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NON-LINEAR ORGANIZATION OF SUBCELLULAR SYSTEMS — THE CONDITION FOR RESPONSE TO WEAK ELECTROMAGNETIC FACTORS*

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The model of transmembrane ion transfer is employed to demonstrate the possibility, in principle, of a non-linearly organized biological system to respond to weak low-frequency electromagnetic radiations (10 V/m, 0.1–100 Hz). The interaction of the biological system of ion transfer with an external electromagnetic field leads to bifurcational changes in the system. The result is a change in the concentration level of the ions in the near-membrane region or the advent of an auto-oscillatory regime. © 1996 Elsevier Science Ltd. All rights reserved.

The Ancients did not doubt the existence of a link between space and terrestrial objects, both animate and inanimate. The modern Indian philosopher, Sri Aurobindo, in line with the Indian philosophical tradition, contends that this link is mediated by the vibrations emitted and perceived by all bodies [1].

There now exist thousands of items of proof of the link between space and terrestrial phenomena. In [2] it is shown that correlations exist between cosmic events and the state of the human body, the bioluminescent activity of bacteria [3] and even the characteristics of radioactive decay [4]. In the last few decades much evidence has appeared in support of the fact that the vibrations binding all material objects are electromagnetic radiations (e.m.r.). The problem of natural science research is to understand the mechanisms of the interaction of often very low-intensity electromagnetic fields coming from space with terrestrial objects. In this case one might justly speak not of correlations but of interactions.

In considering the interaction of space factors with living systems, we see as particularly important the fact that biological systems are essentially non-linear. This mathematical term reflects several circumstances associated with the structural and functional organization of living matter, including the openness and remoteness of living systems from thermodynamic equilibrium. The processes which take place in such systems may be described by non-linear equations and possess properties peculiar to non-linear systems: here multistationary, oscillatory and quasi-stochastic regimes are possible. The parametric regions of the individual patterns of behaviour possess bifurcational boundaries, close to which minor actions on the system may lead to

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qualitative change in the character of their behaviour. The response of living systems to weak space factors must also be considered from such "non-linear" positions.

In considering the interaction of electromagnetic waves with any system we are always dealing with resonance. By resonance in the broad sense of the term, we mean a certain complementarity of the perceiving system and the arriving signal, ensured by a special device of the perceiving system. Depending on the frequency of the signal, this device may have different space and time scales. The e.m.r. of different frequency may be perceived at the level of macromolecules (visible light) or at the level of subcellular systems, for example, cell membranes (low frequencies). The mechanisms of such perception are quite different.

The physics of interaction of visible light with the photosynthetic and visual systems has been quite well studied. On photosynthesis the high energy light quanta take chlorophyll molecules into the excited state, then this energy is stabilized and utilized in the form of the energy of chemical bonds. "Energy" resonance takes place. On visual perception the excited state of the rhodopsin molecule is transformed to the energy of nerve impulses and through a multistep system of regulation and enhancement elicits complex reactions of the higher organism. Konig [5] gives the classical example of a horse negotiating an obstacle in the twilight. The energy of only a few photons "suffices" for the horse to make the jump over the hurdle thanks to the mobilization of the internal energy of the animal with the participation of the complex system of nervous and humoral regulation. Here one may speak of the "informational" resonance of the e.m.r. with the perceiving living system.

In considering the action on a living system of low-frequency e.m.r. the question arises that the energy of the incident radiation is too low to introduce changes into the molecular structure of the perceiving systems. We propose to approach the problem from a different "non-energetic" standpoint, regard the perceiving system as a non-linear macrosystem possessing different types of behaviour as a function of the value of the internal parameters. On exposure to a weak periodic action, the behaviour of such a system may be significantly transformed, in particular, when such an action is experienced by a system close to the bifurcational boundary of its own parameters. The frequency of the action may not correspond to the difference in the energy levels of the molecular structures but be "resonance" for larger scale subcellular systems to which correspond much lower characteristic frequencies.

Below, a non-linear system of transmembrane ion transfer is taken to demonstrate the possibility, in principle, of a subcellular system changing the character of its behaviour in response to a weak low-frequency electric field. The results of the investigation are detailed in [6–8].

We regard as a non-linear system of transmembrane ion transfer the K^+–H^+ antiport across the cell membrane with the participation of the carrier T^-, forming with the ions TH, TK, THK^+ and TH^2 complexes. The rate constants of the corresponding stages are $k_{\pm i}$ ($i = 1, \ldots, 7$). It is assumed that the rates of flows of ions from and into the reaction sphere depend on the electric field voltage in the near-membrane region: $V(\varphi)$.

The subscripts 1 and 2 at concentrations of protons H^+ and potassium K^+ ions correspond to the solution on the two sides of the membrane

$$V_H(\varphi) \underset{k_H}{\rightleftarrows} H_1^+ + T^- \underset{k_{-1}}{\overset{k_{+1}}{\rightleftarrows}} TH \xrightarrow{k_{+2}} T^- + H_2^+ \rightarrow V'_H(\varphi)$$

$$H_1^+ + TH \underset{k_{-7}}{\overset{k_{+7}}{\rightleftarrows}} TH^2$$

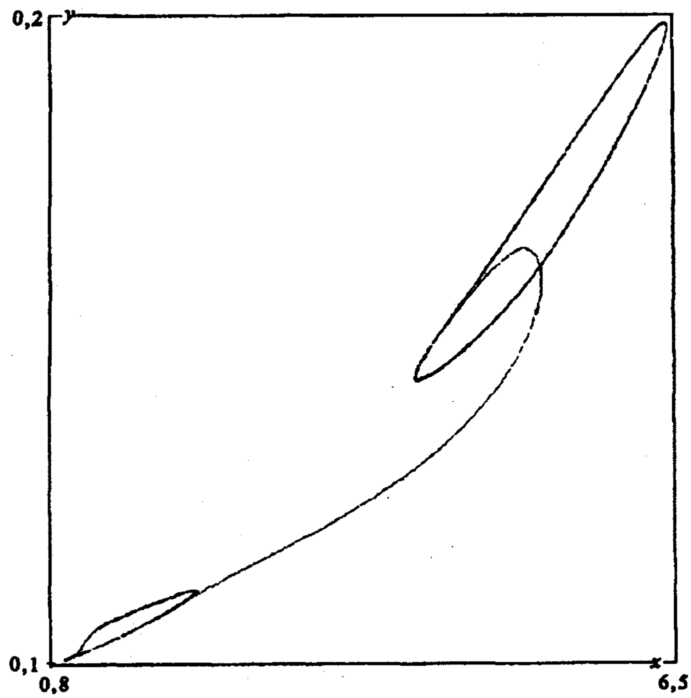

Fig. 1. Phasic portrait of the system of the K^+/H^+ antiport for the case of bistability on e.m.r. exposure; x, dimensionless concentration of protons; y, dimensionless concentration of potassium ions. a, 26.44; $b=0$; $c=0$; $d=0.696$; $V_x=10.637$; $k_x=1$; $V_y=0.0325$. For an amplitude of exposure $A=0.03$ and frequency $\omega=0.047$ the system begins to oscillate about one stable state, but with time passes into the vicinity of another state.

$$k_{-7}$$

$$H_1^+ + TK \underset{k_{-5}}{\overset{k_{+5}}{\rightleftharpoons}} THK^+ \xrightarrow{k_{+6}} TK + H_2^+$$

$$V_K(\varphi) \leftarrow K_1^+ + TH \xleftarrow{k_{+4}} THK^+ \underset{k_{-3}}{\overset{k_{+3}}{\rightleftharpoons}} TH + K_2^+ \leftarrow V_K(\varphi).$$

The set of equations describing the kinetics of the reactions after allowing for the hierarchy of times and the transformatim of equations to the dimensionless form [8] is as follows:

$$dx/d\tau = V_x(\varphi) - k_x x - x(a + by)/(1 + x + xy + cy + dx^2), \quad (1)$$

$$dy/d\tau = V_y(\varphi) - xy/(1 + x + xy + cy + dx^2),$$

where x and y are, respectively, the dimensionless concentrations of protons and potassium ions, combinations of the reaction constants forming the parameters of the system.

With reference to the periodic sinusoidal action of the external electric field on the speed of movement of the ions in the near-membrane region, the system assumes the form:

$$dx/d\tau = V_x(\varphi)(1 + A\sin\omega\tau) - k_x x - x(a + by)/(1 + x + xy + cy + dx^2), \quad (2)$$

$$dy/d\tau = V_y(\varphi)(1 + A\sin\omega\tau) - xy/(1 + x + xy + cy + dx^2),$$

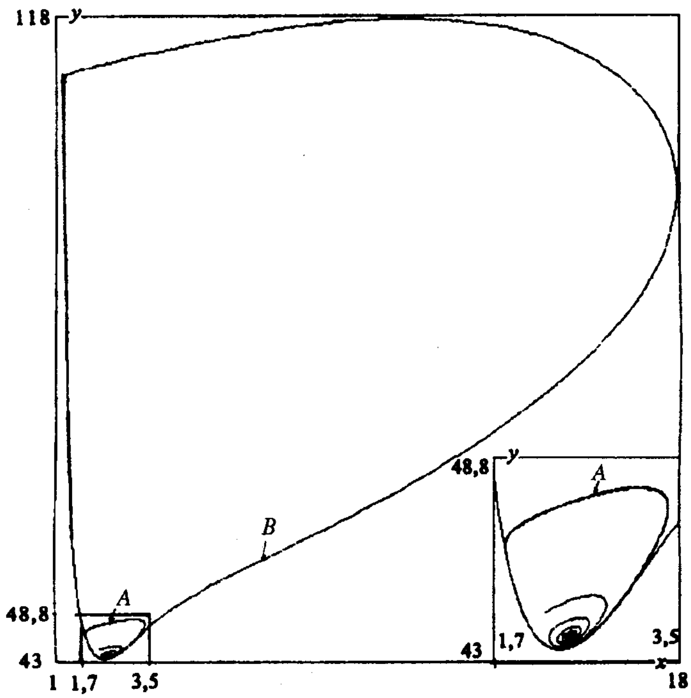

Fig. 2. Phasic portrait of the system of the K^+/H^+ antiport in the case of auto-oscillations for the following values of the speed of influx of protons: $V_x = 0.5241$ (focus); $V_x = 0.5244$ (cycle A); $V_x = -0.5245$ (cycle B); x, dimensionless concentration of protons; y, dimensionless concentration of potassium ions. $a = 0$; $b = 1$; $c = 1$; $d = 10$; $k_x = 1$; $V_y = 0.5$. For the lower critical value of the parameter $V_x = 0.5241$ corresponding to the stable state of the focus, a weak external action ($A = 0.0003$, $\omega = 0.004$) takes the system into the regime of auto-oscillations (cycle A). If the action is carried out when the system is in the regime of auto-oscillations (at V_x close to bifurcational), there is passage from oscillations of low amplitude to those of high amplitude, i.e. transition from cycle A to cycle B.

where A is the dimensionless amplitude and ω is the dimensionless cyclic frequency of the external agent. From the value of the amplitude one may judge how far the voltage of the external electric field makes up the voltage of the electric field proper in the near-membrane region.

Depending on the values of the parameters, the system may have one or three special points, the type and character of the stability of which, are determined by the specific values of the parameters. A detailed investigation of the properties of the system is reported in [8]. A weak periodic field in the system results in minor variations in the concentrations of the ions close to the stable states of the system. With change in the frequency of the acting radiation, resonance amplifications of the variations are possible with switching from one steady state to another (Fig. 1) or oscillations encompassing both these states. Finally, limiting cycles of small and large amplitude may appear (Fig. 2). Critical (resonance) frequencies exist at which the above described changes in the regime of functioning of the system occur, sharply changing the values of the ion concentrations. Evaluation of the parameters of external radiation shows that for a voltage of the electric field in the near-membrane region of the order of 10^4 V/cm [9], the external electric fields of the order of 10 V/cm may produce changes in the intracellular pH by tenths up to unity at resonance frequencies of exposure of the order of 0.1–100 Hz. Much evidence exists indicating the high sensitivity of the cellular processes to pH and ionic strength apparently due to the influence of these magnitudes on the transitions of peripheral proteins from the membrane-bound to the free state in the aqueous phase [10]. The scales of change in the electric field are comparable with the changes in the electric field voltage close to the surface of the ground caused by atmospheric phenomena [11]. Voltages of the acting field of the same order have been used in experiments [12, 13].

However, an important after-effect of exposure to e.m.r. may be not only change in the ion concentration level in the near-membrane layer but also initiation of an auto-oscillatory regime or its cessation. The importance of rhythmic processes in the vital activity of organisms is well known [14]. Often various dysfunctions of the body are connected with disturbance of a particular biological rhythm. The fact that at critical frequencies e.m.r. is an impetus to the advent of auto-oscillations may, to some degree, explain the biological effect of e.m.r.

The enormous diversity of the manifestation of the biological effect of e.m.r. often leads researchers into a blind alley in the search for the mechanisms of such an effect. There is still no single theory capable of embracing the greater part of the accumulated experimental material. The approach proposed in this paper based on the non-linearity of living systems is able, in our view, to explain both the diversity of the responses of biological objects and the low energies of the acting radiations.

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