FREE ENERGY SIMULATIONS WITH QM/MM USING DFTB3, GROMACS AND PLUMED

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The approximative density-functional method DFTB3 has been implemented in the Gromacs package version 5, complementing the existing QM/MM interface. The tight integration within the program gives rise to favorable efficiency, and makes it possible to employ a full PME-based treatment of QM/MM electrostatic interaction. Therefore, unnecessary artifacts are avoided in simulations involving polar or even charged QM regions. An appealing feature is that QM/MM calculations of potentials of mean force are available, both with the Gromacs pull functionality and with the Plumed plugin.

Applications to several testing systems are presented. Free energy for the ultra-fast proton transfer reaction in solvated malonaldehyde is obtained from umbrella sampling as well as free simulations; the choice of reaction coordinate is discussed. The conformation of alanine dipeptide is investigated with both free simulations and metadynamics; QM/MM and pure MM simulations are compared, as are various treatments of QM/MM electrostatics. Finally, a cyclobutane thymine dimer lesion in DNA is simulated, both in a neutral state and as a radical anion, which represents a metastable state.

Also discussed will be the issue of mobile molecules moving between QM and MM regions. A new adaptive QM/MM scheme is introduced as a possible solution, avoiding any discontinuities in the simulations and offering efficient parallelization of the calculation.

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