

Exercises

N.9 Cardiac dynamics.^{1,2} (Computation, Biology, Complexity) ④

Reading: References [6, 11], Niels Otani, various web pages on cardiac dynamics, <http://otani.vet.cornell.edu>, and Arthur T. Winfree, ‘Varieties of spiral wave behavior: An experimentalist’s approach to the theory of excitable media’, *Chaos*, **1**, 303-334 (1991). See also spiral waves in Dictyostelium by Bodenschatz and Franck, <http://newt.ccmr.cornell.edu/Dicty/diEp47A.mov> and <http://newt.ccmr.cornell.edu/Dicty/diEp47A.avi>.

The cardiac muscle is an excitable medium. In each heartbeat, a wave of excitation passes through the heart, compressing first the atria which pushes blood into the ventricles, and then compressing the ventricles pushing blood into the body. In this exercise we will study simplified models of heart tissue, that exhibit *spiral waves* similar to those found in arrhythmias.

An excitable medium is one which, when triggered from a resting state by a small stimulus, responds with a large pulse. After the pulse there is a refractory period during which it is difficult to excite a new pulse, followed by a return to the resting state. The FitzHugh-Nagumo equations provide a simplified model for the excitable heart tissue:³

$$\begin{aligned}\frac{\partial V}{\partial t} &= \nabla^2 V + \frac{1}{\epsilon}(V - V^3/3 - W) & (\text{N.30}) \\ \frac{\partial W}{\partial t} &= \epsilon(V - \gamma W + \beta), & (1)\end{aligned}$$

where V is the transmembrane potential, W is the recovery variable, and $\epsilon = 0.2$, $\gamma = 0.8$, and $\beta = 0.7$ are parameters. Let us first explore the behavior of these equations ignoring the spatial dependence (dropping the $\nabla^2 V$ term, appropriate for a small piece of tissue). The dynamics can be visualized in the (V, W) plane.

(a) Find and plot the nullclines of the FitzHugh-Nagumo equations: the curves along which dV/dt and dW/dt are zero (ignoring $\nabla^2 V$). The intersection of these two nullclines represents the resting state (V^*, W^*) of the heart tissue. We apply a stimulus to our model by shifting the transmembrane potential to a larger value—running from initial conditions $(V^* + \Delta, W^*)$. Simulate the equations for stimuli Δ of various sizes; plot V and W as a function of time t , and also plot $V(t)$ versus $W(t)$ along with the nullclines. How big a stimulus do you need in order to get a pulse?

Excitable systems are often close to regimes where they develop spontaneous oscillations. Indeed, the FitzHugh-Nagumo equations are equivalent to the van der Pol equation (which arose in the study of vacuum tubes), a standard system for studying periodic motion.

(b) Try changing to $\beta = 0.4$. Does the system oscillate? The threshold where the resting state becomes unstable is given when the nullcline intersection lies at the minimum of the V nullcline, at $\beta_c = 7/15$.

Each portion of the tissue during a contraction wave down the heart is stimulated by its neighbors to one side, and its pulse stimulates the neighbor to the other side. This triggering in our model is induced by the Laplacian term $\nabla^2 V$. We simulate the heart on a two-dimensional grid $V(x_i, y_j, t)$, $W(x_i, y_j, t)$, and calculate an approximate Laplacian by taking differences between the local value of V and values at neighboring points.

There are two natural choices for this Laplacian. The five-point discrete Laplacian is generalization of the one-dimensional second derivative,

¹ New exercise supplementing *Statistical Mechanics: Entropy, Order Parameters, and Complexity* by James P. Sethna, copyright Oxford University Press, 2007, page 15. A pdf of the text is available at pages.physics.cornell.edu/sethna/StatMech/ (select the picture of the text). Hyperlinks from this exercise into the text will work if the latter PDF is downloaded into the same directory/folder as this PDF.

²This exercise and the associated software were developed in collaboration with Christopher Myers.

³Nerve tissue is also an excitable medium, modeled using different *Hodgkin-Huxley* equations.

$\partial^2 V / \partial x^2 \approx (V(x+dx) - 2V(x) + V(x-dx)) / dx^2$:

$$\begin{aligned} \nabla_{[5]}^2 V(x_i, y_i) &\approx (V(x_i, y_{i+1}) + V(x_i, y_{i-1}) \\ &\quad + V(x_{i+1}, y_i) + V(x_{i-1}, y_i) \\ &\quad - 4V(x_i, y_i)) / dx^2 \\ &\leftrightarrow \frac{1}{dx^2} \begin{pmatrix} 0 & 1 & 0 \\ 1 & -4 & 1 \\ 0 & 1 & 0 \end{pmatrix} \end{aligned} \quad (2)$$

where $dx = x_{i+1} - x_i = y_{i+1} - y_i$ is the spacing between grid points and the last expression is the *stencil* by which you multiply the point and its neighbors by to calculate the Laplacian. The nine-point discrete Laplacian has been fine-tuned for improved circular symmetry, with stencil

$$\nabla_{[9]}^2 V(x_i, y_i) \leftrightarrow \frac{1}{dx^2} \begin{pmatrix} 1/6 & 2/3 & 1/6 \\ 2/3 & -10/3 & 2/3 \\ 1/6 & 2/3 & 1/6 \end{pmatrix}. \quad (3)$$

We will simulate our partial-differential equation (PDE) on a square 100×100 grid with a grid spacing $dx = 1$.⁴ As is often done in PDEs, we will use the crude Euler time-step scheme $V(t + \Delta) \approx V(t) + \Delta \partial V / \partial t$ (see Exercise 3.12): we find $\Delta \approx 0.1$ is the largest time step we can get away with. We will use ‘no-flow’ boundary conditions, which we implement by setting the Laplacian terms on the boundary to zero (the boundaries, uncoupled from the rest of the system, will quickly turn to their resting state). If you are not supplied with example code that does the two-dimensional plots, you may find them at the text web site [8].

(c) Solve eqn N.30 for an initial condition equal to the fixed-point (V^*, W^*) except for a 10×10 square at the origin, in which you should apply a stimulus $\Delta = 3.0$. (Hint: Your simulation should show a pulse moving outward from the origin, disappearing as it hits the walls.)

If you like, you can mimic the effects of the sinoatrial (SA) node (your heart’s natural pacemaker) by stimulating your heart model periodically (say, with the same 10×10 square). Realistically, your period should be long enough that the old beat finishes before the new one starts.

We can use this simulation to illustrate general properties of solving PDEs.

(d) **Accuracy.** Compare the five and nine-point Laplacians. Does the latter give better circular symmetry? **Stability.** After running for a while, double the time step Δ . How does the system go unstable? Repeat this process, reducing Δ until just before it goes nuts. Do you see inaccuracies in the simulation that foreshadow the instability?

This checkerboard instability is typical of PDEs with too high a time step. The maximum time step in this system will go as dx^2 , the lattice spacing squared—thus to make dx smaller by a factor of two and simulate the same area, you need four times as many grid points and four times as many time points—giving us a good reason for making dx as large as possible (correcting for grid artifacts by using improved Laplacians). Similar but much more sophisticated tricks have been used recently to spectacularly increase the performance of lattice simulations of the interactions between quarks [3].

As mentioned above, heart arrhythmias are due to spiral waves. To generate spiral waves we need to be able to start up more asymmetric states—stimulating several rectangles at different times. Also, when we generate the spirals, we would like to emulate electroshock therapy by applying a stimulus to a large region of the heart. We can do both by writing code to interactively stimulate a whole rectangle at one time. Again, the code you have obtained from us should have hints for how to do this.

(e) Add the code for interactively stimulating a general rectangle with an increment to V of size $\Delta = 3$. Play with generating rectangles in different places while other pulses are going by: make some spiral waves. Clear the spirals by giving a stimulus that spans the system.

There are several possible extensions of this model, several of which involve giving our model spatial structure that mimics the structure of the heart. (One can introduce regions of inactive ‘dead’ tissue. One can introduce the atrium and ventricle compartments to the heart, with the SA node in the atrium and an AV node connecting the two chambers ...) Niels Otani has an exercise with further explorations of a number of these extensions, which we link to from the Cardiac Dynamics web site.

⁴Smaller grids would lead to less grainy waves, but slow down the simulation a lot.