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GLOBAL ANALYSIS ON A CLASS OF MULTI-GROUP SEIR MODEL WITH LATENCY AND RELAPSE

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Abstract. In this paper, we investigate the global dynamics of a multi-group SEIR epidemic model, allowing heterogeneity of the host population, delay in latency and delay due to relapse distribution for the human population. Our results indicate that when certain restrictions on nonlinear growth rate and incidence are fulfilled, the basic reproduction number $\Re_0$ plays the key role of a global threshold parameter in the sense that the long-time behaviors of the model depend only on $\Re_0$. The proofs of the main results utilize the persistence theory in dynamical systems, Lyapunov functionals guided by graph-theoretical approach.

1. **Introduction.** In recent decades, several authors have done a series of works to analyze the multi-group epidemic models, for example [13, 14, 21, 24, 25, 29, 36, 35]. Some of these models are mainly given by systems of ordinary differential equations, and delay differential equations for disease transmission dynamics in heterogeneous host populations [13, 14, 24, 25]. From both the mathematical and epidemiological points of view, multi-group models given by systems of differential equations account for many situations of heterogeneous environments of populations due to many factors: modes of transmission, contact patterns, gender, and professions etc. For example, (i) different contact models among children and adults for childhood diseases (e.g., measles and mumps), children and adults should be treated separately. (ii) different behaviors such as the numbers of sexual partners for some sexually transmitted diseases (e.g., HIV/AIDS, Herpes, Condyloma acuminatum). Host population are generally divided into several homogeneous groups. They can also be formed geographically, such as by schools, communities and cities, so that within-group and inter-group interactions could be modeled separately [24].

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For detailed justifications and more information for multi-group disease models (or other types of heterogeneity epidemic models), we refer the reader to some recent works, see, e.g., [5, 13, 14, 17, 21, 25, 31] and the references therein.

Several authors have analyzed the effect of heterogeneity in the local and global dynamics of the populations, in terms of permanence in each group, bifurcations, effects of group-targeted vaccination strategies on disease control and prevention, and several other features [9, 19, 12]. However, it is well known that global dynamics of multi-group models with higher dimensions, especially the situation for the endemic equilibrium when the threshold is greater than one, is a very challenging subject of intense theoretical analysis [5], if it is not impossible. Especially, Guo et al. [13] developed a graph-theoretic approach, which is known to be an effective tool for the global stability analysis of multi-group epidemic models. Subsequently, a series of good results were produced about multi-group epidemic models in [14, 25, 24, 29, 36, 35, 30]. In [25], the authors studied a class of multi-group SEIR models with distributed delays and bilinear transmission, and it is proved that the endemic equilibrium is globally asymptotically stable if the basic reproduction number is greater than one and without any other additional conditions.

It is more reasonable that many diseases do have a latency period [32]. For example, tuberculosis may take months to develop into the infectious stage. So, it is necessary to consider those individuals that are infected but not infectious yet. Moreover, heterogeneity in the host population can result from many factors during the spread of disease. For diseases such as human and bovine tuberculosis [3, 8, 27], and herpes (a human disease that is transmitted by close physical or sexual contact) [34], recovered individuals may revert back to the infective class due to reactivation of the latent infection or incomplete treatment [8, 34]. There are many clinical studies and evidences that many relapse phenomenon of disease is an important feature of some human and animal diseases, see e.g., [1, 11, 16, 27]. Based on these, it is of interest for us to investigate whether sustained oscillations are the result of models with delays of latency and relapse. This provides us with the motivation to conduct our work.

Under the assumption that the total population size is constant and taking into account the latency and the possibility of relapse, van den Driessche et al. [32] formulated and investigated the following model

$$\begin{cases} S'(t) = \ bN - \beta S(t)\dfrac{I(t)}{N} - bS(t), \\ E(t) = \ \displaystyle\int_0^t \beta S(\xi)\frac{I(\xi)}{N} e^{-b(t-\xi)} P(t-\xi)d\xi, \\ R'(t) = \ rI(t) - (\alpha+b)R(t), \\ I(t) = \ N - S(t) - E(t) - R(t), \end{cases} \tag{1}$$

where $S(t), E(t), I(t)$ and $R(t)$ are the population sizes of susceptible, exposed, infective, and recovered classes, respectively. $\alpha > 0$ is a constant rate at which an individual in the recovered class reverts to the infective class. $b > 0$ is the recruitment rate and the removal rate such that total population remains constant N. $\beta > 0$ denotes the average number of effective contacts of an infective individual per unit time, and $r > 0$ is the rate at which infective individuals recover. $P(t)$ describes the probability that an exposed individual still remains in the exposed class t time units after entering the exposed class, which is based on the fact that the time between new infection and the moment of becoming infectious may differ

from individual to individual. It is assumed in [32] that $P(t)$ satisfies the following reasonable properties.

($\mathbf{H}_1$): $P:\ [0,\infty)\to[0,1]$ is nonincreasing, piecewise continuous with possibly finitely many jumps, satisfies $P(0^+)=1$; $\lim\limits_{t\to\infty}P(t)=0$ and there exists a constant $\epsilon>0$ such that $0<\int_0^\infty P(t)dt<\epsilon$.

Note that the integral in (1) is in the Riemann-Stieltjes sense to allow for possible jump discontinuities of $P(t)$. In [32], van den Driessche et al. numerically verified the global stability of endemic equilibrium but the analytic proof is left as an open problem. Until recently, Liu et al. [26] gave a confirmed answer to the global stability of endemic equilibrium of model (1) with a general nonlinear incidence function $f(S)I$. The proof of main results in [26] used the method of Lyapunov functionals and LaSalle invariance principle, which has been successfully employed in [13, 14, 25].

In [33], van den Driessche and Zou proposed the following system to model a general relapse phenomenon in infectious diseases including herpes:

$$\begin{cases} S'(t) = & b-\beta S(t)I(t)-bS(t),\\ I'(t) = & -(b+r)I(t)+\beta I(t)\big[1-I(t)-\int_0^t rI(\xi)e^{-b(t-\xi)}P(t-\xi)d\xi\big]\\ & -\int_0^t rI(\xi)e^{-b(t-\xi)}d_tP(t-\xi)d\xi,\\ R'(t) = & -bR(t)+rI(t)+\int_0^t rI(\xi)e^{-b(t-\xi)}d_tP(t-\xi)d\xi, \end{cases} \tag{2}$$

where the parameters b,β,r are the same as in model (1). It is assumed that no individuals are initially in the recovered class, i.e., $R(0)=0$. The term $e^{-b(t-\xi)}$ accounts for the death of infective individuals. In model (2), $P(t)$ denotes the fraction of recovered individuals remaining in the recovered class t time units after recovery, which satisfies the assumption ($\mathbf{H}_1$).

By utilizing the theory of asymptotic autonomous system, the authors in [33] studied the dynamic behavior of system (2). Three particular forms for $P(t)$ are investigated, such as a negative exponential function, a function with compact support, and a step function. The multi-group model of (2) was proposed by Wang et al. in [36, 35] with general nonlinear incidence function $f(S)I$ and $f(S,I)$, respectively. An effective tool called graph-theoretic approach is developed in [13, 14], and it is used in the proof of global stability analysis of multi-group epidemic models of (2). As a special case, the global stability of (2) is established by constructing suitable Lyapunov functionals.

Motivated by the work in [13, 14, 26, 25, 32, 33, 29, 35, 36], we propose in the present paper a more general multi-group epidemic model to describe the disease spread in a heterogeneous host population with latency, relapse distribution and general incidence rate. We carry out rigorous mathematical analysis to investigate the global dynamics of the model by constructing suitable Lyapunov functionals. To the best of our knowledge none of the previous multi-group models considered delays in both disease latency and relapse. These concerns differentiate our model from other multi-group models and make it more realistic by allowing it to describe the effects of disease latency and relapse. In an effort to describe a model based on reasonable biological findings on nonlinear incidence function, we formulate our model using the form of $f(S)g(I)$ as used in [29]. Our general multi-group model,

which includes latency and relapse for host population, is formulated in the next section.

The main results in present paper demonstrate that the long time dynamical behaviors of this general model is completely determined by the basic reproduction number $\Re_0$, which is biologically defined by the spectral radius of next generation matrix. More specifically, if $\Re_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable and the disease dies out; if $\Re_0 > 1$, a unique endemic equilibrium exists and is globally asymptotically stable, and the disease persists at the endemic equilibrium. The proofs of the main results utilize construction of Lyapunov functionals and a subtle grouping technique in estimating the derivatives of Lyapunov functionals guided by graph theory, which laid out in [13, 14, 25, 24, 29]. It is very important to highlight the fact that the global stability analysis of such a multi-group epidemic model is thought to be more difficult than that of corresponding single-group epidemic models. As such, this work is of both mathematical and biological interest and importance.

The paper is organized as follows. In Section 2, taking into consideration latency and the possibility of relapse, we propose a multi-group SEIR epidemic model and present preliminary results. Our main results are stated and proved in Section 3. We show that the global dynamics are completely determined by the basic reproduction number. Summary and discussion are given in Section 4.

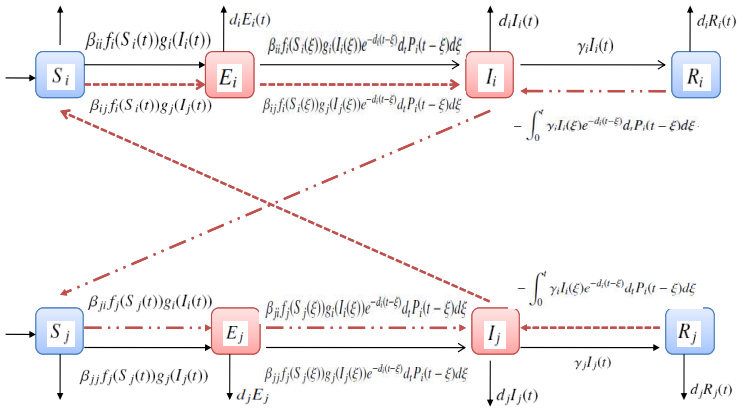

FIGURE 1. Transfer diagram for model (3).

2. **The model derivation and preliminaries.** Inspired by the aforementioned works, we consider a general model that captures the main features of both model (1) and model (2): latency, relapse distribution, and nonlinear intrinsic growth rate and incidence. In the model, the host population is divided into n homogeneous groups. For $i = 1, 2, \ldots, n$, S_i, E_i, I_i and R_i denote the susceptible, exposed, infective, and recovered populations in the i-th group, respectively. Within the i-th group, $\varphi_i(S_i)$ represents the intrinsic growth rate of S_i that accounts for both production and natural death of susceptible individuals. Typical assumptions on $\varphi_i(S_i)$ are the following:

($\mathbf{H_2}$): There exist $S_i^0 > 0$ such that $\varphi_i(S_i^0) = 0$ and

$$\left(\varphi_i(S_i) - \varphi_i(S_i^0)\right)(S_i - S_i^0) < 0, \text{ for } S_i \neq S_i^0, \quad i = 1, 2, \ldots, n.$$

The class of $\varphi_i(S_i)$ that satisfy $(\mathbf{H}_2)$ include both $\lambda_i - d_i^S S_i$ and $\lambda_i - d_i^S S_i + r_i S_i(1 - S_i/N_i)$, $\lambda_i, d_i^S, r_i, N_i > 0$ which have been widely used in the literature [2, 13, 20]. The disease incidence in the i-th group can be calculated as

$$\sum_{j=1}^{n} \beta_{ij} f_i(S_i(t)) g_j(I_j(t)),$$

where the sum takes into account cross-infections from all groups and $\beta_{ij} \geq 0$ represents the transmission coefficient between compartments S_i and I_j, $\beta_{ij} = 0$ if there is no disease transmission between compartments S_i and I_j. The restrictions on nonlinear incidence functions $f_i(S_i(t))g_j(I_j(t))$ as used in [29] are as follows:

$(\mathbf{H}_3)$: $f_i(S_i) \in C$, $g_i(I_i)$ are sufficiently smooth; $f_i(0) = g_i(0) = 0$, and $f_i(S_i) > 0$ for $S_i > 0$, $g_i(I_i) > 0$ for $I_i > 0$, and there exist $0 < c_i \leq \infty$ such that

$$\lim_{I_i \to 0^+} \frac{g_i(I_i)}{I_i} = c_i, \quad i = 1, 2, \ldots, n.$$

$(\mathbf{H}_4)$: $f_i(S_i) < f_i(S_i^0)$ for $0 \leq S_i < S_i^0$, and

$$\sup_{I_i > 0} \frac{g_i(I_i)}{I_i} = c_i, \quad i = 1, 2, \ldots, n.$$

Typical examples of $f_i(S_i(t))g_j(I_j(t))$ that satisfy $(\mathbf{H}_3)$-$(\mathbf{H}_4)$ include common incidence functions such as $S_i I_j$, $S_i^q I_j$, $\eta S_i I_j/(1 + \theta S_i)$ with $q, \eta, \theta > 0$ [13, 2, 20, 37].

To incorporate the delay in latency, and delay due to relapse distribution, the multi-group SEIR epidemic model can be described as the following system of differential and integral equations:

$$\begin{cases} S_i'(t) = \varphi_i(S_i(t)) - \sum_{j=1}^{n} \beta_{ij} f_i(S_i(t)) g_j(I_j(t)), \\ E_i'(t) = \sum_{j=1}^{n} \beta_{ij} f_i(S_i(t)) g_j(I_j(t)) - d_i E_i(t) \\ \qquad + \sum_{j=1}^{n} \int_0^t \beta_{ij} f_i(S_i(\xi)) g_j(I_j(\xi)) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi, \\ I_i'(t) = -\sum_{j=1}^{n} \int_0^t \beta_{ij} f_i(S_i(\xi)) g_j(I_j(\xi)) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi \\ \qquad - \int_0^t \gamma_i I_i(\xi) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi - (d_i + \gamma_i) I_i(t), \\ R_i'(t) = \gamma_i I_i(t) - d_i R_i(t) + \int_0^t \gamma_i I_i(\xi) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi, \\ i = 1, 2, \ldots, n, \end{cases} \tag{3}$$

where d_i denotes the natural death rate of exposed, infective and recovered population in the i-th group, respectively. γ_i denotes the rate of recovery of infectious individuals in the i-th group. All parameter values are assumed to be nonnegative and $d_i, \gamma_i > 0$ for all i. The disease transmission diagram is depicted in Fig. 1. Here, the integrals account for the distributed delays of latency and relapse, respectively. For instance, the integral $-\int_0^t \gamma_i I_i(\xi) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi$ denotes the number of recovered individuals in the i-th group that are relapsed into infective class at time t.

Note that the variables E_i and R_i do not appear in the first and the third equations, together with

$$\int_0^t \gamma_i I_i(\xi) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi = \int_0^t \gamma_i I_i(t-\xi) e^{-d_i\xi} d_\xi P_i(\xi) d\xi,$$

and

$$\begin{aligned} &\int_0^t \beta_{ij} f_i(S_i(\xi)) g_j(I_j(\xi)) e^{-d_i(t-\xi)} d_t P_i(t-\xi) d\xi \\ =& \int_0^t \beta_{ij} f_i(S_i(t-\xi)) g_j(I_j(t-\xi)) e^{-d_i\xi} d_\xi P_i(\xi) d\xi, \end{aligned}$$

which allow us to consider the following reduced system

$$\begin{cases} S_i'(t) = \varphi_i(S_i(t)) - \sum_{j=1}^n \beta_{ij} f_i(S_i(t)) g_j(I_j(t)), \\ I_i'(t) = -\sum_{j=1}^n \int_0^t \beta_{ij} f_i(S_i(t-\xi)) g_j(I_j(t-\xi)) e^{-d_i\xi} d_\xi P_i(\xi) d\xi \\ \qquad - \int_0^t \gamma_i I_i(t-\xi) e^{-d_i\xi} d_\xi P_i(\xi) d\xi - (d_i+\gamma_i) I_i(t), \quad i = 1, 2, \ldots, n. \end{cases} \tag{4}$$

For any initial condition

$$(S_1(0), I_1(0), \ldots, S_n(0), I_n(0)) \in \mathbb{R}_+^{2n},$$

the existence, uniqueness and continuity of the solution of system (4) follow from the standard theory of Volterra integro-differential equation [28]. By using the similar arguments as in [32, Lemma 2.1], we can easily obtain that the solution of (4) with nonnegative initial condition remains nonnegative. Moreover, $S_i(t) > 0$ for all $t > 0, i = 1, 2, \ldots, n$.

Let

$$M_i = \sup_{S_i \in [0, S_i^0]} \varphi_i(S_i), \quad q_i = \min\{M_i/S_i^0, d_i\} \quad \text{for} \quad i = 1, 2, \ldots, n. \tag{5}$$

Next, we show that the solution of system (4) is ultimately bounded in $\mathbb{R}_+^{2n}$. It follows from $(\mathbf{H}_2)$ and the first equation of (4) that $\limsup_{t\to\infty} S_i(t) \le S_i^0$ for all $i = 1, 2, \ldots, n$. For each i, adding the four equations in (3) gives

$$\begin{aligned} S_i'(t) + E_i'(t) + I_i'(t) + R_i'(t) &\le M_i - d_i \left(E_i(t) + I_i(t) + R_i(t)\right) \\ &\le 2M_i - \frac{M_i}{S_i^0} S_i(t) - d_i \left(E_i(t) + I_i(t) + R_i(t)\right) \\ &\le 2M_i - q_i \left(S_i(t) + E_i(t) + I_i(t) + R_i(t)\right). \end{aligned} \tag{6}$$

Thus, $\limsup_{t\to\infty} \left(S_i(t) + E_i(t) + I_i(t) + R_i(t)\right) \le 2M_i/q_i$. It follows from $S_i'(t) \le \varphi_i(S_i)$ and $(\mathbf{H}_2)$ that if $(S_i(t), E_i(t), I_i(t), R_i(t))$ is a solution satisfying $S_i(t_0) \le S_i^0$ for some $t_0 > 0$, then $S_i(t) \le S_i^0$ for all $t > t_0$. By (6), we have, for any $i = 1, 2, \ldots, n$, if $S_i(t_1) + E_i(t_1) + I_i(t_1) + R_i(t_1) \le 2M_i/q_i$ for some $t_1 > 0$, then $S_i(t) + E_i(t) + I_i(t) + R_i(t) \le 2M_i/q_i$ for all $t \ge t_1$. Therefore, we define the

set

$$\Gamma = \Big\{(S_i, E_i, I_i, R_i) \in \mathbb{R}^{4n}_+| \\ 0 \le S_i(t) \le S_i^0, 0 \le S_i(t) + E_i(t) + I_i(t) + R_i(t) \le 2M_i/q_i\Big\}, \quad (7)$$

which is a positively invariant compact absorbing set with respect to the system (3) and all positive semi-orbits are precompact in $\mathbb{R}^{4n}_+$ [4] and thus have non-empty ω-limit sets.

Thus, it follows from (7) that the set

$$\Gamma_0 = \Big\{(S_i, I_i) \in \mathbb{R}^{2n}_+| \ 0 \le S_i(t) \le S_i^0, 0 \le S_i(t) + I_i(t) \le 2M_i/q_i\Big\},$$

is a positively invariant compact absorbing set with respect to the system (4). We can further obtain that all solutions with initial conditions in $\mathbb{R}^{2n}_+$ enter Γ in finite time. Summarizing the above analysis, we arrive at the following result.

Lemma 2.1. *Assume that* $(\boldsymbol{H}_1) - (\boldsymbol{H}_4)$ *hold. Then the region* Γ *is positively invariant and absorbing in* $\mathbb{R}^{2n}_+$ *with respect to system (4).*

Clearly, system (4) always admits a disease-free equilibrium $P_0 = (S_1^0, 0, ..., S_n^0, 0)$ in Γ. We denote

$$Q_i = -\int_0^\infty e^{-d_i\xi} d_\xi P_i(\xi) d\xi. \quad (8)$$

It can be verified that $Q_i \in (0, 1)$ for all $i = 1, 2, \ldots, n$. Define

$$J_i(t) = -\int_t^\infty e^{-d_i\xi} d_\xi P_i(\xi) d\xi, \quad (9)$$

then $J_i(t) \ge 0$ for all $t > 0$, $J_i(0) = Q_i > 0$. An integration by parts yields

$$J_i(t) = e^{-d_i t} P_i(t) - \int_t^\infty d_i e^{-d_i\xi} P_i(\xi) d\xi.$$

It follows from $(\mathbf{H}_1)$ that $0 \le \int_t^\infty d_i e^{-d_i\xi} P_i(\xi) d\xi \le d_i e^{-d_i t} \int_t^\infty P_i(\xi) d\xi \to 0$ as $t \to \infty$. Therefore,

$$\lim_{t\to\infty} J_i(t) = 0 \quad \text{for all} \quad i = 1, 2, \ldots, n.$$

Following Diekmann et al. [10], the basic reproduction number $\Re_0$ for system (4) is defined as the spectral radius of a matrix called the next generation matrix, which describes the expected number of secondary cases produced in an entirely susceptible population by a typical infected individual during its entire infectious period. Thus, the basic reproduction number is given by

$$\Re_0 = \rho(M^0), \quad (10)$$

where

$$M^0 = \begin{pmatrix} \frac{f_1(S_1^0)c_1\beta_{11}Q_1}{d_1+\gamma_1-\gamma_1 Q_1} & \cdots & \frac{f_1(S_1^0)c_n\beta_{1n}Q_1}{d_1+\gamma_1-\gamma_1 Q_1} \\ \vdots & \ddots & \vdots \\ \frac{f_n(S_n^0)c_1\beta_{n1}Q_n}{d_n+\gamma_n-\gamma_n Q_n} & \cdots & \frac{f_n(S_n^0)c_n\beta_{nn}Q_n}{d_n+\gamma_n-\gamma_n Q_n} \end{pmatrix}.$$

Note that (4) may not have an endemic equilibrium for finite time t. According to [28], the following limiting system ensures that (4) has an endemic equilibrium,

$$\begin{cases} S_i'(t) = \varphi_i(S_i(t)) - \sum_{j=1}^{n} \beta_{ij} f_i(S_i(t)) g_j(I_j(t)), \\ I_i'(t) = -\sum_{j=1}^{n} \int_0^\infty \beta_{ij} f_i(S_i(t-\xi)) g_j(I_j(t-\xi)) e^{-d_i\xi} d_\xi P_i(\xi) d\xi \\ \qquad -\int_0^\infty \gamma_i I_i(t-\xi) e^{-d_i\xi} d_\xi P_i(\xi) d\xi - (d_i+\gamma_i) I_i(t), \quad i = 1, 2, \ldots, n. \end{cases} \tag{11}$$

Obviously, system (11) contains infinite delays, thus its associated initial condition needs to be restricted in an appropriate Banach space. To this end, for any $\lambda_i \in (0, d_i)$ with $i = 1, 2, \ldots, n$, we define the following Banach space of fading memory type (see e.g., [4, 18]).

$$\mathcal{C}_i = \Big\{ \phi \in C((-\infty, 0], \mathbb{R}) \ : \ \phi(s) e^{\lambda_i s} \text{ is uniformly continuous for } s \in (-\infty, 0], \text{ and } \sup_{s \le 0} |\phi(s)| e^{\lambda_i s} < \infty \Big\},$$

with norm $\|\phi\|_i = \sup_{s\le 0} |\phi(s)| e^{\lambda_i s}$. For $\phi \in \mathcal{C}_i$, let $\phi_t \in \mathcal{C}_i$ be such that $\phi_t(s) = \phi(t+s)$, $s \in (-\infty, 0]$. The nonnegative cone of $\mathcal{C}_i$ is defined by $\mathcal{C}_i^+ = C((-\infty, 0], \mathbb{R}_+)$. We consider system (11) in the following phase space

$$\mathbb{X} = \prod_{i=1}^{n} (\mathcal{C}_i \times \mathcal{C}_i).$$

Let $\psi_i \in \mathcal{C}_i^+$ and $\phi_i \in \mathcal{C}_i^+$ such that $\psi_i(s) \ge 0$ and $\phi_i(s) \ge 0$ for $s \in (-\infty, 0]$, the standard theory of functional differential equations [18] ensures that system (11) with the initial conditions

$$S_{i0} = \psi_i \in \mathcal{C}_i^+, \quad I_{i0} = \phi_i \in \mathcal{C}_i^+, \quad i = 1, 2, \ldots, n \tag{12}$$

has a unique solution. It can be further verified that the solutions of system (11) with initial conditions (12) are nonnegative and ultimately uniformly bounded in $\mathbb{X}$. Using the similar arguments as in [29, Proposition 3.1], we obtain that the following set is positively invariant for system (11),

$$\Theta = \Big\{ (S_1(\cdot), I_1(\cdot), \ldots, S_n(\cdot), I_n(\cdot)) \in \mathbb{X} |\ 0 \le S_i(s) \le S_i^0, 0 \le S_i(0) + I_i(0) \le \frac{2M_i}{q_i}, \\ I_i(s) \ge 0, s \in (-\infty, 0], i = 1, 2, \ldots, n \Big\},$$

where M_i and q_i are defined in (5). All positive semi-orbits in Θ are precompact in $\mathbb{X}$ [4], and thus have non-empty ω-limit sets.

An equilibrium $P^* = (S_1^*, I_1^*, \ldots, S_n^*, I_n^*)$ in the interior of Θ is called an endemic equilibrium, where $S_i^*, I_i^* > 0$ satisfy the following equilibrium equations

$$\begin{cases} \varphi_i(S_i^*) = \sum_{j=1}^{n} \beta_{ij} f_i(S_i^*) g_j(I_j^*), \\ Q_i \sum_{j=1}^{n} \beta_{ij} f_i(S_i^*) g_j(I_j^*) = (d_i + \gamma_i - \gamma_i Q_i) I_i^*. \end{cases}$$

Next, we will show that under biologically reasonable conditions, the endemic equilibrium P^* is unique.

3. **Main results.** Determining sharp threshold conditions for the global stability of equilibria is generally a challenging problem. In this section, we will tackle this problem for the model (4) and (11). We will demonstrate that $\Re_0$ is the key threshold parameter whose values completely determine the global dynamics of systems (4) and (11). Define

$$H(u) = u - 1 - \ln u. \tag{13}$$

Then $H(u) \geq 0$ for all $u > 0$, and $H(u)$ attains its strict and global minimum at $u = 1$ with $H(1) = 0$.

Theorem 3.1. *Assume that* $(\boldsymbol{H}_1) - (\boldsymbol{H}_4)$ *hold, and* $B = (\beta_{ij})_{n\times n}$ *is irreducible. If* $\Re_0 \leq 1$*, then the disease-free equilibrium* P_0 *of system (4) is globally asymptotically stable in* Γ*; whereas if* $\Re_0 > 1$*, then* P_0 *is unstable.*

Proof. We first illustrate that P_0 is the unique equilibrium of system (4) in Γ if $\Re_0 \leq 1$. Let $S = (S_1, S_2, \ldots, S_n)^T, I = (I_1, I_2, \ldots, I_n)^T, S^0 = (S_1^0, S_2^0, \ldots, S_n^0)^T$, and define matrix-valued function

$$M(S) = \left(\frac{\beta_{ij} f_i(S_i) c_j Q_i}{d_i + \gamma_i - \gamma_i Q_i}\right)_{n\times n}.$$

Then $M(S^0) = M^0$. For $1 \leq i \leq n, 0 \leq S_i \leq S_i^0$, we have $0 \leq M(S) \leq M(S^0) = M^0$. If $S \neq S_0$, then $M(S) < M^0$. On the other side, since $B = (\beta_{ij})_{n\times n}$ is irreducible, then $M(S)$ and M^0 are also irreducible. Moreover, the matrix $M(S) + M^0$ is also irreducible. It follows from the Perron-Frobenius Theorem [6, Corollary 2.1.5] that $\rho(M(S)) < \rho(M^0)$ provided $S \neq S_0$.

If $\Re_0 \leq 1$ and $S \neq S_0$, it follows from the above analysis and $\Re_0 = \rho(M^0)$ that $\rho(M(S)) < 1$. This implies that the equilibrium equation $M(S)I = I$ has only the trivial solution $I = 0$. Therefore the disease-free equilibrium P_0 is the unique equilibrium of system (4) if $\Re_0 \leq 1$.

Next, we prove that the disease-free equilibrium P_0 is globally asymptotically stable in Γ. It follows from [6, Theorem 2.1.4] that the nonnegative irreducible matrix M^0 has a strictly positive left eigenvector $(\omega_1, \omega_2, \ldots, \omega_n)$ corresponding to the spectral radius $\Re_0 = \rho(M^0)$ such that

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

where $\omega_i > 0$ for $i = 1, 2, \ldots, n$. Let

$$k_i = \frac{\omega_i}{d_i + \gamma_i - \gamma_i Q_i} > 0.$$

We consider the following Lyapunov functional $L : \mathbb{X} \to \mathbb{R}$,

$$L = \sum_{i=1}^{n} k_i \left[I_{it}(0) + \gamma_i \int_0^t J_i(\xi) I_{it}(-\xi) d\xi\right],$$

where $S_{it}(\theta) = S_i(t+\theta), I_{it}(\theta) = I_i(t+\theta)$ for $\theta \in (-\infty, 0], i = 1, 2, \ldots, n$, and $J_i(\xi)$ is defined in (9). Obviously, $L \geq 0$ with the equality holds if and only if $S_i(t) \equiv S_i^0$ and $I_i(t) \equiv 0$. Differentiating $\int_0^t J_i(\xi) I_i(t-\xi) d\xi$ along the solutions of system (4) and using integration by parts, we obtain

$$\begin{aligned}\frac{d}{dt}\Big(\int_0^t J_i(\xi)I_i(t-\xi)d\xi\Big) &= J_i(t)I_i(0)+\int_0^t J_i(\xi)\frac{d}{dt}I_i(t-\xi)d\xi\\ &= J_i(t)I_i(0)-\int_0^t J_i(\xi)\frac{d}{d\xi}I_i(t-\xi)d\xi\\ &= Q_iI_i(t)+\int_0^t I_i(t-\xi)e^{-d_i\xi}d_\xi P_i(\xi)d\xi.\end{aligned}$$

Thus the derivative of L along the solutions of system (4) is calculated as

$$\begin{aligned}\frac{dL}{dt}\Big|_{(4)} &= \sum_{i=1}^n k_i\Big[-\sum_{j=1}^n\int_0^t \beta_{ij}f_i(S_i(t-\xi))g_j(I_j(t-\xi))e^{-d_i\xi}d_\xi P_i(\xi)d\xi\\ &\quad -\int_0^t \gamma_iI_i(t-\xi)e^{-d_i\xi}d_\xi P_i(\xi)d\xi\\ &\quad -(d_i+\gamma_i)I_i(t)+\gamma_iQ_iI_i(t)+\int_0^t\gamma_iI_i(t-\xi)e^{-d_i\xi}d_\xi P_i(\xi)d\xi\Big]\\ &\le \sum_{i=1}^n\frac{\omega_i}{d_i+\gamma_i-\gamma_iQ_i}\Big(\sum_{j=1}^n Q_i\beta_{ij}f_i(S_i^0)g_j(I_j)-(d_i+\gamma_i-\gamma_iQ_i)I_i(t)\Big).\end{aligned}$$

Using assumptions $(\mathbf{H}_2)-(\mathbf{H}_4)$, and the expression for $\Re_0$ in (10), we obtain

$$\begin{aligned}\frac{dL}{dt}\Big|_{(4)} &\le \sum_{i=1}^n\frac{\omega_i}{d_i+\gamma_i-\gamma_iQ_i}\Big(\sum_{j=1}^n Q_i\beta_{ij}f_i(S_i^0)c_jI_j(t)-(d_i+\gamma_i-\gamma_iQ_i)I_i(t)\Big)\\ &\le (\omega_1,\omega_2,...,\omega_n)(M^0\mathbf{I}-\mathbf{I})\\ &= (\rho(M^0)-1)(\omega_1,\omega_2,...,\omega_n)\mathbf{I}\le\ 0,\quad \text{if}\ \ \Re_0\le 1,\end{aligned}\tag{14}$$

where $\mathbf{I}=(I_1(t),I_2(t),\dots,I_n(t))^T$. Let

$$Y=\Big\{(S_1,I_1,...,S_n,I_n)\in\Gamma\Big|\ \ \frac{dL}{dt}\Big|_{(4)}=0\Big\}.$$

If $\Re_0=\rho(M^0)<1$, then it follows from (14) that $\frac{dL}{dt}\big|_{(4)}=0$ if and only if $\mathbf{I}=0$. If $\Re_0=\rho(M^0)=1$, then $\frac{dL}{dt}\big|_{(4)}$ implies

$$(\omega_1,\omega_2,...,\omega_n)M(S)\mathbf{I}=(\omega_1,\omega_2,...,\omega_n)\mathbf{I}.\tag{15}$$

If $S\neq S^0$, then $(\omega_1,\omega_2,...,\omega_n)M(S)<(\omega_1,\omega_2,...,\omega_n)M^0=(\omega_1,\omega_2,...,\omega_n)$, which implies that (15) have only the the trivial solution $\mathbf{I}=0$. Thus, if $\Re_0\le 1$, $\frac{dL}{dt}\big|_{(4)}=0$ if and only if $\mathbf{I}=0$ or $S=S^0$. Therefore, the maximal compact invariant set in Y is the singleton $\{P_0\}$. By the LaSalle's invariance principle (see [15, Theorem 5.3.1] or [22, Theorem 3.4.7]), P_0 is globally attractive in Γ. Furthermore, it can be verified that P_0 is locally stable using the same proof as that for Corollary 5.3.1 in [15]. Therefore, P_0 is globally asymptotically stable in Γ.

If $\Re_0=\rho(M^0)>1$ and $\mathbf{I}\neq 0$, we know that

$$(\omega_1,\omega_2,...,\omega_n)(M^0\mathbf{I}-\mathbf{I})=(\rho(M^0)-1)(\omega_1,\omega_2,...,\omega_n)\mathbf{I}>0.$$

From (14), assumption $(\mathbf{H}_2)$ and the continuity of f_i and g_j, it follows that $\frac{dL}{dt}\big|_{(4)}>0$ in a neighborhood of P_0 in the interior of Γ. This implies that P_0 is unstable if $\Re_0>1$. □

Using similar arguments to [36, Theorem 3.2], we can prove the following lemma on the uniform persistence of system (11) if $\Re_0 > 1$, which implies that the disease will persist in all groups.

Lemma 3.2. *Assume that* $(\boldsymbol{H}_1) - (\boldsymbol{H}_4)$ *hold and that* $\Re_0 > 1$. *Then there exists* $\varepsilon > 0$ *such that all solutions of system (11) with initial conditions (12) satisfy*

$$\liminf_{t\to\infty} S_i(t, S_{i,0}) \geq \varepsilon, \quad \liminf_{t\to\infty} I_i(t, \phi_i) \geq \varepsilon, \quad \textit{for} \quad i = 1, 2, \ldots, n.$$

The uniform persistence of system (11), together with the uniform boundedness of solutions in the interior of Θ, implies the existence of a positive equilibrium of (11) (see [7, Theorem 2.8.6]). Summarizing the above analysis, we arrive at the following lemma on the existence of endemic equilibrium.

Lemma 3.3. *Assume that* $(\boldsymbol{H}_1) - (\boldsymbol{H}_4)$ *hold. If* $\Re_0 > 1$, *then system (11) has at least an endemic equilibrium* P^* *in the interior of* Θ.

A difficult mathematical question for system (11) is that of whether the EE P^* is unique if $\Re_0 > 1$, and whether the EE P^* is globally asymptotically stable when it is unique. To answer this question, we arbitrarily choose one endemic equilibrium, still denoted by P^*, and prove global attractivity of P^*. Then we show that P^* is actually the only endemic equilibrium, and it is globally asymptotically stable. The following technical assumptions are required to construct Lyapunov functional for P^*. Let P^* be an arbitrarily chosen endemic equilibrium, assume that for $i = 1, 2, \ldots, n$,

$(\mathbf{H}_5)$: $(\varphi_i(S_i) - \varphi_i(S_i^*))(S_i - S_i^*) < 0$ for $S_i \neq S_i^*$, $S_i \in [0, S_i^0]$.
$(\mathbf{H}_6)$: $(f_i(S_i) - f_i(S_i^*))(S_i - S_i^*) > 0$ for $S_i \neq S_i^*$, $S_i \in [0, S_i^0]$.
$(\mathbf{H}_7)$: $\left(\frac{g_i(I_i(t))}{g_i(I_i^*)} - 1\right)\left(1 - \frac{g_i(I_i^*)I_i}{g_i(I_i(t))I_i^*}\right) \leq 0$ for $I_i > 0$.

Remark 1. The assumption $(\mathbf{H}_5)$ is automatically satisfied if φ_i is strictly monotonically decreasing, namely, $\varphi_i' < 0$, on $[0, S_i^0]$. The assumption $(\mathbf{H}_6)$ is automatically satisfied if f_i is strictly monotonically increasing, namely, $f_i' > 0$, on $[0, S_i^0]$. The assumption $(\mathbf{H}_7)$ is automatically satisfied if g_i is strictly monotonically increasing and concave down, namely, $g_i' > 0$ and $g_i'' < 0$, on $(0, \infty)$. As we shall see later, these technical assumptions are crucial in our proof of globally asymptotic stability result. If some of the conditions are violated, there may exist periodic solutions; see more discussions in [23].

Theorem 3.4. *Assume that* $(\boldsymbol{H}_1)-(\boldsymbol{H}_7)$ *hold, and that* $B = (\beta_{ij})_{n\times n}$ *is irreducible. If* $\Re_0 > 1$, *then for system (11),* P^* *is the unique endemic equilibrium and is globally asymptotically stable in the interior of* Θ.

Proof. Let $P^* = (S_1^*, I_1^*, ..., S_n^*, I_n^*)$ denote an endemic equilibrium whose existence is established in Lemma 3.3. By a graph-theoretical approach to Lyapunov functionals developed by Guo et al. [13, 14] and Li et al. [24], we prove that P^* is globally asymptotically stable when $\Re_0 > 1$. In particular, this implies that the endemic equilibrium is unique in the interior of Θ.

Define a functional $L_{EE}^i : \mathcal{C}_i \times \mathcal{C}_i \to \mathbb{R}$ as follows.

$$L_{EE}^i = L_S^i + L_I^i + L_-^i + L_+^i,$$

where

$$L_S^i = Q_i \int_{S_i^*}^{S_{it}(0)} \frac{f_i(\theta) - f_i(S_i^*)}{f_i(\theta)} d\theta, \quad L_I^i = I_i^* H\left(\frac{I_{it}(0)}{I_i^*}\right),$$

$$L_-^i = \gamma_i \int_0^\infty I_i^* J_i(\xi) H\left(\frac{I_{it}(-\xi)}{I_i^*}\right) d\xi,$$

$$L_+^i = \sum_{j=1}^n \int_0^\infty \beta_{ij} f_i(S_i^*) g_(I_j^*) J(\xi) H\left(\frac{f_i(S_{it}(-\xi)) g_j(I_{jt}(-\xi))}{f_i(S_i^*) g_j(I_j^*)}\right) d\xi,$$

and $S_{it}(\theta) = S_i(t+\theta), I_{it}(\theta) = I_i(t+\theta)$ for $\theta \in (-\infty, 0], i = 1, 2, \ldots, n$. It is clear that $L_{EE}^i \geq 0$ with the equality holds if and only if $S_i(t) \equiv S_i^*$, $I_i(t) \equiv I_i^*$, and L_{EE}^i is bounded for all $t \geq 0$. Differentiating L_S^i along the solution of system (11), we obtain

$$\begin{aligned}\frac{dL_S^i}{dt}\Big|_{(11)} = & \left(1 - \frac{f_i(S_i^*)}{f_i(S_i(t))}\right) \varphi_i(S_i(t)) \\ & + \sum_{j=1}^n \beta_{ij} f_i(S_i^*) g_j(I_j(t)) - \sum_{j=1}^n \beta_{ij} f_i(S_i(t)) g_j(I_j(t)). \end{aligned} \tag{16}$$

Differentiating L_I^i along the solution of system (11), we have

$$\begin{aligned}&\frac{dL_I^i}{dt}\Big|_{(11)} \\ &= \left(1 - \frac{I_i^*}{I_i(t)}\right)\left(- \sum_{j=1}^n \int_0^\infty \beta_{ij} f_i(S_i(t-\xi)) g_j(I_j(t-\xi)) e^{-d_i\xi} d_\xi P_i(\xi) d\xi \right. \\ &\quad \left. - \int_0^\infty \gamma_i I_i(t-\xi) e^{-d_i\xi} d_\xi P_i(\xi) d\xi - (d_i + \gamma_i) I_i(t) \right) \\ &= - \sum_{j=1}^n \int_0^\infty \beta_{ij} f_i(S_i(t-\xi)) g_j(I_j(t-\xi)) e^{-d_i\xi} d_\xi P_i(\xi) d\xi \\ &\quad + \frac{I_i^*}{I_i(t)} \sum_{j=1}^n \int_0^\infty \beta_{ij} f_i(S_i(t-\xi)) g_j(I_j(t-\xi)) e^{-d_i\xi} d_\xi P_i(\xi) d\xi \\ &\quad - \int_0^\infty \gamma_i I_i(t-\xi) e^{-d_i\xi} d_\xi P_i(\xi) d\xi + \frac{I_i^*}{I_i(t)} \int_0^\infty \gamma_i I_i(t-\xi) e^{-d_i\xi} d_\xi P_i(\xi) d\xi \\ &\quad - Q_i \sum_{j=1}^n \beta_{ij} f_i(S_i^*) g_j(I_j^*) \frac{I_i(t)}{I_i^*} \\ &\quad + Q_i \sum_{j=1}^n \beta_{ij} f_i(S_i^*) g_j(I_j^*) + Q_i \gamma_i I_i^* - Q_i \gamma_i I_i(t) \end{aligned} \tag{17}$$

Using integration by parts, we can calculate the derivatives of L_-^i along the solution of system (11) as follows:

$$\begin{aligned}\frac{dL_-^i}{dt}\Big|_{(11)} &= -\gamma_i \int_0^\infty I_i^* J_i(\xi) \frac{d}{d\xi} H\left(\frac{I_i(t-\xi)}{I_i^*}\right) d\xi \\ &= \gamma_i I_i^* Q_i H\left(\frac{I_i(t)}{I_i^*}\right) + \int_0^\infty \gamma_i I_i^* e^{-d_i\xi} d_\xi P_i(\xi) H\left(\frac{I_i(t-\xi)}{I_i^*}\right) d\xi \\ &= \int_0^\infty \gamma_i e^{-d_i\xi} d_\xi P_i(\xi) \left(I_i(t-\xi) - I_i(t) + I_i^* \ln \frac{I_i(t)}{I_i(t-\xi)}\right) d\xi. \end{aligned} \tag{18}$$

Differentiating L_+^i along the solution of system (11), similar to (19) we have

$$\begin{aligned}\frac{dL_+^i}{dt}\Big|_{(11)} = \sum_{j=1}^{n}\int_0^\infty e^{-d_i\xi}d_\xi P_i(\xi)\Big(&\beta_{ij}f_i(S_i(t-\xi))g_j(I_j(t-\xi))\\ &-\beta_{ij}f_i(S_i(t))g_j(I_j(t))\\ &+\beta_{ij}f_i(S_i^*)g_j(I_j^*)\ln\frac{f_i(S_i(t))g_j(I_j(t))}{f_i(S_i(t-\xi))g_j(I_j(t-\xi))}\Big).\end{aligned}\tag{19}$$

Collecting the terms in (16)-(19) gives

$$\begin{aligned}\frac{dL_{EE}^i}{dt}\Big|_{(11)} = {}& Q_i\left(1-\frac{f_i(S_i^*)}{f_i(S_i(t))}\right)(\varphi_i(S_i(t))-\varphi_i(S_i^*))\\ &+2Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)-Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)\frac{f_i(S_i^*)}{f_i(S_i(t))}\\ &+Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j(t))-Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)\frac{I_i(t)}{I_i^*}\\ &+\frac{I_i^*}{I_i(t)}\sum_{j=1}^{n}\int_0^\infty\beta_{ij}f_i(S_i(t-\xi))g_j(I_j(t-\xi))e^{-d_i\xi}d_\xi P_i(\xi)d\xi\\ &+\int_0^\infty I_i^*\gamma_i e^{-d_i\xi}d_\xi P_i(\xi)H\left(\frac{I_i(t-\xi)}{I_i(t)}\right)d\xi\\ &-\sum_{j=1}^{n}\int_0^\infty e^{-d_i\xi}d_\xi P_i(\xi)\beta_{ij}f_i(S_i^*)g_j(I_j^*)\ln\frac{f_i(S_i(t-\xi))g_j(I_j(t-\xi))}{f_i(S_i(t))g_j(I_j(t))}.\end{aligned}$$

Further we have

$$\begin{aligned}&\frac{dL_{EE}^i}{dt}|_{(11)}\\ &=\mathcal{A}+\int_0^\infty I_i^*\gamma_i e^{-d_i\xi}d_\xi P_i(\xi)H\left(\frac{I_i(t-\xi)}{I_i(t)}\right)d\xi+Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)\\ &\quad\times\left(\frac{g_j(I_j(t))}{g_j(I_j^*)}+\frac{g_j(I_j^*)I_j}{g_j(I_j(t))I_j^*}-\frac{I_i(t)}{I_i^*}-\ln\frac{f_i(S_i^*)}{f_i(S_i(t))}-\ln\frac{g_j(I_j^*)I_j(t)}{g_j(I_j(t))I_j^*}\right)\\ &\quad+\sum_{j=1}^{n}\int_0^\infty\beta_{ij}f_i(S_i^*)g_j(I_j^*)e^{-d_i\xi}d_\xi P_i(\xi)\\ &\quad\times\left[H\left(\frac{I_i^*f_i(S_i(t-\xi))g_j(I_j(t-\xi))}{I_i(t)f_i(S_i^*)g_j(I_j^*)}\right)+\ln\frac{I_i^*f_i(S_i(t))g_j(I_j(t))}{I_i(t)f_i(S_i^*)g_j(I_j^*)}+1\right]\\ &=\mathcal{A}+\int_0^\infty I_i^*\gamma_i e^{-d_i\xi}d_\xi P_i(\xi)H\left(\frac{I_i(t-\xi)}{I_i(t)}\right)d\xi\\ &\quad+\sum_{j=1}^{n}\int_0^\infty\beta_{ij}f_i(S_i^*)g_j(I_j^*)e^{-d_i\xi}d_\xi P_i(\xi)H\left(\frac{I_i^*f_i(S_i(t-\xi))g_j(I_j(t-\xi))}{I_i(t)f_i(S_i^*)g_j(I_j^*)}\right)\\ &\quad+Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)\left[\left(\frac{g_j(I_j(t))}{g_j(I_j^*)}-1\right)\left(1-\frac{g_j(I_j^*)I_j(t)}{g_j(I_j(t))I_j^*}\right)\right.\end{aligned}$$

$$+\frac{I_j(t)}{I_j^*}-\ln\frac{I_j(t)}{I_j^*}-\frac{I_i(t)}{I_i^*}+\ln\frac{I_i(t)}{I_i^*}\Big],$$

where

$$\begin{aligned}\mathcal{A}=&Q_i\left(1-\frac{f_i(S_i^*)}{f_i(S_i(t))}\right)(\varphi_i(S_i(t))-\varphi_i(S_i^*))\\&-Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)H\left(\frac{f_i(S_i^*)}{f_i(S_i(t))}\right)\\&-Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)H\left(\frac{g_j(I_j^*)I_j}{g_j(I_j(t))I_j^*}\right).\end{aligned}$$

From the assumptions $(\mathbf{H}_5)$-$(\mathbf{H}_7)$, we have

$$\frac{f(S_i(t))-f(S_i^*)}{f(S_i(t))}(\varphi_i(S_i(t))-\varphi_i(S_i^*))\le 0, \tag{20}$$

and

$$\left(\frac{g_j(I_j(t))}{g_j(I_j^*)}-1\right)\left(1-\frac{g_j(I_j^*)I_j(t)}{g_j(I_j(t))I_j^*}\right)\le 0, \tag{21}$$

which, together with the properties of the function $H(u)$, implies that

$$\frac{dL_{EE}^i}{dt}\Big|_{(11)}\le Q_i\sum_{j=1}^{n}\beta_{ij}f_i(S_i^*)g_j(I_j^*)\left(\frac{I_j(t)}{I_j^*}-\ln\frac{I_j(t)}{I_j^*}-\frac{I_i(t)}{I_i^*}+\ln\frac{I_i(t)}{I_i^*}\right). \tag{22}$$

Set

$$\bar\beta_{ij}=\beta_{ij}f_i(S_i^*)g_j(I_j^*),\quad 1\le i,j\le n,$$

and a Laplacian matrix [24] as

$$\bar B=\begin{bmatrix}\Sigma_{l\neq 1}\bar\beta_{1l} & -\bar\beta_{21} & \cdots & -\bar\beta_{n1}\\ -\bar\beta_{12} & \Sigma_{l\neq 2}\bar\beta_{2l} & \cdots & -\bar\beta_{n2}\\ \vdots & \vdots & \ddots & \vdots\\ -\bar\beta_{1n} & -\bar\beta_{2n} & \cdots & \Sigma_{l\neq n}\bar\beta_{nl}\end{bmatrix}.$$

Note that $\bar B$ is the Laplacian matrix of the matrix $(\bar\beta_{ij})_{n\times n}$. Since $(\beta_{ij})_{n\times n}$ is irreducible, matrices $(\bar\beta_{ij})_{n\times n}$ and $\bar B$ are also irreducible. Let C_{ii} denote the cofactor of the i-th diagonal entry of $\bar B$ for $i=1,\dots,n$. By [13, Lemma 2.1], the linear system $\bar Bv=0$ has a positive solution $v=(v_1,v_2,...,v_n)$, where $v_i=C_{ii}>0$ for $i=1,\dots,n$.

Define a Lyapunov functional $L_{EE}:\ \prod_{i=1}^{n}(\mathbb{R}\times\mathcal{C}_i)\to\mathbb{R}$,

$$L_{EE}=\sum_{i=1}^{n}v_iL_{EE}^i,$$

then the derivative of L_{EE} along the solution of system (11) satisfies

$$\begin{aligned}\frac{dL_{EE}}{dt}\Big|_{(11)}&=\sum_{i=1}^{n}v_i\frac{dL_{EE}^i}{dt}\Big|_{(11)}\\&\le\sum_{i,j=1}^{n}v_iQ_i\bar\beta_{ij}\left(\frac{I_j(t)}{I_j^*}-\ln\frac{I_j(t)}{I_j^*}-\frac{I_i(t)}{I_i^*}+\ln\frac{I_i(t)}{I_i^*}\right).\end{aligned}$$

Using similar arguments in [29, Theorem 4.2], we can prove that $\frac{dL_{EE}}{dt}|_{(11)} \leq 0$, and $\frac{dL_{EE}}{dt}|_{(11)} = 0$ if and only if $S_i(t) \equiv S_i^*, I_i(t) \equiv I_i^*$. Therefore, the largest compact invariant subset of

$$\left\{(S_1, I_1, ..., S_n, I_n) \in \Theta \Big| \ \frac{dL_{EE}}{dt}\Big|_{(11)} = 0\right\}$$

is the singleton $\{P^*\}$. By the LaSalle's invariance principle (see [15, Theorem 5.3.1]), P^* is globally attractive in the interior of Θ, which implies that P^* is the unique endemic equilibrium. Furthermore, by using an argument similar to that in the proof of Theorem 3.1, we can show that the endemic equilibrium P^* is globally asymptotically stable in the interior of Θ if $\Re_0 > 1$. □

4. **Summary and discussion.** The global dynamics of system (4) and (11) are completely determined by the basic reproduction number which is defined as the spectral radius of next generation matrix. More specifically, if $\Re_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable; if $\Re_0 > 1$, a unique endemic equilibrium exists and is globally asymptotically stable. The proofs of our main results utilize construction of Lyapunov functionals and a subtle grouping technique in estimating the derivatives of Lyapunov functionals guided by graph theory, which was recently developed by Guo, Li and Shuai in [13, 14, 25, 24]. Compared with the results in [13, 14], the group structure in system (11) greatly increases the complexity exhibited in the derivatives of the Lyapunov functionals. The key to our analysis is a complete description of the patterns exhibited in the derivative of the Lyapunov functionals using graph theory. Our result generalizes related works [36, 35] in determining the global asymptotic stability of the endemic equilibrium P^* with delay in latency and delay due to relapse distribution.

Biologically, Theorems 3.1 and 3.4 imply that,

- if $\Re_0 \leq 1$, then the disease always dies out from all groups;
- if $\Re_0 > 1$, then the disease always persists in all groups at the unique endemic equilibrium level, irrespective of the initial conditions.

These results also preclude the existence of nonconstant periodic solutions. Note that our model combines two important biological features, latency and relapse, in a heterogeneity host. Moreover, it allows nonlinear growth rate and nonlinear incidence rate. The stability analysis for such model becomes a challenging problem due to the complexity of the system. The Lyapunov functionals in Theorem 3.1 and 3.4 are tactfully designed to incorporate the distributed delays of latency and relapse. Our results also demonstrate that latency, relapse, nonlinearity and group size do not alter the dynamical behaviors of the basic SEIR model.

Note that when $n = 1$, system (4) reduce to a single-group SEIR model with latency, relapse, nonlinear growth rate and incidence rate, which is given by

$$\begin{cases} S'(t) = \ \varphi(S(t)) - \beta f(S(t))g(I(t)), \\ I'(t) = \ -\displaystyle\int_0^t \beta f(S(t))g(I(t))e^{-d(t-\xi)}d_tP(t-\xi)d\xi \\ \qquad\quad -\int_0^t \gamma I(\xi)e^{-d(t-\xi)}d_tP(t-\xi)d\xi - (d+\gamma)I(t). \end{cases} \tag{23}$$

In this model, the basic reproduction number is given by

$$\Re_0^1 = \frac{Q\beta f(S^0)c}{d+\gamma-\gamma Q},$$

where $Q = -\int_0^\infty e^{-d\xi} d_\xi P(\xi) d\xi$. Following the method of constructing Lyapunov functionals, one can determine the global dynamics of single-group SEIR model by

$$V_1 = I_t(0) + \int_0^t J(\xi) I_t(-\xi) d\xi,$$

$$V_2 = Q \int_{S^*}^{S_t(0)} \frac{f(\theta) - f(S^*)}{f(\theta)} d\theta + I^* H\left(\frac{I_t(0)}{I^*}\right) + \gamma I^* \int_0^\infty J(\xi) H\left(\frac{I_t(-\xi)}{I^*}\right) d\xi,$$

where H is defined in (13), and $J(\xi) = -\int_t^\infty e^{-d\xi} d_\xi P(\xi) d\xi$. Applying Theorems 3.1 and 3.4, we obtain the following results but omit the proof.

Theorem 4.1. *Assume that* $(\boldsymbol{H}_1)$*-*$(\boldsymbol{H}_7)$ *hold and* $n = 1$. *Let* $(S(t), I(t))$ *be the solution of system (23) with nonnegative initial condition. If* $\Re_0^1 \le 1$, *then* $\lim_{t\to\infty}(S(t), I(t)) = P_0 = (S^0, 0)$; *If* $\Re_0^1 > 1$, *then* $\lim_{t\to\infty}(S(t), I(t)) = P^* = (S^*, I^*)$.

Theorem 4.1 improves the related results in [26] with constant relapse, which gives part of the proof in the case where $g(I) = I$ of system (11).

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