Autowave Tunneling Through a Non-Excitable Area of Active Media

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Abstract. The mechanisms of autowaves propagation through local non-homogeneities in active media relevant to diverse class of physiological systems were studied by means of a computer simulation The model proposed by Zel'dovich and Frank-Kamenetsky and that of FitzHugh-Nagumo were used for studying autowave tunneling, which in a broad sense implies underbarrier passing It was shown that for every fixed parameter value corresponding to the degree of non-excitability of local area a critical value for non-excitable zone latitude exists An autowave overcomes the barrier and continues to propagate when the value of zone latitude is less than critical

Critical conditions for origination of a source of periodical sequence of impulses in excitable medium were found The source properties, as shown, can be modified by regulation of size of a non-excitable zone and a zone of higher excitability In particular, the conditions when spatial irregularity behaves as a source of unidirectional and/or asynchronous sequence of impulses were explored

Key words: Autowave — Tunneling — Excitable media — Bistability

Introduction

It is well known that self sustained waves (autowaves) play an important role in the regulation of a wide class of physiological systems In that context all physiological systems responsible for signal transduction for macroscopic distances deserve special attention The best example is a nerve impulse, which represents nothing but a self-sustained wave of membrane depolarization (Hodgkin and Huxley 1952) Recently it has been found that calcium autowaves play an extremely important role in intracellular processes (Lechleiter et al 1991)

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Theoretical understanding of mechanisms of autowaves propagation is based on classic works considering the problem of space propagation of a gene bearers of which prevail in the struggle for life (Kolmogorov et al 1937 Fisher 1937). Shortly thereafter Zel'dovich and Frank-Kamenetsky suggested another model which takes into account a critical level of excitation of a stationary state. Initially the model was developed for combustion wave front propagation, which obviously has self sustained autowave nature. It is clear that combustion wave can be initiated only if the excitation of a stationary state exceeds some critical level (here temperature). As it was found later the presence of excitation level is intrinsic to physiological systems on the whole. For example calcium trigger waves are initiated when the concentration of calcium inside a cell exceeds some critical value. From that view point the model of Zel'dovich and Frank-Kamenetsky is more generous and is now widely applied to the majority of trigger processes found in biophysical systems. Today both models mentioned above apply to wide class of biological and physico chemical systems generally named as active media (Marek et al 1995).

As for excitable media the urge for developing of basic mathematical models to describe autowaves regimes in various active media with recovery (excitable media) was initiated after Hodgkin and Huxley had derived their model of the propagation of nervous impulses through the membrane of squid axon. FitzHugh Nagumo model is a simplified (from mathematical standpoint) model of that of Hodgkin and Huxley and is well recognized in theoretical research of cardiac diseases such as ventricular fibrillation ischemia etc. In this paper we treat this model from the general point of view implying common nature of conducting tissue in living organisms i e excitation recovery and capability to support impulse propagation.

Modern autowave studies are primarily oriented at investigating the possibilities of external regulation of autowaves patterns in active media. This branch of biophysics is of great interest due to the perspective of regulation of biological processes on different levels of organization (Murray 1989 Lechleiter et al 1991 Meinhardt 1995). One possible way to govern autowaves behaviour is to perturbate the system during some short period of time (creation of time gradient) (Guria 1993). On the other hand the evolution of autowave process can be influenced by creating a local space non homogeneity in active medium. An important role of local non-homogeneities in physiology of the cardiac tissue was discovered by Wiener and Rosenblueth (Wiener and Rosenblueth 1946). It was found that the mechanism of reverberator generation in cardiac tissue is closely related to local spatial non homogeneities. After this classic work the behaviour of various physiological systems was treated in terms of active media and rather general mathematical models were constructed. The class of most fundamental basic models includes those of Hodgkin Huxley (1952) and FitzHugh-Nagumo (FitzHugh 1961 Nagumo et al 1962). Analyses of basic models of active media show that autowaves propagation properties in locally non homogeneous active media can significantly differ from those in homogeneous active media (Zaikin and Morozova 1979, Babloyantz and Sepulchre 1991, Kogan et al. 1992).

In the present paper the mechanisms of autowaves propagation and transformation in bistable and excitable media with locally non-excitable areas are investigated. The models proposed by Zel'dovich and Frank-Kamenetsky (1938) [for bistable media] and FitzHugh-Nagumo (FitzHugh 1961, Nagumo et al. 1962) [for excitable media] were used to perform the numerical simulations.

Several key questions were confronted before the studies were initiated. Can the qualitatively new autowave regimes result from interaction of an autowave with a local area the properties of which differ from those of the whole medium? How critical is the presence of an affected area (i.e. an area which is not capable of supporting autowave propagation) for autowave existence in the medium considered? What are the possible repercussions of autowave tunneling on the further development of the autowave process?

The exploration was conducted for two types of active media: one-component bistable medium and two-component recoverable active medium (excitable medium). Tunneling effect and the phenomenon of unidirectional conduction of locally non-homogeneous active medium were found in both types of the active media. A source of periodical sequence of impulses at the boundary of zone of higher excitability was shown to originate only in the excitable medium with recovery. Critical conditions which are necessary for the appearance of asynchronous and unidirectional autowave sources were explored.

I. Bistable Media

The widely known model originally proposed by Zel'dovich and Frank-Kamenetsky for wave front propagation was considered

$$\frac{\partial U}{\partial t} = D\frac{\partial^2 U}{\partial x^2} - \delta U\,(U-\alpha)(U-1), \quad 0<\alpha<1 \tag{1}$$

It is well known that bistable media, described by equation (1), support the propagation of a trigger wave which switches the medium from one stable state to another stable state. When the following condition

$$J_0 = -\int_0^1 \delta U(U-\alpha)(U-1)\,\mathrm{d}U > 0 \tag{2}$$

which is equivalent to condition $\alpha < 0.5$ is valid, propagation of an autowave provides for the switch of the system from the initial steady state $U_{\mathrm{st}} = 0$ to state $U_{\mathrm{st}} = 1$. In this case, state $U_{\mathrm{st}} = 1$ is termed "attractive" state of the trigger system (1). The velocity of a trigger wave c_0 is given by the expression

$$c_0 = \frac{1}{2}\sqrt{\delta D}(1-2\alpha) = 6\sqrt{\frac{D}{\delta}}J_0 \tag{3}$$

Let the trigger wave propagate from left to right with a constant velocity c_0. Condition (2) is supposed to be satisfied, state $U_{st} = 1$ is an attractive state for the medium, thus the trigger wave switches the system from state $U_{st} = 0$ to $U_{st} = 1$ Let the properties of some local zone be different from those of the whole medium in such a way that condition (2) for this zone transforms to condition $J_0 < 0$ $(0.5 < \alpha < 1)$ The latter implies that the attractive state for this zone is state $U_{st} = 0$, hence an autowave should switch the system from state $U_{st} = 1$ to $U_{st} = 0$ In other words, within this local area self-sustained wave propagation is only possible in the inverse direction.

For numerical calculations equation (1) was rescaled to the non-dimensional form Equation (1) was solved at the region $x \in [0, L]$ with Neuman boundary condition. Initial value problem has the form:

$$
\begin{aligned}
&\frac{\partial U}{\partial t} = \frac{\partial^2 U}{\partial x^2} - U(U-\alpha)(U-1) \\
&\alpha = \begin{cases} \alpha_2, & x \in [x_1, x_2] \\ \alpha_1, & x \notin [x_1, x_2] \end{cases} \qquad x_1, x_2 \in [0, L] \\
&U(x,0) = \begin{cases} 1, & x \in [0, a] \\ 0, & x \in [a, L] \end{cases} \qquad a \in [0, x_1] \\
&\left.\frac{\partial U}{\partial x}\right|_{x=0} = \left.\frac{\partial U}{\partial x}\right|_{x=L} = 0
\end{aligned} \tag{4}
$$

In all the experiments it was assumed that $\alpha_1 = 0.1$, and $\alpha_2 \in [0.5, 1]$.

Solutions to system (4) at different stages are presented in Fig. 1. The dependence of function U on x is shown at different time values; the change of α

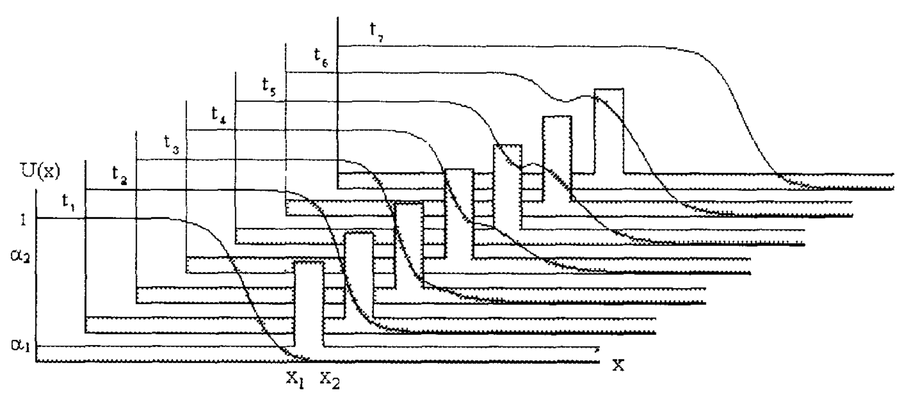

Figure 1. Autowave tunneling through a non-excitable area of bistable medium.

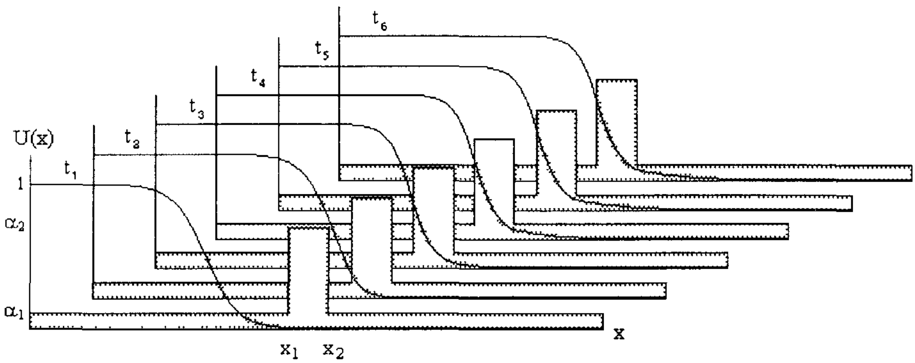

Figure 2. Autowave "locking-up" by an obstacle of supercritical size.

parameter value on interval $[x_1, x_2]$ is shown as a barrier whose height is determined by value of α_2; $\alpha = \alpha_1$ in the whole medium outside the interval $[x_1, x_2]$, the non-excitable zone latitude is $d = x_2 - x_1$. As depicted in Fig. 1, a switch to the repulsive state $U_{st} = 1$ within area $[x_1, x_2]$ takes place, though the attractive state for this zone is $U_{st} = 0$ In a non-homogeneous zone an autowave front is stretching as though it is tempted to go further, and as soon as the excitation in the area behind the barrier exceeds some critical level, the posterior autowave propagation is provided by the autowave support mechanism intrinsic to the model. The process of trigger wave formation in the postbarrier region is initiated before state $U_{st} = 1$ is achieved within the barrier. A newly formed trigger wave "draws out" the points from non-excitable zone, and eventually a stationary regime of propagation is established

Fig 2 shows a case of "locking-up" the autowave by an obstacle with the same value of α_2 parameter (the same barrier height) but for an augmented interval d which exceeds the critical value for the zone latitude. As is evident from Fig 2 excitation in the postbarrier region does not exceed the excitation critical level, and the condition for a new trigger wave formation is thus not satisfied.

Hence, the existence of a critical value of non-excitable zone latitude was revealed If the value of non-excitable zone is less than critical an autowave traverses the barrier and continues to propagate. In this case a delay in time occurs versus the time interval of an autowave propagation in a homogeneous medium. A hypothetical observer situated on the right side from the barrier would see the normally propagating autowave that reaches him with a certain delay The dependence of the time delay on the barrier latitude for the different values of parameter α_2 is shown in Fig 3

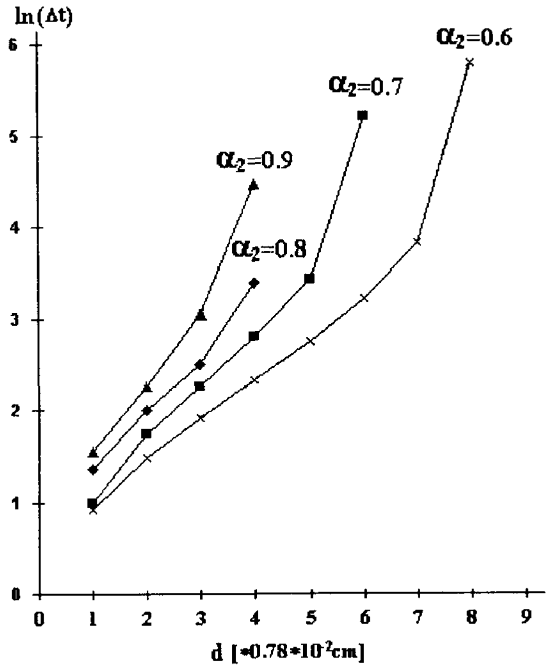

Figure 3. Dependence of time delay of an autowave propagation on the barrier latitude for different values of parameter α_2

The correlation between α_2 and $d_{\mathrm{cr}} = x_2 - x_1$ is shown in Fig. 4. The curve $\alpha_2(d_{\mathrm{cr}})$ divides the parametrical plane into tunneling area (under the curve) and "locking-up" area (above the curve).

Autowave tunneling through a periodical sequence of non-excitable zones

A periodical sequence of non-excitable zones of latitude d with a distance between them h was considered (Fig. 5). It was found that for a fixed barrier height α_2 and a barrier latitude $d < d_{\mathrm{cr}}$, a critical value h_{cr} exists. The tunnel effect occurs when the value of distance h between the obstacles is more than critical. The dependence $h_{\mathrm{cr}}(d)$ for two different values of parameter α_2 is shown in Fig. 7. Each curve divides the parametrical space (h, d) into tunneling area (under the curve) and "locking-up" area (above the curve).

The condition of autowave tunneling through a periodical sequence of non-excitable zones is fully determined by distance h between the obstacles when values of α_2 and d belong to the tunneling area (Fig. 4). The case of an autowave "locking-up" when value of h is more than critical is shown in Fig. 6.

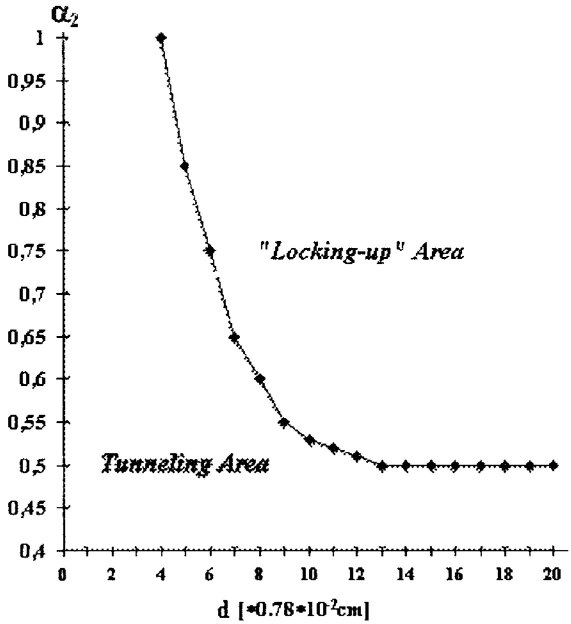

Figure 4. Correlation between critical height and latitude of non excitable zone

Influence on autowave propagation of the barrier form

The interaction of an autowave with a wedge-shaped obstacle with one vertical edge was analyzed. It was found that an obstacle with a right vertical edge will be permeable for autowaves moving from left to right (Fig. 8) while the same obstacle will stop autowaves moving in the opposite direction (Fig. 9). Therefore, the medium with a local non-homogeneity of similar type may serve as a unidirectional autowave filter.

Discussion

In the system considered underbarrier passing, i.e. tunneling takes place though autowave tunneling mechanisms have their own nature and differ from the well known mechanisms of tunneling of a microparticle in quantum mechanics (Leontovich and Mandel'shtam 1928). The fact that an autowave may overcome an obstacle is related to a non-stationary autowave evolution in the local area of inverse attraction. Formation of a new trigger wave in the postbarrier region occurs only when critical conditions for autowave nucleation are satisfied (Belintsev et al. 1978).

Autowave tunneling through a periodical sequence of zones with reduced excitability also resembles to some degree a quantum mechanics problem of interaction of a particle with a potential 'raker'. Tunneling in a chosen direction as in

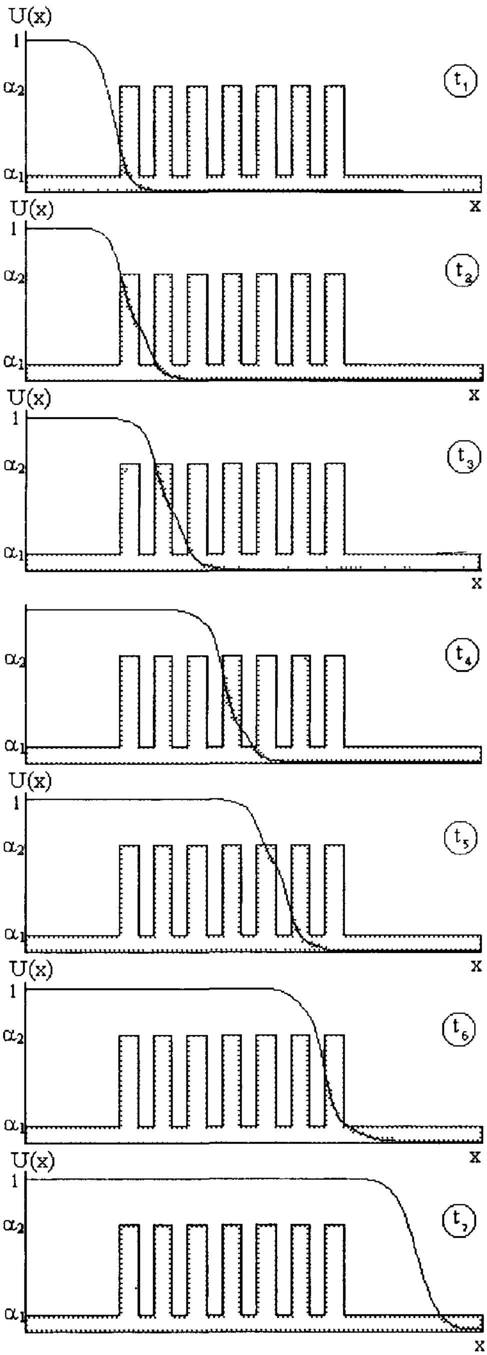

Figure 5. Autowave tunneling through a periodical sequence of barriers

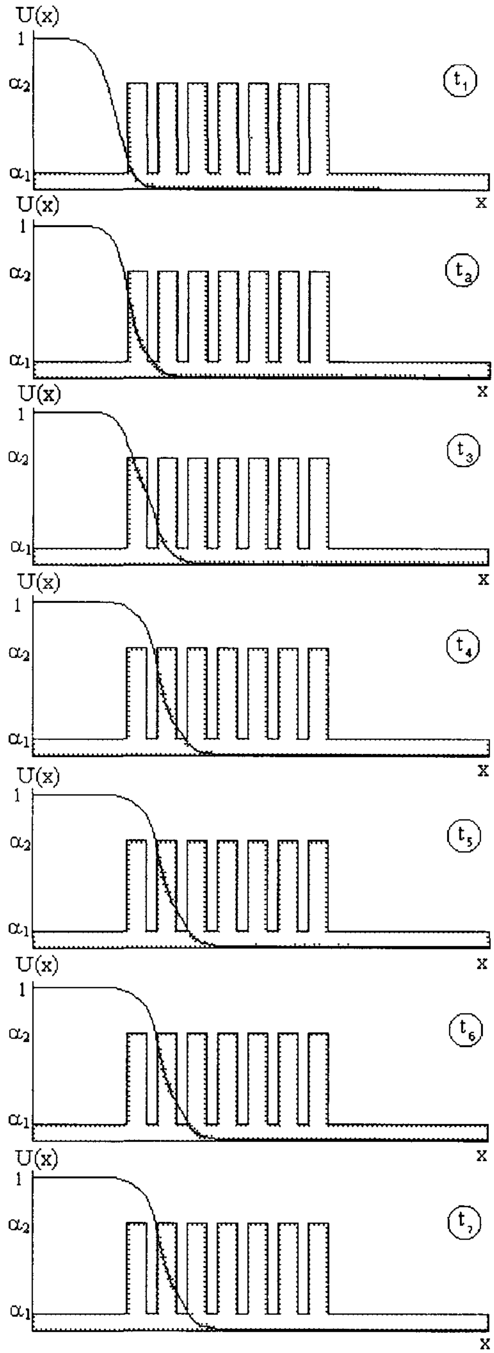

Figure 6. Autowave locking up by a periodical sequence of barriers

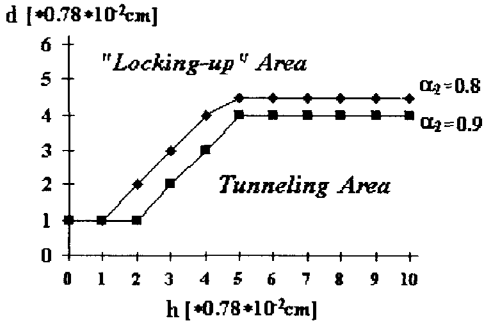

Figure 7. Correlation between barrier latitude d and critical distance h for different values of barrier height α_2

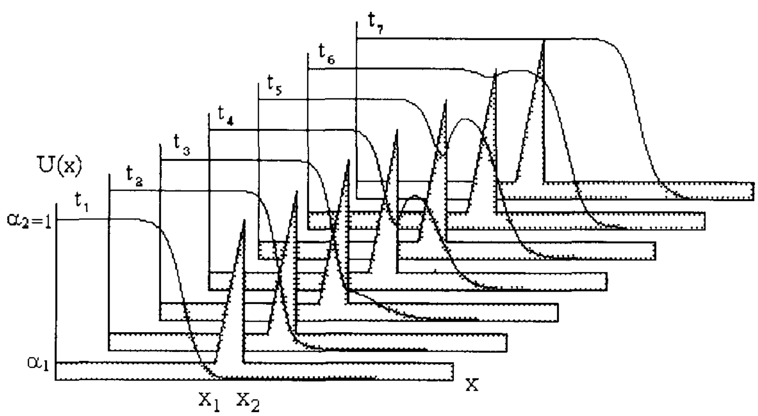

Figure 8. The obstacle is permeable for an autowave moving from left to right

the case of autowave tunneling through an asymmetrical barrier does not have any analogy in microphysics

With respect to biological applications the results obtained seem to be rather important for the interpretation of self-sustained wave propagation in locally inhomogeneous active biological systems Trigger type autowaves passing through a local barrier represent direct model of nerve impulse propagation through the spike The problem of the local inhomogeneities influence on the physiology of spatially extended systems such as human heart and eye facet has been widely discussed (Frank and Shnol' 1967) In this sense the results obtained give the possibility to consider rather general physiological phenomena (in particular, activation wave front propagation and spatio-temporal rearrangements in macroscopic tissues) as a

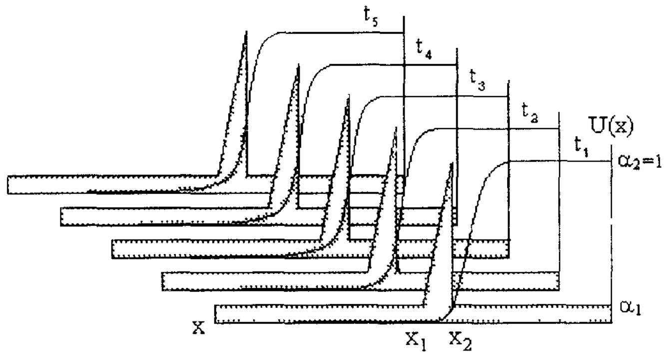

Figure 9. The same obstacle as shown in Fig 8 is not permeable for an autowave moving in the opposite direction

special type of critical phenomena Amplitude, width and form of barrier manifest themselves as the most important critical characteristics (Muller and Plesser 1992)

II. Excitable Medium

FitzHugh-Nagumo model was considered

$$\frac{\partial U}{\partial t} = D\frac{\partial^2 U}{\partial x^2} - U(U-\alpha)(U-1) - W, \qquad 0 < \alpha < 1$$

$$\frac{\partial W}{\partial t} = \beta U - \gamma W$$

where variable U serves as an activator, and W is an inhibitor In a vast region of values of parameters β and γ, system (5) has a single stationary solution which is stable for small perturbations Parameter region where system (5) has autowave solutions has been intensively investigated (McKean 1970 Rauch and Smoller 1978, Miura 1982) The best known autowave solutions to FitzHugh-Nagumo system are single impulses and periodical sequences to impulses (Kuznetsov 1990)

There is a parametrical region where system (5) has two stationary states In this region a supercritical perturbation of one state leads to the initiation of a trigger wave which switches medium from perturbed state to the other stationary state This can occur when the speed of inhibitor production (determined by the value of coefficient β) is too low to recover the first variable to initial state In this case, the system behaviour does not differ from that of system (1) described in the first part of the paper All of the results presented for the Zel'dovich and Frank-Kamenetsky model seem to be applicable to the FitzHugh-Nagumo system at relevant values of parameters corresponding to the bistable mode of system (5)

In this part of the paper, a single impulse propagation through local non homogeneities in excitable medium is investigated by means of numerical analyses of FitzHugh Nagumo model

Model properties with different parameter values

Region ς of parameters β and γ (Fig 10) for fixed value $\alpha = 0$ 1 was found by numerical computation of system (5) For every pair (β γ) belonging to region ς a stable solution in a form of a single impulse exists Region ς is confined by two curves $\gamma^1(\beta)$ $\gamma^2(\beta)$ and by the segment of abscissa $[0\ \beta^*]$ The upper boundary $\gamma^1(\beta)$ is approximated by linear function $\gamma = C\beta$ where $C = 5$ 4 Besides, $\gamma^1(\beta)$ divides the parametrical space (β γ) into two areas which are characterized by different numbers of steady states Under the curve there is an area where system (5) has a single steady state $U_{st} = 0$ $W_{st} = 0$ The area above the curve $\gamma^1(\beta)$ region Ω in Fig 10 corresponds to the bistable mode of the system considered ($U_{st} = 0$, $W_{st} = 0$ and $U_{st} = U^* \neq 0$ $W_{st} = W^* \neq 0$)

When (β γ) $\in \varsigma$ the system is characterized by a single steady state (0,0) and solution to the system is presented by a single impulse A set of parameters (β γ) $\in \vartheta$ corresponds to the case when there are no non-trivial stable stationary solutions to system (5) Every perturbation of steady state (0,0) relaxes in time, so when (β γ) $\in \vartheta$ the medium described by system (5) is actually non-excitable

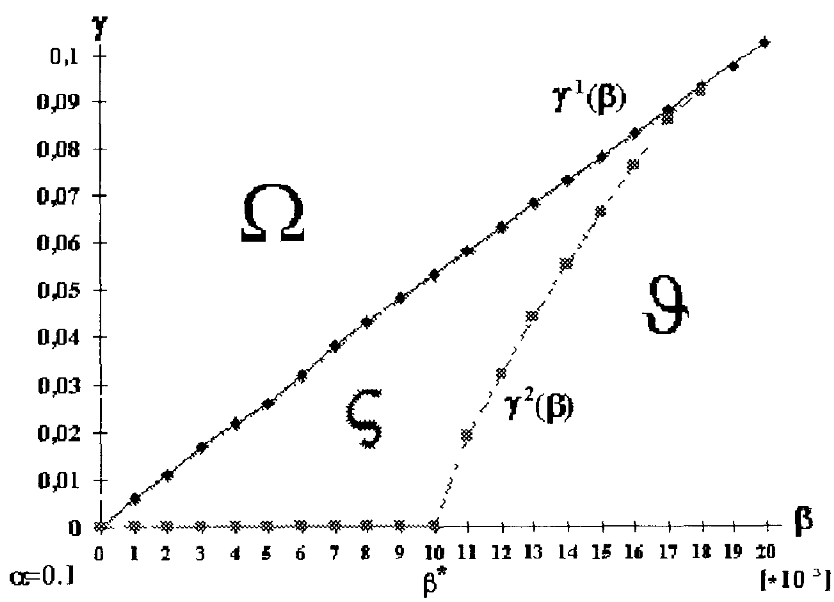

Figure 10. Parametrical space (β γ) for FitzHugh-Nagumo model $\alpha = 0$ 1

Values of parameters β and γ outside the non homogeneity were assumed to belong to area ζ in all numerical experiments described in this part of the paper

Impulse tunneling through a non-excitable area of excitable medium

Let us consider a single impulse instigated by perturbation of initial state ($U_{st} = 0$ $W_{st} = 0$) moving from left to right in the uniform part of excitable medium with a constant velocity c, Let the medium contain a non homogeneity so to speak that there is some local area of size d where excitability is lower than the excitability of the whole medium Let the value of parameter β which determines the speed of inhibitor production be equal to $\beta_1 \in \zeta$ (see Fig 10) in the medium outside the local area Let the value of parameter β in the non excitable zone attain the value $\beta_2 \in \vartheta$ ($\beta_2 > \beta_1$) System (5) has only trivial stable stationary solution $U_{st} = 0$ $W_{st} = 0$ when $(\beta, \gamma) \in \vartheta$ and hence any excitation in this zone should relax to the initial stable state Therefore, it is evident that impulse propagation in rather large non excitable zone, where $(\beta\ \gamma) \in \vartheta$ is impossible

Interaction of a single impulse with a non-excitable zone was studied It was found that for every fixed value of parameter β_2 a critical value of non excitable zone latitude exists An impulse can overcome an obstacle and continue to propagate when the zone latitude is less than the critical value (Fig 11)

Numerical simulations were conducted for system (6)

$$\begin{aligned}
&\frac{\partial U}{\partial t} = D\frac{\partial^2 U}{\partial x^2} - U(U-\alpha)(U-1) - W \qquad 0 < \alpha < 1 \\
&\frac{\partial W}{\partial t} = \beta U - \gamma W \\
&\beta = \begin{cases} \beta_2 & x \in [x_1\ x_2] \\ \beta_1 & x \notin [x_1\ x_2] \end{cases} \qquad x_1\ x_2 \in [0, L] \\
&U(x,0) = \begin{cases} 1, & x \in [0,a] \\ 0, & x \in [a, L] \end{cases} \qquad a \in [0, x_1] \\
&\left.\frac{\partial U}{\partial x}\right|_{x=0} = \left.\frac{\partial U}{\partial x}\right|_{x=L} = 0
\end{aligned} \tag{6}$$

where $\beta_1 = 0\ 005$ Analysis of problem (6) revealed that for any determined value of γ there are two critical values of parameter β_2 β_2^{min} and β_2^{max} When $\beta_2 < \beta_2^{min}$ and $(\gamma, \beta_2) \in \zeta$ non homogeneity is always permeable for a single autowave The higher the value of parameter β_2, the longer the time of tunneling through an obstacle When β_2 is equal or greater than β_2^{max} the obstacle is not permeable for even sufficiently small zone latitude values since the inhibitor production preponderates the activator growing Therefore segment (β_2^{min} β_2^{max}) defines a region of parameter β_2 variation in the computer simulation of system (6)

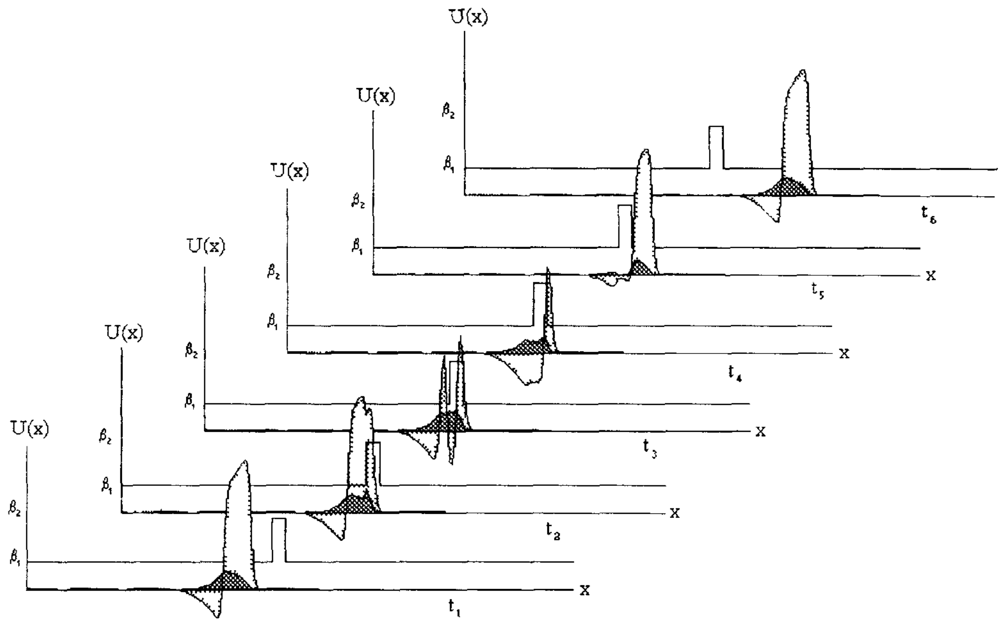

Figure 11. Impulse tunneling through a non-excitable area Concentration profile of activator is indicated in gray, that of inhibitor is in dark gray

When the zone latitude exceeds a critical value, the impulse does not pass through the barrier (Fig 12)

Impulse tunneling through a periodical sequence of non-excitable zones with equal latitudes of d and distances h between them was found to be similar to a trigger wave tunneling through the same "raker". Under a certain combination of zone latitude values and distances between them an impulse can propagate through a sequence of non-excitable zones with some quasistationary effective velocity $c_{\text{eff}} < c_o$

Impulse interaction with a "wedge-shaped" obstacle is also quite similar to that of a trigger wave with the same asymmetrical barrier (see part I). It was found that an obstacle with a left vertical edge is permeable for impulses moving from left to right (Fig 13) while the same obstacle does not permit impulses to traverse when they move in the opposite direction (Fig. 14). It follows from the above that a medium with this kind of non-homogeneity can serve as a unidirectional impulse conductor – an autowave "diode". Potentially, such a medium can be used in different biomedical and technical systems.

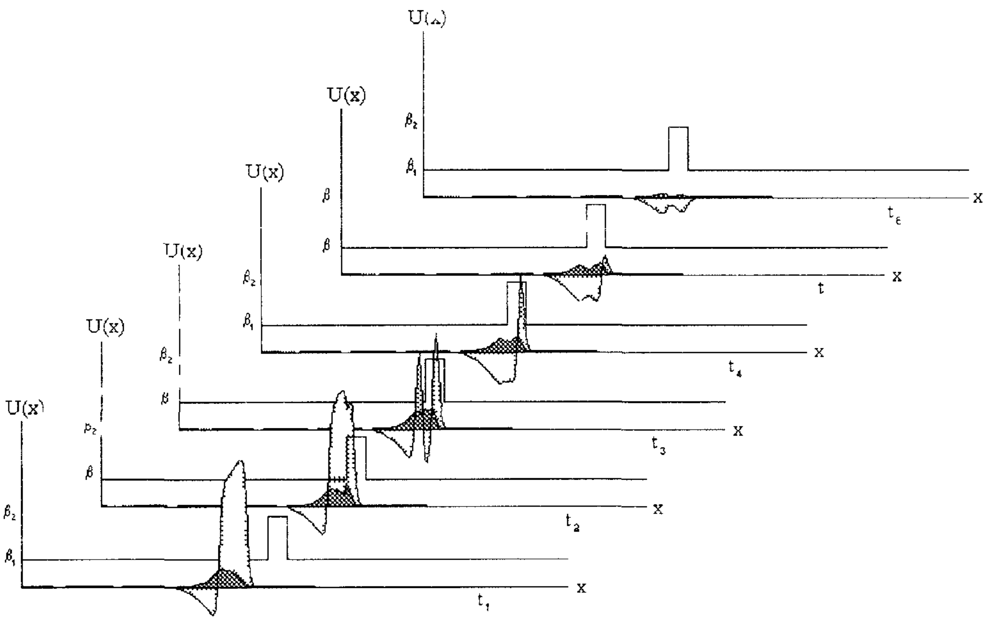

Figure 12 Impulse locking up by a non excitable zone when the zone latitude exceeds critical value

Appearance in medium with a higher excitability zone of a source of periodical impulses

Let some zone $[x_1\ x_2]$ of excitable medium have excitability higher than the outside medium Let the value of parameter β_2 in this zone belong to area Ω (Fig 10) The latter means that the medium considered is bistable i e a definite initial perturbation of a primary stable state (0 0) could switch the system to the other stable state ($U_{st} = U^* \neq 0$ $W_{st} = W^* \neq 0$) The above mentioned zone with increased excitability may become a permanent source of periodical sequence of impulses which propagate in both directions with an equal frequency (Fig 15)

The combination of zone of higher excitability ($(\gamma\ \beta_2) \in \Omega$) with areas of lower excitability ($(\gamma\ \beta_2) \in \vartheta$ or $(\gamma\ \beta_2) \in \zeta$ but $\beta_2 > \beta_1$) makes it possible to regulate the frequency of periodical sequence of impulses For example if a lower excitability zone of subcritical size preceeds a zone of higher excitability (Fig 16) the originated source of periodical sequence of impulses generates impulses with different frequencies

It was found that if the latitude of the zone of lower excitability coincides with

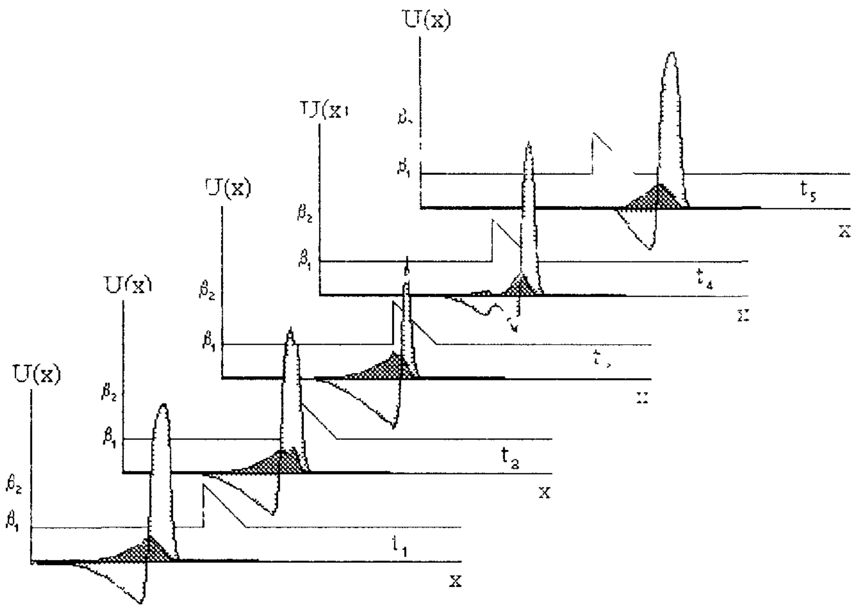

Figure 13. The obstacle is permeable for an impulse moving from left to right

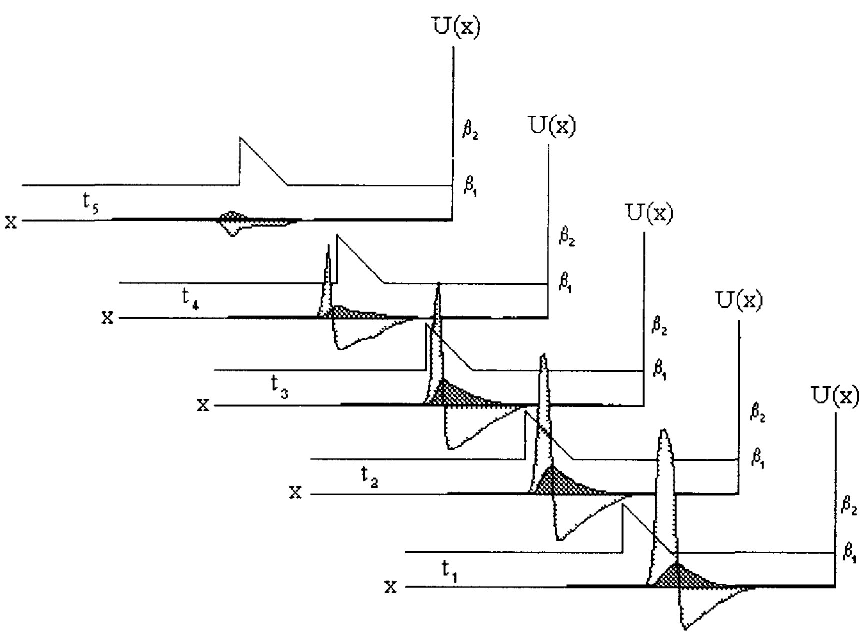

Figure 14. The same obstacle as shown in Fig. 13 is not permeable for an impulse moving in the opposite direction

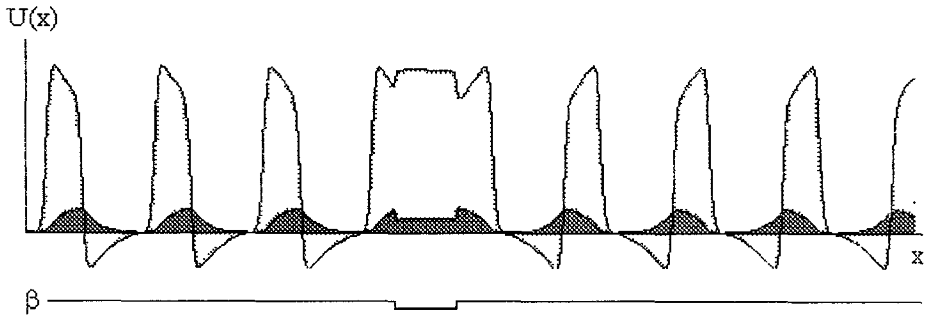

Figure 15. Origination of a source of periodical sequence of impulses in excitable medium with a local zone of higher excitability

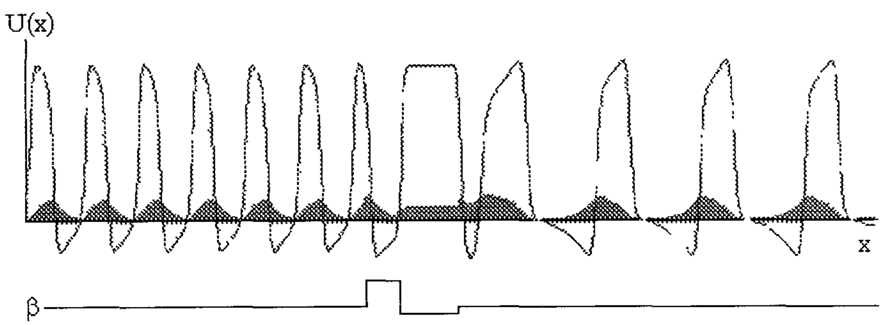

Figure 16. Origination of an asynchronous source of periodical sequence of impulses in excitable medium with local zones of lower and higher excitability

the critical one, the source initiated after the first traversing of an impulse generates a sequence of impulses moving only to the right (Fig. 17*a*) If a zone of lower excitability follows a zone of higher excitability and the barrier is not permeable for an impulse, a source of leftwards moving impulses originates (Fig. 17*b*).

Discussion

At high values of parameter β the conditions for a single impulse formation in the zone of lower excitability are not satisfied. In this case underbarrier passing of an impulse through a non-excitable (prohibited for autowave propagation) area is a special type of tunneling. Any perturbation of a medium inside a non-excitable zone should relax in time to the initial steady state (0,0). Nevertheless it was found that impulse tunneling occurs at some definite values of parameters. Relaxation of excitation in a non-excitable area leads to the appearance in the post-barrier region of a concentration hill of activator significantly diminished in amplitude

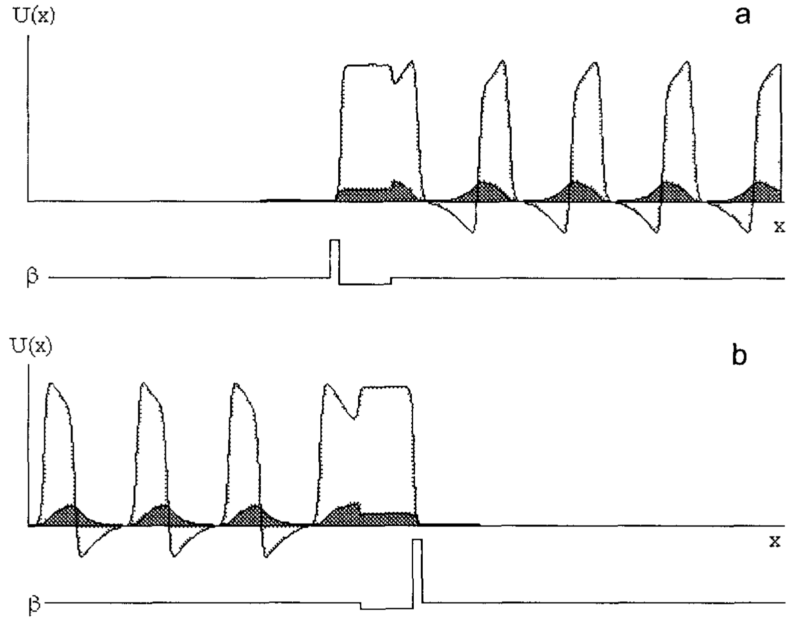

Figure 17*a*, *b*. Origination of an asymmetrical source of periodical sequence of impulses in excitable medium with local zones of lower and higher excitability.

in comparison with its initial value. This postbarrier stimulus predetermines the possibility for a new autowave initiation. The studies conducted revealed that in the region behind the barrier excitation of the medium can be subcritical and hence insufficient for the evolution of an excitation nucleus to form a solitary self-sustained impulse. Therefore the problem of underbarrier tunneling appears to be closely connected with that of autowave nucleation in excitable media.

It was demonstrated that local non-homogeneities in excitable media considered could qualitatively change the patterns of autowave propagation. In particular, they may act as secondary sources of asynchronous or unidirectional waves.

FitzHugh-Nagumo model describes the propagation of an impulse through a cardiac fiber. The first variable U denotes membrane potential, W is a recovery variable. Parameter β can be denoted as the ability of the membrane potential to recover and is actually an inhibitor coefficient of the membrane depolarization process. In a normal functioning cardiac fiber excitation of a cell (membrane depolarization) leads to the formation of an excitation impulse that propagates through the homogeneous cardiac tissue with a constant velocity. Local non-homogeneities for example areas with different recovering properties or areas of bistable mode (once depolarized membrane potential cannot be recovered), could significantly influence the existence of an impulse. Thus, in a cardiac fiber one "bad" cluster of supercritical size can cause impulse damping if it is a zone of lower excitability or become a source of periodic sequence of impulses (for example pacemaker) if it is a non-homogeneity of a trigger type.

The possibility of non-homogeneities acting as sources of secondary waves was first mentioned in the famous work of Wiener and Rosenblueth (1946). The special model of active medium with a local non-homogeneity of a trigger type was later analyzed by Zaikin (1979). Recently, the existence of asynchronous sources has been detected experimentaly in quasi-one-dimensional chemical systems (Perraud 1993, Agladze et al. 1995). Our analysis demonstrate that underbarrier passing in active media with recovery could play an important role in a variety of spatially extended systems far from equilibrium. We hope that the results obtained will find further applications in biophysics and general physiology.

Conclusion

The phenomenon of autowaves underbarrier passing through non-homogeneous areas as well as their transformation into secondary sources present significant interest from both the fundamental standpoint and with respect to their versatile applications in general physiology and biophysics. It should be mentioned that autowaves underbarrier passing mechanisms significantly differ from those of microparticle tunneling effect well known in quantum mechanics (Leontovich and Mandel'shtam 1928). The penetration of a definite microparticle into the postbarrier region is of a probability nature (principally unpredictable) and is defined by the amplitude of the wave function, whereas autowave passing through a non-excitable zone is completely predictable and fully determined. There still is a similarity between the two phenomena: as microparticles can penetrate through areas strongly forbidden by classical mechanics, an autowave may pass through a region of a totally non-excitable medium where there are no facilities for self-sustained wave propagation.

The results obtained seem to be important for various applications. For instance, bistable models originally designed for analysis of combustion wave fronts propagation are nowadays widely used in biophysics. Conductive tissues of living organism such as nervous, cardiac and muscle tissues are examples of excitable media. Malfunction of the propagation of an impulse in cardiac tissue can cause different cardiac diseases such as ischemia and arrhythmia (Winfree 1987). The latter, in particular, can be explained by the presence of local non-excitable areas in the cardiac fibre. The appearance of a source of periodical sequences of impulses can be critical for the heart function as a whole.

Finally, it is worth to mention that regulation of autowave patterns via insertion of local non excitable zones in active media could certainly find an application in the novel class of chemical and biomedical technologies (Luss et al. 1991, 1996; Noskov 1995). The same ideology of insertion of non excitable elements is widely used today to regulate nuclear processes in nuclear power stations around the world. With respect to biomedical application, the method of local perturbation of a spatially distributed excitable biological system (known as acupuncture) has a long standing tradition in the Oriental medicine. The research undertaken will hopefully cast some light on biophysical mechanisms of local spatial non homogeneities influence on macroscopic dynamics of excitable physiological systems.

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