Protein amino acids as a complete (periodic) system

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ABSTRACT

Referring to the results of previous research on the Cipher of genetic code and analogies of genetic and chemical code – two overall complete natural systems – this paper presents the results of the study on the most complete Protein Amino Acids System (PAAS). It is shown that 20 protein amino acids appear to be a complete system – ordered, coherent, and harmonic. In such a system, all chemical distinctions within the system are accompanied by specific arithmetical and algebraic regularities, including the existence of amino acid ordinal numbers from 1 to 20. The classification of amino acids into two decades (1-10 and 11-20) appears to be in a strict correspondence with the balances of the number of atoms. From the existence of harmonic structures and arrangements of AAs, regardless of whether they are or not the constituents of the genetic code follow the conclusions that the genetic code, through its main constituents – 20 AAs and 4 Py-Pu bases – was complete even in prebiotic conditions.

Keywords: Protein amino acids, Amino acid code, Genetic code, Binary tree, Gray code, Golden mean, Fibonacci series.

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Introduction

This paper is a step further in argumentation of the completeness of the system of protein amino acids (AAs),[1] in the sense that it is a Mendeleevian type of system, whose organization is based on the principles of continuity and minimum change, that is, on the principles of balancing the properties[2] of its elements (within the system). In other words, it is a coherent and harmonious system, both in biotic and prebiotic conditions. In this case, the harmonicity is understood as the correspondence with the golden mean and the Fibonacci series.[3] As such, the system is inevitably in relation to one specific periodic system of numbers (PSN) [Figure A1 in relation to Table B5 and Figures C2 & C3], correspondent (analog) with the periodic system of chemical elements (PSE).

„Regarding the application of theoretical-numerical representations, even Mendeleev considered as appropriate to look for an analytical expression for the law of periodicity, based on theory of numbers." (Trifonov, Dmitriev, 1981, p. 237).]

Previously we have shown that the completeness of PAAS is recognized when protein AAs are observed as constituents of the genetic code (GC) (Rakočević, 1998b; 2004a; 2011a, b; 2018a, b). In this paper, however, we are starting with a *working hypothesis* (Box 1) that the same holds true when the set of 20 protein AAs is observed regardless of their positions in the genetic code displays [in the standard Genetic code Table (Crick,

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[1] When we say that the genetic code (GC) was complete even in prebiotic conditions, then we mean on constituents of standard GC, the 20 protein amino acids (AAs) and 4 nucleotide bases. If within this paper we give convincing arguments for the completeness of the system of 20 protein AAs (PAAS), whether they are GC constituents or are just a set of free molecules independent of the positions of the AAs in the Standard GC Table, then we provide evidence also for the completeness of the set of 4 Py-Pu bases, according to the scenario we gave in previous work (Rakočević, 2018a, Section 2, p. 32).

[2] The notions of *balancing* related to the state of the amino acid (genetic) code, as well as the conditions of the system of protein amino acids (PAAS), will be used in the sense of Definitions 1 and 2, given in our previous paper (Rakočević, 2018a, p. 33). Under these assumptions, in this paper we consider that these states are analogous to the same states found in the Periodic system of chemical elements (PSE), when Mendeleev discovered the elements and interpreted their properties by the method of interpolation (Kedrov, 1997, p. 231). [Encyclopedia Britannica: "Interpolation, in mathematics, the determination or estimation of the value of f(x), or a function of x, from certain known values of the function".]

[3] On determination of PSE by the golden mean and the Fibonacci series see in (Trifonov, Dmitriev, 1981) and (Rakočević, 1998a). On the determination of the protein amino acid system (as constituents of the genetic code), also with the golden mean and the Fibonacci series, see in: (Rakočević, 1998b; 2011b).

1966; Rumer, 1966)[4]; in Gray code model of GC (Swanson, 1984) and GC binary tree (Rakočević, 1998b)]. In the argumentation of the working hypothesis, we consider that the coexistence of GC with Boolean spaces (Swanson, 1984; Rakočević, 1994, 1997b, 1998b)[5], analogy with quantum physics (Shcherbak, 1994, 2008),[6] analogy of genetic and chemical code (Rakočević, 2018b) and the existence of "arithmetic inside the universal genetic code" (Shcherbak, 2003) are established facts.

Box 1. *The statements of the working hypothesis*

1. The protein amino acid system (PAAS) is an ordered, coherent, and harmonic system. [Ordered as in Figure 1 in this paper; coherent as in (Rakočević, 2011a, b); harmonic as in (Rakočević, 2004a); with the expectation that all three attributes are applying, while when the protein amino acids are not positioned in the genetic code then they are freely present in the world of molecules.].

2. The order of PAAS is also expressed through the existence of the order of AAs from the first to the 20th [The order according to the logic that each subsequent molecule is similar to the previous one.].

3. "The Little Gauss' algorithm" (Rakočević, 2011b, p. 833) is contained in the Periodic system of numbers (PSN) (Fig. A1)- it is a modified algorithm of "Little Gauss", in the sense that not the numbers are going from 1 to 100 but from 1 to 101. This phenomenon

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[4] The sense of deviation, that is of the degree of freedom in deviation from the standard GC as in: (Rakočević, 2018a, Box 2, p. 41). Under the same "degree of freedom" we can now include the "21th" AA Selenocysteine (encoded by the UGA codon found in every domain of life on Earth), as well as the "22nd" AA Pyrrolysine (coded by UAG in Archaea), and we will not consider them within these considerations. Because they are encoding by stop codons, they do not disturb the order within the system of standard protein AAs. It is quite certain that it makes sense to investigate the possible completeness, coherence and harmony and for the system of "22" protein AAs, as well as the trend towards completeness; also makes sense to investigate the completeness of other potential biomolecular systems (Kostić et al., 1998 a,b, pp. 189-194; 195-200).

[5] Rakočević, 1998b, p. 46: "Swanson (1984) has shown that 'the genetic code is almost an example of a Gray code… an example of minimum change binary code' ... If so, then the genetic code can be represented in the form of a binary-code tree, according to the natural numbers sequence 0–63"; Rakočević, 1994, p. 36: „The basic concept from that we start is the Boolean logical square. This square exists within Gray code model of genetic code, [which] code can be *per se* developed in two types of the binary tree: (1) the binary tree which keeps the logic of the Gray code. ... (2) the binary tree with the logic of natural numbers series"; Rakočević, 1997b, p. 5: „Boolean spaces are the main determinants and invariants of the genetic code".

[6] For details about analogies of genetic code and quantum physics see in preprint form of paper (Rakočević, 2018b), OSF Preprints, DOI: 10.31219/osf.io/mxecj (created on October 07, 2017).

was the only analogy that could be found in relations to results in previous three works (Rakočević, 2006; 2011a,b); however, it can now be shown that this arrangement is "taken off" from the PSN (the right picture in Figure 1 in relation to Figure A1).

4. PAAS correspond with PSN [It refers to the correspondences mentioned in the preceding paragraph, but also to others that is first shown.].

5. The pattern 35-36-61 in the chemical code refers to the number of unstable and stable elements respectively in a set of 61 multi-isotopic elements; and in the genetic code refers to the number of codons encoding less and more complex AAs respectively in a set of 61 amino acid codons; and is also valid for the number of atoms in the PAAS [As stated, and what we found in Darwin's diagram (Rakočević, 2015), *i.e.* in his "computer program" (first two columns in Table C1 in relation to the third quadrant of Table C2].

6. PAAS corresponds to the uniqueness of the six-bit binary tree and correspondent Farey tree (both trees in: Rakočević, 1998b, Figures 1 & 2, pp. 284-285) [The uniqueness of the six-bit tree is in its horizontal and vertical mirror symmetry; it is the first and only possible binary tree with one mirror (010/101), as shown in Figure 2 and Figure A2, on the left. Notice that the mirror symmetry for the binary records on the genetic code of the binary tree (Rakočević, 1998b, Figure 1, p. 284) is a face to back, while for the *amino* or *oxo* functional groups is a face to face: *amino vs. amino* and *oxo vs. oxo* group, in reading the binary tree on the left half: from left to right, and on the right half: from the right to the left; the same logic – *amino vs. amino* and *oxo vs. oxo* is valid in reading two Rumer's octets of nucleotide doublets (Rakočević, 2018a, Table 2A, p. 34). Notice also that the comparable position („terminal position") of the functional group must be the amino group in adenine because it does not have an oxo group.][7].

7. PAAS is (evolutionarily) generated through the unity of the mirror symmetry of the AAs and the mirror symmetry of the correspondent numbers [It is shown that the mirror symmetry 2 *vs.* 5 (010/101) mapped from the six-bit binary tree to the standard Genetic

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[7] "The four [bases] are mutually distinguishable by three main characteristics: the type of base (purine, Pu, or pyrimidine, Py); the type of functional group in terminal position (position 6 in purine, position 4 in pyrimidine) – either oxo or amino; and the number of hydrogen bonds linking them in the system codon-anticodon" (Rakočević, 1988, p. 112).

code Table (GCT) has a quantitative meaning of the number of atoms (Table 3 in relation to Table 7 and Figure 2).].

8. PAAS corresponds with the uniqueness of the decimal number system [The uniqueness of the decimal number system: the 9 non-zero digits correspond to the Cantor triadic set: 123 / 456 / 789, which quantities we found as natural entities (Rakočevič, 2018a, Fig. 4 and Rakočević, 2018b, Equations 1 & 2 and Table 4). Notice that the generation of a binary tree represents *ipso facto* a permanent correspondence with the Cantor triad set.) On the other hand, the decimal number system is the only one that has a direct connection with the golden mean (Table B6, the second row where we find the original golden triangle, whose one cathetus is the square root of number 5. Thus, the first cathetus a = q/2, the second cathetus b = 2 and hypotenuse c = 3 = $\Phi^2 + \phi^2$ (Table B6 in relation to Table A1, second column).

9. PAAS corresponds with the uniqueness of the golden mean and the Fibonacci series of numbers. [This statement applies to PAAS when it is a component of the genetic code we have shown in several papers; we mention now only two (Rakočević, 1998b, 2004b). Here, however, we show that this fact applies to PAAS, regardless of the genetic code.]

The procedure for proving *the working hypothesis* will be realized by presenting the relevant facts in the two main segments of this paper: in the Preliminaries, we give new aspects and new knowledge about the previously presented arrangements of the AAs within the GC and/or outside of it, while in the Section "New insights" we provide new insights into the universal completeness of PAAS.

Preliminaries

Already the act of mapping the Gray code model from "A unifying concept for the amino acid code" (Swanson, 1984) into a binary code tree (Rakočević, 1998b, Figure 1, p. 284) was a hint of the existence of a complete – ordered, coherent and harmonious – system of protein AAs. [The Gray code model as in Figure C2, down on the left.] And when, with this act, the sequence of "golden" AAs, existing on positions ϕ^0 to ϕ^9, on the binary code tree, the sequence (G-Q-T-P-S-L-F), was transmitted in a sequence of Mendeleevian order, according to the growing masses of amino acid molecules: (G-S-T-

P-Q-L-F) (Rakočević, 2011b, Fig. 6, p. 832), then PAAS was obvious (Figure 1 in this paper) (Box 2).

Figure 1. The left picture: Cyclic Invariant Periodic System (CIPS) of AAs (Rakočević, 2011b, Fig. 6, p. 832). The right picture from Rakočević (2011b, Fig. 9, p. 834) (Box 2).

Box 2. *The explanation of Figure 1*

In Figure 1, the left picture from Rakočević (2011b, Fig. 6, p. 832): "The Cyclic Invariant Periodic System (CIPS) of canonical AAs: 1) at the inner side – the atom number within amino acid side chains; 2) in the middle position there are chalcogen AAs (S, T & C, M); 3) follow - in next 'cycle' – the AAs of nonalanine stereochemical types (G, P & V, I); 4) then two double acidic AAs with two their amide derivatives (D, E & N, Q), 5) the two original aliphatic AAs with two amine derivatives (A, L & K, R); and, finally, 6) four aromatic AAs (F,Y & H, W) – two up and two down. The mentioned five classes belong to two superclasses: primary superclass in light areas and secondary superclass in dark areas. Notice that each amino acid position in this CIPS is strictly determined, and none can be changed".[8] New comment, for the left picture: Within "2-3-4-5" rows above plus CM from "1" there are 102 and within "2-3-4-5" down plus ST from "1" also 102 atoms.

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[8] Rakočević, 1998b, p. 289: "Within seven 'golden' amino acids (within side chains) [GSTPQLF] there are 60 atoms; within their seven complements [VCMINAY] there are [60+(1×6)] and within six non-complements [DE, KR, HW] there are {[60+(1×6)]+(2×6)} of atoms. [Notice that the differences are 1×6, 2×6 and 3×6 which means realization of minimum change principle and continuity principle at the same time."]

The right picture from Rakočević (2011b, Fig. 9, p. 834): "Dark tones: Class I of amino acids handled by class I of enzymes aminoacyl-tRNA synthetases [except T]; light tones: Class II [except C]." New comment for the right picture (about exceptions C & M) is given in footnote 9.

New comment for both pictures: going from left to the right picture it is evident that chemically related groups of AAs come down for 0, 1 and 2 steps, respectively; for zero "steps" in aromatics FY-WH; for one step in chalcogen AAs ST-MC and in carboxylic DE-QN (carboxylic AAs D & E in relation with their amides N & Q); for two steps in AL-KR.

In support of the completeness of the system on the left picture goes also the splitting according to the ratio 8:12 (2:3) in molecule number: (FYLA + KRHW = 107 atoms); (QNPI + TMSC + GVDE = 97 atoms). In support of the completeness of the system on the right picture go also the relations within the set of 16 AAs of alanine stereochemical type, the balanced relations between rows and columns:

I. (STLA + KRQN = 81) (LA+MC+QN+WH = 81); $LAQN = 4 \times 9 = 36$; STKR = MCWH = $5 \times 9 = 45$

II. (DEMC + FYWH = 91) (ST+DE+KR+FY = 91); $DEFY = 36+10 = 46$; MCWH = STKR = $5 \times 9 = 45$

(The cited previous papers available in www.rakocevcode.rs)

The determination of the amino acid (genetic) code with the golden mean leads to the CIPS (Cyclic Invariant Periodic System) (Figure 1, the picture on the left), in which the positions of five classes of AAs are strictly determined, two in the less complex and three in the more complex superclass: 1. (**SC-TM**), 2. (GV-PI), 3. (**DE-NQ**), 4. (AL-KR), 5. (**FY-HW**); less complex in the 2nd and 4th class and more complex in the remaining three classes (1st, 3rd and 5th), with the following distinction within the side chains of two super classes: H, C, N / N-O, O, S plus aromatic AAs.

As we can see, the CIPS is indeed a complete amino acid system, but AAs positions within the genetic code determine it, and according to our working hypothesis it must be a Mendeleevian type of system, in which AAs are ordered from the first to the last, the 20th amino acid. This condition is fulfilled in certain percentages by the arrangement of the AAs that we find on the right picture of Figure 1 as if it was mapped from one of the PSN diagonals. (In PSN, Figure A1, this diagonal is in black tones.) At the same time,

this arrangement is identical to the arrangement presented on the right picture of Table B1, if the quartets of the AAs are read in a circular direction (as in the Gray code model within Boolean spaces): STLA, DEMC, KRQN, FYWH. Both these mappings, to some extent, confirms the statements of the working hypothesis: 1, 3, and 4. We say "to some extent" because we still do not have the order of AAs from the first to the last, but we have arrangements of AAs in which their positions are independent of positions in GC (the right picture of Figure 1 in relation to the right illustration in Table B1). [The left illustration of Table B1 also shows the correspondence with the pattern 25-36-61, as it is presented in the legend of Table B1.]

It is noteworthy to mention the fact that in all presented AAs pairs, in right picture of Figure 1, the first member, as a smaller molecule, belongs to the class II of AAs, handled by class II of enzymes aminoacyl-tRNA synthetases, and the second to class I. The exceptions are only T and C.[9] [About two classes of AAs, handled by class I & II of enzymes aminoacyl-tRNA synthetases see in: (Wetzel, 1995) and (Rakočević, 1997a); also, in Box 3 in this paper.]

Box 3. *Aminoacyl-tRNA synthetases*

There are two classes of aminoacyl-tRNA synthetases. Class I consists of synthetases with two highly conserved sequence motifs, which aminoacylate at the 2'-OH of an adenosine nucleotide, and they are usually monomeric or dimeric (one or two subunits, respectively). Class II of synthetases contains three highly conserved sequence motifs, and they aminoacylate at the 3'-OH of the same adenosine, and they are usually dimeric or tetrameric (two or four subunits, respectively). Although phenylalanine-tRNA synthetase belongs to a class II, it aminoacylates at the 2'-OH. Within the standard genetic code's Table it does not follow a full distinction of AAs in relation to two classes of the aminoacyl-tRNA synthetases (Wetzel, 1995, Fig. l, p. 546), but within the ″Codon path cube″ it follows with only one exception (Rakočević, 1997a, Fig. 1, p. 646).

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[9] The 18 AAs are built with four elements, one from the first (H), and three from the second period of PSE (C, N, O). The remaining two AAs have one element more (sulfur). These two sulfur AAs (C-M) have exactly two chemical analogues among the previous 18 AAs (S-T). It would be expected that in both cases, the smaller molecule belongs to Class II, and the larger to Class I; however, this is not the case: a stronger hierarchy (among periods) has the advantage: S-T, which do not reach the third period belong to Class II and C-M, which can be achieved belong to class I.

Presented classification of AAs within CIPS into classes and superclasses (left picture of Figure 1), in correspondence with two classes of aminoacyl-tRNA synthetases, can be continued further to obtain subclasses and families. Such a sophisticated classification can be useful in analyzing the structure and classification of proteins (Rakočević, 2011b, Figure 7, p. 833).

However, apart from the all above, we are now able to present new balances in CIPS. In Survey 1 it was shown that they have the meaning of the distinctions not only of the half the number of molecules *vs.* the second half, in systems and subsystems (in the ratio 1:1), but also of the distinctions with the ratio 4:6 or 6:4 which means 2:3 or 3:2 (Tables B1, B2 and B3 in relation to Table B6). The ratio 2:3/3:2 we find in the second row of Table B6, containing the system of the generalized golden mean; also 2/3 is the harmonic mean of a whole and its half, and 3/2 also represents the limit of "golden numbers" (Moore, 2004, p. 211.)[10]

Survey 1. The relationships within two systems presented in Figure 1

$$(FLQP \quad 46) + (MCVERW \quad 71) = 117$$
$$(YANI \quad 40) + (TSGDKH \quad 47) = 87$$

$$(FLQP \quad 46) + (YANI\ MC \quad 56) = 102$$
$$(WREV \quad 55) + (TSGDKH \quad 47) = 102$$
$$102 \pm 1$$

$$(11+91=102)\ (21+81=102)$$
$$(31+71=102)\ (41+61=102)$$
$$1 \ldots\ldots 51 \ldots\ldots 101$$

$$[(46+55=102\text{-}1)\ (56+47=102\text{+}1)]\ [(56-55=1)\ (47-46=1)]$$

The left area in this Survey (Survey 1) is related to the left picture in Figure 1, and the right area to the right one. The members of AAs pairs are symmetrically distributed (F-Y, L-A, *etc.*). See details in the text.

As it is self-evident (from Table B6), in the special case of generalization, the order values of generalized golden mean are related to the series of natural numbers (0, 1), (1,

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[10] Except of direct relationship of 2/3 (Tables B1 & B2) with the golden mean (Table B6, 2nd row), there is an indirect relationship in the following sense. In the cases presented here: 4 AAs *vs.* 6 AAs. But this is at the same time the 3/2 ratio as: 6 AAs *vs.* 4 AAs, and it is known that 3/2 represents "the limit of the golden numbers" (Moore, 2004, p. 211: "Our concern here is the study of the sequence $\{g_n\}$ of "golden numbers". A computer analysis of this sequence of roots indicated that the odd-indexed subsequence of $\{g_n\}$ was monotonically increasing and convergent to 3/2 from below, while the even-indexed subsequence was monotonically decreasing and convergent to 3/2 from above").

2), (2, 3) *etc.*, and to Hückel rule at the same time (the right illustration in Table B5: the first column in relation to the far right column); also to the squares of natural numbers sequence: (1, 2), (2, 3), (3, 4), ..., when they correspond to the balance "11" (Table A1).

Table 1. The order of protein amino acids based on two classes aminoacyl-tRNA synthetases

G	01	10	V
S	05	05	C
T	08	11	M
P	08	13	I
A	04	13	L
D	07	10	E
N	08	11	Q
K	15	17	R
H	11	18	W
F	14	15	Y

Left / right 81 / 123
zigzag 102±1

61 / 36 / (36+10) [36 = 25 + 11]

(GSTP 22) + (LEQRWY 84) = 107-1
(VCMI 39) + (ADNKHF 59) = 97+1

The left illustration of this Table (Table 1) follows from Rakočević (1998b, Survey 4, p. 290): „On the first (full) zigzag line, there are 102+1 atoms whereas on the second (dotted) line there are 102−1 atoms. The arithmetic means for both: 102±1. Class II handles the smaller amino acids within the pairs (on the left), whereas class I aminoacyl-tRNA synthetases handled the larger amino acids (on the right)." The right illustration is a new arrangement for this paper. See details in the text.

Now we go back to CIPS (left picture of Figure 1 in relation to Survey 1). When the first four of the AAs from the first column are added to six of the AAs from the second one, and *vice versa* (Figure 1 in relation to Survey 1), in these groups of AAs the number of atoms corresponds to the quantities indicated between the fifth and sixth row of Table

A2: 87 as $(97 - 10)$ and 117 as $(107 + 10)$[11] [Notice that $87 = 86 + 01$]. Here, it is particularly interesting the fact that only two sulfur AAs (C & M) appear as a tongue on balance: by moving them from one subgroup to another, the balance 87: 117 turns into a balance of 102: 102. [In the side chains of 20 standard AAs there are 117 hydrogen and 87 non-hydrogen atoms (Sukhodolets, 1985; Rakočević, 2011b, Table 7, p. 830).]. But the balancing also exists when the distinctions from the state 4 *vs.* 6 AAs, or 5 *vs.* 5 (in the shaded and non-shaded space) go on and in a different way as shown in Tables B2 & B3 and the accompanying Survey B1. In doing so, the quantization from the ratio 87: 117 goes to 97: 107.

In the left part of Figure 1, we see also that at the center of the CIPS system, there is a subsystem with high molecular diversity. Two and two AAs of non-alanine types (G-P and V-I) have "captured" the only two sulfur AAs (with sulfur existing in the third period and the sixth group of PSE: cysteine and methionine) and their two oxygen analogues (existing in the second period and a sixth group of PSE: serine and threonine). Realizing that here we have a Mendeleevian order (continuity and minimum change in atom number) with glycine in front: G-S-T-P, it makes sense to bring it in connection also with Mendeleev's based subsystem of the remaining 12 AAs of alanine type, led by alanine and presented in left picture of Table B1. [The only change in this process of connecting the two subsystems is that C and T exchange their positions.] The two subsystems thus connected give a new system, presented in Table 1.

The left illustration in Table 1 was firstly published in 1998, and then in 2004 (Rakočević, 1998b, Survey 4, p. 290; 2004a, Fig. 1, p. 222). With all provided information there, we now show distinctions from the aspect of division into 4: 6 amino acids. The illustration on the right side of Table 1 shows that the pattern 25–36–61 is really "played" here, which we already had with the genetic code and chemical code (Rakočević, 2018a and 2018b). On the right side is the first-class of amino acids, and on

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[11] Relationships with quantities 97/107 we can find in all essential arrangements of AAs: Table 1 & 2, Tables B2 & B3, and Survey B1.

the left side is the second class of amino acids.[12] Each molecule from the second class is smaller than the paring member in the first class.

At the bottom of the first class, there are four amino acids in which there are exactly 61 atoms, and at the top, there is the amino acid quartet which, together, with their in the second-class partners (total of eight amino acids) together also have 61 atoms. The two quartets in the right column are separated by a doublet L-E, while in the left column the quartet A-D-H-F is splitting into doublet A-D and doublet H-F; the H-F exactly with 25 atoms, and A-D with 11 atoms; a total within the quartet of 36 atoms. In two "breakable" doublets (diagonally connected) there is 23+23 = 36+10 atoms. Altogether exactly as it is predicted by working hypothesis (statements 4 & 5), and showed in Table A2 (the fifth and sixth row).

New insights

From a chemical point of view the first step of classification of protein amino acids (AAs), must be the classification into aliphatic and aromatic AAs, where on a hierarchical scale of changes by similarity and complexity, aliphatic AAs must precede the aromatic. For the same reason of the chemical hierarchy, within the class of aliphatic AAs at the beginning must be the hydrocarbon AAs (possessing in the side chain carbon and hydrogen, or hydrogen only, in the case of glycine), and at the end two sulfur AAs, quite different from preceeded non-sulphuric AAs. It means that two sulfur AAs (as the last in the class of aliphatic amino acids) must be found in direct contact to the aromatic.

Full certainty

In the further course of the sequencing of AAs, in terms of changes by similarity, from the aspect of the AAs singlets and/or doublets, *i.e.*, pairs, the appropriate distinctions in three areas should be considered: hydrocarbon, aromatic, and those between them. In the set of aromatic AAs, Phe came the first, as the simplest, followed

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[12] The class I is realized by AAs handled by class I, while class II is realized by AAs handled by class II of enzymes aminoacyl-tRNA synthetases, respectively.

by Tyr, and Trp, all three with possession of a benzene ring.[13] At the very end ultimately must be His, the only one which does not possess the aromatic benzene ring (Table 2 in relation to Survey 2).

In the set of hydrocarbon AAs, at the very beginning must be Gly as the simplest AA, followed by Ala as the first possible case of hydrocarbon series with an open carbon chain. At the same time, for chemical reasons, it seems that Gly-Ala can be considered as a pair of AAs. Then comes the par Val-Pro, both with three carbon atoms in the side chain, rather than Leu and Ile with four carbon atoms. Val with half-cyclic chain precedes Pro. [On the relations between valine and proline, such that the valine is bound by the vertices, and the proline by the side of the isopropyl "triangle" for the amino acid functional group, see in (Rakočević and Jokić, 1996).]

Order uncertainty

After the pair Val-Pro, it follows the pair Leu-Ile or Ile-Leu? One possible solution is that Ile precedes leucine (Table 2) because it has already been demonstrated that Ile chemically best suits to the proline (Rakočević and Jokić, 1996, Survey 1.2), and in addition it is a derivative and pairing-member of valine within a set of only two AAs of the valine stereochemical type (Rakočević and Jokić, 1996; Rakočević, 1998b, Survey 4, p. 290). In this solution, Ile has the status of "the first and only" possible derivative, the valine derivative, from the aspect of the change at the end of the valine side chain ("non-standard" hydrocarbon amino acid in the set of 20 AAs due to the above-mentioned "triangle" in the amino acid side chain); and the leucine has the status of "the first possible case" from the aspect of hydrocarbon chain branching.

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[13] In fact, it is a toluene ring, as a condition of belonging to the alanine stereochemical type, with one CH_2 group between the "head" and "the body" of amino acid molecule (Rakočević and Jokić, 1996. [The 16 AAs of alanine stereochemical type; the 04 AAs of non-alanin stereochemical types: glycine type with only glycine, proline type with only proline and valin type with valine and isoleucine (Popov, 1989; Rakočević and Jokić, 1996).]

Table 2. The order of protein amino acids based
on chemical similarity

(1)	G	01	08	N	(11)
(2)	A	04	07	D	(12)
(3)	V	10	05	S	(13)
(4)	P	08	08	T	(14)
(5)	I	13	05	C	(15)
(6)	L	13	11	M	(16)
(7)	K	15	14	F	(17)
(8)	R	17	15	Y	(18)
(9)	Q	11	18	W	(19)
(10)	E	10	11	H	(20)
		102	102		
(97)	51±1		51±1	(107)	

In both columns: odd 50; even 52

(—— 102) (....... 102)

The 20 protein AAs are arranged into two decades in accordance to ordinal amino acid number, 1-10 and 11-20; the numbers presented outer: the ordinal numbers 1-20; the numbers presented inner: the number of atoms within side chain of the responding amino acid. In red color AAs handled by class I aminoacyl-tRNA synthetases. In both columns: odd 50 and even positions 52 atoms. Within two decades there are 120 atoms in each; in both zigzag lines also 102 and 102 atoms. First four plus six last equals 97/107 respectively [(GAVP) + (CMFYWH) = 97] [(NDST) + (ILKRQE) = 107][VILRQE = CMFYWH = 74] [GAPK = NDST = CMYW = 28][(1 x 74 = 74) (3 x 28 = 84)]. See details in the text.

Another possibility is that Leu precedes the isoleucine to the following logic and chemical similarity: In the relation of Val-Pro *vs*. Leu-Ile, the Leu chemically corresponds more to valine and Ile to proline (Table B4). "Paradoxically," there is a change of status: now Leu has the status of "the first and only" possible derivative, in a set of only two AAs, in the pair of Val-Leu, where happens the splitting into the valine and alanine stereochemical types. In doing so, the derivation occurs at the beginning of the valine side chain, in contact with the amino acid "head", *i.e.*, amino acid functional

group. [This uniqueness of the two-member set also follows from the above said uniqueness of the isopropyl group "triangle".] On the other hand, Ile gets now the status of the "first possible case" from the aspect of the branching.

However, this "paradox" should not be surprising. If the analogy with quantum physics is already on the scene, then this kind of analogy with Heisenberg's uncertainty principle can be expected.

The "between" area

Finally, it remains to determine the chemical distinctions of AAs in "between" area. We have already said that sulfur amino acid pair, Cys-Met, precede aromatic amino acids. As chalcogen AAs, they must be in contact with other two chalcogen amino acids, Ser-Thr. By this, the contact has to be made *via* Cys because it possesses SH group, correspondent to OH group in Ser as well as in Thr.

It is to be understood that a pair of oxygen AAs with the hydroxyl (OH) functional group in side chain must be in contact with a pair of two also oxygen AAs, but which possesses the carboxyl (COOH) functional group: Asp-Glu. However, the problem is that both of these two AAs have their amide derivatives (Asn-Gln) and it is not easy when determining the distinctions, which here proceeds and which follows.

It turns out, however, that the problem is easier to solve when returning to the beginning, in the area of hydrocarbon AAs, to the "point" of the pair Ile-Leu. Further must follow the pair of nitrogen derivatives, Lys-Arg, and Lysine must come first with four carbon atoms in the side chain, which number is also valid for Leucine; and then, with the validity of both principles – the continuity and minimum of change – comes Arginine with three atoms (not counting carbon atom in the guanidino group). Then, chemically speaking, it is very natural that after Arginine comes Gln with its precursor, the glutamic amino acid, both (Gln-Glu) with two carbon atoms in the side chain; it is natural indeed that, in terms of chemical similarity, after 3C atoms occurs changes into 2C atoms, better than into 1C atom, like in the pair Asn-Asp. [As in the case of the guanidino-functional group in arginine, no carbon atom is counting in the carboxylic or

amide functional group.] With this, chemical sequencing of series of 20 AAs closes, starting from the first, glycine, and ending with very different histidine (Table 2).

Survey 2. The relationships in the system presented in Table 2

GAVP 23 CMFYWH 74 **(97)** ILKRQE = 79 NDST = 28 **(107)**	VILRQE 74 / CMYW 49 → 123 GAPK 28 / NDSTFH 53 → 81 74 + 53 = **127** 49 + 28 = **77**
(GAVP 23) + (NDST 28) = 51 x 1 (ILKRQE 79) + (CMFYWH 74) = 51 x 3 (23 + 79 = 51 x 2) / (28 + 74 = 51 x 2)	

The Survey (Survey 2) presents the relationships in Table 2. The key results appear to be in relation to the quantity 97 which follow from the pattern 25-36-61 [(25+36 = 61) (61+36 = 97)]; the adding as in Fibonacci series; cf. Table A2 rows 5 & 6); other balance quantities: 102 and 51 as the ½ and ¼ of quantity 204 as the total number of atoms within 20 amino acid side chains. [Rakočević, 2004a, a legend to Fig. 1, p. 222: "within AAs (side chains) in class II there are 81, whereas in the class I the 0123 of atoms. Notice that 81 (as 9 x 9) is the first possible (zeroth) arithmetic square in module 9, and 0-1-2-3 is the first possible (zeroth) logical square (as 00-01-10-11)."]
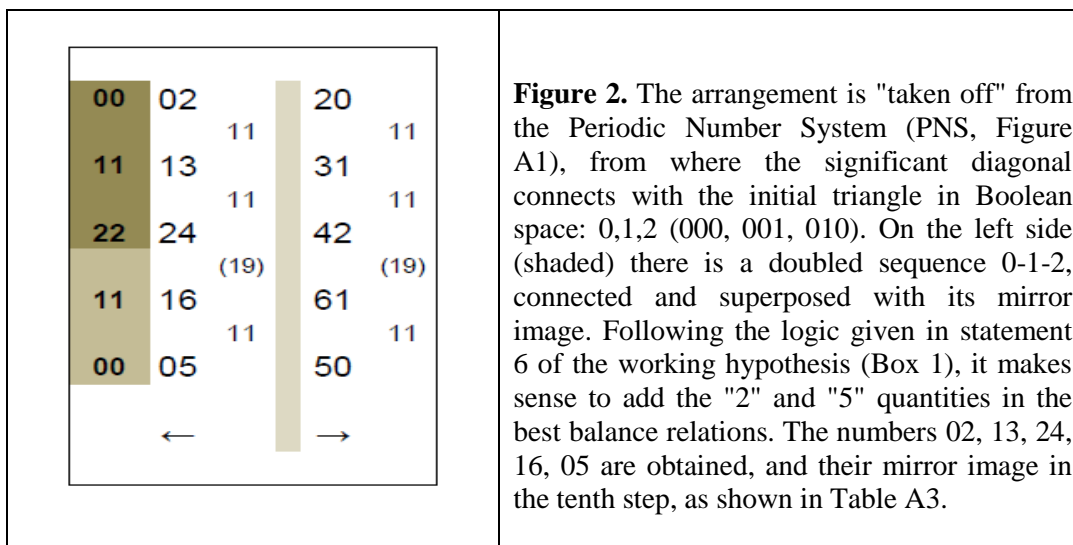
The main result

The main result of this pure chemical sequencing of AAs, presented in Table 2, shows that these chemical distinctions are accompanied by specific arithmetic regularities, including the existence of amino acid ordinal numbers from 1 to 20, with two decades (1-10 and 11-20); and also shows the full balance of the number of atoms in the 20 amino acid molecules: 102±0 atoms in two decades, as well as on two zigzag lines, where such a system with two zigzag lines represents the first possible *periodic system* with two periods.

There is also another result, also directly "taken up" from the Periodic system of numbers (PSN), which simultaneously corresponds to the unique situation in the PSN (Figure A1) and the number of atoms in 20 AAs: 26-42-59-77, within side chains of 4 x 5

of AAs which grouping follows from four amino acid diversity types[14] (Rakočević, 2011b, Figure 3, p. 828). Since these four results are obtained from the "center" of the PSN, it makes sense to compare them with four results obtained from the diagonal of the same system, presented in the right picture of Figure 1 (Equation 1). By this, it makes sense to assume that the quantities "2" and "5" should be understood in the same manner as in Figure 2 (as well as the quantities "1" and "6"), „taken up" from the six-bit binary tree, as shown in Equation 2 (in relation to Figure C3).

$$
\begin{array}{cccc}
31 & 41 & 61 & 71 \\
5 & 1 & 2 & 6 \quad \rightarrow \quad (5+2=1+6=7) \text{............................. (1)} \\
26 & 42 & 59 & 77
\end{array}
$$

$$
\begin{array}{cc}
5 & 6 \\
101 & 110 \quad (101+010=111) \text{... (2)} \\
010 & 001 \quad (110+001=111) \\
2 & 1
\end{array}
$$

00 02		20	
	11		11
11 13		31	
	11		11
22 24		42	
	(19)		(19)
11 16		61	
	11		11
00 05		50	
←		→	

Figure 2. The arrangement is "taken off" from the Periodic Number System (PNS, Figure A1), from where the significant diagonal connects with the initial triangle in Boolean space: 0,1,2 (000, 001, 010). On the left side (shaded) there is a doubled sequence 0-1-2, connected and superposed with its mirror image. Following the logic given in statement 6 of the working hypothesis (Box 1), it makes sense to add the "2" and "5" quantities in the best balance relations. The numbers 02, 13, 24, 16, 05 are obtained, and their mirror image in the tenth step, as shown in Table A3.

---

[14] $(G_1+A_4+C_5+N_8+P_8 = \mathbf{26})$; $(S_5+D_7+T_8+Q_{11}+H_{11} = \mathbf{42})$; $(Y_{15}+M_{11}+E_{10}+V_{10}+L_{13} = \mathbf{59})$; $(W_{18}+R_{17}+F_{14}+I_{13}+K_{15} = \mathbf{77})$. These four sets of AAs follow from four amino acid diversity types (see explanation of Table 6 in Box 4).

Table 3. The order of five quartets of protein amino acids following from Table 2 (I)

[72 (78 − 6)] [12 x 6]					
G (01)	A (04)	N (08)	D (07)	→	20
V (10)	P (08)	S (05)	T (08)	→	31
I (13)	L (13)	C (05)	M (11)	→	42
K (15)	R (17)	F (14)	Y (15)	→	61
Q (11)	E (10)	W (18)	H (11)	→	50
51-1	51+1	51-1	51+1		
[132 (2 x 66)] [22 x 6]					

This Table (Table 3) follows from Table 2 and PSN (Figure A1), from a doubled starting triangle from the top of the last column; triangle switched with its mirror image and superimposed: (00-11-22 / 22-11-00 → 00-11-**22**-11-00 (Table 2 and Table A3). Now we can see that with this arrangement the distinctions and classifications of protein AAs follow another multiplication of number 6 more than was found in the golden mean determination of CIPS (see the legend of Figure 1). Together with the results: (10 x 6 = 60), (11 x 6 = 66), (13 x 6 = 78), we now have the result (12 x 6 = 72). There is still no result (14 x 6 = 84), so if it will occur, then − bingo, the only mirror logical square in the series of natural numbers is reached, also included in Darwin's "computer program". [On the only Darwin's diagram in his famous book *Origin of species*, we see that at the top of the branch "m", between the written numbers 10 and 14, the positions of unwritten numbers 11, 12 and 13 are also indicated (Figure C1).]

Table 4. The order of five quartets of protein amino acids following from Table 2 (II)

120 (2 x 60) [20 x 6]					
G (01)	A (04)	N (08)	D (07)	→	20
V (10)	P (08)	S (05)	T (08)	→	31
I (13)	L (13)	C (05)	M (11)	→	42
K (15)	R (17)	F (14)	Y (15)	→	61
Q (11)	E (10)	W (18)	H (11)	→	50
51-1	51+1	51-1	51+1		
84 (78 + 6) [14 x 6]					

In this Table (Table 4), all is the same as in Table 3, but with the diagonal one step lower. The colors are used to indicate the AAs that are repeated in the "84 atoms" and "120 atoms" quantities in Table 5. From that crossing a specific amino acid distinction follows: at the beginning of dark area the **8** AAs (G, A, V, P, L, N, D, S) as the first possible cases, and at the beginning of light area the **2** AAs (I, K) as "non-standard" AAs: Ile, as the only one derivative within the valine stereochemical type, and Lys as the fourth case, instead of the first as in the Ser and Cys case. In the light area follow the **4** AAs (Q, E, R, W) as the second (Gln, Glu) or different (Arg, Trp); in the dark area follow the **6** AAs (C, M, F, Y, H, T), two sulfur, three aromatic and one with hydroxide functional group. (Cf. legends of Tables 5 & 6.) [It is possible to see the "rotation" in the Ile-Leu pair, depending on which precedes, and which follows in PAAS, presented in Table 2, what is explained in the Section "Order uncertainty".]

Table 5. The order of five quartets of protein amino acids following from Table 2 (III)

[84 (78 + 6)] [14 x 6]					
G (01)	A (04)	N (08)	D (07)	→	20
V (10)	P (08)	S (05)	T (08)	→	31
I (13)	L (13)	C (05)	M (11)	→	42
K (15)	R (17)	F (14)	Y (15)	→	61
Q (11)	E (10)	W (18)	H (11)	→	50
51-1	51+1	51-1	51+1		
[120 (2 x 66)] [22 x 6]					

In this Table (Table 5) all is the same as in Table 3, but with the opposite diagonal in relation to diagonal in Table 3, and colors as in Table 4.

Survey 3. The balance relationships between the arrangements in Tables 4 and 5

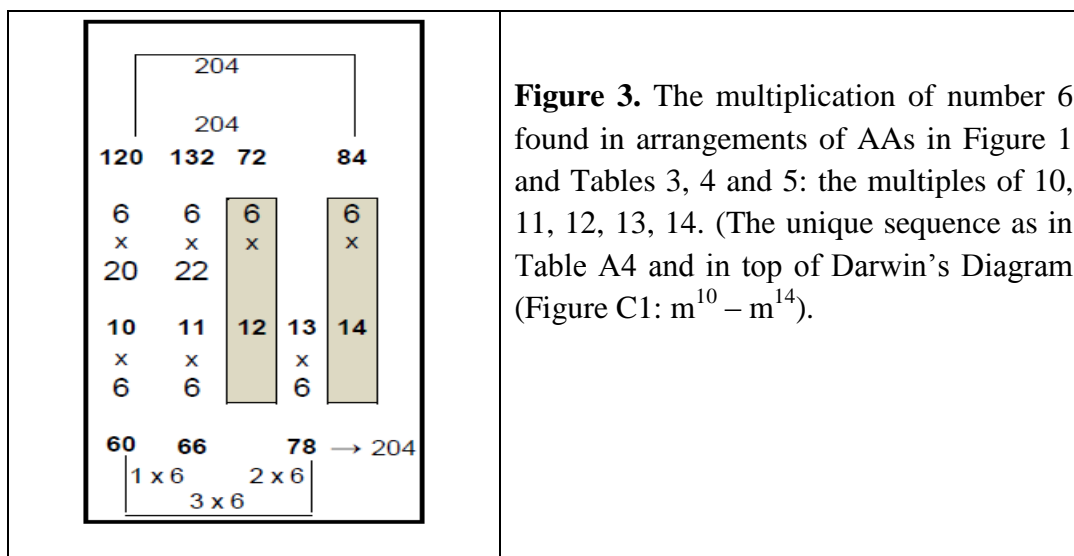| IK QREW GV IK APLNSD	IK 28 + QREW 56 = 84 IK 28 + GVAPLNSD 56 = 84
GVAPLNS CF D TMYH QRE CFWTMYH	GVAPLNSD 56 + CFTMYH 64 = 120 QREW 56 + CFTMYH 64 = 120
[(<u>7</u> x 4 = 28) (<u>7</u> x 8 = 56) (**8** x 8 = 64)] [(**6** x 14 = 84) (**6** x 20 = 120)] (120 − 84 = 36 = **6** x 6)	

Figure 3. The multiplication of number 6 found in arrangements of AAs in Figure 1 and Tables 3, 4 and 5: the multiples of 10, 11, 12, 13, 14. (The unique sequence as in Table A4 and in top of Darwin's Diagram (Figure C1: $m^{10} - m^{14}$).

Table 6. New splitting within the arrangement presented in Table 2

AAs: [(2_{28}), (4_{56}), (6_{64}), (8_{56})]   Atoms: 12–18–22 – (24 x 3)

Box 4. *The explanation of Table 6*

The left illustration in Table 6 follows from Survey 3 and Table 4, while the right illustration follows from Table 2 by rotating the second decade by 180 degrees. [This rotation process is a kind of cyclization; thus, the amino acid arrangement in Table 2 we can call CIPS II versus CIPS I in left picture of Figure 1.] The left illustration contains the result of the crossing of Table 4 with Table 5. Four "new types" of amino acid diversity, comparable to those previously found (Rakočević, 2011b), were obtained. The new types: [(G, A, V, P, L, N, D, S); (C, M, F, Y, H, T); (Q, E, R, W); (I, K)]: the 8 AAs as the first possible cases; the 2 AAs as "non-standard" (as it is explained in the legend of Table 4); the 4 AAs as the second (Gln, Glu) or different (Arg, Trp); the 6 AAs, all the same as the 6 AAs in the "old types" of diversity (Rakočević, 2011b), all but one, Thr instead of Trp. [Thr is the only "black sheep" in the set of 16 AAs of the alanine stereochemical type, given that one of its hydrogen atoms in the CH_2 group, between the head and the body, is replaced by one CH_3 group; on the other hand, Trp is the only "black sheep" in the set of aromatic AAs, having two rings.] "Old type": [(G, P); (A, L, V, I); (C, M, F, Y, W, H); (R, K, Q, N, E, D, T, S)]: the 4 hydrocarbon AAs; the 2 as different, "non-standard" hydrocarbon; the 8 AAs that within the side chain ("body") have a functional group mapped from the "head"; the 6 AAs in which there is no mapping of functional groups from head to body.

Table 7. The generalized Table of standard Genetic code

UUN	F	UCN	S	UAN	Y	UGN	C
	L				CT		CT
CUN	L	CCN	P				W
				CAN	H	CGN	R
(0)		(1)		(4)	Q	(5)	
AUN	I	ACN	T	AAN	N	AGN	S
	M				K		R
		GCN	A				
GUN	V			GAN	D	GGN	G
(2)		(3)		(6)	E	(7)	

Table 7 presents the codon families and their positions on the six-bit binary tree (Rakočević, 1998b, Figure 1). By comparing the positions of codons and AAs on this binary tree, we find that the arrangement is determined by cross-mirror symmetry, in contrast to 000 FLL/111 SRG on the left diagonal and 010 IMV/101 CWR on the right one. In doing so, the key contrasts are: on the least change path Phe UUU 000 000 *vs.* 111 111 GGG Gly crossed with Val GUC 010 101 *vs.* 101 010 UGA "stop" on the path of the maximal changes, when each zero number follows the number one and vice versa. [Notice that "The path of the maximal changes" (101 010 etc., on the correspondent Farey tree is "The golden ruth" as it is presented in Figure 2 in (Rakočević, 1998b).]

Figure 4. This arrangement of PAAS follows from the right illustration in Table 6 (from CIPS II). The expression of the principle of balancing, through the interconnection of the chemical properties of AAs, the number of atoms and the ordinal number of AAs in CIPS II, is self-evident. Confirmation of V. Shcherbak's hypothesis (1994) on the analogy of the amino acid (genetic) code with quantum physics also.

However, the result of the most surprising is the result shown in Table 3 (in relations with Tables 4 & 5). It is indeed a mirror image of our hypothetical result, which we gave with a working hypothesis (the statement 6 in relations to the statements 2, 4, 7 and 8): 20 -31-42-61-50 *vs.* 02-13-24-16-05 (Figure 2 in relation to Table A3). In the system presented in Table A3, the result is found in the 10th step, with sum 204, as well as the number of atoms in 20 AAs, in their side chains. As a curiosity or something more than that, the right neighbor is the number 220 (the first friendly number), the lower vertical

neighbor is the number 284 (the second friendly number) and the top 124 the fourth of the third perfect number (124 x 4 = 496).][15]

Altogether these are systematic natural arrangements, whose organization and determination correspond with the principle of self-similarity.[16] The already well-known facts that genetic code represents an analogy with natural (verbal) language[17] are joined now to the facts about analogies between genetic code arrangements and specific arrangements within the set of natural numbers.[18]

Conclusion

The facts and arguments presented in this paper fully confirm all nine statements of the working hypothesis (Box 1) about the existence of a complete system of protein amino acids (PAAS), both in biotic as well as in prebiotic conditions, *i.e.* within the amino acid (genetic) code, and independently from it. The existence of such facts also supports our hypothesis that the genetic code, viewed through its chemical constituents, was still prebiotic complete (Rakočević, 2004a). Also, everything that is discussed in this paper is in favor of our attitude that both genetic and chemical code corresponds to one specific spontaneous, intelligent design (SPID) (Rakočević, 2018a, Box 4).[19]

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[15] A hypothesis on the determination of the genetic code with the perfect and friendly numbers we have presented in the book (Rakočević, 1997b). (www.rakocevcode.rs) [Perfect numbers: 6, 28, 496, 8128, *etc.*; the pairs of the friendly numbers: (220-284), (1184-1210), (17296-18416) *etc.*]

[16] "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: 1. The principle of systemic self-related and self-similar organization. …" (Rakočević, 2004a, p. 231).

[17] "Rumer (1966) suggests that encoding by dinucleotide aggregations is mediated by 'grammatical' formalism (the relation between words and the root of the word), semantics (one-meaning and multy-meaning codon families) and by semiology, *i.e.* semiotics (the classification of nucleotide doublets after the number of their hydrogen bonds which appear here as 'significant' and 'signifié'" [(Rakočević, 2018a, pp. 31-32 in relation to (De Saussure, 1985, p. 99) (Cf. De Saussure's logical square of natural language in relation with the genetic code language in Figure C2)].

[18] "In determination of the genetic code, except two inherent alphabets – twenty amino acids and four amino bases (two pyrimidines & two purines – is involved still one 'hidden alphabet', the series of natural numbers, with all its regularities and laws" (Rakočević, 2011a, p. 4). An "unfaithless Tomas" may consider this to be numerology, but the facts are the facts. For any theory of probability, it is not possible to prove that all these "downloads" of chemical facts from the Periodic system of numbers (PSN) are mere coincidence.

[19] In further research, it may be possible to get a better term (and notion) by analogy with Carl Jung's term "Synchronizität" ("Synchronicity": Jung, 1993), but with the opposite meaning. This new term could be

Acknowledgment

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"Harmonizität" ("Harmonicity"), but while Synchronicity refers to acausal "meaningful coincidences", the Harmonycity refers to indirect-causal meaningful correspondences. These correspondences follow from interpolation relationships within PSE, with the validity of two Mendeleevian principles (continuity and minimum change), both for chemical elements and for compounds that build complete and consistent molecular systems.

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APPENDIX A

Periodic system of the numbers

The periodic number system (PSN) was originally given in: (Rakočević, 2011a, Table 4, p. 12 and 2011b, Table 4, p. 826), and here is only a different shading and one relevant diagonal with its own source in the double starting "triangle": (00-11-22). [We say "triangle" thinking that this number series corresponds with the first possible "triangle" in Boolean space (0-1-2, i.e. 000-001-010). However, this is a special topic that remains outside of the scope of this paper, for some other occasion.] In both previous presentations, in order to avoid misunderstanding in the scientific public as "pure numerology," I only labeled it "Table of minimal adding". Now I can no longer run back, and here I am presenting it as a PSN, as a reality.

	...											
(-2)	...										...	-22
(-1)	-21	-20	-19	-18	-17	-16	-15	-14	-13	-12	-11	
(0)	-10	-09	-08	-07	-06	-05	-04	-03	-02	-01	**00**	
(1)	01	02	03	04	05	06	07	08	09	10	**11**	
(2)	12	13	14	15	16	17	18	19	20	**21**	**22**	
(3)	23	24	25	**26**	27	28	29	30	**31**	32	33	
(4)	34	35	36	37	38	39	40	**41**	42	43	44	
(5)	45	46	47	48	49	50	**51**	52	53	54	55	
(6)	56	57	58	59	60	**61**	62	63	64	65	66	
(7)	67	68	69	70	**71**	72	73	74	75	76	77	
(8)	78	79	80	**81**	82	83	84	85	86	87	88	
(9)	89	90	**91**	92	93	94	95	96	97	98	99	
(A)	A0	A1	A2	A3	A4	A5	A6	A7	A8	A9	AA	
(B)	B1	B2	B3	B4	B5	B6	B7	B8	B9	BA	BB	

Figure A1. The first three non-negative numbers in the far right column correspond with the zeroth triangle (0,1,2) in Boolean spaces, and the first four (0,1,2,3) with the logical square (as in Figures C2 & C3). The end right column can also be read as (0,1), (1,2), (2,3), (3,4) and so on, as in the last column of Table B5.

Table A1. Possible periodic systems of numbers

q	q/2	squares	addends	diff.
2	1	$1^2 + 2^2$	$(01 + 100)_2$	$(11)_2$
4	2	$2^2 + 3^2$	$(10 + 21)_4$	$(11)_4$
6	3	$3^2 + 4^2$	$(13 + 24)_6$	$(11)_6$
8	4	$4^2 + 5^2$	$(20 + 31)_8$	$(11)_8$
10	5	$5^2 + 6^2$	$(25 + 36)_{10}$	$(11)_{10}$
12	6	$6^2 + 7^2$	$(30 + 41)_{12}$	$(11)_{12}$
14	7	$7^2 + 8^2$	$(37 + 48)_{14}$	$(11)_{14}$
16	8	$8^2 + 9^2$	$(40 + 51)_{16}$	$(11)_{16}$
...				

The row "10" in this Table follows from PSN presented in Table A1; all other rows follow from analog number systems. From the fact that pattern 25-36-61, valid both in genetic and chemical codes, follows the conclusion that in the case of the existence of biomolecules, only decimal number system has "passed" through Darwin's selective sieve. What is surprising, however, is the fact that Darwin's sieve is matched with the "pulse" of Bing Bang.

Table A2. A double Fibonaccian step

1	1					
		3	5	6	9	
2	4					13
		5	13	17	22	6
3	9					19
		7	25	34	41	6
4	16					25
		9	41	57	66	6
5	**25**					31
		11	**61**	**86**	**97**	6
6	**36**					37
		13	85	121	134	6
7	49					43
		15	113	162	177	6
8	64					49
		17	145	209	226	
9	81					

The Table presents – in the red area – a double Fibonaccian step. From the fact that pattern 25-36-61 is valid both in genetic and chemical codes, and patterns 25-36-61-86 & 25-36-61-86-97 are valid in genetic code, follows the conclusion that in Nature realy exists such a double Fibonaccian step. [These are not Fibonacci numbers, but it is the Fibonacci rule.]

Table A3. The source of PAAS mirror symmetry

00	02	04	06	08	10	12
11	13	15	17	19	21	23
22	24	26	28	30	32	34
11	16	21	26	31	36	41
00	05	10	15	20	25	30
44	60	76	92	108	124	140
	12	14	16	18	20	22
	23	25	27	29	31	33
	34	36	38	40	42	44
	41	46	51	56	61	66
	30	35	40	45	50	55
	140	156	172	188	204	220
	22	24	26	28	30	32
	33	35	37	39	41	43
	44	46	48	50	52	54
	66	71	76	81	86	91
	55	60	65	70	75	80
	220	236	252	268	284	300
	32	34	36	38	40	42
	43	45	47	49	51	53
	54	56	58	60	62	64
	91	96	101	106	111	116
	80	85	90	95	100	105
	300	316	332	348	364	380
	...					

The arrangement represents the Table of distinct 2-5 adding (TDA) with starting column 00-11-22-11-00 which follows from PSN (Periodic system of numbers: Figure A1) in decimal number system by overlapping the real sequence of doubled the first possible triangle in Boolean space (0-1-2) with its mirror image through compression and superposition at the point "22". In the 10th step we have a realization of the sequence (20-31-42-61-50), the same with the number of atoms in five AAs classes (20, 31, 42, 61, 50) as it is here presented: all five results in the 10th step are mirror image of the first step. (Cf. Figure 2 and see details in the text.)

Table A4. Mirror symmetry within the sequence 11-12-13-14 in the decimal number system (Rakočević, 1994, p. 235)

0	$11 \times 1 = 11$ $11 \times 2 = 22$ $11 \times 3 = 33$	$11 \times 1 = 11$ $11 \times 2 = 22$ $11 \times 3 = 33$	$11^2 = 121$
1	$12 \times 1 = 12$ $12 \times 2 = 24$ $12 \times 3 = 36$	$21 \times 1 = 21$ $21 \times 2 = 42$ $21 \times 3 = 63$	$12^2 = 144$ $21^2 = 441$
2	$13 \times 1 = 13$ $13 \times 2 = 26$ $13 \times 3 = 39$	$31 \times 1 = 31$ $31 \times 2 = 62$ $31 \times 3 = 93$	$13^2 = 169$ $31^2 = 961$
3	$14 \times 1 = 14$ $14 \times 2 = 28$ $14 \times 3 = ?$	$41 \times 1 = 41$ $41 \times 2 = 82$ $41 \times 3 = ?$	$14^2 = 196$

111	000	(07-00)		(3)	8 x 8	8 x 8	8 x 8
110	011	(06-03)					
101	**010**	**(05-02)**		(2)	4 x 4	4 x 16	16 x 4
100	001	(04-01)					
011	110	(03-06)		(1)	2 x 2	2 x 32	32 x 2
010	**101**	**(02-05)**					
001	100	(01-04)					
000	111	(00-07)		(0)	1 x 1	1 x 64	64 x 1

Figure A2. Mirror symmetry within the binary number record on the Boolean cube (on the left). Mirror symmetry within the codon distribution to a six-bit binary tree; an example: two branches, each with 32 codons *vs.* 32 codon pairs (on the right).

APPENDIX B

Harmonic amino acid structures

Table B1. The distinctions of 16 AAs of alanine stereochemical type

In the Table it is given a classification of 16 AAs of alanine stereochemical type into 8 chemically adequate pairs. In both crossing lines there are 86±0 atoms. [86 + GV 11 = 97 and 86 + PI 21 = 107 (cf. Table A2, 5th and 6th row)]. The differences 8 and 9 (9 - 8 = 1) express the minimum change relation among the amino acids [as in Gray code model of GC (Swanson, 1984, p. 191)]. The order (ordinal number) follows from the atom number hierarchy. Notice that within outer class (2:4 = 1:2 AAs or amino acid pairs) there is a balance of the number of atoms: [(4 + 33 = **37**) + (13 + 25 = **38**) = 75 (86 − 11)]; and within inner class (4:6 = 2:3) [(10 + 38 = **37** + 11) + (19 + 30 = **38** + 11) = 97 (86 + 11)] (All examples as Shcherbak's analogies with quantum physics.) Notice also the realization of 25-36-61 pattern: AME = LCD = 25. [This 25 + (GV 11) from non-alanine types equals 36.]; on the other hand, AAs in green as well as AAs in blue equals 61 atoms. The right illustration contains the algorithm for the generation of a variant ("wobble" variant!) of CIPS as it is the right picture in Figure 1, by reading as from a logical square in the Gray code model: STLA, DEMC, KRQN, FYWH. (Left illustration from: Rakočević and Jokić, 1996, Survey 1, p. 346; right illustration from: Rakočević, 2011b, Table 2.1, p. 823.)

Table B2. The significant distinctions in CIPS (I)

The distinctions of AAs after the ratio 4: 6 = 2:3 on the left and 5:5 = 1:1 on the right. The resulting relationships are analyzed in Table B3 and Survey B1.

Table B3. The significant distinctions in CIPS (II)

The analysis of relationships in Table B2 after crossing of quantities 97 and 107. New order in relation to left picture in Figure 1: [(YF AL) → aliphatic and carboaromatic]; [(QN PI) → the first three nitrogens, the fourth one links P with valine, *i.e. via* isopropyl group "triangle"] [GV DE → *vs.* PI QN]; [RK WH → all are nitrogens]; [On the left (AL FY) → initial aliphatic and initial aromatic; On the right (RK WH) → right end: all are nitrogenous]. In the middle of the system are chalcogenes. All four columns correspond to CIPS on the left picture in Figure 1: two and two rows from top to bottom.

Table B4. The number of conformations (total: 202 + 203 = 405)

(1)	G	04	16	N	(11)
(2)	A	03	10	D	(12)
(3)	V	08	09	S	(13)
(4)	P	02	08	T	(14)
(5)	L	22	21	C	(15)
(6)	I	20	20	M	(16)
(7)	K	66	12	F	(17)
(8)	R	66	12	Y	(18)
(9)	Q	38	24	W	(19)
(10)	E	20	24	H	(20)
(3 x 83)		249 (1 x 93)	156		(4 x 39)
(82 + 56)		138	82		(220)
56 = 028+028		111	74		(185)
		(111 = 3 x 37)	(74 = 2 x 37)		

(a) $(39 + 210 = 249)$ $(64 + 92 = 156)$

$[(b) (39 + 64 = 103) (210 + 92 = 302)]$

(c) $103 = 203 - 100;$ $302 = 202 + 100$

(d) $203 + 001;$ $202 - 001$

(e) $82 + 111 = 203 - 10$

(f) $138 + 74 = 202 + 10$

$[(b) (39 + 64 = 103) (210 + 92 = 302)]$

(g) $39 + 92 = 202 - 71$ (¼ 284)

(h) $64 + 210 = 203 + 71$ (¼ 284)

(i) $203 + 71 = 274$ $(496 - 222)$

(k) $202 - 71 = 131$ $(333 - 202)$

This Table is the same as Table 2, except that Leu proceeds Isoleucine, and instead of the number of atoms in AAs, is given the number of conformations, as in Popov (1989, Table 8, p. 88). The balancing of conformation as follows: From (a) to (c) the difference in the number of conformations in two columns (decades) in relation to the middle pair 202-203, with a change for ± 100; (d) from: (Rakočević, 2004a, Table 8, p. 228) and (Rakočević, 2018a, Table 8, p. 44) where is shown the change in the number of conformations for ± 001 in the GC Table, if the order of AAs follows the order of their coding codons, in the hierarchy of the number of hydrogen bonds; from (e) to (f) the number of conformations in odd positions in relation to multiples of Shcherbak's "Prime quantum 37" with a change for ± 10; from (g) to (h) the number of conformations in relation to the second friendly number; (i) the number of conformations in relation to the second friendly and the third perfect number; (k) the number of conformations in relation to the second friendly number and to the significant determinant of GC, as is the number 333 (Rakočević, 2018a, p. 37: the sixth column in Survey 2).

Survey B1. The relationships within two arrangements presented in Table B2

[(FLTSKH 66) (NIVE 41)] = 107	[(FPTDK 52) (ANCVW 45)] = 97
[(QPGD 27) (YAMCRW 70)] = 97	[(LQSGH 41) (YIMER 66)] = 107

$$(66 + 70 = 68 \times 2 = 136) + (27 + 41 = 68 \times 1) = 204$$
$$(136 = 118 + 018) \, [68 \, / \, 86]$$
$$52 + 66 = 118) + (41 + 45 = 86 \times 1) = 204$$

Survey B2. The determinations on the six-bit binary tree


```
/00 - 07/08 - 15/16 - 23/24 - 31//32 - 39/40 - 47/48 - 55/56 - 63/
    28      92     156     220     284     348     412    476
        64      64      64      64      64      64      64

/00 - 07/00 - 15/00 - 23/00 - 31//00 - 39/00 - 47/00 - 55/00 - 63/
    28     120     276     496     780    1128    1540    2016
        92     156     220     284     348     412     476
```

The Survey follows from (Rakočević, 1997b, Figure 7, p. 60): "The determination of the series of the numbers 0-63. When we look closely into the structure of the sequence 0-63 of the series of the natural numbers we come to the obvious and self-evident explanation of the reason why the genetic code must be six-bit code, no matter if it is the manifestation in the form of the Gray Code model (Swanson, 1984, p 188), or it is in the form of the Binary tree (Rakočević, 1994, p 38). There must be 8 codons, *i.e.* amino acid classes. The structure of the sequence 0-63 is strictly determined by third perfect number (496) and the sum consisted of the first pair of the friendly numbers (220+284). Along with this, the specific Boolean square is being made and it is the restrictive factor, in a sense that it is not possible to 'go on' any further - not ahead, not back: (0) 220+284=504; (1) 156+348=504; (2) 92+412=504; (3) 28+476=504. The key distinctions within the genetic code are obviously self-evident: entity 64 as a series of continuity (correspondent with 64 codons); entity 20 from 496 (III PN)-476=20 (correspondent with 20 amino acids) *etc*."

Table B5. Some number systms: the unique arrangements and situations

(16) $2^4 = 4^2$ (16)		
(64) $2^6 = 4^3$ (64)		
(256) $2^8 = 4^4$ (256)		
(64) $2^6 = 4^3$ (64)		
(4096) $4^6 \neq 8^3$ (512)		
(46656) $6^6 \neq 12^3$ (1728)		

2	1+1	0 + 2	→	0:1
6	3 + 3	2 + 4	→	1:2
10	5 + 5	4 + 6	→	**2:3**
14	7 + 7	6 + 8	→	3:4
18	9 + 9	8 +10	→	4:5
22	11+11	10 +12	→	5:6
	...			

The Table corresponds with PSN (Figure A1) through the ratio 1:2 on the left above and 2:3 on the right, the third row. The left illustration shows unique arrangements and situations corresponding to 16 doublets and 64 triplets of nucleotides in the genetic code. The right illustration shows the changes by ± 1 in relation to $q/2$ of number systems whose numerical basis (q) corresponds to the values that follow from Hükel's rule (the first column). It can be seen that only in the case of the decimal number system we have a direct correspondance with the golden mean (footnote 10).

Table B6. The relationships within Generalized Golden mean (Rakočević, 2004b)

N	x_1	x_2	$\underline{\textit{h}}$	m	r		N	x_1	x_2	$\underline{\textit{h}}$	m	r
0.	$0^2 + 1^2 = \underline{1}$ $(0 + 1)^2 = 1$			0	$\sqrt{1}$		0.	$0^2 + 1^2 = \underline{1}$ $(0 + 1)^2 = 1$			0	$\sqrt{1}$
1.	$1^2 + 2^2 = \underline{5}$ $(1 + 2)^2 = 9$			4	$\sqrt{9}$		1.	$(x_1)^2 + (x_2)^2 = \underline{2}$ $(x_1 + x_2)^2 = 3$			1	$\sqrt{3}$
2.	$2^2 + 3^2 = \underline{13}$ $(2 + 3)^2 = 25$			12	$\sqrt{25}$		2.	$(x_1)^2 + (x_2)^2 = \underline{3}$ $(x_1 + x_2)^2 = 5$			2	$\sqrt{5}$
3.	$3^2 + 4^2 = \underline{25}$ $(3 + 4)^2 = 49$			24	$\sqrt{49}$		3.	$(x_1)^2 + (x_2)^2 = \underline{4}$ $(x_1 + x_2)^2 = 7$			3	$\sqrt{7}$
4.	$4^2 + 5^2 = \underline{41}$ $(4 + 5)^2 = 81$			40	$\sqrt{81}$		4.	$1^2 + 2^2 = \underline{5}$ $(1 + 2)^2 = 9$			4	$\sqrt{9}$
5.	$5^2 + 6^2 = \underline{61}$ $(5 + 6)^2 = 121$			60	$\sqrt{121}$		5.	$(x_1)^2 + (x_2)^2 = \underline{6}$ $(x_1 + x_2)^2 = 11$			5	$\sqrt{11}$
	(...)							(...)				

APPENDIX C

Some additional harmonic structures

The Darwin's equation

Table C1. The key of Darwin's Diagram (I)

Primary				Secondary			
B	00	06	G	B	01	01	G
C	01	02	H	C	01	01	H
D	02	00	K	D	01	01	K
E	10	01	L	E	00	01	L
F	14			F	00		

27 09   03 04

36   (43)   07

(233 + 43 = 276)
(276 + 56 = 332)

99

276 = 216_{down} + 60^{up}

"All branches (primary + secondary) for "other nine species" for the left and the right part of the Diagram, at all 15 levels. The equation 27 + 09 = 36 appears to be a special Darwin's equation, valid to determination of the genetic code (Figure 6, 7 & 8 and Table 6.1); and the equation 03 + 04 = 07 corresponds to the first three members of Lucas number series (Figure D.1). The number 233 comes from Table 4.5 and together with this result (43) makes 276 which is the total number of branches within the Diagram. In addition: 56 = 46 nodes plus 10 branchings, and from that all "branch" entities/quantities equal 332 as a mirror pattern of the 233" (Rakočević, 2015, Table 5, p. 47).
(http://dx.doi.org/10.17605/OSF.IO/QZG69)
(www.rakocevcode.rs)

The Darwin's equation (27 + 9 = 36) is the "missing link" that allows understanding of the pattern 25-36-61, contained in two linear equations, determinants of genetic and chemical code (Rakočević, 2018b, Survey 2a, 2b, 3a and 3b, p. 296). At the same time, it is also the key of Darwin's Diagram (Rakočević, 2015, Figure 1.1, p. 19; here Figure C1).

Table C2. The key of Darwin's Diagram (II)

01	+	00	=	01		09	+	00	=	09
02	+	02	=	04		10	+	06	=	16
03	+	01	=	04		11	+	05	=	16
01	+	00	=	01		05	+	04	=	09
04	+	00	=	04		12	+	04	=	16
02	+	-01	=	01		06	+	03	=	09
...						...				
25	+	00	=	25		49	+	00	=	49
26	+	10	=	36		50	+	14	=	64
27	+	09	=	36		51	+	13	=	64
17	+	08	=	25		37	+	12	=	49
28	+	08	=	36		52	+	12	=	64
18	+	07	=	25		38	+	11	=	49
...						...				

This illustration is from Figure 6 in "Darwin Enigma" (Rakočević, 2015): „The generation of the squares of natural numbers through two linear equations. Darwin's equation is in the third quadrant, in the area of dark tones surrounded by two linear equations valid in the genetic code." Notice that the second member of the equation (the second row in all four quadrants) follows from Hückel's rule (2, 6, 10, 14); the differences between the third and fourth row also from Hückel rule: (3-1 = 2), (11-5 = 6), (**27-17 = 10**), (51-37 = 14). On the other hand, the first member of the equation (2, 10, 26, 50) increases by 8n (n = 1, 2 and 3). Notice also that with the first quadrant we have the generation of the squares of the first two natural numbers 1 and 2, in second 3 and 4, in third 5 and 6 (in relation to the pattern 25-36-61) and in the forth 7 and 8. [The next step in generating would already be in the area of double-digit numbers.]

Table C3. The key of Darwin's Diagram (III)

02	+	02	=	04	10	+	06	=	16
03	+	01	=	04	11	+	05	=	16
01	+	00	=	01	05	+	04	=	09

$$02 + 02 = 04 = 2^2$$
$$01 + 00 = 01 = 1^2$$
$$02 - 02 = 00 = 0^2$$
$$01 - 00 = 01 = 1^2 \ (?!)$$

$$10 + 06 = 16 = 4^2$$
$$05 + 04 = 09 = 3^2$$
$$10 - 06 = 04 = 2^2$$
$$05 - 04 = |01 = 1^2$$

$$1 - (-1) = \mathbf{2}$$

26	+	10	=	36	50	+	14	=	64
27	+	09	=	36	51	+	13	=	64
17	+	08	=	25	37	+	12	=	49

$$26 + 10 = 36 = 6^2$$
$$17 + 08 = 25 = 5^2$$
$$26 - 10 = 16 = 4^2$$
$$17 - 08 = 09 = 3^2$$

$$50 + 14 = 64 = 8^2$$
$$37 + 12 = 49 = 7^2$$
$$50 - 14 = 36 = 6^2$$
$$37 - 12 = 25 = 5^2$$

$$5 - (+3) = \mathbf{2}$$

The Table as in (Rakočević, 2015, Table 5, p. 47): "This Figure follows from the previous. Three linear equations within each of the four quadrants in relation to the quadruplets of natural numbers' squares. In the third quadrant: two equations are valid in the genetic code and one (in the middle position, dark tone) is given as Darwin's equation [Notice a paradox (Darwin's paradox), valid for number 1 in the first quadrant: the negative value of number 1 cannot be – negative?!]."
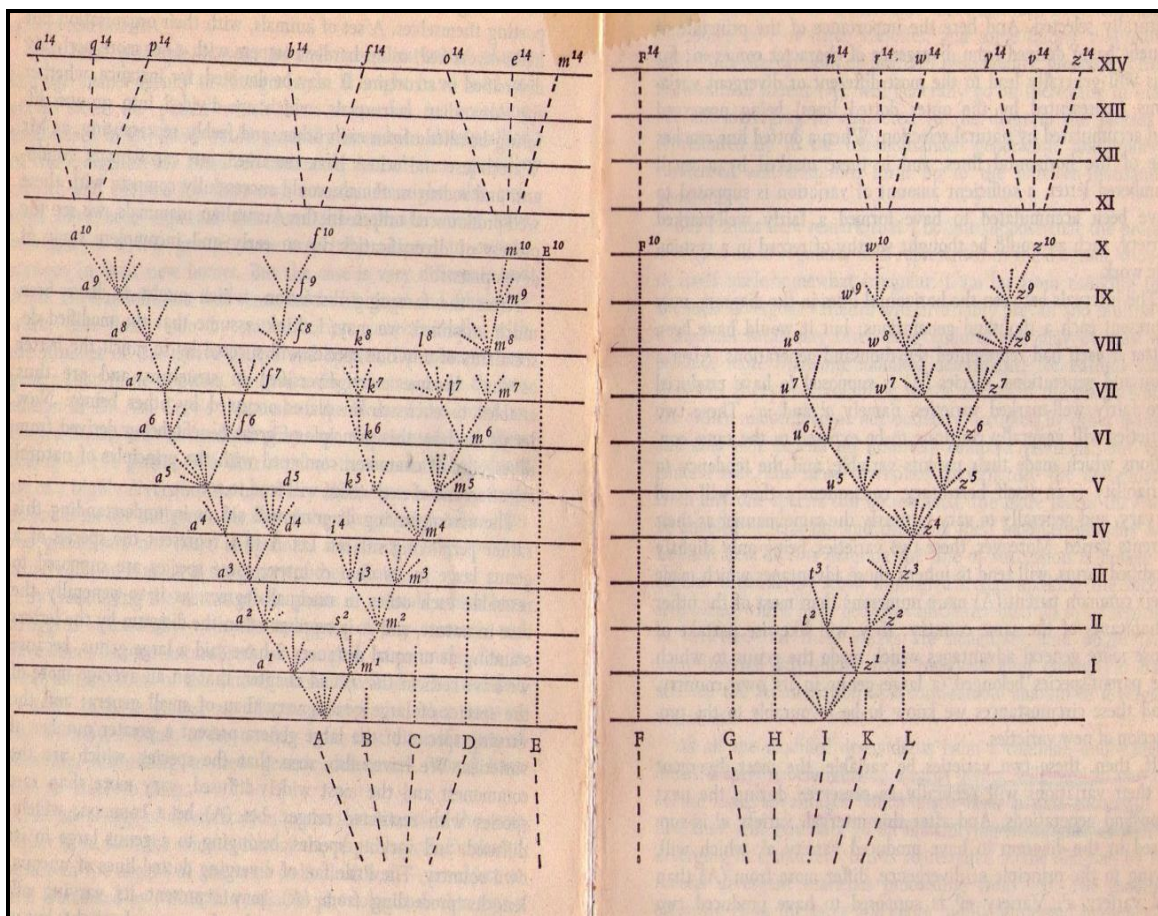
Figure C1. The "accompanying diagram" in Darwin's book "On the Origin of Species" (London, 1859)
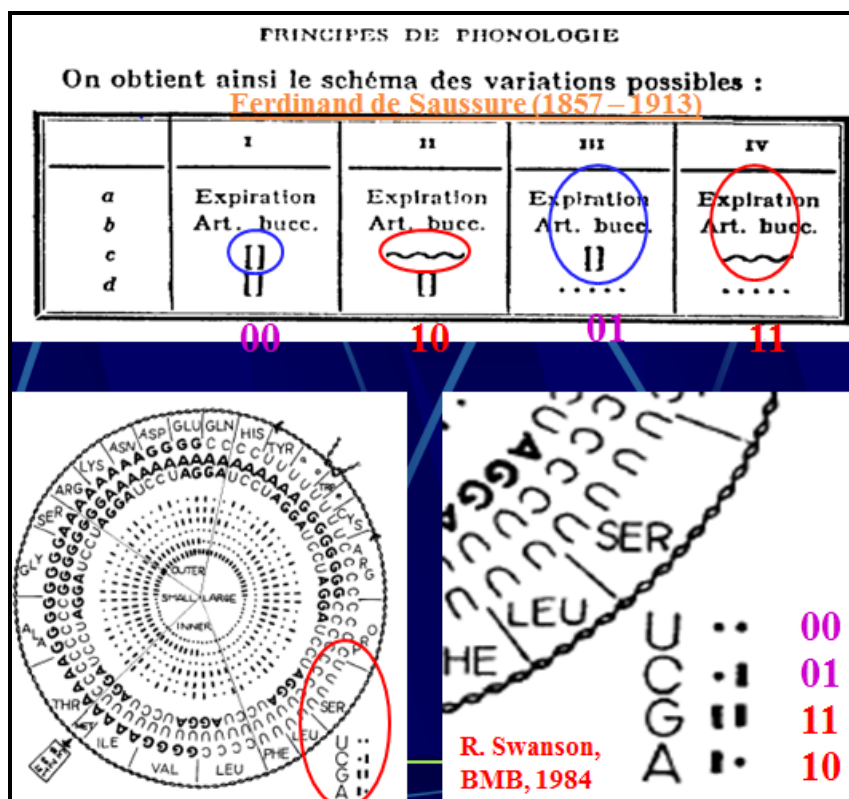
Figure C2. The correspondence with PSN (Fig. A1) through the relations between the logical square 00-01-10-11 and the first four levels in PSN: 00-11-22-33. The binary records of the logical square: up for the human language (De Saussure, 1985, p. 70); down: for the genetc language (Swanson, 1984, p. 188).
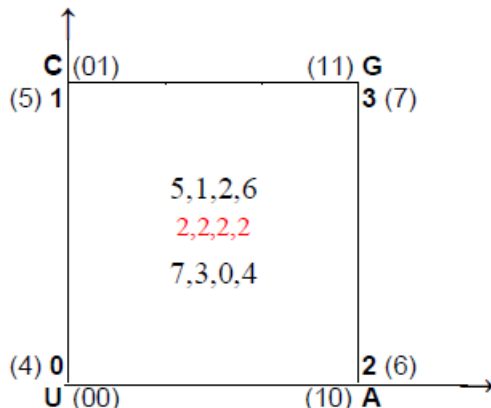
Figure C3. The correspondence with PSN (Figure A1) through the relations between the logical square 00-01-10-11 and the first four levels in PSN: 00-11-22-33. The unit Boolean logical square: **0** (00), **1** (01), **2** (01), **3** (11) in correspondence with the unit Boolean logical cube and/or with eight branches on the binary-code tree of Genetic code (Rakočević, 1998b, Figure 1, p. 284): **0** (000), **1** (001), **2** (010), **3** (011); **4** (100), **5** (101), **6** (110), **7** (111). The mirror symmetry on the binary-code tree of Genetic code: [010 / 101 → AUA / CGC etc.]; [001 / 110 → UCC / GAA etc.]. The Py-Pu logical square: U (00) → simpler ring, simpler H bond; C (01) → simpler ring, more complex H bond; A (10) → more complex ring, simpler H bond; G (11) → more complex ring, more complex H bond. From the 24 permutations of the UCAG sequence, only this, as the first, consistently follows the chemical hierarchy; the remaining 23 are in relation to it. (Cf. footnote 7; also, the sequence 5-1-2-6 with the same sequence in Equation 1.)