OPARIN'S THEORY OF BIOGENESIS: BIOCOLLOIDAL OR BIOMOLECULAR?

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Introduction

There are many definitions of life but no one is quite satisfactory. "Life is a self-sustained chemical system capable of undergoing Darwinian evolution" (1), as NASA defined it; it is also "any autonomous system with open-ended evolutionary capabilities" (2), or "a self-sustained replicative network of chemical reactions whose evolutionary roots lie in some simple primordial replicative system" (3), to list only three of them. However, they are all working definitions. The first is directed to the question which kinds of systems or forms on other planets could be regarded as "alive," and the other two are put forward to direct the line of research on life's origin to particular molecular systems.

But life as such cannot be defined. Its very nature is beyond our comprehension; or as Bergson put it (4):

> Hence should result this consequence that our intellect, in the narrow sense of the word, is intended to secure the perfect fitting of our body to its environment, to represent the relations of external things among themselves—in short, to think matter … We shall see that the human intellect feels at home among inanimate objects, more especially among solids, where our action finds its fulcrum and our industry its tools; that our concepts have been formed on the models of solids … But from this it must also follow that our thought, in its purely logical form, is incapable of presenting the true nature of life, the full meaning of the evolutionary movement.

In the simplest terms, if we want to grasp life logically, intellectually, we have to reduce it to something dead, and so doing we are missing its very essence: life in not a thing, but a process. However, that does not mean that life cannot be studied scientifically—as an empirical fact. It is thus possible to develop a sound, practical and workable model or models of biological processes, and even to find a reliable theory of life's origin on our planet (and possibly elsewhere in the Universe).

Any theory of life's origin has to start with a conception of life, in other words it has to construct model systems, "artificial chemical life," in accordance with that conception (5). If the rising of crops is caused by the putrefaction of seeds (6), it is then possible to produce a manlike creature (*homunculus*) by putrefaction of human semen (7). Or, to refer to modern times, if life is essentially based on RNA molecules—which could be hereditary as well as catalytic molecules, ribozymes (8)—then the origin of life has to be viewed as an evolution of RNA-like molecules to the stage of modern RNA, DNA and proteins (9). If on the other hand life is defined as a complex autocatalytic process, it is crucial to study the evolution of (auto)catalytic systems at the beginning of Earth's history (10). The same holds true for the biocolloidal theory.

Biocolloidal Theory

The finding that proteins are colloids, i.e., that protoplasm is a colloidal solution, led to a quite natural assumption that the colloidal state of the protoplasm is changing in some way due to physiological processes (11). As osmosis was also recognized in biological systems, life at the beginning of the 20th century was comprehended as a colloidal-osmotic phenomenon (12, 13). These observations provided a basis for biocolloidal theory (biocolloidy) (14), which could perhaps be most easily understood from the "chemical" description of human body as an "water solution of certain inorganic and organic compounds in a peculiarly built vessel of so-called colloidal material" (15), as expressed by Croatian biochemist Fran Bubanović (1883-1956) (16, 17). In the light of that theory the cell physiology was tentatively explained by sol-gel transitions of the protoplasm, or by micellar theory (18) proposed in 1858 by Swiss botanist Carl Wilhelm von Nägeli (1817-1891). Even illness has been ascribed to the changes in colloidal state, for "flocculation determines illness and death" (19), and there were attempts to explain narcotic effects by proposing the thixotropic properties (changing sol into gel by shaking, or vice versa) of the protoplasm (20). However, biocolloidy has been poorly supported experimentally (20); in truth there were only vague notions that the colloidal state of the protoplasm has been changed due to external influence (21).

The first complete and sound theory of life's origin, proposed by Russian biochemist Aleksandr Ivanovich Oparin (1894-1980) and explained in his capital book *The Origin of Life* (22, 23), was not focused primarily on prebiotic synthesis (24) but on the evolution of protocellular systems. This is clear from the first sentences of the sixth chapter ("The origin of primary colloidal systems," p 137):

> Attempts to deduce the specific properties of life from the manner of atomic configuration in the molecules of organic substance could be regarded as predestined to failure. … The structure of the protein molecule, its amino and carboxyl radicals, polypeptide or other linkages, etc., determine only the ability of this material to evolve and change into a higher grade of organization, which depends not only on the arrangement of atoms in the molecule but also on the mutual relationship of molecules towards one another.

In other words, there is no "live molecule" as such. Oparin harshly criticized theories that life originated from "live protein," "biogenic molecule" (pp 132, 136), or "free gene," resembling the particle of "filterable virus" (25). It contradicts his materialistic beliefs, starting from an assumption that life came into being by natural law, i.e., by a long process of natural selection, and not by pure chance or a miracle of God. Besides, "protein is by no means living matter, but hidden in its chemical structure is the capacity for further organic evolution which, under certain conditions, may lead to the origin of living things" (p 136).

From the pure chemical point, aggregation of smaller molecules (i.e., polymerization) could not possibly lead to a higher complexity because "successive and repetitive polymerization of separate links can take place only in pure solutions and provided the polymerized substance is isolated" (p 146). As these conditions were not met in the early Earth's history, this was not the way in which life originated. Instead, life was formed from "dirty substances;" the first "live systems" were composed, as they are now, of all kinds of molecules in mutual interactions.

From the above, especially from the cited "mutual relationship of molecules towards one another" it could be concluded that Oparin was adherent to the molecular and not colloidal theory of physiological processes. But this would be wrong. Well acquainted with the polymeric nature of proteins, even with the structure of alpha helix and beta sheet (p 143), as well as many other discoveries in molecular biology (25), Oparin nevertheless paid no attention to the mutual interactions of molecules. Their *colloidal* properties have to be accounted, because (p 148):

> Rubinstein has shown that such properties of the protoplasm as heat coagulation, surface precipitation, permeability, electric properties, etc., cannot be explained on the basis of the properties of some one protoplasmatic component, like the proteins, lipids, etc., but are the resultant of correlation and reciprocal action of different colloidal systems, which make up the protoplasm.

The conclusion is clear: the protoplasm is a colloidal system. Therefore, the aim of theory is to find a colloidal system of enough dynamic complexity to be regarded as "alive," or to say it in his own words: "to attain a higher stage of organization and transition to a colloidal state, which bridges the gap between organic compounds and living things" (p 136) to be further evolved into "colloidal systems with a highly developed physico-chemical organization, namely, the simplest primary organisms" (p 250). Prebiotic evolution is, essentially, the evolution of colloidal systems.

But what were these "colloidal systems," which had, as was said before, emerged from "dirty substances?" They were coacervates, special kind of colloidal systems ("semiliquid colloidal gels"). They were studied by Henrik Gerard Bungenberg de Jong (1893-1977), who clearly distinguished coacervates from the coagulated colloids (26). They were also discussed as possible components of the protoplasm, because (27)

> it certainly seems justifiable to assume that for the structure of living matter, and also for its outer limitation, not only sols and structure elements (gels, fibrils, etc.) have significance, but that by the side of them, likewise coacervates play a part.

In these systems Oparin found a model for the first protocells for coacervates are easily formed in complex mixtures of various organics, as the primordial ocean was assumed to be. Coacervates are prepared by the mixing of colloidal particles with different electrical charges, corresponding to the prebiotic proteinoids and similar polymers of uneven composition (p 159). Moreover, these colloidal systems have "the property of extreme lability, making it possible for them to shift easily in either direction from the equilibrium under the influence of the smallest change in external conditions" (p 153). This means that coacervate droplets in the "primordial soup" of the primitive Earth's ocean were liable to all kinds of changes; they "may actually increase in size, growing at the expense of substances present in the equilibrium liquid, whereby even their chemical composition may undergo a radical change" (p 158). The formation of coacervate droplet was thus "a most important event in the evolution of the primary organic substance and in the process of autogeneration of life" (p 160).

Conclusion

At first it seems strange that Oparin as an enzymologist (28), well acquainted with the structure of protein molecules and the mode of enzyme action, was an adherent of the colloidal and not molecular theory of the protoplasm. But such an assumption is wrong. Oparin very well integrated enzymes in his theory, because the very existence of coacervate droplets depends on their action. Namely, only the droplets with harmonized catalytic, i.e., enzymatic, processes had a real chance to survive and reproduce themselves (due to accumulation of reaction products inside).

> In this way a natural selection of coazervates originated in its most primitive and simplest form, only the dynamically most stable colloidal systems securing for themselves the possibility of continued existence and evolution. (p 191)

Moreover

> Any deviation from this stability resulted in a more or less rapid loss and destruction of the individual system. (p. 191)

These simple systems later developed into more specialized structures, e.g. nucleus, ribosome, or plastid, which are

> only the external visual expression of a gradual unfolding and perfection of an inner physico-chemical structure and organization of colloidal formations (p 198).

The underlying idea is simple. Life has evolved as a system, as a whole, not as an individual molecule or a collection of specific molecules in mutual interactions (29). This means that the first forms characterized as alive were not simple, but complex in a high degree. Such complex forms Oparin found in colloids, or more explicitly in coacervate droplets composed primarily of polyamino acids (proteinoids) (30) with the evolutionary potential to develop catalytic (enzymatic) activity. In this way Oparin did not antagonize but harmonize colloidal and macromolecular theories of physiological chemistry.

References and Notes

1. P. L. Luisi, "About Various Definitions of Life," *Orig. Life Evol. Biosph*., **1998**, *28(4-8)*, 613-622.
2. J. Peretó, "Controversies on the Origin of Life," *Int. Microbiol.*, **2005**, *8*, 23-31.
3. R. Pascal and A. Pross, "The Logic of Life," *Orig. Life. Evol. Biosph*., **2016**, *46*, 507-513.
4. H. Bergson, A. Mitchell, trans., *Creative Evolution*, Dover Publications, Mineola, NY, 1998, ix-xx; originally published as *L'évolution créatrice*, 1907.
5. A. Eschenmoser and M. V. Kisakürek, "Chemistry and the Origin of Life," *Helv. Chim. Acta*, **1996**, *79*, 1249-1259.
6. "Verily, verily, I say unto you, Except a corn of wheat fall into the ground and die, it abideth alone: but if it die, it bringeth forth much fruit" (John 12:24). Such conceptions stem from the theory of spontaneous generation (*generatio equivoca*) which states that animate could be spontaneously created from the inanimate. (J. Bergman, "A Brief History of the Theory of Spontaneous Generation," *CEN Tech. J.*, **1993**, *7(1)*, 73-81.)
7. For example see: a) K. R. Snow, "Homunculus in Paracelsus, 'Tristram Shandy', and 'Faust,'" *J. Engl. Germ. Philology*, **1980**, *79(1*), 67-74; b) M. B. Campbell, "Artificial Men: Alchemy, Transubstantiation, and the Homunculus," *J. Stud. Know. Pol. Arts*, **2010**, *1(2)*, 4-14; c) P. Ball, *The Devil's Doctor: Paracelsus and the World*

of Renaissance Magic and Science, Farrar, Straus and Giroux, New York, 2006.

8. F. H. Westheimer, "Polyribonucleic Acids as Enzymes," *Nature,* **1986**, *319*, 534-536.
9. S. G. Strivatsan, "Modeling Prebiotic Catalysis with Nucleic Acid-like Polymers and Its Implications for the Proposed RNA World," *Pure Appl. Chem.*, **2004**, *76*, 2085-2099.
10. N. Raos and V. Bermanec, "Catalysis in the Primordial World," *Kem. Ind.*, **2017**, *66(11-12)*, 641-654.
11. The first hint of this hypothesis came from the founder of colloid theory Thomas Graham (1805-1869) in his seminal paper T. Graham, "Liquid Diffusion Applied to Analysis," *Phil. Trans. Roy. Soc.,* **1861**, *151*, 183-224. He speculated that colloids might be a necessary ingredient of "substances that can intervene in the organic process of life."
12. L. V. Heilbrunn, *The Colloid Chemistry of Protoplasm*, Gebr. Borntraeger, Berlin, 1928.
13. Conception of life as an osmotic phenomenon resulted in a number attempts to produce "live forms" by preparing various kinds of emulsions and making chemical-garden experiments (L. M. Bange et al., "From Chemical Gardens to Chemobrionics," *Chem. Rev*., **2015**, *115*, 8652-8703). Oparin harshly criticized such experiments: "Of course, all these claims were founded on more or less crude mistakes and have no real value so far as the solution of the problem of the origin of life is concerned. Their interest lies chiefly in a simplified mechanical approach to this problem" (Ref. 22, p 57). However, some modern theories of life's origin are supported by such experiments (e.g., M. J. Russell, A. J. Hall and D. Turner, "*In vitro* Growth of Iron Sulphide Chimneys: Possible Culture Chambers for Origin-of-life Experiments," *Terra Nova*, **1989**, *1*, 238-241).
14. a) U. Deichmann, "'Molecular' Versus 'Colloidal:' Controversies in Biology and Biochemistry, 1900-1940," *Bull. Hist. Chem.*, **2007**, *32(2)*, 105-118; b) C. Tanford and J. Reynolds, "Protein Chemists Bypass the Colloid/Macromolecular Debate," *Ambix*, **1999**, *46*, 33-51.
15. F. Bubanović, *Iz moderne kemije [From Modern Chemistry]*, Matica hrvatska, Zagreb, **1924**, p 117.
16. N. Raos, "Letters of Svante Arrhenius to His Former Croatian Student," *Bull. Hist. Chem.*, **2008**, *33(1)*, 12-16.
17. V. Damjanović, K. Mlinac-Jerković, S. Kalanj Bognar and J. Lovrić, "Fran Bubanović: The Visionary of Medical Chemistry and Biochemistry in Croatia," *Croat. Chem. Acta,* **2017**, *90*, 509-514.
18. C. Nägeli, *Die Micellartheorie*, Akademische Verlagsgesellschaft m.b.h., 1928. This is a reprint edition from the series Ostwald's *Klassiker*. It collects excerpts from papers from 1858-1893.
19. A. Lumière, *Rôle des colloïdes chez les êtres vivants. Essai de biocolloïdologie*, Masson et Cie, Paris, 1921.
20. P. J. Jurašić, "Najnovija istraživanja o biti narkoze [The Most Recent Research on the Essence of Narcosis]," *Priroda*, **1935**, *25(10)*, 296-305. "Colloid chemistry has found that all systems in which life processes take part are characterized by the fact that some parts of these systems are in the colloidal state. … This is the common physical property … which characterizes every living matter from a minuscule bacterium to the protoplasm in the brain cell of a philosopher and a poet." It was assumed that the dispersity of plasma's colloids is lower during narcosis than in an excited state.
21. L. Rhumbler, "Das Protoplasma als physikalisches System," *Ergeb. Physiol.*, **1914**, *14*, 474-617.
22. A. I. Oparin, *The Origin of Life*, translation with annotations by S. Morgulis, 2nd Ed., Dover Publications, Mineola, New York, 1953. Originally published as Возникновение жизни на земле (The Upspring of Life on Earth), 1936.
23. S. L. Miller, J. W. Schopf and A. Lascano, "Oparin's 'Origin of Life': Sixty Years Later," *J. Mol. Evol.*, **1997**, *44*, 351-353.
24. N. Raos, "Carbide Chemistry and Oparin's Theory on the Origin of Life," *Bull. Hist. Chem.*, **2017**, *42(1)*, 57-62.
25. C. B. Lipman, "The Origin of Life," *Sci. Month.*, **1924**, *19*, 357-367. This problem is discussed in length in the second (Russian) edition of his book: А. И. Опарин, Возникновение жизни на земле (The Upspring of Life on Earth), Academy of Science USSR, Moscow, 1941, p 132.
26. H. G. Bungenberg de Jong, "Die Koazervation und ihre Bedeutung für die Biologie," *Protoplasma*, **1932**, *15*, 110-173.
27. H. G. Bungenberg de Jong and H. R. Kruyt, "Coacervation (Partial Miscibility in Colloid Systems)," *Proc. Koninkl. Med. Akad. Wetershap*., **1929**, *32*, 849-856.
28. M. S. Kritsky, "Memoirs of Aleksandr Ivanovich Oparin," *Appl. Biochem. Microbiol*., **2005**, *41(3)*, 316-318.
29. Models based on specific molecular interactions explain the development of particular molecular mechanisms, but give no idea of the system within they have been developed. (See e.g., W. R. Taylor, "Transcription and Translation in an RNA World," *Phil. Trans. Roy. Soc. B*, **2006**, *361*, 1751-1760). However, colloidal (Oparin's) theory has little to say about the real molecules participating in the first metabolic or, even less, in the first reproductive processes; his approach was thus regarded as "extremely bold" (Ref. 1, p 616).
30. In this vein one has to judge Miller's prebiotic synthesis of amino acids (S. L. Miller, "Production of Amino Acids Under Possible Primitive Earth Conditions," *Science*, **1953**, *117*, 528-529), as well as experiments on their po-

lymerization into proteinoids (S. W. Fox, "The Chemical Problem of Spontaneous Generation," *J. Chem. Educ.*, **1957**, *34*, 472-479). These achievements were readily accepted because of the acceptance of Oparin's theory, namely that life evolved from systems of protein-like substances in colloidal (coacervate) state.

About the Author

Nenad Raos is a scientific adviser in chemistry, retired from the Institute for Medical Research and Occupational Health, Zagreb, Croatia. He is a very fluent science writer. Besides hundreds of articles on various topics of science, published in newspapers and magazines, he wrote 13 books in popular science, including *The Cookbook of Life—New Theories on the Origin of Life* (2018).

2019 Is International Year of the Periodic Table

The United Nations General Assembly and its Educational, Scientific and Cultural Organization (UNESCO) have declared 2019 to be the International Year of the Periodic Table. Why 2019? It is the 150th anniversary of Dmitri Mendeleev's first periodic table. For more information, see www.iypt2019.org.

The official opening ceremony was held on January 29 at the UNESCO House in Paris (www.iypt2019.org/opening-ceremony). The official closing ceremony, hosted by the Science Council of Japan IUPAC subcommittee, will take place in Tokyo on December 5 (www.iypt2019.jp/eng/index.html). In addition to conferences on the periodic table (see pp. 31 and 74), a sampling of celebrations still to be held around the world includes:

- Human Periodic Table: On July 15, students and staff of the Physical Sciences department at the Curro Durbanville Independent School in Cape Town, South Africa, will decorate t-shirts, representing elements of the periodic table, and assemble at the sports pavilion to form a human periodic table.
- MacaroNight: An Instagram contest called "Chemistry in stuff!" inviting youth of Macaronesia to upload photos of anything along with an explanation of the elements present in the photo. Winning entries will be recognized at Researchers Night of Macaronesia (September 27). Macaronesia consists of several groups of islands off the west coast of Europe and Africa including the Azores, Canary Islands, Cape Verde, Madeira and the Selvagens Islands.
- Cosmic Origin of the Chemical Elements: A four-day short course for teachers and the general public starting on July 22 at the Universidade Federal de Mato Grosso do Sul (UFMS), Campo Grande, Mato Grosso do Sul, Brazil.
- Days on The Periodic Table: Lectures on the history of the periodic table, its appearance on stamps and art, and its utility as a basic scientific tool. Sponsored by the Phytochemistry & Organic Synthesis Laboratory (POSL) in Béchar, Algeria, November 25 and 26.