28i Solvation Model Based on Order Parameters and Fast Sampling Method for the Calculation of the Solvation Free Energies of the Peptides

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Interactions between peptides and water can contribute a huge amount to the energetics of conformational changes and other processes[1]. The most accurate way to represent these interactions is with explicit solvent models, but these are quite computationally intensive and intractable for adequate sampling of even very small peptides (> 4 residues). Hence, there is a great need for the development of accurate, inexpensive, and simple solvation models that are able to represent the solvation effects quantitatively.

There are three types of models for describing the solvation effects in a more or less quantitative manner: one is computer simulation with explicit solvent molecules[2], which is the most accurate but the most time consuming model; another is the solution of integral equations[3], that is more efficient than the former model, but the accuracy depends the statistical model used to describe the system; the third includes various models based on continuum solvent assumption[4], which is the most efficient method among the three, but not as accurate as the former two.

In this work, we present a simple analytical solvation model as a function of an order parameter which represents the local arrangement of water molecules in the first solvation shell of peptide atoms. The model is combined with a fast sampling method, rotational isomeric state Monte Carlo (RISMC) to sample efficiently the torsional degrees of the peptide backbone. For purpose of validation, solvation free energies of four groups of peptides are calculated by our model, the General Born (GB)[4] model and explicit solvent model. Since our order parameter solvation model regards the local water structure as the major contribution to solvation, it is demonstrated to predictthe solvation free energies of single amino acids and tripeptides with slightly better accuracy then one of the best continuum solvent models, GB. Moreover, due to the inclusion of the efficient sampling approach, the newly proposed method, as a whole, is able to give a much more rapid computation of solvation free energy than thermodynamic integration of GB and explicit solvent models.

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