Modeling and dynamics analyses of immobilized CSTR bioreactor using transfer function model

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***Abstract*—CSTR (Continuous Stirred Tank Reactor) is commonly used in case of immobilized enzyme or immobilized cells. Mathematical model is a useful tool in reactor design, operation condition optimization, and production process automation. Transfer function relates the output and the input and reflects the dynamics of the system. Laplace transforming can make the differential equations into algebra equations, simplifies the solution of the model. In addition, transfer function is simple, easy to use, and able to predict the outputs of various inputs without modification of the transfer function. In this paper, the transfer function for CSTR with immobilized biocatalysts is built as an example for transfer function building and system dynamics analysis.**

Keywords- mathematical model; transfer function; Laplace transformation; CSTR; biocatalysis

I. INTRODUCTION

Biocatalization has the advantages of being at normal temperature, normal pressure, environmental friendly et al., is becoming widely used in fields of food and pharmacy industries, as well as in chemical intermediate production [1]. Immobilized enzyme and immobilized cells are normally used in biocatalization to maintain the biocatalites within the bioreactor for cycling uses, so as to decrease the cost of biocatalites and the difficulties of process operation [2]。 Compared with bath operation, continuous operation has the advantages of higher production efficiency and productivity, and is the optimal operation manner for immobilized biocatalites. Mathematical model is an important tool in bioprocess analysis, bioreactor design, and bioreaction process optimization [3-6]. The mathematical models for bioprocesses are normal differential equation models [3-6], which have sophisticated structure and are difficult in model solving. Transfer function model is easily solved with Laplace transformation of the differential equation model into complex field, and then Laplace reverse transformation is made to transform the model into real field after solving the model. In addition, it is easy to use the transfer function model. The model needs no change when it investigates the process dynamics under different inputs. More important, transfer function model is also used in automatic control system analysis and design [7]. In this paper, the transfer function model for the immobilized CSTR bioreactor is constructed and the dynamics and stability of the reactor operation are analyzed.

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II. DIFFERENTIAL EQUATION MODEL FOR IMMOBILIZED CSTR BIOREACTOR

The bioreactor system is shown in Fig. 1. The differential equation model is as follows:

$$V \cdot \frac{dC}{dt} = F \cdot (C_{in} - C) - V \cdot r_C \qquad (1)$$

$$V \cdot \frac{dP}{dt} = V \cdot r_C - F \cdot P \qquad (2)$$

Where, V, the bioreactor volume (l); C, the substrate concentration (g/l); C_{in}, the substrate concentration in the feeding solution (g/l); F, the substrate feeding speed (l/h); r_c, the reaction speed (g/l/h); P, the product concentration (g/l). Define the dilution rate D as: D=F/V (1/h). Then, the equations (1) and (2) can be transformed into equations (3) and (4):

$$\frac{dC}{dt} = D(C_{in} - C) - r_C \qquad (3)$$

$$\frac{dP}{dt} = r_C - D \cdot P \qquad (4)$$

Where, $F = 2(\text{l/h}), V = 4(1), V_m = 0.5(1/h), K_S = 0.2(g/l)$, $D = F/V = 0.5(1/\text{h})$.

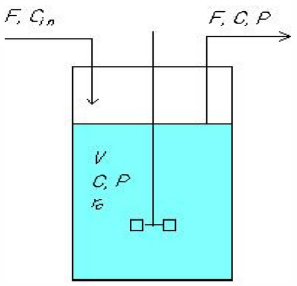

Fig. 1. Schematic diagram of the CSTR.

The immobilized enzyme or cell catalytic reactionrate r_C is defined by Michaelis-Menten equation:

$$r_C = \frac{V_m \cdot C}{K_S + C} \qquad (5)$$

Take equation (5) into equations (3) and (4):

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$$\frac{dC}{dt} = D\left(C_{in} - C\right) - \frac{V_m \cdot C}{K_S + C} \tag{6}$$

$$\frac{dP}{dt} = \frac{V_m \cdot C}{K_S + C} - D \cdot P \tag{7}$$

In the following sections, the CSTR system is analyzed by using $C_{in}(t)$ as the input variable, $C(t)$ and $P(t)$ as the output variables.

III. THE TRANSFER FUNCTION MODEL FOR IMMOBILIZED CSTR BIORACTOR

The transfer function model is based on the zero initial state, constructed by the ratio of Laplace transformed system output over system input. Where, the system output and input are the differences to the values of the balanced state. Under balanced state, dC/dt=0, dP/dt=0. Then, equations (6) and (7) change to:

$$0 = D \cdot \left(\overline{C_{in}} - \overline{C}\right) - \frac{V_m \cdot \overline{C}}{K_S + \overline{C}} \tag{8}$$

$$0 = \frac{V_m \cdot \overline{C}}{K_S + \overline{C}} - D \cdot \overline{P} \tag{9}$$

Where, $\overline{C}_{in}$, $\overline{C}$, $\overline{P}$ are the substrate concentration of the feeding solution, the substrate concentration of the bioreactor, the product concentration of the bioreactor at the balanced state.

The nonlinear equation (5) should be linearized before Laplace transformation. Expansion of r_C by using Taylor series at the concentration $\overline{C}$ of balanced state, ignoring the terms with ranks more than two:

$$r_C = \frac{V_m \cdot \overline{C}}{K_S + \overline{C}} + V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot \left(C - \overline{C}\right) \tag{10}$$

Take equation (10) into equations (8) and (9) to obtain equations (11) and (12):

$$\frac{dC}{dt} = D\left(C_{in} - C\right) - V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot \left(C - \overline{C}\right) - \frac{V_m \cdot \overline{C}}{K_S + \overline{C}} \tag{11}$$

$$\frac{dP}{dt} = \frac{V_m \cdot \overline{C}}{K_S + \overline{C}} + V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot \left(C - \overline{C}\right) - D \cdot P \tag{12}$$

As the inputs and outputs of transfer function are the differences to the values of the balanced state, equations (11) and (12) should subtract equations (8) and (9), producing equations (13) and (14), respectively:

$$\frac{dC}{dt} = D\left[\left(C_{in} - \overline{C}_{in}\right) - \left(C - \overline{C}\right)\right] - V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot \left(C - \overline{C}\right) \tag{13}$$

$$\frac{dP}{dt} = V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot \left(C - \overline{C}\right) - D \cdot \left(P - \overline{P}\right) \tag{14}$$

Let $C_{in}' = C_{in} - \overline{C_{in}}$, $C' = C - \overline{C}$, $P' = P - \overline{P}$, and $dC'/dt = dC/dt$, $dP'/dt = dP/dt$, then equations (13) and (14) are changed to (15) and (16), respectively:

$$\frac{dC'}{dt} = D \cdot \left(C_{in}' - C'\right) - V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot C'$$

$$= D \cdot C_{in}' - \left(D + \frac{V_m}{K_S + \overline{C}} - \frac{V_m \cdot \overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot C' \tag{15}$$

$$\frac{dP'}{dt} = V_m \cdot \left(\frac{1}{K_S + \overline{C}} - \frac{\overline{C}}{\left(K_S + \overline{C}\right)^2}\right) \cdot C' - D \cdot P' \tag{16}$$

Let

$$\frac{1}{\tau_1} = D + \frac{V_m}{K_S + \overline{C}} - \frac{V_m \cdot \overline{C}}{\left(K_S + \overline{C}\right)^2} \tag{17}$$

$$\frac{1}{\tau_2} = D \tag{18}$$

Equations (15) and (16) are Laplace transformed, taken into equations (17) and (18), rearranged into equations (19) and (20), respectively.

$$C'(s) = \frac{\tau_1 / \tau_2}{\tau_1 \cdot s + 1} \cdot C_{in}'(s) \tag{19}$$

$$P'(s) = \frac{1 - \tau_1 / \tau_2}{\left(\tau_2 \cdot s + 1\right) \cdot \left(\tau_1 \cdot s + 1\right)} \cdot C_{in}'(s) \tag{20}$$

The transfer function of equations (21) and (22) can be obtained from equations (19) and (20).

$$G_1 = \frac{\tau_1 / \tau_2}{\tau_1 \cdot s + 1} \tag{21}$$

$$G_2 = \frac{1 - \tau_1 / \tau_2}{\left(\tau_2 \cdot s + 1\right) \cdot \left(\tau_1 \cdot s + 1\right)} \tag{22}$$

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The transfer function model of the CSTR bioreactor is obtained by taking equation (21) and (22) into equation (19) and (20), as in the following:

$$C'(s) = G_1 \cdot C_{in}'(s) \quad (23)$$

$$P'(s) = G_2 \cdot C_{in}'(s) \quad (24)$$

The transfer function model can be easily used in investigating various inputs without modification of the mathematical model.

IV. Dynamics of Immobilized CSTR Bioreactor

At first, the balance state concentrations of $\overline{C}, \overline{P}$ are calculated according to equations (8) and (9). Assuming C_{in} is 1 (g/L) at the beginning of the reaction. Take the values V_m=0.5 (1/h), K_S=0.2 (g/L), D=0.5 (1/h), C_{in}=1 (g/L) into equations (8) and (9), to calculate the substrate and product concentrations at the balanced state, which are $\overline{C}$ =0.358(g/L), $\overline{P}$ =0.642 (g/L). Take the above values into equations (17) and (18), producing τ_1 =1.218 (h) and τ_2 =2 (h). Take τ_1 and τ_2 into equations (21) and (22), producing equations (25) and (26).

$$G_1 = \frac{0.609}{1.218s+1} \quad (25)$$

$$G_2 = \frac{0.391}{(1.218s+1)\cdot(2s+1)} \quad (26)$$

Assuming the substrate changes from 1 (g/L) to 1.5 (g/L) at time 0. The step change of the input is Laplace transformed producing equation (27).

$$C_{in}'(t) = \frac{0.5}{s} \quad (27)$$

Take equations (25), (26) and (27) into equations (23) and (24) producing equations (28) and (29).

$$C'(s) = \frac{0.305}{s\cdot(1.218s+1)} \quad (28)$$

$$P'(s) = \frac{0.196}{s\cdot(1.218s+1)\cdot(2s+1)} \quad (29)$$

Make reverse Laplace transformation of equation (28), (29) to produce equations (30) and (31).

$$C'(t) = 0.305 - 0.305e^{-0,821t} \quad (30)$$

$$P'(t) = 305e^{-0,821t} - 0.501e^{-0,5t} + 0.196 \quad (31)$$

In equations (30) and (31), $C'(t), P'(t)$ are the differences compared with the balanced state. Therefore, $C'(t) = C(t) - \overline{C}(t)$, $P'(t) = P(t) - \overline{P}(t)$. Take $\overline{C}, \overline{P}$ into equations (30) and (31) to produce equations (32) and (33).

$$C(t) = C'(t) + \overline{C} = 0.663 - 0.305e^{-0,821t} \quad (32)$$

$$P(t) = P'(t) + \overline{P} = 0.305e^{-0,821t} - 0.501e^{-0.5t} + 0.838 \quad (33)$$

Equations (32) and (33) are plotted in Fig. 2. The results showed that the substrate and product concentrations are stabilized at 0.66 and 0.84 (g/L), respectively, and there is time delay of the increase of product concentration compared with the increase of substrate concentration. Assuming that the conversion rate of substrate to product is one to one as shown by equations (1) and (2), the results show that the sum of substrate and product is 1.5 g/L at balanced state, which is equivalent to the substrate concentration of the feeding solution at balanced state. The model prediction agrees well with the facts.

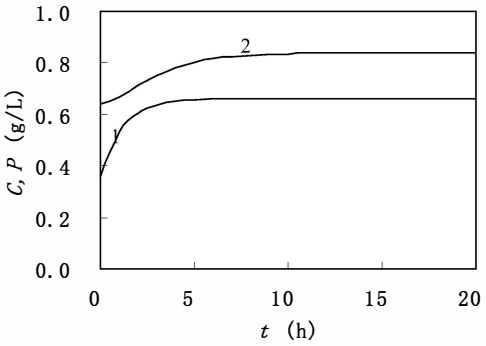

Fig. 2. Model predictions of time series of substrates and product. 1. Substrate; 2. Product.

Assuming that the substrate concentration changes from 1 (g/L) to 0.5 (g/L) at time 0. The Laplace transformation of the step input is shown in equation (34).

$$C_{in}'(t) = -\frac{0.5}{s} \quad (34)$$

Take equations (25), (26), and (34) into equations(23) and (24) producing equations (35) and (36).

$$C'(s) = -\frac{0.305}{s\cdot(1.218s+1)} \quad (35)$$

$$P'(s) = -\frac{0.196}{s\cdot(1.218s+1)\cdot(2s+1)} \quad (36)$$

Laplace transformation of equations (35) and (36) produce equations (37) and (38).

$$C'(t) = -0.305 + 0.305e^{-0,821t} \quad (37)$$

$$P'(t) = -305e^{0,821t} + 0.501e^{-0.5t} - 0.196 \quad (38)$$

Equations (37) and (38) plus the values of the balanced state producing equations (39) and (40), which are the time dependent real concentrations.

$$C(t) = C'(t) + \overline{C} = 0.053 - 0.305e^{-0,821t} \quad (39)$$

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$$P(t) = P'(t) + \overline{P} = -0.305e^{0.821t} + 0.501e^{-0.5t} + 0.446 \quad (40)$$

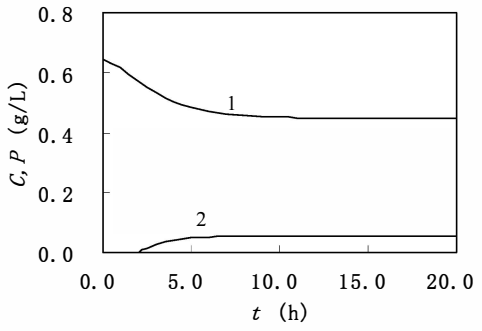

Fig. 3. Model predictions of time series of substrates and product. 1. Substrate; 2. Product.

The plots of equation (39) and (40) are shown in Fig. 3. The results showed that the substrate and product concentrations are stabilized at 0.05 and 0.45 (g/L), respectively. There is time delay on the increase of product concentration. The sum of substrate and product concentrations at balanced state is 0.5 (g/L), which is equivalent to the substrate concentration of the feeding solution at balanced state. It indicates the one to one conversion rate, and the model prediction fits well with the facts.

V. CONCLUSION

Transfer function model can be used in analysis and prediction of the dynamics of biocatalization process. It can investigate the process dynamics under various inputs without changes of the model. By using Laplace transformation, the solution of the model becomes easy. Transfer function model can also be used in automatic control process analysis and design. In this paper, immobilized CSTR bioreactor is used as an example to illustrate the transfer function model construction and process dynamics analysis for bioprocess. This method is also fit for the modeling and analysis of other bioprocesses.

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