438h Stochastic Grey-Box Modelling of Industrial Fermentation

Jan K. Rasmussen, Henrik Madsen, and Sten Bay Jørgensen

Fed-batch processes play a very important role in chemical and biochemical industry. Fermentations are widely used in biochemical industry and these are most often carried out as fed-batch processes. Present control schemes do not utilize the full potential of the production facilities and may often fail to achieve uniform product quality and optimal productivity. Application of advanced multivariable control schemes can help solve this problem. However, the introduction of model based control strategies is considered difficult because suitable models are not readily available without significant experimental investigation and validation.

First principle engineering models can be used in the controller provided that they possess satisfactory predictive capabilities. Parameter estimation in a first principle engineering model can be very time consuming and can require revalidation when scaling up from laboratory to industrial fermenters. Especially parameters for mass and heat transfer models change drastically when the volume of the fermentor is changed. These phenomena can not be investigated in laboratory scale equipment which makes large scale experiments necessary.

The approach used in this work is to combine first principle engineering models with operational data to produce predictive models suited for control purposes. The method described is stochastic grey-box modelling consisting of a set of stochastic differential equations describing the dynamics of the system in continuous time and a set of discrete time measurements[1].

One of the key ideas for the framework is to use all prior information for formulation of an initial first principles engineering model. Unknown parameters for the initial model are then estimated from experimental data and a residual analysis is carried out to evaluate the quality of the resulting model. The next step in the modelling cycle is the model falsification or unfalsification which determines if the model is sufficiently accurate to serve its intended purpose. If the model is unfalsified the model development is completed. In case of falsification the modelling cycle must repeated by reformulating the initial model. In this case statistical tests can be used to provide indications of which parts of the model are deficient. Nonparametric modelling can be applied to estimate which functional relationships are contained in the data and subsequently lead to reformulation of the model. The resulting model must possess good predictive capabilities and is intended for implementation in a Nonlinear Model Predictive Control framework.

The process studied is a cultivation with the filamentous fungus *Aspergillus* for production of the enzyme amylase. The fermenters are equipped with sensors for online measurements of different properties but some values are only available as offline measurements, which makes closed loop control and optimisation more difficult. *Aspergillus* is well characterized in literature and a first principles engineering model by Agger et. al.[2] is used as the initial model in this work.

Experimental data for the fermentation process have been made available by Novozymes A/S. The data are operational data from an actual production facility. To ensure adequate excitation of the process batches representing large variations in feed dosing are investigated using the grey-box modelling framework described. Once the model parameters have been estimated validation will be carried out using batches with different variable trajectories. In case the resulting model lacks sufficient predictive capabilities specific model deficiencies will be pinpointed by the grey-box stochastic modelling framework and the modelling cycle will be repeated.

References:

1. N.R. Kristensen, H. Madsen, S.B. Jørgensen, 2004, A Method for Systematic Improvement of Stochastic Grey-Box Models, Comp. & Chem. Eng., **28 (8)** , 1431-1449

2. T. Agger, A. B. Spohr, M. Carlsen, J. Nielsen, 1998, Growth and Product Formation of Aspergillus oryzae during Submerged Cultivations: Verification of a Morphologically Structured Model Using Fluorescent Probes, Biotechnology and Bioengineering, **57** , 321-329