



## Education Article

# Optimal control of nonlinear switched system in an uncoupled microbial fed-batch fermentation process

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## Abstract

The bio-dissimilation of glycerol to 1,3-propanediol (1,3-PD) is a complex bioprocess due to the multiple inhibitions of substrate and products onto the cell growth. In consideration of both the inhibition mechanisms of 3-hydroxypropionaldehyde (3-HPA) and the transport modes of glycerol and 1,3-PD across the cell membrane, we establish a novel switched system which is represented by a ten-dimensional nonlinear dynamical equation containing both extracellular and intracellular environments. The uncoupled microbial fed-batch fermentation process are modeled using the switched system which the glycerol and alkali are respectively poured into. Taking the feeding rates of glycerol and alkali, the switching times and the mode sequence as the control variables, an optimal control model is proposed with the concentration of the terminal time 1,3-PD as performance index. In order to maximize the yield of 1,3-PD, the control parameterization technique and the exact penalty function method are used to solve the considered problem. Numerical results show that under the obtained optimal feeding rates of glycerol and alkali, switching times and mode sequence, the productivity of 1,3-PD at the terminal time is increased significantly compared with previous results.

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## 1. Introduction

1,3-Propanediol (1,3-PD) has been widely applied in polymers, cosmetics, food, lubricants and medicines. Generally, production methods for 1,3-PD have two categories: chemical

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synthesis and microbial conversion. Compared with chemical synthesis, the microbial conversion of glycerol to 1,3-PD has been given much attention due to its low cost and no pollution. There are three typical cultures for microbial fermentation of glycerol, including batch, continuous and fed-batch cultures, among which the fed-batch fermentation has attracted great interest due to its high productivity [1].

The fed-batch culture starts with batch fermentation, then batch-fed glycerol and alkali are respectively poured into the reactor so that the concentration of glycerol keeps in a proper range and the pH value of the solution in a required level [2]. Thus the system describing the fed-batch culture actually is a nonlinear switched system [3–6]. To improve the productivity of the fed-batch culture, the feeding rates of glycerol and alkali, the feeding instants and sequence should be controlled in a proper level. In consideration of expensive cost, it is impossible to carry out plenty of experiments under various feeding strategies of glycerol and alkali to obtain the optimal one. It has been widely recognized that mathematical modeling is an important tool for simulation and optimization of microbial fermentation. Therefore, a relative accurate mathematical model to formulate the fermentation process becomes a key aspect of the problem. Zeng et al. [7–9] proposed a kinetic model, in which the concentrations of biomass, glycerol and products (1,3-PD, acetic acid and ethanol) in reactor were considered. Xiu and Zeng [10] modified Zeng's model by introducing an excess term to describe the continuous fermentation and batch fermentation. Based on Xiu's model, other researchers investigated the parameter identification, stability of equilibria and phenomena of oscillation and hysteresis for the continuous fermentation [11–15]. According to whether the alkali feeding is coupled with the glycerol feeding or determined by pH logic controller, the fed-batch culture can be classified into the coupled fed-batch culture and the uncoupled one [16]. In recent years, many researchers have studied the former case's modeling, parameter identification, optimal control and so on [17–20]. In 2011, Ye et al. [21] proposed a mathematical model for the uncoupled fed-batch culture and investigated parameter identification and optimal control. However, the above research literatures have taken only the concentrations of extracellular substances into consideration.

In fact, since the microbial growth is subject to multiple inhibitions of substrate and products, the fermentation of glycerol bioconversion to 1,3-PD should cover both extracellular and intracellular environments. Some important intracellular intermediate metabolites and enzymes such as 3-hydroxypropionaldehyde (3-HPA), glycerol dehydratase (GDHt) and 1,3-PD oxydoreductase (PDOR), which play important roles in glycerol metabolism, have never been taken into consideration in the above models. In 2008, taking the concentration of both the extracellular and intracellular substances into account, Sun et al. [22] proposed a mathematical model for the continuous fermentation under the assumptions that glycerol passes the cell membrane by active transport coupled with passive diffusion and 1,3-PD passes the cell membrane by passive diffusion. Since the principle that 3-HPA inhibits the cell growth is still unclear, and the transport mechanisms of glycerol and 1,3-PD are exactly unknown, Zhai et al. [23] established a pathway and parameter identification model based on Sun's model. The most possible pattern is inferred that both glycerol and 1,3-PD pass the cell membrane by active transport coupled with passive diffusion and that there exists an inhibition of 3-HPA to the cell growth, but the inhibitions of 3-HPA to GDHt and PDOR exist only when the 3-HPA concentration reaches a critical concentration. On the basis of these researchers, however, uncoupled microbial fed-batch culture and optimal control with taking the concentrations of the intracellular substances (glycerol, 1,3-PD and 3-HPA) into consideration have never been discussed.

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