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Soliton-like Regimes, Echo and Concave Spiral Waves in Mathematical Models of Biological Excitable Media

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SUMMARY. On the basis of numerical simulations with partial reaction-diffusion equations describing the dynamics of electrical processes in biological excitable tissues, such as a nerve axons and cardiac Purkinje fibers, we have revealed unusual - soliton-like - regimes of interaction of propagating nonlinear excitation waves: reflection of the colliding waves instead of their annihilation. The specific nature of wave dynamics due to the reflection effects in two-dimensional excitable media is considered.

It is well known that nonlinear excitation pulses propagating in chemical and biological excitable media (such as waves in the BZ-like reaction-diffusion systems, nerve fibers, excitable tissues of the heart, etc.) decay (are annihilated) after collisions to each other or/and impermeable boundaries of the medium. This property is such universal that it has been long considered as a characteristic feature distinguishing traveling excitation pulses from solitons - nonlinear waves propagating in conservative media, that escape interactions undestroyed [1, 2)]. Recently results of numerical simulations have refute the indicated opinion. In several works [3-11)] performed with mathematical models of two-component chemical active media, unusual – *soliton-like* – regimes of excitation pulse interaction were revealed: upon collisions to each other the pulses were not annihilated, but reflected. These results raise the question on the possibility of similar effects in biological excitable media. The question is of a great interest, since namely the annihilation phenomena guarantees the stability of unidirectional fluxes of electric signals, excitation pulses, flowing in nerve fibers and in cardiac tissues, and controlling the central nervous system and contractility of the heart. Indeed, if colliding pulses were reflected, then, for example, the directed signal flow in the heart would be irreversibly disorganized with a cascade of re-reflections induced by a single sporadic oncoming pulse;

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apparently, realization of such effects in the heart will lead to cardiac arrhythmias. Our data indicate that the answer to the question mentioned above should be positive.

Below, we outline briefly our results on the soliton-like regimes and echo phenomena revealed numerically in the mathematical models of biological excitable media, described by the reaction-diffusion equations

$$\mathbf{u}_t = \mathrm{D}\Delta \mathrm{u} + \mathrm{f(u)}; \qquad (1)$$

here $\mathbf{u} = (u_1, u_2, ..., u_N)$ is the vector of variables describing the state of the excitable medium (the variable $u_1 \equiv V$ commonly have the sense of the electric potential difference on the membrane of cells forming the excitable tissue, and $u_2, ..., u_N$ are kinetic variables describing the dynamics of membrane ionic electrical currents); the subscript t denotes the first derivative on time t; $\mathrm{D} = \mathrm{diag}\,(D, \underbrace{0, ..., 0}_{N-1})$ is $N \times N$ diagonal matrix with single non-zero term D which is the intracellular electric diffusivity; $\Delta = \partial^2/\partial x_1^2 + ... + \partial^2/\partial x_n^2$ is the Laplacian operator acting on space coordinates (in particular, the values $n = 1$ and $n = 2$ correspond to a one-dimensional excitable fiber and a two-dimensional excitable medium such as the surface of the cardiac muscle walls, respectively); $\mathrm{f} = (f_1, f_2, ..., f_N)$ is the vector of nonlinear kinetic functions (the function f_1 is proportional to the total membrane ionic electrical current density I_i). Note, that in the case of biological excitable media, the expression for the matrix D, indicated above, differs from that is used for description of chemical active media with N diffusive components: in the last case, $\mathrm{D} = \mathrm{diag}(D_1, ..., D_N)$, $D_1 > 0, ..., D_N > 0$ (in refs. 3-11), the case $N = 2$ was considered).

The class of the equations (1) includes both the well-known FitzHugh-Nagumo equations 12, 13) used for qualitative modeling of biological excitable tissues and the Hodgkin-Huxley equations 14) quantitatively describing nerve fibers. Besides, it contains the McAllister-Noble-Tsien and the DiFrancesco-Noble equations 15, 16) presenting adequate quantitative models of cardiac Purkinje fibers.

We have revealed the stable soliton-like regimes in all the equations mentioned. As an example, Fig. 1 indicates both the usual annihilation regime and the soliton-like one, revealed in the FitzHugh-Nagumo model of a one-dimensional excitable fiber 17). The results on numerical simulations of the colliding excitation pulse reflection in the nerve and Purkinje fibers are presented in refs. [18-20) and [21, 22), respectively.

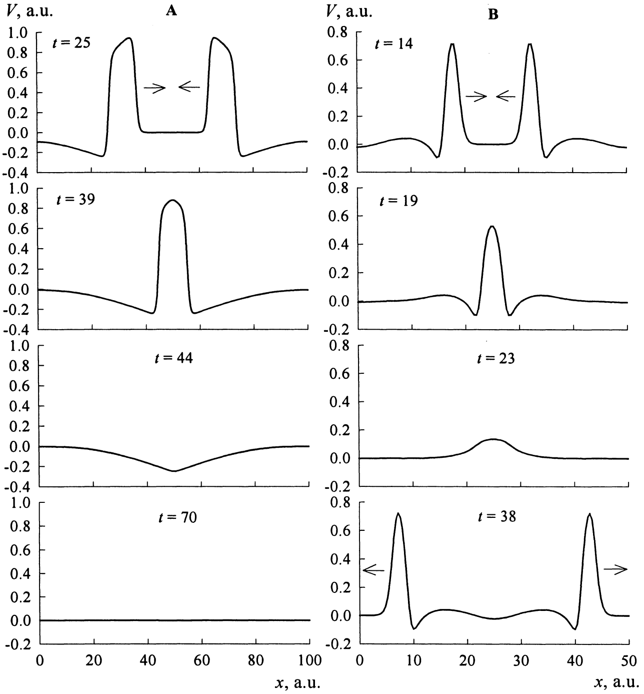

Fig 1. The regimes of interaction of colliding excitation pulses in the FitzHugh-Nagumo model of a one-dimensional excitable fiber. Spatial profiles of the membrane potential difference *V* are presented for the indicated moments of time *t*. The scales of *V* and *t* are given in arbitrary units; arrows indicate the direction of pulse propagation. Column A shows the annihilation regime: two oncoming pulses are annihilated upon collision. Column B presents the soliton-like regime: colliding pulses are reflected. The equations and the conditions of simulations are described in ref. 17).

The phenomenological mechanism of the reflection phenomena can easily be understood by analyzing the spatial profiles of excitation pulses. As Fig. 2 shows, the pulse traveling along the fiber upon the conditions of the soliton-like regime always presents a doublet consisting of a high-amplitude leader followed by a low-amplitude sub-threshold wave. Upon collisions of pulses the leaders are annihilated, but sub-threshold waves summarize becoming super-threshold and initiating two novel echo-pulses traveling in opposite directions. Our numerical simulations confirm the necessity of low-amplitude waves for reflection of colliding pulses: suppression of these waves immediately before collision of the leaders causes their usual annihilation.

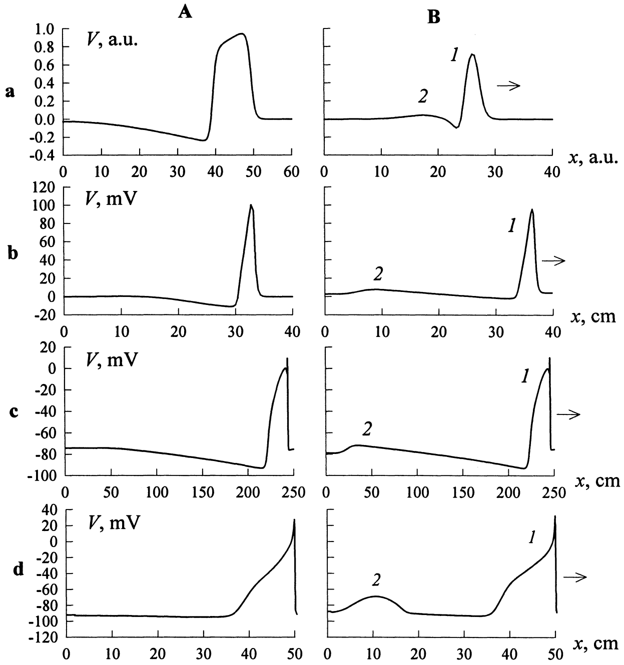

Fig. 2. Spatial profiles of traveling excitation pulses obtained by numerical integration of the FitzHugh-Nagumo equations (row a; see ref. [17]), the Hodgkin-Huxley equations (row b; see refs. [18-20]), the McAllister-Noble-Tsien equations (row c; see refs. [21, 22]), and the DiFrancesco-Noble equations (row d; own unpublished date). Columns A and B correspond to the annihilation regime and to the soliton-like one, respectively (arrows indicate the direction of pulse propagation). It is clear that in the soliton-like regime, a traveling excitation pulse presents the doublet consisting of high-amplitude leader *1* followed by low-amplitude wave *2*.

Note, that the low-amplitude waves following high-amplitude excitation pulses are often recorded in physiological experiments and are called delayed afterdepolarization; in cardiology, this phenomenon is discussed in connection with its possible role in some cardiac rhythm violation – so-called *triggered activity*[23]. However, cardiology has yet clarified neither the intimate mechanisms of triggered activity nor the contribution of delayed afterdepolarization waves to the disturbances of the cardiac rhythm. The numerical simulations performed clarify the situation to some extent: according our hypothesis[21, 22], these waves could provoke arrhythmias by the echo mechanism - due to the collisions of oncoming pulses upon the conditions of the soliton-like regime.

To clarify the possible mechanism of emerging the oncoming pulses in the heart we performed numerical simulations with the simple mathematical model of two-dimensional excitable medium described by the FitzHugh-Nagumo equations upon the conditions of the soliton-like regime. In the simulations, interaction of a plane excitation wave with the local electrically non-conductive inclusion was investigated (in the real heart, such inclusions could be formed in the pathological infarct zones emerging after the healing processes separating electrically living cells from the dead tissue). The qualitative effects revealed are illustrated in Fig. 3, 4. It turns out that the plane wave interacting with the round inclusion of a sub-critical diameter, flows around it without reflection, but generates a secondary echo-wave if the diameter of inclusion is super-critical. The effects revealed are illustrated in Figs. 3, 4. In the medium of size 60×35 the conditions of the soliton-like regime, close to those indicated in ref. [17)], are sustained, and the high-amplitude leading wave (dark stripe in Figs. 3, 4) traveling from the left side to the right one is followed by the low-amplitude sub-threshold wave (gray strip in Figs. 3, 4). In the case of a sub-critical inclusion, presented in Fig. 3, both waves colliding with the obstacle are divided without reflection into two components that flow around the circle and then come off the inclusion conjugating each other. If the diameter of the inclusion have a super-critical value, two components of the leading wave flow around the

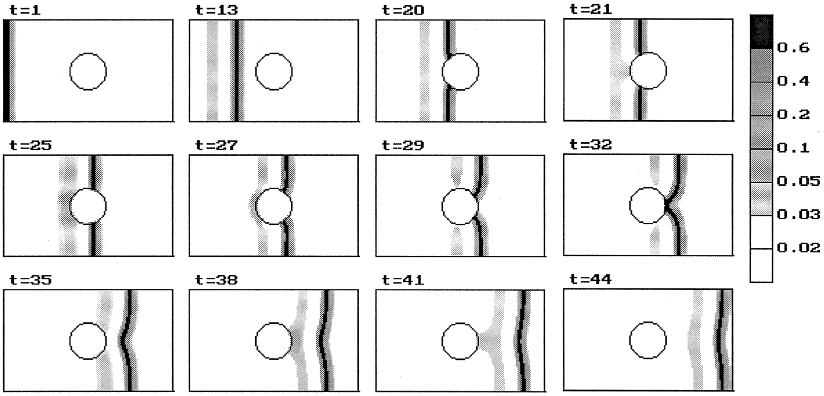

Fig. 3. Interaction of the plane excitation wave propagating in a two-dimensional excitable medium with the local non-conductive impermeable inclusion (open circle) of the sub-critical diameter $d = 12$ upon the conditions of the soliton-like regime. Here and in the following figures, the maps of spatial distribution of the membrane potential difference V in the medium, corresponding to different moments of time t (numbers above the maps) are shown. Here and throughout below, space, time and potential difference V are measured in arbitrary units; palette at the right corresponds to the values of V. The reflection is absent.

inclusion as in the previous case, but the sub-threshold wave colliding with the obstacle initiates a secondary reflected ring wave (see Fig. 4). Upon the conditions of simulations, the critical value d_c of the inclusion diameter proved to be $d_c = 12.4$.

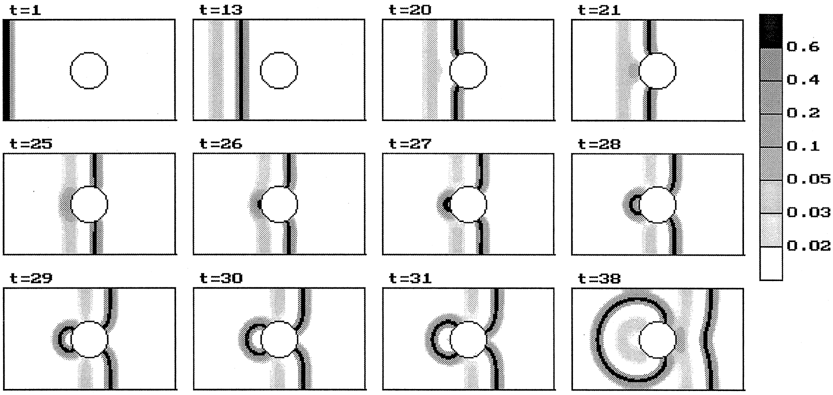

Fig. 4. The same conditions as in Fig. 3, but the diameter of inclusion has the super-critical value $d = 13$. In this case, the low-amplitude wave colliding with the impermeable inclusion initiates a reflected ring wave. Emergence and evolution of the reflected wave is seen in the maps at $t = 21$-38.

In further numerical simulations we have also revealed another unusual, essentially two-dimensional, effect: stable rotation of a *concave spiral wave*. The phenomenon mentioned was observed in the excitable medium described by the FitzHugh-Nagumo equations upon the conditions of the soliton-like regime. Note, that in our preceding work [24)] we already reported on existence of such a wave, but its rotation in those experiments was unstable due to low size (24 x 24) of the medium. In our last experiments, the size of the medium was increased up to 50×50, and the stable concave spiral wave was implemented (see Fig. 5).

The steadily rotating concave spiral wave is a first counterexample to the known theory of stability of propagating excitation waves [25)], which prohibits the stable stationary motion of concave wave fronts. The conflict could be resolved in the following way. The theory mentioned was elaborated using the analysis of local properties of the moving wave fronts only. However, own results of additional numerical experiments omitted here led us to the conclusion that existence of concave spiral wave in the middle of the medium upon conditions of the soliton-like regime is supported by specific interactions of peripheral parts of the wave with the reflecting impermeable boundaries of the medium. Hence, the dynamics of pattern observed is essentially non-local and cannot be described by approximate local theories.

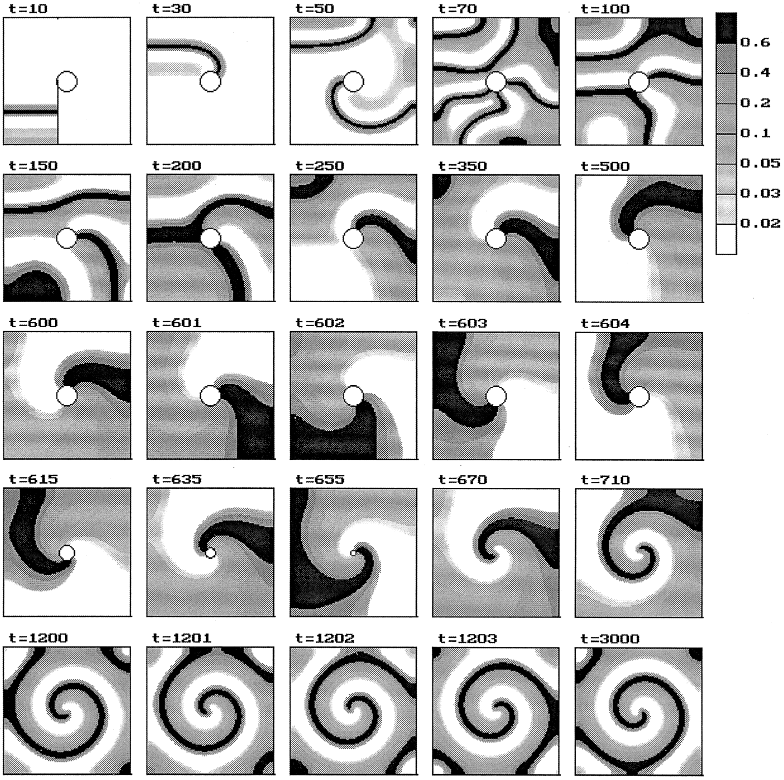

Fig. 5. Concave spiral wave rotating in the excitable medium upon the conditions of the soliton-like regime. The wave is initiated by making a break at the propagating plane wave using the impermeable wall indicated in the map at t = 10 by a thin vertical solid stretch. After the wave penetrates the medium, the wall is deleted; then the high-amplitude leading spiral wave with convex front, followed by the low-amplitude trace spiral wave emerges, and both waves are captured by the impermeable inclusion placed in the middle of the medium (see the map at t = 30; the inclusion is indicated throughout by the open circle). After the moving front of the spiral wave encounters the medium impermeable boundary, the secondary reflected echo-waves appear, and re-reflections of these waves turbulize the medium (see the maps at t = 50 - 100). Paradoxically, the irregular regime is progressively reorganized into the unusual concave spiral wave (t = 150-350) which rotates steadily clockwise around the inclusion (t = 500-604). Now, after the inclusion diameter is decreased gradually to zero (t = 615-670), the concave spiral wave is left free (t = 670, 710) and is stabilized rotating clockwise in the simply connected medium (t = 1200-1203). This rotating structure is conserved in time executing thousands of turns (compare the maps at t = 1200 and t = 3000).

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