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Research Article

Sequential Geometric Programming Method for Parameter Estimation of a Nonlinear System in Microbial Continuous Fermentation

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This paper addresses the problem of parameter estimation for the microbial continuous fermentation of glycerol to 1,3-propanediol. A nonlinear dynamical system is first presented to describe the microbial continuous fermentation. Some mathematical properties of the dynamical system in the microbial continuous fermentation are also presented. A parameter estimation model is proposed to estimate the parameters of the dynamical system. The proposed estimation model is a large-scale, nonlinear, and nonconvex optimization problem if the number of experimental groups is large. A sequential geometric programming (SGP) method is proposed to efficiently solve the parameter estimation problem. The results indicated that our proposed SGP method can yield smaller errors between the experimental and calculated steady-state concentrations than the existing seven methods. For the five error indices considered, that is, the concentration errors of biomass, glycerol, 1,3-propanediol, acetic acid, and ethanol, the results obtained using the proposed SGP method are better than those obtained using the methods in the literature (Xiu et al., Gao et al., Sun et al., Sun et al., Li and Qu, Wang et al., and Zhang and Xu), with improvements of approximately 71.86–95.03%, 52.08–94.87%, 99.70–99.98%, 5.39–90.29%, and 12.67–80.83%, respectively. This concludes that the established dynamical system can better describe the microbial continuous fermentation. We also present that our established dynamical system has multiple positive steady states in some fermentation conditions. We observe that there are two regions of multiple positive steady states at relatively high values of substrate glycerol concentration in feed medium.

1. Introduction

1,3-Propanediol (1,3-PDO) plays a key role in many industry fields, as it has extensive applications on a large commercial scale [1, 2]. In the production of 1,3-PDO, the microbial fermentation of glycerol to 1,3-PDO is attracting extensive attention because of its green production process [1]. In recent years, much research has been directed toward the development of the microbial fermentation process of glycerol, including the metabolic engineering and synthetic biology strategies in the biomanufacturing of 1,3-PDO and the mathematical modeling, optimization, and control of such processes [1, 3–35]. For example, Zhu et al. [1] reviewed the advances in metabolic engineering and synthetic biology techniques in the microbial production of 1,3-PDO. Fokum et al. [3] reviewed the recent developments in the biomanufacturing strategies of 1,3-PDO from glycerol. Wang et al. [4] reprogrammed the metabolism of *Klebsiella pneumoniae* to efficiently produce 1,3-PDO. The conducted metabolic engineering manipulations can dramatically reduce the accumulation of acetate. Lee et al. [5] reviewed the advances in biological and chemical techniques for the 1,3-PDO production from glycerol. Asopa et al. [6] used *Saccharomyces cerevisiae* to produce 1,3-PDO and butyric acid through microbial fermentation of glycerol. Gupta et al. [7] used the new producer, *Clostridium butyricum* L4, to develop a fed-batch fermentation process of crude glycerol into 1,3-PDO. The developed fermentation process can obtain a high yield of 1,3-PDO. Liu et al. [8], Wang et al. [9], Gao et al. [10], and Xu et al. [11] addressed the optimization models and methods to optimize the fermentation processes of glycerol. Pan et al. [12] addressed the theoretical study of feedback control for a two-stage fermentation process of 1,3-PDO. To deal with the challenges of the online measurement of the microbial fermentation process, Zhang et al. [13] presented a robust soft sensor to efficiently predict the concentrations of 1,3-PDO and glycerol. Xu and Li [14] presented the mathematical optimization approach to optimize the metabolic objective for glycerol metabolism into 1,3-PDO production. Xu et al. [15] proposed a two-stage approach to efficiently solve the parameter identification problem of the microbial batch process of glycerol. Pröschle et al. [16] designed the advanced controller to control the fed-batch fermenter of glycerol to 1,3-PDO. Emel'yanenko and Verevkin [17] addressed the thermodynamic properties of 1,3-PDO. Rodriguez et al. [18] proposed the kinetic model to describe the fermentation process of the raw glycerol into 1,3-PDO. Silva et al. [19] addressed the multiplicity study of steady states in a microbial fermentation process of 1,3-PDO. Liu and Zhao [20] presented an optimal switching technique to control the 1,3-PDO fed-batch production. Yuan et al. [21] proposed a robust feedback method to control the nonlinear switched system of 1,3-PDO fed-batch production. Liberato et al. [22] used both crude glycerol and corn steep liquor in 1,3-PDO production using a *Clostridium butyricum* strain.

Xiu et al. [23], Gao et al. [24], Sun et al. [25], Sun et al. [26], Li and Qu [27], Wang et al. [28], and Zhang and Xu [29] used the excess kinetic models, S-system, and fractional-order model to mathematically describe the microbial continuous fermentation of glycerol to 1,3-PDO. However, a comparison study suggested that the steady-state concentrations calculated by these works significantly violate the experimental data (refer to Section 5). For example, the errors of glycerol concentrations reached more than 43% in [24–27]. This concludes that the mathematical models established by these researchers cannot satisfactorily describe the real bioprocess. To better describe the microbial continuous fermentation of glycerol, it is necessary to present new mathematical modeling or parameter estimation methods.

For this purpose, in the present study, we address the problem of parameter estimation for the microbial continuous fermentation of glycerol to 1,3-PDO. First, a nonlinear dynamical system is presented to describe the microbial continuous fermentation. Then, some mathematical properties of the dynamical system in the microbial continuous fermentation are also presented in terms of the estimated parameters, reactant concentrations, and fermentation conditions. Section 3 proposes a parameter estimation model to estimate the value of the parameter vector in the dynamical system of the microbial continuous fermentation. Section 4 proposes a sequential geometric programming (SGP) method to efficiently solve the nonlinear, nonconvex parameter estimation problem. Section 5 presents the computation results obtained using the proposed SGP algorithm and also presents a comparative study to demonstrate that the proposed SGP algorithm can yield smaller errors between the experimental and calculated steady-state concentrations than the other seven methods. Additionally, we investigate the multiple positive steady states of our proposed dynamical system in Section 5. Finally, we provide the conclusions of the present work in Section 6.

2. Nonlinear Dynamical System of Microbial Continuous Fermentation

2.1. Nonlinear Dynamical System. In the microbial continuous fermentation of glycerol to 1,3-PDO by *Klebsiella pneumonia*, the substrate glycerol is continuously added to the fermenter, and equal volumes of substrate glycerol, reaction products, and cells are extracted from the fermenter. The concentration of various substances in the fermenter is in a constant state. The main products of the microbial continuous fermentation include 1,3-PDO, acetic acid, and ethanol [23]. Figure 1 presents the schematic of the microbial continuous fermentation in the fermenter. In this figure, F is the volume flow of feed medium into the fermenter, L/h; y_{sf} denotes the concentration of substrate glycerol in feed medium, mmol/L; V is the volume of fermentation broth, L; y_1 represents the biomass, g/L; and y_2, y_3, y_4, and y_5 represent the concentrations of glycerol, 1,3-PDO, acetic acid, and ethanol, respectively, mmol/L.

A process can be modeled by some modeling methods, such as the neural network modeling techniques [36, 37] and the ODE (ordinary differential equation) methods [38]. Based on the basic conservation law and the previous literature [23], in this study, the material balance equations of the microbial continuous fermentation are written as the following five-dimensional nonlinear ODEs:

$$\frac{\mathrm{d}y_1}{\mathrm{d}t} = r_1 y_1 - d y_1, t \in [0, T], \tag{1}$$

$$\frac{\mathrm{d}y_2}{\mathrm{d}t} = d y_{\mathrm{sf}} - d y_2 - r_2 y_1, t \in [0, T], \tag{2}$$

$$\frac{\mathrm{d}y_3}{\mathrm{d}t} = r_3 y_1 - d y_3, t \in [0, T], \tag{3}$$

$$\frac{\mathrm{d}y_4}{\mathrm{d}t} = r_4 y_1 - d y_4, t \in [0, T], \tag{4}$$

$$\frac{\mathrm{d}y_5}{\mathrm{d}t} = r_5 y_1 - d y_5, t \in [0, T], \tag{5}$$

$$y_i(0) = y_{i,0}, i = 1, 2, \cdots, 5, \tag{6}$$

where t is the fermentation time, h; T represents the terminal time of the microbial continuous fermentation; $d = F/V$ represents the dilution rate, h^{-1}; r_1 is the nonlinear function that denotes the specific growth rate of cells, h^{-1}; r_2 is the nonlinear function representing the specific consumption rate of glycerol, mmol/(g·h); and r_3, r_4, and r_5 are the nonlinear functions denoting the specific formation rates of 1,3-PDO, acetic acid, and ethanol, respectively, mmol/(g·h).

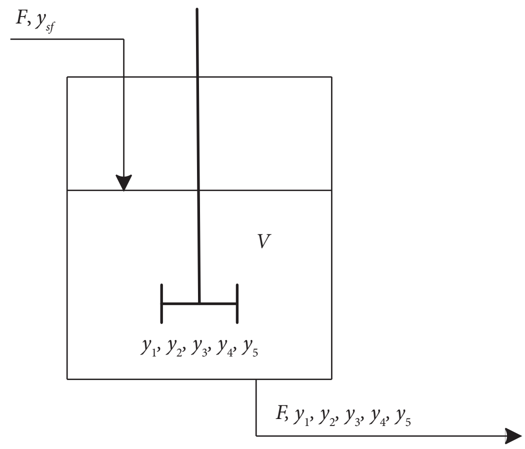

FIGURE 1: Schematic of microbial continuous fermentation in the fermenter.

Considering the nature of the microbial continuous fermentation, we set the rates r_i $(i = 1, 2, \cdots, 5)$ to be $r_i \geq 0$.

The rates r_i $(i = 1, 2, \cdots, 5)$ in (1)–(5) are expressed as the following equations:

$$\begin{aligned} r_1 &= a_1 \frac{y_2}{y_2 + a_2}\left(1 - \frac{y_2}{y_2^*}\right)\left(1 - \frac{y_3}{y_3^*}\right)\left(1 - \frac{y_4}{y_4^*}\right)\left(1 - \frac{y_5}{y_5^*}\right), \\ r_2 &= \theta_1 + \frac{r_1}{\theta_2} + \theta_3 \frac{y_2}{y_2 + \theta_4}, \\ r_3 &= \theta_5 + \theta_6 r_1 + \theta_7 \frac{y_2}{y_2 + \theta_8}, \\ r_4 &= \theta_9 + \theta_{10} r_1 + \theta_{11} \frac{y_2}{y_2 + \theta_{12}}, \\ r_5 &= r_2\left(\frac{\theta_{13}}{\theta_{15} + d y_2} + \frac{\theta_{14}}{\theta_{16} + d y_2}\right). \end{aligned} \tag{7}$$

In these equations, $\theta = (\theta_1, \theta_2, \cdots, \theta_{16})^{\mathrm{T}} \in \Theta$ is the model parameter vector to be estimated later with $\theta_j > 0$ $(j \neq 5, 9)$ and $\theta_j < 0$ $(j = 5, 9)$, where Θ is defined as

$$\Theta = \prod_{j=1}^{16} \left[\theta_j^{\mathrm{L}}, \theta_j^{\mathrm{U}}\right] \subset R^{16}, \tag{8}$$

where $\theta_j^{\mathrm{L}} > 0$ and $\theta_j^{\mathrm{U}} > 0$ when $j \neq 5, 9$ and $\theta_j^{\mathrm{L}} < 0$ and $\theta_j^{\mathrm{U}} < 0$ when $j = 5, 9$.

Under certain experimental conditions, the maximum value of r_1 is a_1 h^{-1}, and the Monod saturation constant is a_2 mmol/L. The critical values of y_1, y_2, y_3, y_4, and y_5 are y_1^* g/L, y_2^* mmol/L, y_3^* mmol/L, y_4^* mmol/L, and y_5^* mmol/L, respectively. Therefore, microbial fermentation system (1)–(6) will work in the subset of R^5, expressed as follows:

$$Y_1 = \left\{y = (y_1, y_2, \cdots, y_5)^{\mathrm{T}} \in R^5 \mid y_1 \in (0, y_1^*], y_2 \in (0, y_2^*], y_3 \in (0, y_3^*], y_4 \in (0, y_4^*], y_5 \in (0, y_5^*]\right\}. \tag{9}$$

In addition, the dilution rate d and glycerol concentration in the feed y_{sf} will stay within certain limits, i.e., $(d, y_{\mathrm{sf}})^{\mathrm{T}} \in Y_2$, where Y_2 is expressed as follows:

$$Y_2 = \left\{(d, y_{\mathrm{sf}})^{\mathrm{T}} \in R^2 \mid d \in \left[d^{\mathrm{L}}, d^{\mathrm{U}}\right], y_{\mathrm{sf}} \in (0, y_2^*]\right\}, \tag{10}$$

where $d^{\mathrm{L}} > 0$ and $d^{\mathrm{U}} > 0$.

By introducing the expressions of functions r_i $(i = 1, 2, \cdots, 5)$ into (1)–(6), we obtain the following reformulations of the microbial continuous fermentation:

$$
\begin{aligned}
\frac{\mathrm{d}y_1}{\mathrm{d}t} &= \frac{a_1 y_1 y_2}{y_2+a_2}\left(1-\frac{y_2}{y_2^*}\right)\left(1-\frac{y_3}{y_3^*}\right)\left(1-\frac{y_4}{y_4^*}\right)\left(1-\frac{y_5}{y_5^*}\right)-dy_1, t\in[0,T],\\
\frac{\mathrm{d}y_2}{\mathrm{d}t} &= dy_{\mathrm{sf}}-dy_2-\left[\theta_1+\frac{a_1 y_2}{\theta_2(y_2+a_2)}\left(1-\frac{y_2}{y_2^*}\right)\left(1-\frac{y_3}{y_3^*}\right)\left(1-\frac{y_4}{y_4^*}\right)\left(1-\frac{y_5}{y_5^*}\right)+\frac{\theta_3 y_2}{y_2+\theta_4}\right]y_1, t\in[0,T],\\
\frac{\mathrm{d}y_3}{\mathrm{d}t} &= \left[\theta_5+\frac{\theta_6 a_1 y_2}{y_2+a_2}\left(1-\frac{y_2}{y_2^*}\right)\left(1-\frac{y_3}{y_3^*}\right)\left(1-\frac{y_4}{y_4^*}\right)\left(1-\frac{y_5}{y_5^*}\right)+\frac{\theta_7 y_2}{y_2+\theta_8}\right]y_1-dy_3, t\in[0,T],\\
\frac{\mathrm{d}y_4}{\mathrm{d}t} &= \left[\theta_9+\frac{\theta_{10} a_1 y_2}{y_2+a_2}\left(1-\frac{y_2}{y_2^*}\right)\left(1-\frac{y_3}{y_3^*}\right)\left(1-\frac{y_4}{y_4^*}\right)\left(1-\frac{y_5}{y_5^*}\right)+\frac{\theta_{11} y_2}{y_2+\theta_{12}}\right]y_1-dy_4, t\in[0,T],\\
\frac{\mathrm{d}y_5}{\mathrm{d}t} &= \left[\theta_1+\frac{a_1 y_2}{\theta_2(y_2+a_2)}\left(1-\frac{y_2}{y_2^*}\right)\left(1-\frac{y_3}{y_3^*}\right)\left(1-\frac{y_4}{y_4^*}\right)\left(1-\frac{y_5}{y_5^*}\right)+\frac{\theta_3 y_2}{y_2+\theta_4}\right]\times\left(\frac{\theta_{13}}{\theta_{15}+\mathrm{d}y_2}+\frac{\theta_{14}}{\theta_{16}+\mathrm{d}y_2}\right)y_1-dy_5, t\in[0,T],\\
y_i(0) &= y_{i,0}, i=1,2,\cdots,5.
\end{aligned}
\tag{11}
$$

Now, we perform some transformations, as follows:

$$
\begin{aligned}
x_1 &= y_2+a_2,\\
x_2 &= 1-\frac{y_2}{y_2^*},\\
x_3 &= 1-\frac{y_3}{y_3^*},\\
x_4 &= 1-\frac{y_4}{y_4^*},\\
x_5 &= 1-\frac{y_5}{y_5^*},\\
x_6 &= y_2+\theta_4,\\
x_7 &= y_2+\theta_8,\\
x_8 &= y_2+\theta_{12},\\
x_9 &= \theta_{15}+dy_{2,}\\
x_{10} &= \theta_{16}+dy_2.
\end{aligned}
\tag{12}
$$

Then, we obtain the following dynamical system with a power function structure:

$$
\begin{aligned}
\frac{\mathrm{d}y_1}{\mathrm{d}t} &= a_1 y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 - dy_1, t\in[0,T],\\
\frac{\mathrm{d}y_2}{\mathrm{d}t} &= dy_{\mathrm{sf}} - dy_2 - \theta_1 y_1 - a_1\theta_2^{-1} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 - \theta_3 y_1 y_2 x_6^{-1}, t\in[0,T],\\
\frac{\mathrm{d}y_3}{\mathrm{d}t} &= \theta_5 y_1 + a_1\theta_6 y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 + \theta_7 y_1 y_2 x_7^{-1} - dy_3, t\in[0,T],\\
\frac{\mathrm{d}y_4}{\mathrm{d}t} &= \theta_9 y_1 + a_1\theta_{10} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 + \theta_{11} y_1 y_2 x_8^{-1} - dy_4, t\in[0,T],\\
\frac{\mathrm{d}y_5}{\mathrm{d}t} &= \theta_1\theta_{13} y_1 x_9^{-1} + a_1\theta_2^{-1}\theta_{13} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 x_9^{-1} + \theta_3\theta_{13} y_1 y_2 x_6^{-1} x_9^{-1} + \theta_1\theta_{14} y_1 x_{10}^{-1}\\
&\quad + a_1\theta_2^{-1}\theta_{14} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 x_{10}^{-1} + \theta_3\theta_{14} y_1 y_2 x_6^{-1} x_{10}^{-1} - dy_5, t\in[0,T],\\
y_i(0) &= y_{i,0}, i=1,2,\cdots,5.
\end{aligned}
\tag{13}
$$

The above dynamical system can be further represented as

$$\frac{dy_i}{dt} = g_i(y, x, d, y_{sf}, \theta), \quad t \in [0, T], i = 1, 2, \cdots, 5, \tag{14}$$

$$x_k = h_k(y, d, \theta), \quad k = 1, 2, \cdots, 10, \tag{15}$$

$$y(0) = y_0. \tag{16}$$

In this representation, $x = (x_1, x_2, \cdots, x_{10})^{\mathrm{T}} \subset R^{10}$, $y_0 = (y_{1,0}, y_{2,0}, \cdots, y_{5,0})^{\mathrm{T}} \subset R^5$, and the functions $g_i(y, x, d, y_{sf}, \theta)$ and $h_k(y, d, \theta)$ are defined as

$$\begin{aligned}
g_1(y, x, d, y_{sf}, \theta) &= a_1 y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 - d y_1, \\
g_2(y, x, d, y_{sf}, \theta) &= d y_{sf} - d y_2 - \theta_1 y_1 - a_1 \theta_2^{-1} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 - \theta_3 y_1 y_2 x_6^{-1}, \\
g_3(y, x, d, y_{sf}, \theta) &= \theta_5 y_1 + a_1 \theta_6 y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 + \theta_7 y_1 y_2 x_7^{-1} - d y_3, \\
g_4(y, x, d, y_{sf}, \theta) &= \theta_9 y_1 + a_1 \theta_{10} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 + \theta_{11} y_1 y_2 x_8^{-1} - d y_4, \\
g_5(y, x, d, y_{sf}, \theta) &= \theta_1 \theta_{13} y_1 x_9^{-1} + a_1 \theta_2^{-1} \theta_{13} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 x_9^{-1} + \theta_3 \theta_{13} y_1 y_2 x_6^{-1} x_9^{-1} \\
&\quad + \theta_1 \theta_{14} y_1 x_{10}^{-1} + a_1 \theta_2^{-1} \theta_{14} y_1 y_2 x_1^{-1} x_2 x_3 x_4 x_5 x_{10}^{-1} + \theta_3 \theta_{14} y_1 y_2 x_6^{-1} x_{10}^{-1} - d y_5, \\
h_1(y, d, \theta) &= y_2 + a_2, \\
h_2(y, d, \theta) &= 1 - \frac{y_2}{y_2^*}, \\
h_3(y, d, \theta) &= 1 - \frac{y_3}{y_3^*}, \\
h_4(y, d, \theta) &= 1 - \frac{y_4}{y_4^*}, \\
h_5(y, d, \theta) &= 1 - \frac{y_5}{y_5^*}, \\
h_6(y, d, \theta) &= y_2 + \theta_4, \\
h_7(y, d, \theta) &= y_2 + \theta_8, \\
h_8(y, d, \theta) &= y_2 + \theta_{12}, \\
h_9(y, d, \theta) &= \theta_{15} + d y_2, \\
h_{10}(y, d, \theta) &= \theta_{16} + d y_2.
\end{aligned} \tag{17}$$

Dynamical system (14)–(16) is a differential-algebraic system.

Remark 1. Compared to the model (1)–(6), the advantages of the transformed dynamical system (14)–(16) are as follows: (1) it is still a nonlinear model that can describe the nonlinear fermentation process and (2) it involves a special power function structure that can be used to propose a novel SGP method for the parameter estimation problem of the microbial continuous fermentation.

2.2. Mathematical Properties of the Dynamical System. In this subsection, we consider the properties of dynamical system (14)–(16).

Property 2. For $\theta \in \Theta$, the functions $g_i(y, x, d, y_{sf}, \theta)$ $(i = 1, 2, \cdots, 5)$ and $h_k(y, d, \theta)$ $(k = 1, 2, \cdots, 10)$ provided in dynamical system (14)–(16) are continuously differentiable on $[0, T]$, i.e., $g_i(y, x, d, y_{sf}, \theta) \in C^1(0, T; R^5)$, $h_k(y, d, \theta) \in C^1(0, T; R^{10})$, and the functions $g_i(y, x, d, y_{sf}, \theta)$ and h_k (y, d, θ) are continuous in θ on Θ.

Proof. By the definitions of the functions $g_i(y, x, d, y_{\mathrm{sf}}, \theta)$ $(i = 1, 2, \cdots, 5)$ and $h_k(y, d, \theta)$ $(k = 1, 2, \cdots, 10)$, it can be easily verified that the conclusion is valid. □

Property 3. For $\theta \in \Theta$, the functions $g_i(y, x, d, y_{\mathrm{sf}}, \theta)$ $(i = 1, 2, \cdots, 5)$ and $h_k(y, d, \theta)$ $(k = 1, 2, \cdots, 10)$ provided in dynamical system (14)–(16) are locally Lipschitz continuous on Y_1 with respect to y.

Proof. Let $\widehat{y}, \widetilde{y} \in Y_1$. By the mean value theorem, there exist $\lambda_i \in (0, 1)$ $(i = 1, 2, \cdots, 5)$ and $\tau_k \in (0, 1)$ $(k = 1, 2, \cdots, 10)$ such that

$$\begin{aligned} \left|g_i(\widehat{y}, x, d, y_{\mathrm{sf}}, \theta) - g_i(\widetilde{y}, x, d, y_{\mathrm{sf}}, \theta)\right| &\leq \left\|\nabla g_i(\widehat{y} + \lambda_i(\widetilde{y} - \widehat{y}), x, d, y_{\mathrm{sf}}, \theta)\right\|_2 \cdot \|\widehat{y} - \widetilde{y}\|_2, \quad i = 1, 2, \cdots, 5, \\ \left|h_k(\widehat{y}, d, \theta) - h_k(\widetilde{y}, d, \theta)\right| &\leq \left\|\nabla h_k(\widehat{y} + \tau_k(\widetilde{y} - \widehat{y}), d, \theta)\right\|_2 \cdot \|\widehat{y} - \widetilde{y}\|_2, \quad k = 1, 2, \cdots, 10. \end{aligned} \tag{18}$$

As Y_1, Y_2, and Θ are bounded sets, the derivatives of $g_i(y, x, d, y_{\mathrm{sf}}, \theta)$ $(i = 1, 2, \cdots, 5)$ and $h_k(y, d, \theta)$ $(k = 1, 2, \cdots, 10)$ are bounded on Y_1 from Property 2. Thus, $\|\nabla g_i(\widehat{y} + \lambda_i(\widetilde{y} - \widehat{y}), x, d, y_{\mathrm{sf}}, \theta)\|_2$ and $\|\nabla h_k(\widehat{y} + \tau_k(\widetilde{y} - \widehat{y}), d, \theta)\|_2$ are bounded. For any $\theta \in \Theta$, let

$$\begin{aligned} L_{g_i} &= \max \left\|\nabla g_i(\widehat{y} + \lambda_i(\widetilde{y} - \widehat{y}), x, d, y_{\mathrm{sf}}, \theta)\right\|_2, \\ L_{h_k} &= \max \left\|\nabla h_k(\widehat{y} + \tau_k(\widetilde{y} - \widehat{y}), d, \theta)\right\|_2. \end{aligned} \tag{19}$$

Then, we have

$$\begin{aligned} \left|g_i(\widehat{y}, x, d, y_{\mathrm{sf}}, \theta) - g_i(\widetilde{y}, x, d, y_{\mathrm{sf}}, \theta)\right| &\leq L_{g_i} \cdot \|\widehat{y} - \widetilde{y}\|_2, \quad i = 1, 2, \cdots, 5, \\ \left|h_k(\widehat{y}, d, \theta) - h_k(\widetilde{y}, d, \theta)\right| &\leq L_{h_k} \cdot \|\widehat{y} - \widetilde{y}\|_2, \quad k = 1, 2, \cdots, 10. \end{aligned} \tag{20}$$

These conclude that $g_i(y, x, d, y_{\mathrm{sf}}, \theta)$ $(i = 1, 2, \cdots, 5)$ and $h_k(y, d, \theta)$ $(k = 1, 2, \cdots, 10)$ are locally Lipschitz continuous on Y_1 with respect to y. □

Property 4. For $\theta \in \Theta$, dynamical system (14)–(16) has a unique solution, expressed by $y(t; y_0, d, y_{\mathrm{sf}}, \theta)$, and $y(t; y_0, d, y_{\mathrm{sf}}, \theta)$ is continuous on Θ with respect to θ.

Proof. For $y_0 \in Y_1$ and $(d, y_{\mathrm{sf}})^{\mathrm{T}} \in Y_2$, we know $g_i(y, x, d, y_{\mathrm{sf}}, \theta) \in C^1(0, T; R^5)$ and $h_k(y, d, \theta) \in C^1(0, T; R^5)$, and the functions $g_i(y, x, d, y_{\mathrm{sf}}, \theta)$ and $h_k(y, d, \theta)$ are continuous in θ on Θ from Property 2. Therefore, dynamical system (14)–(16) has a unique solution, expressed by $y(t; y_0, d, y_{\mathrm{sf}}, \theta)$. According to the continuous dependence of solutions on parameters in nonlinear differential equations, $y(t; y_0, d, y_{\mathrm{sf}}, \theta)$ is continuous on Θ with respect to θ. □

Property 5. Let the solution set of dynamical system (14)–(16) be $Y_3(y_0, d, y_{\mathrm{sf}}) = \{y(t; y_0, d, y_{\mathrm{sf}}, \theta) \in R^5 \mid y(t; y_0, d, y_{\mathrm{sf}}, \theta)$ is the solution of dynamical system (14)–(16) for $\theta \in \Theta\}$.

Then, $Y_3(y_0, d, y_{\mathrm{sf}})$ is a compact set in $C^1(0, T; R^5)$.

Proof. From the definition of set Θ, Θ is a bounded closed set in R^{16}. Therefore, Θ is a compact set in R^{16}. By Properties 2 and 4, we obtain that the mapping from $\theta \in \Theta$ to $y(t; y_0, d, y_{\mathrm{sf}}, \theta) \in Y_3(y_0, d, y_{\mathrm{sf}})$ is continuous. This concludes that $Y_3(y_0, d, y_{\mathrm{sf}})$ is a compact set in $C^1(0, T; R^5)$. □

Property 6. For $\forall (d, y_{\mathrm{sf}})^{\mathrm{T}} \in Y_2$ and $\forall \theta \in \Theta$, the vector function

$$g(y, x, d, y_{\mathrm{sf}}, \theta) = (g_1(y, x, d, y_{\mathrm{sf}}, \theta), g_2(y, x, d, y_{\mathrm{sf}}, \theta), \cdots, g_5(y, x, d, y_{\mathrm{sf}}, \theta))^T, \tag{21}$$

satisfies the following linear growth condition with respect to y:

$$\left\|g(y, x, d, y_{\mathrm{sf}}, \theta)\right\|_2 < b_1\|y\|_2 + b_2, \quad \forall y \in Y_1, \tag{22}$$

where $0 < b_1 < +\infty$ and $0 < b_2 < +\infty$.

Proof. By the derivation of dynamical system (14)–(16) in Section 2.1, we obtain

$$\begin{aligned} g_1(y, x, d, y_{\mathrm{sf}}, \theta) &= r_1 y_1 - d y_1, \\ g_2(y, x, d, y_{\mathrm{sf}}, \theta) &= d y_{\mathrm{sf}} - d y_2 - r_2 y_1, \\ g_3(y, x, d, y_{\mathrm{sf}}, \theta) &= r_3 y_1 - d y_3, \\ g_4(y, x, d, y_{\mathrm{sf}}, \theta) &= r_4 y_1 - d y_4, \\ g_5(y, x, d, y_{\mathrm{sf}}, \theta) &= r_5 y_1 - d y_5. \end{aligned} \tag{23}$$

Then, for $(d, y_{\mathrm{sf}})^{\mathrm{T}} \in Y_2$, $\theta \in \Theta$, and $y \in Y_1$, we have

$$\begin{aligned}\|g(y,x,d,y_{\mathrm{sf}},\theta)\|_2 &= \left\|(g_1(y,x,d,y_{\mathrm{sf}},\theta), g_2(y,x,d,y_{\mathrm{sf}},\theta),\cdots,g_5(y,x,d,y_{\mathrm{sf}},\theta))^{\mathrm{T}}\right\|_2\\ &= \left\|(r_1y_1-dy_1, dy_{\mathrm{sf}}-dy_2-r_2y_1, r_3y_1-dy_3, r_4y_1-dy_4, r_5y_1-dy_5)^{\mathrm{T}}\right\|_2\\ &= \left\|(r_1y_1,-r_2y_1,r_3y_1,r_4y_1,r_5y_1)^{\mathrm{T}}-(dy_1,dy_2,dy_3,dy_4,dy_5)^{\mathrm{T}}+(0,dy_{\mathrm{sf}},0,0,0)^{\mathrm{T}}\right\|_2\\ &\le \left\|(r_1y_1,-r_2y_1,r_3y_1,r_4y_1,r_5y_1)^{\mathrm{T}}\right\|_2+\left\|(dy_1,dy_2,dy_3,dy_4,dy_5)^{\mathrm{T}}\right\|_2+\left\|(0,dy_{\mathrm{sf}},0,0,0)^{\mathrm{T}}\right\|_2\\ &= y_1\left\|(r_1,-r_2,r_3,r_4,r_5)^{\mathrm{T}}\right\|_2+d\|y\|_2+dy_{\mathrm{sf}}.\end{aligned} \tag{24}$$

As $r_1 \ge 0$, $y \in Y_1$, $d \in [d^{\mathrm{L}}, d^{\mathrm{U}}]$, and $\theta \in \Theta$, we obtain

$$\begin{aligned} r_1 &= a_1\frac{y_2}{y_2+a_2}\left(1-\frac{y_2}{y_2^*}\right)\left(1-\frac{y_3}{y_3^*}\right)\left(1-\frac{y_4}{y_4^*}\right)\left(1-\frac{y_5}{y_5^*}\right) < a_1,\\ r_2 &= \theta_1+\frac{r_1}{\theta_2}+\theta_3\frac{y_2}{y_2+\theta_4} < \theta_1+\frac{a_1}{\theta_2}+\theta_3,\\ r_3 &= \theta_5+\theta_6 r_1+\theta_7\frac{y_2}{y_2+\theta_8} < \theta_5+\theta_6 a_1+\theta_7,\\ r_4 &= \theta_9+\theta_{10} r_1+\theta_{11}\frac{y_2}{y_2+\theta_{12}} < \theta_9+\theta_{10} a_1+\theta_{11},\\ r_5 &= r_2\left(\frac{\theta_{13}}{\theta_{15}+dy_2}+\frac{\theta_{14}}{\theta_{16}+dy_2}\right) < \left(\theta_1+\frac{a_1}{\theta_2}+\theta_3\right)\left(\frac{\theta_{13}}{\theta_{15}}+\frac{\theta_{14}}{\theta_{16}}\right). \end{aligned} \tag{25}$$

Then, by $r_i \ge 0$ $(i = 1, 2, \cdots, 5)$, we have

$$\begin{aligned} r_1^2 &< a_1^2,\\ r_2^2 &< \left(\theta_1+\frac{a_1}{\theta_2}+\theta_3\right)^2,\\ r_3^2 &< (\theta_5+\theta_6 a_1+\theta_7)^2,\\ r_4^2 &< (\theta_9+\theta_{10} a_1+\theta_{11})^2,\\ r_5^2 &< \left(\theta_1+\frac{a_1}{\theta_2}+\theta_3\right)^2\left(\frac{\theta_{13}}{\theta_{15}}+\frac{\theta_{14}}{\theta_{16}}\right)^2. \end{aligned} \tag{26}$$

Let $\alpha = \max\{a_1^2, (\theta_1 + a_1/\theta_2 + \theta_3)^2, (\theta_5 + \theta_6 a_1 + \theta_7)^2, (\theta_9 + \theta_{10} a_1 + \theta_{11})^2, (\theta_1 + a_1/\theta_2 + \theta_3)^2 (\theta_{13}/\theta_{15} + \theta_{14}/\theta_{16})^2\}$.

Then, $r_1^2 + r_2^2 + r_3^2 + r_4^2 + r_5^2 < 5\alpha$.

Thus, $\|g(y,x,d,y_{\mathrm{sf}},\theta)\|_2 = y_1\|(r_1,-r_2,r_3,r_4,r_5)^{\mathrm{T}}\|_2 + d\|y\|_2 + \mathrm{d}y_{\mathrm{sf}}$

$$\begin{aligned} &= y_1\sqrt{r_1^2+r_2^2+r_3^2+r_4^2+r_5^2}+d\|y\|_2+dy_{\mathrm{sf}}\\ &< \sqrt{5\alpha}\,y_1+d\|y\|_2+dy_{\mathrm{sf}}\\ &\le \sqrt{5\alpha}\,y_1^*+d\|y\|_2+dy_{\mathrm{sf}}. \end{aligned} \tag{27}$$

Let $b_1 = d$ and $b_2 = \sqrt{5\alpha}y_1^* + dy_{\mathrm{sf}}$, and then we obtain $\|g(y,x,d,y_{\mathrm{sf}},\theta)\|_2 < b_1\|y\|_2 + b_2$. $0 < b_1 < +\infty$ and $0 < b_2 < +\infty$ because $(d, y_{\mathrm{sf}})^{\mathrm{T}} \in Y_2$ and $\alpha > 0$. This completes the proof of Property 6. □

Remark 7. It can be proven that b_1 and b_2 in Property 6 are dependent on the operating parameters d and y_{sf}. Thus, there will be different b_1 and b_2 values for different operating conditions of the microbial continuous fermentation.

Property 8. The functions $g_i(y,x,d,y_{\mathrm{sf}},\theta)$ $(i = 1,2,\cdots,5)$ and $h_k(y,d,\theta)$ $(k = 1, 2,\cdots,10)$ in dynamical system (14)–(16) are signomial functions.

Remark 9. By Property 8, we observe that $g_i(y,x,d,y_{\mathrm{sf}},\theta)$ $(i = 1,2,\cdots,5)$ and $h_k(y,d,\theta)$ $(k = 1, 2,\cdots,10)$ in dynamical system (14)–(16) involve a special structure in the form of signomial functions. This type of mathematical function is often found in geometric programming (GP) problems [39, 40]. In Section 4, we will propose a novel GP method for the parameter estimation problem of the microbial continuous fermentation.

3. Parameter Estimation Model of the Dynamical System

To estimate the value of parameter vector θ in dynamical system (14)–(16) of microbial continuous fermentation, we will first propose a parameter estimation model in this section.

Given certain fermentation condition $(d, y_{\mathrm{sf}})^{\mathrm{T}} \in Y_2$, we can measure the steady-state concentrations of all reactants in the microbial continuous fermentation. Now, we have m different sets of experimental steady-state data that correspond to different fermentation conditions $(d^n, y_{\mathrm{sf}}^n)^{\mathrm{T}} \in Y_2$ $(n = 1, 2,\cdots,m)$. Let $\overline{y}_i^n$ $(\overline{y}_i^n > 0$, $i = 1, 2,\cdots,5$, $n = 1, 2,\cdots,m)$ be the experimental steady-state concentrations of biomass (y_1), glycerol (y_2), 1,3-PDO (y_3), acetic acid (y_4), and ethanol (y_5) under fermentation conditions $(d^n, y_{\mathrm{sf}}^n)^{\mathrm{T}} \in Y_2$, and let y_i^n $(i = 1, 2,\cdots,5, n = 1, 2,\cdots,m)$ be the corresponding steady-state concentrations of variables y_i $(i = 1, 2,\cdots,5)$ calculated by the steady-state conditions. To keep the sum of the squared steady-state concentration deviations from the experimental data $\overline{y}_i^n$ minimized, we propose the following optimization model to estimate parameter θ in dynamical system (14)–(16) of the microbial continuous fermentation:

$$\min_{y^n,x^n,\theta} f = \sum_{n=1}^{m}\sum_{i=1}^{5}\left(y_i^n-\overline{y}_i^n\right)^2, \tag{28}$$

subject to satisfying the $15m$ steady-state constraints:

$$a_1 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n - d^n y_1^n = 0, n = 1, 2, \cdots, m,$$

$$d^n y_{sf}^n - d^n y_2^n - \theta_1 y_1^n - a_1 \theta_2^{-1} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n - \theta_3 y_1^n y_2^n (x_6^n)^{-1} = 0, n = 1, 2, \cdots, m,$$

$$\theta_5 y_1^n + a_1 \theta_6 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \theta_7 y_1^n y_2^n (x_7^n)^{-1} - d^n y_3^n = 0, n = 1, 2, \cdots, m,$$

$$\theta_9 y_1^n + a_1 \theta_{10} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \theta_{11} y_1^n y_2^n (x_8^n)^{-1} - d^n y_4^n = 0, n = 1, 2, \cdots, m,$$

$$\begin{aligned}
&\theta_1 \theta_{13} y_1^n (x_9^n)^{-1} + a_1 \theta_2^{-1} \theta_{13} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_9^n)^{-1} + \theta_3 \theta_{13} y_1^n y_2^n (x_6^n)^{-1} (x_9^n)^{-1} \\
&\quad + \theta_1 \theta_{14} y_1^n (x_{10}^n)^{-1} + a_1 \theta_2^{-1} \theta_{14} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_{10}^n)^{-1} \\
&\quad + \theta_3 \theta_{14} y_1^n y_2^n (x_6^n)^{-1} (x_{10}^n)^{-1} - d^n y_5^n = 0, n = 1, 2, \cdots, m, \\
&x_1^n = y_2^n + a_2, n = 1, 2, \cdots, m, \\
&x_k^n = 1 - \frac{y_k^n}{y_k^*}, k = 2, 3, 4, 5, n = 1, 2, \cdots, m, \\
&x_k^n = y_2^n + \theta_j, (j, k) \in \{(4, 6), (8, 7), (12, 8)\}, n = 1, 2, \cdots, m, \\
&x_k^n = \theta_j + d^n y_2^n, (j, k) \in \{(15, 9), (16, 10)\}, n = 1, 2, \cdots, m,
\end{aligned} \tag{29}$$

and the bound constraints to the $15m + 16$ variables:

$$\begin{aligned}
&\theta \in \Theta, \\
&y^n \in Y_1, \quad n = 1, 2, \cdots, m, \\
&x_k^n > 0, \quad k = 1, 2, \cdots, 10, n = 1, 2, \cdots, m,
\end{aligned} \tag{30}$$

where $y^n = (y_1^n, y_2^n, \cdots, y_5^n)^T \in R^5$ $(n = 1, 2, \cdots, m)$, $x^n = (x_1^n, x_2^n, \cdots, x_{10}^n)^T \in R^{10}$, the equality constraints are the steady-state conditions, and the last three constraints control the corresponding variables to stay within certain limits.

Remark 10. In parameter estimation problem (28)-(30), the number of optimization variables is $15m + 16$, the number of equality constraints is $15m$, the number of lower bound constraints is $15m + 16$, and the number of upper bound constraints is $5m + 16$. Therefore, if the number m of experimental groups is large, then problem (28)-(30) will be a large-scale, nonlinear, and nonconvex optimization problem.

4. SGP Method for the Parameter Estimation Model

As stated previously, proposed parameter estimation model (28)-(30) of the dynamical system is a nonlinear, nonconvex optimization problem. To efficiently solve it, we propose an SGP method in this work.

As there is an implicit requirement that the optimization variables are positive in the framework of GP, we first denote θ with $\omega_j = \theta_j$ $(j \neq 5, 9)$ and $\omega_j = -\theta_j$ $(j = 5, 9)$. Additionally, we replace the expression $\min_{y^n, x^n, \theta} f = \sum_{n=1}^m \sum_{i=1}^5 (y_i^n - \overline{y}_i^n)^2$ with both $\min_{y^n, x^n, \omega, p} p$ and $\sum_{n=1}^m \sum_{i=1}^5 (y_i^n - \overline{y}_i^n)^2 \leq p$. The inequality $\sum_{n=1}^m \sum_{i=1}^5 (y_i^n - \overline{y}_i^n)^2 \leq p$ can be further written as

$$\sum_{n=1}^{m} \sum_{i=1}^{5} \left[(y_i^n)^2 + (\overline{y}_i^n)^2 \right] \leq \sum_{n=1}^{m} \sum_{i=1}^{5} (2 \overline{y}_i^n y_i^n) + p. \tag{31}$$

Then, model (28)-(30) can be represented as the following equivalent formulations:

$$\min_{y^n, x^n, \omega, p} p, \tag{32}$$

subject to satisfying

$$\frac{\sum_{n=1}^m \sum_{i=1}^5 \left[(y_i^n)^2 + (\overline{y}_i^n)^2 \right]}{\sum_{n=1}^m \sum_{i=1}^5 (2 \overline{y}_i^n y_i^n) + p} \leq 1, \tag{33}$$

$$a_1 y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (d^n)^{-1} = 1, \quad n = 1, 2, \cdots, m, \tag{34}$$

$$\frac{d^n y_2^n + \omega_1 y_1^n + a_1 \omega_2^{-1} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_3 y_1^n y_2^n (x_6^n)^{-1}}{d^n y_{\mathrm{sf}}^n} = 1, \quad n = 1, 2, \cdots, m, \tag{35}$$

$$\frac{a_1 \omega_6 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_7 y_1^n y_2^n (x_7^n)^{-1}}{\omega_5 y_1^n + d^n y_3^n} = 1, \quad n = 1, 2, \cdots, m, \tag{36}$$

$$\frac{a_1 \omega_{10} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_{11} y_1^n y_2^n (x_8^n)^{-1}}{\omega_9 y_1^n + d^n y_4^n} = 1, \quad n = 1, 2, \cdots, m, \tag{37}$$

$$\frac{\left[\omega_1\omega_{13} y_1^n (x_9^n)^{-1} + a_1\omega_2^{-1}\omega_{13} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_9^n)^{-1} + \omega_3\omega_{13} y_1^n y_2^n (x_6^n)^{-1} (x_9^n)^{-1} + \omega_1\omega_{14} y_1^n (x_{10}^n)^{-1} + a_1\omega_2^{-1}\omega_{14} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_{10}^n)^{-1} + \omega_3\omega_{14} y_1^n y_2^n (x_6^n)^{-1} (x_{10}^n)^{-1}\right]}{(d^n y_5^n)} = 1, n = 1, 2, \cdots, m, \tag{38}$$

$$\frac{y_2^n + a_2}{x_1^n} = 1, \quad n = 1, 2, \cdots, m, \tag{39}$$

$$\frac{y_k^* x_k^n + y_k^n}{y_k^*} = 1, \quad k = 2, 3, 4, 5, n = 1, 2, \cdots, m, \tag{40}$$

$$\frac{y_2^n + \omega_j}{x_k^n} = 1, (j, k) \in \{(4, 6), (8, 7), (12, 8)\}, \quad n = 1, 2, \cdots, m, \tag{41}$$

$$\frac{\omega_j + d^n y_2^n}{x_k^n} = 1, (j, k) \in \{(15, 9), (16, 10)\}, \quad n = 1, 2, \cdots, m, \tag{42}$$

$$\theta_j^{\mathrm{L}} \le \omega_j \le \theta_j^{\mathrm{U}}, \quad j \in \{1, 2, \cdots, 16\}, j \ne 5, 9, \tag{43}$$

$$-\theta_j^{\mathrm{U}} \le \omega_j \le -\theta_j^{\mathrm{L}}, \quad j = 5, 9, \tag{44}$$

$$y^n \in Y_1, \quad n = 1, 2, \cdots, m, \tag{45}$$

$$x_k^n > 0, \quad k = 1, 2, \cdots, 10, n = 1, 2, \cdots, m, \tag{46}$$

$$p > 0, \tag{47}$$

where $\omega = (\omega_1, \omega_2, \cdots, \omega_{16})^{\mathrm{T}} \in R^{16}$. It can be observed that each of equality constraints (35)–(42) of this problem includes a ratio of certain two posynomials. This type of constraint form is often found in complementary geometric programming. Problem (32)–(47) is an intrinsically nonconvex NP-hard problem.

Replacing each of equality constraints (35)–(42) with two inequality constraints, we can rewrite problem (32)–(47) as

$$\min_{y^n, x^n, \omega, p, u} \; p + \rho \sum_{l=1}^{14m} u_l, \tag{48}$$

subject to satisfying

$$
\begin{aligned}
&\frac{\sum_{n=1}^{m}\sum_{i=1}^{5}\left[\left(y_i^n\right)^2+\left(\overline{y}_i^n\right)^2\right]}{\sum_{n=1}^{m}\sum_{i=1}^{5}\left(2\overline{y}_i^n y_i^n\right)+p}\leq 1,\\
&a_1 y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n\left(d^n\right)^{-1}=1,\quad n=1,2,\cdots,m,\\
&\frac{d^n y_2^n+\omega_1 y_1^n+a_1\omega_2^{-1}y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n+\omega_3 y_1^n y_2^n\left(x_6^n\right)^{-1}}{d^n y_{\mathrm{sf}}^n}\leq 1,\quad n=1,2,\cdots,m,\\
&\frac{d^n y_2^n+\omega_1 y_1^n+a_1\omega_2^{-1}y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n+\omega_3 y_1^n y_2^n\left(x_6^n\right)^{-1}}{d^n y_{\mathrm{sf}}^n}\geq 1-u_n,\quad n=1,2,\cdots,m,\\
&\frac{a_1\omega_6 y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n+\omega_7 y_1^n y_2^n\left(x_7^n\right)^{-1}}{\omega_5 y_1^n+d^n y_3^n}\leq 1,\quad n=1,2,\cdots,m,\\
&\frac{a_1\omega_6 y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n+\omega_7 y_1^n y_2^n\left(x_7^n\right)^{-1}}{\omega_5 y_1^n+d^n y_3^n}\geq 1-u_{m+n},\quad n=1,2,\cdots,m,\\
&\frac{a_1\omega_{10} y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n+\omega_{11} y_1^n y_2^n\left(x_8^n\right)^{-1}}{\omega_9 y_1^n+d^n y_4^n}\leq 1,\quad n=1,2,\cdots,m,\\
&\frac{a_1\omega_{10} y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n+\omega_{11} y_1^n y_2^n\left(x_8^n\right)^{-1}}{\omega_9 y_1^n+d^n y_4^n}\geq 1-u_{2m+n},\quad n=1,2,\cdots,m,\\
&\frac{\left[\omega_1\omega_{13}y_1^n\left(x_9^n\right)^{-1}+a_1\omega_2^{-1}\omega_{13}y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n\left(x_9^n\right)^{-1}+\omega_3\omega_{13}y_1^n y_2^n\left(x_6^n\right)^{-1}\left(x_9^n\right)^{-1}+\omega_1\omega_{14}y_1^n\left(x_{10}^n\right)^{-1}+a_1\omega_2^{-1}\omega_{14}y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n\left(x_{10}^n\right)^{-1}+\omega_3\omega_{14}y_1^n y_2^n\left(x_6^n\right)^{-1}\left(x_{10}^n\right)^{-1}\right]}{\left(d^n y_5^n\right)}\leq 1,\quad n=1,2,\cdots,m,\\
&\frac{\left[\omega_1\omega_{13}y_1^n\left(x_9^n\right)^{-1}+a_1\omega_2^{-1}\omega_{13}y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n\left(x_9^n\right)^{-1}+\omega_3\omega_{13}y_1^n y_2^n\left(x_6^n\right)^{-1}\left(x_9^n\right)^{-1}+\omega_1\omega_{14}y_1^n\left(x_{10}^n\right)^{-1}+a_1\omega_2^{-1}\omega_{14}y_1^n y_2^n\left(x_1^n\right)^{-1}x_2^n x_3^n x_4^n x_5^n\left(x_{10}^n\right)^{-1}+\omega_3\omega_{14}y_1^n y_2^n\left(x_6^n\right)^{-1}\left(x_{10}^n\right)^{-1}\right]}{\left(d^n y_5^n\right)}\geq 1-u_{3m+n},\quad n=1,2,\cdots,m,\\
&\frac{y_2^n+a_2}{x_1^n}\leq 1,\quad n=1,2,\cdots,m,\\
&\frac{y_2^n+a_2}{x_1^n}\geq 1-u_{4m+n},\quad n=1,2,\cdots,m,\\
&\frac{y_k^* x_k^n+y_k^n}{y_k^*}\leq 1, k=2,3,4,5,\quad n=1,2,\cdots,m,\\
&\frac{y_k^* x_k^n+y_k^n}{y_k^*}\geq 1-u_l, (k,l)\in\{(2,5m+n),(3,6m+n),(4,7m+n),(5,8m+n)\},\quad n=1,2,\cdots,m,\\
&\frac{y_2^n+\omega_j}{x_k^n}\leq 1, (j,k)\in\{(4,6),(8,7),(12,8)\},\quad n=1,2,\cdots,m,\\
&\frac{y_2^n+\omega_j}{x_k^n}\geq 1-u_l, (j,k,l)\in\{(4,6,9m+n),(8,7,10m+n),(12,8,11m+n)\},\quad n=1,2,\cdots,m,\\
&\frac{\omega_j+d^n y_2^n}{x_k^n}\leq 1, (j,k)\in\{(15,9),(16,10)\},\quad n=1,2,\cdots,m,\\
&\frac{\omega_j+d^n y_2^n}{x_k^n}\geq 1-u_l, (j,k,l)\in\{(15,9,12m+n),(16,10,13m+n)\},\quad n=1,2,\cdots,m,\\
&\theta_j^{\mathrm{L}}\leq\omega_j\leq\theta_j^{\mathrm{U}},\quad j\in\{1,2,\cdots,16\}, j\neq 5,9,\\
&-\theta_j^{\mathrm{U}}\leq\omega_j\leq-\theta_j^{\mathrm{L}},\quad j=5,9,\\
&y^n\in Y_1,\quad n=1,2,\cdots,m,\\
&x_k^n>0, k=1,2,\cdots,10,\quad n=1,2,\cdots,m,\\
&p>0,\\
&0<u_l<1,\quad l=1,2,\cdots,14m,
\end{aligned}
\tag{49}
$$

where $u=(u_1,u_2,\ldots,u_{14m})^{\mathrm{T}}\in R^{14m}$; $\rho>0$ denotes the weighting coefficient with a sufficiently large value. We can easily observe that if $u_l=0$ $(l=1,2,\cdots,14m)$, then problem (48)-(49) is equivalent to problem (32)–(47). The reason why $u_l>0$ is used here instead of $u_l=0$ is that the optimization variables of GP must be positive. The introduction of the penalty term $\rho\sum_{l=1}^{14m}u_l$ can guarantee that $u_l\approx 0$ at the optimal solution of problem (48)-(49).

By using some derivations to those inequalities involving variables u_l $(l=1,2,\cdots,14m)$, we obtain the equivalent problem, as follows:

$$
\min_{y^n,x^n,\omega,p,u}\ p+\rho\sum_{l=1}^{14m}u_l,
\tag{50}
$$

subject to satisfying

$$
\begin{aligned}
&\frac{\sum_{n=1}^{m}\sum_{i=1}^{5}\left[(y_i^n)^2+(\overline{y}_i^n)^2\right]}{\sum_{n=1}^{m}\sum_{i=1}^{5}(2\overline{y}_i^n y_i^n)+p}\le 1,\\
&a_1 y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (d^n)^{-1} = 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_2^n + \omega_1 y_1^n + a_1\omega_2^{-1} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_3 y_1^n y_2^n (x_6^n)^{-1}}{d^n y_{\mathrm{sf}}^n}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_{\mathrm{sf}}^n}{d^n y_2^n + \omega_1 y_1^n + a_1\omega_2^{-1} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_3 y_1^n y_2^n (x_6^n)^{-1} + d^n y_{\mathrm{sf}}^n u_n}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{a_1\omega_6 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_7 y_1^n y_2^n (x_7^n)^{-1}}{\omega_5 y_1^n + d^n y_3^n}\le 1, n = 1, 2, \cdots, m,\\
&\frac{\omega_5 y_1^n + d^n y_3^n}{a_1\omega_6 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_7 y_1^n y_2^n (x_7^n)^{-1} + \omega_5 y_1^n u_{m+n} + d^n y_3^n u_{m+n}}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{a_1\omega_{10} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_{11} y_1^n y_2^n (x_8^n)^{-1}}{\omega_9 y_1^n + d^n y_4^n}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_9 y_1^n + d^n y_4^n}{a_1\omega_{10} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_{11} y_1^n y_2^n (x_8^n)^{-1} + \omega_9 y_1^n u_{2m+n} + d^n y_4^n u_{2m+n}}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\left[\omega_1\omega_{13} y_1^n (x_9^n)^{-1} + a_1\omega_2^{-1}\omega_{13} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_9^n)^{-1} + \omega_3\omega_{13} y_1^n y_2^n (x_6^n)^{-1}(x_9^n)^{-1} + \omega_1\omega_{14} y_1^n (x_{10}^n)^{-1} + a_1\omega_2^{-1}\omega_{14} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_{10}^n)^{-1} + \omega_3\omega_{14} y_1^n y_2^n (x_6^n)^{-1}(x_{10}^n)^{-1}\right]}{(d^n y_5^n)}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{(d^n y_5^n)}{\left[\omega_1\omega_{13} y_1^n (x_9^n)^{-1} + a_1\omega_2^{-1}\omega_{13} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_9^n)^{-1} + \omega_3\theta_{13} y_1^n y_2^n (x_6^n)^{-1}(x_9^n)^{-1} + \omega_1\omega_{14} y_1^n (x_{10}^n)^{-1} + a_1\omega_2^{-1}\omega_{14} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_{10}^n)^{-1} + \omega_3\omega_{14} y_1^n y_2^n (x_6^n)^{-1}(x_{10}^n)^{-1} + d^n y_5^n u_{3m+n}\right]}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{y_2^n + a_2}{x_1^n}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{x_1^n}{y_2^n + x_1^n u_{4m+n} + a_2}\le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{y_k^* x_k^n + y_k^n}{y_k^*}\le 1, \quad k = 2, 3, 4, 5, \quad n = 1,2, \cdots, m,\\
&\frac{y_k^*}{y_k^* x_k^n + y_k^n + y_k^* u_l}\le 1, (k, l) \in \{(2, 5m+n), (3, 6m+n), (4, 7m+n), (5, 8m+n)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{y_2^n + \omega_j}{x_k^n}\le 1, (j, k) \in \{(4, 6), (8, 7), (12, 8)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{x_k^n}{y_2^n + \omega_j + x_k^n u_l}\le 1, (j, k, l) \in \{(4, 6, 9m+n), (8, 7, 10m+n), (12, 8, 11m+n)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_j + d^n y_2^n}{x_k^n}\le 1, (j, k) \in \{(15, 9), (16, 10)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{x_k^n}{\omega_j + d^n y_2^n + x_k^n u_l}\le 1, (j, k, l) \in \{(15, 9, 12m+n), (16, 10, 13m+n)\}, \quad n = 1, 2, \cdots, m,\\
&\theta_j^{\mathrm{L}} \le \omega_j \le \theta_j^{\mathrm{U}}, j \in \{1,2, \cdots, 16\}, \quad j \ne 5, 9,\\
&-\theta_j^{\mathrm{U}} \le \omega_j \le -\theta_j^{\mathrm{L}}, \quad j = 5, 9,\\
&y^n \in Y_1, \quad n = 1, 2, \cdots, m\\
&x_k^n > 0, k = 1, 2, \cdots, 10, \quad n = 1, 2, \cdots, m,\\
&p > 0,\\
&0 < u_l < 1, \quad l = 1, 2, \cdots, 14m.
\end{aligned}
\tag{51}
$$

It is well known that the standard GP involves a posynomial objective and monomial equality and/or posynomial inequality constraints. This type of optimization problem can be solved very efficiently because it is convex with the logarithmic transformation. Problem (50)-(51) is not a standard GP because many of its inequality constraints are not legal posynomial ones. To deal with this issue, an efficient condensation method is used to transform these inequality constraints into valid posynomial ones. This approach is to approximate every posynomial function in the denominator of inequality constraints by using a monomial function.

Let $z(c) = \sum_e q_e(c)$ be a posynomial where $q_e(c)$ are the monomials. Then, using the arithmetic-geometric mean inequality, we obtain

$$z(c) \geq \tilde{z}(c) = \prod_e \left[\frac{q_e(c)}{\beta_e}\right]^{\beta_e}, \tag{52}$$

where β_e are calculated through

$$\beta_e = \frac{q_e(\bar{c})}{z(\bar{c})}, \quad \forall e. \tag{53}$$

Here, $\bar{c} > 0$ is a given point. We have $\tilde{z}(\bar{c}) = z(\bar{c})$. Inequality (52) implies that $\hat{z}(c)/z(c) \leq 1$ can be replaced with $\hat{z}(c)/\tilde{z}(c) \leq 1$, where $\hat{z}(c)$ is a posynomial.

Applying the approach above to problem (50)-(51), we have the following problem:

$$\min_{y^n, x^n, \omega, p, u} p + \rho \sum_{l=1}^{14m} u_l, \tag{54}$$

subject to satisfying

$$\begin{aligned}
&\frac{\sum_{n=1}^{m}\sum_{i=1}^{5}\left[(y_i^n)^2 + (\bar{y}_i^n)^2\right]}{C_1(y^n, p)} \leq 1,\\
&a_1 y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (d^n)^{-1} = 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_2^n + \omega_1 y_1^n + a_1 \omega_2^{-1} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_3 y_1^n y_2^n (x_6^n)^{-1}}{d^n y_{\mathrm{sf}}^n} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_{\mathrm{sf}}^n}{C_2^n(y^n, x^n, \omega, u)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{a_1 \omega_6 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_7 y_1^n y_2^n (x_7^n)^{-1}}{C_3^n(y^n, \omega)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_5 y_1^n + d^n y_3^n}{C_4^n(y^n, x^n, \omega, u)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{a_1 \omega_{10} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_{11} y_1^n y_2^n (x_8^n)^{-1}}{C_5^n(y^n, \omega)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_9 y_1^n + d^n y_4^n}{C_6^n(y^n, x^n, \omega, u)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\left[\omega_1 \omega_{13} y_1^n (x_9^n)^{-1} + a_1 \omega_2^{-1} \omega_{13} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_9^n)^{-1} + \omega_3 \omega_{13} y_1^n y_2^n (x_6^n)^{-1} (x_9^n)^{-1} + \omega_1 \omega_{14} y_1^n (x_{10}^n)^{-1} + a_1 \omega_2^{-1} \omega_{14} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_{10}^n)^{-1} + \omega_3 \omega_{14} y_1^n y_2^n (x_6^n)^{-1} (x_{10}^n)^{-1}\right]}{(d^n y_5^n)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_5^n}{C_7^n(y^n, x^n, \omega, u)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{y_2^n + a_2}{x_1^n} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{x_1^n}{C_8^n(y^n, x^n, u)} \leq 1, \quad n = 1, 2, \cdots, m,\\
&\frac{y_k^* x_k^n + y_k^n}{y_k^*} \leq 1, k = 2, 3, 4, 5, \quad n = 1, 2, \cdots, m,\\
&\frac{y_k^*}{C_w^n(y^n, x^n, u)} \leq 1, (k, w) \in \{(2, 9), (3, 10), (4, 11), (5, 12)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{y_2^n + \omega_j}{x_k^n} \leq 1, (j, k) \in \{(4, 6), (8, 7), (12, 8)\}, \quad n = 1,2, \cdots, m,\\
&\frac{x_k^n}{C_w^n(y^n, x^n, \omega, u)} \leq 1, (k, w) \in \{(6, 13), (7, 14), (8, 15)\}, \quad n = 1,2, \cdots, m,\\
&\frac{\omega_j + d^n y_2^n}{x_k^n} \leq 1, (j, k) \in \{(15, 9), (16, 10)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{x_k^n}{C_w^n(y^n, x^n, \omega, u)} \leq 1, (k, w) \in \{(9, 16), (10, 17)\}, \quad n = 1,2, \cdots, m,\\
&\theta_j^{\mathrm{L}} \leq \omega_j \leq \theta_j^{\mathrm{U}}, j \in \{1,2, \cdots, 16\}, \quad j \neq 5, 9,\\
&\quad -\theta_j^{\mathrm{U}} \leq \omega_j \leq -\theta_j^{\mathrm{L}}, \quad j = 5, 9,\\
&y^n \in Y_1, \quad n = 1, 2, \cdots, m,\\
&x_k^n > 0, k = 1, 2, \cdots, 10, \quad n = 1, 2, \cdots, m,\\
&p > 0,\\
&0 < u_l < 1, \quad l = 1, 2, \cdots, 14m,
\end{aligned} \tag{55}$$

where C_1 and C_w^n ($w = 2, 3, \cdots, 17$, $n = 1, 2, \cdots, m$) are the monomial functions approximated through (52). Problem (54)-(55) is a standard GP.

We now summarize the proposed SGP method for the parameter estimation model of the dynamical system in the microbial continuous fermentation and provide the following SGP algorithm, denoted as Algorithm 1.

Remark 11. In the implementation of the proposed Algorithm 1, numerical computation problems may occur when $\max_{1\le l\le 14m}\left\{u_l^{(s)}\right\}$ is very small. To deal with this issue, we can transform u_l ($l = 1, 2, \cdots, 14m$) into v_l by $v_l = 1/(1-u_l)$ and obtain the following problem similar to standard GP (54)-(55).

$$\min_{y^n, x^n, \omega, p, v} p + \rho \sum_{l=1}^{14m} v_l, \tag{56}$$

subject to satisfying

$$\begin{aligned}
&\frac{\sum_{n=1}^{m}\sum_{i=1}^{5}\left[(y_i^n)^2 + (\overline{y}_i^n)^2\right]}{D_1(y^n, p)} \le 1,\\
&a_1 y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (d^n)^{-1} = 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_2^n + \omega_1 y_1^n + a_1 \omega_2^{-1} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_3 y_1^n y_2^n (x_6^n)^{-1}}{d^n y_{\mathrm{sf}}^n} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_{\mathrm{sf}}^n}{v_n D_2^n (y^n, x^n, \omega)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{a_1 \omega_6 y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_7 y_1^n y_2^n (x_7^n)^{-1}}{D_3^n (y^n, \omega)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_5 y_1^n + d^n y_3^n}{v_{m+n} D_4^n (y^n, x^n, \omega)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{a_1 \omega_{10} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n + \omega_{11} y_1^n y_2^n (x_8^n)^{-1}}{D_5^n (y^n, \omega)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_9 y_1^n + d^n y_4^n}{v_{2m+n} D_6^n (y^n, x^n, \omega)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{\left[\omega_1 \omega_{13} y_1^n (x_9^n)^{-1} + a_1 \omega_2^{-1} \omega_{13} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_9^n)^{-1} + \omega_3 \omega_{13} y_1^n y_2^n (x_6^n)^{-1} (x_9^n)^{-1} + \omega_1 \omega_{14} y_1^n (x_{10}^n)^{-1} + a_1 \omega_2^{-1} \omega_{14} y_1^n y_2^n (x_1^n)^{-1} x_2^n x_3^n x_4^n x_5^n (x_{10}^n)^{-1} + \omega_3 \omega_{14} y_1^n y_2^n (x_6^n)^{-1} (x_{10}^n)^{-1}\right]}{(d^n y_5^n)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{d^n y_5^n}{v_{3m+n} D_7^n (y^n, x^n, \omega)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{y_2^n + a_2}{x_1^n} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{x_1^n}{v_{4m+n} D_8^n (y^n, x^n)} \le 1, \quad n = 1, 2, \cdots, m,\\
&\frac{y_k^* x_k^n + y_k^n}{y_k^*} \le 1, k = 2, 3, 4, 5, \quad n = 1, 2, \cdots, m,\\
&\frac{y_k^*}{v_l D_w^n (y^n, x^n)} \le 1, (k, w, l) \in \{(2, 9, 5m+n), (3, 10, 6m+n), (4, 11, 7m+n), (5, 12, 8m+n)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{y_2^n + \omega_j}{x_k^n} \le 1, (j, k) \in \{(4, 6), (8, 7), (12, 8)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{x_k^n}{v_l D_w^n (y^n, x^n, \omega)} \le 1, (k, w, l) \in \{(6, 13, 9m+n), (7, 10m+n), (8, 15, 11m+n)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{\omega_j + d^n y_2^n}{x_k^n} \le 1, (j, k) \in \{(15, 9), (16, 10)\}, \quad n = 1, 2, \cdots, m,\\
&\frac{x_k^n}{v_l D_w^n (y^n, x^n, \omega)} \le 1, (k, w, l) \in \{(9, 16, 12m+n), (10, 17, 13m+n)\}, \quad n = 1, 2, \cdots, m,\\
&\theta_j^{\mathrm{L}} \le \omega_j \le \theta_j^{\mathrm{U}}, j \in \{1, 2, \cdots, 16\}, \quad j \ne 5, 9,\\
&\quad -\theta_j^{\mathrm{U}} \le \omega_j \le -\theta_j^{\mathrm{L}}, \quad j = 5, 9,\\
&y^n \in Y_1, \quad n = 1, 2, \cdots, m,\\
&x_k^n > 0, k = 1, 2, \cdots, 10, \quad n = 1, 2, \cdots, m,\\
&p > 0,\\
&v_l > 1, \quad l = 1, 2, \cdots, 14m,
\end{aligned} \tag{57}$$

Step 0. Choose the initial values $(y^n)^{(0)}$, $(x^n)^{(0)}$, $\omega^{(0)}$, $p^{(0)}$, and $u^{(0)}$ $(n = 1, 2, \cdots, m)$ of optimization variables y^n, x^n, ω, p, and u. Given the solution accuracy $\varepsilon > 0$ and initial weighting coefficient $\rho^{(0)} > 0$, set $s = 0$.
Step 1. For the given $(y^n)^{(s-1)}$, $(x^n)^{(s-1)}$, $\omega^{(s-1)}$, $p^{(s-1)}$, and $u^{(s-1)}$ $(n = 1, 2, \cdots, m)$, construct the monomials C_1 and C_w^n $(w = 2, 3, \cdots, 17,\ n = 1, 2, \cdots, m)$ using (52).
Step 2. Solve problem (54)-(55) to attain $(y^n)^{(s)}$, $(x^n)^{(s)}$, $\omega^{(s)}$, $p^{(s)}$, and $u^{(s)}$ $(n = 1, 2, \cdots, m)$ with the weighting coefficient $\rho^{(s-1)}$.
Step 3. If $\max_{1 \le l \le 14m}\{u_l^{(s)}\} \le \varepsilon$, then stop.
Step 4. Update $\rho^{(s)}$ with $\rho^{(s)} > \rho^{(s-1)}$. Set $s = s + 1$ and continue from Step 1.

Algorithm 1: SGP algorithm.

Step 0. Choose the initial values $(y^n)^{(0)}$, $(x^n)^{(0)}$, $\omega^{(0)}$, $p^{(0)}$, and $u^{(0)}$ $(n = 1, 2, \cdots, m)$ of optimization variables y^n, x^n, ω, p, and u. Given the solution accuracy $\varepsilon > 0$ and initial weighting coefficient $\rho^{(0)} > 0$, select $\mu > 0$ $(\mu > \varepsilon)$. Set $s = 0$.
Step 1. For the given $(y^n)^{(s-1)}$, $(x^n)^{(s-1)}$, $\omega^{(s-1)}$, $p^{(s-1)}$, and $u^{(s-1)}$ $(n = 1, 2, \cdots, m)$, construct the monomials C_1 and C_w^n $(w = 2, 3, \cdots, 17,\ n = 1, 2, \cdots, m)$ using (52).
Step 2. Solve problem (54)-(55) to attain $(y^n)^{(s)}$, $(x^n)^{(s)}$, $\omega^{(s)}$, $p^{(s)}$, and $u^{(s)}$ $(n = 1, 2, \cdots, m)$ with the weighting coefficient $\rho^{(s-1)}$.
Step 3. If $\max_{1 \le l \le 14m}\{u_l^{(s)}\} > \mu$, then go to Step 4. Else, go to Step 5.
Step 4. Choose $\rho^{(s)}$ with $\rho^{(s)} > \rho^{(s-1)}$. Set $s = s + 1$ and continue from Step 1.
Step 5. Set $\rho^{(s)} = \rho^{(0)}$, $s = s + 1$ and go to Step 6.
Step 6. For the given $(y^n)^{(s)}$, $(x^n)^{(s)}$, $\omega^{(s)}$, $p^{(s)}$, and $v^{(s)}$ $(n = 1, 2, \cdots, m)$, construct the monomials D_1 and D_w^n $(w = 2, 3, \cdots, 17,\ n = 1, 2, \cdots, m)$ using (52).
Step 7. Solve problem (56)-(57) to attain $(y^n)^{(s+1)}$, $(x^n)^{(s+1)}$, $\omega^{(s+1)}$, $p^{(s+1)}$, and $v^{(s+1)}$ $(n = 1, 2, \cdots, m)$ with the weighting coefficient $\rho^{(s)}$.
Step 8. If $\max_{1 \le l \le 14m}\{v_l^{(s+1)}\} \le 1 + \varepsilon$, then stop. Else, go to Step 9.
Step 9. Choose $\rho^{(s+1)}$ with $\rho^{(s+1)} > \rho^{(s)}$. Set $s = s + 1$ and continue from Step 6.

Algorithm 2: Modified SGP algorithm.

where $v = (v_1, v_2, \ldots, v_{14m})^{\mathrm{T}} \in R^{14m}$; D_1 and D_w^n $(w = 2, 3, \cdots, 17,\ n = 1, 2, \cdots, m)$ are the monomial functions approximated through (52). In problem (56)-(57), the number of upper bound constraints is $5m + 16$, which is fewer than that of (54)-(55).

Based on Algorithm 1 and the above analysis, we present Algorithm 2.

5. Computational Results and Discussion

In this section, we apply the proposed SGP method (Algorithm 2) to solve nonconvex parameter estimation model (28)–(30) of dynamical system (14)–(16). Experimental steady-state data $\overline{y}_i^n$ $(\overline{y}_i^n > 0,\ i = 1, 2, \cdots, 5,\ n = 1, 2, \cdots, 21)$ under 21 different fermentation conditions $(d^n, y_{\mathrm{sf}}^n)^{\mathrm{T}} \in Y_2$ $(n = 1, 2, \cdots, 21)$ were drawn from the literature [23]. Here, the number m of experimental groups is 21, which means that both problems (54)-(55) and (56)-(57) are large-scale, nonlinear optimization problems. Table 1 presents the number N_1 of optimization variables, the number N_2 of equality constraints, the number N_3 of inequality constraints, the number N_4 of lower bound constraints, and the number N_5 of upper bound constraints for problems (54)-(55) and (56)-(57). In the implementation of Algorithm 2, the following parameters were set: $a_1 = 0.67\,\mathrm{h}^{-1}$, $a_2 = 0.28\,\mathrm{mmol/L}$, $y_1^* = 10\,\mathrm{g/L}$, $y_2^* = 2039\,\mathrm{mmol/L}$, $y_3^* = 939.5\,\mathrm{mmol/L}$, $y_4^* = 1026\,\mathrm{mmol/L}$, $y_5^* = 360.9\,\mathrm{mmol/L}$, $d^{\mathrm{L}} = 0.05\,\mathrm{h}^{-1}$, $d^{\mathrm{U}} = 0.5\,\mathrm{h}^{-1}$, $\theta_j^{\mathrm{L}} = 10^{-8}$ $(j \ne 5,9)$, $\theta_j^{\mathrm{U}} = 100$ $(j \ne 5,9)$, $\theta_j^{\mathrm{L}} = -100$ $(j = 5,9)$, $\theta_j^{\mathrm{U}} = -10^{-8}$ $(j = 5,9)$, $\varepsilon = 10^{-6}$, and $\mu = 0.05$. Additionally, we set $\rho^{(s)} = 10000\,(1 + s)$ $(s \ge 0)$ if $\max_{1 \le l \le 14m}\{u_l^{(s)}\} > \mu$. We set $\rho^{(s)} = 10000\,(s - \overline{s})$ if $s \ge \overline{s} + 1$, where $\overline{s} = \min\{s \mid \max_{1 \le l \le 14m}\{u_l^{(s)}\} \le \mu, s \ge 1\}$.

After 53 iterations, Algorithm 2 stops with $p^{(53)} = 56420.232087$ and $\max_{1 \le l \le 14m}\{v_l^{(s+1)}\} = 1 + 8.895892 \times 10^{-7}$ $(\max_{1 \le l \le 14m}\{u_l^{(s)}\} = 8.895884 \times 10^{-7})$. Table 2 presents the optimal values of the estimated parameters θ_j $(n = 1, 2, \cdots, 16)$ obtained using Algorithm 2. Figure 2 provides the comparison between the experimental data and steady-state concentrations calculated using the proposed SGP approach. Table 3 presents the comparison between the proposed SGP method and the approaches used in the literature [23–29]. In this table, E_1, E_2, E_3, E_4, and E_5 denote the error functions of biomass, glycerol, 1,3-PDO, acetic acid, and ethanol, respectively, and are defined as

$$E_i = \left| \frac{\sum_{n=1}^{21} \widetilde{y}_i^n - \sum_{n=1}^{21} \overline{y}_i^n}{\sum_{n=1}^{21} \overline{y}_i^n} \right|, \quad i = 1, 2, \cdots, 5, \tag{58}$$

where $\overline{y}_i^n$ $(\overline{y}_i^n > 0,\ i = 1,2,\cdots,5,\ n = 1,2,\cdots,21)$ are the experimental steady-state concentrations and $\widetilde{y}_i^n$ $(\widetilde{y}_i^n > 0,\ i = 1,2,\cdots,5,\ n = 1,2,\cdots,21)$ are the corresponding positive steady-state concentrations of variables y_i $(i = 1,2,\cdots,5)$ calculated by the steady-state equations with optimal model parameters. As can be observed in Table 3, our proposed

Table 1: Number of optimization variables and constraints for problems (54)-(55) and (56)-(57).

Number	Problem (54)-(55)	Problem (56)-(57)
N_1 (optimization variables)	626	626
N_2 (equality constraints)	21	21
N_3 (inequality constraints)	588	588
N_4 (lower bound constraints)	626	626
N_5 (upper bound constraints)	415	121

Table 2: Optimal parameters obtained using Algorithm 2.

Estimated parameter	Optimal value
θ_1	1.588248
θ_2	0.007800
θ_3	32.070531
θ_4	5.800274
θ_5	−2.573968
θ_6	79.863585
θ_7	23.711599
θ_8	10.998005
θ_9	−0.729023
θ_{10}	30.617914
θ_{11}	5.505295
θ_{12}	70.965262
θ_{13}	0.011729
θ_{14}	8.731747
θ_{15}	0.018555
θ_{16}	46.993338

Table 3: Comparison between the proposed SGP method and the approaches used in the literature [23–29].

Error (%)	Method						
	This paper	[23]	[24]	[25, 26]	[27]	[28]	[29]
E_1	1.39	20.36	—	4.94	—	27.99	18.86
E_2	2.77	5.78	43.76	54.02	44.57	17.46	6.98
E_3	4.68×10^{-3}	6.17	10.41	4.20	1.61	22.22	1.58
E_4	2.28	16.68	14.04	2.41	23.50	13.74	6.42
E_5	5.65	6.59	29.48	8.00	10.67	22.57	6.47
$E_2+E_3+E_4+E_5$	10.7	35.22	97.69	68.63	80.35	75.99	21.45
$E_1+E_2+E_3+E_4+E_5$	12.09	55.58	—	73.57	—	103.98	40.31

SGP approach can produce smaller errors between the experimental and calculated steady-state concentrations than the other seven methods. As observed for the seven error indices considered, E_1, E_2, E_3, E_4, E_5, $E_2+E_3+E_4+E_5$, and $E_1+E_2+E_3+E_4+E_5$ in Table 3, the results obtained using the proposed SGP method are better than those by the methods used in [23–29], with improvements of approximately 71.86–95.03%, 52.08–94.87%, 99.70–99.98%, 5.39–90.29%, 12.67–80.83%, 50.12–89.05%, and 70.01–88.37%, respectively. We can also observe that the methods used in the literature [24–27] yield very large errors of glycerol concentrations reaching more than 43%. These conclude that our established dynamical system can better describe the microbial continuous fermentation.

The experimental studies indicated that in the microbial continuous fermentation, the metabolic overflow of products and their inhibition on cell growth can give rise to multiple steady-state phenomena. To investigate whether our established dynamical system of the microbial continuous fermentation has multiple steady states, we can compute the steady-state equations (i.e., $\mathrm{d}y_i/\mathrm{d}t=0$, $i=1,2,\cdots,5$) to find the positive steady states under different fermentation conditions $(d,y_{\mathrm{sf}})^{\mathrm{T}}$. After some computations, we can observe that our proposed dynamical system has multiple positive steady states in some fermentation conditions $(d,y_{\mathrm{sf}})^{\mathrm{T}}\in Y_2$. As an illustration, Figure 3 presents the experimental and computational results of the microbial continuous fermentation under 1000 different fermentation conditions, where $d=0.1\,\mathrm{h}^{-1}$, $y_{\mathrm{sf}}=2,4,6,\cdots,2000$ mmol/L, and the red squares denote the experimental data. From Figure 3, we can observe that the dynamical system has three types of positive steady states: (1) one positive steady state at $y_{\mathrm{sf}}=2,4,6,\cdots,1110$ mmol/L and $y_{\mathrm{sf}}=1132,1134,\cdots,1734$ mmol/L, (2) three positive steady states at $y_{\mathrm{sf}}=1112,1114,\cdots,1130$ mmol/L, and (3) two positive steady states at $y_{\mathrm{sf}}=1736,1738,\cdots,2000$ mmol/L. This concludes that the proposed dynamical system has multiple positive steady states under some fermentation conditions $(d,y_{\mathrm{sf}})^{\mathrm{T}}$.

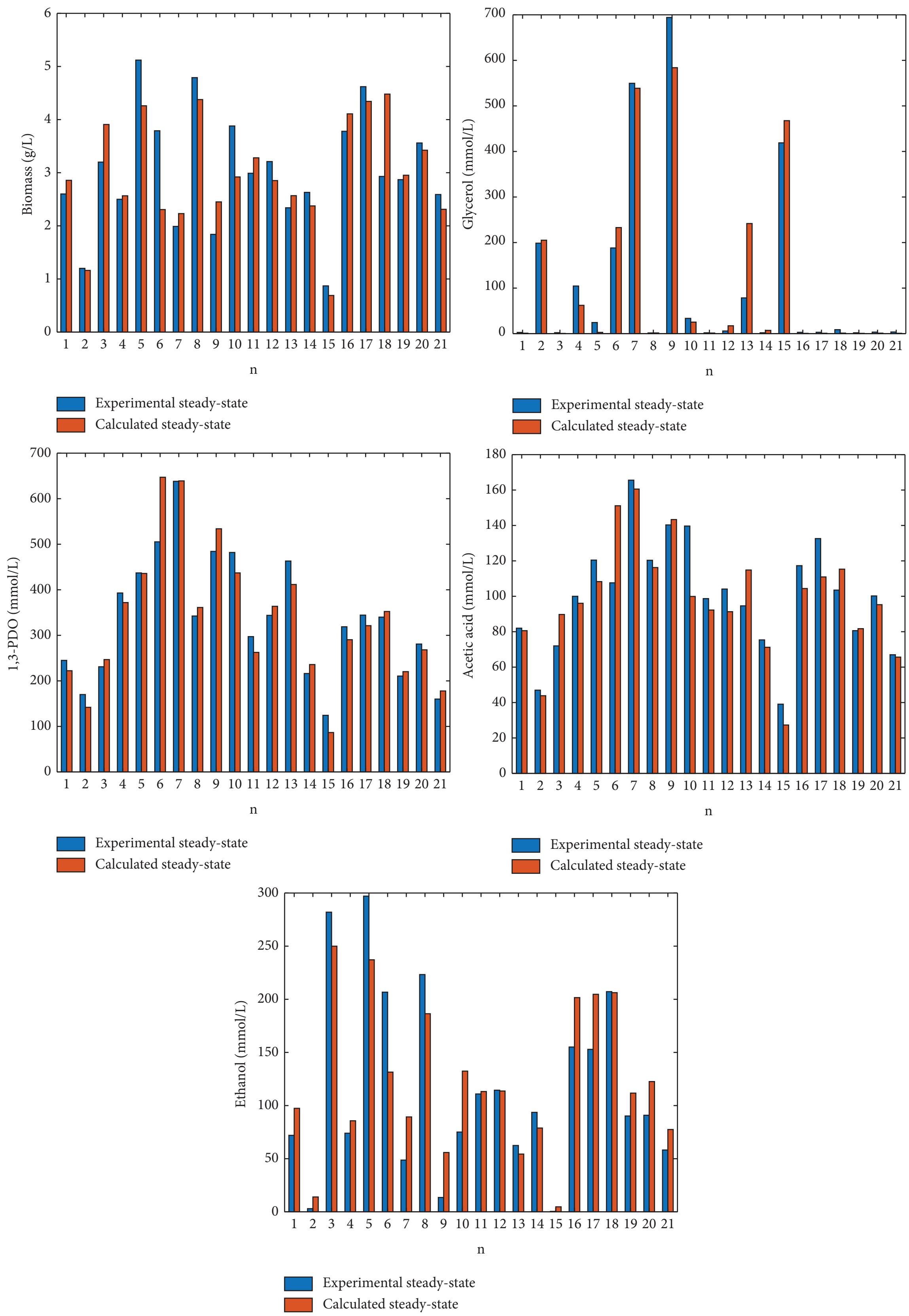

Figure 2: Comparison between the experimental data and steady-state concentrations calculated using the proposed approach.

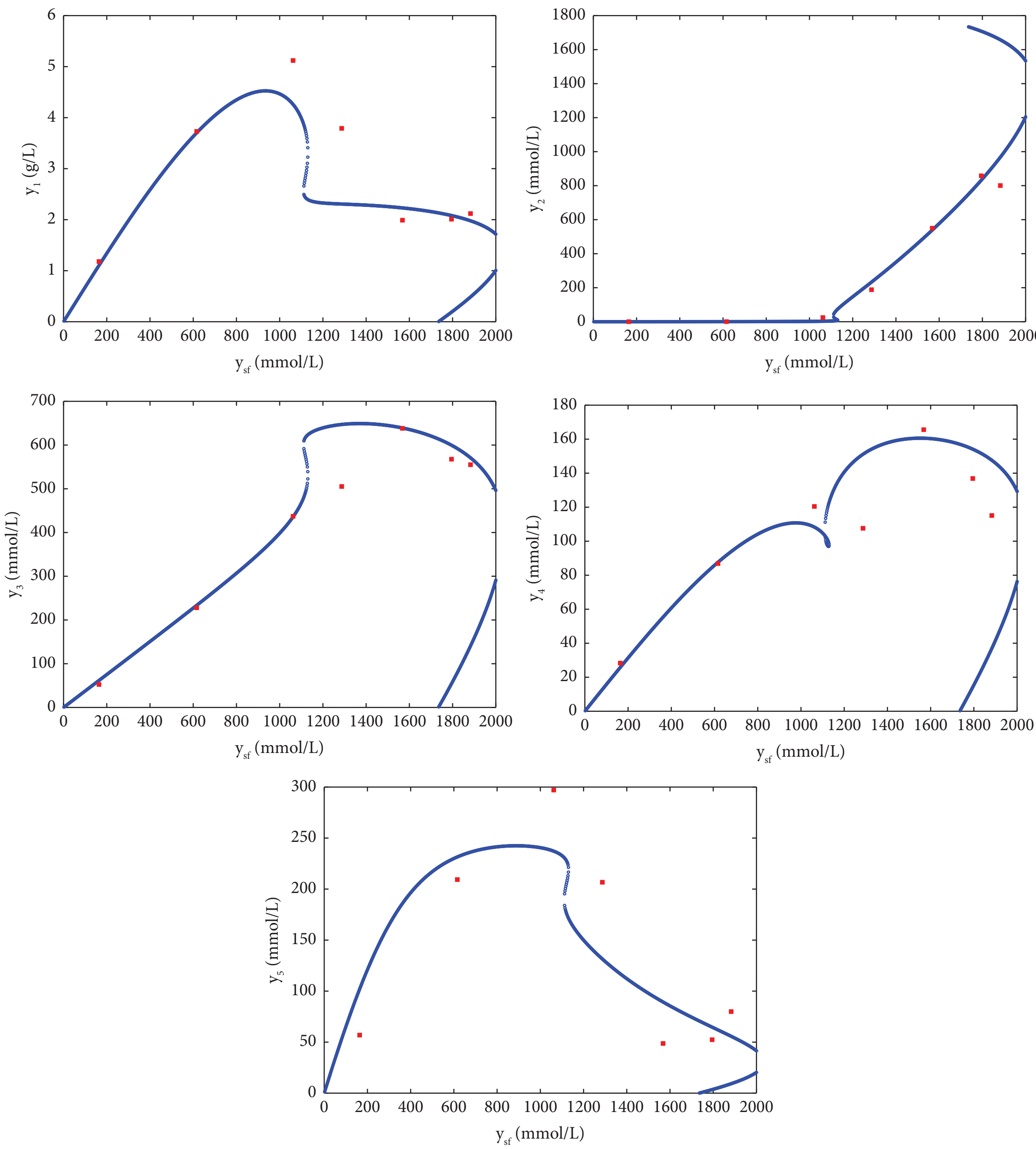

Figure 3: Comparison of the positive steady states between experimental and simulated results under 1000 different fermentation conditions ($d = 0.1\,h^{-1}$ and $y_{sf} = 2, 4, \ldots, 2000$ mmol/L).

6. Conclusions

This work has studied the problem of parameter estimation for the microbial continuous fermentation. A nonlinear dynamical system has been first presented to describe the microbial continuous fermentation. To estimate the value of the parameter vector in the dynamical system, a parameter estimation model as presented in (28)–(30) has been proposed. Model (28)–(30) can minimize the sum of the squared steady-state concentration deviations from the experimental data and has many optimization variables and constraints. Therefore, if the number of experimental groups is large, then problem (28)–(30) will be a large-scale, nonlinear, and nonconvex optimization problem. To efficiently solve problem (28)–(30), an SGP method has been proposed. The results indicated that our proposed algorithm can yield smaller errors between the experimental and calculated steady-state concentrations than the existing methods in the literature [23–29]. This concludes that the established dynamical system can better describe the microbial continuous fermentation and that the proposed SGP method is valid. The proposed framework in this work can also be applied to the parameter estimation of other continuous (bio)chemical processes. We also observe that there are two regions of multiple positive steady-states at relatively high values of substrate glycerol concentration in feed medium.

Data Availability

The data used to support the findings of this study are included within the article and are also available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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