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Comparison of Various Optimization Approaches for Fed-Batch Ethanol Production

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Abstract

Various optimization techniques have been proposed to optimize the feed-rate profile to maximize ethanol production. Among them are the differential algebraic system (DAS) approach, Kelly transformation approach, singular control approach, and on-off control approach. These methods are compared and it is shown that the DAS approach and Kelly transformation method are equivalent. A nonsingular transformation approach is presented. The performance obtained with the nonsingular approach is the same as that obtained with the singular approach and better than those obtained with the DAS and on-off control approaches.

Index Entries: Optimization; differential algebraic system; nonsingular transformation.

Introduction

Several optimization approaches have been proposed for the calculation of optimal feed-rate profiles for the fed-batch fermentation processes *(1–4)*. The complexity of the system model makes the computation of the optimal control profiles quite difficult.

Hong *(5)* applied the singular control theory for the free final-time problem for maximizing the ethanol production and calculated the optimal feed-rate control profile. Since the proposed problem is a volume limitation one, the maximal performance index has been achieved by maximizing the production rate over the substrate consumption rate. Modak et al. *(6)* studied characteristics of the optimal feed-rate profiles and calculated optimal control profiles for various fed-batch fermentation processes by analyzing the singular control and the singular arcs. The optimization of feed-rate profile was reduced to a problem of determining switching times in the bang-bang interval and singular interval. Lim et al. *(7)* also proposed different feed-rate profiles, depending on the characteristics of specific rates of biomass growth and product formation, as well as the initial conditions for models with four state variables. Hong *(5)* has also calculated the optimal control profiles of the singular control problem by considering the conjunction point between the bang-bang and singular arcs. An analytical expression of feed rate was calculated as a function of the concentrations of substrate, cell and product, and volume. However, because of the complexity of the singular control problems, most of the optimizations of the fed-batch fermentation processes have been, so far, limited to low-order processes.

Alternatively, many researchers tried to take state variables other than the feed rate as the control variable. Several researchers have proposed transformation approaches to convert singular control problems into nonsingular ones to overcome the difficulties. One approach is to obtain the solution of the singular control problem from that of the nonsingular problem. Guthke and Knorre *(8)* used the substrate concentration as a control variable but ignored constraints imposed on feed rate and fermentor volume, and the intrinsic properties of the optimization problem therefore have been changed. San and Stephanopoulous *(9)* used the feed substrate concentration as the control variable and derived an optimization algorithm with constraints imposed on the state and control variables. Modak and Lim *(10)* used the culture volume as a control variable instead of the feed rate. Fu and Barford *(11)* proposed a differential algebraic system (DAS) model to convert the singular control problem to a nonsingular one. However, the proposed algorithm is shown to be equivalent to that of the Kelly transformation *(12)*, and as such it can be applied only for some specific problem of which the yield is constant. Chen and Hwang *(13)* proposed the constrained nonlinear programming methods with optimal on-off feeding policy. Instead of using the continuous feed rate, the on-off feeding policy was proposed and the on-off switching time has been calculated with a nonlinear programming method.

Although various methods have been proposed for the optimization of fed-batch fermentation, there has been no attempt to compare those methods. In this article, we compare the performances of various optimization approaches and show the equivalency of a nonsingular transformation algorithm using the DAS and Kelly transformation.

Problem Statement

The fed-batch fermentation process in which ethanol is produced by *Saccharomyces cerevisiae* and the production of ethanol is inhibited by itself *(14)* is considered as a model system. The dynamic behavior of this fed-batch fermentation process is described by the following differential equations:

$$\frac{d(XV)}{dt} = \mu XV \tag{1}$$

$$\frac{d(SV)}{dt} = S_f F - \frac{\mu}{Y_{XS}} XV \tag{2}$$

$$\frac{d(PV)}{dt} = \pi XV \tag{3}$$

and

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

The equations for μ and π were developed by Aiba et al. *(14)*:

$$[\mu_o/(1 + P/K_P)][S/(K_S + S)] \tag{5}$$

and

$$[\pi_o/(1 + P/K_P')][S/(K_S' + S)] \tag{6}$$

where X, S, and P represent the concentrations of the cell mass, substrate, and product, respectively; V is the broth volume; μ is the specific growth rate; π is the specific productivity; Y_{XS} is the yield coefficient; S_f is the substrate concentration of the feed; and F is the feed rate.

For the calculation of the optimal control profile of a given problem, the kinetic constants for *S. cerevisiae* growing on glucose are used. They are as follows: $\mu_o = 0.408$/h; $K_P = 16.0$ g/L; $K_S = 22$ g/L; $\pi_o = 1.0$/h; $K_P' = 71.5$ g/L; $K_S' = 44$ g/L; $Y_{XS} = 0.1$. The initial fermentor volume is 10 L of broth with the 1 g/L and 150 g/L of cell mass and substrate concentrations, respectively. There is no ethanol in the reactor. The maximal reactor volume and maximal feed rate are 200 L and 12 L/h, respectively.

Equality of DAS Model and Kelly Transformation

A nonsingular transformation approach through a DAS was proposed by Fu and Barford *(11)*. They claimed that the DAS is a unique method converting a singular control problem to a nonsingular one, and proposed a numerical method to calculate optimal control profiles. However, we show subsequently that the proposed method through DAS is the same as the Kelly transformation and subject to the same type of limitations. In this section, the nonsingular approach through DAS is shown to be equivalent to the Kelly transformation *(12)*.

DAS Model

Since the proposed system is based on a constant cell mass yield from substrate, Eqs. 1 and 2 can be combined to give

$$S = [(X_o/Y_{XS} + S_o - S_f)V_o/VY_{XS}] + S_o - (X/Y_{XS}) \tag{7}$$

where X_o, S_o, and V_o represent the initial concentrations of cell mass, substrate and broth volume, respectively. Although the proposed problem can be solved without any transformation using the volume as a control variable, we follow the transformation adopted by Fu and Barford *(11)*. The original problem is transformed by defining the transformed state variables: $y_1 = \ln(XV)$, $y_2 = \ln(PV)$, $y_3 = V$, $y_4 = \mu$, and $y_5 = \pi$. The original problem is converted to the following equations:

$$\frac{dy_1}{dt} = y_4 \tag{8}$$

$$\frac{dy_2}{dt} = y_5 \exp(y_1 - y_2) \tag{9}$$

$$\frac{dy_3}{dt} = F \tag{10}$$

and two algebraic equations are developed:

$$0 = y_4 - \mu(y_1, y_2, y_3) \tag{11}$$

$$0 = y_5 - \pi(y_1, y_2, y_3) \tag{12}$$

The performance index of this problem is maximizing the ethanol concentration and is expressed as follows:

$$PI = \underset{F}{\text{Min}}\ [-\exp(y_2(t_f))] \equiv \underset{F}{\text{Min}}\ [-y_2(t_f)] \tag{13}$$

The Hamiltonian of this system is

$$H = \lambda_1 y_4 + \lambda_2 y_5 \exp(y_1 - y_2) + \lambda_3 F + \lambda_4 (y_4 - \mu) + \lambda_5 (y_5 - \pi) \tag{14}$$

The adjoint variables are

$$\frac{d\lambda_1}{dt} = -\lambda_2 y_5 \exp(y_1 - y_2) + \lambda_4 \frac{\partial \mu}{\partial y_1} + \lambda_5 \frac{\partial \pi}{\partial y_1} \tag{15}$$

$$\frac{d\lambda_2}{dt} = -\lambda_2 y_5 \exp(y_1 - y_2) + \lambda_4 \frac{\partial \mu}{\partial y_2} + \lambda_5 \frac{\partial \pi}{\partial y_2} \tag{16}$$

$$\frac{d\lambda_3}{dt} = \lambda_4 \frac{\partial \mu}{\partial y_3} + \lambda_5 \frac{\partial \pi}{\partial y_3} \tag{17}$$

$$0 = -\lambda_2 \exp(y_1 - y_2) - \lambda_5 \tag{18}$$

and

$$0 = -\lambda_1 - \lambda_4 \tag{19}$$

The final conditions of adjoint variables are $\lambda^T(t_f) = \{0, -1, 0, 0, \exp[y_1(t_f) - y_2(t_f)]\}$. Substitution of Eqs. 18 and 19 into Eq. 14 yields:

$$H = \lambda_1\mu + \lambda_2\pi \exp(y_1 - y_2) + \lambda_3 F \tag{20}$$

The optimal control profiles are calculated by making the partial derivative of Hamiltonian with respect to control variable F equal to 0. Therefore, the following relations are derived from Eq. 20:

$$\frac{\partial H}{\partial F} = \lambda_3 = 0 \tag{21}$$

Since $\lambda_3 = 0$, its time derivative also equals 0. Therefore, the optimal control is achieved by satisfying the following conditions:

$$\frac{d\lambda_3}{dt} = \lambda_4 \frac{\partial \mu}{\partial y_3} + \lambda_5 \frac{\partial \pi}{\partial y_3} = -\lambda_1 \frac{\partial \mu}{\partial y_3} - \lambda_2 \exp(y_1 - y_2)\frac{\partial \pi}{\partial y_3} = 0 \tag{22}$$

Since the original control variable, F, does not appear in the optimal control conditions, y_3 can be chosen as a new control variable and this problem is converted to a nonsingular control problem. The optimal control profile is calculated from the calculated time derivative of y_3. This result is a necessary condition of optimality. Fu and Barford *(11)* proposed a linear relationship between the optimal control profile and the adjoint variable λ_3. As in Eq. 21, $\lambda_3 = 0$ for the optimal control and its time derivative is also 0.

Kelly Transformation

Kelly *(12)* proposed a transformation algorithm that reduces the order of the system and converts singular control problems to nonsingular. The transformed control variable is used to calculate the optimal control profile instead of the original control variable. For the proposed system, we can easily choose the transformed control variable that has a mathematical relation with the original control variable.

As shown in Eqs. 8–10, the control variable F is included in Eq. 10 and does not exist in the other equations. Therefore, we can choose V as a new control variable, and the proposed problem is converted to a nonsingular control problem by the Kelly transformation.

The proposed problem is reformulated using the volume as a control variable:

$$\frac{dy_1}{dt} = \mu \tag{23}$$

$$\frac{dy_2}{dt} = \pi \exp(y_1 - y_2) \tag{24}$$

The performance index, maximizing the product concentration, is as follows:

$$PI = \underset{y_3}{\text{Min}} \, [-y_2(t_f)] \tag{25}$$

The feed rate is calculated from the volume profiles:

$$F = (\Delta y_3/\Delta \text{t}) \tag{26}$$

The Hamiltonian of the problem is formulated as follows:

$$H = \lambda_1 \mu + \lambda_2 \pi \exp(y_1 - y_2) \tag{27}$$

The adjoint variables of the system are defined as

$$\frac{d\lambda_1}{dt} = -\lambda_1 \frac{\partial \mu}{\partial y_1} - \lambda_2 \, \pi \exp(y_1 - y_2) - \lambda_2 \frac{\partial \pi}{\partial y_1} \exp(y_1 - y_2) \qquad \lambda_1(t_f) = 0 \tag{28}$$

and

$$\frac{d\lambda_2}{dt} = -\lambda_1 \frac{\partial \mu}{\partial y_2} + \lambda_2 y_5 \exp(y_1 - y_2) - \lambda_2 \frac{\partial \pi}{\partial y_2} \exp(y_1 - y_2) \qquad \lambda_2(t_f) = -1 \tag{29}$$

The optimal control profile is obtained by forcing the derivative of the Hamiltonian with respect to the control variable, y_3, to 0:

$$\frac{\partial H}{\partial y_3} = \lambda_1 \frac{\partial \mu}{\partial y_3} + \lambda_2 \exp(y_1 - y_2) \frac{\partial \pi}{\partial y_3} = 0 \tag{30}$$

which is exactly the same as that of Fu and Barford *(11)* (*see* Eq. 22). Although Fu and Barford *(11)* proposed DAS to convert the singular problem to nonsingular, the proposed DAS is the same as the Kelly transformation *(12)*. Since the proposed problem is a case of constant yield, it is possible to transform it into a nonsingular problem. The substrate concentration is expressed as a function of cell mass and volume owing to the constant yield, and Eq. 2 is therefore eliminated. The Kelly transformation is used to calculate the optimal control profiles by the following numerical procedures.

Numerical Procedures and Results

1. Guess the initial optimal control profiles $y_3^{i}(t)$.
2. Calculate the state variables by forward integration of Eqs. 23 and 24.
3. Calculate the adjoint variables by backward integration of Eqs. 28 and 29.
4. Calculate the derivatives of Hamiltonian from Eq. 27.
5. Update the volume profile using the following control vector iteration with the volume constraint:

$$y_3^{i+1}(t) = y_3^{i}(t) - \varepsilon \left[\frac{dH}{dy_3} \right]^i$$

6. Iterate until the increase in the performance index is less than a specified tolerance (steps 2–5).

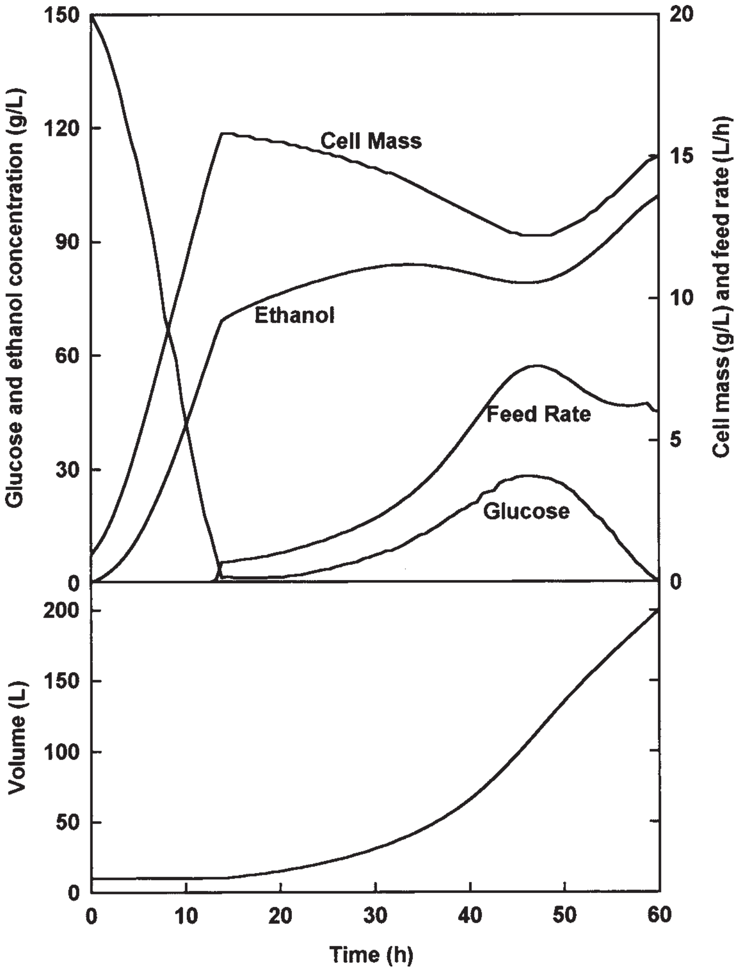

Fig. 1. The optimal control profiles calculated with the Kelly transformation.

Figure 1 shows the optimal control profiles calculated with the volume as a control variable. The proposed gradient algorithm was applied and the feed rate was calculated using Eq. 26. The maximal product concentration at 60 h was 102.13 g/L, and the substrate concentration showed a profile similar to that calculated by Fu and Barford *(11)*. The substrate concentration changed from 0 to 30 g/L. Since substrate concentration deviated from the profile calculated by the singular control algorithm, the final product concentration was less than that calculated by the singular optimal control. The feed rate decreased after 45 h and its profile was different from the singular control profile calculated by Hong *(5)*.

Figure 2 shows the product concentration change with fermentation time. As time increases, performance increases and then decreases after 62 h.

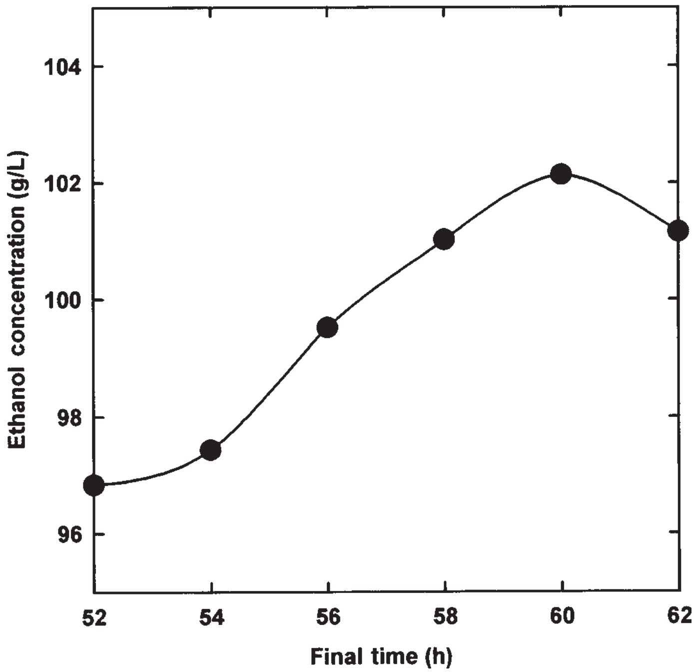

Fig. 2. The performance index changes with the changes of fermentation time with the Kelly transformation.

Nonsingular Transformation Approach

The nonsingular control algorithm developed by Lee et al. *(15)* uses the substrate concentration as a transformed control variable. The volume and control variable constraints are applied for the calculation of optimal control profile. The mathematical derivation and numerical procedures are as follows.

The feed rate determines the substrate concentration in the fermentor and is used to establish the optimum substrate concentration profile. Therefore, the feed-rate control problem can be converted to a substrate concentration control problem. Pontryagin's Minimum Principle is used to determine the optimal substrate concentration trajectory:

$$F = (\sigma XV + V\dot{S})/(S_f - S) \tag{31}$$

Thus, the feed rate can be calculated using Eq. 31 with the known profiles of X, V, and S. We can therefore replace the original mass balance equations with the following set in which Eq. 2 is dropped and a new state variable, X_p, is added. Since the proposed problem is a constant yield problem, the cell mass concentration is calculated from substrate concentration and is shown in Eq. 7.

$$\dot{X}_3 = \pi \cdot XV \qquad X_3(0) = 0 \tag{32}$$

and

$$\dot{X}_P = (\mu / Y_{XS}) \cdot XV, \qquad X_P(0) = 0 \tag{33}$$

where X_P is the amount of substrate consumed. The cell mass and volume changes are expressed as functions of initial conditions, and X_P. $XV = X_o V_o + Y_{XS} X_P$ and $V = (S_f V_o - S_o V_o + X_P)/(S_f - S)$. A state- and control-variable constraint is added to account for the culture volume constraint in Eq. 34:

$$g = [1/(S_f - S)]X_P + [(S_f - S_o)/(S_f - S)]V_o - V_f \leq 0 \tag{34}$$

where S_0 and S_f are the initial and feed substrate concentrations, respectively, and V_0 and V_f are the initial and final fermentor volumes, respectively.

The substrate concentration is constrained by the fixed initial value and also by the minimum and maximum feed rates Eq. 2:

$$S(0) = S_o, \text{ and } S^{\min}(t) \leq S(t) \leq S^{\max}(t) \tag{35}$$

where $S^{\min}(t)$ and $S^{\max}(t)$, the minimum and maximum substrate concentrations, are determined from $F_{\min}$ and $F_{\max}$, respectively.

According to the minimum principle, the Hamiltonian to be minimized is

$$H = (\lambda_2 \pi + \lambda_P \sigma)(X_o V_o + Y_{XS} X_P) + \alpha g = f + \alpha g \tag{36}$$

where $\alpha \begin{cases} \geq 0 & \text{when } g = 0 \\ = 0 & \text{when } g < 0 \end{cases}$

The gradient of substrate concentration is a function of time and determined from the substrate concentration profile. The adjoint equations must satisfy the following ordinary differential equations:

$$-\dot{\lambda} = \frac{\partial H}{\partial \mathbf{X}} \begin{cases} \dfrac{\partial f}{\partial \mathbf{X}} - \alpha \dfrac{\partial g}{\partial \mathbf{X}} & \text{when } g = 0 \\ \dfrac{\partial f}{\partial \mathbf{X}} & \text{when } g < 0 \end{cases} \tag{37}$$

where $\mathbf{X}$ is the vector whose components are X_2 and X_P. Since the Hamiltonian is a nonlinear function of S, a control vector iteration technique can therefore be used to solve this problem. The derivative of Hamiltonian with respect to substrate concentration is as follows:

$$\frac{\partial H}{\partial S} = \frac{\partial f}{\partial S} + \alpha \frac{\partial g}{\partial S} = 0 \tag{38}$$

For $g < 0$, $\alpha = 0$ and Eq. 19 determine the optimal control profile S^*. For $g = 0$, Eqs. 14 and 19 determine the S^* and α, which are needed in Eq. 18.

Numerical Procedure and Results

1. Guess the optimal control profiles $S(t)$.

2. Impose the initial condition, $S(0) = S_0$ and substrate concentration constraints, $S^{min}(t) \leq S(t) \leq S^{max}(t)$, owing to the maximal and minimal feed rates.
3. Calculate the state variables by forward integration of Eqs. 32 and 33.
4. Calculate the adjoint variables and α by backward integration of Eq. 37.
5. Calculate the derivatives of Hamiltonian from Eq. 38.
6. Update the substrate concentration profile using the following control vector iteration:

$$S^{i+1}(t) = S^{i}(t) - \varepsilon \left[\frac{dH}{dS}\right]^{i}$$

7. Iterate until the increase in the performance index is less than a specified tolerance (steps 2–6).

A nonsingular control algorithm with control variable constraint was used to calculate the optimal control profile. The optimal profile of the transformed control variable, substrate concentration, was calculated with the proposed conjugate gradient algorithm. After calculating the optimal substrate concentration profiles, the optimal feed-rate profiles are calculated by Eq. 31. Figure 3 presents the optimization results of this system. Since the substrate concentration starts at the high substrate concentration, a minimal feed rate is applied to decrease it to a lower level and follows the singular arc to maximize the product concentration. The optimal control profiles have been calculated as minimal to singular control, and the conjunction point is automatically determined by imposing the constraint on the transformed control variable.

As shown in Fig. 3, the optimal substrate concentration is almost constant, and it is same as that of Hong *(5)*. The reactor volume reaches its maximal value at 59.5 h, and there is also a 0.5-h final batch fermentation period to consume the residual substrate. However, Hong's *(5)* singular optimal control approach cannot be used for the case of a fixed final time problem. The feed rate cannot be expressed as an explicit functional form of state and adjoint variables for this case.

Using the proposed nonsingular transformation algorithm, the optimal control profile of a fixed final-time optimization problem can be calculated. As the final time changes, the optimal control profile as well as the maximal product concentration change. The product concentration change with fermentation time was calculated and shown in Fig. 4. The final ethanol concentration increased with fermentation time until 60 h. It maintained at the maximum value after 60 h. The calculated optimal final time using nonsingular transformation is almost the same as that calculated by Hong *(5)* (59.67 h).

Since the substrate concentration directly determines the specific cell growth and product formation rates, it was more sensitive to the performance index than feed rate and produced almost an exact optimal profile of this system.

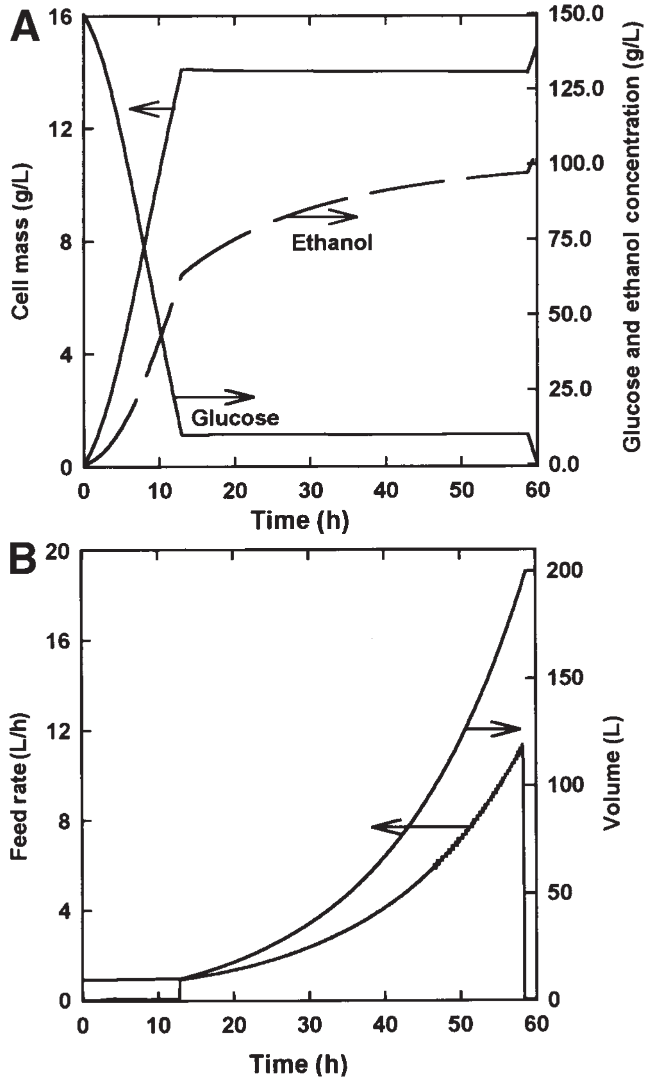

Fig. 3. The optimal control profiles calculated by nonsingular transformation using substrate concentration as a control variable. **(A)** cell mass, glucose, and ethanol profiles; **(B)** volume and feed-rate profiles.

Optimal On-Off Control

As proposed by Chen and Hwang *(13)*, the optimal on-off control for fed-batch fermentation processes is used to maximize the product formation. The dynamic state equation is solved using integration subroutines and the time is divided into 2-h intervals:

$$F(t) = F^{o} \sum_{k=0}^{N-1} [S(t - t_k) - S(t - t_k - \xi_k)] \tag{39}$$

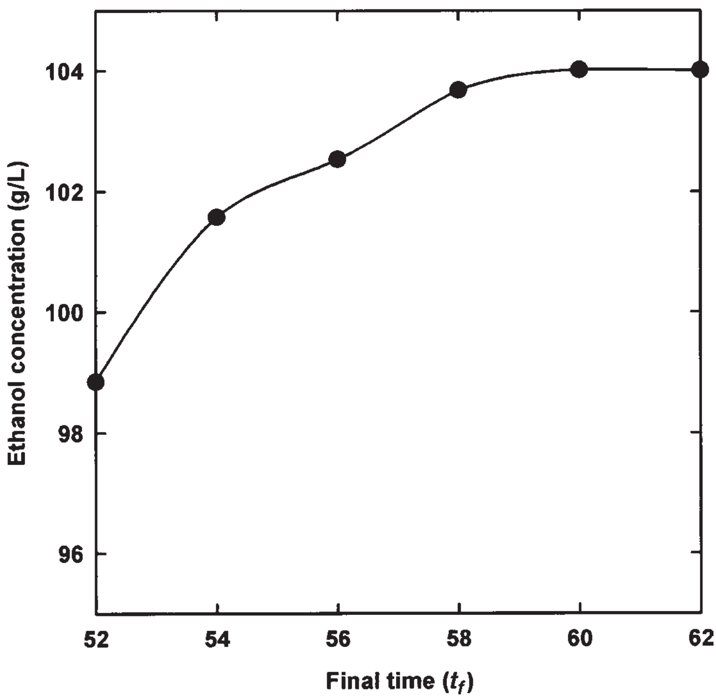

Fig. 4. The change of the performance index with the change of the fermentation time calculated with nonsingular transformation.

The objective function of this system is maximizing the product concentration by controlling F^o and $\xi_{k},\ _{k=1,N}$.

$$\min_{F^o,\ \xi_{k,\, k=1,\, N}} \quad J = [-X_2(t_f)] \tag{40}$$

The optimal search program that uses a simplex search algorithm was used to determine the optimal on-off switching times.

Chen and Hwang *(13)* proposed the on-off optimal control for the optimization of fed-batch fermentation. Since they used a different final time from that of Hong *(5)*, the performance cannot be compared exactly for both optimization approaches. The performance of on-off optimal control approaches for the different final times was calculated.

Figure 5 shows the optimal control results. The initial substrate concentration was started with 150 g/L, decreased during the batch operation, and the on-off control begun to maintain the substrate concentration at a certain level. The period (ξ_k) of maximal feed rate increased exponentially. The results show that the calculated optimal control profile simulated the singular optimal control profiles calculated by Hong *(5)*. Although Chen and Hwang *(13)* claimed that their performance was higher than that of Hong, they did not consider the final product concentration. After the reactor volume reached its maximal volume, there was a short batch period to consume the residual substrate. Figure 6 shows the product concentra-

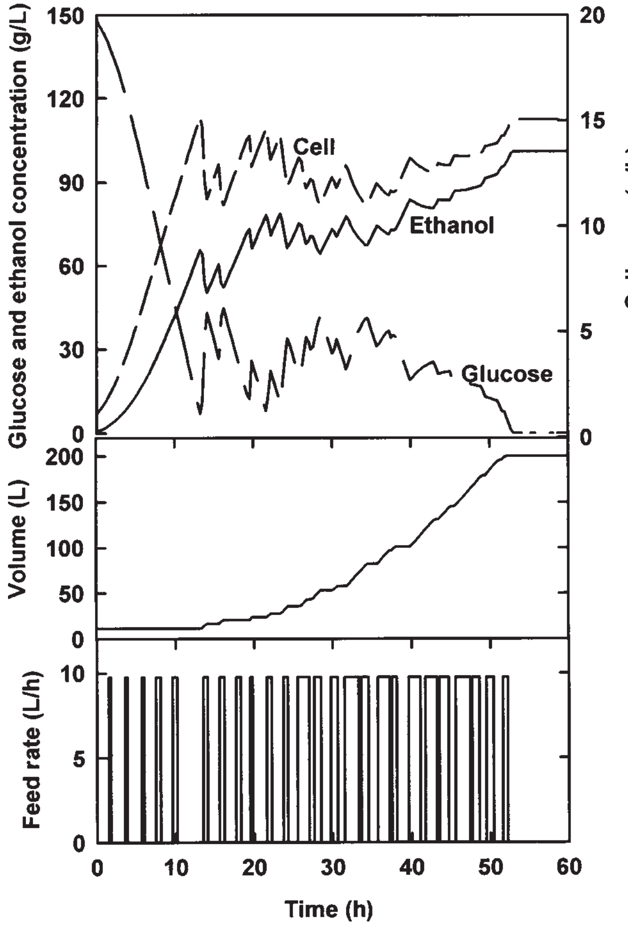

Fig. 5. The optimal control profiles calculated by an on-off optimal control algorithm.

tion changes with the fermentation time. The product concentration increased through 56 h and was maintained at almost the same level. The maximum ethanol concentration was 101.07 g/L and was lower than those of other optimal control approaches. This was owing to the variation of substrate concentration level shown in Fig. 5, which is different from the usual optimal substrate concentration profiles. Higher performance may be achieved by decreasing the step size and making infinite switching times, resulting in similar optimal control profiles. As shown in Fig. 6., the final product concentration is increased as the reaction time increases. Similar to the result of Chen and Hwang *(13)*, the product concentration after 54 h of fermentation was 98.34 g/L.

Ethanol production is not sensitive to the substrate concentration and the maximal production rate can be achieved by maintaining the substrate concentration in a certain range. As a result, not much difference in the ethanol concentration is achieved by using the on-off optimal control.

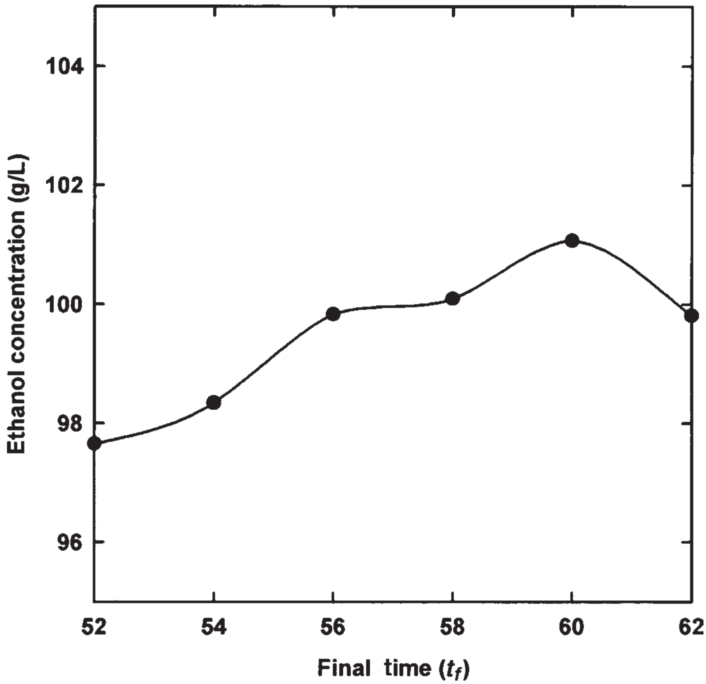

Fig. 6. The change of the performance index with the fermentation time using an on-off optimal control.

Table 1
Final Ethanol Concentrations with Various Optimization Approaches[a]

	t_f (h)					
Approach	52	54	56	58	60	62
Singular optimal control (Hong *[5]*)	—	—	—	—	104.50	—
Kelly transformation (Fu and Barford *[11]*)	96.83	97.43	99.23	101.01	102.13	101.15
Nonsingular transformation	98.85	101.57	102.53	103.68	104.02	104.01
Chen and Hwang *(13)*	97.65	98.34	99.83	100.09	101.07	99.81

[a]Concentrations are in grams/liter.

Conclusion

The final ethanol concentrations obtained by various optimal control approaches are summarized in Table 1. As calculated by Hong *(5)* the performance difference between the control algorithm is a maximum of 5% using the on-off optimal control.

Since Hong *(5)* proposed a free final-time problem, it is possible to calculate optimal control profiles. However, the analytical expression of feed rate cannot be expressed as a function of other state variables for fixed final-time problems. Therefore, other numerical approaches should be used for a fixed final-time problem.

With the Kelly transformation, the volume is used as a control variable. The performance is not as high as that of a singular control profile. This may be owing to the transformed control variable, the volume, which is not as sensitive as the original control variable, the feed rate.

The nonsingular transformation algorithm produces almost the same result as calculated by the singular control algorithm. Since the most sensitive variable, substrate concentration, is used as a control variable, the calculated optimal profile is almost the same as that of the singular control algorithm.

The optimal control profiles using the Kelly transformation and simple on-off optimal control do not maintain the substrate concentration at an optimal level. In this approach, the maximum ethanol concentration calculated was as high as 101 g/L. However, the ethanol concentrations obtained from Hong *(5)* and the nonsingular transformation were 104 and 104.5 g/L, respectively. These results showed that the proposed method by Chen and Hwang *(13)* calculated suboptimal profiles.

In this article, several different types of fed-batch optimization approaches were reviewed, and the optimal control profiles were calculated. From the theoretical evaluation of DAS, the proposed approach by Fu and Barford *(11)* is the same as the Kelly transformation. The performance obtained by Chen and Hwang *(13)* with the on-off optimal control approach is inferior to that of other optimization approaches. The feed rate of the on-off optimal control algorithm simulates the optimal feed-rate profiles by controlling the switching times. As a result, the substrate concentration oscillates around the optimal conditions and the performance cannot exceed the maximum performance. Finally, the optimal control profiles obtained by the nonsingular transformation approach are the same as those of the singular control approach.

Nomenclature

F	substrate feed rate (h^{-1})
H	Hamiltonian
K_P, K_P', K_S, K_S'	Monod constants
P	product concentration (g/L)
PI	performance index
S	substrate concentration (g/L)
S_f	substrate feed concentration (g/L)
V	reactor volume (L)
X	cell mass (g/L)
X_3	reactor volume (L)
Y_{XS}	cell yield (g cell/g substrate)

Greek

α	Lagrangian multiplier
λ	adjoint vector
μ	specific growth rate (h^{-1})
π	specific production rate (h^{-1})
σ	substrate consumption rate (h^{-1})

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