Biophysics, Vol. 45, No. 3, 2000, pp. 483–489. Translated from Biofizika, Vol. 45, No. 3, 2000, pp. 495–501.

Effects of Electric Field on Spatiotemporal Patterning in the Reaction–Diffusion System

A. I. Lobanov[1], T. Yu. Plyusnina[2], T. K. Starozhilova[1], G. Yu. Riznichenko[2], and A. B. Rubin[2]

[1] *Moscow Institute of Physics and Technology, Dolgoprudnyi, Moscow Region, 141700 Russia*
[2] *Biological Faculty, Moscow State University, Moscow, 119899 Russia*

Received April 27, 1999

Abstract—A model is proposed that describes electrodiffusion in the layer adjacent to the cell membrane. The model takes into account chemical reactions at the membrane, Coulomb interactions between particles, their random motion (diffusion), and the effect of an external electric field. Linear analysis of the model shows a possibility of spatiotemporal patterning in the presence of an applied electric field. The dissipative structures formed in the presence and the absence of the electric field differ in a number of characteristics. First, the former structure drifts. Its slow drift proceeds unidirectionally. While it drifts, the number of its structural elements varies. Second, isolated soliton-like structures may emerge in this system, as the dispersion relation contains not only even, but also odd powers of the wavenumber k. In addition to Turing-type diffusion instability, dispersion instability may arise in the presence of an external electric field, also causing spatiotemporal patterning.

Key words: electrodiffusion, layer adjacent to the cell membrane, dissipative structure, dispersion instability

INTRODUCTION

Since the appearance of Turing's classical work *The Chemical Basis of Morphogenesis* and works from the Prigogine–Glansdorff–Nicolis school, it has become clear that, varying the parameters of the distributed reaction–diffusion systems, one may observe generation of structures from an initially uniform stationary state at certain diffusion coefficient ratios [1–3]. Bifurcations in such systems represent alterations of the type of the spatiotemporal regime, e.g., the emergence of a dissipative structure from a homogeneous stationary state, or transitions from a stationary structure to traveling or standing waves.

Bifurcations in the spatiotemporal distributions of ions along the cell membrane or in cell ensembles may be of particular significance in developmental processes. A description of the effects of an external electric field on interacting particles should necessarily include not only their chemical conversions, but also Coulomb interactions with one another and the electric field. These factors may prove to be important in regions where the electroneutrality conditions do not hold. In describing a thin boundary layer of the order of the Debye length adjacent to the cell membrane, it seems useful to employ an approach analogous to those used in description of the processes in electrolytes [4] or commonly used in membrane electrochemistry [5]. The model constructed in these terms provides new insights into the role of electric fields in spatiotemporal bifurcations.

There are studies that consider the spatial scale on which the electroneutrality conditions still hold. Leonetti and Pelce [6] suppose that, compared with the transport processes, chemical reactions proceed much more rapidly. Therefore, the reaction terms may be neglected. As the size of the area they consider is great relative to the Debye length, the condition of

---

Abbreviation: DS, dissipative structure.

bulk electroneutrality allows the authors to reduce the system to two Laplace equations, one describing the concentration and the other the potential, and to set the boundary conditions as a certain combination of fluxes across the membrane. This approach makes it possible to describe the stationary distributions of potentials and ion concentrations at great distances from the membrane; however, it does not apply to the processes in the boundary layer.

In the known nonstationary models [5–8], the electric current density (the electric field strength) is assumed to be uniform. Notwithstanding, in one of these studies, a conclusion is made that appreciable field gradients may develop upon even a minor local disturbance of electroneutrality.

When deriving a set of equations below, we will demonstrate that additional nonlinear terms have to be introduced into the reaction part of the model to describe local perturbations of electroneutrality and that, in the general case, these terms are not small.

MODEL OF PROCESSES IN THE MEMBRANE BOUNDARY LAYER

The main objective of this study was to describe the processes of ion transfer across the cell membrane and the effects of external factors, such as an electric field, on these processes. It is transport of charged particles that is sensitive to the presence of electric fields. To take this fact into account, we have to modify the known set of equations of the reaction–diffusion type.

To derive the equation of motion of charge particles, let us consider an elementary volume Ω with the boundary $\delta\Omega$. The change in the total number of particles in this volume will read:

$$\frac{\partial N}{\partial t} = -\int_{\partial\Omega} (\mathbf{W}, \mathbf{n}) dS + f\Omega, \tag{1}$$

where $N = \Omega n$, with n being the particle density; $\boldsymbol{W}$ denotes the particle flux across the boundary; $\mathbf{n}$ is the outward normal to the volume boundary; and f is the function of the volume source of (or sink for) particles describing their production (utilization) in chemical reactions. Let $\boldsymbol{W}$ be a sum of the diffusion flux $-D\nabla n$, which is associated with chaotic (thermal) motion, and the electrostatic force-driven flux nU, where U is the stationary rate of ion motion in the medium. For positive ions, $U = bE = eBE$, where b is the mobility of a particle in the electric field, e is the electron absolute charge, and B is the proportionality coefficient, which relates the force acting on the particle to its velocity. For negative ions, $U = -bE$.

According to the principle of superposition, the electric field of strength $\boldsymbol{E}$ can be written as a sum of the external field applied to the system and the field created by the moving particles themselves. Let us denote the first summand as $\boldsymbol{E}_{\text{out}}$ and the second as $\boldsymbol{E}_s$. Subscript s in the latter indicates that the field created by particles is self-consistent. As the external field is independent of the charge distribution in the system, its strength satisfies the condition:

$$\operatorname{div}\mathbf{E}_{\text{out}} = 0. \tag{2}$$

For the self-consistent field, we have:

$$\operatorname{div}\mathbf{E}_s = \frac{1}{\varepsilon_0 \varepsilon}\rho = \frac{e}{\varepsilon_0 \varepsilon} n, \tag{3}$$

where ρ is the charge density, ε_0 is the dielectric constant of the medium, and n is the particle concentration.

Dividing equation (1) by the elementary volume Ω and then passing to the limit $\Omega \to 0$, we obtain:

$$\frac{\partial n}{\partial t} = -\operatorname{div}\mathbf{W} + f = D\Delta n - \operatorname{div}(bn\mathbf{E}) + f(n).$$

Equations (2) and (3) allow this equality to be rewritten in the form:

$$\frac{\partial n}{\partial t} = D\Delta n - b(\mathbf{E}_{\text{out}}, \nabla n) - b(\mathbf{E}_s, \nabla n) - \frac{e}{\varepsilon_0 \varepsilon} b n^2 + f(n). \tag{4}$$

The $\boldsymbol{E}_s$ is determined from equation (3). If the system contains differently charged particles, generalization (4) is easily derived analogously, resulting in:

$$\frac{\partial n_i}{\partial t} = D_i \Delta n_i - b_i Z_i (\mathbf{E}_{\text{out}}, \nabla n_i) - b_i Z_i (\mathbf{E}_s, \nabla n_i) - \\ - \frac{e}{\varepsilon_0 \varepsilon} b_i Z_i n_i \sum_{l=1}^{K} Z_l n_l + f_i(n_1, \dots, n_K), \tag{5}$$

$$\operatorname{div}\mathbf{E}_s = \frac{e}{\varepsilon_0 \varepsilon} \sum_{l=1}^{K} Z_l n_l, \tag{6}$$

where subscript i is used to indicate the ith type of ions; b_i and Z_i are the mobility and the valence of the ith ion, respectively (Z_i assumes both positive and negative values).

According to the Einstein formula, the diffusion coefficient of a particle is related to its mobility as

$$D = kTB, \tag{7}$$

where T is the temperature of the medium and k is the Boltzmann constant.

Let us introduce independent scale factors for time (T_0), length (L_0), electric field strength (E_0), and ion concentration (n_0). Note that the concentration of the most abundant ion is chosen to be the ion concentration scale factor. The scale factors for time and electric field strength may be taken in the following forms: $T_0 = \frac{\varepsilon_0}{2e^2 B_1 n_0}$ and $E_0 = eL_0 n_0 \varepsilon_0^{-1}$. Here, B_1 denotes the maximal ion mobility. Rewritten in these terms, equations (5) and (6) appear as

$$\frac{\partial n_i}{\partial \tau} = \frac{d^2 B_i}{L_0^2 B_1}\Delta n_i - \frac{B_i}{2B_1} Z_i(\mathbf{E}_{\text{out}} + \mathbf{E}_s, \nabla n_i) - $$

$$-\frac{B_i}{2\varepsilon B_1} Z_i n_i \sum_{l=1}^{K} Z_l n_l + T_0 f_i(n_1, \ldots, n_K), \tag{8}$$

$$\operatorname{div}\mathbf{E}_s = \frac{1}{\varepsilon}\sum_{l=1}^{K} Z_l n_l .$$

Equations (8) contains the parameter $d = \sqrt{\frac{\varepsilon_0 kT}{2e^2 n_0}}$, which represents the Debye length. The role of this parameter in our problem will be discussed below.

Let us consider the cell membrane in the medium. We assume that the membrane length is much greater than the size of arising inhomogeneities. Our analysis concerns the ion concentration distribution along the outer surface of the membrane. A one-dimensional problem will be considered as a first approximation. Let n_1 and n_2 be, for certainty, the concentrations of positive and negative ions, respectively, and their charge be equal to the electron charge e. The membrane itself is also charged, with the charge surface density of σ. The size of the layer in which the electroneutrality balance may be disturbed by an excess of ions opposite in charge to σ is determined by the Debye length.

Let us consider the membrane boundary layer of the Debye length. In this problem, the Debye number $n_D = n_0 d^3 = \left(\sqrt{\frac{\varepsilon_0 k}{2e^2}}\right)^3 T^{3/2} n_0^{-1/2}$ is small; therefore, collective effects like ambipolar diffusion do not manifest themselves. If so, the formulas written above holds. We also assume that the external field E_{out} is directed along the membrane surface. As the layer is thin, the reactions at the membrane surface are supposed to span the entire layer.

It is convenient to rewrite the equations describing the spatiotemporal dynamics of ion distribution in the following dimensionless form:

$$\frac{\partial n_1}{\partial t} = D_1 \frac{\partial^2 n_1}{\partial x^2} - B_1 E_{\text{out}} \frac{\partial n_1}{\partial x} - B_1 E_s \frac{\partial n_1}{\partial x} - B_1 / \varepsilon \cdot n_1(n_1 - n_2) + f_1(n_1, n_2),$$

$$\frac{\partial n_2}{\partial t} = D_2 \frac{\partial^2 n_2}{\partial x^2} + B_2 E_{\text{out}} \frac{\partial n_2}{\partial x} + B_2 E_s \frac{\partial n_2}{\partial x} - B_2 / \varepsilon \cdot n_2(n_2 - n_1) + f_2(n_1, n_2), \tag{9}$$

$$\frac{\partial E_s}{\partial x} = \frac{1}{\varepsilon}(n_1 - n_2),$$

where D_1 and D_2 are the dimensionless diffusion coefficients, and B_1 and B_2 are the dimensionless mobilities of ions. The external field will be considered to be a given function of time that does not depend on coordinate x.

In its structure, model (9) coincides with the models described in [5–8], differing from them only in the presence of nonlinear terms of the form $B_i/\varepsilon \cdot n_i(n_i - n_j)$. As will be obvious below, these additional terms do not influence the results of the linear analysis of the model; nevertheless, their contribution may be appreciable.

LINEAR ANALYSIS OF THE MODEL

In the vicinity of the spatially homogeneous stationary state, set (9) of equations reads:

$$\frac{\partial u}{\partial t}=D_1\frac{\partial^2 u}{\partial x^2}-B_1E_{\text{out}}\frac{\partial u}{\partial x}+au+cv,$$

$$\frac{\partial v}{\partial t}=D_2\frac{\partial^2 v}{\partial x^2}+B_2E_{\text{out}}\frac{\partial v}{\partial x}+fu+dv.$$

Here, B_1 and B_2 are the mobilities of monovalent ions; E_{out} is the strength of the electric field applied; a, c, d, and f are the elements of the Jacobi matrix of the system calculated for its equilibrium state. Without loss of generality, we can assume that $a+d<0$ and $a>0$. In this case, u may be interpreted as the activator and v as the inhibitor. The effects of the self-consistent field are described by terms of the orders higher than the first one. We can change the characteristic spatial scale and rewrite the set:

$$\frac{\partial u}{\partial t}=\frac{\partial^2 u}{\partial x^2}-b_1E_{\text{out}}\frac{\partial u}{\partial x}+au+cv,$$

$$\frac{\partial v}{\partial t}=\delta\frac{\partial^2 v}{\partial x^2}+b_2E_{\text{out}}\frac{\partial v}{\partial x}+fu+dv.$$

Here, $\delta=D_1/D_2$ and $b_i=B_i/D_1$.

Introducing the variables $\tau=t$ and $\xi=x-b_iE_{\text{out}}t$ gives:

$$\frac{\partial u}{\partial \tau}=\frac{\partial^2 u}{\partial \xi^2}+au+cv,$$

$$\frac{\partial v}{\partial \tau}=\delta\frac{\partial^2 v}{\partial \xi^2}+e\frac{\partial v}{\partial \xi}+fu+dv \qquad (10)$$

where $e=E_{\text{out}}(b_1+b_2)$.

As we will see below from analysis of this model, the wavenumbers k and $-k$ enter the equations nonsymmetrically. This asymmetry is accounted for by the different directions of the ordered motion of positive and negative ions.

Let us Fourier-transform set (10) with respect to variable ξ, as done in Turing's study [1]. Retaining the same designations of the Fourier transforms that used in the study cited, we obtain:

$$\frac{du}{dt}=(-k^2+a)u+cv,$$

$$\frac{dv}{dt}=(-k^2\delta+d-ike)v+fu. \qquad (11)$$

Note that, in the frequency domain, real-valued set (10) corresponds to complex-valued set (11). In the case of the usual diffusion–reaction system, set (10) is real-valued, because it contains only dissipative terms (at $-k^2$).

It is convenient to analyze set (11) using its real-valued representation and introducing the designations $u=u_0+iu_1$ and $v=v_0+iv_1$:

$$\frac{du_0}{dt}=(-k^2+a)u_0+cv_0,$$

$$\frac{du_1}{dt}=(-k^2+a)u_1+cv_1,$$

$$\frac{dv_0}{dt}=(-k^2\delta+d)v_0+fu_0+ekv_1, \qquad (12)$$

$$\frac{dv_1}{dt}=(-k^2\delta+d)v_1+fu_1-ekv_0.$$

Let us consider the conditions under which the spatially homogeneous solution to set (12) loses stability. To do this, we have to find its eigenvalues, which satisfy a biquadratic characteristic equation:

$$\left[(a-k^2-\lambda)(d-k^2\delta-\lambda)-cf\right]^2+ \\ +e^2k^2(-k^2+a-\lambda)^2=0. \qquad (13)$$

For $e=0$, equation (13) is equivalent to the so-called dispersion relation.

A simple way to demonstrate that the system acquires new properties by virtue of a small dispersion summand in equation (13) is as follows.

Let the roots of the equation

$$(a-k^2-\lambda)(d-k^2\delta-\lambda)-cf=0 \qquad (14)$$

be known for the regime calculated without regard for the effects of the external electric field. If the homogeneous state is stable, Re $\lambda<0$ for all k. Let λ^* denote the eigenvalue whose modulus is the smallest one. Obviously, λ^* satisfies equation (14). We shall seek the solution to equation (13) of the form $\lambda^*+\varepsilon$, where ε is a small correction term to account for the effect of the external electric field. In fact, we seek the first term of the series expansion in e. Retaining the bracketed terms of equation (13) that contain ε, we obtain

$$\varepsilon^2(d+a-k^2(1+\delta)-2\lambda^*)^2+e^2k^2(-k^2+a-\lambda^*)^2=0,$$

and, hence,

$$\varepsilon=\frac{\pm iek(a-k^2-\lambda^*)}{(d+a-k^2(1+\delta)-2\lambda^*)}.$$

If k is large, $\varepsilon \sim ik$, that is, the contribution of the correction term is in the imaginary subspace. If k is small and λ is complex, the real part of the eigenvalue is also contributed to. Its sign may change if

$$\alpha = ke\frac{\beta(a-d)+\beta k^2(\delta-1)}{\left[a+d-k^2(\delta+1)-2\alpha\right]^2+4\beta^2}=$$

$$=\frac{ke\left[a-d+k^2(\delta-1)\right]}{4\beta}, \qquad (15)$$

where $\alpha = \mathrm{Re}\,\lambda^*$ and $\beta = \mathrm{Im}\,\lambda^*$. Relationship (15) serves an approximate condition for the loss of dispersion stability upon application of a weak external electric field. Knowing $\lambda^*(k)$ makes it possible to determine the critical value of the wavenumber k whereat the spatially homogeneous solution loses stability. Obviously, if the electric field is reversed in sign, the sign of k is also reversed.

In physical terms, this means a possibility of a dissipative structure (DS) arising in the system. This dissipative structure differs from the structure forming in the absence of the electric field in a number of characteristics.

First, it slowly moves (drifts). The direction of its drift is determined by the signs of the applied electric field and the activator-ion charge.

Second, the dispersion relation contains not only even, but also odd powers of the wavenumber k. For this reason, k and $-k$ enter formula (15) nonsymmetrically. This entails the dependence of the dissipative pattern on the initial conditions, because the initial conditions determine the initial values of functions u_0, u_1, v_0, and v_1. When going over to variables x and t, we obtain structures, which are phase-shifted relative to one another, with the phase shift depending on the initial conditions. In the model without regard for the effect of the external electric field, the eventual dissipative pattern does not depend on the initial conditions.

Third, in addition to the Turing-type diffusion instability, dispersion instability may arise in the presence of an external electric field, also causing spatiotemporal patterning. This situation is feasible when the system, while being stable with respect to Turing-type patterning, comes close to the bifurcation point.

NUMERICAL ANALYSIS OF THE MODEL

We tried to test these predictions using as an example set (9) of equations describing the Brusselator-type kinetics [2, 3]. In these equations, $f_1(n_1, n_2)$ and $f_2(n_1, n_2)$ were specified as follows:

$$f_1(n_1, n_2) = \alpha + n_1^2 n_2 - (\beta + 1)n_1,$$

$$f_2(n_1, n_2) = -n_1^2 n_2 + \beta n_1.$$

The splitting scheme described in [11] and modified to be acceptable in calculating equations with gradient terms was used to numerically solve the set. This allowed the boundary problem of determining the potential to be solved separately.

If ion mobilities were set to zero ($B_1 = B_2 = 0$), the system was insensitive to electric fields, whether external or self-consistent. As a testing example, Figure 1 shows a Turing-type structure formed from the spatially homogeneous stationary state in response to a random perturbation. Specifically, the first reactant (activator u) concentration is shown for the following values of the model parameters: $D_1 = 0.0001$, $D_2 = 0.001$, $\alpha = 1.0$, and $\beta = 3.0$.

To exemplify the first effect, that is, the formation of drifting structures of the Turing type, we examined the same system for $B_1 = 0.001$, $B_2 = 0.01$, $\varepsilon = 1.0$, and $E = 1.0$ while varying the critical value of the wavenumber k. Figure 2 shows the formation of less steeply sloping structures. A decrease in the number of concentration maxima per unit segment is indicative of the decrease in the critical value of the wavenumber k. In addition, the amplitude begins to pulsate. The phase of the drifting structure depends on the initial perturbation.

With E increasing above 1.0, the critical wavenumber becomes lower, as follows from approximate

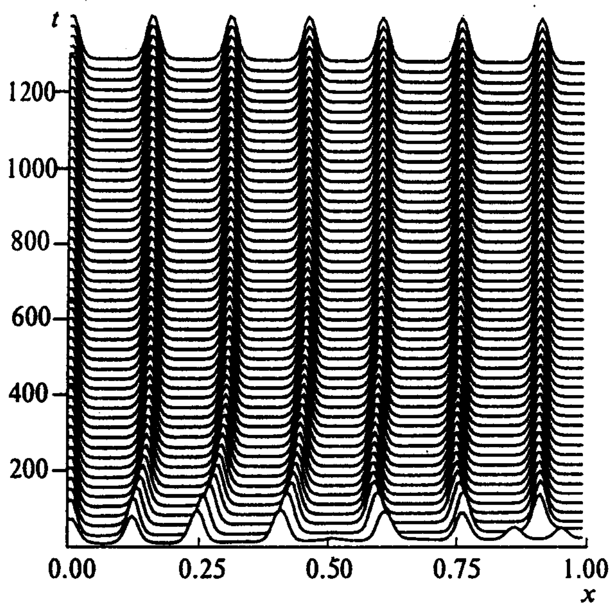

Fig. 1. Dissipative structure arising in the Brusselator-type model constructed without regard for electrostatic interactions: the concentration distribution of activator u in the (x, t) plane. See text for the parameter values.

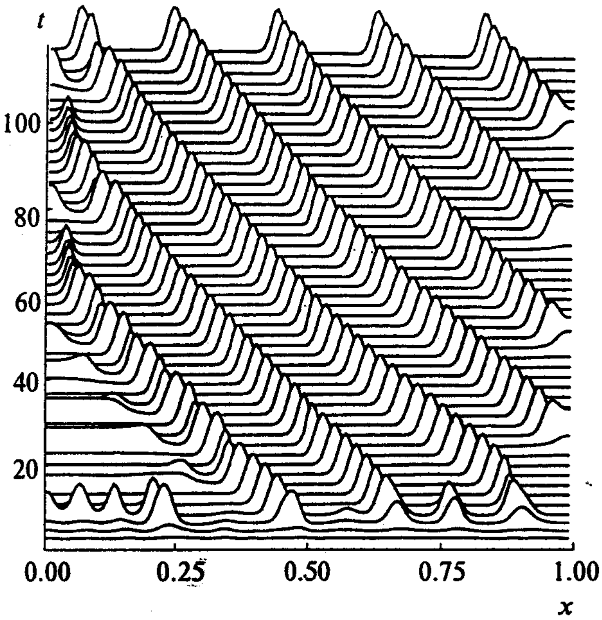

Fig. 2. Dissipative structure arising in the Brusselator-type model modified to take into account the effects of an applied electric field. The solution is shown as the concentration distribution of activator u in the (x, t) plane.

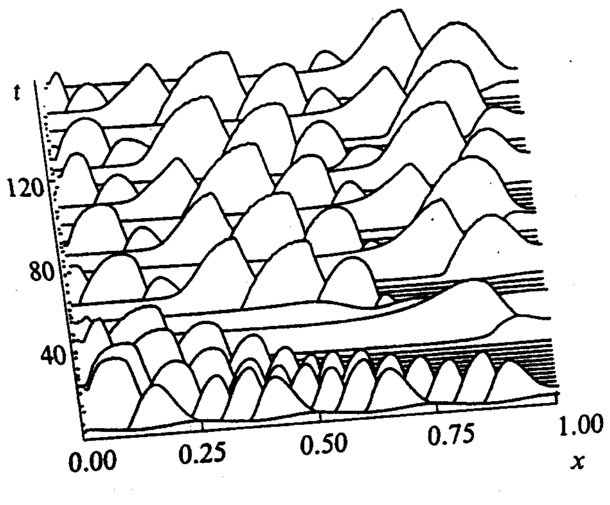

Fig. 3. Solitary structures arising in the modified Brusselator. The solution is shown as the concentration distribution of activator u in the (x, t) plane.

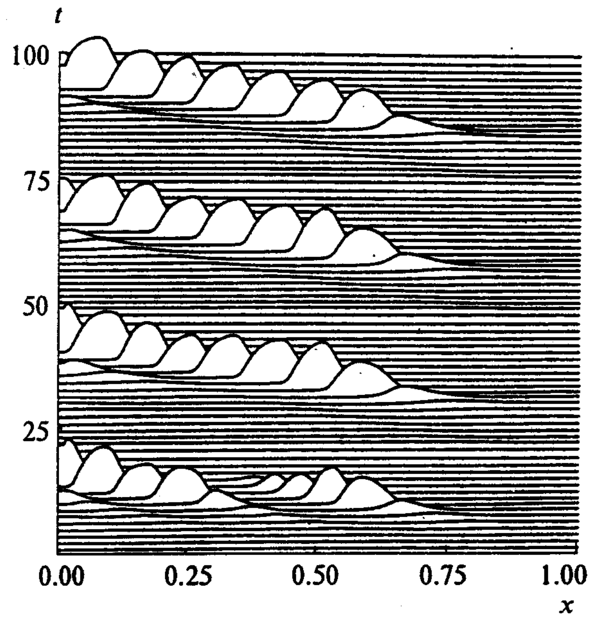

Fig. 4. Pattern formation in the Turing-stable Brusselator in response to application of an electric field. The solution is shown as the concentration distribution of activator u in the (x, t) plane.

formula (15). For $E = 10.0$, only one maximum of u goes into the unit-length segment. The pulse amplitude varies while it drifts (Fig. 3). In appearance, this solution resembles the so-called breathers of the sine-Gordon soliton equation [12]. It is pertinent to the question to recall that the reaction–diffusion equations are known to possess soliton-like solutions [13–15]. Interestingly, such soliton solutions arise in the models that describe nerve pulse propagation [14] or processes in cardiac muscle [15], that is, in the systems in which electrical interactions play a significant part.

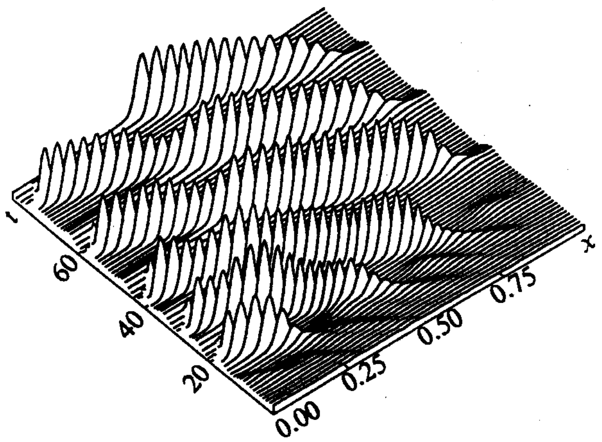

Fig. 5. Pattern formation in the Turing-stable Brusselator in response to application of a high-strength electric field: structures with forerunning small-amplitude pulses. The solution is shown as the concentration distribution of activator u in the (x, t) plane.

An external electric field may cause patterning even in such a reaction–diffusion system that is Turing-stable in its basic form. Let D_1 be 0.00005, D_2 0.0001, α 1.0, β 1.5, B_1 0.001, B_2 0.002, and ε 1.0. In this case, the brusselator has a unique stable stationary solution, and Turing's instability does not manifest itself. In the absence of the external field, all perturbations are rapidly damped. Application of the field leads to the formation of drifting structures. The structure shown in Fig. 4 was generated for $E = 10.0$. With E increasing above 10.0, the number of structural elements going into the unit-length segment decreases, and they arise at longer intervals one after another. Figure 5 shows a fragment of the spatial and time series for $E = 25.0$. Evidently, drifting pulses arise at long time intervals, each with its small-amplitude forerunner.

CONCLUSION

In the boundary membrane layer, ions may either undergo lateral transfer (diffusion and convection) or be involved in transmembrane transport. This study gives a mathematical description of these processes for a one-dimensional case. The results of analytical analysis of the linearized system and of numerical analysis of the initial nonlinear set demonstrate that application of an external electric field may alter both the conditions for the generation of spatiotemporal regimes and their types. Assessing the critical parameter values (electric field strength, ion mobility, etc.) for particular systems will make it possible to reveal the range in which electric fields cause biologically significant effects.

REFERENCES

1. Turing, A.M., *Phil. Trans. Roy. Soc. London*, 1952, vol. 237, pp. 37–72.
2. Nicolis, G. and Prigogine, I., *Self-Organization in Non-equilibrium Systems*, New York: Wiley, 1977. Translated under the Title *Samoorganizatsiya v neravnovesnykh sistemakh*, Moscow: Mir, 1979.
3. Glansdorff, P. and Prigogine, I., *Thermodynamic Theory of Structure Stability and Fluctuations*, London: Wiley, 1971. Translated under the Title *Termodinamicheskaya teoriya struktury, ustoichivosti i fluktuatsii*, Moscow: Mir, 1973.
4. Sivukhin, D.V., *Obshchii kurs fiziki, vol. 3: Elektrichestvo* (General Course of Physics, vol. 3: Electricity), Moscow: Nauka, 1977.
5. Zabolotskii, V.I. and Nikonenko, V.V., *Perenos ionov v membranakh* (Ion Transfer in Membranes), Moscow: Nauka, 1996.
6. Leonetti, M. and Pelce, P., *Biophysics*, 1994, vol. 317, pp. 801–805.
7. Munster, A.F., Hasal, P., Snita, D., and Marek, M., *Phys. Rev. E.*, 1994, vol. 50, no. 1, pp. 546–549.
8. Sevcikova, H., Kosek, J., and Marek, M., *J. Phys. Chem.*, 1996, vol. 100, pp. 1666–1675.
9. Munster, A.F., Waltzl, M., and Schneider, F.W., *Physica Scripta*, 1996, vol. T67, pp. 58–62.
10. Schmidt, B. and Muller, S.C., *Phys. Rev. E*, 1997, vol. 55, no. 4, pp. 4390–4393.
11. Lobanov, A.I., Starozhilova, T.K., and Guriya, G.T., *Mat. Modelirovanie*, 1997, vol. 9, no. 8, pp. 83–95.
12. Lamb, G.L., Jr., *Elements of Soliton Theory*, New York: Wiley, 1980. Translated under the Title *Vvedenie v teoriyu solitonov*, Mogilev: Bibfizmat, 1997.
13. Kerner, B.S. and Osipov, V.V., *Usp. Fiz. Nauk*, 1989, vol. 32, no. 1, pp. 101–138.
14. Mornev, O.A., Aslanidi, O.V., Aliev, R.R., and Chailakhyan, L.M., *Dokl. Akad. Nauk*, 1996, vol. 374, pp. 123–127.
15. Aslanidi, O.V. and Mornev, O.A., *J. Biol. Phys.*, 1999, vol. 25, nos. 2–3, pp. 149–164.