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Source / Izvornik: **Biosystems, 2022, 218**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.1016/j.biosystems.2022.104695

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:217:097800

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Download date / Datum preuzimanja: **2025-01-14**

Repository / Repozitorij:

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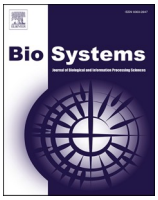
BioSystems 218 (2022) 104695

Contents lists available at ScienceDirect

BioSystems

journal homepage: www.elsevier.com/locate/biosystems



Standard Genetic Code *vs.* Supersymmetry Genetic Code – Alphabetical table *vs.* physicochemical table

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ARTICLE INFO

Keywords:
Standard genetic code
Nuclear genetic code
Mitochondrial genetic code
Genetic code symmetries
Purine
Pyrimidine symmetry
Natural amino acids

ABSTRACT

The fundamental role of symmetry in the genetic code is to decrease disorder between codons and to preserve the integrity of system. The Standard Genetic Code (SGC) table is structured alphabetically in a horizontal and vertical array of U–C-A-G bases only with aesthetic symmetry.

We postulate "the symmetry theory of genetic code" which is based on the unique physicochemical purine – pyrimidine symmetry net between codons of our Supersymmetry genetic code (SSyGC) table. The common purine – pyrimidine symmetry net as "the golden rule" and a core of the SSyGC table is universal, remaining unchanged during all of evolution. It is identical for more than 30 known genetic codes including those that will be discovered in the future, as well as for all RNA and DNA species. The unique SSyGC table has five physicochemical symmetries between bases, codons, and amino acids: 1) purine – pyrimidine symmetry on the principle of the Watson – Crick pairing (A↔U, C↔G), 2) direct – complement symmetry between codons, 3) mirror symmetry between bases and codons, 4) A + T rich and C + G rich symmetry between codons, and 5) symmetry between position of amino acids. Opposite to the SGC table where the third base is inactive, in the SSyGC table the role of the third base in codons is dominant in creation of symmetries. There are also present for the first time the symmetric positions of all boxes with amino acids. Opposite of the SGC table, the SSyGC code table contains three sextets for Serine, Arginine, and Leucine, each with six codons, positioned in continuity. Multi – facet symmetries of the SSyGC table as a natural law exclude the individual random creation of amino acids even in primitive life form. Accordingly, we hypothesize that the contemporary life arose due to common activity of all natural amino acids. With discovery of the unique physicochemical Supersymmetry genetic code table, the new light is shed on the symmetry of the genetic code.

1. Introduction

The full set of relationships between codons that specify the amino acids or stop codons is called the genetic code. Up to present, beside the well-known SGC table, more than 30 slightly alternative nuclear and mitochondrial genetic codes have been reported. They are usually displayed as a table called the genetic code table.

The fundamental role of symmetry in the genetic code is to decrease disorder (entropy) between codons and to preserve the integrity of system during evolution (Rosandić et al., 2013b, 2016, 2019; Rosandić and Paar, 2014, 2021). Einstein's great advance was to put symmetries as a dominant concept in the fundamental law of physics, to regard the symmetry principle as the primary feature of nature. The symmetry principles dictate the form of the laws of nature (Gross, 1996). The relationship between symmetry of the genetic code and evolution was summarized by Koonin and Novozhilov 2009:" Why is the genetic code the way it is and how did it come to be, that was asked over fifty years ago at the dawn of molecular biology and might remain pertinent even in another fifty years". We solved this problem forty years earlier than expected. In our Ideal Symmetry Genetic Code (ISyGC) table, the physicochemical purine-pyrimidine symmetry net between codons is common for all, more than 30 nuclear and mitochondrial genetic codes (Rosandić and Paar, 2021).

However, up to now, the question has remained as to whether the symmetries between amino acids within the genetic code table also exist. The answer to this question, as well as the connection between the

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https://doi.org/10.1016/j.biosystems.2022.104695
Received 7 October 2021; Received in revised form 2 May 2022; Accepted 9 May 2022
Available online 14 May 2022
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creation of amino acids and evolution, is given in this work.

2. The standard genetic code has only aesthetic alphabetical symmetry

The central position in all biology and genetics textbooks is held by the SGC table, which consists of 4 × 4 boxes with 4 codons in each box, where 61 codons are assigned to a specific amino acid and the other three are terminating stop signals. Codons in the SGC table are structured alphabetically in a horizontal and vertical array of U–C-A-G bases. It means that third base in each box has also U– C- A-G alignment. Therefore, the role of the third base was ignored in search of symmetries of SGC table. Thus, each box was differentiated only according to the first two bases. Unfortunately, in this way, the SGC table and all other known genetic code tables built on the U– C- A-G principle suffer from an inability to show the complete physicochemical symmetry between codons. In the SGC table, alphabetic symmetry between all bases (A, G purines; U, C pyrimidines) is only an aesthetic category.

Woese et al. (1966) pointed out that the Standard genetic code is exceedingly highly ordered with respect to the polar requirement with large coherent domains for hydrophobic, intermediate, and polar amino acids. In the recent publication, Štambuk and Konjevoda (2020) also concluded that "marked differences were observed for the hydrophobicity and lipophilicity parameters encoded by the second base of the SGC table. The nucleotide hierarchy U < C < G < A its complement A < G < C < U at the second base correlated best to the amino acid hydrophobicity and polarity. By contrast, the hierarchy C < G < U < A and its reverse A < U < G < C on the second base were associated with the same amino acid parameters of lipophilicity and accessible surface area. No association was observed of the codons at the first and third position with respect to the hydropathy, polarity, lipophilicity, and accessible surface area. The results imply that the second base possesses the majority of information content with respect to the physicochemical properties observed." With respect to the unchanged structure of the SGC table, their results showed only a partial solution related to the physicochemical properties between the second base of codons and amino acids based on polarity.

Our investigation of the genetic code is based on the physicochemical properties of purines and pyrimidines as well as codons based on symmetries. In our completely new SSyGC table the third base also has a very important role, what was ignored already from (Crick, 1968; Lagerkvist, 1978), and is exchanged as purine-pyrimidine on the principle of Watson-Crick pairing (↔), and mirror symmetry (1–4, 2–3): G-A-C-U (1) ↔C–U-G-A (2), and A-G-U-C (3) ↔ U–C-A-G (4). The result is a new construction of the whole SSyGC table which consists of symmetries between bases, codons, and position of amino acids.

The genetic code is degenerate because more than one type of codon (2, 3, 4 or 6) may encode a single amino acid. J.E.M. Hornos and Hornos 1993 introduced, based on an algebraic approach to the SGC table, "the progressive symmetry breaking hypothesis", which explained only the number of codons corresponding to each amino acid, but without finding codon or amino acid symmetries. This model was further extended by other researchers (Hornos et al., 1999; Antoneli and Forger, 2011; Lenstra, 2014; Shu, 2017). In that approach, evolution was related to progressive symmetry breaking.

Our purine - pyrimidine symmetry analysis is based on the principle of codon – anticodon (the Watson – Crick pairing A↔U, C↔G) of genetic code. The purine – pyrimidine symmetry net analysis is a core of the present method which reveals the Supersymmetry genetic code table. With these methods the new mirror symmetry and the symmetry between amino acids are discovered as characteristic for Supersymmetry genetic code table. Quadruplet analysis is based on our classification of trinucleotides (codons) (Rosandić et al., 2013). This manuscript is theoretical approach and not experimental/statistical.

3. Characteristics of the Ideal Symmetry Genetic Code (ISyGC) table

Nirenberg and Matthaei in 1961 identified amino acids corresponding to the 64 nucleotide codons. After that identification, it has been a 60-year challenge for biology to find optimal symmetry of the genetic code. Symmetries were investigated giving emphasis to codons and amino acids distribution in triangular, rectangular, circular, torus form, as well as in binary transformation of nucleotides within codons (Ahmed et al., 2010; Michael and Pirillo, 2010; Castro Chavez, 2012; Nemzer, 2017; Michael, 2017; Shu, 2017; Saier, 2019, Štambuk and Konjevoda, 2020; DiGiulio, 2021), but without results for complete symmetry based on physicochemical properties. The study of all codes of life with the standard methods of science is a new field of research that must be turned into practice (Barbieri, 2014).

After our discovery of the ISyGC table (Rosandić and Paar, 2021), we introduced "symmetry theory of genetic code" which is based on the unique physicochemical purine – pyrimidine symmetry net between codons of the ISyGC table which is identical for all genetic codes as well as for all RNA and DNA species during whole evolution. This was transitional phase in our investigation of genetic code symmetries.

The ISyGC table has also configuration as SGC table with 4 × 4 boxes. But it consists of leading and non-leading groups of codons with four columns of 16 codons each and with unique purine - pyrimidine symmetry net. The leading role between codons has the sextet serine as the single one in whole genetic code table. It encompasses the two neighboring vertical boxes of the ISyGC table, where codons are in direct – complement relationship. Also, with purine ↔ purine and pyrimidine ↔ pyrimidine horizontal transformation, serine determines the positions of all other codons in 4 × 4 boxes of the whole ISyGC table. Therefore, serine was our key for discovering the ISyCG table of codons. Consequently, direct and complement boxes alternate in the whole genetic code. Simultaneously, the pairs of codons in the same box also alternate on direct and complement relationship. Due to the purine - pyrimidine symmetry net, the codons localization in the ISyGC table is strictly defined and amino acids are arranged *in continuo*, but without symmetry between amino acids.

It should be stressed that the purine – pyrimidine symmetry net enables an automatic transformation of the ISyGC table into DNA type two-strand sequences with Watson – Crick pairing (A ↔ U, C ↔ G). This transformation appears automatically by linearizing codons from direct boxes for the top strand, and after that from complement boxes for the bottom strand of the DNA structure. This is also analogous form to the 5'3' codon and the 3'5' anticodons (Rosandić and Paar, 2021). The symmetry-based construction of the ISyGC table automatically places the AUG start signal at the beginning of the genetic code.

The ISyGC table is structured with natural triplet symmetries among bases and codons: purine – pyrimidine symmetry between bases, direct – complement symmetry between bases and codons, and symmetry between A + U rich and C + G rich codons (Rosandić and Paar, 2021).

All RNA and DNA species have the ISyGC table with the common physicochemical purine – pyrimidine symmetry net (Rosandić and Paar, 2021).

4. The unique five symmetries of the supersymmetry genetic code table

The search of symmetries among bases, codons and amino acids within the genetic code table is not like a Rubik's Cube game, but also has implications for understanding the beginning of life and evolution. The genetic code table has revealed during our investigation, step by step, the fascinating symmetry net, as seen from the chronology of our publications from 2013 to today (Rosandić et al., 2013b, 2016, 2019; Rosandić and Paar, 2014, 2021).

From discovery of genetic code (Nirenberg and Matthaei, 1961) most of time was directed to investigations of symmetries between codons

and amino acids. However, our proof of purines and pyrimidines in the form of symmetry net led us also to discovery of symmetrical arrangement of codons and amino acids within genetic code table.

To derive supersymmetry in the SSyGC table, we transformed the ISyGC table with four identical to two identical purine – pyrimidine columns (Fig. 1). This was done so that the non-leading group of codons was moved below the leading group of codons. At the same time, we rotated the non-leading group by 180^{o} in a horizontal and vertical direction. With this rotation we obtained a novel mirror supersymmetry between leading and non-leading group of codons. In this way the horizontal transformation proceeds only once through a purine ↔ purine, pyrimidine ↔ pyrimidine exchange between only two columns. Thus, A + T rich and C + G rich codons are altering between the two columns in the same row. In relation to ISyGC table, the SSyGC table has five symmetries between bases, codons, and amino acids. The vertical transformation does not change the direct – complement symmetry of Watson – Crick pairing between boxes with four codons. The new mirror symmetry is present between the second and third base of all codons. A mirror pairing of the first base of codons in all boxes is to fold alternately over both purines (A ↔ G), and both pyrimidines (U ↔ C) (Fig. 1). The result is the unique core purine – pyrimidine symmetry net with mirror supersymmetry of two identical purine – pyrimidine columns (Fig. 2).

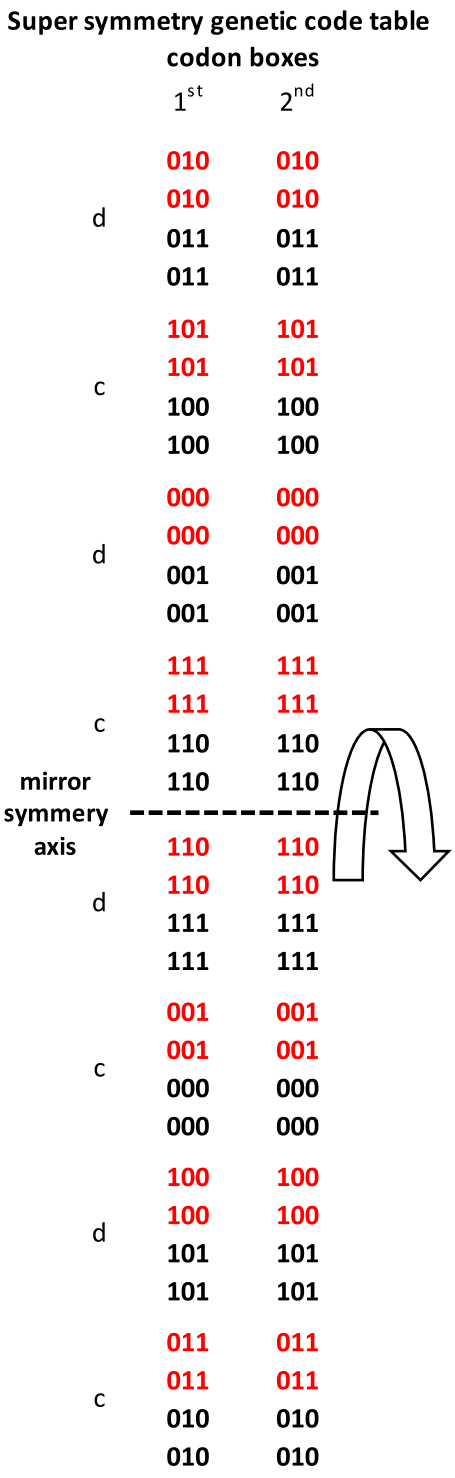
This approach led to a fascinating solution: all amino acids, regardless of the number of associated codons in our proposed two-column Supersymmetry genetic code table, are mutually symmetrically positioned:

- A + T rich pairs of split boxes, mutually in a direct – complement relationship
- C + G rich pairs of non-split boxes, mutually in a direct – complement relationship
- pairs of split boxes with purine ↔ purine, pyrimidine ↔ pyrimidine transformations of bases within codons
- pairs of non-split boxes with purine ↔ purine, pyrimidine ↔ pyrimidine transformations of bases within codons
- split boxes which contain codons for two different amino acids
- non-split boxes which contain four codons for the same amino acid

Box	Amino acid	Codons	Pu/Py	Pu/Py	Codons	Amino Acid
Direct boxes	Start/Met	AUG	010	010	GCA	Ala
	Ile	AUA	010	010	GCG	
		AUC	011	011	GCU	
		AUU	011	011	GCC	
Complement boxes	Tyr	UAC	101	101	CGU	Arg
		UAU	101	101	CGC	
	STOP	UAG	100	100	CGA	
	STOP	UAA	100	100	CGG	
Direct boxes	Glu	GAG	000	000	AGA	Arg
		GAA	000	000	AGG	
	Asp	GAC	001	001	AGU	Ser
		GAU	001	001	AGC	
Complement boxes	Leu	CUC	111	111	UCU	Ser
		CUU	111	111	UCC	
		CUG	110	110	UCA	
		CUA	110	110	UCG	
Direct boxes	Leu	UUA	110	110	CCG	Pro
		UUG	110	110	CCA	
	Phe	UUU	111	111	CCC	
		UUC	111	111	CCU	
Complement boxes	Asn	AAU	001	001	GGC	Gly
		AAC	001	001	GGU	
	Lys	AAA	000	000	GGG	
		AAG	000	000	GGA	
Direct boxes	Gln	CAA	100	100	UGG	Trp
		CAG	100	100	UGA	Stop
	His	CAU	101	101	UGC	Cys
		CAC	101	101	UGU	
Complement boxes	Val	GUU	011	011	ACC	Thr
		GUC	011	011	ACU	
		GUA	010	010	ACG	
		GUG	010	010	ACA	

Mirror symmetry axis

Fig. 1. The Supersymmetry genetic code table. AUG start signal is at the beginning of the Supersymmetry genetic code table. It is the same distribution of purine/pyrimidine profile in both columns, and simultaneously the same profile distribution pairs of codon rows within each box. There are present five symmetries: purine – pyrimidine symmetry between bases and codons, direct – complement symmetry of codons between boxes, and A + U rich and C + G rich symmetry of codons between two columns. There are also present the mirror symmetry between all purines and pyrimidines of the whole code as well as between second and third base of codons. The mirror symmetry simultaneously generated symmetry between amino acids. In such a way for the first time the sextets for Serine, Arginine, and Leucine, each with six codons, are positioned in continuity. 0 pu, purine; 1 py, pyrimidine; bold black line, axis of the mirror symmetry; dark yellow, two pairs of split boxes with direct – complement symmetry between codons; dark blue, two pairs of no-split boxes with direct – complement symmetry between codons; light yellow, two pairs of split boxes with purine ↔purine, pyrimidine ↔ pyrimidine transformation between codons; light blue, two pairs of non-split boxes with purine ↔purine, pyrimidine ↔ pyrimidine transformation between codons.



(caption on next column)

Fig. 2. The fundamental physicochemical purine-pyrimidine symmetry net of the Supersymmetry genetic code table is "the golden rule" of symmetry of genetic code. All distributions of purines and pyrimidines are ordered according to the arrangement in the SSyGC table. There are alternating positions of boxes with direct and complement relationship between purines – pyrimidines within codons on the principle of Watson – Crick pairing; there is also the mirror symmetry between purines and pyrimidines; In the SSyGC table symmetry net of both columns have the same distribution of purine/pyrimidine profile, and simultaneously the same profile distribution pairs of codon rows within each box. The fundamental purine – pyrimidine symmetry net as symmetry core of the SSyGC table is identical for all nuclear and mitochondrial genetic codes as well as for all species from prokaryote and eukaryote, and unchangeable during evolution. 0: purine; 1: pyrimidine; bold black line: axis of the mirror symmetry; red or black are denoted bases of codons with the same purine/pyrimidine profile; d: direct; c: complement.

Because of noticeable all symmetries between the two columns, the SSyGC table has much more natural shape.

The perfection of symmetries is reflected in localization of two boxes which contain codons for 3 amino acids or stop signals:

1. box Tyr UAC, UAU + stop-signal UAG + stop signal UAA
2. box Trp UGG + stop signal UGA + Cys UGC, UGU

As seen, the codons and stop signals between these two boxes also have a mutual mirror symmetry (2:1:1, 1:1:2) and mirror symmetry between purines and pyrimidines (101, 101, 100, 100 : 100, 100, 101, 101) (Fig. 1). The symmetrical position is also between the same boxes within the SSyGC code table (the upper second box in the left column; the lower second box in the right column).

It should be stressed that for the first time our SSyGC code table contains three sextets for Serine, Arginine, and Leucine, each with six codons positioned in continuity. The codons of all other amino acids and signals are also arranged in continuity. The position of the AUG start signal is at the beginning of the Supersymmetry genetic code table.

Opposite of the SSyGC table, the basic difficulty in investigation of the SGC table symmetries is the use of the same U – C – A – G array of the third base in all 16 codon boxes. Therefore, the third base cannot contribute the search for the genetic code symmetries (Lenstra, 2014). Namely, nothing in the nature is alphabetically ordered. The alphabetic ordering of bases in the SGC table cannot reveal natural physicochemical relations between bases and codons. For difference of the third base, the first two bases of all four codons within the same box are equal.

The key role of the third base in creation of symmetries in the SSyGC table is presented in Fig. 3.

5. The common symmetries between DNA genome and genetic code

Our initial investigation of the role of symmetries within the genome and genetic code contains trinucleotide classification with 10 A + T rich and 10 C + G rich quadruplets of DNA molecules (Fig. 4.). Therefore, all members from the same quadruplet are A + T rich or C + G rich. Each quadruplet consists of trinucleotides in the form direct – reverse complement - complement – reverse with purine – pyrimidine and mirror symmetries between them (Rosandić et al., 2016) (Fig. 5). It is manifesting in almost identical relative frequency between direct and reverse complement of trinucleotides in one strand of the DNA molecule as strand symmetry. The unsolved question is how the strand symmetry appears (Chargaff's second parity rule) in an autonomous system, as is the DNA genome. We have shown that under the influence of the natural law, with entrance of each random mutation into one DNA strand, the same mutation must also enter the other strand regardless of localization (Rosandić et al., 2016, 2019) (Fig. 6). Both mutations are binding with their complementary pairs between the two strands of DNA molecule leading to the formation of the quadruplet. The ISGC and SSyGC table

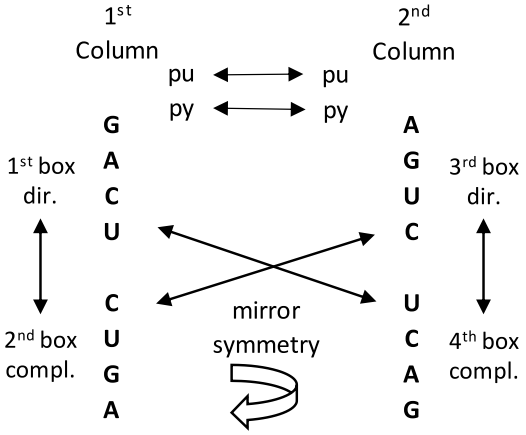


Fig. 3. The third base in all codons of the SSyGC table has a key role in creation symmetries. It is positioned within each box, but also within vertical pairs of alternating boxes of codons (box 1 and 2, as well as 3 and 4) as direct ↔complement on the principle of Watson – Crick pairing, and in horizontal pair of boxes between two columns in the same row on the principle of the purine ↔ purine, pyrimidine ↔ pyrimidine pairing. In this way the mirror symmetry is created. The same motif repeats in boxes 5–8 above the mirror axis of the SSyGC table. All symmetry profile also is repeated below the mirror axis, but in the mirror configuration (see Fig. 1). All bases in this figure are ordered according to the arrangement in the SSyGC table. The SGC table has the same U – C – A – G array of the third base in all 16 codon boxes and therefore cannot contribute the search for the physicochemical symmetries of genetic code.

contain only one copy of 20 quadruplets. We have also shown that the same purine – pyrimidine, direct - complement, A + T rich – C + G rich symmetries, incorporated in the DNA genome are simultaneously present in the ISyGC table as well as in SSyGC table.

One strand RNA viruses as well as double strand DNA viruses, all prokaryotes and eukaryotes have the same common purine – pyrimidine symmetry net (Rosandić and Paar, 2021). Now we show that the same symmetries are present in the SSyGC table, but with the additional mirror symmetry, and the symmetry between amino acids. Because of these additional symmetries the SSyGC table is superior.

Due to the purine – pyrimidine symmetry net it is possible to transform the ISyGC or SSyGC table into the DNA form (Rosandić and Paar, 2021). Therefore, it follows that the DNA and ISyGC table, as well as more sophisticated SSyGC table variant, are like a coin with two faces.

The one strand RNA viruses are short, fragile, and easily mutate because they do not possess quadruplet symmetries (Chargaff's second parity rule) for which the two strands are necessary. A direct example is SARS-CoV-2 RNA virus, which has developed several mutants in less than two years, some of them more infectious. Although one strand viruses, they have identical ISyGC and SSyGC tables and in this way, they have a direction as to how during evolution to transform from RNA to DNA viruses with Watson–Crick A ↔ T, C ↔ G pairing (Rosandić and Paar, 2021).

Klump and coworkers (Klump et al., 2020) and (Breslauer et al., 1986) already also inspired us to compare the symmetries of the free energy codons with our Supersymmetric Genetic code table, the trinucleotides of DNA quadruplets and our classification of trinucleotides/codons. The result is our manuscript on free energy symmetries "The Supersymmetry Genetic Code table and quadruplet symmetries of DNA molecule are unchangeable and synchronized with the codon free energy mapping during all of evolution" which is in the process of publication (Rosandić and Paar, 2022). There we showed that the unchangeable and universal symmetry properties of the genetic code and DNA molecule are linking with the same characteristic of energy code and decreasing disorder and may shed some new light on evolution. On the other hand, the free energy values of codons in the Standard Genetic Code (SGC) table were dispersed, where the simple symmetrical relationship between them was not recognizable. Simultaneously, we presented the interconnectedness of the codon cycles in the form of our classification of codons/trinucleotides regarding the A + T rich and C + G rich quadruplet purine-pyrimidine symmetry (Fig. 4)..

6. The common symmetry net and alternative genetic codes

Our SSyGC table contains also the unique fundamental common purine-pyrimidine symmetry net for all more than 30 slightly alternative variants of nuclear and mitochondrial genetic codes detected up to present (Rosandić and Paar, 2021), including those that will be discovered in the future. Variations of the number of codons for individual amino acids, inserted into the SSyGC table, arise most often by a capture from a neighboring codon from a weak split box or a whole box (Fig. 7), but purine-pyrimidine symmetry net as a core of SSyGC table remaining unchanged during whole evolution. Such usurpation indicates a larger metabolic requirement for individual amino acid.

7. The relationship between the synthetic bacterial genetic code and the SSyGC table

Fredens and coworkers (Fredens, 2019) constructed laboratory *Escherichia coli* with the entire synthetic DNA genome, called Syn 61, that utilized just 61 codons for proton synthesis, compared to the 64 in the natural living organisms. Performing the "synonymous codon compression", they recompile the *E. coli* genome with two (TCG, TCA) out of six codons (AGC, AGT, TCA, TCG, TCT, TCC) encoding serine, and TAG stop signal. Accordingly, this synthetic organism uses 59 codons and TAA, TGA to encode 20 amino acids and 2 start/stop signals. Relative to the parental strain, synthetic DNA organisms displayed only minor changes, with a slower growth rate, slightly elongated cells, and enabled deletion of previously essential tRNA (Fredens, 2019).

What is the nature of relationship between the "laboratory different genetic code" and the SSyGC table? Is it really a different code? If the two codons and one stop signal are omitted from the SSyGC table, the remaining 61 stay at the same positions within the common purine-pyrimidine symmetry net keeping their symmetrical mutual relationship. Simultaneously, the positions of omitted codons and stop signal remain empty, because none of the remaining codons and stop signals can replace them without violating the symmetries; due to symmetries, each codon and stop signal has a strictly defined position within the SSyGC table. In this way, it is not a different genetic code but an abnormal, mutilated and artificial SSyGC table. It is interesting that the experiment was successful omission of TCG and TCA codons of amino acid Serin, which has the special position in the whole SSyGC table. Namely, the two boxes containing four of six codons for Serine are in a unique mutual relationship as direct and complement: TCG (direct) ↔AGC (complement), TCA (direct) ↔AGT (complement). This means that by omission of TCG and TCA from the top strand of DNA molecule, also their complement pairs AGC and AGT in the bottom strand are omitted. However, the same two AGC and AGT codons in the top strand continue to function as a code for Serin. The remaining TCT and TCC codons are intact. In this way, in the synthetic genetic code of *E. coli* four of six codons function for Serine. Serine has important roles in forming glycoproteins and it is involved in the regulation of energy metabolism and fuel storage in the body. The mitochondrial genetic codes for Invertebrate, Trematode, Echinoderm flatworm and Alternative flatworm have even eight codons for Serine (Fig. 7). Therefore, Serine is found in most proteins. Because of its specific position between direct ↔complement neighboring boxes of the SSyGC table, Serin was used as a guideline for creating symmetries in our genetic code table (Rosandić and Paar, 2014, 2021). Similarly, omitting the stop signal TAG, the remaining two stop signals (TGA and TAA) were in function. In this way, the synthetic *E. coli* could survive, but with the mutation marks regarding shape and growth rate.

A+U rich group (I)					C+G rich group (II)				
D	RC(D)	C(D)	R(D)	Subgroup	D	RC(D)	C(D)	R(D)	Subgroup
AUG 010	CAU 101	UAC 101	GUA 010	Ia	GCA 010	UGC 101	CGU 101	ACG 010	IIa
UGA 100	UCA 110	ACU 011	AGU 001		CAG 100	CUG 110	GUC 011	GAC 001	
UAG 100	CUA 110	AUC 011	GAU 001		CGA 100	UCG 110	GCU 011	AGC 001	
UAA 100	UUA 110	AUU 011	AAU 001	Ib	CGG 100	CCG 110	GCC 011	GGC 001	IIb
AAC 001	GUU 011	UUG 110	CAA 100		GGU 001	ACC 011	CCA 110	UGG 100	
AAG 000	CUU 111	UUC 111	GAA 000		GGA 000	UCC 111	CCU 111	AGG 000	
AUA 010	UAU 101	UAU* 101	AUA* 010	Ic	GCG 010	CGC 101	CGC 101	GCG 010	IIc
ACA 010	UGU 101	UGU* 101	ACA* 010		GUG 010	CAC 101	CAC 101	GUG 010	
AGA 000	UCU 111	UCU* 111	AGA* 000		GAG 000	CUC 111	CUC 111	GAG 000	
AAA 000	UUU 111	UUU* 111	AAA* 000		GGG 000	CCC 111	CCC 111	GGG 000	

Fig. 4. Our quadruplet classification of 64 codons (with U-uracil) for genetic code, or trinucleotides (with T-thymine instead of uracil) for RNA and DNA genomes. Each quadruplet is unique and consists of codons or trinucleotides denoted as direct D, and reverse complement from direct RC(D), complement from direct C(D), and reverse from direct R(D). Ten A + U rich (group I) and ten C + G rich (group II) quadruplets are organized in three subgroups. Ia consisting of nonsymmetrical codons/trinucleotides containing four different nucleotides, Ib consisting of nonsymmetrical codons/trinucleotides containing two different nucleotides, Ic, symmetrical codons/trinucleotides which contain duplicated codons/trinucleotides labeled with an asterisk (D = RC, C = R). First four A + U rich quadruplets we generate with start/stop signals: AUG, UGA, UAG and UAA. The C + G rich trinucleotides correspond to purine-purine and pyrimidine-pyrimidine transformation of A + U rich codons/trinucleotides Three symmetries are present in our codon/trinucleotide classification: 1) purine-pyrimidine symmetries in each quadruplet, 2) purine -pyrimidine symmetries within and between A + U rich and C + G rich quadruplets in the same row of the classification; 3) mirror symmetry between direct – reverse and complement – reverse complement in the same quadruplet. For clarity, the white and grey rows are alternating, to order to emphasize pairs of A + T rich and C + G rich codons. 0, purine; 1, pyrimidine. To point out the symmetries this classification is modified with respect to refs. (Rosandić and Paar, 2021). Namely, it is irrelevant which codon/trinucleotide in the quadruplet is direct, because the other three are accordingly adapted.

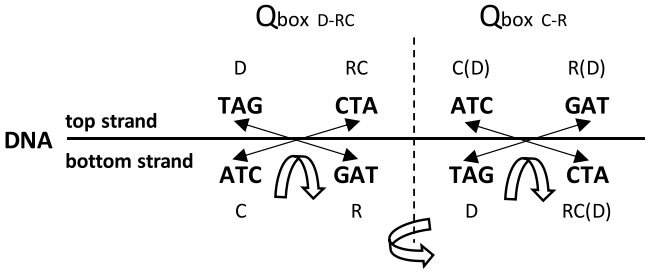


Fig. 5. An example of symmetries in one A + T rich quadruplet from DNA molecule. There are three symmetries: purine – pyrimidine and direct – complement of trinucleotides on the principle of Watson – Crick pairing between both DNA strands. There is also mirror symmetry into $Qbox_{D\text{-}RC}$ as well as $Qbox_{c\ -\ R}$, and between both boxes. The four members of each quadruplet are always the same regardless of which one is chosen as a direct. We named this form of quadruplet "Butterfly symmetry" (Rosandić et al., 2016). The same symmetries exist in the SSyGC table. D, direct; RC, reverse complement; C, complement; R, Reverse; C(D), complement from direct of four trinucleotides; R (D), reverse from direct; RC(D), reverse complement from direct.

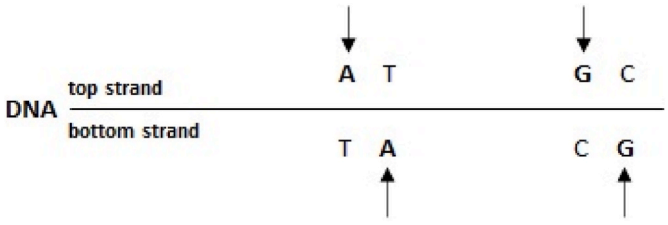


Fig. 6. The scheme for natural law. We have shown that under the influence of natural law the quadruplet of DNA genome, and the strand symmetry (Chargaff's second parity rule) are not violated during evolution. Namely, entrance to each random mutation into one DNA strand, the same mutation must also enter in the other strand regardless of localization (Rosandić et al., 2016). Both mutations are binding with their complementary pairs leading to the formation of the quadruplet. Mononucleotides A ↔ T, and G ↔ C have only two quadruplets (enclosed), dinucleotides six, and trinucleotides 20 (10 A + T rich and 10 C + G rich (Fig. 4)).

8. Concluding remarks

We point out that the purine – pyrimidine multi-symmetry net as the core symmetry of the SSyGC table is unchangeable during whole evolution. After discovery of the Supersymmetry Genetic Code table, we introduced our "symmetry theory of genetic code" which is based on the

Box	Amino acid	Codons	Pu/Py	Pu/Py	Codons	Amino Acid
Direct boxes	Start/Met	AUG	010	010	GCA	Ala
	Met	AUA	010	010	GCG	
	Ile	AUC	011	011	GCU	
		AUU	011	011	GCC	
Complement boxes	Tyr	UAC	101	101	CGU	Arg
		UAU	101	101	CGC	
	STOP	UAG	100	100	CGA	
	STOP	UAA	100	100	CGG	
Direct boxes	Glu	GAG	000	000	AGA	Ser
		GAA	000	000	AGG	
	Asp	GAC	001	001	AGU	Ser
		GAU	001	001	AGC	
Complement boxes	Leu	CUC	111	111	UCU	Ser
		CUU	111	111	UCC	
		CUG	110	110	UCA	
		CUA	110	110	UCG	
Direct boxes	Leu	UUA	110	110	CCG	Pro
		UUG	110	110	CCA	
	Phe	UUU	111	111	CCC	
		UUC	111	111	CCU	
Complement boxes	Asn	AAU	001	001	GGC	Gly
		AAC	001	001	GGU	
		AAA	000	000	GGG	
	Lys	AAG	000	000	GGA	
Direct boxes	Gln	CAA	100	100	UGG	Trp
		CAG	100	100	UGA	Trp
	His	CAU	101	101	UGC	Cys
		CAC	101	101	UGU	
Complement boxes	Val	GUU	011	011	ACC	Thr
		GUC	011	011	ACU	
		GUA	010	010	ACG	
		GUG	010	010	ACA	

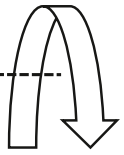


Fig. 7. The mitochondrial trematode code incorporated in the Supersymmetry Genetic Code table. In different genetic codes individual amino acids usually capture a codon from a neighboring amino acid in SSyGC table, points to a larger metabolic requirement, regardless of whether it is for nuclear or mitochondrial genetic codes. But purine – pyrimidine symmetry net always remains unchangeable (Rosandić and Paar, 2021). Methionine (M, Met) expands to the neighboring Isoleucine (Ile) codon AUA; Tryptophan (Trp) expands to the neighboring stop UGA codon; Arginine (Arg) neighboring AGA and AGG codons become 7. and 8. codon for Serine (Ser); Asparagine (Asn) expands to the neighboring AAA codon from Lysine (Lys).

unique physicochemical purine – pyrimidine symmetry net between codons of the SSyGC table, which is identical for all genetic codes as well as for all RNA and DNA species during whole evolution.

Our hypothesis is that life on Earth as we know it today, was developed when all natural amino acids were already present. An example for such an evolutionary path is one of the oldest living organisms, with estimated age of about 2.5 billion years, the single-cell green microalgae *Chlorella Beyerinck*, which consists of 50% proteins and contains all natural amino acids (Bito et al., 2020). This hypothesis is consistent with the SSyGC tables, which with their unique purine – pyrimidine symmetry net is common to all living species from the simplest RNA viruses all the way to *Homo sapiens sapiens*.

The mirror symmetries of purine – pyrimidine net simultaneously generate symmetry between amino acids. This fascinating physicochemical unchangeable symmetry net as “the golden rule” of symmetry of the genetic code table is an argument against the random gradual and individual development of amino acids during the early evolution in the creation of life. Each codon is strictly positioned in the Supersymmetry genetic code table, and therefore, as the whole, can be understood as the natural law. Life was born when all members of the genetic code had been generated.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationship that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Marija Rosandić: Methodology, Conceptualization, Writing – original draft. **Vladimir Paar:** Writing – original draft.

Acknowledgements

We thank to reviewers for very useful comments, stimulating suggestions and recommendations on our manuscript. This work has been fully supported by the Croatian Science Foundation under the project IP-2019-04-2757.

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