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A multiscale model of nucleic acid imaging

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Abstract

The paper describes new results in the field of algebraic biology, where matrix methods are used [Petukhov, 2008, 2012, 2013; Petuhov, He, 2010] with the transition from matrix algebra to discrete geometry and computer visualization of the genetic code. The algorithms allow to display the composition of sequences of nitrogenous bases in parametric spaces of various dimensions. Examples of visualization of the nucleotide composition of genetic sequences of various species of living organisms are given. The analysis was carried out in the spaces of binary orthogonal Walsh functions taking into account the physical and chemical parameters of the nitrogen bases. The results are compared with the rules of Erwin Chargaff concerning genetic sequences in the composition of DNA molecules. The developed method makes it possible to substantiate the relationship between DNA and RNA molecules with fractal and other geometric mosaics, reveals the orderliness and symmetries of polynucleotide chains of nitrogen bases and the noise immunity of their visual representations in the orthogonal coordinate system. The proposed methods can serve to simplify the researchers' perception of long chains of nitrogenous bases through their geometrical visualization in parametric spaces of various dimensions, and also serve as an additional criterion for classifying and identifying interspecific relationships.

Keywords: visualization algorithms, Walsh functions, Chargaff's rules, multidimensional analysis, nucleotide composition, fractals, bioinformatics, DNA, chromosomes, symmetries.

1. Introduction. General information on the nucleotide and nucleotide composition of DNA and RNA

DNA and RNA nucleic acids are sequences of complementary nucleotide pairs that perform the functions of storage and transmission of hereditary genetic information in living organisms [1,17]. These sequences are analyzed, as a rule, by statistical methods. They have a one-dimensional linear character and are displayed as lines consisting of four letters of the alphabet encoding the nucleotides: adenin (A), guanine (G), cytosine (C) and thymine (T) (uracil (U)).

Visual analysis of long runoffs consisting of letters encoding the nucleotides of real genetic sequences is a laborious task. To simplify it, many algorithms and software products have been developed that allow to visualize and to analyze DNA using various histograms, tables and graphs, for example, see [23-26]. These methods are based on machine statistical analysis and are widely used in scientific research. In this paper we have set a task to develop a new method that simplifies the visual analysis of long nucleotide sequences (the question of nucleotide composition interpretation is beyond the scope of this study).

2. Materials and methods. Coding of physico-chemical parameters of nucleotides in symmetric Hadamard matrix

2.1 Genetic coding as a Walsh function system

In [2] it is shown that each nitrous base of genetic code has three variants of its binary representation. These variants of representations, named by S.V. Cock-eared binary sub-alphabets, differ according to the types of binary-opposition properties in the set of nitrogenous bases:

- G = C "3 hydrogen bonds" / A = T "2 hydrogen bonds";
- C = T "pyrimidines" / A = G "purines";
- A = C "amino" / G = T "keto" [20];
- A=T=G=C (presence of phosphate residue).

Taking into account the additional fourth feature, which is not in opposition, the system of genetic subalphavities can be represented in the form of Hadamard's matrix shown in Fig. 1.

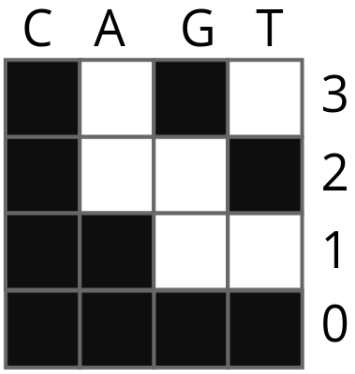


Fig. 1. A variant of the Hadamard matrix displaying the encoding of nucleotide subalphabets. Darkened cells are +1, white cells are -1 (or vice versa depending on the encoding method). Sub-alphabet numbers are denoted as 0, 1, 2 and 3.

This matrix is symmetric, because nucleotides can be replaced by corresponding subalphabets without changing the matrix structure (rows and columns can be changed in places) [3]. Each row and column of the Hadamard Matrix is a Walsh function [4]. Walsh functions are a complete set of orthogonal functions that can be used to represent any discrete function by analogy with the use of trigonometric functions in the Fourier analysis [7]. They are used in digital engineering, in noise immunity coding, in quantum informatics and quantum mechanics.

2.2 Genetic Encoding as a Charghaffe Rule System

Chargaff revealed a system of biochemical regularities within nucleic acid sequences, which describes quantitative relationships between different types of nucleotides [1]. This system of regularities is a set of algebraic relations:

1. The amount of adenin is equal to the amount of thymine, guanine to cytosine:
A = T, G = C or A / T = 1, G / C = 1 (Watson-Crick pairs [17]).

2. The number of purines equals the number of pyrimidines:
A+G ≈ T+C or (A+G) / (C+T) ≈ 1.

3. number of bases with amino groups in position 6 is equal to number of bases with ketogroups in the same position:
A+C ≈ T+G or (A+C) / (G+T) ≈ 1.

4. The ratio (A+T) / (G+C) is a specificity factor and can be different with a predominance of AT or GC pairs depending on a particular organism type, realizing a variety of living forms.

As can be seen from the above, the nucleotide sequence of a living organism is a balanced system representing a double helix (DNA) and having internal symmetries and certain mathematical regularities. Additional information on Hadamard's symmetries and matrices in genetic coding, as well as on genetic algebrae, is detailed in the works of S.V. Petukhov, a biomathematician [2,10,15].
Due to the existence of a connection between algebra and geometry (which means the existence of a connection between genetic algebra and genetic geometries), the author has set and solved the task of developing a method for visualizing nucleic acids. The study was based on the hypothesis that the visualization should reflect the symmetry of the nucleotide composition. The author's method allows investigating the phenomenon of genetic coding from the geometric side.

2.3 Method of scale parametric imaging of nucleic acids

The above method is an algorithm of computer processing of biological information for scale parametric visualization of nucleic acids in coordinate spaces of different dimensions. The main ideas of this method were first proposed by the author in [5]. The steps of the developed algorithm are given below.
1) Scaling. The sequence of symbols {A,G,T,C} encoding nitrogen bases in nucleic acid is divided into fragments of equal length N where N is a free parameter of the algorithm. The obtained fragments of equal length will be called N-meters or N-plates [5].
2) Parametrization. Taking into account the system of genetic subalphabets, the sequence of nitrogenous bases can be represented as three binary sequences consisting of zeros and units. The choice of coding method (what to consider as zero or unit) influences the rotations and other transformations of the final visualization (therefore, for the possibility of adequate comparison of the results obtained, it is necessary to conduct research with reference to the "single coding standard").
3) Geometrization. Binary recording of fragments is their representation in the form of three sequences of decimal or other unambiguously identifying values. Converting binary N-dimensions into decimal numbers allows them to be displayed in any coordinate system. Numerical values specify coordinates of points in parameter space (further - in visualization space or parametric space).
Note 1. The N-factor plays the role of geometric visualization resolution: large N give small number of points, small N give small coordinate grid. This fact allows us to talk about multiscale analysis in parametric spaces.
Note 2: Steps 1 and 2 can be rearranged (first parametrization, then scaling), which affects the computational load when calculating long genetic sequences on a computer.
The visualization algorithm was implemented by the author as a library of programs in Python, Lua, Moonscript and C++ programming languages without interactive editor (GUI) and hardware graphics acceleration. Specialized modules were used to accelerate calculations. The average time required to process genetic information is from several seconds to several hours depending on the scale of N and the length of the analyzed sequence. Sometimes it was necessary to stop the counting due to exceeding the allowed time interval. Some calculations were performed on the supercomputer "MVS-10P" (MSC RAS).
A heuristic formula for calculating the N scale when visualizing L-length nucleotide sequences is proposed:

$$N = \left[\log_2\left(\sqrt{L}\right)\right],$$

where square brackets are the operation of taking an integer part of a number. Width and height of the square image in points:

$$K = 2^N$$

It is proposed to choose all three possible combinations of Walsh basic function pairs as two-dimensional projection spaces. In this case, the most informative variant of the combination of these functions may depend on a particular organism type. At the moment it seems that

there are formal rules for the choice of basic functions, but this question needs to be further studied by analysis of the structure of a large number of DNA of different species of organisms by the proposed method.
The method refers to the development of statistical methods of analysis of nucleotide sequences and is based on parametrization, scaling and geometry of physical and chemical parameters of the molecule. As a result of the method application, the parametric space is given, which is finite, discrete and three-dimensional by the number of binary-opposition features. Combinatorial properties of this space allow to display any polynucleotides for any finite N. Arranged numeric values on coordinate axes display physical and chemical characteristics of N-mers, as they are clearly defined by the properties of binary-opposition subalphabets. The method allows to visualize the nucleotide composition in different projections, with different scales and by different subalphabites and can be used for analysis of RNA and DNA molecules.
The proposed method of conducting research using the developed method: the construction of examples of visualization of long nucleotide sequences from DNA of different organisms on the basis of the proposed method:

–in three-dimensional space of physico-chemical parameters, which is given by three lines of 1, 2 and 3 of Hadamard's matrix in Fig. 1;

–in three-dimensional space of physico-chemical parameters, which is given by three possible combinations of rows 1-2, 1-3 and 2-3 of Hadamard's matrix in Fig. 1;

–in three one-dimensional spaces of physico-chemical parameters, which are given by three rows of 1,2 and 3 of Hadamard's matrix in Fig. 1, considered separately and along the whole length of the molecule, that allows to take into account the location of N-mers in the genetic sequence;

–the zero (bottom) line of the Hadamard matrix in Fig. 1 is not informative, as it does not encode the binary-opposition features, so it is not considered;

–additionally, according to Harmuth's theory of sequential analysis [6] it is possible to visualize by the number of elements (zeros or units), which were found in binary representations of N-platforms in the sequences of nitrogen bases. Due to the fact that this method is based on the total number of some or other parameters in the N-platform, the corresponding visualization spaces will be called integral.

In the course of research, visual patterns were built about a hundred genomes of protozoa, plants, fungi, animals and viruses. In this work, genomes from the NCBI bioinformation database [14] as well as materials kindly provided by the laboratory of Prof. N.S. Zenkin at the Center for Bacterial Cell Biology at Newcastle University (United Kingdom) were used for visualization.

3. Results and discussion. Examples of nucleic acid imaging in parametric spaces of different sizes

3.1 Visualization of nucleic acids in three-dimensional space of physical and chemical parameters of nucleotides

The orthogonal basis {X, Y, Z} selected as a three-dimensional Cartesian coordinate system gives a visualization, an example of which is shown in Fig. 2. Each point corresponds to the generalized characteristics of the considered binary and positional features of the corresponding fragment of the sequence, which allows to display the nucleotide composition of the molecule.

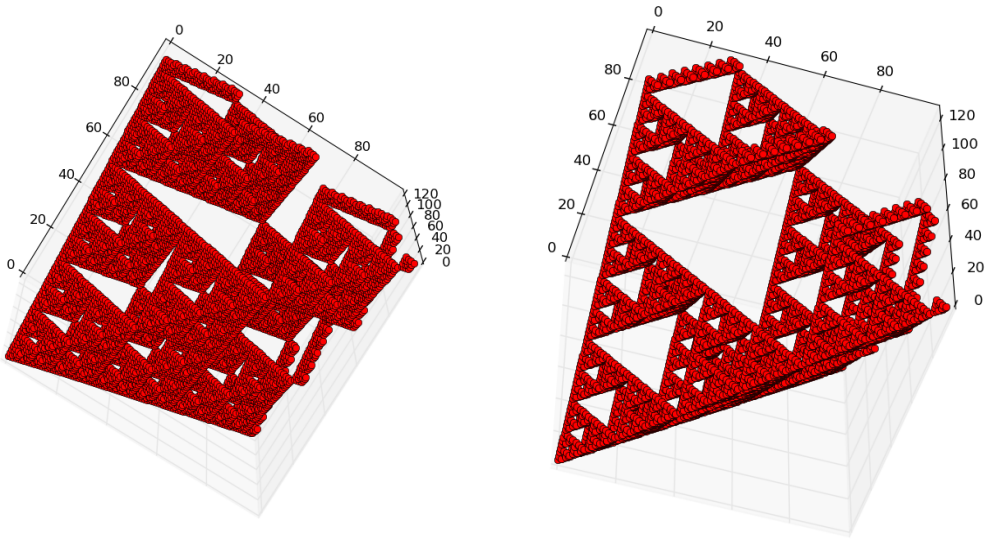
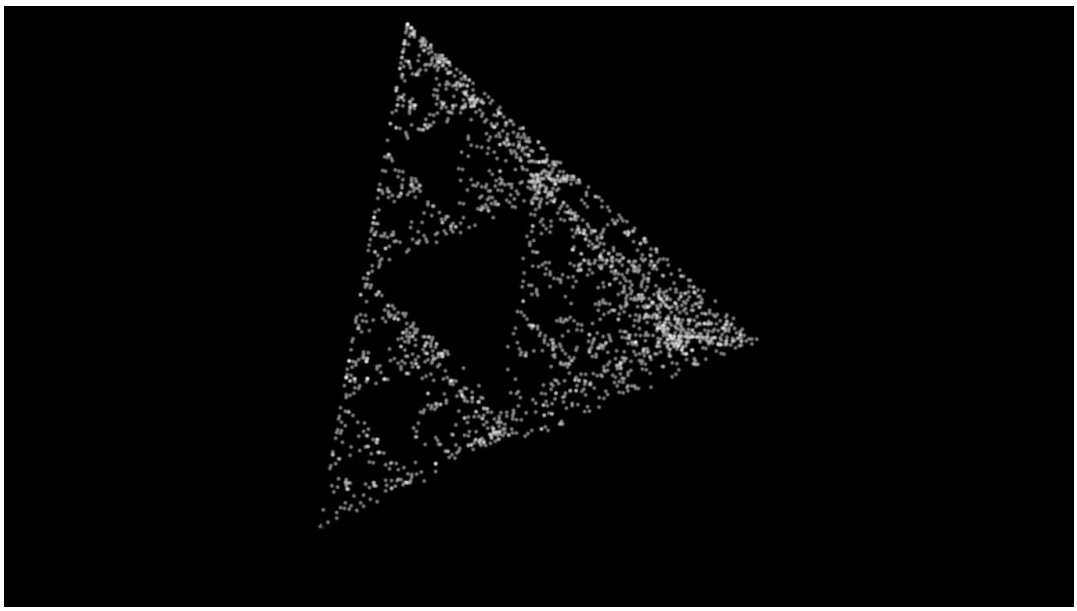


Fig.2. Illustrations of the three-dimensional representation of the nucleotide composition on the example of a chromosome of a living organism in various projections, constructed by the author's algorithm. The X, Y, and Z axes correspond to the ascending orderly decimal representations of the binary coding of N-leafs based on all three binary-opposition subalphabets. Each point of a figure corresponds to N-dimensional which coordinate is set by its proton-numeric characteristics. The analysis of three-dimensional image data is difficult because of the geometry of the object itself. To eliminate this difficulty it is necessary to build two-dimensional projections.

The resulting geometrical figure resembling "Sierpinski's simplex" is typical for three-dimensional visualization of any long nucleotide sequence. The shape of the figure is determined by the properties of binary sub-alphabets and the Hadamard matrix in Fig. 1. The coordinates of each point in the three-dimensional visualization space are given by any pair of its coordinates, because the third coordinate is calculated by adding the two remaining coordinates on the module. This algebraic feature is associated with the redundancy of binary subalphabets used for storing and transmitting genetic information through generations' chains. An animated version of Fig. 2 is presented in animation:



An example of the integral three-dimensional representation of the nucleotide composition of the chromosome of a living organism is given in Fig. 6. 3. It is an object of finite geometry,

each point of which corresponds to a set of N-dimensions of nucleic acid, united by the number of units in binary encoding.

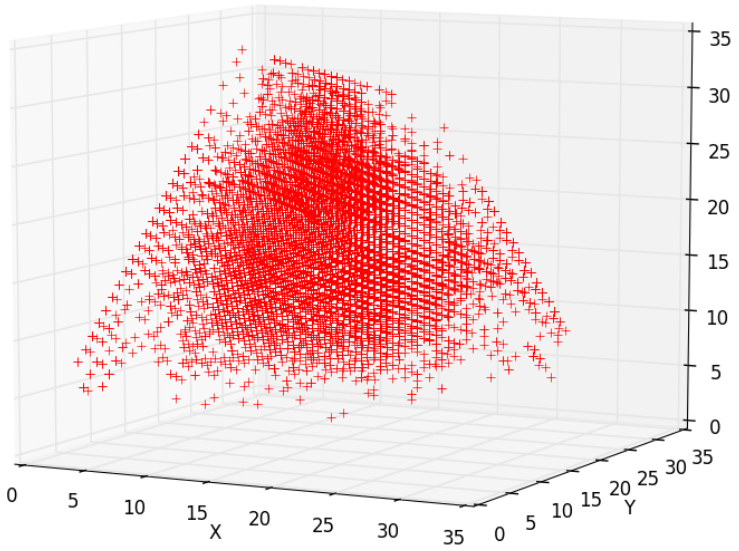
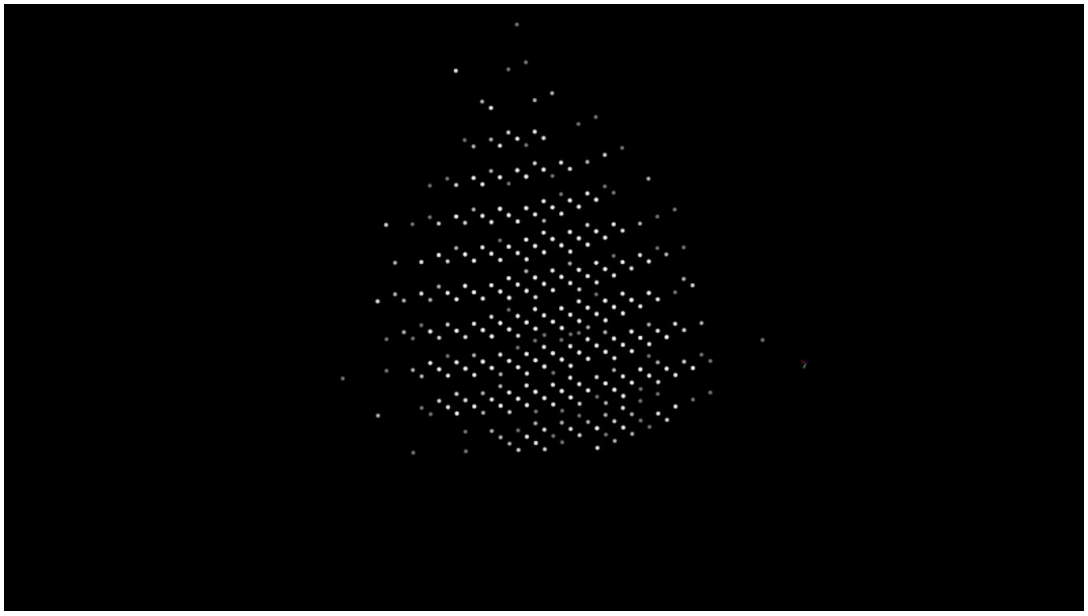


Fig.3. Integral three-dimensional representation of the nucleotide composition of the chromosome. The X, Y, and Z axes correspond to the number of units in the decimal representation of the binary coding of each N-platform using three binary-opposition subalphabets.

Animated version of the picture. 3 is presented in animation:



3.2 Visualization of nucleic acids in three two-dimensional spaces of physical and chemical nucleotide parameters

The properties of parametric space are such that three-dimensional representations are not convenient for perception and analysis of features of long nucleic acids. However, two-dimensional projections of this three-dimensional representation are suitable for displaying the specificity of their structure. In the bases {X, Y}, (X, Z} and {Y, Z} selected as Cartesian coordinate systems, three-dimensional visualization gives three different two-dimensional

projections based on the corresponding sub-alphabets of physical and chemical parameters of nucleotides.

On the basis of the developed method of visualization and computer program it was found out that chromosomes of different kinds of organisms have individual features of structure. Visualization of genomes of different organisms can have a two-dimensional pattern, which is visually similar for all chromosomes and their arbitrary fragments, as well as for the whole considered organism. Fig. 4-9 show examples of two-dimensional visualization of different nucleotide sequences. Next to the figures in the order A, G, T, C there are pairs of Walsh functions, which were used for coding their physico-chemical parameters (Hadamard's matrix rows from Fig. 1).

Based on the noted property of genetic coding (according to which the three binary-opposition sub-alphabets are linked to each other by an addition operation on module 2) any pair of binary representations is sufficient to determine an arbitrary nucleic acid. Therefore, any pair of axes is sufficient for two-dimensional visualization of the nucleotide composition. As it turned out, the question of determining the most informative pair of coordinate axes (and, accordingly, the parameters taken into account) depends on the type of living organism.

As a result of the analysis, it was found that out of three variants of two-dimensional visualization, the most informative and symmetrical mosaics are often mosaics based on information about the external structure of the molecule, i.e. constructed on the elements of structures encoding the features of amino/keto and purine/pyrimidine. Such mosaics have a detailed pattern, in which rectangular forms are usually traced (Figs. 4, 7-9). However, in some cases, the most pronounced and symmetrical mosaics are those based on types of hydrogen bonds representing the internal structure of the double helix DNA. Such mosaics are usually characterized by pronounced diagonal elements of the pattern and are found, for example, in the mitochondria DNA of the plant arabidopsis thaliana (Fig. 5).

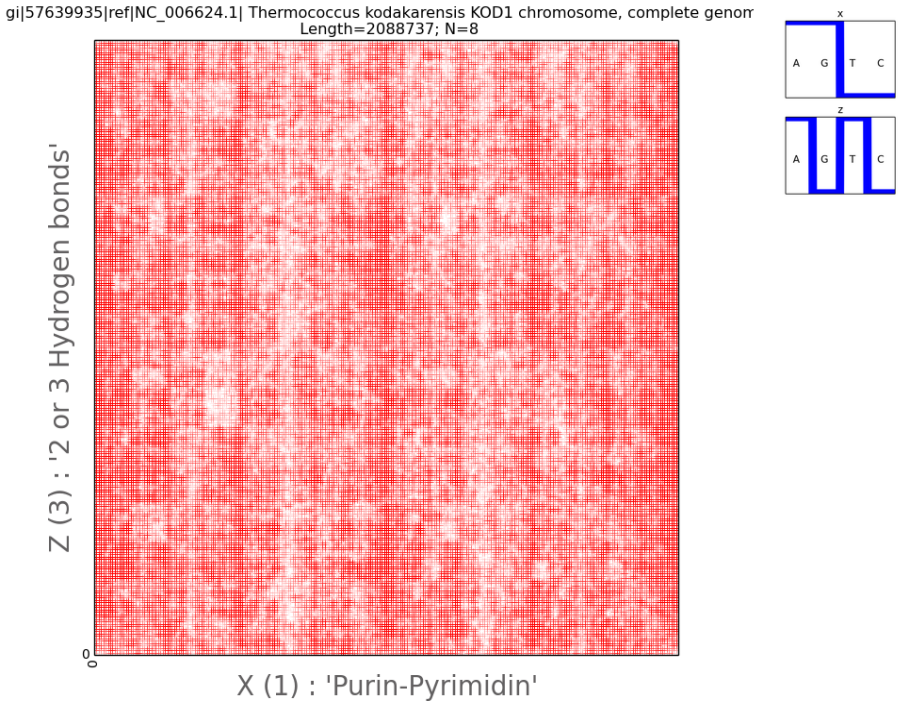


Fig.4. Illustration of two-dimensional representation of the nucleotide composition of the thermophilic archaeology chromosome. A pair of Walsh functions used for parameterization is displayed in the upper right corner. The axes of abscissa and ordinate correspond to the decimal representation of the binary coding of each 8-wire.

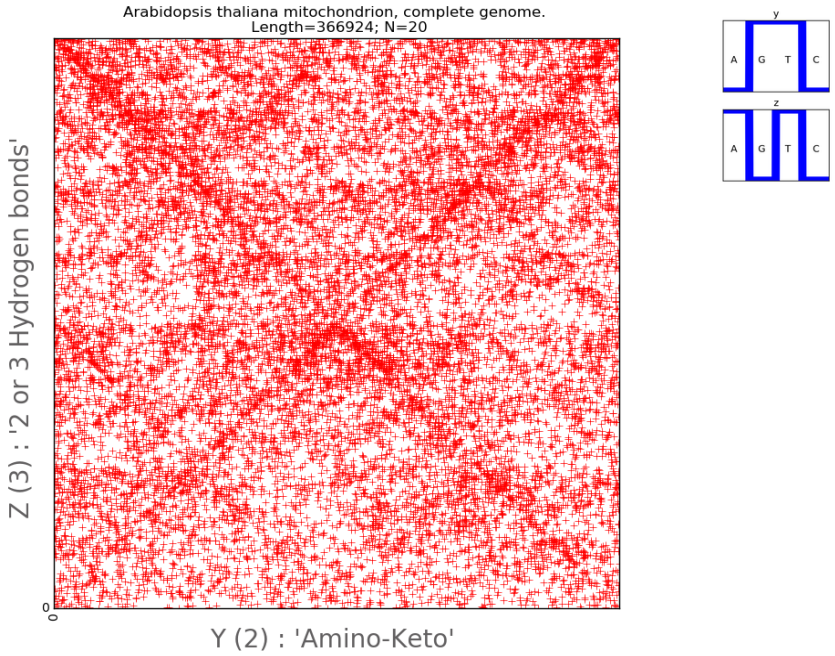


Fig.5. Illustration of two-dimensional representation of the nucleotide composition of the mitochondria genome of the plant Rezuhovidka (Lat. Arabidopsis thaliana) of the cabbage family (Brassicaceae). A pair of Walsh functions used for parameterization is displayed in the upper right corner. The axes of abscissa and ordinate correspond to decimal representations of the binary coding of each 8 weave.

In Fig. 6 and 7, which show a mosaic reflecting the internal structure of chromosomes of two organisms, diagonal elements are well traced. The genome of the bacteria in Fig. 6 shows fractal repetitions of diagonals throughout the pattern. The diagonal elements differ in color depending on the direction and place in the fractal pattern. In Fig. 7, the visualization of the nucleotide composition of the second chromosome of the single-celled microscopic fungus "baker's yeast" shows a different behavior of the diagonal elements: the diagonals are well traced only in one direction, the fractal repetitions of the diagonals are also expressed only in one direction, and they display the absent N-meters. The opposite diagonals responsible for the present N-meters are less clearly traced.

Note that diagonals and other elements of the pattern can be directed in different directions in different organisms while maintaining the general structure of the pattern. This feature can be simulated by reading the complementary DNA filament.

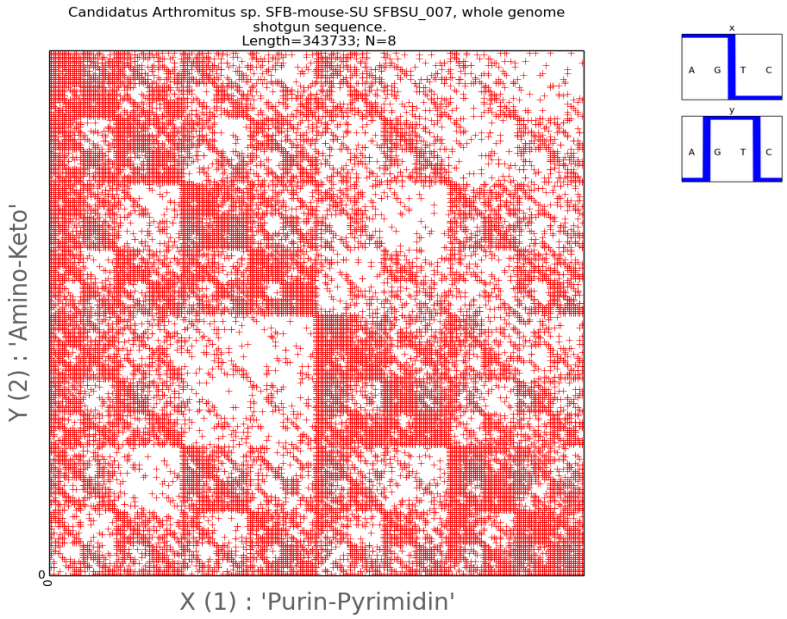


Fig.6. Illustration of two-dimensional representation of the nucleotide composition of the bacterial genome. A pair of Walsh functions used for parameterization is displayed in the upper right corner. The axes of abscissa and ordinate correspond to the decimal representation of the binary coding of each 8-wire.

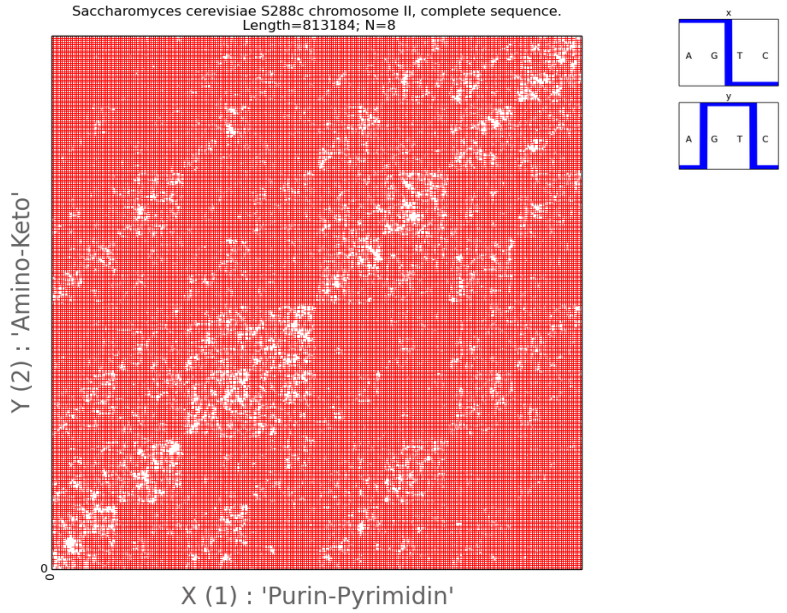


Fig.7. Illustration of two-dimensional representation of nucleotide composition of the second chromosome of single celled microscopic fungus (baking yeast). A pair of Walsh functions used for parameterization is shown in the upper right corner. The axes of abscissa and ordinate correspond to the decimal representations of the binary coding of each 8-wire.

Figures 8 and 9 present visual two-dimensional representations of Ralstonia eutropha (H16 megaplasmid pHG1) and the complete genome of the Burkholderia multivorans protobacter, respectively. Their visual patterns are characterized by pronounced fractality, and the pattern of protobacteria has a bright form - the balance of present and absent 63-dimensions in its DNA is clearly visible (Fig. 9).

General scientific methods of studying nucleic acids, as a rule, concentrate their attention on those fragments that are present in them. The proposed method allows to present in a clear form the phenomenology and features of the deficit and presence of different types of N-

mers. The absent and present N-dimensions of the protobacterial genome in Fig. 9 make up a beautiful fractal. Thus, the geometric approach allows to display the balance of present and absent 63-merials forming structured fractal clusters in Figs. 8 and 9.

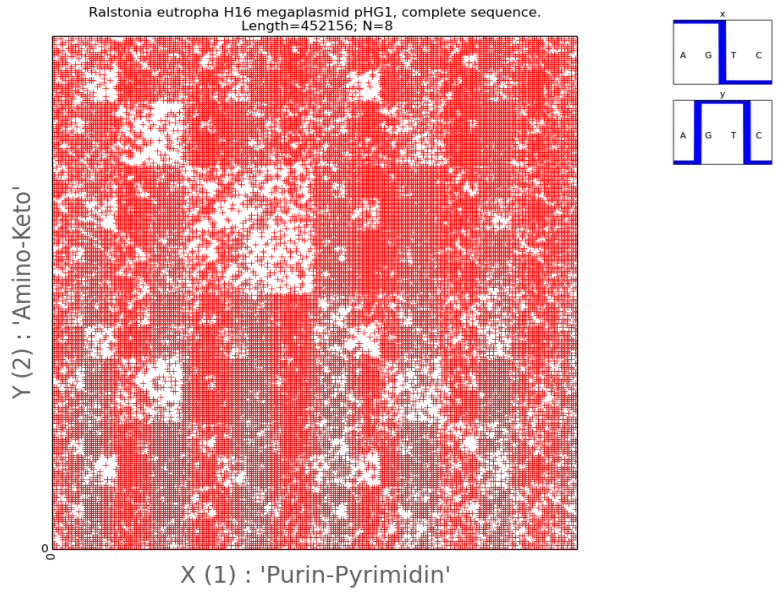


Fig.8. Illustration of two-dimensional representation of the nucleotide composition of the bacterial genome. The axes of abscissa and ordinate correspond to the decimal representation of binary coding of each 8-wire. One of the characteristic patterns having fractal nature.

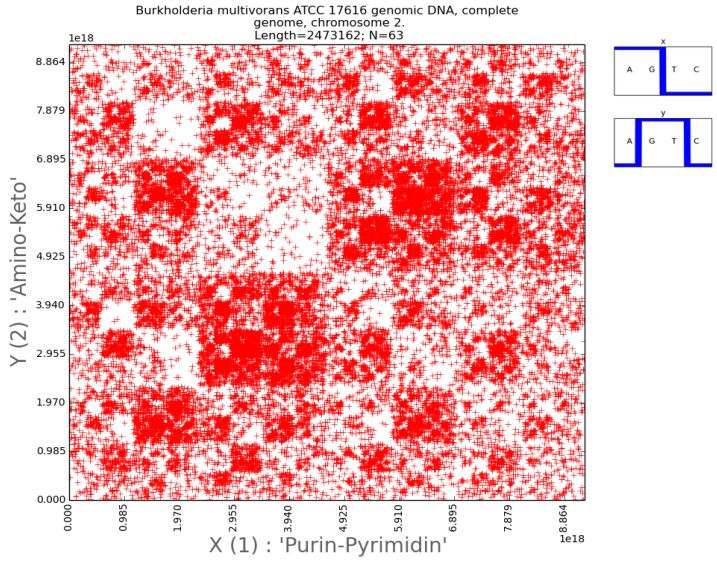


Fig.9. Illustration of two-dimensional representation of nucleotide composition of the second chromosome of protobacteria. It can be seen that in this organism the present and absent 63 wraps form a symmetrical fractal mosaic, the structure of which is stable with respect to the reversal of flowers. To axes of abscissa and ordinate there correspond decimal notions of binary coding of each 63-platform.

The conducted researches and analysis of visualizations of nucleotide sequences of different kinds of living organisms confirm that nucleotide composition can be identical in organisms which are not related in the phylogenetic tree and different in related organisms [12]. A special class of symmetries implemented in long DNA sequences of different organisms is known. In work S.V. Petukhov [22] fractal genetic networks are resulted and tetragroup symmetries are described. Thus, the known scientific data on fractality of DNA are visually displayed on the basis of the offered method.

Fig. 10 shows an example of integral-two-dimensional representation of human chromosome nucleotide composition on one of the visualization planes. Examples of genetic mosaics built in non-position number system are given in [9].

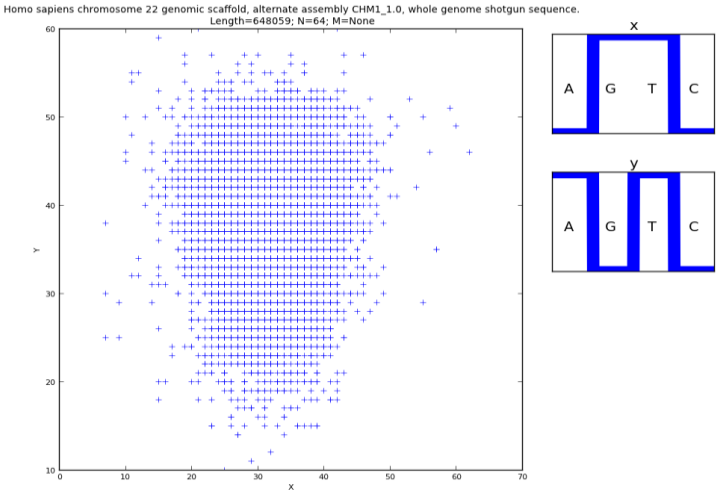
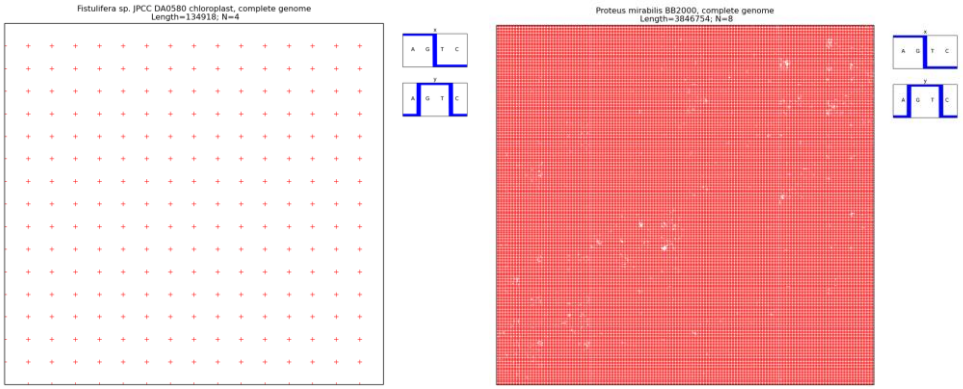


Fig.10. Illustration of integral-double representation of human chromosome nucleotide composition on one of the visualization planes. A pair of Walsh functions used for parameterization is shown on the right. The axes of abscissa and ordinate correspond to the number of units of each 64 wafer using a pair of binary-opposition subalphabets.

Preliminary results of the two-dimensional visualization method allow to draw a conclusion about high stability of the final mosaics at noise of the initial sequence, including at shifts of the sequence reading frame, in cases of removal of arbitrary fragments of the sequence (thinning), at reversing of the whole analyzed chain or its fragments, at different types of rearrangements of N-mers and nucleotides (in some cases up to complete rearrangement of all nucleotides in the sequence). In particular, the stability of mosaic patterns was observed at removal of every second nucleotide, every third nucleotide, etc. In this case, the visualization of nucleic acids in two-dimensional spaces in a number of cases is characterized by pronounced symmetry and stability not only to noise in the original data, but also to different values of the parameter N scale within a certain range - this effect can be seen in the animations:



For further research, random sequences of nitrogenous bases with a length of 100,000 nucleotides were created with the help of the developed computer program, divided into N-brands of 8, 16 and 28. The randomly generated sequences during visualization gave a pattern with all points scattered chaotically (Fig. 11, upper row). Their visual representations are irregular,

chaotic in nature with the complete absence of any mosaics on all subalphabets, which significantly distinguishes them from real long nucleotide sequences.
We have also created pseudo-random nucleotide sequences on the computer, observing the second Chargaff rule, valid for each of the two strands of DNA [1,11]. Fig. 11 shows a comparison of the sequences that were randomly created without observing (bottom row) and with observing (top row) the second Chargaff rule. For these sequences a special type of regularities at different values of N, equal to 6.7 and 20 was visualized. From Fig. 11 we can see that the random pattern, built by the second rule of Chargaff, is structured due to the presence of empty flat areas, which are evenly distributed and especially clearly visible at N = 6 in Fig. 11 in the lower row on the left. At the same time, as noted above, a random pattern created without observing the Chargaff ratio has a chaotic character in the visualization (upper row). From this it is possible to draw a conclusion about geometrical connection of visualization patterns by author's algorithm with algebraic rules of Chargaff.

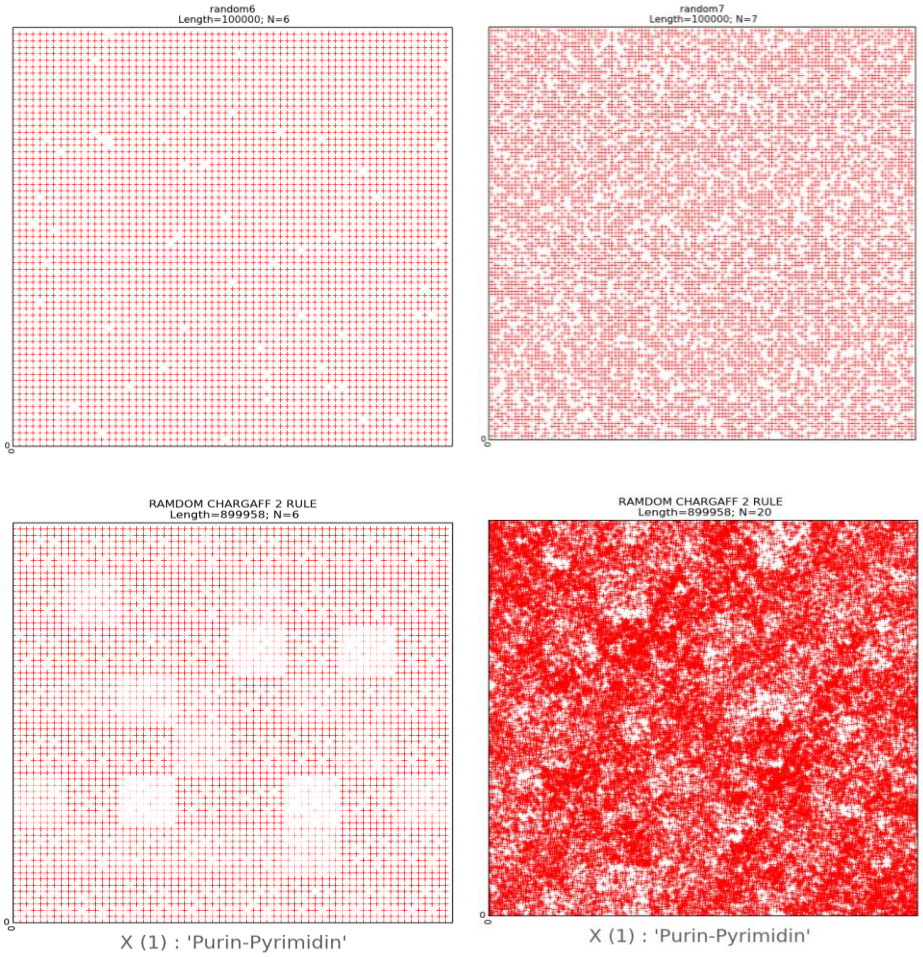


Fig.11. The upper row is an illustration of a two-dimensional representation of the composition of a randomly generated nucleotide sequence without following the Chargaff rules. The lower row is an example of two-dimensional representation of the nucleotide composition of a randomly generated sequence taking into account the second Chargaff rule. The abscissa and ordinate axes correspond to decimal representations of the binary coding of each N-platform.

Thus, two-dimensional visualization of chains of nitrous bases allows to display variants of performance of quantitative rules of Chargaff [1,11] with application of the apparatus of final geometry [21]. This fact can help in the study of internal symmetries and other characteristics of nucleic acids to study complex relationships between living organisms.

We have constructed visual representations of DNA of different kinds of penicillin. The obtained results testify that genomes of this group, as a rule, generate mosaics of high density resembling mosaics of random sequences, which testifies to the high diversity of nucleotide composition. Perhaps the medical value of penicillin is related to this particular feature.
Thus, two-dimensional imaging methods seem useful for studying hidden patterns in chromosomes, as well as for classification and comparative analysis of different genomes with possible applications in biotechnology and medicine.

3.3 Visualization of nucleic acids in three one-dimensional spaces of physical and chemical nucleotide parameters

As noted, binary subalphabets are linked by an addition operation on the module two and set the space with properties in which the coordinates of each point are linked. In this regard, it makes sense to consider each dimension separately. There are three parametrically one-dimensional linked visualisation spaces. Using parametrically one-dimensional coordinate axes {X}, {Y} and {Z} gives three different mappings using corresponding sub-alphabets. The abscissa axis encodes the serial number of the N-platform, the ordinate axis encodes the ascending ordered decimal values of the binary representation of each N-platform (note: the visualization itself is two-dimensional, but the parametric measurement is one).
Figure 12 shows an example of visualization of a human chromosome where areas with different nucleotide composition are clearly visible. These specific regions are marked with arrows in the figure and can be visualized at different scales in two-dimensional imaging spaces for their detailed analysis.

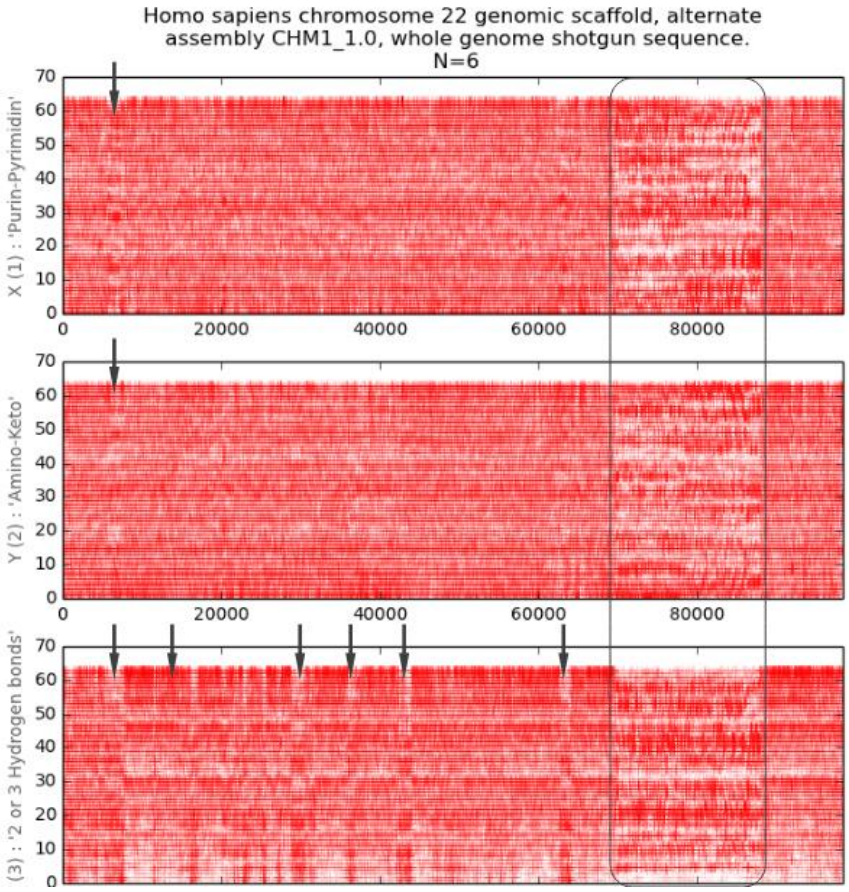


Fig.12. Visualization of the three-channel representation of the nucleotide composition of the 22nd chromosome fragment of Homo Sapiens. Each of the three projections corresponds to a binary-opposition sub-alphabet. In each channel the abscissa axis encodes the ordinate

number of the N-platform, the ordinate axis encodes the ascending ordered decimal values of the binary representation of the N-platform. The arrows highlight some areas with different nucleotide composition. A large area with different nucleotide composition is circled. We can see that in different parts of the chromosome the nucleotide composition may differ for each of the channels.

In Figures 13 and 14, an integral one-dimensional visualization of the total number of units in N-dimensional codes is additionally given for each of the three sub-alphabets. The resulting graphs allow to estimate changes in the nucleotide composition when reading a fragment of a molecule from beginning to end. The depth of registered changes is determined by the scaling parameter N.

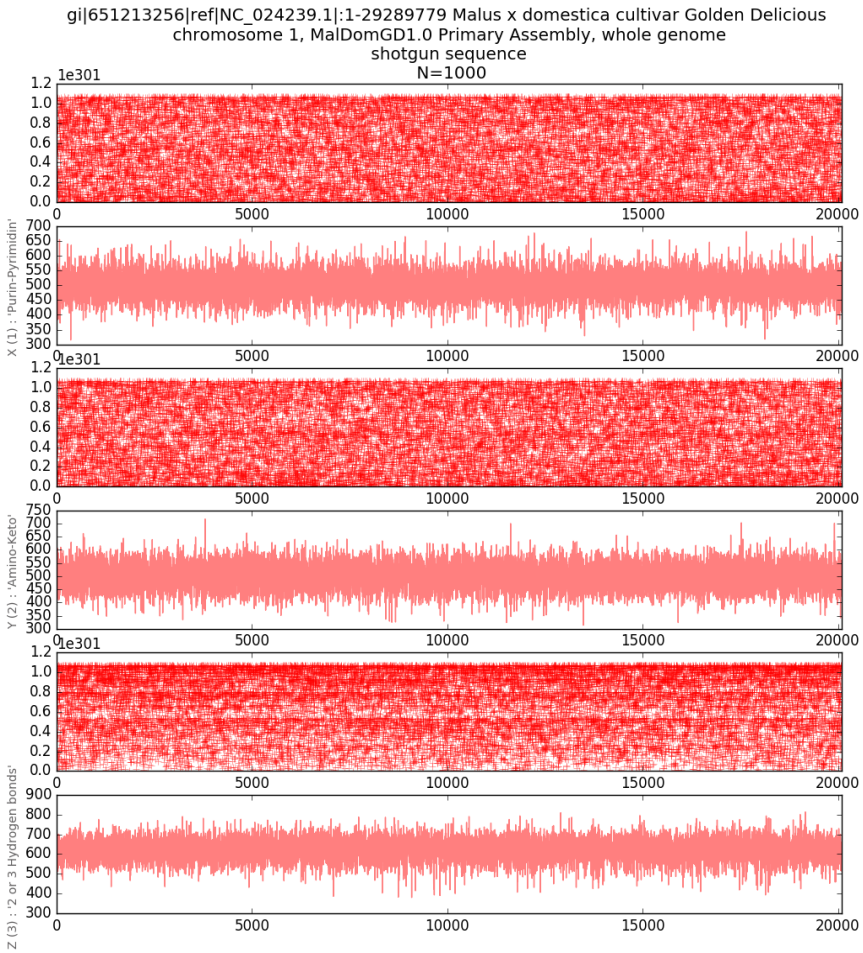


Fig.13. Visualization of the three-channel representation of the nucleotide composition of the apple's 1st chromosome fragment. Each of the three rows corresponds to a binary-opposition sub-alphabet. The abscissa axis encodes the serial number of 1,000-plet, the ordinate axis encodes the number of units in 1,000-plet.

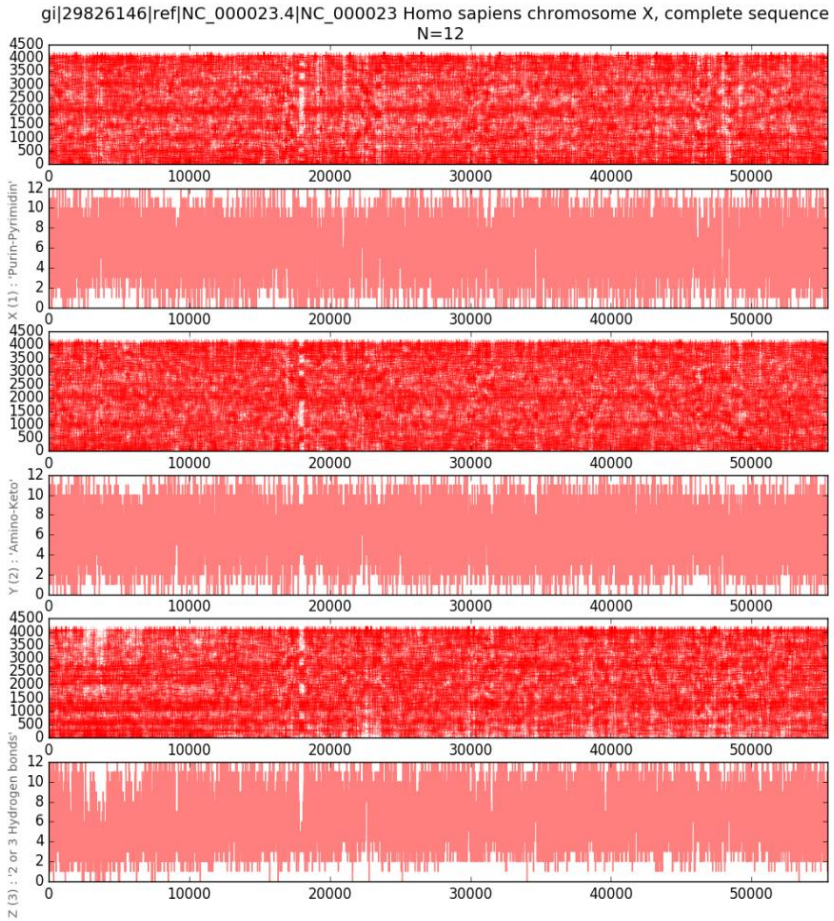


Fig.14. Visualization of the three-channel representation of the nucleotide composition of the human X chromosome. Each of the three rows corresponds to a binary-opposition sub-alphabet. The abscissa axis encodes the serial number of the 12-platform, the ordinate axis encodes the number of units in the 12-platform.

Parametric one-dimensional imaging methods are convenient because they allow to display the nucleotide composition of the chromosome, as it is impossible to display it in two-dimensional and three-dimensional projections. In this regard, the described one-dimensional imaging methods seem to be informative and promising for further studies.
It should be noted that three-channel representation is combined with the classical theory of color perception (RGB), in which it is considered that the eye perceives three basic colors: red, green and blue, and combinations of the three basic colors can get the rest of the colors. This theory is mentioned in [15] in connection with genetic algebra. Each of three channels of one-dimensional visualization can be compared to one of three basic colours. Intensity of colour of each point of two-dimensional visualisation is various, therefore two-dimensional and three-dimensional representations allow to consider combinations of colours. It allows to strengthen color perception in genetics and opens new possibilities for parametric visualization according to the stated method (however, our experiments showed that it considerably increases counting time).
For the author's method of parametric imaging it is proposed to introduce a new term "genetic geometry" or "genometry" as the basis for the corresponding scientific direction in the field of molecular-biological biosemiotics [19].

4. Conclusions

The result of the study is the achievement of the goal to develop methods of visualization of long nucleotide sequences. The connections of molecular genetic systems with Hadamard's binary number system and matrixes are demonstrated. The hypothesis about the possibility of visualizing the internal symmetries in the nucleotide composition was confirmed. Nucleic acids have a visual representation. Parametric visualization of both fragments and entire molecules of DNA and RNA allowed to substantiate their connection with geometric mosaics of different types (see, for example, Fig. 4-9). The proposed method allows to estimate the types of relations between present and absent N-meters in DNA of different organisms (these relations can be characterized by fractal-cluster organization, a vivid example - Fig. 9). The scaling parameter N makes it possible to investigate the genome at many levels of detail to find hidden symmetries and regularities.

The emergence of reasonable methods for comparing geometric representations of genotypes with certain phenotypic features expands the methods of research in molecular genetics. In addition, it opens up the possibility of modeling pseudo-random nucleotide sequences with observance of the phenomenological rules of Charghaff for their visualization and further research. Large-scale parametric visualization of the nucleotide composition contributes to a deeper understanding of genetic phenomena not only by simplifying perception, but also by using adaptive neural network technologies, as the structure of chromosomes of living organisms, represented in the binary code, corresponds to the format of binary artificial neural networks [13].

The author's method of visualization is an additional criterion of classification and detection of interspecific relationships. In this regard, modern ontologies and thesauruses for organization and storage of molecular genetic data can be equipped with visualization options for educational purposes, as well as for presentation and search of biological information. The proposed method can also help advance the understanding of the principles of the immune system in recognizing the nucleotide composition of viruses, DNA of parasites, as well as in food chains and ecosystems. Geometric concepts can help in the study of point mutation mechanisms and CRISPR-Cas systems [16]. It becomes possible due to visual interpretation of basic characteristics of polynucleotide fragments of a certain nucleotide composition with visualization of the final geometry and structure of the genetic code.

The presented results allow us to speak about the author's methods of nucleic acids visualization as a scale-parametric model of DNA, which complements the structural model of the double helix of J. Watson and F. Creek [17,18].

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References

1. Chargaff E, Lipshitz R, Green C (1952). "Composition of the deoxypentose nucleic acids of four genera of sea-urchin" (PDF). J Biol Chem.195 (1): 155–160. PMID 1493836
2. S.V.Petoukhov, M.He. Symmetrical Analysis Techniques for Genetic Systems and Bioinformatics: Advanced Patterns and Applications. 2010, Hershey, USA: IGI Global. 271 p.
3. N.A.Balonin, Y.N.Balonin, D.Z. Djokovic, D.A. Karbovskiy, M.B.Sergeev. Construction of symmetric Hadamard matrices https://arxiv.org/abs/1708.05098
4. Georgiou, S.; Koukouvinos, C.; Seberry, J. (2003). "Hadamard matrices, orthogonal designs and construction algorithms".Designs 2002: Further computational and constructive design theory. Boston: Kluwer. pp. 133–205. ISBN 1-4020-7599-5.
5. I.V. Stepanian, S.V. Petoukhov. The matrix method of representation, analysis and classification of long genetic sequences http://arxiv.org/pdf/1310.8469.pdf
6. H., Harmuth Applying of methods of theory of information in phisics / - Moscow.: Mir, 2016. - p. 344.

7. Ferleger, Sergei V. (March 1998). RUC-Systems In Non-Commutative Symmetric Spaces (Technical report). MP-ARC-98-188.
8. Jeffrey H.J. (1990). Chaos game representation of gene structure. - Nucleic Acids Research, Vol.18, No.8, p. 2163-2170.
9. Feldman, David P. (2012), "17.4 The chaos game", Chaos and Fractals: An Elementary Introduction, Oxford University Press, pp. 178–180, ISBN 9780199566440.
10. G. Darvas, A.A. Koblyakov, S.V.Petoukhov, I.V.Stepanyan. Symmetries in molecular-genetic systems and musical harmony // Symmetry: Culture and Science Vol. 23, No. 3-4, 343-375, 2012 http://symmetry.hu/scs_online/SCS_23_3-4.pdf
11. Rudner, R; Karkas, JD; Chargaff, E (1968). "Separation of B. SubtilisDNA into complementary strands. 3. Direct analysis".Proceedings of the National Academy of Sciences of the United States of America. 60(3): 921–2. doi:10.1073/pnas.60.3.921. PMC 225140. PMID 4970114.
12. Townsend JP, Su Z, Tekle Y (2012). "Phylogenetic Signal and Noise: Predicting the Power of a Data Set to Resolve Phylogeny". Genetics. 61(5): 835–849. doi:10.1093/sysbio/sys036. PMID 22389443.
13. Stepanyan I.V., Ziep N.N. Growing convolutional neural-like structures for problems of recognition of static images // Neurocomputers: development, application. 2018. № 5. pp. 4-11.
14. ftp://ftp.ncbi.nlm.nih.gov/
15. Petukhov, S.V. Matrix genetics, algebra of genetic code, noise immunity. - M.: RHD. - 2008.
16. Ikeda T., Tanaka W., Mikami M., Endo M., Hirano H.-Y. Generation of artificial drooping leaf mutants by CRISPR-Cas9 technology in rice // Genes & Genetic Systems. — 2016. — Vol. 90, no. 4. — P. 231—235. — DOI:10.1266/ggs.15-00030. — PMID 26617267.
17. Crick FH, Wang JC, Bauer WR (April 1979). "Is DNA really a double helix?" (PDF). J. Mol. Biol. 129 (3): 449–57. doi:10.1016/0022-2836(79)90506-0. PMID 458852.
18. Wilkins MH, Stokes AR, Wilson HR (1953). "Molecular Structure of Deoxypentose Nucleic Acids" (PDF). Nature. 171 (4356):738–740. Bibcode: 1953 Natur. 171..738W. doi:10.1038/171738a0. PMID 13054693.
19. Sharov A. (1992). Biosemiotics: functional-evolutionary approach to the analysis of the sense of information. In: Biosemiotics: The Semiotic Web 1991. T.A.Sebeok and J.Umiker-Sebeok (eds.), 345-373. Berlin: Mouton de Gruyter.
20. Waterman M.S. Introduction to Computational Biology. Map, Sequences and Genomes. London: Chapman & Hall, 1995. xvi + 432 pp.
21. Batten, Lynn Margaret (1997), Combinatorics of Finite Geometries, Cambridge University Press, ISBN 0521590140
22. Petoukhov S.V., Petukhova E.S., Svirin V.I. New Symmetries and Fractal-Like Structures in the Genetic Coding System. – Advances in Intelligent Systems and Computing, v. 754, 2018, p. 588-600, https://doi.org/10.1007/978-3-319-91008-6_60
23. Mcdonnell K, Waters N, Howley E, Abram F. Chordomics: a visualisation tool for linking function to phylogeny in microbiomes. Bioinformatics. 2019;
24. Mathema VB, Dondorp AM, Imwong M. OSTRFPD: Multifunctional Tool for Genome-Wide Short Tandem Repeat Analysis for DNA, Transcripts, and Amino Acid Sequences with Integrated Primer Designer. Evol Bioinform Online. 2019;15:1176934319843130.
25. Iacoangeli A, Al khleifat A, Sproviero W, et al. DNAscan: personal computer compatible NGS analysis, annotation and visualisation. BMC Bioinformatics. 2019;20(1):213.
26. Martens KJA, Van beljouw SPB, Van der els S, et al. Visualisation of dCas9 target search in vivo using an open-microscopy framework. Nat Commun. 2019;10(1):3552.