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Transient oscillations induced by delayed growth response in the chemostat*

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Abstract. In this paper, in order to try to account for the transient oscillations observed in chemostat experiments, we consider a model of single species growth in a chemostat that involves delayed growth response. The time delay models the lag involved in the nutrient conversion process. Both monotone response functions and nonmonotone response functions are considered. The nonmonotone response function models the inhibitory effects of growth response of certain nutrients when concentrations are too high. By applying local and global Hopf bifurcation theorems, we prove that the model has unstable periodic solutions that bifurcate from unstable nonnegative equilibria as the parameter measuring the delay passes through certain critical values and that these local periodic solutions can persist, even if the delay parameter moves far from the critical (local) bifurcation values.

When there are two positive equilibria, then positive periodic solutions can exist. When there is a unique positive equilibrium, the model does not have positive periodic oscillations and the unique positive equilibrium is globally asymptotically stable. However, the model can have periodic solutions that change sign. Although these solutions are not biologically meaningful, provided the initial data starts close enough to the unstable manifold of one of these periodic solutions they may still help to account for the transient oscillations that have been frequently observed in chemostat experiments. Numerical simulations are provided to illustrate that the model has varying degrees of transient oscillatory behaviour that can be controlled by the choice of the initial data.

1. Introduction

In this paper, we study the following single-species chemostat model with delay:

$$\begin{aligned} S'(t) &= \big(S^0 - S(t)\big)\, D - p\big(S(t)\big)x(t), \\ x'(t) &= -Dx(t) + \alpha\, p\big(S(t-\tau)\big)x(t-\tau). \end{aligned} \tag{1.1}$$

In this model, $S(t)$ denotes the concentration of the unconsumed nutrient in the growth vessel at time t and $x(t)$ denotes the biomass of the population of microorganisms at time t. The function $p(S)$ represents the species specific per-capita

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nutrient uptake rate. It also models the rate of conversion of nutrient to viable biomass. The growth yield constant has been scaled out for mathematical convenience. The constant $\tau \geq 0$ denotes the time delay involved in the conversion of nutrient to viable biomass. S^0 and D are positive constants and denote, respectively, the concentration of the growth-limiting nutrient and the flow rate of the chemostat (see more details in [19], [51] and [52]). The constant positive constant, $\alpha = e^{-D\tau}$, is required, because it is assumed that the current change in biomass depends on the amount of nutrient consumed τ units of time in the past by the microorganisms that were in the growth vessel at that time and managed to remain in the growth vessel the τ units of time required to process the nutrient.

We show that (1.1) has unstable periodic solutions for certain ranges of the time delay τ. We provide numerical solutions of (1.1) as well, which illustrate how transient oscillatory solutions can be obtained numerically by choosing the initial data appropriately.

The main purpose of this paper is to study the transient behaviour of (1.1) and to give an analytic approach to explain the existence of transient oscillatory solutions. We consider both monotone response functions and nonmonotone response functions. Nonmonotone response functions are important in order to model the inhibitory effects of growth response of certain nutrients when their concentrations are too high. By applying the local Hopf bifurcation theorem, we prove that (1.1) has unstable periodic solutions that bifurcate from unstable nonnegative equilibria as the time delay τ passes through certain critical values. Global Hopf bifurcation is also considered, and it is shown that these local periodic solutions can persist, even if the delay parameter moves far from the critical (local) bifurcation values. The unstable periodic solutions of the model may help to account for the transient oscillations observed in chemostat experiments, provided that the initial data starts close enough to the unstable manifold of one of these periodic solutions. Numerical simulations indicate that the model has varying degrees of transient oscillatory behaviour that can be controlled by the choice of the initial data.

We remark that transient dynamics are usually more difficult to study than the asymptotic behaviour of solutions. As a result, fewer analytic tools are available for studying transient dynamics and most authors have used a numerical approach, despite the fact that transient behaviour is of great importance in understanding microbial growth in the chemostat. One tool to study asymptotic behaviour is to study equations linearized about the equilibrium solution and show that the characteristic equation has complex eigenvalues with negative real parts (see [30], [32], [39] and [41]). This results in solutions that approach the steady state via damped sinusoidal oscillations, provided that the solution starts close enough to the steady state. Results in this paper indicate that unstable periodic solutions can be viewed as sources of transient oscillations, and even though they are unstable, their detection might be useful in understanding transient dynamics.

This paper is organized as follows. In Section 2, we give a brief literature review on transient dynamics for chemostat models. In Section 3, we establish some preliminary results on (1.1) that are used in later sections. In Section 4, we first consider the case where the model has a unique positive equilibrium and explore its global asymptotic behaviour as well as the transient dynamics. The case where the model has two positive equilibrium points is studied in Section 5. Section 6 presents some numerical simulations that illustrate how transient oscillatory solutions can be obtained numerically by choosing initial data appropriately. Finally, in Section 7, we discuss the implications of our results.

2. Transient dynamics: a literature review

Transient growth dynamics are of considerable importance in the study of how microorganisms respond to environmental changes, and are pertinent to understanding the control mechanisms for microbial growth ([40]). Much research, both theoretical and experimental, has been undertaken dealing with transient behaviour of microbial population growth in the chemostat. While the Monod model [37] has some success in describing steady state growth rates (see [26] and [44]), it has been found inadequate to predict transients observed in chemostat experiments where the initial data is not at the globally attracting steady state. It has often been observed that changes in the environmental parameters, such as the input nutrient concentration, dilution rate, and temperature, can give rise to overshoots or transient oscillations in cell numbers ([9], [13], [49]). Lag phases occur in the growth response of microorganisms to changes in the environment ([4]). Cunningham and Maas [13] claim that in order to model such lag phases, it is necessary that transient growth models incorporate some mathematical device that allows the population to "remember" its nutrient history. Hence multicompartment models have been used, where the entire nutrient pool is subdivided into a chain of intracellular compartments through which the limiting nutrient must pass before it catalyzes cell growth. Consequently, the lag phase is modeled by the inevitable time delay introduced during the transfer of nutrient from one compartment to the other.

In [17], while studying the growth-limiting effect of vitamin B_{12} deficiency on the algae, *Monochrysis lutheri*, in the chemostat, Droop formulated a single-compartment model (often called the variable-yield model). In this model, the specific growth rate is decoupled from extracellular nutrient concentration by introducing an intracellular nutrient pool, so that only the internal nutrient is immediately available for cell growth. The model was tested by Droop [17] and showed some empirical superiority to the Monod model. Williams [49] postulated that the population biomass has two basic portions, a synthetic portion and a structured/genetic portion. This led him to formulate a two-compartment model in which the masses of these two portions are taken to be proportional to the two separate intracellular nutrient stores transformed from the outside nutrient supply. Williams tested his model on data for the *Chlorella* populations and, with a few exceptions including transient oscillations in cell numbers, he found good agreement between the model and the actual population dynamics. In [46], Tang and Wolkowicz considered the case where, in the presence of some extracellular enzymes, the external nutrient is first converted to an intermediate product before being absorbed into the cells. Hence the growth rate of the microorganisms is directly related to the concentration of the intermediate product and depends only indirectly on the concentration of the nutrient supply. Compared with the Monod model, this model exhibits different asymptotic behaviour and indicates the importance of the initial concentrations of the populations in determining their final steady states.

From a similar perspective, Barford et. al. [4] concluded that a generalized transient growth model should probably take the form of a structured model in which the biomass is described in terms of a number of intracellular subsections which are internally balanced in the same way the Monod model assumes the overall cell mass to be balanced. Such structured models have been proposed by Ramkrishna et. al. [41] who, in order to introduce a lag phase, assumed that the biomass is composed of two groups of substances which interact with each other and with substances in the environment to produce growth. The structure assigned to the organisms in the model accounts for the dependence of growth on the past history of the cells, and hence it is capable of predicting the lag phases and transient oscillations observed in experiments. In [33], Lee and Jackman also constructed a structured model in which the cells are subdivided into dispersed cells and flocs. Due to different growth rates of the flocs and dispersed cells, sudden changes in either the dilution rate or the nutrient concentration would alter the distribution of the cells in the dispersed state and the floc state. They investigated the responses of the model to step changes in dilution rate and intake nutrient concentration on bacteria growth. The theoretical predictions were in qualitative agreement with the experimental results. Similar two-state models have also been considered by Jäger et. al [30] and Tang et. al. [45]. They incorporated adaptive mechanisms of cells into the modelling equations. Numerical simulations indicate that transient oscillations are possible in the solutions of the models, and they can reproduce the qualitative behaviour of the experimental data from Hansen and Hubbell [26].

Others have *directly* incorporated time delays in the modelling equations and, as a result, the models take the form of delay differential equations. In [9], Caperon studied the growth response of *Isochrysis galbana* in a varying nitrate environment and found a smooth overdamped adjustment in cell numbers after step changes on the flow rate. He used delay differential equations to describe the time lag in the growth response, and the resulting model successfully predicted the population growth in experiment data under dynamic conditions. In an attempt to describe the damped oscillations observed on the transient growth of the unicellular algae, *Chlamydomonas reinhardii*, under nitrogen limitation (see [12]), Cunningham and Nisbet [14] found it is necessary to modify the Droop model [17] by introducing a time delay in the relationship between specific growth rate and the intracellular nutrient supply (see also [38]). The addition of the time delay in the modelling equations brings about oscillations and consequently a qualitative improvement in the behaviour of the model. In [47], Thingstad and Langeland introduced a discrete delay in the Monod model and showed that persistent oscillations are possible. Bush and Cooke [7] also confirmed that autonomous oscillations exist in the model of [47] for growth response functions with inhibitory effects. We refer to MacDonald [35], Wolkowicz and Xia [51], and the references therein, for more detailed discussions on chemostat modeling approaches using delay differential equations.

While delay differential equations have been widely used in modelling population dynamics (see [16],[23] and [25]), some practical problems have to be overcome when applied to models of the chemostat. Cunningham and Nisbet [15] pointed out that the oscillations produced by their time delay model are of the damped sinusoidal form, while the actual oscillatory shape from experiment data is of a more complicated nature. Although time delay models are capable of producing oscillations, they often introduce undesirable features when used for microbial growth in the chemostat. For example, the delay chemostat models studied in [7], [9], [21], [22], [42], [47] and [55] can exhibit stable periodic solutions, although such a form of sustained oscillations has been rarely observed in chemostat experiments (see [35]) performed in accordance with the underlying assumptions in the model. Models of the form (1.1), that incorporate time delay more appropriately, have been proposed and studied in [19], [51], [52] and [53]. The global asymptotic behaviour of the models are completely understood, for both the single-species and the two species competition cases, in the case of monotone growth response functions. It turns out that the global dynamics of these models (with at most two species) are similar to the dynamics of the Monod model. In particular, there are no sustained periodic solutions in such models. However, it was found in [52] that the time delay can affect both the qualitative and quantitative behaviour of the solutions, and numerical simulations illustrate that the models with delay may exhibit slightly more oscillations in the transients, when compared with the models without delay. To the best of our knowledge, the question of how to obtain analytic results on transient oscillations for (1.1) has not been studied, despite the fact that understanding transient microbial growth is just as important as understanding the long term (asymptotic) behaviour as far as controlling microbial population growth is concerned.

3. Preliminary results

Throughout this paper we assume that the growth response function $p(S)$ in (1.1) satisfies:

(3.1) $p : \mathbb{R}^+ \to \mathbb{R}^+$ is continuously differentiable and $p(0) = 0$;
(3.2) there exists a (possibly extended) real number $0 < \eta \leq \infty$ such that $p'(S) > 0$ on $[0, \eta)$ and $p'(S) < 0$ on (η, ∞);
(3.3) there exist uniquely defined positive (possibly extended) real numbers $\lambda_1 \leq \mu_1 \leq \infty$ such that
  (i) $p(S) < De^{D\tau}$, if $S \notin [\lambda_1, \mu_1]$;
  (ii) $p(S) > De^{D\tau}$, if $S \in (\lambda_1, \mu_1)$.

A typical growth response function is shown in Fig. 1. Clearly, when λ_1, μ_1 and η are all finite, $\lambda_1 \leq \eta \leq \mu_1$. Generally λ_1 and μ_1 depend on the delay $\tau \geq 0$. In fact, it can be seen from (3.1)-(3.3) that provided η is finite and $0 < \tau < \frac{1}{D}\ln(\frac{p(\eta)}{D})$, λ_1 and μ_1 are differentiable functions of τ, and if $\lambda_1(\tau) \neq \eta$, then $\lambda_1'(\tau) > 0$ and $\mu_1'(\tau) < 0$.

Let $C_2 := \{\varphi = (\varphi_0, \varphi_1) : [-\tau, 0] \to \mathbb{R}_2$ is continuous$\}$ be the Banach space of continuous functions on $[-\tau, 0]$ with supremum norm. We denote by C_2^+ the nonnegative cone of C_2. By using the method of steps (see Bellman and Cooke [5]), it can be shown that for each $\varphi \in C_2^+$, there is a unique solution of (1.1) through φ, that we call $\pi(\varphi; t) := \big(S(\varphi; t), x(\varphi; t)\big) \in \mathbb{R}_2$, and it is well-defined for all $t \geq 0$

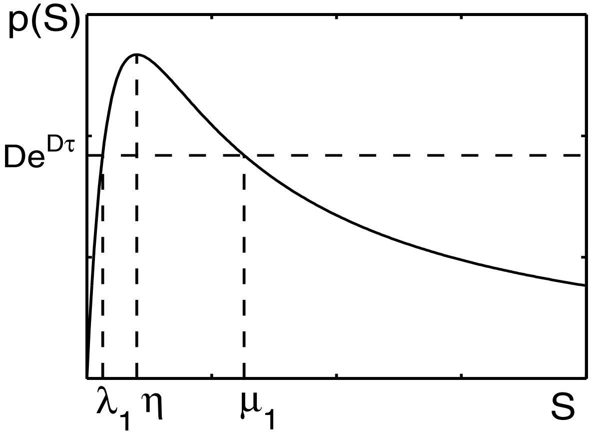

Fig. 1. A typical growth response function $p(S)$ for a fixed $\tau \geq 0$.

and satisfies $\pi(\varphi;\cdot)\mid_{[-\tau,0]}=\varphi$. Moreover, if $\varphi\in C_2^+$, then $\pi(\varphi;t)\in\mathbb{R}_2^+$ for all $t\geq 0$. Throughout, we will also denote by $\big(S(t),x(t)\big)$ the solution $\pi(\varphi;t)$ with $\varphi\in C_2^+$, if no confusion arises. When we say a solution $\pi(\varphi;t)$ or $\big(S(t),x(t)\big)$ of (1.1) is positive, we mean that each component of the solution vector is positive for all $t>0$. By using the variation-of-constant formula, it follows that

$$x(\varphi;t)=\varphi_1(0)e^{-Dt}+\alpha\int_0^t e^{-D(t-\theta)}p\big(S(\theta-\tau)\big)x(\theta-\tau)\,d\theta, \qquad (3.4)$$

from which it follows that the solution $\pi(\varphi;t)$ exists if $\varphi\in\mathbb{R}_2^+$ with $\varphi_1(0)>0$.

Let $\big(S(t),x(t)\big)$ be a given solution (not necessarily nonnegative) of (1.1). Define

$$W(t)=S^0-S(t)-e^{D\tau}x(t+\tau)$$

for all $t\geq 0$. Then it follows from (1.1) that $W'(t)=-DW(t)$ for all $t\geq 0$. Consequently,

$$S(t)+e^{D\tau}x(t+\tau)=S^0+\rho(t),\quad t\geq 0, \qquad (3.5)$$

where $\rho(t)$ is a continuously differentiable function with $\rho(t)\to 0$ exponentially as $t\to\infty$. Thus all nonnegative solutions of (1.1) are bounded for $t>0$.

In what follows, to avoid degeneracy, we assume that λ_1, μ_1 (when they are finite) are distinct from each other and from S^0. Then model (1.1) has at most three nonnegative equilibrium points and they depend on the delay τ and the parameters in the model. The equilibrium $E_{S^0}=(S^0,0)$ corresponds to washout of the single population from the chemostat. We define two other possible positive equilibria:

$$E_{\lambda_1}=\big(\lambda_1,\alpha(S^0-\lambda_1)\big),\quad \text{if } \lambda_1<S^0,$$
$$E_{\mu_1}=\big(\mu_1,\alpha(S^0-\mu_1)\big),\quad \text{if } \mu_1<S^0.$$

where $\alpha = e^{-D\tau}$. The criteria for local stability of these equilibrium points are given in the following theorem.

Theorem 3.1. *For system (1.1):*

- **(i)** *whenever it is defined (i.e., $\lambda_1 < S^0$), the equilibrium E_{λ_1} is locally asymptotically stable;*
- **(ii)** *whenever it is defined (i.e., $\mu_1 < S^0$), the equilibrium E_{μ_1} is unstable;*
- **(iii)** *the equilibrium E_{S^0} is always defined and is locally asymptotically stable if $S^0 \notin [\lambda_1, \mu_1]$, and unstable if $S^0 \in (\lambda_1, \mu_1)$.*

Proof. Let $E^* = (S^*, x^*)$ denote any one of the equilibrium points E_{S^0}, E_{λ_1}, or E_{μ_1}. Linearizing (1.1) about E^* we obtain,

$$\begin{aligned} z_0'(t) &= -\big(D + x^* p'(S^*)\big) z_0(t) - p(S^*) z_1(t) \\ z_1'(t) &= \alpha\, p'(S^*) x^* z_0(t-\tau) - D z_1(t) + \alpha\, p(S^*) z_1(t-\tau). \end{aligned} \tag{3.6}$$

After simplifying, the characteristic equation of (3.6) is $\Delta(\lambda) = 0$, where

$$\Delta(\lambda) = (\lambda + D)\big(\lambda + D - \alpha\, p(S^*) e^{-\lambda\tau} + x^* p'(S^*)\big). \tag{3.7}$$

- *(i)* If $E^* = E_{\lambda_1}$, then $\lambda_1 < S^0$, $\alpha\, p(S^*) = \alpha\, p(\lambda_1) = D$ and $p'(S^*) = p'(\lambda_1) > 0$. As in Ellermeyer [19], we can use Hayes's theorem (see Bellman and Cooke [5] or the appendix of Hale and Lunel [25]) to show that all roots of $\lambda + D - De^{-\lambda\tau} + \alpha(S^0 - \lambda_1)p'(\lambda_1)$ have negative real parts. Therefore, E_{λ_1} is locally asymptotically stable.
- *(ii)* If $E^* = E_{\mu_1}$, then $\mu_1 < S^0$ and $\alpha\, p(S^*) = D,\ p'(S^*) < 0$. Let

  $$f(\lambda) = \lambda + D - De^{-\lambda\tau} + \alpha(S^0 - \mu_1)p'(\mu_1).$$

  We have $f(0) = \alpha(S^0 - \mu)p'(\mu) < 0$ and $\lim_{\lambda\to\infty} f(\lambda) = +\infty$. Thus $f(\lambda)$ has at least one positive real root. This implies that $\Delta(\lambda)$ has a positive real root. Consequently, E_{μ_1} is unstable.
- *(iii)* The proof is similar to (i) and (ii) and so we omit the details. □

Remark 3.1. The above result is similar to the ODEs case (i.e. when $\tau = 0$ in model (1.1)), as shown in Lemma 5.1 of Butler and Wolkowicz [8], who considered the n-species competition case with no delays. However, it is important to note that, unlike the ODEs case, the equilibrium points E_{μ_1} and E_{S^0} for model (1.1) may be non-hyperbolic for some values of the delay τ. In fact, we will show in the next two sections, that a Hopf bifurcation can occur at these two equilibrium points. This indicates the significance of considering delay in the growth response.

When the equilibrium points E_{λ_1} and E_{μ_1} do not exist, we can show that E_{S^0} is globally asymptotically stable (with respect to the non-negative cone C_2^+). In this case, population x will eventually be washed out from the chemostat.

Theorem 3.2. *If* $\lambda_1 > S^0$, *then the equilibrium point* E_{S^0} *is globally asymptotically stable (with respect to* C_2^+*).*

Proof. By Theorem 3.1 (iii), E_{S^0} is locally asymptotically stable. Thus it suffices to show that $\lim_{t\to\infty}\big(S(t), x(t)\big) = (S^0, 0)$ for every positive solution of (1.1), which can be achieved by a similar argument as that given in Theorem 2.3 of [51]. This completes the proof. □

4. The case $\lambda_1 < S^0 < \mu_1$

Throughout this section, we study the global dynamics of model (1.1) under the assumption that $\alpha p(S^0) > D$ so that $\lambda_1(\tau) < S^0 < \mu_1(\tau)$ for all $0 \le \tau < \frac{1}{D}\ln\frac{p(S^0)}{D}$. In this case, the equilibrium point E_{λ_1} sits in the positive cone, but E_{μ_1} does not. We prove that E_{λ_1} is globally asymptotically stable (with respect to C_2^+). Moreover, we also study the dynamical behaviour of solutions near the boundary of C_2^+ in an attempt to better understand certain transient oscillations of solutions in C_2^+.

We begin with the following observation.

Lemma 4.1. *Let* $\big(S(t), x(t)\big)$ *be a positive solution of (1.1). If* $\lambda_1 < S^0 < \mu_1$, *then* $S(t) < S^0$ *for all sufficiently large* t.

Proof. This can be proved by an argument similar to that given for Lemma 2.2 in Wolkowicz and Xia [51]. □

Let $\big(S(t), x(t)\big)$ be an arbitrary positive solution of (1.1). We define $y(t) = e^{D\tau}x(t+\tau),\ t \ge 0$. Then it follows from (3.5) that $S(t) = S^0 - y(t) + \rho(t),\ t \ge 0$. From the second equation of (1.1) it follows that

$$y'(t) = -Dy(t) + \alpha\, p\big(S^0 - y(t) + \rho(t)\big)y(t-\tau). \tag{4.1}$$

We now give a global stability result as follows.

Theorem 4.1. *If* $\lambda_1 < S^0 < \mu_1$, *then* E_{λ_1} *is globally asymptotically stable with respect to the nonnegative cone* C_2^+.

Proof. Since E_{λ_1} is locally asymptotically stable, by Theorem 3.1, it suffices to show that it is globally attractive, i.e. $\lim_{t\to\infty}\big(S(t), x(t)\big) = E_{\lambda_1}$ for every positive solution $\big(S(t), x(t)\big)$ of (1.1). Let $z(t) = e^{D\tau}x(t)$. Then $z(t)$ satisfies (4.1) and is bounded. Define

$$\beta = \liminf_{t\to\infty} z(t), \qquad \gamma = \limsup_{t\to\infty} z(t).$$

Then $0 \le \beta \le \gamma \le S^0$. By Lemma 4.1 and the Fluctuation Lemma of Hirsch, Hanisch and Gabriel [28], assumptions (3.3) and $\lambda_1 < S^0 < \mu_1$, we can proceed as in the proofs of Lemmas 3.4, 3.5 and 3.8 in Wolkowicz and Xia [51], to show that $\beta = \gamma = S^0 - \lambda_1$. Thus $\lim_{t\to\infty} x(t) = \alpha(S^0 - \lambda_1)$ and by (3.5), $\lim_{t\to\infty} S(t) = S^0$. Therefore, $\lim_{t\to\infty} \big(S(t), x(t)\big) = E_{\lambda_1}$ and the proof is complete. □

Remark 4.1. For the case where two species are competing for one limiting resource in the chemostat with general delayed growth functions, Wang and Ma [48] also established a global convergence result by taking advantage of the Fluctuation Lemma.

In the rest of this section, we study the dynamical behaviour of the solutions near the unstable equilibrium point $E_{S^0} = (S^0, 0)$ that lies on the boundary of the nonnegative cone C_2^+. These solutions themselves are not always biologically relevant, since they may involve negative values. However, the oscillatory behaviour of these solutions can be used to help us understand transient oscillations (of other positive solutions) that have been frequently observed in chemostat experiments.

Our idea is to determine when Hopf bifurcations occur at the unstable equilibrium point E_{S^0}. Note that by (3.7), the characteristic equation $\Delta(\lambda) = 0$ of the linearized system at E_{S^0} always has a negative real root $\lambda = -D$. All of the other roots are determined by the equation

$$\lambda + D - A(\tau)e^{-\lambda\tau} = 0, \tag{4.2}$$

where $\alpha = e^{-D\tau}$ and $A(\tau) = \alpha\, p(S^0) > D$, provided that $0 < \tau < \frac{1}{D} \ln \frac{p(S^0)}{D}$.

We look for purely imaginary roots of (4.2). Substitute $\lambda = i\beta,\ \beta > 0$ as a root of (4.2). Considering the real and imaginary parts of (4.2), we obtain

$$\beta + A(\tau)\sin\beta\tau = 0, \quad D - A(\tau)\cos\beta\tau = 0.$$

Equivalently,

$$\cos\beta\tau = \frac{D}{A(\tau)}, \quad \sin\beta\tau = -\frac{\beta}{A(\tau)}. \tag{4.3}$$

Note that since $\cos\beta\tau > 0$ and $\sin\beta\tau < 0$, it follows that $\beta\tau \in ((4n-1)\pi/2, 2n\pi)$ for some positive integer n. Squaring both sides of (4.3) and adding, we obtain

$$\beta = \sqrt{A^2(\tau) - D^2}. \tag{4.4}$$

Therefore, we think of β as $\beta(\tau)$. Now substituting (4.4) into (4.3),

$$\cos\big(\tau\sqrt{A^2(\tau) - D^2}\big) = \frac{D}{A(\tau)}, \ \sin\big(\tau\sqrt{A^2(\tau) - D^2}\big) = -\frac{\sqrt{A^2(\tau) - D^2}}{A(\tau)}. \tag{4.5}$$

Thus, by (4.4), a solution of (4.5) for $0 < \tau < \frac{1}{D} \ln \frac{p(S^0)}{D}$ has $\beta > 0$, and hence yields an imaginary root of (4.2). Therefore, we look for positive solutions of equation (4.5).

Let n be a positive integer. We define $\gamma_n(\tau)$ to be the unique solution of the following equation

$$\sin x = -\frac{x}{\sqrt{x^2 + (D\tau)^2}}, \quad x \in [\tfrac{4n-1}{2}\pi, 2n\pi). \tag{4.6}$$

It follows from the Implicit Function Theorem that for fixed n, $\gamma_n(\tau)$ is continuous on $[0, \infty)$ and differentiable on $(0, \infty)$, with $\gamma_n(0) = (4n-1)\pi/2$ and $\gamma_n(\infty) = 2n\pi$. Moreover, using the fact that $\cos\gamma_n(\tau) = \sqrt{1 - \sin^2\gamma_n(\tau)}$ on $((4n-1)\pi/2, 2n\pi)$, we have

$$\gamma_n'(\tau) = \frac{D\gamma_n(\tau)}{\gamma_n^2(\tau) + D^2\tau^2 + D\tau} > 0. \tag{4.7}$$

Similarly, from (4.7),

$$\gamma_n''(\tau) = -\frac{2D\gamma_n(\tau)\big(\gamma_n(\tau)\gamma_n'(\tau) + D^2\tau\big)}{\big(\gamma_n^2(\tau) + D^2\tau^2 + D\tau\big)^2} < 0,$$

for all $\tau \in (0, \infty)$. Hence $\gamma_n(\tau)$ is strictly increasing and concave down.

Before we characterize the positive solutions of (4.5) we require the following technical lemma.

Lemma 4.2. *Let $\delta = \delta(S^0, D) > 0$ be the unique solution of the equation*

$$p^2(S^0)(1 - Dx) = D^2 e^{2Dx}, \ x > 0,$$

and $N > 0$ be the smallest integer such that

$$p\big(S^0\big)\sqrt{D}\,\delta^{\frac{3}{2}} e^{-D\delta} \le 2N\pi.$$

Consider the function

$$f(\tau) = \tau\sqrt{A^2(\tau) - D^2}, \ \ \tau \in \left[0, \frac{1}{D}\ln\frac{p(S^0)}{D}\right]. \tag{4.8}$$

Then the following hold:

(i) *$\tau\beta = f(\tau) \le p(S^0)\sqrt{D}\,\delta^{\frac{3}{2}} e^{-D\delta}$ with equality if and only if $\tau = \delta$;*
(ii) *$\tau = \tau^* > 0$ is a solution of (4.5) if and only if there exists an integer $0 < n \le N$ such that the graphs of $\gamma_n(\tau)$ and $f(\tau)$ intersect at $\tau = \tau^*$;*
(iii) *If $\gamma_N(\delta) < f(\delta)$, then there are at least N solutions of (4.5) in the interval $(0, \delta)$ and exactly N solutions of (4.5) in the interval $\big(\delta, \frac{1}{D}\ln\frac{p(S^0)}{D}\big)$;*
(iv) *If $\gamma_N(\delta) > f(\delta)$, then there are at least $N-1$ solutions of (4.5) in the interval $(0, \delta)$ and exactly $N-1$ solutions of (4.5) in the interval $(\delta, \frac{1}{D}\ln\frac{p(S^0)}{D})$.*

Proof. *(i)* First note that $f(\tau)$ is always nonnegative and

$$f'(\tau) = \frac{p^2(S^0)(1 - D\tau) - D^2 e^{2D\tau}}{e^{2D\tau}\sqrt{A^2(\tau) - D^2}}. \tag{4.9}$$

So $f(\tau)$ is strictly increasing on $(0, \delta)$ and strictly decreasing on $(\delta, \frac{1}{D}\ln\bigl(p(S^0)/D\bigr)]$. Its maximum value is $f(\delta) = p(S^0)\sqrt{D}\,\delta^{\frac{3}{2}} e^{-D\delta}$.

(ii) Observe that $\tau = \tau^* > 0$ is a solution of (4.5) if and only if

$$\begin{cases} \tau^* A(\tau^*) = \sqrt{f^2(\tau^*) + (D\tau^*)^2}, \\ \sin\bigl(f(\tau^*)\bigr) = -\frac{f(\tau^*)}{\tau^* A(\tau^*)}, \\ f(\tau^*) \in \bigl(\frac{4n-1}{2}\pi, 2n\pi\bigr), \end{cases}$$

for some integer $n > 0$. This means that $f(\tau^*)$ is a solution of (4.6), i.e. the functions $f(\tau)$ and $\gamma_n(\tau)$ intersect at $\tau = \tau^*$. Since $f(\tau) \le f(\delta) = p(S^0)\sqrt{D}\,\delta^{\frac{3}{2}} e^{-D\delta} \le 2N\pi$, any $\gamma_i(\tau)$ with $i \ge N + 1$ cannot intersect the function $f(\tau)$. Hence $n \le N$ and *(ii)* holds.

(iii) If $\gamma_N(\delta) < f(\delta)$, then there are at least $2N$ intersection points of the functions $f(\tau)$ and $\gamma_i(\tau)$, $1 \le i \le N$, with at least N points on each side of $\tau = \delta$, since $f(\tau)$ is always strictly increasing on $[0, \delta)$ and strictly decreasing on $\bigl[\delta, \frac{1}{D}\ln\frac{p(S^0)}{D}\bigr)$, and each $\gamma_i(\tau)$ is strictly increasing. The conclusion now follows from *(ii)* (see Fig. 2).

(iv) This case is similar to *(iii)*. □

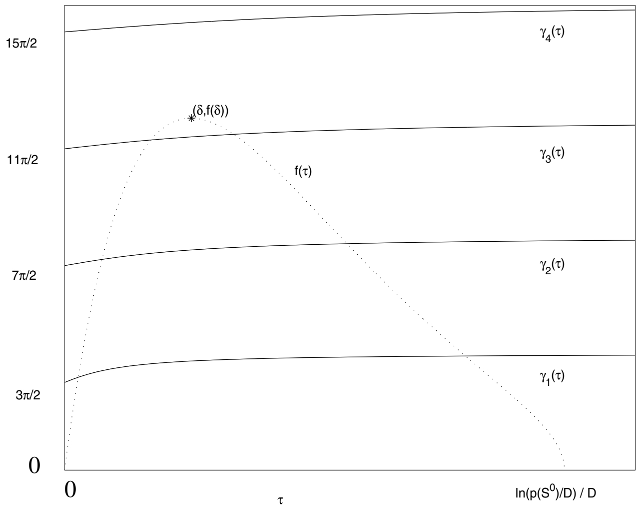

Fig. 2. Intersections of $f(\tau)$ and $\gamma_i(\tau)$.

Remark 4.2. (a) It follows immediately from Lemma 4.2 that $\beta\tau$ is bounded above by $2N\pi$ where N is the smallest positive integer such that $f(\delta) \le 2N\pi$ (see Fig. 2).

(b) Note that $p(S^0) > \sqrt{2}D$ is necessary for the existence of positive solutions of (4.5). In fact, $p(S^0) > \frac{3}{2}\pi e D > \sqrt{2}D$ is necessary. To see this, first note that $\delta^{\frac{3}{2}} e^{-D\delta}$ is an increasing function of δ for $0 \le \delta \le \frac{3}{2D}$. Keeping in mind that $\delta < \frac{1}{D}$, if $p(S^0) \le \delta^{\frac{3}{2}} e^{-D\delta}$, it follows that

$$f(\delta) = p(S^0)\sqrt{D}\,\delta^{3/2}e^{-D\delta} < p(S^0)\sqrt{D}\Big(\frac{1}{D}\Big)^{3/2} e^{-1} = \frac{p(S^0)}{D}e^{-1} \le \frac{3\pi}{2}.$$

Hence $f(\tau) < \gamma_1(\tau)$ for all $\tau \in \big(0, \frac{1}{D}\ln\frac{p(S^0)}{D}\big)$, and by Lemma 4.2 (i), equation (4.5) has no positive solution.

In order to establish analytically that there are only a finite number of positive solutions to (4.5), and that they are distinct and hence isolated, we require a generic transversality condition.

Lemma 4.3. *Let $\delta_0 = \delta_0(S^0, D)$ be the unique solution of the equation*

$$p^2(S^0)(1 - Dx) = 2D^2 e^{2Dx}, \quad x > 0,$$

and let N and δ be the numbers defined in Lemma 4.2. Assume that $p(S^0) > \sqrt{2}D$ and $f(\delta_0) \ne \gamma_i(\delta_0)$ for all $1 \le i \le N$.

- **(i)** *If $\gamma_N(\delta) < f(\delta)$, then there are exactly $2N$ positive solutions of (4.5), namely, $0 < \tau_1^* < \tau_2^* < \cdots < \tau_{2N}^*$ such that $\tau_N^* < \delta_0 < \delta < \tau_{N+1}^*$ and*

$$\gamma_n(\tau_n^*) = f(\tau_n^*), \quad \gamma_n(\tau_{2N-n+1}^*) = f(\tau_{2N-n+1}^*), \quad 1 \le n \le N.$$

- **(ii)** *If $\gamma_N(\delta) > f(\delta)$, then one of the following two conclusions holds.*
  - **(a)** *There are exactly $2(N-1)$ positive solutions $0 < \tau_1^* < \tau_2^* < \cdots < \tau_{2N-2}^*$ such that $\tau_{N-1}^* < \delta_0 < \delta < \tau_N^*$ and*

$$\gamma_n(\tau_n^*) = f(\tau_n^*), \quad \gamma_n(\tau_{2N-n-1}^*) = f(\tau_{2N-n-1}^*), \quad 1 \le n \le N-1;$$

  - **(b)** *There are exactly $2N$ positive solutions $0 < \tau_1^* < \tau_2^* < \cdots < \tau_{2N}^*$ such that $\tau_N^* < \delta_0 < \tau_{N+1}^* < \delta < \tau_{N+2}^*$ and*

$$\gamma_n(\tau_n^*) = f(\tau_n^*), \quad \gamma_n(\tau_{2N-n+1}^*) = f(\tau_{2N-n+1}^*), \quad 1 \le n \le N.$$

Proof. First note that when $p(S^0) > \sqrt{2}D$, it follows that $\delta_0 > 0$. We now show that if $f(\delta_0) \ne \gamma_i(\delta_0)$, $1 \le i \le N$, then the functions $f(\tau)$ and $\gamma_i(\tau)$ intersect transversally. In fact, by (4.7) and (4.9), at any τ such that $f(\tau) = \gamma_i(\tau)$, we have

$$
\begin{aligned}
f'(\tau) - \gamma_i'(\tau) &= \frac{p^2(S^0)(1 - D\tau) - D^2 e^{2D\tau}}{e^{2D\tau}\sqrt{\alpha^2 p^2(S^0) - D^2}} - \frac{D\,\gamma_i(\tau)}{\gamma_i^2(\tau) + D^2\tau^2 + D\tau} \\
&= \frac{p^2(S^0)(1-D\tau)-p^2(\lambda_1)}{e^{2D\tau}\sqrt{\alpha^2 p^2(S^0)-D^2}} - \frac{D\,\tau\sqrt{\alpha^2 p^2(S^0)-D^2}}{\tau^2\big(\alpha^2 p^2(S^0)-D^2\big) + D^2\tau^2 + D\tau} \\
&= \frac{\tau\,\alpha^2}{f(\tau)}\left(p^2(S^0)(1 - D\tau) - p^2(\lambda_1) - \frac{D\big(p^2(S^0) - p^2(\lambda_1)\big)}{\tau\,\alpha^2 p^2(S^0) + D}\right) \\
&= \frac{\tau\,\alpha^2}{f(\tau)}\left(\frac{\tau\,\alpha^2 p^2(S^0)}{\tau\,\alpha^2 p^2(S^0) + D}\big(p^2(S^0) - p^2(\lambda_1)\big) - D\,\tau\, p^2(S^0)\right) \\
&= \frac{\tau^2\,\alpha^2\, p^2(S^0)}{f(\tau)\big(\tau p^2(S^0) + De^{2D\tau}\big)}\big(p^2(S^0)(1 - D\tau) - 2D^2 e^{2D\tau}\big).
\end{aligned}
\tag{4.10}
$$

where $\alpha = e^{-D\tau}$. Define the function

$$g(\tau) = p^2(S^0)(1 - D\tau) - 2D^2 e^{2D\tau}, \quad \tau \geq 0. \tag{4.11}$$

Note that $g(\tau)$ is a decreasing function and $g(\tau) = 0$ if and only if $\tau = \delta_0$. Therefore, if $f(\tau) = \gamma_i(\tau)$, then $f'(\tau) = \gamma_i'(\tau)$ if and only if $\tau = \delta_0$, contradicting the hypothesis that $f(\delta_0) \neq \gamma_i(\delta_0),\ 1 \leq i \leq N$.

(i). From Lemma 4.2(ii), it suffices to show that there is exactly one intersection point of $f(\tau)$ with each $\gamma_i(\tau),\ 1 \leq i \leq N$, on the interval $(0, \delta)$. Suppose not. Then there exists $1 \leq i_0 \leq N$ such that there are at least two τ's in $(0, \delta)$ such that $f(\tau) = \gamma_i(\tau)$. Since there are at least two such τ's, by the transversality of the intersection of $f(\tau)$ with $\gamma_i(\tau)$ shown above and the fact that $f(\delta) > \gamma_{i_0}(\delta)$, there must be at least three such τ's and so we can always select $\tau_+^* > \tau_-^*$ such that $f(\tau_+^*) = \gamma_{i_0}(\tau_+^*)$ and $f(\tau_-^*) = \gamma_{i_0}(\tau_-^*)$, but

$$f'(\tau_+^*) - \gamma_{i_0}'(\tau_+^*) > 0 \quad \text{and} \quad f'(\tau_-^*) - \gamma_{i_0}'(\tau_-^*) < 0.$$

By (4.10), this implies that $g(\tau_+^*) > 0$ and $g(\tau_-^*) < 0$, which is impossible, since $g(\tau)$ is a strictly decreasing function. That $\tau_N^* < \delta_0$, follows since $f'(\tau_N^*) - \gamma_N'(\tau_N^*) > 0$ and this inequality is reversed for $\tau > \delta_0$. This establishes *(i)*.

(ii). Note that $\gamma_{N-1}(\delta) < 2(N-1)\pi < f(\delta)$, and so there are exactly $2(N-1)$ intersections of $\gamma_i(\tau)$ and $f(\tau),\ 1 \leq i \leq N-1$, as in *(i)*. Either $\gamma_N(\tau)$ does not intersect $f(\tau)$ or it does. If there is no intersection, the proof is similar to *(i)*, and conclusion *(a)* follows. Otherwise, it is clear that there must be at least two intersections, since $f(\delta) < \gamma_N(\delta)$. We claim that in this case there are exactly two intersection points of $f(\tau)$ with γ_N. Suppose not, i.e., there are at least three such intersection points, Then we can find $\tau_-^* < \tau_+^* < \delta$ such that $f'(\tau_-^*) - \gamma_N'(\tau_-^*) < 0$ and $f'(\tau_+^*) - \gamma_N'(\tau_+^*) > 0$ and there is a contradiction if one argues as in the previous case. In fact, if there are two such intersections, that $\tau_N^* < \delta_0 < \tau_{N+1}^* < \delta$ follows, since $f'(\tau_N^*) - \gamma_N'(\tau_N^*) > 0$ and $f'(\tau_{N+1}^*) - \gamma_N'(\tau_{N+1}^*) > 0$. This proves *(ii) (b)*.

This completes the proof. □

Lemma 4.4. *Let* $\lambda = \lambda(\tau) = R(\tau) + i\, I(\tau)$ *be a root of the characteristic equation (3.2), with* $R(\tau^*) = 0$ *and* $\beta = I(\tau^*) > 0$ *for some* $\tau^* > 0$. *Then*

$$Sign\big(R'(\tau^*)\big) = Sign\big(f'(\tau^*) - \gamma_i'(\tau^*)\big) \tag{4.12}$$

for some $i \geq 1$, *where* $Sign(x)$ *is the sign function defined by*

$$Sign(x) = \begin{cases} \frac{x}{|x|}, & \text{if } x \neq 0, \\ 0, & \text{if } x = 0. \end{cases}$$

Proof. We differentiate both sides of (4.2) with respect to τ. It follows that

$$\frac{d\lambda}{d\tau} - e^{-\lambda\tau}\frac{dA}{d\tau} + Ae^{-\lambda\tau}\left(\tau\frac{d\lambda}{d\tau} + \lambda\right) = 0.$$

Note that $dA/d\tau = -DA$. Solving for $d\lambda/d\tau$ in the above equation gives

$$\frac{d\lambda}{d\tau} = \frac{-DAe^{-\lambda\tau} - \lambda\, Ae^{-\lambda\tau}}{1 + \tau Ae^{-\lambda\tau}}.$$

By (4.2), $Ae^{-\lambda\tau} = \lambda + D$. Substituting this into the above expression now yields

$$\frac{d\lambda}{d\tau} = -\frac{\big(\lambda + D\big)^2}{1 + \tau\big(\lambda + D\big)}. \tag{4.13}$$

It then follows from (4.13) that at $\tau = \tau^*$, $\lambda = i\,\beta$, and we have

$$\begin{aligned} R'(\tau^*) &= \mathrm{Re}\left(\frac{-\big(i\beta + D\big)^2}{1 + \tau^*\big(i\beta + D\big)}\right) \\ &= -\mathrm{Re}\left(\frac{D^2 - \beta^2 + 2\beta Di}{1 + D\tau^* + \tau^*\beta i}\right) \\ &= -\frac{\big(D^2 - \beta^2\big)\big(1 + D\tau^*\big) + 2D\tau^*\beta^2}{\big(1 + D\tau^*\big)^2 + \big(\tau^*\beta\big)^2} \\ &= -\frac{D^2 - \beta^2 + D^3\tau^* + D\tau^*\beta^2}{\big(1 + D\tau^*\big)^2 + \big(\tau^*\beta\big)^2} \\ &= -\frac{D^2 - \beta^2 + D\tau^*\big(D^2 + \beta^2\big)}{\big(1 + D\tau^*\big)^2 + \big(\tau^*\beta\big)^2}. \end{aligned} \tag{4.14}$$

Note that from (4.4), we have $D^2 + \beta^2 = A^2(\tau^*) = e^{-2D\tau^*}p^2(S^0)$. Therefore, by (4.14), we obtain

$$R'(\tau^*) = -\frac{D^2 - \beta^2 + D\tau^* A^2(\tau^*)}{\big(1 + D\tau^*\big)^2 + \big(\tau^*\beta\big)^2},$$

which leads to

$$\begin{aligned}\operatorname{Sign}\bigl(R'(\tau^*)\bigr) &= \operatorname{Sign}\bigl(\beta^2 - D^2 - D\tau^* A^2(\tau^*)\bigr)\\ &= \operatorname{Sign}\bigl(\beta^2 + D^2 - 2D^2 - D\tau^* A^2(\tau^*)\bigr)\\ &= \operatorname{Sign}\bigl(A^2(\tau^*) - 2D^2 - D\tau^* A^2(\tau^*)\bigr)\\ &= \operatorname{Sign}\bigl(e^{-2D\tau^*} p^2(S^0)(1 - D\tau^*) - 2D^2\bigr)\\ &= \operatorname{Sign}\bigl(p^2(S^0)(1 - D\tau^*) - 2D^2 e^{2D\tau^*}\bigr).\end{aligned}$$

The formula (4.12) follows from (4.10) and Lemma 4.2 (i).

This completes the proof. □

Remark 4.3. As is well-known, $\operatorname{Sign}\bigl(R'(\tau^*)\bigr) \neq 0$ is the *transversality condition* in the classical Hopf bifurcation theorem. It is interesting to note that by formula (4.12), this transversality condition is satisfied if and only if the curves $f(\tau)$ and $\gamma_i(\tau)$ *cross transversally*. Thus this formula gives a way to check the transversality condition geometrically.

Together with Lemmas 4.2 and 4.4, the following theorem gives a sufficient condition for a Hopf bifurcation for model (1.1).

Theorem 4.2. *Let τ^* be a solution of (4.5). Then there exists a unique integer $n \geq 1$ such that $f(\tau^*) = \gamma_n(\tau^*)$. If $f'(\tau^*) \neq \gamma_n'(\tau^*)$, then there is a Hopf bifurcation at $\tau = \tau^*$ of small amplitude periodic solutions bifurcating from the equilibrium E_{S^0}. When τ is sufficiently close to τ^*, these periodic solutions are all unstable and their periods lie in the interval $\bigl(\tau^*/n, 4\tau^*/(4n-1)\bigr)$.*

Proof. Since $\tau^* > 0$ is a solution of (4.5), at $\tau = \tau^*$, (4.2) has a purely imaginary root, βi, and by (4.4) $\beta = \sqrt{A^2(\tau^*) - D^2}$. Moreover, by Lemma 4.2 (i), there exists a unique integer $n \geq 1$ such that $f(\tau^*) = \gamma_n(\tau^*)$. Applying Lemma 4.4, we obtain

$$\frac{d}{d\tau}\bigl(\operatorname{Re}(\lambda)\bigr)\Big|_{\tau=\tau^*} \neq 0,$$

where $\lambda = \lambda(\tau)$ is a root of (4.2) with $\lambda(\tau^*) = \beta i$. Note that

$$\frac{2\pi}{\beta} = \frac{2\pi\tau^*}{\tau^*\sqrt{A^2(\tau^*) - D^2}} = \frac{2\pi\tau^*}{f(\tau^*)} = \frac{2\pi\tau^*}{\gamma_n(\tau^*)},$$

and $\gamma_n(\tau^*) \in \bigl((4n-1)\pi/2, 2n\pi\bigr)$. Therefore, we have

$$\frac{\tau^*}{n} < \frac{2\pi}{\beta} < \frac{4\tau^*}{4n-1}. \tag{4.15}$$

By the Hopf bifurcation theorem for delay differential equations (see, for example, Hale and Lunel [25]), there is a Hopf bifurcation of small amplitude periodic solutions at $\tau = \tau^*$ with periods in $\bigl(\tau^*/n, 4\tau^*/(4n-1)\bigr)$.

Notice that $p(S^0) > D$. The characteristic equation (4.2) always has a positive real root for each $\tau \in \big[0, \frac{1}{D} \ln \frac{p(S^0)}{D}\big)$. This positive real root gives a Floquet multiplier for the small amplitude periodic solutions near E_{S^0} with positive real part (see §4, Chapter VIII of Golubitsky and Schaeffer [24]). Therefore, these bifurcating periodic solutions are all unstable and the proof is complete. □

Remark 4.4. As shown in Theorem 4.1, all positive solutions must converge to the equilibrium E_{λ_1} as $t \to \infty$. Therefore, the periodic solutions bifurcating from E_{S^0} cannot be nonnegative. In fact, as we will see later in this section, in the case $\lambda_1 < S^0 < \mu_1$, any periodic solution of (1.1) must involve negative and positive values and surround the equilibrium $E_{S^0} = (S^0, 0)$. Thus these periodic solutions involve negative values in the initial data and are not themselves biologically relevant. However, these unstable periodic solutions are still of interest for model (1.1), since they may be viewed as "sources" of transient oscillations observed in experiments (see, for example, Hansen and Hubbel [26]). Note that E_{S^0} is on the boundary of C_2^+. It is likely that solutions with positive initial data close to E_{S^0} would also display transient oscillatory behaviour (see Fig. 7).

Remark 4.5. It is also interesting to note that any small amplitude periodic solution obtained via Hopf bifurcation has period less than 2τ. Moreover, as we have discussed in Remark 4.4, the x-component of any such periodic solution must have a zero in the interval $[t, t+\tau]$, for any $t \geq 0$, and must change sign there. In the literature, this type of solution is referred to as a *rapidly oscillating solution* (see, for example, [1]). It has been observed, both numerically and theoretically, that rapidly oscillating periodic solutions seem to be unstable for many delay differential equations. Our result is consistent with this observation.

Note that Theorem 4.2 only gives the existence of periodic solutions *near* the equilibrium E_{S^0}. In what follows, we study the *global continuation* of these local bifurcating periodic solutions. Our main technique is the global Hopf bifurcation theorem proved by Erbe, Geba, Krawcewicz and Wu [20] for functional differential equations. See also Chow and Mallet-Paret [11] and Krawcewicz, Xia and Wu [31].

We begin with the following lemma concerning a-priori bounds of possible periodic solutions of (1.1).

Lemma 4.5. *Let* $\big(S(t), x(t)\big) \in C(\mathbb{R}, \mathbb{R}^+ \times \mathbb{R})$ *be a periodic solution of (1.1). If* $\mu_1(0) < \infty$, *then for all* $t \in \mathbb{R}$, *we have*

$$\lambda_1(0) \leq S(t) \leq \mu_1(0), \quad |x(t)| \leq \max\{S^0 - \lambda_1(0), \mu_1(0) - S^0\}.$$

Proof. Let $W(t) = S^0 - S(t) - e^{D\tau} x(t+\tau)$. Then $W'(t) = -DW(t)$. Since $W(t)$ is periodic, this implies that

$$S(t) + e^{D\tau} x(t+\tau) = S^0, \tag{4.16}$$

for all $t \in \mathbb{R}$. Let $y(t) = e^{D\tau} x(t+\tau)$. Then $y(t) + S(t) = S^0$ for all $t \in \mathbb{R}$, and $y(t)$ satisfies the (scalar) delay differential equation

$$y'(t) = -Dy(t) + \alpha\, p\big(S^0 - y(t)\big) y(t-\tau). \tag{4.17}$$

Suppose that $y(t)$ achieves its minimum at ξ. Then $y'(\xi) = 0$. By Remark 4.4, we must have $y(\xi) < 0$. It now follows from (4.17) that

$$Dy(\xi) = \alpha\, p\big(S^0 - y(\xi)\big)y(\xi - \tau) \geq \alpha\, p\big(S^0 - y(\xi)\big)y(\xi).$$

Cancelling $y(\xi)$ yields $D \leq \alpha\, p\big(S^0 - y(\xi)\big)$, which implies that

$$S^0 - y(\xi) \leq \mu_1(\tau) \leq \mu_1(0).$$

Thus $y(\xi) \geq S^0 - \mu_1(0)$ and

$$x(t) = \alpha\, y(t - \tau) \geq \alpha\big(S^0 - \mu_1(0)\big) \geq S^0 - \mu_1(0). \tag{4.18}$$

Similarly, if $y(t)$ achieves its maximum at ζ, then $y'(\zeta) = 0$. As before, we may assume that $y(\zeta) > 0$. Then (4.17) gives

$$Dy(\zeta) = \alpha\, p\big(S^0 - y(\zeta)\big)y(\zeta - \tau) \leq \alpha\, p\big(S^0 - y(\zeta)\big).$$

Thus $D \leq \alpha p\big(S^0 - y(\zeta)\big)$ and $S^0 - y(\zeta) \geq \lambda_1(\tau) \geq \lambda_1(0)$ by assumption (3.3). Therefore, $y(\zeta) \leq S^0 - \lambda_1(0)$ and

$$x(t) = \alpha\, y(t - \tau) = \alpha\big(S^0 - \lambda_1(0\big) \leq S^0 - \lambda_1(0). \tag{4.19}$$

Therefore, $|x(t)| \leq \max\{S^0 - \lambda_1(0), \mu_1(0) - S^0\}$. That $\lambda_1(0) \leq S(t) \leq \mu_1(0)$ follows from (4.16), (4.18) and (4.19).

This completes the proof. □

Our next lemma excludes periodic solutions of (1.1) with certain periods. Its proof uses an argument similar to that used by Chow and Mallet-Paret [11]. See also Krawcewicz, Xia and Wu [31].

Lemma 4.6. *System (1.1) has no nontrivial $\frac{2\tau}{m}$-periodic solutions in $C(\mathbb{R}, \mathbb{R}^+ \times \mathbb{R})$ for any positive integer m.*

Proof. It suffices to prove the lemma for $m = 1$. Suppose that $\big(S(t), x(t)\big) \in C(\mathbb{R}, \mathbb{R}^+ \times \mathbb{R})$ is a nontrivial 2τ-periodic solution. Let $y(t) = e^{D\tau}x(t + \tau)$. Then $y(t)$ is a nontrivial 2τ-periodic solution of equation (4.17). Let $z(t) = y(t - \tau)$. It follows from (4.17) that

$$\begin{aligned} y'(t) &= -Dy(t) + \alpha\, p\big(S^0 - y(t)\big)z(t), \\ z'(t) &= -Dz(t) + \alpha\, p\big(S^0 - z(t)\big)y(t). \end{aligned}$$

This two-dimensional system of ODEs has an invariant line $\Delta = \{(y, z) \in \mathbb{R}_2;\ y = z\}$. Since there are no nontrivial periodic solutions in one-dimensional autonomous ODEs, we must have $y(t) > z(t)$ for all $t \in \mathbb{R}$, or $y(t) < z(t)$ for all $t \in \mathbb{R}$. In the former case, $y(t) > y(t - \tau)$ for all $t \in \mathbb{R}$, so $y(t - \tau) > y(t - 2\tau) = y(t)$. This leads to $z(t) > y(t)$, a contradiction. The other case leads to a contradiction similarly. Therefore, system (1.1) has no nontrivial 2τ-periodic solutions. This completes the proof. □

The following lemma is concerned with the global stability of a negative equilibrium solution of (1.1). It is useful for describing periodic solutions around the nonnegative equilibrium E_{S^0}.

Lemma 4.7. *Let $\big(S(t), x(t)\big) \in C(\mathbb{R}, \mathbb{R}^+ \times \mathbb{R})$ be a solution of (1.1) with $x(t) < 0$ for all $t \geq -\tau$. Then*

$$\lim_{t\to\infty}\big(S(t), x(t)\big) = \big(\mu_1(\tau), \alpha\,(S^0 - \mu_1(\tau))\big).$$

Proof. First note that $\big(S(t), x(t)\big)$ satisfies (3.5) and $y(t) = e^{D\tau}x(t+\tau)$ is a solution of (4.1). We claim that $y(t)$ is bounded. Since $x(t) < 0$ for all $t \geq -\tau$, clearly $y(t)$ is bounded from above. Suppose now that it is unbounded from below. Let $\varepsilon > 0$ be arbitrarily given. Find $T > \tau$ such that $\rho(t) > -\varepsilon$ for all $t \geq T$. Then for any $L < S^0 - \mu_1 - \varepsilon$, there exists $t_0 \geq T > \tau$ such that $y(t_0) < L$. Define

$$\begin{aligned} M &= \min_{t\in[t_0-\tau, t_0]} y(t) < 0 \ \text{ and} \\ \bar{t} &= \sup\{t \geq t_0 - \tau;\ y(s) \geq M \ \text{ for all } \ s \in [t_0 - \tau, t]\}. \end{aligned}$$

Then $t_0 \leq \bar{t} < \infty,\ M \leq L < S^0 - \mu_1 - \varepsilon$, and

$$\begin{aligned} &y(t) \geq M,\ \ t \in [t_0 - \tau, \bar{t}\,], \\ &y(\bar{t}) = M, \ \ \ y'(\bar{t}) \leq 0. \end{aligned}$$

It now follows from (4.1) that

$$\begin{aligned} DM = D\,y(\bar{t}) &\geq \alpha\, p\big(S^0 - y(\bar{t}) + \rho(\bar{t})\big)y(\bar{t} - \tau) \\ &\geq \alpha\, p\big(S^0 - M + \rho(\bar{t})\big)M. \end{aligned}$$

Since $M < 0$, this implies that $D \leq \alpha\, p\big(S^0 - M + \rho(\bar{t})\big)$. By assumption (3.3), we obtain $S^0 - M + \rho(\bar{t}) \leq \mu_1$. Therefore,

$$M \geq S^0 - \mu_1 + \rho(\bar{t}) > S^0 - \mu_1 - \varepsilon > L,$$

a contradiction. Hence $y(t)$ is also bounded from below.

Let $v(t) = -y(t)$. By (4.1), $v(t)$ now satisfies

$$v'(t) = -D\,v(t) + \alpha\, p\big(S^0 + v(t) + \rho(t)\big)v(t - \tau).$$

Note that $v(t) > 0$ and is bounded for $t > 0$. The following numbers are well-defined:

$$a = \liminf_{t\to\infty} v(t), \quad b = \limsup_{t\to\infty} v(t).$$

Then $0 \leq a \leq b < \infty$. We now argue as in the proofs of Lemmas 3.4, 3.6 and 3.8 of Wolkowicz and Xia [51]. We find that $a = b = \mu_1 - S^0$. Thus $\lim_{t\to\infty} x(t) = \lim_{t\to\infty} \alpha\, y(t) = \alpha \lim_{t\to\infty}\big(-v(t)\big) = \alpha\,(S^0 - \mu_1)$. By (3.5), we obtain $\lim_{t\to\infty} S(t) = \mu_1$. Therefore, $\lim_{t\to\infty}\big(S(t), x(t)\big) = \big(\mu_1, \alpha(S^0 - \mu_1)\big)$, and the proof is complete. □

We are now in the position to state and prove the following theorem about the existence and multiplicity of global (i.e. large amplitude) periodic solutions of (1.1). Note that when we say $\tau^* > 0$ is a *local Hopf bifurcation value* we mean a Hopf bifurcation occurs at $\tau = \tau^*$.

Theorem 4.3. *Let δ, N and δ_0 be the numbers given in Lemmas 4.2 and 4.3, and let $\gamma_i(\tau)$ and $f(\tau)$ be the functions defined by (4.6) and (4.8). Assume that $p(S^0) > \sqrt{2}D$ and $f(\delta_0) \neq \gamma_i(\delta)$ for all $1 \leq i \leq N$. Then the following conclusions hold:*

- **(i)** *If $\gamma_N(\delta) < p(S^0)\sqrt{D}\,\delta^{\frac{3}{2}} e^{-D\delta}$, then there exist exactly $2N$ local Hopf bifurcation values, namely, $0 < \tau_1^* < \tau_2^* < \cdots < \tau_{2N}^* < \frac{1}{D}\ln\frac{p(S^0)}{D}$ such that for each $\tau \in (\tau_n^*, \tau_{2N-n+1}^*)$, $1 \leq n \leq N$, system (1.1) has n periodic solutions with periods in $\big(\tau/m,\ \tau/(m-\frac{1}{2})\big)$, $1 \leq m \leq n$, respectively.*
- **(ii)** *If $\gamma_N(\delta) > p(S^0)\sqrt{D}\,\delta^{\frac{3}{2}} e^{-D\tau}$, then there exist exactly $2K$ local Hopf bifurcation values, namely, $0 < \tau_1^* < \tau_2^* < \cdots < \tau_{2K}^* < \frac{1}{D}\ln\frac{p(S^0)}{D}$ such that for each $\tau \in (\tau_n^*, \tau_{2K-n+1}^*)$, $1 \leq n \leq K$, system (1.1) has n periodic solutions with periods in $\big(\tau/m,\ \tau/(m-\frac{1}{2})\big)$, $1 \leq m \leq K$, respectively, where K is either $N-1$ or N.*

Moreover, any periodic solution $\big(S(t), x(t)\big)$ mentioned above surrounds the equilibrium point E_{S^0} in the $S - x$ phase plane, and for any $t \in \mathbb{R}$, $x(t)$ has a zero in the interval $[t-\tau, t]$ and changes sign there.

Proof. We consider system (1.1) in the Banach space $X = C(\mathbb{R}; \mathbb{R}^+ \times \mathbb{R})$ of bounded and continuous functions with the usual supremum norm, and $\tau \in I := \big(0, \frac{1}{D}\ln\frac{p(S^0)}{D}\big)$ is chosen as a bifurcation parameter. We apply the global Hopf bifurcation theorem for delay differential equations (see Erbe, Geba, Krawcewicz and Wu [20]). For terminology, we refer to [11].

We rewrite system (1.1) in the following form of a general FDE:

$$y'(t) = F(y_t, \tau), \quad (t, \tau) \in \mathbb{R} \times I, \tag{4.20}$$

where $y(t) = \big(S(t), x(t)\big)$, $y_t(\theta) = y(t+\theta)$ for $\theta \in (-\infty, 0]$, and

$$F(\varphi, \tau) = \begin{pmatrix} \big(S^0 - \varphi_0(0)\big)D - \varphi_1(0)p\big(\varphi_0(0)\big) \\ -D\varphi_1(0) + e^{-D\tau}p\big(\varphi_0(-\tau)\big)\varphi_1(-\tau) \end{pmatrix}, \tag{4.21}$$

and $\varphi = (\varphi_0, \varphi_1) \in X$, $\tau \in I$. By identifying the subspace of X consisting of all constant functions from $(-\infty, 0]$ to $\mathbb{R}^+ \times \mathbb{R}$ with $\mathbb{R}^+ \times \mathbb{R}$, we obtain a restricted function

$$\hat{F} := F|_{\mathbb{R}^+ \times \mathbb{R} \times I} : \mathbb{R}^+ \times \mathbb{R} \times I \to \mathbb{R}^2.$$

It can be seen from (4.21) that $\hat{F}$ takes the form

$$\hat{F}(x_0, x_1, x_2) = \begin{pmatrix} (S^0 - x_0)D - x_1 p(x_0) \\ -Dx_1 + e^{-Dx_2}p(x_0)x_1 \end{pmatrix},$$

where $(x_0, x_1, x_2) \in \mathbb{R}^+ \times \mathbb{R} \times I$. We define the set of *stationary solutions* of (4.20) by

$$N(F) = \{(x_0, x_1, x_2) \in \mathbb{R}^+ \times \mathbb{R} \times I;\ \hat{F}(x_0, x_1, x_2) = 0\}. \tag{4.22}$$

It follows from assumption (3.3) and formula (4.22) that

$$N(F) = \{(E_{\lambda_1}, \tau),\ (E_{\mu_1}, \tau),\ (S^0, 0, \tau);\ \tau \in I\},$$

where

$$\begin{aligned} E_{\lambda_1} &= \big(\lambda_1(\tau), e^{D\tau}\big(S^0 - \lambda_1(\tau)\big)\big), \\ E_{\mu_1} &= \big(\mu_1(\tau), e^{D\tau}\big(S^0 - \mu_1(\tau)\big)\big). \end{aligned}$$

Let $D_{(x_0,x_1)}\hat{F}$ denote the derivative of $\hat{F}$ with respect to the first two variables. A direct calculation, together with assumption (3.3), gives

$$\det\Big(D_{(x_0,x_1)}\hat{F}(x_0, x_1, x_2)\Big) = D\big(D - e^{-Dx_3} p(x_0) + x_1 p'(x_0)\big) \neq 0,$$

for any $(x_0, x_1, x_2) \in N(F)$. By the Implicit Function Theorem, there is no bifurcation of stationary solutions from $N(F)$.

(i). Notice that for all $\tau \in I$, E_{λ_1} and E_{μ_1} are hyperbolic and asymptotically stable (see Theorem 3.1 and Lemma 4.7). We need only to look for *centers* in the subset $\{(S^0, 0, \tau);\ \tau \in I\}$ of $N(F)$. Now if $p(S^0) > \sqrt{2}D$ and $f(\delta_0) \neq \gamma_i(\delta_0$ for all $1 \leq i \leq N$, Lemma 4.3 implies that system (4.20) has exactly $2N$ *isolated centers*, namely, $\{(S^0, 0, \tau_n^*);\ 1 \leq n \leq 2N\}$. Moreover, it follows from Lemma 4.4 that the *crossing number* $c_n(S^0, 0, \tau_n^*)$ at each of these centers is

$$\begin{aligned} c_n(S^0, 0, \tau_n^*) &= -\text{Sign}\left(\frac{d}{d\tau}\text{Re }(\lambda)|_{\tau=\tau_n^*}\right) \\ &= -\text{Sign}\big(f'(\tau_n^*) - \gamma_i'(\tau_n^*)\big) \\ &= \begin{cases} -1, & \text{if } 1 \leq n \leq N, \\ \ \ 1, & \text{if } N+1 \leq n \leq 2N, \end{cases} \end{aligned}$$

where $i \in \{1, 2, \ldots, N\}$ is the unique integer such that $f(\tau_n^*) = \gamma_i(\tau_n^*)$.

We now define a closed subset $\Sigma(F)$ of $X \times I \times \mathbb{R}^+$ by

$$\begin{aligned} \Sigma(F) = \mathcal{C}l\{&(y, \tau, p) \in X \times I \times \mathbb{R}^+; \\ &y \text{ is a nontrivial } p\text{-periodic solution of system (4.20)}\} \end{aligned}$$

and consider the connected component $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ of $(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ in $\Sigma(F)$ for each $1 \leq n \leq N$, where $\beta_n = \sqrt{A^2(\tau^*) - D^2}$. By Theorem 4.2, $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ is a nonempty subset of $\Sigma(F)$. To obtain more information about $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$, we apply the global bifurcation theorem (see Theorem 3.3 in [20]). It follows that either

(a) $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ is unbounded in $X \times I \times \mathbb{R}^+$, or
(b) $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ is bounded in $X \times I \times \mathbb{R}^+$ and $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n) \cap \{N(F) \setminus \{(S^0, 0, \tau^*)\}\} \neq \emptyset$,

where, for the sake of convenience, a closed subset of I is said to be unbounded in I if it is non-compact relative to I.

We claim that if (a) occurs, then there exists a constant $c > 0$ such that the projection of $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ onto the parameter space I is $\left(c, \frac{1}{D} \ln \frac{p(S^0)}{D}\right)$. To see this, first note that by Lemma 4.6, system (4.20) has no nontrivial periodic solutions with periods τ/n and $2\tau/(2n-1) = \tau/(n-\frac{1}{2})$. Since

$$\frac{\tau^*}{n} < \frac{2\pi}{\beta_n} < \frac{4\tau^*}{4n-1} < \frac{\tau^*}{n-\frac{1}{2}}$$

(see (4.15)), the connected component $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ must lie in the region between $p = \tau/n$ and $p = \tau/(n-\frac{1}{2})$ in the space $X \times I \times \mathbb{R}^+$. Using Lemma 4.5, we find that the projection of $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ onto the X-space is bounded. Therefore, in order for case (a) to occur, it follows that the projection $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ onto I-space must be unbounded. Note that the functional $F(\varphi, \tau)$ is globally Lipschitz with respect to φ on any bounded subset of X with a Lipschitz constant independent of $\tau \in I$. By a result of Li [34] on the lower bounded on the period of periodic solutions for delay equations, this projection is bounded from below in I. Thus the projection $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ must be $\left(c, \frac{1}{D} \ln \frac{p(S^0)}{D}\right)$ for some constant $c \in I$. (In fact, the constant c can be chosen as $(n-\frac{1}{2})p_0$, where $p_0 > 0$ is a lower bound (independent of τ) on the periods of periodic solutions of (4.20) inside the ball $\|\varphi\| \leq \max\{\mu_1(0), S^0 - \lambda_1(0), \mu_1(0) - S^0\}$.) Therefore, for any $\tau > c$, system (4.20) has a nontrivial periodic solution with period in $(\tau/n, \tau/(n-\frac{1}{2}))$. Clearly, $c \leq \tau_n^*$, and so conclusion *(i)* follows from the fact that

$$\left(\tau_i^*, \tau_{2N-i+1}^*\right) \subset \left(\tau_{i-1}^*, \tau_{2N-i+2}^*\right)$$

for each $2 \leq i \leq N$.

In case (b), we must have

$$\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n) \cap \{\, (E_{\lambda_1}, \tau),\ (E_{\mu_1}, \tau);\ \tau \in I \,\} = \emptyset,$$

since E_{λ_1} and E_{μ_1} are asymptotically stable for all $\tau \in I$. Therefore,

$$\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n) \cap \{\, (S^0, 0, \tau_i^*);\ i \neq n \,\} \neq \emptyset.$$

Now, as we have shown above, $\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n)$ is trapped in the region between $p = \tau/n$ and $p = \tau/(n-\frac{1}{2})$, and in this region there are two Hopf bifurcation values, namely, τ_n^* and τ_{2N-n+1}^*. We are led to

$$\mathcal{C}(S^0, 0, \tau_n^*, 2\pi/\beta_n) \cap N(F) = \{(S^0, 0, \tau_n^*),\ (S^0, 0, \tau_{2N-n+1}^*)\}.$$

This implies that for each $\tau \in (\tau_n^*, \tau_{2N-n+1}^*)$, system (4.20) has a nontrivial periodic solution with period in $(\tau/n, \tau/(n-\frac{1}{2}))$. Consequently, in either case, condition *(i)* holds.

(ii). This can be proved in a similar manner to *(i)* by using Lemma 4.3 (ii).

It remains to show that any periodic solution $\big(S(t), x(t)\big)$ of (4.20) with $S(t) > 0,\ t \in \mathbb{R}$, surrounds the equilibrium E_{S^0}. To see this, we first note that $\big(S(t), x(t)\big)$ must satisfy (4.16) for all $t \in \mathbb{R}$. Then $S(t) - S^0$ must change sign since, otherwise, $x(t)$ will be of the same sign and, by Theorem 4.1 or Lemma 4.7, $\lim_{t\to\infty}\big(S(t), x(t)\big) = E_{\lambda_1}$ or E_{μ_1}, a contradiction. The conclusion now follows from the positive invariance of C_2^+ and $C_2^- = \{(S, x) \in \mathbb{R}^+ \times \mathbb{R};\ x \le 0\}$ and the global asymptotic stability of E_{λ_1} and E_{μ_1} with respect to C_2^+ and C_2^-, respectively.

The proof of the theorem is now complete. □

5. The case $\lambda_1 < \mu_1 < S^0$

Recall that by assumption (3.2), $p(S)$ attains its maximum value at $S = \eta$. Throughout this section, we assume that

$$S^0 > \eta \ \text{ and } \ p(\eta) > D,$$

so that $\lambda_1(\tau) < \mu_1(\tau) < S^0$ for all $\tau \in (\tau_{\min}, \tau_{\max})$, where

$$\tau_{\min} = \max\left(0, \frac{1}{D}\ln\frac{p(S^0)}{D}\right) > 0, \ \text{ and } \ \tau_{\max} = \frac{1}{D}\ln\frac{p(\eta)}{D} > 0.$$

Therefore, the three nonnegative equilibrium points $E_{\lambda_1},\ E_{\mu_1}$, and E_{S^0} are all in the nonnegative cone C_2^+ for $\tau_{\min} \le \tau < \tau_{\max}$.

As indicated in Theorem 3.1, in this case, E_{λ_1} and E_{S^0} are both locally asymptotically stable, and E_{μ_1} is unstable. In this section, we show that the positive equilibrium point E_{μ_1} is not always hyperbolic. As in Section 4, we look for critical values τ at which purely imaginary characteristic values appear and Hopf bifurcation occurs.

Define a function

$$B(\tau) = -\alpha\left(S^0 - \mu_1(\tau)\right)p'\big(\mu_1(\tau)\big), \quad \tau \in [\tau_{\min}, \tau_{\max}], \tag{5.1}$$

where $\alpha = e^{-D\tau}$. Since $\lambda_1(\tau) < \mu_1(\tau) < S^0$ for all $\tau \in (\tau_{\min}, \tau_{\max})$, $B(\tau)$ is always positive. By (3.7), the characteristic equation $\Delta(\lambda) = 0$ of the linearized system at E_{μ_1} has a negative root $\lambda = -D$, and all other roots are determined by the equation

$$\lambda + D - B(\tau) - De^{-\lambda\tau} = 0. \tag{5.2}$$

Since $B(\tau) > 0$, $\lambda = 0$ is not a root. We now look for purely imaginary roots. Substitute $\lambda = \beta i$ in (5.2), where $\beta > 0$. By isolating the real and imaginary parts of equation (5.2), we obtain

$$\cos\beta\tau = \frac{D - B(\tau)}{D}, \ \sin\beta\tau = -\frac{\beta}{D}. \tag{5.3}$$

Since $\sin\beta\tau < 0$, it follows that $\beta\tau \in ((2n-1)\pi, 2n\pi)$ for some positive integer n. Squaring both sides of each equation in (5.3), adding them, and solving for β we obtain

$$\beta = \sqrt{B(\tau)\big(2D - B(\tau)\big)}. \tag{5.4}$$

Substituting (5.4) into (5.3), we obtain

$$\begin{aligned} \cos\Big(\tau\sqrt{B(\tau)\big(2D - B(\tau)\big)}\,\Big) &= 1 - \frac{B(\tau)}{D}, \\ \sin\Big(\tau\sqrt{B(\tau)\big(2D - B(\tau)\big)}\,\Big) &= -\frac{\sqrt{B(\tau)\big(2D - B(\tau)\big)}}{D}. \end{aligned} \tag{5.5}$$

We wish to find positive solutions τ of equation (5.5).

First we consider solutions of

$$\sin x = -\frac{x}{D\tau}, \quad x \in ((2n-1)\pi, 2n\pi) \tag{5.6}$$

for each positive integer n (see Fig. 3). For each fixed n, there is a unique solution of (5.6) if the intersection of the curve $y = \sin x$ and the line $y = -\frac{x}{D\tau}$ occurs at a point where the line is tangent to the curve, i.e., $\cos x = -\frac{1}{D\tau}$. But this implies that $\tan x = x$ at this unique solution. With this in mind, denote by ω_n the unique solution of $\tan x = x$ in the interval $\big((2n-1)\pi, (4n-1)\pi/2\big)$. Since $1 = \sin^2(\omega_n) + \cos^2(\omega_n) = \frac{\omega_n^2}{(D\tau)^2} + \frac{1}{(D\tau)^2}$, solving for τ yields $\tau = \sqrt{\omega_n^2 + 1}/D$. Since the slope of the line $y = -\frac{x}{D\tau}$ is an increasing function of τ and $y = \sin x$ is independent of τ, it is clear that for $\tau < \sqrt{\omega_n^2 + 1}/D$ there are no solutions of (5.6) in the interval $((2n-1)\pi, 2n\pi)$ and for $\tau > \sqrt{\omega_n^2 + 1}/D$ there are always exactly two solutions in the interval $((2n-1)\pi, 2n\pi)$, one less than ω_n and one larger than ω_n (see Fig. 3).

Lemma 5.1. *Let i be a positive integer and $\tau \geq \sqrt{\omega_i^2 + 1}/D$. Define $\gamma_{2i-1} = \gamma_{2i-1}(\tau)$ to be the unique solution of*

$$\sin x = -\frac{x}{D\tau}, \quad x \in \big((2i-1)\pi, \omega_i\big],$$

and $\gamma_{2i} = \gamma_{2i}(\tau)$ to be the unique solution of

$$\sin x = -\frac{x}{D\tau}, \quad x \in \big[\omega_i, 2i\pi\big).$$

Then γ_{2i-1} and γ_{2i} are differentiable functions of τ with domain $\big[\sqrt{\omega_i^2 + 1}/D, \infty\big)$. Moreover, γ_{2i-1} is strictly decreasing and γ_{2i} is strictly increasing with

$$\gamma_{2i-1}\Big(\sqrt{\omega_i^2 + 1}/D\Big) = \gamma_{2i}\Big(\sqrt{\omega_i^2 + 1}/D\Big) = \omega_i, \tag{5.7}$$

$$\gamma_{2i-1}(\infty) = (2i-1)\pi, \quad \gamma_{2i}(\infty) = 2i\pi, \tag{5.8}$$

$$\gamma'_{2i-1}\Big(\sqrt{\omega_i^2 + 1}/D\Big) = -\infty, \quad \gamma'_{2i}\Big(\sqrt{\omega_i^2 + 1}/D\Big) = \infty. \tag{5.9}$$

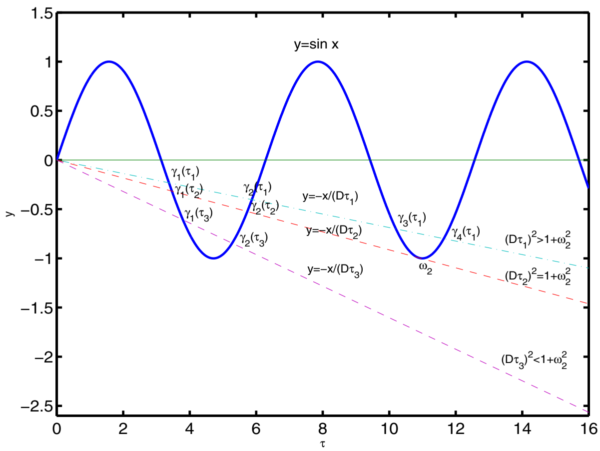

Fig. 3. Solutions of $\sin x = -\frac{x}{D\tau}$.

Proof. That $\gamma_{2i-1}(\tau)$ and $\gamma_{2i}(\tau)$ are well defined, γ_{2i-1} is strictly decreasing and γ_{2i} is strictly increasing, and (5.7) and (5.8) hold follow immediately from the discussion in the paragraph before the statement of the lemma. Also see Fig. 3. By the Implicit Function Theorem, $\gamma_j(\tau),\quad j = 2i-1$ or $2i$ is differentiable and

$$\gamma_j'(\tau) = \frac{\gamma_j(\tau)}{\tau\big(1 + D\tau\cos(\gamma_j(\tau))\big)}. \tag{5.10}$$

Noting that $\cos x$ is increasing on $((2i-1)\pi, 2i\pi)$ and

$$\cos(\gamma_j(\tau))\Big|_{\tau=\frac{1}{D}\sqrt{\omega_i^2+1}} = \cos(\omega_i) = -\frac{1}{D\tau}\Big|_{\tau=\frac{1}{D}\sqrt{\omega_i^2+1}},$$

it follows that $\cos(\gamma_{2i-1}(\tau)) < \cos(\omega_i)$ and $\cos(\gamma_{2i}(\tau)) > \cos(\omega_i)$, for $\tau > \frac{1}{D}\sqrt{\omega_i^2+1}$. Hence (5.9) holds. This establishes the lemma. □

Lemma 5.2. *Let $N > 0$ be the largest integer such that $\sqrt{\omega_N^2+1} < D\tau_{\max}$. Define a function*

$$g(\tau) = \tau\sqrt{B(\tau)\big(2D - B(\tau)\big)}. \tag{5.11}$$

Then the following hold:

(i) *If $\tau = \tau^*$ where $\tau_{\min} < \tau^* < \tau_{\max}$ is a solution of (5.5), then the curve $y = g(\tau)$ must intersect one of the curves $y = \gamma_j(\tau)$, $1 \le j \le 2N$, at $\tau = \tau^*$;*

(ii) *If $y = g(\tau)$ intersects $y = \gamma_j(\tau)$, $1 \le j \le 2N$, ($j = 2i - 1$ or $j = 2i$ for some integer $1 \le i \le N$), at $\tau = \tau^*$ where $\tau_{\min} < \tau^* < \tau_{\max}$, then $\tau = \tau^*$ is a solution of (5.5) if and only if*

$$\begin{cases} B(\tau^*) \ge D, & \text{when } j = 2i-1, \text{ i.e., } j \text{ is odd}, \\ \left(\gamma_j(\tau^*) - \frac{(4i-1)\pi}{2}\right)\left(D - B(\tau^*)\right) \ge 0, & \text{when } j = 2i, \text{ i.e., } j \text{ is even}. \end{cases} \tag{5.12}$$

(iii) *If solutions of*

$$\left(B(\tau) - D\right)\left(\tau B'(\tau) + g'(\tau)g(\tau)\right) = 0, \quad \tau \in (\tau_{\min}, \tau_{\max}) \tag{5.13}$$

are isolated, then there are only a finite number of positive solutions of (5.5).

Proof. (i). If $\tau = \tau^*$, where $\tau_{\min} < \tau^* < \tau_{\max}$, is a solution of (5.5), then

$$\cos\left(g(\tau^*)\right) = 1 - \frac{B(\tau^*)}{D}, \sin\left(g(\tau^*)\right) = -\frac{g(\tau^*)}{D\tau^*},$$

and so $g(\tau^*)$ is a positive solution of $\sin x = -x/(D\tau^*)$. Thus $g(\tau^*) = \gamma_j(\tau^*)$ where $j = 2i - 1$ or $j = 2i$ for some integer $i \ge 1$. Note that the domain of γ_j is $[\sqrt{\omega_i^2 + 1}/D, \infty)$. Since $\tau^* < \tau_{\max}$, it follows that $j \le 2N$ and hence *(i)* holds (see Fig. 4).

(ii). If $y = g(\tau)$ and $y = \gamma_j(\tau)$, $1 \le j \le 2N$, intersects at $\tau = \tau^*$ where $\tau_{\min} < \tau^* < \tau_{\max}$, then $\sin\left(g(\tau^*)\right) = -g(\tau^*)/(D\tau^*)$. This implies that $\tau^* > 0$ satisfies the second equation of (5.5).

If j is odd, by (5.11) $B(\tau^*) > D$. Then $\gamma_j(\tau^*) \in \left((2i-1)\pi, \omega_i\right]$. Thus $g(\tau^*) \in \left((2i-1)\pi, \omega_i\right]$, $\sin\left(g(\tau^*)\right) = -g(\tau^*)/(D\tau^*)$, and $\cos(g(\tau^*)) < 0$.

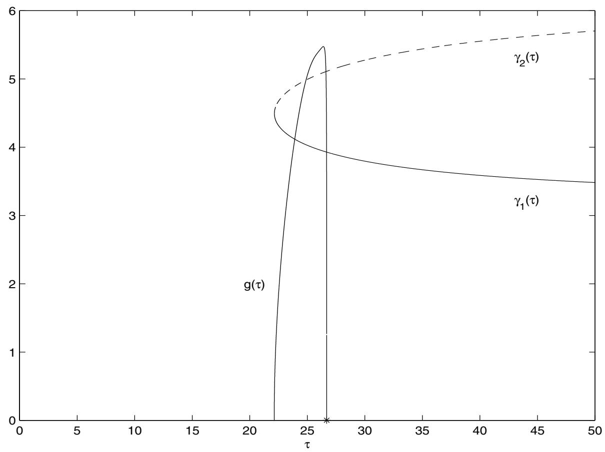

Fig. 4. Intersections of $g(\tau)$ and $\gamma_i(\tau)$.

Therefore,

$$\begin{aligned}\cos\big(g(\tau^*)\big) &= -\sqrt{1-\sin^2\big(g(\tau^*)\big)}\\ &= -\sqrt{1-g^2(\tau^*)/(D\tau^*)^2}\\ &= -\frac{1}{D}\sqrt{D^2-B(\tau^*)\big(2D-B(\tau^*)\big)}\\ &= -\frac{1}{D}\sqrt{(D-B(\tau^*)^2)}\\ &= -\frac{B(\tau^*)-D}{D}\\ &= 1-\frac{B(\tau^*)}{D}.\end{aligned}$$

So τ^* also satisfies the first equation of (5.5). Therefore, τ^* is a positive solution of (5.5).

Now if j is even, from (5.11), either $(B(\tau^*) > D$ and $\gamma_j(\tau^*) \in \big[\omega_i, (4i-1)\pi/2\big))$ or $(B(\tau^*) < D$ and $\gamma_j(\tau^*) \in \big((4i-1)\pi/2, 2i\pi\big))$. In the former case $\cos(g(\tau^*) < 0$ and the proof is the same as in the previous case. In the latter case the proof is similar provided one notes that $\cos(g(\tau^*) > 0$ and so one takes the positive square root and one recalls that $B(\tau^*) < D$ when eliminating the square root.

If (5.12) does not hold, then the sign of the first equation in (5.5) is violated and hence τ^* is not a solution. This completes the proof of (ii).

(iii). Suppose that $y = g(\tau)$ and $y = \gamma_j(\tau)$, $1 \le j \le 2N$, ($j = 2i-1$ or $j = 2i$ for some integer $1 \le i \le N$), intersect at $\tau = \tau^*$ where $\tau_{\min} < \tau^* < \tau_{\max}$. On the domain of definition of g (see equation (5.11)), $g(\tau^*) > 0$ and so $B(\tau^*) < 2D$. Without loss of generality, assume that $\tau^* \neq \sqrt{\omega_i^2 + 1/D}$. Then $\gamma_j'(\tau^*)$ exists and by (5.10), the first equation of (5.5), and the monotonicity of γ_j (see Lemma 5.1),

$$\begin{aligned}\gamma_j'(\tau^*) &= \frac{\gamma_j(\tau^*)}{\tau^*(1+D\tau^*\cos(\gamma_j(\tau^*)))} = \frac{\sqrt{B(\tau^*)(2D-B(\tau^*))}}{1+(D-B(\tau^*))\tau^*}\\ &= \frac{(-1)^j\sqrt{B(\tau^*)(2D-B(\tau^*))}}{|1+(D-B(\tau^*))\tau^*|}.\end{aligned}$$

Therefore,

$$\begin{aligned}g'(\tau^*)-\gamma_j'(\tau^*) &= \sqrt{B(2D-B)}\left(1+\frac{\tau(D-B)B'}{B(2D-B)}-\frac{1}{1+(D-B)\tau}\right)\Bigg|_{\tau=\tau^*}\\ &= \sqrt{B(2D-B)}\left(\frac{\tau(D-B)B'}{B(2D-B)}+\frac{(D-B)\tau}{1+(D-B)\tau}\right)\Bigg|_{\tau=\tau^*}\\ &= \frac{(D-B)(\tau B'+g'(\tau)g(\tau))}{(1+(D-B)\tau)\sqrt{B(2D-B)}}\Bigg|_{\tau=\tau^*}\\ &= \frac{(-1)^j(D-B)(\tau B'+g'(\tau)g(\tau))}{|1+(D-B)\tau|\sqrt{B(2D-B)}}\Bigg|_{\tau=\tau^*}\end{aligned} \tag{5.14}$$

where $B = B(\tau)$ and $B' = B'(\tau)$. Now if solutions to (5.13) are isolated, there are at most a finite number of intersection points of $y = g(\tau)$ and $y = \gamma_j(\tau)$ at which the two graphs are tangent. This implies that $y = g(\tau)$ and $y = \gamma_j(\tau),\ 1 \le j \le 2N$, intersect at only a finite number of points. The conclusion in (iii) now follows from (i).

This completes the proof. □

Remark 5.1. (i) If $B(\tau) > 2D$ for some $\tau \in (\tau_{\min}, \tau_{\max})$, then the domain of $g(\tau)$ is not the whole interval $[\tau_{\min}, \tau_{\max}]$. Since $B(\tau_{\max}) = 0$ (because $p'(\tau_{\max}) = 0$), in this case, the curve $y = g(\tau)$ has more than one disjoint branch and each branch terminates at a point $(\bar{\tau}, g(\bar{\tau})) = (\bar{\tau}, 0)$ with $\tau_{\min} < \bar{\tau} < \tau_{\max}$ satisfying $B(\bar{\tau}) = 2D$;

(ii) It follows from Lemma 5.2 *(i)* that if $y = g(\tau)$ does not intersect $y = \gamma_j(\tau),\ 1 \le j \le 2N$, then the equilibrium E_{μ_1} is hyperbolic.

Lemma 5.3. *Let $\lambda(\tau) = R(\tau) + iI(\tau)$ be a root of (5.2) for each τ near τ^* and $R(\tau^*) = 0,\ I(\tau^*) = \beta > 0$. Then*

$$Sign(\frac{d}{dt}R(\tau^*)) = Sign(B'(\tau^*)\tau^* + g'(\tau^*)g(\tau^*)). \tag{5.15}$$

Proof. Note that $\lambda(\tau)$ satisfies equation (5.2). Differentiating both sides of (5.2) with respect to τ gives

$$\lambda'(\tau) = \frac{B'(\tau) - \lambda D e^{-\lambda\tau}}{1 + \tau D e^{-\lambda\tau}}.$$

Since $De^{-\lambda\tau} = \lambda + D - B$, it follows that

$$\begin{aligned}
\lambda'(\tau^*) &= \left.\frac{B'(\tau) - \lambda(\lambda + D - B(\tau))}{1 + \tau(\lambda + D - B(\tau))}\right|_{\tau=\tau^*} \\
&= \frac{B'(\tau^*) - \beta i(\beta i + D - B(\tau^*))}{1 + \tau^*(\beta i + D - B(\tau^*))} \\
&= \frac{B'(\tau^*)(D - B(\tau^*) - \beta i) - \beta i(\beta^2 + (D - B(\tau^*))^2)}{(D - B(\tau^*) - \beta i) + \tau^*(\beta^2 + (D - B(\tau^*))^2)}.
\end{aligned}$$

We now use (5.3) to obtain $\beta^2 + (D - B(\tau^*))^2 = D^2$. It then follows that

$$\begin{aligned}
\frac{d}{dt}R(\tau^*) &= Re\left(\lambda'(\tau^*)\right) \\
&= Re\left(\frac{B'(\tau^*)(D - B(\tau^*) - \beta i) - D^2\beta i}{D - B(\tau^*) - \beta i + D^2\tau^*}\right) \\
&= Re\left(\frac{B'(\tau^*)(D - B(\tau^*)) - (B'(\tau^*) + D^2)\beta i}{E(\tau^*) - \beta i}\right) \\
&= \frac{1}{E^2(\tau^*) + \beta^2}(B'(\tau^*)(D - B(\tau^*))E(\tau^*) + \beta^2(B'(\tau^*) + D^2)) \\
&= \frac{D^2}{E^2(\tau^*) + \beta^2}(B'(\tau^*)(1 + (D - B(\tau^*))\tau^*) + \beta^2),
\end{aligned} \tag{5.16}$$

where $E(\tau^*) = D^2\tau^* + D - B(\tau^*)$. Note that from (5.4) and (5.11), we have

$$\beta^2 = B(\tau^*)(2D - B(\tau^*))$$

and

$$\begin{aligned} g'(\tau^*)g(\tau^*) &= \tau^*(B'(\tau^*)(D - B(\tau^*)) + B(\tau^*)(2D - B(\tau^*))) \\ &= \tau^*(B'(\tau^*)(D - B(\tau^*))\tau^* + \beta^2). \end{aligned}$$

Substituting this into (5.16), we obtain

$$\frac{d}{dt}R(\tau^*) = \frac{D^2(B'(\tau^*)\tau^* + g'(\tau^*)g(\tau^*))}{\tau^*(E^2(\tau^*) + \beta^2)}, \tag{5.17}$$

which immediately yields (5.15).

This completes the proof. □

Corollary 5.1. *Under the conditions of Lemma 5.2 (i), there exists a unique integer* $1 \le j \le 2N$ *(where* $j = 2i - 1$ *or* $j = 2i$ *for some integer* $1 \le i \le N$*,) such that the curves* $y = g(\tau)$ *and* $y = \gamma_j(\tau)$ *intersect at* $\tau = \tau^*$*. Moreover, if* $\tau \ne \frac{\sqrt{\omega_i^2+1}}{D}$ *or* $\frac{(4i-1)\pi}{2D}$*, then*

$$Sign\left(\frac{d}{dt}R(\tau^*)\right) = \begin{cases} Sign(\gamma_j'(\tau^*) - g'(\tau^*)), & if\ \tau^* \in (\frac{\sqrt{\omega_i^2+1}}{D}, \frac{(4i-1)\pi}{2D}), \\ Sign(g'(\tau^*) - \gamma_j'(\tau^*)), & otherwise. \end{cases} \tag{5.18}$$

Proof. The first point follows directly Lemma 5.2 (i). To obtain (5.18), we first note that it follows from (5.14) and (5.15) that

$$\text{Sign}\left(\frac{d}{dt}R(\tau^*)\right) = \text{Sign}((-1)^j(D - B(\tau^*))(g'(\tau^*) - \gamma_j'(\tau^*))). \tag{5.19}$$

If j is odd, then $\tau^* < \frac{\sqrt{\omega^2+1}}{D}$ and by Lemma 5.2 (ii), $D - B(\tau^*) \le 0$. But $D \ne B(\tau^*)$, because otherwise $\cos(\gamma_j(\tau^*)) = 0$, and so $\gamma_j(\tau^*) = \frac{(4i-1)\pi}{2}$ implying by (5.6) that $\tau^* = \frac{(4i-1)\pi}{2D}$. Thus $D - B(\tau^*) < 0$ and $(-1)^j(D - B(\tau^*)) > 0$. Therefore,

$$\text{Sign}\left(\frac{d}{dt}R(\tau^*)\right) = \text{Sign}(g'(\tau^*) - \gamma_j'(\tau^*)). \tag{5.20}$$

Now if j is even and $\tau^* > \frac{(4i-1)\pi}{2D}$, then $\gamma_j(\tau^*) > \frac{(4i-1)\pi}{2}$. By Lemma 5.2 (ii), $D - B(\tau^*) > 0$ and thus $(-1)^j(D - B(\tau^*)) > 0$. So (5.19) holds. Similarly, if $\tau^* \in \left(\frac{\sqrt{\omega_i^2+1}}{D}, \frac{(4i-1)\pi}{2D}\right)$, then j is even and $\gamma_j(\tau^*) \in \left(\omega_i, \frac{(4i-1)\pi}{2}\right)$. Applying Lemma 5.2 (ii) leads to $(-1)^j(D - B(\tau^*)) < 0$, and (5.18) now follows from (5.19).

This completes the proof. □

We are now ready to give the following local Hopf bifurcation result for model (1.1) in the case that $\lambda_1(\tau) < \mu_1(\tau) < S^0$.

Theorem 5.1. *Assume that $\tau^* > \tau_{\min}$ is a solution of (5.5). Then there exists a unique integer $n \geq 1$ such that $g(\tau^*) = \gamma_n(\tau^*)$. If $\tau^* B'(\tau^*) + g'(\tau^*)g(\tau^*) \neq 0$, $g'(\tau^*) \neq \gamma_n'(\tau^*)$ where $n = 2i - 1$ or $n = 2i$ for some positive integer i and $\tau^* \neq \frac{\sqrt{\omega_i^2+1}}{D}$ or $\frac{(4i-1)\pi}{2D}$, then there is a Hopf bifurcation of the equilibrium E_{μ_1} at $\tau = \tau^*$. Any bifurcating periodic solutions have small amplitude, are positive and unstable, and have period in*

$$\left(\frac{4\tau^*}{2n+1}, \frac{2\tau^*}{n}\right) \quad \text{if } n \text{ is odd,} \tag{5.21}$$

$$\left(\frac{2\tau^*}{n}, \frac{2\tau^*}{n-1}\right) \quad \text{if } n \text{ is even.} \tag{5.22}$$

Proof. The first part follows directly from Lemma 5.3, Corollary 5.1, and the local Hopf bifurcation theorem for delay differential equations (see, for example, [27]). Since E_{μ_1} is a positive equilibrium and these small amplitude periodic orbits are near E_{μ_1}, they must be positive, too. Note that the characteristic equation always has a positive real root and so as in Theorem 4.2, any such bifurcating periodic solutions are unstable. Let $\lambda = \beta i$, $\beta > 0$ be an imaginary root of (5.2) at $\tau = \tau^*$. Then by (5.4), $\beta = g(\tau^*)/\tau^*$, and let $n = 2i - 1$ or $n = 2i$ for some positive integer i. If $n = 2i - 1$, i.e., n is odd, then $g(\tau^*) = \gamma_n(\tau^*) \in (n\pi, \omega_i]$ and therefore

$$\frac{2\pi}{\omega_i} < \frac{2\pi}{\beta} = \frac{2\pi\tau^*}{g(\tau^*)} < \frac{2\tau^*}{n}.$$

Note that $\omega_i < \frac{2n+1}{2}\pi$. The above inequalities imply that (5.21) holds. If n is even, a similar argument shows that (5.22) holds.

This completes the proof. □

In what follows, we consider the global continuation of the periodic solutions bifurcating from the equilibrium E_{μ_1}. In order to apply the global Hopf bifurcation theorem, we need to derive apriori bounds on possible periodic solutions to (1.1) for any $\tau \in (0, \tau_{\max})$. We will require the following notation. Define

$$\|\varphi\|_\infty = \sup_{t\in\mathbb{R}} |\varphi(t)|,$$

where φ is a continuous periodic (scalar) function.

Lemma 5.4. *If $(S(t), x(t))$ is a nonconstant positive periodic solution of (1.1), then*

$$S(t) \geq \lambda_1(\tau) \quad \text{and} \quad x(t) \leq S^0 - \lambda_1(\tau), \quad \text{for all} \quad t \in \mathbb{R}, \quad \tau \in (\tau_{\min}, \tau_{\max}). \tag{5.23}$$

Proof. Let $y(t) = e^{D\tau}x(t+\tau)$. Then $y(t)$ is a solution of (4.17). Let $\xi > 0$ satisfy $y(\xi) = \|y\|_\infty$. Then $y'(\xi) = 0$, and so (4.17) gives

$$Dy(\xi) = e^{-D\tau}p(S^0 - y(\xi))y(\xi - \tau) \le e^{-D\tau}p(S^0 - y(\xi))y(\xi).$$

Since $y(\xi) > 0$, from the above inequality it follows that $p(S^0 - y(\xi)) \ge De^{D\tau}$, which implies that $S^0 - y(\xi) \ge \lambda_1(\tau) \ge \lambda_1(0)$. Thus $y(\xi) \le S^0 - \lambda_1(\tau)$ and $x(t) = e^{-D\tau}y(t-\tau) \le y(\xi) \le S^0 - \lambda_1(\tau)$. The first inequality in (5.23) follows from the fact that $S(t) + y(t) = S^0$ for all $t \in \mathbb{R}$.

This completes the proof. □

We can also show that all positive periodic solutions are bounded away from zero in the $\|\cdot\|_\infty$ norm.

Lemma 5.5. *Assume that $\mu_1(\tau) < S^0$. Then*

$$\|S - S^0\|_\infty \ge S^0 - \mu_1(\tau), \quad \|x\|_\infty \ge e^{-D\tau_{\max}}(S^0 - \mu_1(\tau))$$

for any nonconstant positive solution $(S(t), x(t))$ of (1.1) with $\tau \in (\tau_{\min}, \tau_{\max})$,

Proof. Let $y(t) = e^{D\tau}x(t+\tau)$. As in Lemma 5.4, it follows that $p(S^0 - y(\xi)) \ge De^{D\tau}$, which leads to $S^0 - y(\xi) \le \mu_1(\tau) \le \mu_1(0)$. Thus $y(\xi) \ge S^0 - \mu_1(\tau)$. This implies that

$$\|x\|_\infty = e^{-D\tau}\|y\|_\infty \ge e^{-D\tau_{\max}}(S^0 - \mu_1(\tau)).$$

Note that $y(t) = S^0 - S(t)$, and so $\|S(t) - S^0\|_\infty = \|y(t)\|_\infty \ge S^0 - \mu_1(\tau)$.

This completes the proof. □

We are now ready to state and prove the following global Hopf bifurcation theorem for model (1.1). In what follows, for the ease of exposition, if $b < a$, then the notation (a, b), should be interpreted as the open interval (b, a).

Theorem 5.2. *Let $N > 0$ be the integer defined in Lemma 5.2. Assume that (5.5) has only a finite number of positive solutions. Then the following conclusions hold:*

(i) *For each $1 \le i \le N$ such that $g(\tau)$ intersects $\gamma_j(\tau)$, $j = 2i-1$ or $j = 2i$, there exist an integer $m \ge 1$ and an increasing sequence $\{\tau^*_{n,i}\}_{n=1}^m$ such that $\tau^*_{n,i} \in (\tau_{\min}, \tau_{\max})$, $1 \le n \le m$, are all solutions of (5.5) with $(2i-1)\pi < g(\tau^*_{n,i}) < 2i\pi$.*

(ii) *For the sequence $\{\tau^*_{n,i}\}_{n=1}^m$ in (i), define*

$$\sigma_{n,i} = Sign\big(B'(\tau^*_{n,i})\tau^*_{n,i} + g'(\tau^*_{n,i})g(\tau^*_{n,i})\big),$$

for each $1 \le n \le m$, and let $\tau^*_{0,i} = \tau_{\min}$, $\tau^*_{m+1,i} = \tau_{\max}$. If $\sigma_{n,i} \ne 0$ for all $1 \le n \le m$, then for each $1 \le n \le m$, there exists an integer $\tilde{n} \ne n$, $0 \le \tilde{n} \le m+1$, such that for every $\tau \in (\tau^*_{n,i}, \tau^*_{\tilde{n},i})$, $\tau \ne \tau^*_{k,i}$, $0 \le k \le m+1$, (1.1) has a nonconstant positive periodic solution with period $p \in \left(\frac{\tau}{i}, \frac{2\tau}{2i-1}\right)$.

Proof. (i). This follows immediately from Lemma 5.2.

(ii). We proceed as in the proof of Theorem 4.3. Let $Z = C(\mathbb{R}, \mathbb{R}_2)$ be the Banach space of bounded and continuous functions with the usual supremum norm. We consider system (1.1) in the open subset $Y = C(\mathbb{R}; \mathbb{R}_2^+)$ of Z, and choose $\tau \in J := \big(\tau_{\min}, \tau_{\max}\big)$ as the bifurcation parameter, where $\mathbb{R}_2^+ = (0, \infty) \times (0, \infty)$. Rewrite (1.1) in the following form:

$$y'(t) = F(y_t, \tau), \quad (t, \tau) \in \mathbb{R} \times J, \tag{5.24}$$

where $y(t)$, y_t,and $F(\varphi, \tau)$ with $\varphi \in Y$, are defined as in (4.20) and (4.21). By considering the restricted function $\hat{F} := F|_{\mathbb{R}_2^+ \times J}$, the set of *stationary solutions* of (5.24) is given by

$$N(F) = \{x \in \mathbb{R}_2^+ \times J;\ \hat{F}(x) = 0\} = \{(E_{\lambda_1}, \tau),\ (E_{\mu_1}, \tau),\ (E_{S^0}, \tau);\ \tau \in J\}.$$

Note that $\lambda_1(\tau) < \mu_1(\tau) < S^0$ for all $\tau \in J$. The equilibrium points E_{λ_1} and E_{S^0} are hyperbolic, and $\lambda = 0$ is not a root of the characteristic equation $\Delta(\lambda) = 0$ at E_{μ_1}, where $\Delta(\lambda)$ is given by (3.7). This implies that there is no bifurcation of stationary solutions of $N(F)$.

We now look for centers in the set $N(F)$. Since E_{λ_1} and E_{S^0} are asymptotically stable for all $\tau \in J$, any centers must belong to the subset $\{(E_{\mu_1}, \tau);\ \tau \in J\}$ of $N(F)$. Now for each $1 \le i \le N$ such that $g(\tau)$ intersects $\gamma_j(\tau)$, $j = 2i - 1$ or $j = 2i$, by *(i)*, system (5.24) has exactly m isolated centers $\{\big(E^*_{\mu_1}, \tau^*_{n,i}\big)\}_{n=1}^m$, where

$$E^*_{\mu_1} = \big(\mu_1(\tau^*_{n,i}), e^{-D\tau^*_{n,i}}(S^0 - \mu_1(\tau^*_{n,i}))\big), \quad 1 \le n \le m.$$

Note that $\sigma_{n,i} \neq 0$ for any $1 \le n \le m$. It follows from Lemma 5.3 and [20], that the crossing number $c_n(E^*_{\mu_1}, \tau^*_{n,i})$ at each of these m centers is

$$\begin{aligned} c_n(E^*_{\mu_1}, \tau^*_{n,i}) &= -\mathrm{Sign}\left(\frac{d}{d\tau}\mathrm{Re}\ (\lambda)|_{\tau=\tau^*_{n,i}}\right) \\ &= -\mathrm{Sign}\big(B'(\tau^*_{n,i})\tau^*_{n,i} + g'(\tau^*_{n,i})g(\tau^*_{n,i})\big) \\ &= -\sigma_{n,i} \neq 0. \end{aligned}$$

Next, we define the closed subset $\Sigma(F)$ of $Y \times J \times \mathbb{R}_+$ by

$$\begin{aligned} \Sigma(F) = \mathcal{C}l\{(y, \tau, p) \in Y \times J \times \mathbb{R}_+;\ \ &y \text{ is a nontrivial} \\ &p\text{-periodic solution of system (5.24)}\} \end{aligned}$$

and consider the connected component $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ of $(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ in $\Sigma(F)$ for each fixed $1 \le n \le m$, where $\beta_{n,i} = \sqrt{B(\tau^*_{n,i})(2D - B(\tau^*_{n,i})}$. By the local Hopf bifurcation theorem (Theorem 5.1), we know that $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ is nonempty. Applying the global bifurcation theorem (Theorem 3.3 in [20]), either

- **(a)** $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ is unbounded in $Y \times J \times \mathbb{R}_+$, or
- **(b)** $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ is bounded in $Y \times J \times \mathbb{R}_+$ and the finite set $\Gamma = \mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i}) \cap \{N(F) \setminus \{(E^*_{\mu_1}, \tau^*_{n,i})\}\} \neq \emptyset$.

Here, a closed subset of J or $\mathbb{R}_+$ is said to be unbounded in J or in $\mathbb{R}_+$ if it is non-compact relative to J or $\mathbb{R}_+$. A closed subset S of Y is called bounded if it is bounded and closed in the Banach space Z; S is called unbounded if it is not bounded.

Suppose that (a) holds. We claim that the projection $\mathcal{P}(J)$ of $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ onto the bifurcation parameter $J-$space is unbounded. To see this, first note that by Lemma 4.6, system (5.24) has no nontrivial periodic solutions with periods τ/i and $2\tau/(2i-1)$. By Theorem 5.1, we have $2\pi/\beta_{n,i} \in (\frac{\tau^*_{n,i}}{i}, \frac{2\tau^*_{n,i}}{2i-1})$. This implies that the connected component $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ must lie in the region between $p = \tau/i$ and $p = \tau/(2i-1)$ in the space $Y \times J \times \mathbb{R}_+$. If $\mathcal{P}(J)$ is bounded, then by Lemmas 5.4 and 5.5, we see that the projection $\mathcal{P}(X)$ of $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ onto $X-$space must be bounded. Note that the functional $F(\varphi, \tau)$ is also globally Lipschitz with respect to φ on any bounded subset of Y with a Lipschitz constant independent of $\tau \in J$. As in the proof of Theorem 4.3, it follows that there is a positive lower bound on the period of periodic solutions of (5.24) in any bounded subset of Y. As a result, the projection $\mathcal{P}(p)$ of $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ onto the period parameter $\mathbb{R}_+$-space is also bounded. Hence $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ is bounded, contradicting (a). Therefore, $\mathcal{P}(J)$ must be unbounded. We finally define $\tilde{n}$ to be 0 if $\mathcal{P}(J)$ is bounded away from $\tau_{\max}$, and $m+1$, otherwise. Then $(\tau^*_{n,i}, \tau^*_{\tilde{n},i}) \subset \mathcal{P}(J)$. This implies that for every $\tau \in (\tau^*_{n,i}, \tau^*_{\tilde{n},i})$, $\tau \neq \tau^*_{k,i}$, $1 \leq k \leq m$, system (5.24), and hence (1.1), has a nonconstant periodic solution. Since the periodic solution is in Y, it must be positive.

Now suppose that (b) holds. In this case, we must have

$$\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i}) \cap \{\, (E_{\lambda_1}, \tau),\ (E_{S^0}, \tau);\ \tau \in J \,\} = \emptyset,$$

since E_{λ_1} and E_{S^0} are asymptotically stable for all $\tau \in J$. Therefore,

$$\Gamma = \mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i}) \cap \{\, (E^*_{\mu_1}, \tau^*_{k,i});\ k \neq 0, n, m+1 \,\} \neq \emptyset.$$

Using the argument as in case (a), we can also show that the connected component $\mathcal{C}(E^*_{\mu_1}, \tau^*_{n,i}, 2\pi/\beta_{n,i})$ lies in the the region between $p = \tau/i$ and $p = \tau/(2i-1)$. Note that in this region there are exactly m local Hopf bifurcation values, namely, $\{\tau^*_{n,i}\}_{n=1}^m$. It follows that there must exist $1 \leq k \leq m,\ k \neq n$, such that $(E^*_{\mu_1}, \tau^*_{k,i} 2\pi/\beta_{k,i}) \in \Gamma$. Define $\tilde{n}$ to be any such k that maximizes $|k-n|$. Then we have $(\tau^*_{n,i}, \tau^*_{\tilde{n},i}) \subset \mathcal{P}(J)$, and so (ii) also follows. Therefore, in either case, (ii) must hold.

This completes the proof. □

6. Numerical simulations

In this section, we present some numerical simulations to demonstrate our theoretical results established in this paper and show how to get various transient oscillations via step changes on initial data. We consider

$$\begin{aligned} S'(t) &= \big(S^0 - S(t)\big)\, D - p\big(S(t)\big)x(t), \\ x'(t) &= -Dx(t) + \alpha p\big(S(t-\tau)\big)x(t-\tau), \end{aligned} \tag{6.1}$$

where $D = 0.2079$, and the inhibitory response function $p(S)$ is given by

$$p(S) = \frac{aS}{S^2 + bS + c}$$

with $a = 34.711$, $b = 0.25$, $c = 0.04$. The other two parameters S^0 and τ will be given in the specific computer simulations later. It is easily seen that $p(S)$ is increasing when $S \in [0, \eta)$ and decreasing when $S \in (\eta, \infty)$, where $\eta = 0.2$ and we have $\lambda_1 = \lambda_1(\tau) < \eta < \mu_1 = \mu_1(\tau)$ whenever $\tau \in (0, \frac{1}{D} \ln \frac{p(\eta)}{D}) = (0, 26.69)$. Let $(S(t), x(t))$ be a given solution (not necessarily nonnegative) of (6.1). It follows from (3.5), that

$$S(t - \tau) + e^{D\tau} x(t) \to S^0 \text{ as } t \to \infty.$$

Therefore, in our numerical simulations, we can in fact work on the set $\{S(t - \tau) + e^{D\tau} x(t) = S^0\}$, which results in the following equations

$$x'(t) = -Dx(t) + e^{-D\tau} x(t - \tau) p(S^0 - e^{D\tau} x(t)). \tag{6.2}$$

By the change of the variable $y(t) = x(\tau t)$, we can convert (6.2) to the following delay differential equation with unit delay.

$$y'(t) = -D\tau y(t) + \tau e^{-D\tau} y(t - 1) p(S^0 - e^{D\tau} y(t)). \tag{6.3}$$

All numerical simulations presented here are for system (6.3) and were programmed in Matlab using Euler's method with step size $h = 0.001$ (We also used the Runga-kutta method of 4th order and the results were similar).

We consider three cases: 1) $S^0 < \lambda_1 < \mu_1$; 2) $\lambda_1 < S^0 < \mu_1$; 3) $\lambda_1 < \mu_1 < S^0$.

Case 1): $S^0 < \lambda_1 < \mu_1$. By Theorem 3.2, the dynamic is very simple in this case: $E_{S^0} = (S^0, 0)$ is globally asymptotically stable with respect to C_2^+. For instance, if we choose $S^0 = 0.1$, $\tau = 26.5$, then we have $S^0 = 0.1 < \lambda_1 = 0.1397 < \mu_1 = 0.2862$ and we conclude that $S(t)$ converges to S^0 and the species x eventually goes to extinction. The figure for the numerical simulation is omitted here.

Case 2): $\lambda_1 < S^0 < \mu_1$. Take $S^0 = 1.4$ and $\tau = 19.725$. We can numerically check that $\lambda_1 = 0.0160 < S^0 = 1.4 < \mu_1 = 2.4987$. Theorem 4.1 predicts all positive solutions converge to the equilibrium E_{λ_1} as $t \to \infty$. This can be seen from Fig. 7, where each positive $x(t)$ converges to $x^* = \alpha(S^0 - \lambda_1) = 0.0229$. By Theorem 4.3 (i), we know that there are exactly 12 local Hopf bifurcation values, namely, $0 < \tau_1^* = 0.6024 < \tau_2^* < \cdots < \tau_{12}^* = 19.7262 < \tau_{\max} = \frac{1}{D} \ln \frac{p(S^0)}{D} = 26.6885$ (see Fig. 5).

Note also that $\tau = 19.725 \in (\tau_1^*, \tau_{12}^*) = (0.6024, 19.7262)$ (i.e., $n = 1$ in Theorem 4.3(i)), by Theorem 4.3, there is a periodic solution for system (6.1) which surrounds the equilibrium E_{S^0} and for any $t \in \mathbb{R}$, $x(t)$ has a zero in the interval $[t - \tau, t]$ and changes sign there. This is confirmed in Fig. 6.

As mentioned in Section 1, the unstable periodic solutions bifurcating from E_{S^0} may be regarded as the source of the transient oscillations in solutions that are expected if the initial data are close enough to the unstable manifold of one of these unstable periodic solutions. In fact, our numerical simulations show that

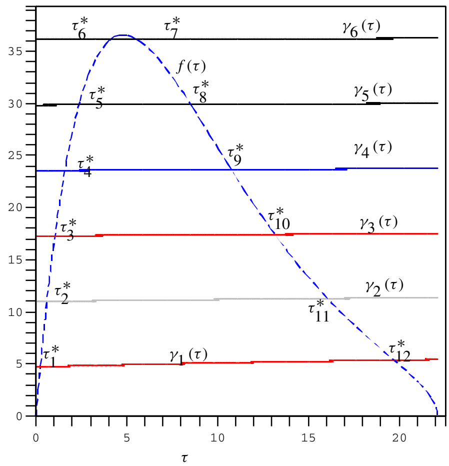

Fig. 5. Intersections of $f(\tau)$ and $\gamma_i(\tau)$. This gives the solutions $\tau_i^*, i = 1, 2, \ldots, 12$, of (4.5).

(6.1) has varying degrees of transient oscillatory behaviour that can be controlled by step changes in the initial data. To this end, we pick the initial data at the mesh points in the following way: $y(\theta) = -0.03$ for $\theta = -1 + ih, i = 0, 1, \ldots, 100$ and take $y(\theta) = y_0$ at the other mesh points. We make step changes on y_0 for each numerical experiment to obtain various degrees of transient oscillatory behaviour and we also detect the existence of a periodic solution. This is shown in Fig. 6, where we used 1) $y_0 = 0.0024$; 2) $y_0 = 0.002359525$; 3) $y_0 = 0.0021$. The figure was plotted in terms of $x(t)$ (i.e., $y(\frac{t}{\tau})$) vs t. Here $x(t)$ obtained from the first set of initial data converges to $\alpha(S^0 - \lambda_1) = 0.0229$ with transient oscillations, the $x(t)$ from the second initial data seems to be a periodic solution oscillating about 0 and the third solution converges to $\alpha(S^0 - \mu_1) = -0.0182$, again with transient oscillations.

In Fig. 7, two sets of positive initial data 1) $y(\theta) = 0.001, \theta < 0$ and $y(0) = 0.01$; 2) $y(\theta) = 0.001, \theta < 0$ and $y(0) = 0.005$ are used to show that every positive solution converges to $\alpha(S^0 - \lambda_1) = 0.0229$ and the transient oscillation happens when the initial data is quite close to unstable manifold of the periodic solution.

Case 3): $\lambda_1 < \mu_1 < S^0$. Take $S^0 = 1.4$ and $\tau = 24.89$. Then $\lambda_1 = 0.0634$ and $\mu_1 = 0.6314$. By Theorem 3.1, we know that E_{S^0} and E_{λ_1} are both locally stable and E_{μ_1} is unstable. We can show that the integer defined in Lemma 5.2 is $N = 1$. As can be seen in Fig. 8, (5.5) has only 4 positive solutions, namely, $\tau_{1,1}^* = 23.9105$, $\tau_{2,1}^* = 24.8883$, $\tau_{3,1}^* = 26.6190$, $\tau_{4,1}^* = 26.6769$, such that $\tau_{n,1}^* \in (\tau_{\min}, \tau_{\max}) = (22.1251, 26.6885)$. Note that $\tau = 24.89 \in (\tau_{2,1}^*, \tau_{3,1}^*)$. By Theorem 5.2, there exists a nonconstant positive periodic solution for (6.1) with period $p \in (\tau, 2\tau) = (24.89, 49.98)$. Changing the initial data slightly, we may obtain

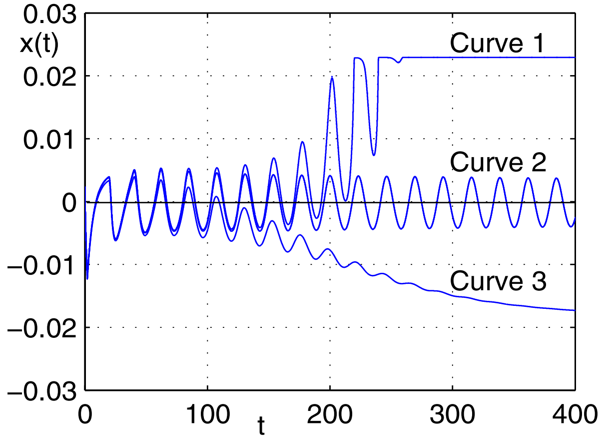

Fig. 6. $\lambda_1 < S^0 < \mu_1$: Transient oscillatory solutions and an unstable periodic solution of (6.1). Euler's method with step size 0.001 was used. Each curve was generated by a different set of initial data. *Curve 1*: $x(\theta) = -0.03$, $\theta \in [-19.725, -17.753]$ and $x(\theta) = 0.0024$, $\theta \in (-17.753, 0]$; *Curve 2*: $x(\theta) = -0.03$, $\theta \in [-19.725, -17.753]$ and $x(\theta) = 0.002359125$, $\theta \in (-17.753, 0]$; *Curve 3*: $x(\theta) = -0.03$, $\theta \in [-19.725, -17.753]$ and $x(\theta) = 0.0021$, $\theta \in (-17.753, 0]$.

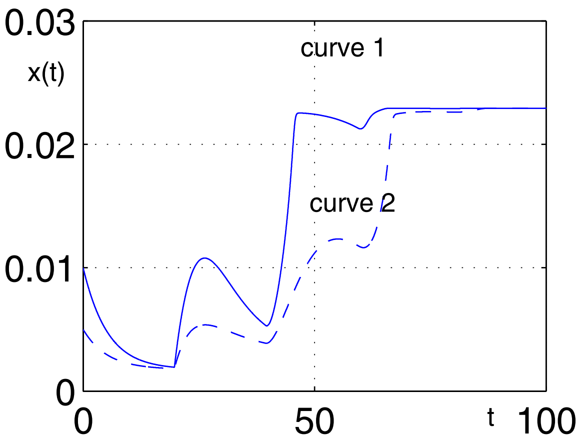

Fig. 7. $\lambda_1 < S^0 < \mu_1$: Transient oscillations in positive solutions of (6.1) Euler's method with step size 0.001 was used. For Curve 1, The initial data is: $x(\theta) = 0.001$, $\theta \in [-19.725, 0)$ and $x(0) = 0.001$; For Curve 2, The initial data is: $x(\theta) = 0.001$, $\theta \in [-19.725, 0)$ and $x(0) = 0.005$.

various transient oscillatory solutions for (6.1). Using the same idea as in Case 2), we obtained the numerical simulations, shown in Figure 9, where we let $y(\theta) = 0.004$ for $\theta < 0$ at the mesh points and $y(0) = y_0$. Step changes were made on y_0 and three sets were used: 1) $y_0 = 0.0055$; 2) $y_0 = 0.0054636757314$; 3) $y_0 = 0.005459$. In the first experiment, $x(t)$ converges to $\alpha(S^0 - \lambda_1) = 0.00756$ with transient

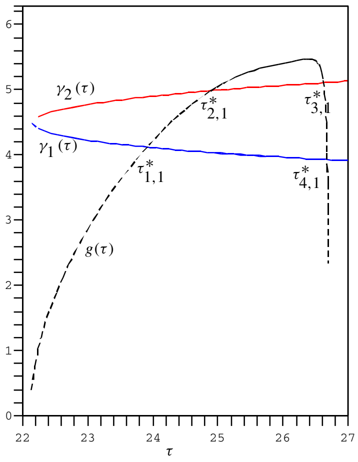

Fig. 8. Intersections of $g(\tau)$ and $\gamma_i(\tau)$. This gives the solutions $\tau^*_{n,1}$, $n = 1, 2, 3, 4$, of (5.5).

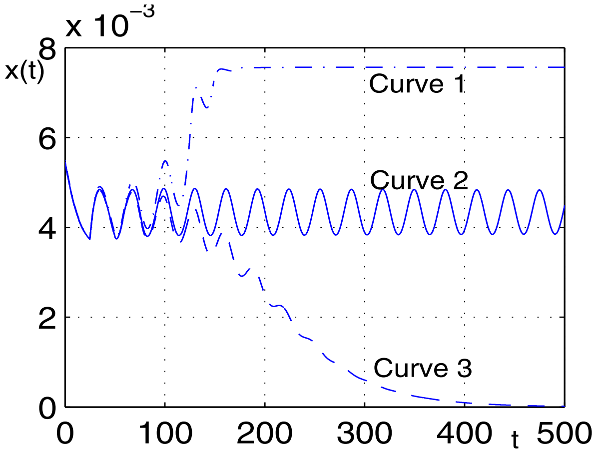

Fig. 9. $\lambda_1 < \mu_1 < S^0$: Transient oscillatory solutions and an unstable positive periodic solution of (6.1). Euler's method with step size 0.001 was used. We used three sets of initial data to get the three curves. *Curve 1*: $x(\theta) = 0.04$, $\theta \in [-24.89, 0)$ and $x(0) = 0.0055$; *Curve 2*: $x(\theta) = 0.04$, $\theta \in [-24.89, 0)$ and $x(\theta) = 0.0054636757314$; *Curve 3*: $x(\theta) = 0.04$, $\theta \in [-24.89, 0)$ and $x(\theta) = 0.005459$.

oscillations, in the second experiment, $x(t)$ is a positive periodic solution. In the third, the solution converges to 0 also with transient oscillations.

7. Discussion

In this paper, we considered a model of microbial growth in the chemostat and studied its transient dynamics, as well as its asymptotic behaviour. The model discussed incorporates a time delay in the growth response that describes the lag involved in the nutrient conversion process. Both monotone response functions and nonmonotone inhibitory response functions were considered. By applying local and global Hopf bifurcation theorems, we proved that unstable periodic solutions exist for certain parameter values. At first thought one might dismiss these solutions as irrelevant, since unstable periodic solutions are themselves not observable in experiments, and these particular periodic solutions may even involve negative values. However, it may in fact be important to understand them. From the continuous dependence of solutions on initial data, it follows that any solution that starts in a neighbourhood of an unstable periodic solution would have transient oscillatory behaviour and the closer the initial data the more oscillatory. Therefore these unstable periodic solutions may be viewed as the *source* of certain actual transient oscillations observed in chemostat experiments. Since it is well known that if delay is not included in the model, even in the case of nonmonotone response functions, no periodic orbits are possible (see e.g., [2], [3], [6], [7], [8], [29], [50], and [54]). We conclude that the delay involved in the the nutrient conversion process might help to account for the transient oscillations observed in chemostat experiments.

Our results can be summarized as follows. First, if $\lambda_1 > S^0$, we showed that the unique non-negative washout equilibrium E_{S^0} is gobally asymptotically stable with respect to the non-negative cone. In this case, the population will eventually be washed out of the chemostat. On the other hand, if $\lambda_1 < S^0 < \mu_1$, then we proved that the unique positive equilibrium E_{λ_1}, is globally asymptotically stable with respect to the non-negative cone. However, it was also shown that unstable periodic solutions exist, that bifurcate from the washout equilibrium E_{S^0}, and these unstable periodic solutions can persist, even if the delay parameter moves far from the critical (local) bifurcation values. Finally, if $\lambda_1 < \mu_1 < S^0$, then there exist two positive equilibrium points E_{λ_1} and E_{μ_1}. The equilibrium E_{λ_1} is locally stable and E_{μ_1} is unstable. In this case, we showed that positive unstable periodic solutions are created that surround E_{μ_1}, as the delay parameter passes through certain bifurcation values, and these periodic solutions may also persist when the delay parameter moves far from the critical bifurcation values. We also provided numerical simulations of the model to demonstrate the existence of the unstable periodic solutions, and showed that the model has varying degrees of transient oscillatory behaviour that can be tuned by choosing appropriate initial data with a step change.

Others have considered transient dynamics of microbial growth modelled using nonmonotone (inhibitory) growth response functions (see [7], [10], [40] and the references cited therein). In particular, Edward [18] discussed various mechanisms causing nutrient inhibition at high concentrations and tested five models against a variety of experimental data for the dependence of the growth rate on an inhibitory nutrient. Chi and Howell [10] also studied transient dynamics experimentally and developed a model describing the transient behaviour of microbial growth in the case of nutrient inhibition. Bush and Cook [7] considered both the effect of a time delay in the growth response and the effect of inhibitory nutrient at high concentrations. While the model of Bush and Cook also predicts oscillations, their model admits stable periodic solutions. However, sustained oscillatory behaviour has not usually been observed in experiments. The results in this paper provide more support for the argument discussed in [19], [51], [52] and [53] that model (1.1) is a more appropriate way of incorporating time delay in the model since we have shown that it can be used to describe both the steady state asymptotic behaviour as well as the transient dynamics of microbial growth in the chemostat. In particular, we proved analytically that unstable periodic solutions exist in the model and our numerical simulations indicate that global periodic solutions also appear to be unstable. This important and useful property of the model, as we discussed above, significantly distinguishes our modeling approach from the approaches taken in [7], [9], [13], [21] and [22] who also incorporate delay in their models.

Note also that discrete delay models can be viewed as the limiting case of certain distributed delay models with kernels given by gamma distributions (see Appendix of [52]). By using the linear chain trick technique [36], these distributed delay models can be converted to systems of ordinary differential equations. Hence, the single discrete time delay in model (1.1) may also be considered to simulate infinitely many intermediate stages in the cell, coupled by a linear chain.

Admittedly, the time delay in model (1.1) may still appear to be too simplistic to model the many complex biochemical pathways, or many different kinetic and genetic interactions within the cell, as we do not use any specific cell physiology in deriving the delay term. Multi-compartment models, or structured models, as mentioned in the Introduction, may be more appropriate and more accurate in describing complex pathways and interactions at different organizational levels of cell control. However, as Cunningham and Maas [13] pointed out, there can be a danger in developing and using such models. Firstly, as they try to treat growth phenomena at a higher and more detailed level of sophistication, these approaches necessarily lead to models of greater complexity. Many compartments or subsections have to be included in these models, involving parameters and variables that cannot be measured. This introduces a large number of parameters that make testing of the models difficult. Secondly, these models would likely involve many differential equations resulting in models that may become analytically intractable. Although numerical solutions can be attempted, many important biological principles rely on an analytical and global analysis of the models. Thirdly, as the number of compartments or the level of the cell structure introduced increases, these models become too specific to apply to a general class of populations. In contrast, our delay differential equations model (1.1) involves only a few parameters that can be measured (see, e.g., [18] for the measurements of inhibitory growth rate, and [19] and [51] for a discussion of how to measure the delay parameter). While the model still may not be satisfactory on a quantitative level, it appears to be an appropriate and generic model that is capable of capturing both asymptotic and transient dynamics observed in experiments, and may be applied to treat a broad range of chemostat populations, since no specific assumptions are made in the model on the internal cell-division process.

Many experimental scientists studying transient dynamics have used the input nutrient concentration S^0 and the dilution rate D as environmental parameters, that they have suddenly perturbed after the chemostat has reached steady state. On the other hand, in our numerical examples shown in Section 6, we produced transient oscillatory solutions through step changes in the initial data. These two approaches are related. In fact, the effect of changing the input nutrient concentration S^0, for example, can be achieved by an appropriate step change of the initial data. To see this, suppose that the chemostat has attained a steady state, say, $E^* = (S^*, x^*)$, from time $t = t_0$. Then $u(t) = \big(S(t), x(t)\big) = E^*, t \geq t_0$, is an equilibrium solution of (1.1), i.e., $F(\varphi^*, \tau) = 0$ for all relevant τ, where $F(\varphi, \tau)$ is the functional defined in (4.20), and $\varphi^* = (S^*, x^*)$ is a constant function. Let $T \geq t_0 + \tau$ be arbitrarily given. If we change S^0 by an amount ΔS^0 at the instant T, then model (1.1) becomes the new system

$$V'(t) = \tilde{F}(V_t, \tau), \quad t \geq T \tag{7.1}$$

where $\tilde{F}(\varphi, \tau)$ is the same functional as defined in (4.20), except that S^0 is replaced by $S^0 + \Delta S^0$. Due to the step change in S^0, the equilibrium solution $u(t)$ of (1.1) can be considered to undergo a sudden change at time T, and then it continues to evolve as a new solution that has as the governing system, (7.1). Denote this new solution by $v(t)$. Then it follows that $v(\theta) = u(\theta) = E^*,\ T - \tau \leq \theta < T$, and the right derivative of $v(t)$ at T is

$$\begin{aligned} v'_+(T) = \tilde{F}(v_T, \tau) &= \begin{pmatrix} \big(S^+ \Delta S^0 - S^*\big)D - x^* p(S^*) \\ -Dx^* + e^{-D\tau} p(S^*)x^* \end{pmatrix} \\ &= \begin{pmatrix} \Delta S^0 D \\ 0 \end{pmatrix} \neq 0. \end{aligned} \tag{7.2}$$

From (7.2), we know that $v(t)$ begins to change from $u(t)$ at $t = T$. Now choose a number $\delta > 0$, and define the initial data ψ as follows

$$\psi(\theta) = \begin{cases} E^*, & \text{for } T - \tau + \delta \leq \theta < T \\ v(\theta), & \text{for } T \leq \theta \leq T + \delta. \end{cases}$$

As such, the function ψ has a "sudden" change at $T + \delta$ if δ is small. However, by the uniqueness of solutions, the solution $w(t),\ t \geq T + \delta$, with initial data ψ, must be the same as $v(t)$, since the two solutions agree on the interval $[T - \tau + \delta, T + \delta]$. Therefore, any transient behaviour of $v(t)$ must also appear in $w(t)$, and vice versa. Consequently, studying solutions obtained after a step change in S^0, can also be done by studying solutions that start with initial data with the appropriate step change.

We remark that although we have proved the existence of periodic solutions which are all unstable when the delay parameter is near the critical bifurcation values, we only have numerical evidence that indicates that global periodic solutions are also unstable. It is still an open problem to show analytically that this is indeed the case. Moreover, the question as to whether or not the unstable periodic solutions are unique and how stable and unstable manifolds are connected is still not resolved.

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