

Template

BioProcess: Biocatalysts for the Enantioselective Construction of Polycyclic Molecules on Synthetically Useful Scales

University of Bristol, School of Chemistry

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Application deadline: 30 April 2026

About the Project

This BioProcess IDLA PhD project will develop tools, knowledge and training in world-class biocatalysis focussed on enzyme-catalysed [4+2]-cycloadditions and deployment of the novel biocatalysts in chemoenzymatic synthesis of bioactive targets. The Diels-Alder reaction of a conjugated diene and dienophile is widely recognised as one of the cornerstone carbon-carbon bond forming reactions for the construction of sp^3 -rich organic compounds enabling the creation of up to 4 new stereocentres in a single step. However, it often requires harsh conditions such as heat, pressure or a Lewis acid and whilst *endo* cycloadducts are usually preferred, complex mixtures may form. Furthermore applications in asymmetric synthesis remain a significant challenge. Diels-Alderase are biocatalysts with potential widespread value for the enantioselective synthesis of libraries of functionalised cyclohexenes under mild conditions.

Building on our recent studies, this project aims to gain insights into the structure, mechanism, scope and synthetic utility of natural and genetically modified enzymes that catalyse both intra- and inter-molecular [4+2]-cycloadditions. A major objective is to transition the *in vitro* biotransformation capability using immobilised enzymes to increase workflow efficiency. We will deploy the Diels-Alderase in chemoenzymatic total synthesis to produce a variety of bioactive scaffolds, and explore enzyme cascades using the immobilisation methods established in this project.

The project supervisors have a long-standing track record of successful collaboration bringing together expertise in computational methods and molecular modelling (Marc van der Kamp), structural and molecular biology (Paul Race) as well as synthesis, spectroscopy and enzyme-catalysed transformations (Chris Willis). This project will give the student opportunity to develop skills at the chemistry-biology interface in all of these areas with training given within a supportive and inclusive environment.

About the programme

Join experts in industry and academia working to sustainably manufacture the complex and diverse molecules needed by modern society.

Industrial manufacturing is at a turning point. Many conventional production routes rely on non-renewable resources, harmful chemicals, and energy-intensive steps. Biocatalysis using engineered enzymes offers a proven solution.

Led by The University of Manchester in collaboration with AstraZeneca, The Universities of Bristol and York alongside other leading industrial partners, BioProcess aims to train the next generation of scientists in the skills needed to realise full the potential of biocatalysis, protein engineering and biomanufacturing for the UK bioeconomy.

Training

BioProcess aims to train the next generation of bio-innovators. Our interdisciplinary programmes prepare PhD students and researchers with the real-world skills to apply biocatalysis, protein engineering and sustainable manufacturing in industry. Alongside the training on the specific project described above,

We offer:

- advanced theoretical and practical skills training provided by a mixture of industry and academic project partners covering structural biology; biophysical and analytical methods; computational modelling; directed evolution; process modelling and development; digital skills
- Access to a network of elite partners and mentors
- A strong track record of impact, including a free online course in industrial biotechnology with over 10,000 learners to date.

Strong foundations in Biocatalysis:

Formerly CoEBio3, our centre has a focus on delivering solutions with real impact in pharmaceutical and chemical manufacturing with our industry partners. Our work has already enabled major industrial advances

Commercialised over 1,000 enzymes

Covering 20+ reaction types, significantly expanding biocatalytic options for manufacturing.

Pioneered metal-free processes

- Reducing reliance on costly and hazardous precious metal catalysts.

Delivered high-performing biocatalysts

- Engineered industry-ready enzymes suitable for large scale pharmaceutical manufacturing.

We've also helped shape national policy. In 2018, our researchers co-authored the UK strategy report Growing the UK Industrial Biotechnology Base, supporting government plans for a £440 billion bio-economy by 2030.

Eligibility

Applicants should have, or expect to achieve, at least a 2.1 honours degree or a master's (or international equivalent) in chemistry and ideally with some experience of organic synthesis.

How to apply

To be considered for this project you'll need complete a formal application through our online application portal.

Applications should be submitted through the BioProcess IDLA Website (<https://www.mib.manchester.ac.uk/research/centres/coebio3/>), where you can find a step-by-step guide to the process.

For informal enquiries about this particular project please contact Prof Chris Willis chris.willis@bristol.ac.uk.

Informal enquiries about the programme and application process can be made by emailing sarah.shepherd@manchester.ac.uk.

Funding Notes

This 4-year PhD project is fully funded and home students, and EU students with settled status, are eligible to apply. The successful candidate will receive an annual tax-free stipend set at the UKRI rate (£20,780 for 2025/26) and tuition fees will be paid. We expect the stipend to increase each year. The start date is September 2026.

References

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2. A. J. Devine, A. E. Parnell, C. R. Back, N. R. Lees, S. T. Johns, A. Z. Zulkepli, R. Barringer, K. Zorn, J. E. M. Stach, M. P. Crump, M. A. Hayes, M. W. van der Kamp, P. R. Race and C. L. Willis, *Angew. Chem. Int. Ed.*, 2023, **62**, e 202213053.
3. S. Z. Mbatha, C. R. Back, A. J. Devine, H. M. Mulliner, S. T. Johns, H. Lewin, Kaiman A. Cheung, K. Zorn, J. E. M. Stach, M. A. Hayes, M. W. van der Kamp, P. R. Race and C. L. Willis *Chem. Sci.* **2024**, *15*, 14009.
4. J. Russell, C. R. Back, C. Perry, K. Cheung, L. Maschio, N. R. Lees, M. A. Hayes, M. van der Kamp, P. R. Race and C. L. Willis, *Chem. Sci.*, **2025**, *16*, 1993.