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COMPLEX SYSTEMS BIOPHYSICS

Negative Refractoriness in Excitable Systems with Cross-Diffusion

M. A. Tsyganov[a], V. N. Biktashev[b], and G. R. Ivanitsky[a]

[a] *Institute of Theoretical and Experimental Biophysics, Pushchino, Moscow Region, 142290 Russia*
[b] *Department of Mathematical Sciences, University of Liverpool, Liverpool L69 7Z L, UK*
e-mail: tsyganov@iteb.ru

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Abstract—The results of numerical experiments with mathematical models of excitable systems with cross-diffusion are presented. It was shown that the refractoriness in such systems may be negative. The effects of negative refractoriness on the propagation and interaction of waves are demonstrated.

Key words: cross-diffusion, refractoriness, excitable media, autowaves, self-organization

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INTRODUCTION

The progress in understanding the phenomena of self-organization in physical, chemical, and biological systems is in the first place associated with the development of the theory of autowaves, i.e. a study of the regularities of generation, propagation, and interaction of nonlinear waves in distributed active (*excitable*) media with diffusion [1–3]. Such media allow recovery of their properties after the passing of a wave pulse. The interval of time necessary for full enough recovery is called the period of refractoriness [4]. Recovery of the properties of the medium takes place at the expense of externally supplied energy. Until the moment of full recovery, usually observed is a period of relative refractoriness, which is characterized by lowered excitability of the medium. Autowaves in media with recovery usually represent themselves as running pulses having finite duration and spatial extension, Theoretical studies of autowaves and self-organization processes in excitable media have been conducted with mathematical models of the "reaction–diffusion" type:

$$\vec{u}_t = \vec{f}(\vec{u}) + D\Delta\vec{u}, \tag{1}$$

where $\vec{u}$ and $\vec{f}$ are vectors, D is diagonal matrix, Δ is Laplacian.

In recent years, broadly studies are excitable systems with cross-diffusion, differing from model (1) in that matrix D is not diagonal [5–16]. The cross-diffusional mathematical models also describe various processes of structural self-organization in physical, chemical, and biological systems, for example, growth and development of tumors [17] (for more detail see reviews [18, 19]). The general form of such systems for two variables in the one-dimensional case is as follows [18]:

$$\begin{aligned} \frac{\partial u}{\partial t} &= f(u, v) + D_1\frac{\partial^2 u}{\partial x^2} + h_1\frac{\partial}{\partial x}\left(Q_1(u, v)\frac{\partial v}{\partial x}\right), \\ \frac{\partial v}{\partial t} &= g(u, v) + D_2\frac{\partial^2 v}{\partial x^2} + h_2\frac{\partial}{\partial x}\left(Q_2(u, v)\frac{\partial u}{\partial x}\right). \end{aligned} \tag{2}$$

At $h_1 = h_2 = 0$ the mathematical model (2) represents a system of the "reaction–diffusion" type with diffusion coefficients $D_1 \geq 0$, $D_2 \geq 0$ (at least one of them is not equal to zero). In the case when at least one of the coefficients $h_i \neq 0$ (the sign may be any), system (2) is cross-diffusional. $Q_i(u, v) = \text{const}$ for $i = 1$, 2 corresponds to linear diffusion; $Q_i(u, v) \neq \text{const}$ for at least one i, to nonlinear diffusion.

In works [5–10] with mathematical models of excitable systems with linear and nonlinear cross-diffusion, studies were made of various wave phenomena characteristic of such systems. On the basis of investigations of mathematical models and experiments with bacterial population, it was proposed to isolate waves in excitable cross-diffusional systems into a special class of nonlinear waves [6,18].

It is known that for excitable systems of the "reaction–diffusion" type (1) in the refractory period the propagation of the next pulse is impossible [4]. In work [20] it has been noted that for excitable systems with nonlinear cross-diffusion the refractoriness may be "negative" in the sense that *in the relatively refractory period the excitability is not lowered as usual, but ele-*

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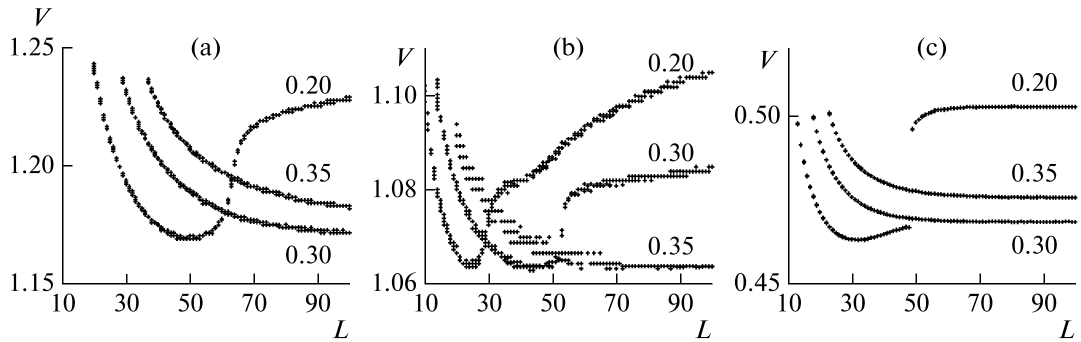

Fig. 1. Dispersion curves for mathematical model (3): (a) $D_u = 1$, $D_v = 1$; (b) $D_u = 1$, $D_v = 0.1$; (c) $D_u = 0.1$, $D_v = 1$. The corresponding values of parameter a are indicated on the plots. Breaks on the plots correspond to the minimal critical lengths of the ring on which wave propagation is possible.

vated. In the present work we present an investigation of refractoriness in excitable systems with linear cross-diffusion.

MATHEMATICAL MODEL AND NUMERICAL EXPERIMENTS

The investigations have been performed with a mathematical model with nonlinearity of the FitzHugh–Nagumo type [21, 22], which is the simplest and the most popular model of excitable media, but instead of the traditional description of the propagation of components of the system as the expense of diffusion, linear cross-diffusion is included [10]:

$$\frac{\partial u}{\partial t} = u(u-a)(1-u) - v + D_v\frac{\partial^2 v}{\partial x^2},$$
$$\frac{\partial v}{\partial t} = \varepsilon(u-v) - D_u\frac{\partial^2 u}{\partial x^2}, \quad (3)$$

where $D_u \geq 0$, $D_v \geq 0$, $\varepsilon \ll 1$, $a < 0.5$.

Numerical experiments with the mathematical model (3) were performed at value $\varepsilon = 0.01$ for three values of parameter a: 0.2; 0.3; 0.35; at three different combinations of the values of cross-diffusion coefficients D_u and D_v: ($D_u = 1$, $D_v = 1$), ($D_u = 1$, $D_v = 0,1$), ($D_u = 0,1$, $D_v = 1$) in a one-dimensional medium $x \in [0, L]$ with impermeable boundaries at $t < t_0$ ($t_0 = 50$ (arb. un. of time) and with periodical boundaries at $t > t_0$. Calculations were conducted in the implicit scheme with spatial and temporal steps $\delta x = 0.2$, $\delta t = 0.005$. To initiate a wave from the left end, the following initial values were chosen: $u(x, 0) = \theta(\delta - x)$, $v(x, 0) = 0$, $\delta = 2$.

Inclusion of periodical boundary conditions allows plotting for mathematical model (3) the dispersion curves, i.e. dependences of the wave propagation rate $V(L)$ on the length of the ring along which the excitation propagates. In our experiments the initial ring length $L = 200$. Reduction of the ring length by $\delta L = 1$ took place with time interval $\delta t = 500$, and then after an intermediate interval $\delta t = 250$ required to reach the established regime, the wave propagation rate was determined with a step $\delta t = 5$.

Presented in Fig. 1 are the dispersion curves for various combinations of parameters a, D_u and D_v. Beginning with a certain value L, the wave propagation rate in the cross-diffusion system (3) rises. In excitable systems of the "reaction–diffusion" type the wave propagation rate always drops with decreasing ring length, i.e. "positive refractoriness" takes place. This happens because of the retardation of the leading front of the wave as a result of its incidence on its own refractory tail [4]. For waves in the cross-diffusional system (3) an increase in the propagation rate, i.e. "negative refractoriness" is possible. In Fig. 1 this corresponds to the so-called anomalous dispersion, i.e. negative slope of the dispersion curves.

In works [6–10] it is shown that characteristic of cross-diffusion systems is the connection of the propagation rate and various interaction regimes with variations in the shape of wave profile.

Presented in Fig. 2 are wave profiles for model (3) corresponding to the parameters given in Fig. 1 for a ring of length $L = 200$. The changes in the wave profile in the course of ring reduction are presented in Fig. 3 for the case $a = 0.2$, $D_u = 1$, $D_v = 1$. It is seen that the transition from a "two-humped" to a one-humped profile correlates with the region of a sharp change of rate V. A sharp change of the wave propagation rate is observed also in the case of the dependence on the medium excitation threshold a on an infinite medium (Fig. 4). A similar singular dependence was observed in the dependence of the wave propagation rate on one of the cross-diffusion coefficients in a system with nonlinear cross-diffusion [6].

Let us consider how negative refractoriness influences the propagation and interaction of two waves on a contracting ring. In Fig. 5a two waves are presented on a ring of length $L = 200$. The distance d between their leading fronts (at the level $u = 0.4$) decreases during slow compression of the ring (Fig. 5b). At ring length $L = 110$–130 there occurs a sharp change of the

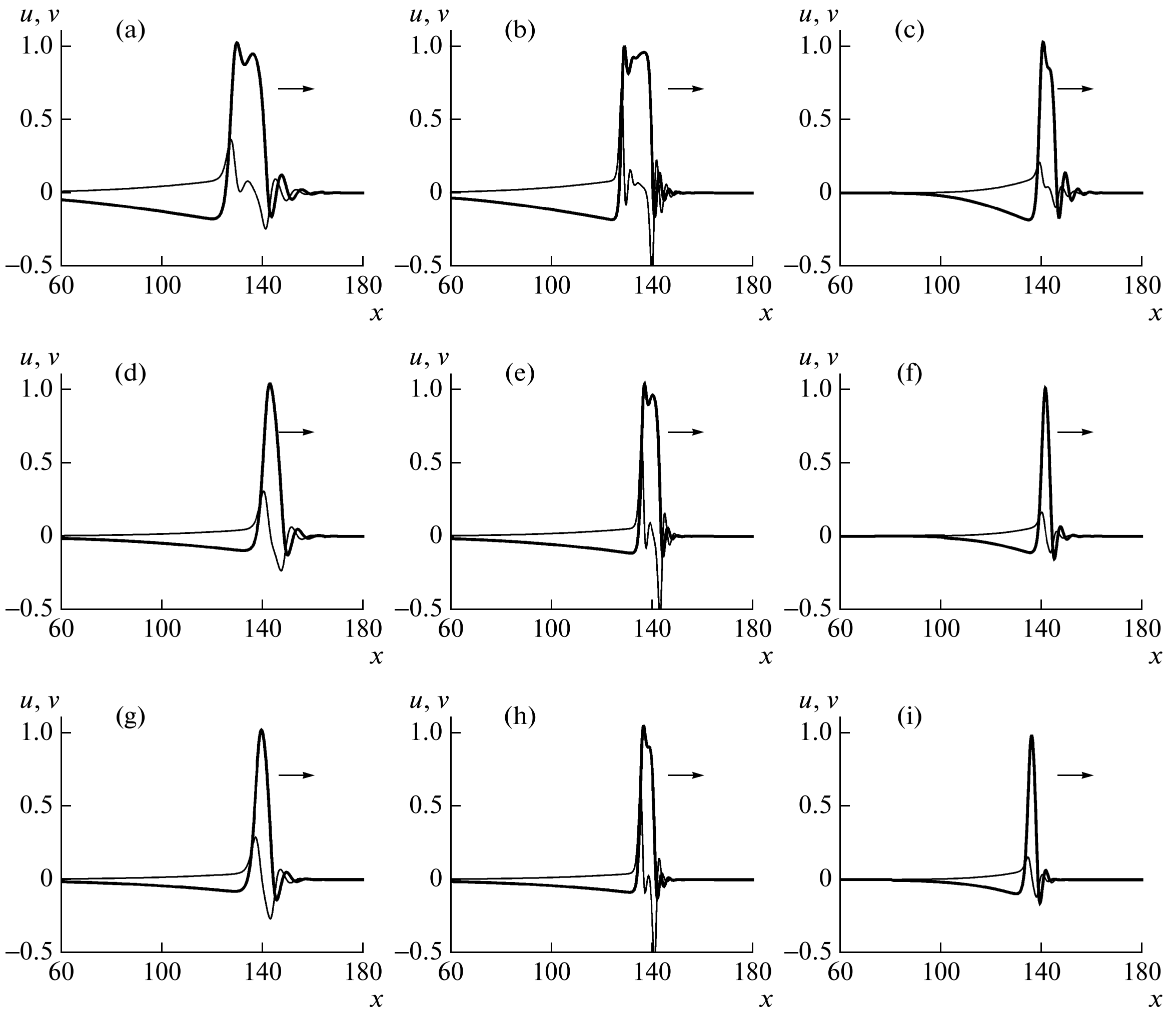

Fig. 2. Wave profiles on a ring $L = 200$ for model (3): (a) $a = 0.2$, $D_u = 1$, $D_v = 1$; (b) $a = 0.3$, $D_u = 1$, $D_v = 1$; (c) $a = 0.35$, $D_u = 1$, $D_v = 1$; (d) $a = 0.2$, $D_u = 1$, $D_v = 0.1$; (e) $a = 0.3$, $D_u = 1$, $D_v = 0.1$; (f) a = 0.35, $D_u = 1$, $D_v = 0.1$; (g) $a = 0.2$, $D_u = 0.1$, $D_v = 1$; (h) $a = 0.3$, $D_u = 0.1$, $D_v = 1$; (i) $a = 0.35$, $D_u = 0.1$, $D_v = 1$. Thick line, variable u; thin line, variable v. Arrows indicate the directions of wave propagation.

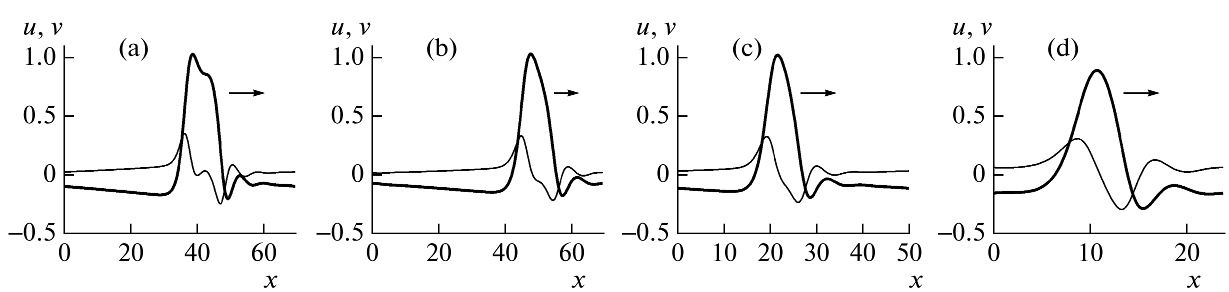

Fig. 3. Wave profiles at different ring lengths: (a) $L = 70$; (b) $L = 60$; (c) $L = 50$; (d) $L = 24$. Parameters of model (3): $a = 0.2$, $D_u = 1$, $D_v = 1$.

propagation rate and rearrangement of the wave profiles (see Figs. 1 and 3 for $L = 50$ and 60). At ring length below critical ($L = 85$) the symmetrical wave propagation becomes unstable. The dynamics of this process is presented in Fig. 6. The shortest distance between waves becomes smaller than half the ring length. At that the hind wave falls in the region of negative refractoriness at the tail of the fore wave, as a

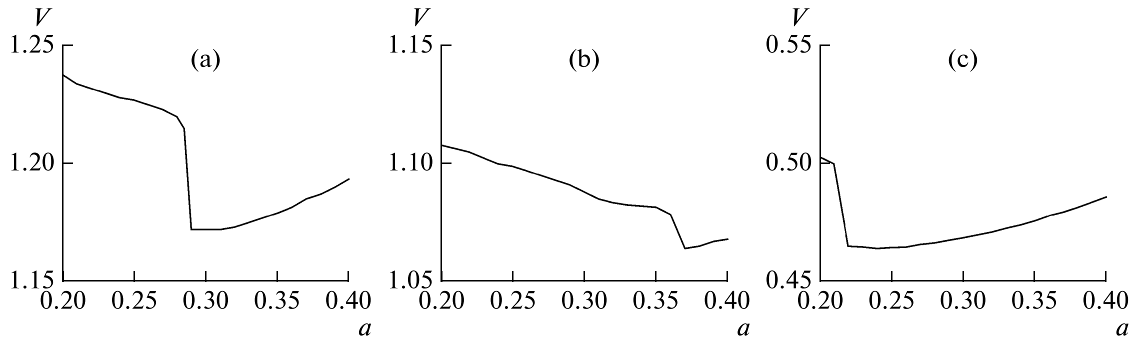

Fig. 4. Dependences of wave propagation rate on excitation threshold a: (a) $D_u = 1$, $D_v = 1$; (b) $D_u = 1$, $D_v = 0.1$; (c) $D_u = 0.1$, $D_v = 1$.

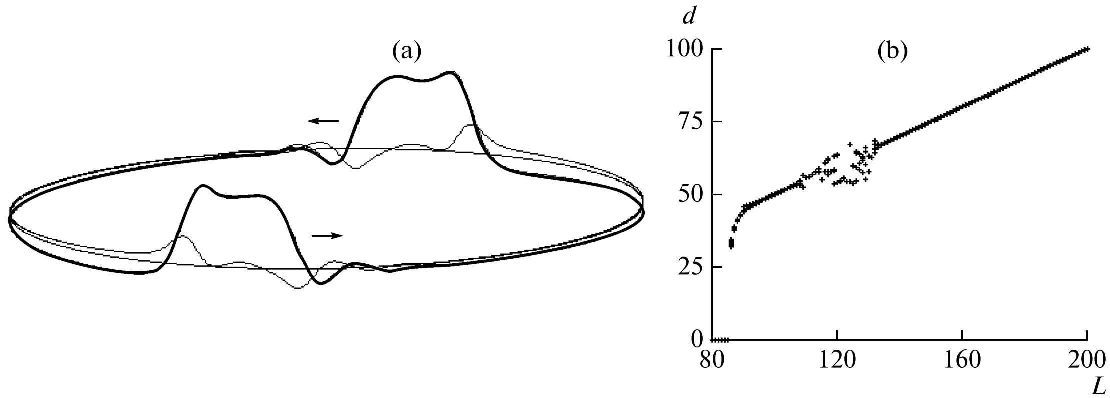

Fig. 5. Two waves ($a = 0.2$, $D_u = 1$, $D_v = 1$ model (3)) on a ring: (a) $L = 200$; (b) dependence of distance d between two waves on ring length L.

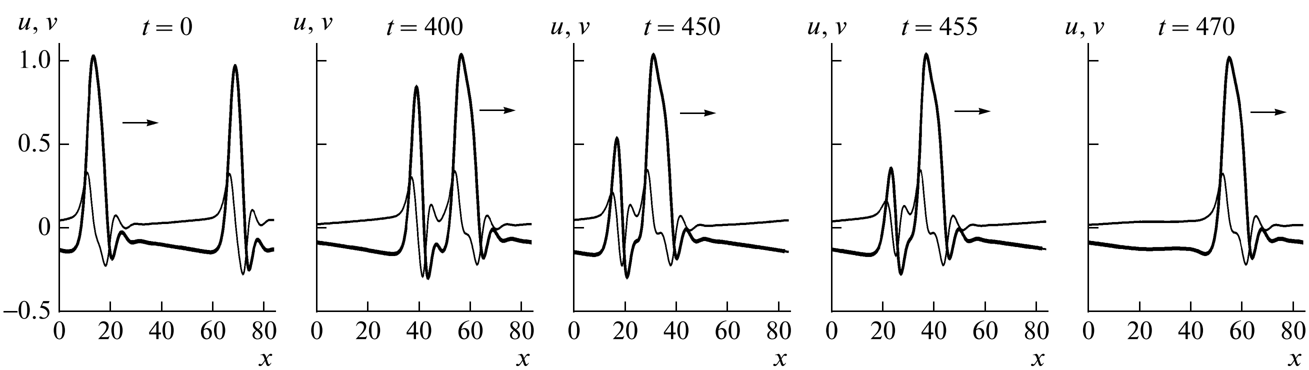

Fig. 6. Dynamics of the decrease in the distance between two waves of model (3) at ring length ($L = 85$) below critical. Model parameters indicated in Fig. 5. The time moment corresponding to the first frame is arbitrarily taken as zero moment.

result of which the rate of the hind wave rises and it overtakes the fore one. Eventually the distance between the waves rapidly decreases, and the hind wave is engulfed by the fore one, and only one wave remains on the ring.

The presence of negative refractoriness explains the new wave phenomenon recently described by us—the "running tail" [20]—a *local stable perturbation stationarily moving in the lateral direction along the trailing front of the wave* (Fig. 7).

In a two-dimensional excitable medium of size $L_x \times L_y$, in which a plane wave of a cross-diffusional system propagates, let us cut a strip $0 \le y \le L_1$, assigning to the variables in this strip the corresponding sta-

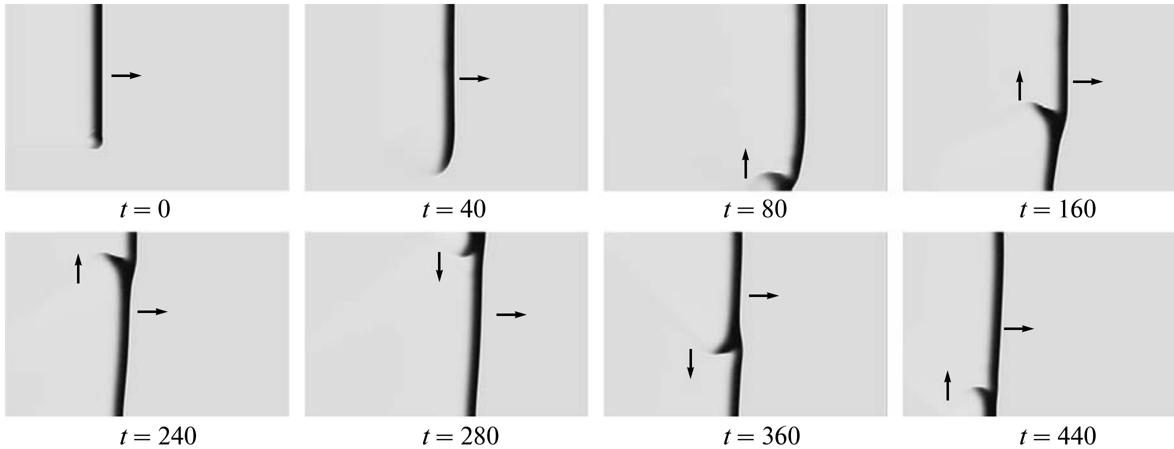

Fig. 7. Formation of a "wave outgrowth" and propagation of the "running tail" along a plane wave, reflection from impermeable boundaries (150 × 100). Medium infinite along axis x, arrows indicate directions of propagation of the plane wave and "running tail" [20].

tionary values (Fig. 7, $t = 5$ is the time moment after section). Considered is the behavior of the wave in an infinite medium along axis x, which is realized by a shift of the whole medium to the left upon the approach of the plane wave to the right boundary for a fixed distance ($L_s = 25$). As a result of in growth and interaction of the free tip of the wave with the impermeable lower boundary ($y = 0$) there forms a wave outgrowth/tail (Fig. 7, $t = 40$, 80). This wave tail propagates along the trailing front of the mother plane wave, consecutively reflecting from impermeable boundaries ($y = L_y$, $y = 0$) (Fig. 7, $t = 160$, 240, 280, 360, 440). The process of propagation of such a "running tail" and its reflection from boundaries goes on without damping [20]. The wave tail may attach to the trailing front of the mother wave analogously to how this happens in Fig. 6 ($t = 450$, 455). But unlike the one-dimensional case shown in Fig. 6, in the two-dimensional medium the "running tail" does not perish completely: apart of propagation in the wake of the mother wave and fusion with it, there is propagation in the perpendicular direction, along the trailing front of the mother wave. Analogously, negative refractoriness leading to engulfment of the hind wave by the fore wave can also explain for cross-diffusional systems the phenomenon of transition of a spiral wave into a concentric one, when the tip of the spiral attaches to the trailing front of the mother wave [8].

CONCLUSIONS

So we have shown that in excitable systems with cross-diffusion the refractoriness can be negative, i.e. there takes place an effect opposite to the one observed in standard autowave systems. By negative refractoriness one can explain a number of wave properties specific for excitable cross-diffusional systems.

The mechanism of negative refractoriness is still unclear. It appears plausible that this phenomenon is somehow connected with other peculiarities characteristic for cross-diffusional systems, such as nonlinear singularity-containing dependences of the wave propagation rate on various parameters, the connection of this rate with the wave front shape, and an oscillating leading front.

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