Harmonic Progression in Bioinformatics and Recurrent Series in Inherited Biostructures

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Abstract. The article is devoted to the study of new approaches to the development of mathematical models in genetic biomechanics, which studies the structural relationships of the genetic coding system with genetically inherited biological forms. More specifically, we are talking about models based on the recurrent harmonic progression whose connection with the information sequences of DNA molecules in the genomes of higher and lower organisms was recently revealed. In particular, the article describes previously unknown connections of the function of natural logarithms with the structures of the molecular genetic system, which allow modelling the main psychophysical logarithmic law by Weber-Fechner and also many other logarithmic structures in genetically inherited biological systems. In physics, the harmonic progression is traditionally considered, first of all, as related to standing waves in resonators. Our results are correlated with Frohlich's vibration-resonant theory about collective quantum effects and long-range communication in biological systems.

1. Introduction

Investigations of symmetries in inherited biological structures are an important component of biomechanics, biophysics, biochemistry, and other sciences of living matter. Many monographs, international forums, including the Nobel Symposium on Symmetries, etc. are devoted to them. The continuation of these studies is an urgent task, which is associated with the disclosure of many secrets of living nature and the creation of new biotechnologies.

In particular, these studies have long drawn attention to the recurrent structure of many inherited biological configurations, which consist of recurrently repeating blocks related, for example, by similarity symmetries; these configurations are abundant in flowers, shells of mollusks, metameric bodies of animal organisms, etc. [1]. The inheritance of configurations relies on the work of the genetic coding system, which allows the reproduction of such forms in a series of generations. Recently, in the genomes of higher and lower organisms, an important rule for the recurrent organization of DNA nucleotide sequences was discovered; these sequences serve for the transfering genetic information [2, 3]. This hyperbolic rule for the relationship of oligomer sums is associated with a long-known harmonic progression (1):

$$1/1, \ 1/2, \ 1/3, \ 1/4, \ ...., \ 1/n \qquad (1)$$

The use of properties of this progression allows building new approches and models in genetic biomechanics, algebraic biology and biotechnologies.

2. Computanional approaches, models

Our computational approaches and models of biological structures are based on the mathematical properties of the harmonic progression (1). Its historically renowned name - "harmonic progression" - derives from its association with a series of harmonics in music (or with a series of standing wavelengths in a vibrating string). It is also indirectly associated with a set of trigonometric functions in the Fourier series. Pythagoras, Orem, Leibniz, Newton, Euler, Fourier, Dirichlet, Riemann and many others were engaged in research of mathematical properties, generalizations and applications of the harmonic progression in various problems. The unexpected discovery of this recurrent harmonic progression in genomes, which are the genetic information basis of living organisms, entails many new scientific issues. The aim and objectives of this study are to study how the mathematical properties of this recurrent genetic progression (1) are able to influence the inherited biomechanical structures bearing the stamp of the structural features of genetic coding. This study leads to the emergence of new model approaches in genetic biomechanics, developing the theme of structural relationships between genetic coding and inherited biomechanical phenomena.

Organisms are cooperative aggregates of a huge number of various molecules that have the ability to reproduce themself in their descendants. Gr. Mendel in experiments on crossing organisms showed that the inheritance of traits to descendants obeys certain algebraic rules. Thus, he actually became the founder of

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algebraic biology, which uses algebraic methods to model inherited biological phenomena. At present, in this regard, an international interdisciplinary seminar "Algebraic biology and systems theory" (https://www.youtube.com/channel/UC8JLsuRzzPsRiH wrwEjMCtw) is functioning in Moscow. According to Mendel's law of independent inheritance of traits, information from the level of genetic DNA molecules dictates the macrostructure of living bodies through many independent channels, despite strong noises and interference. For example, hair, eye, and skin colors are inherited independently of each other. This determinism is provided by unknown algorithms of multichannel noise-immune coding. Accordingly, each organism is a multichannel noise-immune coding machine. Our studies of the properties of genetic inheritance of biological structures and the possibilities of their algebraic modeling are based on the well-known mathematical formalisms of matrix and tensor analysis, recurrent sequences, the theory of information noise-immune coding, as well as on known academic information about genetic and other biological structures.

3. Results and discussion

Let us present some of the possibilities we have studied of using the mathematical properties of harmonic progression (1), which is associated with the organization of genomes of higher and lower organisms, for modeling inherited biological structures and processes.

Harmonic progression is related to the well-known concept of harmonic mean and is a recurrent sequence based on it: knowing two adjacent members of this progression, you can build the entire given progression. Indeed, the harmonic mean x_{n+1} for two numbers x_n and x_{n+2} is expressed by the relation (2):

$$x_{n+1} = ((x_n^{-1} + x_{n+2}^{-1})/2)^{-1} = 2 x_n x_{n+2} /(x_n + x_{n+2}) \quad (2)$$

Knowing two neighboring numbers x_n and x_{n+1} in this triplet of numbers, the third number x_{n+2} is determined, respectively, by the relation (3):

$$x_{n+2} = x_n x_{n+1} /(2x_n - x_{n+1}) \quad (3)$$

Successively applying this recurrence relation (3) to the first terms $x_1 = 1$ and $x_2 = 1/2$ of the harmonic progression (1), we obtain the entire series of its terms. It seems interesting and useful to investigate in the future the harmonic mean ratios in inherited biological structures and processes.

Pairs of numbers n and $1/n$ define points on the plane with coordinates $[n, 1/n]$ in the Cartesian coordinate system belonging to the hyperbola $y = 1/n$, which is closely related to the natural logarithm function $\ln(x)$. As you know, the natural logarithm can be defined for any positive real number $a > 1$ as the area under the hyperbola $y = 1/x$ from 1 to a (Fig. 1) [4].
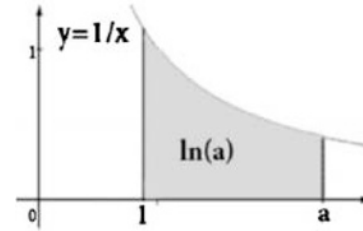

Fig. 1. Illustration of the natural logarithm ln (x) as the area under the hyperbola y = 1/x.

The natural logarithm function is widely used in mathematical biology to model inherited biological phenomena. For example, various types of inherited sensory perceptions - sight, hearing, smell, tactile sense, taste - are subject to the basic psychophysical Weber-Fechner law, which is logarithmic. This law states that the intensity of perception is proportional to the logarithm of the intensity of the stimulus. By virtue of this law, for example, the power of sound in engineering is expressed in a logarithmic decibel scale. The logarithmic nature of perception provides the body with a huge expansion of the range of perceived stimuli, which can differ in intensity by many millions or even billions of times: for example, hammer strikes on a steel plate generate noise that is a hundred billion times louder than the quiet rustle of leaves, and the brightness of a volt arc trillions of times the brightness of a faint star, barely visible in the night sky [5]. It can be assumed that organisms use natural logarithms as the basis for their internal counting.

Taking into account the named connection of the natural logarithm function with the hyperbola $y = 1/x$, we note that the recurrent harmonic progression (1) is conjugate, respectively, with a recurrent sequence of natural logarithms (4):

$$\ln(1), \ln(2), \ln(3), \ldots, \ln(n) \quad (4)$$

Fig. 2 shows this recurrent sequence (4) in graphical form in a polar coordinate system, where an integer positive variable n plays the role of the angular coordinate θ, and $\ln(n)$ plays the role of the radius vector r.

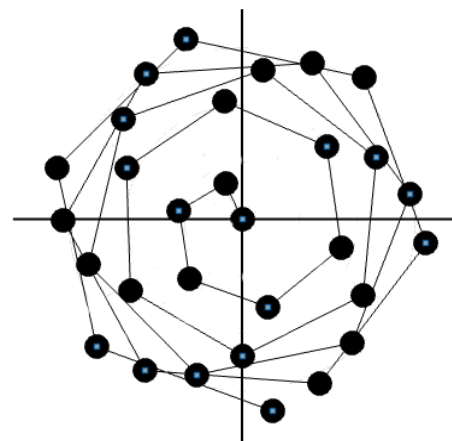**Fig. 2.** The graph of a sequence of discrete values of the natural logarithm ln (n) in a polar coordinat system for n = 1, 2,…, 30.

Turning to discrete values of functions in modeling biological phenomena seems to be fundamentally important due to the discrete nature of the organization of both the genetic coding system (discrete DNA alphabets, etc.) and a variety of biomechanical processes (for example, the seemingly continuous movement of a human hand is provided due to the total effect of discrete contractions of a huge variety of muscle units, each of which has its own threshold of excitability and is contracted out of step with the rest). As is known, for all excitable cells of the body, the genetically inherited universal law of "all or nothing" of a discrete nature is valid: the cell does not respond at all to stimuli of a subthreshold value, but reacts to above-threshold stimuli with full amplitude. These facts indicate that biomechanics, if it takes into account these fundamental features of living tissue, should be developed as the mechanics of discrete sequences and processes, taking into account their relationship with discrete genetic coding.

The use of a polar coordinate system for the graphic representation of biological structures as configurations of a spiral type is justified by the fact that spirals have long been considered as *the curves of life* [6, 7]: spiral and helical configurations are characteristic of DNA molecules, proteins, bones, tendons, muscles, etc. etc. For example, the heart is a holistic spiral muscle that pushes blood by its action of twisting and untwisting, similar to how a washerwoman squeezes water out of laundry by twisting it. Spiral motions (nutation) are observed during the growth of roots and shoots, tendrils of plants are spirally wrapped, a tissue in the trunks of trees grows spirally, etc. Because of spiral configurations, all the fluids in the body (blood, lymph, and urine) are spiral.

Spirals and helices in living matter are quite different from spirals and helices in inanimate nature:

1. They are genetically inherited in the chain of generations and are associated with structures of a molecular-genetic system that is full of spirals and super spirals at different levels of its organization, from DNA to chromosomes;

2. Characteristics of biological spirals are associated with Fibonacci numbers at different levels and branches of the biological evolution, from alpha-peptides to the structure of the integral bodies of plants and animals, which is reflected in the famous bio-mathematical laws of phyllotaxis, to which thousands of publications have been devoted worldwide [8].

The amounts of the initial members of the harmonic progression (1) are termed harmonic numbers H_n. These numbers appear so often in the analysis of algorithms that computer scientists need a special notation for them. The series (5) presents first harmonic numbers H_n:

$$1, 3/2, 11/6, 25/12, 137/60, \dots \qquad (5)$$

Harmonic numbers are related to the harmonic mean in that the n-th harmonic number is also n times the reciprocal of the harmonic mean of the first n positive integers 1, 2, 3, …, n.

Harmonic numbers are connected with the function of natural logarithm: as it is known, the harmonic number H_n is the discrete analog of the continuous function $\ln(x)$. Fig. 3 shows an approximation of the function of the natural logarithm in Fig. 3 by the sum of areas 1, 1/2, 1/3, 1/4, … , 1/n of the shown rectangles; sums of these areas form the series of harmonic numbers H_n (4).
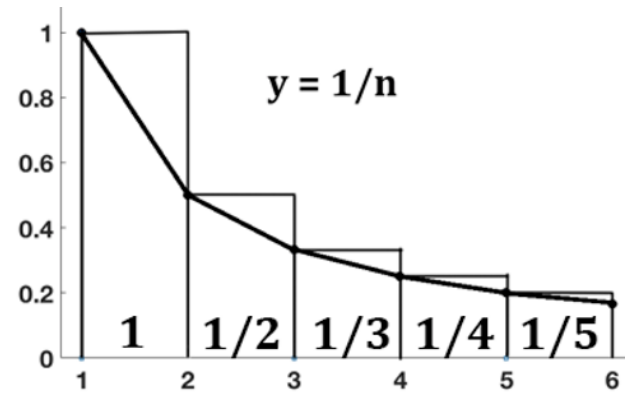

Fig. 3. An approximation of the area under the hyperbola y = 1/x by the sum of areas 1, 1/2, 1/3, 1/4, … , 1/n of the shown rectangles, whose areas form the series of harmonic numbers Hn (4).

In 1740, Euler obtained an asymptotic expression for the harmonic numbers H_n:

$$H_n = \ln(n) + \gamma + \varepsilon \qquad (6)$$

where $\gamma = 0.5772\dots$ is the Euler-Mascheroni constant, and the value ε tends to zero with increasing n. Therefore, with increasing n, the harmonic number H_n is more and more accurately expressed by the sum (6):

$$H_n \approx \ln(n) + 0.5772 = \ln(n) + \ln(1.7810) \qquad (7)$$

To improve an approximation of the logarithmic function $\ln(x)$ by the total area of the rectangles (Fig. 4), you can consider - instead of the classic harmonic progression 1, 2, … , 1/k - more fractional sequences, called the "compressed harmonic progression" (or briefly, the C-harmonic progression):

$$1, 1+1/m, 1+2/m, \dots , 1+k/m, \qquad (8)$$

where the additional factor m can take integer values 1, 2, 3 ,.... The amounts of the initial members of the C-harmonic progression (8) are termed by authors as "compressed harmonic numbers" (or C-harmonic numbers). Fig. 4 shows an improved approximation of the continuous function $\ln(x)$ by C-harmonic numbers $H_n^{[m]}$ at $m = 3$: the area under the hyperbola, representing the natural logarithm, is better approximated by the total area of the rectangles equal to the C-harmonic number $H_n^{[3]}$. The larger the value m, the better the approximation of the continuous function $\ln(x)$ by discrete C-harmonic numbers $H_n^{[m]}$ is provided.
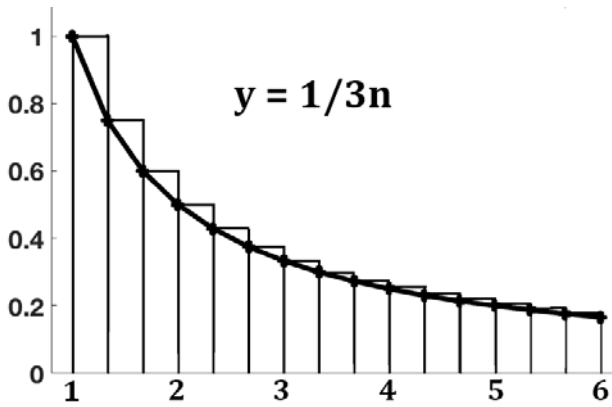
Fig. 4. The approximations of continuous function ln (x), by compressed harmonic numbers Hn[m] under m = 3.

The natural logarithm function $y = \ln(x)$, which is important for modeling inherited biological phenomena, is mutually inverse to the exponent function $x = \exp(y)$, which are also used for a long time to model morphogenetic and other bio-phenomena. Accordingly, the recurrent sequence (4) is mutually inverse to the recurrent sequence (9) of exponentials $\exp(n)$:

$$\exp(1), \exp(2), \exp(3), \ldots, \exp(n) \qquad (9)$$

Fig. 5 shows a continuous exponential function $\exp(x)$ and a discrete recurrent exponential sequence in a polar coordinate system. These graphs correspond to continuous and discrete logarithmic spirals.
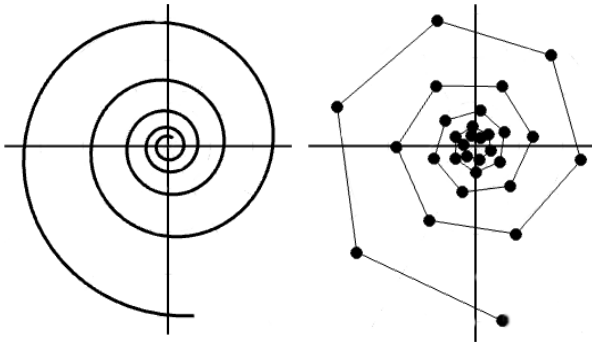

Fig. 5. Graphs of a continuous exponential function exp(0.1x) and discrete sequence exp (0.1n) for n = 1, 2,…, 30.

Logarithmic functions and logarithmic spirals model many genetically inherited biological phenomena, including morphogenetic configurations of phyllotaxis laws [8], which are associated with another recurrent sequence - a series of Fibonacci numbers related to the golden ratio.

Let us add that many cases of biomechanical movements - growth and motor - of living bodies can be modeled as a transition from one discrete recurrent logarithmic spiral to another. This corresponds to the statement of the classic of biomechanics N.A. Bernstein: "The idea that movement is in many respects like an organ seems extremely fruitful" [9].

Mendel discovered in his experiments on the crossing of organisms that the inheritance of their traits occurs according to algebraic rules, despite the colossal complexity and heterogeneity of the molecular structure of living bodies. In this regard, he can be considered the founder of algebraic biology. We believe that algebraic biology is connected with quantum biology, whose history is presented in [10]. The human adult body contains about 100 trillion cells, the ensemble of which behaves as a whole. It seems natural to make a consideration of such complex ensembles from the standpoint of quantum mechanics, to which the carriers of genetic information - DNA molecules - belong.

An important step in the development of quantum biology, to which our study of genetically inherited biological structures belong, was the creation of the theory by H. Frohlich for collective quantum effects in biological systems [11, 12]. This theory testifies in favor that living bodies are a kind of analog of quantum Bose-Einstein condensate. Nobel laureate R. Penrose uses Frolich's theory to substantiate his ideas about the brain as a quantum computer. He writes about it in his book [13, pp. 352 and 367]: «The distinguished physicist Herbert Frohlich suggested a possible role for collective quantum effects in biological systems. … Frohlich was led to propose, in 1968, that there should be vibrational effects within active cells, which would resonate with microwave electromagnetic radiation, at 1011 Hz, as a result of a biological quantum coherence phenomenon. Instead of needing a low temperature, the effects arise from the existence of a large energy of metabolic drive. There is now some respectable observational evidence, in many biological systems, for precisely the kind of effect that Frohlich had predicted in 1968 ... He argued that so long as the energy of metabolic drive is large enough, and the dielectric properties of the materials concerned are sufficiently extreme, then there is the possibility of large-scale quantum coherence similar to that which occurs in the phenomena of superconductivity and superfluidity - sometimes referred to as Bose-Einstein condensation – even at the relatively high temperatures that are present in biological systems… In a Bose-Einstein condensate, large numbers of particles participate collectively in a single quantum state… There is a coherence on a large scale, where many of the strange features of quantum wavefunctions hold at a macroscopic level".

According to Fröhlich, under appropriate conditions a phenomenon quite similar to a Bose condensation may occur in substances, which possess longitudinal electric modes. If energy is fed into these modes and thence transferred to other degrees of freedom of the substance, then a stationary state will be reached in which the energy content of the electric modes is larger than in the thermal equilibrium. This excess energy is found to be channelled into a single mode - exactly as in Bose condensation - provided the energy supply exceeds a critical value. Under these circumstances a random supply of energy is thus not completely thermalized but partly used in maintaining a coherent electric wave in the substance. This theory is supported by many authors, for example [14-17].

Our results about hyperbolic rules of cooperative genomic organization connected with the harmonic progression, which is known in physics of standing waves in resonators, are correlated with ideas of the

article "Genetic code as Language" (see in [11]). It was written by F.Frohlich, the son of H. Fröhlich. This article was devoted to quantum coherence states and long-range communication in genomes. Its author noted that the genome as a whole must contain some sort of long-distance communication. Using H. Frohlich's hypothesis, he wrote that long-range coherent vibrations will lead to resonance between a differentiated cell with its own characteristic vibrations and the chromosome such that the chromosome-particular region responding to this characteristic frequency will be activated or opened up so it can produce the appropriate proteins. Such a resonance could transport the embryological, already partially induced cells to their target and there they would be further fixed into producing the correct proteins for this organ through superimposed resonance and why if it were to o mature, it would not so adapt; there might be degrees of resonance. The conception of multi-resonance genetics was represented also in [18].

4. Some concluding remarks

The work of the laboratory for the research of biomechanical systems of the IMASH RAS (http://eng.imash.ru/) revealed fundamental hyperbolic rules for the organization of DNA information texts in the genomes of higher and lower organisms (eukaryotes and prokaryotes), associated with harmonic progression (1), which is well-known in science in connection with various mathematical and physical problems. The discovery of the important role of the harmonic progression in genetic informatics leads to the development of new mathematical models in genetic biomechanics, which studies the relationship of inherited biomechanical structures with genetic DNA texts, since DNA molecules play a dictatorial role in living organisms, determining their genetically inherited physiological structures [10]. Additionally, we note that harmonic progression plays a prominent role in aesthetics. This progression (1) is important not only for music with its systems of musical harmony and musical overtones. At least since the time of the Pythagorean doctrine of the aesthetics of proportions, there has been an idea that the composer R. Schumann expressed as follows: "*The aesthetics of one art is at the same time the aesthetics of another art; only the material is different*" [19]. In light of this, architecture has long been interpreted as frozen music and music as dynamic architecture. In connection with our research, assumptions arise about the genetic basis of a number of aesthetic parallels in various arts.

The above features of harmonic progression (1) do not exhaust its rich mathematical features, which can serve to create new approaches to the construction and substantiation of models in genetic biomechanics, as well as contribute to the development of algebraic and quantum biology [20].

5. Conclusions

The present study leads us to conclude that

(1) The discovery of the connection of cooperative genomic organization with the recurrent harmonic progression (1) gives new approaches for developing mathematical models of genetically inherited biological structures and also for searching hidden genetic rules;

(2) The connection of the genomic harmonic progression with functions of natural logarithms gives us a new understanding the main psychophysical law by Weber-Fechner and other genetically inherited logarithmic structures in living bodies;

(3) The received results are correlated with Frohlich's vibration-resonant theory about collective quantum effects and long-range communication in biological systems.

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