# Hopf Bifurcation Analysis of a Synthetic Drug Transmission Model with Time Delays 

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#### Abstract

This paper is concerned with the Hopf bifurcation of a synthetic drug transmission model with two delays. Firstly, some sufficient conditions of delay-induced bifurcation for such a model are captured by using different combinations of the two delays as the bifurcation parameter. Secondly, based on the center manifold theorem and normal form theory, some sufficient conditions determining properties of the Hopf bifurcation such as the direction and the stability are established. Finally, to underline the effectiveness of the obtained results, some numerical simulations are ultimately addressed.


## 1. Introduction

Increased use of heroin and other addictive drugs is an issue of concern all over the world. Drug abuse affects not only life quality of the general public but also the overall situation of social stability and economic development [1-3]. The data from the World Drug Report published by the United Nations (U.N.) showed that thirty-five million people worldwide suffer from drug abuse disorders, and only one-seventh has received treatment [4]. It also showed that, in 2017, millions of people around the world injected drugs, including 1.4 million people living with HIV and 5.6 million people suffering from hepatitis C. From the statistical data, it is clear that the adverse health effect due to drug use is more serious and widespread than previous anticipation, and it is urgent to control the prevalence of addictive drugs.

As stated in [5], the spread of heroin habituation and addiction has similar characteristics to an epidemic, including rapid diffusion and clear geographic boundaries. With the help of epidemic models, one could try to simulate and reveal the nature of epidemics and provide theoretical rules and results for preventing and controlling infectious diseases [6]. In recent decades, mathematical modelling technologies based on the infectious disease models have
been developed to understand and combat drug-addiction problems. In [7], White and Comiskey formulated a heroin epidemic model with a standard incidence rate based on principles of mathematical epidemiology. In the succession, Mulone and Straughan [8] found stability conditions for steady states of the proposed model by White and Comiskey. In the subsequent papers, Wang et al. [9-12] studied global stability of a heroin epidemic model with bilinear incidence rate, respectively. Some other works related to the dynamical behaviour of heroin epidemic models with nonlinear incidence rates can be found in [ $3,13-15$ ], and models with age structure can be found in [13, 15-18]. For the analytical study of stochastic heroin epidemic models or some other heroin epidemic models, one can also see [1, 2, 19-22].

All the aforementioned models consider only traditional drugs. Compared with traditional drugs, the relevant works are few. On the other hand, synthetic drugs are addictive more easily because they can directly affect the central nervous system as a new type of mental drug. According to China's Drug Situation Report [23], among drug abuse, methamphetamine is the most common. Methamphetamine abusers accounted for $56.1 \%$ of the existing 2.444 million drug addicts, and methamphetamine has replaced heroin as the most abused drug in China.

Besides, in 2018, the people who relapsed and abused synthetic drugs were accounted for $57.3 \%$ of the total number of drug abuse among the relapsed addicts. Based on the above facts, Ma et al. [24] formulated a synthetic drug transmission model with psychological addicts and general contact rates, and they investigated the local and global stability of the proposed model. However, they assumed that the contact rates of psychological addicts and physiological addicts are equal for the sake of simple calculation and analysis, which is not reasonable because the susceptible individuals who have never taken any drugs are more likely to initiate drug abuse once they contact with the physiological addicts compared to the psychological ones. Based on the work in [24], Saha and Samanta [25] proposed a synthetic drug transmission model with general contact rate and Holling type-II functional responses among susceptible and drug addicts. Recently, Liu et al. [26] proposed the following synthetic drug transmission model with different susceptible compartments:

$$
\left\{\begin{array}{l}
\frac{\mathrm{d} S(t)}{\mathrm{d} t}=\Lambda-\beta_{1} S(t) I(t)-\mu S(t)  \tag{1}\\
\frac{\mathrm{d} Q(t)}{\mathrm{d} t}=\varepsilon I(t)+\delta R(t)-\mu Q(t)-\beta_{2} Q(t) I(t) \\
\frac{\mathrm{d} I(t)}{\mathrm{d} t}=\beta_{1} S(t) I(t)+\beta_{2} Q(t) I(t)+\sigma R(t) \\
\quad-(\varepsilon+\gamma+\mu) I(t) \\
\frac{\mathrm{d} R(t)}{\mathrm{d} t}=\gamma I(t)-(\delta+\sigma+\mu) R(t)
\end{array}\right.
$$

where the meanings of $S(t), Q(t), I(t)$, and $R(t)$ are described concisely in Table 1. All the parameters $\Lambda, \beta_{1}, \mu, \varepsilon, \delta$, $\gamma, \beta_{2}$, and $\sigma$ are positive constants, and their meanings are presented in Table 2. Liu et al. [26] studied the global exponential stability of the drug-free equilibrium and the global stability of the drug-addiction equilibrium, and they showed that special psychological treatment played a very positive role in drug abusers.

It should be pointed out that system (1) assumed that drug abusers can give up drugs instantaneous. This assumption seems not to be realistic since the synthetic drugs are addictive easily and it usually needs a period to give up drugs. Time delays have been incorporated into dynamical models about some other fields by many scholars [27-33]. Generally speaking, delay differential equations exhibit much more complicated dynamics than ordinary differential equations since a time delay could cause the equilibrium of a dynamical model to lose its stability. Hence, it is important to know the critical point at which a synthetic drug transmission model changes its stability. Based on the discussion above, we consider the following synthetic drug transmission model with two time delays:

Table 1: The state variables for system (1).

| Parameter | Description |
| :--- | :---: |
| $S(t)$ | Number of susceptible individuals who have never <br> taken any drugs at time $t$ |
| $Q(t)$ | Number of susceptible individuals who have history <br> of drug abuse |
| $I(t)$ | Number of drug users not in treatment |
| $R(t)$ | Number of individuals who are receiving treatment |

Table 2: The description of parameters for system (1).

| Parameter | Description |
| :--- | :---: |
| $\Lambda$ | Immigration rate of the susceptible |
| $\beta_{1}$ | Probability of transmission from $S$ to $I$ |
| $\mu$ | Natural death rate of all populations |
| E | Self-cure rate from $I$ to $Q$ |
| $\delta$ | Successful treatment rate from $I$ to $Q$ |
| $\gamma$ | Procession rate from $I$ to $R$ |
| $\beta_{2}$ | Probability of transmission from $Q$ to $I$ |
| $\sigma$ | Probability of treatment failure |

$$
\left\{\begin{array}{l}
\frac{\mathrm{d} S(t)}{\mathrm{d} t}=\Lambda-\beta_{1} S(t) I(t)-\mu S(t)  \tag{2}\\
\frac{\mathrm{d} Q(t)}{\mathrm{d} t}=\varepsilon I\left(t-\tau_{1}\right)+\delta R\left(t-\tau_{2}\right)-\mu Q(t)-\beta_{2} Q(t) I(t) \\
\frac{\mathrm{d} I(t)}{\mathrm{d} t}=\beta_{1} S(t) I(t)+\beta_{2} Q(t) I(t)+\sigma R(t)-(\gamma+\mu) I(t) \\
-\varepsilon I\left(t-\tau_{1}\right) \\
\frac{\mathrm{d} R(t)}{\mathrm{d} t}=\gamma I(t)-(\sigma+\mu) R(t)-\delta R\left(t-\tau_{2}\right)
\end{array}\right.
$$

where $\tau_{1}$ is the time delay due to the period that the drug abusers use to give up drugs through self-control. $\tau_{2}$ is the time delay due to the period used to give up drugs through successful treatment. The transfer diagram of system (2) is depicted as in Figure 1. This paper mainly concerns the effect of the delays $\tau_{1}$ and $\tau_{2}$ on the stability of system (2).

The framework of the current paper is arranged as follows. In Section 2, the existence of Hopf bifurcation is discussed in detail by using the different combinations of the two delays as the bifurcation parameters and analyzing the distribution of roots of the associated characteristic equations. In Section 3, the direction of Hopf bifurcation and stability of the bifurcating periodic solutions are determined with the help of the center manifold theorem and normal form theory. In Section 4, the effectiveness of the obtained theoretical findings is certified through numerical simulations. Finally, conclusions are drawn in Section 5.


Figure 1: The transfer diagram of system (2).

## 2. The Existence of Hopf Bifurcation

According to the analysis in the literature [26], we know that system (2) has a unique positive synthetic drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ when

$$
\begin{align*}
R_{0} & =\frac{\beta_{2} \Lambda(\delta+\sigma+\mu)}{\mu((\varepsilon+\gamma+\mu)(\delta+\sigma+\mu)-\gamma \sigma)}>1 \\
S^{*} & =\frac{\Lambda}{\beta_{1} I^{*}+\mu}  \tag{3}\\
Q^{*} & =\frac{\varepsilon(\delta+\sigma+\mu)+\delta \gamma}{(\delta+\sigma+\mu)\left(\mu+\beta_{2} I^{*}\right)} I^{*} \\
R^{*} & =\frac{\gamma}{\delta+\sigma+\mu} I^{*}
\end{align*}
$$

where $I^{*}$ is the positive root of the following equation:

$$
\begin{align*}
a\left(I^{*}\right)^{2}+b I^{*}+c= & 0 \\
a= & \mu \beta_{1} \beta_{2}(\gamma+\delta+\sigma+\mu) \\
b= & \mu^{2}\left(\beta_{1}+\beta_{2}\right)(\gamma+\delta+\mu+\sigma) \\
& +\mu \varepsilon \beta_{1}(\delta+\sigma+\mu)+\mu \beta_{1} \gamma \delta  \tag{4}\\
& -\beta_{1} \beta_{2} \Lambda(\delta+\sigma+\mu), \\
c= & u^{2}(\delta+\sigma+\mu)(\mu+\varepsilon)+\mu^{2} \gamma(\delta+\mu) \\
& -\mu \beta_{1} \Lambda(\delta+\sigma+\mu)
\end{align*}
$$

The linear part of system (2) is

$$
\left\{\begin{array}{l}
\frac{\mathrm{d} S(t)}{\mathrm{d} t}=L_{11} S(t)+L_{13} I(t) \\
\frac{\mathrm{d} Q(t)}{\mathrm{d} t}=L_{22} Q(t)+L_{23} I(t)+M_{23} I\left(t-\tau_{1}\right) \\
\quad+N_{24} R\left(t-\tau_{2}\right), \\
\frac{\mathrm{d} I(t)}{\mathrm{d} t}=L_{31} S(t)+L_{32} Q(t)+L_{33} I(t)+L_{34} R(t)  \tag{5}\\
\quad+M_{33} I\left(t-\tau_{1}\right),
\end{array}\right.
$$

$$
\begin{align*}
\lambda^{4} & +a_{3} \lambda^{3}+a_{2} \lambda^{2}+a_{1} \lambda+a_{0}+\left(b_{3} \lambda^{3}+b_{2} \lambda^{2}+b_{1} \lambda+b_{0}\right) e^{-\lambda \tau_{1}} \\
& +\left(c_{3} \lambda^{3}+c_{2} \lambda^{2}+c_{1} \lambda+c_{0}\right) e^{-\lambda \tau_{2}} \\
& +\left(d_{2} \lambda^{2}+d_{1} \lambda+d_{0}\right) e^{-\lambda\left(\tau_{1}+\tau_{2}\right)}=0 \tag{6}
\end{align*}
$$

where

$$
\begin{aligned}
& a_{0}= L_{11} L_{22}\left(L_{33} L_{44}-L_{34} L_{43}\right)+L_{13} L_{31} L_{22} L_{44}, \\
& a_{1}=\left(L_{34} L_{43}-L_{33} L_{44}\right)\left(L_{11}+L_{22}\right)-L_{13} L_{31}\left(L_{22}+L_{44}\right) \\
&-L_{11} L_{22}\left(L_{33}+L_{44}\right), \\
& a_{2}=\left(L_{11}+L_{22}\right)\left(L_{33}+L_{44}\right)+L_{11} L_{22}+L_{33} L_{44} \\
&-L_{13} L_{31}-L_{34} L_{43}, \\
& a_{3}=-\left(L_{11}+L_{22}+L_{33}+L_{44}\right), \\
& b_{0}= L_{11} L_{44}\left(L_{22} M_{33}-L_{32} M_{23}\right), \\
& b_{1}= L_{32} M_{23}\left(L_{11}+L_{44}\right)-M_{33}\left(L_{11} L_{22}+L_{11} L_{44}+L_{22} L_{44}\right), \\
& b_{2}= M_{33}\left(L_{11}+L_{22}+L_{44}\right)-L_{32} M_{23}, \\
& b_{3}=-M_{33}, \\
& c_{0}= L_{11} L_{22} L_{33} N_{44}+L_{13} L_{31} L_{22} N_{44}+L_{11} L_{32} L_{43} N_{24}, \\
& c_{1}=-N_{44}\left(L_{11} L_{22}+L_{11} L_{33}+L_{22} L_{33}\right)-L_{13} L_{31} N_{44} \\
&-L_{32} L_{43} N_{24}, \\
& c_{2}= N_{44}\left(L_{11}+L_{22}+L_{33}\right), \\
& c_{3}=-N_{44}, \\
& d_{0}= L_{11} N_{44}\left(L_{22} M_{33}-L_{32} M_{23}\right), \\
& d_{1}= L_{32} M_{23} N_{44}-M_{33} N_{44}\left(L_{11}+L_{22}\right), \\
& d_{2}= M_{33} N_{44}, \\
& L_{11}=-\left(\beta_{1} I^{*}+\mu\right), \\
& L_{13}=-\beta_{1} S^{*}, \\
& L_{22}=-\left(\mu+\beta_{2} I^{*}\right), \\
& L_{23}=-\beta_{2} Q^{*}, \\
& L_{31}=\beta_{1} I^{*}, \\
& L_{32}= \beta_{2} I^{*}, \\
& L_{33}= \beta_{1} S^{*}+\beta_{2} Q^{*}, \\
& L_{34}= \sigma, \\
& L_{43}= \gamma, \\
& L_{44}=-(\sigma+\mu), \\
& M_{23}= \varepsilon \\
& M_{33}=-\varepsilon, \\
& N_{24}= \delta, \\
& N_{44}=-\delta, \\
& \\
&
\end{aligned},
$$

$$
\begin{equation*}
\frac{\mathrm{d} R(t)}{\mathrm{d} t}=L_{43} I(t)+L_{44} R(t)+N_{44} R\left(t-\tau_{2}\right) \tag{7}
\end{equation*}
$$

Case 1. $\tau_{1}=\tau_{2}=0$. When $\tau_{1}=\tau_{2}=0$, equation (6) becomes

$$
\begin{equation*}
\lambda^{4}+K_{3} \lambda^{3}+K_{2} \lambda^{2}+K_{1} \lambda+K_{0}=0 \tag{8}
\end{equation*}
$$

where

$$
\begin{align*}
& K_{0}=a_{0}+b_{0}+c_{0}+d_{0} \\
& K_{1}=a_{1}+b_{1}+c_{1}+d_{1} \\
& K_{2}=a_{2}+b_{2}+c_{2}+d_{2}  \tag{9}\\
& K_{3}=a_{3}+b_{3}+c_{3} .
\end{align*}
$$

According to Routh-Hurwitz criterion, the drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ is locally asymptotically stable provided the following conditions are satisfied: $\left(H_{1}\right) K_{0}>0, K_{3}>0, K_{2} K_{3}>K_{1} K_{4}$, and $K_{1} K_{2} K_{3}>K_{1}^{2} K_{4}+$ $K_{0} K_{3}^{2}$.

Case 2. $\tau_{1}>0$ and $\tau_{2}=0$.
We analyze the effect of $\tau_{1}$ on bifurcation for system (2). When $\tau_{1}>0$ and $\tau_{2}=0$, equation (6) becomes

$$
\begin{align*}
& \lambda^{4}+K_{13} \lambda^{3}+K_{12} \lambda^{2}+K_{11} \lambda+K_{10} \\
& \quad+\left(L_{13} \lambda^{3}+L_{12} \lambda^{2}+L_{11} \lambda+L_{10}\right) e^{-\lambda \tau_{1}}=0 \tag{10}
\end{align*}
$$

where

$$
\begin{align*}
K_{10} & =a_{0}+c_{0} \\
K_{11} & =a_{1}+c_{1} \\
K_{12} & =a_{2}+c_{2} \\
K_{13} & =a_{3}+c_{3}  \tag{11}\\
L_{10} & =b_{0}+d_{0} \\
L_{11} & =b_{1}+d_{1} \\
L_{12} & =b_{2}+d_{2} \\
L_{13} & =b_{3}
\end{align*}
$$

Assume that $\lambda=i \omega_{1}\left(\omega_{1}>0\right)$ is a purely imaginary root of equation (10), then it follows that

$$
\left\{\begin{array}{l}
\left(L_{10}-L_{12} \omega_{1}^{2}\right) \cos \omega_{1} \tau_{1}-\left(L_{13} \omega_{1}^{3}-L_{11} \omega_{1}\right) \sin \omega_{1} \tau_{1}  \tag{12}\\
\quad=K_{12} \omega_{1}^{2}-\omega_{1}^{4} \\
\left(L_{10}-L_{12} \omega_{1}^{2}\right) \sin \omega_{1} \tau_{1}+\left(L_{13} \omega_{1}^{3}-L_{11} \omega_{1}\right) \cos \omega_{1} \tau_{1} \\
\quad=K_{11} \omega_{1}-K_{13} \omega_{1}^{3} .
\end{array}\right.
$$

By the aid of equation (12), we have

$$
\begin{equation*}
\omega_{1}^{8}+e_{13} \omega_{1}^{6}+e_{12} \omega_{1}^{4}+e_{11} \omega_{1}^{2}+e_{10}=0 \tag{13}
\end{equation*}
$$

where

$$
\begin{align*}
& e_{10}=K_{10}^{2}-L_{10}^{2} \\
& e_{11}=K_{11}^{2}+2 L_{10} L_{12}-2 K_{10} K_{12}-L_{11}^{2}  \tag{14}\\
& e_{12}=K_{12}^{2}+2 K_{10}+2 L_{11} L_{13}-2 K_{11} K_{13}-L_{12}^{2} \\
& e_{13}=K_{13}^{2}-2 K_{12}-L_{13}^{2}
\end{align*}
$$

Making the substitution $v_{1}=\omega_{1}^{2}$, equation (13) can be rewritten as

$$
\begin{equation*}
v_{1}^{4}+e_{13} v_{1}^{3}+e_{12} v_{1}^{2}+e_{11} v_{1}+e_{10}=0 \tag{15}
\end{equation*}
$$

Define

$$
\begin{equation*}
g_{1}\left(v_{1}\right)=v_{1}^{4}+e_{13} v_{1}^{3}+e_{12} v_{1}^{2}+e_{11} v_{1}+e_{10} \tag{16}
\end{equation*}
$$

In order to establish the main results of this article, it is assumed that $\left(H_{21}\right)$ equation (15) has at least one positive real root. Without loss of generality, assume that equation (15) has four positive roots, denoted by $v_{11}, v_{12}, v_{13}$, and $v_{14}$. Accordingly, $\omega_{1 i}=\sqrt{v_{1 i}}(i=1,2,3,4)$ are the roots of equation (13). From equation (12), one has

$$
\begin{equation*}
\tau_{1 i}^{j}=\frac{1}{\omega_{1 i}} \times \arccos \left\{\frac{f_{11}\left(\omega_{1 i}\right)}{f_{12}\left(\omega_{1 i}\right)}+2 n \pi\right\} \tag{17}
\end{equation*}
$$

with $i=1,2,3,4 ; n=0,1,2, \ldots$; and

$$
\begin{align*}
f_{11}\left(\omega_{1 i}\right)= & \left(L_{12}-K_{13} L_{13}\right) \omega_{1 i}^{6}+\left(K_{11} L_{13}+K_{13} L_{11}\right. \\
& \left.-K_{12} L_{12}-L_{10}\right) \omega_{1 i}^{4}+\left(K_{10} L_{12}+K_{12} L_{10}\right. \\
& \left.-K_{11} L_{11}\right) \omega_{1 i}^{2}-K_{10} L_{10}  \tag{18}\\
f_{12}\left(\omega_{1 i}\right)= & L_{13}^{2} \omega_{1 i}^{6}+\left(L_{12}^{2}-2 L_{11} L_{13}\right) \omega_{1 i}^{4} \\
& +\left(L_{11}^{2}-2 L_{10} L_{12}\right) \omega_{1 i}^{2}+L_{10}^{2}
\end{align*}
$$

Denote

$$
\begin{array}{r}
\tau_{10}=\tau_{1 i_{0}}^{0}=\min \left\{\tau_{1 i}^{0} \mid i=1,2,3,4\right\},  \tag{19}\\
\omega_{10}=\tau_{1 i_{0}} .
\end{array}
$$

Next, we derive the condition of the occurrence for Hopf bifurcation. Differentiating both sides of equation (10) with regard to $\tau_{1}$ and substituting $\lambda=i \omega_{10}$ into the obtained expression, it can be achieved that

$$
\begin{equation*}
\operatorname{Re}\left[\frac{\mathrm{d} \lambda}{\mathrm{~d} \tau_{1}}\right]_{\tau_{1}=\tau_{10}}^{-1}=\frac{g_{1}^{\prime}\left(v_{10}\right)}{\left(L_{13} \omega_{10}^{3}-L_{11} \omega_{10}\right)^{2}+\left(L_{10}-L_{12} \omega_{10}^{2}\right)^{2}} \tag{20}
\end{equation*}
$$

where $v_{10}=\omega_{10}^{2}$. To ensure the condition of the occurrence for Hopf bifurcation, we educe the following hypothesis: $\left(H_{22}\right) g_{1}^{\prime}\left(v_{10}\right) \neq 0$, which suggests that transversality condition is matched. In conclusion, we have the following results.

Theorem 1. For system (2), if the conditions $\left(H_{1}\right),\left(H_{21}\right)$, and $\left(H_{22}\right)$ hold, then drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ is locally asymptotically stable when $\tau_{1} \in\left[0, \tau_{10}\right)$; system (2) undergoes a Hopf bifurcation at the drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ when $\tau_{1}=\tau_{10}$, and a family of periodic solutions bifurcate from the drugaddiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$.

Remark 1. Although the assumptions $\left(H_{21}\right)$ and $\left(H_{22}\right)$ seem to be tedious, however, one can verify the assumptions in numerical simulations.

Case 3. $\tau_{1}=0$ and $\tau_{2}>0$.

Remark 2. When $\tau_{1}=0$ and $\tau_{2}>0$, the analysis of the effect of $\tau_{2}$ on bifurcation for system (2) is similar as that in Case 2. Therefore, we omit it here.

Case 4. $\tau_{1}=\tau_{2}=\tau>0$.
We analyze the effect of $\tau$ on bifurcation for system (2).
When $\tau_{1}=\tau_{2}=\tau>0$, equation (6) becomes

$$
\begin{align*}
\lambda^{4} & +K_{33} \lambda^{3}+K_{32} \lambda^{2}+K_{31} \lambda+K_{30} \\
& +\left(L_{33} \lambda^{3}+L_{32} \lambda^{2}+L_{31} \lambda+L_{30}\right) e^{-\lambda \tau}  \tag{21}\\
& +\left(M_{32} \lambda^{2}+M_{31} \lambda+M_{30}\right) e^{-2 \lambda \tau}=0
\end{align*}
$$

with

$$
\begin{align*}
K_{30} & =a_{0}, \\
K_{31} & =a_{1}, \\
K_{32} & =a_{2}, \\
K_{33} & =a_{3}, \\
L_{30} & =b_{0}+c_{0}, \\
L_{31} & =b_{1}+c_{1},  \tag{22}\\
L_{32} & =b_{2}+c_{2}, \\
L_{33} & =b_{3}+c_{3}, \\
M_{30} & =d_{0}, \\
M_{31} & =d_{1}, \\
M_{32} & =d_{2} .
\end{align*}
$$

By multiplying $e^{\lambda \tau}$ on both sides of equation (21), it can be procured that

$$
\begin{align*}
& L_{33} \lambda^{3}+L_{32} \lambda^{2}+L_{31} \lambda+L_{30} \\
& \quad+\left(\lambda^{4}+K_{33} \lambda^{3}+K_{32} \lambda^{2}+K_{31} \lambda+K_{30}\right) e^{\lambda \tau}  \tag{23}\\
& \quad+\left(M_{32} \lambda^{2}+M_{31} \lambda+M_{30}\right) e^{-\lambda \tau}=0 .
\end{align*}
$$

Suppose $i \omega(\omega>0)$ is the root of equation (23), then one has

$$
\left\{\begin{align*}
J_{41}(\omega) \cos \omega \tau+J_{42}(\omega) \sin \omega \tau & =J_{45}(\omega)  \tag{24}\\
J_{43}(\omega) \sin \omega \tau-J_{44}(\omega) \cos \omega \tau & =J_{46}(\omega)
\end{align*}\right.
$$

where

$$
\begin{align*}
& J_{41}(\omega)=\omega^{4}-\left(K_{32}+M_{32}\right) \omega^{2}+K_{30}+M_{30}, \\
& J_{42}(\omega)=K_{33} \omega^{3}-\left(K_{31}-M_{31}\right) \omega, \\
& J_{43}(\omega)=\omega^{4}-\left(K_{32}-M_{32}\right) \omega^{2}+K_{30}-M_{30}, \\
& J_{44}(\omega)=K_{33} \omega^{3}-\left(K_{31}+M_{31}\right) \omega,  \tag{25}\\
& J_{45}(\omega)=L_{32} \omega^{2}-L_{30}, \\
& J_{46}(\omega)=L_{33} \omega^{3}-L_{31} \omega .
\end{align*}
$$

Using Cramer's rule to solve the above equations, one obtains

$$
\begin{align*}
& \cos \omega \tau=\frac{l_{6} \omega^{6}+l_{4} \omega^{4}+l_{2} \omega^{2}+l_{0}}{\omega^{8}+j_{6} \omega^{6}+j_{4} \omega^{4}+j_{2} \omega^{2}+j_{0}}  \tag{26}\\
& \sin \omega \tau=\frac{l_{7} \omega^{7}+l_{5} \omega^{5}+l_{3} \omega^{3}+l_{1} \omega}{\omega^{8}+j_{6} \omega^{6}+j_{4} \omega^{4}+j_{2} \omega^{2}+j_{0}} \tag{27}
\end{align*}
$$

with

$$
\begin{align*}
j_{0}= & K_{30}^{2}-M_{30}^{2}, \\
j_{2}= & K_{31}^{2}-M_{31}^{2}-2 K_{30} K_{32}+2 M_{30} M_{32}, \\
j_{4}= & 2 K_{30}-M_{32}^{2}-2 K_{31} K_{33}, \\
j_{6}= & K_{33}^{2}-2 K_{32}, \\
l_{0}= & -\left(K_{30}-M_{30}\right) L_{30}, \\
l_{1}= & \left(K_{31}+M_{31}\right) L_{30}-\left(K_{30}+M_{30}\right) L_{31}, \\
l_{2}= & \left(K_{32}-M_{32}\right) L_{30}+\left(K_{30}-M_{30}\right) L_{32}-\left(K_{31}-M_{31}\right) L_{31}, \\
l_{3}= & \left(K_{32}+M_{32}\right) L_{31}+\left(K_{30}+M_{30}\right) L_{33}-\left(K_{31}+M_{31}\right) L_{32} \\
& -K_{33} L_{30}, \\
l_{4}= & \left(K_{31}-M_{31}\right) L_{33}-\left(K_{32}-M_{32}\right) L_{32}+K_{33} L_{31}-L_{30}, \\
l_{5}= & K_{33} L_{32}-L_{31}-\left(K_{32}-M_{32}\right) L_{33}, \\
l_{6}= & L_{32}-K_{33} L_{33}, \\
l_{7}= & L_{33} . \tag{28}
\end{align*}
$$

Squaring both sides of equations (26) and (27), respectively, and adding them together, one has

$$
\begin{align*}
& \omega^{16}+k_{7} \omega^{14}+k_{6} \omega^{12}+k_{5} \omega^{10}+k_{4} \omega^{8}+k_{3} \omega^{6}+k_{2} \omega^{4} \\
& \quad+k_{1} \omega^{2}+k_{0}=0, \tag{29}
\end{align*}
$$

where

$$
\begin{align*}
& k_{0}=j_{0}^{2}-l_{0}^{2}, \\
& k_{1}=2 j_{0} j_{2}-2 l_{0} l_{2}-l_{1}^{2}, \\
& k_{2}=j_{2}^{2}+2 j_{0} j_{4}-l_{2}^{2}-2 l_{0} l_{4}-2 l_{1} l_{3}, \\
& k_{3}=2 j_{0} j_{6}+2 j_{2} j_{4}-2 l_{0} l_{6}-2 l_{2} l_{4}-l_{3}^{2}-2 l_{1} l_{5},  \tag{30}\\
& k_{4}=j_{4}^{2}+2 j_{0}+2 j_{2} j_{6}-l_{4}^{2}-2 l_{2} l_{6}-2 l_{1} l_{7}-2 l_{3} l_{5}, \\
& k_{5}=2 j_{2}+2 j_{4} j_{6}-2 l_{4} l_{6}-l_{5}^{2}-2 l_{3} l_{7}, \\
& k_{6}=j_{6}^{2}+2 j_{4}-l_{6}^{2}-2 l_{5} l_{7}, k_{7}=2 j_{6}-l_{7}^{2} .
\end{align*}
$$

Let $\omega^{2}=v$, then equation (29) becomes

$$
\begin{equation*}
v^{8}+k_{7} v^{7}+k_{6} v^{6}+k_{5} v^{5}+k_{4} v^{4}+k_{3} v^{3}+k_{2} v^{2}+k_{1} v+k_{0}=0 . \tag{31}
\end{equation*}
$$

Suppose that $\left(H_{41}\right)$ equation (29) has at least one positive root. Without loss of generality, assume that equation (31) has eight positive roots, denoted by
$v_{1}, v_{2}, \ldots, v_{8}$. Accordingly, $\omega_{i}=\sqrt{v_{i}}(i=1,2, \ldots, 8)$ are the roots of equation (29). Thus, one has

$$
\begin{equation*}
\tau_{i}^{j}=\frac{1}{\omega_{i}} \times \arccos \left\{\frac{l_{6} \omega_{i}^{6}+l_{4} \omega_{i}^{4}+l_{2} \omega_{i}^{2}+l_{0}}{\omega_{i}^{8}+j_{6} \omega_{i}^{6}+j_{4} \omega_{i}^{4}+j_{2} \omega_{i}^{2}+j_{0}}+2 n \pi\right\} \tag{32}
\end{equation*}
$$

with $i=1,2, \ldots, 8 ; n=0,1,2, \ldots$; and

$$
\begin{array}{r}
\tau_{0}=\tau_{i_{0}}^{0}=\min \left\{\tau_{i}^{0} \mid i=1,2, \ldots, 8\right\},  \tag{33}\\
\omega_{0}=\tau_{i_{0}} .
\end{array}
$$

Differentiating both sides of equation (23) with respect to $\tau$ yields

$$
\begin{equation*}
\left[\frac{\mathrm{d} \lambda}{\mathrm{~d} \tau}\right]^{-1}=-\frac{f_{31}(\lambda)}{f_{32}(\lambda)}-\frac{\tau}{\lambda}, \tag{34}
\end{equation*}
$$

where

$$
\begin{align*}
f_{31}(\lambda)= & 3 L_{33} \lambda^{2}+2 L_{32} \lambda+L_{31}+\left(4 \lambda^{3}+3 K_{33} \lambda^{2}+2 K_{32} \lambda\right. \\
& \left.+K_{31}\right) e^{\lambda \tau}+\left(2 M_{32} \lambda+M_{31}\right) e^{-\lambda \tau}, \\
f_{32}(\lambda)= & \lambda\left(\lambda^{4}+K_{33} \lambda^{3}+K_{32} \lambda^{2}+K_{31} \lambda+K_{30}\right) e^{\lambda \tau} \\
& -\lambda\left(M_{32} \lambda^{2}+M_{31} \lambda+M_{30}\right) e^{-\lambda \tau} . \tag{35}
\end{align*}
$$

Hence, one obtains

$$
\begin{equation*}
\operatorname{Re}\left[\frac{\mathrm{d} \lambda}{\mathrm{~d} \tau}\right]_{\tau=\tau_{0}}^{-1}=\frac{U_{3 R} V_{3 R}+U_{3 I} V_{3 I}}{V_{3 R}^{2}+V_{3 I}^{2}}, \tag{36}
\end{equation*}
$$

with

$$
\begin{align*}
U_{3 R}= & L_{31}-3 L_{33} \omega_{0}^{2}+\left(K_{31}+M_{31}-3 K_{33} \omega_{0}^{2}\right) \cos \omega_{0} \tau_{0} \\
& -\left(2 K_{32} \omega_{0}-2 M_{32} \omega_{0}-4 \omega_{0}^{3}\right) \sin \omega_{0} \tau_{0} \\
U_{3 I}= & 2 L_{32} \omega_{0}+\left(K_{31}-M_{31}-3 K_{33} \omega_{0}^{2}\right) \sin \omega_{0} \tau_{0} \\
& +\left(2 K_{32} \omega_{0}+2 M_{32} \omega_{0}-4 \omega_{0}^{3}\right) \cos \omega_{0} \tau_{0} \\
V_{3 R}= & \left(K_{33} \omega_{0}^{4}-K_{31} \omega_{0}^{2}+M_{31} \omega_{0}^{2}\right) \cos \omega_{0} \tau_{0} \\
& -\left(\omega_{0}^{5}-K_{32} \omega_{0}^{3}-M_{32} \omega_{0}^{3}+K_{30} \omega_{0}+M_{30} \omega_{0}\right) \sin \omega_{0} \tau_{0} \\
V_{3 I}= & \left(K_{33} \omega_{0}^{4}-K_{31} \omega_{0}^{2}-M_{31} \omega_{0}^{2}\right) \sin \omega_{0} \tau_{0} \\
& +\left(\omega_{0}^{5}-K_{32} \omega_{0}^{3}+M_{32} \omega_{0}^{3}+K_{30} \omega_{0}-M_{30} \omega_{0}\right) \cos \omega_{0} \tau_{0} \tag{37}
\end{align*}
$$

In order to obtain the main results, it is necessary to make the following extra assumption ( $H_{42}$ ) $U_{3 R} V_{3 R}+$ $U_{3 I} V_{3 I} \neq 0$, which ensures that transversality condition holds.

Theorem 2. For system (2), if the conditions $\left(H_{1}\right),\left(H_{41}\right)$, and $\left(H_{42}\right)$ hold, then drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ is locally asymptotically stable when $\tau \in\left[0, \tau_{0}\right)$; system (2) undergoes a Hopf bifurcation at the
drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ when $\tau=\tau_{0}$, and a family of periodic solutions bifurcate from the drugaddiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$.

Remark 3. Although the assumptions $\left(H_{41}\right)$ and $\left(H_{42}\right)$ seem to be tedious, however, one can verify the assumptions in numerical simulations.

Case 5. $\tau_{1} \in\left(0, \tau_{10}\right)$ and $\tau_{2}>0$.
Motivated by the work in [34], in this case, we analyze the effect of $\tau_{2}$ on bifurcation for system (2) and fix $\tau_{1} \in\left(0, \tau_{10}\right)$. Suppose $i \omega_{2}^{\prime}\left(\omega_{2}^{\prime}>0\right)$ is the root of equation (6). For convenience, we still denote $\omega_{2}^{\prime}$ as $\omega_{2}$. Then, one has

$$
\left\{\begin{array}{l}
J_{41}\left(\omega_{2}\right) \sin \omega_{2} \tau_{2}+J_{42}\left(\omega_{2}\right) \cos \omega_{2} \tau_{2}=J_{43}\left(\omega_{2}\right)  \tag{38}\\
J_{41}\left(\omega_{2}\right) \cos \omega_{2} \tau_{2}-J_{42}\left(\omega_{2}\right) \sin \omega_{2} \tau_{2}=J_{44}\left(\omega_{2}\right)
\end{array}\right.
$$

where

$$
\begin{align*}
J_{41}\left(\omega_{2}\right)= & c_{1} \omega_{2}-c_{3} \omega_{2}^{3}+d_{1} \omega_{2} \cos \omega_{2} \tau_{1} \\
& -\left(d_{0}-d_{2} \omega_{2}^{2}\right) \sin \omega_{2} \tau_{1}, \\
J_{42}\left(\omega_{2}\right)= & c_{0}-c_{2} \omega_{2}^{2}+d_{1} \omega_{2} \sin \omega_{2} \tau_{1}+\left(d_{0}-d_{2} \omega_{2}^{2}\right) \cos \omega_{2} \tau_{1}, \\
J_{43}\left(\omega_{2}\right)= & a_{2} \omega_{2}^{2}-\omega_{2}^{4}-a_{0}-\left(b_{1} \omega_{2}-b_{3} \omega_{2}^{3}\right) \sin \omega_{2} \tau_{1} \\
& -\left(b_{0}-b_{2} \omega_{2}^{2}\right) \cos \omega_{2} \tau_{1}, \\
J_{44}\left(\omega_{2}\right)= & a_{3} \omega_{2}^{3}-a_{1} \omega_{2}-\left(b_{1} \omega_{2}-b_{3} \omega_{2}^{3}\right) \cos \omega_{2} \tau_{1} \\
& +\left(b_{0}-b_{2} \omega_{2}^{2}\right) \sin \omega_{2} \tau_{1} . \tag{39}
\end{align*}
$$

Squaring both sides of the above equations, respectively, and adding them together, one has

$$
\begin{equation*}
r_{40}\left(\omega_{2}\right)+2 r_{41}\left(\omega_{2}\right) \cos \omega_{2} \tau_{1}+2 r_{42}\left(\omega_{2}\right) \sin \omega_{2} \tau_{1}=0 \tag{40}
\end{equation*}
$$

where

$$
\begin{align*}
r_{40}\left(\omega_{2}\right)= & \omega_{2}^{8}+\left(a_{3}^{2}-2 a_{2}-b_{3}^{2}-c_{3}^{2}\right) \omega_{2}^{6} \\
& +\left(a_{2}^{2}+2 a_{0}-2 a_{1} a_{3}+b_{2}^{2}-2 b_{1} b_{3}\right. \\
& \left.-c_{2}^{2}+2 c_{1} c_{3}-d_{2}^{2}\right) \omega_{2}^{4}+\left(a_{1}^{2}-2 a_{0} a_{2}-2 b_{0} b_{2}+b_{1}^{2}\right. \\
& \left.-c_{1}^{2}+2 c_{0} c_{2}-d_{1}^{2}+2 d_{0} d_{2}\right) \omega_{2}^{2}+a_{0}^{2}+b_{0}^{2}-c_{0}^{2}-d_{0}^{2} \\
r_{41}\left(\omega_{2}\right)= & \left(a_{3} b_{3}-b_{2}\right) \omega_{2}^{6}+\left(a_{2} b_{2}-a_{1} b_{3}-a_{3} b_{1}+b_{0}\right. \\
& \left.-c_{2} d_{2}+c_{3} d_{1}\right) \omega_{2}^{4}+\left(a_{1} b_{1}-a_{2} b_{0}-a_{0} b_{2}+c_{0} d_{2}\right. \\
& \left.-c_{1} d_{1}+c_{2} d_{0}\right) \omega_{2}+a_{0} b_{0}-c_{0} d_{0} \\
r_{42}\left(\omega_{2}\right)= & -b_{3} \omega_{2}^{7}+\left(a_{2} b_{3}+b_{1}-a_{3} b_{2}+c_{3} d_{2}\right) \omega_{2}^{5} \\
& +\left(a_{3} b_{0}+a_{1} b_{2}-a_{2} b_{1}-a_{0} b_{3}-c_{1} d_{2}\right. \\
& \left.+c_{2} d_{1}-c_{3} d_{0}\right) \omega_{2}^{3}+\left(a_{0} b_{1}-a_{1} b_{0}-c_{0} d_{1}+c_{1} d_{0}\right) \omega_{2} . \tag{41}
\end{align*}
$$

Suppose that $\left(H_{51}\right)$ equation (40) has finite positive roots, denoted by $\omega_{21 *}, \omega_{22 *}, \ldots, \omega_{2 i *}$. Thus,

$$
\begin{equation*}
\tau_{2 i *}^{j}=\frac{1}{\omega_{2 i *}} \times \arccos \left\{\frac{J_{41}\left(\omega_{2 i *}\right) \times J_{44}\left(\omega_{2 i *}\right)+J_{42}\left(\omega_{2 i *}\right) \times J_{43}\left(\omega_{2 i *}\right)}{J_{41}^{2}\left(\omega_{2 i *}\right)+J_{42}^{2}\left(\omega_{2 i *}\right)}+2 n \pi\right\}, \tag{42}
\end{equation*}
$$

with $i=1,2, \ldots, k ; n=0,1,2, \ldots$; and

$$
\begin{equation*}
\tau_{2 *}=\tau_{2 i *_{0}}^{0}=\min \left\{\tau_{2 i *}^{0} \mid i=1,2, \ldots, k\right\} . \tag{43}
\end{equation*}
$$

$$
\begin{equation*}
\left[\frac{\mathrm{d} \lambda}{\mathrm{~d} \tau}\right]^{-1}=-\frac{f_{41}(\lambda)}{f_{42}(\lambda)}-\frac{\tau_{2}}{\lambda}, \tag{44}
\end{equation*}
$$

Differentiating equation (6) with respect to $\tau_{2}$, one has

$$
\begin{align*}
f_{41}(\lambda)= & 4 \lambda^{3}+3 a_{3} \lambda^{2}+2 a_{2} \lambda+a_{1}+\left(\left(3 b_{3}-\tau_{1} b_{2}\right) \lambda^{2}-\tau_{1} \lambda^{3}+\left(2 b_{2}-\tau_{1} b_{1}\right) \lambda+b_{1}-\tau_{1} b_{0}\right) e^{-\lambda \tau_{1}} \\
& +\left(\left(2 d_{2}-\tau_{1} d_{1}\right) \lambda-\tau_{1} d_{2} \lambda^{2}+d_{1}-\tau_{1} d_{0}\right) e^{-\lambda\left(\tau_{1}+\tau_{2}\right)}+\left(3 c_{3} \lambda^{2}+2 c_{2} \lambda+c_{1}\right) e^{-\lambda \tau_{2}},  \tag{45}\\
f_{42}(\lambda)= & \lambda\left(c_{3} \lambda^{3}+c_{2} \lambda^{2}+c_{1} \lambda+c_{0}\right) e^{-\lambda \tau_{2}}+\lambda\left(d_{2} \lambda^{2}+d_{1} \lambda+d_{0}\right) e^{-\lambda\left(\tau_{1}+\tau_{2}\right)} .
\end{align*}
$$

Thus, one obtains
with

$$
\begin{equation*}
\operatorname{Re}\left[\frac{\mathrm{d} \lambda}{\mathrm{~d} \tau_{2}}\right]_{\tau_{2}=\tau_{2 *}}^{-1}=\frac{U_{4 R} V_{4 R}+U_{4 I} V_{4 I}}{V_{4 R}^{2}+V_{4 I}^{2}} \tag{46}
\end{equation*}
$$

$$
\begin{align*}
U_{4 R}= & 2 c_{2} \omega_{2 *} \sin \omega_{2 *} \tau_{2 *}+\left(c_{1}-3 c_{3} \omega_{2 *}^{2}\right) \cos \omega_{2 *} \tau_{2 *}+a_{1}-3 a_{3} \omega_{2 *}^{2}+\left(2 d_{2}-\tau_{1} d_{1}\right) \omega_{2 *}\left(\sin \omega_{2 *} \tau_{1} \cos \omega_{2 *} \tau_{2 *}\right. \\
& \left.+\cos \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right)+\left(\tau_{1} d_{2} \omega_{2 *}^{2}+d_{1}-\tau_{1} d_{0}\right)\left(\cos \omega_{2 *} \tau_{1} \cos \omega_{2 *} \tau_{2 *}-\sin \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right) \\
& +\left(\tau_{1} \omega_{2 *}^{3}+\left(2 b_{2}-\tau_{1} b_{1}\right) \omega_{2 *}\right) \sin \omega_{2 *} \tau_{1}+\left(\left(\tau_{1} b_{2}-3 b_{3}\right) \omega_{2 *}^{2}+b_{1}-\tau_{1} b_{0}\right) \cos \omega_{2 *} \tau_{1} \\
U_{4 I}= & 2 c_{2} \omega_{2 *} \cos \omega_{2 *} \tau_{2 *}-\left(c_{1}-3 c_{3} \omega_{2 *}^{2}\right) \sin \omega_{2 *} \tau_{2 *}+2 a_{2} \omega_{2 *}-4 \omega_{2 *}^{3}+\left(2 d_{2}-\tau_{1} d_{1}\right) \omega_{2 *}\left(\cos \omega_{2 *} \tau_{1} \cos \omega_{2 *} \tau_{2 *}\right. \\
& \left.-\sin \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right)-\left(\tau_{1} d_{2} \omega_{2 *}^{2}+d_{1}-\tau_{1} d_{0}\right)\left(\sin \omega_{2 *} \tau_{1} \cos \omega_{2 *} \tau_{2 *}+\cos \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right)  \tag{47}\\
& +\left(\tau_{1} \omega_{2 *}^{3}+\left(2 b_{2}-\tau_{1} b_{1}\right) \omega_{2 *}\right) \cos \omega_{2 *} \tau_{1}-\left(\left(\tau_{1} b_{2}-3 b_{3}\right) \omega_{2 *}^{2}+b_{1}-\tau_{1} b_{0}\right) \sin \omega_{2 *} \tau_{1} \\
V_{4 R}= & \left(d_{0} \omega_{2 *}-d_{2} \omega_{2 *}^{3}\right)\left(\sin \omega_{2 *} \tau_{1} \cos \omega_{2 *} \cos \omega_{2 *}+\cos \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right)-d_{1} \omega_{2 *}^{2}\left(\cos \omega_{2 *} \tau_{1} \cos \omega_{2 *} \tau_{2 *}\right. \\
& \left.-\sin \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right) \\
V_{4 I}= & \left(d_{0} \omega_{2 *}-d_{2} \omega_{2 *}^{3}\right)\left(\cos \omega_{2 *} \tau_{1} \cos \omega_{2 *} \cos \omega_{2 *}-\sin \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right)+d_{1} \omega_{2 *}^{2}\left(\sin \omega_{2 *} \tau_{1} \cos \omega_{2 *} \tau_{2 *}\right. \\
& \left.+\cos \omega_{2 *} \tau_{1} \sin \omega_{2 *} \tau_{2 *}\right) .
\end{align*}
$$

As in Case 4, we make the following extra assumption $\left(H_{52}\right) U_{34} V_{4 R}+U_{4 I} V_{4 I} \neq 0$, which ensures that transversality condition holds.

Theorem 3. For system (2), if $\tau_{1} \in\left(0, \tau_{10}\right)$ and $\tau_{2}>0$ and the conditions $\left(H_{1}\right),\left(H_{51}\right)$, and $\left(H_{52}\right)$ hold, then drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ is locally asymptotically stable when $\tau_{2} \in\left[0, \tau_{2 *}\right)$; system (2) undergoes a Hopf bifurcation at the drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$ when $\tau_{2}=\tau_{2 *}$, and a family of periodic solutions bifurcate from the drug-addiction equilibrium $E^{*}\left(S^{*}, Q^{*}, I^{*}, R^{*}\right)$.

Remark 4. Although the assumptions $\left(H_{51}\right)$ and $\left(H_{52}\right)$ seem to be tedious, however, one can verify the assumptions in numerical simulations.

## 3. Properties of Hopf Bifurcation

In this section, by employing the center manifold theorem and normal form theory, the properties of the Hopf bifurcation at the critical value $\tau_{2 *}$ are determined. Let $t=s \tau$, $S(t)=u_{1}(s \tau), Q(t)=u_{2}(s \tau), I(t)=u_{3}(s \tau), R(t)=u_{4}(s \tau)$, and $\tau=\tau_{2 *}+\varrho$ where $\varrho \in R$. Throughout this section, we
assume that $\tau_{1 *}<\tau_{2 *}$, where $\tau_{1 *} \in\left(0, \tau_{10}\right)$. Then, system (2) becomes the following form:

$$
\begin{equation*}
\dot{u}(t)=L_{\varrho}\left(u_{t}\right)+F\left(\varrho, u_{t}\right), \tag{48}
\end{equation*}
$$

where $L_{\varrho}: C \longrightarrow R^{4}$ and $F: R \times C \longrightarrow R^{4}$ are defined, respectively, by

$$
\begin{align*}
L_{\varrho} \phi= & \left(\tau_{2 *}+\varrho\right)\left(M_{1 \max } \phi(0)+M_{2 \max } \phi\left(-\frac{\tau_{1 *}}{\tau_{2 *}}\right)\right. \\
& \left.+M_{3 \max } \phi(-1)\right), \\
F(\varrho, \phi)= & \left(\begin{array}{c}
-\beta_{1} \phi_{1}(0) \phi_{3}(0) \\
-\beta_{2} \phi_{2}(0) \phi_{3}(0) \\
\beta_{1} \phi_{1}(0) \phi_{3}(0)+\beta_{2} \phi_{2}(0) \phi_{3}(0) \\
0
\end{array}\right), \tag{49}
\end{align*}
$$

with

$$
\begin{align*}
& M_{1 \text { max }}=\left(\begin{array}{cccc}
L_{11} & 0 & L_{13} & 0 \\
0 & L_{22} & L_{23} & 0 \\
L_{31} & L_{32} & L_{33} & L_{34} \\
0 & 0 & L_{43} & L_{44}
\end{array}\right) \text {, } \\
& M_{2 \max }=\left(\begin{array}{cccc}
0 & 0 & 0 & 0 \\
0 & 0 & M_{23} & 0 \\
0 & 0 & M_{33} & 0 \\
0 & 0 & 0 & 0
\end{array}\right) \text {, }  \tag{50}\\
& M_{3 \max }=\left(\begin{array}{cccc}
0 & 0 & 0 & 0 \\
0 & 0 & 0 & N_{24} \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & N_{44}
\end{array}\right) .
\end{align*}
$$

By the Riesz representation theorem in [35], there exists a function $\eta(\theta, \varrho)$ of bounded variation for $\theta \in[-1,0]$ such that

$$
\begin{equation*}
L_{\varrho} \phi=\int_{-1}^{0} \mathrm{~d} \eta(\theta, \varrho) \phi(\theta) . \tag{51}
\end{equation*}
$$

In fact, one can choose

$$
\eta(\theta, \varrho)= \begin{cases}\left(\tau_{2 *}+\varrho\right)\left(M_{1 \max }+M_{2 \max }+M_{2 \max }\right), & \theta=0,  \tag{52}\\ \left(\tau_{2 *}+\varrho\right)\left(M_{2 \max }+M_{3 \max }\right), & \theta \in\left[\frac{\tau_{1 *}}{\tau_{2 *}}, 0\right), \\ \left(\tau_{2 *}+\varrho\right) M_{3 \max }, & \theta \in\left(-1,-\frac{\tau_{1 *}}{\tau_{2 *}}\right), \\ 0, & \theta=-1,\end{cases}
$$

where $\delta$ is defined by

$$
\delta(\theta)= \begin{cases}0, & \theta \neq 0  \tag{53}\\ 1, & \theta=0\end{cases}
$$

For $\phi \in C\left([-1,0], R^{4}\right)$, define

$$
\begin{align*}
& A(\varrho) \phi= \begin{cases}\frac{\mathrm{d} \phi(\theta)}{\mathrm{d} \theta}, & -1 \leq \theta<0, \\
\int_{-1}^{0} \mathrm{~d} \eta(\theta, \varrho) \phi(\theta), & \theta=0\end{cases}  \tag{54}\\
& R(\varrho) \phi= \begin{cases}0, & -1 \leq \theta<0, \\
F(\varrho, \phi), & \theta=0 .\end{cases}
\end{align*}
$$

Then, system (48) is equivalent to

$$
\begin{equation*}
\dot{u}(t)=A(\varrho) u_{t}+R(\varrho) u_{t}, \tag{55}
\end{equation*}
$$

where $u_{t}=u(t+\theta)$.
The adjoint operator $A^{*}(\varrho)$ of $A(\varrho)$ is defined by

$$
A^{*}(\varphi)= \begin{cases}\frac{\mathrm{d} \phi(s)}{\mathrm{d} s}, & 0<s \leq 1  \tag{56}\\ \int_{-1}^{0} \mathrm{~d} \eta^{T}(s, 0) \phi(-s), & s=0\end{cases}
$$

For $\phi \in C\left([-1,0], R^{4}\right)$ and $\varphi \in C^{1}\left([0,1],\left(R^{4}\right)^{*}\right)$, define

$$
\begin{equation*}
\langle\varphi(s), \phi(\theta)\rangle=\bar{\varphi}(0) \phi(0)-\int_{\theta=-1}^{0} \int_{\xi=0}^{\theta} \bar{\varphi}(\xi-\theta) \mathrm{d} \eta \tag{57}
\end{equation*}
$$

$$
\cdot(\theta) \phi(\xi) \mathrm{d} \xi
$$

where $\eta(\theta)=\eta(\theta, 0)$.
From Section 2, it can be seen that $\pm i \tau_{2 *} \omega_{2 *}$ are the eigenvalues of $A(0)$, so $\pm i \tau_{2 *} \omega_{2 *}$ are also the eigenvalues of $A^{*}(0)$. Suppose that $q(\theta)=\left(1, q_{2}, q_{3}, q_{4}\right)^{T} e^{i \tau_{2 *} \omega_{2 *} \theta}$ and $q^{*}(s)=D\left(1, q_{2}^{*}, q_{3}^{*}, q_{4}^{*}\right)^{T} e^{i \tau_{2 *} \omega_{2 *} s}$ be the eigenvectors for $A(0)$ and $A^{*}(0)$ corresponding to $+i \tau_{2 *} \omega_{2 *}$ and $-i \tau_{2 *} \omega_{2 *}$, respectively. Then, one can obtain

$$
\begin{align*}
& q_{2}=\frac{L_{33}\left(i \omega_{2 *}-L_{11}\right)}{L_{13}\left(i \omega_{2 *}-L_{22}-M_{23} e^{-i \tau_{1 *} \omega_{2 *}}-N_{24} e^{-i \tau_{2 *} \omega_{2 *}}\right)}, \\
& q_{3}=\frac{i \omega_{2 *}-L_{11}}{L_{13}}, \\
& q_{4}=\frac{L_{43}\left(i \omega_{2 *}-L_{11}\right)}{L_{13}\left(i \omega_{2 *}-L_{44}-N_{24} e^{-i \tau_{2 *} \omega_{2 *}}\right)},  \tag{58}\\
& q_{2}^{*}=\frac{L_{11}\left(L_{32}+M_{33} e^{i \tau_{1 *} \omega_{2 *}}\right)}{\left(i \omega_{2 *}+L_{31}\right)\left(i \omega_{2 *}+L_{22}+M_{23} e^{i \tau_{1 *} \omega_{2 *}}\right)}, \\
& q_{3}^{*}=-\frac{L_{11}}{i \omega_{2 *}+L_{31}}, \\
& q_{4}^{*}=-\frac{N_{24} e^{i \tau_{2 *} \omega_{2 *}} q_{2}^{*}+L_{34} q_{3}^{*}}{i \omega_{2 *}+L_{44}+N_{44} e^{i \tau_{2 *} \omega_{2 *}}}
\end{align*}
$$

In order to guarantee $\left\langle q^{*}(s), q(\theta)\right\rangle=1$, the value of $D$ needs to be determined. In view of equation (57), we have

$$
\begin{align*}
\bar{D}= & {\left[1+\sum_{i=1}^{4} q_{i}^{*} \bar{q}_{i}+\tau_{1 *} e^{i \tau_{1 *} \omega_{2 *}} \bar{q}_{2}\left(M_{23} q_{2}^{*}+M_{33} q_{3}^{*}\right)\right.}  \tag{59}\\
& \left.+\tau_{2 *} e^{i \tau_{2 *} \omega_{2 *}} \bar{q}_{4}\left(N_{24} q_{2}^{*}+N_{44} Q_{4}^{*}\right)\right]^{-1}
\end{align*}
$$

$$
\begin{align*}
g_{20}= & 2 \bar{D} \tau_{2 *}\left(\bar{q}_{3}^{*}-1\right) \beta_{1} q_{3}+\left(\bar{q}_{3}^{*}-\bar{q}_{2}^{*}\right) \beta_{2} q_{2} q_{3}, \\
g_{11}= & \bar{D} \tau_{2 *}\left(\bar{q}_{3}^{*}-1\right) \beta_{1}\left(q_{3}+\bar{q}_{3}\right)+\left(\bar{q}_{3}^{*}-\bar{q}_{2}^{*}\right) \beta_{2}\left(q_{2} \bar{q}_{3}+\bar{q}_{2} q_{3}\right), \\
g_{02}= & 2 \bar{D} \tau_{2 *}\left(\bar{q}_{3}^{*}-1\right) \beta_{1} \bar{q}_{3}+\left(\bar{q}_{3}^{*}-\bar{q}_{2}^{*}\right) \beta_{2} \bar{q}_{2} \bar{q}_{3},  \tag{60}\\
g_{21}= & 2 \bar{D} \tau_{2 *}\left(\bar{q}_{3}^{*}-1\right) \beta_{1}\left(W_{11}^{(1)}(0) q_{3}+\frac{1}{2} W_{20}^{(1)}(0) \bar{q}_{3}+W_{11}^{(3)}(0)+\frac{1}{2} W_{20}^{(3)}(0)\right)+\left(\bar{q}_{3}^{*}-\bar{q}_{2}^{*}\right) \beta_{2} \\
& \cdot\left(W_{11}^{(2)}(0) q_{3}+\frac{1}{2} W_{20}^{(2)}(0) \bar{q}_{3}+W_{11}^{(3)}(0) q_{2}+\frac{1}{2} W_{20}^{(3)}(0) \bar{q}_{2}\right),
\end{align*}
$$

with $E_{1}$ and $E_{2}$ can be solved by
$W_{20}(\theta)=\frac{i g_{20} q(0)}{\tau_{2 *} \omega_{2 *}} e^{i \tau_{2 *} \omega_{2 *} \theta}+\frac{i \bar{g}_{02} \bar{q}(0)}{3 \tau_{2 *} \omega_{2 *}} e^{-i \tau_{2 *} \omega_{2 *} \theta}+E_{1} e^{2 i \tau_{2 *} \omega_{2 *} \theta}$,
$W_{11}(\theta)=-\frac{i g_{11} q(0)}{\tau_{2 *} \omega_{2 *}} e^{i \tau_{2 *} \omega_{2 *} \theta}+\frac{i \bar{g}_{11} \bar{q}(0)}{\tau_{2 *} \omega_{2 *}} e^{-i \tau_{2 *} \omega_{2 *} \theta}+E_{2}$.

$$
\begin{align*}
& E_{1}=2\left(\begin{array}{cccc}
L_{11}^{*} & 0 & -L_{13} & 0 \\
0 & L_{22}^{*} & L_{23}^{*} & -N_{24} e^{-2 i_{2} \omega_{2} \omega_{2 *}} \\
L_{31} & -L_{32} & L_{33}^{*} & L_{34} \\
0 & 0 & -L_{43} & L_{44}^{*}
\end{array}\right)^{-1} \times\left(\begin{array}{c}
-\beta_{1} q_{3} \\
-\beta_{2} q_{2} q_{3} \\
\beta_{1} q_{3}+\beta_{2} q_{2} q_{3} \\
0
\end{array}\right), \\
& E_{2}=2\left(\begin{array}{cccc}
L_{11} & 0 & L_{13} & 0 \\
0 & L_{22} & L_{23}+M_{23} & N_{24} \\
L_{31} & L_{32} & L_{33}+M_{33} & L_{34} \\
0 & 0 & L_{43} & L_{44}+N_{44}
\end{array}\right)^{-1} \times\left(\begin{array}{c}
-\beta_{1}\left(q_{3}+\bar{q}_{3}\right) \\
-\beta_{2}\left(q_{2} \bar{q}_{3}+\bar{q}_{2} q_{3}\right) \\
\beta_{1}\left(q_{3}+\bar{q}_{3}\right)+\beta_{2}\left(q_{2} \bar{q}_{3}+\bar{q}_{2} q_{3}\right) \\
0
\end{array}\right), \tag{62}
\end{align*}
$$

where

$$
\begin{align*}
& L_{11}^{*}=2 i \omega_{2 *}-L_{11} \\
& L_{22}^{*}=2 i \omega_{2 *}-L_{22}  \tag{64}\\
& L_{23}^{*}=-L_{23}-M_{23} e^{-2 i \tau_{1 *} \omega_{2 *}}  \tag{63}\\
& L_{33}^{*}=2 i \omega_{2 *}-L_{33}-M_{33} e^{-2 i \tau_{1 *} \omega_{2 *}} \\
& L_{44}^{*}=2 i \omega_{0}-L_{44}-N_{44} e^{-2 i \tau_{2 *} \omega_{2 *}}
\end{align*}
$$

Thus, we have

$$
C_{1}(0)=\frac{i}{2 \tau_{2 *} \omega_{2 *}}\left(g_{11} g_{20}-2\left|g_{11}\right|^{2}-\frac{\left|g_{02}\right|^{2}}{3}\right)+\frac{g_{21}}{2}
$$

$$
\mu_{2}=-\frac{\operatorname{Re}\left\{C_{1}(0)\right\}}{\left\{\lambda^{\prime}\left(\tau_{2 *}\right)\right\}}
$$

$$
\beta_{2}=2 \operatorname{Re}\left\{C_{1}(0)\right\}
$$

$$
T_{2}=\frac{\operatorname{Im}\left\{C_{1}(0)\right\}+\mu_{2} \operatorname{Im}\left\{\lambda^{\prime}\left(\tau_{2 *}\right)\right\}}{\tau_{2 *} \omega_{2 *}}
$$



Figure 2: Waveform plots of system (65) with $\tau_{1}=15.2608<\tau_{10}$.


Figure 3: Continued.


Figure 3: Waveform plots of system (65) with $\tau_{1}=16.3642>\tau_{10}$.


Figure 4: Waveform plots of system (65) with $\tau_{2}=20.3665<\tau_{20}$.

In conclusion, we can obtain the following results based on the fundamental results about Hopf bifurcation in the literature [32].

Theorem 4. For system (2), if $\mu_{2}>0\left(\mu_{2}<0\right)$, then the Hopf bifurcation is supercritical (subcritical); if $\beta_{2}<0\left(\beta_{2}>0\right)$, then the bifurcating periodic solutions are stable (unstable); if


Figure 5: Waveform plots of system (65) with $\tau_{2}=23.9608>\tau_{20}$.


Figure 6: Continued.


Figure 6: Waveform plots of system (65) with $\tau=8.4565<\tau_{0}$.


Figure 7: Waveform plots of system (65) with $\tau=8.7807>\tau_{0}$.


Figure 8: Waveform plots of system (65) with $\tau_{2}=10.2508<\tau_{2 *}$ and $\tau_{1}=7.75 \in\left(0, \tau_{10}\right)$.
$T_{2}>0\left(T_{2}<0\right)$, then the period of the bifurcating periodic solutions increases (decreases).

## 4. Numerical Simulation

In this section, numerical simulations are employed to confirm the efficiency of the theoretical analysis in the present paper. Considering the biological significance of the parameters in system (2), we refer to the range of the parameter values provided in the literature [26]. By extracting some values from the literature [26] and considering the biological significance of the parameters and conditions for the occurrence of Hopf bifurcation, we choose $\Lambda=1, \quad \beta_{1}=0.01, \quad \mu=0.02, \quad \varepsilon=0.1, \quad \delta=0.095$, $\beta_{2}=0.008, \sigma=0.0011$, and $\gamma=0.095$. Then, system (2) turns into

$$
\left\{\begin{array}{l}
\frac{\mathrm{d} S(t)}{\mathrm{d} t}=1-0.01 S(t) I(t)-0.02 S(t), \\
\frac{\mathrm{d} Q(t)}{\mathrm{d} t}=0.1 I\left(t-\tau_{1}\right)+0.095 R\left(t-\tau_{2}\right) \\
-0.02 Q(t)-0.008 Q(t) I(t), \\
\frac{\mathrm{d} I(t)}{\mathrm{d} t}=0.01 S(t) I(t)+0.008 Q(t) I(t)+0.0011 R(t) \\
-0.115 I(t)-0.1 I\left(t-\tau_{1}\right), \\
\frac{\mathrm{d} R(t)}{\mathrm{d} t}=0.095 I(t)-0.0211 R(t)-0.095 R\left(t-\tau_{2}\right) .
\end{array}\right.
$$



Figure 9: Waveform plots of system (65) with $\tau=11.3691>\tau_{2 *}$ and $\tau_{1}=7.75 \in\left(0, \tau_{10}\right)$.

Then, one can obtain $R_{0}=2.3530>1$, and equation (4) becomes the following form:

$$
\begin{equation*}
3.3776 e-007\left(I^{*}\right)^{2}-3.6335 e-006 I^{*}-1.3277 e-005=0 \tag{66}
\end{equation*}
$$

from which one gets the unique positive root $I^{*}=13.6396$. Further, we obtain that system (65) has a unique drug-addiction equilibrium $E^{*}(6.3940,18.7755,13.6396$, 11.1607). By delicate calculation, it is obtained that $\omega_{10}=$ 0.1872 and $\tau_{10}=16.0145 ; \omega_{20}=0.9243$ and $\tau_{20}=21.9566$; $\omega_{0}=2.9207$ and $\tau_{0}=8.6947 ; \quad \omega_{2 *}=1.4648$ and $\tau_{2 *}=10.7568$ when $\tau_{1 *}=7.75 \in\left(0, \tau_{10}\right)$.

By Theorem 1, $E^{*}(6.3940,18.7755,13.6396,11.1607)$ is asymptotically stable for system (65) when $\tau_{1}=$ $15.2608<\tau_{10}$, which is depicted in Figure 2. $E^{*}(6.3940$, $18.7755,13.6396,11.1607$ ) is unstable for system (65) and Hopf bifurcation occurs when $\tau_{1}=16.3642>\tau_{10}$, which are simulated in Figure 3. Similar simulations can be shown as in Figures 4 and 5 for Theorem 2, Figures 6 and 7 for Theorem 3, and Figures 8 and 9 for Theorem 4, respectively.

Whereafter, by some complex calculations, we obtain $C_{1}(0)=-13.0664+9.6207 i$ and $\lambda^{\prime}\left(\tau_{2 *}\right)=1.0081-0.6309 i$. By the results in equation (64), it can be derived that $\mu_{2}=12.9614>0, \beta_{2}=-26.1328<0$, and $T_{2}=-0.0916<0$. It
follows from Theorem 4 that the Hopf bifurcation is supercritical since $\mu_{2}>0$, the bifurcating periodic solutions are stable since $\beta_{2}<0$, and the period of the periodic solutions decreases as $\tau_{2}$ increases since $T_{2}<0$.

## 5. Conclusions

In this paper, a delayed synthetic drug transmission model with relapse and treatment is investigated by incorporating two delays into the model proposed in the literature [26]. We consider not only the time delay due to the period that the drug abusers use to give up drugs through self-control but also the time delay due to the period used to give up drugs through successful treatment. Compared with the model in [26], the delayed synthetic drug transmission model in the present paper is more general because it usually needs a period for the drug abusers to give up drugs through either self-control or successful treatment.

It has been shown that, under certain conditions, the drug-addiction equilibrium is locally asymptotically stable when the value of the time delay is below the critical value. In this case, system (2) is in ideal stable state and the synthetic drug transmission can be controlled easily. However, once the value of the time delay is above the critical value, system
(2) will lose its stability and undergo a Hopf bifurcation at the corresponding critical value of the time delay, which is not welcomed in reality. The occurrence of Hopf bifurcation means that the existence of populations in system (2) changes from the drug-addiction equilibrium to a limit cycle, and in this case, the synthetic drug transmission is out of control. Therefore, it is vital to take some necessary measures to postpone and eliminate the occurrence of the Hopf bifurcation for system (2).

Specially, the direction of the Hopf bifurcation and stability of the bifurcating periodic solutions are determined by employing the center manifold theorem and normal form theory. In addition, according to the numerical simulations, it is easily observed that the time delay due to the period that the drug abusers use to give up drugs through self-control is marked because the critical value of $\tau_{1}$ is much smaller when we only consider it. From this point of view, it is strongly recommended that drug abusers should have strong will in the process of giving up drugs.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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