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Comparison of fundamental physical properties of the model cells (protocells) and the living cells reveals the need in protophysiology

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Abstract: A hypothesis is proposed about potassium ponds being the cradles of life enriches the gamut of ideas about the possible conditions of pre-biological evolution on the primeval Earth, but does not bring us closer to solving the real problem of the origin of life. The gist of the matter lies in the mechanism of making a delimitation between two environments – the intracellular environment and the habitat of protocells. Since the sodium–potassium pump (Na^+/K^+-ATPase) was discovered, no molecular model has been proposed for a predecessor of the modern sodium pump. This has brought into life the idea of the potassium pond, wherein protocells would not need a sodium pump. However, current notions of the operation of living cells come into conflict with even physical laws when trying to use them to explain the origin and functioning of protocells. Thus, habitual explanations of the physical properties of living cells have become inapplicable to explain the corresponding properties of Sidney Fox's microspheres. Likewise, existing approaches to solving the problem of the origin of life do not see the need for the comparative study of living cells and cell models, assemblies of biological and artificial small molecules and macromolecules under physical conditions conducive to the origin of life. The time has come to conduct comprehensive research into the fundamental physical properties of protocells and create a new discipline – protocell physiology or protophysiology – which should bring us much closer to solving the problem of the origin of life.

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'Ring the bells that still can ring. Forget your perfect offering. There is a crack, a crack in everything. That's how the light gets in.' – *Leonard Cohen*

Potassium ponds

There is a statement we constantly come across in the scientific and popular-science literature: the ion composition of the internal environment of the body of humans and animals, in which all of its cells are immersed, is close to that of seawater. This observation appeared in the literature even 100 years ago, when it became possible to investigate the ion composition of biological liquids.

This similarity between the internal environment of the body and the sea is quite obvious: in both seawater and blood plasma there are one or two orders of magnitude more Na^+ ions than K^+. It is this composition that can make one think that life originated in the primeval ocean (the memory of which has since been sustained by the internal environment of the body), and the first cells delineated themselves from seawater using a weakly permeable membrane, so that their internal environment became special, suitable for chemical and physical processes needed to sustain life. Indeed, the ratio of the above cations in the cytoplasm is the exact reverse of their ratio in seawater: there is much more K^+ in it than Na^+. In fact, physiological processes can only be possible in an environment where potassium prevails over sodium. Therefore, any theory of the origin of life must explain how such a deep delimitation (distinction) between the two environments could occur: the intracellular environment, wherein vitally important processes take course, and the external environment, which provides the cell with necessary materials and conditions.

For the protocell to separate from seawater, a mechanism must arise that creates and maintains the ion asymmetry between the primeval cell and its environs. We normally consider a mechanism of this kind as the isolating lipid membrane with a molecular ion pump, the Na^+/K^+-ATPase, built into it. If life originated in seawater, the origin of the first cell inevitably comes down to the origin of the sodium pump and any structure supporting it – the lipid membrane – without which the work of any pump would make little sense. It seems that life is born in conditions that are really adverse to it and even ruinous.

The trouble with the idea of life originating in seawater has made one look for alternatives in the hope that the need for the

Highlights

The great basic question of science: Membrane compartment or non-membrane phase compartment (biophase) is a physical basis for origin of life?

1. If life originated in seawater, the origin of the first cell inevitably comes down to the origin of the sodium pump and any structure supporting it – the lipid membrane – without which the work of any pump would make little sense.

2. Since the sodium-potassium pump (Na^+/K^+-ATPase) was discovered, no molecular model has been proposed for a predecessor of the modern sodium pump. Neither Miller's electrical charges, nor Fox's amino-acid condensation, nor building ready-made biomolecules into coacervates; none of this has managed to lead to the self-origination of the progenitor of the ion pump even in favourable lab conditions.

3. In 2007, we saw the simultaneous release of two articles, in which it was posited that life originated not in seawater as previously thought, but in smaller bodies of water with a K^+/Na^+ ratio necessary to sustain life. In this conditions sodium pump is not needed and the pump can originate later. But why the pump is needed if K^+/Na^+ ratio is good? The origin of the sodium pump in conditions where there is no natural need for it may require the agency of Providence.

4. Potassium Big Bang on Earth instead of potassium ponds.

5. Fox's microspheres do not need potassium ponds.

6. Despite the fact that Fox's microspheres have no fully functional membrane with sodium pumps and specific ion channels, they generate action potentials similar to that by nerve cells and in addition have ion channels which open and close spontaneously. This ability of the microspheres contradicts to the generally accepted ideas about the mechanism of generation of biological electrical potentials.

7. Hodgkin-Huxley model of action potentials is similarly well-compatible with both the nerve cell and Fox's microsphere.

8. Biophase as the main subject of protophysiology. In the past they considered the living cell as a non-membrane phase compartment with different physical properties in comparison to the surrounding medium, and this physical difference plays a key role in cell function. According to a new take on an old phase, non-membrane phase compartments play an important role in the functioning of the cell nucleus, nuclear envelope and then of cytoplasm. Somebody sees the compartments even as temporary organelles. According to available data, the phase compartments can play a key role in cell signaling. In this historical context, studies in recent years dedicated to non-membrane phase compartments in the living cells sound sensational.

9. It is essentially a Protocell World which weaves known RNA World, DNA World and Protein World into unity.

10. In the view of non-membrane phase approach, the usage of liposomes and other membrane (non-biophase) cell models to solve the issue of the origin of life is a deadlock way of the investigation.

I would be grateful to those skilled in the field of membrane physiology for comments and criticisms.

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