3BIO-BioControl

*Modelling and Control of Bioprocesses*

Prof. Ph. Bogaerts

**Dynamical models for simulating mammalian cell cultures based on Flux Balance Analysis**

Summary:
Mammalian cell cultures are widely used in biopharmaceutical industries for the production of vaccines and monoclonal antibodies. Dynamical macroscopic models of such processes are of outmost importance for their monitoring, optimization and control. A new strategy for developing simulation models of this process has been proposed at 3BIO-BioControl (A. Richelle et al., submitted to Biochemical Engineering Journal, 2016) and consists in using Flux Balance Analysis (J. D. Orth et al., Nature Biotechnology, 28 (3), 245-248, 2010) for exploiting basic knowledge at the metabolic level. The aim of this work is to investigate the applicability and added value of using more complex metabolic networks (70 fluxes instead of 24) with this new strategy. The metabolic network is available, as well as experimental measurements concerning hybridoma cell fed-batch cultures.

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**Model-based optimization of hybridoma cell fed-batch cultures**

Summary:
Hybridoma cell fed-batch cultures are used in biopharmaceutical industries for producing monoclonal antibodies. Dynamical macroscopic models of such processes are of outmost importance for their monitoring, optimization and control. A first model has been recently identified and validated at 3BIO-BioControl for hybridoma cell fed-batch cultures (Z. Amribt et al., Biochemical Engineering Journal, 70, 196-209, 2013) based on available experimental data. It has been used for determining optimal feeding profiles which maximize the biomass productivity obtained at the end of the process (Z. Amribt et al., Bioprocess and
A second model has been recently proposed (Richelle and Bogaerts, Biochemical Engineering Journal, 100, 41-49, 2015) which involves other factors explaining other activation and inhibition phenomena. The aim of this work is to revisit the process optimization based on this newly available model.

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Model-based shelf life prediction in the food supply chain

Summary:
Predictive food microbiology aims at predicting the growth and/or inactivation of microorganisms in food (J. Ferrer et al., International Journal of Food Microbiology, 134, 2-8, 2009). Primary models describe the time evolution of the microorganism concentration in food while secondary models add the effects of environmental factors (like temperature or pH) on the kinetic parameters (growth rate, lag phase) involved in primary models. Public databases propose experimental data corresponding to different kinds of food, contaminants and environmental conditions. Combase (www.combase.cc) is one of the most important ones. The goal of this work is to build algorithms for predicting the shelf life along the food supply chain, based on i) a microorganism growth model, ii) some (discrete time) measurements (main spoilage microorganism cell density, temperature) and iii) a state observer for estimating unmeasured signals (continuous time spoilage cell density, “bottleneck substance” necessary for the cells to adapt to their environment). The shelf life predictor will be tested on experimental data chosen in the public database Combase.

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