Understanding Rare Events in Complex Systems via Transition path theory

by

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The function of biomolecules depends on their dynamical properties, and especially on their ability to undergo transitions between long-living states, called conformations. A transition network is a reduced model for the dynamical transitions between conformations. These transitions are rare events compared to the timescale of stability of the conformations.

One of the challenges in this field is, besides the identification of conformations and the computation of the transition rates between them, the statistical characterization of the ensemble of /reactive/ (transition) trajectories between conformations. Recently developed for this purpose, transition path theory (TPT) allows to compute the probability distribution of reactive trajectories, the associated reactive probability current and transition rates, and insight into the associated transition pathways. For transitions from set A to set B in state space, the basic object in TPT is the committor function /qAB(x)/ which is the probability to go rather to the set B than to the set A conditioned on the process has started in /x/.

For a Markov diffusion process, the committor satisfies a boundary value problem where the involved partial differential operator is the generator of the discussion process. Solving the committor equation numerically in high dimensions is infeasible and, hence, TPT is impractical for the analysis of high dimensional diffusion processes.

As a remedy, we generalized TPT for Markov jump processes and apply it to reduced models of the biomolecular dynamics under investigation. As a result, the dynamical behavior in state space is described by a discrete transition network. The key steps of the resulting approach is the estimation of the optimal infinitesimal generator underlying the reduced dynamics and the computation of discrete transition pathways via graph algorithms.

The talk will introduce the approach and its biomolecular background, discuss its relations to other fields (e.g. potential theory and short paths algorithms), and illustrate its performance in application to some small peptides.