Hydration in discrete water – mean field, cellular automata based solvent model for calculating hydration free energies.

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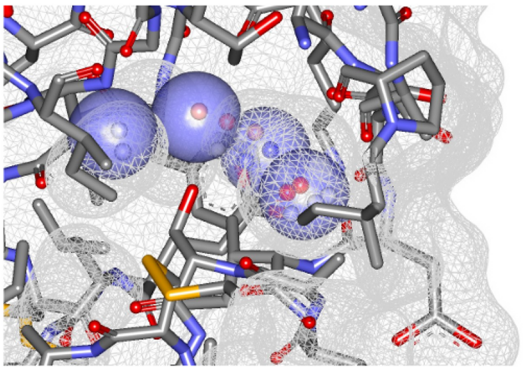
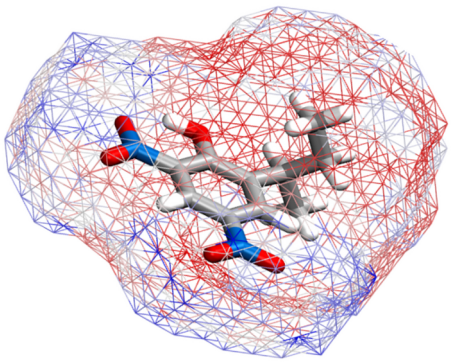
Fast and accurate predictions of hydration free energies are a long standing goal of theoretical biophysics. Despite many years of development, the existing implicit solvent models are still only moderately successful in this area. Here, a solvation model [1] based on a discrete grid of solvent cells will be presented. It utilizes a cellular automata based method to determine the solvent distribution around the solute, and mean field approach to predict the associated hydration free energy. It is computationally efficient and applicable to all compounds described by standard atomistic forcefields, including small drug-like molecules and large biomolecules such as proteins.

In our model, most solvent properties are simplified to the extreme, but those particularly important for molecular hydration: orientation dependent water hydrogen bonding and water-solute electrostatic interactions are explicitly included in the effective Hamiltonian of a solvent cell. The model does not depend on any arbitrary definition of the solute-solvent interface or microscopic surface tension. Instead, nonpolar contributions to the hydration free energies are obtained based on the calculated solvent distribution and solute-solvent dispersion. Apart from providing satisfactory predictions of hydration free energies the model is also able to reproduce some nontrivial aspects of protein hydration like dry hydrophobic cavities or isolated structural water molecules.





[1] P. Setny, M. Zacharias, *J. Phys. Chem. B*, **2010**, *114*, 8667-8675