PROJECT TITLE: Machine Learning, Synthesis and Transport Mechanisms: A Holistic Approach to Aquatic Toxicity Prediction

DTP Research Theme: Changing Planet

Lead Institution: University of Bath

Lead Supervisor: Dr Matthew Grayson, University of Bath, Department of Chemistry

Co-Supervisor: Prof Varinder Aggarwal, University of Bristol, School of Chemistry

Co-Supervisor: Dr Lee Bryant, University of Bath, Department of Architecture & Civil Engineering

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Project keywords: Ecotoxicology & Pollution (Earth Sciences), Environmental Chemistry (Earth Sciences), AI & Machine Learning (Maths & Computing), Synthetic Chemistry (Chemical Sciences), Organic Chemistry (Chemical Sciences), Computational Chemistry (Chemical Sciences), Chemical Toxicology (Chemical Sciences)

Project Background

Animal testing has traditionally been used to assess the safety of chemicals. However, more sustainable approaches to safety testing are required due to the ethical concerns, costs and time scales associated with *in vivo* methods. Global industrialization has resulted in organic pollutants entering aquatic environments. To reduce the number of animals used in toxicity testing, new approaches are required that can assess the potential of organic compounds to cause harm to aquatic life. For such compounds, chemical reactivity contributes significantly towards their toxicological profile through covalent modification of biological nucleophiles. Our previous work led to the development of a fast, computational method for assessing the mutagenic risk of pharmaceutically important organic electrophiles (*J. Chem. Inf. Model.* **2019**, *59*, 5099). DFT-derived LUMO energies and activation barriers for reaction between a model nucleobase and electrophiles showed significant predictivity for the assessment of mutagenic potential. However, DFT calculations are time-consuming and expert-technical knowledge is required to perform them.

Project Aims and Methods

In this project, machine learning (ML) models will be developed that can, once trained, rapidly and easily predict reactivity descriptors for use in the prediction of aquatic toxicity. This work will lead to a new ML protocol for computationally assessing the toxicity of pollutants. Collaboration with Prof. Aggarwal, as a co-supervisor for the project, will focus on validating the new *in silico* prediction models. Predictions about the reactivity of novel electrophiles will be made using these models which will then be tested in the Aggarwal lab at Bristol. Close agreement between the computationally predicted and experimentally determined reactivity for this external test set will provide confidence in using these predictive models in chemical risk assessment. Collaboration with Dr Bryant, as a co-supervisor for the project, will focus on the mass-transport mechanisms by which organic compounds enter aquatic environments on catchment and system scales, using a local drinking-water-supply reservoir as a project study site. Dr Bryant will also support the investigation of the transport and distribution of organic compounds within the water and sediment components of an aquatic system.

The ML and synthesis work will provide insight into mechanism-based toxicity. The work with Dr Bryant will examine exposure mechanisms. Overall, this will provide a more holistic approach to chemical risk assessment, beginning at source and ending at biological endpoint.

Candidate requirements

Experience with coding (any language) is desirable but not essential.

Useful links

Enquiries relating to the project should be directed to the lead supervisor (see email address above for Project Enquiries). Enquiries relating to the application process should be directed to doctoraladmissions@bath.ac.uk.

In order to apply, you should select the relevant University of Bath PhD online application form found here: https://www.bath.ac.uk/study/pg/applications.pl. When completing the form, please state in the 'Finance' section that you wish to be considered for GW4+ DTP funding and quote the project title and lead supervisor's name in the 'Your research interests' section.

Further information about the application process may be found here: http://www.bath.ac.uk/topics/postgraduate-research/

The application deadline is Friday 8 January 2021 at 2359 GMT. Interviews will take place from 8th to 19th February 2021. For more information about the NERC GW4+ Doctoral Training Partnership please visit https://www.nercgw4plus.ac.uk.