Development of a perturbative QM/MM Monte Carlo method for the study of molecules in solution

Ricardo A. Mata[1]

[1] Institut für Physikalische Chemie, Georg-August-Universität Göttingen, Germany

Hybrid quantum mechanics / molecular mechanics (QM/MM) coupled with molecular dynamics (MD) is a widespread method for the study of chemical processes in condensed media. In this methodology, the total system is separated into two regions, a small portion described by quantum mechanics while the remaining environment is represented with classical forcefields. Nevertheless, each time step requires an energy and gradient evaluation, which can be extremely demanding even for the smallest QM regions. The problem is further aggravated by the fact that hundreds of thousands of points are often needed to build a reasonable sampling space. This leads to great computational demands, even though most of the degrees of freedom sampled are located in the MM region.

A possible solution to the problem is the use of Monte Carlo (MC) simulations, whereby the degrees of freedom in the QM and MM regions can be separated. Formulations have been suggested for quite some time,[1, 2] but found no widespread use. We have recently revisited these earlier QM/MM MC formulations and have developed an efficient code for simulations in solution. Our method makes use of a biased sampling dependent on the cost of the electronic structure calculation, rendering the MC simulation in the presence of solvent molecules as accessible as a gas phase run. These developments are particularly promising for the computation of anharmonic vibrational spectra in solution and comparison of conformational isomers of common biomolecules.

[1] Cubero, E., Luque, F., Orozco, M., Gao, J. *J. Phys. Chem. B*, 107:1664, 2003.

[2] Truong, T., Stefanovich, E. *Chem. Phys. Lett.*, 256:348, 1996.