SIMPLE DIGITAL CONTROL OF CELL MASS IN TURBIDOSTAT

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SUMMARY: The application of simple digital control method to the control of cell mass in a continuous stirred tank bioreactor (CSTBR) was experimentally examined. This algorithm based on the time-varying bilinear predictor model was as simple as proportional-integral-derivative (PID) control algorithm and showed better performance.

INTRODUCTION

Because of the self-adaptation and feedback regulations of cell's metabolism to environmental changes the bioreactor system has multiple steady state and complex natures such as unpredictable time-varying characteristics (DiBiasio et al., 1984). These characteristics of biological system dynamics pose many difficult problems to control the CSTBR (Agrawal and Lim, 1984). Especially, significant disturbances are involved in on-line measurement of cell density. Therefore, the controllers with fixed gains such as PID controller are considered not to be sufficient to control the CSTBR at a desired steady state. Hence, for better regulation and more stable operation of CSTBR, it is very important to develop a control algorithm which is robust enough to handle uncertainties in CSTBR dynamic model and measurement errors.

In this work, we propose a new simple digital control algorithm using the concepts of self-tuning adaptation and the bilinearity of predictor model, and also further update this algorithm by introducing the tuning parameter.

DESIGN OF SIMPLE DIGITAL CONTROL ALGORITHM

The material balance on the cell-mass concentration of a constant-volume continuous flow reactor is

\[
dX(t)/dt = \mu(t) X(t) - D(t) X(t) \tag{1}
\]

where \( X \), \( D \), and \( \mu \) represent the cell-mass concentration, the dilution rate, and the specific growth rate, respectively. Using rectangular integration rule with a sampling period \( T \), equation (1) can be discretized as follows:

\[
X(k+1) = (1 + T \mu(k)) X(k) - T D(k) X(k) = a(k) X(k) - T D(k) X(k) \tag{2}
\]

where \( a(k) = 1 + T \mu(k) \). Equation (2) constitutes the basic predictor model for the derivation of the simple digital control algorithm.

Because it is far from easy to measure the value of specific growth rate in real time, we regard \( a(k) \) as the slowly time-varying constant and trace it with projective estimation method (Goodwin and Sin, 1984).

\[
\hat{a}(k) = X(k)/X(k-1) + T D(k-1) \tag{3}
\]

A deadbeat control law (Åström and Wittenmark, 1984) is adopted. At each sampling time the control input \( D(k) \) is computed by setting a one step ahead prediction of cell-mass concentration equal to the prescribed level.
Replacing \( a(k) \) with \( \hat{a}(k) \) in equation (2) and using equation (4), the dilution rate profile is determined as follows:

\[
D(k) = D(k-1) + \frac{X(k)/X(k-1) - X_S/X(k)}{T} \tag{5}
\]

This control law may be sensitive to measurement noises and variations of model parameter. Therefore we introduce a tuning parameter \( \lambda \) to retard the drastic change of the control action. In practice, the control action \( D \) is obviously constrained by the operating condition. Thus the final form of simple adaptive control algorithm is as follows:

\[
D(k) = D(k-1) + \lambda \left( \frac{X(k)/X(k-1) - X_S/X(k)}{T} \right), \quad 0 < \lambda \leq 1.
\]

\[
D(k) = 0 \quad \text{if } D(k) < 0
\]

\[
D(k) = D_{\text{max}} \quad \text{if } D(k) > D_{\text{max}}
\]

\[
D(k) = D(k) \quad \text{otherwise}.
\]

We intend to test the control law of equation (6) and investigate the effects of \( \lambda \) by controlling a laboratory scale CSTBR. If we replace \( X_S \) with \( X_S(k) \), the control law of equation (6) can be used in on-line optimization of cell-mass production in a CSTBR. This algorithm is directly applicable to the control of product or substrate in a CSTBR, if a proper sensor is developed.

**MATERIALS AND METHODS**

A strain of yeast (Saccharomyces cerevisiae, ATCC 24858) was used in this study. The nutrient medium consisted of glucose (20 g/L), yeast extract (5 g/L), malt extract (3 g/L), and Bacto peptone (5 g/L) dissolved in distilled water. The filter-sterilized air was supplied at the rate of 2 vvm. A set-point controlled 2 L fermenter connected with a APPLE II microcomputer was used. The temperature and pH were controlled at 30°C and 5.0, respectively.

The nutrient medium was added to the fermenter using computer-modulated peristaltic pumps. Cell-mass concentrations were determined by measuring optical density with a Spectronic 100 as described by Lee and Lim (1980).

In order to prevent optical density from being noisy, a bubble trap was installed and signals were gathered every 3 min by analog means and averaged digitally. The BASIC language was used in programming the algorithm.

**RESULTS AND DISCUSSION**

As the first experiment, we tried PID control. Since there was no rigorous way to determine the gains of PID controller for highly nonlinear CSTBR, several experiments were repeated by retuning its gains. However, any setting of its gains failed to give stable response. The output response showed nearly sustained oscillation with very long period. Thus experiment with only P-mode was carried out.

Figure 1 shows the performance of P control with high gain and that of control action. The set value was 3.5 g/L. Some output oscillations were observed at initial transient state and the response time was more than 9 hr. For all that, this output response of P control was better than that of PID. DiBiasio et al. (1981) also showed through elaborate simulation and experimental study that the P controller with sufficiently high gain could