Removal of a pinned spiral by generating target waves with a localized stimulus

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Pinning of spiral waves by defects in cardiac muscle may cause permanent tachycardia. We numerically study the removal of a pinned spiral by a localized stimulus at the boundary of a two-dimensional excitable medium. It is shown that target waves may be generated by an external local force, and then the target waves will interact with the pinned spiral. When the external force is appropriately chosen, the generated target waves may suppress the pinned spiral, and the system is finally dominated by the target waves.

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Spiral waves are one kind of interesting patterns in excitable and oscillatory media, which have been observed in the Belousov-Zhabotinsky (BZ) reaction, the catalytic surface processes, and the heart muscle [1–4]. In some cases spiral waves are undesirable because of their harmfulness. For instance, spirals in cardiac muscle are believed to play a vital role in life-threatening situations such as tachycardia and fibrillation [5]. Therefore, it is important to seek some effective methods for spiral wave control [6–13]. In this regard, local periodic forcings may be one of the most desirable methods [14–19] since a local control, especially at the boundary region, is very convenient in practice and can be easily applied in realistic systems. Nevertheless, the local pacing method is not always successful. For example, recent experiments explore the local low-amplitude and high-frequency pacing as an alternative defibrillation technique [20–23]. It is found that the pacing has only a local effect: once the pacing is suspended, the captured local region is reinvaded again by the surrounding electrical activity, and the tissue remains in a state of fibrillation.

Spiral waves in cardiac muscle may be free or their cores may be pinned to a local inhomogeneity (or an anatomical defect) [24–27]. Free spiral waves often drift or meander, and may thus disappear at the boundary, whereupon the heart returns to normal. However, if there exist defective regions in the heart, the spiral may be trapped and its core will remain in a confined region; thereby a so-called anatomical reentry is created when a free rotating wave pins to an anatomical defect, leading to a class of physiological arrhythmias. Recently, Takagi *et al.* [28] showed that a pinned spiral in cardiac tissue can be removed by a weak electric field. It is observed that an electric field creates a pattern of the membrane polarization localized around a defect, and thus unpinning of spiral waves can be achieved.

Then, an interesting question is raised naturally: can local stimulations remove a pinned spiral from the system? Before answering this question, let us consider first the interaction of a wave front with a defect. As shown in computer simulations of the Belousov-Zhabotinsky reaction [29], under appropriate conditions of the excitability, the interaction of a wave front with a defect can lead to fragmentation of this wave front and to form a pair of counterrotating spirals. With a generic model of an excitable medium, Nagy-Ungvarai *et al.* [30] and Pertsov *et al.* [31] studied the conditions under which a propagating wave breaks after colliding with a defect. Depending on the excitability of the system and the characteristics of the defect, there are three main results after the collision between a wave front and a defect [32]:

(a) Upon circumnavigating the defect, the two broken ends of the wave front come together and fuse; the wave front thus recovers its previous shape and moves on.

(b) Upon detachment from the defect, the broken ends move in opposite directions and initiate two counterrotating spirals.

(c) After detaching from the defect, the two fragmented wavelets gradually shrink and die off.

In this paper, we will consider a two-dimensional excitable system described by a modified FitzHugh-Nagumo model with an initial spiral pinned by a defect. A local periodic signal will be injected at the upper boundary of the system. It will be shown that the local periodic signal can generate target waves at the forcing point and the target waves may suppress the pinned spiral. After the spiral is removed, the whole space will be controlled by the target waves: the target wave front breaks into two parts around the defect; then, the two broken ends of the wave front join together and move on. This just corresponds to the case (a) of the collision between a wave front and a defect.

Let us demonstrate our approach with the Barkley model [33]—i.e., a modified FitzHugh-Nagumo model. The model describes the interaction of an activator $u(t,x,y)$ with an inhibitor $v(t,x,y)$ through the following two-dimensional reaction-diffusion equations:

$$\partial u/\partial t = f(u,v) + \nabla^2 u, \tag{1a}$$

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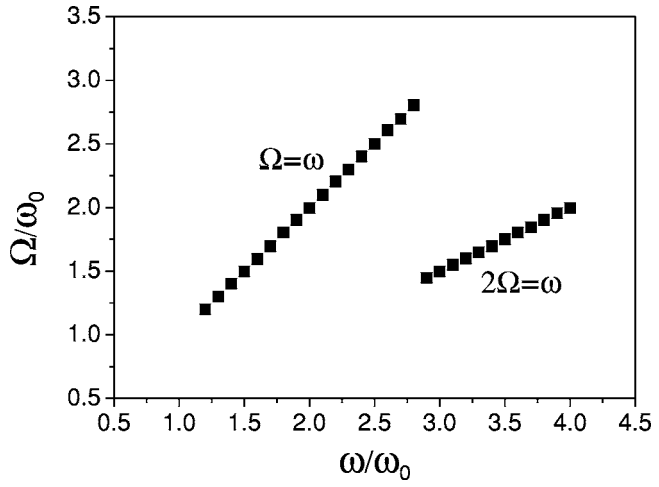

FIG. 1. The ratio of the frequency of the output target waves and the input pacing with $n=5$ and $b_f=0.6$.

$$\partial v/\partial t = g(u,v). \tag{1b}$$

The local reaction kinetics—i.e., the dynamics in the absence of spatial derivatives—is described by

$$f(u,v) = \frac{1}{\varepsilon}u(1-u)[u-(v+b)/a],$$

$$g(u,v) = u - v,$$

where a, b, and ε are three parameters. The local kinetics has a stable but excitable fixed point at the intersection of the nullclines $f(u,v)=0$ and $g(u,v)=0$. The advantage of this model kinetics is that the excitation term can be time stepped with little computational effort. This model permits fast calculations and catches the essential features of excitable media. The simulation is performed on a square grid containing 256×256 grid points and with $\Delta x=0.390625$ (i.e., an area 100×100) and with $\Delta t=0.02$. Zero-flux boundary conditions are considered for u and v at the boundaries. For all results reported in this paper, $a=0.7$, $b=0.1$, and $\varepsilon=0.02$ are used. With these values of the parameters, the system described by Eq. (1) has a solution of a rigidly rotating spiral wave with an angular frequency $\omega_0=0.647\,75$.

Before we study the interaction between target waves and a pinned spiral, we first summarize the main results of a free spiral under the influence of a local periodic forcing. A periodic signal is applied to a small fixed area at the upper boundary of the system for the local control purpose, and this can be realized by replacing parameter $b=b_0=0.1$ with periodic modulation $b(t)=b_0+b_f\cos(\omega t)$ in $n\times n$ sites at the boundary. Numerical simulations show that when the frequency of the local force is higher than that of the spiral and the amplitude of the local force is strong enough, target waves will be generated. Then the generated target waves will drive the spiral out of the boundary, and the system is finally dominated by target waves [17]. In Fig. 1, we give the resonant relation between the external force and target waves

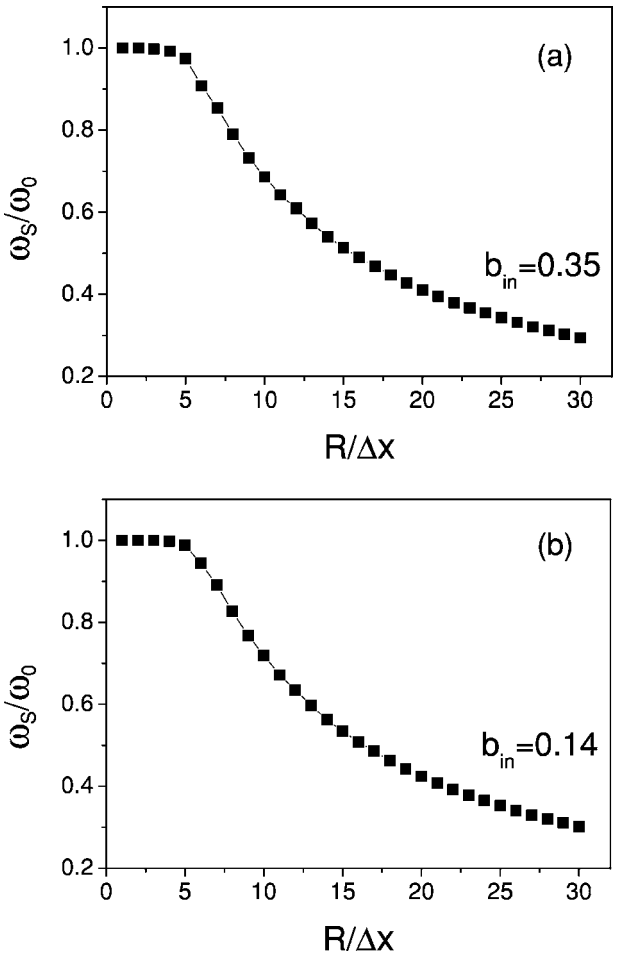

FIG. 2. The angular frequencies ω_s of a pinned spiral vs the radii R of the defect. (a) $b_{in}=0.35$ and (b) $b_{in}=0.14$.

in the presence of a spiral initiation. The single-frequency resonance (the angular frequency of the generated target waves, $\Omega=\omega$) and double-frequency resonances ($2\Omega=\omega$) are observed for $\omega\in[1.2\omega_0, 4\omega_0]$.

Then we need to define a defect in the simulation. In model studies, defects are often represented with Neumann boundary conditions. But in the cardiac muscle, many heterogeneities of various sizes and types are present. In this case, the simplest model of damaged regions is to set the local kinetics less excitable than that of normal tissue. The shape of the defect in the simulation is chosen to be a circle with a radius R. Therefore, the defect is described by two parameters b and R: b ($r<R$, inside the defect) $=b_{in}$ and b ($r\geqslant R$, outside the defect) $=b_0$. An unexcitable defect is with $b_{in}=a/2$, while a partially unexcitable defect is with $b_{in}<a/2$ but bigger than b_0. In Fig. 2(a), we present the angular frequencies of a pinned spiral for different radii of defects with $b_{in}=a/2=0.35$. In Fig. 2(b), the defects are changed to be partially excitable with $b_{in}=0.14$, and one finds no significant change except that the angular frequency of the spiral will be lower. It is shown that the angular frequency of the pinned spiral is lower than that of the free spiral and the angular frequency decreases when we increase the radius of the defect. This is consistent with the prediction by Keener and Tyson [34].

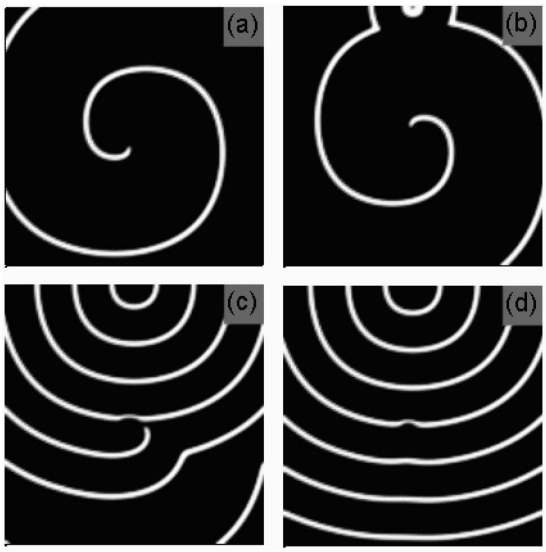

FIG. 3. Suppression of a pinned spiral wave by generating target waves with an external periodic signal. (a) $t=0$, (b) $t=20$ t.u., (c) $t=60$ t.u., and (d) $t=120$ t.u. Parameters read $n=5$, $b_f=0.45$, $\omega=1.8\omega_0$, $R=10\Delta x$, and $b_{in}=0.14$.

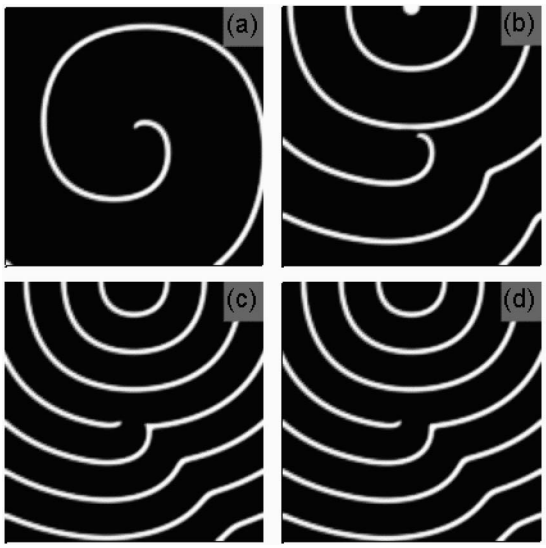

FIG. 4. The final states ($t=1500$ t.u.) of unsuccessful suppressions of a pinned spiral by a local external periodic signal with $n=5$. (a) $b_f=0.35$, $\omega=1.8\omega_0$, $R=10\Delta x$, and $b_{in}=0.14$, (b) $b_f=0.45$, $\omega=1.2\omega_0$, $R=10\Delta x$, and $b_{in}=0.14$ (c) $b_f=0.45$, $\omega=1.8\omega_0$, $R=14\Delta x$, and $b_{in}=0.14$, and (d) $b_f=0.45$, $\omega=1.8\omega_0$, $R=10\Delta x$, and $b_{in}=0.35$.

Now let us consider the interaction of target waves with a pinned spiral. In Fig. 3(a), a pinned spiral is shown. Following the same idea as in the control of a free spiral, our strategy is to apply an external periodic signal to a fixed small area at the boundary of the system. The controlled area is taken to be a square with $n\times n$ sites at the upper boundary. Generally, an external injection into a small local region cannot essentially change the pattern of the dynamic evolution, and the pinned spiral remains the same with slight deformation only. Under certain conditions, however, the state of the system can be dramatically changed by the local periodic forcing, and target waves can be generated in the small controlled area.

We take the pinned spiral wave in Fig. 3(a) as the initial state and inject a external periodic signal with $n=5$, $b_f=0.45$, and $\omega=1.8\omega_0$ at the upper-middle boundary. In Fig. 3, it is shown that target waves moving outward are generated [Fig. 3(b)], and the target waves generated continuously from the controlled region can drive the spiral waves out of the system [Fig. 3(c)]. Finally, the whole space is firmly controlled by the target waves [Fig. 3(d)]. After the external force is turned off from the state in Fig. 3(d), no new target waves will be generated and the existing target waves will move out of the boundary; finally, the whole system evolves to the spatially homogeneous steady state with $u=0$, $v=0$.

The numerical results in Fig. 3 is interesting and the approach is rather simple. We inject only one single signal at the boundary, and the controlled area is not very large. This local control method is convenient and may be useful in terminating physiological arrhythmias with the low amplitude pacing. We note that Fig. 3(d) just corresponds to the case (a) of the collision between a wave front and a defect [32]: upon circumnavigating the defect, the two broken ends of the wave front come together and move on.

To have deeper understanding of the phenomenon in Fig. 3, we now discuss in detail the conditions for a successful suppression of a pinned spiral by target waves.

(1) To generate target waves, the amplitude of the external force should be larger than a threshold. Our numerical simulations show that the threshold of b_f is about 0.4 for $n=5$, $\omega=1.8\omega_0$, $R=10\Delta x$, and $b_{in}=0.14$. For a low-amplitude force, target waves cannot be generated. In Fig. 4(a), an example is given for this case.

(2) The frequency of the local force should be chosen suitably. The frequency ω of the external signal needs to be higher than a threshold Ω_1 for generating target waves at the boundary of the system. Ω_1 is about $0.75\omega_0$ for $n=5$, $b_f=0.45$, $R=10\Delta x$, and $b_{in}=0.14$, while the frequency of the pinned spiral ω_s is $0.72\omega_0$. The condition $\Omega_1>\omega_s$ is similar to the case for the suppression of a free spiral [35,36].

However, Ω_1 is only the threshold for generating target waves, not for suppressing the pinned spiral. There exists another threshold Ω_2 (Ω_2 is about $1.36\omega_0$ for $n=5$, $b_f=0.45$, $R=10\Delta x$, and $b_{in}=0.14$), below which the pinned spiral can not be removed from the defect although target waves can be generated. In Fig. 4(b), such an situation is shown. With a frequency $\omega=1.2\omega_0$ ($\Omega_1<\omega<\Omega_2$), the target wave front breaks into two parts at the defect. One broken part and the initial spiral merge to a wave front and propagate forward. The other broken part will form a new spiral and anchor to the defect. This process repeats continuously and the spiral remains unsuppressed. Generally, higher frequency is better for unpinning a spiral.

(3) The radius R of the defect is very important in the interaction between target waves and the pinned spiral. When the radius R is too big, the local force may fail to unpin the spiral [see Fig. 4(c)]. In this case target waves repetitively remove the spiral and form a new spiral, similar to the case

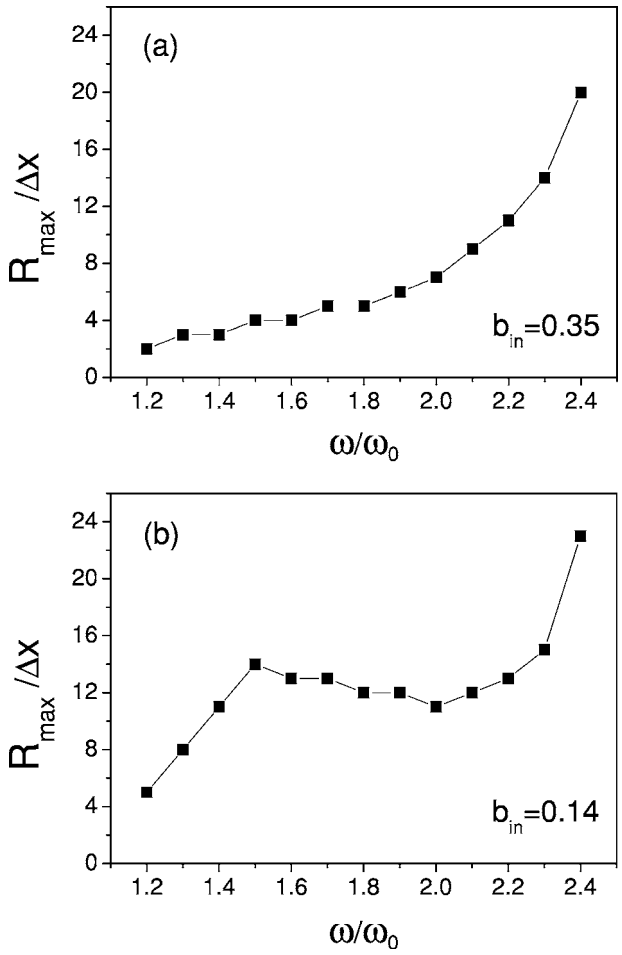

FIG. 5. Dependence of the maximal radius $R_{\max}$ of the defect on the control angular frequency ω. (a) $b_{in}=0.35$ and (b) $b_{in}=0.14$. The other parameters are $n=5$ and $b_f=0.45$.

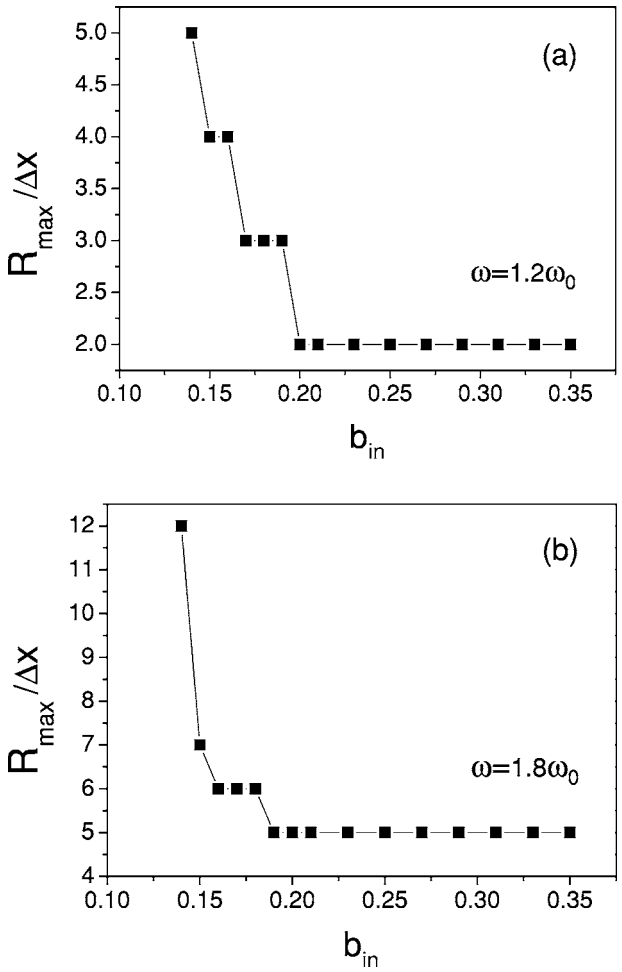

FIG. 6. Variation of the maximal radius $R_{\max}$ of the defect with the parameter b_{in}. (a) $\omega=1.2\omega_0$ and (b) $\omega=1.8\omega_0$. The other parameters are $n=5$ and $b_f=0.45$.

in Fig. 4(b). Numerical simulations show that there exists a critical $R_{\max}$ for fixed b_f, ω, b_{in}, and b_0, and one cannot remove the pinned spiral with the target waves for $R>R_{\max}$.

(4) b_{in} of the defect is also an important parameter. Generally, for a bigger b_{in} (less excitable), it is more difficult to suppress a spiral with target waves. In Fig. 4(d), this case is shown. Target waves cannot unpin the spiral after we after we increase b_{in} from $b_{in}=0.14$ (Fig. 3) to 0.35.

Since the maximal radius $R_{\max}$ of the defect is an important parameter for the local control of a pinned spiral, let us study how $R_{\max}$ varies when we change ω and b_{in}. We first investigate the dependence of $R_{\max}$ on the control angular frequency ω. We inject a signal of $b_f=0.45$, and vary the control frequency in a wide range. In Fig. 5(a), the R_{max}-ω relation is shown for an unexcitable defect of $b_{in}=0.35$. One can see that the maximal radius $R_{\max}$ of the defect increases with the angular frequency ω. In Fig. 5(b), the same relation is shown for a subunexcitable defect of $b_{in}=0.14$. Different from Fig. 5(a), the maximal radius $R_{\max}$ of the defect does not monotonously increase with angular frequency ω. Instead, there are a local maximal value ($\omega=1.5\omega_0$) and a local minimal value ($\omega=2\omega_0$). The dynamic behavior become complicated and there does not exist a clear $R_{\max}$ for $\omega>2.4\omega_0$. For example, for $\omega=2.5\omega_0$ ($b_f=0.45$, $b_{in}=0.35$), locally generated target waves can remove a pinned spiral for $R\in[0,28\Delta x]$ and $R\in[33\Delta x,38\Delta x]$ but fail for $R\in[29\Delta x,32\Delta x]$.

We now turn our attention to the relation between the maximal radius $R_{\max}$ and the parameter b_{in} of the defect. We inject an external signal of $b_f=0.45$ for a defect with different b_{in}. It is found that R_{max} reduces rapidly with the increasing of the parameter b_{in} at the beginning, and then it remains practically unchanged for large b_{in} as shown in Fig. 6. We note that there exists a transition at $b_{in}=0.13$. When b_{in} is close to b_0—e.g., $0.1<b_{in}\leqslant 0.13$—$R_{\max}$ becomes indefinite; i.e., the pinned spiral can be completely suppressed no matter how large the defect is.

In summary, with a modified FitzHugh-Nagumo model of a two-dimensional excitable medium, we have studied the interaction of a pinned spiral and target waves generated by an external periodic force localized at a small boundary region. We show that under certain conditions—i.e., for a suitable choice of b_f, ω, R, and b_{in}—target waves may be generated by the external signal, and then the target waves may drive the pinned spiral out of the excitable medium. And the system is finally controlled by the target waves. In particular,

the relations among the maximal radius $R_{\max}$ of the defect, the angular frequency ω of the external signal, and the parameter b_{in} of the defect are investigated in detail. In addition, we obtain some other interesting results. For example, under certain conditions, the target wave front may break into two parts at the defect, one broken part and the original spiral merge to one wave front and move on, and the other broken part forms a new spiral and is pinned to the defect. Since a spiral pinned to an anatomical defect may create an anatomical reentry that leads to a class of physiological arrhythmias, we expect that the results in this paper may be helpful in the study of terminating physiological arrhythmias by local-low-amplitude and high-frequency pacing.

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