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ADAPTIVE CONTROL FOR FED-BATCH FERMENTATIONS WITH E.COLI WITH TWO PHYSIOLOGICAL STATES

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INTRODUCTION

The fermentation processes with E.coli are known to go through several physiological states, which are described with different operating models. In this study a new adaptive linearizing control algorithm, that reaches target product concentration in the culture medium is proposed. Based on the derived operating models, a key marker - the dynamics of the intermediate metabolite acetate and experimental data of a fed-batch fermentation with E.coli, a cascade structure of software sensors is developed. Its outputs are included in the structure of the linearizing adaptive control algorithm with input -the feeding rate F and output - the glucose concentration. The applicability of the proposed control scheme is demonstrated by simulations.

SOFTWARE SENSORS,MARKER AND ESTIMATORS

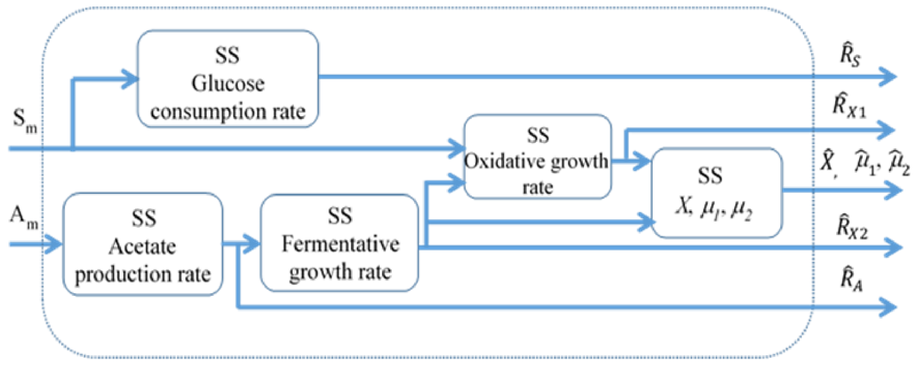

Fig. 1 Cascade structure of the software sensor for monitoring of three metabolic states

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ A \end{bmatrix} = \begin{bmatrix} 1 \\ -k_1 \\ 0 \end{bmatrix} \mu_1(t) X - D \begin{bmatrix} X \\ S \\ A \end{bmatrix} + \frac{F_{in,s}}{W} \begin{bmatrix} 0 \\ S_{in} \\ 0 \end{bmatrix} \quad (1)$$

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ A \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ -k_1 & -k_2 \\ 0 & k_3 \end{bmatrix} \begin{bmatrix} \mu_1(t) \\ \mu_2(t) \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ A \end{bmatrix} + \frac{F_{in,s}}{W} \begin{bmatrix} 0 \\ S_{in} \\ 0 \end{bmatrix}$$

$$R_a = \frac{dA}{dt} + \frac{F_{in,S}}{W} A \quad (2)$$

Ra > 0 oxidative-fermentative growth on glucose
Ra = 0 shows that there is no acetate in the medium and the growth is oxidative only on glucose

$$\frac{d\hat{A}}{dt} = \widehat{R_{ac}} - DA_m + \omega_1(A_m - \hat{A})$$

$$\frac{d\widehat{R_{ac}}}{dt} = \omega_2(A_m - \hat{A}) \quad (3)$$

$$\widehat{R_{X2}} = \frac{\widehat{R_{ap}}}{k_3} \quad (4)$$

$$\frac{d\hat{S}}{dt} = -k_1\widehat{R_{X1}} - k_2\widehat{R_{X2}} - DS_m + \frac{F_{in,S}}{W} S_{in} + \omega_3(S_m - \hat{S}) \quad (5)$$

$$\frac{d\widehat{R_{X1}}}{dt} = \omega_4(S_m - \hat{S}) \quad (6)$$

$$\frac{d\hat{X}}{dt} = \widehat{R_{X1}} + \widehat{R_{X2}} - D\hat{X} \quad (7)$$

$$\frac{d\hat{S}}{dt} = \widehat{R_s} - DS + \frac{F_{in,S}}{W} S_{in} + \omega_5(S_m - \hat{S})$$

$$\frac{d\widehat{R_S}}{dt} = \omega_6(S_m - \hat{S}) \quad (8)$$

$$\widehat{\mu_1} = \frac{\widehat{R_{X1}}}{\hat{X}} \qquad \widehat{\mu_2} = \frac{\widehat{R_{X2}}}{\hat{X}} \quad (9)$$

On figure 1 is shown the structure of the SS derived on the basis of operating models (1) and the new key parameter (2) for monitoring the three physiological states that are shown above. The input information for the software sensor includes real-time measurements of acetate and glucose concentrations. The SS structure is activated depending on the values of Ra, as shown above with the values indicating which of the three metabolic states the process is in. From (3) to (9) are shown the observer-based estimators of unknown kinetic parameters as follows : (3) is estimator for the rate of consumption of acetate, (4) is for the rate of fermentative growth of the biomass, (5) is for the rate of oxidative growth on glucose, (6) is for the concentration of biomass, (7) is estimator for the rate of oxidative growth on acetate, (8) is for the rate of consumption of glucose and (9) shows the estimators for the specific growth rates.

ADAPTIVE CONTROL AND RESULTS

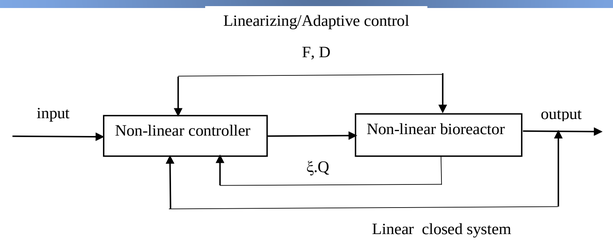

Figure 2. Scheme for adaptive control of the process

On figure 2 is shown the scheme of a closed system with non-linear subject for control. An adaptive control is derived from the estimators shown above. In this case it was picked control based on the concentration of the glucose in the cultural medium and derived from (5) and shown in (10). For the values of S* was picked value of 0.01 and the concentration of glucose in the feed Sin is 250 g/l, chosen from expert's point of view.

$$F = \frac{W.(-\lambda(S^* - S_m) + k_1\hat{R}_{X1} + k_2\hat{R}_{X2})}{S_{in} - S_m} \quad (10)$$

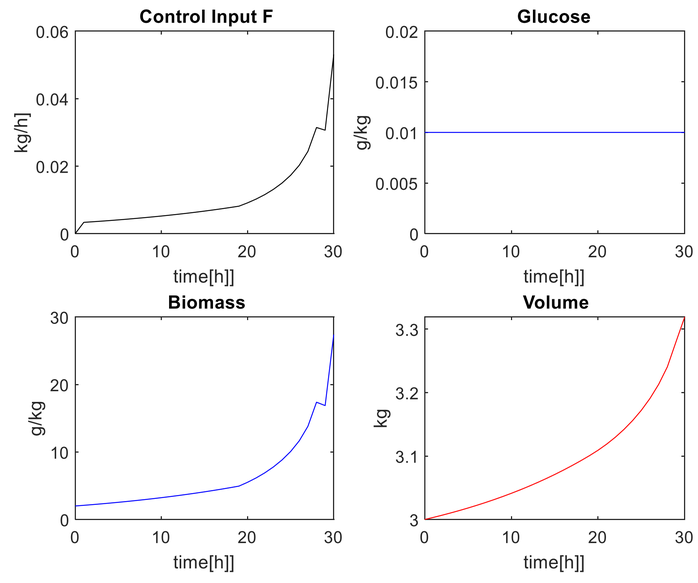

Figure 3 Linearizing control algorithm investigation

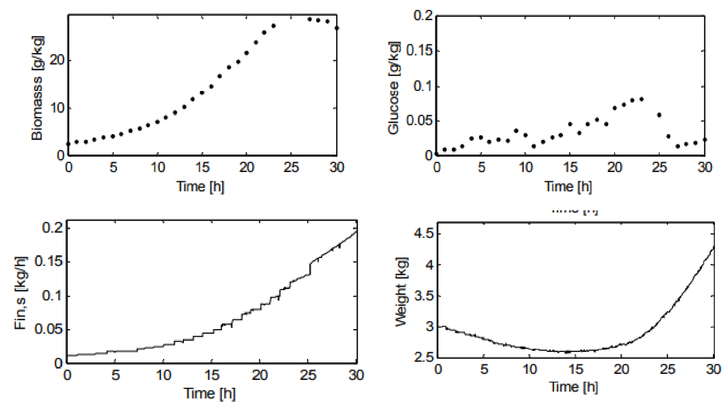

Figure 4 Results for the biomass and glucose concentrations, evolution of the weight in the bioreactor, given the shown feeding profile for the fermentation according the experimental data

Figure 3 shows the results of the simulation studies for the derived adaptive control. From the simulation it can be seen that the control input, which in this case is F is to be started at the beginning of the biotechnological process and as it does not exceed the limitations of the work volume of the bioreactor, which in this case is a total of 5 litres, and the control can be used during the whole fermentation until its conclusion .

A comparison was made with data collected from the literature. It shows that while maintaining a constant value of S* the same results for the concentration of biomass can be reached, at the same time there is less evolution of the weight inside the bioreactor, which leads to better efficiency of the so controlled bioprocess.

At the same time on the two figures can be seen that the biomass concentration continues to grow in steady way without reaching a point with drop in the values.

The results show good fit with the experimental data and the linearizing control algorithm can be used for real application.

CONCLUSION

A linearizing control of fed-batch fermentation by Escherichia coli is proposed. The biotechnological model is identified using the experimental data of batch fermentation. An operational model of the process is derived using the process reaction scheme. This model is used for design of observers of unmeasured biomass concentration and two biomass growth rates included in the structure of derived linearizing adaptive control algorithm.

The results of the simulation studies show that compared to the experiments carried out on the process under consideration, the same biomass concentration can be obtained by maintaining a low value of the glucose concentration in the nutrient medium, a lower value of the feeding rate and therefore a more low production costs.

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