Conformational sampling of complex molecular systems is always a challenge in computer simulations. To tackle this problem, a range of enhanced sampling methods have been developed. However, each method typically only shows distinct advantages in specific systems. Therefore, new approaches aim to combine the complementarity of different enhanced sampling algorithms to achieve a better performance. In this study, we propose a new algorithm to combine the advantages of two Hamiltonian replica exchange methods designed to improve sampling of specific degrees of freedom using biasing potentials and of global conformational properties, including solute-solvent interactions via solute tempering. The new method produces improved sampling for polysaccharides with coupled linkages, including branch points. The method is applied to N-glycans found on the HIV gp120 envelope protein that show potential application in the design of HIV vaccines.

References

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We present a generic solvated coarse-grained protein model that can be used to characterize the driving forces behind protein folding. Each amino acid is coarse-grained with two beads, a backbone and side-chain. While the backbone beads are modeled as polar entities, side-chains are either hydrophobic, polar or charged, thus allowing the exploration of how sequence patterning determines a protein fold. The change in orientation of the atoms of the coarse-grained unit is captured by the addition of two oppositely charged dummy particles inside backbone coarse-grained bead. These two dummy charges represent a dipole which can fluctuate thus introducing structural polarization into the coarse-grained model. Realistic alpha/beta content is achieved de novo without any biases in the force-field toward a particular secondary structure. The dipoles created by the dummy particles interact with each other and drive the protein models to fold into unique structures depending on the amino acid patterning and presence of capping residues. We will present the role of dipole-dipole and dipole-charge interactions in shaping secondary and supersecondary structure of proteins. Since dipole interactions are influenced by the dielectric environment, the model is sensitive to the nature of the environment (low or high dielectric). Results on how changes in dielectric can tune the emergence of different folds will be presented.

Enhanced Conformational Sampling of Carbohydrates using Biasing Potential and Solute Tempering Replica Exchange: Application to the N-glycan on the HIV gp120 Envelope Protein
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Conformational sampling of complex molecular systems is always a challenge in computer simulations. To tackle this problem, a range of enhanced sampling methods have been developed. However, each method typically only shows distinct advantages in specific systems. Therefore, new approaches aim to combine the complementarity of different enhanced sampling algorithms to achieve a better performance. In this study, we propose a new algorithm to combine the advantages of two Hamiltonian replica exchange methods designed to improve sampling of specific degrees of freedom using biasing potentials and of global conformational properties, including solute-solvent interactions via solute tempering. The new method produces improved sampling for polysaccharides with coupled linkages, including branch points. The method is applied to N-glycans found on the HIV gp120 envelope protein that show potential application in the design of HIV vaccines.

References