

Developing a better-than-nature enzyme platform for biocatalysis applications

Supervisory team:

Main supervisor: Dr Christopher Pudney (University of Bath)

Second supervisor: Prof Ross Anderson (University of Bristol)

Prof David Leak (University of Bath)

Host institution: University of Bath

Project description:

Enzymes are outstanding natural catalysts that are fast, highly specific and operate in mild conditions. The industrial use of enzymes in biocatalysis applications is a very significant activity in the UK and comprises a large part of the UK biotech industry. Engineering enzymes is a core activity in the biocatalysis industry and is necessary to improve activity, alter substrate specificity and tune protein stability. Enzymes can be engineered in a number of ways by altering their amino acid composition either by large scale robotic screens of millions of variants, knowledge-based screens that reduce the complexity to hundreds/thousands of variants or selection based assays using error prone PCR approaches. These approaches are typically extremely time and resource intensive and in most cases leads to either only a fractional increase in desired activity, specificity or stability.

Ideally one would like to have a small number of platform enzymes that can be tuned to a range of substrate specificities, activities and stabilities. We aim to generate a biocatalysis platform capable of performing a range of key electron transfer reactions to industrially important substrates and where we are able to tune the stability for specific applications. We propose to develop a novel biocatalysis system based on small, artificial enzymes made up of a four-helix bundle architecture. These systems are highly adaptable with the potential to introduce a range of new activities that are 'better-than-nature'. We will develop systems from the Anderson lab based on a novel approach in protein engineering from the Pudney lab that tunes the dynamics and flexibility of molecules.

The student will use a hybrid computational/experimental approach ensuring broad training in contemporary synthetic biology, protein engineering and biocatalysis as well having the opportunity to interact with a major industrial partner. Time will be spent in the Medicinal and Industrial Biotechnology section at Bath and the Bristol Synthetic Biology centre. The student will be exposed to a truly interdisciplinary environment joining a research team that offers a breadth of experience and training opportunities.