

Equation 5.28 is a pair of coupled finite-difference equations, and they can be iterated to find the solution from any initial condition  $x(0)$ ,  $y(0)$ .

## DYNAMICS IN ACTION

### 15 ACTION POTENTIALS IN NERVE CELLS

To illustrate numerical integration, we will consider a mathematical model of the nerve cell. Nerve cells have a long branch called an axon, which transmits electrical impulses. The axon is an example of an excitable medium (see Section 2.5). Under normal conditions it rests quiescently. Given a small stimulus, it will return to rest almost immediately. However, a sufficiently large stimulus will cause the axon to "fire," after which time it is refractory and returns to rest. The sequence of firing and returning to rest is called an **action potential**.

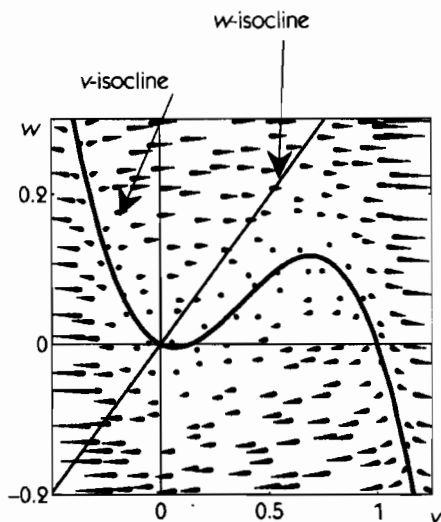
The first detailed and accurate description of the mechanics of the axon was given in a complicated set of equations by A. L. Hodgkin and A. F. Huxley in 1952. This work won them the Nobel prize. A caricature of the Hodgkin-Huxley equations, which nonetheless conveys important aspects of the dynamics, is given by the **Fitzhugh-Nagumo** equation:

$$\begin{aligned}\frac{dv}{dt} &= I - v(v - a)(v - 1) - w, \\ \frac{dw}{dt} &= \epsilon(v - \gamma w).\end{aligned}\tag{5.29}$$

$\gamma$ ,  $\epsilon$ , and  $a$  are parameters, and  $v$  and  $w$  are the dynamical variables.  $v$  is the voltage across the cell membrane, and  $w$  is a recovery variable.  $I$  is the stimulus current that is injected into the cell.

Like the real axon, the equations have a quiescent resting state, and a small stimulus current does not produce an action potential. In our case, we want to see how large a current pulse is needed to generate an action potential when the cell is quiescent.

As you might have anticipated, the quiescent resting state corresponds to a stable fixed point in the differential equations. The figure on the next page shows the isoclines and the flow field when  $I = 0$ . There is a fixed point at  $v = 0$ ,  $w = 0$ .



The isoclines and flow field for the Fitzhugh-Nagumo equations of nerve cell dynamics ( $I = 0$ ).

Linearizing the equations around this fixed point, we find

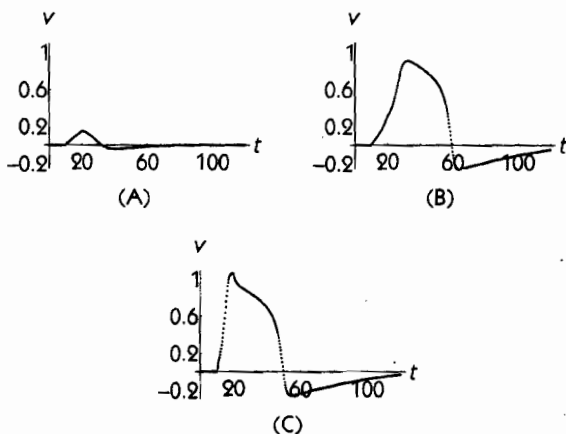
$$\begin{aligned}\frac{dv}{dt} &= -av - w \\ \frac{dw}{dt} &= \epsilon v - \epsilon\gamma w.\end{aligned}$$

The eigenvalues are

$$\lambda = -\frac{a + \epsilon\gamma}{2} \pm \frac{\sqrt{(\epsilon\gamma - a)^2 - 4\epsilon}}{2}.$$

For the resting state to be quiescent, we clearly want to set  $a$ ,  $\gamma$ , and  $\epsilon$  to give stable eigenvalues. Here, we will use the parameters suggested by Rinzel (1977) and set  $\epsilon = 0.008$ ,  $a = 0.139$ , and  $\gamma = 2.54$ . This gives the eigenvalues  $\lambda = -0.797 \pm 0.067i$ . This means that the fixed point is a focus, and since the real part of both eigenvalues is less than 0, we know that the fixed point is stable. Physically, the stable fixed point means that the axon is quiescent; it will stay near the fixed point until a large enough disturbance moves it away. The current stimulus pulse provides this disturbance. What the stability analysis does not tell us is how large the current pulse needs to be to cause an action potential.

The first step in integrating these equations, after picking the parameters  $\epsilon$ ,  $a$ , and  $\gamma$ , is to select a value for the size of the time step,  $\Delta$ . In order for Eq. 5.28 to be a good approximation to Eq. 5.18, we need to pick  $\Delta$  to be as small as possible. On the other hand, in order to keep the amount of computation small, we want to set  $\Delta$  to be as large as possible. One way is to set the value for  $\Delta$  to be some starting value, say  $\Delta = 0.5$ . We carry out the iteration according to Eq. 5.28. Then, we reduce  $\Delta$  by half and repeat the iteration. If we find that the results of the two iterations are approximately the same, then  $\Delta$  is small enough. Otherwise, reduce  $\Delta$  by half again, and repeat. Keep in mind that setting  $\Delta$  too large can have nasty effects; for example, fixed points that are stable in the differential equation can be unstable in the finite-difference approximation if  $\Delta$  is too large.



$v$  versus time in the Fitzhugh-Nagumo model of electrical activity in the nerve cell. Current of amplitude  $I$  is turned on at time  $t = 10$  and turned off at  $t = 20$ . (A)  $I = 0.02$ . No action potential occurs. (B)  $I = 0.03$ . An action potential. (C)  $I = 0.10$ . An action potential.

The iteration according to Eq. 5.28 can be carried out on a computer, or with a calculator, or simply with paper and pencil. Hodgkin and Huxley did their numerical calculations from much more complicated equations using 1950s-era mechanical hand calculators.

In our numerical experiment, we will start the cell at the stable fixed point  $v = 0$ ,  $w = 0$ . At time  $t = 10$ , we will inject current of amplitude  $I$  for 10 time units. Then we will turn off the current and allow the system to evolve autonomously. We want to find what amplitude  $I$  is needed to trigger an action potential.

We will start with a current pulse of amplitude  $I = 0.02$ . The current is turned on at  $t = 10$  and turned off at  $t = 20$ . The figure on the previous page shows transmembrane voltage  $v$  versus time; there is a small deflection in the voltage, which returns to its resting value by  $t = 80$ . In contrast, when a slightly larger current is given,  $I = 0.03$ , the voltage deflection is much larger and lasts much longer. This is an action potential. Increasing the current further to  $I = 0.10$  does not change the amplitude of the action potential by very much.

Equation (5.26) is true only in the limit  $\Delta \rightarrow 0$ . For  $\Delta > 0$ , the equation is only an approximation. One way to make the approximation good is to use very small  $\Delta$ . Another way, beyond the scope of this text, is to use more accurate methods for numerical integration, such as the Runge-Kutta method (Press et al. 1992), instead of the simple Euler method.

## 5.9 ADVANCED TOPIC: DYNAMICS IN THREE OR MORE DIMENSIONS

In the real world, it is unusual to have only a small number of interacting elements. Rather, there are complex networks of interactions. For example, consider the food webs in ecological systems, the multiple synaptic connections in neural networks, or the competition between several businesses in economic systems. In all these circumstances, theoretical models formulated as linear and nonlinear differential equations with more than two variables have been proposed to account for the complex interactions. Even though a great deal of effort has been expended in trying to understand such systems, there remain huge gaps in our mathematical understanding of the dynamics in nonlinear differential equations with three or more interacting variables.

Although much is known about the dynamics in the neighborhood of steady states, and about the bifurcations that arise as a consequence of parametric changes, fundamental mathematical questions involving the classification and the geometry of asymptotic behaviors in the limit  $t \rightarrow \infty$  are still open. In the absence of a complete mathematical theory, there has been a lot of attention on the analysis of particular nonlinear equations. In this section we first give examples of some three-dimensional equations that display chaotic dynamics. Then we show how results concerning analysis of stability in first- and second-order differential equations generalize to higher-dimensional systems.