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Robust identification of enzymatic nonlinear dynamical systems for 1,3-propanediol transport mechanisms in microbial batch culture

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ABSTRACT

In this paper, in view of glycerol bioconversion to 1,3-propanediol (1,3-PD) by *Klebsiella pneumoniae* (*K. pneumoniae*), we study an enzyme-catalytic nonlinear dynamic system with uncertain parameters for formulating the process of batch culture. Some important properties are also discussed. Taking account of the difficulty in accurately measuring the concentrations of intracellular substances and the absence of equilibrium point of the nonlinear system in batch culture, a novel approach is used here to define quantitatively biological robustness of the intracellular substance concentrations for the overall process of batch culture. The purpose of this paper is to identify these uncertain parameters. To this end, taking the defined biological robustness as a performance index, we establish an identification model, which is subject to the nonlinear system. Simultaneously, the existence of optimal solution to the identification model is deduced. We develop an optimization algorithm, based on novel combinations of Nelder–Mead algorithm and the change rate of state variable, for solving the identification model under various experiment conditions. The convergence analysis of this algorithm is also investigated. Numerical results not only show that the established model can be used to describe the process of batch culture reasonably, but also imply that the optimization algorithm is valid.

1. Introduction

1, 3-Propanediol (1,3-PD) is an important chemical raw material which can be used as a solvent, antifreezing agent or fine chemical engineering substance on a large commercial scale, especially as a monomer for polyesters, polyethers and polyurethanes [1]. 1,3-PD produced by fermentation of glycerol was described in 1881, but little attention was paid to this microbial route for over a century. However, its bioconversion process is recently of technical interest due to no harm to environment, high region specificity and cheaply renewable feedstock throughout the world [2]. Among all kinds of microbial production of 1,3-PD, glycerol, a by-product of the soap and detergent industry, which can be converted to 1,3-PD by a number of bacteria such as *Klebsiella pneumoniae, Clostridium butyricum* and *Citrobacter freundii*, has been widely investigated since 1980s due to its high productivity [3–5]. In 1995, Zeng et al. [6] proposed a substrate-sufficient kinetic model to describe the batch culture of substrate consumption and extracellular substances (biomass, glycerol, 1,3-PD, acetate and ethanol) formation. On the basis of Zeng's model, other researchers adopted Zeng's model to provide further investigations

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to parameter identification [7], optimal control [8], hybrid system [9], sensitivity analysis [10], stochastic model [11], time-delay system [12] and multi-stage system [13] for the batch culture.

Little attention is paid to intracellular substances in any of early batch culture references mentioned above. This is obviously a serious limitation, as intracellular substances arising in real-world applications really exist. In view of the difficulties in measuring the concentrations of intracellular substances, we judge the reliability of numerical solution for the concentrations of intracellular substances in terms of some basic characteristics of biological system. Kitano H. argues that biological robustness is a ubiquitously observed property of biological systems [14], and it is a property that allows a system to maintain its functions against internal and external perturbations [15,16]. This point of view, which has been observed for a wide variety of experiments [17,18], is being gradually accepted by experts in the field of biological system. Numerous reports have been published on how robustness is involved in various biological processes and on mechanisms that give rise to robustness in living systems [19–22]. Unfortunately, such reports, which are the lack of the quantitative definition of biological robustness, end with vague semantic references. The biological robustness has been quantitatively defined in the approximately stable state of continue culture [23,24]. None of the above literatures, however, quantitatively defined the biological robustness owing to the lack of equilibrium point in batch culture. So far, the biological robustness defined quantitatively is seldom found in batch culture.

In 2008, Sun et al. [25] firstly proposed a novel enzyme-catalytic mathematical dynamical system, of the batch culture, in which the concentration changes of both extracellular substances and intracellular substances (glycerol, 1,3-PD and 3-hydroxypropionaldehyde (3-HPA)) were all taken into consideration. In this paper, similar to the system formulated in [25], we research an enzyme-catalytic nonlinear dynamic system with uncertain parameters, for formulating the process of batch culture of glycerol to 1,3-PD by *K. pneumoniae*. Some important properties are also discussed. It is difficult to measure accurately the concentrations of intracellular substances. With this in mind, inspired by the qualitative description of the biological robustness given by Kitano [14–16], we put forward a quantitative definition of biological robustness of intracellular substance concentrations in batch culture. The proposed biological robustness, which is defined for the overall process of batch culture due to the absence of equilibrium point, is different from quantitative description of biological robustness of continue culture in the approximately stable state [23,24]. The aim of this paper is to identify these uncertain parameters. To this end, taking the proposed biological robustness as the performance index, we establish an identification model, which is subject to the constraint of the nonlinear system. Simultaneously, the existence of optimal solution to the model is deduced. We propose an optimization algorithm, based on novel combinations of Nelder–Mead algorithm and the change rate of state variable, for solving the identification model under various experiments conditions. The convergence analysis of this algorithm is also investigated. Finally, an illustrative numerical example shows the appropriateness of the model and the validity of the optimization algorithm.

The reminder of this paper is organized as follows. In Section 2, an enzyme nonlinear dynamical system is formulated to describe the batch culture and some important properties are proved. In Section 3, the identification problem is proposed via biological robustness. In Section 4, furthermore, an optimization algorithm is constructed to apply it to the identification problem. In Section 5, numerical results are presented. In Section 6, we draw the conclusions and trace the direction for future works.

2. The multi-stage nonlinear dynamical system and its properties

In the anaerobic conditions, in view of the batch culture of glycerol to 1,3-PD by *K. pneumoniae*, the intracellular main metabolism path includes oxidation and reductive pathways. We mainly consider the batch culture of reductive pathway by the action of enzyme catalysis. We take the mode of transportation by which glycerol transports from extracellular to intracellular as the combination of active transport and passive transport. Transport mechanism of 1,3-PD from intracellular to extracellular is known as passive transport. In the light of the factual experiment, the following conditions will be in force throughout the rest of this paper, whether explicitly mentioned or not.

H1. No medium is pumped inside and outside the bioreactor in the process of batch fermentation.

H2. The concentrations of reactants are uniform in reactor, while time delay and nonuniform space distribution are ignored.

Under the assumptions (**H1**)–(**H2**), the process of batch culture can be formulated by the following system that is similar to the one formulated in[10,25],

$$\begin{cases} \dot{x}(t) = h(x, u_p), t \in [0, t_f], \\ x(0) = x_0, \end{cases} \tag{1}$$

where $x(t) = [x_1(t), \ldots, x_8(t)] \in R^8$ is the state variable, and $x_1(t), \ldots, x_8(t)$ denote the concentrations of biomass, extracellular glycerol, extracellular 1,3-PD, acetate, ethanol, intracellular glycerol, 3-hydroxypropionaldehyde (3-HPA) and intracellular 1,3-PD at time t, respectively. $[0, t_f] \subset R_+$ is the interval of reaction time, and $x_0 \in R^8$, is the initial state. To simplify notation, let $I_n := \{1, 2, \ldots, n\}, \forall n \in \mathbb{N}$.

Now, the mass balances of biomass, substrate and products in batch microbial cultures can be formulated as follows in terms of literature[25]. Namely, the right term of *system* (1) is: