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Physikalische Chemie III
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Aktenzeichen

Ort

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RE: Role of the SAMPL challenges for research in the Kast group (TU Dortmund)

To whom it may concern:

With this letter I want to express my deep gratitude to the organizers of the SAMPL challenges for their effort in providing the community of computational and theoretical chemists with truly meaningful data for testing their models.

My group is engaged in research in the field of liquid state theory for more than 15 years. Our theoretical platform is integral equation theory for describing solvent distributions, which comes in various flavors. Site-site or molecule-site approaches are available using classical or polarizable force fields, but these methods can also be coupled to a quantum-mechanical description of the solute. This latter approach has been termed EC-RISM ("embedded cluster reference interaction site model") by us in 2008 [1] and is now recognized as one of the promising candidates for an (almost) "ab initio" treatment of solvation thermodynamics [2] which extends beyond the limits of established continuum solvation models.

The SAMPL challenges played a key role for validating and further developing the EC-RISM methodology early on. We first contributed to the SAMPL2 challenge in 2009 on the prediction of tautomer preferences of small organic molecules in aqueous solutions [3]. This was a first truly meaningful benchmark of the methodology where we ranked first (averaged over the training set provided and the independent test set to be predicted) [4]. The results revealed subtle details to work on further, such as differing predictive capabilities between 5- and 6-membered rings.

Our next contribution was to SAMPL5 in 2015 on pH-dependent $\log D$ predictions of the distribution of ionizable species between an aqueous and a cyclohexane phase, a very difficult task [5]. Here, we were not prepared sufficiently, ranking in the top 25% with a limited model. The outcome triggered a lot of ongoing work which now makes us confident that we can develop a more complete model covering tautomers, protonation and

conformational equilibria. We are planning to contribute to the upcoming SAMPL6 challenge (likely on $\log D$ predictions between water and octanol), where we are confident to be able to score better than within SAMPL5.

The SAMPL challenges and competitions are therefore of utmost importance for our future work and I strongly support the organizers. The key benefit of SAMPL is **confidence** in methods, not only for us, but also recognized by the wider community, which is even more important. Solid thermodynamic predictions allow for enhanced predictive capabilities in related matters derived from a wave function in solution, such as spectroscopic properties or force field development for condensed phases. In our particular case this led to high-impact publications in the field of NMR [6] and IR [7] spectra calculations for solutions under extreme conditions, or to a recent “editorial pick” publication on the parametrization of force fields suitable for high-pressure systems [8].

We expect a lot more to come, hoping strongly for continuing support of the SAMPL initiative. SAMPL represents what theory in science is all about.

Best regards,



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