Comparison of RESP and IPolQ-Mod Partial Charges by Efficient Molecular Simulations of the Free Energy of Solvation

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The calculation of the Gibbs free energy of solvation ΔG_{solv} by molecular simulation is of great interest as it is linked to a variety of physical properties such as solubility, partition coefficient and activity coefficient. It is described by the free energy difference due to the transfer of a solute from a vacuum with none into a condensed phase with full solute/solvent interactions. If the overlap in configurational space of these thermodynamic states is poor, a linking chain of intermediate states is constructed to scale the solute/solvent interactions stepwise by a parameter λ_i, ranging from 0 to 1. Both the number and spacing of these intermediate states impact the accuracy of the calculations, while 'excessive' sampling should be avoided due to the high computational costs. We present a new scheme to iteratively define a sufficient number of λ_i-states and our new method for adaptive spacing of the intermediate states to allow for efficient and consistent free energy simulations [1].

On the other hand, the accuracy of simulated ΔG_{solv} depends on the description of the solute/solvent interactions and is highly sensitive to the modelling of the electrostatic interactions. Commonly applied additive force fields such as the General Amber Force Field (GAFF) [2] are unable to explicitly account for the polarizations effects due the phase transfer of the solute from the vacuum to the condensed phase. The IPolQ-Mod [3] method is a physically motivated scheme to calculate partial charges for an implicit representation of polarization costs. We compared IPolQ-Mod and RESP [4] charges in combination with GAFF and analyzed their accuracies in ΔG_{solv} predictions for a multitude of various solutes and solvents. For both sets of partial charges, we can identify specific shortcomings, e.g. compounds with nitrile or carbonyl groups are poorly described with GAFF and IPolQ-Mod charges [5]. Thus, our current work is aimed at refitting of Lennard-Jones parameters for an improved description of ΔG_{solv} by GAFF/IPolQ-Mod.

References:

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