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Thesis project:
Comparing popular methods of creating time-dependent metabolic models

Description:
An important aspect of systems & synthetic biology is to understand how biological networks and phenotypes are altered by changes in metabolic state. To this end, large-scale models have been constructed to describe the flow of energy through enzymatic pathways. These models allow us to relate nutrient availability to growth rate and identify bottlenecks in enzymatic pathways that may prevent the efficient use of available resources.

Mathematically, enzymatic reactions are described by ordinary differential equations (ODEs) that relate the change in an enzyme's concentration over time to kinetic rates. However, for large systems, approximating and optimizing reaction rates becomes tricky due to the lack of appropriate data. Thus, methods such as Flux Balance Analysis (FBA) are used to estimate the flux of a pathway given a particular stoichiometry matrix (representing the substrates and products of each reaction). However, FBA methods are limited to predicting steady state flux distributions, i.e. there cannot be any net consumption or production of intermediate metabolites. Hence, whilst results of FBA can provide useful information, such as identifying inefficient reactions or finding optimal growth media for organisms, it does not allow us to understand how enzyme and metabolite concentrations change with time.

In the last decade, dynamic FBA (dFBA) has been formulated to provide insights into how fluxes in an enzyme pathway change over time. However, to the best of our knowledge, there is little research done on a direct comparison of results obtained from dynamic FBA and the classical ODE model formalism.

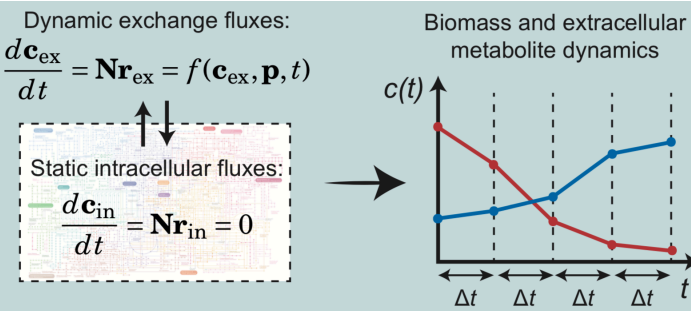

Figure 1: Static-dynamic hybrid modeling.

This project will look to explore how the results of dFBA and ODE models are related, in the context of microbial metabolism: 1. Can optimal solutions using one method be translated to represent optimal solutions using the other? 2. Do limitations exist for one method that can be overcome by the other?

Methods:
Python, Ordinary Differential Equations, Dynamic Flux Balance Analysis, Optimisation.

Requirements:
- Some programming experience required (preferably Python or Matlab)
- Basic familiarity with ordinary differential equations
- One or more of the following courses: Modelling Biological systems I/II, Introduction to Systems and Synthetic Biology, or equivalent

Supervisors:
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References:
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J. A. Gomez et al. (2014) DFBAlab: a fast and reliable MATLAB code for dynamic flux balance analysis. BMC Bioinformatics 15: 409.
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