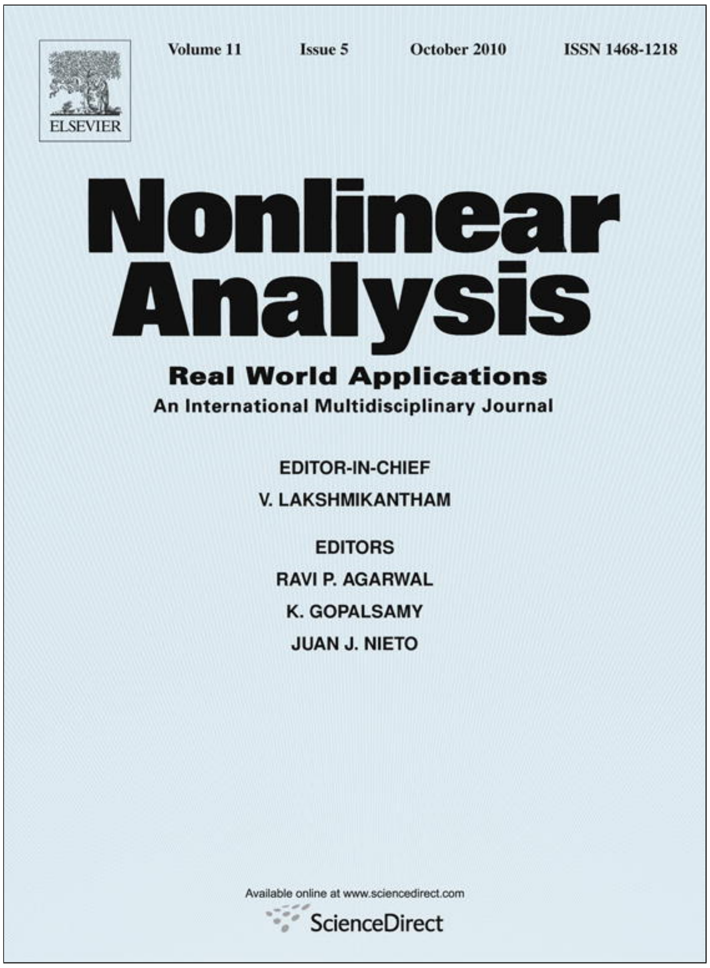

Volume 11 Issue 5 October 2010 ISSN 1468-1218

ELSEVIER

Nonlinear Analysis

Real World Applications

An International Multidisciplinary Journal

Nonlinear Analysis: Real World Applications 11 (2010) 3479–3490

Contents lists available at ScienceDirect

Nonlinear Analysis: Real World Applications

journal homepage: www.elsevier.com/locate/nonrwa

Global threshold property in an epidemic model for disease with latency spreading in a heterogeneous host population

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ARTICLE INFO

Article history:
Received 19 September 2008
Accepted 8 December 2009

Keywords:
Heterogenous host
Epidemic model
Latency
Basic reproduction number
Lyapunov function
Global stability

ABSTRACT

In this paper, a general mathematical model is proposed with detailed justifications to describe the spread of a disease with latency in a heterogeneous host population which includes many existing ones as special cases. For a simpler version that assumes an identical natural death rate for all groups, and with a gamma distribution for the latency, the model is shown to demonstrate the global threshold dynamics in terms of the basic reproduction number $\mathcal{R}_0$ of the model: if $\mathcal{R}_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable in the positive orthant, whereas if $\mathcal{R}_0 > 1$, a unique endemic equilibrium exists and is globally asymptotically stable in the interior of the positive orthant. The proofs of the main results make use of the theory of non-negative matrices, persistence theory in dynamical systems, Lyapunov functions and a subtle grouping technique in estimating the derivatives of Lyapunov functions guided by graph theory, which was recently developed and applied by several authors to some relateted epidemic models.

1. Introduction

One of the typical SIR models for infectious disease has the form

$$\begin{cases} S'(t) = \Lambda - \delta S(t) - \beta S(t)I(t) \\ I'(t) = \beta S(t)T(t) - (\delta + \epsilon + \gamma)I(t) \\ R'(t) = \gamma I(t) - \delta R(t) \end{cases} \tag{1.1}$$

where $S(t)$, $I(t)$ and $R(t)$ denote the populations of the susceptible, infectious and recovered classes respectively at time t. See. e.g., [1,2]. Here recovery may be natural or due to the treatment of infectious individuals. Also in the model, Λ is the recruitment rate, β is the transmission coefficient (average number of effective contacts an infective individual makes per unit time), δ is the natural death rate, ϵ is the disease caused death rate, and γ is the recovery rate. An underlining assumption for this model is that the disease has no latency, and thus, once infected, an individual immediately becomes infectious.

In the real word, many diseases do have a latent period. For example, tuberculosis including bovine tuberculosis (a disease spread from animal to animal mainly by direct contact) may take months to develop to the infectious stage. For such a disease, it is natural to introduce into the model an exposed class, consisting of those individuals that are infected but are not infectious yet. Denote by $E(t)$ the population of this class. Since the time it takes from the moment of new infection to the moment of becoming infectious may differ from individual to individual, it is indeed a random variable. Following

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1468-1218/$ – see front matter
doi:10.1016/j.nonrwa.2009.12.008

the approach in [3], we denote by $P(t)$ the probability (without taking death into account) that an exposed individual still remains in the exposed class t time units after entering the exposed class. Taking into consideration the natural death rate (assuming that the disease does not cause deaths during the latent period), we then have

$$E(t) = \int_0^t \beta S(u)I(u)e^{-\delta(t-u)}P(t-u)\,\mathrm{d}u. \tag{1.2}$$

By its biological meaning, $P(t)$ should be non-decreasing. Taking into account this and the consideration of accommodating those frequently used probability functions and the mathematical tractability, we assume that $P(t)$ satisfies that following:

(A) $P : [0, \infty) \to [0, 1]$ is non-increasing, piecewise continuous with possibly finitely many jumps and satisfy $P(0^+) = 1$, $\lim_{t\to\infty} P(t) = 0$ with $\int_0^\infty P(t)\,\mathrm{d}t$ positive and finite.

Differentiation to (1.2) leads to

$$E'(t) = \beta S(t)I(t) + \int_0^t \beta S(u)I(u)\mathrm{e}^{-\delta(t-u)}P'(t-u)\,\mathrm{d}u - \delta E(t). \tag{1.3}$$

The first term on the right hand side in (1.3) is the rate at which new infected individuals come into the exposed class, and the last term explains the natural deaths. The second term accounts for the rate at which the individuals move to the infectious class (noting that $P'(t-u) \le 0$ due to the property (A)) from the exposed class, implying that the second equation in (1.1) should be replaced by

$$I'(t) = -\int_0^t \beta S(u)I(u)\mathrm{e}^{-\delta(t-u)}P'(t-u)\,\mathrm{d}u - (\delta+\epsilon+\gamma)I(t). \tag{1.4}$$

Let $Q(t) = 1 - P(t)$, the probability that an exposed individual becomes infectious t time units after infection, and let $g(t) = Q'(t)$ which is non-decreasing under assumption (A). Then the above equation becomes

$$I'(t) = \int_0^t \beta S(u)I(u)\mathrm{e}^{-\delta(t-u)}g(t-u)\,\mathrm{d}u - (\delta+\epsilon+\gamma)I(t). \tag{1.5}$$

Replacing the second equation in (1.1) by (1.5) gives a model for diseases with latency

$$\begin{cases} S'(t) = \Lambda - \delta S(t) - \beta S(t)I(t) \\ I'(t) = \displaystyle\int_0^t \beta S(u)I(u)\mathrm{e}^{-\delta(t-u)}g(t-u)\,\mathrm{d}u - (\delta+\epsilon+\gamma)I(t) \\ R'(t) = \gamma I(t) - \delta R(t). \end{cases} \tag{1.6}$$

For a disease without latency, $Q(t) = 0$ for $t > 0$ and $Q(0^+) = 1$, reducing (1.6) to (1.1).

On the other hand, the host population for a disease is often heterogeneous. Therefore, when it comes to modeling of disease transmission in a heterogeneous host population, it is more reasonable and more desirable to divide the host population into groups. Groups can be formed in terms of education levels, ethnic backgrounds, gender, age, and professions etc. They can also be formed geographically, such as by schools, communities and cities. Such a division can better reflect the variance of within group transmission rates and the transmission rate between different groups. For example, for HIV/AIDS, the transmission rate within or to a higher education level group would be lower than that within or to a lower education level group; a flu can spread from one school to another due to after-school activities, but an inter-school transmission rate is usually lower than an intra-school transmission rate. For more and detailed justifications for multi-group disease models, see, e.g., [4–6] and the references therein.

For a heterogeneous host population, the disease can transmit within the same group as well as between groups. Modifying (1.6) in a straightforward way for such a situation lead to the following multi-group model for a disease with latency:

$$\begin{cases} S_k'(t) = \Lambda_k - \delta_k S_k - \displaystyle\sum_{j=1}^m \beta_{kj} S_k I_j, \\ I_k'(t) = \displaystyle\sum_{j=1}^m \beta_{kj} \int_0^t S_k(u)I_j(u)g_j(t-u)\mathrm{e}^{-\delta_j(t-u)}\mathrm{d}u - (\delta_k+\epsilon_k+\gamma_k)I_k, \\ R_k'(t) = \gamma_k I_k - \delta_k R_k, \quad k = 1, \ldots, m. \end{cases} \tag{1.7}$$

Here $S_k(t)$, $I_k(t)$ and $R_k(t)$ denote the numbers of susceptible, infectious, and recovered of individuals at time t in the k-th group, respectively. The non-negative constant β_{kj} is the transmission rate due to the contact of susceptible individuals in the k-th group with infectious individuals in the j-th group. The non-negative constants λ_k, δ_k, ϵ_k, γ_k are the recruitment rates, natural death rates, disease-caused death rates and recovery rates of in the k-th group, respectively. The function $g_k(t)$ is the probability density function for the time (a random variable) it takes for an infected individual in the k-th group to becomes infectious.

Since $R_k(t)$, $k = 1, \dots, m$, are decoupled from the S_k and I_k equations, we only need to consider the sub-system of (1.7) consisting of only the S_k and I_k equations of (1.7):

$$\begin{cases} S_k'(t) = \Lambda_k - \delta_k S_k - \sum_{j=1}^{m} \beta_{kj} S_k I_j, \\ I_k'(t) = \sum_{j=1}^{m} \beta_{kj} \int_0^t S_k(u) I_j(u) g_j(t-u) \mathrm{e}^{-\delta_j(t-u)} \mathrm{d}u - (\delta_k + \epsilon_k + \gamma_k) I_k, \quad k = 1, \dots, m. \end{cases} \tag{1.8}$$

To show the main idea and the approaches more clearly and conveniently, we consider a simpler case in which all groups share the same natural death rate: $\delta_j = \delta$ for $j = 1, \dots, m$. Moreover, we assume that the functions $g_j(u)$ are disease specific only, implying that $g_j(u) = g(u)$ for $j = 1, \dots, m$. In the rest of the paper, we choose the gamma distribution:

$$g(u) = g_{n,b}(u) \equiv \frac{u^{n-1}}{(n-1)! b^n} \mathrm{e}^{-u/b} \tag{1.9}$$

where $b > 0$ is a real number and $n > 1$ is an integer. The reason for this choice is that it is a widely used distribution and it can approximate several frequently used distributions. For example, as $b \to 0^+$, $g_{n,b}(u)$ approaches the Dirac delta function corresponding to the diseases without latency; and when $n = 1$, $g_{n,b}(u)$ becomes an exponentially decaying function corresponding to a typical SEIR multi-group model of ordinary differential equations studied in [5,4] where synchronization, in-phase and out-phase properties are explored via linearization.

Note that the basic demographic model for (1.8), that is, the S_k equations in the absence of disease, is of the form $S'(t) = \lambda - \delta S$ which has the dynamics of global convergence to a positive equilibrium $S^0 = \Lambda/\delta$. In the sequel, we will replace $\Lambda - \delta S$ by a general $\varphi(S)$ that preserves this global convergence property. In other words, in the remainder of this paper, we consider the system:

$$\begin{cases} S_k'(t) = \varphi_k(S_k) - \sum_{j=1}^{m} \beta_{kj} S_k I_j, \\ I_k'(t) = \sum_{j=1}^{m} \beta_{kj} \int_0^t S_k(u) I_j(u) g(t-u) \mathrm{e}^{-\delta(t-u)} \mathrm{d}u - (\delta + \epsilon_k + \gamma_k) I_k, \quad k = 1, \dots, m, \end{cases} \tag{1.10}$$

where $g(u)$ is given by (1.9) and φ_k is a C^1 non-increasing function and there exists $S_k^0 > 0$ such that

$$\varphi_k(S_k^0) = 0, \quad \varphi_k(u) > 0 \quad \text{for } 0 \le u < S_k^0, \quad \text{and} \quad \varphi_k(u) < 0 \quad \text{for } u > S_k^0. \tag{1.11}$$

In Section 2, by using the well-known "linear chain trick", we re-formulate the model system (1.10) into an equivalent ordinary differential equations system, about which the main results will be stated. More precisely, we will identify the basic reproduction number $\mathcal{R}_0$ for the model, and prove that this number completely determines the global dynamics of the model system, as stated in Theorem 2.1.

We point out that this work is motivated by Guo et al. [7] where a SIR type multi-group model was considered. When the function $g(u) = \delta(u)$, the Dirac function at 0, the model (1.10) reduces to a system of the form studied in [7]. The most difficult part is, as in the study of many epidemic models, the proof of the global asymptotic stability of the endemic equilibrium under $\mathcal{R}_0 > 1$. For this, we construct a Lyapunov function which is a very traditional approach. It is well-known that estimating the derivative of a Lyapunov function along the system as efficiently as possible is the key for this classical approach to work out, and better estimate gives better result. By combining the strategy in [7] based on graph theory for organizing terms in the derivative with some subtle skills in maximization of functions, we are able to obtain the optimal estimate leading to the global asymptotic stability of the endemic equilibrium. The same technique has also been successfully applied recently in [8,9] for models with delays in pathogen production within hosts; in [10] to an epidemic model with stage progression which corresponds a special case of (1.8) with $m = 1$ (one group) and $g(u)$ given by (1.9); in [11] to a model for diseases with latency in an homogeneous population, and in [12] to a two-group SIR model with random perturbation. We point out that recent work by [13] is also along this line, but the focus there is on the nonlinear incidence rates, and hence only negatively exponential decay functions are adopted for the probability density functions $g_k(t)$, $k = 1, 2, \dots, m$, leading to an SEIR model with a lower dimension ($3m$ versus $m(n+2)$ with $n \ge 1$).

2. Main results

In this section, we firstly use the "linear chain trick" to transfer (1.10) into a system of ordinary differential equations. To this end, we absorb the exponential term $\mathrm{e}^{-\delta u}$ into the delay kernel by defining

$$\hat{b} \equiv \frac{b}{1 + \delta b}.$$

The second equation in (1.10) can be rewritten as

$$I_k'(t)=\sum_{j=1}^{m}\frac{\beta_{kj}}{(1+\delta b)^n}\int_0^t S_k(u)I_j(u)g_{n,\hat{b}}(t-u)\mathrm{d}u-(\delta+\epsilon_k+\gamma_k)I_k. \tag{2.1}$$

For $l=1,\ldots,n$, let

$$y_{k,l}(t)=\sum_{j=1}^{m}\frac{\beta_{kj}\hat{b}}{(1+\delta b)^n}\int_0^t S_k(u)I_j(u)g_{l,\hat{b}}(t-u)\mathrm{d}u,\quad k=1,2,\ldots,m.$$

Then, for $l\in\{2,\ldots,n\}$,

$$\begin{aligned}y_{k,l}'(t)&=g_{l,\hat{b}}(0)\sum_{j=1}^{m}\frac{\beta_{kj}\hat{b}}{(1+\delta b)^n}S_k(t)I_j(t)+\sum_{j=1}^{m}\frac{\beta_{kj}\hat{b}}{(1+\delta b)^n}\int_{-\infty}^{t}\frac{(l-1)(t-u)^{l-2}}{(l-1)!\hat{b}^l}\mathrm{e}^{-(t-u)/\hat{b}}S_k(u)I_j(u)\mathrm{d}u\\&\quad-\sum_{j=1}^{m}\frac{\beta_{kj}\hat{b}}{(1+\delta b)^n}\int_{-\infty}^{t}\frac{(t-u)^{l-1}}{(l-1)!\hat{b}^{l+1}}\mathrm{e}^{-(t-u)/\hat{b}}S_k(u)I_j(u)\mathrm{d}u\\&=[y_{k,l-1}(t)-y_{k,l}(t)]/\hat{b}.\end{aligned} \tag{2.2}$$

For $l=1$, we have

$$y_{k,1}(t)=\sum_{j=1}^{m}\frac{\beta_{kj}\hat{b}}{(1+\delta b)^n}\int_{-\infty}^{t}\frac{\mathrm{e}^{-(t-u)/\hat{b}}}{\hat{b}}S_k(u)I_j(u)\mathrm{d}u,\quad k=1,2,\ldots,m,$$

yielding

$$\begin{aligned}y_{k,1}'(t)&=\sum_{j=1}^{m}\frac{\beta_{kj}}{(1+\delta b)^n}S_k(t)I_j(t)-\sum_{j=1}^{m}\frac{\beta_{kj}}{(1+\delta b)^n}\int_{-\infty}^{t}\frac{\mathrm{e}^{-(t-u)/\hat{b}}}{\hat{b}}S_k(u)I_j(u)\mathrm{d}u\\&=\sum_{j=1}^{m}\frac{\beta_{kj}}{(1+\delta b)^n}S_k(t)I_j(t)-\frac{1}{\hat{b}}y_{k,1}(t),\quad k=1,2,\ldots,m.\end{aligned} \tag{2.3}$$

Thus, the integro-differential system (1.10) is now equivalent to the following system of ordinary differential equations:

$$\begin{cases}S_k'=\varphi_k(S_k)-\sum_{j=1}^{m}\beta_{kj}S_kI_j,\\ y_{k,1}'=\frac{1}{(1+\delta b)^n}\sum_{j=1}^{m}\beta_{kj}S_kI_j-\frac{1}{\hat{b}}y_{k,1},\\ y_{k,2}'=\frac{1}{\hat{b}}(y_{k,1}-y_{k,2}), & k=1,2,\ldots,m.\\ \cdots\cdots\cdots\\ y_{k,n}'=\frac{1}{\hat{b}}(y_{k,n-1}-y_{k,n}),\\ I_k'=\frac{1}{\hat{b}}y_{k,n}-(\delta+\epsilon_k+\gamma_k)I_k.\end{cases} \tag{2.4}$$

It is easy to show (say, by Theorem 2.1 in page 81 on [14]) that for a set of non-negative initial values, the corresponding solution remains non-negative. Let $\epsilon>0$ be a given real number. By the hypothesis (1.11) on φ_k, for any initial condition in the non-negative orthant there exists a time $T>0$ such that for $t\geq T$ we have $S_k(t)\leq S_k^0+\epsilon$.

Let N_{φ_k} be the maximum of the function φ_k on $\mathbb{R}_+$, and let q be a positive real number such that $q>\hat{b}N_{\varphi_k}$. Denote by Y_k the k-th tube for the system (2.4), that is,

$$Y_k=(S_k,y_{k,1},y_{k,2},\ldots,y_{k,n},I_k).$$

By a similar argument to that in [8], we can show that the set D_ϵ defined by

$$D_\epsilon=\left\{(Y_1,Y_2,\ldots,Y_m)\in\mathbb{R}_+^{m(n+2)}\;\middle|\;\begin{array}{ll}S_k\leq S_k^0+\epsilon, & S_k+(1+\delta b)^n y_{k,1}\leq q+S_k^0,\\ y_{k,l}\leq\dfrac{q+S_k^0+l\epsilon}{(1+\delta b)^n}, & I_k\leq\dfrac{q+S_k^0+(n+1)\epsilon}{\hat{b}(1+\delta)^n(\delta+\epsilon_k+\gamma_k)},\\ k=1,2,\ldots,m, & \text{and for } l=2,3,\ldots,n\end{array}\right\}$$

is a forward invariant compact absorbing set for the system for $\epsilon > 0$, and that the set D_0 (i.e., when $\epsilon = 0$) is a forward invariant compact set.

From the condition (1.11), we know that system (1.10) always has the disease-free equilibrium $P^0 = (S_1^0, 0, S_2^0, 0, \ldots, S_m^0, 0)$, where S_k^0 given in (1.11). An endemic equilibrium P^* of (1.10) is one with the disease related components being positive, that is, P^* has the form $P^* = (S_1^*, I_1^*, S_2^*, I_2^*, \ldots, S_m^*, I_m^*) \in \mathbb{R}^{2m}$ with $S_k^* > 0, I_k^* > 0, k = 1, 2, \ldots, m$. Translating to the equivalent system (2.4), P^0 corresponding to the equilibrium for (2.4):

$$\overline{P}^0 = (S_1^0, 0, \ldots, 0, S_2^0, 0, \cdots, 0, \ldots, S_m^0, 0 \cdots, 0) \in \mathbb{R}^{m(n+2)} \tag{2.5}$$

and P^* corresponding to the equilibrium for (2.4):

$$\overline{P}^* = (S_1^*, y_{1,1}^*, \ldots, y_{1,n}^*, I_1^*, S_2^*, y_{2,1}^*, \ldots, y_{2,n}^*, I_2^*, \ldots, S_m^*, y_{m,1}^*, \ldots, y_{m,n}^*, I_m^*) \tag{2.6}$$

with

$$y_{k,l}^* = \hat{b}(\delta + \epsilon_k + \gamma_k) I_k^* > 0, \quad k = 1, \ldots, m, \ l = 1, \ldots, n. \tag{2.7}$$

In epidemic models, the existence of an endemic equilibrium (EE) is usually closely related to the stability of the disease free equilibrium (DFE) in the sense of equilibrium bifurcation: when the DFE is stable, then there is no EE; and when the DFE becomes unstable, then there will be an EE. The switch of stability of the DFE is usually described by the basic reproduction number—the average number of new infections caused by a single infectious individual during the mean infection time. For model system (2.4) (equivalently model (1.10)), by applying the theory in [15], we can obtain its basic reproduction number as $\mathcal{R}_0 = \rho(M^0)$, the spectral radius of the matrix $M^0 = (M_{ij}^0)_{m\times m}$ where

$$M_{ij}^0 = \frac{\beta_{ij} S_i^0}{(1+\delta b)^n (\delta + \epsilon_i + \gamma_i)}, \quad i, j = 1, \ldots, m. \tag{2.8}$$

We will show that when $\mathcal{R}_0 \le 1$ there is no endemic equilibrium and when $\mathcal{R}_0 > 1$ there is a unique endemic equilibrium. Moreover, in the former case, we will prove that the disease free equilibrium is globally asymptotically stable, while in the latter case, the endemic equilibrium is globally asymptotically stable. These are summarized in the following main theorem, stated in terms of system (2.4).

Theorem 2.1. *Assume that $B = (\beta_{ij})$ is irreducible. Then*

(i) *The disease free equilibrium $\overline{P}^0$ of system (2.4) given by (2.5) is globally asymptotically stable on $\mathbb{R}_+^{m(n+2)}$ if $\mathcal{R}_0 \le 1$, and is unstable if $\mathcal{R}_0 > 1$;*
(ii) *When $\mathcal{R}_0 > 1$, there exists a unique endemic equilibrium $\overline{P}^*$ for (2.4), in the form of (2.6) and (2.7), which is globally asymptotically stable on $\mathbb{R}_+^{m(n+2)}$ excepted for initial values satisfying $y_{k,l}(0) = 0$ for $k = 1, 2, \ldots, m$ and $l = 1, 2, \ldots, n$.*

By the equivalence, we have the following version for (1.10).

Theorem 2.2. *Assume that $B = (\beta_{ij})$ is irreducible. Then*

(i) *The disease free equilibrium P^0 of system (1.10) is globally asymptotically stable on $\mathbb{R}_+^{2m}$ if $\mathcal{R}_0 \le 1$, and is unstable if $\mathcal{R}_0 > 1$;*
(ii) *When $\mathcal{R}_0 > 1$, there exists a unique endemic equilibrium P^* for (1.10) which is globally asymptotically stable on $\mathbb{R}_+^{2m}$ excepted for initial values satisfying $I_k(0) = 0$ for $k = 1, 2, \ldots, m$.*

In Section 2, we will give the proof of Theorem 2.1. We point out that when $\varphi_k(u) = q_k - \lambda_k u$ and $g(u)$ is the Dirac delta function at zero, (i.e., $b \to 0^+$), (1.10) reduces to the multi-group SIR model studied in [7] and Theorem 2.1 reproduces the main results in [7].

3. Proof of main results

By the properties of D_ϵ and D_0 stated in Section 2, we only need to prove the global stability of $\overline{P}^0$ in D_0 when $\mathcal{R}_0 \le 1$, and the global stability of $\overline{P}^*$ in the interior of D_0 (denoted by IntD_0) when $\mathcal{R}_0 > 1$.

For $S = (S_1, \ldots, S_m) \in R_+^m$, let $M(S)$ be the $m \times m$ matrix defined by

$$M(S) = \left(\frac{\beta_{ij} S_i}{(1+\delta b)^n (\delta + \epsilon_i + \gamma_i)} \right)_{m\times m}.$$

It is obvious that $M^0 = M(S^0)$ where $S^0 = (S_1^0, S_2^0, \ldots, S_m^0)$ is specified in the assumption (A). Moreover, if $0 \le S_k \le S_k^0$ for $k = 1, \ldots, m$, then $0 \le M(S) \le M(S_0) = M^0$; and if $S \ne S^0$, then $M(S) < M^0$. Here, the inequalities for matrices are in the component-wise sense. On the other hand, since B is irreducible, using the theory of non-negative matrices in [16], we know that when $S_k > 0$ for $k = 1, \ldots, m$, $M(S)$ and M^0 are irreducible. Furthermore, $M(S) + M^0$ is also irreducible. Therefore, for $S \in D_0$ with $S \neq S^0$, $\rho(M(S)) < \rho(M^0) = \mathcal{R}_0$, and hence, $\rho(M(S)) < 1$ provided that $\mathcal{R}_0 \leq 1$. It follows that

$$M(S)I = I$$

only has the trivial solution $I = 0$ where $I = (I_1, \ldots, I_m)$, and thus, $\overline{P}^0$ is the only equilibrium of system (2.4) in the positive orthant if $\mathcal{R}_0 \leq 1$.

We now consider the stability of $\overline{P}^0$ in D_0 under $\mathcal{R}_0 \leq 1$. By the theory of non-negative matrices, $\rho(M^0)$ is an eigenvalue of M^0, corresponding to which, there is a positive left eigenvector $(\omega_1, \omega_2, \ldots, \omega_m)$, i.e.,

$$(\omega_1, \omega_2, \ldots, \omega_m)\rho(M^0) = (\omega_1, \omega_2, \ldots, \omega_m)M^0.$$

Using this positive eigenvector, we construct the following Lyapunov function

$$V_{DFE} = \sum_{k=1}^{m} \frac{\omega_k}{\delta + \epsilon_k + \gamma_k} \left(\sum_{j=1}^{n} y_{k,j} + I_k \right). \tag{3.1}$$

Computing the derivative of V_{FE} along the trajectories of (2.4) in D_0, we get

$$\begin{aligned} \dot{V}_{DFE} &= \sum_{k=1}^{m} \left[\sum_{j=1}^{m} \frac{\omega_k \beta_{kj}}{(1+\delta b)^n (\delta + \epsilon_k + \gamma_k)} S_k I_j - \omega_k I_k \right] \\ &= (\omega_1, \omega_2, \ldots, \omega_m)[M(S)I - I] \\ &\leq (\omega_1, \omega_2, \ldots, \omega_m)[M^0 I - I] \\ &= [\rho(M^0) - 1](\omega_1, \omega_2, \ldots, \omega_m)I. \end{aligned} \tag{3.2}$$

Thus, under the assumption $\mathcal{R}_0 = \rho(M^0) < 1$, $V'_{FE} \leq 0$; and $V'_{FE} = 0$ if and only if $I = 0$ and $S = S^0$. It can be verified that for (2.4), the only compact invariant subset of the set where $V'_{FE} = 0$ is the singleton $\{\overline{P}^0\}$. It follows from [17] that the disease free equilibrium $\overline{P}^0$ is asymptotically stable in the positive orthant.

If $\mathcal{R}_0 > 1$, then,

$$(\omega_1, \omega_2, \ldots, \omega_m)M_0 - (\omega_1, \omega_2, \ldots, \omega_m) = [\rho(M_0) - 1](\omega_1, \omega_2, \ldots, \omega_m) > 0.$$

By continuity, this implies that

$$V'_{FE} = (\omega_1, \omega_2, \ldots, \omega_m)[M(S)I - I] > 0$$

in a neighborhood of $\overline{P}^0$ in IntD_0, leading to the instability of $\overline{P}^0$. This completes the proof of the Part (i) of the Theorem 2.1.

Assume $\mathcal{R}_0 > 1$. Using the uniform persistence result from [18] and by a similar argument to that in the proof in [7], we can show that, when $\mathcal{R}_0 > 1$, the instability of $\overline{P}^0$ implies the uniform persistence of (2.4). This together with the dissipativity of (2.4) resulted from the forward invariant and compact property of D_0 stated in Section 2, implies (2.4) has an equilibrium in IntD_0, denoted by $\overline{P}^*$ (see,e.g, Theorem D.3 in [19]). In the rest of this paper, we prove that $\overline{P}^*$ is globally asymptotically stable.

For convenience of notations, set

$$\overline{\beta}_{ij} = \beta_{ij} S_i^* I_j^*, \quad 1 \leq i, j \leq m, \tag{3.3}$$

and

$$\overline{B} = \begin{bmatrix} \sum_{l \neq 1} \overline{\beta}_{1l} & -\overline{\beta}_{21} & \cdots & -\overline{\beta}_{m1} \\ -\overline{\beta}_{12} & \sum_{l \neq 2} \overline{\beta}_{2l} & \cdots & -\overline{\beta}_{m2} \\ \vdots & \vdots & \ddots & \vdots \\ -\overline{\beta}_{1m} & -\overline{\beta}_{2m} & \cdots & \sum_{l \neq m} \overline{\beta}_{ml} \end{bmatrix}. \tag{3.4}$$

Then, $\overline{B}$ is also irreducible. By Lemma 2.1 in [7], the solution space of the linear system

$$\overline{B}v = 0 \tag{3.5}$$

has dimension 1 and

$$(v_1, v_2, \ldots, v_m) = (c_{11}, \ldots, c_{mm}), \tag{3.6}$$

gives a base of this space where $c_{kk} > 0$ $(k = 1, 2, \dots, m)$ is the co-factor of the k-th diagonal entry of $\overline{B}$. Using the components of this base, we construct the following Lyapunov function:

$$V_{EE} = \sum_{k=1}^{m} \upsilon_k \left\{ S_k - S_k^* - S_k^* \ln \frac{S_k}{S_k^*} + (1+\delta b)^n \left[\sum_{j=1}^{n} \left(y_{k,j} - y_{k,j}^* - y_{k,j}^* \ln \frac{y_{k,j}}{y_{k,j}^*} \right) + I_k - I_k^* - I_k^* \ln \frac{I_k}{I_k^*} \right] \right\}.$$

This function has a linear part L_{EE} expressed as

$$L_{EE} = \sum_{k=1}^{m} \upsilon_k \left\{ S_k - S_k^* + (1+\delta b)^n \left[\sum_{j=1}^{n} \left(y_{k,j} - y_{k,j}^* \right) + I_k - I_k^* \right] \right\}.$$

The derivative of L_{EE} along the trajectories of (2.4) in $\mathrm{Int}D_0$ can be calculated as

$$L'_{EE} = \sum_{k=1}^{m} \upsilon_k \left[\varphi(S_k) - (1+\delta b)^n (\delta + \epsilon_k + \gamma_k) I_k \right]. \tag{3.7}$$

Using the above and Eq. (2.7), we can further calculate the derivatives of V_{EE} along the solutions of system (2.4) in $\mathrm{Int}D_0$ as follows:

$$\begin{aligned}
V'_{EE} &= L'_{EE} - \sum_{k=1}^{m} \upsilon_k \left\{ \frac{S_k^*}{S_k} S'_k + (1+\delta b)^n \left[\sum_{j=1}^{n} \frac{y_{k,j}^*}{y_{k,j}} y'_{k,j} + \frac{I_k^*}{I_k} I'_k \right] \right\} \\
&= \sum_{k=1}^{m} \upsilon_k [\varphi(S_k) - (1+\delta b)^n (\delta + \epsilon_k + \gamma_k) I_k] - \sum_{k=1}^{m} \upsilon_k \left\{ \left(\varphi(S_k) - \sum_{j=1}^{m} \beta_{kj} S_k I_j \right) \frac{S_k^*}{S_k} \right. \\
&\quad \left. - (1+\delta b)^n \left[\sum_{j=1}^{m} \frac{\beta_{kj}}{(1+\delta b)^n} \frac{S_k I_j y_{k,1}^*}{y_{k,1}} - \frac{y_{k,1}^*}{\hat{b}} - \frac{1}{\hat{b}} \sum_{i=2}^{n} y_{k,i}^* \left(\frac{y_{k,i-1}}{y_{k,i}} - 1 \right) + \frac{1}{\hat{b}} \frac{y_{k,n} I_k^*}{I_k} - (\delta + \epsilon_k + \gamma_k) I_k^* \right] \right\} \\
&= \sum_{k=1}^{m} \upsilon_k \left\{ \varphi(S_k) \left(1 - \frac{S_k^*}{S_k} \right) - \sum_{j=1}^{m} \beta_{kj} S_k^* I_j^* \frac{y_{k,1}^* S_k I_j}{y_{k,1} S_k^* I_j^*} - \frac{(1+\delta b)^n}{\hat{b}} \sum_{i=2}^{n} \frac{y_{k,i}^* y_{k,i-1}}{y_{k,i}} \right. \\
&\quad + \frac{(1+\delta b)^n}{\hat{b}} n y_k^* - \frac{(1+\delta b)^n}{\hat{b}} y_{k,n}^* \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} + (1+\delta b)^n (\delta + \epsilon_k + \gamma_k) I_k^* \\
&\quad \left. + \sum_{j=1}^{m} \beta_{kj} S_k^* I_j - (1+\delta b)^n (\delta + \epsilon + \gamma_k) I_k \right\}.
\end{aligned}$$

From (3.5), we know that

$$\sum_{j=1}^{m} \overline{\beta}_{kj} \upsilon_k = \sum_{j=1}^{m} \overline{\beta}_{jk} \upsilon_j, \quad k = 1, 2, \dots, m.$$

This, together with the fact that

$$\varphi_k(S_k^*) = \sum_{j=1}^{m} \beta_{kj} S_k^* I_j^* = \frac{(1+\delta b)^n}{\hat{b}} y_k^* = (1+\delta b)^n (\delta + \epsilon_k + \gamma_k) I_k^*, \quad k = 1, 2, \dots, m$$

leads to

$$\begin{aligned}
\sum_{k=1}^{m} \upsilon_k \sum_{j=1}^{m} \beta_{kj} S_k^* I_j &= \sum_{k=1}^{m} \sum_{j=1}^{m} (\beta_{jk} S_j{}^* \upsilon_j) I_k = \sum_{k=1}^{m} \left[\sum_{j=1}^{m} (\beta_{jk} S_j{}^* I_k^* \upsilon_j) \right] \frac{I_k}{I_k^*} \\
&= \sum_{k=1}^{m} \left[\sum_{j=1}^{m} (\overline{\beta}_{jk} \upsilon_j) \right] \frac{I_k}{I_k^*} = \sum_{k=1}^{m} \left[\sum_{j=1}^{m} (\overline{\beta}_{kj} \upsilon_k) \right] \frac{I_k}{I_k^*} \\
&= \sum_{k=1}^{m} \left[\sum_{j=1}^{m} (\beta_{kj} S_k^* I_j^*) \right] \frac{\upsilon_k I_k}{I_k^*} = \sum_{k=1}^{m} \upsilon_k (1+\delta b)^n (\delta + \epsilon_k + \gamma_k) I_k.
\end{aligned}$$

Therefore

$$V'_{EE} = \sum_{k=1}^{m} \upsilon_k \left\{ \varphi(S_k) \left(1 - \frac{S_k^*}{S_k} \right) - \sum_{j=1}^{m} \beta_{kj} S_k^* I_j^* \frac{y_{k,1}^* S_k I_j}{y_{k,1} S_k^* I_j^*} - \frac{(1+\delta b)^n}{\hat{b}} y_k^* \sum_{i=2}^{n} \frac{y_{k,i}^* y_{k,i-1}}{y_{k,i} y_{k,i-1}^*} \right.$$

$$
\begin{aligned}
& + \frac{(1+\delta b)^n}{\hat{b}} n y_k^* - \frac{(1+\delta b)^n}{\hat{b}} y_{k,n}^* \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} + \varphi(S_k^*) \Bigg\} \\
&= \sum_{k=1}^m v_k \Bigg\{ \varphi(S_k)\left(1 - \frac{S_k^*}{S_k}\right) - \left(\sum_{j=1}^m \beta_{kj} S_k^* I_j^*\right) \frac{y_{k,1}^* S_k I_j}{y_{k,1} S_k^* I_j^*} - \left(\sum_{j=1}^m \beta_{kj} S_k^* I_j^*\right) \sum_{i=2}^n \frac{y_{k,i}^* y_{k,i-1}}{y_{k,i} y_{k,i-1}^*} \\
& + n \sum_{j=1}^m \beta_{kj} S_k^* I_j^* - \left(\sum_{j=1}^m \beta_{kj} S_k^* I_j^*\right) \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} + \varphi(S_k^*) \Bigg\} \\
&= \sum_{k=1}^m v_k \Bigg\{ \varphi(S_k)\left(1 - \frac{S_k^*}{S_k}\right) - \varphi(S_k^*)\left(1 - \frac{S_k^*}{S_k}\right) \\
& + \sum_{j=1}^m \beta_{kj} S_k^* I_j^* \left[n + 2 - \frac{S_k^*}{S_k} - \frac{S_k I_j y_{k,1}^*}{S_k^* I_j^* y_{k,1}} - \sum_{i=2}^n \frac{y_{k,i}^* y_{k,i-1}}{y_{k,i} y_{k,i-1}^*} - \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} \right] \Bigg\} \\
&= \sum_{k=1}^m v_k \Bigg\{ \frac{(S_k - S_k^*)(\varphi_k(S_k) - \varphi_k(S_k^*))}{S_k} \\
& + \sum_{j=1}^m \overline{\beta}_{kj} \left[n + 2 - \frac{S_k^*}{S_k} - \frac{S_k I_j y_{k,1}^*}{S_k^* I_j^* y_{k,1}} - \sum_{i=2}^n \frac{y_{k,i-1} y_{k,i}^*}{y_{k,i-1}^* y_{k,i}} - \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} \right] \Bigg\} \\
&= \sum_{k=1}^m v_k \frac{(S_k - S_k^*)^2 \varphi_k'(u)}{S_k} + \sum_{k,j=1}^m v_k \overline{\beta}_{kj} \left[n + 2 - \frac{S_k^*}{S_k} - \frac{S_k I_j y_{k,1}^*}{S_k^* I_j^* y_{k,1}} - \sum_{i=2}^n \frac{y_{k,i-1} y_{k,i}^*}{y_{k,i-1}^* y_{k,i}} - \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} \right] \\
&\le \sum_{k,j=1}^m v_k \overline{\beta}_{kj} \left[n + 2 - \frac{S_k^*}{S_k} - \frac{S_k I_j y_{k,1}^*}{S_k^* I_j^* y_{k,1}} - \sum_{i=2}^n \frac{y_{k,i-1} y_{k,i}^*}{y_{k,i-1}^* y_{k,i}} - \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} \right] =: H_m \qquad (3.8)
\end{aligned}
$$

where $u \in [S_k, S_k^*] \subset [0, S_k^0]$ or $u \in [S_k^*, S_k] \subset [0, S_k^0]$. Obviously, the equality in (3.8) holds if and only if $S_k = S_k^*$ for $k = 1, \ldots, m$.

We need to show

$$
\begin{cases} V_{EE}' \le 0 & \text{for } (S_k, y_{k,1}, \ldots, y_{k,m}, I_k) \in \mathrm{Int}\mathbb{R}_+^{n+2} \qquad \text{for } k = 1, 2, \ldots, m; \\ V_{EE}' = 0 & \text{if and only if } (S_k, y_{k,1}, y_{k,2}, \ldots, y_{k,n}, I_k) = (S_k^*, y_{k,1}^*, y_{k,2}^*, \ldots, y_{k,n}^*, I_k^*), \quad k = 1, \ldots, m. \end{cases} \qquad (3.9)
$$

The proof of (3.9) for a general m requires more preparations for notions and results from graph theory (see, e.g., [7] for a proof for general m but for a special case of model (1.10)). In the following, we only give the proofs of (3.9) for $m = 1$, $m = 2$ and $m = 3$, which would give a reader the basic yet clear ideas without being hidden by the complexity of terms caused by larger values of m.

When $m = 1$, $H_1 \le 0$ is a direct result of the inequality between the arithmetical mean and the geometrical mean, and H_1 vanishes if and only if

$$(S_1, y_{1,1}, y_{1,2}, \ldots, y_{1,n}, I_1) = (S_1^*, y_{1,1}^*, y_{1,2}^*, \ldots, y_{1,n}^*, I_1^*).$$

This confirms (3.9) for $m = 1$.

When $m = 2$, we have

$$H_2 = \sum_{k,j=1}^2 v_k \overline{\beta}_{kj} \left[n + 2 - \frac{S_k^*}{S_k} - \frac{S_k I_j y_{k,1}^*}{S_k^* I_j^* y_{k,1}} - \sum_{i=2}^n \frac{y_{k,i-1} y_{k,i}^*}{y_{k,i-1}^* y_{k,i}} - \frac{y_{k,n} I_k^*}{y_{k,n}^* I_k} \right].$$

Formula (3.6) gives $v_1 = \overline{\beta}_{21}$ and $v_2 = \overline{\beta}_{12}$ in this case. Expanding H_2 yields

$$
\begin{aligned}
H_2 &= \overline{\beta}_{21}\overline{\beta}_{11} \left(n + 2 - \frac{S_1^*}{S_1} - \frac{S_1 I_1 y_{1,1}^*}{S_1^* I_1^* y_{1,1}} - \sum_{i=2}^n \frac{y_{1,i-1} y_{1,i}^*}{y_{1,i-1}^* y_{1,i}} - \frac{y_{1,n} I_1^*}{y_{1,n}^* I_1} \right) \\
&+ \overline{\beta}_{21}\overline{\beta}_{12} \left(n + 2 - \frac{S_1^*}{S_1} - \frac{S_1 I_2 y_{1,1}^*}{S_1^* I_2^* y_{1,1}} - \sum_{i=2}^n \frac{y_{1,i-1} y_{1,i}^*}{y_{1,i-1}^* y_{1,i}} - \frac{y_{1,n} I_1^*}{y_{1,n}^* I_1} \right) \\
&+ \overline{\beta}_{12}\overline{\beta}_{21} \left(n + 2 - \frac{S_2^*}{S_2} - \frac{S_2 I_1 y_{2,1}^*}{S_2^* I_1^* y_{2,1}} - \sum_{i=2}^n \frac{y_{2,i-1} y_{2,i}^*}{y_{2,i-1}^* y_{2,i}} - \frac{y_{2,n} I_2^*}{y_{2,n}^* I_2} \right)
\end{aligned}
$$

$$
\begin{aligned}
&+\overline{\beta}_{12}\overline{\beta}_{22}\left(n+2-\frac{S_2^*}{S_2}-\frac{S_2I_2y_{2,1}^*}{S_2^*I_2^*y_{2,1}}-\sum_{i=2}^{n}\frac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}-\frac{y_{2,n}I_2^*}{y_{2,n}^*I_2}\right)\\
&=\overline{\beta}_{21}\overline{\beta}_{11}\left(n+2-\frac{S_1^*}{S_1}-\frac{S_1I_1y_{1,1}^*}{S_1^*I_1^*y_{1,1}}-\sum_{i=2}^{n}\frac{y_{1,i-1}y_{1,i}^*}{y_{1,i-1}^*y_{1,i}}-\frac{y_{1,n}I_1^*}{y_{1,n}^*I_1}\right)\\
&+\overline{\beta}_{12}\overline{\beta}_{22}\left(n+2-\frac{S_2^*}{S_2}-\frac{S_2I_2y_{2,1}^*}{S_2^*I_2^*y_{2,1}}-\sum_{i=2}^{n}\frac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}-\frac{y_{2,n}I_2^*}{y_{2,n}^*I_2}\right)\\
&+\overline{\beta}_{21}\overline{\beta}_{12}\left(2n+4-\frac{S_1^*}{S_1}-\frac{S_1I_2y_{1,1}^*}{S_1^*I_2^*y_{1,1}}-\sum_{i=2}^{n}\frac{y_{1,i-1}y_{1,i}^*}{y_{1,i-1}^*y_{1,i}}-\frac{y_{1,n}I_1^*}{y_{1,n}^*I_1}\right.\\
&\left.-\frac{S_2^*}{S_2}-\frac{S_2I_1y_{2,1}^*}{S_2^*I_1^*y_{2,1}}-\sum_{i=2}^{n}\frac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}-\frac{y_{2,n}I_2^*}{y_{2,n}^*I_2}\right).
\end{aligned}\tag{3.10}
$$

Again by the relation between the arithmetical mean and the geometrical mean, we obtain

$$
\overline{\beta}_{21}\overline{\beta}_{11}\left(n+2-\frac{S_1^*}{S_1}-\frac{S_1I_1y_{1,1}^*}{S_1^*I_1^*y_{1,1}}-\sum_{i=2}^{n}\frac{y_{1,i-1}y_{1,i}^*}{y_{1,i-1}^*y_{1,i}}-\frac{y_{1,n}I_1^*}{y_{1,n}^*I_1}\right)\le 0,\tag{3.11}
$$

$$
\overline{\beta}_{12}\overline{\beta}_{22}\left(n+2-\frac{S_2^*}{S_2}-\frac{S_2I_2y_{2,1}^*}{S_2^*I_2^*y_{2,1}}-\sum_{i=2}^{n}\frac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}-\frac{y_{2,n}I_2^*}{y_{2,n}^*I_2}\right)\le 0,\tag{3.12}
$$

and

$$
\overline{\beta}_{21}\overline{\beta}_{12}\left(2n+4-\frac{S_1^*}{S_1}-\frac{S_1I_2y_{1,1}^*}{S_1^*I_2^*y_{1,1}}-\sum_{i=2}^{n}\frac{y_{1,i-1}y_{1,i}^*}{y_{1,i-1}^*y_{1,i}}-\frac{y_{1,n}I_1^*}{y_{1,n}^*I_1}-\frac{S_2^*}{S_2}-\frac{S_2I_1y_{2,1}^*}{S_2^*I_1^*y_{2,1}}-\sum_{i=2}^{n}\frac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}-\frac{y_{2,n}I_2^*}{y_{2,n}^*I_2}\right)\le 0,\tag{3.13}
$$

which, together with (3.10), imply that $V'_{EE}\le H_2\le 0$. Moreover, by (3.8), (3.10)–(3.13), we see that $V'_{EE}=0$ if and only if $S_k=S_k^*$, $k=1,2$, and $H_2=0$. The irreducibility of matrix B implies $\overline{\beta}_{21}\overline{\beta}_{12}>0$, and consequently, $H_2=0$ if and only if

$$
\begin{cases}
\dfrac{S_1^*}{S_1}=\dfrac{S_1I_1y_{1,1}^*}{S_1^*I_1^*y_{1,1}}=\dfrac{y_{1,i-1}y_{1,i}^*}{y_{1,i-1}^*y_{1,i}}=\dfrac{y_{1,n}I_1^*}{y_{1,n}^*I_1};\\[2mm]
\dfrac{S_2^*}{S_2}=\dfrac{S_2I_2y_{2,1}^*}{S_2^*I_2^*y_{2,1}}=\dfrac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}=\dfrac{y_{2,n}I_2^*}{y_{2,n}^*I_2};\\[2mm]
\dfrac{S_1^*}{S_1}=\dfrac{S_1I_2y_{1,1}^*}{S_1^*I_2^*y_{1,1}}=\dfrac{y_{1,i-1}y_{1,i}^*}{y_{1,i-1}^*y_{1,i}}=\dfrac{y_{1,n}I_1^*}{y_{1,n}^*I_1}\\[2mm]
\dfrac{S_2^*}{S_2}=\dfrac{S_2I_1y_{2,1}^*}{S_2^*I_1^*y_{2,1}}=\dfrac{y_{2,i-1}y_{2,i}^*}{y_{2,i-1}^*y_{2,i}}=\dfrac{y_{2,n}I_2^*}{y_{2,n}^*I_2},
\end{cases}
\quad \text{for } i=2,3,\ldots,n\tag{3.14}
$$

By simple calculation, it follows from (3.8) and (3.14) that $V'_{EE}=0$ if and only if

$$
S_k=S_k^*,\qquad I_k=aI_k^*,\qquad y_{k,i}=\frac{1}{a}y_{ki}^*,\quad k=1,2,\ i=2,\ldots,n\tag{3.15}
$$

where a is a positive number. Substituting $S_k=S_k^*$ and $I_k=aI_k^*$ into the first equation of system (2.4), we obtain

$$
0=\varphi_k(S_k^*)-a\sum_{j=1}^{2}\beta_{kj}S_k^*I_j^*,\quad k=1,2.\tag{3.16}
$$

Since the right-hand-side of (3.16) is strictly decreasing in a, it follows that (3.16) holds if and only if $a=1$. Thus $I_k=I_k^*$ and $y_{k,i}=y_k^*$ for $k=1,2$ and $i=1,2,\ldots,n$. Hence, $V'_{EE}=0$ if and only if $S_k=S_k^*$, $y_{k,i}=y_{k,i}^*$ and $I_k=I_k^*$ for $k=1,2$ and $i=1,2,\ldots,n$, that is, at $\overline{P}^*$. This confirms (3.9) for the case $m=2$.

When $m=3$, we have

$$
H_3=\sum_{k,j=1}^{3}\upsilon_k\overline{\beta}_{kj}\left[n+2-\frac{S_k^*}{S_k}-\frac{S_kI_jy_{k,1}^*}{S_k^*I_j^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right].
$$

By (3.6) and simple calculation, we obtain

$$\begin{aligned} v_1 &= \overline{\beta}_{32}\overline{\beta}_{21} + \overline{\beta}_{31}\overline{\beta}_{21} + \overline{\beta}_{23}\overline{\beta}_{31}, \\ v_2 &= \overline{\beta}_{31}\overline{\beta}_{12} + \overline{\beta}_{13}\overline{\beta}_{32} + \overline{\beta}_{12}\overline{\beta}_{32}, \\ v_3 &= \overline{\beta}_{12}\overline{\beta}_{23} + \overline{\beta}_{21}\overline{\beta}_{13} + \overline{\beta}_{13}\overline{\beta}_{23}. \end{aligned} \tag{3.17}$$

Substituting expression of v_k in (3.17) into H_3, we observe that H_3 is the sum of $3^3 = 27$ terms of forms

$$\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kj}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_jy_{k,1}^*}{S_k^*I_j^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right), \tag{3.18}$$

or

$$\overline{\beta}_{rk}\overline{\beta}_{lk}\overline{\beta}_{kj}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_jy_{k,1}^*}{S_k^*I_j^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right), \tag{3.19}$$

where $\{r, l, k\}$ is a permutation of $\{1, 2, 3\}$, and $1 \le j \le 3$. Write the subindices of $\overline{\beta}_{ij}$'s in (3.18) and (3.19) in the form of transformations

$$\begin{pmatrix} r & l & k \\ l & k & j \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} r & l & k \\ k & k & j \end{pmatrix}, \tag{3.20}$$

respectively. When $j = k$, l or r, both transformations in (3.20) contain cycles of length 1, 2, or 3. In the following, the terms in H_3 will be grouped according to the lengths of cycles appearing in (3.20).

When $j = k$, both transformations in (3.20) have a 1-cycle $\begin{Bmatrix} * & * & k \\ * & * & k \end{Bmatrix}$, and the corresponding 9 terms of the forms (3.18) and (3.19) satisfy

$$\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kk}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_ky_{k,1}^*}{S_k^*I_k^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right) \le 0, \tag{3.21}$$

and

$$\overline{\beta}_{rk}\overline{\beta}_{lk}\overline{\beta}_{kk}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_ky_{k,1}^*}{S_k^*I_k^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right) \le 0. \tag{3.22}$$

When $j = r$, the first transformation in (3.20) produces two distinct 3-cycle patterns $\begin{Bmatrix} r & l & k \\ l & k & r \end{Bmatrix}$ and $\begin{Bmatrix} r & k & l \\ k & l & r \end{Bmatrix}$. Thus, there are 6 terms in H_3 of 3-cycle form, three of them correspond to each cycle pattern and hence have the same coefficients $\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kr}$ or $\overline{\beta}_{rk}\overline{\beta}_{kl}\overline{\beta}_{lr}$. Therefore, the sum of these six terms falls into two parts with each part being a sum of form

$$\begin{aligned} &\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kr}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_ry_{k,1}^*}{S_k^*I_r^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right) \\ &\quad+\overline{\beta}_{lk}\overline{\beta}_{kr}\overline{\beta}_{rl}\left(n+2-\frac{S_r^*}{S_r}-\frac{S_rI_ly_{r,1}^*}{S_r^*I_l^*y_{r,1}}-\sum_{i=2}^{n}\frac{y_{r,i-1}y_{r,i}^*}{y_{r,i-1}^*y_{r,i}}-\frac{y_{r,n}I_r^*}{y_{r,n}^*I_r}\right) \\ &\quad+\overline{\beta}_{kr}\overline{\beta}_{rl}\overline{\beta}_{lk}\left(n+2-\frac{S_l^*}{S_l}-\frac{S_lI_ky_{l,1}^*}{S_l^*I_k^*y_{l,1}}-\sum_{i=2}^{n}\frac{y_{l,i-1}y_{l,i}^*}{y_{l,i-1}^*y_{l,i}}-\frac{y_{l,n}I_l^*}{y_{l,n}^*I_l}\right) \\ &=\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kr}\Bigg(3n+6-\frac{S_k^*}{S_k}-\frac{S_kI_ry_{k,1}^*}{S_k^*I_r^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k} \\ &\quad-\frac{S_r^*}{S_r}-\frac{S_rI_ly_{r,1}^*}{S_r^*I_l^*y_{r,1}}-\sum_{i=2}^{n}\frac{y_{r,i-1}y_{r,i}^*}{y_{r,i-1}^*y_{r,i}}-\frac{y_{r,n}I_r^*}{y_{r,n}^*I_r}-\frac{S_l^*}{S_l}-\frac{S_lI_ky_{l,1}^*}{S_l^*I_k^*y_{l,1}}-\sum_{i=2}^{n}\frac{y_{l,i-1}y_{l,i}^*}{y_{l,i-1}^*y_{l,i}}-\frac{y_{l,n}I_l^*}{y_{l,n}^*I_l}\Bigg) \le 0. \end{aligned} \tag{3.23}$$

When $j = r$, the second transformation in (3.20) has a 2-cycle $\begin{Bmatrix} r & * & k \\ k & * & r \end{Bmatrix}$. Also, when $j = l$, both transformations in (3.20) have a 2-cycle $\begin{Bmatrix} * & l & k \\ * & k & l \end{Bmatrix}$. Thus, there are altogether 12 terms in H_3 corresponding to 2-cycle patterns. Each 2-cycle pattern corresponds to 2 terms in H_3 with the same coefficients (products of $\overline{\beta}$'s). These 12 terms can be grouped into 6 pairs and each pair has a sum of the form

$$\begin{aligned}
&\overline{\beta}_{rk}\overline{\beta}_{lk}\overline{\beta}_{kr}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_ry_{k,1}^*}{S_k^*I_r^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right)\\
&\quad+\overline{\beta}_{kr}\overline{\beta}_{lk}\overline{\beta}_{rk}\left(n+2-\frac{S_r^*}{S_r}-\frac{S_rI_ky_{r,1}^*}{S_r^*I_k^*y_{r,1}}-\sum_{i=2}^{n}\frac{y_{r,i-1}y_{r,i}^*}{y_{r,i-1}^*y_{r,i}}-\frac{y_{r,n}I_r^*}{y_{r,n}^*I_r}\right)\\
&=\overline{\beta}_{rk}\overline{\beta}_{lk}\overline{\beta}_{kr}\left(2n+4-\frac{S_k^*}{S_k}-\frac{S_kI_ry_{k,1}^*}{S_k^*I_r^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right.\\
&\quad\left.-\frac{S_r^*}{S_r}-\frac{S_rI_ky_{r,1}^*}{S_r^*I_k^*y_{r,1}}-\sum_{i=2}^{n}\frac{y_{r,i-1}y_{r,i}^*}{y_{r,i-1}^*y_{r,i}}-\frac{y_{r,n}I_r^*}{y_{r,n}^*I_r}\right)\le 0,
\end{aligned}\tag{3.24}$$

or

$$\begin{aligned}
&\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kl}\left(n+2-\frac{S_k^*}{S_k}-\frac{S_kI_ly_{k,1}^*}{S_k^*I_l^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right)\\
&\quad+\overline{\beta}_{rl}\overline{\beta}_{kl}\overline{\beta}_{lk}\left(n+2-\frac{S_l^*}{S_l}-\frac{S_lI_ky_{l,1}^*}{S_l^*I_k^*y_{l,1}}-\sum_{i=2}^{n}\frac{y_{l,i-1}y_{l,i}^*}{y_{l,i-1}^*y_{l,i}}-\frac{y_{l,n}I_l^*}{y_{l,n}^*I_l}\right)\\
&=\overline{\beta}_{rl}\overline{\beta}_{lk}\overline{\beta}_{kl}\left(2n+4-\frac{S_k^*}{S_k}-\frac{S_kI_ly_{k,1}^*}{S_k^*I_l^*y_{k,1}}-\sum_{i=2}^{n}\frac{y_{k,i-1}y_{k,i}^*}{y_{k,i-1}^*y_{k,i}}-\frac{y_{k,n}I_k^*}{y_{k,n}^*I_k}\right.\\
&\quad\left.-\frac{S_l^*}{S_l}-\frac{S_lI_ky_{l,1}^*}{S_l^*I_k^*y_{l,1}}-\sum_{i=2}^{n}\frac{y_{l,i-1}y_{l,i}^*}{y_{l,i-1}^*y_{l,i}}-\frac{y_{l,n}I_l^*}{y_{l,n}^*I_l}\right)\le 0.
\end{aligned}\tag{3.25}$$

In summary, each term in H_3 corresponds to a transformation in (3.20) which possesses a unique cycle of length 1, 2 or 3 and all terms in H_3 are accounted for in our grouping according to cycle patterns and lengths in (3.20). Therefore, we have shown $H_3 \le 0$. Thus, we see that $V'_{EE} = 0$ if and only if $S_k = S_k^*$, $k = 1, 2, 3$, and $H_3 = 0$. By the irreducibility of $B = (\beta_{ij})$ and a similar argument to that in [7], we know that if $S_k = S_k^*$, $k = 1, 2, 3$, then

$$H_3 = 0 \Leftrightarrow I_k = aI_k^*, \qquad y_{k,i} = \frac{1}{a}y_{k,i}^*, \quad k = 1, 2, 3 \text{ and } i = 1, 2, \ldots, n \tag{3.26}$$

where a is positive number. By the same argument as for the case $m = 2$, we derive that $a = 1$, implying that $I_k = I_k^*$ and $y_{k,i} = y_{k,i}^*$ for $k = 1, 2, 3$ and $i = 1, 2, \ldots, n$. Hence, $V'_{EE} = 0$ if and only if $S_k = S_k^*$, $y_{k,i} = y_{k,i}^*$ and $I_k = I_k^*$ for $k = 1, 2, 3$ and $i = 1, 2, \ldots, n$, that is, at $\overline{P}^*$. Therefore, V'_{EE} is negative along the solutions of (2.4) in $\mathrm{Int}D_0$ except at the endemic equilibrium $\{\overline{P}^*\}$. This completes the proof of Theorem 2.1.

4. Conclusions

In this paper, we have proposed a general epidemic model that allows heterogeneity of the host population and that has taken into consideration latency of the disease. The new model includes many existing ones as special cases. For a simpler version that assumes an identical natural death rate for all groups, and with a gamma distribution for the latency, the global dynamics of the model is fully determined by the basic reproduction number $\mathcal{R}_0$ of the model system: if $\mathcal{R}_0 \le 1$, the disease-free equilibrium is globally asymptotically stable in the positive orthant, whereas if $\mathcal{R}_0 > 1$, a unique endemic equilibrium exists and is globally asymptotically stable in the interior of the positive orthant. The former corresponds to the case in which the disease will eventually die out, and the latter case implies that the disease (with any initial inoculation) will persist in all groups of the population and will eventually settle at a constant level in each group.

Acknowledgements

The first author was supported by the China Scholarship Council, Hunan Province Natural Science Foundation (09JJ3009) and the Scientific Research Foundation for the Returned Overseas Chinese Scholars. The second author was supported by NSERC of Canada, NCE-MITACS of Canada and by PREA of Ontario.

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