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STABILITY ANALYSIS OF AN AGE-STRUCTURED VIRAL INFECTION MODEL WITH LATENCY

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ABSTRACT. Age structure and cell-to-cell transmission are two major infection mechanisms in modeling spread of infectious diseases. We propose an age-structured viral infection model with latency, infection age-structure and cell-to-cell transmission. This paper aims to reveal the basic reproduction number and prove it to be a sharp threshold determining whether the infection dies out or not. Mathematical analysis is presented on relative compactness of the orbit, existence of a global attractor, and uniform persistence of system. We further investigate local and global stability of the infection-free and infection equilibrium.

1. INTRODUCTION

In the past two decades, since the pioneering work of Perelson et al. [20], within-host virus dynamics has attracted considerable attention of researchers. Many mathematical models describing the dynamics inside the host of various infectious diseases such as HIV, HBV have been formulated and studied [15, 16, 18, 19, 22, 29, 35]. The investigation of such models can help better understanding the interaction mechanisms of target cells, infected cells, and free virus particles through time in an infected individual.

The classical viral infection model in Perelson et al. [20] neglects certain features that may be important to consider for HIV, such as *age structure* in the infected cell component. By allowing for mortality rate and viral production rate of infected cells are functions of the infection age of the infected cells instead of constant, Nelson et al. [17], Huang et al. [6], Browne et al. [2], and Wang et al. [32] have studied age-structured model of HIV infection by considering infection age to be a continuous variable. These models generalizes the discrete and distributed delay viral infection model (modeling time delay between viral entry of a target cell and viral production from the newly infected cell. Further, such formulation of a hybrid system of ODEs and PDEs have already made the mathematical analysis very challenging in determining the threshold dynamics of equilibrium in viral infection model, which may allow us to have a good understanding on productively infected cells.

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Recently, HIV latency have been considered together in the viral infection model, which is the main reason that long-term low viral load persistence in patients on antiretroviral therapy. Usually, suppress the plasma viral load to below the detection limit may last half life of months or years [22]. Recent studies reveals the decay dynamics of the latent reservoir, such as latency infected CD4+ T cells, see e.g. Muller et al. [14], Kim and Perelson [9] and Strain et al. [27]. Latently infected cells could be activated by specific antigen. Strain et al. [27] found that cells specific to frequently encountered antigens are activated soon while cells specific to rare antigens are not. It may be important for latently infected cells activation to be more general functions of cellular infection-age. Alshorman et al. [1] introduced latency infection age to model the heterogeneity of latently infected CD4+ T cells.

Recently, based on the facts that HIV latency remains a major obstacle to viral elimination, Wang and Dong [31] considered the model

$$\begin{gathered}
\frac{dT(t)}{dt} = h - dT(t) - \beta T(t)V(t),\\
\Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\Big)e(a,t) = -\theta_1(a)e(a,t),\\
\Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial b}\Big)i(b,t) = -\theta_2(b)i(b,t),\\
\frac{dV(t)}{dt} = \int_0^\infty p(b)i(b,t)\,db - cV(t),
\end{gathered} \tag{1.1}$$

with boundary and initial conditions

$$\begin{gathered}
e(0,t) = f\beta T(t)V(t),\\
i(0,t) = (1-f)\beta T(t)V(t) + \int_0^\infty \xi(a)e(a,t)\,da,\\
T(0) = T_0 \ge 0,\ e(a,0) = e_0(a) \in L^1_+(0,\infty),\\
i(b,0) = i_0(b) \in L^1_+(0,\infty),\ V(0) = V_0 \ge 0,
\end{gathered}$$

where $T(t), e(a,t), i(a,t), V(t)$ the concentration of uninfected CD4+ T cells at time t, latently infected T cells with latency age a at time t, productively infected cells with infection age b at time t, and virions in plasma at t, respectively. The parameter h, d, β and c are the production rate of uninfected CD4+ T cells, the per capita death rate of uninfected cells, infection rate of CD4$^+$ T cells by infectious virus and the viral clearance rate, respectively. In model (1.1), a small fraction $f \in (0,1)$ is assumed to be latency infected cells and that the remaining $1-f$ become productively infected cells (see also in [1]. $\theta_1(a)$ is used to illustrate the decreasing effect of the pool size of latent infected cells when latently infected cells are activated. $\theta_2(b)$ represents the death rate of productively infected cells. $\xi(a)$ denotes the activation rate of latently infected T cells with latency age a. $\int_0^\infty \xi(a)e(a,t)\,da$ denotes the total number of productively infected cells from the activation of latently infected cells. $p(b)$ is the production rate of viral particles with infection age b. $L^1_+(0,\infty)$ is the set of all integrable nonnegative functions on $\mathbb{R}_+ := [0,+\infty)$. In [31], the authors shows that (1.1) has a global attractor, and it is uniformly persistent if the basic reproduction number is greater than one. The threshold dynamics of infection-free and infection equilibrium subject to latently age and infection age are also addressed by Lyapunov functionals techniques.

However, more and more research pay attention to the fact that virus can also spread by direct cell-to-cell transmission [3, 4, 7, 10, 12, 23, 24, 31]. Viral particles can be simultaneously transferred from infected target cells to uninfected ones through virological synapses during cell-to-cell transmission [7]. Some evidences reveal that cell-to-cell transmission may have a lower risk of being neutralized by neutralizing antibodies or cleared by cytotoxic T lymphocytes [12]. Dimitrov et al. [4] found that the infectivity of HIV-1 during cell-to-cell transmission is greater than the infectivity of cell-free viruses. Sigal et al. [24] claimed that cell-to-cell spread of HIV-1 does reduce the efficacy of antiretroviral therapy. Lai and Zou [10] formulated viral infection model incorporating both the virus-to-cell infection and cell-to-cell transmission in the form of discrete and distributed delay differential equations and obtain the threshold dynamics in term of the basic reproduction number. Wang et al. [32] considered the variance in the infectivity with respect to the infection age of the infected cells in the cell-to-cell transmission. Thus, it is natural to consider a model incorporating Latency infection age, infection age and cell-to-cell transmission. This constitutes one motivation of the present paper. Our second motivation comes from a series of works on infection age within host models [17, 6, 2, 21, 32], which are devoted to understanding the joint effects of the age structure and the cell-to-cell transmission on threshold dynamics of these models. Our study is mainly motivated by [31, 32] where the authors proved that the threshold dynamics of the model. It is then interesting to see whether similar results hold for our present model.

In this article, we propose and study the following age-structured HIV infection model with latency and and both cell-free and cell-to-cell transmission modes.

$$
\begin{aligned}
\frac{dT(t)}{dt} &= h - dT(t) - \beta_1 T(t)V(t) - \beta_2 T \int_0^\infty q(b)i(b,t)\,db,\\
\Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\Big)e(a,t) &= -\theta_1(a)e(a,t),\\
\Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial b}\Big)i(b,t) &= -\theta_2(b)i(b,t),\\
\frac{dV(t)}{dt} &= \int_0^\infty p(b)i(b,t)\,db - cV(t),
\end{aligned}
\tag{1.2}
$$

with boundary conditions

$$
\begin{aligned}
e(0,t) &= f\Big(\beta_1 T(t)V(t) + \beta_2 T \int_0^\infty q(b)i(b,t)\,db\Big),\\
i(0,t) &= (1-f)\Big(\beta_1 T(t)V(t) + \beta_2 T \int_0^\infty q(b)i(b,t)\,db\Big) + \int_0^\infty \xi(a)e(a,t)\,da,
\end{aligned}
\tag{1.3}
$$

and initial conditions

$$
\begin{gathered}
T(0) = T_0 \geq 0, \quad V(0) = V_0 \geq 0,\\
e(a,0) = e_0(a) \in L^1_+(0,\infty), \quad i(b,0) = i_0(b) \in L^1_+(0,\infty),
\end{gathered}
$$

where β_1 and β_2 are the infection rate of CD4$^+$ T cells by infectious virus and productively infected cells, respectively. The meaning of other parameters in (1.2) are the same as in (1.1).

We make the following assumptions on the parameters and functions in (1.2).

Assumption 1.1. (i) h, d, β_1, β_2, $c > 0$;

(ii) For $1 = 1, 2$, $q(\cdot), \theta_i(\cdot), p(\cdot), \xi(\cdot) \in L_+^\infty(0,\infty)$ satisfy the conditions:

$$\bar{q} := \operatorname{ess\,sup}_{b\in[0,\infty)} q(b) < \infty, \quad \bar{\theta}_i := \operatorname{ess\,sup}_{a\in[0,\infty)} \theta_i(a) < \infty,$$
$$\bar{p} := \operatorname{ess\,sup}_{a\in[0,\infty)} p(a) < \infty, \quad \bar{\xi} := \operatorname{ess\,sup}_{a\in[0,\infty)} \xi(a) < \infty,$$

(iii) $q(\cdot)$, $p(\cdot)$, $\xi(\cdot)$ are Lipschitz continuous on $\mathbb{R}_+ := [0,\infty)$ with Lipschitz constants M_q, M_p, M_ξ respectively;

(iv) There exists $\mu_0 \in (0, d]$ such that $\theta_1(a), \theta_2(b) \geq \mu_0$ for all $a \geq 0$;

(v) There exists a maximum age $b^+ > 0$ for the viral production such that $p(b) > 0$ for $b \in (0, b^+)$ and $p(b) = 0$ for $b > b^+$.

The remaining part of this article proceeds as follows. In the next Section, we give some preliminary results including solution semi-flow, Volterra formulation of solutions, boundedness of solutions, basic reproduction number and existence of equilibria. Section 3 is devoted to the relative compactness of solution semi-flow and the existence of global attractor. The uniform persistence of (1.2) is proved in Section 4. We obtain the local stability of the infection-free equilibrium and the infection equilibrium in Section 5. Then we establish their global attractivity in Section 6.

2. Preliminaries

2.1. **Semi-flow solution.** We define the state space of (1.2) as

$$\mathcal{Y} = \mathbb{R}_+ \times L_+^1(0,\infty) \times L_+^1(0,\infty) \times \mathbb{R}_+$$

endowed with the norm

$$\|(x,\varphi,\psi,y)\|_{\mathcal{Y}} = |x| + \|\varphi\|_{L^1} + \|\psi\|_{L^1} + |y| \quad \text{for } (x,\varphi,\psi,y) \in \mathcal{Y}.$$

If any initial value $X_0 = (T_0, e_0(\cdot), i_0(\cdot), V_0) \in \mathcal{Y}$ satisfies the coupling equations

$$e(0,0) = f\Big(\beta_1 T_0 V_0 + \beta_2 T_0 \int_0^\infty q(b) i_0(b)\, db\Big),$$
$$i(0,0) = (1-f)\Big(\beta T_0 V_0 + +\beta_2 T_0 \int_0^\infty q(b) i_0(b)\, db\Big) + \int_0^\infty \xi(a) e_0(a) da,$$

then (1.2) is well-posed under Assumption 1.1 according to Iannelli [8] and Magal [11].

In fact, it is easy to show that $(T(t), e(\cdot,t), i(\cdot,t), V(t)) \in \mathcal{Y}$ for each $t \geq 0$. We still assume that the initial values satisfy the coupling equations in the remaining context. Thus we have a continuous solution semi-flow $\Phi : \mathbb{R}_+ \times \mathcal{Y} \to \mathcal{Y}$ defined by

$$\Phi(t, X_0) = \Phi_t(X_0) := (T(t), e(\cdot,t), i(\cdot,t), V(t)), \quad t \geq 0,\ X_0 \in \mathcal{Y}. \tag{2.1}$$

For the ease of notation, we introduce

$$\Omega(a) = e^{-\int_0^a \theta_1(\tau) d\tau}, \quad \Gamma(b) = e^{-\int_0^b \theta_2(\tau) d\tau} \quad \text{for } a, b \geq 0, \tag{2.2}$$

$$\begin{gathered} Q(t) = \int_0^\infty q(b) i(b,t)\, db, \quad M(t) = \int_0^\infty \xi(a) e(a,t)\, da, \\ N(t) = \int_0^\infty p(b) i(b,t)\, db. \end{gathered} \tag{2.3}$$

It follows from (ii) and (v) of Assumption 1.1 that for all $a, b \geq 0$,

$$\begin{aligned} &0 \leq \Omega(a) \leq \mathrm{e}^{-\mu_0 a}, \quad 0 \leq \Gamma(b) \leq \mathrm{e}^{-\mu_0 b}, \\ &\Omega'(a) = -\theta_1(a)\Omega(a), \quad \Gamma'(b) = -\theta_2(b)\Gamma(b). \end{aligned} \tag{2.4}$$

2.2. **Volterra formulation.** Along the characteristic lines $t - a =$ const. and $t - b =$ const., the second and third equations of (1.2) can be calculated as

$$e(a,t) = \begin{cases} f\big[\beta_1 V(t-a) + \beta_2 Q(t-a)\big]T(t-a)\Omega(a) = e(0,t-a)\Omega(a), \\ \quad \text{if } 0 \leq a \leq t, \\ e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}, \\ \quad \text{if } 0 \leq t \leq a; \end{cases} \tag{2.5}$$

and

$$i(b,t) = \begin{cases} i(0,t-b)\Gamma(b), & \text{if } 0 \leq b \leq t, \\ i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}, & \text{if } 0 \leq t \leq b, \end{cases} \tag{2.6}$$

where $i(0,t-b) = \{(1-f)\left[\beta_1 T(t-b)V(t-b) + \beta_2 T(t-b)Q(t-b)\right] + M(t-b)\}$.

2.3. **Boundedness of solutions.**

Proposition 2.1. *Let us define*

$$\begin{aligned} \Xi := \Big\{ &X_0 = (T_0, e_0, i_0, V_0) \in \mathcal{Y} : T_0 + \|e_0(a)\|_{L^1} \leq \frac{h}{\mu_0}, \\ &T_0 + \|e_0(a)\|_{L^1} + \|i_0(b)\|_{L^1} \leq \frac{h}{\mu_1},\ V_0 \leq \frac{\bar{p}h}{c\mu_0} + \frac{h\bar{p}\bar{\xi}}{c\mu_0^2},\ \|\Phi_t(X_0)\|_{\mathcal{Y}} \leq \frac{h}{\tilde{\mu}_0} \Big\}, \end{aligned}$$

where

$$\tilde{\mu}_0 := \frac{\mu_0}{1 + \frac{\bar{\xi}}{\mu_0} + \frac{\bar{p}}{c} + \frac{\bar{p}\bar{\xi}}{c\mu_0}}, \quad \mu_1 := \frac{\mu_0}{1 + \frac{\bar{\xi}}{\mu_0}}.$$

Then Ξ is a positively invariant subset for Φ; that is,

$$\Phi(t, X_0) \in \Xi \quad \textit{for all } t \geq 0 \textit{ and } X_0 \in \Xi.$$

Moreover, Φ is point dissipative and Ξ attracts all points in $\mathcal{Y}$.

Proof. It follows from (2.5) and changing variables that

$$\begin{aligned} \|e(\cdot,t)\|_{L^1} &= \int_0^t e(0,t-a)\Omega(a)\,da + \int_t^\infty e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}da \\ &= \int_0^t e(0,\sigma)\Omega(t-\sigma)\,d\sigma + \int_0^\infty e_0(\tau)\frac{\Omega(t+\tau)}{\Omega(\tau)}d\tau. \end{aligned}$$

Thus

$$\frac{d\|e(\cdot,t)\|_{L^1}}{dt} = e(0,t)\Omega(0) + \int_0^\infty \frac{e_0(\tau)}{\Omega(\tau)}\frac{d\Omega(t+\tau)}{dt}d\tau + \int_0^t e(0,\sigma)\frac{d\Omega(t-\sigma)}{dt}\,d\sigma.$$

It follows from (2.4) and changing of variables that

$$\begin{aligned} \frac{d\|e(\cdot,t)\|_{L^1}}{dt} &= e(0,t)\Omega(0) - \int_0^\infty \frac{e_0(\tau)}{\Omega(\tau)}\theta_1(t+\tau)\Omega(t+\tau)d\tau \\ &\quad - \int_0^t e(0,\sigma)\theta_1(t-\sigma)\Omega(t-\sigma)\,d\sigma \\ &= e(0,t)\Omega(0) - \int_0^\infty \theta_1(a)e(a,t)\,da. \end{aligned} \tag{2.7}$$

This, combined with the first equation in (1.2) and (v) of Assumption 1.1, gives us

$$\begin{aligned}
&\frac{d(T(t)+\|e(\cdot,t)\|_{L^1})}{dt} \\
&= h - dT(t) - \beta_1 T(t)V(t) - \beta_2 T\int_0^\infty q(b)i(b,t)\,db \\
&\quad + f[\beta_1 T(t)V(t) + \beta_2 T\int_0^\infty q(b)i(b,t)\,db] - \int_0^\infty \theta_1(a)e(a,t)\,da \\
&\le h - \mu_0(T(t)+\|e(\cdot,t)\|_{L^1})
\end{aligned}$$

for $t \ge 0$. An application of the variation of constants formula immediately yields

$$T(t)+\|e(\cdot,t)\|_{L^1} \le \frac{h}{\mu_0} - e^{-\mu_0 t}\big\{\frac{h}{\mu_0} - (T_0 + \|e_0\|_{L^1})\big\}, \quad t \ge 0, \tag{2.8}$$

which implies that if $X_0 \in \Xi$ then $T(t)+\|e(\cdot,t)\|_{L^1} \le \frac{h}{\mu_0}$ for $t \ge 0$. Further, we can derive

$$\begin{aligned}
\frac{d\|i(\cdot,t)\|_{L^1}}{dt} &= (1-f)[\beta_1 T(t)V(t) + \beta_2 T\int_0^\infty q(b)i(b,t)\,db] \\
&\quad + \int_0^\infty \xi(a)e(a,t)\,da - \int_0^\infty \theta_2(b)i(b,t)\,db.
\end{aligned}$$

It follows that

$$\begin{aligned}
&\frac{d(T(t)+\|e(\cdot,t)\|_{L^1}) + \|i(\cdot,t)\|_{L^1})}{dt} \\
&= h - dT + \int_0^\infty \xi(a)e(a,t)\,da - \int_0^\infty \theta_1(a)e(a,t)\,da - \int_0^\infty \theta_2(b)i(b,t)\,db.
\end{aligned}$$

From (2.7) and (v) of Assumption 1.1,

$$\begin{aligned}
&\frac{d(T(t)+\|e(\cdot,t)\|_{L^1}) + \|i(\cdot,t)\|_{L^1})}{dt} \\
&\le h + \bar{\xi}\|e(\cdot,t)\|_{L_1} - \mu_0(T(t)+\|e(\cdot,t)\|_{L^1} + i(\cdot,t)\|_{L^1}) \\
&\le h + \bar{\xi}\frac{h}{\mu_0} - \mu_0(T(t)+\|e(\cdot,t)\|_{L^1} + i(\cdot,t)\|_{L^1}).
\end{aligned}$$

Using the variation of constants formula again gives

$$\begin{aligned}
&\|T(t)+\|e(\cdot,t)\|_{L^1}) + \|i(\cdot,t)\|_{L^1} \\
&\le \frac{h+\bar{\xi}\frac{h}{\mu_0}}{\mu_0} - e^{-\mu_0 t}\big\{\frac{h+\bar{\xi}\frac{h}{\mu_0}}{\mu_0} - (T(t)+\|e(\cdot,t)\|_{L^1} + i(\cdot,t)\|_{L^1})\big\}, \quad t \ge 0.
\end{aligned} \tag{2.9}$$

From (2.9), we have $\|i(\cdot,t)\|_{L^1} \le \frac{h}{\mu_0} + \frac{\bar{\xi}h}{\mu_0^2}$. Similarly, it follows from

$$\frac{dV(t)}{dt} \le \bar{p}\|i(\cdot,t)\|_{L^1} - cV(t) \le \bar{p}\Big(\frac{h}{\mu_0} + \frac{\bar{\xi}h}{\mu_0^2}\Big) - cV(t)$$

that

$$\begin{aligned}
V(t) &\le \frac{\bar{p}(\frac{h}{\mu_0} + \frac{\bar{\xi}h}{\mu_0^2})}{c} - e^{-ct}\big\{\frac{\bar{p}h}{c\mu_0} + \frac{h\bar{p}\bar{\xi}}{c\mu_0^2} - V_0\big\} \\
&\le \frac{\bar{p}h}{c\mu_0} + \frac{h\bar{p}\bar{\xi}}{c\mu_0^2} - e^{-\mu_0 t}\big\{\frac{\bar{p}h}{c\mu_0} + \frac{h\bar{p}\bar{\xi}}{c\mu_0^2} - V_0\big\}.
\end{aligned} \tag{2.10}$$

Summing (2.8), (2.9) and (2.10), we conclude that if $X_0 \in \Xi$, then for $t \geq 0$,

$$\begin{aligned} &\|\Phi_t(X_0)\|_{\mathcal{Y}} \\ &\leq \Big(1 + \frac{\bar{\xi}}{\mu_0} + \frac{\bar{p}}{c} + \frac{\bar{p}\bar{\xi}}{c\mu_0}\Big)\frac{h}{\mu_0} - e^{-\mu_0 t}\Big\{\Big(1 + \frac{\bar{\xi}}{\mu_0} + \frac{\bar{p}}{c} + \frac{\bar{p}\bar{\xi}}{c\mu_0}\Big)\frac{h}{\mu_0} - \|X_0\|_{\mathcal{Y}}\Big\} \\ &= \frac{h}{\tilde{\mu}_0} - e^{-\mu_0 t}\big\{\frac{h}{\tilde{\mu}_0} - \|X_0\|_{\mathcal{Y}}\big\} \leq \frac{h}{\tilde{\mu}_0}. \end{aligned} \tag{2.11}$$

Consequently, Ξ is positively invariant with respect to Φ. From (2.9) and (2.11) if follows that $\limsup_{t\to\infty}[T(t) + \|e(\cdot,t)\|_{L^1}] \leq \frac{h}{\mu_1}$ and $\limsup_{t\to\infty}\|\Phi_t(X_0)\|_{\mathcal{Y}} \leq \frac{h}{\tilde{\mu}_0}$ for any $X_0 \in \mathcal{Y}$, that is, Φ is point dissipative and Ξ attracts all points in $\mathcal{Y}$. This completes the proof. $\square$

The following result is a direct consequence of Proposition 2.1, which will be used later.

Proposition 2.2. *Let $A \geq h/\tilde{\mu}_0$ be given. If $X_0 \in \mathcal{Y}$ satisfies $\|X_0\|_{\mathcal{Y}} \leq A$, then the following statements hold for all $t \geq 0$.*

(i) $T(t)$, $\|e(\cdot,t)\|_{L^1}$, $\|i(\cdot,t)\|_{L^1}$, $V(t) \leq A$;
(ii) $M(t) \leq \bar{\xi}A$ *and* $N(t) \leq \bar{p}A$;
(iii) $e(0,t) \leq f\beta A^2$, $i(0,t) \leq (1-f)\beta A^2 + \bar{\xi}A$, *where* $\beta = \beta_1 + \beta_2\bar{q}$.

2.4. **Existence of equilibria.** System (1.2) admits an infection-free equilibrium $P^0 = (T^0, e^0(a), i^0(b), V^0) := (\frac{h}{d}, 0, 0, 0)$.

An equilibrium $(T^*, e^*, i^*, V^*) \in \mathcal{Y}$ of (1.2) should satisfy

$$\begin{gathered} h - dT^* - \beta_1 T^* V^* - \beta_2 T^* \int_0^\infty q(b) i^*(b)\,db = 0, \\ \frac{d}{da} e^*(a) = -\theta_1(a) e^*(a), \\ \frac{d}{db} i^*(b) = -\theta_2(b) i^*(b), \\ \int_0^\infty p(b) i^*(b)\,db = cV^*, \\ e^*(0) = f\beta_1 T^* V^* + f\beta_2 T^* \int_0^\infty q(b) i^*(b)\,db, \\ i^*(0) = (1-f)\beta_1 T^* V^* + (1-f)\beta_2 T^* \int_0^\infty q(b) i^*(b)\,db + \int_0^\infty \xi(a) e^*(a)\,da. \end{gathered} \tag{2.12}$$

where T^*, $e^*(a)$, $i^*(b)$, and V^* are not zero. We denote

$$K = \int_0^\infty \xi(a)\Omega(a)\,da, \quad J = \int_0^\infty p(b)\Gamma(b)\,db, \quad L = \int_0^\infty q(b)\Gamma(b)\,db.$$

We define the basic reproduction number of (1.2) as

$$\mathcal{R}_0 = \frac{(1-f)\beta_1 T^0 J}{c} + (1-f)\beta_2 T^0 L + \frac{f\beta_1 T^0 KJ}{c} + f\beta_2 T^0 KL.$$

After a simple calculation, we see that if $\mathcal{R}_0 > 1$ then (1.2) has a unique infection equilibrium $P^* = (T^*, e^*(a), i^*(b), V^*)$ with

$$T^* = \frac{T^0}{\mathcal{R}_0}, \quad e^*(a) = fh\Big(1 - \frac{1}{\mathcal{R}_0}\Big)\Omega(a), \tag{2.13}$$

$$i^*(b) = (1 - f + fK)h\Big(1 - \frac{1}{\mathcal{R}_0}\Big)\Gamma(b), \quad V^* = \frac{1}{c}\int_0^\infty p(b)i^*(b)\,db. \tag{2.14}$$

Thus we arrive at the following result.

Theorem 2.3. (i) *System* (1.2) *always has an infection-free equilibrium* P^0.

(ii) *If* $\mathcal{R}_0 > 1$, *then* (1.2) *admits a unique infection equilibrium* $P^* = (T^*, e^*(a), i^*(a), V^*)$ *defined by* (2.13).

3. Asymptotic smoothness of $\Phi(t, X_0)$

In this section, we begin with showing the asymptotic smoothness of semiflows, then by [5, Theorem 3.4.6], the semiflow has a compact attractor. In what follows, we adopt the approach in [30, Theorem 4.2 of Chapter IV].

Definition 3.1 ([28]). A set A in $\mathcal{Y}$ is called a compact attractor of a set $B \subseteq X$ if A is compact, invariant, and non-empty and $\Phi_t(B) \to A$ as $t \to \infty$. The last means that, for every open subset U of $\mathcal{Y}$ with $A \subseteq U$, there is some $r > 0$ such that $\Phi_t(B) \subseteq U$ for all $t \ge r$ (i.e. $\Phi([r, \infty) \times B) \subseteq U$).

The following proposition reveals that the functions $M(t)$ and $N(t)$ are Lipschitz continuous. The proof comes from using Proposition 2.1, Assumption 1.1 and [33, Proposition 4.1]. We omit it.

Proposition 3.2. *For any solution of* (1.2), *the functions* $M(t)$, $N(t)$ *and* $Q(t)$ *are Lipschitz continuous on* $\mathbb{R}_+$ *with Lipschitz coefficients* L_M, L_N *and* L_Q.

Next we divide $\Phi : \mathbb{R}_+ \times \mathcal{Y} \to \mathcal{Y}$ into the following two operators Θ, Ψ : $\mathbb{R}_+ \times \mathcal{Y} \to \mathcal{Y}$:

$$\Theta(t, X_0) := (0, \tilde\varphi_e(\cdot, t), \tilde\varphi_i(\cdot, t), 0),$$
$$\Psi(t, X_0) := (T(t), \tilde e(\cdot, t), \tilde i(\cdot, t), V(t)),$$

where

$$\tilde\varphi_e(a,t) = \begin{cases} 0, & \text{if } t > a \ge 0, \\ e(a,t), & \text{if } a \ge t \ge 0; \end{cases} \quad \tilde\varphi_i(b,t) = \begin{cases} 0, & \text{if } t > b \ge 0, \\ i(b,t), & \text{if } b \ge t \ge 0; \end{cases}$$
$$\tilde e(a,t) = \begin{cases} e(a,t), & \text{if } t > a \ge 0, \\ 0, & \text{if } a \ge t \ge 0; \end{cases} \quad \tilde i(b,t) = \begin{cases} i(b,t), & \text{if } t > b \ge 0, \\ 0, & \text{if } b \ge t \ge 0. \end{cases}$$

Then $\Phi(t, X_0) = \Theta(t, X_0) + \Psi(t, X_0)$ for $t \ge 0$. Following the proof of [34, Proposition 3.13], we can arrive at the main result of this section.

Theorem 3.3. *For* $X_0 \in \Xi$, *the orbit* $\{\Phi(t, X_0) : t \ge 0\}$ *has a compact closure in* $\mathcal{Y}$ *if the following two conditions hold:*

(i) *There exists a function* $\Delta : \mathbb{R}_+ \times \mathbb{R}_+ \to \mathbb{R}_+$ *such that, for any* $r > 0$, $\lim_{t\to\infty} \Delta(t, r) = 0$ *and if* $X_0 \in \Omega$ *with* $\|X_0\|_{\mathcal{Y}} \le r$ *then* $\|\Theta(t, X_0)\|_{\mathcal{Y}} \le \Delta(t, r)$ *for* $t \ge 0$;

(ii) *For* $t \ge 0$, $\Psi(t, \cdot)$ *maps any bounded sets of* Ξ *into sets with compact closure in* $\mathcal{Y}$.

Proof. (i) Let $\Delta(t, r) = e^{-\mu_0 t} r$, then $\lim_{t\to\infty} \Delta(t, r) = 0$. By (2.5) and (2.6),

$$\tilde\varphi_e(a,t) = \begin{cases} 0, & \text{if } t > a \ge 0, \\ e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}, & \text{if } a \ge t \ge 0; \end{cases}$$

$$\tilde{\varphi}_i(b,t) = \begin{cases} 0, & \text{if } t > b \geq 0, \\ i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}, & \text{if } b \geq t \geq 0. \end{cases}$$

Then, for $X_0 \in \Xi$ satisfying $\|X_0\|_{\mathcal{Y}} \leq r$ and for $t \geq 0$, we have

$$\begin{aligned}
\|\Theta\left(t, X_0\right)\|_{\mathcal{Y}} &= |0| + \|\tilde{\varphi}_e(\cdot,t)\|_{L^1} + \|\tilde{\varphi}_i(\cdot,t)\|_{L^1} + |0| \\
&= \int_t^\infty |e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}|\,da + \int_t^\infty |i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}|\,db \\
&= \int_0^\infty |e_0(\sigma)\frac{\Omega(\sigma+t)}{\Omega(\sigma)}|\,d\sigma + \int_0^\infty |i_0(\sigma)\frac{\Gamma(\sigma+t)}{\Gamma(\sigma)}|\,d\sigma \\
&= \int_0^\infty |e_0(\sigma)e^{-\int_\sigma^{\sigma+t}\theta_1(\tau)d\tau}|\,d\sigma + \int_0^\infty |i_0(\sigma)e^{-\int_\sigma^{\sigma+t}\theta_2(\tau)d\tau}|\,d\sigma \\
&\leq e^{-\mu_0 t}\|e_0\|_{L^1} + e^{-\mu_0 t}\|i_0\|_{L^1} \\
&\leq e^{-\mu_0 t}\|X_0\|_{\mathcal{Y}}.
\end{aligned}$$

(ii) We next claim that $\Psi\left(t,\cdot\right)$ maps any bounded sets of Ξ into sets with compact closure in $\mathcal{Y}$. It follows from Proposition 2.1 that $T(t)$ and $V(t)$ remains in the compact set $[0, h/\tilde{\mu}_0] \subset [0, A]$. We only need to verify that $\tilde{e}\left(a,t\right)$ and $\tilde{i}\left(b,t\right)$ remain in a precompact subset of $L^1_+\left(0,\infty\right)$, which is independent of $X_0 \in \Xi$. We follow the method of [26, Theorem B.2]) to check the following conditions valid to $\tilde{e}\left(a,t\right)$ and $\tilde{i}\left(b,t\right)$,

(i) The supremum of $\|\tilde{e}\left(\cdot,t\right)\|_{L^1}$ with respect to $X_0 \in \Xi$ is finite;
(ii) $\lim_{h\to\infty}\int_h^\infty \tilde{e}\left(a,t\right)\,da = 0$ uniformly with respect to $X_0 \in \Xi$;
(iii) $\lim_{h\to 0+}\int_0^\infty |\tilde{e}\left(a+h,t\right) - \tilde{e}\left(a,t\right)|da = 0$ uniformly with respect to $X_0 \in \Xi$;
(iv) $\lim_{h\to 0+}\int_0^h \tilde{e}\left(a,t\right)\,da = 0$ uniformly with respect to $X_0 \in \Xi$.

It follows from (2.5), (2.6), Proposition 2.2, and (2.4) that

$$\begin{gathered}
\tilde{e}(a,t) \leq f\beta A^2 e^{-\mu_0 a}, \\
\tilde{i}(b,t) \leq \left[(1-f)\beta A^2 + \bar{\xi}A\right] e^{-\mu_0 b}.
\end{gathered}$$

Thus, (i), (ii), and (iv) are satisfied.

Next we verify condition (iii). For sufficiently small $h \in (0,t)$, we have

$$\begin{aligned}
&\int_0^\infty |\tilde{e}(a+h,t) - \tilde{e}(a,t)|\,da \\
&= \int_0^{t-h} |e(a+h,t) - e(a,t)|da + \int_{t-h}^t |0 - e(a,t)|da \\
&= \int_0^{t-h} \Big|e(0,t-a-h)\Omega(a+h) - e(0,t-a)\Omega(a)\Big|\,da + \int_{t-h}^t \Big|e(0,t-a)\Omega(a)\Big|da \\
&\leq \Delta_1 + \Delta_2 + f\beta A^2 h,
\end{aligned}$$

where

$$\begin{aligned}
\Delta_1 &= \int_0^{t-h} e(0,t-a-h)|\Omega(a+h) - \Omega(a)|\,da, \\
\Delta_2 &= \int_0^{t-h} |e(0,t-a-h) - e(0,t-a)|\Omega(a)\,da.
\end{aligned}$$

We first estimate Δ_1. Directly calculations give

$$\begin{aligned}
\int_0^{t-h} |\Omega(a+h)-\Omega(a)|da &= \int_0^{t-h} \Big(\Omega(a)-\Omega(a+h)\Big)\,da \\
&= \int_0^{t-h} \Omega(a)\,da - \int_h^t \Omega(a)\,da \\
&= \int_0^{t-h} \Omega(a)\,da - \int_h^{t-h} \Omega(a)\,da - \int_{t-h}^t \Omega(a)\,da \\
&= \int_0^h \Omega(a)\,da - \int_{t-h}^t \Omega(a)\,da \le h,
\end{aligned}$$

it follows from Proposition 2.2 that

$$\Delta_1 \le f\beta A^2 h.$$

Next we estimate Δ_2. Rewriting Δ_2 as

$$\begin{aligned}
\Delta_2 &= \int_0^{t-h} |e(0,t-a-h)-e(0,t-a)|\Omega(a)da \\
&= \int_0^{t-h} \Big|\big(f\beta_1 T(t-a-h)V(t-a-h) + f\beta_2 T(t-a-h)Q(t-a-h)\big) \\
&\quad - \big(f\beta_1 T(t-a)V(t-a) + f\beta_2 T(t-a)Q(t-a)\big)\Big|\Omega(a)\,da \\
&\le \int_0^{t-h} \big|f\beta_1 T(t-a-h)V(t-a-h) - f\beta_1 T(t-a)V(t-a)\big|\Omega(a)\,da \\
&\quad + \int_0^{t-h} \big|f\beta_2 T(t-a-h)Q(t-a-h) - f\beta_2 T(t-a)Q(t-a)\big|\Omega(a)\,da.
\end{aligned}$$

Since $T(t)$ and $V(t)$ are both Lipschitz continuous on $\mathbb{R}_+$ with Lipschitz constants $M_T = h + dA + \beta_1 A^2 + \beta_2 \bar{q} A^2$ and $M_V = (\bar{p}+c)A$, respectively. It follows from Proposition 3.2 and [13, Proposition 6] that $T(t)V(t)$is Lipschitz continuous with Lipschitz constants $M_{TV} = AM_V + AM_T$ and $M_{TQ} = AM_Q + \bar{q}AM_T$. Denote that $G = f\beta_1 M_{TV} + f\beta_2 M_{TQ}$. Thus

$$\Delta_2 \le Gh \int_0^{t-h} e^{-\mu_0 a}da \le \frac{Gh}{\mu_0}.$$

Hence

$$\int_0^\infty |\tilde{e}(a+h,t)-\tilde{e}(a,t)|da \le \Big(2f\beta A^2 + \frac{G}{\mu_0}\Big)h,$$

and condition (iii) follows.

As for $\tilde{i}\,(b,t)$, we have

$$\begin{aligned}
&\int_0^\infty |\tilde{i}(b+h,t)-\tilde{i}(b,t)|\,db \\
&= \int_0^{t-h} |i(b+h,t)-i(b,t)|db + \int_{t-h}^t |0-i(b,t)|db \\
&= \int_0^{t-h} \big|i(0,t-b-h)\Gamma(b+h) - i(0,t-b)\Gamma(b)\big|\,db + \int_{t-h}^t \big|i(0,t-b)\Gamma(b)\big|\,db \\
&\le \Upsilon_1 + \Upsilon_2 + \big[(1-f)\beta A^2 + \bar{\xi}A\big]\,h,
\end{aligned}$$

where

$$\Upsilon_1 = \int_0^{t-h} i(0, t-b-h)|\Gamma(b+h) - \Gamma(b)|\, db,$$
$$\Upsilon_2 = \int_0^{t-h} |i(0, t-b-h) - i(0, t-b)|\Gamma(b)\, db.$$

Similarly, we have $\int_0^{t-h} \Big|\Gamma(b+h) - \Gamma(b)\Big| db \le h$. Hence from Proposition 2.2, we can conclude that

$$\Upsilon_1 \le [(1-f)\beta A^2 + \bar{\xi} A]h.$$

For Υ_2, we have

$$\begin{aligned} \Upsilon_2 \le (1-f) \int_0^{t-h} \Big| &\beta_1 \left(T(t-b-h)V(t-b-h) - T(t-b)V(t-b)\right) \\ &+ \beta_2 \left(T(t-b-h)Q(t-b-h) - T(t-b)Q(t-b)\right)\Big|\Gamma(b)\, db \\ &+ \int_0^{t-h} |M(t-b-h) - M(t-b)|\Gamma(b)\, db. \end{aligned}$$

As before, $M_{TV} = AM_V + AM_T, M_{TQ} = AM_Q + \bar{q}AM_T$. Recall that $M(t)$ is Lipschitz continuous on $\mathbb{R}_+$ with Lipschitz constants $L_M = (\bar{\xi} f\beta A + \bar{\xi}\bar{\theta}_1 + M_\xi)A$. Set $H = (1-f)(\beta_1 M_{TV} + \beta_2 M_{TQ}) + L_M$, By a zero-trick, then we have

$$\Upsilon_2 \le Hh \int_0^{t-h} e^{-\mu_0 b} db \le \frac{Hh}{\mu_0}.$$

Finally, we have

$$\int_0^\infty |\tilde{i}(b+h, t) - \tilde{i}(b, t)|\, db \le \big\{2[(1-f)\beta A^2 + \bar{\xi} A] + \frac{H}{\mu_0}\big\}h,$$

thus condition (iii) follows. This completes the proof. □

According to Smith and Thieme [26], we arrive at the following theorem for the existence of global attractors of the semi-flow $\{\Phi(t)\}_{t\ge 0}$.

Theorem 3.4. *The semi-flow $\{\Phi(t)\}_{t\ge 0}$ has a global attractor $\mathcal{A}$ in $\mathcal{Y}$, which attracts any bounded subset of $\mathcal{Y}$.*

4. Uniform persistence

The aim of this section is to show that (1.2) is uniformly persistent when the basic reproduction number is greater than one. Let $\hat{e}(t) := e(0, t)$ and $\hat{i}(t) := i(0, t)$. Then the first three equations of (1.2) can be rewritten as

$$\begin{gathered} \frac{dT(t)}{dt} = h - dT(t) - \frac{1}{f}\hat{e}(t), \\ e(a, t) = \begin{cases} \hat{e}(t-a)\Omega(a), & \text{if } t \ge a \ge 0, \\ e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}, & \text{if } a \ge t \ge 0; \end{cases} \\ i(b, t) = \begin{cases} \hat{i}(t-b)\Gamma(b), & \text{if } t \ge b \ge 0, \\ i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}, & \text{if } b \ge t \ge 0, \end{cases} \end{gathered} \tag{4.1}$$

where

$$\hat{e}(t) = f\Big(\beta_1 T(t)V(t) + \beta_2 T \int_0^\infty q(b)i(b,t)\,db\Big), \tag{4.2}$$

$$\begin{aligned} \hat{i}(t) &= (1-f)\Big(\beta_1 T(t)V(t) + \beta_2 T \int_0^\infty q(b)i(b,t)\,db\Big) \\ &\quad + \int_0^t \xi(a)\Omega(a)\hat{e}(t-a)\,da + \int_t^\infty \xi(a)\frac{\Omega(a)}{\Omega(a-t)} e_0(a-t)\,da. \end{aligned} \tag{4.3}$$

Lemma 4.1. *If $\mathcal{R}_0 > 1$, then there exists a positive constant ϵ_0 such that*

$$\limsup_{t\to\infty} \hat{e}(t) > \epsilon_0. \tag{4.4}$$

Proof. We first get an estimate on $\hat{i}(t)$ as follows. By (4.3), we have

$$\begin{aligned} \hat{i}(t) &\geq (1-f)\Big(\beta_1 T(t)V(t) + \beta_2 T \int_0^\infty q(b)i(b,t)\,db\Big) \\ &\quad + \int_0^t \xi(a)\Omega(a)\hat{e}(t-a)da. \end{aligned} \tag{4.5}$$

It follows from the fourth equation in (1.2) that

$$V(t) \geq \int_0^t e^{-c(t-\tau)} \int_0^\tau p(b)i(b,\tau)\,db\,d\tau = \int_0^t e^{-c(t-\tau)} \int_0^\tau p(b)\Gamma(b)\hat{i}(\tau-b)\,db\,d\tau.$$

This, combined with (4.5), gives us

$$\begin{aligned} &(1-f)\Big(\beta_1 T \int_0^t e^{-c(t-\tau)} \int_0^\tau p(b)\Gamma(b)\hat{i}(\tau-b)\,db\,d\tau + \beta_2 T \int_0^t q(b)\hat{i}(t-b)\Gamma(b)\,db\Big) \\ &+ f\beta_1 \int_0^t \xi(a)\Omega(a)T(t-a) \int_0^{t-a} e^{-c(t-a-\tau)} \int_0^\tau p(b)\Gamma(b)\hat{i}(\tau-b)\,dbd\tau\,da \\ &+ f\beta_2 \int_0^t \xi(a)\Omega(a)T(t-a) \int_0^t q(b)\hat{i}(\tau-b)\Gamma(b)\,dbda \leq \hat{i}(t). \end{aligned} \tag{4.6}$$

Since $\mathcal{R}_0 > 1$, there exists a sufficiently small $\epsilon_1 > 0 (\epsilon_1 = \frac{1}{f}\epsilon_0)$ such that

$$\begin{aligned} &\frac{(1-f)\beta_1}{c}\frac{h-\epsilon_1}{d} \int_0^\infty p(b)\Gamma(b)\,db + \frac{f\beta_1}{c}\frac{h-\epsilon_1}{d} \int_0^\infty \xi(a)\Omega(a)\,da \int_0^\infty p(b)\Gamma(b)\,db \\ &+ (1-f)\beta_2 \frac{h-\epsilon_1}{d} \int_0^\infty q(b)\Gamma(b)\,db \\ &+ f\beta_2 \frac{h-\epsilon_1}{d} \int_0^\infty \xi(a)\Omega(a)\,da \int_0^\infty q(b)\Gamma(b)\,db > 1. \end{aligned} \tag{4.7}$$

We claim that (4.4) holds for this ε_0. Otherwise, there exists a $T > 0$ such that

$$\hat{e}(t) \leq \epsilon_0 \quad \text{for all } t \geq T.$$

Then it follows from (4.1) that $\frac{dT(t)}{dt} \geq h - dT(t) - \epsilon_1$ for $t \geq T$. This implies that $\liminf_{t\to\infty} T(t) \geq \frac{h-\varepsilon_1}{d}$. Thus there exists $\hat{T} > T$ such that $T(t) \geq \frac{h-\epsilon_1}{d}$ for all

$t \ge \hat{T}$ and hence (4.6) becomes

$$
\begin{aligned}
&(1-f)\beta_1 \frac{h-\epsilon_1}{d} \int_0^t e^{-c(t-\tau)} \int_0^\tau p(b)\Gamma(b)\hat{i}(\tau-b)\,db\,d\tau \\
&+ (1-f)\beta_2 \frac{h-\epsilon_1}{d} \int_0^t q(b)\hat{i}(t-b)\Gamma(b)\,db \\
&+ f\beta_1 \frac{h-\epsilon_1}{d} \int_0^t \xi(a)\Omega(a) \int_0^{t-a} e^{-c(t-a-\tau)} \int_0^\tau p(b)\Gamma(b)\hat{i}(\tau-b)\,db d\tau\,da \\
&+ f\beta_2 \frac{h-\epsilon_1}{d} \int_0^t \xi(a)\Omega(a) \int_0^t q(b)\hat{i}(\tau-b)\Gamma(b)\,db\,da \le \hat{i}(t),
\end{aligned} \tag{4.8}
$$

for all $t \ge \hat{T}$. Without loss of generality, we can assume that (4.8) holds for all $t \ge 0$ (just replace X_0 by $\Phi(\hat{T}, X_0)$). Then taking the Laplace transforms on both sides of (4.8), we obtain

$$
\begin{aligned}
\mathcal{L}[\hat{i}] \ge\ & (1-f)\beta_1 \frac{h-\epsilon_1}{d} \frac{1}{c+\lambda} \int_0^\infty e^{-\lambda b} p(b)\Gamma(b)\,db \mathcal{L}[\hat{i}] \\
&+ (1-f)\beta_2 \frac{h-\epsilon_1}{d} \int_0^\infty e^{-\lambda b} q(b)\Gamma(b)\,db \mathcal{L}[\hat{i}] \\
&+ f\beta_1 \frac{h-\epsilon_1}{d} \frac{1}{c+\lambda} \int_0^\infty e^{-\lambda b} p(b)\Gamma(b)\,db \int_0^\infty e^{-\lambda a} \xi(a)\Omega(a)\,da \mathcal{L}[\hat{i}] \\
&+ f\beta_2 \frac{h-\epsilon_1}{d} \int_0^\infty e^{-\lambda b} q(b)\Gamma(b)\,db \int_0^\infty e^{-\lambda a} \xi(a)\Omega(a)\,da \mathcal{L}[\hat{i}].
\end{aligned}
$$

Here $\mathcal{L}[\hat{i}]$ denotes the Laplace transform of $\hat{i}$, which is strictly positive because of (4.2) and Assumption 1.1. Dividing both sides of the above inequality by $\mathcal{L}[\hat{i}]$ and letting $\lambda \to 0$ give us

$$
\begin{aligned}
1 \ge\ & \frac{(1-f)\beta_1}{c} \frac{h-\epsilon_1}{d} \int_0^\infty p(b)\Gamma(b)\,db + (1-f)\beta_2 \frac{h-\epsilon_1}{d} \int_0^\infty q(b)\Gamma(b)\,db \\
&+ \frac{f\beta_1}{c} \frac{h-\epsilon_1}{d} \int_0^\infty p(b)\Gamma(b)\,db \int_0^\infty \xi(a)\Omega(a)\,da \\
&+ f\beta_2 \frac{h-\epsilon_1}{d} \int_0^\infty q(b)\Gamma(b)\,db \int_0^\infty \xi(a)\Omega(a)\,da,
\end{aligned}
$$

which contradicts (4.7). This completes the proof. □

We define a function $\rho : \mathcal{Y} \to \mathbb{R}_+$ on $\mathcal{Y}$ by

$$
\rho(x, \varphi, \psi, y) = f\beta_1 xy + f\beta_2 x \int_0^\infty q(b)\psi(b)\,db, \quad (x, \varphi, \psi, y) \in \mathcal{Y}.
$$

We easily see that $\rho(\Phi_t(X_0)) = \hat{e}(t)$ for $t \ge 0$ and $X_0 \in \mathcal{Y}$. Then Lemma 4.1 tells us that if $\mathcal{R}_0 > 1$ then the semi-flow Φ is uniformly weakly ρ-persistent. Further, from Theorem 3.4 and the Lipschitz continuity of $\hat{i}$ and Smith and Thieme [26, Theorem 5.2], we conclude that the uniform weak ρ-persistence of the semi-flow Φ implies its uniform (strong) ρ-persistence. We have the following result.

Theorem 4.2. *If $\mathcal{R}_0 > 1$, then the semi-flow Φ is uniformly (strongly) ρ-persistent.*

When $\mathcal{R}_0 > 1$, the uniform persistence of (1.2) immediately follows from Theorem 4.2. In fact, it follows from (4.1) that $\|e(\cdot,t)\|_{L^1} \geq \int_0^t \hat{e}(t-a)\Omega(a)\,da$ and hence from a variation of the Lebesgue-Fatou lemma [25, Section B.2] we obtain

$$\liminf_{t\to\infty} \|e(\cdot,t)\|_{L^1} \geq \hat{e}^\infty \int_0^\infty \Omega(a)\,da,$$

where $\hat{e}^\infty = \liminf_{t\to\infty} \hat{e}(t)$. Under Theorem 4.2, there exists a positive constant $\epsilon > 0$ such that $\hat{e}^\infty > \epsilon$ if $\mathcal{R}_0 > 1$ and hence the persistence of $e(a,t)$ with respect to $\|\cdot\|_{L^1}$ follows. By a similar argument, we can prove that $T(t)$ and $V(t)$ are persistent with respect to $|\cdot|$ and $i(a,t)$ is persistent with respect to $\|\cdot\|_{L^1}$. To summarize, we obtain the following result.

Theorem 4.3. *If $\mathcal{R}_0 > 1$, then the semi-flow $\{\Phi(t)\}_{t\geq 0}$ is uniformly persistent in $\mathcal{Y}$, that is, there exists a constant $\epsilon > 0$ such that, for each $X_0 \in \mathcal{Y}$,*

$$\liminf_{t\to\infty} T(t) \geq \epsilon, \quad \liminf_{t\to\infty} \|e(\cdot,t)\|_{L^1} \geq \epsilon, \quad \liminf_{t\to\infty} \|i(\cdot,t)\|_{L^1} \geq \epsilon, \quad \liminf_{t\to\infty} V(t) \geq \epsilon.$$

5. Local stability of infection-free and infection equilibrium

We begin with the local stability of infection-free equilibrium P^0.

Theorem 5.1. *The infection-free equilibrium $P^0 = (h/d, 0, 0)$ is locally asymptotically stable if $\mathcal{R}_0 < 1$ while it is unstable if $\mathcal{R}_0 > 1$.*

Proof. Linearizing (1.2) around the disease-free equilibrium P^0 under introducing the perturbation variables

$$x_1(t) = T(t) - \frac{h}{d}, \quad x_2(a,t) = e(a,t), \quad x_3(b,t) = i(b,t), \quad x_4(t) = V(t),$$

we obtain the system

$$\begin{gathered}
\frac{dx_1(t)}{dt} = -dx_1(t) - \beta_1 \frac{h}{d} x_4(t) - \beta_2 \frac{h}{d} \int_0^\infty q(b) x_3(b,t)\,db, \\
\Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\Big) x_2(a,t) = -\theta_1(a) x_2(a,t), \\
\Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial b}\Big) x_3(b,t) = -\theta_2(b) x_3(b,t), \\
\frac{dx_4(t)}{dt} = \int_0^\infty p(b) x_3(b,t)\,db - cx_4(t), \\
x_2(0,t) = f\Big(\beta_1 \frac{h}{d} x_4(t) + \beta_2 \frac{h}{d} \int_0^\infty q(b) x_3(b,t)\,db\Big), \\
x_3(0,t) = (1-f)\Big(\beta_1 \frac{h}{d} x_4(t) + \beta_2 \frac{h}{d} \int_0^\infty q(b) x_3(b,t)\,db\Big) \\
+ \int_0^\infty \xi(a) x_2(a,t) da,
\end{gathered} \tag{5.1}$$

We set

$$x_1(t) = x_1^0 e^{\lambda t}, \quad x_2(a,t) = x_2^0(a) e^{\lambda t}, \quad x_3(b,t) = x_3^0(b) e^{\lambda t}, \quad x_4(t) = x_4^0 e^{\lambda t}, \tag{5.2}$$

where $x_1^0, x_2^0(a), x_3^0(b), x_4^0$ are to be determined. Plugging (5.2) into (1.1), we have

$$\lambda x_1^0 = -dx_1^0 - \beta_1 \frac{h}{d} x_4^0 - \beta_2 \frac{h}{d} \int_0^\infty q(b) x_3^0(b)\,db,$$

$$
\begin{aligned}
\lambda x_2^0(a) + \frac{dx_2^0(a)}{da} &= -\theta_1(a)x_2^0(a), \\
x_2^0(0) &= f\Big(\beta_1 \frac{h}{d} x_4^0 + \beta_2 \frac{h}{d}\int_0^\infty q(b)x_3^0(b)\,db\Big),
\end{aligned} \tag{5.3}
$$

$$
\begin{aligned}
\lambda x_3^0(b) + \frac{dx_3^0(b)}{db} &= -\theta_2(b)x_3^0(b), \\
x_3^0(0) = (1-f)\Big(\beta_1 \frac{h}{d} x_4^0 &+ \beta_2 \frac{h}{d}\int_0^\infty q(b)x_3^0(b)\,db\Big) + \int_0^\infty \xi(a)x_2^0(a)da,
\end{aligned} \tag{5.4}
$$

$$
\lambda x_4^0 = \int_0^\infty p(b)x_3^0(b)\,db - cx_4^0, \tag{5.5}
$$

By integrating the first equation in (5.3) and (5.4) from 0 to a, we obtain

$$
x_2^0(a) = x_2^0(0)e^{-\lambda a - \int_0^a \theta_1(s)ds}, \tag{5.6}
$$

$$
\begin{aligned}
x_3^0(b) &= x_3^0(0)e^{-\lambda b - \int_0^b \theta_2(s)ds} \\
&= \Big[(1-f)\Big(\beta_1 \frac{h}{d} x_4^0 + \beta_2 \frac{h}{d}\int_0^\infty q(b)x_3^0(b)\,db\Big) \\
&\quad + \int_0^\infty \xi(a)x_2^0(a)da\Big]e^{-\lambda b - \int_0^b \theta_2(s)ds}.
\end{aligned} \tag{5.7}
$$

and from(5.3), (5.5), (5.6), and (5.7), we have

$$
\begin{aligned}
&x_2^0(0) \\
&= \frac{1-f}{\lambda+c}\frac{h\beta_1}{d}x_2^0(0)\int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}db \\
&\quad + \frac{f}{\lambda+c}\frac{h\beta_1}{d}x_2^0(0)\int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da\int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db \\
&\quad + (1-f)\beta_2\frac{h}{d}x_2^0(0)\int_0^\infty q(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db \\
&\quad + f\beta_2\frac{h}{d}x_2^0(0)\int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da\int_0^\infty q(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db.
\end{aligned} \tag{5.8}
$$

It follows that

$$
\mathcal{H}(\lambda) = 1, \tag{5.9}
$$

where

$$
\begin{aligned}
\mathcal{H}(\lambda) &= \frac{1-f}{\lambda+c}\frac{h\beta_1}{d}\int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}db \\
&\quad + \frac{f}{\lambda+c}\frac{h\beta_1}{d}\int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da\int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db \\
&\quad + (1-f)\beta_2\frac{h}{d}\int_0^\infty q(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db \\
&\quad + f\beta_2\frac{h}{d}\int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da\int_0^\infty q(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db.
\end{aligned}
$$

Since $\mathcal{H}$ is a continuously differentiable with $\lim_{\lambda\to\infty}\mathcal{H}(\lambda) = 0$, $\lim_{\lambda\to-\infty}\mathcal{H}(\lambda) = \infty$, and $\mathcal{H}'(\lambda) < 0$, it follows that (5.9) has a unique real root, say λ^*. Moreover, noting $\mathcal{H}(0) = \mathcal{R}_0$, we have $\lambda^* < 0$ if $\mathcal{R}_0 < 1$ and $\lambda^* > 0$ if $\mathcal{R}_0 > 1$, which implies that P^0 is unstable if $\mathcal{R}_0 > 1$. Now suppose that $\mathcal{R}_0 < 1$. Let $\lambda = \mu + \nu i$ be an arbitrary complex root of (5.9). Then

$$1 = |\mathcal{H}(\lambda)| = |\mathcal{H}(\mu + \nu i)| \le \mathcal{H}(\mu),$$

which implies that $0 > \lambda^* \ge \mu$. In other words, all roots of (5.9) have negative real parts and hence P^0 is locally asymptotically stable if $\mathcal{R}_0 < 1$. This completes the proof. $\square$

Theorem 5.2. *The unique infection equilibrium P^* of* (1.2) *is locally asymptotically stable when $\mathcal{R}_0 > 1$.*

Proof. Linearizing the system (1.2) at P^* under introducing the perturbation variables

$$\begin{gathered} y_1(t) = T(t) - T^*, \quad y_4(t) = V(t) - V^*, \\ y_2(a,t) = e(a,t) - e^*(a), \; y_3(b,t) = i(b,t) - i^*(b), \end{gathered}$$

we obtain the system

$$\begin{gathered} \frac{dy_1(t)}{dt} = -d\mathcal{R}_0 y_1(t) - \beta_1 T^* y_4(t) - \beta_2 T^* \int_0^\infty q(b) y_3(b,t)\,db, \\ \Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\Big) y_2(a,t) = -\theta_1(a) y_2(a,t), \\ \Big(\frac{\partial}{\partial t} + \frac{\partial}{\partial b}\Big) y_3(b,t) = -\theta_2(b) y_3(b,t), \\ \frac{dy_4(t)}{dt} = \int_0^\infty p(b) y_3(b,t)\,db - c y_4(t), \\ y_2(0,t) = fd(\mathcal{R}_0 - 1) y_1(t) + f\beta_1 T^* y_4(t) + f\beta_2 T^* \int_0^\infty q(b) y_3(b,t)\,db, \\ \begin{aligned} y_3(0,t) &= (1-f) d(\mathcal{R}_0 - 1) y_1(t) + (1-f)\beta T^* y_4(t) \\ &\quad + (1-f)\beta_2 T^* \int_0^\infty q(b) y_3(b,t)\,db + \int_0^\infty \xi(a) y_2(a,t) da, \end{aligned} \end{gathered} \tag{5.10}$$

We set

$$y_1(t) = y_1^0 e^{\lambda t}, \quad y_2(a,t) = y_2^0(a) e^{\lambda t}, \quad y_3(b,t) = y_3^0(b) e^{\lambda t}, \quad y_4(t) = y_4^0 e^{\lambda t}, \tag{5.11}$$

where $y_1^0, y_2^0(a), y_3^0(b), y_4^0$ are to be determined. Substituting (5.11) into (5.10) yields

$$\lambda y_1^0 = -d\mathcal{R}_0 y_1^0 - \beta_1 T^* y_4^0 - \beta_2 T^* \int_0^\infty q(b) y_3^0(b)\,db, \tag{5.12}$$

$$\begin{gathered} \lambda y_2^0(a) + \frac{dy_2^0(a)}{da} = -\theta_1(a) y_2^0(a), \\ y_2^0(0) = fd(\mathcal{R}_0 - 1) y_1^0 + f\beta_1 T^* y_4^0 + f\beta_2 T^* \int_0^\infty q(b) y_3^0(b)\,db, \end{gathered} \tag{5.13}$$

$$\begin{gathered} \lambda y_3^0(b) + \frac{dy_3^0(b)}{db} = -\theta_2(b) y_3^0(b), \\ \begin{aligned} y_3^0(0) &= (1-f) d(\mathcal{R}_0 - 1) y_1^0 + (1-f)\beta_1 T^* y_4^0 \\ &\quad + (1-f)\beta_2 T^* \int_0^\infty q(b) y_3^0(b)\,db + y_2^0(0) \int_0^\infty \xi(a) e^{-\lambda a - \int_0^a \theta_1(s)ds} da, \end{aligned} \end{gathered} \tag{5.14}$$

$$\lambda y_4^0 = \int_0^\infty p(b) y_3^0(b)\,db - c y_4^0, \tag{5.15}$$

Integrating the first equation of(5.13), (5.14) from 0 to a yields

$$y_2^0(a) = y_2^0(0)e^{-\lambda a - \int_0^a \theta_1(s)ds}, \tag{5.16}$$

$$\begin{aligned}
y_3^0(b) &= y_3^0(0)e^{-\lambda b - \int_0^b \theta_2(s)ds} \\
&= \Big[(1-f)d(\mathcal{R}_0 - 1)y_1^0 + (1-f)\beta_1 T^* y_4^0 + (1-f)\beta_2 T^* \int_0^\infty q(b)y_3^0(b)\,db\Big] \\
&\quad \times e^{-\lambda b - \int_0^b \theta_2(s)ds} + y_2^0(0)\int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da \cdot e^{-\lambda b - \int_0^b \theta_2(s)ds}.
\end{aligned}$$

and from (5.15), we have

$$\begin{aligned}
y_4^0 &= \frac{\int_0^\infty p(b)y_3^0(b)\,db}{\lambda + c} \\
&= \frac{1-f}{\lambda + c}\Big(d(\mathcal{R}_0 - 1)y_1^0 + \beta_1 T^* y_4^0 + \beta_2 T^* \int_0^\infty q(b)y_3^0(b)\,db\Big) \\
&\quad \times \int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}db \\
&\quad + \frac{y_2^0(0)}{\lambda + c}\int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}\,da \int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db.
\end{aligned} \tag{5.17}$$

Substituting (5.12) and (5.13) in (5.17) yields the characteristic equation at P^*,

$$H(\lambda) = (\lambda + d)\mathcal{H}_1(\lambda) - \lambda - d\mathcal{R}_0 = 0, \tag{5.18}$$

where

$$\begin{aligned}
\mathcal{H}_1(\lambda) &= \frac{1-f}{\lambda + c}\beta_1 T^* \int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}db \\
&\quad + \frac{f}{\lambda + c}\beta_1 T^* \int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da \int_0^\infty p(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db \\
&\quad + (1-f)\beta_2 T^* \int_0^\infty q(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db \\
&\quad + f\beta_2 T^* \int_0^\infty \xi(a)e^{-\lambda a - \int_0^a \theta_1(s)ds}da \int_0^\infty q(b)e^{-\lambda b - \int_0^b \theta_2(s)ds}\,db.
\end{aligned}$$

It is sufficient to show that (5.18) has no roots with non-negative real parts. By way of contradiction, suppose that it has a root $\lambda = \mu + \nu i$ with $\mu \geq 0$. Then we have

$$(\mu + \nu i + d)\mathcal{H}_1(\mu + \nu i) - \mu - i\nu - d\mathcal{R}_0 = 0.$$

Separating the real part of the above equality gives

$$\operatorname{Re} \mathcal{H}_1(\mu + \nu i) = \frac{(\mu + d\mathcal{R}_0)(\mu + d) + \nu^2}{(\mu + d)^2 + \nu^2} > 1. \tag{5.19}$$

Noticing that $\mathcal{H}_1(0) = T^* \frac{\mathcal{R}_0}{T_0} = 1$ and $\mathcal{H}_1$ is a decreasing function, we have

$$\operatorname{Re} \mathcal{H}_1(\mu + \nu i) \leq |\mathcal{H}_1(\mu)| = \mathcal{H}_1(\mu) \leq \mathcal{H}_1(0) = 1,$$

which contradicts with (5.19). This completes the proof. $\square$

6. Global stability of the infection-free and infection equilibrium

Set $g(\cdot)$ on $(0,\infty)$ defined by $g(x) = x - 1 - \ln x$ for $x \in (0,\infty)$. Obviously, $g(\cdot)$ has a unique minimum at 1 with $g(1) = 0$.

Theorem 6.1. *The infection-free equilibrium P^0 of (1.2) is globally attractive if $\mathcal{R}_0 < 1$.*

Proof. By Theorem 5.1, it remains to show that P^0 is globally attractive in $\mathcal{Y}$ by the method of Lyapunov function. Consider candidate Lyapunov functional,

$$\mathcal{L}_{IFE}(t) = \mathcal{L}_1(t) + \mathcal{L}_2(t) + \mathcal{L}_3(t) + \mathcal{L}_4(t),$$

where $\mathcal{L}_1(t) = T^0 g\big(\frac{T(t)}{T^0}\big)$, $\mathcal{L}_2(t) = \int_0^\infty \phi(a)e(a,t)\,da$, $\mathcal{L}_3(t) = \int_0^\infty \psi(b)i(b,t)\,db$, and $\mathcal{L}_4(t) = \frac{\beta_1 T^0}{c}V(t)$. Here the nonnegative kernel functions $\phi(a)$ and $\psi(b)$ will be determined later. The derivative of $\mathcal{L}_1$ along the solutions of (1.2) is calculated as follows,

$$\begin{aligned}
\frac{d\mathcal{L}_1(t)}{dt} &= \big(1 - \frac{T^0}{T}\big)\Big(h - dT - \beta_1 T(t)V(t) - \beta_2 T\int_0^\infty q(b)i(b,t)\,db\Big) \\
&= \big(1 - \frac{T^0}{T}\big)\Big(dT^0 - dT - \beta_1 T(t)V(t) - \beta_2 T\int_0^\infty q(b)i(b,t)\,db\Big) \\
&= -dT^0\Big(\frac{T^0}{T} + \frac{T}{T^0} - 2\Big) - \beta_1 TV + \beta_1 T^0 V \\
&\quad - \beta_2 T\int_0^\infty q(b)i(b,t)\,db + \beta_2 T^0\int_0^\infty q(b)i(b,t)\,db.
\end{aligned}$$

By using integration by parts, we have

$$\begin{aligned}
\frac{d\mathcal{L}_2(t)}{dt} &= \int_0^\infty \phi(a)\frac{\partial e(a,t)}{\partial t}da \\
&= -\int_0^\infty \phi(a)\Big[\theta_1(a)e(a,t) + \frac{\partial e(a,t)}{\partial a}\Big]da \\
&= -\phi(a)e(a,t)\Big|_0^\infty + \int_0^\infty \phi'(a)e(a,t)\,da - \int_0^\infty \phi(a)\theta_1(a)e(a,t)\,da \\
&= \phi(0)e(0,t) + \int_0^\infty \Big(\phi'(a) - \phi(a)\theta_1(a)\Big)e(a,t)da.
\end{aligned}$$

Similarly,

$$\frac{d\mathcal{L}_3(t)}{dt} = \psi(0)i(0,t) + \int_0^\infty \Big(\psi'(b) - \psi(b)\theta_2(b)\Big)i(b,t)\,db.$$

It is easy to see that

$$\frac{d\mathcal{L}_4(t)}{dt} = \frac{\beta_1 T^0}{c}\Big(\int_0^\infty p(b)i(b,t)\,db - cV\Big) = \frac{\beta_1 T^0}{c}\int_0^\infty p(b)i(b,t)\,db - \beta_1 T^0 V.$$

Therefore,

$$\begin{aligned}
\frac{d\mathcal{L}(t)}{dt} &= -dT^0\Big(\frac{T^0}{T} + \frac{T}{T^0} - 2\Big) - e(0,t) - i(0,t) \\
&\quad + \int_0^\infty \xi(a)e(a,t)da + \beta_1 T^0 V + \beta_2 T^0\int_0^\infty q(b)i(b,t)\,db \\
&\quad + \frac{d(\mathcal{L}_2(t) + \mathcal{L}_3(t) + \mathcal{L}_4(t))}{dt}
\end{aligned}$$

$$
\begin{aligned}
&= -dT^0\Big(\frac{T^0}{T}+\frac{T}{T^0}-2\Big)\\
&\quad+\big(f\phi(0)+(1-f)\psi(0)-1\big)\Big(\beta_1 TV+\beta_2 T\int_0^\infty q(b)i(b,t)\,db\Big)\\
&\quad+\int_0^\infty\Big(\phi'(a)-\phi(a)\theta_1(a)+\psi(0)\xi(a)\Big)e(a,t)da\\
&\quad+\int_0^\infty\Big(\psi'(b)-\psi(b)\theta_2(b)+\frac{\beta_1T^0}{c}p(b)+\beta_2T^0q(b)\Big)i(b,t)\,db.
\end{aligned}
$$

Now we choose

$$
\begin{gathered}
\psi(b)=\int_b^\infty\Big(\frac{\beta_1T^0}{c}p(u)+\beta_2T^0q(u)\Big)e^{-\int_b^u\theta_2(\omega)d\omega}du,\\
\phi(a)=\int_a^\infty\psi(0)\xi(u)e^{-\int_a^u\theta_1(\omega)d\omega}du.
\end{gathered}
$$

Then $\psi(0)=\frac{\beta_1T^0J}{c}+\beta_2T^0L$, $\phi(0)=\frac{\beta_1T^0KJ}{c}+\beta_2T^0KL$, and ψ and ϕ satisfy

$$
\begin{gathered}
\psi'(b)-\psi(b)\theta_2(b)+\frac{\beta_1T^0}{c}p(b)+\beta_2T^0q(b)=0,\\
\phi'(a)-\phi(a)\theta_1(a)+\psi(0)\xi(a)=0.
\end{gathered}
$$

The derivative of $\mathcal{L}_{IFE}$ along solutions of (1.2) is

$$
\begin{aligned}
\frac{d\mathcal{L}_{IFE}(t)}{dt}&=-dT^0\Big(\frac{T^0}{T}+\frac{T}{T^0}-2\Big)\\
&\quad+\big(f\phi(0)+(1-f)\psi(0)-1\big)\Big(\beta_1TV+\beta_2T\int_0^\infty q(b)i(b,t)\,db\Big)\\
&=-dT^0\Big(\frac{T^0}{T}+\frac{T}{T^0}-2\Big)+\big(\mathcal{R}_0-1\big)\Big(\beta_1TV+\beta_2T\int_0^\infty q(b)i(b,t)\,db\Big)\\
&=-dT^0\Big(\frac{T^0}{T}+\frac{T}{T^0}-2\Big)+\big(\mathcal{R}_0-1\big)\frac{1}{f}e(0,t).
\end{aligned}
$$

Notice that $\frac{d\mathcal{L}_{IFE}(t)}{dt}=0$ implies that $T=T^0$. It can be verified that the largest invariant set where $\frac{d\mathcal{L}_{IFE}(t)}{dt}=0$ is the singleton $\{P^0\}$. Therefore, by the invariance principle, P^0 is globally attractive when $\mathcal{R}_0\le 1$. □

The following result immediately follows from Theorem 5.1 and Theorem 6.1.

Theorem 6.2. *If $\mathcal{R}_0<1$, then the infection-free equilibrium P^0 of* (1.2) *is globally asymptotically stable.*

We next establish the global stability of the infection equilibrium.

Lemma 6.3. *Suppose that $\mathcal{R}_0>1$. Then every solution $(T(t),e(a,t),i(b,t),V(t))$ of* (1.2) *satisfies*

$$
\begin{aligned}
&(1-f)\Big(\beta_1T^*V^*+\beta_2T^*\int_0^\infty q(b)i^*(b)\,db\Big)\big[1-\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)}\big]\\
&+\int_0^\infty\xi(a)e^*(a)\big[1-\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}\big]da=0.
\end{aligned}
\tag{6.1}
$$

Proof. We have

$$\begin{aligned}
&(1-f)\Big(\beta_1 T^* V^* + \beta_2 T^* \int_0^\infty q(b) i^*(b)\,db\Big) \frac{e(0,t) i^*(0)}{e^*(0) i(0,t)} \\
&+ \int_0^\infty \xi(a) e^*(a) \frac{e(a,t) i^*(0)}{e^*(a) i(0,t)} da \\
&= \Big((1-f)(\beta TV + \beta_2 T \int_0^\infty q(b) i(b,t)\,db) + \int_0^\infty \xi(a) e(a,t) da\Big) \frac{i^*(0)}{i(0,t)} \\
&= i^*(0)
\end{aligned}$$

and

$$(1-f)\Big(\beta_1 T^* V^* + \beta_2 T^* \int_0^\infty q(b) i^*(b)\,db\Big) + \int_0^\infty \xi(a) e^*(a) da = i^*(0).$$

This immediately gives (6.1). □

Theorem 6.4. *Assume that $\mathcal{R}_0 > 1$. Then the unique infection equilibrium $P^* = (T^*, e^*(a), i^*(a), V^*)$ of (1.2) defined by (2.13) is globally asymptotically stable.*

Proof. By Theorem 5.2, it suffices to show that P^* is globally attractive. We show this by applying the Lyapunov technique again. Let

$$G[x,y] = x - y - y \ln \frac{x}{y}, \quad \text{for } x, y > 0.$$

It is easy to see that G is non-negative on $(0,\infty) \times (0,\infty)$ with the minimum value 0 only when $x = y$. Furthermore, it is easy to verify that $xG_x[x,y] + yG_y[x,y] = G[x,y]$.

Consider as a candidate the Lyapunov functional

$$\mathcal{L}_{EE}(t) = \mathcal{H}_1(t) + \mathcal{H}_2(t) + \mathcal{H}_3(t) + \mathcal{H}_4(t),$$

where

$$\begin{gathered}
\mathcal{H}_1(t) = G[T, T^*], \quad \mathcal{H}_2(t) = \int_0^\infty \phi_1(a) G\big[e(a,t), e^*(a)\big] da, \\
\mathcal{H}_3(t) = \int_0^\infty \psi_1(b) G\big[i(b,t), i^*(b)\big]\,db, \quad \mathcal{H}_4(t) = \frac{\beta_1 T^*}{c} G[V, V^*],
\end{gathered}$$

with

$$\begin{gathered}
\psi_1(b) = \int_b^\infty \Big(\frac{\beta_1 T^*}{c} p(u) + \beta_2 T^* q(u)\Big) e^{-\int_b^u \theta_2(\omega) d\omega}\,du, \\
\phi_1(a) = \int_a^\infty \psi_1(0) \xi(u) e^{-\int_a^u \theta_1(\omega) d\omega}\,du\,.
\end{gathered}$$

(The reason of this choice is similar to that in the Proof of Theorem 6.1.) One can easily see that $\phi_1(0) = \frac{\beta_1 T^* KJ}{c} + \beta_2 T^* KL$, $\psi_1(0) = \frac{\beta_1 T^* J}{c} + \beta_2 T^* L$,

$$\begin{gathered}
\psi_1'(b) - \psi_1(b)\theta_2(b) = -\frac{\beta_1 T^*}{c} p(b) - \beta_2 T^* q(b), \\
\phi_1'(a) - \phi_1(a)\theta_1(a) = -\psi_1(0)\xi(a).
\end{gathered}$$

Next we calculate the derivative of $\mathcal{H}$ along solutions of (1.2). Firstly, differentiating $\mathcal{H}_1(t)$ along solutions of (1.2) yields

$$\frac{d\mathcal{H}_1(t)}{dt} = \big(1 - \frac{T^*}{T}\big)\Big(h - dT - \beta_1 T(t) V(t) - \beta_2 T \int_0^\infty q(b) i(b,t)\,db\Big)$$

$$= -dT^*\Big(\frac{T^*}{T} + \frac{T}{T^*} - 2\Big) + \frac{1}{f}\big(1 - \frac{T^*}{T}\big)(e^*(0) - e(0,t)).$$

Secondly, using (2.5), we have

$$\begin{aligned}
\mathcal{H}_2(t) &= \int_0^t \phi_1(a)G[e(0,t-a)\Omega(a), e^*(a)]da \\
&\quad + \int_t^\infty \phi_1(a)G[e_0(a-t)e^{-\int_{a-t}^a \theta_1(\omega)d\omega}, e^*(a)]da \\
&= \int_0^t \phi_1(t-r)G[e(0,r)\Omega(t-r), e^*(t-r)]dr \\
&\quad + \int_0^\infty \phi_1(t+r)G[e_0(r)e^{-\int_r^{t+r}\theta_1(\omega)d\omega}, e^*(t+r)]dr \\
&= \mathcal{B}_\infty(t) + \mathcal{B}_\in(t).
\end{aligned}$$

The derivative of $\mathcal{B}_\infty$ and $\mathcal{B}_\in$ take the form

$$\begin{aligned}
&\frac{d\mathcal{B}_\infty(t)}{dt} \\
&= \phi_1(0)G[e(0,t), e^*(0)] + \int_0^t \phi_1'(t-r)G\big[e(0,r)e^{-\int_0^{t-r}\theta_1(\omega)d\omega}, e^*(t-r)\big]\,dr \\
&\quad - \int_0^t \phi_1(t-r)\theta_1(t-r)\Big[e(0,r)e^{-\int_0^{t-r}\theta_1(\omega)d\omega}G_x\big[e(0,r)e^{-\int_0^{t-r}\theta_1(\omega)d\omega}, e^*(t-r)\big] \\
&\quad + e^*(t-r)G_y\big[e(0,r)e^{-\int_0^{t-r}\theta_1(\omega)d\omega}, e^*(t-r)\big]\Big]dr,
\end{aligned}$$

and

$$\begin{aligned}
&\frac{d\mathcal{B}_\in(t)}{dt} \\
&= \int_0^\infty \phi_1'(t+r)G\Big[e_0(r)e^{-\int_r^{t+r}\theta_1(\omega)d\omega}, e^*(t+r)\Big]\,dr \\
&\quad - \int_0^\infty \phi_1(t+r)\theta_1(t+r)\Big[e_0(r)e^{-\int_r^{t+r}\theta_1(\omega)d\omega}G_x\big[e_0(r)e^{-\int_r^{t+r}\theta_1(\omega)d\omega}, e^*(t+r)\big] \\
&\quad + e^*(t+r)G_y\big[e_0(r)e^{-\int_r^{t+r}\theta_1(\omega)d\omega}, e^*(t+r)\big]\Big]\,dr.
\end{aligned}$$

We obtain the derivative of $\mathcal{H}_2(t)$,

$$\begin{aligned}
\frac{d\mathcal{H}_2(t)}{dt} &= \phi_1(0)G[e(0,t), e^*(0)] + \int_0^\infty \big[\phi_1'(a) - \phi_1(a)\theta_1(a)\big]G[e(a,t), e^*(a)]\,da \\
&= \phi_1(0)G[e(0,t), e^*(0)] - \int_0^\infty \psi_1(0)\xi(a)G[e(a,t), e^*(a)]\,da.
\end{aligned}$$

A similar argument as in the derivative of $\mathcal{H}_2$, we calculate the derivative of $\mathcal{H}_3$,

$$\begin{aligned}
\frac{d\mathcal{H}_3(t)}{dt} &= \psi_1(0)G[i(0,t), i^*(0)] + \int_0^\infty \big[\psi'(b) - \psi(b)\theta_2(b)\big]G[i(b,t), i^*(b)]\,db \\
&= \psi_1(0)G[i(0,t), i^*(0)] - \int_0^\infty \Big(\frac{\beta_1 T^*}{c}p(b) + \beta_2 T^* q(b)\Big)G[i(b,t), i^*(b)]\,db.
\end{aligned}$$

We calculate the derivative of $\mathcal{H}_4$,

$$\frac{d\mathcal{H}_4(t)}{dt} = \frac{\beta_1 T^*}{c}\int_0^\infty p(b)i(b,t)\,db - \beta_1 T^* V + \beta_1 T^* V^* - \frac{\beta_1 T^* V^*}{cV}\int_0^\infty p(b)i(b,t)\,db.$$

If follows from $\psi_1(0) = \frac{\beta_1 T^* J}{c} + \beta_2 T^* L$ and $\phi_1(0) = \frac{\beta_1 T^* KJ}{c} + \beta_2 T^* KL$ that

$$\begin{aligned} &\frac{d\mathcal{L}_{EE}}{dt} \\ &= -dT^*\Big(\frac{T}{T^*} + \frac{T^*}{T} - 2\Big) + \frac{1}{f}\big(1 - \frac{T^*}{T}\big)\left(e^*(0) - e(0,t)\right) \\ &\quad + \phi_1(0)G[e(0,t), e^*(0)] - \int_0^\infty \psi_1(0)\xi(a)G[e(a,t), e^*(a)]da \\ &\quad + \psi_1(0)G[i(0,t), i^*(0)] - \int_0^\infty \Big(\frac{\beta_1 T^*}{c}p(b) + \beta_2 T^* q(b)\Big)G[i(b,t), i^*(b)]\,db \\ &\quad + \int_0^\infty \frac{\beta_1 T^*}{c}p(b)i(b,t)\,db + \beta_1 T^* V^* - \beta_1 T^* V \\ &\quad - \frac{V^*}{V}\int_0^\infty \frac{\beta_1 T^*}{c}p(b)i(b,t)\,db. \end{aligned} \tag{6.2}$$

Recall that

$$\begin{aligned} &(1-f)\Big(\beta_1 T^* V^* - \beta_1 TV + \beta_2 T^* \int_0^\infty q(b)i^*(b)\,db - \beta_2 T \int_0^\infty q(b)i(b,t)\,db\Big) \\ &+ \int_0^\infty \xi(a)\big(e^*(a) - e(a,t)\big)\,da \\ &= i^*(0) - i(0,t), \end{aligned}$$

and

$$\begin{aligned} &f\phi_1(0) + (1-f)\psi_1(0) \\ &= \frac{(1-f)\beta_1 T^* J}{c} + (1-f)\beta_2 T^* L + \frac{f\beta_1 T^* KJ}{c} + f\beta_2 T^* KL \\ &= \Big(\frac{(1-f)\beta_1 J}{c} + (1-f)\beta_2 L + \frac{f\beta_1 KJ}{c} + f\beta_2 KL\Big)\frac{T^0}{\mathcal{R}_0} = 1. \end{aligned}$$

Thus (6.2) becomes

$$\begin{aligned} &\frac{d\mathcal{L}_{EE}(t)}{dt} \\ &= -dT^*\Big(\frac{T}{T^*} + \frac{T^*}{T} - 2\Big) + \frac{1}{f}\big(1 - \frac{T^*}{T}\big)\left(e^*(0) - e(0,t)\right) \\ &\quad + \frac{1}{f}G[e(0,t), e^*(0)] - \int_0^\infty \frac{\beta_1 T^*}{c}p(b)G[i(b,t), i^*(b)]\,db \\ &\quad + \psi_1(0)\Big[(1-f)\Big(\beta_1 T^* V^* + \beta_2 T^* \int_0^\infty q(b)i^*(b)\,db\Big)\ln\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)} \\ &\quad + \int_0^\infty \xi(a)e^*(a)\ln\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}da\Big] \\ &\quad + \int_0^\infty \frac{\beta_1 T^*}{c}p(b)i(b,t)\,db + \beta_1 T^* V^* - \beta_1 T^* V \\ &\quad - \frac{V^*}{V}\int_0^\infty \frac{\beta_1 T^*}{c}p(b)i(b,t)\,db. \end{aligned}$$

It follows that

$$
\begin{aligned}
&\frac{d\mathcal{L}_{EE}(t)}{dt} \\
&= -dT^*\Big(\frac{T}{T^*} + \frac{T^*}{T} - 2\Big) \\
&\quad - \frac{1}{f}e^*(0)\Big(\frac{T^*}{T} + \ln\frac{e(0,t)}{e^*(0)}\Big) + \beta_2 T^* \int_0^\infty q(b)i(b,t)\,db \\
&\quad - \int_0^\infty \Big(\frac{\beta_1 T^*}{c}p(b) + \beta_2 T^* q(b)\Big) G[i(b,t), i^*(b)]\,db \\
&\quad + \psi_1(0)\Big[(1-f)\Big(\beta_1 T^* V^* + +\beta_2 T^* \int_0^\infty q(b)i^*(b)\,db\Big)\ln\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)} \\
&\quad + \int_0^\infty \xi(a)e^*(a)\ln\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}da\Big] \\
&\quad + \int_0^\infty \frac{\beta_1 T^*}{c}p(b)i(b,t)\,db + \beta_1 T^* V^* - \frac{V^*}{V}\int_0^\infty \frac{\beta_1 T^*}{c}p(b)i(b,t)\,db.
\end{aligned}
\tag{6.3}
$$

Recall that $e^*(0) = f\big(\beta_1 T^* V^* + \beta_2 T^* \int_0^\infty q(b)i^*(b)\,db\big)$ and $\int_0^\infty p(b)i^*(b)\,db = cV^*$ in (2.12). Collecting the terms of (6.3) yields

$$
\begin{aligned}
\frac{d\mathcal{L}_{EE}(t)}{dt} &= -dT^*\Big(\frac{T}{T^*} + \frac{T^*}{T} - 2\Big) \\
&\quad + \psi_1(0)(1-f)\Big(\beta_1 T^* V^* + \beta_2 T^* \int_0^\infty q(b)i^*(b)\,db\Big)\ln\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)} \\
&\quad + \psi_1(0)\int_0^\infty \xi(a)e^*(a)\ln\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}da \\
&\quad - \beta_2 T^* \int_0^\infty q(b)\Big(i(b,t) - i^*(b) - i^*(b)\ln\frac{i(b,t)}{i^*(b)}\Big)\,db \\
&\quad + \int_0^\infty \frac{\beta_1 T^*}{c}p(b)i^*(b)\Big(2 + \ln\frac{i(b,t)}{i^*(b)} - \frac{T^*}{T} - \ln\frac{e(0,t)}{e^*(0)} - \frac{V^* i(b,t)}{V i^*(b)}\Big)\,db \\
&\quad + \beta_2 T^* \int_0^\infty q(b)i(b,t)\,db - \beta_2 T^* \int_0^\infty q(b)i^*(b)\Big(\frac{T^*}{T} + \ln\frac{e(0,t)}{e^*(0)}\Big)\,db.
\end{aligned}
$$

Further, we have

$$
\begin{aligned}
\frac{d\mathcal{L}_{EE}(t)}{dt} &= -dT^*\Big(\frac{T}{T^*} + \frac{T^*}{T} - 2\Big) \\
&\quad + \beta_2 T^* \int_0^\infty q(b)i^*(b)\Big(1 - \frac{T^*}{T} - \ln\frac{e(0,t)}{e^*(0)} + \ln\frac{i(b,t)}{i^*(b)}\Big)\,db \\
&\quad + \psi_1(0)(1-f)\Big(\beta_1 T^* V^* + \beta_2 T^* \int_0^\infty q(b)i^*(b)\,db\Big) \\
&\quad \times \Big(1 - \frac{e(0,t)i^*(0)}{e^*(0)i(0,t)} + \ln\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)}\Big) \\
&\quad + \psi_1(0)\int_0^\infty \xi(a)e^*(a)\Big(1 - \frac{e(a,t)i^*(0)}{e^*(a)i(0,t)} + \ln\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}\Big)da \\
&\quad + \int_0^\infty \frac{\beta_1 T^* p(b)}{c}i^*(b)\Big(3 - \frac{T^*}{T} + \ln\frac{T^*}{T} - \frac{V^* i(b,t)}{V i^*(b)}
\end{aligned}
$$

$$
\begin{aligned}
&+ \ln \frac{V^*i(b,t)}{Vi^*(b)} - \frac{TVe^*(0)}{T^*V^*e(0,t)} + \ln \frac{TVe^*(0)}{T^*V^*e(0,t)}\Big)\, db \\
&- \psi_1(0)\Big\{(1-f)\Big(\beta_1 T^*V^* + \beta_2 T^* \int_0^\infty q(b)i^*(b)\, db\Big)\big[1 - \frac{e(0,t)i^*(0)}{e^*(0)i(0,t)}\big] \\
&+ \int_0^\infty \xi(a)e^*(a)\big[1 - \frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}\big]da\Big\} \\
&- \int_0^\infty \frac{\beta_1 T^* p(b)}{c} i^*(b)\Big(1 - \frac{TVe^*(0)}{T^*V^*e(0,t)}\Big)\, db.
\end{aligned}
$$

Recall that Lemma 6.3 holds. Putting (6.1) into the above inequality, we have

$$
\begin{aligned}
&\frac{d\mathcal{L}_{EE}(t)}{dt} \\
&= -dT^*\Big(\frac{T}{T^*} + \frac{T^*}{T} - 2\Big) \\
&\quad - \psi_1(0)\Big[\int_0^\infty \xi(a)e^*(a)g\Big(\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}\Big)da \\
&\quad + (1-f)\Big(\beta_1 T^*V^* + \beta_2 T^* \int_0^\infty q(b)i^*(b)\, db\Big)g\Big(\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)}\Big)\, db\Big] \\
&\quad - \int_0^\infty \frac{\beta_1 T^*}{c} p(b)i^*(b)\Big[g\big(\frac{T^*}{T}\big) + g\Big(\frac{V^*i(b,t)}{Vi^*(b)}\Big) + g\Big(\frac{TVe^*(0)}{T^*V^*e(0,t)}\Big)\Big]\, db \\
&\quad - \Big[\int_0^\infty \frac{\beta_1 T^* p(b)}{c} i^*(b)\Big(1 - \frac{TVe^*(0)}{T^*V^*e(0,t)}\Big)\, db \\
&\quad + \beta_2 T^* \int_0^\infty q(b)i^*(b)\Big(1 - \frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)}\Big)\, db\Big] \\
&\quad + \beta_2 T^* \int_0^\infty q(b)i^*(b)\Big(1 - \frac{T^*}{T} - \ln \frac{e(0,t)}{e^*(0)} + \ln \frac{i(b,t)}{i^*(b)} \\
&\quad + 1 - \frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)}\Big)\, db\,.
\end{aligned}
$$

Notice that

$$
\begin{aligned}
&\int_0^\infty \frac{\beta_1 T^* p(b)}{c} i^*(b)\Big(1 - \frac{TVe^*(0)}{T^*V^*e(0,t)}\Big)\, db \\
&+ \beta_2 T^* \int_0^\infty q(b)i^*(b)\Big(1 - \frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)}\Big)\, db = 0
\end{aligned}
$$

and

$$
\begin{aligned}
&1 - \frac{T^*}{T} - \ln \frac{e(0,t)}{e^*(0)} + \ln \frac{i(b,t)}{i^*(b)} + 1 - \frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)} \\
&= 1 - \frac{T^*}{T} + \ln \frac{T^*}{T} + 1 - \frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)} + \ln \frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)} \\
&= -g\big(\frac{T^*}{T}\big) - g\Big(\frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)}\Big)\,.
\end{aligned}
$$

We have

$$
\frac{d\mathcal{L}_{EE}(t)}{dt}
$$

$$
\begin{aligned}
&= -dT^*\Big(\frac{T}{T^*}+\frac{T^*}{T}-2\Big) - \psi_1(0)\Big[\int_0^\infty \xi(a)e^*(a)g\Big(\frac{e(a,t)i^*(0)}{e^*(a)i(0,t)}\Big)da \\
&\quad + (1-f)\Big(\beta_1 T^*V^* + \beta_2 T^*\int_0^\infty q(b)i^*(b)\,db\Big)g\Big(\frac{e(0,t)i^*(0)}{e^*(0)i(0,t)}\Big)\,db\Big] \\
&\quad - \int_0^\infty \frac{\beta_1 T^*}{c}p(b)i^*(b)\Big[g\big(\frac{T^*}{T}\big) + g\Big(\frac{V^*i(b,t)}{Vi^*(b)}\Big) + g\Big(\frac{TVe^*(0)}{T^*V^*e(0,t)}\Big)\Big]\,db \\
&\quad - \beta_2 T^*\int_0^\infty q(b)i^*(b)\Big[g\big(\frac{T^*}{T}\big) + g\Big(\frac{Ti(b,t)e^*(0)}{T^*i^*(b)e(0,t)}\Big)\Big]db \le 0
\end{aligned}
$$

and $\frac{d\mathcal{L}_{EE}(t)}{dt} = 0$ implies that $T = T^*$ and

$$
\frac{i(b,t)}{i^*(b)} = \frac{i(0,t)}{i^*(0)} = \frac{V}{V^*} = \frac{e(0,t)}{e^*(0)} = \frac{e(a,t)}{e^*(a)}, \quad \text{for all } a,b \ge 0.
$$

It is not difficult to check that the largest invariant subset $\{\frac{d\mathcal{L}_{EE}(t)}{dt} = 0\}$ is the singleton $\{P^*\}$. By the invariance principle, P^* is globally attractive and this completes the proof. □

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