New Frontiers for Metalloenzymes: Exploring the synergy between machine learning and biomolecular simulations

Application Reference: MEY21-01

A PhD studentship is available in the group of Dr Antonia Mey (School of Chemistry, The University of Edinburgh; http://mey-research.org)

The studentship is fully funded for 42 months and covers tuition fees and an annual stipend (starting at £15,285 per annum) for a candidate satisfying EPSRC criteria: https://www.epsrc.ac.uk/skills/students/help/eligibility/

Project Summary

The Mey Group (http://mey-research.org) is recruiting an enthusiastic candidate to work on the interface of biomolecular modelling and machine learning; applied to challenges in antimicrobial resistance for a 3.5 year fully funded PhD studentship.

Accurately predicting binding affinities between a protein and a potential inhibitor is crucial in a computer-aided-drug-design process, but still lacks reliability and accuracy for metalloenzymes. Machine learning is changing the way in which computational models are used for modelling and can be used to understand biomolecular processes and design new drugs in a predictive fashion. Successes in protein structure predictions [1], protein ligand binding predictions [2], and design of novel compounds [3] have all been shaped by machine learning. This project will develop new methodologies for modelling metalloproteins using hybrid machine learning and molecular dynamics approaches to efficiently describe active site metal centres and their interactions. The starting point of the project will be based on some preliminary work on combining alchemical free energy methods [4] and quantum machine learning potentials [5] for improving binding affinity predictions between drug-like molecules and target proteins [6]. These improved models will allow to supplant current costly quantum mechanics and molecular dynamics-based hybrid models both in speed and accuracy to model interactions between proteins and ligands as well as other interesting biological processes. The newly developed methods will be used to more accurately predict the efficacy of new inhibitors for metalloproteins. The particular focus of the application of these methodologies will be on metalloproteins implicated in antimicrobial resistance, such as metallo betalactamases.

Interested? Do you have a background in a science discipline and are curious about using mathematical and computational tools to address biomolecular problems? Have you achieved or are you to be expected to get a first-class or high 2.1 honours degree? **Then please direct any informal enquiries or full applications (CV, Cover Letter, and Transcripts) to:**
Dr Antonia Mey (antonia.mey@ed.ac.uk) School of Chemistry, University of Edinburgh, David Brewster Road, Edinburgh EH9 3FJ, UK.

The position will remain open until filled.

References

[1] https://www.nature.com/articles/d41586-020-03348-4, accessed 4/12/2020
[2] Kundu et al. *RSC Adv.,* **8**, 12127-12137 (2018) DOI
[3] Tkatchenko *Nat. Comms.* **11** 4125 (2020) DOI
[4] Mey et al. Living Journal of Computational Molecular Science 2 (1), 18378 DOI
[5] Smith et al. *Chem. Sci.*, **8**, 3192-3203 (2017) DOI
[6] Rufa et al. bioRxiv DOI

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