Atomistic simulations of natively unfolded proteins

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Recently, many proteins that perform essential roles in cellular signaling and regulatory pathways have been found to be natively unfolded, thus challenging the assumption that proteins must fold into well-defined, globular structures in order to carry out their functions.

These proteins fold, or become ordered, only upon binding their partner proteins, suggesting a new paradigm of protein-protein recognition. Understanding this new paradigm is not only fundamental to biology, but could aid the development of therapeutics to prevent the malfunction of natively unfolded proteins due to mutations associated with diseases such as cancer.

Given the difficulty of using experiments to obtain structural details of the conformational changes of proteins upon folding or binding their partners, a natural alternative is to use atomistic molecular dynamics simulations, which provide the time resolution and detail necessary for monitoring the step-by-step progression of conformational changes. Due to the large computational cost required for simulating these conformational changes, we apply methods that take advantage of distributed computing by making effective use of a large ensemble of short, independent simulations.