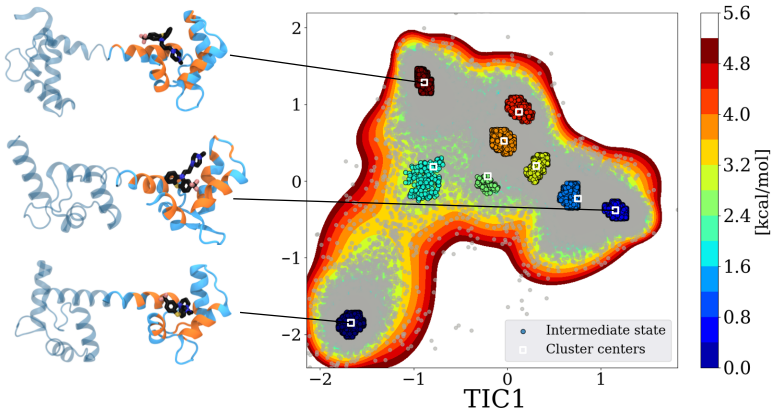
Master degree project in Molecular Dynamics simulations



Background

Calmodulin is a regulatory protein involved in many intracellular pathways that confers calcium sensitivity to target proteins such as ion channels and G-protein coupled receptors. The anti-psychotic drug trifluoperazine binds to calmodulin in several orientations but the molecular mechanisms of binding and unbinding, and of interconversion between binding poses are not well understood. We use molecular dynamics simulations to understand this process with an atomic-level resolution.

Aims

The aims of this project are to run and analyze MD simulations to evaluate these binding pathways under different conditions. Part of the work consists in establishing methodologies that enhance the sampling of simulations, using a combination of machine learning algorithms and enhanced sampling strategies, while the other part consists in extracting the molecular level features that are important for binding and unbinding using data analysis tools.

Methods

In this project you will setup and run molecular dynamics simulations to be able to construct Markov State Models of drug binding to CaM binding. This will be done using mainly the molecular dynamics package Gromacs. Analysis will be performed using python scripts, including the Delemotte lab Demystifying repository: https://github.com/delemottelab/demystifying. Visualization and figure preparation will be done using Pymol and VMD.

Contact

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Research in the Delemotte Lab focuses on understanding the structure and function of membrane proteins, the molecular machines in the cell membranes that enable cellular communication. We are located at SciLifeLab Stockholm and part of a large environment focusing on the development and application of methods in biophysics.
Read more at: https://www.biophysics.se/index.php/projects/delemottelab/