Modeling and Properties of Nonlinear Stochastic Dynamical System of Continuous Culture

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Abstract. The stochastic counterpart to the deterministic description of continuous fermentation with ordinary differential equation is investigated in the process of glycerol bio-dissimilation to 1,3-propanediol by *Klebsiella pneumoniae*. We briefly discuss the continuous fermentation process driven by three-dimensional Brownian motion and Lipschitz coefficients, which is suitable for the factual fermentation. Subsequently, we study the existence and uniqueness of solutions for the stochastic system as well as the boundedness of the Two-order Moment and the Markov property of the solution. Finally stochastic simulation is carried out under the Stochastic Euler-Maruyama method.

Keywords: Continuous Culture, Bioconversion, Nonlinear Stochastic System, Stochastic Simulation.

1 Introduction

Stochastic influences play an important role in bioprocess development (engineering). Biotechnical treatment of microorganisms is commonly described by systems of nonlinear ordinary differential equations(ODEs)[1]. It includes an idealization of the technical system component and a qualitative characterization of the biological part.

Over the past several years, 1, 3-propanediol(1, 3-PD) has been paid attention in microbial production throughout the world because of its lower cost, higher production and no pollution [2,3]. Anping Zeng presented the nonlinear dynamical model for substrate consumption and product formation in the course of the bioconversion of glycerol to 1,3-PD by Klebsiella pneumoniae in continuous culture [4,5]. And then, Zhilong Xiu made simulations for the kinetic model [6] and conducted an investigation into the optimal conditions of continuous glycerol fermentation by using the volumetric productivity of 1,3-PD as an optimziation target based on the nonlinear deterministic dynamical system [3].

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However, different culture states during long term continuous fermentation of glycerol by *K. pneumoniae* under similar initial fermentation conditions are obtained, resulting in randomness of continuous culture. This random phenomena reveal several different patterns and new features compared with those reported in previous literature. In this paper, since 1,3-PD is a monomer for the production of polycondensates in the bioprocess, we propose a stochastic version of the continuous fermentation process which only considers the inherent stochasticity of microorganism. The process is modeled by a stochastic ordinary differential system driven by three-dimensional Brownian motion, which is time independent and suitable for the factual fermentation. And the global Lipschitz and linear growth conditions of the coefficients of the stochastic system are proved to make sure the existence and uniqueness of solution of the stochastic system. Finally computer simulation is used for the stochastic system behind Monte Carlo and Stochastic Euler-Maruyama method. Compared with the results from the deterministic system, numerical results reveal the peculiar role of randomness in the dynamical responses of the continuous culture.

This paper is organized as follows. In section 2, we present a nonlinear stochastic dynamic system of the continuous fermentation process and prove the properties of the stochastic dynamic system as well as the existence and uniqueness of solutions to the stochastic dynamic system. The stochastic continuity, boundedness and Markov property of solutions to the system are also discussed. Section 3 provides numerical examples to simulate the nonlinear stochastic dynamical system of continuous culture. In section 4, we draw the conclusions and trace the direction for future works.

2 Models and Properties

2.1 Deterministic Model

Mass balances of biomass, substrate and product in contionous microbial cultures are written as follows (see [4]).

$$\begin{cases} \dfrac{dX}{dt} = X(\mu - D), \\ \dfrac{dC_s}{dt} = (D(C_{s0} - C_s) - Xq_s, \qquad t \in I = (0,T) . \\ \dfrac{dC_p}{dt} = Xq_p - DC_p, \end{cases} \tag{1}$$

where X, C_{s0}, C_s, C_p, and D are biomass, substrate concentration in medium, substrate concentration in reactor, product concentration in reactor, and dilution rate. The specific growth rate μ of biomass, specific consumption rate of substrate q_s and specific formation rate of product q_p are expressed by Eqs. (2)-(4), respectively.

$$\mu = \mu_{max}(\frac{C_s}{C_s + k_s})(1 - \frac{C_s}{C_s^*})(1 - \frac{C_p}{C_p^*}) . \tag{2}$$

$$q_s = m_s + \frac{\mu}{Y_s^m} + \Delta q_s^m \frac{C_s}{C_s + k_s^*} . \tag{3}$$

$$q_p = m_p + \mu Y_p^m + \Delta q_p^m \frac{C_s}{C_s + k_p^*} . \quad (4)$$

Under anaerobic conditions at $37°C$ and pH=7.0, the maximum specific growth rate of cells μ_{max} is $0.67h^{-1}$, Monod saturation constant k_s is 0.28 mmol$/L$. The critical concentrations of biomass, glycerol, 1,3-PD for cell growth are $X^* = 10g/L$, $C_s^* = 2039mmol/L$, $C_p^* = 939.5mmol/L$, respectively. m_s, m_p Y_s^m, Y_p^m, Δq_s^m, Δq_s^m k_s, k_s^*, k_p^* are parameters given in the previous work [3].

As far as the continuous fermentation is concerned, glycerol is added to the reactor continuously, the broth in reactor pours out at the same rate and the volume of the fermentation broth keeps constant in the whole course of bio-conversation. As a result of fact, the following assumptions can be made:

(H1) The concentrations of reactants are uniform in bio-reactor and only as varied as the fermentation time.
(H2) During the process of continuous culture, the substrate added to the reactor only includes glycerol and the fermentation broth is exported by the dilution rate D.

2.2 Stochastic Model

There are many possibilities to express the stochastic behavior of a system. The natural approach is to take the given d-dimensional deterministic model and simply add a stochastic part, given by a map $G : \mathbb{R}^{d+1} \longrightarrow \mathbb{R}^{dm}$ and an R^m-valued white noise process w_t [7]. This leads to the description as a stochastic differential equation(SDE):

$$\dot{x} = F(t, x) + G(t, x)w_t .$$

being an abbreviating notation for the exact expression

$$x_t = \int_{t_0}^{t} F(\tau, x_\tau)d\tau + \int_{t_0}^{t} G(\tau, x_\tau)dw_\tau + x_{t_0} .$$

for the stochastic process X_t with values in $\mathbb{R}^d$.

In this paper, we want to study only the influence of the noisy parameter $\mu = \bar{\mu} + \sigma_\mu \dot{w}(t)$, and replace it in Eq.(2), Eq.(3) and Eq.(4). This is a standard technique as far as stochastic population modeling is concerned. It introduces stochasticity into the model.

As a result, we get the SDE model for continuous culture,

$$dx = F(x)dt + G(x)dw, \;\; t \in I, \;\; x(0) = x_0 . \quad (5)$$

where

$$F(x) = (X(\mu - D), D(C_{s0} - C_s) - Xq_s, Xq_p - DC_p)^T, \quad (6)$$

$$G(x) = (\sigma_\mu X, \frac{\sigma_\mu X}{Y_s^m}, \sigma_\mu Y_p^m X)^T, \quad (7)$$

$$E(\dot{w}(t)) = 0,$$

$$D(\dot{w}(t)) = 1 .$$

σ_μ is the intensity of the inherent stochasticity disturbance. In Eq. (5), $x = (X, C_s, C_p)^T$ is a stochastic process that reflects the fluctuating trend of the proportion under the inherent stochasticity disturbance.

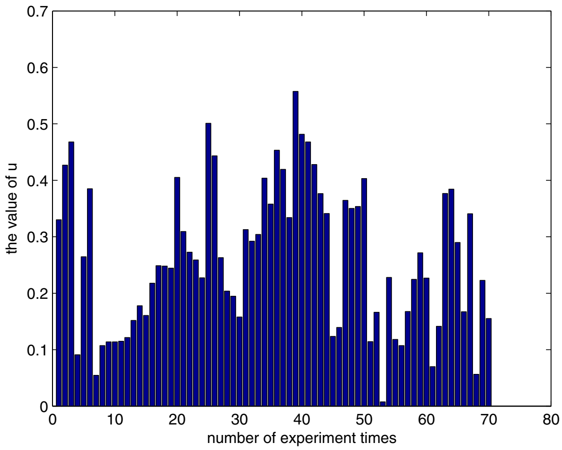

Fig. 1. The variations of the specific growth rate of cells in stable steady state.(data from Ref. [2,3,4])

To determine system noise variances σ_μ additional methods, further experiments are required. Fig. 1 shows the variations of the specific growth rate of cells in stable steady state.

2.3 Existence and Uniqueness of the SDE Solution

Theorem 1. *The vector-valued functions $F(x)$ and $G(x)$ defined by* (6) *and* (7) *are measurable for $t \in I$, $x \in R^3$.*

Proof. It is clear from the continuity of the functions $F(x)$ and $G(x)$ on I.

Theorem 2. *For the vector-valued functions $F(x)$ and $G(x)$ defined by* (6) *and* (7)*, there exist positive constants K and K' such that for $t \in I$ the following conditions hold:*

a) uniform Lipschitz condition

$$\|F(x^1) - F(x^2)\| + \|G(x^1) - G(x^2)\| \le K\|x^1 - x^2\| ,$$

$$\forall\ x^1 \ \mathit{and}\ x^2 \in R^3 .$$

b) growth condition

$$\|F(x)\| + \|G(x)\| \le K'(1 + \|x\|) .$$

Proof. From [8] We conclude that the function $F(x)$ satisfied the uniform Lipschitz condition and growth condition on R^3 a.e. . Let x^1 and x^2 be in R^3, there exists two constants L and C, we have

$$\|F(x^1) - F(x^2)\| \leq L\|x^2 - x^1\| \;\; a.e. \tag{8}$$

$$\|F(x)\| \leq C\|x\| \leq C(1 + \|x\|) \;\; a.e. \tag{9}$$

On the other hand, let $a = max\{1, \frac{1}{Y_s^m}, Y_p^m\}$ and by the definition of the function $G(x)$, we have

$$\|G(x^1) - G(x^2)\| \leq \sigma_\mu a (\sum_{i=1}^{3}(x_i^1 - x_i^2)^2)^{1/2} \leq \sigma_\mu a\|x^2 - x^1\| \; . \tag{10}$$

Thus, it follows from (6), (7) and (10)

$$\|F(x^1) - F(x^2)\| + \|G(x^1) - G(x^2)\| \leq (L + \sigma_\mu a)\|x^2 - x^1\| \; .$$

Let $K = L + \sigma_\mu a$, then we have the following inequality

$$\|F(x^1) - F(x^2)\| + \|G(x^1) - G(x^2)\| \leq K\|x^2 - x^1\| \; .$$

Next, we will show the growth condition of the function $G(x)$. It is clear from the definition of the function $G(x)$

$$\|G(x)\| \leq \sigma_\mu a\|x\| \leq \sigma_\mu a(1 + \|x\|) \; .$$

Therefore, letting $K' = \sigma_\mu a + C$, then we can complete the proof by

$$\|F(x)\| + \|G(x)\| \leq K'(1 + \|x\|) \; . \qquad \square$$

Let the vector-valued functions $F(x)$ and $G(x)$ are defined by (6) and (7). Based on the Theorem 2 and Theorem 5.2.1 [9], we can prove the following theorem.

Theorem 3 (Existence and Uniqueness). *The system* (5) *has a unique solution $x(t)$ satisfying for the initial condition x_0 on I.*

2.4 Properties of Solutions to the Stochastic Dynamic System

Lemma 1. *[10] Suppose $G : R^3 \to L(R^3, R^3)$, $\int_0^r E\|G(x(s))\|^2 dt < \infty$ and $y(t) = \int_0^t G(x(s))dW(s) < \infty$, then*

$$E\|y(t)\|^2 \leq trQ \cdot \int_0^t E\|G(s)\|^2 ds \; .$$

Where $L(R^3, R^3)$ denotes the space of all the bounded linear operators from R^3 to R^3, and Q is the covariance matrix of the Brownian motion $W(t)$ and trQ denotes the trace of $Q^T Q$.

Lemma 2. *[11] Let $\varphi(t)$ and $\alpha(t)$ be measurable bounded functions and for some $L > 0$ assume*

$$\varphi(t) \leq \alpha(t) + L \int_0^t \varphi(s) ds \ .$$

Then

$$\varphi(t) \leq \alpha(t) + L \int_0^t \exp\{L(t-s)\}\alpha(s) ds \ .$$

According to the proof in Theorem 3, Theorem 5.4 [12] and Theorem 5.2 [9], we can prove the following theorems.

Theorem 4 (Markov Property and Boundedness). *Suppose (H_1) and (H_2) hold. The unique solution $x(t)$ is a Markov process on the interval I whose initial probability distribution at $t = 0$ is the distribution of x_0 and $x(t)$ has continuous paths, moreover*

$$(sup_{0 \leq t \leq T} E\|X(t)\|)^2 < B(1 + E\|x_0\|^2) \ .$$

where constant B depends only on K and T.

Theorem 5 (Stochastic Continiuty). *Suppose that assumptions H1 and H2 are satisfied. Then, almost all realizations of $x(t)$ are continuous on I.*

Proof. We begin with another version of the linear growth conditions for the coefficients $F(x)$ and $G(x)$.

By (9) and the definition of the function $G(x)$, we can see that

$$\|F(x)\|^2 \leq C^2 \|x\|^2.$$

and

$$\|G(x)\|^2 \leq \sigma_\mu^2 a^2 \|x\|^2.$$

Hence, let $K_1^2 = C^2 + \sigma_\mu^2 a^2$ it follows that

$$E(\|F(x)\|^2 + \|G(x)\|^2) \leq E[(C^2 + \sigma_\mu^2 a^2)(1 + \|x\|)^2] \leq K_1^2 E\|x\|^2. \tag{11}$$

Suppose $t \in I$ and $\delta > 0$. Let $s \in I$ be such that $|s - t| < \delta$. From (5), we may have that

$$E\|x(s) - x(t)\|^2 = E\| \int_t^s F(x(\tau)) d\tau + \int_t^s G(x(\tau)) dw(\tau)\|^2. \tag{12}$$

Letting $K = \max\{\delta, trQ\}$, it follows from Hölder Inequality, Lemma 1 and Theorem 4 that

$$
\begin{aligned}
E\|x(s)-x(t)\|^2 &\le 4E[\int_t^s \|F(x(\tau))\|d\tau]^2 + 4E[\int_t^s G(x(\tau))dw(\tau)]^2 \\
&\le 4|s-t| \int_t^s E\|F(x(\tau))\|^2 d\tau + 4trQ \int_t^s E\|G(x(\tau))\|^2 d\tau \\
&\le 4K \int_t^s E[\|F(x(\tau))\|^2 + \|G(x(\tau))\|^2] d\tau \\
&\le 4KK_1^2 \int_t^s [1 + E\|x(\tau)\|^2] d\tau \\
&\le 4KK_1^2 B(1+E\|x_0\|^2)|s-t| \,.
\end{aligned}
$$

Set $B' = 4KK_1^2B(1+E\|x_0\|^2)$, thus the above inequality can be as follows:

$$E\|x(s)-x(t)\|^2 \le B'|s-t|,$$

or equivalently,

$$\lim_{s\to t} E\|x(s)-x(t)\|^2 = 0 \,.$$

Thus, for any $\epsilon > 0$, by Tchebycheff inequality, we conclude that

$$\mathcal{P}(\{\omega \in \Omega : \|x(s)-x(t)\| \ge \epsilon\}) \le E\|x(s)-x(t)\|^2/\epsilon^2 \,.$$

which completes the proof. □

3 Numerical Simulation

To elaborate the stochastic nature of continuous fermentation process sufficiently, an numerical example is given. In the example, $D = 0.25$/hour $C_{s0} = 735mmol/L$ and we use Monte Carlo method to generate five thousand random inputs, which consist of the infinitesimal increment of standard Brownian motion $dw(t)$. Afterwards, we solve the proposed stochastic model using the following Stochastic Euler-Maruyama method and obtain five thousand evaluations of the model. Our numerical approximation to $x(\tau_j)$ will be denoted by X_j.

Stochastic Euler-Maruyama method [12]

$$X_j^k = X_{j-1}^k + F(X_{j-1}^k)\triangle t + a_k X_{j-1}^k (W_t^l(\tau_j) - W_t^l(\tau_{j-1})), \quad j = 1, 2, ..., L \,.$$

where $\Delta t = T/L$ for some positive integer L. X^k denotes the k'th component of the x. $\tau_j = j\Delta t$, $a_1 = \sigma_\mu = 0.01638$, $a_2 = \frac{\sigma_\mu}{Y_s^m}$ and $a_3 = \sigma_\mu Y_p^m$. $x_0 = (0.98g/L, 464mmol/L, 184.36mmol/L, 57.83mmol/L, 4.41mmol/L)$, the components of which are the initial concentrations of biomass, substrate, 1,3-PD, acetic acid and Ethanol, respectively. All the parameters of the stochastic system are given in Table 1. Fig. 2 shows the comparison of biomass, substrate and product concentrations between experimental and simulated results, where the points denote the experimental values, written as $y(\tau_i)$=$(y^1(\tau_i)$, $y^2(\tau_i)$, $y^3(\tau_i))$,

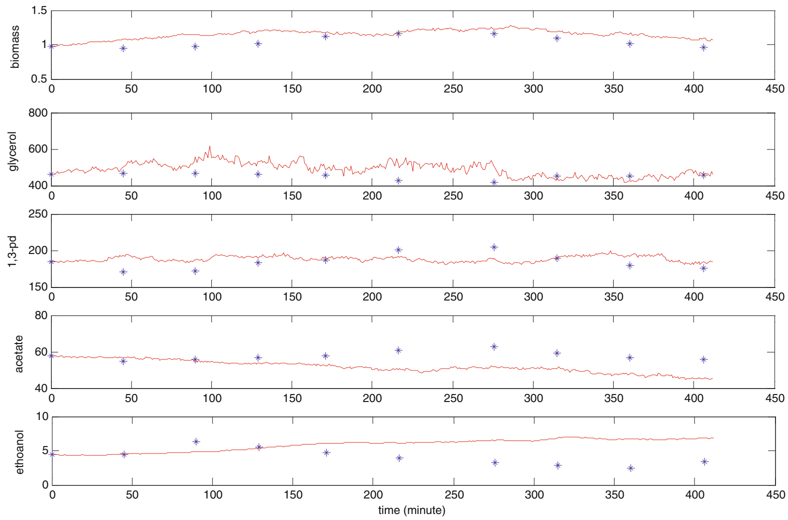

Fig. 2. The comparison of biomass, substrate and product concentrations between experimental and simulated results(acetic acid and ethanol are byproduct)

Table 1. Parameters values of each reactant in the stochastic system

Reactant	μ_m	k_s	m_i^2	Y_i	$\triangle_i$	k_i
Biomass	0.67	0.28	–	–	–	–
Glycerol	–	–	2.20	0.0082	28.58	11.43
$1,3-PD$	–	–	-2.69	67.69	26.59	15.50
Acetic acid	–	–	-0.97	33.07	5.74	85.71
Ethanol	–	–	-0.97	33.07	5.74	85.71

$i = 1, 2..., 10$, and the real lines denote the computational curves $EX^k(t)$, $k \in I_3$. Define errors as follows:

$$e_k = \frac{\sum_{i=1}^{10} |EX^k(\tau_i) - y^k(\tau_i)|}{\sum_{i=1}^{10} y^k(\tau_i)}, \qquad k \in I_3 \ .$$

We obtain the errors $e_1 = 9.37\%$, $e_2 = 6.37\%$, $e_3 = 19.85\%$. Comparing the errors in this paper with the reported results [8], we conclude that the stochastic system is more fit for modeling actual continuous fermentation under investigation.

4 Conclusions

In this paper, we present a nonlinear stochastic dynamical system of continuous culture and demonstrated the existence and uniqueness of solutions to the stochastic system. Further we proved some properties of the solution to the stochastic dynamic system. In the future we will pursue the verification and validation of the proposed stochastic system and make detailed comparison between deterministic and stochastic models of continuous culture. Moreover, we will develop into parameter estimation and stochastic optimal control problem as well as stability for the stochastic system of continuous culture.

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