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Chihua Chen
China University of Petroleum East China - Dongying Campus: China University of Petroleum Huadong
Juan Wang (wangj@upc.edu.cn)
China University of Petroleum East China - Dongying Campus: China University of Petroleum Huadong
https://orcid.org/0000-0003-2968-0380
Feiyan Zhao
China University of Petroleum East China - Dongying Campus: China University of Petroleum Huadong
Jichao Wang
China University of Petroleum East China - Dongying Campus: China University of Petroleum Huadong

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Determination of feeding rate ratio in coupled fed-batch fermentation with pH feedback considering limited number of switches

Chihua Chen[a], Juan Wang*[a], Feiyan Zhao[a] and Jichao Wang[a]

[a] *College of Science, China University of Petroleum, Qingdao 266580, Shandong, China*

Abstract. This paper focuses on binary optimal control of fed-batch fermentation of glycerol by *Klebsiella pneumoniae* with pH feedback considering limited number of switches. To maximize the concentration of 1,3-propanediol at terminal time, we propose a binary optimal control problem subjected to time-coupled combinatorial constraint with the ratio of feeding rate of glycerol to that of NaOH as control variables. Based on time-scaling transformation and discretization, the binary optimal control problem is first transformed into a mixed binary parameter optimization problem consisting not only continuous variables but also binary variables, which is then divided into two subproblems via combinatorial integral approximation decomposition. Finally, a novel fruit fly optimizer with modified sine cosine algorithm and adaptive maximum dwell rounding are applied to solve the obtained subproblems numerically. Numerical results show the rationality and feasibility of the proposed method.

Key Words. Binary control; Fed-batch fermentation; Combinatorial integral approximation; Fruit fly optimization algorithm; Mixed binary optimization.

1 Introduction.

1,3-propanediol (1,3-PD), as an important chemical material, which has a wide range of potential uses in manufacture of polymers, cosmetics, food and lubricants can be produced by glycerol bioconversion by *Klebsiella pneumoniae* [1]. In this bioconversion process, fed-batch culture technology is a widely researched technique that offers distinct advantages over other modes of operation of bioreactors [2]. The fed-batch of bioconversion glycerol to 1,3-PD begins with the cells being grown under the batch culture for some time, then fed process and batch process are carried out alternately according to the given feeding sequence [3] or pH feedback [4].

*Corresponding author: wangj@upc.edu.cn.

In recent decades, optimal control of glycerol bioconversion to 1,3-PD based on fed-batch fermentation process has been a widely investigated problem. Ye et al. took the feeding instants and the terminal time as decision variables to design an optimal control strategy [5]. Gong et al. proposed a switched system with variable switching instants to maximize the concentration of 1,3-PD at terminal time [6]. However, the demand for glycerol is considered as constant in these papers which is obviously unreasonable since the demand for glycerol maybe vary at different fermentation stages. Taking this into account, Liu et al. proposed an open-loop switching system in which the feed rate of glycerol was the control function to maximize the concentration of 1,3-PD at terminal time [3]. Yuan et al. took the feeding rates of glycerol and alkali as continuous control inputs to construct an optimal minimal variation control problem[7]. Gao et al. proposed a nonlinear impulsive dynamical system with continuous variable impulsive instants and volumes of feeding glycerol and alkali [8]. Niu et al. proposed an optimal model with the feeding rates of glycerol and alkali, the switching instants and the mode sequence as control variables to maximize the concentration of the terminal time 1,3-PD [9]. However, such continuous control inputs are difficult to achieve in practical problem. In the present work, we shall take the ratio of the feeding rate of glycerol to that of NaOH as discrete control input which is then transformed into a binary control input via outer convexification. A hybrid system with binary control input and pH feedback is established on the basis of our previous work [10].

In practice, it is of great significance to reduce the cost of frequent switching in industry since the frequent switching may bring great damage to the machine. Thus, some papers have modelled and handled the constraint of switching cost through different methods. In [11], the Euclidean distance between the decision variables of two solutions is defined as the switching cost which is taken as one of the performance indicators to add to the dynamic optimization problem. In [12, 13], a total variation term that measures the switching cost is added to the objective function with a weighting factor. In this paper, for a given maximum number of switches, the switching cost which is defined as the number of switches by total variation can be added to the model in the form of inequality constraint. Then, a binary optimal control problem with constrained total variation is proposed.

To find a solution to binary optimal control problem, in addition to some traditional methods, such as dynamic programming [14, 15] and the methods based on global maximum principle [16, 17], many other excellent methods have been proposed in recent years. Hahn et al. proposed a trust-region steepest descent method to solve binary optimal control problems by iteratively improving on existing solutions [18]. Wu et al. transformed the binary optimal control problem into an equivalent two-level optimization problem involving a combination of a standard optimal control problem and a discrete optimization problem which could be solved by a developed discrete filled function method [19]. Sager et al. proposed a widely-used method, i.e., relaxation first, then discrete and optimize, and finally find the approximate integer solution by the rounding strategy [20]. However, due to the time-coupled combinatorial constraint, the Sum-Up Rounding (SUR) heuristic which is a common strategy to get the approximate integer solution will be not applicable. In this work, the combinatorial integral approximation (CIA) decomposition proposed in [21] shall be used to solve the binary optimal control problem.

This paper focuses on the optimal control of the ratio of feeding rate during fed-batch culture with pH feedback through solving a binary optimal control problem with constrained total variation. Using the time-scaling transformation and discretization technique, a mixed binary optimization problem is obtained. By introducing the CIA decomposition, this problem can be decomposed into a continuous nonlinear program which can be solved easily by the proposed fruit fly optimizer with modified sine cosine algorithm (MSCA-FOA) and an mixed binary linear program (MBLP). Then, base on the relaxed solution of continuous nonlinear program, the MBLP can be solved by adaptive maximum dwell rounding proposed in [21]. Numerical results show the feasibility of optimal strategy and the validity and applicability of the proposed numerical algorithm.

The main contributions of this paper are:

- We propose an optimal control problem considering the limited number of switches which is expressed by the total variation in the inequality constraint.
- The optimal control problem is finally transformed into two tractable subproblems by time-scaling transformation, discretization and CIA decomposition.
- A novel fruit fly optimizer with the modified sine cosine algorithm is proposed to balance convergence speed and global convergence.

This paper is organized as follows. In Section 2, the mathematical model of the fed-batch culture with pH feedback is introduced, and the binary optimal control problem with constrained total variation is proposed based on this model. In Section 3, time-scaling transformation, discretization and CIA decomposition are applied to convert the problem into two subproblems. Section 4 devotes to solving two subproblems numerically using the MSCA-FOA and AMDR, while Section 5 illustrates the numerical results. Conclusions are made in Section 6.

2 Problem formulation

2.1 The nonlinear binary hybrid system

In this work, we consider a fed-batch conversion process of glycerol to 1,3-PD by *Klebsiella pneumoniae* based on our previous work [10], which proposed a nonlinear hybrid system to formulate the coupled fed-batch culture with pH feedback. In this process, if the pH drops below the lower critical concentration pH_*, the fed process is active, while the pH of the solution rises above upper critical concentration pH*, the fed process stops and batch process is active. Let $\mathcal{T} := [t_0, t_f]$ be the entire fermentation time. Let $\mathcal{X} := \mathbb{R}_+^7$ and $\Sigma := \{0, 1\}$ be the continuous state space and the set of discrete states, respectively. Let $\mathbf{x}(t) := (x_1(t), \cdots, x_7(t))^\top \in \mathcal{X}, t \in \mathcal{T}$ be the continuous state vector, in which the components represent the concentrations of biomass, glycerol, 1,3-PD at t in the reactor, the total concentration of acetic acid at t, the concentration of ethanol at t in reactor, the concentration of Na^+ ions coming from the added NaOH and the volume of the solution at t, respectively; $\sigma(t) \in \Sigma, \forall t$ is the discrete state, i.e., 0 represents batch process and 1 represents fed process. Let I_n be the set $\{1, 2, \cdots, n\}$ where n is a natural number.

According to the experimental process, we assume that

(H1) The concentrations of reactants are uniform in reactor, while time delay and nonuniform space distribution are ignored.

(H2) The feeding media includes fixed concentrations of glycerol and alkali.

Under the assumptions (H1)-(H2), according to [10], the nonlinear hybrid system can be described as

$$\begin{cases} \dot{\mathbf{x}}(t) = \mathbf{f}^{\sigma(t)}(\mathbf{x}(t), r(t)), & \mathbf{x} \in \mathcal{X} \backslash \Delta,\ t \in \mathcal{T}, \\ \mathbf{x}(t^+) = \mathbf{x}(t^-),\ \sigma(t^+) = (\sigma(t^-) + 1)\ mod\ 2,\ t \in \Lambda, & \\ \mathbf{x}(t_0) = \mathbf{x}^0,\ \sigma(t_0) = 0, & \end{cases} \tag{2.1}$$

where $\mathbf{x}^0$ denotes the initial state, Δ denotes the set of all switching points, Λ denotes the set of all switching instants, $r(t)$ denotes the ratio of the feeding rate of glycerol to that of NaOH which takes the given values $r_1, \cdots, r_{n_\omega}$. Let $\Omega := \{r_1, \cdots, r_{n_\omega}\}$.

The right hand side of system (2.1) is of the form $\mathbf{f}^\sigma(\mathbf{x}, r) = (f_1^\sigma(\mathbf{x}, r), \cdots, f_7^\sigma(\mathbf{x}, r))^\top$ with the components defined as

$$\begin{cases} f_1^\sigma(\mathbf{x}, r) = (\mu - d)x_1 - \dfrac{(1+r)v_0\sigma}{x_7} x_1, \\ f_2^\sigma(\mathbf{x}, r) = -q_2 x_1 + \dfrac{r v_0 \sigma}{x_7}(C_{s0} - x_2) - \dfrac{v_0\sigma}{x_7} x_2, \\ f_3^\sigma(\mathbf{x}, r) = q_3 x_1 - \dfrac{(1+r)v_0\sigma}{x_7} x_3, \\ f_4^\sigma(\mathbf{x}, r) = q_4 x_1 - \dfrac{(1+r)v_0\sigma}{x_7} x_4, \\ f_5^\sigma(\mathbf{x}, r) = q_5 x_1 - \dfrac{(1+r)v_0\sigma}{x_7} x_5, \\ f_6^\sigma(\mathbf{x}, r) = -\dfrac{r v_0 \sigma}{x_7} x_6 + \dfrac{v_0\sigma}{x_7}(\varrho - x_6), \\ f_7^\sigma(\mathbf{x}, r) = (1+r)v_0\sigma, \end{cases} \tag{2.2}$$

where d denotes the specific decay rate of cells, given in [10], as listed in Table 1, v_0 is the feeding rate of NaOH(L/h), C_{s_0}(mmol/L) and ϱ(mmol/L) are the concentrations of glycerol and NaOH in feed medium, respectively; the specific growth rate of cells μ, specific consumption rate of substrate q_2 and specific formation rate of products q_i, i=3,4,5, are expressed by the following equations according to [4, 22].

$$\mu = \begin{cases} \mu_m \dfrac{x_2}{x_2 + K_s} \displaystyle\prod_{i=1}^{5} \left(1 - \dfrac{x_i}{x_i^*}\right), \text{if } x_i \in [0, x_i^*], i \in I_5, \\ 0, \qquad\qquad\qquad\qquad \text{otherwise,} \end{cases} \tag{2.3}$$

$$q_2 = m_2 + \frac{\mu}{Y_2} + \Delta q_2 \frac{x_2}{x_2 + K_2^*}, \tag{2.4}$$

$$q_i = m_i + \mu Y_i + \Delta q_i \frac{x_2}{x_2 + K_i^*}, i = 3, 4, 5. \tag{2.5}$$

Here, m_i, Y_i, Δq_i and K_i^*, i=2, 3, 4, 5, are kinetic parameters. μ_m is the maximum specific growth rate and K_s is a Monod saturation constant, with values given in [10], as listed in Table 1. x_i^*, i=1, 2, 3, 4, 5, are the critical concentrations of biomass, glycerol, 1,3-PD, acetic acid and ethanol for cell growth, respectively, with values given in [23] ,as listed in Table 1. Let x_6^* and x_7^* be the critical concentration of Na^+ ions coming from the added NaOH and critical volume of the solution, respectively, as listed in Table 1. Let $\mathcal{X}_{ad}$ be the admissible set of the continuous state $\mathbf{x}$, defined by

$$\mathcal{X}_{ad} := \left\{ \mathbf{x}(\cdot) \mid \mathbf{x}(t) \in \prod_{i=1}^{7} [0, x_i^*], \ \forall\, t \in \mathcal{T} \right\}.$$

Table 1: The critical concentrations and the parameters in (2.2)-(2.5).

d	μ_m	K_s	m_2	m_3	m_4	m_5
0.079567	0.69586	0.252	0.9831	−2.1234	−0.0011	−0.2368
Y_2	Y_3	Y_4	Y_5	Δq_2	Δq_3	Δq_4
0.017644	90.2345	18.0174	20.1092	13.0139	7.1623	0.110352
Δq_5	K_2^*	K_3^*	K_4^*	K_5^*	x_1^*	x_2^*
0.0602197	195.592	220.7931	78.9423	92.3576	10	2039
x_3^*	x_4^*	x_5^*	x_6^*	x_7^*		
1300	1026	360.9	1026	10		

Remark 1 *In nature, system (2.1) is a bimodal system, i.e., the fed process is active when* $\sigma = 1$ *and the batch process is active when* $\sigma = 0$*.*

According to [4], since we only discuss the fermentation under acidic environment and the added NaOH is the only basic source, we assume that

(H3) During the whole process of fed-batch culture, there exists a constant $M > 0$ such that $x_4 - \gamma x_6 \geq M$, where $\gamma > 0$ is the ratio of acetic acid concentration to the total acid byproducts concentrations.

(H4) During the whole process of fed-batch culture, there exists a constant $\epsilon_0 \geq \epsilon > 0$ such that $x_6 > \epsilon_0$.

Then, according to [4] the output equation for the pH of the solution is be given as

$$y(\mathbf{x}) := -\lg(K_a) - \lg\frac{x_4 - \gamma x_6}{\gamma x_6}, \tag{2.6}$$

where K_a denotes the averaged dissociation constant of acid byproducts, γ denotes the ratio of acetic acid concentration to the total acid byproducts concentrations.

The following two inequalities must hold during the entire fermentation process to ensure that the pH is restricted in its admissible range.

$$\left.\begin{array}{l} h_0(\mathbf{x}(t)) := \mathrm{pH}^* - y(\mathbf{x}(t)) \geq 0, \\ h_1(\mathbf{x}(t)) := y(\mathbf{x}(t)) - \mathrm{pH}_* \geq 0, \end{array}\right\} t \in \mathcal{T}. \tag{2.7}$$

Then, the set of all switching points and the set of all switching instants can be defined as $\Delta := \{\mathbf{x} \in \mathcal{X} | h_0(\mathbf{x}) = 0 \text{ or } h_1(\mathbf{x}) = 0\}$ and $\Lambda := \{t \in \mathcal{T} | \mathbf{x} \in \Delta\}$, respectively.

According to [24], we shall apply outer convexification to reformulate the non-convex system by introducing a binary function $\omega_i(\cdot)$ for every element r_i of Ω. Let

$$r(t) = \sum_{i=1}^{n_\omega} \omega_i(t) r_i, \tag{2.8}$$

where

$$\sum_{i=1}^{n_\omega} \omega_i(t) = 1,\ \omega(t) \in \{0, 1\}^{n_\omega}, \forall\ t \in \mathcal{T}. \tag{2.9}$$

The discrete-valued control system (2.1) can be equivalently transformed into the following binary control system.

$$\begin{cases} \dot{\mathbf{x}}(t) = \sum\limits_{i=1}^{n_\omega} \mathbf{f}^{\sigma(t)}(\mathbf{x}(t), r_i)\omega_i(t), & \mathbf{x} \in \mathcal{X} \backslash \Delta,\ t \in \mathcal{T} \\ \mathbf{x}(t^+) = \mathbf{x}(t^-),\ \sigma(t^+) = (\sigma(t^-) + 1)\ mod\ 2,\ t \in \Lambda, & \\ \mathbf{x}(t_0) = \mathbf{x}^0,\ \sigma(t_0) = 0, & \end{cases} \tag{2.10}$$

Based on the function $\mathbf{f}^\sigma, \sigma \in \Sigma$, defined in (2.2), it is similar to [4] that the following property can be easily verified.

Property 1 *Under the assumptions (H1)-(H4), for a fixed $\mathbf{x}^0 \in \mathcal{X}$ and a given $\omega(\cdot) \in \{0, 1\}^{n_\omega}$, the system (2.10) has a unique solution, denoted by $\mathbf{x}(\cdot; \omega)$.*

2.2 The nonlinear binary optimal control problem

This paper aims to maximize the concentration of 1,3-PD at terminal time of fermentation under a limited number of switches, which means increasing the output while reducing the switching cost. According to [21], the switching cost can be expressed as total variation as follows

$$v(\omega) := \sup_{P \in \mathcal{P}} \left\{ \frac{1}{2} \sum_{i \in I_{n_\omega}} \sum_{j \in I_{n_P}} |\omega_i(\tau_j) - \omega_i(\tau_{j-1})| \right\}, \tag{2.11}$$

where $P = (\tau_0, \cdots, \tau_{j-1}, \tau_j, \cdots, \tau_{n_P})$ with $\tau_{n_P} = t_f$ is a partition out of the set of all partitions $\mathcal{P}$ of the interval $\mathcal{T}$ and n_P denotes the partition specific number of time points.

Remark 2 *$\omega(\cdot)$ is a binary function that satisfies $\omega_i \in \{0, 1\}$, then the switching cost (2.11) actually represents the total number of switches.*

According to [21], in practice, the total number of switches should be limited so that the inequality constraint so called time-coupled combinatorial constraint can be written as

$$v(\omega) <= \rho_{max}, \tag{2.12}$$

where ρ_{max} denotes maximum number of switches.

Meanwhile, we take the opposite number of the concentration of 1,3-PD at terminal time as the objective function:

$$J(\omega) = -x_3(t_f; \omega). \tag{2.13}$$

Based on the above discussion, let $\mathcal{W}_{ad}$ be the admissible set of binary control ω, defined by

$$\mathcal{W}_{ad} := \Big\{ \omega(\cdot) \mid \omega(t) \text{ satisfies (2.9) and (2.12)}, \ \forall\, t \in \mathcal{T} \Big\},$$

Problem (P1) can be defined formally below.

Problem (P1). Given the hybrid system (2.10), choose a binary control $\omega(\cdot) \in \mathcal{W}_{ad}$ such that the function $J(\omega)$ is minimized subjected to state constraint $\mathbf{x}(\cdot) \in \mathcal{X}_{ad}$.

In **Problem (P1)**, the continuous state inequality constraint $\mathbf{x}(\cdot) \in \mathcal{X}_{ad}$ and the combination constraint of control $\omega(\cdot) \in \mathcal{W}_{ad}$, i.e., convex combination constraint (2.9) and time-coupled combinatorial constraint (2.12), cannot be solved by the standard approaches to solving optimal control problem. In the following sections, we shall discuss how to handle this issue.

Remark 3 *We define the switching sequence and switching instants as the order of the values of $\omega(\cdot)$ along the time and the instants at which it switches from one value to another, respectively. The switching sequence and switching instants of $\omega(\cdot)$ are all decision variables to be optimized.*

3 Problem transformation

Problem (P1) is a binary optimal control problem with point-to-point constraint on state trajectory and combinatorial constraints on control input which can be solved effectively by the combinatorial integral approximation (CIA) decomposition proposed in [21]. Time-scaling transformation and discretization shall be utilized before CIA decomposition as described in the following subsections.

3.1 Time-scaling transformation and Discretization

Divide the entire fermentation time interval $\mathcal{T}$ into n_p subintervals $\mathcal{T}^j := [\tau_{j-1}, \tau_j)$ with $n_p + 1$ partition points denoted by $t_0 = \tau_0 < \tau_1 < \cdots < \tau_{n_p} = t_f$, where $\tau_i, i = 1, \cdots, n_{p-1}$ are the switching instants to be optimized.

A time-scaling transformation method [7, 25, 26] shall be applied to fix these switching instants by introducing a transform which maps from $\tau \in [t_0, t_f]$ into $s \in [0, n_p]$ given by

$$\frac{dt(s)}{ds} = h(s), t(0) = 0, \tag{3.1}$$

where $h(s)$ is given by

$$h(s) = \sum_{j=1}^{n_p} \theta_j \chi_{(j-1,j]}(s), \tag{3.2}$$

with $\theta_j = \tau_j - \tau_{j-1}$, and the characteristic function $\chi_S : \mathbb{R} \to \{0, 1\}$ defined by

$$\chi_S(s) = \begin{cases} 1, \text{if } s \in S, \\ 0, \text{otherwise.} \end{cases}$$

Let θ be the vector whose components are $\theta_j, j \in I_{n_p}$, and Θ be the set of all such θ which satisfy $\theta_j \geq 0$ and $\sum\limits_{j=1}^{n_p} \theta_j = t_f - t_0$. It is easy to see that, for $s \in (j-1, j]$,

$$t(s) = \int_0^s h(\zeta) d\zeta = \sum_{k=1}^{j-1} \theta_k + \theta_k(s - j + 1). \tag{3.3}$$

Let Λ' be the set of all switching instants controlled by pH feedback in the new horizon. Let $\dot{\widetilde{\mathbf{x}}}(s) := \mathbf{x}(t(s))$ and $\widetilde{\omega}(s) := \omega(t(s))$, in new time horizon, hybrid system (2.10) becomes

$$\begin{cases} \dot{\widetilde{\mathbf{x}}}(s) = h(s|\theta) \sum\limits_{i=1}^{n_\omega} \widetilde{\omega}(s) \mathbf{f}^{\widetilde{\sigma}(s)}(\widetilde{\mathbf{x}}(s), r_i), & s \in [0, n_p] \backslash \Lambda' \\ \widetilde{\mathbf{x}}(s^+) = \widetilde{\mathbf{x}}(s^-),\ \widetilde{\sigma}(s^+) = (\widetilde{\sigma}(s^-) + 1)\ mod\ 2, & s \in \Lambda', \\ \widetilde{\mathbf{x}}(0) = \mathbf{x}^0,\ \widetilde{\sigma}(0) = 0, \end{cases} \tag{3.4}$$

where $\widetilde{\omega}(s)$ also satisfies convex combination constraint

$$\sum_{i=1}^{n_\omega} \widetilde{\omega}_i(s) = 1, \ \widetilde{\omega}(s) \in \{0,1\}^{n_\omega}, \ s \in [0, n_p]. \tag{3.5}$$

The total variation (2.11) becomes

$$\widetilde{v}(\widetilde{\omega}) := \frac{1}{2} \sum_{i \in I_{n_\omega}} \sum_{j \in I_{n_p}} |\widetilde{\omega}_i(j) - \widetilde{\omega}_i(j-1)|, \tag{3.6}$$

and inequality constraint (2.12) can be expressed as

$$\widetilde{v}(\widetilde{\omega}) <= \rho_{max}. \tag{3.7}$$

Similarly, let $\widetilde{\mathcal{W}}_{ad}$ denote the admissible set of binary control $\widetilde{\omega}$, defined by

$$\widetilde{\mathcal{W}}_{ad} := \Big\{ \widetilde{\omega}(\cdot) \mid \widetilde{\omega}(s) \text{ satisfies (3.5) and (3.7)}, \ \forall \ s \in [0, n_p] \Big\},$$

By the above time-scaling transformation, **Problem (P1)** with free switching instants is transformed into a new problem with fixed switching instants.

Problem (P2) Given hybrid system (3.4), choose a $\theta \in \Theta$ and a binary control $\widetilde{\omega} \in \widetilde{\mathcal{W}}_{ad}$ such that the cost function

$$\widetilde{J}(\theta, \widetilde{\omega}) = -\widetilde{x}_3(n_p; \theta, \widetilde{\omega}) \tag{3.8}$$

is minimized subjected to state constraint $\widetilde{\mathbf{x}} \in \mathcal{X}_{ad}$.

Based on the time grid adopted in time-scaling transformation, the binary control $\widetilde{\omega}(s)$ is now approximated in the form of a piecewise constant function

$$\widetilde{\omega}(s) \approx \omega^p(s|\eta) = \sum_{j=1}^{n_p} \eta^j \chi_{\mathcal{T}^j}(s), \ s \in [0, n_p], \tag{3.9}$$

where $\eta^j, j = 1, \cdots, n_p$ are the decision variables, satisfying $\eta^j \in \{0,1\}^{n_\omega}$ and $\sum_i^{n_\omega} \eta_i^j = 1$. Define $\eta := \left\{\eta_1^1, \cdots, \eta_{n_\omega}^1, \cdots, \eta_1^{n_p}, \cdots, \eta_{n_\omega}^{n_p}\right\}^\top$ and let Ω' be the set of all such η.

Now the total variation can be rewritten as

$$v^p(\eta) := \frac{1}{2} \sum_{i \in I_{n_\omega}} \sum_{i \in I_{n_p}} |\eta_i^j - \eta_i^{j-1}|, \tag{3.10}$$

which satisfies

$$v^p(\eta) <= \rho_{max}. \tag{3.11}$$

The objective function can be reformulated as

$$J^p(\theta, \eta) = -x_3^p(n_p; \theta, \eta). \tag{3.12}$$

Based on the above discretization, the approximate problem of **Problem (P2)** is given below.

$$
\textbf{Problem (P3)} \quad \min_{\theta,\eta} J^p(\theta,\eta)
$$

$$
\text{s.t.} \begin{cases}
\dot{\mathbf{x}}^p(s) = h(s|\theta) \sum\limits_{i=1}^{n_\omega} \sum\limits_{j=1}^{n_p} \eta_i^j \chi_{\mathcal{T}^j}(s) \mathbf{f}^{\sigma^p(s)}(\mathbf{x}^p(s), r_i), & s \in [0,n_p]\backslash\Lambda', \\
\mathbf{x}^p(s^+) = \mathbf{x}^p(s^-),\ \sigma^p(s^+) = (\sigma^p(s^-)+1)\ mod\ 2, & s \in \Lambda', \\
\mathbf{x}^p(0) = \mathbf{x}^0,\ \sigma^p(0) = 0, \\
0 \le x_i^p(s) \le x_i^*,\ i \in I_7,\ s \in [0,n_p], \\
\sum\limits_{i=1}^{n_\omega} \eta_i^j = 1,\ \eta_i^j \in \{0,1\},\ \theta_j \ge 0, \sum\limits_{j=1}^{n_p} \theta_j = t_f - t_0,\ i \in I_{n_\omega},\ j \in I_{n_p}, \\
v^p(\eta) <= \rho_{max}.
\end{cases}
$$

Finally, we can get a large-scale dynamic parameter optimization problem with $(n_\omega + 1) \times n_p$ decision variables. Once we have obtained the approximate optimal solution (θ^*, η^*) of **Problem (P3)**, the switching sequence and switching instants in **Problem (P1)** can be derived to determine the approximate optimal control strategy $r^*(t)$. Considering the difficulty of inequality constraint coupled with time in **Problem (P3)**, we shall apply a feasible decomposition technique to handle it.

3.2 Problem decomposition

According to the CIA decomposition proposed in [21], **Problem (P3)** can be decomposed into two subproblems i.e., continuous nonlinear program and mixed binary linear program. Based on the solution of the nonlinear continuous program subproblem, a mixed binary linear program subproblem will be solved to obtain the final approximate optimal solution of **Problem (P3)**.

The relaxation of $\eta^j \in \{0,1\}^{n_\omega}$ is given by $\bar{\eta}^j \in [0,1]^{n_\omega}$. We now define the following three sets:

$\bar{\Omega} \triangleq \left\{(\theta,\bar{\eta}) \mid \sum\limits_{i=1}^{n_\omega} \bar{\eta}_i^j = 1,\ \bar{\eta}_i^j \ge 0,\ \sum\limits_{j=1}^{n_p} \theta_j = t_f - t_0,\ \theta_j \ge 0,\ i \in I_{n_\omega},\ j \in I_{n_p}\right\}$,

$\bar{X} \triangleq \{\bar{\mathbf{x}}(\cdot;\theta,\bar{\eta}) \mid \bar{\mathbf{x}}(\cdot;\theta,\bar{\eta})$ is a solution to the system proposed in Problem (P3) with $(\theta,\bar{\eta}) \in \bar{\Omega}\}$,

$\Omega_{ad} \triangleq \{(\theta,\bar{\eta}) \in \bar{\Omega} \mid \bar{\mathbf{x}}(\cdot;\theta,\bar{\eta}) \in \bar{X}$ and $\bar{\mathbf{x}}(\cdot;\theta,\bar{\eta}) \in \mathcal{X}_{ad}\}$.

Then **Subproblem (A)** can be expressed as follows:

$$
\textbf{Subproblem (A)} \quad \min_{\theta,\bar{\eta}} \bar{J}(\theta,\bar{\eta}) \quad \text{s.t.} \ (\theta,\bar{\eta}) \in \Omega_{ad}
$$

Note that the inequality constraint of switching cost is not considered in **Subproblem (A)**, which is the biggest difference from **Problem (P3)**. Once we have obtained the solution of **Subproblem (A)**, we want to convert this solution to a new binary solution that satisfies the inequality constraint through a certain technique, while the error between two solutions need to be minimized. According to [21], based on the solution $(\theta^*, \bar{\eta}^*)$ of **Subproblem (A)**, we shall convert the relaxed solution into the binary solution while considering the maximum number of switches with a special rounding strategy by solving **Subproblem (B)**, so called the CIA problem. **Subproblem (B)** can be expressed as follows:

$$\textbf{Subproblem (B)} \quad \min_{\rho,\psi,\eta} \psi$$

$$\text{s.t.} \quad \begin{cases} \psi \geq \pm \sum\limits_{l \in I_j} (\bar{\eta}^{*l}_{\ i} - \eta_i^l)\Delta_l, \ i \in I_{n_\omega}, \ j \in I_{n_p} \\ \rho_{max} \geq \frac{1}{2} \sum\limits_{i \in I_{n_\omega}} \sum\limits_{j \in I_{n_p}} \rho_{i,j}, \\ \rho_{i,j} \geq \pm(\eta_i^j - \eta_i^{j-1}), \ i \in I_{n_\omega}, \ j \in I_{n_p}, \\ \sum\limits_{i=1}^{n_\omega} \eta_i^j = 1, \ \eta_i^j \in \{0, 1\}, \ i \in I_{n_\omega}, \ j \in I_{n_p}, \end{cases}$$

where Δ_l denotes the interval length of $[\tau_{l-1}, \tau_l]$, $\rho_{i,j}$ are auxiliary variables for introducing a discretized version of the total variation constraint (3.10) and ψ is the approximation error.

According to [21], different from the general rounding problems, the rounding error does not vanish in general with grid length going to zero, and we can easily get the following property.

Property 2 *Let $1 \leq \rho_{max} \leq n_p - 2$ and $n_\omega > 2$. We obtain for the maximum optimal objective value ψ_{max} of **Subproblem (B)**(CIA):*

$$\psi_{max} \geq \begin{cases} \dfrac{(t_f - t_0)}{\rho_{max} + 2}, & \text{if } \rho_{max} \leq n_\omega - 2, \\ \dfrac{(t_f - t_0)}{2\rho_{max} + 4 - n_\omega}, & \text{else.} \end{cases}$$

Property 2 shows the lower bound of the maximum integer approximation error which indicates the importance of designing an appropriate algorithm for rounding. **Subproblem (A)** is a large-scale parameter optimization problem which is devoted to obtaining the relaxed solution without considering the inequality constraint of switching cost, while **Subproblem (B)** focuses on obtaining an approximate integer solution that satisfies the switching cost inequality constraint. In the next section, an efficient and feasible evolutionary algorithm will be introduced to solve **Subproblem (A)**, and a rounding strategy proposed in [21] shall be used to minimize the integer approximation error in **Subproblem (B)** with an appropriate integer solution.

4 Numerical method

In this section, we shall construct a new fruit fly algorithm (FOA) based on the modified sine cosine algorithm (MSCA) proposed in [27], so called MSCA-FOA, to solve **Subproblem (A)**, and an adaptive maximum dwell rounding (AMDR) algorithm proposed in [21] is introduced to solve **Subproblem (B)**.

4.1 The proposed MSCA-FOA

FOA is a new method for finding global optimization based on the food hunting behavior of fruit fly which is an insect that exists widely in temperate and tropical climate zones and is superior to other species in osphresis and vision [28]. During hunting for food, fruit flies exploit the sense of smell to come near to the food source, and exchange odor information with other fruit flies. Then, fruit flies fly towards the fruit fly with the highest odor concentration using its sensitive vision. After several rounds of searching, fruit flies will eventually determine the specific location of the food source. Considering its briefness in calculation process, simplicity in structure, and efficiency in performance, FOA has been applied to handle many practical optimization problems [29, 30]. However, the original FOA usually converges to local optimum, and especially, in the face of high-dimensional problems [31, 32].

To deal with this problem, the sine cosine strategy is combined into the FOA in [32]. The sine cosine algorithm (SCA) is an effective algorithm proposed by Mirjalili [33] in 2016 and has been widely applied to solve practical problems. It creates multiple initial random candidate solutions and requires them to fluctuate outwards or towards the best solution using a mathematical model based on sine and cosine functions.

Although the FOA combined with SCA possesses high performance, the search path of the SCA is nonlinear due to the absolute value term and the trigonometric function term in the position updating equations, which lead to the difficulty that can not limit the search direction of the algorithm. In this paper, a modified SCA proposed in [27] which can improve the efficiency and the accuracy of the search through introducing the linear search path and empirical parameter shall be combined into the original FOA i.e., MSCA-FOA to solve **Subproblem (A)**.

In the proposed MSCA-FOA, the initial positions are generated by the original FOA. After a round of search, the position and smell concentration of the obtained optimal individual will be used as the initial information for the iterative search. In the iteration step, the formula of position updating of the original SCA-FOA is given below according to [32].

$$\xi_{i,j}(k+1) = \begin{cases} \xi_{i,j}(k) + R_1 \times \sin R_2 \times |R_3 \xi^p_{i,j}(k) - \xi_{i,j}(k)|, R_4 < 0.5, \\ \xi_{i,j}(k) + R_1 \times \cos R_2 \times |R_3 \xi^p_{i,j}(k) - \xi_{i,j}(k)|, R_4 \geq 0.5, \end{cases} \quad \xi = X, Y, \tag{4.1}$$

where $\xi_{i,j}(k), \xi^p_{i,j}(k)$ denotes the position of the current solution and the historical best solution in ith individual and jth dimension at kth iteration, respectively. Note that two independent positions $X_{i,j}(k)$ and $Y_{i,j}(k)$ shall be generated by (4.1) according to the principle of FOA. In SCA-FOA proposed in [32], R_2, R_3 and R_4 are uniformly distributed random numbers in the range of $[0, 2\pi], [0, 2]$ and $[0, 1]$, respectively. R_1 is defined by the following formula

$$R_1 = a - k \times \frac{a}{k_{max}}, \tag{4.2}$$

where a is constant, k is the number of current iterations, k_{max} is the maximum number of iterations.

The main difference between our algorithm and SCA-FOA is the updata formula, including the search path and empirical parameter. Using the update formula (4.1), the search path will fluctuate outwards or towards the best solution, rather than go directly towards the best solution, which may make the algorithm fall into the local optimal when solving large-scale problem. The linear search path and empirical parameter are introduced to get rid of the local optimum and improve the searching speed in [27]. Based on this idea, we formulate the position updating in MSCA-FOA as

$$\xi_{i,j}(k+1) = \begin{cases} {R_1}'\xi_{i,j}(k) + c_1 \times \sin R_2 \times (\xi^p_{i,j}(k) - \xi_{i,j}(k)) \\ \qquad + c_2 \times \sin R_2 \times (\xi^e_{i,j}(k) - \xi_{i,j}(k)), \ R_4 < 0.5, \\ {R_1}'\xi_{i,j}(k) + c_1 \times \cos R_2 \times (\xi^p_{i,j}(k) - \xi_{i,j}(k)) \\ \qquad + c_2 \times \cos R_2 \times (\xi^e_{i,j}(k) - \xi_{i,j}(k)), \ R_4 \geq 0.5, \end{cases} \quad \xi = X, Y, \tag{4.3}$$

where $\xi^e_{i,j}(k)$ is the empirical parameter in ith individual and jth dimension at kth iteration. Different from [27], in (4.3), $\xi^e_{i,j}(k)$ is determined by group optimal solution of last iteration instead of randomly selecting from all previous iterations, which can save a mass of storage space. Note that although term $\xi^e_{i,j}(k)$ can help algorithm get rid of the local optimum better, the convergence speed may be reduced. In practice, to balance the globality and convergence speed, we can randomly replace several dimensions of ξ^e with the corresponding dimensions of historical best ξ^p. c_1, c_2 are constants which are determined based on specific problems. ${R_1}'$ is convergence factor to balance prospection and development, defined as follows

$${R_1}' = R_{max} - (R_{max} - R_{min})\frac{k}{k_{max}}, \tag{4.4}$$

where R_{max} and R_{min} are constants which can be adjusted according to specific problems.

After the position update, we will obtain two independent positions $X_i(k)$ and $Y_i(k)$ of ith individual at kth iteration and the smell concentration will be calculated as the fitness value, and then the smell concentration judgment value of ith individual at kth iteration ($S_i(k)$) is calculated.

$$S_i(k) = \frac{1}{\sqrt{X_i(k)^2 + Y_i(k)^2}}. \tag{4.5}$$

The smell concentration $Smell_i(k)$ of the individual position of the fruit fly can be found by substituting $S_i(k)$ into smell concentration judgment function, i.e. the objective function $\bar{J}$.

$$Smell_i(k) = \bar{J}(S_i(k)) = \bar{x}(n_p; S_i(k)). \tag{4.6}$$

Note that the smaller the smell concentration, the better the individual. Based on the smell concentration, the information used for iteration can be obtained. After a given round of iterations, the algorithm will converge to the optimal solution, i.e. the individual with smallest smell concentration. Algorithm 1 summaries the framework of the proposed MSCA-FOA.

4.2 AMDR

Suppose that we have obtained the solution of **Subproblem (A)** $(\theta^*, \bar{\eta}^*)$, then we shall apply AMDR algorithm given in [21] to get the solution η^* of **Subproblem (B)**. According to [21], AMDR runs a maximum dwell rounding (MDR) algorithm iteratively which aims to obtain a solution with the minimum number of switches under the condition of not exceeding the maximum rounding error to get the integer solution. Similar to [21], more specific procedures are divided as follows:

Step 1: Input relaxed control values $\bar{\eta}^*$, optimum tolerance $e > 0$ and allowed number of switches ρ_{max}. Initialize the rounding threshold $b = t_f - t_0$, lower bound $b_l = 0$ and upper bound $b_u = t_f - t_0$.

Step 2: Select a feasible control on the first time interval if $b_u - b_l > e$, otherwise go to step 6. Run MDR if

$$(\bar{\eta}^{*1}_{i_0} - \eta^1_{i_0})\Delta_1 \geq -b,\ i_0 \in I_{n_\omega},$$

and there is no other control $i_1 \neq i_0$ that is

$$\bar{\eta}^{*1}_{i_1}\Delta_1 > b,$$

otherwise, update $b_l = b$ and $b = b_l + 0.5 \cdot (b_u - b_l)$, then repeat step 2.

Step 3: Maximum Dwell Rounding. Initialize $\eta = 0$, $\eta^1_{i_0} = 1$ and $i = i_0$. Set $\eta^j_i = 1$ on other intervals if

$$\sum_{l=1}^{j} (\bar{\eta}^{*l}_i - \eta^l_i)\Delta_l < -b,$$

or there is a control $i_f \neq i$ that is

$$\sum_{l=1}^{j} \bar{\eta}^{*l}_{i_f}\Delta_l - \sum_{l=1}^{j-1} \eta^l_{i_f}\Delta_l \leq b,$$

Algorithm 1 Framework of MSCA-FOA. k is the generation number. $\bar{J}^e$ and S^e represent the Smell concentration and the smell concentration judgment value of group optimal solution of last iteration, respectively. $\bar{J}^p$ and S^p represent the Smell concentration and the smell concentration judgment value of historical best solution, respectively.

Set the total number of fruit flies in the swarm N_{size}, the maximum number of iterations k_{max}, the constants c_1, c_2, R_{max} and R_{min}. Set $k = 1$.
for $i \leq N_{size}$ **do**
  for $j \leq (n_\omega + 1) \times n_p$ **do**
    $X_{axis}(1) = rand(-1, 1)$, $Y_{axis}(1) = rand(-1, 1)$.
    $X_{i,j}(1) = X_{axis}(1) + rand(-10, 10)$, $Y_{i,j}(1) = Y_{axis}(1) + rand(-10, 10)$.
    $j = j + 1$.
  end for
  Calculate $S_i(1)$ and $\bar{J}(S_i(1))$ according to (4.5) and (4.6).
  $S^p = S^e = S_m(1) = \arg\min_{1 \leq i \leq N_{size}} \bar{J}(S_i(1)),\ X^p(1) = X^e(1) = X_m(1),\ Y^p(1) = Y^e(1) = Y_m(1)$.
  $i = i + 1$.
end for
while $k \leq k_{max}$ **do**
  /*the modified sine cosine strategy*/
  for $i \leq N_{size}$ **do**
    Calcultate the convergence factor $R_1{}'$.
    for $j \leq (n_\omega + 1) \times n_p$ **do**
      Set the random numbers R_2 and R_4.
      Update the individual information $X_{i,j}(k)$ and $Y_{i,j}(k)$ using formula (4.1).
      $j = j + 1$.
    end for
    Calculate $S_i(k + 1)$ and $\bar{J}(S_i(k + 1))$ according to (4.5) and (4.6).
    $i = i + 1$.
  end for
  $S_m(k + 1) = \arg\min_{1 \leq i \leq N_{size}} \bar{J}(S_i(k + 1)),\ X^e(k + 1) = X_m(k + 1),\ Y^e(k + 1) = Y_m(k + 1)$.
  if $\bar{J}(S_m(k + 1)) \leq \bar{J}_p$ **then**
    $\bar{J}^p = \bar{J}(S_m(k+1)),\ S^p = S_m(k+1),\ X^p(k+1) = X^e(k+1),\ Y^p(k+1) = Y^e(k+1)$.
  else
    $X^p(k + 1) = X^p(k)$, $Y^p(k + 1) = Y^p(k)$.
  end if
  $k := k + 1$.
end while
Output $\binom{\theta^*}{\bar{\eta}^*} = S^p$.

and $i = \arg\min_{k \in I_{n_\omega}} (\sum_{l=1}^{j} \bar{\eta}^{*l}_{i} \Delta_l - \sum_{l=1}^{j-1} \eta^l_i \Delta_l)$. After MDR, we can get η^j_i on the whole interval, denoted by η_{MDR}. Set $\eta = \eta_{\text{MDR}}$.

Step 4: If η satisfies (3.11) and $\sum_{l=1}^{j} (\bar{\eta}^{*l}_{i} - \eta^l_i)\Delta_l < b_u$ update $\eta_{\text{AMDR}} = \eta$, $b_u = \sum_{l=1}^{j} (\bar{\eta}^{*l}_{i} - \eta^l_i)\Delta_l$ and $b = b_u - 0.5 \cdot (b_u - b_l)$, then go to step 2.

Step 5: Get into the iterative optimization to duplicate steps 2-4. If $b_u - b_1 \le e$, then go to step 6.

Step 6: Output $\eta^* = \eta_{\text{AMDR}}$.

5 Numerical results

To obtain the numerical results, **Subproblem (A)** is solved by the proposed MSCA-FOA, while **Subproblem (B)** is solved by AMDR proposed in [21]. Experimental data and parameters in MSCA-FOA and AMDR are listed in Table 2. All the computations and simulations are performed in Matlab R2020b under 6 cores R5 computational environment with 3.30 GHz CPU.

Table 2: Experimental data and parameter values in MSCA-FOA and AMDR

Experimental data	$\mathbf{x}^0 = (0.14, 430.4673913, 0, 0, 0, 0, 3)^\top$, $\text{pH}_* = 6.48$, $\text{pH}^* = 6.52$, $t_0 = 3$ h, $t_f = 31$ h, $r_1 = 0.3$, $r_2 = 0.5$, $r_3 = 0.8$, $r_4 = 1.0$, $r_5 = 1.2$, $r_6 = 1.5$, $r_7 = 1.8$, $r_8 = 2.1$, $r_9 = 2.5$, $v_0 = 0.10$, $C_{s_0} = 12888$, $\varrho = 5000$, $d = 0.079567$, $\gamma = 0.338$
MSCA-FOA	$c_1 = 0.5$, $c_2 = 0.5$, $R_{max} = 0.8$, $R_{min} = 0.3$, $k_{max} = 30$, $N_{size} = 180$, $(n_\omega + 1) \times n_p = 500$
AMDR	$e = 0.001$, $\rho_{max} = 35$

Table 3: The approximate optimal switching sequence and optimal switching instants of $r^*(t)$.

switching sequence: $(r_1, r_2, r_8, r_1, r_9, r_3, r_1, r_2, r_7, r_1, r_6, r_7, r_3, r_5, r_7, r_9, r_3, r_8, r_9, r_1, r_8, r_6, r_3, r_2, r_8, r_6, r_3, r_1, r_9, r_6, r_7, r_1, r_6, r_5, r_6)^\top$.
switching instants: $(3.0000, 7.6812, 7.7003, 8.0041, 8.7044, 8.8461, 9.3387, 9.4877, 9.5403, 9.5844, 9.8034, 9.8699, 9.9694, 10.3735, 10.5105, 10.6238, 10.9009, 11.4467, 11.5665, 13.2026, 13.4777, 13.5792, 15.2623, 16.7901, 21.6402, 23.5379, 24.1706, 24.2719, 24.5938, 24.6859, 24.7979, 26.0341, 26.2680, 26.9543, 27.2371, 27.9698)^\top$.

By MSCA-FOA and AMDR, the approximate optimal solution (θ^*, η^*) of **Problem (P3)** can be obtained, then the approximate optimal switching sequence and optimal switching instants of $r^*(t)$ can be constructed as listed in Table 3. We can see that the switching occurred only 35 times which can meet the total variation constraint while keeping the 1,3-PD concentration at a high level.

With the progress of fermentation, it seems that high modes only appear in the metaphase of fermentation, and medium modes always appear in the anaphase of fermentation. Especially at the beginning of fermentation, the lowest mode lasted for quite a long time, about 5 hours. We can give a reasonable explanation for this result from a biological point of view. In the early stage of fermentation, the concentration of glycerol is still at a high level, and at this time it is in the substrate inhibition stage, considering the needs of cell growth, the feeding rate of glycerol should not be too high. As fermentation proceeds, the glycerol is continuously consumed and the feeding rate of glycerol should be increased to provide sufficient reactant. As fermentation proceeds further, the number of cells begins to decay and the amount of glycerol consumed decreases. Therefore, the optimal control strategy will show the law as shown in the result.

Fig. 1 and Fig. 2 shows the concentration of glycerol and 1,3-PD during the fed-batch fermentation process under the optimal feeding strategy of glycerol, respectively. Compare with the result 1025.3 mmol/L at terminal time 24.16 h in [3], it can be seen that the concentration of 1,3-PD at terminal time is increased by 10.3% with the result 1131.1 mmol/L at the same moment, which shows the rationality and feasibility of the obtained optimal strategy to enhance the productivity of 1,3-PD. Fig. 3 shows that except at the beginning of the fermentation, the pH is controlled within the acceptable region.

To further explore the influence of the given maximum number of switches on numerical results, the approximate optimal strategy and the concentration of 1,3-PD under three different ρ_{max} are drawn in Fig. 4. We can see that the concentration of 1,3-PD at terminal time decreases gradually as ρ_{max} increases, which indicates that the reduction of switching cost is at the cost of reducing product concentration. Thus, in actual production, these two indicators need to be considered comprehensively to get the maximum benefit.

To test the convergence of MSCA-FOA, the convergence speed of MSCA-FOA and SCA-FOA are drawn in Fig. 5. We can see that MSCA-FOA converges around the 19th iteration, while SCA-FOA converges around the 29th iteration with a nearly equal objective function value. The stability (robustness to initial value) and accuracy of MSCA-FOA and SCA-FOA are also compared under the same parameters. Besides, to gain empirical insight into the influence of the swarm size on the performance of two algorithms, we set N_{size} to four different values of 120, 150, 180, 210, respectively. Table 4 summarizes the mean values and the standard deviations of the two algorithms with 10 independent runs under four different N_{size}. By comparing the mean values, it can be observed that MSCA-FOA can convergence to a better objective function value. The standard deviation measures the stability of the algorithm, which indicates that the convergence results of MSCA-FOA fluctuate less than SCA-FOA in 10 independent runs. Another evaluation indicator running time is also given

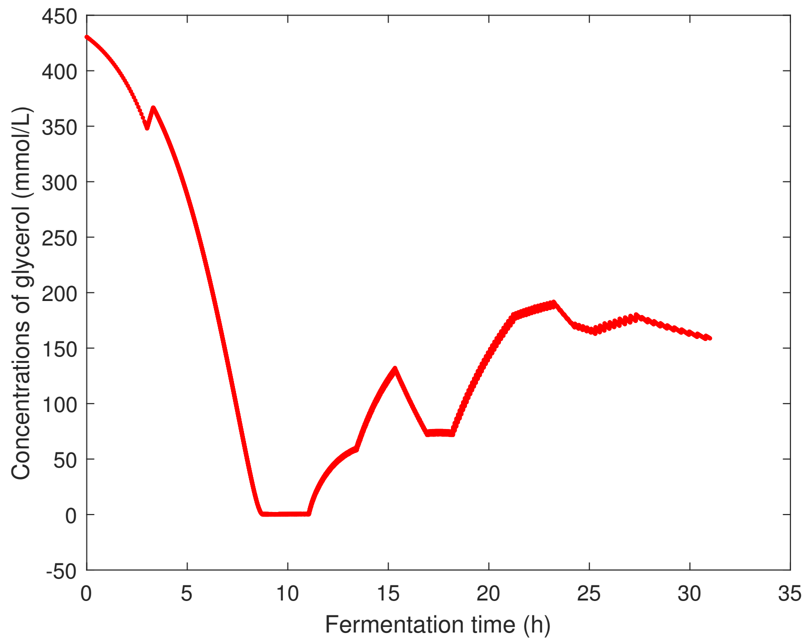


Figure 1: The curve of glycerol concentration with fermentation time under the approximate optimal strategy $r^*(t)$.

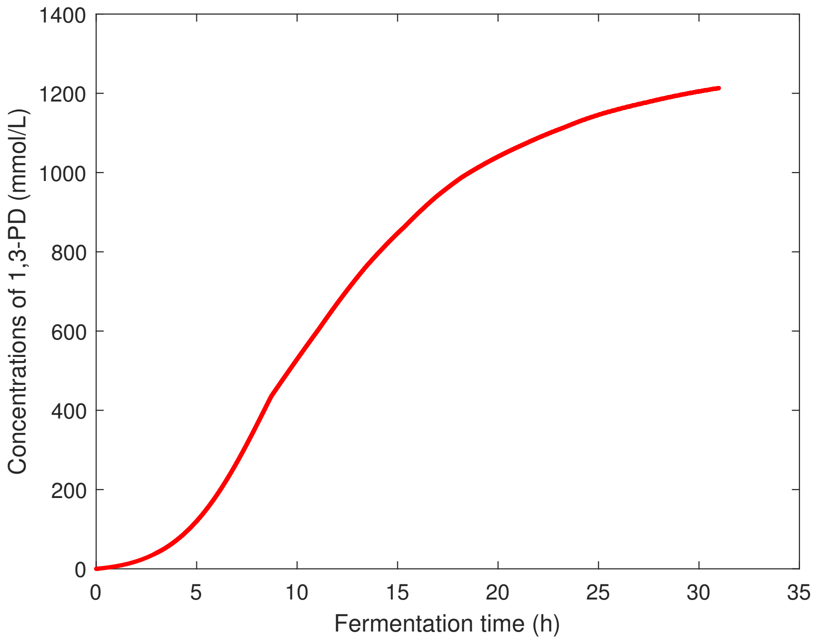


Figure 2: The curve of 1,3-PD concentration with fermentation time under the approximate optimal strategy $r^*(t)$.

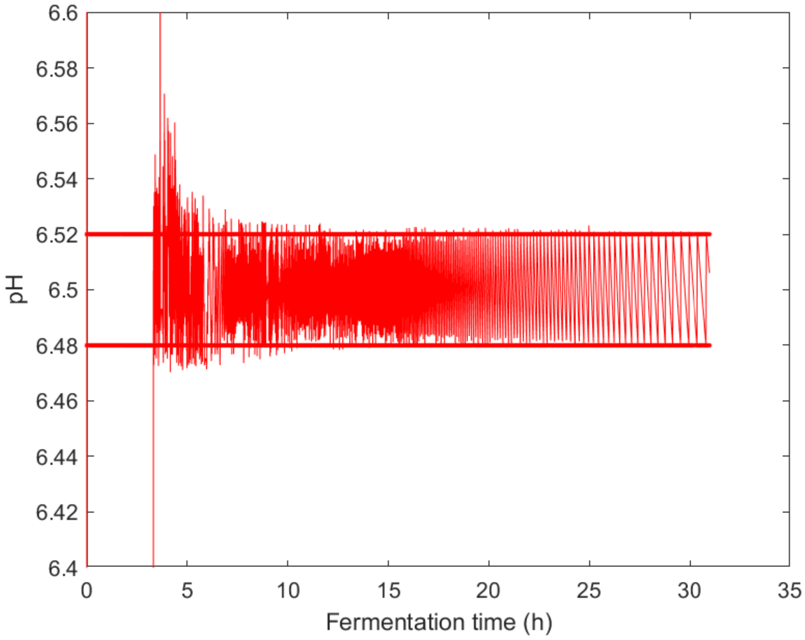
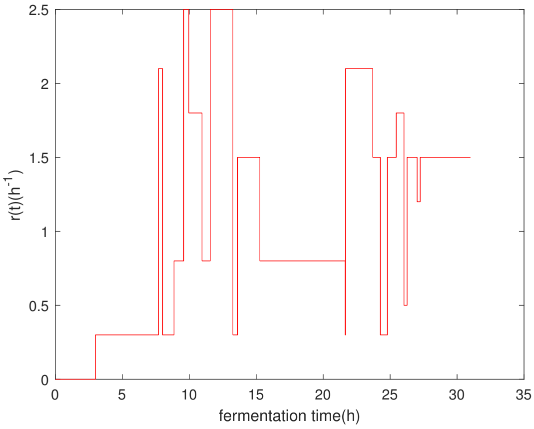


Figure 3: Simulation of the pH during the whole process of fed-batch culture.

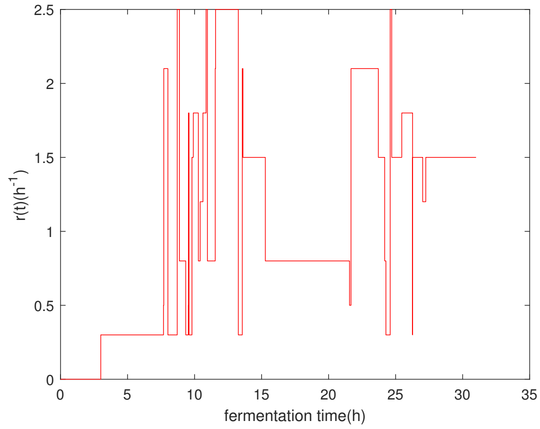
in Table 4, which shows that the running cost of two algorithms are approximately the same. The comparison comes to the conclusion that the proposed MSCA-FOA has better performance than SCA-FOA in terms of convergence speed, accuracy and stability, which verifies the feasibility of the proposed MSCA-FOA in face of the large-scale parameter optimization problem.

Table 4: The experimental results of MSCA-FOA and SCA-FOA.

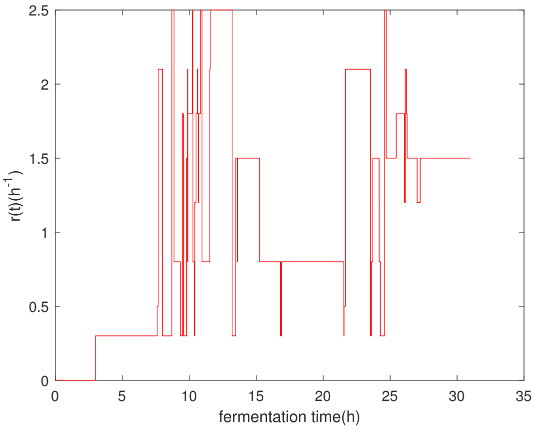
N_{size}	Algorithm	Mean	SD	Time (second)
120	SCA-FOA	-1305.9	5.3277	2715.8645
	MSCA-FOA	-1320.4	0.4435	2704.1235
150	SCA-FOA	-1311.4	3.0395	3366.9897
	MSCA-FOA	-1321.9	0.4726	3366.7073
180	SCA-FOA	-1320.6	1.5127	4077.6961
	MSCA-FOA	-1321.8	0.6028	4121.1946
210	SCA-FOA	-1321.2	0.8605	4771.5866
	MSCA-FOA	-1321.4	0.4272	4793.6620



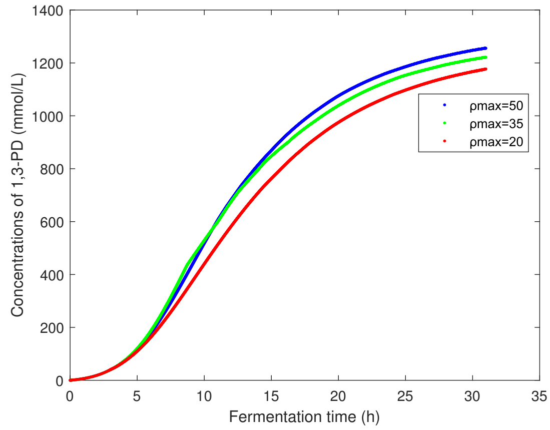
(a) $\rho_{max} = 20$.



(b) $\rho_{max} = 35$.



(c) $\rho_{max} = 50$.



(d) The concentration of 1,3-PD under different ρ_{max}.

Figure 4: Numerical results under three different ρ_{max}

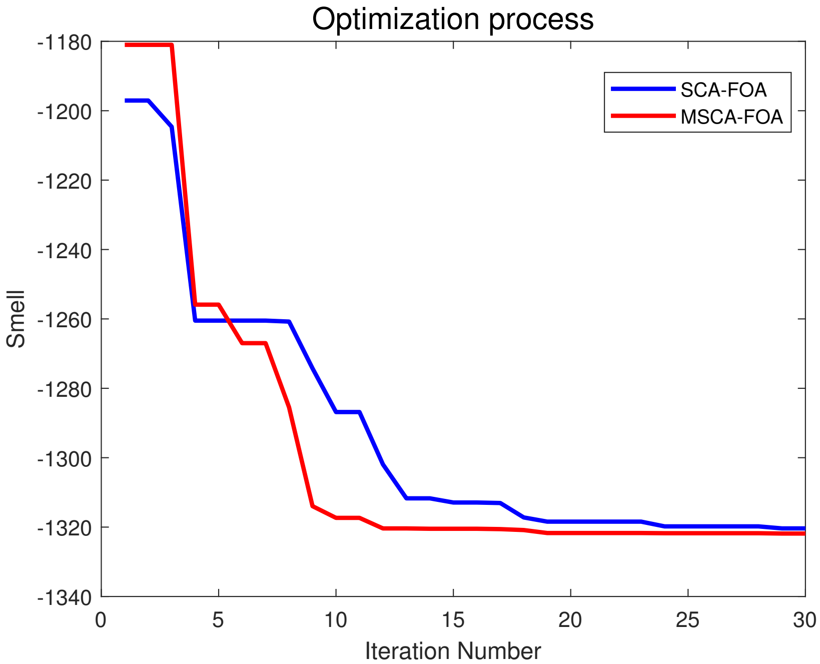


Figure 5: The convergence value of SCA-FOA and proposed MSCA-FOA.

6 Discussions and conclusions

In this paper, we considered limited number of switches to maximize the concentration of 1,3-PD at terminal time via optimizing switching sequence and switching instants simultaneously under fed-batch conversion process coupled with pH feedback. To solve a binary optimal control problem, a combinatorial integral approximation decomposition is introduced to divide it into two subproblems which are a continuous nonlinear program and a mixed binary linear program. We constructed a MSCA-FOA to solve the first subproblem, i.e. **Subproblem (A)**. Compared with the original SCA-FOA, the proposed MSCA-FOA has higher convergence speed and better convergence accuracy in solving **Subproblem (A)**. Numerical results indicate that the optimal strategy is feasible to improve the concentration of 1,3-PD at terminal time within the given number of switches.

For future research, it will be of significant interest to research on the fed-batch fermentation process with glycerol and alkali added separately. Besides, a better way to handle with state constraints will also be considered.

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The datasets generated during and/or analysed during the current study are publicly available.