Project title: Understanding biomolecular interactions with 2D-IR spectroscopy

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Project Description:

Ultrafast 2D-IR spectroscopy combines picosecond ($10^{-12}$ s) time resolution with the ability to resolve structural information of complex molecules, giving the potential to observe biological processes in real time in the solution phase. A PhD studentship opportunity is available that will continue a long-term collaboration between the Hunt group and the Rutherford Appleton laboratory’s Central Laser Facility to explore new directions in using 2D-IR to understand the intermolecular interactions of proteins and DNA while developing new experimental methods at a major national research facility.

Significant recent developments that lay the groundwork for this project include proof of concept testing of real time measurements of DNA and protein molecular dynamics using temperature jump spectroscopy methods to observe biomolecular processes in real time, and demonstration of high throughput 2D-IR screening experiments for DNA-ligand interactions. This project will take the next steps in exploiting internationally-leading laser technology for 2D-IR studies of key biological intermolecular interactions (e.g. protein-small molecule, DNA-small molecule). In addition to new ways of understanding biomolecular processes in solution, these new directions will make 2D-IR techniques more accessible to potential end users, including the commercial sector.

**Strand 1:** High throughput 2D-IR spectroscopy of biomolecular complexes: This strand will develop the use of high throughput 2D-IR methods for observing small molecule binding to proteins. This will extend recent work on DNA-binding systems to the spectroscopically more complex and subtle problem of protein-drug binding. In particular, we will target the use of 2D-IR to report on changes in protein dynamics and intramolecular vibrational coupling upon drug binding, linking spectral observables to biological function or physical phenomena such as binding constants. In addition to expanding our 2D-IR capability, this will further studies linking protein molecular dynamics to antibiotic resistance.

**Strand 2:** Real time measurements of biomolecular interactions: This strand will develop modified T-jump IR and T-jump 2D-IR spectroscopy-based strategies that allow observation of dynamic non-equilibrium responses of biomolecules to steps in temperature, but extend them to allow combined heating/cooling experiments. These will be used to observe examples of dynamic biomolecular structure change in solution both during the initial perturbation but also upon relaxation, giving new access to the process of location of the binding site by the ligand and so direct observation of mechanisms such as induced fit or conformational selection.

The project will suit students with background in spectroscopy, physical chemistry or biophysics and with an interest in multidisciplinary research. The multidisciplinary nature of the work means that the project would also suit students with a background in molecular biology or data analysis methodologies but with the motivation to learn advanced laser spectroscopy techniques.

References

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. In addition, training in ultrafast spectroscopy methods, sample handling and preparation and data analysis methods will be given as part of the project.

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:** This studentship is funded 50% by STFC Central Laser Facility and 50% by a Department of Chemistry Teaching Studentship. It covers: (i) a tax-free annual stipend at the standard Research Council rate (£14,777 for 2018-19), (ii) tuition fees at the UK/EU rate.

**Eligibility:** Studentships are available to any student who is eligible to pay tuition fees at the home rate: [https://www.york.ac.uk/study/postgraduate-research/fees/status/](https://www.york.ac.uk/study/postgraduate-research/fees/status/)

Details of 50% Chemistry Teaching Studentship:

**Role and Responsibilities:**
To assist with undergraduate practical Chemistry teaching for 3 years. This is likely to equate to:

**Undergraduate term time:**
- 37 hours of demonstrating per year in the undergraduate teaching laboratories. Most of your teaching duties will take place in Autumn and Spring term
- 2.5 hours per year of departmental tours for UCAS visit days in the Autumn Term

**Undergraduate vacations:**
Other teaching related duties to enable you to develop your skills, e.g. development of laboratory/Virtual Learning Environment material, assisting with workshops, as well as personal training and development sessions. You will complete a timesheet each term and during the summer vacation and submit them to the Chemistry Graduate Office to record your teaching activities

**Training:**
In common with all graduate students, you will receive training provided by the Chemistry Department and the University’s Research Excellence Training Team (RETT). The Chemistry Department has a Graduate Teaching Assistant (GTA) Training Programme for assisting in laboratory practicals. You will receive additional training specific to developing teaching material online and assessing practical work.

You will have the opportunity to take courses offered by the RETT via the Postgraduates Who Teach programme; e.g. Introduction to Learning and Teaching, Teaching Small Groups, Demonstrating in Science. Further development is possible through engagement with the HEA accredited ‘Preparing Future Academics’ programme.

This training will be complemented by research training integral to your PhD programme. Collectively, experience of research and teaching methods should place you in a strong position for future employment in teaching, academia or other related fields.
Supervision and Mentoring:
Your research will be supervised by your academic supervisor, and you will also be mentored by a second or third year PhD Teaching Student, with overview and input from the Teaching Laboratory Coordinator.

At your Thesis Advisory Panel meetings you will produce a brief one page overview of your teaching activity, and reflect on your skills development in the teaching area. Your Independent Panel Member will take a role in guiding teaching skills development, in consultation with your mentor and the Chair of the Board of Studies.

Candidate selection process:

- You should submit an application for a PhD in Chemistry and a Teaching Studentship Application by **20 August 2018**
- The supervisor may contact their preferred candidates either by email, telephone, web-chat or in person
- The supervisor may nominate up to two candidates to the assessment panel
- Shortlisted candidates will be invited to a panel interview at the University of York on a date to be confirmed
- The 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/