Larger Molecules / Longer Time Scales

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Extending Quantum Chemistry

- Extend accuracy and/or size range of quantum chemistry?
- Remember the canon!

“Right Answer”

Basis set

Minimal Basis Set/Hartree-Fock

Minimal Basis Set Full CI

Complete Basis Set/Hartree-Fock

Electron Correlation
Taking the Canon Seriously

Can we estimate the exact answer?
Hypothesis: One- and Many-particle basis set contributions to energy are additive
Implies that electron correlation and the flexibility of the electronic wfn are independent – cannot be true...
Examples: Gaussian-2 (G2); Complete Basis Set (CBS)

\[
E_{\text{extrapolated}} = E_{HF/SBS} + (E_{Corr/SBS} - E_{HF/SBS}) + (E_{HF/LBS} - E_{HF/SBS}) \\
= E_{Corr/SBS} + E_{HF/LBS} - E_{HF/SBS}
\]

These methods only work well when the SBS is big enough to qualitatively describe correlation, i.e. polarized double-zeta or preferably better

Beyond the Canon...

Can consider a 3-dimensional version of the canon – the new dimension is model size/faithfulness. For example, consider the following sequence of models:

Should not ask about total energy, but rather about energy differences, e.g. $D_e(OH)$ in the above examples. Always looking for $\Delta E$ anyway – total energies are not experimentally observable for molecules.
Extending the Canon - IMOMO

Canon is now a cube...

- Again, assume additivity:
  \[ E_{\text{real/LBS/Corr}} \approx E_{\text{small/SBS/HF}} + (E_{\text{small/LBS/HF}} - E_{\text{small/SBS/HF}})^+ + (E_{\text{small/SBS/Corr}} - E_{\text{small/SBS/HF}})^+ + (E_{\text{real/SBS/HF}} - E_{\text{small/SBS/HF}})^+ \]

- Can be very sensitive to choice of small model...

- Test thoroughly for your problem!

IMOMO Simplified

If we lump basis set and correlation method together, we can just write:

\[ E_{\text{high,real}} \approx E_{\text{low,real}} + E_{\text{high,model}} - E_{\text{low,model}} \]

where high and low are the “high-level” and “low-level” methods and “real” and “model” are the target and truncated molecules.

Example: Proton Affinity – See Lab this afternoon
IMOMO Example

$S_{N2}$ Reaction Energy

IMOMO Example

Geometry optimization (per cycle)

(CH₃Cl)(H₂O)
Pure MP2/b = 5544 sec
ONIOM(MP2/b:B3LYP) = 1178 sec

(CH₃Cl)(H₂O)₂
Pure MP2/b = 15782 sec
ONIOM(MP2/b:B3LYP) = 1602 sec

Single point calculation

(CH₃Cl)(H₂O)
Pure CC/b = 16440 sec
ONIOM(CC/b:MP2) = 1629 sec

(CH₃Cl)(H₂O)₂
Pure CC/b = 104965 sec
ONIOM(CC/b:MP2) = 1922 sec

Errors of approx. 2 kcal/mol per solvent molecule in absolute energies; and 1-2 kcal/mol in reaction energetics
Multi-Level for Transition States?

- Simple variant of previous ideas
  - Optimize w/low-level method (e.g. HF/3-21G)
  - Energies w/high-level method (e.g. CCSD/cc-pvtz)
  - Predict heat of reaction by difference of high-level E
- Why not do the same for TS?
Why do Rxns have Barriers?

It’s the electrons, ...

Simple example: $H_2 + H \rightarrow H + H_2$

\[
\begin{pmatrix}
V_{HH-HH}(R) & V_{12}(R) \\
V_{12}(R) & V_{HH-HH}(R)
\end{pmatrix}
\]

“diabats,” often reasonably approximated as harmonic

\[
V_{HH-HH}(R) = \left\langle \psi_{HH-HH} \right| \hat{H}_{el} \left| \psi_{HH-HH} \right\rangle
\]

\[
V_{12}(R) = \left\langle \psi_{HH-HH} \right| \hat{H}_{el} \left| \psi_{HH-HH} \right\rangle
\]

Adiabatic PES – w/barrier

Crudely approx’ed as constant
Shift and Distort...

To see the point, we need to complicate things...
Consider $XCH_3 + Y^- \rightarrow X^- + H_3CY$

- Correlation and basis set affect frequency and relative energy of diabatic states

TS moves!
Hope springs eternal...

- It turns out that the MEP does not change much...
- Determine MEP at low-level first
- Search along low-level MEP for maximum to get estimate for high-level barrier height – “IRCMax”

Empirical Valence Bond (EVB)

- Parameterize diabats and couplings
- One potential energy surface per bonding topology
- More potential energy surfaces, but advantage is that they are simpler than adiabatic surfaces
- Possible to incorporate solvent effects
- Disadvantages
  - Diagonalize a matrix to get PES
  - Number of diabats quickly gets large unless few reactions are allowed...

Proposed by Warshel and Weiss
Recent applications – Voth, Hammes-Schiffer, others

Large Molecules Directly…

- Is there any way to solve electronic SE for large molecules w/o additivity approximations?
- O(N) Methods
  - Divide and conquer
  - Same ideas are applicable in ALL e⁻ structure methods
  - Generally harder to implement for correlated methods
  - Available in commercial code (e.g. Qchem)
- Pseudospectral Methods
  - Closely related to FFT methods in DFT and wavepacket dynamics
Pseudospectral Methods-Intro

Integral Contractions are major bottleneck in Gaussian-based methods

\[
\hat{F}^{2e} = \sum_i 2\hat{J}_i - \hat{K}_i \quad (pq \mid rs) = \int \frac{\chi_p (r_1) \chi_q (r_1) \chi_r (r_2) \chi_s (r_2)}{|r_1 - r_2|} \, dr_1 \, dr_2
\]

\[
F^{2e,J}_{pq} = \sum_{irs} c^{MO}_{ir} c^{MO}_{is} (pq \mid rs) = \sum_{rs} P_{rs} (pq \mid rs)
\]

Try a numerical grid...

\[
F^{2e,J}_{pq} = \sum_{grs} P_{rs} A_{rs g} R_{pg} R_{qg}
\]

\[
= \sum_g R_{pg} R_{qg} \left( \sum_{rs} P_{rs} A_{rs g} \right)
\]

\[
A_{rs g} = \int \frac{\chi_r (r_1) \chi_s (r_1)}{|r_1 - r_g|} \, dr_1
\]

\[
R_{pg} = \chi_p (r_g)
\]

N^4 work! 2N^3 work!
Pseudospectral Methods

Problem: # grid pts scales w/molecular size, but prefactor is usually very large

Pseudospectral Idea – Don’t think of numerical integration, but of transform between spaces

\[ R\psi_{\text{spectral}} = \psi_{\text{physical}} \]

\[ Q\psi_{\text{physical}} = \psi_{\text{spectral}} \]

\[ \psi_{\text{physical}} = \begin{pmatrix} \psi(r_{g1}) \\ \vdots \\ \psi(r_{gM}) \end{pmatrix} \]

\[ R_{pg} = \chi_p(r_g) \]

Q must be \( R^{-1} \)...

\[ Q = S(R^t wR)^{-1} R^t w \]

Least-squares fitting matrix
Pseudospectral Performance

- PS advantage depends on $N_g/N$ – smaller is better
- Not useful for MBS/small molecules
- HF and Hybrid DFT, $\approx 10x$ faster/100 atoms
- Advantage partly additive w/locality – local MP2 $\approx 30x$ faster/100 atoms
- Only available in commercial code – Jaguar (Schrödinger) (accessible at NCSA)

Eg where PS-B3LYP optimization and PS-LMP2 energy calculations are possible – active site of cytochrome $c$ oxidase

Quantum Effects

- Is there any need for quantum mechanics of nuclei in large molecules?
- Answer not completely known, but certainly yes for:
  - Tunneling – H⁺ transfer
  - Electronic Excited States – Photo-chemistry/biology
- Classical mechanics only works with one PES?!

What *should* happen
Traditional Methods

Need to solve TDSE for nuclear wavefunction:

\[
\frac{i}{\hbar} \frac{\partial}{\partial t} \psi(R,t) = \hat{H} \psi(R,t)
\]

- **Grid methods** (Kosloff and Kosloff, J. Comp. Phys. 52 35 1983)
  - Solve TDSE exactly
  - Require *entire* PES at every time step
  - Only feasible for $< 10$ degrees of freedom
- **Mean-Field** (Meyer and Miller, J. Chem. Phys. 70 3214 1979)
  - Classical Mechanics on Averaged PES
  - Problematic if PES’s are very different

\[
V_{\text{ave}}(R,t) = \sum_{i \in \text{electronic states}} n_i(t)V_i(R)
\]
Spawning Methods

- Classical mechanics guides basis set
- Adaptively increase basis set when quantum effects occur
- Best for t-localized quantum effects
- Effort \( \approx N \) Classical Trajectories, size of \( N \) controls accuracy

\[
\Psi(R;t) = \sum_I \sum_j C^I_j(t) \chi^I_j(R;t) |I\rangle
\]

Nuclear wavefunction

Electronic state

Spawning Application

- Transmembrane protein
- 248 AA/7 helices
- Chromophore: all-trans retinal
- 3762 atoms = 11,286 DOF
- Light-driven proton pump

Light-induced isomerization:
bR Photocycle

Can simulate first steps directly

Initial Geometry of RPSB
Sample Results

![Graph showing energy and dihedral angle changes over time.]

- **Energy / kcal mol⁻¹**
  - 0 10 20 30 40 50 60

- **Dihedral angle / degrees**
  - 0 30 60 90 120 150 180

- **Time / fs**
  - 0 300 600 900 1200

- **Percentage Changes**
  - Asp-212: 9%
  - Asp-85: 62%

- **Structural Diagram**
  - C9, C10, C11, C12, C13, C14, C15, N, H⁺