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Suppression of spatio-temporal chaos in excitable media with nonexcitable cells

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Abstract—Spiral waves and spatio-temporal chaos are the main causes of a serious cardiac arrhythmia. The cardiac muscle has characteristic features of excitable media. It is well known that the fibrosis of myocardium, sets of non-excitable cells, is strongly correlated with an incidence of serious arrhythmias. The present paper examines the suppression of spiral waves and spatio-temporal chaos in excitable media with fibrosis. The boundary periodic pacing is applied to the excitable media. The influence of non-excitable cells on the suppression performance is investigated on numerical simulations. These numerical investigations suggest that the angular frequency of the boundary periodic pacing should be low for the high fibrosis ratio.

1. Introduction

Sudden death is mainly caused by fatal arrhythmias such as the ventricular tachycardia and the ventricular fibrillation. In order to eliminate the ventricular fibrillation, a high-voltage electric shock is applied to a patient. Although this method succeeds in suppressing the fibrillation, it may induce burns and aftereffects to a patient. In recent years, the advanced defibrillation scheme with a low-voltage electric shock is required to avoid such problems.

It is well accepted that the ventricular tachycardia and the ventricular fibrillation would be caused by electrical spiral waves and spatio-temporal chaos occurred in cardiac tissue [1]. As the tissue can be considered as excitable media, the elimination of spiral waves and spatio-temporal chaos in mathematical models of excitable media corresponds to a defibrillation.

There has been growing recognition that such elimination would be a key phenomenon for medical care. It is therefore necessary to find effective methods for the elimination. So far, many researchers have proposed the various methods for eliminating spiral waves and spatio-temporal chaos in mathematical models of excitable media. These are classified into the global and non-global methods: for the global methods, an input signal is applied to the whole media [2, 3, 4]; on the contrary, for the non-global methods, it is applied to some parts of the media [5, 6, 7, 8, 9].

It is generally known that the real cardiac muscle is not homogeneous: the real muscle includes the fibrotic tissue which consists of non-excitable cells. In healthy hearts, the percentage of fibrotic tissue makes up only 5% of the total tissue. During aging and in cardiac diseases, the percentage may increase up to 35% [10]. An increased amount of fibrotic tissue is strongly correlated with an increased incidence of serious arrhythmias [11, 12, 13]. Therefore, the presence of fibrosis should be taken into consideration in developing the defibrillation scheme. Recently, the excitable media with fibrosis are described by the mathematical models: the effect of diffuse fibrosis to the wave propagation has been investigated [14, 15, 16].

The purpose of this work is to investigate the elimination of spiral waves and spatio-temporal chaos in the excitable media with fibrosis. It is shown that the spiral waves and spatio-temporal chaos can be suppressed by applying periodic pacing on media's boundary. This method does not require the measurements and the feedback control mechanism; thus, it would be easily realized in practical situations, such as the implantable cardioverter-defibrillator. The influence of fibrosis on the suppression performance is investigated by numerical simulations.

2. Excitable media with nonexcitable cells

The excitable media can be described by simple mathematical models. The present paper employs a two-dimensional Bär model [17]:

$$\frac{\partial u}{\partial t} = -\frac{1}{\varepsilon}u(u-1)\left(u - \frac{v+b}{a}\right) + \nabla^2 u, \tag{1a}$$

$$\frac{\partial v}{\partial t} = f(u) - v, \tag{1b}$$

$$f(u) = \begin{cases} 0 & u < \frac{1}{3} \\ 1 - 6.75u(u-1)^2 & \frac{1}{3} \le u \le 1 \\ 1 & u > 1 \end{cases}. \tag{2}$$

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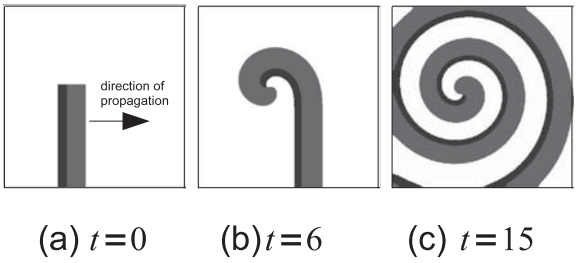

Figure 1: Initial condition and development into spiral waves ($\varepsilon = 0.06$): (a) initial condition; (b)-(c) spiral waves.

Here $\nabla^2 := \partial^2/\partial x^2 + \partial^2/\partial y^2$ is the Laplace operator. $u \in \mathbb{R}$ and $v \in \mathbb{R}$ are the activator and inhibitor variables, respectively. The parameters a and b are related to the excitation threshold, and they are fixed at $a = 0.84$, $b = 0.07$ throughout this paper. As the parameter ε is a small positive value, u is considered as a fast variable compared with the slow variable v. As shown in Fig. 1, the suitable initial conditions lead to a stable spiral wave and a meandering spiral for $\varepsilon < 0.069$. The spiral wave breaks up and then spatio-temporal chaos occurs for $\varepsilon > 0.069$. In our numerical simulations, the time step $\Delta t = 0.002$ and the space step $\Delta x = \Delta y = 0.1$ are used. Further, model (1) has the cell size, $x \in [0, 400]$ and $y \in [0, 400]$, with the no-flux boundary.

The diffuse fibrosis in cardiac tissue was modeled by the presence of nonexcitable obstacles of size 0.1×0.1. These were randomly distributed over the medium, which mainly expresses the aging fibrosis [14]. The ratio of nonexcitable obstacles corresponds to that of fibrosis.

To suppress spiral waves and spatio-temporal chaos, the periodic pacing is applied to the media's boundary [8]. Equation (1a) is modified as

$$\frac{\partial u}{\partial t} = -\frac{1}{\varepsilon}u(u-1)\left(u - \frac{v+b}{a}\right) + \nabla^2 u + F(x,t). \quad (3)$$

The input signal for elimination, $F(x,t)$, is given by

$$F(x,t) = \begin{cases} 15\delta(x)\cos\omega t & t \in [0, 500] \\ 0 & \text{otherwise} \end{cases}, \quad (4)$$

where ω is the angular frequency. The delta function $\delta(x)$ is 1 only at the boundary $x = 0$. The initial condition (i.e., medium state at $t = 0$) is set to a spiral wave or spatio-temporal chaos. The input signal is applied for the period $t \in [0, 500]$. We judge the successful elimination by the fact that the entire medium settles into the rested state by $t = 550$.

3. Numerical simulations

Figure 2 shows the time-space patterns for $\varepsilon = 0.08$ and $\omega = 1.45$. The shaded area represents the excited state ($u \geq 1/3$) and the white area represents the rested state ($u < 1/3$). The suppression occurs with 0% fibrosis as shown in Figs. 2(a)-(d); however, it does not occur with 20% fibrosis (see Figs. 2 (e)∼(h)). For $\varepsilon = 0.08$ and $\omega = 1.20$, the suppression does not occur with 0% fibrosis as shown in Figs. 3 (a)-(d); in contrast, it occurs with 20% fibrosis (see Figs. 3(e)∼(h)). From these results, we notice that the suppression depends on the angular frequency ω and the fibrosis ratio.

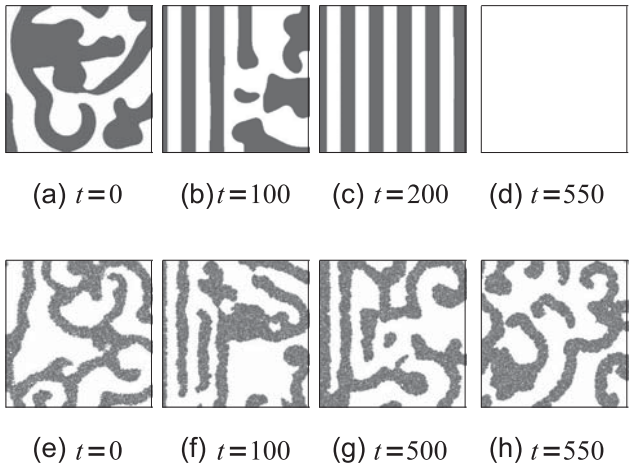

Figure 2: Suppression of spatio-temporal chaos by the boundary periodic pacing ($\varepsilon = 0.08, \omega = 1.45$): (a)-(d) 0% fibrosis; (e)-(h) 20% fibrosis.

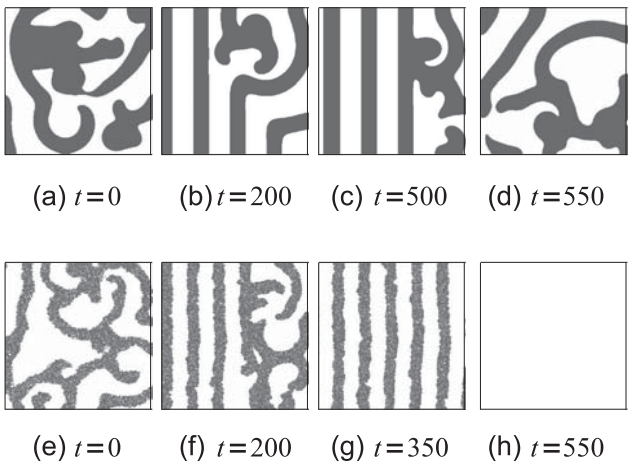

Figure 3: Suppression of spatio-temporal chaos by the boundary periodic pacing ($\varepsilon = 0.08, \omega = 1.20$): (a)-(d) 0% fibrosis; (e)-(h) 20% fibrosis.

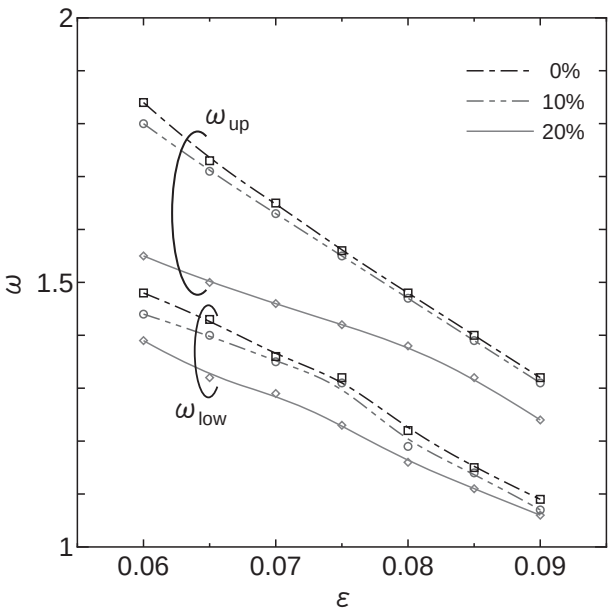

Figure 4: Controllable ranges in ε-ω plane for fibrosis ratio $0, 10, 20$ %.

It was reported that, without fibrosis (i.e., 0%), the controllable angular frequency ω strongly depends on the parameter ε [8]. The present paper shall investigate the influence of the fibrosis ratio on the controllable angular frequency ω. Figure 4 indicates the controllable angular frequency in ε-ω plane for fibrosis ratios $0, 10, 20$ %. The upper (lower) bound of the controllable angular frequency are denoted by $\omega_{\rm up}$ ($\omega_{\rm low}$). The suppression occurs when ω is set to $\omega \in \Delta\omega := [\omega_{\rm low}, \omega_{\rm up}]$. Here, $\Delta\omega$ is called controllable range. The ranges $\Delta\omega$ for the ratios 0% and 10% are almost the same. On the other hand, for the ratio 20%, $\omega_{\rm up}$ decreases greatly and $\omega_{\rm low}$ decreases slightly with an increase in the fibrosis ratio. Further, it is observed that, for the ratio 30%, input signal (4) cannot suppress the spiral waves and the spatio-temporal chaos (i.e., $\Delta\omega = 0$). From these results, we notice that input signal (4) is effective to the excitable medium with fibrosis up to about 20%.

4. Discussion

This section considers the reasons why the upper and lower bounds of the controllable angular frequency, $\omega_{\rm up}$ and $\omega_{\rm low}$, decreases with an increase in the fibrosis ratio.

To begin with, let us consider the reason $\omega_{\rm up}$ decreases. It is obvious that input signal (4) induces the plane waves with the angular frequency ω as indicated in Figs. 2 and 3. Figure 5 shows the time-space pattern on the medium with fibrosis ratio 20% and $\varepsilon = 0.08$ for $\omega = 1.35$, which is under the upper bound $\omega_{\rm up}$. Although the waves are disturbed due to the 20% fibrosis, they still keep their distances. It is clear that these distances become smaller with increasing ω. For over the upper bound $\omega_{\rm up}$, $\omega = 1.40$, the waves' distances become smaller as shown in Fig. 6. Eventually, the disturbed plane waves touch together and collapse their formation. On the other hand, it was reported that the velocity of traveling waves decreases as the fibrosis ratio increases [15]. This report implies that, with increasing the fibrosis ratio, the plane waves' distances become smaller. The disturbance effect and the smaller waves' distances would explain the reason $\omega_{\rm up}$ decreases with an increase in the fibrosis ratio.

It is known that if several waves with different frequencies exist in the medium, a wave with the highest frequency dominates the entire medium [18]. Hence, if the input signal frequency is higher than the spiral/chaotic waves frequencies, the plane wave induced by the input signal dominates the entire medium. This is the fundamental mechanism of suppression with the boundary periodic pacing. Since the frequencies of spiral/chaotic waves decrease with an increase in fibrosis ratio, even low-frequency input signal can suppress them with the high fibrosis ratio. This would be the reason $\omega_{\rm low}$ decreases as the fibrosis ratio increases.

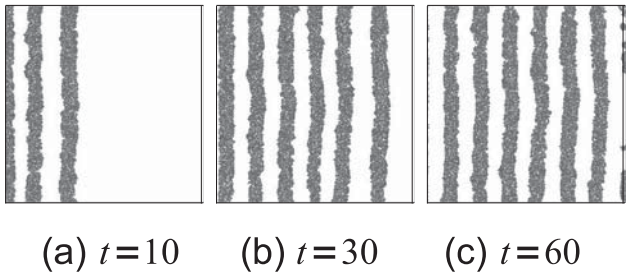

Figure 5: Time-space pattern on the medium with fibrosis ratio 20% and $\varepsilon = 0.08$ for $\omega = 1.35$.

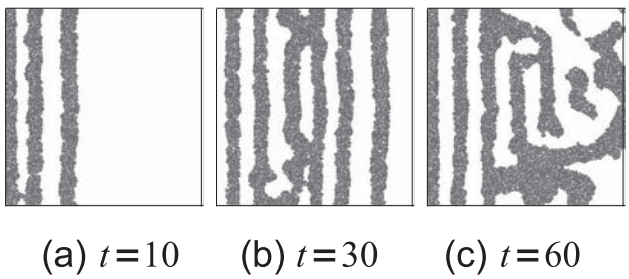

Figure 6: Time-space pattern on the medium with fibrosis ratio 20% and $\varepsilon = 0.08$ for $\omega = 1.40$.

5. Conclusion

The present paper dealt with the suppression of spiral waves and spatio-temporal chaos in excitable media with fibrosis. The influence of non-excitable cells on the suppression performance has been investigated by numerical simulations. According to these numerical investigations, we might suggest that the angular frequency of boundary periodic pacing has to be low for high fibrosis ratio (i.e., aged tissue).

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