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QM(SAC-CI)/MM Calculations with Gaussian: Excited States in Liquids and Enzymes

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When molecular systems are too large to treat on a quantum mechanical (QM) level, the combination with molecular mechanics (MM) can be a good solution. The system is then divided into a small region of interest and treated by QM whereas the bulk is treated by MM. This results in the so-called QM/MM methods. Numerous implementations exist, primarily differing in the way in which broken bonds are treated. Practically all of these methods use a combination of individual QM and MM programs to achieve the desired results. This entails adding an interface to one of these applications and passing information through external files.[1] This is not an ideal situation as both programs have to be obtained and studied how to use. It also means that most of the time two sets of input files have to be maintained.
The aim of this study was the implementation of a QM/MM method within Gaussian, a widely used QM program. It already had the ONIOM method, which can be configured as a special QM/MM method, but has a wider use in multilayer and combined QM/QM applications. For that method, a number of MM force fields were added: AMBER, CFF and DREIDING. Using these, it was possible to implement a QM/MM method all within one program.

All QM methods, be it semi-empirical, Hartree-Fock, or post-Hartree-Fock, can be used to describe the QM region. The MM region can be described either by one of the three internal force fields, by an externally interfaced CHARMM force field or any other external program. The basic implementation uses the same ideas as the ONIOM implementation: atoms are given an MM atom type and added to either the QM or MM region. During geometry optimisations, the atoms of the MM region can be given extra optimisation cycles, so-called microiterations. These are handled in a different way. Depending on whether electronic embedding is used, ONIOM either uses the MM force field as is or it uses ESP-charges as classical charges on the QM atoms. This leads to the use of a different set of forces during the normal optimisation and the microiterations. This is problematic when, for example, during the microiterations the MM region is completely optimised whereas during the normal optimisation this is not yet the case. As such convergence can never be achieved. In the QM/MM method presented, the part of the forces on the MM atoms due to the interactions between the QM electron density and the MM charges is saved. During the microiterations these forces are added to the MM atoms at each iteration. This only solves the problem exactly at the first iteration and still exhibits it at subsequent iterations. This problem, however, cannot be solved exactly without recalculating the entire wavefunction at each microiteration, thereby completely eliminating the advantages of using these microiterations.

The treatment of broken bonds is based on the Linkatom method. It differs from other implementations in three aspects: the set of bonded cross-terms described by the MM force field, the positioning of the linkatoms during geometry optimisations and the treatment of classical charges close to the QM region.[2] These aspects were optimised by comparing geometries, rotational barriers, electron density maps and proton affinities of a set of small molecules. The bonded cross-terms are those used in the GAMESS/CHARMM interface with the omission of the MM valence angle QM-QM-MM. The linkatom is positioned by the

method used in the DYNAMO library: it is kept at a fixed distance from the nearest QM atom and on the broken bond. As its position depends parametrically on the neighbouring QM and MM atoms, its forces can consequently be transferred to these atoms. The charges on the MM atoms close to the QM region are scaled according to a scheme that zeroes out the charge on the nearest MM atom and redistributes this charge to the surrounding atoms while always recovering the total system's charge exactly. The nature of the implementation in Gaussian allows for easily adding different Linkatom methods for a greater diversity of available methods.

The QM/MM method was applied to the study of the excited states of liquids and enzymes. For highly accurate results, the QM region was described by the SAC-CI method, an efficient Coupled-Cluster based method developed specifically for the study of excited states.
A first type of applications is the solvatochromic shift of acetone and 1-naphthol in multiple solvents. Here the solute is described by the SAC-CI method and surrounded by a 20 Å layer of solvent molecules. Although methods exist that are suited more specifically to solvation effects, these applications are a good test for the implementation of the QM/MM method.
For acetone, the ground state geometries were determined using the SAC/D95(d):AMBER method. Afterwards the excitation energies were determined using SAC-CI:AMBER with the cc-pVTZ basis set augmented with one Rydberg s- and p-function on each of the Carbon and Oxygen atoms. For the molecule in the gas phase, an excitation energy of 4.4871 eV was obtained, in excellent agreement with the experimental value of 4.476 ± 0.012 eV.
1-Naphthol was first optimised using the SAC/D95(d):CHARMM method and afterwards the SAC-CI:CHARMM method was used with the cc-pVDZ basis set augmented with two Rydberg s- and p-functions on each of the Carbon and Oxygen atoms to determine the excitation energies. The obtained excitation energy for the molecule in the gas phase was 4.0915 eV, differing slightly from the experimental value of 4.381 eV.
As in other theoretical studies of the solvatochromic shift, when water was used as a solvent, explicit water molecules had to be considered in order to correctly reproduce the type of shift: a blue-shift instead of a red-shift. The results for these calculations will be discussed and compared with the gas-phase structures to determine the exact shift.

Enzymes pose a more challenging situation. In this case bonds have to be broken when dividing the system into QM and MM regions so linkatoms have to be added. The optical properties of the Green Fluorescent Protein (GFP) are actively studied in Nakatsuji Laboratory. The chromophore is the active center and is treated as the QM region in the QM/MM description. This results in a 30 atom QM region connected via two linkatoms to the 3788 atoms of the surrounding MM region. The ground state geometry was obtained using B3LYP/6-31G*:AMBER. The geometry of the lowest excited state (HOMO-LUMO) was determined using CIS/6-31G*:AMBER. The resulting geometry and fluorescence energy will be discussed in detail and compared with experimental values.

[1] B. Swerts, J. Vandroogenbroeck, A. Peeters, C. Van Alsenoy, J. Phys. Chem. A 106 (2002) 424
[2] B. Swerts, Ph. D. Thesis (2004)