Chapter 4

Disease and Epidemic Models

In a structured population model designed to study the spread of a disease through a population, individuals are classified according to a selection of disease-related categories: susceptible, infected, infectious, recovered, quarantined, vaccinated, and so on. Because of the obvious interest and importance of understanding epidemics, there is a huge (and continually growing) amount of literature in which models for innumerable kinds of diseases are derived and analyzed. Almost all of these models structure a population (in some cases the pathogen causing the disease as well) into a finite number of discrete categories. Tracking these subpopulations in continuous time results in models based on differential equations. On the other hand, there is substantial literature on models in discrete time disease as well. This chapter contains a brief introduction to the discrete time modeling of diseases and the dynamics of epidemics, treating the subject in the spirit of and using the analytic methods in Chapters 2 and 3. A good reference for both differential- and difference-equation-based epidemic models is [**9**].

4.1. Preliminaries

For the populations models considered in Chapters 2 and 3, a basic concern is with the extinction or survival of the population (or mathematically, the stability of the extinction equilibrium $\mathbf{x}_e = \mathbf{0}$). For a model

structured by classes related to a disease, the main concern is generally not with the extinction of the population, but instead with the extinction of the infected classes within the population. For this reason, we begin our model building by applying the basic discrete time modeling methodology to the infected classes, which we place in a vector $\mathbf{x}_1 \in R_+^m$. The remaining classes we denote by $\mathbf{x}_2 \in R_+^n$. For example, in the lowest-dimensional case, $\mathbf{x}_1 = [x_1]$ is the (scalar) class of infected (and infectious) individuals, and $\mathbf{x}_2 = [x_2]$ is the (scalar) class of noninfected, but susceptible individuals (and in these one-dimensional cases, we as usual drop the bracket notation). With these epidemic class distinctions, we can write a general epidemic model in the form

$$\begin{array}{ll} \text{(a)} & \mathbf{x}_1(t+1) = \mathbf{f}_1(\mathbf{x}_1(t), \mathbf{x}_2(t)) \\ \text{(b)} & \mathbf{x}_2(t+1) = \mathbf{f}_2(\mathbf{x}_1(t), \mathbf{x}_2(t)). \end{array} \tag{4.1}$$

We assume that infections only occur by transmission from infected individuals so that $\mathbf{0}_m = \mathbf{f}_1(\mathbf{0}_m, \mathbf{x}_2)$. We also assume that in the absence of the disease, the population has a stable equilibrium, that is to say the **disease-free equation**

$$\mathbf{x}_2(t+1) = \mathbf{f}_2(\mathbf{0}_m, \mathbf{x}_2(t)) \tag{4.2}$$

has a (locally asymptotically) stable equilibrium. These requirements are part of our general assumptions on

$$\mathbf{f}(\mathbf{x}) \coloneqq \operatorname{col}(\mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2), \mathbf{f}_2(\mathbf{x}_1, \mathbf{x}_2))$$

for the model equations (4.1) and are summarized as follows.

Assumption 4.1. $\mathbf{f} \in C^2\left(R^{m+n} : R_+^{m+n}\right)$. Furthermore, $\mathbf{0}_m = \mathbf{f}_1(\mathbf{0}_m, \mathbf{x}_2)$ for all $\mathbf{x}_2 \in R_+^n$, and there exists $\mathbf{x}_{2e} \in R_+^n$, $\mathbf{x}_{2e} \neq \mathbf{0}_n$ such that $\mathbf{x}_{2e} = \mathbf{f}_2(\mathbf{0}_m, \mathbf{x}_{2e})$ and $\rho\left(\mathbf{J}_{x_2}\mathbf{f}_2(\mathbf{0}_m, \mathbf{x}_{2e})\right) < 1$, where $\mathbf{J}_{x_2}\mathbf{f}_2$ is the $n \times n$ Jacobian of $\mathbf{f}_2(\mathbf{x}_1, \mathbf{x}_2)$ with respect to $\mathbf{x}_2$.

Under Assumption 4.1, the system of equations (4.1) has the **disease-free equilibrium**

$$\mathbf{x}_e = \begin{bmatrix} \mathbf{0}_m \\ \mathbf{x}_{2e} \end{bmatrix} \in \partial R_+^{m+n}. \tag{4.3}$$

Example 4.2. A Susceptible-Infected (SI) Model. Consider a population of susceptibles x_2 whose dynamics are governed, in the absence

of the disease, by the equation

$$x_2(t+1) = b_0 \frac{1}{1+cx_2(t)} x_2(t) + \sigma_S x_2(t) \tag{4.4}$$

$$\text{with } b_0, c > 0 \text{ and } 0 < \sigma_S < 1$$

(as in Section 1.2). In the presence of the disease, we let φ be the fraction of susceptibles x_2 who do not become infected (per unit time). This fraction (called the **escape probability**) depends, of course, on the number of infected individuals x_1, so we write $\varphi = \varphi(x_1)$. Then the fraction of surviving susceptibles that remain susceptible at $t+1$ is $\sigma_S \varphi(x_1)$, and the equation for the susceptibles x_2 becomes

$$x_2(t+1) = b_0 \frac{1}{1+cx_2(t)} x_2(t) + \sigma_S \varphi(x_1(t)) x_2(t).$$

The fraction of susceptibles that become infected (per unit time), and hence move into the infected class, is $(1-\varphi(x_1))\sigma_S$; thus, the infected class is given by (the newly infected plus the surviving infected)

$$x_1(t+1) = (1-\varphi(x_1(t)))\sigma_S x_2(t)) + \sigma_I x_1(t),$$

where σ_I is the survival probability of infected individuals.

We assume the **escape function** $\varphi(x_1)$ is a decreasing function of x_1 (i.e., $\partial_{x_1}\varphi(x) < 0$ for $x \geq 0$) that equals 1 at $x_1 = 0$ (no infection occurs when no infected individuals are present) and approaches 0 as $x_1 \to \infty$ (the probability of escaping infection drops to 0 as the class of infected individuals increases without bound).

The equations for this suceptible-infected model (or SI model) are

$$\begin{array}{ll} \text{(a)} & x_1(t+1) = (1-\varphi(x_1(t)))\sigma_S x_2(t)) + \sigma_I x_1(t) \quad \text{and} \\ \text{(b)} & x_2(t+1) = b\frac{1}{1+cx_2(t)} x_2(t) + \varphi(x_1(t))\sigma_S x_2(t) \end{array} \tag{4.5}$$

and have the form (4.1) with

$$\mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2) = (1-\varphi(x_1))\sigma_S x_2 + \sigma_I x_1 \quad \text{and}$$
$$\mathbf{f}_2(\mathbf{x}_1, \mathbf{x}_2) = b_0 \frac{1}{1+cx_2} x_2 + \sigma_S \varphi(x_1) x_2.$$

(We drop the bracket notation for one-dimensional vectors.) It is

straightforward to show that Assumption 4.1 is satisfied by the equilibrium

$$x_{2e} = \frac{1}{c}\left(b\frac{1}{1-\sigma_S} - 1\right), \quad b\frac{1}{1-\sigma_S} > 1$$

(which by Theorem 1.26, is in fact globally asymptotically stable on *int* (R_+)). The disease-free equilibrium of the SI model is

$$\mathbf{x}_e = \begin{bmatrix} \mathbf{0} \\ x_{2e} \end{bmatrix} = \begin{bmatrix} \mathbf{0} \\ \frac{1}{c}\left(b\frac{1}{1-\sigma_S} - 1\right) \end{bmatrix}, \quad b\frac{1}{1-\sigma_S} > 1.$$

□

A cycle graph associated with the SI model in example 4.2 appears in Figure 4.1. Note that in this elementary model, it is assumed that newborns are susceptible (i.e., none are born infected), infected individuals do not reproduce, and there is no recovery from the disease.

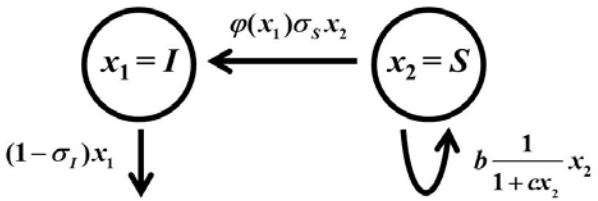

Figure 4.1. A cycle graph for the SI model (4.5).

Remark 4.3. *A remark about notation: In epidemic models, it is common to denote the state variables by (usually uppercase) letters suggestive of their disease-related definitions, such as I for infected, S for susceptible, R for recovered, and so on. With this notation, a common way of writing the basic SI model* (4.5) *is*

$$\begin{aligned} S(t+1) &= b\frac{1}{1+cS(t)}S(t) + \varphi(I(t))\sigma_S S(t) \\ I(t+1) &= (1-\varphi(I(t)))\sigma_S S(t)) + \sigma_I I(t). \end{aligned}$$

While we will occasionally adopt this suggestive notation, we will for the most part keep the state variable notation x_i so as to be notationally consistent with the notation in earlier chapters on structured population dynamics.

4.2. Disease-Free Equilibria and R_0

If the disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} \mathbf{0}_m \\ \mathbf{x}_{2e} \end{bmatrix}$$

is (locally asymptotically) stable, then $\mathbf{x}(0)$ near $\mathbf{x}_e$ implies

$$\lim_{t\to\infty} \mathbf{x}_1(t) = \mathbf{0}_m,$$

that is to say when the susceptible population is at or near its equilibrium, then an infection will ultimate disappear after an invasion by a small population of infected individuals. To attain this desirable result, so as to avoid the disease remaining in the population (i.e., becoming endemic), we are interested in conditions under which the disease-free equilibrium is stable. Towards this end, we apply the Linearization Principle by calculating the Jacobian matrix associated with the model equations (4.1) evaluated at the disease-free equilibrium:

$$\mathbf{J}_x\mathbf{f}(\mathbf{x}_e) \coloneqq \mathbf{J}_x\mathbf{f}(\mathbf{x})\big|_{\mathbf{x}=\mathbf{x}_e}.$$

By Assumption 4.1, we obtain a block diagonal matrix

$$\mathbf{J}_x\mathbf{f}(\mathbf{x}_e) = \begin{bmatrix} \mathbf{J}_{\mathbf{x}_1}\mathbf{f}_1(\mathbf{0},\mathbf{x}_{2e}) & \mathbf{0}_{m\times n} \\ \mathbf{J}_{\mathbf{x}_2}\mathbf{f}_2(\mathbf{0},\mathbf{x}_{2e}) & \mathbf{J}_{\mathbf{x}_2}\mathbf{f}_2(\mathbf{0},\mathbf{x}_{2e}) \end{bmatrix},$$

where $\mathbf{J}_{\mathbf{x}_i}\mathbf{f}_j(\mathbf{x}_0,\mathbf{x}_1)$ is the Jacobian of $\mathbf{f}_j$ with respect to $\mathbf{x}_i$ and evaluated at the disease-free equilibrium (4.3)

$$\mathbf{J}_{\mathbf{x}_i}\mathbf{f}_j\left(\mathbf{0},\mathbf{x}_1^*\right) \coloneqq \mathbf{J}_{\mathbf{x}_i}\mathbf{f}_j(\mathbf{x}_0,\mathbf{x}_1)\big|_{(\mathbf{x}_0,\mathbf{x}_1)=(\mathbf{0},\mathbf{x}_1^*)}.$$

The eigenvalues of $\mathbf{J}_x\mathbf{f}(\mathbf{x}_e)$ consist of the eigenvalues of the diagonal blocks $\mathbf{J}_{\mathbf{x}_1}\mathbf{f}_1(\mathbf{0},\mathbf{x}_{2e})$ and $\mathbf{J}_{\mathbf{x}_2}\mathbf{f}_2(\mathbf{0},\mathbf{x}_{2e})$. Since $\rho\left(\mathbf{J}_{\mathbf{x}_2}\mathbf{f}_2(\mathbf{0}_m,\mathbf{x}_{2e})\right) < 1$ by Assumption 4.1, the eigenvalues of the diagonal block $\mathbf{J}_{\mathbf{x}_2}\mathbf{f}_2(\mathbf{0}_m,\mathbf{x}_{2e})$ all lie within the unit circle of the complex plane, and as a result, the stability of the disease-free equilibrium is determined, according to the Linearization Principle, by the eigenvalues of the remaining diagonal block $\mathbf{J}_{\mathbf{x}_1}\mathbf{f}_1(\mathbf{0},\mathbf{x}_{2e})$. In particular, if $\rho\left(\mathbf{J}_{\mathbf{x}_1}\mathbf{f}_1(\mathbf{0},\mathbf{x}_{2e})\right) < 1$, then the disease-free equilibrium is (locally asymptotically) stable.

The term $\mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2)$ in equation (4.5)(a) describes the dynamics of the infected classes in the vector $\mathbf{x}_1$. We model it by adding newly infected individuals to the surviving infected individuals to get

$$\mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2) = \mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) + \mathbf{s}(\mathbf{x}_1, \mathbf{x}_2).$$

Then we can write the Jacobian as

$$\mathbf{J}_{\mathbf{x}_1}\mathbf{f}_1(\mathbf{0}, \mathbf{x}_{2e}) = \mathbf{F}(\mathbf{0}, \mathbf{x}_{2e}) + \mathbf{T}(\mathbf{0}, \mathbf{x}_{2e}),$$

where we use the notation

$$\begin{aligned} \mathbf{F}(\mathbf{0}, \mathbf{x}_{2e}) &\coloneqq \mathbf{J}_{\mathbf{x}_1}\mathbf{n}(\mathbf{0}, \mathbf{x}_{2e}) \\ \mathbf{T}(\mathbf{0}, \mathbf{x}_{2e}) &\coloneqq \mathbf{J}_{\mathbf{x}_1}\mathbf{s}(\mathbf{0}, \mathbf{x}_{2e}), \end{aligned} \tag{4.6}$$

which is directly analogous to that used in the calculation of R_0 in Section 3.3. (In this analog, $\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e})$ is associated with newly infected individuals rather that with newborns.) As in Chapter 3, we can equivalently determine the stability of the disease-free equilibrium using

$$R_0 = \rho\left(\mathbf{F}(\mathbf{0}_m, \mathbf{x}_{2e})\left(\mathbf{I} - \mathbf{T}(\mathbf{0}_m, \mathbf{x}_{2e})\right)^{-1}\right) \tag{4.7}$$

instead of $\rho\left(\mathbf{J}_{\mathbf{x}_1}\mathbf{f}_1(\mathbf{0}, \mathbf{x}_{2e})\right)$. The entries in $\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e})$ and $\mathbf{T}(\mathbf{0}, \mathbf{x}_{2e})$ are, respectively, per capita rates of new infections and survival with class transitions; therefore, in a properly formulated model, these two matrices will satisfy the assumptions needed for us to apply Theorem 2.15 and Theorem 3.17. We can assign an interpretation of the reproduction number R_0 as the **average number of new infections** (*called secondary infections*) **per infectious individual** over the time spent infectious (see Section 2.3.2).

Theorem 4.4. *Assume Assumption* 4.1 *and that* $\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e})$ *and* $\mathbf{T}(\mathbf{0}, \mathbf{x}_{2e})$ *defined by* (4.6) *satisfy* (2.2) *in Chapter* 2 *with* $\rho(\mathbf{T}(\mathbf{0}, \mathbf{x}_{2e})) < 1$. *Then the disease-free equilibrium is* (*locally asymptotically*) *stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$, *where the reproduction number* R_0 *is defined by* (4.7).

4.3. Examples

In this section, we illustrate further the methodology of building disease models and the use of Theorem 4.4 to study stability properties of disease-free equilibria.

4.3.1. The Susceptible-Infected (SI) Model. As seen in Example 4.2, the SI model described by equations (4.5) has a (unique) disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} \mathbf{0} \\ x_{2e} \end{bmatrix} = \begin{bmatrix} \mathbf{0} \\ \frac{1}{c}\left(b\frac{1}{1-\sigma_S} - 1\right) \end{bmatrix}, \quad b\frac{1}{1-\sigma_S} > 1 \tag{4.8}$$

for which Assumption 4.1 holds. From equation (4.5)(a), we identify

$$\mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) = (1 - \varphi(x_1))\,\sigma_S x_2 \quad \text{and} \quad \mathbf{s}(\mathbf{x}_1, \mathbf{x}_2) = \sigma_I x_1$$

and calculate, using formulas (4.6),

$$\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e}) = -\partial_{x_1}\varphi(0)\,\sigma_S x_{2e} > 0 \quad \text{and} \quad \mathbf{T}(\mathbf{0}, \mathbf{x}_{2e}) = \sigma_I < 1$$

from which, together with formula (4.7), we obtain

$$R_0 = -\partial_{x_1}\varphi(0)\,\sigma_S x_{2e}\frac{1}{1-\sigma_I} > 0.$$

Notice that among the factors that make up R_0 are $-\varphi'(0) > 0$, which is called the **force of infection**, and

$$\frac{1}{1-\sigma_I} = 1 + \sigma_I + \sigma_I^2 + \cdots = \sum_{j=0}^{\infty} \sigma_I^j,$$

which is the **expected time an individual remains infected**.

The elementary SI model in Example 4.2 and Section 4.3.1 assumes the escape function depends only on the number x_1 of infected individuals alone. Another modeling assumption is that φ also depends on the number of susceptibles. For example, consider the following derivation of an escape function for the SI model.

Assume, in a small interval of time Δt, that a susceptible individual comes into contact with at most one other individual and that contact with any individual in the population is equally likely with any other. Assume the probability a contact with another individual occurs is proportional to Δt and write it as $\pi\Delta t$, where $\pi > 0$ is the constant of proportionality. If a contact occurs, then the probability it is with an infected individual equals the fraction of infected individuals in the population (i.e., equals x_1/p, where

$$p = x_1 + x_2$$

is the total population size). With this notation, we have that the probability a susceptible individual contacts an infected individual during a

time interval of length Δt equals

$$\frac{x_1}{p}\pi\Delta t.$$

Will the contact result in an infection? If the probability of infection from a contact with an infected individual is i, then the probability the susceptible individual becomes infected during the time interval Δt is approximately

$$c_i\frac{x_1}{p}\Delta t,$$

where $c_i := i\pi$. It follows that the probability a susceptible escapes infection during the interval Δt is equal to

$$1 - c_i\frac{x_1}{p}\Delta t.$$

In order to avoid infection from t to $t+1$, an individual must avoid infection a total of $1/\Delta t$ times. The probability that this occurs is

$$\left(1 - c_i\frac{x_1}{p}\Delta t\right)^{\frac{1}{\Delta t}}.$$

Letting $\Delta t \to 0$, we have from calculus that

$$\varphi(\mathbf{x}) := \lim_{\Delta t\to 0}\left(1 - c_i\frac{x_1}{p}\Delta t\right)^{\frac{1}{\Delta t}} = \exp\left(-c_i\frac{x_1}{p}\right)$$

is the probability that a susceptible escapes infection from time t to $t+1$.

The equations for the SI model in Example 4.2 with the escape function

$$\varphi(\mathbf{x}) = \exp\left(-c_i\frac{x_1}{p}\right)$$

are

$$\begin{aligned} x_1(t+1) &= \left(1 - \exp\left(-c_i\tfrac{x_1(t)}{p(t)}\right)\right)\sigma_S x_2(t) + \sigma_I x_1(t) \quad \text{and} \\ x_2(t+1) &= b\tfrac{1}{1+cx_2(t)}x_2(t) + \exp\left(-c_i\tfrac{x_1(t)}{p(t)}\right)\sigma_S x_2(t). \end{aligned} \tag{4.9}$$

From

$$\mathbf{n}(\mathbf{x}_1,\mathbf{x}_2) = \left(1 - \exp\left(-c_i\frac{x_1}{x_1+x_2}\right)\right)\sigma_S x_2 \quad \text{and} \quad \mathbf{s}(\mathbf{x}_1,\mathbf{x}_2) = \sigma_I x_1,$$

we see, using formulas (4.6), that

$$\mathbf{F}(\mathbf{0},\mathbf{x}_{2e}) = c_i\sigma_S > 0 \quad \text{and} \quad \mathbf{T}(\mathbf{0},\mathbf{x}_{2e}) = \sigma_I < 1$$

from which, by formula (4.7), we obtain

$$R_0 = c_i \sigma_S \frac{1}{1-\sigma_I}. \tag{4.10}$$

By Theorem 4.4*, the disease-free equilibrium* (4.8) *of* (4.9) *is* (*locally asymptotically*) *stable if* $R_0 < 1$ *and is unstable if* $R_0 > 1$*, where* R_0 *is given by formula* (4.10)*.*

4.3.2. A Susceptible-Infected-Recovered (SIR) Model. The SI model (4.5) in Example 4.2 and Section 4.3.1 is very basic in that it structures the population into only two disease related classes: infected and susceptible individuals. More sophisticated models include any number of other disease related classes, such as individuals who are recovered and immune from the disease, exposed but not yet infectious, exposed but quarantined, immune by vaccination, and so on. In this section, we consider a basic example that includes three classes: infected, susceptible, and recovered individuals.

In this model, $\mathbf{x}_1 = [x_1]$ and $\mathbf{x}_2 = \operatorname{col}(x_2, x_3)$, where the numbers in the classes of infected (and infectious), susceptible, and recovered individuals are denoted by x_1, x_2, and x_3, respectively. We assume an infected individual can recover from the infection. Individuals in the recovered class are neither infected nor susceptible to infection and hence have acquired immunity. We allow in the model, however, for the possibility that immunity is not permanent, and there is a probability that a recovered individual will again become infected. The cycle diagram appears in Figure 4.2.

For the dynamics of x_1, we use the escape function similar to that in the SI model developed in Section 4.3.1:

$$\varphi(\mathbf{x}) = \exp\left(-c_i \frac{x_1}{p}\right),$$

where now the total population size is

$$p = x_1 + x_2 + x_3.$$

Then the equation for the infected class x_1 is

$$x_1(t+1) = \left(1 - \exp\left(-c_i \frac{x_1(t)}{p(t)}\right)\right) \sigma_S x_2(t) + \sigma_I (1-\rho_I) x_1(t),$$

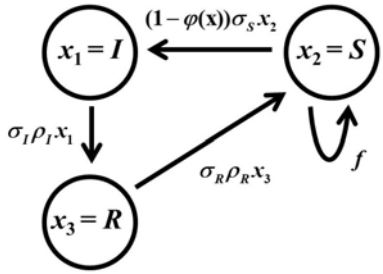

Figure 4.2. A cycle graph for the SIR model (4.11). Only transitions among classes are indicated (removals by deaths are not indicated).

where:

- ρ_I is the probability an infected individual recovers from the disease (per unit time); hence, $1 - \rho_I$ is the probability a (surviving) infected individual remains infected;
- $\mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) = \left(1 - \exp\left(-c_i \frac{x_1}{p}\right)\right)\sigma_S x_2$;
- $\mathbf{s}(\mathbf{x}_1, \mathbf{x}_2) = \sigma_I (1 - \rho_I) x_1$.

For the susceptible class x_2, we have an equation similar to that in the SI model in Section 4.3.1 except with an added input of new susceptibles from the recovered class x_3. Thus,

$$x_2(t+1) = b\frac{1}{1 + cx_2(t)}x_2(t) + \exp\left(-c_i \frac{x_1(t)}{p(t)}\right)\sigma_S x_2(t) + \sigma_R \rho_R x_3(t),$$

where ρ_R is the probability a surviving recovered individual becomes again susceptible (hence, $1 - \rho_R$ is the probability it remains immune) and σ_R is the survival rate of recovered individuals.

Finally, the recovered individuals at time $t + 1$ equals the newly recovered individuals $\sigma_I \rho_I x_1(t)$ from the infected class plus the surviving recovered individuals from time t:

$$x_3(t+1) = \sigma_I \rho_I x_1(t) + \sigma_R (1 - \rho_R) x_3(t).$$

In summary, the equations for this SIR model are

$$
\begin{aligned}
&\text{(a)} \quad x_1(t+1) = \left(1 - \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\right)\sigma_S x_2(t) \\
&\qquad\qquad + \sigma_I(1-\rho_I)x_1(t); \\
&\text{(b)} \quad x_2(t+1) = b\tfrac{1}{1+c(x_2(t)+x_3(t))}(x_2(t)+x_3(t)) \\
&\qquad\qquad + \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\sigma_S x_2(t) + \sigma_R\rho_R x_3(t); \\
&\text{(c)} \quad x_3(t+1) = \sigma_I\rho_I x_1(t) + \sigma_R(1-\rho_R)x_3(t).
\end{aligned}
\tag{4.11}
$$

If $\rho_R = 0$, then the model assumes **permanent immunity** after recovery from the disease. If $\rho_R > 0$, then immunity is only partial. A cycle graph for this model is shown in Figure 4.2.

In Exercise 4.12, the reader is asked to show that the disease-free equilibrium

$$
\mathbf{x}_{2e} = \begin{bmatrix} x_{2e} \\ x_{3e} \end{bmatrix} = \begin{bmatrix} \frac{1}{c}\left(\frac{b}{1-\sigma_S} - 1\right) \\ 0 \end{bmatrix}, \quad \frac{b}{1-\sigma_S} > 1
$$

of the disease-free equilibrium equations

$$
\begin{aligned}
x_2(t+1) &= b\tfrac{1}{1+c(x_2(t)+x_3(t))}(x_2(t)+x_3(t)) \\
&\quad + \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\sigma_S x_2(t) + \sigma_R\rho_R x_3(t) \quad \text{and} \\
x_3(t+1) &= \sigma_I\rho_I x_1(t) + \sigma_R(1-\rho_R)x_3(t)
\end{aligned}
$$

(obtained by setting x_1 equal to 0 in the SIR model equations (4.11)) satisfies Assumption 4.1. From equation (4.11)(a) and formulas (4.6), we have that

$$
\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e}) = c_i\sigma_S > 0 \quad \text{and} \quad \mathbf{T}(\mathbf{0}, \mathbf{x}_{2e}) = \sigma_I(1-\rho_I) < 1;
$$

from formula (4.7), we have that

$$
R_0 = c_i\sigma_S \frac{1}{1-\sigma_I(1-\rho_I)}. \tag{4.12}
$$

We conclude that the disease-free equilibrium $\mathbf{x}_{2e}$ of the SIR model (4.11) *is (locally asymptotically) stable if $R_0 < 1$ and is unstable if $R_0 > 1$, where R_0 is given by the formula* (4.12).

Remark 4.5. *If we use the notation S, I, and R for the classes of susceptible, infectious, and recovered individuals, respectively, then the SIR model equations* (4.11) *are*

$$\begin{aligned} S(t+1) &= b\tfrac{1}{1+c(S(t)+R(t))}\,(S(t)+R(t)) \\ &\quad + \exp\Big(-c_i\tfrac{I(t)}{p(t)}\Big)\sigma_S S(t) + \sigma_R\rho_R R(t), \\ I(t+1) &= \Big(1-\exp\Big(-c_i\tfrac{I(t)}{p(t)}\Big)\Big)\sigma_S S(t) + \sigma_I(1-\rho_I)I(t), \quad \textit{and} \\ R(t+1) &= \sigma_I\rho_I I(t) + \sigma_R(1-\rho_R)R(t). \end{aligned}$$

4.3.3. An SAIR Model. In the SI and SIR models in Sections 4.3.1 and 4.3.2, there is only one infectious class ($m = 1$). This implies that the matrices needed are 1×1, and as a result, the calculation of the next generation map and R_0 is relatively simple. In this section, we extend the SIR to include $m = 2$ infectious classes. This will require us to deal with 2×2 matrices in the calculation of R_0.

In the vector $\mathbf{x}_1 = \mathrm{col}(x_1, x_2)$ of infected individuals, let

- x_1 = infectious but asymptomatic individuals;
- x_2 = infectious but symptomatic individuals.

In the vector $\mathbf{x}_2 = \mathrm{col}(x_3, x_4)$ of noninfected individuals, let

- x_3 = susceptible individuals;
- x_4 = recovered and nonsusceptible individuals.

We assume all newly infected individuals are at first asymptomatic but have probability ρ_A of becoming symptomatic after a unit time.

Let φ_1 and φ_2 be the probabilities that a susceptible individual escapes infection by an asymptomatic individual or by a symptomatic individual, respectively. Then $\varphi_1\varphi_2$ is the probability of escaping infection altogether, and $1-\varphi_1\varphi_2$ is the probability of becoming infected (per unit time). We assume φ_ι *is* a decreasing function of the fraction x_i/p. Specifically, following the derivation in Section 4.3.1, we take

$$\varphi_i\left(\frac{x_i}{p}\right) = \exp\left(-c_i\frac{x_i}{p}\right),$$

where

$$p = x_1 + x_2 + x_3 + x_4$$

is the total population size. Then the escape function is

$$\varphi_1\left(\frac{x_1}{p}\right)\varphi_2\left(\frac{x_2}{p}\right) = \exp\left(-\frac{c_1x_1 + c_2x_2}{p}\right),$$

and we obtain the following extension of the SIR model in Section 4.3.2:

$$\begin{aligned}
&\text{(a)} \quad x_1(t+1) = \left(1 - \exp\left(-\tfrac{c_1x_1(t)+c_2x_2(t)}{p(t)}\right)\right)\sigma_S x_3(t) \\
&\qquad\qquad +\sigma_A(1-\rho_A)x_1(t); \\
&\text{(b)} \quad x_2(t+1) = \sigma_A\rho_A x_1(t) + \sigma_I(1-\rho_I)x_2(t); \\
&\text{(c)} \quad x_3(t+1) = b\tfrac{1}{1+c(x_3(t)+x_4(t))}(x_3(t)+x_4(t)) \\
&\qquad\qquad + \exp\left(-\tfrac{c_1x_1(t)+c_2x_2(t)}{p(t)}\right)\sigma_S x_3(t) \\
&\qquad\qquad +\sigma_R\rho_R x_4(t); \\
&\text{(d)} \quad x_4(t+1) = \sigma_I\rho_I x_2(t) + \sigma_R(1-\rho_R)x_4(t).
\end{aligned} \tag{4.13}$$

In this case, σ_S, σ_A, σ_I, and σ_R are the survival probabilities of susceptible, asymptomatic, symptomatic, and recovered classes, respectively. The coefficients ρ_A, ρ_I, and ρ_R are, respectively, the fractions of asymptomatic individuals that become symptomatic, symptomatic individuals that recover, and recovered individuals that lose immunity and become again susceptible. The cycle graph for the SAIR model (4.13) appears in Figure 4.3.

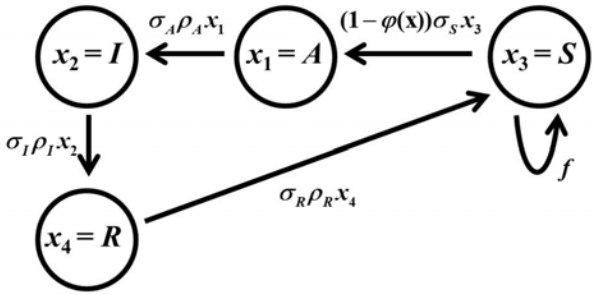

Figure 4.3. A cycle graph for the SAIR model (4.13). Only transitions among classes are indicated (removals by deaths are not indicated).

The disease-free equation (4.2) can be written as the two difference equations

$$\begin{aligned} x_3(t+1) &= b\tfrac{1}{1+c(x_3(t)+x_4(t))}(x_3(t)+x_4(t)) \\ &\quad +\sigma_S x_3(t)+\sigma_R\rho_R x_4(t) \quad \text{and} \\ x_4(t+1) &= \sigma_R(1-\rho_R)x_4(t), \end{aligned}$$

which are mathematically the same as the SIR model of Section 4.3.2 with x_3 and x_4 substituted in place of x_2 and x_3, respectively. By Exercise 4.12, these equations have a (locally asymptotically) stable equilibrium

$$\mathbf{x}_{2e} = \begin{bmatrix} x_{3e} \\ x_{4e} \end{bmatrix} = \begin{bmatrix} \frac{1}{c}\left(\frac{b}{1-\sigma_S}-1\right) \\ 0 \end{bmatrix}, \quad \frac{b}{1-\sigma_S} > 1$$

that satisfies Assumption 4.1. Thus, the SAIR model (4.13) has the disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} x_{1e} \\ x_{2e} \\ x_{3e} \\ x_{4e} \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \frac{1}{c}\left(\frac{b}{1-\sigma_S}-1\right) \\ 0 \end{bmatrix}, \quad \frac{b}{1-\sigma_S} > 1. \tag{4.14}$$

To apply Theorem 4.4, we need to calculate R_0.

The equations (4.13) have the form of the general epidemic model (4.1) with

$$\mathbf{x}_1 = \operatorname{col}(x_1, x_2), \quad \mathbf{x}_2 = \operatorname{col}(x_3, x_4)$$

and

$$\begin{aligned} \mathbf{f}_1(\mathbf{x}_1,\mathbf{x}_2) &= \begin{bmatrix} \left(1-\exp\left(-\frac{c_1x_1+c_2x_2}{x_1+x_2+x_3+x_4}\right)\right)\sigma_S x_3 + \sigma_A(1-\rho_A)x_1 \\ \sigma_A\rho_A x_1 + \sigma_I(1-\rho_I)x_2 \end{bmatrix} \\ \mathbf{f}_2(\mathbf{x}_1,\mathbf{x}_2) &= \mathbf{n}(\mathbf{x}_1,\mathbf{x}_2) + \mathbf{s}(\mathbf{x}_1,\mathbf{x}_2), \end{aligned} \tag{4.15}$$

where

$$\begin{aligned} \mathbf{n}(\mathbf{x}_1,\mathbf{x}_2) &= \begin{bmatrix} \left(1-\exp\left(-\frac{c_1x_1+c_2x_2}{x_1+x_2+x_3+x_4}\right)\right)\sigma_S x_3 \\ 0 \end{bmatrix} \quad \text{and} \\ \mathbf{s}(\mathbf{x}_1,\mathbf{x}_2) &= \begin{bmatrix} \sigma_A(1-\rho_A)x_1 \\ \sigma_A\rho_A x_1 + \sigma_I(1-\rho_I)x_2 \end{bmatrix}. \end{aligned} \tag{4.16}$$

Notice the zero component in $\mathbf{n}(\mathbf{x}_1,\mathbf{x}_2)$, which is the result of the assumption that all newly infected individuals are asymptomatic and

hence lie in the x_1 class. From formulas (4.6), we get the Jacobians

$$\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e}) = \begin{bmatrix} c_1\sigma_S & c_2\sigma_S \\ 0 & 0 \end{bmatrix} \quad \text{and}$$

$$\mathbf{T}(\mathbf{0}, \mathbf{x}_{2e}) = \begin{bmatrix} \sigma_A(1-\rho_A) & 0 \\ \sigma_A\rho_A & \sigma_I(1-\rho_I) \end{bmatrix}.$$

Notice that $\mathbf{F}(\mathbf{0}, \mathbf{x}_{2e})$ has a row of zeros, which produces in a row of zeros in the next generation matrix $\mathbf{F}(\mathbf{0}_2, \mathbf{x}_{2e})(\mathbf{I} - \mathbf{T}(\mathbf{0}_2, \mathbf{x}_{2e}))^{-1}$, which is

$$\begin{bmatrix} \sigma_S c_1 & \sigma_S c_2 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} 1-\sigma_A(1-\rho_A) & 0 \\ -\sigma_A\rho_A & 1-\sigma_I(1-\rho_I) \end{bmatrix}^{-1}$$
$$= \begin{bmatrix} \frac{\sigma_S c_1}{1-\sigma_A(1-\rho_A)} + \frac{\sigma_S c_2 \rho_A}{(1-\sigma_A(1-\rho_A))(1-\sigma_I(1-\rho_I))} & \frac{\sigma_S c_2}{1-\sigma_I(1-\rho_I)} \\ 0 & 0 \end{bmatrix}$$

and whose dominant eigenvalue therefore appears in the upper-left corner as

$$R_0 = \sigma_S c_1 \frac{1}{1-\sigma_A(1-\rho_A)} + \sigma_S c_2 \frac{\rho_A}{(1-\sigma_A(1-\rho_A))(1-\sigma_I(1-\rho_I))}. \tag{4.17}$$

From Theorem 4.4*, we conclude that the disease-free equilibrium* (4.14) *of the SAIR model* (4.13) *is* (*locally asymptotically*) *stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$*, where* R_0 *is given by the formula* (4.17)*.*

Remark 4.6. *If we use the notation S, A, I, and R for the classes of susceptible, infectious asymptomatic, infectious symptomatic, and recovered individuals* (x_3*,* x_1*,* x_2*, and* x_4)*, respectively, then the SAIR model equations* (4.13) *are*

$$\begin{aligned} S(t+1) &= b\tfrac{1}{1+c(S(t)+R(t))}(S(t)+R(t)) \\ &\quad + \exp\Big(-\tfrac{c_1 I(t)+c_2 A(t)}{p(t)}\Big)\sigma_S S(t) \\ &\quad + \sigma_R\rho_R R(t), \\ A(t+1) &= \Big(1-\exp\Big(-\tfrac{c_1 I(t)+c_2 A(t)}{p(t)}\Big)\Big)\sigma_S S(t) + \sigma_A(1-\rho_A)A(t), \\ I(t+1) &= \sigma_A\rho_A A(t) + \sigma_I(1-\rho_I)I(t), \quad \textit{and} \\ R(t+1) &= \sigma_I\rho_I I(t) + \sigma_R(1-\rho_R)R(t). \end{aligned}$$

In this notation, the state variables are listed in the order of disease progression.

In the SAIR model of Section 4.3.3, asymptomatic individuals do not recover without first becoming symptomatic. An alternative would allow that asymptomatic individuals can recover without becoming

symptomatic; see Exercise 4.13. Another extension is to allow newly infected susceptibles to be either asymptomatic or symptomatic; see Exercise 4.14.

4.4. Endemic Equilibria: A Basic Bifurcation Theorem

Theorem 4.4 (and the examples in Section 4.2) focuses on the stability of a disease-free equilibrium. This desirable outcome, when a low-level infection ultimately dies out and a persistent epidemic is avoided, occurs in general when $R_0 < 1$. In this section, we consider the existence and stability of endemic equilibria (i.e., equilibria $\mathbf{x} = \text{col}(\mathbf{x}_1, \mathbf{x}_2) \in R^{m+n}$, $\mathbf{x}_1 \neq \mathbf{0}_m$) of the model equations (4.1):

$$\begin{array}{ll} \text{(a)} & \mathbf{x}_1(t+1) = \mathbf{f}_1(\mathbf{x}_1(t), \mathbf{x}_2(t)); \\ \text{(b)} & \mathbf{x}_2(t+1) = \mathbf{f}_2(\mathbf{x}_1(t), \mathbf{x}_2(t)). \end{array} \tag{4.18}$$

The existence and stability of such an equilibrium would imply that the disease does not ultimately die out and would be endemic in the population.

Theorem 4.4 provides conditions under which a disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} \mathbf{0}_m \\ \mathbf{x}_{2e} \end{bmatrix} \in \partial R^{m+n} \tag{4.19}$$

loses stability as R_0 (defined by (4.7)) increases through 1. Based on the analogous situation with general population dynamic models in Chapter 3, we suspect that this destabilization will result in a (transcritical) bifurcation of endemic equilibria from the disease-free equilibrium and that their stability will be related to the direction of bifurcation. This bifurcation is the subject of Theorem 4.7.

Recall that a diagnostic quantity called κ was key to determining the properties of the bifurcation at $R_0 = 1$ in the general Theorem 3.21 given for population models. The same is true for the bifurcation at $R_0 = 1$ for general disease models. To define this quantity, we start by identifying the entries $p_{ij}(\mathbf{x}_1, \mathbf{x}_2)$ of the Jacobian matrix

$$\mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2) = \left[p_{ij}(\mathbf{x}_1, \mathbf{x}_2) \right].$$

Then we define

$$\kappa := -\mathbf{w}^T \left[\kappa_{ij} \right] \mathbf{v}, \tag{4.20}$$

where

$$\kappa_{ij} := \nabla^0_{\mathbf{x}_1} p_{ij} \cdot \mathbf{v} + \nabla^0_{\mathbf{x}_2} p_{ij} \cdot \left(\mathbf{I} - \mathbf{J}^0_{\mathbf{x}_2} \mathbf{f}_2\left(\mathbf{0}_m, \mathbf{x}_{2e}\right)\right)^{-1} \mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_2\left(\mathbf{0}_m, \mathbf{x}_{2e}\right) \mathbf{v} \tag{4.21}$$

and $\mathbf{w}^T$ and $\mathbf{v}$ are positive left and right eigenvectors of $\mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_1\left(\mathbf{0}_m, \mathbf{x}_{2e}\right)$ associated with the eigenvalue 1. (A superscript "0" now denotes evaluation at the disease-free equilibrium $\mathbf{x} = \operatorname{col}(\mathbf{0}_m, x_{2e})$ when $R_0 = 1$.)

Theorem 4.7. [**64**] *As in Theorem* 4.4*, assume Assumption* 4.1 *and that* $\mathbf{F}\left(\mathbf{0}, \mathbf{x}_{2e}\right)$ *and* $\mathbf{T}\left(\mathbf{0}, \mathbf{x}_{2e}\right)$ (*defined by* (4.6)) *satisfy* (2.2) *in Chapter* 3*. Assume, in addition, that* $\rho\left[\mathbf{T}\left(\mathbf{0}_m, \mathbf{x}_{2e}\right)\right] < 1$ *and* $\kappa \neq 0$*.*

(a) *Then endemic equilibria of equation* (4.18) *bifurcate from the disease-free equilibrium* (4.19) *at* $R_0 = 1$*. Their bifurcation is forward if* $\kappa > 0$ *and backward if* $\kappa < 0$*.*

(b) *If* $\mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_1\left(\mathbf{x}_1, \mathbf{x}_2\right)$ *is primitive, then* $\kappa > 0$ *implies the forward bifurcation is stable, and* $\kappa < 0$ *implies the backward bifurcation is unstable.*

While the technical details of the proof of this theorem are beyond the level of this book, the basic idea behind the proof is straightforward. Solving the equilibrium equation $\mathbf{x}_2 = \mathbf{f}_2\left(\mathbf{x}_1, \mathbf{x}_2\right)$ associated with equation (4.18)(b) for $\mathbf{x}_2$ as a function of $\mathbf{x}_1$ (by means of the Implicit Function Theorem in Appendix A.1) and substituting the answer into the equilibrium equation associated with equation (4.18)(a), we get a matrix equation for $\mathbf{x}_1$, to which we apply the bifurcation Theorems 3.21 and 3.22.

Example 4.8. In Section 4.3.1, we saw that the disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} 0 \\ x_{2e} \end{bmatrix},$$

$$x_{2e} = \frac{1}{c}\left(\frac{b}{1-\sigma_S} - 1\right), \qquad \frac{b}{1-\sigma_S} > 1,$$

of the SI model

$$\begin{aligned} x_1(t+1) &= \left(1 - \exp\left(-c_i \tfrac{x_1(t)}{x_1(t)+x_2(t)}\right)\right)\sigma_S x_2(t) + \sigma_I x_1(t) \\ x_2(t+1) &= b\tfrac{1}{1+cx_2(t)} x_2(t) + \exp\left(-c_i \tfrac{x_1(t)}{x_1(t)+x_2(t)}\right)\sigma_S x_2(t) \end{aligned} \tag{4.22}$$

loses stability as

$$R_0 = c_i \sigma_S \frac{1}{1-\sigma_I}$$

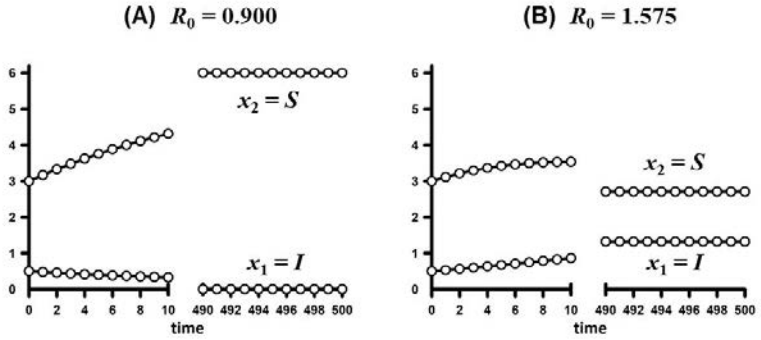

Figure 4.4. Sample solutions of the SI model equations (4.22) with parameter values $\sigma_S = 0.9$, $\sigma_I = 0.8$, $b = 1$, and $c = 1.5$ and initial conditions $x_1(0) = 0.5$ and $x_2(0) = 3$. (A) With force of infection $c_i = 0.2$, the reproduction number $R_0 < 1$, and the disease-free equilibrium $\mathbf{x}_e = \mathrm{col}(0, 6)$ is stable. (B) With force of infection $c_i = 0.35$, the reproduction number $R_0 > 1$, and the disease-free equilibrium $\mathbf{x}_e = \mathrm{col}(0, 6)$ is unstable. In this case, we see that the solution approaches an endemic equilibrium $\mathbf{x}_e = \mathrm{col}(1.321, 2.707)$.

increases through 1. To apply Theorem 4.7, we need to calculate κ from formulas (4.20)–(4.8).

In this example, $m = n = 1$, and the vectors and matrices in these formulas are all scalars, so we drop the bracket notation. In one-dimensional cases such as this, it is always the case that $\mathbf{v} = \mathbf{w} = 1$. From $\mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2) = p_{11}(x_1, x_2)$, where

$$p_{11}(x_1, x_2) = \frac{1 - \exp\left(-c_i \frac{x_1}{x_1 + x_2}\right)}{x_1} \sigma_S x_2 + \sigma_I,$$

we calculate

$$\nabla^0_{\mathbf{x}_1} p_{11} = \lim_{x_1 \to 0} \frac{\partial p_{11}(x_1, x_2^*)}{\partial x_1} = -\frac{1}{2} \sigma_S c_i \frac{c_i + 2}{x_2^*} \quad \text{and}$$

$$\nabla^0_{\mathbf{x}_2} p_{11} = \lim_{x_1 \to 0} \frac{\partial p_{11}(x_1, x_2^*)}{\partial x_2} = 0$$

so that

$$\kappa = \frac{1}{2} \sigma_S c_i \frac{c_i + 2}{x_2^*} > 0.$$

It follows that a forward-stable bifurcation of endemic equilibria occurs at $R_0 = 1$.

See Figure 4.4 for simulation examples that illustrate this bifurcation result. □

Example 4.9. Consider the SAIR model (4.13) in Example 4.3.3. We saw there that the disease-free equilibrium (4.14)

$$\mathbf{x}_e = \begin{bmatrix} 0 \\ 0 \\ x_{3e} \\ 0 \end{bmatrix},$$

$$x_{3e} = \frac{1}{c}\left(\frac{b}{1-\sigma_S} - 1\right), \quad \frac{b}{1-\sigma_S} - 1 > 0,$$

destabilizes as R_0, given by formula (4.17), increases through 1. To determine whether the resulting bifurcation of endemic equilibria is forward (hence stable) or backward (hence unstable) by an application of Theorem 4.7, we calculate the sign of $\varkappa$ given by formulas (4.20)–(4.8). Some lengthy calculations show that from the components

$$\begin{aligned}
p_{11} &= \frac{1 - \exp\left(-\frac{c_1 x_1 + c_2 x_2}{p}\right)}{c_1 x_1 + c_2 x_2} \sigma_S x_3 c_1 + \sigma_A (1 - \rho_A), \\
p_{12} &= \frac{1 - \exp\left(-\frac{c_1 x_1 + c_2 x_2}{p}\right)}{c_1 x_1 + c_2 x_2} \sigma_S x_3 c_2, \\
p_{21} &= \sigma_A \rho_A, \quad \text{and} \\
p_{22} &= \sigma_I (1 - \rho_I)
\end{aligned}$$

of the 2×2 Jacobian matrix $\mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_1 (\mathbf{x}_1, \mathbf{x}_2) = \left[p_{ij} (\mathbf{x}_1, \mathbf{x}_2)\right]$, we obtain the gradients

$$\nabla^0_{\mathbf{x}_1} p_{11} = -\frac{1}{2}\sigma_S \frac{c_1}{x_3} \begin{bmatrix} c_1 + 2 \\ c_2 + 2 \end{bmatrix}, \quad \nabla^0_{\mathbf{x}_2} p_{11} = -\sigma_S \frac{c_1}{x_3} \begin{bmatrix} 0 \\ 1 \end{bmatrix},$$

$$\nabla^0_{\mathbf{x}_1} p_{12} = -\frac{1}{2}\sigma_S \frac{c_2}{x_3} \begin{bmatrix} c_1 + 2 \\ c_2 + 2 \end{bmatrix}, \quad \nabla^0_{\mathbf{x}_2} p_{12} = -\sigma_S \frac{c_2}{x_3} \begin{bmatrix} 0 \\ 1 \end{bmatrix},$$

$$\begin{aligned}
\nabla^0_{\mathbf{x}_1} p_{21} = \nabla^0_{\mathbf{x}_2} p_{21} = \mathbf{0}, \quad \text{and} \\
\nabla^0_{\mathbf{x}_1} p_{22} = \nabla^0_{\mathbf{x}_2} p_{22} = \mathbf{0}
\end{aligned}$$

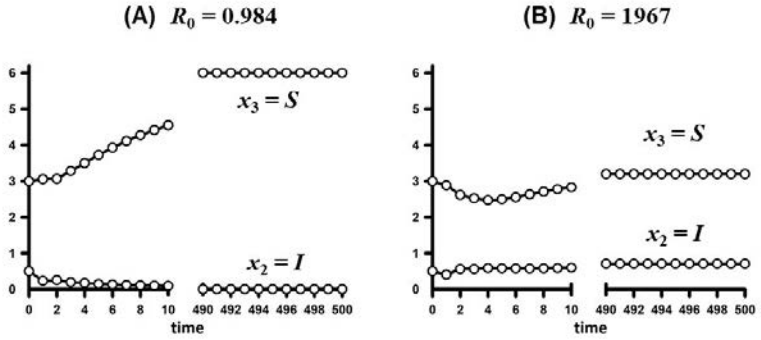

Figure 4.5. Time series plots of the $x_1(t)$ and $x_3(t)$ components of sample solutions of the SAIR model equations (4.13) with parameter values $\sigma_S = 0.9$, $\sigma_A = 0.95$, $\sigma_I = 0.8$, $\sigma_R = 0.5$, $\rho_A = 0.9$, $\rho_I = 0.9$, $\rho_R = 0.5$, $b = 1$, and $c = 1.5$ and initial conditions $x_1(0) = 0.5$, $x_2(0) = 0$, $x_3(0) = 2$, and $x_4(0) = 0$. (A) With forces of infection $c_1 = c_2 = 0.5$, the reproduction number satisfies $R_0 < 1$, and the disease-free equilibrium $\mathbf{x}_e = \text{col}(0, 0, 6, 0)$ is stable. (B) With forces of infection $c_1 = c_2 = 1$, the reproduction number satisfies $R_0 > 1$, and the disease-free equilibrium $\mathbf{x}_e = \text{col}(0, 6)$ is unstable. In this case, we see that the solution approaches an endemic equilibrium $\mathbf{x}_e = \text{col}(0.707, 0.657, 3.197, 0.861)$.

to be used in formula (4.8). Finally from (4.15), we calculate the 2×2 Jacobian matrices

$$\mathbf{J}^0_{\mathbf{x}_1} \mathbf{f}_2(\mathbf{0}_m, \mathbf{x}_{2e}) = \begin{bmatrix} -\sigma_S c_1 & -\sigma_S c_2 \\ 0 & 0 \end{bmatrix} \quad \text{and}$$

$$\mathbf{J}^0_{\mathbf{x}_2} \mathbf{f}_2(\mathbf{0}_m, 0) = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix}.$$

These ingredients in (4.8) give us the matrix

$$\left[\kappa_{ij}\right] = \frac{1}{2}\sigma_S \frac{(c_1 + 2)\, v_1 + (c_2 + 2)\, v_2}{x_{3e}} \begin{bmatrix} -c_1 & -c_2 \\ 0 & 0 \end{bmatrix}.$$

Since this 2×2 matrix has no positive entries, it follows that $\kappa = -\mathbf{w}^T \left[\kappa_{ij}\right] \mathbf{v} > 0$.

By Theorem 4.7, *a forward bifurcation of* (*locally asymptotically*) *stable endemic equilibria bifurcate*

from the disease-free equilibrium as R_0 increases through 1.

See Figure 4.5 for simulation examples that illustrate this bifurcation result. □

4.5. Applications

The two applications in this section illustrate the disease modeling methodology and analysis studied in this chapter. The first application considers a vaccination program in the basic SI and SIR models and the notion of **herd immunity**. The second application concerns a model of a specific disease, namely malaria.

4.5.1. Vaccinations and Herd Immunity. An infection that invades a susceptible population at a low level will not succeed in establishing itself permanently in the population if the disease-free equilibrium is (locally asymptotically) stable (i.e., if $R_0 < 1$). However, if $R_0 > 1$, then one can consider implementing procedures designed to reduce R_0 with the goal of attaining $R_0 < 1$ and a stable disease-free equilibrium. These include vaccination programs, quarantine protocols, cleaning and sterilization procedures, pathogen vector control (such as insecticides), social behavior modification (such as masking and social distancing), and so on. In this section, we look at the use of vaccination programs to reduce R_0 in the basic SI and SIR models introduced in this chapter.

4.5.1.1. *SI Model.* In Section 4.3.1, we saw that SI model

$$\begin{aligned} x_1(t+1) &= \left(1 - \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\right)\sigma_S x_2(t) + \sigma_I x_1(t) \\ x_2(t+1) &= b\tfrac{1}{1+cx_2(t)}x_2(t) + \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\sigma_S x_2(t) \end{aligned} \tag{4.23}$$

has the disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} 0 \\ \frac{1}{c}\left(\frac{b}{1-\sigma_S} - 1\right) \end{bmatrix}, \quad \frac{b}{1-\sigma_S} > 1,$$

and that the reproduction number is

$$R_0 = c_i \sigma_S \frac{1}{1-\sigma_I}.$$

Assume that $R_0 > 1$ so that (by Theorem 4.4) the disease-free equilibrium is unstable. (By Theorem 4.7, there are stable endemic equilibria, at least for $R_0 \gtrapprox 1$.)

Assume that a vaccination program is put in place and succeeds in accomplishing the following: at any given time t, a fraction υ of the susceptibles $x_2(t)$ are vaccinated (during the interval t to $t+1$) and become immune to the disease at time $t+1$. Thus, $(1-\upsilon)x_2(t)$ susceptibles remain at time $t+1$ (if they survive). This assumption replaces the survival probability σ_S in the model equations (4.23) by $(1-\upsilon)\sigma_S$, which now become

$$x_1(t+1) = \left(1 - \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\right)(1-\upsilon)\sigma_S x_2(t) + \sigma_I x_1(t) \quad \text{and}$$
$$x_2(t+1) = b\tfrac{1}{1+cx_2(t)}x_2(t) + \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)(1-\upsilon)\sigma_S x_2(t),$$

and the disease-free equilibrium becomes

$$\mathbf{x}_e = \begin{bmatrix} 0 \\ \frac{1}{c}\left(\frac{b}{1-(1-\upsilon)\sigma_S} - 1\right) \end{bmatrix}, \quad \frac{b}{1-(1-\upsilon)\sigma_S} > 1.$$

We could recalculate R_0 for this vaccination model, but it is easier simply to note that the calculations are the same as those in Section 4.3.2 with σ_S replaced by $(1-\upsilon)\sigma_S$. Consequently, we can use formula (4.12) to obtain the reproduction number

$$R_0(\upsilon) = c_i(1-\upsilon)\sigma_S \frac{1}{1-\sigma_I},$$

which is now a function of the vaccination fraction υ. Note that

$$R_0(\upsilon) = (1-\upsilon)R_0(0), \tag{4.24}$$

where

$$R_0(0) = c_i\sigma_S \frac{1}{1-\sigma_I} > 1 \tag{4.25}$$

is the reproduction number in the absence of the vaccination program. The question is this, If the fraction υ is sufficiently high (close to 1), will an epidemic be avoided? And if so, what is the vaccination threshold?

> *From formula* (4.25)*, we find that* $R_0(\upsilon) < 1$*, and the disease-free equilibrium is stable if the vaccination fraction satisfies*
>
> $$\upsilon > \upsilon_0 := 1 - \frac{1}{R_0(0)}.$$

If this threshold for the fraction of vaccinated individuals is met, it is said that the population has **herd immunity**. Note that the vaccination threshold v_0 can be calculated by this formula from a knowledge of $R_0 = R_0(0)$ in the absence of the vaccination program. See Table 4.1 for examples.

Table 4.1. (Data from Wikipedia: `https://en.wikipedia.org/wiki/Basic_reproduction_number`. Text is available under the Creative Commons Attribution-ShareAlike License 4.0, additional terms may apply.)

Disease	Estimated R_0	Estimated $v_0 = 1 - \frac{1}{R_0}$	Estimated % Needed for Herd Immunity
Measles	$12 - 18$	$\frac{11}{12} - \frac{17}{18}$	$92 - 94\%$
Chickenpox	$10 - 12$	$\frac{9}{10} - \frac{11}{12}$	$90 - 92\%$
Mumps	$10 - 12$	$\frac{9}{10} - \frac{11}{12}$	$90 - 92\%$
Rubella	$6 - 7$	$\frac{5}{6} - \frac{6}{7}$	$83 - 86\%$
Polio	$5 - 7$	$\frac{4}{5} - \frac{6}{7}$	$80 - 86\%$
Covid-19 (variants)	$3 - 8$	$\frac{2}{3} - \frac{7}{8}$	$67 - 88\%$
Pertussis	$5 - 6$	$\frac{4}{5} - \frac{5}{6}$	$80 - 83\%$
Smallpox	$3.5 - 6$	$\frac{5}{7} - \frac{5}{6}$	$71 - 83\%$
Covid-19 (wild type)	$2.4 - 3.4$	$\frac{7}{12} - \frac{12}{17}$	$58 - 71\%$
HIV/AIDS	$2 - 5$	$\frac{1}{2} - \frac{4}{5}$	$50 - 80\%$
SARS	$2 - 4$	$\frac{1}{2} - \frac{3}{4}$	$50 - 75\%$
Common cold	$2 - 3$	$\frac{1}{2} - \frac{2}{3}$	$50 - 67\%$
Diphtheria	$1.7 - 4.3$	$\frac{7}{17} - \frac{33}{43}$	$41 - 77\%$
Ebola	$1.4 - 1.8$	$\frac{2}{7} - \frac{4}{9}$	$29 - 44\%$
Influenza	$1.2 - 1.4$	$\frac{1}{6} - \frac{2}{7}$	$17 - 29\%$

4.5.1.2. *SIR Model.* Consider the SIR model in Section 4.3.2 but with permanent acquired immunity (i.e., with $\rho_R = 0$):

$$\begin{aligned}
&\text{(a)} \quad x_1(t+1) = \left(1 - \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\right)\sigma_S x_2(t) \\
&\qquad\qquad +\sigma_I(1-\rho_I)\,x_1(t); \\
&\text{(b)} \quad x_2(t+1) = b\tfrac{1}{1+c_i(x_2(t)+x_3(t))}(x_2(t)+x_3(t)) \\
&\qquad\qquad + \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\sigma_S x_2(t); \\
&\text{(c)} \quad x_3(t+1) = \sigma_I \rho_I x_1(t) + \sigma_R x_3(t).
\end{aligned} \tag{4.26}$$

In Section 4.3.2, it is shown that this model has the disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} x_{1e} \\ x_{2e} \\ x_{3e} \end{bmatrix} = \begin{bmatrix} 0 \\ \frac{1}{c_i}\left(\frac{b}{1-\sigma_S} - 1\right) \\ 0 \end{bmatrix}, \quad \frac{b}{1-\sigma_S} > 1,$$

and that

$$R_0 = c_i \sigma_S \frac{1}{1-\sigma_I(1-\rho_I)}.$$

If we assume, as in the SI model in Section 4.5.1.1, that a fraction υ of susceptibles becomes immune to the disease by implementation of a vaccination program, then we have the modified SIR model equations

$$\begin{aligned}
&\text{(a)} \quad x_1(t+1) = \left(1 - \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)\right)(1-\upsilon)\,\sigma_S x_2(t) \\
&\qquad\qquad +\sigma_I(1-\rho_I)\,x_1(t); \\
&\text{(b)} \quad x_2(t+1) = b\tfrac{1}{1+c(x_2(t)+x_3(t))}(x_2(t)+x_3(t)) \\
&\qquad\qquad + \exp\left(-c_i \tfrac{x_1(t)}{p(t)}\right)(1-\upsilon)\,\sigma_S x_2(t); \\
&\text{(c)} \quad x_3(t+1) = \sigma_I \rho_I x_1(t) + \upsilon\sigma_S x_2(t) + \sigma_R x_3(t).
\end{aligned} \tag{4.27}$$

Note that the vaccinated individuals υx_2 are placed in the recovered class x_3 (if they survive). The recovered class in this model consists of individuals who have immunity by one of two means: those $\rho_I x_1$ with acquired immunity (i.e., who had and recovered from the disease) and those υx_2 who have been vaccinated.

It is left as Exercise 4.16 to show that the disease-free equilibrium is

$$\mathbf{x}_e = \frac{1}{c}\frac{1}{1-(1-\upsilon)\sigma_S}\left(b - (1-\sigma_R)\frac{1-(1-\upsilon)\sigma_S}{1-\sigma_R+\upsilon\sigma_S}\right)\begin{bmatrix} 0 \\ 1 \\ \upsilon\frac{\sigma_S}{1-\sigma_R} \end{bmatrix}. \tag{4.28}$$

To calculate the reproduction number, we identify from equation (4.27)(a) that

$$\mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2) = \mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) + \mathbf{s}(\mathbf{x}_1, \mathbf{x}_2),$$

where

$$\mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) = \left(1 - \exp\left(-c_i \frac{x_1}{x_1 + x_2 + x_3}\right)\right)(1 - \upsilon)\,\sigma_S x_2.$$

From formulas (4.6), we get the 1×1 Jacobian matrices

$$\mathbf{F}(0, \mathbf{x}_{2e}) = c_i \frac{1 - \sigma_R}{1 - \sigma_R + \upsilon\sigma_S}(1 - \upsilon)\,\sigma_S \quad \text{and}$$
$$\mathbf{T}(0, \mathbf{x}_{2e}) = \sigma_I(1 - \rho_I),$$

and from formula (4.7),

$$R_0(\upsilon) = c_i \frac{1 - \sigma_R}{1 - \sigma_R + \upsilon\sigma_S}(1 - \upsilon)\,\sigma_S \frac{1}{1 - \sigma_I(1 - \rho_I)}.$$

Here we have indicated that the reproduction number $R_0(\upsilon)$ depends on the fraction υ of the population that is vaccinated. Note that

$$R_0(\upsilon) = \frac{1 - \sigma_R}{1 - \sigma_R + \upsilon\sigma_S}(1 - \upsilon)\,R_0(0),$$

where

$$R_0(0) = c_i \sigma_S \frac{1}{1 - \sigma_I(1 - \rho_I)}$$

is the reproduction number if the population is unvaccinated.

Suppose the disease-free equilibrium is unstable if the population is unvaccinated (i.e., suppose $R_0(0) > 1$). Can the disease-free equilibrium be stabilized (and an epidemic avoided) by vaccination? And if so, what level of vaccination will suffice? The answer is that the vaccination fraction will accomplish this if $R_0(\upsilon) < 1$, which occurs when

$$\upsilon > \upsilon_0 := \frac{(1 - \sigma_R)}{\sigma_S + R_0(0)(1 - \sigma_R)}(R_0(0) - 1). \tag{4.29}$$

We conclude from this model the following. Suppose the unvaccinated population is threatened with an epidemic because $R_0(0) > 1$, and therefore, the disease-free equilibrium is unstable. The vaccinated population can avoid an epidemic (i.e., $R_0(\upsilon) < 1$ will be satisfied) provided the vaccination fraction υ exceeds the threshold υ_0 given by formula (4.29).

If we rewrite the vaccination threshold as

$$v_0 := \frac{1}{1 + \frac{\sigma_S}{1-\sigma_R}\frac{1}{R_0(0)}}\left(1 - \frac{1}{R_0(0)}\right),$$

then since

$$\frac{1}{1 + \frac{\sigma_S}{1-\sigma_R}\frac{1}{R_0(0)}} < 1,$$

we see that the threshold $v > v_0$ is met if

$$v > 1 - \frac{1}{R_0(0)}.$$

Thus, the criterion for herd immunity in the SI model is sufficient, but not necessary, to attain herd immunity in the SIR model.

4.5.2. A Malaria Model. The examples in this chapter have not focussed on any specific disease but instead on low-dimensional general models. This is done in order to emphasize the modeling methodology, analytic techniques, and concepts. We close this chapter with a model that is focused on a specific disease, namely malaria. It is a discrete time analog of the ordinary differential equation model studied in [**17**], [**18**], [**19**]. We will direct our attention here solely to the formulation of the model equations and the calculation of R_0 for this rather complicated model.

Mosquitoes are considered the most deadly animal in the world to humans [**86**]. Malaria is the most lethal of many mosquito-borne diseases, which also include dengue, zika, yellow fever, West Nile virus, chikungunya, and equine encephalitis. Malaria is caused by one of several species of protozoan parasites from the genus *Plasmodium*. The parasite is transmitted to a human by the bite of an infected female mosquito of the genus *Anopheles*. After passing through developmental life cycle stages in the human liver, the parasite is transmitted (in the form of gametocytes) back to a mosquito when it bites an infected human. After the parasite passes through more life stages in the mosquito, the mosquito becomes infectious and capable of repeating the cycle by biting a susceptible human. Thus, the disease is spread in humans not by direct contact with the pathogen but by contact with an infected mosquito, which is called a vector for the disease. So our model will account for the dynamics and interactions of both human and mosquito populations.

Because of the latency periods associated with the developmental stages of the parasite, we structure both populations into three classes: susceptibles S, exposed E (infected but not infectious), and infectious I. Humans can recover from malaria, but recovered individuals still have low levels of parasites and can infect mosquitoes. After some time, recovered individuals revert to the susceptible class. Mosquitoes, on the other hand, remain infectious for life. For these reasons, we create a recovered class R for humans but not for mosquitoes. The model for the human population is called an SEIR model, and that for the mosquito population is called an SEI model. A common notational procedure is to list the model equations for these classes in the order of passage for individuals and refer to them as SEIR and SIR models, respectively. However, in keeping with our notation for the calculation of R_0, in which *infected classes are listed first*, we write the state variables in the order

$$\mathbf{x} = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{bmatrix} = \begin{bmatrix} E_h \\ E_m \\ I_h \\ I_m \\ S_h \\ S_m \\ R \end{bmatrix},$$

where a subscript h indicates humans and a subscript m indicates mosquitoes. Using the same modeling methodology used throughout this chapter, we construct the following equations for the components of $\mathbf{x} = \mathbf{x}(t)$ (see graph in Figure 4.6):

$$\begin{aligned}
E_h(t+1) &= (1-\varphi_h(\mathbf{x}(t)))\,\sigma_{Sh}S_h(t) \\
&\quad +(1-\upsilon_{Eh})\,\sigma_{Eh}E_h(t), \\
E_m(t+1) &= (1-\varphi_m(\mathbf{x}(t)))\,\sigma_{Sm}S_m(t) \\
&\quad +(1-\upsilon_{Em})\,\sigma_{Em}E_m(t) \\
I_h(t+1) &= \upsilon_{Eh}\sigma_{Eh}E_h(t)+(1-\upsilon_{Ih})\,\sigma_{Ih}I_h(t), \\
I_m(t+1) &= \upsilon_{Em}\sigma_{Em}E_m(t)+\sigma_{Im}I_m(t), \\
S_h(t+1) &= b_h\tfrac{1}{1+c_hp_h(t)}p_h(t)+\upsilon_{Rh}\sigma_{Rh}R_h(t) \\
&\quad +\varphi_h(\mathbf{x}(t))\,\sigma_{Sh}S_h(t), \\
S_m(t+1) &= b_m\tfrac{1}{1+c_mp_m(t)}p_m(t)+\varphi_m(\mathbf{x}(t))\,\sigma_{Sm}S_m(t), \quad \text{and} \\
R_h(t+1) &= \upsilon_{Ih}\sigma_{Ih}I_h(t)+(1-\upsilon_{Rh})\,\sigma_{Rh}R_h(t).
\end{aligned} \tag{4.30}$$

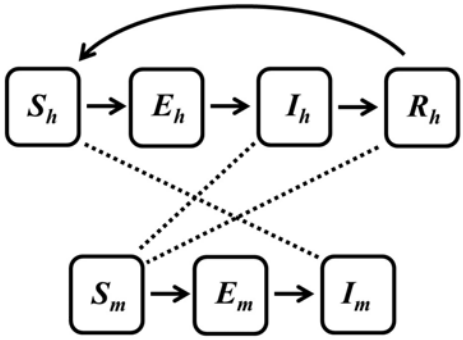

Figure 4.6. The flow diagram for the malaria model (4.30). The dashed lines indicate interactions between humans (top row) and mosquitoes (bottom row).

The time unit is one day. The σ coefficients denote survival probabilities for the class indicated by their subscripts in (4.30), and the υ denote the probability of a transition between classes as indicated their subscripts; see Table 4.2.

What remains for the specification of the model are the infection escape functions φ_h and φ_m. For this purpose, we again use decreasing exponential functions

$$\varphi_h = \exp\left(-\delta_h \frac{I_m}{p_m}\right) \quad \text{and} \quad \varphi_m = \exp\left(-\delta_m \frac{I_h}{p_h}\right),$$

where

$$p_h = S_h + E_h + I_h + R_h \quad \text{and} \quad p_m = S_m + E_m + I_m$$

are total population sizes of humans and mosquitoes, respectively. In this model, the coefficients δ_h and δ_m in the escape functions are related to the number of bites per human per mosquito per day, as given in [**18**], by

$$\begin{aligned} \delta_h &:= \beta_h(p_h, p_m)\, i_{hm} \quad \text{and} \\ \delta_m &:= \beta_m(p_h, p_m)\, i_{mh}, \end{aligned}$$

where

$$\beta_h(p_h, p_m) := \frac{\beta_m p_m \beta_h p_h}{\beta_m p_m + \beta_h p_h} \frac{1}{p_h} \quad \text{and}$$
$$\beta_m(p_h, p_m) := \frac{\beta_m p_m \beta_h p_h}{\beta_m p_m + \beta_h p_h} \frac{1}{p_m}.$$

Thus,

$$\varphi_h(\mathbf{x}(t)) = \exp\left(-\beta_h(p_h, p_m)\, i_{hm} \frac{I_m}{p_m}\right) \quad \text{and}$$
$$\varphi_m(\mathbf{x}(t)) = \exp\left(-\beta_m(p_h, p_m)\, i_{mh} \frac{I_h}{p_h}\right)$$

in (4.30). The interpretation of the coefficients in these expressions appear in Table 4.2.

Note that the disease-free equations for the susceptibles $S_h(t)$ and $S_m(t)$ (obtained by setting E_h, E_m, I_h, I_m, and R_h identically equal to 0) are the two, uncoupled one-dimensional difference equations

$$S_h(t+1) = b_h \frac{1}{1+c_h S_h(t)} S_h(t) + \sigma_{Sh} S_h(t) \quad \text{and}$$
$$S_m(t+1) = b_m \frac{1}{1+c_m S_m(t)} S_m(t) + \sigma_{Sm} S_m(t)$$

Table 4.2. Parameters for the Malaria Model (4.30)

Survival Probabilities	Transition and Infection Probabilities
σ_{Sh} susceptible human	υ_{Eh} exposed human becomes infectious
σ_{Sm} susceptible mosquito	υ_{Em} exposed mosquito becomes infectious
σ_{Eh} exposed human	υ_{Ih} infectious human recovers
σ_{Em} exposed mosquito	υ_{Rh} recovered human becomes susceptible
σ_{Ih} infectious human	i_{mh} mosquito is infected by biting a human
σ_{Im} infectious mosquito	i_{hm} human is infected by a mosquito bite
σ_{Rh} recovered human	
Logistic Growth Coefficients	**Biting Rates**
b_h, b_m birth rates	β_h average bites a human receives per day
c_h, c_m density coefficients	β_m average bites a mosquito gives per day

for the human and mosquito populations. We can analyze both of these equations using the methods of Chapter 1 to find

$$\lim_{t\to\infty} S_h(t) = \begin{cases} 0 & \text{if } \frac{b_h}{1-\sigma_{Sh}} < 1 \\ S_{he} \coloneqq \frac{1}{c_h}\left(\frac{b_h}{1-\sigma_{Sh}} - 1\right) & \text{if } \frac{b_h}{1-\sigma_{Sh}} > 1 \end{cases} \quad \text{and}$$

$$\lim_{t\to\infty} S_m(t) = \begin{cases} 0 & \text{if } \frac{b_m}{1-\sigma_{Sm}} < 1 \\ S_{me} \coloneqq \frac{1}{c_m}\left(\frac{b_m}{1-\sigma_{Sm}} - 1\right) & \text{if } \frac{b_m}{1-\sigma_{Sm}} > 1 \end{cases}$$

for all positive initial conditions $S_h(0) > 0$ and $S_m(0) > 0$. We proceed under the assumption that both populations survive in the absence of the parasite, that is to say that

$$\frac{b_h}{1-\sigma_{Sh}} > 1 \quad \text{and} \quad \frac{b_m}{1-\sigma_{Sm}} > 1.$$

The model equations in (4.30) have the general epidemic model format (4.1) with

$$\mathbf{x} = \begin{bmatrix} \mathbf{x}_1 \\ \mathbf{x}_2 \end{bmatrix},$$

where

$$\mathbf{x}_1 = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{bmatrix} = \begin{bmatrix} E_h \\ E_m \\ I_h \\ I_m \end{bmatrix} \quad \text{and} \quad \mathbf{x}_2 = \begin{bmatrix} x_5 \\ x_6 \\ x_7 \end{bmatrix} = \begin{bmatrix} S_h \\ S_m \\ R_h \end{bmatrix},$$

with

$$\mathbf{f}_1(\mathbf{x}_1, \mathbf{x}_2) = \mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) + \mathbf{s}(\mathbf{x}_1, \mathbf{x}_2) \quad \text{and}$$

$$\mathbf{f}_2(\mathbf{x}_1, \mathbf{x}_2) = \begin{bmatrix} b_h \frac{1}{1+c_h N_h} N_h + \upsilon_{Rh}\sigma_{Rh}R_h + \varphi_h(\mathbf{x})\sigma_{Sh}S_h \\ b_m \frac{1}{1+c_m N_m} N_m + \varphi_m(\mathbf{x})\sigma_{Sm}S_m \\ \upsilon_{Ih}\sigma_{Ih}I_h + (1-\upsilon_{Rh})\sigma_{Rh}R_h \end{bmatrix},$$

and with

$$\mathbf{n}(\mathbf{x}_1, \mathbf{x}_2) = \begin{bmatrix} (1-\varphi_h(\mathbf{x}))\,\sigma_{Sh} S_h \\ (1-\varphi_m(\mathbf{x}))\,\sigma_{Sm} S_m \\ 0 \\ 0 \end{bmatrix} \quad \text{and}$$

$$\mathbf{s}(\mathbf{x}_1, \mathbf{x}_2) = \begin{bmatrix} (1-\upsilon_{Eh})\,\sigma_{Eh} E_h \\ (1-\upsilon_{Em})\,\sigma_{Em} E_m \\ \upsilon_{Eh}\sigma_{Eh} E_h + (1-\upsilon_{Ih})\,\sigma_{Ih} I_h \\ \upsilon_{Em}\sigma_{Em} E_m + \sigma_{Im} I_m \end{bmatrix}.$$

This model has the disease-free equilibrium

$$\mathbf{x}_e = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ x_{5e} \\ x_{6e} \\ 0 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ S_{he} \\ S_{me} \\ 0 \end{bmatrix},$$

which by Theorem 4.4, destabilizes as R_0 increases through 1.

To calculate the reproduction number R_0 using the method in Section 4.2, we calculate (using formulas (4.6)) the Jacobian matrices

$$\mathbf{F}(\mathbf{0}_m, \mathbf{x}_{2e}) = \begin{bmatrix} 0 & 0 & 0 & \frac{S_{he}\beta_{hm}\sigma_{Sh}\beta_h(S_{he},S_{me})}{S_{me}} \\ 0 & 0 & \frac{S_{me}\beta_{mh}\sigma_{Sm}\beta_m(S_{he},S_{me})}{S_{he}} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$\mathbf{T}(\mathbf{0}_m, \mathbf{x}_{2e}) = \begin{bmatrix} (1-\upsilon_{Eh})\,\sigma_{Eh} & 0 & 0 & 0 \\ 0 & (1-\upsilon_{Em})\,\sigma_{Em} & 0 & 0 \\ \upsilon_{Eh}\sigma_{Eh} & 0 & (1-\upsilon_{Ih})\,\sigma_{Ih} & 0 \\ 0 & \upsilon_{Em}\sigma_{Em} & 0 & \sigma_{Im} \end{bmatrix}$$

and the next generation matrix

$$\mathbf{F}(\mathbf{0}_m, \mathbf{x}_{2e})\,(\mathbf{I} - \mathbf{T}(\mathbf{0}_m, \mathbf{x}_{2e}))^{-1} = \begin{pmatrix} \mathbf{N} & * \\ \mathbf{0}_{2\times 2} & \mathbf{0}_{2\times 2} \end{pmatrix},$$

where **N** is the matrix

$$\begin{bmatrix} 0 & \frac{S_{he}}{S_{me}}\frac{\beta_{hm}\sigma_{Sh}\upsilon_{Em}\sigma_{Em}\beta_h(S_{he},S_{me})}{(1-(1-\upsilon_{Em})\sigma_{Em})(1-\sigma_{Im})} \\ \frac{S_{me}}{S_{he}}\frac{\beta_{mh}\upsilon_{\sigma_{Sm}Eh}\sigma_{Eh}\beta_m(S_{he},S_{me})}{(1-(1-\upsilon_{Eh})\sigma_{Eh})(1-(1-\upsilon_{Ih})\sigma_{Ih})} & 0 \end{bmatrix}$$

and the asterisk denotes an unneeded block submatrix. The eigenvalues of this next generation matrix are 0 (with multiplicity 2) and those of **N**, which are $\pm\sqrt{R_{0h}R_{0m}}$, where

$$\begin{aligned} R_{0h} &:= \frac{\beta_{mh}\sigma_{Sh}\upsilon_{Eh}\sigma_{Eh}\beta_h(S_{he},S_{me})}{(1-(1-\upsilon_{Eh})\sigma_{Eh})(1-(1-\upsilon_{Ih})\sigma_{Ih})} \quad \text{and} \\ R_{0m} &:= \frac{\beta_{hm}\sigma_{Sm}\upsilon_{Em}\sigma_{Em}\beta_m(S_{he},S_{me})}{(1-(1-\upsilon_{Em})\sigma_{Em})(1-\sigma_{Im})}. \end{aligned} \tag{4.31}$$

It follows that

$$R_0 = \sqrt{R_{0h}R_{0m}}. \tag{4.32}$$

Note that

$$\begin{aligned} R_{0h} =& [\text{bites per human per unit time}] \\ & \times [\text{probability of human-to-mosquito transmission}] \\ & \times [\text{expected time a human is infectious}] \\ =& \begin{bmatrix} \text{average number of mosquitoes infected} \\ \text{by humans per unit time} \end{bmatrix} \\ & \times [\text{expected time a human is infectious}] \\ =& \begin{bmatrix} \text{average number of mosquitoes infected} \\ \text{by a human per lifetime} \end{bmatrix}, \end{aligned}$$

and similarly, R_{0m} is the average number of humans infected by a mosquito per lifetime.

> *The reproduction number R_0 that determines the stability of the disease-free equilibrium in the malaria model* (4.30) *is the geometric mean* (4.32) *of the two averages R_{0h} and R_{0m} given by formulas* (4.31).

More analysis of the continuous time version of the malaria model (4.30) can be found in [**18**], [**19**].

4.6. Concluding Remarks

In this chapter, we consider an important type of structured population model in which individuals are classified according to various disease-related stages. The focus was on the modeling methodology and the stability properties of a disease-free equilibrium (i.e., an equilibrium of a model in which there a no individuals infected with the pathogen). We describe a general procedure for calculating the famous quantity R_0 (the inherent reproduction number) associated with a specific disease-free equilibrium. The disease-free equilibrium destabilizes as R_0 increases through 1, and this destabilization results in the creation of endemic equilibrium (i.e., equilibria in which the infected class is not empty). This basic (transcritical) bifurcation is analogous to that for matrix models considered in Chapter 3 except that the bifurcation is not of survival equilibria from a population extinction equilibrium but of endemic equilibria from a disease-free equilibrium.

To protect the population from an epidemic, a focus is placed on attaining $R_0 < 1$. It should be remembered, however, that the stability analysis in Theorem 4.4 only guarantees the local stability for initial conditions near the disease-free equilibrium (i.e., for populations near the disease-free equilibrium that are invaded by a small number of diseased individuals). While this might indeed be appropriate for many cases, for other circumstances, $R_0 < 1$ might not guarantee the asymptotic elimination of the disease. A global analysis of the existence and stability of endemic equilibria is needed for such a conclusion.

4.7. Exercises

Exercise 4.10. Assume the disease-free equation in the SI model of Example 4.2 and Section 4.3.1 is the Ricker equation

$$x_1(t+1) = bx(t)\exp(-cx(t))$$

instead of the discrete logistic equation. Calculate R_0 and apply Theorems 4.4 and 4.7.

Exercise 4.11. Prove (4.24) still holds for the vaccination modified SI model (4.23) with a general escape function $\varphi(x_1/p)$ with $\varphi(0) = 1$ and $\varphi'(0) < 0$.

Exercise 4.12. Show that the disease-free equilibrium $\mathbf{x}_{2e}$ of the SAIR model in Section 4.3.3 satisfies Assumption 4.1.

Exercise 4.13. Consider an extension of the SAIR model in Example 4.3.3 in which asymptomatic individuals can also recover and move the recovered class x_4 with a certain probability. Modify the cycle graph in Figure 4.3 to include this possibility. Calculate R_0 and apply Theorems 4.4 and 4.7.

Exercise 4.14. Consider an extension of the SAIR model in Example 4.3.3 in which infected susceptibles can be either asymptomatic or symptomatic. Modify the cycle graph in Figure 4.3 to include this possibility. Calculate R_0 and apply Theorems 4.4 and 4.7.

Exercise 4.15. Consider an extension of the SAIR model in Example 4.3.3 that includes both added features in Exercises 4.13 and 4.14. Modify the cycle graph in Figure 4.3 to include this possibility. Calculate R_0 and apply Theorems 4.4 and 4.7.

Exercise 4.16. Derive the formula (4.28) for the disease-free equilibrium of the vaccination SIR model in Section 4.5.1.2. Also, check the formula by substitution into the disease-free equilibrium equations.