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STABILITY AND OPTIMAL CONTROL OF MICROORGANISMS IN CONTINUOUS CULTURE

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ABSTRACT. The process of producing 1,3-preprandiol by microorganism continuous cultivation would attain its equilibrium state. How to get the highest concentration of 1,3-propanediol at that time is the aim for producers. Based on this fact, an optimization model is introduced in this paper, existence of optimal solution is proved. By infinite-dimensional optimal theory, the optimal condition of model is given and the equivalence between optimal condition and the zero of optimality function is proved.

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1. Introduction

The study of 1,3-propanediol(1,3-PD) from fermentation of glycerol by microorganisms has caused great focus in the world since 1980's. Now many research works have been done in the laboratory, such as kinetics model of product formation, growth of cells, substrate consumption and inhibition(see [1]and[2]). Some theoretical studies have been reported too, such as the analysis of multiplicity, hysteresis, bifurcation et al.(see [3]-[5]), and the effect caused by time delay to the dynamic behavior in continuous culture(see [6]). At the same time, some results on dynamical model and its bifurcations and oscillation of some biology system are reported recently(see[7]-[9]). In the process of continuous culture, the system will attain the equilibrium state by auto-catalysis of microorganisms, at that time, how to get the highest concentration of 1,3-PD by

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controlling the operating conditions is the aim of producers. In this paper, taking the stable equilibrium state of system as mainly constraint condition, the concentration of 1,3-PD as objective function, we give the optimal model, and prove the existence of optimal solution. In order to study the optimal condition of this kind of nonlinear optimal control problem, the optimality function is defined in this paper, and the equivalence between the zero of optimality function and optimal condition is proved by infinite-dimensional optimization theory.

The rest of this paper is organized as follows. In section 2 we give the stability analysis in the continuous culture system and optimal control model. The main results of this paper are presented in section 3, we prove the existence of optimal solution and the equivalence between the zero of optimality function and optimal condition.

2. Stability of continuous culture process and optimal control model

The material balance equations in continuous culture can be written as fellows(only one product 1,3-PD is considered):

$$\begin{cases} \dot{x}_1(t) = h_1(x,u) = (\mu - D)x_1(t) \\ \dot{x}_2(t) = h_2(x,u) = D(x_{20} - x_2(t)) - q_s x_1(t) \\ \dot{x}_3(t) = h_3(x,u) = q_3 x_1(t) - D x_3(t) \end{cases} \quad t \in [0,T] \tag{1}$$

where

$$\begin{cases} \mu = \mu_m \dfrac{x_2(t)}{x_2(t)+k_2}\left(1-\dfrac{x_2(t)}{x_2^*}\right)\left(1-\dfrac{x_3(t)}{x_3^*}\right) \\ q_s = m_s + \dfrac{\mu}{Y_s^m} + g_2 \\ q_3 = m_3 + \mu Y^3 + g_3 \\ g_2 = \Delta q_s^m \dfrac{x_2(t)}{x_2(t)+k_s^*} \\ g_3 = \Delta q_3 \dfrac{x_2(t)}{x_2(t)+k_3} \end{cases} \tag{2}$$

Where the elements of the state variable $x(t) := (x_1(t), x_2(t), x_3(t))^T \in R^3$ are biomass, substrate concentration in reactor, product concentration in reactor, the elements of the control variable $u := (D, x_{20})^T \in R^2$ are dilution rate, substrate concentration in medium, μ, q_s q_3 are the specific growth rate of biomass, the specific consumption rate of substrate, and the specific formation rate of product. $\mu_m = 0.67$ is the maximum specific growth rate, $x_1^* = 10$ is the maximum biomass, $x_2^* = 2039$, $x_3^* = 940$ are the critical concentrations of the substrate and product above which cells cease to grow. $Y_s^m = 0.0082$, $Y^3 = 67.69$, $k_s^* = 11.43$, $k_2 = 0.28$, $k_3 = 15.5$, $\Delta q_s^m = 28.58$, $\Delta q_3 = 26.59$, $m_s = 2.2$, $m_3 = -2.69$ are parameters.

According the fermentation experiment, the ranges of the state variable $x(t)$ and control variable u are $W := (0,\ 10) \times (100,\ 2039) \times (0,\ 940)$ and $U := (0.01,\ 0.67) \times (500,\ 2039)$.

The vector form of model(1):

$$\dot{x}(t) = h(x,u) = (h_1(x,u),\ h_2(x,u),\ h_3(x,u))^T \qquad t \in [0,T] \tag{3}$$

Where $x(t) \in W \subset R^3, u \in U \subset R^2$.

Definition 1. A point $\bar{x} \in W$ is called the *equilibrium point of the system (3)* if there exists a point $\bar{u} \in U$ such that $h(\bar{x},\bar{u}) = 0$.

Xiu(see[3]) had pointed that the system (3) defined by (1)(2) existed equilibrium points. Let $h_i(x,u) = 0 (i = 1,2,3)$ in (1) eliminate x_1 and x_3. Then we can get a polynomial equation of degree 5 of x_2 as fellow:

$$c_0 x_2^5 + c_1 x_2^4 + c_2 x_2^3 + c_3 x_2^2 + c_4 x_2 + c_5 = 0$$

where x_2 is unknown number, $u = (D, x_{20})$ is unknown parameters, and

$$\begin{aligned}
c_0 &:= \mu_m(m_3 + DY^3 + \Delta q_2)\\
c_1 &:= \mu_m\Big((m_3 + DY^3 + \Delta q_2)(k_s^* - x_{20} + x_3^* - x_2^*) + (m_3 + DY^3)k_3\Big)\\
c_2 &:= \mu_m\Big[(k_3k_s^* - x_{20}k_3 + x_3^*k_s^* - k_3x_2^*)(m_3 + DY^3)\\
&\quad +(x_3^*k_3 - x_{20}k_s^* - k_s^*x_2^* + x_{20}x_2^* - x_2^*x_3^*)(m_3 + DY^3 + \Delta q_2)\Big]\\
&\quad +Dx_2^*x_3^*(m_s + D/Y_s^m + \Delta q_s^m)\\
c_3 &:= \mu_m\Big[k_3k_s^*(m_3 + DY^3)(x_3^* - x_{20} - x_2^*)\\
&\quad +x_2^*(x_{20} - x_3^*)(k_s^* + k_3)(m_3 + DY^3)\Big] + \mu_m x_2^*\Delta q_2(x_{20}k_s^* - x_3^*k_3)\\
&\quad +Dx_2^*x_3^*\Big[(k_2 + k_3 + k_s^*)(m_s + D/Y_s^m) + (k_2 + k_3)\Delta q_s^m\Big]\\
c_4 &:= \mu_m x_2^*k_3k_s^*(x_{20} - x_3^*)(m_3 + DY^3)\\
&\quad +Dx_2^*x_3^*\Big[(k_2k_3 + k_s^*k_2 + k_s^*k_3)(m_s + D/Y_s^m) + k_2k_3\Delta q_s^m\Big]\\
c_5 &:= Dx_2^*x_3^*k_s^*k_2k_3(m_s + D/Y_s^m)
\end{aligned}$$

According polynomial theory, above polynomial equation exists at least 1 and at most 5 differentiable real value functions $x_2(u)$ of $u = (D, x_{20}) \in U$. Suppose $k \in N, 1 \le k \le 5$. Let $I := \{1, \ldots, k\}$, $x_2^{(i)}(u) := x_2(u), i \in I$ by (1) and (2), we have that:

$$x_1^{(i)}(u) = \frac{D}{m_s + D/Y_s^m + g_2}\Big(x_{20} - x_2^{(i)}(u)\Big)$$

$$x_3^{(i)}(u) = \frac{m_3 + DY^3 + g_3}{m_s + D/Y_s^m + g_2}\Big(x_{20} - x_2^{(i)}(u)\Big)$$

i.e., $x_1^{(i)}(u)$ and $x_3^{(i)}(u)$ are unique determined by $x_2^{(i)}(u)$.
Let $x^{(i)}(u) := \Big(x_1^{(i)}(u), x_2^{(i)}(u), x_3^{(i)}(u)\Big)$.

Consider the linear approximate system of system (3) on the equilibrium point $\bar{x} = (\bar{x}_1, \bar{x}_2, \bar{x}_3)$:

$$\dot{x}(t) = A(x - \bar{x}) \tag{4}$$

where $A = h_x^{'}(\bar{x}, \bar{u})$.

Suppose $|\lambda I - A| = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3$ is the characteristic polynomial of matrix A where

$$\begin{aligned} a_1 &= \bar{D} + D_1, & (5)\\ a_2 &= \bar{D}D_1 + \frac{\partial\mu}{\partial x_2}\bar{x}_1 q_s + \frac{\partial\mu}{\partial x_3}\bar{x}_1\Big(\frac{g_3^{'}\bar{x}_1}{Y_s^m} - q_3 - Y^3 g_2^{'}\bar{x}_1\Big), & (6)\\ a_3 &= \bar{x}_1\bar{D}\Big(\frac{\partial\mu}{\partial x_2}q_s - \frac{\partial\mu}{\partial x_3}q_3\Big) - \frac{\partial\mu}{\partial x_3}\bar{x}_1^2(q_3 g_2^{'} - q_s g_3^{'}), & (7)\\ D_1 &= \bar{D} + \bar{x}_1\Big(g_2^{'} + \frac{\partial\mu}{\partial x_2}/Y_s^m - \frac{\partial\mu}{\partial x_3}Y^3\Big), & (8) \end{aligned}$$

$\bar{x}$ is asymptotic stable equilibrium point of system (3) when $a_1 > 0,\ a_3 > 0$ and $a_1 a_2 - a_3 > 0$(see[3]).

Now we want to look for an asymptotic stable equilibrium point on which the concentration of 1,3-PD is the highest, i.e. the objective function is $\max\limits_{i\in I}\max\limits_{u\in U} x_3^{(i)}(u)$. For I is finite set, for all $i \in I$, first we consider $\max\limits_{u\in U} x_3^{(i)}(u)$. According (1) we know that $x_2^{(i)}(u) - x_{20} \leq 0$ if and only if $x_1^{(i)}(u) \geq 0$, $x_3^{(i)}(u) \geq 0$, i.e., when $x_2^{(i)}(u) \in [100, x_{20}]$, $x_1^{(i)}(u) \leq x_1^*$, and $x_3^{(i)}(u) \leq x_3^*$, we have $x^{(i)}(u) \in W$. So the following optimal control problem is obtained:

$$\begin{aligned} \text{P:} \qquad & \max\nolimits_{u\in U} \quad J(u) = x_3^{(i)}(u) \\ & s.t. \quad f^1(u) := x_2^{(i)}(u) - x_{20} \leq 0 \\ & \qquad\quad f^2(u) := 100 - x_2^{(i)}(u) \leq 0 \\ & \qquad\quad f^3(u) := x_1^{(i)}(u) - x_1^* \leq 0 \\ & \qquad\quad f^4(u) := x_3^{(i)}(u) - x_3^* \leq 0 \\ & \qquad\quad -a_1 < 0 \\ & \qquad\quad -a_3 < 0 \\ & \qquad\quad a_3 - a_1 a_2 < 0 \\ & \qquad\quad u \in U. \end{aligned}$$

For convenience, for $\varepsilon > 0$ sufficiently small, let $f^5(u) := \varepsilon - a_1,\ f^6(u) := \varepsilon - a_2,\ f^7(u) := \varepsilon + a_3 - a_1 a_2,\ f^0(u) := -x_3^{(i)}(u)$, then P can be written as

$$\text{P1:} \qquad \min_{u\in U}\{f^0(u) | f^j(u) \leq 0, j \in q := \{1, 2, \dots, 7\}\}.$$

3. Existence of optimal solution and optimality condition

For all $i \in I$, let $S_i := \{x^{(i)}(u) | u \in U\}$, $U_i := \{u \in U | x^{(i)}(u) \in S_i \cap W\}$, $U_0 := \{u \in \cup_{i\in I} U_i | a_1 \geq \varepsilon, a_3 \geq \varepsilon, a_1 a_2 - a_3 \geq \varepsilon\}$. Then it is easy to see that $S_i \subseteq R^3$ is close set, $S_i \cap W \subseteq R^3$ is compact set, $U_i, U_0 \subseteq R^2$ are compact sets, and $S_i \cap W$ is equilibrium point set of system (3), U_0 is control variable set which corresponding equilibrium point of system (3) is asymptotic stable. It can be shown(see e.g.[3]) that the system (3) exists asymptotic stable equilibrium points. Thus U_0 is un-empty. Because $x^{(i)}(u) (i \in I)$ is continuous function of $u \in U$, the following conclusion is obtained:

Theorem 1. *The optimal solution of (P1) exists.*

Let $\psi(u) := \max_{j\in q} f^j(u)$, $\hat{F}(u) := \max\{f^0(u) - f^0(\hat{u}), \psi(u)\} = \max\{f^0(u) - f^0(\hat{u}), \max_{j\in q} f^j(u)\}$, where $\hat{u}$ is parameter. If $\hat{u}$ is local minimum of (P1), $\hat{u}$ is the local minimum of $\hat{F}(u)$ too.

Theorem 2. *If $\hat{u}$ is local minimum of (P1), there exists multiplier* $\hat{\mu} \in \sum_0^7 := \left\{ (\mu^0, \mu^1, \dots \mu^7) \middle| \sum_{j=0}^{7} \mu^j = 1, \mu^j \geq 0, j = 0, 1, \dots, 7 \right\}$ *such that*

$$\sum_{j=0}^{7} \mu^j \nabla f^j(\hat{u}) = 0, \tag{9}$$

$$\sum_{j=1}^{7} \mu^j f^j(\hat{u}) = 0. \tag{10}$$

Proof. Suppose $\hat{u}$ is local minimizer of (P1). Then it is the local minimum of $\hat{F}(u)$ too. There must exist minimum $\hat{\mu} \in \sum_0^7$(see [10]) such that

$$\begin{aligned} \mu^0 \nabla (f^0(u) - f^0(\hat{u}))|_{u=\hat{u}} + \sum_{j=1}^{7} \mu^j \nabla f^j(\hat{u}) &= 0, \\ \sum_{j=1}^{7} \mu^j (\hat{F}(\hat{u}) - f^j(\hat{u})) &= 0. \end{aligned}$$

Note that $\nabla (f^0(u) - f^0(\hat{u}))|_{u=\hat{u}} = \nabla f^0(\hat{u})$, $\hat{F}(\hat{u}) = 0$, which completes our proof. □

Let

$$F(u, v) := \max\{f^0(u) - f^0(v) - \gamma\psi(v)_+, \psi(u) - \psi(v)_+\},$$

$$
\begin{aligned}
\psi(v)_+ &:= \max\{0,\psi(v)\},\\
\bar{F}(u,u+h) &:= \max\{\langle\nabla f^0(u),h\rangle-\gamma\psi(u)_+,\\
&\qquad \max_{j\in q}\{f^j(u)-\psi(u)_+ +\langle\nabla f^j(u),h\rangle\}\}+\frac{\delta\|h\|^2}{2},\\
\theta(u) &:= \min_{h\in R^2}\bar{F}(u,u+h), \qquad (11)\\
h(u) &:= argmin\bar{F}(u,u+h) \qquad (12)
\end{aligned}
$$

where $\gamma,\delta\in R_+$, $v\in U, h\in R^2$.

Notice if $\hat{u}$ is local minimum of (P1), then $\psi(\hat{u})\le 0$, and for any $u\in U$, we have $F(u,\hat{u})=\hat{F}(u)$.

We call $\theta(u)$ defined by (11) is the optimality function of (P1). The next Theorem shows the equivalence between the zero of the optimality function and optimal conditions (9)(10).

Theorem 3. *Consider the optimality function $\theta(u)$ defined by (11). Then*

(a) *for all $u\in U$, $\theta(u)\le 0$.*

(b) *for all $u\in U$,*

$$\psi(u)-\psi(u)_+ + d\psi(u;h(u))\le\theta(u)-\frac{1}{2}\delta\|h(u)\|^2\le\theta(u),$$

$$-\gamma\psi(u)_+ + df^0(u;h(u))\le\theta(u)-\frac{1}{2}\delta\|h(u)\|^2\le\theta(u).$$

(c) *an alternative expression for $\theta(u)$ and $h(u)$ are given by*

$$
\begin{aligned}
\theta(u) &= -\min_{\mu\in\sum_q^0}\Big\{\mu^0\gamma\psi(u)_+ +\sum_{j=1}^q\mu^j\psi(u)_+ -\sum_{j=1}^q\mu^j f^j(u)\\
&\qquad +\frac{1}{2\delta}\Big\|\sum_{j=0}^q\mu^j\nabla f^j(u)\Big\|^2\Big\}, \qquad (13)\\
h(u) &= -\frac{1}{\delta}\sum_{j=0}^q\mu^j\nabla f^j(u). \qquad (14)
\end{aligned}
$$

(d) *suppose $\psi(\hat{u})\le 0$. Then equalities (9)and (10)hold if and only if $\theta(\hat{u})=0$.*

Proof. (a) Because $\bar{F}(u,u)=\max\{-\gamma\psi(u)_+,\ \max_{j\in q}\{f^j(u)-\psi(u)_+\}\}\le 0$, then $\theta(u)=\min_{h\in R^2}\bar{F}(u,u+h)\le 0$.

(b) From (11) and (12), we obtain

$$
\begin{aligned}
\theta(u) = &\max\{\langle\nabla f^0(u),h(u)\rangle-\gamma\psi(u),\max_{j\in q}\{f^j(u)-\psi(u)_+ +\langle\nabla f^j(u),h(u)\rangle\}\}\\
&+\frac{1}{2}\delta\|h(u)\|^2.
\end{aligned}
$$

Hence,

$$\theta(u) \geq \langle \nabla f^0(u), h(u)\rangle - \gamma\psi(u)_+ + \frac{1}{2}\delta\|h(u)\|^2, \tag{15}$$

$$\theta(u) \geq \max_{j\in q}\{f^j(u) - \psi(u)_+ + \langle \nabla f^j(u), h(u)\rangle\} + \frac{1}{2}\delta\|h(u)\|^2. \tag{16}$$

Note that

$$df^0(u;h(u)) = \langle \nabla f^0(u), h(u)\rangle,$$
$$d\psi(u;h(u)) = \max_{j\in\hat{q}(u)}\langle \nabla f^j(u), h(u)\rangle$$

where $\hat{q}(u) = \{j \in q | f^j(u) = \psi(u)\}$. Then

$$\max_{j\in q}\{f^j(u) - \psi(u)_+ + \langle \nabla f^j(u), h(u)\rangle\} + \frac{1}{2}\delta\|h(u)\|^2$$
$$\geq \psi(u) - \psi(u)_+ + d\psi(u : h(u)) + \frac{1}{2}\delta\|h(u)\|^2.$$

From inequality (16), we can get

$$\psi(u) - \psi(u)_+ + d\psi(u;h(u)) \leq \theta(u) - \frac{1}{2}\delta\|h(u)\|^2 \leq \theta(u).$$

From inequality(15), we get

$$-\gamma\psi(u)_+ + df^0(u;h(u)) \leq \theta(u) - \frac{1}{2}\delta\|h(u)\|^2 \leq \theta(u).$$

(c) First we know that

$$\theta(u) = \min_{h\in R^2}\Big[\max\Big\{\langle \nabla f^0(u), h\rangle - \gamma\psi(u)_+,$$
$$\max_{j\in q}\{f^j(u) - \psi(u)_+ + \langle \nabla f^j(u), h\rangle\}\Big\} + \frac{1}{2}\delta\|h(u)\|^2\Big].$$

Because the maximum over a finite set is equal to the maximum over their convex hull, we find that

$$\theta(u) = \min_{h\in R^2}\max_{\mu\in\sum_0^7}\Big\{\mu^0\langle \nabla f^0(u), h\rangle - \mu^0\gamma\psi(u)_+ + \sum_{j=1}^{7}\mu^j(f^j(u) - \psi(u)_+$$
$$+\langle \nabla f^j(u), h\rangle) + \frac{1}{2}\delta\|h(u)\|^2\Big\}$$
$$= \min_{h\in R^2}\max_{\mu\in\sum_0^7}\Big\{\sum_{j=1}^{7}\mu^j f^j(u) + \sum_{j=0}^{7}\mu^j\langle \nabla f^j(u), h\rangle - \mu^0\gamma\psi(u)_+$$
$$-\sum_{j=1}^{7}\mu^j\psi(u)_+\frac{1}{2}\delta\|h(u)\|^2\Big\}$$

Applying Corollary 5.5.6 in e.g.[10] to above equality, we conclude that

$$\theta(u) = \max_{\mu\in\sum_0^7} \min_{h\in R^2} \Big\{ \sum_{j=1}^{7} \mu^j f^j(u) + \sum_{j=0}^{7} \mu^j \langle \nabla f^j(u), h\rangle - \mu^0 \gamma\psi(u)_+ - \sum_{j=1}^{7} \mu^j \psi(u)_+ \frac{1}{2}\delta \|h(u)\|^2 \Big\}. \tag{17}$$

Now consider the function

$$g(u) := \min_{h\in R^2} \Big\{ \sum_{j=1}^{7} \mu^j f^j(u) + \sum_{j=0}^{7} \mu^j \langle \nabla f^j(u), h\rangle - \mu^0 \gamma\psi(u)_+ - \sum_{j=1}^{7} \mu^j \psi(u)_+ \frac{\delta}{2} \|h(u)\|^2 \Big\}.$$

Solving above unconstrained minimization problem for h in terms of μ, we find that

$$\delta h = -\sum_{j=0}^{7} \mu^j \nabla f^j(u) \tag{18}$$

and, hence, that

$$g(u) = \sum_{j=1}^{7} \mu^j f^j(u) - \mu^0\gamma\psi(u)_+ - \sum_{j=1}^{7} \mu^j \psi(u)_+ - \frac{1}{2\delta} \left\| \sum_{j=0}^{7} \mu^j \nabla f^j(u) \right\|^2$$

Substituting back into (17), we obtain

$$\begin{aligned} \theta(u) &= \max_{\mu\in\sum_0^7} \Big\{ \sum_{j=1}^{7} \mu^j f^j(u) - \mu^0\gamma\psi(u)_+ - \sum_{j=1}^{7} \mu^j \psi(u)_+ - \frac{1}{2\delta} \left\| \sum_{j=0}^{7} \mu^j \nabla f^j(u) \right\|^2 \Big\} \\ &= -\min_{\mu\in\sum_0^7} \Big\{ \mu^0\gamma\psi(u)_+ + \sum_{j=1}^{7} \mu^j \psi(u)_+ - \sum_{j=1}^{7} \mu^j f^j(u) + \frac{1}{2\delta} \left\| \sum_{j=0}^{7} \mu^j \nabla f^j(u) \right\|^2 \Big\}. \end{aligned}$$

It shows equality (13) holds, it follows from (18) that equality (14) holds.

(d) ($\Rightarrow$). Suppose that $\psi(\hat{u}) \leq 0$, and there exist multiplier $\hat{\mu} \in \sum_0^7$ such that (9) and (10) hold, it means $\psi(\hat{u})_+ = 0$, take it into (13). Then $\theta(\hat{u}) \geq 0$. Note the conclusion (a), we know $\theta(\hat{u}) = 0$.

($\Leftarrow$). Suppose that $\psi(\hat{u}) \leq 0$ and $\theta(\hat{u}) = 0$. It follows from (13) that

$$0 = \min_{\mu \in \sum_0^7} \left\{ -\sum_{j=1}^{7} \mu^j f^j(\hat{u}) + \frac{1}{2\delta} \left\| \sum_{j=0}^{7} \mu^j \nabla f^j(\hat{u}) \right\|^2 \right\}.$$

Since $\psi(\hat{u}) \leq 0$, for all $j \in q$, we have $f^j(\hat{u}) \leq 0$, i.e., $-\sum_{j=1}^{7} \mu^j f^j(\hat{u}) \geq 0$. Because $\left\| \sum_{j=0}^{7} \mu^j \nabla f^j(\hat{u}) \right\|^2 \geq 0$, we know that there must exist $\hat{\mu} \in \sum_0^7$ such that $\sum_{j=1}^{7} \mu^j f^j(\hat{u}) = 0$ and $\sum_{j=0}^{7} \mu^j \nabla f^j(\hat{u}) = 0$. i.e., (9) and (10) hold. □

References

1. W. Wang, J. b. Sun, M. Hartlep, W. D. Deckwer, A. P. Zeng, *Combined use of proteomic analysis of glycerol fermentation by klebsiella pneumoniae*, Biotechnol. Bioeng. , **83** (2003), 525-536.
2. Chen. X, Xiu. Z-L, Wang. J, Zhang. D, Xu. P, *Stoichiometric analysis and experimental investigation of glycerol bioconversion to 1,3-propanediol by Klebsiella pneumoniae under microaerobic conditions*, Enzyme Microbial Technol., **33**(2003), 386-394.
3. Zhi-Long Xiu, An-Ping Zeng, and Wolf-Dieter Deckwer, *Multiplicity and stability analysis of microorganisms in continuous culture: effects of metabolic overflow and growth inhibition*, Biotechnol. Bioeng., **57**(1998), 251-261.
4. Y. F. Ma, L. H. Sun and Z. L. Xiu, *Theoretical analysis of oscillatoyr behavior in process of microbial continuous culture*, J. Eng. Math., **20** (2003), 1-6.
5. L. H. Sun, B. H. Song and Z. L. Xiu, *Study of dynamic behavior in culture of continuous cultivation of microorganisms*, J. Dalian University of Technology, **43**(2003), 433-437.
6. Z. L. Xiu, B. H. Song, L. H. Sun, A. P. Zeng, *Theoretical analysis of effects of metabolic overflow and time delay on the performance and dynamic behavior of a two-stage fermentation process*, Biochem. Eng. J **11** (2002), 101-109.
7. Sándor Kovács, *Bifurcations in a human migration model of Scheurle-Seydel type-II: Rotating waves*, J. Appl. Math. & Computing **16**(2004), 69-78.
8. E. Thandapani, R. Arul and P. S. Raja, *Bounded oscillation of second order unstable neutral type difference equations*, J. Appl. Math. & Computing **16**(2004), 79-90.

9. G. P. Samanta and A. Maiti, *Dynamical model of a single-species system in a polluted environment*, J. Appl. Math. & Computing **16**(2004), 231-242.
10. Elijah Polak, *Optimization algorithms and consistent approximations*, Spring-verlag, New York, inc., 1997.

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