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GLOBAL DYNAMICS OF A GENERAL CLASS OF MULTI-GROUP EPIDEMIC MODELS WITH LATENCY AND RELAPSE

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Abstract. A multi-group model is proposed to describe a general relapse phenomenon of infectious diseases in heterogeneous populations. In each group, the population is divided into susceptible, exposed, infectious, and recovered subclasses. A general nonlinear incidence rate is used in the model. The results show that the global dynamics are completely determined by the basic reproduction number R_0. In particular, a matrix-theoretic method is used to prove the global stability of the disease-free equilibrium when $R_0 \leq 1$, while a new combinatorial identity (Theorem 3.3 in Shuai and van den Driessche [29]) in graph theory is applied to prove the global stability of the endemic equilibrium when $R_0 > 1$. We would like to mention that by applying the new combinatorial identity, a graph of 3n (or 2n+m) vertices can be converted into a graph of n vertices in order to deal with the global stability of the endemic equilibrium in this paper.

1. **Introduction.** In most deterministic epidemic models, the host population is often divided into susceptible, infective and recovered subclasses. For some epidemic diseases, infected individuals can experience incubation before showing symptoms, for example rabies [9, 38], malaria [10], West Nile virus [13], HIV/AIDS [22]. Therefore, it is reasonable to include a latent (or exposed) subclass in the host population. After surviving the latent period, these individuals progress into the infective class, and then recover into the recovered class. However, clinical diagnosis indicates that there may be a recurrence of symptoms for some diseases. Some patients have a remission after treatment during the recovery period, but then, due to the pathogens in the tissue reproduce to certain degree, the early symptoms appeared again - this is called a relapse. Hepatitis B virus relapsed after surgery with a 5-year and 8-year actuarial rate of recurrence of 8% and 21%, respectively. After liver transplantation hepatitis B recurred in 9% treated only with immune globulins and lamivudine [24]. A recurrence of tuberculosis is a second episode of tuberculosis occurring after a

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first episode had been considered cured [17]. The 2-year incidence of recurrence after treatment of pulmonary tuberculosis with rifampicin-containing regimens ranges from 0-27% [11, 31]. The study results also show a high incidence (24%) of recurrent Hepatitis C virus (HCV) viremia in HIV-1-coinfected participants with initial control of HCV, even in some who had previously maintained HCV control for almost two years of observation [14]. In general, there are several reasons about recurrence: (1) Incomplete treatment. Many patients with symptoms will be somewhat better stop treatment because they are afraid of bearing the heavy burden of their expensive medical bills. (2) Resistant. Clinics commonly used some drug for a long time, which causes virus mutations that results in drug resistance. (3) Unhealthy lifestyle habits. Some recovered individuals, once their status became better, will not pay attention to healthy eating, such as overeating, drinking and smoking. (4) Overwork including mental work and physical work. Excessive fatigue will lead to low immunity, then cause infection again.

Van den Driessche et al. [35] in 2007 proposed a mathematical model for a disease with a general exposed distribution and the possibility of relapse. The global attractivity of the disease-free equilibrium (DFE) is proved when the basic reproduction number is less than one. Moreover, assuming that the probability of remaining in the exposed class $P(t)$ is a step-function, they have proved that the system is uniformly persistent and the endemic equilibrium (EE) is locally asymptotically stable (LAS) if the basic reproduction number is larger than one. In particular, they pointed out in the discussion and conclusions section that numerical simulations suggest that the EE is GAS, but no analytic proof is given. Liu et al. [23] extended the above model with a more general nonlinear incidence rate. More importantly, the open problem in [35] was resolved and the result in [23] confirms that the EE is GAS.

Recently, multigroup models have been proposed in the literature to describe the transmission dynamics of some infectious diseases in heterogeneous host populations, such as gonorrhea [3, 16], sexually transmitted diseases [4] and vector borne diseases such as malaria [10], West-Nile disease [13] and cholera [6, 27, 33]. Heterogeneity in host population may be caused by many factors. Groups can be geographical such as communities, cities, and countries, or epidemiological, to incorporate differential infectivity or co-infection of multiple strains of the disease agent. There has been much research on multigroup epidemic models, for example, see [6, 15, 20, 25, 28, 32, 26] and references therein. The question of global stability in higher dimensions models is always a challenging and difficult task. Fortunately, some papers [12, 21, 26, 27, 28, 29] have shown that a graph-theoretic approach may be effective in constructing Lyapunov functions, in particular, the global stability of the unique endemic equilibrium in multigroup models.

The purpose of this paper is to investigate a SEIR model with a general nonlinear incidence rate and relapse in heterogeneous populations. We will carry out a complete mathematical analysis of the model and study its global dynamics. The basic reproduction number R_0 is calculated. Under some biologically reasonable assumptions, it is proved that when $R_0 \leq 1$ the DFE is globally asymptotically stable by using a matrix-theoretic method and applying the Perron eigenvector, and when $R_0 > 1$ the EE is globally asymptotic stability by combining Kirchhoff's matrix tree theorem and a new combinatorial identity.

The article is organized as follows. In section 2, our general model, which includes relapse in heterogeneous populations, is formulated. The basic reproduction number

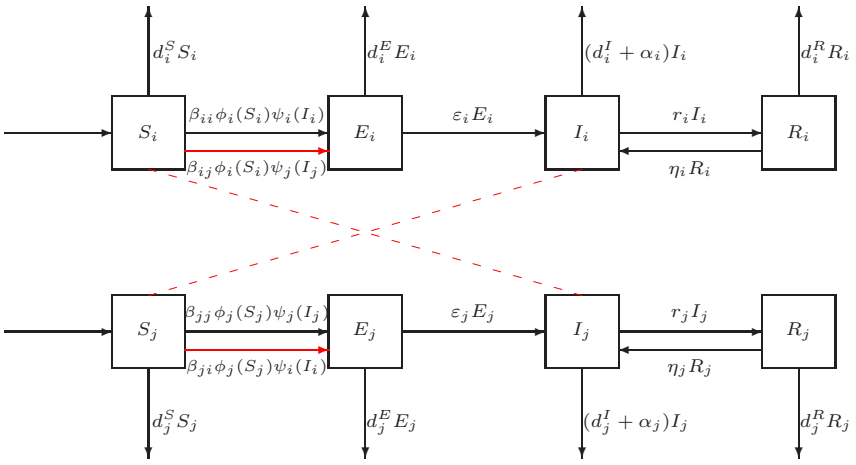

FIGURE 1. Transfer diagram for model (1)

R_0 is calculated and the stability of the disease-free equilibrium is considered in section 3. In section 4, we study the global asymptotic stability of the endemic equilibrium. A brief discussion is given in section 5.

2. **Model formulation.** In order to formulate a general multigroup disease model with relapse, we partition the population into n distinct groups ($n \geq 1$). For $1 \leq i \leq n$, the i-th group is further divided into four compartments: susceptible, exposed, infectious, and recovered, whose numbers of individuals at time t are denoted by $S_i(t), E_i(t), I_i(t)$ and $R_i(t)$, respectively. The disease incidence in the i-th group, assuming a more general nonlinear incidence form, can be calculated as

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

where β_{ij} represents the transmission coefficient between compartments S_i and I_j. The matrix $[\beta_{ij}]$ is the contact matrix, where $\beta_{ij} \geq 0$. Functions f_{ij} describe the incidence for infections occurred among contacts of S_i and I_j. Here, suppose the form of f_{ij} is a nonlinear incidence

$$f_{ij} = \phi_i(S_i)\psi_j(I_j).$$

The new multigroup epidemic model with nonlinear incidence rates and relapse is as follows:

$$\begin{aligned}
S_i' &= \Lambda_i - \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^S S_i, \\
E_i' &= \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^E E_i - \varepsilon_i E_i, \\
I_i' &= \varepsilon_i E_i - (d_i^I + r_i + \alpha_i) I_i + \eta_i R_i, \\
R_i' &= r_i I_i - d_i^R R_i - \eta_i R_i, \quad i = 1, 2, \ldots, n.
\end{aligned} \tag{1}$$

Here Λ_i represents the influx of individuals into the i-th group, d_i^S, d_i^E, d_i^I and d_i^R represent death rates of S, E, I and R populations in the i-th group, respectively. ε_i represents the rate of becoming infectious after a latent period in the i-th group, r_i represents the recovery rate of infectious individuals in the i-th group, α_i represents disease-caused death rate in the i-th group and η_i represents the rate that recovered individuals relapse and regain infectiousness in the i-th group. All parameter values are assumed to be nonnegative and $\Lambda_i, d_i^S, d_i^E > 0$ for all i. Nonnegative functions ϕ_i and ψ_i are assumed to be differentiable and have the following properties:

(H_1) (nonnegativity) All nonnegative functions ϕ_i and ψ_i only vanish at 0.

(H_2) (monotone)ϕ_i and ψ_i are monotonically nondecreasing.

(H_3) (concavity) $\psi_j(I_j)/I_j$ are monotonically nonincreasing.

Classes of $\phi_i(S_i)$, $\psi_j(I_j)$ that satisfy assumptions $(H_1), (H_2)$ and (H_3) include common incidence functions such as $\phi_i(S_i) = S_i$, $\phi_i(S_i) = S_i/(1+\lambda_i S_i)$, $\psi_j(I_j) = I_j^p (0 < p \leq 1)$ and $\psi_j(I_j) = I_j/(1+\alpha_j I_j)$.

Remark 2.1. If the function $\psi_j(I_j)$ $(j = 1, 2, \cdots, n)$ satisfies that the second order derivative $\psi_j''(I_j)$ exists and $\psi_j''(I_j) \leq 0$ for all $I_k \in [0, \infty)$, then we can easily prove that $\psi_j(I_j)/I_j$ is monotonically decreasing on $I_j \in (0, \infty)$.

For biological considerations, we are interested in solutions that are nonnegative and bounded. It can be easily proved that the solutions of model (1) with the initial conditions

$$S_i(0) > 0,\ E_i(0) > 0,\ I_i(0) > 0,\ R_i(0) > 0,\ i = 1, 2, \cdots, n \tag{2}$$

stay nonnegative for all $t \geq 0$.

For each i, adding the four equations in (1) gives

$$\begin{aligned}(S_i + E_i + I_i + R_i)' = &\ \Lambda_i - d_i^S S_i - d_i^E E_i - (d_i^I + \alpha_i) I_i - d_i^R R_i \\ \leq &\ \Lambda_i - d_i^*(S_i + E_i + I_i + R_i),\end{aligned}$$

where $d_i^* = \min\{d_i^S, d_i^E, d_i^I + \alpha_i, d_i^R\}$. Hence $\limsup_{t\to\infty}(S_i + E_i + I_i + R_i) \leq \Lambda_i/d_i^*$. This indicates that the region

$$\Gamma = \{(S_1, E_1, I_1, R_1, \ldots, S_n, E_n, I_n, R_n) \in \mathbb{R}_+^{4n} : S_i + E_i + I_i + R_i \leq \frac{\Lambda_i}{d_i^*}\} \tag{3}$$

is positively invariant with respect to model (1) and the model is well posed. Let Γ° denote the interior of Γ. Our results in this paper will be stated for model (1) in Γ.

3. Basic reproduction number and DFE.

Model (1) always has the disease-free equilibrium

$$P_0 = (S_1^0, 0, 0, 0, S_2^0, 0, 0, 0, \ldots, S_n^0, 0, 0, 0)$$

with $S_i^0 = \Lambda_i/d_i^S$. Following the next generation matrix approach [5, 34] with disesae compartments $x = (E_1, E_2, \ldots, E_n, I_1, I_2, \ldots, I_n, R_1, R_2, \ldots, R_n)^T$ and nondisease compartments $y = (S_1, \ldots, S_n)^T$, define two $3n \times 3n$ matrices F and V :

$$\mathrm{F} = \begin{pmatrix} 0 & F_1 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad \mathrm{V} = \begin{pmatrix} V_1 & 0 & 0 \\ -V_2 & V_3 & -V_4 \\ 0 & -V_5 & V_6 \end{pmatrix}$$

with $F_1 = [\beta_{ij}\phi_i(S_i^0)\psi_j'(0)]$, $V_1 = diag\{d_1^E + \varepsilon_1, \ldots, d_n^E + \varepsilon_n\}$, $V_2 = diag\{\varepsilon_1, \ldots, \varepsilon_n\}$, $V_3 = diag\{d_1^I + r_1 + \alpha_1, \ldots, d_n^I + r_n + \alpha_n\}$, $V_4 = diag\{\eta_1, \ldots, \eta_n\}$, $V_5 = diag\{r_1, \ldots,$

$r_n\}$, and $V_6 = diag\{d_1^R+\eta_1, \ldots, d_1^n+\eta_n\}$. By the inverse operation of block matrices, we can obtain

$$\mathrm{V}^{-1} = \begin{pmatrix} V_1^{-1} & 0 & 0 \\ V_3^{-1}V_4H^{-1}V_5V_3^{-1}V_2V_1^{-1} + V_3^{-1}V_2V_1^{-1} & V_3^{-1}V_4H^{-1}V_5V_3^{-1} + V_3^{-1} & V_3^{-1}V_4H^{-1} \\ H^{-1}V_5V_3^{-1}V_2V_1^{-1} & H^{-1}V_5V_3^{-1} & H^{-1} \end{pmatrix}$$

with $H = -V_5V_3^{-1}V_4 + V_6$. Substituting $V_i (i = 1, \ldots, 6)$ into V^{-1}, we have

$$\mathrm{V}^{-1} = \begin{pmatrix} A & 0 & 0 \\ B & C & D \\ E & F & G \end{pmatrix}$$

where

$$\begin{aligned}
A &= V_1^{-1} = diag\{1/d_1^E + \varepsilon_1, \ldots, 1/d_n^E + \varepsilon_n\}, \\
B &= diag\{l_1, l_2 \ldots, l_n\}, \\
C &= diag\{m_1, m_2, \ldots, m_n\}, \\
D &= diag\{n_1, n_2 \ldots, n_n\}, \\
E &= diag\{r_1\varepsilon_1/\big\{[(d_1^R + \eta_1)(d_1^I + \alpha_1) + d_1^R r_1][d_1^E + \varepsilon_1]\big\}, \ldots, \\
&\qquad r_n\varepsilon_n/\big\{[(d_n^R + \eta_n)(d_n^I + \alpha_n) + d_n^R r_n][d_n^E + \varepsilon_n]\big\}\}, \\
F &= diag\{r_1/\big[(d_1^R + \eta_1)(d_1^I + \alpha_1) + d_1^R r_1\big], \ldots, r_n/\big[(d_n^R + \eta_n)(d_n^I + \alpha_1) + d_n^R r_n\big]\}, \\
G &= diag\{d_1^I + r_1 + \alpha_1/\big[(d_1^R + \eta_1)(d_1^I + \alpha_1) + d_1^R r_1\big], \ldots, \\
&\qquad d_n^I + r_n + \alpha_n/\big[(d_n^R + \eta_n)(d_n^I + \alpha_1) + d_n^R r_n\big]\},
\end{aligned}$$

in which

$$\begin{aligned}
l_i &= \frac{\varepsilon_i(d_i^R + \eta_i)}{[(d_i^R + \eta_i)(d_i^I + \alpha_i) + d_i^R r_i][d_i^E + \varepsilon_i]}, \\
m_i &= \frac{(d_i^R + \eta_i)}{(d_i^R + \eta_i)(d_i^I + \alpha_i) + d_i^R r_i}, \\
n_i &= \frac{\eta_i}{(d_i^R + \eta_i)(d_i^I + \alpha_i) + d_i^R r_i},
\end{aligned}$$

and $i = 1, 2, \ldots, n$. Thus the basic reproduction number can be calculated as

$$R_0 = \rho(FV^{-1}) = \rho(F_1B) = \rho([\beta_{ij}\phi_i(S_i^0)\psi_j'(0)l_j]) \tag{4}$$

and ρ denotes the spectral radius (see [5, 34]).

Remark 3.1. Here R_0 is the spectral radius of the matrix $[\beta_{ij}\phi_i(S_i^0)\psi_j'(0)l_j]_{n\times n}$. From the epidemiological point of view, each entry of this matrix can be interpreted as the product of the adequate contact rate $\beta_{ij}\psi_j'(0)$, with the susceptible $\phi_i(S_i^0)$ at the i-th group, and the death-adjusted mean time

$$\frac{\varepsilon_j(d_j^R + \eta_j)}{[(d_j^R + \eta_j)(d_j^I + \alpha_j) + d_j^R r_j][d_j^E + \varepsilon_j]}$$

in the infective class at the j-th group on multiple passes. Note that a fraction of the last expression is given by the sum of the geometric series

$$\frac{1}{d_j^I + r_j + \alpha_j}\Big(1 + \frac{r_j}{d_j^I + r_j + \alpha_j}\frac{\eta_j}{d_j^R + \eta_j} + \frac{{r_j}^2}{(d_j^I + r_j + \alpha_j)^2}\frac{{\eta_j}^2}{(d_j^R + \eta_j)^2} + \cdots\Big),$$

where $1/(d_j^I + r_j + \alpha_j)$ is the average time in the infective class on the first pass, $r_j/(d_j^I + r_j + \alpha_j)$ is the probability of surviving this class, and $\eta_j/(d_j^R + \eta_j)$ is the probability of surviving the recovered class.

Theorem 3.2. *Suppose that the contact matrix $[\beta_{ij}]$ is irreducible and assumptions $(H_1) - (H_3)$ hold. Then the following results hold for model (1).*

(1) If $R_0 \le 1$, then the DFE P_0 is globally asymptotically stable in Γ.

(2) If $R_0 > 1$, then the DFE P_0 is unstable.

Proof. Since $x' = (F - V)x - f(x, y)$ with

$$\begin{aligned} f(x,y) = \quad & \Big(\sum_{j=1}^{n}\beta_{1j}(\phi_1(S_1)\psi_j(I_j) - \phi_1(S_1^0)\psi_j'(0)I_j), \ldots, \\ & \sum_{j=1}^{n}\beta_{nj}(\phi_n(S_n)\psi_j(I_j) - \phi_n(S_n^0)\psi_j'(0)I_j), 0, \ldots, 0, 0, \ldots, 0\Big)^T. \end{aligned}$$

Since $[\beta_{ij}]$ is irreducible, it follows that the matrix BF_1 is also irreducible. Using the Perron-Frobenius theorem [1], the nonnegative matrix BF_1 has a positive left eigenvector $(\upsilon_1, \upsilon_2, \ldots, \upsilon_n)$ corresponding to the spectral radius $\rho(F_1B) = R_0 > 0$.

Motivated by [25, 29, 26], consider a Lyapunov function for model (1)

$$L = \sum_{i=1}^{n}\upsilon_i l_i E_i + \sum_{i=1}^{n}\upsilon_i m_i I_i + \sum_{i=1}^{n}\upsilon_i n_i R_i.$$

Differentiating L along the solutions of the equation $x' = (F - V)x - f(x, y)$, we have

$$\begin{aligned} L' \quad &= \sum_{i=1}^{n}\upsilon_i l_i \dot{E}_i + \sum_{i=1}^{n}\upsilon_i m_i \dot{I}_i + \sum_{i=1}^{n}\upsilon_i n_i \dot{R}_i \\ &= \sum_{i=1}^{n}\upsilon_i l_i\Big\{ - (d_i^E + \varepsilon_i)E_i + \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^0)\psi_j'(0)I_j \\ &\quad + \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^0)I_j\Big(\frac{\phi_i(S_i)\psi_j(I_j)}{\phi_i(S_i^0)I_j} - \psi_j'(0)\Big)\Big\} \\ &\quad + \sum_{i=1}^{n}\upsilon_i m_i\Big\{\varepsilon_i E_i - (d_i^I + r_i + \alpha_i)I_i + \eta_i R_i\Big\} \\ &\quad + \sum_{i=1}^{n}\upsilon_i n_i\Big\{r_i I_i - (d_i^R + \eta_i)R_i\Big\} \\ &= \sum_{i=1}^{n}\upsilon_i l_i \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^0)I_j\Big(\frac{\phi_i(S_i)\psi_j(I_j)}{\phi_i(S_i^0)I_j} - \psi_j'(0)\Big) \\ &\quad + \sum_{i=1}^{n}\upsilon_i l_i \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^0)\psi_j'(0)I_j - \sum_{i=1}^{n}\upsilon_i I_i \end{aligned}$$

$$
\begin{aligned}
&= \sum_{i=1}^{n} \upsilon_i l_i \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^0) I_j \left(\frac{\phi_i(S_i)\psi_j(I_j)}{\phi_i(S_i^0)I_j} - \psi_j'(0)\right) \\
&\quad + \sum_{j=1}^{n} I_j \sum_{i=1}^{n} \beta_{ij}\phi_i(S_i^0)\psi_j'(0)\upsilon_i l_i - \sum_{i=1}^{n} \upsilon_i I_i \\
&= \sum_{i=1}^{n} \upsilon_i l_i \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^0) I_j \left(\frac{\phi_i(S_i)\psi_j(I_j)}{\phi_i(S_i^0)I_j} - \psi_j'(0)\right) + \sum_{i=1}^{n} (R_0 - 1)\upsilon_i I_i \\
&\leq 0 \quad \text{if } R_0 \leq 1.
\end{aligned} \tag{5}
$$

Let

$$M = \{(S_1, E_1, I_1, R_1, \ldots, S_n, E_n, I_n, R_n) \mid L' = 0\}.$$

If $R_0 < 1$, from the last equality of (5) and $\upsilon_i > 0$, $L' = 0$ implies that $I_i = 0$ for all $1 \leq i \leq n$ and $t \geq 0$. It can be verified that the largest invariant set in M is the singleton $\{P_0\}$.

If $R_0 = 1$, then

$$
\begin{aligned}
L' &= \sum_{i=1}^{n} \upsilon_i l_i \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - \sum_{i=1}^{n} \upsilon_i I_i \\
&= \sum_{j=1}^{n} I_j \sum_{i=1}^{n} \upsilon_i l_i \beta_{ij}\phi_i(S_i)\frac{\psi_j(I_j)}{I_j} - \sum_{j=1}^{n} \upsilon_j I_j.
\end{aligned}
$$

Since in Γ, it holds that $0 \leq S_i \leq S_i^0$, $\psi_i(I_i) \leq \psi_i'(0) I_i$ for $i = 1, 2, \cdots, n$. Let $\tilde{Q} = [\beta_{ij}\phi_i(S_i)\psi_j(I_j)l_i/I_j]$, $Q = F_1 B = [\beta_{ij}\phi_i(S_i^0)\psi_j'(0)l_j]$, we have $0 \leq \tilde{Q} \leq Q$. Since $[\beta_{ij}]$ is irreducible, we obtain that $\tilde{Q}$ and Q are also irreducible. Therefore, $\rho(\tilde{Q}) < \rho(Q) = 1$, provided $S_i \neq S_i^0$ for all $i = 1, 2, \cdots, n$. Moreover, denote $I = (I_1, I_2, \ldots, I_n)^T$, we know that $\tilde{Q}I = I$ only has the trivial solution $I = 0$ if $\rho(\tilde{Q}) < 1$. Furthermore, we have $L' = (\upsilon_1, \upsilon_2, \ldots, \upsilon_n)(\tilde{Q}I - I)$. Therefore, $L' = 0$ implies that $I = 0$ or $S_i = S_i^0$ for $i = 1, 2, \cdots, n$. The same result holds that the largest invariant set in M is the singleton $\{P_0\}$ provided $R_0 = 1$. By LaSalle's Invariance Principle [18], P_0 is globally asymptotically stable in Γ if $R_0 \leq 1$.

If $R_0 > 1$ and $I \neq 0$, it follows that $\sum_{i=1}^{n}(R_0 - 1)\upsilon_i I_i > 0$, which implies that by continuity $L' > 0$ in a small enough neighborhood of P_0 in Γ°. Therefore, P_0 is unstable when $R_0 > 1$. □

Using the uniform persistence result from [7] and a similar argument as in the proof of Proposition 3.3 of [19], we can show that, when $R_0 > 1$, the instability of P_0 implies uniform persistence of model (1).

Remark 3.3. Uniform persistence of model (1), together with the positive invariance of compact set Γ, implies that the existence of an equilibrium of model (1) in Γ° (see Theorem 2.8.6 in [2] or Theorem D.3 in [30]).

Furthermore, we have the following result for model (1).

Theorem 3.4. *Suppose that the contact matrix $[\beta_{ij}]$ is irreducible and assumptions $(H_1) - (H_3)$ hold. If $R_0 > 1$, then model (1) is uniformly persistent in Γ° and there exists at least one endemic equilibrium for model (1) in Γ°.*

4. **Global stability of EE.** By Theorem 3.4, an endemic equilibrium $P^* = (S_1^*, E_1^*, I_1^*, R_1^*, S_2^*, E_2^*, I_2^*, R_1^*, \ldots, S_n^*, E_n^*, I_n^*, R_n^*)$ exists. Here $S_i^* > 0, E_i^* > 0, I_i^* > 0, R_i^* > 0$ $(i = 1, 2, \ldots, n)$ and it satisfies the following equilibrium equations:

$$\begin{aligned}
&\Lambda_i - \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*) - d_i^S S_i^* = 0,\\
&\sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*) - (d_i^E + \varepsilon_i)E_i^* = 0,\\
&\varepsilon_i E_i^* - (d_i^I + r_i + \alpha_i)I_i^* + \eta_i R_i^* = 0,\\
&r_i I_i^* - d_i^R R_i^* - \eta_i R_i^* = 0, \quad i = 1, 2, \ldots, n.
\end{aligned} \tag{6}$$

In this section, we prove that the endemic equilibrium P^* is globally asymptotically stable when $R_0 > 1$. In particular, this result implies that the endemic equilibrium is unique in the interior of Ω when it exists.

Theorem 4.1. *Suppose that the contact matrix $[\beta_{ij}]$ is irreducible and assumptions $(H_1) - (H_3)$ hold. Then, when $R_0 > 1$, the endemic equilibrium P^* is globally asymptotically stable in the interior of Ω.*

Proof. For the convenience of discussion, let us consider three special cases of system (1).

Case 1. $\eta_i > 0$ for all $i = 1, 2, \ldots, n$. Let

$$\begin{aligned}
D_i &= \int_{S_i^*}^{S_i} \frac{\phi_i(z) - \phi_i(S_i^*)}{\phi_i(z)} dz + E_i - E_i^* - E_i^* \ln \frac{E_i}{E_i^*},\\
D_{n+i} &= I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*},\\
D_{2n+i} &= R_i - R_i^* - R_i^* \ln \frac{R_i}{R_i^*}, \quad i = 1, 2, \ldots . n.
\end{aligned}$$

For $i = 1, 2 \ldots, n$, differentiating D_i, D_{n+i} and D_{2n+i} along the solutions of model (1), by the equilibrium equations (6) we obtain

$$\begin{aligned}
D_i' = \quad & (1 - \frac{\phi_i(S_i^*)}{\phi_i(S_i)})\Big\{ - d_i^S(S_i - S_i^*) + \sum_{j=1}^{n} \beta_{ij}\Big(\phi_i(S_i^*)\psi_j(I_j^*) - \phi_i(S_i)\psi_j(I_j)\Big)\Big\}\\
& + (1 - \frac{E_i^*}{E_i})\Big\{ \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^E E_i - \varepsilon_i E_i \Big\}\\
\leq \quad & \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big(1 - \frac{\phi_i(S_i^*)}{\phi_i(S_i)}\Big)\Big(1 - \frac{\phi_i(S_i)\psi_j(I_j)}{\phi_i(S_i^*)\psi_j(I_j^*)}\Big)\\
& + \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big(\frac{\phi_i(S_i)\psi_j(I_j)}{\phi_i(S_i^*)\psi_j(I_j^*)} - \frac{E_i}{E_i^*}\Big)\Big(1 - \frac{E_i^*}{E_i}\Big)\\
= \quad & \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big(2 - \frac{E_i}{E_i^*} - \frac{\phi_i(S_i^*)}{\phi_i(S_i)} - \frac{\phi_i(S_i)\psi_j(I_j)E_i^*}{\phi_i(S_i^*)\psi_j(I_j^*)E_i} + \frac{\psi_j(I_j)}{\psi_j(I_j^*)}\Big)\\
\leq \quad & \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big(\ln \frac{\psi_j(I_j^*)}{\psi_j(I_j)} + \ln \frac{E_i}{E_i^*} - \frac{E_i}{E_i^*} + \frac{\psi_j(I_j)}{\psi_j(I_j^*)}\Big)
\end{aligned}$$

$$
\begin{aligned}
&\leq \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big\{\Big(1-\frac{\psi_j(I_j^*)I_j}{\psi_j(I_j)I_j^*}\Big)\Big(\frac{\psi_j(I_j)}{\psi_j(I_j^*)}-1\Big)\\
&\quad+\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{E_i}{E_i^*}+\ln\frac{E_i}{E_i^*}\Big\}\\
&\leq \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{E_i}{E_i^*}+\ln\frac{E_i}{E_i^*}\Big)\\
&=: \sum_{j=1}^{n}a_{i,n+j}G_{i,n+j},
\end{aligned}
$$

$$
\begin{aligned}
D'_{n+i} &= \Big(1-\frac{I_i^*}{I_i}\Big)\Big\{\varepsilon_iE_i-(d_i^I+r_i+\alpha_i)I_i+\eta_iR_i\Big\}\\
&= \varepsilon_iE_i^*\Big(\frac{E_i}{E_i^*}-\frac{I_i}{I_i^*}\Big)\Big(1-\frac{I_i^*}{I_i}\Big)+\eta_iR_i^*\Big(\frac{R_i}{R_i^*}-\frac{I_i}{I_i^*}\Big)\Big(1-\frac{I_i^*}{I_i}\Big)\\
&\leq \varepsilon_iE_i^*\Big(\frac{E_i}{E_i^*}-\frac{I_i}{I_i^*}-\ln\frac{E_i}{E_i^*}+\ln\frac{I_i}{I_i^*}\Big)+\eta_iR_i^*\Big(\frac{R_i}{R_i^*}-\frac{I_i}{I_i^*}-\ln\frac{R_i}{R_i^*}+\ln\frac{I_i}{I_i^*}\Big)\\
&=: a_{n+i,i}G_{n+i,i}+a_{n+i,2n+i}G_{n+i,2n+i},
\end{aligned}
$$

and

$$
\begin{aligned}
D'_{2n+i} &= \Big(1-\frac{R_i^*}{R_i}\Big)\Big\{r_iI_i-d_i^RR_i-\eta_iR_i\Big\}\\
&= r_iI_i^*\Big(\frac{I_i}{I_i^*}-\frac{R_i}{R_i^*}\Big)\Big(1-\frac{R_i^*}{R_i}\Big)\\
&\leq r_iI_i^*\Big(\frac{I_i}{I_i^*}-\frac{R_i}{R_i^*}-\ln\frac{I_i}{I_i^*}+\ln\frac{R_i}{R_i^*}\Big)\\
&=: a_{2n+i,n+i}G_{2n+i,n+i}.
\end{aligned}
$$

Define the weighted digraph $(\mathcal{G},A)$ here with entries of matrix A given above, and let c_i be the cofactor of the i-th diagonal element of the Laplacian matrix of $(\mathcal{G},A)$. The out-degree $d^+(i)$ is the number of arcs whose initial vertex is i. Since $d^+(2n+i)=1$ for each i (see Figure 2), by Theorem A.3 in the Appendix, $c_{n+i}a_{n+i,2n+i}=c_{2n+i}a_{2n+i,n+i}$. Since $d^+(i)=1$ for each i (see Figure 2), by Theorem A.3 in the Appendix, $c_{n+i}a_{n+i,i}=\sum_{j=1}^{n}c_ia_{i,n+j}$. Thus

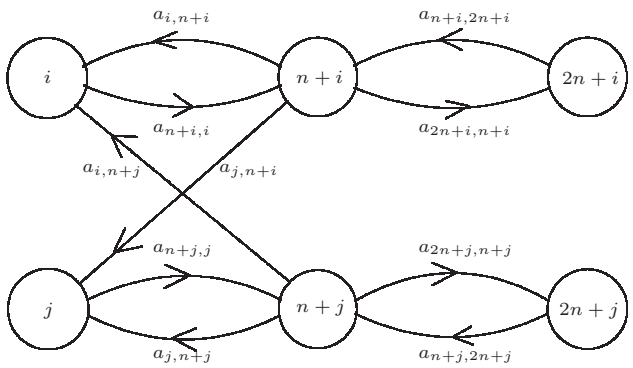

FIGURE 2. The weight digraph $(\mathcal{G},A)$ constructed for model (1) with three groups.

$$D=\sum_{i=1}^{n}c_iD_i+\sum_{i=1}^{n}c_{n+i}D_{n+i}+\sum_{i=1}^{n}c_{n+i}a_{n+i,2n+i}\frac{D_{2n+i}}{a_{2n+i,n+i}}. \tag{7}$$

Since $G_{n+i,2n+i}+G_{2n+i,n+i}=0$ and

$$G_{i,n+j}+G_{n+i,i}=\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{I_i}{I_i^*}+\ln\frac{I_i}{I_i^*},$$

it follows that

$$\begin{aligned}
D'\le\ & \sum_{i=1}^{n}\sum_{j=1}^{n}c_ia_{i,n+j}G_{i,n+j}+\sum_{i=1}^{n}c_{n+i}\Big(a_{n+i,i}G_{n+i,i}+a_{n+i,2n+i}G_{n+i,2n+i}\Big)\\
&+\sum_{i=1}^{n}c_{n+i}a_{n+i,2n+i}\frac{D_{2n+i}}{a_{2n+i,n+i}}\\
\le\ & \sum_{i=1}^{n}\sum_{j=1}^{n}c_ia_{i,n+j}G_{i,n+j}+\sum_{i=1}^{n}c_{n+i}a_{n+i,i}G_{n+i,i}\\
&+\sum_{i=1}^{n}c_{n+i}a_{n+i,2n+i}G_{n+i,2n+i}+\sum_{i=1}^{n}c_{n+i}a_{n+i,2n+i}G_{2n+i,n+i}\\
=\ & \sum_{i=1}^{n}\sum_{j=1}^{n}c_ia_{i,n+j}G_{i,n+j}+\sum_{i=1}^{n}\sum_{j=1}^{n}c_ia_{i,n+j}G_{n+i,i}\\
=\ & \sum_{i=1}^{n}\sum_{j=1}^{n}c_ia_{i,n+j}\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{I_i}{I_i^*}+\ln\frac{I_i}{I_i^*}\Big).
\end{aligned} \tag{8}$$

Let $\tilde{c}_i, i=1,2,\dots,n$, be given as in Proposition A.1 in the Appendix with $(\tilde{\mathcal{G}},\tilde{A})$, where the entry of the $n\times n$ matrix $\tilde{A}=[\tilde{a}_{ij}]$ is defined as $\tilde{a}_{ij}=a_{i,n+j}$. Let

$$\tilde{c}_{n+i}=\sum_{j=1}^{n}\tilde{c}_i\frac{a_{i,n+j}}{a_{n+i,i}}$$

and

$$\tilde{c}_{2n+i}=\tilde{c}_{n+i}\frac{a_{n+i,2n+i}}{a_{2n+i,n+i}}.$$

Now, we claim that

$$\tilde{D}=\sum_{i=1}^{n}\tilde{c}_iD_i+\sum_{i=1}^{n}\tilde{c}_{n+i}D_{n+i}+\sum_{i=1}^{n}\tilde{c}_{2n+i}D_{2n+i}$$

is a Lyapunov function for model (1). In fact, replacing all c_i by $\tilde{c}_i$ in the calculation of (7) yields

$$\tilde{D}'\le\sum_{i=1}^{n}\sum_{j=1}^{n}\tilde{c}_i\tilde{a}_{i,n+j}\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{I_i}{I_i^*}+\ln\frac{I_i}{I_i^*}\Big).$$

Furthermore, by Theorem A.2 in the Appendix, we can obtain that

$$\sum_{i=1}^{n}\sum_{j=1}^{n}\tilde{c}_i\tilde{a}_{i,n+j}\Big(\frac{I_i}{I_i^*}-\ln\frac{I_i}{I_i^*}\Big)=\sum_{i=1}^{n}\sum_{j=1}^{n}\tilde{c}_i\tilde{a}_{i,n+j}\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}\Big).$$

Then

$$\begin{aligned}\tilde{D}' \leq & \sum_{i=1}^{n}\sum_{j=1}^{n}\tilde{c}_i\tilde{a}_{i,n+j}\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{I_i}{I_i^*}+\ln\frac{I_i}{I_i^*}\Big)\\ = & \sum_{i=1}^{n}\sum_{j=1}^{n}\tilde{c}_i\tilde{a}_{i,n+j}\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}\Big)-\sum_{i=1}^{n}\sum_{j=1}^{n}\tilde{c}_i\tilde{a}_{i,n+j}\Big(\frac{I_i}{I_i^*}-\ln\frac{I_i}{I_i^*}\Big)\\ = & 0.\end{aligned}$$

It can be verified that the largest invariant set where $\tilde{D}'=0$ is the singleton $\{P^*\}$. Therefore, by LaSalle's invariance principle, P^* is GAS in the interior of Ω.

Case 2. $\eta_i=0$ for all $i=1,2,\ldots,n$. Then model (1) becomes the following model

$$\begin{aligned}S_i' = & \Lambda_i-\sum_{j=1}^{n}\beta_{ij}\phi_i(S_i)\psi_j(I_j)-d_i^S S_i,\\ E_i' = & \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i)\psi_j(I_j)-d_i^E E_i-\varepsilon_i E_i,\\ I_i' = & \varepsilon_i E_i-(d_i^I+r_i+\alpha_i)I_i,\\ R_i' = & r_i I_i-d_i^R R_i,\quad i=1,2,\ldots,n.\end{aligned}\tag{9}$$

It may be readily seen that the first $3n$ equations in (9) are independent of the variable R_i. Thus, the model can be reduced to the following multi-group system

$$\begin{aligned}S_i' = & \Lambda_i-\sum_{j=1}^{n}\beta_{ij}\phi_i(S_i)\psi_j(I_j)-d_i^S S_i,\\ E_i' = & \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i)\psi_j(I_j)-d_i^E E_i-\varepsilon_i E_i,\\ I_i' = & \varepsilon_i E_i-(d_i^I+r_i+\alpha_i)I_i,\quad i=1,2,\ldots,n.\end{aligned}\tag{10}$$

Let

$$D_i=\int_{S_i^*}^{S_i}\frac{\phi_i(z)-\phi_i(S_i^*)}{\phi_i(z)}dz+E_i-E_i^*-E_i^*\ln\frac{E_i}{E_i^*}+\frac{d_i+\varepsilon_i}{\varepsilon_i}(I_i-I_i^*-I_i^*\ln\frac{I_i}{I_i^*}).$$

For $i=1,2,\ldots,n$, differentiating D_i along the solutions of model (10), by a similar calculation, we have

$$\begin{aligned}D_i'\big|_{(10)} \leq & \sum_{j=1}^{n}\beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{I_i}{I_i^*}+\ln\frac{I_i}{I_i^*}\Big)\\ =: & \sum_{j=1}^{n}a_{ij}\Big(\frac{I_j}{I_j^*}-\ln\frac{I_j}{I_j^*}-\frac{I_i}{I_i^*}+\ln\frac{I_i}{I_i^*}\Big)\end{aligned}$$

with $a_{ij}=\beta_{ij}\phi_i(S_i^*)\psi_j(I_j^*)$. A weighted digraph $\mathcal{G}$ can be constructed to associate with the weighted matrix $A=[a_{ij}]$. Obviously, the irreducibility of $[\beta_{ij}]$ shows that this weighted digraph $(\mathcal{G},A)$ is strongly connected. Furthermore, for $c_i, i=1,2,\ldots,n$, given as in Proposition A.1 in the Appendix, $(\mathcal{G},A)$ is positive by using the Kirchhoff's matrix tree theorem. Thus, we can construct a Lyapunov function

$D = \sum_{i=1}^{n} c_i D_i$, through the similar analysis of (8), it can be proved that P^* is GAS in the interior of Ω.

Case 3. $\eta_i > 0$ for all $i = 1, 2, \ldots, m$ and $\eta_j = 0$ for all $i = m+1, m+2, \ldots, n$ $(1 \le m < n)$. Model (1) becomes the following system

$$\begin{aligned}
S_i' &= \Lambda_i - \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^S S_i,\\
E_i' &= \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^E E_i - \varepsilon_i E_i,\\
I_i' &= \varepsilon_i E_i - (d_i^I + r_i + \alpha_i) I_i + \eta_i R_i,\\
R_i' &= r_i I_i - d_i^R R_i - \eta_i R_i, \qquad\qquad i = 1, 2, \ldots, m,\\
S_i' &= \Lambda_i - \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^S S_i,\\
E_i' &= \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\psi_j(I_j) - d_i^E E_i - \varepsilon_i E_i,\\
I_i' &= \varepsilon_i E_i - (d_i^I + r_i + \alpha_i) I_i, \qquad\qquad i = m+1, m+2, \ldots, n.
\end{aligned} \tag{11}$$

Let

$$D_i = \int_{S_i^*}^{S_i} \frac{\phi_i(z) - \phi_i(S_i^*)}{\phi_i(z)} dz + E_i - E_i^* - E_i^* \ln \frac{E_i}{E_i^*},$$

$$D_{n+i} = I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*}, \qquad\qquad i = 1, 2, \ldots, n.$$

and

$$D_{2n+i} = R_i - R_i^* - R_i^* \ln \frac{R_i}{R_i^*}, \qquad\qquad i = 1, 2, \ldots, m.$$

By similar calculations in the previous cases, we have the following inequalities:

$$D_i' \le \Big(\frac{I_j}{I_j^*} - \ln \frac{I_j}{I_j^*} - \frac{E_i}{E_i^*} + \ln \frac{E_i}{E_i^*}\Big) =: \sum_{j=1}^{n} a_{i,n+j} G_{i,n+j},$$

for all $i = 1, 2, \ldots, n$, and

$$\begin{aligned}
D_{n+i}' &\le \varepsilon_i E_i^* \Big(\frac{E_i}{E_i^*} - \frac{I_i}{I_i^*} - \ln \frac{E_i}{E_i^*} + \ln \frac{I_i}{I_i^*}\Big) + \eta_i R_i^* \Big(\frac{R_i}{R_i^*} - \frac{I_i}{I_i^*} - \ln \frac{R_i}{R_i^*} + \ln \frac{I_i}{I_i^*}\Big)\\
&=: a_{n+i,i} G_{n+i,i} + a_{n+i,2n+i} G_{n+i,2n+i},
\end{aligned}$$

$$D_{2n+i}' \le r_i I_i^* \Big(\frac{I_i}{I_i^*} - \frac{R_i}{R_i^*} - \ln \frac{I_i}{I_i^*} + \ln \frac{R_i}{R_i^*}\Big) =: a_{2n+i,n+i} G_{2n+i,n+i},$$

for all $i = 1, 2, \ldots, m$, and

$$D_{n+i}' \le \varepsilon_i E_i^* \Big(\frac{E_i}{E_i^*} - \frac{I_i}{I_i^*} - \ln \frac{E_i}{E_i^*} + \ln \frac{I_i}{I_i^*}\Big) =: a_{n+i,i} G_{n+i,i},$$

for all $i = m+1, m+2, \ldots, n$. Define a weighted graph $(\mathcal{G}, A)$ associated with the weight matrix $A = [a_{ij}]$, it can be easily obtained that this directed graph $\mathcal{G}$ consists of $2n + m$ vertices (see Figure 3). From Figure 3, we can find that this directed graph $\mathcal{G}$ is strongly connected. Thus, $c_i > 0$ for all $i = 1, 2, \ldots, (2n + m)$ by using the Kirchhoff's matrix tree theorem.

Constructing the following Lyapunov function

$$D = \sum_{i=1}^{n} c_i D_i + \sum_{i=1}^{n} c_{n+i} D_{n+i} + \sum_{i=1}^{m} c_{2n+i} D_{2n+i}. \tag{12}$$

From Figure 3, we can find that $d^+(2n+i) = 1$ for each $i = 1, 2, \ldots, m$ and $d^+(i) = 1$ for each $i = 1, 2, \ldots, n$. Applying Theorem A.3 in the Appendix, we have $c_{n+i}a_{n+i,2n+i} = c_{2n+i}a_{2n+i,n+i}$ for each $i = 1, 2, \ldots, m$ and $c_{n+i}a_{n+i,i} = \sum_{j=1}^{n} c_i a_{i,n+j}$ for each $i = 1, 2, \ldots, n$.

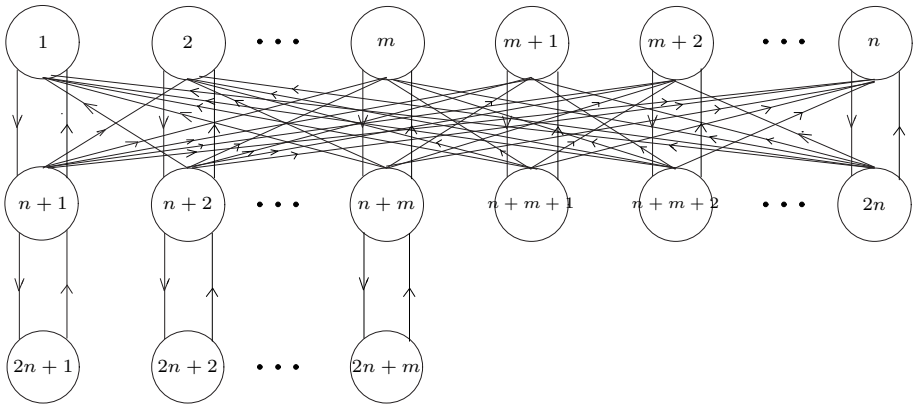

FIGURE 3. The weight digraph $(\mathcal{G}, A)$ constructed for model (11).

Differentiating D along the solutions of model (11) and following the proofs of Cases 1 and 2, we obtain:

$$\begin{aligned} D'|_{(11)} = & \sum_{i=1}^{n} c_i D_i' + \sum_{i=1}^{m} c_{n+i} D_{n+i}' + \sum_{i=m+1}^{n} c_{n+i} D_{n+i}' + \sum_{i=1}^{m} c_{2n+i} D_{2n+i}' \\ \le & \sum_{i=1}^{n}\sum_{j=1}^{n} c_i a_{i,n+j} G_{i,n+j} + \sum_{i=1}^{m} c_{n+i}(a_{n+i,i}G_{n+i,i} + a_{n+i,2n+i}G_{n+i,2n+i}) \\ & + \sum_{i=m+1}^{n} c_{n+i}a_{n+i,i}G_{n+i,i} + \sum_{i=1}^{m} \frac{c_{n+i}a_{n+i,2n+i}}{a_{2n+i,n+i}} a_{2n+i,n+i}G_{2n+i,n+i} \\ = & \sum_{i=1}^{n}\sum_{j=1}^{n} c_i a_{i,n+j}\Big(\frac{I_j}{I_j^*} - \ln\frac{I_j}{I_j^*} - \frac{I_i}{I_i^*} + \ln\frac{I_i}{I_i^*}\Big). \end{aligned} \tag{13}$$

Comparing (8) and (13), we find that the same inequality holds. Therefore, it can also be proved that P^* is GAS in the interior of Ω. □

Remark 4.2. Biologically, Theorems 3.2 and 4.1 imply that if the basic reproduction number $R_0 \le 1$, then the disease will be eradicated in all groups; if the basic reproduction number $R_0 > 1$, then the disease will break out and persist at the unique endemic equilibrium level in all groups, independent of initial values. Furthermore, Theorems 3.2 and 4.1 show that model (1) has the sharp threshold property if the basic reproduction number R_0 is given by (4).

When $n = 1$, $\phi(S) = S, \psi(I) = I$, and $d^S = d^E = d^I = d^R = d$, model (1) reduces to a single-group SEIR model with relapse,

$$\begin{aligned} S' &= \Lambda - \beta SI - dS, \\ E' &= \beta SI - (d+\varepsilon)E, \\ I' &= \varepsilon E - (d+r+\alpha)I + \eta R, \\ R' &= rI - (d+\eta)R \end{aligned} \tag{14}$$

According to (4), R_0 reduces to

$$R_0 = \beta S^0 \frac{\varepsilon(d^R+\eta)}{[(d^R+\eta)(d^I+\alpha)+d^R r][d^E+\varepsilon]}.$$

Applying Theorems 3.2 and 4.1, we have the following result.

Corollary 4.3. *Consider model (14). If $R_0 \le 1$, then the disease-free equilibrium is GAS; If $R_0 > 1$, then the endemic equilibrium is GAS.*

Remark 4.4. Compared to results in section 5 of reference [29], Corollary 4.1 is the same as Theorem 5.1 in [29].

5. **Discussion.** In this paper, we have proposed a general multi-group model to capture the features of some infectious disease with latency and relapse in heterogeneous populations. The model can describe disease progression such as gonorrhea, the co-infection of HIV and HCV, in which individuals can be divided into groups according to distinct numbers of sexual partners.

We carried out a complete mathematical analysis of the model and established its global dynamics. The basic reproduction number R_0 was calculated. It is proved that if $R_0 \le 1$ then the disease-free equilibrium is globally asymptotically stable by using a matrix-theoretic method and applying the Perron eigenvector, and if $R_0 > 1$ then the endemic equilibrium is globally asymptotic stability by combining Kirchhoff's matrix tree theorem and a new combinatorial identity. Our theoretical results show that the disease either dies out or remains endemic completely depending on the value of the basic reproduction number.

Some epidemic models with an arbitrarily distributed exposed stage have been studied in the literature; see for example [35, 36]. It is thus of interest to investigate multi-group models with relapse and a general exposed distribution. Therefore, the following multi-group SEIR epidemic model with relapse and a general exposed distribution

$$\begin{aligned} S_i'(t) &= \Lambda_i - \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i(t))\psi_j(I_j(t)) - d_i S_i(t), \\ E_i'(t) &= \sum_{j=1}^{n} \beta_{ij}\phi_i(S_i(t))\psi_j(I_j(t)) - d_i E_i(t) \\ &\quad + \sum_{j=1}^{n} \int_0^t \beta_{ij}\phi_i(S_i(u))\psi_j(I_j(u)) e^{-d_i(t-u)} d_t P_i(t-u)du, \\ I_i'(t) &= -\sum_{j=1}^{n} \int_0^t \beta_{ij}\phi_i(S_i(u))\psi_j(I_j(u)) e^{-d_i(t-u)} d_t P_i(t-u)du \\ &\quad -(d_i + r_i + \alpha_i)I_i(t) + \eta_i R_i(t), \\ R_i'(t) &= r_i I_i(t) - d_i R_i(t) - \eta_i R_i(t), \quad i = 1, 2, \ldots, n. \end{aligned}$$

will be our further work. As noted in the introduction, a high incidence of HCV relapse is also reported in HIV-1-coinfected patients. It also would be interesting and worthwhile to set up multi-group models to investigate the effect of HIV on the relapse rate in HCV.

Appendix. Some basic concepts from graph theory can be found in [8]. Let $(\mathcal{G}, H)$ be a weighted digraph with n vertices, define the $n \times n$ weight matrix $H = [h_{ij}]$, where $h_{ij} > 0$ if there exists an arc (j, i) from vertex j to vertex i, otherwise $h_{ij} = 0$. Let c_i be the cofactor of the i-th diagonal element of the Laplacian matrix of H which is defined as

$$h_{ij} = \begin{cases} -h_{ij} & \text{for } i \neq j \\ \sum_{k \neq i} h_{ik} & \text{for } i = j \end{cases}$$

[21]. The following result (Kirchhoff's matrix tree theorem) gives the graph-theoretic description of the cofactor c_i.

Proposition A.1. [21] *Assume $n \geq 2$. Then*

$$c_i = \sum_{\mathcal{T} \in \mathbb{T}_i} w(\mathcal{T}), \quad i = 1, 2, \ldots, n,$$

where $\mathbb{T}_i$ is the set of all spanning trees $\mathcal{T}$ of $(\mathcal{G}, \mathcal{H})$ that are rooted at vertex i, and $w(\mathcal{T})$ is the weight of $\mathcal{T}$. In particular, if $(\mathcal{G}, \mathcal{H})$ is strongly connected, then $c_i > 0$ for $1 \leq i \leq n$.

Theorem A.2. [29] *Assume $n \geq 2$. Let c_i be given as in Proposition A.1, and let $\{G_i(z)_{i=1}^n\}$ be any family of functions with $z = (z_1, z_2, \ldots, z_m)^T \in \mathbb{R}^m$. Then*

$$\sum_{i,j=1}^{n} c_i h_{ij} G_i(z) = \sum_{i,j=1}^{n} c_i h_{ij} G_j(z).$$

Theorem A.3. [29] *Assume $n \geq 2$. Let c_i be given as in Proposition A.1. If $h_{ij} > 0$ and $d^+(j) = 1$ for some i, j, then*

$$c_i h_{ij} = \sum_{k=1}^{n} c_j h_{jk}.$$

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