Mathematical Analysis for Epidemic Models with Heterogeneity

非均質性を備える様々な感染症モデルの数理的解析

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January 9, 2013

Acknowledgments

First of all, I would like to thank Professor Hisashi Inaba for his guidance and collaboration during my doctoral program at the University of Tokyo. I would like to thank also Professor Yoshiaki Muroya for his teaching during my bachelor's and master's programs at Waseda University. I would like to thank Dr. Yukihiko Nakata and Dr. Yoichi Enatsu for their kind support and helpful comments.

I would like to thank Professor Mimmo Iannelli for his kind hospitality during my stay in Trento, Italy. I would like to thank Professor Nicolas Bacaër for his helpful comments to my study. I would like to thank all (domestic and abroad) people whom I have met during the past five years of my research life.

Finally, I would like to thank my parents for their undying support and encouragement.

Preface

From the fundamental work by Kermack and McKendrick [48] in 1927, the study of epidemic models as initial-boundary-value problems of nonlinear partial differential equations has been developed focusing on various infectious diseases such as influenza [73], avian influenza [47], measles [92], gonorrhea [58], leishmaniasis [5], SARS [95], HIV [41] and so on. From the application point of view, we have no doubt that the attempt to construct more realistic epidemic models is essentially important for controlling the spread of disease. In this thesis, adding the heterogeneity (e.g., sex, age, position, seasonality and so on) into the usual epidemic models in which the host population is homogeneously divided according to each infection status, we construct more realistic epidemic models with heterogeneity and study their mathematical properties.

One of the most important concepts in this field of mathematical epidemiology is the basic reproduction number $\mathscr{R}_0$ which is epidemiologically defined as the expected number of secondary cases produced by a typical infectious individual during its entire period of infectiousness in a completely susceptible population [18]. From this definition, we can expect intuitively that the disease dies out if $\mathscr{R}_0 < 1$, while it spreads if $\mathscr{R}_0 > 1$. However, whether $\mathscr{R}_0$ defined for each epidemic model keeps such threshold property in a mathematical sense, that is, whether the trivial equilibrium solution called the disease-free equilibrium is (globally) stable if $\mathscr{R}_0 < 1$ and a nontrivial positive equilibrium called an endemic equilibrium is so if $\mathscr{R}_0 > 1$, is not obvious. For the heterogeneous epidemic models we shall study in this thesis, $\mathscr{R}_0$ is mathematically defied by the spectral radius of a positive linear operator called the next generation operator. The main focus of this thesis is on the relation between the size of such $\mathscr{R}_0$ and the (global) stability of each equilibrium of such epidemic models.

The organization of this thesis is as follows. In Part I, which is composed of Chapters 1 and 2, we focus on multi-group epidemic models, in which the heterogeneous host population is divided into several homogeneous groups according to the heterogeneity of each individual. In Part II, which is composed of Chapters 3 and 4, we focus on epidemic models with time-heterogeneity. Under the assumption that parameters are time-periodic, they can be regarded as realistic for seasonal diseases such as influenza and some vector-born diseases.

The author has collaborated with Dr. Yukihiko Nakata (University of Szged) and Professor Hisashi Inaba (University of Tokyo) to obtain results in Chapters 3 and 4, respectively. The author's work is supported by the Japan Society for the Promotion of Science (JSPS) (222176).

Contents

Part I

Multi-Group Epidemic Models

Chapter 1

A multi-group SVIR epidemic model

Abstract In this chapter, we formulate a multi-group SVIR epidemic model that treats the heterogeneity of host population and the effect of immunity induced by vaccination. The basic reproduction number $\mathscr{R}_0$ is defined by the spectral radius of a nonnegative irreducible matrix called the next generation matrix. We show that $\mathscr{R}_0$ plays the role of a perfect threshold in the sense of determining the global asymptotic stability of each equilibrium of the model, that is, the disease-free equilibrium of the model is globally asymptotically stable if $\mathscr{R}_0 \leq 1$, while an endemic equilibrium is so if $\mathscr{R}_0 > 1$. In the proof, we use a classical method of Lyapunov, a recently developed graph-theoretic approach and an approach of max functions.

Keywords Multi-group SVIR epidemic model; Vaccination; The basic reproduction number; Global asymptotic stability; Lyapunov functional; Graph theory

1.1 Introduction

From the beginning of the 20th century, nonlinear mathematical models have played important roles in clarifying the spread pattern of various infectious diseases (see, e.g., the fundamental work by McKendrick [72] and one of the most popular books by Diekmann and Heesterbeek [19]). Multi-group epidemic models, in which a heterogeneous host population is divided into several homogeneous groups according to the heterogeneity (e.g., age, sex, position etc.) of each individual, have gained much attention from many researchers because of their suitability for various realistic situations and rich mathematical properties (see, e.g., [58, 94, 27]). The model we shall consider in this chapter is also a multi-group epidemic model. Dividing total host population into four subpopulations called susceptible S, vaccinated V, infectious I and recovered R, we formulate a multi-group SVIR epidemic model that can consider the effect of immunity induced by vaccination (see, e.g., [53, 4, 1, 68, 65]). For the model, we assume that the immunity is partial, that is, not only a susceptible individual but also a vaccinated individual can be infected by an infectious individual (with weaken force of infection). Although single-group vaccination models similar to the SVIR epidemic model have been studied by several authors (see [53, 4, 1, 68, 65]), to our knowledge, this is the first study that focuses on a multi-group SVIR epidemic model. Here, note that other kinds of multi-group vaccination models have been studied (see, e.g., [15, 22]).

A graph-theoretic approach developed in [27] is known as one of the effective tools for the global stability analysis for multi-group epidemic models. Many researchers have applied the approach to various multi-group epidemic models (see, e.g., [27, 28, 63, 64, 84, 99, 100, 22, 54]). In this chapter, applying the graph-theoretic approach and an approach of max functions, we prove that the model has a threshold value, which is called the basic reproduction number $\mathscr{R}_0$ (see [18, 94]), such that if the value is less than (or equal to) unity, then the disease-free equilibrium of the model is globally asymptotically stable (that is, the disease will eventually die out irrespective of the initial number of infectious individuals), while if the value is greater than unity, then an endemic equilibrium exists for the model and it is unique and globally asymptotically stable (that is, the disease will eventually remain at a fixed size irrespective of the initial number of infectious individuals).

The subsequent sections of this chapter are organized as follows: In Section 1.2, we formulate the multi-group SVIR epidemic model and show some basic facts. In Section 1.3, we prove the global asymptotic stability of the disease-free equilibrium E^0 for $\mathscr{R}_0 \leq 1$. For the proof, we use a classical method of Lyapunov. In Section 1.4, we turn our attention to the case $\mathscr{R}_0 > 1$ and show the existence, uniqueness and global asymptotic stability of an endemic equilibrium E^*. For the proof, we use the graph-theoretic approach and an approach of max functions.

1.2 Preliminaries

1.2.1 The model

Let $n \in \mathbb{N}$ be the number of groups, that is, let us divide a heterogeneous host population into n homogeneous groups. Let $S_i(t)$, $V_i(t)$, $I_i(t)$ and $R_i(t)$ be the numbers of susceptible, vaccinated, infectious and recovered individuals in group $i \in \mathscr{N} := \{1, 2, \cdots, n\}$ at time $t \geq 0$, respectively. Set parameters as

b_i : influx of newborns into group i;

μ_i^S, μ_i^V, μ_i^I, μ_i^R : per capita mortality rates for susceptible, vaccinated, infectious and recovered individuals in group i, respectively;

p_i : fraction at which newborns of group i have the passive immunity;

ν_i : per capita vaccination rate for susceptible individuals in group i;

γ_i : per capita recovery rate for infectious individuals in group i;

β_{ij} : rate of disease transmission between a susceptible individual in group i and an infectious individual in group j;

σ_i : multiplier to the force of infection to vaccinated individuals in group i ($1 - \sigma_i$ is a measure of the vaccine efficacy).

For the parameters, we make the following assumption.

Assumption 1.2.1. (i) b_i, μ_i^S, μ_i^V, μ_i^I, μ_i^R, ν_i and γ_i are positive for all $i \in \mathscr{N}$.

(ii) $p_i \in (0,1)$ and $\sigma_i \in (0,1)$ for all $i \in \mathscr{N}$.

(iii) β_{ij} is nonnegative for all $i, j \in \mathscr{N}$ and n-square matrix $(\beta_{ij})_{1 \leq i,j \leq n}$ is irreducible ([8]).

(i) and (ii) of Assumption 1.2.1 are made for biological justification. (iii) of Assumption 1.2.1 implies that every pair of groups is joined by an infectious path so that the presence of an infectious individual in the first group can cause infection in the second group. Under the above settings, we construct the following nonlinear mathematical model for the epidemic process.

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t} S_i = (1-p_i) b_i - S_i(t) \displaystyle\sum_{j=1}^{n} \beta_{ij} I_j(t) - \left(\mu_i^S + \nu_i\right) S_i(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} V_i = \nu_i S_i(t) - V_i(t) \displaystyle\sum_{j=1}^{n} \sigma_i \beta_{ij} I_j(t) - \mu_i^V V_i(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} I_i = \left(S_i(t) + \sigma_i V_i(t)\right) \displaystyle\sum_{j=1}^{n} \beta_{ij} I_j(t) - \left(\mu_i^I + \gamma_i\right) I_i(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} R_i = p_i b_i + \gamma_i I_i(t) - \mu_i^R R_i(t), \quad i \in \mathscr{N}. \end{cases} \tag{1.2.1}$$

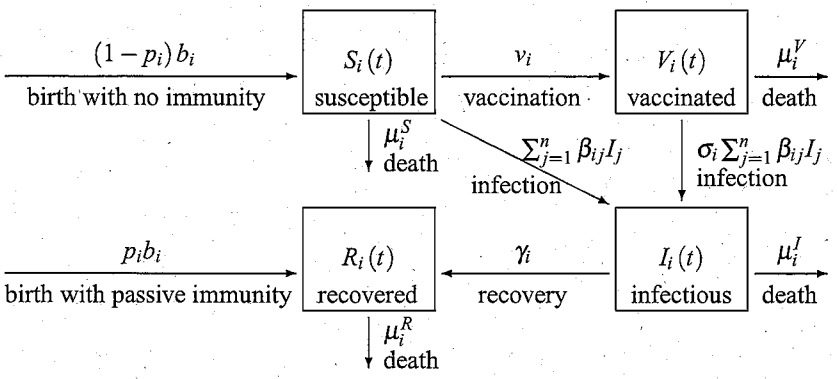


Figure 1.1: Transfer diagram for SVIR epidemic model (1.2.1)

Note that in model (1.2.1) we assume that the vaccine does not wane and the disease confers permanent immunity. This assumption makes the first three equations of (1.2.1) independent of R_i $(i \in \mathcal{N})$ and therefore, the dynamics is governed by the following reduced system:

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t} S_i = (1-p_i) b_i - S_i(t) \sum\limits_{j=1}^{n} \beta_{ij} I_j(t) - \left(\mu_i^S + v_i\right) S_i(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} V_i = v_i S_i(t) - V_i(t) \sum\limits_{j=1}^{n} \sigma_i \beta_{ij} I_j(t) - \mu_i^V V_i(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} I_i = \{S_i(t) + \sigma_i V_i(t)\} \sum\limits_{j=1}^{n} \beta_{ij} I_j(t) - \left(\mu_i^I + \gamma_i\right) I_i(t), \quad i \in \mathcal{N}. \end{cases} \tag{1.2.2}$$

In what follows, we focus on the system (1.2.2).

1.2.2 Equilibria and state-space

Equilibria $(S_1^*, V_1^*, I_1^*, \cdots, S_n^*, V_n^*, I_n^*) \in \mathbb{R}_+^{3n}$ of system (1.2.2) are obtained by solving

$$\begin{cases} 0 = (1-p_i) b_i - S_i^* \sum\limits_{j=1}^{n} \beta_{ij} I_j^* - \left(\mu_i^S + v_i\right) S_i^*, \\ 0 = v_i S_i^* - V_i^* \sum\limits_{j=1}^{n} \sigma_i \beta_{ij} I_j^* - \mu_i^V V_i^*, \\ 0 = (S_i^* + \sigma_i V_i^*) \sum\limits_{j=1}^{n} \beta_{ij} I_j^* - \left(\mu_i^I + \gamma_i\right) I_i^*, \quad i \in \mathcal{N}. \end{cases} \tag{1.2.3}$$

In the situation where $I_i^* = 0$ for all $i \in \mathcal{N}$, the trivial equilibrium $E^0 := \left(S_1^0, V_1^0, 0, \cdots, S_n^0, V_n^0, 0\right) \in \mathbb{R}_+^{3n}$ of system (1.2.2) is obtained, where

$$S_i^0 := \frac{(1-p_i) b_i}{\mu_i^S + v_i}, \quad V_i^0 := \frac{v_i (1-p_i) b_i}{\mu_i^V \left(\mu_i^S + v_i\right)}, \qquad i \in \mathcal{N}.$$

Epidemiologically, this trivial equilibrium E^0 is called *the disease-free equilibrium* ([94]), in which the host population remains in the absence of disease. It is easy to see that E^0 always exists for system (1.2.2).

In the situation where $I_i^* > 0$ for some $i \in \mathscr{N}$, (1.2.3) gives a nontrivial equilibrium called an *endemic* equilibrium ([19]), in which the disease persists. In what follows, we denote it by $E^* := (S_1^*, V_1^*, I_1^*, \cdots, S_n^*, V_n^*, I_n^*) \in \mathbb{R}_+^{3n}$. The existence of E^* is not obvious and therefore shall be discussed in Sections 1.3 and 1.4.

Integrating each equation of (1.2.2), we can easily verify that solutions of system (1.2.2) remain nonnegative, provided that the initial condition satisfies

$$(S_1(0), V_1(0), I_1(0), \cdots, S_n(0), V_n(0), I_n(0)) \in \mathbb{R}_+^{3n}.$$

Therefore, in what follows, we restrict our attention to solutions in $\mathbb{R}_+^{3n}$. Then, from the first and second equations of (1.2.2), we have the following differential inequalities:

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t} S_i \le (1-p_i) b_i - \left(\mu_i^S + \nu_i\right) S_i(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} V_i \le \nu_i S_i(t) - \mu_i^V V_i(t), \quad i \in \mathscr{N}. \end{cases}$$

From the well-known comparison principle (see, e.g., [81, Appendix B]), we see that $\limsup_{t\to+\infty} S_i(t) \le S_i^0$ and $\limsup_{t\to+\infty} V_i(t) \le V_i^0$, $i \in \mathscr{N}$ hold. In addition, adding all equations of (1.2.2), we have

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}(S_i + V_i + I_i) &= (1-p_i) b_i - \mu_i^S S_i(t) - \mu_i^V V_i(t) - \left(\mu_i^I + \gamma\right) I_i(t) \\ &\le (1-p_i) b_i - \mu_i^* \{S_i(t) + V_i(t) + I_i(t)\}, \quad i \in \mathscr{N}, \end{aligned}$$

where $\mu_i^* := \min\left(\mu_i^S, \mu_i^V, \mu_i^I + \gamma_i\right)$, $i \in \mathscr{N}$. Hence, again from the well-known comparison principle, we have

$$\limsup_{t\to+\infty} \{S_i(t) + V_i(t) + I_i(t)\} \le \frac{(1-p_i) b_i}{\mu_i^*}.$$

Based on these arguments, we define a closed set

$$\Omega := \left\{ (S_1, V_1, I_1, \cdots, S_n, V_n, I_n) \in \mathbb{R}_+^{3n} : \ S_i \le S_i^0, \ V_i \le V_i^0, \ S_i + V_i + I_i \le \frac{(1-p_i) b_i}{\mu_i^*}, \ i \in \mathscr{N} \right\}$$

as the state-space for system (1.2.2). The positive invariance of Ω for system (1.2.2) is easily verified. In addition, we define

$$\tilde{\Omega} := \left\{ (S_1, V_1, I_1, \cdots, S_n, V_n, I_n) \in \Omega : \ 0 < S_i < S_i^0, \ 0 < V_i < V_i^0, \ 0 < I_i, \ S_i + V_i + I_i < \frac{(1-p_i) b_i}{\mu_i^*}, \ i \in \mathscr{N} \right\}$$

as an interior of Ω.

1.2.3 The basic reproduction number $\mathscr{R}_0$

Epidemiologically, the basic reproduction number $\mathscr{R}_0$ implies the expected number of secondary cases produced by a typical infectious individual during its entire period of infectiousness in a completely susceptible population (see e.g., [18, 19, 94]). For multi-group epidemic models, it is calculated as the spectral radius of a nonnegative matrix called *the next generation matrix* (see [94]). Therefore, we first define the next generation matrix for system (1.2.2).

Using components of $E^0 := \left(S_1^0, V_1^0, 0, \cdots, S_n^0, V_n^0, 0\right)$, we define an $n \times n$ matrix

$$\mathscr{F} = \begin{pmatrix} \left(S_1^0 + \sigma_1 V_1^0\right) \beta_{11} & \cdots & \left(S_1^0 + \sigma_1 V_1^0\right) \beta_{1n} \\ \vdots & \ddots & \vdots \\ \left(S_n^0 + \sigma_n V_n^0\right) \beta_{n1} & \cdots & \left(S_n^0 + \sigma_n V_n^0\right) \beta_{nn} \end{pmatrix},$$

whose (i,j) entry implies the rate at which an infectious individual in group j produces a new infectious individual in group i. Moreover, we define an n-dimensional diagonal matrix

$$\mathscr{V} = \operatorname{diag}\left(\mu_i^I + \gamma_i\right) = \begin{pmatrix} \mu_1^I + \gamma_1 & 0 & \cdots & 0 \\ 0 & \mu_2^I + \gamma_2 & & 0 \\ \vdots & & \ddots & \vdots \\ 0 & 0 & \cdots & \mu_n^I + \gamma_n \end{pmatrix}.$$

Note that the i-th diagonal entry of the inverse $\mathscr{V}^{-1}$ implies the average length of time an infectious individual in group i spend during its entire period of infectiousness. Therefore, following the definition in [94], we can define the next generation matrix for system (1.2.2) by

$$\mathbf{K} := \mathscr{F}\mathscr{V}^{-1} = \begin{pmatrix} \frac{\left(S_1^0 + \sigma_1 V_1^0\right)\beta_{11}}{\mu_1^I + \gamma_1} & \cdots & \frac{\left(S_1^0 + \sigma_1 V_1^0\right)\beta_{1n}}{\mu_n^I + \gamma_n} \\ \vdots & \ddots & \vdots \\ \frac{\left(S_n^0 + \sigma_n V_n^0\right)\beta_{n1}}{\mu_1^I + \gamma_1} & \cdots & \frac{\left(S_n^0 + \sigma_n V_n^0\right)\beta_{nn}}{\mu_n^I + \gamma_n} \end{pmatrix}.$$

Hence, the basic reproduction number $\mathscr{R}_0$ is obtained as

$$\mathscr{R}_0 = \rho\left(\mathbf{K}\right) = \max\left\{|\lambda|;\ \lambda \in \sigma\left(\mathbf{K}\right)\right\},$$

where $\rho\left(\cdot\right)$ denotes the spectral radius of a matrix and $\sigma\left(\cdot\right)$ denotes the set of eigenvalues of a matrix.

It is easily seen that system (1.2.2) satisfies the conditions (A1)-(A5) of Theorem 2 in [94], and hence, we have the following proposition.

Proposition 1.2.1. *(i) If $\mathscr{R}_0 < 1$, then the disease-free equilibrium E^0 of system* (1.2.2) *is locally asymptotically stable.*

(ii) If $\mathscr{R}_0 > 1$, then the disease-free equilibrium E^0 of system (1.2.2) *is unstable.*

1.3 Global asymptotic stability of the disease-free equilibrium

In this section, we prove the global asymptotic stability of the disease-free equilibrium E^0 for $\mathscr{R}_0 \leq 1$. For the proof, following the way in [27], we use a matrix whose spectral radius equals to that of the next generation matrix, that is, the basic reproduction number $\mathscr{R}_0$. Let

$$\mathbf{M}^0 := \mathscr{V}^{-1}\mathscr{F} = \begin{pmatrix} \frac{\left(S_1^0 + \sigma_1 V_1^0\right)\beta_{11}}{\mu_1^I + \gamma_1} & \cdots & \frac{\left(S_1^0 + \sigma_1 V_1^0\right)\beta_{1n}}{\mu_1^I + \gamma_1} \\ \vdots & \ddots & \vdots \\ \frac{\left(S_n^0 + \sigma_n V_n^0\right)\beta_{n1}}{\mu_n^I + \gamma_n} & \cdots & \frac{\left(S_n^0 + \sigma_n V_n^0\right)\beta_{nn}}{\mu_n^I + \gamma_n} \end{pmatrix}. \tag{1.3.1}$$

Then the following lemma is proved.

Lemma 1.3.1. $\rho\left(\mathbf{M}^0\right) = \rho\left(\mathbf{K}\right) = \mathscr{R}_0$.

Proof. Since the next generation matrix $\mathbf{K}$ is nonnegative and irreducible, it follows from the Perron-Frobenius theorem (see, e.g., [8, Theorem2.1.4]) that $\mathbf{K}$ has a strictly positive eigenvector $\mathbf{w} := \left(w_1, w_2, \cdots, w_n\right)^T$ that corresponds to the spectral radius $\rho\left(\mathbf{K}\right) = R_0$, that is,

$$\mathbf{K}\mathbf{w} = \rho\left(\mathbf{K}\right)\mathbf{w}.$$

Multiplying by $\mathscr{V}^{-1}$ from the left, we obtain

$$\mathbf{M}^0\mathscr{V}^{-1}\mathbf{w} = \rho(\mathbf{K})\mathscr{V}^{-1}\mathbf{w}.$$

Since $\mathscr{V}^{-1}\mathbf{w}$ is a strictly positive vector, it follows again from the Perron-Frobenius theorem that $\rho(\mathbf{K})$ is equal to the spectral radius $\rho(\mathbf{M}^0)$ of matrix $\mathbf{M}^0$ that corresponds to the eigenvector $\mathscr{V}^{-1}\mathbf{w}$. □

Using Lemma 1.3.1, we prove the following theorem, which is one of the main results of this chapter.

Theorem 1.3.1. *If $\mathscr{R}_0 \leq 1$, then the disease-free equilibrium E^0 of system (1.2.2) is globally asymptotically stable in Ω and there is no endemic equilibrium E^*.*

Proof. It follows from Lemma 1.3.1 that $\rho(\mathbf{M}^0) \leq 1$. Let us define an n-dimensional matrix-valued function

$$\mathbf{M}(\mathbf{S},\mathbf{V}) := \begin{pmatrix} \dfrac{(S_1+\sigma_1V_1)\beta_{11}}{\mu_1^I+\gamma_1} & \cdots & \dfrac{(S_1+\sigma_1V_1)\beta_{1n}}{\mu_1^I+\gamma_1} \\ \vdots & \ddots & \vdots \\ \dfrac{(S_n+\sigma_nV_n)\beta_{n1}}{\mu_n^I+\gamma_n} & \cdots & \dfrac{(S_n+\sigma_nV_n)\beta_{nn}}{\mu_n^I+\gamma_n} \end{pmatrix}$$

on $\mathbb{R}_+^{2n}$, where $\mathbf{S} = (S_1,\cdots,S_n)^T \in \mathbb{R}_+^n$ and $\mathbf{V} = (V_1,\cdots,V_n)^T \in \mathbb{R}_+^n$. Here, note that $\mathbf{M}(\mathbf{S}^0,\mathbf{V}^0) = \mathbf{M}^0$, where $\mathbf{S}^0 = (S_1^0,\cdots,S_n^0)^T$ and $\mathbf{V}^0 = (V_1^0,\cdots,V_n^0)^T$. First we claim that there does not exist any endemic equilibrium E^* in Ω. Suppose that $\mathbf{S} \neq \mathbf{S}^0$. Then we have $\mathbf{0} < \mathbf{M}(\mathbf{S},\mathbf{V}) < \mathbf{M}^0$. Since nonnegative matrix $\mathbf{M}(\mathbf{S},\mathbf{V}) + \mathbf{M}^0$ is irreducible, it follows from the Perron-Frobenius theorem (see [8, Corollary 2.1.5]) that $\rho(\mathbf{M}(\mathbf{S},\mathbf{V})) < \rho(\mathbf{M}^0) \leq 1$. This implies that equation $\mathbf{M}(\mathbf{S},\mathbf{V})\mathbf{I} = \mathbf{I}$ has only the trivial solution $\mathbf{I} = \mathbf{0}$, where $\mathbf{I} = (I_1,\cdots,I_n)^T$. Hence the claim is true.

Next we claim that the disease-free equilibrium E^0 is globally asymptotically stable in Ω. From the Perron-Frobenius theorem (see [8, Theorem 2.1.4]) again, it follows that the nonnegative irreducible matrix $\mathbf{M}^0$ has a strictly positive left eigenvector $\ell := (\ell_1,\cdots,\ell_m) \gg \mathbf{0}$ associated with the eigenvalue $\rho(\mathbf{M}^0)$. Let us define a Lyapunov functional

$$\mathbf{L}(\mathbf{I}) := \sum_{i=1}^{n} \ell_i \frac{I_i}{\mu_i^I+\gamma_i}$$

on $C^1(\mathbb{R}_+;\mathbb{R}_+^n)$, whose derivative along the trajectories of system (1.2.2) is

$$\begin{aligned} \mathbf{L}'(\mathbf{I}) &= \sum_{i=1}^{n} \ell_i \left(\frac{(S_i+\sigma_iV_i)\sum_{j=1}^n \beta_{ij}I_j}{\mu_i^I+\gamma_i} - I_i \right) \\ &= \ell\cdot(\mathbf{M}(\mathbf{S},\mathbf{V}) - \mathbf{E}_n)\mathbf{I} \\ &\leq \ell\cdot(\mathbf{M}^0 - \mathbf{E}_n)\mathbf{I} = \ell\cdot(\rho(\mathbf{M}^0)-1)\mathbf{I} \leq 0. \end{aligned} \tag{1.3.2}$$

Here $\mathbf{E}_n$ denotes the $n\times n$ identity matrix and $\cdot$ denotes the inner product of vectors. If $\rho(\mathbf{M}^0) < 1$, then $\mathbf{L}'(\mathbf{I}) = 0$ is equivalent to $\mathbf{I} = \mathbf{0}$. If $\rho(\mathbf{M}^0) = 1$, then from the second equality of (1.3.2) we see that $\mathbf{L}'(\mathbf{I}) = 0$ implies

$$\ell\cdot\mathbf{M}(\mathbf{S},\mathbf{V})\mathbf{I} = \ell\cdot\mathbf{I}. \tag{1.3.3}$$

Hence, if $(\mathbf{S},\mathbf{V}) \neq (\mathbf{S}^0,\mathbf{V}^0)$, then $\ell\cdot\mathbf{M}(\mathbf{S},\mathbf{V}) < \ell\cdot\mathbf{M}^0 = \rho(\mathbf{M}^0)\ell = \ell$ and thus $\mathbf{I} = \mathbf{0}$ is the only solution of (1.3.3). Summarizing these arguments, we conclude that $\mathbf{L}'(\mathbf{I}) = 0$ is equivalent to $\mathbf{I} = \mathbf{0}$ or $(\mathbf{S},\mathbf{V}) = (\mathbf{S}^0,\mathbf{V}^0)$. This implies that the compact invariant subset of the set where $\mathbf{L}'(\mathbf{I}) = 0$ is only the singleton $\{E^0\} \subset \Omega$. Therefore, from the La Salle invariance principle [60], it follows that the disease free equilibrium E^0 of system (1.2.2) is globally asymptotically stable in Ω. □

1.4 Global asymptotic stability of an endemic equilibrium

Next we turn our attention to the case where $\mathscr{R}_0 > 1$. In the case, it follows from Proposition 1.2.1 that the disease-free equilibrium E^0 is unstable. From a uniform persistence result of [24] and an argument as in the proof of Proposition 3.3 of [62], we can deduce that the instability of E^0 implies the uniform persistence of system (1.2.2) in $\tilde{\Omega}$, that is, there exists a positive constant $c > 0$ such that

$$\liminf_{t\to+\infty} S_i(t) \geq c, \quad \liminf_{t\to+\infty} V_i(t) \geq c, \quad \liminf_{t\to+\infty} I_i(t) \geq c, \quad \forall i \in \mathscr{N},$$

provided $(S_1(0), V_1(0), I_1(0), \cdots, S_n(0), V_n(0), I_n(0)) \in \tilde{\Omega}$. The uniform persistence of system (1.2.2) together with the uniform boundedness of solutions in $\tilde{\Omega}$, which follows from the positive invariance of $\tilde{\Omega}$, implies the existence of an endemic equilibrium E^* in $\tilde{\Omega}$ (see Theorem 2.8.6 of [9] or Theorem D. 3 of [81]). Summarizing these statements, we obtain the following proposition.

Proposition 1.4.1. *If $\mathscr{R}_0 > 1$, then system* (1.2.2) *is uniformly persistent and has at least one endemic equilibrium E^* in $\tilde{\Omega}$.*

Using Proposition 1.4.1, we prove the following theorem, which is one of the main results of this chapter.

Theorem 1.4.1. *If $\mathscr{R}_0 > 1$, then the endemic equilibrium E^* of system* (1.2.2) *is unique and globally asymptotically stable in $\tilde{\Omega}$.*

Proof. For $n = 1$, system (1.2.2) is rewritten as

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t} S = (1-p)\, b - \beta S(t) I(t) - \left(\mu^S + v\right) S(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} V = v S(t) - \sigma \beta V(t) I(t) - \mu^V V(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} I = \left(S(t) + \sigma V(t)\right) \beta I(t) - \left(\mu^I + \gamma\right) I(t), \end{cases} \tag{1.4.1}$$

where we omit the subscript $i = 1$ for simplicity. The global asymptotic stability of an endemic equilibrium E^* of system (1.4.1) is shown by constructing a suitable Lyapunov function, although here we omit the proof since it is a simple matter (see [68, Appendix B]).

We proceed to the case where $n \geq 2$. Note that the components of $E^* = (S_1^*, V_1^*, I_1^*, \cdots, S_n^*, V_n^*, I_n^*) \in \mathbb{R}_+^{3n}$ must satisfy

$$(1-p_i)\, b_i = S_i^* \sum_{j=1}^{n} \beta_{ij} I_j^* + \left(\mu_i^S + v_i\right) S_i^*, \tag{1.4.2}$$

$$v_i S_i^* = V_i^* \sum_{j=1}^{n} \sigma_i \beta_{ij} I_j^* + \mu_i^V V_i^*, \tag{1.4.3}$$

$$\left(\mu_i^I + \gamma_i\right) I_i^* = \left(S_i^* + \sigma_i V_i^*\right) \sum_{j=1}^{n} \beta_{ij} I_j^*, \tag{1.4.4}$$

where $i \in \mathscr{N}$. Following [27], we define

$$\theta_{ij} := \left(S_i^* + \sigma_i V_i^*\right) \beta_{ij} I_j^*, \quad i, j \in \mathscr{N} \tag{1.4.5}$$

and

$$\Theta := \begin{pmatrix} \sum_{j\neq 1} \theta_{1j} & -\theta_{21} & \cdots & -\theta_{n1} \\ -\theta_{12} & \sum_{j\neq 2} \theta_{2j} & \cdots & -\theta_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\theta_{1n} & -\theta_{2n} & \cdots & \sum_{j\neq n} \theta_{nj} \end{pmatrix}, \tag{1.4.6}$$

which is a Laplacian matrix whose column sums are zero. It follows from Assumption 1.2.1 that the matrix Θ is irreducible. Therefore, it follows from Lemma 2.1 of [27] that the solution space of linear system

$$\Theta\zeta = 0 \tag{1.4.7}$$

has dimension 1 with a basis

$$\zeta := (\zeta_1, \zeta_2, \cdots, \zeta_n)^T = (c_1, c_2, \cdots, c_n)^T,$$

where c_i ($i \in \mathcal{N}$) denotes the cofactor of the i-th diagonal entry of Θ. Note that from (1.4.6) and (1.4.7) we have

$$\sum_{j=1}^{n} \theta_{ij}\zeta_i = \sum_{j=1}^{n} \theta_{ji}\zeta_j \tag{1.4.8}$$

for all $i \in \mathcal{N}$. Using such $\zeta = (\zeta_1, \cdots, \zeta_n)$, we can define a Lyapunov function

$$W(\mathbf{S}, \mathbf{V}, \mathbf{I}) := \sum_{i=1}^{n} \zeta_i \left(S_i - S_i^* - S_i^* \ln \frac{S_i}{S_i^*} + V_i - V_i^* - V_i^* \ln \frac{V_i}{V_i^*} + I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*} \right)$$

on $\tilde{\Omega}$. We easily see that $W(\mathbf{S}, \mathbf{V}, \mathbf{I}) \geq 0$ for all $(\mathbf{S}, \mathbf{V}, \mathbf{I}) \gg \mathbf{0}$ and the equality $W(\mathbf{S}, \mathbf{V}, \mathbf{I}) = 0$ holds if and only if $(\mathbf{S}, \mathbf{V}, \mathbf{I}) = (\mathbf{S}^*, \mathbf{V}^*, \mathbf{I}^*)$, where $\mathbf{S}^* := (S_1^*, \cdots, S_n^*)^T$, $\mathbf{V}^* := (V_1^*, \cdots, V_n^*)^T$ and $\mathbf{I}^* := (I_1^*, \cdots, I_n^*)^T$. The derivative of $W(\mathbf{S}, \mathbf{V}, \mathbf{I})$ along the trajectories of system (1.2.2) is

$$\begin{aligned} W'(\mathbf{S}, \mathbf{V}, \mathbf{I}) = \sum_{i=1}^{n} \zeta_i \Bigg\{ & (1-p_i) b_i - \mu_i^S S_i - \mu_i^V V_i - (\mu_i^I + \gamma_i) I_i \\ & - (1-p_i) b_i \frac{S_i^*}{S_i} + S_i^* \sum_{j=1}^{n} \beta_{ij} I_j + (\mu_i^S + \nu_i) S_i^* - \nu_i S_i \frac{V_i^*}{V_i} + V_i^* \sum_{j=1}^{n} \sigma_i \beta_{ij} I_j + \mu_i^V V_i^* \\ & - (S_i + \sigma_i V_i) \sum_{j=1}^{n} \beta_{ij} I_j \frac{I_i^*}{I_i} + (\mu_i^I + \gamma_i) I_i^* \Bigg\}. \end{aligned} \tag{1.4.9}$$

Now we claim that

$$\sum_{i=1}^{n} \zeta_i (S_i^* + \sigma_i V_i^*) \sum_{j=1}^{n} \beta_{ij} I_j = \sum_{i=1}^{n} \zeta_i (\mu_i^I + \gamma_i) I_i. \tag{1.4.10}$$

In fact, from (1.4.4), (1.4.5) and (1.4.8), we have

$$\begin{aligned} \sum_{i=1}^{n} \zeta_i (S_i^* + \sigma_i V_i^*) \sum_{j=1}^{n} \beta_{ij} I_j &= \sum_{i=1}^{n} \sum_{j=1}^{n} \zeta_i (S_i^* + \sigma_i V_i^*) \beta_{ij} I_j = \sum_{i=1}^{n} \sum_{j=1}^{n} \zeta_j (S_j^* + \sigma_j V_j^*) \beta_{ji} I_i \\ &= \sum_{i=1}^{n} \sum_{j=1}^{n} \{ (S_j^* + \sigma_j V_j^*) \beta_{ji} I_i^* \} \zeta_j \frac{I_i}{I_i^*} \\ &= \sum_{i=1}^{n} \frac{I_i}{I_i^*} \sum_{j=1}^{n} \theta_{ji} \zeta_j = \sum_{i=1}^{n} \frac{I_i}{I_i^*} \sum_{j=1}^{n} \theta_{ij} \zeta_i = \sum_{i=1}^{n} \zeta_i (\mu_i^I + \gamma_i) I_i. \end{aligned}$$

From (1.4.9) and (1.4.10), we have

$$\begin{aligned} W'(\mathbf{S}, \mathbf{V}, \mathbf{I}) = \sum_{i=1}^{n} \zeta_i \Bigg[& (1-p_i) b_i \left(1 - \frac{S_i^*}{S_i} \right) + \mu_i^S S_i^* \left(1 - \frac{S_i}{S_i^*} \right) + \nu_i S_i^* \left(1 - \frac{S_i}{S_i^*} \frac{V_i^*}{V_i} \right) + \mu_i^V V_i^* \left(1 - \frac{V_i}{V_i^*} \right) \\ & - (S_i + \sigma_i V_i) \sum_{j=1}^{n} \beta_{ij} I_j \frac{I_i^*}{I_i} + (\mu_i^I + \gamma_i) I_i^* \Bigg]. \end{aligned} \tag{1.4.11}$$

Using (1.4.2) and (1.4.4), we can rewrite (1.4.11) as

$$\begin{aligned} W'(\mathbf{S},\mathbf{V},\mathbf{I}) &= \sum_{i=1}^{n}\zeta_i\Bigg[S_i^*\sum_{j=1}^{n}\beta_{ij}I_j^*\left(1-\frac{S_i^*}{S_i}\right)+\mu_i^S S_i^*\left(2-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\right)\\ &\quad +\nu_i S_i^*\left(2-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}\right)+\mu_i^V V_i^*\left(1-\frac{V_i}{V_i^*}\right)\\ &\quad -(S_i+\sigma_i V_i)\sum_{j=1}^{n}\beta_{ij}I_j\frac{I_i^*}{I_i}+(S_i^*+\sigma_i V_i^*)\sum_{j=1}^{n}\beta_{ij}I_j^*\Bigg]. \end{aligned}$$

Hence, from (1.4.3), we have

$$\begin{aligned} W'(\mathbf{S},\mathbf{V},\mathbf{I}) &\le \sum_{i=1}^{n}\zeta_i\Bigg\{\mu_i^S S_i^*\left(2-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\right)+\mu_i^V V_i^*\left(3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_i}{V_i^*}\right)\\ &\quad +S_i^*\sum_{j=1}^{n}\beta_{ij}I_j^*\left(2-\frac{S_i^*}{S_i}-\frac{S_iI_jI_i^*}{S_i^*I_j^*I_i}\right)+\sigma_i V_i^*\sum_{j=1}^{n}\beta_{ij}I_j^*\left(3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_iI_jI_i^*}{V_i^*I_j^*I_i}\right)\Bigg\}\\ &\le W_1+W_2, \end{aligned} \tag{1.4.12}$$

where

$$W_1=\sum_{i=1}^{n}\zeta_i\left\{\mu_i^S S_i^*\left(2-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\right)+\mu_i^V V_i^*\left(3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_i}{V_i^*}\right)\right\}$$

and

$$W_2=\sum_{i=1}^{n}\zeta_i(S_i^*+\sigma_i V_i^*)\sum_{j=1}^{n}\beta_{ij}I_j^*\max\left(2-\frac{S_i^*}{S_i}-\frac{S_iI_jI_i^*}{S_i^*I_j^*I_i},\,3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_iI_jI_i^*}{V_i^*I_j^*I_i}\right)$$

(note that the reason why a max function is used in W_2 is that we have to obtain coefficient $(S_i^*+\sigma_i V_i^*)\beta_{ij}=\theta_{ij}$ in order to apply the graph-theoretic approach as in [27]). It follows from the arithmetic-geometric mean ([10]) that $W_1\le 0$ and the equality holds if and only if $\mathbf{S}=\mathbf{S}^*$ and $\mathbf{V}=\mathbf{V}^*$. Now we claim that $W_2\le 0$. From (1.4.5), we have

$$W_2=\sum_{i=1}^{n}\sum_{j=1}^{n}\zeta_i\theta_{ij}\max\left(2-\frac{S_i^*}{S_i}-\frac{S_iI_jI_i^*}{S_i^*I_j^*I_i},\,3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_iI_jI_i^*}{V_i^*I_j^*I_i}\right).$$

Following the graph-theoretic approach as in [27, 28, 63, 99, 100, 84, 64], we see from the Kirchhoff Matrix Tree Theorem [74, 51] that W_2 is written as

$$W_2=\sum_{K\in\mathbb{K}}w(K)\sum_{(i,j)\in E(CK)}\max\left(2-\frac{S_i^*}{S_i}-\frac{S_iI_jI_i^*}{S_i^*I_j^*I_i},\,3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_iI_jI_i^*}{V_i^*I_j^*I_i}\right),$$

where, for a directed graph $G(\Theta)$ associated with n-square matrix $\Theta=(\theta_{ij})$ as (1.4.6) (that is, $G(\Theta)$ contains n vertices and arcs from vertex i to vertex j if $\theta_{ji}\neq 0$), $\mathbb{K}$ denotes the set of all spanning unicyclic graphs of $G(\Theta)$, $w(K)$ denotes the weight of unicyclic graph K, CK denotes the unique elementary cycle in unicyclic graph K and $E(CK)$ denotes the set of directed arcs in CK (see [64, Theorem 2.2]). Then, in order to prove $W_2\le 0$, it suffices to show that

$$\sum_{(i,j)\in E(CK)}\max\left(2-\frac{S_i^*}{S_i}-\frac{S_iI_jI_i^*}{S_i^*I_j^*I_i},\,3-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\frac{V_i^*}{V_i}-\frac{V_iI_jI_i^*}{V_i^*I_j^*I_i}\right)\le 0 \tag{1.4.13}$$

for all elementary cycles CK containing at most n vertices. As an example, we first consider an elementary cycle $1\to 2\to 1$ that contains two vertices 1 and 2. In this case, $E(CK)=\{(1,2),(2,1)\}$ and the left-hand side of

(1.4.13) is

$$\begin{aligned}
&\max\left(2-\frac{S_1^*}{S_1}-\frac{S_1I_2I_1^*}{S_1^*I_2^*I_1},\ 3-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*}\frac{V_1^*}{V_1}-\frac{V_1I_2I_1^*}{V_1^*I_2^*I_1}\right)+\max\left(2-\frac{S_2^*}{S_2}-\frac{S_2I_1I_2^*}{S_2^*I_1^*I_2},\ 3-\frac{S_2^*}{S_2}-\frac{S_2}{S_2^*}\frac{V_2^*}{V_2}-\frac{V_2I_1I_2^*}{V_2^*I_1^*I_2}\right)\\
&=\max\Big(4-\frac{S_1^*}{S_1}-\frac{S_1I_2I_1^*}{S_1^*I_2^*I_1}-\frac{S_2^*}{S_2}-\frac{S_2I_1I_2^*}{S_2^*I_1^*I_2},\ 5-\frac{S_1^*}{S_1}-\frac{S_1I_2I_1^*}{S_1^*I_2^*I_1}-\frac{S_2^*}{S_2}-\frac{S_2}{S_2^*}\frac{V_2^*}{V_2}-\frac{V_2I_1I_2^*}{V_2^*I_1^*I_2},\\
&\qquad 5-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*}\frac{V_1^*}{V_1}-\frac{V_1I_2I_1^*}{V_1^*I_2^*I_1}-\frac{S_2^*}{S_2}-\frac{S_2I_1I_2^*}{S_2^*I_1^*I_2},\ 6-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*}\frac{V_1^*}{V_1}-\frac{V_1I_2I_1^*}{V_1^*I_2^*I_1}-\frac{S_2^*}{S_2}-\frac{S_2}{S_2^*}\frac{V_2^*}{V_2}-\frac{V_2I_1I_2^*}{V_2^*I_1^*I_2}\Big).
\end{aligned}$$

Here, note that the elements of the max function in the right-hand side are obtained as the possible sum of an element of the first max function and another element of the second max function in the left-hand side. Since it follows from the arithmetic-geometric mean that all of the elements of the max function in the right-hand side are nonpositive, (1.4.13) holds in this case.

We proceed to more general cases. Let $N\in\mathcal{N}$ be an integer. We can describe an elementary cycle CK that contains N vertices by $n_1\to n_2\to\cdots\to n_N\to n_1$, where $n_i\in\{1,2,\cdots,N\}$ and $n_i\neq n_j$ for $i\neq j$. For this CK, we have $E(CK)=\{(n_1,n_2),(n_2,n_3),\cdots,(n_N,n_1)\}$ and hence the left-hand side of (1.4.13) is rewritten as

$$\sum_{i=1}^{N}\max\left(2-\frac{S_{n_i}^*}{S_{n_i}}-\frac{S_{n_i}I_{n_{i+1}}I_{n_i}^*}{S_{n_i}^*I_{n_{i+1}}^*I_{n_i}},\ 3-\frac{S_{n_i}^*}{S_{n_i}}-\frac{S_{n_i}}{S_{n_i}^*}\frac{V_{n_i}^*}{V_{n_i}}-\frac{V_{n_i}I_{n_{i+1}}I_{n_i}^*}{V_{n_i}^*I_{n_{i+1}}^*I_{n_i}}\right),\tag{1.4.14}$$

where $n_{N+1}=n_1$. Similar to the above case, in order to obtain (1.4.13), it suffices to show that all of the possible sum of elements of each max function in (1.4.14) are nonpositive. Let $p,q\in\{1,2,\cdots,N\}$ be arbitrary integers satisfying $p+q=N$. Then, $E(CK)$ can be divided into two subsets $\mathscr{P}$ and $\mathscr{Q}$ that contain p and q elements, respectively, and satisfy

$$\begin{aligned}
&\max\left(2-\frac{S_{n_i}^*}{S_{n_i}}-\frac{S_{n_i}I_{n_{i+1}}I_{n_i}^*}{S_{n_i}^*I_{n_{i+1}}^*I_{n_i}},\ 3-\frac{S_{n_i}^*}{S_{n_i}}-\frac{S_{n_i}}{S_{n_i}^*}\frac{V_{n_i}^*}{V_{n_i}}-\frac{V_{n_i}I_{n_{i+1}}I_{n_i}^*}{V_{n_i}^*I_{n_{i+1}}^*I_{n_i}}\right)\\
&\qquad=\begin{cases}
2-\dfrac{S_{n_i}^*}{S_{n_i}}-\dfrac{S_{n_i}I_{n_{i+1}}I_{n_i}^*}{S_{n_i}^*I_{n_{i+1}}^*I_{n_i}} & \text{if } (n_i,n_{i+1})\in\mathscr{P},\\
3-\dfrac{S_{n_i}^*}{S_{n_i}}-\dfrac{S_{n_i}}{S_{n_i}^*}\dfrac{V_{n_i}^*}{V_{n_i}}-\dfrac{V_{n_i}I_{n_{i+1}}I_{n_i}^*}{V_{n_i}^*I_{n_{i+1}}^*I_{n_i}} & \text{if } (n_i,n_{i+1})\in\mathscr{Q},
\end{cases}
\end{aligned}$$

for all $i\in\{1,2,\cdots,N\}$ and $\mathscr{P}\cap\mathscr{Q}=\emptyset$. We write

$$\mathscr{P}=\{(p_1,p_2),\cdots,(p_p,p_{p+1})\}\ \text{ and }\ \mathscr{Q}=\{(q_1,q_2),\cdots,(q_q,q_{q+1})\}.$$

Note that each of the elements in $\mathscr{P}\cup\mathscr{Q}$ is equal to either one of the elements in

$$E(CK)=\{(n_1,n_2),(n_2,n_3),\cdots,(n_N,n_1)\}.$$

Under these settings, (1.4.14) is calculated as

$$\begin{aligned}
&2p-\frac{S_{p_1}^*}{S_{p_1}}-\frac{S_{p_1}I_{p_2}I_{p_1}^*}{S_{p_1}^*I_{p_2}^*I_{p_1}}-\frac{S_{p_2}^*}{S_{p_2}}-\frac{S_{p_2}I_{p_3}I_{p_2}^*}{S_{p_2}^*I_{p_3}^*I_{p_2}}-\cdots-\frac{S_{p_p}^*}{S_{p_p}}-\frac{S_{p_p}I_{p_{p+1}}I_{p_p}^*}{S_{p_p}^*I_{p_{p+1}}^*I_{p_p}}\\
+\ &3q-\frac{S_{q_1}^*}{S_{q_1}}-\frac{S_{q_1}}{S_{q_1}^*}\frac{V_{q_1}^*}{V_{q_1}}-\frac{V_{q_1}I_{q_2}I_{q_1}^*}{V_{q_1}^*I_{q_2}^*I_{q_1}}-\frac{S_{q_2}^*}{S_{q_2}}-\frac{S_{q_2}}{S_{q_2}^*}\frac{V_{q_2}^*}{V_{q_2}}-\frac{V_{q_2}I_{q_3}I_{q_2}^*}{V_{q_2}^*I_{q_3}^*I_{q_2}}-\cdots-\frac{S_{q_q}^*}{S_{q_q}}-\frac{S_{q_q}}{S_{q_q}^*}\frac{V_{q_q}^*}{V_{q_q}}-\frac{V_{q_q}I_{q_{q+1}}I_{q_q}^*}{V_{q_q}^*I_{q_{q+1}}^*I_{q_q}}\\
\leq\ &2p+3q-(2p+3q)\left(\frac{I_{p_2}\cdots I_{p_{p+1}}I_{q_2}\cdots I_{q_{q+1}}I_{p_1}^*\cdots I_{p_p}^*I_{q_1}^*\cdots I_{q_q}^*}{I_{p_1}\cdots I_{p_p}I_{q_1}\cdots I_{q_q}I_{p_2}^*\cdots I_{p_{p+1}}^*I_{q_2}^*\cdots I_{q_{q+1}}^*}\right)^{1/(2p+3q)}\\
=\ &2p+3q-(2p+3q)\left(\frac{I_{n_1}\cdots I_{n_N}I_{n_1}^*\cdots I_{n_N}^*}{I_{n_1}\cdots I_{n_N}I_{n_1}^*\cdots I_{n_N}^*}\right)^{1/(2p+3q)}\\
=\ &0,
\end{aligned}$$

and thus (1.4.13) holds. Consequently, we have $W_2 \leq 0$ and hence, it follows from (1.4.12) that $W' \leq W_1 + W_2 \leq 0$. Recalling that $W_1 = 0$ if and only if $(\mathbf{S}, \mathbf{V}) = (\mathbf{S}^*, \mathbf{V}^*)$, we see from the graph-theoretic approach as in [27, 28, 63, 99, 100, 84, 64] that $W' = 0$ if and only if $(\mathbf{S}, \mathbf{V}) = (\mathbf{S}^*, \mathbf{V}^*)$ and

$$1 = \frac{I_j^* I_i}{I_j I_i^*}, \text{ that is, } \frac{I_i}{I_i^*} = \frac{I_j}{I_j^*}, \quad \forall\, i, j \in \mathcal{N}.$$

This equation is equivalent to $\mathbf{I} = c\mathbf{I}^*$, where $c > 0$ is an arbitrary constant. Substituting $(\mathbf{S}, \mathbf{I}) = (\mathbf{S}^*, c\mathbf{I}^*)$ into the first equation of system (1.2.2), we have

$$0 = (1 - p_i)\, b_i - c S_i^* \sum_{j=1}^{n} \beta_{ij} I_j^* - \left(\mu_i^S + v_i\right) S_i^*. \tag{1.4.15}$$

Since the right-hand side of (1.4.15) is monotone decreasing with respect to c, it follows from (1.4.2) that equality (1.4.15) holds if and only if $c = 1$. Summarizing the above arguments, we see that $W'(\mathbf{S}, \mathbf{V}, \mathbf{I}) = 0$ holds if and only if the solution $(\mathbf{S}, \mathbf{V}, \mathbf{I})$ of system (1.2.2) is in the singleton $\{(\mathbf{S}^*, \mathbf{V}^*, \mathbf{I}^*)\}$. Hence, from the La Salle invariance principle [60], we see that E^* is globally asymptotically stable in $\tilde{\Omega}$. □

1.5 Discussion

In this chapter, we have shown that the global asymptotic stability of each equilibrium of the multi-group SVIR model (1.2.2) is completely determined by the the basic reproduction number $\mathscr{R}_0$. This result differs from some previous results obtained in [53, 4, 1] for single-group vaccination models, in which it is shown that the backward bifurcation can occur and the disease can persist even if $\mathscr{R}_0 \leq 1$. The cause of this difference might be the existence of a path from vaccinated class V or recovered class R back to susceptible class S, that is, the loss of temporary immunity, which we do not take into account in model (1.2.2). The study of multi-group vaccination models taking into account such effect has been left as a future task.

Acknowledgment

The author would like to thank the editor and the reviewers for their valuable comments and suggestions to the published version [56] of this chapter.

Chapter 2

A multi-group SIR epidemic model with age structure

Abstract For the class of SIR epidemic models with age structure, the global asymptotic stability of an endemic steady state in case where the basic reproduction number $\mathscr{R}_0$ is greater than unity has not been investigated enough. The purposes of this chapter is to construct a multi-group SIR epidemic model with age structure, which is formulated as an initial-boundary value problem of partial differential equation system, and to clarify the relation between its solution dynamics and the basic reproduction number $\mathscr{R}_0$, including the case $\mathscr{R}_0 > 1$. Under some parameter assumptions, discretization of the model with respect to the age variable induces an ODE system, which is regarded as a generalization of the SVIR epidemic model studied in Chapter 1. As in Chapter 1, the methods of a Lyapunov functional, graph theory and a max function can be applied to the global stability analysis for the discretized model. The basic reproduction number $\mathscr{R}_0$ is proved to be a perfect threshold value in the sense of determining the global asymptotic stability of each equilibrium, that is, the global asymptotic stability of the disease-free equilibrium for $\mathscr{R}_0 \leq 1$ and that of an endemic equilibrium for $\mathscr{R}_0 > 1$. We provide a numerical example showing that a numerical value of $\mathscr{R}_0$ for the discretized system tends to that for the original PDE system as the step size of the discretization is decreased.

Keywords Multi-group SIR epidemic model; Age structure; The basic reproduction number; Global asymptotic stability; Discretization; Lyapunov functional

2.1 Introduction

The age structure is thought to be one of the most important concepts that affects the spread pattern of infectious diseases. For example, for measles, the contact rate would be strongly age-dependent due to the increased infection transmission within schools ([79]) and, for HIV, the time scale of the transmission would be so long that the age-dependent demographic change of the host population should not be negligible ([41]). Therefore, many authors have studied various age-structured epidemic models both from the mathematical and epidemiological point of view (see e.g., [72, 2, 19, 90, 79, 41, 26, 39, 12, 13, 11, 87, 3, 14, 31, 23, 21, 92, 33]).

The SIR epidemic model, in which the total host population is divided into susceptible, infectious and recovered classes, is known as one of the most basic epidemic models in this field of mathematical epidemiology. The class of SIR epidemic models with age structure has been studied by many authors for decades (see e.g., [26, 39, 87, 3, 14]). Here, we introduce a typical example of such a SIR epidemic model, which is described by a nonlinear system of

first-order partial differential equations:

$$\begin{cases} \left(\dfrac{\partial}{\partial t}+\dfrac{\partial}{\partial a}\right)S(t,a) = -S(t,a)\displaystyle\int_0^{\omega}\beta(a,\sigma)I(t,\sigma)\,\mathrm{d}\sigma - \mu(a)S(t,a), \\ \left(\dfrac{\partial}{\partial t}+\dfrac{\partial}{\partial a}\right)I(t,a) = S(t,a)\displaystyle\int_0^{\omega}\beta(a,\sigma)I(t,\sigma)\,\mathrm{d}\sigma - (\mu(a)+\gamma(a))I(t,a), \\ \left(\dfrac{\partial}{\partial t}+\dfrac{\partial}{\partial a}\right)R(t,a) = \gamma(a)I(t,a) - \mu(a)R(t,a), \quad t>0, \quad 0<a\leq\omega, \\ S(t,0)=b, \quad I(t,0)=R(t,0)=0, \quad t>0, \end{cases} \tag{2.1.1}$$

Here, $S(t,a), I(t,a)$ and $R(t,a)$ denote the densities of susceptible, infectious and recovered individuals whose age is $a \in [0,\omega]$ ($\omega \in (0,+\infty)$ denotes the maximum attainable age) at time $t>0$, respectively. $\beta(a,\sigma)$ denotes the coefficient of disease transmission between susceptible individuals aged a and infectious individuals aged σ. $\mu(a)$ denotes the age-specific mortality rate. $\gamma(a)$ denotes the age-specific recovery rate and $b>0$ denotes the fixed birth rate, which is obtained under an assumption that the total host population $P(t,a) := S(t,a)+I(t,a)+R(t,a)$ has attained its time-independent demographic steady state $P^*(a)$ from $t=0$ (see, e.g., [39, Section 2] for more details).

For the case of age-independent parameters, it is a classical fact that the global asymptotic stability of each equilibrium of the system (2.1.1) is completely determined by the basic reproduction number $\mathscr{R}_0$, that is, the disease-free equilibrium of the model is globally asymptotically stable if $\mathscr{R}_0 \leq 1$, while an endemic equilibrium of the model is so if $\mathscr{R}_0 > 1$ ([18, 94]). However, for the more general case of age-dependent parameters, such a complete threshold property has not been proved for system (2.1.1). In [39], for the case of constant recovery rate $\gamma(a) \equiv \gamma$, a positive linear integral operator regarded as the next generation operator [19, 18] was obtained and for a threshold valued obtained as the spectral radius of the operator (that is, the basic reproduction number $\mathscr{R}_0$), the global asymptotic stability of the disease-free equilibrium for the value less than unity and the local asymptotic stability of an endemic equilibrium for the value greater than unity were studied. However, the global asymptotic stability of an endemic equilibrium has not been proved. In fact, some authors have pointed out the possibilities of a destabilized endemic equilibrium even for $\mathscr{R}_0 > 1$ (see [87, 3, 14]). These results do not correspond to the case of age-structured SIS epidemic models, for which a complete threshold value determining the global asymptotic stability of each equilibrium is obtained (see, e.g., [12, 13, 11]). Since the methods used for the analysis of such SIS epidemic models are typically relayed on the monotonicity property of solutions for infectious population that is characteristic for such SIS epidemic models, they can not be directly applied to the analysis of SIR epidemic models.

The main purpose of this chapter is to show the possibility of a unique, globally asymptotically stable endemic equilibrium of system (2.1.1) for $\mathscr{R}_0 > 1$. In particular, the analysis shall be carried out for a multi-group system that is regarded as a generalization of system (2.1.1). In the analysis, the PDE system (2.1.1) is discretized with respect to the age variable a into an ODE system, and the global stability of each equilibrium is investigated for the discretized model. The discretized model can be regarded as a generalization of the SVIR epidemic model studied in Chapter (1), and we can apply the classical method of Lyapunov, graph theoretical approach developed by Guo *et al.* [27] and a method of max functions again as in Chapter (1).

The model we shall study in this chapter is the following multi-group SIR epidemic model with age structure,

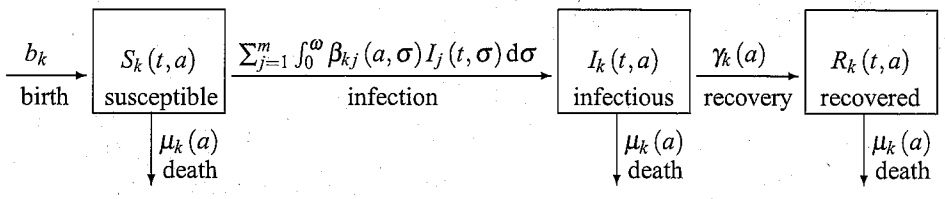


Figure 2.1: Transfer diagram for SIR epidemic model (2.1.2)

which is regarded as a generalization of model (2.1.1):

$$\begin{cases} \left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)S_k(t,a) = -S_k(t,a)\sum_{j=1}^{m}\int_0^{\omega}\beta_{kj}(a,\sigma)I_j(t,\sigma)\,d\sigma - \mu_k(a)S_k(t,a), \\ \left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)I_k(t,a) = S_k(t,a)\sum_{j=1}^{m}\int_0^{\omega}\beta_{kj}(a,\sigma)I_j(t,\sigma)\,d\sigma - (\mu_k(a)+\gamma_k(a))I_k(t,a), \\ \left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)R_k(t,a) = \gamma_k(a)I_k(t,a) - \mu_k(a)R_k(t,a), \quad t>0, \quad 0<a\le\omega, \\ S_k(t,0)=b_k, \quad I_k(t,0)=0, \quad R_k(t,0)=0, \quad t>0, \quad k\in\{1,2,\cdots,m\}. \end{cases} \tag{2.1.2}$$

Here, $S_k(t,a)$, $I_k(t,a)$ and $R_k(t,a)$ denote the densities of susceptible, infectious and recovered individuals of age a in group k at time t, respectively. The meanings of parameters $\mu_k(a)$, $\gamma_k(a)$ and b_k are similar to those in (2.1.1), except for the difference that they are defined for individuals in group k. The disease transmission coefficient is modified as $\beta_{kj}(a,\sigma)$ for the infection between susceptible individuals of age a in group k and infectious individuals of age σ in group j. Thus, the infection is possible to occur beyond the difference of groups.

A multi-group SIS epidemic model with age structure was studied by Feng *et al.* in [23], and the global asymptotic stability of a unique endemic equilibrium was proved under an assumption of quasi-irreducibility. However, similar to the case of single group SIS epidemic models, their proof also relied on the monotonicity property of solutions, and therefore we can not apply their approach directly to the analysis for system (2.1.2). As mentioned above, we discretize (2.1.2) and use the methods of Lyapunov functionals, graph theory and max functions to prove the global asymptotic stability of each equilibrium.

The subsequent sections of this chapter are organized as follows: In section 2.2, we discretize system (2.1.2) into an ODE system, and prove some basic facts. In section 2.3, the global asymptotic stability of each equilibrium of the discretized system is investigated. In section 2.4, providing some numerical examples, we verify the validity of our main stability results. We also provide an example of numerical values of $\mathscr{R}_0$ for the discretized system which approaches to those for the original PDE system (2.1.2) as the step size of the discretization is decreased.

2.2 Preliminaries

2.2.1 Discretization

Let $\mu_k(a)$ and $\gamma_k(a)$ be positive and essentially bounded on $[0,\omega]$ for all k. Let $\beta_{kj}(a,\sigma)$ be nonnegative and essentially bounded on $[0,\omega]\times[0,\omega]$ for all k and j. We make the following assumptions:

Assumption 2.2.1. For all $k,j\in\{1,2,\cdots,m\}$, the disease transmission coefficient $\beta_{kj}(a,\sigma)$ is independent of σ, that is, there exists a $\beta_{kj}\in L^{\infty}_{+}(0,\omega)$ such that $\beta_{kj}(a,\sigma)\equiv\beta_{kj}(a)$.

Assumption 2.2.2. The m-dimensional square matrix $(\beta_{kj}(a))_{1\le k,j\le m}$ is irreducible ([8]) for all $a\in[0,\omega]$.

Assumption 2.2.3. For all $k \in \{1,2,\cdots,m\}$, the sum $\mu_k(a)+\gamma_k(a)$ is age-independent, that is, there exists a positive constant $r_k > 0$ such that $\mu_k(a)+\gamma_k(a) \equiv r_k$.

Assumption 2.2.1 is regarded as a special case of the so-called *proportionate mixing assumption* [21] (or *separable mixing assumption* [18]). Assumption 2.2.2 implies that every pair of groups of same age is joined by an infectious path so that the presence of an infectious individual in the first group causes infection in the second group. Here, note that $\beta_{kj}(a)$ is a strictly positive function if $m = 1$. Assumption 2.2.3 is needed only for the discretization process stated bellow, and thus, it is technical. Biologically, it seems to be too restrictive. However, if we assume that $\gamma_k(a) = \gamma_k$ does not depend on a and is quite larger than $\mu_k(a)$, then $\mu_k(a)+\gamma_k(a) \simeq \gamma_k = r_k$ holds numerically.

Under Assumptions 2.2.1-2.2.3, we can rewrite system (2.1.2) as

$$\begin{cases} \left(\dfrac{\partial}{\partial t}+\dfrac{\partial}{\partial a}\right) S_k(t,a) = -S_k(t,a)\displaystyle\sum_{j=1}^{m}\beta_{kj}(a)\int_0^{\omega} I_j(t,\sigma)\mathrm{d}\sigma - \mu_k(a)S_k(t,a), \\ \left(\dfrac{\partial}{\partial t}+\dfrac{\partial}{\partial a}\right) I_k(t,a) = S_k(t,a)\displaystyle\sum_{j=1}^{m}\beta_{kj}(a)\int_0^{\omega} I_j(t,\sigma)\mathrm{d}\sigma - r_k I_k(t,a), \quad t>0, \quad 0<a\le\omega, \\ S_k(t,0) = b_k, \quad I_k(t,0) = 0, \quad t>0, \quad k\in\{1,2,\cdots,m\}. \end{cases} \tag{2.2.1}$$

Here we omit the equations of R_k $k = 1,2,\cdots,m$ since the solution dynamics of (2.2.1) does not depend on them.

Now we are in a position to discretize (2.2.1). Similar approaches are seen in [92] and [33]. Let us divide the age interval $[0,\omega]$ into n subintervals

$$[0,\omega_1],\ [\omega_1,\omega_2],\cdots,[\omega_{n-1},\omega],$$

which satisfies $0 = \omega_0 < \omega_1 < \cdots < \omega_n = \omega$. Let

$$\beta_{kj}^{(i)} := \beta_{kj}\left(i\frac{\omega}{n}\right), \quad \mu_k^{(i)} := \mu_k\left(i\frac{\omega}{n}\right), \quad i\in\{1,2,\cdots,n\}, \quad k,j\in\{1,2,\cdots,m\}. \tag{2.2.2}$$

Note that $\mu_k^{(i)} > 0$ and $\beta_{kj}^{(i)} \ge 0$ for all k, j and i, and under Assumption 2.2.2, the $m\times m$ matrix $\left(\beta_{kj}^{(i)}\right)_{1\le k,j\le m}$ is irreducible for all i. Using constants (2.2.2), we replace the parameters of system (2.2.1) by the following step functions:

$$\beta_{kj}(a) = \beta_{kj}^{(i)}, \quad \mu_k(a) = \mu_k^{(i)}, \quad \forall a\in(\omega_{i-1},\omega_i), \quad i\in\{1,2,\cdots,n\}, \quad k,j\in\{1,2,\cdots,m\}.$$

Moreover, let us introduce the following functions on $\mathbb{R}_+$:

$$S_k^{(i)}(t) := \int_{\omega_{i-1}}^{\omega_i} S_k(t,a)\mathrm{d}a, \quad I_k^{(i)}(t) := \int_{\omega_{i-1}}^{\omega_i} I_k(t,a)\mathrm{d}a, \quad i\in\{1,2,\cdots,n\}, \quad k\in\{1,2,\cdots,m\}.$$

Let $a^{(i)}$ be the rate at which an individual in the i-th age class moves toward $(i+1)$-th age class, and let it satisfy $S_k(t,\omega_i) = a^{(i)}S_k^{(i)}(t)$ and $I_k(t,\omega_i) = a^{(i)}I_k^{(i)}(t)$, where $a^{(i)} > 0$ for all $i\in\{1,2,\cdots,n-1\}$ and $a^{(n)} = 0$. Under these settings, integrating system (2.2.1) with respect to a from ω_{i-1} to ω_i and adding the differential equations of $I_k^{(i)}$ from $i = 1$ to n, we obtain the following system of ordinary differential equations:

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t}S_k^{(i)}(t) = a^{(i-1)}S_k^{(i-1)}(t) - S_k^{(i)}(t)\displaystyle\sum_{j=1}^{m}\beta_{kj}^{(i)}I_j(t) - \left(\mu_k^{(i)}+a^{(i)}\right)S_k^{(i)}(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t}I_k(t) = \displaystyle\sum_{i=1}^{n}S_k^{(i)}(t)\sum_{j=1}^{m}\beta_{kj}^{(i)}I_j(t) - r_kI_k(t), \\ a^{(0)}S_k^{(0)}(t) = b_k, \quad t>0, \quad i\in\{1,2,\cdots,n\}, \quad k\in\{1,2,\cdots,m\}, \end{cases} \tag{2.2.3}$$

where $I_k(t) := \sum_{i=1}^{n} I_k^{(i)}(t)$. In the subsequent sections of this chapter, we focus on this multi-group SIR epidemic model (2.2.3) with age structure. It is easy to see that, for case $i = 2$, (2.2.3) is equivalent to the multi-group SVIR epidemic model (1.2.2) studied in Chapter 1.

2.2.2 Equilibria, state-space and the basic reproduction number $\mathscr{R}_0$

Let

$$S_{k,0}^{(i)} := \begin{cases} \dfrac{b_k}{\mu_k^{(1)}+a^{(1)}}, & i=1, \\ \dfrac{a^{(i-1)}}{\mu_k^{(i)}+a^{(i)}} S_{k,0}^{(i-1)} = \dfrac{b_k}{\mu_k^{(1)}+a^{(1)}} \displaystyle\prod_{l=2}^{i} \frac{a^{(l-1)}}{\mu_k^{(l)}+a^{(l)}}, & i \in \{2,\cdots,n\}, \end{cases} \qquad k \in \{1,2,\cdots,m\}.$$

Then it is easily seen that the trivial equilibrium, which is obtained by solving

$$\begin{cases} 0 = a^{(i-1)} S_k^{(i-1)*} - S_k^{(i)*} \displaystyle\sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* - \left(\mu_k^{(i)} + a^{(i)}\right) S_k^{(i)*}, \\ 0 = \displaystyle\sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* - r_k I_k^*, \quad i \in \{1,2,\cdots,n\}, \quad k \in \{1,2,\cdots,m\}, \end{cases} \tag{2.2.4}$$

in the situation where $I_k^* = 0$ for all k, is uniquely given by

$$E^0 := \left(S_{1,0}^{(1)}, S_{1,0}^{(2)}, \cdots, S_{m,0}^{(n)}, 0, 0, \cdots, 0\right) \in \mathbb{R}_+^{(n+1)m}, \tag{2.2.5}$$

and E^0 is epidemiologically called *the disease-free equilibrium* [94] of system (2.2.3). A solution of (2.2.4) in the situation where $I_k^* > 0$ for some k is called an *endemic equilibrium* [19] of system (2.2.3), and we denote it by $E^* := \left(S_1^{(1)*}, S_1^{(2)*}, \cdots, S_m^{(n)*}, I_1^*, I_2^*, \cdots, I_m^*\right)$.

Let $\bar{\mu}_k := \min_i \mu_k^{(i)}$ and $d_k := \min\{\bar{\mu}_k, r_k\}$. Then, adding the equations of (2.2.3), we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\sum_{i=1}^{n} S_k^{(i)}(t) + I_k(t)\right) \le b_k - d_k\left(\sum_{i=1}^{n} S_k^{(i)}(t) + I_k(t)\right), \quad k \in \{1,2,\cdots,m\},$$

which implies that $\limsup_{t\to+\infty}(\sum_i S_k^{(i)} + I_k) \le b_k/d_k$. In addition, $(S_k^{(i)})' \le a^{(i-1)} S_k^{(i-1)} - (\mu_k^{(i)} + a^{(i)}) S_k^{(i)}$ is also obtained from ((2.2.3)) and this implies that $\limsup_{t\to+\infty} S_k^{(i)} \le S_{k,0}^{(i)}$. Hence, omega limit sets of system (2.2.3) are contained in a bounded feasible region

$$\Omega := \left\{ \left(S_1^{(1)}, \cdots, S_m^{(n)}, I_1, \cdots, I_m\right) \in \mathbb{R}_+^{(n+1)m} \;\middle|\; 0 < S_k^{(i)} \le S_{k,0}^{(i)}, \; \sum_{i=1}^{n} S_k^{(i)} + I_k \le \frac{b_k}{d_k}, \; i \in \{1,\cdots,n\}, \; k \in \{1,\cdots,m\} \right\}, \tag{2.2.6}$$

which is included in the nonnegative cone of $\mathbb{R}^{(n+1)m}$. It is easy to verify that region Ω is positively invariant for system (2.2.3) (see, e.g., [92]). The existence and uniqueness of the disease-free equilibrium E^0, which is given by (2.2.5), in the boundary $\partial\Omega$ of region Ω is trivial. The existence and uniqueness of an endemic equilibrium E^* in Ω^0 shall be discussed in section 2.3, where

$$\Omega^0 := \left\{ \left(S_1^{(1)}, \cdots, S_m^{(n)}, I_1, \cdots, I_m\right) \in \Omega \;\middle|\; S_k^{(i)} < S_{k,0}^{(i)}, \; \sum_{i=1}^{n} S_k^{(i)} + I_k < \frac{b_k}{d_k}, \; I_k > 0, \; i \in \{1,\cdots,n\}, \; k \in \{1,\cdots,m\} \right\} \tag{2.2.7}$$

is the interior of Ω.

For multi-group system (2.2.3), the basic reproduction number $\mathscr{R}_0$, which is epidemiologically defined as the expected number of secondary cases produced by a typical infected individual during its entire period of

infectiousness in a completely susceptible population (see [2, 18, 19, 94]), is mathematically obtained as the spectral radius of a matrix called *the next generation matrix*. Following [94], we set matrices

$$\mathscr{F} := \left(\sum_{i=1}^{n} S_{k,0}^{(i)} \beta_{kj}^{(i)}\right)_{1\le k,j\le m} = \begin{pmatrix} \sum_{i=1}^{n} S_{1,0}^{(i)} \beta_{11}^{(i)} & \cdots & \sum_{i=1}^{n} S_{1,0}^{(i)} \beta_{1m}^{(i)} \\ \vdots & \ddots & \vdots \\ \sum_{i=1}^{n} S_{m,0}^{(i)} \beta_{m1}^{(i)} & \cdots & \sum_{i=1}^{n} S_{m,0}^{(i)} \beta_{mm}^{(i)} \end{pmatrix},$$

for the new infections produced by infective individuals of each compartment in the linearized system for system (2.2.3) around the disease-free equilibrium E^0, and $\mathscr{V} := \operatorname{diag}(r_1, r_2, \cdots, r_m)$ whose inverse $\mathscr{V}^{-1}$ implies the average length of time each infectious individual spends in each compartment during its lifetime. Then, the next generation matrix $\mathbf{K}$ is given by

$$\mathbf{K} := \mathscr{F}\mathscr{V}^{-1} = \left(\frac{\sum_{i=1}^{n} S_{k,0}^{(i)} \beta_{kj}^{(i)}}{r_j}\right)_{1\le k,j\le m} = \begin{pmatrix} \frac{\sum_{i=1}^{n} S_{1,0}^{(i)} \beta_{11}^{(i)}}{r_1} & \cdots & \frac{\sum_{i=1}^{n} S_{1,0}^{(i)} \beta_{1m}^{(i)}}{r_m} \\ \vdots & \ddots & \vdots \\ \frac{\sum_{i=1}^{n} S_{m,0}^{(i)} \beta_{m1}^{(i)}}{r_1} & \cdots & \frac{\sum_{i=1}^{n} S_{m,0}^{(i)} \beta_{mm}^{(i)}}{r_m} \end{pmatrix} \tag{2.2.8}$$

and the basic reproduction number $\mathscr{R}_0$ for system (2.2.3) is obtained as

$$\mathscr{R}_0 = \rho(\mathbf{K}) = \sup\{|\lambda|;\ \lambda \in \sigma(\mathbf{K})\}, \tag{2.2.9}$$

where $\rho(\cdot)$ denotes the spectral radius of a matris and $\sigma(\cdot)$ denote the set of eigenvalues of a matrix. It is easy to verify that system (2.2.3) satisfies conditions (A1)-(A5) of Theorem 2 of [94]. Hence, we have the following lemma:

Lemma 2.2.1. *Let the disease-free equilibrium E^0 and the basic reproduction number $\mathscr{R}_0$ be defined by (2.2.5) and (2.2.9), respectively. For system (2.2.3), E^0 is locally asymptotically stable if $\mathscr{R}_0 < 1$, while it is unstable if $\mathscr{R}_0 > 1$.*

2.3 Global asymptotic stability of each equilibrium

In this section, we prove the following main theorem of this chapter:

Theorem 2.3.1. *Let the disease-free equilibrium E^0, regions Ω, Ω^0 and the basic reproduction number $\mathscr{R}_0$ be defined by* (2.2.5), (2.2.6), (2.2.7) *and* (2.2.9), *respectively. For system* (2.2.3), *the following statements hold:*

(i) *If $\mathscr{R}_0 \le 1$, then E^0 is globally asymptotically stable in Ω, and there exists no endemic equilibrium E^* in Ω.*

(ii) *If $\mathscr{R}_0 > 1$, then an endemic equilibrium E^* exists uniquely and it is globally asymptotically stable in Ω^0, and E^0 is unstable.*

2.3.1 The disease-free equilibrium

Following [27], we define a matrix

$$\mathbf{M}^0 := \mathscr{V}^{-1}\mathscr{F} = \left(\frac{\sum_{i=1}^{n} S_{k,0}^{(i)} \beta_{kj}^{(i)}}{r_k}\right)_{1\le k,j\le m} = \begin{pmatrix} \frac{\sum_{i=1}^{n} S_{1,0}^{(i)} \beta_{11}^{(i)}}{r_1} & \cdots & \frac{\sum_{i=1}^{n} S_{1,0}^{(i)} \beta_{1m}^{(i)}}{r_1} \\ \vdots & \ddots & \vdots \\ \frac{\sum_{i=1}^{n} S_{m,0}^{(i)} \beta_{m1}^{(i)}}{r_m} & \cdots & \frac{\sum_{i=1}^{n} S_{m,0}^{(i)} \beta_{mm}^{(i)}}{r_m} \end{pmatrix}$$

(see also (1.3.1) in Chapter 1). Then, under Assumption 2.2.2, both of the nonnegative matrices $\mathbf{K}$ and $\mathbf{M}^0$ are irreducible, and hence from the Perron-Frobenius theorem (see e.g., [8]) it follows that their spectral radii are

given by each of their simple eigenvalues. Hence, as in Lemma 1.3.1 in Chapter 1, we obtain $\mathscr{R}_0 = \rho(\mathbf{K}) = \rho\left(\mathscr{F}\mathscr{V}^{-1}\right) = \rho\left(\mathscr{V}^{-1}\mathscr{F}\right) = \rho(\mathbf{M_0})$.

In what follows, for two nonnegative m-square matrices $\mathbf{A} = (a_{ij})$ and $\mathbf{B} = (b_{ij})$, we write $\mathbf{A} \leq \mathbf{B}$ if $a_{ij} \leq b_{ij}$ for all i and j, and $\mathbf{A} < \mathbf{B}$ if $\mathbf{A} \leq \mathbf{B}$ and $\mathbf{A} \neq \mathbf{B}$.

Proof of (i) of Theorem 2.3.1. Let us define a matrix-valued function $\mathbf{M}$ on $\mathbb{R}_+^{n\times m}$ by

$$\mathbf{M}(\mathbf{S}) := \left(\frac{\sum_{i=1}^n S_k^{(i)}\beta_{kj}^{(i)}}{r_k}\right)_{1\leq k,j\leq m} = \begin{pmatrix} \frac{\sum_{i=1}^n S_1^{(i)}\beta_{11}^{(i)}}{r_1} & \cdots & \frac{\sum_{i=1}^n S_1^{(i)}\beta_{1m}^{(i)}}{r_1} \\ \vdots & \ddots & \vdots \\ \frac{\sum_{i=1}^n S_m^{(i)}\beta_{m1}^{(i)}}{r_m} & \cdots & \frac{\sum_{i=1}^n S_m^{(i)}\beta_{mm}^{(i)}}{r_m} \end{pmatrix},$$

where $\mathbf{S} := \left(S_1^{(1)}, S_1^{(2)}, \cdots, S_m^{(n)}\right) \in \mathbb{R}_+^{n\times m}$. Then, we have $\mathbf{M}\left(\mathbf{S}^0\right) = \mathbf{M}^0$, where $\mathbf{S}^0 := \left(S_{1,0}^{(1)}, S_{1,0}^{(2)}, \cdots, S_{m,0}^{(n)}\right) \in \mathbb{R}_+^{n\times m}$.

First we show that there exists no endemic equilibrium E^* in Ω. Suppose that $\mathbf{S} \neq \mathbf{S}^0$. Then, for solutions in Ω, we have $\mathbf{0} < \mathbf{M}(\mathbf{S}) < \mathbf{M}^0$. Since nonnegative matrices $\mathbf{M}(\mathbf{S})$, $\mathbf{M}^0$ and $\mathbf{M}(\mathbf{S}) + \mathbf{M}^0$ are irreducible, it follows from the Perron-Frobenius theorem (see [8, Corollary 2.1.5]) that $\rho(\mathbf{M}(\mathbf{S})) < \rho\left(\mathbf{M}^0\right) = \mathscr{R}_0 \leq 1$. This implies that equation $\mathbf{M}(\mathbf{S})\mathbf{I}^T = \mathbf{I}^T$ has only the trivial solution $\mathbf{I} = \mathbf{0}$, where $\mathbf{I} = (I_1, \cdots, I_m)$ and T denotes the transpose of a vector. Thus, only the disease-free equilibrium E^0 exists in Ω and E^* does not exist.

Next we show that the disease-free equilibrium E^0 is globally asymptotically stable in Ω. Again from the Perron-Frobenius theorem (see [8, Theorem 2.1.4]) we see that the nonnegative irreducible matrix $\mathbf{M}^0$ has a positive left eigenvector $\ell := (\ell_1, \cdots, \ell_m)$ (that is, $\ell_k > 0$ for all k) associated with the eigenvalue $\rho\left(\mathbf{M}^0\right) = \mathscr{R}_0$. Let us define a Lyapunov functional on $C^1\left(\mathbb{R}; \mathbb{R}_+^m\right)$ as $L(\mathbf{I}) = \sum_{k=1}^n \ell_k I_k / r_k$ whose derivative along the trajectories of system (2.2.3) is calculated as

$$\begin{aligned} L'(\mathbf{I}) &= \sum_{i=1}^n \ell_k \left(\frac{\sum_{i=1}^n S_k^{(i)} \sum_{j=1}^n \beta_{kj}^{(i)} I_j}{r_k} - I_k\right) \\ &= \ell \cdot (\mathbf{M}(\mathbf{S}) - \mathbf{E}_n)\mathbf{I}^T \\ &\leq \ell \cdot \left(\mathbf{M}^0 - \mathbf{E}_n\right)\mathbf{I}^T = \ell \cdot \left(\rho(\mathbf{M}^0) - 1\right)\mathbf{I}^T = (\mathscr{R}_0 - 1)\ell \cdot \mathbf{I}^T \leq 0, \end{aligned} \tag{2.3.1}$$

where $\mathbf{E}_n$ and $\cdot$ denote the n-dimensional identity matrix and the inner product of vectors, respectively. If $\mathscr{R}_0 < 1$, then $L'(\mathbf{I}) = 0$ is equivalent to $\mathbf{I} = \mathbf{0}$. Suppose that $\mathscr{R}_0 = 1$. Then from (2.3.1) we see that $L'(\mathbf{I}) = 0$ implies

$$\ell \cdot \mathbf{M}(\mathbf{S})\mathbf{I}^T = \ell \cdot \mathbf{I}^T. \tag{2.3.2}$$

If $\mathbf{S} \neq \mathbf{S}^0$, then we have $\ell \cdot \mathbf{M}(\mathbf{S}) < \ell \cdot \mathbf{M}^0 = \rho(\mathbf{M}^0)\ell = \ell$, and thus the solution of (2.3.2) is only the trivial one $\mathbf{I} = \mathbf{0}$. Summarizing the above, we see that $L'(\mathbf{I}) = 0$ if and only if $\mathbf{I} = \mathbf{0}$ or $\mathbf{S} = \mathbf{S}^0$, and this implies that the compact invariant subset of the set where $L'(\mathbf{I}) = 0$ is only the singleton $\{E^0\}$ in Ω. Hence, from the La Salle invariance principle [60] it follows that the disease free equilibrium E^0 is globally asymptotically stable in Ω. □

2.3.2 An endemic equilibrium

From a uniform persistence result obtained in [24] and an argument as in the proof of Proposition 3.3 in [62], we can deduce that the instability of the disease-free equilibrium E^0 implies the uniform persistence of system (2.2.3) in Ω^0. Uniform persistence of system (2.2.3) together with the uniform boundedness of solutions in Ω^0, which follows from the positively invariance of Ω^0, implies the existence of an endemic equilibrium E^* in Ω^0 (see [9, Theorem 2.8.6] and [81, Theorem D.3]). Summarizing these arguments, from Lemma 2.2.1, we have the following lemma:

Lemma 2.3.1. *Let region Ω^0 and the basic reproduction number $\mathscr{R}_0$ be defined by (2.2.7) and (2.2.9), respectively. If $\mathscr{R}_0 > 1$, then system (2.2.3) has at least one endemic equilibrium E^* in Ω^0.*

The remainder of this section is devoted to the proof of (ii) of Theorem 2.3.1.

Proof of (ii) of Theorem 2.3.1. Let $E^* = \left(S_1^{(1)*}, \cdots, S_m^{(n)*}, I_1^*, \cdots, I_m^*\right) = (\mathbf{S}^*, \mathbf{I}^*) \in \Omega^0$ be an endemic equilibrium of system (2.2.3), whose existence is guaranteed by Lemma 2.3.1. Note that the components of E^* must satisfy

$$b_k = S_k^{(1)*} \sum_{j=1}^{m} \beta_{kj}^{(1)} I_j^* + \left(\mu_k^{(1)} + a^{(1)}\right) S_k^{(1)*}, \tag{2.3.3}$$

$$a^{(i-1)} S_k^{(i-1)*} = S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* + \left(\mu_k^{(i)} + a^{(i)}\right) S_k^{(i)*}, \quad i \in \{2, 3, \cdots, n\}, \tag{2.3.4}$$

$$r_k I_k^* = \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^*, \tag{2.3.5}$$

for $k = 1, 2, \cdots, m$.

First we consider the case where $m = 1$. System (2.2.3) can be rewritten as

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t} S^{(i)}(t) = a^{(i-1)} S^{(i-1)}(t) - S^{(i)}(t) \beta^{(i)} I(t) - \left(\mu^{(i)} + a^{(i)}\right) S^{(i)}(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t} I(t) = \sum\limits_{i=1}^{n} S^{(i)}(t) \beta^{(i)} I(t) - r I(t), \\ a^{(0)} S^{(0)}(t) = b, \quad t > 0, \quad i \in \{1, 2, \cdots, n\}, \end{cases} \tag{2.3.6}$$

where we omit the subscript $k = 1$ for simplicity. Note that $\beta^{(i)}$ is positive for all i under Assumption 2.2.2. Let us now define a Lyapunov function $U : \Omega^0 \to \mathbb{R}_+$ as follows:

$$U(\mathbf{S}, \mathbf{I}) := \sum_{i=1}^{n} \left(S^{(i)} - S^{(i)*} - S^{(i)*} \ln \frac{S^{(i)}}{S^{(i)*}} \right) + I - I^* - I^* \ln \frac{I}{I^*},$$

It is clear that $U(\mathbf{S}, \mathbf{I}) \geq 0$ for all $(\mathbf{S}, \mathbf{I}) \in \Omega^0$ and $U(\mathbf{S}, \mathbf{I}) = 0$ if and only if $(\mathbf{S}, \mathbf{I}) = (\mathbf{S}^*, \mathbf{I}^*)$. The derivative of U along the trajectories of system (2.3.6) is calculated as

$$\begin{aligned} U'(\mathbf{S}, \mathbf{I}) = b - \sum_{i=1}^{n} \mu^{(i)} S^{(i)} - rI + \sum_{i=1}^{n} S^{(i)*} \beta^{(i)} I - b \frac{S^{(1)*}}{S^{(1)}} \\ - \sum_{i=2}^{n} a^{(i-1)} S^{(i-1)} \frac{S^{(i)*}}{S^{(i)}} + \sum_{i=1}^{n} \left(\mu^{(i)} + a^{(i)}\right) S^{(i)*} - \sum_{i=1}^{n} S^{(i)} \beta^{(i)} I^* + rI^*. \end{aligned}$$

From (2.3.5), we have $rI^* = \sum_{i=1}^{n} S^{(i)*} \beta^{(i)} I^*$ and $rI = \sum_{i=1}^{n} S^{(i)*} \beta^{(i)} I$. Hence

$$\begin{aligned} U'(\mathbf{S}, \mathbf{I}) = b \left(1 - \frac{S^{(1)*}}{S^{(1)}}\right) + \sum_{i=1}^{n} \mu^{(i)} S^{(i)*} \left(1 - \frac{S^{(i)}}{S^{(i)*}}\right) \\ + \sum_{i=2}^{n} a^{(i-1)} S^{(i-1)*} \left(1 - \frac{S^{(i-1)}}{S^{(i-1)*}} \frac{S^{(i)*}}{S^{(i)}}\right) + \sum_{i=1}^{n} S^{(i)*} \beta^{(i)} I^* \left(1 - \frac{S^{(i)}}{S^{(i)*}}\right). \end{aligned} \tag{2.3.7}$$

In addition, it follows from (2.3.3) and (2.3.4) that

$$\begin{aligned} b = S^{(1)*} \left(\beta^{(1)} I^* + \mu^{(1)}\right) + a^{(1)} S^{(1)*} &= S^{(1)*} \left(\beta^{(1)} I^* + \mu^{(1)}\right) + S^{(2)*} \left(\beta^{(2)} I^* + \mu^{(2)}\right) + a^{(2)} S^{(2)*} \\ &= \sum_{i=1}^{n} S^{(i)*} \left(\beta^{(i)} I^* + \mu^{(i)}\right), \end{aligned} \tag{2.3.8}$$

and

$$a^{(i-1)} S^{(i-1)*} = S^{(i)*} \left(\beta^{(i)} I^* + \mu^{(i)}\right) + a^{(i)} S^{(i)*} = \sum_{\ell=i}^{n} S^{(\ell)*} \left(\beta^{(\ell)} I^* + \mu^{(\ell)}\right). \tag{2.3.9}$$

Substituting (2.3.8) and (2.3.9) into (2.3.7), we have

$$\begin{aligned} U'(\mathbf{S},\mathbf{I}) &= \sum_{i=1}^{n} S^{(i)*}\left(\beta^{(i)}I^{*}+\mu^{(i)}\right)\left(1-\frac{S^{(1)*}}{S^{(1)}}\right)+\sum_{i=1}^{n}\mu^{(i)}S^{(i)*}\left(1-\frac{S^{(i)}}{S^{(i)*}}\right) \\ &\quad +\sum_{i=2}^{n}\sum_{\ell=i}^{n} S^{(\ell)*}\left(\beta^{(\ell)}I^{*}+\mu^{(\ell)}\right)\left(1-\frac{S^{(i-1)}}{S^{(i-1)*}}\frac{S^{(i)*}}{S^{(i)}}\right)+\sum_{i=1}^{n} S^{(i)*}\beta^{(i)}I^{*}\left(1-\frac{S^{(i)}}{S^{(i)*}}\right) \\ &= \sum_{i=1}^{n} S^{(i)*}\left(\beta^{(i)}I^{*}+\mu^{(i)}\right)\left(i+1-\sum_{\ell=1}^{i}\frac{S^{(\ell-1)}S^{(\ell)*}}{S^{(\ell-1)*}S^{(\ell)}}-\frac{S^{(i)}}{S^{(i)*}}\right). \end{aligned}$$

Hence, from the arithmetic-geometric mean [10], it follows that $U'(\mathbf{S},\mathbf{I}) \le 0$ and the equality $U'(\mathbf{S},\mathbf{I}) = 0$ holds if and only if $\mathbf{S} = \mathbf{S}^*$. Therefore, from the equations for $S^{(i)}$ in (2.3.6), we immediately see that the compact invariant subset of the set where $U'(\mathbf{S},\mathbf{I}) = 0$ is only the singleton $(\mathbf{S}^*,\mathbf{I}^*)$ in Ω^0. Then, it follows from the La Salle invariance principle [60] that the endemic equilibrium E^* is globally asymptotically stable in Ω^0 (which, of course, implies the uniqueness of E^*).

Next we consider the case where $m \ge 2$. Following [27], we set a Laplacian matrix ([64])

$$\Theta := \begin{pmatrix} \sum_{l\neq 1}\theta_{1l} & -\theta_{21} & \cdots & -\theta_{m1} \\ -\theta_{12} & \sum_{l\neq 2}\theta_{2l} & \cdots & -\theta_{m2} \\ \vdots & \vdots & \ddots & \vdots \\ -\theta_{1m} & -\theta_{2m} & \cdots & \sum_{l\neq m}\theta_{ml} \end{pmatrix}, \tag{2.3.10}$$

where

$$\theta_{kj} := \sum_{i=1}^{n} S_k^{(i)*}\beta_{kj}^{(i)}I_j^*, \quad k,j \in \{1,2,\cdots,m\}. \tag{2.3.11}$$

Since matrix Θ is irreducible under Assumption 2.2.2, it follows from Lemma 2.1 in [27] that the solution space of linear system

$$\Theta\mathbf{v} = 0, \tag{2.3.12}$$

has dimension 1, with a basis

$$\mathbf{v} := (v_1, v_2, \cdots, v_m)^T = (c_1, c_2, \cdots, c_m)^T. \tag{2.3.13}$$

Here c_k denotes the cofactor of the k-th diagonal entry of Θ. Now note that, from (2.3.10) and (2.3.12), we have

$$\sum_{j=1}^{m}\theta_{kj}v_k = \sum_{j=1}^{m}\theta_{jk}v_j. \tag{2.3.14}$$

for all $k \in \{1,2,\cdots,m\}$. Let us now consider a Lyapunov function $V : \Omega^0 \to \mathbb{R}_+$ such that

$$V(\mathbf{S},\mathbf{I}) := \sum_{k=1}^{m} v_k\left\{\sum_{i=1}^{n}\left(S_k^{(i)} - S_k^{(i)*} - S_k^{(i)*}\ln\frac{S_k^{(i)}}{S_k^{(i)*}}\right) + I_k - I_k^* - I_k^*\ln\frac{I_k}{I_k^*}\right\},$$

where v_k $(k \in \{1,2,\cdots,m\})$ is a component of the basis defined in (2.3.13). It is obvious that $V(\mathbf{S},\mathbf{I}) \ge 0$ for all $(\mathbf{S},\mathbf{I}) \in \Omega^0$ and the equality $V(\mathbf{S},\mathbf{I}) = 0$ holds if and only if $(\mathbf{S},\mathbf{I}) = (\mathbf{S}^*,\mathbf{I}^*)$. The derivative of V along the trajectories of system (2.2.3) is given by

$$\begin{aligned} V'(\mathbf{S},\mathbf{I}) = \sum_{k=1}^{m} v_k\Bigg\{ & b_k - \sum_{i=1}^{n}\mu_k^{(i)}S_k^{(i)} - r_kI_k - b_k\frac{S_k^{(1)*}}{S_k^{(1)}} + S_k^{(1)*}\sum_{j=1}^{m}\beta_{kj}^{(1)}I_j + (\mu_k^{(1)} + a^{(1)})S_k^{(1)*} \\ & - \sum_{i=2}^{n} a^{(i-1)}S_k^{(i-1)}\frac{S_k^{(i)*}}{S_k^{(i)}} + \sum_{i=2}^{n} S_k^{(i)*}\sum_{j=1}^{m}\beta_{kj}^{(i)}I_j + \sum_{i=2}^{n}\left(\mu_k^{(i)} + a^{(i)}\right)S_k^{(i)*} - \sum_{i=1}^{n} S_k^{(i)}\sum_{j=1}^{m}\beta_{kj}^{(i)}I_j\frac{I_k^*}{I_k} + r_kI_k^*\Bigg\}. \end{aligned} \tag{2.3.15}$$

Now we are in a position to show that

$$\sum_{k=1}^{m} v_k \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j = \sum_{k=1}^{m} v_k r_k I_k. \tag{2.3.16}$$

In fact, from (2.3.5), (2.3.11) and (2.3.14), we have

$$\begin{aligned}\sum_{k=1}^{m} v_k \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j &= \sum_{k=1}^{m} \sum_{j=1}^{m} \sum_{i=1}^{n} v_k S_k^{(i)*} \beta_{kj}^{(i)} I_j = \sum_{k=1}^{m} \sum_{j=1}^{m} \sum_{i=1}^{n} v_j S_j^{(i)*} \beta_{jk}^{(i)} I_k = \sum_{k=1}^{m} \sum_{j=1}^{m} \left(\sum_{i=1}^{n} S_j^{(i)*} \beta_{jk}^{(i)} I_k^* \right) v_j \frac{I_k}{I_k^*} \\ &= \sum_{k=1}^{m} \frac{I_k}{I_k^*} \sum_{j=1}^{m} \theta_{jk} v_j = \sum_{k=1}^{m} \frac{I_k}{I_k^*} \sum_{j=1}^{m} \theta_{kj} v_k = \sum_{k=1}^{m} v_k r_k I_k\end{aligned}$$

and hence, (2.3.16) holds. Substituting (2.3.16) into (2.3.15), we have

$$\begin{aligned}V'(\mathbf{S},\mathbf{I}) &= \sum_{k=1}^{m} v_k \left\{ b_k \left(1 - \frac{S_k^{(1)*}}{S_k^{(1)}} \right) + \sum_{i=1}^{n} \mu_k^{(i)} S_k^{(i)*} \left(1 - \frac{S_k^{(i)}}{S_k^{(i)*}} \right) \right. \\ &\quad \left. + \sum_{i=2}^{n} a^{(i-1)} S_k^{(i-1)*} \left(1 - \frac{S_k^{(i-1)}}{S_k^{(i-1)*}} \frac{S_k^{(i)*}}{S_k^{(i)}} \right) - \sum_{i=1}^{n} S_k^{(i)} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j \frac{I_k^*}{I_k} + r_k I_k^* \right\}. \end{aligned} \tag{2.3.17}$$

Now, note that it follows from (2.3.3) and (2.3.4) that

$$\begin{aligned}b_k = S_k^{(1)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(1)} I_j^* + \mu_k^{(1)} \right) + a^{(1)} S_k^{(1)*} &= S_k^{(1)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(1)} I_j^* + \mu_k^{(1)} \right) + S_k^{(2)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(2)} I_j^* + \mu_k^{(2)} \right) + a^{(2)} S_k^{(2)*} \\ &= \sum_{i=1}^{n} S_k^{(i)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* + \mu_k^{(i)} \right), \end{aligned} \tag{2.3.18}$$

and

$$a^{(i-1)} S_k^{(i-1)*} = S_k^{(i)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* + \mu_k^{(i)} \right) + a^{(i)} S_k^{(i)*} = \sum_{\ell=i}^{n} S_k^{(\ell)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(\ell)} I_j^* + \mu_k^{(\ell)} \right), \tag{2.3.19}$$

respectively. Substituting (2.3.5), (2.3.18) and (2.3.19) into (2.3.17), we obtain

$$\begin{aligned}V'(\mathbf{S},\mathbf{I}) &= \sum_{k=1}^{m} v_k \left\{ \sum_{i=1}^{n} S_k^{(i)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* + \mu_k^{(i)} \right) \left(1 - \frac{S_k^{(1)*}}{S_k^{(1)}} \right) + \sum_{i=1}^{n} \mu_k^{(i)} S_k^{(i)*} \left(1 - \frac{S_k^{(i)}}{S_k^{(i)*}} \right) \right. \\ &\quad \left. + \sum_{i=2}^{n} \sum_{\ell=i}^{n} S_k^{(\ell)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(\ell)} I_j^* + \mu_k^{(\ell)} \right) \left(1 - \frac{S_k^{(i-1)}}{S_k^{(i-1)*}} \frac{S_k^{(i)*}}{S_k^{(i)}} \right) - \sum_{i=1}^{n} S_k^{(i)} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j \frac{I_k^*}{I_k} + \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* \right\}. \end{aligned}$$

Rearranging gives

$$\begin{aligned}V'(\mathbf{S},\mathbf{I}) &= \sum_{k=1}^{m} v_k \left\{ \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* \left(2 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(i)} I_j I_k^*}{S_k^{(i)*} I_j^* I_k} \right) + \sum_{i=1}^{n} \mu_k^{(i)} S_k^{(i)*} \left(2 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(i)}}{S_k^{(i)*}} \right) \right. \\ &\quad \left. + \sum_{i=2}^{n} \sum_{\ell=i}^{n} S_k^{(\ell)*} \left(\sum_{j=1}^{m} \beta_{kj}^{(\ell)} I_j^* + \mu_k^{(\ell)} \right) \left(1 - \frac{S_k^{(i-1)}}{S_k^{(i-1)*}} \frac{S_k^{(i)*}}{S_k^{(i)}} \right) \right\}, \end{aligned}$$

and hence,

$$V'(\mathbf{S},\mathbf{I}) = \sum_{k=1}^{m} v_k \Bigg\{ \mu_k^{(1)} S_k^{(1)*} \left(2 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(1)}}{S_k^{(1)*}} \right) + \mu_k^{(2)} S_k^{(2)*} \left(3 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(1)} S_k^{(2)*}}{S_k^{(1)*} S_k^{(2)}} - \frac{S_k^{(2)}}{S_k^{(2)*}} \right)$$
$$+ \cdots + \mu_k^{(n)} S_k^{(n)*} \left(n+1 - \sum_{i=1}^{n} \frac{S_k^{(i-1)} S_k^{(i)*}}{S_k^{(i-1)*} S_k^{(i)}} - \frac{S_k^{(n)}}{S_k^{(n)*}} \right)$$
$$+ S_k^{(1)*} \sum_{j=1}^{m} \beta_{kj}^{(1)} I_j^* \left(2 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(1)} I_j I_k^*}{S_k^{(1)*} I_j^* I_k} \right) + S_k^{(2)*} \sum_{j=1}^{m} \beta_{kj}^{(2)} I_j^* \left(3 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(1)} S_k^{(2)*}}{S_k^{(1)*} S_k^{(2)}} - \frac{S_k^{(2)} I_j I_k^*}{S_k^{(2)*} I_j^* I_k} \right)$$
$$+ \cdots + S_k^{(n)*} \sum_{j=1}^{m} \beta_{kj}^{(n)} I_j^* \left(n+1 - \sum_{i=1}^{n} \frac{S_k^{(i-1)} S_k^{(i)*}}{S_k^{(i-1)*} S_k^{(i)}} - \frac{S_k^{(n)} I_j I_k^*}{S_k^{(n)*} I_j^* I_k} \right) \Bigg\} =: H_1 + H_2, \tag{2.3.20}$$

where

$$H_1 := \sum_{k=1}^{m} v_k \Bigg\{ \mu_k^{(1)} S_k^{(1)*} \left(2 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(1)}}{S_k^{(1)*}} \right) + \mu_k^{(2)} S_k^{(2)*} \left(3 - \frac{S_k^{(1)*}}{S_k^{(1)}} - \frac{S_k^{(1)} S_k^{(2)*}}{S_k^{(1)*} S_k^{(2)}} - \frac{S_k^{(2)}}{S_k^{(2)*}} \right)$$
$$+ \cdots + \mu_k^{(n)} S_k^{(n)*} \left(n+1 - \sum_{i=1}^{n} \frac{S_k^{(i-1)} S_k^{(i)*}}{S_k^{(i-1)*} S_k^{(i)}} - \frac{S_k^{(n)}}{S_k^{(n)*}} \right) \Bigg\},$$

and H_2 is defined by the remaining terms in the equation (2.3.20). From the arithmetic-geometric mean [10], we easily see that $H_1 \leq 0$ and the equality holds if and only if $\mathbf{S} = \mathbf{S}^*$. Now we claim that $H_2 \leq 0$. Let

$$h_{kj}^{(\ell)} := \ell + 1 - \sum_{i=1}^{\ell} \frac{S_k^{(i-1)} S_k^{(i)*}}{S_k^{(i-1)*} S_k^{(i)}} - \frac{S_k^{(\ell)} I_j I_k^*}{S_k^{(\ell)*} I_j^* I_k}, \quad \ell \in \{1, 2, \cdots, n\}.$$

Then, using a max function, we can evaluate H_2 as

$$\begin{aligned} H_2 &= \sum_{k=1}^{m} v_k \left\{ S_k^{(1)*} \sum_{j=1}^{m} \beta_{kj}^{(1)} I_j^* h_{kj}^{(1)} + S_k^{(2)*} \sum_{j=1}^{m} \beta_{kj}^{(2)} I_j^* h_{kj}^{(2)} + \cdots + S_k^{(n)*} \sum_{j=1}^{m} \beta_{kj}^{(n)} I_j^* h_{kj}^{(n)} \right\} \\ &\leq \sum_{k=1}^{m} v_k \left\{ \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* \max\left(h_{kj}^{(1)}, h_{kj}^{(2)}, \cdots, h_{kj}^{(n)} \right) \right\} \\ &= \sum_{k=1}^{m} \sum_{j=1}^{m} v_k \theta_{kj} \max\left(h_{kj}^{(1)}, h_{kj}^{(2)}, \cdots, h_{kj}^{(n)} \right) =: H_3. \end{aligned}$$

Following the graph-theoretic approach as in [27, 28, 63, 99, 100, 84, 64], we can verify from the Kirchhoff Matrix Tree Theorem [74, 51] that H_3 can be rewritten as

$$H_3 = \sum_{K \in \mathbb{K}} w(K) \sum_{(k,j) \in E(CK)} \max\left(h_{kj}^{(1)}, h_{kj}^{(2)}, \cdots, h_{kj}^{(n)} \right),$$

where, for a directed graph $G(\Theta)$ associated with m-square matrix $\Theta = (\theta_{kj})$ given by (2.3.10) (that is, $G(\Theta)$ contains m vertices and an arc from vertex k to vertex j if $\theta_{kj} \neq 0$), $\mathbb{K}$ denotes the set of all spanning unicyclic graphs of $G(\Theta)$, $w(K)$ denotes the weight of unicyclic graph K, CK denotes the unique elementary cycle in unicyclic graph K and $E(CK)$ denotes the set of arcs in CK. Then, we see that in order to prove that $H_2 \leq H_3 \leq 0$, it suffices to show that

$$\sum_{(k,j) \in E(CK)} \max\left(h_{kj}^{(1)}, h_{kj}^{(2)}, \cdots, h_{kj}^{(n)} \right) \leq 0 \tag{2.3.21}$$

for all elementary cycles CK containing at most m vertices. As an example, we first consider an elementary cycle $1 \to 2 \to 1$ as CK containing two vertices. In this case, $E(CK) = \{(1,2),(2,1)\}$ and the left-hand side of inequality (2.3.21) is

$$\max\left(h_{12}^{(1)}, h_{12}^{(2)}, \cdots, h_{12}^{(n)}\right) + \max\left(h_{21}^{(1)}, h_{21}^{(2)}, \cdots, h_{21}^{(n)}\right).$$

In order to prove its nonpositivity, from the character of sum of max functions, we only have to show that all possible sums of elements of each of the max functions are nonpositive, that is, it suffices to show that $h_{12}^{(p)} + h_{21}^{(q)} \leq 0$ for all $p,q \in \{1,2,\cdots,n\}$. In fact, we have

$$\begin{aligned}
h_{12}^{(p)} + h_{21}^{(q)} &= p+1-\sum_{i=1}^{p} \frac{S_1^{(i-1)} S_1^{(i)*}}{S_1^{(i-1)*} S_1^{(i)}} - \frac{S_1^{(p)} I_2 I_1^*}{S_1^{(p)*} I_2^* I_1} + q+1-\sum_{i=1}^{q} \frac{S_2^{(i-1)} S_2^{(i)*}}{S_2^{(i-1)*} S_2^{(i)}} - \frac{S_2^{(q)} I_1 I_2^*}{S_2^{(q)*} I_1^* I_2} \\
&\leq p+q+2-(p+q+2)\left[\left(\prod_{i=1}^{p} \frac{S_1^{(i-1)} S_1^{(i)*}}{S_1^{(i-1)*} S_1^{(i)}}\right) \frac{S_1^{(p)} I_2 I_1^*}{S_1^{(p)*} I_2^* I_1} \left(\prod_{i=1}^{q} \frac{S_2^{(i-1)} S_2^{(i)*}}{S_2^{(i-1)*} S_2^{(i)}}\right) \frac{S_2^{(q)} I_1 I_2^*}{S_2^{(q)*} I_1^* I_2}\right]^{1/(p+q+2)} \\
&= p+q+2-(p+q+2)\left[\frac{I_1 I_2 I_1^* I_2^*}{I_1 I_2 I_1^* I_2^*}\right]^{1/(p+q+2)} \\
&= 0, \qquad \forall p,q \in \{1,2,\cdots,n\},
\end{aligned}$$

from the arithmetic-geometric mean [10]. Hence (2.3.21) holds in this case. We next proceed to show (2.3.21) for more general cases. Let $N \in \{1,2,\cdots,m\}$ be an arbitrary natural number. An elementary cycle CK containing N vertices can be described by $c_1 \to c_2 \to \cdots \to c_N \to c_1$, where $c_i \in \{1,2,\cdots,m\}$ and $c_i \neq c_j$ for $i \neq j$. In this case, $E(CK) = \{(c_1,c_2),(c_2,c_3),\cdots,(c_N,c_1)\}$ and the left-hand side of inequality (2.3.21) is given by

$$\sum_{i=1}^{N} \max\left(h_{c_i c_{i+1}}^{(1)}, h_{c_i c_{i+1}}^{(2)}, \cdots, h_{c_i c_{i+1}}^{(n)}\right),$$

where $c_{N+1} = c_1$. As in the above example, in order to prove (2.3.21) in this case, it suffices to show that $h_{c_1 c_2}^{(p_1)} + h_{c_2 c_3}^{(p_2)} + \cdots + h_{c_N c_1}^{(p_N)} \leq 0$ for all $p_1, p_2, \cdots, p_N \in \{1,2,\cdots,n\}$. In fact, we have

$$\begin{aligned}
h_{c_1 c_2}^{(p_1)} + h_{c_2 c_3}^{(p_2)} + \cdots + h_{c_N c_1}^{(p_N)} &= p_1+1-\sum_{i=1}^{p_1} \frac{S_{c_1}^{(i-1)} S_{c_1}^{(i)*}}{S_{c_1}^{(i-1)*} S_{c_1}^{(i)}} - \frac{S_{c_1}^{(p_1)} I_{c_2} I_{c_1}^*}{S_{c_1}^{(p_1)*} I_{c_2}^* I_{c_1}} + p_2+1-\sum_{i=1}^{p_2} \frac{S_{c_2}^{(i-1)} S_{c_2}^{(i)*}}{S_{c_2}^{(i-1)*} S_{c_2}^{(i)}} - \frac{S_{c_2}^{(p_2)} I_{c_3} I_{c_2}^*}{S_{c_2}^{(p_2)*} I_{c_3}^* I_{c_2}} \\
&\quad + \cdots + p_N + 1 - \sum_{i=1}^{p_N} \frac{S_{c_N}^{(i-1)} S_{c_N}^{(i)*}}{S_{c_N}^{(i-1)*} S_{c_N}^{(i)}} - \frac{S_{c_N}^{(p_N)} I_{c_1} I_{c_N}^*}{S_{c_N}^{(p_N)*} I_{c_1}^* I_{c_N}} \\
&\leq \sum_{i=1}^{N} p_i + N \\
&\quad - \left(\sum_{i=1}^{N} p_i + N\right)\left[\left(\prod_{i=1}^{p_1} \frac{S_{c_1}^{(i-1)} S_{c_1}^{(i)*}}{S_{c_1}^{(i-1)*} S_{c_1}^{(i)}}\right) \frac{S_{c_1}^{(p_1)} I_{c_2} I_{c_1}^*}{S_{c_1}^{(p_1)*} I_{c_2}^* I_{c_1}} \left(\prod_{i=1}^{p_2} \frac{S_{c_2}^{(i-1)} S_{c_2}^{(i)*}}{S_{c_2}^{(i-1)*} S_{c_2}^{(i)}}\right) \frac{S_{c_2}^{(p_2)} I_{c_3} I_{c_2}^*}{S_{c_2}^{(p_2)*} I_{c_3}^* I_{c_2}}\right. \\
&\qquad \left. \cdots \left(\prod_{i=1}^{p_N} \frac{S_{c_N}^{(i-1)} S_{c_N}^{(i)*}}{S_{c_N}^{(i-1)*} S_{c_N}^{(i)}}\right) \frac{S_{c_N}^{(p_N)} I_{c_1} I_{c_N}^*}{S_{c_N}^{(p_N)*} I_{c_1}^* I_{c_N}}\right]^{1/(\sum_{i=1}^{N} p_i + N)} \\
&= \sum_{i=1}^{N} p_i + N - \left(\sum_{i=1}^{N} p_i + N\right)\left[\frac{I_{c_1} I_{c_2} \cdots I_{c_N} I_{c_1}^* I_{c_2}^* \cdots I_{c_N}^*}{I_{c_1} I_{c_2} \cdots I_{c_N} I_{c_1}^* I_{c_2}^* \cdots I_{c_N}^*}\right]^{1/(\sum_{i=1}^{N} p_i + N)} \\
&= 0,
\end{aligned}$$

for all $p_1, p_2, \cdots, p_N \in \{1,2,\cdots,n\}$. Hence (2.3.21) holds. Consequently, we obtain $H_2 \leq H_3 \leq 0$, and hence, it follows from (2.3.20) that $V'(\mathbf{S},\mathbf{I}) = H_1 + H_2 \leq 0$ and the equality holds if and only if $H_1 = H_2 = 0$. If $(\mathbf{S},\mathbf{I}) =$

$(\mathbf{S}^*, \mathbf{I}^*)$, then it is obvious from (2.3.20) that $H_1 = H_2 = 0$. On the contrary, if $H_1 = H_2 = 0$, then $\mathbf{S} = \mathbf{S}^*$ follows from $H_1 = 0$. Since we can rewrite H_2 as

$$H_2 = \sum_{k=1}^{m} \nu_k \sum_{i=1}^{n} S_k^{(i)*} \sum_{j=1}^{m} \beta_{kj}^{(i)} I_j^* \left(1 - \frac{I_j I_k^*}{I_j^* I_k}\right) = \sum_{k=1}^{m} \sum_{j=1}^{m} \nu_k \theta_{kj} \left(1 - \frac{I_j I_k^*}{I_j^* I_k}\right),$$

it follows again from the graph-theoretic approach as in [27, 28, 63, 99, 100, 84, 64] that $H_2 = 0$ implies

$$\frac{I_j^* I_k}{I_j I_k^*} = \frac{I_j I_k^*}{I_j^* I_k} \Leftrightarrow \frac{I_k}{I_k^*} = \frac{I_j}{I_j^*}, \tag{2.3.22}$$

for all $k, j \in \{1, 2, \cdots, m\}$. From (2.3.22), we have $\mathbf{I} = c\mathbf{I}^*$, where $c > 0$ is a constant. Substituting $(\mathbf{S}, \mathbf{I}) = (\mathbf{S}^*, c\mathbf{I}^*)$ into the first equation of system (2.2.3), we have

$$0 = b_k - cS_k^{(1)*} \sum_{j=1}^{m} \beta_{kj}^{(1)} I_j^* - \left(\mu_k^{(1)} + a^{(1)}\right) S_k^{(1)*}. \tag{2.3.23}$$

Since the right-hand side of (2.3.23) is monotone decreasing with respect to c, it follows from (2.3.3) that (2.3.23) holds if and only if $c = 1$. Summarizing these statements, we see that $V'(\mathbf{S}, \mathbf{I}) = 0$ holds if and only if the solution $(\mathbf{S}, \mathbf{I})$ of system (2.2.3) is in the singleton $\{(\mathbf{S}^*, \mathbf{I}^*)\}$. Hence, it follows from the La Salle invariance principle [60] that E^* is globally asymptotically stable in Ω^0. □

2.4 Numerical examples

In this section, providing some numerical examples, we verify the validity of Theorem 2.3.1. In addition, we provide an example for the comparison of numerical values of the basic reproduction number $\mathscr{R}_0$ for the discretized system (2.2.3) and the original PDE system (2.1.2).

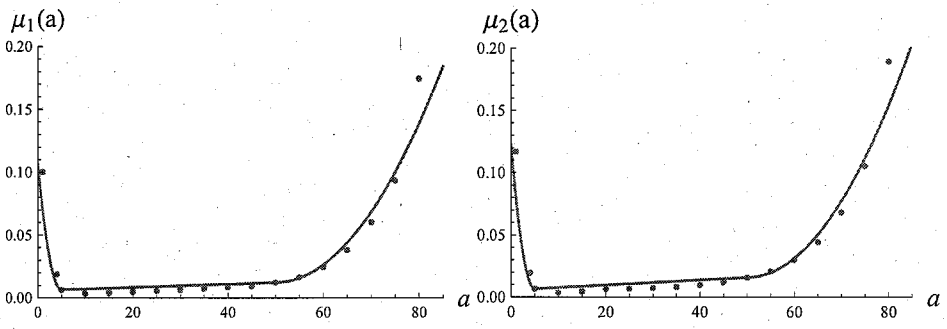
2.4.1 A sexually transmitted disease

Assuming $m = 2$, we simulate the spread of a sexually transmitted disease. Let us relate subscripts 1 and 2 to female and male groups, respectively. Then, the original PDE system (2.1.2) is written as

$$\begin{cases} \left(\dfrac{\partial}{\partial t} + \dfrac{\partial}{\partial a}\right) S_1(t,a) = -S_1(t,a) \displaystyle\sum_{j=1}^{2} \int_0^{\omega} \beta_{1j}(a,\sigma) I_j(t,\sigma) \mathrm{d}\sigma - \mu_1(a) S_1(t,a), \\ \left(\dfrac{\partial}{\partial t} + \dfrac{\partial}{\partial a}\right) I_1(t,a) = S_1(t,a) \displaystyle\sum_{j=1}^{2} \int_0^{\omega} \beta_{1j}(a,\sigma) I_j(t,\sigma) \mathrm{d}\sigma - (\mu_1(a) + \gamma_1(a)) I_1(t,a), \\ \left(\dfrac{\partial}{\partial t} + \dfrac{\partial}{\partial a}\right) S_2(t,a) = -S_2(t,a) \displaystyle\sum_{j=1}^{2} \int_0^{\omega} \beta_{2j}(a,\sigma) I_j(t,\sigma) \mathrm{d}\sigma - \mu_2(a) S_2(t,a), \\ \left(\dfrac{\partial}{\partial t} + \dfrac{\partial}{\partial a}\right) I_2(t,a) = S_2(t,a) \displaystyle\sum_{j=1}^{2} \int_0^{\omega} \beta_{2j}(a,\sigma) I_j(t,\sigma) \mathrm{d}\sigma - (\mu_2(a) + \gamma_2(a)) I_2(t,a), \\ S_1(t,0) = b_1, \quad S_2(t,0) = b_2, \quad I_1(t,0) = I_2(t,0) = 0 \end{cases} \tag{2.4.1}$$

(note that the equations for R_k $(k = 1, 2)$ can be omitted). Set $\omega = 100$. Set the age-specific mortality rates

$$\mu_1(a) = \begin{cases} 0.1000(a-5)^2/25 + 0.0063, & 0 \le a \le 5, \\ 0.0058(a-5)/45 + 0.0063, & 5 \le a \le 50, \\ 0.1622(a-50)^2/1156 + 0.0121, & 50 \le a \le 100, \end{cases} \tag{2.4.2}$$



(a) Age-specific mortality rate $\mu_1(a)$ for female individuals

(b) Age-specific mortality rate $\mu_2(a)$ for male individuals

Figure 2.2: Graphs of the age-specific mortality rates set as (2.4.2) and (2.4.3) (curves) and observed in [25] (dots)

and

$$\mu_2(a) = \begin{cases} 0.1168(a-5)^2/25 + 0.0065, & 0 \le a \le 5, \\ 0.0092(a-5)/45 + 0.0065, & 5 \le a \le 50, \\ 0.1772(a-50)^2/1156 + 0.0157, & 50 \le a \le 100, \end{cases} \tag{2.4.3}$$

so that they can approximate the corresponding observed data obtained in [25] for the population of Zimbabwe (see Figure 2.2). Set $b_1 = 1/46.6495$ and $b_2 = 1/42.9635$ so that the demographic steady states $P_1^*(a) = S_1(t,a) + I_1(t,a) + R_1(t,a)$ of female population and $P_2^*(a) = S_2(t,a) + I_2(t,a) + R_2(t,a)$ of male population satisfy

$$\int_0^{100} P_1^*(a)\mathrm{d}a \simeq \int_0^{100} P_2^*(a)\mathrm{d}a \simeq 1$$

(see, e.g., [39, Section 2]). Set $\gamma_k(a) = 0.4 - \mu_k(a)$ $(k = 1,2)$ so that Assumption 2.2.3 is satisfied.

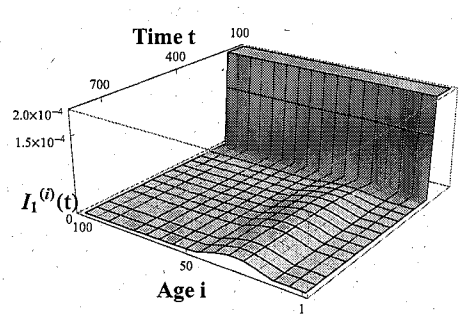
In what follows, we vary the value of the disease transmission coefficient $\beta_{kj}(a,\sigma) = \beta_{kj}(a)$ $(k,j \in \{1,2\})$, which satisfies Assumption 2.2.1, in order to observe the stability change of each equilibrium of system (2.4.1). Let us first set

$$\beta_{11}(a) = \beta_{12}(a) = \beta_{21}(a) = \begin{cases} -0.1(a-30)^2/225 + 0.11, & 15 \le a \le 45, \\ 0.01, & \text{otherwise}, \end{cases}$$

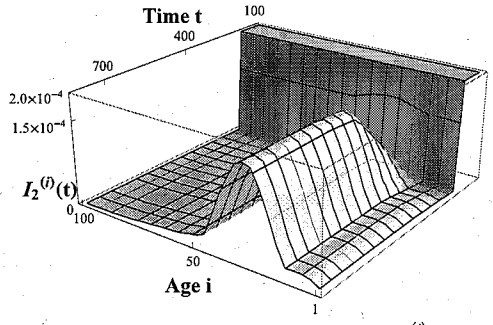
$$\beta_{22}(a) = \begin{cases} -(a-30)^2/225 + 1.1, & 15 \le a \le 45, \\ 0.1, & \text{otherwise}, \end{cases}$$

which satisfies Assumption 2.2.2. Under these settings, we can discretize the PDE system (2.4.1) into an ODE system by using the discretization approach demonstrated in Section 2.2.1. Let us divide the age interval $[0,100]$ into 100 subintervals $[0,1],[1,2],\cdots,[99,100]$. Let $a^{(i)} = 1$ $(i \in \{1,2,\cdots,99\})$ and $a^{(100)} = 0$. Then, system (2.4.1) can be discretized as

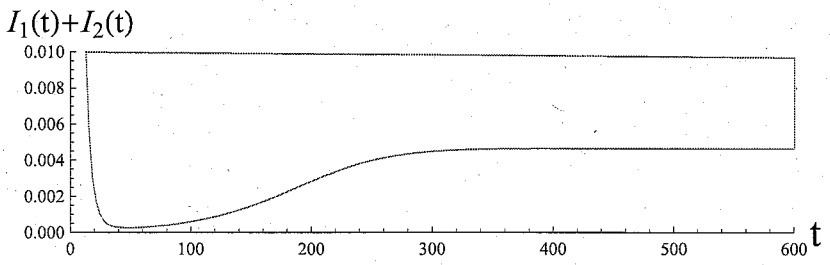
$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t}S_1^{(i)}(t) = S_1^{(i-1)}(t) - S_1^{(i)}(t)\left(\beta_{11}^{(i)}I_1(t) + \beta_{12}^{(i)}I_2(t)\right) - \left(\mu_1^{(i)} + a^{(i)}\right)S_1^{(i)}(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t}I_1(t) = \displaystyle\sum_{i=1}^{100} S_1^{(i)}(t)\left(\beta_{11}^{(i)}I_1(t) + \beta_{12}^{(i)}I_2(t)\right) - 0.4I_1(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t}S_2^{(i)}(t) = S_2^{(i-1)}(t) - S_2^{(i)}(t)\left(\beta_{21}^{(i)}I_1(t) + \beta_{22}^{(i)}I_2(t)\right) - \left(\mu_2^{(i)} + a^{(i)}\right)S_2^{(i)}(t), \\ \dfrac{\mathrm{d}}{\mathrm{d}t}I_2(t) = \displaystyle\sum_{i=1}^{100} S_2^{(i)}(t)\left(\beta_{21}^{(i)}I_1(t) + \beta_{22}^{(i)}I_2(t)\right) - 0.4I_2(t), \\ S_1^{(0)}(t) = \dfrac{1}{46.6495}, \quad S_2^{(0)}(t) = \dfrac{1}{42.9635}, \qquad i \in \{1,2,\cdots,100\}. \end{cases} \tag{2.4.4}$$



(a) Age-distribution of female infectious population $I_1^{(i)}$ $(1 \le i \le 100)$



(b) Age-distribution of male infectious population $I_2^{(i)}$ $(1 \le i \le 100)$



(c) Total infectious population $I_1(t)+I_2(t) = \sum_{i=1}^{100} I_1^{(i)}(t)+I_2^{(i)}(t)$ versus time t

Figure 2.3: Solution behavior of each infectious population for $\mathscr{R}_0 \simeq 1.05425 > 1$

The basic reproduction number $\mathscr{R}_0$ for system (2.4.4) is calculated as the maximum real eigenvalue of the next generation matrix $\mathbf{K}$ defined by (2.2.8), and now $\mathscr{R}_0 \simeq 1.05425 > 1$. For initial condition

$$\left(S_1^{(i)}(0), S_2^{(i)}(0), I_1^{(i)}(0), I_2^{(i)}(0)\right) = (0.009, 0.009, 0.001, 0.001), \quad \forall i \in \{1, 2, \cdots, 100\}, \tag{2.4.5}$$

(note that $I_1 = \sum_{i=1}^{100} I_1^{(i)}$ and $I_2 = \sum_{i=1}^{100} I_2^{(i)}$), we obtain Figure 2.3 that illustrates the age-distributions of each infectious population converging to each endemic steady state. This fits to the statement of (ii) of Theorem 2.3.1 for the global asymptotic stability of an endemic equilibrium E^* of system (2.4.4).

Next we set

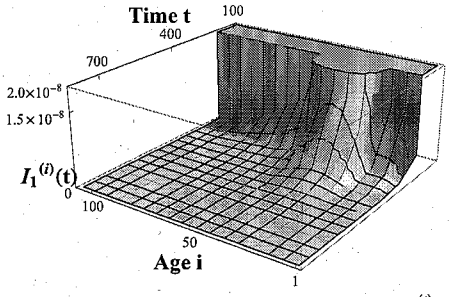
$$\beta_{11}(a) = \beta_{12}(a) = \beta_{21}(a) = \begin{cases} -0.1(a-30)^2/225 + 0.11, & 15 \le a \le 45, \\ 0.01, & \text{otherwise}, \end{cases}$$

$$\beta_{22}(a) = \begin{cases} -(a-30)^2/225 + 0.99, & 15 \le a \le 45, \\ 0.09, & \text{otherwise}. \end{cases}$$

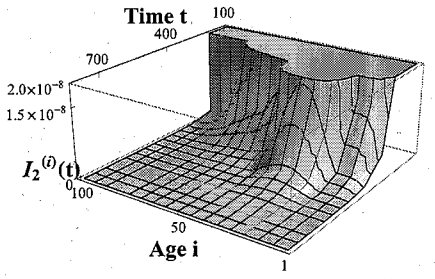
In this case, we have $\mathscr{R}_0 \simeq 0.95143 < 1$ for system (2.4.4). For initial condition (2.4.5), we obtain Figure 2.4 that illustrates the age-distribution of each infectious population converging to zero. This fits to the statement of (i) of Theorem 2.3.1 for the global asymptotic stability of the disease-free equilibrium E^0 of system (2.4.4).

2.4.2 Comparison of $\mathscr{R}_0$

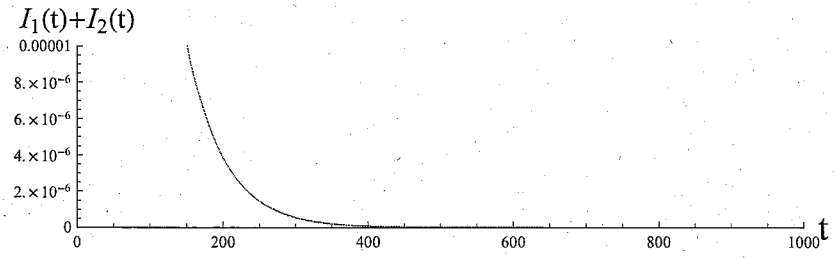
Finally, we compare numerical values of the basic reproduction number $\mathscr{R}_0$ for two systems, that is, the discretized ODE system (2.2.3) and the original PDE system (2.1.2). For simplicity, we assume that $m = 1$ (that is, we consider system (2.1.1). Set $\omega = 100$. For $\mu_2(a)$, $\gamma_2(a)$ and b_2 as in the above examples, we set $\mu(a) = \mu_2(a)$, $\gamma(a) = \gamma_2(a)$



(a) Age-distribution of female infectious individuals $I_1^{(i)}$ $(1 \le i \le 100)$



(b) Age-distribution of male infectious individuals $I_2^{(i)}$ $(1 \le i \le 100)$



(c) Total infectious population $I_1(t)+I_2(t) = \sum_{i=1}^{100} I_1^{(i)}(t) + I_2^{(i)}(t)$ versus time t

Figure 2.4: Solution behavior of each infectious population for $\mathscr{R}_0 \simeq 0.95143 < 1$

and $b = b_2$. Here we fix

$$\beta(a) = \begin{cases} -(a-30)^2/225 + 1.1, & 15 \le a \le 45, \\ 0.1, & \text{otherwise}, \end{cases}$$

which is similar to $\beta_{22}(a)$ in the case of Figure 2.3.

In this simple case, we can explicitly obtain the basic reproduction number $\mathscr{R}_0$ for the PDE system (2.1.1) as the spectral radius of a positive linear integral operator called *the next generation operator* (see e.g., [18, 19]). We have

$$\mathscr{R}_0 = \int_0^\omega \int_\sigma^\omega \beta(\sigma) \frac{\exp\left(-\int_0^\xi \mu(a)\mathrm{d}a\right)}{\int_0^\omega \exp\left(-\int_0^a \mu(\rho)\mathrm{d}\rho\right)\mathrm{d}a} \exp\left(-\int_\sigma^\xi \gamma(a)\mathrm{d}a\right) \mathrm{d}\xi\mathrm{d}\sigma \simeq 0.8894171960411557.$$

Now, let Δa denote the step size of the discretization defined by $\omega/n = 100/n$, where n denotes the number of age subintervals. Then, from (2.2.2), parameters for the discretized ODE system (2.2.3) are obtained as

$$\mu^{(i)} = \mu(i\Delta a), \quad \beta^{(i)} = \beta(i\Delta a), \quad i \in \{1, 2, \cdots, n\}$$

and $r = 0.4$, where we omit the subscript $k = 1$ for simplicity. Let $a^{(i)} = 1/\Delta a$ for all $i \in \{1, 2, \cdots, n-1\}$.

Before comparing the numerical values of $\mathscr{R}_0$, we note the correspondence between the PDE and ODE systems. Under the above settings, rearranging the differential equation for susceptible $S_k^{(i)}$ of (2.2.3), we have

$$\frac{\mathrm{d}}{\mathrm{d}t} S^{(i)}(t) + \frac{S^{(i)}(t) - S^{(i-1)}(t)}{\Delta a} = -S^{(i)}(t)\beta^{(i)} I(t) - \mu^{(i)} S^{(i)}(t), \quad i \in \{1, 2, \cdots, n-1\}, \tag{2.4.6}$$

where we omit the subscript $k = 1$ for simplicity. We see at once that the second term in the left-hand side of equation (2.4.6), which is the backward divided difference with respect to age, corresponds to the partial derivative

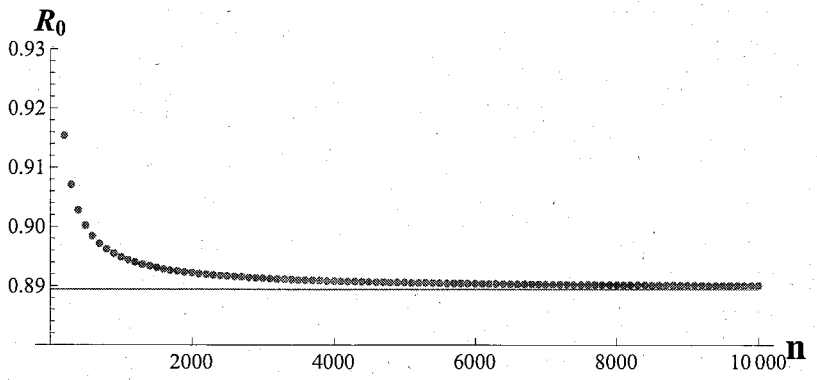


Figure 2.5: Graph of the numerical values of the basic reproduction number $\mathscr{R}_0$ for the original PDE system (2.1.1) (line) and the discretized ODE system (2.2.3) (dots) versus the number n of age subintervals

Table 2.1: Relation between the number n of age subintervals and the numerical values of the basic reproduction number $\mathscr{R}_0$

n	$\mathscr{R}_0$ for the ODE system (2.2.3)
100	0.9384521601853512
1000	0.8948595686884071
10000	0.8899887446988077
50000	0.8895511016452385
100000	0.8894963423122371
$\mathscr{R}_0$ for the PDE system (2.1.1)	0.8894171960411557

term $\partial S/\partial a$ in (2.1.1). Hence, we can expect that, as $\Delta a \to 0$, the numerical values of solutions of the discretized ODE system (2.2.3) converge to those of the original PDE system (2.1.1). Therefore, in the following, we compare the numerical values of $\mathscr{R}_0$ for the two systems with decreasing step size Δa of the discretization.

We obtain Figure 2.5 and Table 2.1. As we expected, the numerical value of $\mathscr{R}_0$ for the discretized ODE system (2.2.3) converges to that for the original PDE system (2.1.1) as the number n of age subintervals increases and the step size $\Delta a = 100/n$ of the discretization decreases.

2.5 Discussion

In this chapter, we have formulated a multi-group SIR epidemic model (2.1.2) and, after the discretization, we have studied the global asymptotic stability of each equilibrium of the discretized model (2.2.3). Our main theorem, Theorem 2.3.1, have stated that the basic reproduction number $\mathscr{R}_0$ defined by (2.2.9) plays the role of a perfect threshold in the sense of determining the global asymptotic stability of each equilibrium, that is, the global asymptotic stability of the disease-free equilibrium E^0 for $\mathscr{R}_0 \leq 1$ and that of an endemic equilibrium E^* for $\mathscr{R}_0 > 1$.

For the class of age-structured SIR epidemic models similar to (2.1.2), any global stability results for E^* for $\mathscr{R}_0 > 1$ have not been obtained (see, e.g., [39, 14, 87] and the references therein). Obviously, our results are only valid for the ODE system (2.2.3) and not for the PDE system (2.1.2), and therefore, the open problem has remained unsolved. However, in the situation where we estimate the pattern of a disease by using numerical calculation, both of the PDE and ODE systems must be discretized similarly, and therefore, we can expect that our results are as

valuable as those for PDE systems for the experimental purpose. In Section 2.4, we have provided an example of converging numerical values of $\mathscr{R}_0$ for the discretized ODE system (2.2.3) to the value for the PDE system (2.1.2) with decreasing step size of the discretization. This suggests us that similar results might be obtained for numerical solutions of both of the PDE and ODE systems, and therefore, the value of our results can be guaranteed again from the numerical point of view.

The future tasks are, for example: to investigate the global asymptotic stability of an endemic steady state of the original PDE system (2.1.2) for $\mathscr{R}_0 > 1$ under assumptions similar to Assumptions 2.2.1-2.2.3; to investigate the global asymptotic stability of an endemic equilibrium of the discretized system corresponding to (2.2.3) under assumptions different from Assumptions 2.2.1-2.2.3; to verify not only the numerical values of $\mathscr{R}_0$ but also of solutions of the discretized system (2.2.3) converge to those for the PDE system (2.1.2) as the step size of the discretization is decreased.

Acknowledgment

The author would like to thank the editor and reviewers for their valuable comments and suggestions to the published version [54] of this chapter. The author would like to thank also Professor Yoshiaki Muroya and Professor Hisashi Inaba for their helpful comments to the earlier version of the paper.

Part II

Epidemic Models in Time-Heterogeneous Environments

Chapter 3

A nonautonomous SEIRS epidemic model

Abstract In this chapter, the long-time behavior of a nonautonomous SEIRS epidemic model is studied. We obtain sufficient conditions for the permanence (uniform persistence) and the extinction of infectious population of the model. Providing some numerical examples, we show that in some cases our results can improve the previous results obtained in [T. Zhang and Z. Teng, On a nonautonomous SEIRS model in epidemiology, Bull. Math. Bio., (2007) 69, 2537-2559]. In addition, we discuss a relation between our results and open questions proposed in the paper. This is a collaborative work with Dr. Yukihiko Nakata in the University of Szeged.

Keywords SEIRS epidemic model; Nonautonomous system; The basic reproduction number; Permanence; Extinction

3.1 Introduction

The model we focus on in this chapter is the following nonautonomous SEIRS epidemic model:

$$\begin{cases} \dfrac{dS(t)}{dt} = \Lambda(t) - \beta(t)S(t)I(t) - \mu(t)S(t) + \delta(t)R(t), \\ \dfrac{dE(t)}{dt} = \beta(t)S(t)I(t) - (\mu(t)+\varepsilon(t))E(t), \\ \dfrac{dI(t)}{dt} = \varepsilon(t)E(t) - (\mu(t)+\gamma(t))I(t), \\ \dfrac{dR(t)}{dt} = \gamma(t)I(t) - (\mu(t)+\delta(t))R(t) \end{cases} \tag{3.1.1}$$

with initial condition

$$S(0) > 0,\ E(0) \geq 0,\ I(0) > 0,\ R(0) \geq 0. \tag{3.1.2}$$

Here $S(t), E(t), I(t)$ and $R(t)$ denote the density of susceptible, exposed (not infectious but infected), infectious and recovered individuals at time $t \geq 0$, respectively. $\Lambda(t)$ denotes the birth rate, $\beta(t)$ denotes the disease transmission coefficient, $\mu(t)$ denotes the mortality, $\varepsilon(t)$ denotes the rate of developing infectivity, $\gamma(t)$ denotes the recovery rate and $\delta(t)$ denotes the rate of losing immunity at time t.

As we saw in the previous chapters, one of the main interests of the field of mathematical epidemiology has been the study of autonomous models (see also, for instance [61, 62, 94, 96, 82, 83] and references therein). In particular, as we saw, the role of the basic reproduction number $\mathscr{R}_0$ as a threshold for the solution behavior of each epidemic model has been gained much attention. For instance, in case where system (3.1.1) is autonomous (that is, all parameters are given by time-independent functions $\Lambda(t) = \Lambda$, $\beta(t) = \beta$, $\mu(t) = \mu$, $\varepsilon(t) = \varepsilon$, $\gamma(t) = \gamma$ and $\delta(t) = \delta$), the basic reproduction number is obtained as

$$\mathscr{R}_0 = \frac{\varepsilon\beta}{(\mu+\varepsilon)(\mu+\gamma)}\frac{\Lambda}{\mu}, \tag{3.1.3}$$

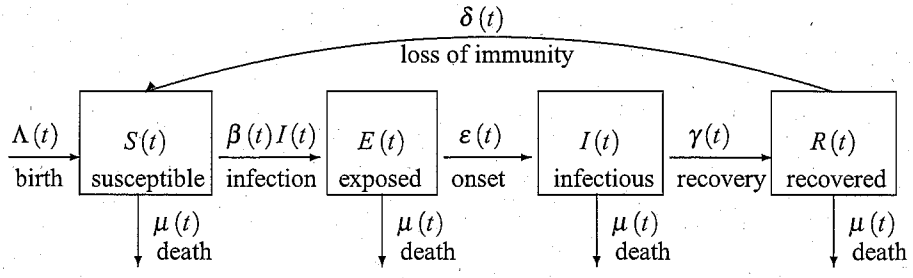


Figure 3.1: Transfer diagram for SEIRS epidemic model (3.1.1)

and a threshold result such that the infectious disease dies out if $\mathscr{R}_0 \leq 1$ and the disease persists if $\mathscr{R}_0 > 1$ for system (3.1.1) is well-known (see, e.g., [67, 83]).

On the other hand, in the real world, many infectious diseases spread seasonally (one of the reasons of such a phenomenon is, for instance, the seasonal change of the number of infectious vectors [5]). In order to model such diseases, many authors have formulated epidemic models with periodicity and studied them enthusiastically (see e.g., [88, 89, 69, 5, 101, 6, 102, 7, 103, 97, 75] and references therein). For periodic epidemic models, the definition of the basic reproduction number $\mathscr{R}_0$ was firstly given by Bacaër and Guernaoui in [5]. For system (3.1.1) in periodic case, Nakata and Kuniya [75] proved that the $\mathscr{R}_0$ defined by Bacaër and Guernaoui plays the role of a threshold for the global dynamics of solutions, that is, the disease-free periodic solution is globally asymptotically stable if $\mathscr{R}_0 < 1$ and the system becomes uniformly persistent if $\mathscr{R}_0 > 1$.

The nonautonomous case we focus on in this chapter is regarded as a generalization of such a periodic case. The definition of $\mathscr{R}_0$ for such general time-heterogeneous epidemic models has recently been given by Thieme [91] and Inaba [46]. Global dynamics of a nonautonomous SEIRS epidemic model similar to (3.1.1) was studied by Zhang and Teng [102]. In their paper, some sufficient conditions for the permanence (uniform persistence) and the extinction of infectious population have been obtained. However, their conditions proposed in Theorems 4.1 and 5.1 in their paper did not correspond to any threshold values such as $\mathscr{R}_0$ even in the autonomous case.

In this chapter, we obtain sufficient conditions different from those in [102] for the permanence and the extinction of infectious population of system (3.1.1). Our conditions correspond to the basic reproduction number $\mathscr{R}_0$ given by (3.1.3) for the autonomous case. Thus, our results can be regarded as the extension of the threshold-type result for the autonomous case. We provide some numerical examples which illustrate that in some cases our results can improve the previous results obtained in [102].

The subsequent sections of this chapter are organized as follows: In Section 3.2 we present preliminary setting and propositions, which we use to analyze the long-time behavior of system (3.1.1). In Sections 3.3 and 3.4 we prove our main theorems on the extinction and permanence of infectious population of system (3.1.1). In Section 3.5, we derive explicit conditions for the existence and permanence of infectious population of system (3.1.1) for some special cases. We prove also that when every parameter is given as a constant parameter our conditions for the permanence and extinction becomes the threshold condition corresponding to the basic reproduction number $\mathscr{R}_0$. In Section 3.6 we provide numerical examples to verify the validity of our results and to show that in some cases our theoretical result can improve the previous results obtained in [102].

3.2 Preliminaries

As in [102] we put the following assumptions for system (3.1.1).

Assumption 3.2.1. **(i)** Functions Λ, β, μ, δ, ε and γ are positive, bounded and continuous on $[0, +\infty)$ and $\beta(0) > 0$.

(ii) There exist constants $\omega_i > 0$ $(i = 1,2,3)$ such that

$$\liminf_{t\to+\infty}\int_t^{t+\omega_1}\beta(s)\mathrm{d}s > 0, \quad \liminf_{t\to+\infty}\int_t^{t+\omega_2}\mu(s)\mathrm{d}s > 0, \quad \liminf_{t\to+\infty}\int_t^{t+\omega_3}\Lambda(s)\mathrm{d}s > 0.$$

In what follows, we denote by $N^*(t)$ the solution of

$$\frac{\mathrm{d}N^*(t)}{\mathrm{d}t} = \Lambda(t) - \mu(t)N^*(t) \tag{3.2.1}$$

with initial value $N^*(0) = S(0) + E(0) + I(0) + R(0) > 0$. By adding equations of (3.1.1), we easily see that $N^*(t) = S(t) + E(t) + I(t) + R(t)$ means the density of total population at time t. From Lemma 2.1, Theorem 3.1 and Remark 3.2 in [102], we have the following results.

Proposition 3.2.1. **(i)** *There exist positive constants $m > 0$ and $M > 0$, which are independent from the choice of initial value $N^*(0) > 0$, such that*

$$0 < m \le \liminf_{t\to+\infty} N^*(t) \le \limsup_{t\to+\infty} N^*(t) \le M < +\infty. \tag{3.2.2}$$

(ii) *The solution $(S(t),E(t),I(t),R(t))$ of system (3.1.1) with initial value (3.1.2) exists, uniformly bounded and*

$$S(t) > 0, \quad E(t) > 0, \quad I(t) > 0, \quad R(t) \ge 0$$

for all $t > 0$.

For $p > 0$ and $t > 0$ we define

$$G(p,t) := \beta(t)N^*(t)p + \gamma(t) - \left(1 + \frac{1}{p}\right)\varepsilon(t)$$

and

$$W(p,t) := pE(t) - I(t), \tag{3.2.3}$$

where E and I are solutions in system (3.1.1).

In Sections 3.3 and 3.4, we use the following lemma in order to investigate the long-time behavior of system (3.1.1).

Lemma 3.2.1. *If there exist positive constants $p > 0$ and $T_1 > 0$ such that $G(p,t) < 0$ for all $t \ge T_1$, then there exists $T_2 \ge T_1$ such that either $W(p,t) > 0$ for all $t \ge T_2$ or $W(p,t) \le 0$ for all $t \ge T_2$.*

Proof. Suppose that there does not exist $T_2 \ge T_1$ such that either $W(p,t) > 0$ for all $t \ge T_2$ or $W(p,t) \le 0$ for all $t \ge T_2$ hold. Then, there necessarily exists an $s \ge T_1$ such that $W(p,s) = 0$ and $\mathrm{d}W(p,s)/\mathrm{d}t > 0$. Hence we have

$$pE(s) = I(s) \tag{3.2.4}$$

and

$$\begin{aligned} & p\{\beta(s)S(s)I(s) - (\mu(s)+\varepsilon(s))E(s)\} - \{\varepsilon(s)E(s) - (\mu(s)+\gamma(s))I(s)\} \\ = \; & I(s)\{\beta(s)S(s)p + (\mu(s)+\gamma(s))\} - pE(s)\left\{(\mu(s)+\varepsilon(s)) + \frac{1}{p}\varepsilon(s)\right\} > 0. \end{aligned} \tag{3.2.5}$$

Substituting (3.2.4) into (3.2.5) we have

$$0 \; < \; pE(s)\left\{\beta(s)S(s)p + \gamma(s) - \left(1 + \frac{1}{p}\right)\varepsilon(s)\right\} \; \le \; pE(s)G(p,s).$$

From (ii) of Proposition 3.2.1, we have $G(p,s) > 0$, which is a contradiction. □

3.3 Extinction of infectious population

In this section, we obtain sufficient conditions for the extinction of infectious population of system (3.1.1). The definition of the extinction is as follows:

Definition 3.3.1. We say that the infectious population of system (3.1.1) is extinct if

$$\lim_{t\to+\infty} I(t) = 0.$$

We give one of the main results of this chapter.

Theorem 3.3.1. *If there exist positive constants $\lambda > 0$, $p > 0$ and $T_1 > 0$ such that*

$$R_1(\lambda,p) := \limsup_{t\to+\infty} \int_t^{t+\lambda} \{\beta(s)N^*(s)p - (\mu(s)+\varepsilon(s))\}\,\mathrm{d}s < 0, \tag{3.3.1}$$

$$R_1^*(\lambda,p) := \limsup_{t\to+\infty} \int_t^{t+\lambda} \left\{\varepsilon(s)\frac{1}{p} - (\mu(s)+\gamma(s))\right\}\mathrm{d}s < 0 \tag{3.3.2}$$

and $G(p,t) < 0$ for all $t \geq T_1$, then the infectious population of system (3.1.1) *is extinct.*

Proof. From Lemma 3.2.1, we only have to consider the following two cases:

(i) $pE(t) > I(t)$ for all $t \geq T_2$,

(ii) $pE(t) \leq I(t)$ for all $t \geq T_2$,

where $T_2 \geq T_1$ is a constant as in Lemma 3.2.1.

First we consider the case (i). From the second equation of system (3.1.1), we have

$$\begin{aligned}\frac{\mathrm{d}E(t)}{\mathrm{d}t} &= \beta(t)(N^*(t)-E(t)-I(t)-R(t))I(t) - (\mu(t)+\varepsilon(t))E(t)\\ &< \beta(t)(N^*(t)-E(t)-I(t)-R(t))pE(t) - (\mu(t)+\varepsilon(t))E(t)\\ &< E(t)\{\beta(t)N^*(t)p - (\mu(t)+\varepsilon(t))\}.\end{aligned}$$

Hence, we obtain

$$E(t) < E(T_2)\exp\left(\int_{T_2}^t \{\beta(s)N^*(s)p - (\mu(s)+\varepsilon(s))\}\,\mathrm{d}s\right) \tag{3.3.3}$$

for all $t \geq T_2$. Now, from (3.3.1), we see that there exist constants $\delta_1 > 0$ and $T_3 > T_2$ such that

$$\int_t^{t+\lambda} \{\beta(s)N^*(s)p - (\mu(s)+\varepsilon(s))\}\,\mathrm{d}s < -\delta_1 \tag{3.3.4}$$

for all $t \geq T_3$. From (3.3.3) and (3.3.4) we have $\lim_{t\to+\infty} E(t) = 0$. Then it follows from $pE(t) > I(t)$ for all $t \geq T_2$ that $\lim_{t\to+\infty} I(t) = 0$.

Next we consider the case (ii). Since we have $E(t) \leq I(t)/p$ for all $t \geq T_2$, it follows from the third equation of system (3.1.1) that

$$\frac{\mathrm{d}I(t)}{\mathrm{d}t} \leq I(t)\left\{\varepsilon(t)\frac{1}{p} - (\mu(t)+\gamma(t))\right\}.$$

Hence we have

$$I(t) \leq I(T_2)\exp\left(\int_{T_2}^t \left\{\varepsilon(s)\frac{1}{p} - (\mu(s)+\gamma(s))\right\}\mathrm{d}s\right) \tag{3.3.5}$$

for all $t \geq T_2$. Now it follows from (3.3.2) that there exist constants $\delta_2 > 0$ and $T_4 > T_2$ such that

$$\int_t^{t+\lambda} \left\{\varepsilon(s)\frac{1}{p} - (\mu(s)+\gamma(s))\right\}\mathrm{d}s < -\delta_2 \tag{3.3.6}$$

for all $t \geq T_4$. From (3.3.5) and (3.3.6) we have $\lim_{t\to+\infty} I(t) = 0$. □

3.4 Permanence of infectious population

In this section, we obtain sufficient conditions for the permanence of infectious population of system (3.1.1). The definition of the permanence is as follows:

Definition 3.4.1. We say that the infectious population of system (3.1.1) is permanent if there exist positive constants $I_1 > 0$ and $I_2 > 0$, which are independent from the choice of initial condition (3.1.2), such that

$$0 < I_1 \leq \liminf_{t\to+\infty} I(t) \leq \limsup_{t\to+\infty} I(t) \leq I_2 < +\infty.$$

The following theorem is also one of the main results of this chapter:

Theorem 3.4.1. *If there exist positive constants $\lambda > 0$, $p > 0$ and $T_1 > 0$ such that*

$$R_2(\lambda,p) := \liminf_{t\to+\infty} \int_t^{t+\lambda} \{\beta(s)N^*(s)p - (\mu(s)+\varepsilon(s))\}\,\mathrm{d}s > 0, \tag{3.4.1}$$

$$R_2^*(\lambda,p) := \liminf_{t\to+\infty} \int_t^{t+\lambda} \left\{\varepsilon(s)\frac{1}{p} - (\mu(s)+\gamma(s))\right\}\mathrm{d}s > 0 \tag{3.4.2}$$

and $G(p,t) < 0$ for all $t \geq T_1$, then the infectious population of system (3.1.1) *is permanent.*

Before the proof of Theorem (3.4.1), we prove the following lemma.

Lemma 3.4.1. *If there exist positive constants $\lambda > 0$, $p > 0$ and $T_1 > 0$ such that* (3.4.1), (3.4.2) *and $G(p,t) < 0$ hold for all $t \geq T_1$, then $W(p,t) \leq 0$ for all $t \geq T_2 \geq T_1$, where T_2 is given as in Lemma 3.2.1.*

Proof. From Lemma 3.2.1 we have only two cases such that $W(p,t) > 0$ for all $t \geq T_2$ or $W(p,t) \leq 0$ for all $t \geq T_2$. Suppose that $W(p,t) > 0$ for all $t \geq T_2$. Then, we have $E(t) > I(t)/p$ for all $t \geq T_2$. It follows from the third equation of system (3.1.1) that

$$\frac{\mathrm{d}I(t)}{\mathrm{d}t} > \varepsilon(t)\frac{1}{p}I(t) - (\mu(t)+\gamma(t))I(t) = I(t)\left\{\varepsilon(t)\frac{1}{p} - (\mu(t)+\gamma(t))\right\}$$

for all $t \geq T_2$. Hence, we obtain

$$I(t) > I(T_2)\exp\left(\int_{T_2}^t \left\{\varepsilon(s)\frac{1}{p} - (\mu(s)+\gamma(s))\right\}\mathrm{d}s\right) \tag{3.4.3}$$

for all $t \geq T_2$. From the inequality (3.4.2), we see that there exist positive constants $\eta > 0$ and $T > 0$ such that

$$\int_t^{t+\lambda} \left\{\varepsilon(s)\frac{1}{p} - (\mu(s)+\gamma(s))\right\}\mathrm{d}s > \eta \tag{3.4.4}$$

for all $t \geq T$. Since the inequality (3.4.3) holds for all $t \geq \max(T_2, T)$, it follows from (3.4.4) that $\lim_{t\to+\infty} I(t) = +\infty$. This contradicts with the boundedness of I, stated in (ii) of Proposition 3.2.1. □

Using Lemma 3.4.1 we prove Theorem 3.4.1.

Proof of Theorem 3.4.1. For a constant $\varepsilon > 0$, let $m_\varepsilon := m - \varepsilon$ and $M_\varepsilon := M + \varepsilon$, where m and M are as in Proposition 3.2.1. Then, from the inequality (3.2.2) of (i) of Proposition 3.2.1, we see that for any $\varepsilon > 0$, there exists a $T > 0$ such that

$$m_\varepsilon < N^*(t) < M_\varepsilon \tag{3.4.5}$$

for all $t \geq T$.

The inequality (3.4.1) implies that for sufficiently small $\eta > 0$, there exists a $T_1 \geq T$ such that

$$\int_t^{t+\lambda} \{\beta(s)N^*(s)p - (\mu(s)+\varepsilon(s))\}\,\mathrm{d}s > \eta \tag{3.4.6}$$

for all $t \geq T_1$.

Define

$$\beta^+ := \sup_{t\geq 0}\beta(t), \quad \mu^+ := \sup_{t\geq 0}\mu(t), \quad \varepsilon^+ := \sup_{t\geq 0}\varepsilon(t), \quad \gamma^+ := \sup_{t\geq 0}\gamma(t).$$

From (3.4.5) and (3.4.6), we see that for some positive constants $\eta_1 < \eta$ and $T_2 \geq T_1$, there exist sufficiently small $\varepsilon_i > 0$ $(i = 1,2,3)$ such that

$$\int_t^{t+\lambda} \{\beta(s)(N^*(s) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3)p - (\mu(s) + \varepsilon(s))\}\,\mathrm{d}s > \eta_1, \tag{3.4.7}$$

$$N^*(t) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3 > m_\varepsilon \tag{3.4.8}$$

hold for all $t \geq T_2$, where $k := 1 + (\beta^+ M_\varepsilon + \gamma^+)\omega_2$. From (ii) of Assumption 3.2.1, ε_2 can be chosen sufficiently small so that

$$\int_t^{t+\omega_2} \{\beta(s)M_\varepsilon\varepsilon_2 - (\mu(s) + \varepsilon(s))\varepsilon_1\}\,\mathrm{d}s < -\eta_1, \tag{3.4.9}$$

$$\int_t^{t+\omega_2} \{\gamma(s)\varepsilon_2 - (\mu(s) + \delta(s))\varepsilon_3\}\,\mathrm{d}s < -\eta_1 \tag{3.4.10}$$

hold for all $t \geq T_2$.

First we claim that

$$\limsup_{t\to+\infty} I(t) > \varepsilon_2.$$

In fact, if it is not true, then there exists a $T_3 \geq T_2$ such that

$$I(t) \leq \varepsilon_2 \tag{3.4.11}$$

for all $t \geq T_3$. Suppose that $E(t) \geq \varepsilon_1$ for all $t \geq T_3$. Then, from (3.4.5) and (3.4.11), we have

$$\begin{aligned} E(t) &= E(T_3) + \int_{T_3}^t \{\beta(s)(N^*(s) - E(s) - I(s) - R(s))I(s) - (\mu(s) + \varepsilon(s))E(s)\}\,\mathrm{d}s \\ &\leq E(T_3) + \int_{T_3}^t \{\beta(s)M_\varepsilon\varepsilon_2 - (\mu(s) + \varepsilon(s))\varepsilon_1\}\,\mathrm{d}s \end{aligned} \tag{3.4.12}$$

for all $t \geq T_3$. From (3.4.9) and (3.4.12), we have $\lim_{t\to+\infty} E(t) = -\infty$, which contradicts with (ii) of Proposition 3.2.1. Therefore, we see that there exists an $s_1 \geq T_3$ such that $E(s_1) < \varepsilon_1$. Suppose that there exists an $s_2 > s_1$ such that $E(s_2) > \varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2$. Then, we see that there necessarily exists an $s_3 \in (s_1, s_2)$ such that $E(s_3) = \varepsilon_1$ and $E(t) > \varepsilon_1$ for all $t \in (s_3, s_2]$. Let n be an integer such that $s_2 \in [s_3 + n\omega_2, s_3 + (n+1)\omega_2]$. Then, from (3.4.9), we have

$$\begin{aligned} &\varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2 \\ &\quad < E(s_2) \\ &\quad = E(s_3) + \int_{s_3}^{s_2} \{\beta(s)(N^*(s) - E(s) - I(s) - R(s))I(s) - (\mu(s) + \varepsilon(s))E(s)\}\,\mathrm{d}s \\ &\quad < \varepsilon_1 + \left\{\int_{s_3}^{s_3+n\omega_2} + \int_{s_3+n\omega_2}^{s_2}\right\} \{\beta(s)M_\varepsilon\varepsilon_2 - (\mu(s) + \varepsilon(s))\varepsilon_1\}\,\mathrm{d}s \\ &\quad < \varepsilon_1 + \int_{s_3+n\omega_2}^{s_2} \beta(s)M_\varepsilon\varepsilon_2\,\mathrm{d}s \\ &\quad < \varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2, \end{aligned}$$

which is a contradiction. Therefore, we have that

$$E(t) \leq \varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2 \tag{3.4.13}$$

for all $t \geq s_1$. In a similar way, from (3.4.10), we can show that there exists a $\tilde{s}_1 \geq T_3$ such that

$$R(t) \leq \varepsilon_3 + \gamma^+ \omega_2 \varepsilon_2 \tag{3.4.14}$$

for all $t \geq \tilde{s}_1$. Now, from Lemma 3.4.1, there exists a $T_4 \geq \max(s_1, \tilde{s}_1)$ such that $W(p,t) = pE(t) - I(t) \leq 0$ for all $t \geq T_4$. Then

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}E(t) &= \{\beta(t)(N^*(t) - E(t) - I(t) - R(t))I(t) - (\mu(t) + \varepsilon(t))E(t)\} \\ &\geq E(t)\{\beta(t)(N^*(t) - E(t) - I(t) - R(t))p - (\mu(t) + \varepsilon(t))\} \\ &\geq E(t)\{\beta(t)(N^*(t) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3)p - (\mu(t) + \varepsilon(t))\} \end{aligned}$$

since it follows from (3.4.11)-(3.4.14) that $E(t) + I(t) + R(t) \leq \varepsilon_1 + k\varepsilon_2 + \varepsilon_3$ for all $t \geq T_4$. Hence, we have

$$E(t) \geq E(T_4) \exp\left(\int_{T_4}^{t} \{\beta(s)(N^*(s) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3)p - (\mu(s) + \varepsilon(s))\} \, \mathrm{d}s \right). \tag{3.4.15}$$

From (3.4.7) and (3.4.15), we have $\lim_{t \to +\infty} E(t) = +\infty$ and this contradicts with the boundedness of E, which is stated in (ii) of Proposition 3.2.1. Therefore, our claim $\limsup_{t \to +\infty} I(t) > \varepsilon_2$ is true.

Next, we claim that

$$\liminf_{t \to +\infty} I(t) \geq I_1,$$

where $I_1 > 0$ is a constant given later. From inequalities (3.4.7)-(3.4.9) and (ii) of Assumption 3.2.1, we see that there exist some constants $\tilde{T}_3 (\geq T_2)$, $\lambda_2 > 0$ and $\eta_2 > 0$ such that

$$\int_t^{t+\lambda_3} \{\beta(s) M_\varepsilon \varepsilon_2 - (\mu(s) + \varepsilon(s))\varepsilon_1\} \, \mathrm{d}s < -M_\varepsilon, \tag{3.4.16}$$

$$\int_t^{t+\lambda_3} \{\gamma(s)\varepsilon_2 - (\mu(s) + \delta(s))\varepsilon_3\} \, \mathrm{d}s < -M_\varepsilon, \tag{3.4.17}$$

$$\int_t^{t+\lambda_3} \{\beta(s)(N^*(s) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3)p - (\mu(s) + \varepsilon(s))\} \, \mathrm{d}s > \eta_2, \tag{3.4.18}$$

$$\int_t^{t+\lambda_3} \beta(s) \mathrm{d}s > \eta_2 \tag{3.4.19}$$

for all $\lambda_3 \geq \lambda_2$ and $t \geq \tilde{T}_3$. Let $C > 0$ be a constant satisfying

$$e^{-(\mu^+ + \varepsilon^+)\lambda_2} m_\varepsilon \nu_2 \eta_2 e^{C\eta_2} > \varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2, \tag{3.4.20}$$

where $\nu_2 = \varepsilon_2 e^{-(\gamma^+ + \mu^+)2\lambda_2}$. Since we proved $\limsup_{t \to +\infty} I(t) > \varepsilon_2$, there are only two possibilities as follows:

(i) $I(t) \geq \varepsilon_2$ for all $t \geq \exists \tilde{T}_4 \geq \tilde{T}_3$.

(ii) $I(t)$ oscillates about ε_2 for large $t \geq \tilde{T}_3$.

In case (i), we have $\liminf_{t \to +\infty} I(t) \geq \varepsilon_2 =: I_1$. In case (ii), there necessarily exist two constants t_1, $t_2 \geq \tilde{T}_3$ $(t_2 \geq t_1)$ such that

$$\begin{cases} I(t_1) = I(t_2) = \varepsilon_2, \\ I(t) < \varepsilon_2 \quad \text{for all } t \in (t_1, t_2). \end{cases}$$

Suppose that $t_2 - t_1 \leq C + 2\lambda_2$. Then, from (3.1.1) we have

$$\frac{\mathrm{d}I(t)}{\mathrm{d}t} \geq -(\mu^+ + \gamma^+) I(t). \tag{3.4.21}$$

Hence, we obtain

$$I(t) \geq I(t_1) \exp\left(\int_{t_1}^{t} -(\mu^+ + \gamma^+) \, \mathrm{d}s \right) \geq \varepsilon_2 e^{-(\mu^+ + \gamma^+)(C + 2\lambda_2)} =: I_1 \tag{3.4.22}$$

for all $t \in (t_1, t_2)$. Suppose that $t_2 - t_1 > C + 2\lambda_2$. Then, from (3.4.21), we have

$$I(t) \geq \varepsilon_2 e^{-(\mu^+ + \gamma^+)(C+2\lambda_2)} =: I_1$$

for all $t \in (t_1, t_1 + C + 2\lambda_2)$. Now, we are in a position to show that $I(t) \geq I_1$ for all $t \in [t_1 + C + 2\lambda_2, t_2)$. Suppose that $E(t) \geq \varepsilon_1$ for all $t \in [t_1, t_1 + \lambda_2]$. Then, from (3.4.16), we have

$$\begin{aligned} E(t_1 + \lambda_2) &\leq E(t_1) + \int_{t_1}^{t_1+\lambda_2} \{\beta(s) M_\varepsilon \varepsilon_2 - (\mu(s) + \varepsilon(s))\varepsilon_1\} ds \\ &< M_\varepsilon - M_\varepsilon = 0, \end{aligned}$$

which is a contradiction. Therefore, there exists an $s_4 \in [t_1, t_1 + \lambda_2]$ such that $E(s_4) < \varepsilon_1$. Then, as in the proof of $\limsup_{t\to+\infty} I(t) > \varepsilon_2$, we can show that $E(t) \leq \varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2$ for all $t \geq s_4$. Moreover, similarly, from (3.4.17), we can show that there exists an $\tilde{s}_4 \in [t_1, t_1 + \lambda_2]$ such that $R(t) \leq \varepsilon_3 + \gamma^+ \omega_2 \varepsilon_2$ for all $t \geq \tilde{s}_4$. Thus, we have

$$E(t) \leq \varepsilon_1 + \beta^+ M_\varepsilon \omega_2 \varepsilon_2, \quad R(t) \leq \varepsilon_3 + \gamma^+ \omega_2 \varepsilon_2 \tag{3.4.23}$$

for all $t \geq t_1 + \lambda_2 \geq \max(s_4, \tilde{s}_4)$. Now, from (3.4.21), we have

$$I(t) \geq v_2 = \varepsilon_2 e^{-(\mu^+ + \gamma^+)2\lambda_2} \tag{3.4.24}$$

for all $t \in [t_1, t_1 + 2\lambda_2]$. Hence, from (3.4.8) and (3.4.24), we have

$$\begin{aligned} \frac{dE(t)}{dt} &= \beta(t)(N^*(t) - E(t) - I(t) - R(t))I(t) - (\mu(t) + \varepsilon(t))E(t) \\ &\geq \beta(t) m_\varepsilon v_2 - (\mu^+ + \varepsilon^+) E(t) \end{aligned}$$

for all $t \in [t_1 + \lambda_2, t_1 + 2\lambda_2]$. Hence, from (3.4.19),

$$\begin{aligned} &E(t_1 + 2\lambda_2) \\ &\geq e^{-(\mu^+ + \varepsilon^+)(t_1 + 2\lambda_2)} \left\{ E(t_1 + \lambda_2) e^{(\mu^+ + \varepsilon^+)(t_1 + \lambda_2)} + \int_{t_1+\lambda_2}^{t_1+2\lambda_2} \beta(s) m_\varepsilon v_2 e^{(\mu^+ + \varepsilon^+)s} ds \right\} \\ &\geq e^{-(\mu^+ + \varepsilon^+)(t_1 + 2\lambda_2)} \int_{t_1+\lambda_2}^{t_1+2\lambda_2} \beta(s) m_\varepsilon v_2 e^{(\mu^+ + \varepsilon^+)s} ds \\ &\geq e^{-(\mu^+ + \varepsilon^+)\lambda_2} \eta_2 m_\varepsilon v_2. \end{aligned} \tag{3.4.25}$$

Now we suppose that there exists a $t_0 > 0$ such that $t_0 \in (t_1 + C + 2\lambda_2, t_2)$, $I(t_0) = I_1$ and $I(t) \geq I_1$ for all $t \in [t_1, t_0]$. Note that from Lemma 3.4.1, without loss of generality, we can assume that t_1 is so large that $W(p,t) = pE(t) - I(t) \leq 0$ for all $t \geq t_1 + 2\lambda_2$. Then, from (3.4.23), we have

$$\begin{aligned} \frac{d}{dt} E(t) &= \{\beta(t)(N^*(t) - E(t) - I(t) - R(t))I(t) - (\mu(t) + \varepsilon(t))E(t)\} \\ &\geq E(t)\{\beta(t)(N^*(t) - E(t) - I(t) - R(t))p - (\mu(t) + \varepsilon(t))\} \\ &\geq E(t)\{\beta(t)(N^*(t) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3)p - (\mu(t) + \varepsilon(t))\} \end{aligned}$$

for all $t \in (t_1 + 2\lambda_2, t_2)$. Hence, from (3.4.18) and (3.4.25), we have

$$\begin{aligned} &E(t_0) \\ &\geq E(t_1 + 2\lambda_2) \exp\left(\int_{t_1+2\lambda_2}^{t_0} \{\beta(s)(N^*(s) - \varepsilon_1 - k\varepsilon_2 - \varepsilon_3)p - (\mu(s) + \varepsilon(s))\} ds \right) \\ &\geq e^{-(\mu^+ + \varepsilon^+)\lambda_2} \eta_2 m_\varepsilon v_2 e^{C\eta_2}. \end{aligned}$$

Hence, from (3.4.23), we have

$$\varepsilon_1 + \omega_2 \beta^+ M_\varepsilon \varepsilon_2 \geq e^{-(\mu^+ + \varepsilon^+)\lambda_2} \eta_2 m_\varepsilon v_2 e^{C\eta_2},$$

which contradicts with (3.4.20). Therefore, $I(t) \geq I_1$ for all $t \in [t_1 + C + 2\lambda_2, t_2)$, which implies $\liminf_{t\to+\infty} I(t) \geq I_1$.

Since $\limsup_{t\to+\infty} I(t) \leq \limsup_{t\to+\infty} N^*(t) < M < +\infty$, the infectious population of system (3.1.1) is permanent. □

3.5 Applications

In this section, we focus on some special cases of system (3.1.1). Applying Theorems 3.3.1 and 3.4.1, we derive some explicit conditions for the extinction and permanence of infectious population of system (3.1.1).

First, we consider the case where all coefficients of system (3.1.1) are given by identically constant functions, that is, the case where (3.1.1) is an autonomous system. We show that, in this case, our results obtained in Sections 3.3 and 3.4 become a well-known threshold-type result corresponding to the basic reproduction number $\mathscr{R}_0$ given by (3.1.3).

For $p > 0$ we define

$$R(p) := \beta\frac{\Lambda}{\mu}p - (\mu+\varepsilon), \quad R^*(p) := \varepsilon\frac{1}{p} - (\mu+\gamma)$$

and

$$G(p) := \beta\frac{\Lambda}{\mu}p + \gamma - \left(1+\frac{1}{p}\right)\varepsilon.$$

Then, one can see that $R_i(\lambda, p) = R(p)$, $R_i^*(\lambda, p) = R^*(p)$ $(i = 1, 2)$ and $G(p,t) = G(p)$ in the autonomous case. We prove the following proposition:

Proposition 3.5.1. *Suppose that functions Λ, β, μ, ε, γ and δ of system* (3.1.1) *are identically positive constant functions. Then we have*

(i) *There exists a $p > 0$ such that $R(p) < 0$, $R^*(p) < 0$ and $G(p) < 0$ if and only if $\mathscr{R}_0 < 1$.*

(ii) *There exists a $p > 0$ such that $R(p) > 0$, $R^*(p) > 0$ and $G(p) < 0$ if and only if $\mathscr{R}_0 > 1$.*

Here $\mathscr{R}_0$ is the basic reproduction number defined by (3.1.3).

Proof. We only prove (i) because (ii) can be proved in a similar manner. Suppose that there exists $p > 0$ such that $R(p) < 0$, $R^*(p) < 0$ and $G(p) < 0$ hold. Then, it follows from $R(p) < 0$ and $R^*(p) < 0$ that

$$\frac{\varepsilon}{\mu+\gamma} < p < \frac{(\mu+\varepsilon)\mu}{\beta\Lambda}. \tag{3.5.1}$$

Hence we obtain $\mathscr{R}_0 < 1$. On the contrary, suppose that $\mathscr{R}_0 < 1$. Then, it is obvious that there exists a $p > 0$ such that (3.5.1) holds. Since we have

$$G\left(\frac{\varepsilon}{\mu+\gamma}\right) = \frac{\varepsilon\beta\Lambda}{(\mu+\gamma)\mu} + \gamma - \left(1+\frac{\mu+\gamma}{\varepsilon}\right)\varepsilon = (\mu+\varepsilon)(R_0 - 1) < 0,$$

there exists a $p > 0$ close enough to $\varepsilon/(\mu+\gamma)$ such that both (3.5.1) and $G(p) < 0$ hold. For such p we have $R(p) < 0$, $R^*(p) < 0$ and $G(p) < 0$. □

Proposition 3.5.1 implies that our conditions for the extinction and permanence for the nonautonomous system (3.1.1) cover the threshold-type result in the autonomous case.

Next we focus on the case where μ, ε and γ are constant functions. In this case, we have the following threshold-type result.

Corollary 3.5.1. Suppose that μ, ε and γ of system (3.1.1) are identically positive constant functions. Then, the following statements hold.

(i) The infectious population of system (3.1.1) is extinct if there exists a $T_1 > 0$ such that

$$\frac{\varepsilon\beta(t)N^*(t)}{(\mu+\varepsilon)(\mu+\gamma)} < 1 \tag{3.5.2}$$

for all $t \geq T_1$.

(ii) The infectious population of system (3.1.1) is permanent if there exists a $T_1 > 0$ such that

$$\frac{\varepsilon\beta(t)N^*(t)}{(\mu+\varepsilon)(\mu+\gamma)} > 1 \tag{3.5.3}$$

for all $t \geq T_1$.

Proof. We only prove (i) because (ii) can be proved in a similar manner. To prove (i), it suffices to show that there exist constants $p > 0$ and $\lambda > 0$ such that (3.3.1) and (3.3.2) hold and $G(p,t) < 0$ for all $t \geq T_1$. From (3.5.2), we have

$$\frac{\varepsilon}{\mu+\gamma} < \frac{\mu+\varepsilon}{\limsup_{t\to+\infty}\int_t^{t+1}\beta(s)N^*(s)\mathrm{d}s}.$$

We choose $p > 0$ such that

$$\frac{\varepsilon}{\mu+\gamma} < p < \frac{\mu+\varepsilon}{\limsup_{t\to+\infty}\int_t^{t+1}\beta(s)N^*(s)\mathrm{d}s}. \tag{3.5.4}$$

Then one can see that (3.3.1) and (3.3.2) with $\lambda = 1$ hold. Next we show that for such p, we have $G(p,t) < 0$ for all $t \geq T_1$. In fact, from (3.5.2), we have

$$\beta(t)N^*(t)\frac{\varepsilon}{\mu+\gamma} - (\mu+\varepsilon) = \beta(t)N^*(t)\frac{\varepsilon}{\mu+\gamma} + \gamma - \left(1+\frac{\mu+\gamma}{\varepsilon}\right)\varepsilon < 0$$

for all $t \geq T_1$. Hence, one can find small enough $\bar{\varepsilon} > 0$ such that $G(p,t) < 0$ holds for

$$p \in \left(\frac{\varepsilon}{\mu+\gamma}, \frac{\varepsilon}{\mu+\gamma}+\bar{\varepsilon}\right) \subset \left(\frac{\varepsilon}{\mu+\gamma}, \frac{\mu+\varepsilon}{\limsup_{t\to+\infty}\int_t^{t+1}\beta(s)N^*(s)\mathrm{d}s}\right)$$

and $t \geq T_1$, because of the continuity of G with respect to p. □

It is easily seen that the existence of $T_1 > 0$ such that (3.5.2) or (3.5.3) hold for all $t \geq T_1$ is a sufficient condition for

$$\limsup_{t\to+\infty}\int_t^{t+\lambda}\{\varepsilon\beta(s)N^*(s) - (\mu+\varepsilon)(\mu+\gamma)\}\mathrm{d}s < 0 \tag{3.5.5}$$

or

$$\liminf_{t\to+\infty}\int_t^{t+\lambda}\{\varepsilon\beta(s)N^*(s) - (\mu+\varepsilon)(\mu+\gamma)\}\mathrm{d}s > 0 \tag{3.5.6}$$

with $\lambda = 1$, respectively, where (3.5.5) and (3.5.6) are conditions proposed in Questions 1 and 2 in [102] for the extinction and permanence of infectious population of system (3.1.1), respectively. However, one can see that those conditions do not imply the conditions given in Corollary 3.5.1. In fact, conditions (3.5.5) and (3.5.6) are not suitable as a threshold condition for the global dynamics of system (3.1.1) because they can overestimate the value of the basic reproduction number $\mathscr{R}_0$ even in the situation where only function $\beta(t)$ is periodic and other coefficients are constant functions (see Section 5.1.2 of [6]). In periodic case, it was shown in [75] that whether the infectious population of system (3.1.1) is extinct or permanent is perfectly determined by $\mathscr{R}_0$.

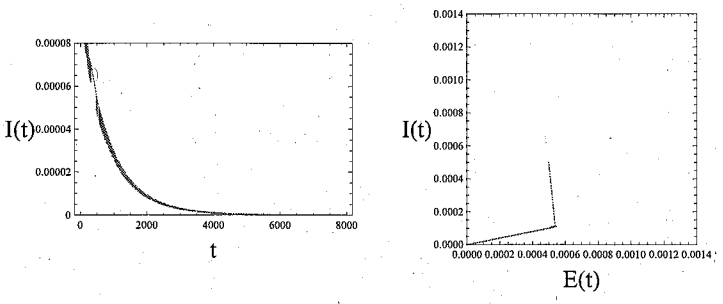


Figure 3.2: Solution behavior of $I(t)$ and $E(t)$ of system (3.1.1) with $E(0) = I(0) = 0.0005$, $\beta(t) = 6.49\,(1+0.5\cos(2\pi t))$ and $p = 0.20011$

3.6 Numerical examples

In this section we perform numerical simulations in order to verify the validity of Theorems 3.3.1 and 3.4.1. We show also that in some special cases, our results can improve the previous results for the permanence and extinction of system (3.1.1) obtained by Zhang and Teng [102].

Fix

$$\Lambda(t) \equiv 1,\ \ \mu(t) \equiv 1,\ \ \varepsilon(t) = 0.3\,(1+0.5\cos(2\pi t)),\ \ \gamma(t) = 0.5\,(1+0.5\cos(2\pi t))$$

and $\delta(t) \equiv 0.1$. Then, from (3.2.1), we have $\lim_{t\to+\infty} N^*(t) = 1$. Here we assume $N^*(0) = 1$ and hence $N^*(t) \equiv 1$.

Let $\beta(t) = 6.49\,(1+0.5\cos(2\pi t))$. Then, system (3.1.1) becomes time-periodic with period 1. We choose $\lambda = 1$ and $p = 0.20011$. Then we have

$$\begin{aligned} R_1(\lambda; p) &= \int_0^1 \{6.49\,(1+0.5\cos(2\pi s)) \times 0.20011 - (1+0.3\,(1+0.5\cos(2\pi s)))\}\,\mathrm{d}s \\ &\backsimeq -0.0012861\cdots < 0, \end{aligned}$$

$$\begin{aligned} R_1^*(\lambda, p) &= \int_0^1 \left\{0.3\,(1+0.5\cos(2\pi s)) \times \frac{1}{0.20011} - (1+0.5\,(1+0.5\cos(2\pi t)))\right\}\mathrm{d}s \\ &\backsimeq -0.000824546\cdots < 0 \end{aligned}$$

and

$$\begin{aligned} G(p,t) &= 6.49\,(1+0.5\cos(2\pi t)) \times 0.20011 + 0.5\,(1+0.5\cos(2\pi t)) \\ &\quad - \left(1+\frac{1}{0.20011}\right) \times 0.3\,(1+0.5\cos(2\pi t)) \\ &\backsimeq -0.000461554\,(1+0.5\cos(2\pi t)) < 0 \end{aligned}$$

for all $t > 0$. From (i) of Theorem 3.3.1, we see that the infectious population of system (3.1.1) is extinct. See Figure 3.2 for a numerical simulation of the solution behavior. In this example we have

$$\frac{\int_t^{t+\lambda} \beta(s)N^*(s)\mathrm{d}s}{\int_t^{t+\lambda} \mu(s)\mathrm{d}s} = \frac{\int_0^1 6.49\,(1+0.5(\cos(2\pi s)))\,\mathrm{d}s}{1} = 6.49 > 1.$$

This implies that a sufficient condition proposed in Theorem 5.1 in [102] for the extinction of infectious population does not hold. Thus, their suggested criterion can not determine the extinction of infectious population in this example.

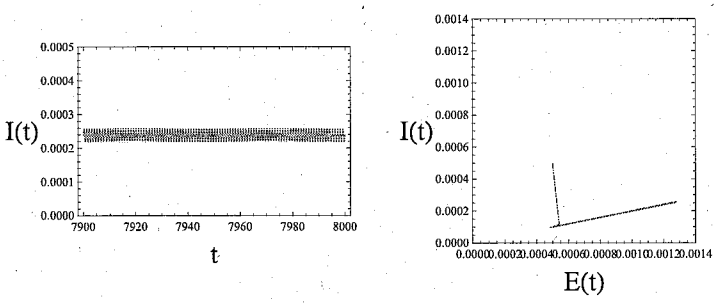


Figure 3.3: Solution behavior of $I(t)$ and $E(t)$ of system (3.1.1) with $E(0) = I(0) = 0.0005$, $\beta(t) = 6.51\,(1+0.5\cos(2\pi t))$ and $p = 0.1997$

Next we set $\beta(t) = 6.51\,(1+0.5\cos(2\pi t))$. We choose $\lambda = 1$ and $p = 0.1997$. Then,

$$\begin{aligned} R_2(\lambda,p) &= \int_0^1 \{6.51\,(1+0.5\cos(2\pi s)) \times 0.1997 - (1+0.3\,(1+0.5\cos(2\pi s)))\}\,\mathrm{d}s \\ &\backsimeq 0.000047\cdots > 0, \end{aligned}$$

$$\begin{aligned} R_2^*(\lambda,p) &= \int_0^1 \left\{0.3\,(1+0.5\cos(2\pi s)) \times \frac{1}{0.1997} - (1+0.5\,(1+0.5\cos(2\pi t)))\right\}\mathrm{d}s \\ &\backsimeq 0.00225338\cdots > 0 \end{aligned}$$

and

$$\begin{aligned} G(p,t) &= 6.51\,(1+0.5\cos(2\pi t)) \times 0.1997 + 0.5\,(1+0.5\cos(2\pi t)) \\ &\quad - \left(1+\frac{1}{0.1997}\right) \times 0.3\,(1+0.5\cos(2\pi t)) \\ &\backsimeq -0.00220638\,(1+0.5\cos(2\pi t)) < 0 \end{aligned}$$

for all $t > 0$. Hence, from (ii) of Theorem 3.4.1, we see that the infectious population of system (3.1.1) is permanent. See Figure 3.3 for a numerical simulation of the solution behavior. On the other hand, one can compute

$$\begin{aligned} &\frac{\int_t^{t+\lambda} 2\sqrt{\beta(s)\varepsilon(s)N^*(s)}\,\mathrm{d}u}{\int_t^{t+\lambda} (\mu(s)+\varepsilon(s)+\mu(s)+\gamma(s))\,\mathrm{d}u} \\ = &\frac{\int_0^1 2\sqrt{6.51\,(1+0.5\cos(2\pi s)) \times 0.3\,(1+0.5\cos(2\pi s))}\,\mathrm{d}s}{\int_0^1 (2+0.8\,(1+0.5\cos(2\pi s)))\,\mathrm{d}s} \backsimeq 0.99821 < 1. \end{aligned}$$

This implies, similar to the previous example, that a sufficient condition proposed in Theorem 4.1 in [102] for the permanence of infectious population fails in this example.

3.7 Discussion

In this chapter, we have investigated the global dynamics of a nonautonomous SEIRS epidemic model (3.1.1). We have obtained sufficient conditions for the extinction and permanence of infectious population of system (3.1.1) in Theorems 3.3.1 and 3.4.1, respectively. In the proofs, we make use of a sign property of a function $W(p,t)$ defined by (3.2.3), see Lemmas 3.2.1 and 3.4.1.

In Section 3.5, we have proved that when every parameter of system (3.1.1) is given as a constant parameter, our conditions in Theorems 3.3.1 and 3.4.1 become the threshold condition corresponding to the basic reproduction

number $\mathscr{R}_0$. Here, we remark that conditions given in Theorems 4.1 and 5.1 in [102] for the permanence and extinction do not give a threshold-type condition even in the autonomous case. In the same section we discussed also a relation between our results and open problems proposed in [102]. For some special cases, we have shown that our conditions are sufficient, but not necessary for (3.5.5) and (3.5.6), which were conjectured as conditions for the permanence and extinction of infectious population in [102]. For the case where every parameter is given as a periodic function, in [75], it was proved that the basic reproduction number $\mathscr{R}_0$ works as a threshold parameter for determining the global stability of the disease-free equilibrium and the permanence of infectious population of the system. An approximation method for the basic reproduction number $\mathscr{R}_0$ in [5] has shown that the conjectured condition in [102] does not determine the permanence and extinction completely, see Section 5 in [75] for the detail.

In Section 3.6 we provided numerical examples to illustrate the validity of our results. In those examples we show also that conditions in Theorems 4.1 and 5.1 in [102] for the permanence and extinction of infectious population of system (3.1.1) are not satisfied.

One may argue that our conditions for the permanence and extinction may not sharp. It is still an open problem that if the basic reproduction number $\mathscr{R}_0$ for (3.1.1) works as a threshold parameter to determine the permanence and extinction of infectious population, similar to the autonomous case.

Acknowledgment

The author would like to thank Professor Yoshiaki Muroya and the reviewers for their valuable comments and suggestions to the published version [55] of this chapter.

Chapter 4

A time-periodic SIS epidemic model with age structure

Abstract The main contribution of this chapter is to obtain a threshold value for the existence and uniqueness of a nontrivial endemic periodic solution of an age-structured SIS epidemic model with periodic parameters. Under the assumption of the weak ergodicity of non-autonomous Lotka-McKendrick system, we formulate a normalized system for infected population as an initial boundary value problem of a partial differential equation. Existence problem for endemic periodic solutions is reduced to a fixed point problem of a nonlinear integral operator acting on a Banach space of locally integrable periodic L^1-valued functions. We prove that the spectral radius of the Fréchet derivative of the integral operator at zero plays the role of a threshold for the existence and uniqueness of a nontrivial fixed point of the operator corresponding to a nontrivial periodic solution of the original differential equation in a weak sense. If the Malthusian parameter of the host population is equal to zero, our threshold value is equal to the well-known epidemiological threshold value, the basic reproduction number $\mathscr{R}_0$. However, if it is not the case, then two threshold values are different from each other and we have to pay attention on their actual biological implications. This is a collaborative work with Professor Hisashi Inaba in the University of Tokyo.

Keywords SIS epidemic model; Age structure; Periodic system; The basic reproduction number; Malthusian parameter

4.1 Introduction

The seasonality of infectious diseases is one of most important research interests in mathematical epidemiology, since the transmission parameters and host population behavior usually depend on season. Therefore many authors have examined differential equations systems with periodic parameters in order to model the seasonal spread of infectious diseases ([29], [32], [59], [5], [6], [97], [75]).

One of the most important concepts in this field is the basic reproduction number $\mathscr{R}_0$. It is epidemiologically defined as the expected number of secondary cases produced by a typical infectious individual during its entire infectious period in a completely susceptible host population, and usually, it is mathematically obtained as the spectral radius of a linear operator, which is called the next generation operator ([18], [19], [94], [20]).

Intuitively speaking, we can expect that the disease can invade into a completely susceptible host population if $\mathscr{R}_0 > 1$, while it cannot if $\mathscr{R}_0 < 1$ in a local sense. This is a principle of invasion threshold based on $\mathscr{R}_0$. Moreover, usually we can also expect that there exists at least one endemic steady state if $\mathscr{R}_0 > 1$, although it may not be a necessary condition for existence of endemic steady states. In fact, endemic steady states can exists under the subcritical condition $\mathscr{R}_0 < 1$ (for instance, see [40], [41]). This endemic threshold result has been widely established among autonomous epidemic systems for age-structured populations ([39], [40], [41], [42], [43]).

On the other hand, the general definition of the basic reproduction number in periodic environments was first successfully established by Bacaër and Guernaoui in 2006 [5], and then it has been extended to the case of more

general time-heterogeneous environments by Thieme [91] and Inaba [46]. As is shown in Inaba [45], the invasion threshold principle for periodic structured epidemic models has been well-established based on the definition of Bacaër and Guernaoui. However, the endemic threshold result for periodic epidemic systems based on $\mathscr{R}_0$ of the definition of Bacaër and Guernaoui has not yet been fully examined for structured population models, although for non-structured population models, Nakata and Kuniya ([75]) have shown existence of periodic endemic solution when $\mathscr{R}_0 > 1$, where $\mathscr{R}_0$ is given by the definition of Bacaër and Guernaoui.

Introduction of age-structure into epidemic models is a crucial point so that we deal with realistic situations. For example, any disease prevention policy depends on age structure of the host population. Due to their relatively complex form, the analysis is difficult and there are not a few open problems on the relation between $\mathscr{R}_0$ and mathematical properties such as the existence, uniqueness, local and global stability of steady states. However, we strongly conjecture that the endemic threshold result for structured population in periodic environments will be properly formulated by $\mathscr{R}_0$ defined by Bacaër and Guernaoui.

The main purpose of this chapter is to obtain threshold results for an age-structured epidemic model with periodic parameters and study the relation between $\mathscr{R}_0$ and the solution behavior of the model.

The model we study in this chapter is an age-structured SIS epidemic model, in which total population is divided into two epidemiological classes, susceptibles and infectives, and individuals recovered from infection do not obtain immunity and directly go back to the susceptible class. The age-structured SIS epidemic models with time-independent parameters have been studied in [11], [34], [13], [36] and [23]. A generalization of such models to a periodic system was given in [59], in which the periodic age-space-structured SIS epidemic model with reaction-diffusion terms is considered, so it has quite a general form. They showed the global asymptotic stability of a nontrivial endemic periodic solution, however, they relied on the assumption of the existence of such a periodic solution (for the case where there is no recruitment from other environments). Thus, the existence of a threshold value like $\mathscr{R}_0$ for the existence of a nontrivial endemic periodic solution has not been investigated for any age-structured SIS periodic epidemic models, and this is the point we focus on in this chapter.

Under the assumption of the weak ergodicity of a nonautonomous Lotka-McKendrick population system, the age-structured SIS periodic epidemic model we shall consider can be normalized to a single equation of fraction of infected population. Integrating it along the characteristic lines, we obtain an expression of the fraction of the infecteds by the force of infection. Substituting the expression into the definition of the force of infection, we obtain an integral equation, which can be a fixed point equation in a Banach space of locally integrable, time-periodic L^1-valued functions. We show that the spectral radius of the Fréchet derivative of the fixed point operator at zero is the desired threshold value, that is, if it is less than one, the trivial disease-free steady state of the normalized system is globally asymptotically stable, while if it is greater than one, there exists a unique nontrivial endemic periodic solution.

In case that the Malthusian parameter of the host population is equal to zero, it is shown that the threshold value is equal to the basic reproduction number $\mathscr{R}_0$ obtained by following to the definition in [5, 91, 45]. However, if it is not equal to zero, they can be different and therefore we have to pay attention to possible cases such as the relatively decreasing but absolutely increasing (or, vice versa) infected population.

The organization of this chapter is as follows: In section 4.2, we formulate the main model of this chapter and normalize it to a single equation as mentioned above. In section 4.3, we show the well-posedness of the time evolution problem. In section 4.4, we obtain the threshold value as mentioned above, and prove the existence of a nontrivial endemic periodic solution of the system in case the threshold value is greater than one. In section 4.5, we prove the uniqueness of such a nontrivial solution in case the threshold value is greater than one. In section 4.6, we prove the global asymptotic stability of the trivial disease-free steady state of the system in case the threshold value is less than one. In section 4.7, we investigate the relation between the threshold value and the basic reproduction number $\mathscr{R}_0$. Finally, in section 4.8, numerical illustration is given.

4.2 The basic model

Let $S(t,a)$ and $I(t,a)$ be the age-densities at time t and age $a \in [0,\omega]$ of susceptible and infective population respectively, where $\omega < \infty$ denotes the maximum attainable age. Let $P(t,a)$ be the age-density of host population at time t and thus we have $P(t,a) = S(t,a) + I(t,a)$. Let $N(t)$ be the total size of population at time t and thus we

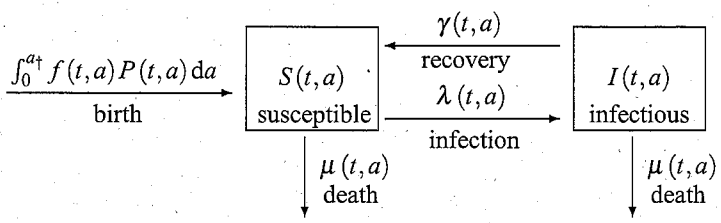


Figure 4.1: Transfer diagram for SIS epidemic model (4.2.1)

have

$$N(t) = \int_0^{\omega} P(t,a)\,\mathrm{d}a.$$

Let $\mu(t,a)$ be the age-specific mortality rate at time t, $\gamma(t,a)$ be the age-specific recovery rate, $k(t,a,\sigma)$ be the transmission coefficient between susceptible individuals aged a and infective individuals aged σ, $f(t,a)$ be the age-specific fertility rate and $\lambda(t,a)$ be the force of infection to susceptible individuals aged a, at time t, respectively. We make the following technical assumption on vital parameters:

Assumption 4.2.1. The basic vital parameters f, γ, μ and k are periodic in time t with period $T > 0$, and we assume that $f(t,\cdot), \gamma(t,\cdot) \in L^{\infty}_{+}(0,\omega)$, $k(t,\cdot,\cdot) \in L^{\infty}_{+}([0,\omega]\times[0,\omega])$ and $\mu(t,a)$ is locally integrable along the characteristic line $t-a=$ const. and

$$\int_0^{\omega} \mu(t+\sigma,\sigma)d\sigma = \infty,$$

for all $t \in \mathbb{R}$, which implies that the cohort survival rate is zero at age ω.

Then the age-structured SIS epidemic model with time-periodic parameters is formulated as follows:

$$\begin{aligned}
&\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)S(t,a) = -\lambda(t,a)S(t,a) - \mu(t,a)S(t,a) + \gamma(t,a)I(t,a),\\
&\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)I(t,a) = \lambda(t,a)S(t,a) - (\mu(t,a)+\gamma(t,a))I(t,a),\\
&\lambda(t,a) = \frac{1}{N(t)}\int_0^{\omega} k(t,a,\sigma)I(t,\sigma)\,\mathrm{d}\sigma,\\
&S(t,0) = \int_0^{\omega} f(t,a)P(t,a)\,\mathrm{d}a,\\
&I(t,0) = 0,\\
&S(0,a) = S_0(a), \quad I(0,a) = I_0(a),
\end{aligned} \tag{4.2.1}$$

where the force of infection is given by the standard type of incidence and the initial data are given by nonnegative integrable functions.

Since we neglect an additional death rate for infecteds, the host population dynamics is described by the Lotka-McKendrick system with periodic coefficients:

$$\begin{aligned}
&\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)P(t,a) = -\mu(t,a)P(t,a),\\
&P(t,0) = \int_0^{\omega} f(t,a)P(t,a)\,\mathrm{d}a,\\
&P(0,a) = P_0(a) := S_0(a) + I_0(a),
\end{aligned} \tag{4.2.2}$$

To simplify the basic model, we introduce the age distribution of ratio for each epidemiological class as follows:

$$s(t,a) := \frac{S(t,a)}{P(t,a)}, \qquad i(t,a) := \frac{I(t,a)}{P(t,a)}. \tag{4.2.3}$$

Now we can rewrite model (4.2.1) as

$$\begin{aligned}
&\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)s(t,a)=-\lambda(t,a)s(t,a)+\gamma(t,a)i(t,a),\\
&\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)i(t,a)=\lambda(t,a)s(t,a)-\gamma(t,a)i(t,a),\\
&\lambda(t,a)=\int_0^{\omega}k(t,a,\sigma)\frac{P(t,\sigma)}{N(t)}i(t,\sigma)\,\mathrm{d}\sigma,\\
&s(t,0)=1,\quad i(t,0)=0,\\
&s(0,a)=s_0(a),\quad i(0,a)=i_0(a).
\end{aligned}\tag{4.2.4}$$

Here we assume that the Lotka–McKendrick system (4.2.2) has a positive persistent solution as

$$P^*(t,a)=\mathrm{e}^{r(t-a)}b(t-a)\mathrm{e}^{-\int_0^a\mu(t-a+\sigma,\sigma)\mathrm{d}\sigma},$$

where the Malthusian parameter r and a positive periodic function $b(t)$ satisfy the characteristic relation:

$$b(t)=\int_0^{\omega}f(t,a)\mathrm{e}^{-ra-\int_0^a\mu(t-a+\sigma,\sigma)d\sigma}b(t-a)\mathrm{d}a.$$

Let $\theta(t,a)$ be the periodic age profile:

$$\theta(t,a):=\frac{P^*(t,a)}{\int_0^{\omega}P^*(t,x)dx}.$$

In this chapter we assume that the age profile of the host population has already attained a periodic stable age profile θ, that is,

$$P(t,a)=N(t)\theta(t,a),$$

holds for all $t\geq 0$. We adopt a technical, but biologically reasonable, assumption as follows:

We remark that if we assume that the non-autonomous system (4.2.2) is *weakly ergodic*, the age profile of the host population converges to a periodic age profile θ in a L^1-sense, that is,

$$\lim_{t\to\infty}\left\|\frac{P(t,\cdot)}{N(t)}-\theta(t,\cdot)\right\|_{L^1}=0.$$

where we use the notation θ neglcting the phase difference.

The stable population model with periodic parameters was first studied by A. J. Coale ([16], [17]) based on the renewal integral equation. The reader may refer to [85], [38], [78], [77] and [45] for the proof of the above statements. Note that our analysis covers a spcial case that only epidemic parameters are periodic and all demographic parameters are time independent, hence the Lotka–McKendrick system (4.2.2) becomes an autonomous system and there exists a disease-free steady state (see Section 4.8).

Since it follows from (4.2.3) that $s(t,a)\equiv 1-i(t,a)$, system (4.2.4) can be reduced to a single equation for $i(t,a)$ as

$$\begin{aligned}
&\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)i(t,a)=\lambda(t,a)(1-i(t,a))-\gamma(t,a)i(t,a),\\
&\lambda(t,a)=\int_0^{\omega}\beta(t,a,\sigma)i(t,\sigma)\,\mathrm{d}\sigma,\\
&i(t,0)=0,\quad i(0,a)=i_0(a),
\end{aligned}\tag{4.2.5}$$

where

$$\beta(t,a,\sigma):=k(t,a,\sigma)\theta(t,\sigma)$$

is a given time-periodic transmission kernel.

It is obvious that system (4.2.5) always has the trivial disease-free steady state $i\equiv 0$. The main interest of this chapter is to investigate the existence and uniqueness of a nontrivial endemic periodic solution of system (4.2.5).

4.3 Abstract formulation

Although the mathematical well-posedness of the initial-boundary value problem (4.2.5) is well known ([11], [36]), here we sketch a method to show it for the readers' convenience. Note that we can reformulate system (4.2.5) as an abstract Cauchy problem in Banach space $E := L^1(0,\omega)$.

Let us define a linear operator $A : D(A) \subset E \to E$ as

$$\begin{cases} (A\varphi)(a) := -\dfrac{\mathrm{d}}{\mathrm{d}a}\varphi(a), \\ D(A) = \{\varphi \in E :\ \varphi \in W^{1,1}(0,\omega),\ \varphi(0) = 0\}, \end{cases} \tag{4.3.1}$$

where $W^{1,1}(0,\omega)$ denotes the set of absolutely continuous functions on $(0,\omega)$. Let C be a closed convex set defined by

$$C := \{\varphi \in E_+ :\ 0 \le \varphi(a) \le 1 \text{ a.e.}\}, \tag{4.3.2}$$

where E_+ denotes the positive cone of E. Let us define family $\{F(t,\cdot)\}_{t\ge 0} : C \subset E \to E$ of nonlinear bounded operators as

$$F(t,\varphi)(a) := \lambda[t,a|\ \varphi](1-\varphi(a)) - \gamma(t,a)\varphi(a), \tag{4.3.3}$$

where

$$\lambda[t,a|\ \varphi] := \int_0^\omega \beta(t,a,\sigma)\varphi(\sigma)\,\mathrm{d}\sigma.$$

Then system (4.2.5) is reformulated as a semilinear nonautonomous Cauchy problem

$$\frac{\mathrm{d}}{\mathrm{d}t}i(t) = Ai(t) + F(t,i(t)), \quad i(0) = i_0 \tag{4.3.4}$$

in E. It is easy to see that operator A is the infinitesimal generator of a C_0-semigroup $\{\mathrm{e}^{tA}\}_{t\ge 0}$ defined by

$$\left(\mathrm{e}^{tA}\varphi\right)(a) = \begin{cases} 0, & t > a, \\ \varphi(a-t), & t < a \end{cases} \tag{4.3.5}$$

on E. Here note that although (4.3.5) is not defined for $t = a$, it does not matter since $\varphi(0) = 0$ always holds for $\varphi \in D(A)$.

From (4.3.5) we immediately have $\mathrm{e}^{tA}(C) \subset C$.

Using the fact that γ and β are bounded above and the same kind of argument as in [11], it is easy to show that the following holds:

Proposition 4.3.1. *$F(t,\cdot) : C \to E$ is Lipschitz continuous for any fixed $t \in \mathbb{R}_+$. There exists a constant $\alpha \in (0,1)$ such that if $\phi \in C$, then $\phi + \alpha F(t,\phi) \in C$.*

Using α appeared in Proposition 4.3.1, we can rewrite problem (4.3.4) as

$$\frac{\mathrm{d}}{\mathrm{d}t}i(t) = \left(A - \frac{1}{\alpha}\right)i(t) + \frac{1}{\alpha}(i(t) + \alpha F(t,i(t))), \quad i(0) = i_0. \tag{4.3.6}$$

Now we are in position to look for a mild solution $i \in C$ of (4.3.6), which is given by the solution of integral equation

$$i(t) = \mathrm{e}^{-\frac{1}{\alpha}t}\mathrm{e}^{tA}i_0 + \frac{1}{\alpha}\int_0^t \mathrm{e}^{-\frac{1}{\alpha}(t-s)}\mathrm{e}^{(t-s)A}\{i(s) + \alpha F(s,i(s))\}\,\mathrm{d}s. \tag{4.3.7}$$

Equation (4.3.7) provides the following scheme for the standard iterative procedure for obtaining mild solution $i \in C$:

$$i^0(t) = i_0,$$

$$i^{n+1}(t) = \mathrm{e}^{-\frac{1}{\alpha}t}\mathrm{e}^{tA}i_0 + \frac{1}{\alpha}\int_0^t \mathrm{e}^{-\frac{1}{\alpha}(t-s)}\mathrm{e}^{(t-s)A}\{i^n(s) + \alpha F(s,i^n(s))\}\,\mathrm{d}s, \quad n = 0,1,2,\cdots.$$

Since it is easy to see that C is invariant with respect to the iteration process, that is, $i^{n+1} \in C$ if $i^n \in C$, according to the argument in [11, 36], we can prove the following theorem ([36]):

Theorem 4.3.1. *Let $i_0 \in C$. Then, abstract Cauchy problem (4.3.4) has a unique mild solution $i(t) = U(t,0)i_0$ in C, where $U(t,s), t \geq s \geq 0$ defines an evolutionary systems with the following property:*

$$U(s,s) = I, \quad U(t,\sigma)U(\sigma,s) = U(t,s), \quad U(t,s)(C) \subset C,$$

$$U(t,s)u \leq U(t,s)v, \quad \text{if} \quad u \leq v.$$

4.4 Existence of an endemic periodic solution

In this section, we investigate the existence of an endemic T-periodic solution of system (4.2.5). Let X_T be the set of locally integrable T-periodic E-valued functions with norm

$$||\varphi||_{X_T} := \int_0^T ||\varphi(t)||_E \mathrm{d}t = \int_0^T \int_0^\omega |\varphi(t,a)| \mathrm{d}a \, \mathrm{d}t,$$

and $X_{T,+}$ be its positive cone. Let Ω_T be the state space given by

$$\Omega_T := \{\varphi \in X_{T,+} : \ 0 \leq \varphi(t,a) \leq 1 \ \text{ a.e.} \}. \tag{4.4.1}$$

If an endemic T-periodic solution $i^* \in \Omega_T \setminus \{0\}$ of system (4.2.5) exists, it satisfies

$$\begin{aligned} \left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right) i^*(t,a) &= \lambda^*(t,a)(1 - i^*(t,a)) - \gamma(t,a)i^*(t,a), \\ \lambda^*(t,a) &= \int_0^\omega \beta(t,a,\sigma) i^*(t,\sigma) \mathrm{d}\sigma, \\ i^*(t,0) &= 0. \end{aligned} \tag{4.4.2}$$

Integrating the first equation of (4.4.2) along the characteristic lines, we have

$$i^*(t,a) = \int_0^a \lambda^*(t-a+\sigma,\sigma) \mathrm{e}^{-\int_\sigma^a [\lambda^*(t-a+\rho,\rho)+\gamma(t-a+\rho,\rho)]\mathrm{d}\rho} \mathrm{d}\sigma. \tag{4.4.3}$$

Note that if a time-periodic E-valued function $\lambda^*(t,\cdot)$ is given, $i^*(t,a)$ calculated from (4.4.3) is differentiable along the characteristic line $t - a = const.$, that is, it follows that

$$Di^*(t,a) = \lambda^*(t,a)(1 - i^*(t,a)) - \gamma(t,a)i^*(t,a), \tag{4.4.4}$$

where operator D is a directional derivative defined by

$$(Df)(t,a) := \lim_{h \to 0} \frac{f(t+h,a+h) - f(t,a)}{h}.$$

In the following, we look for a time-periodic solution of (4.4.2) in a weak sense such that the differential operator $\partial_t + \partial_a$ is interpreted as the directional derivative D. If we assume differentiability of parameter β, the weak solution becomes a classical solution.

Substituting (4.4.3) into the second equation of (4.4.2), we have

$$\begin{aligned} \lambda^*(t,a) &= \int_0^\omega \beta(t,a,\sigma) \int_0^\sigma \lambda^*(t-\sigma+\rho,\rho) \mathrm{e}^{-\int_\rho^\sigma [\lambda^*(t-\sigma+\eta,\eta)+\gamma(t-\sigma+\eta,\eta)]\mathrm{d}\eta} \mathrm{d}\rho \mathrm{d}\sigma \\ &= \int_0^\omega \int_0^\sigma \beta(t,a,\sigma) \lambda^*(t-\tau,\sigma-\tau) \mathrm{e}^{-\int_{\sigma-\tau}^\sigma [\lambda^*(t-\sigma+\eta,\eta)+\gamma(t-\sigma+\eta,\eta)]\mathrm{d}\eta} \mathrm{d}\tau \mathrm{d}\sigma \\ &= \int_0^\omega \int_0^\sigma \beta(t,a,\sigma) \lambda^*(t-\tau,\sigma-\tau) \mathrm{e}^{-\int_0^\tau [\lambda^*(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)]\mathrm{d}\zeta} \mathrm{d}\tau \mathrm{d}\sigma \\ &= \int_0^\omega \int_\tau^\omega \beta(t,a,\sigma) \mathrm{e}^{-\int_0^\tau [\gamma(t-\zeta,\sigma-\zeta)+\lambda^*(t-\zeta,\sigma-\zeta)]\mathrm{d}\zeta} \lambda^*(t-\tau,\sigma-\tau) \mathrm{d}\sigma \mathrm{d}\tau. \end{aligned}$$

Define a nonlinear positive operator

$$\Phi(\varphi)(t,a) := \int_0^\omega \int_\tau^\omega \beta(t,a,\sigma)\, \mathrm{e}^{-\int_0^\tau [\gamma(t-\zeta,\sigma-\zeta)+\varphi(t-\zeta,\sigma-\zeta)]\mathrm{d}\zeta} \varphi(t-\tau,\sigma-\tau)\,\mathrm{d}\sigma\mathrm{d}\tau \tag{4.4.5}$$

on X_T. Then if Φ has a nontrivial fixed point $\lambda^* = \Phi(\lambda^*)$ in $X_{T,+} \setminus \{0\}$, there exists an endemic T-periodic solution i^* in $\Omega_T \setminus \{0\}$ in a weak sense. In fact, if there exists such a fixed point $\lambda^* = \Phi(\lambda^*) \in X_{T,+} \setminus \{0\}$, then from (4.4.3) we easily see that $i^* \geq 0$, $i^* \neq 0$ and

$$\begin{aligned} i^*(t,a) &= \int_0^a (\lambda^*(t-a+\sigma,\sigma) + \gamma(t-a+\sigma,\sigma))\, \mathrm{e}^{-\int_\sigma^a \lambda^*(t-a+\rho,\rho)+\gamma(t-a+\rho,\rho)\mathrm{d}\rho}\mathrm{d}\sigma \\ &\quad - \int_0^a \gamma(t-a+\sigma,\sigma)\, \mathrm{e}^{-\int_\sigma^a [\lambda^*(t-a+\rho,\rho)+\gamma(t-a+\rho,\rho)]\mathrm{d}\rho}\mathrm{d}\sigma \\ &= 1 - \mathrm{e}^{-\int_0^a [\lambda^*(t-a+\rho,\rho)+\gamma(t-a+\rho,\rho)]\mathrm{d}\rho} - \int_0^a \gamma(t-a+\sigma,\sigma)\, \mathrm{e}^{-\int_\sigma^a [\lambda^*(t-a+\rho,\rho)+\gamma(t-a+\rho,\rho)]\mathrm{d}\rho}\mathrm{d}\sigma \leq 1. \end{aligned}$$

Hence $i^* \in \Omega_T \setminus \{0\}$ and it satisfies (4.4.2) in the weak sense. Therefore, in what follows, we investigate the existence of a nontrivial fixed point λ^* of operator Φ in $X_{T,+} \setminus \{0\}$.

Let us define a positive bounded linear operator

$$(K\varphi)(t,a) := \int_0^\omega \int_\tau^\omega \beta(t,a,\sigma)\, \mathrm{e}^{-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta} \varphi(t-\tau,\sigma-\tau)\,\mathrm{d}\sigma\mathrm{d}\tau, \quad \varphi \in X_T, \tag{4.4.6}$$

which is the Fréchet derivative of operator Φ at $\varphi = 0$ and it is a majorant of Φ, that is $\Phi \leq K$. Without loss of generality, we can assume that β is uniformly bounded above, so Φ and K define maps from the positive cone of X_T into itself.

Let $\rho(K)$ be the spectral radius of operator K. Our main purpose here is to show the following proposition.

Proposition 4.4.1. *Suppose that $\rho(K) > 1$. Then operator Φ has at least one nontrivial fixed point $\lambda^* = \Phi(\lambda^*) \in X_{T,+} \setminus \{0\}$.*

For the proof of this proposition, we prepare two lemmas. The first one is as follows.

Lemma 4.4.1. *The operator Φ is monotone nondecreasing on X_T and $\Phi(\varphi)$, $\varphi \in X_{T,+}$ is uniformly bounded.*

Proof. From (4.4.5), we have

$$\begin{aligned} \Phi(\varphi)(t,a) &= \int_0^\omega \beta(t,a,\sigma) \int_0^\sigma \{\varphi(t-\tau,\sigma-\tau) + \gamma(t-\tau,\sigma-\tau)\}\, \mathrm{e}^{-\int_0^\tau \varphi(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\,\mathrm{d}\tau\mathrm{d}\sigma \\ &\quad - \int_0^\omega \beta(t,a,\sigma) \int_0^\sigma \gamma(t-\tau,\sigma-\tau)\, \mathrm{e}^{-\int_0^\tau \varphi(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\mathrm{d}\tau\mathrm{d}\sigma \\ &= \int_0^\omega \beta(t,a,\sigma) \left(1 - \mathrm{e}^{-\int_0^\sigma \varphi(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\right)\mathrm{d}\sigma \\ &\quad - \int_0^\omega \beta(t,a,\sigma) \int_0^\sigma \gamma(t-\tau,\sigma-\tau)\, \mathrm{e}^{-\int_0^\tau \varphi(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\mathrm{d}\tau\mathrm{d}\sigma. \end{aligned} \tag{4.4.7}$$

Then Φ is monotone nondecreasing. Moreover, from (4.4.7), we have

$$\Phi(\varphi)(t,a) \leq \int_0^\omega \beta(t,a,\sigma)\,\mathrm{d}\sigma \leq k^+,$$

where $k^+ := \sup k < +\infty$, which is well defined by Assumption 4.2.1. □

Now we make the following techinical assumption, which is needed to ensure compactness of the fixed point operator and its derivative:

Assumption 4.4.1. For the transmission coefficient k, it holds that

$$\lim_{h\to 0}\int_0^T\int_0^\omega |k(t+h,a+h,\sigma)-k(t,a,\sigma)|\,\mathrm{d}a\mathrm{d}t=0 \quad \text{uniformly for} \quad \sigma\in[0,\omega]. \tag{4.4.8}$$

Lemma 4.4.2. *Under the Assumption 4.4.1, if $\rho(K)>0$, it is a positive eigenvalue of K associated with a positive eigenvector $v_0\in X_{T,+}\setminus\{0\}$.*

Proof. First we show that K is regarded as a compact operator on $L^1([0,T]\times[0,\omega]))$. Observe that K is a linear map from X_T into itself leaving the cone invariant, and we have

$$\begin{aligned}(K\varphi)(t,a) &= \int_0^\omega\int_\tau^\omega \beta(t,a,\sigma)\,\mathrm{e}^{-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\varphi(t-\tau,\sigma-\tau)\,\mathrm{d}\sigma\mathrm{d}\tau\\ &= \int_0^\omega\int_0^{\omega-\tau} \beta(t,a,\tau+x)\,\mathrm{e}^{-\int_0^\tau \gamma(t-\zeta,\tau+x-\zeta)\mathrm{d}\zeta}\varphi(t-\tau,x)\,\mathrm{d}x\mathrm{d}\tau\\ &= \int_{t-\omega}^t\int_0^{\omega-t+s} \beta(t,a,t-s+x)\,\mathrm{e}^{-\int_0^{t-s} \gamma(t-\zeta,t-s+x-\zeta)\mathrm{d}\zeta}\varphi(s,x)\,\mathrm{d}x\mathrm{d}s.\end{aligned} \tag{4.4.9}$$

If we extend the domain of parameter as $\beta(t,a,\sigma)=0$ for $(a,\sigma)\notin[0,\omega]\times[0,\omega]$, we can rewrite (4.4.9) as

$$(K\varphi)(t,a)=\int_{-\infty}^t\int_0^\omega \beta(t,a,t-s+x)\,\mathrm{e}^{-\int_0^{t-s}\gamma(t-\zeta,t-s+x-\zeta)\mathrm{d}\zeta}\varphi(s,x)\,\mathrm{d}x\mathrm{d}s.$$

Note that

$$\int_{-\infty}^t=\int_0^t+\sum_{n=0}^\infty\int_{-(n+1)T}^{-nT},$$

and

$$\begin{aligned}&\int_{-(n+1)T}^{-nT}\int_0^\omega \beta(t,a,t-s+x)\,\mathrm{e}^{-\int_0^{t-s}\gamma(t-\zeta,t-s+x-\zeta)\mathrm{d}\zeta}\varphi(s,x)\,\mathrm{d}x\mathrm{d}s\\ =&\int_0^T\int_0^\omega \beta(t,a,t-s+(n+1)T+x)\,\mathrm{e}^{-\int_0^{t-s+(n+1)T}\gamma(t-\zeta,t-s+(n+1)T+x-\zeta)\mathrm{d}\zeta}\varphi(s-(n+1)T,x)\,\mathrm{d}x\mathrm{d}s\\ =&\int_0^T\int_0^\omega \Psi(t,a,t-s+(n+1)T,x)\,\varphi(s,x)\,\mathrm{d}x\mathrm{d}s,\end{aligned}$$

where Ψ is defined by

$$\Psi(t,a,z,x):=\beta(t,a,z+x)\,\mathrm{e}^{-\int_0^z\gamma(t-\zeta,z+x-\zeta)\mathrm{d}\zeta}. \tag{4.4.10}$$

According to [6], we define

$$\hat{\Psi}(t,a,s,x):=\begin{cases}\displaystyle\sum_{n=0}^\infty \Psi(t,a,t-s+nT,x) & \text{for } t>s,\\ \displaystyle\sum_{n=1}^\infty \Psi(t,a,t-s+nT,x) & \text{for } t<s.\end{cases} \tag{4.4.11}$$

Then $\hat{\Psi}$ is well defined, because the right hand side is a finite sum due to the fact that $\Psi(t,a,z)=0$ for $z>\omega$.

Then it follows from (4.4.9) that

$$(K\varphi)(t,a)=\int_0^T\int_0^\omega \hat{\Psi}(t,a,s,x)\,\varphi(s,x)\,\mathrm{d}x\mathrm{d}s.$$

Hence, we can regard K as an operator on $L^1([0,T]\times[0,\omega])$. From (4.4.8) and the well-known compactness criteria in L^1 (see, for instance, [98], p.275), we see that K is compact. Since K is positive, linear and compact, it follows from the Krein-Rutman theorem ([52]) that if $\rho(K)>0$, it is a positive eigenvalue of K associated with a positive eigenvector $\tilde{v}_0\in L^1_+([0,T]\times[0,\omega])\setminus\{0\}$. That is

$$(K\tilde{v}_0)(t,a)=\rho(K)\,\tilde{v}_0(t,a).$$

Hence, it is easy to see that there exists a periodic eigenvector v_0 in $X_{T,+}\setminus\{0\}$ of K, which is associated with eigenvalue $\rho(K)$ and is the periodization of $\tilde{v}_0$. □

Using the above two lemmas, we prove Proposition 4.4.1.

Proof of Proposition 4.4.1. It follows from Lemma 4.4.2 that for vector $v_0 \in X_{T,+} \setminus \{0\}$ we have

$$(Kv_0)(t,a) = \rho(K) v_0(t,a) = \int_0^T \int_0^\omega \hat{\Psi}(t,a,s,x) v_0(s,x) \,\mathrm{d}x\mathrm{d}s. \tag{4.4.12}$$

Hence, we have

$$\rho(K) v_0(t,a) \le \hat{\Psi}^+ ||v_0||_{X_T}, \tag{4.4.13}$$

where $\hat{\Psi}^+ := \sup \hat{\Psi}(t,a,s,x) < \infty$. Let

$$\lambda_0 := \frac{\rho(K) \log \rho(K)}{\hat{\Psi}^+ \omega} \frac{v_0}{||v_0||_{X_T}} \in X_{T,+} \setminus \{0\}, \tag{4.4.14}$$

whose positivity follows from $\rho(K) > 1$. Then, from (4.4.12)-(4.4.14), we have

$$\begin{aligned}
\Phi(\lambda_0)(t,a) &= \int_0^\omega \int_\tau^\omega \beta(t,a,\sigma) \mathrm{e}^{-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)+\lambda_0(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta} \lambda_0(t-\tau,\sigma-\tau) \,\mathrm{d}\sigma\mathrm{d}\tau \\
&\ge \int_0^\omega \int_\tau^\omega \mathrm{e}^{-\int_0^\omega \lambda_0(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta} \beta(t,a,\sigma) \mathrm{e}^{-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta} \lambda_0(t-\tau,\sigma-\tau) \,\mathrm{d}\sigma\mathrm{d}\tau \\
&= \int_0^\omega \int_\tau^\omega \mathrm{e}^{-\frac{\log\rho(K)}{\hat{\Psi}^+\omega||v_0||_{X_T}} \int_0^\omega \rho(K) v_0(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta} \beta(t,a,\sigma) \mathrm{e}^{-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta} \lambda_0(t-\tau,\sigma-\tau) \,\mathrm{d}\sigma\mathrm{d}\tau \\
&\ge \mathrm{e}^{-\log\rho(K)} (K\lambda_0)(t,a) \\
&= \lambda_0(t,a).
\end{aligned}$$

Hence, from the monotonicity of operator Φ proved in Lemma 4.4.1, we can define a monotone sequence as

$$\lambda_n = \Phi(\lambda_{n-1}), \quad \lambda_0 \le \lambda_1 \le \cdots \le \lambda_n \le \cdots.$$

From Lemma 4.4.1 we see that λ_n is bounded above. Therefore, it follows from B. Levi's theorem that there exists $\lambda^* \in X_{T,+} \setminus \{0\}$ such that $\lim_{n\to\infty} \lambda_n = \lambda^*$ and $\lambda^* = \Phi(\lambda^*)$. □

From Proposition 4.4.1 and the arguments stated in the above, we immediately have the following proposition:

Proposition 4.4.2. *Suppose that $\rho(K) > 1$. Then, system (4.2.5) has at least one endemic T-periodic weak solution.*

4.5 Uniqueness of an endemic periodic solution

Next we investigate the uniqueness of endemic T-periodic solution. For our purpose, we add the following assumptions:

Assumption 4.5.1. There exists a positive number $\varepsilon > 0$ such that $k(t,a,\sigma) \ge \varepsilon$ for all $(t,a,\sigma) \in \mathbb{R} \times \mathbb{R}_+ \times \mathbb{R}_+$.

Biologically speaking, we assume that transmission can occur between every susceptibles and infecteds. In order to prove the uniqueness result, we prepare a following lemma:

Lemma 4.5.1. *If an endemic T-periodic solution $i^* \in \Omega_T \setminus \{0\}$ satisfying (4.4.2) exists, there exist numbers $0 < \alpha_1 = \alpha_1(i^*) < \alpha_2 = \alpha_2(i^*)$ such that $\alpha_1 \le \lambda^* \le \alpha_2$ for the force of infection λ^* corresponding to i^*.*

Proof. Let i^* be a periodic solution of (4.4.2). Observe that

$$\varepsilon V(t) \le \lambda^*(t,a) \le k^+ V(t).$$

where

$$V(t) := \int_0^\omega \theta(t,a) i^*(t,a) da.$$

Then $V(t)$ is the prevalence (proportion of infecteds) at time t, and it is clear $0 \le V \le 1$. To complete our proof, it is sufficient to show $\inf_{t\in\mathbb{R}} V(t) > 0$. Without loss of generality, we can assume that $V(t)$ is a positive, continuous periodic function, since

$$V(t) = \frac{1}{N(t)} \int_0^\omega I^*(t,a) da,$$

where $I^*(t,a) = P^*(t,a) i^*(t,a)$ is a periodic solution of the original system. Then its global minimum is nonnegative. If there exists a time t_0 such that $V(t_0) = 0$, then $i^*(t_0,a) = 0$ for almost all $a \in [0,\omega]$, which implies that $i^*(t,a) = 0$ for all $t \ge t_0$ by the uniqueness of solution. This is a contradiction, so the global minimum of $V(t)$ is positive. □

Lemma 4.5.2. *Let λ^* be the force of infection corresponding to a periodic endemic classical solution i^*. For a number $\kappa \in (0,1)$, there exists a positive number $\eta(i^*) > 0$ such that*

$$\Phi(\kappa\lambda^*)(t,a) \ge \kappa\Phi(\lambda^*)(t,a) + \eta. \tag{4.5.1}$$

Proof. From equation (4.4.5), we have

$$\begin{aligned}
\Phi(\kappa\lambda^*)(t,a) - \kappa\Phi(\lambda^*)(t,a) &= \int_0^\omega \int_\tau^\omega \beta(t,a,\sigma) e^{-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)d\zeta} \kappa\lambda^*(t-\tau,\sigma-\tau) e^{-\int_0^\tau \lambda^*(t-\zeta,\sigma-\zeta)d\zeta} \\
&\quad \times \left(e^{(1-\kappa)\int_0^\tau \lambda^*(t-\zeta,\sigma-\zeta)d\zeta} - 1 \right) d\sigma d\tau \\
&\ge \varepsilon\kappa\alpha_1(i^*) \int_0^\omega d\sigma\theta(t,\sigma) \int_0^\sigma e^{-(\gamma^+ + \alpha_2)\tau} \left(e^{(1-\kappa)\alpha_1\tau} - 1 \right) d\tau,
\end{aligned}$$

where $\gamma^+ := \sup\gamma < \infty$. Then if we define

$$\eta := \varepsilon\kappa\alpha_1(i^*) \int_0^\omega d\sigma\theta(t,\sigma) \int_0^\sigma e^{-(\gamma^+ + \alpha_2)\tau} \left(e^{(1-\kappa)\alpha_1\tau} - 1 \right) d\tau,$$

then $\eta = \eta(i^*)$ is positive. This completes our proof. □

Proposition 4.5.1. *The basic system (4.2.1) has at most one endemic T-periodic classical solution.*

Proof. Suppose that there exist two endemic periodic classical solution. Let λ_1^* and λ_2^* be corresponding force of infections. From the above lemma, there exist positive numbers $\alpha_{jk} = \alpha_{jk}(i_j^*)$, $(j,k = 1,2)$ such that

$$0 < \alpha_{j1} \le \lambda_j^*(t,a) \le \alpha_{j2}, \quad j = 1,2. \tag{4.5.2}$$

From inequality (4.5.2) we have

$$\lambda_1^* \ge \alpha_{11} = \alpha_{11}\alpha_{22}^{-1}\alpha_{22} \ge \alpha_{11}\alpha_{22}^{-1}\lambda_2^*. \tag{4.5.3}$$

Let $\kappa := \inf\{\eta : \lambda_1^* \ge \eta\lambda_2^*\}$. Then $\kappa > 0$ follows from inequality (4.5.3). Suppose that $\kappa < 1$. Then it follows from the above lemma that there exist positive numbers η_1 and η_2 such that

$$\Phi(\kappa\lambda_j^*) \ge \kappa\Phi(\lambda_j^*)(t,a) + \eta_j, \quad j = 1,2.$$

Therefore, from Lemma 4.4.1 and the fact that $\lambda_j^* = \Phi(\lambda_j^*)$, $(j = 1,2)$, we have

$$\lambda_1^* = \Phi(\lambda_1^*) \ge \Phi(\kappa\lambda_2^*) \ge \kappa\Phi(\lambda_2^*) + \eta_2 = \kappa\lambda_2^* + \eta_2\alpha_{22}^{-1}\alpha_{22} \ge \kappa\lambda_2^* + \eta_2\alpha_{22}^{-1}\lambda_2^* = \left(\kappa + \eta_2\alpha_{22}^{-1}\right)\lambda_2^*,$$

which contradicts the definition of κ. Thus, we have $\kappa \ge 1$ and $\lambda_1^* \ge \kappa\lambda_2^* \ge \lambda_2^*$. Exchanging the role of λ_1^* and λ_2^*, we can prove $\lambda_2^* \ge \lambda_1^*$. Therefore, $\lambda_1^* = \lambda_2^*$ and hence $i_1^* = i_2^*$. □

4.6 Global stability of the disease-free steady state

In this section, we investigate the case where $\rho(K) < 1$. First it is easy to see that under the subcritical condition $\rho(K) < 1$, system (4.2.5) does not have any endemic T-periodic solutions. In fact, if we assume that there exists an endemic T-periodic solution $i^* \in \Omega_T \setminus \{0\}$. Then we see that operator Φ has a nontrivial fixed point $\lambda^* = \Phi(\lambda^*) \in X_+ \setminus \{0\}$. Then we have $\lambda^* = \Phi(\lambda^*) \leq K\lambda^*$, which implies $\rho(K) \geq 1$.

As is shown in Theorem 5.6 of [59], we can expect that if system (4.2.5) does not have any endemic T-periodic solutions in $\Omega_T \setminus \{0\}$, then the disease-free steady state $i^* \equiv 0$ of system (4.2.5) is globally asymptotically stable in region Ω_T. In fact, we have the following proposition.

Proposition 4.6.1. *Suppose that $\rho(K) < 1$. Then, the disease-free state $i^* \equiv 0$ of system (4.2.5) is globally asymptotically stable.*

Proof. Instead of (4.2.5), let us consider a linear system as

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right) y(t,a) = -\gamma(t,a)y(t,a) + \int_0^\omega \beta(t,a,\sigma)y(t,\sigma)d\sigma,$$
$$y(t,0) = 0, \quad y(0,a) = i_0(a).$$

Then it is easy to see that $0 \leq i(t,a) \leq y(t,a)$. Integrating along the characteristic line, we obtain an expression:

$$y(t,a) = \begin{cases} \int_0^a \mathrm{e}^{-\int_\sigma^a \gamma(t-a+z,z)dz} B(t-a+\sigma,\sigma)d\sigma, & t-a>0, \\ \mathrm{e}^{-\int_0^t \gamma(\sigma,a-t+\sigma)d\sigma} i_0(a-t) + \int_0^t \mathrm{e}^{-\int_\sigma^t \gamma(z,a-t+z)dz} B(\sigma,a-t+\sigma)d\sigma, & a-t>0. \end{cases}$$

where

$$B(t,a) := \int_0^\omega \beta(t,a,\sigma)y(t,\sigma)d\sigma,$$

is the density of newly infecteds in the linear phase of the normalized system. Inserting the above expression of y into the definition of B and changing the oreder of integrals, we have a renewal equation:

$$B(t,a) = G(t,a) + \int_0^t d\eta \int_\eta^\omega \beta(t,a,\sigma)\mathrm{e}^{-\int_0^\eta \gamma(t-x,\sigma-x)dx} B(t-\eta,\sigma-\eta)d\sigma,$$

where

$$G(t,a) := \int_t^\omega \beta(t,a,\sigma)\mathrm{e}^{-\int_0^t \gamma(z,\sigma-t+z)dz} i_0(\sigma-t)d\sigma, \quad 0<t<\omega,$$

and $G = 0$ for $t > \omega$. Define a time-periodic operator Ψ acting on $L^1(0,\omega)$ as

$$(\Psi(t,\eta)f)(a) := \int_\eta^\omega \beta(t,a,\sigma)\mathrm{e}^{-\int_0^\eta \gamma(t-x,\sigma-x)dx} f(\sigma-\eta)d\sigma,$$

we arrive at an abstract renewal equation for L^1-valued functions:

$$B(t) = G(t) + \int_0^t \Psi(t,\eta)B(t-\eta)d\eta,$$

where $B(t) = B(t,\cdot) \in L^1$, etc. Then we note that the operator K on X_T is expressed as

$$(K\varphi)(t,a) = \int_0^\omega (\Psi(t,\eta)\varphi(t-\eta,\cdot))(a)d\eta, \quad \varphi \in X_T,$$

which is a kind of next generation operator introduced by Bacaër and Guernaoui ([5]). Let us introduse a Laplace transform of Ψ by

$$(\hat{K}(z)\varphi)(t,a) := \int_0^\omega (\mathrm{e}^{-z\eta}\Psi(t,\eta)\varphi(t-\eta,\cdot))(a)d\eta.$$

Using the periodic renewal theorem ([85], [45], [46]), we can conclude that there exists a periodic (vector-valued) function $\varphi_0(t)$ such that $B(t) \sim \mathrm{e}^{r_0 t}\varphi_0(t)$ as $t \to \infty$, where φ_0 is a positive eigenfunction of $\hat{K}(r_0)$ associated with eigenvalue $\rho(K(r_0)) = 1$. Therefore if $\rho(K) = \rho(K(0)) < 1$, the Malthusian parameter r_0 is negative, we have $\lim_{t\to\infty} B(t) = 0$. Therefore we have $\lim_{t\to\infty} y(t,a) = \lim_{t\to\infty} i(t,a) = 0$, which shows the global asymptotic stability of the disease-free state. □

4.7 The basic reproduction number $\mathscr{R}_0$

Here let us introduce the *basic reproduction number* $\mathscr{R}_0$ for the periodic SIS epidemic system (4.2.1) to discuss the relation between $\mathscr{R}_0$ and the threshold parameter $\rho(K)$. Originally, the basic reproduction number is defined as the average number of secondary cases produced by a typical infected individual, introduced into a completely susceptible host population, during its entire period of infectiousness. In this definition, the host population is assumed to be in a demographic steady state ([18], [19]).

Recently, the definition of the basic reproduction number has been extended so that it can be applied to the case of time periodic environments ([5], [6], [45], [46]). However, even in this extended definition for periodic environments, the Malthusian parameter of the host susceptible population is assumed to be zero.

If the Malthusian parameter of host susceptible population is not zero, we have to distinguish two cases of the growth of infected population, absolute growth and relative growth. Based on the general theory of $\mathscr{R}_0$ in a time-heterogeneous environment ([46]), we can calculate the basic reproduction number for a small group of infecteds invading into a growing susceptible population. However, the ratio of infecteds to the total population can go to zero if the growth rate of infecteds is less than the Malthusian parameter of the total population (relative eradication). Therefore we can define another threshold parameter which determines whether the ratio of infecteds can increase or not.

First let us introduce the basic reproduction number $\mathscr{R}_0$ as a threshold value for absolute growth of infected population. Let $y(t,a)$ be a perturbation from the disease-free persistent solution $(P^*(t,a),0)$ of (4.2.1). Then the linearized system around the persistent solution is written as

$$\begin{aligned}\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right)y(t,a) &= v(t,a)-(\mu(t,a)+\gamma(t,a))y(t,a),\\ v(t,a) &= \int_0^\omega \theta(t,a)k(t,a,\sigma)y(t,\sigma)\mathrm{d}\sigma,\end{aligned} \tag{4.7.1}$$

where $v(t,a)$ denotes the density of newly infected individuals in the linear invasion phase.

Integrating the first equation of the linearized system (4.7.1) along the characteristic lines, we have

$$y(t,a)=\int_0^a v(t-a+\sigma,\sigma)\,\mathrm{e}^{-\int_\sigma^a[\mu(t-a+\eta,\eta)+\gamma(t-a+\eta,\eta)]\mathrm{d}\eta}\mathrm{d}\sigma. \tag{4.7.2}$$

Substituting (4.7.2) into the second equation of (4.7.1), we have

$$\begin{aligned}v(t,a) &= \int_0^\omega \theta(t,a)k(t,a,\sigma)\int_0^\sigma v(t-\sigma+\rho,\rho)\mathrm{e}^{-\int_\rho^\sigma[\mu(t-\sigma+\eta,\eta)+\gamma(t-\sigma+\eta,\eta)]\mathrm{d}\eta}\mathrm{d}\rho\mathrm{d}\sigma\\ &= \int_0^\omega\int_\tau^\omega \theta(t,a)k(t,a,\sigma)\,v(t-\tau,\sigma-\tau)\mathrm{e}^{-\int_0^\tau[\mu(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)]\mathrm{d}\zeta}\mathrm{d}\sigma\mathrm{d}\tau\\ &= \int_0^\omega\int_\tau^\omega \theta(t,a)k(t,a,\sigma)\,\mathrm{e}^{-\int_0^\tau[\mu(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}v(t-\tau,\sigma-\tau)\mathrm{d}\sigma\mathrm{d}\tau.\end{aligned} \tag{4.7.3}$$

Let us define linear operator $A(t,\tau)$ from $E=L^1(0,\omega)$ into itself as

$$(A(t,\tau)\varphi)(a):=\int_\tau^\omega \theta(t,a)k(t,a,\sigma)\,\mathrm{e}^{-\int_0^\tau[\mu(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\varphi(\sigma-\tau)\,\mathrm{d}\sigma.$$

Then (4.7.3) can be written as an abstract homogeneous renewal equation:

$$v(t,a)=\int_0^\omega (A(t,\tau)v(t-\tau))(a)\,\mathrm{d}\tau.$$

From the periodic renewal theorem ([85], [45]), $v(t,a)$ is asymptotically proportional to an exponential solution $\mathrm{e}^{r_0 t}w(t)$. The Malthusian parameter r_0 is a real root of the characteristic equation $\rho(\hat{A}(z))=1$, where $\hat{A}(z)$, $z\in\mathbb{C}$ is a linear operator on X_T defined by

$$(\hat{A}(z)\varphi)(t):=\int_0^\omega \mathrm{e}^{-z\tau}A(t,\tau)\varphi(t-\tau)\,\mathrm{d}\tau,$$

and $w \in X_T$ is a positive eigenfunction of $\hat{A}(r_0)$ associated with the positive eigenvalue unity. Therefore the sign relation $\mathrm{sign}(r_0) = \mathrm{sign}(\rho(\hat{A}(0)) - 1)$ holds.

Based on the above observation, $\mathscr{R}_0$ in a periodic environment is defined by the spectral radius of the next generation operator, denoted by K_T, on the space of periodic vector-valued functions X_T ([5, 45]):

$$(K_T\varphi)(t) := (\hat{A}(0)\varphi)(t) = \int_0^\omega A(t,\tau)\varphi(t-\tau)\,\mathrm{d}\tau, \quad \varphi \in X_T.$$

We know that K_T is a positive operator from $X_{T,+}$ into itself:

$$(K_T\varphi)(t,a) = \theta(t,a)\int_0^\omega \int_\tau^\omega k(t,a,\sigma)\mathrm{e}^{-\int_0^\tau [\mu(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)]\mathrm{d}\zeta}\varphi(t-\tau,\sigma-\tau)\,\mathrm{d}\sigma\mathrm{d}\tau. \tag{4.7.4}$$

As is shown in [46], $\mathscr{R}_0 = \rho(K_T)$ gives the asymptotic per generation growth factor of infected population. Now we can establish a following relation between $\mathscr{R}_0 = \rho(K_T)$ and $\rho(K)$:

Proposition 4.7.1. *Suppose that K_T and K are compact positive operators. Then it holds that $\mathscr{R}_0 \geq \rho(K)$ if $r > 0$, $\mathscr{R}_0 = \rho(K)$ if $r = 0$ and $\mathscr{R}_0 \leq \rho(K)$ if $r < 0$.*

Proof. Define a formal multiplication operator $L : \psi \to q\psi$ on X_T, where $q \in X_T$ is given by

$$q(t,a) := \mathrm{e}^{-rt}P^*(t,a) = \mathrm{e}^{-ra}b(t-a)\mathrm{e}^{-\int_0^a \mu(t-\zeta,a-\zeta)d\zeta}.$$

Then we have

$$((K_TL)\psi)(t,a) = \frac{P^*(t,a)}{N(t)}\int_0^\omega \int_\tau^\omega k(t,a,\sigma)\mathrm{e}^{-\int_0^\tau [\mu(t-\zeta,\sigma-\zeta)+\gamma(t-\zeta,\sigma-\zeta)]\mathrm{d}\zeta}q(t-\tau,\sigma-\tau)\psi(t-\tau,\sigma-\tau)\mathrm{d}\sigma\mathrm{d}\tau,$$

where we can observe that

$$q(t-\tau,\sigma-\tau) = \mathrm{e}^{-r(t-\tau)}P^*(t,\sigma)\mathrm{e}^{\int_0^\tau \mu(t-\zeta,\sigma-\zeta)d\zeta}.$$

Therefore we obtain a formal relation that

$$((K_TL)\psi)(t,a) = q(t,a)\int_0^\omega \int_\tau^\omega k(t,a,\sigma)\mathrm{e}^{r\tau-\int_0^\tau \gamma(t-\zeta,\sigma-\zeta)\mathrm{d}\zeta}\frac{P^*(t,\sigma)}{N(t)}\psi(t-\tau,\sigma-\tau)\mathrm{d}\sigma\mathrm{d}\tau.$$

Therefore we have $L^{-1}K_TL > K$ if $r > 0$, $L^{-1}K_TL = K$ if $r = 0$ and $L^{-1}K_TL < K$ if $r < 0$. Since $\rho(L^{-1}K_TL) = \rho(K_T) = \mathscr{R}_0$, we arrive at the conclusion. □

Note that if K and K_T are semi-nonsupporting compact operators, we can apply the comparison theorem by Marek ([71]) to obtain a more sharpe sign relation as

$$\mathrm{sign}(r) = \mathrm{sign}(\mathscr{R}_0 - \rho(K)).$$

If $r = 0$, that is, the Malthusian parameter of the host susceptible population is zero, the threshold value $\rho(K)$ coincides with the basic reproduction number $\mathscr{R}_0$, so we do not need to distinguish absolute growth and relative growth (in the normalized system) of infected population, and we obtain an endemic threshold result that there exists a unique periodic endemic state if $\mathscr{R}_0 > 1$, while the disease-free periodic state is globally stable if $\mathscr{R}_0 < 1$. As is mentioned above, if $r > 0$, there is a possibility that $\rho(K_T) > 1 > \rho(K)$. In this case, the size of infected population increases, but the proportion of infected population to the total population decrease. On the other hand, if $r < 0$ and $\rho(K_T) < 1 < \rho(K)$, the proportion of infected population can increase, although the size of infecteds decreases.

4.8 Numerical examples

In this section, providing some numerical examples, we verify the validity of our results obtained in the previous sections. To simplify, we consider the case where parameters $f(t,a) \equiv f(a)$ and $\mu(t,a) \equiv \mu(a)$ are only age-dependent, $\gamma(t,a) \equiv \gamma$ is constant and $k(t,a) \equiv k(t)$ is only time-periodic.

4.8.1 Calculation of threshold values

In the case of time-independent and age-dependent vital rates $f(a)$ and $\mu(a)$, from the strong ergodicity theorem (see, e.g., [35, 37]), we have

$$\theta(t,a) \equiv \frac{\mathrm{e}^{-ra}\mathrm{e}^{-\int_0^a \mu(\rho)\mathrm{d}\rho}}{\int_0^\omega \mathrm{e}^{-ra}\mathrm{e}^{-\int_0^a \mu(\rho)\mathrm{d}\rho}\mathrm{d}a} =: \theta(a),$$

where r denotes the Malthusian parameter as in the previous sections. Hence, operators K and K_T are given by

$$(K\varphi)(t,a) = k(t)\int_0^\omega \int_\tau^\omega \theta(\sigma)\mathrm{e}^{-\gamma\tau}\varphi(t-\tau,\sigma-\tau)\mathrm{d}\sigma\mathrm{d}\tau \tag{4.8.1}$$

and

$$(K_T\varphi)(t,a) = k(t)\theta(a)\int_0^\omega \int_\tau^\omega \mathrm{e}^{-\int_0^\tau \mu(\sigma-\zeta)\mathrm{d}\zeta-\gamma\tau}\varphi(t-\tau,\sigma-\tau)\mathrm{d}\sigma\mathrm{d}\tau, \tag{4.8.2}$$

respectively, where $\varphi \in X_T$. Since the right-hand side of (4.8.1) is independent of a, the spectral radius $\rho(K)$ is obtained by solving the eigenvalue problem

$$\rho(K)v(t) = k(t)\int_0^\omega \phi_1(\tau)v(t-\tau)\mathrm{d}\tau, \quad v \in X_T, \tag{4.8.3}$$

where

$$\phi_1(\tau) := \int_\tau^\omega \theta(\sigma)\mathrm{d}\sigma\,\mathrm{e}^{-\gamma\tau}. \tag{4.8.4}$$

Moreover, since

$$(K_T v\theta)(t,a) = k(t)\theta(a)\int_0^\omega \left(\int_\tau^\omega \theta(\sigma-\tau)\mathrm{e}^{-\int_0^\tau \mu(\sigma-\zeta)\mathrm{d}\zeta}\mathrm{d}\sigma\right)\mathrm{e}^{-\gamma\tau}v(t-\tau)\mathrm{d}\tau,$$

we see that the basic reproduction number $\mathscr{R}_0 = \rho(K_T)$ is obtained by solving the eigenvalue problem

$$\mathscr{R}_0 v(t) = k(t)\int_0^\omega \phi_2(\tau)v(t-\tau)\mathrm{d}\tau, \quad v \in X_T, \tag{4.8.5}$$

where

$$\begin{aligned}
\phi_2(\tau) &:= \int_\tau^\omega \theta(\sigma-\tau)\mathrm{e}^{-\int_0^\tau \mu(\sigma-\zeta)\mathrm{d}\zeta}\mathrm{d}\sigma\,\mathrm{e}^{-\gamma\tau} \\
&= \int_\tau^\omega \frac{\mathrm{e}^{-r(\sigma-\tau)}\mathrm{e}^{-\int_0^{\sigma-\tau}\mu(\rho)\mathrm{d}\rho}}{\int_0^\omega \mathrm{e}^{-ra}\mathrm{e}^{-\int_0^a \mu(\rho)\mathrm{d}\rho}\mathrm{d}a}\mathrm{e}^{-\int_{\sigma-\tau}^\sigma \mu(\rho)\mathrm{d}\rho}\mathrm{d}\sigma\,\mathrm{e}^{-\gamma\tau} \\
&= \int_\tau^\omega \theta(\sigma)\mathrm{d}\sigma\,\mathrm{e}^{(r-\gamma)\tau}.
\end{aligned} \tag{4.8.6}$$

In what follows we consider the transmission coefficient with form $k(t) = p\{1+q\cos(2\pi t/T)\}$, where $p > 0$, $0 < q < 1$ and $T > 0$. Thus, using the method of [7], we can compute $\rho(K)$ as the largest real root of

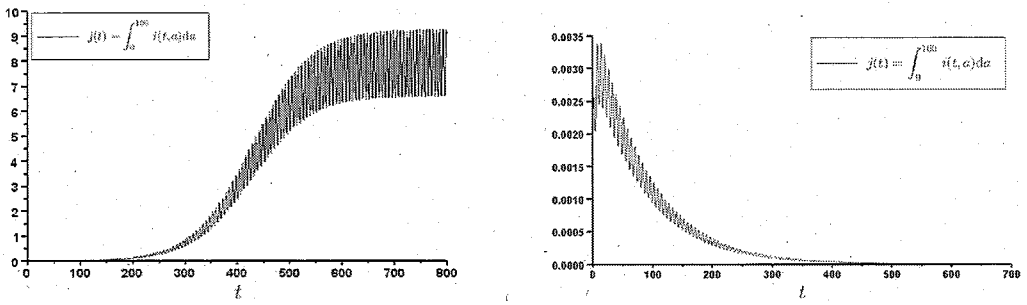
$$\frac{\rho(K)}{\phi_{1,0}} - 1 = 2\mathrm{Re}\cfrac{q^2/4}{\cfrac{\rho(K)}{\phi_{1,1}} - 1 - \cfrac{q^2/4}{\cfrac{\rho(K)}{\phi_{1,2}} - 1 - \cfrac{q^2/4}{\cdots}}},$$

where

$$\phi_{1,n} := p\int_0^\omega \phi_1(\tau)\mathrm{e}^{-i\frac{2\pi}{T}n\tau}\mathrm{d}\tau, \quad n = 0,1,2,\cdots,$$

and $\mathscr{R}_0$ as the largest real root of

$$\frac{\mathscr{R}_0}{\phi_{2,0}} - 1 = 2\mathrm{Re}\cfrac{q^2/4}{\cfrac{\mathscr{R}_0}{\phi_{2,1}} - 1 - \cfrac{q^2/4}{\cfrac{\mathscr{R}_0}{\phi_{2,2}} - 1 - \cfrac{q^2/4}{\cdots}}},$$



(a) Total infected population $j(t) = \int_0^{100} i(t,a)\,da$ versus time t for $\mathscr{R}_0 \simeq \rho(K) \simeq 1.07921 > 1$

(b) Total infected population $j(t) = \int_0^{100} i(t,a)\,da$ versus time t for $\mathscr{R}_0 \simeq \rho(K) \simeq 0.949708 < 1$

Figure 4.2: Solution behavior of $j(t) = \int_0^{100} i(t,a)\,da$ for $\mathscr{R}_0 \simeq \rho(K) \simeq 1.07921 > 1$ (left) and $\mathscr{R}_0 \simeq \rho(K) \simeq 0.949708 < 1$ (right)

where

$$\phi_{2,n} := p\int_0^{\omega} \phi_2(\tau)\,\mathrm{e}^{-i\frac{2\pi}{7}n\tau}\mathrm{d}\tau, \quad n = 0,1,2,\cdots.$$

As in [7], both of them are easily obtained by using the backward iterative algorithm

$$z_n := \frac{x_i}{\phi_{i,n}} - 1, \quad z_{k-1} := \frac{x_i}{\phi_{i,k-1}} - 1 - \frac{q^2/4}{z_k}, \quad i = 1,2, \quad k = n, n-1, \cdots, 2,$$

where $x_1 = \rho(K)$ and $x_2 = \mathscr{R}_0$. From (4.8.4) and (4.8.6), we see that if $r = 0$, then $\phi_1(\tau) = \phi_2(\tau)$ and hence $\rho(K) = \mathscr{R}_0$. This coincides with the statement of Proposition 4.7.1.

4.8.2 Case $r = 0$

In what follows, we fix $\mu(a) = (a-30)^2 \times 10^{-4}$, $\gamma = 0.2$, $\omega = 100$ and vary $f(a)$ and $k(t)$. First we set

$$f(a) = \begin{cases} \dfrac{1}{6.09923}\sin^2\left(\dfrac{a-15}{30}\pi\right), & a \in [15,45], \\ 0, & \text{otherwise} \end{cases}$$

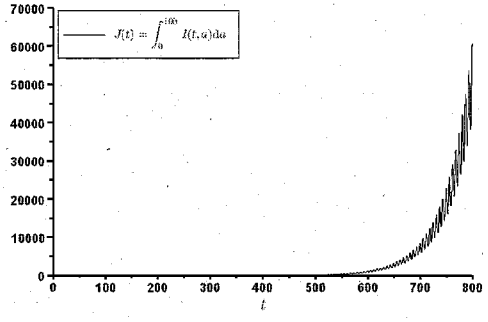
and $k(t) = 0.25(1 + 0.8\cos t)$. In this case, we have $r \simeq 0$ and $\phi_{1,0} \simeq \phi_{2,0} \simeq 1.07885$ and $\mathscr{R}_0 \simeq \rho(K) \simeq 1.07921 > 1$. From Propositions 4.4.2 and 4.5.1, we can expect that system (4.2.5) has a unique periodic solution with period 2π. In fact, (a) of Figure 4.2 exhibits a solution $j(t,a) = \int_0^{100} i(t,a)\,da$ converging to a periodic solution.

Next we change $k(t)$ to $0.22(1 + 0.8\cos t)$. In this case, we have $\phi_{1,0} \simeq \phi_{2,0} \simeq 0.949388$ and $\mathscr{R}_0 \simeq \rho(K) \simeq 0.949708 < 1$. Hence, from Proposition 4.6.1 we can expect that the disease-free steady state of system (4.2.5) is globally asymptotically stable. In fact, (b) of Figure 4.2 exhibits a solution $j(t,a) = \int_0^{100} i(t,a)\,da$ converging to the disease-free steady state 0.

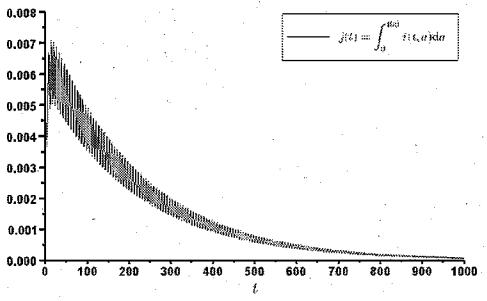
4.8.3 Case $r > 0$

Next we change $k(t)$ to $0.25(1 + 0.8\cos t)$ and $f(a)$ to

$$f(a) = \begin{cases} \dfrac{1}{3}\sin^2\left(\dfrac{a-15}{30}\pi\right), & a \in [15,45], \\ 0, & \text{otherwise.} \end{cases}$$

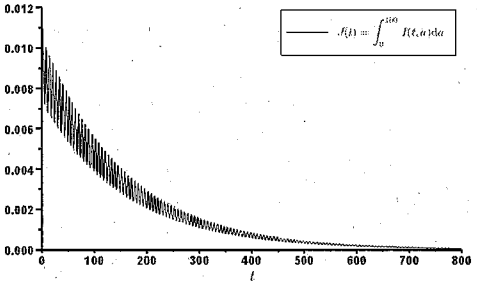


(a) $J(t) = \int_0^{100} I(t,a)\,da$ versus time t for $\mathscr{R}_0 \simeq 1.08716 > 1$

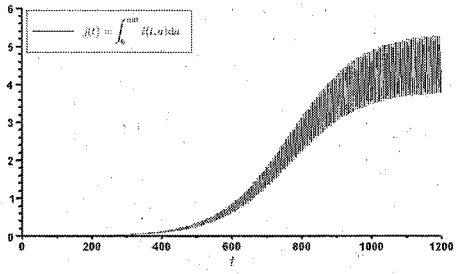


(b) $j(t) = \int_0^{\infty} i(t,a)\,da$ versus time t for $\rho(K) \simeq 0.982352 < 1$

Figure 4.3: Behavior of absolutely growing (a) but relatively decaying (b) infected population for $r \simeq 0.0239891 > 0$, $\mathscr{R}_0 \simeq 1.08716 > 1$ and $\rho(K) \simeq 0.982352 < 1$



(a) $J(t) = \int_0^{100} I(t,a)\,da$ versus time t for $\mathscr{R}_0 \simeq 0.973365 < 1$



(b) $j(t) = \int_0^{\infty} i(t,a)\,da$ versus time t for $\rho(K) \simeq 1.04627 > 1$

Figure 4.4: Behavior of absolutely decaying (a) but relatively growing (b) infected population for $r = -0.016387 < 0$, $\mathscr{R}_0 \simeq 0.973365 < 1$ and $\rho(K) \simeq 1.04627 > 1$

In this case, we have $r \simeq 0.0239891 > 0$. Hence, from Proposition 4.7.1, we can expect that $\mathscr{R}_0 > \rho(K)$. In fact, in this case, we have $\phi_{1,0} \simeq 1.0865 > 0.981739 \simeq \phi_{2,0}$ and $\mathscr{R}_0 \simeq 1.08716 > 1 > 0.982352 \simeq \rho(K)$. This inequality particularly implies the absolutely increasing but relatively decreasing infected population (see Figure 4.3).

4.8.4 Case $r < 0$

Finally we change $k(t)$ to $0.23(1+0.8\cos t)$ and $f(a)$ to

$$f(a) = \begin{cases} \dfrac{1}{10}\sin^2\left(\dfrac{a-15}{30}\pi\right), & a \in [15,45], \\ 0, & \text{otherwise.} \end{cases}$$

In this case, we have $r \simeq -0.016387 < 0$. Hence, from Proposition 4.7.1, we can expect that $\mathscr{R}_0 < \rho(K)$. In fact, in this case, we have $\phi_{1,0} \simeq 0.973187 < 1.04609 \simeq \phi_{2,0}$ and $\mathscr{R}_0 \simeq 0.973365 < 1 < 1.04627 \simeq \rho(K)$. This inequality particularly implies the absolutely decreasing but relatively increasing infected population (see Figure 4.4).

4.9 Discussion

In this chapter, we have formulated an age-structured SIS epidemic model with periodic parameters, and studied the existence of a threshold value which can determine the asymptotic behavior of the model. We have proven that for normalized system (4.2.5), the spectral radius $\rho(K)$ of the linear operator K plays the role of a threshold for the global asymptotic stability of the disease-free steady state and the existence of a unique endemic periodic solution, that is, if $\rho(K) < 1$, then the disease-free steady state of system (4.2.5) is globally asymptotically stable, while if $\rho(K) > 1$, then system (4.2.5) has a unique endemic T-periodic solution $i^* \neq 0$. This is the first endemic threshold result for age-structured periodic epidemic models based on $\mathscr{R}_0$ defined by Bacaër and Guernaoui.

We strongly believe that not only for SIS epidemic models but also for SIR and SEIR age-structured periodic epidemic models, our method might be applied and so the endemic threshold principle will be established under most general conditions by using $\mathscr{R}_0$ defined by Bacaër and Guernaoui.

On the other hand, the reader should note that Hethcote ([29]) studied the non-structured SIS model with periodic coefficients and showed that the disease-free steady state is globally asymptotically stable in the subcritical case, while there is a unique positive periodic solution in the supercritical case, which is globally asymptotically stable. However, this simple dichotomy is only partially true for periodic SIR models. The global stability may be lost when $\mathscr{R}_0 > 1$ because there may exist subharmonic solutions ([80]). In such a case, the main problem is to understand for which class of models the global stability holds.

For our age-dependent case, the global stability of the endemic periodic solution i^* for $\rho(K) > 1$ has been left as an open problem. The corresponding global stability result obtained in [59] is limited to the case of vertically transmitted diseases (the proportion ε of newborn offspring of infective parents who are themselves infective is positive). This implies that their stability result can not be directly applied to our case. However, on the contrary, if our result can be extended to the case of vertically transmitted diseases, their result may be applied to show the global stability result. This is also a future task.

In section 4.7, we have shown that if the Malthusian parameter r equals to zero, then our threshold value $\rho(K)$ equals to the basic reproduction number $\mathscr{R}_0$, while if it is not, then $\rho(K) \neq \mathscr{R}_0$ and this causes possibilities of the relative growth in the sense of percentage of infecteds, but absolute decay (or, vice versa) of infected population. This fact suggests us that in the situation where we estimate the long-time behavior of infected population using a threshold value, we have to pay attention on the host population growth. For age-dependent, autonomous endemic models, the effect of the host population growth on $\mathscr{R}_0$ was considered in [42], [43] and [44], although $\mathscr{R}_0$ introduced in [42] and [43] was not the basic reproduction number, but the threshold value $\rho(K)$ of the normalized system.

Acknowledgments

The author would like to thank the reviewers for their valuable comments and suggestions to the earlier version of this chapter.

Bibliography

[1] M.E. Alexander, C. Bowman, S.M. Moghadas, R. Summers, A.B. Gunmel, B.M. Sahai, A vaccination model for transmission dynamics of influenza, SIAM J. Appl. Dynam. Syst. 3 (2004) 503–524.

[2] R.M. Anderson, R.M. May, Infectious Diseases of Humans: Dynamics and Control, Oxford University Press, Oxford, 1991.

[3] V. Andreasen, Instability in an SIR-model with age-dependent susceptibility, in O. Arino, D. Axelrod, M. Kimmel, M. Langlais (eds), Mathematical Population Dynamics: Analysis of Heterogeneity, Theory of Epidemics, Wuerz Publ., Winnipeg, 1995, pp. 3–14.

[4] J. Arino, C.C. McCluskey, P. van den Driessche, Global results for an epidemic model with vaccination that exhibits backward bifurcation, SIAM J. Appl. Math. 64 (2003) 260–276.

[5] N. Bacaër, S. Guernaoui, The epidemic threshold of vector-borne disease with seasonality, J. Math. Biol. 53 (2006) 421–436.

[6] N. Bacaër, Approximation of the basic reproduction number R_0 for vector-borne diseases with periodic vector population, Bull. Math. Biol. 69 (2007) 1067–1091.

[7] N. Bacaër, R. Ouifki, Growth rate and basic reproduction number for population models with a simple periodic factor, Math. Biosci. 210 (2007) 647–658.

[8] A. Berman, R.J. Plemmons, Nonnegative Matrices in the Mathematical Sciences, Academic Press, New York, 1979.

[9] N.P. Bhatia, G.P. Szego, Dynamical Systems: Stability Theory and Applications, Springer-Verlag, Berlin, 1967.

[10] J.M. Borwein, P.B. Borwein, Pi and the AGM: A Study in Analytic Number Theory and Computational Complexity, John Wiley and Sons, New York, 1987.

[11] S.N. Busenberg, M. Iannelli, H.R. Thieme, Global behavior of an age-structured epidemic model, SIAM J. Math. Anal. 22 (1991) 1065–1080.

[12] S. Busenberg, K. Cooke, Vertically Transmitted Diseases: Models and Dynamics, Springer, Berlin, 1993.

[13] S.N. Busenberg, M. Iannelli, H.R. Thieme, Dynamics of an age structured epidemic model, in: Dynamical Systems, World Scientific, Singapore, 1993, pp. 1–19.

[14] Y. Cha, M. Iannelli, F.A. Milner, Stability change of an epidemic model, Dynam. Syst. Appl. 9 (2000) 361–376.

[15] L. Chow, M. Fan, Z. Feng, Dynamics of a multigroup epidemiological model with group-targeted vaccination strategies, J. Theoret. Biol. 291 (2011) 56–64.

[16] A.J. Coale, The use of Fourier analysis to express the relation between time variations in fertility and the time sequence of births in a closed human population, Demography 7 (1970) 93–120.

[17] A.J. Coale, The Growth and Structure of Human Populations: A Mathematical Investigation, Princeton UP, Princeton, 1972.

[18] O. Diekmann, J.A.P. Heesterbeek, J.A.J. Metz, On the definition and the computation of the basic reproduction ration R_0 in models for infectious diseases in heterogeneous populations, J. Math. Biol. 28 (1990) 365–382.

[19] O. Diekmann, J.A.P. Heesterbeek, Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation, John Wiley and Sons, Chichester, 2000.

[20] O. Diekmann, J.A.P. Heesterbeek, M.G. Roberts, The construction of next-generation matrices for compartmental epidemic models, J. Royal Soc. Interf. 7 (2010) 873–885.

[21] K. Dietz, D. Schenzle, Proportionate mixing models for age-dependent infection transmission, J. Math. Biol. 22 (1985) 117–120.

[22] D. Ding, X. Ding, Global stability of multi-group vaccination epidemic models with delays, Nonlinear. Analysis RWA. 12 (2011) 1991–1997.

[23] Z. Feng, W. Huang, C. Castillo-Chavez, Global behavior of a multi-group SIS epidemic model with age structure, J. Diff. Equat. 218 (2005) 292–324.

[24] H.I. Freedman, S. Ruan, M. Tang, Uniform persistence and flows near a closed positively invariant set, J. Dynam. Diff. Equat. 6 (1994) 583–600.

[25] G.P. Garnett, R.M. Anderson, Balancing sexual partnerships in an age and activity stratified model of HIV transmission in heterosexual populations, IMA J. Math. Appl. Med. Biol. 11 (1994) 161-192.

[26] D. Greenhalgh, Threshold and stability results for an epidemic model with an age-structured meeting rate, IMA J. Math. Appl. Med. Biol. 5 (1988) 81–100.

[27] H. Guo, M.Y. Li, Z. Shuai, Global stability of the endemic equilibrium of multigroup SIR epidemic models, Canadian Appl. Math. Quart. 14 (2006) 259–284.

[28] H. Guo, M.Y. Li, Z. Shuai, A graph-theoretic approach to the method of global Lyapunov functions, Proc. Amer. Math. Soc. 136 (2008) 2793–2802.

[29] H.W. Hethcote, Asymptotic behavior in a deterministic epidemic model, Bull. Math. Biol. 35 (1973) 607–614.

[30] H.W. Hethcote, An immunization model for a heterogeneous population, Theoret. Population Biol. 14 (1978) 338–349.

[31] H.W. Hethcote, H.R. Thieme, Stability of the endemic equilibrium in epidemic models with subpopulations, Math. Biosci. 75 (1985) 205–227.

[32] H.W. Hethcote, S.A. Levin, Periodicity in epidemiological models, in: S.A. Levin, T.G. Hallam, L.J. Gross (Eds.), Applied Mathematical Ecology, Springer, Berlin, 1989, pp. 193–211.

[33] H.W. Hethcote, The mathematics of infectious diseases, SIAM Review. 42 (2000) 599–653.

[34] M. Iannelli, F.A. Milner, A. Pugliese, Analytical and numerical results for the age-structured SIS epidemic model with mixed inter-intracohort transmission, SIAM J. Math. Anal. 23 (1992) 662–688.

[35] M. Iannelli, Mathematical Theory of Age-structured Population Dynamics, Giardini editori e stampatori, Pisa, 1995.

[36] M. Iannelli, M.Y. Kim, E.J. Park, Asymptotic behavior for an SIS epidemic model and its approximation, Nonlinear Anal. 35 (1999) 797–814.

[37] H. Inaba, A semigroup approach to the strong ergodic theorem of the multistate stable population process, Math. Popul. Studies 1 (1988) 49-77.

[38] H. Inaba, Weak ergodicity of population evolution processes, Math. Biosci. 96 (1989) 195–219.

[39] H. Inaba, Threshold and stability results for an age-structured epidemic model, J. Math. Biol. 28 (1990) 411–434.

[40] H. Inaba, H. Sekine, A mathematical model for Chagas disease with infection-age-dependent infectivity, Math. Biosci. 190 (2004) 39–69.

[41] H. Inaba, Endemic threshold results for age-duration-structured population model for HIV infection, Math. Biosci. 201 (2006) 15–47.

[42] H. Inaba, Mathematical analysis of an age-structured SIR epidemic model with vertical transmission, Discrete Cont. Dyn. Syst. B 6 (2006) 69–96.

[43] H. Inaba, Age-structured homogeneous epidemic systems with application to the MSEIR epidemic model, J. Math. Biol. 54 (2007) 101–146.

[44] H. Inaba, H. Nishiura, The basic reproduction number of an infectious disease in a stable population: The impact of population growth rate on the eradication threshold, Mathematical Modelling of Natural Phenomena 7 (2008) 194–228.

[45] H. Inaba, The Malthusian parameter and R_0 for heterogeneous populations in periodic environments, Math. Biosci. Eng. 9 (2012) 313–346.

[46] H. Inaba, On a new perspective of the basic reproduction number in heterogeneous environments, J. Math. Biol. 65 (2012) 309–348.

[47] S. Iwami, Y. Takeuchi, X. Liu, Avian-human influenza epidemic model, Math. Biosci. 207 (2007) 1–25.

[48] W.O. Kermack, A.G. McKendrick, Contributions to the mathematical theory of epidemics I, Proc. Royal Soc. A 115 (1927) 700–721.

[49] W.O. Kermack, A.G. McKendrick, Contributions to the mathematical theory of epidemics II, The problem of endemicity, Proc. Royal Soc. A 138 (1932) 55–83.

[50] W.O. Kermack, A.G. McKendrick, Contributions to the mathematical theory of epidemics III, Further studies of the problem of endemicity, Proc. Royal Soc. A 141 (1933) 94–122.

[51] D.E. Knuth, The Art of Computer Programming, vol. 1, Addison-Wesley, Reading, 1997.

[52] M.G. Krein, M.A. Rutman, Linear operators leaving invariant a cone in a Banach space, Am. Math. Soc. Transl. 10 (1948) 199–325.

[53] C.M. Kribs-Zaleta, J.X. Velasco-Hernández, A simple vaccination model with multiple endemic states, Math. Biosci. 164 (2000) 183–201.

[54] T. Kuniya, Global stability analysis with a discretization approach for an age-structured multigroup SIR epidemic model, Nonlinear Analysis RWA. 12 (2011) 2640–2655.

[55] T. Kuniya, Y. Nakata, Permanence and extinction for a nonautonomous SEIRS epidemic model, Appl. Math. Comput. 218 (2012) 9321–9331.

[56] T. Kuniya, Global stability of a multi-group SVIR epidemic model, Nonlinear Analysis RWA. 14 (2013) 1135–1143.

[57] S.P. Kusmika Kundu, J. Chattopadhyay, Role of standard incidence in an eco-epidemiological system: A mathematical study, Ecol. Model. 199 (2006) 229–239.

[58] A. Lajmanovich, J.A. Yorke, A deterministic model for gonorrhea in a nonhomogeneous population, Math. Biosci. 28 (1976) 221–236.

[59] M. Langlais, S.N. Busenberg, Global behaviour in age structured S.I.S. models with seasonal periodicities and vertical transmission, J. Math. Anal. Appl. 213 (1997) 511–533.

[60] J.P. Lasalle, The Stability of Dynamical Systems, Regional Conference Series in Applied Mathematics, SIAM, Philadelphia, 1976.

[61] M.Y. Li, J.S. Muldowney, Global stability for the SEIR model in epidemiology, Math. Biosci. 125 (1995) 155–164.

[62] M.Y. Li, J.R. Graef, L. Wang, J. Karsai, Global dynamics of a SEIR model with varying total population size, Math. Biosci. 160 (1999) 191–213.

[63] M.Y. Li, Z. Shuai, C. Wang, Global stability of multi-group epidemic models with distributed delays, J. Math. Anal. Appl. 361 (2010) 38–47.

[64] M.Y. Li, Z. Shuai, Global-stability problem for coupled systems of differential equations on networks, J. Diff. Equat. 248 (2010) 1–20.

[65] J. Li, Y. Yang, Y. Zhou, Global stability of an epidemic model with latent stage and vaccination, Nonlinear Analysis RWA. 12 (2011) 2163–2173.

[66] X. Lin, J.W.H. So, Global stability of the endemic equilibrium and uniform persistence in epidemic models with subpopulations, J. Austral. Math. Soc. Ser. B 34 (1993) 282–295.

[67] W.M. Liu, H.W. Hethcote, S.A. Levin, Dynamical behavior of epidemiological models with nonlinear incidence rates, J. Math. Biol. 25 (1987) 359–380.

[68] X. Liu, Y. Takeuchi, S. Iwami, SVIR epidemic model with vaccination strategies, J. Theoret. Biol. 253 (2008) 1–11.

[69] J. Ma, Z. Ma, Epidemic threshold conditions for seasonally forced SEIR models, Math. Biosci. Eng. 3 (2006) 161–172.

[70] T.R. Malthus, An Essay on the Principle of Population, Joseph Johnson, London, 1798.

[71] I. Marek, Frobenius theory of positive operators: Comparison theorems and applications, SIAM J. Appl. Math. 19 (1970) 607–628.

[72] A.G. McKendrick, Application of mathematics to medical problems, Proc. Edinburgh Math. Soc. 44 (1926) 98–130.

[73] C.E. Mills, J.M. Robins, M. Lipsitch, Transmissibility of 1918 pandemic influenza, Nature 432 (2004) 904–906.

[74] J.W. Moon, Counting Labelled Trees, Canadian Mathematical Congress, Montreal, 1970.

[75] Y. Nakata, T. Kuniya, Global dynamics of a class of SEIRS epidemic models in a periodic environment, J. Math. Anal. Appl. 363 (2010) 230–237.

[76] A. Pazy, Semigroups of Linear Operators and Applications to Partial Differential Equations, Springer, Berlin, 1983.

[77] B. Perthame, Transport Equations in Biology, Birkhäuser, Basel, 2007.

[78] R. Rundnicki, M.C. Mackey, Asymptotic similarity and Malthusian growth in autonomous and nonautonomous populations, J. Math. Anal. Appl. 187 (1994) 548–566.

[79] D. Schenzle, An age-structured model of pre- and post- vaccination measles transmission, IMA J. Math. Appl. Med. Biol. 1 (1984) 169–191.

[80] H.L. Smith, Multiple stable subharmonics for a periodic epidemic model, J. Math. Biol. 17 (1983) 179–190.

[81] H.L. Smith, P. Waltman, The Theory of the Chemostat: Dynamics of Microbial Competition, Cambridge University Press, Cambridge, 1995.

[82] M. Song, W. Ma, Y. Takeuchi, Permanence of a delayed SIR epidemic model with density dependent birth rate, J. Comput. Appl. Math. 201 (2007) 389–394.

[83] C. Sun, Y. Lin, S. Tang, Global stability for an special SEIR epidemic model with nonlinear incidence rates, Chaos Solitons Fractals 33 (2007) 290–297.

[84] R. Sun, Global stability of the endemic equilibrium of multigroup SIR models with nonlinear incidence, Comput. Math. Appl. 60 (2010) 2286–2291.

[85] H.R. Thieme, Renewal theorems for linear periodic Volterra integral equations, J. Int. Equat. 7 (1984) 253–277.

[86] H.R. Thieme, Local stability in epidemic models for heterogeneous populations, in: V. Capasso, E. Grosso, S.L. Paveri-Fontana (eds), Mathematics in Biology and Medicine, Lec. Notes in Biomath. 57, Springer, Berlin, 1985, pp. 185–189.

[87] H.R. Thieme, Stability change of the endemic equilibrium in age-structured models for the spread of S-I-R type infectious diseases, in: S. Busenberg, M. Martelli (eds), Differential Equations Models in Biology, Epidemiology and Ecology, Lec. Notes in Biomath. 92, Springer, Berlin, 1991, pp. 139–158.

[88] H.R. Thieme, Uniform weak implies uniform strong persistence for non-autonomous semiflows, Proc. Amer. Math. Soc. 127 (1999) 2395–2403.

[89] H.R. Thieme, Uniform persistence and permanence for non-autonomous semiflows in population biology, Math. Biosci. 166 (2000) 173–201.

[90] H.R. Thieme, Mathematics in Population Biology, Princeton University Press, Princeton, 2003.

[91] H.R. Thieme, Spectral bound and reproduction number for infinite-dimensional population structure and time heterogeneity, SIAM J. Appl. Math. 70 (2009) 188–211.

[92] D.W. Tudor, An age-dependent epidemic model with application to measles, Math. Biosci. 73 (1985) 131–147.

[93] P. Turchin, Does population ecology have general laws?, Oikos 94 (2000) 17–26.

[94] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002) 29–48.

[95] W. Wang, S. Ruan, Simulating the SARS outbreak in Beijing with limited data, J. Theoret. Biol. 227 (2004) 369–379.

[96] W. Wang, X.Q. Zhao, An epidemic model in a patchy environment, Math. Biosci. 190 (2004) 97–112.

[97] W. Wang, X.Q. Zhao, Threshold dynamics for compartmental epidemic models in periodic environments, J. Dynam. Diff. Equat. 20 (2008) 699–717.

[98] K. Yosida, Functional Analysis, Springer, Berlin, 1980.

[99] Z. Yuan, L. Wang, Global stability of epidemiological models with group mixing and nonlinear incidence rates, Nonlinear Analysis RWA. 11 (2010) 995–1004.

[100] Z. Yuan, X. Zou, Global threshold property in an epidemic models for disease with latency spreading in a heterogeneous host population, Nonlinear Analysis RWA. 11 (2010) 3479–3490.

[101] F. Zhang, X.Q. Zhao, A periodic epidemic model in a patchy environment, J. Math. Anal. Appl. 325 (2007) 496–516.

[102] T. Zhang, Z. Teng, On a nonautonomous SEIRS model in epidemiology, Bull. Math. Biol. 69 (2007) 2537–2559.

[103] T. Zhang, Z. Teng, S. Gao, Threshold conditions for a non-autonomous epidemic model with vaccination, Appl. Anal. 87 (2008) 181–199.