## Potential Supervisors

**Professor Philip Biggin – Professor Computational Biochemistry**

Phil is based in the Department of Biochemistry at the University of Oxford. His interests are focussed on the development and application of computational methods with particular respect to membrane proteins and drug-protein interactions. He has over 100 peer-reviewed publications in this field, and has acted as a consultant to BioMedCentral. He is the current Chair of the Molecular Graphics and Modelling Society and a Fellow of the Royal Society of Chemistry (FRSC) as well as a chartered chemist (CChem). He is a member of the British Biophysical Society and the US Biophysical Society. Most of his work has focussed on the use of high-performance computing in molecular dynamics simulations.

## Recent Software Tools and Community Resources Developed

1. **WaterDock** – Many drug-protein interactions are mediated by water molecules. In order to design compounds with higher affinity, a common strategy is try and displace these water molecules – the idea being you obtain higher affinity by increasing the entropy of the system. In order to do this however, one needs to know where the water molecules reside and this information is not always available. WaterDock is a fast and accurate method that predicts the location of water molecules in protein structures. In test sets, WaterDock predicts the position of 80%+ of water molecules correctly (assuming a positional error of 1.5 Å ). In contrast to many software packages, WaterDock is completely free.

2. **Absolute Binding Free Energy (ABFE) resources**. We have recently performed large scale assessments of the performance of absolute binding free energy calculations considering a diverse set of drugs against one target (the bromodomain protein BRD4) and also the selectivity of one compound to 22 different bromodomain proteins. We were able to show that these calculations can predict the affinity of drug-protein interactions to about 1.5 kcal/mol. Given the significance of these results we placed the whole data set online for people to use and reproduce (see for example http://doi.org/10.5281/zenodo.57131) and a tutorial on alchemistry.org on how to perform these kinds of calculations.

3. **LinTools** is a more recent open-source software tool for analysing and drawing time-dependent schematics of protein-ligand molecular dynamics trajectory information. Code is available from https://github.com/bigginlab/lintools-1.

## Involvement of DTC Students

WaterDock was one of the first SABS projects formulated and was undertaken by Greg Ross who after post-doctoral work with Professors Essex (Southampton) and Chodera (Memorial Sloan Kettering Cancer Centre) now works at Schrodinger (New York). Much of the work on ABFE was done by Matteo Aldeghi, now a post-doc at the Max Planck Institute for Biophysical Chemistry. Göttingen, Germany.

## Software-related Contributions to the Research Community

- 2013- HECBioSim Committee Member
- 2011- CCPBioSim Committee Member