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[Valeriy Revo](#) *

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Article

Epithelial Cell—A Repository of Phylogenetic Memory

Valeriy Revo

Retired. Independent. Canada; valeri.revo@gmail.com

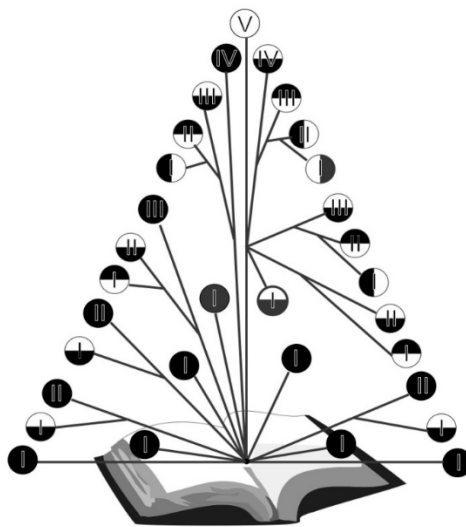
Abstract: Diseases are one of the main attributes of life. Failures in attempts to control these natural phenomena for all living things are due to the epistemological insufficiency of the natural philosophical paradigm. The author's goal is to familiarize specialists with the phylogenetically conditioned quantum nature of disease programs, which is manifested by their pathogenetic pattern. The author's task is to draw the attention of specialists to the possibility of access to the storage of these programs in the body to control them. The solution to this problem is possible only with the interdisciplinary collaboration of specialists capable of developing the appropriate technologies. This publication substantiates the possibilities for this.

Keywords: disease; program; phylogenetic memory; control; cell

1. Summary Statement

One of humanity's greatest mysteries is the origin of life and humans. The author developed the first systemic models of life forms at different stages of phylogenesis. A protein exhibiting spontaneous reversible ultra-high-frequency conformational dynamics of hydration \rightleftharpoons dehydration represents the earliest form of a living organism. This protein's properties align with those of the prion protein PrP^{Sc}.

The author demonstrated that all living organisms, without exception, possess these proteins in their structure by definition, based on the systemic principle of their organization. In the human's systemic model, protein elements at all levels of its organization are first-order subsystems that outnumber other subsystemic elements [1]. See Figure 1.



Legend

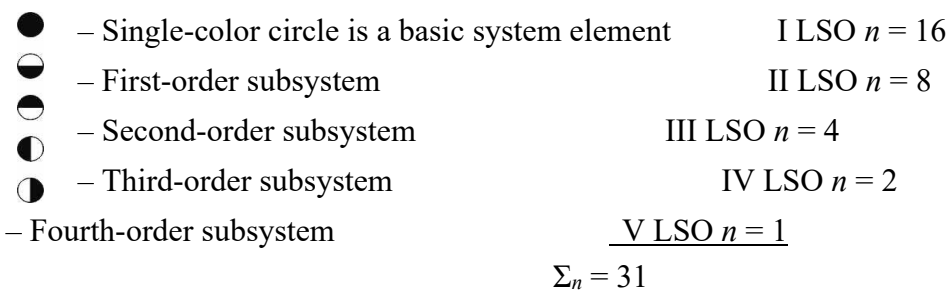


Figure 1. Systemic information models of human (V. Revo, 1986-2024).

Roman numerals indicate the levels of systemic organization (LSO) of the basic information biomechanisms of the living. The basic systemic biomechanism of the I LSO is a system of living protein in a reversible hyper-high-frequency conformational dynamic (hydration \rightleftharpoons dehydration), II LSO – Genetic system, III LSO – Pre-cephalic nervous system (only single neurons, as well as networks, and ganglia), IV LSO – Highly evolved brain system, V LSO – Highly evolved consciousness system in systemic unity with the social form of external memory. The elements on the right side of the model ensure the functioning of the system output, and the elements on the left side of the model ensure the functioning of the system input. The open book at the base of the model represents the social form of external memory.

According to the general law of conservation, the systemic model includes the basic information mechanisms of all previous stages of the development of life on the planet.

This model represents the systemic elements of a human in the dimensions of Newtonian physics. The elements of the quantum dimension are not represented in this model.

Since prions are carriers of phylogenetic memory, their presence in the structure of living organisms along the entire phylogenetic vertical is natural. Prions have also been found in bacteria [2,3]. They are capable of not only forming amyloid fibrils but also of transmitting this property to offspring with subsequent initiation of aggregation of homologous protein molecules.

The author of this message also showed that the quantum level of the systemic organization of life is manifested by some phenomena that science has not yet paid attention to. This is a special type of nutrition, a special mechanism of two-way information communication with the external environment, phylogenetic memory and some other fundamental features that the cells of some tissues of a living organism have, in the structure of which there is a prion protein.

This information opens up new possibilities for its use in research and clinical practice. This is the subject of this paper.

The article addresses biophysicists, physicists, biochemists, biologists, systems engineers, IT specialists, philosophers, doctors, students, postgraduates and doctoral students of specialized universities.

2. Introduction

The German physiologist Emil Dubois-Reymond in his speech "On the Limits of Knowledge of Nature" proclaimed (1872): "... ignoramus et ignorabimus" ("we do not know and will not recognize". He meant the origin of life, the purposefulness of nature, and the mechanism of thinking and language. The successes of science over the past century and a half allow us today to disagree with his statement regarding the origin of life. It has traditionally been considered either in the context of the manifestation of divine will, recognizing its transcendental nature, or believing it to be conditioned by biological laws. However, the so-called biological laws known today have only a natural philosophical content since they do not have the corresponding fundamental natural scientific foundations.

At the same time, some outstanding physicists denied the possibility of understanding the essence of life from the point of view of ordinary laws of physics (E. Schrödinger, 1944) [4]. R.

Oppenheimer (1964) drew attention to the imbalance between our knowledge of the physical world and our knowledge of the living world [5]. The imbalance that Oppenheimer drew attention to is gradually decreasing, which allows us to better understand the content and nature of the processes occurring in living organisms. However, new knowledge has naturally identified new problems.

Today, science can represent life in two dimensions at the same time. This is the scale of the dimensionality of Newtonian physics and the scale of quantum dimensionality. However, objects and phenomena of living Nature of the dimensions of Newtonian physics are studied only by observable effects without considering the fundamental role of relations on the scale of quantum physics. This, as in previous centuries, is the subject of natural philosophy. However, what manifests itself in life at the level of relations on the scale of Newtonian physics is determined by relations on the quantum level. It is these relations that constitute the content of disease programs that arose in the phylogenetic past of a particular living organism.

The conjugation of these relations constitutes the content of life and its manifestations¹. A. Szent-Györgyi (1960) drew attention to the dual nature of life, which can only be understood with a good knowledge of wave mechanics and solid state physics [6]. At the symposium on quantum biology and quantum pharmacology in Florida in 1977, he again drew attention to the fact that from the point of view of physics, the behavior of molecules is determined by their electronic structure [7].

The dual nature of all life must have manifested itself initially in the systemic structure of the first forms of life.

3. Results

3.1. Phylogenetic Past of Life

According to modern concepts, life appeared about 3.7 billion years ago, in the Archean² [8] in a weakly reducing environment [9].

We have sufficient grounds to believe that at the first stage of life development on the planet (\approx 3.7–1.65 billion years ago), various polypeptides and the first living proteins arose, which in their properties corresponded to prions [10]. Prion-like forms occupied a special place among primary life [11].

These are globular proteins, in the secondary structure of which β -sheet forms dominated (43% β -sheets and 30% α -helices) [12]. They received the status of the first living organisms in the format of a living protein.

V. I. Vernadsky called the first forms of life eobionts or protobionts (from the ancient Greek $\eta\acute{\omega}\varsigma$ – dawn, – read as $\epsilon\acute{\omicron}\varsigma$ + $\beta\acute{\iota}\omicron\varsigma$ – a living organism, – read as $\beta\acute{\iota}\omicron\varsigma$). He imagined them as a "substance-creature", but in its basic manifestations, it was a living organism since it had the adaptive attributes of life in the form of information and energy mechanisms.

The environmental conditions during the period of life's emergence were extreme. The Earth had no protective ozone layer; it was exposed to powerful flows of UV and corpuscular radiation. The temperature of the land surface, represented by basalts, reached 80°C. The water in the narrow cracks of the bottom of shallow freshwater bodies on land also had a high temperature. But even in these conditions, such a primary form of life as prion appeared and developed, giving rise to many isomers [13,14].

¹ Diseases in this context are a natural biological phenomenon of quantum nature.

² Such dating is given according to the currently accepted linear continuous time scale. However, according to the systemic information concept of V. V. Revo (1986, 2000), time is discrete and multidimensional, each dimension having its temporal metric. Since these dimensions are unknown today, they cannot be correlated with the linear time scale. Thus, the accepted dating of historical phenomena and processes should be perceived as relative.

Hydrophobic, protease-resistant, free of covalent modifications, and insensitive to extreme living conditions, this primary form of life not only survived but became the basic component of the systemic structure of all life forms that appeared at subsequent stages of phylogenesis.

In small bodies of water on land, the pH of the contents could be higher than that of the slightly acidic World Ocean. The atmosphere during that period was ammonia-carbonic and reducing in nature. The free oxygen content at this stage of phylogenesis was 10^{-3} of the current level³. Such a level of free oxygen was insufficient to exhibit oxidative destructive action on the systems of primary life. Therefore, proteins like PrPSc had the greatest potential for existence under these conditions. They became the progenitors of life on the planet.

The basic systemic features of the structural and functional organization of the first form of life have been preserved in living organisms that emerged at all subsequent stages of phylogenesis leading up to humans [10,15].

The development of life has been accompanied by processes that enhance opportunities for adaptation. One such process is symbiosis in its various forms.

3.2. *Laws of Biosemiotics in the System of Relations of Living Nature*

The phylogenetic vertical of symbiotic relationships consists of the following series of complementary aggregations: Water in the structure of the hydrate shell of a protein molecule → Elements of the genomes of archaic viruses and bacteria in the structure of the genomes of other acceptor organisms → Unicellular organisms of the past in the structure of cell organelles → Individual cells in the structure of a multicellular organism → Multicellular organisms in the structure of communities → Communities in the structure of the biosphere → The biosphere in the structure of Nature.

This sequence represents structural complexes in which integrated elements and the acceptor organisms belong to the same level of systemic organization.

Another phylogenetic series exists, which is the series of systemic integration. This series is fundamentally different from the phylogenetic series of complementary aggregation. The elements of the phylogenetic series of systemic integration are subsystem components of varying ranks within the acceptor organism [16].

This systemic whole represents a higher level of organizational structure. Accordingly, the water of the boundary layer serves as a first-order subsystem within the protein system of the hydration shell; the protein in the hydration shell functions as a first-order subsystem of the genetic apparatus system; the genetic apparatus is a first-order subsystem of the neuron system, and so forth. Elements incorporated into the structure during morphological integration consistently perform the same functions and only at one structural level. Elements incorporated into the structure through systemic integration can create a different semiotic pattern, determined by the systemic rank of these elements. The systemic rank of a protein within a hydration shell depends on the level of systemic organization of the structure it belongs to. Each of these distinct levels serves as an external environment for the protein.

Following the principle of tectological⁴ hostility of the environment (according to A. A. Bogdanov), each level dictates its conditions for protein behavior. For example, the system of protein

³ Today, at sea level, the oxygen content in the atmosphere at the Earth's surface is approximately 21%.

⁴ The term "Tectology" (derived from the Greek root τέχ- in words such as τέκτων – carpenter, builder, creator, read as tekton, and λόγος – word, doctrine, read as lógos) was proposed by E. Haeckel in 1866 to denote the discipline that studies the principles of the structure of living organisms. A. A. Bogdanov, in 1913, suggested using this term to refer to General Organizational Science. According to Bogdanov (1913, 1922), the tectological hostility of the environment is defined by its systemic superiority over any of its parts.

and its hydration shell manifests differently within the body at various systemic levels of organization: 1) as an independent structure, 2) as a first-order subsystem within the genetic apparatus, 3) as a second-order subsystem within the neuron structure, and 4) as a third-order subsystem in the developed brain structure. At each level, it influences these structures in distinct ways. This influence must be differentiated, which is not currently addressed.

Now, we know that the semiotic pattern of each biological phenomenon must be assessed based on the systemic rank of the structures that caused it. Understanding the differences between the mechanisms of morphological integration and systemic integration is a significant resource for managing living organisms.

Various types of biological memory provide the preservation and transmission of these mechanisms to offspring. Phylogenetic memory is one of these types.

3.3. Phylogenetic Memory

Any living organism possesses several specialized forms of memory. A notable type among them is phylogenetic memory, which, among other things, stores programs of all diseases that emerged at previous stages of phylogenesis. This fact enables accurate systemic modeling of diseases that developed in earlier stages of phylogenesis, but it does not permit modeling in living organisms that arose in subsequent stages. Modern experimental pathology does not take this into account.

I described the phenomenon I later termed "phylogenetic memory" in 1986 [15].

I proposed the concept of "Phylogenetic memory" and named it "Phylotheke" (from Greek φυλή – genus, tribe, pronounced fylí, + αποθήκη – depository, pronounced apothíki) on August 5, 2024. This represents a set of systemic biological features of an organism that are transmitted to phylogenetic offspring. One of these features is a repository of disease programs stored in the phylotheke. I referred to it (V. Revo, August 20, 2023) as "Phylopathom" (from the Greek φυλή – tribe, clan, pronounced fylí, + πάθησις – disease, pronounced páthisi + the suffix -om signifies the commonality of something, pronounced om) [14].

In the phylopathom, the programs associated with various diseases can be activated or blocked at different stages of life due to a range of external and internal circumstances. Factors such as syntropic⁵ and dystropic relationships between disease programs, mutations in the genetic structure, traumas of different kinds, including psychological ones, etc., can be significant here. The number of activated disease programs also tends to increase as the organism ages. In this context, I have identified several age stages when the number of activated disease programs rises dramatically [18].

The reasons for this phenomenon deserve the attention of researchers. This should compel us to reconsider the frequency of preventive geriatric measures at an earlier age than currently accepted.

The phylopathom in the body's phylotheke also acts as a storage facility for the innate bank of negentropy [16].

Since the pathogenesis of any disease increases diversity in the body, it reduces entropy. While this favorable circumstance can sometimes be offset by structural and /or/ functional disorders that may be incompatible with life, it illustrates the dual nature of many fundamental phenomena from a human perspective. However, humans are not able to fully comprehend the logic and morality of Nature. They can, nonetheless, understand their physical and biological aspects within certain limits.

The phylotheke also serves the function of storing immune memory in the body.

The carriers of immune memory are quantum-dimensional structures stored in phylogenetic memory, as we do not observe other candidates at the molecular level that can preserve and utilize a vast array of information without delay or distortion. Therefore, we can assert that immune memory retains a "quantum portrait" of millions of exogenous and endogenous antigens encountered throughout all previous stages of phylogenesis.

⁵ Syntropic clusters (V. V. Revo, 1998) is a concept denoting stable group combinations of symptoms, syndromes or nosological forms in a population [17].

These circumstances compel us to reinterpret the ideas of F. M. Barnett (1957) [19] regarding the nature of specific antibodies against various potential antigens somewhat differently.

Since the number of disease programs stored in the phylopathom is unknown, its negentropic potential cannot be calculated.

Among other issues, we face several methodological difficulties here. For example, the dimensionality of the phylotheke and the necessary units of measurement are unclear. According to [20], the reference book includes over 26,000 diseases. There is reason to believe that this number is several orders of magnitude higher [21].

Currently, there are no widely accepted designations for the phylotheke and phylopathom. Such procedural challenges are typical in emerging scientific fields. As the history of science demonstrates, these obstacles can be overcome.

I propose designating the phylotheke as Phm_i and the phylopathom as Phm_p (V. Revo, Jan 11, 2025). I believe that defining a unit of phylogenetic memory is the prerogative of wave mechanics specialists, as both the phylotheke and phylopathom exhibit wave-like nature.

It is possible that the number of nosologies is significantly smaller and aligns with the number of systemoses⁶. In all systemoses, the mutual influence of programs of different phylogenetic origins can lead to a rapid acceleration or deceleration in the deployment rate of subsystem components (V. V. Revo, 2020). This situation is an additional argument supporting the wave nature of disease programs embedded in the organism's phylogenetic memory (V. V. Revo, 2020). The programs of nosologies included in the system of systemoses represent numerous wave isomers. The first living creature on the planet, which possessed phylogenetic memory at its emergence, was a living protein.

3.4. Live Protein

The first living beings were protein-polypeptide prion-like structures that possessed an energy-trophic⁷ mechanism of nutrition and a proton-electron information mechanism for two-way communication with the environment, without which adaptation and, consequently, life are impossible.

Initially, there was no competition among them, as they had no advantages over one another. Furthermore, the energy from the protons of hydrate water was sufficient for all. Competition arose only when the trophic chain developed [15].

I believe that the quality of living protein was achieved through spontaneous reversible ultra-high-frequency (10^{-11} - 10^{-13} sec) conformational dynamics (hydration \rightleftharpoons dehydration). The frequency of this process aligns with the natural oscillation frequency of a single water molecule in proximity to the equilibrium position.

The approximate resonant frequency of a somatic living mammalian cell is $2,39 \cdot 10^{12}$ Hz [22]. Changes in the protein structure alter its resonant frequency. During the conformation of the protein molecule, proton-electron dynamics generate an electromagnetic field at this frequency. This phenomenon can be utilized for diagnostics.

The event when the wall (hydrate) water transferred its frequency feature to the protein occurred at the moment of the systemic metamorphosis of the prion protein at the boundary of the end of the Katarchean and the beginning of the Archean, i.e., approximately 3.7-3.5 billion years ago, according

⁶ Systemoses (V. Revo, 2001) (from Greek *σύνστημα* – a whole consisting of parts, + the suffix - *ώς*, usually used with the ending -*ις*; here, - *ώςις* denotes a slowly developing pathological condition, or chronic disease) – refers to the definition of nosological forms, whose program reflects the basic systemic features of one of the five phylogenetic stages. For example, cancer and the destructive form of tuberculosis are genoses representing proteosis, while peptic ulcer disease and urolithiasis are systemoses of the next phylogenetic level of systemic organization, which is represented by neurosis, etc. [10].

⁷ I first proposed and used this term in my letter to Dr. Barbara Sherwood Lollar on March 13, 2023.

to the accepted continuous linear time scale. This was a one-time event, but from then on, this phenomenon of living protein will manifest in living things at all subsequent stages of phylogenesis.

Science is not aware of any instances of spontaneous or artificial emergence of the primary form of living protein as PrPSc. This serves as evidence that such an event in the history of life on Earth was indeed a one-time incident.

A repetition of this event is impossible because it would require a universal gravitational impulse similar to the one that may have occurred at that distant historical moment. During the first stage of phylogenesis, life, akin to a living protein molecule, faced no competition for nearly two billion years.

The concept of a "living molecule" was introduced by E. F. W. Pflüger in 1871. In his work, he also expressed concern about our limited understanding of the atomic and molecular world within living cells. Concurrently, he believed that nature initially created numerous accumulations of various (primary) living matter and that the most fundamental issues of physiology are actually inherent in the earliest primary matter.

Later, this concept was used by E. Bauer (1935) [24], V. P. Burdakov et al. (2009) [25], and others.

V. I. Vernadsky called the first living organisms "substance-creatures". Indeed, they did not have a cellular structure; they lacked anatomical organs and most of the usual functions. However, they had the basic characteristics of life. This is, first of all, a two-way information connection with the external environment, which was provided by proton-electron flows in the system hydrate (parietal) water \rightleftharpoons living protein. These same flows provided the energy of living protein, maintaining its entropy at a safe level.

Experiments by E. Rapis (1990-2010) showed that protein under nonequilibrium conditions is capable of abiogenic self-organization with synchronous and coherent self-copying, which is necessary during the transition from inert matter to living matter. The DNA-water and RNA-water systems are incapable of this under the same conditions [26].

The PrPSc protein represents such a self-replicating system. It is capable of aggregating and catalyzing the production of each other. At the same time, the infectious form (PrPSc) is thermodynamically more stable and stronger than the normal isoform.

At the second stage of phylogenesis (1.65 – 0.65 billion years ago), systemic metamorphosis⁸ provided part of the biota with a new basic systemic information biomechanism. They received a genetic apparatus. At the same time, a non-infectious form of soluble cellular membrane protein-prion PrPC appeared, consisting of 3% β -sheets and 42% α -helices. The PrPSc molecule can transfer its structure and contagious properties to the PrPC protein upon direct contact. Molecules of the original prion form with a predominance of α -helices in the secondary structure are capable of spontaneous conformation into a different structure, with a predominance of β -flat forms [12]. They are able to transfer the properties they have received to the previously intact prion form. In highly organized animals, this type of conformational rearrangement is observed upon contact of PrPSc (pathological prion) with PrPC (normal cellular form of prion).

The PrPSc form, as an element of the environment, acting on PrPC, transforms it into an infectious prion isomer. In this case, the primary structure, the number of amino acid residues and the molecular weight remain the same⁹. Such isoforms exhibit the ability to combine and form highly structured amyloid fibers while demonstrating the information and energy features inherent in a living protein.

⁸ Systemic metamorphosis of the living is a sudden transition of a part of the biota that appeared at the previous stage of phylogenesis to the next level of systemic organization due to the appearance of a new basic information mechanism in the systemic structure of new living organisms.

⁹ The mature form of PrP consists of 208 amino acid residues and has a molecular mass of 35–36 kDa [28].

3.5. Information and Energy Characteristics of Living Protein

The popular hypothesis of the RNA world of Karl Woese (1968) does not stand up to criticism. After all, the emergence of the initially complex world of ribonucleic acids presupposes the existence of a pre-genetic world of the first living systems. Meanwhile, the probability of forming living RNA constructs in the environment of the primary ocean, which is aggressive for this form of life, is vanishingly small.

The discovery of prions (S. Prusiner, 1982) showed the possibility of the existence of protein systems that do not have a genetic apparatus but have energy and information mechanisms necessary to ensure the temporal continuity of life [27]. Any living system in the process of life requires energy, information, and the maintenance of a sufficient level of entropy, the achievement of a critical level that means death for it [4].

The dominance of layered β -structures in the PrPSc molecule required more energy, which was necessary for aligning several polypeptide chains with the formation of hydrogen bonds between their different sections. This energy was provided in excess by the energy-trophic type of nutrition of the primary living organism due to the protons of the wall (hydrate) water.

At the start of the first stage of phylogenesis, living protein did not have an assimilation apparatus; it used ready-made energy in its pure form from the external environment for its vital functions. I call (2023) this type of nutrition energy-trophic. The donor of this energy for organisms were protons of hydrate (parietal) water, which fed the mechanism of spontaneous reversible ultra-high-frequency conformational dynamics of hydration \rightleftharpoons dehydration of living protein. Since this type of nutrition is a systemic immanent feature of the first living beings, it should also be present in living beings that appeared at all subsequent stages of phylogenesis.

Free protons of hydrate water, as I believe, also perform some important function in membrane (parietal) digestion, which was discovered (1958) by the Russian physiologist A. M. Ugolev (1926-1991) – one of the founders of a new scientific discipline – trophology¹⁰ [29].

Fundamental in its importance, energy-trophic nutrition should not be confused with energy-tropic nutrition, which is a fitness technique when the so-called metabolic drugs are used, increasing the "intensity of energy exchange at the cellular level" (V. S. Sukhorukov, 2007). Such drugs include coenzyme Q10, L-carnitine, various vitamins and other pharmacological agents. However, these drugs exhibit their properties only in organisms that arose at subsequent stages of phylogenesis. They have found application in energy-deficient diatheses, in which "relative individual insufficiency of the cytoenergetic status of the body" is noted (V. S. Sukhorukov, 2006).

Protons and electrons of hydrate water also provide a two-way information connection between the living protein and the environment. After all, any living being must be able to represent its image and the image of the environment in itself and its image in the environment. This is a necessary attribute of adaptation. The adaptation apparatus is especially important in conditions of a tectologically hostile environment [30].

The intrinsic information capacity¹¹ of a living protein is ≈ 898.56 bits, with the presence of 208 amino acid residues in its molecule. The information capacity of the PrPSc protein, consisting of approximately 253 amino acids, is ≈ 1092 bits.

¹⁰ Trophology (from ancient Greek τροφή – nutrition, – read as tropho + λόγος – science, – read as logos) is the theory and practice of adequate nutrition, which, unlike the so-called classical theory of balanced nutrition, involves the use of a systemic general biological and evolutionary approach. Sometimes, the term trophology is used as a synonym for the ecology of nutrition or separate nutrition.

¹¹ The calculation was carried out using the formula: $C = n \cdot \log_2(m)$, where $n = 253$ (number of amino acids), $m=20$ (number of different amino acids).

These are the information resources of only one structural unit of the organism in the dimension of Newtonian physics, while its total information resources are many orders of magnitude greater. In addition, the calculations do not consider the information resources of the structural elements of the organism of quantum dimension. Today, researchers also do not consider the increase in the information potential of the organism due to the development of disease programs in it.

4. Discussion

4.1. Diseases in Ontological and Epistemological Aspects

According to the International Classification of Diseases, latest revision (ICD-11), today, more than 14 thousand different diseases and conditions are taken into account, which are distributed among more than 20 classes and hundreds of headings and subheadings, the number of which is constantly and significantly increasing.

True, this figure, firstly, is immeasurably greater than that presented in ICD-11. Secondly, the semantic pattern of many diseases can differ radically, despite the common systemic basic mechanism.

The construction of this cumbersome classification, like all the previous ones, is based on an organo-morphological, natural-philosophical principle. It does not consider the systemic character and program nature of diseases. Therefore, the strategy of modern medicine is aimed at combating the manifestations of diseases, i.e., combating symptoms and not managing their program basis. In addition, the fight against natural phenomena is ignorance doomed to failure. The systemic status of a part of Nature does not allow it to defeat Nature itself by definition. Man can only manage natural processes to the extent that Nature allows him. This is an axiom. A disease of a living being is a program phenomenon of quantum nature, stored in its phylogenetic memory, the initiation and development of which is manifested at the biological level in the form of specific pathogenesis. See Figure 2.

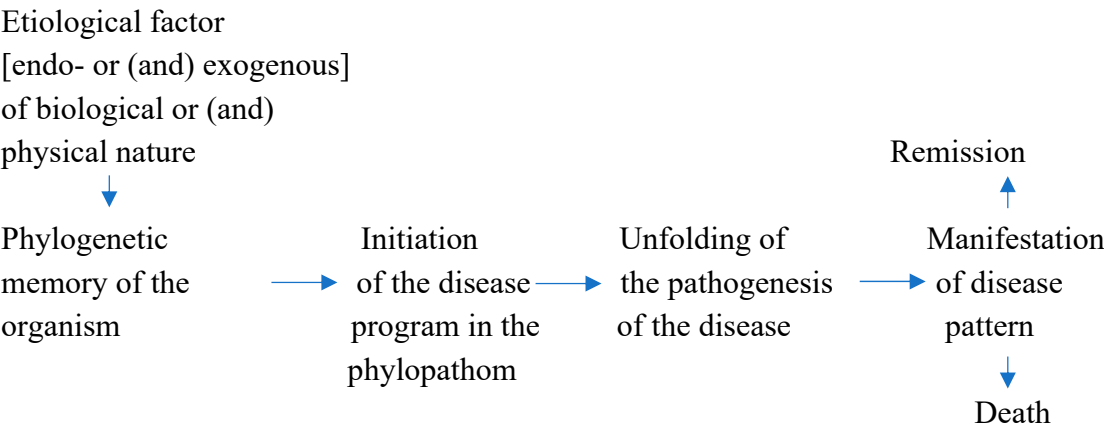


Figure 2. Biodynamics of the disease.

Throughout its history, man has viewed disease exclusively in a negative connotation. Therefore, he built his strategy as a fight against it, without imagining its cause and the content-rich basis of the disease as a natural phenomenon for Nature. Moreover, being a part of Nature, fighting it is reckless and dangerous. By definition, a subsystem element is not capable of overcoming the system. The results of such a fight are known.

Today, symptoms, as manifestations of diseases, have become more or less manageable. But the disease itself not only remained but also continued to cause complications and, ultimately, led to the death of its carrier.

Thus, in an ontological sense, illness is always evil.

But the epistemological assessment is another. Thus, syntropic and dystropic relations of disease programmes can have different manifestations. This can be polymorbidity in syntropies or blocking

of the program of a particular disease with a dystropic relation between them [16]. Increasing diversity in a system always reduces its entropy, taking the organism away from its critical value. True, anatomical and functional disorders in the organism due to the development of a disease can be fatal for it.

I have shown in my works that the manifestation in the organism of a living being of specific relationships at the level of the phenomena of the dimensionality of Newtonian physics in the form of a pathogenetic pattern is caused by the activation of quantum dimensionality programs.

Since diseases are an attribute of life, they appeared when life itself appeared.

Any disease has an internal or external cause. The endogenous factor, depending on the nature of the disease, can manifest itself in two forms. This is either an immediate clinical manifestation of the pathogenesis of the disease after the initiation of its program.

Delayed manifestation of the disease years after the initiation of its program is also well known in clinical practice. For example, cerebral aneurysms manifest mainly at the age of 35-60 years [31]. Other researchers have also drawn attention to this circumstance, for example, [32–34]. Prion diseases and AIDS can also manifest themselves decades after the initiation of their program [35]. There is reason to believe that the nomenclature of diseases with delayed clinical manifestations is more numerous. In this regard, my research is of interest, which, among other things, has shown that it is in the age group of 50 years that the first signs of many severe congenital diseases begin to appear. Among them are hemochromatosis, kidney anomalies, blood vessels, etc. Polymorbidity also manifests itself sharply at this age [18].

This circumstance showed that the age of 50 is critical for a person. I consider this sufficient grounds to begin using geriatric technologies at this age, not at 60, as defined by the World Health Organization [36].

I also drew attention to the fact that some diseases disappear from syntropic clusters at certain periods of a person's life. Previously, I attributed this to the fact that active carriers of these programs died by this age [18].

It cannot be ruled out that another reason within the organism manifests in this way. This is the interference of certain disease programs at this age due to unknown circumstances. In this case, some programs are initiated while others are blocked according to the same physical principles. A similar phenomenon is observed during the expression or suppression of certain genes in different cells [37].

The reasons for this phenomenon require the attention of researchers.

Obviously, the causal mechanism of such phenomena should be sought at the stage of the appearance of the first forms of life. The fundamental role in this was played by hydrate water, as well as a certain level of gravity, which determined its manifestation.

4.2. Hydrate Water and Gravity

Science has not yet addressed the question of the role of gravity in the origin of life. At the same time, one of the most important circumstances determining the possibility of the development of the form of life that developed on Earth is the level of gravity. In conditions of low gravity, there is no possibility of the formation of wall (hydrate) water, the physical and chemical properties of which determine the very possibility of the formation of a dynamic system complex (protein's molecule in hydrate shell).

Wall water, [syn. Hydrate water, Structured water, Biowater (Mascarenhas S., 2005), EZ Water, i.e. Exclusion Zone Water (Zheng J. M. et al., 2006), Boundary layer water (Postnov S. E., 2008), Water in the fourth aggregate state or Water in the fourth phase state (Pollack G. H., 2013)] — definitions of hydrate conformational layered water up to 300 nm thick, which is formed in the wall zone of the bulk mass of water. The structure of this water, as well as of liquid bulk (free) water, is largely not deciphered.

The unusual properties of hydrate water were first discovered at the beginning of the 20th century. The first detailed studies were conducted (1984) at the Central Aerohydrodynamic Institute (CAGI, Russia) when studying the flow of a water-air mixture around bodies (Postnov S. E., 2008).

Regarding its physical and chemical properties, such water differs sharply from bulk (free) liquid water. Hydrate water has a higher density and viscosity than bulk (free) water, but it has lower other characteristics: freezing point, dissolving capacity, permittivity, and thermal conductivity.

Since any living being is, by definition, an open nonequilibrium system located in a tectologically hostile environment, it must adapt to it. To do this, it is necessary to ensure a two-way information connection with the environment.

Centrifugal information flows ensure the systemic integrity of the living and the environment. Centripetal information flows allow scanning the environment, without which adaptation is impossible. Ultra-high-frequency spontaneous reversible conformational dynamics (hydration \rightleftharpoons dehydration) of a living protein molecule allows it to scan the environment at a frequency relevant to it. Two-way proton-electron flows perform this information function. They also provide the energy function of this system.

Water molecules are capable of forming and maintaining cluster structures of various configurations. This allows receiving, storing and transmitting information relevant to their level of systemic organization, i.e., at the quantum level, which is provided by the protons of hydrate water. In this case, the hydrate shell, along with the charge, is a factor in the stability of the protein in a colloidal solution.

I believe that bulk water can transition to the fourth phase state only in the presence of a certain level of gravity. Skupchenko V. V. and Bedareva E. V. showed (1991) that the cells of a living organism are more sensitive to gravity than to the sun, and gravity is of significantly greater importance for living organisms than sunlight [38].

The role of gravity is not limited to this. I have shown that both the start of life itself and the moment of the beginning of each successive stage of phylogenesis for a certain part of the biota were caused by the triggering influence of a jump in gravity in that part of space in which the Earth was located at that time. The long-term research by S. E. Shnol (2009) showed the fact of such events due to space-time fluctuations [39].

Such an event cannot have a temporal duration greater than the Planck time¹² since the systemic metamorphosis of the living at the moment of the beginning of a new stage of phylogenesis does not allow the appearance of intermediate forms. Indeed, even in a thought experiment, it is impossible to imagine an intermediate form of the living, for example, between a living protein and a gene or between a gene and a neuron.

The impossibility of creating a subject model of systemic metamorphosis forces us to use the capabilities of some demons, which are allegories of a thought experiment by J. von Goethe (1811). In this situation, we turn to the resources of the demon¹³ of phylogenesis (syn. demon of systemic metamorphosis), which endows some phylogenetically preceding representatives of the biota with a new basic information mechanism (Revo V. V., 2018) [14].

¹² Planck time (t_p) = $5,391 \cdot 10^{-44}$ s.

¹³ These demons (according to J. von Goethe, 1811) (from the ancient Greek Δαίμων – spirit, divine power, – read as daimōn) are allegories of a thought experiment. The demon of phylogenesis (syn. "Demon of systemic metamorphosis") determines the transcendental imperative of this phenomenon (V. Revo, 2024). This demon 3.7-3.5 billion years ago launched the biomechanism of spontaneous reversible ultra-high-frequency conformational dynamics of hydration \rightleftharpoons dehydration of a protein molecule. From that moment on, this became an immanent property of protein in the systemic structure of any living organism. This demon causes the sudden appearance at a certain moment in a given place of living organisms with a fundamentally new level of systemic organization of the basic information biomechanism. Systemic metamorphosis, by definition, cannot have intermediate forms. For more details on this form of thought experiment, see [14].

This demon endowed the first living organisms with a unique basic mechanism: spontaneous reversible ultra-high-frequency conformational dynamics of hydration \rightleftharpoons dehydration of a protein molecule [40].

Such structures have some specific characteristics, the manifestation of which allows them to be identified.

4.3. Biosignature of Living Protein

The first living thing that had the structure of prions PrPSc should have had a mechanism of protection against proteins with enzymatic properties that were dangerous to them. It cannot be ruled out that prions could mimic inorganic structures under dangerous conditions.

This form of life has been preserved in living organisms that appeared at all subsequent stages of phylogenesis.

Physiochemically, the PrPC form and the PrPSc form represent prion protein in different conformations. They have the same chemical composition and the same molecular weight. Unique frequency features of each form manifest themselves as signature isomerism. In relation to living protein, it can be designated as a "biosignature". Thus, the PrPSc molecule differs from its PrPC isoform only in its secondary and tertiary structure. This circumstance makes it possible to distinguish them from each other by the individual resonant frequency inherent in each of them. Since the secondary and tertiary structure of the protein exhibits conformational dynamics, we can draw an analogy between its conformational transformations and isomerization. Since the isomers of this protein differ from the original forms by their resonant frequency, I proposed (2009) to call them frequency isomers [13].

Although α -helices are thermodynamically more favorable due to the maximum number of hydrogen bonds between amino acid residues within one chain, Nature, at the initial stage of life, chose the form of prion protein with a predominance of β -sheets. I believe that such a choice was due to several circumstances. Firstly, the PrPSc form is stronger and more stable than the PrPC form, especially in the aggressive external environment of that era. Secondly, PrPSc is capable of aggregation and the formation of superstable amyloid structures. Finally, the protons of the parietal (hydration) water in excess provided the energy-trophic type of nutrition for this first form of life.

The PrPC prion is capable of irreversible conformation into the amyloid form of the PrPSc prion upon contact with it. The reverse process is impossible since this would mean a violation of the law of end-to-end irreversibility of development (L. Dollo, 1893). Thus, it is a serious mistake to assume that the PrPC form is phylogenetically older than the PrPSc form. The fact that the synthesis of PrPC is controlled by a genetic mechanism, in particular, the PRNP gene, also indicates the primacy of the PrPSc form, which appeared long before the emergence of the genetic apparatus.

Therefore, the PrPSc form is a fundamental form of organization of life, which, according to the conservation law, must be present in all living organisms, including the human body. Thus, the programs of diseases that arose with the appearance of PrPSc and the energy-trophic type of nutrition were preserved in the phylogenetic memory of all living beings that appeared at subsequent stages of phylogenesis. The latter circumstance is not taken into account today.

Here, the question of the localization of phylogenetic memory in the body naturally arises. We have every reason to believe that its storage is epithelial cells.

4.4. Epithelial Cells of the Body as a Distributed Repository of Phylogenetic Memory

I first proposed the idea of phylogenetic memory as one of the forms of biological memory that emerged during the stages of phylogenesis in 1986 [15]. In 2023, I first presented it as a concept [41].

It is generally accepted that the first living organisms in the form of anaerobic prokaryotes appeared in the Archean era (the era of ancient life) 3.9-3.5 billion years ago. These were already complexly organized living forms, which, by definition, had to have predecessors. I believe that these predecessors were living proteins in the form of PrPSc.

The first multicellular organisms appeared, according to various sources, in the period 2.5 billion - 600 million years ago. It is believed that these were sponges, leading an attached lifestyle, and free-swimming comb jellies, which appeared later.

The cellular elements of sponges are choanocytes and pinacocytes, which provide trophic function (nutrition, respiration and excretion) and informational communication with the external environment. Pinacocytes form pinacoderm, which in its properties corresponds to the epithelium of true multicellular organisms (Latin Eumetazoa).

One of the main functions of the epithelium of true multicellular organisms is to ensure a two-way exchange of energy and information between the organism and the environment. This circumstance allows us to believe that it is the epithelial cells of multicellular organisms of all phylogenetically subsequent products of systemic metamorphosis that represent a distributed repository of phylogenetic memory.

The epithelium develops from all three primary germ layers from blastula cells in multicellular animals. Therefore, already at this level of ontogenesis, one can assume the presence of programs for all diseases inherent in a given organism in accordance with the level of its systemic organization.

Nature successfully uses the ability of prions to maintain their functional activity in extreme environmental conditions by introducing them into the structure of key elements of life, for example, into the egg cell of living organisms throughout the vertical of phylogenesis.

It is known that the eggs of living beings from insects to humans retain their properties when cooled to the temperature of liquid nitrogen ($\approx 196^{\circ}\text{C}$). I believe that this is due to the content of domains of prion-like proteins in them, forming highly ordered fibrillar aggregates. Their important role in ensuring the structural and functional integrity of the egg cell has been convincingly confirmed [42,43].

Phylogenetic memory has a distributed holographic structure. This circumstance ensures the globality of the adaptive redundancy of life since it is the epithelial cell of any organism that is a distributed element of the storage of its phylogenetic memory. Therefore, for experiments with phylogenetic memory, only epithelial cells can be used as a model. This will preserve the lives of millions of experimental living beings and dramatically reduce the costs of experiments. Experimental and clinical biology must take these circumstances into account.

The structure of an adult human body contains $\approx 3.6 \cdot 10^{12}$ – $6 \cdot 10^{14}$ cells, 230 types. All of them, except heart cells and brain neurons, are periodically renewed. Among this cellular array, 20-30% are epithelial cells, which, when dividing, are capable of fully preserving the contents of phylogenetic memory. Only its quantum nature can provide this effect.

What type of epithelial cells is the carrier of phylogenetic memory? This is one of the most important questions for biology and biophysics today. It cannot be ruled out that all seven known types of epithelium are capable of this.

5. Conclusion

The material of this report allows us to draw the following conclusions:

The first living creatures were protein-polypeptide prion-like structures with an energy-trophic mechanism of nutrition and a proton-electron information mechanism of two-way communication with the environment, without which adaptation is impossible, and therefore, life is impossible.

The first living beings were protein-polypeptide prion-like structures with an energy-trophic mechanism of nutrition and a proton-electron information mechanism of two-way communication with the environment, without which adaptation is impossible, and therefore, life is impossible.

For the emergence of this first form of life, three fundamental conditions were necessary. The first condition is a sufficient level of gravity, without which the appearance of hydrated water is impossible. This level could be determined in an experiment in the conditions of the International Space Station. The results of such an experiment would have important scientific and applied significance.

The second condition is the formation of prion protein molecules (PrPSc), capable of spontaneous reversible ultra-high-frequency conformational dynamics of hydration \rightleftharpoons dehydration. Science knows of no examples of the spontaneous or artificial appearance of the primary form of living protein in the form of PrPSc. This is evidence that such an event in the history of life on Earth was a one-time event.

The third condition is a powerful universal gravitational impulse that initiated the launch of the mechanism of spontaneous reversible ultra-high-frequency conformational dynamics of hydration \rightleftharpoons dehydration of prion protein molecules. It is a vital protein for all organisms since it is one of the fundamental systemic elements of life.

Already at this level, the structural elements of life manifested themselves in two dimensions. This is the scale of the dimensionality of Newtonian physics and the scale of quantum dimensionality. Today, objects and phenomena of living Nature of the dimensions of Newtonian physics are studied only by observable effects without taking into account the fundamental role of relations on the scale of quantum physics.

Science does not know of any examples of the spontaneous or artificial appearance of the primary form of living protein in the form of PrPSc. This is evidence that such an event in the history of life on Earth was a one-time event.

The prion protein PrPSc is a vital protein for all organisms because it is one of the fundamental systemic elements of life.

Today, science can represent life in two dimensions at the same time. This is the scale of the dimensionality of Newtonian physics and the scale of quantum dimensionality. However, objects and phenomena of living Nature of the dimensions of Newtonian physics are studied only by observable effects without considering the fundamental role of relations on the scale of quantum physics. This, as in previous centuries, is the subject of natural philosophy. However, what manifests itself in life at the level of relations on the scale of Newtonian physics is determined by relations on the quantum level. It is these relations that constitute the content of disease programs that arose in the phylogenetic past of a particular living organism.

The quantum level of the systemic organization of life is manifested by some phenomena that science has not yet paid attention to. This is the energy-trophic type of nutrition, a special mechanism of two-way information communication with the external environment, phylogenetic memory and some other fundamental features that the cells of a living organism have, in the structure of which there is a prion protein.

The linear continuous time scale accepted today is incorrect since time is discrete and multidimensional, each dimension having its temporal metric. These dimensions are unknown today, so they cannot be correlated with the linear time scale. Thus, the accepted dating of historical phenomena and processes should be perceived as relative.

The basic elements of each level of the systemic organization of a living organism dictate their conditions for the behavior of a protein. For example, the system of a living protein and its hydration shell manifests itself differently in the body at different systemic levels of organization: 1) as an independent structure, 2) as a first-order subsystem in the structure of the genetic apparatus, 3) as a second-order subsystem in the structure of a neuron, 4) as a third-order subsystem in the structure of a developed brain. At each level, it will influence these structures differently. This influence must be differentiated. Today this is not taken into account.

Any living organism has phylogenetic memory in its structure, where, among other things, programs of all diseases that arose at previous stages of phylogenesis are stored. This circumstance allows us to model diseases that arose at previous stages of phylogenesis, but does not allow us to model them on living organisms that arose at subsequent stages, which is a sin of modern experimental pathology.

The phylogenetic memory of any organism has a distributed holographic character.

Phylogenetic memory is stored in epithelial cells.

Phylogenetic memory requires, among other things, the development of its units and the determination of their dimension.

This is the prerogative of wave mechanics specialists since it has a wave nature.

The number of activated disease programs increases as the organism ages. The author noted several age stages when activated disease programs increase abruptly. This should force us to reconsider the frequency of preventive geriatric measures at an earlier age than is currently accepted. The reasons for this phenomenon require the attention of researchers.

The rate of deployment of subsystem components of disease programs of different phylogenetic origin can sharply accelerate or slow down due to mutual influence. Interference of disease programs, which is manifested by the phenomenon of syntropic clusters, is also an additional argument in favor of the wave nature of disease programs located in the phylogenetic memory of the organism. The quantum nature of nosology programs of each phylogenetic level is manifested by wave isomers. Changes in the protein structure change its resonant frequency. In the process of conformation of the protein molecule, proton-electron dynamics form an electromagnetic field of this frequency. This circumstance can be used for diagnostics.

Like all previous editions, the latest edition of the International Classification of Diseases (ICD-11) is based on an organomorphological, natural-philosophical principle. It is fundamentally incorrect since it does not consider the diseases' systemic and programmatic nature. Therefore, the strategy of modern medicine is aimed at combating the manifestations of diseases, i.e., combating symptoms and not managing their programmatic basis.

Attempts to combat natural phenomena are doomed to fail. The systemic status of a part of Nature does not allow it to defeat Nature itself as a systemic whole, by definition. Man can only manage natural processes to the extent that Nature will enable him to. This is an axiom.

Finally, medicine does not yet know the consequences for phylogenetic memory in dermatoses, as well as in mechanical, chemical, thermal, or UHF and microwave acute or chronic effects on epithelial cells. The answer to these questions is within the competence of a collaboration of doctors, biologists, biophysicists, and specialists in systems engineering and wave mechanics. However, the author is not aware of any attempts at such integration.

Finally, the most important conclusion from the presented material is that any drug strategy will not allow for the control of disease programs. In the optimal version, it can control the symptoms more or less, but not the disease program.

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