

## CONTROL OF FERMENTATION PROCESS IN STIRRED TANK BIOREACTOR

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**ABSTRACT:** This paper proposes a nonlinear adaptive controller based on back-stepping method for tracking reference substrate concentration by manipulating dilution rate in a continuous baker's yeast cultivating process in stirred tank bioreactor. Control law is obtained from Lyapunov control function to ensure asymptotical stability of the system. The Haldane model for the specific growth rate depending on only substrate concentration is used in this paper. Due to the uncertainty of specific growth rate, the specific growth rate has been modified as a function including the unknown parameter with known bounded values. The substrate concentration in the bioreactor and feed line are measured. The deviation from the reference is observed when the external disturbance such as the change of the feed is introduced to the system. The effectiveness of the proposed controller is shown through simulation results in continuous system.

### 1. INTRODUCTION

Fermentation is an important process for cultivating microorganisms. Fermentation can be run as a batch, fed-batch and continuous process. In a continuous system, the substrate is supplied to the bioreactor and extracted from the bioreactor. Fermentation process is so complex, time varying, highly nonlinear. Due to pH, dissolved oxygen, temperature, antifoam addition, biomass accumulation, production formation and nutrient depletion during fermentation process, the dynamic behavior is significantly changed. So it is difficult to make a model and control for fermentation process exactly. Specially, the exact estimate of the specific growth rate is so uncertain because it depends on parameters such as biomass concentration, substrate concentration, production formulation, temperature, etc. This uncertainty makes adaptive control theory enable to be applied to fermentation process.

L. Chen, et al., 1991, proposed general adaptive nonlinear method for the ethanol regulation in yeast production process by manipulating dilution rate in fed-batch biological bioreactors when ethanol concentration, dissolve oxygen concentration, CO<sub>2</sub> concentration and gas outflow rate are measured online with fixed known influent substrate concentration, and unknown specific growth rate. M. Maher, et al., 1993 developed adaptive filtering and estimation algorithms using extended Kalman filter, the Dochain-Bastin method and Zeng-Dahou method in a nonlinear fermentation process. G. Roux, et al., 1994, proposed adaptive nonlinear method by using an operation of projection for controlling alcoholic fermentation process in continuous stirred tank bioreactor. The good regulation profiles and tracking the temporal evaluation of certain biological parameters were presented by their proposed method. R. Schneider, et al, 1994, proposed adaptive model-based prediction control to control the state variables of the process around a defined trajectory for the fed-batch

fermentation process. Sliding-mode method for controlling fermentation process has been applied for tracking reference substrate concentration by using dilution rate as control variable<sup>[2-4]</sup>. Miroslav Krstic, 1995, applied adaptive back-stepping method for control of biochemical process with assuming of constant dilution rate and defined specific growth rate function. This function includes two unknown parameters. Yet there is no way of deriving such function from the known models of specific growth rate.

It is important that the concentration of substrate in bioreactor keep constant in continuous fermentation process. Therefore, in this paper, we proposed a nonlinear adaptive controller for tracking substrate concentration by manipulating dilution rate in a continuous baker's yeast cultivating process in stirred tank bioreactor. Control law is obtained from Lyapunov control function to ensure global asymptotical stability of the system by using adaptive nonlinear back-stepping method<sup>[5,6]</sup>. Haldane model as the specific growth rate is used in this paper. It is assumed that the specific growth rate depends only on substrate concentration and the substrate concentration in the bioreactor and feed line are measured. Because of the uncertainty of specific growth rate, the specific growth rate can be modified as a function including the unknown parameter with known bounded values. The deviation from the reference is observed when the external disturbance such as the change of the feed is introduced to the system. The effectiveness of the proposed controller is shown through simulation results in continuous system.

## 2. PROCESS MODEL

Stirred tank bioreactor studied in this paper is shown in Fig. 1. The process considered is a continuous stirred tank in which the growth of microorganism is controlled. The bioreactor is continuously fed with the substrate influent. It is assumed that the rate of outflow is equal to the rate of inflow. The volume of culture remains culture without washout. It is considered that the feeding substrate is diluted in the water stream and the dilution rate is used as the process input. The substrate concentration is regarded as output.

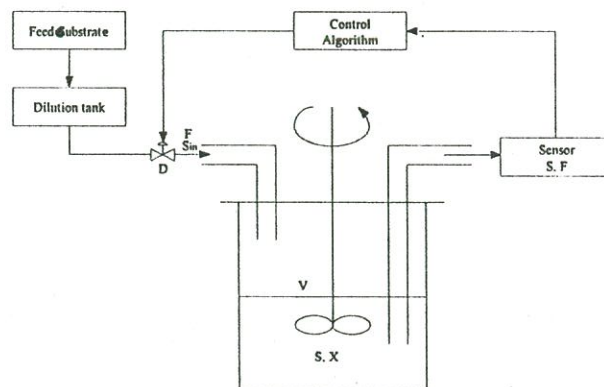


Fig.1 Stirred tank bioreactor system



The system dynamic equations on the substrate and the biomass gives the following nonlinear is given as follows<sup>[3]</sup>

$$\dot{S} = -k\mu(S)X + D(S_m - S) \quad (1)$$

$$\dot{X} = \mu(S)X - DX \quad (2)$$

$$y = S \quad (3)$$

where

- $X$  : biomass concentration in the reactor
- $S$  : substrate concentration in the reactor
- $D$  : dilution rate
- $\mu$  : the specific growth rate
- $k$  : the known yield coefficient
- $S_m$  : external inlet substrate concentration
- $y$  : system output

The specific growth rate is known to be a complex function of plant states and several biological parameters. More than 60 expressions have been suggested such as Monod', Contois', Haldane's law, etc. The choice of an approximate model for  $\mu$  is far from being an easy task. In our case, it is modeled by the Haldane model as the following

$$\mu(S) = \frac{k_i \mu_m S}{k_s k_i + k_i S + S^2} \quad (4)$$

where

- $\mu_m$  : the maximum specific growth rate
- $k_s$  : a saturation constant
- $k_i$  : an inhibition constant

**Control objective and constraints:** *The control objective is to regulate substrate concentration  $S$  in bioreactor as level of reference substrate concentration  $S_{ref}$  by manipulating dilution rate  $D$  based on measurement data of  $S$  and  $X$ . Control constraints are  $0 < D < \mu_m$ ,  $D < \mu$ ,  $X > 0$ ,  $S > 0$  and  $0 < S \leq S_m$  for any  $t \geq 0$ .*

### 3. CONTROLLER DESIGN

Define  $x_1 \equiv S - S_{ref}$  and  $x_2 \equiv X$ . Because of the uncertainty of specific growth rate, the specific growth rate can be modified as a function including the unknown parameter with known bounded values.

$$\mu x_2 \equiv k_u x_2 + \theta \varphi(x_1, x_2) \quad (5)$$

$$\varphi = \frac{k_i \mu_m (x_1 + S_{ref}) x_2}{k_s k_i + k_i (x_1 + S_{ref}) + (x_1 + S_{ref})^2} - k_u x_2 \quad (6)$$

where

$k_u$  : unit conversion parameter

$\theta \in [\theta_{min}, \theta_{max}]$  : adaptation parameter

With Eq. (5) and Eq. (6), the system dynamic equation can be written as:

$$\dot{x}_1 = -k k_u x_2 C - k \theta \varphi + (S_{in} - x_1 - S_{ref}) D - \dot{S}_{ref} \quad (7)$$

$$\dot{x}_2 = k_u x_2 + \theta \varphi - D x_2 \quad (8)$$

Now, we design controller using adaptive back-stepping method as the following.

**Step 1.** Define the first tracking error

$$z_1 = x_1 \quad (9)$$

whose derivative can be expressed as

$$\begin{aligned} \dot{z}_1 &= \dot{x}_1 \\ &= -k k_u x_2 - k \theta \varphi + (S_{in} - x_1 - S_{ref}) D - \dot{S}_{ref} \end{aligned} \quad (10)$$

Choose  $x_2$  as virtual input. By putting Eq. (10) to be  $-c_1 z_1$ ,  $c_1 > 0$  and  $x_2$  can be expressed as

$$x_2 = \frac{c_1 z_1 - k \theta \varphi + (S_{in} - x_1 - x_{1r}) D - \dot{S}_{ref}}{k k_u} \quad (11)$$

If Eq. (11) is replaced by parameter estimate  $\hat{\theta}$  of unknown parameter  $\theta$ , the estimate  $\alpha_1$  of  $x_2$  can be written as

$$\begin{aligned} \alpha_1 &= \alpha_1(x_1, \varphi, \hat{\theta}, D) \\ &= \frac{c_1 z_1 - k \hat{\theta} \varphi + (S_{in} - x_1 - x_{1r}) D - \dot{S}_{ref}}{k k_u} \end{aligned} \quad (12)$$

Introduce the second error variable as

$$z_2 = x_2 - \alpha_1 \quad (13)$$

where  $\alpha_1$  is the stabilizing function for  $x_2$ .

$$\begin{aligned} \dot{z}_1 &= -kk_u x_2 - k\theta \varphi + (S_{in} - x_1 - S_{ref})D - \dot{S}_{ref} \\ &= -c_1 z_1 - kk_u z_2 - k\tilde{\theta} \varphi \end{aligned} \quad (14)$$

Choosing Lyapunov function as the following

$$V_1 = \frac{1}{2} z_1^2 + \frac{1}{2\gamma} \tilde{\theta}^2 \quad (15)$$

where  $\tilde{\theta} = \theta - \hat{\theta}$  is the error of parameter estimation and  $\gamma > 0$  is adaptation gain.

With Eqs. (12) and (13), the first derivative of  $V_1$  along the solution of Eq. (14) is as follows.

$$\begin{aligned} \dot{V}_1 &= z_1 \dot{z}_1 - \frac{1}{\gamma} \tilde{\theta} \dot{\hat{\theta}} \\ &= -c_1 z_1^2 - kk_u z_1 z_2 + \tilde{\theta} \left( -k\varphi z_1 - \frac{1}{\gamma} \dot{\hat{\theta}} \right) \end{aligned} \quad (16)$$

**Step 2.** According to the computation in Step 1, in case that  $\dot{\hat{\theta}} = \gamma \varphi z_1$ ,  $\dot{V}_1$  is non-positive in  $z_1$  when  $z_2 = 0$ . Therefore, we need modify the Lyapunov function to include the error variable  $z_2$ . Therefore, the modified Lyapunov function is chosen as

$$V_2 = \frac{1}{2} z_2^2 + V_1 \quad (17)$$

The derivative of  $z_2 = x_2 - \alpha_1$  is

$$\begin{aligned} \dot{z}_2 &= \dot{x}_2 - \dot{\alpha}_1 \\ &= \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) (k_u x_2 + \theta \varphi - D x_2) \\ &\quad - \left( \frac{c_1 - D}{kk_u} - \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_1} \right) (-c_1 z_1 - kk_u z_2 - k\tilde{\theta} \varphi) + \frac{\varphi}{k_u} \dot{\hat{\theta}} - \frac{\partial \alpha_1}{\partial D} \dot{D} + \frac{1}{kk_u} \ddot{S}_{ref} \end{aligned} \quad (18)$$

where

$$\frac{\partial \alpha_1}{\partial D} = \frac{S_{in} - x_1 - S_{ref}}{kk_u} \quad (19)$$

$$\frac{\partial \varphi}{\partial x_1} = \frac{k_i \mu_m [k_i k_s - (x_1 + S_{ref})^2] x_2}{[k_s k_i + k_i (x_1 + S_{ref}) + (x_1 + S_{ref})^2]^2} \quad (20)$$

$$\frac{\partial \varphi}{\partial x_2} = \frac{k_i \varphi_m (x_1 + S_{ref})}{k_s k_i + k_i (x_1 + S_{ref}) + (x_1 + S_{ref})^2} - k_u \quad (21)$$

The derivative of  $V_2$  is

$$\begin{aligned} \dot{V}_2 = & -c_1 z_1^2 + \tilde{\theta} \left\{ -k \varphi z_1 - \frac{1}{\gamma} \dot{\hat{\theta}} + \left[ \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) \varphi + \left( \frac{c_1 - D}{k k_u} - \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_1} \right) k \varphi \right] z_2 \right\} \\ & + z_2 \left[ -k k_u z_1 + \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) (k_u x_2 + \hat{\theta} \varphi - D x_2) - \left( \frac{c_1 - D}{k k_u} - \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_1} \right) (-c_1 z_1 - k k_u z_2) \right. \\ & \left. + \frac{\varphi}{k_u} \dot{\hat{\theta}} - \frac{\partial \alpha_1}{\partial D} \dot{D} + \frac{1}{k k_u} \ddot{S}_{ref} \right] \quad (22) \end{aligned}$$

where the following update law for parameter estimate eliminates  $\tilde{\theta}$ -term in Eq. (22).

$$\dot{\hat{\theta}} = \gamma \left[ -k \varphi z_1 + \left\{ \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) \varphi + \left( \frac{c_1 - D}{k k_u} - \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_1} \right) k \varphi \right\} z_2 \right] \quad (23)$$

The dynamic feedback controller for system stabilisation is obtained by letting the last bracket in Eq. (22) equal to  $-c_2 z_2$ ,  $c_1 > 0$ . After some rearrangement, we have the control dynamics as

$$\begin{aligned} \dot{D} = & \frac{1}{\frac{\partial \alpha_1}{\partial D}} \left[ - \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) x_2 - \frac{1}{k k_u} (k k_u z_2 + c_1 z_1) \right] D \\ & + \frac{1}{\frac{\partial \alpha_1}{\partial D}} \left[ c_2 z_2 - k k_u z_1 + \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) (k_u x_2 + \hat{\theta} \varphi) + \left( \frac{c_1}{k k_u} - \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_1} \right) (c_1 z_1 + k k_u z_2) + \frac{\varphi}{k_u} \dot{\hat{\theta}} + \frac{1}{k k_u} \ddot{S}_{ref} \right] \quad (24) \end{aligned}$$

With Eqs. (23) and (24),  $\dot{V}_2$  is non-positive as follows

$$\dot{V}_2 = -c_1 z_1^2 - c_2 z_2^2 \leq 0 \quad (25)$$

By Lasalle-Yoshizawa theorem, the global asymptotic stability is guaranteed at  $z_1 = 0$  and  $z_2 = 0$ . So all of trajectories of the closed loop adaptive system are converged to zero.  $\dot{V}_2 = -c_1 z_1^2 - c_2 z_2^2 = 0$  implies that  $\lim z_1(t) = 0$  and  $\lim z_2(t) = 0$  when  $t \rightarrow \infty$ . Because  $z_1 = x_1 - S_{ref}$  and  $z_2 = x_2 - \alpha_1$ , they imply that  $x_1 \rightarrow x_{1r}$  and  $x_2 \rightarrow \alpha_1$ .

The closed loop system equations of the process become the following.



$$\dot{z}_1 = -c_1 z_1 - k k_u z_2 - k \tilde{\theta} \varphi \tag{26}$$

$$\dot{z}_2 = -c_2 z_2 + k k_u z_1 + \tilde{\theta} \left[ \left( 1 + \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_2} \right) \varphi + \left( \left( \frac{c_1 - D}{k k_u} \right) - \frac{\hat{\theta}}{k_u} \frac{\partial \varphi}{\partial x_1} \right) k \varphi \right] \tag{27}$$

This block diagram of the proposed method is shown in Fig. 2.

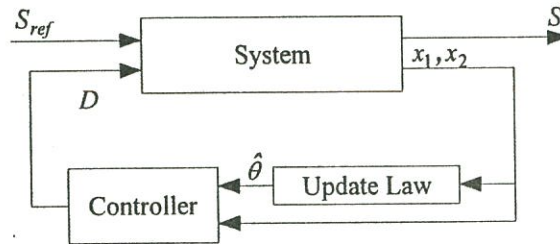


Fig.2 Block diagram of the propose method

#### 4. SIMULATION RESULTS

To verify the effectiveness of the proposed controller, simulations have been done with the changes of reference substrate and influent substrate. The numerical values used for this simulation follow the work of Simutis et al.<sup>[3]</sup> and are given as Table 1.

Table 1 Numerical values for simulation

Parameters	Units	Values
Saturation constant $k_s$	g/l	0.1
Maximum specific growth rate $\mu_m$	1/h	0.3
Yield coefficient $k$		2
Inhibition constant $k_I$	g/l	50
Influent substrate concentration $S_{in}$	g/l	20

The unit conversion value is chosen to be  $k_u=0.275l/(gh)$ , constant in controller are  $c_1=5$ ,  $c_2=1$ , and the adaptation gain is  $\gamma = 0.0115$ . The initial values used for simulation are  $\theta = 1$ ,  $S(1)=2g/l$ ,  $X(1)=0.5g/l$ , and  $\hat{\theta}(1)=1.2$ .

The first simulation has been done to show the tracking performance of the proposed controller. Reference substrate  $S_{ref}$  is assumed to change as a step type as shown in Fig. 3 when the influent substrate concentration is constant. The simulation results are shown in Figs. 3-6. The output substrate concentration  $S$  tracks reference substrate concentration well as shown in Fig. 3. The variation of the biomass concentration  $X$  increase smoothly as shown in Fig. 4. The proposed control input, dilution rate  $D$ , and its derivative,  $dD/dt$  are shown in Figs. 5 and 6. As shown in Figs. 5 and 6, it is shown that the dilution rate varies in an acceptable range of control constraints mentioned previously.

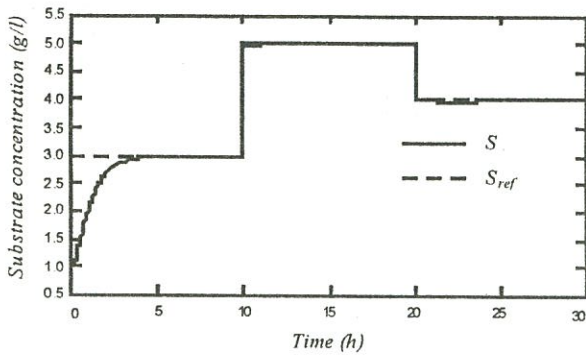


Fig. 3 Output substrate concentration  $S$  during the step change reference substrate concentration  $S_{ref}$

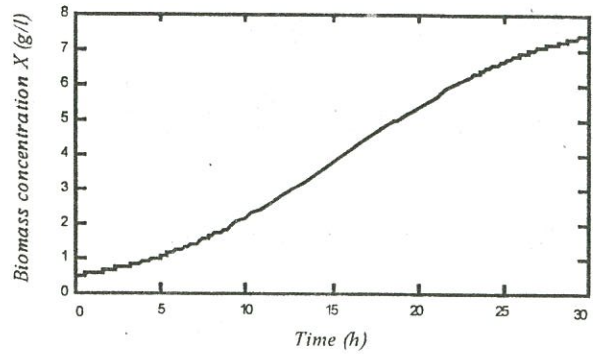


Fig. 4 Biomass concentration  $X$  during the step change reference substrate concentration  $S_{ref}$

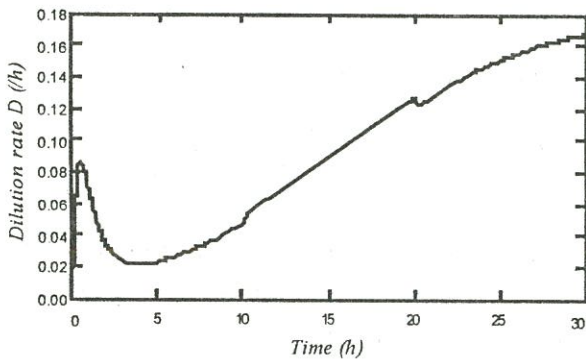


Fig. 5 Dilution rate  $D$  (control input) during the step change reference substrate concentration  $S_{ref}$

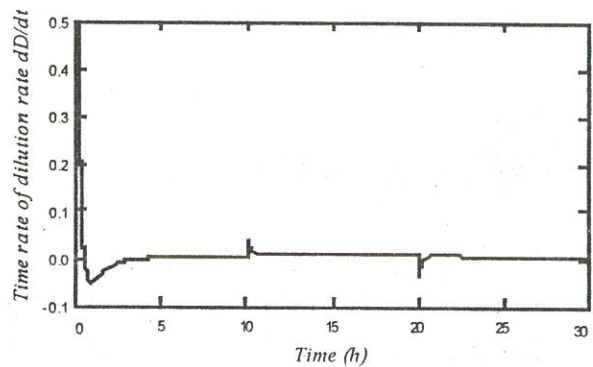


Fig. 6 Time rate of dilution rate  $dD/dt$  during the step change reference substrate concentration  $S_{ref}$

The second simulation has been done with the change of the influent substrate concentration  $S_{in}$  when the reference substrate is unchanged. This simulation has been done to know the controlled system performance under disturbance. The change of  $S_{in}$  is also to be a step type as 20, 18, and 24 g/l during each 10 hours.

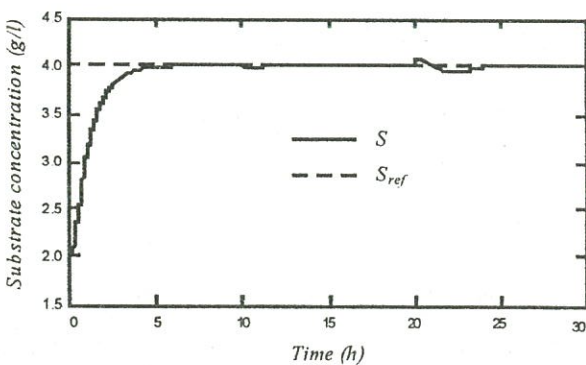


Fig. 7 Output substrate concentration  $S$  during the step change of the influent substrate concentration  $S_{in}$

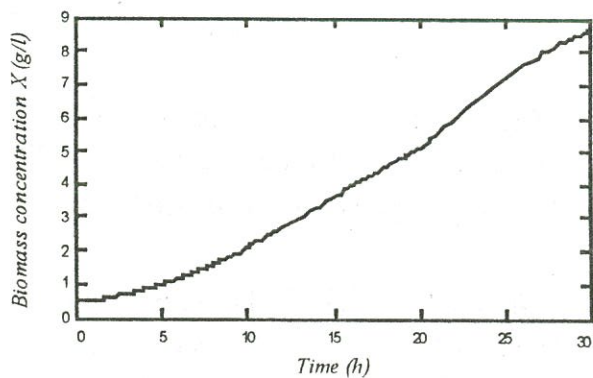


Fig. 8 Biomass concentration  $X$  during the step change of the influent substrate concentration  $S_{in}$



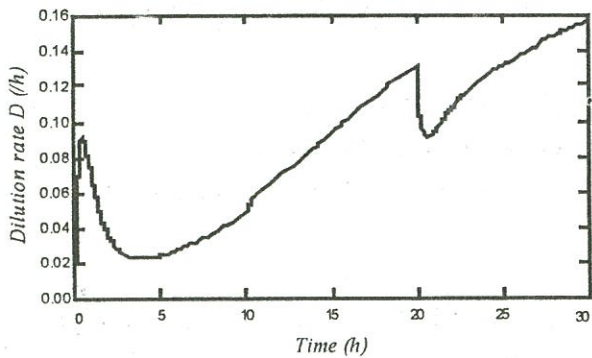


Fig. 9 Dilution rate  $D$  (control input) during the step change of the influent substrate concentration  $S_{in}$

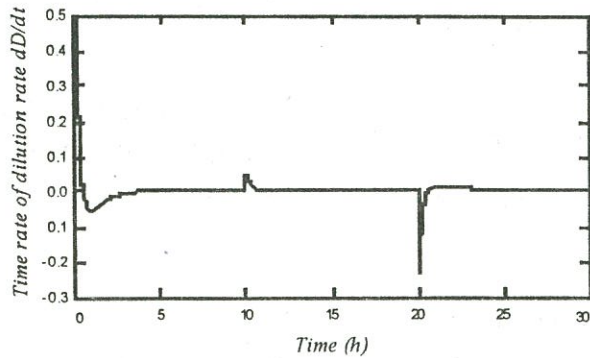


Fig. 10 Time rate of Dilution rate  $dD/dt$  during the step change of the influent substrate concentration  $S_{in}$

The simulation results are shown in Figs. 7-10. Although there are bigger fluctuations at the time with the change of  $S_{ref}$  than at the time with the change of  $S_{in}$ , the simulation result with the change of the influent substrate concentration  $S_{in}$  show similar results with the changes of reference substrate and also show the good tracking performance to reference well.

In simulations, the error estimate parameters  $\tilde{\theta}$  converge to zero as shown in Figs. 11 and 12.

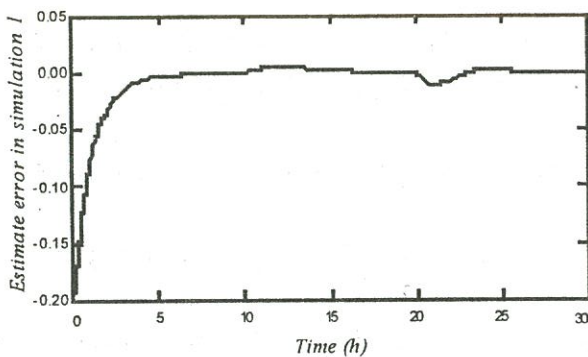


Fig. 11  $\tilde{\theta}$  during the step change reference substrate concentration  $S_{re}$

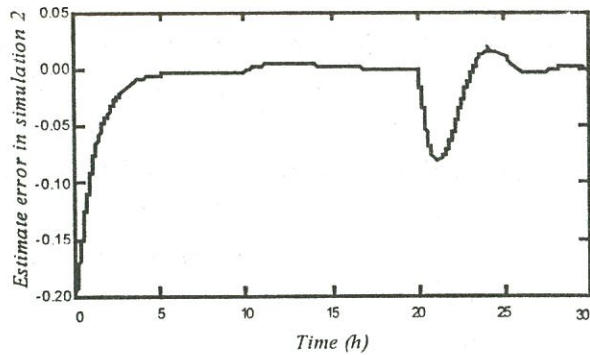


Fig. 12  $\tilde{\theta}$  during the step change of the influent substrate concentration

## 5. CONCLUSION

A nonlinear adaptive controller based on back-stepping method has been introduced for a continuous baker's yeast cultivating process in stirred tank bioreactor. Because of the uncertainty of specific growth rate, the specific growth rate has been modified as a function including the unknown parameter with known bounded values. The simulation results show that the proposed controller can be used for tracking reference substrate concentration with good performance even in the changes of both reference substrate and influent substrate. The proposed controller rejects the effect of the step change of the influent substrate concentration. Smooth biomass concentration is obtained even in both the change of reference substrate concentration and the variation of influent feed substrate concentration for continuous fermentation processes. The dilution rate increases with constant slope except when reference substrate concentration and influent substrate concentration is changed to track the reference substrate concentration.

## ĐIỀU KHIỂN QUÁ TRÌNH LÊN MEN TRONG LÒ PHẢN ỨNG SINH HỌC

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**TÓM TẮT:** Bài báo này giới thiệu bộ điều khiển thích ứng phi tuyến dùng điều khiển quá trình lên men trong lò phản ứng sinh học loại khuấy liên tục. Bộ điều khiển ổn định tiệm cận dựa trên hàm điều khiển Lyapunov. Mô hình đặc tính phát triển Haldane được dùng trong bài báo này. Vì tính bất ổn định, mô hình đặc tính phát triển được xem như là một hàm bao gồm thông số không xác định nhưng biết được phạm vi biến đổi. Nồng độ chất nền trong lò phản ứng và nồng độ chất nền cung cấp vào được đo để xác định luật điều khiển. Sự thay đổi của phản ứng khi có nhiễu ví dụ như sự thay đổi của đầu vào được nghiên cứu. Quá trình mô phỏng được thực hiện để chứng minh hiệu quả của bộ điều khiển.

### REFERENCES

- [1] Kim H.K., Nguyen T.T., Jeong N.S. and Kim S.B., " Nonlinear Adaptive Control of Fermentation Process in Stirred Tank Bioreactor", *Proceedings of ICCAS 2001*, Korea (2001)
- [2] Tham H.J., Hussain M.A. and Ramachandran K.B., "Variable Structure Control for a Continuous Bioreactor", *IEEE*, pp. I-433-I436 (2000)
- [3] Zlateva P., "Sliding-mode Control of Fermentation Process", *Bioprocess Engineering* 16, Springer-Verlag, pp. 383-387 (1997)
- [4] Simutis R., Oliveire R., Manikowski M., et. al, " How to Increase of Performance of Models for Proces Optimization and Control", *Journal of Biotechnology*, Vol. 59, 1997, pp. 73-89.
- [5] Levine W., *The Control Handbook*, Vol. II, CRC Press and IEEE Press, pp. 980-993 (1996)
- [6] Krstic M., Kanellakopoulos I. and Kokotovic P., *Nonlinear and Adaptive control Design*, John Wiley & Sons, Inc., pp. 92-183 (1995)
- [7] Roux G. and Dahhou B., "Adaptive Non-Linear Control of a Real-life Fermentation Process", *Proceedings of the Third IEEE Conference on Control Application*, pp. 909-913 (1994)
- [8] Schneider R., Jale N.A., Munack A. and Leigh J.R., "Adaptive Prediction Control for the Fed-batch Fermentation Process", Vol. 1, *Proceedings of the International IEEE Conference on Control*, pp. 249-254 (1994)
- [9] Maher M., Dahou B. and Zeng F.Y., "Adaptive Filtering and Estimation of Nonlinear Biological System", *Man and Cybernetics Systems*, Vol. 4, pp.235-24 (1993)
- [10] Chen L., Bastin G., Breusegem V.V., "Adaptive Nonlinear Regulation of Fed-Batch Biological Reactor: An Industrial Application", *Proceedings of the 30<sup>th</sup> IEEE Conference on Decision and Control*, 1991, pp. 2130-2134 (1991)