Golden and Harmonic Mean in the Genetic Code

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Abstract

In previous two works (Rakočević, 1998; 2013), we have shown the determination of genetic code by golden and harmonic mean within standard Genetic Code Table, i.e. nucleotide triplet table, whereas in this paper we show the same determination through a specific connection between two tables – of nucleotide doublets Table and triplets Table, over polarity of amino acids, measured by Cloister energy in general, and by hydropathy and polar requirement, partially. [This is the expanded version of the article published in Proceedings of the 2nd International Conference “Theoretical Approaches to BioInformation Systems” (TABIS.2013), September 17–22, 2013, Belgrade, Serbia. That first version is also stored, as Version 1, in OSF Preprints.]

Key words: Cloister Energy; Hydropathy; Polar requirement; Golden mean; Harmonic Mean; Genetic Code; Protein amino acids; Mendeleev system.

1. Introduction

In a previous work we have shown that *golden mean* is a characteristic determinant of the genetic code (GC), regarding on the codons binary tree, 0–63 (Rakočević, 1998). In a second one we showed a splitting of Genetic Code Table (GCT) into three equal and significant parts, using the harmonic mean [$H(a, b) = 2ab/(a + b)$; $a = 63$, $b = 31.5$] (Rakočević, 2013). In this paper, however, we will show that a specific *unity* of golden mean and harmonic mean appears to be the determinant of Rumer’s Table of 16 nucleotide doublets (Rumer, 1966) (Tables 1 & 2 in relation to Tables 3 & 4).

01. G	GG (6)	02. F	UU (4)	03. L
04. P	CC (6)	05. N	AA (4)	06. K
07. R	CG (6)	08. I	AU (4)	09. M
10. A	GC (6)	11. Y	UA (4)	12. St.
13. T	AC (5)	14. H	CA (5)	15. Q
16. V	GU (5)	17. C	UG (5)	18. W
19. S	UC (5)	20. D	GA (5)	21. E
22. L	CU (5)	23. S	AG (5)	24. R

Table 1. Rumer’s Table of nucleotide doublets

01. G	GG (6)	02. F	UU (4)	03. L
04. P	CC (6)	05. N	AA (4)	06. K
07. A	GC (6)	08. Y	UA (4)	09. St.
10. R	CG (6)	11. I	AU (4)	12. M
13. V	GU (5)	14. C	UG (5)	15. W
16. T	AC (5)	17. H	CA (5)	18. Q
19. L	CU (5)	20. S	AG (5)	21. R
22. S	UC (5)	23. D	GA (5)	24. E

Table 2. The modified Rumer’s Table

As we have shown, golden mean "falls" between the 38th and 39th codon (38. CAA, 39. CAG), which code for glutamine (Q), a more complex of only two amide amino acids (AAs); two codons, adjacent to the codons (40.UGU, 41.UGC), which code for one of the only two sulfur AAs, cysteine (C). This "harmonization" of diversity is increased by the harmonic mean, in position 42 on the sequence 0-63. The harmonization extends further to "stop" codon (42.UGA) and to codon (43.UGG) that codes for the most complex AA, tryptophan (W). [The "42" as ending position on the "Golden route" – with Fibonacci numbers – on the Farey tree, corresponding with six-bit GC binary tree (Rakočević, 1998).]

On the other side, the splitting of GCT into three parts through harmonic mean (Rakočević, 2013) makes that AAs are distinguished on the basis of the validity of the evident regularities of key factors, such as polarity, hydrophobicity and enzyme-mediated AAs classification (with parameter values as in Table 5) (Table 2.1 in Rakočević, 2013).

2. A new rearrangement of nucleotide doublet Table

With a minimal modification of Rumer's nucleotide doublets Table (DT) follows the next result: if at the beginning of first sub-system,¹ with 6/4 hydrogen bonds, are GG/UU doublets, chemical reasons require GU/UG doublets at the beginning of the second sub-system, with 5/5 hydrogen bonds, instead of AC/CA. From the same reasons, we have the changes: CG/GC & UC/CU on the left and AU/UA & GA/AG on the right. With the four first doublets we have four outer squares, i.e. codon families ($n_1 = \{GG, UU, GU, UG\}$) in nucleotide triplets Table (TT) which code for nonpolar AAs; the four second doublets give four inner codon families ($n_2 = \{CC, AA, AC, CA\}$), which code for polar AAs (Table 3).² With the four third ($n_3 = \{GC, CU; UA, AG\}$) and four fourth ($n_4 = \{CG, UC; AU, GA\}$) doublets are chosen eight intermediate codon families, the first three code for nonpolar AAs [(CU, AU, GC) $\rightarrow$ (L, I, M, A)] and the second five for polar AAs [(UC, UA, CG, AG, GA) $\rightarrow$ (S, Y, R, D, E)] (Table 4). As we see the polar/nonpolar distribution of squares in Table 3 is realized as 4 ± 0 and in Table 4 as 4 ± 1 . By this, the polarity/nonpolarity is taken after *cloister energy*³ (Table 5) as in R. Swanson's article (Swanson, 1984).⁴

1st	2nd letter				3rd
	U	C	A	G	
U	UUU	UCU	UAU	UGU	U
	UUC	UCC	UAC	UGC	C
	UUA	UCA	UAA	UGA	A
	UUG	UCG	UAG	UGG	G
C	CUU	CCU	CAU	CGU	U
	CUC	CCC	CAC	CGC	C
	CUA	CCA	CAA	CGA	A
	CUG	CCG	CAG	CGG	G
A	AUU	ACU	AAU	AGU	U
	AUC	ACC	AAC	AGC	C
	AUA	ACA	AAA	AGA	A
	AUG	ACG	AAG	AGG	G
G	GUU	GCU	GAU	GGU	U
	GUC	GCC	GAC	GGC	C
	GUA	GCA	GAA	GGA	A
	GUG	GCG	GAG	GGG	G

Table 3. Distributions of AAs after nucleotide doublets presented in Table 2. Four squares with dark tones (outer) contain four first doublets from Table 2 and four light (inner) contain four second doublets. In amino acids (within their side chains) at outer/inner areas there are 369/369 nucleons and 61/61 atoms, respectively. All AAs in outer area are nonpolar whereas those in inner area are polar, measured by cloister energy, except histidine that is neutral, but it is polar from the aspect of hydrophathy.

¹ Two subsystems, each with two quadruplets; in total four quadruplets: two on the left as one-meaning (each nucleotide doublet codes for one AA) and two on the right as two-meaning (each nucleotide doublet codes for two AAs or for one AA and termination in the protein synthesis).

² Histidine (H) is polar in hydrophathy, polar requirement and hydrophobicity; nevertheless, in cloister energy it is neutral, because $H = \pm 0$. [About parameters see in legend of Table 5.]

³ Polarity / non-polarity here follows also by the second two parameters – hydrophathy and polar requirement.

⁴ Cloister energy is “a formal free energy of transfer of the amino acid from the outside of a protein to the inside ... I use cloister energy in preference to other measures of amino acid hydrophobicity-phility because it is an *in situ* measure of the property of interest” (Swanson, 1984).

1st	2nd letter				3rd
	U	C	A	G	
U	UUU UUC F UUA UUG L	UCU UCC S UCA UCG	UAU UAC Y UAA UAG CT	UGU UGC C UGA CT UGG W	U C A G
C	CUU CUC L CUA CUG	CCU CCC P CCA CCG	CAU CAC H CAA CAG Q	CGU CGC R CGA CGG	U C A G
A	AUU AUC I AUA AUG M	ACU ACC T ACA ACG	AAU AAC N AAA AAG K	AGU AGC S AGA AGG R	U C A G
G	GUU GUC V GUA GUG	GCU GCC A GCA GCG	GAU GAC D GAA GAG E	GGU GGC G GGA GGG	U C A G

Table 4. Distributions of AAs after nucleotide doublets presented in Table 2. Four squares with dark tones contain four third doublets from Table 2 and four light contain four fourth doublets; two and two doublets on the right, and two and two on the left. In amino acids (within their side chains), in right/left areas there are 369/369-33 nucleons and 59/58 atoms, respectively. All AAs on the right together with D & E from the left are polar and other on the left are nonpolar. Because the balance is realized in relation to diagonal and not in relation to the type of nucleotide doublets (third or fourth) it follows that positions 3 & 4 in DT are not invariant, but only positions 1 & 2 as it is shown in Table 3.

3. Particles number balances through polarity

Distinctions through polarity, presented in Tables 3 & 4, are followed by the balance of the number of nucleons and atoms. Irrespectively of the Table of nucleotide doublets, V. *shCherbak* showed (Shcherbak, 2008, Fig. 10, p. 173] that it makes sense to display the Table of nucleotide triplets (TT) exactly as in Tables 3 & 4: four squares at the corners and four squares in the center as in Table 3; then, eight squares in middle, i.e. in “between” positions, as in Table 4. After *shCherbak*’s view, the balance of the number of nucleons is the next: AAs in four squares in the corners of TT as well as AAs in four squares in the center of TT have 369 nucleons [(F-91 + L-57 + V-43 + G-01 + W-130 + C-47 = 369); (P-41 + T-45 + K-72 + N-58 + Q-72 + H-81 = 369)].

To this *shCherbak*’s insight, we now add: the same quantity give the AAs in right site of TT; the right site in relation to the diagonal F–G⁵ in TT (S31+Y107+R100+S31+R100 = 369). On the left side of the diagonal there are 336 nucleons (L57+I57+M75+A15+D59+E73=336), what means 33 nucleons less, in relation to 369. With this emergence of difference of "33" on

⁵ Starting from diagonal (F–G) together with two vicinal ones (S–R and L–E) we give a central space (“in” space) in a strict balance with the set of polar AAs, polar through hydrophathy (Kyte and Doolittle, 1982): atom number in two and two sets (“in”, “out” / polar, nonpolar) differs exactly for ±1 and ±10, respectively (Rakočević, 2011, Tab. A.3 and equations 11-14).

the scene appears a specific self-similarity⁶ because the number 33 is an important determinant of the number of atoms in the rows and columns of GCT, i.e. of TT.⁷

To this self-similarity determination by nucleon number we now also add the self-similarity determination by atom number: AAs in four squares in the corners as well as in the center of TT have 61 atoms in amino acid side chains [(F14+L13+V10+G01+W18+C05=61); (P08+T08+K15+N08+Q11+H11=61)]. In relation to the diagonal F–G, in TT, there are 58 and 59 atoms, respectively; on the left: L13+I13+M11+A04+D07+E10=58, and on the right: S05+Y15+R17+S05+R17=59. These quantities (58 and 59) are the same as the quantities of hydrogen atoms in Sukhodolets' system (what is a further self-similarity): 58 in two inner and 59 hydrogen atoms in two outer rows (Rakočević, 2011, Tab. 7, p. 830; Sukhodolets, 1985). (Notice that 58 + 59 = 117 is total number of hydrogen atoms in 20 canonical AAs of GC, within their side chain, what is the self-similarity once more.)

h	+	+	+	+	+	+	+	+	–	+
	0.825	0.943	0.680	0.043	0.251	0.738	0.943	0.880	0.000	0.878
CE	–	–	–	+	+	–	–	+	+	–
	-0.52	-0.54	-0.73	+0.71	+0.91	-0.57	-0.56	+0.42	+0.87	-0.25
HP	+	+	+	•	•	+	+	–	–	+
	+4.2	+3.8	+2.5	-3.5	-3.5	+1.9	+4.5	-1.3	-4.5	-0.9
I	V ₁₀	L ₁₃	C ₀₅	E ₁₀	Q ₁₁	M ₁₁	I ₁₃	Y ₁₅	R ₁₇	W ₁₈
II	G ₀₁	A ₀₄	S ₀₅	D ₀₇	N ₀₈	T ₀₈	P ₀₈	H ₁₁	F ₁₄	K ₁₅
HP	-0.4	+1.8	-0.8	-3.5	-3.5	-0.7	-1.6	-3.2	+2.8	-3.9
	–	–	–	•	•	–	–	–	+	–
CE	-0.16	-0.09	+0.24	+0.69	+0.52	+0.27	+0.46	±0.00	-0.56	+1.46
	+	+	+	–	–	+	+	–	–	+
h	0.501	0.616	0.359	0.028	0.236	0.450	0.711	0.165	1.000	0.283
	–	–	–	–	–	–	–	–	+	–

Table 5. Two classes of amino acids handled by two classes of enzymes aminoacyl-tRNA synthetases. The ordering after class II; the pairing after (Rakočević, 1998, Survey 2.2, p. 289). Class I contains larger amino acids (larger within the pairs), all handled by class I of enzymes. Class II contains smaller amino acids, all handled by class II of synthetases. Within the rows the given values for the parameters are the following: hydrophobicity (h) on a natural scale (0-1) as in Blac and Mould, 2004, and in Chechetkin and Lobzin, 2011; cloister energy, CE (Swanson, 1984) and hidropathy index, HP (Kyte and Doolittle, 1982). The designations “+” and “–” above/below for the number record – more/less within the amino acid pair, respectively. Within the set of “23” AAs, on odd/even pairs, there are 114/125 atoms (with the difference of 11 atoms), exactly as in Table A.4, in Appendix A, what means a self-similarity [(VG + CS₂ + QN + IP + R₂F = 114); (L₂A + ED + MT + YH + WK = 125)]. On the other hand, within first five above there are 62 atoms (Leucine two times in the sum) and within second five 91 of atoms (Arginine two times in the sum);

⁶ “In correspondence with this, Complete Genetic Code must be based on several key principles. We are going to list only those considered to be the most important ...The principle of systemic self-related and self-similar organization. (The “head” of an AA in relation to the first possible ‘organic’ molecule – methane; the functional groups within AAs side chains in relation to functional groups within the AA “head”, and between themselves ...).” Here in the question is a non-fractal self-similarity, although genetic code is *per se* a fractal system at the same time. (Cf., for example, genetic code binary tree as fractal system (Swanson, 1984) and corresponding chapter in our book “GC as a unique system” on our web site: www.rakocevcodes.rs) [Ref. 11]

⁷ If we consider the set of “61” of AAs, then in two rows, YNR & RNY, there are 8 x 33 and in two other, YNY & RNR, 10 x 33 atoms. On the other hand, in two pyrimidine columns, NYN, there are (9 x 33) – 1 and in two purine ones, NRN, (9 x 33) + 1 of atoms [Ref. 13, Tab. 3a, p. 224]. (Y for pyrimidine, R for purine and N for all four types of nucleotides.)

below: 30/56 respectively (Serine two times in the sum); then, with a crossing, there is a balance: $62 + 56 = 119 - 1$ and $30 + 91 = 120 + 1$, what is a change for ± 1 in relation to result 119/120 in Tables A.1, A.2 and A.3 in Appendix A. Regarding to the set of 20 AAs, instead 114/125 there are 92/112 atoms respectively, what also means a balance: 102 ± 10 .

G 01	S 05	Y 15	W 18
A 04	D 07	M 11	R 17
C 05	T 08	E 10	F 14
N 08	Q 11	V 10	I 13
P 08	H 11	L 13	K 15
26	42	59	77
16	17	18	
26 + 42 = 68 x 1			
59 + 77 = 68 x 2			
42 + 59 + 77 = 89 x 2			

Table 6. The Mendeleevian type of arrangement of AAs molecules (MAM) which follows from four diversity types of AAs [(G, P), (A, L, V, I), (C, M, F, Y, W, H), (R, K, Q, N, E, D, T, S)] (Ref. 14, Figs 2 & 3). Within first two and last two columns: 1 x 68 and 2 x 68 atoms, respectively. Within two inner and two outer columns: 102 ± 1 of atoms. All amino acid sequences are of the growing series from the aspect of number of atoms; all but one, in which Q-11 precedes V-10, because different stereochemical types have been distinguished: N-Q belongs to alanine but V-I to valine stereochemical type [analogous to the Mendeleevian situation in which heavier tellurium (127.6) placed in front of the easier iodine (126.9)] (About four stereochemical types of AAs see in Rakočević and Jokić, 1996.)

G 75.07	S 105.09	Y 181.19	W 204.23
A 88.09	D 133.10	M 149.21	R 174.20
C 121.16	T 119.12	E 147.13	F 165.19
N 132.12	Q 146.15	V 117.15	I 131.18
P 115.13	H 155.16	L 131.07	K 146.19
532.57	658.62	725.86	820.99
1258.43 $\approx$ 1258	(34 x 37)		
222			
1479.61 $\approx$ 1480	(40 x 37)		
2738.04 $\approx$ 2738	(74 x 37) (2 x 37 ²)		

Tab. 7. The same arrangement of AAs as in MAM in Table 6, each AA with its molecule mass. From the aspect of self-similarity it makes sense a comparison this Table (a structure of Mendeleevian type, SMT) with “a specific harmonic structure of genetic code” (SHS) [Ref. 13, Tab. 2, p. 223], especially through amino acid molecule mass per columns. So, within two odd columns in SHS the sum is $1258.43 \approx 1258$ (34×37) and in two even $1479.61 \approx 1480$ (40×37). On the other hand within two inner columns here in SMT the sum is $1332.25 \approx 1332$ (36×37) and in two outer columns $1405.66 \approx 1406$ (38×37).

4. Determination through "golden whole"

The splitting of GCT (i.e. TT) into 4 outer, 4 inner and 8 intermediate squares, corresponding to responsible nucleotide doublets, leads us to the following conclusion. Within the set of all n -gons, where n is even number, the case $n = 4$ is only and one case where harmonic mean of "golden whole" ($n^2 - n$)⁸ and its half $[(n^2 - n)/2]$ equals $2n$, and $n^2 - n = 3n$.

⁸ The full equation for “golden whole” can have the next form: $n^2 \pm n = \text{“WHOLE”}$; for $n = 4$, the difference is 12 and the sum 20. In relation to genetic code there are self-similarities expressed through mathematical operations: $(4 \times 4) - 4 = 12$; $(4 \times 4) + 4 = 20$, $(4 \times 4) \times 4 = 64$. [Number 12, correspondent to 4+4+4 doublets in

So, in this case we have that the ratio 2:3 appears to be the harmonic mean within the harmonic mean, and, by this, the sequence " $n_1 - (n_3 \text{ or } n_4) - n_2$ " corresponds with the Cantorian triadic set. Moreover, such a harmonic mean appears to be corresponding with the number of "small squares" within intermediate space in form of only one "ring" as it follows: $[(2 + 2) + (4 \times \underline{0}) = 4]$; $[(\underline{4} + \underline{4}) + (\underline{8} \times \underline{1}) = \underline{16}]$; $[(6+6) + (12 \times \underline{2}) = 36]$; $[(8+8) + (16 \times \underline{3}) = 64]$ etc. As it is self-evident, the symmetrical "out – middle– in" arrangement (1:1:1 of rings) is not possible for $n \neq 4$, neither for n -gons nor for n -letter alphabets.

At the same time here is a self-similarity expressed through the number of "small squares" in the sequence " $n_1 - (n_3 \text{ or } n_4) - n_2$ " and the number of codons within them: four squares per n_1 , n_2 , n_3 , n_4 , each square per four codons. Moreover, there is a self-similarity between golden and harmonic mean versus 4-letter alphabet: $1n$ as 1 square (1 nucleotide doublet), $2n$ as harmonic mean (in the sense said above.), $3n$ as golden whole and $4n$ as the sum $n_1 + n_2 + n_3 + n_4$; all these versus 1 letter of alphabet (as letter minimum), 2 letters as word root (nucleotide doublet), 3 letters as 3-letter word (codon) and 4 letters as letter maximum within alphabet.⁹

5. A possible testing of polarity

Regularities presented above require a testing of polarity parameters, primarily the cloister energy, as follows. In previous papers we have come to a structure of system of the twenty canonical amino acids, which structure is of a Mendeleevian type (Mendeleevian Arrangement of Molecules, MAM): sequences of molecules in rows are given by the number of their atoms (Table 6 in relation to Table 7).¹⁰ We start from four diversity types of AAs, first time presented in (Kyte and Doolittle, 1982): I (G–P), II (A–L, V–I), III (C–M, F–Y, W–H), IV (R–K, Q–N, E–D, T–S)]¹¹ and through some strict symmetry relations we came to Table 6 [Ref. 14, Figs 2 & 3]. The number of atoms per columns (26, 42, 59, 77) is identical with quantities which follow from a strict arithmetical arrangement – by rows and columns – of natural number series (Mendeleevian Arrangement of Numbers, MAN): 1st row: **01**, 02, 03, ..., 11; 2nd row: **12**, 13, 14, ..., 22; 3rd row: **23**, 24, 25, ..., 33; ... ; 9th row: **89**, 90, 91, ..., 99 [Ref. 14, Table 4]. But, as a noteworthy is the fact that all these quantities also follow from a unique algorithm, presented here in Figure 1. If we take this algorithm as an *input algorithm*, then from it follows an *output algorithm* (Figure 2). (Both algorithms as *initial ones*, IA.) And now, a fascinate result: all essential quantities from *output algorithm* appear to be key determinants of a display of AAs through their polarity, measured by cloister energy (Figure 3). Unexpectedly, the self-similarity between two disparate systems?!

sequence " $n_1 - (n_3 \text{ or } n_4) - n_2$ "; number 20 as 20 AAs ($4 \times 4 = 16$ AAs of alanine stereochemical types and 4 of non-alanine stereochemical type); number 64 as 64 codons.]

⁹ By this one can notice that all these self-similarities are possible only for 4-letter alphabet and 3-letter words.

¹⁰ Notice that Mendeleevian regularity (continuity and minimum change) is also valid for first two columns in Table 6: first half of Table is regular and the second one – irregular. (An analogy with two strands of DNA, one coding and one non-coding.) Notice also that the sums of molecules mass per columns in Table 7 (in both systems, SHS and SMT), are determined by multiples of shCherbak's "Prime quantum 37".

¹¹ Notice that AAs from the first and fourth type possess in their side chains the same aliphatic functional groups as in amino acid "head" (Gly H, Pro NH, Ser and Thr OH, Asp and Glu COOH, Asn and Gln CONH₂, Lys and Arg NH₂). (*Aliphatic* functional group in the sense of binding with an *aliphatic* molecule radical.) From this it is clear why two sulfur AAs belong to the third diversity type, together with aromatic AAs, and why there is an atom number balance between two and two diversity types (I & IV vs. II & III) [Ref. 14, Table 8, p. 830].

$$\begin{aligned}
 &x \\
 &x + (x - 10) \\
 &x + (x - 10) + (x - 10) + 1 \\
 &x + [(x - 10) + (x - 10) + 1] + (x - 10) + 2 \\
 &* \\
 &\begin{array}{l}
 (1) \ x \\
 (2) \ 2x - 10 \\
 (3) \ 3x - 19 \\
 (4) \ 4x - 27
 \end{array}
 \end{aligned}$$

26	
42	
59	204
77	

$$\begin{aligned}
 &* \\
 &2(x + (2x - 10)) = (3x - 19) + (4x - 27) \\
 &x = 26
 \end{aligned}$$

Figure 1. Algorithm of Atom Number Uniqueness (ANU), expressed in Mendeleevian arrangement of AAs molecules (MAM) in Table 6.

$26 + 42 + 59 + 77 = 204$ $\begin{array}{ccc} 16 & 17 & 18 \end{array}$ $(1 \times 68) + (2 \times 68)$ $16 + 17 + 18 = 204 : 4$ $26 + 89 + 89 = 204$	$68 + 68 + 68$ $\begin{array}{ccc} (+01) & (\pm 00) & (-01) \end{array}$ $69 + 68 + 67$ $\begin{array}{ccc} (+20) & (-10) & (-10) \end{array}$ $89 + 58 + 57$ <div style="border: 1px dashed black; padding: 5px; display: inline-block;"> $\begin{array}{cc} 31 & \\ & 32 \end{array}$ </div>	<div style="border: 1px solid black; padding: 5px; text-align: center;">ABP</div> <hr/> $57 + 32 = 89$ $58 + 31 = 89$ $\begin{array}{cc} -26 & 26 \end{array}$ $(89)(89)$
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Figure 2. Algorithm of Balance through Polarity (ABP): all quantities are in relations to results presented in Table 6 and Figure 3. [One can notice that reciprocal value of number 89 is unique because it corresponds to Fibonacci series (1: $89 = 0.011235 \dots$).]

31	G 01	05 S	57	G 01	31 (67) 36	05 S
	A 04	07 D		A 04		07 D
	C 05	08 N		C 05		08 N
	V 10	08 T		V 10		08 T
	M 11	08 P		M 11		08 P
<u>H</u> 11		10 E	26	H 11	(69) (68) (137)	10 E
11 Q		11 Q				
58	L 13	15 <u>Y</u>		L 13		15 Y
	I 13			I 13		15 K
	F 14	15 K		F 14		17 R
	W 18	17 R	W 18			
89			89	(89 = 26 + 31+ 32)		

Figure 3.1. Distributions of AAs after polarity, expressed by cloister energy (Swanson, 1984) in relation to quantities presented on the right in Figure 2. Between all presented quantities notice also these characteristic: $31 + 11 = 42$ (42 versus 32); then: $32 + 15 = 47$ (47 versus 57) (57 versus 67) and so on. All other explanations in the text.

<u>G</u> 01	05 <u>S</u>	G 01	31 (67) 36	05 S
A 04	07 D	A 04		07 D
<u>C</u> 05	08 <u>N</u>	C 05		08 N
V 10	08 T	V 10		08 T
<u>M</u> 11	08 <u>P</u>	M 11		08 P
H 11	10 E	H 11	(69) (68) (137)	10 E
<u>L</u> 13	11 <u>Q</u>	L 13		11 Q
I 13	15 Y	I 13		15 Y
<u>F</u> 14	15 <u>K</u>	F 14		15 K
W 18	17 R	W 18		17 R
44 (91) 47	(102±1)			
56 (113) 57				
102 ± 2				

Figure 3.2. Distributions of AAs after polarity, expressed by cloister energy (Swanson, 1984) in relation to odd/even positions (on the left) and to distribution into first ten, second five and third five AAs (on the right).

<u>G</u> 01	05	<u>S</u>	G 01		05 S
A 04	07	D	A 04		07 D
<u>C</u> 05	08	<u>N</u>	C 05	28 (66) 38	08 N
P 08	08	T	P 08		08 T
<u>V</u> 10	10	<u>E</u>	V 10		10 E
M 11	11	Q	M 11		11 Q
<u>L</u> 13	11	<u>H</u>	L 13		11 H
I 13	15	Y	I 13	(69) (69)	15 Y
<u>F</u> 14	15	<u>K</u>	F 14	(138)	15 K
W 18	17	R	W 18		17 R
43 (92) 49 (102+1)					
54 (112) 58 (102-1)					
97 107			[(102±01) (102±10)]		

Figure 4.1. The amino acid ordering is the same as in Figure 3.2, except that histidine "plays" as polar and proline as non-polar amino acid. [(Cf. this Figure with Figure A.5 in Appendix A; also the pattern 92/112 with the same pattern in legend of Table 5.) (Notice that $107 = 117 - 10$, where number 117 represents number of hydrogen atoms in 20 protein AAs, within their side chains. On the other hand, $97 = 87 + 10$, where number 87 represents number of non-hydrogen atoms in 20 protein AAs, within their side chains) (187/197 in whole amino acid molecules, respectively).]

<u>G</u> 01	05	<u>S</u>	G 01	28 (66) 38	05 S
A 04	07	D	A 04		07 D
<u>C</u> 05	08	<u>N</u>	C 05		08 N
P 08	08	T	P 08		08 T
<u>V</u> 10	10	<u>E</u>	V 10		10 E
M 11	11	Q	M 11	(69) (69) (138)	11 Q
<u>L</u> 13	15	<u>K</u>	L 13		11 H
I 13	17	R	I 13		15 Y
<u>F</u> 14	11	<u>H</u>	F 14		15 K
W 18	15	Y	W 18		17 R
43 (92) 49 (102+1)					
54 (112) 58 (102-1)					
97 107 [(102±01) (102±10)]					
187 197 187 non-H & 197 H, in whole molecules					
(87 + 10 / 117 – 10); (87 / 117 atoms in side chains: non-H / H)					

Figure 4.2. The exchange of HY / KR in relation to Figure 4.1, so that the aromatics are at the bottom. But it does not changes any essential fact in the arrangement. Self-similarity in relation to hydrogen and non-hydrogen atom s as in legend of Figure 4.1.

<u>G</u> 01	08 <u>N</u>	G 01		08 N
A 04	08 <u>P</u>	A 04		08 P
<u>S</u> 05	08 <u>T</u>	S 05	22 (66) 44	08 T
C 05	10 <u>V</u>	C 05		10 V
<u>D</u> 07	10 <u>E</u>	D 07		10 E
Q 11	14 <u>F</u>		(102 ± 1)	
<u>M</u> 11	15 <u>Y</u>	Q 11		14 F
H 11	15 <u>K</u>	M 11		15 Y
<u>L</u> 13	17 <u>R</u>	H 11	(59) (79)	15 K
I 13	18 <u>W</u>	L 13	(138)	17 R
		I 13		18 W
37 (95) 58 (102)				
44 (109) 65 (102)				
81 123				

Figure 5. The amino acid arrangement in relation to atom number in molecule: first five AAs on the left, second five on the right, third five on the left and fourth five on the right.

<u>G</u> 01	<u>09</u>	08 <u>N</u>
A 04	12	08 <u>P</u>
<u>S</u> 05	<u>13</u>	08 <u>T</u>
C 05	15	10 <u>V</u>
<u>D</u> 07	<u>17</u>	10 <u>E</u>
13/09	39/27	26/18
04	12	08
Q 11	25	14 <u>F</u>
<u>M</u> 11	<u>26</u>	15 <u>Y</u>
H 11	26	15 <u>K</u>
<u>L</u> 13	<u>30</u>	17 <u>R</u>
I 13	31	18 <u>W</u>
24/35	56/82	32/47
11	13 13	15
39+82 = 121		
27+56 = 83		

Figure 6. The amino acid arrangement as in Figure 5 with further balances.

In relation to *input algorithm* in Figure 1, the next reason is important: If instead of $(x - 10)$ were $(x - y)$, then for the different values for y we gain the different values of x . However, only for $y = 10$ it gives the quantities, which have been found in the genetic code. This supports the hypotheses after that just decimal numbering system is a key determinant of the genetic code [Ref. 19, p. 153: “The genetic code turns out to be a syntactic structure of

arithmetic, the result of unique summations that have been carried out by some primordial abacus at least three and half billion years ago. The decimal place-value numerical system with a zero conception was used for that arithmetic.”], [Ref. 14, p. 831: “It is self-evident that only at the six-bit binary tree the determination with the generalized golden mean is going through module 9, that is through the decimal numbering system. On the other hand, because two golden mean values are calculated from the quadratic equation by square root of the number five (which represents half of the decimal scale of 10 digits) it is reason why decimal numbering system is – the only "golden" numbering system”].

In relation to aromatic Y–H “loop”, i.e. line, at Figure 3, disclosed is a display of a qualitative self-similarity (and quantitative at the same time), expressed through the hierarchy of number of carbon atoms in side chains of *aliphatic* AAs. So, all aliphatic AAs under the line (L, I, K, R) have four carbon atoms in the side chain each, whereas above come M, V, Q, E, P, each with the three carbon atoms; follow P, T, N, D, all with two, then C, A, S with one, and G with zero of carbon atoms.¹²

The display of *aromatic* AAs was realized also in accordance with the principle of self-similarity. More nonpolar AAs, F & W, go together with the nonpolar, L & I. The self-similarity itself is expressed through possession of the same structural motif: "the branching within four carbon atoms." On the other hand more polar Y, which has the same motif of branching as F, exists in the neighborhood of the set of two four-atomic AAs, K-R; two, of which (R) has a quasi-branching in which the central carbon atom, instead with the three carbon, linked to three nitrogen atoms. Ambivalent H, which also has a quasi-branching motif – the central carbon atom is bonded with two carbon and one nitrogen atom – is located in the neighborhood of molecules with three carbon atoms in the side chain.

5.1. Relationships between parameters

With the quantities from *output algorithm* (Figure 2 in relation to Figure 3) are also determined the relationships between key parameters which refer to the polarity. So, if we assign two corner "stones" of the system on left site of Figure 3, G & W, together with the central one (H), we became the scale of polar AAs after the values of their hydropathy index: G–S, D, N, P, T, E, Q, **H–Y**, K, R–W (Kyte and Doolittle, 1982) (cf. Box B.1). On the other hand, the “promotion” of tyrosine (Y) and proline (P) in “partial-nonpolar” amino acids follows from the polar requirement as well as “natural scale” of hydrophobicity of AAs (Box B.2). From the said it must follow a new rearrangement with Histidine (H) as polar and Proline (P) as nonpolar amino acid (Figure 4.1) with new balances and new self-similarities (cf. Figure 4.1 with Table A.5 in Appendix A).

As we see, this testing shows that the key parameter of polarity of amino acid molecule is just *cloister energy*, in relation to other relevant parameters such as *hydropathy index* and "polar requirement"; also in relation to *the natural scale* (0–1) of hydrophobicity. By this, the presented interactions between these parameters correspond to the specific arithmetical

¹² [Ref. 19, p. 162: “The only exception from the general structure of amino acids is provided by proline. It holds its own side chain with two bonds and has one less hydrogen inside the standard block.”] As seen from proline formula one carbon atom, from total 3 in the side chain, exists in amino acid „head“ („standard block“) at the same time.

algorithms, related to golden and harmonic mean and to unique arithmetical and algebraic regularities. All this, and altogether, said us that physicochemical reactions within genetic code are mediated by a *harmonizing system*, in which amino acid molecules as well as nucleotides belong. Moreover, after our *prediction* future researches will show that the arithmetic regularities found in the genetic code by other authors (Sukhodolets, 1985; Dragovich, 2011; Mišić, 2011; Négadi, 2011; Castro-Chavez, 2011) also appear to be, *mutatis mutandis*, in relation to the findings shown here as harmonizing GC system, two initial algorithms as well as the Mendeleeevian Arrangement of Molecules (MAM) and Mendeleeevian Arrangement of Numbers (MAN).

6. Concluding remarks

6.1. The key point in this research is the classification of AAs into four diversity types (as it is shown in the first paragraph of Section 5), with the first two classes in which AAs have (in the side chain) carbon and/or hydrogen, while the other two classes have elements of higher order (N or O, or NO, or S). From this classification follows a strict system of Mendeleeevian type (Tables 6 & 7), and from this system two formal algorithms (Figs 1 & 2), with quantities through which are connected all the important parameters of amino acid polarity (cloister energy, hydropathy index, polar requirement and hydrophobicity "natural scale") (Figs 3.1, 3.2, 4, 5 & 6).

6.2. The approach to the research was achieved through minimal modification of Rumer's DT, and TT is viewed as a set of 61+3 codons and 20, 23 and 61 amino acid molecules at the same time, with respect to their sequence number, in terms of Mendeleeevian arrangements of "numbers", with ascending/descending hierarchy within the rows and columns as it is shown in illustrations within the main text as well as in Appendix A.

6.3. The strict connection of GCT and Codon ring from one site, and the Mutation ring from the other site, as shown in the figures and tables in Appendix B (cybernetic said: a very clear negative feedback) suggests two possible trends in further researches, when it comes to the biological aspects of the results presented in this paper; one theoretical and one practical trend. As a theoretical matter, it is necessary to understand Darwinian selection so that it has been, *per se*, limited by the said negative feedback. Practical uses however could be multilateral, of which we present only a minimum. Starting from the presented relations within Mutation ring it could be made some "golden" simulations in order to realize new protein syntheses where we obtain such proteins which would be "measure" of real life and which would have been useful, at least in the form of precursors, for adequate food additives, for the production of new types of drugs and the similar things.

6.4. This state of affairs in the genetic code caused a proposal for further researches, according to which must not be allowed any "modification" of organisms and organic materials by „ordinary“ laboratory chemistry because it is expected that all of these relationships, contained in the GC, must inevitably be mapped on real proteins and real living processes.

6.5. With the title of the paper is given a working hypothesis that the golden mean (GM) and harmonic mean (HM) are determinants of the genetic code. The findings presented by significant number of illustrations show that this hypothesis is confirmed. However, unlike the previous access to the same determination, it refers not only the analysis of the nucleotide triplet Table, but rather refers to the two tables – Table of doublets (DT) and Table of triplets (TT). In fact, it is precisely presented that these tables are unique in terms of determination just over GM and HM.

6.6. Presented facts are such that ones reaffirm the other and vice versa. All together, they favor the recognition that the chemical reactions that determine the GC are not only "reactions in a tube", but these reactions are associated with a specific balance of the number of particles (atoms and nucleons); balance, determined by unique arithmetic and algebraic regularities and expressed in the form of specific – nonfractal – selfsimilarity ("a harmonized chemistry"). From this it follows further that presented facts also support the hypothesis that the genetic code was from very beginning, in prebiotic times and conditions, a complete code (Sukhodolets, 1985; Rakočević, 2004). On the other hand, the knowledge that "the chemistry of living" is actually a harmonized chemistry requires great care in medicine, agriculture and natural environment, taking into account the fact that this harmonization is strictly immanent to the living as such, mediated by genetic code as such.

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Appendix A

Position non-fractal selfsimilarities

Here we present orderings of AAs in DT and TT and calculated number of atoms in odd and even positions. Self-similarities over the number of atoms in sets of AAs¹³ are immediately apparent: (139/100), (129/110), (119/120), (109/130), (108/131); (115/124), (125/114), (126/113), (116/123), (117/122), (**127/112**), (137/102).¹⁴

6,4 / 5,5 hb				Polarity (a)			
01 <u>G</u>	01	10 <u>V</u>	13	01 <u>G</u>	01	08 <u>P</u>	04
02 <u>F</u>	14	05 <u>C</u>	14	02 <u>F</u>	14	08 <u>N</u>	05
03 <u>L</u>	13	18 <u>W</u>	15	03 <u>L</u>	13	15 <u>K</u>	06
04 <u>P</u>	08	08 <u>T</u>	16	07 <u>A</u>	04	15 <u>Y</u>	08
05 <u>N</u>	08	11 <u>H</u>	17	09 *		17 <u>R</u>	10
06 <u>K</u>	15	11 <u>Q</u>	18	11 <u>I</u>	13	08 <u>T</u>	16
07 <u>A</u>	04	13 <u>L</u>	19	12 <u>M</u>	11	11 <u>Q</u>	18
08 <u>Y</u>	15	05 <u>S</u>	20	13 <u>V</u>	10	05 <u>S</u>	20
09 *		17 <u>R</u>	21	14 <u>C</u>	05	17 <u>R</u>	21
10 <u>R</u>	17	05 <u>S</u>	22	15 <u>W</u>	18	05 <u>S</u>	22
11 <u>I</u>	13	07 <u>D</u>	23	17 <u>H</u>	11	07 <u>D</u>	23
12 <u>M</u>	11	10 <u>E</u>	24	19 <u>L</u>	13	10 <u>E</u>	24
Odd / Even arrangement							
54 (130) 76 (141)				68 (143) 75 (120)			
65 (109) 44 (98)				45 (96) 51 (119)			
119/120				113/126			

Table A.1.1. The ordering after Table 2. On the left as in original Table 2 after the number of hydrogen bonds. On the right the same ordering but with a separation into polar and nonpolar AAs, measured by cloister energy.

¹³ All of these AAs are in standard as well as in mitochondrial GC. Thus, it remains an open question which of the two codes was at the beginning of evolution, and which is a "deviant" one. [Ref. 23, p. 568: "These deviant codes are still closely related to the standard one from which they probably evolved"].

¹⁴ According to our hypothesis the pattern (127/112) we will find in further researches, but the pattern (137/102) we have in standard GCT within two and two columns as well as two and two rows.

6,4 / 5,5 hb				Polarity (b)			
01 <u>G</u> 01	10 <u>V</u> 13			01 <u>G</u> 01	08 <u>N</u> 05		
02 <u>F</u> 14	05 <u>C</u> 14			02 <u>F</u> 14	15 <u>K</u> 06		
03 <u>L</u> 13	18 <u>W</u> 15			03 <u>L</u> 13	15 <u>Y</u> 08		
04 <u>P</u> 08	08 <u>T</u> 16			04 <u>P</u> 08	17 <u>R</u> 10		
05 <u>N</u> 08	11 <u>H</u> 17			07 <u>A</u> 04	08 <u>T</u> 16		
06 <u>K</u> 15	11 <u>Q</u> 18			09 *	11 <u>H</u> 17		
07 <u>A</u> 04	13 <u>L</u> 19			11 <u>I</u> 13	11 <u>Q</u> 18		
08 <u>Y</u> 15	05 <u>S</u> 20			12 <u>M</u> 11	05 <u>S</u> 20		
09 *	17 <u>R</u> 21			13 <u>V</u> 10	17 <u>R</u> 21		
10 <u>R</u> 17	05 <u>S</u> 22			14 <u>C</u> 05	05 <u>S</u> 22		
11 <u>I</u> 13	07 <u>D</u> 23			15 <u>W</u> 18	07 <u>D</u> 23		
12 <u>M</u> 11	10 <u>E</u> 24			19 <u>L</u> 13	10 <u>E</u> 24		
Odd / Even arrangement							
54 (130) 76 (141)				47 (113) 66 (129)			
65 (109) 44 (98)				63 (126) 63 (110)			
119/120				110/129			

Table A.1.2. The ordering after Table 2. On the left as in original Table 2 after the number of hydrogen bonds. On the right the same ordering but with a separation into polar and nonpolar AAs, measured by cloister energy.

6,4 / 5,5 hb			
01 <u>G</u> 01		10 <u>V</u> 13	
02 <u>F</u> 14		05 <u>C</u> 14	
03 <u>L</u> 13		18 <u>W</u> 15	
04 <u>P</u> 08	59/63	08 <u>T</u> 16	
05 <u>N</u> 08	(122)	11 <u>H</u> 17	
06 <u>K</u> 15	(116/123)	11 <u>Q</u> 18	
07 <u>A</u> 04		13 <u>L</u> 19	
08 <u>Y</u> 15		05 <u>S</u> 20	
09 *		17 <u>R</u> 21	
10 <u>R</u> 17	60/57	05 <u>S</u> 22	
11 <u>I</u> 13	(117)	07 <u>D</u> 23	
12 <u>M</u> 11		10 <u>E</u> 24	
Odd / Even arrangement			
54 (130) 76 (141)			
65 (109) 44 (98)			
119/120			

Table A.2. The ordering after Table 2: left site of Table A.1.2 with further balances.

Polarity (a)			
01 <u>G</u> 01	45/71 (116)	08 <u>P</u> 04	04
02 <u>F</u> 14		08 <u>N</u> 05	05
03 <u>L</u> 13		15 <u>K</u> 06	06
07 <u>A</u> 04		15 <u>Y</u> 08	08
09 <u>*</u>		17 <u>R</u> 10	10
11 <u>I</u> 13	(100/139)	08 <u>T</u> 16	16
12 <u>M</u> 11	68/55 (123)	11 <u>Q</u> 18	18
13 <u>V</u> 10		05 <u>S</u> 20	20
14 <u>C</u> 05		17 <u>R</u> 21	21
15 <u>W</u> 18		05 <u>S</u> 22	22
17 <u>H</u> 11		07 <u>D</u> 23	23
19 <u>L</u> 13		10 <u>E</u> 24	24
Odd / Even arrangement			
68 (143) 75 (120)			
45 (96) 51(119)			
113/126			

Table A.3.1. The ordering after Table 2: the right site of Table A.1.1 with further balances.

Polarity (b)		
<u>G</u> 01	40/74 (114)	08 <u>N</u>
<u>F</u> 14		15 <u>K</u>
<u>L</u> 13		15 <u>Y</u>
<u>P</u> 08		17 <u>R</u>
<u>A</u> 04		08 <u>T</u>
<u>*</u>	(95/144)	11 <u>H</u>
<u>I</u> 13	70/55 (125)	11 <u>Q</u>
<u>M</u> 11		05 <u>S</u>
<u>V</u> 10		17 <u>R</u>
<u>C</u> 05		05 <u>S</u>
<u>W</u> 18		07 <u>D</u>
<u>L</u> 13		10 <u>E</u>
Odd / Even arrangement		
47 (113) 66 (129)		
63 (126) 63 (110)		
110/129		

Table A.3.2. The ordering after Table 2: the right site of Table A.1.2. with further balances.

01 <u>F</u> 14		13 <u>L</u> 02
03 <u>L</u> 13		13 <u>I</u> 04
05 <u>M</u> 11		10 <u>V</u> 06
07 <u>S</u> 05	66 / 48	08 <u>P</u> 08
09 <u>T</u> 08	(114)	04 <u>A</u> 10
11 <u>Y</u> 15		* 12
13 <u>H</u> 11	(113/126)	11 <u>Q</u> 14
15 <u>N</u> 08		15 <u>K</u> 16
17 <u>D</u> 07	65 / 60	10 <u>E</u> 18
19 <u>C</u> 05	(125)	18 <u>W</u> 20
21 <u>R</u> 17		05 <u>S</u> 22
23 <u>R</u> 17		01 <u>G</u> 24
<div> <div> <u>68</u> (129) <u>61</u> (124) </div> <div> 63 (110) 47 (115) </div> <div> 131 108 </div> </div>		

Table A.4. The ordering in GCT, within the set of „23“ AAs.

01 <u>F</u> 14		13 <u>L</u> 02
03 <u>I</u> 13		11 <u>M</u> 04
05 <u>V</u> 10	49 / 52	05 <u>S</u> 06
07 <u>P</u> 08	(102-1)	08 <u>T</u> 08
09 <u>A</u> 04		15 <u>Y</u> 10
11 <u>H</u> 11	(102±2)	11 <u>Q</u> 12
13 <u>N</u> 08		15 <u>K</u> 14
15 <u>D</u> 07	48/55	10 <u>E</u> 16
17 <u>C</u> 05	(102+1)	18 <u>W</u> 18
19 <u>R</u> 17		01 <u>G</u> 20
Odd 41 (107)		66 (122)
Even 56 (97)		41 (82)
97		107

Table A.5. The ordering in GCT, within the the set of 20 AAs. Notice the balances through self-similarities of atom number patterns: 97/107 within columns and odd/even positions, 102 ± 1 in up/down halves, 102 ± 2 through the crossing of two and two column halves; also the pattern 82/122 in relation to the pattern 92/112 in Table 5.

Appendix B

Relations between GCT, codon ring, and mutation ring

Here we present Swanson's Mutation ring (Swanson, 1984)¹⁵ (Mutation ring I), and our modification of the same ring (Mutation ring II) (Rakočević, 1997). In the modification we showed additional relationships, for example the relations to Space-3 and Space-4 within Boolean GC cube¹⁶ as well as to essential/nonessential AAs. In addition to the amino acid similarity, presented in (Swanson, 1984), we can now see that the similarity corresponds also to four diversity types of AAs (which types we stated, in the form of amino acid pairs, in the first paragraph of Section 5); and this similarity can be very visible through an expression of amino acid pairs in adequate positioned brackets: (P-G), A{(S-T)[C(V-I)M]}L, F-Y, W-H, R-K, Q-N, D-E). However, as a special, noteworthy fact, is that the mutation ring (as an image and likeness of real proteins) clearly marked division between the polar and non-polar (bold underlined), and partially nonpolar AAs (underlined) (Table B.1).

Figure B.1. Mutation ring I

Figure B.2. Mutation ring II

Explanation of Figure B.1: "Mutation ring. As the codon ring expresses the minimum change relation among codons, so the mutation ring expresses the minimum change relation among the amino acids. The mutation ring shows the broader relationships among the amino acids, as well as the detailed ordering. For this the ring is quartered into the four groups, and for each group the average values of energy and volume are entered. ... The patterns represent progressions in the physical properties of the

¹⁵ "One important measure of amino acid similarity lies in the ability of one residue to replace another in a closely related protein molecule. Dayhoff (1978) has collected data on this subject, and using the method of ancestral sequences, has estimated the odds of any given amino acid remaining unchanged and its odds of being replaced by each of the other 19 in related protein sequences. Presumably, amino acids with high odds of replacing each other are more alike than amino acids with low odds. Dayhoff presents the data in a symmetric 20 x 20 matrix ..." [Ref. 21, p. 190].

¹⁶ Space-3: 011. RCN (T,A) + 001. YCN (S,P) + 010. RUN (I,M,V) + 111. RGN (S,R,G), and Space-4: 100. YAN (Y,H,Q) + 000. YUN (F,L) + 101. YGN (C,W,R) + 110. RAN (N,K,D,E). (Note: Y for pyrimidine, R for purine and N for all four types of nucleotides.)

amino acids. Dark tones are for large residues, light for small. Coarse, checkered or blotchy textures signify external residues, and smooth, delicate or even-textured patterns designate internal” [Ref. 21, Fig. 3, p. 191].

Explanation of Figure B.2: “Everything is the same as on Mutation Ring I, only the S.T.-Q.K. line is shifted by one step on both ends in relation to Mutation Ring I; and P.E.-M.L. line is shifted only on one (the other) end. The squares designate the amino acids from Space-4 and triangles designate the amino acids from Space-3. The empty squares and empty triangles designate the nonessential amino acids, otherwise they designate the essential amino acids; the dots designate the semi-essential amino acids. The lines strictly separate non-essential from essential amino acids; then the lines strictly separate the Space-3 amino acids from Space-4 amino acids. There are the two exceptions: C is full-strayed; R is semi-strayed. One should note that the complementarity principle is applied as follows: outer-inner: non-essential amino acids from Space-4 are complementary with the essential amino acids from Space-3, etc.” [Ref. 11, Fig. 6, p. 28].

Additional explanations of physical facts: Six bold underlined AAs in Table B.1 are nonpolar in all four parameters (Cloister energy, Hydropathy, Hydrophobicity and Polar requirement).¹⁷ Partial nonpolarity of G, A, P and T follows from next facts: A & G have border positions in hydropathy index, whereas A & T in polar requirement. On the other hand, proline (P) is polar in two parameters (Cloister energy and Hydropathy), whereas in other two (Hydrophobicity and Polar requirement) is not (cf. Tables B.1 and B.2).

Additional explanations of chemical facts: Six bold underlined AAs in Table B.1 are nonpolar also from chemical aspects. So, phenylalanine possesses the extremely non-polar benzene ring; valine, leucine and isoleucine have more non-polar methylene and/or methyl groups; two sulfur AAs are the only two AAs that have (within molecule) an atom from the third period of Periodic system of elements (sulfur atom) where the polarity of atoms is much smaller than of atoms in the second period. Partial nonpolarity of G, A, P and T also follows from chemical facts. So glycine is nonpolar through nonpolar hydrogen atom, but polar through direct contact with amino acid functional group (amino acid “head”); similar is with alanine because it possesses only one methyl group. Proline is nonpolar through three methylene groups but polar through a binding of side chain with amino group in amino acid “head”. Finally, threonine (T) is one and only amino acid within the set of 16 AAs of alanine stereochemical type (Rakočević, 1997), with the screen H-C-CH₃ between amino acid “head” and “body” (instead H-C-H) where a CH₃ group is more nonpolar than a H atom. (A possible explanation for serine “deviation” in Mutation ring is that it is a member within the pair S-T, only two aliphatic AAs with OH functional group.)

¹⁷ “We have used both the water-vapor transfer free energies and the interior-exterior distribution of amino acid side chain ... in assigned the final hydropathy values” [Ref. 7, p. 109-110] (cf. adequate relationship in cloister energy: footnote 3).

	III	IV	I	II
GCT	Y,H,Q,N,K,D,E	C,W,R,S,R,G	F,L,L,I,M,V	S, P, T, A
CR	K, N, D, E, Q	H,Y,W,C,R,P,S,L,F	L, V, I, M,	T, A, G, S
MR-I	E, D, N, Q, K	H, R, W, Y, <u>F</u>	<u>L</u> , <u>M</u> , <u>I</u> , <u>V</u> , <u>C</u>	<u>T</u> , <u>S</u> , <u>A</u> , <u>G</u> , <u>P</u>
MR-II	E, D, N, Q	K,H,R, <u>W</u> , <u>Y</u> , <u>F</u> , <u>L</u>	<u>M</u> , <u>I</u> , <u>V</u> , <u>C</u> , <u>T</u>	S, <u>A</u> , <u>G</u> , <u>P</u>
	OUTER	LARGE	INNER	SMALL

Table B.1. Relations between Genetic Code Table, Codon ring and Mutation ring

Explanation of Table B.1: Roman numbers at the top refer to the columns in the standard Genetic Code Table (GCT). In next three rows there are presentations of AAs into four groups as it is designated below. Codon ring (CR) and Mutation ring (MR-I) as in [Ref. 21, Figs 1 & 3, respectively]. The modified Mutation ring (MR-II) as in Ref. 11, Fig. 6.

	I	II	III / IV		
GCT	F,L,L,I,M,V	S, P, T, A	Y,H,Q,N,K,D,E / C,W,R,S,R,G		
DR-I	F,M,L,I,V	<u>C</u> , P, A, T	S,G,D,N	E,Q,K,R	Y,H,W
	large nonpolar	small nonpolar	small polar	large polar	l.m.polar
DR-II	I, V, L, F, C, M, A	G T, W, S, Y, P	H, E, Q, D, N, K, R		
	Cluster III	Cluster II	Cluster I		

Table B.2. Relations between Genetic Code Table and two Doolittle's amino acid rings

Explanation of Table B.2: Roman numbers at the top refer to the columns in the standard Genetic Code Table (GCT). In next rows there are two Doolittle's amino acid rings: DR-I as in (Weaver, 1985) and DR-II as in (Kyte and Doolittle, 1982); l.m.polar = large moderately polar. The correspondence with Mutation ring in Table B.1 is self-evident.

Box B.1. Polarity of amino acids (plus vs minus and vice versa)

Cloister energy (Swanson, 1984):

K +1.46; Q +0.91; R +0.87; E +0.71; D +0.69; N +0.52; P +0.46; Y +0.42; T +0.27; S +0.24; **H ±0.00**

H ±0.00; A -0.09; G -0.16; W -0.25; V -0.52; L -0.54; I -0.56; F -0.56; M -0.57; C -0.73;

Hydropathy index (Kyte and Doolittle, 1982):

R -4.5; K -3.9; D -3.5; E -3.5; N -3.5; Q -3.5; H -3.2; P -1.6; Y -1.3; W -0.9; S -0.8; T -0.7; **G -0.4**

A +1.8; M +1.9; C +2.5; F +2.8; L +3.8; V +4.2; I +4.5

Box B.2. *Polarity of amino acids (first ten more and second ten less polar)*

Hydrophobicity natural scale ((Blac and Mould, 2004), (Chechetkin and Lobzin, 2011)):

R 0.000; D 0.028; E 0.043; H 0.165; N 0.236; Q 0.251; K 0.283; S 0.359; T 0.450; G 0.501

A 0.616; C 0.680; **P 0.711**; M 0.738; V 0.825; W 0.878; **Y 0.880**; L 0.943; I 0.943; F 1.000

Polar requirement ((Woese et al., 1966), (Konopel'chenko and Rumer, 1975)):

D 13.0; E 12.5; K 10.1; N 10.0; R 9.1; Q 8.6; H 8.4; G 7.9; S 7.5; **A 7.0**

T 6.6; P 6.6; V 5.6; **Y 5.4**; M 5.3; W 5.2; F 5.0; L 4.9; I 4.9; C 4.8

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