UNIVERSITY OF BIRMINGHAM

NERC CASE PhD studentship with Thermo Fisher Scientific

Using mass spectrometry and computational biology to discover links between chemical pollutants and environmental health

Project Description: In 2005, Professor Chris Wild at the University of California, Berkeley, introduced the concept of the EXPOSOME – representing the sum of all environmental exposures – as a quantity of critical interest to human and environmental health. This launched a series of major international research programs. With >70,000 synthetic chemicals used by industry, from pharmaceuticals to agrichemicals to consumer products, the challenge to measure the exposome is colossal. Since many of these chemicals enter our environment it is essential to understand the potential impacts of complex chemical mixtures, typically at low levels, on environmental and human health. Specifically, to what extent do these mixtures perturb organism health, and which chemicals are predominantly responsible? Knowing this is essential to strengthen regulation under the European Union's landmark legislation – the Water Framework Directive – the law that governs the monitoring of freshwater across the UK and Europe.

METABOLOMICS is a transformative technology that measures 1000's of metabolites in organisms, yielding information-rich molecular signatures that describe the responses to pollution. Building on the University of Birmingham's decade-long track record in metabolomics, we will adapt mass spectrometry metabolomics approaches to measure both the exposome ('exposure') and metabolome ('effect'). We will then undertake the first ecological Exposome Wide Association Study (EWAS) to discover associations between environmental pollution and health of a sentinel freshwater species, Daphnia magna. This species has multiple benefits: it is a sentinel organism in freshwater ecology and ecotoxicology; lifetime exposures are feasible due to the rapid life cycle; chemically unexposed lab populations exist as negative controls; and all components of the Daphnia's environment can be controlled, including nutrition and pollutant exposure. Overall, this studentship will provide the community with novel methods to characterise the exposome, and build weight of evidence to support the application of EWAS approaches to discover links between pollution and health.

Partners and collaboration: Our CASE PARTNER, Thermo Fisher Scientific (TFS), is a world leader in the development of liquid chromatography and mass spectrometry (LC-MS) and has identified metabolomics as a priority area. In 2013, TFS formed a Technology Alliance Partnership with the University of Birmingham, the first such partnership within Europe. This proposal builds upon four existing iCASE awards with TFS as part of their commitment to graduate training.

Training and skills: Collectively this team will provide SPECIALIST TRAINING: in LC-MS, including unparalleled access to current and pre-released metabolomics technologies; in metabolomics, toxicology and analytical sciences (Viant lab; the largest group in environmental metabolomics nationally).

TRANSFERABLE SKILLS will be taught at both Birmingham, through the extensive courses in the Biosciences Graduate Research School, and at TFS, including business awareness, project management and financial training. This training will be truly MULTIDISCIPLINARY to enrich the student experience. Furthermore the main supervisor is highly experienced, having completed 9 PhDs in the past five years and with 4 current students, several of which are/were NERC CASE.

The student will be integrated within three pre-existing communities of PhD students and researchers, providing an exceptional TRAINING ENVIRONMENT: the growing Environmental Systems Biology network at Birmingham, comprising 7 research groups; the Computational Toxicology community, a network of several research groups from Birmingham and internationally; and the community of ca. 30 scientists who constitute the Partnership with TFS.

Importance of this science: The IMPACTS of this research will be great: economically to TFS through developing and marketing their technologies to study the exposome; socio-economically by developing EWAS approaches that enable a more rigorous assessment of the effects of chemicals on health, of relevance to risk regulation; and by training a scientist who is competent in molecular and computational 'Big Data' science.

Funding Notes

Are you the right person for this PhD? We seek an excellent candidate with a high quality undergraduate or Masters degree in fields such as analytical chemistry, environmental chemistry or forensics, who has a passion to develop bioanalytical approaches and importantly to apply them to a highly relevant 21st century challenge in the environmental sciences.

This studentship is for 3.5 years - to start as soon as possible (ideally by early 2017) - and is funded by NERC and Thermo Fisher Scientific. The studentship covers tuition fees and a stipend of £15,296/year for UK and EU nationals (where the EU nationals have lived in the UK for 3+ years).

Please apply at: View Website

(https://www.findaphd.com/common/clickCount.aspx?theid=4508&type=184&DID=124&url=http%3a%2f%2fwww.birmingham.ac.uk%2fpostgraduate%2fcourses%2fresearch%2fbio%2fbiosciences.aspx)

Application deadline - 30 November 30, 2016

When applying, include the name of the supervisor (VIANT), state the funding source (NERC iCASE) and the project title above.

Additionally, please contact Professor Mark Viant directly - attaching your CV to the email (m.viant@bham.ac.uk)

Recent representative papers from Viant's research team:

D. Southam, R. J. M. Weber, J. Engel, M. R. Jones, M. R. Viant, A complete workflow for high-resolution spectral-stitching nanoelectrospray direct infusion mass spectrometry-based metabolomics and lipidomics. Nature Protocols (accepted, 2016).

M. Clark, U. Sommer, J. Kaur, M. Thorne, S. Morley, M. King, M. R. Viant, L. Peck, Biodiversity in marine invertebrate responses to acute warming revealed by a comparative multi-omics approach. Global Change Biology (accepted, 2016).

J. Zhang, M. A. Abdallah. T. D. Williams. S. Harrad. J. K. Chipman. M. R. Viant, Gene expression and metabolic responses of HepG2/C3A cells exposed to flame retardants and dust extracts at concentrations relevant to indoor environmental exposures. Chemosphere 144, 1996-2003 (2016).

N. S. Taylor, R. Merrifield, T. D. Williams, J. K. Chipman, J. R. Lead, M. R. Viant, Molecular toxicity of cerium oxide nanoparticles to the freshwater alga Chlamydomonas reinhardtii is associated with supra-environmental exposure concentrations. Nanotoxicology 10, 32-41 (2016).

A. Southam, A. Lange, R. Al-Salhi, E. Hill, C. Tyler, M. R. Viant, Distinguishing between the metabolome and xenobiotic exposome in environmental field samples analysed by direct-infusion mass spectrometry based metabolomics and lipidomics. Metabolomics 10, 1050-1058 (2014).

J. A. Kirwan, R. J. M. Weber, D. I. Broadhurst, M. R. Viant, Direct infusion mass spectrometry metabolomics dataset: a benchmark for data processing and quality control. Nature Publishing Group's Scientific Data 1, Article 140012 (2014).

K. L. Poulson-Ellestad, C. M. Jones, J. Roy, M. R. Viant, F. M. Fernández, J. Kubanek, B. L. Nunn, Metabolomics and proteomics reveal impacts of chemically mediated competition on marine plankton. Proceedings National Academy Sciences 111, 9009-9014 (2014).

W. B. Dunn, A. Erban, R. J. M. Weber, D. J. Creek, M. Brown, R. Breitling, T. Hankemeier, R. Goodacre, S. Neumann, J. Kopka, M. R. Viant, Mass appeal: metabolite identification in mass spectrometry-focused untargeted metabolomics. Metabolomics 9, S44-66 (2013).

M. R. Viant, and U. Sommer, Mass spectrometry based environmental metabolomics: A primer and review. Metabolomics 9, S144-158 (2013).

Metabolomics Research at the University of Birmingham

Metabolomics research at the University of Birmingham began in earnest in 2003 and now encompasses several Schools including Biosciences, Environmental Sciences, Medicine, Mathematics and Computer Science. Our metabolomics research spans the development of analytical and informatic methods as well as their application to wide ranging and numerous projects in the Life Sciences. These include studies in mammals, fish, invertebrates, microbes and plants, with a particular emphasis in both **environmental metabolomics** and **clinical metabolomics**. The bioanalytical facilities and expertise in both mass spectrometry and NMR spectroscopy at Birmingham are world class and include several national facilities:

- MRC-funded Phenome Centre Birmingham
- NERC Biomolecular Analysis Facility – Birmingham
- Birmingham Metabolomics Training Centre
- Biomolecular NMR Facility

Collectively these facilities house 20 mass spectrometers and NMR spectrometers for metabolism research, most of which are <3 years old. The bioinformatic facilities and expertise at Birmingham include the new Centre for Computational Biology with and several high performance computing clusters. Our current, highly active research program in metabolomics involves ca. 50 principal investigators, postdoctoral researchers and PhD students.

Further details on the **University of Birmingham's metabolomics research** can be found at here.

The School of Biosciences

The School of Biosciences at the University of Birmingham is the largest biology school in the region, delivering internationally excellent teaching and research across the broad span of modern biology. There is currently an academic staff of approximately 60, conducting research and delivering teaching from the level of individual biological molecules to the study of whole ecosystems. We have a lively research community, with over 70 postdoctoral research fellows and research assistants, and 120 doctoral research students.

Our ground-breaking research ranges from research into cancer and infectious diseases, such as tuberculosis, to studying the movement and behaviour of orangutans. We also offer major high-technology facilities for research in genomics, metabolomics, proteomics, structural biology and optical imaging (see below). The national NERC Biomolecular

Analysis Facility (NBAF) – Birmingham, Phenome Centre Birmingham and the Birmingham Metabolomics Training Centre are all based in the School of Biosciences.

Research in the School centres around four interlinked themes: **BioSystems and Environmental Change;** Microbiology and Infection; Molecular Cell Biology and Signalling; Plant Genetics and Cell Biology.

Current research grant income is around £8 million per year, and comes from a variety of sources including research councils, the European Union and charities. The School has an excellent research profile with 90% assessed as international quality supporting an exciting range of teaching programmes.

The PhD primary supervisor

Prof. Mark R. Viant holds a Chair in Metabolomics, is Director of the NERC Biomolecular Analysis Facility for Metabolomics, Director of the MRC-funded Regional Phenome Centre, and a Past President of the International Metabolomics Society. As a postdoctoral fellow at the University of California, Davis, he pioneered the application of metabolomics to environmental health issues in aquatic organisms. In 2003 he relocated to Birmingham as a NERC Advanced Fellow with the remit to further develop metabolomics in environmental toxicology. With funding from the NERC, BBSRC, MRC, Wellcome Trust, EU, Environment Agency and several companies, he and his group have developed new metabolomics methods in both mass spectrometry and 2-D NMR. His team has primarily applied these techniques to probe toxicant-induced metabolic changes in a range of organisms. He has demonstrated the need for “phenotypic anchoring” in metabolomics and most notably discovered biomarkers of toxic stress that are predictive of whole organism physiological perturbation. He is particularly fascinated by chemical and nanomaterial toxicology in ‘non-animal’ invertebrate model organisms, for example *Daphnia*, and the translation of metabolomics based ‘discovery’ research into mechanistically based tools for chemical safety and environmental diagnostics. Mark has co-authored over 150 publications and his team’s work has recently been recognised by the award of a 2015 Lifetime Honorary Fellowship of the International Metabolomics Society “*In recognition of his pioneering work in environmental metabolomics and for his sustained service to the Society. His vision revolutionized the Society’s operations and reputation, expanding its reach to all corners of the world.*”

Toxicology at the University of Birmingham

The University has a long-standing research and academic focus on Toxicology. Some of the early groundbreaking work in drug metabolism initiated this profile, which evolved into studies of the molecular mechanisms of toxicity relevant to both humans and other organisms. A major current focus is around the development of Adverse Outcome Pathways derived from “Omic” analyses. This area is supported by over £2 million of recent University investment into associated environmental genomics. There are extensive collaborations with other Schools of the University in areas such as nanotoxicology and environmental health. The School has hosted a highly successful Masters programme in Toxicology since 1979, which continues to attract high quality students and that enjoys strong industrial interactions.

Toxicology research in the School currently attracts over £5 million from sources including the EU, NERC, Defra, Industry, NSF and US NIH. Members of the School's Toxicology community have leadership roles within the British Toxicology Society, the International Union of Toxicology, EUROTOX, the international Metabolomics Society and Gordon Conferences. There is School representation on MRC and NERC panels and advisory committees such as the Advisory and Implementation Group NERC Mathematics and Informatics for Environmental 'Omic Data Synthesis Programme. There are strong links with Industry via consultancies and with bodies involved in regulation and policy such as the European Commission's Joint Research Centre (JRC) in Ispra, OECD, the UK Environment Agency, Defra, Department of Health and the Food Standards Agency having made contributions to the UK Committee on Toxicity and the former Committee on Safety of Medicines.

The vision of the University of Birmingham's research group is "to transform environment and health protection by the application of automated higher-throughput biology and omics technologies. This creates a comprehensive database of the effects of all chemicals, advanced materials and their mixtures on biological systems, thereby dramatically reducing uncertainty for industry, policy makers and regulators because of shared knowledge built upon strong scientific principles."

The University

The University of Birmingham was recognised for its commitment to academic excellence and innovation by being named The Times and The Sunday Times University of the Year 2013–14. Our heritage as the UK's first civic university – the original 'redbrick' – is combined with one of the most compelling and ambitious agendas in higher education.

Ranked by QS as 62nd in the world university rankings, Birmingham is a leading member of the Russell Group (the Vice-Chancellor is the current Chair) and a founder member of the Universitas 21 global network of research universities (www.universitas21.com/). The University is a pioneer in sector leading initiatives. These include our 'Birmingham Fellows' programme, which has so far seen 75 of the world's best early-career academics join us; the much emulated unconditional offers strategy to exceptional candidates introduced in 2012–13; and the University School which will open in 2015, and are testament to an institution that rewards and encourages excellence in research and education and which has, unsurprisingly, seen impressive league table rises recently.

As well as our focus on research excellence, we are committed to delivering a first-class experience for our students in every aspect of their university life. This is also why the University has been ranked 11th place in the Times Higher Education Student Experience Survey 2013 and 17th out of 124 UK universities in The Complete University Guide for 2014. These latest league table results further strengthen Birmingham's position as a top 20 university and reflect its recent performance in other highly regarded league tables, such as The Sunday Times University Guide 2014, which ranked the University in 16th place overall.

Areas particularly highlighted in the latest league tables include the excellent student experience and the quality of the courses available. With one of the widest range of offerings in the UK, 17 of our 48 subjects were ranked in the top ten in The Complete University Guide (with two in first place). In addition, the University was ranked tenth place overall and first place for self-made millionaires in the 2013 Wealth-X Survey, which measures the financial success of alumni.

Not only does Birmingham have serious ambition but we also have financial resources to realise those ambitions, and our plans for the future are underpinned by long-established financial probity. We are large: we contribute £1 billion to our region's economy and our turnover was £493 million in 2012–13. Our surpluses and substantial philanthropic support are re-invested into the intellectual and physical fabric of the institution, enabling us to plan with confidence for the future and to continue to invest in the facilities and services that are required for high-quality research, and an outstanding student learning experience.

Led by Vice-Chancellor Professor David Eastwood, the University is structured for swift decision making, enabling us to capitalise on our academic range, financial strength and opportunities that emerge in the fast changing global higher education environment.