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Competition in the bioreactor with general quadratic yields when one competitor produces a toxin

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Microorganisms produce toxins against its competitors sometimes, and variable yields are useful to explain the observed oscillatory behavior in the reactor. In this paper, a model with general quadric yields of competition in the bioreactor of two competitors for a single nutrient where one of the competitors can produce toxin against its opponent, is proposed. We analyze the asymptotic behavior of the model in terms of the relevant parameters. The conditions of the three dimensional Hopf bifurcation, and the existence of limit cycles in the nutrient-organism phase plane are obtained.

KEY WORDS: bioreactor, quadratic yields, toxin, Hopf bifurcation, limit cycles

AMS subject classification: 34C35, 92D25

1. Introduction

The bioreactor is often used in laboratory to manufacture products with genetically altered organisms. In most of the models of bioreactors it is assumed that no toxins are produced by one organism to inhibit the other. However, in nature it is known that microorganisms do produce inhibitors against their rivals. So it is important to consider the toxin issue in these models, because most likely in a bioreactor inhibitors are used to suppress the competitors of the organism manufacturing a product.

Chao and Levin provided basic experiments on anti-bacterial toxins [1]. Hsu and Waltman studied the competition in the bioreactor when one competitor produces a toxin, which destroys the other [2,3]. Lenski and Hattingh [4] proposed a model of the bioreactor with an external inhibitor and used numerical experiments to illustrate the behavior of solutions. Late, the model was analyzed mathematically by Hsu and Luo [5] and Hsu and Waltman [2]. Levin [6] also

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constructed a bioreactor model with some numerical evidence of the presence of bi-stable attractors due to toxins (see figure 1 of [6]).

Some mathematical analysis of the chemostat with an internally produced selective medium was given by Hsu and Waltman [2]. The authors also proposed a model in consideration of redirecting a portion of the consumed nutrient to the production of the inhibitor, the global asymptotic behavior of the model. Equations of the model take the form [7].

$$\begin{aligned} S' &= (S^0 - S)D - \frac{x}{\gamma_1}\frac{m_1 S}{a_1 + S} - \frac{y}{\gamma_2}\frac{m_2 S}{a_2 + S} \\ x' &= x\left(\frac{m_1 S}{a_1 + S} - D - \gamma P\right) \\ y' &= y\left((1-k)\frac{m_2 S}{a_2 + S} - D\right) \\ P' &= ky\frac{m_2 S}{a_2 + S} - DP, \end{aligned} \tag{1}$$

where $S(t)$ denote the concentration of nutrient in the vessel, $x(t)$, the concentration of the toxin sensitive microorganism, $y(t)$, the toxin producing organism, and $p(t)$, the concentration of toxin present. S^0 is the input concentration of nutrient, D is the washout rate, m_i, the maximal growth rates, a_i, the Michaelis–Menten constants and $\gamma_i, i = 1, 2$, the yield constants. This is usually called the Monod Model or the model with Michaelis–Menten dynamics. The constant k represents the fraction of potential growth devoted to producing the toxin. $k = 0$ produces a system asymptotic to the standard chemostat and $k = 1$ represents all effects devoted to producing the toxin and results in no growth and thus extinction. Usually, k is assumed a constant between 0 and 1.

The local and global stability of the equilibrium points of a limiting system of (1) was studied by Hus and Waltman. However, in their simulations no limit cycles have been found. They indicated that "Eliminating this possibility remain an interesting open question" (p. 479, [7]). Since limit cycles correspond to the nonlinear oscillatory phenomena in the reactor, which has been observed in the experiments [9]. Most of the models in bioreactors assume the yields to be constants, but the experimental data indicate that constant yields fail to explain the oscillatory behavior in the chemostat (see [9,10]). Efforts have been mode in this direction for the standard chemastat models (Croode [11,12], Huang [8], Zhu and Huang [13]). But in the case when one competitor produces a toxin there is not any model with variable yields reported in the literature. Furthermore, it is always of interest in both theory and applications to prove the existence of periodic solutions of the n-dimensional differential system. The situation of $n \geqslant 3$ is much complicated than the one of $n = 2$ because the powerful tools in the plane system like Poincare-Bendixson theorem cannot be applied directly in the space.

The goal of this paper is to propose a bioreactor model with a toxin-producing competitor with variable yields: $\gamma_1 = A_1+B_1S+C_1S^2$, $\gamma_2 = A_2+B_2S+C_2S^2$. We shall study the global asymptotic behavior of the model in terms of system parameters, the operating parameters of the bioreactor and the parameters of the organisms. We shall also show that the three dimensional system undergoes a Hopf bifurcation which implies the existence of limit cycles in the three dimensional space. This study is useful in analyzing the nonlinear oscillatory behaviors in the competition when one organism produces toxin. We propose our model in Section 2 and leave the main theorems and the proofs in Section 3.

2. The model

Perform the usual scaling for the chemostat, and let

$$\overline{S} = \frac{S}{S^0}, \qquad \overline{x} = \frac{x}{S^0}, \qquad \overline{y} = \frac{y}{S^0}, \qquad \overline{P} = \frac{P}{S^0}. \qquad \tau = Dt,$$
$$\overline{m}_i = \frac{m_i}{D}, \qquad \overline{a}_i = \frac{a_i}{S^0}, \qquad \overline{\gamma} = \frac{\gamma S^0}{D}, \qquad {}' = \frac{d}{d\tau}.$$

Then drop the bars and replace τ with t, B_iS_0 with B_i, $C_iS_0^2$ with C_i, $i = 1, 2$, system (1) becomes

$$\begin{aligned}
S' &= 1 - S - \frac{x}{A_1 + B_1S + C_1S^2}\frac{m_1S}{a_1 + S} - \frac{y}{A_2 + B_2S + C_2S^2}\frac{m_2S}{a_2 + S} \\
x' &= x\left(\frac{m_1S}{a_1 + S} - 1 - \gamma P\right) \\
y' &= y\left((1 - k)\frac{m_2S}{a_2 + S} - 1\right) \\
P' &= ky\frac{m_2S}{a_2 + S} - P.
\end{aligned} \tag{2}$$

The parameters, which are all positive, have been scaled by the operating environment of the bioreactor, determined by S^0 and D. The variable is non-dimensional and the parameters are scaled relative to this environment. The interaction between the toxin and sensitive organism is of the form $-\gamma Px$, γ is the toxin coefficient. A fraction, k, of the nutrient consumption has been allocated to the production of the growth rate corresponding reduced [7].

It is noted that the form of the equations are such that the positive initial conditions at $t = 0$ result in positive solutions for $t > 0$. Actually, the positive octant

$$\Omega = \left\{ (S, x, y) \,\middle|\, S > 0, x > 0, y > 0 \right\}$$

is positively invariant under (2). This is because that on the part of Ω, where $S = 0$, the vector field is directed strictly insider Ω since $S' = 1$, and the faces $x = 0$ and $y = 0$ are solutions of (2). It is also noted that, for any solutions in $\Omega,\ S' \leqslant 1 - S$, and thus

$$\lim_{t\to\infty} \sup S(t) \leqslant \lim_{t\to\infty} \sup(1 + (S(0) - 1)e^{-t}) = 1.$$

Since each component is non-negative, system (2) is dissipative and thus has a compact, global attractor.

Let us introduce a new variable $z = P - ky/(1-k)$ to simplify the equations of (2), and obtain

$$\begin{aligned} z' &= -z \\ S' &= 1 - S - \frac{x}{A_1 + B_1 S + C_1 S^2}\frac{m_1 S}{a_1 + S} - \frac{y}{A_2 + B_2 S + C_2 S^2}\frac{m_2 S}{a_2 + S} \\ x' &= x\left(\frac{m_1 S}{a_1 + S} - 1 - \gamma z - \frac{\gamma k y}{1 - k}\right) \\ y' &= y\left(\frac{(1-k)m_2 S}{a_2 + S} - 1\right). \end{aligned} \tag{3}$$

By the first equation of (3), $z(t) \to 0$ as $t \to +\infty$, so (3) may be considered as an asymptotically autonomous system with the limiting system

$$\begin{aligned} S' &= 1 - S - \frac{x}{A_1 + B_1 S + C_1 S^2}\frac{m_1 S}{a_1 + S} - \frac{y}{A_2 + B_2 S + C_2 S^2}\frac{m_2 S}{a_2 + S} \\ x' &= x\left(\frac{m_1 S}{a_1 + S} - 1 - y\frac{k\gamma}{1 - k}\right) \\ y' &= y\left((1-k)\frac{m_2 S}{a_2 + S} - 1\right). \end{aligned} \tag{4}$$

Similarly, the form of the equations of (4) guarantees that the positive octant Ω is positively invariant and so are the faces $x = 0$ and $y = 0$. It is noted that system (4) is dissipative which is inherited from (3), and consequence, the global attractor of (3) lies in the set $z = 0$ where (4) is satisfied.

3. Main theorems and proofs

Denote

$$\lambda_1 = \frac{a_1}{m_1 - 1}, \qquad \lambda_2 = \frac{a_2}{(1-k)\,m_2 - 1}, \qquad \hat{\lambda} = \varphi^{-1}(0), \tag{5}$$

where

$$\varphi(\lambda) = \frac{m_1 \lambda}{a_1 + \lambda} - 1 - k\gamma(1 - \lambda)(A_2 + B_2\lambda_2 + C_2\lambda_2^2). \tag{6}$$

$\varphi(\lambda)$ is a monotonic increasing function since $\varphi'(\lambda) > 0$, thus the inverse function φ^{-1} is well defined and the only solution $\hat{\lambda}$ exists. Moreover, since $\varphi(\lambda_1) < 0$, and $\varphi(1) > 0$, it follows that $\lambda_1 < \hat{\lambda} < 1$.

Note that $\lambda_2 < \hat{\lambda}$ implies $\varphi(\lambda_2) < 0$.

System (4) has four possible equilibrium points:

$$\begin{array}{ll} E_0\,(1,0,0)\,,\, E_1\left(\lambda_1, (1-\lambda_1)(A_1 + B_1\lambda_1 + C_1\lambda_1^2), 0\right) & \text{if } \lambda_1 < 1, \\ E_2\left(\lambda_2, 0, (1-\lambda_2)\,(1-k)\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)\right) & \text{if } \lambda_2 < 1, \text{and} \\ E_3\,(\lambda_2, x^*, y^*) & \text{if } \lambda_1 < \lambda_2 < \hat{\lambda}, \end{array}$$

where

$$x^* = \frac{\left(A_1 + B\lambda_2 + C_1\lambda_2^2\right)(a_1+\lambda_2)}{m_1\lambda_2}\left(1-\lambda_2-\frac{1}{k\gamma\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)}\left(\frac{m_1\lambda_2}{a_2+\lambda_2}-1\right)\right)$$

$$y^* = \frac{1-k}{k\gamma}\left(\frac{m_1\lambda_2}{a_1+\lambda_2}-1\right), \text{ (both are positive).} \tag{7}$$

Regarding the stability, denote

$$R_1 = \frac{(1-\lambda_1)\left(\left(1+\frac{C_1\lambda_1}{B_1+C_1\lambda_1}\right)(a_1+\lambda_1)^2 - \lambda_1 m_1 a_1\right) - \lambda_1\,(a_1+\lambda_1)^2}{(a_1+\lambda_1)^2 + (1-\lambda_1)\,m_1 a_1}, \tag{8}$$

$$R_2 = \frac{(1-\lambda_2)\,(1-k)\left(\left(1+\frac{C_2\lambda_2}{B_2+C_2\lambda_2}\right)(a_2+\lambda_2)^2 - \lambda_2 m_2 a_2\right) - \lambda_2\,(a_2+\lambda_2)^2}{(a_2+\lambda_2)^2 + (1-\lambda_2)\,(1-k)\,m_2 a_2}. \tag{9}$$

By a standard argument one can prove:

Theorem 1. (i). E_0 always exists. It is locally asymptotically stable if $\lambda_i > 1, i = 1, 2$, and unstable if either inequality is reversed. (ii). E_1 always exists with a two dimensional stable manifold (the plane $y = 0$); and it is locally asymptotically stable if $\lambda_1 < \lambda_2$ and $A_1/(B_1 + C_1\lambda_1) > R_1$, and unstable if either inequality is reversed. (iii). E_2 exists if and only if $\lambda_2 < 1$. If it exists, it has a two dimensional stable manifold (the plane $x = 0$) and it is locally asymptotically stable if $\lambda_2 < \hat{\lambda}$ and $A_2/(B_2 + C_2\lambda_2) > R_2$, and unstable if either inequality is reversed. (iv) E_3 exists if and only if $\lambda_1 < \lambda_2 < \hat{\lambda}$, and if it exists it is always unstable with a two dimensional stable manifold.

Proof. Most of the proofs are similar to the one of Theorem 1 in [13]. Here we just add some necessary points. In the proof of (iii), the characteristic equation of the variational matrix $J(E_2)$ of (4) is

$$(r-d_2)\left(r^2 + b_2 r + c_2\right) = 0, \tag{10}$$

where

$$d_2 = \frac{m_1\lambda_2}{a_1+\lambda_2} - 1 - (1-\lambda_2)\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)k\gamma = \varphi(\lambda_2).$$

Thus, $d_2 < 0$ implies $\lambda_2 < \hat{\lambda}$. In addition, if $b_2 > 0$, all the eigenvalues are either negative or with negative real parts. Thus, E_2 is stable if $\lambda_2 < \hat{\lambda}$ and $A_2/(B_2 + C_2\lambda_2) > R_2$. E_2 is unstable if $\lambda_2 > \hat{\lambda}$ or if $A_2/(B_2 + C_2\lambda_2) < R_2$.

To determine the stability of E_3, we consider the Jacobian matrix $J(E_3)$ of (4). Since

$$\det(J(E_3)) = \frac{1}{A_1 + B_1\lambda_2 + C_1\lambda_2} \frac{m_1\lambda_2}{a_1+\lambda_2} \frac{x^* k\gamma}{1-k} y^*(1-k) \frac{m_2 a_2}{(a_2+\lambda_2)^2} > 0,$$

there exists at least one positive eigenvalue of $J(E_3)$, which implies that E_3 is always unstable. E_3 is either a repeller or unstable with a two dimensional stable manifold. Since the trace of $J(E_3)$ is negative, the first alternative cannot be true. Thus, E_3 is unstable with a two dimensional stable manifold, which implies the nonexistence of limit cycles around E_3.

For the global statement of (i), we can use the comparison argument. Let $(S(t), x(t), y(t))$ be a solution of (4). Consider

$$\begin{aligned}
&\left(S + \frac{x}{A_1 + B_1\lambda_1 + C_1\lambda_1^2} + \frac{y}{\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)(1-k)}\right)' \\
&\quad = 1 - \left(S + \frac{x}{A_1 + B_1\lambda_1 + C_1\lambda_1^2} + \frac{y}{\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)(1-k)}\right) \\
&\qquad - \frac{xyk\gamma}{\left(A_1 + B_1\lambda_1 + C_1\lambda_1^2\right)(1-k)} \\
&\qquad - x\frac{m_1 S}{a_1+S}\left(\frac{1}{A_1 + B_1 S + C_1 S^2} - \frac{1}{A_1 + B_1\lambda_1 + C_1\lambda_1^2}\right) \\
&\qquad - y\frac{m_2 S}{a_2+S}\left(\frac{1}{A_2 + B_2 S + C_2 S^2} - \frac{1}{A_2 + B_2\lambda_2 + C_2\lambda_2^2}\right) \\
&\quad \leqslant 1 - \left(S + \frac{x}{A_1 + B_1\lambda_1 + C_1\lambda_1^2} + \frac{y}{\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)(1-k)}\right).
\end{aligned} \tag{11}$$

This is because for $\lambda_i > 1 > S$, $i = 1, 2$,

$$\frac{1}{A_i + B_i S + C_i S^2} > \frac{1}{A_i + B_i\lambda_i + C_i\lambda_i^2}.$$

Let $\psi(t)$ be the solution of

$$\begin{aligned} &\psi'(t) = -\psi(t) \\ &\psi(t_0) = 1 - S(t_0) - \frac{x(t_0)}{A_1 + B_1\lambda_1 + C_1\lambda_1^2} - \frac{y(t_0)}{\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)(1-k)}. \end{aligned} \tag{12}$$

For sufficiently large t,

$$0 < 1 - S(t) - \frac{x(t)}{A_1 + B_1\lambda_1 + C_1\lambda_1^2} - \frac{y(t)}{\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)(1-k)} \leqslant \psi(t).$$

Since $\psi(t) \to 0$ as $t \to \infty$, then

$$1 - S(t) - \frac{x(t)}{A_1 + B_1\lambda_1 + C_1\lambda_1^2} - \frac{y(t)}{\left(A_2 + B_2\lambda_2 + C_2\lambda_2^2\right)(1-k)} \to 0 \quad \text{as } t \to \infty.$$

Note that if $\lambda_1 > 1$, so $S < \lambda_1$ and by the second equation of (4),

$$x' < x\left(\frac{m_1 S}{a_1 + S} - 1\right) < x\left(\frac{m_1}{a_1 + 1} - 1\right) < 0.$$

Consider

$$\begin{aligned} &\hat{x}'(t) = \hat{x}(t)\left(\tfrac{m_1}{a_1+1} - 1\right) \\ &\hat{x}(t_0) = x(t_0). \end{aligned} \tag{13}$$

For t sufficiently large, $0 < x(t) < \hat{x}(t)$. Since $\hat{x}(t) \to \infty$ as $t \to \infty$, then so is $x(t)$.

Similarly, $y(t) \to 0$ as $t \to \infty$, and thus $S(t) \to 1$ as $t \to \infty$. The proof of Theorem 1 is completed. □

By Theorem 1, one can see the local stability implies the global stability for the equilibrium E_0. It is also true for E_1 and E_2.

Theorem 2. (i) If $\lambda_1 < \lambda_2$ and $A_1/(B_1 + C_1\lambda_1) > R_1$, then E_1 is globally asymptotically stable. (ii) If $\lambda_2 < \hat{\lambda}$ and $A_2/(B_2 + C_2\lambda_2) > R_2$, then E_2 is globally asymptotically stable.

Proof. We look for a positive invariant set in the positive octant Ω and its boundary $\partial\Omega$. Denote

$$\begin{aligned} \Omega^+ = \{ &(S, x, y) | 0 \leqslant S \leqslant L - x - y,\ 0 \leqslant x \leqslant (1-\lambda_1)(A_1 + B_1\lambda_1 + C_1\lambda_1^2) \\ &+\varepsilon_0, 0 \leqslant y \leqslant (1-\lambda_2)(1-k)(A_2 + B_2\lambda_2 + C_2\lambda_2^2) + \varepsilon_0, \end{aligned}$$

where

$$\varepsilon_0 = \text{const. } L \gg 1\}.$$

If we can prove that any trajectory initiating at the point in $\Omega \cup \partial\Omega$ enters into Ω^+ when t is sufficiently large, then the global stability is established from the local stability. The proof is similar to the one of Theorem 5 in [13]. $\square$

From Theorem 2, it follows that

Theorem 3. (i) If $\lambda_i > 1$, $i = 1, 2$, then $\lim_{t\to\infty} S(t) = 1$, $\lim_{t\to\infty} x(t) = \lim_{t\to\infty} y(t) = 0$;

(ii) If $\lambda_1 < 1$, $\lambda_1 < \lambda_2$ and $\mathrm{A}_1/(\mathrm{B}_1 + \mathrm{C}_1\lambda_1) > \mathrm{R}_1$, then

$$\lim_{t\to\infty} S(t) = \lambda_1, \qquad \lim_{t\to\infty} x(t) = (1-\lambda_1)(A_1 + B_1\lambda_1 + C_1\lambda_1^2),$$
$$\lim_{t\to\infty} y(t) = 0;$$

(iii) If $\lambda_2 < 1$, $\lambda_1 > \lambda_2$ (or $\lambda_1 < \lambda_2 < \hat{\lambda}$) and $\mathrm{A}_2/(\mathrm{B}_2 + \mathrm{C}_2\lambda_2) > \mathrm{R}_2$, then

$$\lim_{t\to\infty} S(t) = \lambda_2, \qquad \lim_{t\to\infty} x(t) = 0,$$
$$\lim_{t\to\infty} y(t) = (1-\lambda_2)(1-k)(A_2 + B_2\lambda_2 + C_2\lambda_2^2).$$

From the standpoint of the operation of the bioreactor, if E_0 or E_1 is globally asymptotically stable, in which $\lim_{t\to\infty} y(t) = 0$, the reactor is not functioning as desired. Conversely, if E_2 is asymptotically stable, y survives and it is manufacturing the desired product.

Regarding the bifurcation for the three dimensional system (4), we shall use the LaSalle corollary to the Liapunov stability theorem (see [14]) to show the stability of E_2 at $A_2/(B_2 + C_2\lambda_2) = R_2$ first. Since the Liapunov function is not necessarily continuous on the closure of the region, we use an extension that was used by Wolkowicz and Lu [14]. The extension states that V is a Liapunov function for a system $\mathrm{d}X/\mathrm{d}t = f(X)$ in a region $G \subset \overline{G}$ if

(i) V is continuous on G;

(ii) V is not continuous at a point $\overline{X} \in \overline{G}$ implies that $\lim_{X\to\overline{X},\, X\in G} V(X) = \infty$;

(iii) $V' = \nabla V \cdot f \leqslant 0$ on G.

Theorem 4. Assume $A_2 \geqslant 1$. If $\lambda_2 < \lambda_1$, the equilibrium E_2 is globally asymptotically stable.

Proof. Let

$$V(S, x, y) = \int_{\lambda_1}^{S} \frac{\eta - \lambda_2}{\eta}\mathrm{d}\eta + c_1 \int_{y*}^{y} \frac{\eta - y*}{\eta}\mathrm{d}\eta + c_2 x + c_3 y, \tag{14}$$

where c_1, c_2, c_3 are determined late, and $y^* = (1-k)(1-\lambda_2)(A_2 + B_2\lambda_2 + C_2\lambda_2^2)$. Then

$$
\begin{aligned}
V' &= \frac{S-\lambda_2}{S}\left(1-S-\frac{x}{A_1+B_1S+C_1S^2}\frac{m_1S}{a_1+S}-\frac{y}{A_2+B_2S+C_2S^2}\frac{m_2S}{a_2+S}\right)\\
&\quad +c_1\frac{y-y^*}{y}y\left((1-k)\frac{m_2S}{a_2+S}-1\right)+c_2x\left(\frac{m_1S}{a_1+S}-1-y\frac{k\gamma}{1-k}\right)\\
&\quad +c_3y\left((1-k)\frac{m_2S}{a_2+S}-1\right)\\
&= \frac{S-\lambda_2}{S}(1-S)-c_1y^*\left((1-k)\frac{m_2S}{a_2+S}-1\right)\\
&\quad +\left(-\frac{S-\lambda_2}{S}\frac{y}{A_2+B_2S+C_2S^2}\frac{m_2S}{a_2+S}+y(c_1+c_3)\left((1-k)\frac{m_2S}{a_2+S}-1\right)\right)\\
&\quad -c_2\frac{k\gamma xy}{1-k}\quad +c_2x\left(\frac{m_1\lambda_2}{a_1+\lambda_2}-1\right)+x\left(c_2\left(\frac{m_1S}{a_1+S}-\frac{m_1\lambda_2}{a_1+\lambda_2}\right)\right.\\
&\quad \left.-\frac{S-\lambda_2}{S}\frac{1}{A_1+B_1S+C_1S^2}\frac{m_1S}{a_1+S}\right)\\
&\equiv V_1+V_2+V_3+V_4+V_5.
\end{aligned}
$$

It easy to see that

$$
(1-k)\frac{m_2S}{a_2+S}-1=\frac{(1-k)m_2-1}{a_2+S}(S-\lambda_2),\quad 1-k=\frac{a_2+\lambda_2}{m_2\lambda_2}. \tag{15}
$$

The sign of each part of V' can be determined as follows:

First choose $c_1=m_2/((1-k)m_2-1)(A_2+B_2\lambda_2+C_2\lambda_2^2)$, and it follows that

$$
\begin{aligned}
V_1 &= \frac{S-\lambda_2}{S}(1-S)-c_1y^*\frac{((1-k)m_2-1)(S-\lambda_2)}{a_2+S}\\
&= (S-\lambda_2)\left(\frac{1-S}{S}-\frac{m_2}{(1-k)m_2-1}(1-k)(1-\lambda_2)(A_2+B_2\lambda_2+C_2\lambda_2^2)\right.\\
&\qquad \left.\times\frac{(1-k)m_2-1}{a_2+S}\right)=(S-\lambda_2)\left(\frac{1-S}{S}-m_2(1-k)(1-\lambda_2)\frac{1}{a_2+S}\right)\\
&\leqslant (S-\lambda_2)\left(\frac{1-S}{S}-m_2\frac{a_2+\lambda_2}{m_2\lambda_2}(1-\lambda_2)\frac{1}{a_2+S}\right)\\
&= -(S-\lambda_2)^2\frac{a_2+S\lambda_2}{\lambda_2S(a_2+S)}\leqslant 0.
\end{aligned}
$$

Also,

$$V_2 = -\frac{S-\lambda_2}{S}\frac{y}{A_2+B_2S+C_2S^2}\frac{m_2S}{a_2+S} + y(c_3+c_1)\frac{(1-k)m_2-1}{a_2+S}(S-\lambda_2)$$
$$= \frac{S-\lambda_2}{a_2+S}\frac{y}{A_2+B_2S+C_2S^2}\big((c_1+c_3)((1-k)m_2-1)(A_2+B_2S+C_2S^2)-m_2\big).$$

Suppose $S \leqslant \lambda_2$, choose

$$c_3 = \frac{m_2}{(1-k)m_2-1}\left(\frac{1}{A_2} - \frac{1}{A_2+B_2\lambda_2+C_2\lambda_2^2}\right),$$

then

$$\left(\frac{m_2}{((1-k)m_2-1)(A_2+B_2\lambda_2+C_2\lambda_2^2)}+c_3\right)((1-k)m_2-1)(A_2+B_2S+C_2\lambda_2^2) \geqslant m_2.$$

Therefore, $V_2 \leqslant 0$.
Suppose $S > \lambda_2$. Choose

$$c_3 = \frac{m_2}{(1-k)m_2-1}\left(\frac{1}{A_2+B_2+C_2} - \frac{1}{A_2+B_2\lambda_2+C_2\lambda_2^2}\right),$$

hence $(c_1+c_3)((1-k)m_2-1)(A_2+B_2S+C_2S^2) < m_2$ that is $V_2 < 0$.

Regarding V_3, V_4 and V_5, one has

$$V_3 = -c_2\frac{k\gamma xy}{1-k} \leqslant 0, \quad V_4 = c_2x\left(\frac{m_1\lambda_2}{a_1+\lambda_2}-1\right) \leqslant 0 \text{ (since } c_2 \geqslant 0,\ \lambda_2 < \lambda_1) \quad \text{and}$$
$$V_5 = x\left(c_2\Big(\frac{m_1S}{a_1+S} - \frac{m_1\lambda_2}{a_1+\lambda_2}\Big) - \frac{S-\lambda_2}{S}\frac{1}{A_1+B_1S+C_1S^2}\frac{m_1S}{a_1+S}\right)$$
$$= \frac{xm_1(S-\lambda_2)}{a_1+S}\left(\frac{c_2a_1}{a_1+\lambda_2} - \frac{1}{A_1+B_1S+C_1S^2}\right).$$

If $S \leqslant \lambda_2$, choose $c_2 = (a_1+\lambda_2)/a_1$, then

$$\frac{c_2a_1}{a_1+\lambda_2} \geqslant \frac{1}{A_1+B_1S+C_1S^2} \quad \text{and} \quad V_5 \leqslant 0.$$

If $S > \lambda_2$, choose $c_2 = (a_1+\lambda_2)/a_1(A_1+B_1+C_1)$, then

$$\frac{c_2a_1}{a_1+\lambda_2} \leqslant \frac{1}{A_1+B_1S+C_1S^2}, \quad \text{and thus} \quad V_5 \leqslant 0.$$

Therefore,

$$V' = V_1+V_2+V_3+V_4+V_5 \leqslant 0, \tag{16}$$

and by the LaSally corollary, all trajectories tend to the largest invariant set in $\Delta = \{(S, x, y) | V' = 0\}$. This requires $S \equiv \lambda_2$ and $x \equiv 0$.

To make $\{S | S = \lambda_2\}$ invariant, under the condition $x = 0$, requires

$$S' = 1 - \lambda_2 - y \frac{1}{(1-k)(A_2 + B_2\lambda_2 + C_2\lambda_2^2)} = 0, \tag{17}$$

which implies $y = (1-k)(1-\lambda_2)(A_2 + B_2\lambda_2 + C_2\lambda_2^2)$. Therefore $\{E_2\}$ is the unique invariant set in Δ. We thus complete the proof of Theorem 4. □

We are now in a position to prove the three dimensional Hopf bifurcation theorem for system (4). We first introduce the following lemma [15].

Lemma 1. Let W be an open set in R^3, $(0,0,0) \in W$. Let $f : W \times (-\mu_0, \mu_0) \to R^3$ be an analytic function on $W \times (-\mu_0, \mu_0)$, where μ_0 is a small positive number. Denote the Jacobian of f at $(X, \mu) = ((0,0,0), 0)$ as $J(f(0,0))$ and assume that

(i) system

$$\frac{\mathrm{d}X}{\mathrm{d}t} = f(X, \mu) \tag{18}$$

has $(0,0,0)$ as its equilibrium point for any μ;

(ii) the eigenvalues of $J(f(0,0))$ are $\pm i\beta(\mu)|_{\mu=0} = \pm i\beta(0), \delta(\mu)|_{\mu=0} = \delta(0)$ with

$$\beta(0) > 0, \quad \delta(0) < 0.$$

Then, if $(0,0,0)$ is asymptotically stable at $\mu = 0$, there exists a sufficiently small μ, $\mu > 0$ such that system $(18)_\mu$ has an asymptotically stable closed orbit surrounding $(0,0,0)$.

The proof of the lemma 1 is based on the Liapunov second method, which can be found in [15].

Theorem 5. If $\lambda_2 < \lambda_1$, system (4) undergoes a three dimensional Hopf bifurcation at $R_2 = A_2/(B_2+C_2\lambda_2)$, and the periodic solution created by the Hopf bifurcation is asymptotically stable for $0 < R_2 - A_2/(B_2 + C_2\lambda_2) \ll 1$.

Proof. Make the change of variables:

$$\overline{S} = S - \lambda_2, \qquad \overline{x} = x, \qquad \overline{y} = y - (1-\lambda_2)(1-k)(A_2 + B_2\lambda_2 + C_2\lambda_2^2),$$

and denote the Jacobian of system (4) in variables $\overline{S}, \overline{x}, \overline{y}$ as $J(\overline{S}, \overline{x}, \overline{y})$.

Choose $\mu = R_2 - A_2/(B_2+C_2\lambda_2)$, R_2 as in (9), as the Hopf bifurcation parameter, and consider system (4) in variables $\overline{S}, \overline{x}, \overline{y}$ as $\frac{\mathrm{d}X}{\mathrm{d}t} = f(X,\mu)$ in $(18)_\mu$. Then

$$J(f(0,0)) = J(\overline{S},\overline{x},\overline{y})\Big|_{\substack{(\overline{S},\overline{x},\overline{y})=(0,0,0)\\ \mu=0}} = J(S,x,y)\Big|_{\substack{(S,x,y)\\ \mu=0}}$$

$$= (\lambda_2, 0, (1-\lambda_2)(1-k)(A_2+B_2\lambda_2+C_2\lambda_2^2)),$$

whose characteristic equation is

$$(r-d_2)\left(r^2+(1-\lambda_2)(1-k)\frac{m_2a_2}{(a_2+\lambda_2)^2}\right)=0. \tag{19}$$

The eigenvalues of (19) are $\pm i\beta(0)$ and $\delta(0)$, where

$$\begin{aligned}\beta(0) &= \frac{1}{a_2+\lambda_2}\sqrt{(1-\lambda_2)(1-k)m_2a_2} > 0,\\ \delta(0) &= \varphi(\lambda_2) < 0,\ \text{(since } \lambda_2<\lambda_1<\hat{\lambda}),\end{aligned} \tag{20}$$

and the hypotheses of the lemma 1 are satisfied. From theorem 4, it follows that: (1) The equilibrium of system (4): $(0,0,0)$ in the $\overline{S},\overline{x},\overline{y}$ coordinate system, or $(\lambda_2, 0, (1-\lambda_2)(1-k)(A_2+B_2\lambda_2+C_2\lambda_2^2))$ in S,x,y coordinates is globally asymptotically stable at $\mu \leqslant 0$; (2) $(0,0,0)$ in $\overline{S},\overline{x},\overline{y}$, or $(\lambda_2,0,(1-\lambda_2)(1-k)(A_2+B_2\lambda_2+C_2\lambda_2^2))$ in S,x,y, is unstable if $\mu>0$ (Theorem 2 (iii)).

Therefore, system $(18)_\mu$, (or (4)), undergoes a Hopf bifurcation at $\mu=0$, (or, $R_2 = A_2/(B_2+C_2\lambda_2)$). Lemma 1 implies that for a sufficient small μ, $\mu>0$, system $(18)_\mu$ has an asymptotically stable closed orbit surrounding $(0,0,0)$, that is, for $0 < R_2 - A_2/(B_2+C_2\lambda_2) < < 1$, system (4) has an asymptotically stable closed orbit surrounding $E_2(\lambda_2, 0, (1-\lambda_2)(1-k)(A_2+B_2\lambda_2+C_2\lambda_2^2))$. Theorem 5 is obtained. □

Regarding the limit cycles in the corresponding stable manifold, following the argument as in [8,13] will result in the next two theorems. It is easy to see that on $x=0$ system (4) is reduced to

$$\begin{aligned}S' &= 1-S-y\frac{1}{A_2+B_2S+C_2S^2}\frac{m_2S}{a_2+S}\\ y' &= y\left(\frac{(1-k)m_2S}{a_2+S}-1\right).\end{aligned} \tag{21}$$

The following theorem holds.

Theorem 6. Assume $0<\lambda_2<1$. System (21) has two equilibrium points: $N_1: (1,0)$, and $N_2: (\lambda_2, (1-\lambda_2)(1-k)(A_2+B_2\lambda_2+C_2\lambda_2^2))$. N_1 is a saddle, and if $A_2/(B_2+C_2\lambda_2) > R_2$, then N_2 is stable; if $A_2/(B_2+C_2\lambda_2) < R_2$, then N_2 is unstable and there exists at least one limit cycle in the stable manifold $x = 0$ surrounding N_2.

Similarly, on the two dimensional stable manifold $y = 0$, system (4) is reduced to

$$\begin{aligned} S' &= 1 - S - \frac{x}{A_1 + B_1 S + C_1 S^2} \frac{m_1 S}{a_1 + S} \\ x' &= x\left(\frac{m_1 S}{a_1 + S} - 1\right). \end{aligned} \tag{22}$$

We have

Theorem 7. If $0 < \lambda_1 < 1$, system (22) has two equilibrium points: $M_1 : (1, 0)$, and $M_2 : (\lambda_1, (1-\lambda_1)(A_1 + B_1\lambda_1 + C_1\lambda_1^2))$. M_1 is a saddle, and M_2 is stable if $A_1/(B_1 + C_1\lambda_1) > R_1$, and unstable if $A_1/(B_1 + C_1\lambda_1) < R_1$. In the case when M_2 is unstable, there is at least one limit cycle of (22) surrounding M_2 on the face $y = 0$.

4. Conclusion

Since the experiments of Chao and Levin [1], the study of the competition in the bioreactor where toxins are produced by one organism to inhibit the other has been interesting to many authors [1–3,5,7,9,13]. However, all these models are assumed that the yields are constants, but the models with constant yields are failed to explain the observed oscillatory behavior in the reactor [8,9,11–13]. We thus modified the model with general quadric yields. We have shown the asymptotic behavior of the model changes with system parameters, and the outcome depends on the initial conditions. We also prove that the three dimensional system undergoes a Hopf bifurcation which creates the existence of limit cycles in the space. Moreover, we investigate that the limit cycles also exist in the nutrient-organism phase plane. Note that the Hopf bifurcation discuss in this paper is for the three dimensional system which is different from the one in [13] which are only in the two dimensional stable manifold.

We observed that in some case the desirable organism is a better competitor without producing an inhibitor so the select medium may not be important (Theorem 2, Section 3). Also, if too much consumption is devoted to producing the inhibitor, λ_2 increases to the point that x wins in spite of the inhibition. Therefore, the inferior competitor can succeed by producing an inhibitor, but only if the initial conditions are suitable.

References

[1] L. Chao and B.R. Levin, Structured habitats and the evolution of anti-competitor toxins in bacteria, Proc. Nat. Acad. Sci. 75 (1981) 6324–6328.

[2] S.B. Hsu and P. Waltman, Analysis of a model of two competitors in a chemostat with an external inhibitor, SIAM J. Appl. Math. 52 (1992) 528–540.
[3] S.B. Hsu and P. Waltman, Competition between plasmid-bearing and plasmid-free organisms in selective media, Chem. Eng. Sci. 52 (1997) 23–35.
[4] R.E. Lenski and S. Hattingh, Coexistence of two competitors on one resource and one inhibitor: a chemostat model based on bacteria and antibiotics, J. Theoret. Biol. 122 (1986) 83–93.
[5] S.B. Hsu and T.K. Luo, Global analysis of a model of plasmid-bearing plasmid-free competition in a chemostat with inhibition, J. Math. Biol. 34 (1995) 41–76.
[6] B.R. Levin, Frequency-dependent selection in bacterial populations, Phil. Trans. Roy. Soc. London 319 (1988) 459–472.
[7] S.B. Hsu and P. Waltman, Competition in the chemostat when one competitor produces toxin, Jpn. J. Indust. Appl. Math. 15 (1998) 471–490.
[8] X.C. Huang, Limit cycles in a continuous fermentation model, J. Math. Chem. 5 (1990) 287–296.
[9] S.S. Pilyugin and P. Waltman, Multiple limit cycles in the chemostat with variable yield, Math. Biosci. 182 (2003) 151–166.
[10] A.G. Dorofeev, M.V. Glagolev, T.F. Bondarenko and N.S. Panikov, Observation and explanation of the unusual growth kinetics of Arthrobacter globiforms, Microbiology 61 (1992) 33–42.
[11] P.S. Crooke, C.-J. Wei and R.D. Tanner, The effect of the specific growth rate and yield expressions on the existence of oscillatory behavior of a continuous fermentation model, Chem. Eng. Commun. 6 (1980) 333–339.
[12] P.S. Crooke and R.D. Tanner, Hopf bifurcations for a variable yield continuous fermentation model, Int. J. Eng. Sci. 20 (1982) 439–443.
[13] L.M. Zhu and X.C. Huang, Relative positions of limit cycles in the continuous culture vessel with variable yield, J. Math. Chem. 38(2) (2005) 119–128.
[14] G.S.K. Wolkowicz and Z. Lu, Global dynamics of a mathematical model of competition in the chemostat: general response functions and differential death rates, SIAM J. Appl. Math. 32 (1992) 222–233.
[15] J. Zhang, *The Geometric Theory and Bifurcation Problem of Ordinary Differential Equation*, (Peking University Press, Beijing, 1987).