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Steady-state Optimization Model and Algorithm of Glycerol Bioconversion to 1,3-Propanediol in Continuous Culture

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Abstract This paper focuses on the improvement of the concentration and productivity of 1,3-propanediol from continuous fermentation of glycerol by Klebsiella pneumoniae. A nonlinear steady-state optimization model is presented according to engineering background. A new linear approximating method has been developed in view of the feature of the optimization model. Computer simulation is used for this paper, and the numerical simulation is in accordance with experimental results. The numerical results illustrate the validity and efficiency of the algorithm. The results presented in this work can be used as guidelines for choosing proper operating parameters to get higher concentration or productivity.

Keywords Steady-state Optimization; Nonlinear Kinetic System; Nonlinear Programming; Linear Approximation Algorithm

1 Introduction

1,3-Propanediol(1,3-PD) has a wide range of potential uses. Polyesters which use 1,3-PD as a monomer have some excellent characters, such as strong capacity of pigmentation, weak capacity of adsorption water, repeating use and so on [14]. Hence the research on it attracts increasing attention all over the world including DuPont and Shell. Originally the main technique to produce 1,3-PD is chemical synthesis. However, there are a lot of drawbacks of this technique such as high cost and serious pollution. Therefore, the researchers focus on the bioconversion technique. In 1990s, the bio-dissimilation of glycerol to 1,3-PD by *Klebsiella Pneumonicae* was proposed, which is a novel technique with low cost, low pollution, easy operation and so on. Since then, the research on it has become more and more popular. In 1995, Zeng and Deckwer provided a kinetic model of the bio-dissimilation of glycerol to 1,3-PD [17]. The phenomena and characteristic of oscillation and hysteresis were studied in [1, 9]. In 2000, Xiu modified Zeng's kinetic model and used the excess kinetic model to describe the continuous fermentation

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and batch fermentation of bio-dissimilation of glycerol to 1,3-PD [16]. Based on Xiu's model, the researchers investigated the parameters identification, stability of equilibrium and phenomena of oscillation and hysteresis of the kinetic model of continuous fermentation in [3, 6, 7, 8]. On the other hand, Gao proposed a nonlinear impulsive dynamical system of the fed-batch fermentation of bio-dissimilation [4]. Moreover, some properties and parameters identification problem of these systems have been studied (see [11, 13]). However, all the works in [1, 3, 4, 6, 7, 8, 11, 13, 16] are intended to prove the kinetic models presented can formulate the real fermentation processes preferably. Because of the high cost of 1,3-PD extraction from aqueous solution, it is necessary to make the concentration and productivity of 1,3-PD reach a higher lever. Tag obtained a maximum 1,3-PD concentration of 393 $mmol \cdot l^{-1}$ at a dilution rate of 0.27 h^{-1} in continuous culture (see [10]). A slightly higher 1,3-PD concentration (about 430 $mmol \cdot l^{-1}$) was obtained at a dilution rate of 0.25 h^{-1}[12]. The highest 1,3-PD concentration achieved 638 $mmol \cdot l^{-1}$ at a dilution rate of 0.1 h^{-1} in [10]. However, the author also mentioned that the productivity decreases sharply as the dilution rate decreases at low values. To the best of our knowledge, the researchers drew these conclusions from experimental point of view, for example, 5 experiments in [10]. Based on the kinetic model of continuous fermentation in [3, 15, 16, 17], we aim to analyze the maximum concentration and productivity of 1,3-PD by optimizing the control parameters in the mathematical literature. Steady state operation of engineering systems is generally around a stable equilibrium point. In numerous books, the standard mathematical definition of an equilibrium point x^* for the dynamical system $\dot{x} = f(x)$ is that it satisfies the equation $f(x^*) = 0$. But it has been shown that this definition may be inadequate from an engineering point-of-view. This paper is to formally propose a definition for kinetic-equilibrium points, which is also intuitively appealing. The basic motivation for the proposed definition of a kinetic-equilibrium solution comes from the fact that the concentrations of each substance keep invariable when the kinetic system reaches its steady state gradually. The amount of material in each steady state remains the same but the process of Glycerol bioconversion to 1,3-PD continues. It is meaningful in biochemical engineering when we just need to concern the concentration of substrate after the kinetic system reaches a steady state. In this paper, we establish an optimization model when the kinetic system of Glycerol bioconversion to 1,3-PD reaches a steady state. We present an efficient algorithm according to the feature of the optimization problem. The numerical results are in accordance with experimental results. The optimization model and algorithm can provide theoretical instruction for controllability of the process of 1,3-PD production by continuous fermentation.

2 Problem description and mathematical model

In a continuous fermentation of glycerol bioconversion to 1,3-PD by *Klebsiella Pneumonicae*, glycerol is added to the reactor continuously, the aqueous solution in reactor pours out at the same rate and the volume of the aqueous solution keeps constant. According to the experimental process, we assume that

$(H1)$ The concentration of reactants are uniform in reactor. Time delay and nonuniform space distribution are ignored.

$(H2)$ During the continuous fermentation, the substrates added into the reactor only include glycerol and alkali, and the aqueous solution is exported by the dilution rate.

Let $x(t) \in R^5$ be a state vector whose components denote the concentration of biomass, glycerol, 1,3-PD, acetate and ethanol at t in reactor, respectively. Let $u = (u_1, u_2)^T \in R^2$ be the control vector, the components of which are glycerol concentration in feed and dilution rate. The control domain is $U_{ad} = [100, 2100] \times [0.01, 0.67]$. Under the assumptions above, the nonlinear dynamical system which describes the continuous fermentation of glycerol to 1,3-PD is given in [3, 15, 16, 17] as follows:

$$\begin{cases} \dot{x}_1 &= (\mu - u_2)x_1, \\ \dot{x}_2 &= u_2(u_1 - x_2) - q_2 x_1, \\ \dot{x}_i &= q_i x_1 - u_2 x_i, i = 3,4,5, \\ x_{t_0} &= x_0, \end{cases} \tag{1}$$

where the coefficients μ, $q_i, i = 2,3,4,5$ are expressed by the following equations

$$\begin{aligned} \mu &= \mu_m \frac{x_2(t)}{x_2(t) + K_s} \prod_{j=2}^{5} (1 - \frac{x_j(t)}{x_j^*}), \\ q_2 &= m_2 + \frac{\mu}{Y_2} + \triangle_2 \frac{x_2(t)}{x_2(t) + k_2}, \\ q_3 &= m_3 + \mu Y_3 + \triangle_3 \frac{x_2(t)}{x_2(t) + k_3}, \\ q_4 &= m_4 + \mu Y_4 + \triangle_4 \frac{x_2(t)}{x_2(t) + k_4}, \\ q_5 &= q_2 (\frac{b_1}{c_1 + u_2 x_2(t)} + \frac{b_2}{c_2 + u_2 x_2(t)}). \end{aligned}$$

Under anaerobic conditions at 37 $^\circ C$ and PH 7.0, μ_m and K_s are the maximum growth rate (0.67 h^{-1}) and saturation constant (0.28 $mmol \cdot l^{-1}$). The critical concentrations are x_1^* =10 $g \cdot l^{-1}$ for biomass, $x_2^* = 2039$ $mmol \cdot l^{-1}$ for glycerol, x_3^* =939.5 $mmol \cdot l^{-1}$ for 1,3-PD, $x_4^* = 1026$ $mmol \cdot l^{-1}$ for acetate, and x_5^* = 360.9 $mmol \cdot l^{-1}$ for ethanol.

We adopt the results after parameters identification in [3]. Some parameters' values of the system are $b_1 = 0.025, b_2 = 5.18, c_1 = 0.06, c_2 = 50.45$. The other parameters see table 1.

Table 1: Value of parameters

	m_i	Y_i	$\triangle_i$	k_i
$i = 2$	2.1854	0.0082	31.2328	11.43
$i = 3$	-2.2942	75.447	24.2336	15.50
$i = 4$	-1.345	30.8599	5.0099	85.71

Let $\Lambda := [0, x_1^*] \times [100, x_1^*] \times [0, x_3^*] \times [0, x_4^*] \times [0, x_5^*]$ and

$$\begin{aligned} f(x,u) := \ & ((\mu - u_2)x_1, u_2(u_1 - x_2) - q_2 x_1, \\ & q_3 x_1 - u_2 x_3, q_4 x_1 - u_2 x_4, q_5 x_1 - u_2 x_5), (x,u) \in \Lambda \times U_{ad}. \end{aligned}$$

When the kinetic system reaches its steady state at some time, the concentrations of each substance is invariable. Equilibrium point at a fixed dilution and an given substrate concentration can be obtained by letting the right hand of Eq.(1) be zero, namely, $f(x,u)=0$. The equilibrium solution is independent of the initial condition, which enables us to introduce the following definition.

Definition 1. *The general solution $x(t)=x(t,t_0,x_0,u)$ of Eq.(1) is said to be kinetic-equilibrious if there exists a $t_f > t_0$ such that $f(x(t),u)=0, t \geq t_f$.*

The objective function is the weighted sum of the concentration and productivity of 1,3-PD relative to the kinetic-equilibrious solutions, that is

$$\phi(x,u) := \mu_1 x_3 + \mu_2 u_2 x_3.$$

where μ_1, μ_2 are weighting scalars and x is a kinetic-equilibrious solution. So we establish the nonlinear programming model of Glycerol Bioconversion to 1,3-PD in continuous culture:

$$\begin{aligned} &\max\ \phi(x,u) \\ &s.t.\ f(x,u)=0 \\ &\quad (x,u) \in \Lambda \times U_{ad} \end{aligned}$$

3 Optimization algorithm

We use $J(x,u)$ to denote the Jacobian matrix of the constraints, that is,

$$J(x,u) = (\nabla f_1, \nabla f_2, \nabla f_3, \nabla f_4, \nabla f_5)^T \in R^{5\times 7}.$$

Assume that (x^k,u^k) is a feasible point. The nonlinear programming model is converted to the following model by linear approximation method.

$$\begin{aligned} &\max\ \phi(x,u) \approx \phi(x^k,u^k) + \nabla\phi(x^k,u^k)^T d \\ &s.t.\ J(x^k,u^k)d = 0 \\ &\quad (x^k,u^k)+d \in \Lambda \times U_{ad} \end{aligned}$$

The linear approximation method may have a greater deviation, which can't guarantee that the iterative sequences satisfy all the constraints. So we need to assess and modify the iterative point to make it satisfy the constraints and guarantee the ascent of objective function. Moreover, the choice of initial point determines how fast the iterative sequences converge to a local optimal solution, so we use uniform design algorithm to generate the initial feasible points. The uniform designs proposed by Fang scatter points uniformly over the experimental domain [2]. They have the advantage of providing a good representation of the experimental domain with fewer runs. Computer experiments using uniform designs have attracted considerable attention in recent years [5]. Traditionally the uniform designs were generated by so-called good lattice point method, cutting method and resolvable balanced incomplete block designs etc.

Since the objective function has only two variables, we can compute the gradient of objective function as the steepest ascent direction. The homogeneous linear system

$J(x,u)d = 0$ with 5 equations in 7 unknowns has a nontrivial solution. Since $rank(J(x,u)) \leq 5$, we can choose the components d_3, d_7 of d to be the ascent direction of objective function(gradient direction). Then we decides how far to move along that direction to get the new feasible point. In order to improve the convergence rate, we use an convergence factor such that the ascent degree of objective function is increased.

The basic steps of the algorithm are given as follows.

Step 1. Given the radius of convergence of Taylor expansion δ, convergence factor α, accuracy $\varepsilon > 0$, terminal condition σ; generate m initial pairs $(x_3^1, u_2^1) \in R^2$ in feasible domain by good lattice point method and let $i = 1, k = 1$.

Step 2. Solve the eqations $f(x,u) = 0$ to get iterative point (x^k, u^k) satisfying all the constraints.

Step 3. Choose $d_3^k = \delta(\mu_1 + \mu_2 u_2^k), d_7^k = \delta\mu_2 x_3^k$ and solve the linear equations $J(x^k, u^k)d^k = 0$ to get the search direction d^k.

Step 4. Let $\tilde{x}_j^k := x_j^k + d_j^k,\ j = 1, \cdots, 5;\ \tilde{u}_j^k := u_j^k + d_{j+5}^k,\ j = 1,2$. If $f(\tilde{x}^k, \tilde{u}^k) < \varepsilon$ and $(\tilde{x}^k, \tilde{u}^k) \in \Lambda \times U_{ad}$, go to Step 5; else, go to Step 8.

Step 5. Let $d^k := \alpha d^k,\ \tilde{x}_j^k := x_j^k + d_j^k,\ j = 1, \cdots, 5;\ \tilde{u}_j^k := u_j^k + d_{j+5}^k,\ j = 1,2.$ go to step 6.

Step 6. If $f(\tilde{x}^k, \tilde{u}^k) < \varepsilon$ and $(\tilde{x}^k, \tilde{u}^k) \in \Lambda \times U_{ad}$, go to Step 5; else, let $\tilde{x}_j^k := x_j^k - d_j^k,\ j = 1, \cdots, 5;\ \tilde{u}_j^k := u_j^k - d_{j+5}^k,\ j = 1,2$, go to Step 7.

Step 7. Let $x_3^{k+1} := \tilde{x}_3^k,\ u_2^{k+1} := \tilde{u}_2^k$ and $k := k+1$, go to Step 2.

Step 8. If $\delta < \sigma$, output (x^k, u^k) and $\phi(x^k, u^k)$, i:=i+1, go to Step 9; else, let $\delta := \beta\delta$, go to Step 3.

Step 9. If $i < m$, go to Step 2; else, output all the local optimal solutions.

4 Numerical results and conclusions

According to the optimization model and the algorithm mentioned above, we have programmed the procedure by *Mathematica* 5 and applied it to the numerical simulation. By comparison of a large quantity of calculation results, we found that the optimal solution doesn't exist if the value of initial point (x_3^1, u_2^1) is too big. It is reasonable because the constraint equation can't be satisfied, which also can be seen from Table 2 and Table 3. But we can obtain the local optimal solutions if $(x_3^1, u_2^1) \in [0, 281.85] \times [0.01, 0.34]$ generated by uniform design algorithm. To compare with the existing results, we mainly choose two extreme of weight scalars. We choose 100 initial points in $[0, 281.85] \times [0.01, 0.34]$ by good lattice point method and get 100 local solutions. These solutions are not exactly the same because of the precision of computing, but we can classify them into four classes or so according to the value of objective function, each of which distribute densely so that can be viewed as one optimal solution.

To compared with Figure 4 in [10], We choose $\mu_1 = 0, \mu_2 = 1$ to get maximal productivity of 1,3-PD at steady state. The optimal value in Table 2 is close to the experimental results and theoretical maximum. The errors between our computational results and the theoretical maximum in [10] is less than 10%, which satisfy the experimental demand well.

Next we choose $\mu_1 = 1, \mu_2 = 0$ to compare the maximal concentration of 1,3-PD with the results in [10, 12] at steady state. We get the maximal 1.3-PD concentration of 440

Table 2: Optimal solutions when $\mu_1 = 0, \mu_2 = 1$

	result1	result2	result3	result4
u_1	524.806	463.844	450.658	459.54
u_2	0.30769	0.30566	0.30527	0.29334
x_1	1.97538	1.92421	1.89755	1.91508
x_2	61.0017	95.8269	117.75	139.328
x_3	425.501	425.983	423.861	438.441
x_4	65.7424	67.6441	68.3169	70.6921
x_5	28.7851	24.889	22.8208	22.3228
$\phi = u_2 x_3$	132.326	131.505	130.687	129.808

$mmol \cdot l^{-1}$ approximately at a dilution rate of 0.29 h^{-1} or so. The concentrations of each components are listed in Table 3.

Table 3: Optimal solutions when $\mu_1 = 1, \mu_2 = 0$

	result1	result2	result3	result4
u_1	459.54	477.881	460.033	469.854
u_2	0.293344	0.286752	0.295097	0.291444
x_1	1.91508	1.96036	1.91845	1.94258
x_2	139.328	118.501	130.897	120.631
$\phi = x_3$	438.441	451.125	437.051	443.874
x_4	70.692	71.2973	70.2582	24.1318
x_5	22.3228	24.8774	22.8188	22.3228

The foregoing examples illustrate very nicely the power of optimization techniques in seeking the optimal control parameters. It is worth mentioning that we have tried genetic algorithm and penalty function method before we conceived of this new method. Because of the equality constraints of great complexity, these two methods are noneffective, even can't generate feasible iterative points. So the new algorithm is efficient and robust to solve the nonlinear programming problem. Future work will focus on the the stability analysis of kinetic-equilibrious solutions.

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