RAPID COMMUNICATIONS

PHYSICAL REVIEW E VOLUME 47, NUMBER 2 FEBRUARY 1993

Interaction between a drifting spiral and defects

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(Received 10 November 1992)

Spiral waves, a type of "reentrant excitation," are believed to be associated with the most dangerous cardiac arrhythmias, including ventricular tachycardia and fibrillation. Recent experimental findings have implicated defective regions as a means of trapping spirals which would otherwise drift and (eventually) disappear. Here, we model the myocardium as a simple excitable medium and study via simulation the interaction between a drifting spiral and one or more such defects. We interpret our results in terms of a criterion for the transition between trapped and untrapped drifting spirals.

PACS number(s): 87.10.+e, 87.22.As, 82.20.Mj

In the United States alone, over 1000 lives are lost daily to sudden cardiac death. Most are initiated by a premature ventricular contraction ("premature systole") and begin with a regular rapid electrical rhythm ("tachycardia") in the thick left ventricular myocardium. Synchrony of the contraction then deteriorates to turbulence with irregular, frenzied heartbeat ("fibrillation"), until finally the heart stops beating for want of oxygen [1].

One possible cause of premature systoles and tachycardia is spiral waves. Myocardial tissue is an excitable medium through which propagate waves of electrical stimulation and muscular contraction; this has been shown by many experiments and simulations [2–4]. In a normally functioning heart the excitations are coherent waves emanating from a pacemaker region near the sinoatrial (SA) node. However, in certain pathological situations, normal function is disturbed and spirals are formed. These spirals generally have a higher frequency than the aforementioned waves [2], which means that the wavefronts are annihilated by collisions with the growing spiral; eventually, the heart tissue will oscillate at the much higher frequency of the spiral [5–7].

It has been suggested [8] that most spirals drift [2] and eventually dissipate at a tissue border, whereupon the heart returns to normal. However, if there exist defective regions in the heart (such as diseased cells due to myocardial infarction), the spiral may be trapped thereby causing permanent tachycardia. This idea motivates us to investigate the interaction between a drifting spiral and defects. Specifically, we wish to obtain some criterion that will distinguish between drifting or trapped spirals as a function of the size and location of these defective regions.

As already mentioned, myocardium behaves in many respects like a generic excitable medium. It can be approximately described, from a biophysical point-of-view, by a set of eight ordinary and partial differential equations, the Beeler-Reuter equations [9], which are a modified version of the Hodgkin-Huxley equations for nerve impulse transmission along axons [10]. At the present it is beyond our ability to numerically tackle the spiral problem in the full Beeler-Reuter model. In addition, even the Beeler-Reuter model is not precise enough for a quantitatively accurate study of the cardiac action potential. However, certain key features of the Beeler-Reuter equations are captured by the much simpler FitzHugh-Nagumo membrane model and therefore, the latter is sufficient to provide a qualitative description of the electric behavior of the heart [4]. This model is

$$\dot{u} = \frac{1}{\epsilon} f(u,v) + D\nabla^2 u, \quad \dot{v} = g(u,v), \tag{1}$$

where the variable u represents membrane potential and v represents a slow recovery process. Here the ventricular myocardium is simplified to be isotropic, though in reality, it is anisotropic due to the elongated shape of the muscle fibers. However, this simplification will not affect the results qualitatively. Also, we restrict ourselves to the two-dimensional (2D) case, although the real heart is undeniably three dimensional. However, the 2D limitation is a good approximation for many experiments performed on slices of epicardium [2].

In the above equations, the parameter ϵ is related to the fact that the time scale of voltage variations (due to fast sodium channels, for example) is much smaller than that of v (due to slow calcium and/or potassium channels). It is well known that the width of the boundary layers, i.e., regions of space where u makes fast jumps, is $(O\sqrt{\epsilon})$ [11] for very small ϵ . Crude estimates of the relevant size of ϵ for myocardium give $\epsilon \sim 10^{-3}$ to 10^{-2}. We will vary ϵ within this range of values.

Finally, we model the local kinetics with [12, 13]

$$f(u,v) = u(1-u)[u - u_{\rm th}(v)], \quad g(u,v) = u - v, \tag{2}$$

where the threshold "voltage" is given by $u_{\rm th}(v) = (v + b)/a$, and a and b are parameters. The local kinetics, i.e., the dynamics in the absence of spatial derivatives, has a stable but excitable fixed point at the intersection of the

nullclines $f(u,v) = 0$ and $g(u,v) = 0$.

As has been stressed by Barkley [13], the advantage of this model kinetics is that the excitation term can be time stepped with little computational effort. At any fixed spatial location, the system spends almost all its time within a very "thin layer" near the left branch of the u nullcline and therefore very little error results from setting $u = 0$ at the update step whenever the system is within $u < \delta$ with $\delta \simeq 10^{-5}$; the advantage gained is that almost every step of the model kinetics requires just one conditional evaluation and one floating-point multiplication. In practice, we have used the program EZ-SPIRAL, obtained from Barkley [14]. One complication is that spirals simulated in this manner show core meandering when b is increased or when a is decreased. In order to focus on the interaction of a spiral with defects, we avoid the regime of parameters that leads to meandering.

Now let us consider a drifting spiral. In order for the spiral to move, there must exist some inhomogeneity in the excitable medium [15, 16]. For example, there is experimental evidence that spiral drift in rabbit myocardium is due to a gradient in the refractory period [17]. The simplest way to introduce such inhomogeneity in our simulation is to set up a gradient in the parameter b. So, we replace b by $b(x) = b_0 + \nu x$, where ν is the gradient. The direction and the magnitude of the drift velocity depend on b_0, ν, ϵ as well as the initial position of the spiral. As an example, one trajectory of a spiral tip is shown in Fig. 1(a), where the spiral tip is defined as the intersection of the two contours $u = \frac{1}{2}$ and $f(u = \frac{1}{2}, v) = 0$. The bigger ν and $b(x)$ are, the faster the spiral drifts, and the larger the size of the spiral core. Again, to avoid meandering, one must be careful not to choose too large a value for ν.

Next we need to define a defect in the simulation. The simplest model of a damaged region of myocardium is that the local kinetics is taken to be less excitable than that of normal tissue. The extreme case is a region of zero excitability. In our model, this consists of replacing $b(x)$ by a constant B. A completely unexcitable defect has $B = B^* \equiv \frac{a}{2}$, while a partially excitable defect has $B < B^*$ but bigger than $b(x)$ around it. One way to see this is to note the condition for minimum excitability required for spiral wave propagation in excitable media is $(v^* - v_s)_{\min} = O(\epsilon^{\frac{1}{3}})$ where v_s is the value of v in the rest state and v^* is that which corresponds to zero wave speed [18]. It is easy to see that for our case $v_s = 0$ and $v^* = b - a/2$. The shape of the defect is chosen to be a circle with variable radius. The simulation is done on a square grid of area L^2 containing N^2 grid points; typically, $N = 101$ and $L = 20$. For all results reported here, $a = 1$, and $b_0 = 0.061$.

Let us first focus on the trapping of a drifting spiral by a completely unexcitable region. We fix the gradient of $b(x)$ (i.e., ν) and ϵ, and vary the size of the defect and the impact parameter of the drifting spiral. To avoid effects merely due to the inhomogeneity of our system, we always start the spiral at the same position and fix the center of the defect circle to lie on a vertical line through the initial position of the center of the spiral core. The impact parameter is evaluated by using a straight-line approximation to the early-time trajectory of the spiral core.

In the simulation, the spiral will either be trapped by the defect or escape to the system boundary. An example of a trapped trajectory is shown in Fig. 1(b). The curving of the trajectory towards the defect, which occurs in almost all cases of either trapped or untrapped spirals, is consistent with an attractive fairly short-range interaction; similar interactions for the spiral-spiral system have been predicted elsewhere [19].

The result of varying the defect size and the impact parameter in this problem is depicted in Fig. 2. There is a critical curve separating capture from escape. Interestingly, when the impact parameter d is large, the critical curve becomes a straight line with slope 1. This is due to the fact that if the defect is large, the only relevant parameter is the distance from the spiral core to the edge of the defect region. Furthermore, this asymptotic

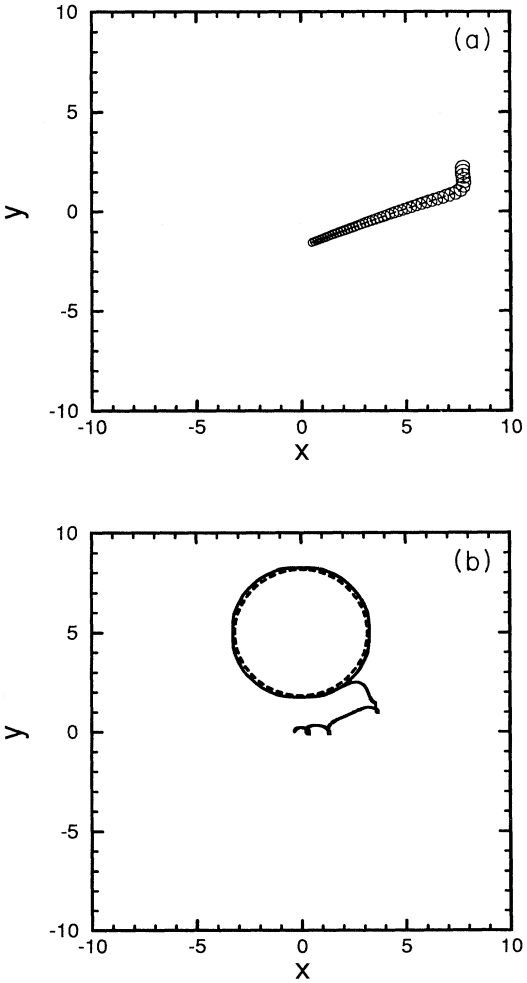

FIG. 1. (a) The tip trajectory of a drifting spiral with $a = 1$, $b_0 = 0.061$, $\nu = 5 \times 10^{-3}$, $\epsilon = 0.02$, and grid parameters $N = 101$, $L = 20$. The spiral starts from the center of the domain, and eventually moves parallel to the no-flux boundary. (b) A trapped spiral for the same parameters. The dashed line represents the contour of the defect.

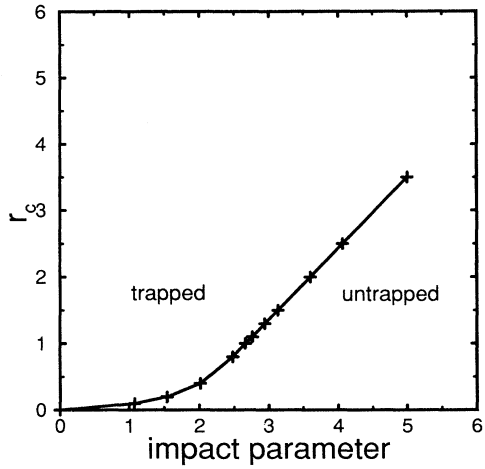

FIG. 2. Critical curve for the spiral trapping.

straight line intersects the r_c axis at a negative value r_c^*. We expect that r_c^* is directly related to the effect of the boundary layer of the spiral, which scales as $\sqrt{\epsilon}$. We vary the value of ϵ and plot r_c^* in Fig. 3. Considering the precision of r_c, the impact parameter, and the drift velocity in the simulation, the data are consistent with $|r_c^*|$ being proportional to the width of the boundary layer.

If we change the defect to be partially excitable, we find no qualitatively significant changes in behavior — of course the trapping will be weaker, the critical line will be shifted, and sometimes the spiral will meander around the defect. We note in passing that the rotation period and the wavelength of the trapped spiral are larger than those of the initial spiral. This is consistent with predictions due to Keener and Tyson [20] as to the effect of defect size on frequency selection. Also, as ϵ decreases the period decreases, again in accord with expected spiral behavior [21].

We have also studied, albeit qualitatively, the scattering of a drifting spiral by two defects. If the (identical) defects are well separated, the spiral will be scattered or trapped by the closer defect as if the second one did not exist. On the other hand, if the two defects are very close to each other, and if the spiral is near enough, the spiral will be trapped and will rotate around the envelope of the two defects. In the intermediate case, the trapped spiral first rotates around two defects and eventually winds up being trapped on only one of them. We have also examined the case in which the two defects have different size. The result is qualitatively the same as above, though the defect with bigger size has a stronger influence on the spiral.

Let us briefly consider the reverse problem of the detrapping of a spiral around a defect. One can imagine that if the gradient increases above a critical value, a trapped spiral will leave the defect and drift away. Unlike the previous simulation, which tested for capture by a bound state, this calculation considers whether a bound state exists at all. We first fix ϵ and increase the gradient ν until we obtain detrapping; if this is done as a function of defect size, this defines the curve ν_c versus r given in Fig. 4. At very large r, the critical gradient decreases; this is due both to the fact that the value of b on the far side of a large defect is changed from its value at the center (and drift speed increases with b at fixed ν) as well as to an intrinsic decrease in binding as the radius of curvature increases. Also, the critical gradient is a decreasing function of $\sqrt{\epsilon}$.

In summary, we have used a modified FitzHugh-Nagumo model to study the interaction between a drifting spiral and defects. Our simulations show that spiral trapping requires a critical defect size that depends on both excitability and inhomogeneity. Though our work was motivated by recent experiments on thin layers of heart muscle, this process can be studied in any excitable medium. Conversely, application to a quantitative description of these processes in the heart would require extensions of this work to more complex models and to three-dimensional geometries.

Note added. After this work was completed, we learned

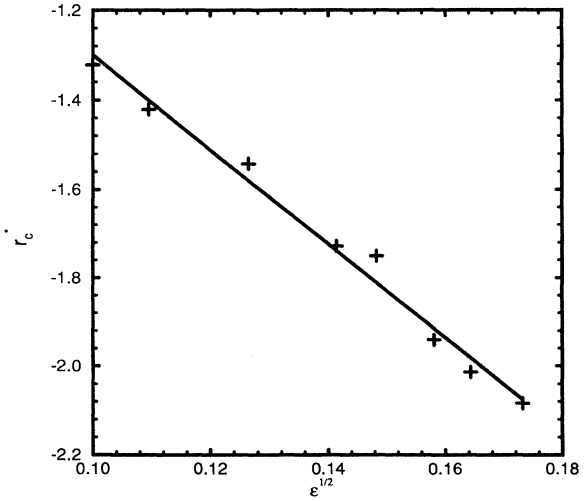

FIG. 3. r_c^* vs $\sqrt{\epsilon}$.

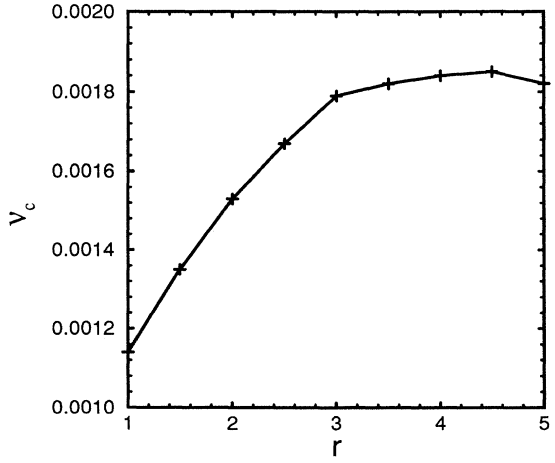

FIG. 4. Critical curve for the spiral detrapping at $\epsilon = 0.02$ and $b_0 = 0.17$.

that the phenomena of the spiral trapping have also been observed by Rogers and McCulloch in their simulations [22], and by Jalife and co-workers in experiments using epicardium [8]. Their (unpublished) results are qualitatively consistent with the findings here.

The authors would like to acknowledge D. Barkley for use of his simulation program, and W. Reynolds for helpful discussions. The work of D.A.K. was supported by the U.S. Department of Energy under Grant No. DE-FG-0285ER54189.

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