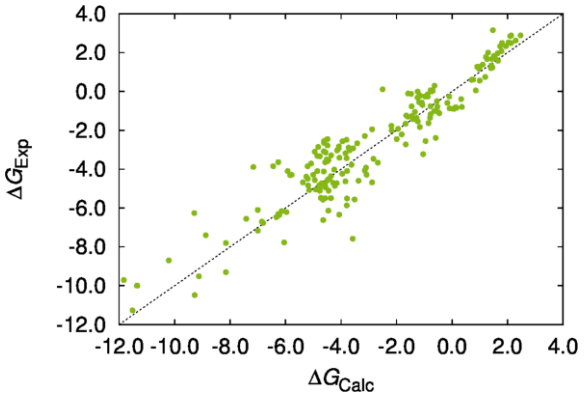
Integral equation-based quantum solvation model for quantitative prediction of hydration free energies

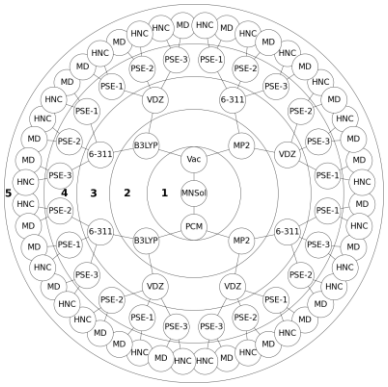
Daniel Tomazic, Stefan M. Kast

Physikalische Chemie III, TU Dortmund, D-44227 Dortmund, Germany

The "embedded cluster reference interaction site model" (EC-RISM) [1] combines statistical-mechanical 3D RISM integral equation (IE) theory and quantum-chemical calculations in a self-consistent manner. In the past, application of approximate closure relations allowed us to compute relative thermodynamic quantities such as pK_a shifts [1,2] and tautomer ratios [3] in aqueous and nonaqueous solution with high accuracy; the quality of the wave function in solution has been demonstrated by successful calculation of chemical shifts related to nuclear magnetic resonance (NMR) spectroscopy. [4]

However, absolute solvation free energies suffer from well-known systematic deficits with available closure approximations. One way to semiempirically compensate for these artifacts is to fit a corrective term related to the partial molar volume (PMV) of the solute [5,6] such that experimentally measured hydration free energies match IE predictions. Since such an approach has not been attempted for a self-consistent quantum solvation model, we here present a two-step correction workflow by fitting EC-RISM hydration free energies to data taken from the MNSOL database [7]. We demonstrate the promising performance in the context of the chosen levels of theory, conformational sampling, and different forms of the PMV correction.





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