======== CELL BIOPHYSICS ========

New Spatiotemporal Modes in the Reaction–Electrodiffusion System

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Abstract—A study was made of the properties of a reaction–electrodiffusion system. A two-component model was developed to describe how interacting charged particles diffuse near the membrane in low-ionic-strength media for which the common assumption of electroneutrality is invalid. Analysis of this model—constructed to take into account the presence a self-consistent field—shows that the latter contributes to the emergence of bistability, localized structures with highly heterogeneous spatial distributions of charges, and spatially and temporally aperiodic modes.

Key words: electrodiffusion, self-consistent field, nonlinear dynamic modes

INTRODUCTION

Involvement of charged molecules in many chemical and biological processes leads to the need to examine the role of the so-called self-consistent field, or electric field arising from interaction of moving charged particles, in producing various dynamic modes.

Ions are essential for live organisms. Among ionic processes in the cell, most important are the generation of potential gradients across the membrane and the movement of electric pulses. There are plant species that form alternating zones of high and low concentrations of some ion (in terms of nonlinear dynamics, such zones are known as dissipative structures). For example, acidic and alkaline regions alternate over the surface of filamentous algae *Nitella* and *Chara* [1–3]. They differ in the membrane potential [4] and the potential of the adjacent layer [5]. These potential variations are a source of additional electric gradients along the membrane. To study the mechanisms of such phenomena, it may be essential not only to know how particular ion channels and membrane carriers operate, but also to understand how the dynamical system behaves as a whole or, in other words, how the spatiotemporal organization of events is affected by the presence of a self-consistent field.

There are two approaches to describing electric phenomena at and near the membrane [6]. One approach called the equivalent electric circuit technique was employed in studies of nerve impulse conduction [7] and of potential profiles in *Chara* cells [5, 8]. The second approach is to use the electrodiffusion equations, as in studies of the effect of external electric fields on chemical reactions in high-ionic-strength solutions [9–13], for which the electroneutrality condition holds. This condition, if fulfilled, markedly simplifies the analysis of problems. However, in biological media, unlike chemical media, this is often not the case. For example, departure from electroneutrality is possible near cell membranes as a result of active ion transport, the presence of the electric double layer, and the presence of fixed charges on integral membrane proteins.

The goal of this study was to demonstrate that self-consistent field-related redistribution of membrane charges and potential gradients gives rise to a number of important biological effects in systems with nonlinear chemical kinetics. We attained this goal by solving reaction–electrodiffusion equations for low-ionic-strength media where the common assumption of electroneutrality is invalid.

REACTION–ELECTRODIFFUSION MODEL

Formulating the Problem

Let us consider a single cell placed in a weak electrolyte solution. The cell membrane is known to carry an electric charge. Assume that its distribution over the cell surface is uniform. To screen the cell surface charge, electrolyte ions of opposite charge accumulate near the cell membrane [14]. The span of this oppositely charged layer can be estimated: it is the Debye radius (length). The Debye radius is usually much smaller than the cell diameter. Therefore, to model the effects produced by ion movement along the cell membrane, we can consider the latter as an infinite boundary carrying an electric charge. This assumption allows us to go over to a one-dimensional problem.

In the system of interest, all reactions altering the concentrations of charged particles proceed on the membrane surface. The electric double layer is supposed to be in equilibrium with the rest of the electrolyte: the flux of ions leaving the layer by virtue of their thermal motion equals the flux of ions arriving from the bulk solution.

Mathematical Model

Let the system under study contain neutral particles along with charged ones. Charged particles may be ions diffusing along the cell membrane and taking part in various chemical reactions. Let the concentration of ions be much lower than that of neutral molecules. In other words, we consider a low-ionic-strength solution.

Variations in ion concentrations are described by the reaction–electrodiffusion equations [13]. With the concentrations of positive and negative ions designated c_1 and c_2, respectively, the set of dimensionless equations with one spatial variable (r) reads

$$\frac{\partial c_1}{\partial \tau} = D_1 \frac{\partial^2 c_1}{\partial r^2} + B_1 \frac{\partial c_1}{\partial r} \frac{\partial \psi}{\partial r} -$$
$$-B_1 \chi c_1 (c_1 - z\gamma c_2) + f(c_1, c_2), \tag{1.1}$$

$$\frac{\partial c_2}{\partial \tau} = D_2 \frac{\partial^2 c_2}{\partial r^2} -$$
$$-B_2 \frac{\partial c_2}{\partial r} \frac{\partial \psi}{\partial r} + B_2 \chi c_2 (c_1 - z\gamma c_2) + g(c_1, c_2), \tag{1.2}$$

$$\frac{\partial^2 \psi}{\partial r^2} = -\chi (c_1 - z\gamma c_2), \tag{1.3}$$

where τ is time; $f(c_1, c_2)$ and $g(c_1, c_2)$ are nonlinear functions that describe the changes in ion concentrations caused by chemical reactions at the membrane; D_1 and D_2 are the diffusion coefficients for positive and negative ions, respectively; B_1 and B_2 are their mobilities in an electric field; γ is the ratio of the characteristic ion concentrations; and z is the valence ratio of ions.

The equations describing changes in ion concentrations were solved for no-flux boundary conditions:

$$J_1(0, \tau) = J_1(1, \tau) = 0$$
$$J_2(0, \tau) = J_2(1, \tau) = 0. \tag{2.1}$$

As the initial condition, we chose the steady-state uniform distribution of ion concentrations, that is, the solution to the algebraic set $f(c_1, c_2) = 0$ and $g(c_1, c_2) = 0$.

The boundary conditions for the Poisson equation were taken in the form

$$\psi(0, \tau) = \psi(1, \tau) = 0, \tag{2.2}$$

implying the absence of electric fields parallel to the membrane surface.

ANALYSIS FOR SELF-SIMILARITY

As shown by Ortoleva and Schmidt [15], the lower the ionic strength, the greater the effect of a self-consistent field. To better understand the patterning in low-ionic-strength media, let us consider self-similar solutions to the set of equations (1.1)–(1.3). This approach allows us to take account of the quadratic terms describing a self-consistent field without the need to assume that the medium is electroneutral.

It is known that, if a set of partial differential equations admits a self-similar solution, the degree of that set can be reduced. For example, it is possible to go over to a set of ordinary differential equations [16]. As such systems are characterized by self-similarity [16], the solutions to the set of ordinary differential equations will reflect the solutions to the original set, provided that large time intervals are considered.

By self-similar solutions we mean the solutions obtained by a generalization of the variable separation technique [17, 18], according to which the solution of the original equation is written as $F(r, \tau) = \phi(\tau)h(\xi)$, where the second multiplier depends only on some combination $\xi(r, \tau)$ of independent dimensionless variables.
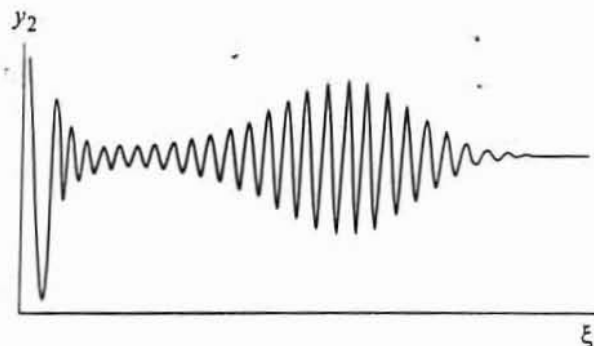
y_2

Fig. 1. Modulated structures, as calculated in the self-similar system (5.1)–(5.3) for $D_1/D_2 = B_1/B_2 = 3$, $p_{11} = 0, p_{12} = 14, p_{13} = 1, p_{21} = 0.5, p_{22} = -24, p_{23} = 2.85$, $z = 1, \gamma = 1$, and $\chi = 0.99$.
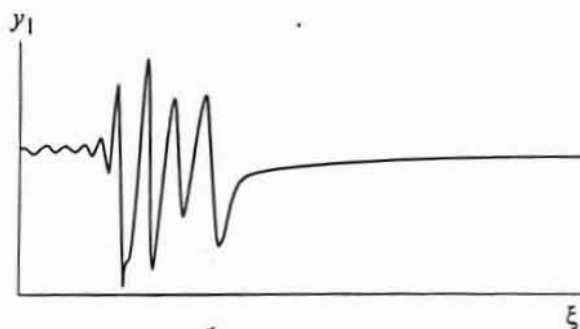
y_1

Fig. 2. Localized structures with high spatial variation in charge density, as calculated in the self-similar system (5.1)–(5.3) for $D_1/D_2 = B_1/B_2 = 2.6$, $p_{11} = 0$, $p_{12} = -25$, $p_{13} = 1, p_{21} = 0.5, p_{22} = -24, p_{23} = 2.85, z = 1, \gamma = 1$, and $\chi = 1.035$.

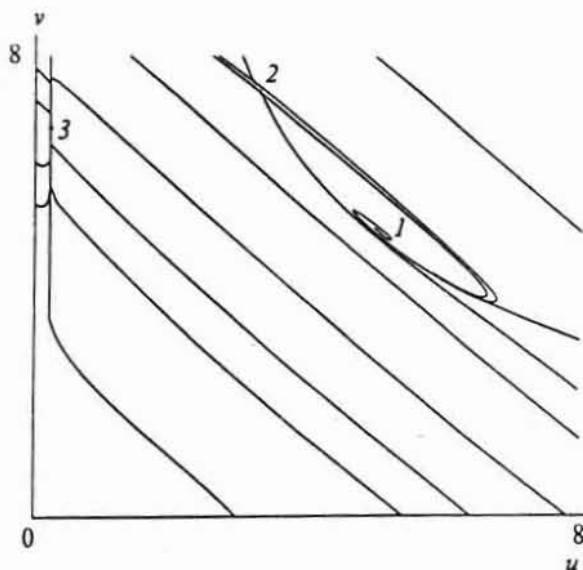**Fig. 3.** Phase portraits of the model describing the local chemical dynamics (*1*) without and (*2, 3*) with regard for the effect of a self-consistent electric field: (*1*) stable focus, (*2*) saddle, and (*3*) stable node. Parameters used in calculations: $a = 5$, $b = 25$, $B_1 = 0.01$, $B_2 = 0.01$, $z = 1$, $\gamma = 1$, and $\chi = 1$.

Let $u(r, \tau)$ and $v(r, \tau)$ be small deviations from the values of c_1 and c_2 corresponding to the uniform steady state (c_1^0 and c_2^0, respectively). Self-similar variables exist in the system (1.1)–(1.3) if its "chemical" part (equations describing the chemical reactions) contains only quadratic terms (that is, if linear terms and terms of the third and higher orders in these equations are negligibly small).

Expanding the right-side functions in powers of the new variables u and v, and retaining only quadratic terms, we obtain

$$\frac{\partial u}{\partial \tau} = D_1 \frac{\partial^2 u}{\partial r^2} + B_1 \frac{\partial u}{\partial r} \frac{\partial \psi}{\partial r} + p_{11}u^2 + p_{12}uv + p_{13}v^2,$$

$$(3.1)$$

$$\frac{\partial v}{\partial \tau} = D_2 \frac{\partial^2 v}{\partial r^2} - B_2 \frac{\partial v}{\partial r} \frac{\partial \psi}{\partial r} + p_{21}u^2 + p_{22}uv + p_{23}v^2,$$

$$(3.2)$$

$$\frac{\partial^2 \psi}{\partial r^2} = -\chi(u - z\gamma v),\quad (3.3)$$

where constants p_{ij} are combinations of the second-order rate constants of the "chemical" part of the system and of the parameters of its "electric" part. The p_{ij} can take on positive and negative values.

The self-similar solution will be sought in the form

$$u(r, \tau) = \frac{1}{\tau} y_1(\xi), \quad v(r, \tau) = \frac{1}{\tau} y_2(\xi),$$

$$\psi(r, \tau) = \frac{1}{\sqrt{\tau}} y_3(\xi), \quad \xi = \tilde{r} = \frac{r}{\sqrt{\tau}}. \quad (4)$$

Functions y_1, y_2, and y_3 are the solution to the following set of ordinary differential equations

$$D_1 y_1'' + \frac{\xi}{2} y_1' + B_1 y_1' y_3' +$$

$$+ y_1 + p_{11}y_1^2 + p_{12}y_1y_2 + p_{13}y_2^2 = 0, \quad (5.1)$$

$$D_2 y_2' + \frac{\xi}{2} y_2' - B_2 z y_2' y_3' + y_2 +$$

$$+ p_{11}y_1^2 + p_{12}y_1y_2 + p_{13}y_2^2 = 0, \quad (5.2)$$

$$y_3' + \chi(y_1 - z\gamma y_2) = 0, \quad (5.3)$$

with the boundary conditions

$$y_1|_{dxi \to +\infty} = 0, \quad y_2|_{\xi \to +\infty} = 0. \quad (6)$$

Note that primes indicate differentiation with respect to the new independent variable ξ.

Conditions (6) imply that we look for localized structures. Far off the coordinate origin, the system remains in a spatially homogeneous steady state.

The solution can be continued into the range of negative ξ values as an even function by setting symmetry conditions at $\xi = 0$:

$$\left.\frac{\partial y_i}{\partial \xi}\right|_{\xi=0} = 0, \quad \left.\frac{\partial \varphi}{\partial r}\right|_{\xi=0} = 0, \quad i = 1, 2.$$

Although we confined ourselves to seeking only self-similar solutions to the full model, this approach allows us to understand some general rules of pattern formation under the action of a self-consistent field in reaction–electrodiffusion systems. Of course, in real systems the roles of linear terms and terms of the third and higher orders cannot be neglected. Expectedly, their contribution would lead either to pattern stabilization, or to significant deviation from self-similar solutions. Still we suppose that real systems may have initial conditions required for bringing into play scenarios close to self-similar ones.

Numerical analysis of the set of self-similar equations (5.1)–(5.3) revealed a number of modes. Described below are those that are analogous to the modes found in the full model (1.1)–(1.3). Non-monotonic structures develop in model (5.1)–(5.3) from special initial conditions called the Cauchy data. The amplitudes of the structural elements depend on the self-similar variable ξ. With increasing ξ, the amplitude first passes through a maximum and then levels off (Fig. 1).

Figure 2 shows more interesting solutions to model (5.1)–(5.3): a localized structure with high spatial variation in the charge distribution. Its size is small compared with the spatial scale of the problem. Beyond the region occupied by this structure, ions remain uniformly distributed.

RESULTS OF NUMERICAL EXPERIMENTS

Analysis of the full system in partial derivatives (1.1)–(1.3) shows that the interplay between particle transfer in an electric field and diffusion gives rise to a variety of modes.

To have nonlinear terms in describing chemical reactions, we chose equations of the Brusselator model:
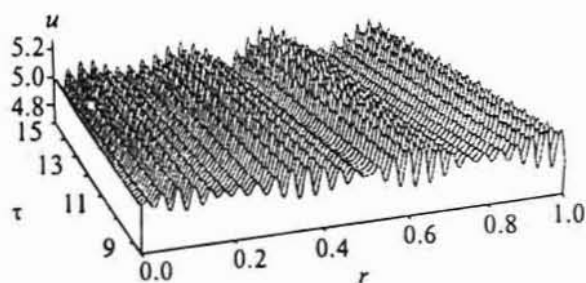
$$f(u, v) = a - (b+1)u + u^2 v,$$

Fig. 4. Structures with modulated amplitude, as calculated in the full system of partial differential equations (1.1)–(1.3) for $a = 5$, $b = 25$, $D_1 = 10^{-4}$, $D_2 = 1.5 \cdot 10^{-4}$, $B_1 = 0.1$, $B_2 = 0.15$, $z = 1$, $\gamma = 1$, and $\chi = 0.99$.
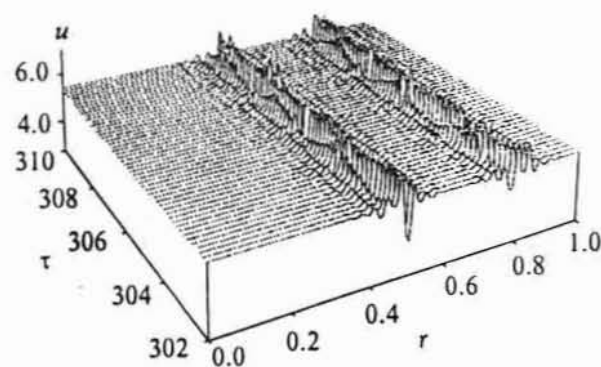

Fig. 5. Localized structures with high spatial variation in charge density, as calculated in the full system of partial differential equations (1.1)–(1.3) for $a = 5.21$, $b = 27.144$, $D_1 = 10^{-4}$, $D_2 = 1.5 \cdot 10^{-4}$, $B_1 = 0.03$, $B_2 = 0.045$, $z = 1$, $\gamma = 1$, and $\chi = 1$.
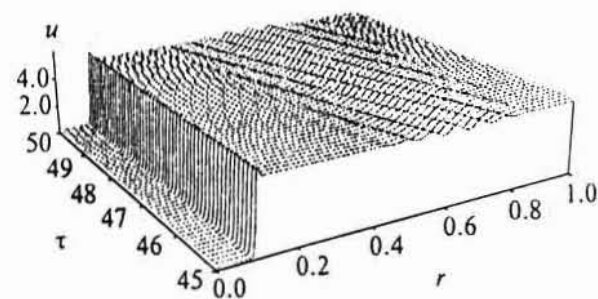

Fig. 6. Step-like distribution of ion concentrations, as calculated in the full system of partial differential equations (1.1)–(1.3) for $a = 5$, $b = 25$, $D_1 = D_2 = 10^{-4}$, $B_1 = B_2 = 0.1$, $z = 1$, $\gamma = 1$, and $\chi = 1$.

$$g(u, v) = bu - u^2 v.$$

Note that the Brusselator is expanded by incorporating the quadratic terms whereby the presence of a self-consistent field is taken into consideration. In the expanded model, more steady states are possible than in the original one (Fig. 3). Specifically, in