Laboratory of Systems and Synthetic Biology
Wageningen University and Research Center
Stippeneng 4 (Building 124)
6708 WE, Wageningen The Netherlands

Erika Gaspari
PhD candidate
erika.gaspari@wur.nl
Room 6032

Master/Bachelor Thesis Project:

Parameter Estimation Strategies to Kineticize Genome-Scale Metabolic Models

Description

Genome-scale Metabolic Models (GEMs) are widely used for the reconstruction of networks of reactions that take place inside living organisms. To analyse the metabolic potential of the organism, constraint-based modelling approaches became very popular; however, these approaches rely on the steady state assumption, give multiple optimal solutions and cannot describe the dynamic changes in metabolite levels.

We are developing an automated Python pipeline to convert genome-scale metabolic models into dynamic models of metabolism that describe the changes of the metabolic fluxes over time. Taking a given network scheme as input, this computational framework automatically searches for known kinetic rates, undergoes a network reduction step and converts the chemical reactions into kinetic equations to then simulate the temporal changes of the metabolic species. However, the number of experimentally-determined kinetic rates is very low. For this reason, strategies for parameters search, estimation from the experimental data and optimization are essential in the construction of an efficient pipeline.

The thesis project focuses on the implementation of one (*bachelor thesis*) or different (*master thesis*) parameter estimation and optimization strategies with the aim of finding the missing parameters and kinetic rates to be included in the automated conversion of genome-scale metabolic models into dynamic models of metabolism. The methods, implemented in Python, will be applied to toy and real metabolic networks.

Methods

Programming skills (Python) and a basic understanding of the principles of genome-scale metabolic modelling and dynamic modelling are required.

References

- Parameter Estimation in Biochemical Pathways: A Comparison of Global Optimization Methods. Moles C.G. et al. (2003). *Genome Res. 13: 2467-2474.*
- Scalable Parameter Estimation for Genome-Scale Biochemical Reaction Networks. Froehlich F. et al. (2017). *PLoS Comput. Biol. 13(1).*
- An Improved Swarm Optimization for Parameter Estimation and Biological Model Selection. Abdullah A. et al. (2013). *PLoS ONE 8(4).*
- Parameter Estimation in Large-scale Systems Biology Models: A Parallel and Self-Adaptive Cooperative Strategy. Penas D.R. et al. (2017). *BMC Bioinformatics 18:52*.