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Research Article

Protein Synthesis: Why the Genetic Code? – from Combinatorial Perspective

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Abstract

Statement of the Problem: Protein type composition, and protein type proliferation and diversification are identified as two goals of protein synthesis. This paper provides the highways to the identified goals. The protein type proliferation and diversification goal in particular has two dissimilar versions, one reached by a district highway and the other reachable by a transcontinental highway.

Method and Theoretical Orientation: Analogy observed between the 10 named digits of number and the 20 named amino acids of protein in the aspect of natural endowment with unrestricted compatibility; whereby the 20 amino acids can stand in any sequence to make a unique protein type, just like the 10 digits standing in any sequence to make sense in the formation of a unique number, is the highway to the first goal of protein type composition. With regard to achievement of protein type proliferation and diversification, the second goal of protein synthesis, theoretical orientation of the method reveals the engagement of permutations, a number enclave, working by the combinatorial input/output multiplicative replication system well-equipped with view mixing techniques for computing factorial complements representing self-proliferation and diversification for specified set (n) and selection (r) i.e. nPr. With the observation in 1953 that the sequence of the four DNA bases A,T,G,C (Adenine, Thymine, Guanine, Cytosine) in the nucleus of a cell influenced the sequence of 20 amino acids of protein in the cellular cytoplasm, the DNA four bases in the setting of substitution phenomenon in science are meant to undergo permutation of 4 from 4 i.e. ${}_4P_4 = 4! = 4 \times 3 \times 2 \times 1 = 24$ quadruplets to provide the genetic code as the district highway to one version of the second goal of protein type proliferation and diversification of protein synthesis. The other version of the second goal of protein type proliferation and diversification of protein synthesis ordinarily involves the set of 20 amino acids undergoing permutation of 20 from 20 i.e. ${}_{20}P_{20} = 20! = 20 \times 19 \times 18 \times 17 \ldots 4 \times 3 \times 2 \times 1 = 2{,}432{,}902{,}008{,}176{,}640{,}000$ protein types, which is a transcontinental highway, not observed in Nature.

Findings: It is the four DNA bases that undergo 4 from 4 permutation to yield a 24-quadruplet genetic code as workforce in protein synthesis and not the 20 amino acids of protein that undergo permutation to achieve protein type proliferation and diversification.

Conclusion and Significance: The genetic code engagement in protein synthesis is in a setting of substitution of 4 DNA bases for 20 amino acids of protein for permutation towards achievement of moderation and adequacy of protein type proliferation and diversification via the avenue of collinearity between the 24-quadruplet version of genetic code and 20 amino acids of protein on one to one correspondence with four spare quadruplets for four time and place based start/stop control signals during protein synthesis.

Keywords: Protein Type; Permutation; Proliferation; Diversification; Input; Output

Introduction

Biological scientists have since named the 20 amino acids that always form protein type, ref, Figure 3 Key, and stated that no two proteins have the same order (sequence) of amino acids. Of interest to us in this paper is the question of the option by which protein types are synthesized so as to be individually characterized by a unique sequence of amino acids. There happens to be two options; one of combinatorial systematic and comprehensive linear repositioning of the constituent 20 amino acids in a sequence by themsel-

ves without external agencies, and the other of selective placement of the respective 20 amino acids in a particular sequence by external set of agencies to make a protein type. The former being merely auto-kinematic is sans "Labour" i.e. without labour while the latter is "Labour intensive". We proceed to consider the likelihood of each option in the light of science, that is, creation based in terms of productivity in so far as protein synthesis borders on productivity. Before then we have some definitions and annotations.

Definitions and Annotations

Definitions

- **Combination:** A group of things chosen from a large number of dissimilar things in which order is not important.
- **Combinatorics:** A sub-discipline of mathematics concerned with the calculation and computation of factorial complements of permutations and combinations of specified set (n) and selection (r) of dissimilar things which is centred on input/output format.
- **Combinatorial computation scheme:** Combinatorial Computation technique capable of producing the factorial complements of permutation, combination and genetic code in fulfillment of the predictions ${}_nP_n = n!$ and ${}_nP_r = \frac{n!}{(n-r)!}$ for permutations, ${}_nC_r = \frac{{}_nP_r}{r!}$ for combinations, ${}_4P_4 = 4! = 4 \times 3 \times 2 \times 1 = 24$ quadruplets for genetic code all based on input/output format.
- **Kinematic:** Of motion considered abstractly without force or mass.
- **Kinematics:** Science of kinematic motion.
- **Permutation:** An arrangement of dissimilar things in which order is important.
- **Tower multiplication:** The factorial complements for permutation in vertical orientation either bottom heavy (gravimetric) or top heavy (antigravimetric) featuring a set of serial terms numbering not less than 3, of which the initial member is called multiplicand while the rest are multipliers. The operation itself, involves the recycling of the preceding product to multiplicand for continuation of the multiplying exercise with the incumbent multiplier for another product in succession
- **Rolling multiplication:** Rolling multiplication either incremental or decremental is the multiplication operation by which a tower multiplication (gravimetric or antigravimetric) is made to yield a multiplication tower complex i.e. Permutation Tower of ${}_nP_n$ or ${}_nP_r$.

Annotations

Rolling incremental multiplication involves the terms in ascending order of magnitude and produces Permutation Tower or fullset selection ${}_nP_n$ ref. Tables 1b and 2b. Rolling decremental multiplication engages the terms in descending order of magnitude and yields Permutation Tower of subset selection nPr ref. Table 1a and 2a.

Count gravimetizer

The count gravimetizer is a numerational apparatus for delineating large figures into counting denominations for speedy expression in words. It consists of a set of "vertical wells" of increasing depth from right to left making abutments with horizontal layers of increasing length from top to bottom such that, the wells at their bottoms carry the packing coefficients of the counting denominations in gravimetric order in the adjoining horizontal layers making the abutments as depicted in figure 1.

Materials and Methods

Materials

The materials consist of the set of 20 named amino acids numbered serially from 1 to 20 as building blocks for a protein type. The numerals for them represent the factorial for the permutation of ${}_{20}P_{20} = 20! = 20 \times 19 \times 18 \times 17 \times 16 \times 15 \times 14 \times 13 \times 12 \times 11 \times 10 \times 9 \times 8 \times 7 \times 6 \times 5 \times 4 \times 3 \times 2 \times 1$. Included also in the materials are the four RNA bases A,U,G,C as input set, being the transcriptions of the DNA four bases A,T,G,C, (Adenine, Thymine, Guanine, Cytosine) in the nucleus of the cell.

Methods

The methods are two-fold: One of Tower multiplication for determining the factorial complements of ${}_{20}P_{20}$; and the other of Square Kinematics for generating an output sequence of permutations of the input set 4 of the four RNA A,U,G,C bases in fullset selection of 4.

(a) Rolling Decremental Multiplication		(b) Rolling Incremental Multiplication	
4	4	1	1
X 3	X 3	X 2	X 2
	12		2
X 2	X 2	X 3	X 3
	24		6
X 1	X 1	X 4	X 4
	24 Ans. Quadruplets		24 Ans. Quadruplets

Table 1: Tower Multiplication of ${}_4P_4 = 4!$ in two varieties.

(a) Rolling Decremental Multiplication		(b) Rolling Incremental Multiplication	
20	20	1	1
X 19	X 19	X 2	X 2
	180		2
	20	X 3	X 3
	380		6
X 18	X 18	X 4	X 4
	3040		24
	380	X 5	X 5
	6840		120
X 17	X 17	X 6	X 6
	47880		720
	6840	X 7	X 7
	116280		5040
X 16	X 16	X 8	X 8
	697680		40320
	116280	X 9	X 9
	1860480		362880
X 15	X 15	X 10	X 10
	9302400		3628800
	1860480	X 11	X 11
	27907200		3628800
X 14	X 14		3628800
	111628800		39916800
	27907200	X 12	X 12
	390700800		79833600
X 13	X 13		39916800
	1172102400		479001600
	390700800	X 13	X 13
	5079110400		1437004800
X 12	X 12		479001600
	10158220800		6227020800
	5079110400	X 14	X 14
	60949324800		24908083200
X 11	X 11		6227020800
	60949324800		87178291200
	60949324800	X 15	X 15
	670442572800		435891456000

X 10	X 10	X 16	87178291200
	6704425728000		1307674368000
X 9	X 9		X 16
	60339831552000		7846046208000
X 8	X 8	X 17	1307674368000
	482718652416000		20922789888000
X 7	X 7		X 17
	3379030566912000		146459529216000
X 6	X 6	X 18	2092278988800
	20274183401472000		167382319004000
X 5	X 5		X 18
	101370917007360000		2845499424768000
X 4	X 4	X 19	355687428096000
	4054836680294400000		6402373705728000
X 3	X 3		X 19
	12164510040883200000		57621363351552000
X 2	X 2	X 20	6402373705728000
	24329020081766400000		121645100408832000
X 1	X 1		X 20
	24329020081766400000 Ans.		24329020081766400000 Ans.
	Twenties		Twenties

Table 2: Tower Multiplication of $_{20}P_{20}$ = 20! in Two Varieties.

Naming the figure 2, 432,902,008,176,640,000 in metric number system (in powers of 1000) using count gravimetizer, depicted in figure 1.

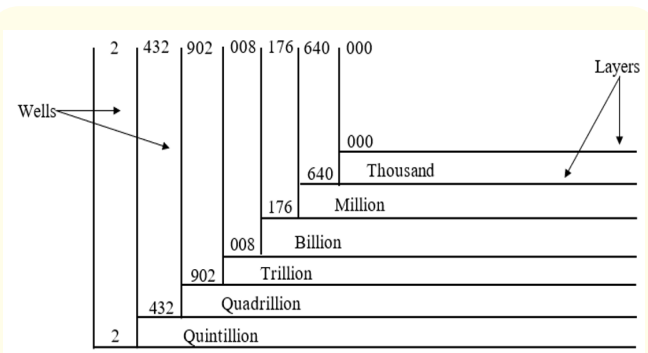

Figure 1: Count Gravimentizer in Action in Metric Number System.

Two quintillion, four hundred and thirty-two quadrillion, nine hundred and two trillion, eight billion, one hundred and seventy-six million, six hundred and forty thousand protein types or sequences.

The same figure in imperial number system (in powers of 1000000) using the count gravimetizer depicted in figure 2.

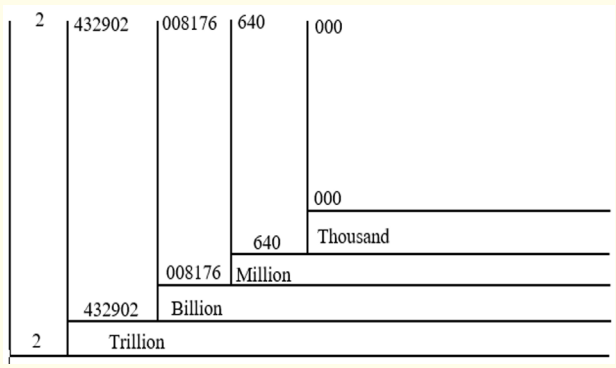

Figure 2: Count Gravimentizer in Action, In Imperial Number system.

Two trillion, four hundred and thirty-two thousand, nine hundred and two billion, eight thousand one hundred and seventy-six million, six hundred and forty thousand protein types or sequences. Note the denominational names are the same in the metric and imperial systems, but they differ in value beyond million, because the higher denominations in the imperial system are in powers of million, while those of metric are in powers of thousand (Table 3).

S/N	Factorial	Orientation	Multiplication Tower	Permutation Tower/Type	Meaning of figure Read-off value	
1	$_{20}P_{20} = 20!$		(a) (b) 20 20 X 19 380 X 18 6840 X 17 116280 X 16 18604880 X 15 27907200 X 14 390700800 X 13 5079110400 X 12 60949324800 X 11 670442572800 X 10 6704425728000 X 9 60339831552000 X 8 482718652416000 X 7 3379030566912000 X 6 20274183401472000 X 5 101370917007360000 X 4 405483668029440000 X 3 1216451004088320000 X 2 2432902008176640000 X 1 2432902008176640000	b	$_{N}P_{R}$ $_{20}P_{1}$ $_{20}P_{2}$ $_{20}P_{3}$ $_{20}P_{4}$ $_{20}P_{5}$ $_{20}P_{6}$ $_{20}P_{7}$ $_{20}P_{8}$ $_{20}P_{9}$ $_{20}P_{10}$ $_{20}P_{11}$ $_{20}P_{12}$ $_{20}P_{13}$ $_{20}P_{14}$ $_{20}P_{15}$ $_{20}P_{16}$ $_{20}P_{17}$ $_{20}P_{18}$ $_{20}P_{19}$ $_{20}P_{20}$	 20 words of 1 amino acid each 380 " " 2 " acids " 6840 " " 3 " " " 116280 " " 4 " " " 1860480 " " 5 " " " 27907200 " " 6 " " " 390700800 " " 7 " " " 5079110400 " " 8 " " " 60949324800 " " 9 " " " 670442572800 " " 10 " " " 6704425728000 " " 11 " " " 60339831552000 " " 12 " " " 482718652416000 " " 13 " " " 3379030566912000 " " 14 " " " 20274183401472000 " " 15 " " " 101370917007360000 " " 16 " " " 405483668029440000 " " 17 " " " 1216451004088320000 " " 18 " " " 2432902008176640000 " " 19 " " " 2432902008176640000 " " 20 " " "
2	$_{20}P_{20} = 20!$	Gravimetric (G)	(A) (B) 1 1 X 2 2 X 3 6 X 4 24 X 5 120 X 6 720 X 7 5040 X 8 40320 X 9 362880 X 10 3628800 X 11 39916800 X 12 479001600 X 13 6227020800 X 14 87178291200 X 15 1307674368000 X 16 20922789888000 X 17 3556874280960000 X 18 6402373705728000 X 19 121645100408832000 X 20 2432902008176640000	b	$_{n}P_{n}$ $_{1}P_{1}$ $_{2}P_{2}$ $_{3}P_{3}$ $_{4}P_{4}$ $_{5}P_{5}$ $_{6}P_{6}$ $_{7}P_{7}$ $_{8}P_{8}$ $_{9}P_{9}$ $_{10}P_{10}$ $_{11}P_{11}$ $_{12}P_{12}$ $_{13}P_{13}$ $_{14}P_{14}$ $_{15}P_{15}$ $_{16}P_{16}$ $_{17}P_{17}$ $_{18}P_{18}$ $_{19}P_{19}$ $_{20}P_{20}$	 1 words of 1 amino acid each 2 " " 2 " acids " 6 " " 3 " " " 24 " " 4 " " " 120 " " 5 " " " 720 " " 6 " " " 5040 " " 7 " " " 40320 " " 8 " " " 362880 " " 9 " " " 362880 " " 10 " " " 39916800 " " 11 " " " 479001600 " " 12 " " " 6227020800 " " 13 " " " 87178291200 " " 14 " " " 13076743680000 " " 15 " " " 20922789888000 " " 16 " " " 355687428096000 " " 17 " " " 6402373705728000 " " 18 " " " 121645100408832000 " " 19 " " " 2432902008176640000 " " 20 " " "

S/N	Factorial	Orientation	Multiplication Tower	Permutation Tower/Type	Meaning of Figure Read-off Values
3	$_4P_4 = 4!$	Gravimetric (G)	(A) (B) 1 1 X2 2 X3 6 X4 24	B	$_nP_n$ $_1P_1$ 1 word of 1 base each $_2P_2$ 2 words " 2 bases each $_3P_3$ 6 " " 3 " " $_4P_4$ 24 " " 4 " "
4	$_4P_4 = 4!$	Antigravmetric (AG)	(A) (B) 4 4 X3 12 X2 24 X1 24	b	$_nP_r$ $_4P_1$ 4 word of 1 base each $_4P_2$ 12 " " 2 " " $_4P_3$ 24 " " 3 " " $_4P_4$ 24 " " 4 " "

Table 3: Indications of the Figures of the permutation tower, viz. Read-off application

A square of convenient size is drawn freehand in accordance with the input set. The columns are numbered 1 to 20 from left to right, while the rows are also numbered 1 to 20 from bottom to top as shown in Figure 3.

The input set of 20 amino acids is assigned 1 to 20 serially as indicated in the key to figure 3. The input sequence is in the serial order of 1 to 20 as carried in row 1.

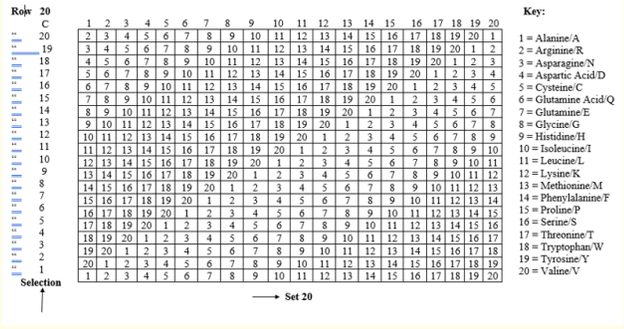

Figure 3: Square Mixerhead, PSI loaded with input set 20 selection 20 of 20 amino acids (1) – (20).
Construction of the square mixerhead for input set 20.

Place-skipped input (PSI) filling of the square mixer head. The square mixer head is loaded in rows from bottom to top. The loading starts at row 1 with item No. 1 and proceeds sequentially towards the right to end at column 20 with item No. 20.

At row 2, column 1 is skipped in compliance with the place skipping loading scheme so that loading starts at row 2 column 2 with item no. 1 and is taken to column 20 which carries item no. 19 and concluded with column 1 item no. 20. The loading is carried on similarly until the top row is done to give the fully loaded mixer head depicted in Figure 3. The mixer head is unloaded in columns from left to right in two views, one up, the other down, to furnish the output material in Chart 1, resulting from amino acid auto kinematic repositioning simulation.

Column 1, view up	1,20,19,18,17,16,15,14,13,12,11,10,9,8,7,6,5,4,3,2, (P1)
Column 1, view down	2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,1 (P2)
…	… …
Col. 20 View up	20,19,18,17,16,15,14,13,12,11,10,9,8,7,6,5,4,3,2,1 P39
" View down	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20 P40

Chart 1: Output of protein types (sequences).

As the foregoing simulation is only to illustrate the auto-kinematic sans labour process of deriving protein types (sequences) by amino acids, it is needless continuing with the pullulation exercise beyond this point of 40 protein types, P40 as conveyed in Chart 1

Derivation of the genetic code from the four RNA bases A,U,G,C by square kinematics for the labour intensive generation of protein types (sequences) is as follows.

Description

Using the set of four RNA bases A,U,G,C as dissimilar objects, a square of convenient size is drawn freehand and the letters (bases)

A,U,G,C are placed at the four corners as depicted in figure 4 in clockwise direction for sequence.

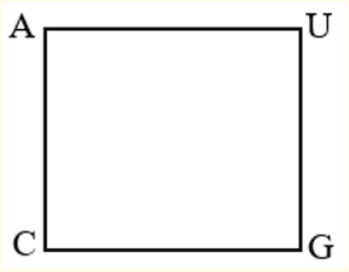

Figure 4: Square A,U,G,C.

Three deployments of square AUGC are designated and depicted as in figure 5.

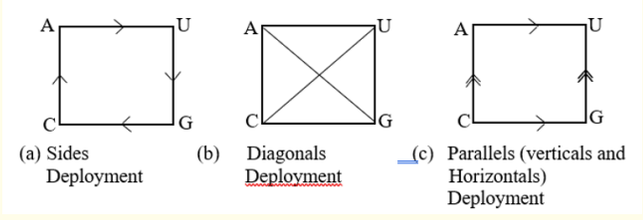

Figure 5

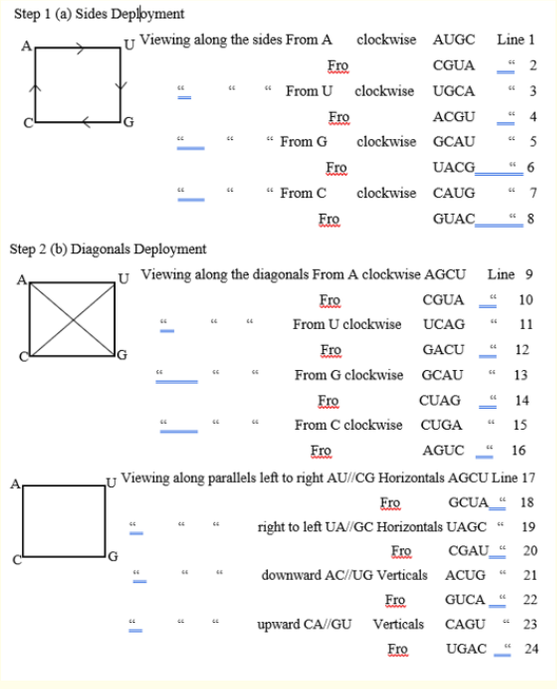

Chart 2: Computation of Genetic Code of 24-quadruplet Codons.

Summary of Valid Codons (Codewords)

Lines 1 – 24 = 24 quadruplets

Factorial ${}_4P_4$ = 4 x 3 x 2 x 1 = 24 quadruplets

Hence Production = Prediction = 24 quadruplets

Results

The results are two: one of the number of protein types (a) that can be synthesized from the 20 amino acids constituting a protein where no labour other than self-repositioning of amino acids is involved; and the other the number of principal "workmen" in the form of codewords (b) that can be raised from the four RNA bases A,U,G,U with a bearing upon the 20 amino acids of protein to execute the protein building project better known as the genetic code. Whence (a) Number of protein types from 20P20 = 20! = 20 x 19 x 18…x 3 x 2 x 1 = 2,432,902,008,176, 640,000 ref. Table 2.

b) 24 quadruplet codewords of the true genetic code from 4P4 = 4! = 4 x 3 x 2 x 1 = 24.

S/N	Codons	Amino acids 20/signals 4
1	AUGC	Allocation yet to be determined
2	CGUA	"
3	UGCA	"
4	ACGU	"
5	UAGC	"
6	UACG	"
7	CAUG	"
8	GUAC	"
9	AGUC	"
10	UCAG	"
11	CUGA	"
12	GACU	"
13	UCGA	"
14	GAUC	"
15	CUGA	"
16	AGUC	"
17	AUCG	"
18	GCUA	"
19	UAGC	"
20	CGAU	"
21	ACUG	"
22	GUCA	"
23	CAGU	"
24	UGAC	"

Table 4: 24 Quadruplet Genetic Code ref Chart 2.

Discussion

The title of this paper is sourced from the Molecular biologists' observation in 1953 that the sequence of the DNA four bases Adenine, Thymine, Guamine, Cytosine (A, T, G, C) in the nucleus of the cell influences the sequence of the 20 amino acids of protein in the cellular cytoplasm. This entails prevalence of variation of DNA base-sequence with attendant protein type diversification due to change of sequence of constituent amino acids. In other words, the DNA four bases undergo permutation to effect protein type diversification and simultaneous proliferation to the achievement of protein synthesis. Whence protein type proliferation and diversification is a goal of protein synthesis. So protein synthesis strategy is equally mined from the same 1953 Molecular Biologists' observation of correlation between sequence of DNA four bases and sequence of 20 Amino Acids of protein.

Protein Synthesis

The 20 named amino acids of protein can stand in any sequence to make sense in the formation of a protein type, just like the 10 named digits of number can stand in any sequence to make sense in the formation of a number. That is to say the 20 amino acids of protein have unrestricted compatibility in linear formation geared to protein type composition which is a basic necessity of protein synthesis. This understood, the crucial issue of protein synthesis is protein type proliferation and diversification to meet the enormous need of protein supply to plants and animals. So Nature has resorted to combinatorial input/output multiplicative replication system using the four nucleotide bases as input set instead of the 20 amino acids of protein to produce a genetic code output of 24-quadruplet codons as workforce in the proliferation and diversification of protein types with moderation and adequacy.

Ordinarily the option would be to resort to the combinatorial input/output multiplicative replication system, whereby the 20 amino acids of a protein type could be used as input set amounting to permutation of 20 from 20 i.e. factorial 20 = 20! = 20 x 19 x 18…3 x 2 x 1 = 2,432,902,008,176, 640,000 protein types. This suggests auto-kinematic process of protein synthesis or formation, where the 20 constituent amino acids of protein through systematic linear self-repositioning produce protein types to the tune of 2,432,902,008,176, 640,000 as factorial complement for $_{20}P_{20}$ = 20! involving no work. This is sans labour and alien to creation and therefore deemed not a tenable option in productivity, and so stands rejected. The genetic code means of protein synthesis or formation, whereby the four RNA bases A,U,G,C positionally related to the 20 amino acids of protein, undergo permutation to yield 24 quadruplet codons as factorial complement of $_4P_4$ = 4! = 4 x 3 x 2 x 1 to be the labour force for building various protein types is in harmony with creation in terms of productivity and it is therefore deemed to be the option to work in NATURE. Moreover, it is viewed that God the Almighty Creator in His infinite wisdom, considering the astronomical figure resulting from 20P20 for auto-kinematic process, unwieldy and cumbersome for man (albeit scientists) to cope with in His divine primordial endowment of man to subdue and take dominion of creation, decided to simplify and streamline protein synthesis or formation by the provision of four DNA bases A,T,G,C (Adenine, Thymine, Guanine, Cytosine) stepped down to RNA four bases of A,U,G,C, all in the nucleus of a cell to control the placement of 20 amino acids that make up protein type in the cytoplasm of the cell. In practice only the four nucleotide bases of DNA (and RNA) undergo permutation in accordance with the factorial formula of $_4P_4$ = 4! = 4 x 3 x 2 x 1 to yield 24 quadruplet permutation codons (genetic code) which outcome is manageable in size and number to save man much rigor. So in protein synthesis, 20 of these 24 quadruplet codons are duty-bound to bring individually associated 20 amino acids for placement at one specific amino acid per particular codon, in a sequence towards the formation of a protein type. The four spare codons serve as four place and time based start/stop signals in the regulation of labour intensive protein synthesis. Moreover, all 24 quadruplet codons are unique (in sequence) being permutations of 4 from 4, as shown in Chart 2 and Table 4.

Why the genetic code option?

The role of genetic code in protein synthesis may be likened to canals in curtailing voyaging around continents. Just as canals such as Panama Canal and Suez Canal cut short voyaging around South America and Africa respectively, so does the genetic code, the true natural one of 24 quadruplet codons, shorten and simplify immensely protein synthesis in favour of man's dealing with it, instead of 2,432,902,008,176,640,000 protein types based on the 20 amino acids of protein for proliferation and diversification by permutation. Moreover, the collinearity the 24 quadruplet genetic code enjoys with the 20 amino acids of protein on one to one correspondence ensures the comprehensive and exhaustive individual engagement of the 20 unique amino acids of protein by 20 of its own 24 unique quadruplet codons with four spare codons for four time and place based start/stop control signals during protein synthesis.

Absenteeism and Underutilization of Bases Per Codon

Absenteeism and underutilization of bases per codon manifest in the 64 triplet genetic code version cannot be a characteristic of the true genetic code structure and constitution. If it were so, there would have been evidence of automation for its operational suste-

nance. Such an arrangement definitely would involve signals several times the codon population of 64 and be a serious complication in discord with the simplification agenda for the genetic code intervention in protein synthesis. So the absenteeism and underutilization only reflect human error in the derivation of the code and therefore mean a high ranking impossibility of the natural code. The 64 triplet degenerate code characterized by numerous irregularities reflecting human errors of derivation, even though fully spelt and adopted since 1968 is out of harmony with the divine agenda of simplification of protein synthesis and it is therefore ruled out as a version of the genetic code option. Besides, it undermines the inerrancy of NATURE by reason of its glaring inaccuracies, whereas the 24-quadruplet genetic code structure upholds the inerrancy of Nature, supported by collinearity between its 24-quadruplet codons and the 20 amino acids of protein with four spare codons for four place/time based start/stop control signals during protein synthesis [1-8].

Conclusion and Significance

The genetic code engagement in protein synthesis is in a setting of substitution of 4 DNA bases for 20 amino acids of protein for permutation towards achievement of moderation and adequacy of protein type proliferation and diversification via the avenue of collinearity between the 24-quadruplet version of genetic code and 20 amino acids of protein on one to one correspondence with four spare quadruplets for four time and place based start/stop control signals during protein synthesis. Thus the transcontinental highway of protein type proliferation and diversification is profitably and successfully avoided by the engagement of the genetic code identified as the district highway to protein synthesis' goal of protein type proliferation and diversification as afforded by permutation of 4 from 4 of DNA four bases.

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