Project proposal

Calibration and Optimisation of Biopharmaceutical Processes

Supervisors:
Juergen Branke (juergen.branke@wbs.ac.uk)

Background: Modern biopharmaceutical drugs offer novel and personalised ways for treating diseases, and the market is expected to increase to $500 billion by 2025. Controlling biopharmaceutical manufacturing processes is a challenge, however, as these processes are complex and usually involve living cells. It is possible to build dynamic mechanistic models (e.g., system dynamics / differential equations) that model cell growth, and then optimise control strategies based on these models. But these models have a number of parameters that need to be tuned.

The standard workflow is thus to first do some lab experiments following a standard experimental design. Then the mechanistic model is calibrated based on the experimental data. And finally, optimisation is used to identify the best possible control strategy.

This approach largely neglects the interdependencies between experiments, calibration and optimisation. If the end goal is to obtain the best possible control strategy, the model doesn't have to be perfect everywhere, but only good enough to reliably identify the best control. And so experimental data collection could be done sequentially, starting with a very sparse experimental design, then identifying what additional experimental data would be most beneficial for identifying a better control strategy.

Mini-project: The mini-project would only look at the second half of the optimisation process, from calibrated model to optimal control strategy. It would start with a given mechanistic model of a biopharmaceutical process (e.g. [1]) and use Bayesian Optimisation to find an optimal control strategy with a minimum number of model simulations. Bayesian Optimisation is a black box optimisation algorithm that starts with a few initial observations (model simulations), and then iteratively samples those potential solutions that have the largest expected value of information [2].

Deliverable: Working code, paper with some empirical results on a simple biopharmaceutical process model.

PhD prospect: In the PhD project, experimental data collection, model calibration, and control policy optimisation should be considered simultaneously. New Bayesian Optimisation algorithms shall be developed that can iteratively decide what additional physical experiment would provide the highest value of information with respect to the quality of the obtainable control policy. This has the potential to generate better control strategies with fewer required expensive physical lab experiments. The problem of combined calibration and optimisation occurs in many domains, so the developed algorithms would be relevant also in a much wider domain.

Student requirements: Programming skills.

References:

[1] A. J. Stacey, E. A. Cheeseman, K. E. Glen, R. L.L. Moore, R. J. Thomas,
Experimentally integrated dynamic modelling for intuitive optimisation of cell based processes and manufacture, Biochemical Engineering Journal, 132, 2018, pp.130-138
[2] B. Shahriari, K. Swersky, Z. Wang, R. P. Adams and N. de Freitas, "Taking the Human Out of the Loop: A Review of Bayesian Optimization," in *Proceedings of the IEEE*, vol. 104, no. 1, pp. 148-175, 2016