Decoding dynamic heterogeneity in single molecule data

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Single molecule time trajectories of biomolecules provide glimpses into complex folding landscapes which are difficult to visualize using conventional ensemble experiments. Recent single molecule data and theoretical analysis have highlighted static or dynamic heterogeneity, a hallmark of rugged energy landscapes, in certain classes of biomolecules. Although data suggestive of molecular heterogeneities from single molecule measurements have recently increased, a systematic method for analyzing such data is currently missing. Here we report a new method to analyze single molecule time trajectories with dynamic heterogeneity such that kinetics of conformational transitions varies along the time due to a slowly changing hidden internal state of the molecule. Our method can detect, if any, the presence of dynamic heterogeneity in each trajectory, identify how many internal states are mixed in the individual trajectories, and enable us to estimate transition rates between internal states as well as the kinetic rates of conformational dynamics of each internal state. Finally, we applied our method to analyze single molecule data of H-DNA whose duplex-triplex transitions exhibit dynamic heterogeneity.

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