Two-Dimensional Differential Equations

In the previous chapter we studied differential equations in which quantities increased or decreased in a monotonic fashion, reaching a fixed point as time increased. We know that in the real world quantities can also oscillate up and down in a regular or irregular fashion. The one-dimensional differential equations in the previous chapter, which have a single variable and a first derivative, cannot produce oscillation. In this chapter we consider differential equations with either a pair of variables and their first derivatives, or a single variable and its first and second derivatives. These two classes of problems are equivalent and are called **second-order** or **two-dimensional ordinary differential equations**.

5.1   THE HARMONIC OSCILLATOR

This section introduces several important concepts by considering a familiar problem from elementary physics courses—a mass on a spring (see Figure 5.1). Although masses and springs are of interest mainly to mechanical
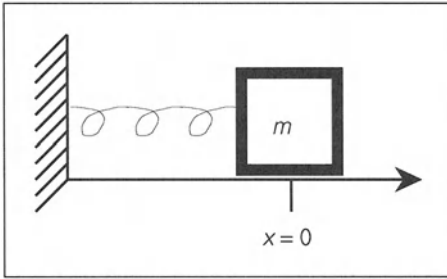
Figure 5.1
The mass on a spring: the archetypical harmonic oscillator.

engineers, the mathematics describing them are fundamental to understanding the dynamics of many other systems. Because the problem is of general interest, it has a general name: the **harmonic oscillator.**

Consider a mass, m, that is attached to a spring resting on a very smooth table so that there is no friction between the mass and the table. If the spring is neither stretched nor compressed, the mass will rest at a steady-state position. Call this position $x = 0$. If the spring is compressed, that is, if $x < 0$, there will be a force tending to increase x, if the spring is stretched, $x > 0$, there will be a force tending to decrease x. According to Hooke's law, familiar from elementary physics, the force, F, is proportional to the position

$$F = -kx,$$

where the constant k is called the **spring constant**. Note that Hooke's law says that there is a *linear* relationship between force and position. Newton's second law of motion says that the acceleration a of a particle of mass m is related to the force on the particle by the famous expression

$$F = ma.$$

In differential calculus, acceleration is simply the second derivative of the position with respect to time. This is because velocity is the rate of change of x with respect to time, $v = \frac{dx}{dt}$, and acceleration is the rate of change of velocity with respect to time, $a = \frac{dv}{dt} = \frac{d^2x}{dt^2}$. Using this fact along with Newton's second law of motion and Hooke's law, we find

$$m\frac{d^2x}{dt^2} = -kx. \tag{5.1}$$

This is a linear, second-order, ordinary differential equation. In general, we want to solve this equation given some initial values of the position and the velocity.

5.2 SOLUTIONS, TRAJECTORIES, AND FLOWS

Let us assume that at $t = 0$ the mass in Figure 5.1 is displaced to a position $x(0)$ and released from rest so that the initial velocity is $v(0) = 0$. We propose the following function as a solution to Eq. 5.1:

$$x(t) = x(0) \cos \omega t \quad \text{where} \quad \omega = \sqrt{\frac{k}{m}}. \tag{5.2}$$

Demonstrating that this is indeed a solution is straightforward: If we substitute this proposed solution into Eq. 5.1 and carry out the second derivative, we find that both sides of the equation are the same. A graph of this solution is shown in Figure 5.2. The solution oscillates without approaching a steady state. The time it takes to complete one cycle of the oscillation is $\frac{2\pi}{\omega}$.

What is the initial condition for this solution? By analogy to Chapter 4, we might say that it is $x(0)$. But this is only half the story. If we placed the mass at position $x(0)$, it might be moving either to the right, to the left, or not at all; to provide a complete description of the initial condition, we also need to specify $v(0)$. In the solution given in Eq. 5.2, we happened to set $v(0) = 0$, but we might ask what are the solutions for other values of $v(0)$.

One way to gain insight into the dynamics of the harmonic oscillator is to consider all the possible initial conditions. Each possible initial condition can be represented as a point on a plane—the (x, v)-plane. The **state** of the harmonic oscillator at time t is the pair of values $(x(t), v(t))$. We can plot out the state as time proceeds simply by plotting $(x(t), v(t))$ in the (x, v)-plane. The path traced out is called the **trajectory**. The (x, v)-plane is called the **phase plane**.

Note that given a solution $x(t)$, we can easily find the velocity $v(t)$ by differentiation:

$$v(t) = -\omega x(0) \sin \omega t. \tag{5.3}$$

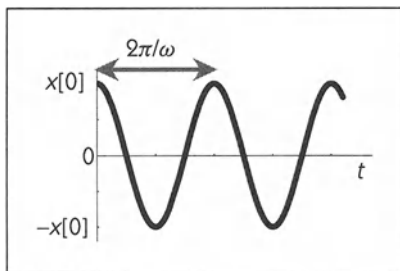From Equations 5.2 and 5.3, and using the trigonometric identity $\sin^2 \omega t +$

Figure 5.2
A solution $x(t)$ to Eq. 5.1.

$\cos^2 \omega t = 1$, we find

$$x^2(t) + \frac{v^2(t)}{\omega^2} = x^2(0). \tag{5.4}$$

This is the equation for an ellipse in the (x, v)-plane (see Section A.8). An example of the trajectory for two different initial conditions is shown in Figure 5.3. Both initial conditions have $v(0) = 0$, but one has $x(0) = 0.5$ while the other has $x(0) = 1.0$. You can see that the two trajectories plotted in Figure 5.3 are both ellipses with the same shape but different sizes; the size is governed by the initial conditions $x(0)$ and $v(0)$.

Recall from physics that the **potential energy** of a mass on a spring is $\frac{1}{2}kx^2$ and the **kinetic energy** is $\frac{1}{2}mv^2$. It follows from Equation 5.4 and $\omega = \sqrt{\frac{k}{m}}$ that

$$\frac{1}{2}kx(t)^2 + \frac{1}{2}mv(t)^2 = \frac{1}{2}kx^2(0).$$

The sum of the potential and kinetic energies is the **total energy**, and we can see from the above equation that "energy is conserved," that is, the total energy does not change. In this case the conservation of energy holds because there is no friction and because nothing is putting energy into the system. The energy always stays at the same value it had originally. In many other systems, energy is not conserved. Later, we will study some such systems.
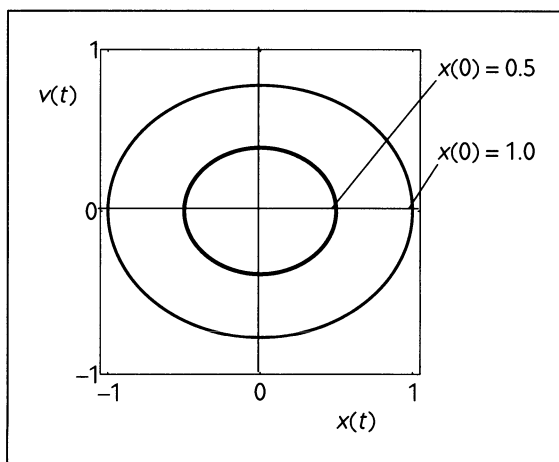

Figure 5.3 The trajectory of two solutions to Eq. 5.1, plotted in the phase plane. One solution has initial condition $x(0) = 0.5$, $v(0) = 0$; the other has initial condition $x(0) = 1.0$, $v(0) = 0$.

One of the consequences of the conservation of energy in the harmonic oscillator concerns the stability of the trajectories. We have already seen that all the trajectories are closed ellipses. These closed ellipses correspond to periodic cycles. Are these cycles stable? Just as in finite-difference equations, a stable cycle is a cycle that is reestablished following a small displacement from the cycle. In the current case, a small displacement leads to another closed ellipsoidal trajectory— the displaced trajectory will not find its way back to the original trajectory. Thus, the cycles in the harmonic oscillator are not stable.

The initial condition is a special case of the state: It is the state at time $t = 0$. So, given the trajectory from an initial condition, we also have the trajectory through many other possible initial conditions—any initial condition that lies on a given trajectory will follow that same trajectory.

A two-dimensional differential equation can be represented as a pattern in the phase plane. The equation can be thought of as a rule that tells us how any given state changes in time. In other words, the equation tells us how a trajectory passes through any point in the phase plane. For any given initial condition, there is only one trajectory; however, the differential equation tells us about all possible trajectories.

We could plot out this information by showing every possible trajectory. This would not be very practical, since the entire phase plane would be covered with ink. Instead, we will draw the trajectory through only a few points, indicating the direction of the trajectory by making the line thicker as time progresses. The entire pattern of trajectories in the phase plane is called the **flow** of the differential equation (analogous to the flow of water). A single trajectory is analogous to the path that would be followed by a (massless) particle if it had been placed in the water; the initial condition is analogous to the place the particle is first placed. Figure 5.4 shows the flow for the harmonic oscillator.

5.3   THE TWO-DIMENSIONAL LINEAR ORDINARY DIFFERENTIAL EQUATION

In the analysis of one-dimensional nonlinear finite-difference equations (Chapter 1) and differential equations (Chapter 4), the basis for the local stability analysis was a firm understanding of the linear system. Similarly, the analysis of two-dimensional nonlinear ordinary equations follows in a straightforward fashion once we understand the linear problem. The linear problem is also of interest in its own right, since many theoretical models in kinetics, mechanics, and electrical circuits are formulated as two-dimensional linear ordinary equations.
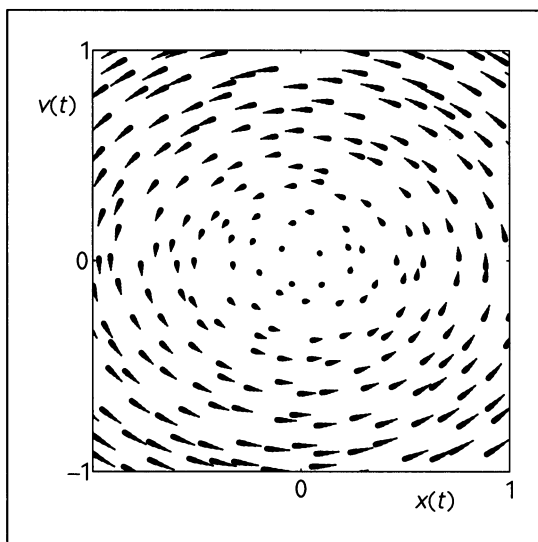
Figure 5.4   The flow of the harmonic oscillator in Eq. 5.1.

The two-dimensional linear ordinary differential equation is written as

$$a\frac{d^2x}{dt^2} + b\frac{dx}{dt} + cx = 0, \tag{5.5}$$

where a, b, and c are constants that we will assume are real numbers. In Chapter 4 we saw that the solution to the one-dimensional linear ordinary differential equation is an exponential. It is an amazing fact that an exponential is also often the solution to higher-dimensional ordinary differential equations—but of course there is a complex twist to the story.

In order to solve Eq. (5.5) we will substitute in a **trial solution:**

$$x(t) = Ce^{\lambda t}. \tag{5.6}$$

Here C and λ represent constants—we do not yet know their value, but we are hoping to be able to find them from the differential equation. We will be able to do so only if Eq. 5.6 is an appropriate form for a solution to Eq. 5.5. Substituting the trial solution into Eq. 5.5 and carrying out the derivatives, we find

$$aC\lambda^2 e^{\lambda t} + bC\lambda e^{\lambda t} + cCe^{\lambda t} = 0.$$

Dividing each term of this equation by $Ce^{\lambda t}$, we obtain an equation that is called the **characteristic equation**, or the **eigenvalue equation**:

$$a\lambda^2 + b\lambda + c = 0, \tag{5.7}$$

If we can find any values for λ that solve this equation, then we know that the trial solution is valid for those values of λ. Of course, Eq. 5.7 is a quadratic equation in λ. The solution for λ as a function of the parameters a, b, and c can be found from the quadratic formula:

$$\lambda_1 = \frac{-b + \sqrt{b^2 - 4ac}}{2a}, \qquad \lambda_2 = \frac{-b - \sqrt{b^2 - 4ac}}{2a}. \tag{5.8}$$

We call λ_1 and λ_2 the **characteristic values**, or **eigenvalues**, of Eq. 5.5.

Since there are two valid values of λ, we have found two solutions to the differential equation. Actually, there is an infinity of possible solutions, which have the general form

$$x(t) = C_1 e^{\lambda_1 t} + C_2 e^{\lambda_2 t}, \tag{5.9}$$

where C_1 and C_2 are constants. Note that the characteristic equation did not put any constraint on C in the trial solution, so any constant value of C gives a valid solution. The actual values of C_1 and C_2 for any given trajectory are set by the initial conditions.

❏ **EXAMPLE 5.1**

Verify that Eq. 5.9 is a solution to Eq. 5.5.

Solution: Taking the first and second derivative of $x(t)$ from Eq. 5.9 and substituting into Eq. 5.5, we find

$$a(C_1\lambda_1^2 e^{\lambda_1 t} + C_1\lambda_2^2 e^{\lambda_2 t}) + b(C_1\lambda_1 e^{\lambda_1 t} + C_1\lambda_2 e^{\lambda_2 t}) + c(C_1 e^{\lambda_1 t} + C_1 e^{\lambda_2 t}) = 0$$

Re-arranging terms gives

$$(a\lambda_1^2 + b\lambda_1 + c)C_1 e^{\lambda_1 t} + (a\lambda_2^2 + b\lambda_2 + c)C_1 e^{\lambda_2 t} = 0.$$

Eq. 5.9 is a solution to Eq. 5.5 only if the above equation is true. But, since the values of λ_1 and λ_2 are chosen to satisfy the characteristic equation (Eq. 5.7), we know that the terms in the parentheses are zero in the above equation, and

so the left-hand side does indeed equal zero. This is true for any values of C_1 and C_2.

◻

Here's the twist in the story: If $b^2 < 4ac$, it follows from Eq. 5.8 that λ_1 and λ_2 are complex numbers. They can be written as

$$\lambda_1 = \alpha + \beta i, \qquad \lambda_2 = \alpha - \beta i,$$

where

$$\alpha = -\frac{b}{2a}, \qquad \beta = \frac{\sqrt{4ac - b^2}}{2a},$$

and of course the infamous $i = \sqrt{-1}$.

You may well be wondering, how can a differential equation that is supposed to describe the real world have a solution that involves imaginary numbers? The answer, in brief, is that C_1 and C_2 are also complex numbers, and that for any real initial conditions, C_1 and C_2 will cancel out the imaginary part of the solution, leaving only the real part.

Many people would feel more comfortable if the solution to Eq. 5.5 could be presented without any mention of imaginary numbers. This real solution is (at least, it's real as long as $b^2 < 4ac$)

$$x(t) = C_3 e^{\alpha t} \cos \beta t + C_4 e^{\alpha t} \sin \beta t, \qquad (5.10)$$

where C_3 and C_4 are now *bona fide* real constants, which can be set from initial conditions. However, if $b^2 > 4ac$, then β in Eq. 5.10 is itself complex, and you have to start worrying about what the sine and cosine of a complex number are. In this case, go back to Eq. 5.9, which will now look like a perfectly ordinary solution in terms of exponential functions of real numbers.

For those readers who are interested in understanding the relationship between Eqs. 5.9 and 5.10, we offer the following information. If we have a complex number $\gamma + \delta i$, then

$$e^{\gamma + \delta i} = e^{\gamma} (\cos \delta + i \sin \delta).$$

(See Problem 5.3 for a derivation of this relationship.) Similarly,

$$\cos \omega t = \frac{1}{2} \left(e^{i\omega t} + e^{-i\omega t} \right)$$

and

$$\sin \omega t = \frac{1}{2i} \left(e^{i\omega t} - e^{-i\omega t} \right).$$

These identities lead to one of the most magical relationships in all of mathematics, which involves the seemingly unrelated irrational numbers e and π, along with $i = \sqrt{-1}$:

$$e^{i\pi} + 1 = 0.$$

❑ EXAMPLE 5.2

In the real world, a harmonic oscillator such as a spring does not swing forever; it eventually slows down due to friction and air resistance. This friction is called "damping," and the equation for a damped spring can be written as

$$\frac{d^2x}{dt^2} + \mu \frac{dx}{dt} + \omega^2 x = 0,$$

where μ is a number that describes how much damping there is. If μ were zero (i.e., no damping), then the solution to the equation would be a sinusoid with a period of oscillation of $\frac{2\pi}{\omega}$. Determine the solution of this equation in the presence of damping, starting from an initial condition of $x(0) = 5$ deg and $\frac{dx}{dt} = 0$ deg/sec.

Solution: The characteristic equation for this system is

$$\lambda^2 + \mu\lambda + \omega^2 = 0.$$

The eigenvalues of this are

$$\lambda_1 = \frac{1}{2} \left[-\mu + \sqrt{\mu^2 - 4\omega^2} \right] \quad \text{and} \quad \lambda_2 = \frac{1}{2} \left[-\mu - \sqrt{\mu^2 - 4\omega^2} \right].$$

If $\mu^2 > 4\omega^2$, both eigenvalues are negative. If $\mu^2 < 4\omega^2$, both eigenvalues are complex conjugates. These two cases are treated differently, as desribed below.

- When $\mu^2 > 4\omega^2$: Call $\alpha = \sqrt{\mu^2 - 4\omega^2}$. The solution can be written as

$$x(t) = C_1 e^{\frac{-\mu+\alpha}{2}t} + C_2 e^{\frac{-\mu-\alpha}{2}t}.$$

From the initial conditions ($x(0) = 5$ and $\frac{dx}{dt} = 0$) we find that

$$C_1 + C_2 = 5; \qquad \left(\frac{-\mu + \alpha}{2}\right) C_1 + \left(\frac{-\mu - \alpha}{2}\right) C_2 = 0.$$

Since there are two equations in the two unknowns, we can solve for C_1 and C_2:

$$C_1 = \frac{5}{2}\left(\frac{\alpha + \mu}{\alpha}\right) \quad \text{and} \quad C_2 = \frac{5}{2}\left(\frac{\alpha - \mu}{\alpha}\right).$$

Therefore, the solution of the equation is

$$x(t) = \frac{5}{2}\left(\frac{\alpha + \mu}{\alpha}\right) e^{\frac{-\mu + \alpha}{2} t} + \frac{5}{2}\left(\frac{\alpha - \mu}{\alpha}\right) e^{\frac{-\mu - \alpha}{2} t}.$$

Since $\mu > \alpha$, both eigenvalues are negative and there is a monotonic approach to $x = 0$. This is illustrated in Figure 5.5.

- When $\mu^2 < 4\omega^2$: Call $\alpha = \sqrt{4\omega^2 - \mu^2}$. Therefore, from Eq. 5.10 we know that the solution is

$$x(t) = C_3 e^{-\frac{\mu t}{2}} \cos \frac{\alpha t}{2} + C_4 e^{-\frac{\mu t}{2}} \sin \frac{\alpha t}{2}.$$

Now applying the initial conditions at $t = 0$, we find

$$C_3 = 5, \qquad \left(\frac{-\mu}{2}\right) C_3 + \left(\frac{-\alpha}{2}\right) C_4 = 0.$$
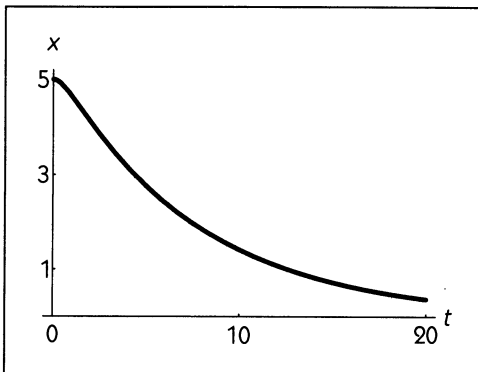

Figure 5.5
The solution of the differential equation for the damped pendulum with $\mu = 2, \omega = 0.5$.
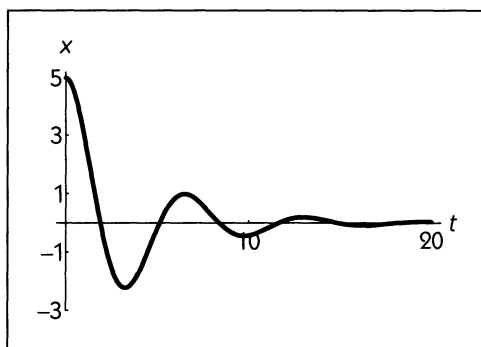
Figure 5.6
The solution to the differential equation for the damped pendulum with $\mu = 0.5, \omega = 1$.

Consequently, we have

$$C_3 = 5 \quad \text{and} \quad C_4 = \frac{5\mu}{\alpha}.$$

Therefore, the solution $x(t)$ is

$$x(t) = 5e^{-\frac{\mu t}{2}} \cos \frac{\alpha t}{2} + \frac{5\mu}{\alpha} e^{-\frac{\mu t}{2}} \sin \frac{\alpha t}{2}.$$

This is an oscillatory decay to $x = 0$, as illustrated in Figure 5.6. $\qquad\square$

5.4 COUPLED FIRST-ORDER LINEAR EQUATIONS

In the case of the mass on a spring, there was one fundamental variable, position, from which the velocity and acceleration could be derived. In other systems there may be more than one fundamental variable, and the rate of change of each of the variables may be a function of the current values all the variables. Here, we will consider the case where there are two such variables. The two variables might represent, for example, two interacting animal species in an ecological system, two different conductances of ion channels in a cell membrane, two different chemicals in a chemical reaction, or the concentration of a drug in two different organs.

Such systems can be represented by a pair of **coupled** ordinary differential equations. In a simple but important case, the derivatives are linear functions of the variables so that

$$\frac{dx}{dt} = Ax + By, \qquad \frac{dy}{dt} = Cx + Dy, \qquad (5.11)$$

where A, B, C, and D are constants. Although Eqs. 5.5 and 5.11 and at first appear to be different, they are completely equivalent. Therefore, once you know how to solve one of them, you can solve the other.

In order to show the equivalence of both formulations, we first compute the second derivative $\frac{d^2x}{dt^2}$ in Eq. 5.11, to obtain

$$\frac{d^2x}{dt^2} = A\frac{dx}{dt} + B\frac{dy}{dt}.$$

Now substituting the value for $\frac{dy}{dt}$ from Eq. 5.11 into the above expression, we find

$$\frac{d^2x}{dt^2} = A\frac{dx}{dt} + BCx + BDy.$$

Finally, since from Eq. 5.11 we know that $By = \frac{dx}{dt} - Ax$, we can substitute this value to obtain finally the expression

$$\frac{d^2x}{dt^2} - (A + D)\frac{dx}{dt} + (AD - BC)x = 0.$$

Thus, Eq. 5.11 is equivalent to Eq. 5.5 as long as

$$-(A + D) = \frac{b}{a} \quad \text{and} \quad AD - BC = \frac{c}{a}.$$

For any a, b, and c, values of A, B, C, and D that satisfy this relationship can always be found, and vice versa.

We can find the solution to Eq. 5.11 in terms of A, B, C, and D by solving the characteristic equation. In the current case, following the same procedure as in the preceding section, the characteristic equation is

$$\lambda^2 - (A + D)\lambda + (AD - BC) = 0, \tag{5.12}$$

so that the eigenvalues are computed from the quadratic equation as

$$\lambda_1 = \frac{A + D}{2} + \frac{\sqrt{(A - D)^2 + 4BC}}{2}$$

$$\lambda_2 = \frac{A + D}{2} - \frac{\sqrt{(A - D)^2 + 4BC}}{2}. \tag{5.13}$$

Thus, the solution for $x(t)$ is given by

$$x(t) = C_1e^{\lambda_1 t} + C_2e^{\lambda_2 t}$$

which is real if λ_1 and λ_2 are real numbers. If $(A - D)^2 + 4BC < 0$, then λ_1 and λ_2 are complex numbers. Let

$$\alpha = \frac{A + D}{2} \quad \text{and} \quad i\beta = \frac{\sqrt{(A - D)^2 + 4BC}}{2}.$$

Then, $\lambda_1 = \alpha + i\beta$ and $\lambda_2 = \alpha - i\beta$ and the solution is

$$x(t) = e^{\alpha t}(C_3 \cos \beta t + C_4 \sin \beta t).$$

C_1 and C_2, or C_3 and C_4 can be found from the initial condition $x(0)$ and $\frac{dx}{dt}(0)$. If λ_1 and λ_2 are real, then

$$x(0) = C_1 + C_2$$
$$\frac{dx}{dt}(0) = \lambda_1 C_1 + \lambda_2 C_2,$$

which can be solved for C_1 and C_2. If λ_1 and λ_2 are complex, then

$$x(0) = C_3$$
$$\frac{dx}{dt}(0) = \beta C_4.$$

DYNAMICS IN ACTION

14 METASTASIS OF MALIGNANT TUMORS

Metastasis of cancer is a process whereby cancer cells spread in the body. In some cases, the cancer cells spread through the bloodstream and are arrested in the capillary bed of an organ. Most of the arrested cells either die or are dislodged from the capillary bed, but some are able to traverse the capillary wall and initiate metastatic foci in the tissue of the organ. Liotta and DeLisi (1977) studied metastasis of radioactively labeled tumor cells to the lungs of laboratory mice. The cells were injected into the tail veins of mice and transported to the lung by the bloodstream. The radioactive labeling allowed the number of tumor cells in the mice's lungs to be measured.
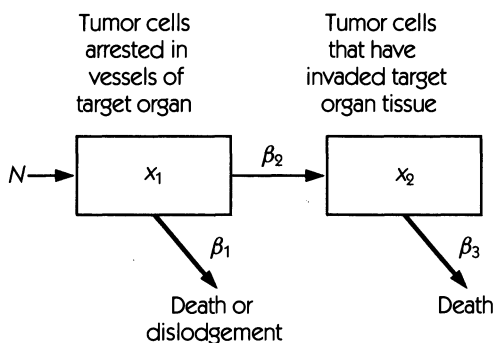
Compartmental model for metastatic spread of cancer cells. x_1 is the number of cancer cells arrested in the vessels of the target organ and x_2 is the number of tumor cells that have invade the target organ tissue. The cells pass between compartments following linear rate laws as described in the text. Adapted from Liotta and Delisi (1977).

The figure on the facing page shows the number of tumor cells plotted on a semilog-arithmic scale. If the data were described by an exponential decay, they would fall on a straight line, but this is not the case. Liotta and DeLisi proposed a more complicated theoretical model accounting for the idea that tumor cells are first arrested in the capillary bed of the lung ("compartment 1"), and then invade the lung tissue itself ("compartment 2").

By measuring the various rates from experimental data, it is possible to assess how effective treatments are in reducing metastasis. Based on their knowledge of the biology of metastasis, Liotta and DeLisi propose the following mathematical description of the kinetics of radioactively labeled cells:

$$\frac{dx_1}{dt} = -(\beta_1 + \beta_2)x_1,$$

$$\frac{dx_2}{dt} = \beta_2 x_1 - \beta_3 x_2.$$

The number of arrested cells is designated x_1 and the number that successfully invade the target tissue is designated x_2. Cells pass from compartment 1 to compartment 2 at a rate $\beta_2 x_1$. Cells are lost from compartment 1 by death or dislodgement at a rate $\beta_1 x_1$, and from compartment 2 at a rate $\beta_3 x_2$. These relationships are schematically represented in the upper figure. The initial conditions are $x_1(0) = N$ and $x_2(0) = 0$. N is the number of cells that are initially arrested in the target organ.
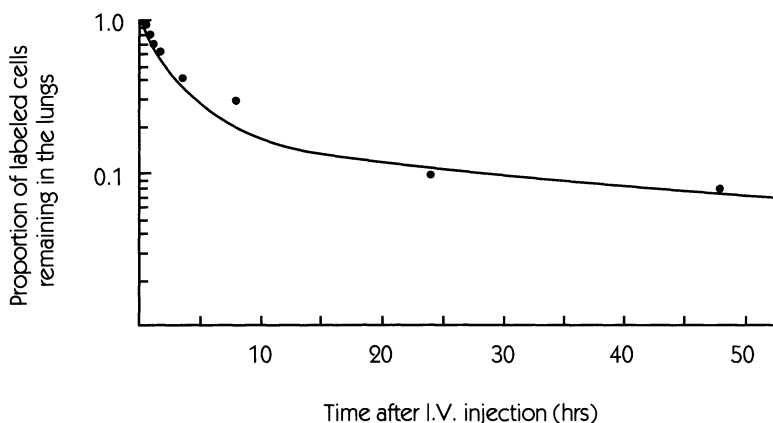
The proportion of labeled cells remaining in the lungs following intravenous injection in the tail veins of mice. The dots show the experimental data, and the line is a fitted solution to the model. Note the semilogarithmic axes. Adapted from Liotta and Delisi (1977) based on Proctor et al. (1976).

Experimentally, the total number of tumor cells in the lung, $x_1(t) + x_2(t)$, is measured. The model can be used to calculate $x_1(t) + x_2(t)$, and the experimental measurement of this number can then be used to estimate the rates in the model.

Since the variable x_1 follows the kinetics of exponential decay, we can use the methods in Chapter 3 to find

$$x_1(t) = Ne^{-(\beta_1 + \beta_2)t}.$$

To find the solution for $x_2(t)$, we notice that the pair of differential equations looks just like Eq. 5.11 with $x_2 = x$ and $x_1 = y$, and

$$A = -\beta_3, B = -\beta_2, C = 0, \text{ and } D = -(\beta_1 + \beta_2).$$

We can sustitute these values for A, B, C, and D into Eq. 5.13 to find

$$\lambda = -\frac{\beta_1 + \beta_2 + \beta_3}{2} \pm \frac{\sqrt{(\beta_1 + \beta_2 - \beta_3)^2}}{2}$$

so that we find the two eigenvalues

$$\lambda_1 = -\beta_3, \qquad \lambda_2 = -(\beta_1 + \beta_2).$$

Therefore, we obtain

$$x_2(t) = C_1 e^{-\beta_3 t} + C_2 e^{-(\beta_1 + \beta_2)t},$$

where C_1 and C_2 are constants that still need to be set from the initial conditions.

At $t = 0$, from the initial conditions stated in the problem we know that $x_2(0) = 0$ and $\frac{dx_2}{dt}(0) = \beta_2 N$. Equating the expression for $x_2(t)$ equal to 0, we find

$$C_1 + C_2 = 0.$$

Taking the derivative of the expression for $x_2(t)$ and equating it to $\beta_2 N$, we find

$$-\beta_3 C_1 - (\beta_1 + \beta_2)C_2 = \beta_2 N.$$

Thus, from the two initial conditions, we have been able to derive two equations that can be solved simultaneously to obtain values for the two unknowns, C_1 and C_2. Carrying out the algebra, we find

$$C_1 = -\phi N, \qquad C_2 = \phi N,$$

where

$$\phi = \frac{\beta_2}{\beta_3 - (\beta_1 + \beta_2)}.$$

Therefore,

$$x_2(t) = \phi N \left[-e^{-\beta_3 t} + e^{-(\beta_1 + \beta_2)t} \right].$$

Consequently, the total amount of radioactive label in the lung as a function of time is

$$x_1(t) + x_2(t) = N \left[(\phi + 1)e^{-(\beta_1 + \beta_2)t} - \phi e^{-\beta_3 t} \right].$$

In the graph on page 227, the solid curve shows the fit to the data with $\beta_1 = 0.32$ hr^{-1}, $\beta_2 = 0.072$ hr^{-1}, and $\beta_3 = 0.02$ hr^{-1}. Therefore, for t sufficiently large that $(\beta_1 + \beta_2)t \gg 1$, we find that the cells have disappeared from compartment 1, and the long time behavior is dominated by the destruction of cells remaining in compartment 2 at a rate β_3.

DETERMINANTS AND EIGENVALUES*

The characteristic equation for a pair of coupled first-order linear differential equations (Eq. 5.11) can also be expressed in terms of **determinants**. The basic idea is simple, but it requires some linear algebra. If you haven't studied linear algebra, keep in mind that you already know the solution to Eq. 5.11 as given by Eq. 5.9 or, equivalently, Eq. 5.10.

Equation (5.11) can be written as a **matrix** equation:

$$\begin{pmatrix} \dfrac{dx}{dt} \\ \dfrac{dy}{dt} \end{pmatrix} = \begin{pmatrix} A & B \\ C & D \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix}. \tag{5.14}$$

Suppose we could define two variables, ξ and η such that for some constants α, β, γ, and δ,

$$x = \alpha\xi + \beta\eta,$$
$$y = \gamma\xi + \delta\eta, \tag{5.15}$$

and such that

$$\begin{pmatrix} \dfrac{d\xi}{dt} \\ \dfrac{d\eta}{dt} \end{pmatrix} = \begin{pmatrix} \lambda_1 & 0 \\ 0 & \lambda_2 \end{pmatrix} \begin{pmatrix} \xi \\ \eta \end{pmatrix}. \tag{5.16}$$

This equation is much easier to solve, because it is two uncoupled equations:

$$\frac{d\xi}{dt} = \lambda_1\xi \quad \text{and} \quad \frac{d\eta}{dt} = \lambda_2\eta.$$

From the previous chapter, we know that these two equations have the solution $\xi(t) = \xi(0)e^{\lambda_1 t}$ and $\eta(t) = \eta(0)e^{\lambda_2 t}$. Now it would be easy to find $x(t)$ and $y(t)$ simply by applying Eq. 5.15.

The problem of finding ξ and η that satisfy Eq. 5.15 and Eq. 5.16 is well known in linear algebra as the **eigenvalue** problem. The solution is routine once one knows the technique. It involves solving the equation

$$\det \begin{vmatrix} A - \lambda & B \\ C & D - \lambda \end{vmatrix} = 0, \tag{5.17}$$

---

*This section employs linear algebra. It gives an alternative and more elegant method to show that the eigenvalues of Eq. 5.11 are those given in Eq. 5.13. Using this method facilitates computations, but it is not essential.

where $\det| \cdot |$ denotes the determinant of the matrix. The determinant of a matrix with two rows and two columns is defined as

$$\det \begin{vmatrix} a & b \\ c & d \end{vmatrix} = ad - bc.$$

Applying the definition of the determinant to Eq. 5.17, we find that it is exactly the same as Eq. 5.12.

5.5   THE PHASE PLANE

Two-dimensional *nonlinear* ordinary differential equations are often written in the form

$$\frac{dx}{dt} = f(x, y),$$

$$\frac{dy}{dt} = g(x, y), \tag{5.18}$$

where $f(x, y)$ and $g(x, y)$ are nonlinear functions of x and y. Just as we saw in Chapter 1, the introduction of nonlinear functions can make it difficult, if not impossible, to find an analytic form for the solution.

A *qualitative* understanding of two-dimensional nonlinear ordinary differential equations can often be gained from studying the **phase plane** of the system. This can provide information about multiple stable and unstable fixed points that is not given by numerical integration. In this section we will describe geometric methods of studying the phase plane. In the following section, we will return to the algebraic method for the analysis of the stability of fixed points. Later, we will describe a numerical method for finding approximate solutions to nonlinear ordinary differential equations.

As an example of the use of geometric phase-plane techniques, consider the interaction of a predator and a prey species. Let x be the population of a prey species and y be the population of a predator species. We assume that if there were no predator, the prey would increase exponentially, and that if there were no prey, the predator would decrease exponentially. By eating the prey, the predator increases its own population and, obviously, decreases the population of the prey. The rate at which predator and prey meet (and therefore the rate at which the prey disappears and the predator thrives) is assumed to be proportional to the product of the populations of the predator and the prey. The justification for this is that if the population of either predator or prey is zero, the meeting rate is zero.

The equations are written as

$$\frac{dx}{dt} = \alpha x - \beta xy,$$

$$\frac{dy}{dt} = \gamma xy - \delta y, \tag{5.19}$$

where $x, y \geq 0$ and α, β, γ, and δ are positive constants. These are the **Lotka-Volterra equations**. The equations were proposed independently by Volterra, who was a mathematician interested in ecology, and Lotka, a chemist interested in oscillatory chemical reactions.

The first step in examining the geometry of the dynamics involves looking at the **isoclines** of the flow. The **x-isocline** is the locus of points in (x, y)-plane along which $\frac{dx}{dt} = 0$. The **y-isocline** is, similarly, the locus of points along which $\frac{dy}{dt} = 0$. Fixed points are values at which both $\frac{dx}{dt} = 0$ and $\frac{dy}{dt} = 0$. Fixed points occur at the points of intersection of the x- and y-isoclines.

Let us now consider the Lotka-Volterra equation as an example of geometrical analysis of the phase plane. Figure 5.7 shows the flow, as well as the x- and y-isoclines. The x-isocline is defined by the expression

$$f(x, y) = \alpha x - \beta xy = 0.$$

This will be satisfied if

$$x = 0 \quad \text{or} \quad \alpha - \beta y = 0,$$

which describes two perpendicular lines in Figure 5.7. Similarly, the y-isocline is found from

$$g(x, y) = \gamma xy - \delta y = 0.$$

This expression is satisfied if

$$y = 0 \quad \text{or} \quad \gamma x - \delta = 0,$$

again, two perpendicular lines.

There are two points of intersections of the x- and y-isoclines, and hence two fixed points. The fixed point at $x = y = 0$ has an obvious biological interpretation: There are no predators and no prey, and therefore nothing would ever change in time. The second fixed point, $y = \frac{\alpha}{\beta}$, $x = \frac{\delta}{\gamma}$, is a point where the populations of predator and prey are exactly balanced. Away from the x- and y-isoclines there will be changes in the population levels of x and y.
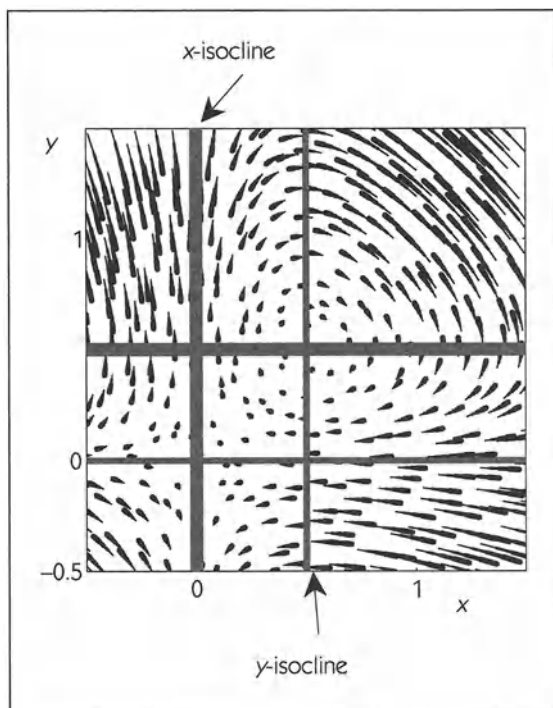
Figure 5.7   The isoclines and flow of the Lotka-Volterra system (Eq. 5.19 with $\beta = \gamma = 2$ and $\alpha = \delta = 1$.) The x-isocline (thick lines) and the y-isocline (thin lines) intersect at the two fixed points of the dynamics.

In order to examine the dynamics away from the isocline, one looks at the flow imposed by the differential equations. This can easily be done. In a short time interval Δ there will be a displacement in the x direction of approximately $x = f(x, y)\Delta$. The displacement in the y direction is approximately $y = g(x, y)\Delta$. The local trajectory through x, y can be found by taking the vector sum of the x and y displacements. For detailed pictures of the sort shown in Figure 5.7, it is convenient to use a computer to draw the picture of the flow in the phase plane.

For understanding the dynamics of a system, a quick, "back-of-the-envelope" picture of the dynamics is often sufficient. This can be drawn as follows:

1. Draw the x- and y-isoclines.

2. On one side of the x-isocline the flow will be to the left and on the other side, the flow will be to the right. Use the equations to decide which side is which, and draw many arrows showing the flow in the x direction. This is shown in Figure 5.8.
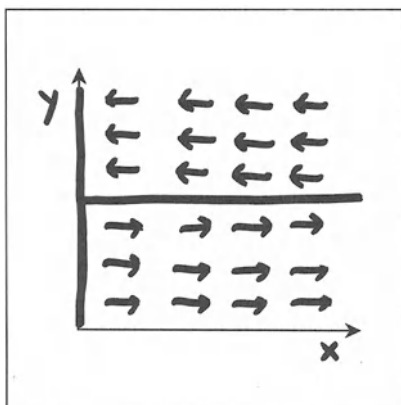
Figure 5.8
The x-isocline and arrows showing the direction of flow in the x direction on each side of the isocline.

3. Similarly, on one side of the y-isocline the flow will be downwards, and on the other side the flow will be up. Draw many arrows showing the flow in the y direction (see Figure 5.9).

4. Combine the x and y arrows to give the vector flow field. This is shown in Figure 5.10.

Of course, it is possible, either by hand or using a computer, to draw a detailed picture of the flow. In the Lotka-Volterra system, by tracing a trajectory through the flow, we see that starting from any point with positive populations, we will cycle around the fixed point, producing oscillations of predator and prey. It is not possible with this geometric method to tell if the cycling will be periodic or will spiral in to the fixed point or away from it. However, additional analysis using a quantity analogous to the energy in the harmonic oscillator shows that in this problem the trajectories are closed paths, just as we found in the ideal
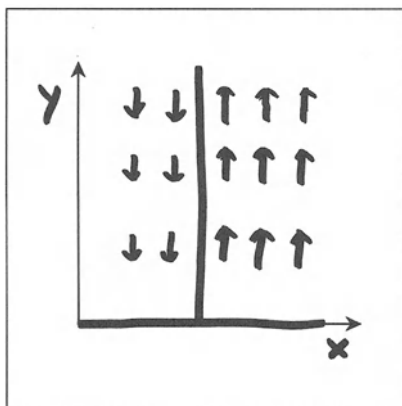

Figure 5.9
The y-isocline and arrows showing the direction of flow in the y direction.
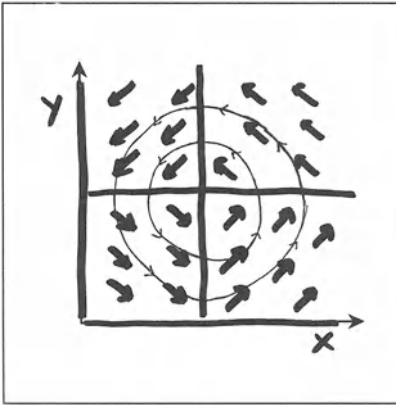
Figure 5.10
Combining the x and y flow gives an idea of what the trajectories look like.

harmonic oscillator. Therefore, the Lotka-Volterra system gives rise to periodic cycles in population. (See Problem 5.28.)

5.6 LOCAL STABILITY ANALYSIS OF TWO-DIMENSIONAL, NONLINEAR DIFFERENTIAL EQUATIONS

The local stability analysis of fixed points in two-dimensional nonlinear ordinary differential equations such as Eq. 5.18 is based on approximating the nonlinear equation by a linear equation in the neighborhood of fixed points of the equation. We can then make use of our understanding of two-dimensional linear equations to determine the dynamics in the neighborhood of the fixed points.

Assume that we are given the nonlinear Eq. 5.18. Let us assume that there is a fixed point (x^*, y^*) for which $f(x^*, y^*) = g(x^*, y^*) = 0$. The linear analysis involves carrying out a Taylor expansion of the nonlinear functions $f(x, y)$ and $g(x, y)$ in the neighborhood of (x^*, y^*). The Taylor expansion of a function $f(x, y)$ is

$$f(x, y) = f(x^*, y^*) + \left.\frac{\partial f}{\partial x}\right|_{x^*, y^*} (x - x^*) + \left.\frac{\partial f}{\partial y}\right|_{x^*, y^*} (y - y^*) + \cdots , \quad (5.20)$$

where the dots represent terms with higher-order derivatives such as $\frac{1}{2}\frac{\partial^2 x}{\partial t^2}(x - x^*)^2$. If we now let

$$X = x - x^*, \qquad Y = y - y^*, \quad (5.21)$$

We can expand Eq. 5.18 to obtain

$$\frac{dX}{dt} = AX + BY + \cdots ,$$

$$\frac{dY}{dt} = CX + DY + \cdots , \qquad (5.22)$$

where

$$A = \left.\frac{\partial f}{\partial x}\right|_{x^*,y^*} \qquad B = \left.\frac{\partial f}{\partial y}\right|_{x^*,y^*}$$

$$C = \left.\frac{\partial g}{\partial x}\right|_{x^*,y^*} \qquad D = \left.\frac{\partial g}{\partial y}\right|_{x^*,y^*} . \qquad (5.23)$$

In the neighborhood of the fixed point, the higher-order terms are negligible in comparison with the linear terms in Eq. 5.22. Consequently, in the neighborhood of the fixed point, the nonlinear equation can be approximated by a linear equation:

$$\frac{dX}{dt} = AX + BY,$$

$$\frac{dY}{dt} = CX + DY. \qquad (5.24)$$

The process of approximating a nonlinear differential equation by equations of the form of Eq. 5.24 is called **linearization.**

The geometry of the vector field in the neighborhood of the fixed points in the phase-plane representation can be classified based on the eigenvalues of the linear approximation given in Eq. 5.24. We have already determined the eigenvalues of the linear equation in Eq. 5.13. We found that the eigenvalues, λ_1 and λ_2, are

$$\lambda_1 = \frac{A+D}{2} + \frac{\sqrt{(A-D)^2 + 4BC}}{2} ,$$

$$\lambda_2 = \frac{A+D}{2} - \frac{\sqrt{(A-D)^2 + 4BC}}{2} .$$

Several different cases can be distinguished. The flows for three different cases are illustrated in Figures 5.11, 5.12, and 5.13.
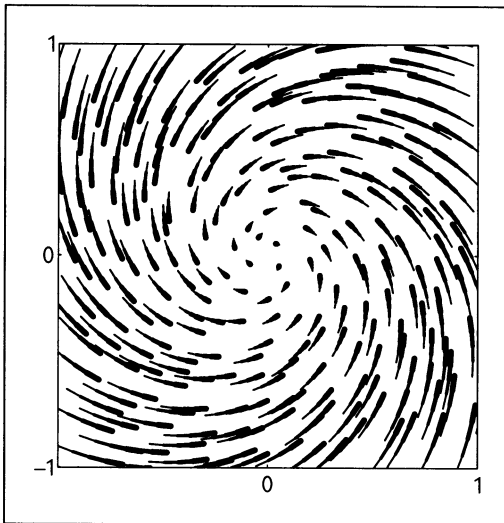
Figure 5.11   A stable focus. $A = -1, B = -1.9, C = 1.9$, and $D = -1$.

Focus $(A - D)^2 + 4BC < 0$. In this case, the eigenvalues are complex numbers. This means that the flow winds around the fixed point (see Figure 5.11). The size of the imaginary part tells how fast the winding occurs. The real part is $\frac{A+D}{2}$. If $\frac{A+D}{2} < 0$ the focus is stable, and if $\frac{A+D}{2} > 0$ the focus is unstable. The special case where $\frac{A+D}{2} = 0$ is called a center.
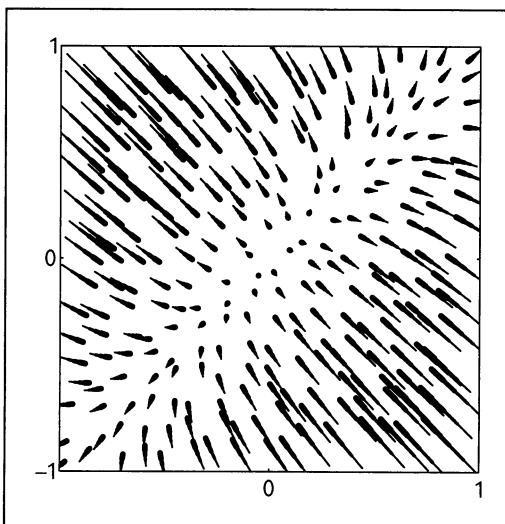

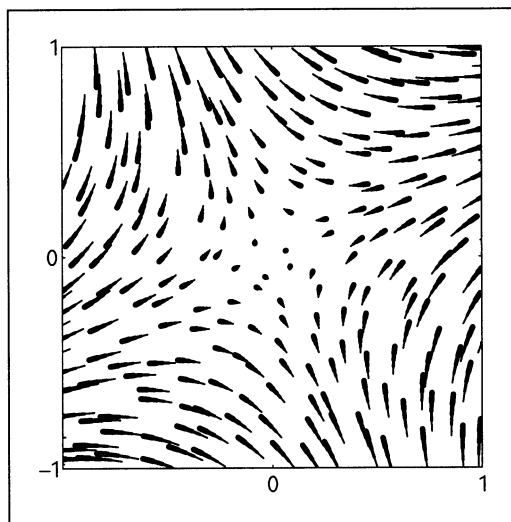**Figure 5.12**   A stable node. $A = -1.5, B = 1, C = 1$, and $D = -1.5$.

Figure 5.13 A saddle point. $A = 1, B = 1, C = 1$, and $D = -1$.

Node $(A - D)^2 + 4BC > 0$ and $|A + D| > \left| \sqrt{(A - D)^2 + 4BC} \right|$.
In this case the eigenvalues are both real and the same sign. If $\frac{A+D}{2} < 0$ the node is stable (see Figure 5.12), and if $\frac{A+D}{2} > 0$ the node is unstable.

Saddle point

$$(A - D)^2 + 4BC > 0 \text{ and } |A + D| < \left| \sqrt{(A - D)^2 + 4BC} \right|.$$

In this case the eigenvalues are both real, but with different signs. The trajectories of the vector field in the neighborhood of the saddle point are similar to the way water would flow on a horse's saddle (see Figure 5.13).

❏ **EXAMPLE 5.3**

Characterize the dynamics of the Lotka-Volterra equations (Eq. 5.19) near the fixed points.

Solution: We found in Section 5.5 that the fixed points occur at $x^\star = 0$, $y^\star = 0$, and at $x^\star = \delta/\gamma$, $y^\star = \alpha/\beta$. We will consider each of these fixed points in turn.

Near a fixed point, the dynamics are well approximated by a linear system

$$\frac{dz}{dt} = Az + Bw, \qquad \frac{dw}{dt} = Cz + Dw$$

where $z = x - x^\star$ and $w = y - y^\star$. The constants $A, B, C,$ and D are found by evaluating the partial derivatives at $(x^\star, y^\star)$:

$$A = \left.\frac{\partial f}{\partial x}\right|_{(x^\star, y^\star)} = \alpha - \beta y^\star \qquad B = \left.\frac{\partial f}{\partial y}\right|_{(x^\star, y^\star)} = -\beta x^\star$$

$$C = \left.\frac{\partial g}{\partial x}\right|_{(x^\star, y^\star)} = \gamma y^\star \qquad D = \left.\frac{\partial g}{\partial y}\right|_{(x^\star, y^\star)} = \gamma x^\star - \delta$$

The fixed point at the origin ($x^\star = 0, y^\star = 0$) is especially important, because it corresponds to extinction of both predator and prey. If this fixed point were stable, then even if both populations were non-zero, the predator-prey dynamics might lead to extinction. At the origin, we have $A = \alpha, B = 0, C = 0,$ and $D = -\delta$. The eigenvalues are therefore

$$\lambda = \frac{\alpha - \delta}{2} \pm \frac{\sqrt{(\alpha + \delta)^2}}{2}$$

or, simplifying,

$$\lambda_1 = \alpha \qquad \lambda_2 = -\delta.$$

Since in the Lotka-Volterra equations, α and δ are both positive, λ_1 is positive and λ_2 is negative. Thus, the fixed point at the origin is a saddle.

The other fixed point occurs at $x^\star = \delta/\gamma$ and $y^\star = \alpha/\beta$, which gives $A = 0, B = -\beta\delta/\gamma, C = \gamma\alpha/\beta, D = 0$. The eigenvalues are therefore

$$\lambda = \pm\sqrt{-\alpha\delta}.$$

These eigenvalues are purely imaginary, meaning that the populations of predators and prey oscillate around the fixed point. Since $(A + D)/2 = 0$, the focus is a center, but this would be meaningful only if the linearized system were exactly faithful to the full nonlinear system. Using an argument analogous to the conservation of energy, it is possible to show that the trajectory consists of closed curves around the fixed point. (See Problem 5.28.)

Since the fixed point at $x^\star = 0, y^\star = 0$ is a saddle, it is unstable in the sense that for almost any nonzero level of predator and prey population near extinction, the system will eventually lead to an increase in both populations. (The "almost any" is intended to exclude the case where the prey population is set to exactly zero. In this case, the predator population will die out exponentially, whatever is its initial value.) This might suggest that predator-prey systems are robust to disturbances; that extinction is difficult. Notice, though, that the seeming robustness is sensitive to details in the model construction. If the model were

changed slightly so that the predator did not depend for sustenance solely on the prey, then extinction is a real possibility for the prey.   ❐

❑ **EXAMPLE 5.4**

In mutual inhibition, there are two variables, each of which inhibits the other. For example, in the lambda bacteriophage (see *Dynamics in Action* 2), the lambda repressor and the cro protein mutually inhibit each other. Here, we shall see how the Boolean network model for the lambda bacteriophage translates into a differential equation model.

A theoretical model for mutual inhibition is

$$\frac{dx}{dt} = f(x) = \frac{\left(\frac{1}{2}\right)^n}{\left(\frac{1}{2}\right)^n + y^n} - x,$$

$$\frac{dy}{dt} = g(x) = \frac{\left(\frac{1}{2}\right)^n}{\left(\frac{1}{2}\right)^n + x^n} - y,$$

where x and y are positive variables and n is a positive constant greater than two. There is a steady state at $x^* = y^* = \frac{1}{2}$. Discuss the bifurcations and sketch the flows in the (x, y)-plane as n varies.

Solution: We linearize around the fixed point at $x^* = \frac{1}{2}$, $y^* = \frac{1}{2}$

$$A = \left.\frac{\partial f}{\partial x}\right|_{(x^*,y^*)} = -1$$

$$B = \left.\frac{\partial f}{\partial y}\right|_{(x^*,y^*)} = -\left.\frac{\left(\frac{1}{2}\right)^n}{\left(\left(\frac{1}{2}\right)^n + y^n\right)^2}ny^{n-1}\right| = -\frac{n}{2}$$

$$C = \left.\frac{\partial g}{\partial x}\right|_{(x^*,y^*)} = -\left.\frac{\left(\frac{1}{2}\right)^n}{\left(\left(\frac{1}{2}\right)^n + x^n\right)^2}nx^{n-1}\right|_{(x^*,y^*)} = -\frac{n}{2}$$

$$D = \left.\frac{\partial g}{\partial y}\right|_{(x^*,y^*)} = -1$$

Using Eq. 5.13, the eigenvalues are $-\frac{2}{2} \pm \frac{\sqrt{4-4+\sqrt{n}}}{2}$, or

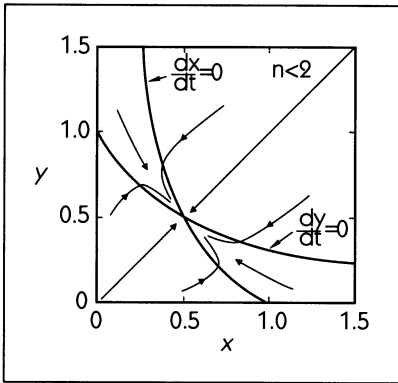$$\lambda_1 = -1 + \frac{n}{2} \qquad \lambda_2 = -1 - \frac{n}{2}.$$

Figure 5.14
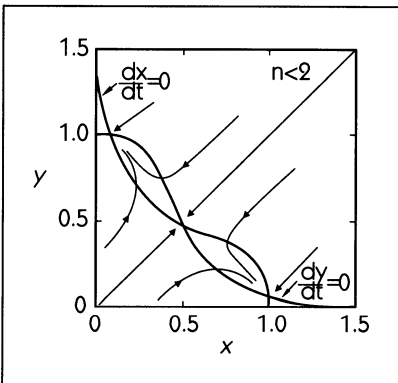Phase plane for mutual inhibition showing a stable node.

Figure 5.15
Phase plane for mutual inhibition showing a saddle point plus two stable nodes.

The steady state is therefore a stable node for $n \leq 2$ and a saddle point for $n > 2$. The trajectories in the (x, y)-plane can be sketched; see Figures 5.14 and 5.15.

 The sketches show that for $n > 2$ there are two additional stable nodes. This is a typical bifurcation in two-dimensional ordinary differential equations in which a stable node splits into a saddle point plus two stable nodes. The biological interpretation is as follows. The larger the value of n, the stronger the inhibitory interactions will be. At strong interactions, one of the variables wins out and reaches a high value, whereas the other variable is at a low value. Such a model captures the essence of mutual inhibition and as such may be important in the analysis of competition of manufacturing production or of ecological species. ☐

 The quantitative analysis of fixed points using linearization and the calculation of eigenvalues provides exact information about the stability of fixed points. For heuristic purposes, the isocline method can also be used to provide qualitative understanding of the behavior near a fixed point. The procedure is quite

simple. First, draw the x- and y-isoclines in the region of their intersection. If the isoclines are not parallel where they intersect, the two isoclines divide the plane into four quadrants. Now, choose one of the quadrants (it doesn't matter which one) and calculate $\frac{dx}{dt}$ and $\frac{dy}{dt}$ in that quadrant. The vector ($\frac{dx}{dt}$, $\frac{dy}{dt}$) indicates the direction of flow in that quadrant.

Repeat this procedure for the other three quadrants. Or, you might note that if ($\frac{dx}{dt}$, $\frac{dy}{dt}$) points in the $(+, +)$ direction in one quadrant, then in the quadrant across the y-isocline, it will point in the $(+, -)$ direction; in the quadrant across the x-isocline, it will point in the $(-, +)$ direction; and in the remaining quadrant it will point in the $(-, -)$ direction. Three cases are shown in Figures 5.16, 5.17, and 5.18.
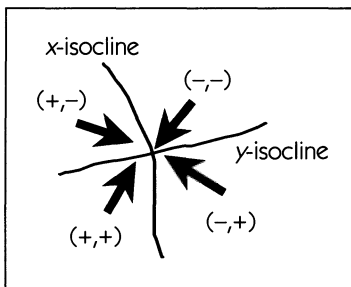

Figure 5.16
The geometry of a node. Flow near the intersection of the x- and y-isoclines. In each quadrant, the sign of $\frac{dx}{dt}$ and $\frac{dy}{dt}$ is shown (for example, $(-, -)$ in the upper-right quadrant) and the corresponding rough direction of the flow in that quadrant is indicated by an arrow.
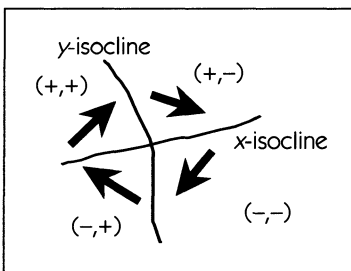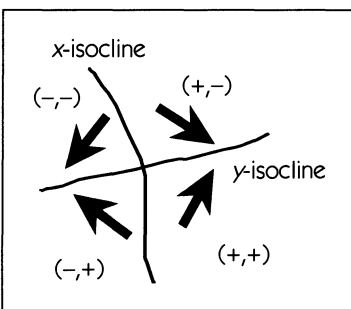

Figure 5.17
The geometry of a focus.

Figure 5.18
The geometry of a saddle.

FLOWS AND VISUAL PERCEPTION

The human visual system is particularly effective at perceiving flow fields. This allows us to experiment with some of the concepts contained in the previous mathematical material without doing any algebra.

We saw in Section 5.5 how the flow field can be sketched by drawing arrows at many places in the phase plane. The eye is capable of seeing flow patterns even when the whole arrow is not sketched. Just putting dots at the positions of the head and tail of the arrow will suffice.

A useful method for generating the visual appearance of a flow field is provided by the superimposition of dot patterns. Figure 5.19 shows three related dot patterns composed of random dots. On the top is a random pattern (A). The pattern in the center (B) is an expanded version of these same random dots (the x- and y-coordinates of all points in A are multiplied by 1.05). Pattern C is formed by multiplying the x coordinate of all points in pattern A by 1.05 and multiplying the y coordinate by 0.95.

Each of the three patterns looks random and shows no sign of a flow field. By placing one pattern over another one, and by rotating the overlaid patterns slightly, it is easy to perceive the geometries of flow fields in the neighborhood of fixed points. By superimposing pattern A on itself, but rotating slightly, there is a circular image; superimposing pattern A on pattern B without rotation gives rise to the geometry of a node; superimposing pattern A on pattern B with rotation gives the geometry of a focus (see Figure 5.20); finally, superimposing pattern A on pattern C gives rise to a saddle point geometry (see Figure 5.21). This shows how simple expansions, contractions, and rotations underlie the various geometries in the neighborhoods of steady states in nonlinear ordinary differential equations. These images, originally described by one of us (Glass) and colleagues, are being studied by scientists who are interested in evaluating the types of computation the brain performs during visual perception.

The best way to explore how contractions and rotations create different sorts of flow fields is to make two photocopies of the random dot patterns in Figure 5.19, one on ordinary paper and the other on transparent film. By aligning the two copies of the different dot patterns with one another (use the square brackets in the top right corner and along the left edge), and rotating them, you will see different flow patterns appear. If you make just one copy and match it up to the printed copies in the book, you may observe that your photocopier rescales the image slightly.
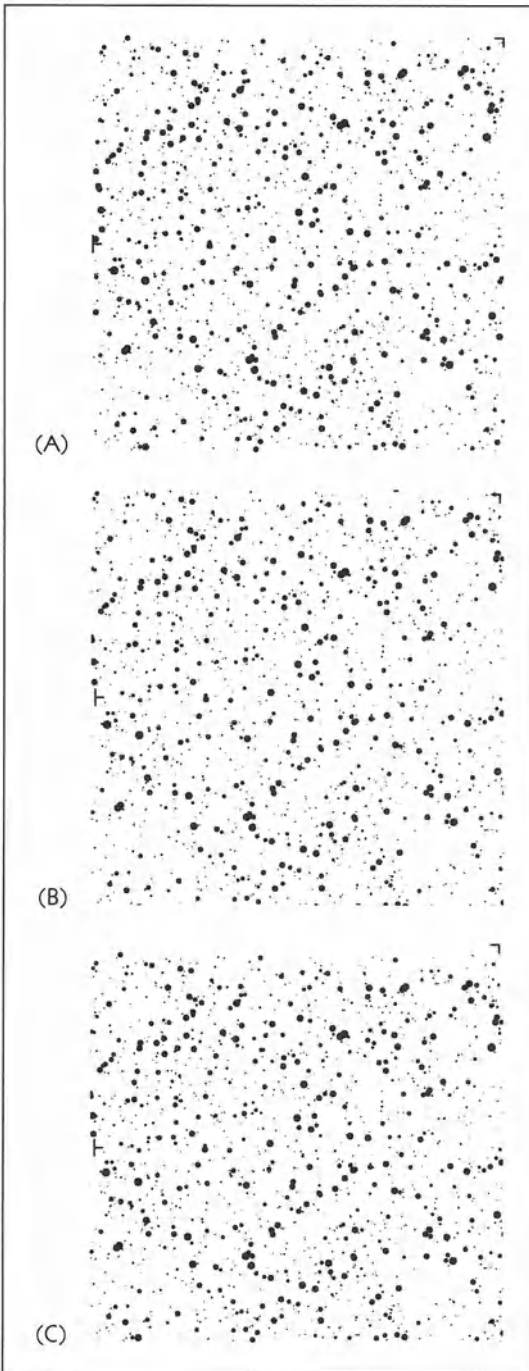
Figure 5.19   The pattern of random dots in (A) is enlarged in both directions in (B) and enlarged in one direction and shrunken in the other in (C).
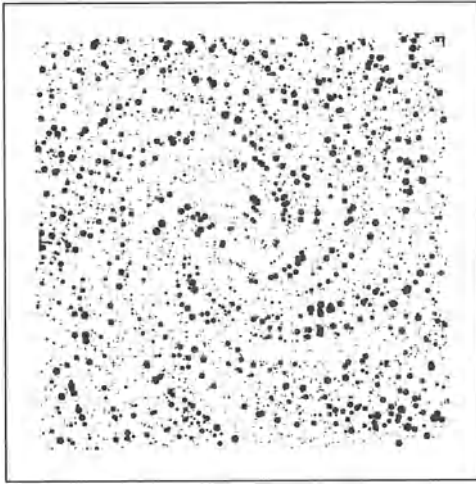
Figure 5.20
Superimposing pattern A on pattern B with a rotation of 0.1 radians creates the flow near a focus.
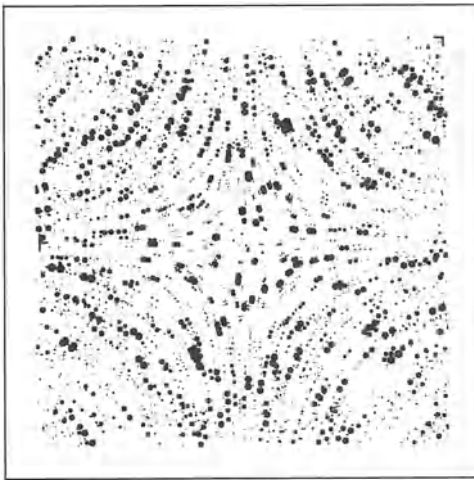

Figure 5.21
Superimposing pattern A on pattern C, with no rotation, creates the flow near a saddle.

5.7 LIMIT CYCLES AND THE VAN DER POL OSCILLATOR

So far we have considered two differential equations that display oscillations—the ideal harmonic oscillator and the Lotka-Volterra equations. In both of these, if some outside disturbance moves the state off of its original trajectory, the new trajectory after the disturbance will be different in amplitude and will never rejoin the original trajectory (unless another outside disturbance happens to do the job). Most biological oscillations show a different behavior. If there is a small outside disturbance, then after sufficient time (i.e., as $t \rightarrow \infty$) the original

trajectory is established. This type of behavior is called a **stable limit cycle.** The French mathematician Henri Poincaré (1854–1912) was the first to realize that this type of behavior could arise in differential equations. You have already seen this type of behavior in *Dynamics in Action* 1.

Figure 5.22, repeated from *Dynamics in Action* 1, gives an example of an electrical shock delivered to oscillating cardiac tissue. The reestablishment of the oscillation with the same period and amplitude as before the shock is an indication that a theoretical formulation for the oscillation should have a stable limit cycle oscillation. Probably the first and simplest theoretical model for cardiac oscillations was proposed by B. van der Pol, an electrical engineer, and his collaborator, J. van der Mark.

The **van der Pol equations** are

$$\frac{dx}{dt} = f(x, y) = \frac{1}{\epsilon}\left(y - \frac{x^3}{3} + x\right),$$

$$\frac{dy}{dt} = g(x) = -\epsilon x, \tag{5.25}$$

where it is usual to assume that $0 < \epsilon \ll 1$.

Even though it is not possible to find an analytic solution of the van der Pol equations, the properties of this equation can be determined using the qualitative methods introduced in the previous two sections. We first sketch the flow in the (x, y)-plane, as shown in Figure 5.23. The x-isocline, found by setting $\frac{dx}{dt} = 0$,
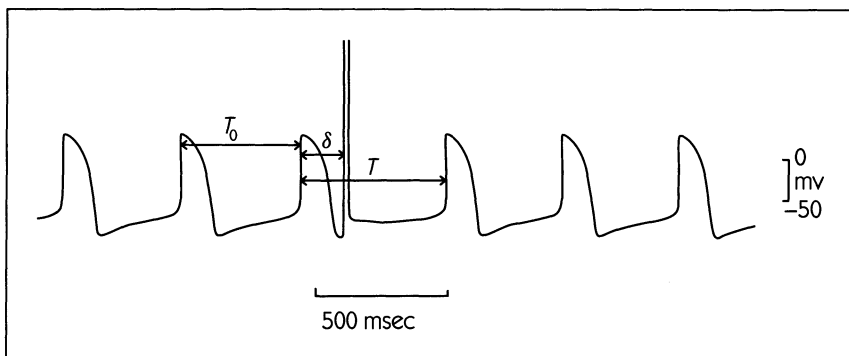

Figure 5.22 Recording of transmembrane voltage from spontaneously beating aggregates of embryonic chick heart cells. The intrinsic cycle length is T_0. A stimulus delivered at a time δ following the start of the third action potential leads to a phase resetting so that the subsequent action potential occurs after time T. After this, the aggregate returns to its intrinsic cycle length. Adapted from Guevara et al. (1981).
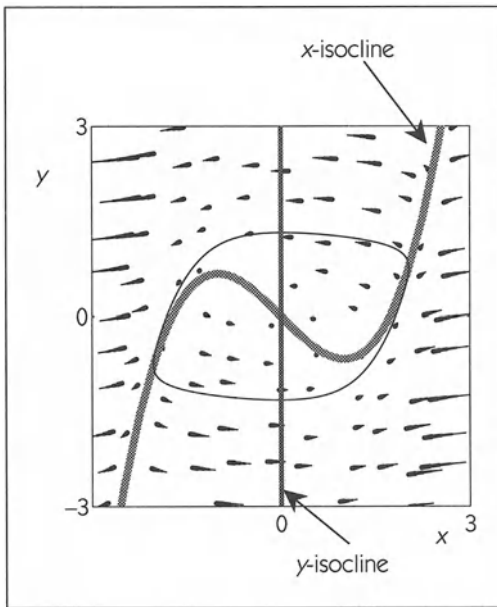
Figure 5.23 The flow and isoclines of the van der Pol equations (Eq. 5.25, $\epsilon = 0.1$). The limit cycle is shown as a thin line.

is the cubic function

$$y = \frac{x^3}{3} - x.$$

Similarly, the y-isocline, found by setting $\frac{dy}{dt} = 0$, is

$$x = 0.$$

There is only one intersection of the x- and y-isoclines, and therefore only one fixed point, which is at $x = y = 0$.

The flow vectors plotted in Figure 5.23, suggest the flow is mostly horizontal, toward the x-isocline. However, there is also a slight vertical component to the flow. Since we are assuming $0 < \epsilon \ll 1$, any initial condition that is not on the x-isocline will lead to relatively rapid changes in the value of x until the state is in the neighborhood of the x-isocline, whereas the vertical component of flow, $\frac{dy}{dt}$, is small. Near the x-isocline $\frac{dx}{dt}$ is small, so there is not much flow in the horizontal direction. In this region, the small vertical component to the flow becomes significant, causing motion along the x-isocline. This motion is either up or down, depending on whether the state is on the left or right limb of the isocline. Once the vertical flow has carried the state near the local extremum

of the x-isocline, the horizontal flow again dominates, producing a jump to the other limb of the x-isocline. Since the fixed point at the origin is unstable (see Example 5.5), we know that trajectories do not spiral into the origin. Instead, there is a stable limit cycle, which is approached no matter what the initial condition.

Figure 5.24 shows x as a function of time. The various segments are labeled to correspond with the region of the phase-plane plot. Note that the oscillation, with its slow drifts in the value of x, interrupted by sudden changes in the value of x, is similar to the recording of cardiac electrical activity. Modifications to the van der Pol equation proposed by several researchers form the basis for theoretical studies of oscillations in cardiac tissue even 70 years after the equations were proposed.

❏ **EXAMPLE 5.5**

Consider the van der Pol equations with $\epsilon > 0$. Evaluate the stability of the fixed point $x^* = y^* = 0$.

Solution: In order to determine the eigenvalues of Eq. 5.25 at the fixed point, we compute

$$A = \left.\frac{\partial f}{\partial x}\right|_{0,0} = \frac{1}{\epsilon}, \qquad B = \left.\frac{\partial f}{\partial y}\right|_{0,0} = \frac{1}{\epsilon},$$

$$C = \left.\frac{\partial g}{\partial x}\right|_{0,0} = -\epsilon, \qquad D = \left.\frac{\partial g}{\partial y}\right|_{0,0} = 0.$$
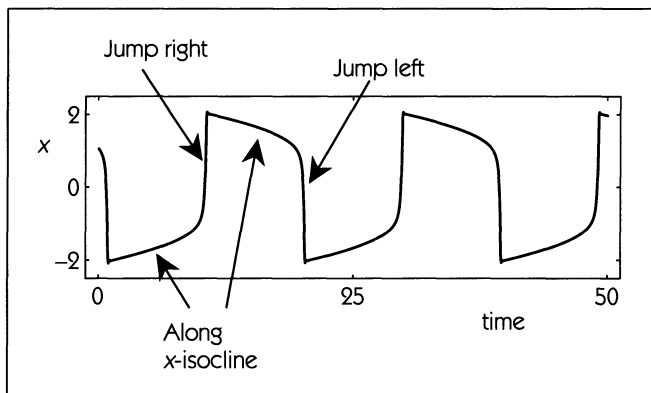

Figure 5.24 x measured from the van der Pol system with $\epsilon = 0.1$.

Using Eq. 5.13, we find the eigenvalues are $\lambda = \frac{1}{2\epsilon} \pm \frac{\sqrt{\frac{1}{\epsilon^2} - 4}}{2}$ or, simplifying,

$$\lambda = \frac{1}{2\epsilon} (1 \pm \sqrt{1 - 4\epsilon^2}).$$

Consequently, for $0 < \epsilon < \frac{1}{2}$ there is an unstable node, and for $\frac{1}{2} < \epsilon$ there is an unstable focus. Notice that the stability analysis gives us a better understanding of the dynamics in the neighborhood of the fixed point than is possible with the phase-plane analysis, but the analysis does not give information about the dynamics in the limit $t \to \infty$. ◻

5.8   FINDING SOLUTIONS TO NONLINEAR DIFFERENTIAL EQUATIONS

We have seen how to use isoclines to understand qualitatively the dynamics of nonlinear differential equations, and how to use linearization and eigenvalues to calculate quantitatively the stability of fixed points. We have not yet seen any general method for calculating solutions to nonlinear differential equations. The reason is that it is generally difficult or impossible to find such solutions algebraically. In Chapter 1, we used the procedure of iteration to find numerical solutions to the nonlinear finite-difference equations we wanted to study. In this section, we shall present an analogous method for finding approximate numerical solutions to nonlinear differential equations. This method can be used to find the trajectory from any given initial condition.

The method for numerical integration of differential equations, called the **Euler method**, is based on the same approximation of the derivative $\frac{dx}{dt}$ that we made in Section 4.6. As there, we define a discrete-time variable $x_t = x(t)$ for $t = 0, \Delta, 2\Delta, \ldots$. Then we have

$$\frac{dx}{dt} = \lim_{\Delta \to 0} \frac{x_{t+1} - x_t}{\Delta}. \tag{5.26}$$

Applying this definition of the derivative in Eq. 5.18, we get the equations

$$x_{t+1} - x_t = f(x_t, y_t)\Delta,$$

$$y_{t+1} - y_t = g(x_t, y_t)\Delta, \tag{5.27}$$

or

$$x_{t+1} = f(x_t, y_t)\Delta + x_t,$$

$$y_{t+1} = g(x_t, y_t)\Delta + y_t. \tag{5.28}$$

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:

$$\frac{dv}{dt} = I - v(v - a)(v - 1) - w,$$

$$\frac{dw}{dt} = \epsilon(v - \gamma w). \tag{5.29}$$

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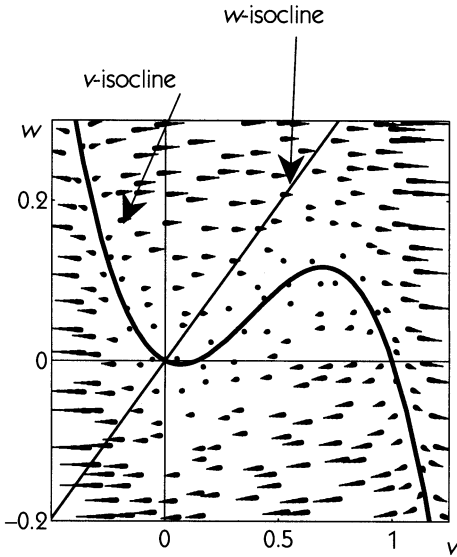
The isoclines and flow field for the Fitzhugh-Nagumo equations of nerve cell dynamics ($I = 0$).

Linearizing the equations around this fixed point, we find

$$\frac{dv}{dt} = -av - w$$

$$\frac{dw}{dt} = \epsilon v - \epsilon \gamma w.$$

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, γ, and ϵ 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 $\gamma = -0797 \pm 0.067i$. 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 is us how large the current pulse needs to be to cause an action potential.

The first step in integrating these equations, after picking the parameters ϵ, a, and γ, is to select a value for the size of the time step, Δ. In order for Eq. 5.28 to be a good approximation to Eq. 5.18, we need to pick Δ to be as small as possible. On the other hand, in order to keep the amount of computation small, we want to set Δ to be as large as possible. One way is to set the value for Δ to be some starting value, say $\Delta = 0.5$. We carry out the iteration according to Eq. 5.28. Then, we reduce Δ by half and repeat the iteration. If we find that the results of the two iterations are approximately the same, then Δ is small enough. Otherwise, reduce Δ by half again, and repeat. Keep in mind that setting Δ 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 Δ is too large.

(A)

(B)

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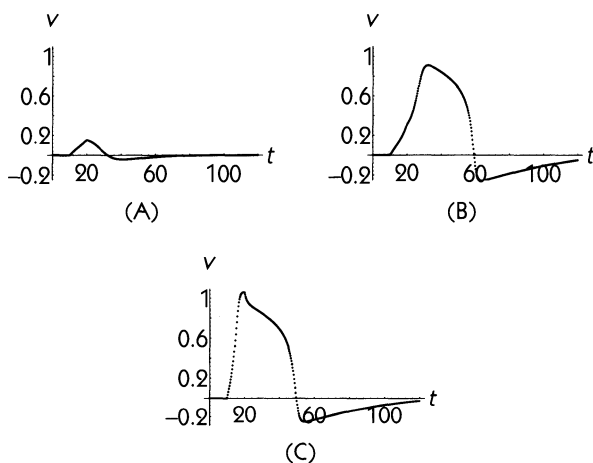
v versus time in the Fitzhugh-Nagumo model of electrical activity in the nerve cell. Current of amplitude I is turned on at time $t = 10$ and turned off at $t = 20$. (A) $I = 0.02$. No action potential occurs. (B) $I = 0.03$. An action potential. (C) $I = 0.10$. An action potential.

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 $\Delta \to 0$. For $\Delta > 0$, the equation is only an approximation. One way to make the approximation good is to use very small Δ. 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 $t \to \infty$ 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.