Suppression of Spiral Waves by Electric Stimulation: A Simulation Study

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Abstract

Recent studies showed that spiral waves could be involved in cardiac fibrillation. Changing the dynamics of spiral waves and stoping them by electric stimulations provide a potential way of defibrillation. However, electric stimulation could bring some serious problems to patient as well. So, our aim in this paper is to determine an optimal stimulation mode, such as the number of required stimulated sites and parameters in order to suppress spiral waves in a cardiac tissue.

1. Introduction

Since years it is well known that cardiac fibrillation can cause some mortal cardiac diseases. However, there are still many aspects of cardiac fibrillation's mechanisms which need to be studied. When the fibrillation happens, the propagation of electrical waves in the heart is severely disrupted [1]. It has been observed that spiral waves involve in cardiac fibrillation. Spiral waves can be induced by electric stimulation in a culture in vitro of cardiac cells [2–5]. Modeling studies proved also that it is possible to induce spiral waves in cardiac model in some certain conditions. According to these investigations, the dynamics of spiral waves can be changed by electric stimulations [6–8]. If spiral waves are terminated, the heart's function could be restored. This provides a potential way of defibrillation. However, electric stimulation could bring some serious problems. The energy delivered by the stimulation process could affect the heart running, so the patient feels uncomfortable or even painful. A possible solution to avoid this problem is to distribute the stimulation energy on the whole heart. Another problem that could be considered is that the stimulation could provoke new spiral waves. In this paper, our aim is to determine the optimal stimulation, such as the number of required stimulated sites and parameters (amplitude and frequency) in order to suppress spiral waves in a localized area of a cardiac tissue. The stimulation amplitude must be carried out under the threshold to avoid the generation of new spiral waves. After a description of the model and methods used in our study (sec. 2), spiral waves have been generated by using a bidimensional FitzHugh-Nagumo (FHN) model. When the stability of these waves has been confirmed, a stimulation function introduced to FHN model delivers a train of monophasic stimulus from electrodes distributed periodically. In (sec. 3), our results suggest that it is possible to suppress spiral waves using a grid of stimulation sites with appropriate stimulating signals. The minimum number of electrodes leading to the electrical resetting of the system is then investigated in function of the stimulation parameters (amplitude, frequency,...). We conclude on the possibility of the optimization of the stimulation process using hybrid strategies based on biological modifications of the cardiac tissue (strength of the intracellular coupling and conductance of sodium current) and an adequate choice of stimulation parameters.

2. Model and methods

In literature, a lot of mathematical models exist, among them, we can cite [9–13] which reproduce the electrical activities and the dynamics of cardiac cells. These models represent an interesting tool for the investigation of heart activity at cellular level but the control of their parameters is quite complex. Then in 1961, FitzHugh suggested a simplified model, which keeps the essential mathematical properties of excitation and propagation from the electrochemical properties of sodium and potassium ion flow. This model permits to view the entire solution on a single phase portrait. Which allows us get a geometrical explanation of important biological phenomena related to action potential [14]. The original model proposed by FitzHugh and modified by Nagumo [15] can be represented by the following coupled differential equations:

$$\begin{cases} \dfrac{\partial V}{\partial t} = D\Delta V - f(V) - W \\ \dfrac{\partial W}{\partial t} = \varepsilon(V - \gamma W) \ , \end{cases} \tag{1}$$

where V is the membrane potential, i.e. the potential difference across the membrane; W is called recovery variable, which indicates the capacity of the medium to revert to its resting state after the propagation of impulsions.

D, a diffusion parameter; Δ , continuous Laplace operator. $f(V) = V(V-\alpha)(V-1)$ is a cubic nonlinear function of the potential, it can model the electrochemical properties of sodium ion flow. It permits the system to produce regenerative self-excitation via a positive feedback. This system is completed by the Neumann boundary conditions at the outer boundary to give vanishing radial components of electric and ion fluxes, so that: $\frac{\partial V}{\partial n} = 0$, where $\frac{\partial V}{\partial n}$ denotes the outer normal derivative at the boundary of the bounded domain.

2.1. Generation of spiral waves

To study how to suppress spiral waves, we need firstly generate spiral waves with our model. In our $2D$ simulation, the system starts with a planar wave. When the traveling plane wave is approximately halfway across the cardiac tissue, a function introduced to reset the upper half of the voltage V and recovery variables W to zero. In this way, spiral waves can be generated. The Fig. 1 shows the spiral wave arising.

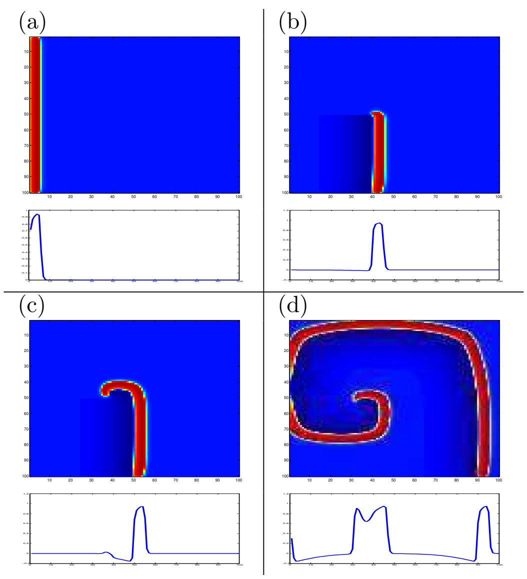

Figure 1. Spiral wave produced by the Fitzhugh-Nagumo equations for (a) $t = 100s$; (b) $t = 900s$; (c) $t = 1100s$; (d) $t = 1900s$. Grid composed of 200×200 cells. The upper figure shows a $2D$ view of the wave propagation and the lower one shows the evolution of the action potential along a line of the tissue.

2.2. Suppression of spiral waves

If a system (eq. 1) is established in a spiral wave scheme, our aim is to suppress spiral waves by sending a train of monophasic stimulus from external electrodes distributed periodically to the system. The cardiac tissue is covered by an electrode network with the same size as the tissue. The electrodes network has a square form but another electrodes pattern can be used. The stimulus function I_{stim} has been introduced to the model (1). The new shape of the model is given by the system (2).

$$\begin{cases} \frac{\partial V}{\partial t} = D\Delta V - k \cdot f(V) - W + I_{stim} \\ \frac{\partial W}{\partial t} = \varepsilon(V - \gamma W) \ , \\ I_{stim} = Arect\left(\frac{t}{\tau}\right) \cdot \sum_{n=0}^{\infty} \delta(t - n\tau), \end{cases} \tag{2}$$

where $Arect\left(\frac{t}{\tau}\right)$ is a rectangular pulse of an amplitude A, a duration τ, and centered in time $t = 0$. The function $\sum_{n=0}^{\infty} \delta(t - n\tau)$ is a Dirac comb corresponding to an infinite series of Dirac delta functions spaced at intervals of τ. Simulating the model "tissue-electrodes network" described by (2), we obtain results given at Fig. 2. This

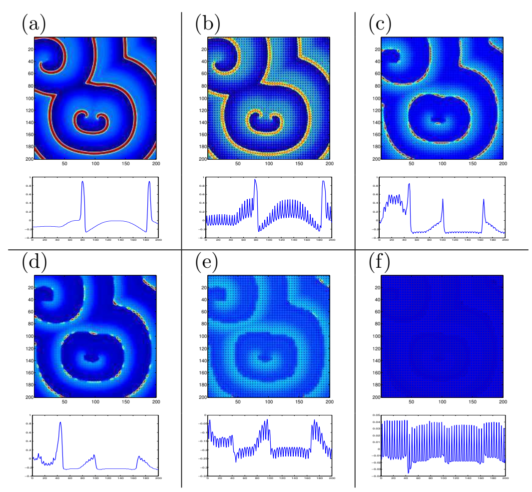

Figure 2. Suppression of Spiral Waves (a) $t = 0s$; (b) $t = 5s$; (c) $t = 30s$; (d) $t = 65s$; (e) $t = 95s$; (f) $t = 155s$.

method, which can be called global stimulation, is based on the hypothesis that there are spiral waves all over the cardiac tissue. It is possible to stimulate just certain region of the tissue, i.e. to perform local stimulation to avoid stressing more the tissue. After introducing the models, in the following, we present and analyze some results.

3. Results

Our simulations were performed with a cardiac tissue which is composed by a cardiac cells grid of 200×200

and are based on a Runge-Kutta scheme. The parameters values used during our simulations are $D = 0.1$, $\varepsilon = 0.005$, $\gamma = 0$ and $\alpha = 0.1$. To illustrate our results, we introduce a term ***Stimulation Rate (SR)***, which is the smallest number of cells needed to stimulate with respect to the total cell number in the cardiac tissue. So, three categories of simulations have been carried out, respectively global stimulation, local stimulation and hybrid stimulation.

3.1. Global stimulation

In this mode, the whole cardiac tissue will be stimulated. Depending on the stimulation parameters (amplitude, frequency and duty cycle of the stimulus function I_{stim}), spiral waves (SW) can be suppressed or not. Analyzing results, the stimulation process does not only suppress SW but can also generate new SW. A frontier corresponding to the suppression or not of SW between each stimulation parameter and the stimulation rate, has been established. The figure (Fig. 3) shows there is a relationship between the energy required in the suppression of SW and the number of electrodes. The energy is function of the amplitude and the frequency of the stimulation. Seeing Fig. 4, the sup-

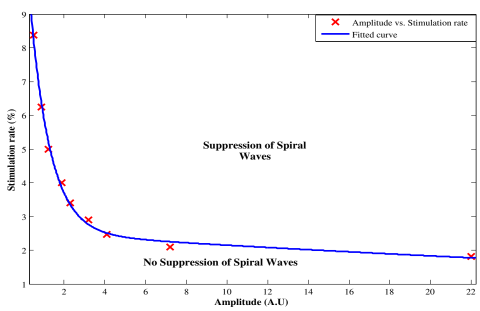

Figure 3. Amplitude vs. SR. $k = 1$, $T = 16$, $duty\ cycle = 0.5$

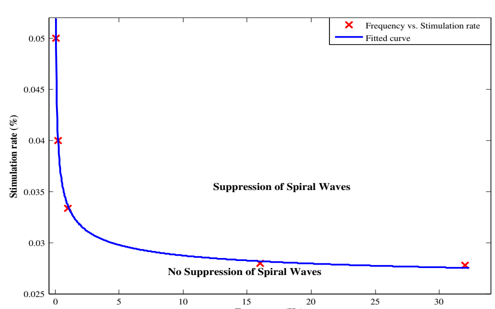

Figure 4. Frequency vs. SR. $A = 2$, $k = 1$, $duty\ cycle = 0.5$

pression process is more sensible of lower frequency than of higher frequency. It's yet another prove of stimulation energy's importance. The duty cycle of the stimulus influences also the suppression of the SW like the amplitude and the frequency (see Fig. 5). But it seemed that it exists

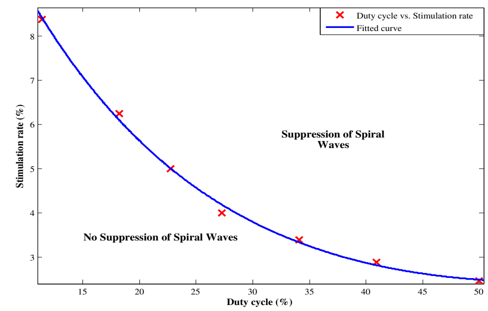

Figure 5. Duty Cycle vs. SR. $A = 2$, $k = 1$, $T = 16$

a stimulation threshold, i.e. when we need to suppress spiral waves on the whole tissue, there's a minimal number of cells to stimulate. Smaller than this number, even the frequency is high enough, the SW cannot be removed and propagate.

3.2. Local stimulation

To avoid the generation of new SW by stimulation process, the stimulation threshold above which a new wave is generated, has been determined. In this investigation, a localized area of the cardiac tissue is considered. The amplitude of the stimulus can be reduced considerably (Fig. 6). The stimulation process under the threshold is interesting because the tissue receives a small quantity of energy and it is not damaged. So, in the following, the results

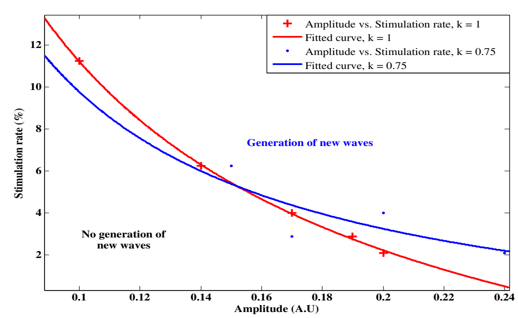

Figure 6. Threshold of generation of new waves for two values of K. Parameters of the stimulus : $T = 16$, $duty\ cycle = 0.5$

corresponding to a third stimulation mode called hybrid stimulation are given.

3.3. Hybrid stimulation

The modification of the dynamic of the sodium current due to the stimulation process has been investigated in this mode. If the value of the parameter k changes, the position and the value of the nullclines are modified in the phase space. Then, the amplitude of the stimulus is greatly reduced (Fig. 7) compared to the first result (Fig. 3). Smaller amplitude could imply less pain to patient.

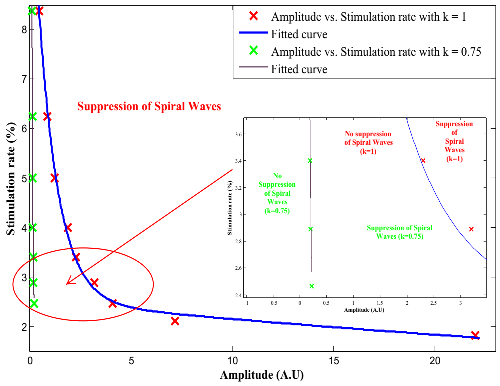

Figure 7. Amplitude vs. SR with two different k values. $T = 16$, $duty\ cycle = 0.5$

The energy required for a stimulation process can be further reduced choosing the amplitude of the stimulus under the threshold and an optimal value of the parameter k (see Fig. 8). Thus, we can suppose that the adequate choice of drugs controlling the activity of the sodium current and the amplitude of the stimulus under the threshold could contribute to the optimize the suppression of the SW.

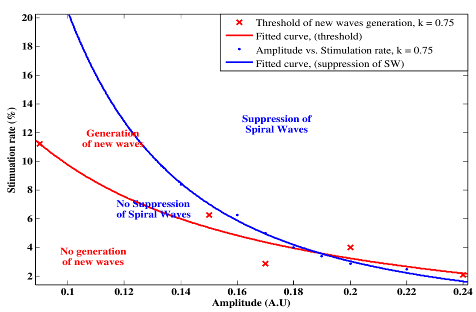

Figure 8. Amplitude vs. SR with $k = 0.75$. $T = 16$, $duty\ cycle = 0.5$

4. Conclusion and Discussion

In this study, the stimulation process has been investigated considering different parameters such as : amplitude, frequency, duty cycle of stimulation impulsions and the parameter k controlling the dynamic of the sodium current. There is some evident results like with an high amplitude of stimulation, the SW can be suppressed because the cardiac cells receive much energy. The size and the geometry of the electrode network have also an important effect on the suppression of spiral waves. The stimulation must be performed under the threshold of generation of the new wave and then to decrease the energy delivered to the tissue. The hybrid strategy could be interesting in the optimization of the defibrillator. In our point of view, hybrid strategy means that in the stimulation process, it should take into account the physical parameters of the stimulation and also the physiological characteristics of the cardiac tissue.

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