Hybrid QM/QM Open-Shell Local Correlation Methods for the Study of Metal Ions with Biomolecular Ligands

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Overview

- Local correlation methods
  - Overview
  - Region calculations

- Reaction mechanism of sulfite oxidase
  - Competing reaction pathways

- Regions calculations on metal sites
  - Sulfite oxidase
  - First open-shell applications
Wave function methods

Hartree-Fock

\[ \Psi_{\text{HF}}(x_1, x_2, \ldots, x_N) = \frac{1}{\sqrt{N!}} \begin{vmatrix} \psi_1(x_1) & \psi_2(x_1) & \ldots & \ldots & \psi_N(x_1) \\ \psi_1(x_2) & \psi_2(x_2) & \ldots & \ldots & \ldots \\ \ldots & \ldots & \ldots & \ldots & \ldots \\ \psi_1(x_N) & \ldots & \ldots & \ldots & \psi_N(x_N) \end{vmatrix} \]

Mean field theory
for molecules with less than 10 atoms, you can safely compute almost everything

- well-defined hierarchy
- formally scales as:
  - HF \( N^4 \)
  - MP2 \( N^5 \)
  - CCSD \( N^6 \)
  - CCSD(T) \( N^7 \)

- CCSD(T) is “gold” standard
Wave function methods

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Local correlation methods

- Electron correlation is a short-range effect, best described with the use of local orbital spaces

- Through the use of local orbitals:
  - The excitation space is truncated (PAO domains)
  - The number of orbital pairs is limited through distance criteria (strong, close, weak, distant, very distant)

- Linear scaling algorithms for LMP2, LCCSD and LCCSD(T) are available
Local correlation methods

**canonical**

**virtual**

**occupied**

**local**
Computational timings

- CCSD Iteration: \( \sim N^7 \) and \( \sim N^6 \)
- LCCSD Iteration: \( \sim N \)
- L(T): \( \sim N \)
Correlation regions

Reaction mechanism of sulfite oxidase
Catalytic cycle of sulfite oxidase

Mo (VI) Fe (III) \[\xrightarrow{\text{SO}_3^{2-} + \text{H}_2\text{O}}\] \[\text{SO}_4^{2-} + 2\text{H}^+\]

Mo (IV) Fe (III) \[\xrightarrow{\text{H}_3\text{C}-\text{S}-\text{O}}\] \[\text{H}_3\text{C}-\text{S}-\text{O}\]

Mo (V) Fe (II) \[\xrightarrow{\text{H}_3\text{C}-\text{S}-\text{O}}\] \[\text{H}_3\text{C}-\text{S}-\text{O}\]

Mo (VI) Fe (II) \[\xrightarrow{\text{H}_3\text{C}-\text{S}-\text{O}}\] \[\text{H}_3\text{C}-\text{S}-\text{O}\]
Molecular mechanism of the oxo transfer

- $S \rightarrow O Mo$ mechanism
  Thapper et al.
  Hernandez-Marin and Ziegler

- $O \rightarrow Mo$ mechanism
  Sarkar et al.

- $S \rightarrow Mo$ mechanism
S → OMo  mechanism
Which mechanism is favorable?

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Transition state</th>
<th>ΔG (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S → OMo</td>
<td>sulfite binding to O-Mo</td>
<td>192.47</td>
</tr>
<tr>
<td>O → Mo</td>
<td>coordination of O-S to Mo</td>
<td>226.30</td>
</tr>
<tr>
<td>S → Mo</td>
<td>bond formation between SO₃ and O</td>
<td>269.58</td>
</tr>
</tbody>
</table>
$S \rightarrow OMo$ mechanism – results

$HSO_3^-$ substrate

$E$ (kJ/mol)

- LCCSD(T0):LMP2
- LCCSD(T0)
- LMP2
- MP2

S -> OMo mechanism

RS TS1 IM1 TS2 PS

Diagram showing energy levels for different states and methods.
First applications in open-shell systems
Binding energies

$$\Delta E_{\text{int}} (L_n) = E([ML_n]^c) + mE(H_2O) - E([M(H_2O)_m])^{2+} - (\Sigma_i E(L_i))^{c-2}$$
Cu$^{2+}$ in linear coordination geometry

\[
\begin{align*}
\text{Cu}^{2+} & \quad \begin{array}{c}
\text{H} \\
\text{O} \\
\text{Cu} \\
\text{O} \\
\text{H} \\
\text{H}
\end{array} \\
\text{H} & \quad \begin{array}{c}
\text{S} \\
\text{C} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H}
\end{array} \\
+ & \quad \begin{array}{c}
\text{H} \\
\text{O} \\
\text{Cu} \\
\text{S} \\
\text{C} \\
\text{H}
\end{array} \\
& \quad \begin{array}{c}
\text{H} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{H} \\
\text{H}
\end{array}
\end{align*}
\]

E (kcal/mol)

-330.00
-320.00
-310.00
-300.00
-290.00

LOCAL METHOD
UCCSD(T)
RMP2
LRMP2:HF
LUCCSD(T)
LUCCSD(T):HF
LUCCSD(T):LRMP2

LRMP2
LRMP2:HF
LUCCSD(T)
LUCCSD(T):HF
LUCCSD(T):LRMP2
$\text{Cu}^{2+}$ in tetrahedral coordination geometry
What’s next?

Target Applications:

● Calibration of lower-level methods for applications in structure refinement

● Calculation of reaction barriers in closed-shell and high-spin open-shell systems

● Study of specific metal-biomolecule interactions, including oligopeptides and oligonucleotides
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