

## Characterization of Alternative Native States of the Villin Headpiece Subdomain using Atomistic Simulation

Ali Sinan Saglam, Alex DeGrave, Thomas Kiefhaber and Lillian T Chong

Recently, triplet-triplet energy transfer experiments have revealed two alternative native states of the villin headpiece subdomain (HP35) that are structurally similar but have different dynamic properties. Here, we have characterized the alternative native states of HP35 as well as the transition state for the interconversion of these native states using atomistic simulations in explicit solvent with enhanced sampling provided by the weighted ensemble path sampling strategy. Preliminary results suggest that the two alternative native states of HP35 differ in the flexibility of their C-termini, residues 32-34, which is caused by the making and breaking of the hydrogen bonds of the third  $\alpha$ -helix. Simulations will be further extended in order to sample the unfolding of the third  $\alpha$ -helix and characterize the transition state ensemble.