

Research Article

Stability and Bifurcation Analysis for a Delay Differential Equation of Hepatitis B Virus Infection

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The stability and bifurcation analysis for a delay differential equation of hepatitis B virus infection is investigated. We show the existence of nonnegative equilibria under some appropriated conditions. The existence of the Hopf bifurcation with delay τ at the endemic equilibria is established by analyzing the distribution of the characteristic values. The explicit formulae which determine the direction of the bifurcations, stability, and the other properties of the bifurcating periodic solutions are given by using the normal form theory and the center manifold theorem. Numerical simulation verifies the theoretical results.

1. Introduction

Recently, a hepatitis B virus (HBV) model with time delay that was proposed and investigated in the literature [1–4] caught the attention of a lot of mathematicians. In practice, the HBV model has suffered time delay caused by the HBV incubation period, which varies from 45 to 180 days, and the delay in viral shedding which both suggest that viral production delay may significantly impact infection dynamics [1]. Precisely, the HBV model with time delay reads as the following:

$$\begin{aligned} \frac{dx(t)}{dt} &= \lambda - dx(t) - \frac{\beta x(t)v(t)}{x(t) + e(t) + y(t)}, \\ \frac{de(t)}{dt} &= -de(t) + \frac{\beta x(t)v(t)}{x(t) + e(t) + y(t)} \\ &\quad - \frac{\beta e^{-d\tau} x(t-\tau)v(t-\tau)}{x(t-\tau) + e(t-\tau) + y(t-\tau)}, \\ \frac{dy(t)}{dt} &= \frac{\beta e^{-d\tau} x(t-\tau)v(t-\tau)}{x(t-\tau) + e(t-\tau) + y(t-\tau)} - ay(t), \end{aligned}$$

$$\frac{dv(t)}{dt} = ky(t) - \mu v(t), \quad (1)$$

where $x(t)$ and $y(t)$ represent the number of uninfected cells and infected cells, respectively. $e(t)$ represents the number of exposed cells, that is, the cells that have acquired the virus but are not yet producing new virions. $v(t)$ denotes the number of free virions. τ is the time delay for virion production. Here, the positive constant λ is the rate at which new uninfected live cells are generated. The positive constant d is the per capita death rate of uninfected live cells. Infected live cells are killed by immune cells at rate ay and produce free virions at rate ky , where k is what so-called “burst” constant. Free virions are cleared by lymphatic and other mechanisms at rate μv , where μ is a constant. $\beta > 0$ is an incidence rate coefficient describing the infection process. The initial conditions for the system (1) are

$$\begin{aligned} x(s) &= x_0(s), & y(s) &= y_0(s), \\ v(s) &= v_0(s), & s &\in [-\tau, 0], \end{aligned} \quad (2)$$

$$E_0 = \beta \int_{-\tau}^0 \frac{e^{ds} v_0(s) x_0(s)}{x_0(s) + y_0(s) + e_0(s)} ds,$$

where x_0 , y_0 , and v_0 are nonnegative functions. Based on some observations of virus particles v , the system (1) is simplified in [1] as the following:

$$\begin{aligned} \frac{dx(t)}{dt} &= \lambda - dx(t) - \frac{\beta kx(t)y(t)}{\mu[x(t)+y(t)]}, \\ \frac{de(t)}{dt} &= -de(t) + \frac{\beta kx(t)y(t)}{\mu[x(t)+y(t)]} \\ &\quad - \frac{\beta ke^{-d\tau}x(t-\tau)y(t-\tau)}{\mu[x(t-\tau)+y(t-\tau)]}, \\ \frac{dy(t)}{dt} &= \frac{\beta ke^{-d\tau}x(t-\tau)y(t-\tau)}{\mu[x(t-\tau)+y(t-\tau)]} - ay(t). \end{aligned} \quad (3)$$

A direct computation shows that the basic infection reproduction number for the system (2) is

$$R_0 = \frac{\beta ke^{-d\tau}}{a\mu}. \quad (4)$$

For the sake of simplicity, let $\bar{x} = x - (\lambda/d)$, and the system (3) is equivalent to the following system:

$$\begin{aligned} \frac{d\bar{x}(t)}{dt} &= -d\bar{x}(t) - \frac{\beta k[\bar{x}(t) + (\lambda/d)]y(t)}{\mu[\bar{x}(t) + (\lambda/d) + y(t)]}, \\ \frac{de(t)}{dt} &= -de(t) + \frac{\beta k[\bar{x}(t) + (\lambda/d)]y(t)}{\mu[\bar{x}(t) + (\lambda/d) + y(t)]} \\ &\quad - \frac{\beta ke^{-d\tau}[\bar{x}(t-\tau) + (\lambda/d)]y(t-\tau)}{\mu[\bar{x}(t-\tau) + (\lambda/d) + y(t-\tau)]}, \\ \frac{dy(t)}{dt} &= \frac{\beta ke^{-d\tau}[\bar{x}(t-\tau) + (\lambda/d)]y(t-\tau)}{\mu[\bar{x}(t-\tau) + (\lambda/d) + y(t-\tau)]} - ay(t), \end{aligned} \quad (5)$$

which has two equilibria: the infection-free equilibrium $E_f = (0, 0, 0)^T$ and the infected equilibrium $E^* = (x^*, e^*, y^*)^T$, where

$$\begin{aligned} x^* &= \frac{\lambda}{d + ae^{d\tau}(R_0 - 1)} - \frac{\lambda}{d}, & e^* &= \frac{a(e^{d\tau} - 1)}{d}x^*, \\ y^* &= (R_0 - 1)x^*. \end{aligned} \quad (6)$$

The following results, Theorems 1 and 2, come from [1].

Theorem 1. *If $R_0 < 1$, the infection-free equilibrium E_f of the system (5) is globally asymptotically stable.*

Theorem 2. *If $R_0 > 1$, the chronic infected equilibrium E^* of the system (5) is locally asymptotically stable.*

The initial conditions for the system (5) are

$$\begin{aligned} (\varphi_1(\theta), \varphi_2(\theta), \psi(\theta)) &\in C_+ = C([- \tau, 0], R_{+0}^3), \\ \varphi_k(0) > 0, \quad \psi(0) > 0, \quad k &= 1, 2, \end{aligned} \quad (7)$$

where $R_{+0}^3 = \{(x_1, x_2, x_3) \in R^3 : x_k > 0, k = 1, 2, 3\}$.

It is straightforward to show the following.

Lemma 3. *The solution of (5) with an initial condition (6) is nonnegative for all $t \geq 0$.*

It is well known that the studies on the dynamical systems not only include the discussion of stabilities, attractivity, and persistence, but also include many dynamical behaviors such as periodic solutions, bifurcations, and chaos. Particularly, the properties of periodic solutions appearing through the Hopf bifurcation in delayed systems are of great interest [5–7]. In the present paper, our main objective is to investigate the bifurcation phenomena of the modified hepatitis B virus (HBV) model with time delay τ .

This paper is organized as follows. In Section 2, by analyzing the characteristic equation of the linearized system of the system (5) at the equilibria, we discuss the stability of the origin and the positive equilibrium and the existence of the Hopf bifurcations occurring at the chronic infected equilibrium. In Section 3, the formulae determining the direction of the Hopf bifurcations and the stability of bifurcating periodic solutions on the center manifold are obtained by using the normal form theory and the center manifold theorem due to Hassard et al. [8]. To verify the obtained results, some numerical simulations are included in Section 4. The paper ends with a brief discussion.

2. Stability of Equilibria and Existence of the Hopf Bifurcation

In this section, we will investigate the stability of the equilibria and the existence of the Hopf bifurcations occurring at the chronic infected equilibrium. Then, it is easy to check that the system (5) has an equilibrium $E_f(0, 0, 0)$ for all nonnegative parameters. The characteristic equation of (5) at E_f is

$$(z + d)^2 \left(z - \frac{\beta ke^{-d\tau}}{\mu} + a \right) = 0. \quad (8)$$

Hence, E_f is a saddle with $\dim W^u(E_f) = 1$, $\dim W^s(E_f) = 2$ for $R_0 < 1$; $W^u(E_f)$ and $W^s(E_f)$ are the local unstable and stable manifolds of E_f , respectively. E_f is locally asymptotically stable for $R_0 < 1$. In fact, E_f is globally asymptotically stable for $R_0 < 1$, see [1, 4].

Now, we will investigate the stability of the chronic infected equilibrium E^* . Linearizing the system (5) at E^* yields the following linear system:

$$\begin{aligned} \frac{d\bar{x}(t)}{dt} &= -d\bar{x}(t) - \left\{ \frac{\beta ky^*(t)}{\mu[x^*(t) + (\lambda/d) + y^*(t)]} \right. \\ &\quad \left. - \frac{\beta k[x^*(t) + (\lambda/d)]y^*(t)}{\mu[x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} \bar{x}(t) \end{aligned}$$

$$\begin{aligned}
 & - \left\{ \frac{\beta k [x^*(t) + (\lambda/d)]}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. - \frac{\beta k [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} y(t), \\
 \frac{de(t)}{dt} = & -de(t) + \left\{ \frac{\beta k y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. - \frac{\beta k [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} \bar{x}(t) \\
 & + \left\{ \frac{\beta k [x^*(t) + (\lambda/d)]}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. + \frac{\beta k [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} y(t) \\
 & - \left\{ \frac{\beta k e^{-d\tau} y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. - \frac{\beta k e^{-d\tau} [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} \bar{x}(t - \tau) \\
 & - \left\{ \frac{\beta k e^{-d\tau} [x^*(t) + (\lambda/d)]}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. - \frac{\beta k e^{-d\tau} [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} y(t - \tau), \\
 \frac{dy(t)}{dt} = & \left\{ \frac{\beta k e^{-d\tau} y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. - \frac{\beta k e^{-d\tau} [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} \bar{x}(t - \tau) \\
 & - \left\{ \frac{\beta k e^{-d\tau} [x^*(t) + (\lambda/d)]}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \right. \\
 & \quad \left. - \frac{\beta k e^{-d\tau} [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2} \right\} y(t - \tau) \\
 & - ay(t), \tag{9}
 \end{aligned}$$

whose characteristic equation reads as

$$\begin{aligned}
 z^3 + (2d + A + a)z^2 + [d(2a + A + d) + aA]z + ad(d + A) \\
 = Be^{-z\tau} e^{-d\tau} [z^2 + 2dz + d^2], \tag{10}
 \end{aligned}$$

with

$$\begin{aligned}
 A &= \frac{\beta k y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \\
 & \quad - \frac{\beta k [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2}, \\
 B &= \frac{\beta k [x^*(t) + (\lambda/d)]}{\mu [x^*(t) + (\lambda/d) + y^*(t)]} \\
 & \quad - \frac{\beta k [x^*(t) + (\lambda/d)] y^*(t)}{\mu [x^*(t) + (\lambda/d) + y^*(t)]^2}. \tag{11}
 \end{aligned}$$

For $\tau = 0$, characteristic equation (10) reduces to

$$\begin{aligned}
 z^3 + (2d + A + a)z^2 + [d(2a + A + d) + aA]z + ad(d + A) \\
 = B(z^2 + 2dz + d^2). \tag{12}
 \end{aligned}$$

By the Routh-Hurwitz criterion, we know that all the roots of (12) have negative real parts, that is, the chronic infected equilibrium E^* is locally asymptotically stable for $\tau = 0$. We now give a definition, which can be found in [2, 9].

Definition 4. The equilibrium E^* is called asymptotically stable if there is an $\varepsilon > 0$ such that

$$\sup_{\tau \leq \theta \leq \infty} [|\varphi_1(\theta) - x_0^*| + |\varphi_2(\theta) - x_1^*| + |\psi(\theta) - y^*|] < \varepsilon \tag{13}$$

implies that

$$\lim_{t \rightarrow \infty} (x_0(t), x_1(t), y(t)) = (x_0^*, x_1^*, y^*), \tag{14}$$

where $(x_0(t), x_1(t), y(t))$ is the solution of the system (5) with an initial condition (6).

Song et al. [10] investigated the distribution of roots of the following equation:

$$z^3 + m_2 z^2 + m_1 z + m_0 + e^{-z\tau} (n_2 z^2 + n_1 z + n_0) = 0, \tag{15}$$

where $m_j, n_j \in R (j = 0, 1, 2)$ and $\sum_{j=0}^2 n_j^2 \neq 0$. When $\tau = 0$, (15) reduces to

$$z^3 + (m_2 + n_2)z^2 + (m_1 + n_1)z + n_0 = 0. \tag{16}$$

Obviously, $i\omega (\omega > 0)$ is a root of (16) if and only if ω satisfies

$$\begin{aligned}
 -\omega^3 i - m_2 \omega^2 + m_1 \omega i + m_0 \\
 + (-n_2 \omega^2 + n_1 \omega i + n_0) (\cos \omega \tau - i \sin \omega \tau) = 0. \tag{17}
 \end{aligned}$$

Separating the real and the imaginary parts, we have

$$\begin{aligned}
 m_2 \omega^2 - m_0 &= -n_2 \omega^2 \cos \omega \tau + n_1 \omega \sin \omega \tau + n_0 \cos \omega \tau, \\
 -\omega^3 + m_1 \omega &= -n_2 \omega^2 \sin \omega \tau - n_1 \omega \cos \omega \tau + n_0 \sin \omega \tau. \tag{18}
 \end{aligned}$$

Squaring the two equations and adding them give

$$\omega^6 + p\omega^4 + q\omega^2 + r = 0, \tag{19}$$

where $p = m_2^2 - 2m_1 - n_2^2$, $q = m_1^2 - 2m_0m_2 + 2n_0n_2 - n_1^2$, and $r = m_0^2 - n_0^2$. Song et al. [10] obtained the following results on the distribution of roots of (15) and (19).

Lemma 5. For the polynomial equation (19),

- (i) if $r < 0$, then (19) has at least one positive root,
- (ii) if $r \geq 0$ and $\Delta = p^2 - 3q \leq 0$, then (19) has no positive roots,
- (iii) if $r \geq 0$ and $\Delta = p^2 - 3q > 0$, then (19) has positive roots if and only if $z_1^* = (-p + \sqrt{\Delta})/3$ and $h(z_1^*) \leq 0$, where

$$h(z) = z^3 + pz^2 + qz + r. \tag{20}$$

Lemma 6. For the transcendental equation (19),

- (i) if $r \geq 0$ and $\Delta = p^2 - 3q \leq 0$, then all roots with positive real parts of (19) have the same sum as those of the polynomial equation (16), for all τ ,
- (ii) if $r < 0$ or $r \geq 0$, $\Delta = p^2 - 3q > 0$, $z_1^* = (-p + \sqrt{\Delta})/3 > 0$ and $h(z_1^*) \leq 0$, then all roots with positive real parts of (19) have the same sum as those of the polynomial equation (16), for $\tau \in [0, \tau_0)$.

From Lemmas 5 and 6, we can have the following lemma.

Lemma 7. (i) The chronic infected equilibrium E^* of the system (5) is absolutely stable if and only if the equilibrium E^* of the corresponding ordinary differential equation (ODE) system is asymptotically stable, and the characteristic equation (10) has no purely imaginary roots for any $\tau > 0$.

(ii) The chronic infected equilibrium E^* of the system (5) is conditionally stable if and only if all roots of the characteristic equation (10) have negative real parts at $\tau = 0$ such that the characteristic equation (10) has a pair of purely imaginary roots $i\omega_0$.

Then, one turns to an investigation of local stability of the chronic infected equilibrium E^* in the case of $R_0 < 1$.

Theorem 8. For $R_0 < 1$ holds, there exists a sequence of values for τ :

$$\tau_0 < \tau_1 < \dots < \tau_k < \dots, \tag{21}$$

such that (10) has a pair of purely imaginary roots $i\omega_0$ when $\tau = \tau_k$, $k = 0, 1, 2, \dots$. That is, the chronic infected equilibrium E^* of the system (5) is conditionally stable.

Proof. From the above arguments, we know that all roots of characteristic equation (10) have negative real parts at $\tau = 0$. Next, we will show that there is a unique pair of purely imaginary roots $i\omega_0$ ($\omega_0 > 0$) for characteristic equation (10).

Assume that for some $\tau > 0$, $i\omega$ ($\omega > 0$) is a root of (10), which implies that

$$\begin{aligned} & -i\omega^3 - (2d + A + a)\omega^2 + [d(2a + A + d) + aA]i\omega \\ & + ad(d + A) = Be^{-i\omega\tau}e^{-d\tau}[-\omega^2 + 2di\omega + d^2]. \end{aligned} \tag{22}$$

Note that $A > 0$, $B > 0$ because of the positivities of the parameters $\lambda, \mu, \kappa, \beta, d$ and the properties $x^*(t) + (\lambda/d) \leq [x^*(t) + (\lambda/d) + y^*(t)]$, $y^*(t) \leq [x^*(t) + (\lambda/d) + y^*(t)]$.

Separating the real and imaginary parts and using Euler's formula give

$$\begin{aligned} & -(2d + A + a)\omega^2 + ad(d + A) \\ & = B(d^2 - \omega^2)e^{-d\tau} \cos \omega\tau + 2Bd\omega e^{-d\tau} \sin \omega\tau, \\ & -\omega^3 + [d(2a + A + d) + aA]\omega \\ & = 2Bd\omega e^{-d\tau} \cos \omega\tau - B(d^2 - \omega^2)e^{-d\tau} \sin \omega\tau, \end{aligned} \tag{23}$$

which is equivalent to

$$\omega^6 + p\omega^4 + q\omega^2 + r = 0, \tag{24}$$

where

$$\begin{aligned} p &= (2d + A + a)^2 - 2[d(2a + A + d) + aA] \\ &= A^2 + 2d^2 + a^2 + 2dA > 0, \end{aligned}$$

$$q = [d(2a + A + d) + aA]^2 - 2(2d + A + a)ad(d + A),$$

$$r = -e^{-2d\tau} [B^2(d^2 - \omega^2)^2 + 8B^2d^2] < 0. \tag{25}$$

In order to solve (24), we first consider the following:

$$\omega^6 + p\omega^4 + q\omega^2 + r_0 = 0, \tag{26}$$

where

$$r_0 = -[B^2(d^2 - \omega^2)^2 + 8B^2d^2] < 0. \tag{27}$$

By Lemma 5, there is a unique positive ω_0 satisfying (26). From (26), we get the corresponding $\tau'_k > 0$ such that (26) has a pair of purely imaginary roots

$$\begin{aligned} \tau'_k &= \frac{1}{\omega_0} \arccos \left\{ \left(ad(d + A) - (2d + A + a)\omega_0^2 - \omega_0^3 \right. \right. \\ & \quad \left. \left. + [d(2a + A + d) + aA]\omega_0 \right) \right. \\ & \quad \left. \times \left(B^2(d^2 - \omega_0^2)^2 + 8B^2d^2 \right)^{-1} \right\} + \frac{2k\pi}{\omega_0} \\ & \quad (k = 0, 1, 2, \dots). \end{aligned} \tag{28}$$

Therefore, by using Rouché's theorem [3], there is a unique positive $\tau_k = \tau'_k + o(1/k)$ satisfying (26), that is, the characteristic equation (10) has a pair of purely imaginary

roots of the form $\pm i\omega_0$ as $k \rightarrow \infty$. By Lemma 7, we complete the proof of Theorem 8.

Next, we turn to show that

$$\left. \frac{d(\operatorname{Re} \lambda)}{d\tau} \right|_{\tau=\tau_k} > 0. \tag{29}$$

This will signify that there exists at least one eigenvalue with positive real part $\tau = \tau_k$. We first consider the following:

$$\begin{aligned} z^3 + (2d + A + a)z^2 + [d(2a + A + d) + aA]z + ad(d + A) \\ = Be^{-z\tau} [z^2 + 2dz + d^2]. \end{aligned} \tag{30}$$

Differentiating (30) with respect to τ , we have

$$\begin{aligned} \left(\frac{d\lambda}{d\tau} \right)^{-1} &= \frac{3z^2 + 2(A + 2d + a)z + [d(2a + A + d) + aA]}{-Bz(d + z)^2 e^{-z\tau}} \\ &+ \frac{\tau e^{-z\tau} B(z + d)^2}{-Bz(d + z)^2 e^{-z\tau}} - \frac{2e^{-z\tau} B(z + d)}{-Bz(d + z)^2 e^{-z\tau}} \\ &= ((d + z) \{ 3z^2 + 2(A + 2d + a)z \\ &\quad + [d(2a + A + d) + aA] \}) \\ &\times (-Bz(d + z)^3 e^{-z\tau})^{-1} \\ &- \frac{2e^{-z\tau} B(z + d)^2}{-Bz(d + z)^3 e^{-z\tau}} - \frac{\tau}{z} \\ &= - (d \{ 3z^2 + 2(A + 2d + a)z \\ &\quad + [d(2a + A + d) + aA] \}) \\ &\times ((d + z) [z^3 + (2d + A + a)z^2 \\ &\quad + [d(2a + A + d) + aA]z \\ &\quad + ad(d + A)])^{-1} \\ &- (z^2 - [d(2a + A + d) + aA]z - 2ad(d + A)) \\ &\times ((d + z) [z^3 + (2d + A + a)z^2 \\ &\quad + [d(2a + A + d) + aA]z \\ &\quad + ad(d + A)])^{-1} \\ &- \frac{\tau}{z}. \end{aligned} \tag{31}$$

For the sake of simplicity, let $a_1 = A + 2d + a$, $a_2 = d(2a + A + d) + aA$, and $a_3 = ad(d + A)$, and (28) can be written as follows:

$$\begin{aligned} \left(\frac{d\lambda}{d\tau} \right)^{-1} &= - \frac{d \{ 3z^2 + 2a_1z + a_2 \}}{(d + z) [z^3 + a_1z^2 + a_2z + a_3]} \\ &- \frac{z^2 - a_2z - 2a_3}{(d + z) [z^3 + a_1z^2 + a_2z + a_3]} - \frac{\tau}{z} \\ &= \frac{-(3d + 1)z^2 - (2a_1d - a_2)z - (a_2d - 2a_3)}{(d + z) [z^3 + a_1z^2 + a_2z + a_3]} - \frac{\tau}{z}. \end{aligned} \tag{32}$$

Therefore,

$$\begin{aligned} \operatorname{sign} \left\{ \left. \frac{d(\operatorname{Re} \lambda)}{d\tau} \right|_{\tau=\tau_k} \right\} &= \operatorname{sign} \left\{ \operatorname{Re} \left(\frac{d\lambda}{d\tau} \right)^{-1} \right\} \Big|_{\tau=\tau_k} \\ &= \operatorname{sign} \operatorname{Re} \left\{ \frac{-(3d + 1)z^2 - (2a_1d - a_2)z - (a_2d - 2a_3)}{(d + z) [z^3 + a_1z^2 + a_2z + a_3]} \right. \\ &\quad \left. - \frac{\tau}{z} \right\} \\ &= \operatorname{sign} \operatorname{Re} \left\{ \left([(3d + 1)\omega_0^2 - i(2a_1d - a_2)\omega_0 \right. \right. \\ &\quad \left. \left. - (a_2d - 2a_3)](d - i\omega_0) \right) \right. \\ &\quad \left. \times (d^2 + \omega_0^2) \right. \\ &\quad \left. \times [(a_3^2 - a_1\omega_0^2)^2 + (a_2\omega_0 - \omega_0^3)^2] \right\}^{-1} \\ &\quad \times [(a_3^2 - a_1\omega_0^2) - i(a_2\omega_0 - \omega_0^3)] \Big\} \\ &= \operatorname{sign} \left\{ \frac{(3d + 1)\omega_0^6 + p^2\omega_0^4 + Bd^2\omega_0^2}{(d^2 + \omega_0^2) [(a_3^2 - a_1\omega_0^2)^2 + (a_2\omega_0 - \omega_0^3)^2]} \right\} > 0. \end{aligned} \tag{33}$$

This root of characteristic equation (9) crosses the imaginary axis from the left to the right as τ continuously varies from a number less than τ_k to one greater than τ_k again by Rouché's theorem [3]. Therefore, the transversality condition holds, and the conditions for Hopf bifurcation [11] are then satisfied at $\tau = \tau_k$. In conclusion, we have the following stability and bifurcation results to (5). \square

Theorem 9. Suppose that $R_0 < 1$ holds. Then, for each fixed $\tau > 0$, there exists a sequence of values for τ :

$$\tau_0 < \tau_1 < \dots < \tau_k < \dots, \tag{34}$$

such that the positive equilibrium E^* is asymptotically stable when $\tau \in [0, \tau_0)$, and unstable when $\tau > \tau_0$. Furthermore, (5) undergoes a Hopf bifurcation at E^* when $\tau = \tau_k = \tau_k' + o(1/k)$, $k = 0, 1, 2, \dots$, where τ_k' is defined by (28).

3. Properties of the Hopf Bifurcations

In this section, we will study the properties of the Hopf bifurcations by using the normal theory and the center manifold theorem due to Hassard et al. [8]. Let $x_1 = \bar{x} - x^*$, $x_2 = e - e^*$, $x_3 = y - y^*$, $\tilde{x}_i(t) = x_i(\tau t)$, $\tau = \tau_k + \vartheta$, and $\vartheta \in R = (-\infty, \infty)$. Then, $\vartheta = 0$ is the Hopf bifurcation value of system. We drop the tildes for simplification of notations, then the system (5) becomes a functional differential equation in $C([-1, 0], R^3)$ as

$$\dot{x}(t) = L_\vartheta(x_t) + f(\vartheta, x_t), \tag{35}$$

where $C([-1, 0], R^3)$ is the Banach space of continuous functions mapping the interval $[-\tau, 0]$ into R^3 , $x(t) = (x_1(t), x_2(t), x_3(t))^T \in R^3$, $x_t(s) = x(t + s)$ for $s \in [-\tau, 0]$ and $L_\vartheta : C \rightarrow R^3$, $f : R \times C \rightarrow R^3$ are read, respectively, as

$$L_\vartheta(\phi) = (\tau_k + \vartheta) \begin{pmatrix} -(d + A) & 0 & -B \\ A & -d & B \\ 0 & 0 & -a \end{pmatrix} \begin{pmatrix} \phi_1(0) \\ \phi_2(0) \\ \phi_3(0) \end{pmatrix} + (\tau_k + \vartheta) \begin{pmatrix} 0 & 0 & 0 \\ -Ae^{-d\tau_k} & 0 & Be^{-d\tau_k} \\ Ae^{-d\tau_k} & 0 & -Be^{-d\tau_k} \end{pmatrix} \begin{pmatrix} \phi_1(-1) \\ \phi_2(-1) \\ \phi_3(-1) \end{pmatrix}, \tag{36}$$

$$f(\vartheta, x_t) = (\tau_k + \vartheta) \times \begin{pmatrix} -\frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} \\ \frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} - \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \\ \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \end{pmatrix}. \tag{37}$$

Obviously, L_ϑ is a continuous linear function mapping C into R^3 , by the Riesz representation theorem, there exists a 3×3 matrix function $\eta(s, \mu)$ of bounded variation for $s \in [-1, 0]$, such that

$$L_\vartheta(\phi) = \int_{-1}^0 d\eta(s, \mu) \phi(s). \tag{38}$$

In fact, we can choose

$$\eta(s, \vartheta) = (\tau_k + \vartheta) \begin{pmatrix} -(d + A) & 0 & -B \\ A & -d & B \\ 0 & 0 & -a \end{pmatrix} \delta(s) + (\tau_k + \vartheta) \begin{pmatrix} 0 & 0 & 0 \\ -Ae^{-d\tau_k} & 0 & Be^{-d\tau_k} \\ Ae^{-d\tau_k} & 0 & -Be^{-d\tau_k} \end{pmatrix} \delta(s + 1), \tag{39}$$

where $\delta(\cdot)$ denotes the Dirac delta function.

If ϕ is any given function in C and $x(\phi)$ is the unique solution of the linearized equation $\dot{x}(t) = L_\vartheta(x_t)$ of (35) with

initial function ϕ at zero, then the solution operator $T(t) : C \rightarrow C$ is defined by $T(t)\phi = x_t(\phi)$, for all $t \geq 0$. It is obvious that $T(t)$, $t \geq 0$, is a strongly continuous semigroup of linear transformation on $[0, +\infty)$ and the infinitesimal generator A_ϑ of $T(t)$, $t \geq 0$, is

$$A_\vartheta = \begin{cases} \frac{d\phi(s)}{ds}, & s \in [-1, 0) \\ \int_{-1}^0 d\eta(s, \mu) \phi(s), & s = 0. \end{cases} \tag{40}$$

For $\phi \in C^1([-1, 0], R^3)$, the space of functions mapping the interval $[-1, 0]$ into R^3 which have a continuous first derivative also defines

$$R_\vartheta(\phi) = \begin{cases} 0, & s \in [-1, 0) \\ f(\vartheta, \phi), & s = 0. \end{cases} \tag{41}$$

Then, system (35) is equivalent to

$$\dot{x}(t) = A_\vartheta x_t + R_\vartheta x_t. \tag{42}$$

For $\psi \in C^1([-1, 0], (R^3)^*)$, the space of functions mapping interval $[0, 1]$ into the three-dimensional row vectors which have continuous first derivative defines

$$A_\vartheta^* = \begin{cases} -\frac{d\psi(s)}{ds}, & s \in (0, 1] \\ \int_{-1}^0 d\eta^T(t, 0) \phi(-t), & s = 0, \end{cases} \tag{43}$$

and a bilinear inner product

$$\langle \psi(\zeta), \phi(s) \rangle = \bar{\psi}(0) \phi(0) - \int_{-1}^0 \int_{\xi=0}^s \bar{\psi}(\xi - s) d\eta(s) \phi(\xi) d\xi, \tag{44}$$

where $\eta(s) = \eta(s, 0)$. Then, $A(0)$ and A^* are adjoint operators. By the discussion in Section 2, we know that z are eigenvalues of $A(0)$. Hence, they are also eigenvalues of A^* . We first need to compute the eigenvectors of $A(0)$ and A^* corresponding to $i\omega_0\tau_k$ and $-i\omega_0\tau_k$, respectively. Suppose that $q(s) = (1, a, b)^T e^{i\omega_0\tau_k s}$ is the eigenvectors of $A(0)$ corresponding to $i\omega_0\tau_k$, then $A(0)q(s) = i\omega_0\tau_k q(s)$. Then, from the definition of $A(0)$ and (36), (38), and (39), we have

$$\begin{aligned} & \tau_k \begin{pmatrix} -(d + A) & 0 & -B \\ A & -d & B \\ 0 & 0 & -a \end{pmatrix} q(0) \\ & + \tau_k \begin{pmatrix} 0 & 0 & 0 \\ -Ae^{-d\tau_k} & 0 & Be^{-d\tau_k} \\ Ae^{-d\tau_k} & 0 & -Be^{-d\tau_k} \end{pmatrix} q(-1) \\ & = i\omega_0\tau_k q(0). \end{aligned} \tag{45}$$

For $q(-1) = q(0)e^{-i\omega_0\tau_k}$, then we obtain

$$\begin{aligned} \rho &= -1 + \frac{1}{B} + \frac{A(d - i\omega_0)(a + i\omega_0)}{B(d^2 + \omega_0^2)}, \\ \sigma &= -\frac{A + d + i\omega_0}{B}. \end{aligned} \tag{46}$$

Similarly, we can obtain the eigenvector $q^*(s) = D(1, \rho^*, \sigma^*)e^{i\omega_0\tau_k}$ of A^* corresponding to $-i\omega_0\tau_k$, where

$$\begin{aligned} \rho^* &= \rho = -1 + \frac{1}{B} + \frac{A(d - i\omega_0)(a + i\omega_0)}{B(d^2 + \omega_0^2)}, \\ \sigma^* &= \sigma = -\frac{A + d + i\omega_0}{B}. \end{aligned} \tag{47}$$

We need to determine the value of D to ensure that $\langle q^*(s), q(s) \rangle = 1$. By (44), we have

$$\begin{aligned} &\langle q^*(s), q(s) \rangle \\ &= \bar{D}(1, \rho^*, \sigma^*) (1, \rho, \sigma)^T \\ &\quad - \int_{-1}^0 \int_{\xi=0}^s \bar{D}(1, \rho^*, \sigma^*) e^{-i\omega_0\tau_k(\xi-s)} d\eta(s) (1, \rho, \sigma)^T \\ &\quad \times e^{i\omega_0\tau_k\xi} d\xi \\ &= \bar{D} \left[1 + |\rho|^2 + |\sigma|^2 \right. \\ &\quad \left. - \int_{-1}^0 (1, \rho^*, \sigma^*) s e^{i\omega_0\tau_k s} d\eta(s) (1, \rho, \sigma)^T \right] \\ &= \bar{D} \left[1 + |\rho|^2 + |\sigma|^2 + e^{-d\tau_k} e^{-i\omega_0\tau_k} (A - B\sigma) (\bar{\rho}^* - \bar{\sigma}^*) \right]. \end{aligned} \tag{48}$$

Therefore, we can choose D as

$$D = \frac{1}{1 + |\rho|^2 + |\sigma|^2 + e^{-d\tau_k} e^{-i\omega_0\tau_k} (A - B\sigma) (\bar{\rho}^* - \bar{\sigma}^*)}. \tag{49}$$

Next, we will compute the coordinate to describe the center manifold C_0 at $\vartheta = 0$. Let x_t be the solution of (42) when $\vartheta = 0$. Define

$$v(t) = \langle q^*(s), x_t \rangle, \quad W(t, s) = x_t(s) - 2 \operatorname{Re} \{v(t) q(s)\}. \tag{50}$$

On the center manifold C_0 , we have

$$W(t, s) = W(v(t), \bar{v}(t), s), \tag{51}$$

where

$$\begin{aligned} &W(v(t), \bar{v}(t), s) \\ &= W_{20}(s) \frac{v^2}{2} + W_{10}(s) v\bar{v} + W_{02}(s) \frac{\bar{v}^2}{2} + \dots \end{aligned} \tag{52}$$

v and \bar{v} are local coordinates for the center manifold C_0 in the direction of q^* and \bar{q}^* . Note that W is real if x_t is real. We only consider real solutions. For solution $x_t \in C_0$ of (42), since $\vartheta = 0$, we have

$$\begin{aligned} \dot{v}(t) &= i\omega_0\tau_k v(t) + \bar{q}^*(0) f(0, W(v, \bar{v}, 0) + 2 \operatorname{Re} \{vq(s)\}) \\ &:= i\omega_0\tau_k v(t) + \bar{q}^*(0) f_0(v, \bar{v}). \end{aligned} \tag{53}$$

For convenience of calculation, let

$$\begin{aligned} &\bar{q}^*(0) f_0(v, \bar{v}) \\ &= f_{20} \frac{v^2}{2} + f_{11}(s) v\bar{v} + f_{02}(s) \frac{\bar{v}^2}{2} + f_{21} \frac{v^2\bar{v}}{2} + \dots \end{aligned} \tag{54}$$

On the other hand, it follows from (50) and (52) that

$$\begin{aligned} x_t(s) &= W(v, \bar{v}, 0) + 2 \operatorname{Re} \{vq(s)\} \\ &= W_{20}(s) \frac{v^2}{2} + W_{10}(s) v\bar{v} + W_{02}(s) \frac{\bar{v}^2}{2} \\ &\quad + (1, a, b)^T e^{i\omega_0\tau_k s} v + (1, \bar{a}, \bar{b})^T e^{-i\omega_0\tau_k s} \bar{v} + \dots \end{aligned} \tag{55}$$

Notice that

$$\begin{aligned} \phi_1(0) &= q_1(0) v + \bar{q}_1(0) \bar{v} + W_{20}^{(1)}(0) \frac{v^2}{2} \\ &\quad + W_{11}^{(1)}(0) v\bar{v} + W_{02}^{(1)}(0) \frac{\bar{v}^2}{2} + \dots, \end{aligned} \tag{56}$$

$$\begin{aligned} \phi_2(0) &= q_2(0)v + \bar{q}_2(0)\bar{v} + W_{20}^{(2)}(0)\frac{v^2}{2} \\ &+ W_{11}^{(2)}(0)v\bar{v} + W_{02}^{(2)}(0)\frac{\bar{v}^2}{2} + \dots, \end{aligned} \quad (57)$$

$$\begin{aligned} \phi_3(0) &= q_3(0)v + \bar{q}_3(0)\bar{v} + W_{20}^{(3)}(0)\frac{v^2}{2} \\ &+ W_{11}^{(3)}(0)v\bar{v} + W_{02}^{(3)}(0)\frac{\bar{v}^2}{2} + \dots, \end{aligned} \quad (58)$$

$$\begin{aligned} \phi_1(-1) &= q_1(0)ve^{-i\omega_0^*\tau_0^*} + \bar{q}_1(0)\bar{v}e^{i\omega_0^*\tau_0^*} \\ &+ W_{20}^{(1)}(-1)\frac{v^2}{2} + W_{11}^{(1)}(-1)v\bar{v} + \dots, \end{aligned} \quad (59)$$

$$\begin{aligned} \phi_2(-1) &= q_2(0)ve^{-i\omega_0^*\tau_0^*} + \bar{q}_2(0)\bar{v}e^{i\omega_0^*\tau_0^*} \\ &+ W_{20}^{(2)}(-1)\frac{v^2}{2} + W_{11}^{(2)}(-1)v\bar{v} + \dots, \end{aligned} \quad (60)$$

$$\begin{aligned} \phi_3(-1) &= q_3(0)ve^{-i\omega_0^*\tau_0^*} + \bar{q}_3(0)\bar{v}e^{i\omega_0^*\tau_0^*} \\ &+ W_{20}^{(3)}(-1)\frac{v^2}{2} + W_{11}^{(3)}(-1)v\bar{v} + \dots, \end{aligned} \quad (61)$$

Taking (37) into account, we can obtain that

$$\begin{aligned} \bar{q}^*(0)f_0(v, \bar{v}) &= \bar{q}^*(0)f(0, x_t) \\ &= \tau_k \bar{D}(1, \bar{\rho}^*, \bar{\sigma}^*) \left(\begin{array}{c} \frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} \\ \frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} - \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \\ \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \end{array} \right) \\ &= \tau_k \bar{D} \left[-\frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} + \bar{\rho}^* \frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} \right. \\ &\quad \left. - \bar{\rho}^* \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} + \bar{\sigma}^* \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \right] \\ &= (\rho^* - 1) \frac{\tau_k \bar{D} \beta k}{\mu \Delta_0} \left[\frac{\lambda}{d} + q_1(0)v + \bar{q}_1(0)\bar{v} + W_{20}^{(1)}(0)\frac{v^2}{2} + W_{11}^{(1)}(0)v\bar{v} + W_{02}^{(1)}(0)\frac{\bar{v}^2}{2} + \dots \right] \\ &\quad \times \left[q_3(0)v + \bar{q}_3(0)\bar{v} + W_{20}^{(3)}(0)\frac{v^2}{2} + W_{11}^{(3)}(0)v\bar{v} + W_{02}^{(3)}(0)\frac{\bar{v}^2}{2} + \dots \right] \\ &\quad \times \left[\frac{\lambda}{d} + q_1(0)v + \bar{q}_1(0)\bar{v} + W_{20}^{(1)}(0)\frac{v^2}{2} + W_{11}^{(1)}(0)v\bar{v} + W_{02}^{(1)}(0)\frac{\bar{v}^2}{2} + \dots + q_3(0)v \right. \\ &\quad \left. + \bar{q}_3(0)\bar{v} + W_{20}^{(3)}(0)\frac{v^2}{2} + W_{11}^{(3)}(0)v\bar{v} + W_{02}^{(3)}(0)\frac{\bar{v}^2}{2} + \dots \right] \\ &\quad + (\sigma^* - \rho^*) \frac{\tau_k \bar{D} \beta k e^{-d\tau_k}}{\mu \Delta_{-1}} \\ &\quad \times \left[\frac{\lambda}{d} + q_1(0)ve^{-i\omega_0^*\tau_0^*} + \bar{q}_1(0)\bar{v}e^{i\omega_0^*\tau_0^*} + W_{20}^{(1)}(0)\frac{v^2}{2} + W_{11}^{(1)}(0)v\bar{v} + \dots \right] \\ &\quad \times \left[q_3(0)ve^{-i\omega_0^*\tau_0^*} + \bar{q}_3(0)\bar{v}e^{i\omega_0^*\tau_0^*} + W_{20}^{(3)}(0)\frac{v^2}{2} + W_{11}^{(3)}(0)v\bar{v} + W_{02}^{(3)}(0)\frac{\bar{v}^2}{2} + \dots \right] \end{aligned}$$

$$\begin{aligned} & \times \left[\frac{\lambda}{d} + q_1(0) e^{-i\omega_0^* \tau_0^*} + \bar{q}_1(0) \bar{v} e^{i\omega_0^* \tau_0^*} + W_{20}^{(1)}(0) \frac{v^2}{2} + W_{11}^{(1)}(0) v\bar{v} + W_{02}^{(1)}(0) \frac{\bar{v}^2}{2} + \dots \right. \\ & \left. + q_3(0) v e^{-i\omega_0^* \tau_0^*} + \bar{q}_3(0) \bar{v} e^{i\omega_0^* \tau_0^*} + W_{20}^{(3)}(0) \frac{v^2}{2} + W_{11}^{(3)}(0) v\bar{v} + W_{02}^{(3)}(0) \frac{\bar{v}^2}{2} + \dots \right], \end{aligned} \tag{62}$$

where

$$\begin{aligned} \Delta_0 = & \left| \frac{\lambda}{d} + q_1(0) v + \bar{q}_1(0) \bar{v} + W_{20}^{(1)}(0) \frac{v^2}{2} + W_{11}^{(1)}(0) v\bar{v} \right. \\ & \left. + W_{02}^{(1)}(0) \frac{\bar{v}^2}{2} + \dots + q_3(0) v + \bar{q}_3(0) \bar{v} \right. \\ & \left. + W_{20}^{(3)}(0) \frac{v^2}{2} + W_{11}^{(3)}(0) v\bar{v} + W_{02}^{(3)}(0) \frac{\bar{v}^2}{2} + \dots \right|^2, \end{aligned}$$

$$\begin{aligned} \Delta_{-1} = & \left| \frac{\lambda}{d} + q_1(0) v e^{-i\omega_0^* \tau_0^*} + \bar{q}_3(0) \bar{v} e^{i\omega_0^* \tau_0^*} + W_{20}^{(1)}(0) \frac{v^2}{2} \right. \\ & \left. + W_{11}^{(1)}(0) v\bar{v} + W_{02}^{(1)}(0) \frac{\bar{v}^2}{2} + \dots \right. \\ & \left. + q_3(0) v + \bar{q}_3(0) \bar{v} + W_{20}^{(3)}(0) \frac{v^2}{2} \right. \\ & \left. + W_{11}^{(3)}(0) v\bar{v} + W_{02}^{(3)}(0) \frac{\bar{v}^2}{2} + \dots \right|^2. \end{aligned} \tag{63}$$

Straightforward calculation leads to

$$\begin{aligned} & \bar{q}^*(0) f_0(v, \bar{v}) \\ & = (\rho^* - 1) \frac{\beta k}{\mu \Delta_0} \\ & \times \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) v^2 + \frac{\lambda}{d} q_1(0) q_3(0) v^2 \right. \\ & \left. + \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(0) \frac{v^2}{2} + \frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) v\bar{v} \right. \\ & \left. + 2 \operatorname{Re} \left\{ \frac{\lambda}{d} q_1(0) q_3(0) \right\} v\bar{v} \right. \\ & \left. + \left(\frac{\lambda}{d} \right)^2 W_{11}^{(3)}(0) v\bar{v} + \dots \right] \\ & + (\sigma^* - \rho^*) \frac{\tau_k \bar{D} \beta k e^{-d\tau_k}}{\mu \Delta_{-1}} \end{aligned}$$

$$\begin{aligned} & \times \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) v^2 + \frac{\lambda}{d} q_1(0) q_3(0) v^2 \right. \\ & \left. + \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(-1) \frac{v^2}{2} + \frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) v\bar{v} \right. \\ & \left. + 2 \operatorname{Re} \left\{ \frac{\lambda}{d} q_1(0) q_3(0) \right\} v\bar{v} \right. \\ & \left. + \left(\frac{\lambda}{d} \right)^2 W_{11}^{(3)}(-1) v\bar{v} + \dots \right]. \end{aligned} \tag{64}$$

Comparing the coefficients with (54), we have

$$\begin{aligned} f_{20} = & (\rho^* - 1) \frac{\beta k}{\mu \Delta_0} \\ & \times \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + \frac{\lambda}{d} q_1(0) q_3(0) \right. \\ & \left. + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(0) \right] \\ & + (\sigma^* - \rho^*) \frac{\tau_k \bar{D} \beta k e^{-d\tau_k}}{\mu \Delta_{-1}} \\ & \times \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + \frac{\lambda}{d} q_1(0) q_3(0) \right. \\ & \left. + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(-1) \right], \\ f_{11} = & \frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + 2 \operatorname{Re} \left\{ \frac{\lambda}{d} q_1(0) q_3(0) \right\} \\ & + \left(\frac{\lambda}{d} \right)^2 W_{11}^{(3)}(-1) + \frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) \\ & + 2 \operatorname{Re} \left\{ \frac{\lambda}{d} q_1(0) q_3(0) \right\} + \left(\frac{\lambda}{d} \right)^2 W_{11}^{(3)}(-1), \\ f_{02} = & (\rho^* - 1) \frac{\beta k}{\mu \Delta_0} \end{aligned}$$

$$\begin{aligned}
 & \times \left[\frac{\lambda}{d} (\bar{q}_1(0) + \bar{q}_3(0)) \bar{q}_3(0) + \frac{\lambda}{d} \bar{q}_1(0) \bar{q}_3(0) \right. \\
 & \quad \left. + \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(0) \frac{\bar{v}^2}{2} \right] \\
 & + (\sigma^* - \rho^*) \frac{\tau_k \bar{D} \beta k e^{-d\tau_k}}{\mu \Delta_{-1}} \\
 & \times \left[\frac{\lambda}{d} (\bar{q}_1(0) + \bar{q}_3(0)) \bar{q}_3(0) + \frac{\lambda}{d} \bar{q}_1(0) \bar{q}_3(0) \right. \\
 & \quad \left. + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(-1) \right], \\
 f_{21} & = (\rho^* - 1) \frac{\beta k}{\mu \Delta_0} \\
 & \times \left[\frac{\lambda}{d} (\bar{q}_1(0) + \bar{q}_3(0)) \bar{q}_3(0) + \frac{\lambda}{d} \bar{q}_1(0) \bar{q}_3(0) \right. \\
 & \quad \left. + \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(0) \frac{\bar{v}^2}{2} \right] \\
 & + (\sigma^* - \rho^*) \frac{\tau_k \bar{D} \beta k e^{-d\tau_k}}{\mu \Delta_{-1}} \\
 & \times \left[\frac{\lambda}{d} (\bar{q}_1(0) + \bar{q}_3(0)) \bar{q}_3(0) + \frac{\lambda}{d} \bar{q}_1(0) \bar{q}_3(0) \right. \\
 & \quad \left. + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 W_{20}^{(3)}(-1) \right]. \tag{65}
 \end{aligned}$$

Since $W_{20}(s)$ and $W_{11}(s)$ are in f_{21} , we still need to compute them. From (40) and (44), we have

$$\begin{aligned}
 \dot{W} & = \dot{x}_t - \dot{v}q - \dot{\bar{v}}\bar{q} \\
 & = \begin{cases} AW - 2 \operatorname{Re} \{ \bar{q}^*(0) f_0 q(s) \}, & s \in [-1, 0), \\ AW - 2 \operatorname{Re} \{ \bar{q}^*(0) f_0 q(s) \} + f_0, & s = 0, \end{cases} \tag{66}
 \end{aligned}$$

that is,

$$\dot{W} = AW + H(v, \bar{v}, s), \tag{67}$$

where

$$H(v, \bar{v}, s) = H_{20}(s) \frac{v^2}{2} + H_{10}(s) v\bar{v} + H_{02}(s) \frac{\bar{v}^2}{2} + \dots \tag{68}$$

Substituting the corresponding series into (67) and comparing the coefficients, we have

$$\begin{aligned}
 (A - 2i\omega_0 \tau_k) W_{20}(s) & = -H_{20}(s), \\
 AW_{11}(s) & = -H_{11}(s), \dots \tag{69}
 \end{aligned}$$

From (67), we know that for $s \in [-1, 0)$,

$$\begin{aligned}
 H(v, \bar{v}, s) & = -\bar{q}^*(s) f_0 q(s) - q^*(s) \bar{f}_0 \bar{q}(s) \\
 & = -f(v, \bar{v}) q(s) - \bar{f}(v, \bar{v}) \bar{q}(s). \tag{70}
 \end{aligned}$$

Comparing the coefficients with (68) gives

$$H_{20}(s) = -f_{20} q(s) - \bar{f}_{02} \bar{q}(s), \tag{71}$$

$$H_{11}(s) = -f_{11} q(s) - \bar{f}_{11} \bar{q}(s).$$

From the definition of A and (69) and (71), we obtain

$$\dot{W}_{20}(s) = 2i\omega_0 \tau_k W_{20}(s) + f_{20} q(s) + \bar{f}_{02} \bar{q}(s). \tag{72}$$

For $q(s) = (1, \rho, \sigma)^T e^{i\omega_0 \tau_k s}$, hence

$$\begin{aligned}
 W_{20}(s) & = \frac{if_{20}}{\omega_0 \tau_k} q(0) e^{i\omega_0 \tau_k s} \\
 & + \frac{i\bar{f}_{02}}{3\omega_0 \tau_k} q(0) e^{-i\omega_0 \tau_k s} \bar{q}(s) + E_1 e^{2i\omega_0 \tau_k s}, \tag{73}
 \end{aligned}$$

where $E_1 = (E_1^{(1)}, E_1^{(2)}, E_1^{(3)})$ is a constant vector. Similarly, we know that

$$W_{11}(s) = -\frac{if_{11}}{\omega_0 \tau_k} q(0) e^{i\omega_0 \tau_k s} + \frac{i\bar{f}_{11}}{\omega_0 \tau_k} q(0) e^{-i\omega_0 \tau_k s} \bar{q}(s) + E_2, \tag{74}$$

where $E_2 = (E_2^{(1)}, E_2^{(2)}, E_2^{(3)})$ is a constant vector.

In what follows, we will calculate E_1 and E_2 . From the definition of A and (69), we have

$$\int_{-1}^0 d\eta^T(s) W_{20}(s) = 2i\omega_0 \tau_k W_{20}(0) - H_{20}(0), \tag{75}$$

$$\int_{-1}^0 d\eta^T(s) W_{11}(s) = -H_{11}(0), \tag{76}$$

where $\eta(s) = \eta(s, 0)$. When $s = 0$, we obtain that

$$\begin{aligned}
 H(v, \bar{v}, 0) & = -2 \operatorname{Re} \{ \bar{q}^*(0) f_0 q(0) \} + f_0 \\
 & = -\bar{q}^*(0) f_0 q(0) - q^*(0) \bar{f}_0 \bar{q}(0) + f_0, \tag{77}
 \end{aligned}$$

that is,

$$\begin{aligned}
 H_{20}(s) \frac{v^2}{2} + H_{11}(s) v\bar{v} + H_{02}(s) \frac{\bar{v}^2}{2} + \dots \\
 = -q(0) \left(f_{20} \frac{v^2}{2} + f_{11}(s) v\bar{v} + f_{02}(s) \frac{\bar{v}^2}{2} + f_{21} \frac{v^2 \bar{v}}{2} \dots \right) \\
 - \bar{q}(0) \left(\bar{f}_{20} \frac{v^2}{2} + \bar{f}_{11}(s) v\bar{v} + \bar{f}_{02}(s) \frac{\bar{v}^2}{2} + f_{21} \frac{v^2 \bar{v}}{2} \dots \right) \\
 + f_0, \tag{78}
 \end{aligned}$$

with

$$f_0 = \tau_k \begin{pmatrix} \frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} \\ \frac{\beta k [\phi_1(0) + (\lambda/d)] \phi_3(0)}{\mu [\phi_1(0) + (\lambda/d) + \phi_3(0)]} - \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \\ \frac{\beta k e^{-d\tau_k} [\phi_1(-1) + (\lambda/d)] \phi_3(-1)}{\mu [\phi_1(-1) + (\lambda/d) + \phi_3(-1)]} \end{pmatrix}. \tag{79}$$

From (50), we have

$$f_0 = \begin{pmatrix} f_{v^2}^1 \\ f_{v^2}^2 \\ f_{v^2}^3 \end{pmatrix} v^2 + \begin{pmatrix} f_{v\bar{v}}^1 \\ f_{v\bar{v}}^2 \\ f_{v\bar{v}}^3 \end{pmatrix} v\bar{v} + \dots, \quad (80)$$

where

$$f_{v^2}^1 = -\frac{\beta k}{\mu \Delta_0} \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + \frac{\lambda}{d} q_1(0) q_3(0) + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 \times \left(\frac{if_{20}}{\omega_0 \tau_k} q(0) e^{i\omega_0 \tau_k s} + \frac{i\bar{f}_{02}}{3\omega_0 \tau_k} q(0) e^{-i\omega_0 \tau_k s} \bar{q}(s) + E_1 e^{2i\omega_0 \tau_k s} \right) \right], \quad (81)$$

$$f_{v^2}^2 = \frac{\beta k}{\mu \Delta_0} \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + \frac{\lambda}{d} q_1(0) q_3(0) + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 \times \left(\frac{if_{20}}{\omega_0 \tau_k} q(0) e^{i\omega_0 \tau_k s} + \frac{i\bar{f}_{02}}{3\omega_0 \tau_k} q(0) e^{-i\omega_0 \tau_k s} \bar{q}(s) + E_1 e^{2i\omega_0 \tau_k s} \right) \right] + \frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + 2 \operatorname{Re} \left\{ \frac{\lambda}{d} q_1(0) q_3(0) \right\} + \left(\frac{\lambda}{d} \right)^2 W_{11}^{(3)}(-1)$$

$$+ \frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + 2 \operatorname{Re} \left\{ \frac{\lambda}{d} q_1(0) q_3(0) \right\} + \left(\frac{\lambda}{d} \right)^2 W_{11}^{(3)}(-1), \quad (82)$$

$$f_{v^2}^3 = -\frac{\beta k e^{-d\tau_k}}{\mu \Delta_{-1}} \left[\frac{\lambda}{d} (q_1(0) + q_3(0)) q_3(0) + \frac{\lambda}{d} q_1(0) q_3(0) + \frac{1}{2} \left(\frac{\lambda}{d} \right)^2 \times \left(\frac{if_{20}}{\omega_0 \tau_k} q(0) e^{i\omega_0 \tau_k s} + \frac{i\bar{f}_{02}}{3\omega_0 \tau_k} q(0) e^{-i\omega_0 \tau_k s} \bar{q}(s) + E_1 e^{2i\omega_0 \tau_k s} \right) \right]. \quad (83)$$

By (70) and (71), we have

$$H_{20}(s) = -f_{20} q(s) - \bar{f}_{02} \bar{q}(s) + f_{v^2}, \quad (84)$$

$$H_{11}(s) = -f_{11} q(s) - \bar{f}_{11} \bar{q}(s) + f_{v\bar{v}}.$$

For $i\omega_0 \tau_k$ is the eigenvalue of $A(0)$ and $q(0)$ is the corresponding eigenvector, we obtain

$$\left[i\omega_0 \tau_k I - \int_{-1}^0 e^{i\omega_0 \tau_k s} d\eta(s) \right] q(0) = 0, \quad (85)$$

$$\left[-i\omega_0 \tau_k I - \int_{-1}^0 e^{-i\omega_0 \tau_k s} d\eta(s) \right] \bar{q}(0) = 0.$$

So substituting (66) and (73) into (68), we obtain

$$\left[2i\omega_0 \tau_k I - \int_{-1}^0 e^{2i\omega_0 \tau_k s} d\eta(s) \right] E_1 = \begin{pmatrix} f_{v^2}^1 \\ f_{v^2}^2 \\ f_{v^2}^3 \end{pmatrix}, \quad (86)$$

that is,

$$\begin{pmatrix} 2i\omega_0 \tau_k + (d + A) & 0 & B \\ A(e^{-d\tau_k} e^{-2i\omega_0 \tau_k} - 1) & 2i\omega_0 \tau_k + d & B(e^{-d\tau_k} e^{-2i\omega_0 \tau_k} - 1) \\ -Ae^{-d\tau_k} e^{-2i\omega_0 \tau_k} & 0 & 2i\omega_0 \tau_k + a + Be^{-d\tau_k} e^{-2i\omega_0 \tau_k} \end{pmatrix} E_1 = \begin{pmatrix} f_{v^2}^1 \\ f_{v^2}^2 \\ f_{v^2}^3 \end{pmatrix}. \quad (87)$$

It follows that

$$\begin{aligned}
 E_1^{(1)} &= \frac{1}{M_1} \det \begin{pmatrix} f_{v^2}^1 & 0 & B \\ f_{v^2}^2 & 2i\omega_0\tau_k + d & B(e^{-d\tau_k}e^{-2i\omega_0\tau_k} - 1) \\ f_{v^2}^3 & 0 & 2i\omega_0\tau_k + a + Be^{-d\tau_k}e^{-2i\omega_0\tau_k} \end{pmatrix}, \\
 E_1^{(2)} &= \frac{1}{M_1} \det \begin{pmatrix} 2i\omega_0\tau_k + (d + A) & f_{v^2}^1 & B \\ A(e^{-d\tau_k}e^{-2i\omega_0\tau_k} - 1) & f_{v^2}^2 & B(e^{-d\tau_k}e^{-2i\omega_0\tau_k} - 1) \\ -Ae^{-d\tau_k}e^{-2i\omega_0\tau_k} & f_{v^2}^3 & 2i\omega_0\tau_k + a + Be^{-d\tau_k}e^{-2i\omega_0\tau_k} \end{pmatrix}, \\
 E_1^{(3)} &= \frac{1}{M_1} \det \begin{pmatrix} 2i\omega_0\tau_k + (d + A) & 0 & f_{v^2}^1 \\ A(e^{-d\tau_k}e^{-2i\omega_0\tau_k} - 1) & 2i\omega_0\tau_k + d & f_{v^2}^2 \\ -Ae^{-d\tau_k}e^{-2i\omega_0\tau_k} & 0 & f_{v^2}^3 \end{pmatrix},
 \end{aligned} \tag{88}$$

where

$$M_1 = \det \begin{pmatrix} 2i\omega_0\tau_k + (d + A) & 0 & B \\ A(e^{-d\tau_k}e^{-2i\omega_0\tau_k} - 1) & 2i\omega_0\tau_k + d & B(e^{-d\tau_k}e^{-2i\omega_0\tau_k} - 1) \\ -Ae^{-d\tau_k}e^{-2i\omega_0\tau_k} & 0 & 2i\omega_0\tau_k + a + Be^{-d\tau_k}e^{-2i\omega_0\tau_k} \end{pmatrix}. \tag{89}$$

Similarly, substituting (67) and (74) into (69), we get

$$\begin{aligned}
 E_2^{(1)} &= \frac{1}{M_2} \det \begin{pmatrix} f_{v\bar{v}}^1 & 0 & B \\ f_{v\bar{v}}^2 & d & B(e^{-d\tau_k}e^{-i\omega_0\tau_k} - 1) \\ f_{v\bar{v}}^3 & 0 & a + Be^{-d\tau_k}e^{-i\omega_0\tau_k} \end{pmatrix}, \\
 E_2^{(2)} &= \frac{1}{M_2} \det \begin{pmatrix} (d + A) & f_{v\bar{v}}^1 & B \\ A(e^{-d\tau_k}e^{-i\omega_0\tau_k} - 1) & f_{v\bar{v}}^2 & B(e^{-d\tau_k}e^{-i\omega_0\tau_k} - 1) \\ -Ae^{-d\tau_k}e^{-i\omega_0\tau_k} & f_{v\bar{v}}^3 & a + Be^{-d\tau_k}e^{-i\omega_0\tau_k} \end{pmatrix}, \\
 E_2^{(3)} &= \frac{1}{M_2} \det \begin{pmatrix} (d + A) & 0 & f_{v\bar{v}}^1 \\ A(e^{-d\tau_k}e^{-i\omega_0\tau_k} - 1) & d & f_{v\bar{v}}^2 \\ -Ae^{-d\tau_k}e^{-i\omega_0\tau_k} & 0 & f_{v\bar{v}}^3 \end{pmatrix},
 \end{aligned} \tag{90}$$

where

$$M_2 = \det \begin{pmatrix} (d + A) & 0 & B \\ A(e^{-d\tau_k} e^{-i\omega_0\tau_k} - 1) & d & B(e^{-d\tau_k} e^{-i\omega_0\tau_k} - 1) \\ -Ae^{-d\tau_k} e^{-i\omega_0\tau_k} & 0 & a + Be^{-d\tau_k} e^{-i\omega_0\tau_k} \end{pmatrix}. \tag{91}$$

Thus, we can determine $W_{20}(s)$ and $W_{11}(s)$ from (66) and (67). Furthermore, we can compute f_{21} by (55). Thus, we can compute the following values:

$$c_{(1)}(0) = \frac{i}{2\omega_0\tau_k} \left(f_{20}f_{11} - 2|f_{11}|^2 - \frac{|f_{02}|^2}{3} \right) + \frac{f_{21}}{2},$$

$$\vartheta_2 = -\frac{\text{Im}\{c_{(1)}(0)\}}{\text{Re}\{\lambda'(\tau_k)\}}, \tag{92}$$

$$\sigma_2 = 2 \text{Re}\{c_{(1)}(0)\},$$

$$T_2 = -\frac{\text{Im}\{c_{(1)}(0)\} + \vartheta_2 \text{Re}\{\lambda'(\tau_k)\}}{\omega_0\tau_k}.$$

Then from [8], we can give the properties of bifurcating periodic solution in the center manifold at the critical values τ_k . More specifically, we have the following theorem.

Theorem 10. *The properties of the Hopf bifurcation are determined by the values in (75).*

- (1) ϑ_2 determines the directions of the Hopf bifurcation: if $\vartheta_2 > 0$ ($\vartheta_2 < 0$), then the Hopf bifurcation is supercritical (subcritical), and the bifurcating periodic solutions exist for $\tau > \tau_k$ ($\tau < \tau_k$).
- (2) ϑ_2 determines the stability of the bifurcating periodic solutions: the bifurcating periodic solutions are stable (unstable) if $\vartheta_2 > 0$ ($\vartheta_2 < 0$).
- (3) T_2 determines the period of the bifurcating periodic solutions: the period increases (decreases) if $T_2 > 0$ ($T_2 < 0$).

4. Numerical Simulations

As an example, we consider the system given in [1] with $\lambda = 1.5 \times 10^5$, $d = 0.011$, $\beta = 9.8 \times 10^{-7}$, $k = 150$, $a = 0.1$, and $\mu = 0.67$, then, there is a chronic infected equilibrium E^* which satisfies the conditions indicated in Theorem 9. When $\tau = 0$, the chronic infected equilibrium $E^* = (-1.3515 \times 10^7, -1.0120 \times 10^5, 1.2090 \times 10^5)$ is asymptotically stable (see Figure 1(a) which is the amplified part of Figure 1(b) during time interval $[0, 30]$). It follows from the discussion in Section 2 that $\omega_0 = 0.6029$, $\tau_0 = 8.1786$ and $\lambda(\tau_0) = 0.2103 - 0.3942i$. From the formulae (92) in Section 3, it follows that $c_1(0) = -0.1052 - 0.3061i$, $\vartheta_2 = 8.2963 > 0$, $\sigma_2 = -0.2103 < 0$, and $T_2 = 1.6737 > 0$. Thus, the chronic infected equilibrium E^* is asymptotically stable when $0 \leq \tau < \tau_0$ as illustrated by the computer simulations (see Figures 2 and 3).

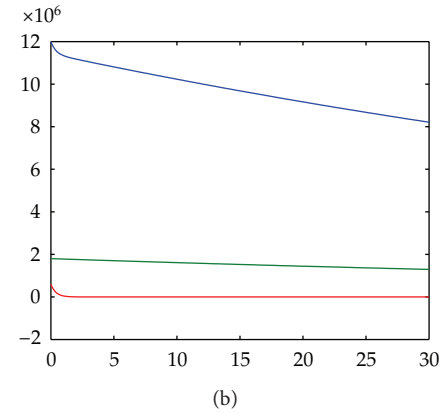
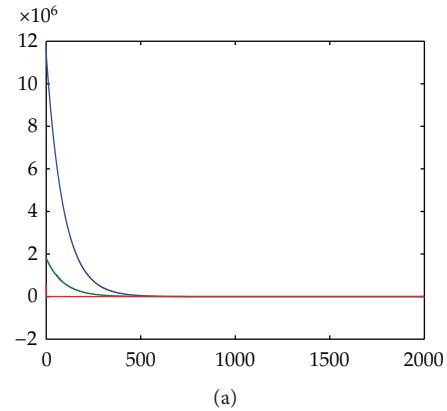


FIGURE 1: The response of the system (5) initial data $(1.2e7, 1.8e6, 6e5)^T$, when $\tau = 0$.

When τ passes through the critical value τ_0 , E^* loses its stability, and a Hopf bifurcation occurs, that is, a family of periodic solutions bifurcate from E^* . Since ϑ_2 and $\sigma_2 = -0.2103 < 0$, the Hopf bifurcation is supercritical, and the direction of the bifurcation is $\tau > \tau_0$, and these bifurcating periodic solutions from E^* at τ_0 are stable, which are depicted in Figures 2 and 3.

In Figure 4, we try to reflect the changes of stability of chronic infected equilibrium E^* as τ increases from 0 to 9. In Figure 4, each vertical blue strip corresponds to component of $\bar{x}(t)$, $e(t)$, and $y(t)$ at each τ , respectively. From Figure 3, we see that if $\tau \in (0, 8.17864293)$, approximately, the vertical amplitudes of $\bar{x}(t)$, $e(t)$, and $y(t)$ are as small as a point, suggesting that E^* is asymptotically stable; if τ increases, the vertical amplitudes of $\bar{x}(t)$, $e(t)$, and $y(t)$ will become larger and larger, showing that E^* becomes more and more unstable. In particular, if $\tau = 8.1787$, points are well distributed

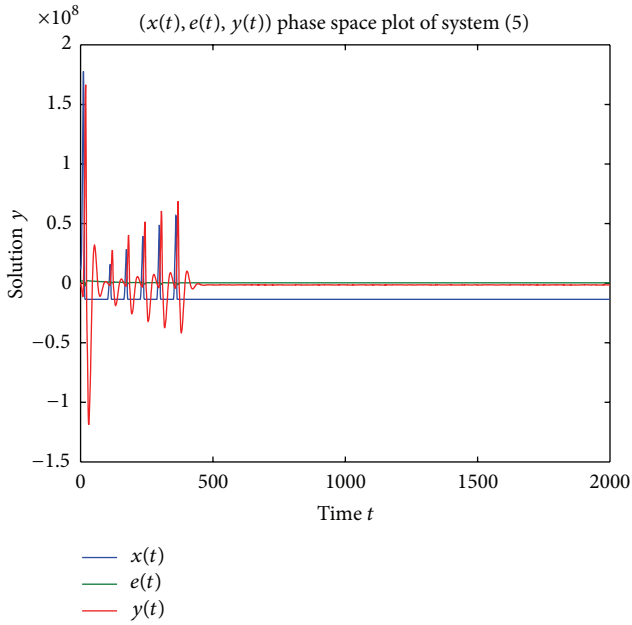


FIGURE 2: The response of the system (5) initial data $(1.2e7, 1.8e6, 6e5)^T$, when $\tau = 8.1786 < \tau_0$.

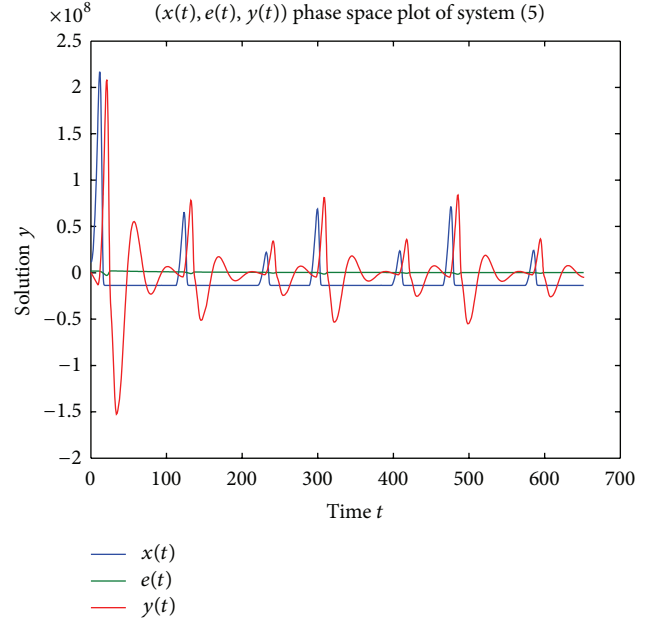


FIGURE 4: The response of the system (5) initial data $(1.2e7, 1.8e6, 6e5)^T$, when $\tau = 8.21 > \tau_0$.

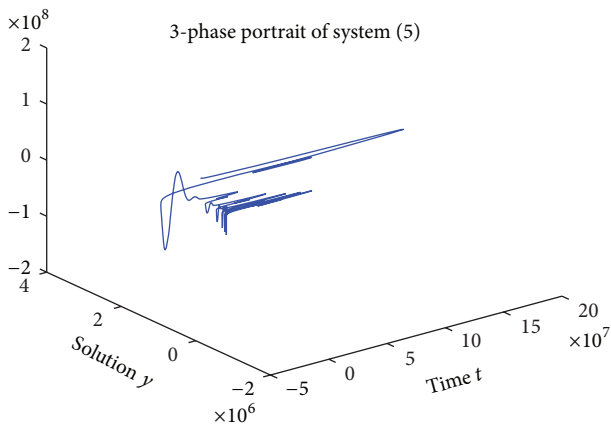


FIGURE 3: 3-phase portrait of the system (5) initial data $(1.2e7, 1.8e6, 6e5)^T$, when $\tau = 8.1786 < \tau_0$.

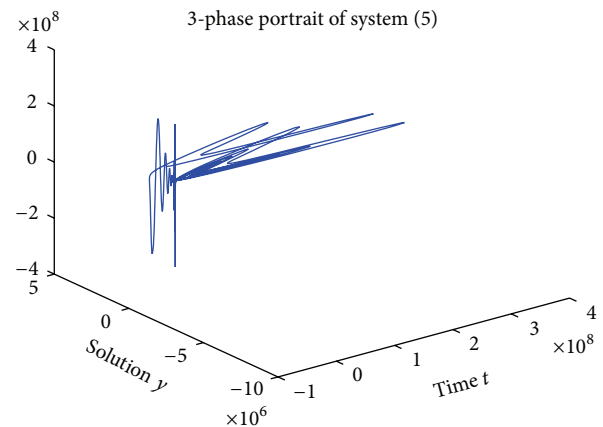


FIGURE 5: 3-phase portrait of the system (5) initial data $(1.2e7, 1.8e6, 6e5)^T$, when $\tau = 8.21 > \tau_0$.

around the positive equilibrium, and their amplitudes are all equivalent. This shows that periodic solution near positive equilibrium may occur.

5. Conclusions

In this paper, a delay differential equation of hepatitis B virus infection is formulated. We analyzed the stability of the equilibria; a sufficient condition was given to guarantee the global stability of the origin. Local stability of the chronic infected equilibrium was considered. By choosing time delay τ as a bifurcated parameter, a sufficient condition has been presented for checking the existence of the Hopf bifurcation. The explicit formulae determining the direction, stability, and other properties of bifurcating periodic solutions were given

by using the normal form theory and the center manifold theorem. Some numerical simulations were performed to support the analytical results found. Although bifurcations in a population dynamics with delay has been investigated by many researchers. However, to the best of our knowledge, there are few papers on the bifurcation of delay differential equation of hepatitis B virus infection dynamics with delay.

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