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Application of Genetic Algorithms to Model Parameter Identification of a Recombinant *E. coli* High-Cell Density Fed-batch Fermentation

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ABSTRACT

In this work, a genetic algorithm was used to estimate both yield and kinetic coefficients of an unstructured model representing a fed-batch high-cell density fermentation of *Escherichia coli* (*E. coli*). The model based on the General State Space Dynamical Model was used to represent the three major metabolic pathways: oxidative growth on glucose, fermentative growth on glucose and oxidative growth on acetate. The structure of the kinetic equations was derived from literature and adapted to represent experimental results. Genetic Algorithm was used to minimize the normalized quadratic differences between simulated and real values of side variables *X*, *A* and *W* by manipulating both yield and kinetic coefficients.

Keywords: *Escherichia coli* (*E. coli*), genetic algorithms, parameter identification

Introduction

Fed-batch fermentation of *E. coli* can be modeled by the following balance equations:

$$\frac{d}{dt} \begin{bmatrix} X \\ S \\ A \\ W \end{bmatrix} = \begin{bmatrix} 1 & 1 & 1 \\ -k_1 & -k_2 & 0 \\ 0 & k_3 & -k_4 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \\ \mu_3 \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ A \\ 0 \end{bmatrix} + D \begin{bmatrix} 0 \\ S_{in} \\ 0 \\ W \end{bmatrix}$$

With *X*, *S* and *A* are biomass, glucose and acetate concentrations; *W* is the culture weight; *D* is the dilution rate, *m* are the specific growth rates and *k* are yield coefficients (Galvanauskas et al., 1998). Parameter estimation can be seen as an optimization problem where the performance criterion is the sum of squared errors between measured and simulated data:

$$J = \frac{\sum_{i=1}^n \frac{[X_{(sim,i)} - X_{exp,i}]^2}{X_{exp,i}^2}}{\sigma_X^2} + \frac{\sum_{i=1}^n \frac{[A_{(sim,i)} - A_{exp,i}]^2}{A_{exp,i}^2}}{\sigma_A^2} + \frac{\sum_{i=1}^n \frac{[W_{(sim,i)} - W_{exp,i}]^2}{W_{exp,i}^2}}{\sigma_W^2}$$

Methods

The experimental setup used to run the fed-batch fermentations with its main components; fermenter, digital control unit, balances, pumps, mass spectrometer, on-line filtration device and FIA system (Bastin & Dochain, 1990).

Simulation of the fermentation was conducted using MATLAB version 6.0 using a Runge-Kutta 4th order integration with fixed stepsize (Rocha & Ferreira, 2002). The Genetic and

Evolutionary Algorithm Toolbox (GEAtbx 3.3) for MATLAB developed by Pohleim was used for optimization purposes.

Results

During optimization, the model described was used to simulate fed-batch fermentations by applying the same feeding profile as in real fermentations. Then, the state variables X, A and W were compared with the real ones using the performance criterion. Genetic algorithms were used to generate an initial population of yield and kinetic coefficients for the simulation and to obtain an optimum set of those parameters. The optimization converged to an optimum after 1000 iterations and the corresponding results from a validation of the identified coefficients are shown below:

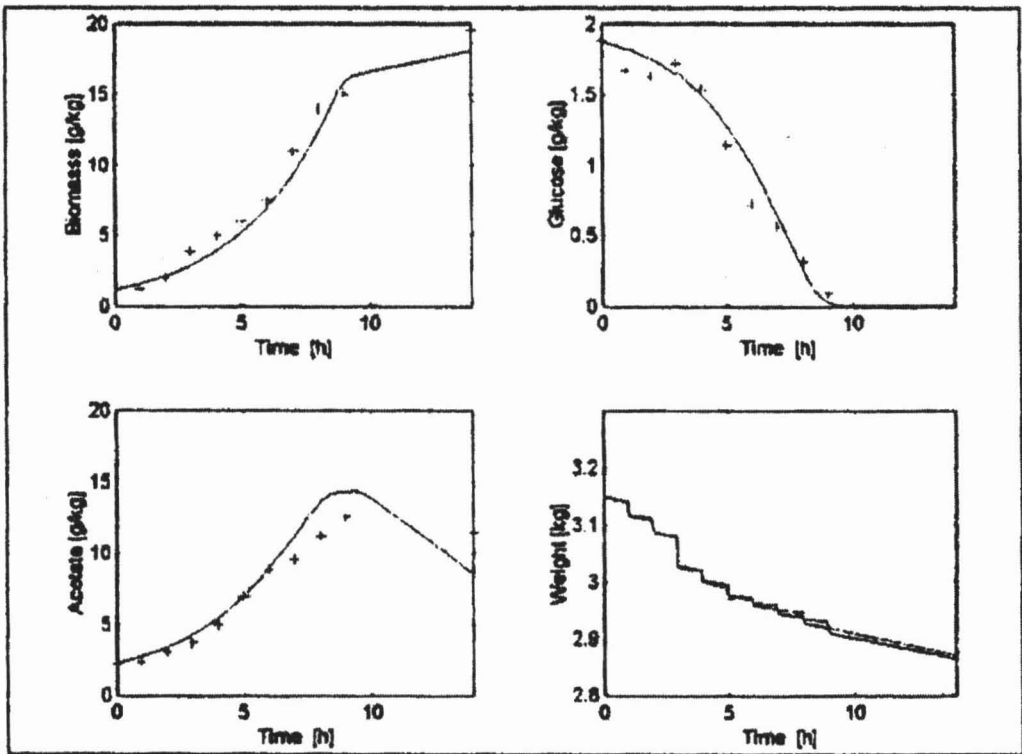


Figure 1: The Optimization Converged to an Optimum after 1000 Iterations

Conclusion

Using this methodology, it is possible to estimate with great accuracy several model parameter, without needing extensive mathematical manipulations of the model. As the results show, there is a very good agreement between real and simulated values for all measured state variables.

References

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