Project title: The electronic mechanism for enzymatic cellulose degradation
Supervisor name(s): Professor Paul Walton, Professor Gideon Davies, Dr Alison Parkin
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**Project Description:**

Sustainable fuel production is a major technological challenge which is of both environmental and politico-economic importance. An appealing prospect is the conversion of cellulose biomass into ethanol, a hydrocarbon which is compatible with existing transport technology. Using biocatalysis to degrade this otherwise highly recalcitrant carbohydrate material is currently the only energetically feasible way in which waste plant materials such as straw can be harvested and utilized as a feedstock for bioethanol production. Lytic polysaccharide monoxygenase enzymes (LPMOs) are important contributors to this bio-catalysed process because they carry out oxidative bond cleavage reactions of recalcitrant polysaccharides, and this aids in the breakdown of the substrate by generating chain ends that can be readily degraded by further classes of enzymes. As recognised by the recent Global Energy Award at the Institution of Chemical Engineers’ (IChemE), Paul Walton and Gideon Davies have already carried out pioneering work in this area, identifying and characterizing the novel copper containing active sites of LPMOs. The aim of this project is to probe how the copper centre in the enzyme must be structured in order to degrade cellulose. In particular, the mechanism via which concerted proton-coupled-electron-transfer is controlled so that an O₂ molecule can be activated to break apart one of the most stable structures in nature will be investigated using a complementary toolkit of molecular biology, spectroscopy, crystallography and electrochemistry. UV-vis and EPR spectro-electrochemical experiments will be used to determine the reduction potentials of the substrate activation reactions, and to probe the structural rearrangements at the active site which support this reactivity. The particularly powerful approach of protein film Fourier transformed alternating current voltammetry (PF-FTacV), which is being pioneered in the Parkin lab, will examine the kinetics of electron transfer in the presence of a soluble substrate (Figure). The FTacV technique is uniquely suited to this study since classical electrochemical methods would be unable to distinguish between electrode-O₂ reduction and rapid, reversible enzyme electron transfer. Comparison between native and variant enzymes will prove which amino acid centres play a vital role in tuning the redox chemistry under interrogation. This insight into the dynamic changes within the enzyme will be complemented with crystallographic studies designed to use appropriate redox reagents to capture snapshots of different states. Overall, this will study therefore aim to derive a blueprint for the design of a copper site capable of activating cellulose using the sustainable input of oxygen and electrons.

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Training:
All research students follow our innovative Doctoral Training in Chemistry (iDTC): cohort-based training to support the development of scientific, transferable and employability skills. All research students take the core training package which provides both a grounding in the skills required for their research, and transferable skills to enhance employability opportunities following graduation. Core training is progressive and takes place at appropriate points throughout a student's higher degree programme, with the majority of training taking place in Year 1. In conjunction with the Core training, students, in consultation with their supervisor(s), select training related to the area of their research.

Walton and Davies have a well-established track record in world leading expertise in the structural characterisation and mechanistic understanding of LPMOs and the successful applicant will be joining a thriving research team. This collaboration is supported by joint group meetings which the student will attend, and this will provide an invaluable introduction to the enzyme system being studied. Broader training in presentation skills and an awareness of other outstanding bio-inorganic and enzymatic research will be provided by the student attending Inorganic and YSBL group meetings and seminars throughout their PhD. External collaboration with Dr Glyn Hemsworth (University of Leeds), and Prof Alan Bond (Monash University, Melbourne) will also provide training in communication and project management. It is expected that the successful applicant will have a desire to attend international conferences and will actively pursue opportunities to present their work.

In terms of practical skills, the interdisciplinary mixture of molecular biology, spectroscopy, structural biology and electrochemical measurements make this a unique project. It will be well supported by the existing expertise within the groups of the three supervisors. Molecular biology training, protein purification and crystallography expertise will be passed on from the Davies group who work in the world leading York Structural Biology Lab (YSBL), which is co-located with the Biology Department. Expertise in protein spectroscopy, data analysis and DFT calculations will be provided by the Walton group. Electrochemical training and support will be provided by the Parkin group.

Equality and Diversity:
The Department of Chemistry holds an Athena SWAN Gold Award and is committed to supporting equality and diversity for all staff and students. The Department strives to provide a working environment which allows all staff and students to contribute fully, to flourish, and to excel. Chemistry at York was the first academic department in the UK to receive the Athena SWAN Gold award, first attained in 2007 and then renewed in October 2010 and in April 2015. This PhD project is available to study full-time or part-time (50%).

Funding:
Value: Studentships are fully funded either by the EPSRC or a Department of Chemistry Teaching Studentship, and cover: (i) a tax-free annual stipend at the standard Research Council rate (£14,553 for 2017-18), (ii) tuition fees at the UK/EU rate.

Eligibility: EPSRC studentships are available to UK and EU students who meet the UK residency requirements. Students from EU countries who do not meet the residency requirements may still be eligible for a fees-only award. Chemistry Teaching Studentships are available to any student who is eligible to pay tuition fees at the home rate. Further information about eligibility for Research Council UK funding can be found at the following website: [http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/](http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/)

Candidate selection process:
- Applicants should submit an application for a PhD in Chemistry by **17:00 on Wednesday 10 January 2018**
- Supervisors will interview their preferred candidates either by email, telephone, web-chat or in person
- Supervisors may nominate up to two candidates to the assessment panel
- The assessment panel will shortlist candidates for interview from all those nominated
- Shortlisted candidates will be invited to a panel interview at the University of York on **13 or 15 February 2018**
- The Chemistry Graduate Awards Panel will award studentships following the panel interviews
- Candidates will be notified of the outcome of the panel’s decision by email

For more information contact chemgrad@york.ac.uk or see our web page: [http://www.york.ac.uk/chemistry/postgraduate/](http://www.york.ac.uk/chemistry/postgraduate/)