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Adaptive Monitoring of Fed-Batch Phytase Production

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Abstract

A new approach to the derivation of algorithms for monitoring processes characterized by different metabolic states has been proposed. Each of them is characterized by a different growth rate and corresponding concentration of biomass. The approach combine z transformations and estimators of multiple specific biomass growth rates depending on the measured variables. The algorithms are applied for dynamics observation of the fed-batch process of phytase production. This approach excludes the use of a process model and related yield coefficients. This leads to the derivation of adaptive monitoring algorithms, which is proven by checking them with another set of experimental data.

Experimental data and reaction scheme of fed-batch phytase production

Two experiments of a periodic feeding process for phytase production were performed. The experimental data are shown in Figure 1 with red and black points. It is noteworthy that in one of the experiments (with black dots) after 11 hours there was a sharp change in metabolism, which is expressed in the cessation of production of the target product (2d) and increase in biomass (2a). This leads to the cessation of glucose consumption. The increase in substrate concentration is due to the periodic cultivation regime. In the second experiment, this effect was avoided. By 14 hours of cultivation, the biomass increases as well as the production of the target product, and the substrate stabilizes at a low level. In the processes with intermediate product (substrate) - acetate, three metabolic states are observed - oxidative growth of biomass on glucose, oxidative-fermentative growth on glucose and oxidative growth on glucose and acetate. The transition from the first to the second metabolic state is initiated with the appearance of acetate (2c). As experimental data for the third metabolic state are not available for one of the experiments (red dots), this gives grounds to consider only the first two metabolic states. In the presented model of the process, the growth of biomass in each physiological state is described by $\mu_1 X_1$ and $\mu_2 X_2$, t.e specific growth rate and corresponding biomass concentration. The model is the basis for outputting software sensors for unmeasured variables - biomass and target product. Glucose and acetate concentrations are measured in real time.

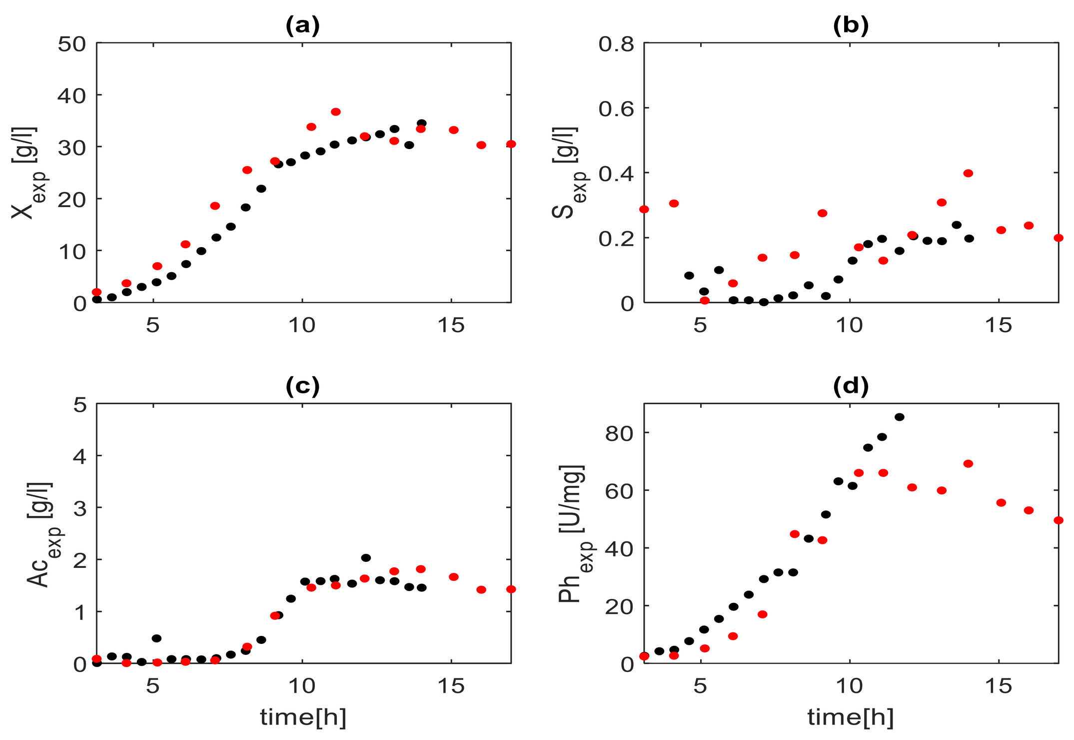

Figure 1

Such processes are characterized by different physiological states during the cultivation and respectively by multiple growth rates (μ_1 - μ_3) of biomass, which is directly related to the target product. The reaction scheme of such process could be presented as set of the following three main reactions (metabolic pathways), which correspond to the process physiological states:

Oxidative growth on glucose, with specific growth rate μ_1:

$$S + O_2 \xrightarrow{\mu 1} X_1$$

Fermentative growth on glucose, with specific growth rate μ_2:

$$S + O_2 \xrightarrow{\mu 2} X_2 + Ac$$

Oxidative growth on acetate, with specific growth rate μ_3:

$$Ac + O_2 \xrightarrow{\mu 3} X_3$$

Results

Adaptive monitoring

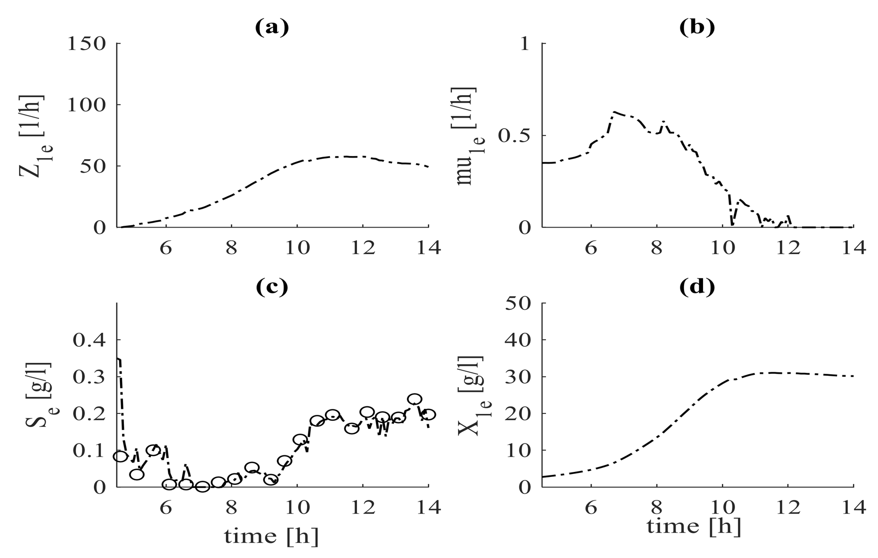

Figure 2a

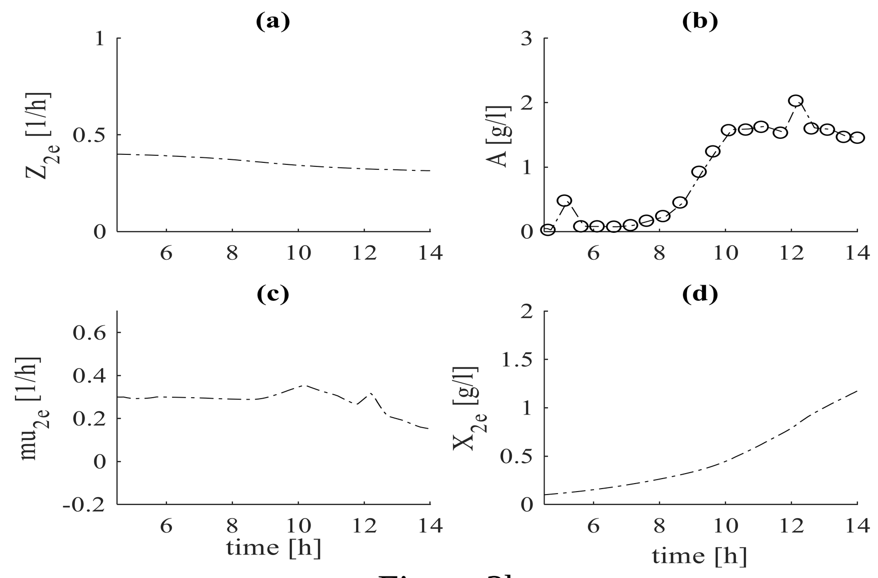

Figure 2b

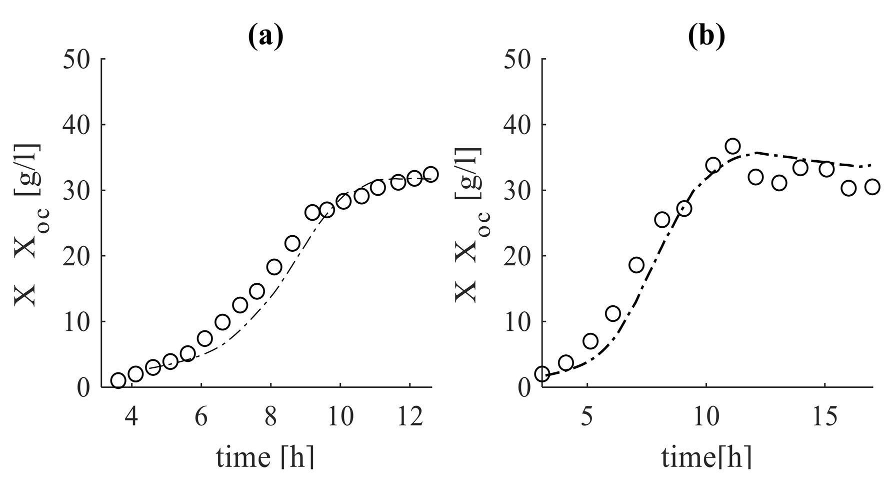

Figure 2c

Verification

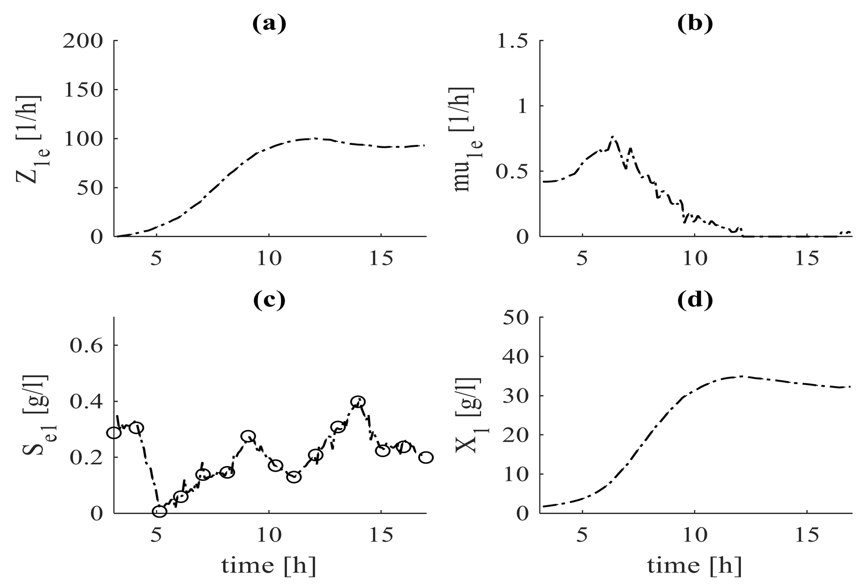

Figure 3a

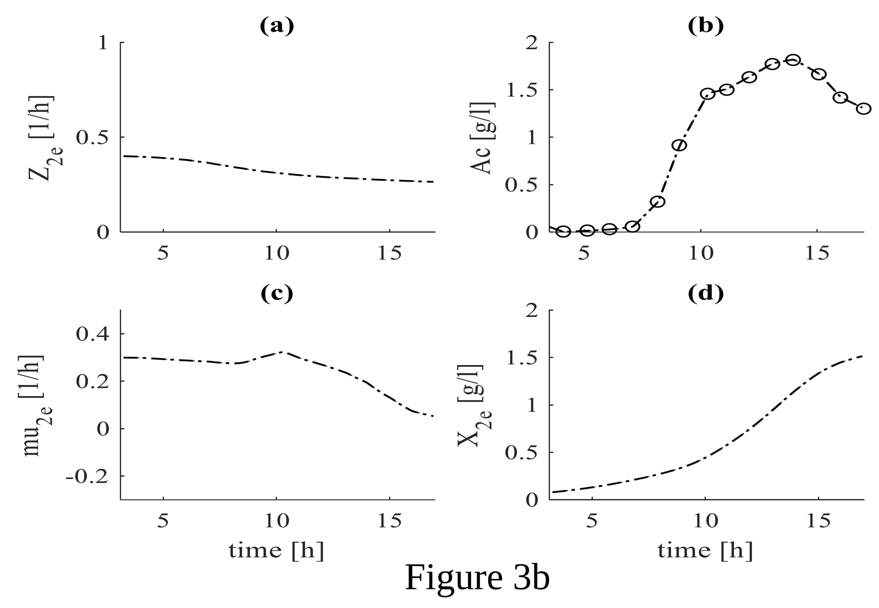

Figure 3b

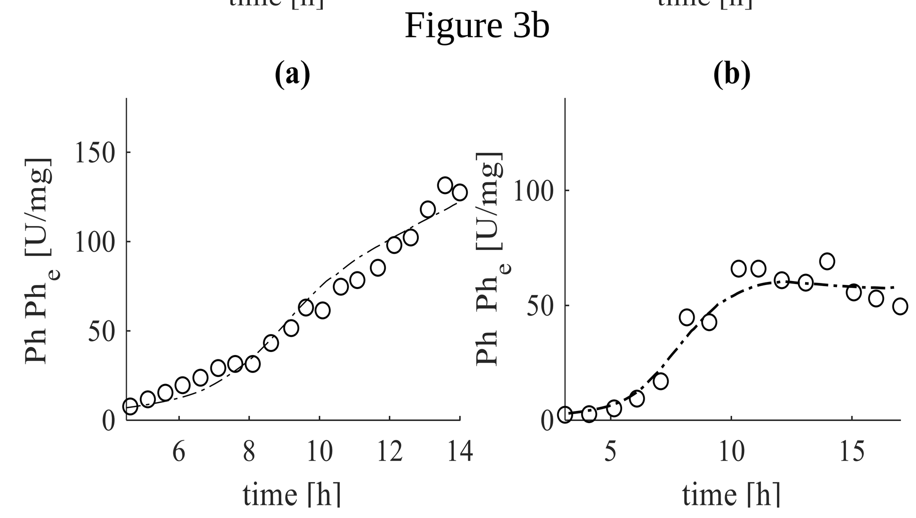

Figure 3c

Discussion

Figure 2 shows the results of the derived algorithms for estimating the kinetics and observers of biomass and phytase from experiment 1 (black dots), and figure 3 shows the results of verification with data from experiment 2 (red dots).

In Figures 2a and 3a the estimates of μ_1 and X_1 based on glucose measurements are shown. In Figures 2b and 3b the estimates of μ_2 and X_2 based on acetate measurement are demonstrated. In Figures 2c and Figures 3c observation and the verification of the biomass and the target product (phytase) are shown respectively. Biomass is calculates as sum of the estimates of the two biomass related to the two phases of the process.

The derived algorithms combine 2 z transformations and estimators of two specific biomass growth rates depending on the measured variable - glucose or acetate.

This approach excludes the use of a process model and related yield coefficients. This leads to the derivation of adaptive monitoring algorithms, which is proven by checking them with another set of experimental data.

Conclusion

The obtained results prove the possibility for deriving adaptive observation of the processes only in the presence of experimental data. The lack of an adequate model of the dynamics of the processes that undergo various metabolic states during cultivation is a common phenomenon in practice. In addition, the moment of their transition from one state to another is different for each experiment. The proposed campaign is robust in terms of such information. This is proven by verifying the derived algorithms with another set of experimental data.

Acknowledgements

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