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MATHEMATICAL ANALYSIS OF AN AGE-STRUCTURED VIRAL INFECTION MODEL WITH LATENCY AND GENERAL INCIDENCE RATE

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Abstract. In this paper, we develop an age-structured viral infection model with latency age, infection age and general incidence rate. The developed model is formulated by ordinary and partial differential equations. The well posedness and the existence of equilibria are rigorously investigated. Moreover, the qualitative properties including uniform persistence, local stability of equilibria as well as the global behavior of the model are fully established.

Keywords: viral infection; age-structure; general incidence rate; uniform persistence; stability analysis.

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1. Introduction

The main objective of this paper is to propose and analyze the dynamics of an age-structured viral infection model with latency and general incidence rate. This model is governed by the following nonlinear system:

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$$\begin{cases} \dfrac{\mathrm{d}x(t)}{\mathrm{d}t} = s - dx(t) - f(x(t),v(t))v(t), \\ \dfrac{\partial e(t,a)}{\partial t} + \dfrac{\partial e(t,a)}{\partial a} = -\delta_1(a)e(t,a), \\ \dfrac{\partial i(t,b)}{\partial t} + \dfrac{\partial i(t,b)}{\partial b} = -\delta_2(b)i(t,b), \\ \dfrac{\mathrm{d}v(t)}{\mathrm{d}t} = \displaystyle\int_0^{\infty} k_2(b)i(t,b)\mathrm{d}b - \mu v(t), \end{cases} \tag{1}$$

with boundary conditions

$$\begin{cases} e(t,0) = \eta f(x(t),v(t))v(t), \\ i(t,0) = (1-\eta)f(x(t),v(t))v(t) + \displaystyle\int_0^{\infty} k_1(a)e(t,a)\mathrm{d}a, \end{cases} \tag{2}$$

and initial conditions

$$x(0) = x_0, \quad e(0,a) = e_0(a), \quad i(0,a) = i_0(a), \qquad v(0) = v_0. \tag{3}$$

Here, the state variables $x(t)$, $e(t,a)$, $i(t,b)$ and $v(t)$ are the concentrations of uninfected target cells, latently infected cells of latency age a, productively infected cells of infection age b and free viruses particles at time t, respectively. The biological meanings of the other parameters in the system (1) are listed in Table 1. The general incidence function $f(x,v)$ denotes the average number of cells which are infected by each virus in unit time. It is assumed to be continuously differentiable in the interior of $\mathbb{R}^2_+$ and satisfies the three fundamental hypotheses given in [1] and used in [2, 3, 4], that are:

(H_1): $f(0,v) = 0$, for all $v \geq 0$,

(H_2): $f(x,v)$ is a strictly monotone increasing function with respect to x, for any fixed $v \geq 0$,

(H_3): $f(x,v)$ is a monotone decreasing function with respect to v, i.e, $\dfrac{\partial f(x,v)}{\partial v} \leq 0$ for all $x \geq 0$ and $v \geq 0$.

TABLE 1. Biological meanings of parameters

Parameter	Biological meaning
s	Recruitment rate of uninfected cells
d	Death rate of uninfected cells
$\delta_1(a)$	Death rate of latently infected cells with latency age a
$\delta_2(b)$	Death rate of productively infected cells with infection age b
$k_1(a)$	Activation rate of latently infected cells with latency age a
$k_2(b)$	Viral production rate of productively infected cells with infection age b
μ	Clearance rate of virions
η	Fraction of infected cells lead to latency

Throughout this paper, we consider the following assumptions:

(i): $s, d, \mu > 0$.

(ii): $\delta_1(\cdot), \delta_2(\cdot), k_1(\cdot), k_2(\cdot) \in L^1_+[0,\infty)$ and

$$\bar{\delta}_1 := \operatorname*{ess\,sup}_{a\in[0,\infty)} \delta_1(a) < \infty, \quad \bar{\delta}_2 := \operatorname*{ess\,sup}_{b\in[0,\infty)} \delta_2(b) < \infty,$$

$$\bar{k_2} := \operatorname*{ess\,sup}_{b\in[0,\infty)} k_2(b) < \infty, \quad \bar{k_1} := \operatorname*{ess\,sup}_{a\in[0,\infty)} k_1(a) < \infty.$$

(iii): There exists $m_0 \in (0,d]$, such that $\delta_1(a), \delta_2(b) \geq m_0$ for all $a, b > 0$.

(iv): There exists a maximum age $b^+ > 0$, such that $k_2(b) > 0$ for $b \in [0, b^+]$, and $k_2(b) = 0$ for $b > b^+$.

It is important to note that our model described by system (1) improves and generalizes the recent age-structured model introduced by Wang and Dong [5] in order to model the dynamics of HIV infection with latency and infection age. More precisely, it suffices to take $f(x,v) = \beta x$, where $\beta > 0$ is the infection rate.

The rest of the paper is organized as follows. The next section deals with preliminaries including properties of solutions and existence of equilibria. Section 3 is devoted to uniform persistence. Section 4 establishes the local and global stability of equilibria. Section 5 closes the paper with an application.

2. Preliminaries

In this section, we present some preliminary results. We first study the existence and uniqueness of solutions of problem (1)-(3).

Let

$$\sigma_1(a) = e^{-\int_0^a \delta_1(\omega)\mathrm{d}\omega} \quad \text{and} \quad \sigma_2(b) = e^{-\int_0^b \delta_2(\omega)\mathrm{d}\omega}, \quad \text{for } a,b \in [0,\infty).$$

According to **(iii)** and **(iv)**, one has

$$0 \le \sigma_1(a) \le e^{-m_0 a} \quad \text{and} \quad 0 \le \sigma_2(b) \le e^{-m_0 b}$$

$$\sigma_1'(a) = -\delta_1(a)\sigma_1(a) \quad \text{and} \quad \sigma_2'(b) = -\delta_2(b)\sigma_2(b).$$

Integrating the second and third equations of (1) along the characteristic lines $t-a=$ constant and $t-b=$ constant, respectively, it yields

$$e(t,a) = \begin{cases} \eta f(x(t-a),v(t-a))v(t-a)\sigma_1(a), & \text{if } t > a, \\ e_0(a-t)\dfrac{\sigma_1(a)}{\sigma_1(a-t)}, & \text{if } t \le a, \end{cases} \tag{4}$$

and

$$i(t,b) = \begin{cases} [(1-\eta)f(x(t-b),v(t-b))v(t-b) + M(t-b)]\sigma_2(b), & \text{if } t > b, \\ i_0(b-t)\dfrac{\sigma_2(b)}{\sigma_2(b-t)}, & \text{if } t \le b, \end{cases} \tag{5}$$

where $M(t) = \int_0^\infty k_1(a)e(t,a)\mathrm{d}a$.

Let

$$G_1(t) = x(t) + \int_0^\infty e(t,a)\mathrm{d}a.$$

Then

$$\begin{aligned} \frac{\mathrm{d}G_1(t)}{\mathrm{d}t} &= s - dx(t) - f(x(t)v(t))v(t) + \eta f(x(t),v(t))v(t) - \int_0^\infty \delta_1(a)e(t,a)\mathrm{d}a \\ &\le s - m_0 G_1(t). \end{aligned}$$

Hence, we have

$$\limsup_{t\to+\infty} G_1(t) \le \frac{s}{m_0}.$$

Next, we define

$$G_2(t) = x(t) + \int_0^\infty e(t,a)\mathrm{d}a + \int_0^\infty i(t,b)\mathrm{d}b.$$

Then

$$\begin{aligned}\frac{\mathrm{d}G_2(t)}{\mathrm{d}t} =& s - dx(t) - f(x(t),v(t))v(t) + \eta f(x(t),v(t))v(t) - \int_0^\infty \delta_1(a)e(t,a)\mathrm{d}a \\ &+ (1-\eta)f(x(t),v(t))v(t) + \int_0^\infty k_1(a)e(t,a)\mathrm{d}a - \int_0^\infty \delta_2(b)i(t,b)\mathrm{d}b \\ =& s - dx(t) + \int_0^\infty k_1(a)e(t,a)\mathrm{d}a \\ &- \int_0^\infty \delta_1(a)e(t,a)\mathrm{d}a - \int_0^\infty \delta_2(b)i(t,b)\mathrm{d}b \\ \leq& s + \bar{k_1}\frac{s}{m_0} - m_0 G_2(t).\end{aligned}$$

Thus,

$$\limsup_{t\to+\infty} G_2(t) \leq \frac{s}{m_0} + \frac{s\bar{k_1}}{m_0^2}.$$

From the fourth equation of system (1), we obtain

$$\begin{aligned}\frac{\mathrm{d}v(t)}{\mathrm{d}t} =& \int_0^\infty k_2(b)i(t,b)\mathrm{d}b - \mu v(t) \\ \leq& \bar{k_2}\left(\frac{s}{m_0} + \frac{s\bar{k_1}}{m_0^2}\right) - \mu v(t).\end{aligned}$$

Then

$$\limsup_{t\to+\infty} v(t) \leq \frac{\bar{k_2}}{\mu}\left(\frac{s}{m_0} + \frac{s\bar{k_1}}{m_0^2}\right).$$

Consequently,

$$\begin{aligned}\Omega = \Bigg\{ &(x,e,i,v) \in \mathbb{R}_+ \times L^1_+(0,\infty) \times L^1_+(0,\infty) \times \mathbb{R}_+ : x(t) + \int_0^\infty e(t,a)\mathrm{d}a \\ &+ \int_0^\infty i(t,b)\mathrm{d}b \leq \frac{s}{m_0} + \frac{s\bar{k_1}}{m_0^2}, \quad v(t) \leq \frac{\bar{k_2}}{\mu}\left(\frac{s}{m_0} + \frac{s\bar{k_1}}{m_0^2}\right), \quad \forall t \geq 0 \Bigg\},\end{aligned}$$

is a positively invariant set of system (1).

In the following, we use the approach introduced by Thieme [6] in order to reformulate the system (1) with the boundary and initial conditions as an abstract Cauchy problem. To this end, define

$$\mathscr{X} = \mathbb{R} \times L^1((0,+\infty),\mathbb{R}) \times \mathbb{R} \times L^1((0,+\infty),\mathbb{R}) \times \mathbb{R} \times \mathbb{R},$$

$$\mathscr{X}_0 = \mathbb{R} \times L^1((0,+\infty),\mathbb{R}) \times \{0\} \times L^1((0,+\infty),\mathbb{R}) \times \{0\} \times \mathbb{R},$$

$$\mathscr{X}_+ = \mathbb{R}_+ \times L^1_+((0,+\infty),\mathbb{R}) \times \mathbb{R}_+ \times L^1_+((0,+\infty),\mathbb{R}) \times \mathbb{R}_+ \times \mathbb{R}_+,$$

and

$$\mathscr{X}_{0+} = \mathscr{X}_+ \cap \mathscr{X}_0.$$

Let $A : \text{Dom}(A) \subset \mathscr{X} \to \mathscr{X}$ be the linear operator defined by

$$A \begin{pmatrix} x \\ \begin{pmatrix} e \\ 0 \end{pmatrix} \\ \begin{pmatrix} i \\ 0 \end{pmatrix} \\ v \end{pmatrix} = \begin{pmatrix} -dx \\ \begin{pmatrix} -e' - \delta_1(a)e \\ -e(0) \end{pmatrix} \\ \begin{pmatrix} -i' - \delta_2(b)i \\ -i(0) \end{pmatrix} \\ -\mu v \end{pmatrix},$$

with $\text{Dom}(A) = \mathbb{R} \times W^{1,1}((0,+\infty),\mathbb{R}) \times \{0\} \times W^{1,1}((0,+\infty),\mathbb{R}) \times \{0\} \times \mathbb{R}$, where $W^{1,1}$ is a Sobolev space. Define $F : \mathscr{X}_0 \to \mathscr{X}$

$$F \begin{pmatrix} x \\ \begin{pmatrix} e \\ 0 \end{pmatrix} \\ \begin{pmatrix} i \\ 0 \end{pmatrix} \\ v \end{pmatrix} = \begin{pmatrix} s - f(x,v)v \\ \begin{pmatrix} 0_{L^1} \\ \eta f(x,v)v \end{pmatrix} \\ \begin{pmatrix} 0_{L^1} \\ (1-\eta)f(x,v)v + \int_0^\infty k_1(a)e(t,a)\mathrm{d}a \end{pmatrix} \\ \int_0^\infty k_2(b)i(t,b)db \end{pmatrix},$$

and

$$u(t) = \begin{pmatrix} x(t) \\ \begin{pmatrix} e(t,.) \\ 0 \end{pmatrix} \\ \begin{pmatrix} i(t,.) \\ 0 \end{pmatrix} \\ v(t) \end{pmatrix}.$$

Rewriting system (1), we obtain the following abstract Cauchy problem:

$$\frac{\mathrm{d}u(t)}{\mathrm{d}t} = Au(t) + F(u(t)), \quad \text{for} \quad t \geq 0, \quad \text{with} \quad u(0) \in \mathscr{X}_{0+}. \tag{6}$$

Using the results in [7, 8, 9], we have the following theorem.

Theorem 2.1. *System (6) generates a unique continuous semiflow $\{U(t)\}_{t\geq 0}$ on $\mathscr{X}_{0+}$ that is bounded dissipative and asymptotically smooth. Furthermore, the semiflow $\{U(t)\}_{t\geq 0}$ has a global attractor $\mathscr{A}$ in $\mathscr{X}_{0+}$, which attracts the bounded sets of $\mathscr{X}_{0+}$.*

Next, we investigate the existence of equilibria of our model. Clearly, system (1) has always one disease-free equilibrium of the form $E^0(x^0,0,0,0)$, where $x^0 = \frac{s}{d}$. Let

$$N_1 = \int_0^\infty k_1(a)\sigma_1(a)\mathrm{d}a \text{ and } N_2 = \int_0^\infty k_2(b)\sigma_2(b)\mathrm{d}b.$$

Hence, we define the basic reproduction number of our model as follows

$$\mathscr{R}_0 = \frac{N_2(1-\eta+\eta N_1)f(x^0,0)}{\mu}. \tag{7}$$

For the biological meaning, $\mathscr{R}_0$ denotes the average number of secondary infections produced by one infected cell during the period of infection when all cells are uninfected, and the disease-free equilibrium E^0 represents the extinction of the viruses.

To find the other equilibrium of system (1), we solve the following

$$s - dx - f(x,v)v = 0, \tag{8}$$

$$\frac{de(a)}{da} = -\delta_1(a)e(a), \tag{9}$$

$$\frac{di(a)}{da} = -\delta_2(a)i(a), \tag{10}$$

$$\int_0^\infty k_2(a)i(a)da - \mu v = 0, \tag{11}$$

$$e(0) = \eta f(x,v)v, \tag{12}$$

$$i(0) = (1-\eta)f(x,v)v + \int_0^\infty k_1(a)e(a)\mathrm{d}a. \tag{13}$$

By (9), (10), (12) and (13), we get

$$e(a) = \eta f(x,v)v\sigma_1(a), \quad i(b) = (1-\eta+\eta N_1)f(x,v)v\sigma_2(b). \tag{14}$$

From (11) and (14), we have

$$(1-\eta+\eta N_1)f(x,v)N_2 = \mu. \tag{15}$$

By (8) and (15), we deduce that

$$v = \frac{N_2(s-dx)(1-\eta+\eta N_1)}{\mu}. \tag{16}$$

Substituting (16) into (15) yields

$$N_2(1-\eta+\eta N_1) f\left(x, \frac{N_2(s-dx)(1-\eta+\eta N_1)}{\mu}\right) = \mu. \tag{17}$$

Since $v = \dfrac{N_2(s-dx)(1-\eta+\eta N_1)}{\mu} \geq 0$, we have $x \leq x^0$. Thus, system (1) has no biological equilibrium if $x > x^0$. Define a function g on the interval $[0, x^0]$ by

$$g(x) \;=\; N_2(1-\eta+\eta N_1) f\left(x, \frac{N_2(s-dx)(1-\eta+\eta N_1)}{\mu}\right) - \mu.$$

We have $g(0) = -\mu < 0$, $g(x^0) = \mu(\mathscr{R}_0 - 1)$ and

$$g'(x) = N_2(1-\eta+\eta N_1)\left(\frac{\partial f}{\partial x} - \frac{dN_2(1-\eta+\eta N_1)}{\mu}\frac{\partial f}{\partial v}\right) > 0.$$

Hence for $\mathscr{R}_0 > 1$, the equation $g(x) = 0$ has a unique solution $x^* \in (0, x^0)$. Then system (1) admits a unique infection equilibrium $E^*(x^*, e^*(a), i^*(b), v^*)$ called the chronic infection equilibrium, where $x^* \in (0, x^0)$, $e^*(a) = \eta f(x^*, v^*) v^* \sigma_1(a)$, $i(b) = (1-\eta+\eta N_1) f(x^*, v^*) v^* \sigma_2(b)$ and $v^* = \dfrac{N_2(s-dx^*)(1-\eta+\eta N_1)}{\mu}$.

In summary, we get the following result.

Theorem 2.2. *Let $\mathscr{R}_0$ be defined by Eq. (7).*

- **(i):** *If $\mathscr{R}_0 \leq 1$, then the system (1) has a unique infection-free equilibrium of the form $E^0(x^0, 0, 0, 0)$, where $x^0 = \dfrac{s}{d}$.*
- **(ii):** *If $\mathscr{R}_0 > 1$, the infection-free equilibrium E^* is still present and the system (1) has a unique chronic infection equilibrium of the form $E^*(x^*, e^*(a), i^*(b), v^*)$ with $x^* \in (0, x^0)$, $v^* = \dfrac{N_2(s-dx^*)(1-\eta+\eta N_1)}{\mu}$, $e^*(a) = \eta f(x^*, v^*) v^* \sigma_1(a)$ and $i^*(b) = (1-\eta+\eta N_1) f(x^*, v^*) v^* \sigma_2(b)$.*

3. UNIFORM PERSISTENCE

This section investigates the uniform persistence of system (1). Let

$$\hat{\mathscr{M}} = \left\{ \begin{pmatrix} x \\ \begin{pmatrix} e \\ 0 \end{pmatrix} \\ \begin{pmatrix} i \\ 0 \end{pmatrix} \\ v \end{pmatrix} \in \mathscr{X}_{0+} : \int_0^{\bar{a}} e(a)da + \int_0^{\bar{b}} i(b)db + v > 0 \right\},$$

and $\partial\hat{\mathscr{M}} = \mathscr{X}_{0+} \setminus \hat{\mathscr{M}}$, where

$$\bar{b} = \inf\left\{ b : \int_b^{\infty} k_1(\theta)d\theta = 0 \right\} \text{ and } \bar{a} = \inf\left\{ a : \int_a^{\infty} k_2(\theta)d\theta = 0 \right\}.$$

Theorem 3.1. *$\partial\hat{\mathscr{M}}$ is positively invariant under the semiflow $\{U(t)\}_{t\geq 0}$ generated by system (6) on $\mathscr{X}_{0+}$. Moreover, the equilibrium* $E^0 \begin{pmatrix} x^0 \\ \begin{pmatrix} 0_{L^1} \\ 0 \end{pmatrix} \\ \begin{pmatrix} 0_{L^1} \\ 0 \end{pmatrix} \\ 0 \end{pmatrix}$ *is globally asymptotically stable for the semiflow $\{U(t)\}_{t\geq 0}$ restricted to $\partial\hat{\mathscr{M}}$.*

Proof. Let $\begin{pmatrix} x_0 \\ \begin{pmatrix} e_0(.) \\ 0 \end{pmatrix} \\ \begin{pmatrix} i_0(.) \\ 0 \end{pmatrix} \\ v_0 \end{pmatrix} \in \partial\hat{\mathscr{M}}$, we have

$$\begin{cases} \dfrac{\partial e(t,a)}{\partial t}+\dfrac{\partial e(t,a)}{\partial a}=-\delta_1(a)e(t,a),\\ \dfrac{\partial i(t,b)}{\partial t}+\dfrac{\partial i(t,b)}{\partial b}=-\delta_2(b)i(t,b),\\ \dfrac{\mathrm{d}v(t)}{\mathrm{d}t}=\displaystyle\int_0^\infty k_2(a)i(t,a)da-\mu v(t),\\ e(t,0)=\eta f(x(t),v(t))v(t),\\ i(t,0)=(1-\eta)f(x(t),v(t))v(t)+\displaystyle\int_0^\infty k_1(a)e(t,a)\mathrm{d}a,\\ e(0,a)=e_0(a),\quad i(0,b)=i_0(b),\quad v(0)=0. \end{cases}$$

Since $x(t)\le x^0$ for large enough time t, it follows that

$$e(t,a)\le\hat{e}(t,a),\quad i(t,b)\le\hat{i}(t,b)\quad\text{and}\quad v(t)\le\hat{v}(t), \tag{18}$$

where

$$\begin{cases} \dfrac{\partial \hat{e}(t,a)}{\partial t}+\dfrac{\partial \hat{e}(t,a)}{\partial a}=-\delta_1(a)\hat{e}(t,a),\\ \dfrac{\partial \hat{i}(t,b)}{\partial t}+\dfrac{\partial \hat{i}(t,b)}{\partial b}=-\delta_2(b)\hat{i}(t,b),\\ \dfrac{\mathrm{d}\hat{v}(t)}{\mathrm{d}t}=\displaystyle\int_0^\infty k_2(a)\hat{i}(t,a)da-\mu \hat{v}(t),\\ \hat{e}(t,0)=\eta f(x^0,0)\hat{v}(t),\\ \hat{i}(t,0)=(1-\eta)f(x^0,0)\hat{v}(t)+\displaystyle\int_0^\infty k_1(a)\hat{e}(t,a)\mathrm{d}a,\\ \hat{e}(0,a)=e_0(a),\quad \hat{i}(0,b)=i_0(b),\quad \hat{v}(0)=0. \end{cases} \tag{19}$$

This yields that

$$\hat{e}(t,a)=\begin{cases} \eta f(x^0,0)\hat{v}(t-a)\sigma_1(a), & 0\le a\le t\\ e_0(a-t)\dfrac{\sigma_1(a)}{\sigma_1(a-t)}, & 0<t\le a \end{cases} \tag{20}$$

end

$$\hat{i}(t,b)=\begin{cases} [(1-\eta)f(x^0,0)\hat{v}(t-b)+\hat{M}(t-b)]\sigma_2(b), & 0\le b\le t\\ i_0(b-t)\dfrac{\sigma_2(b)}{\sigma_2(b-t)}, & 0<t\le b \end{cases} \tag{21}$$

where

$$\hat{M}(t-b)=\eta f(x^0,0)\int_0^{t-b}k_1(a)\hat{v}(t-b-a)\sigma_1(a)\mathrm{d}a+\int_{t-b}^{\infty}k_1(a)\hat{e}_0(a-t+b)\frac{\sigma_1(a)}{\sigma_1(a-t+b)}\mathrm{d}a.$$

From the third equation of (19) and Eqs. (20), (21), we have

$$(22)\qquad \begin{cases} \dfrac{\mathrm{d}\hat{v}(t)}{\mathrm{d}t}=(1-\eta)f(x^0,0)\displaystyle\int_0^t k_2(b)\hat{v}(t-b)\sigma_2(b)db+F_v(t)-\mu\hat{v}(t)\\ \qquad +\eta f(x^0,0)\displaystyle\int_0^t k_2(b)\int_0^{t-b}k_1(a)\hat{v}(t-b-a)\sigma_1(a)\mathrm{d}a\sigma_2(b)\mathrm{d}b\\ \qquad +\displaystyle\int_0^t k_2(b)\int_{t-b}^{\infty}k_1(a)\hat{e}_0(a-t+b)\frac{\sigma_1(a)}{\sigma_1(a-t+b)}\mathrm{d}a\sigma_2(b)\mathrm{d}b,\\ \hat{v}(0)=0, \end{cases}$$

where

$$F_v(t)=\int_t^{+\infty}k(a)i_0(a-t)\frac{\sigma(a)}{\sigma(a-t)}da.$$

According to $\big(k_1(a),k_2(a)\big)\in\big(L^\infty_+((0,+\infty),\mathbb{R})\setminus\{0_{L^\infty}\}\big)^2$, we can obtain that $F_v(t)\equiv 0$ and $\int_{t-b}^{\infty}k_1(a)\hat{e}_0(a-t+b)\frac{\sigma_1(a)}{\sigma_1(a-t+b)}\mathrm{d}a\equiv 0$ for all $t\geq 0$. Then system (22) has a unique solution $\hat{v}(t)=0$. It follows from (20) and (21) that $\big(\hat{e}(t,a),\hat{i}(t,a)\big)=\big(0,0\big)$ for $t>a$. For $t\leq a$,, we get

$$\|\hat{e}(t,a)\|_{L^1}=\left\|e_0(a-t)\frac{\sigma_1(a)}{\sigma_1(a-t)}\right\|_{L^1}\leq e^{-m_0t}\|e_0\|_{L^1},$$

and

$$\|\hat{i}(t,a)\|_{L^1}=\left\|i_0(a-t)\frac{\sigma_2(a)}{\sigma_2(a-t)}\right\|_{L^1}\leq e^{-m_0t}\|i_0\|_{L^1},$$

which means that $\big(\hat{e}(t,a),\hat{i}(t,a)\big)\to(0,0)$ as $t\to\infty$. From (18), we know that $\big(e(t,a),i(t,a)\big)\to(0,0)$ and $v(t)=0$ as $t\to\infty$. Thus, we can show that $x(t)\to x^0$ as $t\to\infty$ from the first equation of system (1). □

Next, we use the method of Magal et al. [10] in order to prove the following result of the uniform persistence.

Theorem 3.2. *Suppose that $\mathscr{R}_0>1$, the semiflow $\{U(t)\}_{t\geq 0}$ generated by system (6) is uniformly persistent with respect to the pair $(\partial\hat{\mathscr{M}},\hat{\mathscr{M}})$, that is, there exists $\varepsilon>0$ such that for each $y\in\hat{\mathscr{M}}$,*

$$\liminf_{t\to+\infty}d(U(t)y,\partial\hat{\mathscr{M}})\geq\varepsilon.$$

Furthermore, the semiflow $\{U(t)\}_{t\geq 0}$ has a compact global attractor $\mathscr{A}_0\subset\tilde{\mathscr{M}}$.

Proof. Since the equilibrium $E^0\begin{pmatrix} x^0 \\ \begin{pmatrix} 0_{L^1} \\ 0 \end{pmatrix} \\ \begin{pmatrix} 0_{L^1} \\ 0 \end{pmatrix} \\ 0 \end{pmatrix}$ is globally asymptotically stable in $\partial\hat{\mathscr{M}}$, by Theorem 4.2 in [11], we only need to show

$$W^s(E^0)\cap\hat{\mathscr{M}}=\emptyset,$$

where

$$W^s(E^0)=\left\{y\in\ \mathscr{X}_{0+}:\lim_{t\to+\infty}U(t)y=E^0\right\}.$$

Assume by contradiction that for each $n\geq 0$, there exists

$$y_n=\begin{pmatrix} x_0^n \\ \begin{pmatrix} e_0^n \\ 0 \end{pmatrix} \\ \begin{pmatrix} i_0^n \\ 0 \end{pmatrix} \\ v_0^n \end{pmatrix}\in\left\{y\in\hat{\mathscr{M}}:\|E^0-y\|\leq\frac{1}{n}\right\}$$

such that

$$\|E^0-U(t)y_n\|\leq\frac{1}{n},\quad \forall t\geq 0.$$

Let

$$\begin{pmatrix} x^n(t) \\ \begin{pmatrix} e^n(t,.) \\ 0 \end{pmatrix} \\ \begin{pmatrix} i^n(t,.) \\ 0 \end{pmatrix} \\ v^n(t) \end{pmatrix}=U(t)y_n.$$

Then, we can get

$$\|x^n(t)-x^0\|\le\frac{1}{n},\quad \|v^n(t)-0\|\le\frac{1}{n}.$$

This implies that $x^0-\frac{1}{n}>0$ for large enough $n>0$. For the given n, there exists $\hat{t}>0$ such that for all $t\ge\hat{t}$, we get

$$x^0-\frac{1}{n}<x^n(t)<x^0+\frac{1}{n},\quad 0\le v^n(t)\le\frac{1}{n}.$$

Applying comparison principle and

$$\begin{aligned}e^n(t,a)&\ge\eta f(x^n(t-a),v^n(t-a))v^n(t-a)\sigma_1(a),\\&\ge\eta f\left(x^0-\frac{1}{n},\frac{1}{n}\right)v^n(t-a)\sigma_1(a),\end{aligned}$$

and

$$\begin{aligned}i^n(t,b)&\ge\left[(1-\eta)f(x^n(t-b),v^n(t-b))v^n(t-b)+M(t-b)\right]\sigma_2(b),\\&\ge(1-\eta)f\left(x^0-\frac{1}{n},\frac{1}{n}\right)v^n(t-b)\sigma_2(b)\\&\quad+\eta f\left(x^0-\frac{1}{n},\frac{1}{n}\right)\int_0^\infty k_1(a)\sigma_1(a)v^n(t-b-a)da\sigma_2(b),\end{aligned}$$

we obtain

$$\hat{v}^n(t)\le v^n(t),$$

where $\hat{v}^n(t)$ is a solution of the following system

$$\begin{cases}\dfrac{\mathrm{d}\hat{v}^n(t)}{\mathrm{d}t}=(1-\eta)f\left(x^0-\frac{1}{n},\frac{1}{n}\right)\displaystyle\int_0^\infty k_2(b)\sigma_2(b)\hat{v}^n(t-b)\mathrm{d}b\\ \qquad+\eta f\left(x^0-\frac{1}{n},\frac{1}{n}\right)\displaystyle\int_0^\infty k_2(b)\sigma_2(b)\int_0^\infty k_1(b)\sigma_1(b)\hat{v}^n(t-b-a)\mathrm{d}a\mathrm{d}b\\ \qquad-\mu\hat{v}^n(t),\\ \hat{v}^n(0)=v^n(0)\ge0.\end{cases}$$

When $\hat{v}^n(0)=0$, we have $\hat{v}^n(t)>0$. Thus, without loss of generality, we take $\hat{v}^n(0)>0$. If $\mathscr{R}_0>1$, then we can choose the large enough n such that

$$N_2(1-\eta+\eta N_1)f\left(x^0-\frac{1}{n},\frac{1}{n}\right)>\mu.$$

From Lemma 3.5 of Browne and Pilyugin [12], we conclude that $\hat{v}^n(t)$ is unbounded. Since $\hat{v}^n(t)\le v^n(t)$, we obtain that $v^n(t)$ is unbounded. This is a contradiction with the boundedness of $v^n(t)$. Hence, $W^s(E^0) \cap \hat{\mathscr{M}} = \emptyset$. By the results of [13], we show that $\{U(t)\}_{t\geq 0}$ is uniformly persistent and there exists a compact set $\mathscr{A}_0 \subset \hat{\mathscr{M}}$ which is a global attractor for $\{U(t)\}_{t\geq 0}$. $\square$

4. Stability Analysis

In this section, we study the local and global stability of equilibria of system (1).

4.1. Local stability.

Theorem 4.1. *The infection-free steady state E^0 is locally asymptotically stable if $\mathscr{R}_0 < 1$ and it is unstable if $\mathscr{R}_0 > 1$.*

Proof. Linearizing system (1) about E^0 and defining the perturbation variables

$$x_1(t) = x(t) - \frac{s}{d}, \qquad i_1(t,a) = i(t,a), \qquad v_1(t) = v(t), \qquad w_1(t) = w(t),$$

we obtain

$$\left\{\begin{array}{l} \dfrac{\mathrm{d}x_1(t)}{\mathrm{d}t} = -dx_1(t) - f(x^0,0)v_1(t), \\ \dfrac{\partial e_1(t,a)}{\partial t} + \dfrac{\partial e_1(t,a)}{\partial a} = -\delta_1(a)e_1(t,a), \\ \dfrac{\partial i_1(t,b)}{\partial t} + \dfrac{\partial i_1(t,b)}{\partial a} = -\delta(b)i_1(t,b), \\ \dfrac{\mathrm{d}v_1(t)}{\mathrm{d}t} = \displaystyle\int_0^\infty k_2(b)i_1(t,b)\mathrm{d}a - \mu v_1(t), \end{array}\right. \tag{23}$$

and

$$\left\{\begin{array}{l} e_1(t,0) = \eta f(x^0,0)v_1(t), \\ i_1(t,0) = (1-\eta)f(x^0,0)v_1(t) + \displaystyle\int_0^\infty k_1(a)e_1(t,a)\mathrm{d}a. \end{array}\right. \tag{24}$$

Look for non-trivial solutions of (23) and (24) of the form

$$x_1(t) = c_1 e^{\lambda t}, \quad e_1(t,a) = e_1^0(a)e^{\lambda t}, \quad i_1(t,b) = i_1^0(b)e^{\lambda t}, \quad v_1(t) = c_2 e^{\lambda t}. \tag{25}$$

Substituting (25) into (23) and (24), it follows that

$$\begin{cases} (\lambda+d)c_1 = -f(x^0,0)c_2, \\ \dfrac{\partial e_1^0(a)}{\partial a} = -(\lambda+\delta_1(a))e_1^0(a), \\ \dfrac{\partial i_1^0(b)}{\partial b} = -(\lambda+\delta_2(b))i_1^0(b), \\ (\lambda+\mu)c_2 = \int_0^\infty k_2(b)i_1^0(b)\mathrm{d}b, \\ e_1^0(0) = \eta f(x^0,0)c_2, \\ i_1^0(0) = (1-\eta)f(x^0,0)c_2 + \int_0^\infty k_1(a)e_1^0(a)\mathrm{d}a. \end{cases} \tag{26}$$

Integrating the second and third equation of (26) yields

$$e_1^0(a) = e_1^0(0)e^{-\int_0^a(\lambda+\delta_1(\theta))d\theta}, \quad i_1^0(b) = i_1^0(0)e^{-\int_0^b(\lambda+\delta_2(\theta))d\theta}. \tag{27}$$

We derive from the fifth and sixth equation of (26) and (27) that

$$\begin{cases} e_1^0(a) = \eta f(x^0,0)c_2 e^{-\int_0^a(\lambda+\delta_1(\theta))d\theta}, \\ i_1^0(b) = f(x^0,0)c_2\big[1-\eta+\eta N_1(\lambda)\big]e^{-\int_0^b(\lambda+\delta_2(\theta))d\theta}. \end{cases} \tag{28}$$

Substituting $e_1^0(a)$ and $i_1^0(b)$ into the fourth equation of (26), we obtain the characteristic equation

$$\left(\frac{\lambda+\mu}{\mu}\cdot\frac{N_2}{N_2(\lambda)}\cdot\frac{1-\eta+\eta N_1}{1-\eta+\eta N_1(\lambda)} - \mathscr{R}_0\right) = 0, \tag{29}$$

where

$$N_1(\lambda) = \int_0^\infty k_1(a)\sigma_1(a)e^{-\lambda a}\mathrm{d}a \text{ and } N_2(\lambda) = \int_0^\infty k_2(a)\sigma_2(a)e^{-\lambda a}\mathrm{d}a.$$

We claim that if $\mathscr{R}_0 < 1$, all roots of equation (29) have negative real parts. Otherwise, equation (29) has at least one root satisfying $Re(\lambda) > 0$, in this case

$$\begin{aligned} \mathscr{R}_0 &= \left|\frac{\lambda+\mu}{\mu}\frac{N_2}{N_2(\lambda)}\frac{1-\eta+\eta N_1}{1-\eta+\eta N_1(\lambda)}\right| \\ &= \left|\frac{\lambda+\mu}{\mu}\right|\left|\frac{N_2}{N_2(\lambda)}\right|\left|\frac{1-\eta+\eta N_1}{1-\eta+\eta N_1(\lambda)}\right| \\ &> 1. \end{aligned}$$

It condradicts with $\mathscr{R}_0 < 1$. Therefore, all roots of equation (29) have negative real parts. Therefore, E^0 is locally asymptotically stable if $\mathscr{R}_0 < 1$ and it is unstable if $\mathscr{R}_0 > 1$. □

Next, we investigate the local and global stability of the chronic infection equilibrium E^* by assuming that $\mathscr{R}_0 > 1$ and the incidence function f satisfies the following hypothesis

(H_4): $f(x,v) + v\dfrac{\partial f(x,v)}{\partial v} \geq 0$, for all $x \geq 0$ and $v \geq 0$.

Theorem 4.2. *Assume $\mathscr{R}_0 > 1$ and (H_4) holds, then the chronic infection equilibrium E^* is locally asymptotically stable.*

Proof. Linearizing system (1) about E^* and defining the perturbation variables

$$x_2(t) = x(t) - x^*, \quad i_2(t,a) = i(t,a) - i^*(a), \quad v_2(t) = v(t) - v^*, \quad w_2(t) = w(t) - w^*,$$

we obtain

$$\left\{\begin{array}{l} \dfrac{dx_2(t)}{dt} = -\left(d + v^*\dfrac{\partial f(x^*,v^*)}{\partial x}\right)x_2(t) - \left(v^*\dfrac{\partial f(x^*,v^*)}{\partial v} + f(x^*,v^*)\right)v_2(t), \\ \dfrac{\partial e_2(t,a)}{\partial t} + \dfrac{\partial e_2(t,a)}{\partial a} = -\delta_1(a)e_2(t,a), \\ \dfrac{\partial i_2(t,b)}{\partial t} + \dfrac{\partial i_2(t,b)}{\partial b} = -\delta_2(b)i_2(t,b), \\ \dfrac{dv_2(t)}{dt} = \displaystyle\int_0^\infty k_2(b)i_2(t,b)db - \mu v_2(t), \end{array}\right. \tag{30}$$

and

$$\left\{\begin{array}{l} e_2(t,0) = \eta v^*\dfrac{\partial f(x^*,v^*)}{\partial x}x_2(t) + \eta\left(v^*\dfrac{\partial f(x^*,v^*)}{\partial v} + f(x^*,v^*)\right)v_2(t), \\ i_1(t,0) = (1-\eta)v^*\dfrac{\partial f(x^*,v^*)}{\partial x}x_2(t) + (1-\eta)\left(v^*\dfrac{\partial f(x^*,v^*)}{\partial v} + f(x^*,v^*)\right)v_2(t) \\ \qquad\qquad \displaystyle\int_0^\infty k_1(a)e_2(t,a)\mathrm{d}a. \end{array}\right. \tag{31}$$

Look for non-trivial solutions of (30) and (31) of the form

$$x_2(t) = c_1e^{\lambda t}, \quad e_2(t,a) = e_2^0(a)e^{\lambda t}, \quad i_2(t,b) = i_2^0(b)e^{\lambda t}, \quad v_2(t) = c_2e^{\lambda t}. \tag{32}$$

By using a similar method to the proof of Theorem 4.1, we obtain the characteristic equation

(33)
$$\frac{\lambda+\mu}{\mu} - \left(\frac{\lambda+d}{\lambda+d+v^*\frac{\partial f(x^*,v^*)}{\partial x}}\right)\left(\frac{N_2(\lambda)\big(1-\eta+\eta N_1(\lambda)\big)}{N_2\big(1-\eta+\eta N_1\big)}\right)\left(\frac{f(x^*,v^*)+v^*\frac{\partial f(x^*,v^*)}{\partial v}}{f(x^*,v^*)}\right) = 0,$$

where

$$N_1(\lambda)=\int_0^\infty k_1(a)\sigma_1(a)e^{-\lambda a}\mathrm{d}a \text{ and } N_2(\lambda)=\int_0^\infty k_2(a)\sigma_2(a)e^{-\lambda a}\mathrm{d}a.$$

If $Re(\lambda)\geq 0$, then we obtain

$$\left|\frac{\lambda+\mu}{\mu}\right|\geq 1,$$

$$\left|\left(\frac{\lambda+d}{\lambda+d+v_1^*\frac{\partial f(x_1^*,v_1^*)}{\partial x}}\right)\left(\frac{N_2(\lambda)\big(1-\eta+\eta N_1(\lambda)\big)}{N_2\big(1-\eta+\eta N_1\big)}\right)\left(\frac{f(x_1^*,v_1^*)+v_1^*\frac{\partial f(x_1^*,v_1^*)}{\partial v}}{f(x_1^*,v_1^*)}\right)\right|$$

$$=\left|\frac{\lambda+d}{\lambda+d+v_1^*\frac{\partial f(x_1^*,v_1^*)}{\partial x}}\right|\left|\frac{N_2(\lambda)\big(1-\eta+\eta N_1(\lambda)\big)}{N_2\big(1-\eta+\eta N_1\big)}\right|\left|\frac{f(x_1^*,v_1^*)+v_1^*\frac{\partial f(x_1^*,v_1^*)}{\partial v}}{f(x_1^*,v_1^*)}\right|<1,$$

which is a contradiction to (33). This implies that the chronic infection equilibrium E^* is locally asymptotically stable. □

4.2. Global stability.

Theorem 4.3. *The infection-free equilibrium E^0 of system (1) is globally asymptotically stable if $\mathscr{R}_0\leq 1$.*

Proof. Considering Lyapunov functional

$$\begin{aligned}L_0(t) &= x(t)-x^0-\int_{x^0}^{x(t)}\frac{f(x^0,0)}{f(\theta,0)}\mathrm{d}\theta+\frac{N_2 f(x^0,0)}{\mu}\int_0^\infty\alpha_1(a)e(t,a)\mathrm{d}a\\ &+ \frac{f(x^0,0)}{\mu}\int_0^\infty\alpha_2(b)i(t,b)\mathrm{d}b+\frac{f(x^0,0)}{\mu}v(t)\end{aligned}$$

where

$$\alpha_1(a)=\int_a^\infty k_1(\theta)e^{-\int_a^\theta\delta_1(\xi)\mathrm{d}\xi}\mathrm{d}\theta \text{ and } \alpha_2(b)=\int_b^\infty k_2(\theta)e^{-\int_b^\theta\delta_2(\xi)\mathrm{d}\xi}\mathrm{d}\theta,$$

Note that $\alpha_1(0)=N_1$ and $\alpha_2(0)=N_2$. Further, $\alpha_1(a)$ and $\alpha_2(a)$ is bounded and its derivative satisfies

$$\alpha_1^{'}(a)=\delta_1(a)\alpha_1(a)-k_1(a) \text{ and } \alpha_2^{'}(a)=\delta_2(a)\alpha_2(a)-k_2(a).$$

Calculating the time derivative of $L_0(t)$ along the solution of system (1)

$$\begin{aligned}
\frac{\mathrm{d}L_0(t)}{\mathrm{d}t} &= \left(1-\frac{f(x^0,0)}{f(x,0)}\right)\frac{dx(t)}{dt}+\frac{N_2 f(x^0,0)}{\mu}\int_0^\infty \alpha_1(a)\frac{\partial e(t,a)}{\partial t}\mathrm{d}a \\
&+ \frac{f(x^0,0)}{\mu}\int_0^\infty \alpha_2(b)\frac{\partial i(t,b)}{\partial t}\mathrm{d}b+\frac{f(x^0,0)}{\mu}\frac{\mathrm{d}v(t)}{\mathrm{d}t} \\
&= \left(1-\frac{f(x^0,0)}{f(x,0)}\right)\big(s-dx-f(x,v)v\big) \\
&- \frac{N_2 f(x^0,0)}{\mu}\int_0^\infty \alpha_1(a)\left(\frac{\partial e(t,a)}{\partial a}+e(t,a)\right)\mathrm{d}a \\
&- \frac{f(x^0,0)}{\mu}\int_0^\infty \alpha_2(a)\left(\frac{\partial i(t,b)}{\partial b}+i(t,b)\right)\mathrm{d}b \\
&+ \frac{f(x^0,0)}{\mu}\int_0^\infty k_2(b)i(t,b)\mathrm{d}b-f(x^0,0)v.
\end{aligned}$$

Using integration by parts and $s=dx^0$, we get

$$\begin{aligned}
\frac{\mathrm{d}L_0(t)}{\mathrm{d}t} &= dx^0\left(1-\frac{x}{x^0}\right)\left(1-\frac{f(x^0,0)}{f(x,0)}\right)+f(x,v)v\big(\mathscr{R}_0-1\big) \\
&+ f(x^0,0)v\left(\frac{f(x,v)}{f(x,0)}-1\right).
\end{aligned}$$

Since the function $f(x,v)$ is strictly monotonically increasing with respect to x and decreasing function with respect to v , we have

$$\left(1-\frac{x}{x^0}\right)\left(1-\frac{f(x^0,0)}{f(x,0)}\right)\leq 0 \text{ and } \frac{f(x,v)}{f(x,0)}-1\leq 0.$$

Therefore, $\dfrac{\mathrm{d}V(t)}{\mathrm{d}t}\leq 0$ for $\mathscr{R}_0\leq 1$. Further, it is easy to show that the largest invariant set where $\dfrac{\mathrm{d}L_0(t)}{\mathrm{d}t}=0$ is the singleton $\{E^0\}$. By the Lyapunov-LaSalle asymptotic stability theorem, the disease-free equilibrium E^0 is globally asymptotically stable for $\mathscr{R}_0\leq 1$. □

Theorem 4.4. *Assume $\mathscr{R}_0>1$ and (H_4) holds, then the chronic infection equilibrium E^* is globally asymptotically stable.*

Proof. From Theorem 3.2, let $u(t)=\left\{\big(x(t),e(t,a),i(t,b),0,v(t)\big)^T\right\}_{t\in\mathbb{R}}\subset\mathscr{A}_0$ be a given entire solution of $U(t)$. It remains to prove that $\mathscr{A}_0=\{u^*\}$. Similar to the proof of Lemma 3.6 and Claim 5.3 in [14], we know that there exist $\Delta_1>0$ and $\Delta_2>0$ such that

$$\Delta_1\leq x(t)\leq\Delta_2,\quad \Delta_1\leq e(t,a)\leq\Delta_2,\quad \Delta_1\leq i(t,b)\leq\Delta_2,\quad \Delta_1\leq v(t)\leq\Delta_2,$$

for all $t \in \mathbb{R}$ and $a, b \geq 0$. Now, we consider the following Lyapunov functional

$$\begin{aligned} L_1(t) &= x(t) - x^* - \int_{x^*}^{x(t)} \frac{f(x^*,v^*)}{f(\theta,v^*)} \mathrm{d}\theta + \frac{N_2 f(x^*,v^*)}{\mu} \int_0^\infty \alpha_1(a) e^*(a) \phi\left(\frac{e(t,a)}{e^*(a)}\right) \mathrm{d}a \\ &\quad + \frac{f(x^*,v^*)}{\mu} \int_0^\infty \alpha_2(b) i^*(b) \phi\left(\frac{i(t,b)}{i^*(b)}\right) \mathrm{d}b + \frac{f(x^*,v^*)}{\mu} v^* \phi\left(\frac{v(t)}{v^*}\right), \end{aligned}$$

where $\phi(x) = x - 1 - \ln x$, $x \in \mathbb{R}^+$. Obviously, $\phi : \mathbb{R}^+ \to \mathbb{R}^+$ attains its strict global minimum at $x = 1$ and $\phi(1) = 0$. Calculating the time derivative of $L_1(t)$ along the solution of system (1), we have

$$\begin{aligned} \frac{dL_1(t)}{dt} &= \left(1 - \frac{f(x^*,v^*)}{f(x,v^*)}\right)\Big(s - dx - f(x,v)v\Big) \\ &\quad - \frac{N_2 f(x^*,v^*)}{\mu} \int_0^\infty \alpha_1(a)\left(1 - \frac{e^*(a)}{e(t,a)}\right)\left(\frac{\partial e(t,a)}{\partial a} + \delta_1(a) e(t,a)\right) \mathrm{d}a \\ &\quad - \frac{f(x^*,v^*)}{\mu} \int_0^\infty \alpha_2(b)\left(1 - \frac{i^*(b)}{i(t,b)}\right)\left(\frac{\partial i(t,b)}{\partial b} + \delta_2(b) i(t,b)\right) \mathrm{d}b \\ &\quad + \frac{f(x^*,v^*)}{\mu}\left(1 - \frac{v^*}{v}\right)\left(\int_0^\infty k(a) i(t,a) \mathrm{d}a - \mu v\right). \end{aligned}$$

Further, we have

$$\begin{aligned} \frac{dL_1(t)}{dt} &= dx^*\left(1 - \frac{x}{x^*}\right)\left(1 - \frac{f(x^*,v^*)}{f(x,v^*)}\right) - f(x,v)v \\ &\quad + f(x^*,v^*)v^*\left(1 - \frac{f(x^*,v^*)}{f(x,v^*)} + \frac{v}{v^*}\frac{f(x,v)}{f(x,v^*)}\right) \\ &\quad + \frac{N_1 N_2 f(x^*,v^*)}{\mu} e^*(0) \phi\left(\frac{e(t,0)}{e^*(0)}\right) \\ &\quad - \frac{N_2 f(x^*,v^*)}{\mu} \int_0^\infty k_1(a) e^*(a) \phi\left(\frac{e(t,a)}{e^*(a)}\right) \mathrm{d}a \\ &\quad + \frac{N_2 f(x^*,v^*)}{\mu} i^*(0) \phi\left(\frac{i(t,0)}{i^*(0)}\right) \\ &\quad - \frac{f(x^*,v^*)}{\mu} \int_0^\infty k_2(b) i^*(b) \phi\left(\frac{i(t,b)}{i^*(b)}\right) \mathrm{d}b \\ &\quad + \frac{f(x^*,v^*)}{\mu} \int_0^\infty k_2(b) i(t,b) \mathrm{d}b - \frac{f(x^*,v^*)v^*}{\mu v} \int_0^\infty k_2(b) i(t,b) \mathrm{d}b \\ &\quad + f(x^*,v^*)v^* - f(x^*,v^*)v. \end{aligned}$$

Recall that

$$i^*(0)-i(0,t)=(1-\eta)\big(f(x^*,v^*)v^*-f(x,v)v\big)+\int_0^{\infty}\big(e^*(a)-e(t,a)\big)\mathrm{d}a$$

and

$$\frac{\eta f(x^*,v^*)N_1N_2}{\mu}+\frac{(1-\eta)f(x^*,v^*)N_2}{\mu}=1.$$

Hence,

$$\begin{aligned}
\frac{dL_1(t)}{dt} &= dx^*\left(1-\frac{x}{x^*}\right)\left(1-\frac{f(x^*,v^*)}{f(x,v^*)}\right)+\frac{1}{\eta}\left(1-\frac{f(x^*,v^*)}{f(x,v^*)}\right)\big(e^*(0)-e(t,0)\big)\\
&+\frac{1}{\eta}e^*(0)\phi\left(\frac{e(t,0)}{e^*(0)}\right)-\frac{f(x^*,v^*)}{\mu}\int_0^{\infty}k_2(b)i^*(b)\phi\left(\frac{i(t,b)}{i^*(b)}\right)\mathrm{d}b\\
&+\frac{N_2f(x^*,v^*)}{\mu}\left[(1-\eta)f(x^*,v^*)v^*\ln\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right)\right]\\
&+\frac{N_2f(x^*,v^*)}{\mu}\int_0^{\infty}k_1(a)e^*(a)\ln\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right)\mathrm{d}a\\
&+\frac{f(x^*,v^*)}{\mu}\int_0^{\infty}k_2(b)i(t,b)\mathrm{d}b-\frac{f(x^*,v^*)v^*}{\mu v}\int_0^{\infty}k_2(b)i(t,b)\mathrm{d}b\\
&+f(x^*,v^*)v^*-f(x,v)v.
\end{aligned}$$

By using $\mu v^*=\int_0^{\infty}k(a)i^*(a)\mathrm{d}a$ and $e^*(0)=\eta f(x^*,v^*)v^*$, we have

$$\begin{aligned}
\frac{dL_1(t)}{dt} &= dx^*\left(1-\frac{x}{x^*}\right)\left(1-\frac{f(x^*,v^*)}{f(x,v^*)}\right)\\
&+\frac{f(x^*,v^*)}{\mu}\int_0^{\infty}k_2(b)i^*(b)\left[1-\frac{f(x^*,v^*)}{f(x,v^*)}+\ln\left(\frac{f(x^*,v^*)}{f(x,v)}\right)\right]\mathrm{d}b\\
&+\frac{f(x^*,v^*)}{\mu}\int_0^{\infty}k_2(b)i^*(b)\left[1-\frac{v^*i(t,b)}{vi^*(b)}+\ln\left(\frac{v^*i(t,b)}{vi^*(b)}\right)\right]\mathrm{d}b\\
&+f(x^*,v^*)v^*\left(-\frac{v}{v^*}+\frac{vf(x,v)}{v^*f(x,v^*)}\right)\\
&+\frac{N_2f(x^*,v^*)}{\mu}(1-\eta)f(x^*,v^*)v^*\left[1-\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}+\ln\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right)\right]\\
&+\frac{N_2f(x^*,v^*)}{\mu}\int_0^{\infty}k_1(a)e^*(a)\left[1-\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}+\ln\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right)\right]\mathrm{d}a.
\end{aligned}$$

Note that

$$(1-\eta)f(x^*,v^*)v^*\left[1-\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right]+\int_0^{\infty}k_1(a)e^*(a)\left[1-\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right]\mathrm{d}b=0,$$

we have

$$
\begin{aligned}
\frac{dL_1(t)}{dt} &= dx^*\left(1-\frac{x}{x^*}\right)\left(1-\frac{f(x^*,v^*)}{f(x,v^*)}\right)\\
&+f(x^*,v^*)v^*\left(-1-\frac{v}{v^*}+\frac{f(x,v^*)}{f(x,v)}+\frac{vf(x,v)}{v^*f(x,v^*)}\right)\\
&-\frac{f(x^*,v^*)}{\mu}\int_0^\infty k_2(b)i^*(b)\left[\phi\left(\frac{f(x^*,v^*)}{f(x,v^*)}\right)+\phi\left(\frac{f(x,v^*)}{f(x,v)}\right)+\phi\left(\frac{v^*i(t,b)}{vi^*(b)}\right)\right]\mathrm{d}b\\
&-N_2(1-\eta)\left(\frac{f(x^*,v^*)}{\mu}\right)^2\int_0^\infty k_2(b)i^*(b)\phi\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right)\mathrm{d}b\\
&-\frac{N_2f(x^*,v^*)}{\mu}\int_0^\infty k_1(a)e^*(a)\phi\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right)\mathrm{d}a.
\end{aligned}
$$

Since $f(x,v)$ is strictly monotonically increasing with respect to x, we have

$$\left(1-\frac{x}{x^*}\right)\left(1-\frac{f(x^*,v^*)}{f(x,v^*)}\right)\leq 0.$$

According to (H_3) and (H_4), we have

$$-1-\frac{v}{v^*}+\frac{f(x,v^*)}{f(x,v)}+\frac{v}{v^*}\frac{f(x,v)}{f(x,v^*)}=\left(1-\frac{f(x,v)}{f(x,v^*)}\right)\left(\frac{f(x,v^*)}{f(x,v)}-\frac{v}{v^*}\right)\leq 0.$$

Since $\phi(x)\geq 0$ for $x>0$, we have $\frac{dL_1(t)}{dt}\leq 0$. Therefore, $L_1(t)$ is a bounded and decreasing map. Arguing similarly as the end of the proof of Theorem 2.2(i) in Demasse and Ducrot [14], we get $u(t)=u^*$, i.e., $\mathscr{A}_0=\{u^*\}$. By using Theorem 4.2, we deduce that E^* is globally asymptotically stable. □

5. Application

In this section, we apply our main results to the following age-structured viral infection model with Hattaf-Yousfi functional response:

$$
(34)\qquad
\begin{cases}
\dfrac{\mathrm{d}x(t)}{\mathrm{d}t}=s-dx(t)-\dfrac{\beta x(t)v(t)}{\alpha_0+\alpha_1x(t)+\alpha_2v(t)+\alpha_3x(t)v(t)},\\
\dfrac{\partial e(t,a)}{\partial t}+\dfrac{\partial e(t,a)}{\partial a}=-\delta_1(a)e(t,a),\\
\dfrac{\partial i(t,b)}{\partial t}+\dfrac{\partial i(t,b)}{\partial b}=-\delta_2(b)i(t,b),\\
\dfrac{\mathrm{d}v(t)}{\mathrm{d}t}=\displaystyle\int_0^\infty k_2(b)i(t,b)\mathrm{d}b-\mu v(t),
\end{cases}
$$

where $\alpha_0, \alpha_1, \alpha_2, \alpha_3 \geq 0$ are the saturation factors measuring the psychological or inhibitory effect and $\beta > 0$ is the infection coefficient. The other parameters have the same biological meanings as those in (1). The boundary condition is as follows:

$$\begin{cases} e(t,0) = \dfrac{\eta\beta x(t)v(t)}{\alpha_0 + \alpha_1 x(t) + \alpha_2 v(t) + \alpha_3 x(t)v(t)}, \\ i(t,0) = \dfrac{(1-\eta)\beta x(t)v(t)}{\alpha_0 + \alpha_1 x(t) + \alpha_2 v(t) + \alpha_3 x(t)v(t)} + \displaystyle\int_0^\infty k_1(a)e(t,a)\mathrm{d}a. \end{cases} \tag{35}$$

The initial conditions of system (34) are similar to that of system (1). Further, the incidence rate of infection is modeled by Hattaf-Yousfi functional response [15] of the form $f(x,v) = \dfrac{\beta x}{\alpha_0 + \alpha_1 x + \alpha_2 v + \alpha_3 xv}$. Moreover, system (34) includes many special cases existing in the literature. For example, when $\alpha_0 = 1$ and $\alpha_1 = \alpha_2 = \alpha_3 = 0$, we get the model of Wang and Dong [5].

On the other hand, it is not hard to see that the Hattaf-Yousfi functional response satisfies the three hypotheses (H_1)-(H_3), In addition, we have

$$f(x,v) + v\frac{\partial f(x,v)}{\partial v} = \frac{\beta(\alpha_0 + \alpha_1 x)}{(\alpha_0 + \alpha_1 x + \alpha_2 v + \alpha_3 xv)^2} \geq 0.$$

Hence, the hypothesis (H_4) is satisfied. From (7), the basic reproduction number of system (34) is given by

$$\bar{\mathscr{R}}_0 = \frac{N_2(1-\eta+\eta N_1)\beta s}{\mu(\alpha_0 d + \alpha_1 s)}. \tag{36}$$

By applying Theorems 4.3 and 4.4, we obtain the following corollary.

Corollary 5.1.

- **(i):** *If $\bar{\mathscr{R}}_0 \leq 1$, then the infection-free equilibrium E^0 of system (34) is globally asymptotically stable.*
- **(ii):** *If $\bar{\mathscr{R}}_0 > 1$, then the infection-free equilibrium E^0 becomes unstable and the chronic infection equilibrium E^* of system (34) is globally asymptotically stable.*

Conflict of Interests

The authors declare that there is no conflict of interests.

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