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Conformational Dynamics of Adenylate Kinase: The Effects of Temperature and Mutation on Friction, Memory, and Reactivity
LUCAS WATKINS, KARL DUDERSTADT, SUCHARITA BHATTACHARYYA, HAW YANG, Department of Chemistry, University of California Berkeley — Enzymes reside on a convoluted free energy surface. This free energy surface generates the conformational dynamics that control activity. We use single molecule Förster Resonance Energy Transfer measurements to study these conformational dynamics and the physics that underly them in a model enzyme, Adenylate Kinase (AK), which catalyzes the disproportionation of ADP into AMP and ATP. Our microscope records time-dependent single-molecule trajectories as a list of single photon arrival times. We treat the distance trajectory that generates this data as a manifestation of a many-dimensional Langevin equation, projected onto the coordinate defined by our two labeling sites. Using a likelihood-based approach, we can then directly extract the potential of mean force and the friction coefficient from the raw photon-by-photon trajectories. Temperature-dependent studies allow calculation of entropy and enthalpy profiles from the measured potentials of mean force, while mutants in functionally-important regions allow us to understand the role of individual residues in dynamics and catalysis. Ultimately, this newly-developed method allows us to begin to draw direct connections between structure, dynamics, and reactivity.

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