TIME-DELAY OPTIMAL CONTROL OF A FED-BATCH PRODUCTION INVOLVING MULTIPLE FEEDS

CHONGYANG LIU¹ and MEIJA HAN²

1. School of Mathematics and Information Science,
   Shandong Technology and Business University, Yantai 264005, China
2. School of Computer Science and Technology,
   Shandong Technology and Business University, Yantai 264005, China

ABSTRACT. In this paper, we consider time-delay optimal control of 1,3-propanediol (1,3-PD) fed-batch production involving multiple feeds. First, we propose a nonlinear time-delay system involving feeds of glycerol and alkali to formulate the production process. Then, taking the feeding rates of glycerol and alkali as well as the terminal time of process as the controls, we present a time-delay optimal control model subject to control and state constraints to maximize 1,3-PD productivity. By a time-scaling transformation, we convert the optimal control problem into an equivalent problem with fixed terminal time. Furthermore, by applying control parameterization and constraint transcription techniques, we approximate the equivalent problem by a sequence of finite-dimensional optimization problems. An improved particle swarm optimization algorithm is developed to solve the resulting optimization problems. Finally, numerical results show that 1,3-PD productivity increases considerably using the obtained optimal control strategy.

1. Introduction. 1,3-Propanediol (1,3-PD) is an odorless viscous liquid for synthesis of polyesters, polyurethanes and heterocyclic compounds [9]. It has numerous applications in solvents, antifreeze, lubricants and other fields [24]. 1,3-PD can be produced from renewable resources such as glycerol using microorganisms with advantages of mild conditions, simple operation, and fewer by-products [2].

Glycerol can be converted to 1,3-PD via one of three microbial production modes: batch production, continuous production and fed-batch production. In particular, fed-batch production is a mixture of the batch and continuous productions. During the bioconversion of glycerol to 1,3-PD, the most efficient cultivation method appears to be a fed-batch culture which corrects pH by alkali addition with glycerol supply [34]. Fed-batch production is commonly used in industrial production due to its ability to overcome catabolite repression or glucose effect which usually occurs during production of fine chemicals. A proper feeding rate, with the right component constitution, is required in order to improve production during the process. Moreover, fed-batch production also gives the operator of freedom of manipulating the process via the feeding rates. Therefore, optimal control of feeding rates in fed-batch production has received extensive attention. Assuming the feeding of substrate only occurs at the impulsive instants, optimal impulsive
control of fed-batch production is discussed in \[1, 4, 27\]. Nonetheless, since the feeding rate of substrate is finite, it is not reasonable to describe the fed-batch production by the impulsive process. In contrast, taking the feeding rate of substrate as a time-continuous process, optimal multistage control of fed-batch production is investigated in \[17\]. Furthermore, regarding the fed-batch production as switching between batch process and feeding process, optimal switched control is studied in \[30\]. However, time-delays are ignored in the above optimal control problems. In fact, like most real processes, fed-batch production is also influenced by time-delays since nutrient metabolization does not immediately lead to the production of new biomass \[28\]. Recently, time-delay optimal control of fed-batch production is discussed in \[15, 18, 19\]. More recently, a published book \[16\] summarizes some optimal control results arising in fed-batch production processes. Although the results obtained are interesting, the control action in the above optimal control problems only includes the feeding rate of substrate glycerol and the feeding rate of alkali is obtained by an empirical velocity ratio of alkali to glycerol. Obviously, this cannot guarantee the obtained feeding rate of alkali to be optimal.

In this paper, we propose a nonlinear time-delay system involving feeds of both glycerol and alkali to formulate 1,3-PD fed-batch production. Taking 1,3-PD productivity as the performance index and the feeding rates of glycerol and alkali as well as the terminal time of process as the controls, we present a time-delay optimal control model subject to control and state constraints. Then, by a time-scaling transformation, we convert the optimal control problem into an equivalent problem with fixed terminal time. Furthermore, by exploiting control parameterization and constraint transcription techniques \[26\], we approximate the equivalent problem by a sequence of finite-dimensional optimization problems. An improved particle swarm optimization (PSO) algorithm is developed to solve the resulting optimization problems. Finally, numerical results show that 1,3-PD productivity increases considerably by utilizing the obtained optimal control strategy.

The organization of this paper is as follows. In Section 2, a nonlinear time-delay system involving multiple feeds for 1,3-PD fed-batch production is formulated. Section 3 gives time-delay optimal control model and its equivalent form. Section 4 develops a numerical solution method to solve the equivalent problem, while Section 5 illustrates the numerical results. Finally, conclusions are provided in Section 6.

### 2. Nonlinear time-delay systems

1,3-PD fed-batch production switches between batch process and feeding process. In batch process, nothing is added to and removed from the reactor. In feeding process, glycerol and alkali are continuously added to provide nutrition and maintain a suitable environment for cells growth. In particular, time-delays exist in the production process \[28\]. According to the production process, we assume that

**Assumption 1.** The concentrations of reactants are uniform in reactor. Nonuniform space distribution is ignored.

**Assumption 2.** Biomass, substrate, 1,3-PD, acetate and ethanol concentrations in reactor at time \(t\) are determined by biomass at time \(t - h\).

Under Assumptions 1 and 2, mass balances of biomass, substrate and products in fed-batch production can be formulated as the following nonlinear time-delay
system:

\[
\begin{align*}
    \dot{x}(t) &= f(t, x(t), x(t-h), u(t)), \\
    u(t) &\in U(t), \quad t \in (0, T], \\
    x(t) &= \phi(t), \quad t \in [-h, 0],
\end{align*}
\]

(1)

where \( x(t) := (x_1(t), x_2(t), x_3(t), x_4(t), x_5(t))^\top \in \mathbb{R}^5 \) is the state vector whose components are, respectively, the concentrations of biomass, glycerol, 1,3-PD, acetic acid and ethanol; \( u(t) := (u_1(t), u_2(t))^\top \in \mathbb{R}^2 \) is the feeding rate vector of glycerol and alkali, the control vector; \( h \) is a given delay argument; \( T \) is the free terminal time; \( \phi : R \to \mathbb{R}^5 \) is a given history function; and

\[
f(t, x(t), x(t-h), u(t)) := \begin{pmatrix} 
    \mu(x(t))x_1(t-h) - D(t, u(t))x_1(t) \\
    D(t, u(t))(c_{s0} - x_2(t)) - q_2(x(t))x_1(t-h) \\
    q_3(x(t))x_1(t-h) - D(t, u(t))x_3(t) \\
    q_4(x(t))x_1(t-h) - D(t, u(t))x_4(t) \\
    q_5(x(t))x_1(t-h) - D(t, u(t))x_5(t)
\end{pmatrix}.
\]

(2)

In (2), \( c_{s0} > 0 \) denotes the concentration of initial feed of glycerol in the medium. \( D(t, u(t)) \) is the dilution rate defined as

\[
    D(t, u(t)) := \frac{u_1(t) + u_2(t)}{V(t)},
\]

(3)

where

\[
    V(t) := V_0 + \int_0^t (u_1(s) + u_2(s))ds,
\]

and \( V_0 \) is the initial volume of culture fluid in the reactor.

Based on the previous work [14], the specific growth rate of cells \( \mu(x(t)) \), the specific consumption rate of substrate \( q_2(x(t)) \), and the specific formation rates of products \( q_\ell(x(t)), \ell = 3, 4, 5, \) are expressed as the following equations:

\[
    \mu(x(t)) = \frac{\Delta_1 x_2(t)}{k_1 + x_2(t)} \prod_{\ell=2}^5 \left(1 - \frac{x_{\ell}(t)}{x^*_\ell}\right),
\]

(4)

\[
    q_2(x(t)) = m_2 + \frac{\mu(x(t))}{Y_2} + \Delta_2 \frac{x_2(t)}{k_2 + x_2(t)},
\]

(5)

\[
    q_\ell(x(t)) = m_\ell + \mu(x(t))Y_\ell + \Delta_\ell \frac{x_2(t)}{k_\ell + x_2(t)}, \quad \ell = 3, 4,
\]

(6)

\[
    q_5(x(t)) = q_2(x(t)) \left( \frac{c_1}{c_2 + \mu(x(t))x_2(t)} + \frac{c_3}{c_4 + \mu(x(t))x_2(t)} \right),
\]

(7)

where \( \Delta_1, k_1, m_2, Y_2, \Delta_2, k_2, m_\ell, Y_\ell, \Delta_\ell, k_\ell, c_1, c_2, c_3, \) and \( c_4 \) are kinetic parameters; and \( x^*_\ell \) are critical concentrations for cells growth.

Let \( 2N + 1 \) be the total number of batch and feeding processes (\( N \) feeding processes and \( N + 1 \) batch processes, since the fed-batch process starts and finishes in batch process) in fed-batch process. Then, we denote the start moment of the batch process by \( t_{2j} \), and the start moment of feeding process by \( t_{2j+1}, j \in \{0, 1, \ldots, N\} \). Note that the number of \( 2N + 1 \) is determined by the terminal time \( T \). Therefore, \( T \in \mathbb{R}^1 \) is called an admissible terminal time if it satisfies the following bound constraint:

\[
    T_{\min} \leq T \leq T_{\max},
\]

(8)
where $T_{\text{min}}$ and $T_{\text{max}}$ are, respectively, the lower and upper bounds of terminal time. Let $\mathcal{T}$ be the set of all such admissible terminal times. Furthermore, define

$$
U_i := \begin{cases} 
[a^1_i, b^1_i] \times [a^2_i, b^2_i], & \text{if } i \text{ is even}, \\
\{0\} \times \{0\}, & \text{if } i \text{ is odd},
\end{cases}
$$

where $a^1_i > 0$ and $b^1_i > 0$ are, respectively, the minimal and maximal feeding rates of glycerol; and $a^2_i > 0$ and $b^2_i > 0$ are, respectively, the minimal and maximal feeding rates of alkali. Thus,

$$
U(t) = U_i, \quad t \in (t_{i-1}, t_i], \quad i = 1, \ldots, 2N + 1.
$$

Any essentially bounded function $u$ from $[0, T_{\text{max}}]$ into $\mathbb{R}^2$ such that $u(t) \in U(t)$ is called an admissible control. Let $U$ be the class of all such admissible controls. Any pair $(u, T) \in U \times \mathcal{T}$ is called an admissible pair for time-delay system (1).

It should be noted that there exist critical concentrations of biomass, glycerol, 1,3-PD, acetate and ethanol, outside which cells cease to grow. Thus, it is biologically meaningful to restrict the concentrations of biomass, glycerol and products within a set $W$ defined as

$$
x(t) \in W := \prod_{\ell=1}^5 [x^\ell_*, x^\ell_*], \quad t \in [0, T],
$$

where $x^\ell_*$ are the lower thresholds for cell growth of biomass, glycerol, 1,3-PD, acetic acid, and ethanol, respectively; and $x^\ell_*$ ($x^1_*, x^2_*, x^3_*$ and $x^5_*$ as used in the formula for $\mu(x(t)))$ are the corresponding upper thresholds.

3. **Time-delay optimal control problems.** Let $x(\cdot|u, T)$ be the continuous solution of time-delay system (1) on $[-h, T]$ corresponding to each $(u, T) \in U \times \mathcal{T}$. It is desired that 1,3-PD productivity is maximized at the terminal time in 1,3-PD fed-batch production process, where 1,3-PD productivity is defined as

$$
\frac{x_3(T|u, T)}{T}.
$$

As a result, taking 1,3-PD productivity as the performance index and incorporating the constraints (8), (10) and (11), we can state the time-delay optimal control problem as follows:

$$
\begin{align*}
\text{(OCP)} \quad \max & \quad J(u, T) = \frac{x_3(T|u, T)}{T} \\
\text{s.t.} & \quad x(t|u, T) \in W, \quad t \in [0, T], \\
& \quad (u, T) \in U \times \mathcal{T}.
\end{align*}
$$

Problem (OCP) is a time-delay optimal control problem with free terminal time in system (1). It is difficult to solve numerically because time-delay system (1) must be integrated over a variable time horizon. To surmount this difficulty, we apply the following time-scaling transformation [20]:

$$
t = Ts,
$$

where $s \in [-\tilde{h}, 1]$ is a new time variable with $\tilde{h} = h/T$. Then, time-delay system (1) can be transformed into an equivalent form as follows:

$$
\begin{align*}
\dot{x}(s) &= \tilde{f}(s, \tilde{x}(s), \tilde{x}(s - \tilde{h}), \tilde{u}(s), T), \\
\tilde{u}(s) &\in \tilde{U}(s), \quad s \in (0, 1], \\
\tilde{x}(s) &= \tilde{\phi}(s), \quad s \in [-\tilde{h}, 0],
\end{align*}
$$

where
where \( \hat{x}(s) := x(Ts); \hat{u}(s) := u(Ts); \hat{f}(s, \hat{x}(s), \hat{x}(s - \hat{h}), \hat{u}(s), T) := Tf(s, \hat{x}(s), \hat{x}(s - \hat{h}), \hat{u}(s)); \) and \( \hat{\phi} := \phi(Ts). \) In addition, \( s_{2N+1} = 1, \) and the switching moments \( t_i \) in original time are converted into \( s_i = t_i/T, \) \( i = 1, \ldots, 2N. \) Accordingly,
\[
\hat{U}(s) = U_i, \ s \in (s_{i−1},s_i], \ i = 1, \ldots, 2N + 1, \tag{15}
\]
and the set of admissible controls becomes
\[
\hat{U} := \{ \hat{u} \in L_{\infty}([0,1], R^2) \mid \hat{u}(s) \in \hat{U}(s), s \in [0,1] \}, \tag{16}
\]
where \( L_{\infty}([0,1], R^2) \) denotes the Banach space of all essentially bounded functions from \([0,1]\) into \( R^2. \)

Let \( \hat{x}(1|\hat{u}, T) \) be the continuous solution of system (14) on \([-\hat{h},1]\) corresponding to each \((\hat{u}, T) \in \hat{U} \times T.\) Then, constraint (11) turns into
\[
\hat{x}(s|\hat{u}, T) \in W, \ s \in [0,1]. \tag{17}
\]
Thus, Problem (OCP) is converted into the following equivalent problem:
\[
\text{(EOCP)} \quad \max \ f(\hat{u}, T) = \frac{\hat{x}_3(1|\hat{u}, T)}{T} \tag{EOCP}
\]
\[
\text{s.t.} \quad \hat{x}(s|\hat{u}, T) \in W, \ s \in [0,1],
\]
\[
(\hat{u}, T) \in \hat{U} \times T. \quad \tag{EOCP}
\]
Note that Problem (EOCP) is a time-delay optimal control problem with fixed terminal time in system (14).

4. Numerical solution methods. Problem (EOCP) is, in essence, an optimal control problem. It is well known that the control parameterization technique is very efficient in solving optimal control problems [6, 5, 7, 13, 26, 31].

The control parameterization is applied to approximating Problem (EOCP) as follows. Let \( \Lambda := \{1, \ldots, 2N + 1, \ldots, p_i \geq 1, \ i \in \Lambda, \) the time subinterval \([s_{i−1}, s_i] \) is divided into \( n_{p_i} \) subintervals with \( n_{p_i} + 1 \) partition points such that
\[
s_{i−1} = p_{i−1} < p_i < \cdots < p_{n_{p_i}} = s_i. \tag{18}
\]
With piecewise-constant basis functions, the control \( \hat{u} \) is approximated as
\[
\hat{u}^p(s|\sigma^p, T) = \sum_{i=1}^{2N+1} \sum_{k=1}^{n_{p_i}} \sigma^{p_{i,k}} \chi(p_{i−1,k}:p_{i,k}]\times(s), \ s \in [0,1], \tag{19}
\]
where \( \sigma^p = (\sigma^{p_1,1}, \ldots, \sigma^{p_{2N}}, T) \) with \( \sigma^{p_i} = (\sigma^{p_{i,1}}, \ldots, \sigma^{p_{i,n_{p_i}}}, T; \) and for a given interval \( I, \) \( \chi_I \) is the characteristic function defined as
\[
\chi_I(s) := \begin{cases} 1, & s \in I, \\ 0, & \text{otherwise}. \end{cases} \tag{20}
\]
From (15), we obtain the following bound constraints on \( \sigma^p: \)
\[
\sigma^{p_{i,k}} \in U_i, \ k = 1, \ldots, n_{p_i}, \ i = 1, \ldots, 2N + 1. \tag{21}
\]
Let \( \Xi^p \) denote the set of all \( \sigma^p \) satisfying constraint (21).

Substituting (19) into system (14) yields
\[
\begin{align*}
\hat{x}(s) &= \hat{f}(s, \hat{x}(s), \hat{x}(s - \hat{h}), \hat{u}(s), T), \ s \in [p_{k−1}, p_{k}], \\
\sigma^{p_{i,k}} &\in U_i, \ k = 1, \ldots, n_{p_i}, \ i = 1, \ldots, 2N + 1, \\
\hat{x}(s) &= \hat{\phi}(s), \ s \in [-\hat{h}, 0]. \tag{22}
\end{align*}
\]
Let \( \tilde{x}(\cdot|\sigma^p, T) \) be the continuous solution of system (22) on \([-\tilde{h}, 1]\) corresponding to each \((\sigma^p, T) \in \Xi^p \times T\). Then, constraint (17) becomes
\[
\tilde{x}(s|\sigma^p, T) \in W, \hspace{1em} s \in [0, 1].
\] (23)

Thus, Problem (EOCP) can be approximated by the following finite-dimensional optimization problem:
\[
\text{(EOCP}(p)) \quad \max \quad J(\sigma^p, T) = \frac{\tilde{x}_3(1|\sigma^p, T)}{T}
\text{ s.t. } \tilde{x}(s|\sigma^p, T) \in W, \hspace{1em} s \in (0, 1], \quad (\sigma^p, T) \in \Xi^p \times T.
\]

Problem (EOCP\((p))\) is a semi-infinite programming involving continuous state inequality constraint (23). As is well known, it is difficult to numerically solve (EOCP\((p))\) directly. By the way, to numerically computation constraint (23), an integral penalty method [3] and an equivalent end-point constraints method [23] were introduced. Nevertheless, a common characteristic of all these techniques is that the penalty terms or end-point constraints introduced have zero gradients with respect to optimization variables at the optimal solution. This, in turn, can result in a reduced convergence rate near the optimal solution. This problem can be dealt with by two approaches: a constraint transcription technique [10, 26, 29]; and an exact penalty method [11, 32]. In this paper, we choose to apply the constraint transcription technique [26] to approximate constraint (23) due to its effectiveness and simplicity. Thus, let
\[
g_\ell(\tilde{x}(s|\sigma^p, T)) := \tilde{x}_\ell(s|\sigma^p, T) - x^*_\ell, \quad g_{5+\ell}(\tilde{x}(s|\sigma^p, T)) := x^*_\ell - \tilde{x}_\ell(s|\sigma^p, T), \hspace{0.5em} \ell = 1, \ldots, 5.
\]

The constraint (23) is equivalent to
\[
G(\sigma^p, T) := \sum_{\ell=1}^{10} \int_0^1 \max \{0, g_\ell(\tilde{x}(s|\sigma^p, T))\} ds.
\] (24)

However, constraint (24) is non-smooth since \(\max\{0, \cdot\}\) is non-differentiable at the origin. Thus, we replace constraint (24) with the following smooth inequality constraint in canonical form:
\[
\tilde{G}^{\epsilon,\gamma}(\sigma^p, T) := \gamma + \sum_{\ell=1}^{10} \int_0^1 \pi_\epsilon(g_\ell(\tilde{x}(s|\sigma^p, T))) ds \geq 0,
\] (25)

where \(\epsilon > 0\) and \(\gamma > 0\) are two adjusting parameters; and
\[
\pi_\epsilon(\eta) := \begin{cases} 
0, & \text{if } \eta < -\epsilon, \\
\frac{(\eta + \epsilon)^2}{4\epsilon}, & \text{if } -\epsilon \leq \eta \leq \epsilon, \\
\eta, & \text{if } \eta > \epsilon.
\end{cases}
\] (26)

For each \(\epsilon > 0\) and \(\gamma > 0\), let Problem (EOCP\(\epsilon,\gamma(p))\) be Problem (EOCP\((p))\) replacing constraint (23) with (25). Note that Problem (EOCP\(\epsilon,\gamma(p))\) can be viewed as a standard mathematical programming. In addition, it can be shown, as in [26], that for each \(\epsilon > 0\), there exists a corresponding \(\gamma(\epsilon) > 0\) such that whenever \(0 < \gamma < \gamma(\epsilon)\), constraint (25) implies constraint (23).
In the numerical computation, the gradients of \( \tilde{G}^{\epsilon,\gamma}(\sigma^p, T) \) with respect to \( \sigma^p \) and \( T \) are required. Define

\[
\tilde{f}(s|\sigma^p, T) := \tilde{f}(s, \tilde{x}(s), \tilde{x}(s - \tilde{h}), \sigma^p, T),
\]

\[
\psi(s|\sigma^p, T) := \begin{cases} 
\tilde{f}(s|\sigma^p, T), & \text{if } s \in [0, 1], \\
\frac{d\tilde{\sigma}(s)}{ds}, & \text{if } s \in [-\tilde{h}, 0].
\end{cases}
\]

Obviously, for almost all \( s \in [-\tilde{h}, 1] \), we have \( \dot{x}(s|\sigma^p, T) = \psi(s|\sigma^p, T) \). Note that, in the sequel, we will use \( \partial \tilde{x} \) to denote partial differentiation with respect to \( \tilde{x}(s - \tilde{h}) \).

The following theorem provides these required gradients.

**Theorem 4.1.** Let \((\sigma^p, T) \in \Xi^p \times T\). Then, for each \( \epsilon > 0 \) and \( \gamma > 0 \),

\[
\frac{\partial \tilde{G}^{\epsilon,\gamma}(\sigma^p, T)}{\partial \sigma^{p,i,k}} = \int_{p_i-1}^{p_i} \lambda^\top(s) \frac{\partial \tilde{f}(s|\sigma^{p,i,k}, T)}{\partial \sigma^{p,i,k}} ds, \\
\frac{\partial \tilde{G}^{\epsilon,\gamma}(\sigma^p, T)}{\partial T} = \int_{p_i-1}^{p_i} \lambda^\top(s) \left( \frac{\partial \tilde{f}(s|\sigma^{p,i,k}, T)}{\partial T} - h \frac{\partial \tilde{f}(s|\sigma^{p,i,k}, T)}{\partial \tilde{x}} \psi(s - \tilde{h}) \right) ds,
\]

where \( \psi(s - \tilde{h}) := \psi(s - \tilde{h}|\sigma^p, T) \); and \( \lambda(s) := \lambda(s|\sigma^p, T) \) is the solution of the following costate system:

\[
\dot{\lambda}(s) = -\sum_{i=1}^{10} \frac{\partial \pi_{\epsilon}(g_l(\tilde{x}(s|\sigma^p, T)))}{\partial \tilde{x}} - \left( \frac{\partial \tilde{f}(s|\sigma^p, T)}{\partial \dot{x}} \right)^\top \lambda(s) \\
- \left( \frac{\partial \tilde{f}(s + \tilde{h}|\sigma^p, T)}{\partial \tilde{x}} \right)^\top \lambda(s + \tilde{h}) \chi_{[0,1-\tilde{h}]}(s), \quad s \in [0, 1],
\]

\[
\lambda(s) = (0, 0, 0, 0, 0)^\top, \quad s \geq 1.
\]

**Proof.** The proof is similar to that given for Theorem 4 in [18].

Based on the above theorem, Problem (OCP) can be solved by a sequence of problems \{\{EOCP^{\epsilon,\gamma}(p)\}\}. Each of \{\{EOCP^{\epsilon,\gamma}(p)\}\} is a smooth mathematical programming problem which can be solved by gradient-based techniques [3, 26]. However, these algorithms are designed to find local optimal solutions. To overcome this difficulty, we introduce an improved PSO algorithm to solve each of \{\{EOCP^{\epsilon,\gamma}(p)\}\}. PSO was developed by Kennedy and Eberhart in the study of artificial life [8, 22]. At present, PSO has attracted wide attention in neural network, optimization and other fields [12, 33]. In PSO, each solution of the considered optimization problem is known as a particle. Each particle flies at a certain velocity according to its own and the swarm’s experience to dynamically adjust the velocity, flying to the global best position, making the optimization problem to achieve the optimal solution. Nevertheless, each of \{\{EOCP^{\epsilon,\gamma}(p)\}\} is an optimization problem with constraints (8), (21) and (25). As a result, traditional PSO cannot be exploited to solve each of \{\{EOCP^{\epsilon,\gamma}(p)\}\}. Based on Theorem 4.1, we propose some improved strategies to solve each of \{\{EOCP^{\epsilon,\gamma}(p)\}\}. Assume that \( N_p \) particles are evolving, the position and velocity of the \( i \)th particle can be expressed in terms of
$\hat{\sigma}_i^p = (\hat{\sigma}_{i,1}^p, \ldots, \hat{\sigma}_{i,n}^p)^\top$ and $\nu_i^p = (\nu_{i,1}^p, \ldots, \nu_{i,n}^p)^\top$, where $k = \sum_{i=1}^{2N+1} 2n_i + 1$. In particular, the lower bound and upper bound of the position are represented by $\hat{\sigma}_{low}$ and $\hat{\sigma}_{upp}$, respectively. In detail, the implementation strategies in the improved algorithm are given as follows.

- **Updating position and velocity**
  
  For the $j$th component of the $i$th particle at the $(k+1)$th iteration, update the position and velocity with the following strategy:
  
  $$
  \nu_{i,j}^p(k+1) = \omega(k)\nu_{i,j}^p(k) + c_1(k)\nu_{i,j}^p(k) + c_2(k)\nu_{i,j}^p(k),
  $$
  
  $$
  \hat{\sigma}_{i,j}^p(k+1) = r_{i,j}^p\hat{\sigma}_{i,j}^p(k) + (1-r_{i,j}^p)\nu_{i,j}^p(k+1),
  $$
  
  where $pb_i^p = (pb_{i,1}^p, \ldots, pb_{i,n}^p)^\top$ is the best position for $i$ particle in history iteration; $gb_i^p = (gb_{i,1}^p, \ldots, gb_{i,n}^p)^\top$ is the best position in the swarm; $r_{i,j}^1, r_{i,j}^2$ and $r_{i,j}^3$ are the random numbers within the range of $[0,1]$; $c_1(k)$ and $c_2(k)$ are two coefficients; and $\omega(k)$ is an inertia weight. The coefficients and inertia weight are defined as
  
  $$
  c_1(k) = \sin^2 \left( \frac{\pi(it_{\text{max}}-k)}{2it_{\text{max}}} \right),
  $$
  
  $$
  c_2(k) = \sin^2 \left( \frac{\pi k}{2it_{\text{max}}} \right),
  $$
  
  where $it_{\text{max}}$ is the maximal number of iterations; $\omega_{\text{max}}$ and $\omega_{\text{min}}$ are, respectively, the maximal and minimal inertia weights.

- **Handling the control constraints**

  At the $k$th iteration, if the position of the $j$th component of the $i$th particle violates the bound constraint, then the position is redefined as:
  
  $$
  \hat{\sigma}_{i,j}^p(k) = \hat{\sigma}_{low,j}, \quad \text{if } \hat{\sigma}_{i,j}^p(k) \leq \hat{\sigma}_{low,j},
  $$
  
  $$
  \hat{\sigma}_{i,j}^p(k) = \hat{\sigma}_{upp,j}, \quad \text{if } \hat{\sigma}_{i,j}^p(k) \geq \hat{\sigma}_{upp,j}.
  $$

- **Handling the state constraints**

  For the position of the $i$th particle at the $k$th iteration, test the value of $G(\hat{\sigma}_i^p(k))$. If $G(\hat{\sigma}_i^p(k)) = 0$, then the position is feasible. Otherwise, $G(\hat{\sigma}_i^p(k)) > 0$ and move the position towards the feasible region based on the gradient formulae in Theorem 4.1, where $\epsilon$ and $\gamma$ are adjusted according to the $\epsilon - \gamma$ process in [20].

- **Stopping criterion**

  The algorithm stops when the maximal iteration $it_{\text{max}}$ is reached.

5. **Numerical results.** Consider a 1,3-PD fed-batch production process by *Klebsiella pneumoniae* reported in [18]. In the numerical simulation, we use the same settings as those to obtain the experimental results to optimize the feeding rates and the terminal time. In particular, the maximal duration of fed-batch process is partitioned into the first batch phase (Ph. I) and phases II-X (Phs. II-X). Within each one of Phs. II-X, all batch processes have 100s minus the duration of the feeding processes, and the same feeding rates of glycerol and allkali are adopted. The characteristics of each phase are given in TABLE 1. The state and costate systems are numerically calculated by Runge-Kutta method of order 4. Lagrange interpolation [25] is used whenever the Runge-Kutta method requires the value of the state or costate at an intermediate time between two adjacent knot points. Here, in time-delay system (1), the history function, the initial volume of culture fluid, the concentration of initial feed of glycerol in the medium, and time-delay are, respectively, $\phi(t) = (0.1115gL^{-1}, 495mmolL^{-1}, 0, 0, 0)^\top$, $V_0 = 5L, c_{s0} = 10762mmolL^{-1}$,
Table 1. Phase characteristics in fed-batch process [18].

| Phase | Start time (h) | End time (h) | Number of processes | Process duration (s) |
|-------|----------------|--------------|---------------------|----------------------|
| I     | 0              | 5.3300       | 0                   | 0                    |
| II    | 5.3300         | 6.1078       | 28                  | 5                    |
| III   | 6.1078         | 7.1356       | 37                  | 7                    |
| IV    | 7.1356         | 8.8300       | 61                  | 8                    |
| V     | 8.8300         | 12.1356      | 119                 | 7                    |
| VI    | 12.1356        | 15.8300      | 133                 | 6                    |
| VII   | 15.8300        | 18.0800      | 81                  | 4                    |
| VIII  | 18.0800        | 23.8300      | 144                 | 2                    |
| IX    | 19.8300        | 24.1633      | 12                  | 1                    |

Table 2. The kinetic parameters and critical concentrations in system (1) [14].

| $\Delta_1$ | $k_1$ | $m_2$ | $\Delta_2$ | $k_2$ | $m_3$ |
|------------|-------|-------|------------|-------|-------|
| 0.8        | 0.28  | 1.927 | 0.0063     | 6.8489| -3.2819|
| $Y_3$      | $\Delta_3$ | $k_3$ | $m_4$ | $Y_4$ | $\Delta_4$ | $k_4$ |
| 80.6096    | 10.3687| 15.50 | -0.97     | 33.07 | 5.74  | 85.71 |

and $h = 0.4652h$. Under anaerobic conditions at $37^\circ C$ and pH 7.0, the kinetic parameters and the critical concentrations for cells growth in system (1) are listed in Table 2.

In the improved PSO algorithm, the number of initial particles swarm $N_p$, the maximal iteration $it_{\text{max}}$ are 50 and 100, respectively. These parameters are derived empirically after numerous experiments. The lower and upper bounds of terminal time are $T_{\text{min}} = 11h$ and $T_{\text{max}} = 24.16h$, respectively. In addition, the lower and upper bounds for the feeding rates of glycerol and alkali are listed in Table 3. In handling the state constraint, $\epsilon = 1.0 \times 10^{-2}$ and $\gamma = 2.5 \times 10^{-3}$ are taken as the initial values. We reduce $\gamma$ by a factor of 2 if the control satisfies (24), or reduce both $\epsilon$ and $\gamma$ by a factor of 10 if the control does not satisfy (24). The $\epsilon - \gamma$ process is terminated when $\epsilon \leq 10^{-8}$.

By applying the improved PSO algorithm with control parameterization method, we obtain the optimal terminal time $T^* = 13.497h$ and the obtained optimal feeding strategy of glycerol and alkali are plotted in Figure 1. Under these optimal feeding rates and terminal time, we obtain that 1,3-PD productivity at the optimal terminal time is 73.397mmol$h^{-1}$, which increases 50.793% compared with the experiment result 48.674mmol$L^{-1}$ in [21]. We also plot the concentration changes of biomass, glycerol and 1,3-PD with respect to the fermentation time in Figure 2. Furthermore, the changes of 1,3-PD productivity with respect to the fermentation.
Table 3. The bounds of feeding rates in Phs. II-X [21].

| Phases | Upper bounds \((u_1, u_2)\) | Lower bounds \((u_1, u_2)\) |
|--------|-----------------------------|----------------------------|
| II-III | 0.2524                      | 0.1682                     |
| IV     | 0.2390                      | 0.1594                     |
| V-VI   | 0.2524                      | 0.1682                     |
| VII    | 0.2657                      | 0.1771                     |
| VIII   | 0.2924                      | 0.1949                     |
| IX-X   | 0.3058                      | 0.2038                     |

Figure 1. Optimal feeding rates of glycerol and alkali in Phs. II-VI.

Time are shown in Figure 3. From Figure 3, we confirm that the obtained 1,3-PD productivity is better than the previous results in [21].
6. Conclusions. This paper has considered time-delay optimal control of 1,3-PD fed-batch production involving multiple feeds. Taking 1,3-PD productivity as the performance index and the feeding rates of glycerol and alkali together with the terminal time of process as the controls, we presented a time-delay optimal control model subject to control and state constraints. To the best of our knowledge, this is the first time-delay optimal control problem involving feeds of glycerol and
alkali in the literature for optimizing the fed-batch production. By applying control parameterization and constraint transcription techniques, the optimal control problem is approximated by a sequence of finite-dimensional optimization problems. Furthermore, an improved PSO algorithm is developed to solve the resulting finite-dimensional optimization problems. Numerical results show that, by employing the obtained optimal control strategy, 1,3-PD productivity increases considerably. However, the time-delay in fed-batch process is generally time-variable. Thus, designing optimal feeding strategy in the presence of variable time-delay is an interesting area to pursue for future research.

Acknowledgments. This work is supported by the Natural Science Foundation of China (No. 11771008), the Shandong Province Natural Science Foundation of China (Nos. ZR2017MA005, ZR2019MA031 and ZR2015FM014) and the Australian Research Council (No. DP190103361).

REFERENCES

[1] B. Bao, H. Yin and E. Feng, Computation of impulsive optimal control for 1,3-PD fed-batch culture, J. Process Contr., 34 (2015), 49–55.
[2] F. Barbirato, E. H. Himmi, T. Conte and A. Bories, 1,3-Propanediol production by fermentation: An interesting way to valorize glycerin from the ester and ethanol industries, Ind. Crop Prod., 7 (1998), 281–289.
[3] A. Bryson and Y. Ho, Applied Optimal Control, Halsted Press, New York, 1975.
[4] C. Gao, E. Feng, Z. Wang and Z. Xiu, Nonlinear dynamical systems of bio-dissimilation of glycerol to 1,3-propanediol and their optimal controls, J. Ind. Manag. Optim., 1 (2005), 377–388.
[5] Z. Gong, C. Liu and Y. Wang, Optimal control of switched systems with multiple time-delays and a cost on changing control, J. Ind. Manag. Optim., 14 (2018), 183–198.
[6] V. K. Gorbunov, The parameterization method for optimal control problems, Comput. Math. Math. Phys., 19 (1979), 18–30.
[7] J. He, W. Xu, Z. Feng and X. Yang, On the global optimal solution for linear quadratic problem of switched system, J. Ind. Manag. Optim., 15 (2019), 817–832.
[8] J. Kennedy and R. C. Eberhart, Particle swarm optimization, Proceedings of the 1995 IEEE International Conference on Neural Networks, Perth, Australia, (1995), 1942–1948.
[9] J. V. Kurian, A new polymer platform for the future-sorona from corn derived 1,3-propanediol, J. Polym. Environ., 13 (2005), 159–167.
[10] B. Li, C. Xu, K. L. Teo and J. Chu, Time optimal Zermelo’s navigation problem with moving and fixed obstacles, Appl. Math. Comput., 224 (2013), 866–875.
[11] B. Li, C. J. Yu, K. L. Teo and G. R. Duan, An exact penalty function method for continuous inequality constrained optimal control problem, J. Optimiz. Theory App., 151 (2011), 260–291.
[12] H. Q. Li, L. Li, T. H. Kim and S. L. Xie, An improved PSO-based of harmony search for complicated optimization problems, Internat. J. Hybrid Inform. Technol., 1 (2008), 57–64.
[13] Q. Lin, R. Loxton and K. L. Teo, The control parameterization method for nonlinear optimal control: A survey, J. Ind. Manag. Optim., 10 (2014), 275–309.
[14] C. Liu, Sensitivity analysis and parameter identification for a nonlinear time-delay system in microbial fed-batch process, Appl. Math. Model., 38 (2014), 1448–1463.
[15] C. Liu, Optimal control of a switched autonomous system with time delay arising in fed-batch processes, IMA J. Appl. Math., 80 (2015), 569–584.
[16] C. Liu and Z. Gong, Optimal Control of Switched Systems Arising in Fermentation Processes, Springer-Verlag, Berlin, 2014.
[17] C. Liu, Z. Gong and E. Feng, Modelling and optimal control for nonlinear multistage dynamical system of microbial fed-batch culture, J. Ind. Manag. Optim., 5 (2009), 835–850.
[18] C. Liu, Z. Gong, K. L. Teo, J. Sun and L. Caccetta, Robust multi-objective optimal switching control arising in 1,3-propanediol microbial fed-batch process, Nonlinear Anal-Hybri., 25 (2017), 1–20.
[19] C. Liu, Z. Gong, H. W. J. Lee and K. L. Teo, Robust bi-objective optimal control of 1,3-propanediol microbial batch production process, *J. Process Contr.*, **78** (2019), 170–182.
[20] C. Liu, R. Loxton and K. L. Teo, A computational method for solving time-delay optimal control problems with free terminal time, *Syst. Contr. Lett.*, **72** (2014), 53–60.
[21] Y. Mu, D. J. Zhang, H. Teng, W. Wang and Z. L. Xiu, Microbial production of 1,3-propanediol by *Klebsiella pneumoniae* using crude glycerol from biodiesel preparation, *Biotechnol. Lett.*, **28** (2006), 1755–1759.
[22] K. E. Parsopoulos and M. N. Vrahatis, Particle swarm optimization method in multiobjective problems, *Proceedings of the 2002 ACM Symp. Appl. Comput.*, 2002, 603–607.
[23] R. W. H. Sargent and G. R. Sullivan, The development of an efficient optimal control package, *Proceedings of the 8th IFIP Conference on Optimization Techniques*, Würzburg, Germany, 7 (2005), 158–168.
[24] R. K. Saxena, P. Anand, S. Saran and J. Isar, Microbial production of 1,3-propanediol: Recent developments and emerging opportunities, *Biotechnol Adv.*, **27** (2009), 895–913.
[25] J. Stoer and R. Bulirsch, *Introduction to Numerical Analysis*, Springer-Verlag, New York, 1980.
[26] K. L. Teo, G. J. Goh and K. H. Wong, *A Unified Computational Approach to Optimal Control Problems*, Longman Scientific & Technical, Essex, 1991.
[27] G. Wang, E. Feng and Z. Xiu, Vector measure as controls for explicit nonlinear impulsive system of fed-batch culture, *J. Math. Anal. Appl.*, **351** (2009), 120–127.
[28] Z. Xiu, B. Song, L. Sun and A. Zeng, Theoretical analysis of effects of metabolic overflow and time delay on the performance and dynamic behavior of a two-stage fermentation process, *Biochem. Eng. J.*, **11** (2002), 101–109.
[29] F. Yang, K. L. Teo, R. Loxton, V. Rehbock, B. Li, C. Yu and L. Jennings, VISUAL MISER: An efficient user-friendly visual program for solving optimal control problems, *J. Ind. Manag. Optim.*, **12** (2016), 781–810.
[30] J. Ye, H. Xu, E. Feng and Z. Xiu, Optimization of a fed-batch bioreactor for 1,3-propanediol production using hybrid nonlinear optimal control, *J. Process Contr.*, **24** (2014), 1556–1569.
[31] C. Yu, Q. Lin, R. Loxton, K. L. Teo and G. Wang, A hybrid time-scaling transformation for time-delay optimal control problems, *J. Optimiz. Theory App.*, **169** (2016), 876–901.
[32] C. Yu, K. L. Teo, L. Zhang and Y. Bai, A new exact penalty function method for continuous inequality constrained optimization problems, *J. Ind. Manag. Optim.*, **6** (2010), 895–910.
[33] J. B. Yu, L. F. Xi and S. J. Wang, An improved particle swarm optimization for evolving feedforward artificial neural networks, *Neural Process Lett.*, **26** (2007), 217–231.
[34] A. P. Zeng and H. Biebl, Bulk-chemicals from biotechnology: The case of microbial production of 1,3-propanediol and the new trends, *Adv. Biochem. Eng. Biotechnol.*, **74** (2002), 239–259.

Received March 2018; revised September 2018.

*Email address: liu_chongyang@yahoo.com*

*Email address: g_shanmeijia@163.com*