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Genetic Biomechanics, Stochastic Rules of Genomes, and Stochastic Resonance

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Abstract. The universal rules and numerical symmetries in the stochastic organization of DNA molecules in the genomes of higher and lower organisms are presented. To understand the dictatorial influence of DNA on inherited macrostructures, a model approach is proposed based on the well-known phenomenon of stochastic resonance, which amplifies weak periodic signals in nonlinear systems by pumping them with energy of surrounded noise. To comprehend a number of bio-phenomena, the concept of stochastic solitons is proposed.

INTRODUCTION

A living organism is a heterogeneous stochastic set of a huge number of molecules of many species, which has the ability to genetically inherit the characteristics of an organism to the next generation. G. Mendel discovered in experiments on the crossing of organisms that the inheritance of traits obeys certain algebraic rules. This testifies to the existence of hidden rules of stochastic processes in living matter, subject to disclosure.

The creators of quantum mechanics P. Jordan and E. Schrödinger pointed out the key difference between living bodies and inanimate ones: inanimate objects are controlled by the average random motion of their millions of particles and the motion of individual particles is not essential for the whole; on the contrary, in a living organism, the chosen - genetic - molecules have a dictatorial influence on the entire organism due to some mechanisms of increasing their influence (see the history of "quantum biology" [1]).

The study of the mechanisms of the dictatorial influence of genetic DNA molecules on inherited biological macrostructures is an urgent task, important for the disclosure of informational patents of wildlife in the interests of biomedical, agro-industrial, engineering and other sciences. Studies of the features of the molecular system of genetic coding and its relationship with the inherited traits of organisms are being carried out with increasing intensity in all developed countries. In particular, the Department of Vibration Biomechanics of the IMASH RAS is carrying out planned work on genetic biomechanics, which analyzes the structural connections of the molecular genetic system with inherited physiological systems bearing the imprint of genetic coding (see, for example, [2-6]). At the same time, special attention of researchers requires the phenomenon of stochastic organization of living bodies, associated, in particular, with the well-known concepts of “gene noise" and "cellular noise”: for example, even genetically identical cells within the same tissue exhibit different levels of protein expression, different sizes and structures because of the stochastic nature of the interactions of individual molecules in cells.

The aim of this study is to identify numeric symmetries and rules in the stochastic organization of nucleotide sequences in the DNA of genomes of higher and lower organisms, as well as to develop model concepts of the inherited mechanisms of the dictatorial influence of genetic structures and processes of the molecular level onto biological macro-objects.

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MATERIALS AND RESEARCH METHODS

In this work, the initial data on the nucleotide sequences of single DNA strands of different genomes were taken from the publicly available GenBank genomic data bank (https://www.ncbi.nlm.nih.gov/genbank/). These genomic DNA sequences consist of many millions of nucleotides (molecular "letters") of four types: adenine A, guanine G, cytosine C and thymine T. This nucleotide system is endowed with binary-oppositional features:

1. two of these molecules are purines (A and G) and the other two are pyrimidines (C and T). Taking into account these oppositions, you can represent C = T = 0, A = G = 1;
2. two molecules are keto molecules (G and T) and the other two are amino molecules (A and C). Taking into account these oppositional indicators, you can present A = C = 0, G = T = 1.

This system of binary oppositions makes it possible to represent DNA alphabets of 4 nucleotides, 16 duplets, 64 triplets, ... in the form of square tables, the rows of which are numbered with binary indicators “pyrimidine or purine” (C = T = 0, A = G = 1), and the columns are numbered by binary indicators “amino or keto” (C = A = 0, T = G = 1). In such tables, all nucleotides (monoplets), duplets, triplets and other n-alphabets of DNA automatically take their strictly individual place (Fig. 1). The resulting family of tables of DNA alphabets turns out to be a tensor family of matrices $[C, A; T, G]^{(n)}$, where (n) is the tensor power [2].

	0	1
0	C	T
1	A	G

;

	00	01	10	11
00	CC	CT	TC	TT
01	CA	CG	TA	TG
10	AC	AT	GC	GT
11	AA	AG	GA	GG

;

	000	001	010	011	100	101	110	111
000	CCC	CCT	CTC	CTT	TCC	TCT	TTC	TTT
001	CCA	CCG	CTA	CTG	TCA	TCG	TTA	TTG
010	CAC	CAT	CGC	CGT	TAC	TAT	TGC	TGT
011	CAA	CAG	CGA	CGG	TAA	TAG	TGA	TGG
100	ACC	ACT	ATC	ATT	GCC	GCT	GTC	GTT
101	ACA	ACG	ATA	ATG	GCA	GCG	GTA	GTG
110	AAC	AAT	AGC	AGT	GAC	GAT	GGC	GGT
111	AAA	AAG	AGA	AGG	GAA	GAG	GGA	GGG

FIGURE 1. Examples of matrices of n-alphabets of DNA from the tensor family of matrices $[C, A; T, G]^{(n)}$.The cases of alphabets of 4 nucleotides, 16 doublets and 64 triplets is presented

A feature of our research approach, which turned out to be effective, is the consideration of each of the genomic nucleotide sequences of a single DNA strand as a set of parallel n-texts, each of which is written in its own n-alphabet. For example, the nucleotide sequence CAGGATCGACGT ... is represented simultaneously as a set of n-texts: a 1-text C-A-G-G-A-T-C-G-A-C-G-T- ..., a 2-text CA-GG-AT-CG-AC-GT- ..., a 3-text CAG-GAT-CGA-CGT- ..., a 4-text CAGG-ATCG-ACGT-… and so on. In each of these n-textual representations of the studied genomic DNA sequence, the percentage of each of the kinds of n-plets, that are members of the corresponding n-alphabet, is calculated using a computer program (created by V.I.Svirin). The resulting set of data on the percents compositions of n-texts is analyzed to identify possible regular relationships of a stochastic nature in it. Then the identified relationships are interpreted from the standpoint of various model approaches.

RESULTS AND DISCUSSION

The described method was used to analyze the percentage of n-texts of the following genomic DNA: 1) all 24 human chromosomes; 2) all the chromosomes of Drosophila, mouse, worm, many plants; 3) 19 genomes of bacteria and archaea; 4) many extremophiles living in extreme conditions, including, for example, radiation with a level exceeding 1000 times fatal to humans. Due to this analysis, the rules and symmetries of the stochastic organization of genomes, common to all these genomic DNAs, and therefore are currently candidates for the role of universal genomic rules, have been identified. Below are some of the obtained rules and symmetries on the example of the nucleotide sequence of single-stranded DNA of human chromosome No. 1, containing about 250 million nucleotides A, C, T, G and taken from GenBan (https://www.ncbi.nlm.nih.gov/ nuccore / NC_000001.11). Figure 2 shows the percentages of each of 4 nucleotides, 16 duplets, and 64 triplets, respectively, in its monoplet, duplet, and triplet representations (i.e., in its 1-textual, 2-textual, and 3-textual representations). These percentages in the form of fractions of one, are shown inserted into the corresponding cells of the matrice of DNA alphabets from Fig. 1

	0	1
0	%C	%T
1	%A	%G

=

	0	1
0	20.85	29.10
1	29.18	20.87

	00	01	10	11
00	%CC	%CT	%TC	%TT
01	%CA	%CG	%TA	%TG
10	%AC	%AT	%GC	%GT
11	%AA	%AG	%GA	%GG

=

	00	01	10	11
00	5.409	7.274	5.033	9.504
01	7.134	1.031	7.429	7.137
10	6.008	6.312	4.402	6.008
11	9.568	7.286	5.046	5.419

	000	001	010	011	100	101	110	111
000	%CCC	%CCT	%CTC	%CTT	%TCC	%TCT	%TTC	%TTT
001	%CCA	%CCG	%CTA	%CTG	%TCA	%TCG	%TTA	%TTG
010	%CAC	%CAT	%CGC	%CGT	%TAC	%TAT	%TGC	%TGT
011	%CAA	%CAG	%CGA	%CGG	%TAA	%TAG	%TGA	%TGG
100	%ACC	%ACT	%ATC	%ATT	%GCC	%GCT	%GTC	%GTT
101	%ACA	%ACG	%ATA	%ATG	%GCA	%GCG	%GTA	%GTG
110	%AAC	%AAT	%AGC	%AGT	%GAC	%GAT	%GGC	%GGT
111	%AAA	%AAG	%AGA	%AGG	%GAA	%GAG	%GGA	%GGG

=

	000	001	010	011	100	101	110	111
000	1.385	1.878	1.524	1.861	1.183	1.977	1.447	3.693
001	1.853	0.291	1.789	2.104	1.622	0.254	2.375	1.988
010	1.758	1.275	0.251	0.227	1.317	1.942	1.441	2.237
011	2.009	2.088	0.259	0.291	2.388	1.781	1.614	1.848
100	1.588	1.964	1.103	1.986	1.255	1.456	0.962	1.960
101	2.226	0.233	1.939	1.284	1.437	0.253	1.327	1.756
110	1.972	1.981	1.457	1.947	0.956	1.115	1.256	1.600
111	3.725	1.884	1.988	1.895	1.445	1.534	1.185	1.382

FIGURE 2. Matrices of the percentage composition of n-texts regarding n-plets) in DNA of human chromosome No. 1, reproducing matrices from Fig. 1 under replacing symbols of n-plets by percentages of these n-plets (n = 1, 2, 3)

At first glance, the set of percentages in the resulting matrices (Fig. 2) is rather chaotic, and, in particualr, the percentage of n-plets presented depends significantly on the order of the letters in them. For example, the percentage of the duplets CG and GC having the same letter composition differs several times: %CG = 1.03 and %GC = 4.40. Likewise, the percentage of triplets of the same letter composition CAT, CTA, ACT, ATC, TCA, TAC differ significantly: %CAT = 1.79, %CTA = 1.27, %ACT = 1.62, %ATC = 1.32, %TCA = 1.96, %TAC = 1.10 and so on.

But, as it turns out, the value of the percentage of nucleotides in the 1-text of this DNA sequence defines with high accuracy the sum of the percentages in special tetra-groupings of n-ples in its n-texts. Table 1 shows, based on the percentage data in Fig. 2, for example, the following:

- The total percentage sum Σ%CN of all 4 duplets CN (hereinafter, the symbol N denotes any of nucleotides A, T, C, and G), that begin with the nucleotide C in the 2-text representation of this DNA, is equal to the percentage of nucleotide C in the 1-text representation of this DNA: Σ%CN ≈ %CC+%CA+%CT+%CG ≈ ≈5.41+7.27+7.13+1.03 ≈20.85 ≈ %C;
- The total percentage sum Σ%NC of all 4 duplets NC, that have nucleotide C in their second position, is also practically equal to %C: Σ%NC ≈ %CC+%AC+%TC+%GC ≈ 5.4+5.03+6.01+4.40 ≈ ≈ 20.85 ≈ % C;
- and so on.

The same is true in the genomic DNA for the percent sums of 16 triplets, as well as 64 tetraplets containing nucleotide C in the first, or second, or third, or fourth positions, that is, for the sums Σ%CNN, Σ%NCN, Σ%NNC, Σ%CNNN, Σ%NCNN, Σ%NNCN, Σ% NNNC, in which the values of the summands are significantly different. Table 1 shows similar equalities between the percentages of each of the four nucleotides C, A, T, G in a 1-text of the DNA, from one side, and the percentage sum of corresponding n-plets groupings in the appropriate n-texts of the same DNA, from the second side (n = 1, 2, 3, 4).

TABLE 1. The percentage of each of the nucleotides C, G, A, T vs the percentage sums of doublets, triplets and tetraplets containing nucleotides in the indicated positions, for the case of the corresponding n-texts of the DNA of human chromosome No. 1. The symbol N denotes any of the 4 nucleotides.

%C ≈ 20.85	%G ≈ 20.87	%A ≈ 29.10	%T ≈ 29.18
Σ%CN ≈ 20.85	Σ%GN ≈ 20.88	Σ%AN ≈ 29.10	Σ%TN ≈ 29.17
Σ%NC ≈ 20.85	Σ%NG ≈ 20.87	Σ%NA ≈ 29.10	Σ%NT ≈ 29.18
Σ%CNN ≈ 20.84	Σ%GNN ≈ 20.88	Σ%ANN ≈ 29.10	Σ%TNN ≈ 29.17
Σ%NCN ≈ 20.85	Σ%NGN ≈ 20.88	Σ%NAN ≈ 29.10	Σ%NTN ≈ 29.17
Σ%NNC ≈ 20.85	Σ%NNG ≈ 20.87	Σ%NNA ≈ 29.10	Σ%NNT ≈ 29.18
Σ%CNNN ≈ 20.85	Σ%GNNN ≈ 20.88	Σ%ANNN ≈ 29.10	Σ%TNNN ≈ 29.17
Σ%NCNN ≈ 20.85	Σ%NGNN ≈ 20.87	Σ%NANN ≈ 29.10	Σ%NTNN ≈ 29.18
Σ%NNCN ≈ 20.85	Σ%NNGN ≈ 20.88	Σ%NNAN ≈ 29.10	Σ%NNTN ≈ 29.18
Σ%NNNC ≈ 20.85	Σ%NNNG ≈ 20.87	Σ%NNNA ≈ 29.10	Σ%NNNT ≈ 29.18

These rules and numerical symmetries in the stochastic tetra-grouping organization of genomic DNA resemble another phenomenon of deterministic stochastics on a different scale of biological organization: meiosis of germ cells, in which one stochastically organized germ cell gives rise to four similar stochastically organized germ cells.

Let us now turn to another kind of numerical symmetries in the stochastic organization of genomic DNA, associated with the binary oppositional (or Yin-Yang) principle. These stochastic symmetries of the Yin-Yang kind are revealed from the analysis of the percentages of different n-plets, which are located in strict orders in the tensor family of alphabetical matrices, whose examples are shown in Fig. 2. Consider the sums of the percentages of n-plets written in those pairs of columns of these matrices, the binary numbering of which is bit-inverted, that is, it differs by the inversion of binary symbols 0 → 1 and 1 → 0. For example, two binary numbers 101 and 010 are bit-inverted. We draw attention to the following phenomenological rule of the stochastic organization of genomes: any two columns of matrices (Fig. 2), which are numbered by bit-reversible binary numbers, have practically identical sums of percentages of n-plets in them (though the individual percentages of n-plets in each of the columns are significantly different). Tables 2 and 3 show examples of this numerical symmetry (equality) of percentage sums of n-plets in columns, which have bit-inverted numberings both in the matrix of percents of duplets in the 2-text of this DNA and in the matrix of percents of triplets in the 3-text of this DNA. Similar numerical symmetries are also valid for rows with bit-inverted numberings in the same matrices in Fig. 2 (see Tables 4 and 5).

TABLE 2. Percents sums of duplets in the columns of the probability matrix of 16 duplets from Fig. 2. Dotted frames mark pairs of columns numbered with bit-inverted numbers. In each of the frames, the percentages in both columns are practically the same.

Column Numbers	Percentage Sums of Duplets in Columns
00	5.409+7.134+6.008+9.568 = 28.119
11	9.504+7.137+6.008+5.419 = 28.068
01	7.274+1.031+6.312+7.286 = 21.903
10	5.033+7.429+4.402+5.046 = 21.910

TABLE 3. Percentage sums in the columns of the probability matrix of 64 triplets from Fig. 2. Dotted frames mark pairs of columns having bit-inverted numberings. In each of the frames, the percentages in both columns are practically the same.

Column Numbers	Percentage Sums of Duplets in Columns
000	1.385+1.853+1.758+2.009+1.588+2.226+1.972+3.725 = 16.516
111	3.693+1.988+2.237+1.848+1.960+1.756+1.600+1.382 = 16.464
001	1.878+0.291+1.275+2.088+1.964+0.233+1.981+1.884 = 11.594
110	1.447+2.375+1.441+1.614+0.962+1.327+1.256+1.185 = 11.607
010	1.524+1.789+0.251+0.259+1.103+1.939+1.457+1.988 = 10.310
101	1.977+0.254+1.942+1.781+1.456+0.253+1.115+ 1.534 = 10.312
011	1.861+2.104+0.227+0.291+1.986+1.284+1.947+1.895 = 11.595
100	1.183+1.622+1.317+2.388+1.255+1.437+0.956+1.445 = 11.603

TABLE 4. Percentage sums in the rows of the probability matrix of 16 duplets from Fig. 2. Dotted frames mark pairs of rows numbered by bit-reversible numbers. In each of the frames, the percentages in both rows are practically the same.

Numbers of Rows	Percentage Sums of Duplets in Rows
00	5.409+7.274+5.033+9.504 = 27.219
11	9.568+7.286+5.046+5.419 = 27.319
01	7.134+1.031+7.429+7.137 = 22.730
10	6.008+6.312+4.402+6.008 = 22.731

TABLE 5. Percentage sums in the rows of the probability matrix of 64 triplets from Fig. 2. Dotted frames mark pairs of rows numbered by bit-inverted numbers. In each of the frames, the percentages in both rows are practically the same.

Numbers of Rows	Percentage Sums of Triplets in Rows
000	1.385+1.878+1.524+1.861+1.183+1.977+1.447+3.693 = 14.946
111	3.725+1.884+1.988+1.895+1.445+1.534+1.185+1.382 = 15.039
001	1.853+0.291+1.789+2.104+1.622+0.254+2.375+1.988 = 12.275
110	1.972+1.981+1.457+1.947+0.956+1.115+1.256+1.600 = 12.285
010	1.758+1.275+0.251+0.227+1.317+1.942+1.441+2.237 = 10.448
101	2.226+0.233+1.939+1.284+1.437+0.253+1.327+1.756 = 10.456
011	2.009+2.088+0.259+0.291+2.388+1.781+1.614+1.848 = 12.277
100	1.588+1.964+1.103+1.986+1.255+1.456+0.962+1.960 = 12.273

These and other data from our research on the rules of the stochastic organization of genomes indicate a special "partially deterministic stochasticity" in living bodies, that is, the stochasticity with elements brought together in blocks of mutually related and predictable integral characteristics.

Let us now turn to the question of the amplification mechanisms that provide the dictatorial influence of DNA and RNA molecules on the inherited macrostructures created on the basis of special stochastic processes. Since we are talking about stochastic organization, it is necessary to look for model approaches to solving this problem in the field of known physical phenomena, in which it is stochastic processes or noises that play an important role. Here the authors are developing - in relation to the problems of genetic informatics - the topic of stochastic resonance [6].

We are talking about the well-known phenomenon of amplification in nonlinear systems of weak periodic signals flowing against a background of noise, the energy of which is partially pumped into these signals. The concept of stochastic resonance appeared in science in 1981. Currently, its theory and applications in various fields, including biomedical, are devoted to over 13000 publications, including a series of articles in the journal Nature [8-17]. In particular, stochastic resonance methods are used in medical clinics and centers in different countries.

The phenomenon of stochastic resonance speaks of the usefulness of noise - in some cases - for transmitting information, contrary to the previous opinion that noise is always a hindrance. For research and applied purposes, the occurrence of stochastic resonance can be controlled by adjusting the appropriate parameters, for example, the intensity of the excitation noise, the structure, and the parameters of nonlinear systems.

A review article in the journal on the successes of physical sciences notes: “From a fundamental scientific point of view, the applications of the theory of stochastic resonance to the study of information processing by biological systems are of the greatest interest. There is reason to believe that in the process of evolution, living organisms have adapted to use the unavoidable internal noise and environmental noise for optimal identification of useful information” [8]. Due to the fact that the genetic system in living bodies has significant specificity, the concept of "genetic stochastic resonance" is introduced by us as a particular case of stochastic resonance for genetically inherited systems. Specific features of the genetic system that should be taken into account in matters of genetic resonance in inherited biological systems include, for example, the biological dissymmetry of left and right isomers discovered by L. Pasteur, which distinguishes living from nonliving structures, as well as the spiral nature of both DNA and inherited biostructures at different levels. It is not for nothing that since the time of W. Goethe spirals have been called lines of life. The DNA double helix is associated with helical antennas used with technology. These antennas generate and receive circularly polarized electromagnetic waves, which makes it possible to exchange information regardless of the spatial orientation of the transmitter and receiver, for example, regardless of the rotation of the spacecraft in space communications. The concept of the double helix of DNA as a helical antenna, emitting and receiving waves of circular polarization, is associated with the aforementioned inherited dissymmetry of left and right forms in living and selective exchange of wave information between biomolecules. Stochastic resonance in such chiral systems with their periodic processes and circular polarization noises has its own specificity, which we study within the framework of the concept of "genetic stochastic resonance", including in connection with the problems of epigenetics in the noise environments of the organism.

To this topic of periodic processes and noises in the body, it can be added that the body is a huge set of coordinated cyclic processes. From the point of view of ancient chrono-medicine, all diseases are the result of irregularities in their coordination. Even proteins are involved in their own life-death cycles, consisting of their periodic breakdown into amino acids and reassembly. So, in humans, the half-life for liver proteins and blood plasma is 10 days, for the hormone insulin - 6-9 minutes, etc. Taking into account this process of constant renewal of the organism, physiologist A.G. Gurvich asserted: “*the main problem of biology is maintaining the form with constant renewal of the substrate*” [18].

But what model approach can be proposed for understanding this phenomenon of maintaining shape with constant renewal of the body compositions? Earlier, in the book on bio-solitons [3], we substantiated - with numerous examples of inherited soliton-like motions in living bodies - the expediency of using the theory of solitons. Solitons are sometimes called "wave atoms" because they simultaneously possess the properties of waves and particles. They have the ability to interact with each other, like charged particles, multiply and die, form ensembles with non-trivial morphology and dynamics of a pulsating and other nature, overcome the tendency to disorder in nonlinear soliton media containing them, etc.

The phenomenon of solitons attracted special attention of the scientific community after the publication of Fermi, Ulam, and Past in 1955 on the computer calculation of oscillations in a simple nonlinear system in the form of a chain of several dozen weights connected by nonlinear springs. The specificity of the behavior of this system was expressed in an unexpected repetitive periodic redistribution of vibrational energy between several lower modes of the excited system. This showed the ability of energy in some media to self-organize into stable ensembles with complex periodic forms of behavior on purely mechanical principles, regardless of the chemical composition of this medium, the configuration of the weights, and everything else that is related to the coefficients of the corresponding soliton equation. Solitons are traps for the energy they absorb, which can be used for external work when a soliton enters a non-soliton medium. Periodic oscillatory processes, shown by Fermi, Ulam, and Pasta on their models, represent an example of important cyclic processes of the solitonic type that are possible in the genetically inherited systems and can be amplified in a noisy environment when part of the noise energy is pumped into them by the mechanism of stochastic resonance. The theory of solitons has already been applied by various authors to modeling the properties of DNA and biological processes (see, for example, [19-22]). The above data on the phenomena of

stochastic block organization of genomic DNA led us to the idea of "stochastic solitons" in genetics, that is, solitons in the form of stable ensembles (blocks) of the percentage composition of genetic elements. This idea, combined with phenomenological data on bio-solitons in inherited macro-systems, seems promising for understanding stochastic genetic structures and phenomena. In our opinion, sine-Gordon solitons, which are the only relativistically invariant type of solitons and which were previously named candidates for the role of fundamental for biology, seem especially promising for modeling in the field of stochastic organization of genetically inherited bio-phenomena [3, p.78-91].

CONCLUSIONS

The nucleotide sequences of DNA molecules in genomes are proposed to be considered as a set of parallel n-texts, each of which is written in its own DNA alphabet, consisting of 4n types of n-lashes. This approach allowed to reveal universal rules and numerical symmetries in the stochastic organization of the percentage composition of n-texts of genomes of higher and lower organisms. The results add the idea of stochastic mechanisms of information coding and the inherited formation of living bodies. These new data led to the concept of the important role of stochastic resonance in providing the dictatorial influence of DNA molecules existing in noise environments on inherited macrostructures. This concept is complemented by the concept of cyclic processes of bio-solitonic type and the concept of stochastic solitons for modeling the phenomena of biological self-organization and maintaining the shape of bio-bodies under a constant renewal of their composition.

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