Optimal control of a batch bioreactor: a study on the use of an imperfect model

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Abstract

This paper presents a numerical study on the performance degradation of a batch bioreactor optimal control strategy when the model used to compute such strategy shows wide variations from the real process. The optimal control was computed using a model that, when exposed to large variations of the control inputs, presents large departures from real process behavior. An improved model based on published experiments was proposed. A new optimal policy was calculated and the behavior of this model when controlled with the earlier policy was studied. Although the earlier control showed a performance degradation with respect to the real optimal control, degradation was modest, and the results are superior to these obtained with other control strategies.

Keywords: Bioreactor; Optimal temperature trajectory; Optimal control

1. Introduction

Although the optimal operation of a process is always a desired feature, off-line computation of optimal control policies has obtained dissimilar acceptance in different disciplines. Optimal control has been used mostly in fields where process models are well known and are subject to negligible perturbations, but it has had little acceptance in biological processes, where model uncertainties and perturbations can be significant.

It is for these reason that few results on optimal control of batch bioreactors have been presented in the literature [1]. Most used the logistic equation and the Luedeking–Piret equation (or slight variations of them) to model cell growth and the formation rate of the desired metabolic product, respectively. For the few published results of batch bioreactor optimal control, the final fermentation time was usually fixed, the objective being to maximize the value of some component of the state vector evaluated at this final time. The control variable was either the broth temperature or the broth pH.

Constantinides et al. [2] presented numerical results obtained on applying optimal temperature control to a penicillin batch fermentation. Their objective was to achieve the maximum penicillin concentration at the final fermentation time, and for that purpose they used the logistic equation as the model for the cell growth and a model for the penicillin formation rate different from the Luedeking–Piret equation. The parameters for both equations were functions of the temperature. The simulation results were good, as they reported increments of 14.7–16.0% in the final concentration of penicillin when compared with the constant temperature operation. They did not present any evidence of the application of optimal temperature control to a real fermentation and gave no estimation of the degradation of the results due to errors in the model. Furthermore, it is evident from their results that the optimal control derived was dependent on the model used.

Lee et al. [3] presented numerical and experimental results of the optimal pH control of a curdlan production batch culture. They used a fixed operation time of

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120 h and values for the specific rates of cell growth, substrate consumption, and curdlan production that were functions of the pH and of the sucrose and ammonium concentration. These functions were developed using data from experiments conducted at different but constant pH, sucrose and ammonium concentration values. They applied the computed pH optimal profile to a batch fermentation, and obtained results in good agreement with those predicted by the model. The curdlan concentration was 78% higher than the concentration obtained when operating with a constant pH.

In a recent work Cacik et al. [4] presented optimal control results for the production of xanthan gum. The goal was to produce a desired amount of gum in minimum time, and the manipulated variable was the temperature of the culture medium. For that purpose a model proposed by Shu and Yang [5], which is dependent on the medium temperature, was used. The numerical results showed the convenience of operating the batch fermentor with a properly designed varying temperature policy instead of the usual constant temperature procedure. Cacik et al. also showed the deviations from the optimal results obtained when the model parameters exhibited small constant departures from the real parameters; such deviations were small and acceptable and the performance degradation was reasonable.

The general criticism of optimal control applications comes from the great dependance of the results on the quality of the model used. Shu and Yang presented results for two fermentations with a non-constant temperature profile, where the parameters behaved rather differently than in their originally proposed model. As a result, Cacik's assumption that the parameters exhibit small variations is not safely applicable.

A possible way to estimate the robustness of the optimal control policy when subject to small parameter variations is to compute the departure of the perturbed objective functional in terms of quantities associated with the nominal model [6] or associated with the solution of the nominal problem [7], when the optimal solution and the associated adjoint variables are differentiable function of the model parameters [8]. Another way, although rather elementary, is to simulate the behavior of a reasonable perturbed model when the nominal optimal control is applied. This course is followed in this work because it is simple and there are available data that permit the building of a reasonable perturbed model.

This work presents a numerical study on the behavior of the computed 'optimal' strategy when applied to the 'real process'. In this context the 'real process' is a new model that fits those two shifted-temperature fermentations results better than the original model of Shu and Yang. The application of different control strategies presented in Cacik et al. to this 'real process' is compared in order to assess their robustness with respect to model errors. It turns out that the original optimal operation performs positively better than other strategies and the degradation with respect to the 'true' optimal is small.

2. Optimal control of batch bioreactors

2.1. Penicillin batch fermentation

Constantinides et al. [2] obtained an optimal temperature profile that maximizes the final penicillin concentration when the model describes the variations of cell concentration X and product concentration P at the temperature T with the following equations:

$$\frac{\mathrm{d}X}{\mathrm{d}t} = b_1(T)\left(1 - \frac{X}{b_2(T)}\right)X \tag{1}$$

$$\frac{\mathrm{d}P}{\mathrm{d}t} = b_3(T)X - b_4(T)P \tag{2}$$

They computed diverse optimal temperature profiles, using different sets of parameters, obtained from various experiments. For the first set of parameters, that conforms (together with Eqs. (1) and (2)) what they call the general model 1F, they assumed, based on results obtained from one fermentation performed at a constant temperature of 25 °C and on several considerations, that b_1, b_2, and b_3 have a parabolic dependance on the temperature, with vertical symmetry axes and maximums at 30 °C for b_1 and b_2, and at 20 °C for b_3. For b_4 they adopted an Arrhenius type relationship.

For the second and third set of parameters, which together with Eqs. (1) and (2) conform to what they call the particular models C2 and S2, they interpolated the parameter values obtained from fermentation runs performed at four and three different constant temperatures, respectively, assuming that, in the intervals defined by the temperatures of those experiments, the logarithm of the parameter values are linear function of the reciprocal of the absolute temperature. It can be seen that simple linear functions of the temperature give similar results than the interpolations used by Constantinides when computed in the temperature ranges defined by their fermentation experiments.

Fig. 1 show the values of the parameters for models 1F, C2 and S2 plotted against the temperature. Different scales were used for the models because their original experimental data were expressed in different units. It is evident from Fig. 1 that the behavior of most of the parameter b_i for model 1F is different from the behavior for models C2 and S2. As a consequence, when computing the optimal control, a different temperature profile is obtained with each model, as can be

seen in Eqs. (3), (5) and (8) of the original paper [2]. Unfortunately, in this case there are no applications of the optimal temperature profiles to the real plant, nor any quantification of the optimal results degradation due to model mismatch. As a result, it is not possible to conclude in this case that the optimal temperature profile computed under such model uncertainty will be an improvement over the traditional constant temperature operation.

2.2. Curdlan batch fermentation

Lee et al. [3] developed a model for the batch production of curdlan, where the cell growth rate and the curdlan production rate were functions of the values of the pH, the sucrose concentration and the ammonium concentration. They computed the pH profile that maximizes the curdlan concentration at the final time (120 h) using the minimum principle of Pontriagyn. This optimizing profile shows two distinct zones, a cell growth phase, where the pH is maintained at a value of 7, and a curdlan production phase, where the pH is maintained at a value of 5.5. As the cell growth phase extends until the available nitrogen is depleted, the pH switching time is the time at which the ammonium concentration approaches zero. This feature gives a robust form to decide the switching time if the ammonium concentration values are readily available.

The reported experimental implementation of the optimal profile shows results in good agreement with these predicted by the model, and improving the final concentration of curdlan by 78% with respect to a fermentation operated at a pH constant value.

2.3. Xanthan gum batch fermentation

Several models have been proposed by different authors to describe the dynamics of the xanthan gum fermentation. The usual state variables are the cell, gum, and main substrate concentrations. The most

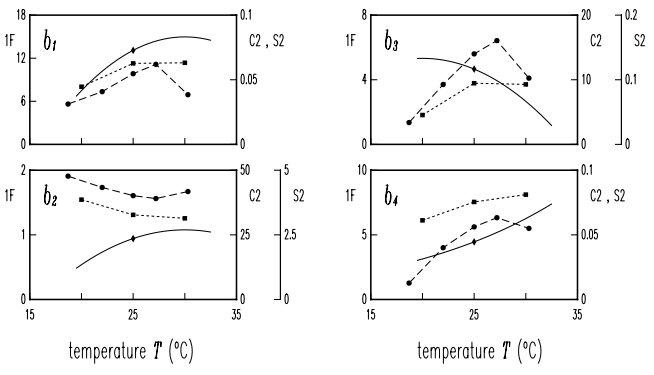

Fig. 1. Parameter functions proposed by Constantinides et al. Models 1F (—), C2 (– – –), and S2 (- - - -); experimental data 1F (◆), C2 (●), and S2 (■).

common approach to describe the dynamics of the biomass in a batch culture is to use a Monod-type specific growth rate coefficient or to use the logistic growth equation. The dynamics of the gum production and the carbon substrate consumption are usually described by relations of the Luedeking–Piret type. Weiss and Ollis [9] presented a thorough analysis proposing the logistic equation, the Luedeking–Piret equation, and a modified Luedeking–Piret equation to describe the biomass, product, and substrate behaviors, respectively. Pons et al. [10] proposed the use of a less empirical model for the product and substrate dynamics than the Luedeking–Piret equation to take into account some of the earlier results and limitations in the oxygen transfer rate. This model includes the principal metabolic pathways and needs a more detailed knowledge of the system, which is not always available, particularly for on-line control purposes. Georgieva and Patarinska [11] presented a model that takes into account the dissolved oxygen concentration. Peters et al. [12] proposed a more elaborated equation for the biomass dynamics, using a Monod-type factor that relates to the ammonium as a growth-limiting substrate, and considering the normal death rate and the death rate induced by oxygen deficiency. For substrate consumption they proposed a different equation, discriminating the usage of the carbon substrate for growth, maintenance and gum production.

Most of the published reports on xanthan gum production suggest the operation of batch reactors at constant temperature, and the effects of temperature levels on the gum production have received little attention. The influence of the temperature on the main processes of the xanthan gum production has been studied by Shu and Yang [5,13]. They experimentally found the production rates of biomass and gum at different temperatures. As a result, they proposed equations of the same type as those used by Weiss and Ollis [9] but with their parameters being functions of the temperature T,

$$\frac{dX}{dt} = k(T)\left(1 - \frac{X}{X_s(T)}\right)X \tag{3}$$

$$\frac{dP}{dt} = a(T)\frac{dX}{dt} + b(T)X \tag{4}$$

$$\frac{dS_c}{dt} = -\left(\alpha(T)\frac{dX}{dt} + \beta(T)X\right) \tag{5}$$

where the state variables are the cell concentration X, the product concentration P, and the carbon substrate concentration S_c. The functional forms of the parameters k, X_s, a, b, α, and β are shown in Shu and Yang [5]. As a result of their experiments, they suggested the convenience of using one temperature level (27 °C) for the trophophase and another level (32 °C) for the idiophase in order to increase the gum production.

Using the model proposed by Shu and Yang, the application of a procedure to compute the temperature operating policy that produces a given amount of xanthan gum in minimum time was presented [4]. The computational experiments showed that the fermentation time required to produce 15 g of gum per litre of medium is, as a result of the application of the mentioned procedure, 16.3% shorter than the fermentation time necessary when the usual constant temperature is used and 12% shorter than the fermentation time necessary when the two-temperatures strategy of Shu and Yang is used.

In order to assess the sensibility of the optimization method to small errors in the parameters, several computations of the optimal temperature profile were performed, where the parameters of Eqs. (3) and (4) had a constant offset (one parameter at a time) from the values of the original model. These runs were called the perturbed model parameter runs. Table 3 of Cacik et al. shows the degradation of the operation obtained when these resulting temperature profiles were applied to the original model. The observed degradation in the fermentation time was negligible, which suggests near optima behavior when confronted with moderate errors in the parameters.

As Shu and Yang [5] performed further experimental fermentations with a temperature step change and reported that their model did not predict correctly the cell concentration dynamics in this case, they re-evaluated the parameters for each of the constant temperature time periods (27 and 32 °C) and found new sets of parameter values. Some of the parameters (mainly X_s, but also b) of Eqs. (3) and (4) show strong departures at 32 °C from their originally proposed values. As a result, the results on sensibility of the optimal control to small errors presented by Cacik et al. do not indicate that a near optimum will be achieved with the obtained trajectory, where a steep increase in the temperature is employed. A simple variation of the Shu and Yang model that fits better the last experimental runs is proposed here. The optimal control operation for this modified model is computed and the outcome obtained when the controls obtained for the original problem are applied to this modified model is studied.

3. A modified model

Equations for X_s and b proposed by Shu and Yang are,

$$X_s = \frac{1.58 + 2.02e^{(29-T)}}{1 + e^{(29-T)}} \tag{6}$$

$$b = 1.61 \times 10^{13} e^{9.58 \times 10^3 T^a} \tag{7}$$

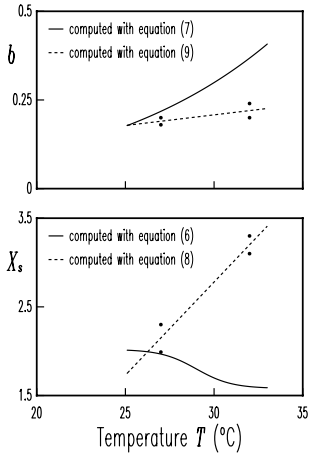

Fig. 2. X_s and b values as functions of the temperature T. (●), values from experiments with temperature shift.

where T is the medium temperature expressed in °C and T^a is the medium absolute temperature expressed in °K. For two fermentations with temperature shifts from 27 to 32 °C results were obtained for values of the parameters X_s and b at the higher temperature level that differ markedly from the values predicted by their proposed Eqs. (6) and (7).

With the main intention of building a different model useful to measure the sensibility of the obtained control to model errors, the equations proposed by Shu and Yang are replaced by simple equations for X_s and b that fit better the experimental data for runs with temperature shift. For that purpose, as there are available values of the parameters at those two temperatures, the following linear function of the temperature is suggested,

$$X_s = -3.52 + 0.21T \tag{8}$$

$$b = 0.028 + 0.006T \tag{9}$$

Fig. 2 shows the values of the parameters X_s and b obtained by Shu and Yang from their experimental fermentations with temperature shifts and listed in their Table 4 [5], the values computed using the model expressed by Eqs. (6) and (7), and the values computed using the linear Eqs. (8) and (9) that are proposed in this work. It is evident from the figure that the equations proposed by Shu and Yang to model the parameters as a function of the temperature represents poorly the behavior of the parameters for runs with temperature shifts.

4. Numerical results with the modified model

4.1. Numerical comparison of model behavior

To validate the proposed models for the temperature dependence of X_s and b, numerical results obtained

with the original model of Shu and Yang and with the modified model were compared with their corresponding experimental data, all for the case when the temperature shift from 27 to 32 °C is performed at 25 h.

Fig. 3 shows Shu and Yang's experimental results for the fermentation with the temperature shift at 25 h and the results of two computer simulations with similar temperature changes, the first simulation uses the original Eqs. (6) and (7) for the parameters X_s and b, and the second simulation uses the linear Eqs. (8) and (9) to compute the values of those parameters. These results manifest, for runs with temperature rises, a better model behavior when using the linear equations than when using the original equations.

Eqs. (8) and (9), together with Eqs. (3) and (4) and the original equations of Shu and Yang for parameters k and a, will be used in the following sections as the 'real process', both to compute the 'real' optimal control, and to compute the performance of the control trajectories presented in the earlier work [4] when they are applied to the 'real process'.

4.2. Optimal temperature trajectory

The optimal temperature control T^* was computed using the model expressed by Eqs. (3) and (4) with the parameters X_s and b given by Eqs. (8) and (9). An iterative procedure to solve the variational problem was applied, as it was done in Cacik et al [4] and outlined in the Appendix, to obtain the temperature trajectory that minimizes the final fermentation time. Such an optimal temperature trajectory is shown in Fig. 4 together with the resulting cell and gum concentration histories. The optimal temperature profile obtained shows a different shape to the optimal temperature profile T^{**} computed earlier using the original Shu and Yang model, which is also shown in Fig. 4. It can be seen that T^* is an increasing temperature profile (as T^{**} is most of the time), favoring cell growth during the initial part of the fermentation with relative medium temperatures, and favoring gum production during the final part with higher temperatures. This optimal control T^* enables a

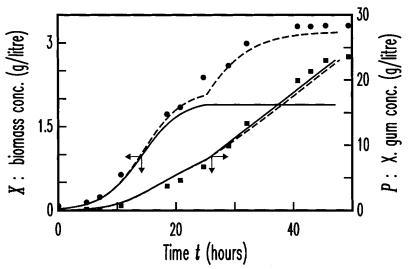

Fig. 3. Fermentation results with temperature shift at 25 h. Experimental data, biomass (●) and gum (■) concentrations. Simulation results: X_s and b computed with Eqs. (6) and (7) (—), X_s and b computed with Eqs. (8) and (9) (- - -).

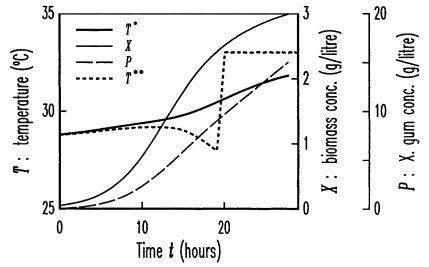

Fig. 4. Optimal operation of the 'real process'.

final gum concentration of 15 g/l to be produced in 27.8 h when the initial cell concentration is 0.05 g/l. This time is 20% shorter than that required when operating at the usual constant temperature of 28 °C.

4.3. Performance of the different control strategies

The temperature trajectories computed and used in Cacik et al., where the models for the parameters X_s and b were not appropriate for fermentations with wide temperature variations, were applied to this new model in order to assess the robustness of such optimal control and compare with the outcomes for other control strategies. The times required to reach the desired gum concentration obtained from these simulations are shown in Table 1. The time necessary to reach the final gum concentration with the earlier optimal temperature profile is only 6.5% longer than the time necessary with the optimal control computed with the improved model. It can also be seen that the earlier optimal temperature profile, when applied to the 'real process', reaches the final gum concentration in a time period 14.7% shorter than the constant temperature strategy and 15.9% shorter than the two temperatures strategy of Shu and Yang.

5. Conclusions

The purpose of this work was to study the robustness of the optimal control of a batch bioreactor with respect to model errors. The optimal control under study was the temperature trajectory obtained using the original model, where this model deviates considerably

Table 1
Different control strategies applied to the 'real' model

Temperature strategy	Final time (h)
Constant temperature (28 °C)	34.7
Two temperatures (27 °C → 32 °C)	35.2
Optimal strategy for original model (T^{**})	29.6
Near-optimum	29.2
Optimal strategy for improved model (T^*)	27.8

from the experimental results when a temperature trajectory with sharp increases, as the optimal one, is applied.

To assess the robustness of that control, an improved model was obtained approximating the behavior of some parameters of the model with simple equations obtained using experimental data presented by other authors.

Numerical simulations were performed applying to the improved model both, the optimal control and other control strategies used or proposed by different authors. The results were compared between them, and against the 'real optimal control' computed with the modified model. It can be concluded that in this case the optimal operation strategy proposed by Cacik et al [4] provides a robust control, showing a modest degradation of the sought objective, and superior results when compared with other operation modes.

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Appendix A. Optimal control formulation

The optimal temperature trajectory for the system is obtained as the solution of the following minimum time problem,

$$\min_{T(t)} t_f$$

subject to, the system equations

$$\frac{dX}{dt} = k(T)\left(1-\frac{X}{X_S(T)}\right)X$$

$$\frac{dP}{dt} = a(T)\frac{dX}{dt} + b(T)X$$

the initial conditions

$$X(t_0) = X_0$$

$$P(t_0) = P_0 = 0$$

the desired final condition

$$P(t_f) = P_f$$

and constraints in the inputs

$$T_l \le T(t) \le T_u$$

The Hamiltonian for this problem is defined as,

$$H = -1 + \lambda' f = -1 + \lambda_1 k(T)\left[1-\frac{X}{X_S(T)}\right]X + \lambda_2\left[a(T)k(T)\left(1-\frac{X}{X_S(T)}\right)X + b(T)X\right]$$

where the vector f is the right hand side of the system equations and λ is the vector of co-states. Consequently, the adjoint equations, defined as $d\lambda/dt = -(\partial H/\partial x)'$ (where x is the state vector, whose components are the state variables X and P), are,

$$\frac{d\lambda_1}{dt} = -\left[\lambda_1 k(T)\left(1-\frac{2X}{X_S(T)}\right) + \lambda_2\left(a(T)k(T)\left(1-\frac{2X}{X_S(T)}\right)+b(T)\right)\right]$$

$$\frac{d\lambda_2}{dt} = 0$$

with the following boundary conditions,

$$\lambda_1(t_f) = 0$$

$$\lambda_2(t_f) = \lambda_{2f} = \left[a(T)k(T)\left(1-\frac{X(t_f)}{X_S(T)}\right)X(t_f) + b(T)X(t_f)\right]^{-1}$$

The temperature $T^*(t)$ that satisfies the problem is a trajectory such that the state and adjoint equations are satisfied and the Hamiltonian can not be improved,

$$\frac{\partial H}{\partial T} = 0 \text{ if } T_l < T^*(t) < T_u$$

$$\frac{\partial H}{\partial T} \ge 0 \text{ if } T^*(t) = T_l$$

$$\frac{\partial H}{\partial T} \le 0 \text{ if } T^*(t) = T_u$$

Such trajectory was obtained using the following iteration scheme:

1. Adopt a temperature profile $T(t)$ that satisfies the temperature constraints.
2. Solve the system equations from $t = t_0$ up to the time t_f such that $P(t_f) = P_f$.
3. Solve the adjoint equations from $t = t_f$ to $t = t_0$.
4. Verify the convergency criteria, if it is not met, $T(t)$ is updated using the gradient of the Hamiltonian $(\partial H/\partial T)$ in such a way that the updated temperature profile satisfies the constraints and the functional value is improved, and steps 2–4 are repeated.

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