

Investigation of Complex Systems by Hybrid QM/MM Molecular Dynamics Simulations

PhD Thesis

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During my PhD study, I was working on two problems inherent to hybrid quantum mechanical-molecular mechanical (QM/MM) simulations: development of a pseudopotential and improvement of sampling. In the first project I developed an appropriate QM/MM potential surface to investigate the properties of negatively charged methanol clusters. The simulations with the new pseudopotential are able to reproduce the most important physical properties (e.g. the optical spectrum, coordination number) of the excess electron in bulk methanol. The static analysis of possible electron binding sites to neutral methanol clusters showed that the excess electron binds to the neutral clusters due to their net dipole moment. The electron occupies very diffuse orbital and the localization exclusively occurs on the surface of the clusters. QM/MM dynamic simulations of the electron-methanol clusters revealed that for larger clusters (above 205 methanol molecules) the electron that initially localized on the surface penetrates into the interior of the clusters and a significant increase of the binding energy can be observed. The results are in a good qualitative agreement with the experimental data and bring one to understand better the physical behavior (i.e. the different trends of the vertical detachment energy in water and methanol clusters with cluster size) of electron-polar solvent clusters in which up to now there is still no consensus. Besides its good predictive power, the pseudopotential has an additional advantage compared to the previous ones, namely the transferability of the parameters. This opens the possibility to construct new pseudopotentials to investigate other electron-polar solvent systems (e.g. ethanol and ammonia) or even biomolecules (e.g. DNA) in a consistent way.

The other project was a methodological improvement, in which I applied a special general reaction coordinate, the energy gap (*Egap*) to investigate the chloride – methyl chloride substitution reaction in gas phase and aqueous solution. Although *Egap* is originally defined on a classical potential energy surface in the framework of the Empirical Valence Bond theory, I was able to apply it successfully on higher level of theory (i.e. QM(PM3) and QM(PM3)/MM level). *Egap* was compared to a geometrical coordinate distance difference (*DD*). The efficiency and hysteresis of the free energy profile of the reaction coordinates were investigated using modern fast PMF methods (Metadynamics and Adaptive Biasing Force). The results showed that free energy profiles of *Egap* converge much faster than those of *DD*. To investigate the correct indication of the transition state (TS) by *Egap* and *DD*, the committor analysis was performed. Although *DD* is widely applied reaction coordinate for this reaction, it has failed the committor test in water solution, while *Egap* behaved as a good reaction coordinate and indicated correctly the TS. The constructed chimera programs give the opportunity to use *Egap* on higher level of theory to investigate reactions in even more complex systems such as enzymatic environments.