

Free Energy Based Quantum Chemical Microsolvation in Arbitrary Solvents

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Much of chemistry takes place in solution. The physical and chemical behavior of the dissolved solute largely depends on the nature of the surrounding solvent. For an accurate description of the system at hand, it is therefore vital that solvent effects are taken into account. In quantum chemical descriptions, this can be done either by treating solvents implicitly, accounting only for bulk properties such as the electrical permittivity, or explicitly by describing an extended condensed phase system. As the latter strategy is often too computationally expensive, quantum chemical microsolvation, also termed cluster approach, has emerged, where only the most important solvent molecules around the solute are considered.

This, however, raises two issues:

1. Where should those solvents be placed?
2. How many are needed to capture the most relevant interactions?

We have developed a computational protocol that quantifies solute-solvent interactions using molecular dynamics simulations and Grid Inhomogeneous Solvation Theory (GIST).^[1] Our algorithm automatically places and orients solvent molecules based on free energy solvation thermodynamics.^[2]

Here, we present the completely revised and extended methodology, which is now capable of identifying favorable solvation sites for the most common (rigid) solvents, such as dichloromethane or DMSO.^[3] We demonstrate the applicability of our method in a number of examples, from organic molecules to transition-metal complexes.

References:

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- [2] M. Steiner, T. Holzknecht, M. Schauerl, M. Podewitz, *Molecules* **2021**, *26*, 1793.
- [3] L. B. Magenheim, R. A. Talmazan, M. Podewitz, *manuscript in preparation* (**2024**).