Quantifying macromolecular conformational transition pathways
SEAN SEYLER, AVISHEK KUMAR, MICHAEL THORPE, OLIVER BECKSTEIN, Arizona State University — Diverse classes of proteins function through large-scale conformational changes that are challenging for computer simulations. A range of fast path-sampling techniques have been used to generate transitions, but it has been difficult to compare paths from (and assess the relative strengths of) different methods. We introduce a comprehensive method (pathway similarity analysis, PSA) for quantitatively characterizing and comparing macromolecular pathways. The Hausdorff and Fréchet metrics (known from computational geometry) are used to quantify the degree of similarity between polygonal curves in configuration space. A strength of PSA is its use of the full information available from the 3N-dimensional configuration space trajectory without requiring additional specific knowledge about the system. We compare a sample of eleven different methods for the closed-to-open transitions of the apo enzyme adenylate kinase (AdK) and also apply PSA to an ensemble of 400 AdK trajectories produced by dynamic importance sampling MD and the Geometrical Pathways algorithm. We discuss the method’s potential to enhance our understanding of transition path sampling methods, validate them, and help guide future research toward deeper physical insights into conformational transitions.

Sean Seyler
Arizona State University

Date submitted: 07 Nov 2014

Electronic form version 1.4