Research Article

Stability and Hopf Bifurcation in a Delayed HIV Infection Model with General Incidence Rate and Immune Impairment

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We investigate the dynamical behavior of a delayed HIV infection model with general incidence rate and immune impairment. We derive two threshold parameters, the basic reproduction number $R_0$ and the immune response reproduction number $R_1$. By using Lyapunov functional and LaSalle invariance principle, we prove the global stability of the infection-free equilibrium and the infected equilibrium without immunity. Furthermore, the existence of Hopf bifurcations at the infected equilibrium with CTL response is also studied. By theoretical analysis and numerical simulations, the effect of the immune impairment rate on the stability of the infected equilibrium with CTL response has been studied.

1. Introduction

In recent years, mathematical models have been proved to be valuable in understanding the dynamics of viral infection (see, e.g., [1–8]). In most virus infections, cytotoxic T lymphocyte (CTL) cells play a significant role in antiviral defense by attacking virus-infected cells. In order to study the role of the population dynamics of the viral infection with CTL response, Nowak and Bangham et al. proposed a basic viral infection model describing the interactions between a replicating virus population and a specific antiviral CTL response, which takes into account four populations: uninfected cells, actively infected cells, free virus, and CTL cells (see, e.g., [1–4, 9, 10]). Now, the population dynamics of viral infection with CTL response has been paid much attention and many properties have been investigated (see, e.g., [11–16]).

Furthermore, the state of latent infection cannot be ignored in many biological models. The infected cells are separated into two distinct compartments, latently infected and actively infected. These latently infected cells do not produce virus and can evade from viral cytopathic effects and host immune mechanisms (see, e.g., [17–20]). Recently, the following model with latent infection and CTL response has been proposed (see, e.g., [11]):

$$
\begin{align*}
\dot{x}(t) &= \lambda - \beta x(t) v(t) - \mu_1 x(t), \\
\dot{u}(t) &= \beta x(t) v(t) - (\sigma + \mu_2) u(t), \\
\dot{y}(t) &= \sigma u(t) - p y(t) z(t) - \mu_3 y(t), \\
\dot{v}(t) &= k y(t) - \mu_4 v(t), \\
\dot{z}(t) &= q y(t) z(t) - \mu_5 z(t),
\end{align*}
$$

where $x(t)$, $u(t)$, $y(t)$, $v(t)$, and $z(t)$ represent the numbers of uninfected cells, latently infected cells, actively infected cells, free virus, and CTLs at time $t$, respectively. Uninfected cells are produced at the rate $\lambda$, die at the rate $\mu_1$, and become infected at the rate $\beta$. The constant $\sigma$ is the rate of latently infected cells translating to actively infected cells and $\mu_3$ is the death rate of actively infected cells. The constant $\mu_2$ represents the death rate of latently infected cells. The constant $p$ is the rate of CTL-mediated lysis and $q$ is the rate of CTL proliferation. The constant $k$ is the rate of production of virus by infected cells and $\mu_5$ is the clearance rate of free virus. The removal rate of CTLs is $\mu_5$. 

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However, in plenty of previous papers, many models are constructed under the assumption that the presence of antigen can stimulate immunity and ignore the immune impairment (see, e.g., [8, 11, 16, 17]). In fact, some pathogens can also suppress immune response or even destroy immunity especially when the load of pathogens is too high such as HIV, HBV (see, e.g., [15, 21–25]). Regoes et al. consider an ordinary differential equation (ODE) model with an immune impairment term $m y z$ (see, e.g., [12, 26, 27]), where $m$ denotes the immune impairment rate. Time delay should be considered in models for CTL response. It is shown that time delay plays an important role to the dynamic properties in models for CTL response (see, e.g., [1, 5, 6, 8, 15]). In fact, antigen stimulation generating CTLs may need a period of time; that is, the CTL response at time $t$ may depend on the numbers of CTLs and infected cells at time $t - \tau$, for a time lag $\tau > 0$ (see, e.g., [1, 5, 13]).

Motivated by the above works, in this paper, we will study a delay differential equation (DDE) model of HIV infection with immune impairment and delayed CTL response. Furthermore, we know that the actual incidence rate is probably not linear over the entire range of $x$ and $v$. Based on the works mentioned above (see, e.g., [21, 28–31]), we propose the following system with general incidence function:

\[
\begin{align*}
\dot{x}(t) &= \lambda - f(x(t), v(t)) v(t) - \mu x(t), \\
\dot{u}(t) &= f(x(t), v(t)) v(t) - (\sigma + \mu_2) u(t), \\
\dot{y}(t) &= \sigma u(t) - p y(t) z(t) - \mu_3 y(t), \\
\dot{z}(t) &= k y(t) - \mu_4 v(t), \\
\dot{v}(t) &= q y(t - \tau) z(t - \tau) - \mu_5 z(t) - m y(t) z(t), \\
\end{align*}
\]

where the state variables $x(t), u(t), y(t), v(t),$ and $z(t)$ and the parameters $\lambda, \sigma, p, k, q, \mu_1, \mu_2, \mu_3, \mu_4,$ and $\mu_5$ have the same biological meaning as in system (1). $m$ is the immune impairment rate. Suppose all the parameters are nonnegative. We assume that the incidence rate is the general incidence function $f(x, v)v$, where $f \in C^1([0, +\infty) \times [0, +\infty], R)$ satisfies the following hypotheses:

(H1) $f(x, v)v \geq 0$, for all $x \geq 0$ and $v \geq 0$, $f(x, v) = 0$ if and only if $x = 0$;

(H2) $\partial f(x, v) / \partial x > 0$, for all $x \geq 0$ and $v \geq 0$;

(H3) $\partial f(x, v) / \partial v \leq 0$, for all $x \geq 0$ and $v \geq 0$;

(H4) $\partial^2 f(x, v)v / \partial v \partial v > 0$, for all $x > 0$ and $v \geq 0$.

Clearly, the hypotheses can be satisfied by different types of the incidence rate including the mass action, the Holling type II function, the saturation incidence, Beddington-DeAngelis incidence function, Crowley-Martin incidence function, and the more generalized incidence functions (see, e.g., [4, 6, 17, 32, 33]). Further, in order to study the global stability of the equilibria of system (2) by the method of Lyapunov functionals, we assume the following hypotheses hold (see, e.g., [28]):

(H5) $\int_{x_0}^{x} (f(s, 0) / f(s, 0)) ds \to +\infty$, as $x \to +\infty$ or $x \to 0^+$;

(H6) $\int_{x_1}^{x} (f(x_1, v_1) / f(s, v_1)) ds \to +\infty$, as $x \to +\infty$ or $x \to 0^+$;

(H7) $\int_{x^*}^{x} (f(x^*, v^*) / f(s, v^*)) ds \to +\infty$, as $x \to +\infty$ or $x \to 0^+$.

The main purpose of this paper is to carry out a complete theoretical analysis on the global stability of the equilibria of system (2). The organization of this paper is as follows. In Section 2, we consider the nonnegativity and boundedness of the solutions and the existence of the equilibria of system (2). In Section 3, we consider the global stability of the infection-free equilibrium $E_0$ and the infected equilibrium without immunity $E_1$ by constructing suitable Lyapunov functionals and using LaSalle invariance principle. In Section 4, we discuss the local stability of the infected equilibrium with CTL response $E^*$ and the existence of Hopf bifurcations. Finally, in Section 5, the brief conclusions are given and some numerical simulations are carried out to illustrate the main results.

2. Basic Results

2.1. The Nonnegativity and Boundedness of the Solutions. According to biological meanings, the initial condition of system (2) is given as follows:

\[
\begin{align*}
x(\theta) &= \varphi_1(\theta), \\
u(\theta) &= \varphi_2(\theta), \\
y(\theta) &= \varphi_3(\theta), \\
v(\theta) &= \varphi_4(\theta), \\
z(\theta) &= \varphi_5(\theta),
\end{align*}
\]

where $\theta \in [-\tau, 0]$ and $(\varphi_1, \varphi_2, \varphi_3, \varphi_4, \varphi_5) \in C = C([-\tau, 0], R^5)$ and $C$ is the Banach space of the continuous functions mapping the interval $[-\tau, 0]$ into $R^5$. $R^5_+ = \{(x_1, x_2, x_3, x_4, x_5) \mid x_i \geq 0, i = 1, 2, 3, 4, 5\}$.

Under the initial condition (3), it easily shows that the solution of system (2) is unique and nonnegative for all $t \geq 0$ and ultimately bounded. It has the following result.

Proposition 1. Under the initial condition (3), the solution of system (2) is unique and nonnegative for all $t \geq 0$ and also ultimately bounded, when (H1)–(H7) are satisfied.

Proof. The uniqueness and nonnegativity of the solution $(x(t), u(t), y(t), v(t), z(t))$ can be easily proved by using the theorems in [34, 35].

Next, for $t \geq 0$, define

\[
\begin{align*}
L(t) &= x(t) + u(t) + y(t) + \frac{\mu_5}{2k} y(t) + \frac{p}{2q} z(t + \tau). 
\end{align*}
\]

By the nonnegativity of the solutions, it follows that, for $t \geq 0,$

\[
\begin{align*}
L'(t) &= \lambda - \mu x(t) - \mu_2 u(t) - \frac{\mu_3}{2} y(t) - \frac{\mu_4}{2k} v(t) - \frac{p \mu_5}{2q} z(t + \tau) - \frac{p}{2} y(t) z(t) \\
&\quad - \frac{pm}{2q} y(t + \tau) z(t + \tau) < \lambda - \gamma L(t),
\end{align*}
\]
where \( y = \min\{\mu_1, \mu_2, \mu_3/2, \mu_4, \mu_5\} \). Thus, it has that \( \limsup_{t \to +\infty} L(t) \leq \lambda/y \), from which it has that the solution \((x(t), u(t), y(t), v(t), z(t)) \) is ultimately bounded.

2.2. The Existence of the Equilibria. Next, we consider the existence of the equilibria. The equilibrium of system (2) satisfies

\[
\begin{align*}
\lambda - f(x, v) - \mu_1 x &= 0, \\
f(x, v) - (\sigma + \mu_2) u &= 0, \\
\sigma u - p y z - \mu_3 y &= 0, \\
k y - \mu_4 v &= 0, \\
q y z - \mu_5 z - m y z &= 0.
\end{align*}
\]

If \( u = 0, y = 0, v = 0, \) and \( z = 0 \), system (2) has only one equilibrium, that is, the infection-free equilibrium \( E_0 = (x_0, 0, 0, 0, 0) \), where \( x_0 = \lambda/\mu_1 \).

If \( u \neq 0, y \neq 0, v \neq 0, \) and \( z = 0 \), we have

\[
\begin{align*}
F(x) &= f\left(x, \frac{k \sigma (\lambda - \mu_1 x)}{\mu_3 \mu_4 (\sigma + \mu_2)} - \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma}\right) = 0, \\
y &= \frac{\sigma (\lambda - \mu_1 x)}{\mu_3 (\sigma + \mu_2)}, \\
u &= \frac{\lambda - \mu_1 x}{\sigma + \mu_2}, \\
v &= \frac{k \sigma (\lambda - \mu_1 x)}{\mu_3 \mu_4 (\sigma + \mu_2)}.
\end{align*}
\]

Since \( \nu > 0 \), we have that \( x < \lambda/\mu_1 \). Hence, we only need to consider the case of \( x < \lambda/\mu_1 \).

Consider the following function defined on the interval \((0, \lambda/\mu_1)\) by

\[
F(x) = f\left(x, \frac{k \sigma (\lambda - \mu_1 x)}{\mu_3 \mu_4 (\sigma + \mu_2)} - \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma}\right).
\]

Under hypotheses (H2) and (H3), we have

\[
F'(x) = \frac{\partial f}{\partial x} + \frac{\partial f}{\partial y} \left( -k \sigma \mu_4 \frac{\sigma}{\mu_3 \mu_4 (\sigma + \mu_2)} \right) > 0.
\]

We know that the function \( F(x) \) is strictly monotonically increasing with respect to \( x \). Denote the basic reproduction number \( R_0 \) of system (2) by

\[
R_0 = \frac{k \sigma f(\lambda/\mu_1, 0)}{\mu_3 \mu_4 (\sigma + \mu_2)}.
\]

Clearly, we have

\[
F(0) = -\frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma} < 0,
\]

\[
F\left(\frac{\lambda}{\mu_1}\right) = f\left(\frac{\lambda}{\mu_1}, 0\right) - \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma} = \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma} (R_0 - 1).
\]

It has that there exists a unique \( x_1 \in (0, \lambda/\mu_1) \) such that \( F(x_1) = 0 \), if \( R_0 > 1 \). Then we can compute \( u_1, y_1 \) and \( v_1 \) by (8). Hence, we get the unique infected equilibrium without immunity \( E_1 = (x_1, u_1, y_1, v_1, z_1, 0) \).

If \( z \neq 0 \) and \( q > m \), we get the following equations:

\[
\begin{align*}
f\left(x, \frac{k \mu_5}{\mu_4 (q - m)}\right) - \frac{k \mu_5}{\mu_4 (q - m)} - \lambda + \mu_1 x &= 0, \\
u &= \frac{\lambda - \mu_1 x}{\sigma + \mu_2}, \\
y &= \frac{\mu_5}{q - m} > 0, \\
v &= \frac{k \mu_5}{\mu_4 (q - m)} > 0, \\
z &= \frac{(\lambda - \mu_1 x)(q - m) - \mu_3 \mu_5 (\sigma + \mu_2)}{\mu_1 (q - m)\sigma}.
\end{align*}
\]

Hence, the existence of the equilibrium requires \( \bar{x} > 0 \) and (13) has a solution on the interval \((0, \bar{x})\).

Denote

\[
\bar{R} = \frac{\lambda (q - m)\sigma}{\mu_3 \mu_5 (\sigma + \mu_2)}.
\]

Hence, if \( \bar{R} > 1 \), it has \( \bar{x} > 0 \). Denote

\[
G(x) = f\left(x, \frac{k \mu_5}{\mu_4 (q - m)}\right) - \frac{k \mu_5}{\mu_4 (q - m)} - \lambda + \mu_1 x.
\]

Under hypothesis (H2), we know that the function \( G(x) \) is strictly monotonically increasing with respect to \( x \). Clearly, we have

\[
G(0) = -\lambda < 0,
\]

\[
G(\bar{x}) = f\left(\bar{x}, \frac{k \mu_5}{\mu_4 (q - m)}\right) - \frac{k \mu_5}{\mu_4 (q - m)} - \lambda + \mu_1 \bar{x}
\]

\[
= f(\bar{x}, \frac{k \mu_5}{\mu_4 (q - m)}) - \frac{k \mu_5}{\mu_4 (q - m)} - \mu_3 \mu_5 (\sigma + \mu_2)
\]

\[
= \frac{\mu_3 \mu_5 (\sigma + \mu_2)}{(q - m)\sigma} \left( R_1 - 1 \right),
\]

where

\[
R_1 = \frac{k \sigma f(\bar{x}, k \mu_5 \mu_4 (q - m))}{\mu_3 \mu_4 (\sigma + \mu_2)}.
\]

Hence, we have that there exists \( x^* \in (0, \bar{x}) \) such that \( G(x^*) = 0 \), if \( \bar{R} > 1 \) and \( R_1 > 1 \). Then we can compute \( u^*, y^*, v^* \), and \( z^* \) by (14) and (15).
Denote the immune response reproduction number of system (2) as \( R_1 \). Therefore, we have that there exists a unique infected equilibrium with CTL response \( E^* = (x^*, u^*, y^*, v^*, z^*) \), if \( R > 1 \) and \( R_1 > 1 \). This proves the following theorem.

**Theorem 2.** Suppose that hypotheses (H1)–(H4) are satisfied; the following conclusions hold.

(i) System (2) always has an infection-free equilibrium \( E_0 \).
(ii) System (2) has an infected equilibrium without immunity \( E_1 \) if \( R_0 > 1 \).
(iii) System (2) has an infected equilibrium with immunity \( E^* \) if \( R > 1 \) and \( R_1 > 1 \).

From hypotheses (H1)–(H3), it is clear that \( R_1 < R_0 \). In order to study the global stability of the infected equilibrium \( E_1 \) in the next section, we give the following remark.

**Remark 3.** Suppose that \( R > 1 \) is satisfied; then the following results hold:

(i) If \( R_1 > 1 \), then \( (q - m)/\mu_5 > 1 \).
(ii) If \( R_1 \leq 1 \), then \( (q - m)/\mu_5 \leq 1 \).

Let us give the proof of Remark 3. Firstly, for Case (i), since \( R_1 > 1 \), then

\[
F(x) = f\left(\frac{\kappa \sigma (\lambda - \mu_1 x)}{\mu_5 \mu_4 (\sigma + \mu_2)} - \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma}\right) = \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma} (R_1 - 1) > 0.
\]

Since the function \( F(x) \) is strictly monotonically increasing with respect to \( x \) and \( F(x_1) = 0 \), we have \( x_1 < x \). Therefore

\[
\lambda - \mu_1 x_1 > \lambda - \mu_1 x = \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{\sigma (q - m)}.
\]

Then

\[
\frac{(q - m) y_1}{\mu_5} = \frac{q - m}{\mu_5} \cdot \frac{\sigma (\lambda - \mu_1 x_1)}{\mu_5 (\sigma + \mu_2)} > 1.
\]

Secondly, for Case (ii), since \( R_1 \leq 1 \), then

\[
F(x) = f\left(\frac{\kappa \sigma (\lambda - \mu_1 x)}{\mu_5 \mu_4 (\sigma + \mu_2)} - \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma}\right) = \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{k \sigma} (R_1 - 1) \leq 0.
\]

We have \( x_1 \geq x \). Therefore

\[
\lambda - \mu_1 x_1 \leq \lambda - \mu_1 x = \frac{\mu_3 \mu_4 (\sigma + \mu_2)}{\sigma (q - m)}.
\]

Then

\[
\frac{(q - m) y_1}{\mu_5} = \frac{q - m}{\mu_5} \cdot \frac{\sigma (\lambda - \mu_1 x_1)}{\mu_5 (\sigma + \mu_2)} \leq 1.
\]

### 3. The Global Stability of the Equilibria

In this section, we study the global stability of the equilibria of system (2). Firstly, we analyze the global stability of the infection-free equilibrium \( E_0 \).

**Theorem 4.** Suppose that hypotheses (H1)–(H7) are satisfied. If \( R_0 \leq 1 \), then the infection-free equilibrium \( E_0 \) is globally asymptotically stable for any time delay \( \tau \geq 0 \). If \( R_0 > 1 \), then the infection-free equilibrium \( E_0 \) is unstable for any time delay \( \tau \geq 0 \).

**Proof.** Let \((x(t), u(t), y(t), v(t), z(t))\) be a positive solution of system (2) with the initial condition (3) for \( t \geq 0 \). Motivated by the works in [14, 28, 31, 36, 37], we consider the following Lyapunov functional:

\[
V_1 = x - x_0 - \left( \int_{x_0}^x f(s, 5) \, ds + u + \frac{\sigma + \mu_2}{\sigma} y + \frac{\mu_2}{k \sigma} q \right) - \frac{\sigma + \mu_2}{q - m} z,
\]

where \( \lambda = \mu_1 x_0 \). By (H1)–(H5), it is obvious that \( V_1 \) is positive definite with respect to \( E_0 \). For \( t \geq 0 \), the time derivative of \( V_1 \) along the solutions of system (2) is

\[
\dot{V}_1 = \left( 1 - \frac{f(x, 0)}{f(x, 0)} \right) x + \dot{u} + \frac{\sigma + \mu_2}{\sigma} y + \frac{\mu_2}{k \sigma} q - \frac{\sigma + \mu_2}{q - m} \dot{z}
\]

\[
+ \frac{\sigma + \mu_2}{\sigma} \frac{p}{q - m} \left[ q y(t) \zeta(t) - q y(t - \tau) \zeta(t - \tau) \right] - \mu_1 \left( 1 - \frac{f(x, 0)}{f(x, 0)} \right) f(x, 0) f(x, v)
\]

\[
+ \frac{\mu_2}{k \sigma} \frac{p}{q - m} \mu_5 z
\]

Since hypotheses (H1)–(H3) and \( R_0 \leq 1 \), we have

\[
\mu_1 \left( 1 - \frac{f(x, 0)}{f(x, 0)} \right) f(x, 0) f(x, v) \leq 0,
\]

\[
1 - \frac{f(x, 0)}{f(x, 0)} R_0 \geq 0.
\]
Therefore, $\dot{V}_1 \leq 0$ if $R_0 \leq 1$. Then it follows from stability theorems in [34, 35] that the infection-free equilibrium $E_0$ is stable for any time delay $\tau \geq 0$ if $R_0 \leq 1$.

Furthermore, note that, for each $t \geq 0$, $\dot{V}_1 = 0$ implies that $x(t) = x_0$, $z(t) = 0$. Let $M$ be the largest invariant set in the set

$$
\Gamma_1 = \{(\varphi_1, \varphi_2, \varphi_3, \varphi_4, \varphi_5) \in C| \dot{V}_1 = 0\} \subset \{(\varphi_1, \varphi_2, \varphi_3, \varphi_4, \varphi_5) \in C| \varphi_1(0) = x_0, \varphi_5(0) \}
$$

Clearly, if $\tau \geq \tau_0$ globally at attractive for any time delay $\tau \geq 0$ if $R_0 \leq 1$.

We have from the first four equations of system (2) and the invariance of $M$ that $M = \{E_0\}$. Since any solution of system (2) is bounded, it follows from LaSalle invariance principle (see, e.g., [34, 35]) that the infection-free equilibrium $E_0$ is also globally attractive for any time delay $\tau \geq 0$ if $R_0 \leq 1$.

The characteristic equation of system (2) at the infection-free equilibrium $E_0$ is

$$
(s + \mu_1)(s + \mu_5)s^3 + (\sigma + \mu_2 + \mu_3 + \mu_4)s^2 + ((\mu_2 + \sigma)(\mu_3 + \mu_4) + \mu_3\mu_4)s + \mu_3\mu_4(\sigma + \mu_2)(1-R_0) = 0.
$$

Clearly, if $R_0 > 1$, (31) has as least a positive real root. Thus, the infection-free equilibrium $E_0$ is unstable.

Next we study the global stability of the infected equilibrium without immunity $E_1$.

**Theorem 5.** Suppose that hypotheses (H1)-(H7) and $R > 1$ are satisfied. If $R_0 > 1 \geq R_1$, then the infected equilibrium without immunity $E_1$ is globally asymptotically stable for any time delay $\tau \geq 0$. If $R_1 > 1$, then the infected equilibrium without immunity $E_1$ is unstable for any time delay $\tau \geq 0$.

Proof. Let $(x(t), u(t), y(t), v(t), z(t))$ be a positive solution of system (2) with the initial condition (3) for $t \geq 0$. Consider the following Lyapunov functional:

$$
V_2 = x - x_1 - \int_{x_1}^{x} \frac{f(x_1, v_1)}{f(s, v_1)} ds + (u-u_1 - u_1 \ln \frac{u}{u_1})
+ \frac{\sigma + \mu_2}{\sigma}(y - y_1 - y_1 \ln \frac{y}{y_1})
+ \frac{\mu_3(\sigma + \mu_2)}{k\sigma}(v - v_1 - v_1 \ln \frac{v}{v_1})
+ \frac{\sigma + \mu_2}{\sigma}p \frac{y}{q - m} z
+ \frac{\sigma + \mu_2}{\sigma} \frac{p q}{q - m} \int_0^t y(\theta) z(\theta) d\theta.
$$

Let $\psi(x) = x - x_1 - \int_{x_1}^{x}(f(x_1, v_1)/f(s, v_1))ds$. Then, $\psi(x)$ has the global minimum at $x = x_1$ and $\psi(x_1) = 0$. Furthermore, $\psi(x) > 0$ for $x > 0$. Hence, $V_2$ is positive definite with respect to $E_1$. For $t \geq 0$, the time derivative of $V_2$ along the solutions of system (2) is

$$
\dot{V}_2 = \left(1 - \frac{f(x_1, v_1)}{f(x, v_1)}\right)x + (1 - \frac{u_1}{u}) \dot{u}
+ \frac{\sigma + \mu_2}{\sigma}(1 - \frac{y_1}{y}) \dot{y} + \frac{\mu_3(\sigma + \mu_2)}{k\sigma}(1 - \frac{v_1}{v}) \dot{v}
+ \frac{\sigma + \mu_2}{\sigma} \frac{p}{q - m} \frac{y}{z}
+ \frac{\sigma + \mu_2}{\sigma} \frac{p q}{q - m} \frac{y}{q - m} \int_0^t y(\theta) z(\theta) d\theta
$$

Note that $\lambda = f(x_1, v_1)v_1 + \mu_1 x_1, f(x_1, v_1)v_1 = (\sigma + \mu_2)u_1$, and $\mu_5 y_1 = \sigma u_1$; we have

$$
\dot{V}_2 = \left(1 - \frac{f(x_1, v_1)}{f(x, v_1)}\right) f(x_1, v_1)v_1 + \mu_1 x_1
- f(x, v) v - \mu_1 x_1 + \left(1 - \frac{u_1}{u}\right) (f(x, v) v
- f(x_1, v_1)v_1) + \frac{\sigma + \mu_2}{\sigma}(1 - \frac{y_1}{y}) (-pyz)
+ f(x_1, v_1) \left(1 - \frac{y_1}{y_1}\right) \frac{u - y}{u_1}
+ \frac{\mu_3(\sigma + \mu_2)}{k\sigma}(1 - \frac{v_1}{v}) (k y - \mu_4 v) + \frac{\sigma + \mu_2}{\sigma}
\cdot \frac{p}{q - m} \left[q y (t - \tau) z (t - \tau) - \mu_5 z
- myz + \frac{\sigma + \mu_2}{\sigma} \frac{q}{q - m} \left[q y (t - \tau) z (t - \tau) - \mu_5 z
- py (t - \tau) z (t - \tau)\right]ight)
\mu_1 \left(1 - \frac{f(x_1, v_1)}{f(x, v_1)}\right) x_1.
that the infected equilibrium without immunity

From hypotheses (H3)-(H4), we have

Thus we have lim \( t \to \infty \) \( \psi_1(s) = 0 \) if \( R_1 > 1 \). Hence, if \( R_1 > 1 \), then \( \psi_1(s) = 0 \) has at least a positive real root; that is, (38) has at least a positive real root. Therefore, the infected equilibrium without immunity \( E_1 \) is unstable.

4. The Local Stability of the Infected Equilibrium and Hopf Bifurcation

The characteristic equation of system (2) at the infected equilibrium with CTL response \( E^* \) is given by

\[
s^5 + A_1 s^4 + A_2 s^3 + A_3 s^2 + A_4 s + A_5 + e^{-\tau} (B_1 s^4 + B_2 s^3 + B_3 s^2 + B_4 s + B_5) = 0,
\]

where

\[
A_1 = A + D + E + \mu_4 + q y^*,
\]

\[
A_2 = (E + \mu_4) q y^* + \mu_4 E + D (E + \mu_4 + q y^*) + A (D + E + \mu_4 + q y^*) - py^* m z^*,
\]

\[
A_3 = \mu_4 E q y^* + D (\mu_4 + E) q y^* - \sigma k B
\]

\[
+ A [(E + \mu_4) q y^* + \mu_4 E + D (E + \mu_4 + q y^*)]
\]

\[
- py^* m z^* (A + D + \mu_4),
\]

\[
A_4 = - B k \sigma q y^* + A [\mu_4 E q y^* + D (\mu_4 + E) q y^* - B k \sigma + C \sigma k (B + H) - py^* m z^* (D \mu_4 + A \mu_4 + AD),
\]

\[
A_5 = C \sigma k (B + H) q y^* - py^* m z^* A D \mu_4 - A B \sigma k q y^*,
\]

\[
B_1 = - q y^*,
\]

\[
B_2 = - q y^* (A + D + \mu_3 + \mu_4),
\]

\[
B_3 = - q y^* [\mu_3 \mu_4 + D (\mu_3 + \mu_4) + A (D + \mu_3 + \mu_4)],
\]

\[
B_4 = - q y^* [D \mu_3 \mu_4 + A (\mu_3 \mu_4 + D \mu_3 + D \mu_4 - \sigma k (B + H)],
\]

\[
B_5 = - q y^* [A D \mu_4 \mu_4 - A \sigma k (B + H) + C \sigma k (B + H)],
\]

\[
a = \frac{\partial f(x^*, v^*)}{\partial x} > 0,
\]

\[
d = \frac{\partial f(x^*, v^*)}{\partial v} \leq 0,
\]

\[
A = av^* + \mu_1,
\]

\[
B = dv^*,
\]

\[
C = av^*,
\]

\[
D = \sigma + \mu_2,
\]

\[
E = \mu_3 + pz^*.
\]
\[
F = (q - m)z^*, \\
H = f (x^*, v^*), \\
M = py^* F.
\]

When \( \tau = 0 \), (40) becomes
\[
s^5 + \alpha_1 s^4 + \alpha_2 s^3 + \alpha_3 s^2 + \alpha_4 s + \alpha_5 = 0, \tag{42}
\]

where
\[
\alpha_1 = A_1 + B_1 = A + D + E + \mu_4 > 0, \\
\alpha_2 = A_2 + B_2 \\
= M + A (D + E + \mu_4) + (E \mu_4 + D \mu_4 + DE) > 0, \\
\alpha_3 = A_3 + B_3 \\
= (A + D + \mu_4) M + A (E \mu_4 + D \mu_4 + DE) - Bk\sigma \geq 0, \tag{43}
\]
\[
\alpha_4 = A_4 + B_4 = (D \mu_4 + A \mu_4 + AD) M + G > 0, \\
\alpha_5 = A_5 + B_5 = AD \mu_4 M > 0, \\
G = CDE\mu_4 - \mu_1 Bk\sigma > 0.
\]

Denote
\[
\Delta_1 = \alpha_1, \\
\Delta_2 = \alpha_1 \alpha_2 - \alpha_3, \\
\Delta_3 = \alpha_3 \Delta_2 + \alpha_1 \alpha_5 - \alpha_2^2 \alpha_4, \\
\Delta_4 = \alpha_4 (\Delta_3 + \alpha_2 \alpha_5 - \alpha_2 \alpha_5 - \alpha_2^2 \alpha_4), \\
\Delta_5 = \alpha_5 \Delta_4. \tag{44}
\]

Since \( \mu_4 (\sigma + \mu_2)(\mu_4 + pz^*) = \sigma k f(x^*, v^*) \) and (H4), we have
\[
\sigma k H = \mu_4 DE, \mu_4 DE + Bk\sigma > 0, \text{ and } ADE\mu_4 - G > 0.
\]

Thus,
\[
\Delta_1 = \alpha_1 > 0, \\
\Delta_2 = EM + A^2 (D + E + \mu_4) + (D + E + \mu_4) [A (D \\
+ E + \mu_4) + D (E + \mu_4) + E \mu_4] - Bk\sigma > 0, \\
\Delta_3 = M \left[ A \left( A^2 E + A^2 E + E^2 \mu_4 + D \mu_4 + EM \\
+ Bk\sigma \right) + D \left( A^2 E + D^2 E + D \mu_4 + AE^2 + DE^2 \\
+ D \mu_4 + EM + Bk\sigma \right) + \mu_4 \left( A^2 E + D^2 E + D \mu_4 + EM \\
+ ADE + AE^2 + DE^2 + D \mu_4 + EM + Bk\sigma \right) + EM + Bk\sigma \right) \right] + \mu_1 (DE \mu_4 + Bk\sigma) (A + D + E \\
+ \mu_4) + \mu_4 \left( A^2 E + A^2 E + AD^2 + ADE + D^2 E \\
+ DE \mu_4 + ADE + AE^2 + DE^2 + EM + Bk\sigma \right) \\
+ ADE \mu_4 (A^2 D + A^2 E + A^2 \mu_4 + AD^2 + ADE) \\
+ ADE \mu_4 + D^2 E + D^2 \mu_4 + ADE + AE^2 + AE \mu_4 \\
+ DE^2 + DE \mu_4 + AD \mu_4 + A \mu_4^2 + DE \mu_4 + D \mu_4^2 \\
+ EM + Bk\sigma \right) \right) + (AE \mu_4 - Bk \sigma) \Delta_2 > 0, \\
\Delta_4 = N_1 M^2 + N_2 M^2 + N_3 M + N_4, \tag{45}
\]

where
\[
N_1 = E \left[ A^2 (D + \mu_4) + (D + \mu_4) (A \mu_4 + D \mu_4 + AD) \right] \\
> 0, \\
N_2 = A^2 D \left( A^2 E + AE^2 \right) + A^2 \mu_4 \left( A^2 E + AE^2 \right) \\
+ D^2 \mu_4 \left( D^2 E + DE^2 + D E \mu_4 + Bk \sigma \right) \\
+ ADE \mu_4 \left( A^2 E + D^2 E + DE^2 \right) + A \mu_4 \left( A^2 E + D^2 E \right) \\
+ ADE + AE^2 + DE^2 + DE \mu_4 + A \mu_4^2 + D \mu_4^2 \\
+ Bk \sigma \right) + D \mu_4^2 \left( D^2 E + DE^2 + DE \mu_4 + E^2 \mu_4 \right) \\
+ DE \mu_4 + E \mu_4^2 + Bk \sigma \right) + \left( A \mu_4^2 + ad \mu_4 \right) \left( A^2 E \right) \\
+ D^2 E + AE^2 + ADE + D^2 E + DE \mu_4 + A \mu_4^2 + E^2 \mu_4 \right) \\
+ A \mu_4 + D \mu_4 \right) + A \left( A \mu_4 + D \mu_4 \right) \left( D \mu_4 \right) \\
+ Bk \sigma \right) > 0, \\
N_3 = \left[ A^2 E + A^2 E + D^3 E + ADE^2 + D^2 E^2 + AE^2 \mu_4 \right. \\
+ E^2 \mu_4^2 + E \mu_4^3 + (A + D + \mu_4) Bk \sigma - EBk \sigma \right] \\
- Bk \sigma \left( ADE + D \mu_4 \right) \left( \Delta_2 - EM \right) + \left( A^2 E \mu_4^2 \right. \\
+ A^2 D^2 E \left( ADE + D \mu_4 + D^2 E + ADE + AE^2 \right) \\
+ A \mu_4 + DE \mu_4 + D^2 E + A \mu_4 + AE \mu_4 + E \mu_4^2 \\
+ DE \mu_4 + A \mu_4 + D \mu_4 + Bk \sigma \right) \\
+ A \mu_4 + D \mu_4 \right) \left( A \mu_4 + D \mu_4 + Bk \sigma \right) \\
+ A \mu_4 + D \mu_4 \right) \left( A \mu_4 + D \mu_4 + Bk \sigma \right) \\
+ A \mu_4 + D \mu_4 \right) \left( A \mu_4 + D \mu_4 + Bk \sigma \right) \\
- G \left( 2D^2 \mu_4^2 + 2AD^2 \mu_4 + 2AD \mu_4^2 + D^3 \mu_4 + D \mu_4^3 \right).
Therefore, \( \Delta_4 > 0, \Delta_2 > 0 \). By Routh–Hurwitz criterion, all the roots of (42) have negative real parts. Hence we have the following result.

**Proposition 6.** When \( \tau = 0 \), if \( \overline{R} > 1, R_1 > 1 \), and (H8) hold, then the infected equilibrium with CTL response \( E^* \) is locally asymptotically stable.

In fact, when \( \tau = 0 \), we can show that if \( \overline{R} > 1 \) and \( R_1 > 1 \) hold, the infected equilibrium with CTL response \( E^* \) is globally asymptotically stable by constructing suitable Lyapunov function.

**Proposition 7.** Suppose that hypotheses (H1)–(H7) and \( \overline{R} > 1 \) are satisfied. If \( R_1 > 1 \), then the infected equilibrium with CTL response \( E^* \) is globally asymptotically stable when \( \tau = 0 \).
and separating the real and imaginary parts, we have
\[ g = \mu_1 (x^* - x) \left( 1 - \frac{f(x^*, v^*)}{f(x, v^*)} \right) + f(x^*, v^*) \]
\[ \nu^* \left( -1 + \frac{f(x, v)}{f(x, v^*)} \frac{v}{v^*} - \frac{f(x, v)}{f(x, v^*)} \frac{v}{v^*} + \frac{f(x, v^*)}{f(x, v)} \right) + f(x^*, v^*) \]
\[ \nu^* \left( \frac{5}{\nu^*} \right) \]
\[ - \frac{f(x^*, v^*)}{f(x, v)} \frac{u^*}{u} - \frac{y^*}{y} \]
\[ - \frac{f(x, v^*)}{f(x, v)} \frac{y^*}{y} \]
\[ \frac{5}{\nu^*} \]
\[ (50) \]

Since the arithmetic mean is greater than or equal to the geometric mean, it has
\[ 5 - \frac{f(x^*, v^*)}{f(x, v^*)} \frac{v}{v^*} - \frac{f(x, v)}{f(x, v^*)} \frac{v}{v^*} + \frac{f(x, v^*)}{f(x, v)} \leq 0. \]
\[ (51) \]

From hypotheses (H3)-(H4), we have
\[ -1 + \frac{f(x, v)}{f(x, v^*)} \frac{v}{v^*} - \frac{f(x, v)}{f(x, v^*)} \frac{v}{v^*} + \frac{f(x, v^*)}{f(x, v)} \]
\[ \frac{f(x, v) - f(x, v^*)}{f(x, v^*)} \frac{v}{v^*} - \frac{f(x, v) - f(x, v^*)}{f(x, v^*)} \frac{v}{v^*} \leq 0. \]
\[ (52) \]

Therefore, \( V_3 \leq 0 \) if \( R_1 > 1 \). Then it follows from stability theorems in [34, 35] that the infected equilibrium CTL response \( E^* \) is stable for \( \tau = 0 \) if \( R_1 > 1 \). Similarly, by LaSalle invariance principle, we can show that the infected equilibrium CTL response \( E^* \) is also globally attractive for \( \tau = 0 \) if \( R_1 > 1 \).

Next, we consider the case when \( \tau > 0 \). Since \( \alpha_3 > 0 \), \( s = 0 \) is not a root of (40). We suppose (40) has a purely imaginary root \( s = i\omega \) (\( \omega > 0 \)) for some \( \tau > 0 \). Substituting \( s = i\omega \) into (40) and separating the real and imaginary parts, we have
\[ \omega^5 - A_4 \omega^3 + A_4 \omega = (B_4 \omega^4 - B_3 \omega^2 + B_5) \sin \omega \tau \]
\[ + (B_2 \omega^3 - B_4 \omega) \cos \omega \tau, \]
\[ A_1 \omega^4 - A_3 \omega^2 + A_5 = -(B_1 \omega^4 - B_3 \omega^2 + B_5) \cos \omega \tau \]
\[ + (B_2 \omega^3 - B_4 \omega) \sin \omega \tau. \]
\[ (53) \]

Squaring and adding the two equations of (53), it follows that
\[ \omega^{10} + C_1 \omega^8 + C_2 \omega^6 + C_3 \omega^4 + C_4 \omega^2 + C_5 = 0, \]
\[ (54) \]

where
\[ C_1 = A_1^2 - 2A_2 - B_1^2, \]
\[ C_2 = A_2^2 + 2A_4 - 2A_1 A_3 + 2B_1 B_3 - B_2^2, \]
\[ C_3 = A_3^2 - 2A_2 A_4 - B_3^2 + 2B_2 B_4 + 2A_1 A_5 - 2B_1 B_5, \]
\[ C_4 = A_4^2 - B_4^2 - 2A_3 A_5 + 2B_3 B_5, \]
\[ C_5 = A_5^2 - B_5^2. \]

Letting \( \nu = \omega^2 \), (54) can be written as
\[ h(\nu) = \nu^5 + C_1 \nu^4 + C_2 \nu^3 + C_3 \nu^2 + C_4 \nu + C_5 = 0. \]
\[ (56) \]

Then we have
\[ h'(\nu) = 5\nu^4 + 4C_1 \nu^3 + 3C_2 \nu^2 + 2C_3 \nu + C_4. \]
\[ (57) \]

Denote
\[ p_1 = -\frac{6}{25} C_1^2 + \frac{3}{5} C_2, \]
\[ q_1 = \frac{8}{25} C_1^3 - \frac{6}{25} C_1 C_2 + \frac{2}{5} C_3, \]
\[ r_1 = -\frac{3}{625} C_1^4 + \frac{3}{125} C_1^2 C_2 - \frac{2}{25} C_1 C_3 + \frac{1}{5} C_4, \]
\[ \Theta_0 = p_1^2 - 4r_1, \]
\[ p_2 = -\frac{1}{3} p_1^2 - 4r_1, \]
\[ q_2 = -\frac{2}{27} p_1^3 + \frac{8}{9} p_1 r_1 - q_1, \]
\[ \Theta_1 = \frac{1}{27} p_2^2 + \frac{4}{9} q_2, \]
\[ s_* = \sqrt{\frac{q_2}{2} + \sqrt{\Theta_1 + \sqrt{\frac{q_2}{2} - \sqrt{\Theta_1 + \frac{1}{3} p_1}}}}, \]
\[ \Theta_2 = -s_* - p_1 + \frac{2q_1}{\sqrt{s_* - p_1}}, \]
\[ \Theta_3 = -s_* - p_1 - \frac{2q_1}{\sqrt{s_* - p_1}}. \]

By a similar argument as that in [38], we have the following results.

**Lemma 8.** For the polynomial equation (56), the following results hold.
(i) Equation (56) has at least one positive root, if one of the following conditions (a)–(d) holds:

(a) $C_5 < 0$.

(b) $C_5 ≥ 0$, $q_1 = 0$, $Θ_3 ≥ 0$, and $p_1 < 0$ or $r_1 ≤ 0$ and there exists $v^* \in \{v_1, v_2, v_3, v_4\}$ such that $v^* > 0$ and $h(v^*) ≤ 0$, where $v_i = y_i - (1/5)C_1 (i = 1, 2, 3, 4)$, and

\[
y_1 = \sqrt{-p_1 + \sqrt{\Theta_0}},
\]

\[
y_2 = -\sqrt{-p_1 + \sqrt{\Theta_0}},
\]

\[
y_3 = \sqrt{-p_1 - \sqrt{\Theta_0}},
\]

\[
y_4 = -\sqrt{-p_1 - \sqrt{\Theta_0}},
\]

(c) $C_5 ≥ 0$, $q_1 ≠ 0$, $s_* > p_1$, $Θ_3 ≥ 0$, or $Θ_3 ≥ 0$ and there exists $v^* \in \{v_1, v_2, v_3, v_4\}$ such that $v^* > 0$ and $h(v^*) ≤ 0$, where $v_i = y_i - (1/5)C_1 (i = 1, 2, 3, 4)$, and

\[
y_1 = \frac{-\sqrt{5s_1 - p_1} + \sqrt{\Theta_0}}{2},
\]

\[
y_2 = \frac{-\sqrt{5s_1 - p_1} - \sqrt{\Theta_0}}{2},
\]

\[
y_3 = \frac{\sqrt{5s_1 - p_1} + \sqrt{\Theta_0}}{2},
\]

\[
y_4 = \frac{\sqrt{5s_1 - p_1} - \sqrt{\Theta_0}}{2},
\]

(d) $C_5 ≥ 0$, $q_1 ≠ 0$, $s_* < p_1$, $q_1^2/4(p_1 - s_*)^2 + (1/2)s_* = 0$, $v > 0$, and $h(v) ≤ 0$, where $v = q_1/2(p_1 - s_*) - (1/5)C_1$.

(ii) If the conditions (a)–(d) of (i) are all not satisfied, then (56) has no positive real root.

Suppose that $h(v) = 0$ has positive real roots. Without loss of generality, we may assume that (56) has $k$ $(1 ≤ k ≤ 5)$ positive real roots, denoted, respectively, as $v_1, v_2, ..., v_k$. Then, (54) has positive real roots $ω_k = \sqrt{r_k}$. From (40), we get

\[
\cos ωτ = \frac{\omega^5 - A_2\omega^3 + A_4\omega}{(B_2\omega^3 - B_4\omega)^2 + (B_4\omega^4 - B_2\omega^2 + B_3)^2} ≡ L(ω).
\]

Therefore, let

\[
t^{(j)}_k = \frac{1}{ω_k} \left[ \arccos L(ω_k) + 2πj \right], \quad (62)
\]

where $k = 1, 2, ..., k$, $j = 0, 1, ...$. Then ±$iω_k$ are a pair of purely imaginary roots of (54) with $τ = t^{(j)}_k$.

Define

\[
t_0 = \min_{k \in [1, 2, ..., k]} \left\{ t^{(0)}_k \right\},
\]

\[
ω_0 = ω_k.
\]

Let $s(τ) = ω(τ) + iω(τ)$ be a root of (40) satisfying $ω(t^{(j)}_k) = 0$ and $ω(t^{(j)}_k) = ω_k$. Differentiating the two sides of (40) with respect to $τ$ and noticing that $s$ is a function of $τ$, it follows that

\[
\left( \frac{ds}{dτ} \right)^{-1} = -\frac{5s^4 + 4A_1 s^3 + 3A_2 s^2 + 2A_3 s + A_4}{s (s^3 + A_1 s^2 + A_2 s^3 + A_3 s^2 + A_4 s + A_5)} + \frac{4B_1 s^3 + 3B_2 s^2 + 2B_3 s + B_4}{s (B_1 s^4 + B_2 s^3 + B_3 s^2 + B_4 s + B_5)} - \frac{τ}{s}.
\]

Thus, we get

\[
\left[ \frac{d \text{Res}(τ)}{dτ} \right]^{-1} \bigg|_{τ = t^{(0)}_k} = \frac{(5ω_k^4 - 3A_2ω_k^2 + A_4)(-ω_k^6 + A_2ω_k^4 - A_4ω_k^2) - (4A_1ω_k^5 - 2A_3ω_k^3 + A_5ω_k)}{(-ω_k^6 + A_2ω_k^4 - A_4ω_k^2)^2 + (A_1ω_k^5 - A_3ω_k^3 + A_5ω_k)^2}
\]

\[
+ \frac{-3B_2ω_k^2 + B_3}{(B_1ω_k^4 - B_3ω_k^2)^2 + (B_4ω_k^5 - B_3ω_k^3 + B_5ω_k)}.
\]
Let us choose
\[
\lambda = 270, \quad \beta = 0.001, \quad k = 6, \quad m = 0.001,
\]
\[
p = 0.04, \quad q = 0.025, \quad \sigma = 0.001, \quad \mu_1 = 0.02, \quad \mu_2 = 0.1, \quad \mu_3 = 0.8, \quad \mu_4 = 1.2, \quad \mu_5 = 0.05.
\]

Direct calculations show that \( R_0 = 0.8354 < 1 \) and \( R_1 = 0.3146 < 1 \); system (2) has the infection-free equilibrium \( E_0 = (13500, 0, 0, 0, 0) \). By Theorem 4, the infection-free equilibrium \( E_0 \) is globally asymptotically stable for any time delay \( \tau \geq 0 \). Figure 1 gives the phase trajectories of system (2) with suitable initial condition.

Next, let us choose the following data:
\[
\lambda = 270, \quad \beta = 0.001, \quad k = 6, \quad m = 0.01,
\]
\[
p = 0.04, \quad q = 0.025, \quad \sigma = 0.002, \quad \mu_1 = 0.02, \quad \mu_2 = 0.1, \quad \mu_3 = 0.8, \quad \mu_4 = 1.2, \quad \mu_5 = 0.05.
\]

Direct computations show that \( R_0 = 1.6544 > 1 \), \( R = 1.9853 > 1 \), and \( R_1 = 0.8211 < 1 \); system (2) has the infected equilibrium without immunity \( E_1 = (8160, 1047.0588, 2.6176, 13.0882, 0) \). Therefore, by Theorem 5, the infected equilibrium without immunity \( E_1 \) is globally asymptotically
Figure 1: Phase trajectories of system (2) with $R_0 \leq 1$.

Figure 2: Phase trajectories of system (2) with $R_0 > 1 \geq R_1$.

Figure 3: Phase trajectories of system (2) with $R_1 > 1$, $\tau = 28$. The initial condition is $(7970, 1000, 2.6, 0.2, 17)$.

Figure 4: Phase trajectories of system (2) with $R_1 > 1$, $\tau = 25 < \tau_0$. The initial condition is $(7970, 1000, 2.6, 0.2, 17)$.

Figure 5: Phase trajectories of system (2) with $R_1 > 1$, $\tau = 28 > \tau_0$. The initial condition is $(7970, 1000, 2.6, 0.2, 17)$.

stable for any time delay $\tau \geq 0$. Figure 2 gives the phase trajectories of system (2) with suitable initial condition.

Furthermore, let us choose the following data:

\[
\lambda = 270, \quad \beta = 0.001, \quad k = 6, \quad m = 0.012,
\]
\[
p = 0.04, \quad q = 0.025, \quad \sigma = 0.004, \quad \mu_1 = 0.02, \quad \mu_2 = 0.1, \quad \mu_3 = 0.8, \quad \mu_4 = 1.2, \quad \mu_5 = 0.05.
\]

Then we have that $R_0 = 3.2452 > 1$, $\overline{R} = 3.375 > 1$, and $R_1 = 2.2837 > 1$ and (56) has no positive root. System (2) has the infected equilibrium with CTL response $E^* = (6882.3529, 1272.6244, 3.84615, 19.2308, 13.0882)$. From Theorem 9(i), the infected equilibrium with CTL response $E^*$ is locally asymptotically stable for any time delay $\tau > 0$. Figure 3 gives the phase trajectories of system (2) with suitable initial condition.

Finally, let us choose the following data:

\[
\lambda = 270, \quad \beta = 0.001, \quad k = 6, \quad m = 0.012,
\]
\[
p = 0.04, \quad q = 0.025, \quad \sigma = 0.004, \quad \mu_1 = 0.02, \quad \mu_2 = 0.1, \quad \mu_3 = 0.8, \quad \mu_4 = 1.2, \quad \mu_5 = 0.05.
\]

Then we have that $R_0 = 3.2452 > 1$, $\overline{R} = 3.8942 > 1$, and $R_1 = 2.4119 > 1$, (56) has two positive roots, and $H'(v_k) \neq 0$. By simple computations, we have $\omega_0 \approx 0.0394$ and $\tau_0 \approx 27.2546$. From Theorem 9(ii), the infected equilibrium with CTL response $E^* = (7363.6364, 1180.0699, 3.3333, 16.6667, 15.4021)$ is asymptotically stable if $0 < \tau < \tau_0$ and unstable if $\tau > \tau_0$. Figure 4 gives the phase trajectories of system (2) with $\tau < \tau_0$ and suitable initial condition. Figure 5 gives the phase trajectories of system (2) with $\tau > \tau_0$ and suitable initial condition and shows the occurrence of the Hopf bifurcations.

Since $v^* = k\mu_5/(\mu_4(q - m))$ and $z^* = \mu_4\mu_3\mu_2(q - m)(R_1 - 1)/(\mu_4\mu_2(q - m) + p\beta k\mu_3)$, it is easy to see that the number of
As immune impairment rate $m$ increases, the CTL response gradually becomes weak and the individuals eventually develop AIDS. Thus, in order to control the HIV infection, we should decrease the value of $m$. Numerical simulations show the similar known results (see, e.g., [22]).

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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