Advances in Hybrid Potential Simulations of Condensed Phase Systems

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• Introduction

• Hybrid Potentials & Dynamo

• Examples

• Adaptive Algorithms
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• The Dynamo team and community
Inspired initially by the approach of Warshel and Levitt.

Hybrid QC/MM Potentials

Boundary

QC

Interactions

MM
QC Potentials:

\[
\hat{H}\Psi = E\Psi
\]

• *Ab initio* DFT and HF — Gaussian basis functions.
• Various semi-empirical methods.

MM Potentials:

• AMBER, CHARMM, OPLS-AA, UFF force fields.

Boundary Methods:

• Periodic boundary conditions.
• Truncated systems.
QC/MM Non-bonding Interactions:

- Electrostatic — full ($e^-$ and $n^+$) or multipole
- Lennard-Jones
- Polarization
QC/MM Methods III

Link Atom Method

Hybrid Orbital Methods
Putting the separate terms together gives, for MO and DFT methods, respectively:

\[ \hat{H}_{\text{Eff}} \Psi = E \Psi \quad \text{where} \quad \hat{H}_{\text{Eff}} = \hat{H}_{\text{QC}} + \hat{H}_{\text{MM}} + \hat{H}_{\text{QC/MM}} \]

\[ E[\rho] = E_{\text{QC}}[\rho] + E_{\text{MM}} + E_{\text{QC/MM}}[\rho] \]

Solving the HF or DFT/KS equations gives the potential energy of the system as well as the wavefunction or electron density. The forces on the particles can be determined from the energy as:

\[ F = -\frac{\partial E}{\partial R} \]

and then used in the appropriate simulation algorithm.


The library is available at:

http://www.pdynamo.org
A platform for the development and testing of simulation algorithms that is *clear, extensible, simple and reasonably efficient*.

- **Python/C:**
  - Python for the majority of operations.
  - C for speed.

- A series of Python packages.

- Object-oriented structure.

- Provides a framework to build complex algorithms:
  - ONIOM, path integrals, replica exchange, ...
Diisopropyl Fluorophosphatase

*JPC B 2014*
Enzymes II

Peptidoglycan Deacetylase

JCP B 2017
Adaptive QC/MM Methods I

A buffer zone in which there is a smooth transition between QC and MM representations.
Existing algorithms include:

- Hot-spot methods of Hofer, Rode et al. (single or double QC calculation with smoothing of forces only).

- Permuted adaptive partitioning method and its derivatives from Heyden, Lin and Truhlar, along with developments by others (Bulo et al, ...).

All methods are either (i) very costly or (ii) numerically inconsistent.
The PAP method considers all $2^N$ possible QC/MM partitionings that arise from the $N$ transformable fragments within the buffer zone. Each fragment is given a weight, $\lambda_I$, that determines its QC ($\lambda_I$) or MM ($1-\lambda_I$) character. This gives the energy:

$$ E_{PAP} = \sum_{P=1}^{2^N} w_P E_P $$

$$ w_P = \prod_{I \in QC} \lambda_I \prod_{J \in MM} (1-\lambda_J) $$

Can we use this scaling idea in a more efficient fashion?
SISPA Algorithm I

Buffer Region

QC Core
\( \lambda = 1 \)

QC \(_i\) \( \lambda_1 \)

QC \(_j\)

\( (1-\lambda_1) \)

\( (1-\lambda_1)^*\lambda_j \)

\( \lambda_1^*\lambda_j \)

MM \(_i\)

\( (1-\lambda) \)

\( (1-\lambda)^*(1-\lambda_j) \)

\( \lambda_1^*(1-\lambda_j) \)

MM Environment
\( \lambda = 0 \)

\( \lambda \)

\( \lambda_i \)

\( \lambda_1 \)

Fragment Corrections

\( -\lambda_i^* \text{MM}_i \)

\( -(1-\lambda_i)^* \text{QC}_i \)
SISPA Algorithm II

Single QC calculation with continuous energy and forces.
SISPA Algorithm III

Results very sensitive to the balance between the QC and MM potentials.
SISPA Algorithm IV

- An adaptive QC/MM algorithm that has approximately the same cost as a fixed partitioning QC/MM method and is numerically consistent.

- Non-trivial to implement.

- Adaptive algorithms, including SISPA, place extra demands on the compatibility of the individual potentials and their coupling.

Thank you for your attention!