



Assessing deterministic and probabilistic optimization methods for dynamic model calibration and data fitting

Supervisors: Dr Henk van Lingen, Dr Rob Smith, Dr Maria Suarez-Diez

Contacts: henk.vanlingen@wur.nl

Type of thesis: Computational

Required competences: Knowledge of ordinary differential equations (ODEs), advanced statistical and numerical optimization skills, and ability to simulate systems in MATLAB, R or Python are desired.

Acquired competences: ODE modelling, deterministic and probabilistic parameter optimization methods, Bayesian analyses, data fitting.

Date: by mutual agreement

Description

For various biological applications, mathematical models are used to test our prior knowledge and study the dynamics of biological networks. For example, modelling of metabolic networks has provided us with insights that can be utilised to aid biopharmaceutical production and improve our understanding of disease (Smith and Van Rosmalen, 2018). Although dynamic models may describe a system in great detail, model structure and parameters may be associated with uncertainty and bias. Estimating model parameters using experimental data is an essential step to streamline these model representation matters. Parameter optimization (the fitting of models to data) is commonly performed by minimizing a goodness of fit measure, for which a wide variety of optimization methods are available (constrained minimisation, simulated annealing, particle swarm optimisation, Bayesian inference, Gaussian processes, etc.). However, despite the specific characteristics (e.g. global vs local and deterministic vs probabilistic optimization), all these methods have trade-offs in terms of computational speed and the level of information about the system their results provide (Gabor and Banga, 2015). We



wish to understand which (set of) method(s) is the most appropriate to use given the research conducted in the department and the data which we have available.

This project will assess the usefulness of various optimization methods for calibrating dynamic models of metabolic systems (e.g. Arhonditsis et al., 2007). Specifically, the student will assess the trade-offs of method regarding accuracy of model parameters and output, parameter identifiability, and computational speed of the optimization. If time allows, the student will also investigate if a combination of these methods will speed up the run time for calibrating a dynamic model. The hope is that this project will help contribute to future research in the group by providing tips, protocols and pipelines for future model development.

References

Smith RW, van Rosmalen RP, et al. (2018) DMPy: a Python package for automated mathematical model construction of large-scale metabolic systems. *BMC Systems Biology* 12:72. Doi:10.1186/s12918-018-0584-8

Gabor and Banga, (2015). Robust and efficient parameter estimation in dynamic models of biological systems. *BMC Systems Biology* 9:74. Doi:10.1186/s12918-015-0219-2

Arhonditsis et al. (2007). Bayesian calibration of mechanistic aquatic biogeochemical models and benefits for environmental management. *Journal of Marine Systems* 73:8-30. Doi:10.1016/j.jmarsys.2007.07.004