ELSEVIER SCIENTIFIC PUBLISHERS IRELAND

BioSystems 31 (1993) 65–73

Bio Systems

Quantum mechanical properties of biosystems: A framework for complexity, structural stability, and transformations

A.U. Igamberdiev

Department of Plant Physiology and Biochemistry, Voronezh State University, Voronezh 394693, Russia

(Received 22 December 1992; revision received 10 March 1993)

Abstract

Internal quantum non-demolition measurements are inherent for biological organization and determine the essential features of living systems. Low energy dissipation in these measurements provided by slow conformational relaxation of biomacromolecular complexes (regarded as measuring devices) is the main precondition of enzyme operation and information transfer determining the steady non-equilibrium state of biosystems. The presence of an internal formal description inside a biosystem, expressed in genetic structures (developmental program), is a consequence of its quantum properties. Incompleteness of this formal description provides the possibility of the generation of new functional relations and interconnections inside the system. This is a logical precondition of an evolutionary process. The quantum mechanical uncertainty that underlies the appearance of bifurcations is considered to be the main physical foundation of complication and irreversible transformation of biosystems.

Key words: Bifurcations; Incompleteness; Non-demolition measurements; Uncertainty principle

1. Introduction

Biological organization is based on the principle of a non-equilibrium steady state (Bauer, 1935). This provides dynamics that require a specific framework for the description of the temporal and spatial characteristics of the biosystem. The logic of such a framework derives from Aristotle, as in his philosophy we find the analysis of fundamental irreversibility and self-determination of living processes.

In a certain sense, the biological system possesses its own internal logic of development, arising from its internal formal system, which is expressed in the genetic structures. The biological system develops according to its internal logic, and the theoretical approach in biology consists of a description of the emergence and operation of this logic. From this statement the metatheoretical character of theoretical biology is evident, and its aim is not one of prediction but rather determination of possible ways of actualization from indefinite states during the process of self-organization. Therefore, traditional logical schemes are insufficient for the description of biological processes. From the analysis of the func-

* Corresponding author.

0303-2647/93/$06.00 © 1993 Elsevier Scientific Publishers Ireland Ltd. All rights reserved.
SSDI 0303-2647(93)01362-W

tion and development of biological structures, Pattee (1968) and Rosen (1977) concluded that its logic should reveal an internal resemblance to the logic of quantum mechanical measurement, in which a non-formal process of mapping physical events into symbols takes place. Biological molecular complexes are operational structures put in correspondence with other molecules and processes. These considerations give a theoretical framework for a description of the complexity, structural stability and transformations of living systems. In the present paper we analyse the possible foundations of this framework.

2. Quantum non-demolition measurements in biosystems

The stability of the biosystem is connected mainly with the reliability of information transfer inside it, determined by specific features of the operation of biomacromolecules and their complexes. Considering the latter as molecular machines, we should also realize that the machine is a device for energy transfer without losses. The specificity of biomacromolecules (enzymes, electron-transferring proteins, etc.) for strictly determined interactions can be explained by low energy dissipation during their operation, which provides registration of signals not distinguished by their energy from the surrounding noise (Elsasser, 1982). In the analysis of operation of these molecular machines we should take into account their quantum properties.

Operation of molecular machines at the quantum level was analysed for the first time by Gray and Gonda (1977). Low energy efficiency seemed to be the main shortcoming of their model. Therefore the improvement of this model should include the explanation of low energy dissipation during the operation of biological macromolecular systems (Vakulenko and Gasteva, 1987).

Conformational relaxation of macromolecular systems is considered to be an elementary action of the bioenergetic process (Blumenfeld, 1983), in which the fast quantum effect (e.g. the capture of an electron by macromolecule) is followed by a slow conformational transition, which is the mechanical motion of a macromolecule. During this transition the energy is not dissipated and remains stored for a total lifetime long enough for the work to be performed (Křemen, 1992). Thus, its motion is many times slower than the initial quantum effect, and the rate of a bioenergetic process is therefore determined by the rate of the conformational relaxation. The latter takes place only after the action of a force converting the system into the new conformational state, i.e. after the generation of a non-equilibrium state resulting from fast initial interaction. From this point of view enzyme specificity is connected with the recognition of specific configurations of electron clouds in certain compounds and should therefore be described using quantum mechanical formalism.

Braginsky et al. (1981) had analysed the conditions necessary for the detection of weak forces. It was shown that according to the Heisenberg uncertainty ratio, interactions between a quantum system and a macroscopic measuring device can take place by a path that provides practically non-demolition registration of strictly determined weak signals. These interactions are characterized by high precision and certainty of the result of measurement, as the sensitivity of the detector is determined by its relaxation properties. Therefore a large class of quantum measurements defined as quantum non-demolition measurements and characterized by low energy dissipation was described. Quantum measurement is connected with low energy dissipation in the case where the relaxation period of a macroscopic oscillator (τ^*) is many times larger than the time interval of measurement ($\hat{\tau}$). Minimal energy dissipation in quantum measurement is calculated as

$$\Delta E_{\min} \approx 2kT \frac{\hat{\tau}}{\tau^*}$$

in the case of zero initial amplitude of oscillations.

Under the condition of quantum non-demolition measurement, internal fluctuations of the oscillator will not unmask the action of detected weak force, and certain motions in a macroscopic oscillator can be transformed into high-frequency vibrations without information loss. This is possible if the relaxation period of the oscillator is many times larger than the initial quantum effect.

Low energy dissipation during the recognition of weak forces is provided by mobile proton states appearing in biomacromolecules. The action of a weak force can be detected via its transformation into high-frequency quanta in an electromagnetic oscillator (Braginsky et al., 1980). It was shown that during enzyme catalysis or electron transport in proteins, the energy of the electron can be transformed without heat production into the energy of coherent vibrational movement, i.e. the macromolecule operates as a quantum generator in which the transition between levels leads to the excitation of coherent electromagnetic oscillations. These intramolecular local excitations in the form of quasi-particles are essential for protein conformational movement in which the α-helical parts of the protein molecule serve as local proton pumps linked with the active site (Warshel, 1984). In all investigated electron transferring proteins, separate pathways exist for electron transfer and proton transfer within the protein molecule (Kim and Rees, 1992). Proton emission during the operation of the electron transport chain can be considered to be a consequence of conformational relaxation.

3. Biomacromolecules as measuring devices

Adequate formalization of quantum measurements was realized in Feynman's (trajectoric) interpretation of quantum mechanics (Mensky, 1983). In this interpretation the probability amplitude of the system's transition from point x to point x' during time period τ is determined by the integral of all possible routes connecting these points in set $I(x', x)$ of the routes parametrized by the time interval $(0, \tau)$:

$$A(x',x) = \int_{I(x',x)} d\{x\} e^{(i/\hbar)S\{x\}}$$

In this formula $S\{x\}$ is the integral of action through this route and $\hbar$ is Planck's constant.

Integral $A(x',x)$ can describe the probability amplitude of electron transition from one point to the other within the boundaries of a substrate molecule in the absence of the enzyme. In the presence of the enzyme the reduction of this set to a subset

$$I_\alpha (x',x) = I_\alpha \cap I (x', x)$$

takes place. Under these conditions the amplitude of particle transition from one point to another will be calculated by the following integral:

$$A_\alpha(x',x) = \int_{I(x',x)} d\{x\} \rho_\alpha\{x\} e^{(i/\hbar)S\{x\}}$$

in which $\rho_\alpha\{x\}$ is a non-negative function characterizing the change in the probability distribution of the electron state function after the action of the enzyme. In an ideal case of measurement without dissipation, this value will be 1 in the set I_α and 0 outside it. In real systems its concrete form will depend on the probability factor of the reaction, determined by chemical group orientation, synchronization of atomic vibration frequences, etc.

Thus, the enzymes determine the boundary conditions that direct the course of a reaction into a certain route. Under these conditions certain states of particle (electron) are not allowed ($\psi(x) = 0$), whereas in a co-ordinate interval defined by the active site, the new wave function is coincident with the one that existed before the action of enzyme. An electron is therefore evolved, being directed into the passage of routes that is determined by the co-ordinate scale defined by an enzyme. This results in the prohibition of some previously probable trajectories of electron movement in the substrate molecule, whereas other trajectories become more probable. This leads to the redistribution of electron density and hence to the internal polarization of the molecule. As a result, proton electron pairs are divided and the subsequent course of the enzymatic reaction is determined by the transition of electron energy into the energy of Coulombic forces of diverse charges. This in turn results in the vectorial movement of charged cations and anions, leading to the formation of reaction products.

The function $\rho_\alpha\{x\}$ in our case describes the evolution of a quantum mechanical system during enzyme action. No Hamiltonian or any differential equation similar to Schrödinger's equation can be put in correspondence to this function (Mensky, 1983). This situation seems analogous to the 'energy-time' uncertainty ratio (de Broglie, 1982).

Rosen (1960) was the first to show that it is not possible to formulate a Hamiltonian for information transition in biological systems. The system's dynamics in this case are not described locally in time, and the reduction cannot be formalized using Schrödinger's equation. The irreversibility of evolution in such a system is determined by the reduction of the quantum mechanical state function itself (Igamberdiev, 1985), as the measurement process is actually irreversible. As shown by Matsuno (1985), the generation of biological information appears as the symmetry breaking of the Hamiltonian originating in the interaction with the exterior through material flow. The latter is related to quantum measurement, which determines the irreversibility of the symmetry-breaking process.

The properties of specific recognition and modulation of biomacromolecules determine the fact that they can integrate many separate processes into systemic units with coherent functions (Marijuán and Westley, 1992). Biomacromolecules, particularly enzymes, acquire these properties according to the quantum-mechanical principles of their operation. As a result they can build massive networks from Boolean functions that are interconnected in a random way (Kauffman, 1987).

Low energy dissipation during the conformational relaxation of biomacromolecules provides for the possibility of long-distance non-locality transfer for electron and proton flows through the metabolic networks. The structural dissymmetry of protein molecules is essential for such long-range transfer of protons and electrons in biosystems (Fisun and Savin, 1992). In such systems a non-locality in the quantum mechanical sense and non-force correlations can arise between subsystems of the biological system in accordance with the Einstein-Podolsky-Rosen (EPR) paradox. It was proposed that these correlations can be a reason for biosystems operating as an entity and even as a physical background of consciousness (Tsekhmistro, 1981; Stapp, 1985).

EPR correlations can appear within systems that realize quantum non-demolition measurements. Two particles arising from a single system (e.g. two electrons with opposite spin values from the same atomic sublevel) can store information about a previous state when they are later non-disturbed, i.e. when non-controlled quantum measurements hiding the initial picture have not happened. Otherwise, information about the whole system will be unavoidably lost. Therefore the preservation of information about the whole system is possible only in the case of non-demolition measurements that are realized on its subsystems, and low energy dissipation during conformational relaxation of biomacromolecules can be considered to be the main precondition for providing and maintaining EPR correlations.

The verification of Bell's inequalities in the biosystem is very important for the confirmation of such an approach. It could be realized for electron transport reactions, for photon absorbtion by receptor proteins, etc., i.e. when it is possible to separate elementary particles as objects of interactions inside the biosystem. A verification procedure such as this could show that certain correlations in biosystems result from non-local interactions arising from EPR effects. Non-force interactions could explain the co-ordination of the parameters of elementary particles during the action of protein molecules and their complexes. Low energy dissipation is considered to be the main condition of these interactions. In the scheme of slow conformational changes, Bell's inequalities can be interpreted as the quantum mechanical background of the operation of macromolecular subsystems in a biological system. The question remains whether EPR correlations are involved in the determination of the holistic properties of living systems and consciousness.

A measuring device operates with a low energy dissipation if we consider only one level of hierarchy, whereas the construction of the device requires interaction between levels. During this interaction, demolition of the previous organization and construction of the following one takes place according to the laws imposed by the formal system inherent in the biological system. Energy dissipation and the increase of entropy are therefore preconditioned to the non-dissipative process. A biological system is simple as an entity but is complex as a structural construction. As stated by Rosen (1979), the system's complexity is

more a result of its representation than of its internal property. The complexity of a biological system being connected with internal measurements can also be a result of its own representation in the construction generated from its internal formal description.

4. Generation of bifurcations in biosystems

From the previous consideration it follows that the entity and stability of a biological system is provided by the realization of the quantum non-demolition measurements within it. The large size and low turnover rates of enzymes are the main necessary preconditions for the realization of the quantum non-demolition measurements that determine the stable operation of a biosystem. These parameters should be optimal in order to provide both for reliability of operation of the biological system and for its capacity for evolutionary transformations; i.e. reliability and ability to change should be optimally equilibrated. The general criterium of optimality cannot be defined, as optimality is dependent on the concrete conditions determined by non-linear competitive process between two diversities, one being dependent on environmental conditions and the other on the parameters of the organism.

The transition from the set of possible worlds to the description of the real world results from the process of reduction of potentialities. During this process the system, considered a device, can generate independent descriptions that are alternative constructions without an implicative relation between them. The point of discrimination between these two descriptions is considered to be the bifurcation point (Rosen, 1979).

In the conditions of quantum non-demolition measurements, i.e. when the system's state is not practically disturbed, the possibility of bifurcations is minimal. In an ideal case of the absence of energy dissipation (which is impossible, as it provides infinitely long time intervals of measurements according to the uncertainty ratio 'energy-time') the system should be found in a state of absolute homeostasis. If relaxation periods are shorter, the system is less stable but it can evolve in a different state. Displacement in this equilibration can lead to differences in evolutionary rates. Therefore the ratio between measurement time and the relaxation period determines the state of equilibration between the stability of the system and its ability to change.

The 'energy-time' uncertainty ratio was determined by Prigogine (1980) as the complementarity ratio between time and alteration. In this ratio, time appears as the time of the observer but not of the quantum system (de Broglie, 1982), which leads to the impossibility of formulation of the Hamiltonian for this ratio. Possibilities of disturbances and bifurcations in the system can arise from this ratio. Irreversibility of time in quantum mechanics appears to be the consequence of subsequent measurements at the stage of information-gathering on the whole sequence of outcomes (Dicke, 1989). Branched evolutionary processes lead to actual irreversibility, which contradicts the formal reversibility of Schrödinger's equation (Toyozawa, 1989), i.e. irreversibility arises at the macroscopic level and is connected with bifurcations. The latter can therefore be considered as the precondition for irreversible development in ontogenesis and evolution and the reason for the complication of organization.

Catastrophe theory claims that at a certain stage of evolution the parameters of the system attain critical values at which the steady state bifurcates and hence stability is lost. In addition to the customary catastrophe-theoretic model of bifurcation, which operates with non-linearities (Poston and Stewart, 1978), it is important to state that the initial instability arises from the non-absolute character of the internal quantum non-demolition measurements. As was shown by Matsuno (1992), local fluctuations are accompanied by the non-vanishing rate of variation because of the uncertainty relationship, and the endogenous transformations refer to the symmetry breaking of the Hamiltonian, which has its own dynamics. Irreversible symmetry-breaking emerges from indefinite states, and indefiniteness is provided by the quantum measurements. Under this consideration, macroscopic bifurcations seem to be the consequence of the quantum properties of the biosystem, and only the measurement process is responsible for the branching behaviour of

biodynamics. At the macroscopic level, the alterations in relaxation processes lead to the redistributions between different steady states within the biosystem. Thus, non-linearity arises from high-order relaxation processes. This leads to instabilities and to initially unpredictable transformations, resulting in macroscopic bifurcations.

In general, a change in relaxation time leads to the alteration in specificity of biomacromolecules to certain interactions, and this can result in branching behaviour. Perturbed versions of the original functions can interact in such way that a property of their commutativity breaks down, and a new global function for the system is generated (Matsuno, 1989).

From the consideration of the branching behaviour of biosystems we should establish the essential difference between the processes of ontogenesis and evolution. Both evolution and ontogenesis are bifurcation phenomena. Ontogenesis can be considered as a sequence of bifurcations strictly determined by the genome and by morphogenetic endogenous and exogenous parameters. In a certain sense it can be defined as an unfolding of a program according to the internal law of the system's organization (Goodwin, 1982). At higher hierarchical levels, interactions with low energy dissipation occur, which provides for the stable operation of the whole system, whereas at lower levels energetic processes demanding external energy inflow take place. For the provision of genetically determined (internalized) bifurcations, the destruction of the previous organization in the developing organism takes place, followed by the construction of novel structures from elements of the previous structure.

The bifurcations that arise during the operation of the genome and enzymes and provided by the non-absolute character of non-demolition measurements (i.e. primarily non-internalized bifurcations) are essential in the evolutionary process. Therefore the evolutionary process seems to be a consequence of the quantum uncertainty that appears at the macroscopic level. An essential difference between the mechanisms of ontogenetic and phylogenetic processes is evident from this consideration.

5. The logic of biological transformations

According to the general principles of synergetics, the bifurcations are considered to be a reason for transformations. The non-absolute specificity of certain enzymes for their substrates determines the creation of bifurcations in metabolic pathways that are considered to be the initial point for the further evolution of the system (Igamberdiev, 1992). If the newly formed type of organization is to be conserved, it must be fixed into the encoding system. The origin of the latter is the central problem for understanding the mechanism of evolutionary transformations.

Bifurcation in a metabolic pathway can be considered as an ontogenic forestalling of phylogenesis (Berg, 1977), which initially is not obligatory but, if it is to be conserved during evolution, must be fixed into the genome. In general, the origin of novel encoding systems cannot be determined or predicted beforehand. However, during the evolution of new systems, structures can be used that previously served other purposes. The possibilities of genomic reconstructions, horizontal gene transfer etc. are the main preconditions for bifurcation fixations in the genome.

Genetic redundancy seems to be important for the internalization of bifurcations. It increases the evolutionary possibilities of the biosystem via self-facilitation of adaptive transformations, as these transformations can be more easily fixed genetically using previous genetic material. According to the 'bootstrap' (self-facilitation) principle (Conrad, 1982), the structure of the biological system becomes increasingly suited to effective evolutionary search through the process of evolution.

The origin of a new formal system is not a subject for strict one-valued causal analysis. Biological systems, because of the purely relative character of their properties, possess evolutionary and cognitive capabilities that exceed those of formal computational systems with fixed components (Kampis, 1991). The transition to a formal system that provides for this advanced organization cannot be completely described by finite means; i.e. the new solution that arises during the evolution of an internal formal description of the biosystem

cannot be obtained only through rearrangements of finite elements. Therefore the evolutionary process cannot be predicted: it can only be forecast with more or less exactness. In this process, pre-existing elements of the formal system (as a word when it is used as a metaphor) can gain new values and change the system to a new level of organization. The fundamental incompleteness (in Gödel's sense) of a formal system that attributes arbitrary values to statements that cannot be proved within the boundaries of the system seems to be the logical foundation of biological transformation. The physical foundation of this process is the uncertainty (in Heisenberg's sense), which cannot be avoided, even in the case of almost non-demolition measurements. This uncertainty provides for the generation of bifurcations in the system and therefore the possibility of creating novel structures. The absence of the nomothetical aspect of the evolutionary process does not follow from the statement about its creative character. Convergent realization of similar structures via different paths only confirms previous considerations about the non-deterministic (emergent or 'creative') character of the evolutionary process. Thus, what we can establish is the impossibility of a formal deduction of a new organization from a pre-existing one.

The evolutionary process is distinguished from other dynamic processes by the indefiniteness of the boundary conditions (Matsuno, 1985), as Heisenberg's uncertainty principle underlies the genesis of evolutionary variability. Only the internal measurement (unpicturable process within the cell) converts the uncertainty relation into an engine for generating de novo variations (Matsuno, 1992). As emphasized by Pattee (1989), measurement itself is a non-formal process and cannot be programmed, but its results are symbols that can be used in a formal system. The appearance of these symbols in living matter and therefore of the semiotic character of the biosystems has been discussed in a previous paper (Igamberdiev, 1992).

It seems evident that constructive logic is inadequate for describing the evolutionary process. Actually, in the latter the trueness (i.e. validity) of the genetic information cannot be preserved in time. Something valid in one condition may not be valid in another. Validity is determined by the falsification of formal systems in Popper's sense, and trueness cannot be represented by correspondence to pre-existing inert reality. The falsification process cannot be analysed in terms of predictability: it corresponds to the actual irreversibility and 'creativity' of the evolutionary process. Interactions between the formal systems of different biosystems generate new relations that correspond to a new environment. Falsification provides not only for the struggle for existence but also for equilibration of contradicting constructs. What can be concluded is that during the evolutionary process, trueness does not exist per se. It has a pragmatic aspect that is a consequence of the inclusion of the system in concrete interactions, being derived from the coordinate of the spatial and temporal continuum. A local change of the properties of this continuum can lead to significant evolutionary transformations. In this we see a radical distinction between biology and physics.

In this context the trueness of the formal (encoding) system resides in its relation to the external world and is determined via the survival of organisms or other biological entities. The unfolding of the genetic program can be considered a verification of this trueness. Irreversibility in the evolutionary process can be explained by its logical foundations. It is determined by the fact that Gödel's formulas cannot be obtained by reversible mathematical operations. On the contrary, for the establishment of these formulas two levels of logical reality are used: subject language and metalanguage. The expression of these formulas by subject language cannot mean their demonstrability via this language (Antipenko, 1986). Therefore progressive evolution always corresponds to the origin of a new hierarchical level in such a way that novel relations cannot be deduced from the laws of the lower level (Pattee, 1970).

The formation of an organism from the zygote is a process of the realization of a construction during which the interaction of the genome with its

cellular environment generates the structure, which cannot be characterized beforehand as true or false. Trueness or falsity are realized after the actualization of the construction. Moreover, the trueness of construction cannot be preserved in time: the constructive knowledge obtained in evolution can lose its significance.

For the description of biological transformations, topoic logic could be convenient. It determines a fundamental logical structure (topos) possessing its own logical calculus with potentially and actually existing elements, in which a certain set of points is stable in relation to topological reconstructions (Goldblatt, 1979). The logical interrelation between ontogenesis and evolution can be represented in the following way. Ontogenesis is realized according to the genetic program, which is constructed during the evolutionary process. This program can be considered as the intrinsic logic of the development of the biosystem. Topological reconstructions during ontogenesis correspond to the actualization of potentialities provided by this intrinsic logic, which takes place according to the logical calculus of corresponding topos. Ontogenesis is characterized by the reproduction of values in the internal logic of a given biosystem. However, evolution corresponds to the process of the gaining of values to the level that is external in relation to the internal logical structure of the biosystem, and to the construction of the corresponding topos for it. Therefore, in biology we are faced with two algebraic levels of logic, and their interconnection can be realized via non-trivial indeterministic interpretation. Under this consideration, evolution can be modelled by the structure of values at the second, external level of logic, whereas the first level (the logical calculus of the biosystem) corresponds to the set of values structuralized during evolution.

The ability of biosystems to undergo evolutionary transformations can therefore be connected with their non-classical properties. The generation of a new hierarchical level represents a transfinite leap in which the traditional causality breaks down. It cannot be determined recursively or simply deduced from the previous organization. It is a process analogous to the creation of a new formula, one that was absent in the initial formalized calculus. The novel property, therefore, is not an adaptation in its trivial sense but rather a forestalling of a new ecological niche that can be forecast but not predicted beforehand.

6. Acknowledgements

The author would like to thank Dr. Vaughan Hurry for critical reading and editing of the manuscript, and the reviewers of this article for their valid comments.

7. References

Antipenko, L.G., 1986, The Problem of Incompleteness of a Theory and its Gnoseological Significance [in Russian] (Nauka, Moscow).

Bauer, E.S., 1935, Theoretical Biology [in Russian] (VIEM, Moscow and Leningrad).

Berg, L.S., 1977, Works on the Theory of Evolution, 1922–1930 [in Russian] (Nauka, Leningrad).

Blumenfeld, L.A., 1983, Physics of Bioenergetic Processes (Springer-Verlag, Berlin).

Braginsky, V.B., Vorontsov, Yu.I. and Thorne, K.S., 1980, Quantum non-demolition measurements. Science 209, 547–557.

Braginsky, V.B., Mitrofanov, V.P. and Panov, V.I., 1981, Systems with Low Dissipation [in Russian] (Nauka, Moscow).

Conrad, M., 1982, Bootstrapping model of the origin of life. BioSystems 15, 209–219.

de Broglie, L., 1982, Les incertitudes d'Heisenberg et l'interprétation probabiliste de la mécanique ondulatoire (Gauthier-Villars, Paris).

Dicke, R.H., 1989, Quantum measurements, sequential and latent. Found. Phys. 19, 385–395.

Elsasser, W., 1982, The other side of molecular biology. J. Theor. Biol. 96, 67–76.

Fisun, O.I. and Savin, A.V., 1992, Homochirality and long-range transfer in biological systems. BioSystems 24, 301–303.

Goldblatt, R., 1979, Topoi: the Categorial Analysis of Logic (North-Holland, Amsterdam).

Goodwin, B.C., 1982, Development and evolution. J. Theor. Biol. 97, 43–55.

Gray, B.F. and Gonda, I., 1977, The sliding filament model of muscle contraction. J. Theor. Biol. 69, 167–230.

Igamberdiev, A.U., 1985, Time in biological systems [in Russian]. Zhurnal Obshchei Biologii [Journal of General Biology] 46, 471–482.

Igamberdiev, A.U., 1992, Organization of biosystems: a semiotic approach, in: Biosemiotics: the Semiotic Web, Th.A. Sebeok and J. Umiker-Sebeok (eds.) (Mouton de Gruyter, Berlin) pp. 125–144.

Kampis, G., 1991, Self-Modifying Systems in Biology and Cog-

nitive Science: a New Framework for Dynamics, Information and Complexity (Pergamon, Oxford).

Kauffman, S.A., 1987, Developmental logics and its evolution. BioEssays 6, 2, 82–87.

Kim, J. and Rees, D.C., 1992, Crystallographic structure and functional implications of the nitrogenase molybdenum-iron protein from *Azotobacter vinelandii*. Nature 360, 553–560.

Křemen, A., 1992, Biological molecular energy machines as measuring devices. J. Theor. Biol. 154, 405–413.

Marijuán, P.C. and Westley, J., 1992, Enzymes as molecular automata: a reflection on some numerical and philosophical aspects of the hypothesis. BioSystems 27, 97–113.

Matsuno, K., 1985, How can quantum mechanics of material evolution be possible?: symmetry and symmetry-breaking in protobiological evolution. BioSystems 17, 179–192.

Matsuno, K., 1989, Protobiology: Physical Basis of Biology (CPC Press, Boca Raton, Florida).

Matsuno, K., 1992, The uncertainty principle as an evolutionary engine. BioSystems 27, 63–76.

Mensky, N.B., 1983, The Group of Paths: Measurements, Fields and Particles [in Russian] (Nauka, Moscow).

Pattee, H.H., 1968, The physical basis of coding and reliability in biological evolution, in: Towards a Theoretical Biology. Vol. 1: Prolegomena, C.H. Waddington (ed.) (Edinburgh University Press) pp. 67–93.

Pattee, H.H., 1970, The problem of biological hierarchy, in: C.H. Waddington (ed.) Towards a Theoretical Biology. Vol. 3, Drafts (Edinburgh University Press) pp. 117–136.

Pattee, H.H., 1989, The measurement problem in artificial world models. BioSystems 23, 281–290.

Poston, T. and Stewart, J. 1978, Catastrophe Theory and Its Applications (Pitman, London).

Prigogine, I., 1980, From Being to Becoming: Time and Complexity in the Physical Sciences (W.H. Freeman, San Francisco).

Rosen, R., 1960, A quantum theoretic approach to genetic problems. Bull. Math. Biophys. 22, 227–255.

Rosen, R., 1977, Observation and biological systems. Bull. Math. Biol. 39, 663–678.

Rosen, R., 1979, Bifurcations and biological observables. Ann. NY Acad. Sci. 316, 178–187.

Stapp, H., 1985, Consciousness and values in the quantum universe. Found. Phys. 15, 35–47.

Toyozawa, Y., 1989, The irreversibility inherent in quantum mechanics. J. Phys. Soc. Japan 58, 2215–2218.

Tsekhmistro, I.Z., 1981, Approaches to the Quantum Concept of Physical Foundations of Consciousness [in Russian] (Vishcha Shkola, Kharkov).

Vakulenko, A.A. and Gasteva, S.V., 1987, On energy dissipation in metabolic systems [in Russian]. Doklady Akademii Nauk SSSR 294, 708–712.

Warshel, A., 1984, Dynamics of enzymatic reactions. Proc. Natl. Acad. Sci. USA 81, 444–448.