Prediction of concentration time profiles in *Saccharomyces cervisiae* fed-batch cultures based on metabolic flux analysis and biomass composition estimation

Summary:
*Saccharomyces cervisiae* fed-batch cultures are widely used in food and biopharmaceutical industries. Dynamical macroscopic models of such processes are of outmost importance for their monitoring, optimization and control. A macroscopic dynamical model has been proposed at 3BIO-BioControl (A. Richelle et al., Computers and Chemical Engineering, 61, 220-233, 2014) for predicting the main species concentration time profiles, taking into account the overflow metabolism phenomenon (fermentation of excess glucose with ethanol production) and the coordinated uptake rates of glucose and nitrogen sources. Another modeling approach is under consideration, based on a selected metabolic network, Flux Balance Analysis and the definition of appropriate constraints linking the intracellular fluxes. Estimation of the biomass composition plays a key role in such a model. The goals of this work are:

- to determine the simplest models of biomass composition as a function of some experimental conditions, e.g. the ammonium feeding concentration, which can be inserted in the above-mentioned metabolic models;
- to compare the complexity and prediction abilities of such a metabolic model with respect to the available macroscopic model.

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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 recently 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 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.

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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).

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