Spiral Breakup in a New Model of Discrete Excitable Media

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The transition from the dangerous cardiac arrhythmia, ventricular tachycardia, to the fatal cardiac arrhythmia, ventricular fibrillation, is believed to be associated with the breakup of spiral waves of excitation into multiple reentrant waves. A new computational method for wave propagation in discrete excitable media employing coupled maps with continuous time is used to derive analytical criteria for parameter ranges in which spiral waves show a stationary rotation, wandering, and breakup into multiple spirals.

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Spiral waves of excitation of the ventricular muscle have been identified as one mechanism underlying ventricular tachycardia, a dangerous cardiac arrhythmia associated with a rapid heart beat.[1,2] Ventricular tachycardia is liable to "degenerate" into ventricular fibrillation, a fatal cardiac arrhythmia. Experimental studies mapping the spread of excitation in the myocardium have identified this transition with the breakup of a spiral wave into multiple reentrant waves propagating in complex and changing pathways.[1,2] Previous studies have modeled wave propagation in the heart by using nonlinear partial differential equations[3-6] and cellular automata.[7-9] Both of these classes of models have deficiencies, since neither captures the spatially discrete, temporally continuous properties of biological tissue. In pathological conditions, the propagation speed of cardiac excitation is reduced, and the cellular myocardium may not be well described by a continuous partial differential equation.[10] These considerations have led us to formulate a novel theoretical model, consisting of coupled maps in continuous time, to study the spread of excitation in discrete cellular media.[11] The theoretical model facilitates numerical and analytical computations concerning wave propagation in excitable media, and allows an explicit computation of stability criteria for rotating spiral waves.

The system is composed of many excitable elements (cells) with an identical property.[12] Each cell is connected to some number of neighboring cells by a conducting cable. The cell can be excited by an incoming pulse from exciting neighboring cells. When a cell gets excited, the cell emits an excitation pulse which conducts through the conducting cable. We assume that the conduction time between the neighboring cells, τ, is given by

$$\tau = f(T)l = \{\alpha \exp(-T/\beta) + \gamma\} l, \text{ if } T \geq \theta, \quad (1)$$

where α, β, and γ are the parameters, l is the distance between the neighboring cells, θ is the refractory time, and T is the recovery time of the cell from the last excitation. Such a relationship is called a recovery curve in cardiac physiology[13] and the functional form in Eq. (1) is often used for the fitting of experimentally measured recovery curves in cardiac physiology.[14] This curve reflects slow conduction velocity for short recovery times, but the ionic mechanisms underling this phenomenon are not well understood. The excitation pulse propagates to every neighboring cell with the same conduction velocity. After a cell is excited, it must spend a constant duration θ to recover its excitability. The next excitation will be induced by the earliest arriving pulse after the refractory period.[15]

At first we consider the simplest case, the circulation of an excitation pulse in a one-dimensional ring of N cells, each of which is connected to two neighboring cells.[16] We assume a homogeneous spacing l between the neighbors. Each cell has a map which gives a conduction time from that cell to its neighbors based on the recovery time. In the ring, the recovery time is equal to the circulation period of the excitation pulse which is given by the sum of the conduction times for each cell. Thus the dynamics of the circulating pulse on the ring is described by N coupled maps. The solution of

$$\tau = f(N\tau)l \quad (2)$$

corresponds to a unidirectional circulation of the excitation pulse (reentry) with a period $T_0 = N\tau$. The conduction time between the neighboring cells τ is the same for all cells. This solution corresponds to a fixed point in the N-dimensional map. There are three criteria that must be satisfied in order for this solution to represent a stable circulating pulse.

(1) Linear stability.—Linear stability analysis of the N-dimensional map shows that the solution of Eq. (2) is a stable attractor provided

$$l \frac{df(T)}{dT}\bigg|_{T=N\tau} > -1. \quad (3)$$

Otherwise, the circulation period begins to oscillate with an exponential growth of its amplitude, and finally the circulation is blocked.

(2) Reentry.—The circulation period must be greater

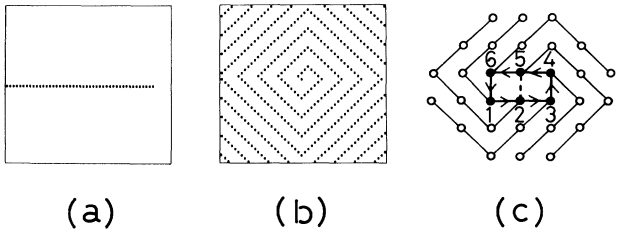

FIG. 1. Evolution of a stable spiral wave for $\alpha=3000$, $\beta=40$ in 50×50 cells. Excited cells at (a) $t=0$ and (b) $t=20000$ are represented by dots. (c) Magnified view of successive motions of tip and arm. One revolution of the spiral wave in (b) takes about 3 s on a DEC station 2100.

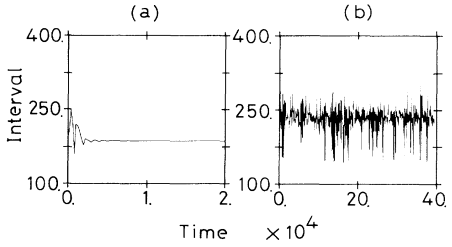

FIG. 2. Time intervals between the successive excitations at the cell in the center of the square as a function of time: (a) $\alpha=3000$, $\beta=40$ (see Fig. 1); (b) $\alpha=6300$, $\beta=40$ (see Fig. 4). Scales of the abscissa are different in the two graphs.

than the refractory time so that

$$N\tau \geq \theta. \tag{4}$$

(3) Unidirectional circulation.—The excitation pulse must be blocked by the refractory duration in the direction opposite to its propagation direction so that

$$2\tau < \theta. \tag{5}$$

We now consider the spread of excitation in two dimensions. In a two-dimensional system, we assume that each cell on a square lattice with a lattice constant l is connected to its four nearest neighbors. We take no-flux boundary conditions, that is, the cells on the boundary are connected to only the inside cells. In the following, we assume $l=1$, $\gamma=2$, and $\theta=140$ and consider the effects of varying α and β. We found that for some parameters, the system has an attractor which is a stationary rotating spiral wave with a constant rotation period T_0. The evolution of a stable spiral wave is shown in Figs. 1(a) and 1(b) for $\alpha=3000$ and $\beta=40$. The simulation starts from the initial condition of a broken wave line propagating downward [Fig. 1(a)], where all cells have spent the same recovery time, 200, and are excitable except those just behind the wave line which have a recovery time 0. After a transient, there is a stationary rotating spiral wave as in Fig. 1(b). The successive motions of the tip are schematically depicted in Fig. 1(c). Here, the tip traverses a closed rectangular ring of six cells. The motion of the tip is the same as the unidirectional circulation with a constant conduction velocity in the one-dimensional case with $N=6$. Therefore the rotation period of the spiral $T_0=N\tau$ is given by the solution of Eq. (2) with $N=6$. Figure 2(a) shows that the time interval between the successive excitations at the cell in the center of the square gradually converges to the rotation period of the spiral, T_0.

These results can be understood by considering analytical criteria for stable reentrant motions of the spiral tips. Figure 3 shows a summary of these calculations with $l=1$, $\gamma=2$, and $\theta=140$ as a function of α and β. Different stable spiral waves are classified by the number of cells, N, in the trace of the tip ($N\geq4$, even integer). The stable regions for the stationary rotating spiral waves with $N=4,6,8$ are shown by different hatchings. Every stable region is determined by three different boundaries determined by three conditions, the first two of which are identical to those obtained for excitation in a one-dimensional system.

(1) Linear stability (solid lines in Fig. 3).—For each N, the spiral wave is linearly stable below the boundary found by Eq. (3) and is unstable above it.

(2) Reentry (dashed lines).—For each value of N, Eq. (4) is satisfied above the boundary.

(3) Premature reentry (dot-dashed lines).—The third criterion in the one-dimensional system must be modified. In the two-dimensional system, as shown in Fig. 1(c) by a dashed line, some cells in the trace of the tip are connected to the cells on the opposite side of the ring as well as the cells in both sides. Stationary circulation is possible only if the conduction of the pulse to the cell on the opposite side is blocked by the refractory duration. Otherwise, the tip reenters into the opposite

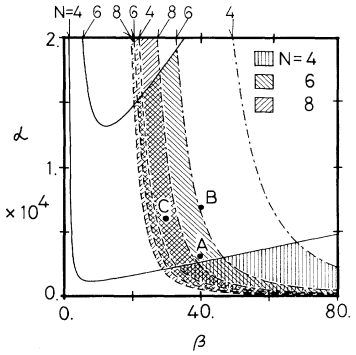

FIG. 3. Phase diagram for spiral waves with $l=1$, $\gamma=2$, and $\theta=140$ as a function of α and β. Stable regions for stationary rotation with $N=4,6,8$ are shown by different hatchings. See text for details.

side prematurely. For example, in Fig. 1(c), when cell 5 receives the excitation pulse from cell 2, it has a recovery time of 4τ which must be less than the refractory time. In general, a spiral wave whose tip passes through N cells must satisfy

$$(N-2)\tau < \theta, \tag{6}$$

to avoid premature reentry. For each N, this condition is satisfied below the boundary.

The above results help in the study of the dynamics in parameter space. The spiral with $N=6$ in Fig. 1 falls at point A in Fig. 3 in the stable region of $N=6$ spirals. At point C in Fig. 3 ($\alpha=6000$, $\beta=30$), we can find both $N=6$ and $N=8$ spirals, depending on the initial conditions, also in accord with the theory. We now consider the dynamics at point B ($\alpha=6300$, $\beta=40$) just above the boundary of premature reentry for $N=6$ spirals, where the system has no attractor of a stable rotating spiral wave. Figures 4(a)-4(f) show the evolution of the excitation waves starting from the same initial condition as Fig. 1(a). At first a single spiral wave appears [Fig. 4(a)]. However, the single spiral is unstable to breakup by a disconnection of the tip from the tail [Fig. 4(b)]. The disconnected tip evolves into a pair of counter-rotating spiral waves [Fig. 4(c)], following escape of the original spiral from the finite two-dimensional space. Such a breakup keeps proceeding at each spiral tip, and finally there coexist many spiral waves [Figs. 4(d)-4(f)]. As seen in Fig. 2(b), the time interval of the successive excitations at a single cell shows an irregular time dependence and the cell sometimes has a short recovery time because of premature reentry. It was also found numerically that the lifetime of the single spiral is prolonged as α is increased with $\beta=40$. For a larger α (~ 20000) the single spiral has a longer lifetime, but wanders around the system in quite an irregular way. In any case the motion is always transient and never enters into any invariant structure. The only invariant set in this dynamical system under these parameters is the complete die out of the excitation over the whole system. However, numerical simulations show that the single spiral evolves to this invariant set only when its tip escapes from the finite two-dimensional system by chance after a long wandering duration. We performed numerical simulations with $\alpha=6300$, $\beta=40$ to determine if the irregular motion is sensitive to initial conditions. From initial conditions in which cells have a recovery time different slightly ($\sim 10^{-5}$) from that of the previous initial arrangements in Fig. 1(a), after a short time (~ 3000), the tip shows a motion different macroscopically from that of the previous simulation. The motion of the tip is sensitive to the initial condition. Premature reentry leads to apparent chaotic motion of the tip and this results in an irregular wandering motion of the spiral. The motion of the tail is relatively simple and regular in any case. However, we have not developed a detailed theory of the spiral breakup.[17]

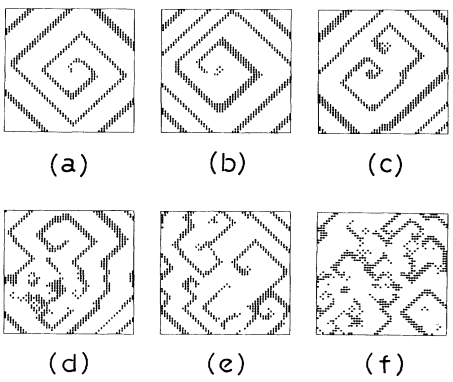

FIG. 4. Evolution of unstable spiral wave and breakup of spirals for $\alpha=6300$, $\beta=40$ in 50×50 cells from the initial condition in Fig. 1(a). Cells which are excited within the interval $(t, t+50)$ are represented by dots at (a) $t=5000$, (b) 8200, (c) 30000, (d) 50000, (e) 200000, and (f) 400000, respectively.

The phenomena discussed here are not artifacts of the regular lattice. We confirmed this by the simulation on a random lattice where the position of each cell is Gaussian distributed around the regular lattice with a standard deviation of 0.05. Even in such a case, the system can have a stationary rotating spiral with a constant period over some parameter ranges. Although the period of the successive excitation is synchronized over the whole space, the timings of the excitation are distributed. The system also shows spiral breakup and wandering of spirals.

The breakup reported here appears to depend on the discrete cellular nature of the excitable medium. The stability boundaries in Fig. 3 depend on the spacing of the cells. As known from the basic equation (1), the system with a cell spacing l under the parameters $(\alpha,\beta,\gamma,\theta)$ shows the identical property as that with a unit-cell spacing under the scaled parameters $(\alpha l,\beta,\gamma l,\theta)$. Thus, if one halves the spacing of the cells for the same parameters used in Fig. 4, spiral breakup is no longer found with $\alpha=6300$, but rather there is a stable spiral. Now spiral breakup appears in the region $\alpha > 13000$.

Spiral breakup has also been found in cellular automata[8] and nonlinear partial differential equations[18] modeling the heart. However, the connections between these earlier observations, the current computations, and the spiral breakup that has been experimentally observed[1,2] are not yet clear. If the same mechanisms for spiral-wave instability described here also hold in the intact heart, then we would expect to find a steep increase of the conduction time for small recovery times for physiological conditions in which spiral breakup occurs. Since all computational approximation schemes studied to date employ spatial discretization, it will be of interest to clar-

ify if spiral breakup can occur in continuous systems such as excitable chemical media.[19] The current paper underscores the relevance of spiral breakup to human health, and the possibility that a theoretical understanding of this phenomenon might be possible.

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