

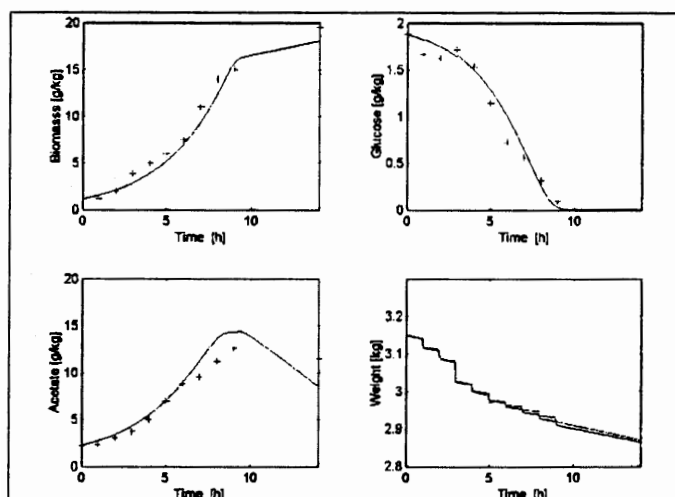
Application of genetic algorithms to model parameter identification of a recombinant *E. coli* high-cell density fed-batch fermentation

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Objectives: 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 *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, and can be represented by four differential equations corresponding to biomass, sugar (glucose), acetate and the culture weight concentration balances. The structure of the kinetic equations was derived from literature and adapted to represent experimental results.

Genetic Algorithms are a stochastic optimization method, based on the biological principle of natural evolution, and were used to minimize the normalized quadratic differences between simulated and real values of the state variables



Biomass, Glucose, Acetate and Weight, by manipulating both yield and kinetic coefficients. The number of optimized parameters was 13.

Results: Data from several fermentation runs were treated with this optimization routine, and after 1000 iterations a new parameter set was obtained that allowed a good description of the process behavior. The next figure represents an example of a fermentation run. Real values of Biomass, Glucose, Acetate, and Weight are compared with the ones simulated using the model with optimized parameters. A normalized difference of only 1% was obtained with this optimized model, when compared to simulations conducted with non-optimized parameters (obtained from literature).

Conclusions: Using this methodology, it is possible to estimate with great accuracy several model parameters, 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.