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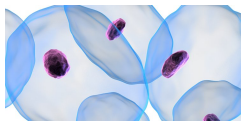

Computational investigation of mutation and rejection rates of synthetic bio-safety tools in cell populations

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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, BCT31806.

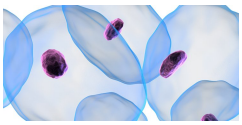
Acquired competences: Ability to simulate stochastic systems, creating hybrid models of systems at different levels, experimental design.

Date: 09-09-2020

Description

A developing research area in fields related to synthetic biology is the safety and stability of synthetic constructs in the natural environment. By incorporating synthetic constructs into their genome, not only is the host cell's function modified, but cell fitness is altered and it is unclear whether the passing of the synthetic construct (and related function) to progeny is stable or will be rejected over generations. This has particular implications in gene drive research, where the genome-inserted gene drive can quickly spread a genetic modification across a population in a non-Mendelian fashion. However, if the gene drive stops working (e.g. due to unwanted mutations in the synthetic construct), the spread of the genetic modification will also cease. As such, it would be desirable to understand how likely it is that mutations in synthetic constructs take place leading to rejection from the genome, the wider implications on cell populations, and whether this can be alleviated through the addition of further synthetic tools or through engineering of the original construct.

This project will look to address these issues with computational modelling. An example of such a modelling strategy in relation to gene drives can be found in Marshall



et al. Ultimately, we are interested in whether this strategy can be extended for further studies. One avenue is to include the addition of anti-gene drives (i.e. the addition of further synthetic constructs) to reverse the effect of the gene drive on the cell population – a potentially crucial control method for gene drives in some circumstances. Another interesting question is whether we can create hybrid models that can simulate changes to the dynamics of synthetic constructs over cell generations (e.g. oscillations of GFP in the Represillator system in Elowitz & Leibler). These questions are open-ended and the student is free to shape the parts of the project around their interests or those of collaborators in SSB and the Laboratory of Microbiology (MIB).

References

Marshall J.M., Buchman A., Sanchez H.M.C. & Akbari O.S. (2017) "Overcoming evolved resistance to population-suppressing homing-based gene drives" *Scientific Reports* **7:** 3776

Elowitz M.B. & Leibler S. (2000) "A synthetic oscillator network of transcriptional regulators" *Nature* **403:** 335-338