Vector Space of the Extended Base-triplets over the Galois Field of five DNA Bases Alphabet

Robersy Sánchez and Ricardo Grau

Abstract—A plausible architecture of an ancient genetic code is derived from an extended base triplet vector space over the Galois field of the extended base alphabet \{D, G, A, U, C\}, where the letter D represents one or more hypothetical bases with unspecific pairing. We hypothesized that the high degeneration of a primeval genetic code with five bases and the gradual origin and improvements of a primitive DNA repair system could make possible the transition from the ancient to the modern genetic code. Our results suggest that the Watson-Crick base pairing and the non-specific base pairing of the hypothetical ancestral base D used to define the sum and product operations are enough features to determine the coding constraints of the primeval and the modern genetic code, as well as the transition from the former to the later. Geometrical and algebraic properties of this vector space reveal that the present codon assignment of the standard genetic code could be induced from a primeval codon assignment. Besides, the Fourier spectrum of the extended DNA genome sequences derived from the multiple sequence alignment allows derive substitution mutations as lineal transformations of the primeval genetic code. We suppose that there was a primeval genetic code then there are not biological reasons to restrict the base alphabet of the primeval RNA and DNA to the present DNA bases. Likewise, there are not biological reasons to restrict the number of codons which code to amino acids. Actually, the environment conditions of the primeval environment could make possible the relative abundance of different bases and their isomers [1]. This richness of bases should increase the success probability of life. The Watson-Crick base pairs G = C and A = U (where each ‘=’ symbolizes a hydrogen bond) characterize the present DNA molecule. The accessibility to five or more bases in the “primeval soup” make plausible the non-Watson-Crick base pairing in a primitive RNA world and later in a primeval DNA molecule.

Piccirilli et al. [2] demonstrated that the alphabet can in principle be larger. C. Switzer et al. [3] have shown an enzymatic incorporation of new functionalized bases into RNA and DNA. This expanded the genetic alphabet from 4 to 6 letters, permits new base pairs, and provides RNA molecules with the potential for greatly increased catalytic power. Actually, a number of alternative base pairs have been proposed. These include isoguanine and isocytosine [2]-[4], diaminopurine and U [2], pseudodiaminopyrimidines (ribose bound to C5 rather than N1) and xanthine [2], A and urazole (1,2,4-triazole-3,5-dione) [5]. According to Levy and Miller, however, to get greater stability it may be necessary to use bases other than these pyrimidines [6].

The existence of uncommon bases in the present RNA and DNA molecules could be the relic genetic fingerprint of a molecular evolution process from primordial cells with an extended DNA base alphabet. At present, minor bases of DNA, 5-Methylcytidine occurs in the DNA of animals and higher plants, N-6-methyladenosine in bacterial DNA, and 5-hydroxymethylcytidine in the DNA of bacteria infected with certain bacteriophages. Ribosomal RNAs characteristically contain a number of specially modified nucleotides, including pseudouridine residues, ribothymidylic acid, and methylated bases. The abundance of bases with non-specific pairing in a primeval DNA molecule could increase the degeneration of coding apparatus and diminished the error frequency during transcription and translation process [2].

On other hand, different algebraic structures of the genetic code have been recently published [7]-[9]. The natural extension of these algebraic structures to gene sequences allows derive substitution mutations as lineal transformations and translations in the N-dimensional DNA sequence vector space (or N-dimensional modulo). In these structures, however, deletion and insertion mutations (indels) can not be analyzed. Now, in order to include these kinds of mutations, we have defined a new Galois field \(GF(5)\) over the set of extended DNA alphabet \(X \in \{D, A, C, G, U\}\), where the letter D can symbolize a deletion or can be considered as a hypothetical base with non-specific pairing present in a
primeval RNA and DNA molecules.

The extended DNA alphabet naturally leads us to an extended set of base-triplets \( X_1X_2X_3 \), i.e. an “extended genetic code”, where \( X_i \in \{ D, A, C, G, U \} \). At this point a new base-triplet vector space over \( GF(5) \) can be derived in analogous way to the genetic code vector space over \( GF(4) \) as appears in [8] and [9]. The extension of this vector space to the DNA sequences should lead, however, to new biological-algebraic insights. The extended DNA sequences appear, normally, during the multiple sequence analysis of genes or genomic sequences. The aligned DNA sequences with gaps resulting of the alignment procedure could be analyzed, integrally, as element of the new vector space.

Here, we shall show that the standard genetic code architecture could be derived from an ancient coding apparatus with an extended alphabet of five bases.

II. THEORETICAL MODEL

A Galois field \( GF(5) \) is defined on the ordered set \( B = \{ D, G, A, U, C \} \). Next, the order in the extended base-triplet is induced by the order in the base set and the vector space of the extended base-triplet set over the Galois field \( GF(5) \) will be defined.

A. The extended base-triplet vector space over the Galois field \( GF(5) \)

If a Galois field algebraic structure is defined on the extended base alphabet subject to the constraint \( A + U = U + A = D \) and \( A \cdot U = U \cdot A = G \) then the sum and product operations can be defined on the sets \( \{ D, G, A, U, C \} \) and \( \{ D, G, A, U, C \} \). That is, it is required that bases \( A \) and \( U \) will be inverses in the sum and product operations with the base \( G \) as neutral element for product. So, these definitions reflect the Watson-Crick base pairs \( UA \) and \( CG \) neutral element for product. So, these definitions reflect the Watson-Crick base pairs \( UA \) and \( CG \) as appears in Table I. By construction, the field defined in the extended triplet set \( \{X,Y,Z\} \) suggest the highly degenerated nature of a primeval coding apparatus. Let \( D \neq \{G, A, U, C\} \) represent the base (or bases) with non-specific pairing with at least two bases of the set \( \{ G, A, U, C \} \) in the DNA molecule. The non-specific pairing of base \( D \) is reflected in the model making it the neutral element of \( (B, +) \).

In the vector space of the extended triplets, the subset with non-specific pairing \( S_{XZ} = \{ XZ \} \) conform a two-dimensional vector subspace, which is contained in the \( XZ \) plane. Likewise, in the coordinated planes \( XY \) and \( YZ \) are contained the bidimensional vector subspaces corresponding to subset with non-specific pairing \( S_{YX} = \{ YX \} \) and \( S_{DZ} = \{ DZ \} \), respectively (see Fig. 1). In particular, the quotient space \( B^3/S_{XZ} \) has the elements:

\[
\{ S_{XZ}, S_{DZ} + X_G, S_{DZ} + X_A, S_{DZ} + X_U, S_{DZ} + X_C \}
\]

Where \( X_G, X_A, X_U \) and \( X_C \) are arbitrary elements of the extended triplet subsets: \{\( XGY \)\}, \{\( XAY \)\}, \{\( XUY \)\} and \{\( XCY \)\} respectively. For instance, codons that belong to the subset \{\( XUY \)\} may be represented by some of the sums.
The horizontal plane subspace SXDZ class has the same number of elements extended triplets into 5 equivalence classes or cosets. Every non-specific pairing subspace and can be obtained from the extended triplets with amino acids with similar properties belong to the same affine subsets triplets, which correspond to the 5 main columns of Table II.

Subsets triplets, which correspond to the 5 main columns of Table II. It can be noticed that, in most of the cases, codons that belong to its vertical line. This conjecture is based on the non-specific pairing of base D in the third codon position. The first two letters of each codon are the primary determinants of specificity, a feature that has some interesting consequences. Analogue situation can be found in nature. The anticodons in some tRNAs include the nucleotide inosinate, which contains the uncommon base hypoxanthine. Inosinate can form hydrogen bonds with three different nucleotides U, G and A, respectively, forming the three base pairs AU, GA and UA, which are akin to the Watson-Crick base pairs. Inosinate can also form a base pair with C, but this is less stable than the AU and GA pairs. The first inosinate triplets that code for the same or similar amino acid belong to the same vertical line. For instance, AUG + SDDZ = {AUD, AUG, AUA, AUU, AUC} and CAG + SDDZ = {CAD, CAG, CAA, CAU, CAC}.

The subset SDDZ = {DDZ} conforms a one-dimensional vector subspace, one of the cube edges, which is inserted in the coordinated Z-axis. So, the SDDZ is a vectorial line, which is generated by the any extended triplets DDZ with Z \neq D. While the quotient vector space B^1/SDDZ of the vector space B^1 is conformed by extended triplet subsets that have fixed the first and the second nucleotides. As can be noticed in Fig. 1, cosets of SDDZ are vertical lines of the cube, which are orthogonal to the plane of YZD extended triplets, i.e. the face inserted in the coordinated plane XY. As a result, there are 25 equivalent classes, having every class 5 extended triplets with non-specific pairing XDY by means of simple translations. So, if the mutation process is described by means of simple translations, the geometrical-geometric features of extended triplet set suggest the transition during the molecular evolution process from a high degenerated primeval code to the present code. The extended triplet of every vertical plane should code, in general, to amino acid with similar physicochemical properties. In particular, the extended triplets with non-specific pairing DXD (X_1 \neq D) should code to any amino acid coded by triplets XYZ (X \neq D, Y = X_2, Z = X_3). The subset extended triplet \{XDY\} (X, Z \in B^1) should not to code to any amino acid.

The quotient space B^1/SDDZ is a partition of the set of extended triplets into 5 equivalence classes or cosets. Every class has the same number of elements SDDZ, i.e. 25 extended triplets, which correspond to the 5 main columns of Table II. Subsets SDDZ + X_G = \{XGZ\}, SDDZ + X_A = \{XAZ\}, SDDZ + X_U = \{XUZ\} and SDDZ + X_C = \{XCZ\} are cosets of the vector subspace SDDZ and, consequently, they are affine subspaces of the vector space B^1, i.e. they are vertical planes with respect to the horizontal plane XY. As a result, there are 25 equivalent classes, having every class 5 extended triplets with non-specific pairing XDY by means of simple translations. So, if the mutation process is described by means of simple translations, the geometrical-geometric features of extended triplet set suggest the transition during the molecular evolution process from a high degenerated primeval code to the present code. The extended triplet of every vertical plane should code, in general, to amino acid with similar physicochemical properties. In particular, the extended triplets with non-specific pairing DXD (X_1 \neq D) should code to any amino acid coded by triplets XYZ (X \neq D, Y = X_2, Z = X_3). The subset extended triplet \{XDY\} (X, Z \in B^1) should not to code to any amino acid.

The quotient space B^1/SDDZ is a partition of the set of extended triplets into 5 equivalence classes or cosets. Every class has the same number of elements SDDZ, i.e. 25 extended triplets, which correspond to the 5 main columns of Table II. Subsets SDDZ + X_G = \{XGZ\}, SDDZ + X_A = \{XAZ\}, SDDZ + X_U = \{XUZ\} and SDDZ + X_C = \{XCZ\} are cosets of the vector subspace SDDZ and, consequently, they are affine subspaces of the vector space B^1, i.e. they are vertical planes with respect to the horizontal plane XY. As a result, there are 25 equivalent classes, having every class 5 extended triplets with non-specific pairing XDY by means of simple translations. So, if the mutation process is described by means of simple translations, the geometrical-geometric features of extended triplet set suggest the transition during the molecular evolution process from a high degenerated primeval code to the present code. The extended triplet of every vertical plane should code, in general, to amino acid with similar physicochemical properties. In particular, the extended triplets with non-specific pairing DXD (X_1 \neq D) should code to any amino acid coded by triplets XYZ (X \neq D, Y = X_2, Z = X_3). The subset extended triplet \{XDY\} (X, Z \in B^1) should not to code to any amino acid.

The quotient space B^1/SDDZ is a partition of the set of extended triplets into 5 equivalence classes or cosets. Every class has the same number of elements SDDZ, i.e. 25 extended triplets, which correspond to the 5 main columns of Table II. Subsets SDDZ + X_G = \{XGZ\}, SDDZ + X_A = \{XAZ\}, SDDZ + X_U = \{XUZ\} and SDDZ + X_C = \{XCZ\} are cosets of the vector subspace SDDZ and, consequently, they are affine subspaces of the vector space B^1, i.e. they are vertical planes with respect to the horizontal plane XY. As a result, there are 25 equivalent classes, having every class 5 extended triplets with non-specific pairing XDY by means of simple translations. So, if the mutation process is described by means of simple translations, the geometrical-geometric features of extended triplet set suggest the transition during the molecular evolution process from a high degenerated primeval code to the present code. The extended triplet of every vertical plane should code, in general, to amino acid with similar physicochemical properties. In particular, the extended triplets with non-specific pairing DXD (X_1 \neq D) should code to any amino acid coded by triplets XYZ (X \neq D, Y = X_2, Z = X_3). The subset extended triplet \{XDY\} (X, Z \in B^1) should not to code to any amino acid.

The quotient space B^1/SDDZ is a partition of the set of extended triplets into 5 equivalence classes or cosets. Every class has the same number of elements SDDZ, i.e. 25 extended triplets, which correspond to the 5 main columns of Table II. Subsets SDDZ + X_G = \{XGZ\}, SDDZ + X_A = \{XAZ\}, SDDZ + X_U = \{XUZ\} and SDDZ + X_C = \{XCZ\} are cosets of the vector subspace SDDZ and, consequently, they are affine subspaces of the vector space B^1, i.e. they are vertical planes with respect to the horizontal plane XY. As a result, there are 25 equivalent classes, having every class 5 extended triplets with non-specific pairing XDY by means of simple translations. So, if the mutation process is described by means of simple translations, the geometrical-geometric features of extended triplet set suggest the transition during the molecular evolution process from a high degenerated primeval code to the present code. The extended triplet of every vertical plane should code, in general, to amino acid with similar physicochemical properties. In particular, the extended triplets with non-specific pairing DXD (X_1 \neq D) should code to any amino acid coded by triplets XYZ (X \neq D, Y = X_2, Z = X_3). The subset extended triplet \{XDY\} (X, Z \in B^1) should not to code to any amino acid.

The quotient space B^1/SDDZ is a partition of the set of extended triplets into 5 equivalence classes or cosets. Every class has the same number of elements SDDZ, i.e. 25 extended triplets, which correspond to the 5 main columns of Table II. Subsets SDDZ + X_G = \{XGZ\}, SDDZ + X_A = \{XAZ\}, SDDZ + X_U = \{XUZ\} and SDDZ + X_C = \{XCZ\} are cosets of the vector subspace SDDZ and, consequently, they are affine subspaces of the vector space B^1, i.e. they are vertical planes with respect to the horizontal plane XY. As a result, there are 25 equivalent classes, having every class 5 extended triplets with non-specific pairing XDY by means of simple translations. So, if the mutation process is described by means of simple translations, the geometrical-geometric features of extended triplet set suggest the transition during the molecular evolution process from a high degenerated primeval code to the present code. The extended triplet of every vertical plane should code, in general, to amino acid with similar physicochemical properties. In particular, the extended triplets with non-specific pairing DXD (X_1 \neq D) should code to any amino acid coded by triplets XYZ (X \neq D, Y = X_2, Z = X_3). The subset extended triplet \{XDY\} (X, Z \in B^1) should not to code to any amino acid.
The primeval life environment could favor the relative abundance of bases different from G, A, U and C. A gradual origin of a primordial coding apparatus without a loss risk of the ancient “genetic information” could be possible by way of the non-specific pairing of these bases.

The present architecture of the standard genetic code is not in disagreement with the plausible architecture of an ancient genetic code like to those proposed in Table II and in Fig. 1. The gradual origin and improvements of a primitive DNA repair system could make possible the transition from the ancient to the modern genetic code.

B. Algebraic partitions of the extended triplet set and architecture of the modern genetic codes

Likewise to the three-dimensional vector space over $\mathbb{P}^3$, the elements $X, Y \in B^3$ are called collinear if $Y_1Y_2Y_3 = \lambda X_1X_2X_3$, where $\lambda \neq D$. The set of all extended triplets can be sorted into 31 subsets of collinear elements (see Table III). The subsets of collinear extended triplet have the general form $S_{CC} = \{X_1X_2X_3, X_{1'A}X_{2'A}X_{3'A}, X_{1'B}X_{2'B}X_{3'B}\}$, where $X_{1'A} = \lambda X_1$, $\lambda \in \mathbb{E}D$ and $X_{1'B} = \lambda X_1$. In particular, the subsets of collinear codons have the general form $S_{CC} = \{X_1GX_3, X_{1'A}X_{2'A}X_{3'A}, X_{1'B}X_{2'B}X_{3'B}\}$, where $X_{1'A} = \lambda X_1$ and $\lambda \in \mathbb{E}D$. That is, the principal partitions of the standard genetic code $\{\{X_1GX_3\}, \{X_1AX_3\}, \{X_1CX_3\}\}$ are represented in every collinear codon subset. In other words: $X_1GX_3 \in \{X_1GX_3\}, X_{1'A}X_{2'A}X_{3'A} \in \{X_1AX_3\}$, $X_{1'B}X_{2'B}X_{3'B} \in \{X_1CX_3\}$. Moreover, the sum operation defined in Table I induces symmetry in every collinear subset (see Table III),

$$X_1GX_3 + X_{1'C}X_{2'C}X_{3'C} = \text{DDD}$$

$$X_{1'A}X_{2'A}X_{3'A} + X_{1'B}X_{2'B}X_{3'B} = \text{DDD}$$

If $X_1X_2X_3 + Y_1Y_2Y_3 = \text{DDD}$, we shall say that the extended triplet $X_1X_2X_3$ and $Y_1Y_2Y_3$ are symmetrical. Likewise, in the $N$-dimensional vector space $(\mathbb{P}^3)^N$ of DNA aligned sequences with length $N$, we shall say that two DNA sequences $\alpha, \beta \in (\mathbb{P}^3)^N$ are symmetrical if $\alpha + \beta = \{\text{DDD}, \text{DDD}, \ldots, \text{DDD}\} \in (\mathbb{P}^3)^N$.

The set of collinear extended triplet subsets can be sorted into two subsets with specific and non-specific pairing, respectively (see Table III). The subset with specific pairing encloses all codons and every collinear subset contains a codon from a different affine subspace. Next, if we define the product operation between extended triplet as the product coordinated by coordinated then the subset of all codons $S_C = \{XYZ | X, Y, Z \in \{G, A, U, C\}\}$, is closed to product operation, i.e. $(S_C, \cdot)$ is a multiplicative group; while the collinear subset $S_{XXX} = \{\text{GGG}, \text{AAA}, \text{UUU}, \text{CCC}\}$ determine the subgroup $(S_{XXX}, \cdot) \subset (S_C, \cdot)$. The quotient subgroup $S_C/S_{XXX}$ split the codon subset $S_C$ into the subset of collinear codons presented in Table III. That is, every collinear subset $\{XYZ\} \in S_C$ can be represented as

$$\{XYZ\} = \{\text{DDD}, \text{DDD}, \ldots, \text{DDD}\} \in (\mathbb{P}^3)^N$$

In the first case codons code to similar amino acid, which belong to the same column in Table II, and, in the second case, each codon belong to a different column of this table.

Fig. 1 Cubic representation of the extended genetic code

There are 61 different encoding codons. Organisms do not have, however, the 61 tRNA species with all possible anticodons. In 1966, Crick proposed the famous “wobble hypothesis”: through non-Watson-Crick base-pairing rules, less tRNA species are needed [10]. Based on observations of characterized yeast tRNAs and modified base-pairing rules, Guthrie and Abelson updated and revised the wobble hypothesis and predicted that 46 different tRNA species would be found in yeast, and perhaps in all eukaryotes [11]. Now, it is known most Eukaryotic cells with sequenced genome follow the revised wobble hypothesis almost perfectly [12]. In vertebrate mitochondria, however, an unusual set of wobble rules allows the 22 tRNAs to decode all 64 possible codons.

B. Algebraic partitions of the extended triplet set and architecture of the modern genetic codes

Likewise to the three-dimensional vector space over $\mathbb{P}^3$, the elements $X, Y \in B^3$ are called collinear if $Y_1Y_2Y_3 = \lambda X_1X_2X_3$, where $\lambda \neq D$. The set of all extended triplets can be sorted into 31 subsets of collinear elements (see Table III). The subsets of collinear extended triplet have the general form $S_{CC} = \{X_1X_2X_3, X_{1'A}X_{2'A}X_{3'A}, X_{1'B}X_{2'B}X_{3'B}\}$, where $X_{1'A} = \lambda X_1$, $\lambda \in \mathbb{E}D$ and $X_{1'B} = \lambda X_1$. In particular, the subsets of collinear codons have the general form $S_{CC} = \{X_1GX_3, X_{1'A}X_{2'A}X_{3'A}, X_{1'B}X_{2'B}X_{3'B}\}$, where $X_{1'A} = \lambda X_1$ and $\lambda \in \mathbb{E}D$. That is, the principal partitions of the standard genetic code $\{\{X_1GX_3\}, \{X_1AX_3\}, \{X_1CX_3\}\}$ are represented in every collinear codon subset. In other words: $X_1GX_3 \in \{X_1GX_3\}, X_{1'A}X_{2'A}X_{3'A} \in \{X_1AX_3\}$, $X_{1'B}X_{2'B}X_{3'B} \in \{X_1CX_3\}$. Moreover, the sum operation defined in Table I induces symmetry in every collinear subset (see Table III),

$$X_1GX_3 + X_{1'C}X_{2'C}X_{3'C} = \text{DDD}$$

$$X_{1'A}X_{2'A}X_{3'A} + X_{1'B}X_{2'B}X_{3'B} = \text{DDD}$$

If $X_1X_2X_3 + Y_1Y_2Y_3 = \text{DDD}$, we shall say that the extended triplet $X_1X_2X_3$ and $Y_1Y_2Y_3$ are symmetrical. Likewise, in the $N$-dimensional vector space $(\mathbb{P}^3)^N$ of DNA aligned sequences with length $N$, we shall say that two DNA sequences $\alpha, \beta \in (\mathbb{P}^3)^N$ are symmetrical if $\alpha + \beta = \{\text{DDD}, \text{DDD}, \ldots, \text{DDD}\} \in (\mathbb{P}^3)^N$.

The set of collinear extended triplet subsets can be sorted into two subsets with specific and non-specific pairing, respectively (see Table III). The subset with specific pairing encloses all codons and every collinear subset contains a codon from a different affine subspace. Next, if we define the product operation between extended triplet as the product coordinated by coordinated then the subset of all codons $S_C = \{XYZ | X, Y, Z \in \{G, A, U, C\}\}$, is closed to product operation, i.e. $(S_C, \cdot)$ is a multiplicative group; while the collinear subset $S_{XXX} = \{\text{GGG}, \text{AAA}, \text{UUU}, \text{CCC}\}$ determine the subgroup $(S_{XXX}, \cdot) \subset (S_C, \cdot)$. The quotient subgroup $S_C/S_{XXX}$ split the codon subset $S_C$ into the subset of collinear codons presented in Table III. That is, every collinear subset $\{XYZ\} \in S_C$ can be represented as

$$\{XYZ\} = \{\text{DDD}, \text{DDD}, \ldots, \text{DDD}\} \in (\mathbb{P}^3)^N$$

In the first case codons code to similar amino acid, which belong to the same column in Table II, and, in the second case, each codon belong to a different column of this table.
TABLE III

<table>
<thead>
<tr>
<th>Specific pairing (codons)</th>
<th>Non-specific pairing</th>
</tr>
</thead>
<tbody>
<tr>
<td>GGG</td>
<td>AAA</td>
</tr>
<tr>
<td>GGA</td>
<td>AAC</td>
</tr>
<tr>
<td>GGU</td>
<td>AAG</td>
</tr>
<tr>
<td>GGC</td>
<td>AAU</td>
</tr>
<tr>
<td>AGG</td>
<td>CAA</td>
</tr>
<tr>
<td>AGA</td>
<td>CAC</td>
</tr>
<tr>
<td>AGU</td>
<td>CAG</td>
</tr>
<tr>
<td>AGC</td>
<td>CAU</td>
</tr>
<tr>
<td>UAG</td>
<td>GCU</td>
</tr>
<tr>
<td>UGU</td>
<td>GUC</td>
</tr>
<tr>
<td>CGU</td>
<td>GUA</td>
</tr>
<tr>
<td>CGG</td>
<td>GUC</td>
</tr>
<tr>
<td>GCG</td>
<td>GUA</td>
</tr>
<tr>
<td>CGA</td>
<td>CUA</td>
</tr>
<tr>
<td>CGC</td>
<td>CUG</td>
</tr>
<tr>
<td>CAG</td>
<td>CGA</td>
</tr>
<tr>
<td>CGT</td>
<td>CGC</td>
</tr>
<tr>
<td>CGP</td>
<td>CGG</td>
</tr>
</tbody>
</table>

The subsets have been sorted into subsets of extended triplets with specific and non-specific pairing. In each subset four extended triplet are found.

\[
\{X\} = X_1X_2X_3 \cdot S_{XXX}
\]

where \(X_1X_2X_3\) is an arbitrary element of \(\{X\}\). For instance, the subset of collinear codons \(\{AGC, CAU, GUA, UCG\}\) and \(\{CGA, UAC, AUG, GCU\}\) can be written, respectively, as

\[
AGC \cdot S_{XXX} \text{ and } CGA \cdot S_{XXX}
\]

These results suggest that the architecture of the modern genetic codes could be determined from the architecture of an ancient genetic code as those proposed here. Actually, the partition of the modern genetic codes is implicit in the structure \((S_C, \cdot)\). The subset of codons \(S_{XGZ} = \{XGZ\}\) determine a subgroup \((S_{XGZ}, \cdot) \subset (S_C, \cdot)\).

The quotient subgroup \(S_C/S_{XGZ}\) is a partition of the set of codons into 4 equivalence classes:

\[
\{S_{XGZ}, XAZ \cdot S_{XGZ}, XUZ \cdot S_{XGZ}, XCZ \cdot S_{XGZ}\}
\]

where, \(XAZ, XUZ\) and \(XCZ\) are arbitrary elements of the codon subsets: \(\{XAZ\}, \{XUZ\}\) and \(\{XCZ\}\), respectively, with \(X, Z \neq D\). Every class has the same number of elements \(S_{XGZ}\), i.e. 16 codons, which correspond to the 4 main columns of codons Table III. These are the 4 main columns of the modern genetic codes tables (see [9]), where each column enclose codons that code, in general, to similar amino acids. For instance, codons that belong to the set \(\{XUZ\}\) may be represented by some of the products,

\[
\{XUZ\} = AUC \cdot S_{XGZ} \subset AUC + S_{XDZ}
\]

or

\[
\{XUZ\} = GUA \cdot S_{XGZ} \subset GUA + S_{XDZ}
\]

which in particular, for codon AUG, means:

\[
AUG = AUC \cdot GGC \text{ or } AUG = GUA \cdot AGU
\]

where \(AUC \in \{XUZ\}, GUA \in \{XUZ\}, GGC \in \{XGZ\}\) and \(AGU \in \{XGZ\}\)

As was pointed out before, codons from the same vertical line code for the same or similar amino acid. Recall that every vertical line encloses five extended triplets one of them having non-specific pairing. The rest of four codons from every vertical line can be getting as classes from the quotient group \(S_C/S_{GGA}\), where

\[
(S_{GGA}, \cdot) = (\{GGG, GGA, GGU, GGC\}, \cdot) \subset (S_{XGZ}, \cdot) \subset (S_C, \cdot)
\]

As a result, the partition of the modern genetic code tables into 16 subsets of codons that code to the same or similar amino acids is also derived from the ancient architecture proposed here (see [9]). That is, it can be written, for instance,

\[
AUG \cdot S_{GGA} = (AUG, AUA, AUU, AUG) \subset AUG + S_{DZD} = (AUD, AUG, AUA, AUUC)
\]

\[
CAG \cdot S_{GGA} = (CAG, CAA, CAU, CAC) \subset CAG + S_{DZD} = (CAD, CAG, CAA, CAUC)
\]

Since, the Watson–Crick base pairing and the non-specific base pairing of the hypothetical ancestral base D are the fundamental features to define the operations of sum and product, our results suggest that these features are enough to determine the coding constraints of the primeval and the modern genetic code, as well as the transition from the former to the later.

C. Some biological remarks

The simpler translation machinery of the mammalian mitochondrial genome suggests that the universal code as we understand it might not have existed at the beginning of the life. Ohno and Epplen [13] propose that life started with the simpler mitochondria-like code involving fewer species of tRNAs and, therefore, fewer anticodons of greater infidelity with respect to their codon recognition. The last suggestions still presume that the Watson–Crick pairing of A with U and of G with C is retained as the basis of genetic template recognition and that these bases were readily available on early Earth. Shapiro [14] argued that presumption is not supported by the existing knowledge of the basic chemistry of these substances. Levy and Miller [6] pointed out that the rates of decomposition of the nucleobases A, U, G, C, and T clearly shows that these compounds are not stable on a geologic time scale at temperatures much above 0°C. Even at 25°C, the rates of hydrolysis of the compounds are fast on the geologic time scale. They conclude that unless the origin of life took place extremely rapidly (<100 yr), a high-temperature origin of life may be possible, but it cannot involve adenine, uracil, guanine, or cytosine.

In our model the letter D means any alternative base with non-specific pairing. The newly emerged prebiotic translation
machinery had to cope with base sequences that were not preselected to be coding sequences [13]. Such regions could increase the length of the primeval coding DNA regions. Following Susumu and Epplen, in a primitive mitochondria-like code the number of chain terminator codons in randomly generated 300-base-long sequences can only specify a number of oligopeptides. Obviously, the number of chain terminators in randomly generated 300-base-long sequences must be decreased in the primeval genes with extended triplets. In addition, the free code regions should decrease the frequency of transcription and translation errors. So, it should not be strange that the primeval genes could have small regions with free code. Translation of every primeval mRNA should produce a set of homolog proteins and the most frequent synthesized amino acid sequence should depend on the amino acids cell concentration.

The primordial cell was the “natural lab test” to design the primitive coding sequences starting from large regions of free code with non-specific pairing. Those primordial cells supporting genome architectures with relatively low frequency of translations and transcription errors could have an advantage over those cells with less fidelity in these molecular processes. The regions of free code with non-specific pairing should confer to the primordial cells high mutability capacities. This feature may plausible that the first speciation should confer to the primordial cells high mutability capacities. The primordial cells enclosing regions of free code with non-specific pairing could come into being the progenotes – the common ancestral forms of the eukaryotes and the two prokaryotic groups: eubacteria and archaea [15]-[16]. The origin and development of the enzymatic mechanisms for recombination and repairs could make plausible the transition from this progenote to the primitive eukaryotes and prokaryotes. The free coding region could have different destinations. In one way, the repair and recombination mechanisms could gradually eliminate the regions of free coding to come into been the primitive prokaryote cells. While, in another way, the repair and recombination mechanisms could gradually replace the free coding regions with bases G, A, T and C to come into been new coding regions or the primitive introns found in eukaryotes cells.

IV. THE POWER SPECTRA OF EXTENDED DNA GENOMIC SEQUENCES

The present highly variable DNA regions with insertions and deletion could be the relict finger printing of the ancient DNA regions of free code. The gaps observed in the alignment of the DNA genome sequences resemble the hypothesized ancient bases. If this hypothesis is right then we must expect that the coding pattern observed in the present DNA genome sequences ought to be conserved in the DNA sequences produced in the multiple alignments, where the gaps are taken as the mark of the ancient bases. In order to verify this conjecture we have obtained the Fourier spectrum from the multiple alignments of 12 HIV-1 genomes and 14 mammal mitochondrial genomes. In every aligned sequence the hypothetical base D of our model replaced the gaps.

It has been pointed out that the relative height of the peak at frequency \( f = 1/3 \) in the Fourier spectrum is a good discriminator of coding potential [17]-[19]. This feature is the called period-3 property of a DNA sequence and it has been used to detect probable coding regions in DNA sequences. Here, we show evidences that the called period-3 property of DNA sequences it is also present in the aligned coding regions of DNA genome sequences including the gaps, which are replaced by the hypothetical base D.

Thus, we can represent the bases of the DNA aligned sequences by the elements of \( C_i \) (see the beginning of section 3). The discrete Fourier transform of a complex representation of a DNA genomic sequence of length \( N \) with parameters \( a \) and \( b \) is defined to be

\[
F(s/N) = \frac{1}{\sqrt{N}} \sum_{n=0}^{N-1} g_n e^{\frac{2\pi i}{N} n s/N}
\]  

where \( s = 0, \ldots, N-1 \) and the frequency \( f = s/N \). The power spectrum is given by \( S(f) = |F(f/N)|^2 \). In Fig 2 the power spectra of the aligned mitochondrial genomes are presented. The hypothetical base D replaced the gaps produced by the multiple alignments. It is notable that the spectrums of those species phylogenetically connected are similar. The power spectra have significant spectral peak at frequency 1/3 and 2/3 not founds in random sequences. In 10100 random sequences, the peak magnitudes at these frequencies are at the white noise level, significantly lesser than the peaks observed in mitochondrial genes. Thus, the extended DNA genomes sequences derived from multiple alignment conserve the coding pattern of original sequences, the period-3 property.

The period-3 property was also found in HIV-1 whole genomes sequences. The power spectra of the three aligned HIV-1 genomes are presented in Fig 3. The three aligned sequences keep the coding pattern with a peak at frequency 2/3. Thus, despite to the non-protein-coding regions (at the beginning and at the end of these sequences) and the superposition of genes, the period-3 property can be detected.
Fig. 2 Power spectra of 13 concatenated and aligned mitochondrial genes of 14 mammals. With similar spectrum A: Homo sapiens (gi|115315570); B: Chimpanzee (gi|5835121), Pygmy chimpanzee (gi|5835135) and Gorilla (gi|5835149; C: Sumatran orangutan (gi|5835834), Orangutan (gi|5835163) and Common gibbon (gi|5835820); D: Bos taurus (gi|60101824), Finback whale (gi|5819095, Blue whale (gi|5834995), Harbor seal (gi|5834857) and Gray seal (gi|5835009); C Mouse (gi|34538597) and D: Opossum (gi|5835037).

Fig. 3 Power spectra of three aligned HIV-1 whole genomes. A, B and C: the power spectra corresponding to the HIV-1 whole genomes sequences with GenBank accession numbers K03455.1 (HXB2), AB023804.1 and U51188.1, respectively. D, E and F: the power spectra corresponding to the same HIV-1 genomes taken from the base position 700 to 9580.
V. CONCLUSIONS

The present genetic code architecture could be derived from an ancient coding apparatus with an extended alphabet of five bases. The Watson-Crick base pairing and the non-specific base pairing of the hypothetical ancestral base D used to define the sum and product operations are enough features to determine the coding constraints of the primeval and the modern genetic code, as well as the transition from the former to the later.

The transition from an ancient DNA coding sequence to the present could be biologically plausible and mathematically determined by an ancient coding apparatus highly degenerated minimizing the transcription and translation errors.

ACKNOWLEDGMENT

This research was supported within the framework of a VLIR-IUS Collaboration Program.

REFERENCES


Robersy Sánchez graduated in Biochemistry at the Havana University in 1991. He hold a Master degree in Applied Mathematics at the Universidad Central de Las Villas (UCLV) and a PhD in Biological Sciences at the Havana University. He is assistant professor at the UCLV and lead Bioinformatic group in INIVIT. His research areas include Mathematical and Computational Biology (genome algebra) and Bioinformatics.

Ricardo Grau received his PhD degrees in Mathematical Physic at the UCLV in 1986. Currently, he is a full professor at the UCLV. His research areas include Mathematical and Computational Biology (genome algebra), Bioinformatics, artificial intelligence, pattern.