Suppress Winfree Turbulence by Local Forcing Excitable Systems

Hong Zhang,[1] Zhoujian Cao,[2] Ning-Jie Wu,[1] He-Ping Ying,[1] and Gang Hu[3,2,*]

[1]*Zhejiang Institute of Modern Physics and Department of Physics, Zhejiang University, Hangzhou 310027, China*

[2]*Department of Physics, Beijing Normal University, Beijing, 100875, China*

[3]*Chinese Center for Advanced Science and Technology (World Laboratory), Beijing 8730, China*

(Received 25 November 2004; published 12 May 2005)

The occurrence of Winfree turbulence is currently regarded as one of the principal mechanisms underlying cardiac fibrillation. We develop a local stimulation method that suppresses Winfree turbulence in three-dimensional excitable media. We find that Winfree turbulence can be effectively suppressed by locally injecting periodic signals to only a very small subset (around some surface region) of total space sites. Our method for the first time demonstrates the effectiveness of local low-amplitude periodic excitations in suppressing turbulence in 3D excitable media and has fundamental improvements in efficiency, convenience, and turbulence suppression speed compared with previous strategies. Therefore, it has great potential for developing into a practical low-amplitude defibrillation approach.

DOI: 10.1103/PhysRevLett.94.188301 PACS numbers: 82.40.Ck, 05.45.−a, 82.20.−w

The problems of pattern formation and transition (including both ordered and turbulent patterns) are central to nonlinear science concerning extended systems. Different patterns represent different functions and properties in realistic systems. Some patterns are beneficial and others harmful. Therefore, the topic of pattern and turbulence control for realizing wanted patterns and avoiding undesirable ones is of broad interest in practical applications. Cardiac systems are typical excitable extended systems and support various patterns including rest patterns, scroll wave patterns, and turbulent patterns [1,2]. Transitions from scroll wave patterns to turbulence (due to spiral wave breakup or scroll wave filament expansion) may induce ventricular fibrillation leading to serious cardiac disease, even to sudden cardiac death [3–8]. Therefore, the problem of scroll wave and turbulence suppression to return the excitable media to a stable rest state is highly relevant to cardiac defibrillation [2].

The only clinical method currently accepted in performing cardiac defibrillation is to apply a large shock to body surface or directly to cardiac muscle [9,10]. These large-amplitude shocks may damage the cardiac tissue and cause serious pains [11]. Therefore, in both nonlinear science and cardiac physiology fields there is a growing experimental and theoretical effort to develop low-amplitude defibrillation methods. However, most of the theoretical works regarding defibrillation of cardiac systems have considered only two-dimensional (2D) systems (or few coupled 2D systems layered together) [12–14], while real ventricles are clearly 3D objects. Global controls in 3D media have been investigated [15,16]. In particular, in [15] the authors have performed suppression of Winfree turbulence by applying global periodic forcing [17]. The difficulty of injecting an external signal into the whole 3D space sites restricts the practical utilization of this global method. A number of previous experiments have explored the use of local-low-amplitude and high-frequency pacing as an alternative defibrillation technique [18]. However, in these experiments, the pacing had only a local effect, resulting in only small areas of organized electrical activity. Once the pacing was suspended, the local region of capture was reinvaded by surrounding electrical activity, and the tissue remains in a state of fibrillation. Calcium channel blocking with a drug has been suggested to improve the effect of local pacing [19]. Nevertheless, how to use local-low-amplitude pacing for globally defibrillating cardiac tissue remains still an unsolved problem.

In the last decade, many local and global control methods, including both feedback [20–23] and nonfeedback [24–26] methods, have been developed for taming chaotic extended systems. Most of the works on spatiotemporal chaos suppression have been restricted in 1D or 2D spatial systems. In this work we propose for the first time to suppress scroll waves and turbulence in 3D excitable media by applying local and periodic excitations and focus on optimizing turbulence suppression in terms of efficiency, convenience, and rapidity.

We use the general Barkley model, a simplified monodomain model, to describe the electrical activities of cardiac tissue [27].

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

where ε is the ratio of the time scale of the activator u (the voltages of cardiac cell membrane) over that of the inhibitor v (the transmembrane currents). Spiral waves of the 2D Barkley model cannot break up to turbulence. On the other hand, in 3D space this model can support scroll waves which can develop to Winfree turbulence with certain parameter combination due to negative-tension instability of vortex filaments [15,28]. Figure 1 demonstrates our attempts in suppressing such turbulence through various local stimulations. An example of Winfree turbulence of the Barkley model is shown in Fig. 1(a), where turbulence formation through the mechanism of filament expansion and stretching is clearly shown (please refer to Fig. 2 of

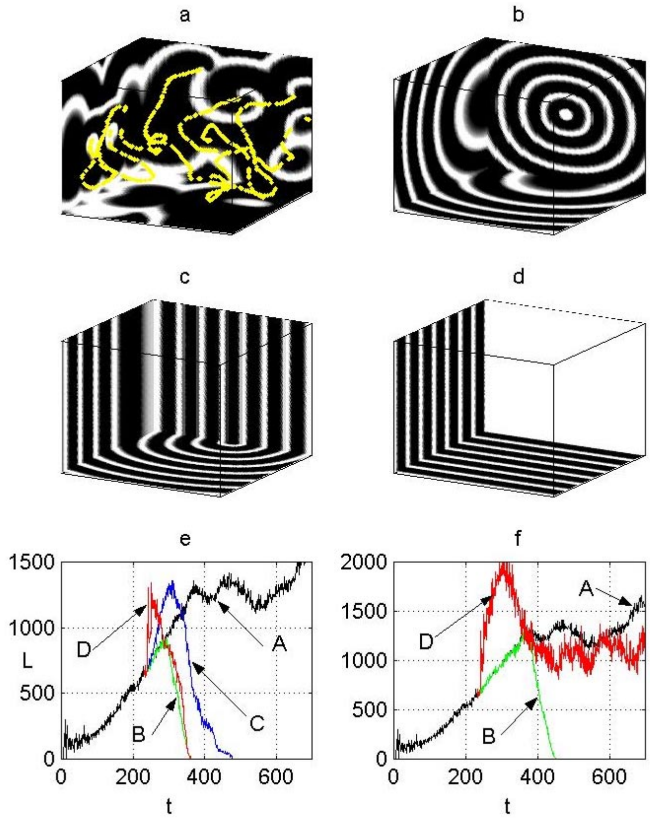

FIG. 1 (color online). (a) Winfree turbulence of the excitable Barkley model. Thin lines show filaments of rotating scroll waves. $a = 1.1$, $b_0 = 0.19$, and $\varepsilon = 0.02$ (these parameters are used in Table I and also in Figs. 2 and 3), at which the rotation frequency of spiral waves is $\omega_0 = 1.19$. A 3D $60 \times 60 \times 60$ cube is considered with space discretization of $150 \times 150 \times 150$ sites in numerical simulations. (b)–(d) Asymptotic states after applying $b(t) = b_0 + b_f \cos(\omega t)$ with $b_f = 0.75$, $\omega = 1.6$ in the controlled sites. (b) A small $6 \times 6 \times 6$ cube around the center of the back surface is injected. (c) A $1 \times 6 \times 150$ strip in the middle line of the back surface is injected. (d) The $1 \times 150 \times 150$ back surface plane is stimulated. (e) The variations of the filament lengths L vs time t. Here all local injections are applied at time $t = 240$, corresponding to the Winfree turbulence of state (a). Curve A: without injection, curve B: local injections on the cube of (b), curve C: local stimulation on the surface strip of (c), and curve D: local stimulation on the surface plane of (d). (f) Same as (e) except for using $b_f = 0.61$ for the cube injection and $b_f = 0.69$ for the surface plane injection.

[15] for a detailed description). In order to suppress the turbulence, previous work [15] applied global excitation to the system by replacing parameter $b = b_0 = 0.19$ with weak periodic modulation

$$b(t) = b_0 + b_f \cos(\omega t) \tag{2}$$

and applying the external signal $b_f \cos(\omega t)$ to all discretization sites. The key strategy of our local periodic forcing is to apply periodic signals to only a small number of sites while leaving most of the sites untouched. The idea is that these local forcings may stimulate some desirable ordered waves first in the injected area, which may propagate in the excitable medium, and then suppress turbulent waves and complex filaments. We apply the periodic signal $b_f \cos(\omega t)$, $b_f = 0.75$ to a small cube [$6 \times 6 \times 6$ sites, Fig. 1(b)], a surface strip [$1 \times 6 \times 150$, Fig. 1(c)], and a surface plane [$1 \times 150 \times 150$, Fig. 1(d)], respectively. It is found that local signals stimulate spherical target waves [1(b)], cylindrical target waves [1(c)], or planar waves [1(d)] and successfully suppress turbulence and scroll waves. These local injections of Fig. 1 are low-amplitude stimuli with the amplitude ($b_f = 0.75$) in the same order of the variables u and v.

Comparing the results of the global excitation in [15] with those of the present local stimulations, the latter methods show a number of advantages. First, the global method needs to inject the external signal to all space sites, and this is inconvenient in many practical situations (e.g., it is difficult to apply electrical impulses to a large area of interior cardiac body). On the contrary, it is much more convenient for our methods to inject signals to partial areas around the surface of the system. Second, the turbulence suppression speed of various local stimulations described in Fig. 1 are 10 times faster than that of the global one in [15]. In Fig. 1(e) we plot the time variations of the total filament lengths L without stimulation and with cubic, surface strip, and surface plane local injections, respectively. The local excitations can reduce filament length to zero for 20–30 rotation periods of the original scroll waves while it takes more than 300 periods for the global forcings to shrink the filament length to close to zero [see Fig. 2(i) of [15]].

For local methods it is crucial to enhance the control efficiency, e.g., to achieve successful turbulence suppression with total power of the injected signals as small as possible. Assuming the total injected power proportional to $M \cdot b_f^2$ with M being the number of the injected sites, we find that the cubic stimulation obviously provides the highest efficiency. In order to reduce filament length to zero with a similar speed, the cubic injection requires signal power that is 2 orders of magnitude lower than that of the surface plane stimulation. The results of Fig. 1(f) are even more striking, where while the $6 \times 6 \times 6$ cubic stimulation can successfully suppress turbulence at the stimulation amplitude $b_f = 0.61$, the $1 \times 150 \times 150$ surface plane stimulation fails at considerably larger amplitude $b_f = 0.69$. The reason for this surprising phenomenon can be understood as follows. It is generally accepted that planar wavefronts can travel faster than convex wave fronts with significant positive curvature [19,29]. However, in order to annihilate turbulence by local excitations, it requires not only fast propagation of wave fronts but also quick formation of a complete seed wave front. Generation of a large planar wave front is much more difficult than that of a

TABLE I. Comparison of various excitation methods. The results denoted by $*$'s are cited from [15].

	Global ($150 \times 150 \times 150$)	Cube area around surface ($6 \times 6 \times 6$)	Strip surface ($1 \times 6 \times 150$)	Plane surface ($1 \times 150 \times 150$)
The optimal frequency	1.2*	1.6	1.63	1.61
Excitation amplitude b_f	0.03*	0.75	0.75	0.75
Number of sites injected M	4.096×10^6	216	800	25 600
Total signal power $Mb_f^2 \approx$	3790	122	450	14 400
Time for turbulence suppression $\approx$	1500*	120	196	120

small spherical wave front. In our case the latter factor turns to be crucial and this leads to the possibility that the overall efficiency of the surface plane stimulation can be considerably lower than that of the cubic stimulation as we see in Figs. 1(e) and 1(f). In order to quantitatively compare the efficiencies of different schemes of turbulence suppression we present Table I which clearly shows that the local pacing on a cube has obviously the best overall properties with both lower power of injected signals and fast suppression of Winfree turbulence. We therefore focus our further effort on the detailed characterization of the cubic stimulation method.

As shown in Fig. 2, we find that with the same Barkley model the results of the cubic stimulation depend on forcing parameters including forcing frequency, forcing amplitude, and injection area. Figure 2 shows the parameter range where local forcing can successfully suppress the existing turbulent scroll waves. There are several characteristic boundaries to this range. First, this range is restricted within a frequency zone [Fig. 2(a)], and frequencies above or below do not provide successful turbulence suppression. The forcing frequency needs to be higher than a threshold ω_0 ($\omega_0 \approx 1.19$ is the rotation frequency in 2D system). This is because target waves generated by the local excitation can suppress existing scroll waves only if its frequency is higher than that of the latter [30]. On the other hand, there is an upper bound to the effective forcing frequency. The target waves are generated by the periodic signals in the presence of turbulence and scroll waves. In order to effectively stimulate target waves, the forcing frequency should not be too far from ω_0 for achieving a 1:1 resonant excitation from the existing scroll wave background. This gives rise to the upper bound of the zone of Fig. 2(a). Second, the injection area and the forcing amplitude need to be sufficiently large. Our cubic stimulation fails for $n \leq 4$ ($n \times n \times n$ sites are injected) and $b_f \leq 0.53$ [Figs. 2(b)–2(d)]. The reasons for these conditions are clear. In order to suppress turbulence with local forcing, the forcing amplitude needs to be larger than a threshold to stimulate spherical target wave fronts. In addition, the injection area needs to be larger than a threshold so that the wave fronts generated have a curvature smaller than a critical value to allow target wave propagation [31]. Nevertheless, when n and b_f are above the thresholds the speed of turbulence annihilation is no longer sensitive to n and b_f. In other words, a further increase of n and b_f does not effectively reduce the suppression time. The thresholdlike behaviors of the local cubic stimulation shown in Figs. 2(b)–2(d) suggest some optimal parameter combination to achieve high control efficiency (e.g., $n = 6$, $b_f = 0.7$). This optimization allows fast turbulence suppression with low signal power, meaning fast curing with low electrical power application and low cardiac tissue disturbance during defibrillation.

Figure 3 demonstrates the mechanism of suppression of Winfree turbulence by local cubic stimulation. The local excitation on a small cube stimulates spherical target wave fronts, which invade the turbulent surrounding and suppress turbulence by pushing the filaments of the scroll waves out of the excitable medium during their propagation [Figs. 3(a)–3(d). In Figs. 3(e) and 3(f) we show how the ordered waves wipe out the remaining filaments and drive the system to the desirable rest state, after lifting the periodic forcing at the turbulent state of Fig. 3(c).

In conclusion, we have developed an effective local periodic forcing method for eliminating Winfree turbulence in 3D excitable media and revealed its desirable advantages of efficiency, convenience, and rapidity.

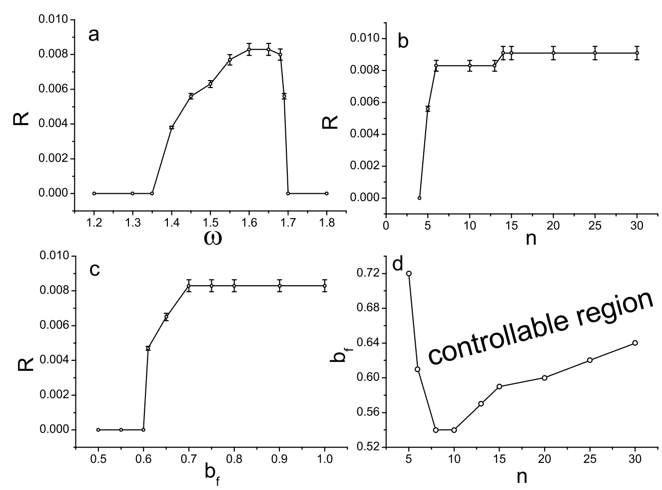

FIG. 2. Turbulence suppression speed $R = 1/T$ of the cubic ($n \times n \times n$) injection plotted for different signal parameters where T is the time needed for turbulence suppression. (a) $n = 6$, $b_f = 0.75$. R plotted vs ω. (b) $b_f = 0.75$, $\omega = 1.6$. R vs n. (c) $\omega = 1.6$, $n = 6$, R vs b_f. (d) The boundary of the controllable region in (b_f, n) plane for $\omega = 1.6$. Controllability is defined such that the filament length shrinks to zero at $t \leq 500$ for the given parameters.

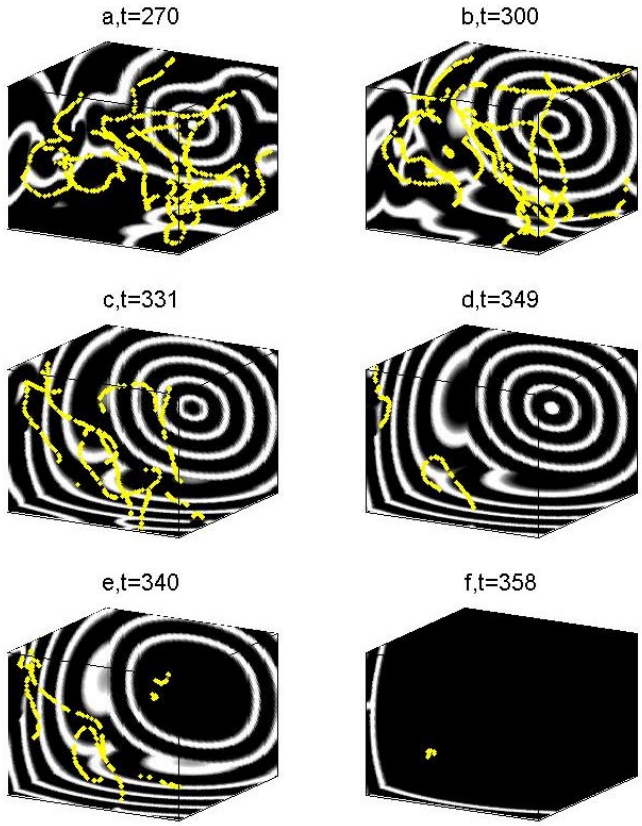

FIG. 3 (color online). (a)–(d) Demonstration of the mechanism of the local cubic injection of Fig. 1(b). Local periodic forcings generate spherical target waves near the injected area, which then propagate in the space and push turbulence and all scroll wave filaments out of the excitable medium. (e),(f) The evolution of the medium after the injection signals are lifted at $t = 331$ [i.e., from state (c)]. The system approaches the desirable rest state without the external forcing, and complete black (indicating the desirable rest state) is observed after $t \approx 360$.

Finally, we emphasize that the model used in this Letter is too simple for simulating actual cardiac systems. In order to give some useful instruction for practical cardiac defibrillation, further investigation taking into account more realistic cardiac activities is needed. On the other hand, since the simplified model catches the general feature of excitable media, our local excitation method is expected to be applicable for suppressing turbulence of excitable systems in wide fields, e.g., chemical reaction systems and neural network systems besides the cardiological ones. For instance, we have checked that our local excitation method works in other excitable and oscillatory models, such as the Bär equation and the Ginzburg-Landau equation.

This work was supported by the National Natural Science Foundation of China and the Nonlinear Science Project of China.

*Corresponding author.
Electronic address: ganghu@bnu.edu.cn
Present address: Beijing-Hong Kong-Singapore Joint Center of Nonlinear and Complex Systems, Beijing Normal University Branch, Beijing.

[1] A. T. Winfree, *When Time Breaks Down* (Princeton University Press, Princeton, NJ, 1987).
[2] For reviews, see Chaos **8**, No. 1 (1998) and **12**, No. 3 (2002).
[3] A. T. Winfree, Science **266**, 1003 (1994).
[4] R. A. Gray *et al.*, Science **270**, 1222 (1995).
[5] A. V. Panfilov and P. Hogeweg, Science **270**, 1223 (1995); Phys. Rev. E **53**, 1740 (1996).
[6] L. Glass, Phys. Today **49**, No. 8, 40 (1996).
[7] R. A. Gray, A. M. Pertsov, and J. Jalife, Nature (London) **392**, 75 (1998).
[8] F. X. Witkowski *et al.*, Nature (London) **392**, 78 (1998).
[9] M. S. Eisenberg *et al.*, Sci. Am. **254**, No. 5, 25 (1986).
[10] L. W. Piller, *Electronic Instrumentation Theory of Cardiac Technology* (Staples Press, London, 1970).
[11] L. Tung, Proc. IEEE **84**, 366 (1996).
[12] V. N. Biktashev and A. V. Holden, J. Theor. Biol. **169**, 101 (1994).
[13] A. V. Panfilov *et al.*, Phys. Rev. E **61**, 4644 (2000).
[14] S. Sinha, A. Pande, and R. Pandit, Phys. Rev. Lett. **86**, 3678 (2001).
[15] S. Alnonso, F. Sagues, and A. S. Mikhailov, Science **299**, 1722 (2003).
[16] M. Vinson *et al.*, Nature (London) **386**, 477 (1997).
[17] Y. Braiman and I. Goldhirsch, Phys. Rev. Lett. **66**, 2545 (1991).
[18] For example, E. G. Daoud *et al.*, Circulation **94**, 1036 (1996); J. M. Kalman *et al.*, J. Cardiovasc. Electrophysiol. **7**, 867 (1996).
[19] A. T. Stamp, G. V. Osipov, and J. J. Collins, Chaos **12**, 931 (2002).
[20] Hu Gang and Qu Zhilin, Phys. Rev. Lett. **72**, 68 (1994).
[21] I. Aranson, H. Levine, and L. Tsimring, Phys. Rev. Lett. **72**, 2561 (1994).
[22] V. S. Zykov *et al.*, Phys. Rev. Lett. **92**, 018304 (2004).
[23] G. M. Hall and D. J. Gauthier, Phys. Rev. Lett. **88**, 198102 (2002).
[24] I. Wygnanski, AIAA Report No. 97-2117.
[25] G. Baier, S. Sahle, and J. Chen, J. Chem. Phys. **110**, 3251 (1999).
[26] H. Zhang, B. Hu, and G. Hu, Phys. Rev. E **68**, 026134 (2003); H. Zhang *et al.*, Phys. Rev. E **66**, 046303 (2002).
[27] D. Barkley, M. Kness, and L. S. Tuckerman, Phys. Rev. A **42**, 2489 (1990).
[28] V. N. Biktashev, A. V. Holden, and H. Zhang, Phil. Trans. R. Soc. A **347**, 611 (1994); F. H. Fenton *et al.*, Chaos **12**, 852 (2002).
[29] J. J. Tyson and J. P. Keener, Physica (Amsterdam) **32D**, 327 (1988).
[30] K. J. Lee, Phys. Rev. Lett. **79**, 2907 (1997); F. Xie, Z. Qu, J. N. Weiss, and A. Garfinkel, Phys. Rev. E **59**, 2203 (1999).
[31] V. S. Zykov, *Simulation of Wave Processes in Excitable Media* (Manchester University Press, New York, 1987), p. 117.