

PhD studentship in biomolecular simulations using large-scale quantum mechanical calculations

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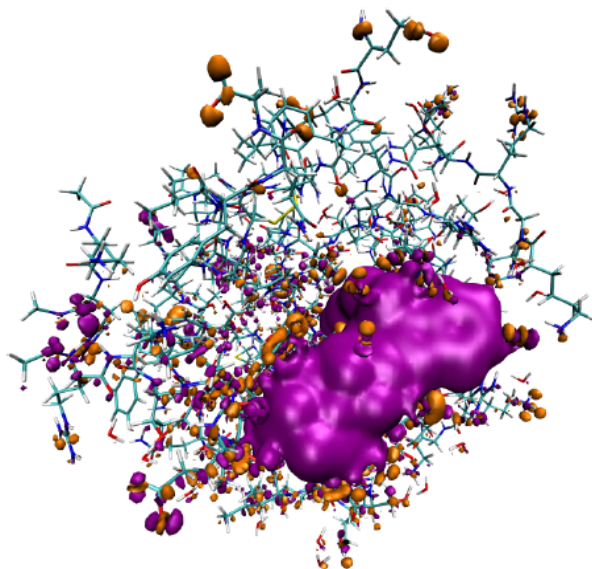
A prestigious four-year BBSRC CASE PhD studentship with a stipend of £15800 per annum is available at the University of Southampton. The project will be supervised by Dr Chris-Kriton Skylaris (<http://www.soton.ac.uk/~compchem/skylaris>) together with senior scientists from Accelrys and pharmaceutical companies.

Simulations of DNA, entire proteins, small molecules (drugs) and their combined interactions are central to the vision that in the next ten years it will become possible to model the behaviour of a minimal living cell (the “e-cell”) in a computer (*in silico*). Molecular mechanics (MM) force fields have allowed much progress towards this goal but they are unable to describe chemical reactions and electronic charge transfer and polarisation. Quantum mechanical (QM) calculations from first principles naturally overcome these limitations but their high computational cost has restricted them to be used in hybrid quantum mechanics/molecular mechanics (QM/MM) schemes where QM is used for a small “important” part of a biomolecule and MM is used for the rest. While QM/MM overcomes some of the limitations of pure MM, it suffers from the arbitrariness in dividing a biomolecule into QM and MM parts and in setting up the interactions (coupling) between them. A reformulation of quantum theory which we have developed and implemented into our ONETEP program makes possible QM calculations with many thousands of atoms and opens the door to a whole new level of simulation as it could be used on entire biomolecules.

In this project you will use ONETEP to simulate the binding affinities of drugs to protein targets for which there is detailed experimental information to compare with. Subsequently more challenging studies of biomolecular targets relevant to therapies will be attempted involving large-scale molecular assemblies such as protein-protein interfaces and proteins in membranes which are ubiquitous components of the cell and their detailed understanding currently has many gaps.

This project is suitable for students with a good degree in chemistry, biochemistry or physics with a keen interest in biomolecular modelling. For informal enquiries related to this project and for further information regarding the nature of this industrially-sponsored studentship, including the periods of placement within the company's European headquarters in Cambridge, please contact Dr Chris-Kriton Skylaris (cks@soton.ac.uk, 023 80599381). The studentship is open to UK students and also to EU students who fulfil the eligibility criteria set by BBSRC:

http://www.bbsrc.ac.uk/funding/studentships/studentship_eligibility.pdf



Electronic density gain (purple) and depletion (orange) upon the binding of a potential drug in the fXa protein