



Implicit solvent models are parametrised to deliver accurate values of the free energy of solvation ( $\Delta\Delta G_{\text{soln}}$ ), but to achieve a reliable output, care must be taken with the input parameters!

### Solvation modelling

- Explicit/discrete** solvent models: Adding individual solvent molecules, each with electronic and nuclear structures, mostly utilised in MM approaches.
- Implicit/continuum** solvent models: Solute is placed in a solvent "field" (a dielectric continuum). Solute wavefunction affected by solvent dielectric constant.

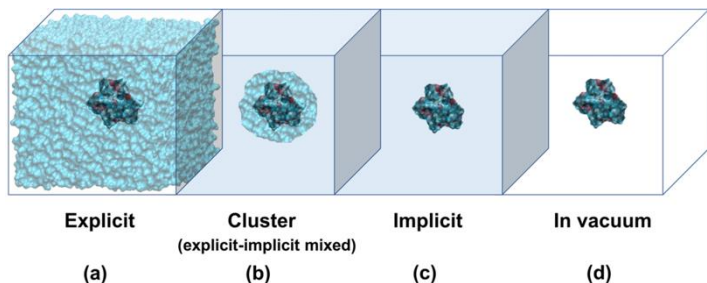


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Phase-change correction from gas-phase standard state (1 atm) to solution-phase standard state (1 mol L<sup>-1</sup>).<sup>1</sup>

$$\Delta G_{\text{soln}} = \Delta G_{\text{gas}} + \Delta\Delta G_{\text{soln}} + RT \ln \frac{RT}{P}$$

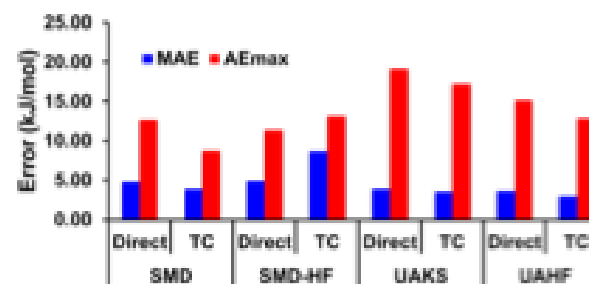
### Implicit solvent models

have been parameterised to deliver accurate values of the *free energies of solvation*, which can be added to accurate values of the *free energies in the gas phase*, to obtain the corresponding solution-phase free energy.

- Polarisable continuum model (PCM): treats the solvent as a polarisable dielectric continuum.
- Solvation model density (SMD): uses full solute density instead of partial charges, implicitly treats dispersion.
- COnductor-like Screening MOdel (COSMO): places the solute in a virtual conductor environment.
- No option** for solvent **mixtures** for PCM/SMD.

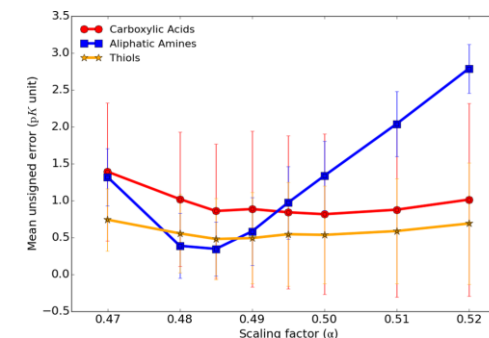
### Recommendations

- Ensure that the energies are computed using **the level of theory that the model was parametrised with!**
- Consider using **thermodynamic cycles** instead of direct computations when aiming for quantitative agreement with experiment.
- Take care when defining the parameters for the cavity constructions, e.g., the surface fitting model (such as the **solvent accessible surface**), the model of the **atomic radii** (UAHF, UAKS, vdW, Bondi, etc.) and the atomic radii **scaling factor**  $\alpha$ . Many codes set the default values arbitrarily.



Comparison of mean and maximum absolute errors (in kJ mol<sup>-1</sup>) of calculated tautomerization energies in water.

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Role of the radii scaling on the SMD accuracy. Reproduced with permission from *J. Phys. Chem. A* **2018**, 122, 4366. © 2018 ACS.

### Defining custom solvents

If the solvent is not in the list,<sup>2</sup> do the following:

- Set the solvent name as **Generic**.<sup>3</sup>
- Solvent parameters can be found from sources such as the CRC Handbooks of Chemistry and Physics, NIST webbooks, and the Minnesota Solvent Descriptor Database.<sup>4</sup>

1. Ho, Klamt, Coote, *J. Phys. Chem. A* **2010**, 114, 13442.

2. SCRF, <http://gaussian.com/scrf/?tabid=Z>. 3. Gaussian Tip: Defining Solvents for SMD Calculations,

<https://gaussian.com/smdtip/>. 4. Minnesota Solvent Descriptor Database,

<https://comp.chem.umn.edu/solvation/mnsddb.pdf>. All links accessed on 03.03.2025.