Dynamic macroscopic modeling of 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 components 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 of this master thesis 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 dynamic macroscopic 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 dynamic macroscopic model will have the following features: description of overflow metabolism phenomena, description of glucose and ammonium coordinated uptakes, description of intracellular TRE accumulation. 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. Parameter identification and model validation will be performed based on experimental data available at 3BIO-BioControl (and possibly data collected from new experimental campaigns). This work is part of a collaboration with Puratos company.

Contacts:
Philippe BOGAERTS (philippe.bogaerts@ulb.ac.be), 3BIO-BioControl, UDS.111a, 02/650.4076
Antoine HUET (antoine.huet@ulb.be), 3BIO-BioControl, UDS.131, 02/650.6608
**Metabolic modeling of intracellular trehalose accumulation in yeast fed-batch cultures**

Summary:
The context of this research is the same as in the former master thesis topic. The difference is that, instead of considering dynamic macroscopic modeling, the goal is to build a metabolic network with input fluxes for glucose and ammonium uptakes, output fluxes for ethanol and biomass production and intracellular fluxes for describing the main intracellular metabolisms (glycolysis, TCA cycle, pentose phosphate pathway, fermentation, amino acid metabolism, transport reactions). Especially, the accumulation of trehalose (TRE) among the carbohydrates will be included in the network. A metabolic network including all the aforementioned fluxes, with the exception of those concerning TRE, has been proposed in a recent PhD thesis in the 3BIO-BioControl group (José Plaza, 2020). A first goal will be to include a more detailed description of carbohydrates metabolism and especially trehalose accumulation. Metabolic Flux Analysis (MFA) and Flux Variability Analysis (FVA) will then performed on the new metabolic network based on experimental data available at 3BIO-BioControl (and possibly data collected from new experimental campaigns). The second goal will consist in analyzing the results so as to determine the culture conditions, i.e. glucose and nitrogen uptake rates, that could lead to increasing the intracellular TRE accumulation. This work is part of a collaboration with Puratos company.

Contacts:
Philippe BOGAERTS (philippe.bogaerts@ulb.ac.be), 3BIO-BioControl, UD5.111a, 02/650.4076
Antoine HUET (antoine.huet@ulb.be), 3BIO-BioControl, UD5.131, 02/650.6608

**Analysis and development of methods for estimating the fluxes in food webs describing the Vietnamese marine ecosystem**

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. Simple linear programs can provide the lower and upper bounds for each of the web fluxes. Sampling
algorithms allow to compute the mean flux distribution and the marginal distribution of each flux. The first goal of this work is to improve the Vietnamese ecosystem model proposed by Anh et al. (Estuarine, Coastal and Shelf Science, 165, 226-236, 2015), especially with new data/information from Nha Trang Ocean Institute and other bibliographical references. The second goal is to test and/or develop different algorithms for determining the food web flows in the aforementioned marine ecosystem, with a special focus on sampling algorithms.

Contacts:
Philippe BOGAERTS (philippe.bogaerts@ulb.ac.be), 3BIO-BioControl, UD5.111a, 02/650.4076
Trang HOANG (katie.hoang.1810@gmail.com), 3BIO-BioControl, UD5.131, 02/650.6608