OF PROTEIN rHu-G-SCF* 320

Morana Drušković

PROČIŠĆAVANJE ZAULJENIH OTPADNIH VODA ELEKTROKEMIJSKIM POSTUPCIMA – *ELECTROCHEMICAL PROCESSES IN OILY WASTERWATER TREATMENT* 322

Valentina Ević

DJELOVANJE MISTRANSLACIJE I OKSIDACIJSKOG STRESA NA RAST I VIJABILNOST BAKTERIJE *Escherichia coli* – *EFFECT OF MISTRANSLATION AND OXIDATIVE STRESS ON GROWTH AND VIABILITY OF BACTERIA Escherichia coli* 324

Mia Gotovuša

UTJECAJ REAKCIJSKIH PARAMETARA NA SINTEZU OKTILNIH ESTERA MASNIH KISELINA – *INFLUENCE OF REACTION PARAMETERS ON THE SYNTHESIS OF OCTYL ESTERS OF FATTY ACIDS* 326

Lucija Hok

UTJECAJ DEUTERACIJE NA AFINITET HISTAMINA PREMA H₂ RECEPTORU: RAČUNALNA STUDIJA – *DEUTERATION AFFECTS HISTAMINE AFFINITY FOR ITS H₂ RECEPTOR: A COMPUTATIONAL STUDY* .. 328

Zoe Jelić Matošević

RAČUNALNE SIMULACIJE TRANSKRIPCISKOG FAKTORA MntR IZ BAKTERIJE *Bacillus subtilis* – *COMPUTATIONAL SIMULATIONS OF THE TRANSCRIPTIONAL REGULATOR MntR FROM THE BACTERIUM Bacillus subtilis* 330

Nikolina Kalčec

ISTRAŽIVANJE INTERAKCIJA RAZLIČITO FUNKCIONALIZIRANIH ZLATNIH NANOČESTICA S DOPAMINOM I L-DOPOM PRIMJENOM FLUORESCENCIJSKE SPEKTROSKOPIJE – *FLUORESCENCE SPECTROSCOPIC STUDY OF THE INTERACTION OF DIFFERENTLY COATED GOLD NANOPARTICLES WITH DOPAMINE AND L-DOPA* 332

Matej Kern

MODELIRANJE ADSORPCIJE FARMACEUTSKI AKTIVNIH TVARI NA UGLJIKOVE NANOMATERIJALE – *MODELLING OF THE ADSORPTION OF PHARMACEUTICALLY ACTIVE COMPOUNDS ON CARBON-BASED NANOMATERIALS* 334

David Klarić

INKLUZIJSKI KOMPLEKSI NABUMETONA S β -CIKLODEKSTRINOM I NJEGOVIM ODABRANIM DERIVATIMA – *INCLUSION COMPLEXES OF NABUMETONE WITH β -CYCLODEXTRIN AND ITS SELECTED DERIVATIVES* 336

Robert Junior Kolman

PRIPRAVA PROPARGILNIH EPOKSIDA – *SYNTHESIS OF PROPARGYLIC EPOXIDES* 338

Milenko Korica

STRUKTURNA KARAKTERIZACIJA MAKROCIKLIČKE SCHIFFOVE BAZE S INKLUDIRANIM AMONIJAKOM, SUMPOROVIM DIOKSIDOM I KLOROM – *STRUCTURAL CHARACTERISATION OF MACROCYCLIC SCHIFF BASE WITH INCLUDED AMMONIA, SULPHUR DIOXIDE AND CHLORINE* 340

Josipa Kosić-Vukšić

ODREĐIVANJE FOSFODIESTERAZA TIP 5 INHIBITORA U DODACIMA PREHRANI PRIMJENOM LC-TOF METODE – *DETERMINATION OF PHOSPHODIESTERASE TYPE 5 INHIBITORS IN DIETARY SUPPLEMENTS USING LC-TOF METHOD* 342

Marta Koščak	
FLUORIMETRIJSKO PREPOZNAVANJE DNA I BSA OVISI O POVEZANOSTI KONJUGATA TRIARILBORANSKOG KATIONA S FLUORESCENTNOM SUPSTITUENTOM ILI SEKVENCOM PEPTIDA – <i>FLUORIMETRIC RECOGNITION BETWEEN DNA AND BSA DEPENDS ON TRIARYLBORONE CATIONE CONNECTIVITY TO FLUORESCENT SUPSTITUENT OR PEPTIDE SEQUENCE</i>	344
Ivana Krošl	
KARAKTERIZACIJA NOVOSINTETIZIRANIH DERIVATA 7-HIDROKSIKUMARINA – <i>CHARACTERISATION OF NEWLY SYNTHESIZED 7-HYDROXYCOUMARIN DERIVATIVES</i>	346
Dino Kuzman	
UTJECAJ REAKCIJSKIH UVJETA NA DOBIVANJE POLIOKSALATOMOLIBDATA RAZLIČITE NUKLEARNOSTI – <i>THE INFLUENCE OF REACTION CONDITIONS ON OBTAINING POLYOXALATOMOLYBDATES OF VARIOUS NUCLEARITY</i>	348
Ana Lozančić	
HOMO- I HETEROPOLINUKLEARNI SPOJEVI DOBIVENI KORIŠTENJEM GRAĐEVNIH BLOKOVA $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ ILI Fe) I ALKIL SUPSTITUIRANIH AMINA – <i>HOMO- AND HETEROPOLYNUCLEAR COMPOUNDS OBTAINED USING $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ OR Fe) AS BUILDING BLOCKS AND ALKYL-SUBSTITUTED AMINES</i>	350
Mirna Mandarić	
POLIOKSOMOLIBDATI RAZLIČITIH NUKLEARNOSTI FUNKCIONALIZIRANI HIDRAZONSKIM KOMPLEKSIMA $Mo(VI)$ – <i>POLYOXOMOLYBDATES OF VARIOUS NUCLEARITIES FUNCTIONALIZED WITH $Mo(VI)$ HYDRAZONE COMPLEXES</i>	352
Mihovil Medić	
UTJECAJ PROPILNIH ESTERA MASNIH KISELINA NA NAPETOST POVRŠINE, VISKOZNOST I GUSTOĆU MJEŠAVINA S DIZELOM – <i>EFFECT OF FATTY ACID PROPYL ESTERS ON SURFACE TENSION, VISCOSITY AND DENSITY OF BLENDS WITH DIESEL FUEL</i>	354
Danijela Mihelec	
PRIPRAVA LIPOFILNIH PREKURSORA ZA SINTEZU NOVIH DESMURAMIL-DIPEPTIDNIH DERIVATA – <i>PREPARATION OF LIPOPHILIC PRECURSORS FOR SYNTHESIS OF NEW DESMURAMYL DIPEPTIDE DERIVATIVES</i>	356
Ana Mikelić	
“ONE POT” PRISTUP SINTEZI MONODENTATNIH OKSAZOLINA S AROMATSKOM JEZGROM- ASIMETRIČNA SUPSTITUCIJA PREKURSORA U JEDNOM KORAKU – „ONE POT“ APPROACH TO SYNTHESIZING MONODENTATE OXAZOLINES WITH AN AROMATIC CORE- ASYMMETRIC SUBSTITUTION OF PRECURSORS IN ONE STEP	358
Martina Miloloža	
BIORAZGRADNJA MIKROPLASTIKE PRIMJENOM GRAM NEGATIVNIH BAKTERIJA RODA <i>Pseudomonas</i> I <i>Delftia</i> – <i>BIODEGRADATION OF MICROPLASTICS BY GRAM NEGATIVE BACTERIA FROM GENERA OF Pseudomonas AND Delftia</i>	360
Ozana Mišura	
UGAĐANJE SAVITLJIVOSTI KRISTALA KOORDINACIJSKOG POLIMERA KADMIJA(II) KOKRISTALIZACIJOM – <i>MODULATING MECHANICAL FLEXIBILITY OF CADMIUM(II) COORDINATION COMPOUND VIA CO-CRYSTALLIZATION</i>	362

Antonija Ožegović

FENIL 3-HIDROKSIPROPIONSKA KISELINA KAO GRAĐEVNI BLOK ZA KIRALNE TEKUĆE KRISTALE SVINUTE GEOMETRIJE – A NOVEL PHENYL-3-HYDROXY PROPIONIC ACID BUILDING BLOCK FOR BENT-SHAPED LIQUID CRYSTALLINE DIMERS 364

Barbara Panić

UTJECAJ STRUKTURNIH I EKSPERIMENTALNIH PARAMETARA NA SAMOUDRUŽIVANJE DERIVATA NITROZOBENZENA NA POVRŠINI ZLATA – INFLUENCE OF STRUCTURAL AND EXPERIMENTAL PARAMETERS ON SELF-ASSEMBLY OF NITROSOBENZENE DERIVATIVES ON GOLD SURFACE..... 366

Antonio Pelesk

KOROZIJSKA ZAŠTITA UGLJIČNOG ČELIKA HLAPLJIVIM INHIBITORIMA KOROZIJE – CORROSION PROTECTION OF CARBON STEEL BY VOLATILE CORROSION INHIBITORS 368

Marijana Pocrnić

ANALIZA INKLUZIJSKIH KOMPLEKSA MELOKSIKAMA I CIKLODEKSTRINA SPEKTROMETRIJOM MASA VISOKOG RAZLUČIVANJA – HIGH RESOLUTION MASS SPECTROMETRIC ANALYSIS OF MELOXICAM – CYCLODEXTRINS INCLUSION COMPLEXES 370

Ivan Pucko

UTJECAJ UDJELA METIL METAKRILATA U POLIMERNOM ADITIVU NA NISKOTEMPERATURNNA SVOJSTVA MINERALNOG DIZELSKOG GORIVA – INFLUENCE OF POLYMER ADDITIVE WITH DIFFERENT AMOUNTS OF METHYL METHACRYLATE ON LOW TEMPERATURE PROPERTIES OF MINERAL DIESEL FUEL 372

Marta Razum

UTJECAJ STRUKTURE NA PRIENOS KALIJEVIH IONA U NIOBIJEVIM FOSFATNIM STAKLIMA – INFLUENCE OF STRUCTURE ON THE TRANSPORT OF POTASSIUM IONS IN NIOBIUM PHOSPHATE GLASSES 374

Lucija Rebrović

UTJECAJ VIŠESTJENČANIH UGLJIKOVIH NANOCIJEVI RAZLIČITIH DIMENZIJA NA SVOJSTVA NANOFLUIDA POLIETILEN GLIKOLA – INFLUENCE OF DIFFERENT SIZE MULTI-WALLED CARBON NANOTUBES ON POLYETHYLENE GLYCOL BASED NANOFLUID PROPERTIES 376

Marko Robić

UBRZANA HIDROLIZA OTOPINA $FeCl_3$ U PRISUTNOSTI IONA Cr^{3+} U KISELOM MEDIJU – FORCED HYDROLYSIS OF $FeCl_3$ SOLUTIONS IN THE PRESENCE OF Cr^{3+} IONS IN ACIDIC MEDIUM 378

Ivana Rubić

NECILJANI METABOLOMSKI PROFIL SERUMA PASA INFICIRANIH S *Babesia canis* POMOĆU GC-MS – UNTARGETED METABOLOMICS PROFILE OF SERUM IN DOGS INFECTED WITH *Babesia canis* BY GC-MS 380

Ivana Šarić

JEZGRA/LJUSKA Ge/Al KVANTNE TOČKE U AMORFNOJ Al_2O_3 MATRICI DOBIVENE MAGNETRONSKIM RASPRAŠENJEM – MAGNETRON SPUTTERING DEPOSITION OF CORE/SHELL Ge/Al QUANTUM DOT LATTICES IN AMORPHOUS Al_2O_3 MATRIX 382

Jakov Slade

DIFUZIJA RADIKALA U PROPILEN KARBONATU I DMF-U – RADICAL DIFUSSION IN PROPYLENE CARBONATE AND DMF 384

Karlo Sović KONFORMACIJSKA ANALIZA DERIVATA KINUKLIDINSKIH KARBAMATA – <i>CONFORMATIONAL ANALYSIS OF QUINUCLIDINE CARBAMATE DERIVATIVES</i>	386
Zlatan Spahić SINTEZA I KARAKTERIZACIJA NOVIH OKSIMSKIH ANTIDOTA PRI OTROVANJU ORGANOFOSFORNIM SPOJEVIMA – <i>SYNTHESIS AND CHARACTERIZATION OF NOVEL OXIME ANTIDOTES FOR ORGANOPHOSPHORUS POISONING</i>	388
Kristina Sušac UTJECAJ SLOJEVITIH SILIKATA ISTIH VELIČINA ČESTICA NA TOPLINSKU VODLJIVOST U NEZASIĆENOJ POLIESTERSKOJ IMIDNOJ SMOLI – <i>INFLUENCE OF SAME PARTICLE SIZE LAYERED SILICATES ON THERMAL CONDUCTIVITY OF UNSATURATED POLYESTER IMIDE RESIN</i>	390
Petar Šutalo FEROCENSKI KROMOFOR KAO POTENCIJALNI SENZOR ZA ODREĐIVANJE ZAVIJENOSTI PEPTIDA – <i>FERROCENE CHROMOPHORE AS A POTENTIAL PROBE FOR THE ASSESSMENT OF HELICITY IN TRIPEPTIDES</i>	392
Lu Turković OPTIMIZACIJA UVJETA ZA ISTOVREMENU EKSTRAKCIJU RIBOCIKLIBA, ANASTROZOLA I LETROZOLA IZ LJUDSKE PLAZME – <i>PARAMETER OPTIMISATION FOR SIMULTANEOUS EXTRACTION OF RIBOCICLIB, ANASTROZOLE AND LETROZOLE FROM HUMAN PLASMA</i>	394
 Matematika/Mathematics	
Angela Bašić-Šiško JEDNODIMENZIONALNI MODEL TOKA VISKOZNOG REALNOG MIKROPOLARNOG PLINA KOJI PROVODI TOPLINU – <i>ONE-DIMENSIONAL MODEL OF VISCOUS AND HEAT-CONDUCTING REAL MICROPOLAR GAS FLOW</i>	396
Dubravka Božić RASPODJELA OPTEREĆENJA BESPILOTNIH LETJELICA PRILIKOM KOOPERATIVNOG PRENOŠENJA TERETA – <i>DISTRIBUTION OF LOAD DURING COOPERATIVE CARGO TRANSFER BY UNMANNED AERIAL VEHICLES</i>	398
Luka Mikec INTERPRETABILNOST – <i>INTERPRETABILITY</i>	400
Damir Mikoč GENERALIZIRANI WRONSKIANI I MODULARNE KRIVULJE GENERALIZED – <i>WRONSKIANs AND MODULAR CURVES</i>	402
Ivana Vukorep O TEORIJI REPREZENTACIJA ALGEBRE $L_{-5/2}(SL(4))$ – <i>ON THE REPRESENTATION THEORY OF $L_{-5/2}(SL(4))$</i>	404

Oceanologija/Oceanology

Anđela Bačinić

STVARANJE Co(II)-LIPIDNOG MIJEŠANOG KOMPLEKSA NA HIDROFOBNOJ POVRŠINI ŽIVINE KAPI –
*FORMATION OF Co(II)-LIPID MIXED LIGAND COMPLEX AT THE MODEL SURFACE OF MERCURY
ELECTRODE* 406

Tonko Bogovac

PREGLED DOHRANJIVANJA PLAŽA U HRVATSKOJ – *AN OVERVIEW OF BEACH NOURISHMENT IN
CROATIA* 408

Nadia Dunato Pejnović

OLUJNI BLOKOV I DUŽ ISTOČNE OBALE JADRANA I NJIHOVO DATIRANJE METODOM ¹⁴C – *STORM
BOULDERS ALONG THE EASTERN COAST OF THE ADRIATIC AND THEIR DATING BY THE
¹⁴C METHOD* 410

Ivana Hazdovac

UTJECAJ NANOČESTICA SREBRA, BAKRA I PLASTIKE NA RAST MORSKE MIKROALGE *Chlorella salina* –
*INFLUENCE OF SILVER, COPPER AND NANOPLASTIC NANOPARTICLES ON THE GROWTH OF THE
MARINE MICROALGA Chlorella salina* 412

Nina Majnarić

IZLAGANJE PLAŠTENJAKA *Clavelina oblonga* MORSKOJ VODI RAZLIČITIH SALINITETA, KAO MOGUĆI
PRIRODAN NAČIN SUZBIJANJA OVE AKTUALNE INVAZIVNE VRSTE – *EXPERIMENTAL EXPOSURE OF
TUNICATE Clavelina oblonga TO REDUCED SALINITIES AS A POSSIBLE ERADICATION MEASURE OF
INVASION IN MUSSEL MARICULTURE* 414

Andrea Milinković

SEZONSKE PROMJENE ATMOSFERSKOG TALOŽENJA DUŠIKA I FOSFORA NA PODRUČJU SREDNJEG
JADRANA I BIOGEOKEMIJSKE POSLJEDICE – *SEASONAL VARIABILITIES OF NITROGEN AND
PHOSPHORUS ATMOSPHERIC DEPOSITION TO THE CENTRAL ADRIATIC AREA AND BIOGEOCHEMICAL
IMPLICATIONS* 416

Lorena Selak

RANJIVOST OBALNIH SLATKOVODNIH SUSTAVA NA PODRUČJU MEDITERANA – MIKROBIOLOŠKO
ISTRAŽIVANJE NA VRANSKOM JEZERU – *THE FRAGILITY OF COASTAL FRESHWATER RESOURCES IN
THE MEDITERRANEAN AREA – A MICROBIAL-BASED CASE STUDY OF LAKE VRANA* 418

Niki Simonović

ORGANSKI UGLJIK KAO INDIKATOR PROMJENA U MORSKOM STRATIFICIRANOM VODENOM OKOLIŠU
– *ORGANIC CARBON AS AN INDICATOR OF CHANGES IN THE MARINE STRATIFIED AQUATIC
ENVIRONMENT* 420

Radionice/workshops

Dejan Vinković

ŽIVOT JE POPUT BOMBONIJERE: OD ASTROFIZIKE DO ZNANSTVENOG PODUZETNIŠTVA - *LIFE IS LIKE A BOX OF CHOCOLATES: FROM ASTROPHYSICS TO SCIENTIFIC ENTREPRENEURSHIP* 423

Paula Dobrinić

KARIJERE IZVAN AKADEMIJE: ISKUSTVO SA SVEUČILIŠTA U OXFORDU - *CAREERS BEYOND ACADEMIA: EXPERIENCE FROM THE UNIVERSITY OF OXFORD* 425

Jelena Čulić-Viskota

KARIJERA U INDUSTRIJI - KLJUČNE VJEŠTINE I NAČIN RAZMIŠLJANJA ZA USPJEH – *CAREER IN INDUSTRY- KEY SKILLS AND MINDSET FOR SUCCESS* 427

Popis sudionika 429

Pozvana predavanja
Invited Lectures

SEISMOLOGY AS A MULTIDISCIPLINARY SCIENCE – RECENT EXAMPLES OF STUDIES OF EARTHQUAKES NEAR ZAGREB AND PETRINJA IN 2020/2021

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Seismology is very young discipline which stands out among sciences by several traits (e.g. the extremely large range of amplitudes and periods of ground motion it studies). It also has three faces – the research one (physics of the Earth's interior), the professional face (recording, locating and cataloguing earthquakes), and the one that deals with seismic hazard assessment and the ways to mitigate seismic risk. Related to these is its distinct multidisciplinary and the need for close cooperation with various professions. Besides the expected physics and mathematics, there are also: geology, civil engineering, geodesy, but also professions such as history, linguistics or archiving.

In the lecture, I will look at how this collaboration materialized during the 2020/2021 earthquake series near Zagreb (ML = 5.5) and Petrinja (ML = 6.2). Joint research with geologists related to locating aftershocks and determining the causal fault will be described, as well as cooperation with colleague geodesists in interpreting the satellite radar measurements (InSAR). The research on the historical seismicity to quantify past important earthquakes that are important in earthquake hazard assessment will be also briefly discussed.

SEIZMOLOGIJA KAO MULTIDISCIPLINARNA ZNANOST – RECENTNI PRIMJERI ISTRAŽIVANJA POTRESA KOD ZAGREBA I PETRINJE 2020/2021. GODINE

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Seizmologija je vrlo mlada znanost koja se ističe i po nekoliko posebnih značajki (npr. izrazito velik raspon amplituda i perioda pomaka koje proučava). Uvjetno rečeno, ona ima i tri lica – istraživačko (fizika unutrašnjosti Zemlje), stručno (bilježenje, lociranje i katalogiziranje potresa), te ono koje se bavi procjenom potresne opasnosti i načinima smanjenja potresne ugroženosti. S time je u vezi i njezina izrazita multidisciplinarnost i nužnost tijesne suradnje s raznim strukama. Od posve očekivanih fizike i matematike, tu su još i: geologija, građevinarstvo, geodezija, ali i struke poput povijesti, lingvistike ili arhivarstva.

Na predavanju ću se osvrnuti na to kako je ova suradnja došla do izražaja tijekom potresnih serija 2020./2021. godine kod Zagreba (ML = 5.5) i Petrinje (ML = 6.2). Opisat će se zajednička istraživanja s geolozima povezana s lociranjem naknadnih potresa i utvrđivanjem uzročnog rasjeda, s kolegama geodetima pri interpretaciji satelitskih radarskih mjerenja (InSAR). Također ću ukratko opisati istraživanja povijesne seizmičnosti radi kvantifikacije prošlih potresa koji su važni pri procjeni potresne opasnosti.

MECHANOBIOLOGY OF THE MITOTIC SPINDLE

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Our bodies are built from around 100 trillion individual cells, each of which contains 46 chromosomes that carry our genetic material. This enormous number of cells originates from a single cell that is the product of fertilization of an egg with a sperm. Thus, cell division is one of the most fundamental processes in the living world. At the onset of division the cell assembles the mitotic spindle, a fascinating and complex micro-machine made of microtubules and the accompanying proteins. The microtubules move the chromosomes around and finally line them up in the middle of the spindle. When all chromosomes are ready, sister chromatids are moved apart towards the opposite spindle poles. The central question in this field of research is how the mitotic spindle manages to divide chromosomes into two equal sets without errors. Understanding how proper chromosome segregation is achieved in cells and how it is controlled will help to identify new strategies for prevention and treatment of diseases such as cancer and genetic disorders caused by chromosome segregation errors. By taking an interdisciplinary approach, in which we combine cell and molecular biology, molecular genetics, cutting-edge microscopy, laser microsurgery, computer science and theoretical physics, my group explores how the mitotic spindle self-assembles and how forces that move the chromosomes are generated.

MEHANOBIOLOGIJA DIOBENOG VRETENA

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Naša su tijela izgrađena od oko 100 bilijuna pojedinačnih stanica, od kojih svaka sadrži 46 kromosoma koji nose naš genetski materijal. Ovaj golemi broj stanica potječe iz jedne stanice koja je proizvod oplodnje jajne stanice spermijem. Stoga je dioba stanica jedan od najvažnijih procesa u živom svijetu. Na početku diobe stanica gradi diobeno vreteno, fascinantno i složen mikrostroj napravljen od mikrotubula i proteina koji se na njima vežu. Mikrotubuli pomiču kromosome po stanici dok ih ne poravnaju po sredini vretena. Kada su svi kromosomi spremni, mikrotubuli razdvajaju sestre kromatide pomičući ih prema suprotnim polovima vretena. Središnje je pitanje u ovom području istraživanja kako diobeno vreteno uspijeva podijeliti kromosome u dva jednaka skupa bez pogrešaka. Razumijevanje kako stanice postižu pravilnu segregaciju kromosoma te kako je kontroliraju pomoći će pronalasku novih strategija za prevenciju i liječenje bolesti poput raka i genetskih poremećaja uzrokovanih pogreškama u segregaciji kromosoma. Uz pomoć interdisciplinarnog pristupa u kojem kombiniramo staničnu i molekularnu biologiju, molekularnu genetiku, vrhunsku mikroskopiju, lasersku mikrokirurgiju, računalnu znanost i teorijsku fiziku moja grupa istražuje kako se diobeno vreteno samoorganizira te kako stvara sile koje pokreću kromosome.

MATHEMATICAL MODELING OF STENTS

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A stent is a mesh that is placed in a narrowed or closed part of a blood vessel to keep the vessel open to restore normal blood flow. There are dozens of stents on the market with a very complex structure and of different sizes, geometries, and then mechanical properties. Testing and designing stents that will meet the prescribed mechanical constraints can be a very demanding task. However, there is a very efficient way for this task, and it is based on the use of a reliable and simple mathematical model. In this talk I will present the path to such a model, and emphasise opportunities it provides. Numerical approximation of the solution of the model allows us to build simulations that can lead us to different conclusions about the global properties of the stent without producing it. Moreover, the simulations allow us to go a step further and look for stents that are optimal in some sense. Thus, on the example of stents, I will approach the three cornerstones for new technologies: modeling, simulation and optimization.

MATEMATIČKO MODELIRANJE STENTOVA

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Stent je mrežica koja se postavlja u suženi ili zatvoreni dio krvne žile s ciljem otvaranja i uspostavljanja normalnog protoka krvi. Na tržištu postoje deseci stentova vrlo složene strukture, različitih veličina i geometrija, a onda i mehaničkih svojstava. Testiranje i dizajniranje stentova koji će zadovoljiti postavljene mehaničke uvjete može biti vrlo zahtjevan proces. Međutim, postoji vrlo efikasan način za ovaj zadatak, a baziran je na korištenju pouzdanog i jednostavnog matematičkog modela stenta. Put do jednog takvog modela predstaviti ću na ovom predavanju, te izložiti njegove dosege. Numerička aproksimacija rješenja modela omogućuje nam simulacije koje nas mogu dovesti do različitih zaključaka o globalnim svojstvima stenta bez da smo ga i efektivno proizveli. Štoviše, simulacije omogućuju da odemo i korak dalje te tražimo stentove optimalne po nekom svojstvu. Tako ću se na primjeru stentova dotaknuti tri temelja razvoja novih tehnologija: modeliranja, simulacija i optimizacije.

EVOLUTION OF GALAXIES THROUGH COSMIC TIME

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Understanding how galaxies form in the early universe and their subsequent evolution through cosmic time is a major goal of modern astrophysics. Panchromatic look-back sky surveys significantly advanced the field in the past decades, leading to a general understanding of galaxy evolution. In the talk I will go through the concepts and results of galaxy evolution studies.

RAZVOJ GALAKSIJA KROZ SVEMIRSKO VRIJEME

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Jedan od glavnih ciljeva moderne astrofizike je razumjeti kako se galaksije stvaraju te kako se razvijaju kroz svemirsku povijest. Višebojni pregledi neba značajno su unaprijedili to područje istraživanja u posljednjim desetljećima, što je dovelo do općeg razumijevanja razvoja galaksija. U predavanju ću proći kroz koncepte i rezultate proučavanja evolucije galaksija.

Usmena izlaganja
Oral presentations



BUTYRYLCHOLINESTERASE - STEPING OUT OF ACETYLCHOLINESTERASE'S SHADOW AS PSEUDOCATALYTIC BIOSCAVENGER OF NERVE AGENTS

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In 1940s cholinesterases became interest of study because of their role in nerve transmission, but it was soon shown that butyrylcholinesterase (BChE) is not so important because even with complete absence of BChE subjects were still alive and healthy. Lacking essential physiological function BChE hasn't been topic of further investigation in the same length as acetylcholinesterase (AChE). Then through years evidence had arisen indicating that BChE has certain role in the development of the symptomatology of Alzheimer's disease (AD). The hypothesis becomes more convincing when cholinesterase inhibitor therapies were shown to be effective in the improvement of main cognitive functions in patient with AD [1]. Except in AD therapy BChE is today associated with many different functions, like its involvement in metabolism of numerous drugs and poison esters even hunger hormone ghrelin, but highest interest was given to acknowledgment of BChE's input against nerve agents' toxicity. BChE placement in plasma gives it ability to act as stoichiometric bioscavenger for organophosphate (OP) before they pass blood brain barrier inhibiting native AChE, causing cholinergic crisis [2]. Due to its ability to act as a stoichiometric bioscavenger, BChE can be administered exogenously in the form of fresh-frozen plasma and thus may aid in recovery from OP poisoning as shown in the case of novichok poisoning [3]. Our hypothesis was that BChE in combination with its efficient reactivator could act as a pseudocatalytic scavenger as medical protection or therapy for detoxification, in this case from excess of OP. Through thorough research we identified efficient oximes based on "click chemistry" synthesis for BChE inhibited with OPs as sarin, cyclosarin, VX, and tabun. Interactions between inhibited BChE and oximes containing alkyne and azide building blocks with triazole linker were kinetically characterized in detail through *in vitro*, *ex vivo* and *in silico* experiments. For several oximes BChE reactivation potency was showed to be promising when compared to the standard oximes used in medical practice. Combination of BChE and oxime with high reactivation potency is appealing pseudocatalytic bioscavenger candidate for OP poisoning because once reactivated BChE is again able to bind OP from blood by which enabling further normal function of AChE.

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BUTIRILKOLINESTERAZA – BIJEG IZ ACETILKOLINESTERAZINE SJENE KAO PSEUDOKATALITIČKO BIOČISTILO ŽIVČANIH OTROVA

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U 1940-ima kolinesteraze postale su zanimljive za proučavanje zbog njihove uloge u prijenosu živčanog impulsa, ali za butirilkolinesterazu (BChE) se ubrzo pokazalo da nije toliko važna jer su čak i uz njezino potpuno odsustvo ispitane skupine bile žive i zdrave. Zbog nedostatka bitne fiziološke funkcije BChE nije bila tema daljnjih ispitivanja u istoj količini kao i acetilkolinesteraza (AChE). Ipak kroz godine su se pojavili dokazi koji ukazuju da BChE ima određenu ulogu u razvoju simptomatologije Alzheimerove bolesti (AD). Hipoteza je postala uvjerljivija kada se pokazalo da su terapije inhibitorima kolinesteraza učinkovite u poboljšanju glavnih kognitivnih funkcija u bolesnika s AD [1]. Osim u AD terapiji, BChE je danas povezana s mnogim različitim funkcijama, poput sudjelovanja u metabolizmu brojnih lijekova i estera otrova, pa čak i hormona gladi grelina, ali najveći interes bio je izazvan učinkom BChE protiv toksičnosti živčanih otrova. Prisutnost BChE u krvnoj plazmi omogućuje da djeluje kao stehiometrijsko biočistilo za organofosphate (OP) prije nego što prođu krvno-moždanu barijeru te inhibiraju nativnu AChE, uzrokujući kolinergičnu krizu [2]. S obzirom na sposobnost da djeluje kao stehiometrijsko biočistilo BChE se može primijeniti egzogeno u obliku svježije smrznute plazme i tako može pomoći pri oporavku kod trovanja OP-om kao što se pokazalo u slučaju trovanja novichokom [3]. Naša je hipoteza bila da BChE u kombinaciji sa učinkovitim reaktivatorom može djelovati i kao pseudokatalitički biočistač te omogućiti medicinsku zaštitu ili terapiju za detoksikaciju, u ovom slučaju od suviška OP. Temeljitim istraživanjem identificirali smo učinkovite reaktivatore, kao oksime temeljene na klik-kemijskoj sintezi, za BChE inhibiranu s OP-ima kao sarin, ciklosarin, VX i tabun. Interakcije između inhibiranih BChE i oksima koji sadrže alkinske i azidne blokove s triazolnim vezom detaljno su kinetički okarakterizirane *in vitro*, *ex vivo* i *in silico* eksperimentima. Reaktivacijska sposobnost nekoliko oksima pokazala se obećavajućom za BChE u usporedbi sa standardnim oksimima koji se koriste u medicinskoj praksi. Kombinacija BChE i oksima s visokim potencijalom reaktivacije privlačan je kandidat za pseudokatalitičko biočistilo u slučaju trovanja OP-om, budući da reaktivirani BChE ponovno je sposoban vezati OP iz krvi i tako osigurati daljnju normalnu funkciju AChE.

ZAHVALE

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ONE-DIMENSIONAL HYDROLOGICAL MODEL OF WATER CONTENT IN KARST SOIL

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Roughly 20-25% of the global population depends largely or entirely on groundwaters obtained from karst areas [1]. Before reaching the aquifer, water passes through soil, epikarst and vadose zone, where is subject to different processes that impact its properties. To better understand water distribution and transport through soil cover, one-dimensional hydrological model at a daily resolution was developed, which simulates water content at 10, 20, 30, 40 and 50 cm depth. The study site is located in central Spain (40°9'15"N, 5°4'20"W) and is characterized by red soil rich in iron minerals that is half meter thick and overlies metamorphosed carbonates [2]. A soil monitoring station was installed at the study site in 2018, with sensors measuring soil water content at depths of 10, 20, 30, 40 and 50 cm. As well, amount of precipitation, temperature, relative humidity, air pressure, wind velocity and direction are recorded every 10-minutes at a meteorological station installed at the study location. In order to develop a hydrological model, it is important to know properties of the media through which water moves. Thus, soil analyses were performed to determine basic soil properties. The development of the model follows an empirical approach which implies construction of mathematical equations based on input and output parameters [3]. Assumed initial soil water content, precipitation, actual evapotranspiration and infiltration are used as input parameters, while modelled soil water content represents the output parameter. Modelled results were compared to measured values and to values modelled in software HYDRUS 1D. Preliminary results show that there is substantial preferential flow on the site, which should be implemented in the later versions of the model. Correlation coefficients show a strong positive relationship between measured and modelled results. Once the model is completed, simulated soil water content and temperature records will be used as input parameters for CO₂ concentration and transport model.

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JEDNODIMENZIONALNI MODEL RASPODJELE VODE U TLU KRŠKOG PODRUČJA

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Otpriblike četvrtina svjetske populacije potpuno je ili djelomično ovisna o zalihama podzemne vode u krškim područjima [1]. Prije nego što dospije do vodonosnika, voda će se kretati kroz tlo, epikršku i vadoznu zonu, te će upravo procesi u navedenim zonama odrediti količinu i svojstva vode koja dospije do vodonosnika. U svrhu razumijevanja raspodjele i kretanja vode u zoni tla, izrađen je jednodimenzionalni dnevni hidrološki model, koji simulira udio vode u tlu na dubinama 10, 20, 30, 40, i 50 cm. Sustav za monitoring postavljen je na lokaciji u središnjoj Španjolskoj (40°9'15"N, 5°4'20"W). Na istraživanoj lokaciji matične stijene izgrađene su od metamorfoziranih karbonata na kojima je razvijeno karakteristično crveno tlo bogato željezovitim mineralima, često dubine preko pola metra [2]. U tlu na dubinama 10, 20, 30, 40 i 50 cm postavljeni su senzori za mjerenje volumnog udjela vode u tlu. Na udaljenosti <100 m od lokacije istraživanja nalazi se meteorološka stanica na kojoj se u 10-minutnim intervalima mjere oborine, temperatura, relativna vlažnost, tlak zraka, te brzina i smjer vjetra. Laboratorijske analize provedene su za određivanje osnovnih karakteristika tla. Razvoj modela slijediti će empirijski pristup, koji podrazumijeva konstrukciju matematičkih jednadžbi proizašlih iz ulaznih i izlaznih parametara [3]. Kao ulazni parametri korišteni su pretpostavljeni početni volumni udio vode u tlu, padaline, stvarna evapotranspiracija i infiltracija, dok izlazni parametar predstavlja modelirani volumni udio vode u tlu. Modelirani rezultati uspoređeni su s izmjerenim vrijednostima i vrijednostima modeliranima u programu HYDRUS 1D. Prvi rezultati pokazuju da na istraživanoj lokaciji postoji preferencijalni tok kojeg će biti potrebno uzeti u obzir prilikom usavršavanja modela. Koeficijenti korelacije pokazuju vrlo dobru do izvrsnu povezanost između izmjerenih i modeliranih rezultata. Nakon usavršavanja, modelirani volumni udio vode u tlu i temperaturni podaci koristiti će se kao ulazni parametri za izradu modela koncentracije i transporta CO₂.

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CHANGES IN THE MICROBIOME OF A SUCCESSFUL INVADER, THE SIGNAL CRAYFISH, ALONG ITS INVASION RANGE

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The microbiome has a key role in maintaining hosts' health and can have a significant impact on its susceptibility to disease [1]. Increasing evidence points out the role of microbiome in biological invasions, since microbes can affect a number of interactions between the host and the environment, and the ecology of the host [2]. On the other hand, the dispersal process and the characteristics of the novel environment may affect the structure and composition of a dispersing invader's microbiome, which may directly and indirectly affect their fitness and invasion success. Invasive species are one of the most significant causes of biodiversity loss, especially in the freshwater ecosystems [3]. Successful and fast dispersing invaders, such as the signal crayfish, have been shown to exhibit changes in population characteristics along the invasion range, indicating that individuals which accumulate on expanding edges (invasion fronts) may possess specific traits that facilitate dispersal and/or population establishment in a novel environment, which may ultimately affect species' future invasion success [4]. In this study we analyzed whether such differences occur in the composition of its microbiome, i.e. whether differences in microbiome occur due to population characteristics (invasion core vs. front), or due to microhabitat characteristics (upstream river section vs. downstream). We collected the samples of crayfish' exoskeletal biofilm, hemolymph, hepatopancreas and intestine from four locations along the Korana River, Croatia and analyzed the microbial composition via 16S rRNA sequencing. Our results reveal that alpha diversity differed significantly between the locations only in the case of hemolymph microbiome. Furthermore, hemolymph also showed significantly different beta diversity between upstream and downstream location, while hepatopancreas and intestine microbiomes differed significantly between core and front populations. Exoskeletal microbiome showed significantly different beta diversity between all locations. In total, our results suggest that the exoskeletal microbiome is shaped by both local environmental characteristic and crayfish density and population structure, while hemolymph microbiome differences may be driven by characteristics of upstream (rural) and downstream (industrial) river environments. Furthermore, hepatopancreas and intestine microbiomes may be determined by population density, since it affects feeding regime and crayfish condition, but may also be dependent upon environmental conditions (i.e. type of available food).

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PROMJENE U MIKROBIOMU USPJEŠNE INVAZIVNE STRANE VRSTE, SIGNALNOGA RAKA, DUŽ NJENOG INVAZIVNOG AREALA

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Mikrobiom ima ključnu ulogu u održavanju zdravlja domaćina i može imati značajan utjecaj na njegovu podložnost bolesti [1]. Sve više dokaza ukazuje na ulogu mikrobioma u biološkim invazijama, budući da mikrobi mogu utjecati na brojne interakcije između domaćina i okoliša te na ekologiju domaćina [2]. S druge strane, proces širenja i karakteristike novog okoliša mogu utjecati na strukturu i sastav mikrobioma invazivne vrste koja se širi, što može izravno i neizravno utjecati na njen fitnes i invazivni uspjeh. Invazivne strane vrste jedan su od najznačajnijih uzroka gubitka biološke raznolikosti, posebice u slatkovodnim ekosustavima [3]. Uspješne invazivne strane vrste, poput signalnoga raka, pokazuju promjene u karakteristikama populacije duž invazivnog areala, što ukazuje da jedinke koje se akumuliraju na rubovima širenja (invazijskim frontama) mogu posjedovati specifične osobine koje olakšavaju širenje i/ili uspostavljanje populacije u novom okolišu, što u konačnici može utjecati na budući invazivni uspjeh vrste [4]. U ovom smo istraživanju analizirali postoje li takve razlike u sastavu mikrobioma vrste, tj. javljaju li se razlike u mikrobiomu zbog karakteristika populacije (invazijsko središte vs. fronta) ili zbog karakteristika mikrostaništa (uzvodni dio rijeke vs. nizvodni). Prikupili smo uzorke egzoskeletnog biofilma, hemolimfe, hepatopankreasa i crijeva rakova sa četiri lokacije duž rijeke Korane u Hrvatskoj i analizirali mikrobni sastav 16S rRNA sekvenciranjem. Naši rezultati otkrivaju da se alfa raznolikost značajno razlikovala između različitih lokacija samo u slučaju mikrobioma hemolimfe. Nadalje, hemolimfa je također pokazala značajno različitu beta raznolikost između uzvodne i nizvodne lokacije, dok su se mikrobiomi hepatopankreasa i crijeva značajno razlikovali između populacija invazijskog središta i fronte. Mikrobiom egzoskeleta pokazao je značajno različitu beta raznolikost među svim lokacijama. Naši rezultati sugeriraju da je egzoskeletni mikrobiom oblikovan i lokalnim okolišnim karakteristikama i gustoćom rakova/strukturom populacije, dok su razlike u mikrobiomu hemolimfe vjerojatnije pod utjecajem karakteristika uzvodnog (ruralnog) i nizvodnog (industrijskog) okoliša rijeke. Nadalje, mikrobiomi hepatopankreasa i crijeva mogu biti određeni gustoćom populacije, budući da ona utječe na režim hranjenja i fiziološko stanje rakova, ali mogu ovisiti i o uvjetima okoliša (tj. tipu dostupne hrane).

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UNIQUENESS AND REGULARITY RESULTS FOR FLUID-RIGID BODY INTERACTION

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We study a nonlinear moving boundary fluid-structure interaction problem where the fluid flow is governed by 3D Navier-Stokes equations, and the structure is a rigid body described by a system of ordinary differential equations called Euler equations for the rigid body.

The fluid-rigid body system has been extensively studied in the last twenty years and some aspects of the well-posedness theory are now well established. The existence of the unique local-in-time (or small data) solution is proven in [2]. On the other hand, it is known that a weak solution of Leray-Hopf type exists and is global in time or exists until the moment of contact between the boundary of the container and the rigid body (see e.g. [1]).

The question of the uniqueness of weak solution is still largely open. Even for the classical case of the 3D Navier-Stokes equations, the uniqueness of the Leray-Hopf weak solution is an outstanding open problem (see e.g. [4]). However, there are classical results of weak-strong uniqueness type (see e.g. [4]) which state that the strong solution (defined in an appropriate way) is unique in the larger class of weak solutions. For the Navier-Stokes equations the weak solutions that satisfy Serrin's conditions are regular. We prove a generalization of the weak-strong uniqueness and regularity results for the Navier-Stokes equations to the fluid-rigid body system.

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REZULTATI JEDINSTVENOSTI I REGULARNOSTI ZA PROBLEME INTERAKCIJE FLUIDA I KRUTOG TIJELA

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Proučavamo nelinearni problem interakcije fluida i strukture u prostoru. Tok fluida je dan Navier-Stokesovim jednadžbama, dok je struktura kruto tijelo opisano sustavom običnih diferencijalnih jednadžbi poznatim kao Eulerove jednadžbe krutog tijela.

Sustavi fluida i strukture predmet su intenzivnog istraživanja u posljednjih dvadeset godina. U [2] je pokazano postojanje jedinstvenog jakog rješenja, ali lokalno po vremenu ili uz male podatke. Također, poznato je da postoji slabo rješenje koje je globalno u vremenu ili postoji do trenutka kontakta s granicom spremnika i krutog tijela (vidi npr. [1]).

Pitanje jedinstvenosti slabog rješenja još uvijek je otvoreno. Čak i za klasični slučaj 3D Navier-Stokesovih jednadžbi, jedinstvenost slabog rješenja istaknut je otvoren problem. Pokazujemo da je slabo rješenje koje dodatno zadovoljava Prodi-Serrinov uvjet jedinstveno u većoj klasi slabih rješenja te da je takvo rješenje glatko, što je poopćenje poznatih rezultata jedinstvenosti i regularnosti za Navier-Stokesove jednadžbe (vidi npr. [4]).

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ALPHA-ACID GLYCOPROTEIN GLYCOSYLATION PATTERN EFFECT ON THE BINDING OF DRUGS DIPYRIDAMOLE AND IMATINIB

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Nowadays, plasma protein binding is increasingly being investigated. There are several plasma proteins in the human body, such as albumin (HAS), α 1-acid glycoprotein (AGP), lipoprotein, transferrin, etc., to which certain drugs bind. Binding of drugs to plasma proteins can influence pharmacokinetics and pharmacodynamics of the drugs. AGP is an acute phase protein and its plasma concentration can be significantly increased in various diseases or traumas. Changes in AGP concentration can potentially affect the free fraction of drugs in plasma, resulting in their different pharmacological action. Unbound fraction or free drug is usually the one that is available for activity or diffusion into the surrounding tissues. Therefore, only the free fraction of the drug is considered as active form, in accordance with "Free Drug Principle". Drug binding to AGP can be altered in a number of pathological and physiological conditions as a result of a change in the glycosylation pattern. Change in concentration of AGP, as well as its high degree of natural structural glycan variability, causes changes in drug binding, particularly in pathological conditions. These changes have been observed in patients with cancer (breast, colon, prostate etc.), depression, infection, renal failure, etc. These examples clearly show the importance of the glycan structure of AGP as one of the major drug transporters in a number of pathophysiological conditions. In this work, we used experimental methods such as fluorescence spectroscopy, mass spectrometry and microscale thermophoresis, to determine the effect and binding constant of AGP glycosylation on the binding of selected drugs and hence predict its impact on pharmacokinetics.

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ISPITIVANJE UTJECAJA GLIKOZILACIJSKOGA OBRASCA ALFA-KISELOG GLIKOPROTEINA NA VEZANJE LIJEKOVA DIPIRIDAMOLA I IMATINIBA

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U današnje vrijeme sve se više istražuje vezanje na proteine plazme. U ljudskom tijelu postoji više proteina plazme poput albumina (HSA), alfa-kiselog glikoproteina (AGP), lipoproteina, transferina odgovornih za vezanje lijekova u cirkulaciji. Vezanje lijekova na proteine plazme važan je korak za sudbinu lijeka zbog utjecaja na njegovu farmakokinetiku i farmakodinamiku. AGP je protein akutne faze upale i njegova koncentracija u plazmi može se značajno povećati kod različitih bolesti ili trauma. Promjene u koncentraciji AGP-a mogu potencijalno utjecati na slobodni udio lijekova u plazmi rezultirajući time na njihovo drugačije farmakološko djelovanje. Nevezana frakcija ili slobodni udio lijeka je onaj za koji se smatra da je raspoloživ za aktivnost ili difuziju u okolna tkiva te se stoga samo slobodna frakcija lijeka smatra aktivnim oblikom, u skladu s tzv. "principom slobodnog lijeka". Uslijed promjene koncentracije AGP-a, omjera njegovih genetskih formi kao i njegovog visokog stupnja prirodne strukturalne varijabilnosti dolazi do promjene vezivanja lijekova za AGP, posebice u patološkim stanjima. Vezanje lijekova za AGP može biti promijenjeno u brojnim patološkim i fiziološkim stanjima kao rezultat promjene u glikozilacijskom uzorku. Promjene u glikozilacijskom obrascu zamijećene su kod pacijenata s brojnim vrstama karcinoma (dojke, kolona, prostate), depresijom, infekcijom, insuficijencijom bubrega itd. Navedeni primjeri jasno pokazuju važnost promjene strukture glikanskog dijela AGP-a kao jednog od glavnih prijenosnika lijekova kod brojnih patofizioloških stanja. U ovome radu koristit će se metode kao što su fluorescencijska spektroskopija, masena spektrometrija i mikroskalarna termoforeza kako bi se odredila konstanta vezanja i utjecaj glikozilacije AGP-a prilikom vezanje odabranih lijekova i posljedično predvidio utjecaj te promjene na terapiju.

ZAHVALE

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DEFECT CREATION IN GRAPHENE WITH SWIFT HEAVY ION IRRADIATION – MD APPROACH

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Classical molecular dynamics (MD) simulation is an established technique for studying changes in graphene structure in picosecond (10^{-12} s) time range. We have applied this method for single layer graphene placed on amorphous SiO_2 substrate irradiated initially with 23 MeV iodine ions. We found the average defect size as well as the average efficiency for formation of defects scales linearly with changing the ion energy, as long it is over the threshold value for defect production. Additionally, we observed individual defect types, their sizes and shapes. We put special emphasis on point defects. Here the trend is not that simple as some defect types preferred specific energy of projectile as well as some specific energy range.



STVARANJE DEFEKATA U GRAFENU S BRZIM TEŠKIM IONIMA – MD PRISTUP

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Simulacije klasične molekularne dinamike (MD) priznate su tehnike za proučavanje promjena u strukturi grafena u vremenskom području pikosekunde (10^{-12} s). Metodu smo primijenili za jednoslojni grafen postavljen na podlogu amornog SiO_2 ozračen ionima joda od 23 MeV-a. Uočili smo da se prosječna veličina defekta, kao i prosječna učinkovitost stvaranja istih skalira linearno s promjenom energije iona, pod uvjetom da je ona iznad granične vrijednosti za nastanak defekta. Pored toga, promatrali smo pojedine vrste defekata, njihove veličine i oblike. Poseban naglasak stavili smo na točkaste defekte. Ovdje trend nije tako jednostavan jer su neke vrste defekata preferirale specifičnu energiju projektila kao i neki specifični raspon energije.



EFFICIENT MECHANOCHEMICAL SYNTHESIS OF GRAPHENE QUANTUM DOTS

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Graphene quantum dots (GQDs) are a latest zero-dimensional (0D) member of the carbon family, consist of single to few layers of graphene sheets with lateral dimensions of <100 nm. GQDs have attracted significant attention due to its intriguing physicochemical properties due to the quantum confinement and edge effects, which makes it a good material for potential applications in bioimaging, sensing, solar cells, photovoltaic devices, photocatalysis and white-light-emitting diodes [1].

Various top-down and bottom-up preparation methods of GQDs have been reported until now, even though limited to the small-scale preparation of GQDs and necessity for the use of strong corrosive acids or organic solvents, harsh synthetic processes and long reaction time.

However, mechanochemistry is becoming more widespread as a technique because it can promote solid state reactions, even on a large scale, quickly and quantitatively [2].

Herein we describe several different mechanochemical routes for a single and few layer GQDs fabrication.

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UČINKOVITA MEHANOKEMIJSKA SINTEZA GRAFENSKIH KVANTNIH TOČKA

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Grafenske kvantne točke (GKT) najnoviji su članovi obitelji OD ugljikovih nanostruktura. GKT sastoje se od jednog do nekoliko slojeva grafenskih plahta dimenzija <100 nm. GKT privukle su značajnu pozornost zbog svojih intrigantnih fizikalno-kemijskih svojstava uzrokovanih efektnom prostornog ograničenja i rubnih učinaka, što ih čini dobrim materijalom za potencijalnu primjenu u sensorima, bio-oslikavanju, solarnim ćelijama, fotonaponskim ćelijama, fotokatalizi i diodama koje emitiraju bijelu svjetlost [1].

Postoje dva generalna pristupa sintezi GKT: pristup odozgo prema dolje i odozdo prema gore. Iako su dosada zabilježeni različiti načini sinteze GKT, ograničeni su nužnom upotrebom jakih korozivnih kiselina ili organskih otapala, korištenjem zahtjevnih sintetskim procesa te dugotrajnošću reakcija uz mogućnost proizvodnje malih količina GKT.

Mehanokemijska sinteza postaje sve raširenija tehnika pošto može kvantitativno potaknuti i ubrzati reakcije u čvrstom stanju, čak i na većim skalama [2].

U ovom radu opisano je nekoliko različitih načina mehanokemijske sinteze jednoslojnih i višeslojnih GKT.

ZAHVALE

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LOCAL RESIDENTS' PERCEPTION TOWARDS TOURISM POTENTIALS AND ECOTOURISM DEVELOPMENT IN PROTECTED NATURAL AREAS IN THE SOUTH BANAT REGION

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Ecotourism is a form of tourism, increasingly developed within protected natural areas due to its ability to minimize negative impacts on the environment and contribute to the preservation and improvement of natural values [1]. In addition to natural potentials, scientific literature emphasizes the importance of the involvement of the local community in ecotourism development, through which multiple socio-economic benefits for the local population are obtained [2, 3]. There are 3 protected natural areas, located very close to each other in the South Banat region - Special Nature Reserve "Deliblato Sands", Special Nature Reserve "Kraljevac" and the Landscape of Outstanding Features "Karas-Nera". They are protected thanks to their specific morphological features, rich biodiversity, rare species and exceptional landscape values [4]. This research examines the attitudes of the inhabitants of the five municipalities in the South Banat region, on whose territories the borders of SNR "Deliblato Sands", SNR "Kraljevac" and LOF "Karas-Nera" are located, about the development of ecotourism, its impact on the environment and community and readiness of local population for direct involvement in ecotourism development. The respondents' attitudes were collected through an online survey, and the results of the research were presented by descriptive analysis. It was determined that the inhabitants of municipalities in the South Banat have a positive attitude towards the development of ecotourism and a proactive approach to direct involvement in further ecotourism development, especially on the territory of Special Nature Reserve "Deliblato Sands".

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PERCEPCIJA LOKALNIH STANOVNIKA O TURISTIČKIM POTENCIJALIMA ZAŠTIĆENIH PRIRODNIH PODRUČJA I RAZVOJU EKOTURIZMA U REGIJI JUŽNI BANAT

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Ekoturizam je oblik turizma, koji se sve više razvija u zaštićenim prirodnim područjima zbog svoje sposobnosti da umanjuje negativne utjecaje na okoliš i doprinese očuvanju i poboljšanju prirodnih vrijednosti [1]. Uz prirodne potencijale, znanstvena literatura naglašava važnost uključivanja lokalne zajednice u razvoj ekoturizma, putem kojeg se postižu višestruke društveno-ekonomske koristi za lokalno stanovništvo [2, 3]. Postoje 3 zaštićena prirodna područja koja se nalaze vrlo blizu jedno drugom u regiji Južni Banat - Posebni rezervat prirode „Deliblatska pješčara“, Posebni rezervat prirode „Kraljevac“ i Pejzaž izvanrednih karakteristika „Karaš-Nera“. Zaštićeni su zahvaljujući svojim specifičnim morfološkim značajkama, bogatoj biološkoj raznolikosti, rijetkim vrstama i iznimnim krajobraznim vrijednostima [4]. Ovo istraživanje ispituje stavove stanovnika pet općina u južnobanatskoj regiji, na čijim se teritorijama nalaze granice PRP „Deliblatska pješčara“, PRP „Kraljevac“ i PIK „Karaš-Nera“, o razvoju ekoturizma, njegovom utjecaju na okoliš i zajednicu i spremnost lokalnog stanovništva za izravno sudjelovanje u razvoju ekoturizma. Stavovi ispitanika prikupljeni su internetskom anketom, a rezultati istraživanja predstavljeni su deskriptivnom analizom. Utvrđeno je da stanovnici općina u Južnom Banatu imaju pozitivan stav prema razvoju ekoturizma i proaktivan pristup izravnom uključivanju u daljnji razvoj ekoturizma, posebno na teritoriju Posebnog rezervata prirode „Deliblatska pješčara“.

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SHINING A LIGHT ON CELL DIVISION USING OPTOGENETICS

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Cell division is a fundamental process in all living organisms during which the genetic material is equally divided into two newly formed daughter cells. To ensure accurate segregation of chromosomes, the cell forms the mitotic spindle—a dynamic micromachine assembled of microtubules and a variety of associated proteins. To study intracellular processes, researchers typically deplete or inhibit a candidate protein and learn about the role of the protein from the resulting phenotype. Over the last decade, RNA interference has been the main tool for revealing the role of spindle proteins. However, the effects of this method are evident only after a longer time period, allowing the cells to compensate for the missing protein, which makes it difficult to interpret the results. Optogenetics is a novel technology that enables fast, reversible, and precise control of protein activity by utilization of light. It implements different genetic modifications of targeted proteins in order to achieve light-induced control of protein function [1].

We designed an optogenetic strategy for rapid and reversible translocation of protein PRC1 from the mitotic spindle to the cell membrane using the blue light of fluorescent microscope. PRC1 protein crosslinks the bundles of microtubules called bridging fibers, which overlap with sister kinetochore fibers that are attached to kinetochores on the chromosome. Upon the optogenetic PRC1 removal, the bridging fibers partially disassemble leading to the loss of chromosome precise alignment in the spindle and the appearance of the lagging chromosomes during the segregation. Tracking of the growing tips of microtubules revealed that after optogenetic PRC1 removal, the overlap regions of bridging microtubules were longer, due to the loss of proteins that regulate microtubule length from the bridging fiber. These results led to a conclusion that PRC1-mediated crosslinking of bridging microtubules and recruitment of associated proteins promote chromosome alignment by overlap length-dependent forces transmitted to the associated kinetochores fibers [2].

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OSVJETLJAVANJE STANIČNE DIOBE KORIŠTENJEM OPTOGENETIKE

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Stanična dioba je temeljni proces svakog živog bića tijekom koje se genetski materijal jednako rasporedi u dvije novonastale stanice kćeri. Da bi osigurala točnu segregaciju kromosoma, stanica stvara diobeno vreteno- dinamični mikrostroj sastavljen od mikrotubula i raznih dodatnih proteina. Unutarstanične procese možemo proučavati tako da inhibiramo ili utišamo ekspresiju proteina od interesa te iz nastalog fenotipa zaključimo koja je njegova uloga. Tijekom zadnjeg desetljeća metoda RNA interferencije se najčešće koristi za proučavanje uloge proteina diobenog vretena. Ali, efekti te metode su vidljivi tek nakon duljeg vremena što omogućuje stanici da se prilagodi i kompenzira ciljani protein što otežava interpretaciju rezultata. Optogenetika je nova tehnika koja omogućuje brzu, reverzibilnu i preciznu kontrolu aktivnosti proteina korištenjem svjetla određene valne duljine. Koriste se genetičke modifikacije ciljanog proteina da bi se postigla kontrola njegove funkcije inducirana svjetlošću [1].

U ovom radu dizajnirali smo optogenetičku strategiju za brzo i reverzibilno premještanje proteina PRC1 s diobenog vretena na staničnu membranu koristeći plavo svjetlo fluorescencijskog mikroskopa. Protein PRC1 povezuje snopove mikrotubula zvanih premošćujući mikrotubuli. Oni rade preklap s kinetohornim vlaknima mikrotubula koja su vezana na sestrinske kinetohore kromosoma. Nakon optogenetičkog uklanjanja proteina PRC1, premošćujuća vlakna su se djelomično rastavila te je došlo do gubitka preciznog poravnanja kromosoma u diobenom vretenu te do pojave zaostajućih kromosoma tijekom segregacije. Promatranjem rastućih krajeva mikrotubula, utvrđeno je da je optogenetičko uklanjanje proteina PRC1 uzrokovalo produljenje premošćujućih mikrotubula jer je došlo do gubitka proteina koji reguliraju duljinu mikrotubula. Došli smo do zaključka da PRC1 povezuje premošćujuće mikrotubule i regrutira dodatne proteine što zajedno potiče poravnanje kromosoma u diobenom vretenu preko sila koje premošćujući mikrotubuli prenose na kinetohorna vlakna [2].

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ROLE OF TYROSYL DNA-PHOSPHODIESTERASE 1 IN THE REPAIR OF THE DNA-PROTEIN CROSSLINKS *IN VIVO*

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Tyrosyl DNA-phosphodiesterase 1 (TDP1) is a protein that primarily repairs trapped topoisomerase 1 on the DNA backbone. Topoisomerase 1 (TOPO1) is an essential enzyme that relaxes the DNA helix during replication and transcription by introducing a temporary single-strand break in DNA. This reaction is reversible: TOPO1 introduces a single-strand break and afterwards dissolves from the DNA backbone followed by repair of the single-strand break. Due to various endogenous and exogenous factors acting on the cell, TOPO1 can remain irreversibly covalently linked to the DNA backbone thus interfering with all DNA transactions. For this reason, cells have TDP1 protein, which through its phosphodiesterase activity destroys the covalent bond formed between tyrosines in TOPO1 protein and 5' phosphates on DNA [1]. Lack of TDP1 protein activity leads to spinocerebellar ataxia with axonal neuropathy (SCAN1 syndrome) [2]. A large number of drugs for the tumor treatments are aimed at inhibiting the activity of TOPO1 enzyme and/or the formation of TOPO1-DNA irreversible covalent bond. Therefore, understanding of this mechanism is crucial for further development of chemotherapeutics [3]. In this study, we tried to answer the questions whether TDP1 removes TOPO1 alone or with the help of other repair factors, and whether TDP1 can remove other proteins that are also cross-linked to the DNA backbone. To answer these questions, we created TDP1 deficient zebrafish models using CRISPR/Cas methods. In one cell stage embryos, we introduced a gRNA-Cas9 complex that specifically cleaves the DNA sequence for TDP1 protein which results in introduction of premature STOP codon in the beginning of the coding sequence. In order to generate catalytically inactive TDP1 protein, we have introduced C23572G i A23573C (H501A) mutations using CRISPR/Cas9 system and homologous recombination which incorporated repair template carrying target mutation in the zebrafish genome. In TDP1 deficient embryos, we have measured the presence and repair of TOPO1-DNA crosslinks after isolation with guanidine chloride (6 M) followed by detection TOPO1-DNA crosslink with TOPO1-DNA crosslink specific antibody and *slot blot* method [4]. Using the CRISPR/Cas9 system and RNA silencing, we are performing corresponding measurements on human cells. We have shown that an increase in the concentration of camptothecin causes the accumulation of TOPO1-DNA complex. The phosphodiesterase activity of TDP1 protein is crucial for the repair of the TOPO1–DNA complex induced by the camptothecin, how this repair takes place and which factors are crucial will be shown by ongoing research.

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ULOGA TIROZILSKE DNA-FOSFODIESTERAZE 1 U POPRAVKU KRIŽNO VEZANIH PROTEINA NA OKOSNICI DNA *IN VIVO*

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Tirozilska DNA-fosfodiesteraza 1 (TDP1) je enzim koji popravljiva križno vezanu topoizomerazu 1 na okosnici DNA. Topoizomeraza 1 (TOPO1) je esencijalni enzim koji relaksira uzvojnica DNA prilikom replikacije i transkripcije uvodeći privremeni jednolančani lom u DNA. Ova reakcija je reverzibilna: TOPO1 uvodi jednolančani lom, zatim se hidrolizom odvoji od DNA nakon čega slijedi popravak jednolančanog loma. Uslijed različitih endogenih i egzogenih čimbenika koji djeluju na stanicu, TOPO1 može ostati ireverzibilno kovalentno vezana na lancu DNA te time ometa sve transakcije koje se odvijaju na DNA. Zbog tog razloga u stanicama se nalazi protein TDP1 koji svojom fosfodiesteraznom aktivnošću razara kovalentnu vezu nastalu između tirozina u TOPO1 i 5' fosfata na DNA[1]. Katalitička mutacija proteina TDP1 uzrokuje spinocerebelarne ataksije s aksonskom neuropatijom (sindrom SCAN1) [2]. Veliki broj lijekova za liječenje tumora upravo je usmjeren na inhibiciju aktivnosti enzima TOPO1 i/ili na stvaranje ireverzibilne kovalentne veze TOPO1-DNA. Stoga je razumijevanje ovog mehanizma ključno za daljnji razvoj kemoterapeutika [3]. U ovom radu odgovorit ćemo na pitanja uklanja li TDP1 TOPO1 sam ili uz pomoć drugih čimbenika DNA popravka te može li TDP1 ukloniti i druge proteine koji su također križno vezani na okosnici DNA. U tu svrhu stvorili smo modele zebrice s deficijencijom proteina TDP1 koristeći CRISPR/Cas sustave. U jednostanične embrije unijeli smo kompleks gRNA-Cas9 koji specifično cijepa sekvencu DNA za protein TDP1 te smo tako uveli preuranjeni STOP-kodon u početak kodirajuće sekvence. Za stvaranje katalitički neaktivnog proteina TDP1 uveli smo mutacije C23572G i A23573C (H501A) pomoću metode CRISPR/Cas9 i homologne rekombinacije kojom se u genom uvodi kalup popravka sa željenom mutacijom. U embrijima s deficijencijom proteina TDP1 mjerili smo prisutnost i popravak kompleksa TOPO1–DNA nakon izolacije pomoću gvanidin-klorida (6 M), te detekcije kovalentnog kompleksa TOPO1–DNA s antitijelom koje specifično prepoznaje križnu vezu TOPO1-DNA pomoću metode *slot blot* [4]. Uz pomoć sustava CRISPR/Cas9 i RNA-utišavanja, paralelna mjerenja radimo na ljudskim stanicama. Pokazali smo da povećanje koncentracije kamptotecina uzrokuje akumulaciju TOPO1–DNA kompleksa. Fosfodiesterazna aktivnost TDP1 proteina ključna je za popravak TOPO1–DNA križnog kompleksa induciranog kemoterapeutikom kamptotecinom, kako se ovaj popravak odvija i koji faktori su ključni pokazat će mjerenja koja su u tijeku.

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3-GROUPS AND HIGHER GAUGE THEORY UNIFICATION OF ALL INTERACTIONS

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We will give a step-by-step overview of the gauge theory construction based on a notion of a 3-group. After we introduce 3-groups in general, we will focus on the relevant example of a 3-group which describes the Standard Model and Einstein-Cartan gravity at the classical level. The 3-group structure features a novel gauge group, intimately connected to the fermion and scalar sectors of the Standard Model. This structure could potentially provide a new insight into the matter sector of the theory, and open new avenues for research on unification of all interactions and matter. Based on the work presented in [1], [2], [3] and [4].

ACKNOWLEDGMENTS

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3-GRUPE I KATEGORIJSKA UNIFIKACIJA INTERAKCIJA

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U ovom predavanju daćemo pregled konstrukcije gejdž teorije zasnovan na kategorijskom uopštenju pojma grupe, 3-grupi. Nakon što uvedemo pojam 3-grupe, fokusiraćemo se relevantan primer koji odgovara klasičnoj teoriji koja opisuje sva fizička polja prisutna u Standardnom Modelu u interakciji sa Ajnštajn-Kartanovom gravitacijom. Struktura 3-grupe daje novu gejdž grupu koja odgovara skalarnim i fermionskim poljima prisutnim u Standardnom Modelu. Ovo je nov i neočekivan rezultat, koji ima potencijal da otvori novi pravac istraživanja i ponudi objašnjenje za strukturu sektora materije prisutne u Standardnom Modelu, kao i izvan. Istraživanje je prezentovano u radovima [1], [2], [3] i [4].

ZAHVALE

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DYNAMICS OF SEDIMENT MICROBIAL COMMUNITIES IN A DECLINING *Cymodocea nodosa* MEADOW

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Seagrass meadow sediments contain diverse and abundant microbial communities [1-3]. Although the diversity of these microorganisms has been described little is known about their response to a meadow decline. Next-generation amplicon sequencing of the V4 16S rRNA region was performed to determine the diversity and dynamics of bacterial and archaeal microbial communities inhabiting sediments of a declining *Cymodocea nodosa* meadow. Sampling was performed in surface sediments from Saline Bay located at the eastern coast of the northern Adriatic Sea (45°7'5" N, 13°37'20" E) from July 2017 to October 2018 at monthly intervals. For comparison, samples from a nearby non-vegetated sediment were also analyzed. Communities differed primarily by sediment depth and secondly by the presence or absence of seagrass vegetation. Although *C. nodosa* declined to a point where almost no leaves were present no notable temporal community changes were observed. Taxonomic analysis showed the dominance of bacterial sequences over archaeal. The most abundant detected archaeal taxa were *Nanoarchaeota*, *Thermoplasmatota*, *Crenarchaeota* and *Asgardarchaeota*, while *Bacteria* were mainly comprised of *Desulfobacterota*, *Proteobacteria*, *Bacteroidota* and *Chloroflexi*. Our results indicate that changing environmental conditions caused by a decline of a seagrass meadow did not have a strong effect on the microbial community composition. The lack of compositional change suggests a response by altering community activity as a mechanism of adaptation to changing conditions.

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DINAMIKA MIKROBNIH ZAJEDNICA SEDIMENTA U PROPADAJUĆOJ LIVADI VRSTE *Cymodocea nodosa*

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Sedimenti livada morskih cvjetnica sadrže brojne i raznolike mikrobne zajednice [1-3]. Iako je raznolikost ovih mikroorganizama opisana saznanja o njihovom odgovoru na propadanje livade su nedovoljna. Sekvenciranjem nove generacije regije V4 gena za 16S rRNA određena je raznolikost i dinamika mikrobnih zajednica bakterija i arheja u sedimentu propadajuće livade vrste *Cymodocea nodosa*. Uzorkovanje površinskog sedimenta provedeno je u uvali Saline smještenoj na istočnoj obali sjevernog dijela Jadranskog mora (45°7'5" N, 13°37'20" E) mjesečno od srpnja 2017. do listopada 2018. Za usporedbu, analizirani su i uzorci obližnjeg nevegetiranog sedimenta. Zajednice su se prvenstveno razlikovale s obzirom na dubinu uzorkovanog sedimenta i prisutnost morske cvjetnice. Iako morska cvjetnica vrste *Cymodocea nodosa* degradirala do stupnja nepostojanja lišća, vremenska promjena zajednice u sedimentu nije uočena. Taksonomskom analizom utvrđena je dominacija nukleotidnih sljedova bakterija u odnosu na arheje. *Nanoarchaeota*, *Thermoplasmata*, *Crenarchaeota* i *Asgardarchaeota* bile su dominantne detektirane skupine arheja, dok su koljeno *Bacteria* uglavnom sačinjavali sljedovi klasificirani u skupine *Desulfobacterota*, *Proteobacteria*, *Bacteroidota* i *Chloroflexi*. Zaključno, promjena okolišnih uvjeta uslijed propadanja livade morske cvjetnice nije imala snažan utjecaj na sastav mikrobne zajednice sedimenta. Nedostatak promjene sastava zajednice implicira promjenu aktivnosti mikroorganizama kao mogući mehanizam prilagodbe na promijenjene uvjete okoliša.

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ANTIPLASMODIAL ACTIVITY OF NOVEL GENERATION OF TRIAZOLE-TYPE HARMICINES

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According to the World Health Organization, malaria, a neglected tropical disease caused by the protozoal parasite *Plasmodium*, was responsible for more than 400 000 deaths in 2019 [1]. Due to the spread of a multidrug-resistant malaria parasite, the development of novel, more effective antimalarials is necessary. Previously, we covalently linked harmine and cinnamic acid derivatives (CADs), compounds with confirmed antimalarial activity, *via* triazole linker into hybrid molecules (harmicines) [2]. The promising antimalarial activity of the prepared hybrids encouraged us to design, synthesize and evaluate the biological activity of a new generation of harmicines differing in the position of substituents at the β -carboline core (Figure 1.). The antimalarial activity of the novel hybrids was evaluated *in vitro* against the erythrocytic stage of the *Plasmodium* life cycle. The hybrids based on 6-substituted β -carboline (**1a-e**) showed better antiplasmodial activity compared to harmine. Among them, *m*-Br-substituted derivative (**1c**) exerted the best antimalarial activity with IC₅₀ value in the low submicromolar range. N9-substituted β -carboline alcohols (**2a-e**) have shown weaker activity compared to harmine. The exception is *m*-Br-substituted derivative (**2c**) which is slightly more active than harmine, but less than its analog at position 6 of the β -carboline core, leading to the conclusion that introduction of the hydroxy group at the position 3 of the β -carboline core resulted in decreased antiplasmodial activity.

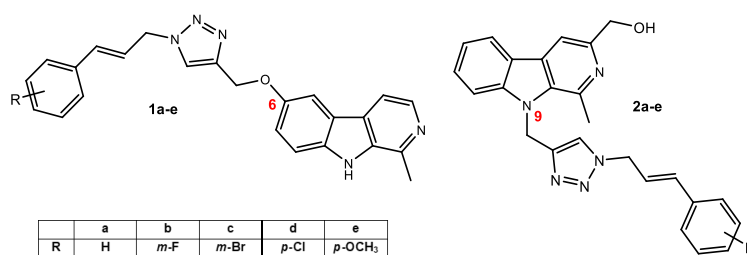


Figure 1. Novel generation of the triazole-type harmicines.

ACKNOWLEDGMENTS

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ANTIPLAZMODIJSKO DJELOVANJE HARMICINA TRIAZOLSKOG TIPA NOVE GENERACIJE

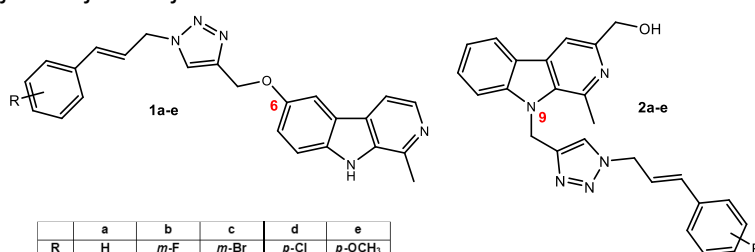
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Prema podacima Svjetske zdravstvene organizacije, malarija, tropska bolest uzrokovana protozom roda *Plasmodium*, bila je odgovorna za više od 400 000 smrtnih slučajeva u 2019. godini [1]. Zbog pojave rezistentnih sojeva plazmodija, razvoj novih i učinkovitijih antimalarika od posebnog je značaja. Prethodno smo, korištenjem triazolskog prstena kao poveznice, kovalentno povezali harmin i derivate cimetine kiseline, molekule s antimalarijskim djelovanjem, u hibridne spojeve (harmicine). Obećavajuće antimalarijsko djelovanje pripremljenih spojeva potaknulo nas je na dizajniranje, sintezu i ispitivanje biološkog djelovanja nove generacije harmicina koji se razlikuju po položaju supstituenata na β -karbolinskom prstenu (Slika 1.). Antimalarijsko djelovanje novih hibrida ispitano je *in vitro* na eritrocitnoj fazi životnog ciklusa plazmodija. C6-supstituirani derivati β -karbolina (**1a-e**) pokazali su bolje antiplazmodijsko djelovanje u usporedbi s harminom. Među njima, najbolje djelovanje pokazao je *m*-Br-supstituirani derivat (**1c**), s IC_{50} vrijednosti u submikromolarnom području. N9-supstituirani β -karbolinski alkoholi (**2a-e**) pokazali su slabije djelovanje u odnosu na harmin. Iznimka je *m*-Br-supstituirani derivat (**2c**) koji je aktivniji od harmina, ali manje od analoga u položaju 6 β -karbolinskog prstena. Može se zaključiti da je uvođenje hidroksilne skupine na β -karbolinski prsten rezultiralo slabijim antimalarijskim djelovanjem hibrida.



Slika 1. Nova generacija harmicina triazolskog tipa.

ZAHVALE

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SPATIAL MODELING OF MOSQUITOES (Culicidae) POPULATIONS USING MATRIX POPULATION MODELS

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Mosquitoes are vectors of numerous zoonotic diseases, indirectly causing more than 700 000 deaths annually across the world. [1] With climate change mosquito distribution is changing as well. With mosquitos' ranges expanding, there is a danger of emergence of novel zoonotic diseases. Therefore, prognostic systems that are able to locate mosquito swarming areas, migration and abundance, are of great research importance. [2] Good stage and age structured models already exist, however they are not spatial. [3] Until recently hardware limitations prevented creation of generalized spatial population models. With parallel processing using general purpose graphic processing units construction of such models is possible. In this work construction of spatial, stage and age structured population model is described, with focus on modelling of mosquito migrations under the influence of wind and spatial attractants. As results, environment dependant simulations of spatial mosquito population dynamics will be presented.

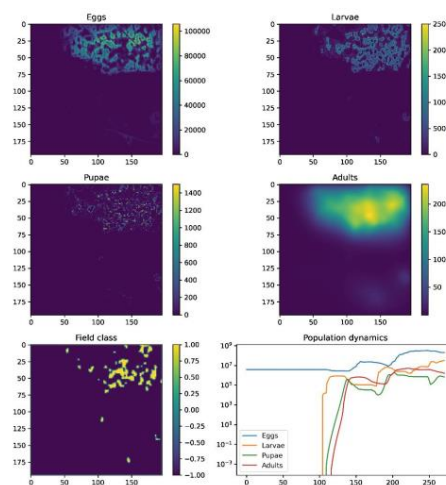


Figure 1. Simulation of the spatial, stage and age mosquito population model

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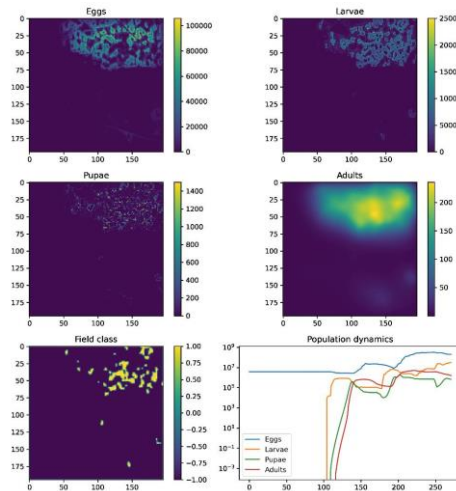
PROSTORNO MODELIRANJE POPULACIJA KOMARACA (*Culicidae*) POMOĆU MATRIČNIH POPULACIJSKIH MODELA

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Komarci su vektori brojnih zoonoza, te godišnje uzrokuju više od 700 000 smrtnih slučajeva diljem svijeta. [1] S klimatskim promjenama se mijenja i rasprostranjenost komaraca, a s prisutnošću komaraca na nekom području povećava se opasnost od pojave bolesti koje prenose komarci. Stoga, istraživanja na području izrade prognostičkih sustava koji mogu predvidjeti i locirati mjesta rojenja komaraca, njihove migracije i brojnost, od izrazite su važnosti [2]. Dobri generalni modeli komaraca koji opisuju starosnu strukturu postoje, no nedostaje im prostorna komponenta. [3] Do nedavno konstrukcija generaliziranih prostornih modela koji istovremeno predviđaju i starosnu strukturu populacija je zbog hardverskih ograničenja bila nezamisliva. Ipak pojavom paralelnog računanja koristeći grafičke procesorske jedinice opće namjene konstrukcija takvih modela postaje moguća. U ovom radu opisati će se konstrukcija prostornog modela komaraca s fokusom na migracije komaraca pod utjecajem vjetrova i atraktanata u prostoru. Prikazati će se rezultati modela, koji uključuju simulacije prostorne dinamike populacija komaraca u dinamičnom okolišu.



Slika 1. Simulacija prostornog modela populacije komaraca

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ANTIMALARIAL ACTIVITY OF NOVEL AMIDE-TYPE HARMICINES

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Malaria is a parasitic infectious disease responsible for more than 400 000 deaths annually [1]. The increasing multidrug resistance of *Plasmodium falciparum*, the most deadly human malaria pathogen, poses a major threat to global efforts to control malaria [2]. One of the promising strategies being pursued to overcome the emergence of resistant parasite strains is the development of hybrid compounds, in which two or more pharmacophores are combined into a single molecule. Harmine is a β -carboline alkaloid and a potent inhibitor of *Plasmodium falciparum* heat shock protein 90 (PfHsp90). On the other hand, covalent binding of cinnamic acid derivatives (CADs) to the known antimalarial drugs results in increased antimalarial activity [3]. Considering all these aspects, novel hybrid compounds composed of harmine and CADs, *i.e.* harmicines (Figure 1.) have been prepared and evaluated for *in vitro* antimalarial activity. Both *N*-harmicines (**5a-f**) and *O*-harmicines (**6a-h**) exerted remarkable activity against the erythrocytic stage of *P. falciparum*. The highest activity exerted *N*-harmicine **5e** with IC₅₀ values in low submicromolar range (0.04 μ M for Pf3D7 strain and 0.17 μ M for the PfDd2 strain).

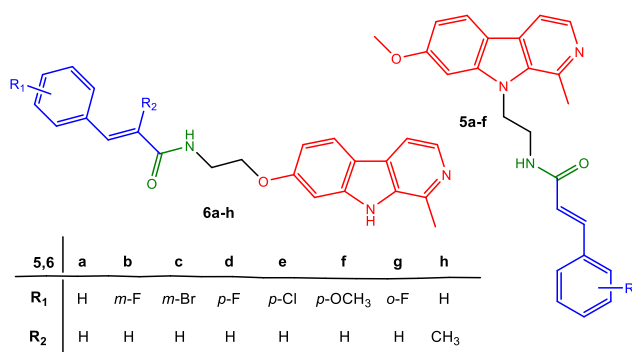


Figure 1. Structures of amide-type harmicines **5a-f** and **6a-h** (red: harmine, blue: cinnamic acid derivative, green: amide bond).

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ANTIMLARIJSKO DJELOVANJE HARMICINA AMIDNOG TIPA

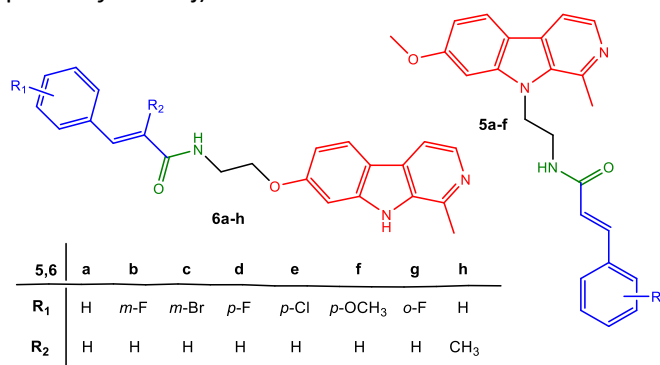
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Malarija je zarazna bolest koja je odgovorna za više od 400 000 smrtnih slučajeva godišnje [1]. Pojava rezistencije *Plasmodium falciparum*, najsmrtonosnijeg parazita koji uzrokuje malariju kod ljudi, glavna je prijetnja globalnim naporima u suzbijanju malarije [2]. Jedan od pristupa koji se koristi kako bi se prevladala pojava rezistencije parazita na postojeće antimalarike je razvoj hibridnih spojeva koji se sastoje od dva ili više farmakofora međusobno povezanih u jedinstvenu molekulu. Harmin je β -karbolinski alkaloid, inhibitor proteina toplinskog šoka 90 plazmodija. S druge strane, dokazano je kako kovalentno povezivanje derivata cimetne kiseline (DCK) s poznatim antimalaricima pojačava njihovo antimalarijsko djelovanje [3]. Uzimajući sve ovo u obzir, sintetizirani su harmicini amidnog tipa, odn. hibridni spojevi građeni od harmina i DCK te je ispitano njihovo antimalarijsko djelovanje *in vitro*. *N*-harmicini (**5a-f**) i *O*-harmicini (**6a-h**) pokazali su značajno antimalarijsko djelovanje protiv *P. falciparum*. Najaktivniji spoj bio je *N*-harmicin **5e** s IC_{50} vrijednostima u submikromolarnim koncentracijama (0,04 μ M za *Pf3D7* soj i 0,17 μ M za *PfDd2* soj).



Slika 1. Strukture harmicina amidnog tipa **5a-f** i **6a-h** (harmin je označen crvenom bojom, derivati cimetne kiseline plavom bojom, a amidna veza zelenom).

ZAHVALE

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TRANSCRIPTOME PROFILING OF *Borrelia burgdorferi* PLEOMORPHIC VARIANTS

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Borrelia burgdorferi is a spirochete bacterium that causes tick-borne Lyme disease. In laboratory cultures, *B. burgdorferi* cells develop several pleomorphic forms (morphotypes). Functional and structural differences between some of the morphotypes have been studied before, but expression changes at the transcriptome level have never been investigated. To address this problem, we grew cultures of different morphotypes (spirochete, round body, bleb and biofilm), harvested their RNA and recovered transcriptomes by RNAseq profiling. We found that spirochetes and round bodies, despite their morphological differences, share similar expression profiles. In contrast, blebs and biofilms showed a significant difference in expression patterns in comparison to each other and in comparison to spirochetes and round bodies each. Regardless of the overall transcriptional similarity to spirochetes, the genes upregulated in round bodies are enriched with transcription and translation functions. Although the total number of upregulated genes is much higher in blebs and biofilms than in round bodies, their function is mainly unknown. Interestingly, the genes that are upregulated in round bodies tend to be localized on the chromosome, while the genes that are upregulated in blebs and biofilms primarily derive from *B. burgdorferi* plasmids. To discern evolutionary imprints of differentially expressed genes we assigned evolutionary age to *B. burgdorferi* genes by phylostratigraphic approach. We found that the round body upregulated genes are enriched for evolutionary old genes common to all life, while the genes upregulated in blebs and biofilms are evolutionary young and specific for Borreliaceae. Our results suggest that spirochete to round body cell morphology transition relies on the delicate regulation of a relatively small number of highly evolutionary conserved genes involved in transcription and translation, while spirochete to bleb and biofilm transition includes substantial reshaping of transcription profiles towards evolutionary young genes of yet unknown function.



TRANSKRIPCijske ZNAČAJKE PLEOMORFNIH VARIJANTI BAKTERIJE *Borrelia burgdorferi*

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Bakterija *Borrelia burgdorferi* vektorski se prenosi putem krpelja i primarni je uzročnik Lajamske bolesti. U laboratorijskim uvjetima stanice *B. burgdorferi* mogu postojati u nekoliko različitih pleomorfni oblika (morfortipova). Dok su funkcionalne i strukturne razlike među nekim morfortipovima već prethodno opisane, ekspresijske razlike na razini transkriptoma do sada nisu istražene. S tim ciljem uzgojili smo laboratorijske kulture različitih morfortipova (spiralni, okrugli, bleb i biofilm), izolirali ukupnu RNA, sekvencirali je te skupili podatke o razlici u ekspresiji na razini transkriptoma. Otkrili smo da unatoč morfološkim razlikama, spiralni i okrugli morfortipovi imaju sličan ekspresijski profil, dok bleb i biofilm morfortipovi pokazuju značajnu razliku u ekspresiji kako međusobno tako i u odnosu na spiralni i okrugli morfortip. Unatoč tome što okrugli morfortip ima transkripciju sličnu spiralnom morfortipu, u okruglom morfortipu su pojačano su ekspimirani geni uključeni u procese transkripcije i translacije. Iako bleb i biofilm morfortipovi imaju veći broj pojačano ekspimiranih gena o odnosu na okrugli oblik, funkcija tih gena je pretežito nepoznata. Geni koji su pojačano ekspimirani u okruglom morfortipu su pretežito locirani na bakterijskom kromosomu, dok se pojačano ekspimirani geni bleb i biofilm morfortipova uglavnom nalaze na plazmidima. Kako bi definirali evolucijsko podrijetlo diferencijalno ekspimiranih gena bakterije *B. burgdorferi* koristili smo genomsku filostratigrafiju. Otkrili smo da su geni koji su pojačano ekspimirani u okruglom morfortipu obogaćeni evolucijski starim genima karakterističnim za sve stanične organizme, dok su geni pojačano ekspimirani u bleb i biofilm morfortipovima evolucijski mlađi i specifični za porodicu Borreliaceae. Naši rezultati upućuju na to da je tranzicija iz spiralnog u okrugli morfortip regulirana malim brojem evolucijski visoko konzerviranih gena koji sudjeluju u transkripciji i translaciji, dok je prijelaz iz spiralnog morfortipa u bleb ili biofilm morfortip popraćen velikim ekspresijskim promjenama koje uključuju pojačanu ekspresiju evolucijski mlađih gena nepoznate funkcije.



STRATEGIES FOR ANALYSIS OF VARIETAL THIOLS IN WINE: DERIVATIZATION AND STABLE ISOTOPE DILUTION ANALYSIS

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Odoriferous compounds: 3-sulfanylhexanol (3-SH), 3-sulfanylhexyl acetate (3-SHA), and 4-methyl-4-sulfanylpentan-2-one (4-MSP) formed during the fermentation of precursors present in grape and must are the most important representatives of the group of varietal thiols. [1] These compounds have a crucial role in the formation of aromatic profile of certain wines and a very low odor detection threshold. Due to the high reactivity, polarity, higher boiling points, and very low abundance in wine, isolation of varietal thiols represents tedious work, difficult to achieve by routine methods. Extraction of varietal thiols almost always involves sophisticated steps of specific extraction, derivatization, purification, and preconcentration. [2, 3] A series of procedures for derivatization of varietal thiols in Sauvignon blanc wine were conducted and validated. Derivatives of varietal thiols were isolated by solid-phase extraction and microextraction. Calibration was performed by standard addition approach combined with stable isotope dilution analysis. Derivatization and extraction of individual varietal thiols from model wine, neutral wines, and varietal wines was optimized. The developed method was successfully used for quantification of varietal thiols by gas chromatography – mass spectrometry with triple quadrupole. Quantification was preceded by the development of a multiple reaction monitoring method. For the first time, concentration of varietal thiols in the samples of Croatian Sauvignon blanc wine was determined, with values ranging from 6 ng L⁻¹ to 135 ng L⁻¹. All the wines show thiol presence above the respective sensory thresholds. The influence of various antioxidants added during the vinification step on the aroma profile of wine and the concentration of varietal thiols was investigated. Best preservation of varietal thiols was achieved in wines treated with a blend of potassium metabisulfite, ascorbic acid, and gallotannins.

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STRATEGIJE ANALIZE SORTNIH TIOLA U VINU: DERIVATIZACIJA I IZOTOPNO RAZRJEĐENJE

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Aromatične tirole 3-sulfanilheksanol (3-SH), 3-sulfanilheksil-acetat (3-SHA) i 4-metil-4-sulfanilpentan-2-on (4-MSP) koji nastaju tijekom alkoholnog vrenja iz prekursora prisutnih u grožđu i moštu nazivamo sortnim tiolima.[1] Sortni tioli imaju snažan učinak na aromu vina određenih sorti i vrlo niske mirisne pragove detekcije. Zbog reaktivnosti sortnih tiola, polarnosti, viših vrelišta i vrlo niske zastupljenosti u uzorku, teško je učinkovito izolirati ove analite rutinskim tehnikama ekstrakcije. Metode ekstrakcije tiola gotovo uvijek kombiniraju složenije korake specifične ekstrakcije, derivatizacije, pročišćavanja uzorka i ukoncentriravanja. [2, 3] Predstavljen je pregled provedenih postupaka derivatizacije i ekstrakcije sortnih tiola u vinu sorte Sauvignon bijeli. Derivati sortnih tiola izolirani su ekstrakcijom na čvrstoj fazi i mikroekstrakcijom na čvrstoj fazi iz prostora iznad otopine. Umjeravanje je provedeno tehnikom dodatka standarda u kombinaciji s tehnikom izotopnog razrjeđenja deuteriranim izotopomerima kao unutarnjim standardima. Uvjeti derivatizacije i ekstrakcije individualnih sortnih tiola optimizirani su testovima na modelnom vinu, neutralnom vinu i sortnim vinima. Kvalitativna i kvantitativna analiza sortnih tiola provedena je plinskom kromatografijom uz detekciju spojeva tandemnom spektrometrijom masa uz prethodni razvoj metode za praćenje višestrukih reakcija. Po prvi puta određene su masene koncentracije sortnih tiola u hrvatskim vinima sorte Sauvignon bijeli, koje su iznosile od 6 ng L⁻¹ do 135 ng L⁻¹, vrijednosti većih od mirisnog praga detekcije. Istražen je utjecaj dodatka različitih vrsta antioksidansa prilikom vinifikacije na koncentraciju i očuvanje arome eksperimentalnih vina. Koncentracije sortnih tiola bile su najviše kod tretmana kombinacijom kalijeva metabisulfita, askorbinske kiseline i galotanina.

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REPRESENTATION THEORY OF p -ADIC GROUPS – LANGLANDS PROGRAM

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The Langlands program consists of far-reaching and important mathematical conjectures which have occupied interests of many mathematicians in the world. It is very active area of research since it connects different areas of mathematics, such as number theory, harmonic analysis and geometry [1]. Although these areas consider different kinds of problems, symmetry is common to all of them. The founder of the program Robert Langlands observed that complicated problems from number theory could be resolved using objects which contain many symmetries. Examples of these objects are automorphic forms which are closely related to harmonic analysis [3].

Representation theory of p -adic groups gives analogues of classical harmonics in terms of irreducible unitary representations collected in a unitary dual [2]. In this way the first step towards understanding harmonic analysis on p -adic groups is to determine unitary dual of a given group. Classical groups over p -adic fields are examples of groups on which significant progress has been made, but unitary duals are still not classified for all of them. Motivated by the description of unitary dual in a case of general linear group, in the thesis we consider representations of a similar form for other classical groups. Hence our main goal is to determine their irreducible parts and select unitary ones.

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TEORIJA REPREZENTACIJA p -ADSKIH GRUPA – LANGLANDSOV PROGRAM

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Langlandsov program se sastoji od dalekosežnih i značajnih slutnji u matematici na kojima rade brojni matematičari u svijetu. Razlog velikoj aktivnosti ovog programa leži u interaktivnosti različitih područja matematike, kao što su teorija brojeva, harmonijska analiza i geometrija [1]. Iako su pitanja kojima se bave različita, imaju zajedničko svojstvo – simetriju. Osnivač programa Robert Langlands je prepoznao da bi se kompleksna pitanja teorije brojeva mogla riješiti objektima koji posjeduju puno simetrija. Primjer takvih objekata su automorfne forme, koje su usko povezane s harmonijskom analizom [3]. Teorija reprezentacija p -adskih grupa opisuje analogone klasičnih harmonika kao ireducibilne unitarne reprezentacije čije klase ekvivalencija čine unitarni dual [2]. Time je osnovni korak prema razumijevanju harmonijske analize na p -adskim grupama odrediti unitarni dual dane grupe. Klasične grupe nad p -adskim poljima su primjeri grupa na kojima se o tome dosta zna, ali je i dalje nisu klasificirani unitarni duali svih klasičnih grupa. Motivirani opisom unitarnog duala u slučaju generalne linearne grupe, u disertaciji proučavamo reprezentacije slične strukture za druge klasične grupe. Prema opisanom, glavni cilj je odrediti njihove ireducibilne dijelove te vidjeti koji od njih su unitarni.

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FROM ICEBERGS TO GEYSERS: THE STORY BEHIND HYDROPHOBIC EFFECT

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The temperature and solvent effect on the complexation of various guests (Figure 1) with α -, β - and γ -cyclodextrin and cucurbit[7]uril was explored experimentally and by means of molecular dynamics simulations. The stability constants of all investigated complexes were by far the highest with cucurbit[7]uril in water. A pronounced temperature dependence of $\Delta_r H^\circ$ and $\Delta_r S^\circ$, resulting in almost complete enthalpy-entropy compensation was observed for most explored host-guest systems. For those systems complexation thermodynamics was in line with the classical rationale of the hydrophobic effect at lower temperatures, and the non-classical explanation at higher ones.^{1,2} The optimized inclusion complex structures corresponded to those deduced by means of NMR spectroscopy and the experimentally obtained and calculated $\Delta_r G^\circ$ were in very good agreement.

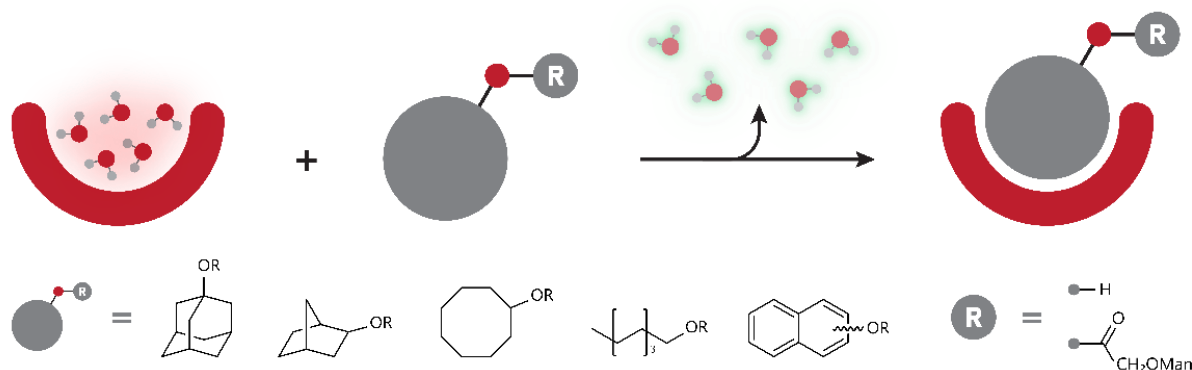


Figure 1. Schematic representation of the complexation process and guest structures.

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OD LEDENJAKA DO GEJZIRA: PRIČA O HIDROFOBONOM EFEKTU

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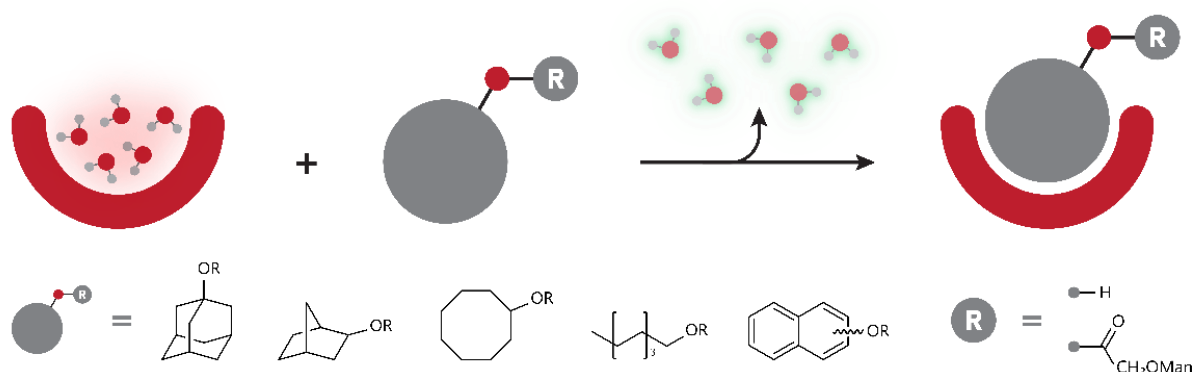
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Utjecaj temperature i otapala na reakcije kompleksiranja raznih gostiju (Slika 1) s α -, β - i γ -ciklodekstrinom i kukurbit[7]urilom istražen je eksperimentalno i simulacijama molekulske dinamike u vodi. Konstante stabilnosti svih proučavanih kompleksa daleko su najveće s kukurbit[7]urilom. Opažena je izražena temperaturna ovisnost $\Delta_r H^\circ$ i $\Delta_r S^\circ$, koja rezultira gotovo potpunom entalpijsko-entropijskom kompenzacijom kod većine istraženih parova gost-receptor. Termodinamika kompleksiranja u opisanim je slučajevima u skladu s klasičnim objašnjenjem hidrofobnog efekta pri nižim, odnosno s neklasičnim objašnjenjem pri višim temperaturama.^{1,2} Optimizirane strukture inkluzijskih kompleksa u skladu su s onima određenima spektroskopijom NMR, a eksperimentalno određene i izračunane $\Delta_r G^\circ$ u dobrom su slaganju.



Slika 1. Shematski prikaz reakcije kompleksiranja i strukture gostiju.

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EFFECTS OF STROBILURIN FUNGICIDES ON SURVIVAL REPRODUCTION AND HATCHING SUCCESS OF *Enchytraeus crypticus*

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Strobilurins, a commonly used class of fungicides, are known to impact an embryonic development of aquatic organisms and show toxicity to different soil organisms [Zhang et al., 2020]. Standard tests for soil invertebrates are usually limited to the assessment of endpoints like survival and number of juveniles, while hatching and embryotoxicity tests have emerged recently [Gonçalves et al., 2015]. Besides earthworms, enchytraeids are the most commonly used bioindicators of soil contamination [Castro-Ferreira et al., 2012]. Their size and short life cycle makes them suitable for this type of research. The aim of the study was to assess the impact of strobilurins on survival, reproduction, and hatching success of enchytraeid *Enchytraeus crypticus*. Standardized OECD reproduction tests with azoxystrobin (AS), pyraclostrobin (PS), and trifloxystrobin (TS) were conducted. Survival was mostly affected by TS (LC₅₀ = 2.34 mg/kg), followed by PS (LC₅₀ = 4.26 mg/kg) and AS (LC₅₀ = >150 mg/kg). Reproduction was affected in the same order (TS EC₅₀ = 0.045 mg/kg, PS EC₅₀ = 1.85 mg/kg, and AS EC₅₀ = 93.10 mg/kg). Exposure to AS and PS demonstrated a negative impact on hatching success and a significant increase in the number of unhatched cocoons was observed at the end of the reproduction experiment. Hence, a prolonged hatching test that was consequently performed. The results showed a hatching delay at lower AS and PS concentrations, while at higher concentrations hatching was prevented and the cocoons were no longer viable. Furthermore, prolonged hatching test enabled discrimination between hatching delay and hatching impairment. The use of prolonged hatching tests can fill the gap between reproduction and multigeneration tests and allow a better understanding of the adverse effects of the tested substances.

ACKNOWLEDGMENTS

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UČINCI STROBILURINSKIH FUNGICIDA NA REPRODUKCIJU, PREŽIVLJAVANJE I IZLJEGANJE VRSTE *Enchytraeus crypticus*

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Strobilurin su jedna od najzastupljenijih skupina fungicida, a dokazano je da utječu na embrionalni razvoj vodenih organizama, te pokazuju toksičnost za različite organizme tla [Zhang i sur., 2020]. Standardni testovi za beskralježnjake tla obično su limitirani na procjenu krajnjih točaka kao što su preživljavanje odraslih i broj juvenilnih, dok su testovi izlijeganja i embriotoksičnosti ustanovljeni tek nedavno [Gonçalves et al., 2015]. Osim gujavica, enhitreje su najčešće korišteni bioindikatori zagađenja tla [Castro-Ferreira et al., 2012]. Nadalje njihova veličina i kratak životni ciklus čine ih pogodnima za ovakvu vrstu istraživanja. Cilj ovog istraživanja bio je utvrditi utjecaj strobilurina na preživljavanje, reprodukciju i izlijeganje kod vrste *Enchytraeus crypticus*. Provedeni su standardizirani OEC reprodukcijски testovi s azoksistrobinom (AS), piraklostrobinom (PS) i trifloksistrobinom (TS). Na preživljavanje je najviše utjecao TS (LC₅₀ = 2.34 mg/kg), te PS (LC₅₀ = 4.26 mg/kg) i AS (LC₅₀ = >150 mg/kg). Izlaganje AS i PS pokazala je negativan utjecaj na uspjeh izlijeganja, a na kraju reprodukcijskog testa zamijećen je značajan porast broja neizležanih kokona. Produljeni test izlijeganja pokazao je odgodu izlijeganja pri nižim koncentracijama AS i PS, dok je pri višim koncentracijama izlijeganje potpuno izostalo, te kokoni više nisu bili izleživi. Produljeni test izlijeganja omogućava razlikovanje odgode izlijeganja i njegovog potpunog izostanka. Osim što su dokazani negativni učinci AS, PS i TS na preživljavanje, reprodukciju i izlijeganje kod vrste *E. crypticus*, dobiveni rezultati ukazuju na potrebu korištenja različitih krajnjih točki. Korištenje produljenog testa izlijeganja može popuniti prazninu između reprodukcijskih i više generacijskih testova i omogućuju bolje razumijevanje štetnih učinaka testiranih tvari.

ZAHVALE

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APPLICATION OF REMOTE SENSING IN MINERAL RESOURCES EXPLORATION

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Spaceborne remote sensing data have a significant role in scientific research. In geology they are used in mineral resources exploration, geological mapping, hydrogeological research, etc. Their main appeal is the ability to interpret and analyze data covering large areas in a rapid and cost-efficient manner. In modern times, remote sensing has been successfully applied in the lithological mapping of arid areas. Similar approaches for lithological mapping in semi-arid regions with a high degree of structural complexity, vegetation and topographic effects are yet to be developed. The primary objective of this study is to combine field-based data derived from the geological mapping program „Map of mineral resources of the Republic Croatia“ with remote sensing imagery in order to derive basic lithological maps of a part of northern Dalmatia. The main lithologies represented in this area are shallow marine Upper Cretaceous to Middle Eocene carbonates, Middle Eocene to Lower Oligocene clastics and freshwater Neogene sediments. Besides mapping of lithological units attempts will be made to distinguish certain types of mineral raw materials such as bauxite, evaporite, phosphorite and coal. To achieve this aim Unsupervised and Supervised Classification will be applied. These approaches have shown great pattern-recognition ability and accurate classification of different lithological groups (Gupta, 2018). The limiting factor in achieving better classification is the spectral and spatial properties of the satellite imagery. Therefore, future research should consider the integration of hyperspectral data and integration of geomorphic products. In the first step this methodology will be applied on Sentinel-2 imagery, in second step on Landsat 8 imagery, and finally on hyperspectral data. All this data will be processed within a GIS (geographic information system) environment. The purpose of the described multidisciplinary research is to study geological properties using a variety of different approaches with as many features as possible to increase the accuracy of lithological unit discrimination and mineral resources mapping. There is no doubt that the growth and development of computers and computer science in general, coupled with advances in GIS technology and geostatistics today play an important role in geological research. This also applies to remote sensing, and such a principle is described in this paper.

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PRIMJENA DALJINSKIH ISTRAŽIVANJA U ISTRAŽIVANJU MINERALNIH SIROVINA

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U geoznanstvenim istraživanjima obrada satelitskih podataka igra vrlo značajnu ulogu. U geologiji se ona odnosi na istraživanje mineralnih resursa, geološko kartiranje, hidrogeološka istraživanja i dr. Glavni razlog sve veće zastupljenosti takvih podataka u znanstvenom istraživanju leži u mogućnosti troškovno prihvatljive interpretacije relativno velikih površina. U današnje vrijeme daljinska istraživanja su uspješno primijenjena kod litološkog kartiranja sušnih područja. Međutim, ono što tek treba znanstveno dokazati je primjena sličnih pristupa u polu sušnim područjima kod kojih je prisutan i visok stupanj strukturnih promjena, vegetacije i površinskih efekata. Primarni cilj ovog rada je pomoću sinteze podataka s terena, a koji su prethodno prikupljeni radom na trajnom znanstveno – istraživačkom projektu “Karta mineralne sirovine Republike Hrvatske” s podacima daljinskih istraživanja, litološki kartirati dio područja sjeverne Dalmacije. Prisutne stijene čine plitkomorski gornjo kredni i srednje eocenski karbonati, srednje eocenski i gornjo eocenski klastiti, Promina naslage i slatkovodni neogenski sediment. Uz litološko kartiranje pokušat će se izdvojiti i prisutne određene vrste mineralnih sirovina kao što su boksiti, evaporiti, fosforiti i ugljen. Za postizanje tog cilja koristiti će se metode nenadzirane i nadzirane klasifikacije. One su pokazale ogroman potencijal za prepoznavanje pojedinačnih litoloških svojstava (Gupta, 2018). Faktor ograničenja su spektralne i prostorne karakteristike dobivenih snimki. Zbog toga će se sagledati i mogućnost implementacije hiperspektralnih setova podataka kao i geomorfoloških obilježja, a sve sa svrhom povećanja točnosti kod litološkog kartiranja. U početnom dijelu istraživanja temelj bi bili podaci Sentinel – 2 satelita, zatim podaci Landsat 8 snimki i na kraju i hiperspektralni podaci. Svi ti podaci biti će obrađeni GIS tehnologijom. Svrha opisanih multidisciplinskih istraživanja je proučavanje geoloških pojava korištenjem nekoliko različitih pristupa sa čim je moguće više značajki s konačnim ciljem povećanja točnost kod izdvajanja litoloških jedinica i kariranja mineralnih sirovina . Nesumnjivo je da rast i razvoj računala i općenito informatike, udružen s napretkom u GIS tehnologiji i geostatistici danas igraju važnu ulogu u geološkim istraživanjima. Navedeno se odnosi i na daljinska istraživanja, te je i takav princip u ovom radu opisan.

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BIOTIPIZATION AND PROTEIN IDENTIFICATION BY MASS SPECTROMETRY ANALYSIS AND PEPTIDE *de novo* SEQUENCING

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Rapid and reliable identification of microorganisms is a key in a clinical diagnostic laboratories as well as in detection of food borne and waterborne pathogens. Matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) is one of the methods commonly used for the identification of microorganisms, but it exhibits several limitations: it has a low discriminatory power in closely related species, and it is limited by the relatively small reference database. We developed a methodology for the identification of microorganisms by MALDI-TOF/TOF tandem mass spectrometry (MS/MS) and peptide *de novo* sequencing which can be used to obtain data of expressed proteins. Accuracy and efficiency of *de novo* sequencing was improved by chemically activated fragmentation (CAF) which enables peptide analysis in positive and negative mass spectrometry ion mode [1]. The newly developed software which performs *de novo* sequencing of positive/negative MS/MS data and matches the elucidated peptide sequences against the analysis is National Centre for Biotechnology Information non redundant database (NCBI *nr*) by a BLASTp tool [2]. The results of the search allowed assignment of experimentally derived peptides to the theoretical protein sequences in the database. The developed pipeline was evaluated on data generated by analysis of relevant clinical bacterial species - *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis* and *Klebsiella pneumoniae*. The results were compared to standard culture methods for bacterial identification and our method correctly identified all the named bacteria in biological triplicate analyses. In addition to correct identification, the results also show information about expressed proteins in the proteome of *E. coli*, *P. aeruginosa*, *P. mirabilis* or *K. pneumoniae* which can be used for functional annotation or homology research.

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BIOTIPIZACIJA I IDENTIFIKACIJA PROTEINA POMOĆU SPEKTROMETRIJE MASA I *de novo* SEKVENCIRANJA PEPTIDA

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Brza i pouzdana identifikacija mikroorganizama ključna je u kliničko-dijagnostičkom laboratoriju, kao i u otkrivanju patogena koji se prenose hranom i vodom. Matricom potpomognuta laserska desorpcija/ionizacija spregnuta s analizatorom koji mjeri vrijeme leta (MALDI-TOF MS) jedna je od metoda koja se obično koristi za identifikaciju mikroorganizama, ali pokazuje nekoliko ograničenja: ima nisku diskriminacijsku moć kod genetički povezanih vrsta te je ograničena relativno malom referentnom bazom podataka. U ovom istraživanju razvijena je metodologija za identifikaciju mikroorganizama tandemskom spektrometrijom masa MALDI-TOF/TOF (MS/MS) i sekvenciranjem peptida *de novo*. Točnost i učinkovitost sekvenciranja *de novo* poboljšana je kemijski aktiviranom fragmentacijom (CAF) koja omogućava analizu peptida u pozitivnom i negativnom načinu rada spektrometrije masa [1]. Novo-razvijeni softver koji vrši *de novo* sekvenciranje pozitivnih/negativnih MS/MS podataka i pomoću algoritma BLASTp sravnava identificirane peptidne sekvence s proteomskom bazom Nacionalnog centra za biotehnološke informacije (NCBI) [2]. Rezultati pretraživanja omogućili su pridruživanje eksperimentalno izvedenih peptida teoretskim proteinskim sekvencama u bazi podataka te identifikaciju mikroorganizma. Za evaluaciju metode korištene su relevantne kliničke bakterije: *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis* i *Klebsiella pneumoniae*. Rezultati su uspoređeni sa standardnom metodom identifikacije bakterija i utvrđeno je da je proteomska metoda ispravno identificirala sve navedene bakterije u biološkim triplikatima. Osim točne identifikacije, rezultati analize također daju informaciju o eksprimiranim proteinima *E. coli*, *P. aeruginosa*, *P. mirabilis* ili *K. pneumoniae* te se iste mogu koristiti za funkcionalnu anotaciju i analize proteinske homologije.

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STEREOCHEMISTRY OF TRIDENTATE LIGAND COMPLEXES WITH COPPER(II) AND ZINC(II)

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Bis-tridentate ligand complexes can form three geometric isomers; *mer*, *trans-fac* and *cis-fac* [1]. For the synthesis of functional complexes incorporating tridentate ligands, understanding the isomer preferences is an important starting point. One way of stabilizing a particular isomer is by non-covalent interactions. In literature, such non-covalent interactions were often found with anions or as π - π interactions in ligands containing aromatic rings [2,3].

In this work, complexes of tridentate bis(2-pyridine-2-ylmethyl)amine (bpa) and 2,2'-iminodiacetamide (imda) ligands were prepared with Cu(II) and Zn(II). The ligands have chiral side chains, with amide groups that enable the formation of hydrogen bonds. The solid-state structures were characterized by single-crystal X-ray diffraction, while the structures in solution were studied by NMR, UV-Vis and CD spectroscopy. Several variations were introduced into the ligand structure, such as length of the CH₂ linker, orientation of the amide group and type of chiral substituent, in order to construct a ligand suitable for the formation of secondary structures.

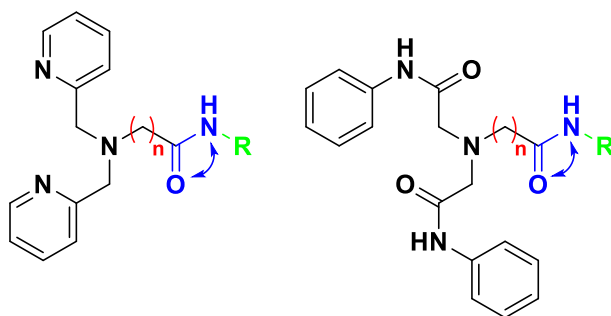


Figure 1. Bis(2-picolyl)amine and iminodiacetamide ligands with R = (S)-1-phenylethylamine or L-Phenylalanine methyl ester and n = 1, 2 or 3.

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STEREOKEMIJA KOMPLEKSA TRIDENTATNIH LIGANADA S BAKROM(II) I CINKOM(II)

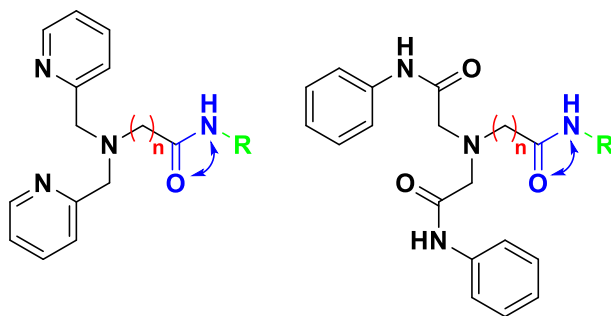
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Bis-koordinirani kompleksi tridentatnih liganada mogu tvoriti tri geometrijska izomera; *mer*, *trans-fac* i *cis-fac* [1]. Za sintezu funkcionalnih kompleksa tridentatnih liganada, razumijevanje nastajanja različitih izomera važna je polazna točka. Jedan od načina stabilizacije određenog izomera su nekovalentne interakcije. U literaturi su takve nekovalentne interakcije često nađene s anionima ili kao π - π interakcije u ligandima koji sadrže aromatske prstenove [2,3].

U ovom radu pripremljeni su kompleksi tridentatnih liganada bis(2-piridin-2-ilmetil)amina (bpa) i 2,2'-iminodiacetamida (imda) s Cu(II) i Zn(II). Ligandi imaju kiralne lance s amidnim skupinama koje omogućuju stvaranje vodikovih veza. Strukture u čvrstom stanju karakterizirane su difrakcijom X-zraka na monokristalu, dok su strukture u otopini proučavane NMR, UV-Vis i CD spektroskopijom. U strukturu liganada uvedene su razne varijacije, poput duljine CH₂ linkera, orijentacije amidne skupine i vrste kiralnog supstituenta, kako bi se dizajnirao ligand prikladan za stvaranje sekundarnih struktura.



Slika 1. Bis(2-pikolil)aminski i iminodiacetamidni ligandi sa skupinom R = (S)-1-feniletanamin ili L-fenilalanin metil ester i n = 1, 2 ili 3.

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LONG-TERM TRENDS OF METAL CONCENTRATIONS AND WATER QUALITY OF THE WASTEWATER IMPACTED KRKA RIVER COURSE

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Krka River is a karst phenomenon due to great variety of travertine waterfalls, lakes and species biodiversity. As a result, a large part of its course was proclaimed national park (NP) in 1985. However, only 2 km upstream of the Krka NP, inadequately purified industrial (screw factory) and municipal wastewaters (Town of Knin) are released into the river endangering the water quality of the protected area [1]. Thus, the aim of the study was to assess the anthropogenic impact on the water quality of the Krka River by measuring physico-chemical parameters and dissolved metals concentrations in water at six locations in three sampling campaigns from 2015 to 2021. Krka River source (KRS) was selected as the reference, while other locations were under different anthropogenic impact: wastewater from the screw factory (IWW), tributary Orašnica (TOR) passing nearby wastewater basins, Krka River downstream of the municipal sewage of the Town of Knin (KRK), tributary Butišnica (TBU) affected by agricultural activity and Brljan Lake (KBL) as downstream location in Krka NP. Water quality was the lowest in effluents from the factory (IWW) in all sampling campaigns. Significantly higher levels of many elements and poorer values of some physico-chemical parameters were recorded at TOR, TBU and KRK compared to KRS, while KBL, due to pronounced lake sedimentation, had relatively low metal concentrations. Also, Hg levels were low at all sites, even below limit of detection. At the affected sites, the highest increase was observed for Co, Fe, Mn, Ni and Zn, metals used in industry, but also for K, Mo, Se, Sb at IWW, TOR and TBU compared to KRS. Long-term research indicated comparable trends, although metal levels slightly declined in the Krka River and its tributaries over the years, as a result of more efficient wastewater treatment. However, increase in metal concentrations downstream of the wastewater discharges indicates potential danger for this sensitive karst ecosystem and the importance of monitoring and protection of the Krka NP.

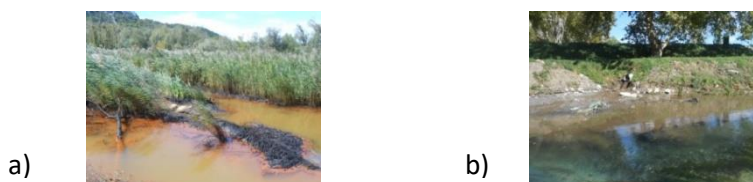


Figure 1. Point sources of pollution at the Krka River: a) industrial, b) municipal wastewaters of Knin

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DUGOROČNI TRENDOMI KONCENTRACIJA METALA I KAKVOĆE VODE RIJEKE KRKE U DIJELU TOKA POD UTJECAJEM OTPADNIH VODA

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Rijeka Krka poznata je kao krški fenomen zahvaljujući velikom bogatstvu sedrenih slapova i jezera te raznolikosti vrsta pa je veći dio toka proglašen nacionalnim parkom (NP) 1985. godine. Međutim, samo 2 km uzvodno od granice NP Krka u rijeku se ispuštaju neadekvatno pročišćene industrijske (tvornica vijaka) i komunalne otpadne vode (grad Knin) koje ugrožavaju i kakvoću vode zaštićenog dijela vodotoka [1]. Stoga je cilj istraživanja bio procijeniti antropogeni utjecaj na kakvoću vode rijeke Krke mjerenjem fizikalno-kemijskih čimbenika te koncentracija otopljenih metala u vodi na šest lokacija tijekom tri uzorkovanja između 2015.-2021. godine. Izvor rijeke Krke (KRS) odabran je kao referentna lokacija, dok su ostale pod različitim antropogenim utjecajima: otpadna voda tvornice vijaka (IWW), pritoka Orašnica (TOR) koja prolazi uz bazene s otpadnom vodom, Krka nizvodno od ispusta komunalnih voda grada Knina (KRK), pritoka Butišnica (TBU) koja je pod utjecajem poljoprivredne djelatnosti i jezero Brljan (KBL) kao nizvodna lokacija unutar NP Krka. Tijekom sva 3 uzorkovanja potvrđena je najlošija kakvoća vode u otpadnoj vodi tvornice (IWW). Značajno više koncentracije mnogih elemenata i lošije vrijednosti pojedinih fizikalno-kemijskih čimbenika u odnosu na izvor zabilježene su i na lokacijama TOR, TBU i KRK, dok je KBL, vezano uz izraženu sedimentaciju u jezeru, imao relativno niske koncentracije metala. Značajno je da su i koncentracije Hg na svim postajama niske, čak i ispod razine detekcije. Najviši porast na postajama pod antropogenim utjecajem zabilježen je za Co, Fe, Mn, Ni i Zn, metale koji se koriste u industriji, kao i višestruko više razine K, Mo, Se na lokacijama IWW, TOR i TBU u odnosu na izvor. Višegodišnje istraživanje ukazuje na slične trendove, iako se tokom godina uočava blagi pad koncentracija metala u rijeci Krki i njezinim pritokama, vjerojatno kao rezultat djelomičnog ulaganja u efikasnije pročišćavanje otpadnih voda. Međutim, zabilježen porast razina metala u blizini ispusta otpadnih voda ukazuje na potencijalnu opasnost za ovaj osjetljivi krški ekosustav i važnost monitoringa i zaštite NP Krka.



Slika 1. Točkasti izvori zagađenja na rijeci Krki: a) industrijske, b) komunalne otpadne vode Knina
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PHYSICO-CHEMICAL AND ECOTOXICOLOGICAL ANALYSIS OF MARINE SEDIMENT IN THE NORTHERN ADRIATIC

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The Republic of Croatia has the binding obligation to achieve and maintain the Good Environmental Status (GES) prescribed by the Marine Strategy Framework Directive (MSFD) of the European Union. The EQS Directive (Environmental Quality Standard) and the Commission Decision 2017/848 [1] provide guidance on the necessary implementation of marine and sediment monitoring, suggesting that the member states should develop their own regulations on the categorization of sediments and maximum permissible concentrations of pollutants by year 2015. As the Republic of Croatia has not yet adopted it, to compensate the lack of the national quantitative and qualitative criteria, we applied the French regulations EQS N1 and N2 [2] in this research. The sediment samples were collected at five locations in the Northern Adriatic Sea off the coast of Rovinj. The granulometric analysis of the sediment, chemical analysis of metals (As, Cd, Hg, Cr, Cu, Ni, Pb, Zn), the analysis of polycyclic aromatic hydrocarbon (PAH) and polychlorinated biphenyls (PCB) were performed, as well as the toxicity risk analysis by GEODRISK software [3]. In addition, the germination test with *Linum ussitatissimum* flax seeds was undertaken to determine the phytotoxicity of the sediment. The results of the chemical analyses (ecotoxic metals, Σ PAH, Σ PCB) compared with the EQS N1 and N2 values by GEODRISK analysis showed the presence of the contaminants in the sediments in concentrations above N1 levels (Cu, Ni, Hg, Cr and Σ PAH), several of them with the values between N1 and N2, and one station contained mercury above the N2 level. Given the obtained values, marine sediments at the research stations presented a low level of pollution without the potential adverse effect on the marine environment. However, the Germination Index (GI) suggested that the pollutants found at the sites exposed to anthropogenic activities had a significant phytotoxic effect: 56.5 % to 84.2 % compared to the S5 control site (GI = 100 %). The conclusion is that the physico-chemical analysis is not sufficient to determine a complete overview of the possible sediment impact on biota, so it is necessary to conduct the selected ecotoxicological tests, as well.

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FIZIKALNO-KEMIJSKA I EKOTOKSIKOLOŠKA ANALIZA MORSKOG SEDIMENTA U SJEVERNOM JADRANU

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Republika Hrvatska (RH) je preuzela obvezu postizanja i održavanja Dobrog stanja okoliša (DSO) propisanu Okvirnom direktivom o morskoj strategiji (ODMS) Europske unije. Direktiva EQS (Environmental Quality Standard) i Odluka EK 2017/848 [1] daju naputak o nužnoj provedbi monitoringa mora i sedimenta uz napomenu kako članice samostalno donose regulativu o kategorizaciji sedimenata i maksimalnim dopuštenim koncentracijama zagađivala do 2015. godine. Kako RH to još uvijek nije učinila, a da bi se nadomjestio nedostatak nacionalnih kvantitativnih i kvalitativnih kriterija, primijenili smo francusku regulativu EQS N1 i N2 [2]. Uzorci sedimenta prikupljeni su na pet lokacija u sjevernom Jadranu u priobalju grada Rovinja. Napravljena je granulometrijska analiza sedimenta, kemijska analiza metala (As, Cd, Hg, Cr, Cu, Ni, Pb, Zn), analiza policikličkih aromatskih ugljikovodika (PAH) i polikloriranih bifenila (PCB) te analiza rizika toksičnosti pomoću softvera GEODRISK [3]. Dodatno, radi utvrđivanja fitotoksičnosti sedimenta proveden je test klijavosti sa sjemenkama lana *Linum ussitisimum*. Rezultati kemijskih analiza (ekotoksični metali, Σ PAH, Σ PCB) uspoređeni s EQS N1 i N2 vrijednostima putem GEODRISK analize pokazali su prisutnost zagađivala u sedimentima u koncentracijama iznad N1 razine (Cu, Ni, Hg, Cr i Σ PAH), nekoliko ih ima vrijednosti između N1 i N2, a jedna postaja sadrži živu iznad N2 razine. S obzirom na dobivene vrijednosti, morski sedimenti na istraživanim postajama pokazuju nisku razinu onečišćenja bez potencijalnog štetnog učinka na morski okoliš. Međutim, Indeks germinacije (GI) sugerira kako prisutna zagađivala na lokacijama pod antropogenim utjecajem imaju značajno fitotoksičan učinak: 56,5 % do 84,2 % u usporedbi s kontrolnom lokacijom S5 (GI =100 %). Može se zaključiti da fizikalno-kemijska analiza nije dostatna za određivanje cjelovite slike o mogućem učinku sedimenta na biotu, stoga je nužno provoditi i odabrane ekotoksikološke testove.

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STEREOSELECTIVE SYNTHESIS OF β,β -DIARYL KETONES WITH β -QUATERNARY STEREOGENIC CENTER

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Stereoselective synthesis of β,β -diaryl ketones with β -quaternary stereogenic center incorporated into isoindolinone moiety is described. *Gem*-diaryl-alkyl isoindolinone derivatives are key skeletons present in numerous naturally occurring and synthetic biologically active molecules. In this context, optically active isoindolinone-derived β,β -diaryl ketones show great potential as the synthetic intermediates of diarylalkyl-containing molecules due to the versatile transformations of the carbonyl and lactame group [1]. The enantioselective Mannich-type reactions of isoindolinone-derived ketimines with carbon nucleophiles – α -azoesters [2], cyclohexenone [3], *N*-acetyl enamides [4] and difluoroenoxyasilanes [5] – provide a direct access to these compounds bearing a chiral quaternary stereogenic center. The main drawbacks of these methodologies are inherent restrictions for the construction of vicinal α,β -stereogenic centers, including the control of its diastereo- and enantioselectivity. Herein we report a chiral Brønsted acid-catalyzed stereoselective addition of ketones to *N*-acyl ketimines for the construction of isoindolinone-derived β,β -diaryl ketones comprising quaternary stereogenic center.

Key to the success of this transformation is the generation of reactive *N*-acyl ketiminium species *in situ* from 3-hydroxy isoindolinones under chiral phosphoric acid catalysis. The addition of enols provides products in excellent yields and enantioselectivities, including compounds with vicinal α,β -stereogenic centers. The stereochemical model of the chiral induction is proposed on the basis of the absolute configuration determined by the X-ray crystallographic analysis. Upon dehydration, *N*-acyl ketiminium ion forms an ion pair with the anion of the catalyst, thus blocking its *si* face. Enol approaches from *re* face of the electrophile, providing yielding products with in diastereo- and enantiomeric ratios.

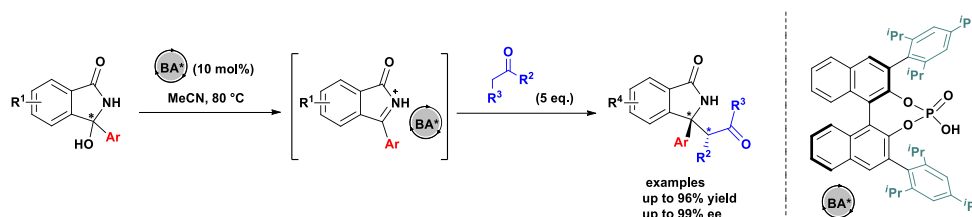


Figure 1. Stereoselective synthesis of β,β -diaryl ketones with β -quaternary stereogenic center catalyzed by chiral Brønsted Acid.

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STEREOSELEKTIVNA PRIPRAVA β,β -DIARIL-KETONA S β -KVATERNIM STEREOGENIM CENTROM

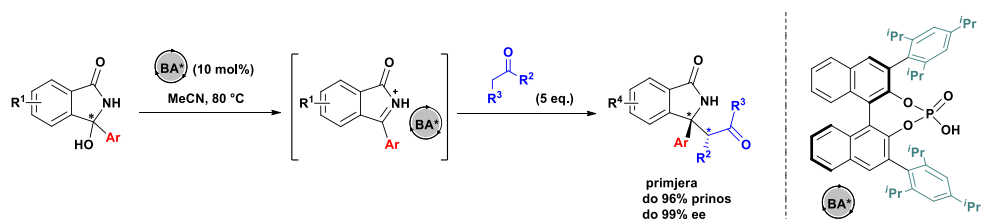
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Gem-diaril-alkilni derivati izoindolinona strukturne su podjedinice brojnih prirodnih i sintetiziranih biološki aktivnih molekula. U tom se kontekstu optički aktivni izoindolinonski derivati β,β -diaril-ketona, zahvaljujući raznovrsnim transformacijama kojima podiježu prisutne funkcionalne skupine - karbonilna i laktamska – ističu kao potencijalni prekursori u sintezi enantiomerno obogaćenih molekula koje sadrže diarilalkilni strukturni motiv [1]. Izravan sintetski pristup ovim spojevima s izoindolinonskim β -kvaternim stereogenim centrom temelji se na stereoselektivnoj Mannichovoj reakciji izoindolinonskih ketimina s različitim ugljikovim nukleofilima - α -azoesterima [2], cikloheksenonima [3], *N*-acetilenamidima [4] i difluorenoksisilanima [5]. Međutim, ograničenja u generiranju vicinalnih α,β -stereogenih centara i kontroli njihove dijastereo- odnosno enantioselektivnosti ističu se kao glavni nedostaci svih navedenih metodologija. Sukladno tome, razvijena je metodologija pripreve izoindolinonskih derivata β,β -diaril-ketona s kvaternim stereogenim centrom temeljena na stereoselektivnoj adiciji ketona na *N*-acil-ketimine u prisustvu kiralne Brønstedove kiseline kao katalizatora.

Uspješnost ove transformacije pripisuje se generiranju reaktivnih vrsta, *N*-acil-ketiminijevih iona *in situ* dehidratacijom 3-hidroksi izoindolinona koja je katalizirana kiralnom fosforom kiselinom. Adicijom enola na *N*-acil-ketimine dobivaju se s visokom enantioselektivnošću produkti u izvrsnim prinosima, uključujući spojeve s vicinalnim α,β -stereogenim centrima. Na temelju apsolutne konfiguracije određene rentgenskom strukturnom analizom predložen je stereokemijski model kiralne indukcije koji uključuje bifunkcionalan način aktivacije supstrata katalizatorom. Nukleofilnim napadom enola preko *re* enantiotopne strane elektrofila, dobivaju se produkti u visokim dijastereo- i enantiomernim omjerima.



Slika 1. Stereoselektivna pripreva β,β -diaril-ketona s β -kvaternim stereogenim centrom katalizirana kiralnom Brønstedovom kiselinom.

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MULTI-FREQUENCY STUDY OF THE STRAIGHT DEPOLARIZATION CANALS IN A SURROUNDING OF THE 3C196 FIELD

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Recent LOFAR (low frequency array) observations show a very rich morphology of Galactic synchrotron emission in polarization [1]. Discovered structures are unraveled by the rotation measure synthesis (RM synthesis), a technique in radio polarimetry that separates the observed polarized emission according to the degree of Faraday rotation. This allows us then to study the relative distribution of the intervening magneto-ionic interstellar medium (ISM) as a function of Faraday depth (so-called Faraday tomography). During this talk we will present a multi-frequency analysis of newly detected Faraday tomography structures observed in a broader area of the 3C196 field. The most striking features that can be seen in maximum polarized intensity images are depolarization canals. The analysis showed that orientation of depolarization canals is very similar to the orientation of plane-of-sky magnetic field and to the orientation of neutral hydrogen filaments. An alignment between these three distinct tracers of the ISM suggests that an ordered magnetic field plays a crucial role in confining different ISM phases. In addition, the starlight polarization correlates with the orientation of depolarization canals in one of the observed fields (Field B), allowing us to constrain the relative distances to the observed structures in Faraday depth.

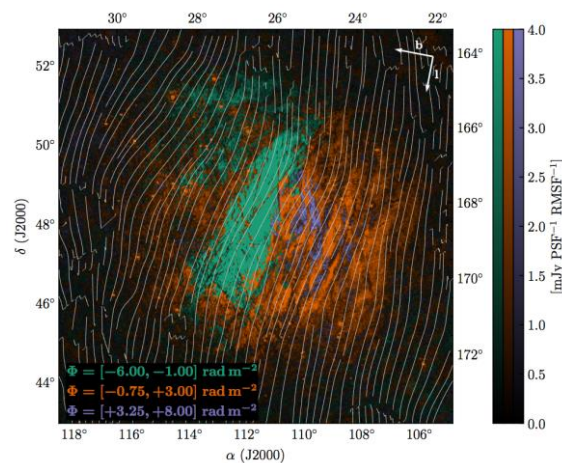


Figure 1. Field A: visualizations of the magnetic field lines in the plane of the sky plotted over Faraday emission sliced into different Faraday dept ranges.

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MULTIFREKVENCIJSKA ANALIZA RAVNIH DEPOLARIZIRANIH KANALA U OKOLINI POLJA 3C196

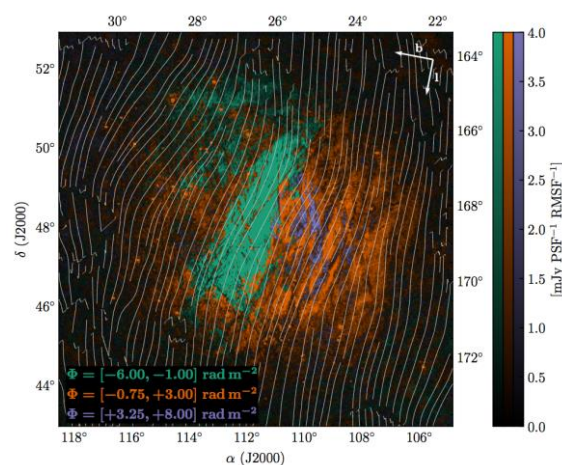
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Nedavna promatranja radioteleskopom LOFAR (eng. low frequency array) otkrila su bogatu morfologiju polariziranog sinkrotronskog zračenja naše galaksije [1]. Otkrivene strukture su raspetljane RM sintezom (eng. rotation measure synthesis), tehnikom u radiopolarimetriji koja razdvaja promatrano polarizirano zračenje prema količini Faradayeve rotacije. To nam onda omogućava proučavanje relativne raspodjele magnetsko-ionske međuzvjezdane tvari (ISM; od eng. interstellar medium) kao funkciju Faradayeve dubine (tzv. Faradayeva tomografija). U ovom izlaganju prezentirat ćemo multifrekvencijsku analizu struktura detektiranih Faradayevom tomografijom u širem području polja 3C196. Najupadljiviji oblici su depolarizirani kanali koje možemo vidjeti u slikama maksimalnog polariziranog intenziteta. Analiza je pokazala da je orijentacija depolariziranih kanala vrlo slična orijentaciji magnetskog polja u ravnini neba i orijentaciji filamenata neutralnog vodika. Poravnanje između ta tri različita sastojka ISM-a nam govori da uređeno magnetsko polje ima važnu ulogu u oblikovanju različitih faza ISM-a. Uz to, polarizirana svjetlost zvijezda korelira s orijentacijom depolariziranih kanala u jednom od promatranih polja (polje B), omogućavajući nam da odredimo granice relativnih udaljenosti do promatranih struktura u Faradayevoj dubini.



Slika 1. Polje A: vizualizacija silnica magnetskog polja u ravnini neba nacrtanih preko Faradayeve emisije iz različitih Faradayevih dubina.

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SYNTHESIS OF C-GLYCOSYL AMINO ACIDS BY POST-CONDENSATION MODIFICATION OF PASSERINI PRODUCTS

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Multicomponent reactions (MCRs) offer an attractive one-pot strategy for generating a library of highly functionalized and complex compounds like glycomimetics. [1] MCRs offer numerous advantages over traditional sequential reactions for the synthesis of diverse structurally demanding compounds. MCRs are applied in the synthesis of small drug-like molecule libraries, but also large and more complex molecules. Isocyanide-based MCRs, particularly Passerini and Ugi reactions, are of special importance, because they provide peptide-like compounds. The utility of the Passerini reaction relies on the mild reaction conditions required for the condensation of a carbonyl compound, a carboxylic acid and an isocyanide to afford peptide-like peptidomimetic products. [2]

The three-component Passerini reaction is a method to convert carbonyl compounds to α -acyloxyamides. [3] Passerini products were synthesized using three different isopropylidene-protected aldehydes (sorbose, galactose and allose derivative) as carbonyl components, amino acid-derived isocyanides (L and D) and acetic acid. Access to highly valuable building blocks, compounds with high degree of structural diversity can be obtained by post-condensation modification of Passerini products. Hydrolysis of Passerini products under basic conditions afforded α -hydroxy C-glycosyl acid derivatives. Further transformations afforded C-glycosyl amino acid dipeptide. Such derivatives are valuable monomers in the synthesis of glycomimetics (Figure 1). Carbohydrates and their derivatives are powerful tools in medicinal chemistry (interaction of proteins and oligosaccharides) and supramolecular chemistry (self-assembly, formation of different types of nanostructures).

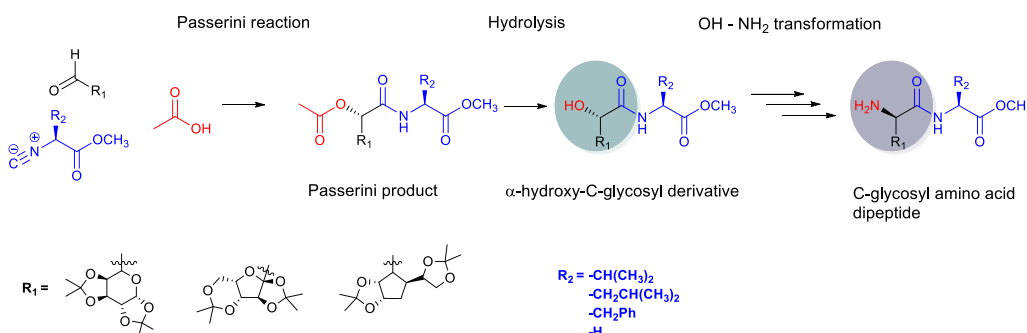


Figure 1. Synthesis to C-glycosyl amino acid derivatives by post-condensation modification of Passerini products.

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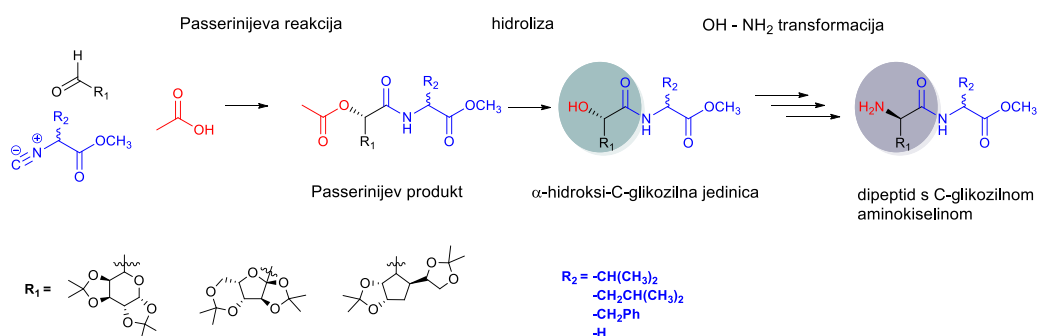
PRIPRAVA C-GLIKOZIL AMINOKISELINA POST-KONDENZACIJSKOM MODIFIKACIJOM PASSERINIJEVIH PRODUKATA

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Višekomponentne reakcije (engl. multicomponent reactions, MCRs) predstavljaju efikasnu metodu za uvođenje kemijskih različitosti i stvaranje biblioteka malih molekula. [1] Osnovni princip MCRs je stvaranje relativno složene strukture iz jednostavnih polaznih spojeva u jednom reakcijskom stupnju. Mnoge MCRs koje se temelje na reakciji izocijanidne skupine (engl. isocyanide-based MCRs - IMCRs) odvijaju se u blagim reakcijskim uvjetima u prisustvu različitih funkcionalnih skupina. Passerinijeva i Ugijeva reakcija su posebno važne reakcije u skupini IMCRs, jer daju peptidima slične produkte-peptidomimetike, koji mogu oponašati strukturu i funkciju prirodnih peptida i proteina. [2] Passerinijevom reakcijom koja uključuje korištenje ugljikohidratnih aldehida dobiveni su α -aciloksi amidi koje nose ugljikohidratnu komponentu direktno vezanu na novi kiralni centar [3]. U Passerinijevoj reakciji kao karbonilna komponenta korišteni su izopropilidenima zaštićeni aldehidi dobiveni iz ugljikohidrata (galaktozni, sorbozni i alozni derivat), aminokiselinski izocijanidi (L i D) te octena kiselina. Post-kondenzacijskim modifikacijama Passerinijevih produkata moguće je pripremiti nove, još složenije strukture. [1] Hidrolizom u baznim uvjetima dobiveni su derivati ugljikohidratnih α -hidroksi kiselina. Daljnjim transformacijama nastaju dipeptidi s C-glikozilnom aminokiselinom. Takvi derivati su vrlo vrijedni monomeri, koji će se koristiti u sintezi peptidomimetika (Slika 1). Ugljikohidratni peptidomimetici imaju potencijalnu primjenu u barem dva područja: medicinska kemija (interakcija proteina i oligosaharida) i supramolekulska kemija (samoudruživanje, formiranje različitih oblika nanostrukture).



Slika 1. Post-kondenzacijska modifikacija Passerinijevih produkata koja daje derivate C-glikozilnih aminokiselina.

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SYNTHESIS AND CHARACTERIZATION OF MACROZONES, NOVEL BIOACTIVE DERIVATIVES OF AZITHROMYCIN

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Macrolides represent a group of antibiotics whose structure is characterized by a macrocyclic lactone ring linked to one or more sugars. Macrolides are bacteriostatic antibiotics, they bind to the 50S subunit of the bacterial ribosome and thus inhibit synthesis of proteins essential for the growth of bacteria. They are effective against Gram-positive and some Gram-negative bacteria. Azithromycin is a semi-synthetic derivative of erythromycin A and belongs to the group of azalides, 15-membered macrolide antibiotics. Azithromycin has excellent pharmacokinetic properties and demonstrates satisfactory biological activity [1]. However, bacterial resistance has emerged due to the frequent use of drugs and there is a need to discover new, more effective antibiotics. As part of this study, macrozones (novel conjugates of azithromycin and thiosemicarbazone) were successfully prepared. Since thiosemicarbazones exhibit antitumor and antibacterial activity [2], they were used to chemically modify azithromycin at three different positions (Figure 1) [3]. Structure and biological activity of macrozones against susceptible and resistant bacterial strains were determined. They showed very good activities against susceptible *S. pneumoniae*, *S. pyogenes* and *E. faecalis* strains, and excellent activity against resistant *S. pneumoniae* and *S. aureus* strains. NMR spectroscopy was used to study interactions of prepared compounds with ribosome and to determine the binding epitopes.

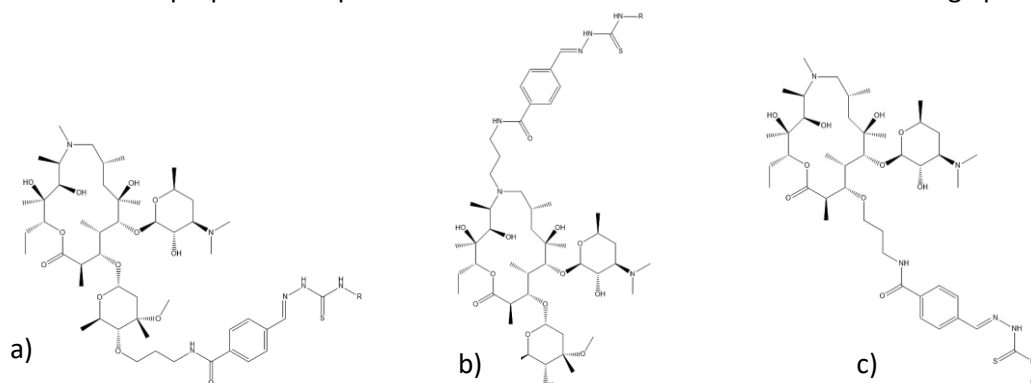


Figure 1. Structures of a) 4''-macrozone, b) 9a-macrozone and c) 3-macrozone.

ACKNOWLEDGMENTS

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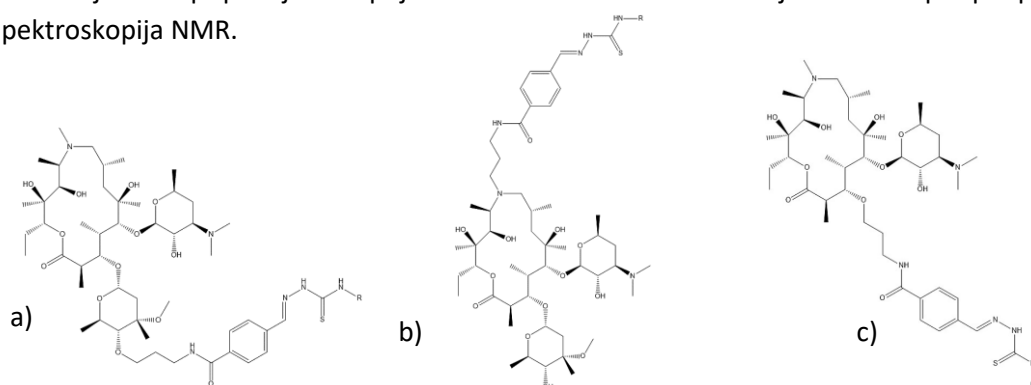
PRIPRAVA I KARAKTERIZACIJA MAKROZONA, NOVIH BIOAKTIVNIH DERIVATA AZITROMICINA

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Makrolidi spadaju u skupinu antibiotika čiju strukturu karakterizira makrociklički laktoski prsten na kojem je vezan jedan ili više šećera. Makrolidi imaju bakteriostatsko djelovanje, vežu se za 50S podjedinicu bakterijskog ribosoma i na taj način sterički sprječavaju sintezu proteina bitnih za rast i razvoj bakterija. Djelotvorni su u liječenju infekcija uzrokovanih Gram-pozitivnim i nekim Gram-negativnim bakterijama. Azitromicin je polusintetski derivat eritromicina A te spada u skupinu azalida, 15-članih makrolidnih antibiotika. Azitromicin ima izvrsna farmakokinetička svojstva i pokazuje zadovoljavajuću biološku aktivnost [1]. Međutim, zbog učestalog i pogrešnog korištenja lijekova došlo je do pojave bakterijske rezistencije te se javlja potreba za otkrićem novih, djelotvornijih antibiotika. U sklopu ovog istraživanja pripremljeni su makrozoni, konjugati azitromicina i tiosemikarbazona. Budući da su tiosemikarbazoni pokazali antitumorsku i antibakterijsku aktivnost [2], korišteni su za kemijsku modifikaciju azitromicina na tri različita položaja (slika 1.) [3]. Pripremljenim makrozonima određena je struktura i biološka aktivnost na susceptibilne i rezistentne bakterijske sojeve. Spojevi su pokazali jako dobru aktivnost na susceptibilne sojeve *S. pneumoniae*, *S. pyogenes* i *E. faecalis*, sličnu ili bolju od azitromicina te izvrsnu aktivnost na rezistentne sojeve *S. pneumoniae* i *S. aureus*. Za istraživanje interakcija novopripremljenih spojeva i ribosoma te određivanje veznih epitopa primjenjena je spektroskopija NMR.



Slika 1. Opća struktura: a) 9a-makrozona, b) 4''-makrozona, i c) 3 makrozona

ZAHVALE

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ANTI-PROLIFERATIVE AND ANGIO-SUPPRESSIVE EFFECT OF RESVERATROL NANOCRYSTALS ON EHRlich ASCITES TUMOR IN MOUSE

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Resveratrol (3,5,4'-trihydroxy-stilbene) is a potential antitumor compound because of his anti-oxidative, anti-inflammatory, anti-angiogenics and anti-proliferation characteristics [1,2]. Due to poor solubility and bioavailability, his potential therapeutic use is very limited [3]. The aim of this research was to investigate effects of resveratrol nanocrystals on fast-growing and angiogenesis-dependent Ehrlich ascites tumour (EAT) in mice. Furthermore, we investigate the relationship between liver and kidney damage levels through histological analysis of the presence of cells in mitosis, apoptosis and necrosis. The tumor was caused by intraperitoneal (i.p.) injection of 2.5×10^6 cells into the abdominal cavity of Swiss albino mice [4]. Treatment of animals with EAT tumor in groups was started the next day by injecting resveratrol or resveratrol nanocrystals at dose of 25 mg/kg every other day for 14 days. The results indicate that resveratrol and resveratrol nanocrystals have an inhibitory effect on tumor cell growth and a protective role in preserving the physiological function of the kidney and liver. Microscopic analysis of the number of blood vessels in the peritoneal sheath confirms the great angi-suppressive potential of resveratrol and its nanocrystals, which in turn leads to inhibition of tumor growth.

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ANTIPROLIFERATIVNI I ANTIANGIOGENI UČINAK NANOKRISTALA RESVERATROLA NA EHRlichOV ASCITESNI TUMOR U MIŠA

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Resveratrol (3,5,4'-trihidroksi-stilben) jest potencijalan protutumorski spoj zbog svoje protuoksidativne, protuupalne, proapoptotičke, antiangiogenetske i antiproliferativne aktivnosti [1,2]. Međutim, njegovu terapijsku primjenu ograničava slaba topljivost i bioraspodivnost [3]. Temeljem navedenog, cilj rada je bio istražiti učinke resveratrola i njegovih nanokristala u dozi od 25 mg/kg na inhibiciju rasta brzo-rastućeg, angiogenski-ovisnog Ehrlichovog ascitesnog tumora (EAT), te istražiti odnos između razine oštećenja jetre i bubrega kroz histološku analizu prisutnosti stanica u mitozu, apoptozu i nekrozu. Tumor smo prouzročili intraperitonealnim (*ip.*) iniciranjem $2,5 \times 10^6$ EAT stanica u trbušnu šupljinu miševa soja Swiss albino [4]. Obrada životinja s EAT tumorom po skupinama započeta je idućeg dana *ip.* iniciranjem resveratrola ili nanokristala resveratrola u dozi od 25 mg/kg svaki drugi dan u periodu od 14 dana. Rezultati ukazuju da resveratrol i nanokristali resveratrola imaju inhibicijski učinak na rast stanica tumora te zaštitnu ulogu u očuvanju fiziološke funkcije bubrega i jetre. Mikroskopska analiza broja krvnih žila u peritonealnoj ovojnici potvrđuje veliki antiangiogeni potencijal resveratrola i njegovih nanokristala što posljedično vodi inhibiciji rasta tumora.

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NOVEL INSIGHTS INTO STRUCTURAL BASIS OF ANTIBIOTIC RESISTANCE IN TYPE II ISOLEUCYL-tRNA SYNTHETASES

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Isoleucyl-tRNA synthetase (IleRS) covalently couples isoleucine, via isoleucyl-adenylate intermediate, to its cognate tRNA^{Ile} in a 2-step aminoacylation reaction. IleRSs cluster into two distinct clades: mupirocin sensitive IleRS1 and mupirocin resistant IleRS2. Mupirocin, a naturally produced antibiotic, binds to the catalytic active site of the enzyme, acting as a competitive inhibitor. The active site resides in the HUP catalytic domain with Rossmann fold topology and is very similar in both IleRS types, despite their different affinity towards mupirocin. Prominent elements of the IleRS active site include conserved amino acid sequences, histidyl-isoleucyl-glycyl-histidine (HIGH) and lysyl-methionyl-seryl-lysyl-serine (KMSKS), which make up structural motifs important for binding of the substrates and the intermediate and in catalysis. The HIGH motif, part of the first helix ($\alpha 1$) of the active site, stabilizes the adenine moiety and phosphate group of the reaction intermediate, whilst the KMSKS motif is part of a flexible loop at the entrance to the active site. To understand the difference in affinity for mupirocin among the two IleRS types, we solved the crystal structures of *Bacillus megaterium* IleRS2 in a complex with the nonhydrolyzable analogue of the reaction intermediate and in a complex with mupirocin. We compared the solved structures with the structure of *Staphylococcus aureus* IleRS1 with bound mupirocin. [1] The comparison revealed that mupirocin binding in IleRS1 and IleRS2, although similar, is not completely analogous. The active site of IleRS1 is compact and preformed for mupirocin binding. On the contrary, binding of mupirocin to the IleRS2 active site is accompanied by the rotational movement of the $\alpha 1$ helix bearing the HIGH motif. This rotation is coupled with energetically disfavoured deformation of additional secondary structure elements in the active site of IleRS2 ($\alpha 2$ helix). The requirement for the $\alpha 1$ - $\alpha 2$ rearrangements might result in a low affinity of the IleRS2 active site towards mupirocin. Analysis of conserved residues in the active site of two IleRS types backs up this hypothesis. The tip of the $\alpha 1$ helix in IleRS2 is flexible due to the lack of a strong hydrogen bond between two sidechains downstream of the HIGH motif in IleRS1. Additionally, in IleRS2, the $\alpha 1$ - $\alpha 2$ helix interface is rich in bulky amino acids, which might necessitate conformational change in the $\alpha 2$ helix following the $\alpha 1$ -helix movement.

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NOVI POGLED NA STRUKTURNE OSNOVE ANTIBIOTSKE OTPORNOSTI IZOLEUCIL-TRNA SINTETAZA TIPA 2

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Izoleucil-tRNA-sintetaza (IleRS) kovalentno veže izoleucin na izoakceptorske tRNA^{le} u dvostupanjskoj reakciji koja se odvija preko adenilatnog intermedijera. Filogenetska analiza dijeli IleRS u dvije kladije: IleRS1 osjetljive na mupirocin i IleRS2 otporne na mupirocin. Mupirocin je prirodni antibiotik koji se veže u aktivno mjesto enzima, djelujući kao kompetitivni inhibitor IleRS. Aktivno mjesto je smješteno u katalitičkoj HUP domeni s Rossmann topologijom, koja je očuvana kod oba tipa IleRS unatoč njihovom različitom afinitetu prema mupirocinu. Najznačajniji elementi aktivnog mjesta IleRS su očuvani aminokiselinski sljedovi, histidil-izoleucil-glicil-histidin (HIGH) i lizil-metionil-seril-lizil-serin (KMSKS), koji grade strukturne motive koji sudjeluju u pozicioniranju supstrata i reakcijskog međuprodukta te u katalizi. Motiv HIGH dio je prve zavojnice aktivnog mjesta ($\alpha 1$) i stabilizira adeninsku jedinicu te fosfatnu skupinu međuprodukta, dok je motiv KMSKS dio fleksibilne omče na ulazu u aktivno mjesto. U cilju rasvjetljavanja razlika u afinitetu dva tipa IleRS prema mupirocinu, riješene su kristalne strukture IleRS2 iz bakterije *Bacillus megaterium* u kompleksu s nehidrolizabilnim analogom reakcijskog međuprodukta te s mupirocinom. Riješene strukture su uspoređene sa strukturom IleRS1 iz bakterije *Staphylococcus aureus* u kompleksu s mupirocinom. [1] Uočeno je da vezivanje mupirocina u aktivno mjesto kod navedena dva tipa IleRS, iako slično, nije potpuno analogno. Aktivno mjesto IleRS1 je kompaktno i preformirano za vezivanje mupirocina s visokim afinitetom. Suprotno tome, vezivanje mupirocina u aktivno mjesto IleRS2 prati rotacija vrha zavojnice $\alpha 1$ s motivom HIGH pri čemu je ta rotacija spregnuta s energetski nepovoljnom deformacijom drugih elemenata sekundarne strukture u aktivnom mjestu IleRS2 (zavojnica $\alpha 2$). Nužnost $\alpha 1$ - $\alpha 2$ rearanžmana mogla bi biti uzrok malog afiniteta IleRS2 prema mupirocinu. Analiza očuvanih pozicija u aktivnim mjestima IleRS1 i IleRS2 potkrjepljuje hipotezu. Vrh zavojnice $\alpha 1$ kod IleRS2 je fleksibilan zbog odsustva vodikove veze bočnih ogranaka očuvanih aminokiselina nizvodno od motiva HIGH, prisutnih kod IleRS1. Također, sučelje interakcije zavojnica $\alpha 1$ i $\alpha 2$ u aktivnom mjestu IleRS2 je bogato sterički zahtjevnim aminokiselinama, zbog čega je konformacijska promjena u zavojnici $\alpha 2$ uslijed pomaka zavojnice $\alpha 1$ očekivana.

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SEMILINEAR EQUATIONS FOR NON-LOCAL OPERATORS: BEYOND THE FRACTIONAL LAPLACIAN

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In this presentation we deal with semilinear equations for non-local operators generated by subordinate Brownian motions. The presentation is based on recent results that can be found in [1,2]. The theory of semilinear equations for Laplacian (which is a local operator) is well-known and has been studied for at least 40 years. The Laplacian commonly arises in many branches of mathematics, and also in many other fields of science such as physics, medicine, economy, etc. In probability theory the Laplacian arises as an infinitesimal generator of the Brownian motion. Hence the solution to the semilinear equation has a nice probabilistic interpretation. However, many phenomena in real life and science need to be modelled by processes with extremely abrupt behavior (such as stock market fluctuations) which is not a characteristic of the Brownian motion. It is natural to model such processes with a discontinuous Markov process, such as a subordinate Brownian motion, which naturally defines a non-local operator through his infinitesimal generator. In our work we deal with operators generated by subordinate Brownian motions and we give necessary (and sufficient) conditions for the existence and uniqueness of a solution of the semilinear equation.

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SEMILINEARNE JEDNADŽBE ZA NELOKALNE OPERATORE: VIŠE OD FRAKCIONALNOG LAPLACEOVOG OPERATORA

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Tema ovog izlaganja su semilinearne jednadžbe za nelokalne operatore generirane subordiniranim Brownovim gibanjem. Izlaganje se temelji na nedavnim rezultatima iz članaka [1,2]. Teorija semilinearnih jednadžbi za Laplaceov operator (koji je lokalnog tipa) dobro je poznata i razvila se u zadnjih 40-ak godina. Laplaceov operator česta je pojava u matematici, ali i u primijenjenim granama znanosti, kao što su fizika, medicina, ekonomija, i sl. U teoriji vjerojatnosti Laplaceov operator je infinitezimalni generator Brownovog gibanja te rješenja jednadžbi za Laplaceov operator imaju lijepu vjerojatnosnu interpretaciju. Međutim, u praksi nam se često nameću prirodni fenomeni koji imaju iznimno isprekidano i skokovito ponašanje (npr. kretanje dionica na burzi) koje odudara od ponašanja Brownovog gibanja. U tim situacijama potrebno je promatrati kompliciranije procese kao što su čisto skokoviti procesi, npr. subordinirano Brownovo gibanje. Takvi procesi prirodno generiraju nelokalne operatore preko svojih infinitezimalnih operatora. U našem radu promatramo operatore dobivene iz subordiniranog Brownovog gibanja te dajemo nužne (i dovoljne) uvjete za postojanje rješenja semilinearnih problema.

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THE ROLE OF BIOLOGICALLY PRODUCED ELEMENTARY SULFUR (S⁰) ON POLYSULPHIDE FORMATION IN THE MARINE EUXINIC ENVIRONMENT (ROGOZNICA LAKE)

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Rogoznica Lake (RL) is a naturally eutrophicated marine lake on the eastern coast of the Adriatic (43°32' N, 15° 58' E) with meromictic and euxinic properties. The main characteristic of the lake is the seasonal thermohaline and chemical stratification of water layers into the upper oxic and lower anoxic layers. Due to intense sulfate reduction, the anoxic layer is rich in dissolved HS⁻ (up to 5 mM). At the oxic-anoxia boundary, a pinkish colored chemocline (up to 50 cm) develops seasonally, and it is characterized by a dense population of purple phototrophic sulfur bacteria (PSB) [1]. PSB are known to store sulfur S(0) intracellularly, which by cell lysis would be released in water, and under euxinic conditions solubilized by HS⁻ in nucleophilic polysulfides, S_x²⁻.

In this work, for the first time in natural samples, differential pulse voltammetry (DPV) was used for direct determination of S_x²⁻ in the euxinic aqueous environment (RL), where concentrations of total reduced sulfur species (RSS) varies between 0.1 and 3 mM (mainly HS⁻). RSS, as well as S_x²⁻ concentrations varied seasonally depending on the chemocline position, light intensity, and HS⁻ concentration. In the summer, when PSB reached maximum abundance, the highest concentrations of S_x²⁻ (up to 0.1 mM polysulfide S(0)) were determined at a depth of about 1 m below the chemocline. Due to sinking of lysed PSB cells, maximum concentration of biologically produced S(0) would be expected at that depth. Vertical mixing usually occurs during autumn or winter when cold, oxygen-rich water from the surface sinks downwards. In such conditions, a dense purple layer of PSB disappears, and S_x²⁻ are not detected. The seasonal dependence of the concentration distribution of S_x²⁻ on physicochemical factors indicates the importance of biologically produced S(0) for the formation and presence of S_x²⁻.

Also, in samples rich in PSB, by acidification procedure used as a standard methodological step [2] in the electroanalytical determination of nonvolatile RSS (RSS_{NV}), an increase in RSS_{NV} concentration of 30-50% was observed. AFM analysis of RL sample with PSB confirmed the presence of intracellular granules of S(0) which are released after cell lysis in induced laboratory conditions by acidification. Released biological S(0) contribute to the RSS_{NV} and the formation of S_x²⁻ in the euxinic layer of RL.

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ULOGA ELEMENTARNOG SUMPORA (S^0) BIOLOŠKOG PORIJEKLA U STVARANJU POLISULFIDA U MORSKOM EUKSINSKOM OKOLIŠU (ROGOZNIČKO JEZERO)

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Rogozničko jezero (RJ) je prirodno eutroficirano morsko jezero na istočnoj obali Jadrana (43°32'N, 15°58'E) s meromiktičnim i euksinskim svojstvima. Glavna karakteristika jezera je sezonsko termohalino i kemijsko raslojavanje vodenog stupca u gornji oksični i donji anoksični sloj. Kao posljedica intenzivne redukcije sulfata, anoksični sloj je bogat otopljenim HS^- (do 5 mM). Na granici oksičnog i anoksičnog sloja, sezonski se formira ljubičasti sloj kemokline (~50 cm), kojeg karakterizira gusta populacija ljubičastih fototrofnih sumpornih bakterija (eng. phototrophic sulfur bacteria, PSB) [1]. PSB unutarstanično pohranjuju $S(0)$, koji se raspadom stanica otpušta u vodeni stupac, te u euksinskim uvjetima s HS^- može stvarati polisulfide (S_x^{2-}).

U ovom radu, po prvi puta u prirodnim uzorcima primijenjena je diferencijalna pulsna voltometrija (DPV) za određivanje S_x^{2-} u euksinskom vodenom okolišu (RJ), u kojem koncentracija ukupnih reduciranih sumpornih specija (RSS) varira od 0.1 do 3 mM (uglavnom u formi HS^-). Koncentracije RSS, kao i koncentracije S_x^{2-} , mijenjaju se sezonski ovisno o poziciji kemokline, intenzitetu svjetlosti i koncentraciji HS^- . U ljetnim mjesecima pri maksimumu abundancije PSB, zabilježene su i najveće koncentracije S_x^{2-} (do 0,1 mM polisulfidnog $S(0)$) na dubini od oko 1 m ispod kemokline. U tom području očekivana je i najveća koncentracija biološki proizvedenog $S(0)$, nastalog uslijed raspada tonućih stanica PSB. Početkom jeseni, sniženjem temperature atmosfere dolazi do hlađenja površinskog sloja RJ obogaćenog kisikom, koji zatim tone, što posljedično dovodi do razbijanja stratifikacije, nestajanja kemokline i miješanja vodenog stupca RJ. U takvim uvjetima nestaje i gusti ljubičasti sloj PSB, te DPV metodom nisu detektirani S_x^{2-} . Sezonska ovisnost raspodjele koncentracija S_x^{2-} o fizikalno-kemijskim čimbenicima ukazuje na važnost biološki proizvedenog $S(0)$ u nastajanju S_x^{2-} . Također, u uzorcima bogatim PSB, postupkom zakiseljavanja koje se koristi kao standardni metodološki korak [2] u elektroanalitičkom određivanju nehlapivih RSS (RSS_{NV}), primijećeno je da dolazi do povećanja koncentracije RSS_{NV} od 30-50%. AFM analizom uzorka RJ s PSB, potvrđeno je prisustvo unutarstaničnih granula $S(0)$ koje se oslobađaju nakon lize stanica u vodeni medij. U našem slučaju liza stanica izazvana je zakiseljavanjem uzorka. Oslobođeni biološki $S(0)$, doprinosi ukupnoj koncentraciji RSS_{NV} i stvaranju S_x^{2-} u euksinskom sloju jezera.

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NEURODEGENERATIVE CHANGES IN THE RAT BRAIN INDUCED BY SEVOFLURANE AND IRON-DEXTRAN

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Inhalation anaesthetics, such as sevoflurane, are commonly used in modern medicine [1]. They are volatile gases that easily diffuse through cell membranes, used as the introduction to anaesthesia or for maintaining it in procedures of unpredictable duration [2]. Aim of this study was to research the effects of sevoflurane, alone or in combination with Fe-dextran, on development of neurodegenerative changes in the rat brain tissue [3][4]. Neurodegeneration was evaluated by: (i) (anti)oxidative status of brain tissue, by measuring the malondialdehyde (MDA) and glutathione (GSH) concentrations, catalase (CAT) and superoxide dismutase (SOD) enzymatic activities; (ii) (anti)genotoxic response in rat lymphocytes, indicating extent of DNA damage; (iii) neuroinflammation, evaluated with relative brain weight compared to healthy control; (iv) toxic effects on haematological and biochemical blood parameters, and osmotic fragility of erythrocytes [5][6]. Results show Fe-dextran causes neuroinflammation and oxidative stress: increases MDA concentration, SOD and CAT activity and decreases GSH. Sevoflurane combined with Fe-dextran causes extensive neuroapoptosis and seemingly low MDA and antioxidant concentrations, with highest blood toxicity and DNA damage [7][8]. In summary, severe neuroinflammation and lipid peroxidation in brain of Fe-dextran treated animals indicate neurotoxicity, whereas combination with sevoflurane causes severe neurodegeneration and permanently affects whole body homeostasis.

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NEURODEGENERATIVNE PROMJENE U MOZGU ŠTAKORA IZAZVANE SEVOFLURANOM I ŽELJEZO-DEKSTRANOM

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Inhalacijski anestetici su lako hlapljive tekućine, a služe za uvod ili održavanje anestezije pri operativnim zahvatima nepredvidljivog trajanja [1][2]. U ovom radu proučavan je utjecaj sevoflurana, samog ili združenog s željezo-dekstranom, na nastanak i razvoj neurodegenerativnih promjena na tkivu mozga štakora [3][4]. Neurodegeneracija je mjerena: (i) promjenama oksidacijskog statusa mjerenjem razine malondialdehida (MDA), glutationa (GSH), te enzimatske aktivnosti katalaze (CAT) i superoksid dismutaze (SOD); (ii) (anti)genotoksičnog odgovora u limfocitima štakora, pokazujući razinu oštećenja DNA; (iii) procjenom razine neuroupale prema relativnoj težini mozga u odnosu na zdravu kontrolu; (iv) procjenom toksičnog učinka na hematološke i biokemijske odrednice u krvi, te osmotsku fragilnost eritrocita [5][6]. Rezultati pokazuju da željezo-dekstran uzrokuje značajnu neuroupalu, te povećanu razinu oksidacijskog stresa: povećava razinu MDA, mijenja aktivnosti antioksidativnih enzima (SOD, CAT) i snižava GSH. Sevofluran u kombinaciji sa Fe-dekstranom pokazuje izraženi gubitak moždanih stanica i prividno niske razine MDA te antioksidansa, kao i značajne toksične učinke na krvne odrednice. Komet test pokazuje najveća oštećenja DNA limfocita pri izlaganju sevofluranu združenim sa željezo-dekstranom [7][8]. Temeljem rezultata može se zaključiti kako jaka neuroupala i pojava lipidne peroksidacije u mozgu životinja obrađenih Fe-dekstranom ukazuju na neurotoksičnost, dok kombinacija sa sevofluranom uzrokuje najteža oštećenja mozga i trajno narušava homeostazu organizma.

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MORPHOLOGICAL CHANGES OF THE ISLAND OF HVAR BEACHES FROM 1834 TO PRESENT DAY

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Beaches are dynamic geomorphological features which are very sensitive to climate change as well as socio-economic activities. Therefore, beaches became a common research topic along the Eastern Adriatic Coast, both in its northern [1] and in its southern part [1],[2]. On the island of Hvar, according to the previous research, the tendency of beach erosion has been observed [3]. In this work, the evolution of beaches was studied in three different points in time: the beginning of the 19th century, middle of 20th century, and in 2020. Three beaches have been analyzed: Lučišće and Mola Milna gravel beaches and Mina, a sand beach formed in aeolian deposits.

The first studied period relates to the beginning of the 19 century. We used the Franciscan Cadastre from the 1834 where each beach is represented by an individual cadastral parcel. The map was georeferenced, digitized, and analyzed in ArcGIS Pro software. The Cadastral Supplement also provides their surface areas in the Klafter Quadrimeter units. The second period was studied by repeat photography method first applied to beaches near Omiš [2]. 7-12 old photographs (between 1910 and 1980) have been obtained for each beach. Using the benchmarks from the photographs the size of the beaches was further estimated. The method is not precise, however, it can provide a reliable estimation of the beach area for the time when it was taken. The recent period was studied by means of UAV method. Beaches were recorded by DJI Phantom 4 Pro v2 in November 2020. Six ground control points were measured on each beach with Trimble GNSS. Precise orthomosaic, Digital surface model, and Digital terrain model were generated in ESRI Drone2Map software and all analyses were done in ArcGIS Pro software.

It was found that Lučišće beach from 1838 m² in 1834 reduced to 1018 m² in 2020; Mina beach from 799 m² to 226 m², and Mola Milna from 1073 m² to 802 m². Consequently, since 1834, the sand beach Mina, reduced in size by 72% while the gravel beaches Lučišće and Mola Milna by 45% and 27% respectively. The analyzes showed that the surface areas of all three beaches decreased during the last ~200 years.

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MORFOLOŠKE PROMJENE ŽALA OTOKA HVARA OD 1834. DO DANAS

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Žala su dinamični geomorfološki oblici, osjetljivi na klimatske promjene, kao i na socio-ekonomske aktivnosti. Danas su sve češća istraživačka tema duž istočne obale Jadrana, kako na njegovom sjevernom dijelu [1], tako i na južnom [1], [2]. Na otoku Hvaru, prema dosadašnjim istraživanjima, uočena je tendencija erozije žala [3]. U ovom radu, promjene žala istražene su kroz 3 različita razdoblja: početak 19. stoljeća, sredina 20. stoljeća i 2020. godina. Analizirana su tri žala: šljunčana žala Lučišće i Mola Milna, te Mina pješćano žalo oblikovano u sedimentima eolskog podrijetla.

Prvo razdoblje odnosi se na početak 19. stoljeća, za koje je korišten Franciskanski katastar iz 1834. godine, u kojem je svako žalo ucrtano kao zasebna katastarska čestica. Katastar je georeferenciran, digitaliziran i analiziran u software-u ArcGIS Pro. Također, korišten je i zapisnik čestica koji sadrži površine žala zapisane u četvornim hvatovima. Drugo razdoblje istraženo je uz pomoć metode ponovljene fotografije, koja je prvi put primijenjena na širem području Omiša [2]. Prikupljeno je 7-12 starih fotografija (od 1910. do 1980. godine) za svako žalo. Koristeći repere sa starih fotografija, procijenjena je površina. Iako metoda nije precizna, daje pouzdanu procjenu površine žala iz vremena kada su snimljene fotografije. Recentno razdoblje istraženo je pomoću bespilotne letjelice. Žala su snimljena s DJI Phantom 4 pro v2.0 u studenom 2020. godine. Trimble GNSS uređajem izmjereno je 6 kontrolnih točaka na svakom žalu. U ESRI Drone2Map software-u generirani su ortomozaik, digitalni model reljefa i digitalni model površina, a sve analize su rađene u ArcGIS Pro software-u.

Utvrđeno je da se žalo Lučišće, s 1838 m² izmjerenih 1834. godine smanjilo na 1018 m² 2020. godine; žalo Mina sa 799 m² na 226 m² i Mola Milna s 1073 m² na 802 m². Posljedično, od 1834., pješćano žalo Mina se smanjilo za 72%, dok su se šljunčana žala Lučišće i Mola Milna smanjili za 45%, odnosno 27%. Analiza je pokazala da su se površine svih triju žala tijekom posljednjih ~200 godina znatno smanjile.

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PERFORMANCE OF THE ADRIATIC SEA AND COAST CLIMATE SIMULATION: OCEAN

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Adriatic Sea and Coast (AdriSC) is a high-resolution atmospheric-ocean model [1] covering the Adriatic and northern Ionian Sea. It was developed with the aim to represent the processes driving the atmospheric and oceanic circulations at different temporal and spatial scales. Further possible applications of the model include extreme event hazard assessment, ecosystem modelling, sediment and larvae transport and others. To quantify climate properties of the Adriatic, 31-year long evaluation run was performed for the 1987-2017 period. The results of ROMS 3-km and 1-km ocean models were first validated on a comprehensive collection of observational data retrieved from available *in situ* measurements and remote-sensing gridded products. Several statistical methods were used in the evaluation of three modelled properties: (i) sea-surface (sea-surface height and temperature), (ii) thermohaline parameters (temperature and salinity) and (iii) dynamical parameters (ocean current speed and direction), quantifying the reliability of the AdriSC ocean model in reproducing the quoted properties, which is a prerequisite for in-depth assessment of processes occurring in the Adriatic-Ionian basin.

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EVALUACIJA KLIMATSKE SIMULACIJE „ADRIATIC SEA AND COAST“: MORE

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Adriatic Sea and Coast (AdriSC) je atmosfersko-oceanski model visoke razlučivosti [1] čije domene prekrivaju Jadransko i sjeverno Jonsko more. Razvijen je s ciljem reprodukcije procesa koji pokreću atmosfersku i oceansku cirkulaciju na različitim vremenskim i prostornim skalama. Daljnje moguće primjene modela uključuju procjene opasnosti od ekstremnih događaja, modeliranje ekosustava, modeliranje transporta sedimenta i ličinki, i drugo. Da bi se opisala klimatska svojstva jadranskog bazena izvršena je 31-godišnja simulacija AdriSC modelom za razdoblje od 1987. do 2017. godine. U svrhu procjene vjerodostojnosti simulacije napravljena je usporedba rezultata oceanskih modela ROMS 3-km i ROMS 1-km s opsežnom bazom podataka prikupljenih iz dostupnih *in situ* mjerenja i satelitskih produkata. U evaluaciji triju modeliranih svojstava: (i) površine mora (visina i temperatura površine mora), (ii) termohalinih parametara (temperatura i salinitet) i (iii) dinamičkih parametara (brzina i smjer morskih struja) korišteno je nekoliko statističkih metoda. Time je kvantificirana sposobnost AdriSC oceanskog modela u reproduciranju navedenih svojstava, što je preduvjet za daljnju analizu pojedinih procesa u jadransko-jonskom bazenu.

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THE INFLUENCE OF HELPER T LYMPHOCYTES ON THE SURVIVAL OF PATIENTS DIAGNOSED WITH FOLLICULAR LYMPHOMA

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Follicular lymphoma (FL) is the second most frequent non-Hodgkin's lymphoma (NHL). It originates from germinal centre B lymphocytes packed in follicles that disrupt the normal structure of lymph nodes [1]. One of the factors that influence the survival of the patients and the progression of FL is the contents of tumour microenvironment (TME) [2]. CD4+ helper T lymphocytes are one of the components of TME that affect the development and progression of the disease. These cells can also express other antigens on their membranes, such as CD69, marker of activated T lymphocytes, and CD57, marker of cells that display a so-called "exhausted" phenotype [3].

The goal of this research was to explore the effect of helper T lymphocytes of various phenotype (activated and exhausted) on the survival of the patients diagnosed with FL. Antigens CD4, CD57 and CD69 were detected by immunohistochemical staining on formalin-fixed, paraffin-embedded tumour tissue samples from 65 patients. After the evaluation of stained slides, Chi-square test and Spearman's rho correlation were used to determine association between the variables.

The results showed that the overall survival of the patients was significantly better in cases where the tumour tissue was infiltrated with a lower number of CD4+ cells, CD57+ cells and CD69+ cells compared to the number of these cell populations in the germinal centre in a non-tumour control tonsil. There was no difference in survival of the patients when the presence of these antigens was observed separately compared to when the presence of all three antigens was observed simultaneously. These results suggest that the activated T lymphocytes which infiltrate tumour tissue in time begin to display exhausted phenotype and lose their ability to successfully battle tumour cells.

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UTJECAJ POMOĆNIČKIH LIMFOCITA T NA PREŽIVLJENJE PACIJENATA S DIJAGNOZOM FOLIKULARNOG LIMFOMA

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Folikularni limfom je drugi najčešći non-Hodgkinov limfom. Podrijetlo ovog limfoma su limfociti B germinalnog centra smješteni u folikule koji narušavaju strukturu limfnog čvora [1]. Jedan od faktora koji utječe na preživljenje pacijenata i progresiju folikularnog limfoma je sastav tumorskog mikrookoliša [2]. Pomoćnički CD4+ limfociti T su jedna od komponenti imunskog sustava koja utječe na razvoj i napredovanje bolesti. Ove stanice mogu na membranama eksprimirati i antigene CD69, koji označava aktivirane limfocite T, i CD57, specifičan za stanice koje pokazuju tzv. „iscrpljeni“ fenotip [3]. Cilj ovog istraživanja bio je istražiti utjecaj pomoćničkih limfocita T različitog fenotipa (iscrpljenog i aktiviranog) na preživljenje pacijenata s dijagnozom folikularnog limfoma. Na uzorcima tumorskog tkiva fiksiranim formalinom i uklopljenim u parafin imunohistokemijskim bojenjem detektirani su antigeni CD4, CD57 i CD69 kod 65 pacijenata. Nakon detekcije i evaluacije signala na uzorcima tkiva, povezanost varijabli određena je χ^2 -testom i Spearmanovom rho korelacijom.

Ustanovljeno je da je ukupno preživljenje pacijenata značajno bolje ukoliko je tumorsko tkivo infiltrirano s manjim brojem CD4+ stanica, CD57+ stanica i CD69+ stanica u odnosu na količinu tih populacija stanica u germinativnom centru tonzile, neovisno o tome promatra li se prisutnost pojedinog markera ili istovremena prisutnost sva tri markera. Ovakvi rezultati sugeriraju da aktivirani limfociti T koji infiltriraju tumorsko tkivo s vremenom počinju pokazivati iscrpljeni fenotip i gube sposobnost uspješne kontrole tumorskih stanica.

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PREPARATION AND CHARACTERIZATION OF POLYELECTROLYTE NANOFILMS

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Polyelectrolytes are macromolecules, usually polymers, with a substantial portion of the constitutional units containing ionic or easily ionizable functional groups. Examples of such macromolecules are PAH – poly(allylamine hydrochloride) and PAA – poly(acrylic acid) whose chemical structures are shown in Figure 1. By alternating adsorption of positively and negatively charged polyelectrolytes on a solid surface, polyelectrolyte multilayers are formed. With this layer-by-layer method [1], nanofilms of desired properties can be designed very precisely. It is for this reason that these nanomaterials have been increasingly researched so that they can be used, for example, in the antibacterial protection of implants [2]. The most commonly used model substrate for the formation of polyelectrolyte films is a silicon wafer on the surface of which a thin oxide layer spontaneously forms. [3]. Therefore, in the first phase of this study, the characterization of the silicon substrate was performed, in order to monitor and investigate the formation of PAH/PAA polyelectrolyte multilayer on substrate in the second phase. Of the numerous methods used, only ellipsometry and atomic force microscopy will be singled out here. By using an ellipsometer, it was determined that there is a layer of oxide about 2 nm thick on the surface of silicon. After that the thickness of the PAH/PAA multilayer during its formation was monitored by the same method. In the end, imaging the surface of the pure substrate and the film-covered substrate with an atomic force microscope provided information on the morphology and surface roughness of the samples, the coverage of the substrate surface with the polyelectrolyte multilayer, and the thickness of the ultrathin film itself.

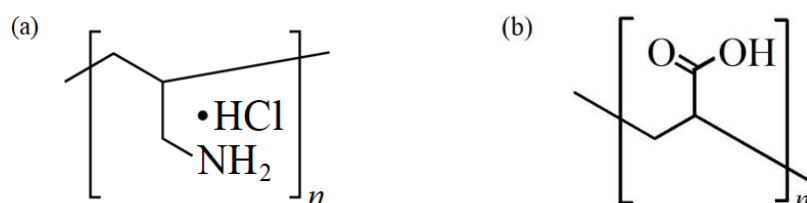


Figure 1. Structure of (a) poly(allylamine hydrochloride) and (b) poly(acrylic acid).

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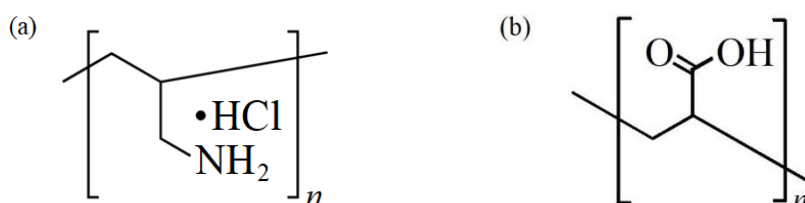
PRIPRAVA I KARAKTERIZACIJA POLIELEKTROLITNIH NANOFILMOVA

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Polielektroliti su makromolekule, najčešće polimeri, kod kojih je prisutan znatan udio gradivnih jedinica koje sadrže ionske ili lako ionizirajuće funkcionalne skupine. Primjeri takvih makromolekula su PAH – poli(alilamin hidroklorid) i PAA – poli(akrilna kiselina) čije su kemijske strukture prikazane na slici 1. Naizmjeničnom adsorpcijom pozitivno i negativno nabijenih polielektrolita na neku čvrstu površinu nastaju polielektrolitni višeslojevi. Ovakvom sloj-po-sloj metodom [1] se mogu veoma precizno dizajnirati nanofilmovi željenih svojstva. Upravo se zbog tog razloga ovi nanomaterijali sve intenzivnije istražuju kako bi se mogli primijeniti primjerice kod antibakterijske zaštite implantanta [2]. Najčešće korišteni modelni supstrat za formiranje polielektrolitnih filmova je pločica silicija na čijoj površini spontano nastaje tanki oksidni sloj [3]. Stoga se u prvoj fazi ove studije provela karakterizacija podloge od silicija, kako bi se u drugoj fazi pratilo i istražilo formiranje PAH/PAA polielektrolitnog višesloja na navedenom supstratu. Od brojnih metoda koje su korištene, ovdje će biti izdvojene samo elipsometrija i mikroskopija atomskih sila. Primjenom elipsometra određeno je da se na površini silicija nalazi oko 2 nm debeli sloj oksida. Potom je istom metodom praćena debljina PAH/PAA višesloja tijekom njegovog formiranja. I na kraju, snimanjem površine čistog supstrata i supstrata prekrivenog filmom mikroskopom atomskih sila dobile su se informacije o morfologiji i hrapavosti površine uzoraka, o prekrivenosti površine supstrata polielektrolitnim višeslojem i o debljini samog ultratankog filma.



Slika 1. Struktura (a) poli(alilamin hidroklorida) i (b) poli(akrilne kiseline).

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IDENTIFICATION, FUNCTION AND INTRACELLULAR LOCALIZATION OF SPONGE HOMOLOG OF HUMAN METASTASIS SUPPRESSOR DRG1

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Sponges (Porifera) are among the simplest multicellular organisms. They possess no real tissues or organs, and are evolutionary almost unchanged since their appearance [1]. Despite having a simple morphology with only a few cell types, sponges possess a "rich" genome containing many genes/proteins similar to their vertebrate homologs, including those that are related to cancer [2, 3]. Thus, sponges represent a good model for studying the evolution of proteins that are linked to cancer [4]. Cancer is a disease of multicellular organisms that is caused by mistakes within the multicellular system, leading to the proliferation of the „selfish“ cell lines. Our research focus is the investigation of evolutionary conserved proteins linked with cancer in humans, such as the metastasis suppressor Developmentally Regulated GTP Binding Protein 1 (DRG1) [5]. Our bioinformatics and phylogenetic analyses showed that DRG1 is conserved across animals. Since DRG1 activity is enhanced by Zinc Finger CCCH-Type Containing protein 15 (LEREPO4) [6], both proteins from sponge as well as their human homologs were cloned and overexpressed in *E. coli*. We confirmed GTPase activity of both sponge and human DRG1 proteins. In addition, transfection of human tumour cells revealed the intracellular localization of both sponge and human DRG1 and LEREPO4 proteins. Further biochemical and biological analyses are ongoing.

Our results will provide a better understanding of the intracellular processes related to the metastasis suppression and pathology of cancer and metastasis.

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IDENTIFIKACIJA, FUNKCIJA I UNUTARSTANIČNA LOKALIZACIJA SPUŽVINOG HOMOLOGA LJUDSKOG SUPRESORA METASTAZIRANJA DRG1

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Spužve (Porifera) su jedne od najjednostavnijih životinja koje ne posjeduju pravo tkivo niti organe te su evolucijski očuvane [1]. Jednostavne su morfologije, građene su od nekoliko tipova stanica, ali posjeduju složen genom sa mnoštvom gena koji pokazuju visoku sačuvanost s homolozima kod kralješnjaka, uključujući i gene povezane s patologijom raka [2, 3]. Stoga spužve predstavljaju dobar modelni organizam za istraživanje gena uključenih u nastanak raka u ljudi [4]. Rak je patološko stanje povezano s pojavom višestaničnosti, čiji su uzrok nastanka „greške“ koje dovode do proliferacije „sebičnih“ staničnih linija. Naš cilj je istraživanje evolucijski očuvanih proteina povezanih s nastankom raka, kao što je supresor metastaziranja DRG1 (od engl. *Developmentally Regulated GTP Binding Protein 1*) [5]. Bioinformatičkim i filogenetskim analizama pokazali smo da je protein DRG1 evolucijski očuvan kod Metazoa. S obzirom da aktivnost proteina DRG1 pojačava protein LEREPO4 (od engl. *Zinc Finger CCCH-Type Containing protein 15*) [6], oba proteina i njihovi homolozi iz čovjeka su klonirani i prekomjerno eksprimirani u *E. coli*. Potvrđena je intrinzična GTP-azna aktivnost spužvinog i ljudskog proteina DRG1. Transfekcijom ljudskih tumorskih stanica pokazali smo unutarstaničnu lokalizaciju spužvinih i ljudskih proteina DRG1 i LEREPO4. Daljnje biokemijske i biološke analize su u tijeku. Naše istraživanje pridonijet će boljem razumijevanju unutarstaničnih procesa supresije metastaziranja, kao i same patologije raka i metastaza.

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TOPOLOGICALLY FRUSTRATED SPIN CHAINS

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In quantum many-body systems with local interactions, the effects of boundary conditions are considered to be negligible, at least for sufficiently large systems. We show examples of the opposite by considering spin-1/2 chains which contain antiferromagnetic interactions and are set on a ring with an odd number of sites – a setting inducing topological frustration. In particular, we focus on the exactly solvable quantum XY chain and other spin chains which possess a global SU(2) symmetry, a quite general condition in the absence of external magnetic fields. We find that topological frustration can destroy local order, create a site-dependent magnetization which varies in space with an incommensurate pattern and induce a quantum phase transition.

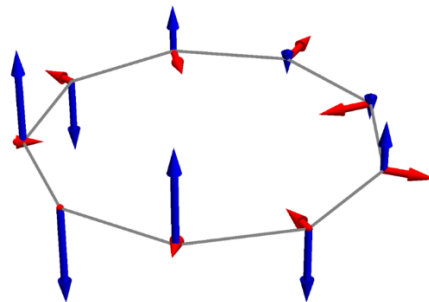


Figure 1. Incommensurate antiferromagnetic order.

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SPINSKI LANCI FRUSTRIRANI TOPOLOGIJOM

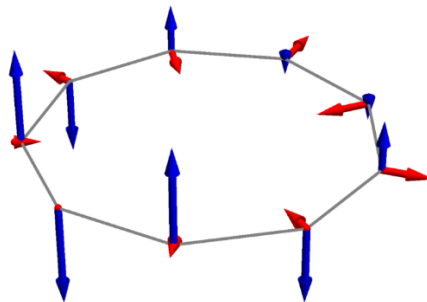
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U višestručnim kvantnim sustavima s lokalnim interakcijama efekti rubnih uvjeta smatraju se zanemarivim, barem u dovoljno velikim sustavima. Mi pokazujemo primjere suprotnog, razmatrajući lance spinova-1/2 koji sadrže antiferomagnetske interakcije i neparan broj čestica te koji su postavljeni na prsten – postavke koje stvaraju topološku frustraciju. Fokusiramo se na egzaktno rješiv XY lanac i druge spinske lance koji posjeduju globalnu SU(2) simetriju, što je poprilično općenito zadovoljen uvjet u odsustvu magnetskih polja. Pronalazimo da topološka frustracija može uništiti lokalno uređenje, stvoriti magnetizaciju koja ovisi o mjestu u rešetci i varira u prostoru, te stvoriti kvantni fazni prijelaz.



Slika 1. Antiferomagnetsko uređenje koje ovisi o mjestu u rešetci i varira u prostoru.

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APPLICATION OF FORAMINIFERAL ASSEMBLAGES IN RESEARCH OF MIOCENE DEPOSITS FROM HRVATSKO ZAGORJE

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Foraminifera are single-celled organisms that live like benthos or plankton and inhabit all seas and oceans, but also brackish and fresh waters. They have great application in geology because their fossil finds are very common, and are significant for biostratigraphy, paleoecology, paleoceanography, and paleoclimatology. During the Middle Miocene area of today's Hrvatsko Zagorje, it was part of the intercontinental sea Paratethys, which extends over a larger area of today's Europe and Asia. Field research and sampling of sediments it was done in the western part of Hrvatsko Zagorje, at five locality: Krapinske Toplice, Razvor, Grešna Gorica, Gaber and Hušnjakovo in Krapina. Sediment samples were processed by method of wet sieving with the intention of isolating whole microfossils. Examination of the microfossil material revealed that the samples from the Razvor and Grešna Gorica locality were suitable for the analysis of foraminiferal assemblages. Due to the poor preservation of fossil record, all analyzes were made at the genus level, and in standardized samples (300 randomly selected individuals), it was analyzed: plankton/benthos (B/P) ratio [1], dominant and common genus, their paleoecological requirements (depth range, infaunal/epifaunal ratio) based on the principle of actualism and bottom water oxygen concentration [2]. At the Razvor locality, infaunal forms of benthic foraminifera predominate and 12 genera were determined, of which the most represented genera are *Gyroidina*, *Nonion*, *Melonis* and *Bolivina*. A high percentage of planktonic foraminifera within the foraminiferal assemblage (more than 80%) indicates a deep-sea marine environment and this is confirmed by the depth ranges of the genera of benthic foraminifera, which indicate a palaeo-depth of up to 180 meters with highly oxic conditions prevailed. At the Grešna Gorica locality, the foraminiferal assemblages lived in a shallow marine environment (planktonic foraminifera have not been recorded, depth ranges of benthic foraminifera indicate depths up to 50 meters). A total of 10 benthic foraminifera genera were identified, of which typical shallow-water genera are dominant *Elphidium*, *Ammonia* and *Porosonion*. Within the assemblage, epifaunal forms predominate and highly oxic condition prevailed at the seabed.

ACKNOWLEDGMENTS

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PRIMJENA FORAMINIFERSKIH ZAJEDNICA U ISTRAŽIVANJU MIOCENSKIH NASLAGA ODABRANIH LOKALITETA HRVATSKOG ZAGORJA

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Foraminifere su jednostanični organizmi koje žive kao bentos ili kao plankton te nastanjuju sva mora i oceane, ali također i bočate i slatke vode. Imaju veliku primjenu u geologiji jer su njihovi fosilni nalazi vrlo česti, te su značajni za biostratigrafiju, paleoekologiju, paleoceanografiju i paleoklimatologiju. Tijekom srednjeg miocena područje današnjeg Hrvatskog zagorja bilo je dio interkontinentalnog Paratethys mora, koje se rasprostiralo na većem području današnje Europe i Azije. Terensko istraživanje i uzorkovanje sedimenata je obavljeno u zapadnom dijelu Hrvatskog zagorja, na pet lokaliteta: Krapinske Toplice, Razvor, Grešna Gorica, Gaber i Hušnjakovo u Krapini. Uzorci sedimenata su obrađeni klasičnom metodom muljenja s namjerom da se izdvoje cijeli mikrofosili. Pregledom mikrofosilnog materijala utvrđeno je da su uzorci s lokaliteta Razvor i Grešna Gorica bili pogodni za analizu foraminiferskih zajednica. Zbog loše očuvanosti fosilnih kućica sve analize napravljene su na nivou rodova, a u standardiziranim uzorcima (300 nasumično odabranih jedinki) razmatran je: odnos plankton/bentos [1], dominantni i srednje zastupljeni rodovi bentičkih foraminifera te njihovi paleoekološki zahtjevi (dubinski rasponi, način života, način ishrane) temeljeni na principu aktualizma [1], te količina kisika pri morskom dnu - indeks kisika bentičkih foraminifera [2]. Na lokalitetu Razvor prevladavaju infaunalni oblici bentičkih foraminifera, a određeno je 12 rodova od kojih su najzastupljeniji rodovi *Gyroidina*, *Nonion*, *Melonis* i *Bolivina*. Visoki udio planktonskih foraminifera unutar foraminiferske zajednice (više od 80%) ukazuje na dubokovodni marinski okoliš, a to potvrđuju i dubinski rasponi rodova bentičkih foraminifera koji ukazuju na dubinu do 180 metara. Na morskom dnu su vladali visoko oksični uvjeti. Na lokalitetu Grešna Gorica foraminiferska zajednica je obitavala u plitkovodnom marinskom okolišu (planktonske foraminifere nisu zabilježene, dubinski rasponi bentičkih foraminifera ukazuju na dubinu do 50 metara). Ukupno je određeno 10 rodova bentičkih foraminifera od kojih su dominantni tipični plitkovodni rodovi *Elphidium*, *Ammonia* i *Porosonion*, Unutar zajednice prevladavaju epifaunalni oblici, a na morskom dnu su vladali visoko oksični uvjeti.

ZAHVALE

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HUMAN PAPILLOMAVIRUS IN NON-SMALL CELL LUNG CANCER WITH *EGFR* GENE MUTATIONS

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Activating mutations/deletions in the epidermal growth factor receptor (*EGFR*) gene are present in 15% of patients diagnosed with non-small cell lung cancer (NSCLC). Exon 19 deletions and codon 858 point mutations of exon 21 are the most common mutations in NSCLC. The presence of point mutations, deletions and insertions within exons 18 - 25 is responsible for a poor response to tyrosine kinase inhibitors. Types 16 and 18 of human papillomavirus (HPV) are considered to be of high risk for cervical cancer development and progression. The aim of this study was to determine the prevalence of HPV infection in NSCLC cells in relation to the presence and frequency of *EGFR* gene mutations. In this study, 34 NSCLC samples with *EGFR* gene mutations and 33 NSCLC samples without *EGFR* gene mutations were analyzed. Furthermore, *EGFR* gene mutations were divided into classical (ex19del; L858R) and rare (G719X; ex20ins; S768I; T790M and ex21). Fragments of the *E7* gene were amplified by PCR for HPV16 and HPV18 DNA detection. The possible higher prevalence of HPV infection in NSCLC patients with *EGFR* mutations, compared to NSCLC patients without *EGFR* mutations, was examined by meta-analysis using data from this and six other studies.

More frequent HPV infection was observed in the NSCLC with *EGFR* gene mutations (HPV16, n=11, p<0.05; HPV18, n=24, p<0.001) compared to the NSCLC without *EGFR* gene mutations. Significant association between smoking and HPV16 infection was observed (p<0.028) in the NSCLC with *EGFR* gene mutations. Among 34 NSCLC samples, 46 mutations in the *EGFR* gene were detected. Classical *EGFR* gene mutations were detected in 20 (58.8%) NSCLC samples and rare mutations in five (14.7%) samples. Nine (26.5%) NSCLC samples had a combination of classical and rare *EGFR* gene mutations. The significant association between the presence of rare *EGFR* gene mutations and HPV16 and/or HPV18 infection (p<0.05) was observed. A meta-analysis confirmed more frequent HPV infection in the NSCLC with *EGFR* gene mutations. The obtained results indicate the need for further research into the role of HPV in the pathogenesis of NSCLC with *EGFR* gene mutations.



LJUDSKI PAPILOMA VIRUS KOD KARCINOMA PLUĆA NEMALIH STANICA S MUTACIJAMA GENA *EGFR*

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Aktivirajuće mutacije/delecije gena *EGFR* prisutne su kod 15% bolesnika s dijagnosticiranim karcinomom pluća nemalih stanica (NSCLC, od eng. *non-small cell lung cancer*). Najčešće mutacije kod NSCLC su delecije eksona 19 i točkasta mutacija kodona 858 u eksonu 21. Točkaste mutacije, delecije i insercije eksona 18 - 25 su odgovorne za loš odgovor na liječenje inhibitorima tirozinske kinaze. Tipovi 16 i 18 ljudskog papiloma virusa (HPV, od eng. *human papillomavirus*) se smatraju visoko rizičnim za nastanak i razvoj karcinoma vrata maternice. Cilj ovog istraživanja bio je utvrditi učestalost infekcije HPV-om u stanicama NSCLC-a u odnosu na prisutnost i učestalost mutacija gena *EGFR*. Analizirana su 34 uzorka NSCLC s dokazanom mutacijom gena *EGFR* i 33 uzorka NSCLC kod kojih nije dokazana mutacija gena *EGFR*. Mutacije gena *EGFR* su dalje podijeljene na klasične (ex19del; L858R) i rijetke (G719X; ex20ins; S768I; T790M i ex21). Metodom lančane reakcije polimerazom (PCR, od eng. *polymerase chain reaction*) su umnažani fragmenti gena *E7* za detekciju DNA HPV16 i HPV18. Moguća veća prevalencija infekcije HPV-om kod NSCLC bolesnika s *EGFR* mutacijama, u usporedbi s NSCLC bolesnicima bez *EGFR* mutacija, ispitana je meta-analizom koristeći podatke iz ove i drugih šest studija. Češća infekcija HPV-om je dokazana kod skupine NSCLC s mutacijama gena *EGFR* (HPV16, n=11, p<0,05; HPV18, n=24, p<0,001) u odnosu na skupinu NSCLC bez mutacija. U skupini NSCLC s mutacijama gena *EGFR* je dokazana statistički značajna povezanost između pušenja i HPV16 infekcije (p<0,028). Kod 34 uzorka NSCLC dokazano je 46 mutacija gena *EGFR*. Kod 20 (58,8%) uzoraka NSCLC su bile prisutne klasične *EGFR* mutacije, a kod pet (14,7%) uzoraka, rijetke mutacije. Kod devet (26,5%) uzoraka NSCLC se radilo o kombinaciji klasičnih i rijetkih mutacija gena *EGFR*. Dokazana je statistički značajna povezanost između prisutnosti rijetkih mutacija gena *EGFR* i HPV16 i/ili HPV18 infekcije (p<0,05). Meta-analiza je potvrdila učestaliju infekciju HPV-om u stanicama NSCLC s mutacijama gena *EGFR*. Dobiveni rezultati ukazuju na potrebu za daljnjim istraživanjima uloge HPV-a u patogenezi NSCLC s mutacijama gena *EGFR*.

**Mikro izlaganja i poster
Flash presentations and posters**



MULTIPLE STRESSOR EFFECTS ON STREAM AQUATIC INSECTS: INSIGHTS FROM A MICROCOSM EXPERIMENT

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Anthropogenic impact and climate change leave a mark on biodiversity and natural resources. Freshwater ecosystems are biodiversity hotspots, a source of drinking water and food for humans, and as such are particularly vulnerable to environmental stressors [1]. Due to increased urbanization and wastewater discharges, freshwater ecosystems are contaminated with various pollutants such as pharmaceuticals, personal care products, pesticides and even hormones [2]. Although the effects of individual stressors on species or populations have been relatively well researched, the understanding of multiple stressors impacts is lacking. Different stressors can interact in many ways, additively, antagonistically, synergistically, thus affecting freshwater ecosystems [1]. The aim of the current study was to investigate the single and combined effects of emerging contaminants (ECs) and elevated temperatures on freshwater invertebrates. We conducted the microcosm experiment with a simplified freshwater food web containing moss and caddisfly larvae (*Micropterna nycterobia*, Trichoptera). Caddisfly larvae, water and moss were collected in spring from temporary river Krčić. After acclimatization, the individuals were assigned randomly to the aquariums according to treatment: a) mixture of ECs; pharmaceuticals (PhACs) and endocrine disrupting compounds (EDCs), b) elevated temperature, c) elevated temperature and mixture of ECs, and d) control. Sampling included initial and several consecutive collections including all life stages (larvae, pupae and adult stage), in accordance with the life cycle of holometabolous caddisflies. We measured body weight of caddisflies and a total protein concentration using the Bradford method [3]. First results show that both male and female adults emerged earlier in treatments with increased water temperature irrespective of the presence of ECs. Furthermore, increased body weight, but decreased protein concentration was observed in larvae and pupae in treatments with ECs mixture. Further analyses that will be conducted include metabolite profiling, total lipid content and fatty acids composition in order to evaluate the response of non-model aquatic insects to selected stressors. Additionally, the quantification of ECs in caddisfly and moss tissues will be conducted in order to assess the bioaccumulation potential of the selected ECs under different water temperature regimes.

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UČINAK VIŠESTRUKIH STRESORA NA VODENE KUKCE: ŠTO MOŽEMO NAUČITI IZ LABORATORIJSKOG POKUSA?

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Antropogeni učinak i klimatske promjene utječu na bioraznolikost i prirodne resurse. Slatkovodni ekosustavi su vruće točke bioraznolikosti, izvor pitke vode i hrane za čovjeka te su posebno ranjivi na antropogene pritiske [1]. Zbog povećane urbanizacije i otpuštanja otpadnih voda, slatkovodni ekosustavi su kontaminirani različitim onečišćujućim tvarima poput farmaceutika, proizvoda za osobnu njegu, pesticida pa čak i hormona [2]. Iako su utjecaji pojedinačnih stresora na razini vrste ili populacije relativno dobro istraženi, utjecaj kombinacije različitih stresora znatno su slabije poznati. Različiti stresori mogu uzajamno djelovati na više različitih načina, aditivno, antagonistički, sinergistički, utječući pritom na slatkovodne ekosustave [1]. Ovim istraživanjem želimo ispitati pojedinačni i kombinirani učinak smjese onečišćujućih tvari i povišene temperature na vodene beskralježnjake. Proveli smo laboratorijski pokus s pojednostavljenom slatkovodnom hranidbenom mrežom koja je uključivala mahovine i ličinke tulara (*Micropterna nycterobia*, Trichoptera), te sljedeće tretmane: a) smjesa onečišćujućih tvari; farmaceutici i endokrini disruptori, b) povišena temperatura, c) povišena temperatura i smjesa onečišćujućih tvari i d) kontrola. Uzorkovanje je organizirano u skladu sa stadijima životnog ciklusa tulara (ličinke, kukuljice i odrasli stadij). Jedinkama tulara izmjerena je masa i koncentracija proteina prema metodi po Bradfordu [3]. Prvi rezultati pokazuju da odrasli mužjaci i ženke emergiraju ranije u tretmanima s povišenom temperaturom neovisno o prisutnosti onečišćujućih tvari. Nadalje, povećana masa, a smanjena koncentracija proteina je primijećena kod ličinki i kukuljica u tretmanima koji sadrže onečišćujuće tvari. Nastavak istraživanja će uključivati analizu metabolita, lipida i određivanje masnih kiselina kako bi procijenili odgovor vodenih kukaca na odabrane višestruke stresore. Izvršit će se kvantifikacija onečišćujućih tvari u tkivima tulara i mahovina kako bi se procijenio bioakumulacijski potencijal odabranih spojeva pod različitim temperaturnim režimom vode.

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CIRCADIAN GENE EXPRESSION IN NON-MODEL INSECTS

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The harmonization of the circadian rhythm with the environment is a prerequisite for the regulation of physiological and metabolic processes, and thus a prerequisite for the survival and adaptation of various organisms [1]. So far, most of the studies that were conducted on a model organism *Drosophila melanogaster* indicated the conservation of molecular mechanisms that regulate circadian rhythm. Crucial part of those mechanisms is autoinhibitory transcription regulation of genes whose products further regulate the expression of other circadian genes. The transcriptional-translational feedback is stimulated and controlled by *Clk/Cyc* and *Per/Tim* dimers [2]. Thus, the aim of this study was to develop a method for detection of *Clk* and *Per* expression in non-model insects. The selected taxa (*Bezzia flavicornis*, *Simulium* sp., *Wiedemannia ouedorum*, *Antocha vitripennis*, *Simulium velutinum* and *Ecdyonurus starmachi*) were taken from the archives stored in alcohol. The RT-qPCR method was used to analyze gene expression using *Rpl32* as endogenous control [3]. RNA isolate from *Drosophila melanogaster* specimens was used as a control sample. Sequences for specific primers used for amplification of selected genes were designed based on the *Drosophila melanogaster* genome [4]. Our results show that genes *Clk* and *Per* can be amplified in non-model insect species *Simulium velutinum* and *Ecdyonurus starmachi* using primers specific for evolutionarily preserved genes whose sequence was determined according to the genome of a related model organism. These results suggest the possibility of implementing circadian genes' expression analysis in non-model organisms in studies assessing the impact of urban stream pollution at the molecular level.

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EKSPRESIJA GENA CIRKADIJANOG RITMA KOD NEMODELNIH KUKACA

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Usklađivanje cirkadijanog ritma s okolišem preduvjet je reguliranja fizioloških i metaboličkih procesa, a time i preduvjet preživljavanja i prilagodbi različitih organizama [1]. Istraživanja od kojih je većina provedena na modelnom organizmu, mušici *Drosophila melanogaster*, ukazala su na konzerviranost molekularnih mehanizama koji reguliraju cirkadijani ritam. Njihov ključni dio je autoinhibicijska regulacija transkripcije gena čiji produkti reguliraju ekspresiju drugih gena cirkadijanog ritma. Transkripcijsko-translacijsku povratnu spregu potiču i vode geni *Clk* i *Cyc* te geni *Per* i *Tim*, čiji produkti stvaraju dimere [2]. Stoga je cilj ovog istraživanja bio razviti metodu za detekciju ekspresije gena *Clk* i *Per* kod nemodelnih kukaca. Odabrane vrste (*Bezzia flavicornis*, *Simulium sp.*, *Wiedemannia ouedorum*, *Antocha vitripennis*, *Simulium velutinum* i *Ecdyonurus starmachi*) uzete su iz arhivskih zbirki u kojima su bile pohranjene u alkoholu. Za analizu ekspresije gena korištena je metoda RT-qPCR pri čemu je *Rpl32* odabran kao endogena kontrola [3]. Kontrolni uzorak bio je izolat RNA iz mušice *Drosophila melanogaster* na temelju čijeg genoma su i odabrane specifične početnice korištene za amplifikaciju odabranih gena [4]. Rezultati su pokazali da je gene *Clk* i *Per* moguće umnožiti u uzorcima nemodelnih kukaca vrsta *Simulium velutinum* i *Ecdyonurus starmachi* korištenjem početnica specifičnih za evolucijski očuvane gene čija je sekvenca određena prema genomu srodnog modelnog organizma. Dobiveni rezultati ukazuju na mogućnost analize ekspresije gena cirkadijanog ritma kod nemodelnih organizama kao načina procjene utjecaja zagađenja urbanih potoka na molekularnoj razini.

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DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF COMPOUNDS AS ACTIVE DRUGS IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM

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Nervous system diseases are caused by the gradual and progressive death of neurons, which in turn leads to dysfunctions of the nervous system and causes problems in the mental and physical functioning of patients. Alzheimer's (AD) and Parkinson's disease and myasthenia gravis are complex neurological disorders currently treated with drugs that inhibit the activity of acetylcholine hydrolyzing enzymes (acetylcholinesterase and butyrylcholinesterase) or are N-methyl-D-aspartate receptor antagonists. However, these drugs act only on the symptoms, not on the course and outcome of the disease. As these are diseases whose development and progression are affected by multiple pathological factors, the pharmaceutical industry and the scientific community have recently made great efforts to find new effective drugs, with a tendency to replace current "single-targeted" drugs with those that act on multi targets – "multi-target-directed ligands" (MTDL).

The primary goal of the HRZZ project IP-2020-02-9343 "Development of bioactive molecules for the treatment of neurodegenerative diseases" is the development of MTDL compounds with the potential to alleviate symptoms and slow down the progression of ND (especially AD). The development of such compounds will have two main goals: the development of compounds active in the central nervous system (CNS) and the development of peripherally active compounds, depending on their ability to cross the blood-brain barrier.

Part of the research is focused on the design and synthesis of biscarbamate compounds, structural analogues of resorcinol, as potential cholinesterase's inhibitors. To date, four groups of compounds with different aliphatic and cyclic substituents in the carbamoyl and amino parts of the molecule have been synthesized. Compounds of appropriate purity (>97%) were kinetically evaluated as human cholinesterase inhibitors and proven to be fast inhibitors of both cholinesterases with inhibition rate constants within $10^6 \text{ M}^{-1} \text{ min}^{-1}$. In addition, the tested compounds showed no toxic effect on liver and neuroblastoma cells at concentrations showing an inhibitory effect on cholinesterases, and some were estimated to be able to cross the blood-brain barrier by active transport. The obtained results will enable the definition of guidelines for structural refining of compounds that could be more effective in the treatment of ND than the currently available drugs.

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DIZAJN, SINTEZA I BIOLOŠKA EVALUACIJA SPOJEVA KAO LIJEKOVA AKTIVNIH U CENTRALNOM I PERIFERNOM ŽIVČANOM SUSTAVU T

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Neurodegenerativne bolesti (ND) uzrokuje postepeno i progresivno odumiranje neurona što posljedično vodi ka disfunkciji živčanog sustava i uzrokuje probleme u mentalnom i fizičkom funkcioniranju oboljelih osoba. Alzheimerova (AD) i Parkinsonova bolest te mijastenija gravis su složeni neurološki poremećaji u liječenju kojih se trenutno primjenjuju lijekovi koji inhibiraju aktivnost enzima koji hidroliziraju acetilkolin (acetilkolinestrase i butirilkolinesteraze) ili su antagonisti N-metil-D-aspartat receptora. Međutim, obje skupine lijekova djeluju samo na simptome, ali ne i na tijek i ishod bolesti. Budući da se radi o bolestima na čije nastajanje i napredak utječu višestruki patološki čimbenici, u novije vrijeme farmaceutska industrija i znanstvena zajednica ulažu velike napore u pronalazak novih učinkovitijih lijekova pri čemu je tendencija da se trenutačni „single targeted“ lijekovi zamijene s onima koji istovremeno djeluju na više ciljeva (eng. *Multi-target-directed ligands* (MTDLs)).

Primarni cilj HrZZ projekta IP-2020-02-9343 „Razvoj bioaktivnih molekula za tretman neurodegenerativnih bolesti“ je razvoj MTDL spojeva s potencijalom ublažavanja simptoma i usporavanja napredovanja ND (naročito AD). Razvoj takvih spojeva imat će dva glavna cilja: razvoj spojeva aktivnih u središnjem živčanom sustavu (CNS) i razvoj periferno aktivnih spojeva, ovisno o sposobnosti spojeva da prijeđu krvno-moždanu barijeru.

Dio istraživanja je obuhvaća dizajn i sintezu biskarbamatnih spojeva, strukturnih analoga rezorcinola, kao potencijalnih inhibitora kolinesteraza. Do sada su sintetizirane četiri skupine spojeva as različitim alifatskim i cikličkim supstituentima u karbamoilnom i amino dijelu molekule. Spojevi odgovarajuće čistoće (>97 %) kinetički su evaluirani kao inhibitori ljudskih kolinesteraza, pri čemu su se pokazali vrlo brzim inhibitorima obiju kolinesteraza s konstantama brzine inhibicije reda veličine $10^6 \text{ M}^{-1} \text{ min}^{-1}$. Testirani spojevi nisu pokazali toksični učinak na jetrene i stanice neuroblastoma u koncentracijama u kojima pokazuju inhibitorni učinak na kolinesteraze, a za neke od spojeva je procijenjeno da mogu proći krvno-moždanu barijeru aktivnim transportom. Dobiveni rezultati će omogućiti definiranje smjernica za strukturnu doradu spojeva koji bi bili učinkovitiji u tretmanu ND od trenutno dostupnih lijekova.

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DIVERSITY OF EPIPHYTIC BACTERIAL COMMUNITIES FOUND ON NORTHERN ADRIATIC FUCACEN SPECIES

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The surface of brown macroalgae is colonized by epiphytic bacteria which are characterized by abilities of fast colonization, quick metabolic response to algal exudates, and adaptation to environmental variations. Epiphytic bacteria found on Fucales differ significantly from bacterial communities found on surrounding abiotic surfaces [1,2]. In addition to the fucacean ecology and the vegetative cycling that significantly influence species resilience to the climate and anthropogenic stress, positive species interactions in the phycosphere can act as a first defense barrier against abiotic stress [3]. The study aimed to determine epiphytic bacterial communities of selected fucacean species (*Treptacanta barbata*, *Carpodesmia crinita*, and *Cystoseira compressa*) and to explore the relationship between the fatty acid profiles of selected fucacean species and their associated epiphytic bacterial communities. The thalli of sampled species were divided into perennial and annual parts. *T. barbata* and *C. crinita* show high contents of mono- and polyunsaturated fatty acids. The branches and apical parts of *C. crinita* demonstrated high proportion of both C18 and C20 polyunsaturated fatty acids but also, *C. crinita* showed the highest unsaturation degree (4.32%) in opposition to the highest proportion of saturated fatty acids which was found in thalli of *C. compressa*. Several representatives of the Gammaproteobacteria class, identified as *Vibrionales*, *Cellvibrionales*, and *Xanthomonadales* were found which contributed strongly to the separation of *T. barbata* apical parts and branches, *C. compressa* receptacles and *C. crinita* branches from the *T. barbata* cauloids and *C. crinita* apical parts and cauloids. The results showed a strong relationship between fatty acid profiles of the analyzed species and phycosphere community structure, underlining the host physiological condition in shaping the biological interactions and maintaining a healthy microbiome.

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DIVERZITET EPIFITSKIH BAKTERIJSKIH ZAJEDNICA PRONAĐENIH NA SMEĐIM ALGAMA SJEVERNOG JADRANA

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Površina smeđih makroalgi je kolonizirana epifitskim bakterijama koje su specifične po brzim kolonizacijama, brzim metaboličkim odgovorima na izlučevine algi te prilagodba na promjene u okolišu. Epifitske bakterije pronađene na smeđim algama se značajno razlikuju od bakterijskih zajednica pronađenih na okolnim abiotičkim površinama [1,2]. Uz ekologiju i vegetativni ciklus smeđih algi, koji značajno utječu na otpornost vrsta na klimatske promjene i antropogene stresore, također su utvrđene i pozitivne interakcije vrsta u pikosferi koje mogu djelovati kao barijera u obrani protiv abiotičkog stresa [3]. Cilj istraživanja bio je utvrditi skupine epifitskih bakterijskih zajednica na odabranim vrstama smeđih algi (*Treptacanta barbata*, *Carpdesmia crinita* i *Cystoseira compressa*) te istražiti poveznicu između profila masnih kiselina navedenih smeđih algi i epifitskih bakterijskih zajednica. Talus uzorkovanih vrsta je podijeljen na trajne i sezonske dijelove. Kod vrsta *T. barbata* i *C. crinita* utvrđena je velika koncentracija mono- i polinezasićenih masnih kiselina. Grane i apikalni vršci vrste *C. crinita* imali su visoke koncentracije C18 i C20 polinezasićenih masnih kiselina te je utvrđen i najviši stupanj nezasićenja (4.32%), za razliku od najvišeg stupnja zasićenosti koji je pronađen u talusu vrste *C. compressa*. Pronađeni su predstavnici razreda Gammaproteobacteria: *Vibrionales*, *Cellvibrionales* i *Xanthomonadales*, što je omogućilo utvrđivanje odvajanja apikalnih vrškova i grana vrste *T. barbata*, receptakula kod vrste *C. crinita*, grana kod vrste *C. crinita* od kaluoida *T. barbata* i apikalnih dijelova i kauloida vrste *C. crinita*. Rezultati su ukazali na snažnu vezu između profila masnih kiselina i analiziranih vrsta s utvrđenom fikosfernom zajednicom, implicirajući važnost fiziološkog stanja domaćina u oblikovanju bioloških interakcija i održavanju zdravog mikrobioma.

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QUANTUM COMMUNICATION WITH ENTANGLED PHOTON PAIRS

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Today, perhaps more than ever before, the security of information and communication is increasingly important. The cryptographic protocols used in classical cryptography are based on mathematical algorithms and can be breached. On the other hand, the laws of quantum physics enable quantum key distribution (QKD) and absolute security of communication based on the fundamental laws of nature can be achieved [1, 2]. Anyone who would eavesdrop on QKD-based communication must perform a measurement and this implies an impact on the system that can be detected by the sender and receiver. In this lecture, I will present an experimental setup for generating a quantum key for communication between two users consisting of a source of polarization entangled photon pairs, an infrastructure for passive analysis of photon polarization states and a detector. Using this setup we measured violation of the Bell's inequality of 114 standard deviations from the classical boundary, which confirms the non-local behavior of the entangled photon pairs [3]. Furthermore, the long-term stability of security communication parameters was achieved, which confirms the security of the communication link. Apart from local quantum communication networks, I will show how this source can also be used to create hybrid connections that can be realized in combination with both optical fibers and free space.

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KVANTNA KOMUNIKACIJA POMOĆU PAROVA KVANTNO PREPLETENIH FOTONA

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Danas, možda više nego ikad prije, sigurnost informacija i komunikacije je sve važnija. Kriptografski protokoli koji se koriste u klasičnoj kriptografiji su temeljeni na matematičkim algoritmima i mogu biti probijeni. S druge strane, zakoni kvantne fizike omogućuju kvantnu distribuciju ključeva (engl. quantum key distribution – QKD) i time apsolutnu sigurnost komunikacije temeljenu na fundamentalnim zakonima prirode. Svatko tko bi prisluškivao komunikaciju temeljenu na QKD-u mora izvršiti mjerenje, a to podrazumijeva utjecaj na sustav koji se može detektirati od strane pošiljatelja i primatelja. U ovom predavanju ću prezentirati eksperimentalni postav za generiranje kvantnog ključa za komunikaciju između dva korisnika koji se sastoji od izvora polarizacijski prepletenih parova fotona, infrastrukture za pasivnu analizu polarizacijskih stanja fotona te detektora. Pomoću navedenog postava izmjereno je narušenje Bell-ove nejednakosti u iznosu od 114 standardnih devijacija od klasične granice čime je potvrđeno ne-lokalno ponašanje prepletenih parova fotona. Nadalje, ostvarena je dugotrajna stabilnost sigurnosnih komunikacijskih parametara čime se potvrdila sigurnost realizirane veze. Osim za lokalne kvantne komunikacijske mreže, izvor se može koristiti i za kreiranje hibridnih veza koje se mogu ostvarivati kombinirano i optičkim vlaknima te slobodnim prostorom.

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BINDING ABILITY OF FERROCENE DERIVATIVES WITH β -CYCLODEXTRINS AS INCLUSION COMPLEXES

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Recent research shows that N-alkylated ferrocene quinoline conjugates exhibited inhibitory effects on selected tumor cell lines.[1] Ferrocene uracil conjugates show similar biological activity. However, due to the high lipophilicity of these compounds, their application is limited. Cyclodextrins have shown great results forming complexes with lipophilic compounds to improve their solubility in water and thus better bio-distribution and pharmacokinetic properties of some drugs. [2, 3 ,4] Complexation was first carried out with ferrocene carboxylic acid in buffer solution pH 7,4 and characterized by UV-spectroscopy. Stability constant was calculated to be 3,6. Further studies included milling as newer method. Its benefits are faster, less toxic and simpler synthesis. The formation of inclusion complex of ferrocene derivatives with β -cyclodextrin was carried out by vibrational mill by grinding and kneading. (Figure 1). Host-guest complexation in the solid state was studied and characterized by NMR spectroscopy, IR and X-ray powder diffraction.

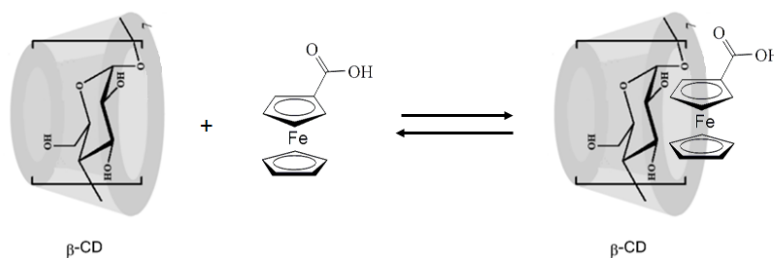


Figure 1. β -cyclodextrin ferrocene derivative complex

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NASTAJANJE INKLUZIJSKIH KOMPLEKSA DERIVATA FEROCENA S β -CIKLODEKSTRINOM

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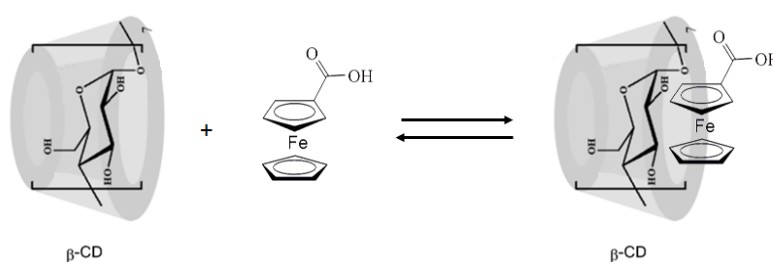
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Novija istraživanja pokazala su sposobnost N-alkiliranih ferocen-kinolinskih konjugata da inhibiraju određene tumorske stanice.[1] Ferocen-uracil konjugati pokazuju sličnu biološku aktivnost, no velika lipofilnost takvih spojeva ograničava njihovu primjenu. Ciklodekstrini su pokazali dobre rezultate u formiranju kompleksa s lipofilnim spojevima kako bi poboljšali njihovu topljivost u vodi i time bolju biodistribuciju i farmakokinetička svojstva lijekova. [2,3,4] Kompleksiranje ferocen derivata provedeno je najprije otopinski s ferocenskom kiselinom u puferu pH 7,4 te je okarakterizirano UV-Vis spektroskopijom iz čega je dobivena konstanta stabilnosti 3,6. Daljnja ispitivanja provedena su novijom metodom – sinteza u čvrstom stanju u mlinu. Prednosti takve metode su korištenje vrlo malih do nikakvih količina otapala što pridonosi bržoj, manje toksičnoj i jednostavnijoj sintezi spojeva. Nastajanje inkluzijskog kompleksa ferocenskog derivata s β -cyclodextrinom provedeno je mljevenjem u vibracijskom mlinu (Slika 1). Inkluzijski kompleks u čvrstom stanju okarakteriziran je NMR spektroskopijom, IR i X-ray difrakcijom praha.



Slika 1. Kompleks derivata ferocena i β -ciklodekstrina

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THE VALUE OF PROTECTED AREAS RANGER SERVICE PERSONNEL FOR BIODIVERSITY MONITORING: CASE STUDY - CAMERA TRAPPING SURVEY OF MAMMALS IN PAKLENICA NATIONAL PARK (CROATIA)

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Paklenica National Park (Paklenica NP) is a part of the Velebit Mountain, represented by 59 mammalian species [1]. The most significant threats to mammals in Croatia are habitat degradation and fragmentation, poaching and pesticide use [2]. To ensure the long-term survival of wild species, it is necessary to conduct systematic research that includes revision of the species richness lists, which was done in this 5 year-long survey in Paklenica NP using camera traps, which were set up and maintained by employees from the NP public institution ranger service (rangers). The aim of this survey was to analyze gathered data on mammal species richness of the Paklenica NP as well as to estimate the quality and quantity of data gathered by rangers. The rangers are not required to have university education in ecology, but they have a very profound knowledge of the specific area. This makes them an irreplaceable segment for biodiversity monitoring, especially when considering their time spent in the field. During the present survey, the camera traps set by rangers recorded 88 % of all medium-large size mammalian species present in the Paklenica NP and recorded in previous research by ecologists. So, the present study identified significant value of rangers for biodiversity monitoring, especially because monitoring of mammal species via camera traps is not very labour intensive (setting and maintaining photo traps) and can be easily incorporated with regular ranger field control tasks.

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VAŽNOST ČUVARA PRIRODE JAVNIH USTANOVA ZAŠTIĆENIH PODRUČJA PRIRODE U MONITORINGU BIORAZNOLIKOSTI: NA PRIMJERU ISTRAŽIVANJA SISAVACA POMOĆU FOTO ZAMKI NA PODRUČJU NACIONALNOG PARKA PAKLENICA (HRVATSKA)

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Nacionalni park Paklenica (NP Paklenica) smješten je na planini Velebit i u njemu je utvrđena prisutnost 59 vrsta sisavaca [1]. Najznačajnije prijetnje sisavcima u Hrvatskoj su degradacija i fragmentacija staništa, krivolov i uporaba pesticida [2]. Kako bi se osigurao dugoročni opstanak divljih vrsta, potrebno je provoditi sustavna istraživanja koja uključuju reviziju popisa bogatstva vrsta, što je provedeno ovim petogodišnjim istraživanjima na području NP Paklenica, i to foto zamkama koje su postavljali i o istima brinuli čuvari prirode. Cilj ovog istraživanja bio je analizirati prikupljene podatke o bogatstvu vrsta sisavaca NP Paklenice, kao i procijeniti kvalitetu i količinu podataka koje su prikupili čuvari prirode NP-a. Čuvari prirode ne moraju imati fakultetsko obrazovanje iz područja ekologije, ali uobičajeno vrlo dobro poznaju područja javnih ustanova u kojima rade. To ih, zajedno s vremenom provedenim na terenu, čini neprocjenjivim segmentom u praćenju biološke raznolikosti. U ovom istraživanju, foto zamkama koje su postavljali čuvari prirode zabilježeno je 88% vrsta srednje-velikih sisavaca od svih prisutnih srednje-velikih vrsta sisavaca u NP Paklenica zabilježenih dosadašnjim istraživanjima ekologa. Stoga, ovo istraživanje je identificiralo značajnu vrijednost čuvara prirode za praćenje biološke raznolikosti foto zamkama, budući da praćenje sisavaca putem foto zamki (postavljanje i održavanje foto zamki) nije fizički zahtjevno i može se lako uklopiti u redovite terenske zadatke čuvara prirode.

ZAHVALE

Zahvaljujemo Javnoj ustanovi „Nacionalni park Paklenica“ na podacima iz foto zamki, kao i studentima Sveučilišta u Zagrebu (Rea Blagajec, Mia Jakopović, Andrijana Čavlović, Darija Jerčić) na pomoći u determinaciji vrsta tijekom analize podataka.

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EFFICIENT AND CONTROLLABLE ENTRAPMENT OF BUCKMINSTERFULLERENE INTO ZIF-8 OF SODALITE TOPOLOGY BY MECHANOCHEMISTRY

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Fullerene and fullerene derivatives are well researched by material science because they show enormous potential for application due to their unique physicochemical properties. Functional materials having fullerene embedded in their structure are usually characterized by enhanced stability, conductivity, magnetism, or catalytic activity, compared to their constitutional components. Metal-organic frameworks (MOFs) are crystalline, porous materials that have proven to be excellent host matrices for the encapsulation of guest molecules. [1] The main problem with current encapsulation strategies is the lack of control over the encapsulation process regarding the solubility of the components used and the fact that the solvent competes with the guest to occupy the pores of the MOFs. [2] Here, a fast and green mechanochemical approach arose as a suitable solution because it requires only traces of solvent. Ball milling allowed stoichiometrically controlled encapsulation and provided four C₆₀@ZIF-8 (zeolitic-imidazolate framework) crystalline materials containing 15, 30, 60, and 100 mol % of fullerene entrapped in the available pores of the sodalite ZIF-8 while solution-based strategies resulted in minimal load. The fullerenes contained within the ZIF-8 matrix show properties of isolated molecules. [3] Therefore, this strategy could serve to fit selected endofullerenes into suitable MOFs for use in advanced spintronics.

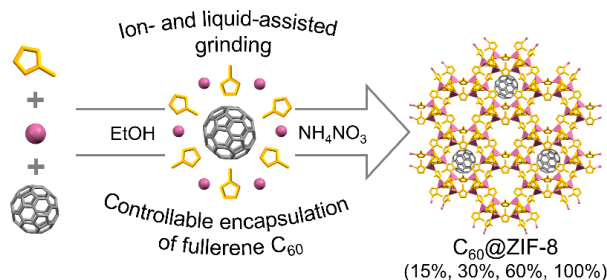


Figure 1. Schematic Representation of the Synthetic Procedure for Encapsulation of Fullerene C₆₀ into ZIF-8

ACKNOWLEDGMENTS

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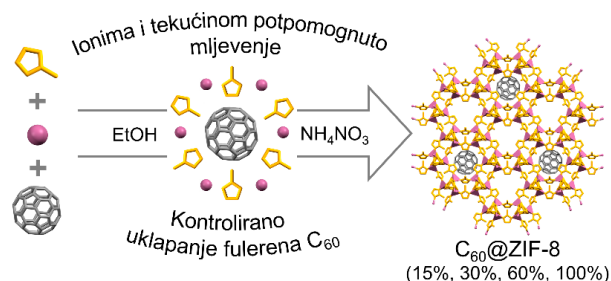
EFIKASNO I KONTROLIRANO UKLAPANJE BUCKMINSTERFULLERENA U ZIF-8 SODALITNE TOPOLOGIJE MEHANOKEMIJSKIM PUTEM

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Fulereni i derivati fulerena dobro su istraženi u znanosti o materijalima jer pokazuju ogroman potencijal za primjenu zbog svojih jedinstvenih fizikalno-kemijskih svojstava. Funkcionalni materijali koji imaju fuleren ugrađen u strukturu obično se odlikuju povećanom stabilnošću, vodljivošću, magnetizmom ili katalitičkom aktivnošću u usporedbi s njihovim sastavnicama. Metal-organske mreže (MOF) su kristalni, porozni materijali koji su se pokazali izvrsnim matricama za uklapanje molekula gostiju. [1] Glavni problem trenutnih sintetskih strategija je nedostatak kontrole nad postupkom uklapanja s obzirom na topljivost korištenih komponenata i činjenicu da su molekule otapala i gosta u kompeticiji za uklapanje u pore MOF-ova. [2] Ovdje se kao prikladno rješenje nameće, brzi i zeleni, mehanokemijski pristup jer koristi otapalo u minimalnim količinama. Mljevenje u vibracijskom mlinu je omogućilo stehiometrijski kontrolirano uklapanje fulerena te je rezultiralo četirima kristalnim materijalima $C_{60}@ZIF-8$ (zeolitna imidazolatna mreža) sa 15, 30, 60 i 100 mol% fulerena uklopljenog u pore sodalitnog ZIF-8 dok su otopinske sintetske strategije rezultirale minimalnim punjenjem. Fulereni uklopljeni u matricu ZIF-8 pokazuju svojstva izoliranih molekula. [3] Stoga bi ova strategija mogla poslužiti za uklapanje odabranih endofulerena u prikladne MOF-ove za upotrebu u naprednoj spintronici.



Slika 1. Shematski prikaz sintetskog postupka uklapanja fulerena C_{60} u ZIF-8

ZAHVALE

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SYNTHESIS OF DIAMONDROID ESTERS FOR SUPRAMOLECULAR SELF-ASSEMBLY

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Diamondoids are a class of compounds incorporating compact cage structures comprised of carbon atoms that structurally resemble the diamond crystal lattice. Since diamondoids are organic molecules, they are easily derivatized and their functionalized scaffolds find application in medicine, material science, nanotechnology, supramolecular chemistry, etc. [1]. Study of diamondoid self-organized assemblies has been of great interest recently as they can be readily applied in material sciences [2]. As part of our investigation dealing with new nanomaterials, we have synthesized novel diamondoid esters by linking two diamondoid cages with a carboxyl moiety. We have also prepared literary known adamantane methyl and *tert*-butyl esters as probes in the study using scanning tunneling microscopy. Our goal is to elucidate the influence of diamondoid structure on the 2D self-organization behavior on various surfaces. The experimental findings will be further supported by computational chemistry tools in order to gain more insight into the structure – self-assembly relationship.

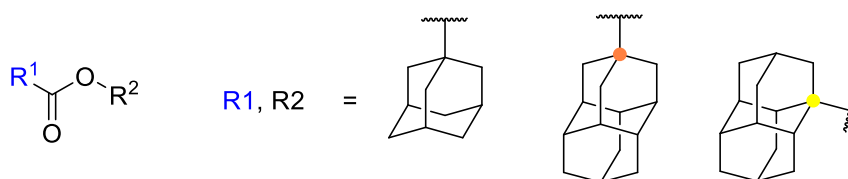


Figure 1. Novel diamondoid esters.

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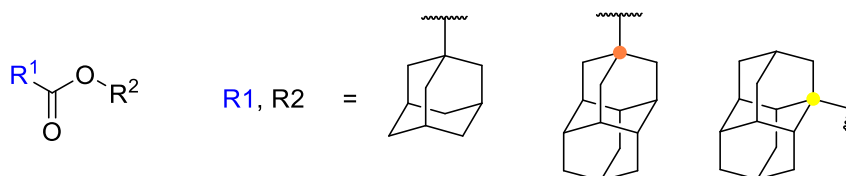
SINTEZA DIAMANTOIDNIH ESTERA ZA SUPRAMOLEKULSKO SAMOUDRUŽIVANJE

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Diamantoidi su klasa spojeva čija kompaktna kavezasta struktura ugljikovih atoma podsjeća na kristalnu rešetku dijamanta. Obzirom da su diamantoidi organske molekule, lako se derivatiziraju te njihovi derivati nalaze primjenu u medicini, znanosti o materijalima, nanotehnologiji, supramolekulskoj kemiji, itd. [1]. Proučavanje samouređenih diamantoidnih sustava u posljednje vrijeme je od značajnog interesa obzirom da takvi sustavi imaju primjenu u razvoju novih materijala. U sklopu našeg istraživanja u području novih nanomaterijala, pripravili smo nove diamantoidne estere povezivanjem dva diamantoidna kaveza esterskom vezom. Također su pripremljeni literaturno poznati metilni i *tert*-butilni ester adamantana kao standardi za studiju koja uključuje korištenje pretražnog mikroskopa s tuneliranjem. Naš cilj je naime razjasniti utjecaj strukture diamantoida na 2D samoorganizaciju molekula na različitim površinama. Eksperimentalno dobiveni podaci bit će potkrijepljeni metodama računalne kemije u svrhu dobivanja boljeg uvida u vezu između strukture i načina na koji se molekule samoudružuju.



Slika 1. Novi diamantoidni esteri.

ZAHVALE

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COMBINED EFFECT OF CISPLATIN AND RESVERATROL ON METALLOPROTEINASE ACTIVITY IN EHRlich ASCITES SOLID MOUSE TUMOR

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The aim of this study was to investigate the combined effect of cytostatic cisplatin [1] and resveratrol [2] on inhibition of angiogenesis and tumor development, increase of host lifespan, and to investigate macrophage activity [3] in tumor tissue through analysis of inducible nitric oxide synthase. In addition, the aim was to determine how the repeated action of cytostatics affects the level of heat shock proteins [4] and whether resveratrol treatment modulates their activity leading to the abolition of tumor cell resistance to cytostatics. The tumor was induced by injecting 1×10^6 EAT cells subcutaneously (sc) into the thighs of Swiss albino mice. Treatment of animals with EAT was initiated by administration of resveratrol *per os* at a dose of 50 mg/kg for 5 consecutive days beginning on day 2 after tumor injection while cisplatin was injected at a dose of 2.5 mg/kg on days 10 and 12 and at a dose of 5 mg/kg on day 15. The results show that cisplatin combined with resveratrol can inhibit angiogenesis, slow tumor growth, and increase host lifespan by enhancing host immunomodulatory activity by modulating heat shock proteins HSP-90 and HSP70 and reducing the adverse effects of cisplatin on normal cells and tissues, which suggest the possibility of clinical use of this combination.

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ZDRUŽENO DJELOVANJE CISPLATINE I RESVERATROLA NA METALOPROTEINAZNU AKTIVNOST U EHRlichOVOM ASCITESNOM SOLIDNOM TUMORU MIŠA

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Cilj ovog istraživanja bio je istražiti združeno djelovanje citostatika cisplatine [1] i resveratrola [2] na inhibiciju angiogeneze i razvoja tumora, povećanje životnog vijeka domaćina, te istražiti aktivnost makrofaga [3] u tkivu tumora kroz analizu inducibilne dušik oksid sintaze. Uz to cilj je bio utvrditi kako višekратно djelovanje citostatika djeluje na razinu proteina toplinskog stresa [4] i da li obrada resveratrolom modulira njihovu aktivnost vodeći dokidanju rezistencije tumorskih stanica na citostatik. Tumor je izazvan injiciranjem 1×10^6 stanica EAT subkutano(sc) u bedro miševa soja Swiss albino. Obrada životinja s EAT započeta je unosom resveratrola *per os* u dozi od 50 mg/kg tijekom 5 dana u nizu s početkom 2. dana od injiciranja tumora dok je cisplatina injicirana u dozi od 2,5 mg/kg 10. i 12. dana te dozom od 5 mg/kg 15. dana. Dobiveni rezultati pokazuju da resveratrol združen s cisplatinom može inhibirati proces angiogeneze, usporiti rast tumora te povećati životni vijek nositelja tumora jačanjem imunomodulatorne aktivnosti domaćina kroz modulaciju proteina toplinskog stresa HSP-90 i HSP-70 i smanjuje štetne učinke cisplatine na normalne stanice i tkiva, što ukazuje na mogućnost kliničke uporabe ove kombinacije.

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ENERGY STATUS IN *Synurella ambulans* POPULATIONS FROM HYPORHEIC ZONE OF SAVA RIVER AND MALA BRŠLJANICA SPRING, CROATIA

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Energy undoubtedly plays a central role in the function of organisms. Many environmental stressors, such as pollution, hypoxia or desiccation, affect the organism's energy status. The adenylate energy charge (AEC) was defined as the ratio of the adenine nucleotides: adenosine mono-, di-, and triphosphate (AMP, ADP, and ATP) [1]. AEC values of 0.8 - 0.9 were ascribed to organisms living in non-polluted environments, while values below 0.5 were indicative of physiological collapse. This study aimed to determine AEC and ATP/ADP ratio and compare them between different populations of the freshwater stygophilous amphipod *Synurella ambulans* from hyporheic zone (HZ) of the Sava River (Medsave and Jarun) and helocene spring Mala Bršljanica sampled in winter. Medsave is located 3 km upstream and Jarun 13 km downstream from the wastewater discharge of the town of Zaprešić, while Mala Bršljanica (13 km from Kutina) is isolated natural spring selected as reference site. AEC values at Mala Bršljanica were 0.44, 0.41 at Medsave and 0.35 at Jarun. Interestingly, *S. ambulans* can survive such low AEC values, predictive of cell death. This lower energy charge (0.3 - 0.4) may be explained by the low efficiency of AMP deaminase in invertebrates when compared to vertebrates (0.5 - 0.6) [2]. Also, harsh environmental conditions in the HZ may affect the energy status of *S. ambulans*. The highest AEC value was observed in Mala Bršljanica, location without known anthropogenic impact. The lowest AEC value noted at Jarun is possibly caused by wastewaters from the pharmaceutical industry and municipal wastewaters. The ATP/ADP ratio reflected the AEC pattern, with the highest value of 1.06 at Mala Bršljanica, 0.91 at Medsave, and the lowest value of 0.72 at Jarun. In summary, the investigated parameters of *S. ambulans* energy metabolism showed that AEC is a sensitive physiological biomarker of organism's response to environmental stress.

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ENERGIJSKI STATUS U POPULACIJAMA *Synurella ambulans* IZ HIPOREIČKE ZONE RIJEKE SAVE I IZVORA MALA BRŠLJANICA, HRVATSKA

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Energija nesumnjivo ima središnju ulogu u funkcioniranju organizama. Mnogi okolišni stresori, poput onečišćenja, hipoksije ili isušivanja, utječu na energijski status organizma. Energijski naboj adenilata (AEC) definiran je kao omjer adeninskih nukleotida: adenozin mono-, di- i trifosfata (AMP, ADP i ATP) [1]. Vrijednosti AEC od 0,8 do 0,9 pronađene su u organizmima koji žive u nezagađenom okolišu, dok vrijednosti ispod 0,5 ukazuju na fiziološki kolaps. Cilj ovog istraživanja bio je odrediti AEC i omjer ATP/ADP te ih usporediti između različitih populacija slatkovodnog stigoofilnog rakušca *Synurella ambulans* iz hipoheičke zone (HZ) rijeke Save (Medsave i Jarun) i helokrenog izvora Mala Bršljanica uzorkovanih zimi. Lokalitet Medsave se nalazi 3 km uzvodno od ispusta otpadnih voda grada Zaprešića, a Jarun 13 km nizvodno od njega, dok je Mala Bršljanica (13 km od Kutine) izolirani prirodni izvor, odabran kao referentna postaja. Vrijednosti AEC na Maloj Bršljanici bile su 0,44, na Medsave 0,41 i na Jarunu 0,35. Zanimljivo je preživljavanje jedinki vrste *S. ambulans* pri tako niskim vrijednostima AEC-a, koje ukazuju na staničnu smrt. Ovakav niži energijski naboj (0,3 - 0,4) može se objasniti niskom učinkovitošću AMP deaminaze kod beskralješnjaka u odnosu na kralješnjake (0,5 - 0,6) [2]. Također, teški okolišni uvjeti u HZ-i mogu utjecati na energijski status jedinki vrste *S. ambulans*. Najviša vrijednost AEC zabilježena je na Maloj Bršljanici, lokaciji bez zabilježenog antropogenog utjecaja. Najniža vrijednost AEC zabilježena na Jarunu vjerojatno je posljedica otpadnih voda iz farmaceutske industrije i komunalnih otpadnih voda. Omjer ATP/ADP je odražavao AEC trend, s najvećom vrijednošću od 1,06 na Maloj Bršljanici, 0,91 na Medsave te najnižom vrijednosti od 0,72 na Jarunu. Zaključno, istraženi parametri energijskog metabolizma vrste *S. ambulans* pokazali su da je AEC osjetljivi fiziološki biomarker odgovora organizma na okolišni stres.

ZAHVALE

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MOTOR PROTEINS GENERATE THE CURVED SHAPE OF THE MITOTIC SPINDLE

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The mitotic spindle is a complex micro-machine made up of microtubules and associated proteins that are highly ordered in space and time to ensure its proper biological functioning. A functional spindle has a characteristic shape, which includes curved bundles of microtubules that are twisted around the pole-to-pole axis [1]. An in-depth understanding of both how the linear and rotational forces define the overall shape of the mitotic spindle and how the twisted shapes arise as a result of interactions between microtubules and motor proteins is still unclear. To answer this, we introduce a model in which motor proteins generate forces at the poles and along the microtubule bundles, thereby regulating the shapes of microtubule bundles. The model provides predictions for forces in the spindle, including that the shape of the entire spindle is predominately determined by rotational forces, and that a difference in bending forces explains the disparity in the shapes of inner and outer bundles.

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MOTORNI PROTEINI SU ZASLUŽNI ZA ZAKRIVLJNE OBLIKE MIKROTUBULA U DIOBENOM VRETENU

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Diobeno vreteno je stanična struktura koja je odgovorna za raspodjelu genetskog materijala među stanicama kćeri, a sastoji se od mikrotubula i pridruženih proteina. Funkcionalno diobeno vreteno ima karakterističan oblik, sastojeći se od zakrivljenih svežnjeva mikrotubula, koji su zakrenuti oko osi vretena [1]. Potpuno razumijevanje linearnih i rotacionih sila, koje određuju cjelokupni oblik diobenog vretena, te koje interakcije između mikrotubula i motornih proteina ih stvaraju, je i dalje otvoreno pitanje. Uvodimo teorijski model diobenog vretena u kojem motorni proteini stvaraju sile i momente sila na polovima i duž svežnjeva mikrotubula, regulirajući time oblike svežnjeva mikrotubula. Iz modela dobivamo predviđanje oblika diobenog vretena, odnosno raspodjelu sila u diobenom vretenu, iz kojih možemo zaključiti da razlika u silama savijanja objašnjava razliku u obliku unutarnjih i vanjskih mikrotubula, te da je cjelokupni oblik vretena većinski rezultat rotacionih sila.

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INTERACTIONS OF BENZOTHAZOLE AMIDINE DERIVATIVES WITH DNA

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Benzothiazoles, a group of compounds containing a benzene ring fused with a thiazole ring, are used as therapeutic compounds with a wide range of biological and potential antitumor activities [1,2]. Their biological activity and binding to DNA can be greatly improved with some substituents, such as amidines, at the end of heteroaromatic substructures [3]. Binding of studied compounds to calf thymus-DNA was monitored with fluorescence spectroscopy. From these data, stability constants of the formed complexes were determined. Titrations with ctDNA yielded fluorescence quenching of all studied compounds. For determination of the binding modes, CD titrations and ΔT_m experiments were used. All compounds showed small or negligible stabilization effect of ctDNA, while some of them (**A2**, **B3** and **B4**) showed great stabilization effect of AT-DNA. Compounds **A4** and **B4** exhibited positive induced CD spectra (ICD) with ctDNA which strongly suggests the minor groove binding to DNA. Addition of compound **A2** to the ctDNA solution resulted in the appearance of a bisignate signal. Such change suggests the binding of the compound in the form of a dimer within the minor groove.

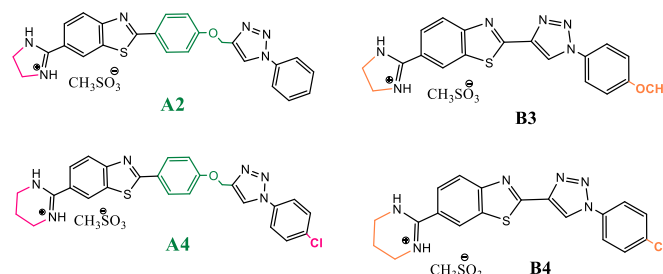


Figure 1. A series of novel benzothiazole amidine derivatives.

ACKNOWLEDGMENTS

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INTERAKCIJE DERIVATA BENZOTIAZOLSKIH AMIDINA S DNA

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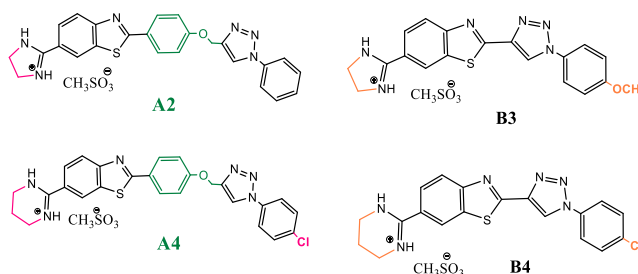
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Benzotiazoli, skupina spojeva koji sadrže benzenski prsten spojen s tiazolnim, poznati su kao spojevi sa širokim spektrom bioloških i potencijalnim antitumorskim aktivnostima [1,2]. Njihova biološka aktivnost i vezanje na DNA uvelike se mogu poboljšati supstumentima, poput amidina, koji se nalaze na kraju heteroaromatskih podstruktura [3]. Vezanje ispitivanih spojeva na DNA goveđeg timusa prati se fluorescentnom spektroskopijom, kojom su dobivene konstante nastalih kompleksa. Titracije s ctDNA rezultirale su gašenjem fluorescencije svih ispitivanih spojeva. Za određivanje načina vezanja korištene su CD titracije i eksperimenti temperaturnog mekšanja. Svi ispitivani spojevi pokazali su mali ili zanemariv stabilizacijski efekt na ctDNA, ali spojevi poput **A2**, **B3** i **B4** zato su pokazali veliki stabilizacijski efekt na AT-DNA. Spojevi **A4** i **B4** dali su pozitivno inducirani CD spektar (ICD) s ctDNA što ukazuje na vezanje u manji utor. Dok je CD titracija spoja **A2** s ctDNA rezultirala pojavom bisignantnog signala čime se može naslutiti vezanje ovog spoja u obliku dimera u mali utor DNA.



Slika 1. Novosintetizirani derivati benzotiazolskih amidina.

ZAHVALE

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ROLE OF BPM1 PROTEIN IN A CONTROL OF METHYLATION PATTERNS OF CML41 AND FWA GENES THROUGH RDDM PATHWAY IN *Arabidopsis thaliana* L.

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Arabidopsis thaliana BPM1 protein belongs to the MATH-BTB family of proteins containing two domains; MATH (*Meprin and TRAF Homology*) and BTB (*Bric-A-Brac, Tramtrack, Broad Complex*). The best-described function of MATH-BTB proteins is within cullin3-based E3 ligases where MATH domain serves as an adapter and binds substrates destined for degradation *via* 26S proteasome [1]. Co-immunoprecipitation and mass spectrometry analysis revealed interaction of BPM1 with DMS3 and RDM1, components of a DDR complex involved in RNA-directed DNA methylation (RdDM) mechanism. The DDR complex recruits polymerase V to chromatin and is indirectly responsible for positioning of methylation machinery at specific genomic locations [2]. The interactions between BPM1 and the aforementioned components of DDR complex are independent of the MATH domain, indicating that DMS3 and RDM1 are not substrates directed for degradation. To further elucidate the role of BPM1 protein in RdDM, two known targets of RdDM, genes CML41 and FWA [3] were selected for methylation pattern analysis by bisulfite conversion, PCR amplification and sequencing. The obtained sequences were processed using CyMATE software. Methylation patterns for each individual methylation position, as well as for each methylation context were compared between wild type, BPM1 overexpressor and a mutant with a dysfunctional DMS3 protein. The results showed significantly higher CHH methylation in BPM1 overexpressing plants and a loss of CHH methylation in DMS3 mutant. Our current goal is to use chromatin immunoprecipitation to identify novel targets of RdDM whose transcription or methylation are influenced by BPM1 and to further correlate methylation patterns with expression profiles in different tissues and mutants.

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ULOGA PROTEINA BPM1 U KONTROLI METILACIJSKIH OBRAZACA GENA CML41 I FWA PUTEM MEHANIZMA RDDM U VRSTI *Arabidopsis thaliana* L.

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Uročnjakov (*Arabidopsis thaliana* L.) protein BPM1 pripada proteinskoj porodici MATH-BTB koju karakteriziraju dvije proteinske domene; MATH (*Meprin and TRAF Homology*) i BTB (*Bric-A-Brac, Tramtrack, Broad Complex*). Najbolje opisana funkcija ovih proteina jest unutar kompleksa kulin3-ovisnih E3 ligaza, gdje domena MATH djeluje kao adapter i veže supstrate usmjerene u degradaciju na 26S proteasomu [1]. Metodama koimunoprecipitacije i spektrometrije masa utvrđena je interakcija proteina BPM1 s proteinima DMS3 i RDM1, koji su dio kompleksa DDR s funkcijom u mehanizmu metilacije DNA posredovanom malim molekulama RNA (RdDM). Kompleks DDR ima ulogu u regrutaciji polimeraze V na kromatin te indirektno sudjeluje u pozicioniranju metilacijske mašinerije na specifične lokacije u genomu [2]. Interakcije proteina BPM1 s komponentama DDR kompleksa ne ovise o domeni MATH, što upućuje na pretpostavku da proteini DMS3 i RDM1 nisu supstrati usmjereni u degradaciju. Kako bi se dodatno razjasnila uloga proteina BPM1 u putu RdDM, analizirani su metilacijski obrasci dvaju gena, CML41 i FWA, čija je metilacija dokazano pod kontrolom mehanizma RdDM [3]. Metilacijski obrasci utvrđeni su metodom bisulfitne konverzije, PCR amplifikacije te sekvenciranja. Dobivene sekvence obrađene su korištenjem CyMATE programa. Razine metilacije analizirane su na razini svakog pojedinog citozina, kao i između različitih metilacijskih konteksta, te uspoređene između linija divljeg tipa, linije s povišenom ekspresijom proteina BPM1 i mutanta s nefunkcionalnim proteinom DMS3. Rezultati su pokazali značajno više razine metilacije CHH konteksta u linijama s povišenom ekspresijom proteina BPM1 te snižene razine CHH metilacije u mutantnoj DMS3 liniji. Trenutni cilj jest metodom kromatinske imunoprecipitacije identificirati nove ciljne regije puta RdDM čija su transkripcija ili metilacija potencijalno regulirane proteinom BPM1, te korelirati metilacijske i ekspresijske obrasce u različitim tkivima i mutantama.

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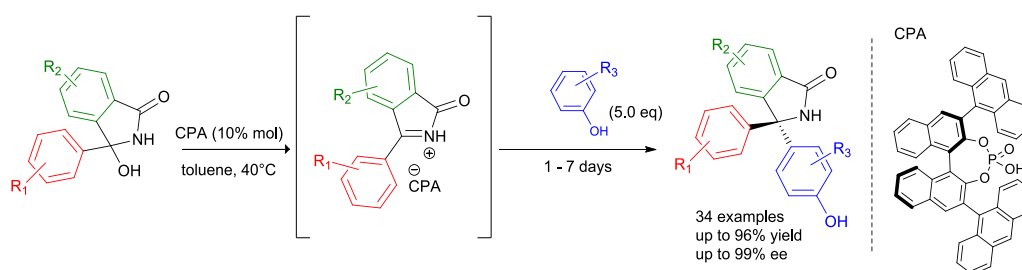
STEREOSELECTIVE ORGANOCATALYTIC SYNTHESIS OF α -TRIARYLMETHANAMINES VIA FORMAL BETTI REACTION

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A stereoselective synthesis of α -triarylmethanamine structural motifs *via* formal Betti reaction is described. Chiral α -triarylmethanamines are represented as ubiquitous building blocks found in a variety of natural products and biologically active molecules [1,2]. Preparation of such compounds has been challenging due to the steric hindrance positioned at the newly formed center of chirality. The catalyst has inherent difficulty in controlling the enantioselectivity of the arylation of ketimines derived from diaryl ketones due to the lack of sufficient steric difference between the two aryl rings. Synthesis of such optically active compounds relies on the usage chiral organometallic complexes of transition metals, such as Rh(I), Pd(II), Ni(II), Zn(II) and Co (II) [3,4]. On the other hand, to the best of our knowledge, there are no reports on the organocatalytic approach to the synthesis of these valuable motifs. Herein, we report a chiral Brønsted acid-catalyzed formal Betti reaction between diaryl ketimines and phenols for the asymmetric construction of α -triarylmethanamines. This type of reaction proceeds *via* direct 1,2-addition of variously substituted phenols to imines resulting in enantioenriched α -triarylmethanamines. The success of this transformation may be attributed to the *in situ* generation of the reactive iminium species from 3-hydroxysubstituted isoindolinones which makes them susceptible to a nucleophilic attack (Scheme 1) [5]. The reaction proceeds in a highly regioselective and enantioselective fashion, showing a broad tolerance of functionalities both in the aromatic ring of the isoindolinone alcohol, as well as on phenol. The absolute configuration of the major enantiomer was unambiguously determined to be (*R*) by single crystal X-ray diffraction analysis. Based on this result, the stereochemical induction in the products stems from the nucleophilic attack of the phenol from *si* face of the electrophile.



Scheme 1. Stereoselective synthesis of α -triarylmethanamine catalyzed by chiral Brønsted Acid.

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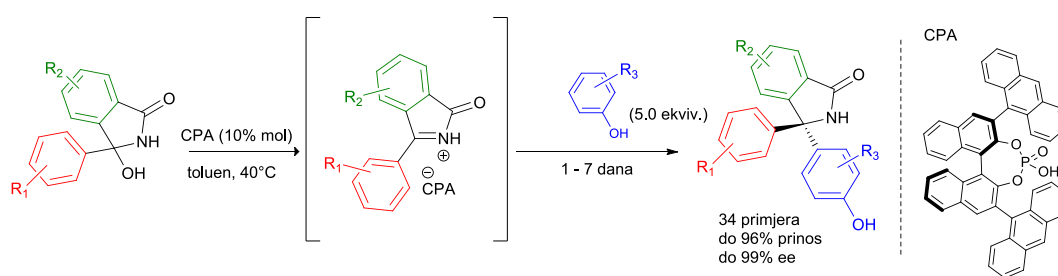
ORGANOKATALITIČKA STEREOSELEKTIVNA SINTEZA α -TRIARILMETANAMINA FORMALNOM BETTIJEVOM REAKCIJOM

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Tetrasupstituirani metanamini prisutni su u velikom broju prirodnih organskih spojeva koji sadrže interesantan strukturalni motiv za sintezu različitih farmakološki aktivnih molekula [1,2]. Zbog velike steričke ometanosti na novosintetiziranom centru kiralnosti, priprava spojeva s kiralnim kvaternim ugljikovim atomom predstavlja veliki izazov u sintetskoj organskoj kemiji. Glavni je problem što katalizator teško prepoznaje enantiotopne strane, jer se fenilni prsteni međusobno malo razlikuju. Uobičajene metode za sintezu takvih optički aktivnih spojeva se oslanjaju na primjeni kiralnih organometalnih kompleksa prijelaznih metala, npr. Rh(I), Pd(II), Ni(II), Zn(II) i Co(II) [3,4]. Međutim, do sada u literaturi nije opisan organokatalitički pristup sintezi enantiomerno čistih α -triarilmetanamina. U tom kontekstu uspješno smo razvili metodologiju za stereoselektivnu Bettijevu reakciju primjenom kiralnih Brønstedovih kiselina (CPA). Reakcija se temelji na izravnoj 1,2-adiciji različito supstituiranih fenola na imin što rezultira nastajanjem enantiomerno obogaćenih α -triarilmetanamina. Uspjeh ove transformacije može se pripisati *in situ* stvaranju *N*-acil ketimina iz 3-hidroksisupstituiranih izoindolinona što ih čini podložnima za nukleofilni napad (Shema 1) [5]. Reakcija je regioselektivna i enantioselektivna, te je tolerantna s obzirom na prisutnost različitih funkcionalnih skupina kako u aromatskom prstenu izoindolinonskog alkohola, tako i na fenolu. Apsolutna konfiguracija određena je primjenom rendgenske strukturne analize, te je utvrđeno da tako opisanom reakcijom pretežito nastaje Bettijev produkt (*R*) konfiguracije. Na temelju dobivenih rezultata zaključili smo da stereokemijska indukcija proizlazi iz nukleofilnog napada fenola preko *si* prokiralne strane elektrofila.



Shema 1. Stereoselektivna sinteza α -triarilmetanamina katalizirana kiralnom Brønstedovom kiselinom.

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PRELIMINARY RESULTS ON POLYBROMINATED DIPHENYL ETHER CONTAMINATION STATUS IN ZAGREB HOUSE DUSTS

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Polybrominated diphenyl ethers (PBDEs) are organic compounds used as additive flame retardants in building and textile materials, and electrical and electronic equipment to prevent fire or slow down its spread. Because they do not form a chemical bond with the materials, they are easily released from household products and bind to organic particles of house dust [1]. In developed cities, people spend most of their time indoors, so inhalation and ingestion of dust is recognized as one of the main routes of human exposure to these compounds, in addition to dietary intake [2]. PBDEs are prone to bioaccumulation in the human body where they disrupt the hormonal balance and affect the endocrine system and neurobehavioral development [1]. Due to significant evidence of negative impact on human health, research into the levels of these compounds in house dust is of great importance.

For this purpose, 20 samples of house dust were collected in Zagreb. Extraction of 7 PBDE congeners (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-183) from 1 g of house dust was performed by microwave-assisted extraction (MAE) using 20 mL of solvent mixture *n*-hexane and acetone (1: 1, v/v) for 20 minutes at 80 °C. Analysis of the purified samples was performed on a gas chromatograph equipped with two capillary columns and two electron capture detectors. The sum of the mass fractions of the detected PBDE congeners in house dust samples ranged from 0.48 ng g⁻¹ to 200.09 ng g⁻¹ dust, and the most common congener was BDE-99. The BDE-183 congener was also detected in most samples, which indicates the presence of the thermolabile and photosensitive congener BDE-209, one of the most common congeners in house dust samples and among whose degradation products is BDE-183 [1,3,4].

ACKNOWLEDGMENTS

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PRELIMINARNI REZULTATI O ONEČIŠĆENJU ZAGREBAČKIH KUĆNIH PRAŠINA POLIBROMIRANIM DIFENIL ETHERIMA

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Polibromirani difenil eteri (PBDE) organski su spojevi korišteni kao aditivni usporivači gorenja u građevnom i tekstilnom materijalu te električnoj i elektronskoj opremi u svrhu sprječavanja nastanka požara ili usporavanja njegovog širenja. Budući da ne stvaraju kemijsku vezu s materijalima lako se otpuštaju sa kućanskih proizvoda i vežu za organske čestice kućne prašine [1]. U razvijenim gradovima ljudi većinu svog vremena provode u zatvorenim prostorima, stoga je udisanje i ingestija prašine prepoznato kao jedan od glavnih putova izloženosti ljudi ovim spojevima, uz unos putem prehrane [2]. Spojevi PBDE sklone su bioakumulaciji u ljudskom organizmu gdje narušavaju hormonsku ravnotežu i utječu na endokrini sustav i neurobihevioralni razvoj [1]. Zbog značajnih dokaza negativnog utjecaja na zdravlje ljudi, istraživanje razina navedenih spojeva u kućnoj prašini od velike je važnosti.

U tu svrhu skupljeno je 20 uzoraka kućne prašine na području Zagreba. Ekstrakcija 7 kongenera PBDE (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154 i BDE-183) iz 1 g kućne prašine provedena je pomoću tehnike mikrovalno potpomognute ekstrakcije (MAE) upotrebom 20 mL smjese otapala *n*-heksan:acetone (1:1, v/v) tijekom 20 minuta na temperaturi od 80 °C. Analiza pročišćenih uzoraka provedena je na plinskom kromatografu opremljenog sa dvije kapilarne kolone i dva detektora zahvata elektrona. Suma masenih udjela detektiranih kongenera PBDE u uzorcima kućne prašine bila je od 0,48 ng g⁻¹ do 200,09 ng g⁻¹ prašine, a najzastupljeniji kongener bio je BDE-99. U većini uzoraka detektiran je i kongener BDE-183 što upućuje na prisutnost termolabilnog i fotoosjetljivog kongenera BDE-209 koji jedan od najzastupljenijih kongenera u uzorcima kućne prašine, a jedan od produkata njegovog raspada je BDE-183 [1,3,4].

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Posterska priopćenja

Poster presentations



ACUTE, BILATERAL LOWER LIMB ISCHEMIA AFTER SARS-CoV-2 INFECTION AND COVID -19: A CASE REPORT

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Acute ischemia of lower extremities is manifested by sudden lack of blood flow or there is not enough blood delivered to the tissue of lower limbs. It is most often caused by thromboembolic events in arterial circulation with the most common source being the heart which is related to atrial fibrillation, myocardial infarction, diseases of heart valves or peripheral atherosclerotic plaques. During the COVID-19 pandemic the higher incidence of acute limb ischemia has been reported due to hypercoagulability that is associated with COVID-19. A case of 85-year-old male patient with confirmed SARS-CoV-2 infection and acute, bilateral lower limb ischemia will be presented. When SARS-CoV-2 infection was confirmed, the patient was showing mild symptoms of the COVID-19 disease, fever to 38° and weakness. Thereafter, the patient fully recovered. Thirty days after confirmed SARS-CoV-2 infection, acute, bilateral lower limb occurred with failed attempt of revascularization.

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AKUTNA, OBOSTRANA ISHEMIJA NOGU NAKON SARS-CoV-2 INFEKCIJE I COVID-19: PRIKAZ SLUČAJA

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Akutnu ishemiju donjih udova obilježava naglo smanjenje ili prestanak protoka krvi u arterijama nogu i najčešće je posljedica tromboembolijskog incidenta u arterijskoj cirkulaciji s najčešćim izvor srčanog porijekla kod fibrilacije atrijske, nakon infarkta miokarda, bolesti srčanih zalistaka, periferne ateroskleroze arterija [1]. Tijekom pandemije koronavirusom primijećena je povećana incidencija akutne ishemije udova što se povezuje s hiperkoaguabilnim stanjem tijekom i nakon bolesti COVID-19 te povećanom učestalosti periferne arterijske tromboze [2,3]. U ovom radu opisat ću bolesnika u dobi od 85 godina s dokazanom infekcijom SARS-CoV-2 i akutnom, obostranom ishemijom nogu. Pri potvrđenoj infekciji SARS-CoV-2 pacijent je imao blage simptome bolesti COVID-19, febrilitet do 38° i opću slabost, nakon čega dolazi do oporavka pacijenta. Trideset dana nakon potvrđene infekcije SARS-CoV-2, pacijent razvija akutnu, obostrano ishemiju nogu uz bezuspješan pokušaj revaskularizacije.

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BIOMARKERS OF EFFECT AND OXIDATIVE STRESS ANALYSIS IN BLOOD OF WHITE STORK (*CICONIA CICONIA*) NESTLINGS FROM CROATIA

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The white stork (*Ciconia ciconia*) is a breeding species in continental Croatia. It feeds usually close to the breeding site with small mammals, amphibians, snakes, fish, earthworms, large insects and their larvae in the flooded river plains, extensively farmed meadows and pastures or water meadows. White stork nestlings can provide quantitative information on the quality of the surrounding environment, and therefore was chosen as a model species for evaluation of molecular biomarkers. Aim of this study was to analyse biomarkers of effect: activities of acetylcholinesterase (AChE) and carboxylesterase (CES), as well as oxidative stress biomarkers: activities of glutathione S-transferase (GST) and glutathione reductase (GR), as well as levels of glutathione (GSH) and reactive oxygen species (ROS). During white stork breeding season in 2020, five sampling locations were visited: Lonjsko polje, Jelas polje, Slavonski Brod - east, Podunavlje and Donje Podravlje. For biomarker analysis and sex determination blood samples (4 mL) were collected from the nestling brachial vein ($n = 109$). All biomarkers were measured in two blood fractions – plasma and S9 homogenate. Nestlings from Podunavlje and Donje Podravlje showed the lowest AChE and CES activity, indicating different presence of inhibitory xenobiotics when compared to different locations. Significant differences were also reported in oxidative stress biomarkers in response to different locations as the highest oxidative stress was recorded in Slavonski Brod - east and Podunavlje. Reported results propose that white stork nestlings could be affected by pollutants from their surrounding environment, due to proximity to metal, petroleum and agricultural industry. However, additional research is needed to confirm this assumption, as this is the first evaluation of blood biochemical parameters in white stork nestling population in Croatia.



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Bijela roda (*Ciconia ciconia*) je gnijezdeća vrsta u kontinentalnoj Hrvatskoj koja se hrani sitnim sisavcima, zmijama, vodozemcima, ribama, gujavicama i kukcima na području poplavnih dolina rijeka, livadama i oranicama koja su pod utjecajem intenzivne poljoprivrede. Ptici bijele rode su indikatori lokalnog zagađenja te daju kvantitativnu procjenu kvalitete okoliša u kojem obitavaju, stoga su izabrane kao modelni organizam za procjenu molekularnih biljega. Cilj ovog istraživanja je određivanje spola i analiza biomarkera učinka: aktivnosti acetilkolinesteraze (AChE) i karboksilesteraze (CES) te analiza biomarkera oksidativnog stresa: aktivnosti glutation S-transferaze (GST) i glutation reduktaze (GR) te razine glutationa (GSH) i reaktivnih kisikovih jedinki (ROS). Tijekom prstenovanja bijele rode u gnijezdećoj sezoni 2020., krv je uzorkovana s 5 različitih lokacija: Lonjsko polje, Jelas polje, Slavonski Brod - istočno, Podunavlje i Donje Podravlje. Uzorkovano je 4 mL krvi iz brahijalne vene ($n = 109$) za analizu navedenih biomarkera te za određivanje spola. Svi navedeni biomarkeri mjereni su u 2 frakcije krvi – plazmi i homogenatu S9. Najniža enzimski aktivnost AChE i CES zabilježena je u ptićima s područja Podunavlja i Donjeg Podravlja, ukazujući na prisutnost inhibitornih ksenobiotika u odnosu na ostale lokacije. Na različitim lokacijama zabilježene su i značajne razlike u odgovoru biomarkera oksidativnog stresa, a najviša razina oksidativnog stresa zabilježena je u Slavonskom Brodu. Navedeni rezultati ukazuju na mogućnost utjecaja zagađivala na ptiće bijele rode s obzirom na blizinu metalne, kemijske i poljoprivredne industrije. Potrebna su dodatna istraživanja kako bi potvrdili ovu pretpostavku, s obzirom na to da je ovo prva analiza biokemijskih parametara u krvi ptića bijele rode na području Hrvatske.



CORRELATION OF BDNF, IL-6 EXPRESSION AND OXIDATIVE STRESS MARKERS IN DEMYELINATING DAMAGE

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BDNF, IL-6 and oxidative stress markers have a distinct role on the process of demyelination in multiple sclerosis [1]. Distinct mechanisms of influence on inflammatory and neurodegenerative phase are not clarified. Around 140 to 200 subjects would be included in this investigation, 70-100 with confirmed demyelinating process according to the criteria of relapse remitting multiple sclerosis and 70-100 with chronic fatigue syndrom as a control group. The levels of the neurotrophin BDNF mRNA (proBDNF and mBDNF), IL-6 and oxidative stress markers (MDA, SOD, GSH, catalase and karbonilated proteins) would be detected from subjects serum and correlated with the number of demyelinating T2 / FLAIR lesions. The aim is to determine the correlation between the ratio of the above physiological parameters with a degree of disability, cognitive deficits and depression in infalamation and degeneration phase of the disease and connection with the disease progression. The hypothesis of this study was that the subjects with relapsing remitting multiple sclerosis have the disorder in proportions BDNF isoforms of IL-6 and markers of oxidative stress, which is directly related to the number of demyelinating MRI lesions.

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MEĐUODNOS EKSPRESIJE BDNF, IL-6 I POKAZATELJA OKSIDACIJSKOG STRESA PRI DEMIJELINIZACIJSKIM OŠTEĆENJIMA

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BDNF, IL-6 i markeri oksidacijskog stresa nedvojbeno imaju utjecaj na demijelinizacijski proces u multiploj sklerozi [1]. Točni mehanizmi utjecaja na upalnu i neurodegenerativnu fazu nisu u potpunosti razjašnjeni. U ovo istraživanje uključilo bi se 140-200 ispitanika, 70-100 s verificiranim demijelinizacijskim oštećenjima koji zadovoljavaju kriterije RRMS-a i 70-100 sa sindromom kroničnog umora kao kontrolnom skupinom. Iz krvi ispitanika određivala bi se razina ekspresije neurotrofina BDNF-a (proBDNF i mBDNF), IL-6 i markera oksidacijskog stresa (MDA, SOD, GSH, katalaze i karboniliranih proteina), te bi se dodatno korelirala s brojem demijelinizacijskih T2/FLAIR lezija. Utvrdila bi se i potencijalna korelacija omjera navedenih fizioloških parametara sa stupnjem onesposobljenosti, kognitivnim deficitom i depresijom u pojedinim fazama i progresiji bolesti. Hipoteza ovog istraživanja je da ispitanici s relapsno remitirajućom multiplom sklerozom imaju poremećaj u omjerima BDNF izoformi, koncentracije IL-6 i markera oksidacijskog stresa koji je u izravnoj vezi sa brojem demijelinizacijskih lezija evidentiranih MR-om.

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GENETIC POLYMORPHISM OF METABOLIC ENZYMES AND TRANSPORTERS IN RENAL TRANSPLANT RECIPIENTS

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Renal transplantation is therapy of choice in treatment of patients with final phase of chronic kidney disease. Genetic variability in some of genes between organ donor and recipient can cause reactions of recipient's immune system and graft rejection. Significant step forward in transplantation medicine started with development of immunosuppressive drugs which enabled better control of immune system and prolongation of survival rate for renal failure patients [1]. Standard immunosuppressive regimen in therapy of renal transplant patients is based on multidrug combination therapy with calcineurin inhibitor (cyclosporine or tacrolimus), mycophenolic acid and steroids. Because of their narrow therapeutic index and significant intra/inter-individual pharmacokinetic variability, their effect needs to be monitored carefully. Therapeutic drug monitoring by measuring drug blood concentration is clinical practice used to minimize pharmacokinetic drug variability by controlling its concentration and to achieve balance between toxic and therapeutic dose, in order to optimise therapeutic effect. Genetic variability of metabolic enzymes and transporters can significantly influence drug absorption, distribution, metabolism and excretion and consequently change benefit/risk ratio by lowering drug effectiveness or causing toxic reactions [2,3]. The aim of this study was to determine the frequency of potentially actionable pharmacogenes in the Croatian renal transplant patients. Study included 158 postrenal transplantation patients treated with immunosuppressants. Genotyping of *ABCB1* (3435C>T), *ABCC2* (-24C>T), *ABCG2* (421C>A), *SLCO1B1* (521T>C), *CYP3A4**22, *CYP3A5**1 and *UGT1A9* (-2152C>T) was performed by TaqMan real-time PCR for discovery of clinically actionable variants: *ABCB1* 3435 CT, *ABCB1* 3435 TT, *ABCC2* 24 CT, *ABCC2* 24 TT, *ABCG2* 421CA, *ABCG2* 421AA, *SLCO1B1* 521TC, *SLCO1B1* 521CC, *CYP3A4**22/*22, *CYP3A4**1/*22, *CYP3A5**1/*1, *CYP3A5**1/*3, *CYP3A5**3/*3, *UGT1A9* 2152CT and *UGT1A9* 2152TT. At least one clinically actionable variant was found in 68 of 150 patients (45%). The frequencies of variant/minor alleles in the observed group were: *ABCB1* (45%), *ABCC2* (28%), *SLCO1B1* (27%), *ABCG2* (12%), *CYP3A5* (12%), *UGT1A9* (3%), *CYP3A4* (1%). Patients with these clinically actionable variants need personalized treatment approach according to their gene variants in order to optimise drug therapy and avoid graft rejection.

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POLIMORFIZAM GENA ZA METABOLIČKE ENZIME I TRANSPORTNE PROTEINE KOD BOLESNIKA S TRANSPLANTIRANIM BUBREGOM

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Transplantacija bubrega je krajnja metoda izbora u liječenju bolesnika koji su u završnoj fazi kronične bubrežne bolesti. Genska nejednakost između darovatelja i primatelja organa dovodi do reakcija imunskog sustava primatelja što rezultira odbacivanjem presatka. Značajan iskorak u transplantacijskoj medicini predstavlja razvoj imunosupresivne farmakoterapije koja omogućava bolju kontrolu imunološkog sustava i uspješnog preživljavanja pacijenata s presađenim bubregom [1]. Standardni imunosupresijski protokol sastoji se od istovremene primjene više lijekova: inhibitora kalcineurina (ciklosporin ili takrolimus), mikofenolne kiseline i kortikosteroida. Obzirom da imunosupresijski lijekovi imaju usku terapijsku širinu, a pokazuju značajnu inter/intraindividulanu farmakokinetičku varijabilnost, potrebno je terapijsko praćenje koncentracije lijeka u krvi kako bi se smanjila farmakokinetička varijabilnost lijekova kontroliranjem njihove koncentracije te postigla ravnoteža između toksične i učinkovite doze lijeka, što dovodi do optimalnog terapijskog učinka. Genetska varijabilnost metaboličkih enzima i transportnih proteina značajno utječe na apsorpciju, distribuciju, metabolizam i izlučivanje lijekova te mijenja omjer rizika i koristi farmakoterapije na način da smanjuje terapijski učinak lijeka ili dovodi do toksičnih reakcija [2,3]. Cilj ovog istraživanja bio je odrediti učestalost genskih polimorfizama metaboličkih enzima (farmakogena) i transportnih proteina u bolesnika s transplantiranim bubregom u Hrvatskoj populaciji. Ispitivanje je uključivalo 158 bolesnika s transplantiranim bubregom koji su na imunosupresijskoj terapiji. Genotipizacija polimorfizama *ABCB1 3435C>T*, *ABCC2 -24C>T*, *ABCG2 421C>A*, *SLCO1B1 521T>C*, *CYP3A4*22*, *CYP3A5*1* i *UGT1A9 -2152C>T* provedena je metodom PCR u stvarnom vremenu (od eng. *real-time PCR*) kako bi se ispitali klinički značajni polimorfizmi ovih gena. Kod 68 od ukupno 150 bolesnika (45%) pojavljuje se najmanje jedan klinički značajan polimorfizam: *ABCB1 3435 CT*, *ABCB1 3435 TT*, *ABCC2 24 CT*, *ABCC2 24 TT*, *ABCG2 421CA*, *ABCG2 421AA*, *SLCO1B1 521TC*, *SLCO1B1 521CC*, *CYP3A4*22/*22*, *CYP3A4*1/*22*, *CYP3A5*1/*1*, *CYP3A5*1/*3*, *CYP3A5*3/*3*, *UGT1A9 2152CT* i *UGT1A9 2152TT*. Učestalost varijantnih alela u promatranoj skupini je: *ABCB1* (45%), *ABCC2* (28%), *SLCO1B1* (27%), *ABCG2* (12%), *CYP3A5* (12%), *UGT1A9* (3%), *CYP3A4* (1%) te ih je potrebno uzeti u obzir prilikom propisivanja lijekova i režima doziranja za pojedinog pacijenta kako bi postigli optimalni učinak farmakoterapije i izbjegli odbacivanje presadka.

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THE EFFECTS OF TRIAZOLE FUNGICIDES ON BEHAVIOUR AND PHYSIOLOGY OF *Daphnia magna*

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Daphnia species are among the most common settlers of freshwater habitats. Due to their high sensitivity to various toxicants, these planktonic crustaceans represent a useful model organism in ecotoxicological research [1]. Recently, *Daphnia* behaviour has gained attention and has been recognized as a sensitive biomarker of toxicity of sublethal concentrations of pollutants [2]. The aim of this study was to investigate the effects of sublethal concentrations of three triazole fungicides (tebuconazole, difenoconazole and fenbuconazole) on swimming activity (average speed, mobility index, number of direction changes, discontinuity of motion etc.) and physiological parameters (heart rate, thoracic limb activity, movement of post-abdominal claw and movement of second antennae) of *Daphnia magna*. The study showed that the applied toxicants caused a decrease in swimming activity in a dose-response manner and also affected the physiological activity of the organisms. The results revealed that the investigated behavioural and physiological endpoints can be used as early biomarkers of exposure to environmentally relevant sublethal concentrations [3] of commonly used commercial triazole fungicides.

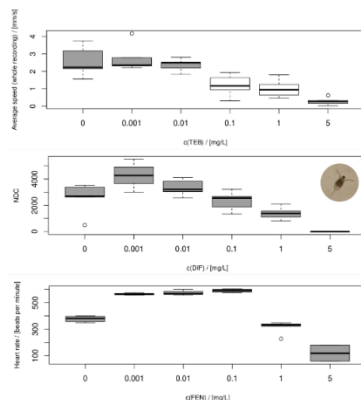


Figure 1. Behavioural and physiological parameters measured in *Daphnia magna* exposed to various concentrations of triazole fungicides.

ACKNOWLEDGMENTS

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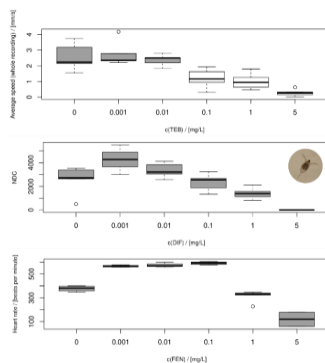
UTJECAJ TRIAZOLNIH FUNGICIDA NA PONAŠANJE I FIZIOLOŠKU AKTIVNOST *Daphnia magna*

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Daphnia (vodenbuhe) su jedna od najbrojnijih skupina u slatkovodnim ekosustavima. Zbog svoje visoke osjetljivosti, ovi planktonski rakovi koriste se kao modelni organizmi u ekotoksikološkim ispitivanjima [1]. U posljednje vrijeme sve su više zastupljena istraživanja temeljena na istraživanju ponašanja *Daphnia* uslijed izloženosti toksikantima, a parametri kretanja prepoznati su kao osjetljiv biomarker izloženosti subletalnim koncentracijama zagađivala [2]. Cilj ovog istraživanja bio je ispitati učinak subletalnih koncentracija tri fungicida iz skupine triazola (tebukonazol, difenkonazol, fenbukonazol) na kretanje (prosječna brzina, indeks pokretljivosti, broj promjena smjera kretanja, diskontinuiranost gibanja itd.) i fiziološke parametre (brzina otkucaja srca, aktivnost filopoda, pomicanje furke i ticala) *Daphnia magna*. Rezultati istraživanja pokazali su da ispitivani toksikanti uzrokuju smanjenje sposobnosti kretanja organizama tipa doza-odgovor, a istovremeno djeluju i na proučavane fiziološke parametre. Rezultati provedenog istraživanja potvrđuju kako se ponašanje i fiziološki parametri *Daphnia* mogu koristiti kao rani biomarkeri izloženosti organizama okolišno relevantnim subletalnim koncentracijama [3] komercijalnih triazolnih fungicida.



Slika 1. Parametri kretanja i fiziološka aktivnost *Daphnia magna* izloženih različitim koncentracijama triazola.

ZAHVALE

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EPIGENOMICS OF HOLOCENTROMERE

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Centromeres are chromosomal regions essential for kinetochore attachment to mitotic spindle and proper chromosome segregation during cell divisions. They are determined epigenetically with centromere-specific variant of histone H3 (CenH3). While centromere function is conserved, CenH3 and underlying DNA evolve rapidly. Most research has been done on sexual species with monocentric chromosomes characterized by a single CenH3-containing region. In contrast, holocentromeres have their function dispersed throughout the entire length of chromosome. In this study, we used holocentric nematodes of the genus *Meloidogyne* as a model organism for the centromere study [1]. CenH3 characterization is done for three closely related, polyploid mitotic parthenogenetic species together with distantly related meiotic parthenogen species. We found that ancestral duplication of CenH3 gene resulted in one conserved CenH3 (α CenH3) and other gene that evolved rapidly into four different CenH3 variants. Immunofluorescence performed on mitotic *M. incognita* revealed a dominant role of α CenH3 histone on its centromere (Figure 1) while the other CenH3s have lost their function. In addition, ChIP-Seq analysis showed that α CenH3-associated DNA is comprised of tandem repeats with divergent monomers but completely conserved 19-bp long box. Preservation of α CenH3 and DNA constituents is also proven for other investigated species. These results elucidate unique characteristics where CenH3 and associated DNA are maintained over long period of time in holocentromeres of exclusively mitotic species. Our findings of centromere evolution in asexual, holocentric organisms thus help building an integrated view on the centromere (epi)genomics.

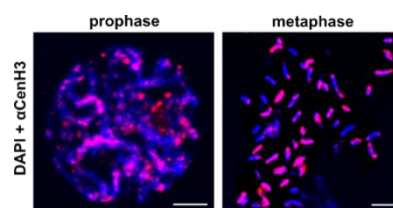


Figure 1. Centromere organization in *Meloidogyne incognita*. Immunofluorescence of α CenH3-containing domains (red) with chromosomes counterstained with DAPI (blue), scale bar=5 μ m.

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EPIGENOMIKA HOLOCENTROMERA

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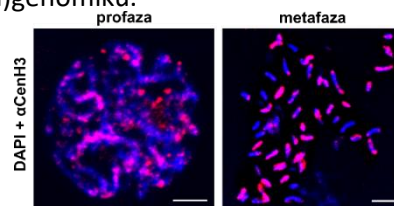
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Centromere su kromosomske regije nužne za vezanje kinetohore za diobeno vreteno i pravilno razdvajanje kromosoma tijekom staničnih dioba. Epigenetički su određene s centromerno-specifičnom varijantom histona H3 (CenH3). Dok je centromerna funkcija očuvana, CenH3 i pripadajuća DNA evoluiraju brzo. Većina istraživanja centromere napravljena su na spolnim vrstama s monocentričnim kromosomima koji imaju jedinstvenu CenH3 regiju. S druge strane, kod holocentričnih kromosoma centromerna funkcija je raspršena njihovom cijelom duljinom. U ovom istraživanju su holocentrični oblici roda *Meloidogyne* korišteni kao modelni organizam za centromerno istraživanje [1]. Karakterizacija histona CenH3 je napravljena za tri blisko srodne poliploidne mitotske partenogenetske vrste zajedno s udaljenom mejotskom partenogenetskom vrstom. Pronađena je ancestralna duplikacija gena *CenH3* koja je rezultirala s jednim konzerviranim histonom CenH3 (α CenH3) i drugim genom koji je evoluirao u četiri različite varijante CenH3. Imunofluorescencijsko bojenje napravljeno na mitotskoj vrsti *M. incognita* otkrilo je dominantnu ulogu histona α CenH3 u centromeri (Slika 1) dok su ostali histoni CenH3 izgubili svoju ulogu. Također, analiza *ChIP-Seq* je pokazala kako se DNA povezana s α CenH3 sastoji od uzastopnih ponavljanja s različitim monomerima, ali uz potpuno sačuvani 19-bp motiv. Očuvanost α CenH3 i vezane DNA potvrđena je i kod ostalih proučavanih vrsta. Ovi rezultati razjašnjavaju jedinstvene karakteristike održavanja povezanosti histona CenH3 i vezane DNA tijekom dugog vremenskog razdoblja u holocentromerama isključivo mitotskih vrsta. Naša otkrića evolucije centromere u nespolnim holocentričnim organizmima pomažu u izgradnji integriranog pogleda na centromernu (epi)genomiku.



Slika 1. Organizacija centromere u vrsti *Meloidogyne incognita*. Imunofluorescencijska α CenH3-pripadajućih domena (crveno) s kromosomima koji su obojani DAPI bojom (plavo), mjera=5 μ m.

ZAHVALE

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GENOME SIZE OF *Festuca bosniaca* (Poaceae) ON THE BALKAN PENINSULA

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The genus *Festuca* is one of the largest genera within the grass family [1]. It is characterized by a complex taxonomy resulting from morphological complexity which includes not only heteromorphism but also convergent morphology of different species inhabiting similar environments. Additional taxonomical confusion is caused by the fact that some species include populations with different degrees of ploidy, resulting in varied morphological characteristics [2]. A different degree of ploidy within the same species may cause a higher ecological adaptability [3].

The aim of our research is to determine the genome size and ploidy degree in *Festuca bosniaca* that is native to the high mountains of the Balkans. Chromosome number in diploids of the species is $2n=14$. Thirty-seven populations of *F. bosniaca* were sampled across its distribution range during the summer months from 2018 to 2020. On average, five individuals were sampled in each population. Genome size measured by flow cytometry showed that in sampled populations, diploids (27 populations) and tetraploids (10 populations) are found. Relative genome size ranged from 1.138 to 1.637 for diploid and 2.255 to 2.627 for tetraploid populations. Diploid populations were found throughout the whole area of species distribution, while tetraploids are limited to the central part of the range, and probably represent relicts from former glacial refugia.

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VELIČINE GENOMA VRSTE *Festuca bosniaca* (Poaceae) NA BALKANSKOM POLUOTOKU

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Rod *Festuca* jedan je od najvećih rodova unutar porodice trava [1]. Karakterizira ga složena taksonomija koja proizlazi iz morfološke kompleksnosti, a koja ne uključuje samo heteromorfno nego i konvergentnu evoluciju morfologije različitih vrsta koje obitavaju u sličnim ekološkim uvjetima. Za dodatnu taksonomsku nejasnoću odgovorna je činjenica da se unutar iste vrste često mogu pronaći populacije različitih stupnjeva ploidijske, što se može odraziti i na različit izgled biljaka [2]. Različiti stupanj ploidijske unutar iste vrste kod biljaka može označavati i veću ekološku prilagodljivost [3].

Cilj našega istraživanja bio je odrediti veličine genoma i stupnjeve ploidijske unutar vrste *Festuca bosniaca* koja je rasprostranjena na visokim planinama Balkana i na Apeninima. Osnovni broj kromosoma kod diploida ove vrste je 14. Ukupno je uzorkovano 37 populacija vrste *F. bosniaca*, koje su sakupljene na većini areala rasprostranjenosti tijekom ljetnih mjeseci od 2018. do 2020. U prosjeku je sakupljeno po pet jedinki po populaciji. Mjerenjem veličine genoma pomoću protočnog citometra određeno je da se unutar uzorkovanih populacija mogu naći diploidi (27 populacija) i tetraploidi (10 populacija). Relativna veličina genoma iznosila je od 1.138 do 1.637 za diploide te 2.255 do 2.627 za tetraploide. Diploidne populacije ustanovljene su na cijelome uzorkovanom području, dok su tetraploidi ograničeni na centralno područje distribucije, a smatraju se reliktima nekadašnjih glacijalnih refugija.

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DYNAMIC ENERGY BUDGET MODELS FOR ENDANGERED NATIVE AND INVASIVE CRAYFISH SPECIES

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Dynamic Energy Budget (DEB) theory postulates the rules of energy acquisition and allocation throughout the life cycle of an organism [1]. Models based on DEB theory have proved to be a powerful and versatile tool in ecology and ecotoxicology, predicting physiological responses of individuals to environmental stressors [2]. In particular, DEB models can predict effects of physiological changes (e.g., responses to stressors such as a disease) to individual growth and reproduction and, through population models, quantify population-level effects [3]. We developed the DEB models for marbled (*Procambarus virginalis*) [4] and stone crayfish (*Austropotamobius torrentium*) [5] and advanced the existing models for noble (*Astacus astacus*) [6] and signal crayfish (*Pacifastacus leniusculus*) [7]. Using given models, we will analyze the effect of exposure to theoretical stressors on endangered native (noble and stone crayfish) and invasive crayfish species (marbled and signal crayfish). We will also incorporate experimental data on effect of sublethal pathogen infection on growth of marbled crayfish into DEB model for marbled crayfish to estimate the energetic costs of defense against pathogens.

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MODELI DINAMIČKIH ENERGIJSKIH BUDŽETA ZA UGROŽENE AUTOHTONE I INVAZIVNE VRSTE RAKOVA

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Teorija Dinamičkih Energijskih Budžeta (DEB) postavlja pravila vezana uz dobivanje i preraspodjelu energije tijekom životnog ciklusa organizma [1]. Modeli temeljeni na DEB teoriji omogućuju predviđanje fizioloških odgovora jedinki na okolišne stresore i pokazali su se korisnim alatom u ekologiji i ekotoksikologiji [2]. Konkretno, DEB modeli mogu predvidjeti učinke fizioloških promjena (npr. odgovora na stres poput bolesti) na rast i reprodukciju jedinki, te u kombinaciji s populacijskim modelima, kvantificirati učinke na razini populacije [3]. Razvili smo DEB modele za mramornog (*Procambarus virginalis*) [4] i potočnog raka (*Austropotamobius torrentium*) [5] te unaprijedili postojeće modele za riječnog (*Astacus astacus*) [6] i signalnog raka (*Pacifastacus leniusculus*) [7]. Pomoću tih modela, analizirat ćemo učinak izloženosti teoretskim stresorima na ugrožene autohtone (riječni i potočni rakovi) i invazivne vrste rakova (mramorni i signalni rakovi). Također ćemo uključiti eksperimentalne podatke o utjecaju subletalne zaraze patogenom na rast mramornih rakova u DEB model mramornog raka, kako bismo procijenili energetske troškove obrane od patogena.

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MOLECULAR BASIS OF VIRULENCE AND ANTIBIOTIC RESISTANCE IN VANCOMYCIN-RESISTANT *ENTEROCOCCUS FAECIUM* FROM WASTEWATER AND RECEIVING BEACH WATER

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Since first identification in 1980s [1], vancomycin-resistant enterococci became one of the most important opportunistic pathogens today [2], and have been detected in clinical and natural environments. Infections caused by vancomycin-resistant *Enterococcus faecium* are particularly difficult to treat, due to its virulence factors, and both intrinsic and acquired resistance to multiple antibiotics including vancomycin as first-line therapy [3]. Prevalence of this pathogen in clinical settings in Croatia increased in recent years to 17% [4]. Thus, the aim of this research was to screen for the first time the presence of vancomycin-resistant *E. faecium* in wastewater outlet and surface water from the nearby public beach located in Kaštela Bay. Isolates were species identified by Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) with MALDI-Biotyper 4.1.80 (PYTH) software version (Bruker Daltonics, Bremen, Germany), and tested for susceptibility to six antibiotics by disc-diffusion method. Isolates were then PCR screened for the presence of genes encoding for virulence (*asa*, *cylA*, *esp*, *gelE*, *ace*, *efaA*, *hyl*, *sprE*), resistance to vancomycin (*vanA*, *vanB*, *vanC1*, *vanC2/C3*) and aminoglycosides (*aph(3')-IIIa*, *ant(4')-Ia*, *aac(6')-Ie-aph(2'')-Ia*, *aph(2'')-Ib*, *aph(2'')-Ic*, *aph(2'')-Id*). Finally, based on results of Sanger sequencing of seven housekeeping genes (*adk*, *atpA*, *ddl*, *gyd*, *gdh*, *purK*, *pstS*) isolates were assigned to sequence types (STs) using multilocus sequence typing (MLST) scheme and reported to PubMLST database (<https://pubmlst.org>).

The presence of virulent and vancomycin-resistant *E. faecium* in surface beach waters represents a serious risk factor for human health, particularly in term of determinants of their virulence and antibiotic resistance characteristic to clinical isolates of this opportunistic pathogen.

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MOLEKULARNA OSNOVA VIRULENCIJE I ANTIBIOTSKE REZISTENCIJE VANKOMICIN-REZISTENTNIH *ENTEROCOCCUS FAECIUM* IZOLATA IZ OTPADNE I MORSKE VODE SA JAVNE PLAŽE

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Od prve identifikacije 1980-ih [1], vankomicin-rezistentni enterokoki među najvažnijim su oportunističkim patogenima današnjice [2], a otkriveni su u kliničkom i prirodnom okolišu. Infekcije uzrokovane vankomicin-rezistentnim *Enterococcus faecium* posebno je teško liječiti zbog čimbenika virulencije, kao i intrinzične i stečene rezistencije na različite antibiotike, uključujući vankomicin kao lijek prve linije [3]. Prevalencija ovog patogena u kliničkim uvjetima u Hrvatskoj povećala se posljednjih godina na 17% [4]. Stoga je cilj ovog istraživanja bio po prvi put provjeriti prisutnost vankomicin-rezistentnog *E. faecium* u otpadnoj vodi i površinskim vodama s obližnje javne plaže smještene u Kaštelanskom zaljevu. Izolati su identificirani do vrste pomoću metode matricom potpomognute ionizacije uz desorpciju laserskim zračenjem i masenom spektrometrijom vremena leta (engl. *matrix-assisted laser desorption/ionization, time of flight mass spectrometry*, MALDI-TOF MS) sa softverskom verzijom MALDI-Biotyper 4.1.80 (PYTH) (Bruker Daltonics, Bremen, Njemačka) te testirani na osjetljivost na šest antibiotika koristeći metodu disk-difuzije. Potom je metodom PCR-a ispitana prisutnost gena koji kodiraju na virulenciju (*asa*, *cyIA*, *esp*, *gelE*, *ace*, *efaA*, *hyl*, *sprE*), rezistenciju na vankomicin (*vanA*, *vanB*, *vanC1*, *vanC2/C3*) i aminoglikozide (*aph (3')-IIIa*, *ant (4')-Ia*, *aac (6')-Ie-aph (2'')-Ia*, *aph (2'')-Ib*, *aph (2'')-Ic*, *aph (2'')-Id*). Konačno, na temelju rezultata Sangerovog sekvenciranja sedam gena za održavanje (*adk*, *atpA*, *ddl*, *gyd*, *gdh*, *purK*, *pstS*) izolati su dodijeljeni tipovima (ST) pomoću sheme za tipizaciju određivanjem sljedova nukleotida na više genskih lokusa (engl. *multilocus sequence typing*, MLST) te prijavljeni u bazu podataka PubMLST (<https://pubmlst.org>).

Prisutnost virulentnih i vankomicin-rezistentnih *E. faecium* izolata u površinskim vodama na javnoj morskoj plaži predstavlja ozbiljan faktor rizika za ljudsko zdravlje, posebno u smislu identificiranih obilježja virulencije i rezistencije na antibiotike karakterističnih za kliničke izolate ovog oportunističkog patogena.

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DIATOM CO-CULTURES: CLOSE ENCOUNTERS OF *ACHNANTHES ELONGATA* AND *PSAMMODYCTION* SP.

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Diatoms (Bacillariophyceae) are unicellular algae almost omnipresent in aquatic and soil ecosystems and are known for their intricate silicate frustules. Along with bacteria, diatoms are the first colonizers of submerged surfaces, often forming mixed diatom species biofilms. Recent studies have shown that diatom biofilms are present on marine vertebrates such as killer whales [1] and loggerhead sea turtles [2] with indications of certain diatom taxa being specific to the host [3, 4]. Loggerhead sea turtles (*Caretta caretta*) have revealed themselves as a peculiar habitat with high potential for new diatom species discovery [2]. The mechanisms surrounding substrate specificity in putative turtle-specific versus non-specific diatom taxa remain unclear. It is known, however, that diatom taxa interactions affect changes in biomass and productivity depending on the biofilm composition [5]. In this study we isolated turtle-associated diatoms (*Achnanthes elongata* and *Psammodyction* sp. strains) from accidentally caught loggerhead sea turtles in the Adriatic Sea. The diatoms were grown as xenic monocultures prior to co-cultivation to estimate the effects co-cultivation on biomass and growth of individual strains. Co-cultivation experiments were performed in 24-well cell culture plates and quantified by Cytation 3 (BioTek) multi-mode reader (bright field images and CY5 fluorescence) which allowed for stable conditions across co-cultivations and higher data output. Preliminary data analysis showed minor changes in growth rates of several *Achnanthes elongata* strains when co-cultured with *Psammodyction* sp., while *Psammodyction* sp. tended to grow slower in co-cultures than in monocultures. Further, co-cultivations of *Achnanthes elongata* and *Psammodyction* sp. indicate the importance of differing life strategies of putative turtle-specific diatom taxa and turtle associated but non-specific diatom taxa.

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KOKULTIVACIJA DIJATOMEJA: BLISKI SUSRETI *ACHNANTHES ELONGATA* I *PSAMMODYCTION* SP.

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Dijatomeje (Bacillariophyceae) su jednostanične alge, intrikatnih silikatnih ljušturica, te su gotovo sveprisutne u vodenim ekosustavima i tlima. Uz bakterije, jedne su od prvih kolonizatora uronjenih površina na kojima često stvaraju miješane dijatomejske biofilme. Nedavna istraživanja ukazala su na prisutnost dijatomejskih biofilмова i na morskim kralješnjacima kao što su orke [1] i glavate želve [2]. Postoje indicacije da su neke od novotkrivenih svojiti dijatomeja specifične za svog domaćina s obzirom da nisu pronađene na drugim potencijalnim staništima [3, 4]. Glavate želve (*Caretta caretta*) su pokazale izniman potencijal kao stanište za dosad neopisane vrste dijatomeja [2] ali mehanizmi koji opisuju prednost nastanjanja dijatomeje na specifičnu površinu domaćina ostaju nepoznati. U ovom istraživanju izolirali smo pojedinačne stanice dijatomeja povezanih s glavatim želvama u Jadranskom moru (sojevi *Achnanthes elongata* i *Psammodyction* sp.) te uspostavili ne-sterilne monokulture prije eksperimenata kako bismo mogli pratiti utjecaj ko-kultivacije na rast i biomasu individualnih sojeva dijatomeja. Ko-kultivacije su postavljene u pločama za uzgoj stanica s 24 jažice i kvantificirane Cytation 3 (Biotek) multi-mode čitačem (svjetlosno polje i CY5 fluorescencija) što nam je omogućilo stabilne uvjete za sve ko-kultivacije i sakupljanje veće količine podataka u usporedbi s tradicionalnijim metodama. Preliminarne analize podataka ukazuju na manje promjene u dinamici rasta nekoliko sojeva *Achnanthes elongata* u ko-kultivaciji s *Psammodyction* sp., dok *Psammodyction* sp. pokazuje usporavanje rate rasta u ko-kulturi (u usporedbi s monokulturom). Nadalje, ko-kultivacije *Achnanthes elongata* i *Psammodyction* sp. upućuju na važnost različitih životnih strategija između svojiti dijatomeja koje smatramo potencijalno specifičnima i onima koje smatramo ne-specifičnima za morske kornjače.

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ANALYSIS OF EXPRESSION OF LNCRNA ANRIL AND PVT1 IN PERIPHERAL CIRCULATION OF PATIENTS WITH CALCIFYING AORTIC VALVE STENOSIS

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In this study, we aimed to analyze the expression of lncRNA ANRIL and PVT1 in the peripheral circulation (plasma) of patients with calcifying aortic valve stenosis (CAVS; n=45) [diagnosed at the Department of Cardiac and Transplant Surgery, Clinical Hospital Dubrava] and the equal number of healthy controls. Signed informed consent was obtained from all participants. The study was approved by the Ethics committee of Clinical Hospital Dubrava and the Medical Faculty, University of Zagreb. Blood was isolated from CAVS patients preoperatively before aortic valve replacement, and from control subjects after signed informed consent for participation in the study. After isolation, peripheral blood samples (vacutainers with sodium citrate) were centrifuged at 3000 g for 15 minutes, and the resulting plasma filtered through 0.2 µm syringe filters to obtain platelet-free plasma (PFP). The PFP samples were aliquoted into 1.5 mL Eppendorf tubes and stored at -80 ° C. The quality and quantity of total RNA isolated from 500 µl of PFP samples by a combination of Trizol reagent (Invitrogen Life Technologies) and miRNAeasy kit (Qiagen) were determined using a NanoDrop spectrophotometer (Thermo Fisher Scientific). Reverse transcription was performed with High fidelity cDNA Reverse Transcription Kit (Thermo Fisher Scientific), and qPCR analysis with CFX96 qRT-PCR (Bio-Rad). All PCR reactions were performed in triplicate using TB Green™ Premix Ex Taq™ II (Tli RNase H Plus) PCR master mix (Takara Biotechnology Co., Ltd) and commercial gene primers. qPCR conditions were as follows: 1: 95 ° C 30 s; 2: 95° C 5 s and 60° C 30 s, 40 cycles. Relative expression of the lncRNAs ANRIL and PVT1 was normalized vs. GAPDH reference gene and the expression data were analyzed using the 2-ΔΔCT method. The expression of lncRNA ANRIL and PVT1 was observed in both CAVS and control PFP samples but no statistically significant difference was observed.



ANALIZA EKSPRESIJE LNCRNA ANRIL I PVT1 U PERIFERNOJ CIRKULACIJI PACIJENATA SA KALCIFICIRAJUĆOM STENOZOM AORTNIH ZALISTAKA SRCA

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U ovom radu analizirana je ekspresija lncRNA molekula ANRIL i PVT1 u perifernoj cirkulaciji (krvnoj plazmi) pacijenata s kalcificirajućom stenozom aortnih zalistaka srca (CAVS; n=45) i zdravih kontrolnih ispitanika (n=45). Od svih ispitanika pribavljen je potpisani informirani pristanak, a dozvolu za istraživanje izdala su Etička povjerenstva Kliničke bolnice Dubrava i Medicinskog fakulteta Sveučilišta u Zagrebu. Krv je od CAVS pacijenata izuzeta predoperativno prije samog zahvata indicirane zamjene aortnog zalistka srca, a od kontrolnih ispitanika prilikom potpisivanja informiranog pristanka za sudjelovanje u navedenom istraživanju. Periferni uzorci krvi (tubice s natrijevim citratom) u periodu do 30 minuta nakon izuzimanja centrifugirani su 15 minuta na 3000 g, a dobivena plazma filtrirana kroz sterilne filtere od 0,2 µm kako bi se dobila plazma bez trombocita (PFP, engl. platelet free plasma). Dobiveni uzorci PFP plazme alikvotirani su u Eppendorf tubice od 1,5 mL i pohranjeni na -80° C za naknadnu analizu lncRNA ekspresije. Kvaliteta i kvantiteta ukupne RNA izolirane iz 500 µl krvne plazme kombinacijom Trizol reagensa (Invitrogen Life Technologies) i miRNAeasy kit-a (Qiagen) određena je uporabom NanoDrop spektrofotometra (Thermo Fisher Scientific). Prepisivanje RNA u cDNA izvršeno je uporabom High fidelity cDNA Reverse Transcription Kit-a (Thermo Fisher Scientific), a qPCR analiza provedena je korištenjem CFX96 qRT-PCR-a (Bio-Rad). Sve PCR reakcije izvedene su u triplikatu korištenjem TB Green™ Premix Ex Taq™ II (Tli RNase H Plus) PCR master mix-a (Takara Biotechnology Co., Ltd) i komercijalnih setova početnica prema sljedećim uvjetima qPCR reakcije: 1: 95° C 30 s; 2: 95° C 5 s i 60° C 30 s, 40 ciklusa. Relativna ekspresija ciljanih gena normalizirana je u odnosu na ekspresiju GAPDH referentnog gena koji se koristio kao endogena kontrola a ekspresijski podaci su analizirani korištenjem 2-ΔΔCT metode. Ekspresija lncRNA ANRIL i PVT1 opažena je i u plazmi CAVS pacijenata i u kontrolnim PFP uzorcima, ali nije primijećena statistički značajna razlika.



USE OF INTEGRATIVE TAXONOMY IN DESCRIPTION OF TWO NEW STENOENDEMIC STONEFLY SPECIES (PLECOPTERA) FROM CROATIA

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Plecoptera are used as a biological indicator for pollution and climate change [1] and since their populations are shrinking (both numerically and by distribution), it is necessary to give special attention to the conservation importance of springs, streams and rivers which they inhabit. Project CroBarFauna (DNA barcoding of biodiversity of Croatian fauna, funded by Croatian Science Foundation: IP-06-2016-988) ongoing since 2017, has contributed to a better understanding of geographic distribution of fauna and has positively impacted the research in taxonomy, systematics, phylogenetics and phylogeography. DNA barcoding (using of cytochrome oxidase subunit I (*COI*) barcode region as a molecular marker) of stoneflies (Plecoptera), with more than 300 analysed specimens, comprising of 70 species (90 % of which were recently found in Croatia [2]) revealed several deeply divergent genetic lineages which accompanied by distinctiveness of the morphological characteristics and ecological features they were identified as new species. The obtained values of uncorrected sequence divergences (p-distances) within the new described species and species described so far is 6-8 %. This exceeds intraspecific divergences (commonly used as a criterion for a delimitation of closely related species in aquatic insects) [3]. Use of integrative taxonomy and rigorous delimitation in describing new species will inevitably yield a better biodiversity inventory [4].

Two newly described species have clearly marked morphological differences from related species and are associated with two different specific habitats (the area along the karstic source of the river Krasulja in Krbava field and the area along the rapids of the river Čabranka in Gorski kotar). The species belong to the genera *Isoptera* and *Taeniopteryx*, characterised by high interspecific genetic diversity. The monophyly of two new species is supported by phylogenetic analysis and for establishing taxonomic relationships, several species delimitation methods were applied. Analysis of more mitochondrial and nuclear markers will contribute to a better understanding of the phylogenetic relationship between species and enable a potential revision of these genera

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PRIMJENA INTEGRATIVNE TAKSONOMIJE U OPISU DVIJU NOVIH STENOENDEMSKIH VRSTA OBALČARA (PLECOPTERA) U HRVATSKOJ

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Obalčari se koriste kao biološki indikatori zagađenja i klimatskih promjena [1], a budući da se njihove populacije smanjuju (po brojnosti i po rasprostranjenosti), potrebno je posvetiti posebnu pozornost očuvanju izvora, potoka i rijeka koje oni nastanjuju. Projekt CroBarFauna (*DNA barkodiranje bioraznolikosti hrvatske faune, sredstva Hrvatske zaklade za znanost: IP-06-2016-988*) koji se provodi od 2017. godine pridonio je boljem razumijevanju geografske rasprostranjenosti faune i pozitivno utjecao na istraživanja u taksonomiji, sistematici, filogeniji i filogeografiji. DNA barkodiranje (primjena gena za podjedinicu I citokrom oksidaze (*COI*) – tzv. barkod regije kao molekularnog biljega) obalčara (Plecoptera) uključilo je analizu više od 300 jedinki i 70 vrsta (što obuhvaća 90 % vrsta koje su nedavno pronađene u Hrvatskoj [2]) dovelo je do otkrića nekoliko divergentnih genskih linija, koje zajedno s istaknutim morfološkim karakteristikama i ekološkim značajkama, predstavljaju nove vrste za znanost. Nekorigirana genska udaljenost (p-distanca) između novo opisanih vrsta i vrsta koje su opisane do sada iznosi 6-8 %. Ta vrijednost premašuje intraspecifičnu gensku udaljenost ($ISD \geq 2\%$) koja se uobičajeno koristi kao kriterij za razgraničavanje srodnih vrsta među skupinama vodenih kukaca [3]. Uporaba integrativne taksonomije i rigoroznog razgraničavanja u opisivanju novih vrsta doprinijet će neminovno boljem uvidu u biološku raznolikost [4].

Dvije novoopisane vrste imaju jasno izražene morfološke karakteristike koji ih razlikuju od srodnih vrsta i povezane su s dva specifična staništa (područje uz krški izvor rijeke Krasulje u Krbavskom polju i područje uz rijeku Čabranku u Gorskom kotaru). Vrste pripadaju rodovima *Isoperla* i *Taeniopteryx*, u kojima vrste pokazuju visoku unutarvrstu gensku varijabilnost. Monofiletsko podrijetlo dviju novih vrsta potkrijepljeno je filogenetskom analizom, a za uspostavljanje taksonomskih odnosa primijenjeno je nekoliko metoda razgraničavanja vrsta. Analizom više mitohondrijskih i nuklearnih pridonijet će boljem razumijevanju filogenetskih odnosa među vrstama i omogućiti potencijalnu reviziju spomenutih rodova.

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OMMOCHROMES – BIOLOGICAL PIGMENTS IN SURFACE RELATIVES OF CAVE-DWELLING ISOPODS (CRUSTACEA)

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Pigmentation loss or albinism is a regressive trait characteristic for cave-adapted animals and a good example of convergent evolution [1]. In order to explain this phenomenon in troglobites, first it is necessary to characterize the type of biological pigments in the phylogenetically closest surface relatives. So far, it has been studied mostly in regard to melanin loss [2,3] while the exact mechanism of ommochrome loss remains mainly unknown. Ommochromes are tryptophan derivate and are generally less studied class of biological pigments so far described in protostomes such as cephalopods, flatworms and some arthropod groups (insects, spiders) [4]. The appearance of these pigments in another arthropod group – crustaceans, was previously proposed in isopod suborders Asellota and Oniscidea [5]. Using a biochemical approach to extract and detect ommochromes along with HPLC-MS analytics, for the first time we have identified ommochromes and their precursors in another isopod suborder – Flabellifera (family Sphaeromatidae). Additionally, ommochromes presence was confirmed in another Oniscidea family – Trichoniscidae, as well as in new Asellota genus - *Proasellus*. Moreover, the pigmented surface isopod groups have subterranean albino relatives in the realm of Dinaric karst, which makes these species pairs a good model for studying molecular mechanisms of albinism as a result of ommochrome deficiency.

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OMOKROMI – BIOLOŠKI PIGMENTI VANJSKIH SRODNIKA ŠPILSKIH JEDNAKONOŽNIH RAKOVA (ISOPODA, CRUSTACEA)

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Gubitak pigmentacije ili albinizam regresivna je osobina životinja prilagođenih životu u špiljama te dobar primjer konvergentne evolucije [1]. Da bi se objasnio ovaj fenomen u troglobiontima, prvo je potrebno okarakterizirati tip bioloških pigmenata u filogenetski najbližim vanjskim srođnicima. Albinizam je do sada proučavan uglavnom s aspekta gubitka melanina [2,3], dok točan mehanizam gubitka omokroma ostaje uglavnom nepoznat. Omokromi su derivati triptofana i općenito su slabije proučavana klasa bioloških pigmenata, koja je do sada opisana u protostomičnim organizmima kao što su glavonošci, plošnjaci te člankonošci - kukci i pauci [4]. Prisutnost ovih pigmenata kod rakova, ranije je bila predložena u podredovima jednakonožnih (izopodnih) rakova: Asellota i Oniscidea [5]. Korištenjem biokemijskog pristupa ekstrakcije i detekcije omokroma zajedno sa HPLC-MS analizom, po prvi smo put identificirali omokrome i njihove prekursore u još jednom podredu izopodnih rakova - Flabellifera (porodica Sphaeromatidae). Uz to, prisutnost omokroma potvrđena je kod porodice Trichoniscidae (Oniscidea), kao i rodu *Proasellus* (Asellota). Štoviše, spomenute pigmentirane skupine izopodnih rakova imaju podzemne albino srođnike na području dinarskog krša, što čini ove parove vrsta dobrim modelom za proučavanje molekularnih mehanizama albinizma kao posljedice nedostatka pigmenta omokroma.

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CYANOBACTERIA ASSOCIATED WITH SEA TURTLES: A DIVERSITY STUDY USING METABARCODING APPROACH

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Cyanobacteria are prokaryotic photosynthesizing organisms that are found in a wide range of habitats. They are well known as one of the first colonizers of underwater surfaces. Although they are an important part of marine microbial communities, there is little information on benthic marine cyanobacteria, especially epizoic cyanobacteria. In recent years, a growing number of studies has shown that epizoic sea turtle biofilms are highly diverse and different from other marine biofilms [1,2]. A sea turtle's carapace and skin can be home to a large variety of macro epibionts (barnacles, green and red algae) and micro epibionts (diatoms, cyanobacteria, proteobacteria, protozoa). However, in those studies, cyanobacteria are completely overlooked in regards to their morphology and phylogeny. Our preliminary research of cyanobacteria within epizoic microbial turtle biofilm was performed by an amplicon sequencing approach using the 16S rRNA marker gene [3]. Skin and carapace scrapings from Mediterranean loggerhead sea turtles (*Caretta caretta*) were used for the investigation of epizoic microbial communities. Samples were collected in 2018 and 2019 from 54 loggerheads inhabiting Adriatic (Croatia and Italy) and the Ionian Sea (Greece). More than 20 cyanobacterial families were found living on Mediterranean loggerheads, with the four most abundant being *Phormidesmiaceae*, *Paraspirulinaceae*, *Xenococcaceae*, and *Limnotrichaceae*. However, there is a large proportion of the sequences that cannot be identified further than class level, due to the lack of matching sequences in the SILVA reference database. In the future, we plan to reduce this knowledge gap by culturing epizoic cyanobacteria sampled from microbial biofilm growing on sea turtles. These cyanobacterial cultures will then be characterized using combined morphological and molecular methods. Marker gene sequences from those cultures will complete the reference database and contribute to more accurate DNA barcoding and metabarcoding hits of cyanobacterial taxa in the future. Hopefully, this research will help us better understand the relationship between cyanobacteria and their host animal.

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CIJANOBakterije NA MORSKIM KORNJAČAMA: ISTRAŽIVANJE RAZNOLIKOSTI METODOM METABARKODINGA

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Cijanobakterije su autotrofni prokariotski organizmi koje nalazimo na širokom rasponu staništa. Poznato je da su jedne od prvih kolonizatora podvodnih površina. Iako su morske bentičke cijanobakterije bitan dio morskih zajednica, manje su istraživane od planktonskih vrsta. O epizojskim morskim cijanobakterijama ima pogotovo malo podataka. Sve veći broj istraživanja biofilмова na morskim kornjačama je pokazao njihovu raznolikost i unikatnost u odnosu na ostale biofilmove pod morem [1,2]. Oklop i koža morskih kornjača predstavljaju stanište različitim makro epibiontima (rakovi vitičari, zelene i crvene alge) i mikro epibiontima (dijatomeje, cijanobakterije, proteobakterije, praživotinje). Epizojske cijanobakterije na morskim kornjačama su u istraživanjima zanemarene te se jako malo zna o njihovoj morfologiji i filogeniji. Za naše preliminarno istraživanje cijanobakterija u mikrobnim obraštajima kornjača koristili smo sekvenciranje amplikona za 16S rRNA [3]. Korišteni su uzorci oklopa i kože od 54 glavate želve (*Caretta caretta*) sakupljeni u 2018. i 2019. godini iz Jadranskog mora (Hrvatska i Italija) te iz Jonskog mora (Grčka). Zabilježeno je više od 20 cijanobakterijskih porodica u tim uzorcima, a četiri najbrojnije porodice su *Phormidesmiaceae*, *Paraspirulinaceae*, *Xenococcaceae* i *Limnotrichaceae*. Također je pronađen veliki broj cijanobakterijskih sekvenci koje se putem metabarkodinga ne mogu identificirati dalje od razine razreda jer sekvence tih cijanobakterija nisu pohranjene u bazama podataka. Kako bi doprinijeli smanjenju broja neidentificiranih sekvenci, plan je izolirati cijanobakterijske kulture iz obraštaja kornjača. Koristit će se kombinirani morfološki i molekularni pristup istraživanja tih kultura, te će njihove sekvence biti pohranjene u bazama podataka. To će doprinijeti preciznijoj identifikaciji cijanobakterija putem DNA barkodinga i metabarkodinga u budućnosti. Također, ova istraživanja će doprinijeti sveukupnom boljem razumijevanju odnosa cijanobakterija i njihovih domaćina, glavatih želvi.

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HYGIENIC AND SANITARY CONDITIONS IN SCHOOL WITH REFERENCE TO COVID-19

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It is the main health and educational task of the schooling process for the students to adopt certain hygiene habits. In this way they can protect themselves from many diseases and preserve their health.^{1,2} One Health as a new initiative, which in fact has deeper roots in human history. The significance of this concept comes from the fact that 6 out of 10 known human contagious diseases are transmitted from animals. During the COVID-19 pandemic, zoonoses are being brought up in the context of the new Corona virus.³ The public health promotion in schools becomes the foundation for improving our health, preventing diseases and ensuring a quality life for each individual. Ensuring the healthy upbringing of children is a great responsibility of the community. Health education should ensure a positive and responsible attitude of students towards health, safety and environmental protection, and thus ensure a healthy upbringing. The right for equal access to health is one of the basic human rights.⁴ The specific goal of this research was to gain new knowledges on health promotion and to investigate, whether the current hygienic and sanitary conditions in schools meet the standards that ensure the proper growth and development of children in schools. The survey was conducted in December 2020. The research conducted of two parts: theoretical and empirical. The obtained data were processed by the method of descriptive statistics. Statistical data processing was performed by the processing software packages MS Access 2016, MS Excel 2016, IBM SPSS 22. The study processed 48 identical questionnaires given to eighth and ninth grade students of Hasan Kikić Elementary School in Zenica, and 6 questionnaires given to school sweepers at the same school. The questionnaires contained closed-ended questions as the participants were asked to circle the letter in front of the proper answer or to write their own opinion. For this purpose we used a written survey consisting of 5 questions for students. Questions were related to their knowledge of personal hygiene in order to prevent infection and 5 questions for school sweepers related to their knowledge of new means of work and their impact on their health. Based on the obtained results we concluded that in the student's population there is a certain fear of infection with a new Corona virus. The study showed that students are partially satisfied with the health related topics through regular classes. Most of the students believe that it is necessary to introduce a separate school subject related to health protection: Health Education. The study also showed that students mostly use face masks that can be washed. On the other hand, it is worrying that students use their personal disinfection on a very low scale. The school sweepers belong to the age population of 50 or over and have reduced working capacity, thus they did not receive timely and complete information on the changed regime of maintaining school hygiene. Respondents cite similar chemicals used for disinfection - quite unknown to them, and stated that they need additional education during a pandemic of COVID 19.



HIGIJENSKO-SANITARNI UVJETI U ŠKOLI SA OSVRTOM NA COVID-19

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Glavni zdravstveno-odgojni zadatci za vrijeme školovanja su da učenici usvoje određene higijenske navike jer se na taj način mogu zaštititi od mnogih bolesti, te sačuvati svoje zdravlje.^{1,2} Jedinstveno zdravlje (engl. *One Health*) kao nova inicijativa, ustvari ima dublje korijene u ljudskoj povijesti. Značaj ovog koncepta proizilazi iz činjenice da 6 od svakih 10 poznatih kontagioznih bolesti ljudi preneseno je od životinja. U doba pandemije COVID-19 aktualiziraju se zoonoze u kontekstu novog Corona virusa.³ Promocija zdravlja u školskim ustanovama temelj je unaprjeđenja zdravlja, sprječavanja bolesti i osiguravanja kvalitetnog života. Osigurati zdravo odrastanje djece velika je odgovornost odraslih. Zdravstvena edukacija treba da osigurava pozitivan i odgovoran odnos učenika prema zdravlju, sigurnosti i zaštiti okoliša, te na taj način osigurava zdravo odrastanje. Pravo na zdravlje jedno je od osnovnih ljudskih prava.⁴ Cilj ovog istraživanja bio je dobiti nova saznanja o promicanju zdravlja te istražiti da li trenutni higijensko-sanitarni uvjeti zadovoljavaju standarde koji osiguravaju pravilan dječji rast i razvoj u školskim ustanovama. Anketiranje je provedeno u mjesecu prosincu 2020. godine. Istraživanje je realizirano iz dva dijela: teorijskog i empirijskog. Dobiveni podaci obrađeni su metodom deskriptivne statistike. Statistička obrada podataka izvršena je obrađivanjem putem softverskih paketa MS Access 2016, MS Excel 2016, IBM SPSS 22. U istraživanju su obrađeni 48 istovjetnih anketnih listova od ispitanika, učenika osmih i devetih razreda OŠ Hasan Kikić u Zenici i 6 zaposlenih spremačica u prethodno imenovanoj školi. Anketni listova su sadržavali pitanja zatvorenog tipa gdje je bilo potrebno zaokružiti slovo odnosno napisati svoje mišljenje. U tu svrhu upotrebljena je pisana anketa koja se sastojala od 5 pitanja za učenike koja su se odnosila o poznavanju osobne zaštite u cilju sprječavanja infekcije i 5 pitanja za školske spremačice koja su se odnosila na poznavanje novih sredstava za rad i utjecaju istih na njihovo zdravlje. Na osnovu dobivenih rezultata izvode se zaključici da u učeničkoj populaciji postoji strah od infekcije sa novim Corona virusom. Učenici su djelomično zadovoljni zdravstvenim temama kroz redovitu nastavu. Većina učenika smatra da je potrebno uvođenje zasebnog nastavnog predmeta: Zdravstveni odgoj. Učenici najviše koriste maske koje je moguće prati. Zabrinjavujuće je da učenici vrlo malo koriste osobnu dezinfekciju. Spremačice pripadaju starosnoj populaciji od preko 50 godina i imaju smanjenu radnu sposobnost, te nisu blagovremeno i u punini dobile informacije o izmjenjenom režimu održavanja školske higijene. Ispitanice navode slična kemijska sredstva koja koriste za dezinfekciju-njima poprilično nepoznata, te su se izjasnile da trebaju dodatnu edukaciju u vrijeme pandemije COVID-19.



THE EFFECTS OF SILVER NANOPARTICLES AND IONS ON *Chlorella vulgaris*

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Silver nanoparticles (AgNPs) are well known for their antimicrobial properties in many commercially available products, but due to their toxicity and reactivity, they can pose a risk to the aquatic environment [1]. The model photosynthetic eukaryotic organism, *Chlorella vulgaris*, was used in this study. To evaluate the effect of AgNPs stabilised with polyvinylpyrrolidone (AgNP-PVP) and silver ions (AgNO₃) on the microalgae, their growth, lipid peroxidation and catalase activity were measured upon exposure to 0.5, 1.0, 1.5 and 2.0 mg L⁻¹ concentrations after 5, 24 and 48 hours in modified liquid BBM nutrient medium. Additionally, the changes of pH, levels of dissolved oxygen and absorbance spectra in the range 300–800 nm in the algae cultures were analysed after the same period of treatment. Since stress conditions negatively affect ribulose biphosphate carboxylase (Rubisco) protein synthesis, to evaluate the fitness of algae upon treatment we used immunoblotting assay to analyze the expression levels of the large Rubisco chain. Furthermore, to visualize ultrastructural changes after the treatments, algae cells were examined using transmission electron microscopy (TEM). After the AgNP-PVP or AgNO₃ treatments, a significant dose-dependent decrease in cell number and an increase in dissolved oxygen and lipid peroxidation were observed. Furthermore, an increase in catalase activity was measured after all of the treatments, while an increase in pH was observed after 24 and 48 hours for treatments with 1.5 and 2.0 mg L⁻¹ of both AgNP-PVP and AgNO₃. Visible light absorbance significantly decreased after the treatment with both AgNP-PVP and AgNO₃, with the decrease most noticeable in the characteristic chlorophyll *a* and *b* absorbance ranges. Immunoblotting revealed significant dose-dependent decrease in the levels of Rubisco large subunit after treatments with both AgNP-PVP and AgNO₃. TEM analyses showed that after 5 hours of exposure to both treatments, cells contained more starch compared to the control, and synthesis of lipid droplets had occurred.

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UTJECAJ NANOČESTICA I IONA SREBRA NA ALGU *Chlorella vulgaris*

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Nanočestice srebra (AgNP) dobro su poznate po svojim antimikrobnim svojstvima u mnogim komercijalno dostupnim proizvodima, ali zbog svoje toksičnosti i reaktivnosti predstavljaju rizik za vodeni okoliš [1]. U ovom istraživanju korištena je modelna fotosintetska alga, *Chlorella vulgaris*. Da bi se procijenio učinak AgNP stabiliziranih polivinilpirolidonom (AgNP-PVP) i ionima srebra (AgNO₃) na alge, izmjeren je njihov rast, lipidna peroksidacija i aktivnost katalaze nakon izlaganja koncentracijama 0.5, 1.0, 1.5 i 2.0 mg L⁻¹ nakon 5, 24 i 48 sati u modificiranom tekućem hranjivom BBM mediju. Nadalje, analizirane su promjene pH, razine otopljenog kisika i spektri apsorpcije u rasponu od 300-800 nm u kulturama algi nakon istog trajanja tretmana. Budući da stresni uvjeti negativno utječu na sintezu proteina ribuloza bisfosfat karboksilaze (Rubisco), koristili smo imunohistokemijsku metodu za analizu ekspresije velikog lanca proteina Rubisco kako bismo procijenili stanje algi nakon tretmana. Nadalje, kako bi se vizualizirale ultrastrukturne promjene nakon tretmana, stanice algi ispitivane su pomoću transmisivne elektronske mikroskopije (TEM). Nakon tretmana s AgNP-PVP ili AgNO₃ primijećeno je značajno smanjenje broja stanica ovisno o dozi tretmana te povećanje peroksidacije lipida i otopljenog kisika. Nadalje, izmjeren je porast aktivnosti katalaze nakon svih tretmana, dok je porast pH primijećen nakon 24 i 48 sati za tretmane s 1,5 i 2,0 mg L⁻¹ AgNP-PVP i AgNO₃. Apsorbancija vidljive svjetlosti značajno se smanjila nakon svih tretmana s AgNP-PVP i AgNO₃, s najočitijim padom u karakterističnim rasponima apsorpcije klorofila a i b. Imunohistokemijska analiza je otkrila značajno smanjenje velike podjedinice proteina Rubisco nakon tretmana s AgNP-PVP ili AgNO₃ čije smanjenje je bilo ovisno o dozi tretmana. Analiza TEM je pokazala da su stanice nakon 5 sati izlaganja tretmanima sadržavale više škroba u usporedbi s kontrolom te da je došlo do sinteze lipidnih kapljica.

LITERATURNI IZVORI

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AUGMIN REGULATES KINETOCHORE TENSION AND SPATIAL ARRANGEMENT OF SPINDLE MICROTUBULES BY NUCLEATING BRIDGING FIBERS

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The mitotic spindle functions as a molecular micromachine that evenly distributes chromosomes into two daughter cells during cell division. Spindle microtubules in human cells are mainly formed at the centrosome and on the lateral surface of existing microtubules by the augmin complex. However, it is unknown how the augmin-mediated nucleation affects functionally distinct microtubule bundles and consequently the forces within the spindle. Here we show, by using siRNA depletion and CRISPR knock-out of the augmin complex subunits HAUS6 or HAUS8, that augmin is crucial for the nucleation of bridging microtubules, which laterally link sister kinetochore fibers. Augmin depletion resulted in a reduction in the number of microtubules within bridging fibers by around 80% and in kinetochore fibers by 40%, suggesting that the bridging microtubules are mainly nucleated at the surface of present microtubules. In augmin-depleted cells, the interkinetochore distance decreased preferentially for kinetochores that lack a bridging fiber, independently of the thickness of their k-fibers, implying that augmin affects forces on kinetochores largely via bridging fibers. Without augmin the number of bridging fibers decreased, with the remaining ones mostly confined to the spindle periphery with an increased overlap length. Additionally, slower poleward flux of microtubules after augmin depletion is indicative of slower sliding within the bridging fiber. Our results demonstrate a critical role of augmin in the formation of bridging microtubules and proper architecture of the metaphase spindle, suggesting a model where sliding of augmin-nucleated bridging microtubules promotes poleward flux of k-fibers and thus tension on kinetochores.

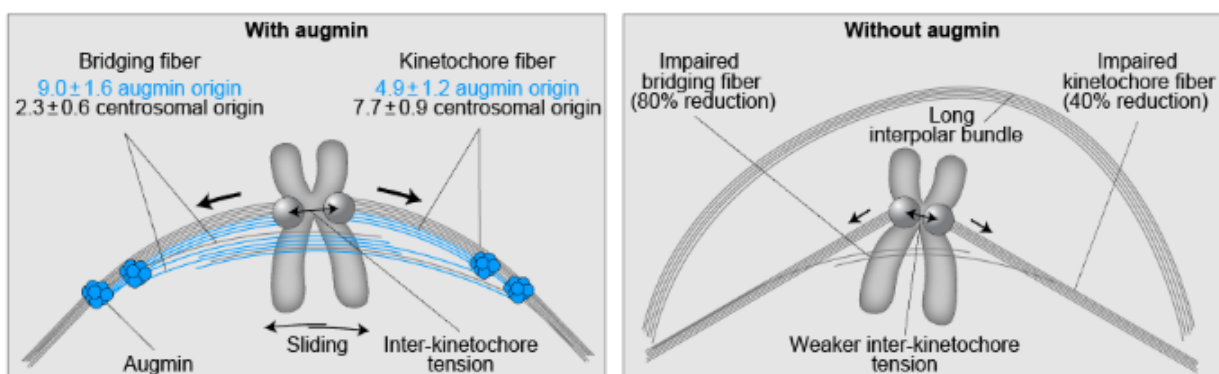


Figure 1. A model of augmin-dependent nucleation of bridging microtubules and their contribution to spindle integrity.



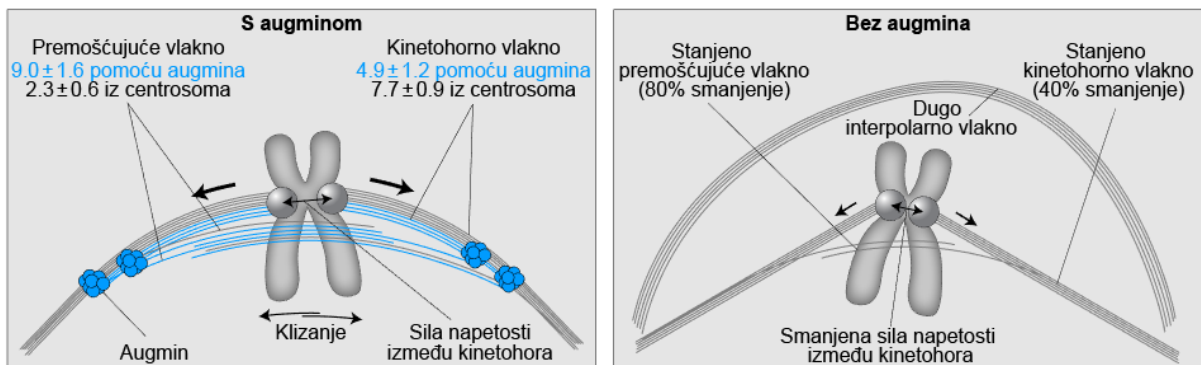
AUGMIN REGULIRA SILU NAPETOSTI IZMEĐU SESTRINSKIH KINETOHORA I PROSTORNI RASPORED MIKROTUBULA NUKLEACIJOM PREMOŠĆUJUĆIH VLAKANA

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Diobeno vreteno složena je molekularna struktura zaslužna za pravilnu raspodjelu kromosoma tijekom stanične diobe na dvije stanice kćeri. Mikrotubuli koji sastavljaju diobeno vreteno u ljudskim se stanicama u najvećoj mjeri stvaraju iz centrosoma te na površini već postojećih mikrotubula pomoću augminskog kompleksa. Unatoč tome, uloga augmina u sastavljanju kinetohornih i premošćujućih vlakana, dvije glavne grupe snopova mikrotubula nužnih za pravilno funkcioniranje diobenog vretena, do danas je velikim dijelom nerazjašnjena. Koristeći siRNA i tehnologiju CRISPR *knock-out* za utišanje podjedinica HAUS6 i HAUS8 augminskog kompleksa, pokazali smo da je augmin nužan za stvaranje premošćujućih vlakana, koja lateralno povezuju dva sestrinska kinetohorna vlakna vezana za kromosome pomoću kinetohora. Utišavanje augmina dovelo je do smanjenja broja mikrotubula u premošćujućim vlaknima za oko 80%, a u kinetohornim vlaknima za oko 40%, sugerirajući da se premošćujuća vlakna u najvećoj mjeri stvaraju na površini već postojećih mikrotubula, dok za kinetohorna vlakna to nije slučaj. U stanicama u kojima je augmin utišan, udaljenost između sestrinskih kinetohora smanjila se primarno na kinetohorima koje nisu imale pripadajuće premošćujuće vlakno, neovisno o debljini njihovih kinetohornih vlakana. Kako je udaljenost između sestrinskih kinetohora mjera za silu napetosti koja se stvara između njih, ustanovili smo da augmin utječe na sile između kinetohora pretežito putem premošćujućih vlakana. Bez augmina, broj premošćujućih vlakana također se smanjio, a ona preostala bila su dulja i smještena na periferiji diobenog vretena. Uz to, sporiji tok mikrotubula prema polu ukazivao je na smanjeno klizanje mikrotubula unutar premošćujućeg vlakna. Ovi rezultati demonstriraju važnu ulogu augmina u stvaranju premošćujućih vlakana i pravilne arhitekture diobenog vretena, sugerirajući model u kojem klizanje premošćujućih vlakana stvorenih pomoću augmina potiče tok mikrotubula prema polu i stvaranje sile napetosti između kinetohora.



Slika 1. Model stvaranja premošćujućih vlakana pomoću augmina i njihovog doprinosa integritetu diobenog vretena.



PHYLOGENY-ONTOGENY CORRELATION DURING CELL DIFFERENTIATION

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Correlations between organismal ontogeny and phylogeny have been observed at the molecular level in different animal phyla, multicellular plants, fungi, and even in bacterial biofilms [1, 2, 3, 4]. All of these studies sampled entire organisms during their developmental (ontogenic) trajectory. However, the phylogeny-ontogeny correspondence has not been specifically studied at the level of single cells, i.e. during cellular ontogeny and differentiation. To address this question we took advantage of single cell RNA sequencing datasets from the non-senescent and constantly self-renewing model organism *Hydra vulgaris* AEP [5], and combined it with genomic phylostratigraphy [6] to calculate transcriptome age index (TAI) [1] for different cell types along their cell differentiation pathways. We showed that stem cells in general express evolutionary the oldest transcriptome, while evolutionary younger transcriptomes are increasingly used along differentiation pathway from progenitors towards fully differentiated neurons, gland cells and nematocytes. The existence of this recapitulative pattern at the cellular level suggests a possible link with phylogeny-ontogeny correlations at the organismal level.

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KORELACIJA FILOGENIJE I ONTOGENIJE TIJEKOM STANIČNE DIFERENCIJACIJE

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Odnos filogenije i ontogenije organizama uočen je na molekularnoj razini u različitim koljenima životinja, višestaničnim biljkama, gljivama i bakterijskim biofilmovima [1, 2, 3, 4] uzorkovanjem cijelih organizama tijekom njihovog razvoja (ontogenije). Korelacija između filogenije i ontogenije, međutim, nije proučavana na razini pojedinačnih stanica, odnosno tijekom stanične ontogenije i diferencijacije. S ciljem određivanja takve korelacije, upotrijebili smo transkriptomске ekspresijske vrijednosti pojedinačnih stanica dobivenih iz organizma koji ne stari i ima sposobnost samoobnavljanja, *Hydra vulgaris* AEP [5]. Ekspresijske vrijednosti kombinirali smo s podacima dobivenim genomskom filostratigrafijom [6] te izračunali indeks starosti transkriptoma (eng. *transcriptome age index*; TAI) [1] za različite tipove stanica tijekom njihove diferencijacije. Rezultati pokazuju da zametne stanice ekspimiraju prosječno najstarije gene, dok se postupno sve mlađi geni ekspimiraju tijekom diferencijacijskog puta od progenitornih do potpuno diferenciranih neurona, žljezdanih stanica te nematocita. Ovaj rekapitulacijski uzorak na staničnoj razini ukazuje na moguću vezu s korelacijom ontogenije i filogenije na razini organizama.

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CHANGES IN ACTIVITIES AND ISOFORM PATTERNS OF ANTIOXIDANT ENZYMES IN TOBACCO PLANTS UPON EXPOSURE TO SILVER NANOPARTICLES AND SILVER NITRATE

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With the rapidly growing utilization of nanomaterials in industry and various consumer products comes a great environmental health risk. Due to their well-known antimicrobial properties, silver nanoparticles (AgNPs) are the most exploited nanomaterial particularly in agriculture and food production [1,2]. However, the release of AgNPs into water or soil raises concerns about their impact on biological systems and indirectly on human health, as they can be transported through plants into the food chain [3]. In this work, *in vitro* grown tobacco (*Nicotiana tabacum* L.) plants were exposed to AgNPs stabilized with cetyltrimethylammonium bromide (CTAB) or polyvinylpyrrolidone (PVP) coating and to ionic silver (AgNO₃) of the same concentrations (25, 50 and 100 μM) in order to determine changes in the antioxidant enzymes system. Spectrophotometric enzyme assays were used to determine the activities of antioxidant enzymes catalase (CAT), ascorbate (APX) and pyrogallol peroxidase (PPX) and superoxide dismutase (SOD) in leaves extracts after exposure to AgNPs or ionic silver, followed by Native Polyacrylamide Gel Electrophoresis, used to determine different isoenzymes and changes in their expression patterns in regard to different treatments. Immunoblotting was used to identify each of the antioxidant enzymes and analyze their expression levels. The results showed that the most prominent changes in activities of SOD and PPX were observed after AgNO₃ treatment, while 100 μM AgNP-CTAB showed the highest increase in both CAT and SOD activities. The form of applied silver seemed to affect the expression of different isoenzymes, while the most notable differences were observed in APX and PPX isoform patterns when comparing Ag⁺ and AgNPs treatment. AgNP-CTAB treatment showed the highest increase in all antioxidant enzyme levels compared to other treatments of the same concentration. Obtained results suggest that oxidative stress is associated with AgNPs toxicity in plants, and cannot be ascribed only to the dissolution of silver ions.

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PROMJENE U AKTIVNOSTI I OBRASCU IZOFORMI ANTIOKSIDACIJSKIH ENZIMA U BILJKAMA DUHANA NAKON IZLAGANJA NANOČESTICAMA SREBRA I IONSKOM SREBRU

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Rastuća primjena nanomaterijala u industriji i raznim potrošačkim proizvodima dovodi do zabrinutosti glede njihovog utjecaja na okoliš. Zbog dobro poznatih antimikrobnih svojstava, nanočestice srebra (AgNP) najčešće su korišteni nanomaterijali, posebno u poljoprivredi i proizvodnji hrane [1,2]. Međutim, otpuštanje AgNP u vodu ili tlo dovodi u pitanje njihov utjecaj na biološke sustave, a posredno i na ljudsko zdravlje, budući da se kroz biljke mogu transportirati u hranidbeni lanac [3]. U ovom radu, *in vitro* uzgojene biljke duhana (*Nicotiana tabacum* L.) tretirane su s AgNP stabiliziranim omotačima cetiltrimetilamonij-bromidom (CTAB) ili polivinilpirolidonom (PVP) i ionskim srebrom (AgNO₃) istih koncentracija (25, 50 i 100 μM) u svrhu ispitivanja promjena u sustavu antioksidacijskih enzima. Spektrofotometrijski su određene aktivnosti antioksidacijskih enzima katalaze (CAT), askorbat (APX) i pirogalol peroksidaze (PPX) i superoksid dismutaze (SOD) u ekstraktima listova nakon izlaganja AgNP ili ionskom srebru, nakon čega je provedena poliakrilamidna gel elektroforeza u nativnim uvjetima, u svrhu određivanja različitih izoenzima i promjena u njihovim obrascima ekspresije uslijed različitih tretmana. Tehnika imunoblotiranja je korištena za identifikaciju svakog od navedenih antioksidacijskih enzima i analizu njihove razine ekspresije. Rezultati su pokazali da su najznačajnije promjene u aktivnostima SOD-a i PPX-a uočene nakon tretmana s AgNO₃, dok je tretman s 100 μM AgNP-CTAB-om pokazao najveći porast aktivnosti CAT i SOD. Pokazalo se da forma primijenjenog srebra utječe na ekspresiju različitih izoenzima, dok su najznačajnije razlike primijećene u obrascima izoformi APX i PPX prilikom usporedbe tretmana Ag⁺ i AgNP. Tretman AgNP-CTAB uzrokovao je najveći porast ekspresije svih antioksidacijskih enzima u usporedbi s drugim tretmanima iste koncentracije. Dobiveni rezultati pokazuju da je oksidativni stres povezan s toksičnošću AgNP-a u biljkama i da se ne može pripisati samo otpuštanju iona srebra.

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APPLICATION OF ASCORBATE-INCORPORATED SOLID LIPID NANOPARTICLES FOR TREATMENT OF CANCER STEM CELLS

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Tumors contain a subpopulation of cells called cancer stem cells (CSCs). They have the ability to self-renew and generate multiple heterogeneous cell lines that create a tumor. Due to their ability to exclude chemotherapeutics and to create metastases, it is thought that their eradication could ease the treatment of patients with tumor. It has been shown that ascorbic acid has a cytotoxic effect on cancer stem cells, however, its delivery can be problematic due to its low stability.

We have synthesized solid lipid nanoparticles (SLN) using the microemulsion technique [1] and incorporated in them ascorbic acid (AA), dehydroascorbic acid (DHA), ascorbyl palmitate (AP) and fluorescent dye coumarin-6. We have analyzed their size, zeta potential, polydispersity and their stability with the conclusion that they are eligible for use and stable during one week. Encapsulation efficiency of all the formulations showed that only ascorbyl palmitate is successfully incorporated into solid lipid nanoparticles. Visualization on a fluorescent microscope confirmed cellular uptake of SLNs. Viability of HEK293, U2OS, hMSC and isolated osteosarcoma stem cells after treatment with SLNs was tested by MTT test and IC50 values were determined.

Results showed that CSCs were more sensitive to treatment with SLN-AP than with ascorbic acid in free form. This shows the potential of ascorbyl palmitate-incorporated solid lipid nanoparticles in cancer stem cell treatment.

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UPOTREBA ČVRSTIH LIPIDNIH NANOČESTICA S UGRAĐENIM ASKORBATOM ZA TRETMAN TUMORSKIH MATIČNIH STANICA

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U tumorima postoji subpopulacija stanica koje su nazvane tumorskim matičnim stanicama (engl. *cancer stem cells*, CSC). One imaju sposobnost samoobnavljanja i stvaranja heterogenih staničnih linija koje sačinjavaju tumor. S obzirom na njihovo svojstvo izbacivanja kemoterapeutika i sposobnost stvaranja metastaza, smatra se da bi se upravo njihovim uklanjanjem moglo lakše pristupiti liječenju tumora u pacijenta. Pokazano je kako askorbinska kiselina ima citotoksičan utjecaj na tumorske matične stanice, ali je doprema askorbinske kiseline problematična zbog njene nestabilnosti.

Stoga smo sintetizirali lipidne nanočestice (SLN) korištenjem tehnike mikroemulzija [1] te smo u te lipidne nanočestice upakirali askorbinsku kiselinu (AA), dihidroaskorbinsku kiselinu (DHA), askorbil palmitat (AP) te fluorescentnu boju coumarin-6. Analizirali smo promjer, zeta potencijal, polidisperzitet i stabilnost nanočestica te smo utvrdili da su karakteristike SLN povoljne za uporabu te da su stabilne tijekom 1 tjedna. Provjerili smo ugradnju AA, DHA i AP te smo utvrdili da se samo AP uspješno ugrađuje u SLN. Ulazak SLN u stanice je potvrđen tretmanom stanica sa SLN-coumarin 6 te vizualizacijom pomoću fluorescentnog mikroskopa. SLN smo testirali na stanicama HEK293, U2OS, hMSC i na izoliranim tumorskim matičnim stanicama izoliranim osteosarkoma. Ispitali smo vijabilnost navedenih stanica metodom MTT nakon izlaganja askorbatu iz AA, DHA i SLN-AP te dobili IC₅₀ vrijednosti.

Usporedili smo rezultate tretmana te utvrdili da je osjetljivost CSC na askorbat veća kada se tretira SLN-AP nego askorbinskom kiselinom u slobodnom obliku. To ukazuje na potencijal u korištenju čvrstih lipidnih nanočestica s ugrađenim askorbil palmitatom u tretmanu tumorskih matičnih stanica.

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GENETIC DIVERSITY AND POPULATION STRUCTURE OF THE NOBLE CRAYFISH IN CROATIA

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The noble crayfish *Astacus astacus* L. is a native European freshwater species whose contemporary distribution and genetics have been shaped by geo-climatic events (i.e. Pleistocene glaciations) and anthropogenic impacts (i.e. translocations, pollution, invasive species). Previous studies revealed that this species harbours highest genetic diversity in the south-eastern Europe, where it survived Pleistocene glaciations [1, 2]. Strong anthropogenic pressure onto its habitats, the presence of non-indigenous invasive crayfish species and climate change are the main reasons for populations decline, therefore the noble crayfish is recognized as threatened and protected by national and international legislation. Maintenance of genetic diversity of a native species in order to protect their adaptive potential is one of the pivotal conservation genetics goals. Guarding in mind declines in population numbers and sizes that cause loss of genetic diversity, we aimed to reveal genetic diversity and structure of the noble crayfish populations in Croatia and identify local genetic hotspots. For that purpose, we used 422 crayfish from 18 populations and 15 recently developed microsatellite loci [3]. Microsatellite analyses revealed moderate level of genetic diversity and differentiation among studied populations reflecting long periods of isolation with restricted gene flow. Moreover, relatively high genetic diversity within populations was recorded. Sampled populations represented two distinct genetic clusters. Results of genetic characterisation will have enabled selection of suitable donor populations for future restocking and/or reintroduction programs. The obtained results help identification of populations and areas with the highest conservation value which should be given the highest priority in protection.

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GENETSKA RAZNOLIKOST I POPULACIJSKA STRUKTURA PLEMENITOG RAKA U HRVATSKOJ

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Plemeniti rak *Astacus astacus* L. je nativna europska slatkovodna vrsta čija je današnja distribucija i genetska raznolikost oblikovana prošlim geo-klimatskim događajima (npr. pleistocenskim glacijacijama) i antropogenim utjecajem (translokacije, onečišćenje, invazivne vrste). Prijašnjim istraživanjima utvrđeno je da ova vrsta posjeduje najveću genetsku raznolikost na području jugoistočne Europe gdje je preživjela pleistocenske oledbe [1, 2]. Snažan antropogeni pritisak na staništa, prisutnost stranih invazivnih vrsta rakova i klimatske promjene su glavni razlozi smanjenja populacija, stoga je plemeniti rak prepoznat kao ugrožen te je zaštićen nacionalnim i međunarodnim zakonodavstvom. Očuvanje genetske raznolikosti i adaptivnog potencijala autohtonih vrsta jedan je od ključnih ciljeva konzervacijske genetike. Imajući u vidu pad broja i veličina populacija koji uzrokuju gubitak genetske raznolikosti, cilj ovog istraživanja bio je utvrditi genetsku raznolikost i populacijsku strukturu plemenitog raka u Hrvatskoj te identificirati lokalna žarišta genetske raznolikosti. Ukupno su uzorkovana 422 raka iz 18 populacija, a genetska raznolikost analizirana je pomoću 15 nedavno razvijenih mikrosatelitnih biljega [3]. Analize mikrosatelitnih lokusa otkrile su srednju razinu genetske raznolikosti i diferencijacije proučavanih populacija što ukazuje na duga razdoblja izolacije s ograničenim protokom gena. Također, zabilježena je relativno visoka genetska raznolikost između jedinki unutar populacija. Uzorkovane populacije predstavljaju dva različita genetska klastera. Rezultati genske karakterizacije omogućit će odabir prikladnih donorskih populacija za buduće programe repopulacije i/ili reintrodukcije. Dobiveni rezultati omogućuju identificiranje populacija i područja s najvećom konzervacijskom vrijednošću kojima treba dati najviši prioritet u zaštiti.

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EFFECTS OF HUMAN PAPILLOMAVIRUS 16 (HPV16) E6 ONCOPROTEIN ON CELL POLARITY REGULATORS IN HEAD AND NECK CANCERS

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Head and neck squamous cell carcinomas (HNSCC) are the sixth most common cancer worldwide caused either by tobacco and alcohol abuse (HPV-negative) or HPV infections, mostly HPV16 type [1]. HPVs are small non-enveloped double stranded DNA viruses linked to almost 100% of cervical cancers, 70% of anogenital cancers, 40-60% of oropharyngeal SCC (OPSCC) and 5% of non-OPSCC [2]. HPV-induced malignancies depend on the co-action of two major viral oncoproteins, E6 and E7, which interact with a number of cellular proteins [3], including tumor suppressors, p53 and pRb, respectively. The process from initial infection to development of malignancy is well understood in cervical area, but is yet under-investigated in tonsillar tissue that, interestingly, shows histological similarities to the cervical mucosa. Currently, p16, a widely used marker for HPV infection seems to be overexpressed both in, HPV-negative and HPV-positive OPSCCs, and thus it should be used only if supported with HPV-genotyping [1]. Therefore, numerous groups are constantly trying to find more reliable biomarkers for predicting disease development or distinguishing HPV-positive from HPV-negative tumors. Other cellular targets of HPV E6, tumor suppressors and cell polarity regulators DLG1 and SCRIB, were investigated in the development of cervical cancer. Some studies suggest that DLG1 expression and cellular localization varies in the HPV-associated lesions [4] and that DLG1 may play an important role in the progression of low-grade cervical intraepithelial lesions [5]. We used immunohistochemical analysis to determine the expression and localization of DLG1 and SCRIB in HPV16-positive and HPV-negative OPSCC samples, which could help enlighten the process of HPV-induced carcinogenesis in head and neck area. DLG1 and SCRIB seem to be predominantly mislocalized from membranes to the cytoplasm in tumors regardless of HPV status. Interestingly, the expression of SCRIB appears to be down-regulated in HPV-positive and in poorly differentiated HPV-negative cancers graded 3/3.

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UTJECAJ ONKOPROTEINA E6 PAPILOMAVIRUSA ČOVJEKA TIP 16 (HPV16) NA REGULATORE STANIČNE POLARNOSTI U TUMORIMA GLAVE I VRATA

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Karcinomi pločastog epitela glave i vrata (HNSCC) šesti su najčešći karcinomi u svijetu uzrokovani prekomjernom uporabom duhana i alkohola (HPV-negativni) ili HPV infekcijama, uglavnom tipom HPV16 [1]. HPV su mali DNA virusi bez ovojnice koji su povezani s gotovo 100% slučajeva raka vrata maternice, 70% anogenitalnih karcinoma, 40-60% karcinoma pločastih stanica orofarinksa (OPSCC) i 5% karcinoma drugih epitelnih stanica u području glave i vrata [2]. HPV-inducirane malignosti posljedica su suradnje dvaju glavnih virusnih onkoproteina, E6 i E7, koji interagiraju s velikim brojem staničnih proteina [3], uključujući tumor supresore, p53 i pRb. Proces od inicijalne infekcije do razvoja malignosti dobro je poznat u vratu maternice, ali je još uvijek nedovoljno istražen u tonzilama koje, zanimljivo, pokazuju histološke sličnosti sa sluznicom vrata maternice. Čini se kako je protein p16, široko korišteni biljeg za HPV infekciju, prekomjerno eksprimiran u HPV-negativnim i HPV-pozitivnim OPSCC, pa bi ga trebalo koristiti samo uz genotipizaciju HPV-a [1]. Stoga brojne skupine neprestano pokušavaju pronaći pouzdanije biomarkere za predviđanje razvoja bolesti ili razlikovanje HPV-pozitivnih od HPV-negativnih tumora. Druge stanične mete proteina E6, tumor supresori i regulatori stanične polarnosti DLG1 i SCRIB istraženi su u procesu razvoja raka vrata maternice. Prema rezultatima pojedinih istraživanja čini se kako se ekspresija i stanična lokalizacija proteina DLG1 razlikuju u lezijama povezanim s HPV-om [4] te kako DLG1 može imati važnu ulogu u progresiji cervikalnih intraepitelnih lezija niskog stupnja (LSIL) [5]. U ovom istraživanju, proveli smo imunohistokemijsku analizu kako bismo odredili razinu ekspresije i lokalizaciju oba proteina, DLG1 i SCRIB u HPV16 pozitivnim i HPV negativnim uzorcima OPSCC, što bi moglo pomoći u rasvjetljavanju procesa karcinogeneze izazvane HPV-om u području glave i vrata. Naši rezultati pokazuju da u tumorima, neovisno o HPV statusu dolazi do promjene lokalizacije oba proteina DLG1 i SCRIB. Zanimljivo, čini se i kako u HPV pozitivnim te u slabo diferenciranim HPV negativnim karcinoma stupnja 3/3 dolazi do potpunog gubitka proteina SCRIB.

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A NOVEL FUNCTION OF THE RASGAP PROTEIN IQGC IN CELL ADHESION

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Proper cell adhesion is crucial for many cellular processes, such as cell migration, phagocytosis and differentiation [1]. In the migrating *Dictyostelium discoideum* cells, transient stationary adhesion foci form on the ventral cell surface underneath the cell body and the pseudopods [2]. These adhesion foci can be discerned from the F-actin-containing puncta presumably involved in transmitting the traction forces to the substratum [3,4]. The adhesion foci contain a number of proteins homologous to those involved in adhesion in higher eukaryotes, such as talin, paxillin, Rap1, and others [2,4,5]. IqgC is a RasGAP protein, which inactivates small GTPase RasG in *D. discoideum* by stimulating the hydrolysis of GTP bound to its active form. We recently showed that IqgC plays an important role in the regulation of large-scale endocytosis [6]. During cultivation in cell-culture dishes, we noticed that IqgC-null cells easily detach from the plastic surface, indicating that IqgC might be involved in the regulation of cell adhesion to the underlying substrata. We therefore proceeded to investigate the involvement of IqgC and its potential interactors in this process. Strength of the cell adhesion to the substratum in wild-type and IqgC-null cells was compared by the shaking assay, which confirmed that cells lacking IqgC are defective in the cell-substratum adhesion, an effect which could be rescued by expressing recombinant IqgC in IqgC-null cells. Cell tracking experiments showed that less adhesive IqgC-null cells migrate faster than wild-type. TIRF (total internal reflection fluorescence) microscopy of cells expressing fluorescently labeled IqgC together with paxillin B or a probe for F-actin demonstrated that IqgC localizes to the paxillin B-containing adhesion foci. The pathways involved in the regulation of cell adhesion in *D. discoideum* are not yet fully elucidated, but it is hypothesized that the small GTPase Rap1 is one of the key regulatory proteins [5,7,8]. Indeed, Rap1 was identified in the IqgC interactome as a potential IqgC binding partner and here we confirmed a direct interaction between IqgC and Rap1 using pull-down and BiFC assays. Here we show that IqgC protein is a positive regulator of the cell adhesion to the underlying substratum in *Dictyostelium discoideum*. Based on the presented results, we hypothesize that IqgC regulates adhesion via binding to small GTPase Rap1.

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ULOGA PROTEINA IQGC PORODICE RASGAP U STANIČNOJ ADHEZIJI

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Pravilna adhezija eukariotskih stanica je nužna za odvijanje fundamentalnih staničnih procesa, kao što su migracija, fagocitoza i diferencijacija [1]. Na ventralnom dijelu stanice *Dictyostelium discoideum* koja se kreće moguće je mikroskopijski razlikovati dvije vrste stacionarnih struktura. Jedno su strukture koje se obično naziva fokalnim adhezijskim strukturama te sadrže razne homologe proteina sisavaca uključenih u nastanak fokalnih adhezija, kao što su paxilin, talin, Rap1 i drugi [2,4,5]. Druga vrsta sličnih struktura su akumulacije filamentoznog (F-) aktina koje se povezuju sa silama trakcije [3,4]. Protein IqgC spada u porodicu proteina RasGAP te inaktivira malu GTPazu RasG u *D. discoideum* stimulacijom hidrolize GTP-a vezanog za aktivni oblik GTPaze. Nedavnim istraživanjem smo pokazali kako IqgC ima važnu ulogu u regulaciji endocitoze na velikoj skali [6]. Tijekom uzgoja stanica deficijentnih za protein IqgC primijetili smo da se stanice lagano ispiru s plastične površine petrijevih zdjelica, što je bila indikacija da je IqgC uključen u regulaciju adhezije stanica za supstrat. Usporedili smo snagu adhezije stanica divljeg tipa i IqgC-deficijentnim stanica ekperimentima rotacijske trešnje i potvrdili da stanice deficijentne za IqgC imaju defekt u ovom procesu, što se može poništiti ponovnom ekspresijom rekombinantnog IqgC-a. Mikroskopijom tamnog polja smo pokazali da slabije adhezivne IqgC-deficijentne stanice migriraju brže nego divlji tip. Mikroskopija TIRF (totalna interna refleksija fluorescencije) sa stanicama koje simultano ekspimiraju fluorescentno obilježeni IqgC i paxilin B ili probu za F-aktin potvrdila je da IqgC lokalizira u adhezijske točke. Signalni putevi uključeni u regulaciju stanične adhezije u *D. discoideum* još uvijek nisu u potpunosti razjašnjeni, ali smatra se da je jedan od glavnih regulatora mala GTPaza Rap1 [4,7,8]. Taj protein smo pronašli u interaktomu proteina IqgC, kao jedan od potencijalnih veznih partnera. Nadalje, koristeći tehnike *pull-down* i BiFC (bimolekularna komplementacija fluorescencije) potvrdili smo interakciju proteina IqgC i Rap1. Ovim istraživanjem pokazujemo da je IqgC pozitivni regulator adhezije stanice za supstrat po kojem se kreće u amebi *Dictyostelium discoideum*. S obzirom na rezultate eksperimenata, predlažemo da IqgC regulira adheziju vezanjem za malu GTPazu Rap1.

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ASSOCIATIONS OF MUSICAL ACTIVITIES ON CORTISOL LEVELS IN PREGNANT WOMEN

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The term "stress" describing a feeling of emotional or physical tensions and exhaustion is nowadays often encountered [1]. It is an established fact that during the periods of stress there is dysregulation of hypothalamic- pituitary-adrenal (HPA) axis leading to raised levels of serum cortisol, "stress hormone" which is involved in many metabolic and immunomodulatory processes [2]. In the last few decades, music has been studied as a non-pharmacological and non-invasive modality known for its calming effect and recognized as a good method of stress reduction [3].

The main goal of this study is to detect and compare cortisol levels in pregnant women in relation to free time spent in listening and creating music. The assumption is that subjects with a higher frequency of musical activities should have better values of biochemical parameters and maintain a normal Body Mass Index (BMI). The research will be conducted on data collected during the implementation of the project "Croatian Island's Birth Cohort Study (CRIBS)" in order to clarify the related factors in the context of the metabolic syndrome that affects an increasing part of the population. Analyzed samples are serum specimens collected from healthy pregnant women in Split-Dalmatia County (Croatia). An analytical protocol for the determination of cortisol in human serum by High-performance liquid chromatography (HPLC) was implemented. Preliminary results revealed a statistically significant moderate negative association between cortisol levels and leisure time (i.e., creating and listening to music) during ($p < 0.05$) and after pregnancy ($p < 0.05$) on mainland, where more frequent exposure to music is associated with lower cortisol level. There is no significant association between cortisol and exposure to music on islands.

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POVEZANOST GLAZBENIH AKTIVNOSTI I RAZINE KORTIZOLA KOD TRUDNICA

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Pojam “stres” se danas često susreće, a označava iscrpljenost uzrokovanu duševnim ili tjelesnim preopterećenjem organizma [1]. Utvrđeno je da tijekom stresnih razdoblja dolazi do disregulacije osi hipotalamus-hipofiza-nadbubrežna žlijezda (HPA) što dovodi do povećane razine kortizola, takozvanog “hormona stresa” koji sudjeluje u mnogim metaboličkim i imunomodulacijskim procesima [2]. Posljednjih desetljeća glazba se proučava kao nefarmakološka i neinvazivna metoda snižavanja stresa, poznata po svom smirujućem učinku [3].

Glavni cilj ovog istraživanja je detekcija i povezanost razine kortizola u trudnica s provođenjem slobodnog vremena u stvaranju i slušanju glazbe. Pretpostavka je da bi ispitanice s većom učestalošću glazbenih aktivnosti trebale imati bolje vrijednosti biokemijskih parametara i održavati normalan indeks tjelesne mase (BMI). Istraživanje će se provoditi na podacima prikupljenim tijekom provedbe projekta “Kohortna studija rođenih na istočnojadranskim otocima (CRIBS)” kako bi se razjasnili čimbenici povezani u kontekstu metaboličkog sindroma koji zahvaća sve veći dio populacije. Analizirani su uzorci seruma prikupljeni od zdravih trudnica u Splitsko-dalmatinskoj županiji (Hrvatska). Primijenjen je analitički protokol za određivanje kortizola u humanom serumu tekućinskom kromatografijom visoke učinkovitosti (HPLC). Preliminarnim rezultatima utvrđena je statistički značajna umjerena negativna povezanost kortizola i provođenja slobodnog vremena (stvaranjem i slušanjem glazbe) tijekom trudnoće ($p < 0.05$) i nakon trudnoće ($p < 0.05$) na kopnu. Veća izloženost glazbi povezana je s nižom razinom kortizola. Nije utvrđena statistički značajna povezanost kortizola i izloženosti glazbi na otocima.

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COMPARISON OF THE ANTIOXIDANT ACTIVITY AND COMPOSITION OF THE ESSENTIAL OIL AND HYDROLATE ISOLATED FROM *Veronica austriaca* ssp. *jacquinii* (BAUMG.) EB. FISH. AND *Veronica saturejoides* VIS. ssp. *satuejoides*

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The genus *Veronica* L. is the largest genus of the Plantaginaceae family and in Croatia about 40 species can be found in various habitats. Some species of this genus, especially *V. officinalis* have been used in folk medicine for the treatment of colds, respiratory diseases, laryngopharyngitis, cough, hernia, cancer, as a diuretic and in the treatment of wounds [1]. According to previous studies, plants of the genus *Veronica* are a potential source of nutrients and functional substances with a variety of biological effects [2]. The aim of this study was to investigate differences in the composition of free volatile compounds of essential oils and hydrosols of the species *Veronica austriaca* ssp. *jacquinii* (Baumg.) Eb. Fish. and *Veronica saturejoides* Vis. ssp. *satuejoides* and to determine the antioxidant activity of the isolated extracts. From the essential oils of selected species, we isolated and identified free volatiles and statistically analyzed the results by using PCA to see which of the isolated extracts were more similar to each other and to relate the results with antioxidant activity. The components of the essential oils and hydrosols were analyzed by gas chromatography (GC-MS and GC-FID instrument) [3]. In both species the major component of the oil is hexahydropharnesyl acetone, while in the hydrosols of *Veronica saturejoides* Vis. ssp. *satuejoides* species, the major component was trans-p-mentha-1 (7), 8-dien-2-ol and in *Veronica austriaca* ssp. *jacquinii*, it was methyl eugenol. For each isolate, antioxidant activity was examined using two methods, ORAC (Oxygen Radical Absorbance Capacity Assay) and DPPH (2,2-diphenyl-1-picrylhydrazyl) solution) [3]. Samples of essential oils isolated from *Veronica saturejoides* Vis. ssp. *satuejoides* showed stronger antioxidant activity by both tested methods at concentration of 10 mg of essential oil per mL of acetone. The antioxidant activity of the hydrosols proved to be similar in all tested samples for both tested plants according to both ORAC and DPPH methods. It is expected that the antioxidant activity of the hydrosol is lower than that of the oil, since hydrosols contain less active substances than the essential oils.

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USPOREDBA ANTIOKSIDATIVNOG DJELOVANJA I SASTAVA ETERIČNOG ULJA I HIDROLATA IZOLIRANIH IZ VRSTA *Veronica austriaca ssp. jacquinii* (BAUMG.) EB. FISCH. I *Veronica saturejoides* VIS. ssp. *saturejoides*

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Rod *Veronica* L. je najveći rod porodice Plantaginaceae, a u Hrvatskoj je rasprostranjeno oko 40 vrsta na raznolikim staništima. Neke vrste ovoga roda, a posebno *V. officinalis*, koristile su se u narodnoj medicini za liječenje prehlade, respiratornih bolesti, laringofaringitisa, kašlja, kile, raka, kao diuretik te u liječenju rana [1]. Prema dosadašnjim istraživanjima, biljke roda *Veronica* su potencijalni izvor nutraceutika i funkcionalnih tvari sa širokim spektrom bioloških djelovanja [2]. Cilj ovog istraživanja je ustanoviti razlike u sastavu slobodnih hlapljivih spojeva eteričnih ulja i hidrolata vrsta *Veronica austriaca ssp. jacquinii* (Baumg.) Eb. Fisch. i *Veronica saturejoides* Vis. ssp. *saturejoides* te ispitati antioksidativnu aktivnost izoliranih ekstrakata. Iz eteričnih ulja odabranih vrsta izolirali smo i identificirali slobodne hlapljive tvari te rezultate statistički obradili PCA analizom da bismo vidjeli koji su od izoliranih ekstrakata sličnija jedni drugima te povezali rezultate sa pokazanom antioksidativnom aktivnosti. Komponente eteričnih ulja i hidrolata su analizirane plinskom kromatografijom (aparatura GC-MS i GC-FID) [3]. Za obje vrste glavna komponenta ulja je heksahidrofarnezil acetone, dok je za hidrolate vrste *Veronica saturejoides* Vis. ssp. *saturejoides* glavna komponenta trans-p-menta-1(7),8-dien-2-ol, a za *Veronica austriaca ssp. jacquinii* metil eugenol. Za svaki izolat ispitana je antioksidativna aktivnost pomoću dvije metode, ORAC (Oxygen Radical Absorbance Capacity Assay) i DPPH ((2,2-diphenyl-1-picrylhydrazyl) otopina) [3]. Uzorci eteričnih ulja izoliranih iz vrste *Veronica saturejoides* Vis. ssp. *saturejoides* pokazali su jače antioksidativno djelovanje za obje testirane metode s koncentracijom 10 mg eteričnog ulja/mL acetona. Antioksidativna aktivnost hidrolata se pokazala sličnom u svim ispitanim uzorcima za obje istraživane biljke i prema ORAC i prema DPPH metodi. Antioksidativna aktivnost hidrolata je očekivano manja nego aktivnost ulja s obzirom da se u hidrolatu nalazi manje aktivnih otopljenih tvari nego u eteričnom ulju.

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INCREASED REARING AND BRAINSTEM DOPAMINE LEVELS IN A RAT MODEL OF MILD NEONATAL NORMOBARIC HYPOXIA

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Prenatal exposure to acute hypoxia can cause developmental disturbances due to hypoxic-ischemic brain injury. Studies on rat models are necessary for a better understanding of the underlying pathological mechanisms of hypoxia and their effects on behavior [1, 2]. The aim of this study was to determine possible behavioral changes (locomotion, learning, anxiety-like, exploratory and social behavior) and analyze brainstem catecholamine levels in a rat non-invasive neonatal hypoxia model, which mimics mild midgestational hypoxic brain injury in humans. 16 experimental Wistar Han rats (8 females, 8 males) were exposed to normobaric hypoxic conditions (8% O₂, 92% N₂), in a warm (≈ 27°C) normobaric chamber, for 2 hours on the first postnatal day (PND1). At the same time 15 control rats (8 females, 7 males) were kept under normoxic conditions (21% O₂, 78% N₂). From PND33 to PND45 rats underwent the battery of behavioral tests: open field, hole-board, T-maze and social choice. On PND50 rats were sacrificed, and brainstem samples were collected for 3-CAT ELISA. In comparison to the control group, hypoxic rats displayed highly significant increase in the number of rearings in the open field test, which was accompanied by significantly increased levels of dopamine in the brainstem, showed by 3-CAT ELISA. With this experiment we demonstrated that acute hypoxia can induce very subtle changes in behavior which may arise because of the dopamine imbalance. Increased number of rearings can indicate disturbed spatial mapping in the hippocampus, the function of which can be disrupted by increased dopamine stimulation [3].

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POVEĆAN BROJ PROPINJANJA I POVEĆANA RAZINA DOPAMINA U MOŽDANOM DEBLU KOD ŠTAKORSKOG MODELA BLAGE NEONATALNE NORMOBARIČNE HIPOKSIJE

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Prenatalna izloženost akutnoj hipoksiji može uzrokovati poremećaje u razvoju uslijed hipoksično-ishemijske ozljede mozga. Istraživanja na štakorskim modelima neophodna su za bolje razumijevanje osnovnih patoloških mehanizama hipoksije i njihovih učinaka na ponašanje [1, 2]. Cilj ovog istraživanja bio je utvrditi moguće promjene u ponašanju (kretanje, učenje, anksioznost, istraživačko i društveno ponašanje) i analizirati razinu katekolamina u moždanom deblu u neinvazivnom štakorskom neonatalnom modelu hipoksije koji oponaša blagu hipoksičnu ozljedu mozga kod ljudi. 16 pokusnih štakora Wistar Han (8 ženki, 8 mužjaka) bilo je izloženo uvjetima normobarične hipoksije (8% O₂, 92% N₂), u toploj ($\approx 27^\circ\text{C}$) normobaričnoj komori, tijekom 2 sata prvog postnatalnog dana (PND1). Istodobno je 15 kontrolnih štakora (8 ženki, 7 mužjaka) bilo u normoksičnim uvjetima (21% O₂, 78% N₂). Od PND33 do PND45 štakori su prošli niz testova ponašanja: test otvorenog polja, test ploče s rupama, T-labirint i test društvenog odabira. Na PND50 štakori su žrtvovani, a uzorci moždanog debla prikupljeni su za 3-CAT ELISA. U usporedbi s kontrolnom skupinom, hipoksični štakori pokazali su značajan porast broja propinjanja u testu otvorenog polja, što je popraćeno značajno povećanom razinom dopamina u moždanom deblu, pokazano 3-CAT ELISA testom. Ovim pokusom pokazali smo da akutna hipoksija može izazvati vrlo suptilne promjene u ponašanju koje mogu nastati zbog neravnoteže dopamina. Povećani broj propinjanja može ukazivati na poremećeno prostorno mapiranje u hipokampusu, čija funkcija može biti poremećena zbog pojačane stimulacije dopaminom [3].

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RECOMBINANT RSV AND HCV VACCINES BASED ON MUMPS VIRUS

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Attenuated mumps virus (*Mumps orthorubulavirus*, family *Paramyxoviridae*) is a promising candidate for the basis of recombinant vector vaccines because it elicits a sustained immune response and does not cause alterations in the host genome. Paramyxoviruses have single-stranded, nonsegmented, negative-sense RNA genome which is encapsidated by the nucleocapsid protein (NP) and further associated with RNA-dependant RNA polymerase (RdRp) consisting of phosphoprotein (P) and large protein (L). Transcription and replication of paramyxoviruses is mediated by the RdRp, which means that a successful production of virions in the host cell requires the presence of viral genome and simultaneous expression of proteins NP, P and L.

For the production of mumps recombinant virus (vMRV2) and recombinant vector vaccines based on vMRV2 we are using a reverse genetics technology called rescue. This method is based on co-transfection of BSRT7 cells with four different plasmids: three expression plasmids that encode NP, P or L proteins and a plasmid with full-length genome of mumps vaccine strain L-Zagreb which does or does not include additional genes. We are using this technology to construct vector vaccines for hepatitis C virus (HCV) and human respiratory syncytial virus (RSV). For RSV vector vaccine, sequence encoding the ectodomain of RSV F protein fused to transmembrane and cytoplasmic region (TMD/CD) of mumps F protein was cloned into the genome of vMRV2. For HCV vaccine, we have inserted a) genomic region of HCV E1 and E2 proteins; or b) sequences encoding ectodomains of HCV E1 and E2 proteins fused to TMD/CD region of mumps F protein. We expect that RSV and HCV genes will be expressed in infected cells and proteins with the addition of TMD/CD of mumps F protein will be incorporated in viral particles.

By using rescue, we have produced recombinant viruses vMRV2 and vF RSV-MRV2 (vector vaccine for RSV); rescue for vCE1E2 HCV-MRV2 (vector vaccine for HCV, plasmid a) and vE1E2TMD HCV-MRV2 (plasmid b) is currently in progress. Viruses vMRV2 and vF RSV-MRV2 were propagated in Vero cell line, virus titer was determined and whole genome sequences were confirmed by next generation sequencing.



REKOMBINANTNA CJEPIVA ZA RSV I HCV TEMELJENA NA VIRUSU MUMPSA

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Atenuirani virus mumpsa (*Mumps orthorubulavirus*, porodica *Paramyxoviridae*) obećavajući je kandidat za bazu rekombinantnih vektorskih cjepiva jer izaziva dobar imunološki odgovor i ne uzrokuje alteracije u genomu domaćina. Genom paramiksovirusa građen je od negativne jednolančane nesegmentirane RNA koja stvara kompleks s nukleokapsidnim proteinom (NP), a na kompleks je vezana RNA-ovisna RNA polimeraza (RdRp) građena od fosfoproteina (P) i velikog proteina (L). Transkripcija i replikacija paramiksovirusa ovisi o aktivnosti kompleksa RdRp te je za nastanak viriona u stanici potrebna prisutnost ne samo virusnog genoma nego i proteina NP, P i L.

Za proizvodnju rekombinantnog virusa mumpsa (vMRV2) i vektorskih cjepiva temeljenih na vMRV2 u našem laboratoriju se koristi tehnologija reverzne genetike, tzv. postupak *rescue*. Metoda se bazira na istovremenoj transfekciji stanica BSRT7 s četiri plazmida: tri su ekspresijska i sadrže gene za proteine NP, P ili L, a četvrti sadrži kompletni genom virusa mumpsa cjepnog soja L-Zagreb u koji mogu biti umetnuti dodatni geni. Ovu tehnologiju koristimo za dizajn vektorskih cjepiva za virus hepatitisa C (HCV) i ljudski respiratorni sincicijski virus (RSV). Cjepivo za RSV dizajnirano je na način da smo u genom cjepnog soja ugradili sekvencu za ektodomenu proteina F RSV-a fuzioniranu na citoplazmatsku i transmembransku domenu (TMD/CD) proteina F mumpsa. Cjepivo za HCV konstruirano je tako da smo u genom mumpsa ugradili a) gensku regiju proteina E1 i E2 virusa HCV-a; ili b) sekvence ektodomena proteina E1 i E2 HCV-a fuzionirane na TMD/CD proteina F mumpsa. Očekujemo da će geni RSV-a i HCV-a biti eksprimirani u inficiranim stanicama, a proteini koji posjeduju TMD/CD proteina F virusa mumpsa će biti i inkorporirani u virusne čestice.

Postupkom *rescue* dobili smo rekombinantne viruse vMRV2 i vF RSV-MRV2 (vektorsko cjepivo za RSV); *rescue* za vCE1E2 HCV-MRV2 (vektorsko cjepivo za HCV, plazmid pod a) i vE1E2TMD HCV-MRV2 (plazmid pod b) je u tijeku. Virusi vMRV2 i vF RSV-MRV2 umnoženi su na stanicama Vero, određen im je titar, a sekvence cijelih virusnih genoma određene su sekvenciranjem nove generacije.



S-ADENOSYL HOMOCYSTEIN HYDROLASE DEFICIENCY

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S-adenosylhomocysteine hydrolase (AHCY) deficiency is a disorder caused by lowered enzymatic activity of AHCY protein due to the mutations in *AHCY* gene. AHCY has a key role in proper functioning of the methionine cycle in the cell, therefore the lack of AHCY function causes severe metabolic disorder. [1] Since AHCY is a single enzyme that hydrolyses SAH (S adenosylhomocysteine), a strong inhibitor of cellular methyltransferases, it has a central role in maintaining the methylation status of the cell. [2] Clinical presentation of this potentially lethal disorder includes a combination of muscular, neurological and hepatic disorders. [3] Despite the essential activity of AHCY, changes in molecular and cellular mechanisms in the state of AHCY deficiency have so far been poorly investigated. [4] Proper activity of AHCY is essential for maintaining the cellular methylation potential, which is determined by the ratio of the S-adenosylhomocysteine (SAH) and S-Adenosylmethionine (SAM) metabolites. The importance of rapid removal of SAH by AHCY has been underscored by the discovery of AHCY deficiency in humans [5] The aim of this research was the analysis and understanding of molecular and cellular roles of AHCY. In order to detect potential biomarkers for this disease in the future, we established lentivirus-delivered stable gene silencing by RNAi in 3 cell lines (MCF7, SW480, HEK293T) and used western method for protein analysis and RNA seq for transcriptome analysis. The goal was to address questions regarding the molecular pathology of AHCY deficiency to which answers are lacking in the context of differential gene expression and deciphering molecular protein networks and pathways. Western analysis showed us that the key proteins involved in cell cycle regulation (CDK2, cyclin B1, Cyclin D1), MAPK signaling proteins (Ras) and DNA damage proteins (P53, pP53) were up regulated. While results of RNA seq analysis showed us that genes involved in NF-kappa B signaling and oxidative stress were the most dysregulated in compare to the control. We can conclude that AHCY dysregulation is connected with changes in MAPK signaling pathway, DNA damage pathway and cell cycle pathway.

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S-ADENOZIL HOMOCISTEIN HIDROLAZNA DEFICIJENCIJA

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Deficijencija S-adenozilhomocistein hidrolaze (AHCY) je poremećaj uzrokovan mutacijama u genu *AHCY* čime je smanjena aktivnost proteina AHCY. AHCY ima ključnu ulogu u pravilnom odvijanju ciklusa aminokiseline metionina u stanici, stoga nedostatak njegove funkcije uzrokuje težak metabolički poremećaj. [1] Kao jedini enzim koji hidrolizira SAH, snažni inhibitor staničnih metiltransferaza, AHCY ima i indirektnu ulogu u održavanju metilacijskog statusa stanice. [2] Klinička slika ovog potencijalno letalnog oboljenja je karakterizirana kombinacijom mišićnih, neuroloških i jetrenih poremećaja. [3] Unatoč dokazanoj esencijalnosti AHCY, promjene u molekularnim mehanizmima stanice u stanju nedostatka su do sada nedovoljno istražene. [4] Ispravna aktivnost AHCY bitna je za održavanje potencijala stanične metilacije, koja se određuje omjerom metabolita S-adenosilhomocisteina (SAH) i S-adenosilmetionina (SAM). Važnost brzog uklanjanja SAH pomoću AHCY naglašena je otkrićem deficijencije AHCY [5] Cilj ovog istraživanja bio je analizirati molekularne i stanične uloge AHCY. Kako bismo u budućnosti detektirali potencijalne biomarkere za ovo oboljenje, generirali smo stabilno utišane stanične linije (MCF7, SW480, HEK293T) uz pomoć lentivirusnih čestica i napravili western analizu kako bismo detektirali promjene na razini proteina te RNA seq za analizu transkriptoma. Na temelju rezultata western analize možemo vidjeti da je povećana količina ključnih proteina uključenih u regulaciju staničnog ciklusa (CDK2, cyclin B1, Cyclin D1), proteina koji sudjeluju u regulaciji aktivacije signalizacije dna oštećenja (P53) te proteina uključenih u MAPK signalizaciju (Ras). Dok nam rezultati RNA seq analize ukazuju na to da je najviše disregulirana transkripcija gena uključenih u NF-kappa B signalizaciju i oksidacijski stres u odnosu na kontrolu. Možemo zaključiti da je AHCY deficijencija povezana sa promjenama u MAPK signalnom putu, putu aktivacije oštećenja DNA te sa regulacijom staničnog ciklusa.

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SEARCHING FOR NEW CERVICAL CANCER BIOMARKERS

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Cervical cancer is one of the most common malignancies in the female population despite existing prevention. It can be divided into two histological types: adenocarcinoma and squamous cell carcinoma (SCC) [1]. SCC is more common and accounts for 70% of all cases [1]. The development of cervical cancer is preceded by precancerous changes called cervical intraepithelial neoplasia (CIN) for several years. CIN is divided into three stages: CIN1 (mild dysplasia), CIN2 (moderate dysplasia), and CIN3 (severe dysplasia) [2]. Cervical cancer and CINs are associated with the high-risk human papillomavirus (HPV) infection that is sexually transmitted and responsible for 90-100% of cervical cancer cases among women, especially those over the age of 35 [1]. HPV types are clinically classified as high-risk (HR) or low-risk (LR) in terms of their association with cancer lesions [1]. HR HPV 16 and 18 are the most common types of HPVs causing cancer [1]. Although cervical cancer can be prevented by vaccination against HR HPVs of teenagers and young women, cytological and also by molecular screening (Pap and/or HPV testing) of sexually active women, there are various limitations of the second preventive measure such as unnecessarily expensive treatment and complications. Therefore, finding new biomarkers that correlate with the degree of lesion would potentially provide better insight into the differentiation of CIN lesions, reduce costs, and improve screening, especially in those women who have been vaccinated. In addition, the biomarkers could aid in the triage of indeterminate cytology or as predictive markers for identifying lesions that are most likely to progress to a high degree of cervical neoplasia [3]. In this preliminary study, the functionality of the antibodies to cellular biomarkers, such as cytokeratin 10, 18, 19 and protein 63 on cervical cancer cell lines and clinical samples, was examined with the MUSE instrument using miniaturized fluorescence detection system and microcapillary cytometry [4]. These biomarkers were examined comparatively in the normal cervical cells and in cervical cancerous cells in order to potentially find proteins that will better distinguish tumour from normal cells and better indicate their proliferation, prevalence and ability to progress to cancer.

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U POTRAZI ZA NOVIM BIOMARKERIMA RAKA VRATA MATERNICE

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Rak vrata maternice je jedan od najčešćih zloćudnih bolesti u ženskoj populaciji unatoč postojećoj prevenciji. Može se podijeliti u dva histološka tipa: adenokarcinom i karcinom skvamoznih stanica (SCC) [1]. SCC je češći i čini 70% svih slučajeva [1]. Razvoju raka vrata maternice prethode prekancerozne promjene koje se nazivaju cervikalnom intraepitelnom neoplazijom (CIN) koje traju više godina. CIN se dijeli u tri stupnja: CIN1 (blaga displazija), CIN2 (umjerena displazija) i CIN3 (teška displazija) [2]. U pozadini raka vrata maternice i CIN-a se nalazi infekcija visokorizičnim humanim papiloma virusom (HPV-om) koja se prenosi spolnim putem te je odgovoran za 90-100% slučajeva raka vrata maternice među ženama, posebno kod onih starijih od 35 godina [1]. Tipovi HPV-a mogu se klinički klasificirati kao visokorizični (HR) ili niskorizični (LR) u smislu njihove povezanosti s karcinomskim lezijama [1]. HR HPV 16 i 18 su najrasprostranjeniji tipovi HPV-a koji uzrokuju rak [1]. Iako je ovo vrsta raka koji se može spriječiti cijepljenjem protiv HR HPV-a kod tinejdžera i mladih žena, citološki i molekularnim probirom (Papa i/ ili HPV testiranje) seksualno aktivnih žena, ipak postoje različita ograničenja u sekundarnim preventivnim mjerama poput nepotrebnog skupog liječenja i komplikacija. Stoga bi pronalazak novih biomarkera koji koreliraju sa stupnjem lezije potencijalno omogućilo bolji uvid u razlikovanje CIN lezija, smanjilo bi troškove i poboljšalo probir, posebno u žena koje su cijepljene. Osim toga, biomarkeri bi mogli pomoći kod trijaže neodređene citologije ili pak kao prediktivni markeri za identifikaciju lezija koje će najvjerojatnije napredovati do visokog stupnja cervikalne neoplazije [3]. U ovom preliminarnom istraživanju ispitana je funkcionalnost antitijela za stanične biljege poput citokeratina 10, 18, 19 i proteina 63 na staničnoj liniji raka vrata maternice i kliničkim uzorcima pomoću MUSE instrumenta koji koristi minijaturiziranu fluorescentnu detekciju i mikrokapilarnu citometriju [4]. Ovi biomarkeri su ispitani usporedno u normalnim stanicama i tumorskim stanicama vrata maternice kako bi se potencijalno pronašli proteini koji će bolje razlikovati tumorske od normalnih stanica i bolje ukazati na njihovu proliferaciju, zastupljenost i mogućnost da napreduju do raka.

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REGULATORY MECHANISMS THAT CONTROL CHROMOSOME SEGREGATION IN *STREPTOMYCES COELICOLOR*

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Streptomyces is the largest genus within the phylum *Actinobacteria*. These filamentous gram-positive bacteria are best known as producers of various secondary metabolites, including more than two-thirds of the natural antibiotics used in medicine, biotechnology and agriculture. *Streptomyces* have a very complex life cycle that begins with spore germination and the formation of vegetative mycelium from which grow areal hyphae that eventually differentiate into long chains of spores.

Currently our research group is investigating the functions, interactions and temporal expression of genes important for DNA metabolism and chromosome segregation during the reproductive phase of *Streptomyces coelicolor* model organism for *Streptomyces* genus. This bacterium contains a linear chromosome with a large number of functional genes (7825). Although the cell division mechanisms are similar to those found in rod-shaped bacterium such as *Escherichia coli*, many aspects that control cell division and its coordination with chromosome segregation are remarkably different. We have identified paralogous single stranded DNA-binding protein (SsbB) as one of key players in chromosome segregation during sporulation in *Streptomyces coelicolor* [1]. To get a better insight into its biological role we have investigated other proteins, such as SMC and ParAB that have been identified to contribute to chromosome organization and distribution during *Streptomyces* sporulation. Our present results indicate how these proteins participate in different cellular mechanisms that control chromosome segregation. Next, we focused on studying segregation and condensation protein (ScpA). This protein is an interested candidate whose role in chromosome segregation is still not well described [2]. Using different molecular methods, our goal was to investigate whether ScpA and SsbB participate in the same regulatory pathway that controls chromosome segregation in the presporogenic compartment. The result of our ongoing project will be presented and discussed.

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REGULATORNI MEHANIZMI KONTROLE SEGREGACIJE KROMOSOMA U *STREPTOMYCES COELICOLOR*

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Streptomyces je najširi rod unutar koljena Aktinobakterija. Ove filamentozne gram-pozitivne bakterije najpoznatiji su proizvođači raznih sekundarnih metabolita uključujući više od dvije trećine antibiotika korištenih u medicini, biotehnologiji i agrokulturi. Rod *Streptomyces* ima vrlo složen životni ciklus koji započinje klijanjem spore te formiranjem vegetativnog micelija iz kojih izrastaju površinske hife koje se na kraju diferenciraju u duge lance spora.

Trenutno naša istraživačka skupina istražuje funkcije, interakcije i ekspresiju gena važnih za metabolizam DNA i segregaciju kromosoma tijekom reproduktivne faze modelnog organizma *Streptomyces coelicolor* za rod *Streptomyces*. Ove bakterije imaju linearan kromosom s velikim brojem funkcionalnih gena (7825). Iako su mehanizmi stanične diobe slični onima koji se nalaze u bakteriji poput *Escherichia coli*, mnogi aspekti koji kontroliraju diobu stanica i njegovu koordinaciju s segregacijom kromosoma su izuzetno različiti. Identificirali smo paralogni protein koji veže jednolančanu DNA (SsbB) kao jedan od ključnih sudionika u segregaciji kromosoma tijekom sporulacije u *Streptomyces coelicolor* [1]. Da bismo imali bolji uvid u njegovu biološku ulogu, istražili smo druge proteine, poput SMC i ParAB, za koje je utvrđeno da doprinose organizaciji i raspodjeli kromosoma tijekom sporulacije. Naši sadašnji rezultati pokazuju kako ti proteini sudjeluju u različitim staničnim mehanizmima koji kontroliraju segregaciju kromosoma. Zatim smo se usredotočili na proučavanje segregacijskog i kondenzacijskog proteina (ScpA). Ovaj protein je interesantan kandidat čija uloga u segregaciji kromosoma još uvijek nije dobro opisana [2]. Korištenjem različitih molekularnih metoda, cilj nam je bio istražiti sudjeluju li ScpA i SsbB na istom regulatornom putu koji kontrolira segregaciju kromosoma u presporogenom odjeljku. Rezultat našeg tekućeg projekta bit će predstavljen i raspravljen.

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RECRUITMENT MECHANISMS OF RasGAP PROTEIN IqgC TO MACROPINOSOMES IN AMOEBA *Dictyostelium discoideum*

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Large-scale endocytosis encompasses nonselective uptake of extracellular fluid or macropinocytosis and particle uptake or phagocytosis. This evolutionary conserved, Ras-regulated process is a primary way of feeding for amoeba *Dictyostelium discoideum* [1]. Wild-type *D. discoideum* isolates predominantly use phagocytosis to feed on bacteria, while their macropinocytosis is not adequate to sustain growth. On the other hand, laboratory strains have strongly upregulated macropinocytosis that enables them to thrive in liquid medium. This is due to a deletion of a gene encoding RasGAP (Ras GTPase activating protein) protein NF1 in axenic strains, which suppresses formation of large macropinosomes and phagosomes in wild-type strains [2]. In our previous study, we have identified a RasG-specific GAP IqgC that negatively regulates large-scale endocytosis in axenic strain [3]. Nevertheless, deletion of *iqgC* induced only modest increase in fluid uptake, possibly because axenic strains already have almost maximally upregulated macropinocytosis. To investigate this, we have generated *iqgC* knock-out in wild-type DdB strain and preliminary results demonstrated increased growth rates in axenic medium. IqgC strongly localizes to nascent macropinosome where it colocalizes with active Ras [3]. However, IqgC remains on the internalized macropinosome after Ras dissociated from the vesicle. Such dynamics suggests that IqgC also functions in early macropinosome maturation, probably in RasG-independent way. To elucidate the mechanism of IqgC recruitment to macropinosomes, we have analysed its localization in *rasG*⁻ cells. The loss of localization demonstrated essential role of RasG in IqgC recruitment to nascent macropinosome. Next, we analysed IqgC domains required for its recruitment to the membrane during macropinosome formation and early maturation. Examination of several fluorescent fusion proteins by confocal microscopy showed that RasGAP and RGCT domains alone, or with adjacent N- and C- terminal ends, are not sufficient for IqgC recruitment to macropinosomes. Since we were unable to demonstrate direct interactions between IqgC and binding partners previously identified in a pull-down assay [3], we performed a protein-lipid overlay assay to see if there are any lipid interactors. We showed that IqgC preferentially binds to phosphatidylinositol 3-phosphate (PI(3)P) and PI-bisphosphates PI(4,5)P₂, PI(3,5)P₂ and PI(3,4)P₂, which are known to be involved in macropinosome formation and early maturation [4]. In summary, IqgC is recruited to nascent macropinosome via interaction with RasG. However, RasG is dispensable for its retention on maturing vesicle, which is probably mediated by phosphoinositides.

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MEHANIZMI REGRUTACIJE RasGAP PROTEINA IqgC NA MAKROPINOSOME U AMEBI *Dictyostelium discoideum*

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Endocitoza na velikoj skali obuhvaća nespecifičan unos izvanstanične tekućine ili makropinocitozu i unos čestica ili fagocitozu. Ovaj evolucijski očuvan proces je reguliran proteinom Ras te je primarni oblik hranjenja amebe *Dictyostelium discoideum* [1]. Divlji sojevi *D. discoideum* dominantno se hrane bakterijama tj. fagocitozom, dok im je makropinocitoza nedovoljna da omogući rast u odsutnosti bakterija. S druge strane, laboratorijski sojevi imaju značajno pojačanu razinu makropinocitoze koja im omogućuje rast u tekućem mediju. Razlog tome je delecija gena koji kodira RasGAP (engl. *Ras GTPase activating protein*) protein NF1 u akseničnim sojevima, a koji u divljim sojevima suprimira formiranje velikih makropinosoma i fagosoma [2]. U prethodnom istraživanju smo identificirali RasGAP protein IqgC koji je specifičan za RasG te negativno regulira endocitozu na velikoj skali u akseničnom soju [3]. Ipak, delecija *iqgC* uzrokuje slabi porast unosa tekućine, vjerojatno zato što aksenični sojevi već imaju skoro maksimalno pojačanu makropinocitozu. Kako bi to istražili, kreirali smo *iqgC* knock-out u divljem soju DdB i preliminarni rezultati pokazuju poboljšanje rasta u akseničnom mediju. IqgC snažno lokalizira na nascentni makropinosom gdje kolokalizira s aktivnim proteinom Ras [3]. No, IqgC ostaje na internaliziranom makropinosomu nakon što je Ras već dislocirao s vezikule. Takva dinamika sugerira da IqgC ima ulogu tijekom ranog sazrijevanja makropinosoma, koja je neovisna o njegovoj interakciji s RasG. Kako bi razjasnili mehanizme regrutacije IqgC na makropinosome, analizirali smo njegovu lokalizaciju u *rasG* stanicama. Gubitak lokalizacije pokazao je da RasG ima ključnu ulogu u regrutiranju IqgC na nascentni makropinosom. Dalje smo istražili koje domene IqgC su potrebne za njegovu regrutaciju na membranu tijekom formiranja i ranog sazrijevanja makropinosoma. Analiza lokalizacije nekoliko skraćenih varijanti proteina fuzioniranih na fluorescentni protein konfokalnom mikroskopijom pokazala je da same RasGAP i RGCT domene, ili u kombinaciji s amino- odnosno karboksi-krajem, nisu dovoljne za regrutaciju IqgC na makropinosome. S obzirom da nismo uspjeli pokazati direktnu interakciju između IqgC i vezujućih partnera, prethodno identificiranih afinitetnim pročišćavanjem [3], testirali smo protein-lipidne interakcije kako bi utvrdili postoje li lipidni interaktori. Pokazali smo da IqgC preferencijalno veže fosfatidilinozitol (3)-fosfat (PI(3)P) i PI-bisfosfate PI(4,5)P₂, PI(3,5)P₂ i PI(3,4)P₂, koji su uključeni u formiranje i rano sazrijevanje makropinosoma [5]. Možemo zaključiti da je RasG potreban za regrutaciju IqgC na nascentni makropinosom, ali nije nužan za njegovo zadržavanje tijekom ranog sazrijevanja makropinosoma, koje je vjerojatno posredovano fosfoinozimidima.

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ALTERED N – GLYCOSYLATION OF IMMUNOGLOBULIN G AND TOTAL PLASMA PROTEINS IN PATIENTS WITH ATRIAL FIBRILLATION

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Atrial fibrillation (AF) is the most common persistent cardiac arrhythmia, affecting more than 1% of population. It is characterized by rapid and disorganized atrial activation leading to impaired atrial function, where myocardial fibrosis is one of the main factors influencing the heart pathophysiological changes. Consequently, AF is a risk factor for embolic stroke and worsening heart failure and has been associated with increased morbidity and mortality [1]. Significant changes in N-glycosylation are known to occur in some of the cardiovascular diseases (CVD), of which Changes in immunoglobulin G (IgG) N-glycome are an independent risk factor for atherosclerotic CVDs [2-3]. Given the importance of glycosylation in CVD and the fact that no studies have been conducted on glycosylation in AF so far, a preliminary analysis of IgG and total plasma protein N-glycans has been performed. The aim of this analysis was to gain insight into the status of IgG and total plasma protein N-glycans in AF, the potential existence of a causal relationship between the abundance of certain N-glycan structures and the degree of fibrosis, and AF recurrence after pulmonary vein isolation. IgG and total protein plasma N-glycans were analyzed by ultra-high performance liquid chromatography with hydrophilic interactions (HILIC-UPLC). The obtained results indicate that altered N-glycosylation occur in patients with AF, especially in IgG N-glycans, which emphasizes the importance of immunoglobulin glycosylation and the potential interaction between the immune response and pathophysiological changes in AF.

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PROMJENE U N-GLIKOZILACIJI IMUNOGLOBULINA G I UKUPNIH PROTEINA PLAZME KOD PACIJENATA S FIBRILACIJOM ATRIJA

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Fibrilacija atrijska (FA) najčešća je dugotrajna srčana aritmija od koje boluje više od 1% populacije. Karakterizirana je brzo i neorganiziranom atrijalnom aktivacijom koja dovodi do poremećaja funkcije atrijske, gdje je fibroza miokarda jedan od glavnih čimbenika koji utječu na patofiziološke promjene srca. Posljedično, AF je faktor rizika za embolijski moždani udar i pogoršanje zatajenja srca te je povezana s povećanim obolijevanjem i smrtnošću od istih [1]. Poznato je da dolazi do značajnih promjena u N-glikozilaciji kod nekih od kardiovaskularnih bolesti (KVB), od kojih su promjene u N-glikomu imunoglobulina G (IgG) neovisan faktor rizika za aterosklerotske KVB [2-3]. S obzirom na važnost glikozilacije u KVB i činjenice da do sada nisu provedena istraživanja o glikozilaciji u FA, napravljena je preliminarna analiza N-glikana IgG-a i ukupnih proteina plazme. Cilj ovog istraživanja je dobiti uvid u status N-glikana IgG-a i ukupnih proteina plazme u fibrilaciji atrijske, te utvrditi potencijalno postojanje uzročno-posljedične veze između zastupljenosti određenih struktura N-glikana i stupnja fibroze te ponovne pojave FA nakon izolacije plućnih vena. N-glikani IgG-a i ukupnih proteina plazme analizirani su visokoprotlačnom metodom tekućinske kromatografije ultravisoke učinkovitosti s hidrofiličnim interakcijama (Engl. HILIC-UPLC). Dobiveni rezultati upućuju da dolazi do promijenjene N-glikozilacije u pacijenata s FA, posebice kod N-glikana IgG-a što naglašava značaj glikozilacije imunoglobulina te potencijalnu međusobnu interakciju između imunološkog odgovora i patofizioloških promjena u fibrilaciji atrijske.

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MORPHOMETRIC CHARACTERISTICS AND CONDITION INDICES OF NOBLE CRAYFISH *Astacus astacus* L. FROM THE PLIVA RIVER

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The protected species, the Noble crayfish (*Astacus astacus*) the IUCN list of endangered species, classified in the third category (VU = vulnerable), is one of the four European species from the family Astacidae that live in freshwater ecosystems of Bosnia and Herzegovina. The aim of this study was to investigate the variability of selected morphometric characteristics of adult male and female crayfish of the species *Astacus astacus* from the upper reaches of the Pliva river. The crayfish were sampled in October of 2019 and then 27 individuals (20 males and 7 females) were caught. Crayfish were analyzed fresh in the field and in the laboratory. The treatment included the measurement of 12 morphometric features: total body length (TBL), weight (W), claw length (CLL), claw width (CLW), carapace length (CPL), carapace width (CPW), rostrum length (ROL), rostrum width (ROW), abdominal length and width (ABL, ABW) and telson length and width (TEL, TEW). The mean body length was 117.12 mm (\pm SD 11.07; min. 91.99 mm; max. 136 mm) in males and 111.55 mm (\pm SD 10.31; min. 94.77 mm; max. 126 mm) in females. The mean recorded body weight was 47.73 g (\pm SD 18.08; min. 22 g; max. 108 g) in males and 36.21 g (\pm SD 10.31; min. 19.3 g; max. 44.2 g) in females. Using the linear regression method, a positive correlation was found between body length and weight ($r = 0.79$), body weight and claws length ($r = 0.82$), as well as carapace width and body length ($r = 0.9$). Using the Mann-Whitney U nonparametric test, a statistically significant difference of the analyzed morphometric parameters was found between the sexes in CLL ($p = 0.003$), ROL ($p = 0.046$) and TEW ($p = 0.02$), which is explained by the pronounced sexual dimorphism of this type of Noble crayfish. The calculated values for Fulton's condition factor and the Crayfish constant indicate that the males are in better fitness, which is in line with the results of previous research in Europe. Data presented in this paper can serve as a basis for further research of *Astacus astacus* in this area.

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MORFOMETRIJSKE ZNAČAJKE I KONDICIJSKI INDEKSI RIJEČNOG RAKA *Astacus astacus* L. IZ RIJEKE PLIVE

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Zaštićena vrsta, riječni rak (*Astacus astacus*) nalazi se na IUCN listi ugroženih vrsta, svrstana u treću kategoriju (VU = ranjiva), jedna je od četiri europske vrste iz porodice Astacidae koje žive u slatkovodnim ekosustavima Bosne i Hercegovine. Cilj ovog rada bio je istražiti varijabilnost odabranih morfometrijskih karakteristika adultnih mužjaka i ženki raka vrste *Astacus astacus* iz gornjeg toka rijeke Plive. Rakovi su uzorkovani u listopadu 2019. godine i tada je ulovljeno 27 jedinki (20 mužjaka i 7 ženki). Rakovi su analizirani u svježem stanju na terenu i u laboratoriji. Obrada je obuhvatila mjerenje 12 morfometrijskih obilježja: totalne dužine tijela (TBL), težine (W), dužine kliješta (CLL), širine kliješta (CLW), dužine karapaksa (CPL), širine karapaksa (CPW), dužine rostruma (ROL), širine rostruma (ROW), dužine i širine abdomena (ABL, ABW) i dužine i širine telzona (TEL, TEW). Prosječna dužina tijela iznosila je 117.12 mm (\pm SD 11.07; min. 91.99 mm; max. 136 mm) kod mužjaka i 111.55 mm (\pm SD 10.31; min. 94.77 mm; max. 126 mm) kod ženki. Prosječna zabilježena težina tijela iznosila je 47.73 g (\pm SD 18.08; min. 22 g; max. 108 g) kod mužjaka i 36.21 g (\pm SD 10.31; min. 19.3 g; max. 44.2 g) kod ženki. Primjenom metode linearne regresije utvrđena je pozitivna korelacija između dužine i težine tijela ($r=0.79$), težine tijela i dužine kliješta ($r=0.82$), kao i širine karapaksa i dužine tijela ($r=0.9$). Primjenom Mann-Whitney U neparametarskog testa utvrđena je statistički značajna razlika analiziranih morfometrijskih parametara između spolova u CLL ($p=0.003$), ROL ($p=0.046$) i TEW ($p=0.02$), što se objašnjava izraženim spolnim dimorfizmom ove vrste rakova. Izračunate vrijednosti za Fultonov kondicijski faktor i Konstantu dekapodnog raka ukazuju da su mužjaci u boljem kondicijskom stanju, što je sukladno sa rezultatima dosadašnjih istraživanja u Europi. Podaci predstavljeni u ovom radu mogu poslužiti kao osnova za dalja istraživanja vrste *Astacus astacus* na ovom području.

ZAHVALE

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CHROMOSOME SEGREGATION ERRORS IN CELLS WITH VARYING CELL-TO-CELL CONTACT LEVELS

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The mitotic spindle is a microtubule-based structure that allows accurate division of genetic material between two daughter cells. Disruption of division mechanisms threaten cell viability or lead to cellular transformation if not detected and eliminated. Improper establishment and maintenance of kinetochore-microtubule attachments can give rise to erroneously attached chromosomes, which lag in anaphase which threatens segregation fidelity [1]. Here, we investigate the importance of cell environment for accurate chromosome segregation in epithelial healthy and cancer cell lines, based on previous research on organoid systems [2]. By using cell micropatterning of U2OS cells and growing both U2OS and MDCKII cells on fibronectin-coated coverslips in varying densities, we determined error rates in isolated cells and cells grown in confluent monolayers. In U2OS cells, chromosome bridges are the most frequently observed error, while the occurrence of lagging chromosomes is low in both groups of cells. Spindle geometry and interkinetochore distance are not influenced by cellular environment. However, anaphase spindles are less well centered in tightly surrounded MDCKII cells than in isolated ones, indicating defects in spindle positioning. Cortical actin levels are differently influenced by cell environment depending on the cell type. Future experiments should reveal to what extent and how forces from the cortex are transmitted via astral microtubules to the central spindle and kinetochores.

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GREŠKE U RAZDVAJANJU KROMOSOMA U STANICAMA S RAZLIČITIM RAZINAMA MEĐUSTANIČNOG KONTAKTA

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Mitotsko vreteno je struktura građena od mikrotubula koja omogućuje preciznu raspodjelu genskog materijala na stanice kćeri. Poremećeni mehanizmi diobe prijete opstanku stanice ili vode transformaciji ukoliko ih stanica ne primijeti i ukloni. Nepravilno uspostavljanje i održavanje veza između mikrotubula i kinetohora može dovesti do pogrešno prihvaćenih kromosoma koji zaostaju za sestrinskim kinetohorama koje se razdvajaju i prijete vjernosti diobe. [1]. Na temelju saznanja ostvarenih na sustavima organoida, istražujemo važnost stanične okoline za pravilnu raspodjelu kromosoma u zdravim i tumorskim staničnim linijama epitela. [2]. Koristeći metodu staničnog *micropatterninga* na U2OS stanicama te od nedavno, U2OS i MDCKII stanice uzgajane na fibronektinu u različitim gustoćama, odredili smo pojavnost grešaka u diobi u izoliranim stanicama te stanicama u konfluentnim jednoslojima. U U2OS stanicama, najzastupljeniji su kromosomski mostovi, dok je pojavnost kromosoma koji zaostaju u anafazi niska u obje grupe stanica. Stanično okruženje ne utječe na geometriju vretena i interkinetohornu udaljenost. Međutim, anafazna vretena u MDCKII stanicama su lošije centrirana u čvrsto okruženim stanicama, nego u izoliranim što ukazuje da imaju defekte u pozicioniranju vretena. Gustoća kortikalnog aktina ovisi o okruženju i različito je regulirana u dvjema tipovima stanica. Budući eksperimenti trebaju pokazati u kojoj se mjeri i na koji način sile s korteksa prenose preko astralnih mikrotubula na središte vretena i kinetohore.

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PHYLOGEOGRAPHIC DISTRIBUTION OF *CYP2D6* HAPLOTYPES

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The *CYP2D6* gene is located on chromosome 22q13.1 and consists of nine exons with an open reading frame of 1491 bp coding for a 497-amino acid protein [1]. This gene encodes CYP2D6 enzyme, which is responsible for metabolism of 25% of clinically prescribed drugs, although accounting for around 2% of total CYP content in the liver [2]. Due to difference in pharmacogenetic distribution of CYP2D6, we wanted to determine a phylogeographic distribution of SNP variation in this gene.

The 1000 Genomes Project Phase 3 data on 26 worldwide populations with different genetic ancestry were used in this study. 271 polymorphic SNPs were identified and phased into haplotypes (PHASE v2.1). Reconstructed haplotypes were analysed using population genetics softwares in order to explore inter- and intra-population characteristics.

In worldwide sample, 433 haplotypes were reconstructed. The highest nucleotide diversity was found in Africa. Highest haplotype diversity was detected in African ancestry populations and lowest in East Asian populations. F_{ST} pairwise differences grouped East Asian populations separately from other populations. Principal component analysis showed continental clustering for all but Central and South American populations. Tests of neutrality showed no background selection in any of investigated populations, while mismatch distribution suggests bottleneck effect in East Asian populations.

Haplotype distribution showed significant differences between continental population groups. Phylogeographic differences of *CYP2D6* gene suggest greater impact of demography than evolutionary forces like selection on SNP variation in this gene.

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FILOGEOGRAFSKA DISTRIBUCIJA HAPLOTIPOVA GENA *CYP2D6*

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Gen *CYP2D6* se nalazi na kromosomu 22q13.1, sadrži 9 egzona s otvorenim okvirom čitanja od 1491 parova baza i kodira za protein veličine 497 aminokisline [1]. Enzim *CYP2D6* je odgovoran za metabolizam oko 25% klinički najčešće propisanih lijekova iako čini samo oko 2% svih citokroma u jetri čovjeka [2]. S obzirom na različite farmakogenetičke karakteristike gena *CYP2D6*, cilj ovog istraživanja bio je odrediti filogeografsku distribuciju polimorfizama jednog nukleotida (SNP) ovog gena.

U istraživanju smo koristili podatke iz javno dostupne baze podataka (*The 1000 Genomes Project Phase 3*) iz 26 svjetskih populacija različitog porijekla. Pronađena je 271 SNP varijanta gena *CYP2D6*. Pomoću programa Phase v2.1 rekonstruirani su haplotipovi u svrhu određivanja intra- i interpopulacijskih karakteristika metodama populacijske genetike.

Najveća raznolikost nukleotida gena *CYP2D6* pronađena je u populacijama afričkog porijekla. Na ukupnom uzorku rekonstruirano je 433 haplotipova. Najveća raznolikost haplotipova pronađena je u populacijama afričkog porijekla, a najmanja u populacijama Istočne Azije. Genetičke različitosti (F_{ST}) između parova populacija odvojile su populacije istočne Azije od ostalih populacija. Analiza glavnih komponenti (PCA) pokazala je kontinentalno grupiranje svih populacija osim populacija Srednje i Južne Amerike. Testovi neutralnosti nisu detektirali utjecaj selekcije na nijednu istraživanu populaciju, dok test *mismatch distribution* upućuje na učinak uskog grla u populacijama Istočne Azije.

Distribucija haplotipova je pokazala značajnu različitost među kontinentalnim grupama populacija. Filogeografske različitosti gena *CYP2D6* upućuju na veći utjecaj demografije nego evolucijskih sila poput selekcije na varijabilnost ovog gena.

ZAHVALE

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TELOMERE LENGTH AND AGE AT DEATH IN VERY OLD INDIVIDUALS

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Ageing is a complex biological process characterized by a progressive deterioration of all bodily functions. Many theories of ageing have been proposed, with one of the most widely supported being the theory of programmed ageing caused by the shortening of telomeres [1]. Telomeres are repetitive sequences of DNA on the ends of the chromosomes that get shortened in every cell division [2]. Telomere DNA is bound with proteins of the shelterin complex, and together they comprise protective caps for the ends of the DNA molecule. Shorter telomeres have been associated with an increased morbidity and mortality risk of many age-related diseases [3].

Within the HECUBA project (CSF IP-01-2018-2497) relative telomere length (RTL) has been determined on DNA samples of 314 very old persons (85+ years of age), with 100 young individuals (aged 20-35) as a referent sample. DNA for all the samples was extracted from peripheral blood by the salting out method [4]. As the sample of the long-lived individuals was collected in the period between 2007 and 2009, age at death for each individual has been determined 10 years after the initial sampling. This data is valuable, as it enables us to compare telomere lengths between truly long-lived individuals that had lived beyond 90 and 95 years of age, and individuals that died before reaching 90 years of age, thus determining whether telomere length is a key component for extreme longevity.

RTL was determined by a quantitative polymerase chain reaction [5]. It is a method for amplifying desired DNA fragments while monitoring the amplification process in real time. To determine the RTL, two reactions were necessary – one in which specific primers were used to amplify the telomere repeats, and the other in which the primers were specific for a beta-globin gene, a gene which has only one copy in the human genome. RTL was expressed as a factor by which each sample differed from a reference DNA sample in its ratio between amplified telomere DNA and amplified single copy gene DNA [5]. This ratio is proportional to the average telomere length. Preliminary results of the statistical analysis show that in this sample of very old individuals there is a negative correlation between RTL and the age at death ($r=-0.114$; $p=0.043$), with longer telomeres being a negative predictor for reaching 95 years of age ($p=0.024$). These results indicate that in advanced age RTL is not a good biomarker of ageing and cannot be used as a predictor for achieving extreme longevity.

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DULJINA TELOMERA I DOB SMRTI KOD OSOBA DUBOKE STAROSTI

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Starenje je kompleksan biološki proces kojeg karakterizira progresivno slabljenje svih funkcija organizma. Mnoštvo je predloženih teorija starenja, a među njima je jedna od najbolje istraženih ona o programiranom starenju uzrokovanom skraćivanjem telomera [1]. Telomere su repetitivne sekvencije DNA na krajevima kromosoma koje vezane s proteinima shelterin kompleksa čine zaštitne kape na krajevima molekule DNA, a skraćuju se prilikom svake diobe stanice [2]. Mnoga istraživanja su potvrdila povezanost kraćih telomera s povećanim rizikom obolijevanja i smrti od mnogih bolesti povezanih sa starenjem [3].

U okviru projekta HECUBA (HRZZ IP-01-2018-2497) provedeno je određivanje relativne duljine telomera (RTL) na DNA uzorcima 314 osoba duboke starosti (85+ godina), dok je kao referentni uzorak poslužila DNA 100 mladih osoba (20-35 godina). DNA svih uzoraka izolirana je iz periferne krvi metodom izoliranja [4]. Kako je uzorak osoba duboke starosti prikupljen u razdoblju 2007. - 2009., za svakog od uključenih nakon 10 godina utvrđena je dob smrti, što omogućava usporedbu duljine telomera osoba koje su doživjele 90. i 95. godinu života u odnosu na one koje su preminule prije navršene 90. godine života.

Relativna duljina telomera određena je kvantitativnom lančanom reakcijom polimerazom [5]. To je metoda za umnožavanje željenih fragmenata DNA uz praćenje reakcije u stvarnom vremenu. Za izračun RTL za svaki su uzorak bile potrebne dvije reakcije – reakcija u kojoj se specifičnim početnicama umnažaju telomerna ponavljanja, i ona u kojoj se umnožava gen koji se u ljudskom genomu ponavlja samo jednom (ovdje, gen za beta-globin). RTL je izražena faktorom koji predstavlja razliku omjera umnožene telomerne DNA i DNA referentnog gena mjerenih uzoraka u odnosu na referentni uzorak [5]. Dobiveni faktor proporcionalan je prosječnoj duljini telomera svakog ispitanika. Preliminarni rezultati obrade podataka pokazuju da u uzorku osoba duboke starosti (85+ g.) postoji negativna korelacija između RTL i dobi smrti ($r=-0,114$; $p=0,043$), a dulje telomere su se pokazale kao negativan prediktor za doživljenje 95. godina starosti ($p=0,024$). Ovi rezultati upućuju da u dubokoj starosti duljina telomera nije više biomarker starenja organizma te ne može poslužiti kao prediktor dostizanja ekstremne dugovječnosti.

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RNA-Seq ANALYSIS OF FIBROBLASTS FROM PATIENT WITH S-ADENOSYLHOMOCYSTEINE HYDROLASE DEFICIENCY

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S-adenosylhomocystein hydrolase (AHCY) is an enzyme that catalyzes hydrolysis of S-adenosyl-L-homocysteine (SAH) to adenosine and homocysteine. [1] Since SAH is the product and competitive inhibitor of all S-adenosyl methionine-dependent transmethylation reactions, its removal is crucial for maintaining cells' methylation potential and normal organism function. [2] Reduced AHCY activity leads to inhibition of S-adenosyl methionine-dependent transmethylation reactions which leads to severe metabolic disorders and pathological conditions in humans. This clinical presentation is also characterized with increased concentrations of SAH, S-adenosyl methionine (SAM) and methionine in plasma. This severe and hereditary metabolic disease caused by insufficient AHCY activity was described for the first time in Croatia in 2004. [3] So far, several mutations that lead to reduced AHCY activity have been found (R49C, R49H, G71S, D86G, A89V, Y143C, Y328D and W112Ter). To gain insight into possible consequences on the patient's transcriptome due to insufficient AHCY activity caused by mutations Y328D and Y143C, RNA extracted from patient's dermal fibroblasts was sequenced (RNA-seq.). This was done on Illumina NextSeq System, using three biological replicas. RNA extracted from healthy fibroblasts was used as control (WT). The obtained raw data was processed using commercially available applications RNA-Seq alignment (Illumina, Inc.), DeSeq 2 (BaseSpace Labs.) and iPathwayGuide (Advaita Bio). RNA-Seq alignment was used to align obtained sequences which were then analyzed with DeSeq2 to obtain a list of differentially expressed genes. 50 differentially expressed genes with highest absolute log₂-fold change value (out of 1692 observed, with p<0,05) were analyzed using iPathwayGuide. Cell pathways that can be assumed to be most altered in patient's fibroblasts are PI3K-Akt signaling pathway, focal adhesion and ECM-receptor interaction. Based on this results it can be concluded that cell cycle regulation and synthesis of collagens, laminins and integrins is disturbed in patient's fibroblasts. Disturbed regulation of key extracellular proteins might lead to infringed adhesion and cell-extracellular matrix interaction.

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ANALIZA FIBROBLASTA PACIJENTA S NEDOSTATNOM AKTIVNOSTI S-ADENOZILHOMOCISTEIN-HIDROLAZE METODOM RNA-Seq

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S-adenozilhomocistein-hidrolaza (SAHH) katalizira reakciju hidrolize S-adenozilhomocisteina (SAH) na adenzin i homocistein [1]. Budući da je SAH produkt svih reakcija transmetilacije ovisnih o adenzilmetioninu i njihov kompetitivni inhibitor, njegovo uklanjanje ključno je za održavanje normalnog metilacijskog potencijala stanice te za normalnu funkciju organizma. [2] Do sada je pronađeno nekoliko mutacija koje uzrokuju smanjenje aktivnosti SAHH (R49C, R49H, G71S, D86G, A89V, Y143C, Y328D i W112Ter). Nedostatna aktivnost SAHH dovodi do inhibicije reakcija transmetilacije ovisnih o adenzilmetioninu što uzrokuje teške metaboličke poremećaje te patološka stanja kod ljudi. Također, teškoj kliničkoj slici doprinose i biokemijski poremećaji kao što su povećana koncentracija SAH, S-adenozilmetionina (SAM) te metionina u krvnoj plazmi. Ova teška i nasljedna metabolička bolest uzrokovana nedostatnom aktivnosti enzima SAHH prvi put je opisana u Hrvatskoj 2004. godine. [3] Kako bismo dobili uvid u moguće promjene transkriptoma pacijenta kojem je dijagnosticiran poremećaj uzrokovan nedostatnom aktivnosti SAHH uslijed pojave mutacija Y328D i Y143C, sekvencirana je RNA izolirana iz kožnih fibroblasta pacijenta (RNA-seq). Za sekvenciranje je korišten uređaj Illumina NextSeq, te su sekvencirane tri biološke replike. Kao kontrola korištena je RNA izolirana iz kožnih fibroblasta zdrave osobe (divlji tip, WT). Dobiveni podaci obrađeni su korištenjem programa RNA-Seq alignment (Illumina, Inc.), DeSeq 2 (BaseSpace Labs.) i iPathwayGuide (Advaita Bio). Programom RNA-Seq alignment poravnate su dobivene sekvence, a potom je programom DeSeq2 generirana lista diferencijalno eksprimiranih gena. 50 gena s najvećom apsolutnom *log2-fold change* razlikom (od ukupno 1692, uz $p < 0,05$) analizirano je pomoću programa iPathwayGuide. Stanični putevi za koje se može pretpostaviti da su najviše promijenjeni u fibroblastima pacijenta su PI3K-Akt signalni put, fokalna adhezija te interakcija ekstracelularnog matriksa i receptora. Na temelju dobivenih rezultata može se zaključiti da je u fibroblastima pacijenta narušena regulacija staničnog ciklusa te sinteza kolagena, laminina i integrina. Narušena regulacija ključnih ekstracelularnih proteina dovodi do narušene adhezije i interakcije stanica s ekstracelularnim matriksom.

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APOBEC MUTATIONAL SIGNATURE AFFECTS PREDICTION OF CELL OF ORIGIN IN DIFFERENT MOLECULAR GROUPS OF BREAST CANCER

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One of the main challenges in cancer biology is the identification of the cell-of-origin (COO) of cancers. It has been shown that cell type of origin of a cancer can be accurately determined based on the distribution of mutations along its genome [1]. Novel approaches based on machine learning methods can successfully identify COO by utilizing different epigenetic features of the COO and somatic mutations, since the distribution of mutations reflects the chromatin structure of the cell-of-origin. However, these models can not explain well the variance in somatic mutations across the genome in certain cancers, such as breast cancer [2]. Often in human cancers, there is a biological noise in the genome due to hypermutation phenomena and specific mutational processes, such as those due to the APOBEC family of cytidine deaminases [3], which is especially present in breast cancers. This noise can negatively affect the outcome of predicting the cell-of-origin in cancers.

The goal of this research is to explore the impact of genomic regions with high APOBEC mutational signature on the outcome of the models for predicting the cell-of-origin in different subtypes of breast cancer (basal and non-basal breast cancers). Mutational signatures are characteristic patterns of somatic mutations caused by distinct mutational processes. Random forest regression was used to model the distribution of somatic mutations in 1 Mb windows using the chromatin profiles from various normal tissues. Since mutations that are due to APOBEC activity may lower the prediction accuracy of the model, the modelling was performed with removed regions containing the APOBEC signature above a certain threshold. For each subtype of breast cancer, the best cutoff value of percentage of APOBEC signature for a region was determined based on the performance of the model. Both basal-like breast tumors and non-basal-like tumors had an increase in overall explained variance when removing regions with a high percentage of APOBEC signature. However, the best cut-off values for subtypes vary, for basal breast tumors the cut-off value is 10% while for non-basal tumors it is about 40%. Basal-like breast tumors have significantly smaller amounts of APOBEC signature compared to non-basal-like tumors therefore this difference in cutoff values is expected. Analysis of genomic regions with different proportions of APOBEC signature indicates that the mutations that result from APOBEC activity, primarily occur in open chromatin regions. Together these results indicate the importance of characteristics of regions and mutations which can be used to improve the prediction of cell-of origin in cancers.

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UTJECAJ MUTACIJSKOG POTPISA PROTEINA APOBEC NA PREDVIĐANJE ISHODIŠNE STANICE RAZLIČITIH MOLEKULARNIH SKUPINA RAKA DOJKE

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Jedan od glavnih izazova u biologiji raka je identifikacija ishodišne stanice (*cell-of-origin*, COO) karcinoma. Pokazalo se da se stanični tip podrijetla raka može točno odrediti na temelju raspodjele mutacija duž njegovog genoma [1]. Novi pristupi koji se temelje na metodama strojnog učenja mogu uspješno identificirati COO koristeći različite epigenetske značajke COO i somatske mutacije, budući da raspodjela mutacija odražava strukturu kromatina ishodišne stanice raka. Međutim, ovi modeli ne mogu dobro objasniti odstupanje somatskih mutacija u genomu kod određenih karcinoma, poput raka dojke [2]. Često kod karcinoma u ljudi postoji biološki šum u genomu zbog pojava hipermutacije i specifičnih mutacijskih procesa, poput onih zbog porodice citidin deaminaza APOBEC [3], koja je posebno prisutna kod karcinoma dojke. Ova buka može negativno utjecati na ishod predviđanja ishodišne stanice karcinoma.

Cilj ovog istraživanja je istražiti utjecaj genomskih regija s visokim APOBEC mutacijskim potpisom na ishod modela za predviđanje ishodišne stanice u različitim podtipovima karcinoma dojke (bazalni i ne-bazalni karcinom dojke). Mutacijski potpisi su karakteristični obrasci somatskih mutacija uzrokovani različitim mutacijskim procesima. Šuma slučajnih stabala korištena je za modeliranje raspodjele somatskih mutacija u prozorima veličine 1 Mb pomoću kromatinskog profila iz različitih normalnih tkiva. Budući da mutacije koje su posljedica aktivnosti proteina APOBEC mogu smanjiti preciznost modela, modeliranje je provedeno s uklonjenim regijama koje sadrže mutacijski potpis proteina APOBEC iznad određenog praga. Za svaku podvrstu karcinoma dojke određena je najbolja granična vrijednost postotka mutacijskog potpisa proteina APOBEC po regiji na temelju izvedbe modela. I bazalni tumori dojke i ne-bazalni tumori imali su porast ukupne objašnjene varijance pri uklanjanju regija s visokim postotkom potpisa APOBEC. Međutim, najbolje granične vrijednosti za podtipove variraju, za bazalne tumore dojke granična vrijednost je 10%, dok za nebazalne tumore iznosi oko 40%. Bazalni tumori dojke imaju znatno manje količine potpisa APOBEC u usporedbi s ne-bazalnim tumorima, pa je i očekivana ova razlika u graničnim vrijednostima. Analiza genomskih regija s različitim udjelima potpisa APOBEC-a pokazuje da mutacije koje proizlaze iz aktivnosti APOBEC-a uglavnom se pojavljuju u otvorenim kromatinskim regijama. Zajedno ovi rezultati ukazuju na važnost karakteristika regija i mutacija koje se mogu koristiti za poboljšanje predviđanja ishodišne stanice karcinoma.

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POLAR CHROMOSOMES PIVOT THEIR WAY TOWARDS THE SPINDLE BODY

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During mitosis, the cell forms a spindle that equally segregates chromosomes into two daughter cells. Soon after nuclear envelope breakdown microtubules nucleated at the centrosomes of the spindle pole capture kinetochores, protein complexes on chromosomes. Some chromosomes immediately find themselves in the area between two spindle poles, yet others positioned at the periphery first need to approach the spindle pole in order to congress, or in other words, travel to the spindle equatorial plane. The question remains how these polar chromosomes located at the back of the spindle make their way across the spindle pole and reach the spindle body, from where they can continue their congression towards the equator. By using tubulin specific dyes in RPE1 cells stably expressing CENP-A-GFP and Centrin1-GFP, markers for kinetochores and centrosomes, respectively, we demonstrate that polar chromosomes, together with the microtubules they are attached to, pivot around the centrosome towards the spindle body. The angle that the polar chromosomes form with the spindle axis changed faster during the period of rapid spindle elongation, indicating a mechanism in which spindle elongation creates a hydrodynamic drag force that brings kinetochores to the spindle body. This mechanism also ensured timely mitosis, as kinetochores that failed to pivot by the end of spindle elongation significantly delayed anaphase onset. Altogether, we propose a model in which pivoting of microtubules around the spindle pole, driven by spindle elongation, promotes the movement of peripheral chromosomes towards the spindle body and consequently their proper congression to the spindle equator [1].

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PIVOTIRANJE KAO MEHANIZAM DOLASKA POLARNIH KROMOSOMA NA DIOBENO VRETENO

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Tijekom mitoze stanica formira diobeno vreteno potrebno za ravnomjernu segregaciju kromosoma u stanice kćeri. Ubrzo nakon puknuća jezgrine ovojnice, mikrotubuli nukleirani na centrosomima polova diobenog vretena hvataju i vežu kinetohore, proteinske komplekse na kromosomima. Neki kromosomi su odmah smješteni u prostoru između dva pola diobenog vretena, dok kromosomi smješteni na periferiji prvo moraju prići polu vretena kako bi mogli nastaviti kongresiju, tj. putovanje prema ekvatorskoj ravnini vretena. Još uvijek je otvoreno pitanje na koji način polarni kromosomi smješteni iza pola vretena dolaze do tijela vretena gdje nastavljaju kongresiju prema ekvatoru kada postoje centrosomi kao fizička prepreka. Koristeći boje specifične za tubulin u stanicama RPE1 koje stabilno eksprimiraju CENP-A-GFP i Centrin1-GFP, markere za kinetohore i centrosome, pokazali smo kako polarni kromosomi, zajedno s mikrotubulima za koje su vezani, pivotiraju oko centrosoma prema vretenu. Kut koji zatvaraju polarni kromosomi zajedno s osi vretena mijenja se brže tijekom bržeg produljenja vretena, što ukazuje da se radi o mehanizmu u kojemu elongacija vretena uzrokuje hidrodinamičku silu koja dovodi kromosome do tijela diobenog vretena. Ovaj mehanizam također osigurava pravilno odvijanje mitoze, s obzirom da su kinetohore zaostale na polu vretena nakon njegove elongacije značajno produljile vrijeme početka anafaze. Na temelju toga predlažemo model u kojemu pivotiranje mikrotubula oko pola vretena, kao rezultat elongacije vretena, promiče kretanje perifernih kromosoma prema vretenu te daljnju ispravnu kongresiju prema ekvatoru vretena [1].

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IDENTIFICATION, BIOCHEMICAL CHARACTERIZATION AND INTRACELLULAR LOCALIZATION OF SPONGE HOMOLOG OF HUMAN RRAS2

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Cancer is one of the most extensively studied diseases that occurs in almost all multicellular organisms. It is most likely that cancer appeared in parallel with multicellularity and the development of true tissues and organs [1]. Thus, investigation of proteins involved in processes of intercellular cooperation, cell division control and multicellularity is crucial for better understanding of the disease. Comparative genomic analyses have shown that most genes/proteins associated with human cancer emerged during the early evolution of Metazoa [2,3,4]. Hence, the study of these proteins in simpler organisms, such as sponges, provides a new approach in understanding cancer. Sponges are important model organisms because of their simple morphology and a complex genome with many genes/proteins highly similar to their vertebrate homologs [5,6,7]. Using bioinformatics tools, we identified a homolog of human RRAS2 (*Ras-related protein R-Ras2*), a cancer-related protein, in the freshwater cave sponge *Eunapius subterraneus*. RRAS2 (also known as TC21) belongs to the subfamily of RAS-related proteins. When constitutively expressed and activated, it has a regulatory role in cell proliferation and migration, and is often overexpressed in human cancers [8]. Our aim is to understand the physiological functions of RRAS2 protein in humans using sponges as a model system and to gain a better insight into the evolution of this oncogene. Bioinformatics analysis showed high conservation of RRAS2 protein and its homologs among Metazoa. The sponge cDNA encoding RRAS2 protein was successfully cloned into the expression vector and overexpressed. We confirmed GTPase activity of sponge RRAS2 protein. Additionally, cDNA was cloned into vectors for biological characterization of RRAS2. Intracellular localization of sponge RRAS2 protein was determined in transfected human tumour cells using immunofluorescence and confocal microscopy.

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IDENTIFIKACIJA, BIOKEMIJSKA KARAKTERIZACIJA I UNUTARSTANIČNA LOKALIZACIJA SPUŽVINO G HOMOLOGA LJUDSKOG PROTEINA RRAS2

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Rak je jedna od najintenzivnije proučavanih bolesti koja se javlja u gotovo svim višestaničnim organizmima. Budući da se smatra kako se rak pojavio upravo prilikom prijelaza na višestaničnost i razvojem prvih pravih tkiva i organa, za bolje razumijevanje bolesti ključno je proučavanje proteina odgovornih za procese međustanične komunikacije, kontrolu diobe stanica i nastanak višestaničnosti [1]. Komparativnim genomskim analizama utvrđeno je da se većina gena/proteina povezanih s nastankom raka kod ljudi pojavila tijekom rane evolucije Metazoa [2,3,4], pa nam tako proučavanje navedenih proteina u jednostavnijim organizmima, poput spužvi, pruža novi pristup [5]. Spužve predstavljaju dobar modelni organizam jer su jedne od morfološki najjednostavnijih životinja, no imaju kompleksan genom te većina gena iz spužvi pokazuje značajnu očuvanost s homolozima kod kralješnjaka [5,6,7]. Bioinformatičkim analizama identificirali smo gen/protein iz slatkovodne špiljske spužve *Eunapius subterraneus* čiji je homolog kod čovjeka RRAS2 (od engl. *Ras-related protein R-Ras2*) povezan s nastankom raka. Protein RRAS2 (poznat i kao TC21) pripada subobitelji RAS-srodnih proteina. Kada je konstitutivno eksprimiran i aktiviran, ključan je za regulaciju staničnih procesa poput proliferacije i migracije stanica, a često je prekomjerno eksprimiran u različitim vrstama raka [8]. Cilj je razjasniti osnovne fiziološke funkcije proteina RRAS2 kod čovjeka na modelu spužve te steći što bolji uvid u evoluciju ovog onkogeno. Bioinformatička analiza pokazala je visoku očuvanost ovog proteina i njegovih konzerviranih regija kod Metazoa. Spužvina cDNA koja kodira za protein RRAS2 uspješno je uklonirana u odgovarajući ekspresijski vektor te je napravljena prekomjerna ekspresija proteina. Potvrđena je GTPazna aktivnost proteina RRAS2. Također je uklonirana cDNA za RRAS2 u odgovarajuće vektore s ciljem biološke karakterizacije proteina. Transfekcijom ljudskih tumorskih stanica metodama imunofluorescence i konfokalne mikroskopije određen je unutarstanični smještaj spužvinog proteina RRAS2.

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MORPHOLOGICAL VARIABILITY IN *Dianthus sylvestris* Wulfen s. l. ON THE BALKAN PENINSULA

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Dianthus sylvestris complex includes ten subspecies [1,2] whose delimitation is still challenging and full of controversy. Its important diversity centre is in the central Mediterranean area. Identification of *D. sylvestris* subspecies continues to be problematic due to great morphological variability between subspecies, and complex patterns of variation with respect to ecological preferences and geographic distribution [3]. This study is focused on Balkan populations of six subspecies (*D. sylvestris* ssp. *alboroseus*, *D. sylvestris* ssp. *bertisceus*, *D. sylvestris* ssp. *kozjakensis*, *D. sylvestris* ssp. *nodosus*, *D. sylvestris* ssp. *syvestris* and *D. sylvestris* ssp. *tergestinus*), which have been treated inconsistently in previous taxonomic accounts. Qualitative and quantitative morphological characters were examined on plants collected in the field and deposited in ZA herbarium. The multivariate analyses based on 15 morphological characters (2 qualitative, 5 continuous, 6 ratios and 2 meristic) were used to describe and identify patterns of morphological variation in *D. sylvestris* complex, including 461 individuals from 97 populations across the Balkan Peninsula. When considering the subspecies in two-dimensional ordination space, a separation of southern Balkan and northern Balkan subspecies along PC1 (27% of variation) was detected, as well as a vast amount of overlap along PC2 (19% of variation). Calyx length, petal denticulation, and number and shape of epicalyx scales turned out to capture the greatest extent of morphological variability between individuals. However, they should not be considered as taxonomically reliable, since individual values can fall within the variability range of several subspecies. Subspecies such as *D. sylvestris* ssp. *nodosus*, *D. sylvestris* ssp. *syvestris* and *D. sylvestris* ssp. *tergestinus*, have similar morphologies and share parts of their geographic distributions, and cannot be clearly differentiated using quantitative morphological concepts. However, a different flowering period differentiates *D. sylvestris* ssp. *tergestinus*, suggesting it to be a sympatric taxon, which is supported by our preliminary results of genetic analyses. Therefore, we suggest treating *D. sylvestris* complex on the Balkan Peninsula as a single morphologically variable species, while only *D. sylvestris* ssp. *tergestinus* deserves infraspecific rank.

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MORFOLOŠKA VARIJABILNOST *Dianthus sylvestris* Wulfen s. l. NA BALKANSKOM POLUOTOKU

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Kompleks *Dianthus sylvestris* uključuje deset podvrsta [1,2] čije je razgraničenje i dalje izazovno i puno kontroverzi. Važno središte njegove raznolikosti nalazi se na području središnjeg Mediterana. Identifikacija podvrsta ove grupe problematična je zbog velike morfološke varijabilnosti te kompleksnog obrasca varijabilnosti s obzirom na ekološke preferencije i geografsku rasprostranjenost [3]. Ovo je istraživanje usredotočeno na balkanske populacije šest podvrsta (*D. sylvestris* ssp. *alboroseus*, *D. sylvestris* ssp. *bertisceus*, *D. sylvestris* ssp. *kozjakensis*, *D. sylvestris* ssp. *nodusus*, *D. sylvestris* ssp. *sylvestris* i *D. sylvestris* ssp. *tergestinus*), koje su dosada tretirane taksonomski nedosljedno kao. Kvalitativne i kvantitativne morfološke osobine izmjerene su na jedinkama sakupljenim na prirodnim staništima, a čuvaju se u herbaru ZA. Multivarijatne analize temeljene na 15 morfoloških osobina (2 kvalitativne, 5 kontinuiranih, 6 omjernih i 2 merističke) korištene su za opisivanje i identifikaciju obrazaca morfološke varijabilnosti *D. sylvestris* s.l. na Balkanskom poluotoku, uključujući 461 jedinku iz 97 populacija. Razmatranjem svih šest podvrsta u dvodimenzionalnom ordinacijskom prostoru, vidljivo je odvojeno grupiranje podvrsta iz južnog i sjevernog dijela Balkanskog poluotoka duž PC1 osi (27% varijabilnosti), te preklapanja duž PC2 osi (19% varijabilnosti). Osobine koje su obuhvatile najveći raspon morfološke varijabilnosti među jedinkama su dužina čaške, nazubljenost latica te broj i oblik ljusti epikaliksa. Međutim, ove osobine ne bi se trebale smatrati taksonomski pouzdanima, budući da se individualne vrijednosti mogu nalaziti unutar raspona varijabilnosti nekoliko podvrsta. Podvrste kao npr. *D. sylvestris* ssp. *nodusus*, *D. sylvestris* ssp. *sylvestris* i *D. sylvestris* ssp. *tergestinus* dijele sličnu morfologiju i geografsku distribuciju te ih nije moguće jasno razlikovati temeljem kvantitativnih morfoloških osobina. Međutim, *D. sylvestris* ssp. *tergestinus* se izdvaja prema različitom razdoblju cvatnje, sugerirajući da se radi o simpatričkoj svojti, što potvrđuju naši preliminarni rezultati genetičkih analiza. Stoga predlažemo da se kompleks *D. sylvestris* na Balkanskom poluotoku tretira kao jedna morfološki varijabilna vrsta, dok samo *D. sylvestris* ssp. *tergestinus* zaslužuje rang podvrste.

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EFFECT OF INCREASED TEMPERATURE ON *Arabidopsis thaliana*, *Brassica rapa* AND *Solanum lycopersicum* SEEDLINGS

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Temperature is one of the major parameters influencing plant life alongside relative humidity and light. It varies geographically and changes with time. Here, the effect of heat stress on growth and physiology of model plant *Arabidopsis thaliana* (thale cress), and two globally important crop species, *Solanum lycopersicum* (tomato) and *Brassica rapa* (chinese cabbage) was investigated. Seedlings were exposed to a moderate elevated temperature of 37 °C, a temperature common for the summer season in the Mediterranean, and to a severe elevated temperature of 45 °C. This extreme temperature regime was chosen based on literature data and the highest recorded temperature in Croatia [1,2]. Timeframes of seedling survival at such an extreme condition were evaluated. In heat treated seedlings, prolin content and levels of lipid peroxidation were measured. Both parameters show an increase in heat treated seedlings in comparison to controls. As a consequence of global warming, environmental temperatures have risen in recent years and continue to do so. Thus, these results, together with previous research, will provide a clearer picture of heat tolerance and response in plants.

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UTJECAJ POVIŠENE TEMPERATURE NA KLIJANCE VRSTA *Arabidopsis thaliana*, *Brassica rapa* I *Solanum lycopersicum*

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Temperatura, kao važan čimbenik za rast i razvoj biljaka, varira s geografskom širinom i stalno se mijenja. Uz relativnu vlagu i svjetlost, vanjska temperatura ima presudnu ulogu u adaptaciji biljaka na okolišne uvjete. Istražen je učinak povišene temperature na rast i fiziološke promjene klijanaca uročnjaka *Arabidopsis thaliana* koji je modelna biljka te dviju poljoprivredno važnih vrsta, rajčice *Solanum lycopersicum* i kineskog kupusa *Brassica rapa*. Klijanci su tretirani umjereno povišenom temperaturom od 37 °C, uobičajenom tijekom ljetnog razdoblja na sredozemnom području, te temperaturom od 45 °C. Tretman ekstremnom temperaturom od 45 °C izabran je na temelju literaturnih podataka i apsolutne najviše izmjerene temperature u Hrvatskoj [1,2], te je određen vremenski okvir u kojem klijanci preživljavaju ekstremne uvijete. U klijancima izloženim povišenim temperaturama, izmjeren je sadržaj prolina i stupanj lipidne peroksidacije te je pokazan porast oba parametra pod utjecajem toplinskog stresa. U posljednje vrijeme, a kao posljedica globalnog zatopljenja, okolišna temperatura je u stalnom porastu, a ovo će istraživanje, uz dosadašnja saznanja, dati jasniju sliku o toleranciji i odgovoru biljaka na toplinski stres.

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IDENTIFICATION, CHARACTERIZATION AND LOCALIZATION OF SATELLITE DNA SEQUENCES OF THE PACIFIC OYSTER *CRASSOSTREA GIGAS* (Thunberg, 1793)

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Bivalve mollusks are a large group of economically and ecologically important invertebrates, which made them particularly interesting as model organisms for genomic research. So far, 31 bivalve genomes have been sequenced, the first one being the genome of the Pacific oyster *Crassostrea gigas* (Thunberg, 1793), now assembled to the level of chromosomes. Repetitive DNA sequences constitute the largest part of the most eukaryotic genomes. Satellite DNAs (satDNAs) are the most numerous and usually build very long arrays of tandemly repeated monomers preferentially located in the heterochromatin [1]. Although they are involved in important functions regarding the stability of chromatin, due to their repetitive nature and almost identical monomers they are very often underrepresented in the genome assemblies making them still quite unexplored. Low content of heterochromatin [2] and the association of satDNAs with transposable elements [3], make the genome of the Pacific oyster an interesting research topic.

In order to identify a complete set of satDNAs (satellitome) of the Pacific oyster, we isolated genomic DNA and sequenced it using next-generation sequencing platform. The obtained reads were analyzed using TAREAN (*Tandem Repeat Analyzer*) pipeline yielding a set of 52 satDNAs. All satDNAs were compared to an online base of repetitive sequences, *Repbase*. More than 50% of satDNAs showed similarity to DNA transposons, half of which were Helitrons. The whole set of identified satDNAs was localized *in silico* on publicly available chromosomes of the Pacific oyster, and several were localized on metaphase chromosomes using fluorescence *in situ* hybridization. Chromosomal distribution exhibiting mostly interspersed pattern is related to the association of satDNAs with mobile elements. In this work, we identified and characterized the satellitome of the Pacific oyster and localized several satDNAs of interest, furthering our knowledge about the unexplored genome components of the Pacific oyster.

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IDENTIFIKACIJA, KARAKTERIZACIJA I LOKALIZACIJA SATELITNIH SEKVENCIJA DNA GENOMA PACIFIČKE KAMENICE *CRASSOSTREA GIGAS* (Thunberg, 1793)

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Školjkaši su ekonomski i ekološki važni beskralješnjaci što ih čini iznimno zanimljivim modelnim organizmima za genomska istraživanja. Do sada je sekvenciran 31 školjkaški genom, a prvi među njima bio je genom pacifičke kamenice *Crassostrea gigas* (Thunberg, 1793), koji je sada sastavljen do razine kromosoma. Repetitivne sekvencije DNA čine najveći dio većine eukariotskih genoma. Među njima su najbrojnije satelitne DNA (satDNA) i najčešće grade vrlo duge nizove uzastopno ponovljenih monomera te su preferencijalno smještene u heterokromatinu [1]. Uključene su u važne funkcije vezane uz stabilnost kromatina. Zbog repetitivne organizacije i gotovo identičnih monomera vrlo često su izostavljene iz sastavljenih genoma i stoga slabo istražene. Niska zastupljenost heterokromatina [2] i povezanost satDNA i pokretnih genetičkih elemenata [3] čine genom vrste *C. gigas* zanimljivim područjem istraživanja.

Kako bismo u potpunosti identificirali ukupnu satDNA (satelitom) genoma vrste *C. gigas*, izolirali smo genomsku DNA i primijenili sekvenciranje nove generacije. Dobivena očitavanja analizirana su računalnim alatom TAREAN (*Tandem Repeat Analyzer*) kojim smo identificirali 52 satDNA. Sve dobivene satDNA uspoređene su s bazom repetitivnih sekvenci *Repbases*. Više od 50 % satDNA pokazalo je sličnost s DNA transpozonomima, od kojih su polovica bili Helitroni. Cijeli satelitom lokaliziran je *in silico* na javno dostupne kromosome vrste *C. gigas*. Nekoliko satDNA lokalizirano je na metafaznim kromosomima vrste *C. gigas* fluorescencijskom hibridizacijom *in situ*. Lokalizacije *in situ* i *in silico* pokazale su raspršenu distribuciju po kromosomima što se može pripisati povezanosti satDNA s pokretnim genetičkim elementima. U ovom smo radu identificirali i okarakterizirali satelitom vrste *C. gigas* te nekoliko satDNA lokalizirali na kromosomima. Dobivenim rezultatima pridonijeli smo dosadašnjim saznanjima o ovom nedovoljno istraženom dijelu genoma vrste *C. gigas*.

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MACROPHYTES AS STORAGE UNITS FOR EMERGING CONTAMINANTS

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Emerging contaminants, like pharmaceuticals and endocrine disrupting chemicals have been detected worldwide in surface waters, and mostly originate from sewage effluents [1]. Behavior and effects of these contaminants on aquatic biota are poorly understood. Furthermore, knowledge regarding their trophic transfer in aquatic food webs is insufficient. It is known that many aquatic organisms bioaccumulate different contaminants [2]–[4]. Macrophytes, aquatic plants and mosses, are proven to accumulate various contaminants from the environment they live in, and are often observed in phytoremediation experiments [5], [6]. However, information on bioaccumulation potential of pharmaceuticals and endocrine disrupting chemicals in macrophytes is limited. Macrophytes could act like storage units for some of these chemicals and could secondly reintroduce them into environment through food webs. In order to discover additional information on this matter, a field study was conducted on five rivers and ten sampling sites in Croatia. The sites were selected to represent effluent impacted watercourses and upstream clean controls. Given the possible different distribution of accumulated compounds in different parts of mosses and aquatic plants, plant roots and leaves, as well as lower old and upper new shoots of moss were sampled separately. Water and biofilm samples were collected as well. Samples will be screened for contaminants using an ultra-performance liquid chromatography (UPLC) system coupled to a hybrid quadrupole linear ion trap mass spectrometer. The results will contribute to a better understanding of the role primary producers have in accumulation of pharmaceuticals and endocrine disrupting contaminants. Moreover, results will provide new insights on transfer of pharmaceuticals and endocrine disruptors within the aquatic food webs and aquatic-terrestrial habitat linkage.

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MAKROFITI KAO SPREMNICI ZA ONEČIŠĆUJUĆE TVARI

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Onečišćujuće tvari, poput farmaceutika i endokrinih disruptora, prisutne su u površinskim vodama širom svijeta, a uglavnom potječu iz komunalnih otpadnih voda i otpadnih voda iz stočarstva [1]. Ponašanje tih spojeva u vodi te njihov utjecaj na vodene organizme, još nisu dovoljno istraženi. Osim toga, vrlo malo se zna i o njihovom trofičnom prijenosu u vodenim hranidbenim mrežama. Utvrđeno je da mnogi vodeni organizmi mogu bioakumulirati različite onečišćujuće spojeve [2]–[4]. Dokazano je da makrofiti, vodene biljke i mahovine, akumuliraju različite kontaminante iz okoline u kojoj žive te se zbog toga često istražuju u vidu fitoremedijacije [5], [6]. Međutim, podaci o potencijalu bioakumulacije farmaceutika i endokrinih disruptora u makrofitima su ograničeni. Makrofiti bi mogli djelovati kao spremnici za neke od ovih spojeva, te ih na taj način reintoducirati u vodeni okoliš putem prehrambenih mreža. S ciljem utvrđivanja novih činjenica vezanih uz ovo područje, provedeno je terensko istraživanje na deset lokacija na pet rijeka u Hrvatskoj. Lokacije uzorkovanja su odabrane tako da predstavljaju vodotoke pod utjecajem onečišćenja otpadnim vodama i čiste kontrole uzvodno. S obzirom na moguću različitu raspodjelu akumuliranih onečišćujućih spojeva u različitim dijelovima mahovina i vodenih biljaka, odvojeno su uzorkovani korijen i lišće biljaka, te donji stari i gornji novi izdanci mahovina. Na svim lokacijama uzorkovanja prikupljeni su i uzorci vode i obraštaja. Onečišćujuće tvari u uzorcima će se odrediti pomoću sustava tekućinske kromatografije visokog učinka spregnutog sa sustavom tandemске spektrometrije masa. Rezultati će doprinijeti boljem razumijevanju uloge koju primarni proizvođači imaju u akumulaciji farmaceutika i endokrinih disruptora. Štoviše, rezultati će pružiti nove uvide o prijenosu farmaceutika i endokrinih disruptora unutar slatkovodnih hranidbenih mreža, te u kopnene ekosustave.

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ANALYSIS OF THE SATELLITOME OF THE FLOUR BEETLE *TRIBOLIUM FREEMANI* BY HIGH-THROUGHPUT SEQUENCING

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Satellite DNA (satDNA) are noncoding sequences located primarily in the heterochromatic regions of eukaryotic chromosomes. Due to their noncoding nature, they were often regarded as “junk” DNA, but recent studies have shown the important role of satDNA in chromosomal architecture and proper chromosome segregation [1]. The tandem organization of satellite monomers in eukaryotic genomes also presents a great technical challenge for researchers, and therefore satDNAs have often been omitted from the genome assemblies. However, due to the development of new sequencing technologies, research on satDNA has become more prevalent.

The genome of the flour beetle *Tribolium freemani* is composed of huge heterochromatic blocks, which makes it a great model organism for studying satellite sequences. The main satDNA of the species *T. freemani*, making up 31% of the genome, has been described almost three decades ago. The existence of other satDNA in the genome of the *T. freemani* beetle has not yet been confirmed [2].

The goal of this study was to reveal the satellitome, the collection of satDNA in the *T. freemani* genome by using high-throughput sequencing of the second and third generation. Whole-genome sequencing was carried out using the Illumina and PacBio platforms. Short (151 bp) paired-end reads obtained by Illumina sequencing were analyzed by the bioinformatics tool TAREAN which is capable of identifying new satellites based on short unassembled reads [3]. Using PacBio sequencing we obtained ultra-long high-fidelity (HiFi) reads which were used to study the organization of the satellite monomers in the genome. By combining the aforementioned analyses, we defined 10 new low-copy satellites. Their portions in the genome vary between 0.013-0.24%, while their monomer sizes range from 63 to 266 bp. The tandem organization of these satDNA has been successfully proven by using the Southern blot method, and their chromosomal location was determined by fluorescence *in situ* hybridization. The new satellites are found dispersed in the genome, comprising arrays spanning more than 10 kilobases, but also show higher order repeat (HOR) structures. To conclude, by using the high-throughput sequencing, the *T. freemani* satellitome has been deciphered. Characterization of the previously unknown DNA sequences paves the way for a comprehensive understanding of the *T. freemani* genome as well as for further studies on the function of its hidden genome parts.

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ANALIZA SATELITOMA KUKCA BRAŠNARA *TRIBOLIUM FREEMANI* VISOKOPROTOČNIM SEKVENCIRANJEM

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Satelitne DNA (satDNA) nekodirajuće su sekvence smještene prvenstveno u heterokromatskim dijelovima eukariotskih kromosoma. Zbog svoje nekodirajuće prirode često su nazivane „otpadnom“ DNA, ali istraživanja novijeg datuma otkrivaju važnu ulogu satDNA u kromosomskoj arhitekturi i pravilnom razdvajanju kromosoma [1]. Uzastopno ponovljena organizacija satelitnih monomera u genomu predstavlja velik metodološki izazov te su ove sekvence često zapostavljene u genomskim istraživanjima i nedostaju u sastavljenim eukariotskim genomima. Međutim, razvojem novih tehnologija sekvenciranja, satDNA postaju predmetom sve intenzivnijih studija.

Kukac brašnar *Tribolium freemani* odlikuje se visokim udjelom heterokromatina u genomu što ga čini odličnim modelom za proučavanje satelitnih sekvenca. Prije tri desetljeća eksperimentalnim metodama opisana je glavna satDNA vrste *T. freemani* koja izgrađuje čak 31% genoma, no postojanje drugih satDNA u genomu ove vrste dosad nije dokazano [2].

Cilj ovog istraživanja bio je upotrebom metoda visokoprotočnog sekvenciranja druge i treće generacije istražiti satelitom, ukupnu zbirku satelitnih DNA, u genomu vrste *T. freemani*. Ukupnu genomsku DNA sekvencirali smo pomoću platforma Illumina i PacBio. Kratka očitavanja duljine 151 para baza (pb) dobivena Illumina sekvenciranjem analizirana su bioinformatičkim programom TAREAN koji identificira nove satelite na temelju kratkih neposloženih očitavanja [3]. PacBio sekvenciranje rezultiralo je dugim očitavanjima velike točnosti (HiFi, *high fidelity reads*) na temelju kojih je proučena organizacija satelitnih monomera unutar genoma. Kombinirajući spomenute analize definirali smo 10 novih nisko zastupljenih satDNA čiji pojedinačni udjeli u genomu iznose 0,013-0,24 %, dok im monomeri duljinom nukleotidnog slijeda variraju između 63-266 pb. Uzastopno ponovljena genomska organizacija ovih satDNA eksperimentalno je potvrđena metodom hibridizacije po Southernu, dok je kromosomski smještaj otkriven metodom fluorescencijske hibridizacije *in situ*. Novodetektirani sateliti raspršeni su u genomu u nizovima dugim i do nekoliko desetaka kilobaza pokazujući također organizaciju višeg reda. Zaključno, visokoprotočnim sekvenciranjem rasvijetljen je satelitom kukca *T. freemani*, a karakterizacija dosad nepoznatih DNA sekvenci utire put cjelokupnom sagledavanju genoma ove vrste kao i daljnjim proučavanjima funkcije njegovih zakučastih dijelova.

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EFFECT OF STRESS CONDITIONS ON PHOTOSYNTHETIC EFFICIENCY OF *Arabidopsis thaliana* SEEDLINGS WITH MODIFIED *BPM1* GENE EXPRESSION

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Six genes encoding BPM proteins are present in the *Arabidopsis thaliana* genome. Previous studies have shown that the BPM1 protein plays an important role in the regulation of various developmental processes, as well as in the phenotypic and physiological adaptability of plants to adverse environmental conditions [1, 2]. Depending on the severity and duration, different stress conditions can have negative effects on plant metabolism. One of the most likely effects is reduced photosynthesis, resulting in decreased plant growth, development, and productivity. Today, there are several methods for determining photosynthetic efficiency. One of the most commonly used is the measurement of chlorophyll *a* (Chl *a*) fluorescence by the OJIP test. The method is based on recording of polyphasic Chl *a* fluorescence induction curve during high-intensity illumination of dark-adapted leaves [3]. The aim of this work was to study the effect of heat, salinity, and osmotic stress on the photosynthetic efficiency of *Arabidopsis* seedlings using the OJIP test. To question the possible role of BPM1 protein in plant response to stress conditions, two lines were used – the wild type (wt) and the line with overexpressed BPM1 gene (*oeBPM1*). Chlorophyll *a* fluorescence was measured 12th day after the beginning of germination. The effect of heat stress was studied on 12-day-old seedlings exposed to a temperature of 43 °C for one hour. For salinity and osmotic stress, seedlings were cultured from day 5 to day 12 on medium containing 75 mM NaCl and 150 mM mannitol, respectively. Regardless of the stress condition applied, seedlings of both lines showed a decrease in performance index (PI_{ABS}) compared to non-stressed plants. From several measured parameters (φ_{PO} , F_0 , V_j , M_0), the amount of active reaction centers of photosystem II was calculated. The results obtained indicate a decrease in their amount due to stress conditions, which could explain the decrease in PI_{ABS}. Measurement of Chl *a* fluorescence by the OJIP test revealed no difference between the wt and *oeBPM1* lines in response to the stress conditions studied.

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UČINAK STRESNIH UVJETA NA FOTOSINTETSKU UČINKOVITOST KLIJANACA UROČNJAKA (*Arabidopsis thaliana*) S PROMIJENJENOM EKSPRESIJOM GENA *BPM1*

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U genomu uročnjaka (*Arabidopsis thaliana*) prisutno je šest gena koji kodiraju proteine BPM. Dosadašnja istraživanja pokazala su da protein BPM1 ima važnu ulogu u regulaciji različitih razvojnih procesa, ali i u fenotipskoj i fiziološkoj prilagodljivosti biljaka na nepovoljne okolišne uvjete [1, 2]. Različiti stresni uvjeti mogu imati negativne učinke na biljni metabolizam što ovisi o njihovoj jačini i trajanju. Jedan od najznačajnijih učinaka je smanjena učinkovitost fotosinteze što može dovesti do usporavanja rasta i razvoja te pada biljne produktivnosti. Danas su dostupne različite metode za određivanje učinkovitosti fotosintetskih reakcija, a jedna od često korištenih je mjerenje fluorescencije klorofila *a* (Chl *a*) metodom OJIP. Temelji se na mjerenju polifaznog rasta fluorescencije Chl *a* prilikom kontinuiranog osvjjetljavanja listova biljaka aklimatiziranih na tamu [3]. Cilj ovog rada bio je istražiti utjecaj toplinskog, solnog i osmotskog stresa na učinkovitost fotosintetskih reakcija u klijanaca uročnjaka primjenom metode OJIP. U istraživanju su korištene dvije linije – klijanci divljeg tipa (*wt*) i klijanci s pojačanom ekspresijom gena *BPM1* (*oeBPM1*) kako bi se istražila potencijalna uloga proteina BPM1 u odgovoru biljke na stresne uvjete. Fluorescencija Chl *a* mjerena je 12. dana od početka isključavanja. Učinak toplinskog stresa istraživao je na klijancima koji su 12. dana izloženi temperaturi od 43 °C tijekom jednog sata. Za istraživanje solnog i osmotskog stresa, klijanci su od 5. do 12. dana uzgajani na podlozi koja je sadržavala 75 mM NaCl, odnosno 150 mM manitol. Neovisno o primijenjenom stresnom uvjetu, klijanci obje linije pokazali su pad fotosintetske učinkovitosti (PI_{ABS}) u usporedbi s biljkama koje nisu bile izložene stresnim uvjetima. Iz nekoliko izmjerenih parametara (φ_{PO} , F_0 , V_J , M_0) izračunata je količina aktivnih reakcijskih centara fotosustava II. Dobiveni rezultati ukazuju na smanjenje njihove količine zbog djelovanja stresnih uvjeta čime se može objasniti pad PI_{ABS} . Mjerenjem fluorescencije Chl *a* metodom OJIP nije utvrđena razlika između linija *wt* i *oeBPM1* u odgovoru na istraživane stresne uvjete.

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LONG-RANGE ORGANISATION OF HOLOCENTROMERES

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The centromere is a specific region of every eukaryotic chromosome essential for efficient segregation of chromosomes during cellular division. The main role of the centromere is organization of kinetochore protein attachment to the chromosomes as well as the kinetochore attachment to the spindle apparatus. Regarding centromere architecture, the majority of species have monocentric chromosomes characterized by a single regional centromere. In contrast, holocentric chromosomes, with the centromere function distributed at multiple sites along the chromosome length, were observed in some nematode, insect, and plant species. In general, centromere is determined by a centromere variant of histone protein (CenH3) and centromeric DNA. Recent ChIP-seq analyses in nematode *Meloidogyna incognita* revealed cluster-like organization of CenH3 domains in holocentromere. The centromeric clusters are composed of divergent tandem repeats which share a completely conserved 19 bp-long box [1]. In order to disclose the long-range organisation of *M. incognita* holocentromere, we have performed whole genome sequencing with the Pacific Biosystems High-Fidelity (HiFi) technology [2]. We have obtained 535,322 reads containing 8,700,000 base pairs (50x coverage of the genome). The reads were assembled into contigs using HiCanu [3]. In order to disclose the patterns of sequences that lie in-between centromeric clusters we performed extensive bioinformatics analyses and found that these large regions are highly conserved. Moreover, we found that the regions surrounding the centromeric tandem repeats represent dispersed repetitive sequences highly similar in size and composition. In conclusion, consistent with the polycentromere model, *M. incognita* centromere is organized in a form of short tandem arrays embedded in environment composed of dispersed non-centromeric repeats.

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ORGANIZACIJA HOLOCENTROMERE U DUGIM POTEZIMA

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Centromera je specifična regija eukariotskih kromosoma bitna za njihovo učinkovito razdvajanje tijekom stanične diobe. Glavna uloga centromere je organizacija vezanja kinetohornih proteina na kromosome te posljedično na diobeno vreteno. Što se tiče same strukture centromere, većina vrsta ima monocentrične kromosome koje karakterizira jedna lokalizirana centromera. S druge strane holocentrični kromosomi s centromernom funkcijom raspoređenom duž kromosoma, primijećeni su u nekih vrsta oblika, insekata i biljaka. Općenito, centromera je determinirana centromernom varijantom histonskog proteina (CenH3) i centromernom DNA. Nedavne *ChIP-seq* analize na obliću *Meloidogyna incognita* otkrile su *cluster-like* organizaciju CenH3 domena u holocentromeri. Centromerni klasteri sastoje se od divergentnih tandemskih ponavljanja koji imaju potpuno očuvani motiv dug 19 bp [1]. Kako bismo otkrili organizaciju holocentromere u dugim potezima kod *M. incognita*, izvršili smo sekvenciranje cijelog genoma koristeći tehnologiju *High-Fidelity (HiFi) Pacific Biosystems* [2]. Dobili smo 535 322 očitavanja koja sadrže 8700000 baznih parova (50x pokrivenost genoma). Očitavanja su sastavljena u duge sljedove (eng. *contig*) pomoću algoritma HiCanu [3]. Kako bismo otkrili obrasce sekvenci koje se nalaze između centromernih klastera, izveli smo opsežne bioinformatičke analize i otkrili da su ta područja vrlo očuvana. Štoviše, otkrili smo da područja oko centromernih uzastopnih ponavljanja predstavljaju raspršene ponavljajuće sekvence vrlo slične po veličini i sastavu. Zaključno, u skladu s modelom policentromere, centromera vrste *M. incognita* organizirana je u obliku kratkih nizova uzastopno ponovljenih sekvenci koji su uklopljeni u okoliš sastavljen od raspršenih ne-centromernih ponavljanja.

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THERAPEUTIC POTENTIAL OF NEUROSTEROIDS AND NEUROTROPHINS IN DEMENTIA

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Dementia is a syndrome of progressive cognitive decline that usually affects older people [1]. It will become one of the leading global problems in the future due to accelerated aging of the population and increase of life expectancy [2]. Alzheimer's disease (AD) is the most common progressive and incurable neurodegenerative disease. [3]. Neuroimaging techniques have shown a decrease in brain volume and weight in AD patients, as well as dilation of lateral brain chambers, while post-mortem studies have found extracellular accumulations of amyloid beta (A β) in senile plaques and intracellular neurofibrillary tangles as a result of accumulating hyperphosphorylated tau protein [4]. Current available therapy is based on symptomatic treatment or alleviation of disease symptoms and numerous studies of new effective drugs have failed [5]. Dehydroepiandrosterone (DHEA) and its sulfate (DHEAS), the most abundant steroids in human blood whose concentrations decrease significantly with aging [6], are involved in brain functions such as neural plasticity, learning, memory and behavior and have anti-inflammatory, antioxidant and anti-glucocorticoid effects [7]. Brain-derived neurotrophic factor (BDNF) is one of trophic factors that is involved in various aspects of neuronal development and differentiation, as well as plasticity and repair mechanisms [8]. BDNF promotes the survival and differentiation of neurons that are damaged in AD [9]. The purpose of this study is to investigate the neuroprotective potential and mechanisms of action of DHEA(S) and BDNF in dementia, through a combination of cellular, animal and human experiments. Currently, we are conducting *in vitro* experiments in which we study the protective effects of DHEA(S) and BDNF on isolated primary neurons from C57BL/6 mouse strain, treated with toxic A β -oligomers.

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TERAPIJSKI POTENCIJAL NEUROSTEROIDA I NEUROTROFINA U DEMENCIJI

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Demencija predstavlja sindrom progresivnog propadanja kognitivnih sposobnosti koji obično pogađa osobe starije životne dobi [1]. Obzirom na ubrzano starenje stanovništva i produljenje životnog vijeka, demencija će u budućnosti postati jedan od vodećih globalnih problema [2]. Alzheimerova bolest je najčešća progresivna i neizlječiva neurodegenerativna bolest [3]. Neuroslikovne tehnike su pokazale smanjenje volumena i težine mozga osoba oboljelih od ove bolesti, kao i proširenje lateralnih moždanih komora, dok su post-mortem studije utvrdile izvanstanične nakupine beta-amiloida (A β) u senilnim plakovima i unutarstanične neurofibrilarne snopiće kao posljedicu akumulacije hiperfosforiliranog proteina tau [4]. Trenutna terapija temelji se na simptomatskom liječenju, odnosno ublažavanju simptoma bolesti, a brojne studije novih učinkovitih lijekova za sada su bezuspješne [5]. Dehidroepiandrosteron (DHEA) i njegov sulfat (DHEAS), najzastupljeniji steroidi u krvi čovjeka čija koncentracija značajno opada sa starenjem [6], uključeni su u moždane funkcije poput neuralne plastičnosti, učenja, pamćenja i ponašanja te imaju antiupalno, antioksidativno i antiglukokortikoidno djelovanje [7]. Moždani neurotrofni čimbenik (BDNF) je neurotrofin uključen u različite aspekte razvoja neurona i diferencijacije te plastičnosti i mehanizama popravka [8]. BDNF promovira preživljenje i diferencijaciju neurona koji propadaju tijekom Alzheimerove bolesti [9]. Svrha ovog istraživanja je istražiti neuroprotektivni potencijal i mehanizme djelovanja DHEA(S)-a i BDNF-a u demenciji, kombinacijom staničnih i animalnih istraživanja te istraživanja na ispitanicima. Trenutno radimo *in vitro* istraživanje u kojem proučavamo protektivno djelovanje DHEA(S)-a i BDNF-a na izoliranim primarnim neuronima miša soja C57BL/6 koje tretiramo toksičnim A β -oligomerima.

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UNDERSTANDING COMPLEX TIME SERIES INTERACTIONS THROUGH THE LENS OF DEEP LEARNING

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The adaptation of deep learning models within safety-critical systems cannot rely only on good prediction performance but needs to provide interpretable and robust explanations for their decisions. When modeling complex sequences, attention mechanisms are regarded as the established approach to support deep neural networks with intrinsic interpretability [1-2]. In this presentation we will try to demonstrate how these models can not only achieve satisfying prediction performance, but they also can give explanation of their prediction. Using this explanation, we can understand how underlying data is generated [3]. Application of these models to physics and biophysics could help us understand problems that before were out of reach. Furthermore, physical approaches to the study of dynamical systems can provide new insights into the design of new architectures and concepts of deep learning models.

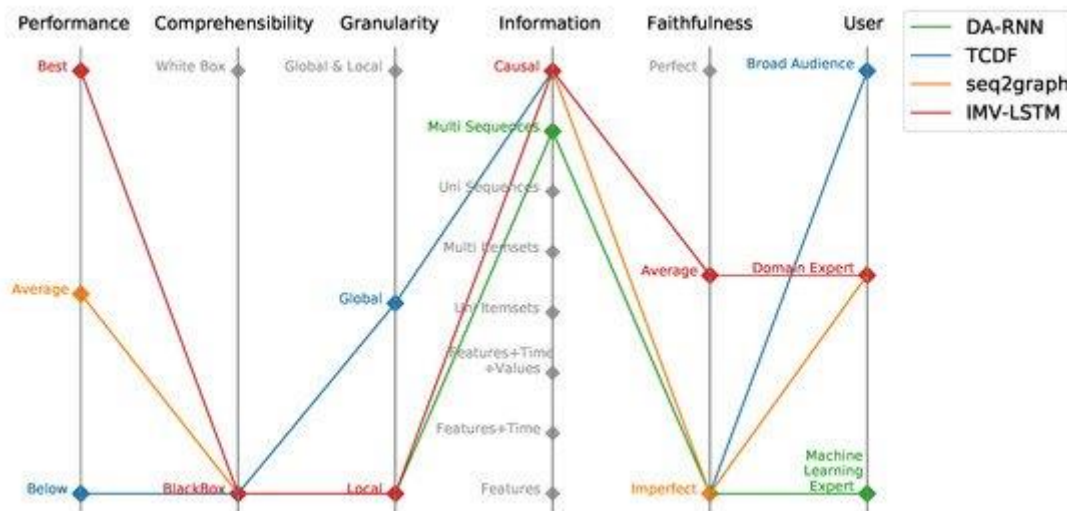


Figure 1. Performance-Explainability chart for considered models.

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RAZUMIJEVANJE SLOŽENIH INTERAKCIJA VREMENSKIH SERIJA KROZ LEĆU DUBOKOG UČENJA

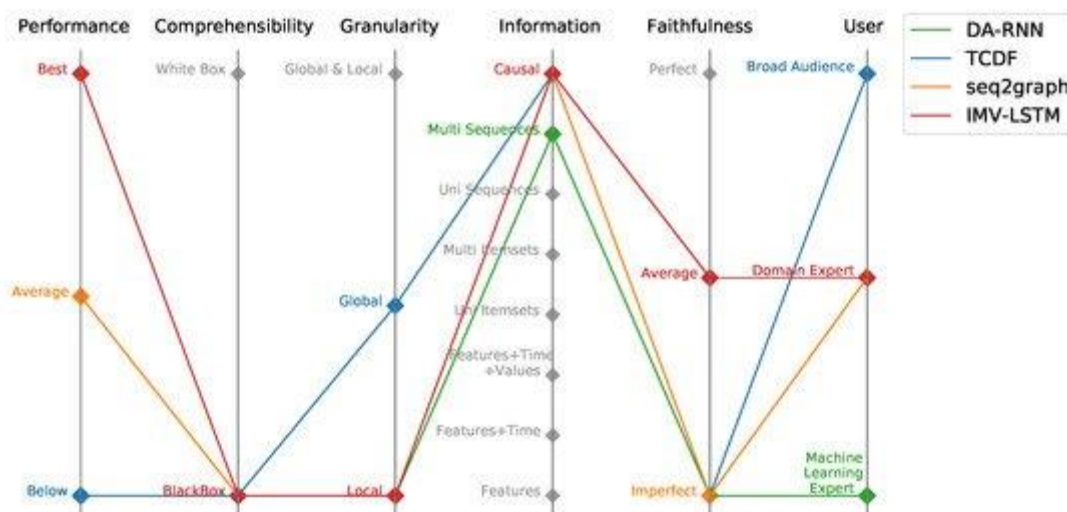
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Primjena modela dubokog učenja u sustavima kritične važnosti ne može se samo osloniti na njihove dobre prediktivne performanse, već modeli ujedno moraju pružiti razumljiva i robusna objašnjenja svojih odluka. Pri modeliranju složenih sekvenci, mehanizmi pažnje (attention) smatraju se jednim od osnovnih pristupa uspostavljanja dubokih neuronskih mreža s inheretnom interpretabilnosti [1-2]. U ovom izlaganju pokazat će se kako ovi modeli, osim što postižu zadovoljavajuće performanse predikcije, mogu dati i objašnjenje svog predviđanja. Koristeći ovo objašnjenje, možemo razumjeti dinamiku podataka[3]. Primjena ovih modela u fizici i biofizici mogla bi nam pomoći da razumijemo probleme koji su prije bili nedostižni. Nadalje, fizikalni pristupi proučavanja dinamičkih sustava mogu dati nove uvide u oblikovanje novih arhitektura i koncepata modela dubokog učenja.



Slika 1. Graf točnosti-objašnjivosti za analizirane modele

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PAIRING CORRELATIONS IN THE HEAVY-ION TRANSFER REACTION

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The pairing interaction induces nucleon-nucleon correlations that are essential in defining the properties of finite quantum many-body systems close to their ground states. A very specific probe of this pairing component in the nuclear interactions, which ties up nucleons in a highly correlated state, the nuclear Cooper pairs, is the two-nucleon transfer reactions. How pairing correlations can be probed in heavy-ion collisions, is still an open question. Several experiments have been performed in the past, searching for signatures mainly via extraction of the enhancement coefficients, defined as the ratio of the actual transfer cross section and the prediction of the model using uncorrelated states. Unfortunately, experimental evidence of these factors is marred by the fact that all existing studies involve reactions at energies higher than the Coulomb barrier, where the reaction mechanism is the result of the interplay between nuclear and Coulomb interactions. With the development of the new instrumentation, it nowadays became possible to measure the heavy-ion transfer reaction with high efficiency and good ion identification even at very low bombing energies where nuclei interact at large distances [1]. Multinucleon transfer reactions were measured in the $^{206}\text{Pb} + ^{118}\text{Sn}$ system at the INFN-LNL accelerator complex. The measurement has been performed in the inverse kinematic, by using the heavy ^{206}Pb beam, and by detecting the lighter reaction fragments in the magnetic spectrometer PRISMA. The total cross sections of different transfer channels will be extracted in an energy range from above to well below the Coulomb barrier (see figure 1 which shows the experimental yields of the identified neutron and proton transfer channels). By direct comparison of one- and two-nucleon transfer probabilities (one expects that the probability for the two-nucleon channel is proportional to the square of the single-particle one) we will extract the enhancement factors at the large distances. In the second stage, the experimental results will be compared with the state-of-the-art microscopical calculations which include correlations [2].

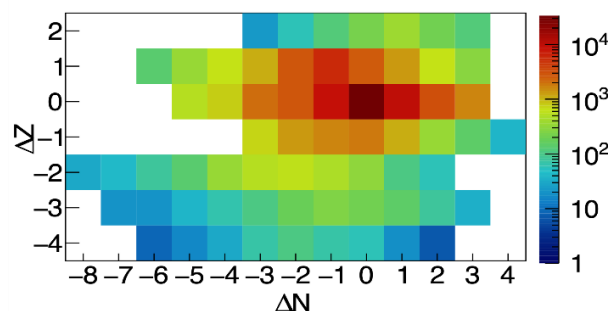


Figure 1. The figure shows the neutron and proton transfer yield.

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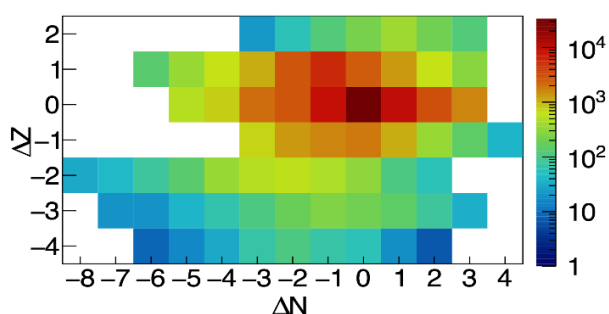
PRIJENOS KORELIRANIH PAROVA NUKLEONA U TEŠKO-IONSKIM REAKCIJAMA

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Sila sparivanja i s njome povezane korelacije između nukleona, koje vežu nukleone u jako korelirana stanja, tzv. Cooperove parove, definiraju svojstva konačnih kvantnih višestrukih sustava u blizini njihovih osnovnih stanja. Reakcije prijenosa dva nukleona jedan su od najboljih alata za istraživanje efekta sparivanja. Još je uvijek otvoreno pitanje kako se korelacije između nukleona mogu istražiti u sudarima teških iona. U prošlosti su izvedena mjerenja, u kojima su se proučavale korelacije preko izvedenosti koeficijenta pojačanja, definiranih kao omjer mjerenog udarnog presjeka prijenosa i onog predviđenog modelom za prijenos nezavisnih nukleona. Nažalost, eksperimentalni dokaz ovih efekata narušen je činjenicom da sve postojeće studije uključuju reakcije na energijama većim od kulonske barijere, gdje je mehanizam reakcije kompleksan zbog snažnog međudjelovanja nuklearne i kulonske sile. Razvojem novih mjernih instrumenata postalo je moguće mjeriti teško-ionske reakcije prijenosa s visokom učinkovitošću i dobrom identifikacijom iona čak i pri vrlo niskim energijama, gdje jezgre međudjeluju na velikim udaljenostima [1]. Reakcije prijenosa mnogo nukleona mjerene su u sustavu $^{206}\text{Pb} + ^{118}\text{Sn}$ u akceleratorском postrojenju INFN-LNL. Mjerenje je izvedeno u inverznoj kinematici, korištenjem snopa ^{206}Pb te detekcijom lakših fragmenata reakcije u magnetskom spektrometru PRISMA. Ukupni udarni presjeci različitih kanala prijenosa dobit će se u energetskom rasponu od iznad do znatno ispod kulonske barijere (vidi sliku 1 koja prikazuje eksperimentalne doprinose identificiranih kanala prijenos neutrona i protona). Izravnom usporedbom vjerojatnosti prijenosa jednog i dva nukleona (očekuje se da je vjerojatnost za dvonukleonski kanal proporcionalna kvadratu prijenosa jednog nukleona) izvući ćemo faktore pojačanja na velikim udaljenostima. U drugoj će se fazi eksperimentalni rezultati uspoređivati s najsuvremenijim mikroskopskim izračunima koji uključuju korelacije kako bi se izvrijednio efekt prijenosa koreliranog para nukleona [2].



Slika 1. Slika prikazuje doprinose neutronske i protonske kanala prijenosa.

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SEARCH FOR SMALL-AMPLITUDE LONG-PERIOD VARIABILITY

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We report the results of a search for small-amplitude, long-period ($P > 100$ days) variability in SDSS Stripe 82 region. The SDSS coverage of Stripe 82 [1] enables such a search because there are on average 20 observations per band in ugriz bands for about 1 million sources, collected over 6 years, with a competitive faint limit ($r \sim 22$) and precisely calibrated 1 - 2% photometry. We calculated periods for candidate variable sources in this data sample using Lomb - Scargle periodogram [2] and kept 3 highest periodogram peaks per gri filter as relevant. Only those with gri periods agreeing with each other to within 0.1% were later studied. We focus our search on periodic variability with periods $100 < P < 600$ days and uniform distribution of data points in phased light curves. We present recovered candidates with periodic variability and their periods that are in good agreement with other surveys such as ZTF [3].

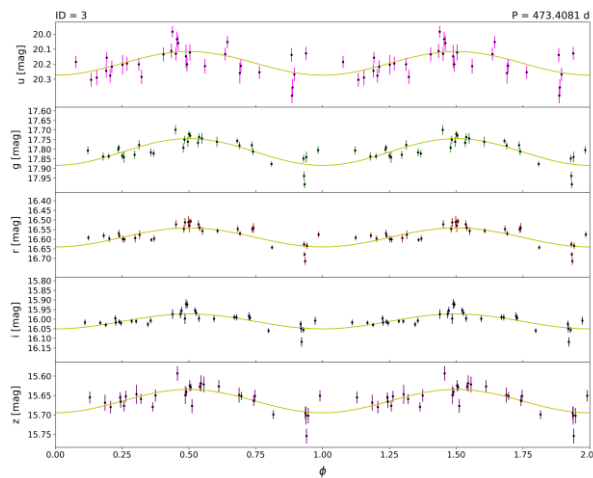


Figure 1. Light curve of a plausible pulsating variable source

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POTRAGA ZA PROMJENJIVIM IZVORIMA S MALIM AMPLITUDAMA I DUGIM PERIODIMA

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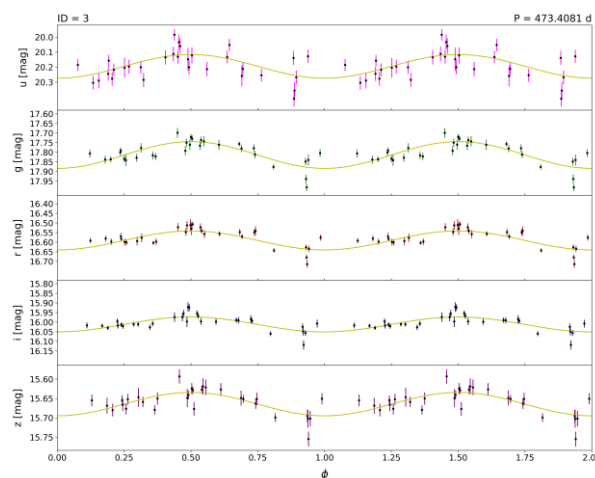
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Izveštavamo rezultate potrage za promjenjivim izvorima s malim amplitudama i dugim periodima ($P > 100$ dana) u SDSS Stripe 82 području. Takva je potraga moguća s SDSS-ovim snimanjem Stripe 82 područja [1] zato što za svaki od ugriz filtera postoji u prosjeku 20 opažanja za otprilike milijun izvora prikupljenih u periodu od 6 godina s granicom na magnitudu od $r \sim 22$ mag te precizno kalibriranom fotometrijom. Izračunali smo periode za kandidate promjenjivih izvora iz ovih podataka koristeći Lomb-Scargle periodogram [2] i zadržali tri najviša vrha u periodogramu za gri filtere. Samo oni kandidati čiji su se gri periodi slagali unutar 0.1% su kasnije analizirani. Fokusirali smo se na potragu za periodički promjenjivim izvorima s periodima između 100 i 600 dana te s jednoliko raspoređenim podacima u faznoj krivulji. Prezimiramo pronađene kandidate s periodičnim promjenama i njihove periode koji su u dobrom slaganju s podacima iz drugih promatranja neba kao što je to ZTF[3].



Slika 1. Krivulja sjaja jednog uvjerljivog promjenjivog izvora

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BLUMENBERG'S GENESIS OF THE AMBIGUITY OF HEAVEN

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Cosmology, especially as a pre-Copernican question of metaphysics, represented one of the central questions of thought throughout the history of the Western horizon: the relationship between metaphysics and cosmology was questioned with Copernicus major work on cosmology and especially in post-Copernican literature where the position of metaphysics alone was questioned. Following this, Hans Blumenberg (†1996) in his work "Genesis of the Copernican world" presented the history of cosmos thinking from ancient cosmology through the relationship of cosmos and tragedy to the postclassical idealistic development of science and cosmology within the field of natural science, encyclopedically presenting the results of his research.

The main hypothesis of this paper is reflected in proving how Blumenberg, by expounding the genesis of the Copernican world and presenting the thesis of the "ambiguity of heaven", actually sets out the preconditions for the development of modern science in the field of natural science thinking. Namely, modern science is in fact the result of a history of thought with all its essential principles on the path of clarity and certainty, and finally to the pinnacle of science which is theoretically manifested in exactness. The ultimate goal of the paper is to present the genesis of the ambiguity of heaven to modern cosmology and cosmological research in modern times, especially - on the example of Blumenberg's work.

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BLUMENBERGOVA GENEZA DVOSMISLENOSTI NEBA

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Kozmologija, poglavito kao predkopernikansko pitanje metafizike, predstavljala je jedno od centralnih pitanja mišljenja tijekom povijesti horizonta Zapada: sa Kopernikovim glavnim djelom o kozmologiji doveden je u pitanje odnos metafizike i kozmologije, a poglavito u postkopernikanskoj literaturi kada je doveden u pitanje i status same metafizike. Na tomu tragu, Hans Blumenberg (†1996) u svojem djelu „Geneza kopernikanskoga svijeta“ jeste predstavio povijest mišljenja kozmosa od antičke kozmologije kroz odnos kozmosa i tragedije do postklasičnoidealističkog razvoja znanosti i kozmologije unutar područja prirodne znanosti, a pri tomu enciklopedijski predočavajući rezultate svojih istraživanja.

Glavna hipoteza ovoga rada ogleda se u dokazivanju kako Blumenberg izlažući genezu kopernikanskoga svijeta i iznoseći tezu o „dvosmislenosti neba“ zapravo izlaže pretpostavke za razvoj moderne znanosti u području prirodno-znanstvenog mišljenja. Naime, suvremena znanost jeste zapravo rezultanta jedne povijesti mišljenja sa svim njenim bitnim zasadama ka putu jasnosti i izvjesnosti, pa na koncu do vrhunca znanosti koji se teorijski očituje u egzaktnosti. Krajnji cilj rada jeste - na primjeru djela Blumenberga - predočiti genezu dvosmislenosti neba do suvremene kozmologije i kozmoloških istraživanja u suvremenosti, napose.

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[3] Frederick Copleston, *Istorija filozofije*, BIGZ, Beograd, 1999.



RECENT WEAKENING IN THE WINTER ENSO TELECONNECTION OVER THE NORTH ATLANTIC-EUROPEAN REGION

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New observational evidence for variability of the atmospheric response to wintertime El Niño-Southern Oscillation (ENSO) is found. Using different approaches and datasets, a weakening in the recent ENSO teleconnection over the North Atlantic-European (NAE) region is demonstrated. Changes in both pattern and strength of the teleconnection indicate a turning point in the 1970s, with a shift from a response resembling the North Atlantic Oscillation (NAO) to an anomaly pattern with very weak or statistically non-significant values; and to nearly non-existent teleconnection in the most recent decades. Results show the importance of the background sea surface temperature (SST) state and sea-ice climatology having opposite effects in modulating the ENSO-NAE teleconnection. As indicated with targeted simulations, the recent change in the SST climatology in the Atlantic and Arctic has contributed to the weakening of the ENSO effect. The findings of this study can have implications on our understanding of the modulation of ENSO teleconnections and ENSO as a source of predictability in the NAE sector.

ACKNOWLEDGMENTS

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NEDAVNO SLABLJENJE DALJINSKE VEZE EL NIÑO-JUŽNE OSCILACIJE ZIMI NAD PODRUČJEM SJEVERNOG ATLANTIKA I EUROPE

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Na temelju izmjerenih podataka pokazana je varijabilnost atmosferskog odziva na El Niño-Južnu oscilaciju (ENSO – El Niño-Southern Oscillation) tijekom zime. Korištenjem različitih metoda i skupova podataka uočeno je slabljenje ENSO daljinske veze nad područjem sjevernog Atlantika i Europe (NAE – North Atlantic-Europe) u posljednjih 50-ak godina. Promjena snage i oblika prostornog polja ove daljinske veze ukazuje na prekretnicu oko 1970. godine kada se dogodio pomak od odziva nalik na Sjevernoatlantsku oscilaciju (NAO – North Atlantic Oscillation) do prostornog polja anomalija s vrlo slabim vrijednostima, dok je u posljednja dva desetljeća opaženo gotovo potpuno iščezavanje ove daljinske veze. Rezultati ukazuju na važnost suprotnih učinaka koje pozadinsko stanje površinske temperature mora i klimatologija morskog leda imaju na opaženu promjenu ENSO-NAE daljinske veze. Ciljane simulacije modelom opće cirkulacije atmosfere pokazuju da je nedavna promjena u klimatologiji površinskih temperatura mora u Atlantiku i Arktiku doprinijela slabljenju utjecaja ENSO događaja na promatrano područje. Rezultati ovog istraživanja korak su prema razumijevanju promjene ENSO daljinske veze te uloge ENSO događaja kao izvora prediktabilnosti na području sjevernog Atlantika i Europe.

ZAHVALE

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INVESTIGATION OF GAGG:CE SCINTILLATORS FOR APPLICATIONS IN GAMMA IMAGING SYSTEMS

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Inorganic scintillating crystals are most commonly used detector materials for medical imaging systems based on gamma detection, such as Positron Emission Tomography (PET). Their properties - high light yield, high stopping power and fast decay time, allow for particularly good energy and timing resolution of a detector. Today, the most used such material is Lutetium Yttrium Oxyorthosilicate (LYSO:Ce). Potential candidate for replacing LYSO:Ce is Gadolinium Aluminum Gallium Garnet doped with Cerium (GaGG:Ce). It is a relatively new material and compared to LYSO:Ce offers a significantly higher light output, along with its other promising characteristics, such as non-hygroscopicity and no intrinsic radioactivity. To investigate energy and coincidence time resolution of GaGG:Ce crystals coupled to Silicon Photomultipliers (SiPM), we assembled two detector modules. Each module consisted of 64 polished GaGG:Ce crystals, 3 mm x 3 mm x 20 mm in size, assembled in 8x8 matrices, with a 0.2 mm reflector material made of epoxy resin, resulting in a matrix pitch of 3.2 mm. In one module, crystals were coupled with SiPM using 1 mm thick silicon pad, and in the other, the optical coupling material was optical cement. Signals were obtained with a ²²Na source at various SiPM operating voltages, acquired and processed by TOFPET2 ASIC system. The mean energy resolution of 9.8 ± 0.6 % at 511 keV was observed, and the best energy resolution of a single crystal was 9.2%. Module coupled with optical cement performed better overall, achieving higher energy resolutions at every operating voltage, which suggests that the difference is driven by optical coupling. The coincidence time resolution achieved with the setup was 384 ± 33 ps, which is comparable to resolutions of the most commercial PET systems. GaGG:Ce crystals thus proved to be a promising candidate for further development of imaging systems, in particular ones based on Compton imaging, where the performance critically depends on energy. [1]

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ISPITIVANJE GAGG:CE SCINTILATORA ZA PRIMJENE U SUSTAVIMA ZA OPAŽANJE GAMA ZRAČENJA

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Anorganski scintilacijski kristali su najčešće korišteni materijal za izradu detektora korištenih u medicinskim sustavima za oslikavanje koji koriste gama zračenje, poput pozitronske emisijske tomografije (PET). Njihova svojstva – jak svjetlosni odgovor, visoka zaustavna snaga i kratko vrijeme relaksacije omogućuju izradu detektora koji imaju posebno dobru energijsku i vremensku rezoluciju. Danas najčešće korišteni takav materijal je lutecij itrij oksidot-silikat (LYSO:Ce). Potencijalni kandidat za zamjenu LYSO:Ce-a je gadolinij aluminij galij granat (GaGG:Ce). To je relativno novi materijal koji ima jači svjetlosni odgovor od LYSO:Ce-a, a te druge prednosti poput nehigroskopsnosti i nepostojeće intrinzične radioaktivnosti. Da bi proučili energijsku i vremensku rezoluciju GaGG:Ce kristala povezanih sa silicijskim fotomultiplikatorom (SiPM), izrađena su dva detektorska modula. Svaki od modula sastoji se od 64 polirana GaGG:Ce kristala, veličine 3 mm x 3 mm x 20 mm. Kristali su postavljeni u 8x8 matricu, sa 0.2 mm reflektirajućeg materijala od epoksi smole. U jednom modulu, kristali su povezani sa SiPM-om putem silikonskog jastučića debljine 1 mm, dok je u drugom modulu, optički vezivni materijal bio optički cement. Signali su dobiveni iz ²²Na izvora na različitim narinutim naponima na SiPM-u, te su prikupljeni i procesuirani pomoću TOFPET2 ASIC sustava. Opažena je srednja energijska rezolucija od 9.8 ± 0.6 % na 511 keV, dok je najbolja energijska rezolucija pojedinog kristala iznosila 9.2%. Drugi modul općenito je dao bolje rezultate, jer je postigao višu energijsku rezoluciju na svim promatranim naponima, što sugerira da razlika dolazi od optičkog veziva. Koincidenzijska vremenska rezolucija postignuta s ovim postavom bila je 384 ± 33 ps, što je usporedivo s rezolucijama većine komercijalnih PET sustava. GaGG:Ce se tako pokazao obećavajućim kandidatom za budući razvoj sustava za oslikavanje, posebno onih zasnovanih na komptonском oslikavanju, gdje učinak jako ovisi o energiji.[1]

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LASER COOLING OF ATOMS INSIDE AN OPTICAL RESONATOR USING A FREQUENCY COMB

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Mechanical action of laser radiation on atoms presents a central part of research in atomic physics for the last few decades. Radiation force is a foundation of laser cooling and trapping of atoms, which allowed the creation of dense and cold atomic samples [1]. Several Nobel prizes have been awarded for new discoveries and research in this area. Cold atomic samples allowed the creation of new states of matter, like Bose-Einstein Condensate (BEC) and degenerate Fermi gases, which set a foundation of a very prosperous and productive area of science. These samples form a basis of modern research in quantum technologies, including quantum simulators and sensors, as well as quantum information [2]. However, these standard cooling techniques are limited to a small number of atomic species, as their efficiency relies heavily on the structure of atomic energy levels, and the availability of laser radiation in the wavelength region needed for the cooling. Due to their complex energy structures and transitions in the deep UV region, cooling and trapping of molecules is still unavailable. Manipulation and control of molecules like oxygen or nitrogen would be of great interest in the research of ultracold chemistry.

It is our goal to investigate novel cooling techniques that would allow bypassing of the mentioned limitations. When placed inside an optical resonator (two mirrors of high reflectivity between which the light waves can bounce back and forth for a large number of cycles before leaking out), the interaction of atoms and the resonator light can show exciting new phenomena, including a cooling mechanism independent of the atomic energy structure. This mechanism could, in theory, be applied to any polarizable particle, as long as it acts as a scatterer of light [3].

The resonator cooling technique is not without limitations, which we want to investigate using a different type of laser. Instead of using a laser of continuous emission and of single emitted frequency in its spectrum, we plan to use a pulsed laser whose spectrum consists of a large number of equidistant modes – a so called frequency comb [4]. The modes of the frequency comb can be matched with the resonator modes, giving rise to new, still unexplored phenomena and possibilities of controlling and manipulation of atoms.

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LASERSKO HLAĐENJE ATOMA UNUTAR OPTIČKOG REZONATORA POMOĆU FREKVENTNOG ČEŠLJA

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Mehaničko djelovanje laserskog zračenja na atome predstavlja središnji dio istraživanja u području atomske fizike već zadnjih nekoliko desetljeća. Sila zračenja čini osnovu za lasersko hlađenje i zarobljavanje atoma, čime je omogućeno stvaranje gustih i hladnih atomskih uzoraka [1]. Nekoliko je Nobelovih nagrada dodjeljeno za istraživanja u ovome području. Hladni atomski uzorci omogućili su stvaranje novih stanja materije, kao što su Bose-Einsteinov kondenzat (BEC) i degenerirani Fermijevi plinovi, čime je uspostavljeno vrlo perspektivno i produktivno područje znanosti. Ti su uzorci temelj modernih istraživanja kvantnih tehnologija, koje uključuju kvantne simulatore i senzore, kao i kvantne informacije [2].

Ipak, standardne tehnike hlađenja ograničene su na malen broj atomskih vrsta jer je za njihovu efikasnost bitna struktura atomskih energijskih razina, kao i dostupnost laserskog zračenja u području valnih duljina potrebnih za hlađenje. Zbog njihove složene strukture i energijskih prijelaza u dubokom UV području, hlađenje i zarobljavanje molekula i dalje je nedostupno. Manipulacija i kontrola molekula poput kisika i dušika bili bi od velikog značaja u istraživanjima ultrahladne kemije.

Naš je cilj istražiti nove tehnike hlađenja koje bi omogućile nadilaženje navedenih ograničenja. Kada se atomi nalaze unutar optičkog rezonatora (dva visokorefleksna zrcala među kojima se svjetlosni valovi mogu odbijati i kružiti velik broj ciklusa prije nego se izgube), njihovo međudjelovanje sa svjetlošću unutar rezonatora dovodi do novih zanimljivih fenomena, a jedan od njih je mehanizam hlađenja neovisan o energijskoj strukturi atoma. Taj bi se mehanizam mogao, u teoriji, primjeniti na bilo koju polarizabilnu česticu, sve dok se ponaša kao raspršivač svjetlosti [3].

Tehnika hlađenja u rezonatoru nije bez ograničenja, koje želimo istražiti koristeći drugačiji tip lasera. Umjesto uobičajenih lasera kontinuiranog zračenja i jedne frekvencije u svom spektru, planiramo koristiti pulsni laser čiji se spektar sastoji od velikog broja jednako udaljenih modova – tzv. frekventni češalj [4]. Modovi frekventnog češlja mogu se uskladiti i vezati s modovima rezonatora, što dovodi do novih, neistraženih fenomena i mogućnosti kontrole i manipulacije atoma.

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SEISMIC SHAKING SCENARIOS FOR CITY OF ZAGREB, CROATIA

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The wider area around the city of Zagreb is one of the seismically most active regions in Croatia where many strong events have been reported in the past. Due to the large population and socio-economic importance of this region, advanced seismic hazard and risk assessment for this area is of high importance. And since the 1880, $M_w = 6.2$ earthquake is the most significant event, de-facto governing hazard assessment for the wider Zagreb area, our goal is to answer the ongoing question about its source location, but also explore effects of such an occurrence happening today. To facilitate this, we assemble a detailed 3D seismic model of the crust for the city of Zagreb and its surrounding region. We test the performance of the model by comparing the synthetic waveforms obtained using both newly defined 3D and a simple 1D model. We then simulate full broadband ground motions using a hybrid technique for the Zagreb March 22nd 2020, $M_w = 5.3$ event and four smaller ($3.0 < M_w < 5.0$) events. We compare these data with the observed seismograms and validate results by calculating goodness of fit scores. Since simulations using the 3D model and our methodology proved to be successful, we then compute synthetic seismograms for the 1880, $M_w = 6.2$ earthquake at two different hypocenter locations - North Medvednica and Kašina fault. We plot the shakemaps to establish if the main expected ground-motion features are well-represented with our approach. By comparing the estimated intensities with the observed data, we determine the more probable source location of the 1880 event. Lastly, due to the events that occurred in the Petrinja epicentral area at the end of 2020, we extend our 3D model to cover the area of interest. We will present the preliminary results of the simulation for the December 29th 2020 $M_w = 6.4$ earthquake, as well as our plans for further research.

ACKNOWLEDGMENTS

The authors would like to thank Prof. Marijan Herak and Robert W. Graves for the advice and help they provided us to conduct this research. For the simulation purposes, we used GP method which is implemented within SCEC Broadband Platform software system [1, 2] and the SPECFEM3D Cartesian wave propagation code [3]. This research was performed using the resources of computer cluster Isabella based in SRCE - University of Zagreb University Computing Centre. The seismograms used in the study were recorded by seismological stations of the Croatian Seismograph Network.

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SIMULACIJA POTRESNE TREŠNJE ZA GRAD ZAGREB, HRVATSKA

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Šire zagrebačko područje jedno je od seizmički najjaktivnijih regija u Hrvatskoj u kojem je zabilježeno mnogo snažnih potresa u prošlosti. S obzirom na velik broj stanovnika i ekonomski značaj ovog područja, napredne metode procjene seizmičkog hazarda i rizika od velike su važnosti. Kako je potres $M_w=6.2$ iz 1880. jedan od najvažnijih potresa koji iznimno utječe na procjenu seizmičkog hazarda šireg zagrebačkog područja, cilj ovoga rada bio je odgovoriti na pitanje o lokaciji njegovog izvora te istražiti učinke kada bi se ovakva pojava dogodila danas. U svrhu toga sastavljen je detaljan 3D seizmički model kore za grad Zagreb i okolno područje. Primjenjivost modela u simulacijama testirana je usporedbom sintetičkih seizmograma dobivenih novim 3D modelom te jednostavnim 1D modelom. Nadalje, napravljena je simulacija širakopojasnih zapisa gibanja tla korištenjem hibridne metode za zagrebački potres iz 22. ožujka 2020., $M_w = 5.3$ te četiri manja ($3.0 < M_w < 5.0$) potresa. Provjera rezultata provedena je usporedbom mjerenih podataka sa sintetičkim seizmogramima te računanjem vrijednosti mjere kvalitete sličnosti. S obzirom da su se rezultati simulacija provedenih korištenjem 3D modela i metode pokazali uspješnim, izračunati su i sintetički seizmogrami za potres iz 1880., $M_w = 6.2$ na dvije različite lokacije hipocentra - Sjeverni rubni medvednički i Kašinski rasjed. Kako bi se utvrdilo jesu li glavne očekivane značajke gibanja tla dobro simulirane, nacrtane su karte trešnje te usporedbom procijenjenih intenziteta s opaženim podatcima, određena je lokacija izvora potresa iz 1880. Uslijed događanja koja su zadesila petrinjsko epicentralno područje krajem 2020., naš 3D model proširen je tako da obuhvaća područje od interesa. Preliminarni rezultati simulacije potresa 29. prosinca 2020., $M_w = 6.4$, te planovi za daljanje istraživanje, također će biti predstavljeni u ovom izlaganju.

ZAHVALE

Autori zahvaljuju prof. Marijanu Heraku i Robertu W. Graves-u na savjetima i pomoći koju su nam pružili za provedbu ovog istraživanja. U svrhu provedbe simulacija korištena je GP metoda dostupna unutar SCEC Broadband Platform softverskog sustava [1, 2] te SPECFEM3D Cartesian kod [3]. U okviru izrade ovog istraživanja korišteni su resursi računalnog klastera Isabella koji održava Sveučilišni računski centar Sveučilišta u Zagrebu (Srce). Seizmogrami korišteni u ovome istraživanju zabilježeni su seizmološkim postajama Hrvatske seizmografske mreže.

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ESTIMATING CONTRIBUTION OF HIGH-FREQUENCY SEA-LEVEL OSCILLATIONS TO THE EXTREME SEA LEVELS IN THE ADRIATIC SEA

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Extreme sea levels are known to hit the Adriatic Sea and to occasionally cause floods that produce severe material damage. Whereas the contribution of longer-period ($T > 2$ h) sea-level oscillations to the phenomena has been well researched, the contribution of the shorter period ($T < 2$ h) oscillations is yet to be determined. With this aim, data of 1-min sampling resolution were collected for 20 tide gauges, 10 located at the Italian (north and west) and 10 at the Croatian (east) Adriatic coast. Analyses were done on time series of 3 to 15 years length, with the latest data coming from 2020, and with longer data series available for the Croatian coast. Sea level data were thoroughly checked, and spurious data were removed.

For each station, extreme sea levels were defined as events during which sea level surpasses its 99.9 percentile value. The contribution of short-period oscillations to extremes was then estimated from corresponding high-frequency ($T < 2$ h) series. Additionally, for four Croatian tide gauge stations (Rovinj, Bakar, Split, and Dubrovnik), for period of 1956-2015, extreme sea levels were also determined from the hourly sea level time series, with the contribution of short-period oscillations visually estimated from the original tide gauge charts.

Spatial and temporal distribution of contribution of short-period sea-level oscillations to the extreme sea level in the Adriatic were estimated. It was shown that short-period sea-level oscillation can significantly contribute to the overall extremes and should be considered when estimating flooding levels.



PROCJENA DOPRINOSA VISOKOFREKVENTNIH OSCILACIJA RAZINE MORA EKSTREMNIM RAZINAMA U JADRANSKOM MORU

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Poznato je da ekstremne razine mora pogađaju Jadransko more i povremeno uzrokuju poplave koje proizvode veliku materijalnu štetu. Doprinos dugo-periodičkih razina mora ($T > 2$ h) je dobro istražen, dok se doprinos kratko-periodičkih oscilacija ($T < 2$ h) ukupnoj razini mora tek treba utvrditi. S tim ciljem prikupljeni su 1-minutni podaci razine mora mjereni na 20 mareografskih postaja u Jadranskom moru. Od ukupnog broja postaja, 10 je smješteno na talijanskoj (sjevernoj i zapadnoj), a 10 na hrvatskoj (istočnoj) obali Jadranskog mora. Analize su izvršene na vremenskim nizovima duljine od 3 do 15 godina, s tim da su najnoviji podaci iz 2020. godine. Duži nizovi podataka dostupni su za hrvatsku obalu. Podaci o razini mora temeljito su provjereni, a loši podaci su uklonjeni.

Ekstremne razine mora definirane su za svaku postaju kao razdoblja tijekom kojih razina mora prelazi 99,9 percentil. Doprinosi kratko periodičkih oscilacija ekstremima procijenjeni su iz odgovarajućih visoko-frekventnih nizova ($T < 2$ h). Uz to, za četiri mjerne postaje (Rovinj, Bakar, Split i Dubrovnik), za razdoblje od 1956. do 2015. godine, ekstremne razine mora utvrđene su i iz satnih vremenskih nizova razine mora, pri čemu je doprinos kratko-periodičkih oscilacija dodatno određen iz izvornih mareografa.

Procijenjena je prostorna i vremenska raspodjela doprinosa kratko-periodičkih oscilacija razine mora ekstremnoj razini mora na Jadranu. Pokazano je da kratko-periodičke oscilacije razine mora mogu značajno pridonijeti ukupnim ekstremima i treba ih uzeti u obzir pri procjeni razine poplava.



AGN LUMINOSITY FUNCTIONS AND THEIR EVOLUTION

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We study the space density evolution of active galactic nuclei (AGN) through cosmic time by constructing their luminosity functions. An emphasis is placed on the difference in evolution between the high and the low luminosity end of the sample. The luminosity functions were constrained using the parametric approach via the likelihood function. The fitting of the model parameters was done in a Bayesian framework, using the Dynesty program package [1]. In order to test the methodology, we first used it on simulated data. It can be seen that the estimation of luminosity functions from simulated data works well. We also show the benefits of using multiple surveys of varying depth and area to constrain the luminosity functions better. We discuss the application of this method onto real observed astronomical data, with emphasis on the XXL-Survey [2].

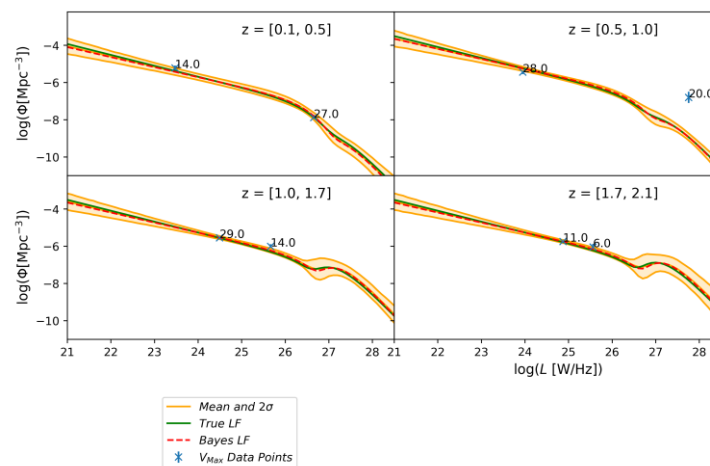


Figure 1. Luminosity functions re-created from simulated data.

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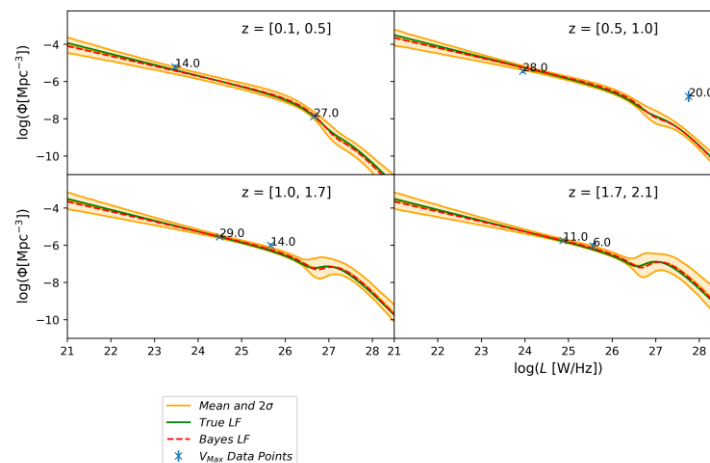
FUNKCIJE LUMINOZITETA AKTIVNIH GALAKTIČKIH JEZGRI I NJIHOVA EVOLUCIJA

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Istražujemo evoluciju u gustoći aktivnih galaktičkih jezgri kroz kozmičko vrijeme konstrukcijom njihovih funkcija luminoziteta. Pritom je naglasak na razlici u evoluciji visoko i nisko luminozitetnih izvora unutar pojedinoga uzorka. Funkcije luminoziteta određene su putem parametarske metode, koristeći funkciju vjerojatnosti (*engl.* likelihood function). Prilagodba modela na podatke vršila se Bayesovom metodom putem Dynesty programskog paketa [1]. Kako bismo bolje utvrdili metodologiju, koristili smo simulirane podatke. Određivanje funkcija luminoziteta na simuliranim podacima daje dobre rezultate. Također je vidljivo da korištenje većeg broja istraživanja raznih dubina i površina ima povoljan efekt na ograničavanje funkcija luminoziteta. Diskutiramo i primjenu ove metodologije na prave opažene astronomske podatke, s naglaskom na XXL-Istraživanju [2].



Slika 1. Funkcije luminoziteta konstruirane na simuliranim podacima.

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DEPOSITION OF THIN ALUMINA FILMS CONTAINING 3D ORDERED NETWORK OF NANOPORES ON DIFFERENT SUBSTRATES

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Self-supporting thin films containing nanopores are very promising materials to be used for multiple applications. Here we present a method for the production of nanomembranes containing a 3D ordered network of nanopores in an alumina matrix, with a diameter of about 1 nm, and body centered tetragonal structure of the network nodes [1]. The material is produced by magnetron sputtering deposition of a 3D ordered network of Ge nanowires in alumina matrix, followed by a specific annealing process resulting in the evaporation of Ge. We demonstrate that the films can be easily grown on different substrates, including porous ones. We believe that these films have a potential for applications in the fields of filtration, separation and sensing.

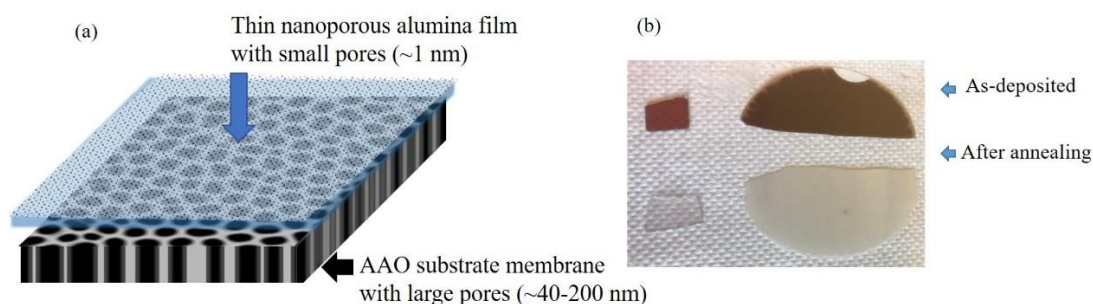


Figure 1. (a) Scheme of the material structure. Thin nanoporous alumina film (pore size ~ 1 nm) is deposited on the porous anodic aluminum oxide (AAO) substrate with large pores (40-200 nm); (b) Image of the prepared thin films deposited on porous AAO (right) and quartz (left) before and after annealing. The change in the color is due to the evaporation of Ge out of the film during annealing.

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DEPOZICIJA TANKIH FILMOVA SA UREĐENOM 3D MREŽOM NANOPORA NA RAZLIČITE SUPSTRATE

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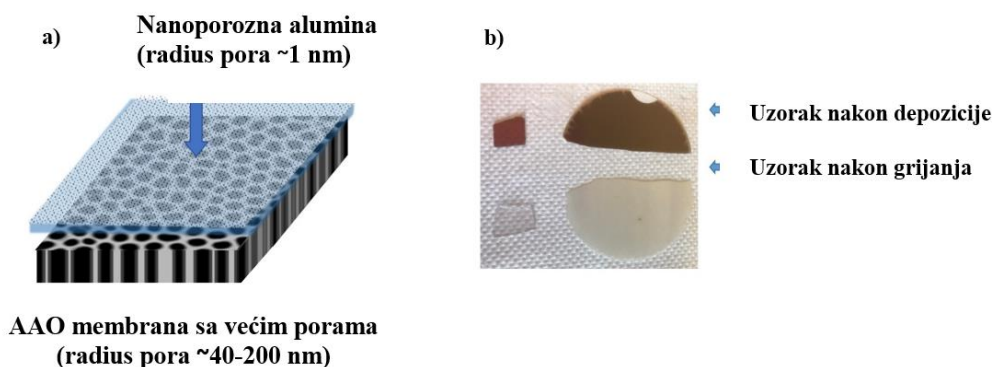
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U ovom je radu predstavljena metoda dobivanja prostorno uređene mreže nanopora u alumini. Promjer dobivenih nanopora u alumini je oko 1 nm, a čvorišta mreže uređuju se tako da formiraju kvazi BCT rešetku [1]. Tanki filmovi dobiveni su metodom magnetronskog raspršenja. Kao supstrat korišten je kristalni silicij, kvarc i komercijalno dostupna porozna alumina čiji je promjer pora u rasponu 20-200 nm. Nakon grijanja u niskom vakuumu germanij izlazi iz uzoraka. Ovakvi porozni tanki filmovi mogli bi se koristiti u različite svrhe u kojima je poželjan manji radijus pora kao što su različiti kemijski senzori ili za nanofiltraciju.



Slika 1. (a) Shematski prikaz strukture tankog filma na poroznom supstratu. Promjer pora u tankom filmu je oko 1 nm dok je promjer pora poroznog substrata 20-200 nm,; (b) Slike uzoraka nakon depozicije i nakon grijanja. Filmovi su smeđe obojeni nakon depozicije zbog Ge prisutnog u njima. Nakon grijanja uzorci su transparentni zbog izlaske Ge iz uzoraka.

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EXPLORING CLUSTERING IN NEUTRON RICH BERYLLIUM ISOTOPES BY REACTIONS OF ${}^9\text{Li}$ BEAM ON LiF TARGET

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Light nuclei, due to small number of relevant degrees of freedom, present excellent framework in which to study the basic principles of nuclear interaction and structure: from single-particle dynamics and correlations to the appearance of clustering and molecular like structures in the nuclei. A promising way to study these structural phenomena, even in neutron-rich light nuclei, is to explore the sensitivity of transfer reactions to the structure of the nuclei in the entrance channel. Evolution of the clustering phenomena with the addition of neutrons in beryllium isotopes is an important benchmark to our understanding of the nuclear structure [1,2]: from the alpha-alpha two-center clustering in ${}^8\text{Be}$ to the molecular like alpha-Xn-alpha structure in ${}^{10}\text{Be}$ and ${}^{12}\text{Be}$ [3,4,5]. With the aim to study these structures experiment S1620 was performed at ISAC-II facility at TRIUMF, using the ${}^9\text{Li}$ beam and LiF target. Many interesting decay channels of the neutron-rich light nuclei are populated in this reaction, the ${}^{12}\text{Be}$ being preeminent as it could be produced by triton transfer to the ${}^9\text{Li}$ beam. Large solid angle silicon detector array, comprised of six wedge shaped telescopes covering 16-48 degrees in polar angle had been used. Results of the observed helium-helium cluster decays of the ${}^{10,12}\text{Be}$ excited states will be presented, with the indications of possible existence of the exotic cluster states in these isotopes.

ACKNOWLEDGMENTS

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ISTRAŽIVANJE KLASTERSKE GRAĐE NEUTRONSKI BOGATIH IZOTOPA BERILIJA REAKCIJAMA SNOPA ${}^9\text{Li}$ NA LiF METI

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Lake jezgre, zbog malog broja relevantnih stupnjeva slobode, predstavljaju odličan sistem za proučavanje osnovnih principa nuklearne interakcije i strukture: od jedno-nukleonske dinamike i više-nukleonskih korelacija, preko pojave klasteriranja i evolucije samog efekta s porastom broja neutrona u jezgri, do egzotičnih struktura kao što su nuklearne molekule. Obećavajuća metoda za proučavanje navedenih strukturnih fenomena je iskorištavanje osjetljivosti reakcija prijenosa na strukturu jezgara u ulaznom kanalu. Evolucija efekta klasteriranja povećanjem broja neutrona u izotopima berilija važan je test našeg razumijevanja nuklearne strukture [1,2]: od alfa-alfa klusterske strukture s dva centra u ${}^8\text{Be}$ do molekulske alfa-Xn-alfa strukture u ${}^{10}\text{Be}$ i ${}^{12}\text{Be}$ [3,4,5]. S ciljem proučavanja ovakvih strukturnih fenomena izveden je eksperiment S1620 na akceleratorском postrojenju ISAC-II na TRIUMF-u, koristeći neutronske bogati snop ${}^9\text{Li}$ na LiF meti. Mnogi su interesantni kanali raspada neutronske bogatih lakih jezgara proizvedeni u ovoj reakciji, među kojima je raspad ${}^{12}\text{Be}$ najznačajniji, a mogao se proizvesti prijenosom tritona na ${}^9\text{Li}$ snop. Korištenjem detektorskog postava velikog kutnog raspona, sastavljenog od šest teleskopa od po dva silicijska detektora klinastog oblika, postignuto je pokrivanje od 16-48 stupnjeva u polarnom kutu. Rezultati opaženih klusterskih raspada helij-helij za ${}^{10,12}\text{Be}$ biti će prezentirani, te ukazuju na moguće postojanje egzotičnih klusterskih stanja u tim izotopima.

ZAHVALE

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THE IMPACT OF POPULATION POLICIES ON FAMILY SIZE IN SERBIA IN THE 21st CENTURY

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The modern family consists of the nuclear family, which is composed of parents and their children [1]. The average size of the family in Serbia is 2.9 members [2]. This research aims to determine whether the measures adopted in the Strategy for Birth Incentives in 2008 [3] influenced the family size in Serbia, and to what extent. Given the fact that the population replacement required that a woman gives birth to at least one female child during their reproductive period and the net reproduction rate is equal to one [4]. To ensure the replacement level, it is necessary that a woman during her reproductive period gives birth to 2.1 children [5]. Serbia is below that minimum with a total fertility rate of 1.46 children per woman [6], which indicates that the implementation of the adopted strategies (2008, 2018) is exceptionally important for improving the demographic picture in Serbia. However, the measures adopted by the Birth Incentive Strategy in 2008 were not significantly contributing to the regulation of family size in Serbia. The Strategy for Encouraging Birth was adopted in 2008 and there was no time to achieve the goals until 2011 when the last Census in the Republic of Serbia was conducted.

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UTJECAJ POPULACIJSKE POLITIKE NA VELIČINU OBITELJI U SRBIJI U 21. STOLJEĆU

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Moderna obitelj sastoji se od nuklearne obitelji koju čine roditelji i njihova djeca [1]. Veličina obitelji u Srbiji u prosjeku iznosi 2,9 članova [2]. Cilj rada i istraživanja je utvrditi jesu li mjere usvojene Strategijom poticanja rađanja 2008. godine [3] utjecale na regulaciju veličine obitelji u Srbiji i u kojoj mjeri. S obzirom na činjenicu da je za jednostavnu smjenu generacija potrebno da jedna žena rodi barem jedno žensko dijete tijekom reproduktivnog razdoblja, tj. da neto stopa reprodukcije bude jednaka jedinici [4]. Da bi se osigurala razina zamjene, potrebno je da žena tijekom reproduktivnog razdoblja rodi 2,1 djece [5]. Srbija je ispod tog minimuma s ukupnom stopom plodnosti od 1,46 djece po ženi [6], što ukazuje da je provedba usvojenih strategija (2008., 2018.) izuzetno važna za poboljšanje demografske slike u Srbiji. Međutim, mjere usvojene Strategijom poticanja rađanja 2008. godine nisu značajno doprinijele regulaciji veličine obitelji u Srbiji. Kako je Strategija poticanja rađanja usvojena tek 2008. godine, nije bilo vremena za postizanje ciljeva do 2011. godine, kada je održan posljednji popis stanovništva u Republici Srbiji.

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ADAPTATION OF FOREIGN STUDENTS TOWARD THE SERBIAN SYLLABUS

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In Serbian education system primary education covers the period of compulsory education (it lasts 8 years). After eight years of elementary school, students start three or four year secondary schools [1]. Foreign students' adaptation to the new education environment was covered in some studies relating to sociocultural and psychological adaptation of students [2,3] and contingency of the academic progress and social adaptation. Some studies deal with such questions as the elaboration of models of friendly behavior among foreign students [3,4], cross-cultural adaptation of students [3,5] as well as with the questions of a cultural shock and stress that foreign students experience while changing the education environment [3,6]. This article aim is to show the adaptation of foreign students toward the Serbian syllabus. Views of foreign students are of remarkable importance for this paper, so the survey was used as an instrument. Because of global pandemic COVID-19 survey was also conducted online. The survey was conducted in one international school in Novi Sad. The research was conducted during school year 2020/2021. The sample was random. After the completion of the field survey and online survey, there were a total number of 41 properly filled in surveys. The field survey was completed among preschool and elementary school students and online survey among secondary school students. Most of the respondents have between 10 and 14 years and their first language is English. Also, 24.5% of students consider Serbian syllabus very easy. Most of the respondents are bilingual and multilingual. Students in the survey have more support from teachers than from parents adapting to the Serbian syllabus. According to respondents the Serbian syllabus is not harder, and it's not too extensive than the one in their country which makes their adaptation much easier. Also, In Serbia foreign students have more written than verbal knowledge testing and they don't find Serbian grading system hard. Students in a survey consider their new teachers a big advantage, while written and verbal knowledge testing big disadvantage.

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LATE MIOCENE FLOURISHING OF FRESHWATER COCKLES (BIVALVIA: CARDIIDAE) IN THE PANNONIAN LAKE

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The Pannonian Lake existed for about 7 million years, from the end of the Middle Miocene to the beginning of the Early Pliocene, and during that geological time it changed significantly geographically and biologically [1]. It was formed by the closure of the Paratethys Sea and its gradual change in salinity, as a result of which many stenohaline organisms became extinct, and euryhaline organisms, including cockles, began to develop rapidly and their number and species diversity increased [2]. Most lake mollusks experience their maximum during the Late Miocene. Croatian Natural History Museum stores a rich collection of Miocene and Pliocene freshwater mollusks, including over 2000 specimens of freshwater cockles, mostly members of the Lymnocardiinae subfamily. About 100 species have been determined, and the first results indicate that the largest number originates from the youngest Miocene Rhomboidea deposits [3,4]. Species that stand out with the number of specimens are *Lymnocardium mayeri* (245), *L. riegeli* (202), *L. rogenhoferi* (110), *L. diprosopum* (94) and *Pseudocatillus simplex* (136). Due to the fragmentation and shell deficiencies, 97 specimens were determined at the genus level. The main findings of these fossil shells are located around the hills in Northern Croatia, which during the Late Miocene represented the islands in the lake. They inhabited a part of the neritic zone, which indicates the coastline relief that can be traced along the sites and which has changed over time. A big difference in the number of freshwater cockles through different stages of the existence of the Pannonian Lake in the wider area can be correlated with the salinity changes and their ability to adapt to new environments [5].

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KASNOMIOCENSKI PROCVAT SLATKOVODNIH SRČANKI (BIVALVIA: CARDIIDAE) U PANONSKOM JEZERU

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Panonsko jezero postojalo je oko 7 milijuna godina, od kraja srednjeg miocena do početka ranog pliocena i kroz to se geološko vrijeme značajno geografski i biološki mijenjalo [1]. Nastalo je zatvaranjem Paratethys mora i njegovim postupnim oslađivanjem, zbog čega mnogi stenohalini organizmi izumiru, a eurihalini organizmi, među kojima i srčanke, započinju ubrzani razvoj i njihov se broj i raznolikost vrsta povećava [2]. Većina jezerskih mekušaca doživljava svoj maksimum tijekom mlađeg miocena. U fundusu Hrvatskoga prirodoslovnog muzeja čuva se bogata zbirka miocenskih i pliocenskih slatkovodnih mekušaca, među kojima i preko 2000 primjeraka slatkovodnih srčanki, najviše pripadnika podporodice Lymnocardiinae. Determinirano je oko 100 vrsta, a prvi rezultati ukazuju da najveći broj potječe iz najmlađih miocenskih Rhomboidea naslaga [3,4]. Po broju primjeraka ističu se vrste *Lymnocardium mayeri* (245), *L. riegeli* (202), *L. rogenhoferi* (110), *L. diprosopum* (94) i *Pseudocatillus simplex* (136). Zbog fragmentiranosti i nedostataka elemenata ljušture, 97 primjeraka određeno je na razini roda. Glavna nalazišta ovih školjkaša smještena su oko uzvisina na prostoru sjeverne Hrvatske, koja su u mlađem miocenu predstavljala otoke u jezeru. Oni su naseljavali dio neritičke zone, što ukazuje na reljef obalne linije, koji se može pratiti uz nalazišta i koji se s vremenom mijenjao. Velika razlika u brojnosti slatkovodnih srčanki kroz različite etape postojanja Panonskog jezera na širem prostoru može se korelirati s promjenom saliniteta i njihovom mogućnošću prilagodbe novonastalim okolišima [5].

ZAHVALE

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MOBILITY OF OXYANIONS FROM AN AGED INDUSTRIAL WASTE IN CROATIA (ŠTRMAC, ISTRIA)

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Leaching of trace elements from industrial waste is the main mechanism of contaminant transport from waste to the environment [1]. Oxyanions (As, Cr, Mo, Se, S, V) are of particular concern if the waste is alkaline as they are the most mobile in those conditions [2]. An aged alkaline waste, located in Istria (Croatia), was generated in the second half of the 20th century during Raša coal combustion [3] and has caused pollution of the local area [4]. Aged waste has different characteristics compared to the waste disposed of [5]. Therefore, leaching of oxyanions was tested on the surface samples that have signs of early pedogenesis. Considering that several extract concentrations of analyzed oxyanions were above the regulatory limit, the waste still poses a threat to the local area, even decades after disposal (fig.1.). The mineralogical analysis showed that mineral transformation occurred due to exposure to environmental conditions, changing the mobility pattern of several elements.

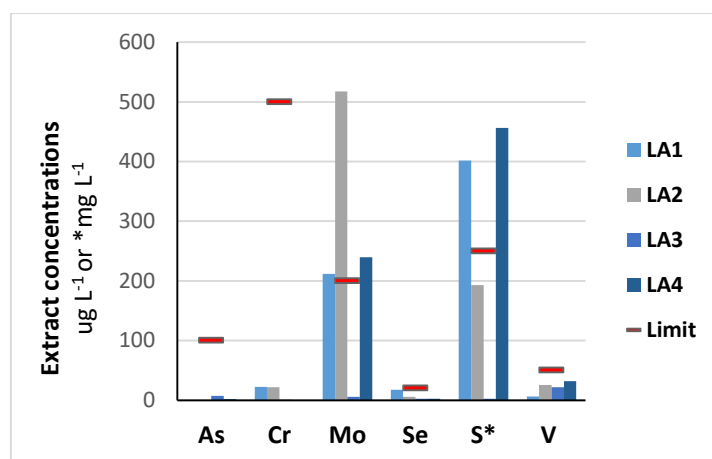


Figure 1. Extract concentrations of analyzed oxyanions from different samples.

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MOBILNOST OKSIANIONA IZ OSTARJELOG INDUSTRIJSKOG ODLAGALIŠTA U HRVATSKOJ (ŠTRMAC, ISTRA)

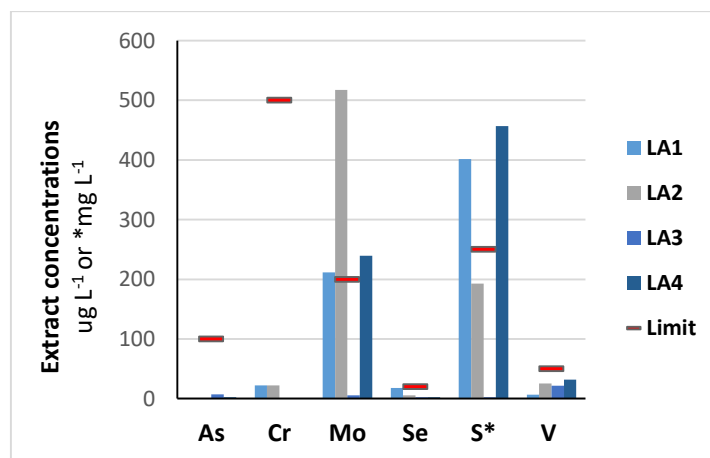
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Procjedne vode glavni su mehanizam transporta zagađivala iz otpada u okoliš [1]. Oksianioni (As, Cr, Mo, Se, S, V) su najmobilniji u alkalnim uvjetima te ih treba ispitati ako je otpad alkalni [2]. Ostarjeli alkalni otpad nalazi se u Istri (Hrvatska), a nastao je u drugoj polovici 20. stoljeća tijekom izgaranja Raškog ugljena [3]. Prijašnja istraživanja pokazala su da je taj otpad jedan od izvora onečišćenja lokalnog područja [4]. Ostarjeli otpad ima različite karakteristike u odnosu na otpad koji se odložio [5]. Zato je ispiranje oksianiona testirano na površinskim uzorcima koji pokazuju znakove rane pedogeneze. Koncentracije pojedinih elemenata bile su iznad regulatorne granice, što znači da je otpad i dalje prijetnja lokalnom okolišu, čak i desetljećima nakon odlaganja (sl.1). Provedena mineraloška analiza ukazuje da je došlo do transformacije minerala zbog izloženosti otpada okolišnim uvjetima, što je utjecalo na pokretljivost elemenata.



Slika 1. Koncentracije elemenata u ekstraktima različitih uzoraka.

ZAHVALE

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SUBMERGED LANDSCAPE OF THE PROKLJAN LAKE

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The Krka River located on the Eastern Adriatic shore (central Dalmatia) is typical karstic river that creates about 24 km long estuary. The Holocene transgression formed this very stratified estuary that covers the area of two wider parts, Šibenik Channel and the Prokljan Lake, up to the relatively narrow part of an ancient river valley, the Skradinski buk waterfall [1]. A multiproxy approach based on high resolution acoustic methods, including multibeam echosounder (MBES), side scan sonar (SSS) and sub-bottom profiler (SBP), coupled with piston sediment cores and bottom samples, were used to provide ground truth data, interpret the geomorphological evolution and reconstruct 6,2 km² of submerged landscape of the Prokljan Lake and upper part of the estuary. A detailed high resolution bathymetry and backscatter maps were made over a depth range from 5 m b.s.l. in the northern part of estuary to 25 m b.s.l. in the southern part of the estuary. The bathymetry and side scan sonar indicate that the submerged paleolandscape consists of tuffa barriers (partly buried by estuarine sediments), waterfalls and small lakes that are similar to the recent barriers of Skradinski buk waterfall and of carbonate mounds and channels. The submerged tuffa barriers can be more than 15 m high and began forming during early Holocene or even during the transition from the Pleistocene into Holocene. The geophysical survey consisted of a total of 70 km of seismic profiles, including 5 long (4-9 m long) piston sediment cores in the lake area. Three sedimentary units were generally identified: fluvial, brackish and marine (spaning up to 9000 y BP), up to thickness of 15 m. Ground-truth data were provided in form of 36 grab samples and seafloor images. Sediment samples were analyzed for grain size, magnetic susceptibility, bulk density, carbon and nitrogen concentrations and mineralogical XRD analysis. The flooding of the river canyons (Gudača River and Krka river) due to sea level rise, in Prokljan lake started at 9300 y BP and the estuary was formed at approx. 7500 BP. This multiproxy approach will enable a better understanding of the paleoenvironmental evolution and predicting the estuary response to future climate change and sea level rise.

ACKNOWLEDGMENTS

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POTOPLJENI KRAJOLIK PROKLJANSKOG JEZERA

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Rijeka Krka je tipična krška rijeka smještena na istočnoj obali Jadranskog mora (sredšnja Dalmacija) s estuarijem dužine otprilike 24 km. Vrlo stratificirani estuarij rijeke Krke nastao je poplavlivanjem tijekom holocenske transgresije, a obuhvaća 2 šira područja, Šibenski kanal i Prokljansko jezero, te relativno uže područje nekadašnjeg korita sve do Skradinskog buka [1]. Koristeći multidisciplinarni pristup istraživanja koji obuhvaća visokorezolucijske akustične metode, poput dubinomjera višestrukog snopa (MBES), panoramskog dubinomjera (SSS) i geološkog dubinomjera (SBP), ali i jezgre sedimentata te površinske uzorke, omogućit će kartiranje morskog dna, interpretaciju geomorfološke evolucije i rekonstrukciju 6,2 km² potopljenog krajolika Prokljanskog jezera i gornjeg dijela estuarija. Batimetrijska karta i karta povratnog raspršenja ("backscatter") obuhvaćaju područja dubine od 5 m u sjevernom dijelu estuarija, pa do 25 m dubine u južnom dijelu estuarija. Batimetrija te snimke panoramskog dubinomjera ukazuju na prisutnost potopljenih sedrenih barijera (djelomično zatrpane sedimentima estuarija) slapova i malih jezerca koji su vrlo slični recentnim barijerama Skradinskog buka te na karbonatne bioherme ("mounds") i riječne kanale. Potopljene sedrene barijere visine do 15 m počele su se stvarati tijekom ranog holocena ili čak na prijelazu pleistocena u holocen. Tijekom geofizičkog istraživanja snimljeno je ukupno 70 km seizmičkih profila visoke rezolucije te uzorkovano 5 jezgara sedimentata koje ukazuju da je ovo područje građeno od 3 sedimentne jedinice, odnosno riječne, brakične i marinske, starosti do 9000 g i ukupne debljine do 15 m. Prikupljeno je ukupno 36 površinskih uzoraka te je na tim lokacijama podvodnom kamerom snimljeno podmorje. Na površinskim uzorcima provedene su sljedeće analize: distribucija veličine čestica, magnetski susceptibilitet, gustoća uzorka, koncentracije ugljika i dušika te analize mineraloškog sastava primjenom metode rendgenske difrakcije na prahu (XRD), s ciljem izrade geološke karte podmorja. Poplavlivanje riječnih kanala rijeke Krke i Guduče u Prokljanskom jezeru započelo je otprilike prije 9300 g, a formiranje estuarija prije otprilike 7500 g. Ovo istraživanje omogućit će bolje razumijevanje paleokolišne evolucije estuarija, a također i predviđanje utjecaja budućih klimatskih promjena te porasta razine mora na estuarij.

ZAHVALE

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EARLY AND MIDDLE MIOCENE VOLCANICLASTIC RECORD ON MTS. KALNIK AND POŽEŠKA GORA

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The formation and evolution of the Pannonian Basin as part of the Carpathian-Pannonian Region (CPR) was accompanied by voluminous silicic eruptions during Early and Middle Miocene [1]. Silicic pyroclastic material, which covered much of the CPR, can be found in Miocene deposits in the North Croatian Basin (NCB, SW part of Pannonian Basin). This research is focused on two main outcrops of volcanoclastic rocks on Mts. Kalnik and Požeška Gora. Samples are in a process of analyses using a "multi-proxy" approach, combining sedimentological, petrological and paleontological data, high-precision zircon geo(petro)chronology, ⁴⁰Ar/³⁹Ar radiometric dating along with geochemistry and isotopic composition of volcanic glass and minerals. First results from Mt. Kalnik volcanoclastic deposits characterized them as massive rhyolitic ignimbrites with a CA-ID-TIMS U-Pb zircon age of 18.06 ± 0.023 Ma [2]. These results indicate that potentially correlative volcanoclastic deposits are intercalated with marine sediments in the Hrvatsko Zagorje Basin and lake sediments in the Sinj Basin. Guided by results from Avanić [3] and de Leeuw [4], we sampled nine additional volcanoclastic outcrops.

Furthermore, deposits that might be correlative with Mt. Požeška gora primary volcanoclastic turbidites are found on Mt. Medvednica intercalated in marine sediments of Central Paratethys. New CA-ID-TIMS zircon ages indicates that the initial Middle Miocene marine flooding of the western part of the NCB (Mt. Medvednica) could have occurred contemporaneously with its eastern part (Mt. Požeška Gora, 15.345 ± 0.02 Ma, [2]). Integrated data will enable more reliable tephrochronological and volcanic provenance, as well as petrogenetic reconstructions of Mts. Kalnik and Požeška Gora volcanoclastic deposits.

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VULKANOKLASTIČNI ZAPISI DONJEG I SREDNJEG MIOCENA NA KALNIKU I POŽEŠKOJ GORI

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Nastanak Panonskog bazena kao dijela Karpatsko-Panonske regije (CPR) popraćeno je snažnim voluminoznim kiselim erupcijama. Kiseli piroklastični materijal koji je pokrивao veći dio CPR može se pronaći i u miocenskim naslagama Sjevernohrvatskog bazena (NCB, JZ dio Panonskog bazena). Naše istraživanje provodi se na dva glavna izdanka vulkanoklastičnih naslaga na Kalniku i Požeškoj gori. Uzorci se analiziraju koristeći “multi-proxy” pristup koji uključuje sedimentološke, petrološke i paleontološke analize, visoko preciznu geokronologiju cirkona, $^{40}\text{Ar}/^{39}\text{Ar}$ radiometrijsko datiranje te geokemiju vulkanskog stakla i minerala. Prvim rezultatima na lokalitet Kalnik utvrđeno je da se radi o masivnom riolitnom ignimbritu s CA-ID-TIMS U-Pb cirkon starosti od 18.06 ± 0.023 Ma [1]. Ovi rezultati ukazuju na potencijalno korelativne naslage interkalirane u marinskim sedimentima Bazena Hrvatskog zagorja i jezerskim sedimentima Sinjskog bazena. Na temelju podataka koje su zabilježili Avanić [2] i de Leeuw [3], uzorkovali smo devet dodatnih izdanaka vulkanoklastičnih naslaga.

Potencijalno istovremene naslage s vulkanoklastičnim turbiditima Požeške gore interkaliranima s marinskim naslagama Centralnog Paratethysa pronađene su na Medvednici. Starost određena na cirkonima ukazuje na to da se prva srednjomiocenska marinska transgresija NCB-a u zapadnom dijelu (Medvednica) dogodila u slično vrijeme kao i u istočnom dijelu (Požeška gora, 15.345 ± 0.02 Ma, [1]) bazena. Podatci koji će se dobiti ovim istraživanjem dat će detaljniji uvid u vulkansku provenijenciju i petrografsku rekonstrukciju vulkanoklastičnih naslaga Kalnika i Požeške gore.

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METHODOLOGICAL APPROACH TO THE RESEARCH OF IMPACTS ON THE TUFA ENVIRONMENT IN THE SLUNJČICA RIVER BASIN

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From a scientific and aesthetic point of view, tufa barriers formed on karst watercourses represent geological and geomorphological formations of outstanding universal value [1]. However, they are extremely sensitive parts of karst ecosystems, and nowadays there are increasing anthropogenic pressures on rivers. Water pollution and interventions on watercourses alter natural conditions of habitats and flow regimes, affecting the speed and continuity of tufa precipitation. In such changed conditions, the growth of tufa can be completely stopped. The tufa of the river Slunjčica has not been systematically investigated so far, but fifteen years ago papers were published mentioning the distribution of metals in some sediments of the river Slunjčica [2] and oncoids as some forms of tufa in Rastoke [3]. The new research of the tufa-forming environment in the Slunjčica river basin includes a multi-criteria analysis based on field work, laboratory analyzes as well as on the theoretical basis of tufa precipitation. The conditions of tufa precipitation in the Slunjčica river basin are investigated, with an emphasis on sedimentation characteristics at the mouth of the Slunjčica river and with special review to the influence of ecotoxic metal content in the water-sediment system. In the context of the spatial distribution of tufa, the geological, hydrogeological and hydrological characteristics of the basin are considered. The type of tufa and facies are determined *in situ* and using micropetrographic analysis of tufa samples. Hydrochemical studies of catchment waters include *in situ* and laboratory analyzes (stable isotopes, ionic composition, trace elements, suspended solids). The composition and characteristics of laminated and homogeneous tufa deposited on artificial structures are analyzed. Within the spatial-temporal interpretation of hydrochemical data, the concentrations of ecotoxic metals and changes of these concentrations in the water-sediment system are determined. The aim of the study is to determine whether these changes are comparable to changes of tufa growth rate. The sequence of the above procedures generates a logical set of analytical methods that are graphically combined into a research model. The applied model serves to interpret the recent deposition conditions and the annual growth rate of tufa. The ultimate purpose is to contribute to the development of scientific research models in the subject field of science.

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METODOLOŠKI PRISTUP ISTRAŽIVANJU UTJECAJA NA SEDROTVORNI OKOLIŠ U SLIVU SLUNJČICE

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Sedrene barijere formirane na krškim vodotocima predstavljaju geološke i geomorfološke tvorbe izvanredne univerzalne vrijednosti iz znanstvenog i estetskog pogleda [1]. Međutim, one su izuzetno osjetljivi dijelovi krških ekosustava, a u današnje vrijeme sve su veći antropogeni pritisci na rijeke. Onečišćenja voda i intervencije na vodotocima mijenjaju prirodne uvjete staništa i režime protoka, što utječe na brzinu i kontinuiranost precipitacije sedre. U tako promijenjenim uvjetima rast sedre može biti i potpuno zaustavljen. Sedra Slunjčice do sada nije sustavno istraživana, ali su prije petnaestak godina objavljeni radovi u kojima se spominje raspodjela metala u nekim sedimentima Slunjčice [2] i onkoidi kao neki od pojavnih oblika sedre u Rastokama [3]. Nova istraživanja sedrotvornog okoliša u slivu Slunjčice podrazumijevaju višekriterijsku analizu koja se oslanja na terenski rad, laboratorijske analize i teorijske osnove sedrenja. Istražuju se uvjeti precipitacije sedre u slivu Slunjčice, s naglaskom na značajke osedranja na ušću Slunjčice i uz poseban osvrt na utjecaj sadržaja ekotoksičnih metala u sustavu voda-sediment. U kontekstu prostorne raspodjele sedre sagledavaju se geološke, hidrogeološke i hidrološke značajke sliva. Tip sedre i facijes određuju se *in situ* i mikropetrografski na uzorcima sedre. Hidrokemijska istraživanja voda u slivu uključuju *in situ* i laboratorijske analize (stabilni izotopi, ionski sastav, elementi u tragovima, suspendirane tvari). Analiziraju se sastav i značajke laminirane i homogene sedre istaložene na umjetnim objektima. U okviru prostorno-vremenske interpretacije hidrokemijskih podataka, utvrđuju se koncentracije i promjene koncentracija ekotoksičnih metala u sustavu voda-sediment. Cilj je utvrditi jesu li te promjene usporedive s promjenama stope rasta sedre. Slijed navedenih postupaka generira logičan skup analitičkih metoda koje se grafički objedinjuju u istraživački model. Primijenjeni model služi za interpretaciju recentnih uvjeta taloženja i godišnje stope prirasta sedre. Krajnja svrha je doprinos razvoju znanstveno-istraživačkih modela u predmetnom području znanosti.

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„ONE POT“ APPROACH TO SYNTHESIZING MONODENTATE OXAZOLINES WITH AN AROMATIC CORE- ASYMMETRIC SUBSTITUTION OF PRECURSORS IN ONE STEP

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The application of oxazoline ligands in asymmetric catalysis is successfully carried out in many important reactions with very high enantioselectivities [1]. However, the research accumulated so far has mainly been focused on utilizing bidentate bisoxazoline derivatives in catalysis, leaving the monodentate oxazoline ligands widely unexplored. Syntheses of more complex organic molecules often demand introduction of protection groups due to the large number of functional groups, which react in a non-selective fashion with various reagents. The introduction of protecting groups can be avoided by careful choice of the reagents and adjustment of reaction conditions.

Following our work on metal-organic catalysts in which noncovalent interactions induce chirality [2,3] we have synthesized monodentate oxazoline ligands for application in asymmetric catalysis. In this study we present a comparison of synthetic approaches via protecting groups and the “one pot” method for asymmetric substitution of benzene and naphthalene rings with oxazoline and peptide substituents with different substitution patterns. The prepared compounds are characterized using spectroscopic methods, namely ¹H and ¹³C NMR, as well as mass spectrometry.

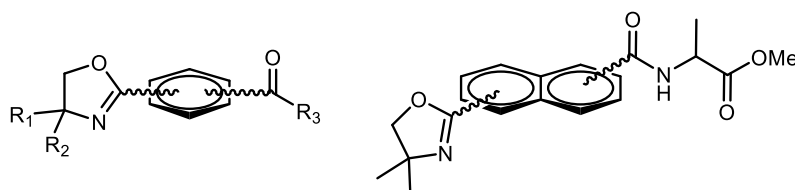


Figure 1. Ligands with benzene (left) and naphthalene (right) central structural unit and different substitution motifs (left: 1,3-, 1,4-; right: 1,4-, 1,5-, 2,6-, 2,7-). R₁= Me, *i*-Pr, Ph, Bn, R₂= H, Me, R₃ = NH-Ala-OMe, NH-Gly-Val-Phe-OMe.

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“ONE POT” PRISTUP SINTEZI MONODENTATNIH OKSAZOLINA S AROMATSKOM JEZGROM-ASIMETRIČNA SUPSTITUCIJA PREKURSORA U JEDNOM KORAKU

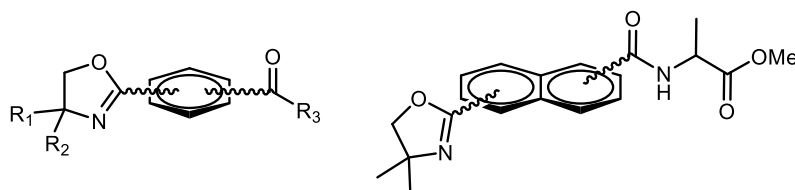
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Primjenom oksazolinskih liganda uspješno se provodi asimetrična kataliza velikog broja različitih važnih reakcija s visokim enantioselektivnostima [1]. Ipak, fokus većine radova je na korištenju bidentatnih bisoksalinskih derivata u katalizi, dok su monodentatni oksazolinski derivati još uvijek slabo istraženi. Sintaza kompliciranijih organskih molekula nerijetko zahtijeva uvođenje zaštitnih skupina zbog prisutnosti većeg broja funkcionalnih skupina koje neselektivno reagiraju s raznim reagensima. Uvođenje zaštitnih skupina moguće je izbjeći pažljivim odabirom samih reagensa i prilagodbom reakcijskih uvjeta.

Nastavljajući naše istraživanje metal-organskih katalizatora u kojima nekovalentne privlačne interakcije induciraju kiralnost [2,3], sintetizirali smo monodentatne oksazolinske ligande za primjenu u asimetričnoj katalizi. Unutar ovog posterskog priopćenja bit će uspoređeni sintetski postupci provedeni korištenjem zaštitnih skupina i tzv. „one pot“ metode za asimetričnu supstituciju benzenskog i naftalenskog prstena oksazolinskim i peptidnim supstituentima različitih supstitucijskih motiva. Dobiveni spojevi karakterizirani su spektroskopskim metodama, prije svega ¹H i ¹³C NMR te spektrometrijom mase.



Slika 1. Ligandi s benzenskom (lijevo) i naftalenskom (desno) centralnom strukturnom jedinicom različitih supstitucijskih motiva (lijevo: 1,3-, 1,4-; desno: 1,4-, 1,5-, 2,6-, 2,7-). R₁ = Me, i-Pr, Ph, Bn, R₂ = H, Me, R₃ = NH-Ala-OMe, NH-Gly-Val-Phe-OMe.

ZAHVALE

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BIS(TRIAZOLYLPYRENE)-DERIVED PSEUDOPEPTIDES AS POTENTIAL FLUORESCENT SENSORS: APPLICATION IN CELL IMAGING

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Fluorescence imaging is emerging as promising and powerful means for monitoring various bioactive molecules in living systems, which is thanks to its remarkable advantages, such as easy operation, high sensitivity and high temporal-spatial resolution [1]. In recent years, many fluorescent probes for various bioactive molecules have been reported, which has facilitated advances in cell biology and therapeutic imaging [2]. Polyaromatic chromophores are one of the most researched groups of fluorophores due to their different emission properties. Pyrene derivatives are intensively used as signal units in structural studies of biomolecules and molecule sensing, due to their properties [3]. Pyrene is an efficient chromophore with excellent fluorescent quantum yield, high detection sensitivity and efficient excimer emission that makes it useful as a fluorescence sensor. To regulate the fluorescence behaviors of pyrene-derived fluorophores, the assistance of self-complementary groups has been proved to be an efficient way to modulate the aggregating states of pyrene-related fluorophores [4].

With purpose of developing the new chemosensor molecules, we report on the design and synthesis of novel bis(triazolypyrene)-derived pseudopeptide fluorophores, their photophysical and self-aggregation properties, as well as confocal fluorescence microscopy studies (Figure 1).

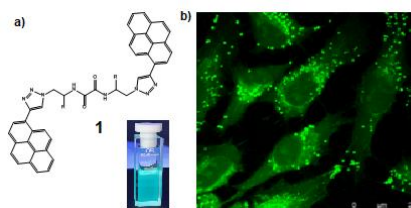


Figure 1. (a) Structure of **1** (R = iso-butyl) and (b) confocal image of MDA-MB-435S cells incubated with **1**.

ACKNOWLEDGMENTS

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BIS(TRIAZOLILPIRENSKI)-DERIVATI PSEUDOPEPTIDA KAO FLUORESCENTNI SENZORI: PRIMJENA U VIZUALIZACIJI STANICA

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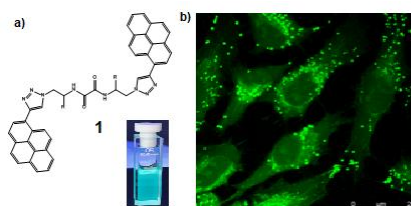
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Fluorescentno snimanje pojavljuje se kao obećavajuće i moćno sredstvo za praćenje različitih bioaktivnih molekula u živim sustavima, zahvaljujući svojim izvanrednim prednostima, poput jednostavnog rada, visoke osjetljivosti i visoke vremensko-prostorne razlučivosti [1]. Posljednjih godina otkrivene su mnoge fluorescentne sonde za različite bioaktivne molekule, što je olakšalo napredak u staničnoj biologiji i terapijskoj vizualizaciji [2]. Poliaromatski kromofori su jedna od najistraživanijih skupina kemosenzorskih molekula zbog različitih emisijskih svojstava. Derivati pirena se zbog svojih svojstava intenzivno koriste kao signalne jedinice u strukturnim istraživanjima biomolekula i osjetljivosti molekula [3]. Piren je učinkovit kromofor s izvrsnim kvantnim prinosom fluorescencije, visokom osjetljivošću detekcije i učinkovitom emisijom ekscimera, što ga čini korisnim kao fluorescentni senzor. Da bi se reguliralo fluorescencijsko ponašanje pirenskih derivata, pokazalo se da je dodatak samo-komplementarnih skupina učinkovit način modulacije agregatnih stanja fluorofora koji sadrže piren [4].

U svrhu razvoja novih kemosenzorskih molekula, izvješćujemo o dizajnu i sintezi novih bis(triazolilpirenskih) pseudopeptidnih fluorofora, njihovim fotofizičkim i samoagregirajućim svojstvima, kao i o rezultatima konfokalne fluorescencijske mikroskopije (Slika 1).



Slika 1. (a) struktura spoja **1** (R = izo-butil) i (b) konfokalna slika stanica MDA-MB-435S inkubiranih sa spojem **1**.

ZAHVALE

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QUALITY ASSESSMENT OF TURMERIC DIETARY SUPPLEMENTS AND FOOD SAMPLES

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Regulation of dietary supplements regarding their quality is still not well developed worldwide [1]. Many such products, mostly those available online, are not subjected to quality control and are either fraudulently underdosed, demonstrating no efficacy, or adulterated with synthetic active substances or alien herbal species, possibly leading to overdosage and toxicity. Furthermore, inadequate dissolution of active substances can lead to decreased bioavailability. The aims of this work were, therefore, to assess the content of curcuminoids and piperine, active substances of turmeric and black pepper (often used in conjunction with turmeric as piperine enhances the absorption of curcuminoids [2]), in widely used marketed turmeric dietary supplements and food samples, as well as to examine the dissolution of tableted and capsulated products according to the United States Pharmacopoeia (USP). A total of 20 dietary supplement and 13 food samples were investigated. High-performance liquid chromatography with spectrophotometric detection was the technique of choice. Firstly, optimization of extraction of active substances from a representative food sample (as the more complex sample type) was performed using Box-Behnken response surface methodology. After model optimization, maximum yield for all substances was achieved using 76.9% (V/V) ethanol as extraction solvent, 75 °C as extraction temperature and 30 min as sonication time. Food samples contained 1.7 to 4.7% curcuminoids (of turmeric rhizome mass) save for two purchased online, which showed higher content (9.1 and 10.5%, possibly implying adulteration). The content of piperine ranged from 3.9 to 5.8% of black pepper fruit mass. Only 9 of 20 and 1 of 8 dietary supplement samples conformed to the USP regulations of 90 to 110% of declared curcuminoid and piperine content, respectively. Dissolution studies using USP Apparatus 2 revealed only 3 of 15 formulated products conformed to minimum of 75% active substance release, which could be due to lower expected curcuminoid amounts present in products on the American market. In conclusion, more than half of the investigated samples failed to conform to active substance content and/or dissolution criteria of relevant regulations, which points to an increased need of quality control of herbal preparations and dietary supplements.

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PROCJENA KAKVOĆE DODATAKA PREHRANI I PREHRAMBENIH PROIZVODA NA BAZI KURKUME

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Regulativa dodataka prehrani u aspektu kakvoće još nije dovoljno razvijena diljem svijeta [1]. Mnogi proizvodi, ponajviše oni dostupni putem internetske prodaje ne podlažu kontroli kakvoće te su ili poddozirani, ne pokazujući učinkovitost, ili krivotvoreni dodatkom sintetskih aktivnih tvari ili stranih biljnih vrsta, što može dovesti do predoziranja i toksičnosti. Nadalje, nedostatno oslobađanje aktivnih tvari može dovesti do smanjene bioraspodivnosti. Stoga su ciljevi ovog rada procijeniti sadržaj kurkuminoida i piperina, aktivnih tvari kurkume i crnog papra (često primjenjivanog uz kurkumu jer piperin povećava apsorpciju kurkuminoida [2]) u široko korištenim dodacima prehrani i prehrambenim proizvodima koji sadrže kurkumu, kao i ispitati oslobađanje tabletiranih i kapsuliranih proizvoda prema Američkoj farmakopeji (USP). Ispitano je 20 uzoraka dodataka prehrani i 13 uzoraka prehrambenih proizvoda. Kao tehnika izbora odabrana je tekućinska kromatografija visoke djelotvornosti uz spektrofotometrijsku detekciju. Prvotno je provedena optimizacija ekstrakcije aktivnih tvari iz reprezentativnog uzorka prehrambenog proizvoda (kao složenije vrste uzorka) putem Box-Behnken metodologije površine odaziva. Nakon optimizacije modela, najveći prinos aktivnih tvari je postignut korištenjem 76.9 % (V/V) etanola kao ekstrakcijskog otapala, 75 °C kao ekstrakcijske temperature i 30 minuta kao vremena sonikacije. Uzorci prehrambenih proizvoda sadržavali su 1,7 do 4,7 % kurkuminoida (mase podanka kurkume), osim dva nabavljena putem internetske prodaje koja su pokazala viši sadržaj (9,1 i 10,5 %, ukazujući na moguće krivotvorenje). Sadržaj piperina bio je od 3,9 do 5,8 % mase ploda crnog papra. Samo 9 od 20, odnosno 1 od 8 uzoraka dodataka prehrani zadovoljilo je regulativu USP od 90 do 110 % deklariranog sadržaja kurkuminoida, odnosno piperina. Studije oslobađanja korištenjem USP aparature 2 pokazale su kako samo 3 od 15 formuliranih proizvoda odgovara minimalno 75 % oslobođenih aktivnih tvari, što može biti zbog nižeg sadržaja kurkuminoida u proizvodima na američkom tržištu. Zaključno, više od polovice ispitanih uzoraka nije zadovoljilo kriterije sadržaja i/ili oslobađanja aktivnih tvari, što ukazuje na povećanu potrebu za kontrolom kakvoće biljnih pripravaka i dodataka prehrani.

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MICROWAVE DRYING OF SEWAGE SLUDGE

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The trend of the construction of wastewater treatment plants (WWTP) has created problems with generation of significant amounts of sludge (SS). According to EUROSTAT statistics, the total SS production from WWTP at the level of 28 EU Member States can be estimated at around 10 million tonnes of dry matter (DM) per annum [1]. Thermal treatment reduces the mass and volume of SS, and removes or destroys most of potentially hazardous substances from SS, promotes the use of by-products and their material recovery to protect the environment, optimize land use, reduce CO₂ emissions and protect groundwater. High-temperature SS treatment processes (incineration, gasification, pyrolysis) require SS with lower moisture content, and SS drying requires significant energy consumption. Therefore, further research to improve energy efficiency is considered as essential. In the drying process of materials with high moisture content, microwave drying has certain benefits due to its rapid heating and low energy consumption. Unlike other heating sources, microwaves at a frequency of 2.4 GHz heat volumetrically, not from surface, and have a penetration depth of a few centimeters, as evidenced by the drying of SS from WWTP [2]. Microwave drying effectively destroys microorganisms, stabilizes harmful substances in dehydrated SS and has a positive effect on the environment [3]. This paper analyses the efficiency of both drying procedures. SS from WWTP Zagreb and Karlovac was analyzed with respect to the convection drying at a temperature of $T = 105\text{ °C}$ and microwave drying at a power of $P = 360\text{ W}$. Microwave drying achieved a 14 times shorter drying time of sludge mass of 600 g compared to conventional drying with lower energy consumption.

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- [3] H. F. Wang, J. J. Lu, K. F. Chen, H. L. Duan, METALURGIJA 54 (2015) 3, 459-461



MIKROVALNO SUŠENJE MULJA S UPOVA I SVOJSTVA MIKROVALNO OSUŠENOG MULJA

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Trend izgradnje uređaja za pročišćavanje otpadnih voda (UPOV) stvorio je probleme nastanka značajnih količina mulja. Prema statističkim podacima EUROSTAT-a ukupna proizvodnja mulja s UPOV-a na razini 28 država članica EU, može se približno procijeniti na oko 10 milijuna tona suhe tvari (ST)[1]. Termičkom obradom smanjuje se masa i volumen mulja, te se izdvajaju ili uništavaju potencijalno opasne tvari iz mulja, promiče se ponovna uporaba nusproizvoda i njihovo recikliranje radi zaštite okoliša, optimizira se korištenje zemljišnih resursa, smanjuju se emisije CO₂ i štite se podzemne vode. Visokotemperaturni procesi obrade mulja (spaljivanje, uplinjavanje, piroliza) zahtijevaju mulj s nižim udjelom vlage, a sušenje mulja zahtijeva značajan utrošak energije. Stoga su daljnja istraživanja poboljšanja energetske učinkovitosti od izuzetne važnosti. Kod sušenja materijala s visokim udjelom vlage posebno se ističe mikrovalno sušenje zbog brzog zagrijavanja i niske potrošnje energije. Za razliku od ostalih izvora zagrijavanja, mikrovalovi na frekvenciji 2,4 GHz zagrijavaju volumetrijski, a ne površinski, te imaju dubinu prodiranja nekoliko centimetara, što je dokazano sušenjem mulja s UPOV-a [2]. Mikrovalno sušenje efikasno uništava mikroorganizme, stabilizira štetne tvari u dehidriranom mulju i pozitivno utječe na okoliš [3]. U ovom radu analiziran je utjecaj različitih postupaka sušenja na svojstva mulja. Mulj s UPOV-a Zagreb i Karlovac podvrgavan je konvencionalnom načinu sušenja konvekcijom pri temperaturi T=105 °C te mikrovalnom sušenju mulja pri snazi P=360 W. Mikrovalnim sušenjem postignuto je kraće vrijeme sušenja mase mulja 600 g za čak 14 puta u odnosu na konvencijsko sušenje, uz manju potrošnju energije.

ZAHVALE

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A DFT APPROACH TO PLASMONIC PROPERTIES TUNING BY ALLOYING

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Plasmonic nanostructures show great potential in the fields of photocatalysis, solar energy harvesting and sensing because of their properties such as near field enhancement, strong light absorption and scattering, as well as efficient hot carrier generation [1,2]. The nanostructure properties can be tuned for a desired purpose by alloying plasmonic metals. Using a density functional theory (DFT) based approach we showed that the modulation of plasmonic properties by alloying can be relatively well predicted. Moreover, the DFT calculation results showed that increased optical losses in the IR range occur for all the studied alloys even when they are composed of metals for which this effect is not present in the pure state, which makes it an emergent property of alloying. Based on the connection between alloy composition, (effective) band structure and optical properties we showed the causes of increased absorption in the IR range, as well as the change of properties in the UV and visible range. The results of DFT calculations were used as a basis for electrodynamic simulations of several different nanostructures. The standard method based on the PBE functional was showed as inferior in comparison with equally efficient method in which the GLLB-SC functional is used. We therefore propose the GLLB-SC functional as the new standard for high throughput DFT calculations of metal alloy plasmonic properties.

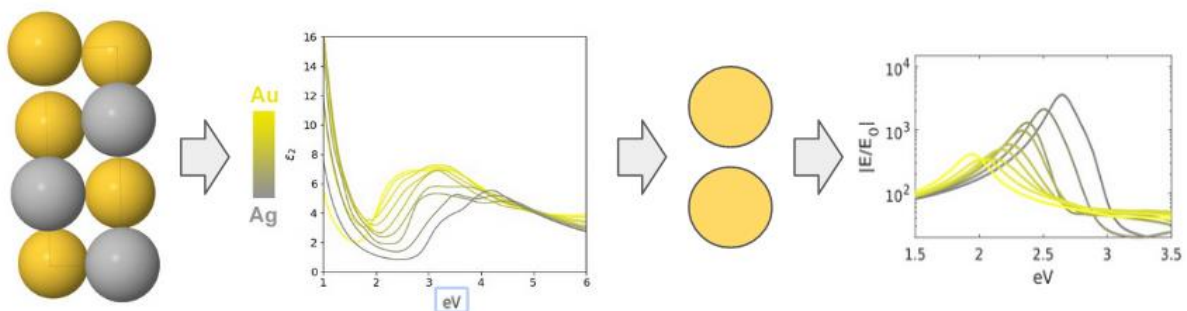


Figure 1. Scheme of the approach used in this work

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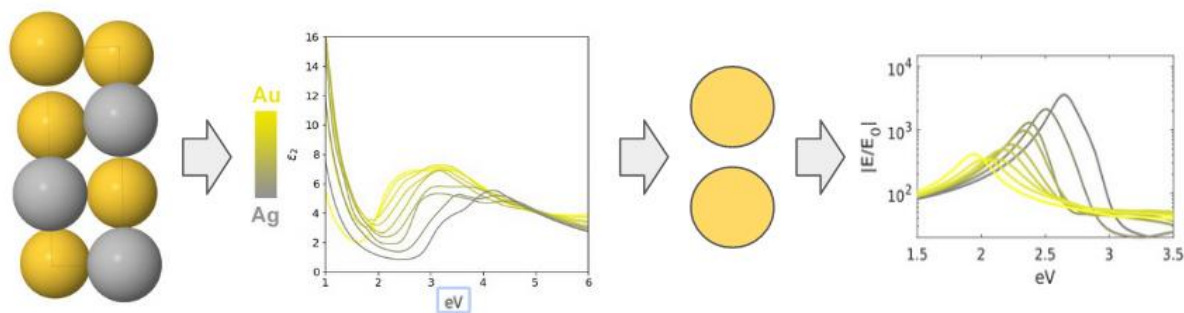
DFT PRISTUP PODEŠAVANJU PLAZMONIČKIH SVOJSTAVA LEGIRANJEM

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Plazmoničke nanostrukture pokazuju velik potencijal u području fotokatalize, solarne energije i senzora zbog svojstava poput pojačanja bliskog polja, snažne apsorpcije i raspršenja svjetla te učinkovitog stvaranja “vrućih” nosioca naboja [1,2]. Legiranje plazmoničkih metala omogućava podešavanje svojstava nanostrukture za željenu primjenu. Pristupom temeljenim na teoriji funkcionala gustoće (*eng. density functional theory, DFT*) pokazali smo da se promjena plazmoničkih svojstava s legiranjem može relativno dobro predvidjeti. Uz to, rezultati DFT računa pokazali su da se kod svih legura javljaju pojačani optički gubici u IR području zbog prijelaza između elektronskih vrpki čak i kada ih tvore metali kod kojih taj efekt u čistom stanju nije prisutan, što ih čini emergentnim svojstvom legiranja. Na temelju poveznice sastava legure, (efektivne) strukture elektronskih vrpki i optičkih svojstava pokazali smo što uzrokuje veću apsorpciju u IR području, kao i promjenu svojstava u UV i vidljivom području. Rezultati DFT računa iskorišteni su kao temelj za elektrodinamičke simulacije nekoliko različitih nanostrukture. Standardna metoda temeljena na PBE funkcionalu pokazala se kao lošija u odnosu na jednako učinkovitu metodu u kojoj se koristi GLLB-SC funkcional. GLLB-SC funkcional stoga predlažemo kao novi standard za *high throughput* DFT račune plazmoničkih svojstava metalnih legura.



Slika 1. Shema pristupa korištenog u ovom radu

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AGING OF POLYSTYRENE MICROPLASTIC BY ADVANCED OXIDATION PROCESSES

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Plastic is considered to be all organic polymers synthesized from fossil raw materials such as oil, natural gas and coal. Excellent properties and low cost have made plastic inevitable in everyday life, but due to improper and inadequate disposal, a large amount of plastic material accumulates in the environment. An increasing threat to the living world is posed by plastic particles smaller than 5 mm called microplastics (MP). Plastic is a stable material, but in the environment it is exposed to various conditions that cause decomposition and aging of material (change of physical and chemical properties) [1]. In nature, several factors affect change of the MPs properties. UV light and oxidation are one of them. In this paper, advanced oxidation processes (AOP) are used for treatment of MPs. AOP are oxidation processes in an aqueous medium, where highly reactive radicals are formed under the influence of energy with main purpose of removing or decomposing organic pollutants, in this case MP [2]. Applying this approach aims to gain a better insight into the MPs aging process. The investigation of certain factors that occur in nature, such as light, oxidizing agents, pH-value and exposure time to the aging of polystyrene MP (PS), has been examined. Two types of advanced oxidation processes were investigated: UV / H₂O₂ and UV / S₂O₈²⁻ according to the Box-Behnken design of experiments for determining the optimal aging conditions of PS. To determine the changes in the properties and surface of PS, various methods of analysis were used such as SEM, FTIR spectrometry and TOC analysis.

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STARENJE MIKROPLASTIKE POLISTIRENA NAPREDNIM OKSIDACIJSKIM PROCESIMA

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Plastikom se smatraju svi organski polimeri sintetizirani iz fosilnih sirovina poput nafte, zemnog plina i ugljena. Izvrsna svojstva i niska cijena omogućili su da plastika postane neizbježna u svakodnevnom životu. Zbog nepravilnog odlaganja i neadekvatnog zbrinjavanja dolazi do akumulacije velike količine plastičnog materijala u okolišu. Sve veću prijetnju živome svijetu predstavljaju čestice plastike manje od 5 mm koje se nazivaju mikroplastikom (MP). Plastika je stabilan materijal, ali je u okolišu izložena različitim uvjetima koji uzrokuju razgradnju i starenje materijala (promjena fizikalnih i kemijskih svojstava) [1]. U prirodi nekoliko čimbenika utječe na promjenu svojstava MP-a. UV svjetlost i oksidacija su jedan od njih. U ovom radu napredni oksidacijski procesi (AOP) koriste se za obradu MP-a. To su procesi oksidacije u vodenom mediju, gdje pod utjecajem energije dolazi do stvaranja vrlo reaktivnih radikala čiji je cilj uklanjanje ili razgradnja onečišćujućih tvari, u ovome slučaju MP-a [2]. Primjenjujući ovakav pristup želi se dobiti bolji uvid u procese starenja MP-a. Provedeno je ispitivanje pojedinih faktora koji se javljaju u prirodi kao što su svjetlost, oksidacijski agensi, pH-vrijednost i vrijeme izlaganja na starenje MP-a polistirena (PS). Ispitane su dvije vrste naprednih oksidacijskih procesa: UV/H₂O₂ i UV/S₂O₈²⁻ prema Box – Behnken eksperimentalnom planu kako bi se odredili optimalni uvjeti starenja PS-a. Za utvrđivanje promjene svojstva i površine PS-a, korištene su različite metode analize poput FTIR spektrometrije i TOC analize.

ZAHVALA

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AGITATION INDUCED REVERSIBLE SELF-ASSOCIATION OF PROTEIN *rHu-G-SCF*

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Granulocyte colony-stimulating factor (rHuG-CSF), or so-called filgrastim, is a member of the class of cytokines that stimulates the synthesis of granulocytes in the human body. Filgrastim is structurally composed of 175 amino acids and can be used as a drug for the treatment of neutropenia. While affected by different types of stressors, the monomeric protein form of filgrastim has a tendency to self-associate and produce dimers, trimers, tetramers, and other complex aggregates. A stressor such as heat can induce the formation of irreversible filgrastim aggregates, while agitation stimulates the reversible self-association mechanism. Produced irreversible forms can emerge due to the formation of covalent bonds of monomer protein structures, of which the most significant are disulfide bridges. Further on, reversible filgrastim aggregate forms occur due to the non-covalent bonds, i.e. hydrogen bonds, electrostatic, hydrophobic, and van der Waals interactions. Researchers have discovered that reversible self-associated proteins in the human body can promote the development of Alzheimer's, Parkinson's, Huntington's, and prion's diseases, as well as amyotrophic lateral sclerosis [1], however, the complexity of the filgrastim structure makes the understanding of aforementioned self-association processes extremely challenging. Therefore, to examine the mechanism of the reversible protein binding reaction, the filgrastim aqueous solution was agitated at a constant rate increasing the agitation time by 60-600 s. The analysis was performed immediately after agitation by high performance liquid chromatography (HPLC) and the obtained results were normalized by a mathematical model that derives a more precise quantitative analysis of chromatographic peaks in four steps. Such a mathematical model enabled the illustration of the Lumry-Eyring equation framework that explains the mechanism of an aggregation process of filgrastim.

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AGITACIJOM POTAKNUTO REVERZIBILNO POVEZIVANJE PROTEINA *rHu-G-CSF*

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Faktor rasta granulocitnih kolonija (*rHuG-CSF*), ili skraćeno filgrastim, je protein skupine citokina koji u ljudskom organizmu stimulira sintezu granulocita. Strukturno je građen od 175 aminokiselina te se koristi kao lijek za liječenje neutropenije. Prilikom utjecaja različitih stresora, monomerni protein filgrastim ima tendenciju samo-udruživanja čime nastaju dimeri, trimeri, tetrameri i ostalih složeni agregati. Stresora poput toplinske energije može potaknuti stvaranje ireverzibilnih agregata filgrastima, dok agitacija stimulira reverzibilni mehanizam samo-udruživanja. Ireverzibilne forme nastaju uslijed kovalentnih povezivanja monomernih proteinskih struktura, od kojih je najznačajnije povezivanje uslijed formiranja disulfidnih mostova. Nadalje, reverzibilni oblici agregata filgrastima mogu nastati uslijed povezivanja ne-kovalentnim vezama, tj. vodikovim vezama te elektrostatskim, hidrofobnim i van der Waals-ovim interakcijama. Znanstvenici su otkrili kako reverzibilni samo-udruženi proteini u ljudskom organizmu potiču nastajanje Alzheimer-ove, Parkinson-ove, Huntington-ove te prion-ove bolesti kao i amiotropne lateralne skleroze [1] no kompleksna struktura proteina filgrastima onemogućuje detaljno poznavanje spomenutih procesa samo-udruživanja. Kako bi se ispitaio mehanizam reverzibilne reakcije povezivanja proteina, vodena otopina filgrastima agitirana je konstantnom brzinom povećavajući vrijeme agitacije od 60–600 s. Analiza je vršena neposredno nakon agitacije tekućinskom kromatografijom visoke djelotvornosti (HPLC), a dobiveni rezultati normalizirani su matematičkim modelom koji u četiri koraka vrši precizniju kvantitativnu analizu kromatografskih pikova. Takav matematički model omogućio je ilustraciju Lumry-Eyring mehanističkog modela koji pojašnjava mehanizam povezivanja proteina filgrastima.

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ELECTROCHEMICAL PROCESSES IN OILY WASTERWATER TREATMENT

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Today's trends are focused on investigating the efficiency of oily wastewater treatment with electrochemical processes due to the fact that they do not depend on temperature changes of the influent, do not require the addition of chemicals and do not require pH adjustment during treatment. Among different electrochemical processes, state-of-the-art confirms the high efficiency of electrocoagulation (EC) process. The use of Fe and Al electrodes achieves a relatively high efficiency of oil and grease removal, as well as COD removal. However, there is a need to investigate the efficiency of hybrid processes that combine different electrochemical processes, such as advanced oxidation processes (AOP) and EC. In this paper, oily wastewater from oil and grease separators was used, and the treatment was performed on a pilot plant using a combination of electrochemical AOP and EC processes. Two tests were performed, the first analysing the treatment efficiency of oily wastewater, which was completely mixed without pretreatment, and the second analysing the effect of primary sedimentation (1st stage of treatment) on the overall treatment efficiency. In the treatment of oily wastewater by applied electrochemical processes without primary sedimentation, the removal efficiency of total oil and grease was about 70%, and COD about 50%. With additional primary sedimentation prior to AOP-EC process, the total removal efficiency of total oil and grease was about 90%, and COD about 70%. The results indicate the high efficiency of oily wastewater treatment by a hybrid AOP and EC process, and the application of primary sedimentation has been proven with higher overall treatment efficiency.

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PROČIŠĆAVANJE ZAULJENIH OTPADNIH VODA ELEKTROKEMIJSKIM POSTUPCIMA

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Današnji trendovi su usmjereni na istraživanje učinkovitosti pročišćavanja zauljenih otpadnih voda s elektrokemijskim postupcima s obzirom na činjenicu da ne ovise o temperaturnim promjenama influenta, ne zahtijevaju dodavanje kemikalija i ne zahtijevaju prilagodbu pH u toku obrade [1]. Među različitim elektrokemijskim postupcima, dosadašnja svjetska istraživanja potvrđuju visoku učinkovitost procesa elektrokoagulacije (EK). Korištenjem Fe i Al elektroda postiže se relativno visoka učinkovitost uklanjanja ulja i masti, te KPK [2,3]. Međutim, uočava se potreba za istraživanjem učinkovitosti hibridnih procesa koji kombiniraju različite procese, poput elektrokemijskih naprednih oksidacijskih procesa (NOP) i EK. U ovom je radu korištena zauljena otpadna voda iz separatora ulja i masti, a pročišćavanje je provedeno na pilot uređaju koji koristi kombinaciju NOP i EK procesa. Provedena su dva ispitivanja, pri čemu je u prvom ispitana učinkovitost pročišćavanja zauljene otpadne vode, koja je potpuno izmiješana bez prethodnog predtretmana, a u drugom je ispitan utjecaj prethodnog taloženja (1. stupnja pročišćavanja) na cjelokupnu učinkovitost pročišćavanja. Pri pročišćavanju zauljenih otpadnih voda primijenjenim elektrokemijskim postupcima bez prethodnog taloženja ostvarena je učinkovitost uklanjanja ukupnih ulja i masti u iznosu oko 70%, a KPK oko 50%. Uz dodatno prethodno taloženje sirove zauljene vode, ostvarena je ukupna učinkovitost uklanjanja ukupnih ulja i masti u iznosu oko 90%, a KPK oko 70%. Dobiveni rezultati ukazuju na visoku učinkovitost pročišćavanja zauljenih otpadnih voda hibridnim NOP i EK procesom, a dokazana je i opravdanost primjene prethodnog taloženja.

ZAHVALE

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EFFECT OF MISTRANSLATION AND OXIDATIVE STRESS ON GROWTH AND VIABILITY OF BACTERIA *Escherichia coli*

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Translation is a cellular process in which nucleotide sequence is translated to protein sequence whereby enzymes aminoacyl-tRNA synthetases play an important role in catalysis of aminoacyl-tRNA synthesis. During translation process, incorporation of the wrong amino acid in the polypeptide chain can occur. Mistranslation is usually associated with deleterious effects it has on a cell, but there are few examples of beneficial effects of mistranslation in stress conditions [1].

Escherichia coli strain expressing mutant isoleucyl-tRNA synthetase with inactivated editing domain produces mistranslated proteins if proteinogenic amino acid valine or nonproteinogenic norvaline, which are structurally similar to isoleucine, are added to the media [2]. Mistranslation was induced by adding different concentrations of valine or norvaline and oxidative stress was induced by adding H₂O₂. Bacteria observed under microscope displayed morphological change in oxidative and, more significantly, in mistranslation stress conditions. The cells were considerably longer compared to control with size increasing in a concentration-dependent manner by adding valine or norvaline. To observe the effect of stress on cell proliferation and viability, growth curves were measured, and survival assays were performed. The results indicate that there is mistranslation-induced preadaptation to oxidative stress, albeit only in a narrow range of valine and norvaline concentrations. Further work will be focused on identification of cellular mechanisms that allow better survival under oxidative stress due to mistranslation.

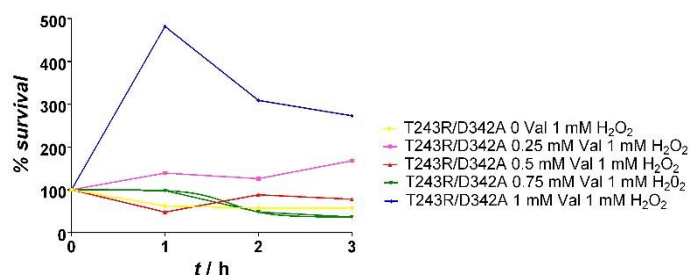


Figure 1. Survival percentage of mistranslating *E. coli* mutant after treatment with 1 mM H₂O₂ for various periods of time.

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DJELOVANJE MISTRANSLACIJE I OKSIDACIJSKOG STRESA NA RAST I VIJABILNOST BAKTERIJE *Escherichia coli*

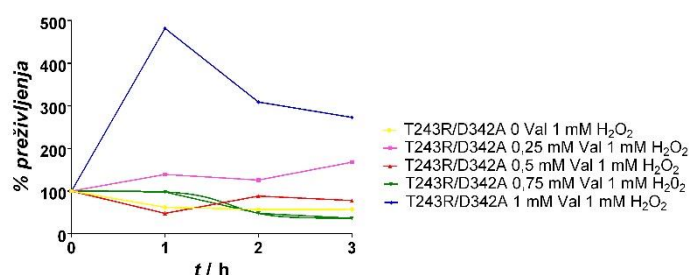
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Translacija je stanični proces prevođenja nukleinskog slijeda mRNA u aminokiselinski slijed proteina, pri čemu važnu ulogu imaju enzimi aminoacil-tRNA-sintetaze koji kataliziraju nastajanje aminoacilirane tRNA. U procesu translacije može doći do pogreške, odnosno do ugradnje krive aminokiseline u polipeptidni lanac. Mistranslacija se obično veže uz štetne učinke na stanicu, no poznato je više primjera korisnog učinka mistranslacije u uvjetima stresa [1].

Soj bakterije *Escherichia coli* koji eksprimira mutiranu inačicu izoleucil-tRNA-sintetaze, u kojoj je inaktivirana domena za popravak pogreške, proizvodi mistranslatirane proteine ukoliko su u medij dodane aminokiseline valin (proteinogena aminokiselina) ili norvalin (neproteinogena aminokiselina) koje su strukturno slične izoleucinu [2]. Mistranslacija je inducirana dodatkom različitih koncentracija valina ili norvalina, a oksidacijski stres induciran je dodatkom H₂O₂. Bakterije su promatrane pod mikroskopom te je uočena promijenjena morfologija u oksidacijskom i osobito u mistranslacijskom stresu. Stanice su značajno izdužene u odnosu na kontrolne uvjete, a veličina im se povećava s koncentracijom dodanog valina i norvalina. Utjecaji na proliferaciju i vijabilnost stanica praćeni su određivanjem krivulja rasta i udjela preživljenja. Rezultati ukazuju da postoji adaptacija na oksidacijski stres prethodnom mistranslacijskom, ali samo u uskom području koncentracije dodanog valina i norvalina. Daljnja istraživanja bit će usmjerena na identifikaciju staničnih mehanizama koji omogućuju bolje preživljenje u oksidacijskom stresu uslijed mistranslacije.



Slika 1. Grafički prikaz postotka preživljenja mistranslatirajućeg mutanta bakterije *E. coli* nakon inkubacije s 1 mM H₂O₂ tijekom različitih vremenskih perioda.

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INFLUENCE OF REACTION PARAMETERS ON THE SYNTHESIS OF OCTYL ESTERS OF FATTY ACIDS

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Alkyl esters of fatty acids or biodiesel have been more intensively investigated in recent decades as a renewable source of energy that can be combined with diesel [1]. Possessing similar properties to diesel, smaller modifications are needed for biodiesel to be used solely or as a part of binary or ternary blends with diesel and/or alcohol in diesel engines [2, 3]. Biodiesel is chemically obtained with the reaction of transesterification that yields long-chained esters of fatty acids from initial feedstock (vegetable oil, bioalcohol or waste animal fat), in the presence of appropriate catalyst [4]. Mostly used alcohols for this reaction are methanol and ethanol although the potential for the improvement of biodiesel properties rises with the chain length of the alcohol, which is demonstrated here with the use of octanol [5]. The influence of molar ratio of the reactants and weight fraction of the catalyst on the conversion was investigated by comparing the experiments conducted at the same temperatures and throughout the same times. Experiments showed that the increase in the molar ratio from 4 : 1 to 10 : 1, at $T = 40\text{ °C}$, $t = 2\text{ h}$ and $w_{\text{cat}} = 2\%$, results in the conversion increasing from 32 % to 99 %. While the increase in temperature from 40 °C to 80 °C , at $t = 2\text{ h}$, $A : U = 4 : 1$ and $w_{\text{cat}} = 2\%$, results in the increase of the conversion from 32 % to 55 %.

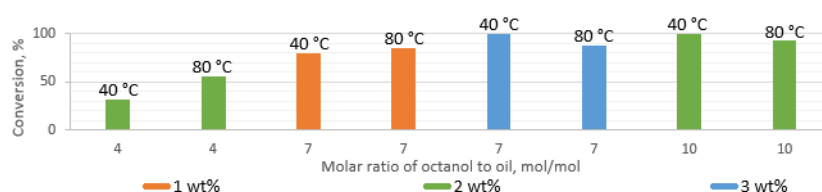


Figure 1. The influence of the reaction parameters on reaction conversion

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UTJECAJ REAKCIJSKIH PARAMETARA NA SINTEZU OKTILNIH ESTERA MASNIH KISELINA

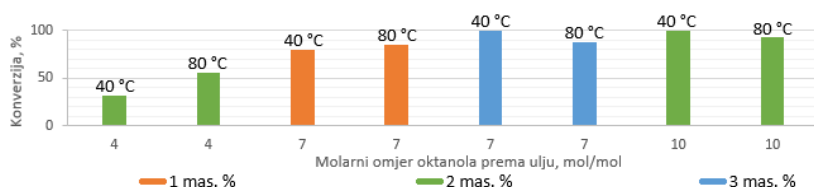
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Alkilni esteri masnih kiselina, odnosno biodizel, posljednjih su desetljeća intenzivnije istraživani kao obnovljivi izvor energije koji bi mogao koristiti u kombinaciji s dizelom [1]. Posjedujući slična svojstva dizelu, potrebne su manje modifikacije kako bi se biodizel, bilo samostalno, ili kao komponenta binarne ili ternarne smjese s dizelom i/ili alkoholom, koristio kao gorivo u dizel motorima [2, 3]. Biodizel se kemijski dobiva reakcijom transesterifikacije, kojom od polazišne biosirovine (biljnog ulja, bioalkohola ili otpadne životinjske masti), u prisutnosti odgovarajućeg katalizatora, nastaju dugolančani alkilni esteri masnih kiselina [4]. Najčešće korišteni alkoholi za ovu reakciju su metanol i etanol, međutim potencijal prema poboljšanju svojstva biodizela s porastom duljine alkoholnog lanca potaknuo je istraživanja usmjerena primjeni viših alkohola, poput ovdje primijenjenog oktanola [5]. Istražen je utjecaj molarnog omjera reaktanata i masenog udjela katalizatora na iskorištenje usporedbom eksperimenata provedenih na istoj reakcijskoj temperaturi, pri istim vremenima. Rezultati eksperimenata su pokazali da povećanjem molarnog omjera reaktanata s 4 : 1 na 10 : 1, pri $T = 40\text{ }^{\circ}\text{C}$, $t = 2\text{ h}$ i $w_{\text{kat}} = 2\%$, iskorištenje reakcije raste s 32 % na 99 %, dok povećanje temperature na $80\text{ }^{\circ}\text{C}$, uz $t = 2\text{ h}$, $A : U = 4 : 1$ i $w_{\text{kat}} = 2\%$, rezultira rastom iskorištenja s 32 % na 55 %.



Slika 1. Utjecaj reakcijskih parametara na iskorištenje reakcije

ZAHVALE

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DEUTERATION AFFECTS HISTAMINE AFFINITY FOR ITS H₂ RECEPTOR: A COMPUTATIONAL STUDY

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In the past few years, deuteration has become one of the most promising tools in medicinal chemistry to overcome problems in terms of metabolism-mediated toxicity, low bioactivation, and drug interactions. Furthermore, precise deuteration goes beyond the pure and simple amelioration of the pharmacokinetic properties, providing an opportunity to decrease the degree of racemisation, reduce the dose of coadministered boosters, and contribute to the investigation of mechanisms of action for various endo- and xenobiotics [1].

In this work, we used a range of computational techniques to reveal an increased histamine affinity for its H₂ receptor upon nonselective deuteration, which was interpreted through altered hydrogen bonds within the receptor and the aqueous solution preceding the binding [2].

Molecular docking procedure identified the area between third and fifth transmembrane α -helices as the likely binding site. The subsequent molecular dynamics simulation recognized Asp98 as the most dominant residue, whose persistent hydrogen bond with the histamine $-\text{NH}_3^+$ group accounts for the 40% of the total binding energy, and is further stabilised through interaction with Tyr250 (Figure 1). Lastly, quantum-chemical calculations supported the deuteration-induced affinity increase by calculating the difference in the binding free energy of $-0.85 \text{ kcal mol}^{-1}$, which is in excellent agreement with an experimental value of $-0.75 \text{ kcal mol}^{-1}$. All these calculations confirm the initial hypothesis that hydrogen bonds are crucial in the H₂ receptor activation and underline precise deuteration as a useful tool to improve drug efficiency.

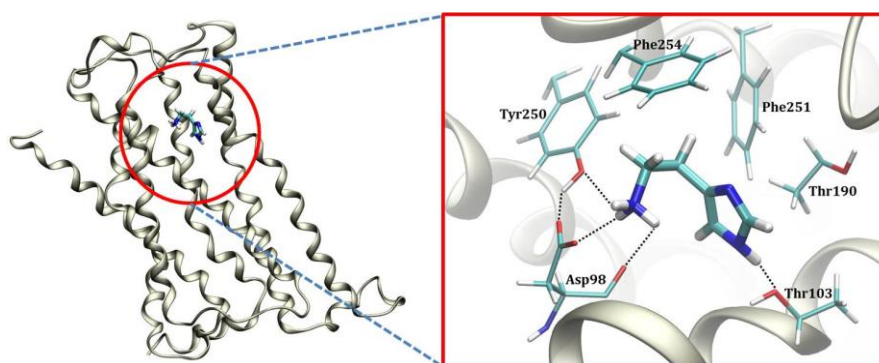


Figure 1. Histamine hydrogen bonds within the H₂ receptor active site.

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UTJECAJ DEUTERACIJE NA AFINITET HISTAMINA PREMA H₂ RECEPTORU: RAČUNALNA STUDIJA

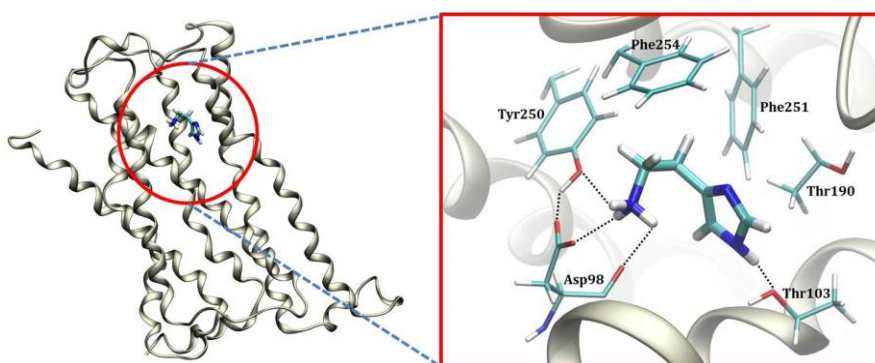
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U posljednjih nekoliko godina, deuteracija je postala jedan od najperspektivnijih alata u rješavanju učestalih problema u farmaceutskoj kemiji, kao što su metabolizmom-posredovana toksičnost, niska bioaktivacija te interakcija među lijekovima. Nadalje, ciljane deuteracije nadilazi samo poboljšanje farmakokinetičkih svojstava, pružajući mogućnost smanjenja stupnja racemizacije enantiomernih lijekova, reducirajući dozu *booster* supstancija te uvelike pridonoseći istraživanju mehanizma djelovanja različitih endo- i ksenobiotika [1].

U ovom smo radu koristili niz različitih računalnih tehnika kako bismo objasnili povećani afinitet histamina za H₂ receptor nakon neselektivne deuteracije, za što smo pretpostavili da je posljedica promijenjenih vodikovih veza u receptoru i vodenoj otopini koja prethodi vezanju u aktivno mjesto [2]. Docking procedurom identificirano je područje između treće i pete transmembranske α -uzvojnice kao vezno mjesto histamina. Naknadne molekulske-dinamičke simulacije izdvojile su Asp98 kao aminokiselinski ostatak koji najviše doprinosi vezanju, čak 40% ukupne energije, a njegova trajna vodikova veza s histaminskom $-NH_3^+$ skupinom dodatno je stabilizirana interakcijom s Tyr250 (Slika 1). Kvantno-kemijski računi predviđjeli su veći afinitet histamina nakon deuteracije, procjenjujući razliku u energiji vezanja od -0.85 kcal mol⁻¹, što je u izvrsnom slaganju s eksperimentalno dobivenom vrijednošću od -0.75 kcal mol⁻¹. Svi prethodno navedeni izračuni potvrđuju početnu pretpostavku da su vodikove veze ključne za aktivaciju H₂ receptora te naglašavaju ulogu ciljane deuteracije u poboljšanju efikasnosti lijekova.



Slika 1. Vodikove veze histamina unutar aktivnog mjesta H₂ receptora.

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COMPUTATIONAL SIMULATIONS OF THE TRANSCRIPTIONAL REGULATOR MntR FROM THE BACTERIUM *Bacillus subtilis*

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Metal ion homeostasis is essential for all microorganisms. Transition metal ions are crucial for normal cellular functioning, on the other hand, high concentrations of the same ions can be toxic. Thus, organisms have developed sensitive mechanisms for regulating cellular metal ion concentrations. Metal homeostasis in bacteria is most commonly regulated by metallo-sensors – transcription factors whose DNA-binding affinity depends on the binding of its cognate metal ions [1]. Bacterium *Bacillus subtilis*, the model organism for gram-positive bacteria, can be found in the soil and as a gut commensal. Manganese homeostasis in *B. subtilis* is regulated by the transcription factor MntR, whose DNA binding affinity is enhanced upon the binding of manganese ions [2]. MntR is a dimer in solution and each subunit binds two manganese ions in a binuclear binding site [3, 4]. Molecular dynamics simulations were employed to study the allosteric effects Mn²⁺ ion binding.

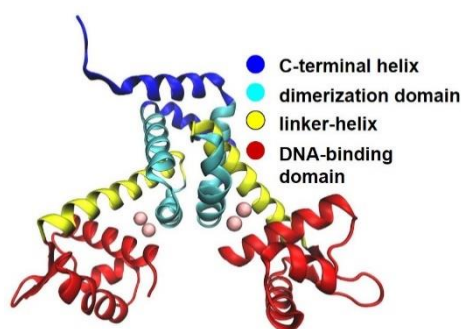


Figure 1. The protein MntR from the bacterium *Bacillus subtilis*.

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RAČUNALNE SIMULACIJE TRANSKRIPCIOJSKOG FAKTORA MntR IZ BAKTERIJE *Bacillus subtilis*

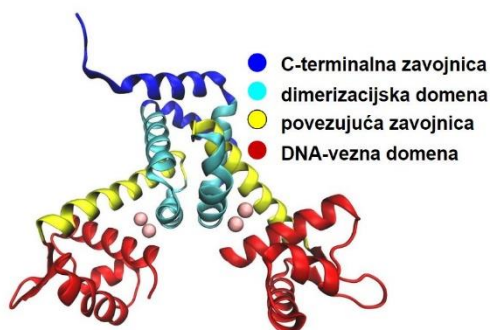
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Homeostaza iona prijelaznih metala od esencijalne je važnosti za mikroorganizme. Naime, ioni prijelaznih metala nužni su za normalno funkcioniranje stanice, ali visoke koncentracije istih mogu biti toksične. Stoga su razvijeni osjetljivi mehanizmi kontrole i regulacije stanične koncentracije iona prijelaznih metala. Kod bakterija se homeostaza metala najčešće regulira metalosenzorima – transkripcijskim faktorima čiji afinitet za vezanje DNA ovisi o vezanju metalnih iona [1]. Bakterija *Bacillus subtilis* živi u tlu i kao crijevni komenzal te je modelni organizam za gram-pozitivne bakterije. U *B. subtilis* homeostaza mangana regulirana je transkripcijskim faktorom MntR, čiji se afinitet za DNA povećava uslijed vezanja manganovih iona [2]. MntR se u otopini nalazi kao dimer, a svaka podjedinica veže dva iona mangana u binuklearnom veznom mjestu [3, 4]. Simulacijama molekulske dinamike istraženi su alosterički efekti koje izaziva vezanje Mn^{2+} iona u vezna mjesta MntR proteina.



Slika 1. Protein MntR iz bakterije *Bacillus subtilis*.

ZAHVALE

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FLUORESCENCE SPECTROSCOPIC STUDY OF THE INTERACTION OF DIFFERENTLY COATED GOLD NANOPARTICLES WITH DOPAMINE AND L-DOPA

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Efficient and safe treatment of patients suffering from Parkinson's disease possess many challenges. Common therapy that includes external administration of L-dopa to Parkinson's disease patients is limited due to poor blood-brain barrier (BBB) penetration and lack of targeting ability [1-2]. To overcome these issues, gold nanoparticles (AuNPs) represent an attractive platform for targeted drug delivery into the brain, as they enter the central nervous system (CNS) by penetration through the BBB [3-4]. For this purpose, AuNPs functionalized with polyethylene glycol (PEG), adamantane derivatives, and peptidoglycan monomer (PGM) were prepared [5]. In this study, the ability of novel AuNPs to be used as delivery systems for dopamine and L-dopa was evaluated considering their binding capabilities. Steady-state fluorescence spectroscopy was employed to investigate the binding interaction of dopamine and L-dopa on differently coated AuNPs. The strongest interaction was observed between L-dopa/dopamine and AuNPs functionalized with PGM. The intermolecular forces between L-dopa or dopamine and differently coated AuNPs were estimated by thermodynamic analysis. The binding predominantly occurred through Van der Waals interactions or hydrogen bonds, while positive entropy change that is indicative for electrostatic interactions was seen only in a few instances. In all cases, interactions were exothermic and spontaneous since enthalpy change and Gibbs free energy were negative, respectively.

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ISTRAŽIVANJE INTERAKCIJA RAZLIČITO FUNKCIONALIZIRANIH ZLATNIH NANOČESTICA S DOPAMINOM I L-DOPEOM PRIMJENOM FLUORESCENCIJSKE SPEKTROSKOPIJE

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Učinkovit i siguran tretman u liječenju Parkinsonove bolesti nailazi na brojne prepreke. Poznata terapija koja uključuje primjenu L-dope ograničena je zbog ograničenog prolaska kroz krvno-moždanu barijeru, odnosno nedostatne mogućnosti ciljanja određenih tkiva [1-2]. Kako bi se zaobišle ove prepreke, zlatne nanočestice mogu poslužiti kao učinkovit sustav za ciljanu dostavu lijekova u mozak zbog mogućnosti prolaska preko krvno-moždane barijere i ulaska u centralni živčani sustav [3-4]. U tu svrhu pripravljene su zlatne nanočestice koje su funkcionalizirane s polietilen glikolom, derivatima adamantana i peptidoglikan monomerom (PGM) [5]. Jakost vezanja L-dope i dopamina na nosivno funkcionalizirane zlatne nanočestice procijenjena je primjenom fluorescencijske spektroskopije u svrhu dobivanja najpogodnijeg sustava za ciljanu dostavu lijekova. Uočeno je da konstante vezanja ovise o različitoj funkcionalizaciji zlatnih nanočestica. Najjača interakcija vidljiva je između L-dope/dopamina i zlatnih nanočestica koje su funkcionalizirane s PGM-om. Termodinamičkom analizom utvrđeno je da su interakcije između L-dope i dopamina sa zlatnim nanočesticama većinom van der Waalsove interakcije ili vodikove veze, osim u par slučajeva gdje su primijećene elektrostatske interakcije na što je ukazivala pozitivna vrijednost promjene entropije. U svim slučajevima, promjena entalpije i promjena Gibbsove energije bila je negativna, što ukazuje da su interakcije egzotermne i spontane.

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MODELLING OF THE ADSORPTION OF PHARMACEUTICALLY ACTIVE COMPOUNDS ON CARBON-BASED NANOMATERIALS

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A wide range of pharmaceuticals enter water systems and consequently impact both aquatic and terrestrial ecosystems [1]. Carbon based nanomaterials (CNMs) have emerged as effective next-generation adsorbents, receiving increasing attention due to their potential in water and wastewaters treatment applications [2]. Understanding and acquiring knowledge about the adsorption of pharmaceuticals on CNMs is imperative to the chemical engineering applications of CNMs, as well as to risk assessment and pollution control of both CNMs and pharmaceuticals. Here we provide a computational assessment of the mechanism and thermodynamics of the adsorption of 18 most common pharmaceuticals on four different CNMs (pristine/functionalized graphene and carbon nanotube) in two different solvents (water and *n*-octanol). We show that the adsorption of pharmaceuticals on pristine CNMs is controlled by dispersion forces, π interactions and hydrophobic interaction. On the other hand, adsorption on functionalized CNMs is controlled by hydrogen bonding and Coulombic ionic interactions. Furthermore, we demonstrate how functionalization of CNM, CNM curvature and background solution properties modulate the intensity of non-covalent interactions and their contribution towards adsorption Gibbs free energy. With this knowledge, we pinpoint functionalized graphene at environmental pH as the most effective setting for the removal of a given set of PhACs from water and wastewater. Finally, we show that CNMs may transport pharmaceuticals into living organisms and release them in nonpolar mediums such as cellular membranes and fat cells. The obtained theoretical insights expand and complement experimental observations and provide important information which will contribute to further exploration into the adsorbent properties of CNMs, the evaluation of CNMs toxicity, and towards the development of predictive adsorption models.

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MODELIRANJE ADSORPCIJE FARMACEUTSKI AKTIVNIH TVARI NA UGLJIKOVE NANOMATERIJALE

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Širok spektar farmaceutski aktivnih tvari koje dospijevaju u vodne puteve imaju značajan utjecaj na vodene i kopnene ekosustave [1]. Ugljikovi nanomaterijali pokazali su se kao učinkoviti adsorbenti nove generacije, privlačeći sve više pozornosti zbog potencijala koji imaju u primjeni pri tretiranju vode i otpadnih voda [2]. Prikupljanje znanja i razumijevanje adsorpcije farmaceutski aktivnih tvari na ugljikove nanomaterijale od ključne je važnosti za kemijsko inženjerstvo primjene tih materijala kao i u ocjeni rizika zagađenja i kontroli zagađenja ugljikovim nanomaterijalima i farmaceutski aktivnim tvarima. U ovom radu predstavljamo analizu mehanizma i termodinamike adsorpcije 18 najčešćih farmaceutika na četiri ugljikova nanomaterijala u dva različita otapala metodama računalne kemije. Pokazujemo da je adsorpcija farmaceutika na netaknuti grafen pretežito kontrolirana disperznim interakcijama, π interakcijama te hidrofobnim efektom. Adsorpcija na grafen oksid, sa druge strane, kontrolirana je vodikovim vezama te ionskim interakcijama. Nadalje, demonstriramo kako utjecaj funkcionalizacije, zakrivljenosti ugljikovih nanomaterijala te svojstva otopine utječu na snagu nekovalentnih interakcija te njihov doprinos ukupnoj Gibbsovoj energiji adsorpcije. Ovaj uvid omogućuje nam da ukažemo na grafen oksid kao najefektivniji ugljikov nanomaterijal za uklanjanje danih farmaceutika iz otpadnih voda pri pH okoliša. U konačnici pokazujemo da ugljikovi nanomaterijali mogu prenijeti farmaceutike u žive organizme te ih otpustiti u nepolarnim medijima poput staničnih membrana i masnih stanica. Stečeni teoretski uvidi proširuju i nadopunjuju eksperimentalna opažanja te pružaju bitne informacije koje doprinose daljnjim istraživanjima adsorpcije na ugljikove nanomaterijale, procjene toksičnosti ugljikovih nanomaterijala te razvoju prediktivnih modela adsorpcije.

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INCLUSION COMPLEXES OF NABUMETONE WITH β -CYCLODEXTRIN AND ITS SELECTED DERIVATIVES

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Nabumetone (NAB) is a nonsteroidal anti-inflammatory prodrug which is clinically used for reducing pain and inflammation in the treatment of patients with osteoarthritis or rheumatoid arthritis. Its main active metabolite, 6-methoxy-2-naphthylacetic acid acts as a strong inhibitor of cyclo-oxygenase isoenzymes [1]. Since NAB possesses low aqueous solubility [2], it can be classified as a Class 2 drug substance according to The Biopharmaceutics Classification System.

Cyclodextrins (CDs) are group of cyclic oligosaccharides containing six (α -CD), seven (β -CD) or eight (γ -CD) D-glucopyranose units which are α -(1,4)-linked in a ring formation. Their structure is visualized as a truncated cone with hydrophilic outer surface and hydrophobic central cavity. Their ability of forming water soluble inclusion complexes with lipophilic drug molecules has been intensively studied [3].

Inclusion complexes of NAB with α -CD [4], γ -CD [2], β -CD and its derivatives [4, 5] have already been studied, as was the influence of α -CD and γ -CD on the enhancement of NAB solubility in unbuffered aqueous solution [6].

The aim of this study is to evaluate influence of β -CD and its hydroxypropyl (HP β CD), sulfobutylether (SBE β CD) and randomly methylated (RM β CD) derivatives on intrinsic solubility of NAB in water and in buffered aqueous solutions (simulated gastric fluid, pH 1.0.; simulated duodenal fluid, pH 4.5 and simulated intestinal fluid, pH 6.8) by means of phase-solubility analysis according to the existing Higuchi-Connors method [7]. In order to evaluate total drug solubility changes in the presence of increasing CD concentration phase-solubility diagrams were constructed. Quantitative determination of NAB was performed by developed UV/Vis spectrophotometric and spectrofluorimetric methods. Complexation of NAB with selected β -CDs was studied by fluorescence spectroscopy since CD-induced variation of native NAB fluorescence was noticed. In order to determine formation constants Benesi-Hildebrand plots were constructed [7].

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INKLUZIJSKI KOMPLEKSI NABUMETONA S β -CIKLODEKSTRINOM I NJEGOVIH ODABRANIM DERIVATIMA

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Nabumeton (NAB) je nesteroidni protuupalni predlijek koji se koristi za smanjivanje boli i upala prilikom liječenja pacijenata koji boluju od osteoartritisa ili reumatoidnih artritisa. Njegov glavni aktivni metabolit, 6-metoksi-2-naftiloctena kiselina djeluje kao snažan inhibitor izoformi enzima ciklooksigenaze [1]. Budući da je NAB slabo topljiv u vodi [2] on prema biofarmaceutskom sustavu klasifikacije djelatnih tvari spada u skupinu 2.

Ciklodekstrini (CD) čine skupinu cikličkih oligosaharida koji su građeni od šest (α -CD), sedam (β -CD) ili osam (γ -CD) D-glukopiranoznih jedinica koje su α -(1,4)-glikozidnom vezom povezane u prsten. Ciklodekstrini imaju oblik krnjeg stošca pri čemu je vanjska strana molekule hidrofilnog, dok je središnja šupljina hidrofobnog karaktera. Njihova sposobnost tvorenja topljivih inkluzijskih kompleksa s lipofilnim molekulama lijekova se već duže vrijeme intenzivno proučava [3].

Inkluzijski kompleksi NAB s α -CD [4], γ -CD [2], β -CD i njegovim derivatima [4, 5] su već proučavani, kao što je proučavan i utjecaj α -CD i γ -CD na poboljšanje njegove topljivosti u vodi [6].

Cilj ovog rada je utvrđivanje utjecaja β -CD i njegovog hidroksipropiliranog (HP β CD), alkilsulfoniranog (SBE β CD) i nasumično metiliranog (RM β CD) derivata na topljivost NAB u vodi te u puferiranim vodenim otopinama (simulirani želučani medij, pH 1,0.; simulirani duodenalni medij, pH 4,5 i simulirani intestinalni medij, pH 6,8) analizom poboljšanja topljivosti prema postojećoj Higuchi-Connors metodi [7]. Kako bi se utvrdile promjene u intrinzičnoj topljivosti lijeka u prisutnosti ciklodekstrina sa sukcesivnim porastom koncentracije konstruirani su dijagrami topljivosti. Kvantitativno određivanje NAB provedeno je razvijenim UV/Vis spektrofotometrijskim i spektrofluorimetrijskim metodama.

Kompleksiranje NAB s odabranim β -CD proučavano je fluorescencijskom spektroskopijom budući da je opažen utjecaj CD na nativnu sposobnost fluorescencije NAB. Kako bi se izračunale odgovarajuće konstante kompleksiranja konstruirani su Benesi-Hildebrand dijagrami [7].

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SYNTHESIS OF PROPARGYLIC EPOXIDES

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The synthesis of substituted propargylic epoxides for the purpose of stereoselective and regioselective ring opening by enzyme halohydrin dehalogenase was described. Using different nucleophiles, enantiomerically pure propargylic azidoalcohols and bicyclic triazole derivatives (N_3^-), propargylic oxazolidinone derivatives (OCN^-) and propargylic nitriloalcohols (NC^-) could be obtained [1]. Phenyl-, *tert*-butyl- and cyclopentyl- substituted epoxides were synthesized from the corresponding terminal acetylenes by introduction and epoxidation of a double bond. Also, *p*- and *m*-tolyl derivatives were synthesized in a similar reaction sequence, starting from the corresponding iodotoluene and trimethylsilylacetylene. Furthermore, attempts to prepare the phenyl derivative in two ways (in a reaction sequence similar to the synthesis of tolyl derivatives; and by derivatization of propargyl alcohol, oxidation of the obtained alcohol to aldehyde in several ways and its cyclization by sulfonium ylides), as well as the *p*-tolyl derivative by reacting *p*-iodotoluene with ethynylmagnesium bromide, were described.

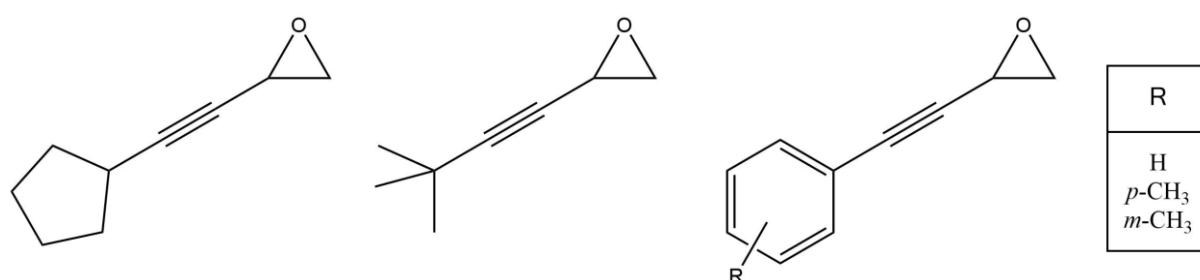


Figure 1. Synthesized propargylic epoxides

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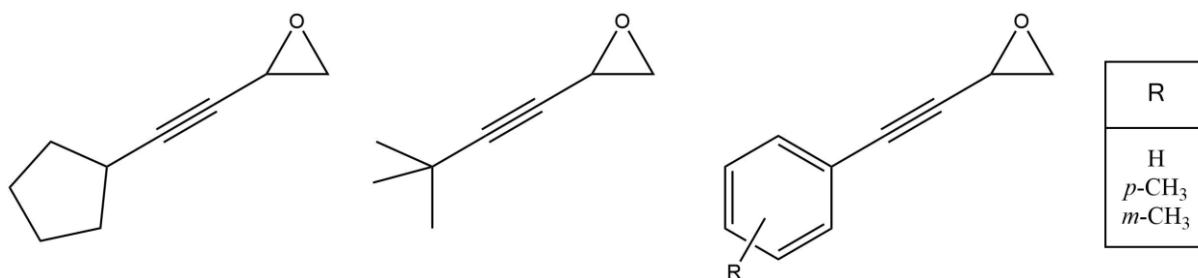
PRIPRAVA PROPARGILNIH EPOKSIDA

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Opisana je priprava supstituiranih propargilnih epoksida u svrhu stereoselektivnog i regioselektivnog otvaranja prstena pomoću enzima halohidrin dehalogenaze. Korištenjem različitih nukleofila, na ovaj način mogli bi se dobiti enantiomerno čisti propargilni azidoalkoholi i biciklički derivati triazola (N_3), propargilni derivati oksazolidinona (OCN), te propargilni nitriloalkoholi (NC) [1]. Fenil-, *tert*-butil- i ciklopentil-supstituirani epoksidi pripremljeni su iz odgovarajućih terminalnih acetilena uvođenjem i epoksidacijom dvostruke veze. Također su pripremljeni *p*- i *m*-tolilni derivati sličnim reakcijskim slijedom, plazeći od odgovarajućeg jodtoluena i trimetilsililacetilena. Nadalje, opisani su pokušaji priprave fenilnog derivata (reakcijskim slijedom sličnim pripravi tolilnih derivata; te derivatizacijom propargilnog alkohola, oksidacijom dobivenog alkohola do aldehida na nekoliko načina i njegovom ciklizacijom pomoću sulfonijevih ilida) te *p*-tolilnog derivata reakcijom *p*-jodtoluena i etinilmagnezijevog bromida.



Slika 1. Pripremljeni propargilni epoksidi

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STRUCTURAL CHARACTERISATION OF MACROCYCLIC SCHIFF BASE WITH INCLUDED AMMONIA, SULPHUR DIOXIDE AND CHLORINE

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Porous macrocycles are very interesting among the researchers in last years, mainly because of their potential applications in environmental sustainability. These materials can be classified as organic zeolites. Most of the investigations in this particular research area are based on the shape-persistent macrocycles that have a noncollapsible backbone and a well-defined inner void in the size range from less than 1 up to several nanometers [1]. Because of their rigid structure, organic zeolites have potential application as host materials. Furthermore, the size of voids can be rationally designed by utilization of supramolecular forces or by simple increase or decrease of a number of atoms in the macrocyclic ring [2]. The promising field of research in this area are macrocyclic Schiff bases that can be relatively easily synthesized by simple condensation reactions of suitable formyl and amino precursors. Among these materials, there is a great interest in macrocycles that can form porous structures and subsequently bind gaseous species [3]. This paper addresses synthetic procedures for obtaining a macrocyclic Schiff base, essentially built from dialdehyde and diamine precursors with included gases such as ammonia, sulfur dioxide, and chlorine. In this, presentation we report synthesis and crystallization of a large macrocyclic Schiff base, derived from *p*-phenyldiamine and 2-[5-(2-formylphenoxy)pentoxy]benzaldehyde. The compound was treated with ammonia, chlorine and sulfur dioxide vapors inside a sealed chamber for 3 hours to form a host-guest complex with those gases. The crystal and molecular structure of gas included compounds was determined by single-crystal X-ray analysis. The amount of absorbed gases was determined by TGA. In addition, the guest-free compound and gas loaded compound were characterized by FTIR to verify the stability of the organic framework.

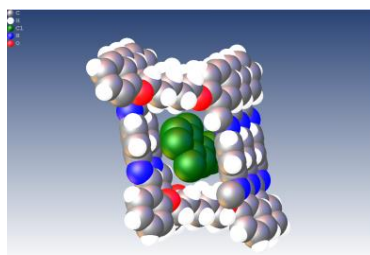


Figure 1. The molecular structure of Cl₂ included compound

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STRUKTURNA KARAKTERIZACIJA MAKROCIKLIČKE SCHIFFOVE BAZE S INKLUDIRANIM AMONIJAKOM, SUMPOROVIM DIOKSIDOM I KLOROM

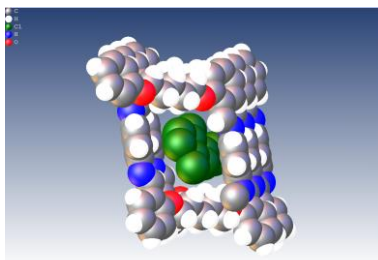
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Porozni makrociklički spojevi vrlo su zanimljivi među istraživačima posljednjih godina, uglavnom zbog njihove potencijalne primjene u kemiji okoliša. Ovi materijali mogu klasificirati kao organski zeoliti. Većina istraživanja u ovom području temelji se na makrociklima postojana oblika koji imaju rigidnu okosnicu i dobro definiranu unutarnju šupljinu u rasponu od 1 do nekoliko nanometara [1]. Zbog svoje rigidne strukture, organski zeoliti imaju potencijalnu primjenu kao materijali domaćini. Veličina šupljina može se dizajnirati korištenjem supramolekulskih interakcija ili jednostavnim povećanjem ili smanjenjem broja atoma u makrocikličkom prstenu [2]. Zanimljivi spojevi ovom području su makrocikličke Schiffove baze koje se mogu relativno lako sintetizirati jednostavnim reakcijama kondenzacije pogodnih formilnih i amino prekursora. Među tim materijalima postoji veliki interes za spojeve koji mogu tvoriti porozne strukture i potom vezati plinovite vrste [3]. Ovaj se rad bavi sintetskim postupcima za dobivanje makrocikličke Schiffove baze, koja je sintetizirana od dialdehida i diamina te su određenim postupcima u pore spoja ugrađeni plinovi amonijak, sumporni dioksid i klor. U ovom izlaganju prezentirani su sinteza i kristalizaciji makrocikličke Schiffove baze, izvedene iz p-fenilendiamina i 2-[5-(2-formilfenoksi)pentoksi] benzaldehida. Spoj je tretiran parama amonijaka, klora i sumporova dioksida unutar zatvorene komore tijekom 3 sata pri čemu nastaju domaćin-gost kompleksi s tim plinovima. Kristalna i molekulska struktura spojeva određena je rendgenskom strukturnom analizom. Količina apsorbiranih plinova određena je pomoću TGA. FTIR analizom potvrđena je stabilnost spoja pri ugradnji plinovitih vrsta.



Slika 1. Molekulska struktura spoja s ugrađenim molekulama klora.

ZAHVALE

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DETERMINATION OF PHOSPHODIESTERASE TYPE 5 INHIBITORS IN DIETARY SUPPLEMENTS USING LC-TOF METHOD

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Phosphodiesterase type 5 (PDE-5) inhibitors are used for the treatment of erectile dysfunction (ED) and represent an important group of adulterants in herbal dietary supplements.[1] The use of herbal dietary supplements has significantly increased during the last few decades and poses a serious health risk.[2] The aim of this study was to investigate herbal dietary supplements sold in the Croatian market for the presence of PDE-5 inhibitors and their analogues in the period 2017-2020. Chromatographic separation was achieved on Inertsil ODS-4 C18 column (150 mm x 2,1 mm; 3 μm) using a gradient elution with 5 mM ammonium formate and 0,1% (v/v) formic acid in water and acetonitrile with 0,1% formic acid as mobile phases at a flow rate of 0,3 mL min⁻¹. The detection was performed with time of flight (TOF) mass spectrometer in positive polarity equipped with electrospray interface. Identification was based on accurate mass measurement of protonated ion [M+H]⁺ and LC retention time of the analyte compared to the standard. In-source collision induced dissociation (CID) was used to generate fragment ions. The developed method has been successfully applied to examine 37 commercial “all natural” dietary supplements, and 20 (54%) of them proved to contain synthetic PDE-5 inhibitors. Sildenafil and tadalafil were most detected. Data obtained indicate that regular and consistent monitoring of the use of herbal dietary supplements is needed.

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ODREĐIVANJE FOSFODIESTERAZA TIP 5 INHIBITORA U DODACIMA PREHRANI PRIMJENOM LC-TOF METODE

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Inhibitori fosfodiesteraze tipa 5 (PDE-5) koriste se za liječenje erektilne disfunkcije (ED) i predstavljaju važnu skupinu patvoritelja u biljnim dodacima prehrani. [1] Korištenje biljnih dodataka prehrani znatno se povećalo tijekom posljednjih nekoliko desetljeća i predstavlja ozbiljnu opasnost za zdravlje ljudi. [2] Cilj ove studije bio je istražiti biljne dodatke prehrani koji se prodaju na hrvatskom tržištu u periodu 2017-2019 na prisutnost inhibitora PDE-5 i njihovih analoga. Kromatografsko odvajanje postignuto je na koloni Inertsil ODS-4 C18 (150 mm x 2,1 mm; 3 µm) uporabom gradijentne elucije s 5 mM amonijevog formata i 0,1% (v / v) mravlje kiseline u vodi i acetonitrila s 0, 1% mravlje kiseline kao pokretne faze pri brzini protoka od 0,3 ml min⁻¹. Detekcija je provedena uz analizator masa mjerenjem vremena preleta (TOF) u pozitivnom modu uz ionizaciju elektroraspršenjem. Identifikacija se temeljila na mjerenju točne mase protoniranog iona [M + H]⁺ i vremena zadržavanja analita u usporedbi sa standardom. Kolizijom inducirana disocijacija u izvoru (CID) korištena je za stvaranje fragmentnih iona. Razvijena metoda uspješno je primijenjena za ispitivanje 37 komercijalnih „prirodnih“ dodataka prehrani, u 20 (54%) uzoraka je potvrđena prisutnost sintetskih PDE-5 inhibitora. Najčešće su bili prisutni sildenafil i tadalafil. Dobiveni podaci pokazuju da je potrebno redovito i dosljedno praćenje primjene biljnih dodataka prehrani.

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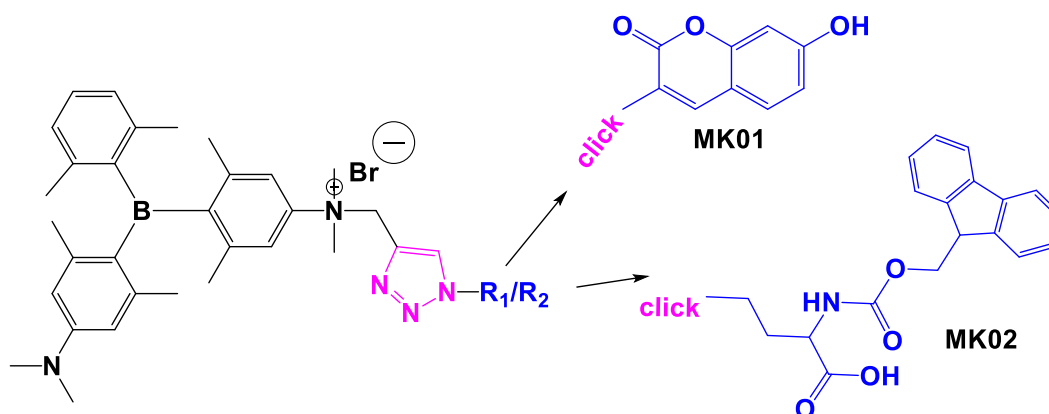
FLUORIMETRIC RECOGNITION BETWEEN DNA AND BSA DEPENDS ON TRIARYLBORONE CATIONE CONNECTIVITY TO FLUORESCENT SUPSTITUENT OR PEPTIDE SEQUENCE

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Small molecule fluorescent probes targeting DNA/RNA and proteins became unavoidable tools for monitoring biological processes due to their biochemical and biomedical applications. Until recently boron-containing polycyclic π -systems were considered unstable in water, but in 2012 was shown that planarised triarylboranes can be stable in water [1,2] and subsequently we showed that such dyes are intriguing fluorescent probes for biomacromolecules [3]. Here, we designed and prepared two novel conjugates of triarylborane cation, differing in type of “click” attached substituent (Scheme 1). Both conjugates showed fluorimetric selectivity between ds-DNA (*ct*-DNA) and protein (BSA), whereby MK02 excelled by complete quenching emission for DNA and strong increase for BSA.



Scheme 1. General structure of prepared triarylboranes conjugates.

ACKNOWLEDGMENTS

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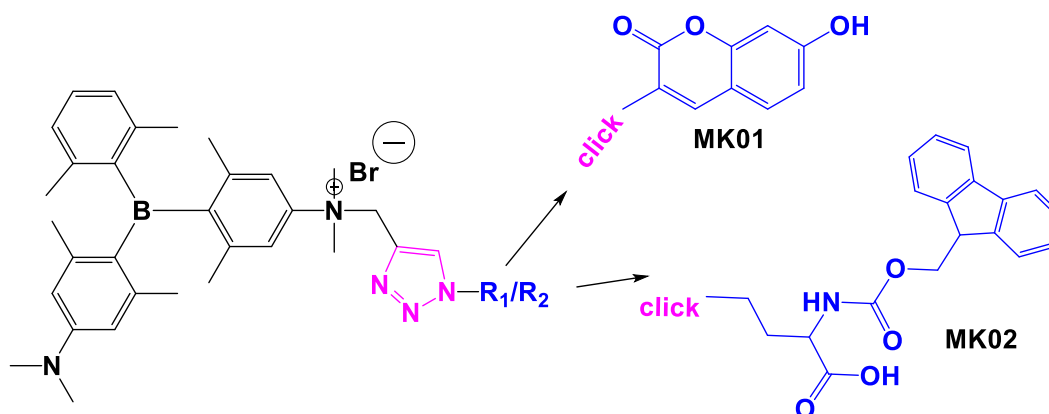


FLUORIMETRIJSKO PREPOZNAVANJE DNA I BSA OVISI O POVEZANOSTI KONJUGATA TRIARILBORANSKOG KATIONA S FLUORESCENTNOM SUPSTITUENTOM ILI SEKVENCOM PEPTIDA

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Male fluorescentne probe koje se nekovalentno vežu za DNA/RNA i proteine postale su nezaobilazan alat za praćenje brojnih bioloških procesa zbog svoje primjenjivosti u različitim biokemijskim i biomedicinskim procesima. Do nedavno su borovi policiklički aromatski sustavi (PAH) smatrani nestabilnima u vodi, no 2012. godine dokazano je da su planarni triarilborani stabilni u vodi [1,2] te da stvaraju nekovalentne interakcije s biomakromolekulama [3]. U sklopu našeg rada pripravljena su dva nova konjugata triarilboranskog kationa koji se međusobno razlikuju u vezanim supstituentima (Shema 1). Oba konjugata su pokazala različitu fluorimetrijsku selektivnost prema dvolančanoj DNA (*ct*-DNA) u odnosu na protein (BSA), pri čemu je MK02 pokazao potpuno gašenje emisije za DNA i snažni porast emisije za BSA.



Shema 1. Opća struktura ispitivanih triarilboranskih konjugata.

ZAHVALE

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CHARACTERISATION OF NEWLY SYNTHESIZED 7-HYDROXYCOUMARIN DERIVATIVES

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Phe-Arg-His motif (**1**) is known for forming a complex with Cu²⁺, which helps to protect synapses from copper-related oxidative damage, by resisting ROS generation. [1] Our goal was to synthesize a fluorescent marker that will also complex Cu²⁺ and bind to DNA/RNA, possibly cleaving backbone under controlled conditions. Arginine is replaced by lysine, to keep positive charge at pH 7, while avoiding interaction of guanidine with Cu²⁺. Histidine is replaced by triazole (moiety of similar ability to coordinate Cu²⁺), which is a product of click reaction and thus allows easy introduction of a variety of fluorescent markers, but in this work we attached well-known fluorescent sensor – 7-hydroxycoumarin (Figure 1).

The tautomeric equilibrium of 7-hydroxycoumarin, sensitive to solvent and pH, yields characteristic changes in its UV/Vis and fluorescence spectra. [2,3] Our newly synthesized compounds **2** and **3** showed not only expected pH-dependent changes in their UV/Vis fluorescence spectra but also up till now unprecedented analogous temperature dependence changes. Fluorimetric titrations at pH 7 showed that peptide-analogue **3** interacts with ds-DNA, at variance to single amino acid analogue **2**, stressing the importance of the Phe-Lys part for efficient DNA-binding. Study of **2** and **3** interactions with Cu²⁺, as well as corresponding **2**, **3**/Cu²⁺ complexes with ds-DNA, is in progress.

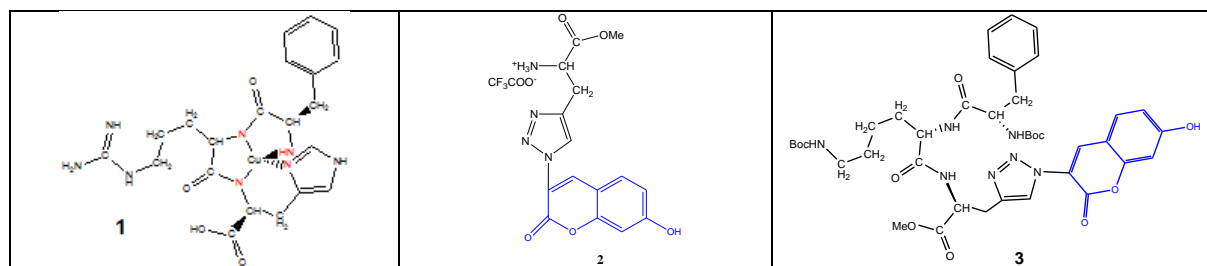


Figure 1.A: naturally occurring Cu-binding motif; **1**, new amino acid; **2**, peptide mimicking structure; **3**

ACKNOWLEDGMENTS

We thank HrZZ IP-2018-01-5475 for financial support.

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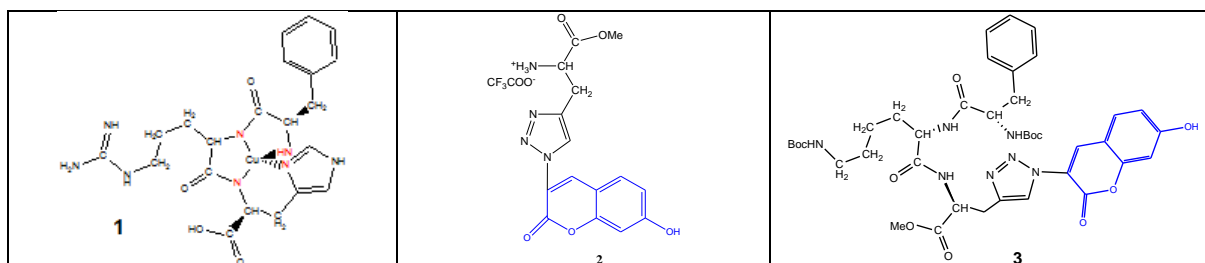
KARAKTERIZACIJA NOVOSINTETIZIRANIH DERIVATA 7-HIDROKSIKUMARINA

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Phe-Arg-His tripeptid, **1** poznat je po kompleksiranju Cu^{2+} , te pomaže u zaštiti sinapsi od oksidativnih oštećenja povezanih s bakrom, na način da sprječava generiranje ROS čestica. [1] Naš cilj je bio sintetizirati fluorescentnu probu koja će također kompleksirati Cu^{2+} i raditi interakcije s DNA/RNA, uz moguće cijepanje okosnice u kontroliranim uvjetima. Arginin je zamijenjen lizinom, kako bi se zadržao pozitivan naboj pri pH=7, ujedno i izbjegavajući reakciju gvanina s Cu^{2+} . Histidin je zamijenjen triazolom (koji ima sličnu sposobnost koordinacije Cu^{2+}), koji je produkt 'click' reakcije i stoga dopušta jednostavno uvođenje raznih fluorescentnih markera, ali u ovom radu smo uveli poznat fluorescentni senzor – 7-hidroksikumarin. Tautomerna ravnoteža 7-hidroksikumarina, osjetljivog na otapalo i pH, daje karakteristične promjene u spektru UV/Vis i fluorescencije. [2,3] Naši nosintetizirani spojevi **2** i **3** pokazali su, ne samo očekivane promjene pH vrijednosti u spektru fluorescencije UV / Vis, već i dosad neviđene analogne promjene ovisnosti o temperaturi. Fluorimetrijske titracije pri pH 7 pokazale su da peptid-analog **3** stupa u interakciju s ds-DNA, u suprotnosti s aminokiselinskim analogom **2**, naglašavajući važnost Phe-Lys dijela za učinkovito vezivanje DNA. U toku je proučavanje **2** i **3** interakcija s Cu^{2+} , kao i odgovarajućih **2,3** / Cu^{2+} kompleksa s ds-DNA.



Slika 1. Prirodni tripeptid koji kompleksira Cu^{2+} ; **1**, nova aminokiselina; **2**, spoj koji oponaša peptid; **3**

ZAHVALE

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THE INFLUENCE OF REACTION CONDITIONS ON OBTAINING POLYOXALATOMOLYBDATES OF VARIOUS NUCLEARITY

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The main driving forces responsible for the formation of polyoxomolybdates (POMos) are various interactions and self-assembly processes between $[\text{MoO}_4]^{2-}$ anions. Most common synthetic methods involve acidification of aqueous solutions containing $[\text{MoO}_4]^{2-}$ anion or neutralization of the molybdenum trioxide solution [1]. The main goal of modern POMo studies is the synthesis of materials with specific properties and applications. In our previous research we have postulated that hydrogen bonding capacity of counterions and reaction conditions greatly influence the condensation processes in POMo chemistry [2,3] which led us to use $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]^+$ and $[\text{Co}(\text{CO}_3)(\text{NH}_3)_4]^+$ as a counterion in POMo synthesis from $[\text{MoO}_4]^{2-}$ units in the presence of different molar ratios of oxalic acid. Solution-based synthesis reactions were performed in an aqueous medium at room temperature or at 110°C. Depending on the reaction conditions (method, pH, concentration of oxalic acid), following products were isolated and characterized: $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{MoO}_4]$, $[\text{Co}^{\text{III}}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{Co}^{\text{II}}(\text{C}_2\text{O}_4)_2(\text{H}_2\text{O})_2]$, $\text{Na}_3[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4][\text{Mo}_2\text{O}_4(\mu\text{-O})_2(\text{C}_2\text{O}_4)_2]$, $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_4[\text{Mo}_3\text{O}_6(\mu\text{-O})_2(\text{C}_2\text{O}_4)_3(\text{H}_2\text{O})_2]$ and $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{Mo}_2\text{O}_5(\text{C}_2\text{O}_4)_2(\text{H}_2\text{O})_2]$.

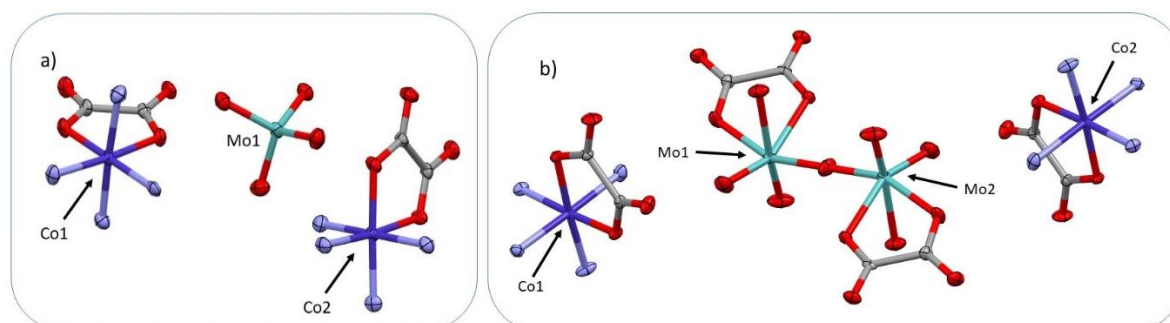


Figure 1. ORTEP plot of $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{MoO}_4]$ (a) and $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{Mo}_2\text{O}_5(\text{C}_2\text{O}_4)_2(\text{H}_2\text{O})_2]$ (b) with a partial numbering scheme (numbering for metal atoms only is shown; hydrogen atoms were omitted for clarity).

ACKNOWLEDGMENTS

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UTJECAJ REAKCIJSKIH UVJETA NA DOBIVANJE POLIOKSALATOMOLIBDATA RAZLIČITE NUKLEARNOSTI

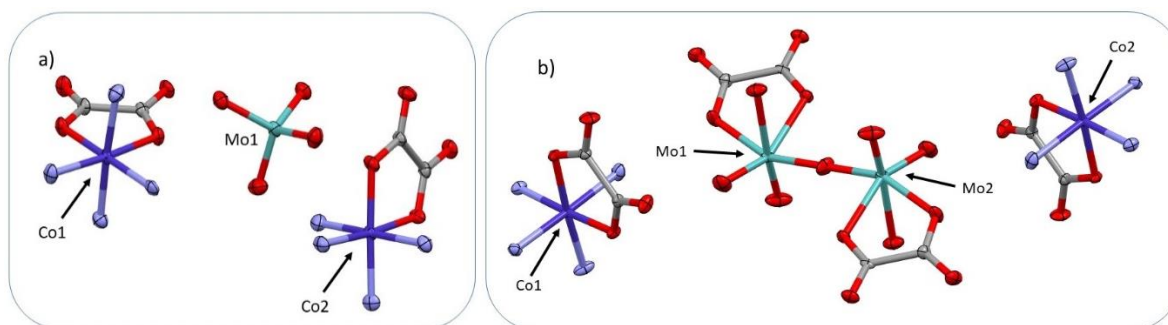
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Glavne sile odgovorne za formiranje polioksomolibdata (POMo) su razne interakcije i procesi samoudruživanja $[\text{MoO}_4]^{2-}$ aniona. Najčešće metode pripreme takvih spojeva uključuju zakiseljavanje vodenih otopina koje sadrže $[\text{MoO}_4]^{2-}$ anion te neutralizaciju otopine molibdenova trioksida [1]. Cilj modernih istraživanja POMo je sinteza materijala specifičnih svojstava i primjena. U našim prethodnim istraživanjima postulirali smo da reakcijski uvjeti i sposobnost protuiona da stvaraju vodikove veze uvelike utječu na procese kondenzacije u kemiji POMo [2,3] što nas navodi na korištenje $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]^+$ i $[\text{Co}(\text{CO}_3)(\text{NH}_3)_4]^+$ kationa kao protuiona u sintezi POMo iz $[\text{MoO}_4]^{2-}$ jedinica uz prisustvo različitih molarnih omjera oksalne kiseline. Otopinske sinteze su provedene u vodenim medijima pri sobnoj temperaturi ili pri 110°C . Ovisno o reakcijskim uvjetima (metoda, pH, koncentracija oksalne kiseline), izolirani su i okarakterizirani sljedeći produkti: $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{MoO}_4]$, $[\text{Co}^{\text{III}}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{Co}^{\text{II}}(\text{C}_2\text{O}_4)_2(\text{H}_2\text{O})_2]$, $\text{Na}_3[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4][\text{Mo}_2\text{O}_4(\mu\text{-O})_2(\text{C}_2\text{O}_4)_2]$, $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_4[\text{Mo}_3\text{O}_6(\mu\text{-O})_2(\text{C}_2\text{O}_4)_3(\text{H}_2\text{O})_2]$ te $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{Mo}_2\text{O}_5(\text{C}_2\text{O}_4)_2(\text{H}_2\text{O})_2]$.



Slika 1. ORTEP prikaz $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{MoO}_4]$ (a) i $[\text{Co}(\text{C}_2\text{O}_4)(\text{NH}_3)_4]_2[\text{Mo}_2\text{O}_5(\text{C}_2\text{O}_4)_2(\text{H}_2\text{O})_2]$ (b) s djelomičnom numeracijom atoma (prikazana je samo numeracija metalnih atoma; atomi vodika su izostavljeni radi preglednosti).

ZAHVALE

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HOMO- AND HETEROPOLYNUCLEAR COMPOUNDS OBTAINED USING $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ or Fe) AS BUILDING BLOCKS AND ALKYL-SUBSTITUTED AMINES

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Multifunctional properties of the coordination polymers can often be achieved by combining the intrinsic properties of the host, especially the magnetic ones, with an additional functionalities coming from the selected guest molecules [1]. The oxalate group, $C_2O_4^{2-}$, has been demonstrated to be one of the most versatile ligands used in the preparation of these systems. Due to its various coordination modes towards the metal centres as well as its ability to mediate magnetic interactions between paramagnetic metal ions, a large number of oxalate-based transition-metal species of different nuclearity, connectivity and dimensionality have been synthesized and characterized, many of them having tunable magnetic frameworks [2].

Since their discovery, homo- and heterometallic 2D and 3D oxalate-based extended networks of a general formula $[M_a^{I/III}M_b^{I/III}(C_2O_4)]_n^{2n-/n-}$, obtained from a combination of tris(oxalato)metalates, $[M^{III}(C_2O_4)_3]^{3-}$, with other metallic ions, using different template cations, have attracted a lot of attention. The anionic networks provide magnetic properties (ferro-, antiferro-, or ferrimagnetic ordering) depending on the nature of the connected metal ions. Furthermore, these reported polymers are mostly negatively charged and therefore can be combined with different (functional) molecular cations in order to afford salts combining cooperative magnetism with a second property of interest hence forming multifunctional materials. Recently published oxalate-based networks have shown high humidity-dependent proton conductivity related to the presence of substituted ammonium and/or crystallization water which form hydrophilic layers that enabled conductive pathways of protons [2,3].

To achieve our final goal – the development of materials containing noteworthy structural, magnetic and/or electrical features, novel homo- and heteropolynuclear oxalate-based systems have been synthesized using tris(oxalato)metalates, $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ or Fe), as ligands towards second transition metal ion (Mn^{II} or Cu^{II}) and *N,N*-diethylmethylamine or *N,N*-dimethylethylamine. In addition to the single crystal X-ray diffraction study, characterization of the new complexes has been accomplished by means of the IR spectroscopy and thermal analysis.

ACKNOWLEDGMENTS

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HOMO- I HETEROPOLINUKLEARNI SPOJEVI DOBIVENI KORIŠTENJEM GRAĐEVNIH BLOKOVA $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ ili Fe) I ALKIL SUPSTITUIRANIH AMINA

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Višefunkcionalna svojstva koordinacijskih polimera mogu se često dobiti kombiniranjem unutarnjih svojstava domaćina, kao što je magnetizam, sa svojstvima molekula gosta [1]. U pripravi ovih sustava veliku važnost ima oksalatna skupina, $C_2O_4^{2-}$. Zbog različitih načina koordiniranja na metalne centre kao i sposobnosti posredovanja u magnetskoj interakciji između paramagnetskih metalnih iona, sintetiziran je i okarakteriziran veliki broj oksalatnih spojeva prijelaznih metala različite nuklearnosti, povezivanja i dimenzionalnosti, dok mnogi od njih imaju prilagodljive magnetske mreže [2].

Otkada su otkrivene homo- i heterometalne 2D- i 3D-oksalatne mreže opće formule $[M_a^{II/III}M_b^{I/II}(C_2O_4)]_n^{2n-/n-}$, priređene korištenjem tris(oksalato)metalatnih aniona, $[M^{III}(C_2O_4)_3]^{3-}$, u reakciji s drugim metalnim ionima, uz dodatak različitih templatirajućih kationa, plijene veliku pažnju. Anionska mreža osigurava magnetska svojstva (fero-, antifero-, ili ferimagnetsko uređenje) ovisna o prirodi premoštenih metalnih iona. Nadalje, ovako priređeni polimeri su uglavnom negativno nabijeni te se kombiniraju s različitim funkcionalnim kationskim molekulama kako bi se dobili funkcionalni materijali koji pored kooperativnog magnetizma sadrže i drugo svojstvo od interesa. Nedavno su istražene oksalatne mreže koje pokazuju veliku protonsku vodljivost u ovisnosti o vlažnosti, kao posljedicu prisutnosti supstituiranog amonijaka i/ili molekula kristalnih vode, koji tvore hidrofilne slojeve omogućavajući tako protonima vodljive putove [2,3].

Kako bi se postigao naš konačni cilj – razvoj materijala sa zanimljivim strukturnim, magnetskim i / ili električnim svojstvima, priređeni su novi homo- i heteropolinuklearni oksalatni spojevi korištenjem tris(oksalato)metalatnih aniona, $[M^{III}(C_2O_4)_3]^{3-}$ ($M^{III} = Cr$ ili Fe), kao liganada prema drugim prijelaznim metalnim ionima (Mn^{II} ili Cu^{II}), i *N,N*-dietilmetilamina ili *N,N*-dimetiletilamina. Za karakterizaciju novih kompleksnih spojeva, uz difrakciju rendgenskih zraka u monokristalu, korištena je infracrvena spektroskopija te termička analiza.

ZAHVALA

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POLYOXOMOLYBDATES OF VARIOUS NUCLEARITIES FUNCTIONALIZED WITH Mo(VI) HYDRAZONE COMPLEXES

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The development of novel synthetic routes to achieve polyoxometalate (POM) architectures is an attractive research field because POMs are, among others, materials with catalytic, magnetic, bioactive, and energy storage properties. There are two ways of functionalizing inorganic-organic hybrid POMs, one being by the formation of polyoxometalate salt with organic or metal-organic cation and the other one by the substitution of the oxo atoms [1,2]. Bearing in mind previously stated facts, the tendency of dioxobis(pentane-2,4-dionato)molybdenum(VI) towards hydrolysis in wet acetonitrile solutions, as well as the solubility of hydrazones [3] we hypothesized the possible formation of hexamolybdate and octamolybdate hybrides functionalised by the hydrazone complexes. All hybrides were achieved by using aroylhydrazone ligands derived from (iso)nicotinoylhydrazide and differently substituted salicylaldehydes. Structurally diverse POMs with cations of various protonation states were obtained. Characteristic bands in the IR spectra showed facile differentiation of POMs with different nuclearities whereas crystal and molecular structures were unambiguously determined by single-crystal X-ray diffraction.

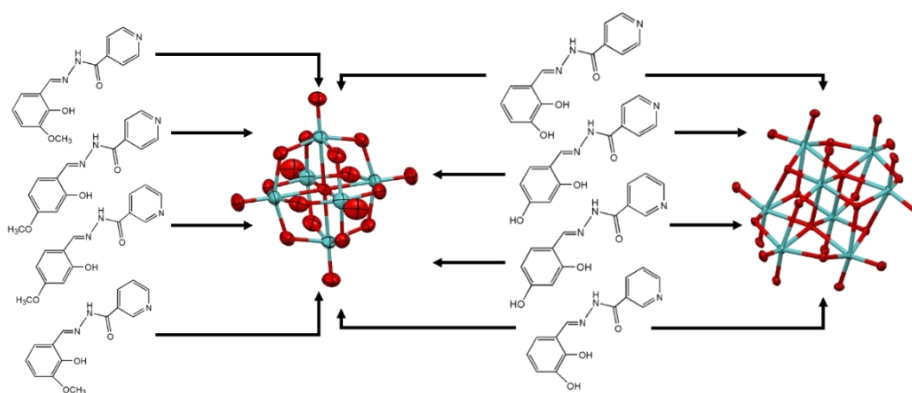


Figure 1. Formation of hexa- and octamolybdate species dependent on the ligand used.

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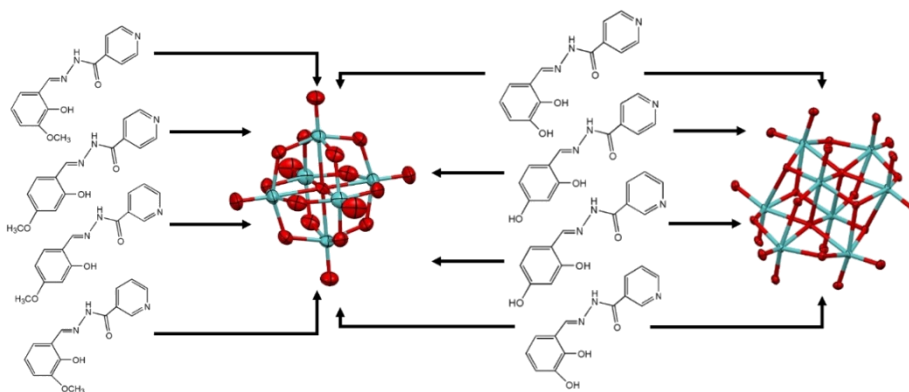
POLIOKSOMOLIBDATI RAZLIČITIH NUKLEARNOSTI FUNKCIONALIZIRANI HIDRAZONSKIM KOMPLEKSIMA Mo(VI)

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Razvoj novih sintetskih metoda za pripremu polioksometalnih (POM) struktura je atraktivno područje istraživanja jer POM-ovi, između ostalih, posjeduju katalitička, magnetska, biološki aktivna i svojstva za pohranu energije. Dva su načina funkcionalizacije anorgansko-organskih hibridnih POM-ova, jedan je nastajanjem soli polioksometalata s organskim ili metalo-organskim kationom, a drugi zamjenom terminalnog okso atoma [1,2]. Imajući na umu prethodno spomenuto, kao i tendenciju ka hidrolizi dioksobis(pentan-2,4-dionato)molibdena(VI) u vlažnom acetonitrilu te topljivost hidrazona [3], pretpostavili smo mogućnost nastanka heksamolibdatnih i oktamolibdatnih vrsta funkcionaliziranih s hidrazonato kompleksnim kationima. Svi hibridi priređeni su s arilhidrazonskim liganadima nastalim reakcijom (izo)nikotinhidrazida s derivatima salicilaldehidima. Dobiveni su strukturno različiti POM-ovi u čijim su strukturama kationi različitog stupnja protonacije. Karakteristične vrpce u IR spektrima ukazale su na jednostavno razlikovanje POM-ova različitih nuklearnosti dok su kristalne i molekulske strukture nedvojbeno određene difrakcijom rentgenskog zračenja u jediničnim kristalima.



Slika 1. Formiranje heksa- i oktamolibdatnih vrsta ovisno o korištenom ligandu.

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EFFECT OF FATTY ACID PROPYL ESTERS ON SURFACE TENSION, VISCOSITY AND DENSITY OF BLENDS WITH DIESEL FUEL

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The advantages of biomass are that it contains negligible amounts of sulfur, nitrogen and metals and it is a renewable source of carbon that can be converted into liquid fuel. Vegetable oils are produced from plant biomass by extraction, but their high viscosity disables its direct application in diesel engines. [1] This disadvantage is overcome by transesterification of triglycerides from vegetable oils and alcohols, mostly methanol, thus result in fatty acid alkyl esters, i.e. biodiesel. Although methanol and ethanol are predominantly used, advantages of propanol, due to the additional carbon atom in its structure, are better blending capabilities, higher cetane number and calorific value. [2] Considering that and the fact that Croatia has high yields of sunflower crops, transesterification is carried out with sunflower oil in the presence of a basic catalyst (KOH). The aim of this study was to investigate the addition of propanol and propyl esters on application properties of blends with diesel fuel for use in internal combustion engines. By increasing the content of propyl esters, surface tension values increased which can have a negative influence on fuel injection in engines. Also, the addition of propyl esters caused an increase in kinematic viscosity which can result in better lubricity.



Figure 1. Pendant drop images of blends

ACKNOWLEDGMENTS

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UTJECAJ PROPILNIH ESTERA MASNIH KISELINA NA NAPETOST POVRŠINE, VISKOZNOST I GUSTOĆU MJEŠAVINA S DIZELOM

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Prednost je biomase što sadrži zanemarive količine sumpora, dušika i metala te obnovljivi je izvor ugljika koji se može pretvoriti u tekuće gorivo. Biljna ulja dobivaju se preradom biomase, postupkom ekstrakcije, no njihova velika viskoznost onemogućava izravnu primjenu u dizelskom motoru.[1] Taj nedostatak prevladan je reakcijom transesterifikacije triglicerida iz biljnih ulja s alkoholima, metanolom, čime nastaju alkilni esteri masnih kiselina, odnosno biodizel. Iako su najčešće korišteni alkoholi metanol i etanol, propanol zbog dodatnog ugljikovog atoma u lancu posjeduje određene prednosti poput bolje mješljivosti s dizelom, većeg cetanskog broj i toplinske vrijednosti.[2] Uzevši to u obzir i činjenicu da Hrvatska ima visoke prinose suncokreta, reakcija transesterifikacije provedena je u suncokretovom ulju uz bazični katalizator (KOH). Cilj je bio ispitati utjecaj dodataka propanola i propilnih estera na svojstva mješavina s mineralnim dizelom za primjenu u motorima s unutarnjim izgaranjem. Ispitivanjem je utvrđeno povećanje napetosti površine s povećanjem udjela propilnih estera što može negativno utjecati na raspršivanje kapi u motoru. Također, dodatkom propilnih estera došlo je do povećanja vrijednosti kinematičke viskoznosti što može rezultirati boljom mazivošću.



Slika 1. Snimke visećih kapi namješanih uzoraka

ZAHVALE

Projekt Hrvatske zaklade za znanost Razvoj funkcionalnih biogoriva i (bio)aditiva te ispitivanje primjenskih svojstava mješavina s mineralnim gorivima (FunBioFA, UIP-2019-04-5242)

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PREPARATION OF LIPOPHILIC PRECURSORS FOR SYNTHESIS OF NEW DESMURAMYL DIPEPTIDE DERIVATIVES

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Adjuvants are substances that are added to vaccines to improve the human immune response. The well-known adjuvants are muramyl dipeptide derivatives (MDP, *N*-acetylmuramyl-L-alanyl-D-isoglutamine) as well as desmuramyl dipeptide derivatives (L-Ala-D-isoGln), MDP analogs without the sugar *N*-acetylmuramyl unit [1]. L-Ala-D-isoGln pharmacophore is essential for the immunostimulatory properties and the introduction of lipophilic substituent can increase its adjuvant activity [2]. So far, some of lipophilic derivatives have been prepared in our laboratory and their adjuvant activity was tested *in vivo*, primarily the adamantyl-triazole derivative with or without mannose subunit.

Our further research is focused on modifying the mannosylated desmuramyl dipeptide by different lipophilic subunits that are linked to α -position of D-isoGln subunit through an amide bond via triazole ring (Figure 1). For this purpose, various lipophilic (hexadecyl, dodecyl, cholesteryl and 2-(adamantan-1-yl)ethyl) 1,4-disubstituted triazole subunits have been prepared by click-reaction from corresponding pre-prepared azides with propargylamine. [3] Click-reactions were performed in the presence of di-*tert*-butyl dicarbonate (Boc₂O) wherein, in addition to the formation of a substituted triazole ring, propargylamine amino group was protected *in situ*. Target lipophilic propargylamine derivatives were prepared by removal of the Boc protection in the last step. They will be used as precursors for the synthesis of new triazole desmuramyl dipeptide and mannosylated desmuramyl dipeptide derivatives which will be tested for their adjuvant activity.

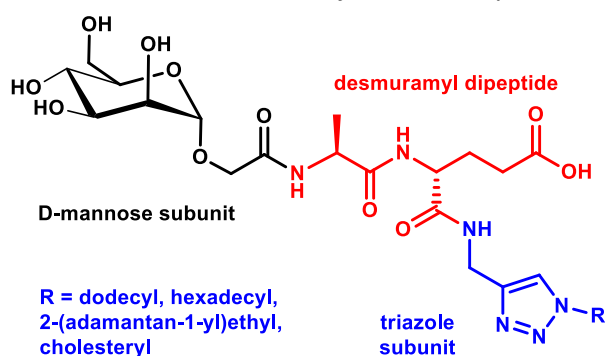


Figure 1. Lipophilic triazole derivatives of desmuramyl dipeptide with mannose subunit

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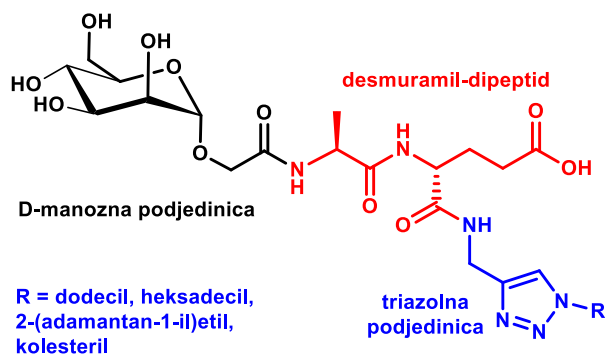
PRIPRAVA LIPOFILNIH PREKURSORA ZA SINTEZU NOVIH DESMURAMIL-DIPEPTIDNIH DERIVATA

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Adjuvanti su tvari koje se dodaju cjepivima radi pojačavanja imunološkog odgovora. Derivati muramil-dipeptida (*N*-acetilmuramil-L-alanil-D-izoglutamin, MDP) kao i derivati desmuramil-dipeptida (L-Ala-D-*iso*Gln), MDP-a bez šećerne *N*-acetilmuraminske komponente spadaju među poznatije adjuvante [1]. L-Ala-D-*iso*Gln podjedinica nužna je za imunostimulacijska svojstva, a uvođenjem lipofilnih podjedinica može se povećati njezina adjuvantska aktivnost [2]. Do sada su u našem laboratoriju pripremljeni neki lipofilni derivati, prije svega adamantil-triazolni derivat, sa ili bez manozne podjedinice, te im je ispitan adjuvantski učinak.

Daljnje istraživanje usmjereno je na modificiranje desmuramil-dipeptida različitim lipofilnim podjedinicama vezanim amidnom vezom preko triazolnog prstena na α -položaj D-*iso*Gln podjedinice (Slika 1). U tu svrhu klik-reakcijom iz prethodno pripremljenih azida i propargilamina dobivene su različite lipofilne (heksadecil, dodecil, kolesteril i 2-(adamantan-1-il)etil) 1,4-disupstituirane triazolne podjedinice [3]. Klik-reakcije provedene su u prisutnosti di-*tert*-butil-dikarbonata (Boc₂O) pri čemu je, uz nastajanje supstituiranog triazolnog prstena, *in situ* zaštićena i amino-skupina propargilamina. Uklanjanjem Boc zaštite u posljednjem koraku pripremljeni su ciljni lipofilni derivati propargilamina. U daljnjim istraživanjima oni će poslužiti kao prekursori za sintezu novih triazolnih derivata desmuramil-dipeptida i manoziliranih desmuramil-dipeptida kojima će biti ispitana adjuvantska aktivnost.



Slika 1. Lipofilni triazolni derivati desmuramil-dipeptida s manoznom podjedinicom

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MACHINE LEARNING-BASED PREDICTION OF MULTI-TARGET ANTIMICROBIAL ACTIVITY

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Reduced space of multi-target antimicrobial activities was used as a dependent variable for estimation of *Cinchona* alkaloids derivatives [1] activities. A panel of various Gram-positive and Gram-negative bacteria provided activity data whose principal components were extracted by 2nd-order tensor decomposition. These principal components were regressed on the theoretically computed energy fingerprints of all compounds.

Extensive machine learning procedure was applied for generation of multivariate linear regression models with linear combination of original variables as well as their higher-order polynomial terms. Regression models of antimicrobial activity in dependence on molecular dynamics data were builded and thoroughly validated by *leave-one-out cross-validation* technique (LOO-CV) [2]. The most optimal representation was selected on the basis of R^2 values and LOO-CV mean squared error and is presented on Fig. 1.

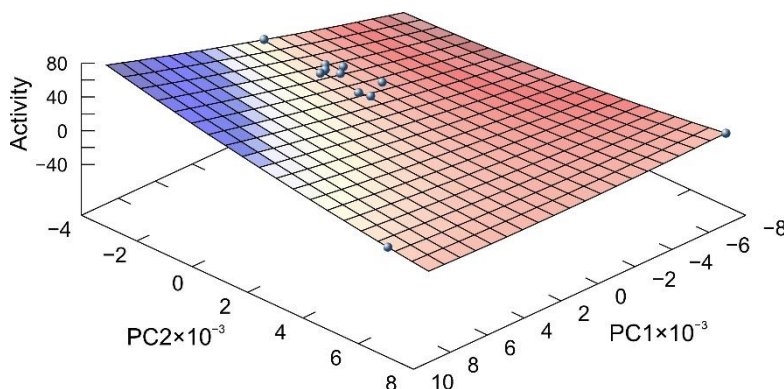


Figure 1. 2D cut of regression model.

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ODREĐIVANJE VIŠECILJNE ANTIMIKROBNE AKTIVNOSTI PRIMJENOM STROJNOG UČENJA

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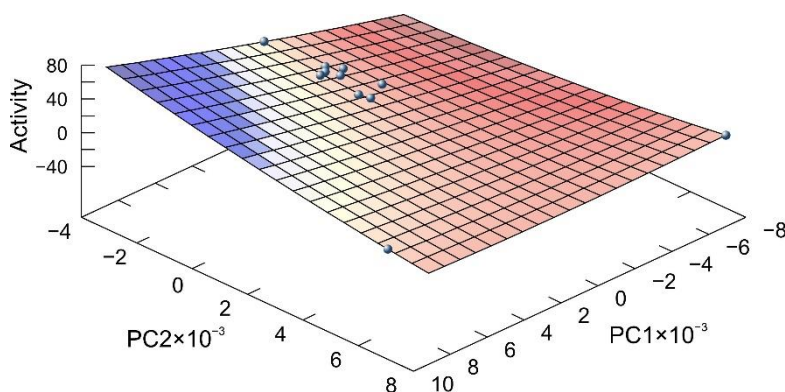
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Reducirani prostor višeciljnih antimikrobnih aktivnosti iskorišten je kao ovisna varijabla za procjenu aktivnosti derivata *Cinchona* alkaloida [1]. Za panel Gram-pozitivnih i Gram-negativnih bakterija određeni su podaci o aktivnosti čije su glavne komponente izračunane dekompozicijom tenzora drugog reda. Regresijskom analizom ispitana je korelacija između tih glavnih komponenata i teorijski izračunanih energijskih "otisaka prsta" svih spojeva.

Ekstenzivna procedura strojnog učenja primjenjena je za modele multivarijatne linearne regresije s linearnim kombinacijama originalnih varijabli kao i njihovim polinomnim članovima višeg reda. Napravljeni su regresijski modeli antimikrobne aktivnosti u ovisnosti o podacima dobivenim molekularnom dinamikom te su ti modeli detaljno validirani tehnikom *leave-one-out cross-validation* (LOO-CV) [2]. Na temelju vrijednosti R^2 i srednje kvadratne pogreške LOO-CV odabrana je najoptimalnija reprezentacija podataka (prikazana na slici 1).



Slika 1. Dvodimenzijski presjek regresijskog modela.

ZAHVALE

Rad izrađen je u okviru projekata Hrvatske zaklade za znanost: "Projekt razvoja karijera mladih istraživača - izobrazba novih doktora znanosti" (ESF-DOK-2018-09-3416) te "Aktivnošću i in silico usmjeren dizajn malih bioaktivnih molekula" (IP-2016-06-3775).

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BIODEGRADATION OF MICROPLASTICS BY GRAM NEGATIVE BACTERIA FROM GENERA OF *Pseudomonas* AND *Delftia*

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Large amounts of discarded plastics in the environment, as a consequence of human globalization and development and poor waste management, are directly influenced by abiotic and biotic factors within ecosystems resulting in the formation of plastic particles smaller than 5 mm defined as microplastics [1]. These particles cannot be easily detected, identified and removed from the environment, and due to their toxic effects they can have detrimental effects on ecosystem components as well as on ecological balance. Biodegradation is one of the most commonly used method for removing microplastics from the environment, and in order to be highly effective, it is necessary to optimize significant process parameters. The biological degradation of microplastics depends on their physical and chemical properties and on the properties of the microorganisms themselves [2]. In this study, biodegradation of polyethylene (PE) and polystyrene (PS) by bacteria *Pseudomonas aeruginosa*, *Pseudomonas alcaligenes*, and *Delftia acidovarans* was investigated. During 57 days of the experiment, pH-value, temperature, concentration of dissolved oxygen, colony forming units (CFU), total organic carbon (TOC), inorganic carbon (IC), ionic composition and HPLC analysis of aquatic phase were monitored. Functional groups in the PE and PS structures were analyzed by FTIR-ATR analysis. The obtained results indicate that tested bacterial cultures have the ability to degrade PE and PS.

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BIORAZGRADNJA MIKROPLASTIKE PRIMJENOM GRAM NEGATIVNIH BAKTERIJA RODA *Pseudomonas* I *Delftia*

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Velike količine odbačene plastike u okolišu, kao posljedica ljudske globalizacije i razvitka te lošeg gospodarenja otpadom, pod direktnim su utjecajem abiotičkih i biotičkih faktora unutar ekosustava što rezultira nastankom čestica plastike manjim od 5 mm definiranom kao mikroplastika [1]. Te čestice nije jednostavno detektirati, identificirati i ukloniti iz okoliša, a zbog toksičnih efekata mogu imati štetno djelovanje na sastavnice ekosustava, kao i na ekološku ravnotežu. Biorazgradnja je jedna od najčešće primjenjivanih metoda za uklanjanje mikroplastike iz okoliša, a da bi se postigao visok postotak uklanjanja potrebno je optimirati značajne procesne parametre. Biološka razgradnja mikroplastike ovisi o njihovim fizikalnim i kemijskim svojstvima te o svojstvima samih mikroorganizama [2]. U ovome je radu istraživana biorazgradnja polietilena (PE) i polistirena (PS) primjenom bakterija *Pseudomonas aeruginosa*, *Pseudomonas alcaligenes* i *Delftia acidovarans*. Tijekom 57 dana provedbe eksperimenta, praćena je pH-vrijednost, temperatura, koncentracija otopljenoga kisika, broj živih stanica bakterija (CFU), ukupni organski ugljik (TOC), anorganski ugljik (IC), ionski sastav te HPLC analiza vodene faze. Funkcionalne skupine u strukturi PE i PS analizirane su FTIR-ATR analizom. Dobiveni rezultati ukazuju da ispitivane bakterijske kulture imaju sposobnost razgraditi PE i PS.

ZAHVALE

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MODULATING MECHANICAL FLEXIBILITY OF CADMIUM(II) COORDINATION COMPOUND *via* CO-CRYSTALLIZATION

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Flexibility of crystals with inner metal-organic structure has hit the spotlight in the last few years with respect to mechanical response of organic crystals that already have somewhat broader scope of investigation regarding this topic. [1, 2] Since it has been known that mechanical properties of materials could be controlled *via* fine interplay between building blocks and intermolecular interactions in the crystal structure, understanding those correlations is of crucial importance in establishing unambiguous paths for rational design of solid-state architecture with desired properties e.g. bendability. This engineering approach is of great importance today since the interest of knowing and determining properties of molecular solids spans over different areas of research in which it can be applicable (e.g. optical waveguides, flexible electronics and others). [3]

It appears that introducing co-former in the crystal structure of cadmium(II) iodide coordination polymer equipped with iodopyrazine molecules (i.e. co-crystallization of the initial polymer) changes the degree of flexible response when comparing with the bending strain of the starting coordination polymer, which has been reported in literature [2]. To explain modified mechanical properties, relations between molecular structure and intermolecular interactions in the crystal structures of prepared co-crystals were studied and some guidelines have been proposed for targeting specific supramolecular connectivities to modulate the flexible response of metal-organic solids.

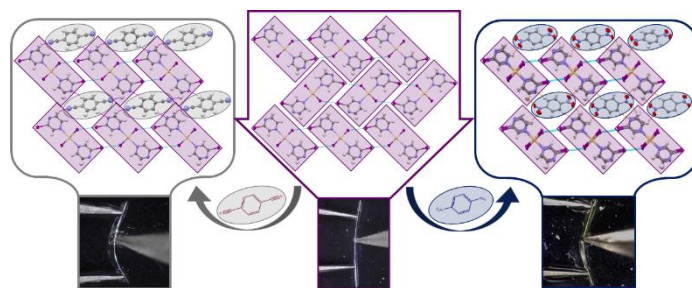


Figure 1. Structure and mechanical responsiveness of the starting coordination polymer (middle) and prepared co-crystals (left and right).

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UGAĐANJE SAVITLJIVOSTI KRISTALA KOORDINACIJSKOG POLIMERA KADMIJA(II) KOKRISTALIZACIJOM

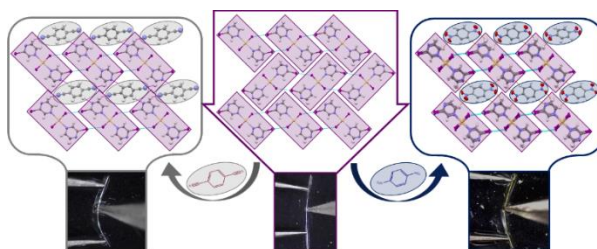
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U posljednjih je nekoliko godina savijanje kristala metalo-organskih krutina u središtu istraživanja, za razliku od mehaničkog odziva kristala organskih krutina, čija su fleksibilna svojstva istraživana relativno dulji niz godina [1, 2]. Za dizajn krutina željenih mehaničkih svojstava ključno je utvrditi jednoznačne načine ostvarivanja supramolekulske povezanosti budući da se ugađanjem jakosti i usmjerenosti međumolekulskih interakcija omogućuje ciljana izgradnja kristalne strukture o kojoj ovise mehanička svojstva, kao na primjer savitljivost materijala. Ovakav inženjerski pristup poželjan je budući da obuhvaća mnoga područja u kojima je dobivanje kristalnih krutina specifičnih svojstava od velikog značaja (npr. optička vlakna, fleksibilna elektronika i slično). [3]

Mehanički je odziv kokristala koordinacijskog polimera kadmijevog(II) jodida s jodpirazinom i koformera ispitan i kvantificiran, te je uspoređen s literaturno dostupnim stupnjem fleksibilnog odziva polaznog koordinacijskog polimera. [2] Da bi se objasnio modificiran stupanj fleksibilnog odziva, uspoređene su međumolekulske interakcije ostvarene u kristalnim strukturama kokristala s kristalnim pakiranjem polaznog koordinacijskog spoja, na temelju čega su predložene strukturne značajke koje utječu na prirodu i stupanj fleksibilnog odziva kristala.



Slika 1. Struktura i mehanički odziv polaznog koordinacijskog polimera (sredina) i priređenih kokristala (lijevo i desno).

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A NOVEL PHENYL-3-HYDROXY PROPIONIC ACID BUILDING BLOCK FOR BENT-SHAPED LIQUID CRYSTALLINE DIMERS

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Liquid crystals (LC) are the substances that exhibit a state between solid and liquid in which molecules have a greater degree of order than those in liquids, but less than those in crystals.[1] Materials with liquid crystal properties have a great technological application and are used in the displays, thermometers, lasers, as parts of photovoltaic cells, etc. The chiral LC structures were mainly achieved by connecting cholesterol mesogenic unit[2] or incorporating a methyl group[3] utilising enantiopure starting material. The structural variations of materials with cholesterol mesogenic unit are limited what diminish detail investigation of structure-property relations. Incorporation of the methyl group in the terminal chain or spacer resulted in branching and suppressed LC phase formation in dimers.[4] Here we focus on developing the synthetic pathway to dimers incorporating 3-hydroxy propionic ester moiety as a source of chirality. The targeted molecules *rac*-**12a, b** were synthesized using a convergent approach in which alkoxy benzoic acids **3a, b**, protected 3-[4-(benzyloxy)phenyl]propionic acid **8** and alcohol 3-[4-(benzyloxy)phenyl]propan-1-ol **5** were separately synthesized then brought together to form final compound (Scheme 1). Investigation of the mesomorphic behaviour reveal that *rac*-**12a** exhibits a monotropic SmC_A phase, while **12b**, shows only direct transition from crystal to isotropic liquid. In further work we'll modify the structure of the molecule in order to stabilize mesogenic properties and to investigate the influence of the chiral center on chiral self-organization.

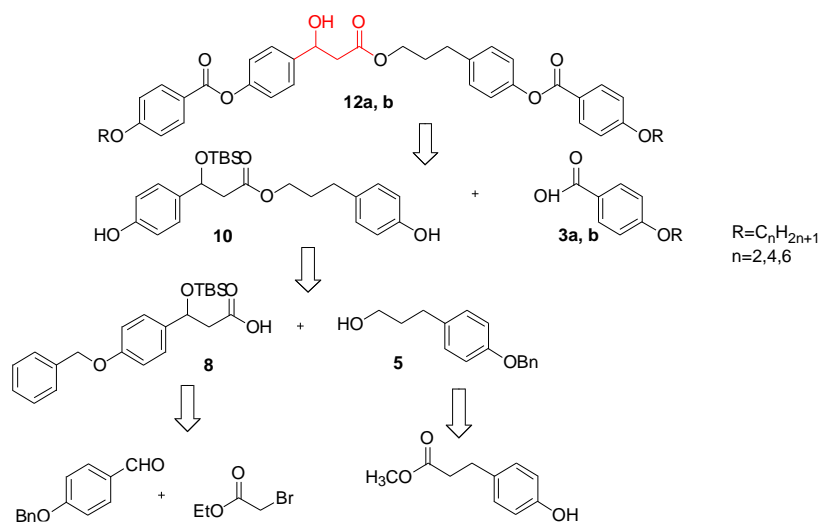


Figure 1. Schematic representation of the retrosynthesis of molecules **12a, b**.

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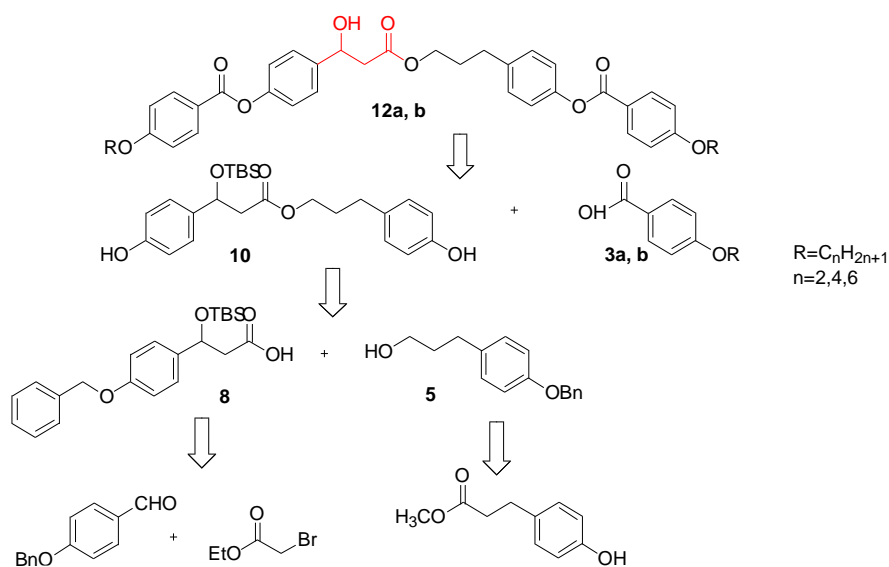
FENIL 3-HIDROKSIPROPIONSKA KISELINA KAO GRAĐEVNI BLOK ZA KIRALNE TEKUĆE KRISTALE SVINUTE GEOMETRIJE

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Tekući kristali (LC) su tvari koje posjeduju stanje između krutog i tekućeg u kojem molekule imaju veći stupanj uređenosti i orijentacije od onog u tekućinama, ali manji od onog u kristalima.[1] Materijali sa svojstvima tekućih kristala imaju veliku tehnološku primjenu te se koriste u izradi zaslona, kao termometri, laseri, dijelovi fotonaponskih ćelija itd. Kiralni tekući kristali uglavnom su postignuti uvođenjem kolesterola kao mezogene jedinice[2] ili uvođenjem metilne skupine[3]. Strukturna raznolikost materijala s kolesterolom je umanjena te je ograničeno proučavanje odnosa strukture i svojstava, a uvođenje metilne skupine u terminalni lanac ili razmaknicu dovodi do grananja strukture i destabilizacije LC faze kod dimera.[4] U okviru istraživanja razvijamo sintetski put za pripremu dimera s 3-hidroksi propionatnim esterom kao izvorom kiralnosti. Za sintezu ciljanih molekula korišten je konvergentan pristup te su zasebno sintetizirane alkoksi-benzojeve kiseline **3a,b**, zaštićena 3-[4-(benziloksi)fenil]propanska kiselina **8** i alkohol, 3-[4-(benziloksi)fenil]propan-1-ol **5**, koji su potom kondenzirani (slika 1). Ispitivanjem mezogenih svojstava pokazano je kako *rac*-**12a** posjeduje monotropnu Sm_CA fazu dok spoj **12b** direktno iz kristalnog stanja prelazi u izotropnu tekućinu. Daljnjim radom modificirat će se struktura molekule kako bi se stabilizirala mezogena svojstva i istražio utjecaj kiralnog centra na kiralnu samoorganizaciju.



Slika 1. Shematski prikaz retrosinteze konačnih molekula **12a, b**.

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INFLUENCE OF STRUCTURAL AND EXPERIMENTAL PARAMETERS ON SELF-ASSEMBLY OF NITROBENZENE DERIVATIVES ON GOLD SURFACE

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Self-assembled monolayers (SAMs) are formed by the adsorption of organic molecules on metal surfaces and their spontaneous organization into highly ordered two-dimensional structures. The most studied systems are SAMs of organic molecules with sulphur, which are bound to the flat gold surface through Au-S bond. It has recently been found that molecules of aromatic C-nitroso compounds functionalized by a sulfur-containing group form ordered SAMs on the gold (111) surface. Owing to the property of aromatic C-nitroso monomers to dimerize to the corresponding azodioxides, it is also possible to form self-assembled bilayers (SABs) by interactions of nitroso groups exposed at the monolayer interface and free nitroso groups in solution through azodioxy bonds [1-3].

In order to gain deeper insight into the formation mechanism and growth kinetics of nitroso/azodioxy adlayers, the influence of structural and experimental parameters (adsorption time and concentration of the solution) on the formation of SAMs and SABs of nitrosobenzene derivatives on the gold (111) surface was investigated. For this purpose, three nitrosobenzene derivatives with alkyl chains of different lengths in *para*-position relative to the nitroso group, ending with thiocyanate headgroups for adsorption on gold (111) surface, were synthesized. Molecular layers were prepared by immersing the gold (111) substrate in a solution of the corresponding nitrosobenzene derivative of known concentration for a defined time. The morphology, structural features and the thickness of the molecular layers of nitrosobenzene derivatives on the gold (111) surface were investigated by atomic force microscopy (AFM) and ellipsometry.

ACKNOWLEDGMENTS

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UTJECAJ STRUKTURNIH I EKSPERIMENTALNIH PARAMETARA NA SAMOUDRUŽIVANJE DERIVATA NITROZOBENZENA NA POVRŠINI ZLATA

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Samoudruženi molekularni jednoslojevi (engl. *self-assembled monolayer*, SAM) nastaju adsorpcijom organskih molekula na metalne površine te njihovom spontanom organizacijom u visoko uređene dvodimenzijske strukture. Najčešće proučavani sustavi su SAM-ovi organskih molekula sa sumporom koje su vezane na ravnu površinu zlata preko veze Au-S. Nedavno je utvrđeno da molekule aromatskih C-nitrozo spojeva funkcionalizirane skupinom koja sadrži sumpor formiraju uređene SAM-ove na površini zlata (111). S obzirom na svojstvo aromatskih C-nitrozo monomera da dimeriziraju u odgovarajuće azodiokside, moguće je i stvaranje samouređenih molekularnih dvoslojeva (engl. *self-assembled bilayer*, SAB) interakcijama nitrozo skupina izloženih na međupovršini jednosloja s nitrozo skupinama slobodnih molekula iz otopine preko azodioksidnih veza [1-3].

Kako bi se stekao dublji uvid u mehanizam i kinetiku nastajanja nitrozo/azodioksidnih slojeva, ispitan je utjecaj strukturnih i eksperimentalnih parametara (vremena adsorpcije i koncentracije otopine) na nastajanje SAM-ova i SAB-ova derivata nitrozobenzena na površini zlata (111). U tu svrhu sintetizirana su tri derivata nitrozobenzena koji u *para*-položaju s obzirom na nitrozo skupinu sadrže alkilne lance različitih duljina na čijim krajevima se nalaze tiocijanatne skupine koje omogućuju adsorpciju spojeva na površinu zlata preko sumpora. Molekularni slojevi pripremljeni su uranjanjem supstrata zlata (111) u otopinu odgovarajućeg derivata nitrozobenzena poznate koncentracije na određeno vrijeme. Morfologija, strukturne značajke i debljina molekularnih slojeva derivata nitrozobenzena na površini zlata (111) istražene su mikroskopijom atomskih sila (AFM) te elipsometrijom.

ZAHVALE

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CORROSION PROTECTION OF CARBON STEEL BY VOLATILE CORROSION INHIBITORS

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The most common types of corrosion are pitting and uniform corrosion, especially pitting corrosion in low carbon steel. Low carbon steel is widely used as the main material for atmospheric storage tank floors, and the atmospheric storage tanks play an irreplaceable role in storage and transportation of crude oil and oil derivatives [1,2]. In the industry, the protection of steel structures has always been a challenge. In order to achieve protection, VCIs (volatile corrosion inhibitors) are increasingly applied in closed systems affected by atmospheric corrosion. VCI is not yet a recognized standard method for the protection of steel and as such has no limitations in its installation and operation, other than environmental ones. VCI is most often applied in quantities, forms and dosages that are mainly based on practical experience rather than scientific research. This research aims to improve the understanding of the impact of a specific inhibitor under specific application conditions and corrosive environments. This work will investigate the effect of commercial powder corrosion inhibitors on corrosion of cleaned and corroded carbon steel commonly used for oil tanks. VCI protects the metal in such a way that forms an invisible protective film on the metal surface, thus not affecting the physical properties or functionalities of the metal. The adsorbed monolayer can change the rate of electrochemical reactions such as metal oxidation or oxygen reduction. The tests were performed by electrochemical methods EIS (electrochemical impedance spectroscopy) and Tafel polarization in a cell with aqueous electrolyte (acid rain pH = 6.5; aqueous solution of 1% NaCl). Two vapour phase inhibitors at different concentrations were dissolved in corrosive media in order to study their inhibiting efficiency.

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KOROZIJSKA ZAŠTITA UGLJIČNOG ČELIKA HLAPLJIVIM INHIBITORIMA KOROZIJE

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Najčešći tipovi korozije su točkasta i jednolika korozija, posebno točkasta korozija u niskougličnom čeliku. Niskouglični čelik naširoko se koristi kao glavni materijal za podnice u atmosferskim skladišnim spremnicima, a atmosferski spremnici igraju nezamjenjivu ulogu u skladištenju i prijevozu sirove nafte i naftnih derivata [1,2]. U industriji zaštita čeličnih konstrukcija je oduvijek bila izazov. Kako bi se zaštita postigla sve češće su prisutni VCI (hlapljivi inhibitori korozije) u dijelovima konstrukcije koja je pod najvećim djelovanjem korozije. VCI još nije standardna metoda za zaštitu čelika i kao takav nema ograničenja u svom postavljanju i djelovanju, osim onih ekoloških. VCI je najčešće prisutan u količinama, oblicima i doziranjima koja su uglavnom bazirana na iskustvu iz prakse, nego znanstvenog istraživanja. Ovo istraživanje ima za cilj poboljšati razumijevanje utjecaja određenog inhibitora u određenim uvjetima primjene i korozivnih okoliša. U radu će se ispitivati djelovanje komercijalnih praškastih inhibitora korozije na koroziju čiste i korodirale površine ugljičnog čelika. VCI štiti metal tako da formira nevidljivi zaštitni film, a na taj način ne utječe na fizička svojstva ili funkcionalnosti metala. Adsorbirani monosloj može promijeniti brzinu elektrokemijskih reakcija kao što je oksidacija metala ili redukcija kisika. Ispitivanja su provedena elektrokemijskim metodama EIS (elektrokemijska spektroskopija impedancije) i Tafel polarizacijom u ćeliji s vodenim elektrolitom (kisela kiša pH=6.5; vodena otopina 1% NaCl). Dva hlapiva inhibitora ispitivala su se pri različitim koncentracijama u korozivnom okruženju kako bi se proučila njihova inhibicijska učinkovitost.

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HIGH RESOLUTION MASS SPECTROMETRIC ANALYSIS OF MELOXICAM - CYCLODEXTRINS INCLUSION COMPLEXES

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Meloxicam (MEL) is a non-steroidal anti-inflammatory drug used in treatment of rheumatoid arthritis and osteoarthritis. According to Biopharmaceutical Classification System it is a Class II drug, or a drug with low solubility and high permeability [1].

Cyclodextrins (CD) are cyclic oligosaccharides containing 6 (α -CD), 7 (β -CD) or 8 (γ -CD) glucose subunits linked with (α -1,4)-glycosidic bond. Their cone like shape with hydrophobic cavity and hydrophilic surface enables formation of inclusion complexes with drugs, which affects physicochemical properties of drugs, such as solubility and stability [2].

Electrospray ionization mass spectrometry can be used to investigate inclusion complexes and to determine their stoichiometry. In combination with other complementary techniques (NMR, UV-Vis, molecular modeling) it enables confirmation of formation of inclusion complexes as well as their characterization [3].

Mass spectrometry (MS) was used to detect meloxicam inclusion complexes with natural occurring cyclodextrins (α -CD, β -CD and γ -CD), but only low resolution mass spectra of complexes were acquired [1]. The objective of this research was a detailed study of meloxicam complexes with β -CD and its more soluble derivatives, hydroxypropyl- (HP β CD) and randomly methylated β -CD (RM β CD). High resolution quadrupole time-of-flight mass spectrometer (QTOF) was used to obtain MS and MS/MS spectra, wherever possible. Corresponding breakdown curves were constructed.

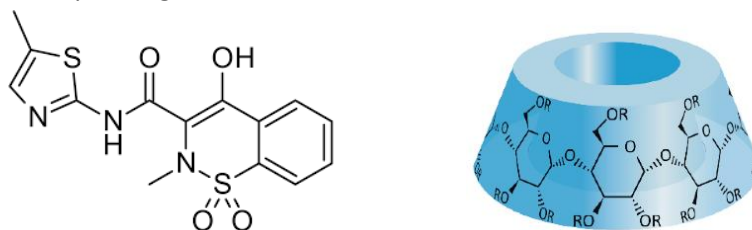


Figure 1. Meloxicam and β -cyclodextrin

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ANALIZA INKLUZIJSKIH KOMPLEKSA MELOSIKAMA I CIKLODEKSTRINA SPEKTROMETRIJOM MASA VISOKOG RAZLUČIVANJA

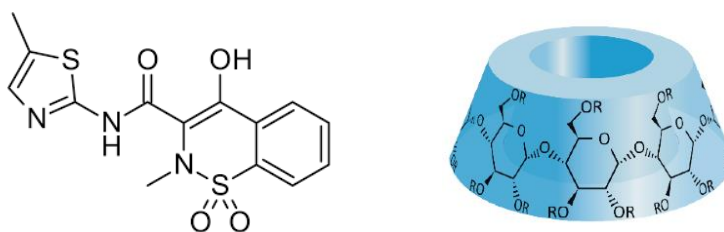
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Meloksikam (MEL) pripada skupini nesteroidnih protuupalnih lijekova te se koristi u liječenju reumatoidnog artritisa i osteoartritisa. Po biofarmaceutskom sustavu klasifikacije pripada skupini II, odnosno lijekovima slabe topljivosti i dobre permeabilnosti [1].

Ciklodekstrini (CD) su ciklički oligosaharidi koji se sastoje od 6 (α -CD), 7 (β -CD) ili 8 (γ -CD) glukoznih podjedinica povezanih (α -1,4)-glikozidnom vezom. Zbog svoje strukture u obliku stošca sa hidrofobnom unutrašnjosti i hidrofilnom površinom, stvaraju inkluzijske komplekse s lijekovima i time im mijenjaju fizikalno-kemijska svojstva, kao što su topljivost i stabilnost [2].

Spektrometrija masa uz ionizaciju elektroraspršenjem koristi se za analizu inkluzijskih kompleksa I određivanje njihove stehiometrije. U kombinaciji s drugim, komplementarnim tehnikama (NMR, UV-Vis, molekulska modeliranje) potvrđuje nastanak inkluzijskih kompleksa te njihovu karakterizaciju [3]. U literaturi su objavljeni samo spektri masa niskog razlučivanja inkluzijskih kompleksa melosikama s prirodnim ciklodekstrinima (α -CD, β -CD i γ -CD) [1]. Cilj ovog rada bio je detaljnija analiza inkluzijskih kompleksa melosikama s β -CD i njegovim topljivijim derivatima, hidroksipropil- (HP β CD) i nasumično metiliranim β -CD (RM β CD). Spektri masa visokog razlučivanja snimljeni su hibridnim spektrometrom masa s kvadrupolom i analizatorom vremena leta (QTOF). Gdje je bilo moguće, snimljeni su MS/MS spektri te konstruirane krivulje ovisnosti intenziteta iona kompleksa o kolizijskoj energiji.



Slika 1. Melosikam i β -ciklodekstrin

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INFLUENCE OF POLYMER ADDITIVE WITH DIFFERENT AMOUNTS OF METHYL METHACRYLATE ON LOW TEMPERATURE PROPERTIES OF MINERAL DIESEL FUEL

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Mineral diesel fuel is a product of oil refining and is characterized by higher density and higher boiling point compared to petrol fuel. In its composition, which primarily consists of a petroleum fraction and a light gas fraction, it contains a small portion of long - chain hydrocarbons (C₁₅ - C₂₅) that crystallize into paraffin crystals at low temperatures [1]. They agglomerate and clog the pores of the fuel filter. This prevents the normal engine operation, and due to agglomeration, sediment is formed in the fuel tank. To eliminate these problems additives are added to improve the low temperature properties. As additives, the most commonly used copolymers are ethylene-vinyl acetate, copolymers of maleic anhydride and poly- α -olefins and their derivatives. In recent research, the interest shifted to methacrylate copolymers [2,3]. Their effectiveness depends on the ratio of polar and non-polar segments and the length of the alkyl chain in the structure, and their properties are greatly influenced by the structural composition. In this study, we investigated the influence of the content of methyl methacrylate in a polymer additive consisting of a short-chain, long-chain and functional monomer. There was a substantial improvement in the cold flow plugging point by 12 ° C and the pour point by 33 ° C compared to non-additive mineral diesel fuel. The results are promising and the synthesized additives will be used for further investigation in motor engines.

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UTJECAJ UDJELA METIL METAKRILATA U POLIMERNOM ADITIVU NA NISKOTEMPERATURNNA SVOJSTVA MINERALNOG DIZELSKOG GORIVA

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Mineralno dizelsko gorivo proizvod je prerade nafte, a karakterizira ga veća gustoća i više vrelište u odnosu na benzinsko gorivo. U svome sastavu koji se primarno sastoji od petrolejske frakcije i frakcije lakog plinskog ulja, sadrži manji udio dugolančanih ugljikovodika ($C_{15} - C_{25}$) koji pri niskim temperaturama kristaliziraju u parafinske kristale [1]. Njihovom aglomeracijom dolazi do začepljenja pora filtra goriva. To onemogućava normalan rad motora, a uslijed aglomeracije dolazi i do stvaranja taloga u spremniku goriva. Spomenuti problemi rješavaju se dodatkom aditiva za poboljšavanje niskotemperaturnih svojstava. Kao aditivi, najčešće su korišteni kopolimeri etilen-vinil acetata, kopolimeri anhidrida maleinske kiseline te poli- α -olefini i njihovi derivati. U novijim istraživanjima sve više pažnje usmjerava se na metakrilatne kopolimere [2,3]. Djelotvornost im ovisi o omjeru polarnih i nepolarnih segmenata te duljini alkilnog lanca u strukturi, a na njihova svojstva uvelike utječe sastav. U provedenom istraživanju ispitan je utjecaj udjela metil metakrilata u polimernom aditivu koji se sastoji od kratkolančanog, dugolančanog i funkcionalnog monomera. Došlo je do značajnog sniženja točke filtrabilnosti za 12 °C te točke tečenja za 33 °C u odnosu na neaditivirano mineralno dizelsko gorivo. Rezultati su obećavajući te će se sintetizirani aditivi koristiti u svrhu daljnjih istraživanja u automobilskom motoru.

ZAHVALA

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INFLUENCE OF STRUCTURE ON THE TRANSPORT OF POTASSIUM IONS IN NIOBIUM PHOSPHATE GLASSES

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Niobium phosphate glasses belong to an important class of oxide glasses and have been investigated for a wide range of applications, such as the waste form for radioactive waste immobilization, glass fibers, and optical lenses, and electrode/electrolyte materials for solid-state batteries [1]. In this study, structural and electrical properties of glasses with composition $x\text{Nb}_2\text{O}_5-(100-x)[0.45\text{K}_2\text{O}-0.55\text{P}_2\text{O}_5]$, $x=10-50$ mol% were investigated by Raman and impedance spectroscopies. Glasses were synthesized by microwave heating of starting chemicals $\text{NH}_4\text{H}_2\text{PO}_4$, Nb_2O_5 , and KOH in a microwave oven with a nominal power of 1100 W for 30 min. The melts were quenched in the air by pouring them into steel molds and were annealed for 3 h at 773 K [2]. Raman spectra reveal that the glass structure changes from predominantly orthophosphate ($x \leq 20$ mol%) to predominantly niobate ($x=50$ mol%) with increasing Nb_2O_5 content. In the glass network, niobium forms NbO_6 octahedra which becomes mutually interconnected *via* Nb-O-Nb bonds at higher Nb_2O_5 content. The DC conductivity of glasses decreases with the increase in Nb_2O_5 due to a decrease in the concentration of potassium ions, however, this decrease is not linear indicating that glass structure strongly influences their mobility. While glasses with predominantly orthophosphate structure and those with predominantly niobate glass network exhibit a slight decrease in DC conductivity with increasing Nb_2O_5 content, the intermediate glass compositions exhibit a strong drop in DC conductivity which could be attributed to the hampering effect of the mixed niobate-phosphate network on the diffusion of potassium ions. Interestingly, a predominantly niobate glass network exhibits a rather facilitating effect which is evidenced not just in the trend of DC conductivity but also in the features of the frequency-dependent conductivity and typical hopping lengths of potassium ions.

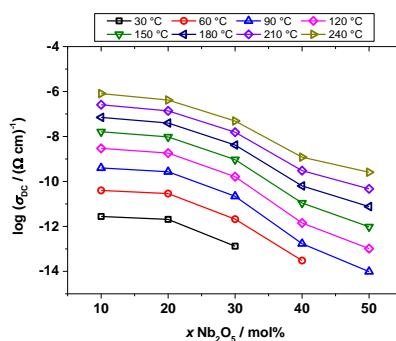


Figure 1. DC conductivity at various temperatures as a function of the Nb_2O_5 content.

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UTJECAJ STRUKTURE NA PRIJENOS KALIJEVIH IONA U NIOBIJEVIM FOSFATNIM STAKLIMA

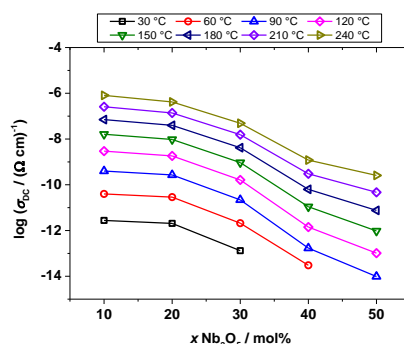
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Niobijeva fosfatna stakla važna su skupina oksidnih stakala koja pokazuju potencijal za primjenu u različitim područjima, npr. u imobilizaciji radioaktivnog otpada, kao staklena vlakna i optičke leće, te elektrode/elektroliti u čvrstim baterijama [1]. U ovom istraživanju strukturalna i električna svojstva stakala sastava $x\text{Nb}_2\text{O}_5-(100-x)[0.45\text{K}_2\text{O}-0.55\text{P}_2\text{O}_5]$, $x = 10-50$ mol% istražena su Ramanovom i impedancijskom spektroskopijom. Stakla su pripravljena mikrovalnim zagrijavanjem početnih spojeva $\text{NH}_4\text{H}_2\text{PO}_4$, Nb_2O_5 i KOH u mikrovalnoj pećnici snage 1100 W tijekom 30 minuta. Taline su izlivena u čelične kalupe na zraku i potom napuštane 3 h na 773 K [2]. Ramanovi spektri pokazuju da se s povećanjem udjela Nb_2O_5 struktura stakla postepeno mijenja iz dominantno ortofosfatne ($x \leq 20$ mol%) u dominantno niobatnu ($x = 50$ mol%). Niobij u strukturalnoj mreži stakla tvori NbO_6 oktaedre koji se pri većim udjelima Nb_2O_5 međusobno povezuju Nb-O-Nb vezama. DC provodnost stakala smanjuje se s porastom udjela Nb_2O_5 što je posljedica smanjenja koncentracije kalijevih iona, međutim pad provodnosti nije linearan što ukazuje na snažan utjecaj strukture na njihovu mobilnost. Tako kod stakala s dominantno ortofosfatnom i dominantno niobatnom strukturom dolazi do blagog smanjenja DC provodnosti, a stakla s miješanom niobatno-fosfatnom mrežom pokazuju snažan pad DC provodnosti što ukazuje na otežanu difuziju kalijevih iona. S druge strane, dominantno niobatna strukturalna mreža stakla ima pozitivan utjecaj na pokretljivost kalijevih iona što utječe ne samo na DC provodnost već i na svojstva frekvencijski ovisne provodnosti te tipični prostorni doseg skoka kalijevih iona.



Slika 1. DC provodnost pri različitim temperaturama u ovisnosti o udjelu Nb_2O_5 .

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INFLUENCE OF DIFFERENT SIZE MULTI-WALLED CARBON NANOTUBES ON POLYETHYLENE GLYCOL BASED NANOFLUID PROPERTIES

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For the potential use of nanofluids in cooling processes, thermal conductivity and rheological properties have to be well investigated [1]. Carbon nanotubes can be used as nanoparticles in nanofluids due to their outstanding thermal conductivity [2]. Aim of this work was to investigate properties of nanofluids of polyethylene glycol of molar mass 200 g/mol (PEG-200) with multi-walled carbon nanotubes (MWCNTs) differentiating in their length and width. Nanofluids were prepared by ultrasonic mixing in the concentration range 0.1-10 wt%. First type of MWCNTs was short (length 10-20 μm) and wide (diameter > 50 nm), and second was long (length 50 μm) and thin (diameter 8-15 nm). Thermal conductivity and rheological properties of prepared nanofluids and the base fluid were studied. It was found that the nanofluids with short and wide MWCNTs have better heat transfer properties compared to the nanofluids containing long and thin ones. For the highest concentration of 10 wt% of MWCNTs in nanofluids, thermal conductivity of those containing short and wide MWCNTs increased by 133 % in reference to the base fluid. For the same concentration, nanofluids with long and thin MWCNTs had a three times smaller increase, by only 40 %. Nanofluids in the concentration range 0.01-1 wt% of MWCNTs exhibit Newtonian behaviour, while those of higher concentrations show different types of non-Newtonian behaviour. Samples with short and wide MWCNTs show shear-thickening behaviour, and samples of long and thin ones shear-thinning.

ACKNOWLEDGMENTS

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UTJECAJ VIŠESTJENČANIH UGLJIKOVIH NANOCIJEVI RAZLIČITIH DIMENZIJA NA SVOJSTVA NANOFLUIDA POLIETILEN GLIKOLA

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Nanofluidi se primijenjuju u rashladnim procesima te im je važno poznavati svojstva poput toplinske vodljivosti i reološkog ponašanja [1]. Ugljikove nanocijevi su nanočestice kod kojih je primijećena izvrsna toplinska vodljivost zbog čega se mogu koristiti kao sastavnica nanofluida [2]. Cilj ovoga rada bio je pripremiti i istražiti svojstva nanofluida polietilen glikola i različitih vrsta višestjenčanih ugljikovih nanocijevi (engl. *multi-walled carbon nanotubes* (MWCNTs)) pri udjelima MWCNTs 0,1 – 10 mas. %. Nanofluidi su pripremljeni ultrazvučnim miješanjem polietilen glikola prosječne molekulske mase 200 g/mol (PEG-200) s jednom vrstom širokih (>50 nm) i kratkih (10 – 20 μm) MWCNT te drugom vrstom uskih (8 – 15 nm) i dugih (50 μm). Istražena su reološka svojstva i toplinska vodljivost nanofluida i baznog fluida. Primijećeno je da nanofluidi sa širokim i kratkim MWCNTs ostvaruju bolji prijenos topline u usporedbi s nanofluidima s uskim i dugim nanocijevima. U usporedbi s toplinskom vodljivošću baznog fluida, za najveću istraženu koncentraciju od 10 mas. % MWCNTs, toplinska vodljivost nanofluida sa širokim i kratkim MWCNTs se povećava za 133 %. U slučaju nanofluida sa uskim i dugačkim nanocijevima dolazi do tri puta manjeg povećanja, za samo 40 %. Kod nanofluida koncentracija 0,01 – 1 mas. % MWCNTs primijećeno je newtonsko ponašanje, dok se nanofluidi viših koncentracija s kratkim i širokim nanocijevima ponašaju dilatantno, a nanofluidi s dugačkim i uskim nanocijevima pseudoplastično.

ZAHVALE

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FORCED HYDROLYSIS OF FeCl_3 SOLUTIONS IN THE PRESENCE OF Cr^{3+} IONS IN ACIDIC MEDIUM

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Forced hydrolyses of FeCl_3 solutions in the presence of Cr^{3+} ions without alkali addition were investigated at 200°C. These precipitation systems were compared to corresponding reference systems. The isolated precipitates were characterized with XRD, ^{57}Fe Mössbauer, FT-IR, FE SEM and photocatalytic measurements. Although chromium was not detected by EDS (Energy Dispersive X-ray Spectroscopy), the analysis of samples precipitated in the presence of Cr^{3+} ions showed several effects which can be attributed to the presence of these ions in the starting solutions. Autoclaving of FeCl_3 solutions in the presence of Cr^{3+} impeded the transformation kinetics $\beta\text{-FeOOH}$ to $\alpha\text{-Fe}_2\text{O}_3$. Relative intensities of prominent diffraction lines 104 and 110 of $\alpha\text{-Fe}_2\text{O}_3$ changed as a result of the presence of Cr^{3+} ions. Changes in the size and formation of lemon-like particles instead of cube-like $\alpha\text{-Fe}_2\text{O}_3$ particles were also noticed (Figure 1). The presence of Cr^{3+} ions in hydrolysing FeCl_3 solution influenced the photocatalytic degradation of rhodamine B. Since no specific adsorption of Cr^{3+} ions occurred in the acidic pH medium [1], it was inferred that traces of Cr^{3+} ions enter into the structural tunnels of $\beta\text{-FeOOH}$ crystals. It can be assumed that $\alpha\text{-Fe}_2\text{O}_3$ crystals start to grow on very fine and thin $\beta\text{-FeOOH}$ crystallites [2] which were not completely dissolved, but were previously affected by Cr^{3+} ions.

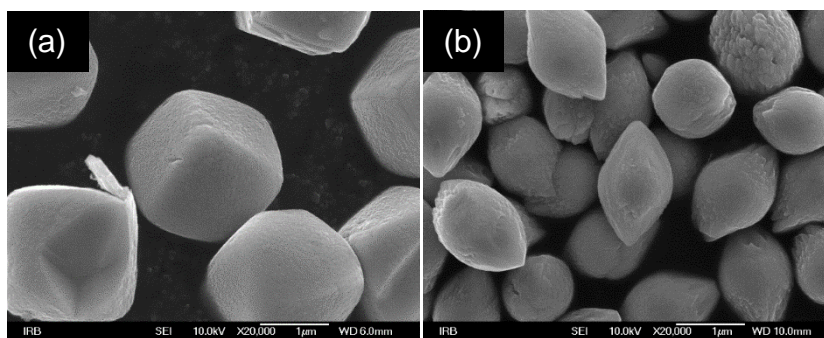


Figure 1. (a) $\alpha\text{-Fe}_2\text{O}_3$ cube-like particles (obtained without the presence of Cr^{3+}) and (b) lemon-like $\alpha\text{-Fe}_2\text{O}_3$ particles (obtained in the presence of Cr^{3+}).

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UBRZANA HIDROLIZA OTOPINA FeCl_3 U PRISUTNOSTI IONA Cr^{3+} U KISELOM MEDIJU

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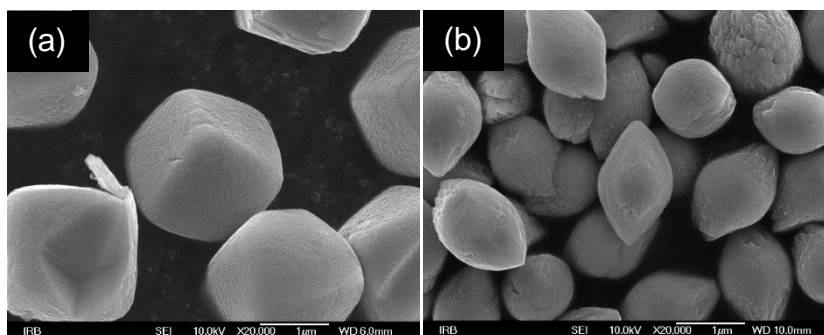
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Istražene su ubrzane hidrolize vodenih otopina FeCl_3 u prisutnosti iona Cr^{3+} bez dodatka lužine pri 200°C . Navedeni taložni sustavi su uspoređeni sa odgovarajućim referentnim sustavima. Svojstva dobivenih taloga ispitana su metodama XRD, ^{57}Fe Mössbauer, FT-IR, FE SEM te fotokatalitičkim mjerenjima. Iako krom nije detektiran pomoću EDS-a (Energy Dispersive X-ray Spectroscopy), analiza uzoraka dobivenih u prisutstvu iona Cr^{3+} pokazuje nekoliko efekata koji se mogu pripisati prisutnosti spomenutih iona u početnim otopinama. Autoklaviranjem otopina FeCl_3 u prisutnosti iona Cr^{3+} usporava se kinetika transformacije $\beta\text{-FeOOH}$ u $\alpha\text{-Fe}_2\text{O}_3$. Relativni odnosi intenziteta istaknutih difrakcijskih linija 104 i 110 koje pripadaju $\alpha\text{-Fe}_2\text{O}_3$ su promijenjeni zbog prisutnosti iona Cr^{3+} . Osim toga, primijećeno je kako dolazi do promjene u veličini čestica te kako umjesto kockastih $\alpha\text{-Fe}_2\text{O}_3$ čestica nastaju čestice nalik limunu (Slika 1). Prisutnost iona Cr^{3+} u hidrolizirajućim otopinama FeCl_3 pokazuje utjecaj na fotokatalitičku razgradnju rodamina B. S obzirom da nema specifične adsorpcije iona Cr^{3+} u kiselom mediju [1], može se zaključiti kako vrlo mala količina iona Cr^{3+} ulazi u strukturne tunele kristala $\beta\text{-FeOOH}$. Može se pretpostaviti kako kristali $\alpha\text{-Fe}_2\text{O}_3$ počinju rasti na jako finim i tankim kristalićima $\beta\text{-FeOOH}$ [2] koji se nisu u potpunosti otopili, a na čiji su nastanak utjecali ioni Cr^{3+} .



Slika 1. (a) kockaste čestice $\alpha\text{-Fe}_2\text{O}_3$ (dobivene bez prisutnosti Cr^{3+}) i (b) čestice $\alpha\text{-Fe}_2\text{O}_3$ nalik limunu (dobivene u prisutnosti Cr^{3+}).

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UNTARGETED METABOLOMICS PROFILE OF SERUM IN DOGS INFECTED WITH *BABESIA CANIS* BY GC-MS

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Babesiosis is a tick-borne disease, caused by protozoan pathogens from the genus *Babesia canis* [1]. The disease can be clinically classified into uncomplicated and complicated forms. The innovative, post-genomic technologies, has led to the development of strategies aimed at identifying specific and sensitive biomarkers in biological fluids and tissues. Metabolomics is one of the most frequently applied approaches in the field of systems biology for the identification and quantitation of small molecules [2]. The goal was to examine the difference of serum metabolome between dogs infected with *B. canis* and healthy dogs using non-targeted approach on the GC-MS platform.

Serum was collected from 12 dogs infected with *B. canis* and 12 healthy dogs. Briefly, 50 µL of each sample was mixed with 250 µL of a solvent water/methanol/chloroform (1:2.5:1 ratio) and then the mixture was incubated at 1 200 rpm for 30 min at 37°C. After incubation, samples were centrifuged at 16.000 x g for 5 min at 4°C. The extraction solution (225 µL) was mixed with 200 µL of distilled water, shaken at 1.200 rpm for 30 min at 37°C and then were centrifuged at 16.000 x g for 5 min at 4°C. The supernatant was vacuum-dried before analysis. Samples were analysed on a GC-MS QP2010 Ultra Gas Chromatograph Mass Spectrometer (Shimadzu, Kyoto, Japan).

The metabolomics analysis resulted in the identification of 26 metabolites using GC-MS Metabolite Mass Spectral Database (Shimadzu Co). Total of 6 metabolites were showed significant differences ($p < 0.05$) between dogs with *B. canis* infection and healthy controls. Some of the most significant metabolites were Myo-Inositol, Phenylalanine and Stearic acid.

The study confirmed that host-pathogen interactions can be studied by metabolomics approach with the main aim of discovering new biomarkers with potential diagnostic and/or prognostic meaning and better understood the researched disease. The GC-MS method is useful in investigating the serum metabolome of dogs infected with *B. canis*.

ACKNOWLEDGMENTS

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NECILJANI METABOLOMSKI PROFIL SERUMA PASA INFICIRANIH S *BABESIA CANIS* POMOĆU GC-MS

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Babezioza je bolest koja se prenosi krpeljima, a uzrokovana je protozoama roda *Babesia canis* [1]. Bolest se klinički može manifestirati u nekompliciranom i kompliciranom obliku. Inovativne postgenomske tehnologije dovele su do razvoja strategija usmjerenih na prepoznavanje specifičnih i osjetljivih biomarkera u biološkim tekućinama i tkivima. Metabolomika je jedan od najčešće primjenjivanih pristupa u području sistemske biologije za identifikaciju i kvantifikaciju malih molekula [2]. Cilj ovog istraživanja je otkriti nove biomarkere u pasa inficiranih s *B. canis* i zdravih pasa koristeći neciljani metabolomski pristup pomoću GC-MS platforme.

Serum je prikupljen od 12 pasa inficiranih s *B. canis* i 12 zdravih pasa. Ukratko, 50 uL svakog uzorka pomiješano je s 250 uL otapala voda / metanol / kloroform (omjer 1: 2,5: 1), a zatim je smjesa inkubirana na 1.200 okretaja u minuti 30 minuta na 37°C. Nakon inkubacije, uzorci su centrifugirani na 16.000 x g tijekom 5 minuta na 4°C. Ekstrakcijska otopina (225 uL) pomiješana je s 200 uL destilirane vode, mućkala se na 1.200 o/min 30 minuta na 37 °C, a zatim centrifugirala na 16.000 x g 5 minuta na 4°C. Supernatant je osušen u vakuumu prije analize. Uzorci su analizirani sa plinskim kromatografom vezanim na spektrometar masa, GC-MS QP2010 (Shimadzu, Kyoto, Japan).

Neciljani metabolomski pristup rezultirao je identifikacijom 26 metabolita korištenjem GC-MS baze podataka za istraživanje metabolita, a pri tome je 6 metabolita pokazalo značajnu razliku između pasa s *B. canis* infekcijom i zdravih kontrola. Neki od najznačajnijih metabolita bili su mio-inozitol, fenilalanin i stearinska kiselina.

Istraživanje je potvrdilo da se interakcije između patogena i domaćina mogu proučavati metabolomskim pristupom kako bi se otkrili novi biomarkeri s potencijalnim dijagnostičkim i/ili prognostičkim značajem te bolje razumjela istraživana bolest. GC-MS metoda je korisna u istraživanju serumskog metaboloma pasa inficiranih s *B. canis*.

ZAHVALE

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MAGNETRON SPUTTERING DEPOSITION OF CORE/SHELL Ge/Al QUANTUM DOT LATTICES IN AMORPHOUS Al₂O₃ MATRIX

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In this study, we demonstrate the production of thin films made of 3D-ordered Ge/Al core/shell quantum dots embedded in an alumina matrix. The films were produced by a magnetron sputter deposition of the Ge/Al/Al₂O₃ multilayer. The Ge core size was tuned by varying the Ge-layer deposition time while the other parameters were kept constant. The influence of the Ge core size on the structural, optical, and electrical properties of the films was investigated. The results confirm the formation of Ge/Al core/shell quantum dots, differing by the sizes of the core and shell, that are arranged in a 3D-ordered network. The optical properties of the materials, their photo-generation ability and quantum efficiency show strong dependence on the Ge core size. The materials bandgap is strongly tuneable by the size of the Ge core. The investigated materials are very promising for application in solar cells, photodetectors, and sensors.

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JEZGRA/LJUSKA Ge/Al KVANTNE TOČKE U AMORFNOJ Al_2O_3 MATRICI DOBIVENE MAGNETRONSKIM RASPRAŠENJEM

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Tema ovog istraživanja su tanki filmovi načinjeni od kvantnih točaka strukture jezgra/ljuska u matrici od alumine. Filmovi su pripremljeni tehnikom magnetronskog rasprašenja Ge/Al/ Al_2O_3 multi sloja. Veličina Ge jezgre mijenjana je promjenom vremena depozicije jezgre, dok su ostali parametri ostali isti. Promatran je utjecaj veličine jezgre na strukturna, optička i električna svojstva istraživanih filmova. Dobiveni rezultati su potvrdili nastajanje Ge/Al jezgra/ljuska kvantnih točaka složenih u 3D uređene mreže. Optička svojstva materijala i kvantna efikasnost pokazala su značajnu ovisnost o veličini jezgre. Također, promjenom veličine Ge jezgre značajno se utjecalo na širinu energijskog procjepa. Ovi materijali jako su interesantni zbog mogućnosti široke primjene, pa ih je tako moguće primijeniti u solarnim ćelijama, foto detektorima i senzorima.

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RADICAL DIFFUSION IN PROPYLENE CARBONATE AND DMF

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Diffusion is a random translational motion of molecules observed in all aggregate states, the rate of which is described by the diffusion coefficient - diffusivity. If long-lived radicals are dissolved in the liquid, their diffusion can be studied by Electron Paramagnetic Resonance (EPR) spectroscopy. The diffusion of radicals in a liquid changes the strength of the magnetic interactions between the spins of their unpaired electrons and thus affects the shape of the EPR spectrum of the radicals. The method of determining diffusivity through spectral analysis was published in [1] and can be applied to various nitroxide radicals and solvents. In this study, we determined by EPR the diffusivity of the deuterated nitroxyl radical Tempon (2,2,6,6-tetramethyl-4-oxopiperidin-1-oxyl) in propylene carbonate (PC) and dimethyl formamide (DMF). The diffusivity of the radicals in solvent is compared with the literature data on temperature-dependent self-diffusion coefficients of solvents, determined by the pulse NMR technique [2].

By cooling liquids, two different phenomena can occur: crystallization and glass transition [3]. Crystallization is the process of transition from a liquid to a solid state of a high degree of organization, and glass transition, which occurs by rapid cooling, is a transition to a solid amorphous state. Propylene carbonate is a cyclic carbonate ester that belongs to the glass-forming liquids, while dimethyl formamide is a good example of a crystallizing liquid that does not form glass [4]. In this study, we examined the relationship between Tempon diffusivity and self-diffusion coefficients for PC and DMF. These relationships differ (Figure 1) which is possibly due to different cooling behavior and solid structure formation [3].

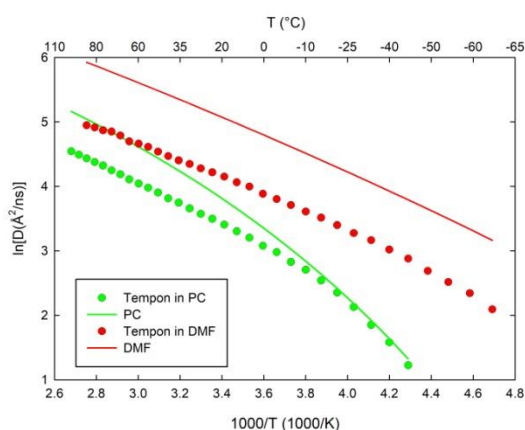


Figure 1. Curves of Tempon diffusivity and self-diffusion coefficients for PC and DMF

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DIFUZIJA RADIKALA U PROPILEN KARBONATU I DMF-U

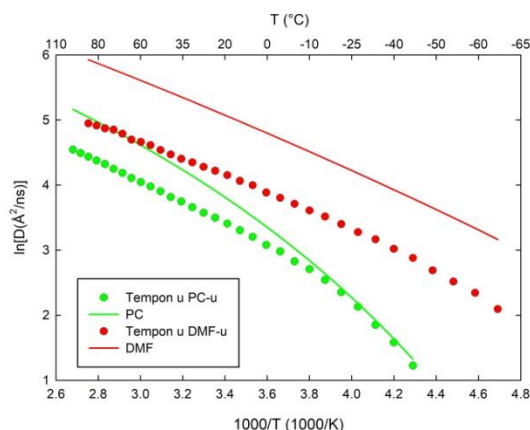
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Difuzija je nasumično translacijsko gibanje molekula koje se opaža u svim agregatnim stanjima, a čiju brzinu opisuje difuzijski koeficijent – difuzivnost. Ako su u tekućini otopljeni dugoživi radikali, njihovu difuziju moguće je proučavati spektroskopijom elektronske paramagnetske rezonancije (EPR). Difuzija radikala u tekućini mijenja jačinu magnetskih interakcija između spinova njihovih nesparenih elektrona i tako utječe na oblik spektra EPR-a radikala. Metoda određivanja difuzivnosti analizom spektara objavljena je u članku [1] i može se primjenjivati se na različite nitroksidne radikale i otapala. U ovom istraživanju, metodom EPR-a određivali smo difuzivnost deuteriranog nitroksilnog radikala Tempon-a (2,2,6,6-tetrametil-4-oksopiperidin-1-oksil) u propilen karbonatu (PC) i dimetil formamidu (DMF). Difuzivnost radikala u otapalu uspoređuje se s literaturnim podacima o temperaturno ovisnim koeficijentima samodifuzije otapala, određenih tehnikom pulsne NMR-a[2].

Hlađenjem tekućina može doći do dvije različite pojave: kristalizacije i staklastog prijelaza [3]. Kristalizacija je proces prijelaza iz tekućeg u čvrsto stanje visokog stupnja organizacije, a staklasti, do kojega dolazi brzim hlađenjem, je prijelaz u čvrsto amorfno stanje. Propilen karbonat ciklički je karbonatni ester koji spada među stakloformirajuće tekućine, dok je dimetil formamid dobar primjer kristalizirajuće tekućine koja ne tvori staklo [4]. U istraživanju smo ispitali odnos između difuzivnosti Tempon-a i koeficijenta samodifuzije za PC i DMF. Ti odnosi se razlikuju (slika 1) što je moguće posljedica različitog ponašanja pri hlađenju i formiranja čvrste strukture [3].



Slika 1. Krivulje difuzivnosti tempona i koeficijenta samodifuzije za PC i DMF

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CONFORMATIONAL ANALYSIS OF QUINUCLIDINE CARBAMATE DERIVATIVES

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Conformational analysis of quinuclidine carbamate derivatives was performed by grid search of the potential energy surface spanned by the corresponding torsional coordinates via rigid and relaxed scan. A grid search of an N -dimensional surface implies systematic variation in torsional degrees of freedom for a defined displacement. Two algorithms used in this paper differ in the method of implementation and the type of quantum chemical calculation (single point or optimization). Rigid scan includes systematic search of all defined points in the N -dimensional surface spanned by relevant torsional coordinates for which a single point calculation is performed at each point. Relaxed scan has a guided search of defined points in the N -dimensional surface and optimization of the molecular geometry is performed at each point, namely for those atoms that do not participate in the definition of torsional coordinates. Local minima were determined from the generated surfaces at the semiempirical level of the theory using PM7 method [1]. Corresponding structures were further subjected to geometry optimization at the B3LYP/6-311++G(d,p) level of the theory with Grimme's D3 dispersion correction [2]. The results of these conformational analyses were compared and the conformers relative content was determined using the Maxwell-Boltzmann distribution at the room temperature.

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KONFORMACIJSKA ANALIZA DERIVATA KINUKLIDINSKIH KARBAMATA

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Konformacijska analiza derivata kinuklidinskih karbamata provedena je holističkim pretraživanjem plohe potencijalne energije razapete odgovorajućim torzijskim koordinatama putem *rigid scan* te *relaxed scan* algoritma. Holističko pretraživanje N -dimenzionalne plohe podrazumijeva sistematičnu pretragu plohe po svim dimenzijama za definirani pomak. Dva algoritma koja su korištena u ovom radu razlikuju se u načinu provedbe i vrsti kvantno-kemijskog proračuna (statički proračun ili optimizacija). *Relaxed scan* algoritam ima usmjereno pretraživanje definiranih točaka N -dimenzionalne plohe i pritom se u svakoj točki vrši optimizacija promatrane geometrije, i to onih atoma koji ne sudjeluju u definiciji torzijskih koordinata. *Rigid scan* algoritam uključuje kombinatornu pretragu svih definiranih točaka N -dimenzionalne plohe razapete torzijskim koordinatama te se u svakoj točki izvršava statički proračun. Iz generiranih ploha na semiempirijskoj razini teorije s PM7 [1] hamiltonijanom određeni su minimumi i odgovarajuće strukture su nadalje podvrgnute optimizaciji geometrije na B3LYP/6-311++G(d,p) razini teorije s Grimmeovom D3 disperzijskom korekcijom [2]. Rezultati navedenih pretraga su međusobno uspoređeni i konformerima je određena relativna zastupljenost preko Maxwell-Boltzmannove raspodjele na sobnoj temperaturi.

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SYNTHESIS AND CHARACTERIZATION OF NOVEL OXIME ANTIDOTES FOR ORGANOPHOSPHORUS POISONING

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In attempt to find new, more potent antidotes against organophosphorus poisoning [1], series of novel, quaternary imidazole-2-aldoxime based compounds have been prepared. *N*-alkylation of commercially available imidazole was carried out with benzyl bromide in THF with sodium hydride as a base. *N*-benzylimidazole was converted to 2-carbaldehyde derivative by the reaction with *n*-butyllithium and DMF [2]. *N*-benzylimidazole-2-aldoxime was synthesized using hydroxylamine hydrochloride in solution and without solvent in mechanochemical reaction [3]. Quaternization of *N*-benzylimidazole-2-aldoxime with methyl iodide and benzyl bromides substituted with fluorine atoms and trifluoromethyl groups resulted in the desired novel quaternary compounds [1, 4]. Structures of compounds were deduced from FTIR, ATR, one- and two-dimensional NMR spectra. Furthermore, molecular modelling was used to predict the most probable orientations of compounds within the active site of the enzyme to determine the potency to reactivate phosphorylated human plasma butyrylcholinesterase (BChE). The optimized geometries for complexes of all prepared oximes with BChE have been proposed. Structural characteristics of an efficient oxime reactivator, differences in orientation and relative energies will be presented and discussed.

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SINTEZA I KARAKTERIZACIJA NOVIH OKSIMSKIH ANTIDOTA PRI OTROVANJU ORGANOFOSFORNIM SPOJEVIMA

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S ciljem pronalaska novih, učinkovitijih antidota pri trovanju organofosforinim spojevima [1], pripravljena je serija novih spojeva na bazi kvaternih imidazol-2-aldoksima. *N*-alkiliranje komercijalno dostupnog imidazola provedeno je s benzil-bromidom uz natrijev hidrid kao bazu i tetrahidrofuran kao otapalo. Derivat 2-karbaldehida dobiven je iz pripravljenog *N*-benzilimidazola u reakciji s *n*-butillitijem i dimetilformamidom [2]. *N*-benzilimidazol-2-aldoksim sintetiziran je u reakcijama s hidroksilamin-hidrokloridom uz upotrebu otapala te mehanokemijskim reakcijama bez upotrebe otapala [3]. Kvaternizacijom *N*-benzilimidazol-2-aldoksima s metil-jodidom i benzil-bromidom bez ili sa supstituentima na benzenskom prstenu (jednim ili više atoma flouora ili triflourmetilnim skupinama) dobiveni su novi kvaterni spojevi. Strukture novih spojeva određene su FTIR, ATR, 1D i 2D NMR spektroskopijom. Nadalje, molekulskim modeliranjem određena je usmjerenost sintetiziranih spojeva unutar aktivnog mjesta enzima butilkolinesteraze iz ljudske plazme. Predložena je optimirana geometrija svih kompleksa oksim-enzim. Prezentirat će se i raspraviti potrebne strukturne karakteristike, orijentacije i relativne energije unutar aktivnog mjesta enzima za dizajn novih, efikasnih oksimskih reaktivatora.

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INFLUENCE OF SAME PARTICLE SIZE LAYERED SILICATES ON THERMAL CONDUCTIVITY OF UNSATURATED POLYESTER IMIDE RESIN

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The properties of polymer materials can be improved by adding particles of micrometer and nanometer dimensions without impairing the existing properties, hence developing new composite materials. Unsaturated polyester resins are often research for their application in the impregnation industry due to good electrical resistance and mechanical properties as well as good thermal stability. By incorporating thermally conductive nano/microparticles into the polymer phase, the thermomechanical properties of the polymer composite can be changed as a result of increased concentration of thermal phonons, resulting a more thermally conductive material. We investigated the thermal conductivity and microparticles distribution in samples of duromer systems with different microparticles of layered silicates with the same diameter. The continuous phase represents the unsaturated polyester imide resin, while the discontinuous phases are particles of biotite, phlogopite, fluorophlogopite and muscovite with an average microparticles diameter of 45 μm . The results of the thermal conductivity for 1 and 10 wt% composites show that highest conductivity is obtained for muscovite filler (10.8 % and 129.4 % respectively), while for the 5 wt% composites fluorophlogopite shows the highest increase in thermal conductivity (44.1 %). To determine the homogeneity of filler distribution and evaluate the quality of preparation procedure of composite systems, the top and bottom parts of the sample were analyzed with thermogravimetric analysis. The system with muscovite particles showed the best particle distribution.

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UTJECAJ SLOJEVITIH SILIKATA ISTIH VELIČINA ČESTICA NA TOPLINSKU VODLJIVOST U NEZASIĆENOJ POLIESTERSKOJ IMIDNOJ SMOLI

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Polimerni materijali mogu se poboljšati svojstva dodatkom čestica mikrometarskih i nanometarskih dimenzija bez narušavanja postojećih svojstava tvoreći kompozitni materijal. Nezasićene poliesterske smole učestali su predmet istraživanja za industriju impregnacije zbog dobre električne izolacije, mehaničkih svojstava i dobre toplinske stabilnosti. Ugradnjom toplinski vodljivih nano/mikročestica u duromernu poliestersku fazu, mijenjaju se termomehanička svojstva novonastalog polimernog kompozita povećanjem koncentracije toplinskih fonona pri čemu kompozitni materijal postaje toplinski vodljiviji. Istraživanjem duromernog sustava s različitim mikročesticama slojevitih silikata istog promjera, prati se utjecaj vrste kristalne strukture mikročestica na toplinsku vodljivost polimernog kompozita kao i na raspodijeljenost diskontinuirane faze u kontinuiranoj. Kontinuirana faza je nezasićena poliesterska imidna smola dok diskontinuirane faze čine čestice biotita, flogopita, fluoroflogopita i muskovita s prosječnom veličinom čestica od 45 μm . Rezultati ispitivanja toplinske vodljivosti pokazali su da s 1 i 10 mas. % punila toplinska vodljivost najviše se povećava za sustav gdje je prisutan muskovit (za 10,8 % i 129,4 %). S 5 mas.% fluoroflogopita, toplinska vodljivost kompozita povećala se u odnosu na čistu smolu za 44,1 %. Kako bi se odredila homogenost raspodjele punila i ocjena kvalitete pripreme kompozitnih sustava nakon umrežavanja, provedena je termogravimetrijska analiza gornjeg i donjeg dijela polimeriziranog uzorka. Najbolja raspodjela čestica prisutna je kod sustava s česticama muskovita.

ZAHVALE

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FERROCENE CHROMOPHORE AS A POTENTIAL PROBE FOR THE ASSESSMENT OF HELICITY IN TRIPEPTIDES

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Helicity is particularly important for the biological activity of peptides. However, the helicity of conformers in equilibrium for a particular system is often difficult to determine experimentally. Some organic chromophores can act as chiroptical probes for identification of screw-sense preference of peptides by circular dichroism (CD) spectroscopy.[1,2] Significant number of disubstituted ferrocene peptidomimetics show a positive Cotton effect at 450 nm for the *P*-helix. Recent research in our group has shown that even small monosubstituted ferrocene-based peptidomimetics synthesized from ferrocenamine show a signal in CD spectra near the absorption maximum of the ferrocene chromophore.[3]

To gain a better insight into the key structural properties and geometric parameters associated with a sign of CD spectra of the ferrocene chromophore acting as a probe for determining the helicity of small peptides, Boc-Pro-Pro-Ala-HNFC stereoisomers were studied theoretically. The conformer distribution of each stereoisomer was obtained by a hierarchical approach, searching the conformational potential energy surface employing molecular mechanics and further reoptimized using DFT and implicit solvent model. Quantum theory of atoms in molecules (QTAIM) has confirmed the existence of β -turns in the ensemble of the most stable conformers. TD-DFT calculated average CD spectra corroborated the experimental findings. Absorption maximum near 470 nm can be assigned to the d-d transition of ferrocene unit in which directly attached amide group also participates. An origin of the sign change in circular dichroism spectra near the absorption maximum of ferrocene chromophore is strongly related to the sign of dihedral angle describing deviation of the directly attached amide plane from planarity of cyclopentadienyl ring.

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FEROCENSKI KROMOFOR KAO POTENCIJALNI SENZOR ZA ODREĐIVANJE ZAVIJENOSTI PEPTIDA

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Iako je poznato da heličnost ima važnu ulogu u biološkoj aktivnosti peptida, vrlo je teško eksperimentalno odrediti heličnost ravnotežnih konformera u određenom sustavu. Organski kromofori mogu djelovati kao kirooptički senzori kojima se spektroskopijom cirkularnog dikroizma (CD) može odrediti smjer uzvojnice heličnog peptida.[1,2] Veliki broj disupstituiranih ferocenskih peptidodimetika pokazuje pozitivni Cottonov efekt pri 450 nm za *P*-uzvojnica. Nedavna istraživanja u našoj grupi pokazala su da čak i mali monosupstituirani peptidodimetici izvedeni iz ferocenamina pokazuju signal u CD spektrima u području ferocenskog kromofora.[3]

Kako bi se dobio bolji uvid u ključna strukturna svojstva i geometrijske parametre koji su povezani s predznakom CD spektra ferocenskog kromofora kao senzora za određivanje heličnosti malih peptida, teorijski su proučeni stereoizomeri Boc-Pro-Pro-Ala-HNFC. Raspodjela konformera pojedinog stereoizomera određena je hijerarhijskim pristupom pretraživanjem konformacijske plohe potencijalne energije molekulskom mehanikom, te reoptimizacijom najstabilnijih konformera DFT metodom u implicitnom otapalu. Kvantna teorija atoma u molekulama (QTAIM) potvrdila je postojanje β -okreta u najstabilnijim konformerima. TD-DFT metodom izračunati prosječni CD spektri pokazuju dobro slaganje s eksperimentalno određenim spektrima. Apsorpcijski maksimum pri 470 nm može se pripisati d-d prijelazima ferocenske jezgre uz sudjelovanje izravno vezane amidne skupine. Promjena predznaka signala u CD spektru blizu apsorpcijskog maksimuma ferocenskog kromofora povezana je s promjenom predznaka diedarskog kuta kojim je opisano uvijanje između amidne ravnine i ravnine ciklopentadienilnog prstena.

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PARAMETER OPTIMISATION FOR SIMULTANEOUS EXTRACTION OF RIBOCICLIB, ANASTROZOLE AND LETROZOLE FROM HUMAN PLASMA

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Development of bioanalytical methods is challenging due to the complexity of the sample matrix which requires a clean-up to remove interferences and improve analytical system performance. [1] Ribociclib coupled with an aromatase inhibitor (anastrozole, letrozole) is used in hormone receptor (HR) positive and human epidermal growth factor receptor 2 (HER2) negative breast cancer treatment. [2] In need of environmental acceptability, lower price and ability to work with small sample volumes, a special type of extraction - dispersive liquid-liquid microextraction (DLLME) has been developed. In DLLME, an extracting solvent is used with a dispersing solvent to create an emulsion when injected into a water sample. This facilitates fast extraction of analytes from the water sample. Parameters affecting DLLME must be optimized for the analytes of interest. [3] DLLME is used in this study for the simultaneous extraction of ribociclib, anastrozole and letrozole. Acetonitrile is used for protein precipitation in a volume at least four times larger than that of the human plasma sample. The produced supernatant is evaporated, dispersed in water and used as a starting water phase for extraction. Combinations of chloroform or dichloromethane as the extracting solvent and acetonitrile or methanol as the dispersing solvent were tested. The mixture of chloroform and acetonitrile showed the best recovery, thus it was used for further optimization. During optimization, effects of different ratios of chloroform and acetonitrile, as well as volume and pH value of the starting water sample, added NaCl concentration and ultrasonication duration on analyte recovery were examined. High performance liquid chromatography coupled with diode array detector and fluorescence detector (HPLC-DAD-FLD) was used to assess the recoveries of the extracted analytes. The obtained results can serve as a foundation for the development of therapeutic drug monitoring methods for stated substances in human plasma.

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OPTIMIZACIJA UVJETA ZA ISTOVREMENU EKSTRAKCIJU RIBOCIKLIBA, ANASTROZOLA I LETROZOLA IZ LJUDSKE PLAZME

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Razvoj bioanalitičke metode je zahtjevan zbog kompleksnog matriksa uzorka koji je prije analize potrebno pročistiti kako bi se postigla zadovoljavajuća selektivnost i osjetljivost metode. [1] Ribociklib se u kombinaciji s inhibitorom aromataze (anastrozol, letrozol) koristi u terapiji raka dojke pozitivnog na hormonski receptor i negativnog na HER2. [2] U svrhu ekološke prihvatljivosti, niže cijene i mogućnosti rada s malim volumenima uzorka razvijena je disperzivna mikroekstrakcija tekuće-tekuće (engl. *dispersive liquid-liquid microextraction*, DLLME). U DLLME ekstrakcijsko otapalo se koristi pomiješano s disperznim sredstvom kako bi injektiranjem u vodeni uzorak došlo do stvaranja emulzije. Time se osigurava brza ekstrakcija analita iz vodenog uzorka. Uvjeti trebaju biti optimizirani za pojedine analite. [3] Upravo DLLME se u ovom radu koristi za simultanu ekstrakciju ribocikliba, anastrozola i letrozola. Za taloženje proteina iz plazme koristi se acetonitril u volumenu barem četiri puta većem od volumena uzorka plazme. Dobiveni se supernatant uparava do suhoga, dispergira u vodi te koristi kao polazna vodena faza za ekstrakciju. Isprobane su kombinacije kloroforma ili diklormetana kao ekstrakcijskog otapala s acetonitrilom ili metanolom kao disperznim sredstvom te su najveći prinosi dobiveni smjesom kloroforma i acetonitrila, koja je odabrana za daljnju optimizaciju. Tijekom optimizacije, proučavan je utjecaj različitih udjela kloroforma i acetonitrila, kao i volumena i pH polazne vodene faze, koncentracije dodanog NaCl te vremena soniranja na prinose ovih triju analita. Ekstrakti su analizirani tehnikom tekućinske kromatografije visoke djelotvornosti spregnute s detektorom niza dioda i fluorescencijskim detektorom (engl. *High performance liquid chromatography coupled with diode array detector and fluorescence detector*, HPLC-DAD-FLD). Dobiveni rezultati mogu poslužiti kao temelj daljnjem razvoju metoda za terapijsko praćenje navedenih lijekova u plazmi pacijenata.

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ONE-DIMENSIONAL MODEL OF VISCOUS AND HEAT-CONDUCTING REAL MICROPOLAR GAS FLOW

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Classical fluid flow models based solely on Navier-Stokes equations are widely used to analyze the behavior of fluids at the macroscopic level. Recently, with the progress of technology, there is a need for models that more accurately describe the behavior of fluids at the micro-level by considering local micro effects.

In the micropolar fluid model, additional fields of internal structure such as body torque per unit mass and couple stress are defined. Unlike other attempts at modeling the micro-continuum, the micropolar fluid model proved to be applicable and suitable for analysis since only microrotations are taken into account, while microdeformations are neglected.

Instead of the ideal gas model assumed in the previous studies of compressible micropolar fluid, in this work we consider a real gas characterized by a generalized equation of state in which the pressure is proportional to the product of the temperature and a power of the density.

We first present a general three-dimensional model of a viscous, heat-conducting micropolar real gas that is polytropic in the thermodynamic sense. Then we consider a special case of one-dimensional flow, for which we introduce the conditions under which the governing system of equations allows the existence and uniqueness of the generalized solution. We also analyze our problem numerically whereby we construct approximate solutions by the Faedo-Galekin method and discuss the influence of micropolarity and the generalized equation of state on the fluid behavior using several numerical experiments.

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JEDNODIMENZIONALNI MODEL TOKA VISKOZNOG REALNOG MIKROPOLARNOG PLINA KOJI PROVODI TOPLINU

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Klasični model fluida primjenjuje se u matematici i brojnim drugim znanostima za analizu ponašanja fluida. Međutim, pokazuje se da model nije dovoljno dobar za opisivanje svih elemenata toka fluida, primjerice efekta krutih čestica raspršenih u fluidu na tok s malom karakterističnom dimenzijom.

U modelu mikropolarnog fluida, uz standardene hidro i termodinamičke aspekte, u obzir se uzimaju lokalni mikroefekti odnosno unutarnja torzija i kontaktno naprezanje. Model se pokazao pogodnim za analizu i primjenu budući da se razmatraju samo mikrorotacije, dok se deformacije čestica zanemaruju. U dosadašnjim istraživanjima u području kompresibilnog mikropolarnog fluida, isključivo je korištena jednadžba stanja idealnog plina. U ovom istraživanju razmatramo model realnog plina koji je karakteriziran generaliziranom jednadžbom stanja i u kojem je tlak proporcionalan umnošku temperature i eke potencije gustoće mase.

U prvom dijelu opisujemo opći trodimenzionalni model viskoznog politrponog realnog mikropolarnog plina koji provodi toplinu, a zatim izvodimo specijalan slučaj modela jednodimenzionalnog toka. Za dobiveni inicijalno rubni problem iskazujemo i dokazujemo teoreme o lokalnoj i globalnoj egzistenciji te jedinstvenosti rješenja. Naposljetku izvodimo i analiziramo algoritam za numeričko rješavanje sustava temeljen na Faedo-Galerkinovoj metodi. Korištenjem numeričkih simulacija ispituje se na koji način generalizirana jednadžba stanja i mikropolarost utječu na tok fluida.

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DISTRIBUTION OF LOAD DURING COOPERATIVE CARGO TRANSFER BY UNMANNED AERIAL VEHICLES

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Unmanned aerial vehicles (UAV), i.e. drones, are used to transfer medical equipment, collect meteorological data, geodetic surveys, tourist needs, perform agricultural work, transfer various types of cargo and other activities. It is estimated that in the EU by 2035, approximately 200 million shipments will be annually delivered by drones [1]. Greater use of drones is expected both in areas without infrastructure and in urban densely populated areas. A necessary prerequisite for the use of drones is a sufficient level of safety and reliability of their operation. In order to contribute to the safety and reliability of drones, a mathematical model of drone cargo transfer in an uncharacterized environment has been developed. The model describes the transfer of small loads by a pair of drones. The cargo is linked, to both drones, with inextensible ropes. Part of the analysis of cargo transfer by drones has already been performed [2]. During cargo transportation by drones, the generated thrusts generally are different. The load factor is the proportion of the weight carried by one of the drones and it takes the values from 0 to 1. The limit amounts are corresponding to cases where only one of the drones carries cargo, and the amount of 1/2 refers to the case when both drones are equally loaded. Any change in the values of model parameters causes a change in the load factor. Less sensitivity to environmental conditions is associated with greater safety and reliability.

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RASPODJELA OPTEREĆENJA BESPILOTNIH LETJELICA PRILIKOM KOOPERATIVNOG PRENOŠENJA TERETA

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Bespilotne letjelice tj. dronovi koriste se za prijenos medicinske opreme, prikupljanje meteoroloških podataka, geodetske izmjere, turističke potrebe, izvođenje poljoprivrednih radova, prijenos raznih vrsta tereta i za druge djelatnosti. Predviđa se kako će u EU do 2035. godine otprilike 200 milijuna pošiljaka godišnje biti isporučivano dronovima [1]. Očekivana je veća primjena dronova kako u područjima bez infrastrukture tako i u urbanim gusto naseljenim sredinama. Nužan preduvjet za uporabu dronova je postignuta dovoljna razina sigurnosti i pouzdanosti njihova rada. Kako bi se doprinijelo sigurnosti i pouzdanosti rada dronova razvijen je matematički model prijenosa tereta dronovima u nekarakteriziranoj okolini. Model opisuje prijenos tereta malih dimenzija parom dronova. Teret je nerastezljivim konopcima vezan za oba drona. Dio analize prijenosa tereta parom dronova već je prethodno proveden [2]. Prilikom prenošenja tereta dronovima potisci koje dronovi ostvaruju općenito se razlikuju. Faktor opterećenja je udio težine tereta kojeg nosi jedan od dronova i poprima iznose od 0 do 1. Granični iznosi odgovaraju slučajevima kada samo jedan od dronova nosi teret, a iznos od $\frac{1}{2}$ odnosi se na slučaj kada su oba drona jednako opterećena. Svaka promjena iznosa parametara modela uzrokuje promjenu faktora opterećenja. Manja osjetljivost na uvjete okoline povezuje se s većom sigurnošću i pouzdanošću rada.

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INTERPRETABILITY

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Most formal theories appearing in mathematics and elsewhere, such as various theories of numbers, exhibit self-referential behaviour. In a certain sense which can be made fully precise, these theories are able to comprehend their own features, occasionally giving rise to seemingly paradoxical, and, at the very least, unexpected, properties thereof; most notably, Gödel's incompleteness theorems.

One can consider any such theory and ask: how much can this theory prove about itself, or, to put it informally, 'how much is this theory self-aware?' A certain result in this field or research can be informally understood as saying that any sufficiently strong (and here the requirements are very modest) has exactly the same amount of 'self-awareness' as any other such theory. This implies that making a theory stronger, e.g. by appending additional axioms, cannot increase the theory's level of 'self-awareness'.

This uniformity is lost when we consider not only what the theory is aware of concerning itself, but include being able to prove properties concerning other theories. The specific notion we study is *formal relativised interpretability*. The major open question is: what can *every* theory prove regarding the interpretability of its finite extensions? The answer is known for many specific theories, but here the problem is determining the intersection of these answers across all theories.

We will sketch the problems we worked on and the results obtained ([1], [2], [3], [4], [5], [6]).

ACKNOWLEDGMENTS

Most results have been obtained in collaboration with: Marta Bílková, Evan Goris, Joost J. Joosten, Fedor Pakhomov, Tin Perkov, Albert Visser, and Mladen Vuković.

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INTERPRETABILNOST

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Većina matematičkih i drugih formalnih teorija, poput primjerice raznih teorija brojeva, manifestira neku razinu auto-referencijalnog ponašanja. U smislu koji bi se mogao precizno iskazati, ove teorije mogu rezonirati o vlastitim svojstvima, što povremeno dovodi do naizgled paradoksalnih i, u najmanju ruku, neočekivanih, svojstava tih teorija; poput Gödelovih teorema o nepotpunosti.

Razmatramo li pojedinu teoriju, možemo se pitati: što sve ova teorija može dokazati o sebi, ili, neformalnije rečeno, "koliko je ova teorija svjesna same sebe?". Jedan rezultat iz ovog područja istraživanja može se neformalno shvatiti kao rezultat da bilo koja dovoljno snažna (uvjeti su za to vrlo niski) teorija posjeduje jednaku količinu znanja o samoj sebi kao i bilo koja druga teorija. To implicira da činjenje teorije snažnijom, primjerice dodavanjem novih aksioma, ne može povećati takvo znanje teorije.

Ova je uniformnost izgubljena kad razmatramo ne samo čega je teorija "svjesna" u vezi same sebe, već u to uključimo i sposobnost dokazivanja svojstava drugih teorija. Specifičan pojam koji istražujemo zove se formalna relativizirana interpretabilnost. Važno otvoreno pitanje je: što svaka teorija može dokazati u vezi interpretabilnosti njenih konačnih proširenja? Odgovor je poznat za brojne konkretne teorije, ali nas zanima određivanje presjeka tih odgovora za sve teorije.

Skicirat ćemo probleme na kojima smo radili i rezultate ([1], [2], [3], [4], [5], [6]).

ZAHVALE

Većina rezultata uspostavljena je u kolaboraciji s: Marta Bílková, Evan Goris, Joost J. Joosten, Fedor Pakhomov, Tin Perkov, Albert Visser i Mladen Vuković.

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GENERALIZED WRONSKIANS AND MODULAR CURVES

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The Weierstrass points on the algebraic curve X of the genus $g > 2$, as well as their generalizations q -Weierstrass point are of fundamental importance in the analysis of the properties of the curve X . The point P on the curve is Weierstrass if and only if its Weierstrass weight is positive. The key fact is that the Weierstrass weight of the point P is equal to the order of annulment of the determinant of the Wronski matrix (see [1]). The Wronskian matrix contains elements of the base space of holomorphic differentials as well as their derivatives. For q -Weierstrass points ($q > 1$) we observe the space of holomorphic q -differentials and the corresponding Wronskian obtained from the base elements of that space.

In this paper, the focus is on modular curves. It is natural to invest them in projective space using modular forms of the same weight (see [4]). Consequently, instead of the Wronskian differential, we observe the Wronskian of the corresponding cusp forms.

By the term generalized Wronskian we mean Wronskian of any modular forms which is a generalization of the usual notion of the Wronskian of cusp modular forms [7], [6], [3], [5]. For computation with modular forms we use the mathematical software SAGE [8].



Figure 1. Curve of genus 2 contains Weierstrass point.

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GENERALIZIRANI WRONSKIANI I MODULARNE KRIVULJE

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Weierstrassove točke na algebarskoj krivulji X genusa $g > 2$, kao i njihove generalizacije q -Weierstrassove točke od temeljne su važnosti u analizi svojstava krivulje X . Proširenje ovoga je pojam Weierstrassove težine koja je nenegativan cijeli broj. Točka P na krivulji je Weierstrassova ako i samo ako je njena Weierstrassova težina pozitivna. Ključna činjenica glasi da je Weierstrassova težina točke P jednaka redu poništavnja determinante matrice Wronskiana (vidi [1]). Matrica Wronskiana u sebi sadrži elemente baze prostora holomorfnih diferencijala kao i njihove derivacije. Za q -Weierstrassove točke ($q > 1$) promatramo prostor holomorfnih q -diferencijala i pripadni Wronskian dobiven od elemenata baze toga prostora.

U ovom radu fokus je na modularnim krivuljama. Njih je prirodno ulagati u projektivni prostor pomoću modularnih formi iste težine (vidi [4]). Slijedom toga umjesto Wronskiana diferencijala promatramo Wronskian pripadnih kusp formi.

Pod pojmom generalizirani Wronskian smatramo Wronskian bilo kojih modularnih formi što je generalizacija uobičajenog pojma Wronskiana kasp modularnih formi [7], [6], [3], [5]. Za račune s modularnim formama koristimo matematički software SAGE [8].



Slika 1. Krivulja genusa 2 ima Weierstrassovu točku

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ON THE REPRESENTATION THEORY OF $L_{-5/2}(\mathfrak{sl}(4))$

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Representation theory of simple affine vertex algebra $L_k(\mathfrak{g})$, for arbitrary simple Lie algebra \mathfrak{g} and general level k , is a very interesting problem in vertex algebra theory. In this talk we consider simple affine vertex algebra $L_{-5/2}(\mathfrak{sl}(4))$. This case is of particular interest since it appears in conformal embeddings of affine vertex algebras [1]. Using an explicit formula for a singular vector, Zhu's theory and the conformal embeddings, we obtain classification of irreducible $L_{-5/2}(\mathfrak{sl}(4))$ -modules in the category \mathcal{O} . We also determine the fusion rules for irreducible $L_{-5/2}(\mathfrak{sl}(4))$ -modules in the category of ordinary modules.

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O TEORIJI REPREZENTACIJA ALGEBRE $L_{-5/2}(sl(4))$

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Teorija reprezentacija proste afine verteks algebre $L_k(\mathfrak{g})$, za prostu Liejevu algebru \mathfrak{g} i nivo k , jedan je od vrlo zanimljivih problema u teoriji verteks algebri. U ovom radu proučavamo prostu afinu verteks algebru $L_{-5/2}(sl(4))$. Ta algebra je od posebne važnosti jer se javlja kod konformnih ulaganja afinih verteks algebri. Koristeći eksplicitnu formulu za singularni vektor, Zhuovu teoriju i konformna ulaganja, klasificiramo ireducibilne module u kategoriji O . Određujemo i pravila fuzije za ireducibilne $L_{-5/2}(sl(4))$ -module u kategoriji jakih modula.

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FORMATION OF Co(II)-LIPID MIXED LIGAND COMPLEX AT THE MODEL SURFACE OF MERCURY ELECTRODE

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Cell membrane represents boundary between the cell and its environment. It consists of a phospholipid bilayer in which are embedded functional molecules as membrane proteins, carbohydrates, protein channels, glycolipids which enable various membrane functions from which selective permeability for ions and organic molecules is important for our work [1]. Cell physiology is strongly dependent on the interaction of hydrophobic cell membranes with hydrophilic inorganic ions. The key lipid-type defining membrane bilayers are phospholipids. Among which phosphatidylglycerol, phosphatidylethanolamin and phosphatidylcholine (PC) which is the subject of our investigation, are the most important, especially in algae species [2]. Investigation of cobalt complexation with phosphatidylcholine was performed by cathodic stripping voltammetry in 0.55 mol dm⁻³ NaCl solution at static mercury electrode used as a model of hydrophobic cell membrane. Penetration of cobalt ions into the PC layer was facilitated by the formation of hydrophilic Co-Phenanthroline (Phen) complex in the subphase, followed by the mixed ligand Co-Phen-PC complex formation at the hydrophobic interface. Complex Co-Phen was registered within pH range from 4 to 10 at -1.0 V. Stoichiometry, stability and complex kinetics were determined. Co(II)-Phen-PC complex reduces irreversibly indicating a two-electron transfer chemical reaction at -1.5 V vs Ag/AgCl including reactant adsorption with complex dissociation. Investigation of Co(II) lipid mixed complex adsorbed at the mercury electrode hydrophobic surface is a significant contribution to the understanding of the processes occurring on the hydrophobic surface of cell membranes [3].

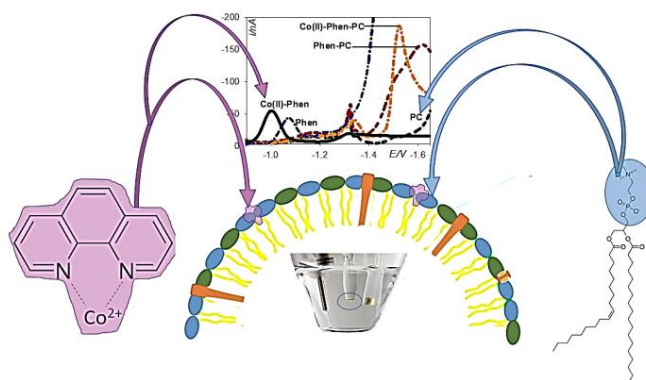


Figure 1. Scheme of the Co(II)-phosphatidylcholine interaction

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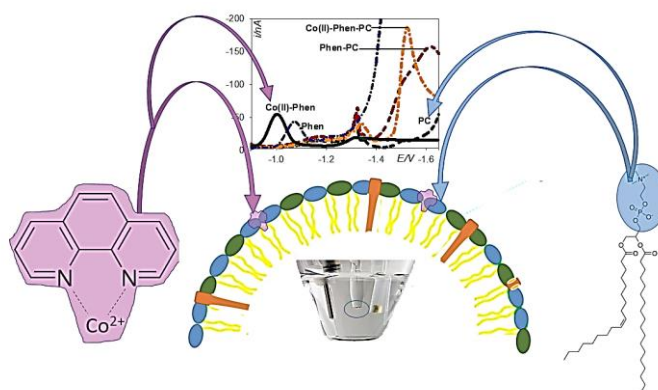
STVARANJE Co(II)-LIPIDNOG MIJEŠANOG KOMPLEKSA NA HIDROFOBNOJ POVRŠINI ŽIVINE KAPI

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Stanična membrana predstavlja granicu između stanice i njezine okoline. Sastoji se od fosfolipidnog dvosloja unutar kojeg su ugrađene funkcionalne molekule kao što su: membranski proteini, ugljikohidrati, proteinski kanali, glikolipidi koje membrani omogućavaju obavljanje različitih funkcija od kojih je za ovo istraživanje bitna selektivna propusnost za ione i organske molekule [1]. Stanična fiziologija značajno ovisi o interakcijama hidrofobne stanične membrane s hidrofilnim anorganskim ionima. Ključni lipidi za tvorbu dvosloja su fosfolipidi. Fosfatidilglicerol, fosfatidiletanolamin, te fosfatidilkolin (predmet ovog istraživanja) su posebno važni za stanice algi [2]. Istraživanje kompleksiranja kobalta Co(II) s fosfolipidom fosfatidilkolinom (PC) provedeno je voltametrijom katodnog otapanja u vodenoj otopini 0,5 M NaCl na statičnoj živinoj elektrodi (SMDE) korištenoj kao modelu hidrofobne stanične membrane. Prolaz kobaltovih iona u fosfolipidni sloj olakšan je stvaranjem hidrofilnog kompleksa Co-fenantrolina (Phen) u otopini dok je miješani kompleks Co(II)-Phen-PC formiran samo na hidrofobnoj površini. Kompleks Co-Phen vidljiv je u pH području od 4 do 10 na potencijalu redukcije -1,0 V prema Ag/AgCl te su određivane stehiometrija kompleksa, stabilnost i kinetika formiranja. Co(II)-Phen-PC kompleks se reducira u ireverzibilnom dvoelektronskom procesu na potencijalu -1,5 V prema Ag/AgCl uz adsorpciju reaktanta na živinu kap te disocijaciju kompleksa nakon redukcije Co(II). Voltametrijsko praćenje stvaranja Co(II) lipidnog miješanog kompleksa na hidrofobnoj površini živine kapi omogućuje bolje razumijevanje prirodnih procesa koji se odvijaju na hidrofobnoj površini staničnih membrana [3].



Slika 1. Shematski prikaz interakcije Co(II)-fosfatidilkolina

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AN OVERVIEW OF BEACH NOURISHMENT IN CROATIA

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Beach nourishment is a commonly accepted beach management practice intended to counter beach erosion. Many countries in Europe perform beach nourishment [1] and it has become the dominant beach management measure performed today, replacing hard beach management practices dominant at the beginning of the past century. Beach nourishment is considered an ecologically safe measure in comparison to other practices [2], but it is mostly performed on sand beaches. It is predicted that the frequency of beach nourishment will increase following the impact of climate change predicted by the IPCC, including sea level rise and an increase in frequency of extreme weather events [3]. The Republic of Croatia is also performing beach nourishment, but the lack of strict government regulation and the pressure of the tourism industry have resulted in beach nourishment being performed without monitoring or planning. This poster will present a review of beach nourishment in Croatia based on more than 250 beaches nourished throughout 2015-2019 on more than 800 occasions depicting how much resources (money, materials) is being spent on beach nourishment in Croatia and how it is done.

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PREGLED DOHRANJIVANJA PLAŽA U HRVATSKOJ

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Dohrana plaža je učestala i prihvaćena praksa upravljanja plažama korištena kao protumjera njihovoj eroziji. Brojne zemlje u Europi provode dohranu plaža [1], te je ona postala glavni postupak u upravljanju plažama danas, u potpunosti zamjenjujući čvrsta rješenja koja su prevladavala u prošlom stoljeću. Dohrana se smatra ekološki prihvatljivim postupkom u usporedbi s ostalim metodama [2] i pretežito se provodi na pješčanim plažama. Učestalost dohrane plaža će rasti sukladno utjecaju klimatskih promjena na priobalno područje koje predviđa IPCC, a koje obuhvaćaju rast morske razine i povećanje učestalosti olujnih događaja [3]. Republika Hrvatska također provodi dohranu plaža, međutim nedostatak zakonske regulative [4] i pritisak turističke industrije doveo je do učestalog provođenja dohrane plaža bez planiranja ili praćenja. Na ovom posterskom izlaganju prezentirat će se pregled dohrane plaža u Hrvatskoj temeljen na podacima više od 250 plaža dohranjenih u razdoblju 2015.-2019. godine u preko 800 navrata, te će se opisati količine korištenih resursa (novca, materijala) i prevladavajuće prakse.

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STORM BOULDERS ALONG THE EASTERN COAST OF THE ADRIATIC AND THEIR DATING BY THE ^{14}C METHOD

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Due to the increasingly dense population of the coast and its growing construction, the assessment of risks arising from natural phenomena is crucial for the adequate management of the coastal area. Given climate change and the increasing occurrence of extreme weather events, the ability to identify the negative aspects of storm episodes through the study of their impacts on coastal accumulation and erosion processes is of paramount importance. The energy of storm waves and their ability to erode rocky shores and move large blocks of rock toward land have been documented in some places around the world. In the south of the Istrian peninsula, on Cape Kamenjak, storm blocks weighing 7 to 15 tons were thrown in places up to 70 meters from the coast. Cape Kamenjak is also the first locality where storm blocks have been recorded in the northern Adriatic, which can be considered a semi-enclosed and relatively shallow basin [1]. In the study of storm blocks, the timing of when they are thrown ashore is of paramount importance. Precise dating of storm blocks and reconstruction of the line of the former shores, despite the use of different methods, still presents great difficulties. Shells of marine organisms in overgrowth on rocks, very often, represent immediately available sources of information by the method of dating using the ^{14}C isotope and allow the definition of the time range in which the blocks could be broken off and transported. Also, by analyzing the community of organisms in overgrowth, it is possible to determine the depths from which the blocks originally originated. As part of this research, a field reconnaissance of the locality of Cape Kamenjak was conducted. After the potentially most interesting area of the ejected blocks was determined, GPS markers were set up and photography was carried out to monitor changes in the movement of the ejected blocks and the possible appearance of new ones. The main tracking method relates to the creation of successive 3D models of a selected field of blocks. All blocks were inspected to determine the presence and composition of organisms involved in bioerosion / biocorrosion or bioconstruction. The selected blocks were sampled for fouling: a random bulk sample of fouling and a parallel shell of the found organisms were sent from each block for analysis. To obtain the most accurate results, the collected samples were pre-treated by physical cleaning and detailed examination using a stereomicroscope. After the obtained results, other locations of storm blocks along the eastern Adriatic coast will continue to be processed.

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OLUJNI BLOKOVI DUŽ ISTOČNE OBALE JADRANA I NJIHOVO DATIRANJE METODOM ¹⁴C

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Zbog sve gušće naseljenosti obale i njene sve brže izgradnje, procjena rizika proizašlih iz prirodnih pojava od ključne je važnosti za adekvatno upravljanje obalnim područjem. Uzmu li se u obzir klimatske promjene i sve učestalija pojava ekstremnih vremenskih pojava, sposobnost prepoznavanja negativnih aspekata olujnih epizoda kroz proučavanje njihovih utjecaja na akumulacijske i erozijske procese na obali od iznimne je važnosti. Energija olujnih valova i njihova sposobnost erozije stjenovitih obala i pomicanja velikih blokova stijena prema kopnu dokumentirane su na nekim mjestima u svijetu. Na jugu istarskog poluotoka, na Rtu Kamenjak olujni blokovi teški i do 15 tona, mjestimice su izbačeni i do 70 metara od obale. Rt Kamenjak je ujedno i prvi takav lokalitet na kojem je zabilježena pojava olujnih blokova u sjevernom Jadranu, koji se može smatrati poluzatvorenim i relativno plitkim bazenom [1].

U proučavanju olujnih blokova od iznimne je važnosti odredba vremena kad su izbačeni na obalu. Precizno datiranje olujnih blokova te rekonstrukcija linije nekadašnjih obala, unatoč korištenju različitih suvremenih metoda i dalje predstavlja veliki izazov. Sačuvane ljuštore morskih organizama u obraštaju na stijenama čine kvalitetne arhive za datiranje pomoću izotopa ¹⁴C te omogućavaju definiranje vremenskog raspona u kojem su blokovi mogli biti odlomljeni i transportirani. Također, analizom zajednice organizama u obraštaju moguće je odrediti i dubine s kojih su blokovi izbačeni iz mora. U sklopu ovog istraživanja provedena je terenska reambulacija lokaliteta rta Kamenjak. Nakon što je utvrđeno potencijalno najzanimljivije područje izbačenih blokova, postavljene su GPS oznake te je provedeno fotografiranje radi praćenja promjena pomicanja izbačenih blokova i eventualna pojava novih. Glavna metoda praćenja odnosi se na izradu uzastopnih 3D modela odabranog polja blokova. Svi su blokovi pregledani kako bi se na njima utvrdilo prisustvo i sastav organizama koji sudjeluju u bioeroziji/biokoroziji ili biokonstrukciji. Odabranim blokovima je uzorkovan obraštaj: sa svakog bloka na analizu je poslan nasumičan uzorak obraštaja i usporedno ljuštura zatečenih organizama. Kako bi se dobili što precizniji rezultati, napravljena je predobrada prikupljenih uzoraka fizičkim čišćenjem te detaljnim pregledom pomoću stereo mikroskopa. Nakon analize dobivenih rezultata nastaviti će se s obradom i drugih lokaliteta s olujnim blokovima duž istočne obale Jadrana.

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INFLUENCE OF SILVER, COPPER AND NANOPLASTIC NANOPARTICLES ON THE GROWTH OF THE MARINE MICROALGA *Chlorella salina*

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In the last two decades engineered nanoparticles (NPs) have become ubiquitous in everyday life. They have found their application in almost all sectors of industry, such as biotechnology, medicine, textile, and cosmetics industry due to their unique size and physicochemical properties [1]. It is increasingly likely that NP will enter the aquatic environment and be transported from wastewater, through freshwater, to marine waters with the corresponding potential to come into contact with a wide range of organisms [2]. For this reason, and the fact that NP may be toxic to biota, the influence of metal, metal oxide and polymer nanoparticles has been studied in the marine microalga *Chlorella salina*. Microalgae are important test organisms as they encompass primary production as autotrophs, and any changes to this biomass production can affect the entire marine ecosystem [3].

To determine the effects of variously-coated silver (Ag-NPs), citrate and polyvinylpyrrolidone (PVP) – stabilized Ag-NPs of diameter 20, 40, 60, and 80 nm were tested in the concentration range 0.01–10 µg / L. To examine the effect of nanoparticle oxidation state on *C. salina* different copper (Cu-NPs) were examined: Cu, CuO and Cu₂O, with concentrations ranging from 1 to 1000 µg / L. Furthermore, synthesized polystyrene (PS-NPs) of 20 and 40 nm, and polymethylmethacrylate (PMMA-NPs) of 20 nm, were used to study the effect of nanoplastics in the concentration range 0.25–5 mg / L. Results show that silver and copper have a strong negative effect on algal growth kinetics, while polymer NP had a less pronounced impact. Significant disturbance of photosynthesis electron transfer processes in *C. salina* was noted after treatment with metal and metal oxide NP, indicating a route by which growth of algal biomass was hindered. The results indicate the potential deleterious effects of NP reaching the aquatic environment and have broader implications for marine food webs of which microalgae form the base level. Moreover, bioaccumulation of these NP in microalgae followed by trophic transfer represents a threat to other organisms such as, for example, mussels and sea urchins.

ACKNOWLEDGMENTS

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UTJECAJ NANOČESTICA SREBRA, BAKRA I PLASTIKE NA RAST MORSKE MIKROALGE *Chlorella salina*

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Posljednja dva desetljeća sve se više istražuju nanočestice (NPs) koje su sveprisutne u svakodnevnom životu. Svoju primjenu našle su u gotovo svim sektorima industrije, poput biotehnologije, medicine te u tekstilnoj i kozmetičkoj industriji zbog svoje jedinstvene veličine, kao i fizikalno-kemijskih svojstava [1]. Većina NPs dolazi u morski okoliš iz otpadnih voda te prilikom transporta čestica može potencijalno doći do kontakta s više vrsta organizama [2]. Iz navedenih razloga, proučavan je utjecaj nanočestica metala, metalnih oksida i plastike na morsku mikroalgu *Chlorella salina*. Mikrolage su od iznimne važnosti u oceanima, jer čine osnovu biomase, a bilo kakve promjene strukture fitoplanktonske zajednice ili produkcije mogu izravno utjecati na cijeli morski ekosustav [3].

Kako bi se utvrdio utjecaj srebra (AgNP), korištene su NPs veličine 20, 40, 60 i 80 nm s omotačem od citrata i polivinilpirolidona (PVP) u rasponu koncentracija od 1 do 1000 µg / L. Za ispitivanje utjecaja oksidacijskog broja korišten je bakar (CuNPs) : Cu, CuO i Cu₂O, s koncentracijama u rasponu od 1 do 1000 µg / L, dok su za proučavanje utjecaja nanoplastike korištene sintetizirane čestice polistirena (PS) NP veličine 20 i 40 nm i polimetilmetakrilata (PMMA) NP veličine 20 nm, koncentracije od 0.25 do 5 mg / L. Rezultati pokazuju kako NPs srebra i bakra imaju snažan negativan učinak na kinetiku rasta *C. salina*, dok NPs plastike imaju manje izražen utjecaj. Poremećaj procesa prijenosa elektrona fotosinteze u *C. salina* zabilježen je nakon tretiranja NPs metala i metalnih oksida, što ukazuje na ometan rast alga. Rezultati ukazuju na potencijalne štetne učinke NPs na vodeni okoliš i imaju širu primjenu na hranidbeni mrežu gdje mikroalge čine osnovnu razinu. Nadalje, bioakumulacija ovih NPs u mikroalgama praćena trofičkim prijenosom predstavlja prijetnju drugim organizmima kao što su primjerice školjkaši i ježinci.

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EXPERIMENTAL EXPOSURE OF TUNICATE *Clavelina oblonga* TO REDUCED SALINITIES AS A POSSIBLE ERADICATION MEASURE OF INVASION IN MUSSEL MARICULTURE

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A new invasive species of tunicate was observed in summer 2020 in mariculture on the western and eastern coast of Istria, Croatia. After field inspection it was confirmed that the identified species is invasive tunicate *Clavelina oblonga* Herdman, 1880 (Ascidiacea, Enterogona, Clavelinidae) previously recorded in the Gulf of Trieste and Piran in 2015 [1]. Due to its fast growth, *C. oblonga* outgrows and overgrows mussels, physically restricting their growth and feeding, and increasing the weight on load-bearing infrastructure. This species is described as sensitive to lowered salinity [2]. Cultivators in Lim bay have a known practice of transferring their mussels to the beginning of the bay, exposing them to brackish waters in order to reduce overgrowth [3]. During an experimental laboratory exposure of *C. oblonga* to different salinities for a period of 14 days, followed by 14 days recovery, no sexual reproduction was noted, while sea water salinities 20 and 11 caused disruption in food uptake and digestion which led to change of colour, tissue necrosis and finally body fragmentation. Based on our preliminary research, field observations and available literature we assume and conclude that translocation of mussel holding nets with tunicates *C. oblonga* overgrowth to locations of lower sea water salinity (<20) for 7-10 days, can be a natural and effective way/measure for eradication of this invasive species.



Figure 1. Morphology of *C. oblonga* after 14 days exposure to different salinities: A) 37, B) 30, C) 20 and D) 11 (upper row), and after 14 days recovery at 37 (lower row).

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IZLAGANJE PLAŠTENJAKA *Clavelina oblonga* MORSKOJ VODI RAZLIČITIH SALINITETA, KAO MOGUĆI PRIRODAN NAČIN SUZBIJANJA OVE AKTUALNE INVAZIVNE VRSTE

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Nova invazivna vrsta plaštenjaka primijećena je ovog ljeta u marikulturi na zapadnoj i istočnoj obali Istre. Nakon terenskog uviđaja potvrđeno je da se radi o invazivnoj vrsti plaštenjaka *C. oblonga* Herdman, 1880 (Ascidiacea, Enterogona, Clavelinidae) prethodno zabilježenoj u Tršćanskom zaljevu i Savudrijskoj vali 2015. godine [1]. Zbog brzog rasta *C. oblonga* obrasta i prerasta dagnje, fizički ograničava njihov rast i hranidbu te dodatno opterećuje nosivu infrastrukturu. Ova vrsta je opisana kao osjetljiva na snižene salinitete mora [2]. Poznato je da su nekad uzgajivači u Lirskom zaljevu premještali pergolare s školjkašima na sam početak zaljeva i ostavljali pergolare i rešte izložene bočatoj morskoj vodi na tretman uništavanja obraštajnih organizama [3]. Eksperimentalno izlaganje *C. oblonga* različitim salinitetima je pokazalo da tijekom ukupnog vremena promatranja (14 dana izlaganja nižim salinitetima i 14 dana oporavka) nije bilo spolnog razmnožavanja, morska voda saliniteta 20 i 11 uzrokovala je poremećaj u prihvatu hrane i samom hranjenju, što je dovelo do promjene boje i nekroze tkiva, a konačno i do raspadanja te fragmentacije korpusa. Generalno na temelju naših preliminarnih rezultata, terenskih zapažanja i dostupne literature, možemo aproksimirati i zaključiti da bi translokacija pergolar dagnji/školjkaša sa plaštenjakom *C. oblonga* i izlaganje obraštaja sniženom salinitetu (<20) kroz 7-10 dana bio moguć prirodan način/mjera suzbijanja ove aktualne invazivne vrste.



Slika 1. Morfologija plaštenjaka *C. oblonge* nakon 14 dana izlaganja različitim salinitetima: A) 37, B) 30, C) 20 i D) 11 (gornji red) te nakon 14 dana oporavka na 37 (donji red slika).

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SEASONAL VARIABILITIES OF NITROGEN AND PHOSPHORUS ATMOSPHERIC DEPOSITION TO THE CENTRAL ADRIATIC AREA AND BIOGEOCHEMICAL IMPLICATIONS

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The atmosphere is not only a significant, but in some cases the dominant pathway by which natural and anthropogenic material is transported from the continents to the coastal areas and open seas [1, 2]. Once deposited through dry and wet processing, atmospheric particles provide the aqueous ecosystems with an external source of macronutrients (N and P) [3]. This, in turn, influences the quality and quantity of organic matter (OM) produced by the phytoplankton within the photic zone, changes CO₂ uptake and indirectly affects the climate. The input of atmospheric deposition (AD) can be of particular importance in oligotrophic regions such as the Mediterranean Sea (Med) which continuously receives anthropogenic aerosols from European regions. The impacts of human activities, including open-field biomass burning (BB) from wildfires and agricultural practices, are thought to be stronger in the Med than in any other sea in the world. The effect of the AD inputs to oligotrophic surface waters of Adriatic Sea is generally unknown.

Atmospheric particulate matter as well as bulk and wet atmospheric deposition samples were collected simultaneously during a field campaign conducted from February to July 2019 at the coastal zone of the Šibenik archipelago (Central Adriatic) in order to assess the AD impact of nutrients on sea surface responses of this oligotrophic coastal region. The first comprehensive insight into concentration levels of dissolved inorganic N (DIN) and P in atmospheric samples, their transport history, and dry and wet deposition fluxes to the investigated Central Adriatic area will be presented. The results suggest that dissolved inorganic N and P deposited from the atmosphere to the central Adriatic coastal area can theoretically support up to 8% of new primary production. However, considering the highest values of total DIN and P deposition fluxes related to the intense BB events which occurred during the investigated period, atmospheric nutrient fluxes can sustain up to 12% of primary production in this coastal area. Regional open-field BB episodic emissions commonly occurring at the coastal Adriatic area, accompanied with the rainfalls, could significantly enhance already imbalanced atmospheric N and P deposition and appears to have a significant role in altering nutrient availability and strengthening P limitation in sea surface layers of coastal areas.

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SEZONSKE PROMJENE ATMOSFERSKOG TALOŽENJA DUŠIKA I FOSFORA NA PODRUČJU SREDNJEG JADRANA I BIOGEOKEMIJSKE POSLJEDICE

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Atmosfera ne predstavlja samo značajan, već često i dominantan put kojim se prirodne i antropogene tvari prenose s kopna na obalna područja i otvoreno more [1, 2]. Jednom uneseni putem mokrog i suhog taloženja, atmosferske lebdeće čestice postaju važan izvor hranjivih soli (N i P) [3] čime mogu utjecati na kvalitetu i kvantitetu organskog materijala koju proizvodi fitoplankton u fotičkoj zoni, mijenjati doseg pohrane CO₂ te posredno utjecati na klimu. Unos atmosferskim taloženjem (AT) može biti od posebne važnosti u oligotrofnim područjima kao što je Sredozemno more (Med) koje je pod kontinuiranim utjecajem donosa antropogenih aerosola Europe. Utjecaj ljudskih aktivnosti, uključujući otvoreno sagorijevanje biomase uslijed šumskih požara i poljoprivrednih aktivnosti, značajniji je u Med nego i u jednom drugom svjetskom moru. Unatoč tome, učinci donosa atmosferskog materijala putem AT na oligotrofne površinske vode Jadranskog mora općenito su slabo poznati.

Uzorci atmosferskih čestica te ukupnog i mokrog atmosferskog taloženja prikupljeni su istovremeno tijekom terenske kampanje provedene od veljače do srpnja 2019. godine u obalnom pojasu šibenskog arhipelaga (srednji Jadran) kako bi se procijenio utjecaj AT hranjivih soli na promjenu bioloških i kemijskih svojstava morske površine ovog oligotrofnog obalnog područja. Predstaviti će se prvi sveobuhvatni uvid u razine koncentracija otopljenog anorganskog N (engl. *dissolved inorganic nitrogen*, DIN) i P u atmosferskim uzorcima, projekcije njihovog dalekosežnog prijenosa te tokovi suhog i mokrog taloženja na ispitivano područje. Rezultati ove studije ukazuju da otopljeni anorganski N i P, koji se iz atmosfere talože na obalno područje srednjeg Jadrana, mogu biti teoretski odgovorni za do 8% nove primarne proizvodnje. Međutim, uzimajući u obzir najviše vrijednosti tokova ukupnog DIN i P taloženja izmjerene tijekom intenzivnih otvorenih požara koji su se dogodili tijekom promatranog perioda, atmosferski tokovi hranjivih soli mogu biti odgovorni za i do 12% primarne proizvodnje u ovom obalnom području. Povremeni intenzivni požari otvorenog tipa koji su česti za obalna područja Jadrana, a posebno oni praćeni kišom, mogli bi značajno pospješiti ionako neuravnoteženo atmosfersko taloženje N i P te utjecati na biodostupnost hranjivih soli, kao i jačanje uloge P kao ograničavajuće hranjive soli u površinskim slojevima obalnih mora.

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THE FRAGILITY OF COASTAL FRESHWATER RESOURCES IN THE MEDITERRANEAN AREA – A MICROBIAL-BASED CASE STUDY OF LAKE VRANA

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Mediterranean freshwater systems (coastal lakes or springs) as scarce water resources are experiencing an increase in anthropogenic and climate change-caused pressures, leading to increased productivity and consequent deterioration of the trophic state [1]. Coastal lakes are centers of carbon circulation and transformation managed to a large degree by microbial populations intertwined in a network of interactions [2]. The trophic state of the coastal Lake Vrana is under the influence of several counteracting drivers. In the summer months, at least 50% of the surface area is covered by macrophytes [3] that utilize large amounts of nutrients and thereby mitigate eutrophication. On the other hand, the largest agricultural complex in the region with the water discharge system feeding into the lake and excessive water pumping at local springs can considerably enhance the natural eutrophication process [4]. High-throughput sequencing of 16S and 18S rRNA genes revealed the effect of several environmental pressures on the microbial community structural change, including salinity, and dissolved organic carbon (DOC) concentrations. While the connection between microbial primary producers and heterotrophic bacteria was deciphered through DOM perturbation, the lake's precipitation-evaporation imbalance caused the seawater intrusion and the introduction of marine species and allochthonous DOM input.

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RANJIVOST OBALNIH SLATKOVODNIH SUSTAVA NA PODRUČJU MEDITERANA – MIKROBIOLOŠKO ISTRAŽIVANJE NA VRANSKOM JEZERU

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Slatkovodni mediteranski sustavi (obalna jezera i izvori), kao rijetki vodni resursi bilježe promjene usred povećanja antropogenog pritiska te posljedice klimatskih promjena, koje dovode do povećane produktivnosti i progresije u trofičkom stanju [1]. Jezera na obalama su središta cirkulacije i transformacije ugljika kojom upravljaju mikrobne populacije isprepletene međusobnim interakcijama [2]. Na trofičko stanje Vranskog jezera kod Biograda na moru utječe nekoliko parametara. U ljetnim mjesecima najmanje je 50% površine jezera pokriveno makrofitima [3], koji koriste velike količine hranjivih tvari i time ublažavaju eutrofikaciju. S druge strane, najveći poljoprivredni kompleks u regiji s drenažnim kanalima koji usmjeravaju višak vode u jezero te prekomjernim crpljenjem vode s lokalnih izvora može znatno ubrzati proces eutrofikacije [4]. Visoko-protočnom metodom sekvenciranja 16S i 18S rRNA gena otkriven je utjecaj više okolišnih parametara na promjenu strukture mikrobne zajednice, uključujući salinitet i otopljeni organski ugljik (DOC). Dok je veza između mikrobnih primarnih proizvođača i heterotrofnih bakterija otkrivena kroz stvaranje nove i metaboliziranje prisutne otopljene organske tvari (DOM), narušavanje precipitacijsko-evaporacijske ravnoteže jezera uzrokovalo je ulaz morske vode i pojavu morskih vrsta te unos alohtonog DOM-a.

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ORGANIC CARBON AS AN INDICATOR OF CHANGES IN THE MARINE STRATIFIED AQUATIC ENVIRONMENT

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Monitoring of organic matter (OM) in the marine system can be based on measurements of dissolved organic matter (DOC) and its surface-active fraction (SAS) (1). In seawater, OM is a complex mixture of organic substances (proteins, carbohydrates, lipids, humic and fulvic acids), which have different surface-active properties (1). In the aquatic environment, we distinguish between dissolved and suspended particulate OM. The boundary between solute and particulate matter is 0.7 μm and the fractions are separated by filtration. OM with surface active properties (SAS) is also distributed between the dissolved and the particle fractions. The OM (SAS) in the sea is autochthonously produced by biological activity (primary production, releases of secondary metabolites under feeding pressure), but part of the OM is of allochthonous origin and is introduced into the aquatic environment (mainly terrestrial origin). The main property of SAS is that it contains hydrophobic (e.g. fatty acid chains, aromatic rings or hydrocarbons) and hydrophilic functional groups (e.g. $-\text{NH}_2$, $-\text{COOH}$, $-\text{OH}$ or $-\text{SH}$) that allow the accumulation of SAS at different phase boundaries (e.g. marine surface-atmosphere, particle-aqueous phase, bottom layer-sediment, pycnocline in a stratified water column). By adsorption processes, SAS affects the bioavailability of metals as well as other OMs and their further distribution in natural waters.

This presentation will present a unique long-term set of DOC and SAS measurement data in the water column samples of the unique marine and euxinic (free sulfide in the water column) system on the Adriatic coast, Rogoznica Lake (43°32'N 15°58'E) (2). Analysis of long-term data indicates that the lake reflects climate change observed through the water column warming, accumulation of toxic sulfides and ammonia (3), and DOC in the bottom euxinic layer. Since the early 1990s, when this lake was first explored, the volume of the anoxic water layer has increased by 4-5 times. The analysis of a set of long-term data (1992-2020) on the reactivity of the OM (based on the analysis of the hydrophobicity of the present OM) shows a trend of accumulation of SAS in the oxic layer and a decrease in the concentration of SAS in the anoxic layer. Comparison of SAS and DOC in the same samples or layers of the water column of Lake Rogoznica indicates certain changes in the biological activity and biogeochemical cycle of organic matter.

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ORGANSKI UGLJIK KAO INDIKATOR PROMJENA U MORSKOM STRATIFICIRANOM VODENOM OKOLIŠU

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Praćenje organske tvari (OT) u morskom sustavu može se bazirati na mjerenjima otopljenog organskog ugljika (eng. *dissolved organic matter*, DOC) te njegove površinsko aktivne frakcije (PAT) (1). U morskoj vodi OT je složena smjesa organskih tvari (bjelančevina, ugljikohidrata, lipida, huminske i fulvinske kiseline), koje imaju različita površinski aktivna svojstva (1). U vodenom okolišu razlikujemo otopljenu OT i suspendiranu partikulatnu OT. Granica između otopljene i partikularne tvari je 0.7 μm te se filtriranjem razdvajaju frakcije. OT s površinski aktivnim svojstvima (PAT), također, se raspoređuje između otopljene i frakcije čestica. Prisutna OT (PAT) u moru je autohtono proizvedena biološkom aktivnošću (primarna proizvodnja, otpuštanja sekundarnih metabolita pod pritiskom hranjenja), ali dio OT je alohtonog porijekla te je unesen u vodeni okoliš (kopneno i atmosfersko porijeklo). Glavno svojstvo PAT je da sadrži hidrofobne (npr. lanci masnih kiselina, aromatski prstenovi ili ugljikovodici) i hidrofilne funkcionalne skupine (npr. $-\text{NH}_2$, $-\text{COOH}$, $-\text{OH}$ ili $-\text{SH}$) koje omogućuju nakupljanje PAT na različitim granicama faza (npr. morska površina-atmosfera, čestica-vodena faza, pridneni sloj-sediment, piknoklina u stratificiranom vodenom stupcu). Adsorpcijskim procesima PAT utječe na bioraspoloživost metala kao i drugih OT te utječe na njihovu daljnju raspodjelu u prirodnim vodama.

U ovom radu bit će prikazani jedinstveni dugoročan skup podataka mjerenja DOC i PAT u uzorcima vodenog stupca jedinstvenog morskog i euksinskog (milimolarne konc. slobodnog sulfida u vodenom stupcu) sustava na Jadranskoj obali, Rogozničkog jezera ($43^{\circ}32'N$ $15^{\circ}58'E$) (2). Analiza dugoročnih podataka ukazuje na to da jezero odražava klimatske promjene uočene preko zagrijavanja vodenog stupca, akumulacije toksičnih sulfida i amonijaka (3), te DOC-a u pridnenom euksinskom sloju. Volumen anoksičnog vodenog sloja od ranih devedesetih godina, od kada se istražuje ovo jezero porastao je za 4-5 puta. Analiza skupa dugoročnih podataka (1992.-2020.) o reaktivnosti OT (bazirano na analizi hidrofobnosti prisutne OT) pokazuje trend akumulacije PAT-a u oksičnom sloju, odnosno smanjenje koncentracije PAT u anoksičnom sloju. Usporedba PAT i DOC u istim uzorcima odnosno slojevima vodenog stupca Rogozničkog jezera ukazuje na određene promjene u biološkoj aktivnosti i biogeokemijskom ciklusu organske tvari.

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Radionice Workshops

LIFE IS LIKE A BOX OF CHOCOLATES: FROM ASTROPHYSICS TO SCIENTIFIC ENTREPRENEURSHIP

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When I was a university professor, I often got a question from Croatian astrophysics and astronomy students about their possibilities for future careers. Their view was that astrophysics gives you only a path toward work as a professional scientist and nothing else. In reality, astrophysics and astronomy give you a very diverse set of skills that are highly valuable in private sector. Advanced work with data and math, understanding sensors, programming, solving problems, data acquisition techniques, etc., all these are highly prized skills. But life is more complicated than this simple story. We seek life security and predictability, but dream about adventures and exciting uncertainties. Today, we live in a world of truly amazing possibilities, but this means that more responsibility is put on us, on our personal life choices and decisions.

ŽIVOT JE POPUT BOMBONIJERE: OD ASTROFIZIKE DO ZNAJSTVENOG PODUZETNIŠTVA

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Dok sam bio sveučilišni profesor, često sam od hrvatskih studenata astrofizike i astronomije dobivao pitanja o mogućnostima za njihovu buduću karijeru. Njihovo je mišljenje bilo da vam astrofizika daje samo put ka poslu profesionalnog znanstvenika i ništa drugo. U stvarnosti, astrofizika i astronomija daju vam vrlo raznolik niz vještina koje su iznimno vrijedne u privatnom sektoru. Napredno poznavanje rada s podacima i matematikom, razumijevanje senzora, programiranje, rješavanje problema, tehnike prikupljanja podataka itd., sve su to vrlo cijenjene vještine. Ali život je složeniji od ove jednostavne priče. Težimo sigurnosti i predvidljivosti u životu, ali sanjamo o pustolovinama i uzbudljivim neizvjesnostima. Danas živimo u svijetu doista nevjerojatnih mogućnosti, ali to znači da se na nas stavlja više odgovornosti, na naše osobne životne odabire i odluke.

CAREERS BEYOND ACADEMIA: EXPERIENCE FROM THE UNIVERSITY OF OXFORD

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During my undergraduate studies and later PhD, I was picturing myself pursuing a long-term career as an academic researcher. Becoming a group leader and maybe a lecturer seemed like an obvious path for someone who loves and enjoys scientific research. However, a postdoc experience at the University of Oxford opened my eyes to other possibilities. I had a chance to meet and hear from many former researchers who left academia after their PhD or postdoc, and were thriving in their new roles. Moreover, the University is providing lots of support for students and staff who want to employ their unique set of skills to pursue careers outside of academia. Focus on personal and professional development of researchers is becoming increasingly important to major funders and scientific institutions in the UK. I would like to share personal experience of how this environment shaped my own thinking about my future career.

KARIJERE IZVAN AKADEMIJE: ISKUSTVO SA SVEUČILIŠTA U OXFORDU

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Tijekom svog preddiplomskog studija, a kasnije i doktorata, vidjela sam se kako nastavljam dugogodišnju karijeru akademske istraživačice. Postati voditelj grupe i možda predavač, činilo se očitim putem za nekoga tko voli i uživa u znanstvenim istraživanjima. Međutim, iskustvo usavršavanja na poslijedoktorskoj razini na Sveučilištu u Oxfordu, otvorilo mi je oči za druge mogućnosti. Imala sam priliku upoznati se i razgovarati s brojnim bivšim istraživačima koji su napustili akademsku zajednicu nakon doktorata ili poslijedoktorata i koji su s uspjehom napredovali u novim ulogama. Štoviše, Sveučilište pruža veliku podršku studentima i osoblju koje žele primijeniti svoje jedinstvene vještine za nastavak karijere izvan akademske zajednice. Stavljajući fokus na osobni i profesionalni razvoj istraživača postaje sve važnije za velike donatore i znanstvene institucije u Velikoj Britaniji. Željela bih podijeliti osobno iskustvo o tome kako je ovo okruženje oblikovalo moje vlastito razmišljanje o mojoj budućoj karijeri.

CAREER IN INDUSTRY- KEY SKILLS AND MINDSET FOR SUCCESS

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When I wistfully look back on my academic years, my present-day self would have liked to have known what key skills to prioritize for professional successes. Technical education- is the foundational base to a career in STEM disciplines- but the real distinguishers are a number of skills and methodologies that academia tends to fail to systematically teach. In this workshop, I will share my view on which skills are important to successfully navigate your career- both in industry and academia.

KARIJERA U INDUSTRIJI - KLJUČNE VJEŠTINE I NAČIN RAZMIŠLJANJA ZA USPJEH

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Kad se sjetno osvrnem na svoje akademske godine, moje bi današnje ja voljelo znati koje ključne vještine vrijedi prioretizirati za profesionalni uspjeh. Tehničko obrazovanje temeljna je osnova za karijeru u STEM disciplinama, ali brojne vještine i metodologije koje akademska zajednica ne uspijeva sustavno podučavati su ključne za poslovni uspjeh. Na ovoj radionici podijelit ću „tajnu” o tome koje su vještine važne za uspješni razvoj karijere - kako u industriji, tako i u akademskoj zajednici - a često su zanemarene.

Popis sudionika

Ančić, Daniela	115, 116	Dragičević, Paula	61, 62
Antičević, Ivan	75, 76	Drušković, Morana	322, 323
Bačinić, Anđela	406, 407	Dunato Pejnović, Nadia	410, 411
Bakija, Marija	308, 309	Dželalija, Mia	191, 192
Bakšić, Marta	175, 176	Đerđ, Tamara	183, 184
Barić, Domjan	271, 272	Ević, Valentina	324, 325
Bašić-Šiško, Angela	396, 397	Fatović, Marta	275, 276
Begić, Valerija	144, 145	Filek, Klara	193, 194
Belovari, Mateja	310, 311	Gazdek, Nika	152, 153
Beljan, Silvestar	133, 134	Gizdavec, Nikola	97, 98
Beriša, Arben	170, 171	Gotovuša, Mia	326, 327
Biočić, Ivan	119, 120	Grbić, Safer	277, 278
Biščan, Matko	154, 155	Grgurić, Jasenka	195, 196
Bjedov, Dora	177, 178	Gršković, Paula	129, 130
Bogoje Raspopović, Andrijana	179, 180	Hackenberger Kutuzović, Domagoj	83, 84
Bogovac, Tonko	408, 409	Harabajsa, Suzana	139, 140
Borić Bilušić, Ana	181, 182	Hazdovac, Ivana	412, 413
Bošnjak, Barbara	91, 92	Hlebec, Dora	197, 198
Božić, Dubravka	398, 399	Hok, Lucija	328, 329
Brkić, Alojzije	117, 118	Ivasić, Sara	279, 280
Brusač, Edvin	312, 313	Ivec, Arian	164, 165
Bubalo, Anđelina	314, 315	Iveković, Damjan	67, 68
Bubaš, Matej	316, 317	Jagić, Karla	172, 173
Bule, Kristina	318, 319	Jelić Matošević, Zoe	330, 331
Burić, Nataša	158, 159	Jarić, Anja	298, 299
Colić, Ivana	111, 112	Jovović, Lada	199, 200
Čadež, Tena	57, 58	Junior Kolman, Robert	338, 339
Čorak, Nina	87, 88	Kalčec, Nikolina	332, 333
Despot-Slade, Evelin	185, 186	Kanjer, Lucija	201, 202
Diklić, Josipa	273, 274	Karić, Mirnes	203, 204
Doboš, Marko	187, 188	Kerep, Robert	66, 67
Dobrović, Ana	189, 190	Kern, Matej	334, 335
Dončević, Lucija	320, 321	Klačić, Tin	131, 132

Klarić, David	336, 337	Mijošek, Tatjana.....	103, 104
Kokotović, Iva	142, 143	Mikec, Luka	400, 401
Komazec, Bruno.....	205, 206	Mikelić, Ana	358, 359
Koprivec, Isabella.....	207, 208	Mikoč, Damir.....	402, 403
Korica, Milenko.....	340, 341	Mikulandra, Ivana	113, 114
Koska, Sara	209, 210	Milinković, Andrea	416, 417
Kosić-Vukšić, Josipa	342, 343	Miloloža, Martina.....	360, 361
Košćak, Marta	344, 345	Mišura, Ozana	362, 363
Košpić, Karla	211, 212	Mrdjen-Hodžić, Rafaela	221, 222
Kovačević, Marija.....	95, 96	Nazlić, Marija	223, 224
Kožuljević, Ana Marija	281, 282	Nikolić, Barbara.....	225, 226
Kralj, Magdalena.....	69, 70	Ožegović, Antonija	364, 365
Krošl, Ivona	346, 347	Pali, Dorotea	227, 228
Kruljac, Mateo	283, 284	Panić, Barbara.....	366, 367
Kučan, Darko	160, 161	Pantalon Juraj, Natalija	101, 102
Kuzman, Dino	348, 349	Pavičić, Ivana.....	229, 230
Latečki, Helena	285, 286	Pelesk, Antonio	368, 369
Ledinski, Maja.....	213, 214	Pelikan, Jadranka	105, 106
Lesar, Nikola	123, 124	Peranić, Matej.....	150, 151
Lovrenčić, Leona.....	215, 216	Pešut, Ena	231, 232
Lozančić, Ana	350, 351	Petrović, Marija.....	300, 301
Lulić, Lucija	217, 218	Pipalović, Goran	233, 234
Majnarić, Nina	414, 415	Pocnić, Marijana	370, 371
Mandarić, Mirna.....	352, 353	Poje, Goran	81, 82
Marić, Vanja.....	135, 136	Pranić, Petra.....	127, 128
Marinović, Marina	85, 86	Pritišanac, Ena.....	148, 149
Markovski, Marsej.....	79, 80	Pucko, Ivan.....	372, 373
Martinčić, Jelena	71, 72	Putar, Darija	235, 236
Martinez, Valentina	156, 157	Radenković, Tijana	77, 78
Mateša, Sarah.....	121, 122	Radošević, Ana	63, 64
Matišić, Mateja.....	107, 108	Radovani, Barbara.....	237, 238
Matošević, Ana	146, 147	Razum, Marta	374, 375
Medić, Mihovil.....	354, 355	Rebrović, Lucija	376, 377
Mićunović, Marin.....	125, 126	Redžović, Zuzana.....	162, 163
Mihelec, Danijela.....	356, 357	Robić, Marko.....	378, 379
Mijanović, Lucija	219, 220	Roljić, Rajko.....	239, 240

Rubić, Ivana	380, 381	Švob, Mirna.....	59, 60
Ruić, Krešimir.....	287, 288	Talajić, Antea.....	253, 254
Sabol, Jurica	137, 138	Terlević, Ana	255, 256
Sekulić, Milena.....	295, 296	Tkalčević, Marija	291, 292
Selak, Lorena	418, 419	Tokić, Mirta.....	257, 258
Simonović, Niki	420, 421	Trinajstić, Nina	304, 305
Slade, Jakov	384, 385	Trpčić, Marina	306, 307
Sošić, Iva	241, 242	Tunjić Cvitanić, Monika.....	259, 260
Sović, Karlo	386, 387	Turić, Luka.....	109, 110
Spahić, Zlatan	388, 389	Turković, Lu.....	394, 395
Stajić, Stefan	297	Usenik, Andrea.....	93, 94
Stojanović Marković, Anita.....	243, 244	Veseli, Marina	261, 262
Sušac, Kristina.....	390, 391	Veseljak, Damira	263, 264
Svetličić, Ema.....	99, 100	Viskić, Marko.....	89, 90
Šarić, Ivana.....	382, 383	Vitko, Sandra.....	265, 266
Šenolt, Natalia	302, 303	Volarić, Marin	267, 268
Šetinc, Maja	245, 246	Vuić, Barbara.....	269, 270
Šimunić, Ena	247, 248	Vuk, Tamara.....	168, 169
Šlaus, Bruno.....	289, 290	Vukman, Nikola.....	293, 294
Štancl, Paula	249, 250	Vukorepa, Ivana	404, 405
Štimac, Valentina.....	251, 252	Zeljковиć, Marija.....	71, 72
Šutalo, Petar	392, 393	Zonjić, Iva	166, 167

