MATHEMATICAL ANALYSIS OF AN AGE-STRUCTURED HIV MODEL WITH INTRACELLULAR DELAY

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Abstract. In this paper, we study an age-structured HIV model with intracellular delay, logistic growth and antiretroviral therapy. We first rewrite the model as an abstract non-densely defined Cauchy problem and obtain the existence of the unique positive steady state. Then through the linearization arguments we investigate the asymptotic behavior of steady states by determining the distribution of eigenvalues. We obtain successfully the globally asymptotic stability for the null equilibrium and (locally) asymptotic stability for the positive equilibrium respectively. Moreover, we also prove that Hopf bifurcations occur around the positive equilibrium under some conditions. In addition, we address the persistence of the semi-flow by showing the existence of a global attractor. Finally, some numerical examples are provided to illustrate the main results.

1. Introduction. In this paper, we study an age-structured HIV model with logistic growth, antiretroviral therapy and intracellular delay. More precisely, we shall investigate the long-time behavior for the following age-structured HIV model.

\[
\begin{aligned}
\frac{dT(t)}{dt} &= h - d_1 T(t) - (1 - \eta_0) \beta T(t - \tau_1) V_I(t - \tau_1) \\
&\quad + r T(t) \left( 1 - \frac{T(t) + \int_0^{+\infty} i(t,a) da}{K} \right), \\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -d_2 i(t,a), \quad t \geq 0, \quad a \geq 0, \\
\frac{dV_I(t)}{dt} &= (1 - \eta_1) \int_0^{+\infty} \alpha(a) i(t,a) da - d_3 V_I(t), \quad t \geq 0, \\
\frac{dV NI(t)}{dt} &= \eta_1 \int_0^{+\infty} \alpha(a) i(t,a) da - d_4 V NI(t), \quad t \geq 0, \\
i(t,0) &= (1 - \eta_0) \beta T(t - \tau_1) V_I(t - \tau_1), \quad t \geq 0.
\end{aligned}
\]
with the initial condition
\[
\begin{align*}
T_0(\theta) &= \phi(\theta) \in C([-\tau_1, 0], \mathbb{R}^+), \\
i(0, a) &= i_0(a) \in L^1((0, +\infty), \mathbb{R}^+), \\
V_0(\theta) &= \psi(\theta) \in C([-\tau_1, 0], \mathbb{R}^+), \\
V_{NI}(0) &= V_{NI} \geq 0.
\end{align*}
\]
where \( T(t) \), \( V_I(t) \) and \( V_{NI}(t) \) represent the concentration of \( T \)-cells, infectious and non-infectious virus at time \( t \), respectively. \( i(t, a) \) is the density of infected target cells of infection age \( a \) at time \( t \). The logistic growth term describes the mitotic division of uninfected cells. The parameters in model (1) are explained as follows. \( h \) is the constant recruitment rate of susceptible CD4\(^+\) T cells, \( \beta \) is the rate at which an uninfected cell becomes infected by an infectious virus, \( d_1, d_2, d_3 \) and \( d_4 \) are the natural death rate of uninfected cells, infected cells, infectious and non-infectious virus. Here \( \tau_1 \) is the intracellular delay denoting the time from initial interaction to that uninfected cells becomes infected by infectious virus, and \( \eta_0, \eta_1 \in [0, 1] \) are the efficacy of reverse transcriptase (RT) inhibitor and protease inhibitor of antiretroviral therapy separately. \( \alpha(a) \) is the viral production rate of an infected cell with infection age \( a \), which is given by
\[
\alpha(a) = \begin{cases} \alpha^*, & a \geq \tau_2, \\ 0, & \text{otherwise,} \end{cases}
\]
where \( \tau_2 \) presents the time from initial infection to the release of new free virus particles by infected CD4\(^+\) T cells, and \( K_0 = \int_0^{+\infty} \alpha(a)e^{-d_2 a} da \) denotes the total number of virus particles produced by an infected cell during its life-span. We make the following assumptions biologically on the parameters in (1):
\[
h, \ d_k, (k = 1, 2, 3, 4), \ \beta, \ r > 0, \text{ and } 0 \leq \eta_i < 1 \ (i = 0, 1).
\]
Note that the non-infectious virus \( V_{NI} \) does not exist in the first three equations of System (1). Therefore, we turn to consider the following subsystem of System (1)
\[
\begin{align*}
dT(t) &= h - d_1 T(t) - (1 - \eta_0) \beta T(t - \tau_1) V_I(t - \tau_1) \\
&\quad + r T(t) \left( 1 - \frac{\int_0^{+\infty} i(t,a) da}{K} \right), \\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -d_2 i(t,a), \ t \geq 0, \ a \geq 0, \\
\frac{dV_I(t)}{dt} &= (1 - \eta_1) \int_0^{+\infty} \alpha(a) i(t,a) da - d_3 V_I(t), \ t \geq 0, \\
i(t,0) &= (1 - \eta_0) \beta T(t - \tau_1) V_I(t - \tau_1), \ t \geq 0.
\end{align*}
\]
with the initial conditions
\[
\begin{align*}
T_0(\theta) &= \phi(\theta) \in C([-\tau_1, 0], \mathbb{R}^+), \\
i(0, a) &= i_0(a) \in L^1((0, +\infty), \mathbb{R}^+), \\
V_0(\theta) &= \psi(\theta) \in C([-\tau_1, 0], \mathbb{R}^+).
\end{align*}
\]
It is well known that Acquired Immune Deficiency Syndrome (AIDS) is an infectious disease which threatens public health heavily. HIV, the virus causing AIDS, damages the body’s immune system, leading to humoral and cellular immune function loss. At present, the best treatment for HIV is the simultaneous administration of two or more anti-viral drugs, which generally consist of reverse transcriptase (RT)
inhibitors that impede the infection of target T-cells by infectious virus and protease inhibitors (PIs) that cause infected cells to produce virus particles that are noninfectious.

The classic HIV infection model is proposed in [7, 17, 19, 20], which describes the virus dynamics by an ordinary differential equation

\[
\begin{align*}
\frac{dT(t)}{dt} &= h - d_T T(t) - \beta T(t)V(t), \\
\frac{dT_*(t)}{dt} &= \beta T(t)V(t) - \delta T_*(t), \\
\frac{dV(t)}{dt} &= bT_*(t) - cV(t),
\end{align*}
\]

where \( T(t), T_*(t), \) and \( V(t) \) represent uninfected CD4\(^+\) T cells, infected T cells and free virion at time \( t \), respectively. \( h \) is the source of T cells from precursors, and \( d_T \) is death rates for the uninfected T cells, which are infected by free virions at a rate \( \beta \). For infected cells, they produce the free viral particles at a constant rate \( b \). Besides, the infected T cells and free virions die out at rates \( \delta \) and \( c \), respectively.

For this model, the basic reproduction number \( R_0 \) plays a decisive role for the virus dynamics. Precisely, if \( R_0 < 1 \), the infection cannot go on, i.e. \( V(t) \to 0 \) and \( T_*(t) \to 0 \). If \( R_0 > 1 \), the virus will persist in the host (see [7]).

During these years, the system (5) has been extended in various ways to better HIV models. In particular, in the systems studied in [8, 9, 10, 15, 28], intracellular delays have been incorporated into the incidence term in finite or distributed form. Their analysis showed that the intracellular delay can cause stability switches in the positive steady state. Meanwhile, many authors explored the HIV models by taking the drug therapy into account and their work revealed that antiretroviral drugs play an important role in impeding the infection process, see [15, 16, 28] for example.

On the other hand, some age-structured HIV models have also been considered extensively by many authors in the past years, see [4, 14, 21, 25, 26, 27, 29, 30], for instance. Among them, Guo et al. discussed an age-structured HIV system with logistic growth in [4] in the following form

\[
\begin{align*}
\frac{dT(t)}{dt} &= h - d_1 T(t) - \beta T(t)V(t) + rT(t) \left( 1 - \frac{T(t) + \int_0^{+\infty} i(t,a)da}{K} \right), \\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -d_2 i(t,a), \\
\frac{dV(t)}{dt} &= \int_0^{+\infty} \alpha(a) i(t,a)da - d_3 V(t), \\
i(t,0) &= \beta T(t)V(t),
\end{align*}
\]

where \( \alpha(a) \) is defined as (2). They proved that if the basic reproduction number \( R_0 < 1 \), the boundary equilibrium is locally asymptotically stable for all \( \tau_2 \geq 0 \). They also found that Hopf bifurcations will occur at the positive steady state when bifurcation parameter \( \tau_2 \) crosses the critical value.

Inspired by the above mentioned work, we are going to investigate in this article the asymptotic behavior of the foregoing described age-structured HIV model (3), which is obtained by incorporating intracellular delay and antiretroviral therapy into the system (6). There is no doubt that it is reasonable and natural to introduce these factors in to the model. Our main purpose is to study the influences of the intracellular delay upon the dynamical behavior of age-structured HIV model. It
is seen that logistic growth, antiretroviral therapy and intracellular delay are now commonly involved into the system (3) so that it catches the main aspects of the HIV systems stated above. Apparently it is more suitable and realistic to describe the dynamical behavior than those systems such as (6).

We shall study the asymptotic behavior of System (3), as usual, employing the linearization techniques. Based on the existence of equilibria, we first linearize the system around the null and positive steady state respectively, and then investigate the asymptotic behavior of solutions of (3) around the equilibria by determining the distribution of eigenvalues of the linearized equation. The main work carried on in this paper lies in:

1. We first consider the local and global asymptotic stability of the disease-free equilibrium. Here, since there is a complicate logistic growth term, we discuss the global attractiveness by the approximation method, rather than constructing Liapunov functions as in [25, 26, 27, 29]. We will prove that the disease-free equilibrium $E_0 = (T_0, 0, 0)$ of System (3) is globally asymptotically stable when $R_0 < 1$, and it is unstable if $R_0 > 1$ (see Theorem 4.1 and 4.2).

2. By performing some estimations and applying theory of infinite dynamical systems we explore the weak and strong persistence problems for the considered system which is clearly biologically meaningful. Our discussion shows that, under some conditions concerning $R_0$ and time delay, any solution $(T(t), i(t, a), V_I(t))$ of (3) can be uniformly strongly persistent (see Theorem 5.7).

3. We also study the local asymptotic stability for the positive equilibrium $E_*$ of (3) and the topic of Hopf bifurcations about $E_*$ regarding the intracellular delay $\tau_1 = \tau_2$ (the time from initial infection to the release of new free virus particles by infected CD4$^+$ T cells) as the bifurcation parameters. It is interesting to see that, when they cross through the threshold parameter $(\tau^*)$ (given by (62)), Hopf bifurcations will occur for the system (3) around $E_*$. Besides, the achieved result manifests clearly their dependence on the time delay (see Theorem 6.4). We emphasis here that, as the system is infinite dimensional, the center manifold theorem founded in [12] is employed to reduce the linearize system to an ODE system so that Hassard’s Hopf bifurcation theorem works well for this system.

It is clear that the HIV model discussed here is more general and accurate than the existing ones mentioned above and the obtained results extend and improve directly the conclusions appearing in literature such as [4, 10, 25, 26, 27, 28, 30]. Moreover, the results obtained in this paper are also richer than [4, 28]. In addition, it is worth mentioning that, because the system involves time delay, we need to consider the issues in phase space of finite delay. This makes the computations much more complicated, see the sections 5 and 6.

Subsequently the paper is organized as follows. In Section 2 we first transform the system (3) into an abstract Cauchy problem to obtain the well-posedness of its solutions. Then in Section 3, we prove the existence of equilibria for the system under some conditions and linearize the abstract equation around the equilibria. Following that, in Section 4, we discuss the stability of the disease-free steady state. The problems of persistence of solutions of the system is considered and proved in Section 5, while the stability and the existence of Hopf bifurcation around the
We first prove that the solutions are ultimately bounded. Theorem 2.1. Let \( \alpha \geq 0 \) and \( \beta \geq 0 \), and consider the distribution \( \hat{T}(\hat{t}) = T(\tau_2 \hat{t}), \hat{V}_I(\hat{t}) = T(\tau_2 \hat{t}) \) and \( \hat{i}(\hat{t}, \hat{a}) = \tau_2 i(\tau_2 \hat{t}, \tau_2 \hat{a}) \).

We first normalize \( \tau_2 \) by time-scaling and age-scaling, that is, set
\[
\hat{a} = \frac{a}{\tau_2}, \hat{t} = \frac{t}{\tau_2},
\]
and consider the distribution
\[
\hat{T}(\hat{t}) = T(\tau_2 \hat{t}), \hat{V}_I(\hat{t}) = T(\tau_2 \hat{t}) \text{ and } \hat{i}(\hat{t}, \hat{a}) = \tau_2 i(\tau_2 \hat{t}, \tau_2 \hat{a}).
\]

Then System (3) is transformed into the following system by dropping the hat and putting \( r_0 = \frac{\tau_2}{\tau_2} \):

\[
\begin{align*}
\frac{dT(t)}{dt} &= \tau_2 (h - d_1 T(t) - (1 - \eta_0)\beta T(t - r_0)V_I(t - r_0)) \\
&\quad + rT(t) \left( 1 - \frac{T(t) + \int_0^{+\infty} i(t,a)da}{K} \right), \\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -\tau_2 d_2 i(t,a), \quad t \geq 0, \quad a \geq 0, \\
\frac{dV_I(t)}{dt} &= \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a) i(t,a)da - \tau_2 d_3 V_I(t), \quad t \geq 0, \\
i(t,0) &= \tau_2 (1 - \eta_0)\beta T(t - r_0)V_I(t - r_0), \quad t \geq 0.
\end{align*}
\]

with the initial condition
\[
\begin{align*}
T_0(\theta) &= \phi(\theta) = \int_{0}^{+\infty} \rho_0(\theta,a)da \in C([-r_0, 0], \mathbb{R}^+), \\
i(0,a) &= i_0(a) \in L^1((0, +\infty), \mathbb{R}^+), \\
V_{I0}(\theta) &= \psi(\theta) = \int_{0}^{+\infty} \mu_0(\theta,a)da \in C([-r_0, 0], \mathbb{R}^+),
\end{align*}
\]

Notice that the function \( \alpha(\cdot) \) is then correspondingly given by
\[
\alpha(a) = \begin{cases} 
\alpha^*, & a \geq 1, \\
0, & \text{otherwise},
\end{cases}
\]
with \( \alpha^* = K_0 d_2 e^{d_2 \tau_2} \) from (2).

We now prove the following essential result showing that all solutions of System (7) remain positive and bounded with initial conditions (8), which implies the solutions are biologically reasonable. To this end, we make the assumption about the initial function \( \psi \), i.e. \( \psi(\theta) \in C([-r_0, 0], \mathbb{R}^+); \psi(0) > 0, \|\psi\| \leq K \). On the other hand, we always suppose that \( h \geq (1 - \eta_0)\beta K \left[ K + \frac{1 - \eta_0}{d_3} \right] \) in the following discussion.

**Theorem 2.1.** Let \( h \geq (1 - \eta_0)\beta K \left[ K + \frac{1 - \eta_0}{d_3} \right] \). Then every solution of System (7) with initial conditions (8) remains non-negative for all \( t \geq 0 \) and is ultimately bounded.

**Proof.** We first prove that \( T(t) \) is non-negative for all \( t \geq 0 \). Indeed, from the third equation of System (7), we have
\[
V_I'(t) \leq \tau_2 (1 - \eta_1)\alpha^* I(t) - \tau_2 d_3 V_I(t) \leq \tau_2 (1 - \eta_1)\alpha^* K - \tau_2 d_3 V_I(t),
\]
and
...
which implies \( (V(t)e^{\tau_2 dt})' \leq \tau_2(1 - \eta_1)\alpha^*Ke^{\tau_2 dt} \). Then
\[
V(t) \leq \psi(0)e^{-\tau_2 dt} + \frac{(1 - \eta_1)\alpha^*K}{d_3}(1 - e^{-\tau_2 dt}).
\]
As, naturally, \( \psi(0) > 0 \) and \( \|\psi\| \leq K \), we get
\[
|V(t)| \leq \|\psi\| + \frac{(1 - \eta_1)\alpha^*K}{d_3} \leq K + \frac{(1 - \eta_1)\alpha^*K}{d_3}, \quad \text{for any } t \geq 0.
\]
Suppose now that there exists \( t_1 \) such that \( T(t_1) = 0 \), and \( T(t) > 0 \) for any \( t \in (0, t_1) \), then from the first equation of System (7), we see
\[
T'(t_1) = \tau_2 [h - (1 - \eta_0)\beta T(t_1 - r_0) V_I(t_1 - r_0)].
\]
Since it is assumed \( h \geq (1 - \eta_0)\beta K \bigl[ K + \frac{(1 - \eta_1)\alpha^*K}{d_3} \bigl], \) we derive \( T'(t_1) \geq 0 \), which is a contradiction.

Similarly, we can obtain that \( V_I(t) \geq 0 \) for any \( t \geq 0 \). If there is a \( t_2 \) such that \( V_I(t_2) = 0 \), and \( V_I(t) > 0 \) for all \( t \in (0, t_2) \), then from the third equation of System (7), it gives that \( V_I'(t_2) = \tau_2(1 - \eta_1) \int_0^{\infty} a(\alpha) i(t_2, a) da \). On the other hand, \( i(t, a) \) can be solved by integrating the second equation of System (7) along the characteristic line, which yields that
\[
i(t, a) = \begin{cases} i(t - a, 0)e^{-\tau_2 da}, & a \leq t, \\ i_0(a - t)e^{-\tau_2 dt}, & a > t. \end{cases}
\]
Thus from initial and boundary condition of \( i(t, a) \), we obtain that
\[
i(t_2, a) = \begin{cases} \tau_2(1 - \eta_0)\beta T(t_2 - a - r_0) V_I(t_2 - a - r_0)e^{-\tau_2 da}, & a \leq t_2, \\ i_0(a - t_2)e^{-\tau_2 dt_2}, & a > t_2, \end{cases}
\]
which implies that \( i(t_2, a) \) remains non-negative for non-negative initial conditions. It then follows that \( V_I'(t_2) \geq 0 \), a contradiction. So we have that \( V_I(t) \geq 0 \), for any \( t \geq 0 \). Hence, \( i(t, a) \) is also non-negative for all \( t \geq 0 \) from (9).

We next prove that the solutions of (7) are ultimately bounded. Due to \( \lim_{a \to -\infty} i(t, a) = 0 \), we deduce from System (7) that
\[
\begin{align*}
(T(t) + I(t))' &= \tau_2 h - \tau_2 d_1 T(t) - i(t, 0) + \tau_2 r T(t)(1 - \frac{T(t) + I(t)}{K}) \\
& \quad + \int_0^{\infty} \left( -\frac{\partial i(t, a)}{\partial a} - \tau_2 d_2 i(t, a) \right) da \\
& = \tau_2 h - \tau_2 d_1 T(t) - \tau_2 d_2 I(t) + \tau_2 r T(t)(1 - \frac{T(t) + I(t)}{K}).
\end{align*}
\]
From (25) in Section 4, we obtain that \( \lim \sup_{t \to +\infty} T(t) \leq T_0 \) (the total number of uninfected cells in disease-free steady state given in Theorem 3.2). Consequently there exists \( T_1 > 0 \) such that, for \( t > T_1 \),
\[
\begin{align*}
(T(t) + I(t))' &\leq \tau_2 h - \tau_2 d_1 T(t) - \tau_2 d_2 I(t) + \tau_2 r T_0 \\
& \quad \leq \tau_2 h + \tau_2 r T_0 - \min \{ \tau_2 d_1, \tau_2 d_2 \} (T(t) + I(t)).
\end{align*}
\]
Therefore,
\[
\limsup_{t \to +\infty} (T(t) + I(t)) \leq \frac{h + r T_0}{\min \{ d_1, d_2 \}}. \tag{10}
\]
Note that
\[
\frac{dV_I(t)}{dt} \leq \tau_2(1-\eta_1)\alpha^*I(t) - \tau_2d_3V_I(t) \leq \tau_2(1-\eta_1)\alpha^* \frac{h + rT_0}{\min\{d_1, d_2\}} - \tau_2d_3V_I(t)
\]
for \( t \) is sufficiently large, we also have that
\[
\limsup_{t \to +\infty} V_I(t) \leq \frac{(1-\eta_1)\alpha^*(h + rT_0)}{d_3\min\{d_1, d_2\}}.
\]
(11)
Then every solution of System (7) is ultimately bounded. 

Before formulating (7) as an abstract equation, we introduce here some notations and basic facts on operator semigroups (see [13] and [18] for more details). Let \( \rho(A) \) and \( \sigma(A) = \mathbb{C} \setminus \rho(A) \) denote respectively the resolvent set and the spectrum of a linear operator \( A \). In particular, the point spectrum of \( A \) is defined as
\[
\sigma_p(A) : = \{ \lambda \in \sigma(A) : A(\lambda I - A) \neq \{0\} \}.
\]

**Definition 2.2.** (see [13]) Let \( A : D(A) \subseteq X \rightarrow X \) be a linear operator on a Banach space \( (X, \|\cdot\|) \), \( A \) is called a Hille-Yosida operator if there exist constants \( M \geq 1, \) and \( \omega \in \mathbb{R}, \) such that \( (\omega, +\infty) \subseteq \rho(A), \) and
\[
\| (\lambda - A)^{-n} \| \leq \frac{M}{(\lambda - \omega)^n}, \text{ for all } n \in \mathbb{N}_+ \text{ and } \lambda > \omega.
\]

For a Hille-Yosida operator one has that

**Lemma 2.3.** (see [18]) Let \( (A, D(A)) \) be a Hille-Yosida operator on a Banach space \( X \) and \( B \in \mathcal{L}(X) \), the set of all bounded linear operators on \( X \), then the sum \( C = A + B \) is a Hille-Yosida operator as well.

Let \( A_0 \) be the part of \( A \) on \( X_0 := \overline{D(A)} \), which is defined by
\[
A_0x = Ax, \forall x \in D(A_0) = \{ x \in D(A) : Ax \in X_0 \}.
\]
Then \( A_0 \) is a infinitesimal generator of a strongly continuous semigroup \( (C_{00}-\text{ semi- group}) \) from the following lemma.

**Lemma 2.4.** (see [18]) If \( (A, D(A)) \) is a Hille-Yosida operator, then its part \( (A_0, D(A_0)) \) generates a \( C_0 \)-semigroup \( (T_0(t))_{t \geq 0} \) on \( X_0 \).

Now we set about to transform (7) into an abstract Cauchy problem. Let \( \rho(t, a) \) be the density of susceptible CD4\(^+\) T cells of age \( a \) at time \( t \), and \( \mu(t, a) \) denotes the density of infectious virus of age \( a \) at time \( t \). Then
\[
T(t) = \int_0^{+\infty} \rho(t, a)da, \quad V_I(t) = \int_0^{+\infty} \mu(t, a)da.
\]
From the first equation of (7), we have
\[
\begin{align*}
\frac{\partial \rho(t, a)}{\partial t} + \frac{\partial \rho(t, a)}{\partial a} &= -\tau_2d_1\rho(t, a), \quad t \geq 0, \\
\rho(t, 0) &= Q(\rho(t, a), i(t, a), \mu(t, a)), \\
\rho(0, a) &= \rho_0(\theta, a) \in L^1((0, +\infty), \mathbb{R}), \quad \theta \in [-r_0, 0],
\end{align*}
\]
where

\[ Q(\rho(t,a), i(t,a), \mu(t,a)) \]

\[ = \tau_2 h + \tau_2 r \int_0^{+\infty} \rho(t,a)da \left( 1 - \int_0^{+\infty} \rho(t,a)da + \int_0^{+\infty} \frac{i(t,a)da}{K} \right) \]

\[ - \tau_2 (1 - \eta_0) \beta \int_0^{+\infty} \rho(t - r_0, a)da \int_0^{+\infty} \mu(t - r_0, a)da. \]

Similarly, from the third equation of (7) we can obtain the following system on \( \mu(t,a) \).

\[ \begin{cases} \frac{\partial \mu(t,a)}{\partial t} + \frac{\partial \mu(t,a)}{\partial a} = -\tau_2 d_3 \mu(t,a), \ t \geq 0, \\ \mu(t,0) = \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a)i(t,a)da, \\ \mu(0,a) = \mu_0(\theta,a) \in L^1((0, +\infty), \mathbb{R}), \ \theta \in [-r_0, 0], \end{cases} \]

Set \( w(t,a) = (\rho(t,a), i(t,a), \mu(t,a))^T \) and \( w_t(\theta,a) = w(t + \theta, a) \) for \( t \geq 0 \) and \( \theta \in [-r_0, 0] \), we then have that

\[ \begin{cases} \frac{\partial w(t,a)}{\partial t} + \frac{\partial w(t,a)}{\partial a} = - Dw(t,a), \ t \geq 0, \\ w(t,0) = B(w_t(\theta,a)), \\ w_0(\theta,a) = (\rho_0(\theta,a), i_0(\theta,a), \mu_0(\theta,a))^T \in C \left([-r_0, 0], L^1((0, +\infty); \mathbb{R})^3 \right), \end{cases} \]

in which

\[ D = \begin{pmatrix} \tau_2 d_1 & 0 & 0 \\ 0 & \tau_2 d_2 & 0 \\ 0 & 0 & \tau_2 d_3 \end{pmatrix} \]

and

\[ B(w_t(\theta,a)) = \begin{pmatrix} \tau_2 (1 - \eta_0) \beta \int_0^{+\infty} \rho(t - r_0, a)da \int_0^{+\infty} \mu(t - r_0, a)da \\ \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a)i(t,a)da \end{pmatrix}. \]

Let now \( Y := \mathbb{R}^3 \times L^1((0, +\infty); \mathbb{R})^3 \) endowed with the usual product norm \( \| (c,f) \| = \| c \|_{\mathbb{R}^3} + \| f \|_{L^1} \), for any \( (c,f)^T \in Y \) and define the linear operator \( L : D(L) \subset Y \rightarrow Y \) as

\[ L \left( \begin{pmatrix} c \\ f \end{pmatrix} \right) = \begin{pmatrix} c \| c \|_{\mathbb{R}^3} + \| f \|_{L^1} \end{pmatrix} \]

with \( D(L) = \{0\} \times W^{1,1}((0, +\infty); \mathbb{R})^3 \). In the sequel, we always denote \( C := C([-r_0,0], Y) \) and \( C^0 = \{(0, \psi(\theta))^T \in C, \psi \in C \left([-r_0,0], L^1((0, +\infty); \mathbb{R})^3 \right) \} \). On \( C^0 \) we introduce the operator \( F : C^0 \rightarrow C \) by

\[ F \left( \begin{pmatrix} 0 \\ \psi(\theta) \end{pmatrix} \right) = \begin{pmatrix} B(\psi(\theta)) \\ 0_{L^1} \end{pmatrix}. \]

Thus, setting \( y(t,a) = (0, w(t,a))^T \in Y \), we can rewrite (12) immediately as

\[ \begin{cases} \frac{d}{dt} y(t,a) = L(y(t,a)) + F(y_t(\theta,a)), \ t \geq 0, \\ y_0(\theta,a) = \begin{pmatrix} 0 \\ w_0(\theta,a) \end{pmatrix} \in C^0, \end{cases} \]

which is an abstract delayed differential equation if the variable \( a \) is considered as a parameter. It is observed that (13) can further be converted into an ODE on the
space $C^0$ so that the operator semigroup theory might be well applied. To do so, we put $x(t, \theta)(a) = y(t + \theta, a)$ and substitute it into \((13)\) to get
\[
\begin{align*}
\frac{\partial x(t, \theta)}{\partial t} - \frac{\partial x(t, \theta)}{\partial \theta} &= 0, \quad \theta \in [-r_0, 0], t \geq 0, \\
\frac{\partial x(t, 0)}{\partial \theta} &= L(x(t, 0)) + F(x(t, \theta)), \quad t \geq 0, \\
x(0, \theta) &= y_0(\theta, a), \quad \theta \in [-r_0, 0].
\end{align*}
\] (14)
Next we rewrite \((14)\) into an abstract ODE as follows. Let $Z := Y \times C$ with the usual product norm $\| (y, \phi)^T \| = \| y \|_Y + \| \phi \|_C$, and define the linear operator $A : D(A) \subset Z \to Z$ as
\[
A \left( \begin{pmatrix} 0 \\
\phi \end{pmatrix} \right) = \left( \begin{pmatrix} -\phi'(0) \\
\phi' \end{pmatrix} \right),
\]
with the domain
\[
D(A) = \{ 0_Y \} \times \{ \phi \in C^1([-r_0, 0], Y), \phi(0) \in D(L) \}. 
\]
Obviously, $A$ is non-densely defined, since
\[
Z_0 := \overline{D(A)} = \{ 0_Y \} \times C^0 \neq Z.
\]
We further introduce the operator $H : Z_0 \to Z$ by $H \left( \begin{pmatrix} 0_Y \\
\phi \end{pmatrix} \right) = \left( \begin{pmatrix} F(\phi) \\
0_{C^0} \end{pmatrix} \right)$, and set
\[
z(t) := \begin{pmatrix} 0 \\
x(t) \end{pmatrix}
\]
with $x(t) = x(t)(\theta) = x(t, \theta)$, then \((14)\) is readily transformed into
\[
\begin{align*}
\frac{d}{dt} z(t) &= Az(t) + H(z(t)), \quad t \geq 0, \\
z_0 := z(0) &= \begin{pmatrix} 0_Y \\
y_0 \end{pmatrix} \in Z_0,
\end{align*}
\] (15)
which is an ODE in space $Z$.

Note that, generally speaking, it is difficult to find a strong solution for an abstract differential equation like \((15)\), so alternatively we turn to consider the existence of integrated solutions for \((15)\), which have the form
\[
z(t) = z_0 + A \int_0^t z(s) \, ds + \int_0^t H(z(s)) \, ds.
\] (16)
Now we are in the condition to discuss the well-posedness of solutions for System (15). Let
\[
d := \min\{ \tau_2 d_1, \tau_2 d_2, \tau_2 d_3 \} > 0 \quad \text{and } \quad \Omega := \{ \lambda \in \mathbb{C}; Re(\lambda) > -d \}.
\]
and denote
\[
Y_+ := \mathbb{R}_+^3 \times L^1((0, +\infty); \mathbb{R}_+^3), \quad Z_+ := Y_+ \times C([-r_0, 0], Y_+), \quad Z_{0+} := Z_0 \cap Z_+.
\]
Then for the operator $(A, D(A))$ in \((15)\) we have the following conclusion.

**Theorem 2.5.** The operator $(A, D(A))$ in \((15)\) is a Hille-Yosida operator and so its part $(A_0, D(A_0))$ generates a $C_0$-semigroup $(T(t))_{t \geq 0}$ on $D(A)$.

**Proof.** Firstly, we prove $(L, D(L))$ in \((13)\) is a Hille-Yosida operator. Let $\lambda \in (-d, +\infty)$, then we have, for any $(c, f_1)^T \in Y$, $(0, f)^T \in D(L),
\[
(\lambda I - L) \begin{pmatrix} 0 \\
f_1 \end{pmatrix} = \begin{pmatrix} c \\
f \end{pmatrix} \iff \begin{pmatrix} f' + (\lambda I + D)f \\
f_1 \end{pmatrix} = \begin{pmatrix} c \\
f_1 \end{pmatrix},
\]
which implies that
\[ f(a) = e^{-(\lambda I + D)a}c + \int_0^a e^{-(\lambda I + D)(a-s)}f_1(s)ds. \]
So by integrating this equation with regard to the age variable \( a \) from 0 to \(+\infty\), we obtain
\[
\|f\|_{L^1} = \sum_{i=1}^3 \int_0^{+\infty} \left| e^{-(\lambda + \tau_d i)a}c_i + \int_0^a e^{-(\lambda + \tau_d i)(a-s)}f_1(s)ds \right| da \\
\leq 3 \int_0^{+\infty} e^{-(\lambda + d)a}da|c| + \sum_{i=1}^3 \int_0^{+\infty} \int_0^a e^{-(\lambda + d)(a-s)}|f_1(s)|ds da \\
= 3 \int_0^{+\infty} e^{-(\lambda + d)a}da|c| + \sum_{i=1}^3 \int_{+\infty}^{+\infty} \int_{+\infty}^{a} e^{-(\lambda + d)(a-s)}da|f_1(s)|ds \\
\leq \frac{3}{\lambda + d}(|c| + \|f_1\|_{L^1}).
\]
It follows that
\[
\left\| (\lambda I - L)^{-1} \right\| \leq \frac{3}{\lambda + d}, \text{ for } \lambda > -d,
\]
showing \((L, D(L))\) is a Hille-Yosida operator.

By applying the similar arguments as in the proofs of Lemma 3.6 in [3], we deduce that the operator \((A, D(A))\) is also a Hille-Yosida operator. Hence, from Lemma 2.4, the part of \((A, D(A))\) generates a \(C_0\)-semigroup \((T(t))_{t \geq 0}\) on \(D(A)\). Then the proof is completed. \(\square\)

Accordingly, we conclude the following well-posedness theorem for the system (15) and (3).

**Theorem 2.6.** For any \(z_0 \in Z_{0+}\), the system (15) has a unique solution \(z \in C([0, +\infty), Z_{0+})\) (equivalently the system (3) has \((T(t), i(t, a), V_1(t)) \in C(\mathbb{R}_+ \times \mathbb{R}_+, \mathbb{R}_+ \times L^1((0, +\infty), \mathbb{R}_+) \times \mathbb{R}_+)\). Moreover, the family \((U(t))_{t \geq 0}\) of maps \(U(t) : Z_{0+} \mapsto Z_{0+}\) defined by \(U(t)z_0 = z(t, z_0)\) is a continuous semi-flow, that is, there hold

(i) \(U(t) \circ U(s) = U(t + s)\), for any \(t, s \geq 0\), and \(U(0) = I\);
(ii) \((t, z_0) \mapsto U(t)z_0\) is continuous from \([0, +\infty) \times Z_{0+}\) into \(Z_{0+}\).

3. Equilibriums and linearized equations. As mentioned in Section 1, we shall carry on our investigation mainly employing the linearization arguments. In this section, we will linearize System (15) around the steady states. To do so, we need to find all the equilibria of System (15).

Clearly, an equilibrium \(\bar{z} = (0, \bar{d})^T \in D(A)\) of (15) must satisfy
\[
A\bar{z} + H(\bar{z}) = 0,
\]
or equivalently,
\[
\begin{cases}
-\bar{d}(0) + L\bar{d}(0) + F(\bar{d}) = 0, \\
\bar{\phi} = 0.
\end{cases}
\]
Since \( \bar{\omega}(0) \in D(L) \), we can write \( \bar{\omega} = (0, \bar{\psi})^T \) for \( \bar{\psi} \in C^1([-r_0, 0], L^1((0, +\infty); \mathbb{R})^3) \), and hence (17) becomes that

\[
\begin{cases}
-\bar{\psi}(0)(0) + B(\bar{\psi}(0))(a) = 0, \\
-\bar{\psi}(0)'(a) - D\bar{\psi}(0)(a) = 0.
\end{cases}
\]  

(18)

From the second equation of (18), we obtain that \( \bar{\psi}_i'(0)(a) = C_i e^{-\tau_2 d_i a}(i = 1, 2, 3) \). Substituting them into the first equation of (18) yields that

\[
\begin{cases}
- \frac{r}{\tau_2 d_i^2} C_i^2 + \left( \frac{r}{d_i^2} - 1 \right) C_i - \frac{r}{\tau_2 d_1 d_2 K} C_1 C_2 - \frac{(1 - \eta_0) \beta}{\tau_2 d_1 d_3} C_1 C_3 + \tau_2 h = 0, \\
- \tau_2 d_1 d_3 C_i C_3, \\
- \tau_2 d_1 d_3 C_i C_3, \\
- C_i + (1 - \eta_1) K_0 C_i = 0.
\end{cases}
\]

Solving the above equation with regard to \( C_i \) by direct but tedious computations, we can infer that

**Lemma 3.1.** *The system (15) always has an equilibrium*

\[
\bar{z}_0 = \left( \begin{array}{c}
0_Y \\
0_{g^3} \\
C_1 e^{-\tau_2 d_1 a}
\end{array} \right)
\]

with

\[
C_1 = \frac{\tau_2 d_1 K (r - d_i) + \tau_2 d_1 K \sqrt{(r - d_1)^2 + \frac{4hr}{K}}}{2r}.
\]

(19)

*And additionally, it has a unique positive equilibrium*

\[
\bar{z}_* = \left( \begin{array}{c}
0_Y \\
0_{g^3} \\
\bar{\psi}_1(\theta) \\
\bar{\psi}_2(\theta) \\
\bar{\psi}_3(\theta)
\end{array} \right)
\]

if and only if

\[(H1) \, \beta > \frac{1}{2h(1 - \eta_0)(1 - \eta_1) K_0} \cdot \left( \sqrt{(r - d_1)^2 + \frac{4hr}{K}} - (r - d_1) \right),\]

where \( \bar{\psi}_i \) are given by \( \bar{\psi}_i'(0)(a) = C_i^* e^{-\tau_2 d_i a}(i = 1, 2, 3) \) with

\[
C_1^* = \frac{\tau_2 d_1 d_3}{(1 - \eta_0)(1 - \eta_1) \beta K_0},
\]

\[
C_2^* = \frac{\tau_2 (1 - \eta_0)(1 - \eta_1) K_0 K \beta [h(1 - \eta_0)(1 - \eta_1) K_0 \beta + (r - d_1) d_3] - r d_2^3 d_2^2}{(1 - \eta_0)^2 (1 - \eta_1) K_0 K \beta^2 + (1 - \eta_0)(1 - \eta_1) r d_2 d_3 K_0 \beta},
\]

\[
C_3^* = (1 - \eta_1) K_0 C_2^*.
\]

**Proof.** Note that the numerator of \( C_2^* \) is a quadratic polynomial with respect to \( \beta \), it is positive if and only if \( (H1) \) holds true. Hence, \( C_i^* > 0 \) \( (i = 1, 2, 3) \) are equivalent to the condition \( (H1) \) and so it ensures the existence of the positive equilibrium. \( \square \)

As a result, we draw the following conclusion.
Then linearize (20) to obtain Definition 3.4.\(A\) (see [11] for more details).

Theorem 3.3. We further consider the compactness of the generated \(C_0\)-semigroups \((S(t))_{t \geq 0}\), which will play an important role in our later discussions. For this purpose, we introduce the definition of quasi-compact semigroups and a basic result about it (see [11] for more details).

**Theorem 3.3.** The operator \(A + DH(\bar{z})\) is a Hille-Yosida operator on \(Z\). And, therefore, the part of operator \((A + DH(\bar{z})), D(A + DH(\bar{z}))\) on \(Z_0\) generates \(C_0\)-semigroup \((S(t))_{t \geq 0}\) on the space \(Z_0\).

\[DH(\bar{z})\]

\[
\begin{pmatrix}
\frac{d}{dt} \bar{z}(t) = A\bar{z}(t) + H(\bar{z}(t) + \bar{z}) - H(\bar{z}), \ t \geq 0, \\
\bar{z}_0 := \bar{z}(0) = \begin{pmatrix}
y_0 - \phi \\
y_0 \end{pmatrix} \in Z_0.
\end{pmatrix}
\]

Then linearize (20) to obtain

\[
\begin{pmatrix}
\frac{d}{dt} \bar{z}(t) = A\bar{z}(t) + DH(\bar{z})\bar{z}(t), \ t \geq 0, \\
\bar{z}_0 \in Z_0,
\end{pmatrix}
\]

in which

\[
DH(\bar{z})\begin{pmatrix}
0_y \\
\phi(t)
\end{pmatrix} = \begin{pmatrix}
DF(\bar{\phi})(\phi(t)) \\
0_{C^0}
\end{pmatrix} = \begin{pmatrix}
\begin{pmatrix}
DB(\bar{w})(w_t(\theta,a))
\end{pmatrix} \\
0_{L_1} \\
0_{C^0}
\end{pmatrix}
\]

\[
DB(\bar{w})(w_t(\theta,a)) = \begin{pmatrix}
\begin{pmatrix}
-\beta \bar{V}_I & 0 & -\beta \bar{T} \\
-\beta \bar{V}_I & 0 & \beta \bar{T} \\
0 & 0 & 0
\end{pmatrix}^+ \int_0^{+\infty} w(t - r_0, a) da \\
0 & 0 & 0 \\
T_2(1 - \eta_1) & 0 & 0 \\
\end{pmatrix} \end{pmatrix} \int_0^{+\infty} \alpha(a)w(t,a) da \\
+ \begin{pmatrix}
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & 0 & 0
\end{pmatrix} \int_0^{+\infty} \tau_2(1 - \eta_1) w(t,a) da \\
+ \begin{pmatrix}
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & 0 & 0
\end{pmatrix} \int_0^{+\infty} \tau_2 \begin{pmatrix}
\begin{pmatrix}
1 - \frac{2T + I}{K} & 0 & 0 \\
0 & 0 & 0 \\
0 & 0 & 0
\end{pmatrix} \end{pmatrix} \int_0^{+\infty} w(t,a) da.
\]

Clearly, here \(DH(\bar{z})\) is a compact bounded linear operator on \(Z_0\). Hence from Lemmas 2.3, 2.4 and Theorem 2.5, we infer immediately that

**Theorem 3.3.** The operator \(A + DH(\bar{z})\) is a Hille-Yosida operator on \(Z\). And, therefore, the part of operator \((A + DH(\bar{z})), D(A + DH(\bar{z}))\) on \(Z_0\) generates \(C_0\)-semigroup \((S(t))_{t \geq 0}\) on the space \(Z_0\).

We further consider the compactness of the generated \(C_0\)-semigroups \((S(t))_{t \geq 0}\), which will play an important role in our later discussions. For this purpose, we introduce the definition of quasi-compact semigroups and a basic result about it (see [11] for more details).

**Definition 3.4.** A \(C_0\)-semigroup \((S(t))_{t \geq 0}\) is called quasi-compact if \(S(t) = S_1(t) + S_2(t)\) with the operator families \(S_1(t)\) and \(S_2(t)\) satisfying separately that

(i) \(\|S_1(t)\| \to 0\) as \(t \to +\infty\),

(ii) \(S_2(t)\) is eventually compact, that is, there is \(t_0 > 0\) such that \(S_2(t)\) is compact for all \(t > t_0\).
Lemma 3.5. Let \((L,D(L))\) be the infinitesimal generator of a quasi-compact \(C_0\)-semigroup \((\mathcal{T}(t))_{t \geq 0}\). Then, for some \(\epsilon > 0\), \(e^{\epsilon t}\|\mathcal{T}(t)\| \to 0\) as \(t \to +\infty\) if and only if each eigenvalue of \(L\) has strictly negative real part.

From Theorem 2.5, we have \(\|\mathcal{T}(t)\| \leq M e^{-\delta t}\), and clearly \(DH(\bar{z})\mathcal{T}(t) : Z_0 \to Z\) is compact for any \(t > 0\). Since

\[
\mathcal{S}(t) = e^{DH(\bar{z})t} \mathcal{T}(t) = \mathcal{T}(t) + \sum_{k=1}^{+\infty} \frac{(DH(\bar{z})t)^k}{k!} \mathcal{T}(t),
\]

we see that \((\mathcal{S}(t))_{t \geq 0}\) is quasi-compact. Therefore by Lemma 3.5 we derive that, for some \(\delta > 0\), \(e^{\delta t}\|\mathcal{S}(t)\| \to 0\) as \(t \to +\infty\) if and only if all the eigenvalues of \((A + DH(\bar{z}))\) have strictly negative real part.

In light of the above arguments, we then conclude that

**Theorem 3.6.** The solution semi-flow \(U(t)(z_0)\) of System (15), described in Theorem 2.6, satisfies the following properties.

(i) If each eigenvalue of \((A + DH(\bar{z}))\) has strictly negative real part, then the steady state \(\bar{z}\) is locally asymptotically stable.

(ii) If there is at least one eigenvalue with strictly positive part for \((A + DH(\bar{z}))\), then the steady state \(\bar{z}\) is unstable.

4. **Stability of disease-free steady state.** Based on the preparations in Section 3, from now on we study the long-time behavior of solutions for System (15) (or System (3)). To begin with, we focus on in this part the stability of disease-free steady state by considering linearized equation of System (15) around \(\bar{z}_0\). The first main result of this section is

**Theorem 4.1.** If \((1-\eta_0)(1-\eta_1)\beta T_0 K_0 < 1\), then the equilibrium \(\bar{z}_0\) of System (15), equivalently, the disease-free equilibrium \(E_0 = (T_0,0,0)\) of System (3), is locally asymptotically stable. If, however, \((1-\eta_0)(1-\eta_1)\beta T_0 K_0 > 1\), \(\bar{z}_0\) (or \(E_0\)) is unstable.

**Proof.** Let \(\tilde{z}(t) = z(t) - \bar{z}_0 = \begin{pmatrix} 0 & 0 & \tilde{w}(t)(.) \end{pmatrix}^T\), we can simplify the linearizing system (21) for System (15) at \(\bar{z}_0\) by some direct calculations. And then we can derive that for \(\tilde{w}(t)(.)\)

\[
\frac{\partial \tilde{w}(t,a)}{\partial t} + \frac{\partial \tilde{w}(t,a)}{\partial a} = -D \tilde{w}(t,a),
\]

\[
\tilde{w}(t,0) = W_1 \int_0^t \tilde{w}(t-r_0) da + W_2 \int_r^{+\infty} \tilde{w}(t,r) da + W_3 \int_r^{+\infty} \alpha(a) \tilde{w}(t,a) da,
\]

in which

\[
W_1 = \begin{pmatrix} 0 & 0 & -\tau_2 (1 - \eta_0) \beta T_0 \\ 0 & 0 & \tau_2 (1 - \eta_0) \beta T_0 \\ 0 & 0 & 0 \end{pmatrix},
\]

\[
W_2 = \begin{pmatrix} \tau_2 r \left(1 - \frac{2T_0}{\alpha} \right) & -\tau_2 r T_0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},
\]

\[
W_3 = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & \tau_2 (1 - \eta_1) & 0 \end{pmatrix},
\]

with \(T_0 = \int_0^{+\infty} C_1 e^{-\tau_2 d_r a} da\) given in Theorem 3.2.
Substitute \( \tilde{\rho}(t, a) = \tilde{\rho}_0(a)e^{\lambda t}, \tilde{i}(t, a) = \tilde{i}_0(a)e^{\lambda t} \), \( \tilde{\mu}(t, a) = \tilde{\mu}_0(a)e^{\lambda t} \) into (22) to find that

\[
\begin{cases}
\tilde{\rho}_0(a) = -(\lambda + \tau_2d_1)\tilde{\rho}_0(a), \\
\tilde{i}_0(a) = -(\lambda + \tau_2d_2)\tilde{i}_0(a), \\
\tilde{\mu}_0(a) = -(\lambda + \tau_2d_3)\tilde{\mu}_0(a), \\
\tilde{\rho}_0(0) = \tau_2\left(1 - \frac{\tau_2d_1}{K_0}\right)\int_0^{\infty} \tilde{\rho}_0(a)da - \frac{\tau_2}{\tau_0}\tilde{\rho}_0(0), \\
\tilde{i}_0(0) = \tau_2(1 - \eta_0)\int_0^{\infty} \tilde{\mu}_0(a)da, \\
\tilde{\mu}_0(0) = \tau_2(1 - \eta_1)\int_0^{\infty} \alpha(a)\tilde{i}_0(a)da.
\end{cases}
\]

Solving the first three equations of (23), then we have

\[ \tilde{\rho}_0(a) = \tilde{\rho}_0(0)e^{-(\lambda + \tau_2d_1)a}, \quad \tilde{i}_0(a) = \tilde{i}_0(0)e^{-(\lambda + \tau_2d_2)a}, \quad \tilde{\mu}_0(a) = \tilde{\mu}_0(0)e^{-(\lambda + \tau_2d_3)a}. \]

Thus, from the fifth equation of (23) it follows that

\[ \tilde{i}_0(0) = \tau_2(1 - \eta_0)\beta T_0 \tilde{\rho}_0(0) e^{-(\lambda + \tau_2d_2)a}. \]

Substituting it into the last equation of (23) we find, since \( \tilde{\mu}_0(0) \) is arbitrary, that

\[ \Delta_0(\lambda) := \frac{\tau_2^2(1 - \eta_0)(1 - \eta_1)\beta T_0}{\lambda + \tau_2d_3} \int_0^{\infty} \alpha(a)e^{-(\lambda + \tau_2d_2)a}da \cdot e^{-\lambda t} - 1 = 0, \]

which is the characteristic equation of (22).

It is easy to see that

\[ \lim_{\lambda \to +\infty} \Delta_0(\lambda) = -1, \quad \Delta_0(0) = \frac{(1 - \eta_0)(1 - \eta_1)\beta T_0 K_0}{d_3} - 1. \]

Hence, if \( \frac{(1 - \eta_0)(1 - \eta_1)\beta T_0 K_0}{d_3} > 1 \), there exists at list one positive real root for the characteristic equation (24). Thus, from Theorem 3.6, \( z_0 \) is unstable. If, however, \( \frac{(1 - \eta_0)(1 - \eta_1)\beta T_0 K_0}{d_3} < 1 \), we prove below that all the complex solutions of (24) has strictly negative real part. In fact, assume conversely that \( \lambda = \alpha + bi \) with \( \alpha \geq 0 \) is a complex root of (24), then

\[
1 = |\Delta_0(\lambda)| + 1 = \frac{\tau_2^2(1 - \eta_0)(1 - \eta_1)\beta T_0}{\alpha + bi + \tau_2d_3} \int_0^{\infty} \alpha(a)e^{-(\alpha + bi + \tau_2d_2)a}da \cdot e^{-(\alpha + bi)\tau_0} \\
\leq \frac{\tau_2^2(1 - \eta_0)(1 - \eta_1)\beta T_0}{|\alpha + bi + \tau_2d_3|} \int_0^{\infty} \alpha(a) \left| e^{-(\alpha + bi + \tau_2d_2)a} \right| da \cdot e^{-\alpha \tau_0} \\
= \frac{\tau_2^2(1 - \eta_0)(1 - \eta_1)\beta T_0}{\sqrt{(\alpha + \tau_2d_3)^2 + b^2}} \int_0^{\infty} \alpha(a)e^{-(\alpha + \tau_2d_2)a}da \cdot e^{-\alpha \tau_0} \\
\leq \frac{\tau_2^2(1 - \eta_0)(1 - \eta_1)\beta T_0}{\alpha + \tau_2d_3} \int_0^{\infty} \alpha(a)e^{-(\alpha + \tau_2d_2)a}da \cdot e^{-\alpha \tau_0} \\
= \Delta_0(a) + 1 \leq \Delta_0(0) + 1 < 1,
\]

which is a contradiction. So the assertion follows, which implies that equilibrium \( z_0 \) of system (15) (and hence \( E_0 \) of (3)) is locally asymptotically stable when \( \frac{(1 - \eta_0)(1 - \eta_1)\beta T_0 K_0}{d_3} < 1 \). The proof is completed. \( \square \)

Now we set

\[ R_0 := \frac{T_0}{T_0} = \frac{(1 - \eta_0)(1 - \eta_1)\beta T_0 K_0}{d_3}. \]

As we know, \( \eta_0, \eta_1 \in (0, 1) \) represent the efficacy of the RT inhibitor and the protease inhibitors, respectively. \( T_0 \) is the total number of uninfected cells in disease-free steady state, and the uninfected cells are infected by free virus at a rate \( \beta \).

In addition, \( K_0 \) is the total number of viral particles produced by an infected cell.
which shows that \( i \) means the life-span of a virus. So \( R_0 \) represents the total number of newly infected cells under antiretroviral therapy and therefore it is the basic reproduction number for the considered system.

Actually, using the asymptotic autonomous semi-flow theory, we can further show that the disease-free equilibrium is globally asymptotically stable. That is,

**Theorem 4.2.** If \( R_0 < 1 \), then the equilibrium \( z_0 \) of system (15), equivalently, the disease-free equilibrium \( E_0 = (T_0, 0, 0) \) of System (3), is globally asymptotically stable.

**Proof.** From Theorem 4.1 it is sufficient to prove that \( z_0 \) is globally attractive, i.e. \( \lim_{t \to +\infty} z(t) = z_0 \), or equivalently, \( \lim_{t \to +\infty} (T(t), i(t, a), V_I(t)) = (T_0, 0, 0) \).

From the first equation of (7), it follows that

\[
\frac{dT(t)}{dt} \leq \tau_2 \left( h - d_1 T(t) + r T(t) \left( 1 - \frac{T(t)}{K} \right) \right),
\]

which together with the comparison principle implies that

\[
\limsup_{t \to +\infty} T(t) \leq T_0. \tag{25}
\]

So, for any \( \varepsilon > 0 \), there exists \( t_1 \) such that \( T(t - r_0) \leq T_0 + \varepsilon \), for all \( t \geq t_1 + r_0 \). It then follows that

\[
i(t, a) \leq \tau_2 \left( 1 - \eta_0 \right) \beta (T_0 + \varepsilon) V_I(t - r_0), \quad \text{for } t \geq t_1 + r_0.
\]

Next we consider the system

\[
\begin{cases}
\frac{\partial i(t, a)}{\partial t} + \frac{\partial i(t, a)}{\partial a} = -\tau_2 d_2 \dot{i}(t, a), \quad t \geq 0, \quad a \geq 0, \\
d \dot{V_I}(t) = \tau_2 (1 - \eta_1) \int_0^{a} \alpha(a) \dot{i}(t, a) da - \tau_2 d_3 V_I(t), \quad t \geq 0, \\
i(t, 0) = \tau_2 (1 - \eta_0) \beta (T_0 + \varepsilon) V_I(t - r_0), \quad t \geq 0.
\end{cases} \tag{26}
\]

Adopting the similar methods as in the proof of Theorem 4.1, we can show that there exists a solution for System (26) in the form \( (i(t, a), \dot{V}_I(t)) = (i_0(a)e^{\lambda_0 t}, \dot{V}_{I0} e^{\lambda_0 t}) \), in which \( i_0(a) \) and \( \dot{V}_{I0} \) are nonnegative and \( \lambda_0 \) is a root of the characteristic equation of System (26), i.e.

\[
\Delta_0(\lambda_0, \varepsilon) := \frac{\tau_2^2 (1 - \eta_0) (1 - \eta_1) \beta (T_0 + \varepsilon)}{\lambda_0 + \tau_2 d_3} \int_0^{+\infty} \alpha(a) e^{-(\lambda_0 + \tau_2 d_2) a} e^{-\lambda_0 r_0} - 1 = 0. \tag{27}
\]

Solving \( i(t, a) \) by integrating the second equation in the system (7) finds that

\[
i(t, a) = \begin{cases}
\dot{i}(t-a, 0) e^{-\tau_2 d_2 a}, & a \leq t, \\
\dot{i}_0(a-t) e^{-\tau_2 d_2 t}, & a > t,
\end{cases}
\]

which shows that \( i(t, a) \leq \dot{i}(t, a) \) for any \( t \geq t_1 + r_0 \). Therefore, we have \( V_I(t) \leq \dot{V}_I(t) \) by the comparison principle again and the third equation of (7). Thus

\[
(i(t, a), V_I(t)) \leq (\dot{i}_0(a) e^{\lambda_0 t}, \dot{V}_{I0} e^{\lambda_0 t}), \quad t \geq t_1 + r_0.
\]

Since, from (27), \( \lambda_0 < 0 \) as long as \( \varepsilon \in \left( 0, \frac{1 - R_0}{R_0} T_0 \right) \), we see that

\[
\lim_{t \to +\infty} (i(t, a), V_I(t)) = (0, 0).
\]
Hence, when \( t \to +\infty \), the first equation in (7) converges to the equation

\[
\frac{dT'(t)}{dt} = \tau_2 \left( h - d_1 T(t) + r T(t) \left( 1 - \frac{T(t)}{K} \right) \right),
\]

which implies that

\[
\lim_{t \to +\infty} T(t) = T_0.
\]

Finally, applying the asymptotic autonomous semi-flow theory (see Corollary 4.3 in [22]), we deduce that

\[
\lim_{t \to +\infty} T(t) = T_0.
\]

Consequently, if \( R_0 < 1 \), then

\[
\lim_{t \to +\infty} (T(t), i(t, a), V_I(t)) = (T_0, 0, 0).
\]

The proof is completed. \( \square \)

5. **Uniform persistence of infection.** In this section, we would like to establish the sufficient conditions guaranteeing the persistence of System (3).

Firstly, we observe that, for a solution \( z(t) \) of System (15),

\[
\|z(t)\|_Z = \|x(t)\|_C = \max_{\theta \in [-r_0, 0]} \|y_i(\theta, a)\|_Y = \max_{\theta \in [-r_0, 0]} \|w_i(\theta, a)\|_{L^1} = \max_{\theta \in [-r_0, 0]} \left( \|\mu_i(\theta, a)\|_{L^1} + \|\iota_i(\theta, a)\|_{L^1} \right).
\]

Then from Theorem 2.1, we obtain

\[
\limsup_{t \to +\infty} \|z(t)\|_Z \leq \frac{h + r T_0}{\min\{d_1, d_2\}} \left( 1 + \frac{(1 - \eta_1)\alpha^*}{d_3} \right),
\]

which means that \( z(t) \) is ultimately bounded. Now we set

\[
\Gamma = \left\{ z(t) : z(t) \in Z_{0+}, \|z(t)\|_Z \leq \frac{h + r T_0}{\min\{d_1, d_2\}} \left( 1 + \frac{(1 - \eta_1)\alpha^*}{d_3} \right) \right\}
\]

then the omega limit set of (15) is contained in \( \Gamma \).

We first establish the result of weak persistence in the sequel. For this we prove that

**Lemma 5.1.** If \( R_0 > 1 \) and \( \frac{h}{d_1 T_0} R_0 > 1 \), then there exists a constant \( \varepsilon_0 > 0 \) such that any solution \((T(t), i(t, a), V_I(t))\) of (7)-(8) satisfies that

\[
\limsup_{t \to +\infty} (1 - \eta_0)\beta V_I(t) > \varepsilon_0.
\]

**Proof.** Assume conversely that for any \( \varepsilon \in \left( 0, \frac{h \min\{d_1, d_2\}}{h + r T_0} \right) \), there exists a sufficiently large constant \( T_1 > 0 \) such that

| (28) |

\[
T'(t) \geq \tau_2 h - \tau_2 d_1 T(t) - \tau_2 \varepsilon T(t - r_0).
\]

In addition, from (10), there exists a \( T_2 > 0 \) such that \( T(t - r_0) \leq \frac{h + r T_0}{\min\{d_1, d_2\}} \) for \( t \geq T_2 + r_0 \). Hence we further obtain that

\[
T'(t) \geq \tau_2 h - \tau_2 \varepsilon \frac{h + r T_0}{\min\{d_1, d_2\}} - \tau_2 d_1 T(t), \text{ for all } t \geq \max\{T_1, T_2\} + r_0,
\]

\[
\frac{dT'(t)}{dt} = \tau_2 \left( h - d_1 T(t) + r T(t) \left( 1 - \frac{T(t)}{K} \right) \right),
\]

which implies that

\[
\lim_{t \to +\infty} T(t) = T_0.
\]

Finally, applying the asymptotic autonomous semi-flow theory (see Corollary 4.3 in [22]), we deduce that

\[
\lim_{t \to +\infty} T(t) = T_0.
\]

Consequently, if \( R_0 < 1 \), then

\[
\lim_{t \to +\infty} (T(t), i(t, a), V_I(t)) = (T_0, 0, 0).
\]

The proof is completed. \( \square \)
which implies
\[ (T(t)e^{\tau_2 d_1 t})' \geq \tau_2 \left( h - \varepsilon \frac{h + r T_0}{\min\{d_1, d_2\}} \right) e^{\tau_2 d_1 t}. \]

Then, integrating the above equation from \( t - r_0 \) to \( t \), we find
\[ T(t) \geq e^{-d_1 \tau_1} T(t - r_0) + \frac{1 - e^{-d_1 \tau_1}}{d_1} \left( h - \varepsilon \frac{h + r T_0}{\min\{d_1, d_2\}} \right) \]
for \( t \geq \max\{T_1, T_2\} + 2r_0 \). Substituting (29) into (28), we infer that, for \( t \geq \max\{T_1, T_2\} + 2r_0 \)
\[ T'(t) \geq \tau_2 h + \frac{\tau_2 \varepsilon (e^{d_1 \tau_1} - 1)}{d_1} \left( h - \varepsilon \frac{h + r T_0}{\min\{d_1, d_2\}} \right) - \tau_2 \left( d_1 + \varepsilon e^{d_1 \tau_1} \right) T(t) \]
which yields that
\[ \limsup_{t \to +\infty} T(t) \geq \liminf_{t \to +\infty} T(t) \geq \frac{h}{d_1 + \varepsilon e^{d_1 \tau_1}}. \]
Set \( \kappa(t) = i(t, 0) \), then from the fourth equation of (7) we have
\[ \kappa(t) \geq \frac{\tau_2 (1 - \eta_0) \beta h}{d_1 + \varepsilon e^{d_1 \tau_1}} V_I(t - r_0), \]
provided \( t \) is sufficiently large. Thus from the third equation of (7) and (9), it follows that
\[ V'_I(t) \geq \tau_2 (1 - \eta_1) \int_0^t \alpha(a) \kappa(t - a) e^{-\tau_2 d_2 a} da - \tau_2 d_3 V_I(t). \]
Conducting Laplace transforms on both sides of (30) and (31) gives that
\[ \hat{\kappa}(s) \geq \frac{\tau_2 (1 - \eta_0) \beta h e^{-r_0 s}}{d_1 + \varepsilon e^{d_1 \tau_1}} \hat{V}_I(s), \]
in which \( \hat{A}(s) = \int_0^{+\infty} \alpha(a) e^{-\tau_2 d_2 a} da \), \( \hat{\kappa}(s) \) and \( \hat{V}_I(s) \) denote the Laplace transform of \( \kappa \) and \( V_I \), respectively. Due to (32) and (33), we then deduce that
\[ \hat{\kappa}(s) \geq \frac{\tau_2^2 (1 - \eta_0) (1 - \eta_1) \beta h e^{-r_0 s} \hat{A}(s)}{(d_1 + \varepsilon e^{d_1 \tau_1}) (\tau_2 d_3 + s)} \hat{\kappa}(s) + \frac{\tau_2 (1 - \eta_0) \beta h e^{-r_0 s}}{(d_1 + \varepsilon e^{d_1 \tau_1}) (\tau_2 d_3 + s)} \hat{V}_I(s) \]
Define now \( K(\varepsilon, s) = \frac{\tau_2^2 (1 - \eta_0) (1 - \eta_1) \beta h e^{-r_0 s} \hat{A}(s)}{(d_1 + \varepsilon e^{d_1 \tau_1}) (\tau_2 d_3 + s)} \), then from the assumption \( \frac{h}{d_1 + \varepsilon e^{d_1 \tau_1}} R_0 \geq 1 \) we get easily
\[ \lim_{\varepsilon, s \to 0} K(\varepsilon, s) = \frac{(1 - \eta_0) (1 - \eta_1) \beta h}{d_1 d_3} K_0 = \frac{h}{d_1 T_0} R_0 \geq 1, \]
which is impossible, since \( K(\varepsilon, s) \) should be strictly less than 1 from (8) and (34). Consequently, there exists a constant \( \varepsilon_0 > 0 \) such that for all solutions \( (T(t), i(t, a), V_I(t)) \) of (7), with initial conditions (8) satisfy
\[ \limsup_{t \to +\infty} (1 - \eta_0) \beta V_I(t) > \varepsilon_0. \]
\[ \Box \]
By virtue of this lemma, we can now study readily the weak uniform persistence for System (3). Indeed, based on (11), there exists a $T_3 > 0$ such that $V_I(t-r_0) \leq \frac{(1-\eta_0)\mu_1(h+rT_0)}{d_3 \min\{d_1,d_2\}} := \mu$ for $t \geq T_3 + r_0$. Therefore,

$$T'(t) \geq \tau_2 h - \tau_2 d_1 T(t) - \tau_2 \mu_0 T(t-r_0),$$

where $\mu_0 = (1 - \eta_0)\beta \mu$. From Lemma 5.1, we have already known that $T(t-r_0) \leq \frac{h+rT_0}{\min\{d_1,d_2\}}$ for $t \geq T_2 + r_0$. Thus it follows from (36) that

$$T'(t) \geq \tau_2 h - \tau_2 \mu_0 \frac{h + rT_0}{\min\{d_1,d_2\}} - \tau_2 d_1 T(t),$$

for all $t \geq \max\{T_2, T_3\} + r_0$, which implies

$$(T(t)e^{-\tau_2 \int t_0^t})' \geq \tau_2 \left(h - \mu_0 \frac{h + rT_0}{\min\{d_1,d_2\}}\right) e^{-\tau_2 \int t_0^t}.$$ 

So we can infer that

$$T(t) \geq e^{-d_1 \tau_1} T(t-r_0) + \frac{1 - e^{-d_1 \tau_1}}{d_1} \left(h - \mu_0 \frac{h + rT_0}{\min\{d_1,d_2\}}\right),$$

for $t \geq \max\{T_2, T_3\} + 2r_0$. Then, from (36) and (37), we obtain that, for $t \geq \max\{T_2, T_3\} + 2r_0$,

$$T'(t) \geq \tau_2 h + \frac{\tau_2 \mu_0 (e^{d_1 \tau_1} - 1)}{d_1} \left(h - \mu_0 \frac{h + rT_0}{\min\{d_1,d_2\}}\right) - \tau_2 (d_1 + \mu_0 e^{d_1 \tau_1}) T(t).$$

Hence, if we assume that $h + \frac{\mu_0 (e^{d_1 \tau_1} - 1)}{d_1} \left(h - \mu_0 \frac{h + rT_0}{\min\{d_1,d_2\}}\right) > 0$, we then derive

$$\limsup_{t \to +\infty} T(t) \geq \frac{m}{d_1 + \mu_0 e^{d_1 \tau_1}}.$$ 

(38)

On the other hand, combining (35) with (38) implies that $\kappa(t)$ satisfies

$$\limsup_{t \to +\infty} \kappa(t) \geq \frac{\tau_2 m \eta_0}{d_1 + \mu_0 e^{d_1 \tau_1}},$$

which shows that

$$\limsup_{t \to +\infty} \int_0^t i(t,a) \, da = \limsup_{t \to +\infty} \int_0^t \kappa(t-a) e^{-\tau_2 \int a^t} \, da \geq \frac{m \eta_0}{d_2 (d_1 + \mu_0 e^{d_1 \tau_1})} > 0.$$ 

(39)

Now, in view of Lemma 5.1, (38) and (39), we arrive at the following result on the weak uniform persistence of System (7) and (3).

**Theorem 5.2.** If $R_0 > 1$, $\frac{h}{d_1 T_0} R_0 \geq 1$ and $h + \frac{\mu_0 (e^{d_1 \tau_1} - 1)}{d_1} \left(h - \mu_0 \frac{h + rT_0}{\min\{d_1,d_2\}}\right) > 0$, then there exists a constant $\eta > 0$ such that any solution $(T(t), i(t,a), V_I(t))$ of (7)-(8) (equivalently of System(3)), satisfies

$$\limsup_{t \to +\infty} T(t) \geq \eta, \limsup_{t \to +\infty} \|i(t,a)\|_{L_1} \geq \eta, \limsup_{t \to +\infty} V_I(t) \geq \eta.$$

In what follows, we further investigate the uniformly strong persistence of System (15) by proving the existence of a global attractor. To this end, we present here some basic definitions and results on infinite-dimensional dynamical systems (see [5]). Let $(T(t))_{t \geq 0}$ be a semi-flow on Banach space $X$.

**Definition 5.3.** The semi-flow $T(t)$ is asymptotically smooth if for any nonempty, bounded and closed set $B \subset X$ for which $T(t)(B) \subset B$, there is a compact set $C \subset B$ such that $C$ attracts $B$. 

For a semi-flow \((T(t))_{t \geq 0}\), one has that

**Proposition 1.** Suppose that, for each \(t \geq 0\), the semi-flow \(T(t) = T_1(t) + T_2(t)\) verifies

(i) There is a continuous function \(g : \mathbb{R}_+ \times \mathbb{R}_+ \mapsto \mathbb{R}_+\) with \(k(t, r) \to 0\) as \(t \to +\infty\), such that \(T_1(t) x \leq k(t, r)\), for \(|x| < r\).

(ii) \(T_2(t)\) is completely continuous.

Then \(T(t), t \geq 0\), is asymptotically smooth on \(X\).

**Definition 5.4.** The semi-flow \(T(t)\) is said to be point dissipative on \(X\) if there is a bounded set \(B \subset X\) such that \(B\) attracts every point of \(X\) under \(T(t)\).

**Definition 5.5.** An invariant set \(A\) is said to be a global attractor if \(A\) is a maximal compact invariant set which attracts each bounded set \(B \subset X\).

The following proposition is a powerful tool of proving the existence of a global attractor.

**Proposition 2.** If \(T(t) : X \mapsto X, t \geq 0\), is asymptotically smooth, point dissipative and orbits of bounded sets are bounded, then there exists a global attractor \(A\) for the semi-flow \((T(t))_{t \geq 0}\).

To discuss the strong persistence result for System (15), we need first to establish the existence of a global attractor for the solution semi-flow of (15) and, correspondingly, we require the initial functions satisfy more conditions on smoothness and monotony to some extent. That is, we impose in this part the following initial conditions on (15).

\[
\begin{align*}
T_0(\theta) &= \phi(\theta) \in C^1([-r_0, 0], \mathbb{R}_+), \\
i(0, a) &= i_0(a) \in L^1((0, +\infty), \mathbb{R}_+), \\
V_0(\theta) &= \psi(\theta) \in C^1([-r_0, 0], \mathbb{R}_+), \psi' \geq 0.
\end{align*}
\]

Then we have the result on existence of a global attractor for (15) as below.

**Lemma 5.6.** The solution semi-flow \((U(t))_{t \geq 0}\) of System (15) has a global attractor.

**Proof.** To prove this assertion, we show that \((U(t))_{t \geq 0}\) satisfies the assumptions of Proposition 2.

First of all, since the solutions of (15) are all contained in \(\Gamma\) from our previous discussion, the semi-flow \((U(t))_{t \geq 0}\) defined in Theorem 2.6 is point dissipative. Meanwhile, it’s obvious that the orbits from bounded sets are bounded for \((U(t))_{t \geq 0}\) from the proof of Theorem 2.1.

Now we apply Proposition 1 to prove that \((U(t))_{t \geq 0}\) is asymptotically smooth. To do so, we first decompose (12) into two parts as

\[
\begin{align*}
\begin{cases}
\frac{\partial \hat{w}(t, a)}{\partial t} + \frac{\partial \hat{w}(t, a)}{\partial a} = -D \hat{w}(t, a), \\
\hat{w}(t, 0) = 0, \\
\hat{w}_0(\theta, a) = w_0(\theta, a);
\end{cases} & \quad (41) \\
\begin{cases}
\frac{\partial \hat{w}(t, a)}{\partial t} + \frac{\partial \hat{w}(t, a)}{\partial a} = -D \hat{w}(t, a), \\
\hat{w}(t, 0) = B(\hat{w}_l(\theta, a)), \\
\hat{w}_0(\theta, a) = 0.
\end{cases} & \quad (42)
\end{align*}
\]
It is clear that (41) and (42) can be respectively transformed into the following Cauchy problems in the similar ways as in Section 2.

\[
\begin{aligned}
\frac{d}{dt} \tilde{z}(t) &= \Lambda \tilde{z}(t), \quad t \geq 0, \\
\tilde{z}_0 := \tilde{z}(0) &= z_0 \in Z_0; \\
\frac{d}{dt} \hat{z}(t) &= \Lambda \hat{z}(t) + H(\hat{z}(t)), \quad t \geq 0, \\
\hat{z}_0 := \hat{z}(0) &= 0 \in Z_0.
\end{aligned}
\] 

Equations (43) and (44) can be respectively transformed into the following inequalities.

Let \( U_1(t) \) and \( U_2(t) \) be the solution semi-flows of Systems (43) and (44), respectively. Then we have \( U(t) = U_1(t) + U_2(t) \).

Next we verify for \( U(t) \) that all the conditions of Proposition 1 are fulfilled. Set

\[
\nu(t) = \int_0^{+\infty} \hat{\rho}(t,a) da + \int_0^{+\infty} \hat{i}(t,a) da + \int_0^{+\infty} \hat{\mu}(t,a) da,
\]

we can obtain the inequality \( \nu'(t) \leq d\nu(t) \) from the first equation of (41). Hence, \( \nu(t) \leq \max_{\theta \in [-r_0, 0]} \nu(0) e^{-dt} \). Consequently,

\[
\|U_1(t)z_0\| = \|\tilde{z}(t)\| \leq \max_{\theta \in [-r_0, 0]} \nu(0) e^{-dt} = \|z_0\| e^{-dt},
\]

which implies the condition (i) of Proposition 1 is satisfied.

Subsequently we show that \( U_2(t) \) is completely continuous on \( Z_{0+} \) for each \( t \).

Namely, for any bounded set \( B \subset Z_{0+}, \overline{U} := \{U_2(t)z_0 : z_0 \in B\} \) is relatively compact in \( Z_{0+} \). Obviously, we just need to show the set \( \overline{X} := \{\hat{x}(t) : (0, \hat{x}(t))^T \in \overline{U}\} \) is relatively compact in \( C([-r_0, 0]; Y) \). We employ the Ascoli-Arzelà theorem to prove this in two steps as below.

**Step 1.** We show that \( \overline{Y} := \{\hat{x}(t, \theta) : \hat{x}(t) \in \overline{X}\} \) is relatively compact in \( Y \) for any \( \theta \in [-r_0, 0] \).

Initially from (42) we have

\[
\hat{i}(t,a) = \begin{cases} 
\hat{k}(t-a) e^{-\tau_2 d_{2a}}, & a \leq t, \\
0, & a > t,
\end{cases}
\]

where \( \hat{k}(t) = \hat{i}(t, 0) = \tau_2 (1 - \eta_0) \beta T(t - r_0) V_I(t - r_0) \). Since for \( z_0 \in B, \hat{k}(t), T(t), V_I(t) \) and \( I(t) \) are all bounded for \( t \geq 0 \) or \( t \geq -r_0 \) with initial conditions (40), and so do \( T'(t) \) and \( V_{II}(t) \). Then

\[
|\hat{k}'(t)| = |\hat{i}(t, 0)| = \tau_2 (1 - \eta_0) \beta |T'(t - r_0) V_I(t - r_0) + T(t - r_0) V_{II}(t - r_0)|
\]

is bounded as well. Thus, from (45), there exists a constant \( \delta_1 > 0 \) such that

\[
\left\| \frac{\partial \hat{i}(t,a)}{\partial a} \right\|_{L^1} \leq \int_0^{+\infty} |\hat{k}'(t, a)| e^{-\tau_2 d_{2a}} da + \tau_2 d_2 \int_0^{+\infty} \hat{k}(t, a) e^{-\tau_2 d_{2a}} da \leq \delta_1
\]

which implies \( \frac{\partial \hat{i}(t,a)}{\partial a} \) is bounded in \( L^1((0, +\infty), \mathbb{R}) \). Hence we have \( |I'(t)| \) is also bounded, because

\[
|I'(t)| = \left| \int_0^{+\infty} \frac{\partial \hat{i}(t,a)}{\partial t} da \right| = \left| \int_0^{+\infty} -\frac{\partial \hat{i}(t,a)}{\partial a} - \tau_2 d_2 i(t,a) da \right| 
\]

\[
\leq \left\| \frac{\partial \hat{i}(t,a)}{\partial a} \right\|_{L^1} + \tau_2 d_2 I(t).
\]
On the other hand, one has

\[ \hat{\rho}(t, a) = \begin{cases} \hat{\chi}(t - a)e^{-\tau_2 d_1 a}, & a \leq t, \\ 0, & a > t, \end{cases} \tag{46} \]

where \( \hat{\chi}(t) = \hat{\rho}(t, 0) = \tau_2 h + \tau_2 r T(t) \left( 1 - \frac{T(t) + I(t)}{K} \right) - \tau_2 (1 - \eta_0) \beta T(t - r_0) V_I(t - r_0). \)

Since

\[ \hat{\chi}'(t) = \tau_2 r T(t) \left( 1 - \frac{T(t) + I(t)}{K} \right) - \tau_2 r T(t) \left( \frac{r' T(t) + I'(t)}{K} \right) - \hat{\kappa}'(t), \]

it follows immediately that \( |\hat{\chi}(t)| \) and \( |\hat{\chi}'(t)| \) are both bounded. Hence from (46), we infer that there is a constant \( \delta_2 > 0 \) such that

\[ \left\| \frac{\partial \hat{\rho}(t, a)}{\partial a} \right\|_{L^1} \leq \int_0^{+\infty} |\hat{\chi}'(t - a)| e^{-\tau_2 d_1 a} da + \tau_2 d_1 \int_0^{+\infty} \hat{\chi}(t - a) e^{-\tau_2 d_1 a} da \leq \delta_2. \]

As for \( \hat{\mu}(t, a) \), we find

\[ \hat{\mu}(t, a) = \begin{cases} \hat{\vartheta}(t - a)e^{-\tau_2 d_3 a}, & a \leq t, \\ 0, & a > t, \end{cases} \tag{47} \]

in which \( \hat{\vartheta}(t) = \hat{\mu}(t, 0) = \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a) i(t, a) da. \) Utilizing

\[ \left| \hat{\vartheta}'(t) \right| = \left| \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a) \frac{\partial i(t, a)}{\partial t} da \right| \leq \tau_2 (1 - \eta_1) \alpha^* |I'(t)|, \]

we see readily that \( |\hat{\vartheta}'(t)| \) is bounded too. Hence from (47), we have

\[ \left\| \frac{\partial \hat{\mu}(t, a)}{\partial a} \right\|_{L^1} \leq \int_0^{+\infty} |\hat{\vartheta}'(t - a)| e^{-\tau_2 d_3 a} da + \tau_2 d_3 \int_0^{+\infty} \hat{\vartheta}(t - a) e^{-\tau_2 d_3 a} da \leq \delta_3, \]

for some constant \( \delta_3 > 0 \). Now concluding the above estimates we deduce that

\[ \|\hat{\psi}(t + \theta, a + h) - \hat{\psi}(t, a)\|_{L^1} \leq \int_0^{+\infty} \left| \hat{\rho}(t + \theta, a + h) - \hat{\rho}(t + \theta, a) \right| + \left| \hat{\vartheta}(t + \theta, a + h) - \hat{\vartheta}(t + \theta, a) \right| \] \( \leq \int_0^{+\infty} \left( \left\| \frac{\partial \hat{\rho}(t + \theta, a)}{\partial a} \right\|_{L^1} + \left\| \frac{\partial \hat{\vartheta}(t + \theta, a)}{\partial a} \right\|_{L^1} \right) \cdot |h| \rightarrow 0, \text{ as } h \rightarrow 0. \]

(48)

It then follows from Fréchet-Kolmogorov theorem that \( W = \{\hat{\psi}_l(\theta, a) : (0, \hat{\psi}_l(\theta, a))^T \in \bar{Y} \} \) is precompact in \( L_1 \), and therefore \( \{\hat{x}(t, \theta) : \hat{x}(t) \in \bar{X} \} \) is precompact in \( Y \) for any \( \theta \in [-r_0, 0] \) too.

**Step 2.** We prove that the family \( \bar{X} \) is equicontinuous on \( C([-r_0, 0]; Y) \).

Let \( \theta_1, \theta_2 \in [-r_0, 0] \), then due to the computations in step 1 we get

\[ \|\hat{x}(t, \theta_1) - \hat{x}(t, \theta_2)\|_Y = \|\hat{\psi}(t, \theta_1) - \hat{\psi}(t, \theta_2)\|_Y = \|\hat{\psi}_l(\theta_1, a) - \hat{\psi}_l(\theta_2, a)\|_{L^1} \]

\[ = \int_0^{+\infty} \left| \frac{\partial \hat{\psi}(t + \theta_1, a)}{\partial t} - \frac{\partial \hat{\psi}(t + \theta_2, a)}{\partial t} \right| da + \int_0^{+\infty} \left| \frac{\partial \hat{\psi}_l(t + \theta_1, a)}{\partial t} - \frac{\partial \hat{\psi}_l(t + \theta_2, a)}{\partial t} \right| da + \int_0^{+\infty} \left| \frac{\partial \hat{\psi}(t + \theta_1, a)}{\partial a} - \frac{\partial \hat{\psi}(t + \theta_2, a)}{\partial a} \right| da \]

\[ = \left( \int_0^{+\infty} \left| \frac{\partial \hat{\psi}(t + \theta_1, a)}{\partial t} \right| da + \int_0^{+\infty} \left| \frac{\partial \hat{\psi}_l(t + \theta_1, a)}{\partial t} \right| da + \int_0^{+\infty} \left| \frac{\partial \hat{\psi}(t + \theta_1, a)}{\partial a} \right| da \right) \cdot |\theta_1 - \theta_2|, \tag{49} \]

from which the claim follows immediately.

So, by virtue of Ascoli-Arzéla theorem, we have \( \bar{X} = \{\hat{x}(t) : (0, \hat{x}(t))^T \in \bar{U} \} \) is relatively compact in \( C([-r_0, 0]; Y) \). Consequently \( U_2(t) \) is completely continuous.
for each \( t \geq 0 \). Thus, the assumption (ii) of Proposition 1 is also satisfied and the assertion of this lemma follows. \( \square \)

Now we are in the position to discuss the strong persistence results for System (15). As the following result reveals, the solutions of System (15) have actually the strong persistent property under the same condition of Theorem 5.2.

**Theorem 5.7.** If \( R_0 > 1, \frac{h}{d_1} R_0 \geq 1 \) and \( h + \frac{\mu_0 (e^{d_1 r_1} - 1)}{d_1} \left( h - \frac{\mu_0}{\min \{d_1, d_2\}} \right) > 0 \), then there exists a constant \( \eta > 0 \) such that any solution \((T(t), i(t, a), V_I(t))\) of (7)-(40) (equivalently of System (3)), satisfies

\[
\liminf_{t \to +\infty} T(t) \geq \eta, \quad \liminf_{t \to +\infty} ||i(t, a)||_{L_1} \geq \eta, \quad \liminf_{t \to +\infty} V_I(t) \geq \eta.
\]

**Proof.** We first prove that there exists a positive constant \( \zeta > 0 \) such that

\[
\liminf_{t \to +\infty} (1 - \eta_0) \beta V_I(t) > \zeta.
\]

Define a function \( \rho : Z_{0+} \to \mathbb{R}_+ \) as

\[
\rho(U(t)z_0) := (1 - \eta_0) \beta \max_{\theta \in [r_0, 0]} \|\mu_I(\theta, a)\|_{L_1} = (1 - \eta_0) \beta \max_{\theta \in [r_0, 0]} V_I(t + \theta).
\]

Then from Lemma 5.1 the semi-flow \((U(t))_{t \geq 0}\) of System (15) is uniformly weakly persistent in \( Z_0 \), while lemma 5.6 shows that the semi-flow \((U(t))_{t \geq 0}\) has a global attractor. In addition, by the third equation of System (7), we see easily that \( V_I(t) e^{\tau_2 d_3 t} \) is increasing for \( t \geq -r_0 \). Hence, we have

\[
(1 - \eta_0) \beta \max_{\theta \in [r_0, 0]} V_I(t + \theta) \geq (1 - \eta_0) \beta \max_{\theta \in [r_0, 0]} V_I(s + \theta) e^{-\tau_2 d_3 (t-s)}, \text{ for } t > s.
\]

So \( \rho(U(t)z_0) > 0 \) if \( \rho(U(s)z_0) > 0 \). Then the solution semi-flow \((U(t))_{t \geq 0}\) is uniformly strongly \( \rho \)-persistent by Theorem 2.6 in [23], i.e. there exists a constant \( \eta > 0 \) such that \( \liminf_{t \to +\infty} \rho(U(t)z_0) > \zeta \), which means

\[
\liminf_{t \to +\infty} (1 - \eta_0) \beta V_I(t) > \zeta. \tag{50}
\]

Furthermore, from (38) and (50), we have

\[
\liminf_{t \to +\infty} \frac{i(t, 0)}{t} = \liminf_{t \to +\infty} \frac{\tau_2 (1 - \eta_0) \beta T(t - r_0) V_I(t - r_0)}{1 - \eta_0} \geq \frac{\tau_2 m \zeta}{d_1 + \mu_0 e^{\tau_2 r_1}}.
\]

Therefore, from a variation of the Lebesgue-Fatou Lemma ([24] Section B.2), we obtain

\[
\liminf_{t \to +\infty} ||i(t, a)||_{L_1} \geq \int_0^{+\infty} \liminf_{t \to +\infty} \frac{i(t, a)}{t} da \geq \int_0^{+\infty} \liminf_{t \to +\infty} \frac{i(t - a, 0) e^{-\tau_2 d_3 s}}{d_1 + \mu_0 e^{\tau_2 r_1}} da \geq \frac{m \zeta}{d_2 (d_1 + \mu_0 e^{\tau_2 r_1})}.
\]

Then the proof is completed. \( \square \)

6. **Stability of the positive equilibrium and Hopf bifurcations.** In this section, we investigate the stability and the existence of Hopf bifurcation around \( \bar{z}_* \). We stress here that, as the \( C_0 \)-semigroup \((S(t))_{t \geq 0}\) associated to the linearized system is quasi-compact, we can apply the center manifold Theorem 4.21 and Proposition 4.22 in [12] to reduce the linearized system to an ODE system in finite dimension. As a result, we are able to utilize the Hassard’s Hopf bifurcation theorem in [6] to analyse whether Hopf bifurcations will occur for our situation.
Firstly, we consider the stability of the positive equilibrium by computing the characteristic equation for the linearizing system (21) at \( \bar{W} \) as we did in Section 4. Let \( \tilde{z}(t) = z(t) - \bar{z} = (0 \eta \ 0 g_3 \ \tilde{w}(t)(.)^T \) , then we can derive that for \( \tilde{w}(t)(.) \)

\[
\begin{align*}
\frac{\partial \tilde{w}(t, a)}{\partial t} + \frac{\partial \tilde{w}(t, a)}{\partial a} &= -D \tilde{w}(t, a), \\
\tilde{w}(t, a) &= W_1^* \int_0^{+\infty} \tilde{w}(t, a) da + W_2^* \int_0^{+\infty} \tilde{w}(t, a) da + W_3^* \int_0^{+\infty} \alpha(a) \tilde{w}(t, a) da.
\end{align*}
\]

where

\[
W_1^* = \tau_2 (1 - \eta_0) \begin{pmatrix} -\beta V_{t*} & 0 & -\beta T_{t*} \\ \beta V_{1*} & 0 & \beta T_{t*} \\ 0 & 0 & 0 \end{pmatrix}, \quad W_2^* = \begin{pmatrix} \tau_2 (1 - \frac{2 T_{t*} + T_{x}}{\lambda}) & -\frac{2 T_{t*}}{\lambda} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \\
W_3^* = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ \tau_2 (1 - \eta_1) & 0 \end{pmatrix}.
\]

Substitute \( \tilde{\rho}(t, a) = \tilde{\rho}_0(a) e^{\lambda t} \), \( \tilde{i}(t, a) = \tilde{i}_0(a) e^{\lambda t} \), \( \tilde{\mu}(t, a) = \tilde{\mu}_0(a) e^{\lambda t} \) into (51) to yield that

\[
\begin{align*}
\tilde{\rho}_0(a) &= -(\lambda + \tau_2 d_1) \tilde{\rho}_0(a), \\
\tilde{i}_0(a) &= -(\lambda + \tau_2 d_2) \tilde{i}_0(a), \\
\tilde{\mu}_0(a) &= -(\lambda + \tau_2 d_3) \tilde{\mu}_0(a), \\
\tilde{\rho}_0(0) &= \tau_2 \left( r (1 - \frac{2 T_{t*} + T_{x}}{\lambda}) - (1 - \eta_0) \beta V_{1*} e^{-\lambda \tau_0} \right) \int_0^{+\infty} \tilde{\rho}_0(a) da - \frac{2 T_{t*}}{\lambda} \int_0^{+\infty} \tilde{i}_0(a) da - \tau_2 (1 - \eta_0) \beta T_{t*} e^{-\lambda \tau_0} \int_0^{+\infty} \tilde{\mu}_0(a) da, \\
\tilde{i}_0(0) &= \tau_2 (1 - \eta_0) \beta V_{1*} e^{-\lambda \tau_0} \int_0^{+\infty} \tilde{\rho}_0(a) da + \tau_2 (1 - \eta_0) \beta T_{t*} e^{-\lambda \tau_0} \int_0^{+\infty} \tilde{\mu}_0(a) da, \\
\tilde{\mu}_0(0) &= \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a) \tilde{i}_0(a) da.
\end{align*}
\]

Solving the first three equations of (52), we have

\[
\tilde{\rho}_0(a) = \tilde{\rho}_0(0) e^{-(\lambda + \tau_2 d_1) a}, \quad \tilde{i}_0(a) = \tilde{i}_0(0) e^{-(\lambda + \tau_2 d_2) a}, \quad \tilde{\mu}_0(a) = \tilde{\mu}_0(0) e^{-(\lambda + \tau_2 d_3) a}.
\]

which together with the last three equations in (52) implies that

\[
\begin{align*}
\tilde{\rho}_0(0) &= \frac{\tau_2 r (1 - \frac{2 T_{t*} + T_{x}}{\lambda})}{\lambda + \tau_2 d_1} \tilde{\rho}_0(0) - \frac{\tau_2 r T_{t*}}{\lambda + \tau_2 d_2} \tilde{i}_0(0) - \frac{2 T_{t*}}{\lambda} \tilde{i}_0(0), \\
\tilde{i}_0(0) &= \frac{\tau_2 (1 - \eta_0) \beta V_{1*} e^{-\lambda \tau_0}}{\lambda + \tau_2 d_1} \tilde{\rho}_0(0) + \frac{\tau_2 (1 - \eta_0) \beta T_{t*} e^{-\lambda \tau_0}}{\lambda + \tau_2 d_2} \tilde{\mu}_0(0), \\
\tilde{\mu}_0(0) &= \tau_2 (1 - \eta_1) \int_0^{+\infty} \alpha(a) e^{-(\lambda + \tau_2 d_3) a} da.
\end{align*}
\]

Then we obtain from the first equation and the last two equations in (53), respectively,

\[
\left( \frac{\tau_2 r T_{t*}}{\lambda + \tau_2 d_2} + 1 \right) \tilde{i}_0(0) = \left( \frac{\tau_2 r (1 - \frac{2 T_{t*} + T_{x}}{\lambda})}{\lambda + \tau_2 d_1} - 1 \right) \tilde{\rho}_0(0),
\]

\[
\tilde{i}_0(0) = \frac{\tau_2 (1 - \eta_0) \beta V_{1*} e^{-\lambda \tau_0}}{\lambda + \tau_2 d_1} \tilde{\rho}_0(0) + \frac{\tau_2 (1 - \eta_0) (1 - \eta_1) \beta T_{t*} e^{-\lambda \tau_0}}{\lambda + \tau_2 d_3} \int_0^{+\infty} \alpha(a) e^{-(\lambda + \tau_2 d_3) a} da \tilde{i}_0(0).
\]
In addition, we have known that

\[ \frac{\tau T}{\lambda + \tau d_1} + 1 \]

Multiplying \( \frac{\tau T}{\lambda + \tau d_1} + 1 \) on the both sides of (55) and combining with (54), we find that

\[ \frac{\tau^2 r (1 - 2T + I_3)}{\lambda + \tau d_1} = 1 = \left( \frac{\tau T}{\lambda + \tau d_1} + 1 \right) \frac{r_2 (1 - \eta_0) \beta V_{1 \ast} e^{-\lambda_0}}{\lambda + \tau d_1} \]

By some complex calculations, we then get the characteristic equation as

\[ \Delta_1(\lambda) = \frac{\lambda^3 + \tau_2 a_1 \lambda^2 + \tau_2 a_2 \lambda + \tau_2 a_3 + (\tau_2 a_4 \lambda^3 + \tau_2 a_5 \lambda + \tau_2 a_6) e^{-\lambda \eta_0} + (r_2 a_2 \lambda + \tau_2 a_6) e^{-\lambda_0} e^{-\lambda}}{(\lambda + \tau d_1)(\lambda + \tau d_2)(\lambda + \tau d_3)} \]

where

\[ \begin{align*}
    a_1 &= (d_1 + d_2 + d_3) - r(1 - \frac{2T + I_3}{K}), \\
    a_2 &= (d_1 d_2 + d_2 d_3 + d_1 d_3) - (d_2 + d_3)r(1 - \frac{2T + I_3}{K}), \\
    a_3 &= d_2 d_3[d_1 - r(1 - \frac{2T + I_3}{K})], \\
    a_4 &= (1 - \eta_0) \beta V_{1 \ast}, \\
    a_5 &= (1 - \eta_0) \beta V_{1 \ast}(d_2 + d_3 + \frac{r}{K} T_\ast), \\
    a_6 &= (1 - \eta_0) \beta V_{1 \ast}(d_2 d_3 + \frac{r}{K} T_\ast d_3), \\
    a_7 &= -(1 - \eta_0)(1 - \eta_1) \beta T_\ast d_2 K_0, \\
    a_8 &= -(1 - \eta_0)(1 - \eta_1) \beta T_\ast d_2 K_0[d_1 - r(1 - \frac{2T + I_3}{K})].
\end{align*} \]

We always assume in this part that

(H2) \( (a_1 - a_4)(a_2 - a_5 + a_7) \neq a_3 - a_6 + a_8, \)

(H3) \( a_6 + (a_2 + a_7)a_4 - a_1 a_5 < 0. \)

In addition, for simplicity we only consider in this section the situation that \( \tau_1 = \tau_2 = \tau \). So \( f(\lambda) \) becomes now

\[ f(\lambda) = \lambda^3 + \tau_2 a_1 \lambda^2 + \tau_2 a_2 \lambda + \tau_2 a_3 + (\tau_2 a_4 \lambda^3 + \tau_2 a_5 \lambda + \tau_2 a_6) e^{-\lambda} + (\tau_2 a_2 \lambda + \tau_2 a_6) e^{-\lambda_0} e^{-\lambda}. \]

Let \( \lambda = \tau \zeta \), then \( f(\lambda) = 0 \) is equivalent to

\[ h(\zeta) := \zeta^3 + a_1 \zeta^2 + a_2 \zeta + a_3 + (a_4 \zeta^2 + a_5 \zeta + a_6) e^{-\zeta \tau} + (a_7 \zeta + a_8) e^{-2\zeta \tau} = 0. \]  \tag{56} \]

We first discuss the case that \( \tau = 0 \). For this case, (56) becomes

\[ h(\zeta) = \zeta^3 + (a_1 + a_4) \zeta^2 + (a_2 + a_5 + a_7) \zeta + a_3 + a_6 + a_8. \]  \tag{57} \]

Next we examine for this situation the conditions ensuring all the roots of (57) have negative part. Substituting \( E_\ast \) into the first equation in System (7), we get

\[ d_1 = \frac{h}{T_\ast} + r(1 - \frac{T_\ast + I_3}{K}) - (1 - \eta_0) \beta V_{1 \ast}. \]

In addition, we have known that

\[ T_\ast = \int_0^{+\infty} C_{\ast} e^{-\tau_2 d_1 a} da = \frac{C_{\ast}}{\tau_2 d_1} = \frac{d_3}{(1 - \eta_0)(1 - \eta_1) \beta K_0}. \]
Therefore, by some computations, we find that
\[ a_1 + a_4 = d_1 + d_2 + d_3 - r(1 - \frac{2T_0}{K} + \frac{R}{K}) + (1 - \eta_0)\beta V_1 = d_2 + d_3 + \frac{r T_0}{K} + \frac{h}{T_0} > 0, \]
\[ a_2 + a_3 + a_7 = (d_2 + d_3)(\frac{r T_0}{K} + \frac{h}{T_0}) + (1 - \eta_0)\beta V_1 > 0, \]
\[ a_3 + a_6 + a_8 = (1 - \eta_0)\beta V_1(d_2d_3 + \frac{r T_0}{K}T_0d_3) = a_6 > 0. \]

Thus, applying the Routh-Hurwitz criterion, we see that every root of (57) has strictly negative real part if and only if
\[ (a_1 + a_4)(a_2 + a_3 + a_7) > (a_3 + a_6 + a_8). \] (58)

Hence we obtain immediately that

**Theorem 6.1.** If \( \tau_1 = \tau_2 = 0 \), the condition (H1), (58) are satisfied, then the positive equilibrium \( \bar{z}_* \) of the system (15) (equivalently, \( E_* \) of System (3)) is locally asymptotically stable.

In the case of \( \tau_1, \tau_2 > 0 \), some roots of \( h(\zeta) \) may cross the imaginary axis to the right part. Let \( \zeta = \pm i \omega > 0 \) be purely imaginary roots of (56), then \( \omega \) satisfies
\[ -\omega^3 - a_1\omega^2 + a_2\omega + a_3 + (-a_4\omega^2 + a_5\omega + a_6) e^{-\omega \tau_1} + (a_7\omega + a_8) e^{-2\omega \tau_1} = 0. \]

Note that (H2) implies \( \frac{\omega^3}{2} \neq \frac{\pi}{2} + j\pi, j \in \mathbb{Z} \). Set \( \kappa = \tan \frac{\omega^3}{2} \), then \( e^{-i\omega \tau} = \frac{1-i\kappa}{1+i\kappa}, e^{i\omega \tau} = \frac{1+i\kappa}{1-i\kappa} \). Now, separating the real and imaginary parts, we find that \( \kappa \) satisfies
\[
\begin{cases}
(a_1 - a_4)\omega^2 - (a_3 - a_5 + a_7)\omega & [2\omega^3 - 2(a_2 - a_7)\omega] \kappa = (a_1 + a_4)\omega^2 - (a_3 + a_6 + a_8), \\
\omega^3 - (a_2 - a_5 + a_7)\omega & [-2a_1\omega^2 + 2(a_3 - a_8)\omega] \kappa = \omega^3 - (a_2 + a_5 + a_7)\omega.
\end{cases}
\] (59)

Put
\[
M = \begin{pmatrix}
(a_1 - a_4)\omega^2 - (a_3 - a_5 + a_7)\omega & 2\omega^3 - 2(a_2 - a_7)\omega & (a_1 + a_4)\omega^2 - (a_3 + a_6 + a_8) \\
\omega^3 - (a_2 - a_5 + a_7)\omega & -2a_1\omega^2 + 2(a_3 - a_8)\omega & \omega^3 - (a_2 + a_5 + a_7)\omega
\end{pmatrix},
\]
\[
M_1 = \begin{pmatrix}
(a_1 - a_4)\omega^2 - (a_3 - a_6 + a_8) & 2\omega^3 - 2(a_2 - a_7)\omega \\
\omega^3 - (a_2 - a_5 + a_7)\omega & -2a_1\omega^2 + 2(a_3 - a_8)\omega
\end{pmatrix},
\]
\[
M_2 = \begin{pmatrix}
(a_1 + a_4)\omega^2 - (a_3 + a_6 + a_8) & 2\omega^3 - 2(a_2 - a_7)\omega \\
\omega^3 - (a_2 + a_5 + a_7)\omega & -2a_1\omega^2 + 2(a_3 - a_8)\omega
\end{pmatrix},
\]
\[
M_3 = \begin{pmatrix}
(a_1 - a_4)\omega^2 - (a_3 - a_6 + a_8) & (a_1 + a_4)\omega^2 - (a_3 + a_6 + a_8) \\
\omega^3 - (a_2 - a_5 + a_7)\omega & \omega^3 - (a_2 + a_5 + a_7)\omega
\end{pmatrix}.
\]

and \( D(\omega) = \det(M_1), E(\omega) = \det(M_2), F(\omega) = \det(M_3). \)

If \( D(\omega) = 0 \), then \( E(\omega) = F(\omega) = 0 \), i.e.
\[
F(\omega) = \det(M_3)
= -2a_4\omega^5 + 2(a_6 + a_2a_4 - a_1a_5 + a_4a_7)\omega^3 + 2[(a_3 + a_8)a_5 - a_6(a_2 + a_7)]\omega = 0.
\]

Suppose \( \omega_1^2, \omega_2^2 \) are two roots of the above equality, then
\[
\omega_1^2 + \omega_2^2 = \frac{a_6 + (a_2 + a_7)a_4 - a_1a_5}{a_4},
\]
which trivially contradicts (H3). So we have \( D(\omega) \neq 0 \), thus from (59) we obtain that
\[
\kappa^2 = \frac{E(\omega)}{D(\omega)}, \kappa = \frac{F(\omega)}{D(\omega)}.
\]
which implies that
\[ D(\omega)E(\omega) = F(\omega)^2. \] (60)

Now, simplifying (60) by direct and tedious computations, we find \( \omega \) satisfies
\[ \omega^{12} + S_1 \omega^{10} + S_2 \omega^8 + S_3 \omega^6 + S_4 \omega^4 + S_5 \omega^2 + S_6 = 0. \]

where
\[
S_1 = 2a_1^2 - 4a_2 - a_4,
S_2 = a_1^3(a_1^2 - 4a_2 - a_4^2) + 2a_4(a_6 + a_2a_4 + a_1a_7) + (6a_2^2 - a_4^2 - 2a_7^2) + a_3(a_4 - 2a_1) - (2a_1 + a_4),
S_3 = [a_1(a_1 - a_4)(-2a_2 - a_3)](a_6 + 2a_4(1 - a_8) + (a_2 - a_7)(a_2 + a_5 + a_7))
- [a_2(a_1 + a_4) - (2a_2 + a_3)](a_6 + a_3(a_4 - a_8) - (a_2 - a_7)(a_2 + a_5 + a_7)]
- 2a_4a_6(a_2 + a_7) - (a_6 + a_2a_4 - a_1a_5 + a_4a_7)^2,
S_4 = [a_1(a_6 + 2a_4(1 - a_8))][a_1(2a_3 - a_4) - a_4(a_3 - a_8) - (a_2 - a_7)(a_2 + a_5 + a_7)]
- (a_2 - a_7)(a_2 + a_5 + a_7)[a_1(2a_3 - a_4) - a_4(a_3 - a_8) - (a_2 - a_7)(a_2 + a_5 + a_7)]
+ 2(a_3 - a_8)(a_5a_{10} - a_4a_6) + 2a_6(a_6 + a_2a_4 - a_1a_5 + a_4a_7)(a_2 - a_7),
S_5 = -a_6(a_3 - a_8)a_1(2a_3 - a_4) - a_4(a_3 - a_8) - (a_2 - a_7)(a_2 + a_5 + a_7)]
+ a_6(a_3 - a_8)[a_1(2a_3 - a_4) + a_4(1 - a_8) - (a_2 - a_7)(a_2 + a_5 + a_7)] - a_6^2(a_2 + a_7)^2,
S_6 = -a_6^2(a_3 - a_8)^2 < 0.
\]

Put \( z = \omega^2 \), then \( z \) clearly satisfies
\[ z^6 + S_1 z^5 + S_2 z^4 + S_3 z^3 + S_4 z^2 + S_5 z + S_6 = 0. \] (61)

Notice that \( g(z) := z^6 + S_1 z^5 + S_2 z^4 + S_3 z^3 + S_4 z^2 + S_5 z + S_6 \) is a real valued continuous function with \( g(0) = S_6 < 0 \), so (61) has one positive real root \( \omega^2 \).

From the above discussions, we arrive at the following result.

**Lemma 6.2.** If (H1) – (H3) hold, then (59) has a real root \( \theta_\ast \), and then (56) has a pair of roots \( \pm i \omega_\ast \) when
\[
\tau^j = \begin{cases} 
\frac{2 \arctan \theta_\ast + j 2 \pi}{\omega_\ast}, & j \in \mathbb{N} \ \text{and} \ \omega_\ast > 0, \\
\frac{2 \arctan \theta_\ast + 2(j+1) \pi}{\omega_\ast}, & j \in \mathbb{N} \ \text{and} \ \omega_\ast < 0.
\end{cases}
\] (62)

In the sequel we verify the transversality condition for (56). More precisely, set
\[
\mathcal{G}(\omega, \theta) := \begin{vmatrix} [a_6 - a_4 \omega^2(1 + \theta^2) + 2a_8(-1 - \theta^2 + 4a_7 + \theta)] & [a_4 \omega(1 + \theta^2) + a_1 \omega(1 - \theta^2) + (a_2 - a_7 - 3\omega^2) \theta] \\ [a_5 \omega(1 + \theta^2) + 2a_7 \omega(1 - \theta^2 - 4a_8 \theta)] & [a_3 \omega(1 + \theta^2) + a_2 \omega(1 + 3\omega^2) - \theta^2 - 4a_1 \omega] \end{vmatrix},
\]
we then have that

**Lemma 6.3.** If \( \mathcal{G}(\omega_\ast, \theta_\ast) \neq 0 \), there exists \( \lambda(\tau) = \alpha(\tau) + i \omega(\tau) \) which is the root of (56) for \( \tau \in (\tau^j - \varepsilon, \tau^j + \varepsilon) \) for some small \( \varepsilon > 0 \) satisfying \( \alpha(\tau^j) = 0, \omega(\tau^j) = \omega_\ast \).
Moreover,
\[
\left. \frac{d \text{Re} \lambda(\tau)}{d \tau} \right|_{\tau = \tau^j} > 0, \ j \in \mathbb{N}, \ \text{when} \ \mathcal{G}(\omega_\ast, \theta_\ast) > 0;
\left. \frac{d \text{Re} \lambda(\tau)}{d \tau} \right|_{\tau = \tau^j} < 0, \ j \in \mathbb{N}, \ \text{when} \ \mathcal{G}(\omega_\ast, \theta_\ast) < 0.
\]

**Proof.** This lemma can be proved by applying the similar ways as in the proof of Lemma 2.10 in [2], we omit it here.

Accordingly, we conclude the second main result of this part as follows.

**Theorem 6.4.** Let (H1) – (H3) be satisfied, then the following statements hold true.
(1) If (58) hold, then the positive equilibrium $E_*$ of System (3) is locally asymptotically stable for $\tau \in [0, \tau^0)$.

(2) For any small enough $\varepsilon > 0$, the equilibrium $E_*$ of System (3) is unstable for $\tau \in (\tau^0, \tau^0 + \varepsilon)$.

(3) If $\mathcal{G} (\omega_*, \theta_*) \neq 0$, then there exist a sequence $(\tau_j)_{j \geq 0} \subset (0, +\infty)$ given by (62), such that System (3) undergoes a Hopf bifurcation at the positive equilibrium $E_*$ whenever $\tau$ crosses through $\tau_j$.

7. Numerical simulations. In this part, we provide some numerical simulations to illustrate the theoretical results given in Theorems 4.2, 5.7 and 6.4.

Figure 1. Solutions of the system (3) go to the disease-free steady state, where “T” represents the uninfected T cells, “I” represents the infected T cells, “$V_I$” represents the infectious viral.

(1) We first choose the parameters satisfying the conditions in Theorem 4.2 as follows.

$$h = 2, r = 2, \beta = 0.001, d_1 = 0.3, d_2 = 0.4, d_3 = 0.6,$$
$$\eta_0 = 0.4, \eta_1 = 0.6, K = 30, K_0 = 1, \tau_1 = \tau_2 = 0.4.$$ 

Then we have $R_0 = 0.009 < 1$, and due to Theorem 4.2 the disease-free equilibrium $E_0 = (26.627, 0, 0)$ of System (3) is globally asymptotically stable which is shown well in Fig. 1. Here $(T, I, V_I)$ are the solutions of System (3) with initial conditions

$$T_0 (\theta) = \phi (\theta) \equiv 28, \theta \in [-\tau_1, 0]; I(0) = 2; V_0 (\theta) = \psi (\theta) \equiv 2, \theta \in [-\tau_1, 0].$$

(2) Now we take the parameters as

$$h = 4, r = 0.5, \beta = 0.03, d_1 = 0.5, d_2 = 0.4, d_3 = 0.4,$$
$$\eta_0 = 0.01, \eta_1 = 0.0001, K = 50, K_0 = 2, \tau_1 = \tau_2 = 0.01.$$ 

Then the conditions of Theorem 5.7 are satisfied since $R_0 = 2.967 > 1$, $h + \mu_0 \frac{h+\tau_0}{d_1} R_0 = 1.187 \geq 1$ and $m = h + \mu_0 \frac{h+\tau_0}{d_1} \left( h - \mu_0 \frac{h+\tau_0}{\min\{d_1, d_2\}} \right) = 2.558 > 0$. So, from
Theorem 5.7, the solutions \((T, I, V)\) are persistent as shown by Fig. 2 below. Here the initial conditions are respectively
\[ T_0(\theta) = \phi(\theta) = 20 + \theta, \theta \in [-\tau_1, 0]; \quad I(0) = 0.5; \quad V_0(\theta) = \psi(\theta) = 0.5 + \frac{\theta}{10}, \theta \in [-\tau_1, 0]. \]

**Figure 2.** The infection is persistent.

(3) If we choose the parameters as
\[ h = 2.3, r = 2, \beta = 0.03, d1 = 0.2, d2 = 0.4, d3 = 0.4, \]

\( \eta_0 = 0.05, \eta_1 = 0.5, K = 100, K_0 = 3. \)

It then follows that \((H1) - (H3)\) and \((58)\) are well verified which is certified by some complicated computations. Moreover, we obtain \(\omega_\ast = 1.326, \tau^0 = 0.654.\)

So, according to Theorem 6.4, the positive equilibrium \(E_\ast\) of System (3) is locally asymptotically stable for \(\tau_1, \tau_2 \in (0, \tau^0)\), see Fig. 3. If \(\tau_1, \tau_2\) increase to \(\tau^0 > 1\), the equilibrium \(E_\ast\) of System (3) becomes unstable. In particular, the solutions of System (3) will oscillate periodically, and Hopf bifurcation occurs in this situation around \(E_\ast\), see Fig. 4.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig4.png}
\caption{The solutions oscillate periodically for \(\tau_1 = \tau_2 = 1.\)}
\end{figure}

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