Biophysical experiments and biomolecular simulations: A perfect match?

Kresten Lindorff-Larsen

Structural Biology and NMR Laboratory, Linderstrøm-Lang Centre for Protein Science, Univ. of Copenhagen

Abstract:
Biological macromolecules are dynamic entities and I will discuss methods and applications for how simulations and experiments can be used synergistically to study protein and RNA dynamics [1,2]. Functional protein motions are often described as an exchange between a ground state structure and minor states. The structural and biophysical properties of these transiently and sparsely populated states are, however, difficult to study, and an atomic-level description of those states is challenging. Using proteins with extensive NMR data available as test systems, we have shown how enhanced sampling simulations can be used to capture accurately complex conformational changes in proteins, and I will briefly discuss such examples [3,4].

Despite recent progress, one may still find that a simulation does not quantitatively match experiments. Then, experiments and simulations may be combined in a very direct fashion to provide a description of the molecular motions that combines the details of atomic simulations with the accuracy afforded by experiments [1,2]. The resulting conformational ensembles may provide novel insight into biomolecular systems that are not obtainable by simulations of experiments alone. I will discuss how this may be achieved [5], and give examples of the application of such approaches using both NMR and small-angle scattering experiments to describe both proteins [6,7] or RNA [8,9], and possible future approaches to include timescales of motion [10]

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