Resonance Induced Pacemakers: A New Class of Organizing Centers for Wave Propagation in Excitable Media

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Propagation of waves in an extended excitable system is considered. It is shown that traveling wave fronts can be triggered and maintained via local periodic modulations of an appropriate system parameter. For a finite range of perturbation frequencies, this new class of pacemakers introduces spatiotemporal self-organization in an otherwise quiescent medium. Excitation waves of activity similar to those observed in heart tissue cultures and other biological preparations can emerge in the presence of these pacemakers.

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Wave propagation in excitable media provides an excellent example of spatiotemporal self-organization. Target wave fronts have been observed in both biological [1–4] and chemical systems [5–7]. The underlying mechanisms for the inception of these patterns are of practical interest as they provide valuable insight into relevant problems such as ventricular tachycardias [4]. For example, paroxysmal starting and stopping of circulating waves of activity can give rise to serious complex rhythms in the cardiac system [8]. Although, wave propagation from a source point is reasonably well understood, some curiosity persists regarding the emergence of the pacemaker (source) regions [1]. The two common triggers for the emergence of pacemakers discussed in the literature [9,10] are diffusive instability and local physical/chemical inhomogeneities.

Inception of wave fronts in a quiescent excitable media is traditionally achieved via a large stimulus provided to an accessible control parameter [11,12]. This usually involves parametrically crossing the bifurcation point separating the homogeneous and oscillatory states. In this Letter, we report a new mechanism for creating pacemakers capable of inducing spontaneous pattern formation in a steady state. Instead of superthreshold perturbation with a large amplitude, small amplitude modulation of a control parameter with an appropriate tuning frequency (bifurcation point in parameter space of the autonomous system is not crossed). For this class of organizing centers the quiescent excitable system, upon inspection, abruptly starts exhibiting wave propagation without the mandatory large amplitude parameter gradient between the pacemaker region and the surrounding environment. Spontaneous (abrupt) spatiotemporal self-organization [13] of a quiescent excitable media in the absence of known factors such as random concentration fluctuations and physical defects [14] could be attributed to such pacemakers.

In order to study the effect of a resonance induced wave propagation on an extended excitable system we use the modified Oregonator equations [15] accounting for the photosensitivity [16,17] of the Beluosov-Zhabotinsky reaction. After a series of scalings and stoichiometric approximations, the dimensionless spatiotemporal model can be expressed as

$$
\begin{aligned}
\epsilon \partial_\tau x &= x(1 - x) + y(q - x) - \epsilon \kappa_f x + p_2 \phi \\
&\quad + \epsilon D_x \nabla^2 x\,, \\
\epsilon' \partial_\tau y &= 2hz - y(q + x) + \epsilon' \kappa_f (y_0 - y) + p_1 \phi \\
&\quad + \epsilon' D_y \nabla^2 y\,, \\
\partial_\tau z &= x - z - \kappa_f z + \left(\frac{p_1}{2} + p_2\right)\phi + D_z \nabla^2 z\,,
\end{aligned}
\tag{1}
$$

where

$$
x = \frac{2k_{O4}}{k_{O3}A} X, \qquad y = \frac{k_{O2}}{k_{O3}A} Y\,,
$$

$$
z = \frac{k_{O4}k_{O5}M}{(k_{O3}A)^2} Z, \qquad \tau = k_{O5}Mt
$$

are the rescaled dimensionless variables, and

$$
\epsilon = \frac{k_{O5}M}{k_{O3}A}, \quad \epsilon' = \frac{2k_{O4}k_{O5}M}{k_{O2}k_{O3}A}, \quad q = \frac{2k_{O1}k_{O4}}{k_{O2}k_{O3}}\,,
$$

$$
y_0 = \frac{k_{O2}}{k_{O3}A} Y_0, \quad \kappa_f = \frac{1}{k_{O5}M} k_f, \quad \phi = \frac{2k_{O4}}{(k_{O3}A)^2} \Phi\,,
$$

$$
p_1 = \frac{V}{0.089 + V + 15H^2A}\,,
$$

$$
p_2 = \frac{15H^2A}{0.089 + V + 15H^2A}
$$

are the dimensionless system parameters. To integrate associated partial differential equations [Eq. (1)] the system size was chosen to be 1 cm (one spatial dimension) and then divided into 100 grid elements for simulation using a 3rd-order Runge-Kutta algorithm subjected to Neumann boundary conditions. A constant step size in time ($\Delta = 0.005$) was used.

The dynamics of the temporal part of the model system were studied using linear stability analysis and numerical integration. Scanning the system dynamics as a function of light intensity (ϕ) reveals the existence of a subcritical Hopf bifurcation point [15]. Consequently, the system is oscillatory for $\phi < 8.0 \times 10^{-7}$, bistable between a stable focus and a stable limit cycle $8.0 \times 10^{-7} < \phi < 8.05 \times 10^{-7}$, and exhibits steady state dynamics for $\phi > \phi_c$ where $\phi_c = 8.05 \times 10^{-7}$. Analogously, the spatiotemporal system [Eq. (1)] exhibits traveling wave and steady state behavior at corresponding parameter values. It needs to be pointed out that in all of our simulations, parameter regions of bistability and oscillatory dynamics are intentionally precluded as the control parameter $\phi > \phi_c$ where $\phi_c = 8.05 \times 10^{-7}$.

A frequency and amplitude scan in the vicinity of the subcritical Hopf bifurcation reveals the extent in parameter space where resonance induced excitation can be observed. The U-shaped curve in Fig. 1 represents the parameter domain where nonlinear resonance lowers the threshold for the observance of the firing pattern. The existence of the optimum frequency is intimately related to the fact that the excitable system [Eq. (1)] has a resonance (nonlinear) at a frequency close to the imaginary part of the eigenvalues of the flow dynamics linearized around its fixed point.

Detailed investigation of the invoked dynamics within the U-shaped curve reveals behavior consistent with two-frequency nonlinear resonance. Figure 2(a) shows three induced time series and the corresponding forcing functions responsible for their generation. Moreover, we calculated the firing number (No. of excitations/No. of perturbations) as a function of the forcing frequency in the U-shaped curve. It reveals a devil's staircase as shown in Fig. 2(b). The existence of a devil's staircase with clearly demarcated phase-locked domains is typical of forced oscillatory/excitatory dynamics.

For resonance induced pacemakers we choose $\phi > \phi_c$ such that the extended excitable media is quiescent. Subsequently parameter ϕ is modulated sinusoidally for a finite subregion of the excitable media (first ten oscillators),

$$\phi = \phi_0[1 + \alpha \sin(2\pi\nu\tau)], \qquad (2)$$

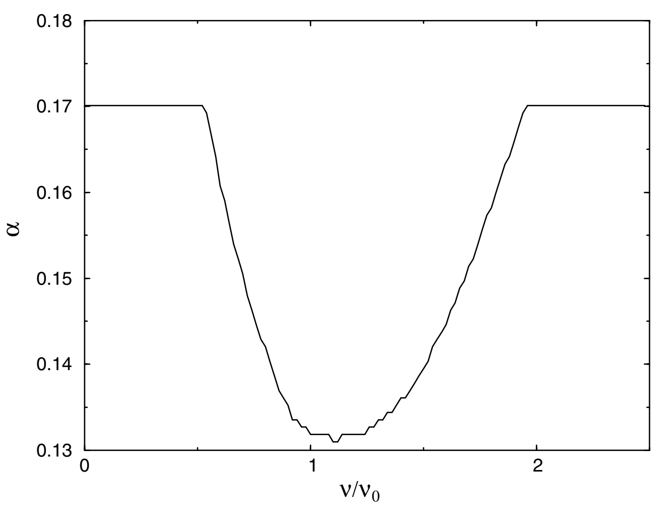

FIG. 1. The U-shaped curve encapsulates the region in parameter space (amplitude-frequency domain) where subthreshold modulations of ϕ triggers excitation in the model system ($\phi_0 = 9.7 \times 10^{-7}$). The model parameters of the autonomous system are: $k_{O1} = (2\ \mathrm{M}^{-3}\,\mathrm{s}^{-1})\mathrm{H}^2$, $k_{O2} = (3 \times 10^6\ \mathrm{M}^{-2}\,\mathrm{s}^{-1})\mathrm{H}$, $k_{O3} = (42\ \mathrm{M}^{-2}\,\mathrm{s}^{-1})\mathrm{H}$, $k_{O4} = 3 \times 10^3\ \mathrm{M}^{-1}\,\mathrm{s}^{-1}$, $k_{O5} = 5\ \mathrm{M}^{-1}\,\mathrm{s}^{-1}$, $k_f = 1.05 \times 10^{-3}\,\mathrm{s}^{-1}$, $\nu_0 = 0.02\,\mathrm{s}^{-1}$, $h = 0.5$, $H = 0.37$ M, $A = 0.15$ M, $M = 0.2\ \mathrm{M}^{-1}$, and $V = 0.05$ M. Initial conditions: $X_0 = 0$ M, $Y_0 = 1 \times 10^{-4}$ M, and $Z_0 = 0$ M, while frequency and amplitude of the superimposed periodic perturbations are scanned. $\alpha = 0.17$ corresponds to the parameter threshold that ensures that $\phi > \phi_c$ where $\phi_c = 8.05 \times 10^{-7}$.

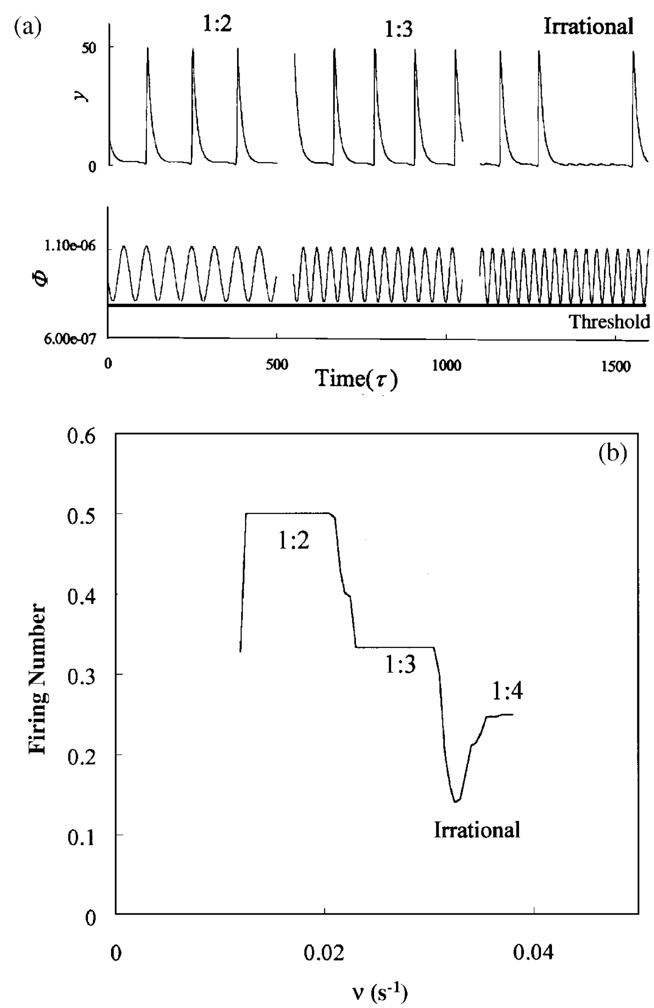

FIG. 2. Details within the U-shaped curve reveal different types of phase-locked dynamics consistent with the existence of a nonlinear resonance between the frequency of the external forcing and that of the damped oscillations. (a) Time series for different firing patterns invoked by corresponding periodic modulations. (b) Devil's staircase encapsulated by the U-shaped region for resonance induced excitation. It indicates the inception of both rational and irrational firing numbers under the influence of periodic modulations.

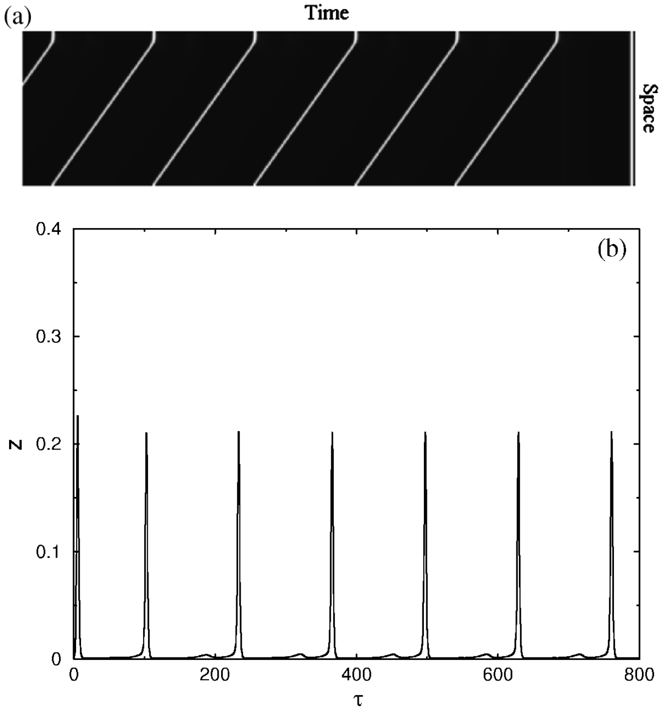

FIG. 3. (a) Space-time plot of the excitable media (100 oscillators) in one spatial dimension (system size = 1 cm) under Neumann boundary conditions. It indicates inception of wave propagation in the homogeneous state by virtue of periodic modulations of the light flux. The model parameters are same as Fig. 1, Initial conditions: $X_0 = 0$ M, $Y_0 = 1 \times 10^{-4}$ M, and $Z_0 = 0$ M. Diffusion parameters: $D_x = 1.5 \times 10^{-5}$, $D_y = 1.68 \times 10^{-5}$, and $D_z = 8.75 \times 10^{-6}$. Control parameters: $\nu = (1.1 \times \nu_0)$ where $\nu_0 = 0.02$ s^{-1} and $\alpha = 0.165$. (b) Local time series of the first oscillator for the space-time plot of (a).

ensuring that ϕ never crosses the excitation threshold of the autonomous system (ϕ_c) in parameter space. Such stimuli are known to evoke a harmonic response [18,19] in the homogeneous media. However, consistent with results of the temporal model, for a range of forcing frequencies (U-shaped resonance curve), perturbations can induce excitation waves that initiate at the site of stimulation and subsequently traverse the entire system.

Figure 3(a) shows the space-time plot for the extended excitable system of 100 diffusively coupled oscillators in one spatial dimension. The perturbations are superimposed locally, i.e., only the first ten oscillators are modulated parametrically. This results in the emergence of wave propagation in the previously homogeneous state. The local time series of the first oscillator is shown in Fig. 3(b). It indicates inception of a constant velocity propagating pulse in the excitable media.

To reiterate, excitation in our case occurs via resonance between the damped oscillations around the stable fixed point and the periodic perturbations with an appropriate tuning frequency. In our model system, this resonance amplifies the invoked oscillations of the state variables in the neighborhood of the excitable fixed point. For systems with low excitability these resonant oscillations may grow larger such that the system crosses the semicircular separatrix in the state space and consequently triggers an excitation wave. This however does not preclude the emergence of activation waves in highly excitable systems where the stable focus is located at almost the minima of the N-shaped null cline. Continuous periodic perturbations are necessary in order to sustain these waves.

The distinction between the present work and the pioneering work of Kádár *et al.* [17] is twofold: In their work the parameter threshold is being crossed by virtue of the superimposed noise. In this sense their results are similar to the concept of coherence resonance [20] in a spatiotemporal system. Secondly the noisy perturbations in their work are superimposed globally on the extended excitable system. In contrast our simulations involve invoking pattern formation using resonant periodic perturbations that are locally superimposed.

Our results indicate that apart from the existing notions of random concentration fluctuations and defects, local periodic perturbations with an appropriate tuning frequency can also induce wave propagation in a quiescent media. This new class of organizing centers does have stringent prerequisites for inception, hence they could emerge in a number of excitable media. They need to be considered, included, and studied as one of the probable causes for spontaneous pattern formation in an excitable media. This is of practical interest in biological (excitable) media where such abrupt pattern formation could have pathological implications [4,8]. For example, it is possible to envisage a scenario where a part of the media is active (exhibiting oscillations) and the remaining is passive (fixed point behavior). Because of the intrinsic mutual coupling within the two regimes, the oscillations in the active region could translate as an external forcing for the units in the passive region. If this forcing has the right frequency, it could result in the inception and subsequent propagation of the excitation waves in the previously passive domain even if the coupling strength (amplitude) is small.

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