Computationally efficient and accurate 3D-RISM calculations

Jochen Heil, Roland Frach, Daniel Tomazic, Franziska Hoffgaard, Stefan M. Kast

Physikalische Chemie III, Technische Universität Dortmund

The three-dimensional "reference interaction site model" (3D-RISM) integral equation theory is a statistical-mechanical approach to predict liquid state structural and thermodynamic features [1]. It is based on approximate solute-solvent correlation functions to be computed on a 3D grid as a function of the interaction potential between the solute and the solvent sites, circumventing the need of costly sampling of explicit solvent degrees of freedom. In combination with quantum-chemical calculations within the embedded cluster (EC-) RISM framework [2], the theory also allows for studying chemical reactions in solution, outperforming traditional continuum solvation methods, for instance pK_a shift calculations and conformational equilibria [2], and the prediction of tautomer ratios [3].

Extending the scope of 3D-RISM applications to very large systems such as those involving biological macromolecules as well as to non-aqueous environments poses particular challenges on both the conceptual and the software implementation side. At the same time, it is necessary to systematically improve the inherent 3D-RISM approximations and to add typical capabilities used in computational chemistry in order to make the theory routinely usable. Here we show that we can make progress by developing novel methodical and software features:

- The expensive treatment of long-range Coulomb interactions is circumvented by implementing a "particle-mesh Ewald" (PME) approach [4] that exploits the computational efficiency of the fast Fourier transformation (FFT). Furthermore, a multipole renormalization scheme eliminates the need to compute the costly real-space potential at any stage of the calculations.
- The performance of key routines is improved by implementing MPI parallelization in order to facilitate porting of the 3D-RISM software to massively parallel hardware architectures.
- Semi-empirical free-energy functionals for improved accuracy are currently parametrized with respect to quantitative agreement between simulated and 3D-RISM free energies of solvation [5,6].
- Gradient formulations [7] for geometry optimization in solution are developed in order to allow for characterizing reaction thermodynamics and mechanisms.

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