Chapter 2
Introduction to Epidemic Modeling

2.1 Kermack–McKendrick SIR Epidemic Model

Introduction to epidemic modeling is usually made through one of the first epidemic models proposed by Kermack and McKendrick in 1927, a model known as the SIR epidemic model [84].

2.1.1 Deriving the Kermack–McKendrick Epidemic Model

When a disease spreads in a population, it splits the population into nonintersecting classes. In one of the simplest scenarios, there are three such classes:

- The class of individuals who are healthy but can contract the disease. These are called *susceptible individuals* or *susceptibles*. The size of this class is usually denoted by S.
- The class of individuals who have contracted the disease and are now sick with it, called *infected individuals*. In this model, it is assumed that infected individuals are also *infectious* (see Chap. 1 for distinction between infected and infectious individuals). The size of the class of infectious/infected individuals is denoted by I.
- The class of individuals who have recovered and cannot contract the disease again are called *removed/recovered individuals*. The class of recovered individuals is usually denoted by R.

The number of individuals in each of these classes changes with time, that is, $S(t)$, $I(t)$, and $R(t)$ are functions of time t. The total population size N is the sum of the sizes of these three classes:

$$N = S(t) + I(t) + R(t).$$

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To formulate a model, we have to make assumptions to simplify reality. The first assumption for the Kermack–McKendrick model is that infected individuals are also infectious. The second assumption of the model is that the total population size remains constant.

Epidemiological models consist of systems of ODEs that describe the dynamics in each class. One of the simplest models involves the dynamics of susceptible, infectious, and recovered individuals. The model was first proposed by Kermack and McKendrick in 1927 [84].

To derive the differential equations, we consider how the classes change over time. When a susceptible individual enters into contact with an infectious individual, that susceptible individual becomes infected with a certain probability and moves from the susceptible class into the infected class. The susceptible population decreases in a unit of time by all individuals who become infected in that time. At the same time, the class of infectives increases by the same number of newly infected individuals. The number of individuals who become infected per unit of time in epidemiology is called *incidence*, and the rate of change of the susceptible class is given by

$$S'(t) = -\text{incidence}.$$

How can we represent the incidence? Consider one infectious individual. Assume:

- cN is the number of contacts per unit of time this infectious individual makes. Here we assume that the number of contacts made by one infectious individual is proportional to the total population size with per capita contact rate c.
- $\frac{S}{N}$ is the probability that a contact is with a susceptible individual. Thus,
- $cN\frac{S}{N}$ is number of contacts with susceptible individuals that one infectious individual makes per unit of time. Not every contact with a susceptible individual necessarily leads to transmission of the disease. Suppose p is the probability that a contact with a susceptible individual results in transmission. Then,
- pcS is number of susceptible individuals who become infected per unit of time per infectious individual.
- βSI is the number of individuals who become infected per unit of time (incidence). Here we have set $\beta = pc$.

If we define $\lambda(t) = \beta I$, then the number of individuals who become infected per unit of time is equal to $\lambda(t)S$. The function $\lambda(t)$ is called the *force of infection*. The coefficient β is the constant of proportionality called the *transmission rate constant*. The number of infected individuals in the population $I(t)$ is called the *prevalence* of the disease.

There are different types of incidence depending on the assumption made about the form of the force of infection. One form is called *mass action incidence*. With this form of incidence, we obtain the following differential equation for susceptible individuals:

$$S'(t) = -\beta IS.$$

The susceptible individuals who become infected move to the class I. Those individuals who recover or die leave the infected class at constant per capita probability

per unit of time α, called the *recovery rate*. That is, αI is the number of infected individuals per unit of time who recover. So,

$$I'(t) = \beta IS - \alpha I.$$

Individuals who recover leave the infectious class and move to the recovered class

$$R'(t) = \alpha I.$$

Thus, the whole model is given by the following system of ODEs:

$$\begin{aligned} S'(t) &= -\beta IS, \\ I'(t) &= \beta IS - \alpha I, \\ R'(t) &= \alpha I. \end{aligned} \tag{2.1}$$

To be well defined mathematically, this system is equipped with given initial conditions $S(0)$, $I(0)$, and $R(0)$.

When we formulate a model, we need to be concerned with the units of the quantities involved. Units are also helpful when we estimate parameters from data. The units of both sides of the above equations must be the same. All derivatives have units number of people per unit of time (why?). Hence, each term on the right-hand side should have the same units. From the first equation, we see that since I and S have units number of people, the units of β must be 1/[number of people$\times$unit of time]. Since $\beta = pc$ and p is a probability, which has no units, the units of c must be 1/[number of people$\times$unit of time]. Thus the contact rate cN has units 1/unit of time. Similarly, from the second equation, we see that the units of α are 1/unit of time, so the term αI has units number of people/unit of time.

Loosely speaking, a differential equation model such as the model (2.1) is *well posed* if through every point (initial condition), there exists a unique solution. Differential equation models must be well posed to be mathematically acceptable and biologically significant. Because the dependent variables in the model denote physical quantities, for most models in biology and epidemiology, we also require that solutions that start from positive (nonnegative) initial conditions remain positive (nonnegative) for all time.

We denote by N the total population size at time zero $N = S(0) + I(0) + R(0)$. Adding all three equations in system (2.1), we obtain $N'(t) = S'(t) + I'(t) + R'(t) = 0$. Hence, $N(t)$ is constant and equal to its initial value, $N(t) = N$. This model is called the SIR model or SIR system. It is a special type of model called a *compartmental model*, because each letter refers to a "compartment" in which an individual can reside. Each individual can reside in exactly one compartment and can move from one compartment to another. Compartmental models are schematically described by a diagram often called a *flowchart*. Each compartment in a flowchart is represented by a box indexed by the name of the class. Arrows indicate the direction of movement of individuals between the classes. The movement arrows are typically labeled by the transition rates (see Fig. 2.1).

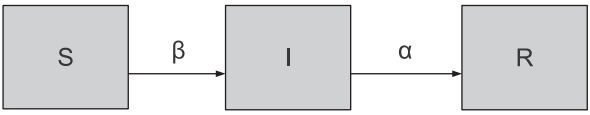

Fig. 2.1 Flowchart of the Kermack–McKendrick SIR epidemic model

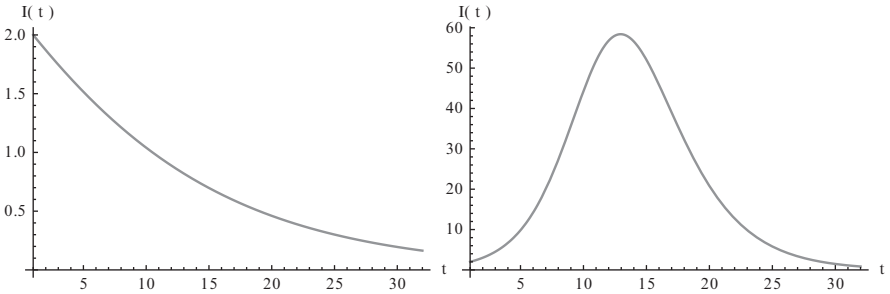

Fig. 2.2 *Left:* shows the prevalence monotonically decreasing. *Right:* shows the prevalence first increasing and then decreasing to zero

2.1.2 Mathematical Properties of the SIR Model

The Kermack–McKendrick epidemic model (2.1) has very distinctive dynamics. Because $S' < 0$ for all t, the number of susceptible individuals is always declining, independently of the initial condition $S(0)$. Since $S(t)$ is monotone and positive, we have

$$\lim_{t\to\infty} S(t) = S_\infty.$$

The number of recovered individuals also has monotone behavior, independently of the initial conditions. Since $R' > 0$ for all t, the number of recovered individuals is always increasing. Since the number of recovered is monotone and bounded by N, we have

$$\lim_{t\to\infty} R(t) = R_\infty.$$

On the other hand, the number of infected individuals may be monotonically decreasing to zero, or may have nonmonotone behavior by first increasing to some maximum level, and then decreasing to zero (see Fig. 2.2). The prevalence first starts increasing if $I'(0) = (\beta S(0) - \alpha)I(0) > 0$. Hence, a necessary and sufficient condition for an initial increase in the number of infecteds is $\beta S(0) - \alpha > 0$, or

$$\frac{\beta S(0)}{\alpha} > 1.$$

This sudden increase in the prevalence and then a decline to zero is a classical model of an **epidemic** or **outbreak**. Threshold conditions for an epidemic to occur are

common in epidemiology, and we will discuss them in detail later on. To determine the limits S_∞ and R_∞, we divide the equation for S and the equation for R. Hence,

$$\frac{dS}{dR} = -\frac{\beta}{\alpha}S.$$

Solving, we have

$$S = S(0)e^{-\frac{\beta}{\alpha}R} \geq S(0)e^{-\frac{\beta}{\alpha}N} > 0.$$

We conclude that $S_\infty > 0$. The quantity S_∞ is called the **final size of the epidemic**. We see that the epidemic does not end, because *all* susceptible individuals have been infected and are now immune. Some individuals always escape a disease—an observation that was made in practice is also confirmed by the SIR model.

Finally, we show that the epidemic dies out. If

$$\lim_{t\to\infty} I(t) = I_\infty,$$

then $I_\infty = 0$. This is evident from the plots in Fig. 2.2, but a mathematical argument can establish the result for all parameters. To see this, we integrate the first equation in (2.1):

$$\begin{aligned}
\int_0^\infty S'(t)dt &= -\beta\int_0^\infty S(t)I(t)dt,\\
S_\infty - S_0 &= -\beta\int_0^\infty S(t)I(t)dt,\\
S_0 - S_\infty &= \beta\int_0^\infty S(t)I(t)dt,\\
S_0 - S_\infty &\geq \beta S_\infty\int_0^\infty I(t)dt. \qquad (2.2)
\end{aligned}$$

The last inequality implies that $I(t)$ is integrable on $[0,\infty)$. Hence, $\lim_{t\to\infty} I(t) = 0$.

The Kermack–McKendrick model is based on several assumptions: (1) There are no births and deaths in the population. (2) The population is **closed**, that is, no one from the outside enters the population, and no one leaves the population, and finally, (3) All recovered individuals have complete immunity and cannot be infected again. These assumptions seem very restrictive, but within limits, they can be satisfied. We will see a specific example in Sect. 2.3. Diseases that lead to permanent immunity and are well modeled by the SIR epidemic model are most diseases typical of childhood years, often called **childhood diseases**. These include chickenpox, smallpox, rubella, and mumps.

To solve the system, we first notice that the variable R does not participate in the first two equations. Thus we can consider only the equations for S and I, which are coupled, and leave out the equation for R. The variable R can then be obtained in this model from the relation $R = N - S - I$:

$$\begin{aligned} S'(t) &= -\beta IS, \\ I'(t) &= \beta IS - \alpha I. \end{aligned} \tag{2.3}$$

Dividing the two equations, we obtain

$$\frac{I'}{S'} = \frac{\beta SI - \alpha I}{-\beta SI} = -1 + \frac{\alpha}{\beta S}.$$

Separating the variables, we have

$$I' = \left(-1 + \frac{\alpha}{\beta S}\right) S'.$$

Integrating leads to

$$I = -S + \frac{\alpha}{\beta} \ln S + C,$$

where C is an arbitrary constant. Thus, the orbits of the solution are given implicitly by the equation

$$I + S - \frac{\alpha}{\beta} \ln S = C. \tag{2.4}$$

The Kermack–McKendrick model is equipped with initial conditions: $S_0 = S(0)$ and $I_0 = I(0)$. Those are given. We also have that $\lim_{t\to\infty} I(t) = 0$, while $S_\infty = \lim_{t\to\infty} S(t)$ gives the final number of susceptible individuals after the epidemic is over. The above equality holds both for (S_0, I_0) and for $(S_\infty, 0)$. Thus,

$$I_0 + S_0 - \frac{\alpha}{\beta} \ln S_0 = C.$$

Consequently,

$$I_0 + S_0 - \frac{\alpha}{\beta} \ln S_0 = S_\infty - \frac{\alpha}{\beta} \ln S_\infty.$$

Rearranging terms, we get

$$I_0 + S_0 - S_\infty = \frac{\alpha}{\beta} (\ln S_0 - \ln S_\infty).$$

Therefore,

$$\frac{\beta}{\alpha} = \frac{\ln \frac{S_0}{S_\infty}}{S_0 + I_0 - S_\infty}. \tag{2.5}$$

We note that since $S(t)$ is a decreasing function, we have $S_\infty < S_0 + I_0$. The implicit solution also allows us to compute the maximum number of infected individuals that is attained. This number occurs when $I' = 0$, that is, when

$$S = \frac{\alpha}{\beta}.$$

From

$$I + S - \frac{\alpha}{\beta} \ln S = I_0 + S_0 - \frac{\alpha}{\beta} \ln S_0,$$

substituting the expression for S and moving all terms but I to the right-hand side leads to

$$I_{\max} = -\frac{\alpha}{\beta} + \frac{\alpha}{\beta} \ln \frac{\alpha}{\beta} + S_0 + I_0 - \frac{\alpha}{\beta} \ln S_0. \tag{2.6}$$

Here $I_{\max}$ is the maximum number of infected individuals reached in the epidemic. It signifies the maximum severity of the epidemic. If we are able to estimate $I_{\max}$ for a newly occurring infectious disease, we will know when the number of infections will begin to decline.

2.2 The Kermack–McKendrick Model: Estimating Parameters from Data

When we are given specific disease and time series data for it, we can estimate the parameters of the SIR model and compare the solution of the model with the data. This section follows the description in [27]. See [27] for a different example.

2.2.1 Estimating the Recovery Rate

For many diseases, information about the mean duration of the exposed period or the infectious period can easily be obtained. For instance, for influenza, the duration of the infectious period is 3–7 days with mean 4–5 days. How can that help us estimate the recovery rate α? To approach that question, let us assume that there is no inflow in the infectious class and a certain number of individuals I_0 have been put in the infectious class at time zero. Then the differential equation that gives the dynamics of this class is given by

$$I'(t) = -\alpha I, \qquad I(0) = I_0.$$

This equation can be easily solved. Therefore, the number of people in the infectious class at time t is given by

$$I(t) = I_0 e^{-\alpha t}.$$

Consequently,

$$\frac{I(t)}{I_0} = e^{-\alpha t}$$

for $t \geq 0$ gives the proportion of people who are still infectious at time t, or in probability language, it gives the probability of being still infectious at time t. We can compute the fraction of individuals who have left the infectious class,

$$1 - e^{-\alpha t},$$

or in probability terms,

$$F(t) = 1 - e^{-\alpha t} \qquad t \geq 0$$

is the probability of recovering/leaving the infectious class in the interval $[0,t)$. Clearly, $F(t)$ is a probability distribution (if defined as zero for $t < 0$). The probability density function is $f(t) = dF/dt$. Consequently,

$$f(t) = \alpha e^{-\alpha t}.$$

Note: $f(t) = 0$ for $t < 0$. Furthermore, the average time spent in the infectious class is given by the mean (expected value of a random variable X, denoting time to exiting the infectious class),

$$E[X] = \int_{-\infty}^{\infty} t f(t) dt.$$

Therefore, computing that integral yields

$$\int_{-\infty}^{\infty} t f(t) dt = \int_{-\infty}^{\infty} t \alpha e^{-\alpha t} dt = \frac{1}{\alpha}.$$

Thus we conclude that

mean time spent in the infectious class = $\frac{1}{\alpha}$.

For influenza, we are sick with it for 3–7 days. Say that the mean time spent as infectious is 5 days. Thus the recovery rate, measured in units of $[\text{days}]^{-1}$, is 1/5.

Estimating the transmission rate β is quite a bit more difficult. Estimating β is possible for the Kermack–McKendrick model, because that model is relatively simple. In particular, we can obtain an implicit solution. An implicit solution is rarely obtainable for epidemic models, and estimating parameters for epidemic models requires techniques different from the one presented below. We will discuss these techniques in Chap. 6.

2.2.2 The SIR Model and Influenza at an English Boarding School 1978

In January and February 1978, an epidemic of influenza occurred in a boarding school in the north of England. The boarding school housed a total of 763 boys, all of whom were at risk during the epidemic. The spring term began on January 10. The boys returned from their Christmas vacation spent at many different locations in the world. A boy returning from Hong Kong exhibited elevated temperature during the period 15–18 January. On January 22, three boys were sick. Table 2.1 gives the number of boys ill on the nth day beginning January 22 ($n = 1$).

Table 2.1 Daily number of influenza-infected boys

Day	No. infected[a]	Day	No. infected
3	25	9	192
4	75	10	126
5	227	11	71
6	296	12	28
7	258	13	11
8	236	14	7

[a]Data taken from "Influenza in a Boarding School," *British Medical Journal*, 4 March 1978

The number of boys who escaped influenza was 19. The average time spent sick was 5–6 days. However, since boys were isolated in the infirmary, they spent perhaps about 2 days as infectious. A swab taken from some of the boys revealed that they were infected with H1N1 influenza A virus. The staff of the boarding school remained healthy, with only one staff member displaying symptoms of illness.

These data give the following values: $S_3 = 738$, $I_3 = 25$, $S_\infty = 19$.

From the computations above, we have

$$\frac{\beta}{\alpha} = \frac{\ln \frac{S_3}{S_\infty}}{S_3 + I_3 - S_\infty} = \frac{\ln \frac{738}{19}}{763 - 19} = 0.00491869. \tag{2.7}$$

We measure time in days. We take $t_0 = 0$ to be January 21. The first datum is given on January 22, which gives $t = 1$. We have that $t_{\text{end}} = 14$ is the February 4, 1978.

We take the infective period to be 2.1 days. This value can be obtained as the best fit as values around 2 days are tried with the procedure below. After we fix the duration of the infectious period, we compute α as the reciprocal of the time spent as an infectious individual (infectious period):

$$\alpha = \frac{1}{2.1} = 0.476.$$

From Eq. (2.7) and using the value for α, we can obtain the value for β:

$$\beta = 0.004918\alpha = 0.004918 * 0.476 = 0.002342.$$

From Eq. (2.6) for the $I_{\max}$, we can estimate the maximum number of infectives during the epidemic. First, notice that $\alpha/\beta = 203.306$. Thus,

$$I_{\max} = -203.306 + 203.306 \ln 203.306 + 738 + 25 - 203.306 \ln 738 = 298.$$

Notice that the data give the maximum number of infective individuals as 296. We illustrate the fit between the model and the data in Fig. 2.3.

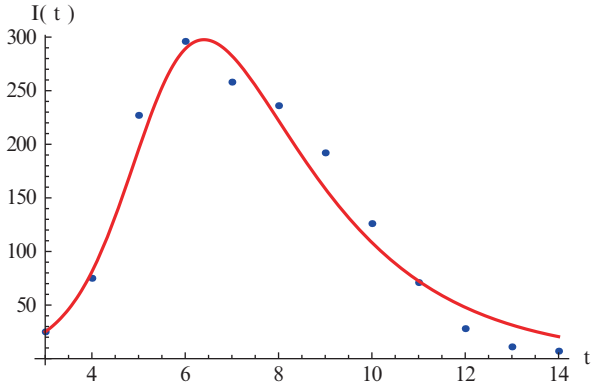

Fig. 2.3 English boarding school influenza epidemic: agreement between Kermack–McKendrick SIR epidemic model and data

2.3 A Simple SIS Epidemic Model

We want to relax the assumption for permanent immunity after recovery to model diseases that can infect us repeatedly, such as influenza. We may assume in the simplest scenario that individuals who recover become immediately susceptible again. Thus, individuals who are susceptible may become infected (and infectious) and then recover into being susceptible again. The model is described with the flowchart in Fig. 2.4.

The model takes the form

$$\begin{aligned} S'(t) &= -\beta IS + \alpha I, \\ I'(t) &= \beta IS - \alpha I. \end{aligned} \tag{2.8}$$

System (2.8) is called an SIS epidemic model and is perhaps the simplest model in mathematical epidemiology. Here, if $N = S + I$ and we add the two equations, we

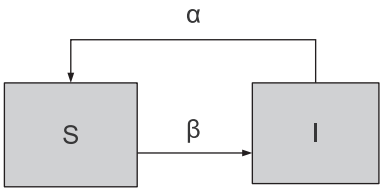

Fig. 2.4 Flowchart of a simple SIS epidemic model

again obtain $N' = 0$. Hence the total population size is N, where N is a constant in time. The system is equipped with initial conditions $S(0)$ and $I(0)$, so that $N = S(0) + I(0)$.

2.3.1 Reducing the SIS Model to a Logistic Equation

Because the total population size is constant and known, the system (2.8) can be reduced to a single equation. This technique is commonly used for the reduction of the dimension of an epidemiological model. We express S as $S = N - I$ and substitute it in the second equation. The resulting equation is a variant of the **logistic equation**:

$$I'(t) = \beta I(N - I) - \alpha I. \tag{2.9}$$

We rewrite this equation in the form of a logistic equation,

$$I'(t) = rI\left(1 - \frac{I}{K}\right),$$

where $r = \beta N - \alpha$ and $K = r/\beta$. To see this, first factor out I and then $r = \beta N - \alpha$. The logistic equation is one of the classical models in population dynamics. It typically models the total population size of a population of individuals. We will use it later on for models in which the total population size does not remain constant. The parameter r is often referred to as the *growth rate*. We can see that r can be positive or negative, so we consider two cases.

$r < 0$ If the growth rate is negative, $r < 0$, then the number of infected individuals $I(t)$ tends to 0 as $t \to \infty$. To see this, notice that if $r < 0$, then $K < 0$. Hence,

$$I'(t) \leq rI(t).$$

The solutions of this simple differential inequality are $I(t) = I(0)e^{rt}$, and they approach zero for $r < 0$. This implies that if $r < 0$, the disease gradually disappears from the population on its own.

$r > 0$ The logistic equation can be solved, and in this case, we need to solve it to have an explicit expression for $I(t)$. The logistic equation is a differential equation of separable type. It is solved by a method called *separation of*

variables. To separate the variables I and t, we move all terms that contain I to the left-hand side of the equation, and all terms that contain t, namely dt, to the right-hand side:

$$\frac{1}{I\left(1-\frac{I}{K}\right)}dt = rdt.$$

Notice that while dividing by $\left(1-\frac{I}{K}\right)$, we have assumed that $I(t) \neq K$. But $I(t) = K$ is a solution of the original logistic equation. On the other hand, $I = K$ is not a solution of the derived equation above, so it will have to be artificially added to the solution set.
Using partial fraction decomposition, we can integrate both sides of that equation:

$$\int \left(\frac{1}{I} + \frac{1}{K-I}\right) dI = r \int 1 dt.$$

Hence,

$$\ln \frac{I}{|K-I|} = rt + C,$$

where C is an arbitrary constant of integration, and the absolute value in the logarithm is necessary, since we can compute logarithms only of positive values, but we do not know whether $K-I$ is positive. To determine C, we use the initial conditions. Assuming that the initial conditions are given at 0, we have

$$\ln \frac{I(0)}{|K-I(0)|} = C.$$

Replacing C with the above expression, we obtain

$$\ln \frac{I}{|K-I|} - \ln \frac{I(0)}{|K-I(0)|} = rt.$$

Hence,

$$\ln \frac{I|K-I(0)|}{I(0)|K-I|} = rt.$$

The absolute values above can be disregarded, since $K-I(0)$ and $K-I$ have the same sign: they are both positive or both negative. Taking an exponent, we obtain

$$\frac{I}{K-I} = \frac{I(0)}{K-I(0)} e^{rt}.$$

Finally, we solve for I to obtain an explicit solution for $I(t)$ in terms of the initial conditions, r and K:

$$I(t) = \frac{KBe^{rt}}{1+Be^{rt}},$$

where $B = I(0)/(K - I(0))$. We see from this that

$$\lim_{t\to\infty} I(t) = K,$$

and the disease remains in the population indefinitely.

The threshold condition $r > 0$ can be rewritten as $\mathscr{R}_0 > 1$, where

$$\mathscr{R}_0 = \frac{\beta N}{\alpha}$$

is called *basic reproduction number* of the disease. Mathematically, the reproduction number plays the role of a threshold value for the dynamics of the system and the disease. If $\mathscr{R}_0 > 1$, the disease remains in the population, and the number of infecteds stabilizes around K. In this case, we say that the disease has become **endemic** in the population. This implies that the simple SIS model is a model of endemic disease. If $\mathscr{R}_0 < 1$, the number of infecteds gradually declines to zero, and the disease disappears from the population.

Epidemiologically, the reproduction number gives the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individuals.

To see this interpretation in the formula for $\mathscr{R}_0$, notice that the number of new cases per unit of time produced by all infectious individuals is given by the incidence βSI. If there is only one infectious individual, we have $I = 1$, and the number of secondary cases produced by one infectious individual will be βS. If the entire population consists of susceptible individuals, we have $S = N$. Hence, the number of secondary cases one infectious individuals will produce in a unit of time is βN. Since one infectious individual remains infectious for $1/\alpha$ time units, the number of secondary cases it will produce during its lifespan is $\mathscr{R}_0 = \beta N/\alpha$.

2.3.2 *Qualitative Analysis of the Logistic Equation*

The information we derived about the behavior of the solutions was obtained from the explicit solution. Many single-equation models in biology cannot be solved explicitly. We need tools to deduce the properties of the solutions directly from the differential equation. These tools can readily be extended to systems of equations.

From the explicit solution of the logistic equation, we saw that in the long run, the disease will become endemic and persist in the population if $\mathscr{R}_0 > 1$. We also learned that in the long run, the number of infected individuals in the population will be approximately $K = (\beta N - \alpha)/\beta$. Furthermore, if $\mathscr{R}_0 < 1$, the disease will die out. Ideally, we would like to be able to obtain such results without having to solve the equation explicitly.

A nonlinear differential equation model with constant coefficients typically has time-independent solutions, that is, solutions that are constant in time. Such solutions are called **equilibrium points**. Equilibrium points play an important role in the long-term behavior of the solutions. They are easy to find from the differential equation even if we don't know the explicit solution, since their derivative with respect to time is zero. Thus, for the equation $\frac{dI}{dt} = f(I)$, the equilibria are the solutions of the equation $f(I) = 0$. We set the right-hand side of Eq. (2.9) equal to zero:

$$\beta I(N-I) - \alpha I = 0.$$

This equation has two solutions, $I_1^* = 0$ and $I_2^* = K$, which give the two equilibrium points. The equilibrium I_1^* always exists. In the mathematical epidemiology literature, the equilibrium I_1^* is referred to as a **disease-free equilibrium**, since the disease is not present in the population, and the entire population is susceptible. The equilibrium I_2^* exists only if $\mathscr{R}_0 > 1$. The equilibrium I_2^* is called an **endemic equilibrium**, since the disease is present in the population.

In the case $\mathscr{R}_0 > 1$, both $I_1(t) = 0$ and $I_2(t) = K$ are solutions to Eq. (2.9). Since the model is well posed, no other solution can cross them. So solutions that start in the interval $(0,K)$ stay in that interval for all time:

$$0 < I(0) < K \Longrightarrow 0 < I(t) < K.$$

Furthermore, solutions that start from a value above K stay above K:

$$I(0) > K \Longrightarrow I(t) > K.$$

If $0 < I(t) < K$, then $f(I) > 0$, which means that $\frac{dI}{dt} > 0$. This means that the solutions in that interval are increasing functions of time. Since $I(t)$ is increasing and bounded, it follows that $I(t)$ converges to a finite limit as $t \to \infty$. To deduce the behavior of the derivative, we use the following corollary.

Corollary 2.1 (Thieme [151]). *Assume that $f(t)$ converges as $t \to \infty$. Assume also that $f'(t)$ is uniformly continuous. Then $f'(t) \to 0$ as $t \to \infty$.*

It can be shown (see (2.10) below) that the second derivative $\frac{d^2I}{dt^2}$ is continuous and bounded. Hence, the corollary above implies that $I'(t) \to 0$ and the limit of $I(t)$, say L, satisfies the equilibrium equation $f(L) = 0$. This implies that $L = 0$ or $L = K$. Since $I(t)$ is positive and increasing, we have $I(t) \to K$ as $t \to \infty$. If $I(0) > K$, then $I(t) > K$ for all t. Thus, $\frac{dI}{dt} < 0$, and $I(t)$ is decreasing and bounded below by K. Similar reasoning as above implies that $I(t) \to K$.

We can further investigate the concavity of the solutions by looking at the second derivative:

$$\frac{d^2I}{dt^2} = r\left(1 - \frac{2I}{K}\right)\frac{dI}{dt} = r^2\left(1 - \frac{2I}{K}\right)I\left(1 - \frac{I}{K}\right). \tag{2.10}$$

For solutions in the interval $0 < I(t) < K$, the second derivative changes sign when $I(t)$ crosses the horizontal line $y = \frac{K}{2}$. Thus, for values of t such that $I(t) < \frac{K}{2}$, the

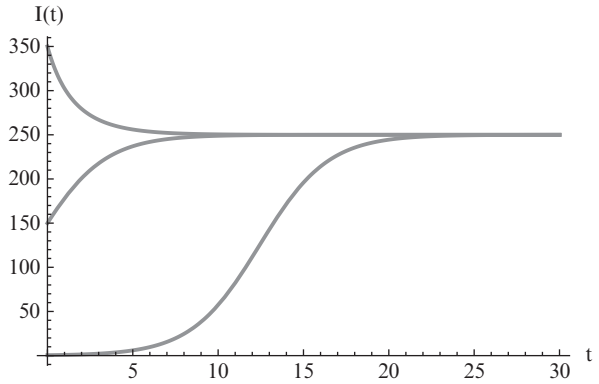

Fig. 2.5 Solutions to the logistic equation (2.9) converge to the endemic equilibrium

second derivative of I is positive, and $I(t)$ is concave up. For values of t for which $I(t) > \frac{K}{2}$, the second derivative of I is negative, and $I(t)$ is concave down. This is illustrated in Fig. 2.5. For solutions for which $I(t) > K$, the second derivative $\frac{d^2I}{dt^2}$ is positive. Consequently, $I(t)$ is decreasing and concave up.

2.3.3 General Techniques for Local Analysis of Single-Equation Models

We saw that if $\mathscr{R}_0 < 1$, then all solutions of Eq. (2.9) approach the unique equilibrium $I^* = 0$. That is, *all* solutions converge to zero, $I(t) \to 0$, for *every* initial condition $I(0) > 0$. In this case, we say that the disease-free equilibrium is **globally stable**. In the case $\mathscr{R}_0 > 1$, there are two equilibria: the disease-free $I_1^* = 0$ and the endemic equilibrium $I_2^* = K$. We see that all solutions that start from $I(0) > 0$ move away from the disease-free equilibrium. Hence, the disease-free equilibrium in this case is **unstable**. At the same time, all solutions that start from $I(0) > 0$ approach the endemic equilibrium $I_2^* = K$. In this case, we call the endemic equilibrium **globally stable**.

For many models, even models given by a single equation, we may not be able to solve the equation(s) explicitly or perform detailed analysis of the behavior of the solutions. In addition, if there are multiple endemic equilibria, there may not be a globally stable equilibrium. In these cases, the concept of a locally stable equilibrium is an applicable and useful tool. Loosely speaking, an equilibrium is locally asymptotically stable if solutions that *start close* to the equilibrium approach that equilibrium as $t \to \infty$. Stability of a nonlinear system can often be inferred from the stability of a corresponding linear system obtained through the process of **linearization**. For a general differential equation

$$x'(t) = f(x), \tag{2.11}$$

x^* is an equilibrium if and only if $f(x^*) = 0$. The idea of the linearization is to shift the equilibrium to zero. Thus, we denote by $u(t) = x(t) - x^*$ the perturbation that gives the deviation of a solution of (2.11) from an equilibrium. Solutions of (2.11) starting from a neighborhood of x^* approach x^* if $u(t)$ approaches zero. The perturbation $u(t)$ is assumed small. Notice that $u(t)$ can be positive or negative, even if $x(t) > 0$. We have $x(t) = u(t) + x^*$. We replace $x(t)$ with its equal in the differential equation and expand f around x^* in a Taylor series, assuming that f is sufficiently differentiable:

$$u'(t) = f(x^*) + f'(x^*)u(t) + \frac{f''(\xi)}{2!}(u(t))^2,$$

where ξ is between x^* and $x^* + u(t)$. Assuming that f has two continuous derivatives, the second derivative f'' is bounded, and the last term in the expansion with $(u(t))^2$ is small and can be neglected. Since x^* is an equilibrium, we also have $f(x^*) = 0$. Thus, the equation for the perturbations becomes

$$u'(t) = f'(x^*)u(t). \tag{2.12}$$

This is the linearized equation of the nonlinear equation (2.11). This equation is linear in the dependent variable $u(t)$. The quantity $f'(x^*)$ is a given known constant. If we define $\lambda = f'(x^*)$ then the linearized equation becomes

$$u'(t) = \lambda u(t),$$

whose solution is $u(t) = u(0)e^{\lambda t}$. These solutions approach ∞ or $-\infty$ exponentially, depending on $u(0)$, if $\lambda > 0$ and approach zero if $\lambda < 0$. Thus, if $\lambda < 0$, then $u(t) \to 0$. Hence, $x(t) - x^* \to 0$ or $x(t) \to x^*$ as $t \to \infty$. We conclude that solutions of (2.11) that start from an initial condition that is sufficiently close to the equilibrium converge to this equilibrium if $\lambda < 0$. In this case, the equilibrium x^* is called **locally asymptotically stable**. If $\lambda > 0$, then $|u(t)| \to \infty$, and $x(t)$ moves away from the equilibrium x^*. In this case, the equilibrium x^* is called **unstable**. We summarize this result in the following theorem.

Theorem 2.1. *An equilibrium x^* of the differential equation $x'(t) = f(x)$ is locally asymptotically stable if $f'(x^*) < 0$ and is unstable if $f'(x^*) > 0$.*

This theorem does not tell us anything about the stability of the equilibrium x^* if $f'(x^*) = 0$. An equilibrium for which $f'(x^*) \neq 0$ is called **hyperbolic**. If $f'(x^*) = 0$, the equilibrium is called **nonhyperbolic**.

We apply Theorem 2.1 to the logistic version of Eq. (2.9). If $\mathscr{R}_0 < 1$, we found only one equilibrium $I_1^* = 0$. If $\mathscr{R}_0 > 1$, we found two equilibria: $I_1^* = 0$ and $I_2^* = K$. We compute the derivative of $f(I)$,

$$f'(I^*) = r\left(1 - \frac{I^*}{K}\right) - \frac{r}{K}I^*,$$

and its value of each equilibrium,

$$f'(0) = r \qquad\qquad f'(K) = -r.$$

We conclude that if $\mathscr{R}_0 < 1$, the disease-free equilibrium is locally asymptotically stable. If $\mathscr{R}_0 > 1$, the disease-free equilibrium is unstable, while the endemic equilibrium is locally asymptotically stable.

The problem of determining equilibria and their stability has a very elegant graphical solution. For the equation $x' = f(x)$, if we plot the function $f(x)$ as a function of x, then the places where $f(x)$ intersects the x-axis give the equilibria. The stability of each equilibrium can then be read off the graph from the slope of the graph as it passes through the equilibrium. If the slope of the tangent line to the graph at the point of the equilibrium is positive, then that equilibrium is unstable; if the slope of the tangent is negative, then that equilibrium is locally stable. If the slope of the tangent to the graph at the equilibrium is zero, then the stability of that equilibrium cannot be inferred from the graph. To illustrate this concept, consider the equation $x' = f(x)$, where $f(x)$ is plotted in Fig. 2.6. The equilibria and their stability are explained in the figure caption.

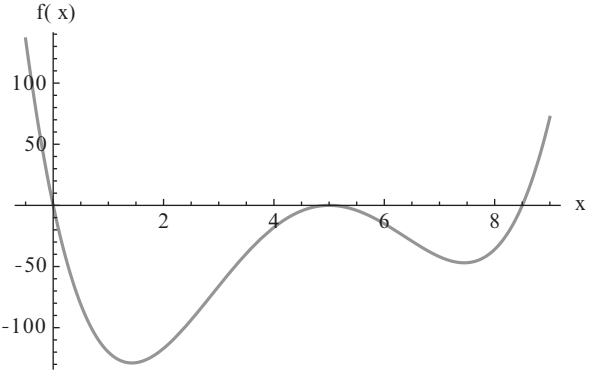

Fig. 2.6 Graph of the function $f(x)$. Figure shows that equilibria are $x_1^* = 0$, $x_2^* = 5$, and $x_3^* = 8.5$. The equilibrium x_1^* is locally stable because the slope of the tangent to x_1^* is negative. The slope of the tangent to x_2^* is zero, so its stability cannot be determined from the graph. Equilibrium x_3^* is unstable, since the slope of the tangent to x_3^* is positive

2.4 An SIS Epidemic Model with Saturating Treatment

We illustrate the concepts of the previous section on an SIS model with saturating treatment/recovery rate. Suppose that in model (2.8), the per capita recovery rate α depends on treatment. In this case, we may assume that treatment resources are

limited and the per capita treatment rate α is not constant, but is decreasing with the number of infected individuals. A reasonably simple form of such a function would be

$$\alpha(I) = \frac{\alpha}{1+I},$$

where the constant α is the treatment/recovery rate when there are few infectives. We use this function in model (2.8) to obtain the following SIS model with saturating treatment:

$$\begin{aligned} S'(t) &= -\beta IS + \frac{\alpha I}{1+I}, \\ I'(t) &= \beta IS - \frac{\alpha I}{1+I}. \end{aligned} \tag{2.13}$$

System (2.13) is called an SIS epidemic model with saturating treatment. Here, if $N = S+I$ and we add the two equations, we again obtain $N' = 0$. Hence the total population size is N, where N is a constant in time. The system is equipped with initial conditions $S(0)$ and $I(0)$, so that $N = S(0)+I(0)$.

2.4.1 Reducing the SIS Model with Saturating Treatment to a Single Equation

Since the total population size in model (2.13) is a given constant, we may write $S(t) = N - I(t)$ and substitute it in the second equation of system (2.13). Therefore, we obtain a single equation in the number of infected individuals:

$$I'(t) = \beta I(N-I) - \frac{\alpha I}{1+I}. \tag{2.14}$$

In principle, Eq. (2.14) is a separable equation and can be solved. However, to illustrate common methodologies, we will try to investigate the properties of this equation without solving it. First, we look for the equilibria. We denote by $f(I)$ the right-hand side:

$$f(I) = \beta I(N-I) - \frac{\alpha I}{1+I}.$$

To find the equilibria, we set $f(I) = 0$. Clearly, $I_1^* = 0$ is an equilibrium. This gives the disease-free equilibrium of the equation. To look for endemic equilibria, we cancel one I and we rewrite the equation $f(I) = 0$ as an equality of two functions:

$$\beta(N-I) = \frac{\alpha}{1+I}.$$

This equation can be rewritten as a quadratic equation, which can have zero, one, or two positive roots. We will investigate graphically the options and the conditions

for each to occur. We rewrite the above equation as

$$(N-I)(1+I) = \frac{\alpha}{\beta}. \tag{2.15}$$

Let $g(I) = (N-I)(1+I)$. Then $g(I)$ is a parabola that opens downward. Clearly, $g(0) = N$. The right-hand side of the above equation is $y = \dfrac{\alpha}{\beta}$ and can be graphed as a horizontal line.

- If $g(0) = N > \dfrac{\alpha}{\beta}$, then Eq. (2.15) always has a unique positive solution I_2^*. Then the system (2.13) has one endemic equilibrium. We define the reproduction number of the system as

  $$\mathscr{R}_0 = \frac{\beta N}{\alpha}.$$

  Hence, if $\mathscr{R}_0 > 1$, there is a unique endemic equilibrium. We illustrate this situation in Fig. 2.7.

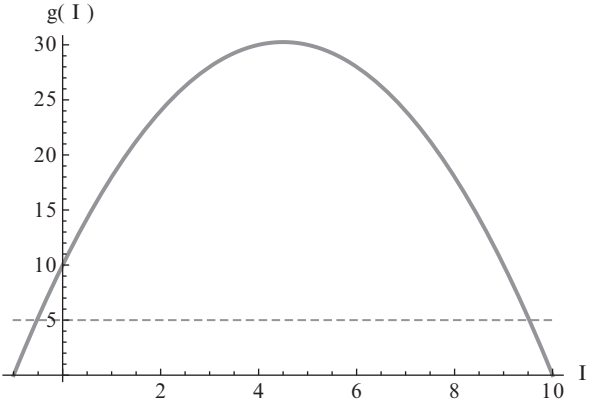

Fig. 2.7 Graph of the function $g(I)$ and the horizontal line $y = \dfrac{\alpha}{\beta}$. The figure shows the existence of a unique intersection for positive I, giving a unique positive equilibrium

- If $g(0) = N < \dfrac{\alpha}{\beta}$, then Eq. (2.15) has either two or zero solutions. In this case,

  $$\mathscr{R}_0 < 1.$$

  To specify additional conditions so that Eq. (2.15) has two positive solutions, we must notice that we need two things to happen:
  (1) The maximum of the parabola must be to the right of the y-axis. The parabola intersects the x-axis at the points N and -1. Hence, its maximum occurs at their average,

  $$I_m = \frac{N-1}{2} > 0.$$

This poses the requirement that $N > 1$. (2) The line $y = \dfrac{\alpha}{\beta}$ must lie below the maximum of the parabola. That is, we must have

$$(N - I_m)(1 + I_m) > \frac{\alpha}{\beta}. \tag{2.16}$$

Therefore, if $\mathscr{R}_0 < 1$, $N > 1$, and condition (2.16) are satisfied, then the system (2.13) has two endemic equilibria I_{11}^* and I_{12}^*; otherwise, it has no endemic equilibria. We illustrate these two situations in Fig. 2.8.

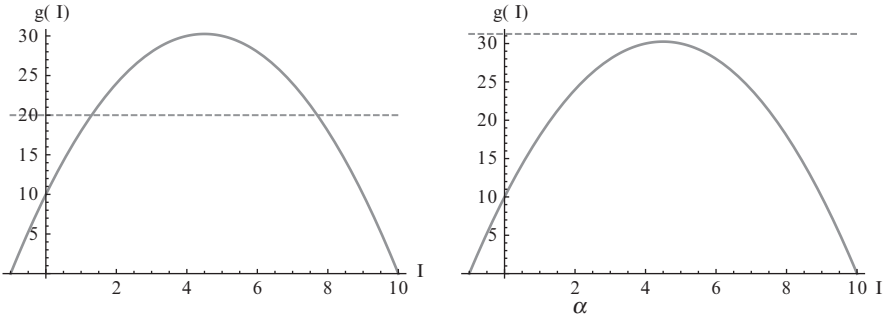

Fig. 2.8 Graph of the function $g(I)$ and the horizontal line $y = \dfrac{\alpha}{\beta}$. *Left:* the existence of two intersections for positive I, giving two positive equilibria. *Right:* no intersections of the function $g(I)$ and the horizontal line $y = \dfrac{\alpha}{\beta}$. Thus, there are no positive equilibria

2.4.2 Bistability

To decide the stability of equilibria, we have to derive the sign of $f'(I^*)$ for each equilibrium I^*. That may not be an easy task to do analytically. Fortunately, the stability of the equilibria can be read off the graph of the function $f(I)$ for each of the three cases above. If $\mathscr{R}_0 < 1$ and there are no nontrivial equilibria, then all solutions of Eq. (2.15) are attracted by the disease-free equilibrium. So the disease-free equilibrium is globally stable in this case. For each of the other two cases, we graph the function $f(I)$ in Fig. 2.9. Looking at Fig. 2.9, we see that in the case $\mathscr{R}_0 > 1$ (left figure), we have $f'(0) > 0$. Hence, the disease-free equilibrium is unstable. Furthermore, $f'(I_2^*) < 0$. Hence, the endemic equilibrium is locally stable. We can argue, as we did in the case of the logistic equation, that the equilibrium is globally stable. In the case $\mathscr{R}_0 < 1$, there are three equilibria: $I_1^* = 0$, $I_{11}^* < I_{12}^*$. For solutions $I(t)$ that start from $I(0) = I_0$ satisfying $0 < I_0 < I_{11}^*$, we have $0 < I(t) < I_{11}^*$ for all t. Furthermore, $f(I) < 0$ for such solutions (the graph of $f(I)$ is below the x-axis), so that $\frac{dI}{dt} < 0$. Hence, $I(t)$ is decreasing and $\lim_{t\to\infty} I(t) = 0$. For solutions $I(t)$ that start from $I(0) = I_0$ satisfying $I_{11}^* < I_0 < I_{12}^*$, we have $I_{11}^* < I(t) < I_{12}^*$ for all t.

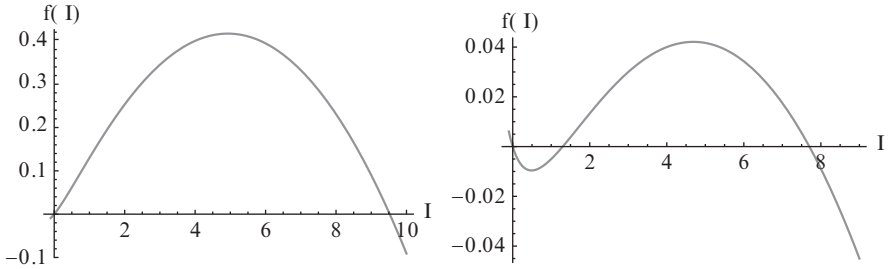

Fig. 2.9 Graph of the function $f(I)$. *Left:* the case $\mathscr{R}_0 > 1$ and the existence of two intersections for nonnegative I, giving two nonnegative equilibria. *Right:* the case $\mathscr{R}_0 < 1$ and three intersections of the function $f(I)$ and the x-axis, giving three nonnegative equilibria. Stabilities explained in text

Furthermore, $f(I) > 0$ for such solutions (the graph of $f(I)$ is above the x-axis), so that $\frac{dI}{dt} > 0$. Hence, $I(t)$ is increasing and $\lim_{t\to\infty} I(t) = I^*_{12}$. For solutions $I(t)$ that start from $I(0) = I_0$ satisfying $I^*_{12} < I_0$, we have $I^*_{12} < I(t)$ for all t. Furthermore, $f(I) < 0$ for such solutions (the graph of $f(I)$ is below the x-axis), so that $\frac{dI}{dt} < 0$. Hence, $I(t)$ is decreasing and $\lim_{t\to\infty} I(t) = I^*_{12}$. We notice that depending on the initial conditions, we have solutions that converge to the disease-free equilibrium and solutions that converge to the endemic equilibrium. Such a situation is called **bistability**. In this case, there is no globally stable equilibrium. The region $0 < I_0 < I^*_{11}$ is called a *domain of attraction* of the disease-free equilibrium. The region $I^*_{11} < I_0$ is called a *domain of attraction* of the endemic equilibrium.

Problems

2.1. Show that the model (2.1) is well posed.

2.2. Use a computer algebra system to graph the solutions (2.4).

2.3. The simplest model of malaria assumes that the mosquito population is at equilibrium and models the proportion of the infected humans I with the following equation:

$$I' = \frac{\alpha\beta I}{\alpha I + r}(1 - I) - \mu I,$$

where r is the natural death rate of mosquitoes, μ is the death rate of humans, β is the transmission rate from infected mosquitoes to susceptible humans, and α is the transmission rate from humans to mosquitoes.

(a) Compute the reproduction number of malaria.
(b) Find the equilibria of the model and their stabilities.
(c) Use a computer algebra system to graph several solutions.

2.4. Consider the model of malaria in Problem 2.3 and assume that saturating treatment is applied:

$$I' = \frac{\alpha\beta I}{\alpha I + r}(1 - I) - \mu I - \frac{\gamma I}{A + I},$$

where r is the natural death rate of mosquitoes, μ is the death rate of humans, β is the transmission rate from infected mosquitoes to susceptible humans, α is the transmission rate from humans to mosquitoes, γ is the treatment rate, and A is the half-saturation constant.

(a) Compute the reproduction number of malaria with saturating treatment.
(b) Find the equilibria of the model and the conditions for their existence.
(c) Find the stabilities of the equilibria.
(d) Use a computer algebra system to graph several solutions.

2.5. Consider the SIS model with constant population size N and saturating incidence in the size of the susceptibles:

$$\begin{aligned} S'(t) &= -\frac{\beta IS}{1 + \sigma S} + \alpha I, \\ I'(t) &= \frac{\beta IS}{1 + \sigma S} - \alpha I. \end{aligned} \tag{2.17}$$

(a) Reduce the SIS model to a single equation.
(b) Determine the threshold condition for the existence of endemic equilibria.
(c) Use a computer algebra system to plot the solutions of (2.17) for $N = 100$, $\beta = 0.5$, $\sigma = 0.01$, $\alpha = 0.05$.

2.6. Consider the SIS model with constant population size N:

$$\begin{aligned} S'(t) &= -\frac{\beta I^p S}{1 + \sigma I^q} + \alpha I, \\ I'(t) &= \frac{\beta I^p S}{1 + \sigma I^q} - \alpha I. \end{aligned} \tag{2.18}$$

(a) Reduce the SIS model to a single equation.
(b) For the case $p < 1$, $q = p - 1$, determine the threshold condition for the existence of endemic equilibria.
(c) For the case $p > 1$, $p = q$, determine the threshold condition for the existence of endemic equilibria.

2.7. Plague in Eyam [27]
The Derbyshire village of Eyam, England, suffered an outbreak of bubonic plague in 1665–1666. The source of that plague was believed to be the Great Plague of London. The village is best known for being the "plague village" that chose to isolate itself when the plague was discovered there in August 1665 rather than let the

infection spread. Detailed records were preserved. The initial population of Eyam was 350. In mid-May 1666, nine months after the beginning of the epidemic, there were 254 susceptibles and 7 infectives. The data about the epidemic in the remaining months are given in Table 2.2. The infective period of the bubonic plague is 11 days.

(a) Estimate α
(b) Use the implicit solution of the SIR model to estimate β.
(c) Plot S and I alongside the data. Do they fit?

2.8. A first-order differential equation is given by $x'(t) = f(x)$, where $f(x)$ is defined by Fig. 2.10.

(a) Determine the equilibria of the model $x' = f(x)$.
(b) Determine the local stabilities of the equilibria of the model $x' = f(x)$.
(c) Graph the solutions $x(t)$ of the model $x' = f(x)$ as a function of time.
(d) What is the limit

$$\lim_{t\to\infty} x(t)$$

if $x(0) = 15$? What about if $x(0) = 1$?

Table 2.2 Number of susceptible and infected individuals during the Great Plague of Eyam

Date 1666	No. susceptible	No. infected
Mid-May	254	7
July 3/4	235	14.5
July 19	201	22
August 3/4	153.5	29
August 19	121	21
September 3/4	108	8
September 19	97	8
October 3/4	Unknown	Unknown
October 20	83	0

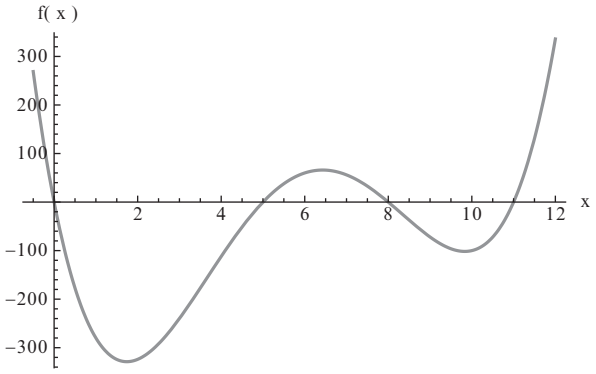

Fig. 2.10 Graph of the function $f(x)$

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