Transfer free energies between aqueous and nonaqueous phases from an integral equation-based quantum solvation model

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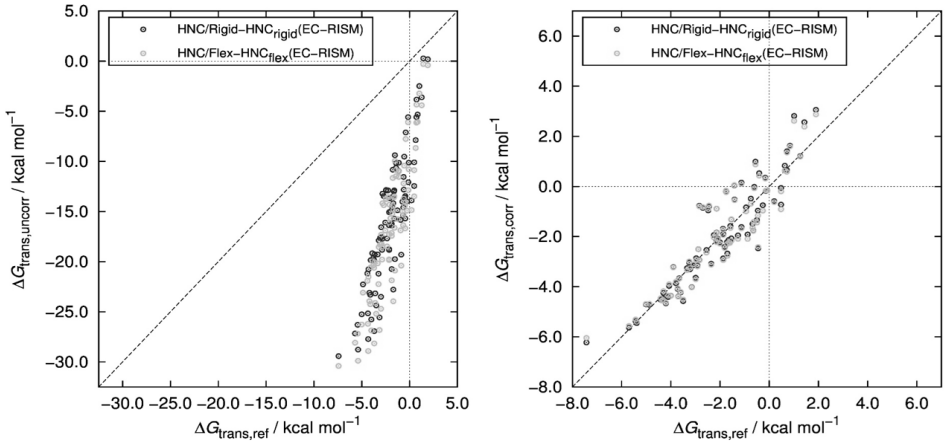
Reliable yet fast prediction of free energies of solvation or of partition coefficients of molecules between immiscible or partly miscible phases such as water and *n*-octanol requires proper theories as for instance provided by the integral equation approach to fluid phase thermodynamics [1]. To accurately model the solvation of small molecules we here combine such a statistical-mechanical description of the solvent with a quantum level description of the solute in the form of the "embedded cluster reference interaction site model" (EC-RISM). This combination takes into account both the electronic relaxation and the excess chemical potential governing the solvation process for predicting the free energy of solvation [2].

To extend the scope of EC-RISM theory to complex solvents other than water we here examine several models for *n*-octanol, taking molecular flexibility into account. This is achieved by parameterizing suitable analytical expressions for the intramolecular distribution functions with respect to reference data from explicit molecular dynamics simulations. One known drawback of the RISM formalism is an overestimation of the free energy contribution accompanying the formation of the solute cavity, leading to significant errors in the absolute free energy of solvation. This error is highly correlated with the partial molar volume (PMV) of the solute [3]. To address this issue we parametrize a PMV correction to increase the accuracy of the calculated free energies of solvation within the EC-RISM context. We discuss the application of this framework to the calculation of the octanol-water partition coefficients (log *P*) for a structurally and chemically diverse set of compounds.



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