MODELING AND PARAMETER IDENTIFICATION FOR MULTISTAGE SIMULATION OF MICROBIAL BIOCONVERSION IN BATCH CULTURE

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The bioconversion of glycerol to 1,3-propanediol is a complex bioprocess. The item of product inhibition in the equation of Specific rate of cell growth is overlapped in [L. Wang, J. X. Ye, E. M. Feng and Z. L. Xiu, An improved model for multistage simulation of glycerol fermentation in batch culture and its parameter identification, Nonlinear Anal. Hybrid Syst. 3(4) (2009) 455–462]. Therefore, in this work, the specific rate of cell growth is modified by the mechanism of multistage simulation of microbial bioconversion and the previous time-dependent model is converted to the autonomous standard form. The properties of the solutions for the nonlinear dynamic system are discussed and the identifiability of the parameters is proved. Finally the feasible optimization algorithm is constructed to find the optimal parameters for the system. Numerical result shows that the improved model with identified parameters can describe the batch culture better, compared with the previous results.

Keywords: Batch culture; specific rate of cell growth; nonlinear dynamical system; parameters identification.
1. Introduction

The bioconversion of glycerol to 1,3-propanediol (1,3-PD) has recently received more and more attention throughout the world due to its environmental safety, high region specificity, cheaply available feedstock, and relatively high theoretical molar yield [19]. Many researchers have been carried out including the quantitative description of the cell growth kinetics of multiple inhibitions, the metabolic overflow kinetics of substrate consumption and product formation [15, 18, 20], existence of equilibrium points and stability [17], time delay [6], optimization of biochemical systems [16], inherent stochasticity of microorganism [11] and feedback control and pulse feeding [10] for the models of the continuous cultures, feeding strategy of glycerol [1], optimal control [12] and optimality condition [13] in fed-batch culture and so on.

Compared with continuous and feed-batch cultures, glycerol fermentation in batch culture can obtain the highest production concentration and molar yield 1,3-PD to glycerol [3]. So nonlinear dynamical systems in this culture have been extensively considered in recent years [2, 4, 5]. The typical cell growth in batch culture includes several growth phases, which are defined as the lag, exponential growth, decreased growth and death phases [14]. However, it should be mentioned that, in [20], the microbial growth inhibited by several inhibitors described by the item \( \prod_{i=2}^{5} (1 - \frac{x_i(t)}{x_i^*}) \) and in [9], the equation of improved Specific rate of cell growth also demonstrated the multiproduct-inhibition. Therefore, in our previous work [14], the product inhibition was overlapped. Additionally, only two new introduced parameters were identified, every system parameter in the improved model need to be identified.

In this paper, based on the previous model in [14], we modify the specific rate of cell growth and convert the novel model to the autonomous standard form in [8] in order to prove the existence, uniqueness and boundedness of solutions to the system and the continuity of solutions with respect to the parameters by using the conclusion of [8]. A parameter identification model for every system parameter is developed and its identifiability is proved. Subsequently, we construct a modified Hooke–Jeeves algorithm to solve the parameter identification problem. Numerical result shows the effectiveness of the algorithm and demonstrates that the improved model can describe the batch culture better, compared with the previous results.

This paper is organized as follows. In Sec. 2, a nonlinear dynamical system of batch culture is proposed. In Sec. 3, the existence, uniqueness, boundedness and regularity of solutions to the system are proved. In Sec. 4, we propose a parameter identification model for the system and construct a feasible algorithm to solve it. Finally, Sec. 5 concludes.
2. Nonlinear Dynamical System

Mass balances of biomass, substrate and products in batch culture are written as follows (see [14]):

\[
\dot{x}(t) = f(t, x(t), u), \quad t \in [0, t_f], \quad x(0) = \xi, \quad (2.1)
\]

where

\[
f(t, x, u) = (f_1(t, x, u), f_2(t, x, u), f_3(t, x, u), f_4(t, x, u), f_5(t, x, u))^T
\]

\[
= (\mu x_1(t), -q_2 x_1(t), q_2 x_1(t), q_4 x_1(t), q_5 x_1(t))^T, \quad (2.2)
\]

where \(x_1(t), x_2(t), x_3(t), x_4(t)\) and \(x_5(t)\) are biomass, glycerol, 1,3-PD, acetate and ethanol concentrations at time \(t\) in the reactor, respectively. \(u = (t_l, t_m)\) are starting moment of lag growth phase and the time when \(\mu\) reaches the maximum, respectively. \(\xi\) denotes the initial state. The specific growth rate of cells \(\mu\), specific consumption rate of substrate \(q_2\) and specific formation rate of products \(q_i\), \(i = 3, 4, 5\), are expressed by the following equations on the basis of [2, 14].

\[
\mu = \mu_m \exp\left(\frac{-(t - t_m)^2}{2t_l^2}\right) \prod_{i=2}^{5} \left(1 - \frac{x_i(t)}{x_i}\right), \quad (2.3)
\]

\[
q_2 = m_2 + \frac{\mu}{Y_2}, \quad (2.4)
\]

\[
q_i = m_i + \mu Y_i, \quad i = 3, 4, 5. \quad (2.5)
\]

In Eq. (2.3), \(\prod_{i=2}^{5} \left(1 - \frac{x_i(t)}{x_i}\right)\) denotes the product inhibition as well as the \(\exp\left(\frac{-(t - t_m)^2}{2t_l^2}\right)\). On the basis of the analysis in [9], we make a modify on (2.3) as follows:

\[
\mu = \mu_m \exp\left(\frac{-(t - t_m)^2}{2t_l^2}\right). \quad (2.6)
\]

Under anaerobic conditions at 37°C and pH = 7.0, the maximum specific growth rate of cells \(\mu_m = 0.67h^{-1}\). \(t_l, t_m, m_i\) and \(Y_i\), \(i = 2, 3, 4, 5\), are parameters to be identified later in Eqs. (2.4)–(2.6), defined as:

\[
k = (t_l, t_m, \mu_m, m_2, m_3, m_4, m_5, Y_2, Y_3, Y_4, Y_5)^T \in K \subset R^{11}.
\]

Here, the parameter values in [2] are used as initial values, that is, \(k_0 \triangleq (1.769, 2.944, 0.67, 2.20, -2.69, -0.97, 5.26, 0.0082, 67.69, 33.07, 11.66)^T \in U\). The parameters to be identified range in

\[
K_{ad} = \prod_{i=1}^{11} [k_{0i} - \Delta k_{0i}, k_{0i} + \Delta k_{0i}] \subset R^{11},
\]

where \(\Delta k_{0i} = 0.5 k_{0i}\) in this paper.
According to the factual experiment, we make the following assumptions:

**H1** The concentrations of reactants are uniform in reactor, while time delay and nonuniform space distribution are ignored.

**H2** No medium is pumped inside and outside the bio-reactor in the process of batch fermentation.

Let $y(s) = (y_1(s), y_2(s), y_3(s), y_4(s), y_5(s), y_6(s))^T \in R^6$ be the state variable, $s \in I \triangleq [0, 1]$, here $\bar{x} = (y_1(s), y_2(s), y_3(s), y_4(s), y_5(s))$, $\tilde{t} = y_6(s)$. Let $\zeta \triangleq (\xi, 0)$ and $h \triangleq (\tilde{t}_f(l, \bar{x}(l), k), t_f)^T$. Thus, under assumptions (H1), (H2) and based on Eq. (2.1) and Eqs. (2.4)–(2.6), the batch culture can be formulated as the following nonlinear dynamical system

$$
\dot{y}(s) = h(y(s), k), \quad s \in I, \quad y(0) = y_0 \triangleq (\xi, 0).
$$

Based on [8], we can show that, if $y(s)$ is a solution of system (2.7), then $x(t) = \bar{x}(t/t_f), t \in [0, t_f]$ is a solution of system (2.1).

Since the concentrations of biomass, glycerol and products are restricted in a certain range according to the practical production, we consider the properties of the system on a subset of $R^6$, $W \triangleq \{y \in R^6 \mid y_1 \in [0.001, x^*_1], y_6 \in [0, x_6^*], i = 2, 3, 4, 5\}$, where $x_1^* = 10$ g/L, $x_2^* = 2039$ mmol/L, $x_3^* = 939.5$ mmol/L, $x_4^* = 1026$ mmol/L and $x_5^* = 360.9$ mmol/L are the critical concentrations of biomass, glycerol, 1,3-PD, acetate and ethanol for cell growth, respectively.

Let $C_b([0, T], R^6)$ denote the space of continuous bounded functions on $[0, T]$ with values in $R^6$, equipped with the sup norm topology, that is, for $z \in C_b([0, T], R^6)$, $\|z\|_c = \sup\{\|z(t)\|, t \in [0, T]\}$, where $\|\cdot\|$ is the Euclidean norm.

### 3. Properties of the Solution for the System

In this section, we study the questions of existence, uniqueness and boundedness of solutions to the system (2.7). To begin with, we discuss some properties of the function $h(y, k)$.

**Proposition 3.1.** For fixed $u \in U$, the function $h(y, k)$ defined by (2.7) satisfies that

(a) $h \in C^2(W \times U, R^6)$;
(b) $h$ satisfies linear growth condition in $y$, that is, there exists a constant $0 < K < \infty$ such that for all $y \in W$,

$$
\|h(y, k)\| \leq K'(\|y\| + 1).
$$

**Proof.** (a) It is easy to verify that the function $h \in C^2(W \times U, R^6)$ by definition and Eqs. (2.4)–(2.6).
Proposition 3.3. Suppose Definition 3.2.

(b) It follows from system (2.7) that

\[ \|h(y, k)\| = \left( \sum_{j=1}^{6} h_j^2(y, k) \right)^{1/2} \leq |y_1| (\mu^2 + q_3^2 + q_4^2 + q_5^2)^{1/2} + |t_f|. \]

Set \( a_1 = \max\{\frac{1}{2}, Y_3, Y_4, Y_5, 1\} \), \( a_2 = \max\{m_2, m_3, m_4, m_5, 0\} \). Since \( \exp(-\frac{\|t-m\|^2}{2t_f^2}) \leq 1 \), we have \( q_i^2 \leq (a_1\mu + a_2)^2 \), \( i = 2, 3, 4, 5 \). Then,

\[ \|h(y, k)\| \leq |x_1| \sqrt{a} (a_1\mu + a_2) + |t_f|. \]

Similarly, let \( K' = \max\{\sqrt{a}(a_1\mu + a_2), |t_f|\} \), it follows from above expression that

\[ \|h(y, k)\| \leq K'(\|y_1\| + 1) \leq K'(\|y\| + 1). \]

Definition 3.2. Suppose \( y_0 \in W, k \in K \), the set of admissible initial-state-control pairs \((y_0, k)\) is denoted by \( H \triangleq W \times K \). \( y(t; y_0, k) \in C_b([0, T], R^d) \) is said to be a solution of (2.7), if it satisfies the following integral equation:

\[ y(s; y_0, k) = y_0 + \int_0^s h(y(\tau), k) d\tau, \quad s \in I. \]  

Proposition 3.3. The function \( h(y, k) \) satisfies that there exists a constant \( M \in [1, \infty) \) such that for all \( y_1, y_2 \in W \) and \( k_1, k_2 \in K \), the following three relations hold:

\[ \|h(y_1, k_1) - h(y_2, k_2)\| \leq M (\|y_1 - y_2\|_c + \|k_1 - k_2\|), \]

\[ \|h(y_1, k_1) - h(y_2, k_2)\| \leq M (\|y_1 - y_2\|_c + \|k_1 - k_2\|), \]

and

\[ \|h_u(y_1, k_1) - h_u(y_2, k_2)\| \leq M (\|y_1 - y_2\|_c + \|k_1 - k_2\|). \]

Proof. Let \( y_2 = y_1 + \Delta y \) and \( k_2 = k_1 + \Delta k \). It is easy to verify that the function \( h \in C^2(H, R^d) \) by definition and Eqs. (2.4)–(2.6) and follows from the Mean Value Theorem that

\[ \|h(y_2, k_2) - h(y_1, k_1)\| = \left\| \frac{\partial h}{\partial y}(y^1 + \theta_1 \Delta y, k) \Delta y \right\| + \left\| \frac{\partial h}{\partial u}(y^1, k + \theta_2 \Delta k) \Delta k \right\| \]

\[ \leq \left\| \frac{\partial h}{\partial y}(y^1 + \theta_1 \Delta y, k) \right\| \|\Delta y\| + \left\| \frac{\partial h}{\partial u}(y^1, k + \theta_2 \Delta k) \right\| \|\Delta k\|. \]

The continuous differentiability of the function \( h \) imply existence of positive constants \( M_1 \) and \( M_2 \) such that

\[ \left\| \frac{\partial h}{\partial y}(y^1 + \theta_1 \Delta y, k) \right\| \leq M_1, \quad \left\| \frac{\partial h}{\partial u}(y^1, k + \theta_2 \Delta k) \right\| \leq M_2. \]
Hence, letting $M \triangleq \max\{M_1, M_2\}$ we can have

$$\|h(y^2, k^2) - h(y^1, k^1)\| \leq M(\|y^2 - y^1\|_c + \|k^2 - k^1\|).$$

Then by (2.7), direct calculations show that $\|\partial^2 h/\partial y^2\|, \|\partial^2 h/\partial k^2\|$ and $\|\partial^2 h/\partial y \partial u\|$ are all bounded on $H$, and we will see that

$$\|h_y(y^1, k^1) - h_y(y^2, k^2)\| \leq M(\|y^1 - y^2\|_c + \|k^1 - k^2\|),$$

$$\|h_u(y^1, k^1) - h_u(y^2, k^2)\| \leq M(\|y^1 - y^2\|_c + \|k^1 - k^2\|).$$

Note that (3.2) implies that there exists a $M' < \infty$ such that for all $y \in R^n$ and $k \in K$,

$$\|h(y, k)\| \leq M'(\|y\| + 1).$$

**Lemma 3.4.** Consider the system (2.7), with $(y_0, k) \in H$, and based on Proposition 3.3, given any absolutely continuous function $x_0: I \rightarrow R^n$ (so that $x_0(\cdot)$ is differentiable almost everywhere), there exists a solution $y(s; y_0, k)$ of (2.7) such that, for all $s \in I$,

$$\|y(s; y_0, k) - x_0(s)\| \leq e^K\epsilon(x_0, y_0, k)$$

with $K$ as in (3.2), and

$$\epsilon(x_0, y_0, k) \triangleq \|x_0(0) - y_0\| + \int_0^1 \|\dot{x}(s) - h(x(s), k)\| ds.$$

**Proof.** See [8, Picard Lemma 5.6.3].

**Proposition 3.5.** For any $(y_0, k) \in H$, the system (2.7) has a unique solution $y(\cdot; y_0, k) \in C_b(I, R^n)$ and $y(\cdot; y_0, k)$ is continuous in $k$ on $K$.

**Proof.** It is easy to verify that the solution $y(\cdot; y_0, k)$ is continuous. Then, we will prove the existence, uniqueness of the solutions. First, it follows from Lemma 3.4 that the existence of solutions is proved. Subsequently, we will verify the uniqueness. Let $y^1(s; y_0, k)$ and $y^2(s; y_0, k)$ be two solutions of (2.7). For all $s \in I$, we can conclude from (3.1) that

$$\|y^1(s; y_0, k) - y^2(s; y_0, k)\|_c \leq \int_0^t \|h(s, y_1, k) - h(s, y^2, k)\| ds$$

$$\leq L \int_0^t \|y^1(s; y_0, k) - y^2(s; y_0, k)\|_c ds.$$

Bellman Gronwall inequality is applied to the above inequality, which implies that $\|y^1(s; y_0, k) - y^2(s; y_0, k)\|_c = 0$ for all $s \in I$, that is, the solution of (3.1) is unique.


**Proposition 3.6.** For any \((y_0, k) \in H\), the solutions of the system (2.7) satisfy that
\[
\|y(\cdot; y_0, k)\|_c \leq (1 + \|y_0\|)e^K,
\]
with \(K\) as in Proposition 3.3.

**Proof.** Now, we prove the boundedness of solutions to the system (2.7). By the definition of solutions of differential equation, it suffices to show that the solutions of the following integral equation
\[
y(s; y_0, k) = y_0 + \int_0^s h(\tau, x, k)d\tau, \quad s \in I
\]
are bounded. From the above equation and Proposition 3.3, we can have that
\[
\|y(s; y_0, k)\|_c \leq \|y_0\| + \int_0^s \|h(\tau, x, k)\|d\tau \leq \|y_0\| + K \int_0^s \|y(\tau; y_0, k)\|_c d\tau.
\]
Letting \(\tilde{h}(s) = \|y(s; y_0, k)\|_c + 1\), we conclude that
\[
\tilde{h}(s) \leq \tilde{h}(0) + K \int_0^s \tilde{h}(\tau)d\tau.
\]
By Bellman Gronwall inequality, for all \(s \in I\), we can obtain \(\tilde{h}(s) \leq \tilde{h}(0)e^K\) and hence, that \(\|y(\cdot; y_0, k)\|_c \leq (1 + \|y_0\|)e^K\).

4. Parameter Identification Model and Optimization Algorithm

Although the object function in this paper is formally accord with \(J(u)\) in [14], the proposed algorithm cannot be directly utilized. In [14], only two parameters need to be identified and the monotonicity is no longer valid. Therefore, in this section, a parameter identification model for the system (2.7) is proposed and a modified Hooke–Jeeves algorithm is constructed to solve it.

For given \(y_0^i, i = 1, 2, \ldots, N\), we measured \(N_i\) groups of experimental data in batch culture and denoted the experimental values of the concentrations of reactants as \(y^i_1(t_{j_1}), y^i_2(t_{j_2}), y^i_3(t_{j_3}), y^i_4(t_{j_4}), y^i_5(t_{j_5}), y^i_6(t_{j_6}), j_1 = 1, 2, \ldots, N_i\), correspondingly. Let \(y^i(t_{j}) = (y^i_1(t_{j}), y^i_2(t_{j}), y^i_3(t_{j}), y^i_4(t_{j}), y^i_5(t_{j}), y^i_6(t_{j}))^T \in \mathbb{R}^6\), and for given \(y_0^i \in W\), define
\[
S_1(y_0^i) \triangleq \{y(\cdot; y_0^i, k) \in C_b(I, \mathbb{R}^6) | y(\cdot; y_0^i, k) \}
\]
is the solution to the system (2.7), \(k \in K\).

According to Proposition 3.5 and the compactness of \(K\), we can easily obtain the following consequence.

**Lemma 4.1.** For given \(y_0^i \in W\), the set \(S_1(y_0^i)\) defined in (4.1) is compactness in \(C_b(I, \mathbb{R}^6)\).

Since intermittent feeding of alkali into the reactor to maintain the pH value at 7 or so greatly affects the extracellular concentrations of acetic acid and ethanol, this work is only concerned with the relative error between the experimental data
and computational values of the first three substances. Thus, the parameter identification problem can be formulated as

$$(IP) : \inf_{k} J(k) \triangleq \sum_{i=1}^{3} \sum_{j=1}^{N} |y(t_j; y_0^i, k) - y_i^j(t_j)|$$

s.t. $y(t; y_0^l, k) \in S(y_0^l), \quad l = 1, 2, \ldots, N,$

$$0 \leq t_l \leq t_m \leq t_f.$$  

On the basis of the factual fermentation, we make the following assumption.

(H3) For given $y_0^l, y(t; y_0^l, k) \in S(y_0^l), l = 1, 2, \ldots, N$, the system (2.7) is controllable and observable.

**Theorem 4.2.** Under assumptions (H3), there exists an optimal solution of (IP), that is, there exists $k^* \in K$ such that

$$J(k^*) \leq J(k), \quad \forall k \in K. \quad (4.1)$$

**Proof.** It follows from Proposition 3.5 that the mapping from $k \in K$ to $y(:; y_0^l, k) \in S(y_0^l)$ is continuous, $l = 1, 2, \ldots, N$. In view of the continuity of the mapping from $y(:; y_0^l, k)$ to $J(k) \in R$ and the compactness of $S(y_0^l)$, we conclude that (IP) has an optimal solution, denoted by $k^*$, that is, $J(k^*) \leq J(k), \forall k \in K$.  

Since the parameter optimization problem (IP) is subject to a nonlinear dynamical system and its performance index $J(k)$ cannot be explicitly expressed by $k$, it is impossible to solve this problem by methods related to the gradient of $J(k)$. Hooke–Jeeves algorithm is a pattern search method to unconstrained optimization of nonlinear functions that are not necessarily continuous or differentiable. It does not require the derivatives of the objective function, and the iterative operation is very simple. For each iteration, the algorithm goes through a series of exploratory (directional) searches and one pattern search. However, its convergence rate is slow, and what we want to solve is the optimization in a bounded domain. To overcome these problems, we take some modifications to the Hooke–Jeeves algorithm. Suppose $k_0$ is the above give initial parameter, $k_0$ is the initial step size, $\alpha$ is an acceleration factor, $\varepsilon$ is the computational precision and $r_{\max}$ is the maximal iterative time, thus we can construct the optimization algorithm to solve the problem (IP), which is given by the following basic steps:

**Algorithm 1**

**Step 1.** Set constants $\alpha \in (0, 1), \delta \in (0, 1)$ and $\varepsilon \in (0, 1)$. Set $r = 0, w^{(1)} = k^{(1)} = k_0$. Let $e_i$ be coordinate vector, $i = 1, 2, \ldots, n$, then goto Step 2.

**Step 2.** Set $r := r + 1$, if $r > r_{\max}$ then let $k^* = k^{(r-1)}$, stop. Otherwise, set $j = 1$, goto Step 3.

**Step 3.** If $J(w^{(j)} + \delta e_j) < J(w^{(j)})$, then $w^{(j+1)} = w^{(j)} + \delta e_j$, else if $J(w^{(j)} - \delta e_j) < J(w^{(j)})$, then $w^{(j+1)} = w^{(j)} - \delta e_j$, else $w^{(j+1)} = w^{(j)}$, goto Step 4.
Step 4. If $j < n$, then $j := j + 1$, goto Step 3, else goto Step 5.

Step 5. If $J(w^{(n+1)}) < J(k^{(r)})$, then $k^{(r+1)} = w^{(n+1)}$, $w^{(1)} = k^{(r+1)} + \alpha(k^{(r+1)} - k^{(r)})$, goto Step 2, else goto Step 6.

Step 6. If $d > \varepsilon$, then $k^{(r+1)} = k^{(r)}$, $d = d/2$, then goto Step 2, else $k^* = k^{(r)}$, stop.

On the basis of two groups of experimental data, we obtain the optimal parameters by the use of Algorithm 1, listed in Table 1. In the Algorithm 1, the parameters, $\alpha$, $d$ and $\varepsilon$, needed in the computation are 0.8, 0.1 and 0.005, respectively. The definitions of $e_i$ in Table 1 are as follows:

$$e_i = \frac{\sum_{l=1}^{N} \sum_{j_l=1}^{N_l} |x(t_{j_l}; x_{l0}, k) - y_{l_i}(t_{j_l})|}{\sum_{l=1}^{N} \sum_{j_l=1}^{N_l} y_{l_i}(t_{j_l})}, \quad i = 1, 2, 3.$$  \hspace{1cm} (4.2)

<table>
<thead>
<tr>
<th>Substrate/products</th>
<th>$t_l$</th>
<th>$t_m$</th>
<th>$\mu_m$</th>
<th>$m_i$</th>
<th>$Y_i$</th>
<th>% $e_i$</th>
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<tr>
<td>$i = 1$ (Biomass)</td>
<td>1.7924</td>
<td>2.4508</td>
<td>0.9192</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>$i = 2$ (Glycerol)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.358</td>
<td>0.01558</td>
<td>4.39</td>
</tr>
<tr>
<td>$i = 3$ (1,3-PD)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—8.9346</td>
<td>64.69</td>
<td>5.30</td>
</tr>
</tbody>
</table>

Table 1. Parameters values in dynamical system (2.7).

Fig. 1. Comparison of biomass, substrate and product concentrations between the first group experimental data and computational results.
L. Wang et al.

Fig. 2. Comparison of biomass, substrate and product concentrations between the second group experimental data and computational results.

The objective function $J(k_0) = 1.1739$, $J(k^*) = 0.403416$ and $J$ achieves its optimal value at $k^*$.

Figures 1 and 2 show the comparison of biomass, substrate and product concentrations between experimental data and computational results. Comparing the errors in this paper with the reported results [14], which are $e_1 = 4.57\%$, $e_2 = 5.30\%$, and $e_3 = 10.59\%$, we conclude that the improved model is more fit for describing the factual batch fermentation under investigation. In particular, it can simulate the growth of cell much better.

5. Conclusions

In this paper, on the basis of the previous model, we modify the specific rate of cell growth to avoid repeated consideration of substance inhibition and convert the novel model to the autonomous standard form in order to readily prove the existence, uniqueness and boundedness of solutions to the system and the continuity of solutions with respect to the parameters. The structure of the modified model is more simple and easy to calculate than the previous ones and the biological significance of the parameters is specific and concision. For all the biological parameters
in this system, we present a parameter identification model and construct a feasible optimization algorithm to find the optimal parameters for the system. Numerical result shows that the improved model with identified parameters can describe the batch culture better, compared with the previous results.

Our current tasks accommodate the modeling and simulation of the fermentation process. Moreover, the stability and reachability of the improved model need to be discussed. In particular, the objective of our efforts is to delve into optimal control problem for the nonlinear dynamical system of batch culture.

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References


L. Wang et al.


