Computation of the Genetic Code

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Computation of the Genetic Code

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Abstract. One of the problems in the development of mathematical theory of the genetic code (summary is presented in [1], the detailed -to [2]) is the problem of the calculation of the genetic code. Similar problems in the world is unknown and could be delivered only in the 21st century. One approach to solving this problem is devoted to this work. For the first time provides a detailed description of the method of calculation of the genetic code, the idea of which was first published earlier [3]), and the choice of one of the most important sets for the calculation was based on an article [4]. Such a set of amino acid corresponds to a complete set of representations of the plurality of overlapping triple gene belonging to the same DNA strand. A separate issue was the initial point, triggering an iterative search process all codes submitted by the initial data. Mathematical analysis has shown that the said set contains some ambiguities, which have been found because of our proposed compressed representation of the set. As a result, the developed method of calculation was limited to the two main stages of research, where in the first stage only the of the area were used in the calculations. The proposed approach will significantly reduce the amount of computations at each step in this complex discrete structure.

1. Introduction
First, con First of all, the question arose: what sets can be used in this case. Our approach was based on the search for all codes satisfying the set of amino acids that record overlapping genes. The author has studied the subject matter of the mathematical analysis of such genes for a number of years [2], and it was this analysis that led to the formulation of this problem.

From the very beginning it was clear that the discussion would mainly focus on the iterative process. Since overlapping of genes contains two, three, etc., amino acids, right up to 6, the first task was to find those overlaps where the same amino acid participates (in overlaps, it participates with different encodings, according to the genetic code). On this occasion, a special study was conducted.

2. Theorem for homogeneous overlaps
We consider unusual ways of recording genetic information - overlapping genes, when the same DNA portion corresponds to more than one protein. We investigated all 5 possible cases of overlapping of genes resolved by DNA structure, which were studied earlier [5]. This study was based on a mathematical analysis of all 5 possible overlap cases and relied on sets of so-called elementary genetic overlaps-e.o., or overlaps corresponding to a pair of single amino acids. In [6] a brief analysis of such sets is presented, and the final version in [2]. In Fig. 1. A description of the structure of the sets W1-W5 is presented, and are presented by the 4th e.o.. In each of these sets.
The principal position of this research is indicated in [2], where it was shown that the presented list of elementary overlaps can cost any (!) allowed by the structure of the genetic code, overlapping not only 2 but also all admissible overlap from 3 to 6 genes. The urgency of the problems is due to the current situation: overlapping genes common in viruses, mitochondria, bacteria and plasmids were found in eukaryotic large genomes, including humans, with the

Description of the structure of sets W1-W5. Two analysis of a set of elementary overlaps for 3 genes overlapping in the same DNA chain. It is established that there are only 307 such overlaps. On the basis of these overlaps, a new problem was posed, connected with the calculation of the genetic code by mathematical methods [11, 12]. The question of why exactly such a set was chosen to calculate the code was based on a theorem that was published relatively recently [4]. We are talking about the calculation and analysis of all homogeneous e.o.o.chs. From 2 to 6 genes. Are e.o. which correspond to the same amino acid. Its solution is given by the following theorem.

We call an e.o. -elementary overlap for i amino acids, where, i ∈ (2,6). Thus, the e.o. introduced earlier in [2]. Will be referred to as e.o.-2. Figure 1 shows the general representation for e.o.-6.

Fig.1. General presentation for e.o.-6. (See the text) - 5 e.o.-2 for overlaps from one DNA chain:

For the amino acid Ama (isolated by hatching) encoded by the triplet n1n2n3, there are 5 alternative amino acids Ama1- Ama5, the encodings of which are formed by -1, +1 shifts in the same DNA chain (→) and -1, 0, +1 in the complementary DNA strand (←). The designations ni, i ∈ (0,4) are the nucleotides from the set A, T, C, G; N; n’i, i ∈ (0,4) - complementary components: i.e. For n’1 = A; n2 = T ; n3 = C, n4 = G for any i ∈ (0,4) and vice versa. In order to sequentially isolate e.o.-2 for all 5 cases of pair overlaps from [2,3], one should consistently leave one of the 5 pairs of amino acids: (Ama, Ama), i ∈ (1,5). In order to sequentially isolate all overlap cases for e.o.-3, it is necessary to leave Ama and a pair of amino acids out of 5 possible ones or we have 10 cases of triple overlap, etc. We turn to the search for a homogeneous subset for all possible e.o.-2-6, or subsets, in each e.o.. Which is the same amino acid. We denote it by W2,6. To represent homogeneous elementary overlaps, the following notation is used: Y: T, C; X: A, G; N: A, G, C, T.

First of all, it is necessary to exclude from consideration all homogeneous overlaps in which two strands of DNA participate. Consideration of these overlaps requires the introduction of a double strand of DNA - this is an additional condition in the problem. Eliminating such homogeneous overlaps, we proceed from the principle of constructing an algorithm with a minimum number of conditions. Therefore, in our examination there remain only homogeneous overlaps belonging to the same DNA chain: for pairs of amino acids (1), there are only 5 of them and similar overlaps for three amino acids (3) -th total of 4. Thus, we selected the main working sets E.o., namely, those in which these homogeneous overlaps are present. The final version of these sets is presented on pages 312-319 in [2].

Contains two nucleotides n1n2; The codon n2n3n4 for Ama2 overlaps with codon n1n2n3 for Ama - the overlap contains two nucleotides n2n3. As a result, the triple overlap contains only one common position n2.

B. Elements of sets of combinations of amino acids, formed on the basis of elementary overlap. On the left there is one element of the set U1, in the center there are two elements of the set U2 and to the right one element of the set U3.
Amino acids shown in Table 1. Elements are given in the view that is used in this task. Each of the elements consists of three lines: upper, middle and lower. The named amino acids Met and Arg are shown in the middle line.

**Table 1.** Steps 1-9 of the iterative process of calculating the genetic code. The last line indicates the number of calculated codons after this step.

|   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| Met |   |   |   |   | abd |   |   |   |   |
| Trp |   |   |   |   | bdd |   |   |   |   |
| Phe | bbb |   | bbY |   |   |   |   |   |   |
| Tyr |   |   | baY |   |   |   |   |   |   |
| His |   |   | caY |   |   |   |   |   |   |
| Asn |   |   | aaY |   |   |   |   |   |   |
| Asp |   |   | daY |   |   |   |   |   |   |
| Cys |   |   |   |   | bY |   |   |   |   |
| Gln |   |   | caX |   |   |   |   |   |   |
| Lys | aaa | aaX |   |   |   |   |   |   |   |
| Glu |   |   | daX |   |   |   |   |   |   |
| Ile |   |   | abM |   |   |   |   |   |   |
| Val |   |   | dbN |   |   |   |   |   |   |
| Pro | ccc | ccN |   |   |   |   |   |   |   |
| Thr |   |   |   |   | acN |   |   |   |   |
| Ala |   |   | dcN |   |   |   |   |   |   |
| Gly | ddd | ddN |   |   |   |   |   |   |   |
| Ser |   |   | bca | bec | bde | bce |   |   |   |
| Leu |   |   | cbX | cbb | bbX | cbe |   |   |   |
| Arg |   |   | cdN | adX |   |   |   |   |   |
| Σ  | 4 | 12 | 24 | 27 | 31 | 35 | 43 | 58 | 61 |

Notation: X: a, d; Y: b, c; M: a, b, c; N: a, b, c, d.

### 3. Formulation of the problem

Let’s have a set of 4 letters: N: a, b, c, d, and also triplets - any triples of these letters, there are 64 in all. Moreover, each of the 20 canonical amino acids can be encoded by an arbitrary combination of such triplets. The task is to search for all the genetic codes that correspond to all the elements designated above the three sets U1, U2, U3, corresponding to the genetic experiments.

For the future, we use standard three-letter abbreviations for each of the 20 amino acids.

In [11] we talked about ste.o.s to calculate this problem, but did not say how the required elements were selected at the ste.o. For such a selection, a special re.o.resentation of the basic working set was introduced. This result is published in detail for the first time.

We introduce one concise re.o.resentation for 307 elements of the principal set-U3. For each Ama of this set (it is indicated in the corresponding cell), the amino acid Ama1 is plotted along the abscissa axis, and the ordinate is Ama2. It turned out that the resulting re.o.resentation is not homogeneous, but contains multiple ambiguities: these are cases when more than one Ama value corresponds to the same Ama1 and Ama2 values. It turned out that the number of ambiguities in the range from 2 to 4. All
these cases are shaded in Fig. 2 and they are denoted by A1 - A13, and their decoding is given in the caption to this figure.

It should be noted that these ambiguities correspond to the values of Ser, Leu, Arg, both along the abscissa axis and along the ordinate axis. However, the most significant area, which corresponds to the cases where on both axes there is none of the amino acids from the Ser, Leu, Arg. For our calculations, the last region is reduced, eliminating from it all cells containing Ser, Leu, Arg. The shading corresponds to the three amino acids mentioned, and the non-zero elements of the unshaded region have the following property: each Ama value is unique for the corresponding pair Ama1 and Ama2.

The above property allowed us to refer to the first stage of the calculation, when the calculation of the encodings for all elements is made Ama value on the basis of the encodings for the corresponding pair Ama1 and Ama2. The results of the ste.o.-by-ste.o. solution of the problem are presented in Table 2, but the most important stage of the study was the question of finding the initial approximation.

4. Solution of the problem

We use the standard three-letter abbreviations for each of the 20 amino acids listed in the first column of Table 1. We have a set

$$A_0: A_{mai}, i (1,20).$$  \hspace{1cm} (1)

We introduce the definition. Let us turn to the previously introduced homogeneous overlaps. As before, we call a combination of amino acids, constructed on the basis of an elementary genetic overlap, homogeneous if the same amino acid participates in it. For homogeneous elements of the set we have

Property. Let the encodings $A_{ma}$ for homogeneous $u_3$ have one of the following three representations:

$$n_1N_1N_2, \quad N_3n_2N_4 , \quad N_5N_6n_3$$ \hspace{1cm} (2)

Where small letters denote the unit components of the set $N$, and large - some subsets of this set, up to $N$. Then homogeneous $u_3$ can exist only if at least one base triplet or triplet with three identical letters is used.

For the proof we successively substitute each of the representations (2) in $u_3$:

$$A_{ma} \quad A_{ma} \quad A_{ma}$$  \hspace{1cm} (3)

Where $n'_i$ is the single component of the set $N_i$, where $i \in (1,6)$, and the string na. - nucleotide sequences that are formed after this substitution. In the first case, in (3), the base codon $n_1n_1n_1$ was used for encoding amino acid $A_{ma}$ from the bottom position, in the second - $n_2n_2n_2$ - from the middle position, and in the third - $n_3n_3n_3$ - from the top position.

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![Fig.2.](image-url)
We turn to homogeneous u3 from the set U3, which turned out to be 4:

\[
\begin{align*}
\text{Lys} & \quad \text{Phe} & \quad \text{Pro} & \quad \text{Gly} \\
\text{Lys} & \quad \text{Phe} & \quad \text{Pro} & \quad \text{Gly} \\
\text{Lys} & \quad \text{Phe} & \quad \text{Pro} & \quad \text{Gly}
\end{align*}
\]  
(4)

Within the framework of the assumption specified in the Property, the following step-by-step process of searching for a genetic code is proposed; See Table 2. Step 1. Amino acids from (4) will assign the corresponding base codons. This assignment is not unique. However, in our approach, the set of letters N: a, b, c, d is not correlated with the canonical set of 4 nucleotides; This will be discussed at the end of the paper. Therefore, we will continue to operate with only one of the representations for the amino acids from (4), which we assign respectively the following basic triplets:

\[
\begin{align*}
\text{Lys: aaa, Phe: bbb, Pro: ccc, Gly: ddd}
\end{align*}
\]  
(5)

For further calculations, we turn to some generalized data on the sets U2 and U1, which are given in Table 1.

Step 2. From Table 1 it follows that, as in column m12 (the number and the list of overlapping amino acids on 1 and 2 bases are indicated), and in column m23 (similar data for 2 and 3 bases) do not contain mutual overlap between amino acids from (4). Such overlaps take place only one position and belong to the set U1. We have:

\[
\begin{align*}
\text{Lys} & \quad \text{Phe} & \quad \text{Pro} & \quad \text{Gly} \\
\text{Lys} & \quad \text{Phe} & \quad \text{Pro} & \quad \text{Gly} \\
\text{Lys} & \quad \text{Pro} & \quad \text{Phe} & \quad \text{Gly}
\end{align*}
\]  
(6)

See [2]:

\[
\begin{align*}
\text{Lys: aaX, Phe: bbY, Pro: ccN, Gly: ddN}
\end{align*}
\]  
(7)

Step 3-by-step 7 calculation in the uniqueness domain

The solution search in step 3 is illustrated in Fig. 2 (step. 3), where the reduced reduced ambiguity region is presented. For each of the four amino acids from (5) we carry out two bands (gray hatching in Fig.) For Ama1 (horizontal strip, figure 2 outside the figure indicates the step number) and Ama2 (vertical strip). As a result, at the intersections of these bands we find only 4 amino acids: Gln, Glu, Val, Ala, which are shown in the figure as bold. Taking into account the accepted standard record and the codings from (5), we have:

\[
\begin{align*}
\text{Lys} & \quad \text{Lys} & \quad \text{Phe} & \quad \text{Pro} \\
\text{Gln} & \quad \text{Glu} & \quad \text{Val} & \quad \text{Ala} \\
\text{ccaa} & \quad \text{ddaa} & \quad \text{ddbb} & \quad \text{ddcc}
\end{align*}
\]  
(8)

Where n.s. is the nucleotide sequence. From (8) we have single-valued encodings for 4 amino acids: Gln, Glu, Val, Ala, and with (9) we find:

\[
\begin{align*}
\text{Gln:caX, Glu:daX, Val:dbN, Ala:dcN}
\end{align*}
\]  
(9)

Thus, it is shown that the use of the introduced reduced set leads to minimal costs in the step, compared to a direct search for 307 elements of the main set - U3.

Step 4-Steh 7-on analog

Search for a solution in the field of ambiguity

Step 8. Finding solutions in an area where the values of Ama1 and Ama2 belong not only to these 17 amino acids. On the basis of Fig.2 We get:

\[
\begin{align*}
\text{Gln} & \quad \text{Pro} & \quad \text{Ala} & \quad \text{Val} \\
\text{Ser} & \quad \text{Ser} & \quad \text{Ser} & \quad \text{Ser}
\end{align*}
\]
| Phe | Ile | Gln | Gln |
|-----|-----|-----|-----|
| Tyr | Phe | Trp | Tyr | Trp |
| Leu | Leu | Leu | Leu | Leu |
| Thr | Ala | Pro | Val | Val |
| Glu | Val | Ala | Gly | Gly | Gly |
| Arg | Arg | Arg | Arg | Arg |
| Lys | Ala | Ala | Pro | Thr | Lys |

(10)

From these overlappings we find the following encodings:

Ser: bca,bbc,adY; Leu: cbX,cbb,bbX; Arg: cdN,adX.   (11)

Step 9. From the ambiguity region in Fig. 2, we select cases containing two amino acids from the set Ser, Leu, Arg and giving solutions different from (11). We have:

Arg Leu Ser
Ser Ser Leu
Val Ile Pro                                           (12)

When passing from the set of letters a, b, c, d to the canonical nucleotides A, C, T, G, 24 similar genetic codes can be obtained. Only one of them is standard, with a = A, b = T, c = C, d = G, and triplets baX, bda become TAA, TAG, TGA; They play a role.

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