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Studies on optimal control approach in a fed-batch fermentation

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Abstract−Fed-batch operation of fermentation processes has been receiving a great deal of interest as it offers the possibility to control a substrate concentration at a desired condition. However, control of a fed-batch fermentation reactor has been known to be a difficult task due to its highly nonlinear and complicated behavior. This work addresses an optimization-based control strategy for a fed-batch bioreactor where an ethanol fermentation process is chosen as a case study. The optimal control problem is formulated to determine the optimal feeding rate policy giving the highest product yield. The resulting optimization problem is solved by using an efficient sequential approach with a piecewise constant control parameterization. Due to the limitation of the sequential approach to cope with inequality path constraints, comparative studies of the methods for handling such constraints are carried out. Furthermore, the impact of time interval and switching time on the solution of the optimal control is investigated.

Key words: Optimal Control, Path Constraints, Fed-Batch Reactor, Fermentation Process

INTRODUCTION

A fermentation process has been receiving much attention for many years as it can be widely applied for the production of many bioproducts including pharmaceutical and agricultural products. In general, fermentation processes can be operated in batch, fed-batch and continuous mode [Rani and Rao, 1999]. However, the fed-batch operation which the inlet feed is supplied to a reactor while products generated remain in the reactor until the end of the operation is preferable to the others, especially in the case that i) high substrate levels inhibit the product formation, and ii) undesired components are produced in parallel with a desired components [Lee and Yoo, 1994]. For such circumstances, it is found that changing feeding rate of the substrate affects the productivity and yield of the desired product.

In order to obtain high productivity, a fed-batch fermentation reactor must operate efficiently. However, most fed-batch reactors are currently operated at constant feed rate using heuristic process understanding gained by experience or laboratory experimental data [Vemuri, 2004]. However, a heuristic approach cannot always guarantee optimal operation. On the contrary, with an advance in optimization techniques, an optimization-based control technique can be used to identify the optimal feeding policy of the reactor, resulting in the highest desired product at the end of operation time [Zavala et al., 2005]. Generally, the optimal feeding profile is determined by solving an optimal control problem that is formulated based on dynamic models of the system to be controlled. However, achieving the optimal feeding profile is known to be quite difficult and challenging due to the highly nonlinear and complicated dynamic behavior of the reactor. In the past, the Pontryagin's maximum principle (indirect method) was usually used to solve such the optimal control problems; however, the presence of many state constraints makes the solution via this approach difficult [Patkar et al., 1993]. As a result, an alternative method that considers the optimal control problem as a direct optimization problem has been proposed. In general, the direct optimization method can be classified into two approaches, simultaneous and sequential, depending on the degree of discretization [Carvantes and Biegler, 1999].

In the simultaneous approach, state and control variables are parameterized and the model solution and optimization problem are solved simultaneously. Based on an orthogonal collocation on finite elements that is used to parameterize both state and control variables, and a sequential quadratic programming (SQP) that is used to solve the resulting optimization problems, Cuthrell and Biegler [1984] applied this approach for solving the optimal control of a fed-batch reactor in penicillin production. In contrast to the simultaneous approach, only control variables are parameterized in the sequential method [Arpornwichanop et al., 2005]. Following this approach, the model solution and optimization are solved sequentially. Chen and Hwang [1990] proposed a method based on a piecewise constant control parameterization to convert the original optimal control problem into a sequence of finite dimensional nonlinear programming problems (NLP) that were solved by a SQP algorithm. To illustrate the proposed solution method, they solved an optimal control problem related to a fed-batch reactor for ethanol production.

It is to be noted that the main advantage of the sequential approach is that the formulated optimization is a small scale NLP problem since only the discretized control profile is considered as decision variables. However, the limitation of this approach is the difficulty to handle a constraint on state variables (path constraints), because the state variables are not directly included in an NLP problem.

In this work, an optimal control strategy for a fed-batch reactor in an ethanol production is presented. The optimal control problem is formulated so as to determine an optimal feed rate policy and solved by using a sequential model solution and optimization technique. Due to the limitation of this approach to handle path constraints, this present work investigates two methods, a penalty function method and an equivalent end-point constraint method, for deal-

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ing with such a difficulty. In addition, the influences of time interval and switching time on the solution of the optimal control are studied.

PROCESS MODEL

The present work is focused on the production of ethanol in a fed-batch reactor. The dynamic reactor model developed by Hong [1986] for describing the ethanol fermentation by *Saccharomyces cerevisiae* in the fed-batch culture is used in simulation studies. The mathematical models consisting of differential and algebraic equations are given as follows:

$$\frac{dx}{dt} = \mu x - \frac{x}{V}u \tag{1}$$

$$\frac{ds}{dt} = -\frac{\mu x}{Y} + \frac{(s_0 - s)}{V}u \tag{2}$$

$$\frac{dp}{dt} = \eta x - \frac{p}{V}u \tag{3}$$

$$\frac{dV}{dt} = u \tag{4}$$

$$\mu = \frac{\mu_0 s}{\left(1 + \frac{p}{K_p}\right)(K_s + s)} \tag{5}$$

$$\eta = \frac{\eta_0 s}{\left(1 + \frac{p}{K_p'}\right)(K_s' + s)} \tag{6}$$

where x, s and p are the concentration of cell mass, substrate, and product (ethanol), respectively, V is the liquid volume within the reactor, μ is the specific growth rate, η is the specific productivity, Y is the yield coefficient (=0.1), s_0 is the feed concentration of substrate, and u is the feed flow rate into the fed-batch reactor which is the only manipulated input in this process.

Table 1 shows the values of initial conditions and kinetic parameters of the process models.

OPTIMAL OPERATING STRATEGY

To determine an optimal feeding policy, the optimal control problem of the fed-batch reactor with a fixed terminal time is formulated as shown below:

Find u(t) over $t \in [t_0, t_f]$ maximizing

$$J = p(t_f)V(t_f) \tag{7}$$

Table 1. Initial conditions and kinetic constants used in the process model

Initial conditions	Kinetic constant
x(0)=1 g/L	K_p=16.0 g/L
s(0)=150 g/L	K_s=0.22 g/L
p(0)=0 g/L	K_p'=71.5 g/L
V(0)=10 L	K_s'=0.44 g/L
μ_0=0.408 h^{-1}	
η_0=1 h^{-1}	

subject to

the fed-batch reactor models (Eqs. (1)-(6)) (8)

$$0 \le u(t) \le 12 (L/hr) \tag{9}$$

$$V(t_f) \le 200 (L) \tag{10}$$

$$t_f = 63 \text{ hr} \tag{11}$$

Eqs. (9)-(10) indicate the constraints on the rate of substrate feed (u) into the fed-batch reactor and on the volume of the fed-batch reactor, respectively.

1. Sequential Approach

As mentioned earlier, in the sequential approach, only the control variables are discretized. Typically, a piecewise constant approximation over equally spaced time intervals is made for the control variables. The basic algorithm of the sequential approach shown in Fig. 1 can be summarized as follows:

Step 1. Specify the initial conditions for state variables and guess the initial value for a set of control parameters.

Step 2. Solve the process model by Gear's type method to determine the trajectory of state variables at each iteration of optimization. This provides information of the objective function and constraints to a nonlinear programming solver. Further, an efficient adjoint variable approach [Morrison, 1984] is employed to evaluate the gradient information of the objective function and constraints with respect to the decision variables.

Step 3. Determine a new set of control parameters. It should be noted that the resulting nonlinear program (NLP) is solved by using the successive reduced quadratic programming solver.

Step 4. Go to step 2 and recalculate based on the new set of control parameters until the optimum is found.

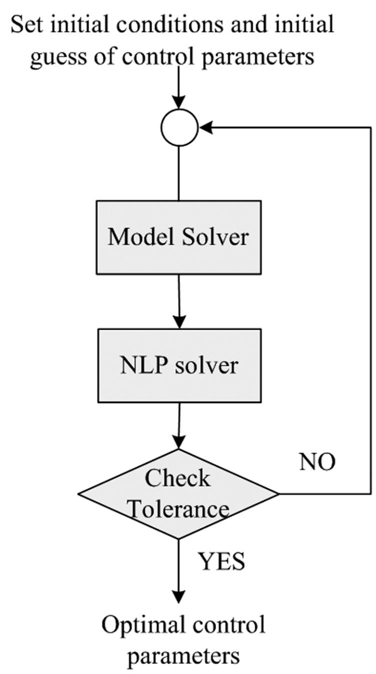

Fig. 1. Sequential approach to the solution of optimal control problems.

2. Path Constraints Handing

For general optimal control problems, path constraints usually occur when a certain process variable cannot exceed a given limit for the entire processing period [Aziz and Mujtaba, 2002]. There are two kinds of path constraints: equality and inequality path constraints. To deal with the equality path constraints, Bryson and Ho [1975] introduced an integral penalty term in the objective function to be minimized in order. Nevertheless, this approach often leads to numerical difficulties due to the use of the penalty term. Sargent and Sullivan [1997] introduced an alternative method concerning the conversion of the path constraint to an equivalent end point constraint.

For inequality path constraints, the same techniques as for handling equality path constraints can be applied. Thus, the management of inequality path constraints usually relies upon defining a measure of the constraint violation over the entire horizon and penalizing it in the objective function (a penalty function method), or forcing it directly to zero through an end point constraint (an equivalent end point constraint method) [Aziz and Mujtaba, 2002].

In the penalty function method, the violation of path constraints is added in the objective function by the penalty terms which are associated with the inequality path constraints. The augmented objective function is as follows:

$$\min_{u(t)} J_{aug} = p(t_f)V(t_f) + \lambda\int_0^{t_f} VT\ dt \tag{12}$$

where λ is the penalty terms and VT is the violation term which can be defined as shown below:

$$VT(t) = \begin{cases} V(t) - V_{max} & \text{if } V(t) \geq V_{max} \\ 0 & \text{if } V(t) < V_{max} \end{cases} \tag{13}$$

where V(t) is the liquid volume in the reactor at any t and V_{max} is the maximum allowable liquid volume within the reactor (V_{max}= 200 L). It is noted that the penalty term reflects the violation of the constraints and assigns higher costs of the penalty function to the objective function.

In the equivalent end point constraint method, the total accumulation of the violation over the entire period is considered and can be expressed in the following equation.

$$V_T = \int_{t_0}^{t_f} VT(t)\ dt \tag{14}$$

Eq. (14) can be rearranged in a differential equation form as given in Eq. (15) which is further added to the process model equations presented earlier.

$$\frac{dV_T}{dt} = VT(t) = \max(V(t) - V_{max}, 0) \tag{15}$$

In order to handle the inequality path constraint on the reactor liquid volume with this approach, the following additional end point constraint is included in the optimal control problem to ensure that V(t) will always be less than V_{max}

$$V_T(t_f)=0 \tag{16}$$

SIMULATION RESULTS

1. Optimal Control Performance

The simulation results obtained from solving the optimal control problem are divided into two cases according to the method that is used to handle the path constraint. Under the nominal condition, the operation time is divided into 10 equal stages and the control variable profile is approximated by a piecewise constant function.

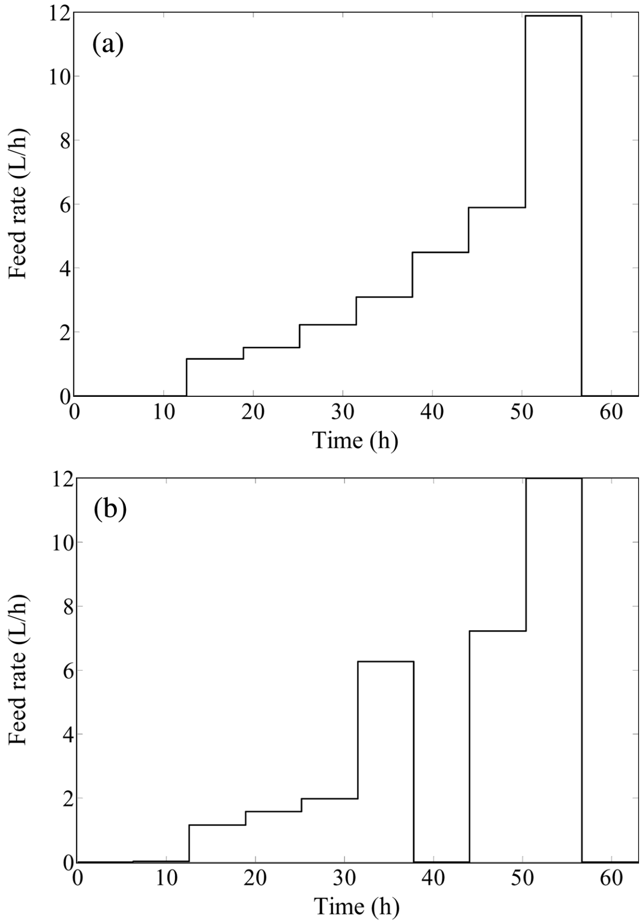

Fig. 2. Optimal feed profile by using (a) penalty function method, (b) equivalent end-point constraint method.

Figs. 2(a) and 2(b) show the optimal feed profiles of the substrate which are obtained from the solution of the optimal control problem by using a penalty function method and an equivalent end-point constraint method, respectively, and the corresponding concentration profiles are given in Figs. 3(a) and 3(b). In both cases, the substrate feed rate at the end of the batch time is close to zero, signifying the liquid volume does not exceed 200 L which is the maximum capacity of the reactor volume. It can be seen from Fig. 3 that when the substance which is used for cell growth and ethanol production is completely consumed, the concentration of ethanol and cell is constant.

From the simulation results, the control performance index obtained in case of the penalty function method (=20747) is better than that with the equivalent end-point constraint method (20480). It seems that the penalty function method is more suitable than the equivalent end-point constraint method in handling path constraints of this process. Table 2 presents the control results of the proposed method, in term of performance index, compared with other methods which are reported in the literature: IDP method [Luus, 1993], ICRS/DS method [Banga et al., 1997] and CAFNN method [Xiong

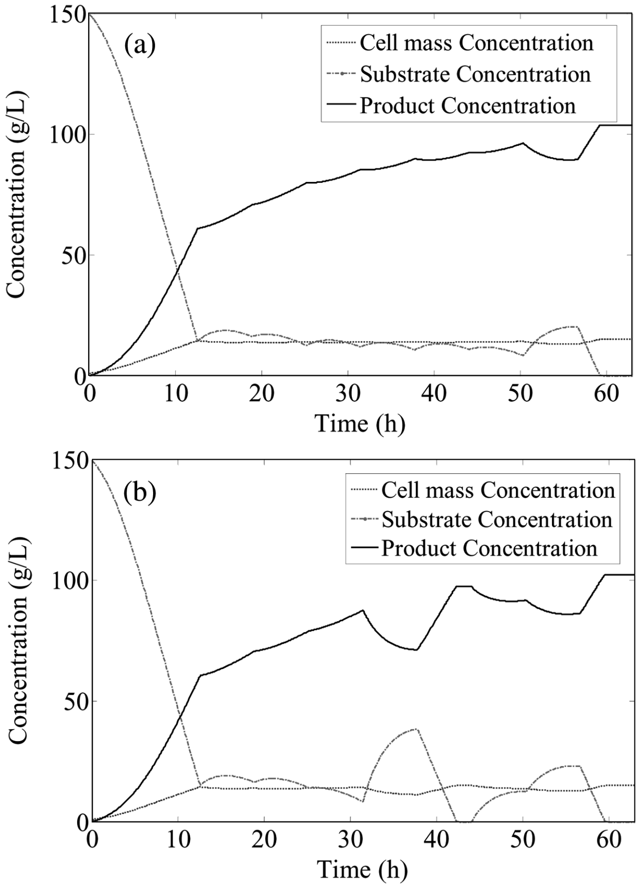

Fig. 3. Concentration profile under the optimal control by using (a) penalty function method, (b) equivalent end-point constraint method.

Table 2. The results of different solution methods of optimal control problem

Method	Performance index
IDP	20,841
ICRS/DS	20,715
CAFNN	20,627
Present study	20,747

and Zhang, 2004]. It can be seen that the proposed method using the penalty function method to handle the path constraint gives better control performance compared to the ICRS/DS and CAFFNN method. However, although the IDP method provides the best value of performance index, its computational time is longer than that used in the proposed method.

2. Effect of Time Interval

In the previous section, the optimal control problem of a fed-batch reactor is formulated as a fixed final time with equally spaced time interval of 6.3 hr. In this section, the effect of the time interval on the control performance is studied. Fig. 4 shows the response of the optimal feed rate profile computed by using a time interval of 3.15 hr. It is found that the control performance (=20841) is improved; the performance index equals that obtained from the IDP method. This can be explained as follows: as the length of time intervals decreases, the approximated optimal profile with piecewise constant policy is closer to the actual optimal profile.

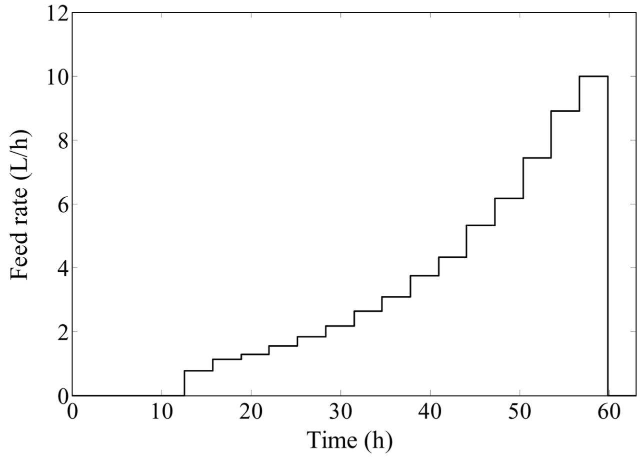

Fig. 4. Optimal feed profile with a penalty function method in case of decreased time interval.

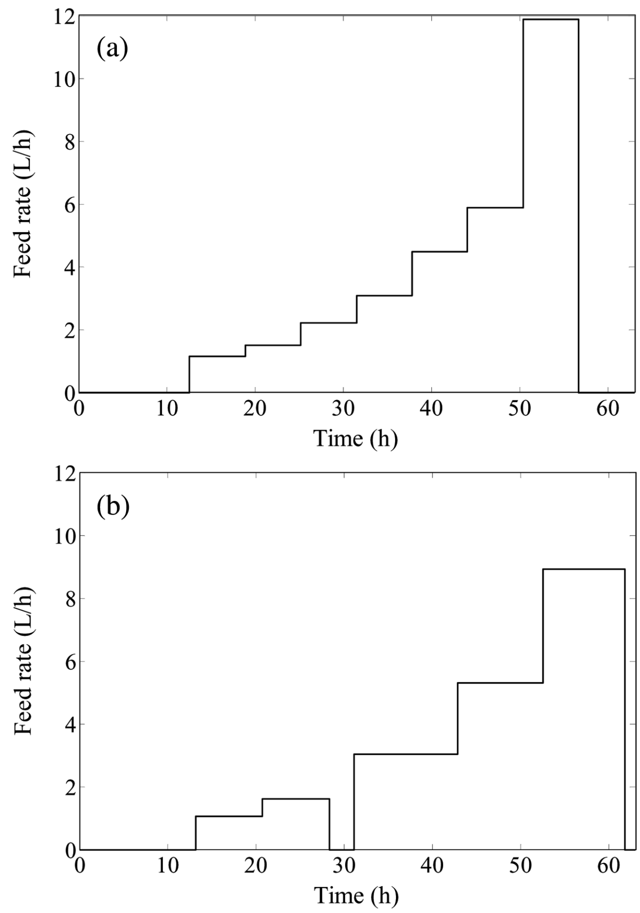

Fig. 5. Optimal feed profile with a penalty function method: (a) uniform control vector parameterization (fixed switching time), (b) non-uniform control vector parameterization (free switching time).

3. Effect of Switching Time

In this section, a non-uniform control vector parameterization is studied in order to improve the performance of the optimal control.

Figs. 5(a) and 5(b) show the response of the optimal control of the feeding rate obtained by using the uniform control vector parameterization (fixed switching time) and the non-uniform control vector parameterization (free switching time). With the non-uniform control vector parameterization, the optimal feeding rate does not reach the upper limit and its control performance (=20798) is slightly higher than that using the uniform control vector parameterization (=20747). This is due to more degrees of freedom (i.e., the switching time) for determining the solution of the optimization problem.

CONCLUSIONS

The optimal control of a fed-batch reactor for ethanol production has been studied in this work. The solution of the optimal control problem is computed by using a sequential model solution and optimization method. Due to the difficulty of this approach in handling path constraints, two methods--the path constraints are defined as a penalty function and as an equivalent end-point constraint--for coping with these constraints are studied. It has been found that the optimal control with the penalty function method gives a better value of performance index. To improve the control performance, the effects of a time interval and switching time are also investigated. From the results, it can be seen that decreasing the time interval and using non-uniform control vector parameterization (free switching time) result in better control performance.

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NOMENCLATURE

J : performance index
K_p : kinetic constant of product [g/L]
K_s : kinetic constant of substrate [g/L]
p : product concentration [g/L]
s : substrate concentration [g/L]
t : time [h]
u : feedrate [L/h]
V : volume of reactor [L]
x : cell mass concentration [g/L]
Y : yield coefficient
μ : specific growth rate [h^{-1}]
η : specific productivity [h^{-1}]

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