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Stability and Bifurcation Analysis for a Hepatitis C Virus Transmissions Model with Time Delay

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Abstract

In this paper, we propose a Hepatitis C virus transmissions model with time delay. Firstly, we get the condition for the existence and local stability of equilibria of the system. Secondly, by choosing the time delay τ as a bifurcation parameter, we show that Hopf bifurcation will occur as the time delay τ passes through some critical values. Thirdly, by use of normal form theory and central manifold argument, we establish the direction and stability of Hopf bifurcation. At last, some numerical simulations is provided to verify the theoretical results.

Keywords: Hepatitis C virus; time delay; Hopf bifurcation; normal form theory; center manifold theory.

2010 Mathematics Subject Classification: 92D30; 34K20

1 Introduction

Infection with Hepatitis C virus (HCV) is a major global public health problem. The WHO estimates that up to 3% of the world's population has been infected with the virus, equating to more than 170 million carriers of HCV worldwide [1]. HCV has been recognized as a major cause of chronic liver disease since there is strong evidence demonstrating the association of chronic HCV infection to cirrhosis and hepatocellular carcinoma (HCC) [2,3]

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HCV is a single-stranded ribonucleic acid (RNA) virus that is transmitted primarily through direct percutaneous exposures to blood. In many countries, the two most common exposures associated with transmission of HCV are injecting-drug use and transfusion of blood from unscreened donors. Transmission can also result from occupational, perinatal, and sexual exposures [4,5].

Most of newly infected persons are asymptomatic (and are unaware of their infection) with a minority having symptoms such as jaundice, dark urine, fatigue, nausea, vomiting, and abdominal pain [6]. Approximately 10-20% spontaneously clear the virus and develop natural immunity. Following the acute period, a high proportion of HCV-infected persons develops chronic infection.

Mathematical modeling and quantitative analysis of Hepatitis C infections has been explored extensively over the last decade. Martcheva and Castillo-Chavez introduced an epidemiologic model of hepatitis C with chronic infectious stage in a varying population [7]. Their model does not include a recovered or immune class and falls within the susceptible-infected-susceptible (SIS) category of models. A susceptible-infected-removed (SIR) model is used by Kretzschmar and Wiessing to study the transmission of HCV among injecting drug users (IDUs) [8]. Models that allow for waning immunity of the susceptible-infected-removed-susceptible (SIRS) type are used in [9,10]. For Hepatitis C infections, on adequate contact with an infectious individual, a susceptible becomes exposed for a while; that is, infected but not yet infectious [11]. Thus it is worthy to introducing a time delay τ to simulate latent compartment. So, in the article we will analyze a Hepatitis C virus transmissions model with time delay.

The organization of this paper is as follows: In section 2, the model is formulated. In section 3, we consider the existence and stability of equilibria of the system. In section 4, by use of normal form theory and central manifold argument, we illustrate the direction and stability of Hopf bifurcation. In Section 5, some numerical simulations is provided to verify the theoretical results.

2 Model Formulation

A susceptible individual acquires acute HCV infection primarily through effective exposure to infected blood of a temporary or a chronic HCV disease, shifts to the latent period averaging 6-10 weeks and then becomes acute HCV state which is relatively short in comparison to the chronic stage [12]. By convention, prolonged chronic Hepatitis is believed to have developed when the serum enzymes remain abnormal for at least 6 months.

We construct a Hepatitis C virus transmissions model with time delay instead of latent compartment. The population is divided into three classes: susceptible to infection (S), acutely infected (I), persistently (chronically) infected (P). We choose a simple demographic model with a constant rate Λ of recruitment in the naive class and exit rate μ for all classes. Susceptible persons are infected at a rate β_i, respectively. Upon infection, the host moves into the I compartment and progresses to chronic stage at rate ϵ. The model can be described by the following delay differential equations:

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta_1 SI(t-\tau) - \beta_2 SP(t-\tau) - \mu S, \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = \beta_1 SI(t-\tau) + \beta_2 SP(t-\tau) - (\mu+\epsilon)I, \\ \dfrac{\mathrm{d}P}{\mathrm{d}t} = \epsilon I - \mu P. \end{cases} \tag{2.1}$$

3 Local Stability of Equilibriums and the Existence of Hopf Bifurcation

By simple calculation, we know that system (2.1) always has a disease-free equilibrium $E_0(\frac{\Lambda}{\mu}, 0, 0)$ and if the basic reproduction number

$$R_0 = \frac{\Lambda(\mu\beta_1 + \epsilon\beta_2)}{\mu^2(\mu + \epsilon)} > 1,$$

then system (2.1) has a unique endemic equilibrium

$$E^*(S^*, I^*, P^*) = E^*(\frac{\Lambda}{\mu R_0}, \frac{\Lambda}{\mu + \epsilon} - \frac{\mu^2}{\mu\beta_1 + \epsilon\beta_2}, \frac{\epsilon}{\mu} I^*).$$

3.1 Local stability of E_0

In this subsection, we will analyze the local stability of equilibrium E_0. Linearizing system (2.1) at E_0 yields the following linear system

$$\begin{cases} \frac{\mathrm{d}S}{\mathrm{d}t} = -\mu S - \frac{\Lambda\beta_1}{\mu} I(t-\tau) - \frac{\Lambda\beta_2}{\mu} P(t-\tau), \\ \frac{\mathrm{d}I}{\mathrm{d}t} = \frac{\Lambda\beta_1}{\mu} I(t-\tau) + \frac{\Lambda\beta_2}{\mu} P(t-\tau) - (\epsilon + \mu) I, \\ \frac{\mathrm{d}P}{\mathrm{d}t} = \epsilon I - \mu P, \end{cases} \tag{3.1}$$

and its characteristic equation is

$$\begin{vmatrix} \lambda + \mu & \frac{\Lambda\beta_1}{\mu} e^{-\lambda\tau} & \frac{\Lambda\beta_2}{\mu} e^{-\lambda\tau} \\ 0 & \lambda - \frac{\Lambda\beta_1}{\mu} e^{-\lambda\tau} + (\epsilon + \mu) & -\frac{\Lambda\beta_2}{\mu} e^{-\lambda\tau} \\ 0 & -\epsilon & \lambda + \mu \end{vmatrix} = 0,$$

or equivalently,

$$(\lambda + \mu)\left[\lambda^2 + (2\mu + \epsilon - \frac{\Lambda\beta_1}{\mu} e^{-\lambda\tau})\lambda + \mu(\mu + \epsilon - \frac{\Lambda\beta_1}{\mu} e^{-\lambda\tau}) - \frac{\epsilon\Lambda\beta_2}{\mu} e^{-\lambda\tau}\right] = 0. \tag{3.2}$$

We will consider this characteristic equation for two cases:

Case 1 $\tau = 0$, then the equation (3.2) reduces to

$$(\lambda + \mu)\left[\lambda^2 + (2\mu + \epsilon - \frac{\Lambda\beta_1}{\mu})\lambda + \mu(\mu + \epsilon - \frac{\Lambda\beta_1}{\mu}) - \frac{\epsilon\Lambda\beta_2}{\mu}\right] = 0.$$

It is easy to see that the eigenvalues satisfy

$$\lambda_1 = -\mu < 0,$$
$$\lambda_2 + \lambda_3 = -(2\mu + \epsilon - \frac{\Lambda\beta_1}{\mu}) < 0,$$
$$\lambda_2\lambda_3 = \mu(\mu + \epsilon - \frac{\Lambda\beta_1}{\mu}) - \frac{\epsilon\Lambda\beta_2}{\mu}$$

Hence, by Routh-Hurwitz criterion, we get that if $R_0 > 1$, then $\lambda_2\lambda_3 < 0$, which indicates that there is one positive eigenvalue; if $R_0 < 1$, then $\lambda_2\lambda_3 > 0$, which indicates that both eigenvalues have negative real part.

Case 2 $\tau > 0$, then the sign of the real part of the eigenvalues can not be determined, which means that this equilibrium may be locally stable or unstable.
According to the above discussion, we get the following result.

Theorem 3.1. *(i) For $\tau = 0$, if $R_0 < 1$, the disease-free equilibrium of system (2.1) is locally asymptotically stable; if $R_0 > 1$, it is unstable.*
(ii) For $\tau > 0$, the local stability of the disease-free equilibrium in unknown.

3.2 Local stability of E^* and existence of Hopf bifurcation

In this subsection, we investigate the the stability of the endemic equilibrium and the existence of Hopf bifurcation.

We make the following assumptions:

(H1)$R_0 > 1$, which indicates that system (2.1) has a unique endemic equilibrium.
(H2)Equation (3.8) has at least one positive real root.
Linearizing system (2.1) at the equilibrium E^*, we will get

$$\begin{cases} \frac{\mathrm{d}S}{\mathrm{d}t} = -(\beta_1 I^* + \beta_2 P^* + \mu)S - \beta_1 S^* I(t-\tau) - \beta_2 S^* P(t-\tau), \\ \frac{\mathrm{d}I}{\mathrm{d}t} = (\beta_1 I^* + \beta_2 P^*)S + \beta_1 S^* I(t-\tau) - (\epsilon+\mu)I + \beta_2 S^* P(t-\tau), \\ \frac{\mathrm{d}p}{\mathrm{d}t} = \epsilon I - \mu P. \end{cases} \tag{3.3}$$

We will consider two cases.

Case 1 When $\tau = 0$, the characteristic equation of system (3.3) is

$$(\lambda+\mu)[\lambda^2 + (2\mu+\epsilon+\beta_1 I^* + \beta_2 P^* - \beta_1 S^*)\lambda + \mu^2 - \mu\beta_1 S^* + \epsilon\beta_1 I^* + \mu(\epsilon+\beta_1 I^* + \beta_2 P^*)] = 0. \tag{3.4}$$

When $R_0 > 1$, we get that all of the eigenvalues of equation (3.4) have negative real part, which means that E^* is locally stable for system (2.1).

Case 2 When $\tau > 0$, the characteristic equation of system (3.3) is

$$\lambda^3 + D\lambda^2 + E\lambda + F = e^{-\lambda\tau}(G\lambda^2 + H\lambda + J), \tag{3.5}$$

where

$$\begin{array}{llll} D & = 3\mu + \epsilon + \beta_1 I^* + \beta_2 P^*, & & E = 3\mu^2 + 2\mu\epsilon + (2\mu+\epsilon)(\beta_1 I^* + \beta_2 P^*), \\ F & = \mu(\mu+\epsilon)(\beta_1 I^* + \beta_2 P^*), & & G = \beta_1 S^*, \\ H & = \mu\beta_1 S^* + \epsilon\beta_2 S^*, & & J = \mu\beta_2 S^* + \epsilon\mu\beta_2 S^*. \end{array}$$

Suppose that there is a pure imaginary root $\lambda = i\omega$, $\omega > 0$, then we get

$$-i\omega^3 - D\omega^2 + E\omega i + F = e^{-\omega\tau}(-G\omega^2 + H\omega i + J).$$

Separating the real and imaginary parts, we have

$$\begin{cases} -D\omega^2 + F = (-G\omega^2 + J)\cos\omega\tau - H\omega\sin\omega\tau, \\ -\omega^3 + E\omega = -\left[H\omega\cos\omega\tau + (-G\omega^2 + J)\sin\omega\tau\right]. \end{cases} \tag{3.6}$$

Adding the square of the above two equations, we obtain

$$\omega^6 + \omega^4(D^2 - 2E - G^2) + \omega^2(E^2 - 2DF + 2JG - H^2) + F^2 - J^2 = 0. \tag{3.7}$$

Denote $p=\omega^2$, then equation (3.7) becomes

$$p^3+p^2(D^2-2E-G^2)+p(E^2-2DF+2JG-H^2)+F^2-J^2=0. \tag{3.8}$$

Let $K(p)=p^3+p^2(D^2-2E-G^2)+p(E^2-2DF+2JG-H^2)+F^2-J^2$.

According assumption (H2), we know that equation (3.8) has at least one positive real root, and it is denoted as p_0. Then equation (3.7) has a positive root ω_0, and then the characteristic equation (3.5) has a pair of purely imaginary of the form $\pm\, \mathrm{i}\omega_0$. From (3.6), we get the corresponding $\tau_0>0$ such that the the characteristic equation (3.5) has a pair of purely imaginary, and here

$$\tau_0=\frac{1}{\omega_0}[\arccos\frac{H\omega_0(\omega_0^3-E\omega_0)+(G\omega_0^2-J)(F-D\omega_0^2)}{(H\omega_0)^2+(G\omega_0^2-J)^2}].$$

Differentiating equation (3.5) with respect t, we get

$$(3\lambda^2+2D\lambda+E)\frac{\mathrm{d}\lambda}{\mathrm{d}t}=(-\tau\frac{\mathrm{d}\lambda}{\mathrm{d}t}-\lambda)e^{-\lambda\tau}(G\lambda^2+H\lambda+J)+e^{-\lambda\tau}(2G\lambda+H)\frac{\mathrm{d}\lambda}{\mathrm{d}t},$$

and form which we have

$$\begin{aligned}(\frac{\mathrm{d}\lambda}{\mathrm{d}\tau})^{-1} &= \frac{3\lambda^2+2D\lambda+E-e^{-\lambda\tau}(2G\lambda+H)}{-\lambda e^{-\lambda\tau}(G\lambda^2+H\lambda+J)}-\frac{\tau}{\lambda}\\ &= \frac{3\lambda^2+2D\lambda+E}{-\lambda e^{-\lambda\tau}(G\lambda^2+H\lambda+J)}+\frac{2G\lambda+H}{\lambda(G\lambda^2+H\lambda+J)}-\frac{\tau}{\lambda}\\ &= \frac{2\lambda^3+D\lambda^2-F}{-\lambda^2(\lambda^3+D\lambda^2+E\lambda+F)}+\frac{G\lambda^2-J}{\lambda^2(G\lambda^2+H\lambda+J)}-\frac{\tau}{\lambda}.\end{aligned}$$

Therefore

$$\begin{aligned}\mathrm{sign}\{\frac{\mathrm{d(Re}\lambda)}{\mathrm{d}\tau}\}_{\tau=\tau_0} &= \mathrm{sign}\{\mathrm{Re}(\frac{\mathrm{d}\lambda}{\mathrm{d}\tau})^{-1}\}_{\lambda=i\omega_0}\\ &= \mathrm{sign}\{\mathrm{Re}[\frac{2\lambda^3+D\lambda^2-F}{-\lambda^2(\lambda^3+D\lambda^2+E\lambda+F)}]_{\lambda=i\omega_0}+\mathrm{Re}[\frac{G\lambda^2-J}{\lambda^2(G\lambda^2+H\lambda+J)}]_{\lambda=i\omega_0}\}\\ &= \mathrm{sign}\{\frac{2\omega_0^3(\omega_0^3-E\omega_0)-(F^2-D^2\omega_0^4)}{\omega_0^2[(-D\omega_0^2+F)^2+(\omega_0^3-E\omega_0)^2]}+\frac{-(G\omega_0^2)^2+J^2}{\omega_0^2[(G\omega_0^2+J)^2+H^2\omega_0^2]}\}\\ &= \mathrm{sign}\{\frac{2\omega_0^6+\omega_0^4(D^2-2E-G^2)-(F^2-J^2)}{\omega_0^2[(-G\omega_0^2+J)^2+(H\omega_0)^2]}\}.\end{aligned}$$

From assumption (H2), we have $\frac{\mathrm{d(Re}\lambda)}{\mathrm{d}\tau}|_{\tau=\tau_0}>0$. This result means that there exists a root of characteristic equation (3.5) crosses the imaginary axis from the left to the right as τ continuously varies from a number less than τ_0 to one greater than τ_0 by Rouché's theorem [13]. Thus, we get the following result.

Theorem 3.2. *If assumptions (H1) and (H2) hold, then we have*

(i) The endemic equilibrium E^* of system (2.1) is locally asymptotically stable for $\tau\in[0,\tau_0)$.
(ii) The endemic equilibrium E^* of system (2.1) undergoes a Hopf bifurcation when $\tau=\tau_0$.

4 Direction and Stability of the Hopf Bifurcation

In this section, we will analyze the direction of Hopf bifurcation and stability of bifurcation periodic solution by using the normal theory and the center manifold theorem [14].

Let $u_1=S-S^*$, $u_2=I-I^*$, $u_3=P-P^*$, $\bar{u}_i(t)=u_i(\tau t)$, $\tau=\nu+\tau_k$, and dropping the bars for simplification of notations, then system (2.1) becomes a functional differential equation in $C = C([-1, 0], R^3)$ as

$$\dot{u}(t) = L_\nu(u_t) + f(\nu, u_t), \tag{4.1}$$

where $u(t) = (u_1(t), u_2(t), u_3(t))^T \in \mathbb{R}^3$, $L_\mu : C \to R$, $f : \mathbb{R} \times C \to \mathbb{R}^3$, and

$$\begin{aligned} L_\nu(\phi) \quad &= \quad (\tau_k + \nu) \begin{pmatrix} -(\beta_1 I^* + \beta_2 P^* + \mu) & 0 & 0 \\ \beta_1 I^* + \beta_2 P^* & -(\epsilon + \mu) & 0 \\ 0 & \epsilon & -\mu \end{pmatrix} \begin{pmatrix} \phi_1(0) \\ \phi_2(0) \\ \phi_3(0) \end{pmatrix} \\ &\quad + (\tau_k + \mu) \begin{pmatrix} 0 & -\beta_1 S^* & -\beta_2 S^* \\ 0 & \beta_1 S^* & \beta_2 S^* \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \phi_1(-1) \\ \phi_2(-1) \\ \phi_3(-1) \end{pmatrix}, \end{aligned} \tag{4.2}$$

$$f(\mu, \phi) = (\tau_k + \mu) \begin{pmatrix} -\beta_1 \phi_1(0)\phi_2(-1) - \beta_2 \phi_1(0)\phi_3(-1) \\ \beta_1 \phi_1(0)\phi_2(-1) + \beta_2 \phi_1(0)\phi_3(-1) \\ 0 \end{pmatrix}, \tag{4.3}$$

where $\phi(\theta) = (\phi_1(\theta), \phi_2(\theta), \phi_3(\theta))^T \in C$. By the Riesz representation theorem, there exists a function $\eta(\theta, \mu)$ of bounded variation for $\theta \in [-1, 0]$, such that

$$L_\mu(\phi) = \int_{-1}^{0} d\eta(\theta, \mu)\phi(\theta), \quad \text{for } \phi \in C. \tag{4.4}$$

In fact, we can choose

$$\begin{aligned} \eta(\theta, \mu) \quad &= \quad (\tau_k + \mu) \begin{pmatrix} -(\beta_1 I^* + \beta_2 P^* + \mu) & 0 & 0 \\ \beta_1 I^* + \beta_2 P^* & -(\epsilon + \mu) & 0 \\ 0 & \epsilon & -\mu \end{pmatrix} \delta(\theta) \\ &\quad - (\tau_k + \mu) \begin{pmatrix} 0 & -\beta_1 S^* & -\beta_2 S^* \\ 0 & \beta_1 S^* & \beta_2 S^* \\ 0 & 0 & 0 \end{pmatrix} \delta(\theta + 1), \end{aligned} \tag{4.5}$$

where δ is the Dirac delta function. For $\phi \in C^1([-1, 0], R^3)$, define

$$A(\mu)\phi = \begin{cases} \dfrac{d\phi(\theta)}{d\theta}, & \theta \in [-1, 0), \\ \displaystyle\int_{-1}^{0} d\eta(s, \mu)\phi(s), & \theta = 0, \end{cases}$$

and

$$R(\mu)\phi = \begin{cases} 0, & \theta \in [-1, 0), \\ f(\mu, \phi), & \theta = 0. \end{cases}$$

Then system (2.1) is equivalent to

$$\dot{u}_t = A(\nu)u_t + R(\nu)u_t, \tag{4.6}$$

where $u_t(\theta) = u(t + \theta), \theta \in [-1, 0]$. For $\psi \in C^1([0, 1], (R^3)^*)$, define

$$A^*\psi(s) = \begin{cases} -\dfrac{\mathrm{d}\psi(s)}{\mathrm{d}s}, & s \in (0, 1], \\ \displaystyle\int_{-1}^{0} \psi(-\tau)\mathrm{d}\eta(t, 0), & s = 0, \end{cases}$$

and a bilinear inner product

$$\langle\psi(s),\phi(\theta)\rangle=\bar{\psi}(0)\phi(0)-\int_{-1}^{0}\int_{\xi=0}^{\theta}\bar{\psi}(\xi-\theta)\mathrm{d}\eta(\theta)\phi(\xi)\mathrm{d}\xi, \tag{4.7}$$

where $\eta(\theta)=\eta(\theta,0)$. Then $A(0)$ and A^* are adjoint operators. By the discussion in Section 3, we know $\pm i\omega_0\tau_0$ are eigenvalues of $A(0)$. Thus, they are also eigenvalues of A^*. We need to compute the eigenvector of $A(0)$ and A^* corresponding to $i\omega_0\tau_0$ and $-i\omega_0\tau_0$, respectively.

Suppose that $q(\theta)=(1,q_1,q_2)^T e^{i\omega_0\tau_0\theta}$ is the eigenvalues of $A(0)$ corresponding to $i\omega_0\tau_0$, then $A(0)q(\theta)=i\omega_0\tau_0 q(\theta)$. It follows the definition of $A(0)$ and (4.2), (4.4)and(4.5), we have

$$\tau_0\begin{pmatrix}-(\beta_1I^*+\beta_2P^*+\mu) & 0 & 0\\ \beta_1I^*+\beta_2P^* & -(\epsilon+\mu) & 0\\ 0 & \epsilon & -\mu\end{pmatrix}q(0)+\tau_0\begin{pmatrix}0 & -\beta_1S^* & -\beta_2S^*\\ 0 & \beta_1S^* & \beta_2S^*\\ 0&0&0\end{pmatrix}q(-1)=i\omega_0\tau_0q(0),$$

because of $q(-1)=q(0)e^{-i\omega_0\tau_0}$, then we get

$$\begin{cases} q_1=\dfrac{(i\omega_0+\mu)[-i\omega_0-(\beta_1I^*+\beta_2P^*+\mu)]}{\beta_1(i\omega_0+\mu)+\epsilon\beta_2]S^*e^{-i\omega_0\tau_0}},\\ q_2=\dfrac{-i\epsilon\omega_0-\epsilon(\beta_1I^*+\beta_2P^*+\mu)}{[\beta_1(i\omega_0+\mu)+\epsilon\beta_2]S^*e^{-i\omega_0\tau_0}}.\end{cases}$$

Similarly, let $q^*(\theta)=D(1,q_1^*,q_2^*)^T e^{i\theta\omega_0\tau_0}$ be the eigenvalues of A^* corresponding to $-i\omega_0\tau_0$, according to the definition of A^* we get

$$\begin{aligned}&\tau_0\begin{pmatrix}-(\beta_1I^*+\beta_2P^*+\mu) & \beta_1I^*+\beta_2P^* & 0\\ 0 & -(\epsilon+\mu) & \epsilon\\ 0 & 0 & -\mu\end{pmatrix}q^*(0)\\ &+\tau_0\begin{pmatrix}0&0&0\\ -\beta_1S^* & \beta_1S^* & 0\\ -\beta_2S^* & \beta_2S^* & 0\end{pmatrix}q^*(-1)=-i\omega_0\tau_0q^*(0).\end{aligned}$$

Then,

$$\begin{cases} q_1^*=\dfrac{-i\omega_0+(\beta_1I^*+\beta_2P^*+\mu)}{\beta_1I^*+\beta_2P^*},\\ q_2^*=\dfrac{\beta_2S^*(\omega_0i+e^{-i\omega_0\tau_0})[-i\omega_0+(\beta_1I^*+\beta_2P^*+\mu)]}{(\mu-\omega_0i)(\beta_1I^*+\beta_2P^*)}.\end{cases}$$

In order to assure $\langle q^*(s),q(\theta)\rangle=1$, we need to determine the value of D. By (4.7), we have

$$\begin{aligned}\langle q^*(s),q(\theta)\rangle &=\bar{D}(1,\bar{q}_1^*,\bar{q}_2^*)(1,q_1,q_2)^T-\textstyle\int_{-1}^{0}\int_{\xi=0}^{\theta}\bar{D}(1,\bar{q}_1^*,\bar{q}_2^*)e^{-i\omega_0\tau_0(\xi-\theta)}\mathrm{d}\eta(\theta)(1,q_1,q_2)^Te^{i\omega_0\tau_0\xi}\mathrm{d}\xi\\ &=\bar{D}\{1+q_1\bar{q}_1^*+q_2\bar{q}_2^*-\textstyle\int_{-1}^{0}(1,\bar{q}_1^*,\bar{q}_2^*)\theta e^{i\omega_0\tau_0\theta}\mathrm{d}\eta(\theta)(1,q_1,q_2)^T\}\\ &=\bar{D}\{1+q_1\bar{q}_1^*+q_2\bar{q}_2^*+\tau_0e^{-i\omega_0\tau_0}S^*(q_1\beta_1+q_2\beta_2)(-1+\bar{q}^*)\}.\end{aligned}$$

Therefore, we can choose D as

$$D=\frac{1}{1+\bar{q}_1q_1^*+\bar{q}_2q_2^*+\tau_ke^{i\omega_0\tau_0}S^*(\bar{q}_1\beta_1+\bar{q}_2\beta_2)(-1+q^*)}.$$

Next, we will compute the coordinate to describe the center manifold C_0. Let u_t be the solution of (4.6). Define

$$Z(t) = \langle q^*, u_t\rangle, \quad W(t,\theta) = u_t(\theta) - 2\mathrm{Re}\{Z(t)q(\theta)\}. \tag{4.8}$$

On the center manifold C_0, we have

$$W(t,\theta) = W(Z(t), \bar{Z}(t), \theta),$$

where Z and $\bar{Z}$ are local coordinates for center manifold C_0 in the direction of $q^*(s)$ and $\bar{q}^*$. Note that W is real if u_t is real. We only consider real solutions. For the solution $u_t \in C_0$ of (4.6), since $\nu = 0$, we have

$$\begin{array}{rcl} \dot{Z}(t) & = & i\omega_0\tau_0 Z + \bar{q}^*(0)f(0, W(Z,\bar{Z},0)) + 2\mathrm{Re}\{Zq(\theta)\} \\ & = & i\omega_0\tau_0 Z + \bar{q}^*(0)f_0(Z,\bar{q}^*) \\ & = & i\omega_0\tau_0 Z(t) + g(Z,\bar{q}^*,), \end{array}$$

where

$$g(Z,\bar{Z}) = \bar{q}^*(0)f_0(Z,\bar{Z}) = g_{20}\frac{Z^2}{2} + g_{11}Z\bar{Z} + g_{02}\frac{\bar{Z}^2}{2} + g_{21}\frac{Z^2\bar{Z}}{2} + \cdots. \tag{4.9}$$

From (4.8) and (4.9), we have

$$\begin{array}{rcl} u_t(\theta) & = & W(t,\theta) + 2\mathrm{Re}\{Z(t)q(\theta)\} \\ & = & W_{20}(\theta)\frac{Z^2}{2} + W_{11}(\theta)Z\bar{Z} + W_{02}(\theta)\frac{\bar{Z}^2}{2} \\ & & +(1,q_1,q_2)^T e^{i\omega_0\tau_0\theta}Z + (1,\bar{q}_1,\bar{q}_2)^T e^{-i\omega_0\tau_0\theta}\bar{Z} + \cdots, \end{array}$$

It follows together with (4.3) that

$$\begin{array}{rcl} g(Z,\bar{Z}) & = & \bar{q}^*(0)f_0(Z,\bar{Z}) = \bar{q}^*(0)f(0,u_t) = \tau_0\bar{D}(1,\bar{q}_1^*,\bar{q}_2^*)\begin{pmatrix} -\beta_1u_{1t}(0)u_{2t}(-1) - \beta_2u_{1t}(0)u_{3t}(-1) \\ \beta_1u_{1t}(0)u_{2t}(-1) + \beta_2u_{1t}(0)u_{3t}(-1) \\ 0 \end{pmatrix} \\ & = & \tau_0\bar{D}\left[\beta_1(\bar{q}_1^*-1)u_{1t}(0)u_{2t}(0) + \beta_2(\bar{q}_1^*-1)u_{1t}(0)u_{3t}(-1)\right] \\ & = & \tau_0\bar{D}\Big[\beta_1(\bar{q}_1^*-1)\left(W_{20}^{(1)}(0)\frac{Z^2}{2} + W_{11}^{(1)}(0)Z\bar{Z} + W_{02}^{(1)}(0)\frac{\bar{Z}^2}{2} + Z + \bar{Z} + \cdots\right) \\ & & \times\left(W_{20}^{(2)}(-1)\frac{Z^2}{2} + W_{11}^{(2)}(-1)Z\bar{Z} + W_{02}^{(2)}(-1)\frac{\bar{Z}^2}{2} + q_1e^{-i\omega_0\tau_0}Z + \bar{q}_1e^{i\omega_0\tau_0}\bar{Z} + \cdots\right) \\ & & +\beta_2(\bar{q}_1^*-1)\big(W_{20}^{(2)}(0)\frac{Z^2}{2} + W_{11}^{(2)}(0)Z\bar{Z} + W_{02}^{(2)}(0)\frac{\bar{Z}^2}{2} + Z + \bar{Z} + \cdots\big) \\ & & \times\big(W_{20}^{(3)}(-1)\frac{Z^2}{2} + W_{11}^{(3)}(-1)Z\bar{Z} + W_{02}^{(3)}(-1)\frac{\bar{Z}^2}{2} \\ & & +q_2e^{-i\omega_0\tau_0}Z + \bar{q}_2e^{i\omega_0\tau_0}\bar{Z} + \cdots\big)\Big]. \end{array} \tag{4.10}$$

Comparing the coefficients with (4.9), we obtain

$$\begin{array}{rcl} g_{20} & = & \tau_0\bar{D}\left(\bar{q}_1^*-1\right)(\beta_1e^{-i\omega_0\tau_0} + \beta_2e^{-i\omega_0\tau_0}) \\ g_{11} & = & 2\tau_0\bar{D}\left(\bar{q}_1^*-1\right)[\beta_1\mathrm{Re}\{q_1e^{-i\omega_0\tau_0}\} + \beta_2\mathrm{Re}\{q_2e^{-i\omega_0\tau_0}\})] \\ g_{02} & = & \tau_0\bar{D}\left(\bar{q}_1^*-1\right)[\beta_1\bar{q}_1e^{i\omega_0\tau_0} + \beta_2\bar{q}_2e^{i\omega_0\tau_0}] \\ g_{21} & = & \tau_0\bar{D}(\bar{q}_1^*-1)[\beta_1\left(W_{20}^{(1)}(0)\bar{q}_1e^{i\omega_0\tau_0} + W_{11}^{(1)}(0)q_1e^{-i\omega_0\tau_0} + W_{11}^{(2)}(-1) + W_{20}^{(2)}(-1)\right) \\ & & +\beta_2\big(W_{20}^{(1)}(0)\bar{q}_2e^{i\omega_0\tau_0} + W_{11}^{(1)}(0)q_2e^{-i\omega_0\tau_0} + W_{11}^{(3)}(-1) + W_{20}^{(3)}(-1))\big]. \end{array}$$

In order to determine g_{21} we need to compute $W_{20}(\theta)$, and $W_{11}(\theta)$. From (4.6) and (4.8), we have

$$\begin{array}{rcl} \dot{W} & = & \dot{u}_t - \dot{Z}q - \dot{\bar{Z}}\bar{q} = \begin{cases} A(0)W - 2\mathrm{Re}\{\bar{q}^*(0)f_0q(\theta)\}, & \theta \in [-1,0), \\ A(0)W - 2\mathrm{Re}\{\bar{q}^*(0)f_0q(\theta)\} + f_0, & \theta = 0., \end{cases} \\ & \doteq & A(0)W - H(z,\bar{z},\theta), \end{array} \tag{4.11}$$

where

$$H(Z,\bar{Z},\theta) = H_{20}(\theta)\frac{Z^2}{2} + H_{11}(\theta)Z\bar{Z} + H_{02}\frac{\bar{Z}^2}{2} + \cdots. \tag{4.12}$$

Note that on the center manifold C_0 near the origin,

$$\dot{W} = W_Z \dot{Z} + W_{\bar{Z}} \dot{\bar{Z}},$$

thus we obtain

$$(A(0) - 2i\omega_0\tau_0)W_{20}(\theta) = -H_{20}(\theta), \quad A(0)W_{11}(\theta) = -H_{11}(\theta). \tag{4.13}$$

By (4.11) we know that for $\theta \in [-1, 0)$

$$H(Z, \bar{Z}, \theta) = -\bar{q}^*(0) f_0 q(\theta) - q_0^* \bar{f}_0 \bar{q}(\theta) = -g(Z, \bar{Z}) q(\theta) - \bar{g}(Z, \bar{Z}) \bar{q}(\theta). \tag{4.14}$$

Comparing the coefficients with (4.12)gives that

$$H_{20}(\theta) = -g_{20} q(\theta) - \bar{g}_{02} \bar{q}(\theta), \quad H_{11}(\theta) = -g_{11} q(\theta) - \bar{g}_{11} \bar{q}(\theta). \tag{4.15}$$

From (4.13), (4.15) and the definition of A, we have

$$\dot{W}_{20}(\theta) = 2i\omega_0\tau_0 W_{20}(\theta) + g_{20} q(\theta) + \bar{g}_{02} \bar{q}(\theta).$$

Noting $q(\theta) = q(0)e^{i\omega_0\tau_0\theta}$, hence

$$W_{20}(\theta) = \frac{ig_{20}}{\omega_0\tau_0} q(0) e^{i\omega_0\tau_0\theta} + \frac{i\bar{g}_{02}}{3\omega_0\tau_0} \bar{q}(0) e^{-i\omega_0\tau_0\theta} + E_1 e^{2i\omega_0\tau_0\theta}, \tag{4.16}$$

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

$$W_{11}(\theta) = \frac{i\bar{g}_{11}}{\omega_0\tau_0} \bar{q}(0) e^{-i\omega_0\tau_0\theta} + E_2, \tag{4.17}$$

where $E_2 = (E_2^{(1)}, E_2^{(2)}, E_2^{(3)})^T$ is also a constant vector. In the following, we will find out E_1 and E_2.

From the definition of A and (4.13), we can obtain

$$\int_{-1}^{0} \mathrm{d}\eta(\theta) W_{20}(\theta) = 2i\omega_0\tau_0 W_{20}(0) - H_{20}(0), \tag{4.18}$$

and

$$\int_{-1}^{0} \mathrm{d}\eta(\theta) W_{11}(\theta) = -H_{11}(\theta), \tag{4.19}$$

where $\eta(\theta) = \eta(\theta, 0)$. From (4.11) we know that when $\theta = 0$,

$$\begin{aligned} H(Z,\bar{Z},0) &= -2\mathrm{Re}\{\bar{q}^*(0)f_0q(0)\}+f_0 \\ &= -\bar{q}^*(0)f_0q(0)-q^*(0)\bar{f}_0\bar{q}(0)+f_0 \\ &= -g(Z,\bar{Z})q(0)-\bar{g}(Z,\bar{Z})\bar{q}(0)+f_0, \end{aligned} \tag{4.20}$$

that is,

$$\begin{aligned} & H_{20}(0)\frac{Z^2}{2}+H_{11}(0)Z\bar{Z}+H_{02}(0)\frac{\bar{Z}^2}{2}+\cdots \\ &= -q(0)\left(g_{20}\frac{Z^2}{2}+g_{11}Z\bar{Z}+g_{02}\frac{\bar{Z}^2}{2}+\cdots\right)-\bar{q}(0)\left(\bar{g}_{20}\frac{\bar{Z}^2}{2}+\bar{Z}g_{11}Z\bar{Z}+\bar{g}_{02}\frac{Z^2}{2}+\cdots\right)+f_0. \end{aligned} \tag{4.21}$$

By (4.3), we have

$$f_0=\tau_0\begin{pmatrix} -\beta_1u_{1t}(0)u_{2t}(-1)-\beta_2u_{1t}(0)u_{3t}(-1) \\ \beta_1u_{1t}(0)u_{2t}(-1)+\beta_2u_{1t}(0)u_{3t}(-1) \\ 0 \end{pmatrix}.,$$

By (4.8), we have

$$\begin{aligned} u_t(\theta) &= W(t,\theta)+2Re\{Z(t)q(\theta)\} \\ &= W(t,\theta)+Z(t)q(\theta)+\bar{Z}(t)\bar{q}(\theta) \\ &= W_{20}(\theta)\frac{Z^2}{2}+W_{11}(\theta)Z\bar{Z}+Z(t)q(\theta)+\bar{Z}(t)\bar{q}(\theta)+\cdots. \end{aligned}$$

Then we have

$$f_0=\tau_0\begin{pmatrix} -\beta_1u_{1t}(0)u_{2t}(-1)-\beta_2u_{1t}(0)u_{3t}(-1) \\ \beta_1u_{1t}(0)u_{2t}(-1)+\beta_2u_{1t}(0)u_{3t}(-1) \\ 0 \end{pmatrix} \tag{4.22}$$

By equations (4.21) and (4.22) we have

$$H_{20}(0)=-g_{20}q(0)-\bar{g}_{02}\bar{q}(0)+\tau_ke^{-i\omega_0\tau_0}\begin{pmatrix} -\beta_1q_1 \\ -\beta_2q_2 \\ 0 \end{pmatrix}, \tag{4.23}$$

$$H_{11}(0)=-g_{11}q(0)-\overline{g}_{11}\bar{q}(0)+2\tau_0\begin{pmatrix} \beta_1\mathrm{Re}\{q_1e^{-i\omega_0\tau_0}\} \\ \beta_2\mathrm{Re}\{q_2e^{-i\omega_0\tau_0}\} \\ 0 \end{pmatrix}. \tag{4.24}$$

Since $i\omega_0\tau_0$ is the eigenvalues of $A(0)$ and $q(0)$ is the corresponding eigenvector, we obtain

$$\left(i\omega_0\tau_0I-\int_{-1}^{0}e^{i\omega_0\tau_0\theta}\mathrm{d}\eta(\theta)\right)q(0)=0$$

and

$$\left(-i\omega_0\tau_0I-\int_{-1}^{0}e^{-i\omega_0\tau_0\theta}\mathrm{d}\eta(\theta)\right)\bar{q}(0)=0.$$

Thus, substituting (4.16) and (4.23) into (4.18), we have

$$\left(2i\omega_0\tau_0I-\int_{-1}^{0}e^{2i\omega_0\tau_0\theta}\mathrm{d}\eta(\theta)\right)E_1=2\tau_0e^{-i\omega_0\tau_0}\begin{pmatrix} -\beta_1q_1 \\ -\beta_2q_2 \\ 0 \end{pmatrix}.$$

That is,

$$\begin{aligned} &\begin{pmatrix} 2i\omega_0+\beta_1I^*+\beta_2P^*+\mu & \beta_1S^*e^{-2i\omega_0\tau_0} & \beta_2S^*e^{-2i\omega_0\tau_0} \\ -\beta_1I^*-\beta_2P^* & 2i\omega_0-\beta_1S^*e^{-2i\omega_0\tau_0}+\epsilon+\mu & -\beta_2S^*e^{-2i\omega_0\tau_0} \\ 0 & -\epsilon & \mu \end{pmatrix}E_1 \\ &= 2e^{-i\omega_0\tau_0}\begin{pmatrix} -\beta_1q_1 \\ -\beta_2q_2 \\ 0 \end{pmatrix}, \end{aligned}$$

from which we obtain

$$E_1 = 2e^{-i\omega_0\tau_0}\begin{pmatrix} 2i\omega_0+\beta_1 I^*+\beta_2 P^*+\mu & \beta_1 S^* e^{-2i\omega_0\tau_0} & \beta_2 S^* e^{-2i\omega_0\tau_0} \\ -\beta_1 I^*-\beta_2 P^* & 2i\omega_0-\beta_1 S^* e^{-2i\omega_0\tau_0}+\epsilon+\mu & -\beta_2 S^* e^{-2i\omega_0\tau_0} \\ 0 & -\epsilon & \mu \end{pmatrix}^{-1} \times \begin{pmatrix} -\beta_1 q_1 \\ -\beta_2 q_2 \\ 0 \end{pmatrix}.$$

Similarly, substituting (4.17) and (4.24) into (4.19), we have

$$\begin{pmatrix} \beta_1 I^*+\beta_2 P^*+\mu & \beta_1 S^* & \beta_2 S^* \\ -\beta_1 I^*-\beta_2 P^* & -\beta_1 S^*+\epsilon+\mu & -\beta_2 S^* \\ 0 & -\epsilon & \mu \end{pmatrix} E_2 = 2\tau_0 \begin{pmatrix} \beta_1 \mathrm{Re}\{q_1 e^{-i\omega_0\tau_0}\} \\ \beta_2 \mathrm{Re}\{q_2 e^{-i\omega_0\tau_0}\} \\ 0 \end{pmatrix},$$

from which we can get

$$E_2 = 2\begin{pmatrix} \beta_1 I^*+\beta_2 P^*+\mu & \beta_1 S^* & \beta_2 S^* \\ -\beta_1 I^*-\beta_2 P^* & -\beta_1 S^*+\epsilon+\mu & -\beta_2 S^* \\ 0 & -\epsilon & \mu \end{pmatrix}^{-1} \times \begin{pmatrix} \beta_1 \mathrm{Re}\{q_1 e^{-i\omega_0\tau_0}\} \\ \beta_2 \mathrm{Re}\{q_2 e^{-i\omega_0\tau_0}\} \\ 0 \end{pmatrix}.$$

Thus, we can determine $W_{20}(\theta)$ and $W_{11}(\theta)$ from equations (4.16) and (4.17). Furthermore, g_{21} can be expressed by the parameters and delay. Thus, we can compute the following values:

$$\begin{aligned} c_1(0) &= \frac{i}{2\omega_0\tau_0}(g_{20}g_{11} - 2|g_{11}|^2 - \frac{|g_{02}|^2}{3}) + \frac{g_{21}}{2}, \\ \alpha_2 &= -\frac{\mathrm{Re}\{c_1(0)\}}{\mathrm{Re}\{\lambda'(\tau_0)\}}, \\ \gamma_2 &= 2\mathrm{Re}\{c_1(0)\}, \\ T_2 &= -\frac{\mathrm{Im}\{c_1(0)\} + \mu_2 \mathrm{Im}\{\lambda'(\tau_0)\}}{\omega_0\tau_0}, \end{aligned} \tag{4.25}$$

which determine the qualities of bifurcating periodic solution in the center manifold at critical value τ_0, i.e, α_2 determine the direction of the Hopf bifurcation: if $\alpha_2 > 0(\alpha_2 < 0)$, then the Hopf bifurcation is supercritical (subcritical) and the bifurcating periodic solution exists for $\tau > \tau_0(\tau < \tau_0)$; γ_2 determines the stability of the bifurcating periodic solution: the bifurcating periodic solution is stable (unstable) if $\gamma_2 < 0(\gamma_2 > 0)$; and T_2 determines period of the bifurcating periodic solution: the period increases (decreases) if $T_2 > 0(< 0)$.

5 Numerical Investigations

Here, we choose the following parameter values: $\Lambda = 2.5$, $\beta_1 = 1.8$, $\beta_2 = 1.3$, $\mu = 0.8$, $\epsilon = 0.5$. By simple calculation we get $R_0 = 3.906$, $\omega_0 = 0.247$, and $\tau_0 = 8.96$. From Fig. 1, we see that when $\tau = 8.5 < \tau_0$, the endemic equilibrium is locally stable. From Eig. 2, we see that when $\tau = 15 > \tau_0$, the endemic equilibrium is unstable.

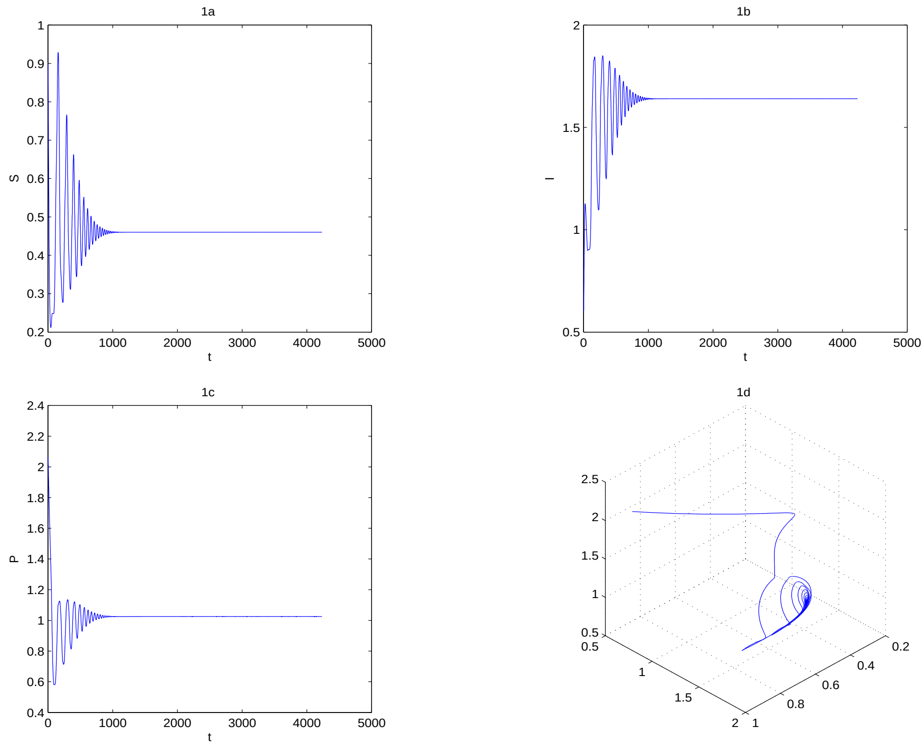

Fig. 1. When $\tau = 8.5 < \tau_0$, E^* is locally asymptotically stable.

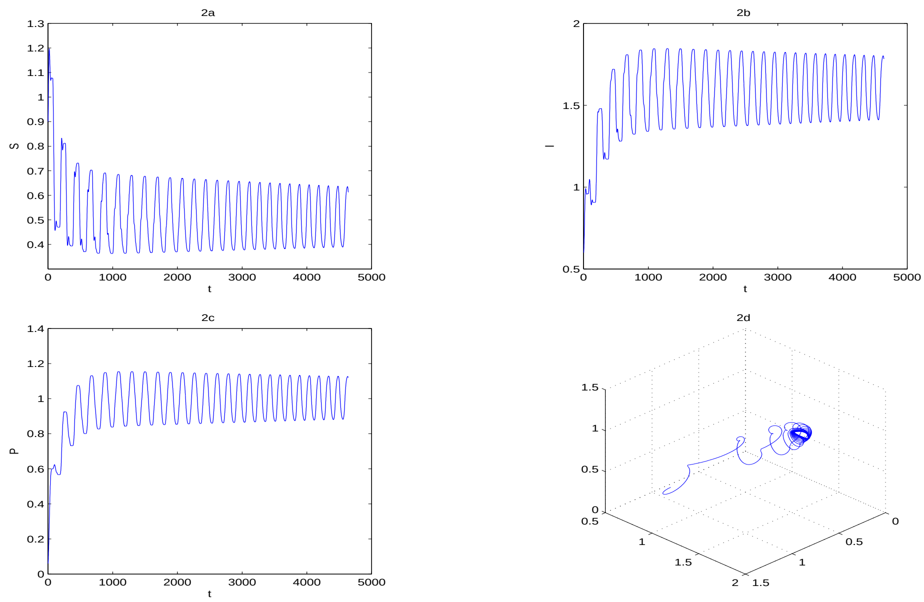

Fig. 2. When $\tau = 15 > \tau_0$, E^* is unstable.

6 Conclusion

In this paper, we propose a three-dimensional Hepatitis C virus transmissions model with time delay. Firstly, we analyze the existence and local stability of the equilibria of the system. Secondly, the condition for the existence of a Hopf bifurcation is obtained. Thirdly, by use of normal form theory and central manifold argument, we establish the formulae for the direction and the stability of the Hopf bifurcation. At last, we give some numerical simulations to verify our mathematical results.

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Competing Interests

The authors declare that no competing interests exist.

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