Biotechnology and Bioprocess Engineering 17: 1238-1243 (2012)
DOI 10.1007/s12257-012-0290-0

RESEARCH PAPER

Joint Estimation in Batch Culture by Using Unscented Kalman Filter

Xi Zhu and Enmin Feng

Received: 2 May 2012 / Revised: 7 July 2012 / Accepted: 23 July 2012

Abstract The disturbances caused by uncertain factors are inevitable in microbial fermentation. In this paper, we study the joint estimation problem for state and parameter in the bio-dissimulation process of glycerol to 1,3-PD in batch culture. Based on the nonlinear stochastic dynamic system model, we establish the corresponding iteration equations of Joint Unscented Kalman Filter (UKF) by referring to the Extended Kalman Filter (EKF), which is generally applied in microbial fermentation. Through numerical computation, both the state estimations and the uncertain model parameter estimations are obtained. Furthermore, the results of different parameter identification methods are compared. The results show that Joint UKF is more feasible for the process of controlling the glycerol fermentation.

Keywords: batch culture, nonlinear stochastic system, unscented kalman filter, joint estimation

1. Introduction

1,3-propanediol possesses potential applications on a large commercial scale, especially as a monomer of polyesters or polyurethanes, its microbial production has been recently paid attention to in the world for its low cost, high production, no pollution, and *etc.*[1-3]. Since the 1980s, several mathematical models have been established to describe this bioconversion process [4-7]. As more accurate developments of system models have been presented, the corresponding research works, *e.g.*, parameter identification, stability analysis and optimal control, have been investigated [8-12]. Compared with continuous and feed-batch cultures, glycerol fermentation in batch culture can obtain the highest production concentration and molar yield 1,3-PD [13]. Because the deterministic model implies some hidden assumptions, different culture states during long term continuous fermentation of glycerol by *K. pneumoniae* under similar initial fermentation conditions are obtained, resulting in randomness of batch culture [7]. The stochastic version of the batch fermentation process is more suitable for the factual fermentation.

Although statistical methods for parameter estimation of linear models in biological dynamic systems have been developed intensively in recent years, the estimation of both states and parameters of nonlinear dynamic systems remains a challenging task [14]. Kalman filter can be used for state estimation in microbial fermentation to reduce the interferences, which are caused by random errors, and to achieve the purpose of controlling the fermentation process more accurately. However, the general Kalman filter theory is merely to determine the state estimation of linear system, and the fluctuations of model parameters cannot be observed and justified. So the general Kalman filter theory is not suitable to solve the optimal estimation problem of the nondeterministic model. In order to deal with the nonlinear stochastic dynamical system in glycerol batch fermentation, by expanding the system state variables with model parameter, Extended Kalman filter (EKF) can be applied to estimate the state and model parameters, simultaneously. But EKF has some limitations. For example, it can only solve weakly nonlinear problem. Therefore, it is necessary to develop a more effective nonlinear filter dedicated to the fermentation processes.

This paper is organized as follows. In Section 2, the five-dimensional stochastic dynamical system is presented. In Section 3, Joint EKF method is applied to estimate state and model parameters of the established system. In Section 4, the iteration equations of Joint UKF method are

Xi Zhu*, Enmin Feng
School of Mathematical Sciences, Dalian University of Technology, Liaoning 116-024, China
Tel: +86-411-8470-8354; Fax: +86-411-8470-8354
E-mail: zhuxi81@163.com/emfeng@dlut.edu.cn

established. In Section 5, numerical calculations based on parameter sensitivity analysis are provided to simulate the nonlinear stochastic system of batch culture. Some conclusions are presented in the last section.

2. Materials and Methods

2.1. Modeling for nonlinear stochastic dynamical system

In batch fermentation, the medium is pumped at the beginning of fermentation and the working volume of fermentation keeps constant in the whole course of bioconversion. As a result of fact, the following assumptions can be made:

(H1) The medium is adequately intermixed. Moreover, the concentrations of reactant are uniform in bio-reactor and only as varied as the fermentation time.

(H2) No medium is pumped inside and outside the bioreactor in the process of batch fermentation. Therefore, mass balances of biomass, substrate and products in batch microbial culture are written as follows [15]:

$$\begin{cases} \dot{x}_1(t) = \mu x_1(t), \\ \dot{x}_2(t) = -q_2 x_1(t), \quad t \in [0, t_f] \\ \dot{x}_i(t) = q_i x_1(t), \quad i = 3, 4, 5 \end{cases}$$
$$x_i(0) = x_i^0, \quad i \in I_5, \tag{1}$$

where the specific growth rate of cells μ, specific consumption rate of substrate q_2 and specific formation rate of product q_i are expressed as follows,

$$\mu = \mu_m \frac{x_2(t)}{x_2(t)+k_s} \prod_{i=2}^{5} \left(1 - \frac{x_i(t)}{x_i^*}\right),$$
$$q_2 = m_2 + \frac{\mu}{Y_2} + \Delta_2 \frac{x_2(t)}{x_2(t)+k_2},$$
$$q_i = m_i + \mu Y_i \quad i = 3, 4, 5 \tag{2}$$

where x_1, x_2, x_3, x_4, and x_5 are the concentration of biomass, glycerol, 1,3-PD, acetic acid and ethanol at time t in reactor, respectively. $x_0 \in R^5$ denotes the initial state. Under anaerobic conditions at 37°C and $PH = 7$, $\mu_m = 0.67$ is the maximum specific growth rate of cells, and $k_s = 0.28$ is Monod saturation constant. The critical concentrations of biomass, glycerol, 1,3-PD, acetic acid and ethanol for cell growth are $x_1^* = 10$ g/L, $x_2^* = 2039$ mmol/L, $x_3^* = 939.5$ mmol/L, $x_4^* = 1026$ mmol/L and $x_5^* = 360.9$ mmol/L, respectively [15,16]. m_i, Y_i, i = 2, 3, 4, 5 are system parameters to be identified. Here, the parameters are described by $p = (p_1, p_2, ..., p_8)^T := (m_2, m_3, m_4, m_5, Y_2, Y_3, Y_4, Y_5)^T \in P_{ad} \subset R^8$ conveniently.

However, the deterministic model brings forth some inaccuracy that different culture states, during long term continuous fermentation under similar initial fermentation conditions, are obtained. Thus, stochastic system plays a key role in describing the randomness of microbial growth. In order to construct a stochastic system, a normal method, which is simply to add a stochastic part to the deterministic model, can be chosen, *e.g.* the system (1) can be driven by 5 scalar white noise sources. Under assumptions (H1) and (H2), the course of batch culture with uncertain perturbations can be formulated as the following nonlinear stochastic dynamical system [7]:

$$\dot{x}(t) = F(t, x(t), p) + G(t, x(t))\dot{W}(t), \tag{3}$$

where $F(t, x(t), p) = (\mu x_1(t), -q_2 x_1(t), q_3 x_1(t), q_4 x_1(t), q_5 x_1(t))^T$, $E(\dot{W}(t)) = 0$, $D(\dot{W}(t)) = 1$, G(t, x(t)) is a dispersion matrix, W(t) is a Brownian motion. By using the following Stochastic Euler-Maruyama method, the equation is scattered as:

$$x_{k+1} = x_k + F(x_k, p_k)\Delta t + w_k, \tag{4}$$

where w_k is a white noise with a power spectral density $Q'_k \in R^{5\times5}$.

In more general, the nonlinear stochastic discrete model is given by

$$x_{k+1} = f(x_k, p_k) + w_k, \tag{5}$$

where $f(x_k, p_k) = x_k + F(x_k, p_k)\Delta t$.

2.2. EKF for joint estimation

In order to apply the mechanics of the Kalman filter to nonlinear problems, the Extended Kalman filter (EKF) was developed [17]. EKF is a method of linearizing the dynamic system at the last state estimation by using Taylor series to obtain a group of iterative equations, which are similar to Kalman Filter equations of linear system.

In the joint Extended Kalman filter [18], by extending the state variables with the model parameter vector p, the stochastic dynamical system in batch microbial culture can be described as:

$$z_{k+1} = \begin{bmatrix} x_{k+1} \\ p_{k+1} \end{bmatrix} = \begin{bmatrix} F(x_k, p_k) \\ p_k \end{bmatrix} + \begin{bmatrix} w_k \\ \eta_k \end{bmatrix} = g(z_k) + \xi_k, \tag{6}$$

where the state and parameter vector are concatenated into a single, joint state vector: $z_k^T = [x_k^T\ p_k^T]$. η_k is a white noise with a power spectral density $Q''_k \in R^{8\times8}$. After extended, $\xi_k^T = [w_k^T\ \eta_k^T]$, which is the dynamic system's white noise with covariance matrix $Q_k = \begin{bmatrix} Q'_k & \\ & Q''_k \end{bmatrix}$. And the observation equation becomes

$$y_k = Hz_k + v_k, \tag{7}$$

where $H = [I\ 0] \in R^{5\times 8}$, $I \in R^{5\times 5}$ is a unit matrix, $0 \in R^{5\times 3}$ is a null matrix, and vector y is used to compare with the experimental data. Assuming that the white noise w_k and v_k are mutually independent, v_k is an uncorrelated Gaussian noise with variance matrix $R_k \in R^{5\times 5}$. In order to obtain the convenient numerical computing form, by using the first-order Taylor series, the state equation (6) is changed into

$$z_{k+1} = \Gamma_k z_k + o(z_k) + \xi_k, \tag{8}$$

where Γ_k is the Jacobian matrix of $g(z_k)$ at the point z_k, and $o(z_k)$ is an infinitesimal of higher order. Then, the joint EKF algorithm for the nonlinear stochastic dynamical system exhibits as follows,

Prediction:

$$\begin{aligned} \hat{z}_{k/k-1} &= g(\hat{z}_{k-1/k-1}) \\ P_{k/k-1} &= \Gamma_{k-1} P_{k-1/k-1} \Gamma_{k-1}^T + Q_{k-1} \end{aligned} \tag{9}$$

Update:

$$\begin{aligned} K_k &= P_{k/k-1} H^T (H P_{k/k-1} H^T + R_k)^{-1} \\ \hat{z}_k &= \hat{z}_{k/k-1} + K_k (y_k - H\hat{z}_{k/k-1}) \\ P_k &= (I - K_k H)\Gamma_{k-1}[I - K_k H]^T + K_k R_k K_k^T \end{aligned} \tag{10}$$

where,

$\hat{z}_{k/k-1}$ and $P_{k/k-1}$ are the predicted mean and variance of the extended state, respectively, on the time step k before seeing the measurement.

$\hat{z}_k$ and P_k are the estimated mean and variance of the extended state, respectively, on the time step k before seeing the measurement.

K_k is the Kalman Filter gain matrix, on the step k.

When the time steps k=0, there is only the prior distribution $\hat{z}_0 \sim N(z_0, P_0)$ without measurement.

The EKF can be viewed as providing "first-order" approximations to the optimal terms. While "second-order" versions of the EKF exist, their increased implementation and computational complexity tend to prohibit their use. In general, the EKF methods may obtain only local optimum, rather than global optimal solutions [14]. In many circumstances, the EKF cannot satisfy the accuracy of nonlinear problem.

2.3. UKF for joint estimation

In order to avoid the flaws of the EKF discussed above, the unscented transform (UT) can be used for forming a Gaussian approximation to the joint distribution of random variables z and y, which are defined with equations (6, 7). For calculating the statistics of a random variable, which undergoes a nonlinear transformation, a random variable x (dimension n) is considered propagating through a nonlinear function, y = g(x). Assuming x has a mean $\bar{x}$ and variance P_x, the statistics of y is calculated as the form of a matrix χ of 2n+1 sigma vectors χ_i (with corresponding weights W_i), the transformation procedure is as follows [19]:

$$\begin{aligned} \chi_0 &= \bar{x} \\ \chi_i &= \bar{x} + (\sqrt{(n+\lambda)P_x})_i \quad i = 1, ..., n \\ \chi_i &= \bar{x} - (\sqrt{(n+\lambda)P_x})_{i-n} \quad i = n+1, ..., 2n \\ W_0^{(m)} &= \lambda/(n+\lambda) \\ W_0^{(c)} &= \lambda/(n+\lambda) + (1-\alpha^2+\beta) \\ W_i^{(m)} &= W_i^{(c)} = 1/(2(n+\lambda)) \quad i = 1, ..., 2n, \end{aligned} \tag{11}$$

where λ is a scaling parameter, which is defined as $\lambda = \alpha^2(n+\kappa) - n$. α determines the spread of the sigma points around $\bar{x}$ and is usually set to a small positive value. κ is a secondary scaling parameter, which is usually set to 0, and β is used to incorporate prior knowledge of the distribution of x ($\beta = 2$ is optimal for Gaussian distributions). $(\sqrt{(n+\lambda)P_x})_i$ is the ith row of the matrix square root. And the mean and variance for y are approximated using the weighted sample mean and variance of the sigma vectors, which are propagated through the nonlinear function [20],

$$\begin{aligned} y_i &= g(\chi_i) \quad i = 0, 1, ..., 2n \\ \bar{y} &\approx \sum_{i=0}^{2n} W_i^m y_i \\ P_y &\approx \sum_{i=0}^{2n} W_i^c (y_i - \bar{y})(y_i - \bar{y})^T. \end{aligned} \tag{12}$$

So dealing with the equations (6, 7), the joint UKF algorithm for the nonlinear stochastic dynamical system exhibits as follows,

Prediction:

$$\begin{aligned} \chi_i(k|k-1) &= g[\chi_i(k-1|k-1)] \quad i = 0, 1, ..., 2n \\ \hat{z}_{k/k-1} &= \sum_{i=0}^{2n} W_i \chi_i(k|k-1) \\ P_{k/k-1} &= \sum_{i=0}^{2n} W_i [\chi_i(k|k-1) - \hat{z}_{k/k-1}][\chi_i(k|k-1) - \hat{z}_{k/k-1}]^T + Q_{k-1} \end{aligned} \tag{13}$$

Update:

$$\hat{y}(k|k-1) = \sum_{i=0}^{2n} W_i^{(m)} H\chi_i(k|k-1)$$
$$P_{\bar{y}_k\bar{y}_k} = \sum_{i=0}^{2n} W_i^{(c)} [H\chi_i(k|k-1) - \hat{y}(k|k-1)][H\chi_i(k|k-1) - \hat{y}(k|k-1)]^T$$
$$P_{z_k y_k} = \sum_{i=0}^{2n} W_i^{(c)} [\chi_i(k|k-1) - \hat{z}(k|k-1)][H\chi_i(k|k-1) - \hat{y}(k|k-1)]^T$$
$$S_k = P_{\bar{y}_k\bar{y}_k} + R_{k-1}$$
$$K_k = P_{z_k y_k} S_k^{-1}$$
$$\hat{z}_k = \hat{z}_{k/k-1} + K_k(y_k - \hat{y}(k|k-1))$$
$$P_k = P_{k/k-1} - K_k S_k K_k^T \quad (14)$$

where,

$\hat{z}_{k/k-1}$ and $P_{k/k-1}$ are the predicted mean and variance of the extended state, respectively, on the time step k before seeing the measurement.

$\hat{z}_k$ and P_k are the estimated mean and variance of the extended state, respectively, on the time step k before seeing the measurement.

K_k is the Kalman filter gain matrix, on the step k.

When the time steps k = 0, there is only the prior distribution $\chi_0 \sim N(z_0, P_0)$, without measurement.

The UKF may provide a more accurate estimate through direct approximation of the expectation of the Hessian [20]. Furthermore, it is much less difficult to implement without the need to perform any analytic differentiation to gain the Jacobian or Hessian.

3. Results and Discussion

Before numerical computing, both noise variance matrix Q_0 and R_0 must be chosen first. The quality of the selecting noise intensity matrix has a direct impact on filter accuracy that it affects the convergence rate and tracking performance; the more inaccurate the dynamic model, the greater the impact. Generally, a better estimation of SNR (signal to noise ratio computing by Q/R) can be made through experiments and modeling analysis. Choosing parameter noise matrix must obey the following criterion: (1) while the parameters merely fluctuate stochastically in a small range, the amendment to them must be smaller than to the state variables, and (2) the ratio between the parameters is basically determined by their sensitivities, as the parameters with lower sensitivities should be carried out with bigger variance. According to the conclusion of kinetic parameter sensitivity analysis in [21], parameters p_1, p_4, p_5, p_7, p_8 are identified as sensitive. On the other hand, p_2, p_3, p_6 are insensitive. Furthermore, basing on the crude numerical computing result in [16], the order of magnitude of the error variance matrix of state variables is estimated as σ_μ.

As the same importance to the initialization, the efficiency of EKF or UKF is seriously depended on its starting value estimation, which contains the initial mean Z_0 and the initial variance matrix P_0 in the prediction equations (9, 13). An appropriate starting value can greatly reduce the convergence time of the filter. The estimation of the starting values of the parameters must be more accurate [22]. While the variables have already been set by the reaction condition at time 0, the starting value of parameter variables can call the identified parameter estimation in [8]. Through the above analysis and repeated experiments, the SNR is assumed as $Q/R = 0.2$. The corresponding initial values are assumed as follows:

$R_0 = diag(0.819, 49.635, 32.89, 3.719, 2.4945)$,
$P_0 = diag(3, 30, 10, 10, 10, 0.1, 0.1, 0.1, 0.1, 0.1, 0.1, 0.1, 0.1)$,
$Q_0 = diag(0.1638, 9.927, 6.578, 0.7438, 0.4989, 0.000001, 0.000025, 0.000025, 0.00001, 0.00001, 0.000025, 0.00001, 0.00001)$,
$z_0 = [0.2245, 509.8913, 0, 0, 0, 2.2, -2.69, -0.97, 5.26, 0.0082, 67.69, 33.07, 11.66]^T$.

By using MATLAB, the results are as fellows. Fig. 1 shows the comparison between two estimation methods for system state variables, where the points denote the experimental values, and the real lines denote the computational curves. Fig. 2 shows the comparison between two estimation methods for parameters. The results of the parameter estimation in nonlinear stochastic dynamic system are listed in Table 1.

As shown in the pictures, Joint UKF process can track the experimental data much better than Joint EKF. As the filter time continues the error caused by EKF accumulates, the filter tracking curves appears to detach from the experimental data. Especially, x_2 (glycerol) descends below zero, which would not be allowed in real experiments. Simultaneously, some parameters (p4, p5, p8), which are indicated by dashed lines, diverge at the terminal of Joint EKF process. N/A is substituted for the inaccuracy result in Table 1.

Table 1. The parameter estimations in batch fermentation

Method	p1	p2	p3	p4	p5	p6	p7	p8
JEKF	2.04	-16.94	-9.40	N/A	N/A	56.62	29.78	N/A
JUKF	2.21	-4.61	-2.19	1.43	0.0084	56.29	27.56	6.50

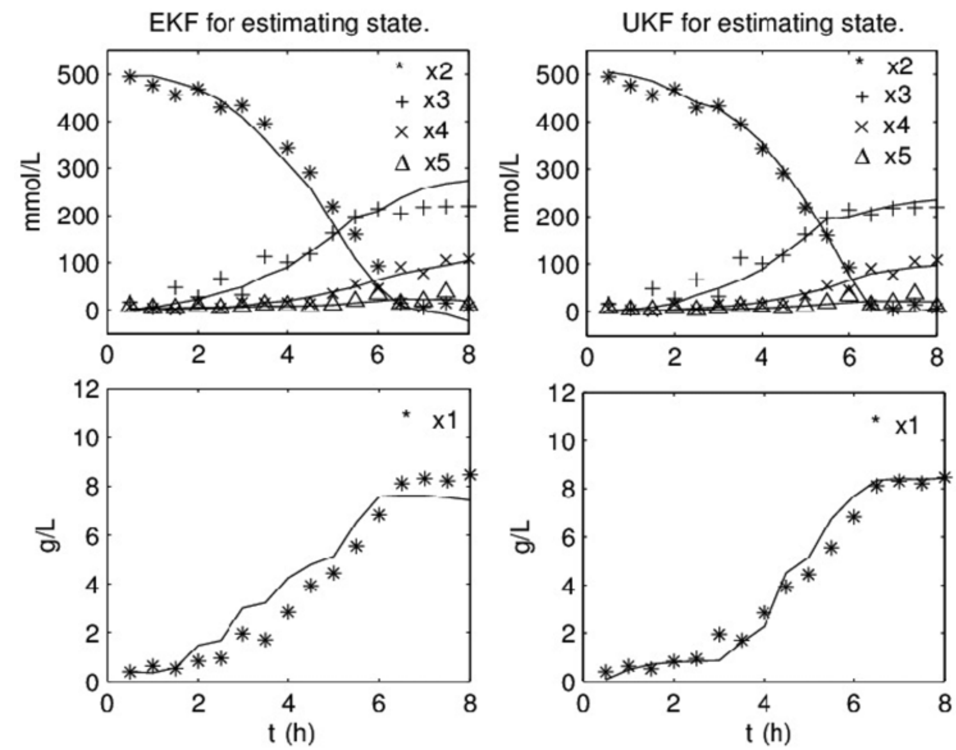

Fig. 1. The comparison between two methods for system state variables.

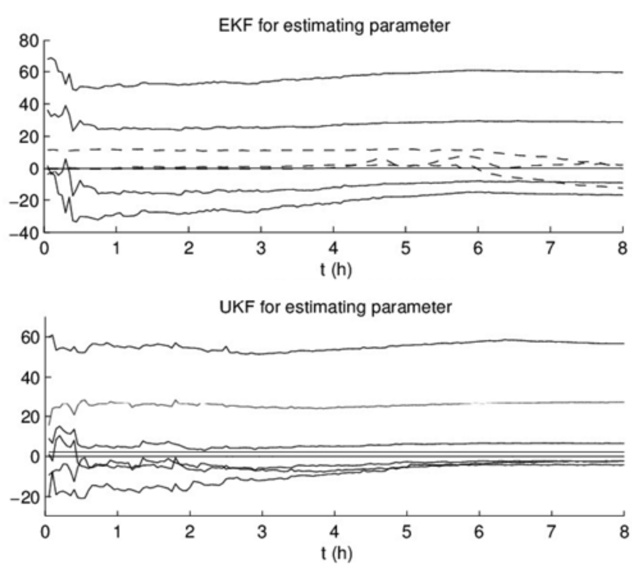

Fig. 2. The comparison between two methods for parameters.

4. Conclusion

In this paper, based on Joint EKF method, Joint UKF for the stochastic system of batch culture is designed. Both methods can eliminate random interference and estimate the state variables. When it comes to estimation for the system parameters, without the errors caused by the first order truncation, the Joint UKF has a much better effect, compared with the Joint EKF. But there are some unavoidable limitations, a mass of repeated experiments are needed to obtain the initial variance matrixes, and some sensitive parameters may tend to filter divergence as filter time increases. Further adaptive Kalman Filter algorithm and H_2/H_∞ mixed filter design will be the research emphases. The dynamic system model will also be reasonably improved.

Acknowledgements

This work was supported by 863 Program (Grant No. 2007AA02Z208), 973 Program (Grant No. 2007CB714304), the National Natural Science Foundation of China (Grant Nos. 11171050 and 10871033).

References

1. Reimann, A. and H. Biebl (1996) Production of 1,3-propanediol by clostridium butyricum DSM5431 and product tolerant mutants in fed batch culture, feeding strategy for glycerol and ammonium. *Biotechol. Lett*. 18: 297-298.
2. Zhilong, X., A. Zeng, and W. Deckwer (1998) Multiplicity and stability analysis of microorganisms in continuous culture: Effects of metabolic overflow and growth inhibition. *Biotechnol. Bioeng*. 57: 251-261.

3. Anping, Z. and H. Biebl (2002) Bulk-chemicals from biotechnology: the case of microbial production of 1,3-propanediol and the new trends. *Adv. Biochem. Eng. Biotechnol*. 74: 237-257.
4. Zeng, A. P. and W. D. Deckwer (1995) A kinetic model for substrate and energy consumption of microbial growth under substrate-suffcient condition. *Biotechnol. Prog*. 11: 71-79.
5. Xiu, Z., A. Zeng, and L. An (2000) Mathematical modeling of kinetics and research on multiplicity of glycerol bioconversion to 1,3-propanediol. *J. Dalian Univ. Technol*. 40: 428-433.
6. Wang, G., E. M. Feng, and Z. L. Xiu (2008) Modelling and parameter identification of microbial bioconversion in fed-batch cultures. *J. Proc. Contr*. 18: 458-464.
7. Lei, W., E. Feng, and Z. Xiu (2009) Nonlinear stochastic dynamical system of bio-dissimilation of glycerol to 1,3-propanediol in batch culture and its viable set. *Bioinformatics and Biomedical Engineering. 3rd International Conference*. June 11-13.
8. Gao, C., W. Zongtao, F. Emnin, and X. Zhilong (2006) Parameter identification and optimization of process for bio-dissimilation of glycerol to 1,3-propanediol in batch culture. *J. Dalian Univ. Technol*. 46: 771-775.
9. Zhaohua, G., C. Liu, and E. Feng (2009) Modeling in microbial batch culture and its parameter identcation. *Joint 48th IEEE Conference on Decision and Control and 28th Chinese Control Conference Shanghai*. P. R. China.
10. Xiaofang, L., R. Qu, and E. Feng (2011) Hopf bifureation of a ve-dimensional delay differential system. *Internat. J. Comp. Math.* 1: 79-96.
11. Juan, W., J. Ye, H. Yin, E. Feng, and L. Wang (2010) Sensitivity analysis and identification of kinetic parameters in batch fermentation of glycerol. *J. Computational and Appl. Math.* 9: 2268-2276.
12. Lei, W. (2012) Modelling and regularity of nonlinear impulsive switching dynamical system in fed-batch culture. *Abstract and Appl. Anal*. doi:10.1155/2012/295627.
13. Gtinzel, B. (1991) *1,3-propandiol durch Clostridium butyricum und adsorptive Abtremutng von Diolen.* Ph. D. Thesis. TU Braunschweig, Germany.
14. Sun, X., L. Jin, and M. Xiong (2008) Extended Kalman filter for estimationof parameters in nonlinear state-space models of biochemicalnetworks. *PLoS ONE*. 3: 3758.
15. Li, X. H. and E. M. Feng (2005) Optimal control and property of nonlinear dynamic system for microorganism in batch culture. *OR Transaction*. 9: 67-79.
16. Lei, W. (2009) *Nonlinear dynamical systems and influence of stochastic noise in microbial fermentation.* Ph. D. Dissertation. Dalian: Dalian University of Technology.
17. Jazwinski, A. H. (1970) *Stochastic Processes and Filtering Theory*. Academic Press.
18. Matthews, M. B. and G. S. Moschytz (1990) Neural-network nonlinear adaptive filtering using the extended Kalman filter algorithm. *Signal Proc. Lett*. 13: 445-448.
19. Julier, S. J. and J. K. Uhlmann (1997) A new extension of the kalman filter to nonlinear systems. *In Proceedings of AeroSense: The 11th International Symposium on Aerospace/Defence Sensing, Simulation and Controls*. Orlando, Florida.
20. Wan, E. A. and R. van der Merwe (2000) The unscented kalman filter for nonlinear estimation. *In Proceedings of IEEE Symposium 2000 (AS-SPCC).* October 1-4.
21. Juan, W., J. Ye, H. Yin, E. Feng, and L. Wang (2010) Sensitivity analysis and identification of kinetic parameters in batch fermentation of glycerol. *J. Comp. Appl. Math.* 9: 2268-2276.
22. Bellgardt, K. H., W. Kuhlmann, H. D. Meyer, K. Schügerl, and M. Thoma (1986) Application of an extended Kalman filter for state estimation of a yeast fermentation. *IEE Proc.* 133: 226-234.