

# Quantum Chemical Microsolvation by Automated Solvent Placement

Maren Podewitz<sup>a</sup>, Miguel Steiner<sup>a</sup>, Michael Schauerl<sup>a,b</sup>, Klaus R. Liedl<sup>a</sup>

<sup>a</sup>*Institute of General, Inorganic and Theoretical Chemistry, University of Innsbruck, Austria*

<sup>b</sup>*Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, USA*

maren.podewitz@uibk.ac.at

Many chemical reactions take place in solvent and the chemically relevant solution-phase conformation of the reactant may differ significantly from its gas phase or solid-state conformation. To accurately account for their reactivity an explicit incorporation of solvent molecules may be required. This is in particular true for biomolecules and biochemical reactions, that take place in water. Defining the number of solvent molecules and its exact location is a great challenge. Thus, we developed a physics based approach to microsolvation, where we deduced the number and location of solvent molecules in an automated way based on the free energy solvation thermodynamics derived from Molecular Dynamics (MD) Simulations and Grid Inhomogeneous Solvation Theory (GIST). This enabled us to rigorously define the number and positions of individual solvent molecules for subsequent quantum chemical investigations, which is a prerequisite to study large bioinorganic structures and their reactivity that cannot be accessed by ab initio MD due to its size. We showcased the applicability of this computational protocol for a number of biologically relevant molecules, including urea, aspartate, and benzoic acid.[1]

## References

1. Miguel Steiner, Michael Schauerl, Klaus R. Liedl, Maren Podewitz, Explicit Solvation By Automated Water Placement Based On Free Energy, 2019, *Manuscript in Preparation*.