AN IMPROVED NONLINEAR COMPLEX SYSTEM OF MICROBIAL BIOCONVERSION PROCESS IN FED-BATCH CULTURE

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Abstract. The purpose of this paper is to explore the properties of a new model which can describe the multistage of population growth of microorganisms. The improved model is developed based on the time dependent changes of the specific growth rate. Considering the discontinuity of the process of adding glycerol and alkali, a nonlinear complex kinetic system (CKS) of fed-batch fermentation is investigated. Then the existence, uniqueness and boundedness of solutions to the CKS and the Lipschitz continuity and differentiability of solutions with respect to the initial-state-control pairs are discussed. Finally, a numerical example is employed to carry out numerical simulation for the CKS.

Keywords. Fed-batch culture, Bioconversion, Nonlinear complex kinetic system.

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1 Introduction

The anaerobic conversion of glycerol to 1,3-propanediol (1,3-PD) is a complex bioprocess of industrial interest and recently has been receiving more and more attention throughout the world because of its lower cost, higher production and no pollution [1]. Among various microbial production methods of 1,3-PD, dissimilation of glycerol to 1,3-PD by Klebsiella pneumoniae has been widely investigated since the 1980s [2], including experimental investigations of the multiple inhibitions in the fermentation [3, 4] and quantitative analysis of this complex bioprocess [5, 6].

The advantages of the process simulation of microbial fermentation have been performed for a long time now [7, 8, 9, 10, 11], and it is possible to find recent examples of applications of modeling and simulation to the performance and optimization [12, 13] and predictive control [14] of a bioprocess. In recent years, the nonlinear kinetic system of glycerol fed-batch fermentation by Klebsiella pneumoniae has extensively been considered. In [15] and [16], nonlinear impulsive and hybrid kinetic systems were proposed based on the fed-batch culture respectively. In addition, some properties of solutions to
the impulsive and hybrid systems were discussed. However, the previous theoretical work was based on Monod kinetics and some of its modifications, which can only be used under very restrictive conditions such as a steady state chemostat [17]. So we improve a new model to describe the batch culture. The improved model has two parameters which have clear physiological meanings and are easy to calculate. Consequently, in terms of the features of fed-batch culture, a nonlinear complex kinetic system of fed-batch culture is proposed based on the nonlinear kinetic system of batch culture and continuous culture. Subsequently, we do some theoretical and numerical analysis to guide the practices.

The rest of the paper is organized as follows. In Section 2, some notations and terminologies are given. In Section 3, a nonlinear complex kinetic system of fed-batch culture is proposed. In Section 4, the existence, uniqueness, boundedness and regularity of solutions to the CKS are proved. In Section 5, we present a numerical example to show that the errors can be decreased by use of a nonlinear complex kinetic system. Finally, Section 6 concludes.

2 Some notations and terminologies

Let $C_b([0,T], R^5)$ denote the space of continuous bounded functions on $[0,T]$ with values in $R^5$. Equipped with the sup norm topology, that is, for $z \in C_b([0,T], R^5)$, $\|z\|_c = \sup\{\|z(t)\|, t \in I\}$. Let $L_2[0,T]$ be the space of Lebesgue square integrable functions from $[0,T]$ to $R$. The $L_2[0,T]$ inner product $\langle u, u' \rangle_{2}$ is defined by

$$\langle u, u' \rangle_{2} = \int_{0}^{T} u(t)v(t)dt$$

As a result, the $L_2[0,T]$ norm $\|u\|_2$ is defined by $\|u\|_2 = \langle u, u \rangle_2$. Let $L_\infty[0,T]$ denote the space of equivalence classes of Lebesgue measurable, essentially bounded functions from $[0,T]$ to $R$, with norm $\|u\|_\infty$ defined by $\|u\|_\infty = \text{ess sup}_{t \in I} |u(t)|$.

To carry out our analysis for the complex system of fed-batch culture, we let $H_2 = R^5 \times L_\infty[0,T]$. The inner product $\langle \cdot, \cdot \rangle_{H_2}$ and norm $\cdot \cdot_{H_2}$ on $H_2$ can be defined as follows. For any $\eta = (\xi, u) \in H_2$ and $\eta' = (\xi', u') \in H_2$,

$$\langle \eta, \eta' \rangle_{H_2} \triangleq \langle \xi, \xi' \rangle + \langle u, u' \rangle_{2}$$

where $\langle \xi, \xi' \rangle$ denotes the Euclidean inner product. The norm $\cdot \cdot_{H_2}$ is defined below. For any $\eta = (\xi, u) \in H_2$, $\|\eta\|_{H_2} \triangleq \langle \eta, \eta \rangle_{H_2} = \|\xi\|^2 + \|u\|_{L_\infty}^2$.

Now, we define the subspace of $H_2$ to be the pre-Hilbert space $H_\infty,2$ consisting of the elements $\eta = (\xi, u) \in H_2$ such that $u \in L_\infty[0,T]$ and endowed with the same inner product and norm as $H_2$, that is,

$$H_\infty,2 \triangleq R^5 \times L_\infty,2[0,T] \triangleq (R^5 \times L_\infty[0,T], \langle \cdot, \cdot \rangle_{H_2}, \cdot \cdot_{H_2})$$
where $L_{\infty,2}[0,T] \triangleq (L_{\infty}[0,T],\langle \cdot, \cdot \rangle_{H_2}, \| \cdot \|_{H_2})$ is a pre-Hilbert space with the same elements as $L_{\infty}[0,T]$, but equipped with the inner product and norm of $L_2[0,T]$.

Finally, let $U \triangleq \{ u \in L_{\infty,2}[0,T] | u(t) \in [0,\rho_{\text{max}}] \}$, where $\rho_{\text{max}} \in (0,\infty)$ is sufficiently large to ensure that all the control functions take values in the interior of the closed interval $[0,\rho_{\text{max}}]$. The set of admissible initial-state-control pairs $\eta \triangleq (\xi, u)$ is denoted by $H \triangleq R^5 \times U \subset H_{\infty,2}$.

For differentiability statements, we define the subset of $H$ as

$$H^0 \triangleq \{ \eta = (\xi, u) \in H | \|u\|_\infty < \gamma \rho_{\text{max}} \}$$

where $\gamma \in (0,1)$ is near unity.

3 Nonlinear complex kinetic system

The fed-batch culture of glycerol bioconversion to 1,3-PD begins with batch fermentation, then batch-fed glycerol and alkali are discontinuously added to the reactor every so often in order that the glycerol concentration keeps in a given range and pH value in the bioreactor maintains 7 or so. Therefore, the whole process includes batch fermentation in the early stage and later fed-batch culture. Mass balances of biomass, substrate and products in batch cultures are written as follows (see [5]):

$$\begin{align*}
\dot{x}_1(t) &= \mu x_1(t) \\
\dot{x}_2(t) &= -q_2 x_1(t) \\
\dot{x}_i(t) &= q_i x_1(t) \\
x(0) &= x_0 \\
t &\in (0,t_1), \ i = 3, 4, 5
\end{align*}$$

(1)

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. $x_0$ denotes the initial state. The specific growth rate of cells $\mu$, specific consumption rate of substrate $q_2$ and specific formation rate of product $q_i$, $i = 3, 4, 5$, are expressed by the following equations on the basis of [5]

$$\mu = \mu_m \left( \frac{x_2(t)}{x_2(t) + k_2} \right) \prod_{i=2}^{5} \left( 1 - \frac{x_i(t)}{x_i^{*}} \right)$$

(2)

$$q_2 = m_2 + \frac{\mu}{Y_2} + \Delta_2 \frac{x_2(t)}{x_2(t) + k_2}$$

(3)

$$q_i = m_i + \mu Y_i + \Delta_2 \frac{x_2(t)}{x_2(t) + k_i}, \ i = 3, 4$$

(4)

$$q_5 = q_2 \left( \frac{b_1}{c_1 + \mu x_2(t)} + \frac{b_2}{c_2 + \mu x_2(t)} \right)$$

(5)
During the process of fed-batch culture, the substrates added to the reactor and nonuniform space distribution are ignored. The concentrations of reactants are uniform in reactor, while time delay process.

The typical cell growth in batch culture includes several growth phases, the lag growth phase is that when the cells are transferred into a new environment the cells need some time to synthesize new enzymes for adaptation to the new environment. The lag growth phase occurs during the initial period of cultivation when the value of \( \mu \) is zero or near to zero. The physiological explanation of the lag growth phase is that when the cells are transferred into a new environment the cells need some time to synthesize new enzymes for adaptation to the new environment. \( \mu \) increases gradually from zero or a small value, then enters into increased growth phase and finally the exponential growth phase reaching its maximum value \( \mu_m \). When the decrease of \( \mu \) from \( \mu_m \) to zero, cell growth enters the stationary growth and decreased phases [18]. We can easily find out the value of \( x_2 \) will decrease below zero using equation (2). This model can not predict the stationary growth and death phase, so we modified equation (2) in the form given in [19] as follows:

\[
\dot{x}_2(t) = \frac{x_2(t)}{x_2(t) + k_s} \prod_{i=2}^{5} (1 - \frac{x_i(t)}{x_i^*}) \exp\left(\frac{-(t - t_m)^2}{2t_l^2}\right)
\]

where \( t_l \) is the time of lag growth phase and \( t_m \) is the time when \( \mu \) reaches the maximum.

In the course of fed-batch culture, the flow of glycerol and alkali is continuous when adding glycerol and alkali starts, which can be described by the kinetic system of continuous culture. Mass balances of biomass, substrate and products in continuous culture are given below (see [20]):

\[
\begin{align*}
\dot{x}_1(t) &= (\mu - D)x_1(t) \\
\dot{x}_2(t) &= (D(C_{i0} - x_2(t)) - q_2x_1(t) \\
\dot{x}_i(t) &= q_i x_1(t) - Dx_i(t), \quad i = 3, 4, 5
\end{align*}
\]

where \( D \) is referred to the dilution rate and \( C_{i0} \) is the initial glycerol concentration in feed. \( T \in (0, \infty) \) denotes the terminal moment of the fermentation process.

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) During the process of fed-batch culture, the substrates added to the reactor and nonuniform space distribution are ignored. The concentrations of reactants are uniform in reactor, while time delay process.

where \( n_i \in \mathbb{N} \) and \( 1 \leq n_i \leq 5, i = 1, 2, 3, 4, 5 \). Under anaerobic conditions at \( 37^0C \) and \( pH = 7.0 \), the maximum specific growth rate of cells \( \mu_m = 0.67h^{-1} \), and Monod saturation constant \( k_s = 0.28 \text{mmol}/L \). The critical concentrations of biomass, glycerol, 1,3-PD, acetate and ethanol for cell growth are \( x_1^* = 10g/L, x_2^* = 2039\text{mmol}/L, x_3^* = 939.5\text{mmol}/L, x_4^* = 1026\text{mmol}/L \) and \( x_5^* = 360.9\text{mmol}/L \), respectively. \( b_1, b_2, c_1, c_2, m_i, Y_i, \Delta_i, k_i, i = 2, 3, 4, 5 \) are parameters given in [2]. 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 \( \mathbb{R}^5 \), \( W = \{ x \in \mathbb{R}^5 \mid x_1 \in [0.001, x_1^*], x_2 \in [100, x_2^*], x_3 \in [0, x_3^* + \epsilon], x_i \in [0, x_i^*], i = 4, 5 \} \), where \( \epsilon \) is a positive constant.

The typical cell growth in batch culture includes several growth phases, which are defined as the lag, exponential growth, decreased growth and death phases. The lag growth phase occurs during the initial period of cultivation when the value of \( \mu \) is zero or near to zero. The physiological explanation of the lag growth phase is that when the cells are transferred into a new environment the cells need some time to synthesize new enzymes for adaptation to the new environment. \( \mu \) increases gradually from zero or a small value, then enters into increased growth phase and finally the exponential growth phase reaching its maximum value \( \mu_m \). With the decrease of \( \mu \) from \( \mu_m \) to zero, cell growth enters the stationary growth and decreased phases [18]. We can easily find out the value of \( x_2 \) will decrease below zero using equation (2). This model can not predict the stationary growth and death phase, so we modified equation (2) in the form given in [19] as follows:

\[
\mu = \mu_m (\frac{x_2(t)}{x_2(t) + k_s}) \prod_{i=2}^{5} (1 - \frac{x_i(t)}{x_i^*}) \exp\left(\frac{-(t - t_m)^2}{2t_l^2}\right)
\]

where \( t_l \) is the time of lag growth phase and \( t_m \) is the time when \( \mu \) reaches the maximum.
reactor only include glycerol and alkali.

(H3) The feed rate of glycerol and speed of adding alkali are both uniform at various discrete time intervals.

Under assumptions (H1), (H2) and (H3), the discrete process of adding glycerol and alkali is embedded into the kinetic system of continuous culture and hence the complex system of fed-batch culture can be obtained. Let $x(t) = (x_1(t), x_2(t), x_3(t), x_4(t), x_5(t)) \in \mathbb{R}^5$ be the state variable, $I$ is $[0, T]$, $t_i$ is the moment of adding glycerol, at which the fermentation process switches to continuous culture from batch culture, $t_i'$ denotes the moment of ending the flow of glycerol from the beginning of time $t_i$, at which the fermentation process jumps into batch culture from continuous culture, and $0 = t_0 < t_1 < t_1' < \ldots < t_n' < t_{n+1} = T, i \in I_n = \{1, 2, \ldots, n\}$. Let $I_i = [t_{i-1}, t_i]$ be the time interval of batch culture, $I'_i = [t_i, t_i']$ be the time interval of continuous culture, $i \in I_n$. Thus, based on (1) and (2), the fed-batch culture can be formulated as the following nonlinear complex system

$$\dot{x}(t) = F(x(t), u(t)), \quad t \in I, \quad x(0) = \xi$$

(8)

where

$$F(x(t), u(t)) = (F_1(x(t), u(t)), F_2(x(t), u(t)), F_3(x(t), u(t)), F_4(x(t), u(t)), F_5(x(t), u(t)))$$

$$= ((\mu - u(t))x_1(t), u(t)(x_20 - x_2(t)) - q_2x_1(t), q_3x_1(t) - u(t)x_3(t),$$

$$q_4x_1(t) - u(t)x_4(t), q_5x_1(t) - u(t)x_5(t)) \in \mathbb{R}^5$$

(9)

$$u(t) = \begin{cases} 
(pv_i + u_i)(t - t_i)/\left(\sum_{j=1}^{i-1} \rho(F_j + v_j) + (pv_i + u_i)(t - t_i) + \rho V_0\right), & t \in I'_i, \\
0, & t \in I_i.
\end{cases}$$

(10)

$$\mu(t) = \begin{cases} 
\mu_m \left(\frac{x_2(t)}{x_2(t) + k_2}\right) \prod_{i=2}^{n} \left(1 - \frac{z_i(t)}{x_1(t)}\right), & t \in I'_i, \\
\mu_m \left(\frac{x_2(t)}{x_2(t) + k_2}\right) \prod_{i=2}^{n} \left(1 - \frac{z_i(t)}{x_1(t)}\right) \exp \left(-\frac{(t - t_m)^2}{2\sigma^2}\right), & t \in I_i.
\end{cases}$$

Here $u(t)$ is dilution rate. $v_i(g/s)$ and $v_i(ml/s)$ are the velocity of adding glycerol and alkali in $I'_i$, respectively. $t_i$ is the time of lag growth phase and $t_m$ is the time that $\mu$ reaches the maximum in each batch culture stage. $F_j$ and $V_j$ are the volumes of glycerol and alkali added at $t_j$ before $t_i$, respectively, $i \in I_n$. $V_0$ is the initial volume of fermentation broth and $\rho$ is the density of glycerol added.

4 Existence, uniqueness, boundedness and regularity properties

In this section, we study the questions of existence, uniqueness and boundedness of solutions to system (8). Here, we will denote the solutions of (8)
corresponding to a particular \( \eta \in H \) by \( x^0(\cdot) \). First, we discuss some properties of the function \( F(x, u) \).

**Lemma 4.1** Suppose \( \eta = (\xi, u) \in H \). Then, given any absolutely continuous function \( x^0 : I \to \mathbb{R}^5 \), there exists a solution \( x^0(\cdot) \in C_b(I, \mathbb{R}^5) \) such that, for all \( t \in I \),

\[
\|x^0(t) - x^0(t)\| \leq \exp\{K\} \varepsilon(x^0, \eta)
\]

with \( K > 0 \), and

\[
\varepsilon(x^0, \eta) \triangleq \|x^0(t) - \xi\| + \int_0^1 \|\dot{x}(t) - F(x^0(t), u(t))\|dt
\]

**Proof.** See [21, Picard Lemma 5.6.3].

**Proposition 4.1** The function \( F(x, u) \) defined by (9) satisfies that

i.) the function \( F(\cdot, \cdot) \) is continuously differentiable,

ii.) \( F(\cdot, \cdot) \) satisfies linear growth conditions in \( x \), that is, there exists a constant \( 0 < K' < \infty \) such that for all \( x \in \mathbb{R}^5 \) and \( u \in U \),

\[
\|F(x, u)\| \leq K'(\|x\|_C + 1).
\]

**Proof.**

i.) It is easy to verify that the function \( F \) is continuously differentiable by the definition.

ii.) For any \( u \in U \), it follows from (9) that

\[
\|F(x, u)\| = (\sum_{j=1}^{5} F_j(x, u))^2 \leq \sum_{j=1}^{5} |F_j(x, u)|.
\]

Set \( K_1 \triangleq \mu_m + \rho_{\max} \), \( L_2 \triangleq |m2| + |1/Y_2| + |\Delta_2| \) and \( K_2 \triangleq \max\{L_2 + \rho_{\max}, \rho_{\max} C_0\} \), we can obtain

\[
|F_1(x, u)| = |(\mu - u(t))x_1| \leq |\mu + u(t)||x_1| \leq (\mu_m + \rho_{\max})\|x\|_C
\]

\[
\leq K_1(1 + \|x\|_C)
\]

\[
|F_2(x, u)| = |u(t)(C_{s0} - x_2(t)) - q_2x_1| \leq |u(t)||C_{s0} - x_2(t)| + |q_2||x_1|
\]

\[
\leq K_2(1 + \|x\|_C)
\]

Similarly, let \( L_3 \triangleq m_i + \mu_m Y_i + \Delta_i \) \( (i = 3, 4) \), \( L_5 \triangleq C_2(b1/c1 + b2/c2) \) and \( K_i \triangleq \rho_{\max} + C_i \), and we have

\[
|F_i(x, u)| = |q_i x_i - u(t)x_i| \leq L_i|x_i| + \rho_{\max}|x_i| \leq K_i(1 + \|x\|_C).
\]

Finally, set \( K' \triangleq \max\{K_1, K_2, \ldots, K_5\} \), then we can have that

\[
\|F(x, u)\| \leq K'(\|x\|_C + 1).
\]

\( \square \)
Proposition 4.2  For any $\eta \in H_2$, the solutions of system (8) satisfy that

$$\|x^n(t)\|_C \leq (1 + \|\xi\|) \exp\{K'\},$$

with $K'$ as in Proposition 4.1.

Proof. Now, we prove the boundedness of solutions to system (8). By the definition of solutions of differential equation, it suffices to show that the solutions of the following integral equation:

$$x^n(t) = \xi + \int_0^t F(x^n(s), u(s))ds, \quad t \in I$$

are bounded. From the above equation and Proposition 4.1, we can have that

$$\|x^n(t)\| \leq \|\xi\| + \int_0^t \|F(x^n(s), u(s))\|ds \leq \|\xi\| + K' \int_0^t \|x^n(s) + 1\|ds$$

Letting $y(t) = \|x^n(t)\| + 1$, we conclude that

$$y(t) \leq y(0) + K' \int_0^t y(s)ds.$$

By Bellman Gronwall inequality, for all $t \in I$, we can obtain $y(t) \leq y(0)e^{K'}$ and hence, that $\|x^n(t)\|_C \leq (1 + \|\xi\|) \exp K'$.  \qed

Proposition 4.3  The function $F(x, u)$ defined in (9) satisfies that there exists a constant $K \geq 1$ such that for all $x_1, x_2 \in W$, and $u_1, u_2 \in U$, the following three relations hold:

$$\|F(x_1, u_1) - F(x_2, u_2)\| \leq K(\|x_1 - x_2\|_C + \|u_1 - u_2\|_2),$$

$$\|F_x(x_1, u_1) - F_x(x_2, u_2)\| \leq K(\|x_1 - x_2\|_C + \|u_1 - u_2\|_2),$$

and

$$\|F_u(x_1, u_1) - F_u(x_2, u_2)\| \leq K(\|x_1 - x_2\|_C + \|u_1 - u_2\|_2)$$

Proof. Let $x_2 = x_1 + \Delta x$ and $u_2 = u_1 + \Delta u$. It follows from the Mean Value Theorem that

$$\|F(x_2, u_2) - F(x_1, u_1)\| = \|\frac{\partial F}{\partial x}(x_1 + \theta_1 \Delta x, u) \Delta x\| + \|\frac{\partial F}{\partial u}(x_1, u + \theta_2 \Delta u) \Delta u\|$$

$$\leq \|\frac{\partial F}{\partial x}(x_1 + \theta_1 \Delta x, u)\| \|\Delta x\| + \|\frac{\partial F}{\partial u}(x_1, u + \theta_2 \Delta u)\| \|\Delta u\|$$

Proposition 4.2 and the continuous differentiability of the function $F$ imply existence of positive constants $M_1$ and $M_2$ such that

$$\|\frac{\partial F}{\partial x}(x_1 + \theta_1 \Delta x, u)\| \leq M_1, \quad \|\frac{\partial F}{\partial u}(x_1, u_1 + \theta_2 \Delta u)\| \leq M_2$$
Hence, letting $K \triangleq \max\{M_1, M_2\}$ we have

$$\|F(x_2, u_2) - F(x_1, u_1)\| \leq K(\|x_2 - x_1\|_C + \|u_2 - u_1\|_2)$$

Then by (8), direct calculations show that $\|\partial^2 F/\partial x^2\|$, $\|\partial^2 F/\partial u^2\|$ and $\|\partial^2 F/\partial x\partial u\|$ are all bounded on $H$, and we will see that

$$\|F_+(x_1, u_1) - F_+(x_2, u_2)\| \leq K(\|x_1 - x_2\|_C + \|u_1 - u_2\|_2),$$
$$\|F_+(x_1, u_1) - F_+(x_2, u_2)\| \leq K(\|x_1 - x_2\|_C + \|u_1 - u_2\|_2).$$

**Theorem 4.1** For any $\eta = (\xi, u) \in H$, system (8) has a unique solution $x^\eta(\cdot) \in C_b(I, R^3)$.

**Proof.** First, it follows from Lemma 1 that the existence of solutions is proved. Subsequently, we will verify the uniqueness. Let $x^\eta_1(t)$ and $x^\eta_2(t)$ be two solutions of (8). For all $t \in I$, we can conclude that from (10)

$$\|x^\eta_1(t) - x^\eta_2(t)\| \leq \int_0^t |F(x^\eta_1(s), u(s)) - F(x^\eta_2(s), u(s))| ds \leq K \int_0^t |x^\eta_1(s) - x^\eta_2(s)| ds$$

Bellman Gronwall inequality is applied to the above inequality, which implies that $\|x^\eta_1(t) - x^\eta_2(t)\| = 0$ for all $t \in I$, that is, the solution of (8) is unique.

Next, we explore the question of Lipschitz continuity of solutions relative to the set $H$.

**Theorem 4.2** For all $\eta, \eta' \in H$ and all $t \in I$, there exists a constant $0 < L < \infty$ such that

$$\|x^\eta(t) - x^{\eta'}(t)\| \leq L\|\eta - \eta'\|_{H_2}$$

**Proof.** First, we let $x_0(t) \triangleq x^\eta(t)$. Next, since by Theorem 4.1 the solution of (7) is unique, we can deduce from Lemma 1 that, for all $t \in I$, $\|x^\eta(t) - x^{\eta'}(t)\| \leq e^K \varepsilon(x^\eta(t), \eta)$. Now we find that

$$\varepsilon(x^\eta(t), \eta) = \|\xi - \xi'\| + \int_0^1 |F(x^\eta(t), u(t)) - F(x^{\eta'}(t), u'(t))| dt \leq \|\xi - \xi'\| + K \int_0^1 |u(t) - u'(t)| dt$$

By Schwartz inequality and H"older inequality, we can have

$$\int_0^1 |u(t) - u'| dt \leq (\int_0^1 1 dt)^{1/2} (\int_0^1 |u(t) - u'|^2 dt)^{1/2}$$

$$\varepsilon(x^\eta(t), \eta) \leq \|\xi - \xi'\| + K\|u - u'\|_2 \leq \sqrt{2}K\|\xi - \xi'\|_{H_2}$$

Letting $L \triangleq \sqrt{2}K \exp\{K\}$, we complete the proof. \[\Box\]
5 Numerical results

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. In the following example, the medium composition, cultivation conditions, determination of biomass, substrate and metabolites have been reported in [16]. The initial value $\xi = (0.115g/L, 494.5mmol/L, 0)$. Fed-batch began at $t_1 = 5.33h$. The flow time $t_i$, the flow stopping time $t'_i$, and the speeds $u_i$ and $v_i$ of adding glycerol and alkali, $i \in \Lambda_{785}$, are determined by the experiment. Fig.1 shows the comparison of biomass, substrate and product concentrations between experimental data and computational results, where the stars denote the experimental values, written as $y(\tau_j) = (y_1(\tau_j), y_2(\tau_j), y_3(\tau_j))$, $\tau_j = 2jh, j \in \Lambda_{15}$. The dashing lines denote the computational curves in [15], and the real lines denote the computational curves $x_k(t), k \in \Lambda_3$ in this work. Define errors as follows:

$$e_k = \frac{\sum_{i=1}^{15} |x_k(\tau_i) - y_k(\tau_i)|}{\sum_{i=1}^{15} y_k(\tau_i)}, \quad k \in \Lambda_3.$$ 

We obtain the errors $e_1 = 7.39\%$, $e_2 = 14.19\%$, $e_3 = 10.68\%$. Comparing the errors in this paper with the reported results [15], we conclude that the CKS is fitter for modeling actual fed-batch fermentation under investigation.

Figure 1: Comparison of biomass, glycerol, 1,3-PD concentrations between experimental data and computational results.
6 Conclusions

In this paper we have presented a nonlinear CKS of fed-batch culture. Then we demonstrated the existence, uniqueness, boundedness and regularity of solutions to the CKS. At last, a numerical simulation for the CKS illustrates the improvements between our efforts and those in [15] and [16] where the impulsive and hybrid system of fed-batch culture are considered.

Our current tasks accommodate the modeling and simulation of CKS. Moreover, the stability and reachability of the CKS need to be discussed. In particular, the objective of our efforts is to delve into parameter identification and optimal control problem for the CKS of fed-batch culture.

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8 Reference

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