New Methods of Suppression of the Spiral Wave Activity in Cardiac Tissue

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Abstract— *We present an approach to the problem of the suppression of the fibrillating activity in the heart by weak local external stimulations. Such a low-energy strategy has a great advantage in comparison with other widespread methods because it, in particular, does not require the knowledge of the frequency of re-entrant waves. To overcome the dependence of the suppression success on the position of the local stimulation we propose to use moving external sources.*

I. Introduction

Any abnormality in the cardiac rhythm is said to be arrhythmia. It can develop by several reasons, the dominant of which consists of the change in the intrinsic properties of the excitable tissue. In this case the destruction of the excitation wave fronts is possible such that the fibrillation phenomenon may appear. It is well known that the fibrillation is the prevalent mode of death among patients with cardiovascular diseases. Thus, an immediate medical care is required. In this case the application of high–energy electrical stimulation to the patient's heart (through his chest or in extreme cases, to the open heart) is commonly used to suppress the fibrillation and restore the normal heartbeat. However, high–energy shock can cause the necrosis of myocardium or give rise to functional damage manifested as disturbances in atrioventricular conduction.

Electrical pulses for the termination of fibrillations are also used in implantable cardioverter defibrillators (ICDs) initiating low-power electrical pacing pulses automatically when they detect dangerous activity. However, the ICD action is very painful and occurs even in the case of complex arrhythmias that are not associated with fibrillation. Therefore, a very important factor in the design of modern ICDs is reduction of the stimulation amplitude in order to avoid painful shocks and damage to the heart itself and surrounding tissues. Thus, the main purpose is to develop a universal technology of fibrillation suppression by low energy impulses with amplitudes of the same order as the impulses from sinoatrial node.

The dominating hypothesis in the current theory of excitable systems is that fatal cardiac arrhythmias, fibrillations, occur due to the creation of numerous autowave sources, so-called re-entry, which are spiral waves or vortex structures (i.e., spatiotemporal chaos, see, e.g., [1, 2] and references therein), in cardiac tissue. Therefore, to resolve the described problem we may relay upon the modern theory of chaos. Theoretical studies suggest that low-energy defibrillation protocols are also possible at exploiting the dynamical properties of re-entrant waves under electrical forcing, known as feedback-driven resonant drift [3]. However, in practice the major problem is the change of the resonant frequency with the position of a rotating wave, especially close to unexcitable boundaries.

The qualitatively different approach to the low–amplitude suppression of spiral wave turbulence lies in parametric perturbations (see [4] and refs cited therein). Although both parametric suppressing (non-feedback) and controlling (feedback) lead to the stabilization of complex dynamics, they are not realizable for defibrillation. The matter is that, such a way implies variations of parametric values in every medium element.

The recent investigations offer new opportunities for defibrillation: The amplitude of the external stimulation can be essentially decreased such that the turbulent regime in excitable systems is suppressed by a weak non-feedback periodic forcing applied globally [5, 6] or locally [7–11] (see also Refs. therein). By these manners, it is possible to stabilize the turbulent dynamics and reestablish the initial cardiac rhythm, because such a strategy leads to the relaxation of the medium to the rest state.

II. The model

As it is supposed, fibrillation of the cardiac tissue corresponds to spatio–temporal chaos in excitable medium. Our scheme consists of introduction of weak local excitations into this medium (Fig.1). All the simulations were performed in two dimensions for a modified FitzHugh-Nagumo model.

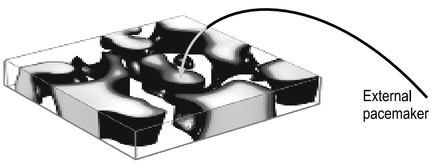

Fig. 1. A weak local stimulation of the turbulent medium.

The FitzHugh-Nagumo–type system can be written as follows:

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

To get correlation with the heart tissue, usually the following admissions are applied, and so-called Panfilov-Hogeweg modification is used:

$$f(u) = \begin{cases} C_1 u, & u < u_1, \\ -C_2 u + a, & u \in [u_1, u_2), \\ C_3(u-1), & u \geq u_2, \end{cases}$$
$$g(u,v) = \begin{cases} G_1, & u < u_2, \\ G_2, & u \geq u_2, \\ G_3, & u < u_1, \nu < \nu_1. \end{cases} \tag{2}$$

Here u and ν are activator and inhibitor variables, respectively. The parameter values are $C_1 = 20$; $C_2 = 3$; $C_3 = 15$; $u_1 = 0.0026$; $u_2 = 0.837$; $\nu_1 = 1.8$; $k = 3$; $G_2 = 1$. Parameters $G_1 \in [1/75, 1/30]$ and $G_3 \in [0.1, 2.0]$ remain to be free.

One of the advantages of this model is the presence of two independent relaxation parameters. One of them, G_3, takes into account a relative relaxation period for small values u and ν. The other one, G_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. In spite of its simplicity, this model describes real experimental data sufficiently well even for the myocardium tissues of mammals [12].

Numerical simulations were carried out in two-dimensional (2D) grids of 175×175 and 350×350 elements with periodic (torus) and zeroth boundary conditions.

III. Spatio–temporal chaos

Our analysis of the turbulent and regular dynamics is based on the consideration of the number N of phase singularities (PS). These singularities can be found by a so-called Bray algorithm [13]. This method is based on the fact that the tip of the spiral wave (as well as any point of discontinuity of the wave front) is a singularity for the phase field $\varphi(x,y,t) = \arctan 2\,(U((x,y,t) - U^*), V((x,y,t) - V^*))$. Then the quantity

$$N = \frac{1}{\pi} \oint \nabla\varphi dl$$

is the topological charge. It is not equal to zero only if such a singularity is located within the integration contour. In this case, N is an integer, whose sign determines the chirality of the spiral wave.

During the numerical analysis we have found that at certain parameter values of the model (1), (2) an initial spiral wave breaks into complex turbulent pattern. The number N of phase singularities as a function of time is shown in Fig.2. The final regime appearing at $t > 1000$ was used for the further analysis as the initial state of the system when we study the possibility of the suppression of turbulence dynamics.

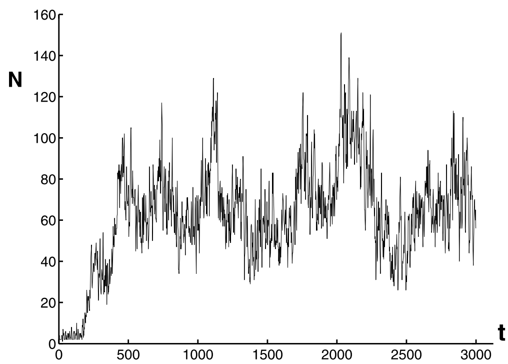

Fig. 2. The number of PS as a function of time.

IV. Novel approach to the defibrillation problem

In our previous works we have described that suppression of spiral wave chaos in the system (1), (2) is possible [4, 8]. We found that the suppression effectiveness strongly depends on the stimulation frequencies (which should be the maximal possible) and the amplitude, it was found that if these values are chosen by an appropriate way, the turbulent wave activity can be quickly and easily eliminated. This is a very important qualitative result, which gives us the hope to resolve the defibrillation problem in the future.

However, unfortunately, there are some very essential limitations. For example, let us imagine a situation, when an external pacemaker is surrounded by several vortices such that the space around it is always occupied by wave fronts of surrounding spirals.

In this case the external source may be suppressed for a sufficiently long time.

To solve this problem we propose two independent directions of further investigations: to use several pacemakers and moving pacemakers. The first way consists of the increasing of the number of external pacemakers in the medium. However, after careful numerical experiments we have come to the conclusion that stationary pacemakers (even a comparably large number) can not guarantee the chaos suppression in the investigated systems.

Therefore, we concentrated on the case of one/several moving pacemakers. The law of their motion used is $\xi = \xi_0 \sin\omega(\Omega_r, t)$, where ξ is parallel to either vertical or horizontal axis. The pacemaker described by this formula is moving along the axis ξ periodically with the frequency Ω_r. However, in this case it is necessary to remember that we should use not the maximum possible frequencies for the given medium parameters, but the ones close to them. The matter is that, if we choose the maximal possible frequency, then the medium will be saturated with the wave fronts. In other words, the space between the excitation regions will be always occupied by the elements in the refractory state such that elements in the rest state can not exist here. In this case the motion of external pacemakers leads to the creation of spiral waves. As a result, the recovery of the turbulent dynamics takes place.

Let us consider the system (1), (2) with two pacemakers located on a vertical line with the distance of 176 points between them. Let these pacemakers move along a horizonal line with the amplitude $\xi_0 = 10$ and frequency $\Omega_r = 2.5 \cdot 10^{-4}$. Then, for the medium with $G_1 = 0.01$, $G_3 = 0.5$, we get the suppression phenomenon during 3300 ms. If, however, we take the same condition for horizontally located pacemakers which are vertically moving, the suppression of turbulent dynamics is not observed. It can be achieved by increasing the frequency up to, for example, $\Omega_r = 3.0 \cdot 10^{-4}$. However, in this case the chaotic dynamics is extruded after 9500 ms.

The dependence on the position of pacemakers and the frequency of their motion remains to be carefully explored [14]. Preliminary investigations show that this dependency is essentially nonlinear.

Finally, we present the effectiveness of the suppression phenomenon as a function of τ (Fig.3). Here by efficiency we mean the fraction $10\,000/T_{supp}$. Here T_{supp} is the suppression time and τ defines the external impulse shape: $I = A \cdot (2\theta(t - T\tau) - 1)$, where θ is the Heaviside step function.

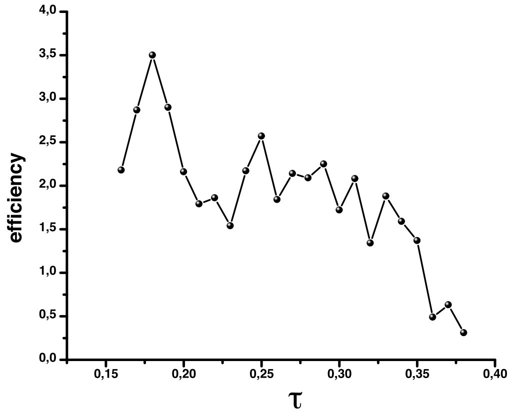

Fig. 3. Dependence of the suppression efficiency on τ.

V. Discussion

First of all, it should be emphasized that the investigated model is a rough approximation of the cardiac tissue properties. That is the reason why, the spiral-wave turbulence may not adequately describe the real fibrillation phenomenon. Also, the main difference of our approach from the real cardiac tissue is that in our analysis we used only a homogeneous excitable medium. This medium is characterized, in particular, by the property that the maximal frequency is the same at every point. Therefore, a special consideration should be given to the robustness of the proposed method in relation to heterogeneities.

In the end, here we give some ideas concerning the reasons of suppression of the spiral–wave turbulence by the described method.

We have analyzed a response of the medium to external periodic pulses of period $T = 2\pi/\omega_{in}$. To put it differently, we have studied the signal processing by the excitable medium. The medium is more sensitive at specified (characteristic) frequencies. This phenomenon is connected with synchronization of the medium dynamics and the pacemaker frequency. The first peak corresponds to the frequency locking $1 : 1$, when the medium has its response to each source action. When the maximum possible frequency is achieved, the medium cannot respond to every impulse. With the further increase of the frequency ω_{in} of the external pacemaker, the wave propagation is possible when the medium in the neighborhood of the pacemaker is in the rest state. This is the case when the synchronization $2 : 1$ is attained. And so on. However, owing to the complexity of the system, the synchronization with higher source frequencies is not possible, so that the graph $\omega_{out} = f(\omega_{in})$ loses its regular structure.

Thus, if we choose the source frequencies far from maxima of the dependence $\omega_{out} = f(\omega_{in})$ then, generally speaking, we do not get the suppression phenomenon. In a certain sense the piece–wise picture of the nonlinear response is said to be resonance (Arnol'd) tongues known in nonlinear dynamics [15]. This is due to the fact that each medium has its own characteristic time of the signal processing, i.e. the time of pulse propagation.

Consider now a *stable* medium with a certain number of spiral waves. Because this medium is stable, spirals will neither drift nor decay. As is known, for *periodic* boundary conditions the existence of a single spiral wave or their odd number is forbidden. The birth of pairs of waves with the opposite chirality is only possible. Then, in principle, due to the resonant drift, the suppression of the medium dynamics in such a configuration is always possible except for special cases when several waves turn out to be localized in different medium regions (say, when one spiral wave is surrounded by three pacemakers and the second wave is also surrounded by another three pacemakers). This means that there is no way to suppress a single spiral wave. It is necessary the collision of phase singularities of waves with different chirality.

For the *sable* medium with *zeroth* boundary conditions the question about the suppression of spiral waves can be resolved not only depending on the number of waves with positive and negative chiralities. This is due to the fact that in this medium spiral waves, being displaced into the boundary, should vanish. Thus, the suppression result is strongly determined by the pacemaker(s) location. In some cases one can displace spiral waves into the medium boundary, in the others — not, but the action of external pacemakers leads to the collision of phase singularities and their mutual disappearance. For example, in a stable medium in the form of a square it is not possible to suppress a single spiral wave by four sources located in the square corners. But, if we have several spiral waves of one and the same chirality, their suppression by the displacement into the periphery is possible.

Thus, in the stable medium with both, periodic and zeroth boundary conditions the suppression success strongly depends on different special situations. If, finally, each spiral turns out to be blocked in different regions by target waves generated by pacemakers, the suppression is not possible.

In *unstable* media spiral waves are being destroyed with time, so that the spatio–temporal chaos appears. In this case we have not found a fundamental difference which boundary conditions (periodic or zeroth ones) we consider, in spite of the fact that the medium with periodic conditions is quantitatively more complex. If there is a proper choice of the location of the external sources and plenty of time, the suppression of the spiral–wave turbulence (at the resonance frequencies of the applied stimulation for the given medium parameters) can be obtained. However, usually in applications these conditions turn out to be a intractable problem. Nevertheless, the preformed simulations with *moving pacemakers* have demonstrated that there is a quite simple way to stabilize the spatio–temporal chaos in some 2D excitable media.

Thus, our conjecture consists of the following. To find domains of turbulence in the space of model parameters corresponding to the spiral wave solution. Being in one of this domains, one has to perturb weakly a small part of the medium in a predefined way by a moving source. Under such additional conditions this procedure may result in squeezing of spiral waves out from the cardiac tissue. In the applications this means, actually, defibrillation. Prolonged influence of stimulation of the proposed kind prevents return of fibrillation and provides conditions for regeneration of the damaged cardiac tissue in the long–term period.

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