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Global stability of multi-group epidemic models with distributed delays

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ABSTRACT

We investigate a class of multi-group epidemic models with distributed delays. We establish that the global dynamics are completely determined by the basic reproduction number $\mathcal{R}_0$. More specifically, we prove that, if $\mathcal{R}_0 \leqslant 1$, then the disease-free equilibrium is globally asymptotically stable; if $\mathcal{R}_0 > 1$, then there exists a unique endemic equilibrium and it is globally asymptotically stable. Our proof of global stability of the endemic equilibrium utilizes a graph-theoretical approach to the method of Lyapunov functionals.

1. Introduction

In the literature of mathematical epidemiology, multi-group epidemic models have been proposed to describe the spread of many infectious diseases in heterogeneous populations, such as measles, mumps, gonorrhea, and HIV/AIDS. A heterogeneous host population can be divided into several homogeneous groups according to modes of transmission, contact patterns, or geographic distributions, so that within-group and inter-group interactions could be modeled separately. One of the earliest multi-group models is proposed by Lajmanovich and Yorke [15] for the transmission of gonorrhea. For a class of n-group SIS models, they have completely established the global dynamics and proved the global stability of a unique endemic equilibrium using a quadratic global Lyapunov function. Various forms of multi-group models have subsequently been studied. One of main mathematical challenges in the analysis of multi-group models is the global stability of the endemic equilibrium [2,11,12,14,17,23,24]. A complete resolution of this problem has been elusive until recently. In [8,9], for a class of multi-group SEIR models described by ordinary differential equations, a graph-theoretic approach to the method of global Lyapunov functions was proposed and used to establish the global stability of a unique endemic equilibrium.

In the present paper, a more general multi-group epidemic model than that in [9] is proposed to describe the disease spread in a heterogeneous host population with general age-structure and varying infectivity. The host population is divided into several homogeneous groups. Let S_k, E_k, I_k and R_k denote the susceptible, infected but non-infectious, infectious, and recovered populations in the k-th group, respectively. Let $i_k(t,r)$ denote the population of infectious individuals in the k-th group with respect to the age of infection r at time t, and $I_k(t) = \int_{r=0}^{\infty} i_k(t,r)\,dr$. Let $h_k(r) \geqslant 0$ be a continuous kernel function that represents the infectivity at the age of infection r. The disease incidence in the k-th group, assuming a bilinear incidence form, can be calculated as

$$\sum_{j=1}^{n} \beta_{kj} S_k(t) \int_{r=0}^{\infty} h_j(r) i_j(t,r)\,dr, \tag{1.1}$$

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where the sum takes into account cross-infections from all groups and β_{kj} represents the transmission coefficient between compartments S_k and I_j. In the special case $h_k(r) \equiv 1$, the incidence in (1.1) becomes $\sum_{j=1}^{n} \beta_{kj} S_k(t) I_j(t)$ as in [9]. Therefore, the model in [9] can be generalized to the following system of differential equations

$$\begin{aligned}
S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} h_j(r) i_j(t,r)\,dr - d_k^S S_k,\\
E_k' &= \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} h_j(r) i_j(t,r)\,dr - \big(d_k^E + \epsilon_k\big) E_k,\\
I_k' &= \epsilon_k E_k - \big(d_k^I + \gamma_k\big) I_k,\\
R_k' &= \gamma_k I_k - d_k^R R_k, \quad k = 1, 2, \ldots, n.
\end{aligned} \tag{1.2}$$

Here Λ_k represents influx of individuals into the k-th group, d_k^S, d_k^E, d_k^I and d_k^R represent death rates of S, E, I and R populations in the k-th group, respectively, ϵ_k represents the rate of becoming infectious after a latent period in the k-th group, and γ_k represents the recovery rate of infectious individuals in the k-th group. All parameter values are assumed to be nonnegative and Λ_k, d_k^S, $d_k^E > 0$ for all k. For detailed discussions of the model, we refer the reader to [9,22] and references therein. Note that

$$\begin{aligned}
&\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial r}\right) i_k(t,r) = -\big(d_k^I + \gamma_k\big) i_k(t,r),\\
&i_k(t,0) = \epsilon_k E_k(t),
\end{aligned}$$

whose solution is

$$i_k(t,r) = i_k(t-r,0) e^{-(d_k^I + \gamma_k) r} = \epsilon_k E_k(t-r) e^{-(d_k^I + \gamma_k) r}. \tag{1.3}$$

Substituting (1.3) into (1.2) we obtain

$$\begin{aligned}
S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} h_j(r) \epsilon_j E_j(t-r) e^{-(d_j^I + \gamma_j) r}\,dr - d_k^S S_k,\\
E_k' &= \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} h_j(r) \epsilon_j E_j(t-r) e^{-(d_j^I + \gamma_j) r}\,dr - \big(d_k^E + \epsilon_k\big) E_k,\\
I_k' &= \epsilon_k E_k - \big(d_k^I + \gamma_k\big) I_k,\\
R_k' &= \gamma_k I_k - d_k^R R_k, \quad k = 1, 2, \ldots, n.
\end{aligned} \tag{1.4}$$

Since the variables I_k and R_k do not appear in the first two equations of (1.4), we can consider the following reduced system with distributed time delays and general kernel functions

$$\begin{aligned}
S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} f_j(r) E_j(t-r)\,dr - d_k^S S_k,\\
E_k' &= \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} f_j(r) E_j(t-r)\,dr - \big(d_k^E + \epsilon_k\big) E_k, \quad k = 1, 2, \ldots, n.
\end{aligned} \tag{1.5}$$

Here the kernel function $f_k(r) \geqslant 0$ is continuous and $\int_{r=0}^{\infty} f_k(r)\,dr = a_k > 0$. While system (1.5) is derived from a general age of infection model (1.2), it can also be interpreted as a multi-group model for an infectious disease whose latent period r in hosts has a general probability density function $\frac{1}{a_k} f_k(r)$, for the k-th group. We will establish the global dynamics of system (1.5).

The basic reproduction number $\mathcal{R}_0$ is defined as the expected number of secondary cases produced in an entirely susceptible population by a typical infected individual during its entire infectious period [7]. Intuitively, if $\mathcal{R}_0 < 1$, the disease dies out from the host population, and if $\mathcal{R}_0 > 1$, the disease will persist. Let $S_k^0 = \frac{\Lambda_k}{d_k^S}$, $a_k = \int_{r=0}^{\infty} f_k(r)\,dr$. The next generation matrix for system (1.5) is

$$M_0 = \left(\frac{\beta_{kj} S_k^0 a_k}{d_k^E + \epsilon_k}\right)_{n \times n}. \tag{1.6}$$

Motivated by [7,25,26], we define the basic reproduction number as the spectral radius of M_0,

$$\mathcal{R}_0 = \rho(M_0). \tag{1.7}$$

In the special case of a single-group model, the definition of $\mathcal{R}_0$ in (1.7) agrees with that in [22]. In the special case when $f_k(r)$ is an exponential function, $\mathcal{R}_0$ reduces to that for the resulting ODE models as given in [9,25]. For system (1.5), we will establish that the dynamical behaviors are completely determined by values of $\mathcal{R}_0$. More specifically, if $\mathcal{R}_0 \leqslant 1$, the disease-free equilibrium is globally asymptotically stable and the disease dies out; if $\mathcal{R}_0 > 1$, a unique endemic equilibrium exists and is globally asymptotically stable, and the disease persists at the endemic equilibrium. Our proof demonstrates that the graph-theoretical approach developed in [8,9] for systems of ordinary differential equations is applicable to delay differential systems like (1.5).

The paper is organized as follows. In the next section, we prove some preliminary results for system (1.5). Our main results are stated in Section 3. In Section 4, the global stability of the disease-free equilibrium is proved. The global stability of the endemic equilibrium is proved in Section 5. For the convenience of the reader, we include in Appendix A results from graph theory that are needed for our proof.

2. Preliminaries

We make the following assumption on the kernel function $f_k(r)$ in (1.5):

$$\int_{r=0}^{\infty} f_k(r)e^{\lambda_k r}\,dr < \infty, \tag{2.1}$$

where λ_k is a positive number, $k = 1, 2, \ldots, n$. Define the following Banach space of fading memory type (see e.g. [1] and references therein)

$$C_k = \Bigl\{\phi \in C\bigl((-\infty, 0], \mathbb{R}\bigr)\colon \phi(s)e^{\lambda_k s} \text{ is uniformly continuous on } (-\infty, 0], \text{ and } \sup_{s\leqslant 0}\bigl|\phi(s)\bigr|e^{\lambda_k s} < \infty\Bigr\}, \tag{2.2}$$

with norm $\|\phi\|_k = \sup_{s\leqslant 0}|\phi(s)|e^{\lambda_k s}$. For $\phi \in C_k$, let $\phi_t \in C_k$ be such that $\phi_t(s) = \phi(t+s)$, $s \in (-\infty, 0]$. Let $S_{k,0} \in \mathbb{R}_+$ and $\phi_k \in C_k$ such that $\phi_k(s) \geqslant 0, s \in (-\infty, 0]$. We consider solutions of system (1.5), $(S_1(t), E_{1t}, S_2(t), E_{2t}, \ldots, S_n(t), E_{nt})$, with initial conditions

$$S_k(0) = S_{k,0}, \qquad E_{k0} = \phi_k, \quad k = 1, 2, \ldots, n. \tag{2.3}$$

Standard theory of functional differential equations [13] implies $E_{kt} \in C_k$ for $t > 0$. We consider system (1.5) in the phase space

$$X = \prod_{k=1}^{n}(\mathbb{R} \times C_k). \tag{2.4}$$

It can be verified that solutions of (1.5) in X with initial conditions (2.3) remain nonnegative. In particular, $S_k(t) > 0$ for $t > 0$. From the first equation of (1.5), we obtain $S_k'(t) \leqslant \Lambda_k - d_k^S S_k(t)$. Hence, $\limsup_{t\to\infty} S_k(t) \leqslant \frac{\Lambda_k}{d_k^S}$. For each k, adding the two equations in (1.5) gives $(S_k(t) + E_{kt}(0))' \leqslant \Lambda_k - d_k^*(S_k(t) + E_{kt}(0))$, where $d_k^* = \min\{d_k^S, d_k^E + \epsilon_k\}$. Hence, $\limsup_{t\to\infty}(S_k(t) + E_{kt}(0)) \leqslant \frac{\Lambda_k}{d_k^*}$. Therefore, the following set is positively invariant for system (1.5),

$$\Theta = \left\{\bigl(S_1, E_1(\cdot), \ldots, S_n, E_n(\cdot)\bigr) \in X \;\middle|\; 0 \leqslant S_k \leqslant \frac{\Lambda_k}{d_k^S},\ 0 \leqslant S_k + E_k(0) \leqslant \frac{\Lambda_k}{d_k^*},\ E_k(s) \geqslant 0,\ s \in (-\infty, 0],\ k = 1, \ldots, n\right\}. \tag{2.5}$$

All positive semi-orbits in Θ are precompact in X [1], and thus have non-empty ω-limit sets. We have the following result.

Lemma 2.1. *All positive semi-orbits in Θ have non-empty ω-limit sets.*

Let

$$\mathring{\Theta} = \left\{\bigl(S_1, E_1(\cdot), \ldots, S_n, E_n(\cdot)\bigr) \in X \;\middle|\; 0 < S_k < \frac{\Lambda_k}{d_k^S},\ 0 < S_k + E_k(0) < \frac{\Lambda_k}{d_k^*},\ E_k(s) > 0,\ s \in (-\infty, 0],\ k = 1, \ldots, n\right\}. \tag{2.6}$$

It can be shown that $\mathring{\Theta}$ is the interior of Θ.

The equilibria of (1.5) are the same as those of the associated ODE system

$$S_k' = \Lambda_k - \sum_{j=1}^{n} \beta_{kj} a_j S_k E_j - d_k^S S_k,$$

$$E_k' = \sum_{j=1}^{n} \beta_{kj} a_j S_k E_j - \left(d_k^E + \epsilon_k\right) E_k, \quad k = 1, 2, \ldots, n. \tag{2.7}$$

System (2.7) is similar to a multi-group SIR model considered in [8] with E_k relabeled as I_k. Results established in [8] can be readily applied to system (2.7). In the positively invariant region

$$\Gamma = \left\{ (S_1, E_1, \ldots, S_n, E_n) \in \mathbb{R}_+^{2n} \;\middle|\; S_k \leqslant \frac{\Lambda_k}{d_k^S},\ S_k + E_k \leqslant \frac{\Lambda_k}{d_k^*},\ 1 \leqslant k \leqslant n \right\}, \tag{2.8}$$

system (2.7) has two possible equilibria: the disease-free equilibrium $P_0 = (S_1^0, 0, \ldots, S_n^0, 0)$, where $S_k^0 = \frac{\Lambda_k}{d_k^S}$, and the endemic equilibrium $P^* = (S_1^*, E_1^*, \ldots, S_n^*, E_n^*)$, where $S_k^*, E_k^* > 0$ and satisfy

$$\Lambda_k = \sum_{j=1}^{n} \beta_{kj} a_j S_k^* E_j^* + d_k^S S_k^*, \tag{2.9}$$

$$\sum_{j=1}^{n} \beta_{kj} a_j S_k^* E_j^* = \left(d_k^E + \epsilon_k\right) E_k^*. \tag{2.10}$$

We assume that the transmission matrix $B = (\beta_{kj})$ is irreducible. This is equivalent to assuming that for any two distinct groups k and j, individuals in E_j can infect those in S_k directly or indirectly. The following result is proved in [8].

Proposition 2.2. *(See Guo, Li, Shuai [8].) Assume that $B = (\beta_{kj})$ is irreducible.*

(1) *If $\mathcal{R}_0 \leqslant 1$, then P_0 is the only equilibrium for system (2.7) and it is globally asymptotically stable in Γ.*
(2) *If $\mathcal{R}_0 > 1$, then P_0 is unstable and there exists a unique endemic equilibrium P^* for system (2.7). Furthermore, P^* is globally asymptotically stable in the interior of Γ.*

Since the delay system (1.5) and the ODE system (2.7) share the same equilibria, the following result follows from Proposition 2.2.

Proposition 2.3. *Assume that $B = (\beta_{kj})$ is irreducible.*

(1) *If $\mathcal{R}_0 \leqslant 1$, then P_0 is the only equilibrium for system (1.5) in Θ.*
(2) *If $\mathcal{R}_0 > 1$, then there exist two equilibria for system (1.5) in Θ: the disease-free equilibrium P_0 and a unique endemic equilibrium P^* defined by Eqs. (2.9) and (2.10).*

3. Main result

The global dynamics of system (1.5) are completely established in the following result.

Theorem 3.1. *Assume that $B = (\beta_{kj})$ is irreducible.*

(1) *If $\mathcal{R}_0 \leqslant 1$, then the disease-free equilibrium P_0 of system (1.5) is globally asymptotically stable in Θ. If $\mathcal{R}_0 > 1$, then P_0 is unstable.*
(2) *If $\mathcal{R}_0 > 1$, then the endemic equilibrium P^* of system (1.5) is globally asymptotically stable in $\mathring{\Theta}$.*

Biologically, Theorem 3.1 implies that, if the basic reproduction number $\mathcal{R}_0 \leqslant 1$, then the disease always dies out from all groups; if $\mathcal{R}_0 > 1$, then the disease always persists in all groups at the unique endemic equilibrium level, irrespective of the initial conditions. The proof of the first part of Theorem 3.1 will be given in the next section, and the second part in Section 5.

Theorem 3.1 includes several previous results. Choose the kernel function as

$$f_k(r) = \epsilon_k e^{-(d_k^I + \gamma_k) r}$$

and let $\tilde{I}_k = \int_{r=0}^{\infty} f_k(r) E_k(t-r)\,dr$. Then (1.5) gives

$$S_k' = \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \tilde{I}_j - d_k^S S_k, \qquad E_k' = \sum_{j=1}^{n} \beta_{kj} S_k \tilde{I}_j - \big(d_k^E + \epsilon_k\big) E_k.$$

Using integration by parts we obtain

$$\tilde{I}_k' = \int_{r=0}^{\infty} f_k(r) \frac{\partial E_k(t-r)}{\partial t}\,dr = -\int_{r=0}^{\infty} f_k(r) \frac{\partial E_k(t-r)}{\partial r}\,dr = \epsilon_k E_k - \big(d_k^I + \gamma_k\big)\tilde{I}_k.$$

System (1.5) is thus reduced to a multi-group SEIR model governed by the system of ordinary differential equations considered in [9]. Note that

$$a_k = \int_{r=0}^{\infty} f_k(r)\,dr = \frac{\epsilon_k}{d_k^I + \gamma_k},$$

the basic reproduction number in (1.7) becomes

$$\mathcal{R}_0 = \rho\left(\frac{\beta_{kj}\epsilon_k \Lambda_k}{(d_k^E + \epsilon_k)(d_k^I + \gamma_k)\, d_k^S}\right)_{1\leqslant k, j\leqslant n},$$

which agrees with that given in [8,9]. Thus the global stability results in [8,9] are special cases of Theorem 3.1.

In the case $n = 1$, system (1.5) reduces to a single-group SEIR or SIR model with distributed delays studied in [3–5,18–20, 22]. Theorem 3.1 generalizes the global stability results in [19,20] to multi-group models.

4. Proof of Theorem 3.1(1)

Since B is irreducible, we know that matrix

$$N = \left(\frac{\beta_{kj} S_k^0 a_j}{d_k^E + \epsilon_k}\right)_{n\times n}$$

is also irreducible, and has a positive left eigenvector $(\omega_1, \omega_2, \ldots, \omega_n)$ corresponding to the spectral radius $\rho(N) > 0$. In particular, $\rho(N) = \rho(M_0)$, where M_0 is defined in (1.6), and thus $\rho(N) = \mathcal{R}_0 \leqslant 1$. Let

$$c_k = \frac{\omega_k}{d_k^I + \gamma_k} > 0 \quad \text{and} \quad \alpha_k(r) = \int_{\sigma=r}^{\infty} f_k(\sigma)\,d\sigma.$$

Consider a Lyapunov functional

$$L = \sum_{k=1}^{n} c_k \left(S_k - S_k^0 - S_k^0 \ln\frac{S_k}{S_k^0} + E_k + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} \alpha_j(r) E_j(t-r)\,dr\right). \tag{4.1}$$

Note that $\Lambda_k = d_k^S S_k^0$, $\alpha_k(0) = \int_{\sigma=0}^{\infty} f_k(\sigma)\,d\sigma = a_k$, and $\frac{S_k}{S_k^0} + \frac{S_k^0}{S_k} \geqslant 2$ with equality holding if and only if $S_k = S_k^0$. Differentiating L along the solution of system (1.5) and using integration by parts, we obtain

$$\begin{aligned}
L' &= \sum_{k=1}^{n} c_k \Bigg(\Lambda_k - d_k^S S_k - \Lambda_k \frac{S_k^0}{S_k} + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} f_j(r) E_j(t-r)\,dr + d_k^S S_k^0 \\
&\qquad - \big(d_k^E + \epsilon_k\big) E_k + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} \alpha_j(r) \frac{\partial E_j(t-r)}{\partial t}\,dr\Bigg) \\
&= \sum_{k=1}^{n} c_k \Bigg[d_k^S S_k^0\left(2 - \frac{S_k}{S_k^0} - \frac{S_k^0}{S_k}\right) + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} f_j(r) E_j(t-r)\,dr \\
&\qquad - \big(d_k^E + \epsilon_k\big) E_k + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} \alpha_j(r)\left(-\frac{\partial E_j(t-r)}{\partial r}\right) dr\Bigg]
\end{aligned}$$

$$= \sum_{k=1}^{n} c_k \Bigg[d_k^S S_k^0 \bigg(2 - \frac{S_k}{S_k^0} - \frac{S_k^0}{S_k} \bigg) + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr$$

$$- \big(d_k^E + \epsilon_k\big) E_k + \sum_{j=1}^{n} \beta_{kj} S_k^0 \bigg(a_j E_j - \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr \bigg) \Bigg]$$

$$\leqslant \sum_{k=1}^{n} \frac{\omega_k}{d_k^I + \gamma_k} \Bigg(\sum_{j=1}^{n} \beta_{kj} a_j S_k^0 E_j - \big(d_k^E + \epsilon_k\big) E_k \Bigg) = (\omega_1, \omega_2, \ldots, \omega_n)(NE - E)$$

$$= \big(\rho(N) - 1\big)(\omega_1, \omega_2, \ldots, \omega_n) E \leqslant 0, \quad \text{if } \mathcal{R}_0 \leqslant 1. \tag{4.2}$$

Here $E(t) = (E_1(t), E_2(t), \ldots, E_n(t))^T$. Denote

$$Y = \big\{ \big(S_1, E_1(\cdot), \ldots, S_n, E_n(\cdot)\big) \in \Theta \;\big|\; L' = 0 \big\},$$

and Z be the largest compact invariant set in Y. We will show $Z = \{P_0\}$. From inequality (4.2) and $c_k > 0$, $L' = 0$ implies $2 - \frac{S_k(t)}{S_k^0} - \frac{S_k^0}{S_k(t)} = 0$ for all $1 \leqslant k \leqslant n$ and $t \geqslant 0$, and thus $S_k(t) \equiv S_k^0 = \frac{\Lambda_k}{d_k^S}$. Hence, from the first equation of (1.5), we obtain

$$\sum_{j=1}^{n} \beta_{kj} \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr = 0,$$

and thus

$$\beta_{kj} \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr = 0,$$

for $1 \leqslant k, j \leqslant n$. Then, by irreducibility of B, for each j, there exists $k \neq j$ such that $\beta_{kj} \neq 0$, thus

$$\int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr = 0.$$

This implies that in Z, $E_{jt}(s) = 0$, $s \in (-\infty, 0]$, $j = 1, 2, \ldots, n$. Therefore, $Z = \{P_0\}$.

Using Lemma 2.1 and the LaSalle–Lyapunov Theorem (see [16, Theorem 3.4.7] or [10, Theorem 5.3.1]), we conclude that P_0 is globally attractive in Θ if $\mathcal{R}_0 \leqslant 1$. Furthermore, it can be verified that P_0 is locally stable using the same proof as one for Corollary 5.3.1 in [10]. In fact, we can show that there exists a nonnegative monotone increasing continuous function $a(r)$ such that $a(|(S_1(t), E_1(t), \ldots, S_n(t), E_n(t))|) \leqslant L(S_1(t), E_{1t}, \ldots, S_n(t), E_{nt}) \leqslant L(S_1(0), E_{10}, \ldots, S_n(0), E_{n0})$. Therefore, P_0 is globally asymptotically stable if $\mathcal{R}_0 \leqslant 1$. On the other hand, if $\mathcal{R}_0 > 1$, then $-L$ serves as a Lyapunov functional for system (1.5). The same proof as in Theorem 5.3.3 of [10] can be used to show that P_0 is unstable.

5. Proof of Theorem 3.1(2)

The global stability of the endemic equilibrium of the single-group model with delays has been proved in [19,20]. In the following, we consider the case $n \geqslant 2$. Let $P^* = (S_1^*, E_1^*, \ldots, S_n^*, E_n^*)$ denote the unique endemic equilibrium of system (1.5). Set

$$\bar{\beta}_{kj} = \beta_{kj} a_j S_k^* E_j^*, \quad 1 \leqslant k, j \leqslant n,\ n \geqslant 2, \tag{5.1}$$

and

$$\overline{B} = \begin{bmatrix} \sum_{l \neq 1} \bar{\beta}_{1l} & -\bar{\beta}_{21} & \cdots & -\bar{\beta}_{n1} \\ -\bar{\beta}_{12} & \sum_{l \neq 2} \bar{\beta}_{2l} & \cdots & -\bar{\beta}_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{\beta}_{1n} & -\bar{\beta}_{2n} & \cdots & \sum_{l \neq n} \bar{\beta}_{nl} \end{bmatrix}. \tag{5.2}$$

Note that $\overline{B}$ is the Laplacian matrix of the matrix $(\bar{\beta}_{kj})$ (see Appendix A). Since (β_{kj}) is irreducible, matrices $(\bar{\beta}_{kj})$ and $\overline{B}$ are also irreducible. Let C_{kj} denote the cofactor of the (k, j) entry of $\overline{B}$. We know that system $\overline{B} v = 0$ has a positive solution $v = (v_1, v_2, \ldots, v_n)$, where $v_k = C_{kk} > 0$ for $k = 1, 2, \ldots, n$, by Theorem A of Appendix A. Consider a Lyapunov functional

$$V = V_1 + V_2, \tag{5.3}$$

where

$$V_1 = \sum_{k=1}^{n} v_k \left(S_k - S_k^* - S_k^* \ln \frac{S_k}{S_k^*} + E_k - E_k^* - E_k^* \ln \frac{E_k}{E_k^*} \right), \tag{5.4}$$

$$V_2 = \sum_{k,j=1}^{n} v_k \beta_{kj} S_k^* \int_{r=0}^{\infty} \alpha_j(r) \left(E_j(t-r) - E_j^* - E_j^* \ln \frac{E_j(t-r)}{E_j^*} \right) dr, \tag{5.5}$$

and

$$\alpha_j(r) = \int_{\sigma=r}^{\infty} f_j(\sigma)\, d\sigma.$$

Differentiating V_1 along the solution of system (1.5) and using equilibrium equations (2.9) and (2.10), we obtain

$$\begin{aligned} V_1' &= \sum_{k=1}^{n} v_k \Bigg(\Lambda_k - d_k^S S_k - \frac{\Lambda_k S_k^*}{S_k} + \sum_{j=1}^{n} \beta_{kj} S_k^* \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr + d_k^S S_k^* \\ &\quad - \left(d_k^E + \epsilon_k\right) E_k - \frac{E_k^*}{E_k} \sum_{j=1}^{n} \beta_{kj} S_k \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr + \left(d_k^E + \epsilon_k\right) E_k^* \Bigg) \\ &= \sum_{k=1}^{n} v_k \Bigg[d_k^S S_k^* \left(2 - \frac{S_k^*}{S_k} - \frac{S_k}{S_k^*} \right) + \sum_{j=1}^{n} \beta_{kj} S_k^* E_j^* \Bigg(a_j \left(2 - \frac{S_k^*}{S_k} - \frac{E_k}{E_k^*} \right) \\ &\quad + \frac{1}{E_j^*} \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr - \frac{S_k E_k^*}{S_k^* E_k E_j^*} \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr \Bigg) \Bigg]. \end{aligned} \tag{5.6}$$

Differentiating V_2 along the solution of system (1.5) and using integration by parts, we obtain

$$\begin{aligned} V_2' &= \sum_{k,j=1}^{n} v_k \beta_{kj} S_k^* \int_{r=0}^{\infty} \alpha_j(r) \frac{\partial}{\partial t} \left(E_j(t-r) - E_j^* - E_j^* \ln \frac{E_j(t-r)}{E_j^*} \right) dr \\ &= \sum_{k,j=1}^{n} v_k \beta_{kj} S_k^* \int_{r=0}^{\infty} \alpha_j(r) \left[-\frac{\partial}{\partial r} \left(E_j(t-r) - E_j^* - E_j^* \ln \frac{E_j(t-r)}{E_j^*} \right) \right] dr \\ &= \sum_{k,j=1}^{n} v_k \beta_{kj} S_k^* E_j^* \left(\frac{a_j E_j}{E_j^*} - \frac{1}{E_j^*} \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr - \int_{r=0}^{\infty} f_j(r) \ln \frac{E_j(t)}{E_j(t-r)}\, dr \right). \end{aligned} \tag{5.7}$$

Combining (5.6) and (5.7) and using expression (5.1), we have

$$\begin{aligned} V' &= \sum_{k=1}^{n} v_k d_k^S S_k^* \left(2 - \frac{S_k^*}{S_k} - \frac{S_k}{S_k^*} \right) + \sum_{k,j=1}^{n} v_k \beta_{kj} S_k^* E_j^* \Bigg[a_j \left(2 - \frac{S_k^*}{S_k} - \frac{E_k}{E_k^*} + \frac{E_j}{E_j^*} \right) \\ &\quad - \frac{S_k E_k^*}{S_k^* E_k E_j^*} \int_{r=0}^{\infty} f_j(r) E_j(t-r)\, dr - \int_{r=0}^{\infty} f_j(r) \ln \frac{E_j(t)}{E_j(t-r)}\, dr \Bigg] \\ &\leqslant \sum_{k,j=1}^{n} v_k \beta_{kj} S_k^* E_j^* \int_{r=0}^{\infty} f_j(r) \Bigg[\frac{E_j}{E_j^*} - \frac{E_k}{E_k^*} - \ln \frac{S_k^*}{S_k} \cdot \frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*} \cdot \frac{E_j(t)}{E_j(t-r)} \\ &\quad + \left(1 - \frac{S_k^*}{S_k} + \ln \frac{S_k^*}{S_k} \right) + \left(1 - \frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*} + \ln \frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*} \right) \Bigg] dr \end{aligned}$$

$$\leqslant \sum_{k,j=1}^{n} v_k\bar{\beta}_{kj}\left(\frac{E_j}{E_j^*}-\frac{E_k}{E_k^*}\right)-\sum_{k,j=1}^{n} v_k\bar{\beta}_{kj}\ln\frac{E_k^*E_j}{E_kE_j^*}$$
$$=: H_1 - H_2. \tag{5.8}$$

In the above derivation, we have used two facts: $\frac{S_k^*}{S_k}+\frac{S_k}{S_k^*}\geqslant 2$ with equality holding if and only if $S_k=S_k^*$, and $1-x+\ln x\leqslant 0$ for all $x>0$ with equality holding if and only if $x=1$.

We first show $H_1\equiv 0$ for all $E_1,E_2,\dots,E_n>0$. It follows from $\overline{B}v=0$ that

$$\sum_{j=1}^{n}\bar{\beta}_{jk}v_j=\sum_{i=1}^{n}\bar{\beta}_{ki}v_k,$$

or, using $\bar{\beta}_{jk}=\beta_{jk}a_kS_j^*E_k^*$,

$$\sum_{j=1}^{n}\beta_{jk}a_kS_j^*E_k^*v_j=\sum_{i=1}^{n}\beta_{ki}a_iS_k^*E_i^*v_k,\quad k=1,2,\dots,n.$$

This implies that

$$\sum_{k,j=1}^{n}v_k\beta_{kj}a_jS_k^*E_j=\sum_{k=1}^{n}E_k\sum_{j=1}^{n}\beta_{jk}a_kS_j^*v_j=\sum_{k=1}^{n}\frac{E_k}{E_k^*}\sum_{i=1}^{n}\beta_{ki}a_iS_k^*E_i^*v_k=\sum_{k,j=1}^{n}v_k\beta_{kj}a_jS_k^*E_j^*\frac{E_k}{E_k^*},$$

and thus $H_1\equiv 0$ for all $E_1,E_2,\dots,E_n>0$.

Next we show $H_2\equiv 0$ for all $E_1,E_2,\dots,E_n>0$. Let G denote the directed graph associated with matrix $(\bar{\beta}_{kj})$. G has vertices $\{1,2,\dots,n\}$ with a directed arc (k,j) from k to j iff $\bar{\beta}_{kj}\neq 0$. $E(G)$ denotes the set of all directed arcs of G. Using Kirchhoff's Matrix-Tree Theorem (see Theorem A in Appendix A), we know that $v_k=C_{kk}$ can be interpreted as a sum of weights of all directed spanning subtrees T of G that are rooted at vertex k. Consequently, each term in $v_k\bar{\beta}_{kj}$ is the weight $w(Q)$ of a unicyclic subgraph Q of G, obtained from such a tree T by adding a directed arc (k,j) from the root k to vertex j. Note that the arc (k,j) is part of the unique cycle CQ of Q, and that the same unicyclic graph Q can be formed when each arc of CQ is added to a corresponding rooted tree T. Therefore, the double sum in H_2 can be reorganized as a sum over all unicyclic subgraphs Q containing vertices $\{1,2,\dots,n\}$, that is,

$$H_2=\sum_{Q}H_Q, \tag{5.9}$$

where

$$H_Q=w(Q)\cdot\sum_{(k,j)\in E(CQ)}\ln\frac{E_k^*E_j}{E_kE_j^*}=w(Q)\cdot\ln\left(\prod_{(k,j)\in E(CQ)}\frac{E_k^*E_j}{E_kE_j^*}\right). \tag{5.10}$$

Since $E(CQ)$ is the set of arcs of a cycle CQ, we have

$$\prod_{(k,j)\in E(CQ)}\frac{E_k^*E_j}{E_kE_j^*}=1,\quad\text{and thus}\quad \ln\left(\prod_{(k,j)\in E(CQ)}\frac{E_k^*E_j}{E_kE_j^*}\right)=0.$$

This implies $H_Q=0$ for each Q, and hence $H_2\equiv 0$ for all $E_1,E_2,\dots,E_n>0$. Therefore, we obtain $V'\leqslant 0$ for all $(S_1,E_1(\cdot),\dots,S_n,E_n(\cdot))\in\mathring{\Theta}$. Furthermore, if $\beta_{kj}\neq 0$, then, by (5.8), $V'=0$ implies

$$\left(1-\frac{S_k^*}{S_k}+\ln\frac{S_k^*}{S_k}\right)+\left(1-\frac{S_kE_k^*E_j(t-r)}{S_k^*E_kE_j^*}+\ln\frac{S_kE_k^*E_j(t-r)}{S_k^*E_kE_j^*}\right)=0,$$

for all $r\in[0,\infty)$ and $t>0$. Using the fact that $1-x+\ln x\leqslant 0$ for all $x>0$ with equality holding iff $x=1$, we obtain

$$S_k=S_k^*,\qquad\frac{E_k}{E_k^*}=\frac{E_j(t-r)}{E_j^*},\quad r\in[0,\infty),\ t>0. \tag{5.11}$$

Now let p and q denote any two distinct groups, namely, two distinct vertices of the directed graph G associated with the irreducible matrix $(\bar{\beta}_{kj})$. Then, by the strong connectivity of G, there exists an oriented path between p and q. Applying (5.11) to each arc (k,j) of such a path, we can see that

$$S_p=S_p^*,\qquad\frac{E_p(t-r)}{E_p^*}=\frac{E_q(t-r)}{E_q^*}=c,\quad r\in[0,\infty),\ t>0,\ \text{for all } p,q.$$

Therefore, $V' = 0$ if and only if

$$S_k = S_k^*, \qquad E_k(t-r) \equiv cE_k^*, \quad k = 1, 2, \ldots, n, \ r \in [0, \infty), \ t > 0, \tag{5.12}$$

where $c > 0$ is an arbitrary number. Substituting (5.12) into the first equation of system (1.5), we obtain

$$0 = \Lambda_k - c\sum_{j=1}^{n} \beta_{kj} a_j S_k^* E_j^* - d_k^S S_k^*. \tag{5.13}$$

The right-hand side of (5.13) is strictly decreasing in c. By (2.9), we know that (5.13) holds iff $c = 1$, namely at P^*. Therefore, the only compact invariant subset of the set where $V' = 0$ is the singleton $\{P^*\}$. By a similar argument as in Section 4, P^* is globally asymptotically stable in $\mathring{\Theta}$ if $R_0 > 1$. This establishes Theorem 3.1(2).

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Appendix A. Kirchhoff's Matrix-Tree Theorem

Given a nonnegative matrix $A = (a_{ij})$, the *directed graph* $G(A)$ associated with $A = (a_{ij})$ has vertices $\{1, 2, \ldots, n\}$ with a directed arc (i, j) from i to j iff $a_{ij} \neq 0$. It is *strongly connected* if any two distinct vertices are joined by an oriented path. Matrix A is irreducible if and only if $G(A)$ is strongly connected [6].

A *tree* is a connected graph with no cycles. A subtree T of a graph G is said to be *spanning* if T contains all the vertices of G. A *directed tree* is a tree in which each edge has been replaced by an arc directed one way or the other. A directed tree is said to be *rooted* at a vertex, called the root, if every arc is oriented in the direction towards to the root. An *oriented cycle* in a directed graph is a simple closed oriented path. A *unicyclic graph* is a directed graph consisting of a collection of disjoint rooted directed trees whose root are on an oriented cycle. We refer the reader to [21] for more details of these concepts.

For a given nonnegative matrix $A = (a_{ij})$, let

$$L = \begin{bmatrix} \sum_{l\neq 1} a_{1l} & -a_{21} & \cdots & -a_{n1} \\ -a_{12} & \sum_{l\neq 2} a_{2l} & \cdots & -a_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -a_{1n} & -a_{2n} & \cdots & \sum_{l\neq n} a_{nl} \end{bmatrix} \tag{A.1}$$

be the Laplacian matrix of the directed graph $G(A)$ and C_{ij} denote the cofactor of the (i, j) entry of L. For the linear system

$$Lv = 0, \tag{A.2}$$

the following result holds, see [9].

Theorem A *(Kirchhoff's Matrix-Tree Theorem). Assume that $n \geqslant 2$ and that A is irreducible. Then following results hold*:

(1) *The solution space of system* (A.2) *has dimension* 1, *with a basis* $(v_1, v_2, \ldots, v_n) = (C_{11}, C_{22}, \ldots, C_{nn})$.
(2) *For* $1 \leqslant k \leqslant n$,

$$C_{kk} = \sum_{T\in\mathbb{T}_k} w(T) = \sum_{T\in\mathbb{T}_k} \prod_{(r,m)\in E(T)} a_{rm} > 0, \tag{A.3}$$

where $\mathbb{T}_k$ is the set of all directed spanning subtrees of $G(A)$ that are rooted at vertex k, $w(T)$ is the weight of a directed tree T, and $E(T)$ denotes the set of directed arcs in T.

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