

# THE UNIVERSITY OF MANCHESTER

# PARTICULARS OF APPOINTMENT

# **FACULTY OF SCIENCE & ENGINEERING**

### SCHOOL OF CHEMISTRY

#### MANCHESTER INSTITUTE OF BIOTECHNOLOGY

### RESEARCH ASSOCIATE IN TIME-RESOLVED STRUCTURAL BIOLOGY

### VACANCY REF: S&E-14250

Salary:	Grade 6 £32,236 to £39,609 per annum according to experience
Hours:	Full time
Duration:	Fixed Term from 1 October 2019 for 60 months
Location:	As part of the collaborative grant the Research Associate will spend 2 years of this 5 year contract working in France. The remaining 3 years will be spent in Manchester.
Reports To:	Professor Nigel Scrutton, Professor David Leys and Dr Derren Heyes

Enquiries about the vacancy, shortlisting and interviews: Name: Professor Nigel Scrutton Email: <u>nigel.scrutton@manchester.ac.uk</u> Or: Name: Professor David Leys Email: <u>david.leys@manchester.ac.uk</u>

#### **Project Title:**

Time-resolved structural biology of photoreceptor proteins

### **Project Description:**

This project is based on recent research at Manchester on understanding the molecular mechanism of photoreceptor proteins, essential components of future industrial biotechnology applications. We have reported the complete reaction cycles of a number of bilin-containing photoreceptors using time-resolved spectroscopies. We showed that the photochemistry is coupled to long timescale structural change to enable downstream biological signalling. In addition, having previously investigated the photochemistry of coenzyme  $B_{12}$  alone and bound to  $B_{12}$  containing enzymes, we recently reported the photochemistry and mechanism of CarH (a member of a new superfamily of  $B_{12}$  photoreceptors). This provided a mechanistic basis for the emerging field of  $B_{12}$  photobiology and a new class of optogenetic tools for the control of gene expression. We are now well placed to map pathways of structural change in these and



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related, but more complex, multicentre photoreceptor proteins. Multicentre photoreceptors have recently been identified in the new family of  $B_{12}$  photoreceptor proteins but the basis of the photobiological response, is currently unknown and in particular how the photochemical events couple to protein structural change. This will require structural determination of the protein at each stage of their photocycles, together with the timescales of these structural changes.

In this project we aim to develop a detailed dynamic structural understanding of a small number of target photoreceptors. We have teamed up with world-leading experts in the field of time-resolved structural biology at the IBS, who have pioneered the use of X-ray and neutron-based techniques to follow atomic motions in proteins on the ps-ms timescale. We will initially obtain high resolution (crystallographic) structural information of these proteins at Manchester and will take these forward for time-resolved structural studies together with the project partners in Grenoble, also making full use of the recently established XFEL hub at Diamond led by Dr Allen Orville. Active crystals will provide the opportunity for unprecedented, high impact time-resolved structural studies using laser pulses to trigger the photoresponse and coupled pulses from synchrotron and XFEL sources to probe conformational changes along the reaction pathway. We will also use time-resolved X-ray scattering (TRXS) measurements on the proteins in solution to follow large-scale structural changes (*e.g.* domain reorganisation) on µs-s timescales. The work builds on our established collaboration with the project partners in Grenoble in our studies of structural and dynamical changes in a light-activated enzymes and phytochrome photoreceptors.

#### **Overall Purpose of the Job:**

The appointee will drive the structural and time resolved structural biology analysis of selected photoreceptor proteins. This will involve overproduction, purification and (micro)crystallisation of the target proteins, data collection and structure determination, rational design and production of variant proteins and time-resolved studies of structural change. A full time technician will support the more basic biochemical aspects of the project. Consequently we are seeking candidates with proven expertise in structural biology.

#### Key Responsibilities, Accountabilities or Duties:

#### Main responsibilities

- To take initiatives in the planning of research (design and perform experiments).
- To identify and develop suitable techniques, and apparatus, for the collection and analysis of data.
- To ensure the validity and reliability of data at all times.
- To maintain accurate and complete records of all findings.
- To actively read the scientific literature relating to (and around) the project.
- To write reports for submission to research sponsors and industrial collaborators.
- To prepare material for presentation in oral and poster formats, and present findings to colleagues, collaborators, and at conferences.
- To attend relevant meetings, including regular meetings with industrial collaborators.
- To draft publications and prepare them for submission to refereed journals.
- To contribute to writing bids for research grants.
- To undertake instruction of PhD students, supervise practical work and advise students on techniques as agreed.



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- To attend relevant workshops and conferences as necessary.
- To work alongside the PI and other colleagues in a collegiate manner and build rapport within the team and the wider Faculty.
- To undertake any necessary training and/or development.
- To maintain safe workplace practice and procedures in accordance with the requirements of Health and Safety legislation.
- Any other duties commensurate with the grade of the post as directed by PI / supervisor.

# PERSON SPECIFICATION

# **Essential Knowledge, Skills and Experience:**

- Hold (or expect to hold shortly) a PhD in one of the following areas: Structural biology, especially X-ray crystallography
- Experience/skills in conventional protein purification, basic spectroscopy and associated biochemical methods (electrophoresis; recombinant DNA work etc)
- Proven ability to use initiative to efficiently plan, optimise and progress project and communicate findings.
- Extensive IT skills.
- Excellent interpersonal and communication skills and ability to work with colleagues at all levels.
- Good written and spoken English.

#### Desirable

• Theoretical and practical knowledge of time resolved approaches (post 1); mutagenesis and /or spectroscopy) post 2

#### **Background Information:**

#### The University of Manchester

The University of Manchester was the world's first 'industrial city' and has since been a prodigious source of pioneers and innovators. Many major advances in the 20th century began in the University's laboratories, such as the work by Rutherford leading to the splitting of the atom and the development of the world's first stored programme computer by Williams and Kilburn. Today, research remains at the heart of The University of Manchester.

On October 1st 2004, The University of Manchester, created as a result of the merger of the Victoria University of Manchester and UMIST, became the largest in the UK, with an income of £600 million, more than 35,000 students and 11,000 staff. We have used the golden opportunity of its creation, and a £600 million capital programme to plan a revolutionary agenda. We have modernised management and administration, made long-term academic plans for all subjects, established key priorities for interdisciplinary research in areas of science and technology at the

cutting edge of progress in industry and commerce, and set a target to more than double the volume of research activity performed in collaboration with external partners. By 2020, The University of Manchester aims to hold a world-class leading research profile and be among the top 25 universities worldwide. The University is pursuing this agenda in the context of the city of Manchester's dramatic regeneration over the past 20 years. The aim is to make the



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world's first industrial city a great post-industrial city. A vibrant culture of creative industries, entrepreneurs, and technology-based start-ups is served by iconic buildings and a remodelled city centre – and now by a powerful, consolidated research university. Now and in the coming years we look forward to welcoming the very best staff, students and industrial partners from around the world.

Further information about the University and its faculties may be found on the University's website (www.manchester.ac.uk).

# **Manchester Institute of Biotechnology**

Biotechnology is a field of biology that involves the manipulation of living organisms and bioprocesses in engineering, technology, medicine and other fields for human benefit. Interdisciplinary in nature it draws on the pure biological sciences and in many instances is dependent upon knowledge and methods outside of biology at the engineering and physical sciences interface.

The strong interdisciplinary focus and mode of operation in the MIB enables our scientists and engineers to drive state-of-the-art biotechnology research through establishing new types of collaboration. The MIB's approach is pluralistic, integrative and non-exclusive functioning flexibly as a partner to researchers across a broad spectrum of disciplines which are fluid and constantly evolving. Using advanced quantitative methods to explore the relationship between the macro behaviour of biological systems and the properties of their nanoscale components we see this understanding as a basis for developing new biotechnologies that will find applications in areas such as human health, the energy economy, food security, industrial transformations and the environment. A defining feature of our mission is the incorporation of rigorous, cutting-edge principles and technologies derived from the physical sciences, engineering, mathematics and computation into novel approaches to elucidating the molecular mechanisms that underpin living processes and systems. An extensive programme of technology development lies at the heart of our research programmes, driven by expertise from the quantitative sciences and engineering, allowing us to accelerate progress through the implementation of state-of-the-art enabling technologies.

Further information can be found at http://www.mib.manchester.ac.uk/

#### Lab environment

The mission of the host lab is to understand the catalytic power of enzymes and synthetic biology/metabolic engineering, and to exploit the use of enzymes in sustainable chemicals biosynthesis and industrial biotechnology programmes.

Further information can be found at https://www.sites.google.com/site/scruttonlab/home