

Modelling a blue light-controlled synthetic biology circuit for the purpose of metabolic reprogramming

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Type of thesis: Computational

Required competences: Knowledge of ordinary differential equations (ODEs) and their analysis, ability to simulate systems in MATLAB or Python. These are taught in courses, e.g., SSB30806, SSB31806, BCT20306.

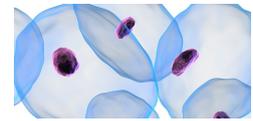
Acquired competences: Ability to analyse data and simulations of mathematical models. Designing experiments to test model predictions.

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Description

Optogenetics is the use of light-responsive proteins (photoreceptors) to synthetically control biology. Recently, researchers have experimentally characterised a blue-light responsive system with the capabilities of controlling metabolic pathways (Lalwani et al., 2020). In this work, the blue-light system was shown to produce a larger amount of GFP compared to chemical inducers (IPTG), whilst the addition of a negative feedback loop reduced the background “leakage” from the system – which is undesirable if we want tight control over biological processes. The authors went on to apply the tool to perturb the production of isobutanol and mevalonate.

Even though the experimental design of the network showed promising results, a mathematical model can help understand the next steps for system development. Optogenetic circuits are often modelled to help understand their robustness and for experimental design (e.g. Baaske et al., 2018). In this project, we would like to model the system published in Lalwani et al. Once the model has shown it can match the current experimental data, we will consider how the system can be further improved, or look to design experiments that yield a desired amount of metabolic outputs.



References

Lalwani MA, et al. (2020) Optogenetic control of the *lac* operon for bacterial chemical and protein production. *Nature Chemical Biology* doi: 10.1038/s41589-020-0639-1

Baaske J, et al. (2018) Dual-controlled optogenetic system for the rapid downregulation of protein levels in mammalian cells. *Scientific Reports* doi: 10.1038/s41598-018-32929-7