References - Postdoctoral Fellow Update

In this guide

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This is a paper for discussion. It does not represent the views of the Committee and should not be cited.

References

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PhD Student Update

TOX-AI : Geometric deep learning applied to toxicology, for developing next-generation tools and databases for aiding chemical risk assessment of molecules found in food and drink.

Why and how are you associated with the FSA?

12. The Food Standards Agency (FSA) is jointly funding this PhD project, alongside the Biotechnology and Biological Sciences Research Council (BBSRC), as an iCASE (industrial CASE) project under the LIDo (London Interdisciplinary Doctoral programme) consortium, with the PhD project itself based at King’s College

London, while the FSA is named as an industrial partner. Dr Olivia Osborne, Dr David Gott (now retired) and Ms Claire Potter, of the FSA, are all formally named as part of the supervisory team, in addition to other supervisors. This project shall contribute to the FSA's interests, in developing innovative Artificial Intelligence (AI) based New Approach Methodologies (NAMs) for next-generation chemical risk assessment of molecules found in food and drink, to assist in improving consumer safety while simultaneously reducing reliance on animal testing. It is intended that, in addition to numerous publications of interest, a corresponding database of high-quality predictions for certain food and drink molecules shall be released for the FSA's use, alongside an open-source software tool.

Broad Overview of PhD

13. The primary aim of this PhD project is to develop novel Quantitative Structure-Activity Relationship (QSAR) models, using innovative AI, which may reliably predict toxicological properties of molecules found in food drink, over a diverse range of endpoints of interest. The project started by developing QSAR models of mutagenicity, using relatively simple deep learning approaches, before exploring use of more advanced deep learning approaches for navigating more challenging toxicological endpoints, such as neurotoxicity, developmental toxicity, reproductive toxicity, hepatotoxicity, nephrotoxicity, cardiotoxicity and more. A particular research focus has emerged, on using geometric deep learning algorithms via Graph Neural Networks (GNNs), to construct QSAR models that can directly handle molecular graphs and similar data as inputs. Additionally, specific chemical classes of concern have been investigated via the developed models, as part of targeted case studies; these have so far included Brominated Flame Retardants (BFRs), Selective Androgen Receptor Modulators (SARMs) and Tropane Alkaloids (TAs), while more may be included in the near-future. It is ultimately intended that the final models produced by this project will be as accurate as possible in their predictions, while also providing unique insights into toxicological space, compared to existing models in literature. It is furthermore aimed that the final developed QSAR models will be explainable and easily interpretable, via use of Explainable AI (XAI), along with reliable quantifications of uncertainty on particular predictions. The final QSAR models shall also be made available via open-source, accompanied by open-access datasets of associated predictions for certain molecules. The methods, results and other materials are being developed in close collaboration with the FSA, with a placement within the FSA actively taking place, while all materials are to be published in open-access publications and/or presented at relevant conferences.

Main Work Up to this Point:

14. The main work up to the present is composed of 4 parts: (1) Development of QSAR models of mutagenicity, using feed-forward neural networks and an exploration of dimensionality reduction techniques, before moving on to Graph Convolutional Networks (GCNs) and mining of Structural Alerts (SAs), (2) Case study on BFRs, using Graph Attention Networks (GATs) to predict in-vivo doses and concentrations relevant to neurotoxicity, developmental toxicity and reproductive toxicity, via both graph-regression over molecular graphs and node-regression over knowledge graphs containing numerous molecules; (3) Case study on SARMs, using transfer learning on GCNs to predict Drug-Induced Liver Injury (DILI), Drug-Induced Renal Injury (DIRI) and Drug-Induced Cardiotoxicity (DICT); (4) Exploration of different GNN architectures – GCNs, GATs and Graph Isomorphism Networks (GINs), in order to characterise the most advantageous GNN architectures for navigating varying toxicological assay data environments.

Papers and/or Conferences in Progress:

- Society of Toxicology (SOT) 2025.

- 3 papers in progress, relating to work on BFRs, work on SARMs and work on exploring novel GNN architectures.

References

Kalian, A.D., Benfenati, E., Gott, D., Potter, C., Dorne, J.L., Osborne, O.J., Guo, M. and Hogstand, C., 2024. P05-37 Graph attention networks using knowledge graphs, for predicting novel points of departure for brominated flame retardants. Toxicology Letters, 399, pp.S146-S147.

Kalian, A., Osborne, O.J., Dorne, J.L.C., Gott, D., Potter, C., Guo, M. and Hogstrand, C., 2023. Improving accuracy scores of neural network driven QSAR models of mutagenicity. Computer Aided Chemical Engineering, pp.2717-2722.

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