Journal of Biomolecular Structure & Dynamics, ISSN 0739-1102
Volume 29, Issue Number 4, February 2012

Comment

Thermodynamic Inversion and Self-Reproduction with Variations: Integrated View on the Life-Nonlife Border

http://www.jbsdonline.com

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The excellent work by Trifonov (1) adds to the discussion of extremely important questions: "What is life?", or "What is the difference between life and nonlife?" At present these questions have acquired practical sense, in particular, due to plural experiments on prebiotic chemistry and efforts to obtain an artificial cell. Where is the border between a non-living prebiotic microsystem and the simplest living unit? In the origin-of-life field these both types of systems are often fused into the infinitive term "protocell", no border between them. The Trifonov's minimalistic definition "*Life is self-reproduction with variation*", in my opinion, represents a profound insight into the foundation of life. It may serve as an important criterion for the distinguishing an actually alive molecular structure/system, who in the future will inevitably be obtained in laboratory conditions.

Some aspects of fundamental biology, Trifonov arises in his article, should be discussed in more detail.

Definition of Life or Properties of Life?

There exist more than 100 definitions of life. Most of them are true but none is comprehensive. In the opinion of the author of this comments life is such a phenomenon that can not be embraced with an exhaustive definition. Due to this reason, the author in his works (2, 3) deliberately did not give a definition of life. Instead, four key biological properties were formulated on the basis of the comparison of biological and non-biological systems: 1) the ability to concentrate free energy and information; 2) the ability to exhibit an intensified counteraction to external influences; 3) expedient behavior; 4) regular self-renovation on the various levels, including self-reproduction. The essence of the properties could be expressed by the author in the following thesis (or definition): a living system concentrates free energy and information using the ability to exhibit an intensified and expedient reaction to external changes extending its own existence through self-renovation. In fact, the above-mentioned set of four fundamental biological properties provides more opportunities for investigation of the origin of life than the single thesis. The author's goal consisted in consideration of the transition "nonliving $\rightarrow$ living systems" from different sides; for this purpose the integrative consideration of several properties was preferable in comparison with a single definition. As for the Trifonov's work, apparently, his goal is different: to provide the most compact and objective definition through creative integration of previous efforts in this area. And this goal has been achieved by him.

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Life-Nonlife Border

Trifonov emphasizes two independent notions: *self-reproduction* and *changes (evolution)*; they, actually, exclude one another, as self-reproduction is exact copying, no changes, while changes can not relate to exact copying (1). These combined notions are considered by him as a unique attribute of life, or the border between life and non-life: all is life that copies itself and changes. According to the author's inversion approach to the origin of life, the decisive step in the transformation of prebiotic microsystems into the simplest living units (probionts) took place due to the thermodynamic inversion, *i.e*. radical change of the balances "free energy contribution/entropy contribution" and "information contribution/informational entropy contribution" into negative entropy values (2-4). The thermodynamic inversion changes the direction of free energy, information and entropy transfer in the interchanging processes between the microsystem and its surroundings: free energy and information start to be imported into the microsystem, while entropy is exported outside. Simultaneously the exchange of substances is reorganized to facilitate extraction from the surrounding energy-rich compounds, providing molecules suitable for constructing new structures in the microsystem. Since the inversion, functional processes arose and connected the main types of biopolymers – sequences of nucleotides and proteins. Unlike a polynucleotide or proteinoid chain artificially synthesized *in vitro,* a functional sequence is meaningful (5). Functional sequences produce function at their destination (binding site or ribosomal translation site). Algorithmic optimization (selection of each symbol in the sequence specifically for function) occurred in the course of internal circulation of bioinformation, through continuous recombination and selection. In this way the inverse prebiotic microsystem becomes an active constituent with respect to the medium. Simultaneously the environment becomes part of the physical medium that is being actively influenced by life.

The Trifonov's definition and the author's origin-of-life concept are two different approaches to understanding of distinction between living and non-living systems. In spite of the difference between them, they can be integrated.

The Author's Interpretation of the Trifonov's Definition

Why are the two opposite attributes, *self-reproduction* and *changes,* in the foundation of life, according to the Trifonov's definition? How could they arise? A possible answer can be found in the inversion approach to the origin of life (2-4). The approach offers that thermodynamic inversion might occur only in a prebiotic microsystem oscillating around the bifurcation point under far-from-equilibrium conditions. In the case of balanced oscillations the microsystem acquires a bifurcate structure because of its intermediate position between two attractors – the initial and (potential) new states (Figure 1). There appears a paradoxical organization "stabilized instability" that preceded its transformation into the living unit in the course of thermodynamic inversion. Oscillations of the microsystem around the bifurcation point are not symmetrical: the forward transition over the bifurcation point

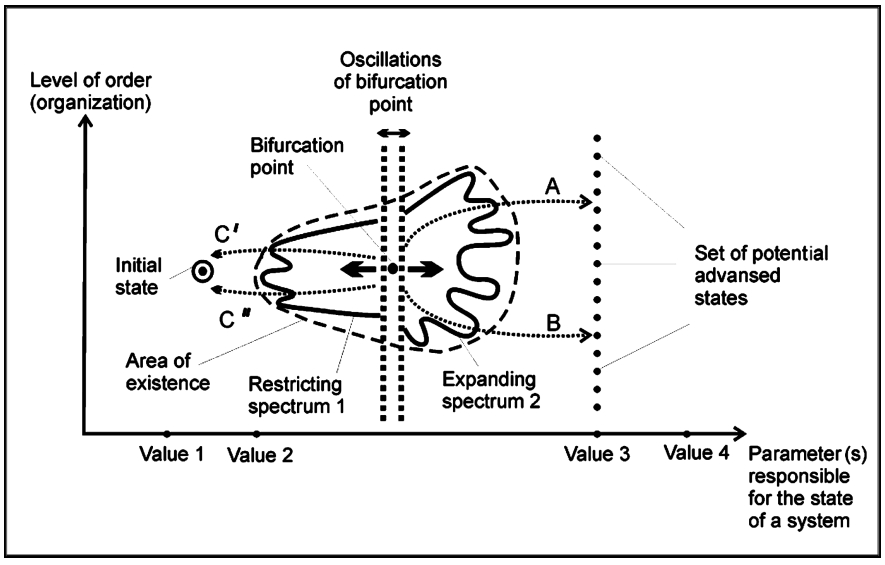

Figure 1: Spectrums of the potential states of a chemical system oscillating around the bifurcation point (*in the course of nonequilibrium transition from the initial stable state into advanced stable state through the unstable point of bifurcation*). **A** – trend to advanced higher-organized state; **B** – trend to advanced lower-organized state; **C'** and **C''** – reverse trends to the approximately initial state. On the left (from the bifurcation point) – restricting spectrum 1 focused on the initial state, on the right – expanding spectrum 2 directed to the set of potential advanced states.

brings new accidental change that reflects in the expanding spectrum of the potential advanced states (Figure 1, right part). The back transition is characterized with the restricting spectrum of the potential states because the system strives to return closer to the initial state (Figure 1, left part). Continuous oscillations lead to appearance of new and new changes in the microsystem due to the expanding spectrum of forward transitions; some of them are conserved in congruence with the restricting spectrum of the back transitions. As a result, such an oscillating prebiotic microsystem obtains two opposite tendencies – to conservation and modification, at the same time. In the author's opinion, the compact Trifonov's definition of life reflects the consequences of prebiotic processes on the early Earth.

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