Orig Life Evol Biosph (2008) 38:343–353
DOI 10.1007/s11084-008-9139-0

THEORETICAL MODELING

Early Stages of the Evolution of Life: a Cybernetic Approach

Alexey V. Melkikh · Vladimir D. Seleznev

Received: 5 February 2008 / Accepted: 2 May 2008 /
Published online: 3 June 2008

Abstract Early stages of the evolution of life are considered in terms of control theory. A model is proposed for the transport of substances in a protocell possessing the property of robustness with regard to changes in the environmental concentration of a substance.

Keywords Protocell · Control theory · Robustness · Active transport of ions · Minimal cell

Introduction

According to modern ideas, the initiation of chemical processes on the planet was the start point of the chemical evolution. The major result of the first phase was the integration of simple H, C, N and P atoms into relatively complex organic molecules. The next evolutionary process consisted in their integration into macromolecules. Some molecules, which were formed in the protoatmosphere, combined into chains: polypeptides and polynucleotides were formed while they were constantly competing with the chains-breaking process of hydrolysis.

Two possible basic scenarios of the later evolution can be suggested. By the first scenario, an isolated protocell (a coacervate droplet or a microsphere) appeared first and only then it acquired the multiplication capability (Fox 1965, 1980, 1988; Fox and Dose 1972; Oparin 1964). The reverse sequence is adopted in the second scenario, that is, a simplest system capable of producing its replicas (a replicator) was formed first and then it got a membrane and was isolated from the environment. Networks of polynucleotides and polypeptides—hypercycles—probably appeared (Eigen 1971; Eigen and Schuster 1979). Abiogenic polypeptides could have been decisive for the acceleration of the synthesis and replication processes. Modifications of initial components arising from small errors of replication and the subsequent selection of favorable variants played an important role.

A. V. Melkikh (✉) · V. D. Seleznev
Ural State Technical University, Mira str. 19, Yekaterinburg, Russia 620002
e-mail: melkikh2008@rambler.ru

A number of models in the literature have described the evolution of self-reproducing molecules or replicators (see, e.g., Fontanari et al. 2006; Szathmary and Demeter 1987; Szathmary 1992).

The importance of metabolism to primitive molecules has been noted earlier (Morovitz et al. 2000). Some authors think that just metabolism rather than the replication capability was the first property of living systems.

Thus, the gradual complication of molecular complexes led to the formation of protocells (eobionts), which were isolated from the environment by a membrane. Those simplest organisms could perform elementary operations with substances (the energy conversion and the transport).

However, even the simplest organisms existing today are very complex. This brought up the problem of finding the minimum complexity of an organism or a "minimal cell" (Murtas 2007; Glass et al. 2006). This problem can reasonably be tackled in terms of control theory, according to which the control is a function of a system that allows retaining its structure. As applied to living systems, the control should ensure both the invariability of the spatial structure and some sequence of changes with time, which is connected with the reproduction process.

From the viewpoint of vital functions of a cell, one of its most important functions consists in provision of constant intracellular conditions primarily by the composition of substances. For this purpose, it is necessary to provide an active transport of ions through the cell membrane so that this transport depends little on casual changes in the environmental composition (i.e. the robustness is ensured). It should be remembered that closed membranes of water-dissolved phospholipids can be formed in equilibrium conditions as well. However, in these conditions the membrane has some average lifetime τ_0 and its intra- and extracellular compositions are the same. In this case, a minimum step for organization of a "living" cell can be assumed to be the establishment of a control system that would maintain the concentrations of substances on both sides of the membrane at different levels. It can be expected in this case that the intracellular composition is preserved such that the membrane life to failure increases and the system will begin increasing its concentration in the environment. The process of the geographical proliferation of this system can be initiated as its lifetime is longer than τ_0 corresponding to the equilibrium. For this process to occur it suffices that a molecule, which acts as an ion pump absorbing the sunlight or some other energy, is built into the material of the cell membrane. Also, the spatial spreading requires that the intracellular composition and, hence, chemical reactions in the cell depend little on changes in the environment and other extracellular conditions, which are inevitable during the proliferation.

Let us consider physicochemical processes in such a minimal cell and discuss conditions necessary for commencement of the further process of the biological evolution.

A Model of the Simplest Transport System in a Minimal Cell

Undoubtedly one of the basic functions of protocells was the conversion of energy from one type to another. One of distinctive properties of living systems is their organization providing a highly efficient (almost 100%) conversion of energy at the molecular level. Molecular complexes, which perform this conversion, are conventionally referred to as molecular machines. Cells of contemporary organisms have a plethora of various molecular machines.

One more critical property of living systems is their robustness, i.e. a weak sensitivity of their properties to fluctuations of environmental properties (see, e.g., Kitano 2004; Stelling et al. 2004) or the ability to keep the intracellular medium unchanged.

Let us consider a model of the simplest molecular machine, which can transport substances to (or from) a protocell thanks to an external energy source. We shall show that the properties of robustness and efficiency in this system are mutually complementary: a fully efficient system cannot be robust or vice versa.

Models of the active transport of ions in different types of cells have been constructed (Melkikh and Seleznev 2005, 2006a, b, 2008). We shall simulate the active transport in a protocell using analogous models. The basic provisions of the model of the active transport of ions are listed below:

1. A transfer macromolecule capable of the ion transport has two conformational states corresponding to the position of an ion sorption center inside and outside the cell.
2. The motive force of the ion transport is the difference of the ATP–ADP chemical potentials (another source is also possible in this case). The ATP energy is almost fully imparted to the transfer molecule, which then passes with a high probability to the state corresponding to the position of the ion sorption center outside the cell.
3. After the ion has passed to the solution, the macromolecule returns to its initial state (the ion center resides predominantly in the cell).

The model of the active transport is based on the Boltzmann distribution for a two-level system and the probability of finding the macromolecule in either state under nonequilibrium conditions (when the ATP–ADP chemical potentials are different).

Let us conceive a simplest protocell whose membrane hosts one pump transferring some substances from the external solution to the cell inside. At the start of the evolution this pump could be not too specific and probably was unable to recognize some molecules. An immediate analog of such a system among the currently existing systems is synaptic vesicles transporting neuromediators in neurons (Melkikh and Seleznev 2007).

We shall assume the existence of a permanently maintainable source of energy, which could be presented by the sunlight or some energy-rich molecules. Such a universal molecule in contemporary cells is ATP. Let us use the same designation remembering that ATP can be replaced by another molecule whose chemical formula is not of principal importance in the given model. That is, the energy source will be simulated as an ATP molecule, which can transform to ADP through hydrolysis. The motive force of this source is the difference of the chemical potentials, $\Delta\mu_A$. It is important (again for efficiency reasons) that the reaction must be catalytic and take place in a transfer molecular machine rather than in the solution. Figure 1 shows an efficient transport system in a protocell.

In this case, the active flow of a substance to the inside of a vesicle can be written in the form (according to Melkikh and Seleznev 2005):

$$J_a = C\frac{\exp\left(\frac{\Delta\mu_A+\varphi e}{kT}\right)n_o - n_{in}}{\left[1+\exp\left(\frac{\Delta\mu_A+\varphi e-Q}{kT}\right)\right]}, \quad (1)$$

where φ is the electrical potential at the vesicle membrane (if the transferred substance has a charge); n_{in} and n_0 are concentrations of the substance in the external environment and on the inside of the vesicle; Q is the difference between energy levels of the ion-transporting macromolecule. We shall assume first that the passive flow of this actively transferred

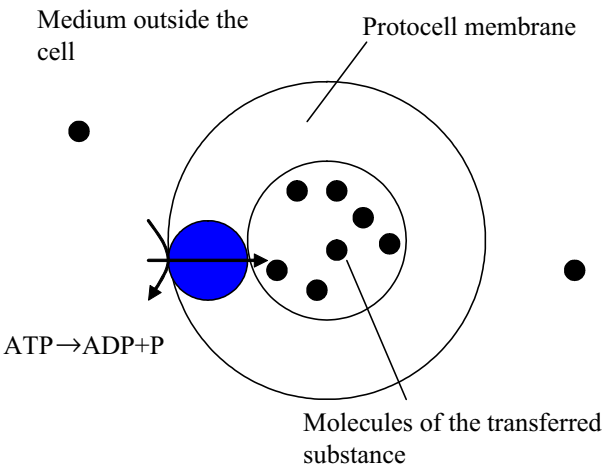

Fig. 1 The efficient transport system in a protocell

substance is small as compared to its active flow. This assumption follows from efficiency considerations because otherwise much energy would be lost.

Equating the active flow (Eq. 1) to zero from the condition of conservation of the number of particles gives the ratio of the molecule concentrations on the inside and the outside of a protocell:

$$\frac{n_{\text{in}}}{n_0} = \exp\left(\frac{\Delta\mu_{\text{A}} + \varphi e}{kT}\right). \tag{2}$$

Let us assume for simplicity that the prebiotic soup includes only two types of ions, namely a positive ion (actively transferred to the protocell) and a negative ion, which passively penetrates through the cell membrane. Then the electroneutrality condition

$$\begin{aligned} n_0^+ &= n_0^- \\ n_{\text{in}}^+ &= n_{\text{in}}^- \end{aligned}, \tag{3}$$

should be fulfilled both in the external environment and on the inside of the protocell.

The second (negative) component will be distributed inside the protocell in accordance with the Boltzmann law:

$$n_{\text{in}}^- = n_0^- \exp\left(-\frac{\varphi e}{kT}\right). \tag{4}$$

Then from Eqs. 1–4 we have

$$\varphi e = \frac{\Delta\mu_{\text{A}}}{2}, \tag{5}$$

$$\frac{n_{\text{in}}^+}{n_0^+} = \exp\left(\frac{\Delta\mu_{\text{A}}}{2kT}\right). \tag{6}$$

It can easily be shown from Eqs. 5 and 6 that the free energy consumed for the transfer of one ion through the membrane equals exactly $\Delta\mu_{\text{A}}$. This means that the efficiency of the process is unity (for more details see Melkikh and Seleznev 2006a, b).

If the transferred molecule is uncharged, from Eq. 2 we have

$$\frac{n_{\text{in}}}{n_0} = \exp(\Delta\mu_{\text{A}}). \tag{7}$$

In this case, the electrical portion of the free energy is absent, but the energy consumption again equals $\Delta\mu_{\text{A}}$.

In both cases this pump provides a large concentration of the transferred substance inside the protocell (or removes harmful substances from the protocell). For example, if $\Delta\mu_{\text{A}} \approx$ 20 kT (a typical value for currently existing cells), we obtain that the ratio between the intra- and extracellular concentrations of uncharged molecules will be approximately 5×10^8. The free energy of the substance, thus obtained, can be used in further operations (work, synthesis of other substances, etc.).

Notice that at this stage of the evolution the high efficiency of the molecular machine does not necessarily results from selection. It can simply be due to a certain structure of molecules participating in the process of the active transport and the subsequent chemical metabolism. This structure can exist even before replication.

Let us turn to the problem of robustness of this ion transport system. It is seen from Eq. 7 that the intracellular concentration of ions is directly proportional to the concentration of ions outside the cell. In other words, this system is not robust since it has not a mechanism that would inhibit the change of the intracellular concentrations with varying extracellular concentrations. If such a pump is present, the pumping effect, which arises with varying environmental composition, can lead to the failure of the membrane because of the change in the osmotic pressure, the electrical breakdown of the membrane or a critical intracellular composition impairing the metabolism processes.

A Model of the Simplest System for Control of Transport Processes in a Cell. Robustness of Transport Processes as the Basic Property of a Minimal Cell

Thus, a protocell should have the simplest system for control of the active transport of ions, reducing the breaking action of environmental variations.

One of the most important characteristics of the control system is the controller, which is a device ensuring the required behavior of dynamic systems by means of a feedback (Dorf and Bishop 2004). A classical diagram of the feedback control system is shown in Fig. 2.

There is a multitude of controllers (integral, proportional, PID, etc.) based on different dependences of regulating functions on parameters of the system and the time.

However, a controller is the simplest when the control variable is time independent (i.e. the controller is quasistationary). We shall consider just this quasistationary controller in the model describing the system of control of transport processes in a minimal cell.

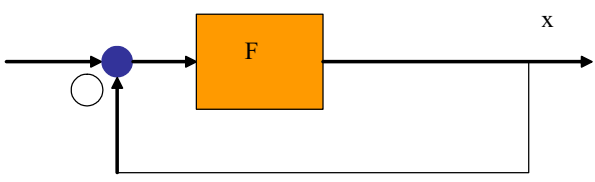

Fig. 2 Diagram of the feedback control system

The control device in this system can be the presence of passive penetrability of the actively transferred ion or one more system of the active transport. Let us consider these two mechanisms while limiting ourselves to the transport of an uncharged molecule.

Write the equation for the stationary flow of an uncharged substance through the cell biomembrane taking into account the passive transport. The full flow will be the sum of the active (the first term) and passive (the second term) flows:

$$C(x\exp(\Delta\mu_A) - y) + P(y)(x - y) = 0, \tag{8}$$

where C is a constant characterizing the pump speed; $P(y)$ is penetrability of the biomembrane by actively transferred molecules; x is the concentration of the substance inside the protocell; y is the concentration of the substance in the external environment. Assume the membrane penetrability to be a function of the extracellular concentration. It is necessary to find the function $P(y)$ providing a constant concentration of the substance in the protocell. The presence of such dependence means that, e.g., the protocell biomembrane has a variable-penetrability ion channel in addition to the ion-transferring pump. Such channels are very frequent in contemporary cells.

It can be shown (see Appendix) that the proper selection of the penetrability $P(y)$ as a function of the extracellular concentration readily gives the dependence of the intracellular concentration on the extracellular one and this dependence is much like the homeostatic curves for different living systems (Fig. 3; Cannon 1932). Figure 3 presents the dependence $x(y)$ near the critical point (x_0=2, y_0=1).

This system has the property of robustness near the said point as only the term proportional to ($y - y_0$) is left after the function has been expanded as a power series. For example, if fluctuations of y amount to 10%, the value of x remains essentially unchanged.

Then the active transport with a controller in the protocell can be sketched diagrammatically as in Fig. 4.

One more possibility of constructing the controller is the presence of two different pumps for one type of molecules. Let us write the equation for the flow of molecules

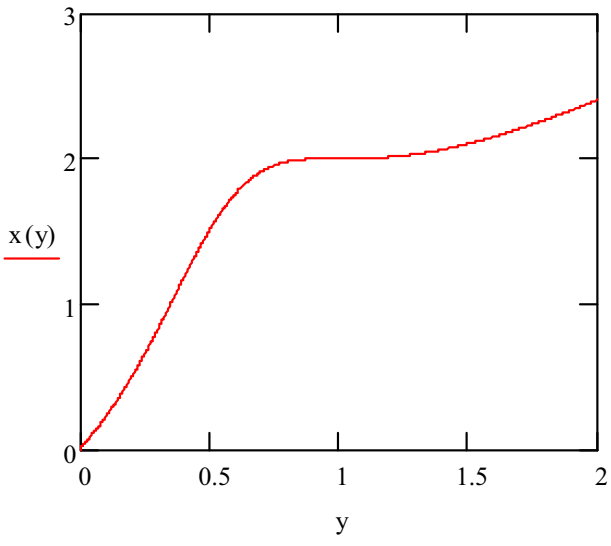

Fig. 3 The dependence $x(y)$ near the critical point (x_0=2, y_0=1)

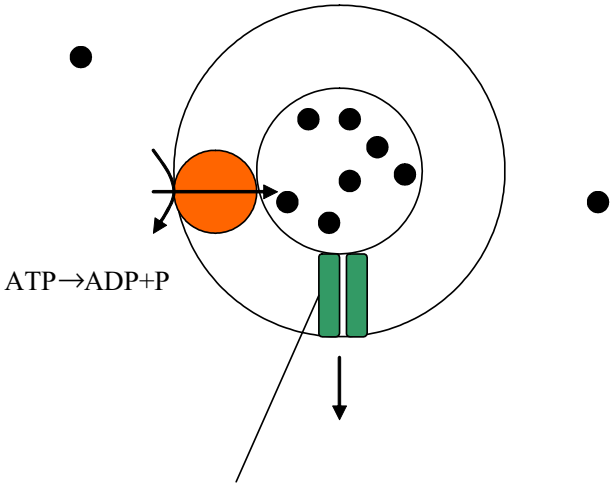

Fig. 4 A sketch of the active transport with a controller in the protocell

considering that the actuation frequency of one (or both) of the pumps depends on the extracellular concentration of molecules:

$$C_1(x\exp(\Delta\mu_A) - y) + C_2(y)(x\exp(\Delta\mu_B) - y) = 0. \quad (9)$$

The larger is the value of $\Delta\mu_B$, the easier the robustness conditions are fulfilled and the wider is the interval of values when these conditions can be fulfilled. By way of example, Fig. 5 shows the dependence $x(y)$ for $\Delta\mu_A$=2 and $\Delta\mu_B$=2.3.

In this case, the coefficient C_0 is negative and this means that the pumps will operate in opposite directions.

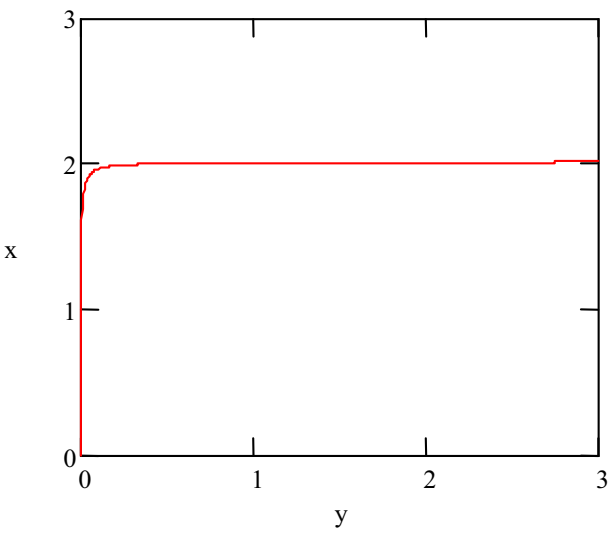

Fig. 5 The dependence $x(y)$ for $\Delta\mu_A$=2 and $\Delta\mu_B$=2.3

At the same time, if $\Delta\mu_A=\Delta\mu_B$, the system of the active transport becomes degenerate and is not liable to optimization.

The same results can be achieved if we use one and the same value of $\Delta\mu_A$, but different stoichiometries of the molecule transfer by two systems of the active transport. In this case, the value of $\Delta\mu_B$ or the stoichiometry constants will present a control instrument providing one more opportunity to increase robustness. The scheme of the control system in the presence of two different systems of the active transport of a substance is shown in Fig. 6.

Significantly, the system cannot be 100% efficient if any of the above types of the controllers is present. This is because any possibility to control the process requires energy consumption.

An especially evident case is when two pumps operate virtually towards one the other. This situation can probably be realized in the nature only when the consistency of some value is very important and the inputs to maintaining this consistency are justified.

It is known that many processes in a cell exhibit a self-oscillation behavior. Since a cell represents an open system, properties of these self-oscillations will depend on environmental conditions. The presence of the self-oscillation process, which is weakly sensitive to external perturbations, is of fundamental importance for vital functions of cells. Invariability of the amplitude and the period of self-oscillations is important for cells.

Notice that the presence of at least one control system in a matter can be taken as a definition of life. Indeed, all existing control systems are either living systems or systems subsisting on living systems (technical, economical). In this sense, a minimal cell can be implied to be a system, in which substances are transported at the expense of external energy sources, while the concentration of at least one substance is maintained within some limits as its concentration changes considerably in the external medium. It is precisely this property that distinguishes such a minimal cell from molecules and molecular complexes, which cannot be thought of as living ones. The structure of this minimal cell is much simpler than structures of currently available cells. In other words, its evolution had taken a sufficiently long time before the advent of simplest cells (e.g., archaebacteria) as we understand them today.

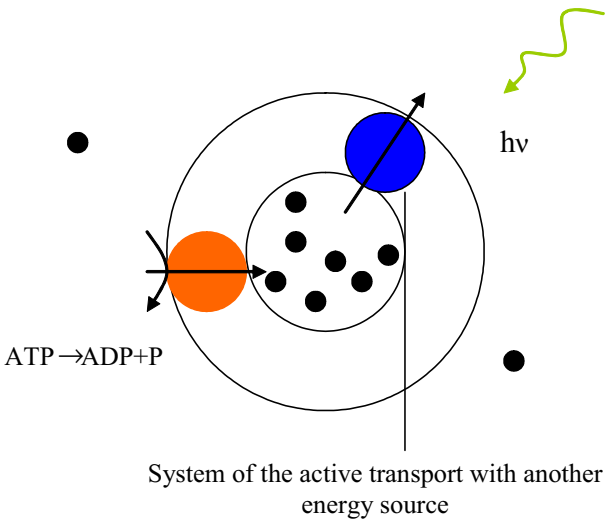

Fig. 6 The scheme of the control system in the presence of two different systems of the active transport of a substance

Conclusion

A system having a closed membrane with a built-in molecular machine and a control system, which would maintain a constant intracellular composition that is different from the environmental composition and changes little with variations of the latter, has been proposed as a minimal cell. Physicochemical processes occurring in this minimal cell have been considered. A highly efficient use of external energy sources and the independence of the intracellular composition from the extracellular composition were shown to be competing requirements. The efficiency is impaired with growing robustness. This property appears to be typical of more complex systems as well.

Appendix

A Mathematical Model of the Work of a Control System

According to Eq. 8, the dependence of x on y will have the form:

$$x = y\frac{P(y) + C}{P(y) + C\exp(\Delta\mu_A)}. \tag{A1}$$

Suppose there is an intracellular value of x_0, which must be maintained constant. It has the corresponding value of y_0.

Expand penetrability as a power series in $y-y_0$:

$$P(y) = P_0 + \alpha(y - y_0) + \frac{\beta}{2}(y - y_0)^2, \tag{A2}$$

where

$$P_0 = C\frac{x_0\exp(\Delta\mu_A) - y_0}{y_0 - x_0}. \tag{A3}$$

For the weak sensitivity it is required that the first and second derivatives of the intracellular concentration with respect to the extracellular concentration equal zero.

Then we have

$$\frac{\partial}{\partial y}x = 0,\ \frac{\partial^2}{\partial y^2}x = 0. \tag{A4}$$

The coefficients α and β can be found from the conditions (A4) and equation (A1):

$$\alpha = C_1 x_0\frac{1 - \exp(\Delta\mu_A)}{(y_0 - x_0)^2}, \tag{A5}$$

$$\beta = \frac{2x_0 C}{(y_0 - x_0)^3}(\exp(\Delta\mu_A) - 1). \tag{A6}$$

Thus, the dependence of the intracellular concentration of the substance on its extracellular concentration with account taken of the controller has the form

$$x = y\frac{P_0 + C_1 x_0 \frac{1-\exp(\Delta\mu_A)}{(y_0-x_0)^2}(y-y_0) + \frac{1}{2}\frac{2x_0 C}{(y_0-x_0)^3}(\exp(\Delta\mu_A)-1)(y-y_0)^2 + C}{P_0 + C_1 x_0 \frac{1-\exp(\Delta\mu_A)}{(y_0-x_0)^2}(y-y_0) + \frac{1}{2}\frac{2x_0 C}{(y_0-x_0)^3}(\exp(\Delta\mu_A)-1)(y-y_0)^2 + C\exp(\Delta\mu_A)}. \tag{A7}$$

In the second case, when only one of the pumps is variable, we have analogously for the intracellular concentration:

$$x = y\frac{C_2(y) + C_1}{C_2(y)\exp(\Delta\mu_B) + C_1\exp(\Delta\mu_A)}. \tag{A8}$$

Expand $C_2(y)$ as a power series in y–y_0:

$$C_2(y) = C_0 + \alpha(y-y_0) + \frac{\beta}{2}(y-y_0)^2, \tag{A9}$$

where

$$C_0 = C_1\frac{x_0\exp(\Delta\mu_A) - y_0\exp(\Delta\mu_B)}{y_0 - x_0\exp(\Delta\mu_B)}. \tag{A10}$$

Equating the derivative $\partial x/\partial y$ to zero gives the expression for α:

$$\alpha = C_1 x_0\frac{\exp(\Delta\mu_B) - \exp(\Delta\mu_A)}{(x_0\exp(\Delta\mu_B) - y_0)^2}. \tag{A11}$$

Equating the second derivative to zero gives the expression for β:

$$\beta = \frac{2x_0 C_1}{(y_0 - x_0\exp(\Delta\mu_B))^3}(\exp(\Delta\mu_A) - \exp(\Delta\mu_B)). \tag{A12}$$

References

Cannon WB (1932) The wisdom of the body. Kegan Paul, Trench, Trubner, London

Dorf RC, Bishop RH (2004) Modern control systems, 10th edition. Prentice-Hall Inc, Englewood Cliffs, New Jersey

Eigen M (1971) Self-organization of matter and the evolution of macromolecules. Naturwissenschafen 58:465–523

Eigen M, Schuster P (1979) The hypercycle: a principle of natural self-organization. Springer, Berlin

Fontanari JF, Santos M, Szathmary E (2006) Coexistence and error propagation in pre-biotic vesicle models: a group selection approach. J Theor Biol 239:247–256

Fox SW (1965) Simulated natural experiments in spontaneous organization of morphological units from protenoid. In: Fox SW (ed) The origins of prebiological systems and their molecular matrices. Academic, New York, pp 361–382

Fox SW (1980) The origins of behavior in macromolecules and protocells. Comp Biochem Physiol 67B:423–436

Fox SW (1988) The emergence of life: darwinian evolution from the inside. Basic, New York

Fox SW, Dose K (1972) Molecular evolution and the origin of life. Freeman, San Francisco

Glass JI, Assad-Garcia N, Alperovich N, Yoosefph S, Lewis MR, Maruf M, Hutchison CA III, Smith HO, Craig Venter J (2006) Essential genes of a minimal bacterium. PNAS 103(2):425–430

Kitano H (2004) Biological robustness. Nature 5:826–837
Melkikh AV, Seleznev VD (2005) Models of active transport of ions in biomembranes of various types of cells. J Theor Biol 324(3):403–412
Melkikh AV, Seleznev VD (2006a) Model of active transport of ions in biomembranes based on ATP-dependent change of height of diffusion barriers to ions. J Theor Biol 242(3):17–626
Melkikh AV, Seleznev VD (2006b) Requirements on models and models of active transport of ions in biomembranes. Bull Math Biol 68(2):385–399
Melkikh AV, Seleznev VD (2007) Models of active transport of neurotransmitters in synaptic vesicles. J Theor Biol 248(2):350–353
Melkikh AV, Seleznev VD (2008) Nonequilibrium statistical model of active transport of ions and ATP production in mitochondria. J Biol Physics 33:161–170 DOI 10.1007/s10867-007-9053-0
Morovitz HJ, Kostelnik JD, Yang J, Cody GD (2000) The origin of intermediary metabolism. PNAS 97 (14):7704–7708
Murtas G (2007) Question 7: construction of a semi-synthetic minimal cell: a model for early living cells. Origins of Life and Evolution of Biospheres 37(N 4–5):419–422 DOI 10.1007/s11084-007-9090-5
Oparin AI (1964) Life: its nature, origin and development. Academic
Stelling J, Sauer U, Szallasi Z, Doyle FJ, Doyle J (2004) Robustness of cellular functions. Cell 118:675–685
Szathmary E (1992) Natural selection and the dynamical coexistence of defective and complementing virus segments. J Theor Biol 157:383–406
Szathmary E, Demeter L (1987) Group selection of early replicators and the origin of life. J Theor Biol 128:463–486