Control of turbulence in heterogeneous excitable media

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Control of turbulence in two kinds of typical heterogeneous excitable media by applying a combined method is investigated. It is found that local-low-amplitude and high-frequency pacing (LHP) is effective to suppress turbulence if the deviation of the heterogeneity is minor. However, LHP is invalid when the deviation is large. Studies show that an additional radial electric field can greatly increase the efficiency of LHP. The underlying mechanisms of successful control in the two kinds of cases are different and are discussed separately. Since the developed strategy of combining LHP with a radial electric field can terminate turbulence in excitable media with a high degree of inhomogeneity, it has the potential contribution to promote the practical low-amplitude defibrillation approach.

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I. INTRODUCTION

The excitability is one of the main dynamical principles behind a variety of biological functions. The most well known example of excitable media in biology is the heart tissue. Ventricular fibrillation continues to be the leading cause of sudden cardiac death. Investigations over the past decade have suggested that ventricular fibrillation is associated with broken spiral turbulence [1–4]. Consequently, the requirement for defibrillation has attracted much attention to developing methods to terminate spiral turbulence.

The complex structure of cardiac tissue makes it heterogeneous, which results in a spatially inhomogeneous distribution of the excitability [5–13] and gives rise to complicated dynamic behavior. For example, some investigations have claimed that cardiac fibrillation can be characterized by multiple stable spiral waves with different frequencies resulting from an inhomogeneous excitability [12,13]. Documented studies concentrated on two types of heterogeneities. The first one results from ischemia, fibrosis, or sarcoidosis in cardiac tissue and is treated as in non- or sub-excitable regions. The existence of this type of heterogeneity may induce serious consequences. It may break the excitable planar wave with a simultaneous pinned reentry spiral [14–17] or turbulence [7,18]. Therefore, from the view of actual practice, various methods to suppress spiral and turbulence have been put forward [19–21], such as exciting waves on heterogeneities by a pulsed electric field [22], high frequency stimulation as antitachycardia pacing [23–25], and so on. The second type of heterogeneity contains a “hot” region where the excitability is higher than that in the rest region [10,26–29]. Deleterious results may also be induced by this type of heterogeneity since it negatively affects the stability of propagating waves [8]. However, less concerns are put on this case and the corresponding control means.

In clinics, electric shocks with high intensity are applied to body surface or directly to cardiac muscle for cardiac defibrillation [30,31]. These large amplitude shocks have drawbacks: they may damage the cardiac tissue and cause serious pains [32]. As a low field treatment, trains of low-amplitude pulses are then widely used as an antitachycardia pacing. A big challenge of antitachycardia pacing is that it usually fails to terminate high-frequency arrhythmias and developed chaos if the media are heterogeneous [25]. The first type of heterogeneity will block (or break) the trains of low-amplitude pulses and then protect the existing turbulence behind it. The second kind of heterogeneity may act as another source of pacemaker emitting irregular waves preventing the attempt at antitachycardia pacing. For these drawbacks of antitachycardia pacing, it is necessary and meaningful to develop strategies to suppress turbulence in heterogeneous media.

In this paper, a radial electric field, in addition to the method of local-low-amplitude and high-frequency pacing (LHP), is proposed as a combined strategy to terminate spiral turbulence in both types of heterogeneous media. It will be found that the radial electric field greatly improves the effectiveness of the local pacing. The mechanisms of suppression of turbulence in two types of heterogeneous media are different and discussed separately.

II. MODEL

In our simulation, a modified FitzHugh-Nagumo model introduced by M. Bär and Eiswirth is used to describe the electrical activities of cardiac tissue [33]:

\[
\frac{\partial u}{\partial t} = f(u,v) + \nabla^2 u, \quad \frac{\partial v}{\partial t} = g(u) - v, \tag{1}
\]

where the functions \(f(u,v)\) and \(g(u)\) take the following forms:

\[
f(u,v) = \frac{1}{\varepsilon(x,y)} u(1-u) \left( u - \frac{v + b}{a} \right), \tag{2}
\]

\[
g(u) = \begin{cases} 
0, & 0 \leq u < 1/3 \\
1 - 6.75u(u - 1)^2, & 1/3 \leq u < 1 \\
1, & 1 \leq u. 
\end{cases} \tag{3}
\]
Here, \( u \) and \( v \) are the activator and the inhibitor variables, respectively. Parameters \( a = 0.84 \) and \( b = 0.07 \) are fixed to ensure the medium is excitable.

The parameter \( \varepsilon \) can characterize the excitability of the medium which exhibits various distinctive characteristics as \( \varepsilon \) is varied. The bigger the \( \varepsilon \), the smaller the excitability is. When \( \varepsilon \) is in \([0.02,0.07]\), the medium supports stable or meandering spiral with suitable initial conditions. Due to the Doppler effect for \( \varepsilon > 0.071 \), spiral waves will break up and the system will quickly fall into a turbulent state. As \( \varepsilon \) crosses the threshold of backfiring at about 0.1, the system can not support the propagation of regular waves. In our model, \( \varepsilon(x,y) \) characterizes the spatially distributed excitability of the two-dimensional medium. To simulate a heterogeneous excitable medium, the \( \varepsilon(x,y) \) is presented as

\[
\varepsilon(x,y) = \begin{cases} 
\varepsilon_0, & 0 \leq x < L_1 \\
\varepsilon_H, & L_1 \leq x \leq L_2 \\
\varepsilon_0, & L_2 < x \leq L.
\end{cases}
\]

The size of the square medium is \( L = 100 \) (\( L_1 = 46 \) and \( L_2 = 58 \)). The stripe with \( \varepsilon_H \) acts as the heterogeneity. Local pacing \( F(t) = \tau \cos(\omega t) \) with fixed amplitude \( \tau = 2.0 \) is imposed on a small square region (3 \( \times \) 3 grids) with a central point at grid \( (x_0,y_0) = (31,47) \). The radial electric field with the same center point is imposed. At point \( (x,y) \), the radial electric field can be divided into two directions along the \( x \) and \( y \) axes, that is, \( E_x = E \cos \theta = E(x-x_0)/d \) and \( E_y = E \sin \theta = E(y-y_0)/d \), where \( d = \sqrt{(x-x_0)^2 + (y-y_0)^2} \). One can find the detailed information in the sketches in Fig. 1.

\[
\frac{\partial u}{\partial t} = f(u,v) + \nabla^2 u + F(t) - E_x \frac{\partial u}{\partial x} - E_y \frac{\partial u}{\partial y}, \\
\frac{\partial v}{\partial t} = g(u) - v.
\]

III. RESULTS AND DISCUSSION

1. Heterogeneity with a higher excitability

First, we study the control of turbulence in the second type of heterogeneous media containing hot regions with a higher excitability than that in the rest region, that is, \( \varepsilon_0 > \varepsilon_H \). The value \( \varepsilon_0 \) is fixed to be 0.075, while \( \varepsilon_H \) is changed to alter the degree of heterogeneity. Since we focus on the suppression of turbulence, we give chaotic states as initial conditions.

As an alternative defibrillation technique, the strategy of LHP has been explored in a number of previous experiments [34]. It is found that target waves with a high frequency generated by LHP are effective in terminating turbulence when the medium is homogeneous (the value \( \Delta \varepsilon = 0 \) [35]). We present an example with a fixed \( \varepsilon_0 = 0.075 \) and gradually decrease \( \varepsilon_H \) to increase the excitability of the heterogeneity. With a small deviation of the excitability \( \Delta \varepsilon < 0.015 \), the target waves growing from LHP succeed in wiping away turbulence in the system, which can be seen from the evolution in the upper row of Fig. 2. In this process, the frequency of LHP is always bigger than \( \omega_T(\varepsilon_0) \) and \( \omega_T(\varepsilon_H) \) that are the frequencies of turbulence in the \( \varepsilon_0 \) region and heterogeneity, respectively. However, the effort of suppression fails when \( \Delta \varepsilon \) crosses a critical value 0.015 (the corresponding critical \( \varepsilon_{H1} = 0.06 \)). This is shown in the lower row of Fig. 2 where the excitability of the heterogeneity is just the same as the critical value. Spiral waves spontaneously appear in

\[
\text{FIG. 2. (Color online) Evolution of turbulence in an inhomogeneous medium controlled by LHP with } \omega_{T1} = 1.45, \varepsilon_0 = 0.075 \text{ is fixed while } \varepsilon_H = 0.062 \text{ in the upper row and } 0.06 \text{ in the lower row.}
\]
the heterogeneity, which protect against the target waves from LHP. The coexistence of target waves and spiral waves indicates they have identical frequencies. A more obvious example showing the failure of LHP is presented in the upper row of Fig. 5 where the heterogeneity has a much higher excitability ($\epsilon_H = 0.04$). The target wave can not grow since it is suppressed by turbulence with a high frequency from the heterogeneity.

The condition to ensure the validity of LHP depends on its characteristic, namely, high frequency waves. However, this condition may break down in a heterogeneous medium containing hot regions where the frequency of turbulence is higher than that of the target waves. To clarify this point and put forward possible control strategy, we present the dispersion relation in Fig. 3. To suppress turbulence surrounding the pacing points (in the region with $\epsilon_H$), the frequency of target waves $\omega_{LHP}$ from LHP should be higher than $\omega_T(\epsilon_H)$. Terminating turbulence in the heterogeneity requires $\omega_{LHP} > \omega_T(\epsilon_H)$. It is easy to reach these two requirements if the medium is homogeneous or the deviation is small. In the upper row of Fig. 2, these two conditions are fulfilled: $\omega_{LHP} > \omega_T(\epsilon_H) > \omega_T(\epsilon_0)$, namely, $1.45 > 1.43 > 1.22$. However, there is an additional requirement for a heterogeneous medium, that is, $\omega_{LHP}$ should also be smaller than $\omega_{max}(\epsilon_0)$. Otherwise, the pacing is so fast that the next pacing stimulus S2 falls in the refractory tail of the previous wave S1, which is called S1S2 stimulation [36]. Then, the target wave can not be generated until the third stimulus is applied. Consequently, the frequency of target waves will be halved, which will result in the failure of suppressing turbulence. In order to make use of LHP to the most degree, we always select the condition $\omega_{LHP} = \omega_{max}(\epsilon_0)$. Thus, the first condition is fulfilled automatically. From Fig. 3, one can see that the frequency of turbulence in the heterogeneity is increased when $\epsilon_H$ is decreased. By continually increasing the deviation of the excitability, which results from a decrease of $\epsilon_H$ ($\epsilon_0$ is fixed), the value $\omega_T(\epsilon_H)$ will inevitably exceed $\omega_{max}(\epsilon_0)$ and $\omega_{LHP}$. The condition $\omega_T(\epsilon_H) = \omega_{LHP}$ in the lower row of Fig. 2 and $\omega_T(\epsilon_H) > \omega_{LHP}$ in the upper row of Fig. 5 results in the failure of suppression. From the dispersion relation, one can get the critical value of $\epsilon_H$ ($=0.06$) (see the auxiliary lines). The analysis is consistent with the simulation result in Fig. 2 where we exactly find the critical value $\epsilon_H$ is 0.06.

From the discussion mentioned above, one way to suppress turbulence in heterogeneous media with a large deviation of the excitability is to increase the $\omega_{max}(\epsilon_0)$ so that the value $\omega_{LHP}$ can be subsequently increased to make the condition $\omega_{LHP} > \omega_T(\epsilon_H)$ fulfilled. In our strategy, the radial electric field with the center located on the LHP points is applied to play the role of increasing $\omega_{max}(\epsilon_0)$. To show the influence of the radial electric field, one loop of the target wave is plotted in Fig. 4. In Fig. 4(a), it is evident that applying the radial electric field results in expanding the refractory tail, which has the same effect as decreasing $\epsilon_0$ [33]. Note that the decrease of $\epsilon_0$ will correspondingly decrease the deviation $\Delta \epsilon = (\epsilon_0 - \epsilon_H)$. It seems as if the deviation of the excitability is moderated once the radial electric field is applied. On the other hand, one can find that the recovery of excitation to the $v = 0$ state becomes faster after the radial electric field is applied. This point is distinctive in Figs. 4(b) and 4(c) where the evolutions of $u$ and $v$ are plotted. Compared to the case without the radial electric field, the duration of excitation with the radial electric field is dramatically decreased (marked by the $\Delta T_U$ and $\Delta T_V$). We can take advantage of this effect to increase the $\omega_{max}(\epsilon_0)$: when trains of pulses are generated from LHP, the front of the second wave will reach the refractory tail of the previous wave if its frequency $\omega_{LHP}$ is bigger than $\omega_{max}(\epsilon_0)$. Now, the radial electric field decreases the duration of the waves, which makes LHP generate trains of waves with higher frequencies possible. In the inset of Fig. 3, it is found that the maximum frequency of the target wave by LHP [identical with $\omega_{max}(\epsilon_0)$] can be greatly increased by the radial electric field monotonously. The maximum frequency $\omega_{max}(\epsilon_0)$ at different $\epsilon_0$ with the same intensity as the radial electric field is also plotted in Fig. 3. Comparing the curve $\omega_{max}(\epsilon_0)$ with $\omega_{max}(\epsilon_0)$, one can find the enhancement is obvious.

In terms of this mechanism, we can utilize the radial electric field to suppress turbulence in heterogeneous media with a big deviation. An example with a big $\Delta \epsilon$ is shown in Fig. 5. Without the radial electric field in the upper row of Fig. 5, the target waves can not grow since $\epsilon_H = 0.04$ is much smaller than the critical value ($\epsilon_H = 0.06$). Once the radial electric field is applied in the lower row of Fig. 5, the target waves with
higher frequencies dramatically enter into the heterogeneity and suppress turbulence in the medium. In the simulation, we decrease the value of $\varepsilon_H$ until the combined method loses its effect when $\varepsilon_H$ crosses a critical value which is labeled as $\varepsilon_{H2}$. A surprising thing is that the value of $\varepsilon_{H2}$ from the simulation is 0.025, which is smaller than that from the analysis of the dispersion relation in Fig. 3 where the intersection marked by one arrow $\varepsilon_{H2}$ shows its value 0.037. To evaluate the efficiency of the radial electric field, we plot the value $\Delta \varepsilon$ as a function of the intensity of the radial electric field. It is found that the $\Delta \varepsilon$ depends on the amplitude of the radial electric field, which has been illustrated in Fig. 6 where a monotonically increasing curve is obtained. Compared to the value $\Delta \varepsilon = 0.015$ without the radial electric field, the value $\Delta \varepsilon$ is increased to 0.065 under the radial electric field with $E = 1.0$, which means the deviation is greatly enhanced. Thus, we can conclude that the combination of local pacing and the radial electric field can suppress turbulence in an inhomogeneous medium with very hot heterogeneity.

2. Heterogeneity with a lower excitability

We divert our attention to the first type of heterogeneity with the excitability lower than that in the rest region ($\varepsilon_0 < \varepsilon_H$, $\varepsilon_0 = 0.04$ is fixed). Traditionally, this kind of heterogeneity is called an “obstacle” since it blocks the propagation of waves. Certainly, turbulence can be suppressed if the deviation $\Delta \varepsilon = (\varepsilon_H - \varepsilon_0)$ is small. In the top row of Fig. 7, we show the evolution of target waves by LHP with a suitable frequency in a medium with $\Delta \varepsilon = 0.023$ ($\varepsilon_H = 0.063$). The growing target waves propagate into the heterogeneity and eliminate the initially existing turbulence. Now, the question is posed again: can the LHP suppress turbulence if the excitability of the heterogeneity is very low, namely, the deviation $\Delta \varepsilon$
is very big? In middle row of Fig. 7, the $\Delta \varepsilon$ is enhanced from 0.023 to 0.04 ($\varepsilon_H$ is increased from 0.063 to 0.08). One can see that the target waves by LHP can not enter into the heterogeneity any longer. The blocking of the heterogeneity makes the effort fail although the frequency of LHP is higher than that of the existing turbulence in any region [$\omega_{\text{LHP}} = 1.76$, $\omega_T(\varepsilon_0) = 1.75$, and $\omega_T(\varepsilon_H) = 1.18$]. No matter what frequencies of LHP are selected, the target waves can not achieve suppressing turbulence in the heterogeneity. The simulation gives the critical value $\varepsilon_{H1} = 0.065$.

Then we make use of the radial electric field again in heterogeneous media with a high deviation of excitability. In the bottom row of Fig. 7 where $\Delta \varepsilon = 0.04$, we utilize the radial electric field and decrease the frequency of LHP. Now, the target waves successfully pass through the heterogeneity and wipe away turbulence. Thus, it is interesting that the radial electric field is also effective for this type of heterogeneity.

The radial electric field increases the critical value $\varepsilon_{H1}$ so far. We label the new critical value after the radial electric field is imposed as $\varepsilon_{H2}$ and $\Delta \varepsilon(E) = \varepsilon_{H2}(E) - \varepsilon_0$. From Fig. 8, it is found that the $\Delta \varepsilon$ increases with the intensity of the radial electric field. The deviation parameter $\Delta \varepsilon$ is greatly extended, i.e., $\Delta \varepsilon = 0.12$ when the amplitude of the radial electric field is 1.0. Compared with the efficiency of LHP, $\Delta \varepsilon$ is increased almost five times by means of the combined method.

In order to have an insight into the underlying mechanism of successful control in this type of heterogeneity, we plot the dispersion relation in Fig. 9 again. It is clear that suppressing turbulence requires the frequency of LHP $\omega_{\text{LHP}}$ to be higher than $\omega_T(\varepsilon_0)$. [Since $\omega_T(\varepsilon_0)$ is bigger than $\omega_T(\varepsilon_H)$, the condition $\omega_{\text{LHP}} > \omega_T(\varepsilon_H)$ is fulfilled automatically.] However, the increase of the deviation $\Delta \varepsilon$ will simultaneously decrease the $\omega_{\text{max}}(\varepsilon_H)$. Once the $\varepsilon_H$ crosses the critical value $\varepsilon_{H1}$, $\omega_{\text{LHP}}$ will be bigger than $\omega_{\text{max}}(\varepsilon_H)$. This is not permitted since the frequency of target waves will be halved in the heterogeneity, which results in the failure of terminating turbulence in the heterogeneity by LHP. Thus, $\varepsilon_{H1}$ is the maximum value for the method of LHP. For example, $\varepsilon_{H1}$ is about 0.065 when $\varepsilon_0$ is fixed to be 0.04, which shows a maximum deviation $\Delta \varepsilon = 0.025$ (see the auxiliary lines). The simulation results illustrated in the top and middle rows of Fig. 7 confirm this point. In contrast to the increase of the frequency of LHP in the second type of heterogeneity, in this case, the alternative is to decrease $\omega_T(\varepsilon_0)$ so that we can decrease $\omega_{\text{LHP}}$ correspondingly to ensure the conditions $\omega_{\text{max}}(\varepsilon_0) > \omega_{\text{LHP}} > \omega_T(\varepsilon_0)$ and $\omega_{\text{max}}(\varepsilon_H) > \omega_{\text{LHP}} > \omega_T(\varepsilon_H)$ to be both fulfilled. That is what we have done in the bottom row in Fig. 7 where the $\omega_{\text{LHP}}$ is decreased from 1.76 to 1.73 [note $\omega_T(\varepsilon_0)$ is 1.75] with the radial electric field and $\omega_T^2(\varepsilon_0)$ is 1.48 with the radial
electric field. Indeed, the radial electric field can decrease the principal frequency of turbulence in the $\varepsilon_0$ region. The radial electric field acts in the role of the radial gradient force, which is indicated in Eq. (5). The essential influence of the gradient force is to make defects and waves move along the gradient direction [37]. It reduces the principal frequencies of turbulent waves of the system due to the Doppler effect, which has been illustrated in the Fig. 9 (see the curve $\omega_0^E$ and curve in the inset). The principal frequency of turbulence decreases when the intensity of the radial electric field is increased, which is shown in the inset of Fig. 9. We simulate the principal frequencies of turbulence $\omega_0^E(\varepsilon_0)$ at different $\varepsilon$ after the radial electric field with $E = 0.5$ is imposed and plot them in Fig. 9. From the new dispersion relation, we can get the $\varepsilon_{H2} = 0.08$ if $\omega_{LHP}^E = 1.73$ and $\varepsilon_{H2} = 0.092$ if $\omega_{LHP}^E = \omega_0^E(\varepsilon_0)$, which are also confirmed by the simulation results. If we add the curve $\omega_0^E(\varepsilon_0)$ in Fig. 3 and consider the curve $\omega_0^E(\varepsilon_0)$ instead of $\omega_0^E(\varepsilon_0)$ in the second type of heterogeneity, then the $\varepsilon_{H2}$ in terms of the dispersion relation is 0.025, which is consistent with the simulation.

3. Suppression of turbulence in media with two types of heterogeneities

From the results and discussion, it is shown that the utilizing of the radial electric field can greatly contribute to suppressing turbulence in both types of heterogeneous media with a large deviation of excitability. Therefore, even if the excitability of the medium is distributed in a very wild range, the combined method is also proved to be effective. For the complexity of cardiac tissues, the spatial distribution of different excitabilities is possible, which makes it interesting to develop some efficient ways to suppress turbulence under various conditions. In Fig. 10, we consider the coexistence of both types of heterogeneities. The medium is divided into three regions. The excitability is highest in the left region and lowest in the right region. The LHP points are located in the middle region. The simulation shows that the smallest value of $\varepsilon_l$ in the left region is 0.025 and the largest value of $\varepsilon_r$ in the right region is 0.13. Note that the deviation of $(\varepsilon_r - \varepsilon_l)$ in this case shows a very big value 0.095. Furthermore, it should be pointed that the turbulence can not be terminated by LHP in the backfiring regime ($\varepsilon > 0.1$) without an auxiliary means. However, the suppression of turbulence in the right region demonstrates that the radial electric field can contribute to avoid this drawback.

IV. CONCLUSION

In conclusion, we have studied the suppression of turbulence in inhomogeneous media containing two kinds typical of heterogeneities in which the excitability is higher or lower than that in the rest region. The LHP is a general method if the deviation of excitability is small while it fails when the deviation is large. Then, a combined strategy, including LHP and the radial electric field, is put forward as a method with a very high efficiency. Another advantage is that, compared to high intensity electric shocks, the required energy of the combined method to terminate ventricular fibrillation (VF) is quite small. The underlying mechanism of successful control is different in different heterogeneous media and discussed in terms of dispersion relations. In the second type of heterogeneity, the utilization of the radial electric field increases the frequency of target waves from LHP. In the first one, the radial electric field decreases the frequency of turbulence. The simulation is consistent with the analysis.

We point out that it is not clear whether one can use this combined method for cardiac defibrillation. How to design a device to combine local pacing and the radial electric field in experiments is a question. In addition, the model is too simple for simulating actual cardiac systems although it catches the general features of excitable media. We hope our studies can offer some useful instructions for experiments and simulations on practical cardiac defibrillation.

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