



3BIO-BioControl

Modelling and Control of Bioprocesses

Prof. Ph. Bogaerts

Mathematical modeling for optimizing intracellular trehalose accumulation in yeast fed-batch cultures

Summary:

The general context of this study concerns yeast cell cultures in fed-batch bioreactors, i.e. within reactors which are fed over time with liquid culture medium containing the required species for an efficient yeast growth. There exist a lot of applications, from baker's yeast production to the one of therapeutic molecules, or biofuels. The general goal is to mathematically analyze the key factors influencing the accumulation of trehalose (TRE) within *Saccharomyces cerevisiae* cells cultured in bioreactor, and to deduce feeding profiles which allow maximizing this accumulation. Several studies have proved the key role of TRE whose accumulation allows increasing yeast cell resistance to diverse stresses caused by the surrounding environment. The main goal is to build a mathematical model which allows predicting the time profiles of *S. cerevisiae* yeast concentration, of the main extracellular species involved in the bioreactor culture medium (glucose, ammonium, ethanol) and of intracellular TRE. This model will have the following features: description of overflow metabolism phenomena, description of glucose and ammonium coordinated uptakes, description of intracellular TRE accumulation, use of continuous differentiable kinetic models. It will take inspiration on former results obtained at 3BIO-BioControl (A. Richelle et al., Computers and Chemical Engineering, 61, 220-233, 2014). The model will be used to determine the optimal bioreactor feeding conditions which maximize TRE accumulation. Experimental validation of the obtained results will be performed based on data available at 3BIO-BioControl (and possibly data collected from new experimental campaigns). This work is part of a collaboration with Puratos company. **POSSIBILITY TO LINK THIS THESIS WITH A THREE-MONTH INTERNSHIP** (information coming soon from Puratos).

Contact: Philippe BOGAERTS (philippe.bogaerts@ulb.ac.be), 3BIO-BioControl, UD5.111a, 02/650.4076

Metabolic 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. Macroscopic models have been identified and validated at 3BIO-BioControl for hybridoma cell fed-batch cultures (Z. Amribt et al., *Biochemical Engineering Journal*, 70, 196-209, 2013; Richelle and Bogaerts, *Biochemical Engineering Journal*, 100, 41-49, 2015) based on available experimental data. The first one 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 Biosystems Engineering*, 37, 1637-1652, 2014). Another dynamical model has been recently developed based on a simplified metabolic network and metabolic flux analysis tools (Bogaerts et al., *Journal of Process Control*, 60, 34-47, 2017). The aim of this work is to revisit the process optimization based on this newly available model and to compare optimal solutions derived from macroscopic models and metabolic models.

Contact: Philippe BOGAERTS (philippe.bogaerts@ulb.ac.be), 3BIO-BioControl, UD5.111a, 02/650.4076

Analysis and development of methods for estimating the fluxes in food webs describing coastal ecosystems

Summary:

The analysis of marine ecosystems involves food webs which describe the mass flows between different trophic compartments. For low trophic levels, these compartments are phytoplankton, zooplankton, bacteria, detritus, etc., while for higher trophic levels they concern different fish species which are directly linked to the former levels through the zooplankton they predate. Quantifying these web flows allows understanding the behavior of many types of marine and coastal ecosystems and the impact of natural and anthropogenic changes (climate, fishery intensity, nutrient enrichment, etc.). Similarly to metabolic networks, food webs are generally underdetermined as the number of unmeasured web fluxes is higher than the available linear equality constraints (mass balances and available measurements). Even by considering the inequality constraints representing physiological constraints like lower and upper bounds on bacterial growth efficiency or detritus degradation rate, it is not possible to determine unique values for the web fluxes. Linear Inverse Models (LIMs) consist of the set of equality and inequality equations which link the web fluxes (van Oevelen et al., *Ecosystems*, 13, 32-45, 2010). Different algorithms have been proposed to tackle the underdeterminacy problem. The goal of this work is to test and/or develop different algorithms for determining the food web flows in some practical case studies for which the food web and data / constraints are available in the literature (e.g., Soetaert and van Oevelen, *Oceanography*, 22(1), 128-143, 2009).

Contact: Philippe BOGAERTS (philippe.bogaerts@ulb.ac.be), 3BIO-BioControl, UD5.111a, 02/650.4076