Coexistence of multiple spiral waves with independent frequencies in a heterogeneous excitable medium

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We studied the interactions and coexistence of stable spiral waves with independent frequencies in a heterogeneous excitable medium, using numerical simulations of a spatial system based on the FitzHugh-Nagumo cell model. When the heterogeneity of the medium exceeded a critical value, a transition took place from a single dominant spiral wave to a coexistence of multiple spiral waves with independent frequencies and $n:n-1$ wave conduction blocks. In this case, multiple spiral waves could coexist because they are ''insulated'' from each other by chaotic regions.

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Spiral waves, and their three-dimensional analogs, scroll waves, have been extensively observed in spatial systems, including chemical and biological systems [1,2]. They have been actively investigated for several reasons, one of which is their potential clinical relevance to cardiac arrhythmias, especially ventricular fibrillation, the leading cause of sudden cardiac death in industrialized countries [2,3]. Some studies have claimed that cardiac fibrillation can be characterized by multiple stable spiral waves, with differing frequencies [4], but these claims have not been supported by previous numerical and theoretical studies [5–10]. In particular, previous simulation studies in generic excitable media suggested that when multiple spirals were induced, the fastest stable spiral always swept away all slower spirals in the system. This interaction resulted in a single dominant spiral wave, and a single frequency in the system [5–10]. So far, it is not clear how multiple stable spirals with independent frequencies can coexist. In addition, it is not clear how these spirals interact at the boundaries of different frequency domains.

In this paper, we investigate this problem using the Bär model (a modified FitzHugh-Nagumo model), which 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 [11],

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

where the function $f(u)$ takes the following form

$$f(u)=\begin{cases}0 & 0\leqslant u<1/3\\ 1-6.75u(u-1)^2, & 1/3\leqslant u\leqslant 1\\ 1, & 1<u,\end{cases} \tag{2}$$

and $D=0.5$, $a=0.84$, and $b=0.07$. $\varepsilon(x,y)$ is a spatial parameter representing the heterogeneity of the system. In realistic excitable systems such as cardiac tissue, the heterogeneity is very complex [12]. Here, in order to study the interactions between different spiral waves systematically, we simplified $\varepsilon(x,y)$ as

$$\varepsilon(x,y)=\begin{cases}\varepsilon_1, & 0\leqslant x<L_x/3, \quad 0\leqslant y\leqslant L_y,\\ \varepsilon_1+(\varepsilon_2-\varepsilon_1)(x-L_x/3)/(L_x/3), & L_x/3\leqslant x\leqslant 2L_y/3, \quad 0\leqslant y\leqslant L_y,\\ \varepsilon_2, & 2L_x/3\leqslant x\leqslant L_x, \quad 0\leqslant y\leqslant L_y,\end{cases} \tag{3}$$

and the size of the medium is $L_x=L_y=L=52.5$. Equation (1) was integrated by an explicit scheme with fixed time step $\Delta t=0.005$, and spatial step $\Delta x=\Delta y=0.25$. No-flux boundary conditions were used in all simulations. To study spiral wave interactions, two spiral waves were initiated in the left and right domains by perpendicular waves, respectively.

As $\varepsilon_2\equiv\varepsilon_1$, the system (1) recovers to a homogeneous excitable medium, which exhibited various interesting spiral wave behaviors as ε was varied [11,13,14]. When ε was in [0.02, 0.06], the spiral wave in the homogeneous medium was *stable*, that is, a *stationary* spiral wave, whose tip motion traced a complete circle. In this paper, we fixed $\varepsilon_1\equiv 0.02$, and varied ε_2 in the above range to study the interactions of spiral waves.

Since the two spiral waves were initiated in the left and right halves of the medium, their interaction strongly depended on the degree of heterogeneity of the medium, created by ε_2. For ε_2 below 0.042, each wave generated by the left spiral was able to propagate to the right edge of the medium, so the right spiral wave was swept away by the left spiral, after a transient. Figure 1(a) shows the interaction of two spiral waves in the medium for $\varepsilon_2=0.038$. Due to the

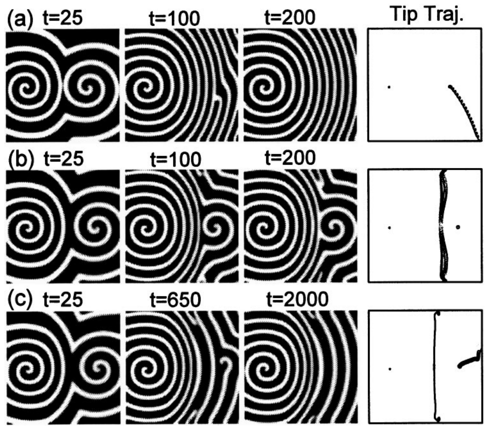

FIG. 1. Evolution of interacting spiral waves (left 3 columns) and the corresponding spiral tip trajectories (right column). (a) $\varepsilon_2 = 0.038$. (b) $\varepsilon_2 = 0.048$. (c) $\varepsilon_2 = 0.056$.

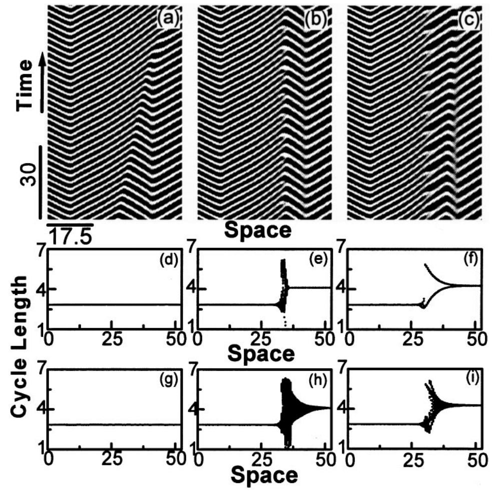

FIG. 2. (a)–(c) Space time plots of the value of the variable u (after transients) on the line $y = L/2$ for Figs. 1(a) and 1(b), respectively. (d)–(f) corresponding plots of cycle length on the line $y = L/2$. (h)–(j) superimposed (i.e., averaged) cycle lengths for all y values. Note the disorder in (e), (h), and (i).

difference of spiral rotation period [often called ''cycle length'' (CL)], wavefronts from the faster spiral ''unwind'' the slower one, eventually arriving at the core area of the slower spiral. These wavefronts then drove the slower spiral to drift toward the boundary with a nearly constant drift velocity, until it finally disappeared off the boundary. The tip activity of the two spirals is shown in the right column. It is clear that the tip of right spiral drifted to the bottom right corner of the medium, but the left one stayed permanently on the left-hand side. This finding, that the faster spiral drives out the slower, has been found in many previous studies [5–10].

When ε_2 was beyond 0.042, but below 0.052, not all wavefronts in the high heterogeneity regions could follow in 1:1 propagation, resulting in wave conduction block in these regions. But in the right-hand region beyond the heterogeneity, the waves reorganized and formed new frequencies, whose average was nearly equal to the frequency of the right spiral. Thus, *the wavebreak region prevented the faster spiral from ''unwinding'' the slower one, and the two spirals with independent cycle lengths could therefore coexist, insulated from one another by the wavebreak in the middle region*. As can be seen in Fig. 1(b) ($\varepsilon_2 = 0.048$), the tips of the two spirals traced circular paths, but wavebreak occured between them, resulting in a highly disordered middle region. The most interesting finding was that as ε_2 was increased beyond 0.052, the original right-hand spiral was swept away by the newly formed wavefronts again, but the frequency of the newly formed wave in the right-hand region was different from that of the faster spiral in the left-hand region. Figure 1(c) shows this behavior for $\varepsilon_2 = 0.056$. The difference in wavelength between the left and right regions, and the wavebreak in the middle region, are both clear.

To understand these interactions, we explored how waves propagate through the middle region. Figures 2(a)–2(c) shows space time plots of wave propagation. We plotted the value of the variable u, restricted to the line $y = L/2$ (after transients have died away). Figures 2(d)–2(f) are the corresponding plots of cycle length on along $y = L/2$, and in Figs. 2(g)–2(i), all cycle lengths (for each y coordinate) are superimposed on the x axis. For $\varepsilon_2 = 0.038$, the spiral wave source in the right-hand region [Fig. 2(a)] was forced to drift to the boundary, and finally disappeared off it. Cycle lengths, evaluated on the line $y = L/2$, are the same as for the whole medium (2.84), so the system has a unique frequency. However, as shown in Fig. 2(b) for $\varepsilon_2 = 0.048$, when two spirals were initiated with independent frequencies in the left- and right-hand regions, they always coexisted, due to the conduction failure in the middle. In the middle region, different degrees of block were intermingled with each other; first three 3:2 blocks, then one 4:3 block, then a repetition of this process. This ''intermingling'' feature is more clearly seen in the enlarged spatiotemporal evolution in Fig. 3(a) with the same parameters as Fig. 2(b). In Figs. 2(e) and 2(h), the cycle lengths in the left- and right-hand regions each remained constant, but in the middle wavebreak region, the cycle length plots showed a very narrow zone of disorder. This disordered zone in the superimposed cycle length plots was wider. Disorder can also be easily observed [Fig. 3(b)] in the spatially averaged plots of the variable u. For ε_2

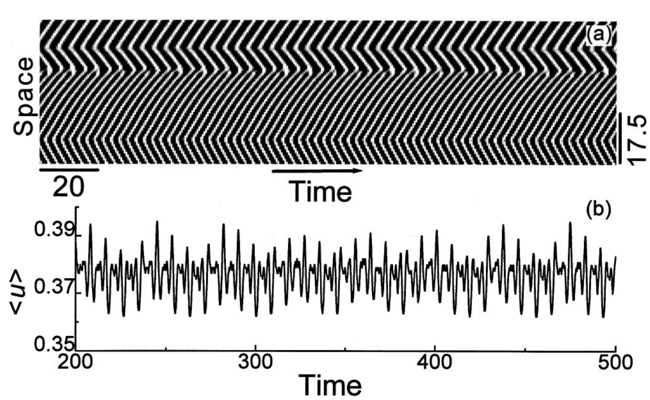

FIG. 3. (a) Enlargement of Fig. 2(b). (b) average value of u for the whole medium, versus time. The intermingling of 4:3 and 3:2 conduction wave blocks is clear.

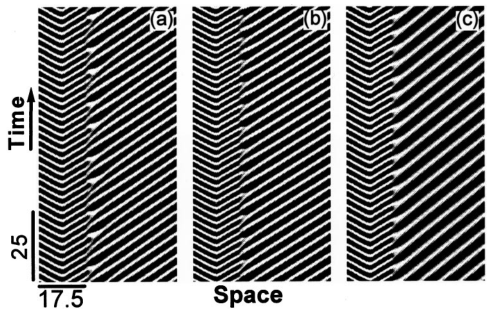

FIG. 4. n:n-1 wave conduction block in excitable medium with heterogeneity given by Eq. (4). (a) 4:3 and 3:2 block intermingled, $\varepsilon_2 = 0.044$. (b) 3:2 block, $\varepsilon_2 = 0.046$. (c) 2:1 block, $\varepsilon_2 = 0.080$.

$=0.052$ in Fig. 2(c), the wave source in the right-hand region was forced to drift to the boundary by these newly formed waves after wavebreak in the middle region. After the right-hand spiral disappeared off the boundary, *the conduction wave block in the middle region was exactly 3:2*, which made the cycle length in the right-hand region 1.5 times that in the left [Fig. 2(f)]. It is interesting to note that the cycle length in the middle region displayed period-2 alternation, but this period-2 decayed to a fixed point as the x coordinate increased to the right. Since the period-2 distribution along the y coordinate was different, the corresponding superimposed cycle lengths in the middle region were a little disordered [Fig. 2(i)].

As the heterogeneity of the medium was increased above the threshold value at which wave conduction failure occurred, wave propagation in the medium displayed a number of interesting conduction blocks. Figure 4 showed a set of n:n-1 blocks with small n, where the heterogeneity of the medium was described by

$$\varepsilon(x,y)=\begin{cases}0.02, & x\leqslant L/3, \quad 0\leqslant y\leqslant L,\\ \varepsilon_2, & x>L/3, \quad 0\leqslant y\leqslant L,\end{cases} \tag{4}$$

and only one spiral wave was initiated at the left region of the medium, where the spiral has the faster frequency. When ε_2 was a little larger than the threshold for wave break, wave propagation displayed various 4:3 and 3:2 intermingled conduction blocks. Figure 4(a) shows a combination of 4:3 and 3:2 blocks for $\varepsilon_2 = 0.044$. If ε_2 was increased to 0.046, wave conduction block was exactly 3:2 [Fig. 4(b)]. Finally, as ε_2 became more large, the conduction block was 2:1, which is shown in Fig. 4(c) for $\varepsilon_2 = 0.08$.

The mechanism of wave break in this paper is essentially different from that of spiral wave breakup in a homogeneous medium. The latter is caused by inherent dynamical instabilities in spiral wave propagation [14,15]. Here, wave break was produced purely by the heterogeneity. It can be described quantitatively as follows. First, consider a wave being paced in a homogeneous medium with a pacing cycle CL. For each ε, there is a minimum pacing cycle length ($\mathrm{CL}_{\min}$), such that waves can successfully propagate in the medium *only if the pacing cycle length was above* $\mathrm{CL}_{\min}$; otherwise, conduction block occurs. The $\mathrm{CL}_{\min}$ versus ε measured from one-dimensional cable simulations is shown

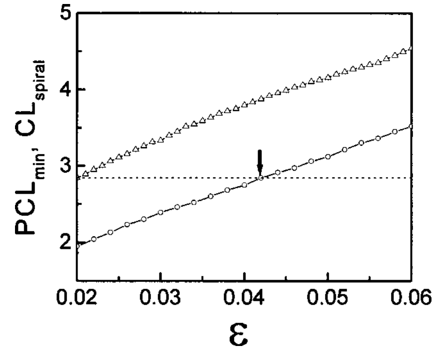

FIG. 5. The minimum pacing cycle length (circles) and the cycle length of an induced spiral wave (triangles) versus ε in a homogeneous excitable medium. The dotted line represents the spiral wave cycle length or period at $\varepsilon = 0.02$.

in Fig. 5 with open circles. The triangles in Fig. 5 represent the cycle length of spiral wave ($\mathrm{CL}_{\mathrm{spiral}}$) or period in homogeneous medium. Both $\mathrm{CL}_{\min}$ and $\mathrm{CL}_{\mathrm{spiral}}$ increased linearly with ε. Second, in a *heterogeneous* medium, the minimum cycle length necessary to support a propagated wave varied with the degree of heterogeneity. In this paper, the parameter ε in the left-hand region was set equal to 0.02, less than in the other regions. As the spiral wave was initiated at the left region, the cycle length of spiral wave was 2.84, shown in Fig. 5, with a dotted line. At this cycle length, we found numerically that the maximum ε_2 in the medium [see Eq. (2)] for which the wave can successfully propagate through the whole medium, was near 0.042. This critical value of this transition was exactly the same as that we predicted by the intersection point (down arrow) between the dotted line and minimum cycle length line in Fig. 5. As ε_2 was increased above 0.042, not all waves in the high ε region can follow in 1:1 propagation, so some waves must be broken. But the several waves following immediately *after* a wave break can propagate through that region, due to the quick recovery of the excitable medium from wave break. However, these waves, reorganized after conduction block, formed new frequencies. In Fig. 1(b), the average cycle length of new waves was around 4.10, which was the same as the frequency of the right spiral wave with CL=4.10; thus the newly formed waves were unable to unwind the right-hand spiral. As the degree of heterogeneity (ε_2) was continuously increased, the cycle length of the right spiral was also increased, so the corresponding frequency decreased. When this frequency was below the average frequency of the newly formed (post wave break) waves, the right spiral wave was once again swept away, this time by the newly formed waves [Fig. 1(c) for $\varepsilon_2 = 0.056$].

The most important finding reported in this paper is that two stable spiral waves with independent frequencies could coexist in a *hetero*geneous excitable medium, if the multiple waves were ''insulated'' from one another by the disordered wave propagation generated by the wave conduction block in an intervening border region [Figs. 2(b), 2(e), and 2(h)]. The type of heterogeneity we studied, where an intervening region is subject to conduction block, may be particularly relevant to cardiac tissue, in which the ''M cell'' layer separating subendocardial from subepicardial tissue has a long refractory period [12]. In this situation, conduction block, which occurred in several $n:n-1$ block patterns such as 4:3, 3:2, and 2:1, is dependent on the degree of heterogeneity of the medium. In principle, it should be possible to find $n:n-1$ block of any order, but this paper did not find any higher than 4:3. The reason may be that higher-order block is located in a very narrow range of heterogeneity, which makes it difficult to detect in numerical simulations.

We also found that a situation [for example, see Fig. 1(c)] in which a stable rotor persists on the left-hand side, but no stable rotor can form on the right. Instead, new wave breaks continue to form on the right, with a consistent 3:2 block pattern. Thus, this situation appears to model the existence of ''fibrillatory conduction'' [16,17], in which most of the apparent irregularity results from conduction block rather than from an inherent dynamical instability. However, the waveform on the right remains highly periodic under these conditions, which is not the case in cardiac fibrillation. In addition, it is not clear whether actual cardiac tissue possesses the high degree of heterogeneity required for this scenario.

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