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CONFERENCE REPORT

Cellular Life Could Have Emerged from Properties of Vesicles

Saša Svetina

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Abstract It is indicated why it is plausible to assume that the initiation of cellular life was based on properties of vesicles. Vesicle properties relevant for the process of vesicle self-reproduction are revealed. Some open questions related to the idea that vesicle self-reproduction is an evolutionary process that includes the elements of the Darwinian selection are put forward, and some suggestions are made for possible directions of further research.

Keywords Vesicles · Self-reproduction · Darwinian selection · Evolution · Emergence of cells

There is a general quest to reveal which properties of molecules or their supramolecular structures have been decisive for the emergence of life. In this contribution we hypothesize that the core features of cellular life, i.e. growth, self-replication and evolution, could have emerged on the basis of properties of vesicles. Vesicles are macroscopic objects in which their aqueous interior is separated from their aqueous environment by a thin flexible membrane. They can form spontaneously with their membranes made of amphiphilic molecules such as surfactants, lipids or polymers (Walde 2006). The possible role of lipids in the origin of life has been indicated by their primordial availability (Deamer 1997). Vesicles were instrumental for the transition from inanimate to living matter at least by supplying the necessary compartmentalization. However, their role could have been much more important: it was demonstrated that they can grow and self-reproduce (Berclaz et al. 2001); they exhibit compositional inheritance as their splitting may produce offspring with identical composition (Segré et al. 2001); it is possible to ascribe to self-reproducing vesicles the principle of natural selection based on the condition for vesicle self-reproduction that interrelates a vesicle's intrinsic physical parameters and the parameters that also depend on the properties of their environment (Božič and Svetina 2004, 2007).

The notion about involving the selectivity principle suggests that vesicles have the capacity to evolve. Vesicle evolution could have operated on the basis of the selection

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S. Svetina (✉)
Institute of Biophysics, Faculty of Medicine, University of Ljubljana and Jožef Stefan Institute, Ljubljana, Slovenia
e-mail: sasa.svetina@mf.uni-lj.si

between vesicle populations that could have existed in a given prebiotic environment and differed with respect to the physical and chemical characteristics of their vesicles. A possible method to study the relative importance of different vesicle properties in the establishment of the corresponding vesicle populations is to develop models of vesicle self-reproduction based on the existing knowledge of vesicle behaviour. In our theoretical models proposed previously (Božič and Svetina 2004, 2007) the conditions for vesicle self-reproduction were obtained from the requirement that a growing vesicle, while doubling its size, must also prepare itself for division. This it does by changing its shape from a sphere into a budded shape that is composed of two spheres connected by a narrow neck. By breaking this neck a vesicle with a laterally homogeneous membrane divides into two spherical daughter vesicles that have the same composition. In the simplest case, the prototype model of vesicle self-reproduction (Božič and Svetina 2004), vesicle growth was assumed to occur due to constant incorporation of new molecules into its membrane causing an exponential increase of its area. Vesicle volume was passively changing due to the flow of water through the membrane dragged by the transmembrane pressure difference. The analysis showed that at the time of the doubling of membrane area and vesicle volume a vesicle can attain the budded twin shape (the shape involving two equal connected spheres) if the condition that relates model parameters assumes a certain fixed value. At smaller values than this a growing vesicle would attain shapes (Peterlin et al. 2009) which cannot lead to its self-reproduction, whereas at higher values the budded shapes obtained would be composed of two unequal spheres. Analogous behavior was predicted also with a generalization of the prototype model that included a membrane permeable solute (Božič and Svetina 2007).

The cited models of vesicle self-reproduction identified the requirement for relationships between parameters of the system that balance the growth of the membrane, the increasing of the vesicle volume and the concomitant transformation of the vesicle shape. The nature of these relationships can be particularly well elucidated by the analysis of the prototype model because its four parameters (membrane spontaneous curvature, membrane bending constant, membrane hydraulic permeability and membrane doubling time) symbolize four different aspects of the self-reproducing process. Membrane spontaneous curvature (Helfrich 1973) is a membrane structural property measuring membrane asymmetry which drives the membrane into a definitely curved conformation. It is therefore the determinant of the size of the self-reproducing vesicle. It is also one of the two determinants of vesicle shapes that correspond to the minimum of the membrane bending energy. More strictly, the shape determining parameter is the dimensionless reduced spontaneous curvature, which is proportional to the product of the membrane spontaneous curvature and the square root of its area (Deuling and Helfrich 1976). Because of the growth of the membrane area the reduced spontaneous curvature during the self-reproduction process is constantly increasing. Consequently the rate of growth of membrane area must be related to the change of the reduced spontaneous curvature from its value for the initial sphere to its value of the final budded shape. The remaining two parameters of the model, membrane bending constant and hydraulic permeability, influence vesicle shape by affecting the reduced vesicle volume defined as the ratio between vesicle volume and the maximum vesicle volume at a given membrane area, which is the second shape defining parameter. The values of membrane bending constant and hydraulic permeability must be such that the doubling time defined by the rate of the growth of the membrane area is matched also with the time needed for the doubling of the vesicle volume. In the prototype model both of the described requirements are united into a single relationship between the four model parameters. In the model with the included solute the simple relationship between model parameters is replaced by a set of two equations.

The analyses described strongly indicated that vesicle self-reproduction is an evolutionary process which includes the elements of the Darwinian selection. However, full acceptance of this idea requires further experimental and theoretical verification. In the following we shall state some related open problems and indicate some possible ways to resolve them.

Although vesicle shape behaviour is an emergent property of membranous systems and thus does not depend essentially on the type of amphiphilic molecules that have constituted different primordial membranes, it is still of interest to ask what kind of molecules could have been responsible for the generation of their spontaneous curvature. Membrane spontaneous curvature can be expressed in terms of the intrinsic shapes of membrane constituting lipids as well as of molecules which are intercalated into the membrane or bound to its surface (Kovačič et al. 2010). A possible origin of membrane spontaneous curvature is the asymmetric binding of dissolved molecules to the two leaflets of a bilayer membrane. These molecules could have been small peptides that bound only to the outer layer of the bilayer membranes. Such a prebiotic situation is appealing because it could have led to the development of the membrane catalyzed metabolic processes, and then potentially also to the formation of pore forming peptides and eventually to curvature forming proteins (McMahon and Gallop 2005).

Another still unresolved vesicle problem concerns the mechanism of breaking the neck that connects the two spherical parts of the budded shape. It is possible for this process to occur spontaneously due to specific composition of the vesicle membrane (Sakuma and Imai 2011). However, for most membranes the spontaneous breaking of the neck is not expected and it is thus plausible to assume that the primordial causes for breaking the neck were the external, possibly cyclic mechanical agitations.

The important aspect of the process of vesicle self-reproduction concerns the mechanism responsible for the increase of vesicle volume due to the water inflow. Water can be dragged into the vesicle due to the osmotic imbalance caused by the transmembrane transport of solutes as well as by the pressure difference between the vesicle outside and inside. The analysis of the model of vesicle self-reproduction that included a solute (Božič and Svetina 2007) indicated that the water influx must be a combination of both these causes. Membranes with the corresponding permeability behaviour have not yet been constructed.

In early vesicle evolution the selection between vesicle populations most probably operated on the basis of their rates of the growth. As a consequence, an initially polydisperse vesicle population must have gradually become monodisperse, with the winning vesicles being those of the shortest generation time. The generation time could have decreased due to the increase of the growth rates. In order for the relationships between the system parameters to keep the prescribed fixed value, the decrease of the generation time could have only happened by increasing the value of some other system parameter, e.g. membrane hydraulic permeability. For such an evolutionary process to proceed, it must have started with vesicles with relatively long generation times. Also, for vesicles to exhibit the growth process, the system had to be far from equilibrium. It can thus be deduced that the primordial vesicle membranes had to be formed from molecules with as low CVCs (critical vesicle concentrations) as possible (Svetina 2012).

At the level of vesicle populations it will have to be still found which properties of vesicular systems are essential for the establishment of conditions that allow for their constant exponential growth. Vesicles can be formed after the solution concentration of their constituents reaches their CVC. After that the total vesicle mass would be increasing proportionally to the rate of formation of vesicle constituents. For exponential growth the formation of new constituents of vesicle membranes should be proportional to the total amount of these membranes. This could have been realized if vesicles by themselves became involved in the formation of relevant membrane constituents. It is not impossible for this to happen because vesicles might also possess the capacity to increase their complexity, for example by acquiring in addition to the function of self-reproduction some other cell-like functions such as surface enhanced catalysis (Svetina 2007). In this respect it can be pointed out that in the process of vesicle complexification an important role might have been played by their ability to fuse. Fusion of vesicles carrying different extra acquired functions could have produced a new vesicle inheriting characteristics of both parent vesicles.

In conclusion, vesicles involve properties that allow for the Darwinian evolution. Thus it is not impossible for cells to have evolved from a simple vesicular physico-chemical system to the complex contemporary entities in a single evolutionary route. However, the complete scenario of how vesicle properties have been utilized in the course of the development of the cellular life is still to be worked out.

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