Project title:

A posteriori extraction of molecular kinetic and thermodynamic properties from trajectory data

PIs:

Julien Michel (**JM**), School of Chemistry, University of Edinburgh

Ben Leimkuhler (**BL**), School of Mathematics, University of Edinburgh

Project description:

This project is concerned with the use of classical molecular dynamics (MD) simulations to study the interactions of synthetic molecules with biological molecules. Theories have been developed to build from raw MD data discrete time master equations, or Markov state models. Analysis of such Markov state models allows extraction of the thermodynamic and kinetic properties of a molecular system. There are however several numerical challenges to overcome when applying such theories to model biological molecules in condensed-phases.

MD simulations of the c-myc biological molecule have been performed in the group of Julien Michel; these have revealed mechanisms by which small molecules modify the structure and dynamics of c-myc, which helps to identify important interactions. Such information is important to guide the design of novel putative anti-cancer agents targeting c-myc. Julien's group has furthermore built Markov State Models of c-myc conformational dynamics and performed spectral analysis of the resulting transition matrix to compute equilibrium and kinetic properties. However, the resulting properties have large statistical errors and the goal of this project is therefore to find alternative mathematical analyses which may improve resolution. Drawing on B. Leimkuhler's expertise in molecular modelling the researcher employed on this project will re-analyse ('post-process') Julien's molecular trajectory data using improved methods to compute kinetic and thermodynamic properties, in addition attempting to quantify the error in the current model. Methods will be explored based on techniques which enable us to identify a few relevant collective variables to describe important transitions.