ROCKY MOUNTAIN
JOURNAL OF MATHEMATICS
Volume 38, Number 5, 2008

STABILITY ANALYSIS OF THE NONLINEAR IMPULSIVE SYSTEM IN MICROBIAL FED-BATCH FERMENTATION

CAIXIA GAO AND ENMIN FENG

ABSTRACT. In this study, the nonlinear impulsive dynamical system of fed-batch fermentation is investigated in the process of bio-dissimilation of glycerol to 1,3-propanediol. Several stability criteria are established by employing the method of Lyapunov functions. The ranges of parameters' value in the system are obtained according to the actual microbial fermentation.

1. Introduction. 1,3-propanediol(1,3-PD) possesses potential applications on a large commercial scale, especially as a monomer of polyesters or polyurethanes. Its microbial production has recently been paid worldwide attention for its low cost, high production and no pollution, etc. [**1**]. Among all kinds of microbial production of 1,3-PD, dissimilation of glycerol to 1,3-PD by *Klebsiella pneumoniae* has been widely investigated since the 1980s due to its high productivity [**5, 6**]. Experimental investigations showed that the fermentation of glycerol by *K. pneumoniae* is a complex bioprocess, since the microbial growth is subjected to multiple inhibitions of substrate and products. Research concerning fermentation includes the quantitative description of cell growth kinetics of multiple-inhibitions, metabolic overflow kinetics of substrate consumption and product formation in continuous cultures, feeding strategy of glycerol in fed-batch culture, and so on [**4**]. In this research on fed-batch culture, all numerical results are based on continuous dynamical models, and big errors exist between computational and experimental results. In fact, impulsive phenomena exist in fed-batch culture, so the process characterized by continuous models is not fit for the actual process any longer. In order to characterize the actual process, impulsive differential equations are applied to the fed-batch fermentation [**2**]. Parameters in the continuous system are not fit for

2000 AMS *Mathematics subject classification.* Primary 34K45, 49N25, 49N90.
Keywords and phrases. Stability, Lyapunov function, nonlinear impulsive system.
Received by the editors on August 19, 2007.
DOI:10.1216/RMJ-2008-38-5-1377

the impulsive system, so parameter identification is necessary. Usually, ranges of parameters change in the neighborhood of initial values during the identification process. But we can't ensure the system is stable under the given ranges of parameters. Thus, stability of the system becomes a fundamental issue in system analysis and design that is necessary for system identification and optimal control.

In this paper, we consider the impulsive dynamical system in [**2**] as preliminaries. In order to ensure stability of the system during parameter identification, we use the method of Lyapunov functions to establish several impulsive stabilization criteria for the impulsive system concerned.

This paper is organized as follows. In Section 2, we introduce some notations, definitions and a lemma. In Section 3, we formulate the problem of the impulsive system and establish several stability criteria for the impulsive system. And the ranges of the parameters' values in the system are obtained.

2. Preliminaries. Consider the impulsive dynamical system

$$
\begin{aligned}
\dot{x}(t) &= f(t, x(t)), && t \neq t_k, \\
\Delta x &= I_k(x), && t = t_k,\ k = 1, 2, \dots , \\
x(t_0) &= x_0,
\end{aligned}
\tag{1}
$$

where $x \in R^n$ is the state variable, $f(t, x(t)) : R_+ \times R^n \to R^n$ is a continuous function, $\Delta x(t_k) = x(t_k^+) - x(t_k^-)$, $x(t_k^+) = \lim_{t \to t_k^+} x(t)$ and $x(t_k^-) = \lim_{t \to t_k^-} x(t)$. Without loss of generality, we assume $f(t, 0) \equiv 0$ so that system (1) admits a trivial solution.

Definition 2.1. The impulsive differential system (1) is said to be

(i) stable, if for all $\varepsilon > 0$, $t_0 \in R_+$, there exists a $\delta = \delta(t_0, \varepsilon) > 0$, such that $\|x_0\| < \delta$ implies $\|x\| < \varepsilon$, $t > t_0$, where $x(t) = x(t, t_0, x_0)$ satisfies system (1);

(ii) uniformly stable, if δ in (i) is independent of t_0;

(iii) asymptotically stable, if system (1) is stable and for all $t_0 \in R_+$, there exists a $\sigma(t_0) > 0$ such that $\|x_0\| < \sigma$ implies $\lim_{t\to\infty} x(t) = 0$;

(iv) uniformly asymptotically stable, if system (1) is uniformly stable and there exists a $\sigma > 0$, for any $\eta > 0$ and $t_0 \in R_+$. We can find a $T = T(\eta) > 0$ such that $\|x_0\| < \sigma$ implies $\|x(t)\| < \eta$ and $t \geq t_0 + T$.

Definition 2.2. A function $V(t,x)$ is said to be (i) decrescent if there exists a function $a : R_+ \to R_+$ such that

$$V(t,x) \leq a(\|x\|), \quad (t,x) \in R_+ \times s(\rho).$$

(ii) positive definite if there exists a continuous function $b : R_+ \to R_+$ such that

$$\begin{aligned} &b(\|x\|) \leq V(t,x), && (t,x) \in R_+ \times s(\rho) \\ &V(t,0) \equiv 0, && t \in R_+. \end{aligned}$$

We denote by Σ the class of functions $V : R_+ \times R^n \to R_+$ such that V is positive definite, locally Lipschitz in x and continuous everywhere except possibly at a sequence of points t_k at which $V(t,x)$ is left continuous and the right limit $V(t_k^+, x)$ exists for all $x \in R^n$. For $\rho > 0$, let $s(\rho) = \{x \in R^n \mid \|x\| < \rho\}$.

We define the upper righthand generalized derivative of a function $V(t,x)$ along solutions of $\dot{x}(t) = f(t, x(t))$ by

$$D^+V(t,x) = \limsup_{\delta \to 0^+} \frac{1}{\delta}[V(t+\delta, x+\delta) f(t,x) - V(t,x)]. \tag{2}$$

If $V(t,x)$ is continuously differentiable, then (2) reduces to

$$D^+V(t,x) = \frac{\partial}{\partial t}V(t,x) + \frac{\partial}{\partial x}V(t,x) \cdot f(t,x). \tag{3}$$

Lemma 2.1 [**3**]. *Assume that* (i) $V \in \sum$. *There exist* $\lambda_k \in R$ *and a continuous function* $c_k : R_+ \to R_+$ *such that*

$$D^+V(t,x) \leq \frac{\lambda_k}{\Delta t_k} c_k(V(t,x)), \quad (t,x) \in (t_{k-1}, t_k) \times s(\rho);$$

(ii) *there exist* $v_k \in R$ *and a continuous function* $d_k : R_+ \to R_+$ *such that*

$$V(t_k^+, x + I_k(x)) \leq V(t_k, x) + v_k d_k(V(t_k, x)), \quad x \in s(\rho);$$

(iii) $\lambda_k + v_k \le 0$, *for* $s \in (0,\rho)$, $c_k(s) \le d_k(s)$ *if* $v_k < 0$ *and* $c_k(s) \ge d_k(s)$ *if* $u_k < 0$. *Then system* (1) *is stable. Suppose further that*

(iv) $V(t,x)$ *is decrescent and for any* $\eta > 0$, *there exists a* $\sigma > 0$ *such that*

$$s + |v_k| d_k(s) < \eta, \text{ for all } s \in (0,\sigma), \quad k = 1,2,\dots .$$

Then system (1) *is uniformly stable.*

3. Problem formulation and stability criteria. The fed-batch culture of glycerol bioconversion to 1,3-PD begins with batch fermentation, then glycerol is added to the reactor at different discrete instants during the culture process in order for the glycerol concentration to remain in a given range. At the end of fermentation, glycerol is expected to convert to 1,3-PD as much as possible. The whole process includes batch fermentation in the early stage and later fed-batch culture. The dynamical system of batch culture can be formulated as follows [**5**]

$$\begin{cases} \dot{x}_1(t) = \mu x_1(t) = \mu_m \frac{x_2(t)}{x_2(t)+k_s} \prod_{i=2}^{5} (1 - \frac{x_i(t)}{x_i^*}) x_1(t) \\ \dot{x}_2(t) = -q_2 x_1(t) = -(m_2 + \frac{\mu}{Y_2} + \Delta_2 \frac{x_2(t)}{x_2(t)+k_2}) x_1(t) \\ \dot{x}_3(t) = q_3 x_1(t) = (m_3 + \mu Y_3 + \Delta_3 \frac{x_2(t)}{x_2(t)+k_3}) x_1(t) \\ \dot{x}_4(t) = q_4 x_1(t) = (m_4 + \mu Y_4 + \Delta_4 \frac{x_2(t)}{x_2(t)+k_4}) x_1(t) \\ \dot{x}_5(t) = q_5 x_1(t) = q_2 (\frac{b_1}{c_1 + \mu x_2(t)} + \frac{b_2}{c_2 + \mu x_2(t)}) x_1(t) \\ x_1(0) = x_{10}, x_2(0) = x_{20}, x_3(0) = x_{30}, x_4(0) = x_{40}, x_5(0) = x_{50}, \end{cases}$$

where the expressions of μ, q_i, $i = 2,3,4,5$ and μ_m, k_s, m_i, Y_i, Δ_i, k_i, $i = 2,3,4$, b_i, c_i, $i = 1,2$, x_i^*, $i \in I_5$ are on the basis of previous work (see Xiu et al. [**5**]). Let $x(t) = (x_1(t), x_2(t), x_3(t), x_4(t), x_5(t)) \in R^5$, the initial state $x(0) = x_0 = (x_{10}, x_{20}, x_{30}, x_{40}, x_{50}) \in R^5$. We can formulate the dynamical system as follows.

$$\begin{cases} \dot{x}(t) = f(x(t)), \\ x(0) = x_0, \end{cases} \tag{4}$$

where

$$f(x(t)) = (\mu x_1(t), \ -q_2 x_1(t), \ q_3 x_1(t), \ q_4 x_1(t), \ q_5 x_1(t)) \in R^5.$$

Let $I_1 = [0, t_1)$ be the interval of batch fermentation, $I_2 = [t_1, T]$ the interval of the later fed-batch fermentation, $I = I_1 \cup I_2$, $D = \{t_1, t_2, \dots, t_{n-1}\} \subset [t_1, T)$, t_i, $i \in I_{n-1} = \{1, 2, \dots, n-1\}$, are the times of occurrence of impulses. $t_n = T$. Thus, the fed-batch culture including batch fermentation can be formulated as the following nonlinear impulsive system.

$$
\begin{cases} \dot{x}(t) = f(x(t)) & t \in I \backslash D,\ x(0) = x_0, \\ \Delta x(t_i) = I_i(x(t_i)) & 0 = t_0 < t_1 < t_2 < \cdots < t_n < t_{n+1} = T, \end{cases} \tag{5}
$$

where

$$
\begin{aligned}
f(x(t)) &= (\mu x_1(t),\ -q_2 x_1(t),\ q_3 x_1(t),\ q_4 x_1(t),\ q_5 x_1(t)), \\
I_i(x(t_i)) &= (-u_i x_1(t_i),\ -u_i x_2(t_i) + c u_i,\ -u_i x_3(t_i), \\
&\qquad\qquad\qquad\qquad - u_i x_4(t_i),\ -u_i x_5(t_i)),
\end{aligned}
$$

and $\Delta x(t_i) = x(t_i + 0) - x(t_i - 0) = x(t_i + 0) - x(t_i)$ denotes the jump of state variable at t_i, $x_0 \in R^5$ is the initial state and c is the initial glycerol concentration in feed. $u_i = F_i / (\sum_{k=1}^{i} F_k + V)$ is the dilution rate at t_i, where F_i is the volume of glycerol added at t_i, $i = 1, 2, \dots, n$. V is the initial volume of fermentation broth.

Theorem 3.1. *The dynamical system* (5) *is impulsively stable if parameters in system* (5) *satisfy that* $(b_1/c_1) + (b_2/c_2) < 1$ *and* $1 + (1/Y_2)(a+1) + Y_3 + Y_4 > 0$.

Proof. Define Lyapunov function

$$
V(x) = \frac{1}{2}(x_1 - x_2)^2 + x_1 x_3 + x_1 x_4 + x_1 x_5. \tag{6}
$$

Then $V(x)$ is positive-definite and decrescent. Along solutions of (4), we have

$$
\begin{aligned}
D^+ V(x) = \frac{\partial}{\partial x} V(x) \cdot f(x) &= (x_1 - x_2 + x_3 + x_4 + x_5)\mu x_1 \\
&\quad - q_2 x_1 (x_2 - x_1) + q_3 x_1^2 + q_4 x_1^2 + q_5 x_1^2.
\end{aligned}
$$

Let $a = (b_1/c_1) + (b_2/c_2)$ to express q_5. Since $a < 1$, $1 + (1/Y_2)(a+1) + Y_3 + Y_4 > 0$ and $(\Delta_i x_2/x_2 + k_i)$, $i = 2, 3, 4$, is increasing about x_2, we have

$$\begin{aligned} D^+V(x) \le \Bigg[&(a+1)m_2 + m_3 + m_4 + \left(1 + \frac{1}{Y_2}(a+1) + Y_3 + Y_4\right)\mu_m \\ &+ (a+1)\frac{\Delta_2 x_2^*}{x_2^* + k_2} + \frac{\Delta_3 x_2^*}{x_2^* + k_3} + \frac{\Delta_4 x_2^*}{x_2^* + k_4}\Bigg] x_1^2 \\ &+ \mu_m x_1 x_2 + \mu_m x_1 x_3 + \mu_m x_1 x_4 + \mu_m x_1 x_5. \end{aligned}$$

Let $\lambda_0 = (a+1)m_2 + m_3 + m_4 + (1 + (1/Y_2)(a+1) + Y_3 + Y_4)\mu_m + (\Delta_3 x_2^*/x_2^* + k_3) + (\Delta_4 x_2^*/x_2^* + k_4)$ and $\lambda^* = \max\{2\lambda_0, \mu_m\}$. Thus, by (6),

$$D^+V(x) \le \lambda^* V(x). \tag{7}$$

This implies, by the definition of $I_i(x(t_i))$, that

$$\begin{aligned} V(x + I_i(x)) &= V(x_1(1-u_i), cu_i + x_2(1-u_i), x_3(1-u_i), \\ &\qquad x_4(1-u_i), x_5(1-u_i)) \\ &= (1-u_i)^2 V(x) - cu_i(1-u_i)x_1 + \frac{1}{2}c^2 u_i + cu_i x_2(1-u_i). \end{aligned} \tag{8}$$

Hence, $V \in \sum$. Let $\lambda_i = \Delta t_i \lambda^*$ and $c_k(s) = s$. Condition (i) of Lemma 2.1 is satisfied from (7).

There are two cases to consider for Condition (ii) of Lemma 2.1.

Case 1. $x_1 < x_2$. *Choose* u_i *that satisfies* $u_i \le (2x_1 - 2x_2 - c/2x_1 - 2x_2)$*, which implies, in view of* (8)*, that*

$$V(x + I_i(x)) \le V(x) - u_i(2-u_i)V(x). \tag{9}$$

Case 2. *For* $x_1 \ge x_2$*, we can also choose the controllable variable* u_i *such that* (9) *is satisfied.*

Let $v_i = -u_i(2-u_i)$ and $d_k(s) = s$. Then Condition (ii) of Lemma 2.1 is satisfied from (9).

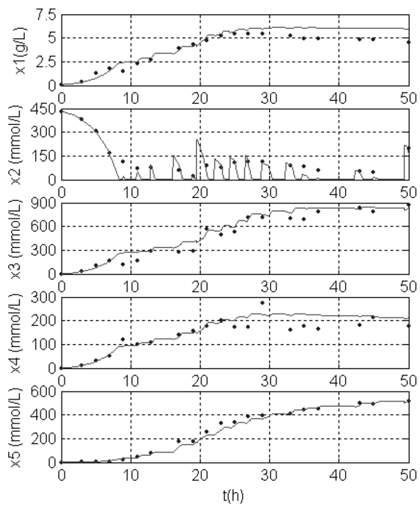

FIGURE 1. Comparison of concentrations between experimental and simulated results.

We can also choose the controllable variable u_i such that $u_i \geq 1 - \sqrt{1 - \lambda^* \Delta t_i}$, when $\lambda_i + v_i = \Delta t_i \lambda^* - u_i(2 - u_i) \leq 0$. We get $c_i(s) = d_i(s)$ if $v_i < 0$. Thus, Condition (iii) of Lemma 2.1 is satisfied. Hence system (5) is impulsively stable by Lemma 2.1.

Theorem 3.2. *Under the conditions of Theorem* 3.1, *system* (5) *is uniformly stable.*

Proof. From Definition 2.2, the function $V(x)$ of Theorem 3.1 is decrescent and $s + |v_i| d_i(s) = s + u_i(2 - u_i)s$. Let $\sigma = \eta/2$. We have

$$s + |v_i| d_i(s) \leq 2s < \eta.$$

This implies that condition (iv) of Lemma 2.1 is satisfied, and system (5) is uniformly stable. $\square$

4. Conclusion. The conditions of the parameters are given by Theorem 3.1. Under these conditions, parameter identification is realized for the fermentation process. Numerical simulation shows that the impulsive dynamical system presented in this paper can characterize the process of 1,3-propanediol production by fermentation (see Figure 1). In Figure 1, the points denote the experimental values and the real lines denote the computational curves. We obtain the errors $e_1 = 6.82$ percent, $e_2 = 15.92$ percent, $e_3 = 11.39$ percent, $e_4 = 16.23$ percent and $e_5 = 9.44$ percent. But the errors of substrate values reached 50 percent or so in [**6**]. Comparing the errors in this paper with the reported results, we conclude that the impulsive system is more fit for formulating fed-batch fermentations.

Acknowledgments. This work was supported by the Natural Science Foundation of Inner Mongolia (grant no. 200607010114), the College Project of Research in Inner Mongolia (grant no. NJZY07012) and the 513 Program Project of Inner Mongolia University.

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Department of Mathematics, College of Science, Inner Mongolia University, Hohhot, Inner Mongolia, 010021, P.R. China
Email address: gaocx0471@163.com

Department of Applied Mathematics, Dalian University of Technology, Dalian, Liaoning, 116024, P.R. China
Email address: emfeng@dlut.edu.cn