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Mathematical analysis for a multi-group SEIR epidemic model with age-dependent relapse

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We consider a multi-group SEIR epidemic model in which recovered population relapse back to infectives depending on the time elapsed since the recovery. This leads to a hybrid system for which we can determine the basic reproduction number $\Re_0$ by the spectral radius of the next generation matrix and prove the threshold behaviours. The key idea to prove the global asymptotic stability of each equilibrium is the usage of the graph-theoretic approach to construct suitable Lyapunov functionals. The necessary arguments, including the existence of an endemic equilibrium, the asymptotic smoothness of the semi-flow, the uniform persistence of the system and the existence of a global attractor are also addressed.

Keywords: SEIR epidemic model; multi-group model; age-dependent relapse; global asymptotic stability; Lyapunov functional

AMS Subject Classifications: 35Q92; 37N25; 92D30

1. Introduction

In epidemic models, heterogeneity of host population (for example, sex, position, age and so on) plays an important role in transmission of infection, which result from different contact modes (e.g.,measles and mumps) or different behaviors (e.g., herpes and condyloma acuminatum). Taking into account the different contact patterns, or different geography, it is more suitable to divide individual hosts into groups. Recently, multi-group epidemic models have attracted much attention of many authors (see e.g., [6, 7, 11, 14–16, 25, 30–32] and the references therein). The global stability analysis of endemic equilibrium of such models has been studied by a novel approach using the graph theory, see as in [6, 7, 14]. Recently, diseases with latency and relapse have been included in multi-group epidemic models in [11, 30–32].

Age of infection (time elapsed since since infection began) has been included in many epidemic models. These models are usually formulated as hybrid systems of ordinary differential equations and partial differential equations, see, for instance, [16] for a two-group model with infection age; [18] for an SIR epidemic model with infection age; [15, 20] for SEIR epidemic models with infection age; [4] for an SIRS epidemic model with infection age; [2, 29, 35] for infection age models of cholera; [1, 10, 21, 22, 27, 28] for viral infection models; and the references therein). For

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such age of infection models, from the mathematical viewpoint, this leads to the difficulties in analyzing the uniform persistence of the system, the existence of a global attractor, the asymptotic smoothness of the orbit and the local and global asymptotic stability of each equilibrium. A model has been developed by Vargas-De-León [26] to describe a disease (human herpes virus, HSV-1 and HSV-2) with relapse rate of recovered individuals in which depends on asymptomatic-infection-age. They obtained global behavior of solutions by defining the explicit formulas for the basic reproductive number and by constructing Volterra-type Lyapunov functionals.

Introducing age-structure into multi-group epidemic models makes the global stability analysis more difficult. To the best of our knowledge, there are few studies on multi-group SEIR epidemic models with age of infection (see [15] for a single-group SEIR epidemic model with age-dependent latency and relapse). In this study, we assume that recovered individuals can go back to the infectious class because of the relapse of infection. The time until relapse may depend on the heterogeneity of each individual, it is thus of interest to account for duration of relapse as continuous variable and relapse rate depends on the time since recovery. The "age" is defined as the time elapsed since the recovery and we refer this structuring variable as *relapse-age* for short. We assume that the newly recovered individuals enter the recovered class with relapse-age zero.

Our purpose in this paper is to describe a multi-group SEIR epidemic model in which it is assumed that there is an age-structure in the recovered population. Total number of groups is fixed to be n and each group is labeled by subscript $i \in \{1, 2, ..., n\}$. Denote by $S_i(t)$, $E_i(t)$, and $I_i(t)$ the susceptible, exposed and infectious populations in group i at time t, respectively. Let $r_i(t, \omega)$ be the recovered population of relapse-age ω in group i at time t. Then, the total recovered population in group i at time t is given by $R_i(t) = \int_0^{+\infty} r_i(t, \omega)\mathrm{d}\omega$. More precisely, $\int_{\omega_1}^{\omega_2} r_i(t, \omega)\mathrm{d}\omega$ denotes the recovered population between age ω_1 and ω_2 in group i at time t. The relapse rate of the recovered individuals in group i, which is denoted by $\gamma_i(\omega)$, is assumed to depend on the relapse-age ω. The total number of individuals which go back to the infectious class due to the relapse in group i at time t is given by $\int_0^{+\infty} \gamma_i(\omega) r_i(t, \omega)\mathrm{d}\omega$.

Under these assumptions, the model to be studied in this paper is formulated in the following form:

$$\begin{cases} \dfrac{\mathrm{d}S_i(t)}{\mathrm{d}t} = \Lambda_i - \mu_i S_i(t) - \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i(t) I_j(t), \\ \dfrac{\mathrm{d}E_i(t)}{\mathrm{d}t} = \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i(t) I_j(t) - (\mu_i + \sigma_i) E_i(t), \\ \dfrac{\mathrm{d}I_i(t)}{\mathrm{d}t} = \sigma_i E_i(t) - (\mu_i + \kappa_i) I_i(t) + \displaystyle\int_0^{+\infty} \gamma_i(\omega) r_i(t, \omega)\mathrm{d}\omega, \\ \dfrac{\partial r_i(t, \omega)}{\partial t} + \dfrac{\partial r_i(t, \omega)}{\partial \omega} = -(\mu_i + \gamma_i(\omega)) r_i(t, \omega), \\ r_i(t, 0) = \kappa_i I_i(t), \\ S_i(0) = S_{i,0},\ E_i(0) = E_{i,0},\ I_i(0) = I_{i,0},\ r_i(0, \omega) = r_{i,0}(\omega), \quad 1 \le i \le n. \end{cases} \tag{1}$$

The meaning of each parameter is listed as follows:

Λ_i: the constant recruitment into group i;
μ_i: the mortality of individuals in group i;
β_{ij}: the transmission coefficient between susceptible individuals in group i and infectious individuals in group j;

σ_i: the rate of the onset of illness for exposed individuals in group i;
κ_i: the recovery rate for infectious individuals in group i;
$\gamma_i(\cdot)$: the age-dependent relapse rate for recovered individuals in group i.

For these parameters, we make the following assumption.

Assumption 1.1 (i) Λ_i, μ_i, σ_i, and κ_i are positive for all $i \in \{1, 2, \cdots, n\}$.

(ii) $\gamma_i(\cdot)$ is non-negative and bounded with upper bound $\gamma_i^+ \in (0, +\infty)$ for all $i \in \{1, 2, \cdots, n\}$.

(iii) β_{ij} is nonnegative for all $i, j \in \{1, 2, \cdots, n\}$ and n-square matrix $(\beta_{ij})_{1 \le i,j \le n}$ is irreducible [3].

From the point of applications, it is particularly relevant to study the stability and attractivity of a positive endemic equilibrium of system (1), if it exists. We characterize the threshold condition of the system (1) with the basic reproductive number of infection in the sense that it determines the stability of the equilibria. It is easy to see that system (1) always has the disease-free equilibrium $P^0 = (S_1^0, S_2^0, \cdots, S_n^0, 0, \cdots, 0)$, where $S_i^0 = \Lambda_i/\mu_i$, $1 \le i \le n$. Let $P^* = (S_1^*, S_2^*, \cdots, S_n^*, E_1^*, E_2^*, \cdots, E_n^*, I_1^*, I_2^*, \cdots, I_n^*, r_1^*(\omega), r_2^*(\omega), \cdots, r_n^*(\omega))$ be a positive endemic equilibrium of (1). Then, the following algebraic equations hold:

$$\begin{cases} \Lambda_i = \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i^* I_j^* + \mu_i S_i^*, \\ (\mu_i + \sigma_i) E_i^* = \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i^* I_j^*, \\ (\mu_i + \kappa_i) I_i^* = \sigma_i E_i^* + \displaystyle\int_0^{+\infty} \gamma_i(\omega) r_i^*(\omega) \mathrm{d}\omega, \\ \dfrac{\mathrm{d} r_i^*(\omega)}{\mathrm{d}\omega} = -(\mu_i + \gamma_i(\omega)) r_i^*(\omega), \quad r_i^*(0) = \kappa_i I_i^*, \quad 1 \le i \le n. \end{cases} \tag{2}$$

Now, we define the basic reproduction number $\Re_0$, which implies the expected number of secondary cases produced in an entirely susceptible population by a typical infected individual during its entire infectious period [5, 25]. For system (1), we can calculate it as the spectral radius of a nonnegative matrix called the next generation matrix. Let

$$\mathcal{F} = \begin{pmatrix} \beta_{11} S_1^0 & \cdots & \beta_{1n} S_1^0 \\ \vdots & \ddots & \vdots \\ \beta_{n1} S_n^0 & \cdots & \beta_{nn} S_n^0 \end{pmatrix} \quad \text{and} \quad \mathcal{V} = \mathrm{diag}((\mu_i + \kappa_i(1 - \theta_i)) F_i),$$

where

$$\theta_i = \int_0^{+\infty} \gamma_i(\omega) e^{-\int_0^{\omega} (\mu_i + \gamma_i(\sigma)) \mathrm{d}\sigma} \mathrm{d}\omega \quad \text{and} \quad F_i = \frac{\mu_i + \sigma_i}{\sigma_i}, \quad 1 \le i \le n. \tag{3}$$

Note that

$$0 \le \theta_i = \int_0^{+\infty} \gamma_i(\omega) e^{-\int_0^{\omega} (\mu_i + \gamma_i(\sigma)) \mathrm{d}\sigma} \mathrm{d}\omega \le \int_0^{+\infty} \gamma_i(\omega) e^{-\int_0^{\omega} \gamma_i(\sigma) \mathrm{d}\sigma} \mathrm{d}\omega \le 1, \quad 1 \le i \le n.$$

Then, the next generation matrix is given by

$$\mathcal{F}\mathcal{V}^{-1} = \begin{pmatrix} \dfrac{\beta_{11} S_1^0}{(\mu_1 + \kappa_1(1 - \theta_1)) F_1} & \cdots & \dfrac{\beta_{1n} S_1^0}{(\mu_n + \kappa_n(1 - \theta_n)) F_n} \\ \vdots & \ddots & \vdots \\ \dfrac{\beta_{n1} S_n^0}{(\mu_1 + \kappa_1(1 - \theta_1)) F_1} & \cdots & \dfrac{\beta_{nn} S_n^0}{(\mu_n + \kappa_n(1 - \theta_n)) F_n} \end{pmatrix}.$$

Hence, the basic reproduction number of model (1) is defined by the spectral radius of the next generation matrix:

$$\Re_0 = r(\mathcal{F}\mathcal{V}^{-1}), \tag{4}$$

where $r(\cdot)$ denotes the spectral radius of a matrix.

The main theoretical result to be proved in this paper is stated as follows.

THEOREM 1.1 *Let $\Re_0$ be defined by (4).*

(i) If $\Re_0 > 1$, then system (1) *has a unique endemic equilibrium P^* which is globally asymptotically stable;*

(ii) If $\Re_0 \le 1$, then the disease-free equilibrium P^0 is globally asymptotically stable.

The organization of this paper is as follows. In Section 2, we show the existence of the endemic equilibrium P^* when $\Re_0 > 1$ by reformulating (2) into a fixed-point problem. In Section 3, we show the well-posedness of the problem (1) by using the integrated semigroup approach as in Thieme [24]. In Section 4, we prove the asymptotic smoothness of the semi-flow by using the method as in [23, 33, 34]. In Section 5, we prove the the uniform persistence and the existence of a compact global attractor under the condition $\Re_0 > 1$ by using the method of Hale and Waltman [9]. In Section 6, we investigate the global asymptotic stability of each equilibrium and give the proof of Theorem 1.1. In Section 7, we give numerical examples to verify the validity of Theorem 1.1.

2. Existence of the endemic equilibrium

We first introduce the following notations, which will be used throughout the paper:

$$\begin{aligned}
&\mathbf{S} = (S_1, S_2, \cdots, S_n)^T, \quad \mathbf{E} = (E_1, E_2, \cdots, E_n)^T, \quad \mathbf{I} = (I_1, I_2, \cdots, I_n)^T,\\
&\mathbf{r} = (r_1, r_2, \cdots, r_n)^T, \quad \mathbf{\Lambda} = (\Lambda_1, \Lambda_2, \cdots, \Lambda_n)^T, \quad \mathbf{D}(1) = \mathrm{diag}(1, 1, \cdots, 1),\\
&\mathcal{M} = \mathrm{diag}(\mu_1, \mu_2, \cdots, \mu_n), \quad \mathcal{B} = (\beta_{ij})_{n\times n}, \quad \Sigma = \mathrm{diag}(\sigma_1, \sigma_2, \cdots, \sigma_n),\\
&K = \mathrm{diag}(\kappa_1, \kappa_2, \cdots, \kappa_n), \quad \Gamma(\omega) = \mathrm{diag}(\gamma_1(\omega), \gamma_2(\omega), \cdots, \gamma_n(\omega)),
\end{aligned} \tag{5}$$

where T denotes the transpose of a vector.

As stated above, the disease-free equilibrium P^0 of system (1) always exists. To investigate the existence of endemic equilibrium P^*, we rewrite (2) into a fixed-point problem of $\mathbf{I}^* := (I_1^*, I_2^*, \cdots, I_n^*)^T$. It follows from (2) that, for $1 \le i \le n$,

$$S_i^* = \frac{\Lambda_i}{\sum\limits_{j=1}^n \beta_{ij} I_j^* + \mu_i}, \quad E_i^* = \frac{1}{\mu_i + \sigma_i} \frac{\Lambda_i \sum\limits_{j=1}^n \beta_{ij} I_j^*}{\sum\limits_{j=1}^n \beta_{ij} I_j^* + \mu_i}, \quad r_i^*(\omega) = \kappa_i I_i^* e^{-\int_0^\omega (\mu_i + \gamma_i(l))dl}. \tag{6}$$

Hence, from the third equation of (2), we have

$$(\mu_i + \kappa_i) I_i^* = \frac{1}{F_i} \frac{\Lambda_i \sum\limits_{j=1}^n \beta_{ij} I_j^*}{\sum\limits_{j=1}^n \beta_{ij} I_j^* + \mu_i} + \theta_i \kappa_i I_i^*, \quad 1 \le i \le n,$$

where θ_i and F_i are defined as in (3). Hence, we obtain the following equation of

I_i^*:

$$I_i^* = \frac{1}{(\mu_i + \kappa_i(1-\theta_i))\,F_i} \frac{\Lambda_i \sum_{j=1}^{n} \beta_{ij} I_j^*}{\sum_{j=1}^{n} \beta_{ij} I_j^* + \mu_i}, \quad 1 \leq i \leq n.$$

Now, let us define the following nonlinear operator Θ on $\mathbb{R}^n$:

$$\Theta(\varphi) := \left(\frac{1}{(\mu_i + \kappa_i(1-\theta_i))\,F_i} \frac{\Lambda_i \sum_{j=1}^{n} \beta_{ij} \varphi_j}{\sum_{j=1}^{n} \beta_{ij} \varphi_j + \mu_i} \right)_{1 \leq i \leq n}, \quad \varphi = (\varphi_1, \varphi_2, \cdots, \varphi_n)^T \in \mathbb{R}^n.$$

If the operator Θ has a positive fixed-point $\varphi^* \,(= \Theta(\varphi^*))$, then it is no other than $(I_1^*, I_2^*, \cdots, I_n^*)^T$ and the existence of the endemic equilibrium P^* follows by substituting it to (6). It is easy to see that the Frećhet derivative of Θ at $\mathbf{0}$ is the next generation matrix:

$$\Theta'[\mathbf{0}]\varphi = \left(\frac{\frac{\Lambda_i}{\mu_i} \sum_{j=1}^{n} \beta_{ij} \varphi_j}{(\mu_i + \kappa_i(1-\theta_i))\,F_i} \right)_{1 \leq i \leq n} = \left(\frac{S_i^0 \sum_{j=1}^{n} \beta_{ij} \varphi_j}{(\mu_i + \kappa_i(1-\theta_i))\,F_i} \right)_{1 \leq i \leq n} = \mathcal{F}\mathcal{V}^{-1}\varphi.$$

We prove the following theorem:

THEOREM 2.1 *Let $\Re_0$ be defined by* (4)*. If $\Re_0 > 1$, then system* (1) *has at least one endemic equilibrium P^*.*

Proof. It is obvious that the nonlinear operator Θ is monotone nondecreasing (that is, $\Theta(\varphi) \geq \Theta(\psi)$ if $\varphi \geq \psi$, where the inequality between vectors implies that the same inequality holds for each entry of the vectors). Then, we see that

$$\|\Theta(\varphi)\| \leq \sum_{i=1}^{n} \frac{\Lambda_i}{(\mu_i + \kappa_i(1-\theta_i))\,F_i}, \tag{7}$$

where $\|\cdot\|$ denotes the usual Euclidean norm in $\mathbb{R}^n$ defined by $\|\mathbf{x}\| = \sum_{i=1}^{n} |x_i|$, $\mathbf{x} = (x_1, x_2, \cdots, x_n)^T \in \mathbb{R}^n$. The inequality (7) implies that the operator Θ is uniformly bounded. It follows from the Perron-Frobenius theorem that $\Re_0 = r\left(\mathcal{F}\mathcal{V}^{-1}\right) > 1$ is the eigenvalue of matrix $\mathcal{F}\mathcal{V}^{-1}$ associated with a positive eigenvector $\mathbf{w} := (w_1, w_2, \cdots, w_n)^T$ such that $\mathcal{F}\mathcal{V}^{-1}\mathbf{w} = \Re_0 \mathbf{w}$. Note that since $\Re_0 > 1$, there exists a sufficiently small constant $c > 0$ such that $c \sum_{j=1}^{n} \beta_{ij} w_j + \mu_i \leq \Re_0 \mu_i$ for all $i = 1, 2, \cdots, n$. Let $\tilde{\mathbf{w}} := c\mathbf{w}$. Then

$$\begin{aligned}
\Theta(\tilde{\mathbf{w}}) &= \left(\frac{1}{(\mu_i + \kappa_i(1-\theta_i))\,F_i} \frac{\Lambda_i \sum_{j=1}^{n} \beta_{ij} c w_j}{\sum_{j=1}^{n} \beta_{ij} c w_j + \mu_i} \right)_{1 \leq i \leq n} \\
&\geq c \left(\frac{1}{(\mu_i + \kappa_i(1-\theta_i))\,F_i} \frac{\Lambda_i \sum_{j=1}^{n} \beta_{ij} w_j}{\Re_0 \mu_i} \right)_{1 \leq i \leq n} = \frac{c}{\Re_0} \mathcal{F}\mathcal{V}^{-1}\mathbf{w} = \frac{c}{\Re_0} \Re_0 \mathbf{w} = \tilde{\mathbf{w}}.
\end{aligned}$$

Hence, from the monotonicity of Θ, we can construct the monotone nondecreasing sequence $\{\Theta^n(\tilde{\mathbf{w}})\}_{n=0}^{+\infty}$ such that $\Theta^n(\tilde{\mathbf{w}}) \leq \Theta^{n+1}(\tilde{\mathbf{w}})$. Since Θ is uniformly bounded, the sequence converges to a limit $\mathbf{w}^*$ which satisfies $\mathbf{w}^* = \Theta(\mathbf{w}^*)$. It is no other than the desired fixed-point and the existence of the endemic equilibrium P^* follows. ■

3. Well-posedness of the problem

Since system (1) is an infinite dimensional dynamical system, its associated initial conditions and boundary conditions need to be restricted in an appropriate phase space. Let us consider the following Banach spaces and their positive cones:

$$\mathcal{X} = \mathbb{R}^n \times \mathbb{R}^n \times \mathbb{R}^n \times \mathbb{R}^n \times L^1(0,+\infty;\mathbb{R}^n),\ \mathcal{X}_+ = \mathbb{R}^n_+ \times \mathbb{R}^n_+ \times \mathbb{R}^n_+ \times \mathbb{R}^n_+ \times L^1(0,+\infty;\mathbb{R}^n_+),$$

$$\mathcal{Y} = \mathbb{R}^n \times \mathbb{R}^n \times \mathbb{R}^n \times L^1(0,+\infty;\mathbb{R}^n),\quad \mathcal{Y}_+ = \mathbb{R}^n_+ \times \mathbb{R}^n_+ \times \mathbb{R}^n_+ \times L^1(0,+\infty;\mathbb{R}^n_+).$$

The norms are defined as $\|(\mathbf{x},\mathbf{y},\mathbf{z},\varphi,\psi)^T\|_{\mathcal{X}} = \|\mathbf{x}\| + \|\mathbf{y}\| + \|\mathbf{z}\| + \|\varphi\| + \|\psi\|_{L^1}$ and $\|(\mathbf{x},\mathbf{y},\varphi,\psi)^T\|_{\mathcal{Y}} = \|\mathbf{x}\| + \|\mathbf{y}\| + \|\varphi\| + \|\psi\|_{L^1}$, where $\mathbf{x},\mathbf{y},\mathbf{z},\varphi \in \mathbb{R}^n$ and $\psi \in L^1(0,+\infty;\mathbb{R}^n)$.

Denote by $N_i(t) := S_i(t) + E_i(t) + I_i(t) + \int_0^{+\infty} r_i(t,\omega)\mathrm{d}\omega$ the total population in group i at time t. From (1) we easily see that $N_i(t)$ satisfies the ordinary differential equation $\mathrm{d}N_i(t)/\mathrm{d}t = \Lambda_i - \mu_i N_i(t)$. Hence, we have $\lim_{t\to+\infty} N_i(t) = \Lambda_i/\mu_i = S_i^0 =: N_i^*$, $1 \le i \le n$. In what follows, for simplicity, we assume that $N_i(0) = N_i^*$ and hence, $N_i(t) = N_i^*$ for all $t \ge 0$, $1 \le i \le n$. Then, to show the well-posedness of the model (1), it suffices to consider the following reduced system:

$$\begin{cases} \dfrac{\mathrm{d}E_i(t)}{\mathrm{d}t} = \displaystyle\sum_{j=1}^{n} \beta_{ij}\left(N_i^* - E_i(t) - I_i(t) - \int_0^{+\infty} r_i(t,\omega)\mathrm{d}\omega\right) I_j(t) - (\mu_i+\sigma_i)E_i(t), \\ \dfrac{\mathrm{d}I_i(t)}{\mathrm{d}t} = \sigma_i E_i(t) - (\mu_i+\kappa_i)I_i(t) + \displaystyle\int_0^{+\infty} \gamma_i(\omega) r_i(t,\omega)\mathrm{d}\omega, \\ \dfrac{\partial r_i(t,\omega)}{\partial t} + \dfrac{\partial r_i(t,\omega)}{\partial \omega} = -(\mu_i + \gamma_i(\omega)) r_i(t,\omega), \quad r_i(t,0) = \kappa_i I_i(t), \\ E_i(0) = E_{i,0},\ I_i(0) = I_{i,0},\ r_i(0,\omega) = r_{i,0}(\omega), \quad 1 \le i \le n. \end{cases} \tag{8}$$

As in the approach introduced by [19], we reformulate the system (8) into a semi-linear abstract Cauchy problem in $\mathcal{Y}$. Let $A : D(A) := \mathbb{R}^n \times \mathbb{R}^n \times \{\mathbf{0}_{\mathbb{R}^n}\} \times W^{1,1}(0,+\infty;\mathbb{R}^n) \subset \mathcal{Y} \to \mathcal{Y}$ be a linear operator defined by

$$Au := \begin{pmatrix} -\mathcal{M}\mathbf{x} \\ -\mathcal{M}\mathbf{y} \\ -\psi(0) \\ -\frac{d}{\mathrm{d}\omega}\psi(\omega) - \mathcal{M}\psi(\omega) \end{pmatrix}, \quad u = \begin{pmatrix} \mathbf{x} \\ \mathbf{y} \\ \mathbf{0}_{\mathbb{R}^n} \\ \psi \end{pmatrix} \in D(A), \tag{9}$$

where $\mathcal{M}$ is an n-diagonal matrix defined in (5). Note that the domain of the operator A is not dense in $\mathcal{Y}$ since $\overline{D(A)} = \mathbb{R}^n \times \mathbb{R}^n \times \{\mathbf{0}_{\mathbb{R}^n}\} \times L^1(0,+\infty;\mathbb{R}^n) \neq \mathcal{Y}$. Let us define a nonlinear operator $F : \overline{D(A)} \to \mathcal{Y}$ by

$$F(u) := \begin{pmatrix} \left(\mathbf{N}^* - \mathbf{x} - \mathbf{y} - \int_0^{+\infty} \psi(\omega)\mathrm{d}\omega\right)^T \mathcal{B}\mathbf{y} - \Sigma\mathbf{x} \\ \Sigma\mathbf{x} - K\mathbf{y} + \int_0^{+\infty} \Gamma(\omega)\psi(\omega)\mathrm{d}\omega \\ K\mathbf{y} \\ -\Gamma(\omega)\psi(\omega) \end{pmatrix}, \quad u = \begin{pmatrix} \mathbf{x} \\ \mathbf{y} \\ \mathbf{0}_{\mathbb{R}^n} \\ \psi \end{pmatrix} \in \overline{D(A)}, \tag{10}$$

where $\mathcal{B}$, Σ, K and $\Gamma(\omega)$ are matrices defined in (5) and $\mathbf{N}^* = (N_1^*, N_2^*, \cdots, N_n^*)^T$. By setting $U(t) := (\mathbf{E}(t), \mathbf{I}(t), \mathbf{0}_{\mathbb{R}^n}, \mathbf{r}(t,.))^T$, we rewrite problem (8) into the following non-densely defined abstract Cauchy problem in $\mathcal{Y}$:

$$\frac{\mathrm{d}U(t)}{\mathrm{d}t} = AU(t) + F(U(t)), \quad t > 0, \quad U_0 := U(0). \tag{11}$$

We define the following closed space in $\mathcal{Y}$:

$$\Omega := \left\{ u = (\mathbf{x}, \mathbf{y}, \varphi, \psi)^T \in \mathcal{Y}_+ : \ 0 \le x_i + y_i + \varphi_i + \int_0^{+\infty} \psi_i(\omega) \mathrm{d}\omega \le N_i^*, \quad 1 \le i \le n \right\}. \tag{12}$$

To show the well-posedness of the problem (11), we apply Theorems 2.3 and 3.2 in [24]. To this end, we first prove the following lemma:

Lemma 3.1 *A is a Hille-Yosida operator which satisfies*

$$\|(\lambda I - A)^{-1}\| \le \frac{1}{\lambda + \underline{\mu}}, \quad \lambda > -\underline{\mu}, \tag{13}$$

where $\underline{\mu} := \min_{1 \le i \le n}(\mu_i)$. Furthermore, $\lambda(\lambda I - A)^{-1}$ maps Ω into itself for sufficiently large λ.

Proof. For any $u = (\mathbf{x}, \mathbf{y}, \varphi, \psi)^T \in \mathcal{Y}$ and $\lambda > -\underline{\mu}$, denote $\tilde{u} := (\lambda I - A)^{-1} u$. Since $\tilde{u} \in D(A)$, we can write $\tilde{u} = \left(\tilde{\mathbf{x}}, \tilde{\mathbf{y}}, \mathbf{0}_{\mathbb{R}^n}, \tilde{\psi}\right)^T \in D(A)$. Then, since $u = (\lambda I - A)\tilde{u}$, we have

$$\tilde{x}_i = \frac{x_i}{\lambda + \mu_i}, \ \tilde{y}_i = \frac{y_i}{\lambda + \mu_i}, \ \tilde{\psi}_i(\omega) = e^{-(\lambda + \mu_i)\omega} \varphi_i + \int_0^{\omega} e^{-(\lambda + \mu_i)(\omega - s)} \psi_i(s) \mathrm{d}s, \ 1 \le i \le n. \tag{14}$$

Then, we can verify the following inequality:

$$\begin{aligned} \left\|(\lambda I - A)^{-1} u\right\|_{\mathcal{Y}} &= \ \|\tilde{u}\|_{\mathcal{Y}} \\ \le \ & \sum_{i=1}^{n} \left(\frac{|x_i| + |y_i|}{\lambda + \mu_i} + \int_0^{+\infty} e^{-(\lambda + \mu_i)\omega} \mathrm{d}\omega |\varphi_i| + \int_0^{+\infty} \int_0^{\omega} e^{-(\lambda + \mu_i)(\omega - s)} |\psi_i(s)| \, \mathrm{d}s \mathrm{d}\omega \right) \\ \le \ & \sum_{i=1}^{n} \left(\frac{|x_i| + |y_i| + |\varphi_i| + \int_0^{+\infty} |\psi_i(s)| \, \mathrm{d}s}{\lambda + \underline{\mu}} \right) \ = \ \frac{1}{\lambda + \underline{\mu}} \|u\|_{\mathcal{Y}}. \end{aligned}$$

This implies that inequality (13) holds.

From (14) we see that if $u \in \Omega$ and $\tilde{u} = (\lambda I - A)^{-1} u$ for $\lambda > 0$, then $\lambda \tilde{x}_i = \lambda x_i / (\lambda + \mu_i) \in [0, x_i]$, $\lambda \tilde{y}_i = \lambda y_i / (\lambda + \mu_i) \in [0, y_i]$ and

$$\int_0^{+\infty} \lambda \tilde{\psi}_i(\omega) \mathrm{d}\omega = \frac{\lambda \varphi_i}{\lambda + \mu_i} + \frac{\lambda \int_0^{+\infty} \psi_i(s) \mathrm{d}s}{\lambda + \mu_i} \in \left[0, \ \varphi_i + \int_0^{+\infty} \psi_i(s) \mathrm{d}s\right], \quad 1 \le i \le n.$$

Hence, we have

$$0 \ \le \ \lambda \left(\tilde{x}_i + \tilde{y}_i + 0 + \int_0^{+\infty} \tilde{\psi}_i(\omega) \mathrm{d}\omega \right) \ \le \ x_i + y_i + \varphi_i + \int_0^{+\infty} \psi_i(s) \mathrm{d}s \ \le \ N_i^*, \quad 1 \le i \le n.$$

This implies that $\lambda (\lambda I - A)^{-1} (\Omega) \subset \Omega$ and the proof is complete. ∎

We next prove the following lemma:

Lemma 3.2 *F is Lipschitz continuous on $\overline{D(A)} \cap \Omega$. That is, there exists a constant $L > 0$ such that $\|F(u) - F(\tilde{u})\|_{\mathcal{Y}} \le L \|u - \tilde{u}\|_{\mathcal{Y}}$ for any $u, \tilde{u} \in \overline{D(A)} \cap \Omega$. Furthermore, $\lim_{\alpha \to 0+} (1/\alpha) \mathrm{dist}\,(u + \alpha F(u), \Omega) = 0$ for any $u \in \overline{D(A)} \cap \Omega$, where $\mathrm{dist}(u, \Omega) := \inf_{\tilde{u} \in \Omega} \|u - \tilde{u}\|_{\mathcal{Y}}$.*

Proof. We omit the proof of the first part (Lipshitz continuity) since it be easily proved by letting $L := \max(N^+ \beta^+ + 2\sigma^+, \ 2N^+ \beta^+ + 2\kappa^+, \ N^+ \beta^+ + 2\gamma^+)$, where $N^+ := \max_{1\le i\le n} N_i^*$, $\beta^+ := \max_{1\le i,j\le n}\beta_{ij}$, $\sigma^+ := \max_{1\le i\le n}\sigma_i$, $\kappa^+ := \max_{1\le i\le n}\kappa_i$, and $\gamma^+ := \max_{1\le i\le n}\gamma_i^+$.

To prove the remaining part of the lemma, it suffice to show that $u+\alpha F(u)\in\Omega$ for sufficiently small α. For any $u = (\mathbf{x},\mathbf{y},\mathbf{0}_{\mathbb{R}^n},\psi)^T \in \overline{D(A)}\cap\Omega$, let us define $\tilde{u} = \left(\tilde{\mathbf{x}},\tilde{\mathbf{y}},\tilde{\varphi},\tilde{\psi}\right)\in\mathcal{Y}$ by $\tilde{u} := u+\alpha F(u)$. Then, we have for $1\le i\le n$ that

$$\begin{aligned}0 \le&\tilde{x}_i+\tilde{y}_i+\tilde{\varphi}_i+\int_0^{+\infty}\tilde{\psi}_i(\omega)\mathrm{d}\omega\\ \le& x_i+y_i+\int_0^{+\infty}\psi_i(\omega)\mathrm{d}\omega+\alpha\sum_{j=1}^n\beta^+N_j^*\left(N_i^*-x_i-y_i-\int_0^{+\infty}\psi_i(\omega)\mathrm{d}\omega\right)\ \le\ N_i^*\end{aligned}$$

if $\alpha < 1/(\sum_{j=1}^n\beta^+N_j^*)$. This implies that $u+\alpha F(u)\in\Omega$, which completes the proof. ■

From Lemmas 3.1 and 3.2, we can use Theorems 2.3 and 3.2 in [24] to obtain the following proposition:

Proposition 3.3 *For system (8), there exists a unique strongly continuous semi-flow $\{\Phi(t)\}_{t\ge0}:\overline{D(A)}\cap\Omega\to\mathcal{Y}_+$ such that for each $U_0\in\overline{D(A)}\cap\Omega$, the function $U\in C([0,+\infty),\mathcal{Y}_+)$ defined by $U(\cdot)=\Phi(\cdot)U_0$ is a mild solution of (8). That is, it satisfies $\int_0^t U(s)\mathrm{d}s\in D(A)$ and $U(t)=U_0+A\int_0^t U(s)\mathrm{d}s+\int_0^t F(U(s))\mathrm{d}s$ for all $t\ge0$.*

This proposition implies the mathematical well-posedness of the original problem (1) for any initial condition in $\mathbb{R}^n\times(\overline{D(A)}\cap\Omega)$.

4. Asymptotic smoothness of semi-flows

To prove the asymptotic smoothness of semi-flow $\{\Phi(t)\}_{t\ge0}$ generated by (8), we use the method as in [8, 23, 33, 34]. We divide $\{\Phi(t)\}_{t\ge0}$ into two parts: $\Phi(t)U_0 = \mathcal{W}_1(t)U_0+\mathcal{W}_2(t)U_0$, where $\mathcal{W}_1(t)U_0 := \left(\mathbf{0}_{\mathbb{R}^n},\mathbf{0}_{\mathbb{R}^n},\mathbf{0}_{\mathbb{R}^n},\tilde{\psi}(t,\cdot)\right)^T$ and $\mathcal{W}_2(t)U_0 := (\mathbf{E}(t),\mathbf{I}(t),\mathbf{0}_{\mathbb{R}^n},\tilde{\mathbf{r}}(t,\cdot))^T$. Here

$$\tilde{\psi}(t,\omega)=(\psi_1(t,\omega),\psi_2(t,\omega),\cdots,\psi_n(t,\omega))^T,\quad \tilde{\psi}_i(t,\omega)=\begin{cases}0, & 0\le\omega\le t;\\ r_i(t,\omega), & t<\omega,\end{cases}\quad 1\le i\le n$$

and

$$\tilde{\mathbf{r}}(t,\omega)=(\tilde{r}_1(t,\omega),\tilde{r}_2(t,\omega),\cdots,\tilde{r}_n(t,\omega))^T,\quad \tilde{r}_i(t,\omega)=\begin{cases}r_i(t,\omega), & 0\le\omega\le t;\\ 0, & t<\omega,\end{cases}\quad 1\le i\le n.$$

Now we introduce the following result, which comes from [8, Lemma 3.2.3 and Theorem 3.4.6].

Theorem 4.1 ([8]) *The semi-flow $\{\Phi(t)\}_{t\ge0}:\overline{D(A)}\cap\Omega\to\mathcal{Y}_+$ is asymptotically smooth if the following properties hold:*

(i) $\lim_{t\to+\infty}\operatorname{diam}\mathcal{W}_1(t,\Omega)=0$;

(ii) there exists a $t_\Omega\ge0$ such that $\mathcal{W}_2(t,\Omega)$ has compact closure for each $t\ge t_\Omega$.

To verify the conditions in Theorem 4.1, we first prove the following lemma.

LEMMA 4.2 *There exists a real-valued function* $\Delta : \mathbb{R}_+ \times \mathbb{R}_+ \to \mathbb{R}_+$ *such that* $\lim_{t\to+\infty} \Delta(t,r) = 0$ *and* $\|\mathcal{W}_1(t)U_0\|_{\mathcal{Y}} \le \Delta(t,r)$ *hold for any* $r > 0$ *and* $t \ge 0$ *and* $U_0 \in \overline{D(A)} \cap \Omega$ *such that* $\|U_0\|_{\mathcal{Y}} \le r$.

Proof. Integrating the equation of r_i in system (8) along the characteristic line $t - \omega =$ constant, we have

$$\tilde{\psi}_i(t,\omega) := \begin{cases} 0, & 0 \le \omega \le t; \\ r_{i,0}(\omega - t)\,\mathrm{e}^{-\int_0^t \{\mu_i + \gamma_i(\omega - t + \sigma)\}\mathrm{d}\sigma}, & t < \omega, \end{cases} \quad 1 \le i \le n.$$

Hence, for $U_0 \in \overline{D(A)} \cap \Omega$ satisfying $\|U_0\|_{\mathcal{Y}} \le r$,

$$\begin{aligned}\|\mathcal{W}_1(t)U_0\|_{\mathcal{Y}} &= \|\mathbf{0}_{\mathbb{R}^n}\| + \|\mathbf{0}_{\mathbb{R}^n}\| + \|\mathbf{0}_{\mathbb{R}^n}\| + \left\|\tilde{\psi}(t,\cdot)\right\|_{L^1} = \sum_{i=1}^n \int_0^{+\infty} \left|\tilde{\psi}_i(t,\omega)\right| \mathrm{d}\omega \\ &= \sum_{i=1}^n \int_t^{+\infty} |r_{i,0}(\omega - t)|\,\mathrm{e}^{-\int_0^t \{\mu_i + \gamma_i(\omega - t + \sigma)\}\mathrm{d}\sigma}\mathrm{d}\omega \\ &\le \mathrm{e}^{-\underline{\mu}t} \sum_{i=1}^n \int_0^{+\infty} |r_{i,0}(\omega)|\,\mathrm{d}\omega \ \le\ \mathrm{e}^{-\underline{\mu}t}\,\|U_0\|_{\mathcal{Y}} \ \le\ \mathrm{e}^{-\underline{\mu}t}\,r.\end{aligned}$$

Hence, the assertion holds for $\Delta(t,r) := \mathrm{e}^{-\underline{\mu}t}\,r$. ■

We next prove the following lemma.

LEMMA 4.3 *For all* $t \ge 0$, $\mathcal{W}_2(t)$ *maps any bounded subsets of* $\overline{D(A)} \cap \Omega$ *into sets with compact closure in* $\mathcal{Y}$.

Proof. For U_0 in any bounded subset of $\overline{D(A)} \cap \Omega$, it follows from (12) that $\mathbf{E}(t)$, $\mathbf{I}(t)$ remain in the compact set $\left\{\mathbf{x} = (x_1, \cdots, x_n)^T \in \mathbb{R}^n_+ :\ 0 \le x_i \le \Lambda_i/\mu_i,\ 1 \le i \le n\right\}$ for all $t \ge 0$. Therefore, it suffices to show that $\tilde{\mathbf{r}}(t,\cdot)$ remains in a pre-compact subset of $\mathcal{Y}$ which is independent of U_0. Now, integrating the equation of r_i in system (8) along the characteristic line $t - \omega =$ constant gives

$$\tilde{r}_i(t,\omega) = \begin{cases} \kappa_i I_i(t - \omega)\mathrm{e}^{-\int_0^\omega \{\mu_i + \gamma_i(\sigma)\}\mathrm{d}\sigma}, & 0 \le \omega \le t; \\ 0, & t < \omega, \end{cases} \quad 1 \le i \le n. \tag{15}$$

To complete the proof, it suffices to show the following four properties (see Smith and Thieme [23, Theorem B.2]):

(i) The supremum of $\sum_{i=1}^n \int_0^{+\infty} \tilde{r}_i(t,\omega)\,\mathrm{d}\omega$ for all initial data $U_0 \in \overline{D(A)} \cap \Omega$ is finite.

(ii) $\lim_{h\to+\infty} \sum_{i=1}^n \int_h^{+\infty} \tilde{r}_i(t,\omega)\,\mathrm{d}\omega = 0$ uniformly for $U_0 \in \overline{D(A)} \cap \Omega$.

(iii) $\lim_{h\to+0} \sum_{i=1}^n \int_0^{+\infty} |\tilde{r}_i(t,\omega + h) - \tilde{r}_i(t,\omega)|\,\mathrm{d}\omega = 0$ uniformly for $U_0 \in \overline{D(A)} \cap \Omega$.

(iv) $\lim_{h\to+0} \sum_{i=1}^n \int_0^h \tilde{r}_i(t,\omega)\,\mathrm{d}\omega = 0$ uniformly for $U_0 \in \overline{D(A)} \cap \Omega$.

Now, from (15), we have $0 \le \tilde{r}_i(t,\omega) \le \kappa_i\Lambda_i\mathrm{e}^{-\underline{\mu}\omega}/\mu_i$, $1 \le i \le n$ and hence, it is easy to see that (i), (ii) and (iv) follow.

We prove (iii). Since we shall consider $h \to +0$, we can assume that $h \in (0,t)$

without loss of generality. From (15), we have

$$\begin{aligned}
&\sum_{i=1}^{n}\int_{0}^{+\infty}\left|\tilde{r}_i\left(t,\omega+h\right)-\tilde{r}_i\left(t,\omega\right)\right|\mathrm{d}\omega\\
=&\sum_{i=1}^{n}\int_{t-h}^{t}\left|0-\tilde{r}_i\left(t,\omega\right)\right|\mathrm{d}\omega+\sum_{i=1}^{n}\int_{0}^{t-h}\left|\tilde{r}_i\left(t,\omega+h\right)-\tilde{r}_i\left(t,\omega\right)\right|\mathrm{d}\omega\\
\leq&\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i h}{\mu_i}+\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i}{\mu_i}\int_{0}^{t-h}\left|\mathrm{e}^{-\int_0^{\omega+h}\{\mu_i+\gamma_i(\sigma)\}\mathrm{d}\sigma}-\mathrm{e}^{-\int_0^{\omega}\{\mu_i+\gamma_i(\sigma)\}\mathrm{d}\sigma}\right|\mathrm{d}\omega\\
\leq&\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i h}{\mu_i}+\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i}{\mu_i}\int_{0}^{t-h}\left|\int_{0}^{\omega+h}\left\{\mu_i+\gamma_i\left(\sigma\right)\right\}\mathrm{d}\sigma-\int_{0}^{\omega}\left\{\mu_i+\gamma_i\left(\sigma\right)\right\}\mathrm{d}\sigma\right|\mathrm{d}\omega\\
\leq&\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i h}{\mu_i}\left\{1+\mu_i\left(t-h\right)\right\}+\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i}{\mu_i}\int_{0}^{t-h}\int_{\omega}^{\omega+h}\gamma_i(\sigma)\mathrm{d}\sigma\mathrm{d}\omega\\
\leq&\sum_{i=1}^{n}\frac{\kappa_i\Lambda_i h}{\mu_i}\left\{1+\mu_i\left(t-h\right)+\gamma_i^{+}\left(t-h\right)\right\}\ \rightarrow 0\ \text{ as }\ h\rightarrow+0.
\end{aligned}$$

Note that we used the relation $\left|\mathrm{e}^{-a}-\mathrm{e}^{-b}\right|\leq|a-b|$. Since the right-hand side of the above inequality is independent from $U_0\in\overline{D(A)}\cap\Omega$, (iii) is proved and the proof is complete. ■

From Lemmas 4.2 and 4.3, we can use Theorem 4.1 to conclude that the semiflow $\{\Phi(t)\}_{t\geq 0}$ is asymptotically smooth:

Proposition 4.4 *The strongly continuous semiflow* $\{\Phi(t)\}_{t\geq 0}:\overline{D(A)}\cap\Omega\rightarrow\mathcal{Y}_+$ *generated by system* (8) *is asymptotically smooth.*

5. Uniform persistence of the system and existence of a global attractor

In this section, for $\Re_0>1$, we prove the uniform persistence and the existence of a compact global attractor by using the methods proposed in Hale and Waltman [9]. Set

$$\Omega_0:=\left\{(\mathbf{x},\mathbf{y},\mathbf{0}_{\mathbb{R}^n},\psi)^T\in\Omega:\ x_i>0\ \text{ or }\ y_i>0\ \text{ or }\ \int_0^{+\infty}\psi_i(\omega)\mathrm{d}\omega>0\ \text{ for some } i\right\},$$
$$\partial\Omega:=\Omega\setminus\Omega_0,\quad M_0:=\overline{D(A)}\cap\Omega_0,\quad \partial M_0:=\overline{D(A)}\cap\partial\Omega. \tag{16}$$

We first prove the following lemma.

Lemma 5.1 *Let* M_0 *and* ∂M_0 *be defined as in* (16)*. The following properties hold:*

(1) $\Phi(t)\left(\partial M_0\right)\subset\partial M_0$ *for all* $t>0$*;*
(2) If $U_0=\left(\boldsymbol{E}_0,\boldsymbol{I}_0,\mathbf{0}_{\mathbb{R}^n},\boldsymbol{r}_0(.)\right)^T\in M_0$*, then* $E_i(t)>0$ and $I_i(t)>0$ *for all* $i\in\{1,2,\cdots,n\}$ *and* $t>0$*.*

Proof. First, to prove (i), let $U_0=\left(\mathbf{E}_0,\mathbf{I}_0,\mathbf{0}_{\mathbb{R}^n},\mathbf{r}_0(.)\right)^T\in\partial M_0$. Then, $E_{i,0}=I_{i,0}=$

$\int_0^{+\infty} r_{i,0}(\omega)\mathrm{d}\omega = 0$ for all $i \in \{1, 2, \cdots, n\}$. Integrating (8), we have

$$\begin{cases} E_i(t) = \displaystyle\int_0^t \sum_{j=1}^n \beta_{ij} \left(N_i^* - E_i(s) - I_i(s) - \int_0^{+\infty} r_i(s,\omega)\mathrm{d}\omega \right) I_j(s)\mathrm{e}^{-(\mu_i+\sigma_i)(t-s)}\mathrm{d}s, \\ I_i(t) = \displaystyle\int_0^t \left(\sigma_i E_i(s) + \int_0^{+\infty} \gamma_i(\omega) r_i(s,\omega)\mathrm{d}\omega \right) \mathrm{e}^{-(\mu_i+\kappa_i)(t-s)}\mathrm{d}s, \\ r_i(t,\omega) = \begin{cases} \kappa_i I_i(t-\omega)\mathrm{e}^{-\int_0^\omega (\mu_i+\gamma_i(\sigma))\mathrm{d}\sigma}, & 0 \le \omega \le t; \\ 0, & t < \omega, \end{cases} \quad 1 \le i \le n. \end{cases} \tag{17}$$

Substituting the third equation into the second equation, we have

$$I_i(t) = \int_0^t \left(\sigma_i E_i(s) + \int_0^t \gamma_i(\omega)\kappa_i I_i(t-\omega)\mathrm{e}^{-\int_0^\omega (\mu_i+\gamma_i(\sigma))\mathrm{d}\sigma}\mathrm{d}\omega \right) \mathrm{e}^{-(\mu_i+\kappa_i)(t-s)}\mathrm{d}s. \tag{18}$$

From (17)-(18) and the continuity, we see that $E_i(t) = I_i(t) = \int_0^{+\infty} r_i(t,\omega)\mathrm{d}\omega = 0$ for all $i \in \{1, 2, \cdots, n\}$ and $t > 0$. This implies that $\Phi(t)(\partial M_0) \subset \partial M_0$ for all $t > 0$.

Next, to prove (ii), let $U_0 \in M_0$. If $E_{j,0} > 0$ for some j, then $E_j(t) \ge E_{j,0}\mathrm{e}^{-(\mu_j+\sigma_j)t} > 0$ for all $t > 0$ and hence, $I_j(t) \ge \int_0^t \sigma_j E_j(s)\mathrm{e}^{-(\mu_j+\kappa_j)(t-s)}\mathrm{d}s > 0$ for all $t > 0$. From the first equation of (17) and the irreducibility of matrix $(\beta_{ij})_{1\le i,j\le n}$ (see Assumption 1.1 (iii)), we see that $E_i(t) > 0$ for all $i \in \{1, 2, \cdots, n\}$ and $t > 0$. Then, from the second equation of (17), we see that $I_i(t) > 0$ for all $i \in \{1, 2, \cdots, n\}$ and $t > 0$.

If $I_{j,0} > 0$ for some $j \in \{1, 2, \cdots, n\}$, then in a completely similar way, we can show that $E_i(t) > 0$ and $I_i(t) > 0$ for all $i \in \{1, 2, \cdots, n\}$ and $t > 0$.

If $\int_0^{+\infty} r_{j,0}(\omega)\mathrm{d}\omega > 0$ for some j, then $I_j(t) \ge \int_0^t \int_s^{+\infty} \gamma_j(\omega) r_{j,0}(\omega - s)\mathrm{e}^{-\int_0^s (\mu_j+\gamma_j(\omega-s+\sigma))\mathrm{d}\sigma}\mathrm{d}\omega\ \mathrm{e}^{-(\mu_i+\kappa_i)(t-s)}\mathrm{d}s > 0$ for all $t > 0$. The remaining part of the proof is similar as in the above cases. ■

According to [17, Theorem 3.7] and [9, Theorem 4.2], we are able to show the following theorem about the uniform persistence.

THEOREM 5.2 *If $\Re_0 > 1$, then the semi-flow $\{\Phi(t)\}_{t\ge 0}$ is uniformly persistent in M_0. That is, there exists an $\underline{U} > 0$ such that $\liminf_{t\to+\infty} \|\Phi(t)U_0\|_{\mathcal{Y}} \ge \underline{U}$ for all $U_0 \in M_0$.*

Proof. We show that $\mathbf{0}$ is isolated in $\overline{D(A)} \cap \Omega$ and that $M_0 \cap W^s(\mathbf{0}) = \emptyset$, where $W^s(\mathbf{0})$ denotes the stable manifold of $\mathbf{0}$ defined by $W^s(\mathbf{0}) := \left\{ U_0 \in \overline{D(A)} \cap \Omega : \lim_{t\to+\infty} \Phi(t)U_0 = \mathbf{0} \right\}$. To this end, suppose that $\limsup_{t\to+\infty} \|\Phi(t)U_0\|_{\mathcal{Y}} \le \varepsilon$ for some $U_0 \in M_0$ and sufficiently small $\varepsilon > 0$ and show a contradiction. There exists a sufficiently large $T > 0$ such that $\|\Phi(t)U_0\|_{\mathcal{Y}} \le \varepsilon$ for all $t \ge T$. Then, from the positivity of the solution, we have $E_i(t) + I_i(t) + \int_0^{+\infty} r_i(t,\omega)\mathrm{d}\omega \le \varepsilon,\ 1 \le i \le n$ for all $t \ge T$. Hence, by integrating (8), we have for $1 \le i \le n$ that

$$\begin{cases} E_i(t) \ge \displaystyle\int_0^t \sum_{j=1}^n \beta_{ij} \left(N_i^* - \varepsilon \right) I_j(s)\mathrm{e}^{-(\mu_i+\sigma_i)(t-s)}\mathrm{d}s, \\ I_i(t) \ge \displaystyle\int_0^t \left(\sigma_i E_i(s) + \kappa_i \int_0^t \gamma_i(\omega) I_i(t-\omega)\mathrm{e}^{-\int_0^\omega (\mu_i+\gamma_i(\sigma))\mathrm{d}\sigma}\mathrm{d}\omega \right) \mathrm{e}^{-(\mu_i+\kappa_i)(t-s)}\mathrm{d}s \end{cases} \tag{19}$$

for all $t \ge T$. Without loss of generality, regarding $\Phi(T)U_0$ as the new initial value, we can consider that (19) holds for all $t \ge 0$. Let us denote by $\mathcal{L}[f](\lambda) := \int_0^{+\infty} \mathrm{e}^{-\lambda t} f(t)\mathrm{d}t, \lambda > 0$ the Laplace transform of function $f(t)$. Then, from (19), we have for $1 \le i \le n$ that

$$\begin{cases} \mathcal{L}[E_i](\lambda) \ge \dfrac{\sum_{j=1}^n \beta_{ij}(N_i^* - \varepsilon)\mathcal{L}[I_j](\lambda)}{\mu_i + \sigma_i + \lambda} = \dfrac{\sum_{j=1}^n \beta_{ij}(S_i^0 - \varepsilon)\mathcal{L}[I_j](\lambda)}{\mu_i + \sigma_i + \lambda}, \\ \mathcal{L}[I_i](\lambda) \ge \dfrac{\sigma_i \mathcal{L}[E_i](\lambda)}{\mu_i + \kappa_i + \lambda} + \dfrac{\kappa_i \mathcal{L}[I_i](\lambda) \int_0^{+\infty} \gamma_i(\omega) \mathrm{e}^{-\int_0^\omega (\mu_i + \gamma_i(\sigma))\mathrm{d}\sigma - \lambda\omega} \mathrm{d}\omega}{\mu_i + \kappa_i + \lambda}. \end{cases} \tag{20}$$

Note that $\mathcal{L}[E_i](\lambda)$ and $\mathcal{L}[I_i](\lambda)$, $1 \le i \le n$ exist for all $\lambda > 0$ because of the uniform boundedness of the solution in M_0, that is,

$$0 < \max(\mathcal{L}[E_i](\lambda), \mathcal{L}[I_i](\lambda)) \le \int_0^{+\infty} \mathrm{e}^{-\lambda t} N_i^* \mathrm{d}t = \frac{N_i^*}{\lambda} < +\infty, \quad 1 \le i \le n.$$

For $1 \le i \le n$, let

$$\ell_\lambda := \begin{pmatrix} \mathcal{L}[I_1](\lambda) \\ \mathcal{L}[I_2](\lambda) \\ \vdots \\ \mathcal{L}[I_n](\lambda) \end{pmatrix}, \quad F_{i,\lambda} := \frac{\mu_i + \sigma_i + \lambda}{\sigma_i}, \quad \theta_{i,\lambda} := \int_0^{+\infty} \gamma_i(\omega) \mathrm{e}^{-\int_0^\omega (\mu_i + \gamma_i(\sigma))\mathrm{d}\sigma - \lambda\omega} \mathrm{d}\omega,$$

$$\mathcal{K}_{\varepsilon,\lambda} := \begin{pmatrix} \dfrac{\beta_{11}(S_1^0 - \varepsilon)}{(\mu_1 + \kappa_1(1 - \theta_{1,\lambda}) + \lambda)F_{1,\lambda}} & \cdots & \dfrac{\beta_{1n}(S_1^0 - \varepsilon)}{(\mu_n + \kappa_n(1 - \theta_{n,\lambda}) + \lambda)F_{n,\lambda}} \\ \vdots & \ddots & \vdots \\ \dfrac{\beta_{n1}(S_n^0 - \varepsilon)}{(\mu_1 + \kappa_1(1 - \theta_{1,\lambda}))F_{1,\lambda} + \lambda} & \cdots & \dfrac{\beta_{nn}(S_n^0 - \varepsilon)}{(\mu_n + \kappa_n(1 - \theta_{n,\lambda}) + \lambda)F_{n,\lambda}} \end{pmatrix}.$$

Then, from (20), we have $\ell_\lambda \ge \mathcal{K}_{\varepsilon,\lambda}\ell_\lambda$. It is easy to see that $\mathcal{K}_{0,0} = \mathcal{F}\mathcal{V}^{-1}$. Hence, if $\Re_0 = r(\mathcal{F}\mathcal{V}^{-1}) > 1$, then from the continuity we can choose sufficiently small $\varepsilon > 0$ and $\lambda > 0$ so that $r(\mathcal{K}_{\varepsilon,\lambda}) > 1$. Let $\tilde{\ell}_{\varepsilon,\lambda}$ be the positive left eigenvector of matrix $\mathcal{K}_{\varepsilon,\lambda}$ associated with the eigenvalue $r(\mathcal{K}_{\varepsilon,\lambda})$, which existence is guaranteed by the Perron-Frobenius theorem. Multiplying $\tilde{\ell}_{\varepsilon,\lambda}$ to the both sides of the inequality $\ell_\lambda \ge \mathcal{K}_{\varepsilon,\lambda}\ell_\lambda$ from the left, we have $\tilde{\ell}_{\varepsilon,\lambda}\ell_\lambda \ge \tilde{\ell}_{\varepsilon,\lambda}\mathcal{K}_{\varepsilon,\lambda}\ell_\lambda = r(\mathcal{K}_{\varepsilon,\lambda})\tilde{\ell}_{\varepsilon,\lambda}\ell_\lambda > \tilde{\ell}_{\varepsilon,\lambda}\ell_\lambda$, which is a contradiction. Thus, $\mathbf{0}$ is isolated in $\overline{D(A)} \cap \Omega$ and $M_0 \cap W^s(\mathbf{0}) = \emptyset$. By [17], $\{\Phi(t)\}_{t\ge0}$ is uniformly persistent. ■

Furthermore, we can conclude for our case that there exists a compact set $\mathcal{A}_0 \subset \mathcal{Y}$ which is a global attractor for $\{\Phi(t)\}_{t\ge0}$ in $\mathcal{Y}$:

PROPOSITION 5.3 *The semi-flow $\{\Phi(t)\}_{t\ge0}$ has a compact global attractor $\mathcal{A}_0 \subset \mathcal{Y}$, which attracts any bounded sets of $\mathcal{Y}_+$.*

6. Proof of Theorem 1.1

For the proof of Theorem 1.1, we return our attention to the original system (1) which includes the susceptible populations $S_i(t)$, $1 \le i \le n$. Of course, our theoretical results obtained in the previous sections (the existence of equilibria, the asymptotic smoothness of the semi-flow, the uniform persistence of the system and the existence of a compact global attractor) still hold true for the original system (1).

In the proof, we use function $G(z) = z - 1 - \ln z$, which is nonnegative for all $z > 0$ and equal to zero if and only if $z = 1$. In the calculation, for simplicity, we denote $\partial r_i(t,\omega)/\partial\omega \to \partial_\omega r_i(t,\omega)$, $\partial r_i(t,\omega)/\partial t \to \partial_t r_i(t,\omega)$ and $\mathrm{d}r_i^*(\omega)/\mathrm{d}\omega \to \mathrm{d}_\omega r_i^*(\omega)$.

Let $\alpha_i(\omega) = \mu_i + \gamma_i(\omega)$ and $\rho_i(\omega) = e^{-\int_0^\omega \alpha(\tau)d\tau}$, $1 \le i \le n$. The fourth and fifth equations of (2) can be rewritten to $\mathrm{d}_\omega r_i^*(\omega) = -\alpha_i(\omega)r_i^*(\omega)$ and $r_i^*(0) = \kappa_i I_i^*$, respectively. Hence, we have $r_i^*(\omega) = \kappa_i I_i^* \rho_i(\omega)$, $1 \le i \le n$. Let

$$\zeta_i(\omega) = \int_\omega^{+\infty} \gamma_i(\nu) e^{-\int_\omega^\nu \alpha_i(\phi) d\phi} \mathrm{d}\nu, \quad 1 \le i \le n, \tag{21}$$

which will be used in the construction of Lyapunov functionals. Note that $\zeta_i(\omega) \ge 0$ for $\omega \ge 0$ and $\zeta_i(0) = \theta_i$, $1 \le i \le n$. The derivative of $\zeta_i(\omega)$ satisfies

$$\mathrm{d}_\omega \zeta_i(\omega) = \zeta_i(\omega)\alpha_i(\omega) - \gamma_i(\omega), \quad 1 \le i \le n. \tag{22}$$

6.1. *Proof of (i) of Theorem 1.1*

Based on the graph-theoretic approach developed by [6, 7, 14], we construct a Lyapunov functional. First we set $\tilde{\beta}_{ij} := \beta_{ij} S_i^* I_j^*$, $1 \le i, j \le n$ and a Laplacian matrix

$$\tilde{B} := \begin{pmatrix} \sum_{k\ne 1} \tilde{\beta}_{1k} & -\tilde{\beta}_{21} & \cdots & -\tilde{\beta}_{n1} \\ -\tilde{\beta}_{12} & \sum_{k\ne 2} \tilde{\beta}_{2k} & & -\tilde{\beta}_{n2} \\ \vdots & & \ddots & \vdots \\ -\tilde{\beta}_{1n} & -\tilde{\beta}_{2n} & \cdots & \sum_{k\ne n} \tilde{\beta}_{nk} \end{pmatrix}.$$

Then, from [6, Lemma 2.1], we see that the solution space of a linear system $\tilde{B}\mathbf{v} = \mathbf{0}$, $\mathbf{v} = (v_1, v_2, \dots, v_n)^T$. has dimension 1 and one of its basis is given by $\mathbf{v} = (v_1, v_2, \dots, v_n)^T = (c_{11}, \dots, c_{nn})^T$, where $c_{ii} > 0$, $i = 1, 2, \cdots, n$ denotes the cofactor of the i-th diagonal entry of matrix $\tilde{B}$. Using this $\mathbf{v}$, we construct the following Lyapunov functional: $V_1(\mathbf{S}, \mathbf{E}, \mathbf{I}, \mathbf{r}(\omega)) = \sum_{i=1}^n v_i \Big[L_{1,i}(t) + C_i L_{2,i}(t)\Big]$, where

$$\begin{cases} L_{1,i}(t) = & S_i^* G\Big(\dfrac{S_i}{S_i^*}\Big) + E_i^* G\Big(\dfrac{E_i}{E_i^*}\Big) + C_i I_i^* G\Big(\dfrac{I_i}{I_i^*}\Big), \\ L_{2,i}(t) = & \displaystyle\int_0^{+\infty} \zeta_i(\omega) r_i^*(\omega) G\Big(\dfrac{r_i(t,\omega)}{r_i^*(\omega)}\Big) \mathrm{d}\omega, \qquad\qquad 1 \le i \le n. \\ C_i = & \displaystyle\sum_{j=1}^n \dfrac{\beta_{ij} S_i^* I_j^*}{\sigma_i E_i^*}, \end{cases}$$

Note that by virtue of the uniform persistence of the system as shown in Theorem 5.2, functions $L_{2,i}, 1 \le i \le n$ are well-defined.

Using equilibrium equations (2), we first calculate the derivative of $L_{1,i}(t)$, $1 \le i \le n$ as

$$\begin{aligned} & L_{1,i}'(t) \\ = & \Big(1 - \frac{S_i^*}{S_i}\Big)\Big[\mu_i S_i^* \Big(1 - \frac{S_i}{S_i^*}\Big) + \sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big(1 - \frac{S_i I_j}{S_i^* I_j^*}\Big)\Big] + \Big(1 - \frac{E_i^*}{E_i}\Big)\sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big(\frac{S_i I_j}{S_i^* I_j^*} - \frac{E_i}{E_i^*}\Big) \\ & + C_i \Big(1 - \frac{I_i^*}{I_i}\Big)\Big[\sigma_i E_i^* \Big(\frac{E_i}{E_i^*} - \frac{I_i}{I_i^*}\Big) + \int_0^{+\infty} \gamma_i(\omega) r_i^*(\omega) \Big(\frac{r_i(t,\omega)}{r_i^*(\omega)} - \frac{I_i}{I_i^*}\Big)\mathrm{d}\omega\Big] \\ = & \mu_i S_i^* \Big(2 - \frac{S_i}{S_i^*} - \frac{S_i^*}{S_i}\Big) + C_i \int_0^{+\infty} \gamma_i(\omega) r_i^*(\omega) \Big[\frac{r_i(t,\omega)}{r_i^*(\omega)} - \frac{I_i}{I_i^*} - \frac{I_i^* r_i(t,\omega)}{I_i r_i^*(\omega)} + 1\Big]\mathrm{d}\omega \\ & + \sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big[3 - \frac{S_i^*}{S_i} + \frac{I_j}{I_j^*} - \frac{E_i^* S_i I_j}{E_i S_i^* I_j^*} - \frac{I_i}{I_i^*} - \frac{I_i^* E_i}{I_i E_i^*}\Big] \\ = & -\mu_i S_i^* \Big[G\Big(\frac{S_i}{S_i^*}\Big) + G\Big(\frac{S_i^*}{S_i}\Big)\Big] + C_i \int_0^{+\infty} \gamma_i(\omega) r_i^*(\omega) \Big[\frac{r_i(t,\omega)}{r_i^*(\omega)} - \frac{I_i}{I_i^*} - \frac{I_i^* r_i(t,\omega)}{I_i r_i^*(\omega)} + 1\Big]\mathrm{d}\omega \\ & - \sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big[G\Big(\frac{S_i^*}{S_i}\Big) + G\Big(\frac{I_i^* E_i}{I_i E_i^*}\Big) + G\Big(\frac{E_i^* S_i I_j}{E_i S_i^* I_j^*}\Big) + \frac{I_i}{I_i^*} - \frac{I_j}{I_j^*} + \ln \frac{I_i^* I_j}{I_i I_j^*}\Big], \quad 1 \le i \le n. \end{aligned} \tag{23}$$

Next, calculating the derivative of $L_{2,i}(t)$, $1 \le i \le n$, we have

$$
\begin{aligned}
L'_{2,i}(t) =& \int_0^{+\infty} \zeta_i(\omega)\Big(1 - \frac{r_i^*(\omega)}{r_i(t,\omega)}\Big)\partial_t r_i(t,\omega)\mathrm{d}\omega \\
=& -\int_0^{+\infty} \zeta_i(\omega)\Big(1 - \frac{r_i^*(\omega)}{r_i(t,\omega)}\Big)\Big(\partial_\omega r_i(t,\omega) + \alpha_i(\omega) r_i(t,\omega)\Big)\mathrm{d}\omega, \quad 1 \le i \le n.
\end{aligned}
$$

Since $\partial_\omega G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big) = \Big(1 - \frac{r_i^*(\omega)}{r_i(t,\omega)}\Big)\Big(\frac{\partial_\omega r_i(t,\omega)}{r_i^*(\omega)} - \frac{r_i(t,\omega)\mathrm{d}_\omega r_i^*(\omega)}{r_i^*(\omega) r_i^*(\omega)}\Big)$ and $\mathrm{d}_\omega r_i^*(\omega) = -\alpha_i(\omega) r_i^*(\omega)$, $1 \le i \le n$, we have

$$
r_i^*(\omega)\partial_\omega G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big) = \Big(1 - \frac{r_i^*(\omega)}{r_i(t,\omega)}\Big)\Big(\partial_\omega r_i(t,\omega) + \alpha_i(\omega) r_i(t,\omega)\Big), \quad 1 \le i \le n.
$$

Hence,

$$
L'_{2,i}(t) = -\int_0^{+\infty} \zeta_i(\omega) r_i^*(\omega)\partial_\omega G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega, \quad 1 \le i \le n. \tag{24}
$$

Using integration by parts and (22), we have

$$
\begin{aligned}
&\int_0^{+\infty} \zeta_i(\omega) r_i^*(\omega)\partial_\omega G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega \\
&= \zeta_i(\omega) r_i^*(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\Big|_{\omega=0}^{+\infty} - \int_0^{+\infty} \mathrm{d}_\omega[\zeta_i(\omega) r_i^*(\omega)] G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega \\
&= \zeta_i(\omega) r_i^*(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\Big|_{\omega=0}^{+\infty} - \int_0^{+\infty} \Big[r_i^*(\omega)\mathrm{d}_\omega \zeta_i(\omega) + \zeta_i(\omega)\mathrm{d}_\omega r_i^*(\omega)\Big] G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega \\
&= \zeta_i(\omega) r_i^*(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\Big|_{\omega=+\infty} - \zeta_i(0) r_i^*(0) G\Big(\frac{r_i(t,0)}{r_i^*(0)}\Big) \\
&\quad - \int_0^{+\infty} \Big[r_i^*(\omega)\zeta_i(\omega)\alpha_i(\omega) - r_i^*(\omega)\gamma_i(\omega) + \zeta_i(\omega)\mathrm{d}_\omega r_i^*(\omega)\Big] G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega, \quad 1 \le i \le n.
\end{aligned}
$$

Using the equalities $\zeta_i(0) = \theta_i$, $r_i^*(0) = \kappa_i I_i^*$, $r_i(t,0) = \kappa_i I_i(t)$, $\mathrm{d}_\omega r_i^*(\omega) = -\alpha_i(\omega) r_i^*(\omega)$, $1 \le i \le n$, we have

$$
\begin{aligned}
&\int_0^{+\infty} \zeta_i(\omega) r_i^*(\omega)\partial_\omega G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega \\
&= \zeta_i(\omega) r_i^*(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\Big|_{\omega=+\infty} - \theta_i \kappa_i I_i^* G\Big(\frac{I_i(t)}{I_i^*}\Big) + \int_0^{+\infty} r_i^*(\omega)\gamma_i(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\mathrm{d}\omega.
\end{aligned} \tag{25}
$$

Substituting (25) in (24), we obtain

$$
\begin{aligned}
L'_{2,i}(t) =& -\zeta_i(\omega) r_i^*(\omega) G\left(\frac{r_i(t,\omega)}{r_i^*(\omega)}\right)\Big|_{\omega=+\infty} + \theta_i \kappa_i I_i^* G\Big(\frac{I_i(t)}{I_i^*}\Big) \\
&+ \int_0^{+\infty} r_i^*(\omega)\gamma_i(\omega)\Big[-\frac{r_i(t,\omega)}{r_i^*(\omega)} + 1 + \ln\frac{I_i^* r_i(t,\omega)}{I_i(t) r_i^*(\omega)} + \ln\frac{I_i(t)}{I_i^*}\Big]\mathrm{d}\omega.
\end{aligned} \tag{26}
$$

Combining (23) and (26), we have

$$
\begin{aligned}
V_1'(t) = & \sum_{i=1}^n v_i \Big[L_{1,i}'(t) + C_i L_{2,i}'(t)\Big] = \sum_{i=1}^n v_i \bigg\{ -\mu_i S_i^* \Big[G\Big(\frac{S_i}{S_i^*}\Big) + G\Big(\frac{S_i^*}{S_i}\Big)\Big] \\
& - \sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big[G\Big(\frac{S_i^*}{S_i}\Big) + G\Big(\frac{I_i^* E_i}{I_i E_i^*}\Big) + G\Big(\frac{E_i^* S_i I_j}{E_i S_i^* I_j^*}\Big) + \frac{I_i}{I_i^*} - \frac{I_j}{I_j^*} + \ln \frac{I_i^* I_j}{I_i I_j^*}\Big] \\
& - C_i \zeta_i(\omega) r_i^*(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\Big|_{\omega=+\infty} - C_i \int_0^{+\infty} r_i^*(\omega)\gamma_i(\omega) G\Big(\frac{I_i^* r_i(t,\omega)}{I_i(t) r_i^*(\omega)}\Big) \mathrm{d}\omega \\
& - C_i \int_0^{+\infty} r_i^*(\omega)\gamma_i(\omega) G\Big(\frac{I_i(t)}{I_i^*}\Big) \mathrm{d}\omega + C_i \theta_i \kappa_i I_i^* G\Big(\frac{I_i(t)}{I_i^*}\Big) \bigg\}.
\end{aligned}
$$

Since $r_i^*(\omega) = \kappa_i I_i^* \rho_i(\omega)$ and $\theta_i = \int_0^{+\infty} \gamma_i(\omega)\rho_i(\omega)\mathrm{d}\omega$, $1 \le i \le n$, the terms including $G\Big(I_i(t)/I_i^*\Big)$ are canceled. Finally we get

$$
\begin{aligned}
V_1'(t) = & \sum_{i=1}^n v_i \bigg\{ -\mu_i S_i^* \Big[G\Big(\frac{S_i}{S_i^*}\Big) + G\Big(\frac{S_i^*}{S_i}\Big)\Big] \\
& - \sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big[G\Big(\frac{S_i^*}{S_i}\Big) + G\Big(\frac{I_i^* E_i}{I_i E_i^*}\Big) + G\Big(\frac{E_i^* S_i I_j}{E_i S_i^* I_j^*}\Big) + \frac{I_i}{I_i^*} - \frac{I_j}{I_j^*} + \ln \frac{I_i^* I_j}{I_i I_j^*}\Big] \\
& - C_i \zeta_i(\omega) r_i^*(\omega) G\Big(\frac{r_i(t,\omega)}{r_i^*(\omega)}\Big)\Big|_{\omega=+\infty} - C_i \int_0^{+\infty} r_i^*(\omega)\gamma_i(\omega) G\Big(\frac{I_i^* r_i(t,\omega)}{I_i(t) r_i^*(\omega)}\Big) \mathrm{d}\omega \bigg\}.
\end{aligned} \tag{27}
$$

Due to [6], it follows from $\tilde{B}\mathbf{v} = 0$ that $\sum_{j=1}^n \tilde{\beta}_{ji} v_j = \sum_{j=1}^n \tilde{\beta}_{ij} v_i$ and hence, $\sum_{j=1}^n \beta_{ji} S_j^* I_i^* v_j = \sum_{j=1}^n \beta_{ij} S_i^* I_j^* v_i$, $1 \le i \le n$. This implies that

$$
\begin{aligned}
& \sum_{i,j=1}^n \beta_{ij} S_i^* I_j^* v_i \frac{I_j}{I_j^*} = \sum_{i,j=1}^n \beta_{ij} S_i^* I_j v_i = \sum_{i=1}^n I_i \sum_{j=1}^n \beta_{ji} S_j^* v_j = \sum_{i=1}^n \frac{I_i}{I_i^*} \sum_{j=1}^n \beta_{ji} S_j^* I_i^* v_j \\
& = \sum_{i=1}^n \frac{I_i}{I_i^*} \sum_{j=1}^n \beta_{ij} S_i^* I_j^* v_i = \sum_{i,j=1}^n \beta_{ij} S_i^* I_j^* v_i \frac{I_i}{I_i^*}
\end{aligned}
$$

and thus, $\sum_{i=1}^n v_i \sum_{j=1}^n \beta_{ij} S_i^* I_j^* \Big(I_j/I_j^* - I_i/I_i^*\Big) = 0$. Hence, (27) can be evaluated as

$$
V_1'(t) \;\le\; -\sum_{i,j=1}^n v_i \beta_{ij} S_i^* I_j^* \ln \frac{I_i^* I_j}{I_i I_j^*} \;=\; -\sum_{i,j=1}^n v_i \bar{\beta}_{ij} \ln \frac{I_i^* I_j}{I_i I_j^*}.
$$

By using the graph-theoretic approach as in Guo et al. [6] and Li and Shuai [14], we can prove that the right-hand side of this inequality is equal to zero. That is, the positive-definite function $V_1(t)$ has nonpositive derivative $\mathrm{d}V_1(t)/\mathrm{d}t$. It is easy to see that the equality $\mathrm{d}V_1(t)/\mathrm{d}t = 0$ holds if and only if $(\mathbf{S}(\cdot), \mathbf{E}(\cdot), \mathbf{I}(\cdot), \mathbf{r}(\cdot,\omega)) = (\mathbf{S}^*, \mathbf{E}^*, \mathbf{I}^*, \mathbf{r}^*(\omega))$. By virtue of the asymptotic smoothness of the semi-flow as shown in Proposition 4.4, we can apply the invariance principle (see [33, Theorem 4.2 in Chapter IV]) to conclude that the endemic equilibrium P^* is globally asymptotically stable. ■

6.2. *Proof of (ii) of Theorem 1.1*

Let us define matrix $M^0 := \left(\beta_{ij}S_i^0/(\mu_i+\kappa_i(1-\theta_i))F_i)\right)_{1\le i,j\le n} = \mathcal{V}^{-1}\mathcal{F}$ and matrix-valued function $M(\mathbf{S}) := (\beta_{ij}S_i/(\mu_i+\kappa_i(1-\theta_i))F_i))_{1\le i,j\le n}$. It is easy to see that $M(\mathbf{S}^0) = M^0$, where $\mathbf{S}^0 := \left(S_1^0, S_2^0, \cdots, S_n^0\right)^T$. Since $r(\mathcal{F}\mathcal{V}^{-1}) = r(\mathcal{V}^{-1}\mathcal{F})$, we see that $r(M^0) = \Re_0$.

First we claim that there does not exist any endemic equilibrium P^* if $\Re_0 \le 1$. Suppose that $\mathbf{S} \neq \mathbf{S}^0$. Then, under Assumption 1.1, we have $\mathbf{0} < M(\mathbf{S}) < M^0$, where we denote $\mathbf{A} < \mathbf{B}$ for any two matrices $\mathbf{A} = (a_{ij})_{1\le i,j\le n}$ and $\mathbf{B} = (b_{ij})_{1\le i,j\le n}$ if $a_{ij} \le b_{ij}$ for all $i, j \in \{1, 2, \cdots, n\}$ and $\mathbf{A} \neq \mathbf{B}$.

Since matrix $M(\mathbf{S}) + M^0$ is nonnegative and irreducible under Assumption 1.1, it follows from the Perron-Frobenius theorem (see Corollary 2.1.5 of [3]) that $r(M(\mathbf{S})) < r(M^0) = \Re_0 \le 1$. This implies that equation $M(\mathbf{S})\mathbf{I} = \mathbf{I}$ has only the trivial solution $\mathbf{I} = 0$ and the claim is true. Here, note that the equation $M(\mathbf{S})\mathbf{I} = \mathbf{I}$ can be obtained by rearranging the equations in (2).

Next we claim that the disease-free equilibrium P^0 is globally asymptotically stable. Since M_0 is irreducible, the Perron-Frobenius theorem guarantees that there exists a positive left eigenvector $(\omega_1, \omega_2, \cdots, \omega_n)$ of matrix M^0 associated with the eigenvalue $r(M_0) = \Re_0 \le 1$, that is, $(\omega_1, \omega_2, \cdots, \omega_n)M^0 = r(M^0)(\omega_1, \omega_2, \cdots, \omega_n)$. Let $c_i = \omega_i/(\mu_i+\kappa_i(1-\theta_i))F_i > 0,\ 1 \le i \le n$. Let us define a Lyapunov functional,

$$V_2(\mathbf{S}, \mathbf{E}, \mathbf{I}, \mathbf{r}(\omega)) = \sum_{i=1}^{n} c_i\Big[E_i + F_iI_i + F_i\int_0^{+\infty}\zeta_i(\omega)r_i(t,\omega)\mathrm{d}\omega\Big] \tag{28}$$

where $F_i = (\mu_i+\sigma_i)/\sigma_i,\ 1 \le i \le n$. Calculating the derivative of $V_2(t)$ along the solution of system (1), we obtain

$$\begin{aligned} V_2'(t) = &\sum_{i=1}^{n} c_i\Big[\sum_{j=1}^{n}\beta_{ij}S_iI_j - (\mu_i+\kappa_i)F_iI_i + F_i\int_0^{+\infty}\gamma(\omega)r_i(t,\omega)\mathrm{d}\omega \\ &- F_i\int_0^{+\infty}\zeta_i(\omega)(\partial_\omega r_i(t,\omega) + \alpha_i(\omega)r_i(t,\omega))\mathrm{d}\omega\Big]. \end{aligned} \tag{29}$$

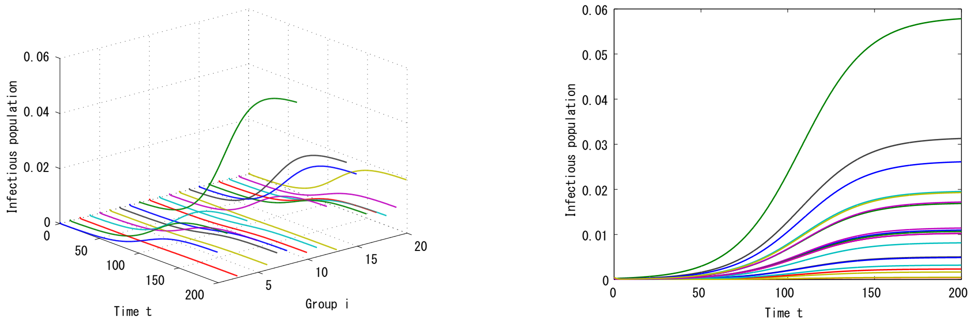
Using integration by parts, we obtain

$$\begin{aligned} \int_0^{+\infty}\zeta_i(\omega)\partial_\omega r_i(t,\omega)\mathrm{d}\omega =& \zeta_i(\omega)r_i(t,\omega)\Big|_{\omega=0}^{+\infty} - \int_0^{+\infty}\mathrm{d}_\omega\zeta_i(\omega)r_i(t,\omega)\mathrm{d}\omega \\ =& -\theta_i\kappa_iI_i(t) - \int_0^{+\infty}[\zeta_i(\omega)\alpha_i(\omega) - \gamma_i(\omega)]r_i(t,\omega)\mathrm{d}\omega,\ 1 \le i \le n. \end{aligned} \tag{30}$$

Substituting the expression (30) into (29) yields

$$\begin{aligned} V_2'(t) =& \sum_{i=1}^{n} c_i\Big[\sum_{j=1}^{n}\beta_{ij}S_iI_j - (\mu_{i_i}+\kappa_i(1-\theta_i))F_iI_i\Big] = \sum_{i=1}^{n}\omega_i\left[\frac{\sum_{j=1}^{n}\beta_{ij}S_iI_j}{\mu_{i_i}+\kappa_i(1-\theta_i)F_i} - I_i\right] \\ =& (\omega_1, \omega_2, \cdots, \omega_n)\cdot(M(\mathbf{S}) - \mathcal{E}_n)\mathbf{I} \le (\omega_1, \omega_2, \cdots, \omega_n)\cdot(M_0 - \mathcal{E}_n)\mathbf{I} \\ =& (\omega_1, \omega_2, \cdots, \omega_n)\cdot(r(M_0) - 1)\mathbf{I} \le 0, \end{aligned} \tag{31}$$

where $\mathcal{E}_n$ denotes the $n \times n$ identity matrix and $\cdot$ denotes the inner product of vectors. If $r(M_0) < 1$, then it is easy to see from (31) that $V_2'(t) = 0$ if and only if



(a) Infectious population $I_i(t)$ versus time t and group i

(b) Infectious population $I_i(t), 1 \le i \le 20$ versus time t

Figure 1. Time variation of infectious population $I_i(t), 1 \le i \le 20$ of model (1) with parameters (33) when $\Re_0 \approx 1.0864 > 1$

$\mathbf{I} = 0$. Suppose that $r(M_0) = 1$. Then it follows from (31) that $V_2'(t) = 0$ implies

$$(\omega_1, \omega_2, \cdots, \omega_n) \cdot M(\mathbf{S})\mathbf{I} = (\omega_1, \omega_2, \cdots, \omega_n) \cdot \mathbf{I}. \tag{32}$$

If $\mathbf{S} \neq \mathbf{S}^0$, then

$$(\omega_1, \omega_2, \cdots, \omega_n) \cdot M(\mathbf{S}) < (\omega_1, \omega_2, \cdots, \omega_n) \cdot M^0 = r(M^0)(\omega_1, \omega_2, \cdots, \omega_n) = (\omega_1, \omega_2, \cdots, \omega_n),$$

which implies that (32) has only the trivial solution $\mathbf{I} = \mathbf{0}$. Therefore, $V_2'(t) = 0$ if and only if $\mathbf{I} = 0$ or $\mathbf{S} = \mathbf{S}^0$ provided $r(M^0) = 1$. This implies that the only compact invariant subset of the set where $V_2'(t) = 0$ is the singleton $\{P^0\}$. Hence, using the LaSalle's invariance principle, we can conclude that the disease-free equilibrium P^0 is globally asymptotically stable. ■

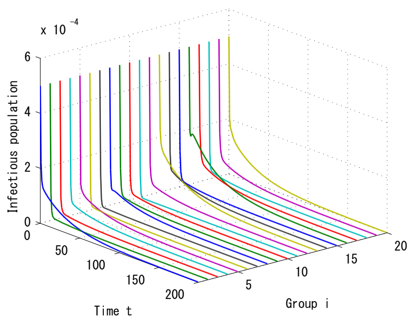
7. Numerical simulation

In this section, we perform numerical simulation to show the validity of Theorem 1.1. Let $n = 20$. Using uniform random variable $X \in (0, 1)$, we choose each parameter as follows (X is different in each choice):

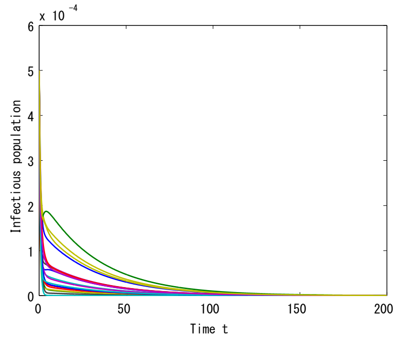
$$\begin{aligned}
&\Lambda_i = 1 + (0.5 - X), \quad \mu_i = 1 + (0.5 - X), \quad \sigma_i = 1 - X, \quad \kappa_i = 1 - X, \\
&\beta_{ij} = 0.45\,(1 - X), \quad \gamma_i(\omega) = \begin{cases} 0, & \omega < 10, \\ 0.5\,(1 - X), & \omega \ge 10, \end{cases} \\
&S_{i,0} = \frac{0.99}{20}, \quad E_{i,0} = 0, \quad I_{i,0} = \frac{0.01}{20}, \quad r_{i,0}(\omega) \equiv 0, \quad 1 \le i \le 20.
\end{aligned} \tag{33}$$

In one example, $\Re_0 \approx 1.0864 > 1$ and we obtain Figure 1. In this case, we see that the infectious population $I_i(t), 1 \le i \le n$ converges to the equilibrium solution $I_i^*, 1 \le i \le n$ as time evolves. This implies the global asymptotic stability of the endemic equilibrium P^* as shown in Theorem 1.1 (i).

In another example, $\Re_0 \approx 0.9526 < 1$ and we obtain Figure 2. In this case, we see that the infectious population $I_i(t), 1 \le i \le n$ converges to 0 as time evolves. This implies the global asymptotic stability of the disease-free equilibrium P^0 as shown in Theorem 1.1 (ii).



(a) Infectious population $I_i(t)$ versus time t and group i



(b) Infectious population $I_i(t), 1 \leq i \leq 20$ versus time t

Figure 2. Time variation of infectious population $I_i(t), 1 \leq i \leq 20$ of model (1) with parameters (33) when $\Re_0 \approx 0.9526 < 1$

8. Discussion

In this paper we have formulated multi-group SEIR epidemic model (1) with relapse-age-structure and studied its global stability. We have defined the basic reproduction number $\Re_0$ by the spectral radius of the next generation matrix (see (4)) and proved Theorem 1.1, which states that the endemic equilibrium P^* is globally asymptotically stable when $\Re_0 > 1$, whereas the disease-free equilibrium P^0 is so when $\Re_0 \leq 1$. This result implies that the relapse-age-structure has no effect on global asymptotic stability of both of the equilibria. Compared the previous studies, relapse leads the difficulties in analysis of existence of the endemic equilibrium, we used fixed-point problem to study it when $\Re_0 > 1$. The asymptotic smoothness of the semi-flow, the uniform persistence and the existence of a compact global attractor are also obtained by standard and rigorous analysis. For the proof of Theorem 1.1, we have constructed suitable Lyapunov functionals based on the graph theoretic approach as in [6, 7, 14].

Corresponding to the multi-group model (1), the single-group SEIR model with relapse-age structure (when $n = 1$) takes the following form.

$$\begin{cases} \dfrac{\mathrm{d}S(t)}{dt} = \Lambda - \beta S(t)I(t) - \mu S(t), \\ \dfrac{\mathrm{d}E(t)}{dt} = \beta S(t)I(t) - (\mu + \sigma)E(t), \\ \dfrac{\mathrm{d}I(t)}{dt} = \sigma E(t) - (\mu + \kappa)I(t) + \displaystyle\int_0^{+\infty} \gamma(\omega) r(t,\omega)\mathrm{d}\omega, \\ \dfrac{\partial r(t,\omega)}{\partial t} + \dfrac{\partial r(t,\omega)}{\partial \omega} = -(\mu + \gamma(\omega))r(t,\omega), \\ r(t,0) = \kappa I(t) \\ S(0) = S_0 > 0, \ E(0) = E_0 > 0, \quad I(0) = I_0 > 0, \quad r(0,\omega) = r_0(\omega) \geq 0. \end{cases} \tag{34}$$

This model is consistent with the special case of the model studied in [15] (see model (6.3) in the reference). The global behavior of (34) has been already clarified from [15, Theorems 5.2 and 5.6]. That is, the basic reproduction number $\Re_0$ governs the global dynamics of (34), as shown more generally in Theorem 1.1 of this paper.

In the last of this paper, we give a discussion on the discretization of our model. If we assume that recovered individuals are partitioned into m age stages defined by the age intervals $[\omega_{k-1}, \omega_k)$ where $0 = \omega_0 < \omega_1 < \cdots < \omega_{m-1} < \omega_m = \infty$, and we further assume that for $\omega \in [\omega_{k-1}, \omega_k)$, the functions $\gamma_i(\omega)\,(1 \leq i \leq n)$

are constants such that $\gamma_i(\omega) = \gamma_i^{(k)}$. Then, denoting $R_i^{(k)}(t) = \int_{\omega_{k-1}}^{\omega_k} r_i(t,\omega)d\omega$ and integrating the fourth equation of system (1) in the age interval $[\omega_{k-1}, \omega_k)$, respectively, yields

$$r_i(t,\omega_k) - r_i(t,\omega_{k-1}) + \frac{dR_i^{(k)}(t)}{dt} = -(\gamma_i^{(k)} + \mu_i)R_i^{(k)}(t), \quad 1 \le i \le n, \quad 1 \le k \le m.$$

Denote by c_k the transfer rate from the k-th age stage to the $(k+1)$-th age stage such that $r(t,\omega_k) = c^{(k)}R_i^{(k)}(t)$, where $c^{(m)} = 0$. By using the boundary condition in system (1), we can obtain the following ordinary equations for $S_i(t), E_i(t), I_i(t)$ and $R_i^{(k)}(t)$.

$$\begin{cases} \dfrac{\mathrm{d}S_i(t)}{\mathrm{d}t} = \Lambda_i - \mu_i S_i(t) - \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i(t) I_j(t), \\ \dfrac{\mathrm{d}E_i(t)}{\mathrm{d}t} = \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i(t) I_j(t) - (\mu_i + \sigma_i)\, E_i(t), \\ \dfrac{\mathrm{d}I_i(t)}{\mathrm{d}t} = \sigma_i E_i(t) - (\mu_i + \kappa_i)\, I_i(t) + \displaystyle\sum_{k=1}^{m} \gamma_i^{(k)} R_i^{(k)}(t), & 1 \le i \le n. \\ \dfrac{dR_i^{(1)}(t)}{\mathrm{d}t} = \kappa_i I_i(t) - (c^{(1)} + \gamma_i^{(1)} + \mu_1) R_i^{(1)}(t), \\ \dfrac{dR_i^{(k)}(t)}{\mathrm{d}t} = c^{(k-1)} R_i^{(k-1)}(t) - \left(c^{(k)} + \gamma_i^{(k)} + \mu_i\right) R_i^{(k)}(t), \quad 2 \le k \le m, \end{cases} \tag{35}$$

The model (35) is thought to be essentially equivalent to our model (1). Therefore, we can expect that global stability results similar to Theorem 1.1 may hold for (35). Although we do not analyze (35) in this paper, the advantage of analyzing ODEs model (35) is that we can ease the proof of existence of the solution, asymptotic smoothness of the semi-flow and uniform persistence of the system. In usual, in the analysis of multi-group ODEs models, we can concentrate our attention to the construction of Lyapunov functions. For the other papers on the global stability analysis of a multi-group SIR epidemic model with age-structure in the discretized case and the continuous case, please see [12] and [13], respectively. An extension to our model involving the latency age will be an avenue for future work.

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