Chapter 1

Basic Knowledge and Modeling on Epidemic Dynamics

Zhien Ma and Jia Li

1.1. Introduction

The spread of infectious diseases has always been of concerns and a threat to public health. It has caused serious problems for the survival of human beings and other species, and for the economic and social development of the human society. The Antonine Plague, 165–180 AD, was an ancient pandemic, either of smallpox or measles, brought back to the Roman Empire by troops returning from campaigns in the Near-East. The epidemic invaded the Roman Empire, claimed the lives of two Roman emperors and caused drastic population reduction and economic hardships which led to disintegration of the empire because of disorganization that facilitated invasions of barbarians [Wikipedia (2008)]. In the early 1500s, smallpox was introduced into the Caribbean by the Spanish armies led by Cortez, from where it spread to Mexico, Peru, and Brazil. It is probable that smallpox was one of the factors that resulted in widespread deaths among the Incas. The population of Mexico was reduced from up to 30 million to less than 2 million during a period of 50 years after the Spanish invasion, smallpox being the principal cause of death [Brauer and Castillo-Chavez (2001); Geddes (2006)]. The Black Death (bubonic plague) had spread four times in Europe. It had caused the death of more than 10000 people every day and a half of the population there in 600 AD, and the death of as much as one-third of the population between 1346 and 1350. The disease recurred regularly in various parts of Europe and, particularly, led to the death of one-sixth of the population in London between 1665 and 1666. The last outbreak of the bubonic plague happened between 1720 and 1722 in France,
which had taken the lives as much as a half of the population in Marseilles, 60% nearby Toulon, 44% in Arles, and 30% in Aix and Avignon [Brauer and Castillo-Chavez (2001); Snell (2008)].

The fighting with infectious diseases has had a long history, and great progresses had been achieved, especially during the 20th century. While smallpox outbreaks have occurred from time to time for thousands of years, the disease is now eradicated after a successful worldwide vaccination program [HHS (2008)]. In 1991, World Health Assembly passed a resolution to eliminate leprosy as a public health problem by the year 2000, where elimination of leprosy as a public health problem is defined as a prevalence rate of less than one case per 10 000 persons. The target was achieved on time [WHO (2008a)]. Poliomyelitis (polio) is a highly infectious viral disease, which mainly affects young children. When the Global Polio Eradication Initiative was launched in 1988, wild poliovirus was endemic in more than 125 countries on five continents, paralyzing more than 1000 children every day. As a result of the Global Polio Eradication Initiative — the single largest, internationally coordinated public health project to date — by the end of 2006, only four countries remained which had never interrupted endemic transmission of wild poliovirus (Nigeria, India, Pakistan, and Afghanistan). In 2006, less than 2000 cases were reported [WHO (2008c)]. There are some other infectious diseases, such as diphtheria, measles, pertussis, and tetanus (lockjaw), that can be serious and fatal, but have been significantly under control in many countries.

While the great achievement and progresses in the prevention and control of infectious diseases are promising and inspiring, there is a long way to go to completely eradicate infectious diseases in the world.

An estimated 1.5 million people died from tuberculosis in 2006 [WHO (2007)]. Malaria is by far the world’s most important tropical parasitic disease. Approximately, 40% of the world’s population, mostly those living in the world’s poorest countries, are at risk of malaria. Every year, more than 500 million people become severely ill with malaria, and between 1 and 1.5 million people die from it. Malaria kills more people than any other communicable disease except tuberculosis [WHO (2008b)]. Over 22 million people have died from AIDS. The United Nations estimates that, currently, there are 14 million AIDS orphans and that there will be 25 million by 2010 [UNTIL (2008)].

To prevent and to control infectious diseases more effectively, it is important to first fully understand the mechanism of the spread and the
transmission dynamics of the diseases, and then provide useful predictions and guidance so that better strategies can be established.

The research in infectious diseases can be basically classified as descriptive, analytic, experimental, and theoretic. Epidemic dynamics study is an important theoretic approach to investigate the transmission dynamics of infectious diseases. It formulates mathematical models to describe the mechanisms of disease transmissions and dynamics of infectious agents. The mathematical models are based on population dynamics, behavior of disease transmissions, features of the infectious agents, and the connections with other social and physiologic factors. Through quantitative and qualitative analysis, sensitivity analysis, and numeric simulations, mathematical models can give us good understanding of how infectious diseases spread, discover general principles governing the transmission dynamics of the diseases, and identify more important and sensitive parameters, to make reliable predictions and provide useful prevention and control strategies and guidance.

Compared to the classic statistic analysis in epidemic research, employing the well-developed modern theory of dynamic systems and utilizing high-speed computing facilities, epidemic dynamics studies provide deeper understanding of transmission mechanisms and global analysis of transmission dynamics. Further qualitative and quantitative investigations, and sensitivity analysis on model parameters can help us to make more realistic simulations and reliable long-term transmission prediction which may not be feasible by experiments or field studies. Moreover, the combination of epidemic dynamics, epidemiologic theory, biostatistics, and computer simulations will significantly contribute to further improvement of our knowledge of transmission patterns of epidemics, development of epidemiology, and more effective methods in controlling infectious diseases.

While mathematical modeling of infectious diseases can be traced back to 1760 when Bernoulli used mathematical models for smallpox [Bernoulli (1760)], the research on infectious diseases, using deterministic mathematical models, actually began in the 20th century. Hamer formulated a discrete-time model for the spread of measles in 1906. A physician, Dr. Ross, used a differential equation model to describe the transmissions of malaria between human beings and mosquitoes in 1911, and determined that there exists a threshold of the size of mosquitoes below which the spread of malaria can be controlled. It was because of his outstanding contributions in the research of the transmission dynamics of malaria, Dr. Ross was awarded his second Nobel Prize in medicine. Kermack and
McKendrick formulated a well-known and well-recognized SIR (susceptible–infective–recovered) compartmental model, in 1926, to study the outbreak of Black Death in London during the period of 1665–1666, and the outbreak of plague in Mumbai in 1906. They later, in 1932, formulated an SIS compartment model and, based on the investigation of this model, formally introduced the concept of thresholds that determines whether a disease spreads in a given population [Kermack and McKendrick (1932)]. The concept of thresholds established the fundamentals of the theory of epidemic dynamics. More intensive studies on epidemic dynamics took place after the middle of the 20th century. A remarkable and landmark publication is the book by Bailey with the first edition in 1957, and the second edition in 1975.

More developments and progresses have been particularly made during the past 20 years. Massive mathematical models have been formulated and developed to study various infectious diseases, ranging from more theoretic, general ones [Waltman (1974); Burnett and White (1974); Hoppensteadt (1975); Frauenthal (1980); Anderson and May (1982); Evans (1982); Webb (1985); Kranz (1990); Busenberg and Cooke (1993); Capasso (1993); Isham and Medley (1996); Daley and Gani (1999); Diekmann and Heesterbeek (2000)] to more specific ones especially for measles, malaria, tuberculosis, sexually transmitted diseases (STD), or AIDS/HIV [Hethcote and Yorke (1984); Hethcote (2000); Hyman and Stanley (1988); Brauer and Castillo-Chavez (2001); Brauer et al. (2008)]. The modeling of infectious diseases has shown rich dynamic behavior and phenomena.

From the perspective of transmission mechanisms, those models have included a variety of factors. For example, contact, vertical, and vector transmissions have been considered. Models incorporating incubation or latent periods, isolations, quarantines, vaccination with or without immunity loss, and infection within groups or between groups, or different population dynamics that epidemic modeling bases on have been formulated. More sophisticated models with age structure, infection-age structure, or spatial structure have also been studied.

From the perspective of mathematical structures of the models, while most deterministic models are based on ordinary differential equations, first- and second-order partial differential equations and delayed differential equations have been used for age-structured, spatial-structured, or reaction–diffusion models, and models with latent or incubation periods, respectively. Impulse differential systems have also been applied to evolution processes with a short-term perturbation.
As the deterministic epidemic models based on dynamic systems are developed and applied extensively, the functional extreme value problems from the theories of optimal control and optimization have been used for finding the best strategies in prevention and control of disease transmissions. Moreover, stochastic epidemic modeling and network epidemiologic models have also been employed.

Mathematical models can also be categorized, based on the described diseases, populations, and environments, as linear, nonlinear, autonomous, or nonautonomous models. There exist, moreover, modeling variations in each category.

The analysis of deterministic mathematical models has been focused on the wellposedness of the models and their solutions, persistence of diseases, existence and stability of steady states, which characterize the diseases spreading or being endemic, existence and stability of periodic solutions, which describe the oscillations of disease transmissions, and occurrence of bifurcations or chaotic behavior.

In earlier deterministic mathematical models for epidemic transmissions, a constant population size was usually assumed. It took the advantage of the tractability of the mathematical analysis. Those models are also good approximations for short-term predictions in closed populations or in the cases where the birth and death are relatively balanced and/or the disease-induced deaths are negligible. As progresses are being made in epidemic modeling, more advanced mathematical tools have been developed and are ready to be applied. More realistic mathematical models for infectious diseases have been dramatically developed lately. More specifically, (1) factors and structures, such as latent periods and time delays, age, infection-age, gender, other physiologic structures, and effects of isolations, quarantine, vaccination, or treatment, have been further included; (2) the dimensions of the models have been greatly increased, which allows for studying epidemic transmission dynamics between populations and species in depth; (3) more thorough and detailed investigations have been conducted on specific infectious diseases, such as AIDS/HIV and vector-borne diseases. Nevertheless, as the epidemic models become closer to reality and more biological and social factors are included, the model features and behavior become more complex. Hence, more advanced mathematical techniques, such as the theories of bifurcation, chaos, degree, and semigroup, have been broadly employed and utilized in the model analysis, and high-speed computers have also been used for more complicated simulations.
Dynamical Modeling and Analysis of Epidemics

The theory of epidemic dynamics is so rich that it is impossible for us to cover all of its aspects. We only introduce basic mathematical disease models, the ideas for modeling, and fundamental concepts and techniques for the model analysis in this chapter. More sophisticated models and techniques will be gradually provided in later chapters.

1.2. The Fundamental Forms of Epidemic Models

1.2.1. Two fundamental dynamic models of epidemics

Dynamic models for infectious diseases are mostly based on compartment structures that were initially proposed by Kermack and McKendrick (1927, 1932) and developed later by many other biomathematicians.

To formulate a dynamic model for the transmission of an epidemic disease, the population in a given region is often divided into several different groups or compartments. Such a model describing the dynamic relations among these compartments is called a compartment model.

1.2.1.1. Kermack–Mckendrick SIR compartment model

In the compartment model studied by Kermack and Mckendrick in 1927, the population is divided into three compartments: a susceptible compartment, labeled $S$, in which all the individuals are susceptible if they contact with a disease; an infected compartment, labeled $I$, in which all the individuals are infected by the disease and infectious; and a removed compartment, labeled $R$, in which all the individuals are removed or recovered from the infection. Denote the numbers of individuals in the compartments $S$, $I$, and $R$, at time $t$, as $S(t)$, $I(t)$, and $R(t)$, respectively. The following three assumptions were made by them:

1. The disease spreads in a closed environment; that is, there is no emigration nor immigration, and neither birth nor death in the population, so that the total population remains a constant $K$ for all $t$, that is, $S(t) + I(t) + R(t) \equiv K$.
2. The number of susceptibles who are infected by an infected individual per unit of time, at time $t$, is proportional to the total number of susceptibles with the proportional coefficient (transmission coefficient) $\beta$, so that the total number of newly infectives, at time $t$, is $\beta S(t)I(t)$.
3. The number removed (recovered) individuals from the infected compartment per unit time is $\gamma I(t)$ at time $t$, where $\gamma$ is the recovery rate coefficient, and the recovered individuals gain permanent immunity.
Based on these assumptions, the flow chart of the model is shown in Fig. 1.1, and the corresponding model equations are given in the system

\[
\begin{align*}
\frac{dS}{dt} &= -\beta SI, \\
\frac{dI}{dt} &= \beta SI - \gamma I, \\
\frac{dR}{dt} &= \gamma I. 
\end{align*}
\] (1.1)

Because the equation for variable \( R \) is decoupled from the first two equations of system (1.1), we only need to consider the system

\[
\begin{align*}
\frac{dS}{dt} &= -\beta SI, \\
\frac{dI}{dt} &= \beta SI - \gamma I. 
\end{align*}
\] (1.2)

While system (1.2) is oversimplified, useful information can still be obtained as shown below.

From Eq. (1.2), we have

\[
\frac{dI}{dS} = -1 + \frac{\rho}{S},
\] (1.3)

where \( \rho = \gamma / \beta \). The solution curves of Eq. (1.3) in the \( SI \) phase plane are shown in Fig. 1.2. All curves of \( I(S) \) reach the maximum when \( S = \rho \).

It follows from Fig. 1.2 that there is a threshold \( S = \rho \) such that if the initial number of susceptibles \( S(0) = S_0 > \rho \), the number of infectives increases; if \( S(0) = S_0 < \rho \), the number of infectives decreases. Define

\[
R_0 = \frac{1}{\gamma} S_0 = \frac{S_0}{\rho},
\]

then the epidemic spreads when \( R_0 > 1 \) and dies out when \( R_0 < 1 \).

We note that \( \gamma I \) is the number of recovered individuals who move from the infected compartment \( I \), per unit of time, at time \( t \). Hence after the period of time \( 1/\gamma \), all the infectives \( I(t) \) recover. Therefore, \( 1/\gamma \) is actually
the mean duration of infection, and $R_0 = \beta S_0 / \gamma$ is the number of newly infectives infected by an infected individual during the whole infection period when all of the individuals in the population are initially susceptible. This quantity $R_0$ determines the thresholds for disease transmissions. The number of infectives decreases if $R_0 < 1$ and increases if $R_0 > 1$. Therefore, to control the spread of an epidemic, one of the key factors is to estimate the value of $R_0$ and then reduce it to $< 1$.

The estimation of $R_0$ is not an easy task in practice because it involves biological parameters some of which may not be easily measured. We introduce an approximate method and use the model governed by system (1.1) to illustrate the method as follows.

The solution of Eq. (1.3) with the initial value $(S_0, I_0)$ is

$$I - I_0 = -(S - S_0) + \rho \ln \frac{S}{S_0}. \tag{1.4}$$

It follows from the second equation of (1.2) that $I(t) \to 0$, as $t \to \infty$, if $R_0 < 1$. Then since $S(t)$ is monotone decreasing and bounded below, $\lim_{t \to \infty} S(t) = S_\infty$. Writing $S_0 + I_0 = K$ and taking the limit in (1.4), we have

$$K - S_\infty + \rho \ln \frac{S_\infty}{S_0} = 0. \tag{1.5}$$
It is easy to verify that there is one and only one positive real root $S_{\infty}$ to Eq. (1.5). It follows also from Eq. (1.5) that

$$\rho = \frac{K - S_{\infty}}{\ln S_0 - \ln S_{\infty}}. \tag{1.6}$$

Suppose that $S_0$ and $S_{\infty}$ are measured clinically. Then we can determine the quantity $\rho$ by (1.6) and then $R_0$ from $R_0 = S_0/\rho$. If the average infection period $1/\gamma$ is estimated, then the transmission coefficient $\beta$ can be also determined by $\beta = \gamma/\rho$.

For example, the village of Eyam near Sheffield, England suffered an outbreak of bubonic plague in 1665–1666 [Brauer and Castillo-Chavez (2001)]. Preserved records show that the initial numbers of susceptibles and infectives were 254 and 7 in the middle of May 1666, respectively, and only 83 persons survived in the middle of October 1666. Hence, the parameters in (1.6) can be estimated as $S_0 = 254$, $S_{\infty} = 83$, and $K = 261$, so that $\rho = 153$ and $R_0 = S_0/\rho = 1.66$. The records also show that the infective period was 11 days such that

$$\beta = \gamma = \frac{1}{\gamma} \times \frac{1}{153} = 0.000594(1/\text{day}) = 0.0178(1/\text{month}).$$

It follows from (1.3) that the number of infectives $I$ reaches the maximum as $S = \rho$. Thus from (1.4), we estimate the number of the infectives at the high peak of the epidemic to be

$$I_m = I_0 + S_0 - \rho + \rho \ln \frac{\rho}{S_0} = K - \rho(1 + \ln R_0) = 261 - 153(1 + \ln 1.66) = 31(\text{persons}).$$

1.2.1.2. *Kermack–Mckendrick SIS compartment model*

For viral diseases, such as influenza, measles, and chickenpox, the recovered individuals, in general, gain immunity to the same virus. Then the SIR model described in Sec. 1.2.1.1 is applicable. However, for bacterial diseases, such as encephalitis, and gonorrhea, the recovered individuals gain no immunity and can be reinfected. To study the transmission dynamics of these diseases, Kermack and Mckendrick (1932) proposed an SIS model. The flow chart of an SIS model is shown in Fig. 1.3, and the corresponding
model equations are given:
\[
\frac{dS}{dt} = -\beta SI + \gamma I, \\
\frac{dI}{dt} = \beta SI + \gamma I. 
\] (1.7)

Since \( S + I \equiv K \), system (1.7) can be reduced to
\[
\frac{dS}{dt} = \beta(K - S)(\rho - S), \quad \text{where} \ \rho = \frac{\gamma}{\beta}. 
\] (1.8)

Then it is easy to see that when \( \rho \geq K \), Eq. (1.8) has only one equilibrium \( S = K \), which is globally asymptotically stable, such that \( S(t) \) with any initial value \( S_0 \in (0, K) \) increases monotonically to \( K \), and \( I(t) \) decreases monotonically to zero. Hence the epidemic dies out.

When \( \rho < K \), Eq. (1.8) has two positive equilibria, \( S = K \) and \( S = \rho \). \( S = K \) is unstable and \( S = \rho \) is globally asymptotically stable. Solution \( S(t) \) starting from any initial value \( S_0 \in (0, K) \) tends to \( \rho \) as \( t \to \infty \), and \( I(t) \) tends to \( K - \rho \). In this case, the epidemic persists and the infectives eventually approach \((1 - \rho)\). Hence the disease becomes endemic.

Let \( R_0 = K/\rho = \beta K/\gamma \). Then it is easy to see that this \( R_0 \) has the same biological meaning as the \( R_0 \) in the SIR model in Sec. 1.2.1.1.

1.2.2. **Fundamental forms of compartment models**

Fundamental forms of epidemic compartment models can be classified as the following types. We list them by their flow charts.

1.2.2.1. **Models without vital dynamics**

When a disease, such as influenza, measles, rubella, or chickenpox, spreads in a population rapidly, for a relatively short time, usually the vital dynamic...
factors, such as birth and natural death of the population, can be neglected in the models.

**Models without latent periods.** In these models, infected individuals become infectious immediately.

**SI model** In this model, the infectives cannot be recovered from infection. The flow chart of the transmission dynamics is shown in Fig. 1.4.

**SIS model** The infectives are recovered but gain no immunity after recovery. The flow chart is shown in Fig. 1.3.

**SIR model** The infectives obtain permanent immunity to the disease after recovered from infection. The flow chart is shown in Fig. 1.1.

**SIRS model** The recovered individuals have only temporary immunity after they recovered from infection. The immunity will be lost eventually. If the number of individuals who lose their immunity per unit time is $\delta R(t)$ at time $t$, they enter the susceptible compartment again. The flow chart is shown in Fig. 1.5, where $1/\delta$ is the mean immunity period.

**SIRI model** For some diseases, such as tuberculosis, infectives cannot get permanent recovery after infection. The individuals who recover temporarily may get recurrence under some conditions, say, tiredness. Suppose that the recurrence rate coefficient is $\delta$, then the flow chart of the SIRI model is shown in Fig. 1.6.

**Remark 1.1.** The difference between the SIRS and the SIS models is the following. For the SIS model, the individuals of infectives become susceptible again immediately after they are recovered from the infection,
but for the SIRS model, the recovered individuals are not susceptible to the same disease until they lose their immunity.

Models with latent periods. In these models, an exposed compartment, in which all of the individuals have been infected but have not yet infectious, is introduced. Let $E(t)$ denote the number of individuals in the exposed compartment at time $t$. Corresponding to the above models without latent periods, we may introduce SEI, SEIS, SEIR, and SEIRS models with latent periods, respectively. For example, the flow chart in Fig. 1.7. illustrates an SEIRS model with a latent period, where $\omega$ is the progression rate coefficient for individuals from compartments $E$ to $I$, such that $1/\omega$ is the mean latent period.

1.2.2.2. Models with vital dynamics

Constant population size. If we assume that the birth and death rates of a population are equal during the epidemic period of a disease, and that there is no disease-induced death, then the population size in a closed environment keeps constant, denoted by $K$. Two examples for this case are given below:

SIR model without vertical transmission In this model, we assume that the disease is not inherited from parents to their new generations, so that all the newborns are susceptible. The corresponding flow chart of the model is shown in Fig. 1.8.
Basic Knowledge and Modeling on Epidemic Dynamics

SIR model with vertical transmission For many diseases, such as AIDS, hepatitis B, and hepatitis C, newborns from the infected individuals can be infected as well. Such transmission is called vertical transmission. Suppose that a fraction, $k$, of newborns is infected, and the rest is only susceptible to the disease. Then the flow chart of the model is shown in Fig. 1.9.

Variable population size. If the birth and death rates of a population are different, there is a migration to the population, or there is a disease-induced death to the population, then the population size varies. We give two examples as follows:

SIS model with vertical transmission, input, output, and disease-induced death The flow chart of the model is shown in the Fig. 1.10, where $b$ is the birth rate coefficient, $\mu$ the natural death rate coefficient, $\alpha$ the coefficient of death rate caused by the disease, $A$ the input rate of the total population, $B$ the output rate coefficient of the susceptibles and the infected, and the other coefficients are the same as before.

---

**Fig. 1.8.** Flow chart of the SIR model without vertical transmission.

**Fig. 1.9.** Flow chart of the SIR model with vertical transmission.

**Fig. 1.10.** Flow chart of the SIS model with vertical transmission, input, output and disease-induced death.
Here we introduce a new compartment $M$, in which all newborns have passive immunity, which means that the newborns have several months congenital immunity coming from their maternal antibodies, but they become susceptible after these months. Suppose that the fraction of newborns with passive immunity is $p$ such that the mean period of passive immunity is $1/\delta$. The flow chart of the corresponding model is shown in Fig. 1.11.

1.3. Basic Concepts of Epidemiologic Dynamics

1.3.1. Adequate contact rate and incidence

An infectious diseases is, in general, transmitted through direct contacts. The number of individuals contacted by an infective per unit of time is called a contact rate of the infection, denoted by $U(N)$. It usually depends on the population size $N$ in a given environment. If the individuals contacted by an infective are susceptible, they may be infected. Suppose that the probability of infection by each contact is $\beta_0$. Then the function $\beta_0 U(N)$ is called an adequate contact rate, which describes the infection strength of the infectives and usually depends on the toxicity of the virus or bacterium and the situation of the environment. Because diseases are only transmitted to susceptibles by contacting with infectives, and the fraction of the susceptibles in the population is $S/N$, the mean adequate contact rate of an infected individual to a susceptible is $\beta_0 U(N) S/N$. This rate is called an infection rate. Then the total new infectives infected by all individuals in the infected compartment, per unit of time, at time $t$ is $\beta_0 U(N) S I / N$, which is called an incidence of the disease.

There are two types of incidence often used in disease modeling:

If $U(N) = k N$, that is, the contact rate is proportional to the total population size, the incidence is $\beta S(t) I(t)$, where $\beta = \beta_0 k$ is called the transmission coefficient. This type of incidence is called bilinear incidence or simple mass action incidence.

**MSEIR model with passive immunity**  Here we introduce a new compartment $M$, in which all newborns have passive immunity, which means that the newborns have several months congenital immunity coming from their maternal antibodies, but they become susceptible after these months. Suppose that the fraction of newborns with passive immunity is $p$ such that the mean period of passive immunity is $1/\delta$. The flow chart of the corresponding model is shown in Fig. 1.11.
If \( U(N) = k' \), that is, the contact rate is a constant, in this case, the incidence becomes \( \beta SI/N \), where \( \beta = \beta_0 k' \), and it is called **standard incidence**. For instance, in modeling of STDs in most circumstances, the standard incidence is often used, due to the fact that the number of sexual contacts per individual is approximately constant.

As Anderson and May (1986) pointed out, the standard incidence may be more suitable for human beings, or animals who live in groups. The incidence formed by \( \beta N^\alpha SI/N \) was used in modeling of five types of infectious diseases in a human community which has 1000 to 400000 people. Their results showed that \( \alpha \) was estimated as between 0.03 and 0.07 [Anderson and May (1982, 1986)], closer to be 0 rather than 1. This study shows that, for many infectious diseases, the size of a human population where a disease is transmitted has little effects to the incidence. Hence the standard incidence is more suitable than the bilinear form for diseases transmitted in human populations, although the incidence \( \beta N^{0.05} SI/N \) was used and its suitability was confirmed in [Anderson and May (1982)].

The so-called saturation contact rate, \( U(N) = \alpha N/(1+\omega N) \), is also used, which is between the proportional and constant contact rates [Dietz (1982)]. When the population size \( N \) is small, function \( U(N) \) is close to \( U(N) = \alpha N \), and it tends to the saturation value \( \alpha/\omega \) for large \( N \). Moreover, Heesterbeek and others considered some stochastic factors in the contacts and proposed the following form of contact rate: \( U(N) = \alpha N/(1+bN+\sqrt{1+2bN}) \) [Heesterbeek and Metz (1993)]. All of the contact rates listed above satisfy the following conditions:

1. \( (H_1) \): \( U(N) \) is a nonnegative nondecreasing continuous function as \( N \geq 0 \) and is continuously differentiable for \( N > 0 \).
2. \( (H_2) \): \( D(N) = U(N)/N \) is a nonincreasing continuously differentiable function as \( N > 0 \), \( D(0^+) \neq 0 \) and \( U'(N) + |D'(N)| \neq 0 \).

Therefore, we can also consider a contact rate in a more general form \( U(N) \), and assume that it satisfies conditions \( H_1 \) and \( H_2 \), and the saturation condition: \( \lim_{N \to +\infty} U(N) = U_0 \).

To describe transmission dynamics of diseases in more details, and understand mechanism of transmissions of diseases, other nonlinear incidences are also proposed. These incidences are more plausible for some special cases. Capasso and Serio (1978) used a saturated incidence of the form of \( \beta IS/(1+\beta I) \), Liu and his coworkers (1986, 1987) proposed nonlinear incidences of the form of \( kIPS/(1+\alpha I) \) and \( \beta IPS^q \). More generalized
incidences $\beta g(I)S$ and $\beta g(I)S^p/N$ were also used [Wang (2006a); Hethcote and van den Driessche (1991); Alexander and Moghadas (2004, 2005)].

In short, what type of incidence is more suitable and to be chosen, when we investigate a specific epidemic, depend on the disease and the environment, and is determined by real data we obtained. Many forms of functional responses used in the studies of population dynamics may inspire us to construct different forms of contact rates for various diseases and environments.

1.3.2. Basic reproductive number and modified reproductive number

1.3.2.1. Basic reproductive number

We have seen a very important number, $R_0$, in the study of Kermack–Mckendrick SIR and SIS models in Sec. 1.2.1. A disease dies out if $R_0 < 1$ and spreads if $R_0 > 1$. To better understand this number $R_0$, we first provide the following two examples, through which we also introduce a qualitative method which is often used in planar differential systems for disease transmission dynamics.

Example 1.1. Consider the SIR model demonstrated in Fig. 1.8 in Sec. 1.2.2. The corresponding model is

\[
\frac{dS}{dt} = bK - \beta SI - \mu S, \\
\frac{dI}{dt} = \beta SI - \mu I - \gamma I, \\
\frac{dR}{dt} = \gamma I - \mu R,
\]

where we assume $b = \mu$. Since the variable $R$ is not included in the first two equations of (1.9), and we are only interested in the spread of the disease, we only investigate the system consisting of the first two equations

\[
\frac{dS}{dt} = \mu K - \beta SI - \mu S := P(S, I), \\
\frac{dI}{dt} = (\beta S - \mu - \gamma)I := Q(S, I),
\]

where $(S, I) \in D = \{(S, I) : S > 0, I \geq 0, S + I \leq K\}$.

Equilibria of system (1.10) can be solved by letting the right side of each of the equations equal zero, so that possible equilibria of the system...
(1.10) are

\[ E_0(K, 0) \quad \text{and} \quad E_1\left(\frac{\mu + \gamma}{\beta}, \frac{\mu(\beta K - (\mu + \gamma))}{\beta(\mu + \gamma)}\right). \]

We then discuss the dynamics of these equilibria as follows:

1. Assume \( \beta K/(\mu + \gamma) < 1 \). Then there is only one equilibrium \( E_0 \) in region \( D \). The Jacobian matrix of (1.10) at this equilibrium, \( E_0 \), is given by

\[
J(E_0) = \begin{pmatrix}
-\mu & -bK \\
0 & \beta K - \gamma - \mu
\end{pmatrix}.
\]

It is easy to see that \( J(E_0) \) has two eigenvalues \( \lambda_1 = -\mu < 0 \) and \( \lambda_2 = \beta K - (\gamma + \mu) \).

Since \( A_2 < 0 \) for \( \beta K/(\mu + \gamma) < 1 \), equilibrium \( E_0 \) is locally asymptotically stable. Because there is only one equilibrium \( M_0 \) in the region \( D \) in this case, it is impossible to have a closed orbit of system (1.10), and we note that region \( D \) is positively invariant for system (1.10) such that all orbits of (1.10) started inside \( D \) cannot go out of \( D \). Then equilibrium \( E_0 \) is globally asymptotically stable in \( D \). This implies that no matter how many initial infectives in this population, the epidemic cannot persist and dies out eventually. The point \( E_0(K, 0) \) is called a disease-free equilibrium.

2. If \( \beta K/(\mu + \gamma) > 1 \), in addition to \( E_0 \), there is a positive equilibrium \( E_1 \) in region \( D \). The Jacobian matrix of (1.10) at the equilibrium \( E_1 \) is given by

\[
J(E_1) = \begin{pmatrix}
-\mu \frac{\beta K}{\mu + \gamma} & -(\mu + \gamma) \\
\frac{\mu(\beta K - (\mu + \gamma))}{\mu + \gamma} & 0
\end{pmatrix}.
\]

Thus, it follows from \( \text{tr}(J(E_1)) = -\mu \beta K/(\mu + \gamma) < 0 \) and \( \text{det}(J(E_1)) = \mu[\beta K - (\mu + \gamma)] > 0 \), in this case, the equilibrium \( E_1 \) is locally asymptotically stable if it exists. Since region \( D \) is a positive invariant set of the system (1.10), to show the global stability of equilibrium \( E_1 \), we need only to prove that there is no closed orbit of system (1.10) in the interior of \( D \). Taking the Dulac function \( B(S, I) = 1/I \), we obtain

\[
\frac{\partial(BP)}{\partial S} + \frac{\partial(BQ)}{\partial I} = -\beta - \frac{\mu}{I} < 0 \quad \text{for} \quad (S, I) \in \text{int} \ D.
\]
By the qualitative theory of planar differential systems, equilibrium $E_1$ is globally asymptotically stable in region $D$. This implies that once the disease invades the population, the epidemic persists, and the susceptibles and infectives eventually approach the numbers $(\mu + \gamma)/\beta$ and $\mu[\beta K - (\mu + \gamma)]/|\beta(\mu + \gamma)|$, respectively, so that the disease become endemic. The point $E_1$ is called an endemic equilibrium.

Let $R_0 := \beta K/(\mu + \gamma)$. Then $R_0 = 1$ is a threshold that determines whether a disease persists or goes extinct. The epidemic does not persist if $R_0 < 1$, and spreads and eventually forms an endemic if $R_0 > 1$. This can be interpreted from the biological point of view as follows.

From the second equation of system (1.9), we can see that $1/(\mu + \gamma)$ is the mean infective period, or the mean course of infection, $K$ is the number of the individuals in the population, also the number of susceptibles at the disease-free equilibrium $E_0$. Therefore, $R_0 = \beta K/(\mu + \gamma)$ is actually the average number of secondary infections produced by one infected individual during the mean course of infection in a completely susceptible population, and is called the basic reproductive number, or simply the reproductive number. If $R_0 < 1$, then on average, the number of new infections by one infected individual over the mean course of the disease is $< 1$, which implies that the disease dies out eventually. If $R_0 > 1$, then the number of new infections produced by one infected individual is $> 1$, which leads to the persistence of the infection.

We have seen from above example that the number of susceptibles, when all the members of the population are susceptible (this usually is assumed at the initial time of the epidemic), and the number of susceptibles at the disease-free equilibrium are the same, both are $K$. However it is not always the case and we show it in Example 1.2.

**Example 1.2.** Consider the following SIR model with vaccination:

\[
\begin{align*}
\frac{dS}{dt} &= \mu K - \beta SI - \mu S - pS, \\
\frac{dI}{dt} &= \beta SI - (\gamma + \mu)I, \\
\frac{dR}{dt} &= \gamma I - \mu R + pS,
\end{align*}
\]

where $p$ is the vaccinating rate coefficient for the susceptibles.
System (1.11) has, in addition to the disease-free equilibrium $E_0(\mu K/(\mu + p), 0, pK/(\mu + p))$, a positive equilibrium

$$E_1\left(\frac{\gamma + \mu}{\beta}, \frac{\beta\mu K - (\mu + p)(\mu + \gamma)}{\beta(\mu + \gamma)}, \frac{\beta K\gamma - (\mu + \gamma)(\gamma - p)}{\beta(\mu + \gamma)}\right),$$

if $\beta\mu K/[(\mu + p)(\mu + \gamma)] > 1$.

Let $R_0 = \beta\mu K/[(\mu + p)(\mu + \gamma)]$. Then it is not difficult to prove that if $R_0 < 1$, the disease-free equilibrium $E_0$ is stable, and that if $R_0 > 1$, $E_0$ is unstable, and the endemic equilibrium $E_1$ is stable.

In summary, we have the following conclusions:

1. The number of susceptibles at the disease-free equilibrium $E_0$ is $\mu K/(\mu + p)$, but adding the three equations of system (1.11) and denoting $S(t) + I(t) + R(t) = N(t)$, we have

$$\frac{dN}{dt} = \mu(K - N).$$

Then the number of all individuals in the population is $K$, not equal to $\mu K/(\mu + p)$, the number of susceptibles, because of the proportion of vaccination.

2. The threshold that determines whether the disease dies out ultimately is $R_0 = \beta\mu K/[(\mu + p)(\mu + \gamma)] = 1$ rather than $\beta K/(\mu + \gamma) = 1$. Notice that $\mu K/(\mu + p) = S_0$ is the number of susceptibles at the disease-free equilibrium, so that $R_0 = \beta S_0/(\mu + \gamma)$ is the average number of secondary infections provided by one infected individual during the mean course of infection in the case where the number of susceptibles is counted from the disease-free equilibrium; that is, the total susceptibles of the population when disease is free. It is not the number of susceptibles in the case where all individuals of the population are susceptible. The number $R_0 = \beta S_0/(\mu + \gamma)$ is the reproductive number which we defined above.

3. Here, the reproductive number $R_0 = \beta S_0/(\mu + \gamma) = 1$ is also a threshold to determine whether the positive equilibrium exists. If $R_0 < 1$ there exists only the disease-free equilibrium $E_0$. A positive equilibrium $E_1$ appears, in addition to $E_0$, if $R_0 > 1$. Furthermore, $R_0 = 1$ also differentiates the stability and instability of the disease-free equilibrium $E_0$. If $R_0 < 1$, $E_0$ is stable, whereas $E_0$ is unstable and $E_1$ is stable if $R_0 > 1$, all of which are the mathematical representations of the extinction or persistence of the disease.
We need to point out that while conclusion (3) is true, in general, for some other epidemic models, \( R_0 = 1 \) may not be a threshold as we state above. For some models, when \( R_0 > 1 \) there is an endemic equilibrium, but when \( R_0 < 1 \), a positive equilibrium, or even more positive equilibria, may appear. This is called a backward bifurcation, which will be further discussed in Sec. 2.7.1.

There are two methods often used to determine the basic reproductive number of epidemic models. One method is to find conditions for the local stability of the disease-free equilibrium of the model. The other method is to use a next-generation operator [Diekmann et al. (1990); Diekmann and Heesterbeek (2000); van den Driessche and Watmough (2002)], applications of which are given in Sec. 2.3.2. Moreover, the basic reproductive number can also be determined either by finding the conditions on the existence of an endemic equilibrium or epidemiologic meaning of parameters in the model.

1.3.2.2. Modified reproductive number

Before introducing a new concept of modified reproductive numbers in this section, we give an example below.

**Example 1.3.** Consider the following SIRS model with exponential birth, natural death, disease-induced death rates, standard incidence. The compartmental diagram is shown in Fig. 1.12.

The corresponding differential equations are

\[
\frac{dS}{dt} = bN - \mu S - \frac{\beta SI}{N} + \delta R, \\
\frac{dI}{dt} = \frac{\beta SI}{N} - (\alpha + \mu + \gamma)I, \\
\frac{dR}{dt} = \gamma I - (\mu + \delta)R, \\
\frac{dN}{dt} = (b - \mu)N - \alpha I.
\]

(1.12)

where \( b \) and \( \mu \) are the birth rate and the natural death rate coefficients, respectively, \( \alpha \) the disease-induced death rate coefficient, \( \gamma \) is the recovery rate coefficient, \( \delta \) is the immunity loss rate coefficient, and \( N(t) = S(t) + I(t) + R(t) \) is the total population size. From system (1.12), we have
Then, the population size $N(t)$ declines exponentially to zero if $b < \mu$, may approach zero, remain finite, or grow exponentially to infinity, depending on the infectives $I(t)$, if $b > \mu$.

System (1.12) has no equilibrium if $b > \mu$. However, we can still determine whether the disease dies out or not by analyzing the changing tendency of the infective fraction $I(t)/N(t)$ in the total population, such that the disease persists if the limit $\lim_{t \to \infty} I(t)/N(t)$ is greater than 0, and dies out if the limit is 0.

Let

$$x = \frac{S}{N}, \quad y = \frac{I}{N}, \quad z = \frac{R}{N}.$$ 

Then system (1.12) is transformed to

$$\frac{dx}{dt} = b - bx - \beta xy + \delta z + \alpha xy,$$

$$\frac{dy}{dt} = \beta xy - (b + \alpha + \gamma) y + \alpha y^2,$$

$$\frac{dz}{dt} = \gamma y - (b + \delta) z + \alpha yz,$$

which is equivalent to the following two-dimensional system

$$\frac{dy}{dt} = \beta(1 - y - z)y - (b + \alpha + \gamma) y + \alpha y^2,$$

$$\frac{dz}{dt} = \gamma y - (b + \delta) z + \alpha yz,$$

since $x + y + z = 1$. It is easy to see that region $D = \{(y, z) : y \geq 0, z \geq 0, y + z < 1\}$ is invariant for system (1.13).
Define
\[ R_1 := \frac{\beta}{b + \alpha + \gamma}. \]

It can be shown (see [Mena-Lorca and Hethcote (1992)]) that system (1.13) has only the disease-free equilibrium \( E_0(0,0) \), which is globally asymptotically stable in \( D \), if \( R_1 \leq 1 \). This disease-free equilibrium, \( E_0 \), becomes unstable, and there appears a positive equilibrium \( E^*(y^*, z^*) \), which is globally asymptotically stable in the interior of \( D \) if \( R_1 > 1 \).

The fact that the disease-free equilibrium \( E_0 \) is globally asymptotically stable implies that \( \lim_{t \to \infty} y(t) = \lim_{t \to \infty} I(t)/N(t) = 0 \) for any initial values of \( I_0 > 0 \) and \( N_0 > 0 \); that is, the infective fraction goes to 0. In this sense, the disease dies out finally no matter whether the total population size keeps finite, goes to 0, or grows infinitely. Similarly, the global asymptotic stability of \( E^* \) implies that \( \lim_{t \to \infty} I(t)/N(t) = y^* > 0 \), which means that the infective fraction in the population goes to a positive constant, so the disease persists and becomes an endemic, no matter whether the total population size keeps finite, or grows infinitely.

For the model in (1.12), the transmission coefficient is \( \beta \) and the mean course of infection is \( 1/(\alpha + \mu + \gamma) \). Hence, the average number of secondary infections produced by one infected individual during the mean course of infection in a fully susceptible population is \( R_0 = \beta/(\alpha + \mu + \gamma) \), not equal to \( R_1 \), while the threshold to determine whether the disease dies out is \( R_1 = 1 \). This number \( R_1 = \beta/(b + \alpha + \gamma) \) is then defined as a modified reproductive number.

1.3.3. Average lifespan and average infection age

Average lifespan. Suppose that \( N(a) \) is the number of individuals of a population who have survival until age \( a \), and that \( \mu \) is the natural death rate coefficient, that is, the proportion of the individuals who die in the population, per unit of time. We notice that time and age have the same scales. Then we have
\[
\frac{dN(a)}{da} = -\mu N(a),
\]
where the minus sign implies the decrease of \( N \) with respect to age \( a \) due to the natural death. Assume \( N(0) = N_0 \). Solving differential equation (1.14),
we obtain
\[ N(a) = N_0 e^{-\mu a}, \] 
that is, \( e^{-\mu a} = \frac{N(a)}{N_0} \),
so that \( e^{-\mu a} \) expresses the probability of survivals of the population at age \( a \). Hence, the probability of death of the population in the age interval \([0, a]\) is \( 1 - e^{-\mu a} \). Thinking of the age at death as a random variable and denoting it by \( \xi \), we have probability \( P(0 < \xi \leq a) = 1 - e^{-\mu a} = \int_0^a \mu e^{-\mu x} dx \), so that the probability density function of the random variable \( \xi \) is \( \mu e^{-\mu a} \), and thus the mathematical expectation of the random variable \( \xi \) is
\[ \int_0^{+\infty} a\mu e^{-\mu a} da = -\mu e^{-\mu a} \bigg|_0^{+\infty} + \int_0^{+\infty} e^{-\mu a} da = \frac{1}{\mu}. \]
From the meaning of mathematical expectation, \( 1/\mu \) is the average death age of the population, that is, the average lifespan. This can be also seen from the definition of the death rate. It follows from (1.14) that the number of deaths of the population \( N \) with age \( a \) per unit of time is \( \mu N(a) \) because of the same scale for time and age. Hence those individuals of age \( a \) die completely after time period \( 1/\mu \). Therefore, their average life-span is \( 1/\mu \).

In summary, if \( \mu \) is the natural death rate coefficient, then \( e^{-\mu a} \) is the probability of the individuals who survive up to age \( a \), \( 1/\mu \) is the average lifespan of this population, and \( 1/\mu = \int_0^{+\infty} e^{-\mu a} da \).

Similarly, if \( \gamma \) is a recovery rate coefficient, then \( 1/\gamma \) is the mean course of infection or the average period of infection in the absence of death, and \( e^{-\gamma t} \) is the probability that those individuals are not recovered until time \( t \). Moreover, if \( \delta \) is an immunity loss rate coefficient, then \( 1/\delta \) is the mean immunity period in the absence of death, and \( e^{-\delta t} \) is the probability that those individuals still have the immunity until time \( t \). It should be pointed out, however, that if the death is considered, the mean course of infection or mean immunity period will decrease. For instance, if the natural death rate coefficient \( \mu \) is incorporated, the mean course of infection is \( 1/(\gamma + \mu) \).

**Average infection age.** Let us explain this concept using Example 1.1, where we have seen that if \( R_0 > 1 \) there exists a positive equilibrium \( E_1(S^*, I^*) \) with
\[ S^* = \frac{\mu + \gamma}{\beta}, \quad I^* = \frac{\mu[\beta K - (\mu + \gamma)]}{\beta(\mu + \gamma)}. \]
It is easy to understand that $\beta I^* S^*$ is the number of infectives per unit of time at the steady state when $R_0 > 1$, so that $\beta I^*$ is the probability of a susceptible being infected per unit of time at the steady state. It is similar to the average lifespan, from the meaning of mathematical expectation, we know that $e^{-\beta I^*a}$ is the probability that susceptibles are not infected until age $a$, and $1/\beta I^*$ is the average infection age of the susceptibles. It is also called a waiting time.

For some diseases in a given area, the average lifespan and average infection age may be obtained by statistic data, so that the reproductive number $R_0$ can be estimated accordingly.

For instance, the reproductive number is

$$R_0 = \frac{\beta K}{\mu + \gamma} = \frac{K}{S^*},$$

(1.16)

in Example 1.1. It follows from Eq. (1.15) that

$$S^* = \frac{K}{1 + \beta I^*/\mu}.$$

If we denote the average infective age as $A$ and the average lifespan as $L$, then

$$A = \frac{1}{\beta I^*}, \quad L = \frac{1}{\mu}.$$

Thus (1.16) can be rewritten as

$$R_0 = 1 + \frac{L}{A}. \quad (1.17)$$

Consider the example by Brauer and Castillo-Chavez (2001), in some urban communities in England and Wales between 1956 and 1969. The average age of contracting measles was 4.8 years. If average lifespan in that area is assumed to be 70 years, then the reproductive number can be calculated, by the formula (1.17), as $R_0 = 15.6$.

To control an epidemic, we need to reduce the reproductive number $R_0$. It follows from formula (1.17), we can see that because the average lifespan in a given area is almost fixed during a short period, reducing $R_0$ implies increasing the average infection age. However, as it is pointed out by Brauer and Castillo-Chavez (2001), some diseases such as rubella (German measles) have more serious effects on adults than children. Then, as we intend to reduce $R_0$, a possible negative impact of such an effort needs to be considered.
1.4. Epidemic Models with Various Factors

1.4.1. Epidemic models with latent period

In general, SEIR and SEIRS models with latent periods cannot be reduced to planar differential equation systems. The qualitative analysis for such models can be difficult, and, as a result, few complete analytic results have been obtained. Nevertheless, if such a model is a competitive system under certain conditions, then the global stability of its steady states may be investigated by means of study of their orbital stability, the second additive compound matrix, or the method of ruling out the existence of periodic solutions, developed, for example, by Muldowney (1990) and Li and Muldowney (1995b, 1996).

Consider the SEIR model in (1.18) with the saturating contact rate \( C(N) = bN/[1 + bN + \sqrt{1 + 2bN}] \). The transfer flow chart is shown in Fig. 1.13.

\[
\begin{align*}
\frac{dS}{dt} &= A - \frac{a_0 SI}{h(N)} - \mu S, \\
\frac{dE}{dt} &= \frac{a_0 SI}{h(N)} - \varepsilon_0 E - \mu E, \\
\frac{dI}{dt} &= \varepsilon_0 E - \gamma_0 I - \mu I - \alpha_0 I, \\
\frac{dR}{dt} &= \gamma_0 I - \mu R,
\end{align*}
\]  

(1.18)

where \( a_0 = \beta b, h(N) = 1 + bN + \sqrt{1 + 2bN} \). Let \( a = a_0/\mu, \varepsilon = \varepsilon_0/\mu, \gamma = \gamma_0/\mu, \alpha = \alpha_0/\mu, \) and \( \mu \cdot \frac{dt}{d\tau} = d\tau \). Notice that \( N(t) = S(t) + E(t) + I(t) + R(t) \). Then model (1.18) can be rewritten as

\[
\begin{align*}
\frac{dE}{d\tau} &= \frac{a(N - E - I - R)I}{h(N)} - (1 + \varepsilon)E, \\
\frac{dI}{d\tau} &= \varepsilon E - (1 + \gamma + \alpha)I, \\
\frac{dR}{d\tau} &= \gamma I - R, \\
\frac{dN}{d\tau} &= \frac{A}{\mu} - N - \alpha I.
\end{align*}
\]  

(1.19)
We can find the reproductive number for model (1.19) as

\[ R_0 = \frac{a\epsilon A}{\mu \delta \omega h (A/N)} = \beta C(N) \frac{S}{N} \left( \frac{A}{\mu} \right) \frac{\epsilon_0}{(\mu + \gamma_0 + \alpha_0)(\mu + \epsilon_0)}, \]

where \( \delta = 1 + \gamma + \alpha, \omega = 1 + \epsilon \). We can also prove that the disease-free equilibrium \( P_0(0, 0, 0, A/\mu) \) is globally asymptotically stable in the region \( \Gamma = \{(E, I, R, N) \in R^4_+ : 0 \leq E + I + R \leq N \leq A/\mu \} \) if \( R_0 \leq 1 \), and \( P_0 \) is unstable and there exists a unique, globally asymptotically stable endemic equilibrium \( P^*(E^*, I^*, R^*, N^*) \) in the region \( \Gamma \) if \( R_0 > 1 \) [Zhang and Ma (2003)].

A more general SEIR model was considered by Zhang et al. (2006) with the flow chart shown in Fig. 1.14, where the recruitment enters not only to \( S \) but also to compartments \( E, I \) and \( R \), and the contact rate \( C(N) \) satisfies the conditions \((H_1)\) and \((H_2)\) in Sec. 1.3.1.

The corresponding system is

\[
\begin{align*}
\frac{dS}{dt} &= (1 - p - q - b)A - \beta C(N) \frac{S}{N} I - \mu S, \\
\frac{dE}{dt} &= qA + \beta C(N) \frac{S}{N} I - \mu E - qE, \\
\frac{dI}{dt} &= pA + \epsilon E - \mu I - \alpha I - \gamma I, \\
\frac{dR}{dt} &= bA + \gamma I - \mu R, \\
N(t) &= S(t) + E(t) + I(t) + R(t).
\end{align*}
\]
The reproductive number of system (1.20), $R_0$, is given by

$$R_0 = \frac{\beta C}{\mu + \varepsilon} \cdot \frac{1}{\mu + \gamma + \alpha},$$

if $p + q + b = 0$. The disease-free equilibrium is globally asymptotically stable in $\Gamma = \{(S, E, I, R) \in R_+^4 : 0 \leq S + E + I + R = N \leq A/\mu\}$ if $R_0 \leq 1$. It is unstable and there exists a unique, globally asymptotically stable endemic equilibrium in $\Gamma$, if $R_0 > 1$, for $p + q + b = 0$. In the case of $0 < p + q < 1 - b$, model (1.20) has no disease-free equilibrium (because of the recruitment) and only a globally asymptotically stable endemic equilibrium, $P^*(S^*, E^*, I^*, R^*)$, in $\Gamma$ [Zhang et al. (2006)].

### 1.4.2. Epidemic models with time delay

Inclusion of time delay in epidemic models considers the fact that the transmission dynamic behavior of a disease at time $t$ depends not only on the state of time $t$ but also on the state of previous time. We consider two types of time delays. One of such time delays is a discrete delay or fixed delay. In models with a discrete or fixed delay, the dynamic behavior of the model at time $t$ depends also on the state at time $t - \tau$, where $\tau$ is a fixed constant. For example, the number of newborns at time $t$ depends on the state of population and environment at time $t - \tau$, where $\tau$ is the period of pregnancy; the number of infectives at time $t$ for some diseases also depends on the number of infectives at time $t - \tau$, where $\tau$ is the latent period. The other type of time delays is a continuous delay or distributed delay. In a model with a continuous or distributed delay, the dynamic behavior of the model at time $t$ depends also on the states during the whole period prior to time $t$.

To better understand the biological meaning of time delay in epidemiologic models, we deduce the Kermack–Mckendrick SIS model to its integral form as follows. As we introduced in Sec. 1.2.1, the Kermack–Mckendrick SIS model has the form of

$$\frac{dS}{dt} = -\beta SI + \gamma I,$$

$$\frac{dI}{dt} = \beta SI - \gamma I,$$

where $\gamma$ is the recovery rate coefficient. Regarding the term $\beta SI$ in the second equation as a known function and solving this equation formally, we
obtain

\[ I(t) = I_0 e^{-\gamma t} + \int_0^t \beta S(u)I(u)e^{-\gamma(t-u)}du, \quad (1.21) \]

where \( I_0 = I(0) \) is the number of infectives at time \( t = 0 \). It follows from Sec. 1.3.3 that the first term in the right side of the expression (1.21), \( I_0 e^{-\gamma t} \), is the number of the infectives who were infected at \( t = 0 \) and have not been recovered until time \( t \). Since \( e^{-\gamma(t-u)} \) is the probability that the individuals who were infectives at \( t = u \) have not been recovered after the time period \( t - u \), that is, at time \( t \), and \( \beta S(u)I(u) \) is the number of secondary infections at time \( u \) per unit of time, the number of secondary infections during the time period \( [u, u + du] \) is \( \beta S(u)I(u)du \), and those who have not been recovered, at time \( t \), is \( \beta S(u)I(u)e^{-\gamma(t-u)}du \). Hence, the integral on the right side of expression (1.21) is the number of the individuals who are infected during the time period \( [0, t] \) and have not been recovered at time \( t \). Therefore, the number of total infectives at time \( t \), \( I(t) \), is given in (1.21).

Let \( P(t) \) be a general probability function which is monotone decreasing with respect to time \( t \) and \( P(0) = 1 \). (\( P(t) = e^{-\gamma t} \) in (1.21).) Then we have

\[ I(t) = I_0 P(t) + \int_0^t \beta S(u)I(u)P(t - u)du. \quad (1.22) \]

By means of mathematical expectation we can prove that the mean course of infection is \( \int_0^{+\infty} P(t)dt \).

1.4.2.1. Ideas for the modeling

Models with fixed time delay. There are two types of probability functions often used in epidemic models. One is of the exponential form \( P(t) = e^{-\gamma t} \) used in (1.21), where the recovered rate coefficient is \( \gamma \). It implies the number of the recovered to be subject to the exponential law. The other form of probability functions is the step function

\[ P(t) = \begin{cases} 1 & \text{for } 0 \leq t < \tau, \\ 0 & \text{for } t \geq \tau, \end{cases} \quad (1.23) \]
where \( \tau = 1/\gamma \) is the mean course of infection. Using this probability function in (1.23) implies that all of the infectives are recovered with no more infectivity after time period \( \tau \), but have the same infectivity during the course of infection, \( 0 < t < \tau \).

Based on \( P(t) \) in (1.23), we know

\[
P(t-u) = \begin{cases} 
1 & \text{for } 0 \leq t-u < \tau, \\
0 & \text{for } t-u \geq \tau,
\end{cases}
\]

or

\[
P(t-u) = \begin{cases} 
1 & \text{for } t - \tau < u \leq t, \\
0 & \text{for } 0 \leq u \leq t - \tau.
\end{cases}
\]

Notice \( I_0 P(t) = 0 \) when \( t \geq \tau \). Then Eq. (1.22) becomes

\[
I(t) = \int_0^t \beta S(u)I(u)P(t-u)du = \int_{t-\tau}^t \beta S(u)I(u)du,
\]

for \( t \geq \tau \), where \( I(0) = \int_{-\tau}^0 \beta S(u)I(u)du \) is required to ensure the continuity of \( I(0) \). Taking the derivatives of both sides of Eq. (1.24) with respect to \( t \), we obtain

\[
\frac{dI}{dt} = \beta S(t)I(t) - \beta S(t-\tau)I(t-\tau).
\]

Equation (1.25) is an ordinary differential equation with time delay \( \tau \), which is also called a differential-difference equation, a special but important form of functional differential equations. The reader is referred to Bellman and Cooke (1963), Hale (1977), and Kuang (1993).

The biological meaning of Eq. (1.25) is clear. \( \beta S(t)I(t) \) is the number of secondary infections who were infected at time \( t \) per unit of time, \( \beta S(t-u)I(t-u) \) is the number of secondary infections who were infected at time \( t-u \) per unit of time. Since all the infectives are recovered after time period \( \tau \), and there are no birth and death considered, the rate of change of infectives, that is, the recovery rate of the infectives at time \( t \) should be the difference between \( \beta S(t)I(t) \) and \( \beta S(t-u)I(t-u) \). Therefore, Eq. (1.25) can be also formulated directly according to its biological meaning. In this way, if the vital factors of the population are not considered, then the SIS
model with fixed course of infection is

\[
\frac{dS}{dt} = -\beta S(t)I(t) + \beta S(t-\tau)I(t-\tau),
\]
\[
\frac{dI}{dt} = \beta S(t)I(t) - \beta S(t-I)I(t-\tau).
\] (1.26)

If the natural death rate coefficient \(\mu\) and the disease-induced death rate coefficient \(\alpha\) are included in the model, then the recovery rate of the infectives at time \(t\) is \(\beta S(t-\tau)I(t-\tau)e^{-(\mu+\alpha)\tau}\), where the factor \(e^{-(\mu+\alpha)\tau}\) is the probability that the infectives survive during the time period \(\tau\). Then, in this case, model (1.26) becomes

\[
\frac{dS}{dt} = -\beta S(t)I(t) - \mu S(t) + \beta S(t-\tau)I(t-\tau)e^{-(\mu+\alpha)\tau},
\]
\[
\frac{dI}{dt} = \beta S(t)I(t) - (\mu + \alpha)I(t) - \beta S(t-I)I(t-\tau)e^{-(\mu+\alpha)\tau}.
\] (1.27)

Models with distributed delay. The case that all the individuals have the same course of infection is special. Usually, the course of infection varies. Assume \(P(\tau)\) is the probability that individuals were infected at time \(t=0\) and have not recovered at time \(t=\tau\). Then \(P(0) = 1\) and \(\beta S(t-\tau)I(t-\tau)e^{-(\mu+\alpha)\tau}\) is the number of those individuals who were infected during the time period \([t-(\tau+d\tau), t-\tau]\) and still remain in the infected compartment at time \(t\). Hence the number of the total infectives at time \(t\) is

\[
I(t) = \int_{0}^{+\infty} \beta S(t-\tau)I(t-\tau)P(\tau)d\tau
= \int_{-\infty}^{t} \beta S(u)I(u)P(t-u)du.
\] (1.28)

Assume \(P(\tau)\) is differentiable and define \(f(\tau) := -P'(\tau)\). Then, by differentiating (1.28), we have

\[
\frac{dI}{dt} = \beta S(t)I(t) + \int_{-\infty}^{t} \beta S(u)I(u)P'(t-u)du
= \beta S(t)I(t) - \int_{0}^{+\infty} \beta S(t-\tau)I(t-\tau)f(\tau)d\tau,
\]
and we arrive at the corresponding SIS model described by

\[
\frac{dS}{dt} = -\beta S(t)I(t) + \int_{0}^{+\infty} \beta S(t-\tau)I(t-\tau)f(\tau)d\tau,
\]

\[
\frac{dI}{dt} = \beta S(t)I(t) - \int_{0}^{+\infty} \beta S(t-\tau)I(t-\tau)f(\tau)d\tau.
\]

Here we notice that \(\int_{0}^{+\infty} f(\tau)d\tau = \int_{0}^{+\infty} [-P'(\tau)]d\tau = 1\), and \(\int_{0}^{+\infty} \tau P(\tau)d\tau\) is the course of infections.

Similarly to the case with discrete delays, if the natural death rate coefficient \(\mu\) and the disease-induced death rate coefficient \(\alpha\) are included in the model, then the corresponding SIS model becomes

\[
\frac{dS}{dt} = -\beta S(t)I(t) - \mu S(t) + \int_{0}^{+\infty} \beta S(t-\tau)I(t-\tau)f(\tau)e^{-\left(\mu + \alpha\right)\tau}d\tau,
\]

\[
\frac{dI}{dt} = \beta S(t)I(t) - (\mu + \alpha)I(t) - \int_{0}^{+\infty} \beta S(t-\tau)I(t-\tau)f(\tau)e^{-\left(\mu + \alpha\right)\tau}d\tau.
\]

**Epidemic models based on integral equations.** Integral equation (1.28) can be used directly to formulate epidemic models. For example, suppose that the input rate of a population is \(A\), the natural and disease-induced death-rate coefficients are \(\mu\) and \(\alpha\), respectively, the probability that those infectives who were infected at time \(u\), \(u \leq t\), and after time period \(t - u\) still remain in the infective compartment at time \(t\) in the absence of death, is \(P(t - u)\), satisfying \(P(t - u)|_{u=0} = 1\), and \(\int_{0}^{+\infty} P(t - u)du = \tau\), the mean course of infection. Then the number of individuals, who had been infected during the time interval \([0, t]\), remain in the infective compartment, and are still alive at time \(t\), is \(\int_{0}^{t} \beta S(u)I(u)P(t - u)e^{-\left(\mu + \alpha\right)(t-u)}du\). Since the number of individuals who were already infective at \(t = 0\), remain in the infective compartment, and are still alive at time \(t\), is \(I_{0}P(t)e^{-\left(\mu + \alpha\right)t}\), the total number of infectives who are alive at time \(t\) is

\[
I(t) = I_{0}P(t)e^{-\left(\mu + \alpha\right)t} + \int_{0}^{t} \beta S(u)I(u)P(t - u)e^{-\left(\mu + \alpha\right)(t-u)}du.
\]

Let \(N(t) = I(t) + S(t)\) be the total number of individuals in the population at time \(t\). Due to recruitment and deaths, the rate of change of
the population size is
\[ \frac{dN}{dt} = A - \mu N(t) - \alpha I(t). \]

Formally solving this equation, we obtain
\[ N(t) = N_0 e^{-\mu t} + \int_0^t [A - \alpha I(u)]e^{-\mu(t-u)}du. \]

Hence, the SIS model with population dynamics can be expressed in terms of the following integral equations:
\[ I(t) = I_0 P(t)e^{-(\mu+\alpha)t} + \int_0^t \beta [N(u) - I(u)]P(t-u)e^{-(\mu+\alpha)(t-u)}du, \]
\[ N(t) = N_0 e^{-\mu t} + \int_0^t [A - \alpha I(u)]e^{-\mu(t-u)}du. \]

### 1.4.2.2. Examples of models with time delay

**SIS model with birth and death and a constant period of recovery.**
Suppose that the birth rate of the population is constant, denoted by \( A \), and the natural death rate is \( \mu N \). For convenience, we let \( K := A/\mu \). Then we have
\[ \frac{dN}{dt} = \mu K - \mu N = \mu (K - N). \]

We can see that \( K = A/\mu \) is the carrying capacity of the environment for the population such that the population stops growing when \( N = K \) and decays when \( N > K \).

An SIS model usually consists of compartments of susceptibles \( S \) and infectives \( I \). Since \( S(t) + I(t) = N(t) \), it can be convenient, in some cases, if we choose either \( S \) or \( I \), in addition to \( N \), as variables.

We consider a case where there is neither disease-induced death nor vertical transmission. Let the course of infection, that is, the period of recovery, be constant, denoted by \( \tau \). Then the individuals, who were infected at time \( t - \tau \), recover at time \( t \). On the other hand, there are individuals who were infected at time \( t - \tau \), are alive and recovered at time \( t \) is \( \beta I(t-\tau)S(t-\tau)e^{-\mu \tau} \). Then the SIS model, based on
these assumptions, is described by the following system:

\[
\frac{dI}{dt} = \beta I(t)[N(t) - I(t)] - \beta I(t - \tau) \\
\times [N(t - \tau) - I(t - \tau)]e^{-\mu\tau} - \mu I(t),
\]

\[
\frac{dN}{dt} = \mu[K - N(t)].
\]

If the disease-induced death, with coefficient \(\alpha\), is considered in the model, the model equations become

\[
\frac{dI}{dt} = \beta I(t)[N(t) - I(t)] - \beta I(t - \tau) \\
\times [N(t - \tau) - I(t - \tau)]e^{-(\mu+\alpha)\tau} - (\mu + \alpha)I(t),
\]

\[
\frac{dN}{dt} = \mu[K - N(t)] - \alpha I(t),
\]

or, in terms of variables \(S\) and \(I\),

\[
\frac{dS}{dt} = \mu[K - S(t)] - \beta S(t)I(t) + \beta S(t - \tau)I(t - \tau)e^{-(\mu+\alpha)\tau},
\]

\[
\frac{dI}{dt} = \beta S(t)I(t) - \beta S(t - \tau)I(t - \tau)e^{-(\mu+\alpha)\tau} - (\mu + \alpha)I(t).
\]

The basic reproductive number for model (1.29) is

\[
R_0 = \frac{\beta K[1 - e^{-(\mu+\alpha)\tau}]}{\mu + \alpha}.
\]

Instead of a constant input, if the birth rate of the population is proportional to the population size, \(bN(t)\), and the standard incidence is chosen, then the SIS model becomes

\[
\frac{dS}{dt} = bN(t) - \mu S(t) - \beta S(t)I(t) - \beta S(t - \tau)I(t - \tau)e^{-(\mu+\alpha)\tau},
\]

\[
\frac{dI}{dt} = \frac{\beta S(t)I(t)}{N(t)} - (\mu + \alpha)I(t) - \frac{\beta S(t - \tau)I(t - \tau)}{N(t - \tau)}e^{-(\mu+\alpha)\tau}.
\]

In case where there exists vertical transmission, then the birth rate \(bN(t)\) will be divided into two parts, \(bS(t)\) and \(bI(t)\), which will be added to the equations of \(dS/dt\) and \(dI/dt\), respectively.
SEIR model with constant latent period $\omega$ and constant course of infection $\tau$. Notice that the individuals in the compartment $I$ are the infectives with infectivity, whereas the individuals in the compartment $E$ are infectives without infectivity. An individual who enters compartment $I$ at time $t$ should have been infected at time $t - \omega$, and an individual who recovers at time $t$ should enter the compartment $I$ at time $t - \tau$, and been infected at time $t - \omega - \tau$. Hence, if the birth rate of the population is $A := \mu K$, the natural death rate coefficient is $\mu$, the disease-induced death rate coefficient is $\alpha$, and there is no vertical transmission, then the corresponding SEIR model is

\[
\begin{align*}
\frac{dS}{dt} &= \mu[K - S(t)] - \beta S(t)I(t), \\
\frac{dE}{dt} &= \beta S(t)I(t) - \beta S(t - \omega)I(t - \omega)e^{-\mu\omega} - \mu E(t), \\
\frac{dI}{dt} &= \beta S(t - \omega)I(t - \omega)e^{-\mu\omega} - \beta S(t - \omega - \tau) \\
&\quad \times I(t - \omega - \tau)e^{-\mu(\omega + \tau)}e^{-\alpha\tau} - (\mu + \alpha)I(t), \\
\frac{dR}{dt} &= \beta S(t - \omega - \tau)I(t - \omega - \tau)e^{-\mu(\omega + \tau)}e^{-\alpha\tau} - \mu R(t).
\end{align*}
\]

SIRS model with constant period of immunity. Suppose that the recovery and the immunity loss rate coefficients are $\gamma$ and $\delta$, respectively. Then the corresponding SIRS model is

\[
\begin{align*}
\frac{dS}{dt} &= \mu[K - S(t)] - \beta S(t)I(t) + \delta R(t), \\
\frac{dI}{dt} &= \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t), \\
\frac{dR}{dt} &= \gamma I(t) - \mu R(t) - \delta R(t),
\end{align*}
\]

where the other parameters are defined the same as before. This is a differential equation system without time delay. It follows from the immunity loss rate $\delta R$ that the proportion of immunity loss of the recovered individuals is distributed exponentially as $e^{-\delta t}$, and the mean period of immunity without death is $1/\delta$. 
If the period of immunity is a constant $\tau = 1/\delta$, then the corresponding model is described by the following time-delay system:

$$\frac{dS}{dt} = \mu [K - S(t)] - \beta S(t) I(t) + \gamma I(t - \tau)e^{-\mu \tau},$$

$$\frac{dI}{dt} = \beta S(t) I(t) - (\mu + \alpha + \gamma) I(t),$$

$$\frac{dR}{dt} = \gamma I(t) - \mu R(t) - \gamma I(t - \tau)e^{-\mu \tau}.$$

If the recovery period, that is, the course of infection without death, is also a constant, denoted by $\omega = 1/\gamma$, then the corresponding model becomes

$$\frac{dS}{dt} = \mu [K - S(t)] - \beta S(t) I(t) + \beta S(t - \tau - \omega)
\times I(t - \tau - \omega)e^{-\mu(\tau + \omega)}e^{-\alpha \omega},$$

$$\frac{dI}{dt} = \beta S(t) I(t) - \beta S(t - \omega) I(t - \omega)e^{-(\mu + \alpha)\omega} - (\mu + \alpha) I(t),$$

$$\frac{dR}{dt} = \beta S(t - \omega) I(t - \omega)e^{-(\mu + \alpha)\omega} - \mu R(t)
- \beta S(t - \tau - \omega) I(t - \tau - \omega)e^{-\mu(\tau + \omega)}e^{-\alpha \omega}.$$ (1.30)

It is straightforward to show that the basic reproductive number of model (1.30) is

$$R_0 = \frac{\beta K [1 - e^{-(\mu + \alpha)\omega}]}{\mu + \alpha}.$$ 

If more factors such as vertical transmission, latent period, density dependence of the population, or some measures of prevention and control for the disease are incorporated, the models become more complicated. Some of the examples will be given later.

### 1.4.3. Epidemic models with prevention, control, or treatment

Two effective methods, quarantine, and vaccination and treatment, are more widely used in controlling and preventing the spread of diseases. We explain the ideas of their modeling as follows.
1.4.3.1. Models with quarantine

Early studies on the effects of quarantine on disease transmissions were carried out by Feng and Thieme (1995), Nuno et al. (2005), and Wu and Feng (2000). In those papers, they introduce a quarantined compartment, $Q$, and assume that all the infectives go to the quarantined compartment before going to the recovery compartment $R$, or becoming susceptibles again. Hethcote et al. (2002) considered a more realistic case where a part of the infectives are quarantined, whereas the others, not quarantined, either enter the recovery compartment or go back to the susceptible compartment after treatment. They analyzed six SIQS and SIQR models with bilinear, standard, or quarantine-adjusted incidence, and found that only the SIQR model with quarantine-adjusted incidence might have a Hopf bifurcation, comparing to the other five models with disease-induced death, each of which has a globally stable disease-free or endemic equilibrium, and their necessary and sufficient stability conditions were obtained.

As an example, we consider an SIQR model with quarantine-adjusted incidence (Fig. 1.15).

In Fig. 1.15, $Q$ is the quarantine compartment. A part of the infectives are quarantined with the rate $\delta I$, and the rest of the infectives still remain unquarantined and are recovered with the rate $\gamma I$. We assume that the mean course of infection without death is $1/\gamma$, the mean period of quarantine without death is $1/\varepsilon$, and the disease-induced death rate coefficient for the individuals in $Q$ is $\alpha_1$, which is different from $\alpha$, in $I$, due to different treatments. Here we use the so-called quarantine-adjusted incidence $\beta SI/(N - Q) \equiv \beta SI/(S + I + R)$, instead of the standard incidence $\beta SI/N$, because the individuals in the quarantine compartment

\[
\begin{align*}
A & \quad S \\
& \quad \mu S
\end{align*}
\]

\[
\begin{align*}
& \quad I
\end{align*}
\]

\[
\begin{align*}
& \quad Q
\end{align*}
\]

\[
\begin{align*}
& \quad R
\end{align*}
\]

\[
\begin{align*}
\delta I & \quad \gamma I \\
& \quad \mu I \\
& \quad \alpha I \\
& \quad \mu Q \\
& \quad \alpha_1 Q \\
& \quad \mu R
\end{align*}
\]

Fig. 1.15. Flow chart of the SIQR model with quarantine-adjusted incidence.
Q cannot contact others. Thus the corresponding model is

\[
\begin{align*}
\frac{dS}{dt} &= A - \frac{\beta SI}{S + I + R} - \mu S, \\
\frac{dI}{dt} &= \frac{\beta SI}{S + I + R} - (\mu + \alpha + \gamma + \delta)I, \\
\frac{dQ}{dt} &= \delta I - (\mu + \alpha_1 + \varepsilon)Q, \\
\frac{dR}{dt} &= \gamma I + \varepsilon Q - \mu R.
\end{align*}
\]

(1.31)

The quarantine reproductive number \( R_q \) for model (1.31) is defined as

\[
R_q = \frac{\beta}{\mu + \alpha + \gamma + \delta}.
\]

1.4.3.2. Models with vaccination

Vaccination is considered to be the most effective and cost-effective method of preventing infectious diseases. To model transmission dynamics of diseases with vaccines, ordinary differential equations, delay differential equations, and pulse differential equations are often used. Here, we introduce ideas for the modeling based on the first two kinds of equations as follows, and consider the pulse differential equations models later. The reader for further details are referred to Li et al. (2006) and Li and Ma (2002, 2003, 2004a, 2006a).

Ideas for the modeling. In general, we can use SIR models to describe the transmission dynamics of the diseases if the vaccination leads to permanent immunity. For example, we assume that a portion of susceptibles, \( pS \), go to the removed compartment \( R \) directly, due to permanent immunity obtained from vaccination. The model flow chart is shown in Fig. 1.16.

In case where the vaccination leads to only temporary immunity — that is, vaccinated individuals lose their immunity and become susceptibles again after a period of time — and if we use SIRS models to describe the transmission dynamics of the diseases, it implies that we assume the same probability for immunity loss for recovered and vaccinated individuals.
However, the two rates are different in most cases. Then, one of the modeling ideas is to introduce another compartment $V$ which consists of the vaccinated susceptibles. A flow chart of a such model is given in Fig. 1.17.

The corresponding model equations are

$$\frac{dS}{dt} = A - \mu S - \beta SI - pS + \delta_1 R + \delta_2 V,$$

$$\frac{dI}{dt} = \beta SI - (\mu + \alpha + \gamma) I,$$

$$\frac{dR}{dt} = \gamma I - \mu R - \delta_1 R,$$

$$\frac{dV}{dt} = pS - \mu V - \delta_2 V,$$

(1.32)

where constants $1/\delta_1$ and $1/\delta_2$ are the periods of immunity of the recovereds and vaccinated susceptibles, respectively.

**SIS-VS models.** Figure 1.18 is the flow chart of an SIS-VS model, where $V$ is the compartment of vaccinated individuals, where we assume that the
vaccination is given to both the newborns and the susceptibles. We use $A$ to represent the birth rate, $q$ the fraction of the vaccinated newborns, so that $qA$ enters compartment $V$, while the rest of newborns $(1-q)A$ enters compartment $S$, and $p$ the fraction of the vaccinated susceptibles. We assume that the vaccinated individuals have temporary immunity and $Q(t)$ is the probability that a vaccinated individual remains in the compartment $V$ at least $t$ time units before returning to the compartment $S$, so that $1-Q(t)$ is the probability of those vaccinated individuals who lose immunity within $t$ time units. The corresponding model is then described by the following system:

$$
\frac{dI}{dt} = \beta SI - (\mu + \alpha + \gamma)I,
$$

$$
V(t) = V_0(t) + \int_0^t [qA + pS(u)]Q(t-u)e^{-\mu(t-u)}du,
$$

$$
\frac{dN}{dt} = A - \mu N - \alpha I,
$$

$$
N = S + I + V
$$

where $V_0(t)$ is the number of the individuals who were vaccinated before $t = 0$ and are still alive and remain immune until time $t$, and $\int_0^t [qA + pS(u)]Q(t-u)e^{-\mu(t-u)}du$ are the individuals who were vaccinated in the time period $(0, t]$ and are still alive and remain immune until time $t$.

Suppose we have $Q(t)$ as an exponential distribution with $Q(t) = e^{-\delta t}$. Then

$$
V_0(t) = V_0(0)e^{-\delta t}e^{-\mu t} = V_0(0)e^{-(\mu + \delta)t},
$$
and model (1.33) can be written as

\[
\frac{dI}{dt} = pSI - (\mu + \alpha + \gamma)I,
\]

\[
V(t) = V_0(0)e^{-(\delta + \mu)t} + \int_0^t [qA + pS(u)]e^{-(\mu + \delta)(t-u)}\mu u,
\]

\[
\frac{dN}{dt} = A - \mu N - \alpha I,
\]

or

\[
\frac{dS}{dt} = (1-q)A - \beta SI - (p + \mu)S + \gamma I + \delta V,
\]

\[
\frac{dI}{dt} = \beta SI - (\mu + \alpha + \gamma)I,
\]

\[
\frac{dV}{dt} = qA + pS - (\delta + \mu)V,
\]

\[
\frac{dN}{dt} = A - \mu N - \alpha I.
\]

In system (1.35), the third equation is obtained by differentiating both sides of the second equation in system (1.34), and the first equation is derived from the last three equations in (1.35) according to its biological definition. The vaccination reproductive number of the model (1.35) is defined as

\[
R_v = \frac{A}{\mu} \frac{\beta[\xi + \mu(1-q)]}{(\mu + \gamma + \alpha)(\mu + \delta + p)}.
\]

If we take \(Q(t)\) as a step function

\[
Q(t) = \begin{cases} 
1 & \text{for } t \in [0, \tau), \\
0 & \text{for } t \geq \tau,
\end{cases}
\]

where \([0, \tau)\) is the period of immunity, which means that the period of immunity is uniformly distributed for all the vaccinated individuals, and all the vaccinated individuals lose their immunity and become susceptible.
again after time $\tau$. In this case, model (1.33) becomes

$$\frac{dI}{dt} = \beta SI - (\mu + \alpha + \gamma)I,$$

$$V(t) = \int_{t-\tau}^{t} [qA + pS(u)] e^{-\mu(t-u)}du, \quad \text{for } t \geq \tau,$$

(1.36)

$$\frac{dN}{dt} = A - \mu N - \alpha I,$$

where

$$Q(t-u) = \begin{cases} 1 & \text{for } t-\tau < u \leq t, \\ 0 & \text{for } 0 \leq u \leq t-\tau, \end{cases}$$

and the function $V_0(t)$ in system (1.33) vanishes for $t \geq \tau$, where $V(0) = \int_{-\tau}^{0} [qA + pS(u)] e^{\mu u}du$ is imposed to ensure the continuity of $V(t)$. Similarly to system (1.35), system (1.36) can be written as a differential equations system with time delay:

$$\frac{dS}{dt} = (1-q)A - (p+\mu)S(t) - \beta S(t)I(t)$$

$$+ \gamma I(t) + [qA + pS(t-\tau)]e^{-\mu \tau},$$

$$\frac{dI}{dt} = \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t),$$

(1.37)

$$\frac{dV}{dt} = qA + pS(t) - [qA + pS(t-\tau)]e^{-\mu \tau} - \mu V(t),$$

$$\frac{dN}{dt} = A - \mu N(t) - \alpha I(t).$$

The vaccination reproductive number of the model (1.37) is defined as

$$R_v = \frac{\beta A [1 - q(1 - e^{-\mu \tau})]}{(\mu + \alpha + \gamma) [\mu + p(1 - e^{-\mu \tau})]}.$$

**SIR-VS and SIRS-VS models.** Figure 1.19 is the flow chart for an SIR-VS model, where we assume that only the susceptibles are vaccinated with temporary immunity, and that the recovereds have permanent immunity.
The corresponding model is described by the system

\[
\frac{dI}{dt} = \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t),
\]

\[
\frac{dR}{dt} = \gamma I(t) - \mu R(t),
\]

\[
V = V_0(t) + \int_0^t pS(u)Q(t-u)e^{-\mu(t-u)}du,
\]

\[
\frac{dN}{dt} = A - \mu N(t) - \alpha I(t),
\]

where \(V_0(t)\) is the individuals who were vaccinated before \(t = 0\) and stay in the vaccination compartment until time \(t\).

The model shown in Fig. 1.17 can be generalized to the SIRS-VS model as shown in Fig. 1.20.

---

**Fig. 1.19.** Flow chart for an SIR-VS model.

**Fig. 1.20.** Flow chart for a more general SIRS-VS model.
The corresponding model equations are

\[ \frac{dI}{dt} = \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t), \]

\[ R = R_0(t) + \int_0^t \gamma I(u)Q_1(t-u)e^{-\mu(t-u)}du, \]

\[ V = V_0(t) + \int_0^t pS(u)Q_2(t-u)e^{-\mu(t-u)}du, \]

\[ \frac{dN}{dt} = A - \mu N(t) - \alpha I(t). \]

(1.38)

If the probability function \( Q_i \) has the form of \( e^{-\delta_i t}, \ i = 1, 2 \), we have \( R_0(t) = R_0(0)e^{-\delta_1 t}e^{-\mu t} \) and \( V_0(t) = V_0(0)e^{-\delta_2 t}e^{-\mu t} \). Then the time-delayed equations in (1.38) are reduced to the ordinary differential equations in (1.32). If the probability function \( Q_i \) is a step function

\[ Q_i(t) = \begin{cases} 1 & \text{for } t \in [0, \tau_i), \\ 0 & \text{for } t \geq \tau_i, \end{cases} \ i = 1, 2, \]

then, for \( t \geq \tau_i \) the second and third equations in (1.38) become

\[ R(t) = \int_{t-\tau_i}^t \gamma I(u)e^{-\mu(t-u)}du, \]

\[ V(t) = \int_{t-\tau_2}^t pS(u)e^{-\mu(t-u)}du. \]

Similarly as in (1.36), the initial conditions

\[ R(0) = \int_{-\tau_1}^0 \gamma I(u)e^{\mu u}du \quad \text{and} \quad V(0) = \int_{-\tau_2}^0 pS(u)e^{\mu u}du \]

are imposed.
Differentiating both sides of the equations for $R$ and $V$ in (1.38), we obtain the following system with time delay:

\[
\begin{align*}
\frac{dI}{dt} &= \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t), \\
\frac{dR}{dt} &= \gamma I(t) - \mu R(t) - \gamma I(t - \tau_1)e^{-\mu\tau_1}, \\
\frac{dV}{dt} &= pS(t) - \mu V(t) - pS(t - \tau_2)e^{-\mu\tau_2}, \\
\frac{dN}{dt} &= A - \mu N(t) - \alpha I(t), \\
\frac{dS}{dt} &= A - \beta S(t)I(t) - \mu S(t) - pS(t) \\
&\quad + \gamma I(t - \tau_1)e^{-\mu\tau_1} + pS(t - \tau_2)e^{-\mu\tau_2},
\end{align*}
\]

or

\[
\begin{align*}
\frac{dI}{dt} &= \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t), \\
\frac{dR}{dt} &= \gamma I(t) - \mu R(t) - \gamma I(t - \tau)e^{-\mu\tau}, \\
\frac{dV}{dt} &= pS(t) - \mu V(t) - pS(t - \tau_2)e^{-\mu\tau_2}.
\end{align*}
\]

**SIS models with vaccination and vaccine efficacy.** In the models discussed above, we assumed that the vaccines have full efficacy, but in reality, the efficacy of a vaccine is usually not 100%. Hence, we need to take this into account when we formulate epidemic models with vaccination.

We give an example whose flow chart is shown in Fig. 1.21, where we suppose that the birth rate coefficient is $r$, the natural death rate coefficient depends on the population size $N$, denoted by $f(N)$, the vaccination is given to both newborns and susceptibles; standard incidence is chosen, the mean period of immunity without death is $1/\delta$, and the vaccine is not completely efficacious and $\sigma(0 \leq \sigma \leq 1)$ describes the inefficaciousness of the vaccine such that the infection incidence from the inefficaciously vaccinated individuals is $\sigma\beta VI/N$. 

---

DYNASTICAL MODELING AND ANALYSIS OF EPIDEMICS
© World Scientific Publishing Co. Pte. Ltd.
http://www.worldscibooks.com/medsci/6799.html
The model of corresponding to Fig. 1.21 is given by
\[
\begin{align*}
\frac{dS}{dt} &= bN - \beta \frac{SI}{N} - [p + f(N)]S + \gamma I + \varepsilon V, \\
\frac{dI}{dt} &= \beta \frac{SI}{N} + \sigma \beta \frac{VI}{N} - [\gamma + \alpha + f(N)]I, \\
\frac{dV}{dt} &= pS - \sigma \beta \frac{VI}{N} - [\varepsilon + f(N)]V, \\
\frac{dN}{dt} &= [b - f(N)]N - \alpha I.
\end{align*}
\]

The modified reproductive number of model (1.39) is defined as
\[
R_v = \frac{\beta (\varepsilon + \sigma p + b)}{(\alpha + b + \gamma)(p + b + \varepsilon)}.
\]

1.4.3.3. Models with treatment

In classic epidemic models, the treatment rate of the infectives is assumed to be proportional to the number of the infectives. This is based on the assumption of sufficient resource available for treatment when the number of the infectives is large. Nevertheless, this involves the best strategy or optimal available resource for treatment for every community. A community wastes resource for treatment if the resource is prepared for too large, but may have a risk of an outbreak of a disease if the available resource is too small. Thus, it is important to determine optimal resource supplies, or capacity, for the treatment of a disease.
Suppose that the capacity for the treatment of a disease in a community is a constant and the recovery rate coefficient due to the treatment is \( r \). We further assume that the treatment rate is proportional to the number of the infectives when the capacity of the treatment has not been reached, and saturates to a constant when the number of the infectives is so large that the capacity of the treatment is exceeded. With these assumptions, the following SIR model was constructed [Wang (2006b)] as

\[
\begin{align*}
    \frac{dS}{dt} &= A - \mu S - \beta SI, \\
    \frac{dI}{dt} &= \beta SI - (\mu + \gamma + T(I))I, \\
    \frac{dR}{dt} &= \gamma I + T(I) - \mu R,
\end{align*}
\]

(1.40)

where

\[
T(I) = \begin{cases} 
    rI, & \text{if } 0 \leq I \leq I_0, \\
    rI_0, & \text{if } I > I_0,
\end{cases}
\]

(1.41)

is the recovery rate due to the treatment and \( \gamma I \) is recovery rate due to other reasons. \( I_0 \) reflects the capacity of the treatment. The investigation of the effects of \( I_0 \) on the transmission dynamics was investigated [Wang (2006b)], and is shown in Sec. 2.6.3.

1.4.4. **Epidemic models with multiple groups**

If a disease is transmitted among multiple interactive populations or multiple subpopulations of a population, then the number of variables is increased, and the structure of the models becomes more complex. Hence the analysis becomes more difficult and new dynamic features may appear. We introduce some modeling ideas below.

1.4.4.1. **Models with different subgroups**

**DS-SIR model with differential susceptibility.** Many mechanisms lead to differential susceptibility (DS). For example, genetic variation of susceptible individuals may lead to their differentiation of susceptibility to infection. The efficacy of available vaccinations for many infectious diseases is not perfect. Vaccinated individuals may still contract the disease and
the susceptibility varies from individual to individual. To address the DS in modeling of infectious diseases, DS models are formulated where the susceptible population is partitioned into $n$ subgroups, $S_i$, $i = 1, \ldots, n$, according to their susceptibilities. It is assumed that the input rate of each subgroup $S_i$ is $\mu S_0^i$, and the incidence is $\beta k_i S_i I / N$, where $k_i$, $i = 1, \ldots, n$, characterizes the susceptibility of individuals in the subgroup $S_i$ [Hyman and Li (2005)]. The flow chart of DS models is given in Fig. 1.22.

The corresponding model equations are

$$
\frac{dS_i}{dt} = \mu (S_0^i - S_i) - \frac{\beta k_i S_i I}{N}, \quad i = 1, 2, \ldots, n,
$$

$$
\frac{dI}{dt} = \sum_{i=1}^{n} \frac{\beta k_i S_i I}{N} - (\mu + \alpha + \gamma) I,
$$

$$
\frac{dR}{dt} = \gamma I - dR.
$$

The basic reproductive number of (1.42) is defined as

$$
R_0 = \frac{\beta \sum_{i=1}^{n} k_i S_0^i}{(\mu + \alpha + \gamma) \sum_{i=1}^{n} S_0^i}.
$$

Fig. 1.22. Flow chart of the DS-SIR model.
SIR models with variations in infectiousness. In the studies of the transmission dynamics of HIV, two fundamental hypotheses for variations in infectiousness have been employed. Based on other clinical findings and blood serum level studies, the differential infectivity (DI) hypothesis assumes that the population of infectives is divided into several groups, depending on their infectivity. Infected individuals enter one of the groups and stay in that group until they develop AIDS. Another hypothesis is the staged-progression (SP) hypothesis, in which the infected individuals sequentially pass through a series of stages, being highly infectious in the first few weeks after their own infection, then having low infectivity for many years, and finally becoming gradually more infectious as their immune system breaks down and they progress to AIDS. Both deterministic DI and SP models have been formulated and studied to understand the impact of the DI and the disease progression on the spread of HIV. (See [Hyman et al. (1999); Hyman and Li (2000); Ma et al. (2003)] and references therein.)

In a DI model, it is assumed that individuals in each infective compartment $I_i$ contact susceptibles with different adequate contact rate. However, the secondary infectives infected by the infectives in $I_i$ are not necessarily belong to the same infective compartment $I_i$, and the probability that the total secondary infections enter to the compartment $I_i$ is $p_i$ ($\sum_{i=1}^{n} p_i = 1$). The flow chart of a DI model is shown in Fig. 1.23.

![Flow chart of the DI-SIR model.](image-url)
The corresponding model equations are
\[
\begin{align*}
\frac{dS}{dt} &= \mu(S^0 - S) - \lambda S, \\
\frac{dI_i}{dt} &= p_i \lambda S - (\mu + \alpha_i + \gamma_i)I_i, \quad i = 1, 2, \ldots, n, \\
\frac{dR}{dt} &= \sum_{i=1}^{n} \gamma_i I_i - \mu R,
\end{align*}
\]
where
\[
\lambda = \sum_{i=1}^{n} \frac{\beta_i I_i}{N}, \quad N = S + \sum_{k=1}^{n} I_k.
\]

The basic reproductive number of infection for the DI model in (1.43) is defined as
\[
R_0 = S^0 \sum_{i=1}^{n} \frac{\beta_i p_i}{\mu + \alpha_i + \gamma_i}.
\]

In an SP model, infectives sequentially pass through a series of stages, which implies that this model is a Markov chain model, and hence the population of infectives is divided into subgroups, \( I_i \) (\( i = 1, 2, \ldots, n \)), with different infection stages such that infected susceptible individuals enter the first subgroup \( I_1 \) and then gradually progress from subgroup \( I_1 \) finally to subgroup \( I_n \). The infectives in stage \( I_i \) contact the susceptibles and the incidence of \( I_i \) is \( \beta_i S I_i \). (See [Hyman et al. (1999); Hyman and Li (2000)] for details.) The flow chart of an SP model is shown in Fig. 1.24.

The corresponding model equations are
\[
\begin{align*}
\frac{dS}{dt} &= \mu S^0 - \lambda S - \mu S, \\
\frac{dI_1}{dt} &= \lambda S - (\mu + \alpha_1 + \gamma_1)I_1, \\
\frac{dI_i}{dt} &= \gamma_{i-1} I_{i-1} - (\mu + \alpha + \gamma_i)I_i, \quad i = 2, \ldots, n, \\
\frac{dR}{dt} &= \gamma_n I_n - \mu R,
\end{align*}
\]
where
\[ \lambda = r \sum_{i=1}^{n} \frac{\beta_i I_i}{N}, \quad N = S + \sum_{k=1}^{n} I_k, \]
and \( r \) is the number of contacts. The basic reproductive number of infection for the SP model in Sec. 1.4.4.1 is defined as
\[ R_{S0}^S = r \sum_{k=1}^{n} \frac{\beta_k q_k}{\gamma_k + \mu}, \]
where
\[ q_i := \prod_{j=1}^{i-1} \frac{\gamma_j}{\mu + \gamma_j}. \]

**SIS models with differential susceptibilities and infectivities.**
There are also cases in which diseases are transmitted among both different susceptible groups and different infective groups. We briefly describe a DS-DI model as follows. The reader is referred to [Hyman and Li (2006)] for further details.

We consider the spread of a disease in a randomly mixing population that approaches a steady state, \( S^0 \), if there is no disease infection. We assume that infected individuals become fully immune or are removed from the susceptible population after they recover from the infection. We approximate the transmission dynamics with an SIR model. We assume that susceptibles may have different susceptibility and divide them into \( n \) groups, \( S_1, S_2, \ldots, S_n \). Here, the individuals in each group have homogeneous susceptibility, but the susceptibilities of individuals from different groups are distinct. The susceptibles are distributed into the \( n \) susceptible subgroups, based on their inherent susceptibility, in such a way that the input flow into group \( S_i \) is \( p_i \mu S^0 \) with \( \sum_{i=1}^{n} p_i = 1 \). The infectives are divided into \( m \) groups, \( I_1, I_2, \ldots, I_m \), such that a susceptible individual in group \( S_i \) can be infected by infectives in all groups, and upon infection, enters group \( I_j \) with probability \( q_{ij} \) and stays in this group until becoming recovered or removed, where \( \sum_{j=1}^{m} q_{ij} = 1 \), for \( i = 1, 2, \ldots, n \).
We assume full immunity of recovered individuals or complete isolation after individuals are infected and diagnosed, and we group all these individuals to group $R$. The transmission dynamics of infection are governed by the system of differential equations

$$\frac{dS_i}{dt} = \mu(p_iS^0 - S_i) - \lambda_iS_i, \quad i = 1, \ldots, n,$$

$$\frac{dI_j}{dt} = \sum_{i=1}^{n} q_{ij}\lambda_iS_i - (\mu + \delta_j + \nu_j)I_j, \quad j = 1, \ldots, m,$$

$$\frac{dR}{dt} = \sum_{j=1}^{m} \nu_jI_j - (\mu + \delta_r)R,$$

where $\mu$ is the natural death rate coefficient in the absence of infection, $\nu_j$ is the recovery or removal rate coefficient for infectives in group $I_j$, and $\delta_j$ and $\delta_r$ are the disease-induced death rate coefficients. The rate of infection for susceptibles in group $S_i$ is given by

$$\lambda_i = c(N)\sum_{j=1}^{m} \alpha_i\beta_j I_j = \frac{c(N)}{N} \alpha_i \sum_{j=1}^{m} \beta_j I_j,$$

where $c(N)$ is the contacts rate with $N = \sum_{i=1}^{n} S_i + \sum_{j=1}^{m} I_j + R$, $\alpha_i$ is the susceptibility of susceptible individuals in group $S_i$, and $\beta_j$ is the infectiousness of infected individuals in group $I_j$. The choice of the function $c(N)$ depends on the modeled disease or situations investigated.

The reproductive number of infection for model (1.44) is defined as

$$R_0 = \sum_{i=1}^{n} p_i c(S^0)\alpha_i \sum_{j=1}^{m} q_{ij}\beta_j \mu + \delta_j + \nu_j.$$
Dynamical Modeling and Analysis of Epidemics

classified as one of the following three types of systems according to the relation between the two populations: predator-prey systems, competitive systems, and cooperative systems. We explain the concepts using the following simple but famous Volterra system:

\[
\begin{align*}
\frac{dx}{dt} &= x(r_1 - a_1 x - c_1 y), \\
\frac{dy}{dt} &= y(r_2 - a_2 x - c_2 y),
\end{align*}
\]  

(1.46)

where \( x \) and \( y \) are, respectively, the numbers of total individuals in the two populations, \( r_i = b_i - \mu_i, \ i = 1, 2, \) are the so-called intrinsic growth rate coefficients with \( b_i \) and \( \mu_i \) being the birth and death rate coefficients, \( a_1 \) and \( c_2 \) are the density dependence coefficients, which are both positive so that the two populations follow the logistic dynamics (see below) in the absence of interaction, and \( c_1 \) and \( a_2 \) are the interactive coefficients.

1. If \( c_1 > 0 \) and \( a_2 < 0 \), system (1.46) is a predator-prey system with \( x \) and \( y \) regarded as the numbers of prey and predators, respectively. Then, \( c_1 x \) is the number of prey eaten by one predator per unit of time at time \( t \), and is called the functional response of predators to prey. \(-a_2 xy\) is the production of predators per unit of time at time \( t \), which comes from the predation \( c_1 xy \). Here \(-a_2 = kc_1 \), with \( k \) being the transform rate coefficient from eating the prey to the production of the predator. The functional response \( c_1 x \) is proportional to the number of prey population size, which may not be appropriate if \( x \) is very large. Hence we sometimes consider the saturation of the predation, and use some other functional responses. The Holling-II functional response \( \phi(x) = ax/(1 + bx) \) is often used, and the ratio functional response \( \phi\left(\frac{x}{y}\right) = \frac{ax/y}{1 + bx/y} \)

is also used and even probably more appropriate in some cases.

2. If \( c_1 > 0 \) and \( a_2 > 0 \), system (1.46) is a competitive system. The two populations \( x \) and \( y \) compete for same limited resource in an environment such that the appearance of population \( x(y) \) affects the growth of the other population \( y(x) \).

3. System (1.46) is a cooperative system if \( c_1 < 0 \) and \( a_2 < 0 \). The two populations are cooperative with each other. The existence of population \( x(y) \) increase the growth of the other population \( y(x) \), as the cooperation between bees and flowers.
It should be pointed out that the density dependence affects not only the birth but also the death of the populations. Hence, we need to separate the effects of the density dependence, in some cases. For example, we may have

\[ a_1x^2 = a_1[p + (1 - p)]x^2, \]  

where the part \( p \) affects the birth rate and the part \( (1 - p) \) affects the death rate. Thus the first equation in model \( (1.46) \) can be rewritten as

\[ \frac{dx}{dt} = (b_1 - a_1px) - [\mu_1 + (1 - p)a_1x]x - cxy. \]

It also should be pointed out that without predation, the first equation in the system \( (1.46) \) can be written as

\[ \frac{dx}{dt} = x(r_1 - a_1x) = r_1x \left(1 - \frac{x}{K}\right) \]  

and is called the logistic equation, where \( K = r_1/a_1 \) is the carrying capacity of the environment to the population \( x \), that is the maximum size of the population the environment can support. This can be seen from the logistic equation that the population grows if \( x < K \), stops growing at \( x = K \), and decays if \( x > K \).

It follows from \( (1.47) \), logistic equation \( (1.48) \) can be rewritten as

\[ \frac{dx}{dt} = x \left[ (b_1 - prx/K) - \left(\mu_1 + (1 - p)rx/K\right) \right]. \]

This decomposition has been introduced by Gao and Hethcote (1992), which implies that population satisfies the logistic equation with the birth rate coefficient \( b_1 - prx/K \) and the death rate coefficient \( \mu_1 + (1 - p)rx/K \), where \( r = b_1 - \mu_1 > 0 \) and \( 0 \leq p \leq 1 \). The density dependence affects only the death when \( p = 0 \), the birth when \( p = 1 \), and both when \( 0 < p < 1 \).

**Disease spreads only in the prey population.** Anderson and May incorporated the spread of infectious disease into a predator–prey model in 1986. In that model, they assume that the disease is transmitted only within the prey species, and that the incidence is bilinear. The model is
given by the system
\[
\frac{dH}{dt} = rX - (\mu_1 + \alpha)Y - c[(1 - f)X + Y]P - \mu_1 X,
\]
\[
\frac{dY}{dt} = \beta XY - (\mu_1 + \alpha)Y - cYP,
\]
\[
\frac{dP}{dt} = \delta HP - \mu_2 P,
\]
where \( H \) is the prey population size, \( X \) and \( Y \) are the numbers of the susceptibles and infectives in the prey population, respectively, with \( H = X + Y \) and \( P \) is the predator population size. The parameters \( r, \mu_1, \) and \( \alpha \) are the birth, natural death, and disease-induced death rate coefficients of the prey population, respectively. The parameter \( \mu_2 \) is the natural death rate coefficient of the predators, \( \delta \) is the conversion rate coefficient of the prey to predator, and \( c \) the catching rate coefficient of the predators. The parameter \( f \) describes the catching difference between the susceptible and infected prey. It is assumed that the infected prey individuals have no fertility and incidence \( \beta XY \) is bilinear.

The results of their study show that the disease dies out when the prey population size \( H \) is reduced to a certain level \( H_T \) due to predation. Nevertheless, the predator population goes to extinct if the level \( H_T \) is too low. Moreover, it is shown that model (1.49) has a stable limit cycle which implies that the presence of the disease may result in a stable periodic oscillation of the two species.

Xiao and Chen (2001a, 2002a) investigated prey–predator models with a disease spreads only in the prey population, where time delays are included which describe the conversion of the prey to predator. The model equations [Xiao and Chen (2001a)] are
\[
\frac{dS}{dt} = rS \left( 1 - \frac{S + I}{K} \right) - \beta SI - p_1 SY,
\]
\[
\frac{dI}{dt} = \beta SI - cI - p_2 IY,
\]
\[
\frac{dY}{dt} = -dY + kp_1 S(t - \tau)Y(t - \tau) + kp_2 I(t - \tau)Y(t - \tau),
\]
where \( S \) and \( I \) are the numbers of susceptibles and infectives in the prey population and \( Y \) is the number of individuals in the predator population. The parameters \( K \) and \( r \) are the carrying capacity of the environment.
and the intrinsic growth rate of the prey population, \( c \) is the death rate coefficient of the infected prey, \( \mu \) is the nature death rate coefficient of the predators, \( p_1S \) and \( p_2I \) are the functional response of the predators to the susceptible and infective prey, respectively, \( \beta \) is the adequate contact rate coefficient for the prey population, and \( k \) is the conversion rate coefficient of the prey to predator.

Local stability of the equilibria of the models, stability switch caused by the time delay and Hopf bifurcation are investigated by Xiao and Chen (2001a, 2002a).

They also studied a ratio-dependent predator–prey model with disease in the prey and proved the existence of Hopf bifurcation and local stability for the model.

**Disease spreads in both predator and prey populations.** Hadeler and Freedman (1989) investigated a predator–prey model with disease spreading in both prey and predator populations, in which it is assumed that the predators are infected when swallowing the infected prey, and that the prey are infected by contacting the excrement of the infected predators. The model equations are given by

\[
\begin{align*}
\frac{dx_0}{dt} &= ax - a \frac{x_0 x}{K} - \frac{x_0}{A + x_0 + ex_1} y - \beta x_0 y_1, \\
\frac{dy_0}{dt} &= -c \frac{B}{B + A} y_0 + c \frac{x_0 + ex_1}{A + x_0 + ex_1} y - k \frac{ex_1}{A + x_0 + ex_1} y_0, \\
\frac{dx_1}{dt} &= \beta y_1 x_0 - \frac{ax_1 x}{K} - \frac{ex_1}{A + x_0 + ex_1} y, \\
\frac{dy_1}{dt} &= -c \frac{B}{B + A} y_1 + k \frac{ex_1}{A + x_0 + ex_1} y_0,
\end{align*}
\]

(1.50)

where \( x_0 \) and \( x_1 \) are the numbers of the susceptibles and infectives in prey population, \( y_0 \) and \( y_1 \) are the numbers of the susceptibles and infectives in predator population, \( x = x_0 + x_1 \) and \( y = y_0 + y_1 \) are the total sizes of the prey and predators, respectively, \( a \) is the birth rate coefficient of the prey population, \( K \) is the carrying capacity of the environment to the prey populations, \( cB/(B + A) \) is the natural death rate coefficient of the predator population, \( x_0/(A + x_0 + ex_1) \) and \( ex_1/(A + x_0 + ex_1) \) are the functional responses of predators to the susceptible and infected prey, respectively, constant \( e > 1 \) represents the fact that the infected prey are easier to be catched, \( c \) is the conversion rate coefficient from the prey to
Dynamical Modeling and Analysis of Epidemics

It is assumed that the infection of the prey population is caused by intraspecific contacts, and that of the predator population is caused by, in addition to intraspecific contacts, swallowing infected prey. As an example, we only present an SIS model with standard incidence described by the following system:

\[
\frac{dS_1}{dt} = \left( b_1 - a_1 r_1 N_1 \right) \frac{N_1}{K_1} - \left[ \mu_1 + (1 - a_1) \frac{r_1 N_1}{K_1} \right] S_1 - a N_2 S_1 - \beta_1 \frac{S_1}{N_1} I_1 + \gamma_1 I_1,
\]

\[
\frac{dI_1}{dt} = \beta_1 \frac{S_1}{N_1} I_1 - \gamma_1 I_1 - \left[ \mu_1 + (1 - a_1) \frac{r_1 N_1}{K_1} \right] I_1 - a N_2 I_1,
\]

\[
\frac{dN_1}{dt} = \left[ r_1 \left( 1 - \frac{N_1}{K_1} \right) - a N_2 \right] N_1,
\]

\[
\frac{dS_2}{dt} = k a N_1 N_2 - \alpha S_2 I_2 - \mu_2 S_2 - \beta_2 \frac{S_2 I_2}{N_2} + \gamma_2 I_2,
\]

\[
\frac{dI_2}{dt} = \beta_2 \frac{S_2 I_2}{N_2} - \mu_2 I_2 + \alpha \frac{S_2 I_1}{N_2} - \gamma_2 I_2,
\]

\[
\frac{dN_2}{dt} = (k a N_1 - \mu_2) N_2,
\]

\[
N_i = S_i + I_i, \quad i = 1, 2,
\]

\[
r_1 = b_1 - \mu_1 > 0, \quad 0 \leq a_1 \leq 1,
\]
where \(N_1\) and \(N_2\) are the population sizes of the prey and predators, respectively, \(a\) is the coefficient of predation, \(\beta_i, i = 1, 2\), are the adequate intraspecific contact rate coefficients, \(\alpha\) is the adequate interspecific contact rate coefficient, and \(k\) is the conversion rate coefficient.

Here the density dependence in the prey population is introduced as follows. The term \(\left(\frac{a_1 r_1 N_1}{K_1}\right) N_1\) is for the density-dependent birth rate of the prey population. The density-dependent death \(\left(1 - a_1\right) r N_1\) is further divided into two parts: \(\left(1 - a_1\right) r N_1 S_1 / K_1\) and \(\left(1 - a_1\right) r N_1 I_1 / K_1\), which represent the natural death rates of the susceptibles and infectives in the prey population, respectively. We note that density dependence is not considered in the predator population.

Since \(N_i = S_i + I_i\), model (1.51) can be simplified to

\[
\frac{dI_1}{dt} = \beta_1 \left(\frac{N_1 - I_1}{N_1}\right) I_1 - \gamma_1 I_1 - \left[\mu_1 + (1 - a_1) \frac{r_1 N_1}{K_1}\right] I_1 - aN_2 I_1,
\]

\[
\frac{dN_1}{dt} = \left[r_1 \left(1 - \frac{N_1}{K_1}\right) - aN_2\right] N_1,
\]

\[
\frac{dI_2}{dt} = \beta_2 \left(\frac{N_2 - I_2}{N_2}\right) I_2 - \mu_2 I_2 - \gamma_2 I_2 + \alpha \frac{(N_2 - I_2)}{N_2} I_1,
\]

\[
\frac{dN_2}{dt} = (ka N_1 - \mu_2) N_2,
\]

\(N_i \geq I_i \geq 0, \quad i = 1, 2, \quad 0 \leq a_1 \leq 1\).

Model (1.52) has five boundary equilibria and one positive equilibrium. Threshold conditions, which determine the global stability of each equilibrium, and other results were obtained [Han et al. (2001)].

**Disease spread in two competing populations.** In 2003, Han and coworkers discussed the spread of a disease in two competitive populations to formulate SIS and SIRS models with bilinear incidence and standard incidence and obtained more completed results [Han et al. (2001, 2003)]. We introduce an SIS model with standard incidence as an example. The model is the following

\[
\frac{dI_1}{dt} = \frac{N_1 - I_1}{N_1} \left(\beta_1 I_1 + \beta_2 I_2\right) - \gamma_1 I_1 - \left[\mu_1 + (1 - a_1) \frac{r_1 N_1}{K_1}\right] I_1 - mN_2 I_1,
\]

\[
\frac{dN_1}{dt} = \left[r_1 \left(1 - \frac{N_1}{K_1}\right) - mN_2\right] N_1,
\]
\[ \frac{dI_2}{dt} = \frac{N_2 - I_2}{N_2} \left( \beta_{21} I_1 + \beta_{22} I_2 \right) - \gamma_2 I_2 - \left[ \mu_2 + (1 - a_2) \frac{r_2 N_2}{K_2} \right] I_2 - nN_1 I_2, \]

\[ \frac{dN_2}{dt} = \left[ r_2 \left( 1 - \frac{N_2}{K_2} \right) - nN_1 \right] N_2, \]

\( N_i \geq I_i \geq 0, \quad 0 \leq a_i \leq 1, \quad i = 1, 2, \)

where \( m \) and \( n \) are the coefficients of competition, \( \beta_{ii}, \ i = 1, 2, \) are the adequate contact rate coefficients for the contacts within species and \( \beta_{ij}, \ i \neq j, \) are for those between species.

The model (1.53) exists six boundary equilibria and one positive equilibrium. The existence and global attractivity of each equilibrium have been discussed completely [Han et al. (2001)].

1.4.4.3. Models with vector-host

There are diseases whose infections are acquired through vectors rather than the direct contacts within the infectives in a population. For instance, the transmission of malaria to human beings is from infected mosquitoes, the transmission of schistosomiasis to human beings is from infected snails. In the following, we introduce the idea for modeling of these vector-borne diseases by a simple malaria model proposed first by Ross (1911).

Let \( N_h(t) \) denote the human population size in a given region at time \( t \), \( I_h(t) \) the proportion of the infective human beings at time \( t \), \( N_m(t) \) the number of female mosquitoes at time \( t \) (only female mosquitoes bite human beings because they need blood to produce eggs), and \( I_m(t) \) the proportion of infective mosquitoes. Then \( k := N_m/N_h \) is the average number of female mosquitoes possessed by a host (human). Suppose that \( a \) is the biting rate per female mosquito, that is, the number of bites per female mosquito, per unit of time, \( \beta_h \) and \( \beta_m \) are the probabilities that a bite leads to infection to a susceptible human and to a susceptible mosquito, respectively, \( \gamma \) is the recovery rate coefficient of infective humans, and \( \mu \) is the death rate coefficient of mosquitoes. Hence, the average number of bites by female mosquitoes per human, per unit of time, is \( aN_m/N_h \), and the probability of infection for one susceptible person per unit of time is \( \beta_h aN_m I_m/N_h = \beta_h ak I_m \). Noticing that the proportion of the susceptible human beings at
time $t$ is $1 - I_h(t)$, we obtain the following system of equations:

\[
\begin{align*}
\frac{dI_h}{dt} &= \beta_h a_k I_m(1 - I_h) - \gamma I_h, \\
\frac{dI_m}{dt} &= \beta_m a I_h(1 - I_m) - \mu I_m.
\end{align*}
\]

(1.54)

Model (1.54) always has a disease-free equilibrium $(0, 0)$. When the reproductive number $R_0 := \frac{a^2 \beta_m \beta_h k}{\gamma \mu} > 1$, (1.54) also has a unique endemic equilibrium $E^*(I^*_h, I^*_m)$, where

\[
I^*_h = \frac{a_k \beta_h (1 - 1/R_0)}{a_k \beta_h + \gamma}, \quad I^*_m = \frac{a \beta_m (1 - 1/R_0)}{a \beta_m + \mu}.
\]

It can be proved that if the reproductive number $R_0 < 1$, the disease-free equilibrium $E_0(0, 0)$ is asymptotically stable, and if $R_0 > 1$, $E_0$ becomes unstable, and the endemic equilibrium $E^*(I^*_h, I^*_m)$ is asymptotically stable. It is easy to see that when the biting rate of a mosquito during its whole lifespan, $a/\mu$, increases, the reproductive number $R_0$, the proportions of the infected humans $I^*_h$ and the infected mosquitoes $I^*_m$ (if $R_0 > 1$) all increase. Unfortunately, this does not always agree with the reality. It follows from the data acquired by experiments that the proportion of the infected mosquitoes is less than 10% even if in highly infected regions. This can be improved by introducing latent periods in the infected mosquitoes. We explain it as follows.

During the life-cycle of malaria transmission, gametocytes are ingested by a mosquito when it ingests human blood. Within the mosquito the gametocytes develop into gametes that fuse to form zygotes. They become motile ookinete form which bore through the gut wall of the vector and form an oocyst from which large numbers of sporozoites are released. These sporozoites then invade the salivary glands of the mosquito from which they are injected into human host when the vector feeds. Hence, there is a latent period, denoted by $\tau$, between a mosquito being infected and becoming infectious. Let $E_m(t)$ be the proportion of the mosquitoes in the exposed (latent) compartment. Model (1.54) can be modified to as the following model with time delay:

\[
\begin{align*}
\frac{dI_h}{dt} &= \beta_h a_k I_m(1 - I_h) - \gamma I_h, \\
\frac{dE_m}{dt} &= a \beta_m I_h(t)[1 - I_m(t) - E_m(t)] - \mu E_m(t) \\
&\quad - a \beta_m I_h(t - \tau)[1 - I_m(t - \tau) - E_m(t - \tau)]e^{-\mu \tau}, \\
\frac{dI_m}{dt} &= a \beta_m I_h(t - \tau)[1 - I_m(t - \tau) - E_m(t - \tau)]e^{-\mu \tau} - \mu I_m(t).
\end{align*}
\]

(1.55)
It can be shown that the reproductive number of infection for model (1.55) is
\[ \bar{R}_0 = R_0 e^{-\mu \tau} = \frac{a^2 \beta_h \beta_m k}{\gamma} \times \frac{e^{-\mu \tau}}{\mu}, \]
and the corresponding components \( I^*_{h} \) and \( I^*_{m} \) are
\[ I^*_{h} = \frac{ak \beta_h e^{-\mu \tau} (1 - 1/\bar{R}_0)}{ak \beta_h e^{-\mu \tau} + \gamma}, \quad I^*_{m} = \frac{a \beta_m e^{-\mu \tau} (1 - 1/\bar{R}_0)}{a \beta_m e^{-\mu \tau} + \mu}. \]

Another point of view to investigate the epidemic models for vector-borne diseases, such as malaria, is to transform approximately the infected mosquitoes into the infective hosts by means of transformation of time scales. In this way, we need only to investigate the host population in the model.

Let us explain it, using an example [Takeuchi et al. (2000)], as follows.

Consider an SIR malaria model with vital dynamics included in the human population where the human population size is a constant, \( N \), such that the death rate and birth rate coefficients are the same, denoted by \( \bar{\mu} \), and assume that all human newborns are susceptible. We also assume a constant mosquito population, \( V_T \), such that the death rate and birth rate coefficients are the same, denoted by \( \delta \), and assume \( V_T \) is sufficiently larger than \( N \) so that \( q = N/V_T \ll 1 \). We divide the mosquito population into two groups: susceptibles, \( V_s \), and infectives, \( V_i \), and let \( \tau \) be the latent period for an infected mosquito to become infectious. Under these assumptions, we have the following equations for the human population
\[
\begin{align*}
\frac{dS}{dt} & = -\tilde{\beta} S(t) V_i(t) - \bar{\mu} S(t) + \mu N, \\
\frac{dI}{dt} & = \tilde{\beta} S(t) V_i(t) - \tilde{\lambda} I(t), \\
\frac{dR}{dt} & = \tilde{\lambda} I(t) - \bar{\mu} R(t),
\end{align*}
\]
where \( \tilde{\beta} \) is the transmission rate coefficient from mosquitoes to humans, \( \tilde{\lambda} \) is the recovery rate, and \( N(t) = S(t) + I(t) + R(t) = N(t_0) \); and the following equations for the mosquito population:
\[
\begin{align*}
\frac{dV_s}{dt} & = -ke^{\delta \tau} I(t - \tau) V_s(t - \tau) - \delta V_s(t) + \delta [V_s(t) + V_i(t)], \\
\frac{dV_i}{dt} & = ke^{\delta \tau} I(t - \tau) V_s(t - \tau) - \delta V_i(t),
\end{align*}
\]
where \( k \) is the the transmission rate coefficient from humans to mosquitoes, \( \delta \) is the birth and death rate coefficient, and \( V_s(t) + V_i(t) = V_T(t) = V_T(0) \), and the term \( ke^\delta \tau I(t - \tau) V_s(t - \tau) \) is the number of mosquitoes who were infected at time \( t - \tau \), are still alive after the latent period \( \tau \), and become infectious, at time \( t \).

Now we set the two models in dimensionless forms by the transformations

\[
s(t) = \frac{S(t)}{N}, \quad i(t) = \frac{I(t)}{N}, \quad r(t) = \frac{R(t)}{N};
\]

and

\[
v_s(t) = \frac{V_s(t)}{V_T}, \quad v_i(t) = \frac{V_i(t)}{V_T}.
\]

Notice that the time scales for human beings and mosquitoes are quite different, where \( \sigma = kNt \) (slow scale) such that \( \sigma = \frac{1}{kt} \), which is the mean duration of infection for human beings; \( \rho = kV_T t \) (fast scale) such that \( \rho = \frac{1}{kV_T} \), which is the mean duration of infection for mosquitoes. Hence, \( t_\rho = qt_\sigma \) and \( q = N/V_T \ll 1 \). We uniform the two scales by using the slow scale \( \sigma \).

Now, we let \( t = \frac{\rho}{kV_T} \). It follows from model (1.57) that

\[
\frac{dv_i}{d\rho} = q \left[ e^{-\delta \tau i(t - \tau)}v_s(t - \tau) - \frac{\delta}{kN} v_i(t) \right],
\]

\[
\frac{dv_s}{d\rho} = -\frac{dv_i(t)}{d\rho}. \tag{1.58}
\]

It can be derived easily from the first expression of (1.58) that

\[
-\frac{q\delta}{kN} \leq \frac{dv_i}{d\rho} \leq q e^{-\delta t},
\]

and hence

\[
\frac{dv_i}{d\rho} \to 0 \quad \text{if} \quad q \to 0.
\]

Thus, when \( q = N/V_T \) is small enough,

\[
\frac{dv_i}{d\rho} = q \left[ e^{-\delta \tau i(t - \tau)}v_s(t - \tau) - \frac{\delta}{kN} v_i(t) \right] \approx 0,
\]

that is,

\[
v_i(t) \approx \frac{kN}{\delta} e^{-\delta \tau i(t - \tau)} v_s(t - \tau). \tag{1.59}
\]
Since \( v_s(t) + v_i(t) \equiv 1 \), \( v_s \approx 1 \) if the death rate coefficient \( \delta \) for mosquitoes is sufficiently large such that \( kN e^{-\delta \tau} / \delta \ll 1 \), that is, \( \delta e^{\delta \tau} \gg kN \). (Note that the assumption of a large death rate for mosquitoes is more realistic.) Hence, it follows from (1.59) that

\[
v_i(t) \approx \frac{kN}{\delta} e^{-\delta \tau} i(t - \tau). \tag{1.60}
\]

Next, let \( t = \frac{\sigma}{kN} \) and denote

\[
s(t) := s \left( \frac{\sigma}{kN} \right) = \tilde{s}(\sigma), \quad i(t) := \tilde{i}(\sigma), \quad r(t) := \tilde{r}(\sigma). \tag{1.61}
\]

By straightforward calculations and using the approximate equality (1.60), models (1.56) and (1.57) can be combined into the following system:

\[
\begin{align*}
\frac{d\tilde{s}(\sigma)}{d\sigma} &= -\beta \tilde{s}(\sigma) \tilde{i}(\sigma - \tau) - \mu \tilde{s}(\sigma) + \mu, \\
\frac{d\tilde{i}(\sigma)}{d\sigma} &= \beta \tilde{s}(\sigma) \tilde{i}(\sigma - \tau) - \mu \tilde{i}(\sigma) + \lambda \tilde{i}(\sigma), \\
\frac{d\tilde{r}(\sigma)}{d\sigma} &= \lambda \tilde{i}(\sigma) - \mu \tilde{r}(\sigma),
\end{align*}
\]

where

\[
\beta = \frac{\bar{\beta} V e^{-\delta \tau}}{\delta}, \quad \mu = \frac{\bar{\mu}}{kN}, \quad \lambda = \frac{\bar{\lambda}}{kN}.
\]

System (1.61) represents a vector-borne SIR model with an incubation time \( \tau \).

Model (1.61) can be further more realistically improved as follows. Assume that the incubation time \( \tau \) is not the same for whole vector population, but distributed over the interval \([0, h]\), where \( h \in R_+ \) is the superior limit of incubation time. Then, if we replace the incidence \( \beta s(\sigma) i(\sigma - \tau) \) by \( \beta s(\sigma) \int_0^h f(\tau) i(\sigma - \tau) d\tau \), system (1.61) becomes

\[
\begin{align*}
\frac{d\tilde{s}(\sigma)}{d\sigma} &= -\beta \tilde{s}(\sigma) \int_0^h f(\tau) i(\sigma - \tau) d\tau - \mu \tilde{s}(\sigma) + \mu, \\
\frac{d\tilde{i}(\sigma)}{d\sigma} &= \beta \tilde{s}(\sigma) \int_0^h f(\tau) i(\sigma - \tau) d\tau - \mu \tilde{i}(\sigma) + \lambda \tilde{i}(\sigma), \\
\frac{d\tilde{r}(\sigma)}{d\sigma} &= \lambda \tilde{i}(\sigma) - \mu \tilde{r}(\sigma),
\end{align*}
\]

where \( f \) is the distribution function of incubation time \( \tau \) among the vector, \( \int_0^h f(\tau) d\tau = 1 \).
System (1.62) needs the following appropriate initial conditions: 
\[ x_{\sigma_0} = \phi(\theta), \theta \in [-h,0], \]
where 
\[ x_{\sigma_0} = (\bar{s}(\sigma_0 + \theta), \bar{i}(\sigma_0 + \theta), \bar{r}(\sigma_0 + \theta)), \]
for any \( \sigma_0 \in R \), 
\[ \phi \in C: [-h,0] \rightarrow \Omega = \{ x \in \mathbb{R}^{1}_{+} : \bar{s} + \bar{i} + \bar{r} \leq 1, x = (\bar{s}, \bar{i}, \bar{r}) \}. \]

Note that model (1.62) neglects a possible latent component for the human population as pointed out by Takeuchi et al. (2000). Further improvement of the model is needed.

1.4.5. **Epidemic models with age structure**

Age is one of the most important characteristics in the modeling of populations and infectious diseases. Individuals with different ages may have different reproductive and survival capacities. Diseases may have different infection rates and mortality rates for different age groups. Individuals of different ages may also have different behaviors. Young individuals tend to be more active in interactions within or between populations, and in disease transmissions. STDs are spread through partner interactions with pair formations, and the pair formations are clearly age dependent in most cases. Most AIDS cases occur in the group of young people. Childhood diseases, such as measles, chickenpox, and rubella, are spread mainly by contacts between children of similar ages. More than half of the deaths attributed to malaria are in children under 5 years of age due to their weaker immune systems [Anderson and May (1991)]. All of these suggests that age structure needs to be incorporated into epidemic models in many cases [Gurtin and MacCamy (1985); Webb (1985); Charlesworth (1994); Iannelli (1995); Hethcote (2000); Li and Brauer (2008)].

In this section, we consider three types of age-structured epidemic models: those with discrete age structure, continuous age structure, and age groups or stages, respectively.

To have better understanding of epidemic models with age structure, we first introduce age-structured population models.

1.4.5.1. **Population models with age structure**

**Discrete age-structured population growth model.** We partition the age interval into \( n \) equal subintervals, and discretize the time interval with the step size as same as the length of the age subintervals, starting with \( t_0 \). Let \( N_{ij} \) (\( i = 1, 2, \ldots, n; j = 1, 2, 3, \ldots \)) be the number of individuals whose age is in the \( i \)th age subinterval at time \( j \), \( p_i \) is the probability that individuals at the \( i \)th age subinterval survive to the \((i+1)\)th age subinterval,
that is, \( N_{i+1,j+1} = p_i N_{ij} \), and \( B_i \) is the number of newborns produced by an individual at \( i \)th age subinterval. We assume density independence. Then the discrete age-structured population growth model is given by

\[
\begin{align*}
N_{1,j+1} &= B_1 N_{1j} + B_2 N_{2j} + \cdots + B_n N_{nj}, \\
N_{2,j+1} &= p_1 N_{1j}, \\
& \vdots \\
N_{n,j+1} &= p_{n-1} N_{n-1,j},
\end{align*}
\]

or in the vector form

\[
N_{j+1} = A N_j, 
\]

(1.63)

where

\[
N_j = \begin{bmatrix}
N_{1j} \\
N_{2j} \\
\vdots \\
N_{nj}
\end{bmatrix}, \quad A = \begin{bmatrix}
B_1 & B_2 & B_3 & \cdots & B_{n-1} & B_n \\
p_1 & 0 & 0 & \cdots & 0 & 0 \\
0 & p_2 & 0 & \cdots & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \cdots & p_{n-1} & 0
\end{bmatrix}.
\]

Equation (1.63) is called the **Leslie matrix model** [Leslie (1945, 1948)].

**Continuous age-structured population growth model.** When population size is sufficiently large or generations overlap, models with a continuous distribution in age are more appropriate for modeling of population growth.

Let \( f(a,t) \, da \) be the number of individuals whose age is between \( a \) and \( a + da \), at time \( t \), where \( f(a,t) \) is called the age distribution function such that the number of individuals whose age is between \( a - da \) and \( a \) at time \( t \) is \( f(a - da, t) \, da \). Suppose that the probability of death for individuals whose age is between \( a - da \) and \( a \) in unit of time is \( \mu(a - da) \), such the number of deaths for those individuals growing from age interval \([a - da, a]\) to \([a, a + da]\) is

\[
\mu(a - da) f(a - da, t) \, da.
\]
Thus we have

\[ [f(a-da,t) - f(a,t+dt)]da = \mu(a-da)f(a-da,t)da dt. \] (1.64)

Notice that age and time have the same scale so that \( da = dt \). Then, expanding the both sides of (1.64) in Taylor series, keeping the terms of first degree, and factoring out \( dt \), we obtain

\[ \frac{\partial f}{\partial t} + \frac{\partial f}{\partial a} + \mu(a)f = 0. \] (1.65)

Equation (1.65) is a hyperbolic partial differential equation with first order. To find the boundary condition, let \( B(a)da \) express the mean number of offspring produced by an individual with age between \( a \) and \( a + da \). Notice that \( f(0,t)da \) is the number of all newborns in the population at time \( t \). Thus

\[ f(0,t) = \int_0^{+\infty} B(a)f(a,t)da. \]

Therefore, the system with definite conditions satisfied by the age distribution function of the population is the following:

\[ f_t + f_a + \mu(a)f = 0, \]

\[ f(0,t) = \int_0^{+\infty} B(a)f(a,t)da, \] (1.66)

\[ f(a,0) = f_0(a), \]

where \( f_0(a) \) is an initial age distribution.

**Population growth model with age groups or stages.** In many circumstances, vital dynamics of individuals are approximately homogeneous in a given age interval, but significantly different compared to those in a different age interval. Then, under certain conditions, the age-structured partial differential equation model (1.66) can be reduced to a system of ordinary differential equations [Hethcote (1997); Li and Hallam (1988); Tudor (1985)].

Partition the age interval into \( n \) subintervals \([0,a_1), [a_1,a_2), \ldots, [a_{n-1}, a_n)\), where \( a_n \leq \infty \).
Define the group of individuals with ages in interval \([a_{i-1}, a_i]\), where \(a_0 = 0\), by \(N_i(t)\) such that \(N_i(t) = \int_{a_{i-1}}^{a_i} f(t,a)da, \ i = 1, \ldots, n\). Then integrating the partial differential equation in (1.66) from 0 to \(a_1\), we have

\[
\frac{dN_1(t)}{dt} + f(t,a_1) - f(t,a_0) + \int_0^{a_1} \mu(t,a)f(t,a)da = 0. \tag{1.67}
\]

Assume that individuals with ages in each interval have the same vital rates such that \(B(a) = B_i, \ \mu(t,a) = \mu_i\), for \(a \in [a_{i-1}, a_i], \ i = 1, \ldots, n\). Here \(B_i\) and \(\mu_i\) are age independent, but may be density dependent. Then, in age interval \([0, a_1]\), we have

\[
f(t,0) = \sum_{i=1}^{n} B_i N_i(t), \quad \int_0^{a_1} \mu f(t,a)da = \mu_1 N_1(t),
\]

which leads to

\[
\frac{dN_1}{dt} = \sum_{i=1}^{n} B_i N_i - m_1 N_1 - \mu_1 N_1. \tag{1.68}
\]

Here \(m_1\) is the age progression rate from groups 1 to 2, defined by \(m_1 = f(t,a_1)/N_1(t)\), and we assume it is time independent.

Integrating (1.66) from \(a_{i-1}\) to \(a_i\) for \(2 \leq i \leq \infty\), we have

\[
\frac{dN_i}{dt} = m_{i-1} N_{i-1} - (m_i + \mu_i) N_i, \quad i = 2, \ldots, n, \tag{1.69}
\]

where \(m_i\) is the age progression rate from groups \(i\) to \(i + 1\), and we let \(m_n = 0\). Then the system (1.66) is reduced into a system of ordinary differential equations.

1.4.5.2. Epidemic models with age structure

**Epidemic models with continuous age structure.** There are many studies on continuous age-structured epidemic models in the literature. See for example, [Busenberg et al. (1988, 1991); Capasso (1993); Dietz and Schenzle (1985); Iannelli et al. (1992, 1999); Langlais (1995); Li et al. (2003); Muller (1998)]. The ideas for modeling are similar as those in the previous sections, but all individuals in every compartment are of continuously age distributed. The following SIS model without disease-induced death is an example [Busenberg et al. (1985, 1988)].
Let $s(a,t)$ and $i(a,t)$ be the age distributions of the susceptibles and infectives in a population at time $t$, and assume that the disease is only transmitted between individuals with the same age. According to the ideas for age-structured population growth models and epidemic compartment SIS models, we have

$$\frac{\partial s(a,t)}{\partial a} + \frac{\partial s(a,t)}{\partial t} = -\mu(a)s(a,t) - k_0(a)i(a,t)s(a,t) + \gamma(a)i(a,t),$$

$$\frac{\partial i(a,t)}{\partial a} + \frac{\partial i(a,t)}{\partial t} = k_0(a)i(a,t)s(a,t) - (\gamma(a) + \mu(a))i(a,t),$$

$$s(0,t) = \int_0^A B(a)[s(a,t) + (1-q)i(a,t)]da,$$

$$i(0,t) = \int_0^A qB(a)i(a,t)da,$$

$$s(a,0) = s_0(a), \quad i(a,0) = i_0(a),$$

where $\mu(a)$ and $B(a)$ are, respectively, the natural death and birth rate coefficients of the individuals with age $a$, $\gamma(a)$ is the recovery rate coefficient at age $a$, $A$ is the maximum age of all individuals in the population, and $k_0(a)$ is the infection rate coefficient of the infectives with age $a$. It also assumed that there exists a vertical transmission with $q$ being the vertical transmission coefficient.

Define $R_0 := q \int_0^A B(a)e^{\int_0^\infty [(\mu(\sigma)+\gamma(\sigma)) + p_\infty(\sigma)]d\sigma}da$, where $p_\infty(\sigma) = b_0e^{-\int_0^\infty \mu(\sigma)d\sigma}$ with $b_0 \geq 0$, a constant. It is proved in [Busenberg et al. (1988)] that the disease-free equilibrium solution is globally asymptotically stable if $R_0 < 1$, unstable if $R_0 > 1$, and there exists an endemic equilibrium solution which is globally asymptotically stable if $R_0 > 1$.

In general, a disease can be transmitted between individuals with different ages. In such a case, the incidence $k_0(a)i(a,t)s(a,t)$ in model (1.70) should be replaced by the term $k_1(a)\int_0^A k_2(a')i(a',t)da'$, which is the sum of infective forces of all the infectives to the susceptibles with age $a$.

For some diseases, the course of infection is long and infectives with different infection stages have different infectivities. Then in addition to the chronologic ages, we should also consider infection ages.

Let $c$ denote the infection age, that is the time since infected, and let $f(a,c,t)$ be the distribution function of chronologic age $a$ and infection age $c$. (We call chronologic age simply age for convenience hereafter.)
We then consider the following epidemic model with age and infection age structures, which was studied by [Zhou et al. (2001)]. It is assumed that there is no disease-induced death and all newborns are susceptibles:

\[
\begin{align*}
\frac{\partial s}{\partial t} + \frac{\partial s}{\partial a} &= -\mu(a)s(a, t) - G(a, t) + \gamma(a) \int_0^a i(a, c, t) dc, \\
\frac{\partial i}{\partial t} + \frac{\partial i}{\partial a} &= -\gamma(a)i(a, c, t), \\
s(0, t) &= \int_{A_1}^{A_2} B(a, P(t))p(a, t) da, \\
i(a, 0, t) &= G(a, t) = C(a)S(a, t) \int_0^A \int_0^{a'} \beta(a', c) \frac{i(a', c, t)}{p(a', t)} \rho(a, a', t) dc da', \\
s(a, 0) &= s_0(a), \quad s(A, t) = 0, \\
i(A, c, t) &= 0, \quad i(a, c, 0) = i_0(a, c),
\end{align*}
\]

where \(s(a, t)\) and \(i(a, c, t)\) are the density functions for susceptibles and infectives, respectively,

\[
p(a, t) = s(a, t) + \int_0^a i(a, c, t) dc
\]

is the total population density function such that \(P(t) = \int_0^A p(a, t) da\) is the total population size at time \(t\), \(B(a, P(t))\) is the density-dependent age-specific birth rate, \(C(a)\) is the age-specific contact rate, \(s_0(a)\) and \(i_0(a, c)\) are the initial distributions, \([A_1, A_2]\) is the period of fecundity, \(0 < A_1 < A_2 < A\) with \(A\) the maximum age, \(\beta(a, c)\) is the age-specific probability that a susceptible becomes infected through a contact with an infective with age \(a\) and infection-age \(c\), and \(\rho(a, a', t)\) is the probability that an individual of age \(a\) has contact with an individual of age \(a'\), at time \(t\).

We assume proportionate mixing [Busenberg and Castillo-Chavez (1991)] such that

\[
\rho(a, a', t) = \rho(a', t) = \frac{C(a')p(a', t)}{\int_0^A C(a)p(a, t) da}.
\]

Then the reproductive number of infection for model (Sec. 1.4.5.2) is derived as

\[
R_0 = \int_0^A \int_0^{a'} C(a' - c)p_{\infty}(a' - c) \frac{C(a')\beta(a'c)}{\int_0^A C(a)p_{\infty}(a') da'} \pi(a', c) dc da',
\]

DYNAMICAL MODELING AND ANALYSIS OF EPIDEMICS
© World Scientific Publishing Co. Pte. Ltd.
http://www.worldscibooks.com/medsci/6799.html
Basic Knowledge and Modeling on Epidemic Dynamics

where

\[ p_\infty = P_\infty \frac{\exp(-\int_0^a \mu(\tau) d\tau)}{\exp(-\int_0^a \mu(\tau) d\tau) da} \]

is the total population at its demographic steady-state, with \( P_\infty \) a positive contact, and

\[ \pi(a', c) = \exp \left( - \int_{a' - c}^{a'} [\mu(a) + \gamma(a)] da \right) \]

is the survival probability of an infective surviving from \( a' - c \) to \( a' \). The global stability of the disease-free steady-state and endemic steady-state are investigated under certain conditions. The reader is referred to [Zhou et al. (2001)] for further details.

Epidemic models with discrete age structure. Since the time unit of collection of data about epidemic transmission is usually days or months, it is more natural and convenient to use models with discrete age structure. Moreover, parameters for discrete age-structure models can be, in general, relatively analyzed and computed easier. In the meantime, many discrete age-structures models exhibit richer dynamics. While continuous age-structured models have been widely used and well developed, taking advantage of the advanced theories of differential equations, integral equations, and dynamic systems, however, theoretic development of discrete systems in epidemic modeling is still in an infant stage, and existing results are relatively fewer. Now we introduce a discrete age-structured SIS model without vertical transmission and disease-induced death in the example below. [See Zhou and Fergola (2004) for further details.]

Let \( A \) be the maximum age of the lifespan of individuals, and partition equally the maximum age interval \([0, A]\) into \( n + 1 \) subintervals. Let \( \beta_i \lambda_j \) be the adequate contact rate coefficient for the contact between an infected individual whose age in the interval \([iA/(n + 1), (i + 1)A/(n + 1)]\) \((i = 0, 1, \ldots, n)\) and an individual with age in the interval \([jA/(n + 1), (j + 1)A/(n + 1)]\); \( j = 0, 1, \ldots, n, \gamma_j \) be the recovery rate coefficient of the infective with age in the interval \([jA/(n + 1), (j + 1)A/(n + 1)]\), \( \mu_j \) and \( b_j \) be the natural death and birth rate coefficients, respectively, and \( p_j = 1 - \mu_j \). Then, according to the ideas of constructing population growth models with discrete age structure and
the epidemic compartment models, an SIS model with discrete age structure can be formulated as

\[
S_i(t + 1) = \sum_{k=0}^{n} b_k [S_k(t) + I_k(t)],
\]

\[
I_0(t + 1) = 0,
\]

\[
S_{i+1}(t + 1) = p_i S_i(t) - \lambda_i \sum_{k=0}^{n} \beta_k I_k(t) \frac{S_i(t)}{N_i(t)} + \gamma_i I_i(t), \quad i = 0, 1, \ldots, n - 1,
\]

\[
I_{i+1}(t + 1) = p_i I_i(t) + \lambda_i \sum_{k=0}^{n} \beta_k I_k(t) \frac{S_i(t)}{N_i(t)} - \gamma_i I_i(t), \quad i = 0, 1, \ldots, n - 1,
\]

\[
S_i(0) = S_{i0} \geq 0, \quad I_i(0) = I_{i0} \geq 0, \quad S_{i0} + I_{i0} = N_i, \quad i = 0, 1, \ldots, n.
\]

(1.71)

Consider the function

\[
f(x) = \beta_1 \lambda_0 + \beta_2 [\lambda_1 + \lambda_0 q_1(x)] + \beta_3 [\lambda_1 q_2(x) + \lambda_0 q_1(x) q_2(x)] + \cdots
\]

\[
+ \beta_n [\lambda_{n-1} + \lambda_{n-2} q_{n-1}(x) + \lambda_{n-3} q_{n-2}(x) q_{n-1}(x) + \cdots
\]

\[
+ \lambda_1 q_2(x) q_3(x) \cdots q_{n-1}(x) + \lambda_0 q_1(x) q_2(x) \cdots q_{n-1}(x),
\]

where \( q_i(x) = p_i - \gamma_i - \lambda_i x / N_i, \quad i = 1, 2, \ldots, n - 1 \). By defining the basic reproductive number \( R_0 = f(0) \), it is proved [Zhou and Fergola (2004)] that the disease-free steady-state is globally asymptotically stable if \( R_0 < 1 \), unstable if \( R_0 > 1 \), and that there exists a small endemic steady-state if \( R_0 \) is greater and near one. Although sufficient conditions for the uniqueness and global stability of an endemic steady-state have not been obtained for model (1.71), the authors introduced another reproductive number \( R_{02} \) and proved that the disease-free steady-state is globally asymptotically stable if \( R_{02} < 1 \), and the endemic steady-state is globally asymptotically stable if \( R_{02} > 1 \), for the special case \( n = 2 \).

**Epidemic models with discrete age groups or stages.** Epidemic models with age groups or stages have been studied by many authors [Xiao and Chen (2001b, 2002b, 2003); Xiao et al. (2002); Lu et al. (2003)]. In the following, we introduce an SIS model to show the idea of modeling. The reader is referred to Xiao and Chen (2003) for further details.

Consider a population consisting of only two stages, larva and adult, and assume that a disease is transmitted only among the larvae. Let \( x_1(t) \)
denote the numbers of the susceptibles in the larvae at time $t$, $x_2(t)$ the number of adults at time $t$, $y(t)$ the number of the infected larvae at time $t$, $\tau$ the maturation period, $b$ and $\mu$ the birth and natural death rate coefficients, respectively, $\alpha$ the disease-induced death rate coefficient, $\gamma$ the recovery rate coefficient, and $c$ the coefficient for the density dependence in the adults.

Since the maturation period of the larvae is $\tau$, the number of individuals progressing out of the larva class at time $t$ is just the number of the newborns $bx_2(t-\tau)$ at time $t-\tau$ multiplied by the probability $e^{-\mu\tau}$ of those newborns who survive to time $t$. Thus the corresponding model can be described by the following system:

\[
\begin{align*}
\frac{dx_1(t)}{dt} &= bx_2(t) - be^{-\mu\tau}x_2(t-\tau) - \mu x_1(t) - \beta x_1(t)y(t) + \gamma y(t), \\
\frac{dy(t)}{dt} &= \beta x_1(t)y(t) - \mu y(t) - (\gamma + \alpha)y(t), \\
\frac{dx_2(t)}{dt} &= be^{-\mu\tau}x_2(t-\tau) - cx_2^2(t).
\end{align*}
\]

Here, it is assumed that the density dependence affects only the death rate of the adults. Results of determining whether the disease dies out or persists have been obtained [Xiao and Chen (2003)].

1.4.6. Epidemic models with impulses

Impulse can describe phenomena with sudden, rapid changes in continuous processes, such as changes during seasonal reproductives of some marine animals, and vaccinations given at certain fixed time of a year. In such cases, it is more appropriate to describe their dynamics by means of impulsive differential equations.

1.4.6.1. Concepts of impulsive differential equations

Impulsive equations can be classified into two types if the classification is according to the happening time of impulse: equations with fixed times or nonfixed times. If the classification is on the bases of the category of equations, then there are impulsive ordinary differential equations, impulsive delay differential equations, impulsive integral equations, and
so on. In the following, we only introduce impulsive ordinary differential equations with fixed times, which is often used in the population and epidemic models.

In general, differential equations with impulses happening at a fixed times take the following form:

$$\frac{dx}{dt} = f(t, x), \quad t \neq \tau_k,$$

$$\Delta x_k = I_k(x(\tau_k)), \quad t = \tau_k, \quad k = 1, 2, \ldots,$$

$$x(t_0) = x_0,$$  \hspace{1cm} (1.72)

where $f \in C[R \times R^n, R^n]$ satisfies the Lipschitz condition, $t_0 < \tau_1 < \tau_2 < \cdots$, $I_k \in C[R^n, R^n]$, $\Delta x_k = x(\tau_k^+) - x(\tau_k)$, $x_0 \in R^+$, $x(\tau_k^+) = \lim_{h \to 0^+} x(\tau_k + h)$.

Function $x(t)$ is called a solution of system (1.72) if it satisfies

1. $\frac{dx}{dt} = f(t, x(t))$ for $t \in [\tau_k, \tau_{k+1})$;
2. $\Delta x_k = x(\tau_k^+) - x(\tau_k)$ for $t = \tau_k$, that is, $x(\tau_k^-) = x(\tau_k)$ and $x(\tau_k^+) = x(\tau_k) + \Delta x_k$.

Since impulsive differential equations are nonautonomous, they have no equilibria. When $\Delta \tau_k = \tau_k - \tau_{k-1}$ is a constant, the existence and stability of the periodic solutions are often of interest. For further comprehension with respect to impulsive differential equations, see the related references [Lakshmikantham et al. (1989); Bainov and Simeonov (1995)].

1.4.6.2. **Epidemic models consist of impulsive differential equations**

**Epidemic models with impulsive birth.** We introduce the ideas of the modeling in terms of an SIS model by showing the following example.

Let $b$ and $\mu$ denote the birth and natural death rate coefficients, respectively, and $k$ be the carrying capacity of the environment. Assume that there are neither vertical transmission nor disease-induced death, the density dependence only affects the birth, and $\Delta \tau_k = 1$. Notice that the birth happens only at time $t = \tau_k$. Then the impulsive conditions
and the density dependent birth should also only take place at \( t = \tau_k \). Thus a corresponding model, investigated by [Han (2002)](http://www.worldscibooks.com/medsci/6799.html), is given as follows.

\[
\begin{align*}
\frac{dN}{dt} &= -\mu N(t), \quad t \neq k, \\
\frac{dS}{dt} &= -\mu S(t) - \beta S(t)I(t) + \gamma I(t), \quad t \neq k, \\
\frac{dI}{dt} &= \beta S(t)I(t) - (\mu + \gamma)I(t), \quad t \neq k, \quad k = 1, 2, 3, \ldots, \\
N(t^+) &= \left[ 1 + b - \frac{rN(t)}{K} \right] N(t), \quad t = k, \\
S(t^+) &= S(t) + \left[ b - \frac{rN(t)}{K} \right] N(t), \quad t = k, \\
I(t^+) &= I(t), \quad t = k,
\end{align*}
\]

where we write \( r = b - \mu \). Since \( N = S + I \), we only need to study the following system:

\[
\begin{align*}
\frac{dN}{dt} &= -\mu N(t), \quad t \neq k, \\
\frac{dI}{dt} &= \beta [N(t) - I(t)]I(t) - (\mu + \gamma)I(t), \quad t \neq K, \quad k = 1, 2, 3, \ldots, \\
N(t^+) &= \left[ 1 + b - \frac{rN(t)}{K} \right] N(t), \quad t = k, \\
I(t^+) &= I(t), \quad t = k.
\end{align*}
\]

This model always has a disease-free periodic solution \( (N_1^*(t), 0) \), and there also exists an endemic periodic solution \( (N_2^*(t), I_2^*(t)) \), provided \( \int_0^1 A(t)dt > 0 \), where \( A(t) = \beta N_1^*(t) - (\mu + \gamma) \).

**Epidemic models with impulsive vaccinations.** Assume, in a population, a fraction, \( p \), of the susceptibles is vaccinated at time \( t = k \), \( k = 0, 1, 2, \ldots, \) and enters into the removed compartment. Then we have an SIR epidemic model with impulsive vaccinations as
follows:
\[
\frac{dS}{dt} = \mu K - \mu S(t) - \beta S(t)I(t), \quad t \neq k,
\]
\[
\frac{dI}{dt} = \beta S(t)I(t) - (\mu + \alpha + \gamma)I(t), \quad t \neq k,
\]
\[
\frac{dR}{dt} = \gamma I(t) - \mu R(t), \quad t \neq k,
\]
\[k = 0, 1, 2, \ldots\]
\[
S(t^+) = (1 - p)S(t), \quad t = k,
\]
\[
I(t^+) = I(t), \quad t = k,
\]
\[
R(t^+) = R(t) + pS(t), \quad t = k,
\]
where \(\mu K = A\) represents recruitment, \(\mu\) and \(\alpha\) are the natural death and disease-induced death rate coefficients, respectively. It is proved in [Jin (2001)] that system (1.73) always has a disease-free periodic solution, \((S^*(t), 0, R^*(t))\), with period 1 and it is globally asymptotically stable if \(\sigma < 1\), where
\[
\sigma = \frac{\beta K}{\mu + \alpha + \gamma} \left[ 1 - \frac{p(e^\mu - 1)}{\mu(e^\mu - 1 + p)} \right].
\]

1.4.7. Epidemic models with migration

The models in the previous sections do not include the diffusion or migration of individuals in space. In fact, with the migration of individuals, the influence of individual diffusions on the spread of a disease should not be neglected. Here, we simply introduce two types of diffusions into the epidemic models.

1.4.7.1. Epidemic models with migration among different patches

Although Hethcote (1976) established an epidemic model with migration between two patches, more intensive studies dealing with this aspect only happened in recent years. To explain the ideas of the modeling and the main questions that people are interested in, we introduce the following SIS model as an example.

Wang and Zhao (2004) considered an SIS model with immigration among \(n\) patches. It is assumed that in the absence of migration among
patches; that is, the patches are isolated, the dynamic model in the $i$th patch, $i = 1, 2, \ldots, n$, are given by
\[
\frac{dS_i}{dt} = B_i(N_i)N_i - \mu_i S_i - \beta_i S_i I_i + \gamma_i I_i,
\]
\[
\frac{dI_i}{dt} = \beta_i S_i I_i - (\gamma_i + \mu_i)I_i,
\]
where the birth rate coefficient $B_i(N_i)$, for $N_i > 0$, $i = 1, \ldots, n$, satisfies the following common hypothesis:
\[
B_i(N_i) > 0, \quad B_i(N_i) \in C^1(0, +\infty), B_i'(N_i) < 0 \quad \text{and} \quad B_i(+\infty) < \mu_i.
\]
If the $n$ patches are connected with each other; that is, the individuals between any two patches can migrate, then an SIS epidemic model with migration among the $n$ patches can be formulated as
\[
\frac{dS_i}{dt} = B_i(N_i)N_i - \mu_i S_i - \beta_i S_i I_i + \gamma_i I_i + \sum_{j=1}^{n} a_{ij} S_j,
\]
\[
\frac{dI_i}{dt} = \beta_i S_i I_i - (\mu_i + \gamma_i)I_i + \sum_{j=1}^{n} b_{ij} I_j,
\]
where $a_{ii}$ and $b_{ii}$ ($a_{ii} \leq 0$, $b_{ii} \leq 0$) denote the emigration rates of the susceptibles and the infectives from the $i$th patch to other patches, respectively; $a_{ij}$ and $b_{ij}$ ($a_{ij} \geq 0$, $b_{ij} \geq 0$) denote the immigration rates of the susceptibles and the infectives from the $j$th patch to the $i$th patch, respectively. Model (1.74) assumes that the disease is not fatal, and the death and birth of individuals in the process of migration are neglected. Since the individuals emigrating from the $i$th patch will move dispersedly to the other $n - 1$ patches, we have
\[
-a_{ii} = \sum_{j=1}^{n} a_{ji}, \quad -b_{ii} = \sum_{j=1}^{n} b_{ji}.
\]
Under the assumptions that the matrices $(a_{ij})$ and $(b_{ij})$ are all irreducible, Wang and Zhao (2004) obtained conditions for the local and global stability of the disease-free equilibrium, and the conditions under which the disease persists in all patches.

For the sake of better understanding, we consider a model with migration only between two patches. In this case, from (1.75) we know

\[
-a_{ii} = \sum_{j=1, j \neq i}^{n} a_{ji}, \quad -b_{ii} = \sum_{j=1, j \neq i}^{n} b_{ji}.
\]
that

$$-a_{11} = a_{21}, \quad -a_{22} = a_{12}, \quad -b_{11} = b_{21}, \quad -b_{22} = b_{12}.$$  

Assume that the birth rates satisfy

$$B_i(N_n)N_i = b_i + c_i N_i, \quad c_i < \mu_i, \quad N_i = S_i + I_i, \quad i = 1, 2.$$  

Then model (1.75) is simplified as

$$\frac{dS_1}{dt} = b_1 + c_1 I_1 - (\mu_1 - c_1 - a_{11})S_1 - \beta_1 S_1 I_1 + \gamma_1 I_1 - a_{22} S_2,$$

$$\frac{dI_1}{dt} = \beta_1 S_1 I_1 - (\mu_1 + \gamma_1 - b_{11}) I_1 - b_{22} I_2,$$

$$\frac{dS_2}{dt} = b_2 + c_2 I_2 - (\mu_2 - c_2 - a_{22})S_2 - \beta_2 S_2 I_2 + \gamma_2 I_2 - a_{11} S_1,$$

$$\frac{dI_2}{dt} = \beta_2 S_2 I_2 - (\mu_2 + \gamma_2 - b_{22}) I_2 - b_{11} I_1,$$  

where $a_{ii} \leq 0, b_{ii} \leq 0$, and other parameters are all nonnegative.

In system (1.74), we actually assumed that $S_i$ and $I_i$ are residents in patch $i$, and that an individual who moves to a new patch will become a resident of the new patch.

Another type of epidemic models with migration describe the transmission from traveling rather than residence. During traveling, susceptibles may get infection when they contact infectives in other patches, and traveling infectives may also transmit a disease to others. We discuss an epidemic model [proposed by Sattenspiel and Dietz (1995)], to describe such situations as follows.

Let $S_{ii}$ be the number of susceptibles, who are the residents in the patch $i$. They travel to other patches at a rate $\sigma_i$ per unit of time. These visitors are distributed among the $n - 1$ patches with probability $v_{ij}$ to patch $j$, where $0 \leq v_{ij} \leq 1$, $v_{ii} = 0$, and $\sum_{j=1}^{n} v_{ij} = 1$. Let $\rho_{ij}$ be the rate of the traveling individuals residing in patch $i$, who return from patch $j$ to patch $i$, with $\rho_{ii} = 0$. Let $I_{jk}$ be the number of infectives presently in patch $k$ who are residents in patch $j$. $\beta_{ijk}$ be the transmission coefficient of an infective from patch $j$ contacting a susceptible from the patch $i$ in patch $k$. If we omit the death rate, the corresponding SIR epidemic model
Basic Knowledge and Modeling on Epidemic Dynamics

77

with standard incidence can be described as in the following system:

\[
\frac{dS_{ii}}{dt} = \sum_{k=1}^{n} \rho_{ik}S_{ik} - \sigma_{i}S_{ii} - \sum_{j=1}^{n} \beta_{iji} \frac{S_{ii}I_{ji}}{N_{i}^{*}},
\]

\[
\frac{dS_{ik}}{dt} = \sigma_{ijk}S_{ii} - \rho_{ik}S_{ik} - \sum_{j=1}^{n} \beta_{ijk} \frac{S_{ik}I_{jk}}{N_{k}^{*}},
\]

\[
\frac{dI_{ii}}{dt} = \sum_{k=1}^{n} \rho_{ik}I_{ik} - \sigma_{i}I_{ii} + \sum_{j=1}^{n} \beta_{iji} \frac{S_{ii}I_{ji}}{N_{i}^{*}} - \gamma I_{ii},
\]

\[
\frac{dI_{ik}}{dt} = \sigma_{ijk}I_{ii} - \rho_{ik}I_{ik} + \sum_{j=1}^{n} \beta_{ijk} \frac{S_{ik}I_{jk}}{N_{k}^{*}} - \gamma I_{ik},
\]

\[
\frac{dR_{ii}}{dt} = \sum_{k=1}^{n} \rho_{ik}R_{ik} - \sigma_{i}R_{ii} + \gamma I_{ii},
\]

\[
\frac{dR_{ik}}{dt} = \sigma_{ijk}R_{ii} - \rho_{ik}R_{ik} + \gamma I_{ik},
\]

where \( N_{k}^{*} = \sum_{m=1}^{k}(S_{mk} + I_{mk} + R_{mk}) \), \( \gamma \) is the recovery rate coefficient. The term \( \rho_{ik}S_{ik} \) in the first equation of (1.77) is the number of the residents in patch \( i \) who travel back from patch \( k \) per unit of time and have not been infected, so that \( \sum_{k=1}^{n} \rho_{ik}S_{ik} \) is the number of all susceptibles traveling back from other patches per unit of time, the term \( \sigma_{i}S_{ii} \) represents the number of susceptible residents in patch \( i \) who travel out per unit of time, and the term \( \sum_{j=1}^{n} \beta_{iji} \frac{S_{ii}I_{ji}}{N_{i}^{*}} \) represents the number of newly infected residents in patch \( i \) who are infected by the infectives traveling from all other patches. The meanings of terms in the other equations in (1.77) are similar.

In the second equation of the system (1.77), \( S_{ik} \) is the number of susceptibles presently in patch \( k \) who are residents in patch \( i \), the term \( \sigma_{ij}v_{ij}S_{ii} \) is the number of susceptibles who presently in patch \( k \) but are residents and traveling from patch \( i \) per unit of time, \( \rho_{ik}S_{ik} \) is the number of susceptibles who traveled to patch \( k \) and now return to their home patch \( i \) per unit of time, and the term \( \sum_{j=1}^{n} \beta_{ijk} \frac{S_{ik}I_{jk}}{N_{k}^{*}} \) represents the number of newly infected residents in patch \( i \) who traveled to and infected in patch \( k \) by infective visitors from all other patches. The meanings of terms in the other equations in (1.77) are similar.

1.4.7.2. Epidemic models with continuous diffusion in space

We supposed that individuals in a population and the adequate contacts in a given environment are uniformly distributed in the previous sections.
Nevertheless, it is not always the case in reality. The distribution of individuals and their interactions depend on not only time $t$, but also location $x$, in given space $\Omega$. In the following, we explain the idea of modeling by using an SIR model as an example.

Let $S(x, t)$, $I(x, t)$, and $R(x, t)$ be the numbers of susceptibles, infectives, and recovereds at time $t$ and location $x \in \Omega$, respectively, $\Delta$ represent the Laplace operator, $\mu_i$, $i = 1, 2, 3$, represent the diffusion rate coefficients, and assume that, at time $t$ and location $x$, the susceptibles can be infected by infectives at any location $y \in \Omega$ with the adequate contact rate $K(x, y)$. Then an SIR epidemic model with diffusion in space and without death can be described by the system

$$
\frac{\partial S}{\partial t} = d_1 \Delta S - S(x, t) \int_{\Omega} I(y, t)K(x, y)dy,
$$

$$
\frac{\partial I}{\partial t} = d_2 \Delta I + S(x, t) \int_{\Omega} I(y, t)K(x, y)dy - \gamma I(x, t),
$$

$$
\frac{\partial R}{\partial t} = d_3 \Delta R + \gamma I(x, t),
$$

(1.78)

under the boundary value conditions

$$
\frac{\partial S}{\partial n}(x, t) = \frac{\partial I}{\partial n}(x, t) = \frac{\partial R}{\partial n}(x, t) = 0, \quad (x, t) \in \partial \Omega \times (0, +\infty),
$$

and initial conditions

$$
S(x, 0) = S_0(x), \quad I(x, 0) = I_0(x), \quad R(x, 0) = R_0(x), \quad x \in \Omega.
$$

For some diseases, the infectives at location $x \in \Omega$ at the present time $t$ may be infected at another location $y \in \Omega$ at an earlier time $t - \tau$ with the adequate contact rate $K(x, y, t - \tau)$. In this case, the corresponding SIR model may be described by the system

$$
\frac{\partial S}{\partial t} = d_1 \Delta S - S(x, t) \int_{-\infty}^{t} \int_{\Omega} I(y, \tau)K(x, y, t - \tau)dyd\tau,
$$

$$
\frac{\partial I}{\partial t} = d_2 \Delta I + S(x, t) \int_{-\infty}^{t} \int_{\Omega} I(x, \tau)K(x, y, t - \tau)dyd\tau - \gamma I(x, t),
$$

$$
\frac{\partial R}{\partial t} = d_3 \Delta R + \gamma I(x, t),
$$

(1.79)

under suitable boundary and initial conditions [Takeuchi et al. (2007)].
For diffusion models, such as (1.78) and (1.79), the interesting problems to be studied are the stability of the disease-free equilibrium and the existence of traveling waves.

1.4.8. 

Epidemic models with time-dependent coefficients

In many real situations, the growth of a population and the transmission of a disease vary seasonally, which implies that it is more appropriate to assume coefficients of some epidemic models to be time-dependent, and more specifically, to be continuous and bounded periodic functions of time \( t \). In such cases, the corresponding models become nonautonomous differential systems and the model analysis is more difficult. It seems, to our knowledge, that few results appeared in the literature so far for this kind of epidemic models. In the following, we explain some ideas by means of two examples.

1.4.8.1. 

SIR model with time-dependent coefficients

First, we consider the following simple SIR model:

\[
\frac{dS}{dt} = \mu(t) - \mu(t)S - \beta(t)SI,
\]

\[
\frac{dI}{dt} = \beta(t)SI - \gamma(t)I - \mu(t)I,
\]

\[
\frac{dR}{dt} = \gamma(t)I - \mu(t)R,
\]

(1.80)

where we assume that \( \mu(t), \beta(t), \) and \( \gamma(t) \) are all continuous functions with upper bounds and positive lower bounds, and that \( S(t) + I(t) + R(t) = N(t) \equiv 1 \).

To control the spread of an epidemic, we intend to find conditions under which the number of infectives \( I(t) \) tends to zero.

We can see, from the second equation of model (1.80), that

\[
\frac{dI}{dt} = \left[ \frac{\beta(t)S(t)}{\gamma(t) + \mu(t)} - 1 \right] [\gamma(t) + \mu(t)]I(t).
\]

Then, if there exists a \( t_0 \) such that \( \beta(t_0)/[\gamma(t_0) + \mu(t_0)] < 1 \) and \( S(t_0) \approx 1 \), \( I(t) \) decreases in a neighborhood of \( t_0 \). Hence if we want \( I(t) \) to
be decreasing with \( t \) for any initial value, then we only need
\[
R_{\text{max}} = \max_{t} \left[ \frac{\beta(t)}{\gamma(t) + \mu(t)} \right] < 1.
\]
Notice that to make \( R_{\text{max}} < 1 \) we need to spend more energy and it costs more.

The following results obtained by [Ma and Ma (2006)] gives a threshold to determine whether the disease dies out or not.

Define
\[
\bar{R} = \frac{\langle \beta \rangle}{\langle \gamma \rangle + \langle \mu \rangle}.
\]
Then the disease-free solution \((1, 0, 0)\) of model (1.80) is unstable if \( \bar{R} > 1 \), and globally asymptotically stable if \( \bar{R} < 1 \), where
\[
\langle f \rangle = \lim_{t \to \infty} \frac{1}{t} \int_{0}^{t} f(u) \, du
\]
is defined as the long-term average of function \( f \). We assume that \( \langle \beta \rangle, \langle \gamma \rangle, \) and \( \langle \mu \rangle \) all exist.

It is easy to see that if \( \beta, \gamma, \) and \( \mu \) are all constants, then \( \bar{R} = \beta / (\gamma + \mu) \) is the basic reproductive number. For the nonautonomous system (1.80), the number \( \bar{R} \) is actually the basic reproductive number of the following long-term average system:
\[
\begin{align*}
\frac{dS}{dt} &= \langle \mu \rangle - \langle \mu \rangle S - \langle \beta \rangle SI, \\
\frac{dI}{dt} &= \langle \beta \rangle SI - \langle \gamma \rangle I - \langle \mu \rangle I, \\
\frac{dR}{dt} &= \langle \gamma \rangle I - \langle \mu \rangle R.
\end{align*}
\]

For the following SIRS model with disease-induced death, different birth and natural death rate coefficients, and standard incidence,
\[
\begin{align*}
\frac{dS}{dt} &= b(t)N - \mu(t)S - \frac{\beta(t)SI}{N} + \delta(t)R, \\
\frac{dI}{dt} &= \frac{\beta(t)SI}{N} - \mu(t)I - \alpha(t)I - \gamma(t)I, \\
\frac{dR}{dt} &= \gamma(t)I - \mu(t)R - \delta(t)R.
\end{align*}
\]
it is proved by [Ma and Ma (2006)] that the modified reproductive number for the corresponding long-term average system

\[ \tilde{R}_1 = \frac{\langle \beta \rangle}{\langle b \rangle + \langle \alpha \rangle + \langle \gamma \rangle} = 1 \]

is still the threshold to distinguish between the instability and global stability of the disease-free solution of model (1.81).

Next, we consider the following simple SEIRS model with latent compartment \( E \) and no death:

\[ \begin{align*}
\frac{dS}{dt} &= -\beta(t)SI + \delta R, \\
\frac{dE}{dt} &= \beta SI - \sigma E, \\
\frac{dI}{dt} &= \sigma E - \gamma I, \\
\frac{dR}{dt} &= \gamma I - \delta R.
\end{align*} \]

(1.82)

We suppose that \( S(t) + E(t) + I(t) + R(t) \equiv 1, \) and \( \langle \beta \rangle = \bar{\beta} \) exists.

The corresponding long-term average system of model (1.82) is

\[ \begin{align*}
\frac{dS}{dt} &= -\bar{\beta}SI + \delta R, \\
\frac{dE}{dt} &= \bar{\beta}SI - \sigma E, \\
\frac{dI}{dt} &= \sigma E - \gamma I, \\
\frac{dR}{dt} &= \gamma I - \delta R.
\end{align*} \]

(1.83)

It is easy to see that the basic reproductive number of model (1.83) is \( \bar{R}_0 = \bar{\beta}/\gamma \) and that the disease-free equilibrium \( E_0 \) is globally asymptotically stable if \( \bar{R}_0 < 1 \), and unstable if \( \bar{R}_0 > 1 \). However, for model (1.82), is \( \bar{R}_0 = \bar{\beta}/\gamma \) still a threshold to determine the stability of the disease-free solution? It is, unfortunately, not necessary! A counterexample was given by [Ma and Ma (2006)]. Nevertheless, the condition of \( \bar{R}_0 = \bar{\beta}/\gamma < 1 \) is
still sufficient to guarantee the global stability of the disease-free solution of model (1.82), although it is not necessary.

We would like to point out that, actually, for model (1.82), the threshold should be

\[ R_0 = \frac{\sigma \langle \omega \rangle}{\gamma} = 1, \]

where \( \omega(t) \) is a solution of the equation

\[ \frac{d\omega}{dt} = \beta(t) - (\sigma - \gamma)\omega - \sigma \omega^2. \]

Even though we may not be able to find an explicit formula for the threshold analytically, a numeric approximation can provide useful information to prevent and control the disease.