THE UNIVERSITY of EDINBURGH

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''A hybrid molecular simulation/machine learning framework for the rational discovery of allosteric modulators of protein function''

42-month fully funded PhD studentship, September 2020

<u>Supervisor:</u> Dr Julien Michel, School of Chemistry, University of Edinburgh.

Applications are invited for a PhD studentship in the Michel lab (http://www.julienmichel.net) in the area of biomolecular simulations and computer-aided drug design. The EaStCHEM school of Chemistry at the University of Edinburgh is among the top ranked departments within the EU.

This project will focus on developing a computational methodology that combines molecular simulation, information theory and machine learning methods for predicting how the binding of drug-like small molecules to different locations on the surface of a protein will modulate the biological function of the protein. Such so-called allosteric modulators are of particular interest to tackle challenging drug targets. The computational methodology will be applied to compounds binding to pharmaceutically important enzymes or protein-protein interactions. We are particularly interested in characterising the potential of 'hit' molecules, weak binders typically identified at the early stage of a drug discovery campaign by fragment screens, to be developed into potent allosteric modulators. The work will build on molecular dynamics simulation and free energy calculation methodologies the Michel lab has recently used to elucidate allosteric effects in proteins (*Chem. Commun. 2019*), and to guide rational drug design efforts (*Chem. Sci. 2019*). The project will be carried out in collaboration with the biopharmaceutical company UCB and involve placements at their R&D site. This is an exciting opportunity to develop, validate and apply next-generation computer-aided drug design software and methodologies. Upon completion of the studentship, the successful applicant will have gained strong technical expertise in molecular modelling and learned to work closely with the pharmaceutical industry sector. This will prepare him or her well for a future career in academia or industry.

Applicants with an excellent academic record in a chemistry/biochemistry/physics are encouraged to apply. The ideal candidate will have: interest in computer programming (Python) and evidence of strong programming abilities, strong knowledge in physical chemistry and/or biophysical chemistry; relevant research experience; excellent written and oral communication skills; enthusiasm for rational drug design, computational chemistry and scientific computing.

Applications will be considered until an excellent candidate has been identified. Candidates should normally be UK resident, with or about to obtain a 2.i or 1st class degree in a relevant discipline. EU candidates may be considered, provided they demonstrate an outstanding academic record (within top 5% of your class) and strong written/spoken English language skills.

To apply, please submit initially by email a CV, covering-letter describing your previous research experience, reasons to apply and justifying your eligibility, as well as the names and email address of two referees in pdf format to Dr. Julien Michel julien.michel@ed.ac.uk. Informal enquiries are encouraged.