Protein Folding Properties from Molecular Dynamics Simulations

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Abstract. Our understanding of protein folding has improved tremendously due to computer simulations of molecular dynamics (MD), but determining protein folding kinetics and thermodynamics from all-atom MD simulations without using experimental data still represents a formidable scientific challenge. Simulations can easily get trapped in local minima on rough free energy landscapes and folding events may only rarely be observed. This necessitates the computation of multiple simulation trajectries (tens to thousands), which can be independent from each other or coupled in some manner, as for example in the Replica Exchange MD (REMD) method [1–3]. We have recently reported simulations of the complete folding of the polypeptide Chignolin from the extended state to the native conformation [4]. Here we present results obtained with new analysis tool that allows the deduction of faithful kinetic information from a heterogeneous ensemble of simulation trajectories. The method is demonstrated on the decapeptide Chignolin [5] for which we predict folding and unfolding time constants of 1.0±0.3 and 2.6±0.4 μs, respectively. We also derive the energetics of folding, and calculate a realistic melting curve for Chignolin. This new method greatly expands our capabilities to extract information from MD simulations.

References

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