Leveraging structural data by decoupling structure thermodynamics and dynamics

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Abstract

Decoupling structure, thermodynamics and dynamics to study the function of biomolecules allows leveraging specific structural data to focus on certain aspects. As a result, one typically obtain insights that might remain elusive for strategies applying a unique tool, say molecular dynamics, to study all aspects at once. In this talk, I will discuss several recent developments illustrating this perspective.

In the first part, I will introduce a novel distance measure for conformations [1], as well as novel analysis shedding light on the multiscale structural conservation that may be present in conformational changes [2]. Applied to crystal structures of (homologous) proteins, these tools provide insights on dynamics without explicitly resorting to dynamics [3].

In the second part, I will argue that these insights may be used to stratify degrees of freedom (dof) i.e. internal coordinates into active / passive, and that the active ones may be exploited by basin hopping related methods to tame down the usual concentration phenomena in high dimensional conformational spaces. Novel methods to perform conformational exploration and analysis will be presented [4, 5, 6].

Finally, to bridge the gap to thermodynamics, I will introduce novel improvements to importance sampling / multi-phase Monte Carlo methods aiming at speeding up free energy calculations for (groups of) basins from the potential energy landscape [7].

Pointers to software tools implemented within the Structural Bioinformatics Library will be given [8].

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