Enhancing Solute Sampling via Higher-Dimension Generalized Ensemble Methods

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Generalized ensemble simulation methods accelerate sampling of conformational processes via the promotion of energy fluctuations. To more specifically focus the activation of conformational vibrations on major events, various "focusing sampling" (or "locally sampling") strategies have been proposed in order to overcome the associated diffusion sampling problem, which is caused by sampling space enlargement. For the fact that solute configuration transitions can be governed by diverse interplays between solute-solute internal interactions and solute-solvent interactions, none of the existing "focusing sampling" methods can robustly enable efficient visits of essential states of a target solute. In this work, we developed a high-dimension generalized ensemble scheme to effectively capture such pivotal energetic interplays. We demonstrate the effectiveness of this novel scheme in the context of the essential energy space random walk algorithm (C. L. & W. Y., J. Chem. Phys. 2012 in press). Based on the present new higher-dimension treatment, we further developed a generalized orthogonal space sampling method, which allows slow protein motions to be efficiently sampled in commonly affordable simulation length. Both model systems and realistic protein systems are employed to demonstrate the above strategies.