Tracing and shaping the evolutionary paths of engineered biology

Supervisory team:
Main supervisor: Dr Thomas Gorochowski (University of Bristol)
Second supervisor: Prof Tiffany Taylor (University of Bath)
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Host institution: University of Bristol

Project description:
No biological system can avoid evolution, yet most engineered biology to date completely overlooks its impact. This project aims to address this failing by helping us better understand how design choices when implementing synthetic genetic circuits affect the routes that evolution takes once the system is deployed. To do this, the project will develop a mixture of experimental and modelling approaches to recover the evolutionary paths of an engineered population of cells and use this data to guide future circuit designs that lessen or exploit the impact of evolutionary change.

The project will consist of two major parts. First, we will develop new nanopore sequencing methods that allow for the accurate reconstruction of evolutionary trajectories by sampling long-term evolutionary experiments. Nanopore sequencing has historically been branded as having a relatively poor read accuracy. However, recent improvements in sequencing chemistry and nanopore design have resulted in the ability to generate long reads >10kb with accuracies >99%. In addition, it is possible to use unique molecular identifiers (UMIs) to increase this accuracy further through consensus reconstruction, where starting DNA molecules are amplified and barcoded simultaneously via PCR. We plan to assess both these methods and develop supporting computational analyses and mathematical models to take this longitudinal data and reconstruct evolutionary trajectories of an entire population at a scale and fidelity rarely seen.

Building on this capability, the second part of the project will employ experimental evolution techniques using a wide range of cells transformed with different synthetic genetic circuits. The circuits will be selected to implement a range of functionalities (e.g., combinatorial logic and oscillations) using a variety of different biochemical processes to achieve similar behaviours. By assessing how these different circuits evolve under a range of environmental conditions, we aim to elucidate principles for creating more robust genetic systems and potentially exploiting predictable patterns in evolution to engineer robustness and adaptation into our systems.

This project will be supported by a supervisory team that brings a wealth of complementary experience covering the design/assembly of synthetic genetic circuits and novel applications of nanopore sequencing (Dr Gorochowski, University of Bristol) to experimental evolution and the mapping of evolutionary paths taken by biological systems (Professor Taylor, University of Bath). Overall, this project provides a foundation for integrating evolution into biological design workflows and will support the creation of more adaptable and robust engineered biology.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.