

Free Energy Profiles from Single-molecule CryoEM

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Single-particle cryo-electron microscopy has the great advantage of taking projection images of individual molecules. Because the freezing process is done very rapidly, these molecules can be trapped in different conformations, which are typically distributed according to the Boltzmann factor at the temperature prior to freezing. In this work, we define a conformational path that transitions from representative states of the system. We present a Bayesian formalism to extract the free energy profile using individual cryoEM particles given the predetermined path. We apply the method over a diverse set of systems, finding that the particle-pose accuracy and signal-to-noise ratio are key factors to extract accurate profiles.