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Spiral breakup in a modified FitzHugh–Nagumo model

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In a modified FitzHugh–Nagumo model for excitable tissue a spiral wave is found to break up into an irregular spatial pattern. The main difference between our equations and the standard FitzHugh–Nagumo model is that we use two different time constants: one for the relative refractory period and another for the absolute refractory period. Breakup occurs when the relative refractory period is short. The effect is numerically stable at least for a five-fold decrease in the space integration step.

1. Introduction

Spiral waves in excitable media provide an important example of self-organization phenomena in spatially distributed biological, physical and chemical systems [1]. Usually, spiral waves occur either because of inherent heterogeneity in the excitable tissue, or because of some special initial conditions [2]. However, in some cases, spirals can be generated even in homogeneous systems. Recent studies have demonstrated that a spiral can break up, and spontaneously generate complicated spatio-temporal patterns [3–10]. This process of spiral breakup has been observed in some sophisticated equations for cardiac tissue [4–7] and in several cellular automata models [3,8–10]. However, the mechanism involved is unknown, but the breakup is believed to be associated with the discrete nature of the model [8], or in some cases to be connected with the presence of two inward ionic currents [7]. One way of studying the mechanism underlying this effect is to reproduce it in simple minimal partial differential equation models of excitable tissue, which allow us to study the influence of discrete effects, pulse shape, dispersion relation, etc., on the process of spiral breakup. However, recent computations by Winfree show that this effect is unlikely to exist in classical FitzHugh–Nagumo equations [11]. Here we show that it is possible to obtain the spiral breakup in a simple two-component model of excitable tissue by modifying the dynamics of the recovery variable.

2. Mathematical model and method of computation

For numerical computation we use FitzHugh–Nagumo-type equations with piecewise linear "Pushchino kinetics" [12,13],

$$\partial e/\partial t=\nabla^2 e-f(e)-g\,,$$

$$\partial g/\partial t=\epsilon(e,g)(ke-g)\,, \tag{1}$$

with $f(e)=C_1 e$ when $e<e_1$; $f(e)=-C_2 e+a$ when $e_1\leqslant e\leqslant e_2$; $f(e)=C_3(e-1)$ when $e>e_2$, and $\epsilon(e,g)=\epsilon_1$ when $e<e_2$; $\epsilon(e,g)=\epsilon_2$ when $e>e_2$, and $\epsilon(e,g)=\epsilon_3$ when $e<e_1$ and $g<g_1$. The parameters determining the shape of the function $f(e)$ are $e_1=0.0026$, $e_2=0.837$, $C_1=20$, $C_2=3$, $C_3=15$, $a=0.06$ and $k=3$. With these parameter values the function $f(e)$ is continuous. The shape of the function $f(e)$ specifies fast processes such as the initiation of the action potential. The dynamics of the recovery variable g in (1) is determined by the function $\epsilon(e,g)$. In $\epsilon(e,g)$ the parameter ϵ_3^{-1} specifies the recovery time constant for small values of e and g. This region approximately corresponds to the relative refractory period. Similarly, ϵ_1^{-1} specifies the recovery time constant for relatively large values of g and intermediate values of e. This region approximately corresponds to the wave front, wave back and to the ab-

solute refractory period. The main difference between model (1) and the previous model [13] is that model (1) uses two independent constants ϵ_1^{-1} and ϵ_3^{-1} for the refractory state. The values of these parameters were fixed at $\epsilon_1^{-1}=75$, $\epsilon_2^{-1}=1$, $g_1=1.8$, and $0.5<\epsilon_3^{-1}<10$.

For numerical computations we used the explicit Euler method with Neumann boundary conditions, and the rectangular grid measured from 100×100 elements up to 1000×700 elements. To initiate the first spiral we used initial data corresponding to a 2D broken wave front, the break being located in the middle of the excitable tissue.

3. Results and discussion

We found that the spiral breakup occurred spontaneously in the excitable media that have a shortened relative refractory period. In our computations we fixed the time constant for the absolute refractory period at $\epsilon_1^{-1}=75$, and we varied the value of the time constant for the relative refractory period ϵ_3^{-1}. We found that spiral breakup occurred if ϵ_3^{-1} was less than 5.5. Figure 1 shows the evolution of a spatial pattern in a medium with $\epsilon_3^{-1}=2.8$. In this case the wave makes several rotations with pronounced meandering and begins to fragment close to the centre of the spiral (fig. 1c). However, at this moment in time, there is not enough recovered space and the wave breaks disappear. Later, at time $t=111$, a larger fragment of the wave breaks away (fig. 1e), initiating two new spirals. This process continues, and at $t=183$ we see five interacting rotating spatial waves (fig. 1f).

In a large excitable medium, the behaviour of the system becomes more complicated. Figure 2 shows the same computation as in fig. 1, but on a grid of 1000×700 elements. The final structure comprises many wave breaks of various sizes and a complicated spatial distribution of the recovery variable. This picture evolves in time, new breaks occur continuously and disappear; generically, however, the picture remains similar. Note that in this case the

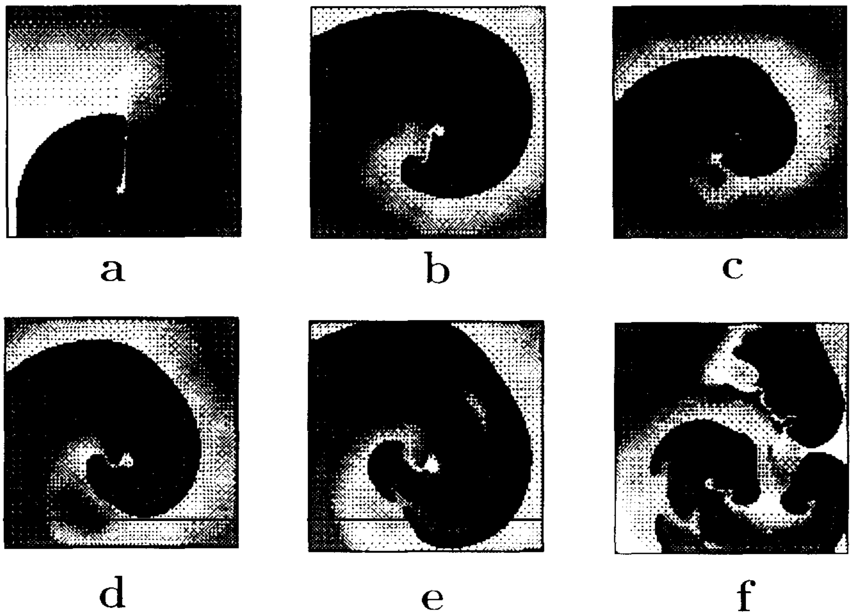


Fig. 1. The spiral breakup in model (1). The pictures are at time (a) $t=27$, (b) 67, (c) 82, (d) 107, (e) 111, (f) 183. Numerical integration with space step $h_s=0.5$ and time step $h_t=0.0222$ on the grid of 120×120 elements. The black area represents the excited state of the tissue ($e>0.6$), dark grey shows the region where $g>1.8$ (close to the absolute refractory state) and intermediate shading from grey to white shows different levels of g, $0<g<1.8$ (estimate for the relative refractory period).

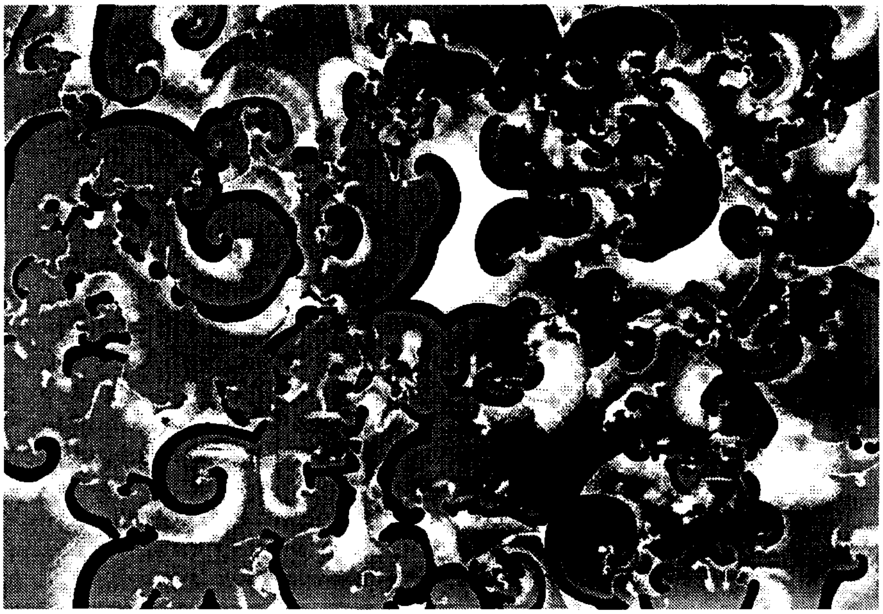


Fig. 2. The spatial pattern that occurred spontaneously due to the spiral breakup in the excitable medium measuring 1000×700 elements at the time $t=1554$. All other settings are the same as in fig. 1.

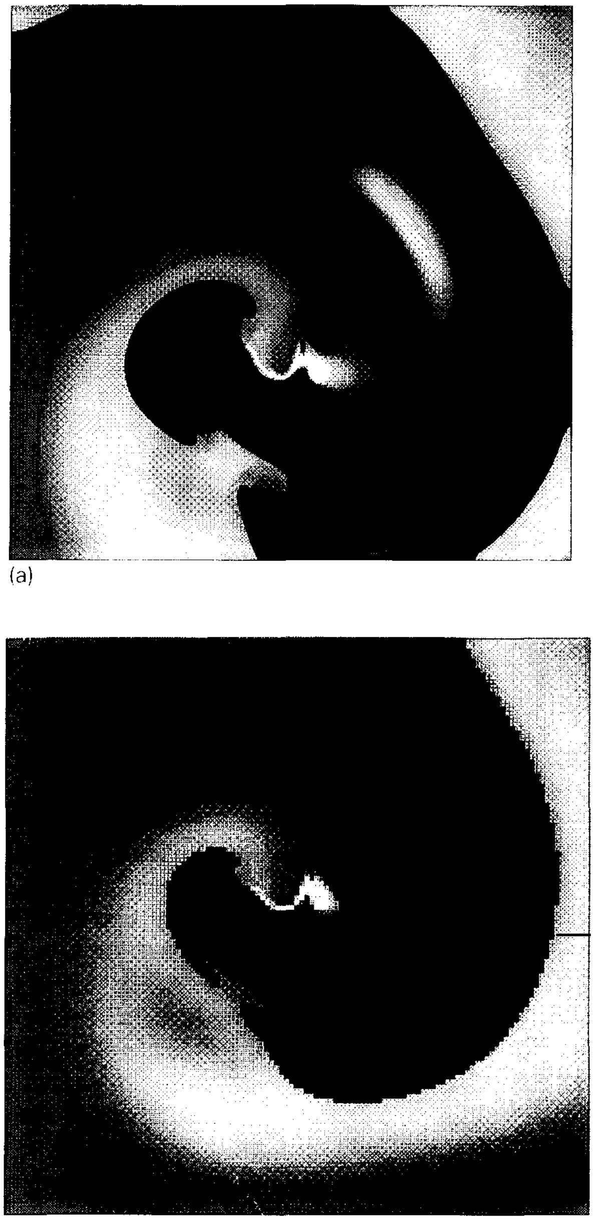
process of spiral breakup also started close to the centre of the initial spiral, and spread out over the entire medium.

We studied the stability of spiral breakup at various spatial and time integration steps. Figure 3a shows the same computation as fig. 1 but with the space step decreased five-fold and the time step decreased 25-fold. In both cases the picture of the first major breakup is similar. (Compare fig. 3a and fig. 1e.) The error in these computations, estimated using the difference between the computed and the saturated value for the velocity of plane wave propagation, is less than 0.2% for space step $h_s=0.1$ and less than 5% for $h_s=0.5$.

Because the difference in the time constants of the absolute and relative refractory periods is important for the effect studied in this paper, we looked for a possible source of numerical instability: the region of abrupt change from ϵ_3 and ϵ_1. We made a computation in which we used linear interpolation from the value of $\epsilon_1^{-1}=75$ to the value of $\epsilon_3^{-1}=2.8$. In this case the excitable tissue spends about 30% of time at the region where ϵ_3^{-1} changes to ϵ_1^{-1}. Figure 3b shows that this modification of recovery did not affect the results of our computation. The first major breakup appeared in the same way as in figs. 3a and 1e.

For the breakup of spirals, it is not necessary for the two nullclines in eq. (1) to be parallel to each other ($k=C_2=3$); however, the slope of the nullcline for the slow variable affects the process of spiral breakup. We found the effect of breakup at $k=4.5$ and $C_2=3$, but it was less pronounced. The first major breakup in this situation occurred at time $t=305$, whereas in fig. 1 it occurred at $t=111$. The threshold of the excitable medium (the parameter a) was also important for the process of spiral breakup. We did observe the breakup when the threshold was increased three-fold ($a=0.18$); however, the first major breakup in this situation occurred later, at $t=360$. Another parameter that is important for spiral breakup is relative refractoriness (dependence of ϵ on the variables e and g). As we mentioned above, increasing the time constant for the relative refractory period makes the breakup impossible at $\epsilon_3^{-1}>5.5$.

The effect of spiral breakup is not a unique property of model (1) with particular piecewise linear "Pushchino kinetics". Modifying the dynamics of the



(a)

(b)

Fig. 3. The first major breakup of a spiral wave at various integration steps (a) and recovery kinetics (b). (a) Computation of eqs. (1) with $h_s=0.1$, $h_t=0.000888$, grid 600×600 elements. (b) Computation with linear interpolation from the value of $\epsilon_1^{-1}=75$ to the value of $\epsilon_3^{-1}=2.8$: $\epsilon(e,g)^{-1}=\epsilon_1^{-1}$ when $e<e_2$ and $g<2.1$; $\epsilon(e,g)^{-1}=\epsilon_3^{-1}+(\epsilon_1^{-1}-\epsilon_3^{-1})(g-1.5)/0.6$ when $e<e_2$ and $1.5<g<2.1$; $\epsilon(e,g)^{-1}=\epsilon_3^{-1}$ when $e<e_1$ and $g<1.5$. $h_s=0.5$, $h_t=0.0222$, grid 120×120 elements; both pictures are at time $t=111$.

recovery variable (using two independent constants for relative and absolute refractory periods), we were able to observe the effect of spiral breakup in the FitzHugh–Nagumo model, with the standard function $f(e)$ in the form of a cubic parabola ($f(e)=20e(e-0.1)(e-1)$). We can see (fig. 4) that the picture which occurs in this situation is similar to figs. 1 and 2.

The mechanism underlying spiral breakup is not quite clear; however, in our case it is connected with functional heterogeneity of the tissue with respect to the refractory period, the heterogeneity being induced by the spiral itself. The patch in the refractory period (fig. 1d) at which the wave later breaks up can be seen clearly. We presume that this kind of heterogeneity is associated with some kind of bifurcation in the pulse propagation during high frequency forcing. Figure 5 shows the time–space course of one-dimensional wave propagation during forcing with period $t_p=24.5$. The length of the forcing period is within the range of periods of a meandering spiral at these parameter values. We see (fig. 5) small oscillations in the velocity and duration of the excited

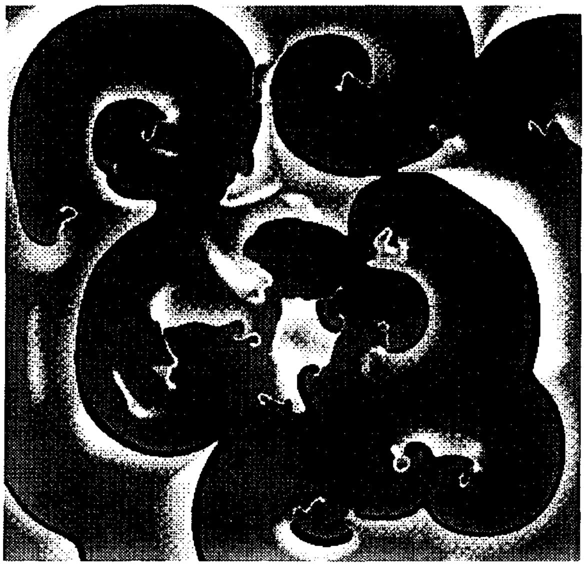


Fig. 4. The spatial pattern that occurred spontaneously due to the spiral breakup in the excitable medium measuring 500×500 elements at the time $t=2266$. Numerical integration with the function $f(e)=20e(e-0.1)(e-1)$; the other parameters are: $k=4.5$, $e_1=0.049$, $e_2=0.685$, $\epsilon_2^{-1}=1.5$. All other settings are the same as in fig. 1.

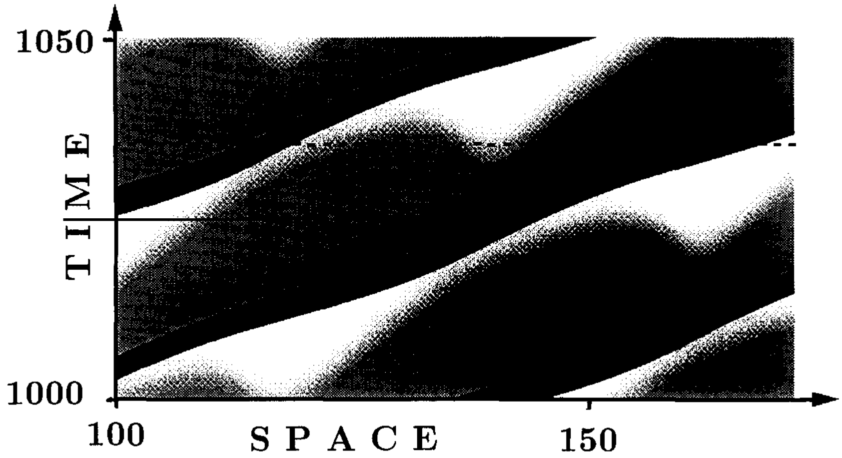


Fig. 5. Pulse propagation during periodic forcing with period $t_p = 24.5$. $h_s = 0.1$, $h_t = 0.000888$; gray scale coding is the same as in fig. 1. Space and time are measured in nondimensional units. The dotted line corresponds to moment $t = 1038$ in time.

state of the pulse, and large oscillations in the refractory period. The important feature of these oscillations is the nonmonotonic dependence on space of the edge of the absolute refractory period. In fig. 5 we can see clearly the maxima and minima in the absolute refractory period profile and the excitation propagating steadily upward and to the right. This means that if we consider the spatial state of this one-dimensional excitable medium at some moment of time $t = 1038$, we will find a refractory patch behind the propagating pulse. So, the patch can be considered as a heterogeneity with respect to refractoriness at this moment in time. We think that such heterogeneities break up the two-dimensional spiral. The other important feature of this "patch heterogeneity" is that it disappears quickly, providing recovered space in which the new breaks can survive.

Note that the spiral breakup observed here is similar to the onset of the complicated spatio-temporal patterns observed in cellular automata models for a process of evolution [9] and for spread of excitation in cardiac tissue [8]. Studies of the models [8,9] have also revealed that relative refractory period plays an important role in the process of spiral breakup.

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