Adaptive Solvent QM/MM MD with AMBER

Andreas W. Götz†, Rosa E. Bulo‡, and Ross C. Walker†

†San Diego Supercomputer Center, University of California San Diego, 9500 Gilman Dr, 92036 La Jolla, CA, USA
Email: {agoetz,rcw}@sdsc.edu

‡Department of Theoretical Chemistry, Faculty of Sciences, VU University Amsterdam, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands
Email: bulo@few.vu.nl

QM/MM
Quantum mechanical (QM) methods for molecular dynamics (MD) simulations are required to overcome the primary limitations of classical molecular mechanics (MM) potential energy functions. This includes the ability to
- describe charge transfers
- break/form chemical covalent bonds

QM methods require none or less parameters than MM based approaches and can be applied to systems which are typically not covered by traditional force fields such as proteins that employ co-enzymes and catalytic or structural metal centers.

Because of far higher computation time of the QM Hamiltonian relative to MM, one uses coupled QM/MM [1,2,3] potential based simulations.

\[ E = E_{QM} + E_{MM} + E_{QM/MM} \]
in which the reactive or structurally important part is described with a QM based potential while the surrounding protein and solvent region is treated with an MM potential.

QM/MM Solvent Diffusion Problem

The established static QM/MM partitioning into QM solute or QM reactive center and MM solvent cannot be applied if
- the solvent is part of a reaction
- QM interactions between solute and solvent are important

Inclusion of some solvent molecules into the QM region is problematic because they
- can diffuse away from the solute or reactive center into the MM region

on the time scales that are of relevance for the observation of reactions or structural changes.

Adaptive QM/MM Method

Solute molecules are allowed to change their QM character during the simulation, depending on their position relative to a permanent QM region (solute or reactive center). In order to obtain a smooth potential energy surface and avoid discontinuities in the forces, we employ a transition region around the permanent quantum region within which solvent molecules gradually change their character from QM to MM.

We are using the difference based adaptive (DAS) solvation approach [3]. The QM character of solvent molecule \(i\) is described by a position-dependent coefficient with a sigmoid switching function:

\[ \lambda_i(r_i) = \begin{cases} 0 & r_i < R_1 \\ \frac{r_i - R_1}{R_2 - R_1} & R_1 \leq r_i \leq R_2 \\ 1 & r_i > R_2 \end{cases} \]

The energy is a weighted average of QM/MM energies for different partitionings which successively include all solvent molecules in the transition region:

\[ E(r) = \sum_{i=1}^{N} \sigma_i(r_i)E_{i} \]

The weight for each partitioning is determined by the quantum character of the molecules in the transition region such that normalization is guaranteed:

\[ \sigma_i = \lambda_{i+1} - \lambda_i \]

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