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Optimization of a fed-batch bioreactor for 1,3-propanediol production using hybrid nonlinear optimal control

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ABSTRACT

A nonlinear hybrid system was proposed to describe the fed-batch bioconversion of glycerol to 1,3-propanediol with substrate open loop inputs and pH logic control in previous work [47]. The current work concerns the optimal control of this fed-batch process. We slightly modify the hybrid system to provide a more convenient mathematical description for the optimal control of the fed-batch culture. Taking the feeding instants and the terminal time as decision variables, we formulate an optimal control model with the productivity of 1,3-propanediol as the performance index. Inequality path constraints involved in the optimal control problem are transformed into a group of end-point constraints by introducing an auxiliary hybrid system. The original optimal control problem is associated with a family of approximation problems. The gradients of the cost functional and the end-point constraint functions are derived from the parametric sensitivity system. On this basis, we construct a gradient-based algorithm to solve the approximation problems. Numerical results show that the productivity of 1,3-propanediol can be increased considerably by employing our optimal control policy.

1. Introduction

1,3-Propanediol (1,3-PD) has wide applications for a large volume of markets, especially as a monomer for polyesters, polyethers and polyurethanes [19]. Generally, 1,3-PD is produced by chemical or biotechnological route. Compared with chemical synthesis, the bioconversion of glycerol to 1,3-PD is more attractive to industry since it is environmentally safe and has renewable feedstock [49]. 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 [10].

To improve the productivity of the fed-batch culture, the concentration of the substrate should be controlled in a proper level. In the laboratory, the addition of the substrate is determined by a preassigned sequence of feeding times, which is usually given on an empirical basis. With consideration of expensive cost, it is impossible to carry out plenty of experiments under various glycerol feeding strategies to obtain the optimal one. For this reason, mathematical modelling and optimal control of this microbial process become necessary.

Over the past decades, model-based optimization of biological processes has been attracted the attention of many scientists and engineers [1,3,9]. Banga et al. [2] presented an excellent review of various methods for bioreactor optimization. Recently, researchers have also put great effort on multiple objective optimal control of bioprocesses [25,26,28]. Modelling and optimization of glycerol fermentation by *Klebsiella pneumoniae* have been considered by Gao et al. [16], Wang et al. [40], Yan et al. [46], Liu et al. [24] and Wang et al. [41–43]. However, most of the previous researches on this bioprocess only considered the technique with both open loop inputs of glycerol and alkali. Till now, the technique with open loop glycerol inputs and pH logic control is seldom discussed, and the existing theoretical work in this aspect includes the nonlinear hybrid modelling [47] and the continued parameter identification in Ref. [48]. Yet optimal control of this bioprocess has not been discussed.

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To address optimal control problems, there are in general two categories of methods: indirect methods, which are based on solving Pontryagin's necessary conditions [8], and direct method, in which the infinite dimensional optimization problem is reduced to a finite dimensional one by using control parameterization [17] or complete discretization [31,36].

Control parameterization methods (known as sequential methods) have been extensively studied from both theoretical and applied aspects over the past decades. See, for example, Refs. [4,5,27,37]. In control parameterization, only the controls are discretized and the dynamic system is decoupled from the optimization stage. Given initial conditions and a set of control parameters, the dynamic system is solved within an inner loop controlled by an NLP solver, and parameters representing the control variables are updated by the NLP solver itself. One of the advantages of control parameterizations scheme is that a good approximation of the state variables can be obtained without affecting the size of the NLP problem. However, if the inequality path constraints are involved, the solution would become much more complicated due to the potential high-index DAEs composed of the active path constraints and the original ODEs or DAEs. To overcome this problem, Feehery and Barton [14,15] have proposed an approach based on the dummy derivatives to deal with high-index DAEs. Other practical methods are included in Ref. [11] and the references therein. In general, handling the path constraints by using DAE solver would reduce the number of decision variables in the combined NLP solver, because part of the decision variables may be directly determined in the DAE solver. Therefore, this method for handling path constraints would be much more efficient than that including the path constraints in the master NLP [15].

In complete discretization (known as simultaneous approach) the state variables are discretized at the same level of the control variables. Tsang et al. [36] used collocation to discretize the dynamic system. Biegler [6] applied global orthogonal collocation and Lagrange polynomials for the approximation of the continuous variables. An efficient simultaneous solution strategy based on multiple shooting and reduced SQP was proposed by Leineweber et al. [22,23]. An excellent review of simultaneous strategies can be founded in Biegler [7]. The simultaneous approaches have several advantages: firstly, simultaneous approaches directly couple the solution of ODE/DAE system with the optimization problem, the dynamic system needs to be solved only once during the optimization procedure; secondly, simultaneous approaches can deal with instabilities that occur for a range of inputs; thirdly, simultaneous approaches such as multiple shooting method have advantages for singular control problems and problems with high index path constraints. In particular, the simultaneous strategy is the relative ease in handling path constraints by including them directly in the optimization problem as a set of point constraints [14]. Recent work [12] has also shown that the simultaneous approaches have advantages in parallel computing. However, it has been well recognized that the simultaneous approaches lead to large scale NLP that requires efficient optimization strategies [7].

The optimization of glycerol fed-batch process considered in this work is a dynamic optimization of switching times due to the special control method of this bioprocess. In the laboratory, since it is hard to control the flow rate of glycerol precisely by the pump, the flow rate is set to be a fixed constant and the inlet flow is controlled by on/off switches of the pump. Therefore, the decision variables are the feeding instants and the terminal time, and the considered problem is essentially an optimal parameter selection problem (OPSP) with inequality path constraints arising from biochemical limitations on the system. It is therefore not necessary to use discretization technique for this problem. In addition, it is not suitable for OPSP to directly handle the path constraints in the DAE solver. The reason is that one often fails to determine part of the decision variables due to the possible over-determination in the DAE system.

In this work, we firstly modify the hybrid system proposed in our previous work [47] on the basis of a control method that is much easier to be implemented on the equipment of our laboratory. Then, taking the feeding instants and the terminal time as decision variables, we formulate a free-time optimal control model with the productivity of 1,3-PD as performance index, in which inequality path constraints are involved. An auxiliary state-based impulsive system is introduced to derive the sensitivity functions of the hybrid system with respect to the decision variables, and the inequality path constraints are transformed into a group of end-point constraints. The original optimal control problem is finally associated with a family of approximation ones, parameterized by a tolerance error for the end-point constraints. A gradient-based algorithm is constructed to solve the approximation problem. Numerical results show that the algorithm can solve the optimal control problem efficiently.

This paper is organized as follows. In Section 2, we present the nonlinear hybrid dynamical system of the fed-batch culture and the basic properties of the system. In Section 3, an optimal control model with path constraints is formulated, and the corresponding approximation problems are deduced. Section 4 is devoted to the algorithm of the approximation problems and Section 5 shows the corresponding numerical results. Discussions and conclusions are presented at the end of this paper.

2. Reformulation of the nonlinear hybrid dynamical system in fed-batch culture

The fermentation of glycerol by *K. pneumoniae* is a complex bioprocess, since microbial growth is subjected to multiple inhibitions of substrate and products [49]. Among most of the literature, the considered states are the biomass, the substrate glycerol, the product 1,3-PD, the inhibitory metabolites acetate and ethanol [40,41,49]. In our previous work [47], we introduced two additional states, Na^+ ions and the volume of the solution, so as to formulate the logic control of the pH of the solution in the reactor.

In the fed-batch culture, the substrate glycerol is discontinuously added to the reactor every so often in order that glycerol concentration keeps in a given range. Alkali (NaOH solution) is also fed into the reactor from time to time for neutralizing the formed acid byproduct such as acetic acid, lactic acid, succinic acid and so on. The inputs of glycerol and alkali are determined by a preassigned time sequence and a pH logic controller, respectively. The flows of alkali and glycerol are set to be constant rates. According to the above description, the fermentation switches among the following four different operating modes throughout the entire fed-batch process.

Mode 0. Batch process (no glycerol or alkali feeding);
Mode 1. Semibatch process with alkali feeding only;
Mode 2. Semibatch process with feeding glycerol only;
Mode 3. Semibatch process with both glycerol and alkali feeding.

Some notations are adopt as follows. Let $[t_0, T]$ be the entire time horizon of the fed-batch fermentation, and let $T_{ad} := [T_*, T^*]$ be the admissible set of T, which is known a prior in the laboratory. Let $x(t) := (x_1(t), x_2(t), \ldots, x_7(t))^\top$ be the continuous state vector at time t,