**"**A high-throughput FEP pipeline for optimisation of hits into leads for novel drug targets''
3.5-year fully funded CASE PhD studentship, September 2021, stipend ca. £15.5k pa

Supervisors: Dr Julien Michel, School of Chemistry, University of Edinburgh ; Dr Tahsin Kellici & Dr Inaki Morao, Evotec

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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 research project will be carried out in collaboration with the pharmaceutical company Evotec.

**Free Energy Perturbation (FEP) methods** are increasingly used in industry to guide potency optimisation of preclinical candidate compounds. FEP methods are well suited to optimise compounds for novel drug targets amenable to structure-based drug design as they can deliver high accuracy potency predictions without requiring a prior training set of active compounds. However the performance of FEP varies across target classes (e.g. kinases, GPCRs) and can be affected by the choice of the FEP implementation. Currently significant technical expertise is required to deploy FEP effectively in an industrial R&D setting.

The goal of this research is to develop an optimised open source FEP implementation for robust performance across broad range of drug target classes of current interest to Evotec. Systematic comparison of leading FEP implementations (available via e.g. Amber, Gromacs, OpenMM) will be facilitated by development of easy to use **automated pipelines for high throughput FEP studies** using the BioSimSpace framework for biomolecular simulation (www.biosimspace.org). We will also exploit recent advances in **machine learning** to implement next-generation potential energy functions and sampling algorithms in our in-house FEP software SOMD (www.siremol.org) to significantly improve the accuracy of and scope of FEP calculations. Through periods of placement at Evotec the student will deploy the new software onto internal computing resources and **help molecular modellers apply the methodology to real world drug discovery projects.**

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 the student well for a future career in academia or industry.

Applicants with an excellent academic record in a chemistry/engineering/biochemistry/physics/high performance computing degree are encouraged to apply. The ideal candidate will have: a background in scientific computing; knowledge in physical chemistry; relevant research experience; excellent written and oral communication skills. Previous experience and keen interest in computer programming (e.g. Python, C++) is desirable.

**Applications will be considered until a suitable candidate has been identified**. Candidates should have or be about to obtain a 2.i or 1st class degree in a relevant discipline. To apply, please submit initially by email a CV, covering-letter describing your previous research experience, reasons to apply, as well as the names and email address of two referees to Dr. Julien Michel julien.michel@ed.ac.uk. Informal enquiries are encouraged.