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Review Article

Fractal Biology — Evolution from Molecular to Cognitive, and Psychological Dimensions

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Biological and artificial intelligence (BI and AI) share the fundamental principles of space-time information processing based on symmetry transformation. Therefore, cognitive-science-inspired AI represents a promising area of exploration. A convincing example is the fractal structure of human languages and protein assembly. The temporal and spatial plasticity of biological processes links them to the basic laws of physics. Continuous advances in fundamental physical theories allow for the understanding of all aspects of space-time symmetry (STS) natively intertwined with the principles of relativity and causality.

Spatial aspects of symmetry, represented by three sub-domains such as chirality, fractality, and topology, are widely studied in biology. The role of chirality in biology has been analyzed in several recent reviews. However, the fractals and topological states of biological structures are a relatively new and fast-developing branch of science. Here, we trace publications exploring the role of fractal symmetry in all hierarchical states of biological organization, including at the molecular, cellular, morphological, physiological, perceptual, cognitive, and psychological levels. The coverage of the above-listed areas in current studies is sharply unequal and unsystematic. A broad view of biological fractality opens a unique opportunity to discriminate between a healthy state and a wide range of disease conditions. Psychiatric, neurological, and immune disorders are associated with aberrant molecular assembly and morphological changes in neural circuits, suggesting that the chain of chirality/fractality transfer through all levels of physiological organization deserves persistent attention.

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Abbreviations

Amino acids (AAs). Artificial intelligence (AI). Biological intelligence (BI). Biological symmetry (BS). Deoxyribonucleic acid (DNA). Elementary particles (EPs). General theory of relativity (GTR), scale relativity theory (SRT), space-time symmetry (STS), space-time symmetry and relativity (STSR), standard model theory (SMT), string theory (StT).

Introduction

Biological and artificial intelligence (BI and AI) research are becoming more intertwined in the search for methods of mutual information transfer and adaptation. Notably, the fundamental principles of such interaction are based on the conservative space-time symmetrical transformations [1][2][3][4][5]. Biological symmetry (BS) comprises an enormous network of incidents covering physiologically relevant space-time scales. Proper navigation in this multidimensional continuum requires researchers to stand on the generalized (i.e., philosophical) frame of reference. The first necessary step of generalization is the notion of the universe's integrity, which allows for distinguishing the timing of the prebiotic and biotic periods, pointing to the origin of (BS). Second is understanding the evolution of the biological world from the time of molecular condensation to the appearance of bilateral organisms possessing consciousness and the mind [3]. The time-dependent unfolding of the universe from the pre-biotic to biotic state assumes the existence of the fundamental determinants common to both evolutionary periods. The appearance of journals devoted to biological and molecular psychiatry (1969-1997) opened a new era in the study of the link between molecular physiology, cognitive functions, the psychological state of the human being, and the fundamental laws of Nature. This review explores the long-time efforts of interpretation (analysis) of key events of biological evolution through reference to the fundamental determinants of matter space-time symmetry. The mathematical concepts and theorems utilizing this approach discriminate the contribution of chiral [3][4], topological [6], and fractal [7] symmetry interacting and competing along the evolutionary time scale.

In the 1980s, mathematician Benoit Mandelbrot published the seminal work titled *The Fractal Geometry of Nature* [8]. Currently, fractal theories are adopted by scientists from diverse branches of knowledge, including aesthetics, astrophysics, economics, protein folding, neuroscience, medicine, social media, climatology, human physiology, and psychology [9][10][11][12][13][14][15][16]. Impressive success is grounded on the universal significance of space-time symmetry and relativity (STSR) principles [15][16]. The significance of manifold space-time symmetry (STS) is recognized practically in all branches of science. The symmetry determinants in biology are studied (known) in many sub-fields, starting from molecular X recognition to the physiological, perceptual, cognitive, and psychological functions of humans. From a geometrical perspective, symmetry determinants can be segregated into different categories, the main ones of which are devoted to chirality, fractality, and topology. Chirality is the most studied form of biological symmetry, spreading its impact from molecular biology to psychology [3][4][14][16]. The possibility of mutual transformation of an achiral to a chiral tetrahedron suggests the distinction between absolute and relative chirality. Experimentally observed artificial modulation of molecular chirality by "chiral switches" points to the possibility of regulation of molecular, physiological, and psychological processes by internal (genetic) and external (such as the natural and social environment) factors [17][18]. Fractal psychology is on the way to its mature state.

Fractal Physics

A generalized approach to STSR points to fundamental determinants of biological symmetry (Fig. 1) [13][14]. Symmetry-based physical theories, including standard model theory (SMT) and string theory (StT), contain chiral, fractal, and topological branches [17][18][19]. The dominance of string theories in physics, achieved by mathematical definitions and experimental exploration of direct and indirect isometries and chirality (mirror symmetry ¹), works for any metric space [20][21][22][23]. Not surprisingly, the same categories of patterning are found in biological objects. The link between physical and biological space-time fractal symmetry is the main point of our interest. Fractal geometry describes the symmetry of structures based on the concept of scale invariance, frequently referred to as "scale-symmetry," "self-similarity," "similarity, or symmetry up to scale," and "similarity in the small and in the large" [24]. The fractality is a distinct, discrete symmetry of physical and chemical interactions, providing self-similarities of the complex systems of different natures and hierarchies [24]. Considering fractals in space-time physics is necessary for a broader view of the general theory of relativity (GTR) [25][26], standard model theory (SMT), and gauge field theories [23]. Gauge theory is, in fact, a consequence of the inclusion of fractal dimension in the space-time symmetry structure [27]. The theory of scale relativity describes space-time as a non-differential "manifold," which implies that its geometry is fractal [28][29]. The mathematical apparatus of SMT links the internal properties of elementary particles (EPs), their interactions with each other, and the features of corresponding fundamental forces of nature to the concept of STSR [30]. The family of EPs adequately describes the physical world at microscopic and cosmological scales [4][31]. Many natural phenomena exhibit repeating patterns of similarity across a wide range of spatial scales. The illustrative example is the chain of chirality transfer from the molecular, cellular, and morphological levels to the level of physiological, cognitive, and psychological functions [3][4][14]. This similarity across the scale is traditionally associated with diverse symmetry transformation forms, including chirality, fractality, topology, and the principle of relativity [4][32][33][34] and causality [35][36]. The geometrical representation of gravitational force in Einstein's SRT and GTR showed that space-time was curved. Both theories are based on the notion that position, orientation, movement, and acceleration cannot be defined in an absolute way but only relative to a frame (system) of reference. The scale relativity theory of Nottale overcomes the limitations of the principle of relativity associated with SRT and GRT by extending space-time geometry to fractal dimensions—an approach that allows mathematical interpretation of quantum physics [37]. The theory of scale relativity and fractal space-time extend the principle of relativity to scale transformations of the reference system [38][39]. The scale-symmetry (as well as chirality) is observable in the galaxy shape evolution [32] and structures formed by the interaction of EPs [40] complemented by the various intermediate scales, including all domains of biological levels of organization (Fig. 2) [41]. Re-evaluation of the STS appearance in cosmology [42][43][44] and the micro world [45] highlights symmetry's determining role in all biology domains [13], including perception, cognition, and physiology [46] and ecology [25]. The universal significance of spatial determinants suggests EPs as the root of the origin of biological symmetry.



Fig. 1. (GA Legend). Allegorical/metaphorical representation of four fundamental determinants (driving forces) of biological evolution. Space, time, symmetry, and relativity are considered as the elements of a tetrahedral meta-structure (adopted from [2] with alteration).

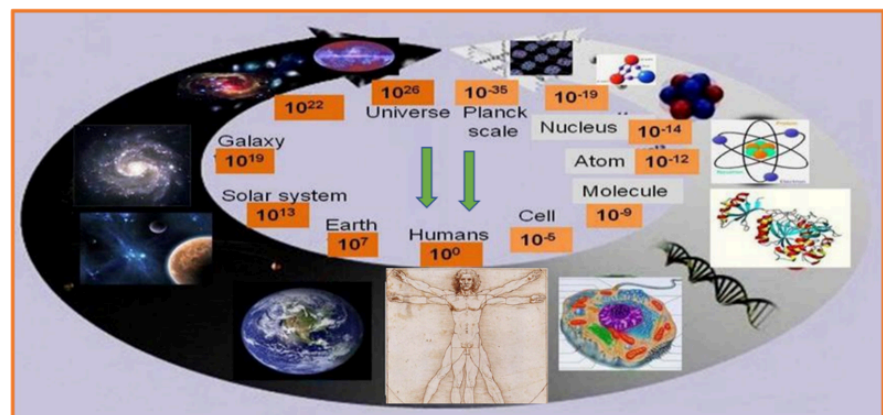


Fig. 2. The dimensions of the Universe {from extremely small (right part) to unthinkable large (left part), with humans seemingly in the middle} revealing different forms of space-time-symmetry. Adopted from [42] with modification.

Biological Symmetry

Biological symmetry occurs in numerous unique forms and refers to the conjunct dynamics of geometrical patterns including mirror symmetry (chirality), fractality, and topology. All the above-mentioned forms of

symmetries are observed in the structure of organisms (including plants, animals, fungi, and bacteria) and viruses. Our consideration is primarily focused on the fractal biology of humans, where the fine morphology of multiple neural circuits underlies cognitive abilities and psychological functions ^[48]. Highly prevalent in physical and biological objects, fractal patterns possess self-similar components that repeat at varying size scales. Increasing attention to fractal physiology ^{[11][49]} and fractal neuroscience ^{[50][51]} opens a window to studying fractality perception and related cognitive and psychological effects ^{[52][53]}. All living organisms contain splendid examples of fractal structures at different hierarchical levels of biological organization. The most known include glycogen's structure, the cytoskeleton network, the axonal-dendritic complex, the lung alveolar structure, and the capillary network ^{[46][54][55]}. Fractality at the molecular level is observed in the assembly of peptides adopting the beta-sheet conformation experimentally ^{[56][57][58]}. This observation suggests that at the molecular level, we could expect the interaction of different forms of STSR ^[59]. The symmetry determinants are evident in the prevalent chirality of DNA, proteins, and lipids. Homochiral protein systems are made from the chiral structure of DNA ^[60]. Proteins of all organisms contain mostly the L-isofom of amino acids (AAs).

However, a small quantity of selected AAs ^{[4][14]} plays a critical role in development and biological information processing. Currently, the impact of AAs and protein handedness on molecular fractality is practically overlooked. Many actual questions, such as the impact of protein racemization on fractal-based molecular assembly or the structure-function link in pyramidal neurons, still need to be systematically addressed. At the organism level, the symmetry determinants are observed in the structures of physiological systems and the bilateral morphology and functions of higher animals. Recently, complex physiological systems (e.g., neurological, respiratory, visual, and cardiovascular) have been shown to exhibit fractal dimensions. The quantitative assessment of spatiotemporal fractality allows for distinguishing between physiological function and dysfunction ^[46]. The interplay of continuous and discrete forms of symmetry in living organisms is responsible for the networks of links between the prevalence of bio-molecular handedness and the bilateral morphology and functions. The bilateral design of the nervous system in humans exhibits balanced patterns of symmetry and asymmetry, culminating in the laterality of perceptual, cognitive, and psychological functions. Notably, at all levels of organization from molecular, morphological, and functional, biological symmetry is always not absolute (i.e., relative). In bilateral organisms, predominant molecular chirality (the most studied form of biological symmetry) is traditionally considered to contribute to anatomical handedness and nervous system laterality. The transfer of chirality from the enzyme-protein level to the higher levels of biological organization is a well-studied process ^{[60][61][62][63]}. Spontaneous racemization was shown to disrupt proteins' physiological functions ^{[4][14][61]}, leading to age-associated neurodegeneration. The less studied form of biological symmetry at the organism level is fractality. The transfer of fractality from molecular to higher levels of biological organization is rarely addressed. We will analyze (currently limited) publications tracing the possible contribution of fractal geometry to biological symmetry at the molecular, cellular ^{[64][65]}, morphological ^[66], and perceptual ^{[67][68]} levels at physiological ^[46] and disease conditions ^[69]. The interaction of chiral and

fractal-based assembly is a promising pathway in molecular biology [54][55]. Fractality at the morphological level is studied in microorganisms (including viruses [70], bacteria [71], fungi [72], parasites [73], plants, and organs of animals [74][75][76]. Animal evolution, on the demand for information about the spatial and temporal structure of the external world, provided the mechanisms of the common and domain-specific perception of time and space determinants. At the level of brain information processing, time-space perception exhibits hemispheric asymmetry. Spatial and temporal stimuli predominantly activate the right cortical hemisphere, preserving the opportunity for discrimination between spatial and temporal inputs [77][78][79]. A broader view of fractality is provided in systems biology. The scale relativity theory (SRT), (known as the theory of biological relativity), explores bi-directional causation in the hierarchy of biological events. SRT is based on the assumption that the space-time geometry has a fractal dimension (i.e., explicitly scale-dependent) [80][81][82].

Conclusion

According to Meijer, the fundamental building blocks of Nature constitute a triad of energy, matter, and information [47]. In the development of his idea, we conclude that the fractal symmetry of space-time, evident in non-biological and biological objects, is associated with the scale-invariant laws of Nature. STSR is closely associated with Heisenberg's uncertainty principle [83][84]. The implication of space-time relativity for other fields of inquiry, including topics in biological information processing, cognition, and social science, is at the front line of neuroscience and psychology [29][84]. Convincing results are presented at the molecular level. Over 500 Protein Data Bank entries show the fractal-like structure [85] associated with molecular surface irregularity at the ligand-binding site involved in protein-protein interfaces [86]. For the small amyloid beta fragments (40 and 42 amino acids), fractal structures are predicted in the plaque-forming aggregates [87][88]. However, the specific role of fractal symmetry in the mechanism of protein aggregation, biological aging, and the pathology of cognitive and psychological functions remains to be studied. The coherent appearance of fractal determinants at the neuronal network connectivity [52], physiological functions [46] and in all lower levels of biological organization, including molecular and cellular assembly patterns, suggests the crucial role of fractal symmetry in physiological, perceptual [67][68], cognitive [89][90][91], and psychological [91][15] levels. At the molecular level, actin network assembly participates in many critical cellular processes, including the establishment and maintenance of cell junctions and cell shape. Relatively recently, it was discovered that an actin cytoskeleton (human embryonic kidney (HEK 293) cells) comprises a fractal structure [92]. In the neuronal dendritic spine, the actin network is organized into fractal patterns [93][94][95]. It is reasonable to assume that in pyramidal neurons (PyrNs), the actin cytoskeleton contributes to the formation of the soma shape. However, so far, there is no experimental support for this idea. The appearance of fractal determinants at all lower levels of biological organization [46][55] is in agreement with the evidence that the immune system, represented by the complex network of organs, cells, and molecular assemblies (proteins, DNA, lipids), exhibits distinct fractal patterns in health and disease conditions [96][97]. Many actual questions, such as the impact of protein racemization on fractal-based molecular assembly or the structure-

function link in pyramidal neurons, still need to be systematically addressed. Returning to the broad view, we can restate that, highly persistent in non-animate and animate nature, fractal patterns possess self-similar components that repeat across varying spatial and temporal scales. Fractal geometry encompasses physical, biological, and psychological realms. Not surprisingly, biological evolution selects a complex of the molecular, sensory, cognitive, and psychological mechanisms of corresponding perceptions and responses [98]. The environmental and human-made spaces, exhibiting fractal patterns, are associated with the spectrum of physiological [99], perceptual [100], and psychological experiences [101][102]. Until recently, experimental observation of molecular assembly into fractals was restricted to synthetic systems. The discovery of the fractal structure of protein aggregates opens a new dimension in studying pyramidal neuron soma genesis [3] and molecular psychology [7].

Statements and Declarations

Competing interests

The authors declare no conflict of interest.

Author Contributions

VV.D-S.: Conceptualization, Investigation, Writing – Original Draft, Writing – Review & Editing.

Data Availability

No new data were created or analyzed in this study. Data sharing is not applicable to this article as all information discussed is derived from previously published research cited within the text.

Footnotes

I. Mirror symmetry is a particular incident of a more generalized mathematical property of STS (referred to as T duality) [20].

In scale relativity theory, space-time geometry is considered continuous but non-differentiable; therefore, it is fractal (i.e., explicitly scale-dependent). A fundamental result of scale relativity is to propose a minimum and maximum scale in physics, invariant under dilations, in a very similar way as the speed of light is an upper limit for speed.

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