Solvation effects on chemical shifts by 3D RISM theory

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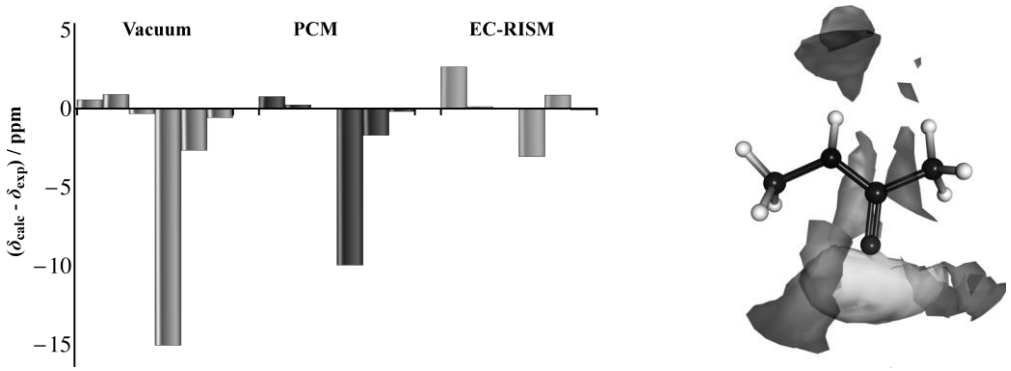
Accurate predictions of chemical shifts are relevant for the interpretation of nuclear magnetic resonance (NMR) spectra not only of small molecules, but even more so for structure predictions of bioorganic and polymeric entities since their chemical shift distribution increases in complexity due to the conformational freedom. In order to capture environmental effects adequately, quantum-chemical calculations of NMR parameters have to be combined with an accurate solvent model that reflects directional interactions such as hydrogen bonds that can have substantial influence on chemical shifts.



To retain the solvent granularity, which is neglected in continuum solvation models, we developed the "embedded cluster reference interaction site model" (EC-RISM) [1] that combines statistical-mechanical 3D-RISM integral equation theory and quantum-chemical calculations in a self-consistent manner. EC-RISM theory is capable of calculating thermodynamic quantities such as pK_a shifts and tautomer ratios [2,3] in aqueous and in nonaqueous solution with affordable computational costs. Here we use EC-RISM to increase the accuracy of quantum-chemical nuclear magnetic shielding calculations for small bioorganic building blocks in comparison with continuum solvation data and with results from computationally demanding cluster approaches combined with molecular dynamics simulations [4]. We discuss statistical evaluation schemes and illustrate the relation between chemical shift and solvent structure.

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[4] A. Frank, H. M. Möller, T. E. Exner, *J. Chem. Theory Comput.*, **2012**, *8*, 4818-4827.