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Suppression of spatio-temporal chaos in simple models of re-entrant fibrillations

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Abstract.
On the basis of the FitzHugh-Nagumo–type model we investigate the possibility of suppression of the spiral wave turbulence by weak pacemaker excitations. We consider different ways of media stabilization and study the dependence of the suppression efficiency on the excitation shape and the media parameters. Also, we analyze the frequency of target waves in the unperturbed media as a function of the external force frequency. Applications of the obtained results to cardiac rhythm pathologies are considered.

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1. Introduction

One of the remarkable examples of excitable media is the cardiac tissue. Because the stability of its behavior is vitally important, investigations of processes occurring in the cardiac muscle attract a considerable scientific interest. Owing to extraordinary complexity of the system, many alternative models have been tested. One of them treats the cardiac tissue as an active system. The other models rely upon the property of conductivity (see [1] and. Refs. cited therein).

Cardiovascular diseases (CVDs) are responsible for 4 million deaths each year. A major group of CVDs involve disturbances of the normal cardiac rhythm (arrhythmias). Some of arrhythmias can develop via the destruction of excitation wave fronts. In this case the fibrillation phenomenon appears. The fibrillation is the prevalent mode of death among patients with CVD.

To suppress the heart fibrillation, the application of high-energy electrical stimulation through the patient's chest is commonly used. However, high-energy shock can cause the necrosis of myocardium or give rise to functional damage manifested as disturbances in atrioventricular conduction. So, it is necessary to find another method of stimulation of the fibrillative heart.

Following the contemporary conjecture, the cardiac fibrillation phenomenon is represented by a quite large number of spiral or scroll waves [2–4] (i.e. by spatio–tempotal chaos or spiral–wave turbulence). The last investigations in the active medium theory offer new possibilities: sometimes the amplitude of the external pulse can be *essentially* decreased [5]. Moreover, the turbulent regime in excited media may be stabilized by a sufficiently weak parametric excitation [6, 7] or external forcing applied to some media area [8–12]. In this way, it is possible not only to suppress spatio–temporal chaos and stabilize the media dynamics, but also in some cases to reestablish the initial cardiac rhythm, because after stabilization the media goes to the spatially homogeneous steady state.

In the present article we show that it is possible to suppress spatio–temporal chaos in active media that appears via coexistence of a large number of spiral waves. We used the two variable reaction-diffusion model of the FitzHugh-Nagumo–type:

$$\begin{aligned} \frac{\partial u}{\partial t} &= \triangle u - f(u) - \nu, \\ \frac{\partial \nu}{\partial t} &= e(u, \nu)(ku - \nu). \end{aligned} \tag{1}$$

Lately, generalizations of this model are used. According these generalizations, f and e are taken as piece–wise linear functions [13]. Then, to correspond to the real systems (say, a cardiac tissue) usually the following admissions are applied: $f(u) = C_1 u$ if $u < u_1$, $f(u) = -C_2 u + a$ if $u_1 \leq u \leq u_2$, $f(u) = C_3(u - 1)$ if $u \geq 1$, and $e(u, \nu) = e_1$ if $u < u_2$, $e(u, \nu) = e_2$ if $u > u_2$, $e(u, \nu) = e_3$ if $u < u_1$ and $\nu < \nu_1$. Here u and ν are activator and inhibitor variables, respectively. The parameter values are $C_1 = 20$;

$C_2 = 3$; $C_3 = 15$; $u_1 = 0.0026$; $u_2 = 0.837$; $\nu_1 = 1.8$; $k = 3$; $e_2 = 1$. Parameters $e_1 \in [1/75, 1/30]$ and $e_3 \in [0.1, 2.0]$ remain to be free.

One of the advantages of this model is the presence of two independent relaxation parameters. One of them, e_3, takes into account a relative relaxation period for small values u and ν. The other one, e_1, gives an absolute relaxation period for large values of ν and intermediate values of u that corresponds to the leading and trailing fronts of the wave.

Numerical simulations were carried out in a two-dimensional (2D) grid of 175×175 and 350×350 elements with periodic (torus) boundary conditions. Torus topology of the area allowed us to exclude the influence of some boundary effects such as wave attenuation.

At the analysis of the spatially extended systems, the main problem is to obtain correctly the chaoticity characteristics. As it was noted above, for the excitable medium the spatio–temporal chaos appears via a set of spiral waves. As is known, each of them has a phase singularity (tip, or filament) [14]. In the present paper, to analyze the turbulent and regular dynamics we use the consideration of the number N of phase singularities. This allows us to attain more effective control over the system dynamics. The main advantage of this method consists of the availability of the well developed algorithms. Our investigations showed that the number of phase singularities may serve as a rather simple and the visual estimation of the efficiency of the turbulence suppression.

2. Suppression of the turbulent dynamics

Let us consider the problem of the detection of the perturbation frequencies, which provide the effective stabilization. Because the search of the suppressing frequencies at random is ineffective, we used the method, which allowed us to find the frequency intervals ensured the high efficiency of the chaos suppression. The idea of our method consists of the known properties of the active media (see [8]). Following that, for the observation of the chaos suppression phenomenon it is necessary that the wave frequency in the medium would be close to the maximal possible frequency for the given system parameters.

To find such frequencies we generated pacemakers in the *two-dimensional medium volume* and determined the frequency ω_{cw} of the obtained waves as a function of the pacemaker frequency ω_{ef} (Fig.1, Fig.2). One can expect that in the frequency intervals near the maxima of this dependence the spatio-temporal chaos can be suppressed by the point external perturbation.

During our investigations we found that the initial distribution taken in the form of the plane half-wave is transformed into spatio-temporal chaos after about 2000 time units. Such a final system state (turbulence) has been considered as the initial one. Then, we added the external *point* periodic force with the frequency ω_{ef} and the amplitude A to the first equation of the system (1). This force was applied to a small

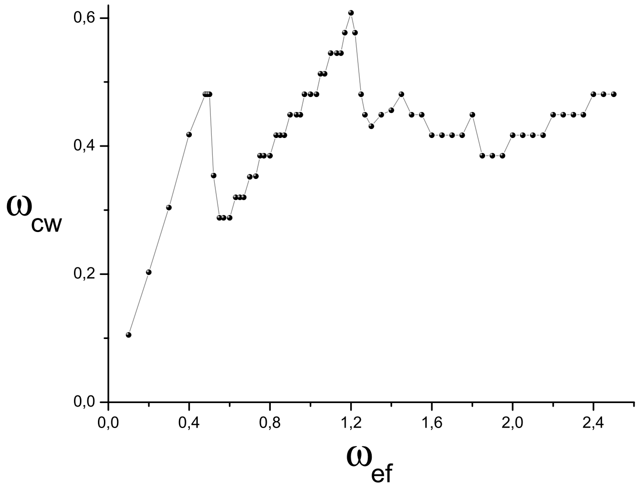

Figure 1. The frequency ω_{cw} of target waves in the medium as a function of the external force frequency ω_{ef}, $e_1 = 1/30$, $e_3 = 1.0$

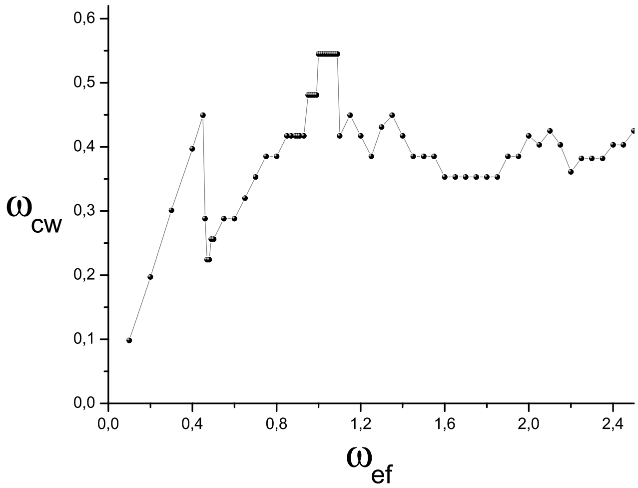

Figure 2. The frequency ω_{cw} of target waves as a function of the external force frequency ω_{ef}. $e_1 = 1/30$, $e_3 = 0.5$

area (2×2 nodes) located in the grid center. This means that to stabilize the spatio–temporal chaotic dynamics we generated a single external pacemaker in the medium.

We used periodic impulses with period T of two different types: $I_{-+}(t) = A\cdot(2\theta(t-T\tau)-1)$ and $I_{+}(t) = A\cdot\theta(t-T\tau)$ where θ is the Heaviside step function and τ is varied between 0.1 and 0.9 (Fig.3).

The result of the point excitation on the turbulent active media is shown in Fig.4.

To be more precise, we consider the number N of phase singularities. These

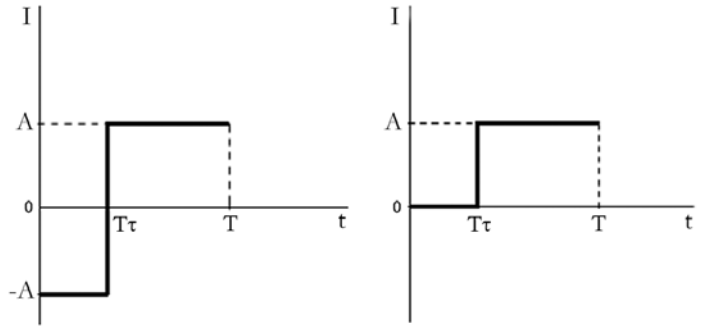

Figure 3. The shapes of the excitation impulses: $I_{-+}(t)$ (left) and $I_{+}(t)$ (right)

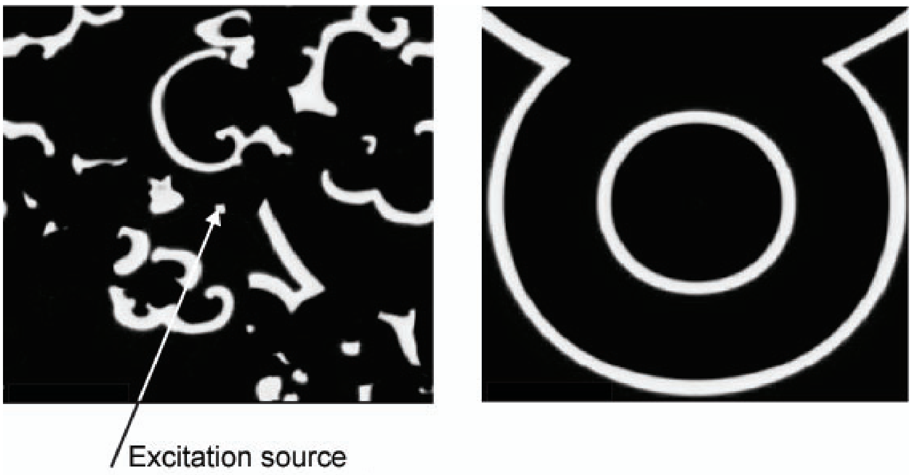

Figure 4. The result of the excitation of the medium point 2×2.

singularities can be found by a so-called Bray algorithm [14]. It relies upon the fact that the kernel of the spiral wave (and also any point of the wave front gap) is a singular point, and the topological charge is not zero if the contour of integration includes such a singularity. The number N of phase singularities as a function of time in the system with the external point perturbation ($e_1 = 1/30$, $e_3 = 1.0$, $A = 6$) is shown in Figs.5a,b. In these Figs., the starting points of the curves corresponds to the established turbulent regime of the medium.

One can see that for $\omega_{ef} = 1.2$ that exactly corresponds to the maximum of the function shown in Fig.1, the suppression efficiency is very high, and during a quite short period of time the external pacemaker completely eliminates all the spiral waves. However, at $\omega_{ef} = 0.48$ that corresponds to the second maximum it is impossible to suppress the turbulence during he observation time.

In Fig.2 ω_{cw} as a function of ω_{ef} but for the other medium parameters $e_1 = 1/30$, $e_3 = 0.5$, $\omega_{ef} = 1.2$, $A = 6$ are shown. As before, the obtained curve has maxima: at $\omega_{ef} = 0.45$ and $1.0 \leq \omega_{ef} < 1.1$. For the frequency $\omega_{ef} = 1.05$ the external pacemaker can annihilate the turbulence (see Fig.6).

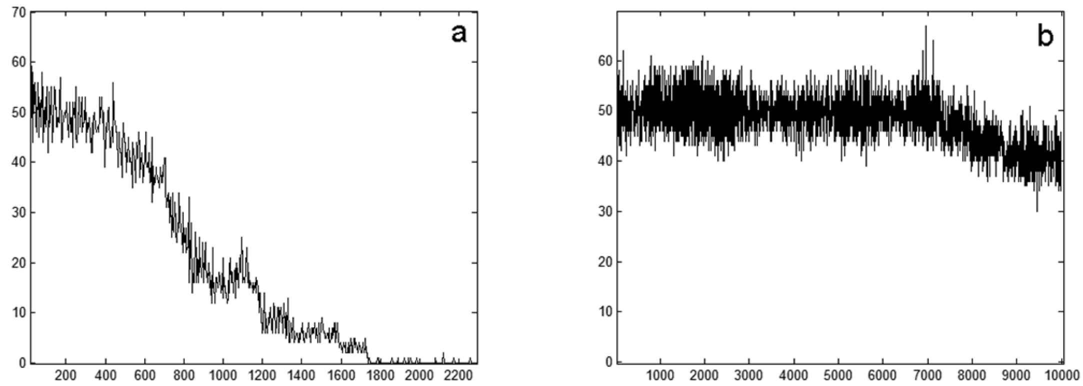

Figure 5. The number N of phase singularities as a function of time for the system with the following parameters: $e_1 = 1/30$, $e_3 = 1.0$, $\omega_{ef} = 1.2$ (a) and $\omega_{ef} = 0.48$ (b).

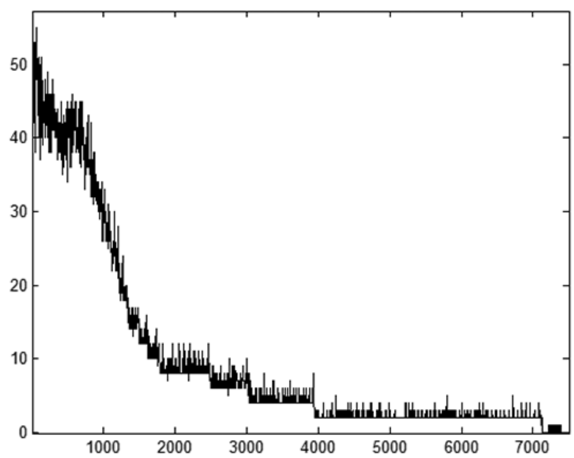

Figure 6. Dynamics of phase singularities. $e_1 = 1/30$, $e_3 = 0.5$, $\omega_{ef} = 1.05$.

Thus, considering Fig.5a and Fig.6 one can see that in the first case the suppression effectiveness is significantly higher than for the latter one ($\omega_{ef} = 1.05$), although both curves look qualitatively the same.

As to the impulse shape, it is necessary to say the following. We found that the suppression phenomenon exists only in the sufficiently narrow interval $\tau \in (0.7, 0.75)$. In other words, the impulses should be short enough. Simultaneously, for the excitation form I_+ the suppression time is in approximately twice as much than for I_{-+}.

Finally, in the case of two pacemakers (2×2 nodes) acting in antiphase at distances from 5 to 200 nodes, the suppression efficiency is increasing with the distance.

3. Conclusion

The properties of spiral waves in the excitable media can be exploited for the development of novel approaches to the defibrillation of the cardiac muscle. The elimination of spiral wave re-entrant arrhythmias is a very important clinical problem. That is the reason why, in the recent years a number of studies have been concentrated on the theoretical understanding of how the application of an electric current defibrillates the heart. One of our aims in present investigation is to develop new methods of internal stimulation which reduce the defibrillation threshold.

On the basis of the FitzHugh-Nagumo medium we showed that it is quite possible to realize stabilization of the spatio-temporal chaotic dynamics by external point excitations. This approach permits to eliminate spiral waves and restore the regular behavior in the system. The main problem here is to find the excitation frequencies. But this problem is easily solved by the preliminary localization (Sect.2).

Thus, the obtained results make possible to predict the dynamics of active systems, depending on their parameter values. Moreover, using the proposed approach one can develop a quite general theory of the chaos suppression for the distributed media by point excitations. In the nearest future we plan to get analogous results in application to more realistic models [15].

Finally, some words about applications to cardiology. The theory of non-linear dynamical systems could be the key for more advance in understanding fibrillation and its therapy. The standard method to stop chaos in cardiac muscle — defibrillation — does not distinguish normal waves and reentries, anatomical and functional reentries. Estimation have shown that energy required by the new approaches may be less then the standard defibrillation energy by two orders of magnitude. This gives a good expectation for success, even if significant amount of estimated energy gain will be eaten by technical limitations. A new word in the solution of the problem of sudden death due to the fibrillation phenomena is so-called implanted cardio-defibrillators (ICD). They are placed in the body and realize the monitoring of cardiac rhythm. Since very important factor in the construction of the modern ICD is decreasing their mass and sizes, the main task is to find such an impulse form that can allow to defibrillate miocardium. Some specific impulse forms of high voltage can realize low-energy defibrillation but, at the same time can induce the miocardium depression. Therewith, the energy decrease is not a unique task. In addition, it is necessary to reduce a painful feeling in the heart. This problem can be resolved employing the difference in the nervous tissue and miocardium excitability.

Our conjecture consists of the following: To find domains of turbulence in the space of model parameters corresponding to the spiral wave solution (i.e. fully developed spatially-temporal chaos). Being in one of this domains, one has to perturb weakly a small part of the medium in a predefined way. Under such additional conditions this procedure may result in squeezing of spiral waves out from the body of the cardiac tissue to its boundaries where these waves will die out completely because they can exist only as waves in a 3D media. In the short-time term this means, actually, defibrillation. Prolonged influence of stimulation of this kind prevents returns of fibrillation and provides conditions for regeneration of the damaged cardiac tissue in the long-time term.

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