Bifurcation analysis on a survival red blood cells model

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Abstract

In this paper, we consider a model described the survival of red blood cells in animal. Its dynamics are studied in terms of local and global Hopf bifurcations. We show that a sequence of Hopf bifurcations occur at the positive equilibrium as the delay crosses some critical values. Using the reduced system on the center manifold, we also obtain that the periodic orbits bifurcating from the positive equilibrium are stable in the center manifold, and all Hopf bifurcations are supercritical. Further, particular attention is focused on the continuation of local Hopf bifurcation. We show that global Hopf bifurcations exist after the second critical value of time delay.

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1. Introduction

In order to describe the survival of red blood cells in animal Wazewska-Czyzewska and Lasota [11] proposed the following autonomous functional differential equation

$$\frac{dN}{dt} = -\delta N(t) + \rho e^{-\gamma N(t-\tau)}, \quad t \geq 0, \quad \delta > 0, \quad \rho > 0, \quad \gamma > 0, \quad \tau > 0,$$

(1)

where \(N(t)\) denotes the number of red blood cells at time \(t\), \(\delta\) is the rate of the red blood cells, \(\rho\) and \(\gamma\) describe the production of red blood cells per unite time and \(\tau\) is the time required to produce a red blood cell. There is an extensive literature concerning oscillation, global attractivity and periodicity of Eq. (1) and its general case with periodic coefficients (see, for example, [1,4–8,10] and references therein). As far as we know, there are few papers on the bifurcation analysis of Eq. (1), especially global Hopf bifurcation. In this paper, both local and global Hopf bifurcations are studied.

To be specific and to make statement easy, let

$$\sigma = \frac{\delta}{\gamma \rho}, \quad \nu = \tau \gamma \rho, \quad u(t) = \gamma N\left(\frac{t}{\gamma \rho}\right).$$

Then Eq. (1) is transformed into

$$u'(t) = -\sigma u(t) + e^{-u(t-\nu)}, \quad t \geq 0, \quad \sigma > 0, \quad \nu > 0,$$

(2)

and we only consider Eq. (2) in the sequel. It is easy to verify that Eq. (2) has an unique steady state \(u_*\), which is positive and satisfies

$$\sigma u_* = e^{-u_*}.$$

(3)

It is worth mentioning that using a fixed theorem, Chow [1] has shown that if \(0 < \sigma < 1/e\), then there exists an \(H, H > 2/\sigma u_*\), such that for every \(\nu > H\) there exists a non-constant periodic solutions. However, the stability and direction of local Hopf bifurcations were not considered in [1]. In the present paper, we compute the reduced system on the center manifold associated with the pair of conjugate complex, purely imaginary solutions. By this reduction, we are able to determine stability and direction of local Hopf bifurcations. Further, we use a different approach, the degree theory, to study the global existence of periodic solutions of Eq. (2). We show that if \(0 < \sigma < 1/e\), then Eq. (2) has at least \(k\) periodic solutions after the \(k\)th \((k \geq 1)\) critical value of the delay \(\nu\).

2. Existence of local Hopf bifurcations

By the translation \(y(t) = u(t) - u_*\), Eq. (2) is written as

$$y'(t) = -\sigma y(t) + \sigma u_*\left(e^{-y(t-\nu)} - 1\right).$$

(4)

It is well known that the stability of the positive steady state and local Hopf bifurcations can be determined by the distribution of the roots associated with the characteristic equation of its linearization, and the positive steady state \(u_*\) of Eq. (2) is stable if and only if the zero steady state of Eq. (4) is stable. Thus, we consider linearization of Eq. (4) at \(y = 0\):
\[ y'(t) = -\sigma y(t) - \sigma u^* y(t - \nu). \quad (5) \]

The characteristic equation of (5) is
\[ \lambda + \sigma + \sigma u^* e^{-\lambda \nu} = 0. \quad (6) \]

For \( \nu = 0 \), the only root of (5) is \( \lambda = -\sigma - \sigma u^* < 0 \). We first examine when Eq. (6) has pure imaginary roots \( \lambda = \pm i\omega (\omega > 0) \). Obviously, \( i\omega \) is a root of (6) if and only if
\[ i\omega + \sigma + \sigma u^* (\cos(\omega \nu) - i \sin(\omega \nu)) = 0. \]

Separating the real and imaginary parts, we obtain
\[ -\sigma = \sigma u^* \cos(\omega \nu), \quad \omega = \sigma u^* \sin(\omega \nu), \quad (7) \]

which lead to
\[ \omega^2 = \sigma^2 (u^*^2 - 1). \]

By (3), it is easy to show that \( u^* > 1 \) if and only if \( \sigma < 1/e \). Hence, \( \omega = \sigma \sqrt{u^*^2 - 1} \) if
\[ 0 < \sigma < \frac{1}{e}. \]

Let
\[ \nu_k = \frac{1}{\sigma \sqrt{u^*^2 - 1}} \left[ \arccos \left( -\frac{1}{u^*} \right) + 2k\pi \right], \quad k = 0, 1, 2, \ldots, \quad (8) \]

and
\[ \omega_0 = \sigma \sqrt{u^*^2 - 1}. \quad (9) \]

Then Eq. (6) has a pair of purely imaginary roots \( \pm \omega_0 i \) provided that \( 0 < \sigma < 1/e \) and \( \nu = \nu_k \).

Let \( \lambda = \eta(\nu) + i\omega(\nu) \) denote a root of (6) near \( \nu = \nu_k \), such that
\[ \eta(\nu_k) = 0, \quad \omega(\nu_k) = \omega_0. \]

Substituting \( \lambda_k \) into (6) and differentiating with respect to \( \nu \), we have
\[ \frac{d\lambda}{dv} - \sigma u^* \left( \lambda + \nu \frac{d\lambda}{dv} \right) e^{-\lambda \nu} = 0. \]

It follows that
\[ \left( \frac{d\lambda}{dv} \right)^{-1} = \frac{1}{\lambda \sigma u^* e^{-\lambda \nu}} - \frac{\nu}{\lambda}. \]

This, together with (7), yields
\[ \text{Re} \left( \frac{d\lambda}{dv} \right)^{-1} \bigg|_{\nu = \nu_k} = \text{Re} \left( \frac{1}{\omega_0 i (\sigma u^* \cos(\omega \nu) - \sigma u^* \sin(\omega \nu))} \right) = \text{Re} \left( \frac{1}{-\omega_0 i (\sigma + i\omega_0)} \right) \]
\[ = \frac{1}{\sigma^2 + \omega_0^2} = \frac{1}{(\sigma u^*)^2}, \]
where we have used the fact that $\omega_0^2 = \sigma^2 (u_0^2 - 1)$. Thus, we have

$$\text{sign} \left\{ \frac{d \text{Re} \lambda}{d \nu} \right\}_{\nu = \nu_k} = \text{sign} \left\{ \text{Re} \left( \frac{d \lambda}{d \nu} \right)_{\nu = \nu_k}^{-1} \right\} = \text{sign} \left\{ \frac{1}{(\sigma u_*)^2} \right\} = 1,$$

i.e.,

$$\frac{d \text{Re} \lambda}{d \nu} \bigg|_{\nu = \nu_k} > 0. \quad (10)$$

From the above discussions, we can state the lemma below.

**Lemma 2.1.** If $\sigma \geq 1/e$, then all roots of the characteristic Eq. (6) have negative real parts. If $0 < \sigma < 1/e$, then the following hold.

(i) When $\nu = \nu_k$ ($k = 0, 1, 2, \ldots$), Eq. (6) has a pair of simple imaginary roots $\pm i \alpha_0$.

(ii) When $\nu \in [0, \nu_0)$, all roots of Eq. (6) have negative real parts, and when $\nu = \nu_0$, all roots of Eq. (6), except $\pm i \omega_0$, have negative real parts. But when $\nu \in (\nu_k, \nu_{k+1})$, Eq. (6) has $2(k+1)$ roots with positive real parts.

From Lemma 2.1 and the transversality condition (10), we may easily obtain the following results about the stability of the positive equilibrium and the local Hopf bifurcation for (2).

**Theorem 2.1.** If $\sigma \geq 1/e$, then the steady state $u_*$ is asymptotically stable for all $\nu \geq 0$. If $0 < \sigma < 1/e$, then we have

(i) the steady state $u_*$ is asymptotically stable for $\nu \in [0, \nu_0)$, and unstable for $\nu > \nu_0$; and

(ii) (2) undergoes a Hopf bifurcation at the positive equilibrium $u_*$ when $\nu = \nu_k$, for $k = 0, 1, 2, \ldots$.

3. Direction and stability of the Hopf bifurcation

From Theorem 2.1, we know that when $0 < \sigma < 1/e$ (equivalently, $u_* > 1$), Eq. (2) undergoes Hopf bifurcation at $\nu = \nu_k$, $k = 0, 1, \ldots$. We want now to determine the direction, stability of the bifurcating non-trivial periodic solutions at $\nu = \nu_k$. To accomplish this, we use the normal form procedure described in [2,3], where the algorithm used here can be found.

For convenience, let $x(t) = y(\nu t)$ and $\nu = \nu_k + \alpha$. Then (4) can be written as an FDE in $C = C([-1, 0], R)$ as

$$x'(t) = L_\alpha (x(t)) + F(x(t), \alpha), \quad (11)$$

where $L_\alpha : C \to R$, $f : R \times C \to R$ are given respectively by

$$L_\alpha (\phi) = -(\nu_k + \alpha) \sigma \phi(0) - (\nu_k + \alpha) \sigma u_* \phi(-1), \quad (12)$$
and

\[ F(\phi, \alpha) = (v_\kappa + \alpha)\sigma u_* \left[ \frac{1}{2!}\phi^2(-1) - \frac{1}{3!}\phi^3(-1) + O(\phi^4(-1)) \right]. \quad (13) \]

Clearly, when \( \alpha = 0 \), the characteristic equation of (11) at the zero steady state has two simple, purely imaginary characteristic roots \( \pm i\omega_0\nu_k \). Thus, the center manifold considered is two dimensional. Following [3], let

\[ B(\nu_k, \sigma u_*) = \frac{1}{2i\omega_0\nu_k - L_0(e^{2i\omega_0\nu_k}\theta)} \]

and thus, we can compute the reduced system on the center manifold in polar coordinates \((\rho, \xi)\) (see [3, p. 194]):

\[ \dot{\rho} = \alpha \frac{d}{dv} \left\{ \text{Re} \lambda(v_k) \right\} \rho + K\rho^3 + O(\alpha^2 \rho + |(\rho, \alpha)|), \]

\[ \dot{\xi} = -v_\kappa \omega_0 + O\left(|(\rho, \alpha)|\right), \quad (15) \]

where

\[ K = \text{Re} \left[ \frac{1}{L_0(\theta e^{i\omega_0\nu_k}\theta)} \left( B_{(2,1,0,0)} - \frac{B_{(1,1,0,0)}B_{(1,0,1,0)}}{L_0(1)} + \frac{B_{(2,0,0,0)}B_{(0,1,0,1)}}{2i\omega_0\nu_k - L_0(e^{2i\omega_0\nu_k}\theta)} \right) \right]. \]

It is well known (e.g., [3]) that the sign of \( K \) determines the direction of the bifurcation (supercritical if \( K \) > 0, subcritical if \( K < 0 \)), and that the sign of \( K \) determines the stability of the bifurcating periodic orbits (stable if \( K < 0 \), unstable if \( K > 0 \)). From (10), \( \frac{d}{dv}\left\{ \text{Re} \lambda(v_k) \right\} > 0 \). So, it suffices to determine the sign of \( K \).

By (13), for \( (x_1, x_2, x_3, x_4) \in R^4 \)

\[ F(x_1 e^{i\omega_0\nu_k}\theta + x_2 e^{-i\omega_0\nu_k}\theta + x_3 1 + x_4 e^{2i\omega_0\nu_k}\theta, 0) \]

\[ = v_\kappa \sigma u_* \left[ \frac{1}{2} \left( x_1 e^{-i\omega_0\nu_k} + x_2 e^{i\omega_0\nu_k} + x_3 + x_4 e^{-2i\omega_0\nu_k} \right)^2 \right. \]

\[ - \frac{1}{6} \left( x_1 e^{-i\omega_0\nu_k} + x_2 e^{i\omega_0\nu_k} + x_3 + x_4 e^{-2i\omega_0\nu_k} \right)^3 + \cdots \]

\[ = v_\kappa \sigma u_* \left( \frac{1}{2} e^{-2i\omega_0\nu_k} x_1^2 + x_1 x_2 + e^{-i\omega_0\nu_k} x_1 x_3 + e^{-i\omega_0\nu_k} x_2 x_4 - \frac{1}{2} e^{-i\omega_0\nu_k} x_1^2 x_2 + \cdots \right). \]

Comparing with (14), we have \( B_{(2,0,0,0)} = \frac{1}{2} v_\kappa \sigma u_* e^{-2i\omega_0\nu_k} \), \( B_{(1,1,0,0)} = v_\kappa \sigma u_* \), \( B_{(1,0,1,0)} = v_\kappa \sigma u_* e^{-i\omega_0\nu_k} \), \( B_{(0,1,0,1)} = v_\kappa \sigma u_* e^{-i\omega_0\nu_k} \), \( B_{(2,1,0,0)} = -\frac{1}{2} v_\kappa \sigma u_* e^{-i\omega_0\nu_k} \). This, together with (6) and (12), means

\[ K = \frac{A}{B}, \quad (16) \]

where
\[ B = 2C^2(1 + u_*)^2[(1 + C)^2 + C^2(u_*^2 - 1)](5u_* - 4) > 0, \]
\[ A = -C\left(2k\pi + \arccos\left(-\frac{1}{u_*}\right)\right)^2 \left\{ (u_* - 4)(u_* + 1)\left(1 + \frac{u_*^2(2k\pi + \arccos(-\frac{1}{u_*}))}{\sqrt{u_*^2 - 1}}\right) \right. \\
\left. - \frac{1}{u_*^2 - 1}(1 + u_*)^2 \left[ 4 - 4u_* - u_*^2(3 - 2u_* + \frac{\pi(u_*^2 + 2u_* - 2)}{2\sqrt{u_*^2 - 1}}) \right] \right\} > -C\left(2k\pi + \arccos\left(-\frac{1}{u_*}\right)\right)^2 \left\{ (u_* - 4)(u_* + 1)\left(1 + \frac{\pi u_*^2}{2\sqrt{u_*^2 - 1}}\right) \right. \\
\left. - \frac{1}{u_*^2 - 1}(1 + u_*)^2 \left[ 4 - 4u_* - u_*^2(3 - 2u_* + \frac{\pi(u_*^2 + 2u_* - 2)}{2\sqrt{u_*^2 - 1}}) \right] \right\}, \]
where \( C = \frac{\arccos(-1/u_*) + 2k\pi}{\sqrt{u_*^2 - 1}} \).

Let
\[ g(u_*) = (5u_* - 4)(u_* + 1)\left(1 + \frac{\pi u_*^2}{2\sqrt{u_*^2 - 1}}\right) \\
- \frac{(1 + u_*)^2}{u_*^2 - 1}\left[ 4 - 4u_* - u_*^2(3 - 2u_* + \frac{\pi(u_*^2 + 2u_* - 2)}{2\sqrt{u_*^2 - 1}}) \right], \]
from which we obtain that when \( u_* > 1 \), \( g(u_*) \) has a unique minimum \( g(\tilde{u}_*) \approx 93.368 \), where \( \tilde{u}_* \approx 1.35952 \) (see Fig. 1). Thus, \( A < 0 \) as \( u_* > 1 \). It follows from (16) that \( K < 0 \) provided that \( u_* > 1 \). As a consequence, we obtain the following theorem.

**Theorem 3.1.** If \( 0 < \sigma < 1/e \), then, on the center manifold for (11) (or (2)) the periodic orbits bifurcating from the zero steady state (or \( u_* \)) at \( \nu_k \) are stable, and the Hopf bifurcations are supercritical.

**Example 1.** Consider Eq. (2) with \( \sigma = 0.3 \),
\[ u'(t) = -0.3u(t) + e^{-u(t-v)}. \] (17)
Fig. 2. The steady state $u_*$ of (17) is orbitally, asymptotically stable when $\nu = 18 < \nu_0 \doteq 19.2089$.

Fig. 3. The bifurcating periodic solution is orbitally, asymptotically stable when $\nu_0 \doteq 19.2089 < \nu = 20 < \nu_1 = 25.492$, near $\nu_0$.

Fig. 4. The bifurcating periodic solution is orbitally, asymptotically stable when $\nu_1 = 25.492 < \nu = 26 < \nu_2 \doteq 31.7752$, near $\nu_1$.

From Section 2, we have

$$u_* \doteq 1.10454, \ \nu_0 \doteq 19.2089, \ \nu_1 \doteq 25.492, \ \nu_2 \doteq 31.7752, \ \nu_3 \doteq 38.0584, \ldots$$

By Theorems 2.1 and 3.1, the steady state $u_*$ is stable for $\nu \in [0, \nu_0)$ (see Fig. 2), and the Hopf bifurcation occurs as $\nu$ crosses $\nu_k$ to the right, with stable non-trivial periodic solutions, as plotted in Figs. 3 and 4. Generally speaking, these obtained bifurcating peri-
Fig. 5. The bifurcating periodic solution exists when $v_0 = 19.2089 < v = 25 < v_1 = 25.492$, near $v_1$.

Fig. 6. The bifurcating periodic solution exists when $v_1 = 25.492 < v = 28 < v_2 = 31.7752$.

Fig. 7. The bifurcating periodic solution still exists when $v_1 = 25.492 < v = 31 < v_2 = 31.7752$, far away from the critical value $v_1$.

Periodic solutions only exist in the left small neighborhood of the critical value since the Hopf bifurcations are supercritical. However, the numerical simulations show that the bifurcating periodic solutions still exist when the delay $v$ is far away from the critical value (see Figs. 5–7). In the next section, we investigate the global existence of periodic solutions, motivated by these numerical simulations and the previous success of Ruan and Wei [9], Wei and Li [12], and Wu [13].
4. Global continuation of local Hopf bifurcations

In this section, we study the global continuation of periodic solutions bifurcating from the positive equilibrium \( u^* \). Let \( x(t) = u(\nu t) \). Then Eq. (2) becomes

\[
\dot{x}(t) = -\nu \left[ \sigma x(t) - e^{x(t-1)} \right].
\]

(18)

Throughout this section, we follow closely the notations used in Wu [13]. For simplification of notations, we rewrite (18) as the following functional differential equation

\[
\dot{x}(t) = F(x_t, \nu, T),
\]

(19)

where \( x_t(\theta) = x(t + \theta) \in C([-1, 0], \mathbb{R}) \) and \( F(x_t, \nu, T) = -\nu [\sigma x(t) - e^{x(t-1)}] \). Clearly, the characteristic equation of Eq. (19) at the unique steady state \( x^* = u^* \) is

\[
\lambda + \nu \sigma + \nu \sigma u^* e^{-\lambda} = 0.
\]

Following the work of Wu [13], we need to define

\[
X = C([-1, 0], \mathbb{R}),
\]

\[
\Sigma = \text{Cl}\{ (x, \nu, T) \in X \times R \times R^+; x \text{ is a } T\text{-periodic solution of (19)} \},
\]

\[
M = \{ (\bar{x}, \nu, T); F(\bar{x}, \nu, T) = 0 \},
\]

\[
\Delta(\bar{x}, \nu, T)(\lambda) = \lambda + \nu \sigma + \nu \sigma \bar{x} e^{-\lambda}.
\]

From [13], we know that \((\bar{x}, \nu, T)\) is called a center if \((\bar{x}, \nu, T) \in u\) and \(\Delta(\bar{x}, \nu, T)(\lambda) = 0\). A center \((\bar{x}, \nu, T)\) is said to be isolated if it is the only center in some neighborhood of \((\bar{x}, \nu, T)\). For the benefit of the readers, we first state the global Hopf bifurcation theory due to Wu [13] for functional differential equations.

Lemma 4.1 (Wu [13]). Assume that \((\bar{x}, \nu, T)\) is an isolated center satisfying the hypotheses \((A_1)-(A_4)\) in Wu [13, p. 4814]. Denote by \(\ell(\bar{x}, \nu, T)\) the connected of \((\bar{x}, \nu, T)\) in \(\Sigma\). Then either

(i) \(\ell(\bar{x}, \nu, T)\) is unbounded, or

(ii) \(\ell(\bar{x}, \nu, T)\) is bounded, \(\ell(\bar{x}, \nu, T) \cap u\) is finite and

\[
\sum_{(\bar{x}, \nu, T) \in \ell(\bar{x}, \nu, T) \cap M} \gamma_m(\bar{x}, \nu, T) = 0
\]

for all \( m = 1, 2, \ldots \), where \( \gamma_m(\bar{x}, \nu, T) \) is the \( m \)-th crossing number of \((\bar{x}, \nu, T)\) if \( m \in J(\bar{x}, \nu, T) \), or it is zero if otherwise.

Clearly, if (ii) in Lemma 4.1 is not true, then \(\ell(\bar{x}, \nu, T)\) is unbounded. Thus, if the projections of \(\ell(\bar{x}, \nu, T)\) onto \(x\)-space and onto \(T\)-space are bounded, then the projection of \(\ell(\bar{x}, \nu, T)\) onto \(\nu\)-space is unbounded. Further, if we can show that the projection of \(\ell(\bar{x}, \nu, T)\) onto \(\nu\)-space is away from zero, then the projection of \(\ell(\bar{x}, \nu, T)\) onto \(\nu\)-space must include interval \([\nu, \infty)\). In the following, we follow this ideal to prove our main results about the
global Hopf bifurcation. From Section 2, it is easy to see that $(u_*, v_k, 2\pi/(v_k\omega_0))$ are isolated centers, and the connected component $\ell_{(u_*, v_k, 2\pi/(v_k\omega_0))}$ through the isolated center $(u_*, v_k, 2\pi/(v_k\omega_0))$ in $\Sigma$ is non-empty, where $v_k$ is defined in (8). The remainder of this section, we show that the projection of $\ell_{(u_*, v_k, 2\pi/(v_k\omega_0))}$ onto $v$-space must include interval $[v_k, \infty)$ provided that $0 < \sigma < 1/e$ and $k \geq 1$.

**Lemma 4.2.** All periodic solutions of (18) are uniformly bounded.

**Proof.** For a periodic function $x(t)$, define
\[
x(\xi) = \min\{x(t)\}, \quad x(\eta) = \max\{x(t)\}.
\]
Let $x(t)$ be a non-constant periodic solution of (18). Then, $x'(\xi) = 0$ and $x'(\eta) = 0$. That is
\[
\begin{align*}
\sigma x(\xi) - e^{-x(\xi-1)} &= 0, \quad (21) \\
\sigma x(\eta) - e^{-x(\eta-1)} &= 0. \quad (22)
\end{align*}
\]
Equation (21) yields
\[
x(\xi) > 0,
\]
which leads to
\[
x(\eta - 1) \geq x(\xi) > 0.
\]
This, together with (22), implies
\[
x(\eta) < \frac{1}{\sigma}, \quad (23)
\]
from which, together with (21), we have
\[
x(\xi) > \frac{1}{\sigma} \exp \left\{ -\frac{1}{\sigma} \right\}. \quad (24)
\]
Equations (23) and (24) show that if $x(t)$ be a non-constant periodic solution of (18), then
\[
\frac{1}{\sigma} \exp \left\{ -\frac{1}{\sigma} \right\} < x(t) < \frac{1}{\sigma}. \quad (25)
\]
This completes the proof. \qed

**Lemma 4.3.** Equation (18) has no periodic solutions of period 1.

**Proof.** This result easily follows from the fact that the ordinary differential equation
\[
x'(t) = -v[\sigma x(t) - e^{-x(t)}]
\]
has a no non-trivial periodic solution. \qed

**Theorem 4.1.** If $0 < \sigma < 1/e$, then, for each $v > v_k$ ($k \geq 1$), Eq. (18) has at least $k$ periodic solutions, where $v_k$ is defined by (8).
**Proof.** To obtain the above result, it is sufficient to prove that the projection of \( \ell(u_*, v_k, 2\pi/(v_k\omega_0)) \) onto \( v \)-space is \([\bar{v}, \infty)\) for each \( k \geq 1 \).

For an isolated center \((u_*, v_k, 2\pi/(v_k\omega_0))\), it follows from Section 2 that there exist \( \epsilon > 0, \delta > 0 \) and a smooth curve \( \lambda: (v_k - \delta, v_k + \delta) \rightarrow C \) such that \( \Delta(\lambda(v)) = 0, |\lambda(v) - iv_k\omega_0| < \epsilon \) for all \( v \in [v_k - \delta, v_k + \delta] \) and

\[
\lambda(v_k) = v_k\omega_0i, \quad \frac{d(Re \lambda(v))}{dv} \bigg|_{v=v_k} > 0.
\]

Let

\[
\Omega_{\epsilon, 2\pi/v_k\omega_0} = \left\{ (\eta, T): 0 < \eta < \epsilon, \left| T - \frac{2\pi}{v_k\omega_0} \right| < \epsilon \right\}.
\]

It is easy to verify that on \([v_k - \nu, v_k + \nu] \times \partial\Omega_{\epsilon, 2\pi/(v_k\omega_0)}\),

\[
\Delta(u_*, v, T) \left( \eta + \frac{2\pi}{T}i \right) = 0 \quad \text{if and only if} \quad \eta = 0, \quad v = v_k, \quad T = \frac{2\pi}{v_k\omega_0}.
\]

Therefore, the hypotheses \((A_1) \sim (A_4)\) in Wu [13] are satisfied for \( m = 1 \). Moreover, if we define

\[
H^\pm(u_*, v_k, \frac{2\pi}{v_k\omega_0}) \left( \eta, T \right) = \Delta(u_*, v_k \pm \delta, T) \left( \eta + \frac{2\pi}{T} \right),
\]

then we have the crossing number of the isolated center \((u_*, v_k, 2\pi/(iv_k\omega_0))\) as follows

\[
\gamma \left( u_*, v_k, \frac{2\pi}{v_k\omega_0} \right) = \deg_B \left( H^- \left( u_*, v_k, \frac{2\pi}{v_k\omega_0} \right), \Omega_{\epsilon, 2\pi/v_k\omega_0} \right) - \deg_B \left( H^+ \left( u_*, v_k, \frac{2\pi}{v_k\omega_0} \right), \Omega_{\epsilon, 2\pi/v_k\omega_0} \right) = -1,
\]

where \( \deg_B \) denotes the Brouwer degree. Thus, we have

\[
\sum_{(\bar{x}, \bar{v}, \bar{T}) \in \ell(u_*, v_k, 2\pi/(v_k\omega_0))} \gamma(\bar{x}, \bar{v}, \bar{T}) < 0,
\]

where \((\bar{x}, \bar{v}, \bar{T})\), in fact, has the form as \((u_*, v_k, 2\pi/(iv_k\omega_0))\) \((k = 0, 1, \ldots)\). It follows from Lemma 4.1 that the connected component \( \ell(u_*, v_k, 2\pi/(v_k\omega_0)) \) through \((u_*, v_k, 2\pi/(iv_k\omega_0))\) in \( \Sigma \) is unbounded. From (8), we have

\[
v_k\omega_0 = \arccos \left( -\frac{1}{u_*} \right) + 2k\pi > 2\pi, \quad \text{for} \ k \geq 1.
\]

Thus, there exists an \( n_k \in N \) such that

\[
\frac{1}{n_k} < \frac{2\pi}{v_k\omega_0} < 1.
\]

This, together with Lemma 4.3, implies that \( 1/n_k < T < 1 \) if \((x, v, T) \in \ell(u_*, v_k, 2\pi/(v_k\omega_0))\). In addition, from Lemma 4.2, we known that the projection of \( \ell(u_*, v_k, 2\pi/(v_k\omega_0)) \) onto \( x \)-space is bounded. Thus, if the connected component \( \ell(u_*, v_k, 2\pi/(v_k\omega_0)) \) is unbounded, then its
projection onto the $\nu$-space must be unbounded and includes $[\tau_k, \infty)$. The above discussion shows that, for each $\nu > \nu_k$, Eq. (18) has a non-constant periodic solution with a period in $(1/n_k, 1)$. This completes the proof. \hfill \Box

5. Conclusions

In this paper, we investigated local and global Hopf bifurcations in a survival red blood cells model. We have shown that, as the delay $\nu$ increases, the positive equilibrium $u_*$ loses its stability and a sequence of Hopf bifurcations (local) occur at $u_*$. Using center manifold reduction, we have shown that the periodic orbits bifurcating from the steady state $u_*$ at $\nu_k$ are stable on the center manifold, and the Hopf bifurcation occurs as $\nu$ crosses $\nu_k$ to the right. In particular, the stability of the bifurcating periodic solutions of Eq. (2) is coincidence with that on the center manifold at the first critical value. Recently, numerous researchers have studied the Hopf bifurcation in a delay-differential equation. However, most of them only dealt with the local Hopf bifurcation. Namely, their obtained results remain valid only when the parameter is in a small neighborhood of the critical value. In the present paper, the existence of periodic solutions for $\nu$ far away from the local Hopf bifurcation values was also established. More specifically, we have shown that, for each $\nu \in [\nu_k, \infty) \ (k \geq 1)$, Eq. (2) has at least $k$ periodic solutions. Unfortunately, there are the following questions which the authors have not been able to investigate completely.

1. For $\nu \in [\nu_0, \nu_1)$, we only knew that Eq. (2) has orbitally asymptotically stable periodic solutions when $\nu > \nu_0$ and close to $\nu_0$. But it is unknown that whether Eq. (2) has a periodic solution for any $\nu \in [\nu_0, \nu_1)$.

It is the main difficulty to answer this question that we cannot rule out 4-periodic solutions of Eq. (18). For a contradiction, suppose that $x(t)$ is a periodic solution to Eq. (18) of period 4. Set $u_j(t) = x(t - j + 1), j = 1, 2, 3, 4$. Then $u(t) = (u_1(t), u_2(t), u_3(t), u_4(t))$ is a periodic solution to the following system of ordinary differential equations

\[
\begin{align*}
    u_1'(t) &= -\nu \sigma [u_1(t) - \frac{1}{\sigma} e^{-u_2(t)}], \\
    u_2'(t) &= -\nu \sigma [u_2(t) - \frac{1}{\sigma} e^{-u_3(t)}], \\
    u_3'(t) &= -\nu \sigma [u_3(t) - \frac{1}{\sigma} e^{-u_4(t)}], \\
    u_4'(t) &= -\nu \sigma [u_4(t) - \frac{1}{\sigma} e^{-u_1(t)}],
\end{align*}
\]

whose orbits, by (25), belong to the region

\[
G = \left\{ u \in R^4 \mid \frac{1}{\sigma} \exp \left\{ -\frac{1}{\sigma} \right\} < u_j < \frac{1}{\sigma}, \ j = 1, 2, 3, 4 \right\}. \tag{27}
\]

Clearly, it is still very difficult to prove the non-existence of non-constant periodic solutions of system (26) even though the similar problem has been solved in [12].
2. From the global Hopf bifurcation theory due to Wu [13], we obtained the existence of periodic solutions for a large range \( \nu \in [\nu_1, \infty) \), but this approach seems to generate little information for the stability.

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References