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Research Article

Optimal Control for Multistage Nonlinear Dynamic System of Microbial Bioconversion in Batch Culture

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In batch culture of glycerol biodissimilation to 1,3-propanediol (1,3-PD), the aim of adding glycerol is to obtain as much 1,3-PD as possible. Taking the yield intensity of 1,3-PD as the performance index and the initial concentration of biomass, glycerol, and terminal time as the control vector, we propose an optimal control model subject to a multistage nonlinear dynamical system and constraints of continuous state. A computational approach is constructed to seek the solution of the above model. Firstly, we transform the optimal control problem into the one with fixed terminal time. Secondly, we transcribe the optimal control model into an unconstrained one based on the penalty functions and an extension of the state space. Finally, by approximating the control function with simple functions, we transform the unconstrained optimal control problem into a sequence of nonlinear programming problems, which can be solved using gradient-based optimization techniques. The convergence analysis and optimality function of the algorithm are also investigated. Numerical results show that, by employing the optimal control, the concentration of 1,3-PD at the terminal time can be increased, compared with the previous results.

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 [1]. Many researchs 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 [2–4], open-loop substrate input and pH logic control [5], enzyme-catalytic reductive pathway and transport of glycerol and 1,3-propanediol across cell membrane [6], parameter identification of biochemical systems [7] and feedback control and pulse feeding

[8] for the models of the continuous cultures, feeding strategy of glycerol [9], and optimal control [10] and optimality condition [11] in fed-batch culture.

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 [12]. So nonlinear dynamical systems in this culture have been extensively considered in recent years [13–15]. In batch culture of glycerol biodissimilation to 1,3-propanediol (1,3-PD), the aim of adding glycerol is to obtain as much 1,3-PD as possible. In this paper, based on the previous model in [16], taking the yield intensity of 1,3-PD as the performance index and the initial concentration of biomass, glycerol and terminal time as the control vector, we propose an optimal control model subject to a multistage nonlinear dynamical system and constraints of continuous state. A computational approach is constructed to seek the solution of the above model in two aspects. On the one hand transform the optimal control problem into the one with fixed terminal time and transcribe it into an unconstrained one based on the penalty functions and an extension of the state space; on the other hand, by approximating the control function with simple functions, we transform the unconstrained optimal control problem into a sequence of nonlinear programming problems, which can be solved using gradient-based optimization techniques. The convergence analysis and optimality function of the algorithm are also investigated. Numerical results show that, by employing the optimal control, the concentration of 1,3-PD at the terminal time can be increased, compared with the previous results.

This paper is organized as follows. In Section 2, a nonlinear dynamical system of batch culture is proposed. In Section 3, we propose an optimal control model, develop a computational approach to solve the optimal control model, and prove the convergence of algorithm. Section 4 illustrates the numerical results. Finally, conclusions are provided in Section 5.

2. Nonlinear Dynamical System

On the basis of our previous literature(see [16]), mass balances of biomass, substrate, and products in batch culture can be formulated as the following nonlinear dynamical system:

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

$$\begin{aligned} f(t, x(t)) &= \left(f_1(t, x(t)), f_2(t, x(t)), f_3(t, x(t)), f_4(t, x(t)), f_5(t, x(t))\right)^T \\ &= \left(\mu x_1(t), -q_2 x_1(t), q_3 x_1(t), q_4 x_1(t), q_5 x_1(t)\right)^T, \end{aligned} \tag{2.2}$$

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. $\xi = (\xi_1, \xi_2, \xi_3, \xi_4, \xi_5)^T$ denotes the initial state, and t_f is the terminal time of the fermentation process. $x \triangleq (x_1, x_2, x_3, x_4, x_5)^T \in R_+^5$ is as state vector. The specific growth rate of cells μ, 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 [13, 16]:

$$\mu = \mu_m \exp\left(\frac{-(t - t_m)^2}{2t_l^2}\right)\prod_{i=2}^{5}\left(1 - \frac{x_i}{x_i^*}\right),$$
$$q_2 = m_2 + \frac{\mu}{Y_2},$$
$$q_i = m_i + \mu Y_i, \quad i = 3, 4, 5. \tag{2.3}$$

In batch culture, the initial concentrations of biomass, glycerol, and the terminal time can be chosen as control variables. Let $u = (u_1, u_2, u_3)^T \triangleq (\xi_1, \xi_2, t_f)^T \in R_+^3$ be the control vector. The solution of system (2.1) with respect to control vector is defined by $x(\cdot, u)$.

Based on the factual fermentation, there exist critical concentrations, outside which cells cease to grow, of biomass, glycerol, 1,3-PD, acetate and ethanol. Hence, it is biologically meaningful to restrict the concentrations of biomass, glycerol, products, and the volume of culture fluid in a set W and the control vector in a admissible control set U defined respectively, as follows:

$$x(t, u) \in W \triangleq \prod_{i=1}^{5}\left[x_{*i}, x_i^*\right] \subset R_+^5, \quad \forall t \in I = \left[0, t_f\right].$$
$$u \in U \triangleq \prod_{i=1}^{3}\left[u_{*i}, u_i^*\right] \subset R_+^3. \tag{2.4}$$

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 $z \in C_b([0, T], R^5)$, $\|z\|_c = \sup\{\|z(t)\|, t \in [0, T]\}$, where $\|\cdot\|$ is the Euclidean norm.

3. Optimal Control Problem

The optimal control problem using the yield intensity of 1,3-PD at the terminal time as cost functional, based on the controlled multistage nonlinear dynamical system (2.1), can be formulated as follows:

$$\begin{aligned} \inf \quad & J(u) \triangleq -\frac{x_3(u_3, u)}{u_3} \\ \text{s.t.} \quad & \dot{x}(t) = f(t, x(t, u)) \\ & x(0) = \xi, \\ & x(t) \in W, \quad t \in [0, u_3] \\ & u \in U. \end{aligned} \tag{OCP}$$

From the theory on continuous dependence of solutions on parameters and our previous literature (see [16]), we know that $x(\cdot, u)$ is continuous relative to u, so $J(u)$ is continuous on $u \in U$. Moreover, U is a closed bounded convex subset of R_+^3. Hence we know the optimal control must exist, namely, $\exists u^* \in U$ such that $J(u^*) \leq J(u)$, for all $u \in U$.

3.1. Differentiability with respect to the Control Vector

In this subsection, our aim is to show the differentiability and the gradient information of solutions of the system (2.1) with respect to the control vector. To begin with, we discuss some properties of the function $f(t, x(t, u))$.

Proposition 3.1. *For the system* (2.1), $f(t, x(t, u))$ *and* $(\partial f/\partial x_i)(t, x(t, u))$ $(i = 1, 2, \ldots, 5)$ *are continuous in* (t, x) *on an open set* Δ *in* $R_+ \times W$.

Proof. It follows by inspection that the function $f \in C^2(R_+ \times W, R^5)$ by definition and (2.3). □

Using Theorems I-1-4 and II-1-2 in [17], we can show that the system (2.1) has a unique solution $x = x(t, u)$, and the solution satisfies the integral equation

$$x(t, u) = \xi + \int_0^t f(s, x(s, u))ds, \quad t \in I. \tag{3.1}$$

$u_1 = \xi_1$ and $u_2 = \xi_2$ are the initial value of the system (2.1), due to the differentiability of $x(t, u)$ with respect to the initial vector, and we have

$$\frac{\partial f}{\partial \xi_j}(t, x(t, \xi, u)) = e_j + \int_0^t \frac{\partial f}{\partial x}(s, x(t, \xi, u))\frac{\partial x}{\partial \xi_j}(s, x(t, \xi, u))ds, \tag{3.2}$$

where e_j is the vector in R^5 with entries 0 except for 1 at the jth entry, and $\partial f/\partial x$ is the 5×5 matrix whose ith column is $\partial f/\partial x_i$, $i, j = 1, 2, \ldots, 5$. From this speculation, we obtain the following result.

Proposition 3.2. *Partial derivatives* $\partial x/\partial u_1$ *and* $\partial x/\partial u_2$ *exist and are continuous in* (t, u). *Furthermore,* $\partial x/\partial \xi_j$ *is the unique solution of the initial-value problem*

$$\dot{z} = \frac{\partial f}{\partial x}(t, x(t, u))z, \quad z(0) = -e_j. \tag{3.3}$$

By virtue of the result of Proposition 3.2, we can obtain the value of $\partial x/\partial u_1$ and $\partial x/\partial u_2$. The following Proposition gives a formula to compute the value of $\partial x/\partial u_3$.

Proposition 3.3. *Partial derivatives* $\partial x/\partial u_3$ *exist and are continuous in* (t, u). *Furthermore,*

$$\frac{\partial x}{\partial u_3} = f(u_3, x(u_3, u)). \tag{3.4}$$

Proof. The existence and continuity of $\partial x/\partial u_3$ can be directly obtained by the function $f \in C^2(R_+ \times W, R^5)$ and implicit function theorem. Next, we derive the formula (3.4), for $\forall t \in I$, and we have:

$$x(u_3, u) = \xi + \int_0^{u_3} f(s, x(s, u))ds,$$
$$x(u_3 + \Delta t, u) = \xi + \int_0^{u_3+\Delta t} f(s, x(s, u))ds, \tag{3.5}$$

then, by the integral mean value theorem, there exists a constant $\theta \in [0, 1]$, such that

$$x(u_3 + \Delta t, u) - x(u_3, u) = \int_{u_3}^{u_3+\Delta t} f(s, x(s, u))ds = f(u_3 + \theta\Delta t, x(u_3 + \theta\Delta t, u))\Delta t. \tag{3.6}$$

Let $\Delta t \to 0$, then

$$\frac{\partial x}{\partial u_3} = \lim_{\Delta t \to 0} \frac{x(u_3 + \Delta t, u) - x(u_3, u)}{\Delta t} = \lim_{\Delta t \to 0} f(u_3 + \theta\Delta t, x(u_3 + \theta\Delta t, u)) = f(u_3, x(u_3, u)). \tag{3.7}$$

We obtain the desired result. □

3.2. Model Transformation

The optimal control problem (3.5) is not a standard case because the terminal time t_f is free. Using the method in Section 6.8.1 of [18], the (3.5) can be transformed into the one with fixed terminal time. Treating t_f as an unknown parameter and using the transformation $t = t_f\tau$, the (3.5) is converted to (3.8) as follows:

$$\begin{aligned} \inf \quad & J(u) \triangleq -\frac{x_3(1, u)}{u_3} \\ \text{s.t.} \quad & \dot{x}(\tau) = t_f f(t_f\tau, x(t_f\tau, u)) \\ & x(0) = \xi, \\ & x(\tau) \in W, \quad \tau \in [0, 1] \\ & u \in U. \end{aligned} \tag{OCP$'$}$$

3.3. Semi-Infinite Optimization with Inequality Constrained

For the optimal control problem $J(u)$, it is difficult to cope with the continuous state inequality constraints, that is, this is a semi-infinite optimization problem. To overcome the difficulty, let

$$\begin{aligned} g_i(x(\tau,u)) &:= x_i(\tau,u) - x_i^*, \\ g_{5+i}(x(\tau,u)) &:= x_{*i} - x_i(\tau,u), \quad i = 1,2,\dots,5. \end{aligned} \tag{3.8}$$

The condition, $x(\tau,u) \in W$, for all $\tau \in [0,1]$, is equivalently transcribed into

$$G(u) = 0, \tag{3.9}$$

where $G(u) = \sum_{l=1}^{10} \int_0^1 \max\{0, g_i(x(\tau,u))\} dt$.

However, $G(u)$ is nonsmooth in $g_i(x(\tau,u)) = 0$. By the standard optimization routines [19, 20], the following smoothing technique is to replace $\widehat{g}_{i,\epsilon}(x(\tau,u))$ with $\max\{0, g_i(x(\tau,u))\}$, where

$$\widehat{g}_{i,\epsilon}(x(\tau,u)) = \begin{cases} 0 & \text{if } g_i(x(\tau,u)) < -\epsilon, \\ \dfrac{\left(g_i(x(\tau,u)) + \epsilon\right)^2}{4\epsilon} & \text{if } -\epsilon \le g_i(x(\tau,u)) \le \epsilon, \\ g_i(x(\tau,u)) & \text{if } g_i(x(\tau,u)) > \epsilon. \end{cases} \tag{3.10}$$

Note that

$$G_\epsilon(u) = \sum_{l=1}^{10} \int_0^T \widehat{g}_{l,\epsilon}(x(\tau,u)) dt \tag{3.11}$$

is a smooth function in u. Let

$$\begin{aligned} W_\epsilon &\triangleq \{u \in U \mid G_\epsilon(u) = 0\} \\ &= \left\{u \in U \mid g_l(x(\tau,u)) \le -\epsilon,\ l = 1,2,\dots,10,\ \tau \in [0,1]\right\}. \end{aligned} \tag{3.12}$$

Clearly, $W_\epsilon \subseteq W \cap U$ for each $\epsilon > 0$.

We now define an approximate problem denoted by (3.13), where the smoothed state constraint is treated as the penalty function:

$$\begin{aligned}
\inf \quad & J_{\epsilon,\gamma}(u) := -x_3(1,u) + \gamma G_\epsilon(u) \\
\text{s.t.} \quad & \dot{x}(t) = t_f f\left(t_f \tau, x\left(t_f \tau, u\right)\right), \\
& x(0) = \xi, \\
& u \in W_\epsilon.
\end{aligned} \tag{$\mathrm{OCP}_{\epsilon,\gamma}$}$$

By similar arguments as those given in [21], (3.13) is coincident with (3.5) as $\epsilon \to 0$. On this basis, (3.5) can be explored by solving a sequence of approximate (3.13). Each of these (3.13) is viewed as a smooth nonlinear mathematical programming problem.

3.4. Optimization Algorithm

In this subsection, similar with the approach based on gradient in [22, 23], we proposed an algorithm based on gradient of $J_{\epsilon,\gamma}(u)$ to solve the (3.13). $\partial J_{\epsilon,\gamma}(u)/\partial u \triangleq J_g(u)$ can be derived by solving the ordinary differential equation (3.3) and computing (3.4). The admissible control set U can be called a "box" because of its rectangular shape, we use the classic gradient projection method to cope with "box."

The projection of an arbitrary u onto the feasible set U is defined as follows. The ith component is given by

$$p(u, u_*, u^*)_i = \begin{cases} u_{i*} & \text{if } u_i < u_{i*}, \\ u_i & \text{if } u_i \in \left[u_{i*}, u_i^*\right], \\ u_i^* & \text{if } u_i > u_i^*. \end{cases} \tag{3.13}$$

Thus, the control variable $u(t)$ obtained by projecting the steepest descent direction at u onto the feasible set U is given by

$$u(\lambda) = p\left(u - \lambda J_g, u_*, u^*\right), \tag{3.14}$$

where λ is optional step size.

On the basis of the above analysis, we can obtain an optimal control for (3.13) as shown in the following algorithm.

Algorithm 3.4.

Step 1. Set constants $\alpha, \delta \in (0,1)$, and $r_{\max}$ is positive constant. Set $r = 0$, compute $J_g(u_r)$ by equations (3.3) and (3.4), if $J_g(u_r) < \delta$, stop. Else, then go to Step 2.

Step 2. Compute the step-size $\lambda(r) = \beta^{k_r}$ with Armijo line search rules, where k_r is any integer such that

$$J_{\epsilon,\gamma}\left(u(r) + \beta^{k_r} J_g(u_r)\right) - J_{\epsilon,\gamma}(u(r)) \leq -\beta^{k_r}\alpha J_g^T(u_r) J_g(u_r), \tag{3.15}$$

$$J_{\epsilon,\gamma}\left(u(r) + \beta^{k_r} J_g(u_r)\right) - J_{\epsilon,\gamma}(u(r)) > -\beta^{k_{r-1}}\alpha J_g^T(u_r) J_g(u_r), \tag{3.16}$$

go to Step 3.

Step 3. If $r > r_{\max}$, stop. Otherwise, compute $u(r+1) = p(u(r) - \lambda(r) J_g(u_r), u_*, u^*)$ using the equation defined by (3.14), replace r by $r+1$, and go to Step 1.

Note that, due to the boundedness of the function $J_{\epsilon,\gamma}(\cdot)$, it is very easy to find a k_r satisfying (3.15) and (3.16), using the following subprocedure, which uses the last used step length $\lambda_{r-1} = \beta^{k_{r-1}}$, as the starting point for the computation of the next one.

Subprocedure of Algorithm 3.4

Step 1. If $r = 0$, set $k' = 0$. Else, set $k' = k_{r-1}$.

Step 2. If $k_r = k'$ satisfies (3.15) and (3.16). Else, set $k' = k_{r-1}$, stop.

Step 3. If $k_r = k'$ satisfies (3.15) and not (3.16), replace k' by $k' - 1$, and go to Step 2. If $k_r = k'$ satisfies (3.16) and not (3.15), replace k' by $k' + 1$, and go to Step 2.

For Algorithm 3.4, we see that $-J_g^T J_g(\cdot)$ is continuous, that $-J_g^T J_g(u) \leq 0$ for all $u \in U$, and that $-J_g^2(u) = 0$ if and only if $J_g(u) = 0$, that is, that $-J_g^2(\cdot)$ is an optimality function for the problem (3.13). So, we have the following theorem to guarantee the convergence of the algorithm.

Theorem 3.5. *If u_r is such that $J_g \neq 0$, then λ_r is computed by Algorithm 3.4 using a finite number of function evaluations and any accumulation point $\widehat{u}$ of this sequence satisfies $J_g(\widehat{u}) = 0$.*

Proof. We apply Theorem 1.2.24a in [24] with $\theta(\cdot) = -J_g^T J_g(\cdot)$, then the desired result can be obtained immediately. □

Remark 3.6. Although the approach we are using here to deal with the constraints of continuous state is similar with the one mentioned in [19], There are still three main difference between them. First of all, our approach is applied for the batch culture, while the one in [19] is used for the fed-batch culture. Secondly, the control variables in the two approaches are different. Our variable controls the initial and terminal points, and their variable controls the switching time. Finally, we use the gradient-based algorithm to numerically solve the problem. Their algorithm is an improved Particle Swarm Optimization (PSO) algorithm, not gradient based.

Table 1: Parameters values in dynamical system (2.1).

Substrate/products	t_l	t_m	μ_m	m_i	Y_i
$i = 1$ (Biomass)	1.7924	2.4508	0.9192	—	—
$i = 2$ (Glycerol)	—	—	—	1.358	0.01558
$i = 3$ (1,3-PD)	—	—	—	−8.9346	64.69
Acetic acid	—	—	—	2.1098	4.541
Ethanol	—	—	—	−0.183	3.046

4. Numerical Results

According to the model and algorithm mentioned above, we have programmed the software and applied it to the optimal control problem of microbial fermentation in batch culture. The system parameters are listed in Table 1 (see [9, 16]).

The basic data are listed, respectively, as follows.

Boundary Value of Control Vector

$u_{*1} = 0.01\,\text{mmol/L}$, $u_1^* = 1\,\text{mmol/L}$, $u_{*2} = 200\,\text{mmol/L}$, $u_2^* = 939.5\,\text{mmol/L}$, $u_{*3} = 2h$, and $u_3^* = 10\,\text{h}$.

Boundary Value of State Vector

$x_{*1} = 0.001\,\text{mmol/L}$, $x_1^* = 2039\,\text{mmol/L}$, $x_{*2} = 0.001\,\text{mmol/L}$, $x_2^* = 939.5\,\text{mmol/L}$, $x_{*3} = 0.01\,\text{mmol/L}$, $x_3^* = 10\,\text{mmol/L}$. $u_{*4} = 0.01\,\text{mmol/L}$, $u_4^* = 1026\,\text{mmol/L}$, and $u_{*5} = 200$, $u_5^* = 360.9\,\text{mmol/L}$.

We adopt $\alpha = 0.4, \delta = 0.00001$, and $r_{\max} = 1000$ in the procedure. Then, by Algorithm 3.4, the optimal control vector $\overline{u}$ and objective function $J_{\epsilon,\gamma}(\overline{u})$ are $(0.973186, 547.04, 5.17509)^T$ and 54.5911, respectively. Numerical results show that, by employing the optimal control, the concentration of 1,3-PD at the terminal time can be increased, compared with the previous results.

5. Conclusions

In this paper, based on the previous model in [16], taking the yield intensity of 1,3-PD as the performance index and the initial concentration of biomass, glycerol, and terminal time as the control vector, we propose an optimal control model subject to a multistage nonlinear dynamical system and constraints of continuous state. A computational approach is constructed to seek the solution of the above model in two aspects. The convergence analysis and optimality function of the algorithm are also investigated. Numerical results show that, by employing the optimal control, yield intensity of 1,3-PD at the terminal time can be increased, 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.

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