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Global dynamics for a class of infection-age model with nonlinear incidence*

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Abstract. In this paper, we propose an HBV viral infection model with continuous age structure and nonlinear incidence rate. Asymptotic smoothness of the semi-flow generated by the model is studied. Then we calculate the basic reproduction number and prove that it is a sharp threshold determining whether the infection dies out or not. We give a rigorous mathematical analysis on uniform persistence by reformulating the system as a system of Volterra integral equations. The global dynamics of the model is established by using suitable Lyapunov functionals and LaSalle's invariance principle. We further investigate the global behaviors of the HBV viral infection model with saturation incidence through numerical simulations.

Keywords: age structure, saturation incidence, asymptotic smoothness, Lyapunov functional, global stability.

1 Introduction

Over the past few years, within-host virus models have been studied extensively to describe the dynamics inside the host of various infectious diseases such as HIV, HBV and so on. For it is not easy to obtain accurate information of patients, specific hypotheses testing based on clinical data is an arduous task. Therefore, many researchers have made great efforts by mathematical models in this area of research [4, 8, 10, 13, 15–17, 26], presenting assumptions that the death rate and virus production rate of infected cells are both constant in their works. However, biological observations show that the death rate of

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infected cells has been different during the period of infection, and there exists a maximal bud rate of viruses when virus particles gradually bud out of the host cell until the cell is dead. Thus, age structure is employed to make HBV infection model more realistic. In particular, the fact has been explained that the mortality rate and viral production rate of infected cells are functions of the infection age of the infected cells instead of constants.

It is worth noting that there exists direct cell-to-cell infection in vivo spread of the virus. Besides, the infection is more potent and efficient means of virus propagation than the virus-to-cell infection mechanism. Viral particles can be simultaneously transferred from infected target cells to uninfected ones through virological synapses during cell-to-cell infection. Thus, it is necessary to understand the viral dynamics in terms of applications. There exist less age-structured virus models to take both virus-to-cell and cell-to-cell infection into consideration. Recently, Wang et al. [20] established an HIV infection model containing the two modes of infection and allowing age-dependent death rate of infected cells and age-dependent production rate of virus. Meanwhile, considering antiretroviral therapy of HIV, Xu et al. [27] has proposed the following model:

$$
\begin{aligned}
T'(t) &= \lambda - dT(t) - (1-\eta_{rt})\beta_1 T(t)V_I(t) - T(t)\int_0^\infty \bigl(1-\eta_p^{(2)}\bigr)\beta_2(a)i(t,a)\,\mathrm{d}a,\\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -\delta(a)i(t,a),\\
i(t,0) &= (1-\eta_{rt})\beta_1 T(t)V_I(t) + T(t)\int_0^\infty \bigl(1-\eta_p^{(2)}\bigr)\beta_2(a)i(t,a)\,\mathrm{d}a,\\
V_I'(t) &= \bigl(1-\eta_p^{(1)}\bigr)\int_0^\infty p(a)i(t,a)\,\mathrm{d}a - \mu V_I(t),\\
V_{NI}'(t) &= \eta_p^{(1)}\int_0^\infty p(a)i(t,a)\,\mathrm{d}a - \mu V_{NI}(t).
\end{aligned}
$$

There is no certain observation suggesting that viruses infect cells with linear incidence rate. Motivated by this fact, several within-host virus dynamics models have been constructed to investigate the dynamics of models to take saturation incidence rate or other nonlinear incidence rate into consideration [2, 6, 7, 9, 19, 21–25, 28, 29]. However, almost none of these investigations take both age structure and cell-to-cell infection into account. For biological consideration, we introduce a more general incidence rate to formulate the following model:

$$
\begin{aligned}
x'(t) &= \lambda - dx(t) - \beta_1 x(t)f(v_I) - x(t)\int_0^\infty \bigl(1-\eta_p^{(2)}\bigr)\beta_2(a)i(t,a)\,\mathrm{d}a,\\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -\delta(a)i(t,a),
\end{aligned}
\tag{1a}
$$

$$
\begin{aligned}
i(t,0) &= \beta_1 x(t) f(v_I) + x(t) \int_0^\infty \bigl(1-\eta_p^{(2)}\bigr)\beta_2(a) i(t,a)\,\mathrm{d}a, \\
v_I'(t) &= \bigl(1-\eta_p^{(1)}\bigr) \int_0^\infty p(a) i(t,a)\,\mathrm{d}a - \mu v_I(t), \\
v_{NI}'(t) &= \eta_p^{(1)} \int_0^\infty p(a) i(t,a)\,\mathrm{d}a - \mu v_{NI}(t)
\end{aligned}
\tag{1b}
$$

with initial condition

$$
\begin{aligned}
&x(0) = x_0 \geqslant 0, \qquad i(0,a) = i_0(a) =: \varphi(a) \in L_+^1(0,\infty), \\
&v_I(0) = v_{I0} \geqslant 0, \qquad v_{NI}(0) = v_{NI0} \geqslant 0.
\end{aligned}
\tag{2}
$$

Here $x(t)$, $v_I(t)$, $v_{NI}(t)$ denote the concentration of susceptible cells, infectious virions and noninfectious virions at time t, respectively. The density of infected target cells of infection age a (i.e., the time that has elapsed since an HBV virion has penetrated cell) at time t is denoted by $i(t,a)$. λ is the recruitment rate of healthy susceptible cells, d is the per capita death rate of uninfected cells, $\delta(a)$ is the age-dependent remove rate of infected cells, μ is the clearance rate of virions, β_1 is the infection rate of free virus. $\eta_p^{(1)}$ denotes the efficacy of the PI inhibitor. We also assume that the efficacy of the PI inhibitor, which blocks the cell-to-cell infection is denoted by $\eta_p^{(2)}$. The function $\beta_2(a) \in L_+^\infty(0,\infty)$ is the infection-age specific transmission rate of reproductively infected cells, which is Lipschitz continuous and has a finite essential upper bound. $p(a)$ is the viral production rate of an infected cell with age a. We also assume that functions $p(a)$ and $\delta(a)$ are all Lipschitz continuous and satisfy the conditions: (i) $\delta(a)$, $p(a) \in L_+^\infty(0,\infty)$ and $\delta^+ := \operatorname{ess\,sup}_{a\in[0,\infty)} \delta(a) < +\infty$, $p^+ := \operatorname{ess\,sup}_{a\in[0,\infty)} p(a) < +\infty$; (ii) there exits a positive constant $\delta_{\min}$ such that $\delta(a) \geqslant \delta_{\min}$ for all $a \geqslant 0$; (iii) there exits a maximum age $\hat{a} > 0$ for the viral production such that $p(a) > 0$ for $a \in (0,\hat{a})$.

Evidently, the last equation of system (1) is independent to the others because $v_{NI}(t)$ does not exist in the first four equations of system (1). Let $k(a) = (1-\eta_p^{(2)})\beta_2(a)$ and $q(a) = (1-\eta_p^{(1)})p(a)$ to simplify the notation. Then we consider the following reduced

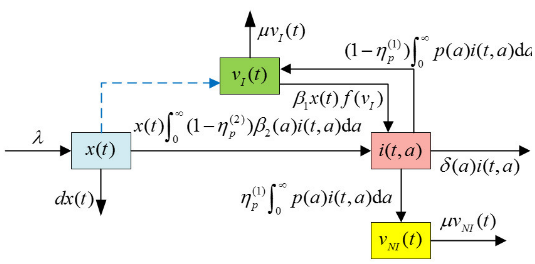


Figure 1. Flowchart of HBV infection in system (1).

system:

$$
\begin{aligned}
&x'(t) = \lambda - dx(t) - \beta_1 x(t) f(v_I) - x(t) \int_0^\infty k(a) i(t,a)\,\mathrm{d}a,\\
&\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} = -\delta(a) i(t,a),\\
&i(t,0) = \beta_1 x(t) f(v_I) + x(t) \int_0^\infty k(a) i(t,a)\,\mathrm{d}a,\\
&v_I'(t) = \int_0^\infty q(a) i(t,a)\,\mathrm{d}a - \mu v_I(t).
\end{aligned} \tag{3}
$$

Denote function space $\mathcal{Z} = \mathbb{R}^+ \times L^1_+(0,\infty) \times \mathbb{R}^+$ equipped with the norm

$$
\big\|(z_1, z_2, z_3)\big\|_{\mathcal{Z}} = z_1 + \int_0^\infty \big|z_2(a)\big|\,\mathrm{d}a + z_3.
$$

By the standard theory of age-structured model, it can be verified that system (3) with initial condition (2) has a unique nonnegative solution. Thus, system (3) generates a continuous semi-flow $\Phi : \mathbb{R}^+ \times \mathcal{Z} \to \mathcal{Z}$, which takes the form $\Phi(t, z_0) = \Phi_t(z_0) = (x(t), i(t,\cdot), v_I(t))$, $t \geqslant 0$, $z_0 = (x_0, i_0(\cdot), v_I(0)) \in \mathcal{Z}$, with

$$
\big\|\Phi_t(z_0)\big\|_{\mathcal{Z}} = \big\|\big(x(t), i(t,\cdot), v_I(t)\big)\big\|_{\mathcal{Z}} = x(t) + \int_0^\infty \big|i(t,a)\big|\,\mathrm{d}a + v_I(t).
$$

The organization of this paper is as follows. In Section 2, we present some preliminaries results of the system (3). Asymptotic smoothness of the semi-flow generated by system (3) is analyzed. Then we study the existence of equilibria and obtain the expression of the basic reproduction number $\mathcal{R}_0$. In Section 3, the global stability of equilibria is proved. More details concerning the global stability analysis of virus models, we refer readers to [5–7, 9, 14, 18–25, 28, 29].

2 Preliminaries

To study the global dynamics of the model, it is necessary to make assumptions about $f(v_I)$ as follows.

Assumption 1. We assume that:

(i) $f(v_I)$ is a continuously differentiable nonnegative function;
(ii) $f(0) = 0$;
(iii) $f'(v_I) v_I \leqslant f(v_I) \leqslant f'(0) v_I$.

Set $I(t) = \int_0^\infty i(t,a)\,\mathrm{d}a$, which represents the total number of infected cells at time t. Biologically, there exists a finite maximum age, thus it is reasonable to assume that $\lim_{a\to\infty} i(t,a) = 0$. Then from system (3) we have

$$\begin{aligned}\big(x(t)+I(t)\big)' &= \lambda - dx(t) - i(t,0) + \int_0^\infty \left(-\frac{\partial i(t,a)}{\partial a} - \delta(a)i(t,a)\right)\mathrm{d}a \\ &= \lambda - dx(t) - \int_0^\infty \delta(a)i(t,a)\,\mathrm{d}a \\ &\leqslant \lambda - \min\{d,\delta_{\min}\}\big(x(t)+I(t)\big).\end{aligned}$$

Thus, $x(t) + \int_0^\infty i(t,a)\,\mathrm{d}a \leqslant \lambda/\min\{d,\delta_{\min}\}$.

According to the assumption of $p(a)$ and the fourth equation of system (3), it is easy to get

$$v_I'(t) \leqslant \big(1-\eta_p^{(1)}\big)p^+ \int_0^\infty i(t,a)\,\mathrm{d}a - \mu v_I(t),$$

thus, we have $v_I(t) \leqslant (1-\eta_p^{(1)})p^+\lambda/(\mu\min\{d,\delta_{\min}\})$. Integrating the second equation of system (3) along the characteristic line $t-a = \mathrm{const}$ yields

$$i(t,a) = \begin{cases} i(t-a,0)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}, & t \geqslant a, \\ i_0(a-t)\mathrm{e}^{-\int_{a-t}^a \delta(\tau)\,\mathrm{d}\tau}, & a > t. \end{cases} \tag{4}$$

Obviously, $i(a,t)$ remains nonnegative for nonnegative initial condition. Suppose that there exists t_0 such that $x(t_0) = 0$ and $x(t) > 0$ for $t \in [0,t_0)$. Then $x'(t_0) = \lambda > 0$, which implies that $x(t) \geqslant 0$ for all $t \geqslant 0$. Furthermore, from the forth equation of system (3) we have $v_I'(t) + \mu v_I(t) = \int_0^\infty q(a)i(t,a)\,\mathrm{d}a$, which gives $\mathrm{d}(v_I(t)\mathrm{e}^{\mu t})/\mathrm{d}t = \mathrm{e}^{\mu t}\int_0^\infty q(a)i(t,a)\,\mathrm{d}a$, then we have $v_I(t) = \mathrm{e}^{-\mu t}v_I(0) + \int_0^t \mathrm{e}^{-\mu(t-s)}\int_0^\infty q(a)i(t,a)\,\mathrm{d}a\,\mathrm{d}s$. Thus, $v_I(t) \geqslant 0$ for all positive initial data, and $f(v_I(t)) \geqslant 0$ for all positive initial data, which implies that $i(t,a) \geqslant 0$. Then the positive invariant set of system (3) can be given as

$$\mathcal{D} = \left\{(x,i,v_I)\colon x + \int_0^\infty i(t,a)\,\mathrm{d}a \leqslant \frac{\lambda}{\min\{d,\delta_{\min}\}},\ v_I \leqslant \frac{(1-\eta_p^{(1)})p^+\lambda}{\mu\min\{d,\delta_{\min}\}}\right\}.$$

2.1 Asymptotic smoothness

To analyze the global dynamics of system (3), it is necessary to prove the smoothness of the semi-flow generated by system (3). Firstly, we introduce some lemmas as follows.

Lemma 1. *For each $t \geqslant 0$, suppose $\Phi(t) = \Theta(t) + U(t) : \mathcal{Z} \to \mathcal{Z}$ has the property that $U(t)$ is complete continuous and there is a continuous function $g : \mathbb{R}^+ \times \mathbb{R}^+ \to \mathbb{R}^+$ such that $g(t,r) \to 0$ as $t \to 0$ and $\Theta(t)\chi \leqslant g(t,r)$ if $|\chi| < r$. Then $\Phi(t)$ is asymptotically smooth.*

Lemma 2. *If $\Phi(t) : \mathcal{Z} \to \mathcal{Z}$, $t \geqslant 0$ is asymptotically smooth point dissipative and orbits of bounded sets are bounded, then there exists a global attractor $\mathcal{A}_0$. If $\Phi(t)$ is also one-to-one on $\mathcal{A}_0$, then $\Phi(t)/\mathcal{A}_0$ is a C^r-group. In addition, if $\mathcal{Z}$ is a Banach space, then $\mathcal{A}_0$ is connected.*

By using the similar method in [1, 12], we can state the following result, which shows that system (3) has a global compact attractor.

Lemma 3. *Assume that $\mathcal{R}_0 > 1$, then there exists $\mathcal{A}_0$, a compact subset of $\mathcal{Z}_0$, which is a global attractor for the semi-flow of system* (3) *in $\mathcal{Z}_0$. Moreover, $\mathcal{A}_0$ is invariant under the semi-flow, that is,*

$$\Psi(t, \chi_0) \subseteq \mathcal{A}_0 \quad \forall \chi_0 \in \mathcal{A}_0,\ t \geqslant 0.$$

Proof. Denote

$$\Psi\big(t, x_0, i_0(\cdot), v_{I0}\big) = \big(x(t), i(t, \cdot), v_I(t)\big),$$

$\Psi : [0, \infty) \times \mathcal{Z}_0 \to \mathcal{Z}_0$ with $\Psi(t, \Psi(s, \cdot)) = \Psi(t + s, \cdot)$ for all $t, s \geqslant 0$, and $\Psi(0, \cdot)$ being the identity map. In order to utilize Lemmas 1 and 2, we decompose the solution semi-flow into two parts $\Psi = \hat{\Psi}(t, \chi_0) + \tilde{\Psi}(t, \chi_0)$. This decomposition is done in such a way that $\lim_{t\to\infty} \hat{\Psi}(t, \chi_0) = 0$ for every $\chi_0 \in Z_0$, and for a fixed t and any bounded set Ω in Z_0, then the set $\{\tilde{\Psi}(t, \chi_0)\colon \chi_0 \in \Omega\}$ is precompact. Here $\hat{\Psi}$ and $\tilde{\Psi}$ are defined as follows:

$$\begin{aligned}
\hat{\Psi}(t, x_0, i_0(\cdot), v_{0I}) &= \big(0, \hat{i}(t, \cdot), 0\big),\\
\tilde{\Psi}(t, x_0, i_0(\cdot), v_{0I}) &= \big(x(t), \tilde{i}(t, \cdot), v_I(t)\big).
\end{aligned}$$

Notice that $x(t)$ and $v_I(t)$ satisfy system (3) with $i(t, a) = \hat{i}(t, a) + \tilde{i}(t, a)$. The function $\hat{i}(t, a)$ is the solution of the following system:

$$\begin{aligned}
&\hat{i}_t(t, a) + \hat{i}_a(t, a) = -\delta(a)\hat{i}(t, a),\\
&\hat{i}(t, 0) = 0, \qquad \hat{i}(0, a) = i_0(a),
\end{aligned} \tag{5}$$

and $\tilde{i}(t, a)$ is the solution of the following system:

$$\begin{aligned}
&\tilde{i}_t(t, a) + \tilde{i}_a(t, a) = -\delta(a)\tilde{i}(t, a),\\
&\tilde{i}(t, 0) = \beta_1 x f(v_I) + \int_0^\infty k(a)\tilde{i}(t, a)\,\mathrm{d}a, \qquad \tilde{i}(0, a) = 0.
\end{aligned} \tag{6}$$

It is easy to obtain that $\hat{i}(t, a)$ and $\tilde{i}(t, a)$ are nonnegative. Let $w(t) = \int_0^\infty \hat{i}(t, a)\,\mathrm{d}a$. Thus, (5) implies that $w'(t) \leqslant -\delta_{\min} w(t)$. Therefore, we have $\lim_{t\to\infty} \hat{\Psi}(t, \chi_0) = 0$ for every $\chi_0 \in \mathcal{Z}_0$. In order to show that the set $\{\tilde{\Psi}(t, \chi_0)\colon x_0 \in \Omega\}$ is precompact for that fixed t and any bounded set Ω in $\mathcal{Z}_0$, we only need to verify the set $\{\tilde{\Psi}(t, \chi_0)\colon \chi_0 \in \mathcal{Z}_0,\ \text{fixed } t\}$ is precompact by utilizing Fréchet–Kolmogorov theorem. On the one hand, it holds that $\{\tilde{\Psi}(t, \chi_0)\colon \chi_0 \in \mathcal{Z}_0,\ \text{fixed } t\} \subset \mathcal{Z}_0$, and $\{\tilde{\Psi}(t, \chi_0)\colon \chi_0 \in \mathcal{Z}_0,\ \text{fixed } t\}$ is bounded due to that $\mathcal{Z}_0$ is bounded. On the other hand, from (6) we have $\tilde{i}(t,a) = 0$ for $a > t$. The third condition of Fréchet–Kolmogorov theorem is satisfied. Furthermore, in order to verify the second condition, we need to show that the L^1-norm of $\partial\tilde{i}(t,a)/\partial a$ is bounded. Actually, from (6) we obtain that

$$\tilde{i}(t,a) = \begin{cases} \tilde{\phi}(t-a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}, & t \geqslant a, \\ 0, & t < a, \end{cases} \tag{7}$$

where $\tilde{\phi}(t) = x(t)(\beta_1 f(v_I) + \int_0^t k(a)\tilde{\phi}(t-a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a)$. Since, $\tilde{\phi}(t)$ is bounded for $x_0 \in \mathcal{Z}_0$, and $x(t)$, $v_I(t)$ are bounded. Thus, we obtain from (7) that

$$\tilde{\phi}(t) \leqslant \xi_1 \int_0^t \tilde{\phi}(t-a)\,\mathrm{d}a + \xi_2, \qquad \left|\tilde{\phi}'(t)\right| \leqslant \xi_3 \int_0^t \left|\tilde{\phi}'(t-a)\right|\mathrm{d}a + \xi_4,$$

where ξ_i ($i = 1,2,3,4$) are constants that depend on the bounds of the parameters as well as the bounds of the solution.

Making use of Gronwall's inequality, we have

$$\tilde{\phi}(t) \leqslant \xi_2\mathrm{e}^{\xi_1 t}, \qquad \tilde{\phi}'(t) \leqslant \xi_4\mathrm{e}^{\xi_3 t}. \tag{8}$$

Equation (7) implies that

$$\left|\frac{\partial\tilde{i}(t,a)}{\partial a}\right| = \begin{cases} |\tilde{\phi}'(t-a)|\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau} + \tilde{\phi}(t-a)\delta(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}, & t \geqslant a, \\ 0, & t < a. \end{cases} \tag{9}$$

Together with (8) and (9), we have

$$\left\|\frac{\partial\tilde{i}(t,a)}{\partial a}\right\| \leqslant \xi_4\mathrm{e}^{\xi_3 t} \int_0^\infty \mathrm{e}^{-\int_0^a \delta(\tau)}\,\mathrm{d}a + \xi_2\mathrm{e}^{\xi_1 t} \int_0^\infty \delta(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a < \xi.$$

Notice that

$$\int_0^\infty \left|\tilde{i}(t,a+h) - \tilde{i}(t,a)\right|\mathrm{d}a \leqslant \left\|\frac{\partial\tilde{i}(t,a)}{\partial a}\right\| |h| \leqslant \xi|h|.$$

Thus, it is easy to show that the above integral can be made arbitrary small uniformly in the family of functions. This completes the proof of Lemma 3. □

2.2 Existence and uniqueness

Define the basic reproduction number

$$\mathcal{R}_0 = \frac{\lambda(\beta_1 f'(0)\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + \mu\int_0^\infty k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a)}{d\mu},$$

which means the average number of secondary infection produced by one infected cell during its period of infection. From the expression of $\mathcal{R}_0$ it is easy to see that the virus-to-cell infection always exists and the cell-to-cell infection can be prevented by increasing the dose of PI (protease inhibitor).

System (3) always has a infection free steady state $E_0 = (x^0, i^0(a), v_I^0)$, where $x^0 = \lambda/d$, $i^0(a) = 0$, $v_I^0 = 0$. Moreover, there may exist a nonnegative steady state $E^* = (x^*, i^*(a), v_I^*)$, where x^*, $i^*(a)$, v_I^* are nonnegative and satisfy the following equations:

$$\begin{aligned}
&\lambda - dx^* - \beta_1 x^* f(v_I^*) - x^* \int_0^\infty k(a) i^*(a)\,\mathrm{d}a = 0,\\
&\frac{\mathrm{d}i^*(a)}{\mathrm{d}a} = -\delta(a) i^*(a), \qquad \int_0^\infty q(a) i^*(a)\,\mathrm{d}a - \mu v_I^* = 0,\\
&i^*(0) = \beta_1 x^* f(v_I^*) + x^* \int_0^\infty k(a) i^*(a)\,\mathrm{d}a.
\end{aligned} \tag{10}$$

From the first equation of (10) we get

$$x^* = \frac{\lambda}{d + \beta_1 f(v_I^*) + \int_0^\infty k(a) i^*(a)\,\mathrm{d}a}.$$

Solving the second equation of (10) yields

$$i^*(a) = i^*(0)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}. \tag{11}$$

From the third equation of (10) we have

$$i^*(0) = \frac{\mu v_I^*}{\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}.$$

From the first and the fourth equations of (10) we get

$$\begin{aligned}
\lambda - dx^* - i^*(0) &= \lambda - \frac{d}{\frac{\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}{\mu v_I^*}\beta_1 f(v_I^*) + \int_0^\infty k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}\\
&\quad - \frac{\mu v_I^*}{\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}\\
&= \lambda - \frac{\mu d v_I^*}{\beta_1 f(v_I^*)\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + \mu v_I^* \int_0^\infty k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}\\
&\quad - \frac{\mu v_I^*}{\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}\\
&= 0.
\end{aligned}$$

Let $q = \int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a$, $k = \int_0^\infty k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a$. Set

$$g(v) = \lambda - \frac{\mu dv}{q\beta_1 f(v) + \mu kv} - \frac{\mu v}{q}.$$

Then

$$g'(v) = -\mu dq\beta_1 \frac{f(v) - vf'(v)}{(q\beta_1 f(v) + \mu kv)^2} - \frac{\mu}{q}.$$

According to the Assumption 1, $f(v) - vf'(v) \geqslant 0$, $g'(v)$ remains negative for nonnegative initial condition

$$g(0) = \lim_{v\to 0} g(v) = \lambda - \frac{d\mu}{q\beta_1 f'(0) + \mu k} > 0 \quad \text{if } \mathcal{R}_0 > 1.$$

Therefore, when $\mathcal{R}_0 > 1$, there always exists a nonnegative v_I^* satisfying $g(v_I^*) = 0$.

Theorem 1. *System* (3) *always has a steady state* $E_0(x^0, 0, 0)$; *system* (3) *has a unique positive steady state* $E^*(x^*, i^*(a), v_I^*)$ *if and only if* $\mathcal{R}_0 > 1$.

3 Stability analysis of steady states

In this section, we study the local and global stability of the infection-free steady state E_0 and the infection steady state of system (3). The local stability of the two steady states is studied by using the method of characteristic equations, while the global dynamics of system (3) is discussed by constructing Lyapunov functionals.

3.1 Stability of infection-free steady state

Theorem 2. *If* $\mathcal{R}_0 < 1$, *then the infection-free steady state* E_0 *of system* (3) *is locally asymptotically stable. Otherwise, it is unstable.*

Proof. Let $x_1(t) = x(t) - x^0$, $i_1(t,a) = i(t,a)$, $v_1(t) = v_I(t)$. Linearizing system (3) at E_0 leads to the following system:

$$\begin{aligned}
x_1'(t) &= -dx_1(t) - \beta_1 x^0 f'(0) v_1(t) - x^0 \int_0^\infty k(a) i_1(t,a)\,\mathrm{d}a,\\
\frac{\partial i_1(t,a)}{\partial t} &+ \frac{\partial i_1(t,a)}{\partial a} = -\delta(a) i_1(t,a),\\
v_1'(t) &= \int_0^\infty q(a) i_1(t,a)\,\mathrm{d}a - \mu v_1(t),\\
i_1(t,0) &= \beta_1 x^0 f'(0) v_1(t) + x^0 \int_0^\infty k(a) i_1(t,a)\,\mathrm{d}a.
\end{aligned}$$

To analyze the asymptotic behavior of E_0, we set $x_1(t) = x_1\mathrm{e}^{ut}$, $i_1(t,a) = i_1(a)\mathrm{e}^{ut}$ and $v_1(t) = v_1\mathrm{e}^{ut}$. Thus, we get the following equations:

$$\begin{aligned}
(u+d)x_1 &= -\beta_1 x^0 f'(0)v_1 - x^0 \int_0^\infty k(a)i_1(a)\,\mathrm{d}a,\\
\frac{\mathrm{d}i_1(a)}{\mathrm{d}a} &= -\big(u+\delta(a)\big)i_1(a),\\
(u+\mu)v_1 &= \int_0^\infty q(a)i_1(a)\,\mathrm{d}a,\\
i_1(0) &= \beta_1 x^0 f'(0)v_1 + x^0 \int_0^\infty k(a)i_1(a)\,\mathrm{d}a.
\end{aligned} \tag{12}$$

Solving (12) gives

$$\begin{aligned}
i_1(a) &= i_1(0)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau},\\
v_1 &= \frac{i_1(0)}{u+\mu}\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a.
\end{aligned} \tag{13}$$

Substituting (13) into the last equation of (12), we can get

$$\begin{aligned}
&\frac{1}{u+\mu}\beta_1\frac{\lambda}{d}f'(0)\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\\
&\quad + \frac{\lambda}{d}\int_0^\infty k(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a = 1.
\end{aligned} \tag{14}$$

Define a function $G(u)$ that denotes the left hand of (14). Obviously, $G(u)$ is a continuously differentiable function with $\lim_{u\to\infty} G(u) = 0$. It is easy to see that $G(0) = \mathcal{R}_0$, and by direct computation, it shows that $G'(u) < 0$, and therefore, $G(u)$ is a decreasing function. Hence, any real solution of (14) is negative if $\mathcal{R}_0 < 1$, and positive if $\mathcal{R}_0 > 1$. Thus, if $\mathcal{R}_0 > 1$, the infection-free steady state E_0 is unstable. Next, we show that (3.3) has no complex solutions with nonnegative real part if $\mathcal{R}_0 < 1$. Set

$$F(a) = \beta_1\frac{\lambda}{d}f'(0)q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}, \qquad H(a) = \frac{\lambda}{d}k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}.$$

Thus, we have

$$G(u) = \frac{1}{u+\mu}\int_0^\infty \mathrm{e}^{-ua}F(a)\,\mathrm{d}a + \int_0^\infty \mathrm{e}^{-ua}H(a)\,\mathrm{d}a.$$

For $\mathcal{R}_0 < 1$, let $u = \xi + \eta\mathrm{i}$ be an arbitrary complex root to (14) with $\xi \geqslant 0$. Then

$$\begin{aligned}
|G(u)| &= \left| \frac{1}{u+\mu} \int_0^\infty \mathrm{e}^{-ua} F(a)\,\mathrm{d}a + \int_0^\infty \mathrm{e}^{-ua} H(a)\,\mathrm{d}a \right| \\
&\leqslant \left| \frac{1}{|\xi + \eta\mathrm{i} + \mu|} \int_0^\infty \mathrm{e}^{-(\xi+\eta\mathrm{i})a} F(a)\,\mathrm{d}a \right| + \left| \int_0^\infty \mathrm{e}^{-(\xi+\eta\mathrm{i})a} H(a)\,\mathrm{d}a \right| \\
&= \frac{1}{\sqrt{(\xi+\mu)^2 + \eta^2}} \int_0^\infty \left|\mathrm{e}^{-(\xi+\eta\mathrm{i})a}\right| F(a)\,\mathrm{d}a + \int_0^\infty \left|\mathrm{e}^{-(\xi+\eta\mathrm{i})a}\right| H(a)\,\mathrm{d}a \\
&\leqslant \frac{1}{\xi+\mu} \int_0^\infty \mathrm{e}^{-\xi a} F(a)\,\mathrm{d}a + \int_0^\infty \mathrm{e}^{-\xi a} H(a)\,\mathrm{d}a \\
&= |G(\xi)| \leqslant G(0) = \mathcal{R}_0 < 1. \qquad (15)
\end{aligned}$$

It follows from (15) that (14) has a solution $u = \xi + \eta\mathrm{i}$ only if $\xi < 0$. Thus, any solution of (14) must have a negative real part. Therefore, the infection-free steady state E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$. □

Theorem 3. *If $\mathcal{R}_0 \leqslant 1$, then the infection-free steady state E_0 of system* (3) *is globally asymptotically stable.*

Proof. We consider the following Lyapunov functional $V_1 = V_{11} + V_{12} + V_{13}$, where

$$V_{11} = x - x^0 - x^0 \ln\frac{x}{x^0}, \qquad V_{12} = \int_0^\infty \Phi(a) i(t,a)\,\mathrm{d}a, \qquad V_{13} = \beta_1 \frac{x_0}{\mu} f'(0) v_I.$$

Here the nonnegative kernel function $\Phi(a)$ will be determined later. Using (10), differentiating V_1 along the solutions of system (3) yields

$$\begin{aligned}
V_{11}' &= \left(1 - \frac{x^0}{x}\right)\left(dx^0 - dx - \beta_1 x f(v_I) - x\int_0^\infty k(a) i(t,a)\,\mathrm{d}a\right) \\
&= -\frac{d}{x}\left(x - x^0\right)^2 - \beta_1 x f(v_I) - x \int_0^\infty k(a) i(t,a)\,\mathrm{d}a \\
&\quad + \beta_1 x^0 f(v_I) + x^0 \int_0^\infty k(a) i(t,a)\,\mathrm{d}a \\
&= -\frac{d}{x}\left(x - x^0\right)^2 - i(t,0) + \beta_1 x^0 f(v_I) + x^0 \int_0^\infty k(a) i(t,a)\,\mathrm{d}a.
\end{aligned}$$

Using (4), V_{12} becomes

$$V_{12} = \int_0^\infty \Phi(a) i(t,a)\,\mathrm{d}a$$
$$= \int_0^t \Phi(a) i(t-a,0) \mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + \int_t^\infty \Phi(a) i_0(a-t) \mathrm{e}^{-\int_{a-t}^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a$$
$$= \int_0^t \Phi(t-r) i(r,0) \mathrm{e}^{-\int_0^{t-r} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}r + \int_0^\infty \Phi(t+r) i_0(r) \mathrm{e}^{-\int_r^{t+r} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}r.$$

Differentiating V_{12} yields

$$V_{12}' = \Phi(0) i(t,0) + \int_0^t \Phi'(t-r) i(r,0) \mathrm{e}^{-\int_0^{t-r} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}r$$
$$- \int_0^t \delta(t-r)\Phi(t-r) i(r,0) \mathrm{e}^{-\int_0^{t-r} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}r$$
$$+ \int_0^\infty \Phi'(t+r) i_0(r) \mathrm{e}^{-\int_r^{t+r} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}r$$
$$- \int_0^\infty \delta(t+r)\Phi(t+r) i_0(r) \mathrm{e}^{-\int_r^{t+r} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}r$$
$$= \Phi(0) i(t,0) + \int_0^\infty \left(\Phi'(a) - \delta(a)\Phi(a)\right) i(t,a)\,\mathrm{d}a.$$

Also, using (10), differentiating V_{13} along the solutions of system (3) yields

$$V_{13}' = \beta_1 \frac{x^0}{\mu} f'(0) \frac{\mathrm{d}v_I}{\mathrm{d}t} = \beta_1 \frac{x^0}{\mu} f'(0) \left(\int_0^\infty q(a) i(t,a)\,\mathrm{d}a - \mu v_I \right)$$
$$= \beta_1 \frac{x^0}{\mu} f'(0) \int_0^\infty q(a) i(t,a)\,\mathrm{d}a - \beta_1 x^0 f'(0) v_I.$$

According to Assumption 1, it is easy to get

$$V_{13}' \leqslant \beta_1 \frac{x^0}{\mu} f'(0) \int_0^\infty q(a) i(t,a)\,\mathrm{d}a - \beta_1 x^0 f(v_I).$$

Adding V_{11}, V_{12}, V_{13} together gives

$$\begin{aligned}
V_1' &= -\frac{d}{x}(x-x^0)^2 - i(t,0) + x^0\int_0^\infty k(a)i(t,a)\,\mathrm{d}a + \beta_1 x^0 f(v_I) \\
&\quad + \Phi(0)i(t,0) + \int_0^\infty \big(\Phi'(a) - \delta(a)\Phi(a)\big)i(t,a)\,\mathrm{d}a \\
&\quad + \beta_1\frac{x^0}{\mu}f'(0)\int_0^\infty q(a)i(t,a)\,\mathrm{d}a - \beta_1 x^0 f'(0)v_I \\
&\leqslant -\frac{d}{x}\big(x-x^0\big)^2 - i(t,0) + x^0\int_0^\infty k(a)i(t,a)\,\mathrm{d}a + \Phi(0)i(t,0) \\
&\quad + \int_0^\infty \big(\Phi'(a) - \delta(a)\Phi(a)\big)i(t,a)\,\mathrm{d}a + \beta_1\frac{x^0}{\mu}f'(0)\int_0^\infty q(a)i(t,a)\,\mathrm{d}a \\
&= -\frac{d}{x}\big(x-x^0\big)^2 + \big(\Phi(0)-1\big)i(t,0) \\
&\quad + \int_0^\infty \left(\beta_1\frac{x^0}{\mu}f'(0)q(a) + x^0k(a) + \Phi'(a) - \delta(a)\Phi(a)\right)i(t,a)\,\mathrm{d}a.
\end{aligned}$$

Now let

$$\Phi(a) = \int_a^\infty \left(\beta_1\frac{x^0}{\mu}f'(0)q(\theta) + k(\theta)x^0\right)\mathrm{e}^{-\int_a^\theta \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}\theta.$$

By differentiating the above equation, it can be verified that

$$\Phi'(a) = -\beta_1\frac{x^0}{\mu}f'(0)q(a) - x^0k(a) + \delta(a)\Phi(a).$$

Notice that $\Phi(0) = \mathcal{R}_0$. Hence, it follows that

$$V_1' \leqslant -\frac{d}{x}\big(x-x^0\big)^2 + (\mathcal{R}_0 - 1)i(t,0) \leqslant 0 \quad \text{if } \mathcal{R}_0 \leqslant 1.$$

Therefore, $\mathcal{R}_0 \leqslant 1$ ensures that $V_1'(t) \leqslant 0$. It can be verified that the largest invariant set where $V_1' = 0$ is the singleton E_0. Thus, all solutions of system (3) converge to the infection-free steady state E_0. Therefore, E_0 is globally asymptotically stable when $\mathcal{R}_0 \leqslant 1$. □

3.2 Local stability of infection steady state

Theorem 4. *If $\mathcal{R}_0 > 1$, then the infection steady state E^* of system* (3) *is locally asymptotically stable.*

Proof. To show the local stability, we linearize the system (3) around the infection steady state E^*. In particular, we introduce the perturbation variables $x_2(t) = x(t) - x^*$, $i_2(t,a) = i(t,a) - i^*(a)$, $v_2(t) = v_I(t) - v_I^*$, which leads to

$$\begin{aligned}
x_2'(t) &= -dx_2(t) - \beta_1 x^* f'(v_I^*) v_2(t) - x^* \int_0^\infty k(a) i_2(t,a)\,\mathrm{d}a \\
&\quad - \beta_1 f(v_I^*) x_2(t) - x_2(t) \int_0^\infty k(a) i^*(a)\,\mathrm{d}a, \\
\frac{\partial i_2(t,a)}{\partial t} &+ \frac{\partial i_2(t,a)}{\partial a} = -\delta(a) i_2(t,a), \\
v_2'(t) &= \int_0^\infty q(a) i_2(t,a)\,\mathrm{d}a - \mu v_2(t), \\
i_2(t,0) &= \beta_1 x^* f'(v_I^*) v_2(t) + x^* \int_0^\infty k(a) i_2(t,a)\,\mathrm{d}a \\
&\quad + \beta_1 f(v_I^*) x_2(t) + x_2(t) \int_0^\infty k(a) i^*(a)\,\mathrm{d}a.
\end{aligned}$$

To analyze the asymptotic behavior of E^*, we look for solutions of the form $x_2(t) = x_2 \mathrm{e}^{ut}$, $i_2(t,a) = i_2(a)\mathrm{e}^{ut}$ and $v_2(t) = v_2 \mathrm{e}^{ut}$. Thus, we can consider the following eigenvalue problem:

$$\begin{aligned}
ux_2 &= -dx_2 - \beta_1 x^* f'(v_I^*) v_2 - x^* \int_0^\infty k(a) i_2(a)\,\mathrm{d}a - \beta_1 f(v_I^*) x_2 \\
&\quad - x_2 \int_0^\infty k(a) i^*(a)\,\mathrm{d}a, \\
\frac{\mathrm{d}i_2(a)}{\mathrm{d}a} &= -u i_2(a) - \delta(a) i_2(a), \\
uv_2 &= \int_0^\infty q(a) i_2(a)\,\mathrm{d}a - \mu v_2, \\
i_2(0) &= \beta_1 x^* f'(v_I^*) v_2 + x^* \int_0^\infty k(a) i_2(a)\,\mathrm{d}a + \beta_1 f(v_I^*) x_2 \\
&\quad + x_2 \int_0^\infty k(a) i^*(a)\,\mathrm{d}a.
\end{aligned} \tag{16}$$

Solving (16), we have

$$
\begin{aligned}
&i_2(a) = i_2(0)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau},\\
&x_2 = -\frac{i_2(0)}{u+d}, \qquad v_2 = \frac{i_2(0)}{u+\mu}\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a.
\end{aligned}
\tag{17}
$$

Substituting (17) into the last equation of (16) yields

$$
\begin{aligned}
&-\frac{\beta_1 f(v_I^*) + \int_0^\infty k(a)i^*(a)\,\mathrm{d}a}{u+d} + \frac{\beta_1 x^* f'(v_I^*)}{u+\mu}\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\\
&\quad + x^*\int_0^\infty k(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a = 1.
\end{aligned}
$$

We rewrite the equation in the following form:

$$
\begin{aligned}
&\frac{\beta_1 x^* f'(v_I^*)}{u+\mu}\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + x^*\int_0^\infty k(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\\
&= \frac{u+d+\beta_1 f(v_I^*) + \int_0^\infty k(a)i^*(a)\,\mathrm{d}a}{u+d}.
\end{aligned}
\tag{18}
$$

It is not hard to see that for u with Re $u \geqslant 0$, the right side of the characteristic equation (18) satisfies the following inequation:

$$
\left|\frac{u+d+\beta_1 f(v_I^*) + \int_0^\infty k(a)i^*(a)\,\mathrm{d}a}{u+d}\right| > 1.
$$

With respect to the left side of (18), for u with $\mathrm{Re}\,u \geqslant 0$, we have

$$
\begin{aligned}
&\left|\frac{\beta_1 x^* f'(v_I^*)}{u+\mu}\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + x^*\int_0^\infty k(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\right|\\
&\quad \leqslant \frac{\beta_1 x^* f'(v_I^*)}{|u+\mu|}\left|\int_0^\infty q(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\right| + \left|x^*\int_0^\infty k(a)\mathrm{e}^{-ua}\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\right|\\
&\quad \leqslant \frac{\beta_1 x^* f'(v_I^*)}{\mu}\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + x^*\int_0^\infty k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\\
&\quad \leqslant \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + x^*\int_0^\infty k(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\\
&\quad = 1.
\end{aligned}
$$

Hence, for u with $\operatorname{Re} u \geqslant 0$, the right side of (18) is strictly larger than one, while the left side of (18) is smaller than 1. Therefore, the contradiction implies that the characteristic equation (18) has no roots with non-negative real part. Thus, we have proved that the infection steady state E^* is locally asymptotically stable. □

To establish the global stability of the infection steady state E^*, we define the following Lyapunov functional:

$$V_2 = V_{21} + V_{22} + V_{23},$$

where

$$\begin{aligned} V_{21} &= G(x, x^*), \qquad V_{22} = \int_0^\infty \Phi(a) G\bigl(i(t,a), i^*(a)\bigr)\,\mathrm{d}a, \\ V_{23} &= \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}\left(v - \int_{v^*}^{v} \frac{f(v^*)}{f(\eta)}\,\mathrm{d}\eta\right), \qquad G(x,y) = x - y - y\ln\frac{x}{y}, \\ \Phi(a) &= \int_a^\infty \left(\frac{\beta_1 x^* f(v_I^*) q(\theta)}{\mu v_I^*} + k(\theta) x^*\right) \mathrm{e}^{-\int_a^\theta \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}\theta. \end{aligned} \tag{19}$$

Before making use of the Lyapunov functional V_2 defined above to establish the global stability of infection steady state, it should be shown that the Lyapunov functional is well defined. To this end, we first show the uniform persistence of system (3).

3.3 Persistence

In this section, we investigate the uniform persistence of system (3) by using the persistence theory for infinite dimensional dynamical system. Define

$$\bar a_1 = \inf\left\{a\colon \int_a^\infty k(u)\,\mathrm{d}u = 0\right\}, \qquad \bar a_2 = \inf\left\{a\colon \int_a^\infty \delta(u)\,\mathrm{d}u = 0\right\},$$
$$\bar a_3 = \inf\left\{a\colon \int_a^\infty q(u)\,\mathrm{d}u = 0\right\}.$$

Since $k(a), \delta(a), q(a) \in L_+^1(0,\infty)$, we have $\bar a_1, \bar a_2, \bar a_3 > 0$. Furthermore, let

$$\tilde{\mathcal{Z}} = L_+^1(0,\infty) \times \mathbb{R}^+, \qquad \bar a = \max\{\bar a_1, \bar a_2, \bar a_3\},$$
$$\tilde{\mathcal{Y}} = \left\{\bigl(i(t,\cdot), v_I(t)\bigr)^{\mathrm{T}} \in \tilde{\mathcal{Z}}\colon \int_0^{\bar a} i(t,a)\,\mathrm{d}a > 0 \text{ or } v_I(t) > 0\right\},$$

and

$$\mathcal{Y} = \mathbb{R}^+ \times \tilde{\mathcal{Y}}, \qquad \partial\mathcal{Y} = \mathcal{Z} \setminus \mathcal{Y}, \qquad \partial\tilde{\mathcal{Y}} = \tilde{\mathcal{Z}} \setminus \tilde{\mathcal{Y}}.$$

It is not difficult to verify the following result.

Proposition 1. *The subsets $\mathcal{Y}$ and $\partial\mathcal{Y}$ are both positively invariant under the semi-flow $\{\Phi(t)\}_{t\geqslant 0}$, namely, $\Phi(t,\mathcal{Y}) \subset \mathcal{Y}$ and $\Phi(t,\partial\mathcal{Y}) \subset \partial\mathcal{Y}$ for $t \geqslant 0$.*

Furthermore, the following result is useful for the proof of uniform persistence.

Theorem 5. *The disease-free steady state E_0 of system* (3) *is globally asymptotically stable for the semi-flow $\{\Phi(t)\}_{t\geqslant 0}$ restricted to $\partial\mathcal{Y}$.*

Proof. Letting $(x_0, i_0(\cdot), v_{I0}(\cdot)) \in \partial\mathcal{Y}$, namely, $(i_0(\cdot), v_{I0}(\cdot)) \in \partial\tilde{\mathcal{Y}}$, we consider the following system:

$$\begin{aligned}
&\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} = -\delta(a) i(t,a),\\
&i(t,0) = \beta_1 x(t) f\bigl(v_I(t)\bigr) + x(t)\int_0^\infty k(a) i(t,a)\mathrm{d}a,\\
&v'_I(t) = \int_0^\infty q(a) i(t,a)\mathrm{d}a - \mu v_I(t),\\
&i(0,a) = i_0(a), \qquad v_I(0) = v_{I0}.
\end{aligned}$$

Since $x(t) \leqslant \lambda/d$ as t tends to infinity, by comparison, we have $i(t,a) \leqslant \tilde{i}(t,a)$, $v_I(t) \leqslant \tilde{v}_I(t)$, where $\tilde{i}(t,a)$ and $\tilde{v}_I(t)$ satisfy the following auxiliary system:

$$\begin{aligned}
&\frac{\partial \tilde{i}(t,a)}{\partial t} + \frac{\partial \tilde{i}(t,a)}{\partial a} = -\delta(a)\tilde{i}(t,a),\\
&\tilde{i}(t,0) = \beta_1 \frac{\lambda}{d} f\bigl(\tilde{v}_I(t)\bigr) + \frac{\lambda}{d}\int_0^\infty k(a)\tilde{i}(t,a)\mathrm{d}a,\\
&\tilde{v}'_I(t) = \int_0^\infty q(a)\tilde{i}(t,a)\mathrm{d}a - \mu \tilde{v}_I(t),\\
&\tilde{i}(0,a) = i_0(a), \qquad \tilde{v}_I(0) = v_{I0}.
\end{aligned} \tag{20}$$

Similar to (4), solving the first equation of (20) yields

$$\tilde{i}(t,a) = \begin{cases} \tilde{L}(t-a)\mathrm{e}^{-\int_0^a \delta(\tau)\mathrm{d}\tau}, & t \geqslant a,\\ i_0(a-t)\mathrm{e}^{-\int_{a-t}^a \delta(\tau)\mathrm{d}\tau}, & a > t, \end{cases} \tag{21}$$

where

$$\tilde{L}(t) = \frac{\lambda}{d}\left(\beta_1 f(\tilde{v}_I(t)) + \int_0^\infty k(a)\tilde{i}(t,a)\,\mathrm{d}a\right). \tag{22}$$

Substituting (21) into (22) yields

$$\tilde{L}(t) = \frac{\lambda}{d}\left(\beta_1 f\bigl(\tilde{v}_I(t)\bigr) + \int_0^t k(a)\tilde{L}(t-a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\right) + G(t), \tag{23}$$

where

$$G(t) = \frac{\lambda}{d}\int_0^t k(a)i_0(a-t)\mathrm{e}^{-\int_{a-t}^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a.$$

Since $(i_0(\cdot), v_{I0}(\cdot)) \in \partial\tilde{\mathcal{Y}}$, we have $G(t) \equiv 0$ for all $t \geqslant 0$. From (23) we obtain that

$$\tilde{L}(t) = \frac{\lambda}{d}\left(\beta_1 f(\tilde{v}_I(t)) + \int_0^t k(a)\tilde{L}(t-a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a\right). \tag{24}$$

It is easy to show that (24) has a unique solution $\tilde{L}(t) \equiv 0$, in which $\tilde{v}_I(t) = 0$. From (21) we have $\tilde{i}(t,a) = 0$. For $a \geqslant t$, it follows that

$$\bigl\|\tilde{i}(t,a)\bigr\|_{L^1} = \bigl\|\mathrm{e}^{-\int_{a-t}^a \delta(\tau)\,\mathrm{d}\tau} i_0(a-t)\bigr\|_{L^1} \leqslant \mathrm{e}^{-\delta_{\min} t}\|i_0\|_{L^1},$$

which implies that $\tilde{i}(t,a) = 0$ as $t \to \infty$. Noting that $i(t,a) \leqslant \tilde{i}(t,a)$, $v_I(t) \leqslant \tilde{v}_I(t)$, we have $i(t,a) \to 0$ and $v_I(t) \to 0$ as $t \to \infty$. It follows from the first equation of system (3) that $x(t) \to x^0$ as $t \to \infty$. Thus, E_0 is globally asymptotically stable in $\partial\mathcal{Y}$. □

Theorem 6. *If $\mathcal{R}_0 > 1$, then the semi-flow $\{\Phi(t)\}_{t\geqslant 0}$ is uniformly persistent with respect to $(\mathcal{Y}, \partial\mathcal{Y})$, i.e., there exists an $\varepsilon > 0$, which is independent of initial values such that $\lim_{t\to\infty}\|\Phi(t,z)\|_{\mathcal{Z}} \geqslant \varepsilon$ for $z \in \mathcal{Y}$. Furthermore, there is a compact subset $\mathcal{A}_0 \subset \mathcal{Y}$, which is a global attractor for $\{\Phi(t,z)\}_{t\geqslant 0}$ in $\mathcal{Y}$.*

Proof. It follows from Theorem 5 that E_0 is globally asymptotically stable in $\partial\mathcal{Y}$. Applying Theorem 4.2 in [3], we need only to show that $W^s(E_0) \cap \mathcal{Y} = \emptyset$, where

$$W^s(E_0) = \Bigl\{z \in \mathcal{Y}\colon \lim_{t\to\infty} \Phi(t,z) = E_0\Bigr\}.$$

Otherwise, there exists a solution $y \subset \mathcal{Y}$ such that $\Phi(t,y) \to E_0$ as $t \to \infty$. In this case, there exists a sequence $\{y_n\} \subset \mathcal{Y}$ such that $\|\Phi(t,y_n) - E_0\|_{\mathcal{Z}} < 1/n$ for $t \geqslant 0$. Denote $\Phi(t,y_n) = (x_n(t), i(t,\cdot), v_{In}(t))$ and $y_n = (x_n(0), i(0,\cdot), v_{In}(0))$. Since $\mathcal{R}_0 > 1$, we can choose n sufficiently large satisfying $x^0 > 1/n$ and

$$\left(\frac{\lambda}{d} - \frac{1}{n}\right)\frac{\beta_1 f'(0)\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a + \mu\int_0^\infty \mathrm{k(a)}\mathrm{e}^{-\int_0^{\mathrm{a}} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{d}a}{\mu} > 1, \tag{25}$$

where $x^0 = \lambda/d$. For such a $n > 0$, there exists a $T > 0$ such that for $t > T$, $x^0 - 1/n < x_n(t) < x^0 + 1/n$. Consider the following auxiliary system:

$$\begin{aligned}
&\frac{\partial \hat{i}(t,a)}{\partial t} + \frac{\partial \hat{i}(t,a)}{\partial a} = -\delta(a)\hat{i}(t,a),\\
&\hat{i}(t,0) = \left(\frac{\lambda}{d} - \frac{1}{n}\right)\left(\beta_1 f\big(\hat{v}_I(t)\big) + \int_0^\infty k(a)\hat{i}(t,a)\,\mathrm{da}\right),\\
&\hat{v}_I'(t) = \int_0^\infty q(a)\hat{i}(t,a)\,\mathrm{da} - \mu\hat{\mathrm{v}}_{\mathrm{I}}(\mathrm{t}).
\end{aligned} \tag{26}$$

Looking for solutions of system (26) of the form $\hat{i}(t,a) = \hat{i}(a)\mathrm{e}^{ut}$ and $\hat{v}_I(t) = \hat{v}_I\mathrm{e}^{ut}$, where the function $\hat{i}(a)$ and the constant $\hat{v}_I$ will be determined later, we obtain the following linear eigenvalue problem:

$$\begin{aligned}
&\frac{d\hat{i}(a)}{da} = -\big(u + \delta(a)\big)\hat{i}(a),\\
&\hat{i}(0) = \left(\frac{\lambda}{d} - \frac{1}{n}\right)\left(\beta_1 \frac{f(\hat{v}_I)}{\mathrm{e}^{ut}} + \int_0^\infty k(a)\hat{i}(a)\,\mathrm{da}\right),\\
&(u+\mu)\hat{v}_I = \int_0^\infty q(a)\hat{i}(a)\,\mathrm{da}.
\end{aligned} \tag{27}$$

Solving the first equation of system (27) yields

$$\hat{i}(a) = \hat{i}(0)\mathrm{e}^{-\int_0^a (u+\delta(s))\,\mathrm{d}s}. \tag{28}$$

Substitution (28) into the last two equations of (27), we obtain the characteristic equation of system (3) at the steady state E_0 as follows:

$$f(u) = 1, \tag{29}$$

where

$$\begin{aligned}
f(u) &= \left(\frac{\lambda}{d} - \frac{1}{n}\right)\frac{\beta_1 f(\hat{v}_I)\int_0^\infty q(a)\mathrm{e}^{-\int_0^a (u+\delta(s))\,\mathrm{d}s}\,\mathrm{da}}{\mathrm{e}^{ut}(u+\mu)\hat{v}_I}\\
&\quad + \left(\frac{\lambda}{d} - \frac{1}{n}\right)\int_0^\infty k(a)\mathrm{e}^{-\int_0^a (u+\delta(s))\,\mathrm{d}s}\,\mathrm{da}.
\end{aligned}$$

Clearly, we have $\lim_{u\to\infty} f(u) = 0$. From (25) and Assumption 1, there exists a $n > 0$ and a $T > 0$ such that

$$f(0) = \left(\frac{\lambda}{d} - \frac{1}{n}\right)\frac{\beta_1 f'(0)\int_0^\infty q(a)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{da} + \mu\int_0^\infty \mathrm{k(a)}\mathrm{e}^{-\int_0^{\mathrm{a}} \delta(\tau)\,\mathrm{d}\tau}\,\mathrm{da}}{\mu} > 1.$$

Hence, if $\mathcal{R}_0 > 1$, (29) has at least one positive root. This implies that the solution $(\hat{i}(t,\cdot), \hat{v}_I(t))$ of system (26) is unbounded. By comparison, the solution $\Phi(t, y_n)$ of system (3) is unbounded, which contradicts to the boundedness of system (3). Therefore, the semi-flow $\Phi(t)_{t\geqslant 0}$ generated by system (3) is uniformly persistent. Furthermore, there is a compact subset $\mathcal{A}_0 \subset \mathcal{Y}$, which is a global attractor for $\Phi(t)_{t\geqslant 0}$ in $\mathcal{Y}$. This completes the proof. □

3.4 Global stability of the infection steady state

Now we are ready to establish the global stability of the steady state E^*. The following theorem summarizes the result.

Theorem 7. *If $\mathcal{R}_0 > 1$, then the infection steady state E^* of system* (3) *is globally asymptotically stable.*

Proof. Using (10), we take the derivative of each part of the Lyapunov functional V_2 defined in (19) along the solutions of system (3) separately

$$\begin{aligned} V_{21}' &= \left(1 - \frac{x^*}{x}\right)\bigl(\lambda - dx - i(t,0)\bigr) \\ &= \left(1 - \frac{x^*}{x}\right)\bigl(dx^* + i^*(0) - dx - i(t,0)\bigr) \\ &= -\frac{d}{x}(x - x^*)^2 + i^*(0) - i(t,0) - i^*(0)\frac{x^*}{x} + i(t,0)\frac{x^*}{x}. \end{aligned} \tag{30}$$

Using (4), it follows that

$$\begin{aligned} V_{22} &= \int_0^t \Phi(a) G\bigl(i(t-a,0)\mathrm{e}^{-\int_0^a \delta(\tau)\,\mathrm{d}\tau},\, i^*(a)\bigr)\,\mathrm{d}a \\ &\quad + \int_t^\infty \Phi(a) G\bigl(i_0(a-t)\mathrm{e}^{-\int_{a-t}^a \delta(\tau)\,\mathrm{d}\tau},\, i^*(a)\bigr)\,\mathrm{d}a \\ &= \int_0^t \Phi(t-r) G\bigl(i(r,0)\mathrm{e}^{-\int_0^{t-r} \delta(\tau)\,\mathrm{d}\tau},\, i^*(t-r)\bigr)\,\mathrm{d}r \\ &\quad + \int_0^\infty \Phi(t+r) G\bigl(i_0(r)\mathrm{e}^{-\int_r^{t+r} \delta(\tau)\,\mathrm{d}\tau},\, i^*(t+r)\bigr)\,\mathrm{d}r. \end{aligned}$$

From (11) and the fact that $xG_x(x,y) + yG_y(x,y) = G(x,y)$, differentiating V_{22} yields

$$V_{22}' = \Phi(0)G\bigl(i(t,0), i^*(0)\bigr) + \int_0^t \Phi'(t-r) G\bigl(i(r,0)\mathrm{e}^{-\int_0^{t-r} \delta(\tau)\,\mathrm{d}\tau},\, i^*(t-r)\bigr)\,\mathrm{d}r$$

$$
\begin{aligned}
&- \int_0^t \Phi(t-r)\delta(t-r)\big[i(r,0)\mathrm{e}^{-\int_0^{t-r}\delta(\tau)\,\mathrm{d}\tau} G_x\big(i(r,0)\mathrm{e}^{-\int_0^{t-r}\delta(\tau)\,\mathrm{d}\tau},\, i^*(t-r)\big) \\
&\quad + i^*(t-r)G_y\big(i(r,0)\mathrm{e}^{-\int_0^{t-r}\delta(\tau)\,\mathrm{d}\tau},\, i^*(t-r)\big)\big]\,\mathrm{d}r \\
&+ \int_0^\infty \Phi'(t+r)G\big(i_0(r)\mathrm{e}^{-\int_r^{t+r}\delta(\tau)\,\mathrm{d}\tau},\, i^*(t+r)\big)\,\mathrm{d}r \\
&- \int_0^\infty \Phi(t+r)\delta(t+r)\big[i_0(r)\mathrm{e}^{-\int_r^{t+r}\delta(\tau)\,\mathrm{d}\tau} G_x\big(i_0(r)\mathrm{e}^{-\int_r^{t+r}\delta(\tau)\,\mathrm{d}\tau},\, i^*(t+r)\big) \\
&\quad + i^*(t+r)G_y\big(i_0(r)\mathrm{e}^{-\int_r^{t+r}\delta(\tau)\,\mathrm{d}\tau},\, i^*(t+r)\big)\big]\,\mathrm{d}r \\
&= \Phi(0)G\big(i(t,0), i^*(0)\big) + \int_0^\infty \big(\Phi'(a) - \delta(a)\Phi(a)\big)G\big(i(t,a),\, i^*(a)\big)\,\mathrm{d}a.
\end{aligned}
$$

Notice that $\Phi(0) = 1$ and

$$
\Phi'(a) = -\left(\frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*} q(a) + x^* k(a)\right) + \delta(a)\Phi(a).
$$

Then we have

$$
\begin{aligned}
V_{22}' = {}& \int_0^\infty \left(\frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*} q(a) + x^* k(a)\right)\left(i^*(a) - i(t,a) + i^*(a)\ln\frac{i(t,a)}{i^*(a)}\right)\mathrm{d}a \\
&+ i(t,0) - i^*(0) - i^*(0)\ln\frac{i(t,0)}{i^*(0)}.
\end{aligned} \tag{31}
$$

Similarly, differentiating V_{23} along the solutions of system (3) yields

$$
\begin{aligned}
V_{23}' &= \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}\left(1 - \frac{f(v_I^*)}{f(v_I)}\right)\left(\int_0^\infty q(a)i(t,a)\,\mathrm{d}a - \mu v_I\right) \\
&= \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}\left(\int_0^\infty q(a)i(t,a)\,\mathrm{d}a\right. \\
&\quad \left. - \frac{f(v_I^*)}{f(v_I)}\int_0^\infty q(a)i(t,a)\,\mathrm{d}a - \mu v_I + \mu v_I\frac{f(v_I^*)}{f(v_I)}\right).
\end{aligned} \tag{32}
$$

Adding (30), (31) and (32) together yields

$$
\begin{aligned}
V_2' = {}& -\frac{d}{x}(x-x^*)^2 - i^*(0)\frac{x^*}{x} + i(t,0)\frac{x^*}{x} - i^*(0)\ln\frac{i(t,0)}{i^*(0)} \\
&+ \int_0^\infty \left(\frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}q(a) + x^* k(a)\right)\left(i^*(a) - i(t,a) + i^*(a)\ln\frac{i(t,a)}{i^*(a)}\right)\mathrm{d}a \\
&+ \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}\left(\int_0^\infty q(a)i(t,a)\,\mathrm{d}a - \frac{f(v_I^*)}{f(v_I)}\int_0^\infty q(a)i(t,a)\,\mathrm{d}a - \mu v_I + \mu v_I\frac{f(v_I^*)}{f(v_I)}\right).
\end{aligned}
$$

Then we can get

$$
\begin{aligned}
V_2' = {}& -\frac{d}{x}(x-x^*)^2 - i^*(0)\frac{x^*}{x} - i^*(0)\ln\frac{i(t,0)}{i^*(0)} - \beta_1 x^* f(v_I^*) \\
&+ \int_0^\infty \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}q(a)i^*(a)\left(2 + \ln\frac{i(t,a)}{i^*(a)} - \frac{f(v_I^*)}{f(v_I)}\frac{i(t,a)}{i^*(a)}\right)\mathrm{d}a \\
&+ \int_0^\infty x^* k(a)i^*(a)\left(1 + \ln\frac{i(t,a)}{i^*(a)}\right)\mathrm{d}a - \frac{\beta_1 x^* f(v_I^*)v_I}{v_I^*} + \frac{\beta_1 x^* f^2(v_I^*)v_I}{v_I^* f(v_I)} \\
={}& -\frac{d}{x}(x-x^*)^2 \\
&+ \int_0^\infty \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}q(a)i^*(a)\left(2 - \frac{x^*}{x} - \ln\frac{i(t,0)}{i^*(0)} + \ln\frac{i(t,a)}{i^*(a)} - \frac{f(v_I^*)}{f(v_I)}\frac{i(t,a)}{i^*(a)}\right)\mathrm{d}a \\
&+ \int_0^\infty k(a)x^* i^*(a)\left(1 - \frac{x^*}{x} + \ln\frac{i(t,a)}{i^*(a)} - \ln\frac{i(t,0)}{i^*(0)}\right)\mathrm{d}a \\
&+ \beta_1 x^* f(v_I) - \beta_1 x^* f(v_I^*) - \frac{\beta_1 x^* f(v_I^*)v_I}{v_I^*} + \frac{\beta_1 x^* f^2(v_I^*)v_I}{v_I^* f(v_I)}.
\end{aligned}
$$

Notice that

$$
\begin{aligned}
&\int_0^\infty \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*}q(a)i^*(a)\left(1 - \frac{x}{x^*}\frac{f(v_I)}{f(v_I^*)}\frac{i^*(0)}{i(t,0)}\right)\mathrm{d}a \\
&\qquad + \int_0^\infty x^* k(a)i^*(a)\left(1 - \frac{x}{x^*}\frac{i(t,a)}{i^*(a)}\frac{i^*(0)}{i(t,0)}\right)\mathrm{d}a
\end{aligned}
$$

$$
\begin{aligned}
&= \beta_1 x^* f(v_I^*) + x^* \int_0^\infty k(a) i^*(a)\,\mathrm{d}a - \beta_1 x f(v_I) \frac{i^*(0)}{i(t,0)} \\
&\quad - \frac{i^*(0)}{i(t,0)} \int_0^\infty k(a) i(t,a)\,\mathrm{d}a = i^*(0) - i(t,0)\frac{i^*(0)}{i(t,0)} \\
&= 0.
\end{aligned}
$$

Therefore, we have

$$
\begin{aligned}
V_2' = {}& -\frac{d}{x}(x-x^*)^2 - \frac{\beta_1 x^* f(v_I^*)}{\mu v_I^*} \\
&\times \int_0^\infty q(a) i^*(a) \left[g\left(\frac{x^*}{x}\right) + g\left(\frac{f(v_I^*) i(t,a)}{f(v_I) i^*(a)}\right) + g\left(\frac{x f(v_I) i^*(0)}{x^* f(v_I^*) i(t,0)}\right)\right] \mathrm{d}a \\
&- x^* \int_0^\infty k(a) i^*(a) \left[g\left(\frac{x^*}{x}\right) + g\left(\frac{x i^*(0) i(t,a)}{x^* i(t,0) i^*(a)}\right)\right] \mathrm{d}a \\
&+ \beta_1 x^* f(v_I) - \beta_1 x^* f(v_I^*) - \frac{\beta_1 x^* f(v_I^*) v_I}{v_I^*} + \frac{\beta_1 x^* f^2(v_I^*) v_I}{v_I^* f(v_I)}.
\end{aligned}
$$

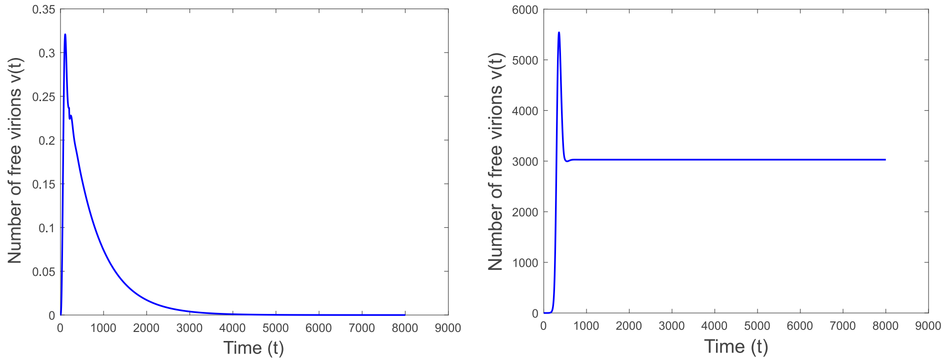
Obviously,

$$
\begin{aligned}
&\beta_1 x^* f(v_I) - \beta_1 x^* f(v_I^*) - \frac{\beta_1 x^* f(v_I^*) v_I}{v_I^*} + \frac{\beta_1 x^* f^2(v_I^*) v_I}{v_I^* f(v_I)} \\
&\quad = \beta_1 x^* \big(f(v_I) - f(v_I^*)\big) + \frac{\beta_1 x^* f(v_I^*) v_I}{v_I^* f(v_I)} \big(f(v_I^*) - f(v_I)\big) \\
&\quad = \frac{\beta_1 x^* v_I}{f(v_I)} \big(f(v_I) - f(v_I^*)\big) \left(\frac{f(v_I)}{v_I} - \frac{f(v_I^*)}{v_I^*}\right) \leqslant 0.
\end{aligned}
$$

It is easy to see that $g(x) = x - 1 - \ln x \geqslant 0$ for all $x > 0$ with equality holding if and only if $x = 1$. Then it can be verified that the largest invariant set of $V_2' = 0$ is the singleton E^*. It then follows from [11] that the compact global attractor $\mathcal{A}_0 = E^*$, which implies E^* is globally asymptotically stable. □

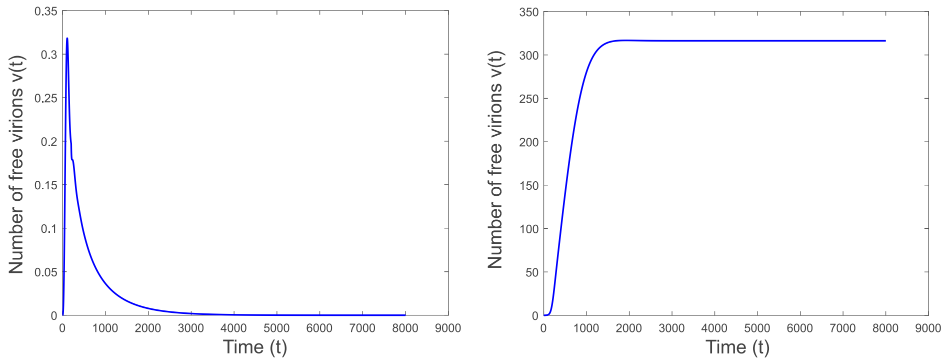
4 Numerical simulations

In this section, to illustrate the valid of theoretical results of this paper, we present corresponding numerical simulations. The backward Euler and linearized finite difference method will be used to discretize the ODEs and PDE in system (3), and the integral will be numerically calculated using Simpson's rule. Furthermore, we focus on the age-infection model with saturation incidence. Let $f(v_I) = v_I/(1+\alpha v_I)$. Following [1]



(a) (b)

Figure 2. The dynamical behavior of free virions $v_I(t)$, where $\alpha = 0$.



(a) (b)

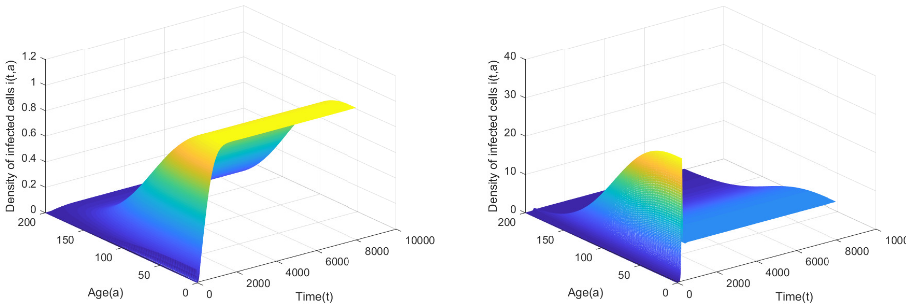
Figure 3. The dynamical behavior of free virions $v_I(t)$, where $\alpha = 0.9$.

and references therein [12, 22], we fix the following coefficients: $\lambda = 10$, $d = 0.09$, $\beta_1 = 0.0025$, $\mu = 2.4$.

Furthermore, we set the maximum age for the viral production as $\hat{a} = 10$ and $\delta(a) = 0.4(1 + \sin((a-5)\pi/10))$, $p(a) = 300(1 + \sin((a-5)\pi/10))$, $0 \leqslant a \leqslant 10$, so that each of the averages is equal to 0.4 and 300, respectively, which were used in [30]. Then we observe the dynamical behavior of solutions as follows when α varies.

We obtain that basic reproduction number $\mathcal{R}_0$ is approximately calculated as 0.8603 and less than one. From Theorem 2 we know that infection-free steady state is locally asymptotically stable. In fact, we can observe in Figs. 2(a) and 3(a) that free virion $v_I(t)$ converges to 0.

In another case, through direct calculation, we get the basic reproduction number $\mathcal{R}_0$, which is near 86.0316 and greater than one. From Theorem 4 we obtain that the positive steady state is locally asymptotically stable. From Figs. 2(b) and 3(b) we find that free virion $v_I(t)$ converges to the positive steady state. From Figs. 4(a) and 4(b) it is easy to



(a) $\alpha = 0$ (b) $\alpha = 0.9$

Figure 4. The dynamical behavior of infected cells $i(t, a)$.

see that the infected cells $i(t, a)$ converges to the positive steady state whether $\alpha = 0$ or $\alpha = 0.9$, just reaching different peak level.

References

1. L. Cai, M. Martcheva, X. Li, Epidemic models with age of infection, indirect transmission and incomplete treatment, *Discrete Contin. Dyn. Syst., Ser. B*, **18**:2239–2265, 2013.
2. R.V. Culshaw, S. Ruan, G. Webb, A mathematical model of cell-to-cell spread of HIV-1 that includes a time delay, *J. Math. Biol.*, **46**:425–444, 2003.
3. J.K. Hale, P. Waltman, Persistence in infnite dimensional systems, *SIAM J. Math. Anal.*, **20**(2):388–395, 1989.
4. A.V. Herz, S. Bonhoeffer, R.M. Anderson, R.M. May, M.A. Nowak, Viral dynamics in vivo: Limitations on estimations on intracellular delay and virus delay, *Proc. Natl. Acad. Sci. USA*, **93**:7247–7251, 1996.
5. G. Huang, X. Liu, Y. Takeuchi, Lyapunov functions and global stability for age-structured HIV infection model, *SIAM J. Appl. Math.*, **72**:25–38, 2012.
6. X. Lai, X. Zou, Modeling HIV-1 virus dynamics with both virus-to-cell infection and cell-to-cell transmission, *SIAM J. Appl. Math.*, **74**:898–917, 2014.
7. X. Lai, X. Zou, Modeling cell-to-cell spread of HIV-1 with logistic target cell growth, *J. Math. Anal. Appl.*, **426**:563–584, 2015.
8. P.D. Leenheer, H.L. Smith, Virus dynamics: A global analysis, *SIAM J. Appl. Math.*, **63**:1313–1327, 2003.
9. F. Li, J. Wang, Analysis of an HIV infection model with logistic target-cell growth and cell-to-cell transmission, *Chaos Solitons Fractals*, **81**:136–145, 2015.
10. M.Y. Li, H. Shu, Global dynamics of an in-host viral model with intracellular delay, *Bull. Math. Biol.*, **72**:1492–1505, 2010.
11. P. Magal, C.C. McCluskey, G. Webb, Lyapunov functional and global asymptotic stability for an infection-age model, *Appl. Anal.*, **89**:1109–1140, 2010.

12. M. Martcheva, X.Z. Li, Competitive exclusion in an infection-age structured model with environmental transmission, *J. Math. Anal. Appl.*, **408**:225–246, 2013.
13. J.E. Mittler, B. Sulzer, A.U. Neumann, A.S. Perelson, Influence of delayed virus production on viral dynamics in HIV-1 infected patients, *Math. Biosci.*, **152**:143–163, 1998.
14. P.W. Nelson, M.A. Gilchrist, D. Coombs, J.M. Hyman, A.S. Perelson, An age structured model of HIV infection that allows for variations in the production rate of viral particles and the death rate of productively infected cells, *Math. Biosci. Eng.*, **1**:267–288, 2004.
15. P.W. Nelson, J. Murray, A.S. Perelson, A model of HIV-1 pathogenesis that includes an intracellular delay, *Math. Biosci.*, **163**:201–215, 2000.
16. A.S. Perelson, P.W. Nelson, Mathematical analysis of HIV-1 dynamics in vivo, *SIAM Rev.*, **41**:3–44, 1999.
17. A.S. Perelson, A.U. Neumann, M. Markowitz, J.M. Leonard, D.D. Ho, HIV-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time, *Science*, **271**:158–286, 1996.
18. L.B. Rong, Z.L. Feng, A.S. Perelson, Mathematical analysis of age-structured HIV-1 dynamics with combination antiretrovial therapy, *SIAM J. Appl. Math.*, **67**:731–756, 2007.
19. J. Wang, M. Guo, X. Liu, et al., Threshold dynamics of HIV-1 virus model with cell-to-cell transmission, cell-mediated immune responses and distributed delay, *Appl. Math. Comput.*, **291**:149–161, 2016.
20. J. Wang, J. Lang, X. Zou, Analysis of a structured HIV infection model with both virus-to-cell infection and cell-to-cell transmission, *Nonlinear Anal., Real World Appl.*, **34**:75–96, 2017.
21. J. Wang, J. Yang, T. Kuniya, Dynamics of a PDE viral infection model incorporating cell-to-cell tranmission, *J. Math. Anal. Appl.*, **444**:1542–1564, 2016.
22. J. Wang, R. Zhang, T. Kuniya, Global dynamics for a class of age-infection HIV models with nonlinear infection rate, *J. Math. Anal. Appl.*, **432**:289–313, 2015.
23. J. Wang, R. Zhang, T. Kuniya, Mathematical analysis for an age-structured HIV infection model with saturation infection rate, *Electron. J. Differ. Equ.*, **33**:1–19, 2015.
24. J. Wang, R. Zhang, T. Kuniya, The dynamics of an svir epidemiological model with infection age, *IMA J. Appl. Math.*, **81**:321–343, 2016.
25. J. Wang, R. Zhang, T. Kuniya, A note on dynamics of an age-of-infection cholera model, *Math. Biosci. Eng.*, **1**:227–247, 2016.
26. Y. Wang, Y. Zhou, Oscillatory viral dynamics in a delayed HIV pathogenesis model, *Math. Biosci.*, **219**:104–112, 2009.
27. J. Xu, Y. Geng, Y. Zhou, Global dynamics for an age-structured HIV virus infection model with cellular infection and antiretroviral therapy, *Appl. Math. Comput.*, **305**:62–83, 2017.
28. Y. Yang, L. Zou, S. Ruan, Global dynamics of a delayed within-host viral infection model with both virus-to-cell and cell-to-cell transmissions, *Math. Biosci.*, **270**:183–191, 2015.
29. T. Zhang, X. Meng, T. Zhang, Global dynamics of a virus dynamical model with cell-to-cell transmission and cure rate, *Comput. Math. Methods Med.*, **10**:45–48, 2015.
30. X. Zhou, J. Cui, Global stability of the viral dynamics with Crowley–Martin functional response, *Bull. Korean Math. Soc.*, **48**:555–574, 2011.