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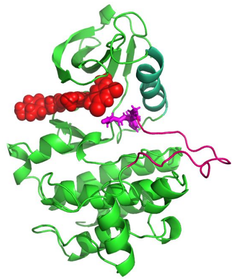
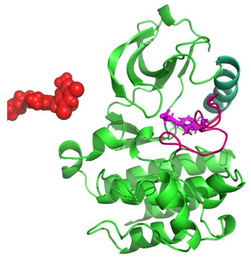
Technology, Social Impact

Minimum Energy Path in Kinase conformations

ABSTRACT

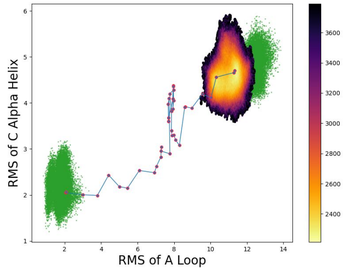
The Kinase takes on many different conformations, out of which 2 are known to be of interest. The active and inactive, separated by a few differences, are very well researched, and the transitional pathway between them, even more. We attempt to find the Minimum Energy Pathway between the two conformations in this project.

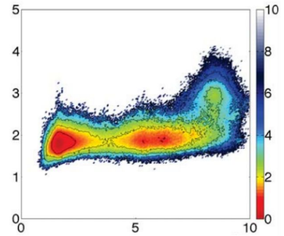


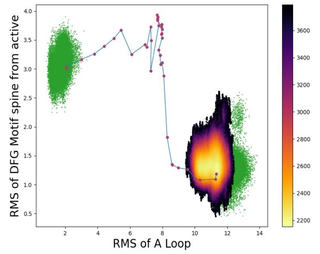


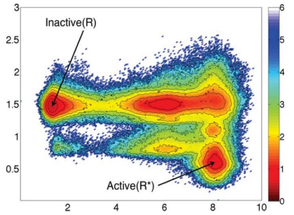
OBJECTIVE

A Minimum Energy Pathway between 2 conformations is one which requires the least amount of energy for the initial state to the final state. Here we use the Nudged Elastic Band method, implemented in the Molecular Dynamics software package AMBER, in order to find this minimum energy pathway.









METHOD

Input : 2 conformations with same number of atoms but different positional coordinates.
Output : M + 2 conformations (M, hyperparameter), each one being one of the intermediates in the Minimum Energy Path conformation.
A simulated annealing protocol is used for this purpose, where we first linearly interpolate positional coordinates for each atom, and then heat it to a high temperature in order for it to explore potential local minima, and then cool it back, all while keeping a constraint that the conformations don't all fall into the same minima.

- A value of M = 40 was used.
- The conformations were then mapped to 2 order parameters of interest in the transition, and compared with free energy surfaces that were validated in reference research papers.

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