# Global Hopf bifurcation for differential-algebraic equations with state dependent delay 

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#### Abstract

We develop a global Hopf bifurcation theory for differential equations with a state-dependent delay governed by an algebraic equation, using the $S^{1}$-equivariant degree. We apply the global Hopf bifurcation theory to a model of genetic regulatory dynamics with threshold type state-dependent delay vanishing at the stationary state, for a description of the global continuation of the periodic oscillations.


Key words: state-dependent delay, Hopf bifurcation, differential-algebraic equations, $S^{1}$-equivariant degree, regulatory dynamics

## 1 Introduction

Consider the following system of differential-algebraic equations (DAEs) with statedependent delay,

$$
\left\{\begin{array}{l}
\dot{x}(t)=f(x(t), x(t-\tau), \sigma),  \tag{1.1}\\
\tau(t)=g(x(t), x(t-\tau), \sigma),
\end{array}\right.
$$

where $f: \mathbb{R}^{N} \times \mathbb{R}^{N} \times \mathbb{R} \rightarrow \mathbb{R}^{N}$ and $g: \mathbb{R}^{N} \times \mathbb{R}^{N} \times \mathbb{R} \rightarrow \mathbb{R}$ are continuously differentiable with $f(0,0, \sigma)=0$ and $\sigma \in \mathbb{R}$. The state-dependent delay of system (1.1) arises in several applications. To mention a few, in the model of turning processes [7], the delay $\tau$ is the time duration for one around of cutting; In the echo control model [16], the state-dependent delay is the echo traveling time between the object's positions when $\star$

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the sound is emitted and received. See [4] for a review. To model diffusion processes in genetic regulatory dynamics with time delay, we considered in [5] the following system:

$$
\left\{\begin{align*}
\frac{\mathrm{d} x(t)}{\mathrm{d} t} & =-\mu_{m} x(t)+f_{0}(y(t-\tau))  \tag{1.2}\\
\frac{\mathrm{d} y(t)}{\mathrm{d} t} & =-\mu_{p} y(t)+g_{0}(x(t-\tau)) \\
\tau(t) & =\epsilon_{0}+c(x(t)-x(t-\tau))
\end{align*}\right.
$$

where $f_{0}, g_{0}: \mathbb{R} \rightarrow \mathbb{R}$ are three times continuously differentiable functions; $\mu_{m}, \mu_{p}, c$ and $\epsilon_{0}$ are positive constants. The time delay $\tau(t)=\epsilon_{0}+c(x(t)-x(t-\tau))$ models the homogenization time of the substances produced in the regulatory processes. Since the equation for $\tau$ can be written as

$$
\begin{equation*}
\int_{t-\tau(t)}^{t} \frac{1-c \dot{x}(s)}{\epsilon_{0}} \mathrm{~d} s=1 \tag{1.3}
\end{equation*}
$$

we call $\tau$ a threshold type state-dependent delay and we have shown in [5 that using the time transformation $t \mapsto \int_{0}^{t}(1-c \dot{x}(s)) \mathrm{d} s$ system (1.2) can be transformed into a system with constant delay and distributed delay under certain conditions. In such a case, the theory we developed in [1] is applicable to system (1.2) for a local and global Hopf bifurcation theory. However, if $\epsilon_{0}=0$ in (1.2) and the integral equation for $\tau$ becomes

$$
\begin{equation*}
\int_{t-\tau(t)}^{t}(1-c \dot{x}(s)) \mathrm{d} s=0 \tag{1.4}
\end{equation*}
$$

which cannot be employed to remove the state-dependent delay using the time transformation $t \mapsto \int_{0}^{t}(1-c \dot{x}(s)) \mathrm{d} s$. Thus the global Hopf bifurcation theory developed in [1] is no longer applicable. We remark that if we obtain a differential equation of $\tau$ from $\tau(t)=\epsilon_{0}+c(x(t)-x(t-\tau))$, the resulting system will have a foliation of equilibrium and at least one zero eigenvalue. The global Hopf bifurcation theory developed in [6] is not applicable either. With these facts, we are motivated to develop a global Hopf bifurcation theory for system (1.1) and apply it to an extended three dimensional Goodwin's model with state-dependent delay where the delay vanishes at equilibrium. (See system (4.1) at Section 4 for a quick note.)

We organize the remaining part of the paper as following: Using the framework for a Hopf bifurcation theory established in [6], we develop a local Hopf bifurcation theory for system (1.1) in Section 2, and develop a global Hopf bifurcation theory in Section 3. In Section 4 we apply the developed local and global Hopf bifurcation to the prototype system (1.2) with $\epsilon_{0}=0$. We conclude the discussion by Section (5.

## 2 Local Hopf Bifurcation for DAEs with State-dependent Delay

We begin with definitions of notations. Denote by $C\left(\mathbb{R} ; \mathbb{R}^{N}\right)$ the normed space of continuous functions from $\mathbb{R}$ to $\mathbb{R}^{N}$ equipped with the usual supremum norm $\|x\|=$ $\sup _{t \in \mathbb{R}}|x(t)|$ for $x \in C\left(\mathbb{R} ; \mathbb{R}^{N}\right)$, where $|\cdot|$ denotes the Euclidean norm. We also denote by $C^{1}\left(\mathbb{R} ; \mathbb{R}^{N}\right)$ the normed space of continuously differentiable bounded functions from $\mathbb{R}$ to $\mathbb{R}^{N}$ equipped with the usual $C^{1}$ norm

$$
\|x\|_{C^{1}}=\max \left\{\sup _{t \in \mathbb{R}}|x(t)|, \sup _{t \in \mathbb{R}}|\dot{x}(t)|\right\}
$$

for $x \in C\left(\mathbb{R} ; \mathbb{R}^{N}\right)$. We denote by $V=C_{2 \pi}\left(\mathbb{R} ; \mathbb{R}^{N}\right)$ the space of $2 \pi$-periodic continuous functions from $\mathbb{R}$ to $\mathbb{R}^{N}$ equipped with the supremum norm. We denote by $C_{2 \pi}^{1}\left(\mathbb{R} ; \mathbb{R}^{N}\right)$ the Banach space of $2 \pi$-periodic and continuously differentiable functions equipped with the $C^{1}$ norm.

We write $\partial_{i} f=\frac{\partial}{\partial \theta_{i}} f$ for $i=1,2$, and similarly we define $\partial_{i} g$ for $i=1,2$. We assume that
(S1) The map $f: \mathbb{R}^{N} \times \mathbb{R}^{N} \times \mathbb{R} \ni\left(\theta_{1}, \theta_{2}, \sigma\right) \rightarrow f\left(\theta_{1}, \theta_{2}, \sigma\right) \in \mathbb{R}^{N}$ is $C^{2}$ (twice continuously differentiable).
(S2) The map $g: \mathbb{R}^{N} \times \mathbb{R}^{N} \times \mathbb{R} \ni\left(\gamma_{1}, \gamma_{2}, \sigma\right) \rightarrow g\left(\gamma_{1}, \gamma_{2}, \sigma\right) \in \mathbb{R}$ is continuous.
We assume that for a fixed $\sigma_{0} \in \mathbb{R},\left(x_{\sigma_{0}}, \tau_{\sigma_{0}}\right)$ (or, for simplifcity, $\left(x_{\sigma_{0}}, \tau_{\sigma_{0}}, \sigma_{0}\right)$ ) is a stationary state of (1.1). That is,

$$
f\left(x_{\sigma_{0}}, x_{\sigma_{0}}, \sigma_{0}\right)=0, \quad g\left(x_{\sigma_{0}}, x_{\sigma_{0}}, \sigma_{0}\right)=\tau_{\sigma_{0}}
$$

We also assume that

$$
\begin{equation*}
\left.\left(\frac{\partial}{\partial \theta_{1}}+\frac{\partial}{\partial \theta_{2}}\right) f\left(\theta_{1}, \theta_{2}, \sigma\right)\right|_{\sigma=\sigma_{0}, \theta_{1}=\theta_{2}=x_{\sigma_{0}}} \text { is nonsingular, } \tag{S3}
\end{equation*}
$$

which implies that there exists $\epsilon_{0}>0$ and a $C^{1}$-smooth curve $\left(\sigma_{0}-\epsilon_{0}, \sigma_{0}+\epsilon_{0}\right) \ni \sigma \mapsto$ $\left(x_{\sigma}, \tau_{\sigma}\right) \in \mathbb{R}^{N+1}$ such that $\left(x_{\sigma}, \tau_{\sigma}\right)$ is the unique stationary state of (1.1) in a small neighborhood of ( $x_{\sigma_{0}}, \tau_{\sigma_{0}}$ ) for $\sigma$ close to $\sigma_{0}$.

We wish to drop the part of the algebraic equation in (1.1) for the application of $S^{1}$-equivariant degree and show that
Lemma 2.1 Assume that (S2) holds. For every $(x, \sigma) \in C\left(\mathbb{R} ; \mathbb{R}^{N}\right) \times \mathbb{R}$, where $x$ is periodic, there exists $\tau \in C(\mathbb{R} ; \mathbb{R})$ such that $\tau(t)=g(x(t), x(t-\tau(t)), \sigma)$.

Proof Fix an arbitrary $t \in \mathbb{R}$ and let $a=\tau(t)$. Consider the graphs of $h=a$ and $h=g(x(t), x(t-a), \sigma)$ in the $h-a$ plane. The graphs must have an intersection since $x \in C\left(\mathbb{R} ; \mathbb{R}^{N}\right)$ is periodic and $h=g(x(t), x(t-a), \sigma)$ is continuous and bounded with respect to $a$. By the implicit function theorem, the solution of $a=g(x(t), x(t-a), \sigma)$ for $a$ is continuous with respect to $(t, \sigma)$.

In light of Lemma 2.1, we assume in the following that if $x \in C\left(\mathbb{R} ; \mathbb{R}^{N}\right)$ is periodic, we choose $\tau \in C(\mathbb{R} ; \mathbb{R})$ such that $\tau(t)=g(x(t), x(t-\tau(t)), \sigma), t \in \mathbb{R}$ and call $x$ a solution if the chosen $(x, \tau)$ satisfies system (1.1).

For a stationary state $x_{0}$ of system (1.1) with the parameter $\sigma_{0}$, we say that $\left(x_{0}, \sigma_{0}\right)$ is a Hopf bifurcation point of system (1.1), if there exist a sequence $\left\{\left(x_{k}, \sigma_{k}, T_{k}\right)\right\}_{k=1}^{+\infty} \subseteq$ $C\left(\mathbb{R} ; \mathbb{R}^{N}\right) \times \mathbb{R}^{2}$ and $T_{0}>0$ such that

$$
\lim _{k \rightarrow+\infty}\left\|\left(x_{k}, \sigma_{k}, T_{k}\right)-\left(x_{0}, \sigma_{0}, T_{0}\right)\right\|_{C\left(\mathbb{R} ; \mathbb{R}^{N}\right) \times \mathbb{R}^{2}}=0
$$

and $\left(x_{k}, \sigma_{k}\right)$ is a nonconstant $T_{k}$-periodic solution of system (1.1).
Due to the nature of the same approach of using the $S^{1}$-equivariant degree, the presentation of the remaining part of this section is similar to that of [6], even though the systems in question are different. We study Hopf bifurcation of (1.1) through the formal linearization [2] obtained from its part of the differential equations. Namely, we freeze the state-dependent delay in system (1.1) at its stationary state and linearize the resulting differential equation of $x$ with constant delay at the stationary state. For $\sigma \in\left(\sigma_{0}-\epsilon_{0}, \sigma_{0}+\epsilon_{0}\right)$, the following formal linearization of system (1.1) at the stationary point $x_{\sigma}$ :

$$
\begin{equation*}
\dot{x}(t)=\partial_{1} f(\sigma)\left(x(t)-x_{\sigma}\right)+\partial_{2} f(\sigma)\left(x\left(t-\tau_{\sigma}\right)-x_{\sigma}\right), \tag{2.1}
\end{equation*}
$$

where

$$
\partial_{1} f(\sigma):=\partial_{1} f\left(x_{\sigma}, \tau_{\sigma}, \sigma\right), \partial_{2} f(\sigma):=\partial_{2} f\left(x_{\sigma}, \tau_{\sigma}, \sigma\right), \tau_{\sigma}=g\left(x_{\sigma}, x_{\sigma}, \sigma\right)
$$

Letting $x(t)=e^{\omega t} . C+x_{\sigma}$ with $C \in \mathbb{R}^{N}$, we obtain the following characteristic equation of the linear system corresponding to the inhomogeneous linear system (2.1),

$$
\begin{equation*}
\operatorname{det} \Delta_{\left(x_{\sigma}, \sigma\right)}(\omega)=0 \tag{2.2}
\end{equation*}
$$

where $\Delta_{\left(x_{\sigma}, \sigma\right)}(\omega)$ is an $N \times N$ complex matrix defined by

$$
\begin{equation*}
\Delta_{\left(x_{\sigma}, \sigma\right)}(\omega)=\omega I-\partial_{1} f(\sigma)-\partial_{2} f(\sigma) e^{-\omega \tau_{\sigma}} . \tag{2.3}
\end{equation*}
$$

A solution $\omega_{0}$ to the characteristic equation (2.2) is called a characteristic value of the stationary state $\left(x_{\sigma_{0}}, \sigma_{0}\right)$. If zero is not a characteristic value of $\left(x_{\sigma_{0}}, \sigma_{0}\right),\left(x_{\sigma_{0}}, \sigma_{0}\right)$ is said to be a nonsingular stationary state. We say that $\left(x_{\sigma_{0}}, \sigma_{0}\right)$ is a center if the set of nonzero purely imaginary characteristic values of $\left(x_{\sigma_{0}}, \sigma_{0}\right)$ is nonempty and discrete. $\left(x_{\sigma_{0}}, \sigma_{0}\right)$ is called an isolated center if it is the only center in some neighborhood of $\left(x_{\sigma_{0}}, \sigma_{0}\right)$ in $\mathbb{R}^{N} \times \mathbb{R}$.

If $\left(x_{\sigma_{0}}, \sigma_{0}\right)$ is an isolated center of (2.1), then there exist $\beta_{0}>0$ and $\delta \in\left(0, \epsilon_{0}\right)$ such that

$$
\operatorname{det} \Delta_{\left(x_{\sigma_{0}}, \sigma_{0}\right)}\left(i \beta_{0}\right)=0
$$

and

$$
\begin{equation*}
\operatorname{det} \Delta_{\left(x_{\sigma}, \sigma\right)}(i \beta) \neq 0 \tag{2.4}
\end{equation*}
$$

for any $\sigma \in\left(\sigma_{0}-\delta, \sigma_{0}+\delta\right)$ and any $\beta \in(0,+\infty) \backslash\left\{\beta_{0}\right\}$. Hence, we can choose constants $\alpha_{0}=\alpha_{0}\left(\sigma_{0}, \beta_{0}\right)>0$ and $\varepsilon=\varepsilon\left(\sigma_{0}, \beta_{0}\right)>0$ such that the closure of the set $\Omega:=\left(0, \alpha_{0}\right) \times\left(\beta_{0}-\varepsilon, \beta_{0}+\varepsilon\right) \subset \mathbb{R}^{2} \cong \mathbb{C}$ contains no other zero of $\operatorname{det} \Delta_{\left(x_{\sigma_{0}}, \sigma_{0}\right)}(\cdot)$ in $\partial \Omega$. We note that $\operatorname{det} \Delta_{\left(x_{\sigma}, \sigma\right)}(\omega)$ is analytic in $\omega$ and is continuous in $\sigma$. If $\delta>0$ is small enough, then there is no zero of $\operatorname{det} \Delta_{\left(x_{\sigma_{0} \pm \delta}, \sigma_{0} \pm \delta\right)}(\omega)$ in $\partial \Omega$. So we can define the number

$$
\gamma_{ \pm}\left(x_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)=\operatorname{deg}_{B}\left(\operatorname{det} \Delta_{\left(x_{\sigma_{0} \pm \delta}, \sigma_{0} \pm \delta\right)}(\cdot), \Omega\right)
$$

and the crossing number of $\left(x_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)$ as

$$
\begin{equation*}
\gamma\left(x_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)=\gamma_{-}-\gamma_{+} \tag{2.5}
\end{equation*}
$$

where $\operatorname{deg}_{B}$ is the Brouwer degree in finite-dimensional spaces. See, e.g., 8], for details. To formulate the Hopf bifurcation problem as a fixed point problem in the space of continuous functions of period $2 \pi$, we normalize the period of the $2 \pi / \beta$-periodic solution $x$ of (1.1) and the associated $\tau \in C(\mathbb{R} ; \mathbb{R})$ by setting $(x(t), \tau(t))=(y(\beta t), z(\beta t))$ and obtain

$$
\begin{equation*}
\binom{\dot{y}(t)}{z(t)}=\binom{\frac{1}{\beta} f(y(t), y(t-\beta z(t)), \sigma)}{g(y(t), y(t-\beta z(t)), \sigma)} . \tag{2.6}
\end{equation*}
$$

Define $N_{0}: V \ni(y, \sigma, \beta) \times \mathbb{R}^{2} \rightarrow N_{0}(y, \sigma, \beta) \in V$ by

$$
\begin{equation*}
N_{0}(y, \sigma, \beta)(t)=f(y(t), y(t-\beta z(t)), \sigma) \tag{2.7}
\end{equation*}
$$

Then the part of differential equations of system (2.6) is rewritten as

$$
\begin{equation*}
\dot{y}(t)=\frac{1}{\beta} N_{0}(y, \sigma, \beta)(t) . \tag{2.8}
\end{equation*}
$$

Correspondingly, (2.1) is transformed into

$$
\begin{equation*}
\dot{y}(t)=\frac{1}{\beta} \tilde{N}_{0}(y, \sigma, \beta)(t) \tag{2.9}
\end{equation*}
$$

where $\tilde{N}_{0}: V \ni(y, \sigma, \beta) \times \mathbb{R}^{2} \rightarrow \tilde{N}_{0}(y, \sigma, \beta) \in V$ is defined by

$$
\tilde{N}_{0}(y, \sigma, \beta)(t)=\partial_{1} f(\sigma)\left(y(t)-y_{\sigma}\right)+\partial_{2} f(\sigma)\left(y\left(t-\beta z_{\sigma}\right)-y_{\sigma}\right)
$$

with $\left(y_{\sigma}, z_{\sigma}\right)=\left(x_{\sigma}, \tau_{\sigma}\right)$. We note that $y$ is $2 \pi$-periodic if and only if $x$ is $(2 \pi / \beta)$ periodic.

Let $K: V \rightarrow \mathbb{R}^{N}$ be defined by

$$
\begin{equation*}
K(y)=\frac{1}{2 \pi} \int_{0}^{2 \pi} y(t) \mathrm{d} t \tag{2.10}
\end{equation*}
$$

Define the map $\tilde{\mathcal{F}}: V \times \mathbb{R}^{2} \rightarrow V$ by

$$
\begin{equation*}
\tilde{\mathcal{F}}(y, \sigma, \beta):=y-\left(L_{0}+K\right)^{-1}\left[\frac{1}{\beta} \tilde{N}_{0}(y, \sigma, \beta)+K(y)\right] . \tag{2.11}
\end{equation*}
$$

We call the set defined by

$$
B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)=\left\{(y, \sigma, \beta):\left\|y-y_{\sigma}\right\|<r,\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|<\rho\right\},
$$

a special neighborhood of $\widetilde{\mathcal{F}}$, if it satisfies
i) $\tilde{\mathcal{F}}(y, \sigma, \beta) \neq 0$ for every $(y, \sigma, \beta) \in \overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)}$ with $\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|=$ $\rho$ and $\left\|y-y_{\sigma}\right\| \neq 0$;
ii) $\left(y_{0}, \sigma_{0}, \beta_{0}\right)$ is the only isolated center in $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)}$.

Before we state and prove our local Hopf bifurcation theorem, we cite some technical Lemmas from [6] with necessary notational adaptions.
Lemma 2.2 ( [6] ) Let $L_{0}: C_{2 \pi}^{1}\left(\mathbb{R} ; \mathbb{R}^{N}\right) \rightarrow V$ be defined by $L_{0} y(t)=\dot{y}(t), t \in \mathbb{R}$ and let $K: V \rightarrow \mathbb{R}^{N}$ be defined at (2.10). Then $L_{0}+K$ has a compact inverse $\left(L_{0}+K\right)^{-1}: V \rightarrow V$.
Lemma 2.3 ( [6] ) For any $\sigma \in \mathbb{R}$ and $\beta>0$, the map $N_{0}(\cdot, \sigma, \beta): V \rightarrow V$ defined by (2.8) is continuous.
Lemma 2.4 ( [6] ) If system (2.1) has a nonconstant periodic solution with period $T>0$, then there exists an integer $m \geq 1, m \in \mathbb{N}$ such that $\pm i m 2 \pi / T$ are characteristic values of the stationary state $\left(x_{\sigma}, \tau_{\sigma}, \sigma\right)$.

For the purpose of establishing the $S^{1}$-degree on some special neighborhood near the stationary state, we have
Lemma 2.5 Assume (S1)-(S3) hold. Let $L_{0}$ and $K$ be as in Lemma 2.2 and $\tilde{N}_{0}: V \times$ $\mathbb{R}^{2} \rightarrow V$ be as in (2.9). Let $\tilde{\mathcal{F}}: V \times \mathbb{R}^{2} \rightarrow V$ be defined at (2.11). If $B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)$ is a special neighborhood of $\widetilde{\mathcal{F}}$ with $0<\rho<\beta_{0}$, then there exist $r^{\prime} \in(0, r]$ such that the neighborhood

$$
B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)=\left\{(u, \sigma, \beta):\left\|y-y_{\sigma}\right\|<r^{\prime},\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|<\rho\right\}
$$

satisfies

$$
\dot{y}(t) \not \equiv \frac{1}{\beta} f(y(t), y(t-\beta z(t)), \sigma)
$$

for $(y, \sigma, \beta) \in \overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$ with $y \neq y_{\sigma}$ and $\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho$.

Proof. We prove by contradiction. Suppose the statement is not true, then for any
$0<r^{\prime} \leq r$, there exists $(y, \sigma, \beta)$ such that $0<\left\|y-y_{\sigma}\right\|<r^{\prime},\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho$ and

$$
\begin{equation*}
\dot{y}(t)=\frac{1}{\beta} f(y(t), y(t-\beta z(t)), \sigma) \text { for } t \in \mathbb{R} . \tag{2.12}
\end{equation*}
$$

Then there exists a sequence of nonconstant periodic solutions $\left\{\left(y_{k}, \sigma_{k}, \beta_{k}\right)\right\}_{k=1}^{\infty}$ of (2.12) such that

$$
\begin{equation*}
\lim _{k \rightarrow+\infty}\left\|y_{k}-y_{\sigma_{k}}\right\|=0,\left|\left(\sigma_{k}, \beta_{k}\right)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho \tag{2.13}
\end{equation*}
$$

and

$$
\begin{equation*}
\dot{y}_{k}(t)=\frac{1}{\beta_{k}} f\left(y_{k}(t), y_{k}\left(t-\beta_{k} z_{k}(t)\right), \sigma_{k}\right) \text { for } t \in \mathbb{R} \tag{2.14}
\end{equation*}
$$

where $z_{k}$ is chosen according to $y_{k}$ in light of Lemma [2.1]so that $\left(y_{k}, z_{k}\right)$ is a solution of system (2.6).

Note that $0<\rho<\beta_{0}$ implies that $\beta_{k} \geq \beta_{0}-\rho>0$ for every $k \in \mathbb{N}$. Also, since the sequence $\left\{\sigma_{k}, \beta_{k}\right\}_{k=1}^{\infty}$ belongs to a bounded neighborhood of $\left(\sigma_{0}, \beta_{0}\right)$ in $\mathbb{R}^{2}$, there exists a convergent subsequence, still denoted by $\left\{\left(\sigma_{k}, \beta_{k}\right)\right\}_{k=1}^{\infty}$ for notational simplicity, that converges to $\left(\sigma^{*}, \beta^{*}\right)$ so that $\left|\left(\sigma^{*}, \beta^{*}\right)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho$ and $\beta^{*}>0$. Then we have

$$
\begin{equation*}
\lim _{k \rightarrow+\infty}\left\|y_{k}-y_{\sigma_{k}}\right\|=0, \lim _{k \rightarrow+\infty}\left|\left(\sigma_{k}, \beta_{k}\right)-\left(\sigma^{*}, \beta^{*}\right)\right|=0 \tag{2.15}
\end{equation*}
$$

and

$$
\begin{equation*}
\dot{y}_{k}(t)=\frac{1}{\beta_{k}} f\left(y_{k}(t), y_{k}\left(t-\beta_{k} z_{k}(t)\right), \sigma_{k}\right) \text { for } t \in \mathbb{R} . \tag{2.16}
\end{equation*}
$$

In the following we show that the system

$$
\begin{equation*}
\dot{v}(t)=\frac{1}{\beta^{*}} \partial_{1} f\left(\sigma^{*}\right) v(t)+\frac{1}{\beta^{*}} \partial_{2} f\left(\sigma^{*}\right) v\left(t-\beta^{*} z_{\sigma^{*}}\right) \tag{2.17}
\end{equation*}
$$

has a nonconstant periodic solution which contradicts the assumption that ( $y_{\sigma_{0}}, \sigma_{0}, \beta_{0}$ ) is the only center of $\left(\sqrt{2.9)}\right.$ in $\overline{B_{M}\left(u_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)}$.
$\operatorname{By}(\mathrm{S} 1), f: \mathbb{R}^{N} \times \mathbb{R}^{N} \times \mathbb{R} \ni\left(\theta_{1}, \theta_{2}, \sigma\right) \rightarrow f\left(\theta_{1}, \theta_{2}, \sigma\right) \in \mathbb{R}^{N}$ is $C^{2}$ in $\left(\theta_{1}, \theta_{2}\right)$. It follows from the Integral Mean Value Theorem that

$$
\begin{align*}
\dot{y}_{k}(t)= & \frac{1}{\beta_{k}} \int_{0}^{1} \partial_{1} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s\left(y_{k}(t)-y_{\sigma_{k}}\right) \\
& +\frac{1}{\beta_{k}} \int_{0}^{1} \partial_{2} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s\left(y_{k}\left(t-\beta_{k} z_{k}(t)\right)-y_{\sigma_{k}}\right), \tag{2.18}
\end{align*}
$$

where

$$
\left.\partial_{1} f_{k}\left(\sigma_{k}, s\right)(t):=\partial_{1} f\left(y_{\sigma_{k}}+s\left(y_{k}(t)-y_{\sigma_{k}}\right), y_{\sigma_{k}}+s\left(y_{k}\left(t-z_{k}(t)\right)-y_{\sigma_{k}}\right), \sigma_{k}\right)\right)
$$

$$
\left.\partial_{2} f_{k}\left(\sigma_{k}, s\right)(t):=\partial_{2} f\left(y_{\sigma_{k}}+s\left(y_{k}(t)-y_{\sigma_{k}}\right), y_{\sigma_{k}}+s\left(y_{k}\left(t-z_{k}(t)\right)-y_{\sigma_{k}}\right), \sigma_{k}\right)\right)
$$

Put

$$
\begin{equation*}
v_{k}(t)=\frac{y_{k}(t)-y_{\sigma_{k}}}{\left\|y_{k}-y_{\sigma_{k}}\right\|} \tag{2.19}
\end{equation*}
$$

Then we have

$$
\begin{equation*}
v_{k}\left(t-\beta_{k} z_{k}(t)\right)=\frac{y_{k}\left(t-\beta_{k} z_{k}(t)\right)-y_{\sigma_{k}}}{\left\|y_{k}-y_{\sigma_{k}}\right\|} \tag{2.20}
\end{equation*}
$$

By (2.18) and (2.20) we have

$$
\begin{equation*}
\dot{v}_{k}(t)=\frac{1}{\beta_{k}} \int_{0}^{1} \partial_{1} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s v_{k}(t)+\frac{1}{\beta_{k}} \int_{0}^{1} \partial_{2} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s v_{k}\left(t-\beta_{k} z_{k}(t)\right) \tag{2.21}
\end{equation*}
$$

We claim that there exists a convergent subsequence of $\left\{v_{k}\right\}_{k=1}^{+\infty}$. Indeed, by (2.13) and system (2.6), we know that $\left\{z_{k}, \beta_{k}\right\}_{k=1}^{+\infty}$ is uniformly bounded in $C(\mathbb{R} ; \mathbb{R}) \times \mathbb{R}$ and hence $\lim _{t \rightarrow+\infty}\left[t-\beta_{k} z_{k}(t)\right]=+\infty$. Then by (2.19) and (2.20), we have

$$
\left\|v_{k}\right\|=1,\left\|v_{k}\left(\cdot-\beta_{k} z_{k}(\cdot)\right)\right\|=1
$$

Recall that $\partial_{i} f\left(\sigma^{*}\right)$ and $\partial_{i} g\left(\sigma^{*}\right), i=1,2$, are defined in (2.1). By (2.15), we know that $\left(y_{\sigma_{k}}+s\left(y_{k}(t)-y_{\sigma_{k}}\right), y_{\sigma_{k}}+s\left(y_{k}\left(t-z_{k}(t)\right)-y_{\sigma_{k}}\right), \sigma_{k}\right)$ converges to the stationary state $\left(y_{\sigma^{*}}, y_{\sigma^{*}}, \sigma^{*}\right)$ in $C\left(\mathbb{R} ; \mathbb{R}^{2 N}\right) \times \mathbb{R}$ uniformly for all $s \in[0,1]$. By (S1) we know that $f\left(\theta_{1}, \theta_{2}, \sigma\right)$ is $C^{2}$ in $\left(\theta_{1}, \theta_{2}, \sigma\right)$ and $\partial_{1} f\left(\theta_{1}, \theta_{2}, \sigma\right)$ is $C^{1}$ in $\sigma$. Also, by (2.13), the sequence $\left\{u_{k}, \beta_{k}, \sigma_{k}\right\}_{k=1}^{+\infty}$ is uniformly bounded in $C\left(\mathbb{R} ; \mathbb{R}^{N+1}\right) \times \mathbb{R}^{2}$. Then there exists a constant $\tilde{L}_{1}>0$ so that

$$
\begin{aligned}
& \left|\partial_{1} f_{k}\left(\sigma_{k}, s\right)(t)-\partial_{1} f\left(\sigma^{*}\right)\right| \\
\leq & \tilde{L}_{1}\left|\left(y_{\sigma_{k}}+s\left(y_{k}(t)-y_{\sigma_{k}}\right), y_{\sigma_{k}}+s\left(y_{k}\left(t-z_{k}(t)\right)-y_{\sigma_{k}}\right), \sigma_{k}\right)-\left(y_{\sigma^{*}}, y_{\sigma^{*}}, \sigma^{*}\right)\right|
\end{aligned}
$$

for all $t \in \mathbb{R}, k \in \mathbb{N}$ and $s \in[0,1]$. Therefore, we have $\lim _{k \rightarrow+\infty} \| \partial_{1} f_{k}\left(\sigma_{k}, s\right)-$ $\partial_{1} f\left(\sigma^{*}\right) \|=0$ uniformly for $s \in[0,1]$. By the same argument we obtain that

$$
\begin{equation*}
\lim _{k \rightarrow+\infty}\left\|\partial_{1} f_{k}\left(\sigma_{k}, s\right)-\partial_{1} f\left(\sigma^{*}\right)\right\|=0, \lim _{k \rightarrow+\infty}\left\|\partial_{2} f_{k}\left(\sigma_{k}, s\right)-\partial_{2} f\left(\sigma^{*}\right)\right\|=0 \tag{2.22}
\end{equation*}
$$

uniformly for $s \in[0,1]$. From (2.22) we know that $\left\|\partial_{1} f_{k}\left(\sigma_{k}, s\right)\right\|$ and $\left\|\partial_{2} f_{k}\left(\sigma_{k}, s\right)\right\|$ are both uniformly bounded for all $k \in \mathbb{N}$ and $s \in[0,1]$. Then it follows from (2.21) that there exists a constant $\tilde{L}_{2}>0$ such that $\left\|\dot{v}_{k}\right\|<\tilde{L}_{2}$ for any $k \in \mathbb{N}$. By the Arzela-Ascoli Theorem, there exists a convergent subsequence $\left\{v_{k_{j}}\right\}_{j=1}^{+\infty}$ of $\left\{v_{k}\right\}_{k=1}^{+\infty}$. That is, there exists $v^{*} \in\{v \in V:\|v\|=1\}$ such that

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left\|v_{k_{j}}-v^{*}\right\|=0 \tag{2.23}
\end{equation*}
$$

By the Integral Mean Value Theorem, we have

$$
\left|v_{k_{j}}\left(t-\beta_{k_{j}} z_{k_{j}}(t)\right)-v_{k_{j}}\left(t-\beta^{*} z_{\sigma^{*}}\right)\right|
$$

$$
\begin{align*}
& =\left|\int_{0}^{1} \dot{v}_{k_{j}}\left(t-\theta\left(\beta_{k_{j}} z_{k_{j}}(t)-\beta^{*} z_{\sigma^{*}}\right)\right) \mathrm{d} \theta\left(\beta_{k_{j}} z_{k_{j}}(t)-\beta^{*} z_{\sigma^{*}}\right)\right| \\
& \leq\left\|\dot{v}_{k_{j}}\right\| \cdot\left|\beta_{k_{j}} z_{k_{j}}(t)-\beta^{*} z_{\sigma^{*}}\right| \\
& \leq \tilde{L}_{2}\left(\beta_{k_{j}}\left|z_{k_{j}}(t)-z_{\sigma^{*}}\right|+\left|\beta_{k_{j}}-\beta^{*}\right| z_{\sigma^{*}}\right) . \tag{2.24}
\end{align*}
$$

By (2.15) and (2.24) we have

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left\|v_{k_{j}}\left(\cdot-\beta_{k_{j}} z_{k_{j}}(\cdot)\right)-v_{k_{j}}\left(\cdot-\beta^{*} z_{\sigma^{*}}\right)\right\|=0 \tag{2.25}
\end{equation*}
$$

Therefore, it follows from (2.23) and (2.25) that

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left\|v_{k_{j}}\left(\cdot-\beta_{k_{j}} z_{k_{j}}(\cdot)\right)-v^{*}\left(\cdot-\beta^{*} z_{\sigma^{*}}\right)\right\|=0 \tag{2.26}
\end{equation*}
$$

It follows from (2.15), (2.22), (2.23) and (2.26) that the right hand side of (2.21) converges uniformly to the right hand side of (2.17). Therefore, $v^{*}$ is differentiable and we have

$$
\lim _{k \rightarrow+\infty}\left|\dot{v}_{k}(t)-\dot{v}^{*}(t)\right|=0
$$

and

$$
\begin{equation*}
\dot{v}^{*}(t)=\frac{1}{\beta^{*}} \partial_{1} f\left(\sigma^{*}\right) v^{*}(t)+\frac{1}{\beta^{*}} \partial_{2} f\left(\sigma^{*}\right) v^{*}\left(t-\beta^{*} z_{\sigma^{*}}\right) . \tag{2.27}
\end{equation*}
$$

Since by (S3) the matrix $\partial_{1} f\left(\sigma^{*}\right)+\partial_{2} f\left(\sigma^{*}\right)$, is nonsingular, $v=0$ is the only constant solution of (2.27). Also, we have $v^{*} \in\{v \in V:\|v\|=1\},\left\|v^{*}\right\| \neq 0$. Therefore, $\left(v^{*}(t), \sigma^{*}, \beta^{*}\right)$ is a nonconstant periodic solution of the linear equation (2.27). Then by Lemma $2.4\left(y_{\sigma^{*}}, \sigma^{*}, \beta^{*}\right)$ is also a center of (2.9) in $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)}$. This contradicts the assumption that $B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)$ is a special neighborhood of (2.6). This completes the proof.

To apply the homotopy argument of $S^{1}$-degree, we show the following
Lemma 2.6 Assume (S1)-(S3) hold. Let $L_{0}, K, \tilde{N}_{0}, \tilde{\mathcal{F}}$ be as in Lemma 2.5 and $N_{0}: V \times \mathbb{R}^{2} \rightarrow V$ be as in (2.6). Define the map $\mathcal{F}: V \times \mathbb{R}^{2} \rightarrow V$ by

$$
\mathcal{F}(y, \sigma, \beta):=y-\left(L_{0}+K\right)^{-1}\left[\frac{1}{\beta} N_{0}(y, \sigma, \beta)+K(y)\right] .
$$

If $\mathcal{U}=B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right) \subseteq V \times \mathbb{R}^{2}$ is a special neighborhood of $\tilde{\mathcal{F}}$ with $0<\rho<\beta_{0}$, then there exists $r^{\prime} \in(0, r]$ such that $\mathcal{F}_{\theta}=(\mathcal{F}, \theta)$ and $\tilde{\mathcal{F}}_{\theta}=(\tilde{\mathcal{F}}, \theta)$ are homotopic on $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$, where $\theta$ is a completing function (or Ize's function) defined on $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$ which satisfies
i) $\theta\left(y_{\sigma}, \sigma, \beta\right)=-\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|$ if $\left(y_{\sigma}, \sigma, \beta\right) \in \overline{\mathcal{U}}$;
ii) $\theta(y, \sigma, \beta)=r^{\prime}$ if $\left\|y-y_{\sigma}\right\|=r^{\prime}$.

Proof. Since $\mathcal{U}=B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right) \subseteq V \times \mathbb{R}^{2}$ is a special neighborhood of $\tilde{\mathcal{F}}$ with $0<\rho<\beta_{0}$, then by Lemma [2.5, both $\mathcal{F}_{\theta}=(\mathcal{F}, \theta)$ and $\tilde{\mathcal{F}}_{\theta}=(\mathcal{F}, \theta)$ are $\mathcal{U}$-admissible.

Suppose, for contradiction, that the conclusion is not true. Then for any $r^{\prime} \in(0, r]$, $\mathcal{F}_{\theta}=(\mathcal{F}, \theta)$ and $\tilde{\mathcal{F}}_{\theta}=(\mathcal{F}, \theta)$ are not homotopic on $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$. That is, any homotopy map between $\mathcal{F}_{\theta}$ and $\tilde{\mathcal{F}}_{\theta}$ has a zero on the boundary of $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$. In particular, the linear homotopy $h(\cdot, \alpha):=\alpha \mathcal{F}_{\theta}+(1-\alpha) \tilde{\mathcal{F}}_{\theta}=(\alpha \mathcal{F}+(1-\alpha) \tilde{\mathcal{F}}, \theta)$ has a zero on the boundary of $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$, where $\alpha \in[0,1]$.

Note that $\theta(y, \sigma, \beta)<0$ if $\left\|y-y_{\sigma}\right\|=r^{\prime}$. Then, there exist $(y, \sigma, \beta)$ and $\alpha \in[0,1]$ such that $\left\|y-y_{\sigma}\right\|<r^{\prime},\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho$ and

$$
\begin{equation*}
H(y, \sigma, \beta, \alpha):=\alpha \mathcal{F}+(1-\alpha) \tilde{\mathcal{F}}=0 \tag{2.28}
\end{equation*}
$$

Since $r^{\prime}>0$ is arbitrary in the interval $(0, r]$, there exists a nonconstant sequence $\left\{\left(y_{k}, \sigma_{k}, \beta_{k}, \alpha_{k}\right)\right\}_{k=1}^{\infty}$ of solutions of (2.28) such that

$$
\begin{equation*}
\lim _{k \rightarrow+\infty}\left\|y_{k}-y_{\sigma_{k}}\right\|=0,\left|\left(\sigma_{k}, \beta_{k}\right)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho, 0 \leq \alpha_{k} \leq 1 \tag{2.29}
\end{equation*}
$$

and

$$
\begin{equation*}
H\left(y_{k}, \sigma_{k}, \beta_{k}, \alpha_{k}\right)=0, \text { for all } k \in \mathbb{N} \tag{2.30}
\end{equation*}
$$

Note that $0<\rho<\beta_{0}$ implies that $\beta_{k} \geq \beta_{0}-\rho>0$ for every $k \in \mathbb{N}$. From (2.29) we know that $\left\{\left(\sigma_{k}, \beta_{k}, \alpha_{k}\right)\right\}_{k=1}^{\infty}$ belongs to a compact subset of $\mathbb{R}^{3}$. Therefore, there exist a convergent subsequence, denoted for notational simplicity by $\left\{\left(\sigma_{k}, \beta_{k}, \alpha_{k}\right)\right\}_{k=1}^{\infty}$ without loss of generality, and $\left(\sigma^{*}, \beta^{*}, \alpha^{*}\right) \in \mathbb{R}^{3}$ such that $\beta^{*} \geq \beta_{0}-\rho>0, \alpha^{*} \in[0,1]$ and

$$
\begin{equation*}
\lim _{k \rightarrow+\infty}\left|\left(\sigma_{k}, \beta_{k}, \alpha_{k}\right)-\left(\sigma^{*}, \beta^{*}, \alpha^{*}\right)\right|=0 \tag{2.31}
\end{equation*}
$$

By the same token for the proof of Lemma 2.5, we show that the system

$$
\begin{equation*}
\dot{v}(t)=\frac{1}{\beta^{*}} \partial_{1} f\left(\sigma^{*}\right) v(t)+\frac{1}{\beta^{*}} \partial_{2} f\left(\sigma^{*}\right) v\left(t-\beta^{*} z_{\sigma^{*}}\right) \tag{2.32}
\end{equation*}
$$

with $\partial_{i} f\left(\sigma^{*}\right), \partial_{i} g\left(\sigma^{*}\right), i=1,2$, defined at (2.1), has a nonconstant periodic solution which contradicts the assumption that $B_{M}\left(u_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)$ is a special neighborhood which contains an isolated center of (2.9).

By (2.30), we know that the subsequence $\left\{\left(y_{k}, \sigma_{k}, \beta_{k}, \alpha_{k}\right)\right\}_{k=1}^{\infty}$ satisfies

$$
\begin{equation*}
H\left(y_{k}, \sigma_{k}, \beta_{k}, \alpha_{k}\right)=0 \tag{2.33}
\end{equation*}
$$

By (S1), $f: \mathbb{R}^{N} \times \mathbb{R}^{N} \times \mathbb{R} \ni\left(\theta_{1}, \theta_{2}, \sigma\right) \rightarrow f\left(\theta_{1}, \theta_{2}, \sigma\right) \in \mathbb{R}^{N}$ is $C^{2}$ in $\left(\theta_{1}, \theta_{2}\right)$. Then it follows from the Integral Mean Value Theorem and from (2.33) that

$$
\dot{u}_{k}(t)=\frac{\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{1} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s\left(y_{k}(t)-y_{\sigma_{k}}\right)
$$

$$
\begin{align*}
& +\frac{\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{2} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s\left(y_{k}\left(t-\beta_{k} z_{k}(t)\right)-y_{\sigma_{k}}\right) \\
& +\frac{1-\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{1} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s\left(y_{k}(t)-y_{\sigma_{k}}\right) \\
& +\frac{1-\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{2} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s\left(y_{k}\left(t-\beta_{k} z_{\sigma_{k}}\right)-y_{\sigma_{k}}\right) \tag{2.34}
\end{align*}
$$

where

$$
\begin{aligned}
& \left.\partial_{1} f_{k}\left(\sigma_{k}, s\right)(t):=\partial_{1} f\left(y_{\sigma_{k}}+s\left(y_{k}(t)-y_{\sigma_{k}}\right), y_{\sigma_{k}}+s\left(y_{k}\left(t-\beta z_{k}(t)\right)-y_{\sigma_{k}}\right), \sigma_{k}\right)\right), \\
& \left.\partial_{2} f_{k}\left(\sigma_{k}, s\right)(t):=\partial_{2} f\left(y_{\sigma_{k}}+s\left(y_{k}(t)-y_{\sigma_{k}}\right), y_{\sigma_{k}}+s\left(y_{k}\left(t-\beta z_{k}(t)\right)-y_{\sigma_{k}}\right), \sigma_{k}\right)\right)
\end{aligned}
$$

Put

$$
\begin{equation*}
v_{k}(t)=\frac{y_{k}(t)-y_{\sigma_{k}}}{\left\|y_{k}-y_{\sigma_{k}}\right\|} \tag{2.35}
\end{equation*}
$$

Then we have

$$
\begin{equation*}
v_{k}\left(t-\beta_{k} z_{k}(t)\right)=\frac{y_{k}\left(t-\beta_{k} z_{k}(t)\right)-y_{\sigma_{k}}}{\left\|y_{k}-y_{\sigma_{k}}\right\|} \tag{2.36}
\end{equation*}
$$

By (2.34) and (2.36), we have

$$
\begin{align*}
\dot{v}_{k}(t)= & \frac{\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{1} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s v_{k}(t) \\
& +\frac{\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{2} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s v_{k}\left(t-\beta_{k} z_{\sigma_{k}}\right) \\
& +\frac{1-\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{1} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s v_{k}(t) \\
& +\frac{1-\alpha_{k}}{\beta_{k}} \int_{0}^{1} \partial_{2} f_{k}\left(\sigma_{k}, s\right)(t) \mathrm{d} s v_{k}\left(t-\beta_{k} z_{\sigma_{k}}\right) \tag{2.37}
\end{align*}
$$

We show that there exists a convergent subsequence of $\left\{v_{k}\right\}_{k=1}^{+\infty}$. Indeed, by (2.29) we know that $\left\{z_{k}, \beta_{k}\right\}_{k=1}^{+\infty}$ is uniformly bounded in $C(\mathbb{R} ; \mathbb{R}) \times \mathbb{R}$. Therefore we have

$$
\begin{equation*}
\lim _{t \rightarrow+\infty} t-\beta_{k} z_{k}(t)=+\infty \tag{2.38}
\end{equation*}
$$

By (2.35), (2.36) and (2.38), we have $\left\|v_{k}\right\|=1,\left\|v_{k}\left(\cdot-\beta_{k} z_{k}\right)\right\|=1$. Note that by (S1) and (2.31) and by an argument similar yielding (2.22), we know that

$$
\begin{equation*}
\lim _{k \rightarrow+\infty}\left\|\partial_{1} f_{k}\left(\sigma_{k}, s\right)-\partial_{1} f\left(\sigma^{*}\right)\right\|=0, \lim _{k \rightarrow+\infty}\left\|\partial_{2} f_{k}\left(\sigma_{k}, s\right)-\partial_{2} f\left(\sigma^{*}\right)\right\|=0 \tag{2.39}
\end{equation*}
$$

uniformly for $s \in[0,1]$. We know from (2.39) that $\left\|\partial_{1} f_{k}\left(\sigma_{k}, s\right)\right\|,\left\|\partial_{2} f_{k}\left(\sigma_{k}, s\right)\right\|$, are both uniformly bounded for every $k \in \mathbb{N}$ and $s \in[0,1]$. It follows from (2.37) that there exists $\tilde{L}_{3}>0$ such that $\left\|\dot{v}_{k}\right\|<\tilde{L}_{3}$ for every $k \in \mathbb{N}$. By the Arzela-Ascoli

Theorem, there exists a convergent subsequence $\left\{v_{k_{j}}\right\}_{j=1}^{+\infty}$ of $\left\{v_{k}\right\}_{k=1}^{+\infty}$. That is, there exists $v^{*} \in\{v \in V:\|v\|=1\}$ such that

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left\|v_{k_{j}}-v^{*}\right\|=0 \tag{2.40}
\end{equation*}
$$

By the Integral Mean Value Theorem, we obtain for all $t \in \mathbb{R}$,

$$
\begin{align*}
& \left|v_{k_{j}}\left(t-\beta_{k_{j}} z_{k_{j}}(t)\right)-v_{k_{j}}\left(t-\beta^{*} z_{\sigma^{*}}\right)\right| \\
= & \left|\int_{0}^{1} \dot{v}_{k_{j}}\left(t-\beta^{*} z_{\sigma^{*}}-\theta\left(\beta_{k_{j}} z_{k_{j}}(t)-\beta^{*} z_{\sigma^{*}}\right)\right) \mathrm{d} \theta\left(\beta_{k_{j}} z_{k_{j}}(t)-\beta^{*} z_{\sigma^{*}}\right)\right| \\
\leq & \left\|\dot{v}_{k_{j}}\right\| \cdot\left|\beta_{k_{j}} z_{k_{j}}(t)-\beta^{*} z_{\sigma^{*}}\right| \\
\leq & \tilde{L}_{3}\left(\beta_{k_{j}}\left|z_{k_{j}}(t)-z_{\sigma^{*}}\right|+\left|\beta_{k_{j}}-\beta^{*}\right| z_{\sigma^{*}}\right) . \tag{2.41}
\end{align*}
$$

Then by (2.31) and (2.41) we have

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left\|v_{k_{j}}\left(\cdot-\beta_{k_{j}} z_{k_{j}}(\cdot)\right)-v_{k_{j}}\left(\cdot-\beta^{*} z_{\sigma^{*}}\right)\right\|=0 \tag{2.42}
\end{equation*}
$$

From (2.40) and (2.42) we have

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left\|v_{k_{j}}\left(\cdot-\beta_{k_{j}} z_{k_{j}}(\cdot)\right)-v^{*}\left(\cdot-\beta^{*} z_{\sigma^{*}}\right)\right\|=0 \tag{2.43}
\end{equation*}
$$

It follows from (2.31), (2.39), (2.40) and (2.43) that the right hand side of (2.37) converges uniformly to the right hand side of (2.32). Therefore,

$$
\begin{equation*}
\lim _{j \rightarrow+\infty}\left|\dot{v}_{k_{j}}(t)-\dot{v}^{*}(t)\right|=0 \tag{2.44}
\end{equation*}
$$

and

$$
\begin{equation*}
\dot{v}^{*}(t)=\frac{1}{\beta^{*}} \partial_{1} f\left(\sigma^{*}\right) v^{*}(t)+\frac{1}{\beta^{*}} \partial_{2} f\left(\sigma^{*}\right) v^{*}\left(t-\beta^{*} \tau_{\sigma^{*}}\right) . \tag{2.45}
\end{equation*}
$$

Noticing that $v^{*} \in\{v:\|v\|=1\}$, we have $\left\|v^{*}\right\| \neq 0$. Since the matrix $\partial_{1} f\left(\sigma^{*}\right)+$ $\partial_{2} f\left(\sigma^{*}\right)$ is nonsingular, $v^{*}$ is a nonconstant periodic solution of (2.45). Then by Lemma $2.4\left(y_{\sigma^{*}}, \sigma^{*}, \beta^{*}\right)$ is also a center of (2.9) in $\overline{B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)}$. This contradicts the assumption that $B_{M}\left(y_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)$ is a special neighborhood of (2.9) which contains only one center $\left(y_{0}, \sigma_{0}, \beta_{0}\right)$. This completes the proof.

Now we are in the position to prove the local Hopf bifurcation theorem.
Theorem 2.7 Assume (S1)-(S3) hold. Let $\left(x_{\sigma_{0}}, \sigma_{0}\right)$ be an isolated center of system (2.1). If the crossing number defined by (2.5) satisfies

$$
\gamma\left(x_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right) \neq 0
$$

then there exists a bifurcation of nonconstant periodic solutions of (1.1) near $\left(x_{\sigma_{0}}, \sigma_{0}\right)$. More precisely, there exists a sequence $\left\{\left(x_{n}, \sigma_{n}, \beta_{n}\right)\right\}$ such that $\sigma_{n} \rightarrow \sigma_{0}, \beta_{n} \rightarrow \beta_{0}$ as
$n \rightarrow \infty$, and $\lim _{n \rightarrow \infty}\left\|x_{n}-x_{\sigma_{0}}\right\|=0, \lim _{n \rightarrow \infty}\left\|\tau_{n}-\tau_{\sigma_{0}}\right\|=0$, where

$$
\left(x_{n}, \sigma_{n}\right) \in C\left(\mathbb{R} ; \mathbb{R}^{N}\right) \times \mathbb{R}
$$

is a nonconstant $2 \pi / \beta_{n}$-periodic solution of system (1.1).

Proof. Let $(x, \tau)$ be a solution of system (1.1) with $x$ being $2 \pi / \beta$-periodic and $\beta>0$. Let $(x(t), \tau(t))=(y(\beta t), z(\beta t))$. Then system (1.1) is transformed to

$$
\left\{\begin{array}{l}
\dot{y}(t)=\frac{1}{\beta} f(y(t), y(t-\beta z(t)), \sigma)  \tag{2.46}\\
z(t)=g(y(t), y(t-\beta z(t)), \sigma)
\end{array}\right.
$$

Then $x$ is a $2 \pi / \beta$-periodic solution of system (1.1) if and only if $y$ is a $2 \pi$-periodic solution of system (2.46).

Let $V=C_{2 \pi}\left(\mathbb{R} ; \mathbb{R}^{N}\right)$. For any $\xi=e^{i \nu} \in S^{1}, u \in V,(\xi u)(t):=u(t+\nu)$. The idea of the proof in the sequel is to verify all the conditions (A1)-(A6) for applying Theorem 2.4 on Hopf bifurcation developed in [6].

Recall that $\delta$ and $\varepsilon$ are defined before (2.5). Let $\mathscr{D}\left(\sigma_{0}, \beta_{0}\right)=\left(\sigma_{0}-\delta, \sigma_{0}+\delta\right) \times\left(\beta_{0}-\right.$ $\left.\varepsilon, \beta_{0}+\varepsilon\right)$ and define the maps

$$
\begin{aligned}
L_{0} y(t) & :=\dot{y}(t), y \in C_{2 \pi}^{1}\left(\mathbb{R} ; \mathbb{R}^{N}\right) \\
N_{0}(y, \sigma, \beta)(t) & :=f(y(t), y(t-\beta z(t)), \sigma), y \in V \\
\tilde{N}_{0}(y, \sigma, \beta)(t) & :=\partial_{1} f(\sigma)\left(y(t)-y_{\sigma}\right)+\partial_{2} f(\sigma)\left(y\left(t-\beta z_{\sigma}\right)-y_{\sigma}\right), y \in V
\end{aligned}
$$

where $(\sigma, \beta) \in \mathscr{D}\left(\sigma_{0}, \beta_{0}\right)$ and $t \in \mathbb{R}$, and $\left(y_{\sigma}, z_{\sigma}\right)$ is the stationary state of the system at $\sigma$ such that $y_{\sigma_{0}}=x_{\sigma_{0}}$. The space $V$ is a Banach representation of the group $G=S^{1}$.

Define the operator $K: V \rightarrow \mathbb{R}^{N}$ by

$$
K(y):=\frac{1}{2 \pi} \int_{0}^{2 \pi} y(t) d t, y \in V
$$

By Lemma [2.2, the operator $L_{0}+K: C_{2 \pi}^{1}\left(\mathbb{R} ; \mathbb{R}^{N}\right) \rightarrow V$ has a compact inverse $\left(L_{0}+K\right)^{-1}: V \rightarrow V$. Then, finding a $2 \pi / \beta$-periodic solution for the system (1.1) is equivalent to finding a solution of the following fixed point problem:

$$
\begin{equation*}
y=\left(L_{0}+K\right)^{-1}\left[\frac{1}{\beta} N_{0}(y, \sigma, \beta)+K(y)\right], \tag{2.47}
\end{equation*}
$$

where $(y, \sigma, \beta) \in V \times \mathbb{R} \times(0,+\infty)$.
By (S1) we know that the linear operator $\tilde{N}_{0}$ is continuous. By Lemma 2.3, we know that $N_{0}(\cdot, \sigma, \beta): V \rightarrow V$ is continuous. Moreover, by Lemma 2.2 the operator $\left(L_{0}+\right.$
$K)^{-1}: V \rightarrow V$ is compact and hence $\left(L_{0}+K\right)^{-1} \circ\left(\frac{1}{\beta} N_{0}(\cdot, \alpha, \beta)+K\right): V \rightarrow V$ and $\left(L_{0}+K\right)^{-1} \circ\left(\frac{1}{\beta} \tilde{N}_{0}(\cdot, \alpha, \beta)+K\right): V \rightarrow V$ are completely continuous and hence are condensing maps. That is, (A2) and (A4) are satisfied.

Define the following maps $\mathcal{F}: V \times \mathbb{R} \times(0,+\infty) \rightarrow V$ and $\tilde{\mathcal{F}}: V \times \mathbb{R} \times(0,+\infty) \rightarrow V$ by

$$
\begin{aligned}
\mathcal{F}(y, \sigma, \beta) & :=y-\left(L_{0}+K\right)^{-1}\left[\frac{1}{\beta} N_{0}(y, \sigma, \beta)+K(y)\right], \\
\widetilde{\mathcal{F}}(y, \sigma, \beta) & :=y-\left(L_{0}+K\right)^{-1}\left[\frac{1}{\beta} \tilde{N}_{0}(y, \sigma, \beta)+K(y)\right],
\end{aligned}
$$

which are equivariant condensing fields. Finding a $2 \pi / \beta$-periodic solution of system (1.1) is equivalent to finding the solution of the problem

$$
\mathcal{F}(y, \sigma, \beta)=0, \quad(y, \sigma, \beta) \in V \times \mathbb{R} \times(0,+\infty)
$$

Since $\left(x_{\sigma_{0}}, \sigma_{0}\right)=\left(y_{\sigma_{0}}, \sigma_{0}\right)$ is an isolated center of system (2.1) with a purely imaginary characteristic value $i \beta_{0}, \beta_{0}>0,\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right) \in V \times \mathbb{R} \times(0,+\infty)$ is an isolated $V$ singular point of $\tilde{\mathcal{F}}$. That is, $\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)$ is the only point in $V$ such that the derivative $D_{y} \mathcal{F}\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)$ is not an automorphism of $V$. One can define the following twodimensional submanifold $M \subset V^{G} \times \mathbb{R} \times(0,+\infty)$ by

$$
M:=\left\{\left(y_{\sigma}, \sigma, \beta\right): \sigma \in\left(\sigma_{0}-\delta, \sigma_{0}+\delta\right), \beta \in\left(\beta_{0}-\varepsilon, \beta_{0}+\varepsilon\right)\right\},
$$

such that the point $\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)$ is the only $V$-singular point of $\tilde{\mathcal{F}}$ in $M . M$ is the set of trivial solutions to the system (2.1) and satisfies the assumption (A3).

Since $\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right) \in V \times \mathbb{R} \times(0,+\infty)$ is an isolated $V$-singular point of $\tilde{\mathcal{F}}$, for $\rho>0$ sufficiently small, the linear operator $D_{u} \tilde{\mathcal{F}}\left(y_{\sigma}, \sigma, \beta\right): V \rightarrow V$ with $\mid(\sigma, \beta)-$ $\left(\sigma_{0}, \beta_{0}\right) \mid<\rho$, is not an automorphism only if $(\sigma, \beta)=\left(\sigma_{0}, \beta_{0}\right)$. Then, by the Implicit Function Theorem, there exists $r>0$ such that for every $(y, \sigma, \beta) \in V \times \mathbb{R} \times(0,+\infty)$ with $\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho$ and $0<\left\|y-y_{\sigma}\right\| \leq r$, we have $\tilde{\mathcal{F}}(y, \sigma, \beta) \neq 0$. Then the set $B_{M}\left(x_{0}, \sigma_{0}, \beta_{0} ; r, \rho\right)$ defined by

$$
\left\{(y, \sigma, \beta) \in V \times \mathbb{R} \times(0,+\infty) ;\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|<\rho,\left\|y-y_{\sigma}\right\|<r\right\}
$$

is a special neighborhood for $\tilde{\mathcal{F}}$.
By Lemma 2.5, there exists a special neighborhood $\mathcal{U}=B_{M}\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)$ such that $\mathcal{F}$ and $\tilde{\mathcal{F}}$ are nonzero for $(y, \sigma, \beta) \in \overline{B_{M}\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0} ; r^{\prime}, \rho\right)}$ with $y \neq y_{\sigma}$ and $\left|(\sigma, \beta)-\left(\sigma_{0}, \beta_{0}\right)\right|=\rho$. That is, (A5) is satisfied.

Let $\theta$ be a completing function on $\mathcal{U}$. It follows from Lemma 2.6 that $(\mathcal{F}, \theta)$ is homotopic to $(\tilde{\mathcal{F}}, \theta)$ on $\mathcal{U}$.

It is known that $V$ has the following isotypical direct sum decomposition

$$
V=\overline{\bigoplus_{k=0}^{\infty} V_{k}}
$$

where $V_{0}$ is the space of all constant mappings from $\mathbb{R}$ into $\mathbb{R}^{N}$, and $V_{k}$ with $k>0$, $k \in \mathbb{N}$ is the vector space of all mappings of the form

$$
x \cos k \cdot+y \sin k \cdot: \mathbb{R} \ni t \rightarrow x \cos k t+y \sin k t \in \mathbb{R}^{N}
$$

where $x, y \in \mathbb{R}^{N}$. Then $V_{k}, k>0, k \in \mathbb{N}$, are finite dimensional. Then, (A1) is satisfied.

For $(\sigma, \beta) \in \mathscr{D}\left(\sigma_{0}, \beta_{0}\right)$, we denote by $\Psi(\sigma, \beta)$ the map $D_{y} \widetilde{\mathcal{F}}(y(\sigma), \sigma, \beta): V \rightarrow V$. Then we have $\Psi(\sigma, \beta)\left(V_{k}\right) \subset V_{k}$ for all $k=0,1,2, \cdots$. Therefore, we can define $\Psi_{k}: \mathscr{D}\left(\sigma_{0}, \beta_{0}\right) \rightarrow L\left(V_{k}, V_{k}\right)$ by

$$
\Psi_{k}(\sigma, \beta):=\left.\Psi(\sigma, \beta)\right|_{V_{k}}
$$

We note that $V_{k}, k \geq 1, k \in \mathbb{N}$, can be endowed with the natural complex structure $J: V_{k} \rightarrow V_{k}$ defined by

$$
J(x \cos k \cdot+y \sin k \cdot)=-x \sin k \cdot+y \cos k \cdot), x y \in \mathbb{R}^{N}
$$

By extending the linearity of $J$ to the vector space spanned over the field of complex numbers by $e^{i k \cdot} \cdot \epsilon_{j}: \mathbb{R} \ni t \rightarrow e^{i k t} \cdot \epsilon_{j} \in \mathbb{C}^{N}, j=1,2, \cdots, N$, we know that

$$
\left\{e^{i k \cdot} \cdot \epsilon_{j}, J\left(e^{i k \cdot} \cdot \epsilon_{j}\right)\right\}_{j=1}^{N}=\left\{e^{i k \cdot} \cdot \epsilon_{j}, i e^{i k \cdot} \cdot \epsilon_{j}\right\}_{j=1}^{N}
$$

is a basis of $V_{k}$, where $\left\{\epsilon_{1}, \epsilon_{2}, \cdots, \epsilon_{N}\right\}$ denotes the standard basis of $\mathbb{R}^{N}$. Then we identify $V_{k}$ with the vector space over the complex numbers spanned by $e^{i k} \cdot \epsilon_{j}, j=$ $1,2, \cdots, N$.

Then we have for $v_{k} \in V_{k}, k \in \mathbb{Z}, k \geq 1$,

$$
\begin{aligned}
\Psi_{k}(\sigma, \beta) v_{k} & =v_{k}-\left(L_{0}+K\right)^{-1}\left(\frac{1}{\beta} D_{u} \tilde{N}_{0}(u(\sigma), \sigma, \beta)+K\right) v_{k} \\
& =v_{k}-\frac{1}{\beta}\left(L_{0}+K\right)^{-1}\left(\partial_{1} f(\sigma) v_{k}+\partial_{2} f(\sigma)\left(v_{k}\right)_{\beta z_{\sigma}}\right)
\end{aligned}
$$

where $\left(v_{k}\right)_{\beta z_{\sigma}}=v_{k}\left(\cdot-\beta z_{\sigma}\right)$. Then we have, for $e^{i k \cdot} \epsilon_{j} \in V_{k}$,

$$
\begin{aligned}
& \Psi_{k}(\sigma, \beta)\left(e^{i k \cdot} \epsilon_{j}\right) \\
= & \frac{1}{i k \beta}\left(i k \beta \operatorname{Id}-\partial_{1} f(\sigma)-\partial_{2} f(\sigma) e^{-i k \beta z_{\sigma}}\right) \cdot\left(e^{i k \cdot} \epsilon_{j}\right) \\
= & \frac{1}{i k \beta} \Delta_{(u(\sigma), \sigma)}(i k \beta) \cdot\left(e^{i k \cdot} \epsilon_{j}\right),
\end{aligned}
$$

where the last equality follows from (2.3). Therefore, the matrix representation $\left[\Psi_{k}\right]$ of $\Psi_{k}(\sigma, \beta)$ with respect to the ordered $\mathbb{C}$-basis $\left\{e^{i k \cdot} \cdot \epsilon_{j}\right\}_{j=1}^{N}$ is given by

$$
\frac{1}{i k \beta} \Delta_{\left(y_{\sigma}, \sigma\right)}(i k \beta) .
$$

Next we show that there exists some $k \in \mathbb{Z}, k \geq 1$, such that $\mu_{k}\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right):=$ $\operatorname{deg}_{B}\left(\operatorname{det}_{\mathbb{C}}\left[\Psi_{k}\right]\right) \neq 0$.

Define $\Psi_{H}: \mathscr{D}\left(\sigma_{0}, \beta_{0}\right) \rightarrow \mathbb{R}^{2} \simeq \mathbb{C}$ by

$$
\Psi_{H}(\sigma, \beta)=\operatorname{det} \Delta_{\left(y_{\sigma}, \sigma\right)}(i \beta) .
$$

The number $\mu_{1}\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)$ can be written as follows (see Theorem 7.1.5 of [8]):

$$
\mu_{1}\left(u\left(\sigma_{0}\right), \sigma_{0}, \beta_{0}\right)=\epsilon \cdot \operatorname{deg}\left(\Psi_{H}, \mathscr{D}\left(\sigma_{0}, \beta_{0}\right)\right)
$$

where $\epsilon=\operatorname{sign} \operatorname{det} \Psi_{0}(\sigma, \beta)$ for $(\sigma, \beta) \in \mathscr{D}\left(\sigma_{0}, \beta_{0}\right)$. For a constant map $v_{0} \in V_{0}$,

$$
\Psi_{0}(\sigma, \beta) v_{0}=-\frac{1}{\beta}\left(\partial_{1} f(\sigma)+\partial_{2} f(\sigma)\right) v_{0}
$$

Then, by (S3), we have $\epsilon \neq 0$ and therefore (A6) is satisfied.
Note that $\alpha_{0}, \beta_{0}, \delta$ and $\varepsilon$ are chosen at (2.5). Define the function $H:\left[\sigma_{0}-\delta, \sigma_{0}+\right.$ $\delta] \times \bar{\Omega} \rightarrow \mathbb{R}^{2} \simeq \mathbb{C}$ by

$$
H(\sigma, \alpha, \beta):=\operatorname{det} \Delta_{\left(y_{\sigma}, \sigma\right)}(\alpha+i \beta)
$$

where $\Omega=\left(0, \alpha_{0}\right) \times\left(\beta_{0}-\varepsilon, \beta_{0}+\varepsilon\right), \alpha_{0}=\alpha_{0}\left(\sigma_{0}, \beta_{0}\right)>0$. By the same argument for (2.4) and (2.5), we know that $H$ satisfies all the conditions of Lemma 2.1 of [6] (or Lemma 7.2 .1 of [8]) by the choice of $\alpha_{0}, \beta_{0}, \varepsilon$ and $\delta$. So we have

$$
\operatorname{deg}\left(\Psi_{H}, \mathscr{D}\left(\sigma_{0}, \beta_{0}\right)\right)=\gamma\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right) \neq 0
$$

Thus, $\mu_{1}\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right) \neq 0$ which, by Theorem 2.4 of [6], implies that $\left(y_{\sigma_{0}}, \sigma_{0}, \beta_{0}\right)$ is a bifurcation point of the system (2.46). Consequently, there exists a sequence of nonconstant periodic solutions $\left(x_{n}, \sigma_{n}, \beta_{n}\right)$ such that $\sigma_{n} \rightarrow \sigma_{0}, \beta_{n} \rightarrow \beta_{0}$ as $n \rightarrow \infty$, and $x_{n}$ is a $2 \pi / \beta_{n}$-periodic solution of (1.1) such that the associated pair $\left(x_{n}, \tau_{n}\right)$ satisfies (1.1) with $\lim _{n \rightarrow+\infty}\left\|\left(x_{n}, \tau_{n}\right)-\left(x_{\sigma_{0}}, \tau_{\sigma_{0}}\right)\right\|=0$.

## 3 Global Bifurcation of DAEs with State-dependent Delays

In this section we use Rabinowitz type global Hopf bifurcation Theorem 2.5 developed in [6] to describe the maximal continuation of bifurcated periodic solutions with large
amplitudes when the bifurcation parameter $\sigma$ is far away from the bifurcation value. We show that there is a lower bound for the periods of periodic solutions of system (1.1).

Lemma 3.1 (Vidossich, [19]) Let $X$ be a Banach space, $v: \mathbb{R} \rightarrow X$ be a p-periodic function with the following properties:
(i) $v \in L_{l o c}^{1}(\mathbb{R}, X)$;
(ii) there exists $U \in L^{1}\left(\left[0, \frac{\mathrm{p}}{2}\right] ; \mathbb{R}_{+}\right)$such that $|v(t)-v(s)| \leq U(t-s)$ for almost every (in the sense of the Lebesgue measure) $s, t \in \mathbb{R}$ such that $s \leq t, t-s \leq \frac{\mathrm{p}}{2}$;
(iii) $\int_{0}^{\mathrm{p}} v(t) \mathrm{d} t=0$.

Then

$$
\mathrm{p}\|v\|_{L^{\infty}} \leq 2 \int_{0}^{\frac{\mathrm{p}}{2}} U(t) \mathrm{d} t
$$

We make the following assumption on system (1.1):
(S4) There exists constant $L_{f}>0$ such that

$$
\left|f\left(\theta_{1}, \theta_{2}, \sigma\right)-f\left(\bar{\theta}_{1}, \bar{\theta}_{2}, \sigma\right)\right| \leq L_{f}\left(\left|\theta_{1}-\bar{\theta}_{1}\right|+\left|\theta_{2}-\bar{\theta}_{2}\right|\right)
$$

for every $\theta_{1}, \theta_{2}, \bar{\theta}_{1}, \bar{\theta}_{2}, \sigma \in \mathbb{R}$.
Lemma 3.2 Suppose that system (1.1) satisfies the assumption (S4) and $x$ is a nonconstant periodic solution. The following statements are true.
i) If $\|\tau\|_{L^{\infty}}<\frac{1}{2 L_{f}}$, then the minimal period p of $x$ satisfies

$$
\mathrm{p} \geq \frac{2}{1-2 L_{f}\|\tau\|_{L^{\infty}}}
$$

ii) If $\tau$ is continuously differentiable in $\mathbb{R}$, then the minimal period p of $x$ satisfies

$$
\mathrm{p} \geq \frac{4}{L_{f}\left(2+|\dot{\tau}|_{L^{\infty}}\right)}
$$

iii) Suppose there exists a constant $L_{g}>0$ such that

$$
\left|g\left(\theta_{1}, \theta_{2}, \sigma\right)-g\left(\bar{\theta}_{1}, \bar{\theta}_{2}, \sigma\right)\right| \leq L_{g}\left(\left|\theta_{1}-\bar{\theta}_{1}\right|+\left|\theta_{2}-\bar{\theta}_{2}\right|\right)
$$

for every $\theta_{1}, \theta_{2}, \bar{\theta}_{1}, \bar{\theta}_{2}, \sigma \in \mathbb{R}$. If $\|\dot{x}\|_{L^{\infty}}<\frac{1}{L_{g}}$, then the minimal period p of $x$ satisfies

$$
\mathrm{p} \geq \frac{2\left(1-L_{g}|\dot{x}|_{L^{\infty}}\right)}{L_{f}}
$$

Proof. Assume that $x$ is a nonconstant periodic solution with minimal period p . Let $v(t)=\dot{x}(t)$. Then we have $\int_{0}^{\mathrm{p}} v(t) \mathrm{d} t=0$. For $s \leq t$, by (S4) and the Integral Mean

Value Theorem, we have

$$
\begin{align*}
|v(t)-v(s)| & \leq|\dot{x}(t)-\dot{x}(s)| \\
& \leq L_{f}(|x(t)-x(s)|+|x(t-\tau(t))-x(s-\tau(s))|) \\
& \leq L_{f}|\dot{x}|_{L^{\infty}}(t-s)+L_{f}|\dot{x}|_{L^{\infty}}(t-s+|\tau(t)-\tau(s)|) \\
& \leq\left(2 L_{f}|\dot{x}|_{L^{\infty}}+L_{f}|\dot{x}|_{L^{\infty}} \cdot|\dot{\tau}|_{L^{\infty}}\right)(t-s) . \tag{3.1}
\end{align*}
$$

i) If $\|\tau\|_{L^{\infty}}<\frac{1}{2 L_{f}}$, then by (3.1) we have

$$
\begin{aligned}
|v(t)-v(s)| & \leq L_{f}|\dot{x}|_{L^{\infty}}(t-s)+L_{f}|\dot{x}|_{L^{\infty}}(t-s+|\tau(t)-\tau(s)|) \\
& \leq 2 L_{f}|\dot{x}|_{L^{\infty}}(t-s)+2 L_{f}|\tau|_{L^{\infty}} \cdot|\dot{x}|_{L^{\infty}} .
\end{aligned}
$$

Let

$$
U(t)=2 L_{f}|\dot{x}|_{L^{\infty}} t+2 L_{f}|\tau|_{L^{\infty}} \cdot|\dot{x}|_{L^{\infty}}
$$

Then, by Lemma 3.1, we obtain

$$
\mathrm{p}|\dot{x}|_{L^{\infty}} \leq 2 \int_{0}^{\frac{\mathrm{p}}{2}} U(t) \mathrm{d} t=\frac{\mathrm{p}^{2}}{4} \cdot 2 L_{f}|\dot{x}|_{L^{\infty}}+\mathrm{p} \cdot 2 L_{f}|\tau|_{L^{\infty}} \cdot|\dot{x}|_{L^{\infty}}
$$

Therefore,

$$
\mathrm{p} \geq \frac{2}{\left(1-2 L_{f}|\tau|_{L^{\infty}}\right)}
$$

ii) If $\tau$ is continuously differentiable in $\mathbb{R}$, then we have $|\dot{\tau}|_{L^{\infty}}<\infty$. Moreover, by (3.1) we have

$$
\begin{aligned}
|v(t)-v(s)| & \leq L_{f}|\dot{x}|_{L^{\infty}}(t-s)+L_{f}|\dot{x}|_{L^{\infty}}(t-s+|\tau(t)-\tau(s)|) \\
& \leq\left(2+|\dot{\tau}|_{L^{\infty}}\right) L_{f} \cdot|\dot{x}|_{L^{\infty}}(t-s)
\end{aligned}
$$

Let

$$
U(t)=\left(2+|\dot{\tau}|_{L^{\infty}}\right) L_{f} \cdot|\dot{x}|_{L^{\infty}} t
$$

Then, by Lemma 3.1, we obtain

$$
\mathrm{p}|\dot{x}|_{L^{\infty}} \leq 2 \int_{0}^{\frac{\mathrm{p}}{2}} U(t) \mathrm{d} t=\frac{\mathrm{p}^{2}}{4} \cdot\left(2+|\dot{\tau}|_{L^{\infty}}\right) L_{f} \cdot|\dot{x}|_{L^{\infty}}
$$

Therefore,

$$
\mathrm{p} \geq \frac{4}{L_{f}\left(2+|\dot{\tau}|_{L^{\infty}}\right)}
$$

iii) If $g$ is Lipschitz continuous, then we have

$$
\begin{aligned}
|\tau(t)-\tau(s)| & \leq L_{g}|x(t)-x(s)|+L_{g}|x(t-\tau(t))-x(s-\tau(s))| \\
& \leq L_{g}|\dot{x}|_{L^{\infty}}(t-s)+L_{g}|\dot{x}|_{L^{\infty}}(t-s+|\tau(t)-\tau(s)|) .
\end{aligned}
$$

If $|\dot{x}|_{L^{\infty}}<\frac{1}{L_{g}}$, then we have

$$
\begin{equation*}
|\tau(t)-\tau(s)| \leq \frac{2 L_{g}|\dot{x}|_{L^{\infty}}(t-s)}{1-L_{g}|\dot{x}|_{L^{\infty}}} . \tag{3.2}
\end{equation*}
$$

By (3.1) and (3.2)

$$
\begin{aligned}
|v(t)-v(s)| & \leq L_{f}|\dot{x}|_{L^{\infty}}(t-s)+L_{f}|\dot{x}|_{L^{\infty}}(t-s+|\tau(t)-\tau(s)|) \\
& \leq 2 L_{f} \cdot|\dot{x}|_{L^{\infty}}(t-s)+\frac{2 L_{f} L_{g}|\dot{x}|_{L^{\infty}}^{2}(t-s)}{1-L_{g}|\dot{x}|_{L^{\infty}}} \\
& =\frac{2 L_{f}|\dot{x}|_{L^{\infty}}}{1-L_{g}|\dot{x}|_{L^{\infty}}}(t-s) .
\end{aligned}
$$

Let

$$
U(t)=\frac{2 L_{f}|\dot{x}|_{L^{\infty}}}{1-L_{g}|\dot{x}|_{L^{\infty}}} t
$$

We obtain

$$
\mathrm{p}|\dot{x}|_{L^{\infty}} \leq 2 \int_{0}^{\frac{\mathrm{p}}{2}} U(t) \mathrm{d} t=\frac{\mathrm{p}^{2}}{4} \cdot \frac{2 L_{f}|\dot{x}|_{L^{\infty}}}{1-L_{g}|\dot{x}|_{L^{\infty}}},
$$

and

$$
\mathrm{p} \geq \frac{2\left(1-L_{g}|\dot{x}|_{L^{\infty}}\right)}{L_{f}}
$$

To describe the minimal periods of the periodic solutions near the bifurcation point, we need the following result which was first established in [9] for ordinary differential equations and was extended to other types of delay differential equations in [6, 20].
Lemma 3.3 Suppose that system (1.1) satisfies (S1-S4). Assume further that there exists a sequence of real numbers $\left\{\sigma_{k}\right\}_{k=1}^{\infty}$ such that:
(i) For each $k$, system (1.1) with $\sigma=\sigma_{k}$ has a nonconstant periodic solution $x_{k} \in$ $C\left(\mathbb{R} ; \mathbb{R}^{N+1}\right)$ with the minimal period $T_{k}>0$, and one of the conditions i), ii) and iii) at Lemma 3.2 is satisfied by $\left(x_{k}, \tau_{k}\right)$;
(ii) $\lim _{k \rightarrow \infty} \sigma_{k}=\sigma_{0} \in \mathbb{R}, \lim _{k \rightarrow \infty} T_{k}=T_{0}<\infty$, and $\lim _{k \rightarrow \infty}\left\|x_{k}-x_{0}\right\|=0$, where $x_{0}: \mathbb{R} \rightarrow \mathbb{R}^{N}$ is a constant map with the value $x_{0}$.

Then $x_{0}$ is a stationary state of (1.1) and there exists $m \geq 1, m \in \mathbb{N}$ such that $\pm i m 2 \pi / T_{0}$ are the roots of the characteristic equation (2.2) with $\sigma=\sigma_{0}$.

Proof. By Lemma 3.2 and the uniform convergence of $\left\{\left(x_{k}, \sigma_{k}, T_{k}\right)\right\}_{k=1}^{\infty}$ we conclude that there exists $T^{*}>0$ such that $T_{k} \geq T^{*}$ and therefore $T_{0} \geq T^{*}$. We can show that
$\left(x_{0}, \sigma_{0}\right)$ is a stationary state of (1.1), and that the following linear system

$$
\begin{equation*}
\dot{v}(t)=\partial_{1} f\left(\sigma_{0}\right) v(t)+\partial_{2} f\left(\sigma_{0}\right) v\left(t-\tau_{0}\right) \tag{3.3}
\end{equation*}
$$

has a nonconstant periodic solution, the proofs of which are just simplified versions of the proof for Lemma 4.3 in [6] without the equations for $\tau_{k}$. Hence we omit the details here. Then by Lemma [2.4, there exists $m \geq 1, m \in \mathbb{N}$, such that $\pm i m 2 \pi / T_{0}$ are characteristic values of (2.2). This completes the proof.

Now we can describe the relation between $2 \pi / \beta_{k}$ and the minimal period of $u_{k}$ in Theorem 2.7.
Theorem 3.4 Assume (S1-S4) hold and every point in the sequence $\left\{\left(x_{k}, \tau_{k}\right)\right\}_{k=1}^{\infty}$ at Theorem 2.7 satisfies one of the conditions among i), ii) and iii) at Lemma 3.2, then every limit point of the minimal period of $x_{k}$ as $k \rightarrow+\infty$ is contained in the set

$$
\left\{\frac{2 \pi}{\left(n \beta_{0}\right)}: \pm i m n \beta_{0} \text { are characteristic values of }\left(x_{0}, \sigma_{0}\right), m, n \geq 1, m, n \in \mathbb{N}\right\}
$$

Moreover, if $\pm i m n \beta_{0}$ are not characteristic values of $\left(x_{0}, \sigma_{0}\right)$ for any integers $m, n \in$ $\mathbb{N}$ such that $m n>1$, then $2 \pi / \beta_{k}$ is the minimal period of $u_{k}(t)$ and $2 \pi / \beta_{k} \rightarrow 2 \pi / \beta_{0}$ as $k \rightarrow \infty$.

Proof. Let $T_{k}$ denote the minimal period of $x_{k}(t)$. Then there exists a positive integer $n_{k}$ such that $2 \pi / \beta_{k}=n_{k} T_{k}$. Since $T_{k} \leq 2 \pi / \beta_{k} \rightarrow 2 \pi / \beta_{0}$ as $k \rightarrow \infty$, there exists a subsequence $\left\{T_{k_{j}}\right\}_{j=1}^{\infty}$ and $T_{0}$ such that $T_{0}=\lim _{j \rightarrow \infty} T_{k_{j}}$. Since $2 \pi / \beta_{k_{j}} \rightarrow 2 \pi / \beta_{0}$, $T_{k_{j}} \rightarrow T_{0}$ as $j \rightarrow \infty, n_{k_{j}}$ is identical to a constant $n$ for $k$ large enough. Therefore, $2 \pi / \beta_{0}=n T_{0}$. Thus $T_{k_{j}} \rightarrow 2 \pi /\left(n \beta_{0}\right)$ as $j \rightarrow \infty$. By Lemma3.3, $\pm i m 2 \pi / T_{0}= \pm i m n \beta_{0}$ are characteristic values of $\left(x_{0}, \sigma_{0}\right)$ for some $m \geq 1, m \in \mathbb{N}$.

Moreover, if $\pm i m n \beta_{0}$ are not characteristic values of ( $u_{0}, \sigma_{0}$ ) for any integers $m \in \mathbb{N}$ and $n \in \mathbb{N}$ with $m n>1$, then $m=n=1$. Therefore, for $k$ large enough $n_{k_{j}}=1$ and $2 \pi / \beta_{k}=T_{k}$ is the minimal period of $x_{k}(t)$ and $2 \pi / \beta_{k} \rightarrow 2 \pi / \beta_{0}$ as $k \rightarrow \infty$. This completes the proof.

The following lemma shows that we can locate all the possible Hopf bifurcation points of system (1.1) with state-dependent delay at the centers of its corresponding formal linearization. Since the proof is similar to that for Lemma 4.5 in [6], we omit the details here.
Lemma 3.5 Assume (S1-S3) hold. If $\left(x_{0}, \sigma_{0}\right)$ is a Hopf bifurcation point of system (1.1), then it is a center of (2.1).

Now we are in the position to consider the global Hopf bifurcation problem of system (1.1). Letting $(x(t), \tau(t))=\left(y\left(\frac{2 \pi}{\mathrm{p}} t\right), z\left(\frac{2 \pi}{\mathrm{p}} t\right)\right)$, we can reformulate the problem as a
problem of finding $2 \pi$-period solutions to the following equation:

$$
\begin{equation*}
\dot{y}(t)=\frac{\mathrm{p}}{2 \pi} N_{0}(y(t), \sigma, 2 \pi / \mathrm{p}), \tag{3.4}
\end{equation*}
$$

where the $z$ satisfies the algebraic equation $z(t)=g\left(y(t), y\left(t-\frac{\mathrm{p}}{2 \pi} z(t)\right), \sigma\right)$. Accordingly, the formal linearization (2.1) becomes

$$
\begin{equation*}
\dot{x}(t)=\frac{\mathrm{p}}{2 \pi} \tilde{N}_{0}(x(t), \sigma, 2 \pi / \mathrm{p}) \tag{3.5}
\end{equation*}
$$

Using the same notations as in the proof of Theorem 2.7, we can define $\mathscr{N}_{0}(x, \sigma, \mathrm{p})=$ $N_{0}(x, \sigma, 2 \pi / \mathrm{p}), \tilde{\mathcal{N}}_{0}(x, \sigma, \mathrm{p})=\tilde{N}_{0}(x, \sigma, 2 \pi / \mathrm{p})$.

Then the following system

$$
\begin{equation*}
L_{0} x=\frac{\mathrm{p}}{2 \pi} \mathscr{N}_{0}(x, \sigma, \mathrm{p}), \mathrm{p}>0 \tag{3.6}
\end{equation*}
$$

is equivalent to (3.4) and

$$
\begin{equation*}
L_{0} x=\frac{\mathrm{p}}{2 \pi} \tilde{\mathscr{N}}_{0}(x, \sigma, \mathrm{p}), \mathrm{p}>0 \tag{3.7}
\end{equation*}
$$

is equivalent to (3.5). Let $\mathcal{S}$ denote the closure of the set of all nontrivial periodic solutions of system (3.6) in the space $V \times \mathbb{R} \times \mathbb{R}_{+}$, where $\mathbb{R}_{+}$is the set of all nonnegative reals. It follows from Lemma 3.2 that the constant solution $\left(x_{0}, \sigma_{0}, 0\right)$ does not belong to this set if the sequence $\left\{\left(x_{k}, \tau_{k}\right)\right\}_{k=1}^{\infty}$ in Theorem [2.7] satisfies one of the conditions among i), ii) and iii) at Lemma 3.2. Consequently, we can assume that problem (3.6) is well posed on the whole space $V \times \mathbb{R}^{2}$, in the sense that if $\mathcal{S}$ exists in $V \times \mathbb{R}^{2}$, then it must be contained in $V \times \mathbb{R} \times \mathbb{R}_{+}$.

Then by the global Hopf bifurcation theorem 2.5 developed in [6] and with similar arguments leading to Theorem 4.6 in [6], we obtain the following global Hopf bifurcation theorem for system (1.1) with state-dependent delay.
Theorem 3.6 Suppose that system (1.1) satisfies (S1-S4) and (S3) holds at every center of (3.7). Assume that all the centers of (3.7) are isolated and every periodic solution $x$ of system (1.1) satisfies one of the conditions among i), ii) and iii) at Lemma 3.2. Let $M$ be the set of trivial periodic solutions of (3.6) and $M$ is complete. If $\left(x_{0}, \sigma_{0}, \mathrm{p}_{0}\right) \in M$ is a bifurcation point, then either the connected component $C\left(x_{0}, \sigma_{0}, \mathrm{p}_{0}\right)$ of $\left(x_{0}, \sigma_{0}, \mathrm{p}_{0}\right)$ in $\mathcal{S}$ is unbounded, or

$$
C\left(x_{0}, \sigma_{0}, \mathrm{p}_{0}\right) \cap M=\left\{\left(x_{0}, \sigma_{0}, \mathrm{p}_{0}\right),\left(x_{1}, \sigma_{1}, \mathrm{p}_{1}\right), \cdots,\left(x_{q}, \sigma_{q}, \mathbf{p}_{q}\right)\right\}
$$

where $\mathrm{p}_{i} \in \mathbb{R}_{+},\left(x_{i}, \sigma_{i}, \mathrm{p}_{i}\right) \in M, i=0,1,2, \cdots, q$. Moreover, in the latter case, we have

$$
\sum_{i=0}^{q} \epsilon_{i} \gamma\left(x_{i}, \sigma_{i}, 2 \pi / \mathrm{p}_{i}\right)=0
$$

where $\gamma\left(x_{i}, \sigma_{i}, 2 \pi / \mathbf{p}_{i}\right)$ is the crossing number of $\left(x_{i}, \sigma_{i}, \mathrm{p}_{i}\right)$ defined by (2.5) and

$$
\epsilon_{i}=\operatorname{sgn} \operatorname{det}\left(\partial_{1} f\left(\sigma_{i}\right)+\partial_{2} f\left(\sigma_{i}\right)\right)
$$

## 4 Global Hopf bifurcation of a model of regulatory dynamics

We consider the following extended Goodwin's model for regulatory dynamics:

$$
\left\{\begin{align*}
\frac{\mathrm{d} x(t)}{\mathrm{d} t} & =-\mu_{m} x(t)+\frac{\alpha_{m}}{1+\left(\frac{z(t-\tau)}{\tilde{z}}\right)^{h}}  \tag{4.1}\\
\frac{\mathrm{~d} y(t)}{\mathrm{d} t} & =-\mu_{p} y(t)+\alpha_{p} x(t-\tau) \\
\frac{\mathrm{d} z(t)}{\mathrm{d} t} & =-\mu_{e} z(t)+\alpha_{e} y(t-\tau) \\
\tau(t) & =c(x(t)-x(t-\tau))
\end{align*}\right.
$$

where $x$ is the concentration of mRNA, $y$ is the concentration of the related protein; $z$ is the concentration of an active enzyme which controls the level of the metabolite functioning as repressor at the DNA level; $\mu_{m}, \mu_{p}$ and $\mu_{e}$ are nonnegative degradation rates; $\alpha_{m}, \alpha_{p}$ and $\alpha_{e}$ are positive coefficients for the inhibition/activation terms; $c$ and $\tilde{z}$ are positive constants; $h$ is an even positive integer. The Goodwin's model [3] without delay $(\tau=0)$ has been extensively studied in system biology modeling various regulatory dynamics. Note that if we freeze the delay $\tau$ at the stationary state in system (4.1), it becomes the classic Goodwin's model without delay.

We are interested in the onset and termination of each Hopf bifurcation branch of periodic solutions which are described as one of the alternatives given in Theorem 3.6. To be specific, we need to obtain the boundedness or unboundedness of the connected component of the pairs of nonconstant periodic solution and parameter in the product space of the state and the parameter space. In the following, we first analyze the local Hopf bifurcation of system (4.1) and then consider the boundedness of periodic solutions of system (4.1) for a global Hopf bifurcation in light of Theorem 3.6.

### 4.1 Local Hopf bifurcation

Note that $h$ is an even positive integer. Every stationary point ( $x, y, z$ ) of System (4.1) satisfies that

$$
\left\{\begin{align*}
-\mu_{m} x+\frac{\alpha_{m}}{1+\left(\frac{z}{\tilde{z}}\right)^{h}} & =0  \tag{4.2}\\
-\mu_{p} y+\alpha_{p} x & =0 \\
-\mu_{e} z+\alpha_{e} y & =0
\end{align*}\right.
$$

and $(x, y, z)=\left(x_{0}, \frac{\alpha_{p}}{\mu_{p}} x_{0}, \frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}} x_{0}\right)$, where by Descartes' rule of signs we know that $x=x_{0}$ is the unique solution of

$$
\mu_{m}\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}}\right)^{h} x^{h+1}+\mu_{m} x-\alpha_{m}=0 .
$$

Freezing the delay of system (4.1) at $\tau=0$ and linearizing the resulting nonlinear system at the stationary state $(x, y, z)=\left(x_{0}, \frac{\alpha_{p}}{\mu_{p}} x_{0}, \frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}} x_{0}\right)$ lead to the characteristic polynomial

$$
\begin{align*}
& \operatorname{det}\left(\lambda I-\left[\begin{array}{ccc}
-\mu_{m} & 0 & -\frac{h \alpha_{m} z^{h-1}}{\tilde{z}^{h}\left(1+\left(\frac{z}{\bar{z}}\right)^{h}\right)^{2}} \\
\alpha_{p} & -\mu_{p} & 0 \\
0 & \alpha_{e} & -\mu_{e}
\end{array}\right]\right) \\
= & \left(\lambda+\mu_{m}\right)\left(\lambda+\mu_{p}\right)\left(\lambda+\mu_{e}\right)+\frac{h \alpha_{m} z^{h-1}}{\tilde{z}^{h}\left(1+\left(\frac{z}{\tilde{z}}\right)^{h}\right)^{2}} \tag{4.3}
\end{align*}
$$

which has a unique negative root and a pair of imaginary roots. In the following, we discuss the existence of purely imaginary eigenvalues as the parameter $\alpha_{m}$ varies. We have
Lemma 4.1 Let $(x, y, z)$ be a stationary state of system 4.1). Then the following equation of $\left(x, \alpha_{m}\right)$

$$
\left\{\begin{align*}
\left(\mu_{m}+\mu_{p}\right)\left(\mu_{e}+\mu_{p}\right)\left(\mu_{e}+\mu_{m}\right) & =\frac{h \alpha_{m}^{3}}{\tilde{z}^{h} \mu_{m}^{2}} \cdot\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}}\right)^{h-1} x^{h-3},  \tag{4.4}\\
\mu_{m} x & =\frac{\alpha_{m}}{1+\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}} x\right)^{h}},
\end{align*}\right.
$$

has a unique solution for $\left(x, \alpha_{m}\right)=\left(x^{*}, \alpha_{m}^{*}\right)$.
Proof Noticing that by the second equation of (4.4), $\frac{\alpha_{m}}{x}=\mu_{m}\left(1+\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}} x\right)^{h}\right)$, we rewrite the first equation of (4.4) into

$$
x^{h}\left(1+\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}} x\right)^{h}\right)^{3}=\frac{\left(\mu_{m}+\mu_{p}\right)\left(\mu_{e}+\mu_{p}\right)\left(\mu_{e}+\mu_{m}\right)}{\frac{h \mu_{m}}{\tilde{z}^{h}}\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}}\right)^{h-1}},
$$

which has a unique positive solution for $x^{h}$ and hence for $x$ with $x=x^{*}$ for some $x^{*}>0$. Then $\alpha_{m}=\alpha_{m}^{*}$ with $\alpha_{m}^{*}=x^{*} \mu_{m}\left(1+\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}} x^{*}\right)^{h}\right)$. The solution of (4.4) is $\left(x, \alpha_{m}\right)=\left(x^{*}, \alpha_{m}^{*}\right)$.
Lemma 4.2 Let $\alpha_{m}^{*}$ be as in Lemma 4.1 and $\lambda=u \pm i v$ be the imaginary roots of the characteristic polynomial at 4.3). Then $u$ and $v$ are continuously differentiable
with respect to $\alpha_{m}$ and $u=0$ if and only if $\alpha_{m}=\alpha_{m}^{*}$. Moreover,

$$
\left.\frac{\mathrm{d} u}{\mathrm{~d} \alpha_{m}}\right|_{\alpha_{m}=\alpha_{m}^{*}}>0 .
$$

Proof Let $(x, y, z)=\left(x_{0}, \frac{\alpha_{p}}{\mu_{p}} x_{0}, \frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}} x_{0}\right)$ be a stationary state of System (4.1) and let

$$
F\left(\lambda, \alpha_{m}\right)=\left(\lambda+\mu_{m}\right)\left(\lambda+\mu_{p}\right)\left(\lambda+\mu_{e}\right)+\frac{h \alpha_{m} z^{h-1}}{\tilde{z}^{h}\left(1+\left(\frac{z}{\tilde{z}}\right)^{h}\right)^{2}} .
$$

Noticing that $z=\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}} x_{0}$ and

$$
\frac{\mathrm{d} x_{0}}{\mathrm{~d} \alpha_{m}}=\frac{1}{\mu_{m}+\mu_{m}(h+1)\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}}\right)^{h} x_{0}^{h}},
$$

we know that $F$ is continuously differentiable with respect to $\left(\lambda, \alpha_{m}\right)$. Let $\left(\lambda, \alpha_{m}\right)$ be such that $F\left(\lambda, \alpha_{m}\right)=0$. Then we have

$$
\begin{aligned}
\frac{\mathrm{d} F}{\mathrm{~d} \lambda}= & \left(\lambda+\mu_{m}\right)\left(\lambda+\mu_{p}\right)\left(\lambda+\mu_{e}\right)\left(\frac{1}{\lambda+\mu_{m}}+\frac{1}{\lambda+\mu_{p}}+\frac{1}{\lambda+\mu_{e}}\right) \\
& =-\frac{h \alpha_{m} z^{h-1}}{\tilde{z}^{h}\left(1+\left(\frac{z}{\tilde{z}}\right)^{h}\right)^{2}}\left(\frac{1}{\lambda+\mu_{m}}+\frac{1}{\lambda+\mu_{p}}+\frac{1}{\lambda+\mu_{e}}\right) .
\end{aligned}
$$

Next we show that $\frac{\mathrm{d} F}{\mathrm{~d} \lambda} \neq 0$ at every solution of $F\left(\lambda, \alpha_{m}\right)=0$. Otherwise, $F$ has a repeated root and the root satisfies

$$
\frac{1}{\lambda+\mu_{m}}+\frac{1}{\lambda+\mu_{p}}+\frac{1}{\lambda+\mu_{e}}=0
$$

which lead to two distinct negative roots:

$$
\lambda=\frac{-\left(\mu_{m}+\mu_{p}+\mu_{e}\right) \pm \sqrt{\left(\mu_{m}+\mu_{e}\right)^{2}+\mu_{p}^{2}-\mu_{p}\left(\mu_{m}+\mu_{e}\right)}}{3} .
$$

This is a contradiction. Then by the Implicit Function Theorem, $\lambda$ is continuously differentiable with respect to $\alpha_{m}$.

Next we bring $\lambda=u+i v$ into the characteristic polynomial at (4.3) we have

$$
\left\{\begin{array}{l}
\left(\left(u+\mu_{m}\right)\left(u+\mu_{p}\right)-v^{2}\right)\left(u+\mu_{e}\right)-\left(\mu_{m}+\mu_{p}+2 u\right) v^{2}+c_{0}=0  \tag{4.5}\\
{\left[\left(u+\mu_{m}\right)\left(u+\mu_{p}\right)-v^{2}+\left(u+\mu_{e}\right)\left(\mu_{m}+\mu_{p}+2 u\right)\right] v=0}
\end{array}\right.
$$

where $c_{0}=\frac{h \alpha_{m} z^{h-1}}{\tilde{z}^{h}\left(1+\left(\frac{z}{z}\right)^{h}\right)^{2}}=\frac{h \alpha_{m}^{3}}{z^{h} \mu_{m}^{2}} \cdot\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}}\right)^{h-1} x^{h-3}$. If $u=0$, then (4.5) leads to

$$
\left\{\begin{align*}
\left(\mu_{m}+\mu_{p}\right)\left(\mu_{e}+\mu_{p}\right)\left(\mu_{e}+\mu_{m}\right) & =c_{0}  \tag{4.6}\\
\mu_{m} \mu_{p}+\mu_{e}\left(\mu_{m}+\mu_{p}\right) & =v^{2}
\end{align*}\right.
$$

where $x$ satisfies $\mu_{m} x=\frac{\alpha_{m}}{1+\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} z} x\right)^{h}}$. By Lemma 4.4, we have $\alpha_{m}=\alpha_{m}^{*}$. By the uniqueness of $\alpha_{m}^{*}, u=0$ if and only if $\alpha_{m}=\alpha_{m}^{*}$.

To compute $\frac{\mathrm{d} u}{\mathrm{~d} \alpha_{m}}$ at $\alpha_{m}=\alpha_{m}^{*}$, we take derivatives with respect to $\alpha_{m}$ on both sides of the equations at (4.5) and then let $u=0$, we obtain

$$
\left\{\begin{array}{c}
{\left[\left(\mu_{e} \mu_{p}+\mu_{e} \mu_{m}+\mu_{m} \mu_{p}\right)-3 v^{2}\right] u^{\prime}-2 v\left(\mu_{m}+\mu_{p}\right) v^{\prime}+c_{0}^{\prime}=0} \\
{\left[2\left(\mu_{m}+\mu_{p}+\mu_{e}\right) v\right] u^{\prime}+\left[\left(\mu_{e} \mu_{p}+\mu_{e} \mu_{m}+\mu_{m} \mu_{p}\right)-3 v^{2}\right] v^{\prime}=0 .}
\end{array}\right.
$$

Then we have

$$
\left.\frac{\mathrm{d} u}{\mathrm{~d} \alpha_{m}}\right|_{\alpha_{m}=\alpha_{m}^{*}}=\frac{-c_{0}^{\prime}\left(\left(\mu_{e} \mu_{p}+\mu_{e} \mu_{m}+\mu_{m} \mu_{p}\right)-3 v^{2}\right)}{\left[\left(\mu_{e} \mu_{p}+\mu_{e} \mu_{m}+\mu_{m} \mu_{p}\right)-3 v^{2}\right]^{2}+4 v^{2}\left(\mu_{m}+\mu_{p}\right)\left(\mu_{m}+\mu_{p}+\mu_{e}\right)} .
$$

By the second equation of (4.6), we have

$$
\left.\frac{\mathrm{d} u}{\mathrm{~d} \alpha_{m}}\right|_{\alpha_{m}=\alpha_{m}^{*}}=\frac{2 c_{0}^{\prime}\left(\mu_{e} \mu_{p}+\mu_{e} \mu_{m}+\mu_{m} \mu_{p}\right)}{\left[\left(\mu_{e} \mu_{p}+\mu_{e} \mu_{m}+\mu_{m} \mu_{p}\right)-3 v^{2}\right]^{2}+4 v^{2}\left(\mu_{m}+\mu_{p}\right)\left(\mu_{m}+\mu_{p}+\mu_{e}\right)} .
$$

Noticing that

$$
\begin{aligned}
c_{0} & =\frac{h \alpha_{m}^{3}}{\tilde{z}^{h} \mu_{m}^{2}} \cdot\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}}\right)^{h-1} x^{h-3} \\
& =\frac{h}{\tilde{z}^{h} \mu_{m}^{2}} \cdot\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}}\right)^{h-1} x^{h}\left(\frac{\alpha_{m}}{x}\right)^{3} \\
& =\frac{h \mu_{m}}{\tilde{z}^{h}} \cdot\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p}}\right)^{h-1} x^{h}\left(1+\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} \tilde{z}} x\right)^{h}\right)^{3}
\end{aligned}
$$

can be regarded as a fourth order polynomial of $x^{h}$ with positive coefficients, and that $\frac{\mathrm{d} x_{0}}{\mathrm{~d} \alpha_{m}}=\frac{1}{\mu_{m}+\mu_{m}(h+1)\left(\frac{\alpha_{e} \alpha_{p}}{\mu_{e} \mu_{p} z}\right)^{h} x_{0}^{h}}>0$, we have

$$
\left.\frac{\mathrm{d} c_{0}}{\mathrm{~d} \alpha_{m}}\right|_{\alpha_{m}=\alpha_{m}^{*}}>0,
$$

hence $\left.\frac{\mathrm{d} u}{\mathrm{~d} \alpha_{m}}\right|_{\alpha_{m}=\alpha_{m}^{*}}>0$.
Notice that $\left.\frac{\mathrm{d} u}{\mathrm{~d} \alpha_{m}}\right|_{\alpha_{m}=\alpha_{m}^{*}}>0$ implies the crossing number at the stationary point $\left(x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right)\right)$ satisifes:

$$
\gamma\left(x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right), \alpha_{m}^{*}, v\left(\alpha_{m}^{*}\right)\right) \neq 0 .
$$

Moreover, we can check that conditions $(S 1-S 3)$ for Theorem 2.7 are satisfied. Then we have the following local Hopf bifurcation theorem for system (4.1).
Theorem 4.3 Let $\alpha_{m}^{*}$ be as in Lemma 4.1. Then system 4.1) undergoes Hopf bifurcation near the stationary point $\left(x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right)\right)$ as $\alpha_{m}$ varies near $\alpha_{m}^{*}$.

### 4.2 Global Hopf bifurcation

In this section, we develop a global Hopf bifurcation theory for system (4.1). By Lemma 4.4 and Theorem 4.3, we know that $\left(x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right)\right)$ is the only Hopf bifurcation point and is an isolated center. To apply the global Hopf bifurcation theorem [3.6, it remains to check condition (S4) and one of the conditions among i), ii) and iii) at Lemma 3.2. We first consider the boundedness of periodic solutions.

Theorem 4.4 Let $(x, y, z)$ be a periodic solution of system 4.1). Then $(x, y, z)$ satisfies for every $t \in \mathbb{R}$,

$$
0<x(t) \leq \frac{\alpha_{m}}{\mu_{m}}, 0<y(t) \leq \frac{\alpha_{p} \alpha_{m}}{\mu_{p} \mu_{m}}, 0<z(t) \leq \frac{\alpha_{e} \alpha_{p} \alpha_{m}}{\mu_{e} \mu_{p} \mu_{m}} .
$$

Proof Note that $h>0$ is an even integer. We have $\dot{x}(t) \leq-\mu_{m} x(t)+\alpha_{m}$, which by Gronwall's inequality leads to

$$
\begin{equation*}
x(t) \leq e^{-\mu_{m} t} x(0)+\frac{\alpha_{m}}{\mu_{m}}\left(1-e^{-\mu_{m} t}\right) \tag{4.7}
\end{equation*}
$$

Since $x$ is periodic, there exists $p>0$ such that $x(t)=x(t+p)$ for every $t \in \mathbb{R}$ and for every $n \in \mathbb{N}$, we have $x(t)=x(t+n p)$. Then for every $t \in \mathbb{R}$ we have $x(t)=x(t+n p) \leq e^{-\mu_{m}(t+n p)} x(0)+\frac{\alpha_{m}}{\mu_{m}}\left(1-e^{-\mu_{m}(t+n p)}\right) \rightarrow \frac{\alpha_{m}}{\mu_{m}}$ as $n \rightarrow \infty$. Therefore, we have $x(t) \leq \frac{\alpha_{m}}{\mu_{m}}$ for every $t \in \mathbb{R}$.

By the same token, with $x(t-\tau) \leq \frac{\alpha_{m}}{\mu_{m}}$, we obtain from the second equation of system (4.1) that $y(t) \leq \frac{\alpha_{p} \alpha_{m}}{\mu_{p} \mu_{m}}, t \in \mathbb{R}$, and subsequently from the third equation of system (4.1) that $z(t) \leq \frac{\alpha_{e} \alpha_{p} \alpha_{m}}{\mu_{e} \mu_{p} \mu_{m}}$ for every $t \in \mathbb{R}$.

To obtain lower bounds of $x, y$ and $z$, let $\bar{x}=-x, \bar{y}=-y$ and $\bar{z}=-z$. Then system (4.1) becomes

$$
\left\{\begin{align*}
\frac{\mathrm{d} \bar{x}(t)}{\mathrm{d} t} & =-\mu_{m} \bar{x}(t)-\frac{\alpha_{m}}{1+\left(\frac{\bar{z}(t-\tau)}{\bar{z}}\right)^{h}}  \tag{4.8}\\
\frac{\mathrm{~d} \bar{y}(t)}{\mathrm{d} t} & =-\mu_{p} \bar{y}(t)+\alpha_{p} \bar{x}(t-\tau) \\
\frac{\mathrm{d} \bar{z}(t)}{\mathrm{d} t} & =-\mu_{e} \bar{z}(t)+\alpha_{e} \bar{y}(t-\tau) \\
\tau(t) & =c(\bar{x}(t-\tau)-\bar{x}(t))
\end{align*}\right.
$$

We have $\dot{\bar{x}}(t)<-\mu_{m} \bar{x}(t)$, which leads to

$$
\begin{equation*}
\bar{x}(t)<e^{-\mu_{m} t} \bar{x}(0) . \tag{4.9}
\end{equation*}
$$

Note that $\bar{x}$ is also $p$-periodic. For every $t \in \mathbb{R}$ we have

$$
\bar{x}(t)=\bar{x}(t+n p)<e^{-\mu_{m}(t+n p)} \bar{x}(0) \rightarrow 0 \text { as } n \rightarrow \infty .
$$

Therefore, we have $\bar{x}(t) \leq 0$ for every $t \in \mathbb{R}$. By the same token, with $\bar{x}(t-\tau) \leq 0$, we obtain from the second equation of system (4.8) that $\bar{y}(t) \leq 0, t \in \mathbb{R}$, and subsequently from the third equation of system (4.8) that $\bar{z}(t) \leq 0$ for every $t \in \mathbb{R}$. Then by the definition of $(\bar{x}, \bar{y}, \bar{z})$, we obtain that for every $t \in \mathbb{R}, x(t) \geq 0, y(t) \geq 0, z(t) \geq 0$.

If there exists $t_{0} \in \mathbb{R}$ such that $x\left(t_{0}\right)=0$, then by the first equation of system (4.1) we have $\dot{x}\left(t_{0}\right)>0$. By the continuity of $\dot{x}$, there exists $\delta>0$ such that $x$ is strictly increasing in $\left(t_{0}-\delta, t_{0}+\delta\right)$. so that $x(t)<0$ for $t \in\left(t_{0}-\delta, t_{0}\right)$. This is a contradiction. By the same token we have $y(t)>0$ and $z(t)>0$ for every $t \in \mathbb{R}$.
Lemma 4.5 Let $f_{0}: \mathbb{R}^{3} \times \mathbb{R}^{3} \times \mathbb{R} \rightarrow \mathbb{R}^{3}$ be defined by

$$
f_{0}\left(\theta_{1}, \theta_{2}\right)=-\left(\begin{array}{c}
\mu_{m} \\
\mu_{p} \\
\mu_{e}
\end{array}\right) \cdot \theta_{1}+\left(\begin{array}{c}
\frac{\alpha_{m}}{1+\left(\frac{z_{2}}{z}\right)^{h}} \\
\alpha_{p} x_{2} \\
\alpha_{e} y_{2}
\end{array}\right)
$$

where $\theta_{1}=\left(x_{1}, y_{1}, z_{1}\right)$ and $\theta_{2}=\left(x_{2}, y_{2}, z_{2}\right)$. Then $f_{0}$ is Lipschitz continuous with a Lipschitz constant

$$
L_{f}=\max \left\{\mu_{m}, \mu_{p}, \mu_{e}, \alpha_{p}, \alpha_{e}, \frac{\alpha_{m} h_{0}}{\tilde{z}}\right\}
$$

where $h_{0}=\frac{h\left(1-\frac{2}{h+1}\right)^{\frac{h-1}{h}}}{\left(1+\frac{h-1}{h+1}\right)^{2}}$.
Proof We use the Mean Value theorem for integrals to obtain a Lipschitz constant. Let $\tilde{\theta}_{1}=\left(\tilde{x}_{1}, \tilde{y}_{1}, \tilde{z}_{1}\right)$ and $\tilde{\theta}_{2}=\left(\tilde{x}_{2}, \tilde{y}_{2}, \tilde{z}_{2}\right)$. Then we have

$$
\begin{align*}
\left|f_{0}\left(\theta_{1}, \theta_{2}\right)-f_{0}\left(\tilde{\theta}_{1}, \tilde{\theta}_{2}\right)\right| \leq & \max \left\{\mu_{m}, \mu_{p}, \mu_{e}\right\}\left|\theta_{1}-\tilde{\theta}_{1}\right| \\
& +\max \left\{\alpha_{p}, \alpha_{e}, \sup _{z_{2}}\left|\frac{\mathrm{~d}}{\mathrm{~d} z_{2}} \frac{\alpha_{m}}{1+\left(\frac{z_{2}}{z}\right)^{h}}\right|\right\}\left|\theta_{2}-\tilde{\theta}_{2}\right| . \tag{4.10}
\end{align*}
$$

We have

$$
\frac{\mathrm{d}}{\mathrm{~d} z_{2}} \frac{\alpha_{m}}{1+\left(\frac{z_{2}}{\tilde{z}}\right)^{h}}=\frac{\alpha_{m} h}{\tilde{z}} \frac{\left(\frac{z_{2}}{\tilde{z}}\right)^{h-1}}{\left(1+\left(\frac{z_{2}}{\tilde{z}}\right)^{h}\right)^{2}}
$$

. Noticing that the map $\mathbb{R} \ni t \rightarrow \frac{t^{h-1}}{\left(1+t^{h}\right)^{2}}$ vanishes at $t=0$ and $t=\infty$ and that

$$
\frac{\mathrm{d}}{\mathrm{~d} t} \frac{t^{h-1}}{\left(1+t^{h}\right)^{2}}=0
$$

if and only if $t= \pm\left(1-\frac{2}{h+1}\right)^{\frac{1}{h}}$, we obtain that $\sup _{z_{2}}\left|\frac{\mathrm{~d}}{\mathrm{~d} z_{2}} \frac{\alpha_{m}}{1+\left(\frac{z_{2}}{\tilde{z}}\right)^{h}}\right|=\frac{\alpha_{m} h_{0}}{\tilde{z}}$ with

$$
h_{0}=\frac{h\left(1-\frac{2}{h+1}\right)^{\frac{h-1}{h}}}{\left(1+\frac{h-1}{h+1}\right)^{2}}
$$

and the supremum is achieved at $\frac{z_{2}}{\tilde{z}}=\left(1-\frac{2}{h+1}\right)^{\frac{1}{h}}$. Then by (4.10) $f_{0}$ is Lipschitz continuous with a Lipschitz constant $L_{f}=\max \left\{\mu_{m}, \mu_{p}, \mu_{e}, \alpha_{p}, \alpha_{e}, \frac{\alpha_{m} h_{0}}{\tilde{z}}\right\}$.

To apply the global Hopf bifurcation theorem, we also use Lemma 3.2 to show the closure of all nontrivial periodic solutions bifurcating from the stationary point $\left(x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right)\right)$ will not include constant solution with zero period.
Lemma 4.6 Let $(x, y, z)$ be a periodic solution of system 4.1). If $\alpha_{m}<\frac{1}{c}$, then $\tau: \mathbb{R} \rightarrow \mathbb{R}$ given by $\tau(t)=c(x(t)-x(t-\tau(t)))$ exists and is continuously differentiable.

Proof The existence and continuity of $\tau$ follows from Lemma 2.1, Let $f_{1}: \mathbb{R}^{2} \rightarrow \mathbb{R}$ be defined by

$$
f_{1}(\tau, t)=\tau-c(x(t)-x(t-\tau))
$$

Then $f_{1}$ is continuously differentiable with respect to $(\tau, t)$. Moreover, by (4.11) we have

$$
\frac{\partial f_{1}(\tau, t)}{\partial \tau}=1-c \dot{x}(t-\tau)
$$

By the first equation of system (4.1) and by Lemma 4.4 we have for every $t \in \mathbb{R}$, $\dot{x}(t)<\alpha_{m}$ and

$$
\begin{equation*}
\dot{x}(t) \geq-\mu_{m} \frac{\alpha_{m}}{\mu_{m}}+\frac{\alpha_{m}}{1+\left(\frac{\alpha_{e} \alpha_{p} \alpha_{m}}{\mu_{e} \mu_{p} \tilde{z}}\right)^{h}}>-\alpha_{m} . \tag{4.11}
\end{equation*}
$$

Then we have $|\dot{x}|<\alpha_{m}$ and by (4.11) we have

$$
\frac{\partial f_{1}(\tau, t)}{\partial \tau}=1-c \dot{x}(t-\tau)>0
$$

By the Implicit Function Theorem, $\tau$ is continuously differentiable at $t \in \mathbb{R}$.
It follows from Lemma 4.6 and ii) of Lemma 3.2 that if $\alpha_{m}<\frac{1}{c}$, then the period p of every nonconstant periodic solution satisfies $\mathrm{p}>\frac{4}{L_{f}\left(2+\|\dot{\tau}\|_{L^{\infty}}\right)}>0$.

Now we are in the position to state the global Hopf bifurcation theorem.
Theorem 4.7 Let $\alpha_{m}^{*}$ be as in Lemma 4.1 and $p^{*}=\frac{2 \pi}{v^{*}}$ where $v^{*}>0$ is the imaginary part of eigenvalue of the formal linearization of system (4.1) at $\alpha_{m}=\alpha_{m}^{*}$. Suppose that $\alpha_{m}^{*}<\frac{1}{c}$. There exists a connected component $\mathcal{C}$ of the closure of all nonconstant periodic solution of system (4.1) bifurcating from $\left(\alpha_{m}^{*}, p^{*}, x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right)\right) \in$ $\mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$, which satisfies that
i) either the projection of $\mathcal{C}$ onto the parameter space of the period p is unbounded.
$i)$ or the projection of $\mathcal{C}$ onto the parameter space of $\alpha_{m}$ does not cross $\alpha=0$ but is not contained in any compact subset of the interval ( $0, \frac{1}{c}$ );

Proof We first show that if $\alpha_{m}=0$, system (4.1) has no nonconstant periodic solutions. Otherwise, let $(x, y, z)$ be a nonconstant periodic solution with $\alpha_{m}=0$. Then from system (4.1) $\dot{x}=-\mu_{m} x$ implies that $x=0$ and subsequently $y=z=0$. This is a contradiction.

In the following we consider $\alpha_{m}$ in $\left(0, \frac{1}{c}\right)$ and introduce the following change of variables:

$$
\begin{equation*}
\alpha_{m}=q(\alpha)=\frac{2}{c \pi}\left(\arctan \alpha-\frac{\pi}{2}\right)+\frac{1}{c}, \tag{4.12}
\end{equation*}
$$

where $q$ is an increasing function of $\alpha$ with $\lim _{\alpha \rightarrow-\infty} q(\alpha)=0$ and $\lim _{\alpha \rightarrow+\infty} q(\alpha)=\frac{1}{c}$. Then system (4.1) is rewritten as

$$
\left\{\begin{align*}
\frac{\mathrm{d} x(t)}{\mathrm{d} t} & =-\mu_{m} x(t)+\frac{q(\alpha)}{1+\left(\frac{z(t-\tau)}{\tilde{z}}\right)^{h}}  \tag{4.13}\\
\frac{\mathrm{~d} y(t)}{\mathrm{d} t} & =-\mu_{p} y(t)+\alpha_{p} x(t-\tau) \\
\frac{\mathrm{d} z(t)}{\mathrm{d} t} & =-\mu_{e} z(t)+\alpha_{e} y(t-\tau) \\
\tau(t) & =c(x(t)-x(t-\tau))
\end{align*}\right.
$$

with $\alpha \in \mathbb{R}$ and $\alpha^{*}=q^{-1}\left(\alpha_{m}^{*}\right)$ the critical value of $\alpha$ for a unique Hopf bifurcation point. By Theorem 4.3 There exists a connected component $\mathcal{C}_{0}$ of the closure of all nonconstant periodic solution of system (4.13) bifurcating from the stationary point $\left(\alpha^{*}, p^{*}, x\left(\alpha^{*}\right), y\left(\alpha^{*}\right), z\left(\alpha^{*}\right)\right) \in \mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$.

By Lemma 4.5, condition (S4) is satisfied by system (4.13). By Lemma 4.6, the function $\tau$ defined by $\tau(t)=c(x(t)-x(t-\tau(t)))$ for a nonconstant periodic solution $(x, y, z)$ of system (4.13) is continuously differentiable. Hence by Lemma 3.2, the period p of every nonconstant periodic solution $(x, y, z)$ of system (4.13) is positive. Notice that $\left(\alpha^{*}, p^{*}, x\left(\alpha^{*}\right), y\left(\alpha^{*}\right), z\left(\alpha^{*}\right)\right)$ is the only bifurcation point of system (4.13), by Theorem 3.6, the connected component $\mathcal{C}_{0}$ is unbounded in $\mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$.

Notice that by Theorem4.4, the projection of $\mathcal{C}_{0}$ onto the space of $(x, y, z) \in C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$ is bounded. The unboundedness of $\mathcal{C}_{0}$ is either because of the unbounded projection onto the parameter space of the period p , or the projection of $\mathcal{C}$ onto the parameter space of $\alpha$.

Notice that $q$ induce a homeomorphism $(q, i d): \mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right) \rightarrow \mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$ defined by

$$
(q, i d)(\alpha, h)=(q(\alpha), h)
$$

The image $\mathcal{C}=(q, i d)\left(\mathcal{C}_{0}\right)$ of $\mathcal{C}_{0}$ under $(q, i d)$ is a connected component of the closure of all nonconstant periodic solution of system (4.1) bifurcating from the bifurcation point $\left(\alpha_{m}^{*}, p^{*}, x\left(\alpha_{m}^{*}\right), y\left(\alpha_{m}^{*}\right), z\left(\alpha_{m}^{*}\right)\right) \in \mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$, which satisfies that either the projection of $\mathcal{C}$ onto the parameter space of the period p is unbounded, or the projection of $\mathcal{C}$ onto the parameter space of $\alpha_{m}$ does not cross the hyperplane $\alpha_{m}=0$ but is not contained in any compact subset of the interval ( $0, \frac{1}{c}$ ).

## 5 Concluding remarks

Motivated by the extended Goodwin's model with a state-dependent delay governed by an algebraic equation, we developed a global Hopf bifurcation theory for differential-algebraic equations with state-dependent delay, using the $S^{1}$-equivariant degree. This is based on the framework described in [6] where the technique of formal linearization is employed to obtain auxiliary linear systems at the stationary states which indicate local and global Hopf bifurcation using a homotopy argument.

The local and global Hopf bifurcation theories are applied to the extended Goodwin's model which describes intracellular processes in the genetic regulatory dynamics. We obtained two alternatives for the connected component $\mathcal{C}$ of periodic solutions in the Fuller space $\mathbb{R}^{2} \times C\left(\mathbb{R} ; \mathbb{R}^{3}\right)$. Namely, the projection of $\mathcal{C}$ onto the parameter space of the period $\mathbf{p}$ is unbounded, or the projection onto the parameter space of $\alpha_{m}$ is not contained in any compact subset of the interval $\left(0, \frac{1}{c}\right)$. We remark that in the previous case, there exists a sequence of periodic solutions with periods going to $\infty$. From (3.6), system (4.1) can be represented as

$$
\frac{2 \pi}{\mathrm{p}} \frac{\mathrm{~d} x}{\mathrm{~d} t}=\mathscr{N}_{0}\left(x, \alpha_{m}, \mathrm{p}\right), \mathrm{p}>0
$$

where $x$ is normalized to be $2 \pi$-periodic. Notice from the definition of $\mathscr{N}_{0}$ at (2.7) that p appears only in the time domain of $\mathscr{N}_{0}$. Note also that the periodic solutions are uniformly bounded with $\alpha_{m} \in\left(0, \frac{1}{c}\right)$. Then with $\mathrm{p} \rightarrow \infty$, this alternative implies the possibility that the system has a sequence of nonconstant periodic solutions with the limiting profile satisfying the algebraic equation $\mathscr{N}_{0}\left(x, \alpha_{m}, \mathrm{p}\right)=0$. See ( [10, [11], [12]) for a discussion of limiting profiles for differential equations with state-dependent delays.

If the projection of $\mathcal{C}$ onto the parameter space of the period $p$ is bounded, we have the latter alternative that the projection of $\mathcal{C}$ onto the parameter space of the period $\alpha_{m}$ is not contained in any compact subset of the interval $\left(0, \frac{1}{c}\right)$. Since $\mathcal{C}$ will not cross the hyperplane $\alpha_{m}=0$, and will not blow up at $\alpha_{m}=\frac{1}{c}$ with the boundedness of the solutions and periods, $\mathcal{C}$ must cross the hyperplane $\alpha_{m}=\frac{1}{c}$ leaving the solutions at $\alpha_{m} \geq \frac{1}{c}$ out of the scope of the discussion.

We also remark that the state-dependent delay in system (1.1) may be negative or
positive and is not a priori advanced or retarded type delay differential equations. It remains open to investigate this type of systems in general settings for a qualitative theory including existence and uniqueness of solutions. For systems with mixed type constant delays, see, among many others, [13, 14].

## References

[1] Balanov, Z., Hu, Q. and Krawcewicz, W., Global Hopf bifurcation of differential equations with threshold-type state-dependent delay, J. Differential Equations, 257 (2014), 2622-2670.
[2] Cooke, K., and Huang, W., On the problem of linearization for state-dependent delay differential equations. Proceedings of the American Mathematical Society 124, 5 (1996), 1417-1426.
[3] Goodwin, B., Oscillatory behavior in enzymatic control processes, Advances in Enzyme Regulation, 3 (1965), 425-438.
[4] Hartung, F., Krisztin, T., Walther, H.-O., and Wu, J., Chapter 5: Functional Differential Equations with State-Dependent Delays: Theory and Applications. In Handbook of Differential Equations: Ordinary Differential Equations, P. D. A. CaÑada and A. Fonda, Eds., vol. 3. North-Holland, 2006, pp. 435-545.
[5] Hu, Q., A model of regulatory dynamics with threshold type state-dependent delay, submitted, 2017.
[6] Hu, Q., and Wu, J., Global Hopf bifurcation for differential equations with statedependent delay. J. Differential Equations 248, 12 (2010), 2801-2840.
[7] Insperger, T., Stépán, G., and Turi, J., State-dependent delay in regenerative turning processes. Nonlinear Dyn. 47 (2007), 275-283.
[8] Krawcewicz, W. and Wu, J., Theory of degrees with applications to bifurcations and differential equations, Canadian Mathematical Society Series of Monographs and Advanced Texts, John Wiley \& Sons, New York, 1997.
[9] Mallet-Paret, J. and Yorke, A. J., Snakes: oriented families of periodic orbits, their sources, sinks, and continuation, J. Differential Equations 43 (1982), 419-450.
[10] Mallet-Paret, J., and Nussbaum, R. Boundary layer phenomena for differentialdelay equations with state-dependent time lags, I. Archive for rational mechanics and analysis 120, 2 (1992), 99-146.
[11] Mallet-Paret, J., and Nussbaum, R. Boundary layer phenomena for differentialdelay equations with state dependent time lags: II. Journal fur die Reine und Angewandte Mathematik (1996), 129-197.
[12] Mallet-Paret, J., and Nussbaum, R. Boundary layer phenomena for differentialdelay equations with state-dependent time lags: III. Journal of Differential Equations 189, 2 (2003), 640-692.
[13] Mallet-Paret, J. The Fredholm alternative for functional differential equations of mixed type. J. Dynamics and Differential Equations, 11 (1999), 1-47.
[14] Rustichini, A. Hopf bifurcation for functional differential equations of mixed type. J. Dynamics and Differential Equations, 1 (1989), 145-177.
[15] Smith, H., Structured population models, threshold-type delay and functionaldifferential equations. Delay and differential equations, AMS, IA, 1991 (1992), 52 -64 .
[16] Walther, H., Stable periodic motion of a system using echo for position control, Journal of Dynamics and Differential Equations 15 (2003), no. 1, 143-223
[17] Walther, H., Smoothness properties of semiflows for differential equations with statedependent delays, Journal of Mathematical Sciences 124 (2004), 5193-5207.
[18] Smith, H. L., Reduction of structured population models to threshold-type delay equations and functional differential equations: a case study. Mathematical Biosciences 113, 1 (1993), 1 - 23.
[19] Vidossich, V., On the structure of periodic solutions of differential equations, $J$. Differential Equations 21 (1976), 263 - 278.
[20] Wu, J., Global continua of periodic solutions to some differential equations of neutral type, Tôhoku Math J., 45 (1993), 67-88.

