# Bifurcation Analysis for a Physiological Control System with Delay 

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Abstract-In this paper, a delayed physiological control system is investigated. The sufficient conditions for stability of positive equilibrium and existence of local Hopf bifurcation are derived. Furthermore, global existence of periodic solutions is established by using the global Hopf bifurcation theory. Finally, numerical examples are given to support the theoretical analysis.

Keywords-Physiological control system; global Hopf bifurcation; periodic solutions.

## I. Introduction

IN order to describe some physiological control systems, Mackey and Glass proposed the following three first order nonlinear delay differential equations as their appropriate models in [1]:

$$
\begin{align*}
\frac{d N(t)}{d t} & =\lambda-\frac{\alpha V_{m} N(t) N^{k}(t-\tau)}{\theta^{k}+N^{k}(t-\tau)}  \tag{1}\\
\frac{d N(t)}{d t} & =\frac{V_{m} \theta^{k}}{\theta^{k}+N^{k}(t-\tau)}-\delta N(t)  \tag{2}\\
\frac{d N(t)}{d t} & =\frac{V_{m} \theta^{k} N(t-\tau)}{\theta^{k}+N^{k}(t-\tau)}-\delta N(t) \tag{3}
\end{align*}
$$

Here, all the coefficients are positive constants. Details for the derivation of these equations can be found in [1]. Subsequently, many results from various angles have been obtained, such as the main theorems in [2-5]. Local and global Hopf bifurcations for system (1) and (2) were studied by regarding $\tau$ as the bifurcation parameter in [2-3]. For system (3), boundedness of solutions and global stability of positive equilibrium were considered. Besides, existences of periodic and chaotic solutions were derived by regarding $\tau$ and $k$ as bifurcation parameters in [1] and [5], respectively.

The aim of this paper is to investigate the stability of positive equilibrium and existences of local and global Hopf bifurcation for system (3) with the help of bifurcation theory [6-7]. Detailed mathematical analysis and numerical examples will be given.

## II. Stability of positive equilibrium

Obviously, system (3) has the unique positive equilibrium $N_{*}$ when $V_{m}>\delta$. The linear part of system (3) at $N_{*}$ is

$$
\dot{N}(t)=\delta\left(1+\frac{k \delta}{V_{m}}-k\right) N(t-\tau)-\delta N(t)
$$

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then the characteristic equation is

$$
\begin{equation*}
\lambda+\delta+\delta\left(k-1-\frac{k \delta}{V_{m}}\right) e^{-\lambda \tau}=0 \tag{4}
\end{equation*}
$$

When $\tau=0$, we have $\lambda=k \delta\left(\frac{\delta}{V_{m}}-1\right)<0$. Next, we will discuss the distribution of characteristic roots when $\tau>0$. Let $\lambda=i \omega(\omega>0)$ be a root of equation (4), then

$$
i \omega=-\delta+\delta\left(1+\frac{k \delta}{V_{m}}-k\right)(\cos \omega \tau-i \sin \omega \tau)
$$

Separating the real and imaginary parts, we have

$$
\left\{\begin{array}{l}
\delta=\delta\left(1+\frac{k \delta}{V_{m}}-k\right) \cos \omega \tau \\
\omega=-\delta\left(1+\frac{k \delta}{V_{m}}-k\right) \sin \omega \tau
\end{array}\right.
$$

and

$$
\omega^{2}=\delta^{2}\left(1+\frac{k \delta}{V_{m}}-k\right)^{2}-\delta^{2}
$$

Thus, equation (4) has a pair of purely imaginary roots $\pm i \omega_{0}$ when $k\left(1-\frac{\delta}{V_{m}}\right)>2$, where

$$
\omega_{0}=\delta \sqrt{k\left(\frac{\delta}{V_{m}}-1\right)\left(2+\frac{k \delta}{V_{m}}-k\right)}
$$

Denote

$$
\tau_{j}=\frac{1}{\omega_{0}}\left[\arccos \frac{1}{1+\frac{k \delta}{V_{m}}-k}+2 j \pi\right], j=0,1,2 \ldots
$$

Differentiating both sides of (4) with respect to $\tau$, we can get

$$
\frac{d \lambda}{d \tau}=\frac{\delta\left(k-1-\frac{k \delta}{V_{m}}\right) \lambda}{e^{\lambda \tau}-\delta\left(k-1-\frac{k \delta}{V_{m}}\right) \tau}
$$

Hence,

$$
\left.\operatorname{Re}\left\{\frac{d \lambda}{d \tau}\right\}\right|_{\lambda=i \omega_{0}, \tau=\tau_{j}}=\frac{\omega_{0}^{2}}{A^{2}+\sin ^{2} \omega_{0} \tau_{j}}>0
$$

where $A=\cos \omega_{0} \tau_{j}-\delta\left(k-1-\frac{k \delta}{V_{m}}\right) \tau_{j}$.
According to the Corollary 2.4 in [7], the sum of the orders of zeros on the open right half plane can change only if a zero appears on or crosses the imaginary axis. We can conclude the following lemma.
Lemma 1 (i) If $k\left(1-\frac{\delta}{V_{m}}\right) \leq 2$, then all roots of (4) have strictly negative real parts.
(ii) If $k\left(1-\frac{\delta}{V_{m}}\right)>2$, then all roots of (4) have strictly
negative real parts only when $\tau \in\left[0, \tau_{0}\right)$; equation (4) has a pair of purely imaginary roots when $\tau=\tau_{0}$; equation (4) has $2(j+1)$ roots with positive real parts when $\tau \in\left(\tau_{j}, \tau_{j+1}\right]$.
Moreover, we can establish the stability of positive equilibrium of system (3) from the Hopf bifurcation theorem in [7].
Theorem 1 (i) If $V_{m}>\delta$ and $k\left(1-\frac{\delta}{V_{m}}\right) \leq 2$, then $N_{*}$ is absolutely stable.
(ii) If $V_{m}>\delta$ and $k\left(1-\frac{\delta}{V_{m}}\right)>2$, then $N_{*}$ is asymptotically stable when $\tau \in\left[0, \tau_{0}\right)$ and unstable when $\tau>\tau_{0}$.
(iii) $\tau=\tau_{j}(j=0,1,2, \ldots)$ are the critical values and Hopf bifurcation occurs.

## III. Global existence of Hopf bifurcation

In this section, we mainly focus on the global existence of periodic solutions bifurcating from positive equilibrium. Throughout this section, we closely follow the notation in [6] and define

$$
X=C([-\tau, 0], \mathbf{R})
$$

$\Sigma=C l\{(x, \tau, p): x$ is $p$-periodic solution of system (3) $\} \subset X \times \mathbf{R}_{+} \times \mathbf{R}_{+}$,

$$
\begin{aligned}
& N=\left\{(\hat{x}, \tau, p): V_{m} \theta^{k}-\delta \theta^{k}-\delta \hat{x}^{k}=0\right\}, \\
& \Delta=\lambda+\delta+\delta\left(k-1-\frac{k \delta}{V_{m}}\right) e^{-\lambda \tau} .
\end{aligned}
$$

Let $C\left(N_{*}, \tau_{j}, \frac{2 \pi}{\omega_{0}}\right)$ denote the connected component of $\left(N_{*}, \tau_{j}, \frac{2 \pi}{\omega_{0}}\right)$ in $\Sigma$. By the Lemma 3 in [4], we have the following lemma.
Lemma 2 If $\frac{k \delta}{k-1}<V_{m} \theta<\delta \frac{k+1}{k-1}$, then all the periodic solutions of (3) are uniformly bounded.
Lemma 3 System (3) has no nontrivial $\tau$ - periodic solutions when $k$ is a positive integer.
Proof The nontrivial $\tau$-periodic solution of system (3) is also the nonconstant periodic solution of the following ordinary differential equation,

$$
\begin{equation*}
\dot{N}(t)=N(t)\left(\frac{V_{m} \theta^{k}}{\theta^{k}+N^{k}(t)}-\delta\right) \tag{5}
\end{equation*}
$$

On one hand, when $N(t)>0$, we have $\dot{N}(t)<0$ with $N(t)>$ $N_{*}$ and $\dot{N}(t)>0$ with $N(t)<N_{*}$. On the other hand, when $N(t)<0$, we can obtain that $\dot{N}(t)$ is definitely positive or definitely negative when $k$ is an integer. Therefore, system (5) has no nonconstant periodic solution. This completes the proof.
Theorem 2 If $V_{m}>\delta k\left(1-\frac{\delta}{V_{m}}\right)>2, \frac{k \delta}{k-1}<V_{m} \theta<$ $\delta \frac{k+1}{k-1}$ and $k$ is a positive integer, then periodic solutions of system (3) still exist when $\tau>\tau_{j}$.
Proof First of all, define $F\left(x^{t}, \tau, p\right)=\frac{V_{m} \theta^{k} N(t-\tau)}{\theta^{k}+N^{k}(t-\tau)}-\delta N(t)$. The assumptions $\left(A_{1}\right)-\left(A_{3}\right)$ in [8] hold. Let $\left(\hat{x}_{0}, \alpha_{0}, p\right)=$ $\left(N_{*}, \tau_{j}, \frac{2 \pi}{\omega_{0}}\right)$ and it is easy to verify that $\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right)$ is the only isolated center. There exist $\varepsilon>0, \delta>0$ and a smooth function $\lambda:\left(\tau_{j}-\delta, \tau_{j}+\delta\right) \rightarrow \mathbf{C}$, such that

$$
\Delta(\lambda(\tau))=0, \quad\left|\lambda(\tau)-i \omega_{0}\right|<\varepsilon
$$

for any $\tau \in\left[\tau_{j}-\delta, \tau_{j}+\delta\right]$, and

$$
\lambda\left(\tau_{j}\right)=i \omega_{0}, \quad \frac{d \operatorname{Re}(\lambda(\tau))}{d \tau}>0
$$

Define $p_{j}=2 \pi / \omega_{0}$ and $\Omega_{\varepsilon, p_{j}}=\{(0, p): 0<u<\varepsilon, \mid p-$ $\left.p_{j} \mid<\varepsilon\right\}$. Obviously, if $\left|\tau-\tau_{j}\right| \leq \delta$ and $(u, p) \in \partial \Omega_{\varepsilon}$, then $\Delta_{\left(N_{*}, \tau, p\right)}(u+2 \pi i / p)=0$ if and only if $\tau=\tau_{j}, u=0$, $p=p_{j}$. Thus the assumptions $\left(A_{4}\right)$ in [8] holds.

Putting

$$
H^{ \pm}\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right)(u, p)=\Delta_{\left(N_{*}, \tau_{j} \pm \delta, p\right)}(u+i 2 \pi / p)
$$

then we can calculate the crossing number as follows

$$
\begin{aligned}
\gamma\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right)= & \operatorname{deg}_{B}\left(H^{-}\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right), \Omega_{\varepsilon, p_{j}}\right) \\
& -\operatorname{deg}_{B}\left(H^{+}\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right), \Omega_{\varepsilon, p_{j}}\right) \\
= & -1
\end{aligned}
$$

By Lemma 2, the projection of $C\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right)$ onto the $x$-space is bounded. When $j>0$, we have $0<$ $2 \pi / \omega_{0}<\tau_{j}$. Thus, the projection of $C\left(N^{*}, \tau_{j}, 2 \pi / \omega_{0}\right)$ onto the $p$-space is bounded. Lemma 3 reveals that the projection of $C\left(N_{*}, \tau_{j}, 2 \pi / \omega_{0}\right)$ onto $\tau$-space must be positive and has no upperbound. As a result, system (3) still has nontrivial periodic solutions when $\tau>\tau_{j}$.

## IV. Numerical simulation

Consider the following system

$$
\begin{equation*}
\frac{d N(t)}{d t}=\frac{4 \cdot 0.45^{3} N(t-\tau)}{0.45^{3}+N^{3}(t-\tau)}-N(t) \tag{6}
\end{equation*}
$$

system (6) has the unique positive equilibrium $N_{*}=0.6490$. By direct computation, we can get $\omega_{0}=0.75, \tau_{0}=3.3308$, $\tau_{1}=11.7084, \tau_{2}=20.0859, \tau_{3}=28.4635, \tau_{4}=36.8411 \cdots$. The equilibrium is stable when $\tau$ is small as shown in Fig.1. and periodic solution exists when $\tau$ passes through the first critical value $\tau_{0}$ as shown in Fig.2. When $\tau$ is sufficiently large, periodic solutions still exist as shown in Fig.3-4.


Fig. 1. Numerical solutions of system (6) with $\tau=2.5$.


Fig. 2. Numerical solutions of system (6) with $\tau=4$.


Fig. 3. Numerical solutions of system (6) with $\tau=12$.


Fig. 4. Numerical solutions of system (6) with $\tau=38$.

## V. Conclusions

In this paper, existences of local and global Hopf bifurcations for a physiological control system are established. When the time delay $\tau$ varies, the positive equilibrium loses its stability and Hopf bifurcation occurs at that equilibrium. The results show the existence of periodic solutions for $\tau$ far away from the local Hopf bifurcation values.

Thus, the bifurcating periodic solutions of three delayed models proposed by Mackey and Glass all have been investigated.

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