Rare event sampling problems for biomolecules

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For efficiently sampling “rare events” in complex molecular systems on rugged energy landscapes, it is inevitable to devise advanced methods based on the idea of “paths”, such as transition path sampling [1] or the (finite-temperature) string methods [2]. Though such methods require huge computational resources, it has become feasible with current technology using massively parallel environments. Here we encapsulate our recent attempts for developing new path sampling methods and show some applications of such methods to (bio)molecular systems.

First we discuss the molecular detail of the conformational change of an enzyme, adenylate kinase, using the “on-the-fly” string method [2]. Employing several principal components, known as good order parameters to characterize the conformational change of proteins, as collective variables, we can identify the minimum free energy pathways with full molecular detail including solvent water molecules, and estimate free energy barrier along the pathways. We then scrutinize the molecular detail of the transition (the transition state) with and without the ligand molecule [3]. In addition, we present a preliminary result of applying the string method to a huge membrane protein, AcrB.

We also discuss our recent studies for path sampling using the Onsager-Machlup action functional [4,5], which is a basic tool to analyze dynamic trajectories. The basic idea of this method is to consider a path probability (weight) for an individual trajectory and to formulate the dynamical system problems regarding nonequilibrium situations as equilibrium ones. We show some applications of this method to model systems.

References

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