Larger Molecules / Longer Time Scales

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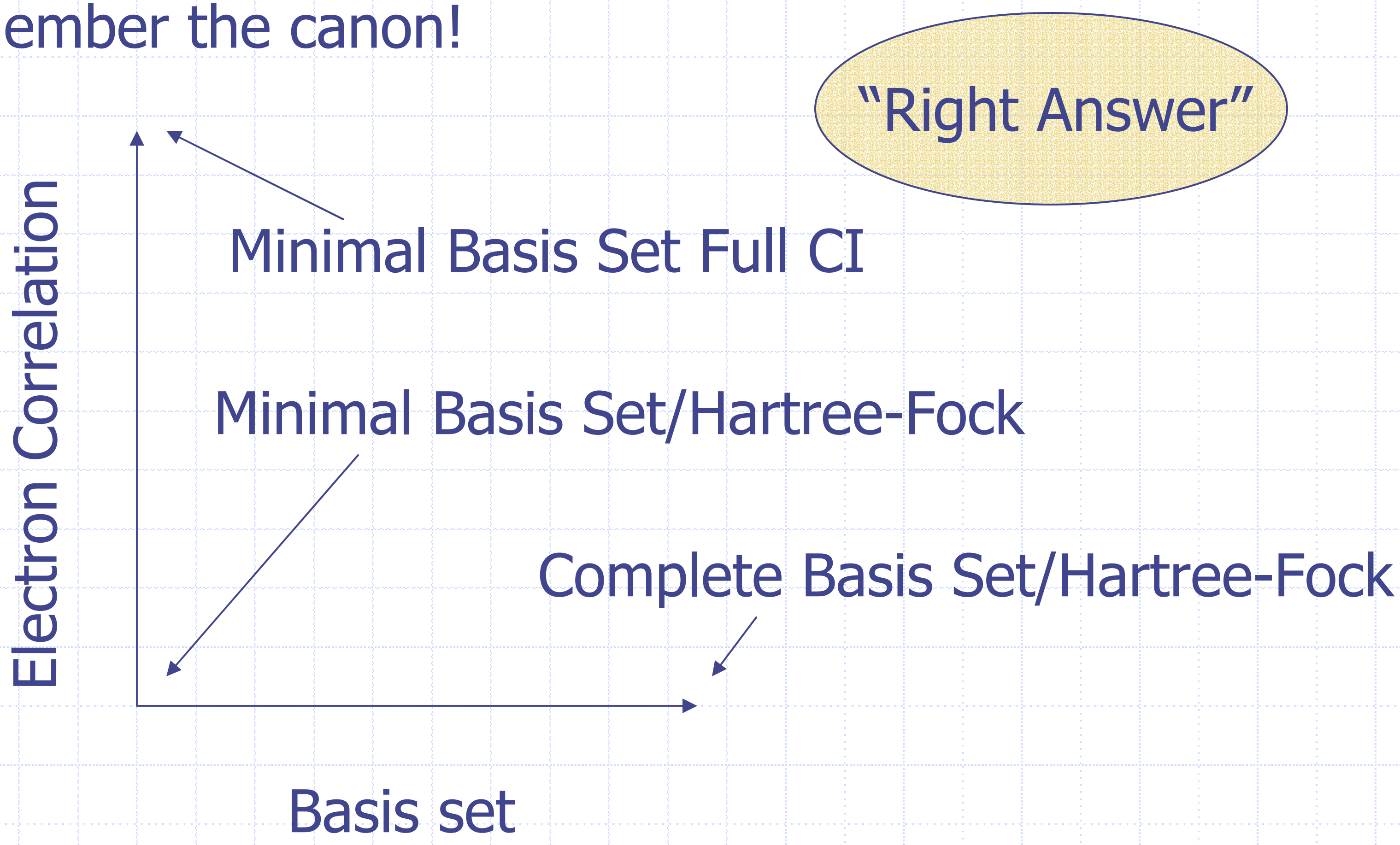
Extending Quantum Chemistry

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



"Right Answer"

Minimal Basis Set Full CI

Minimal Basis Set/Hartree-Fock

Complete Basis Set/Hartree-Fock

Electron Correlation

Basis set

Taking the Canon Seriously

Can we estimate the exact answer?

Hypothesis: One- and Many-particle basis set contributions to energy are additive

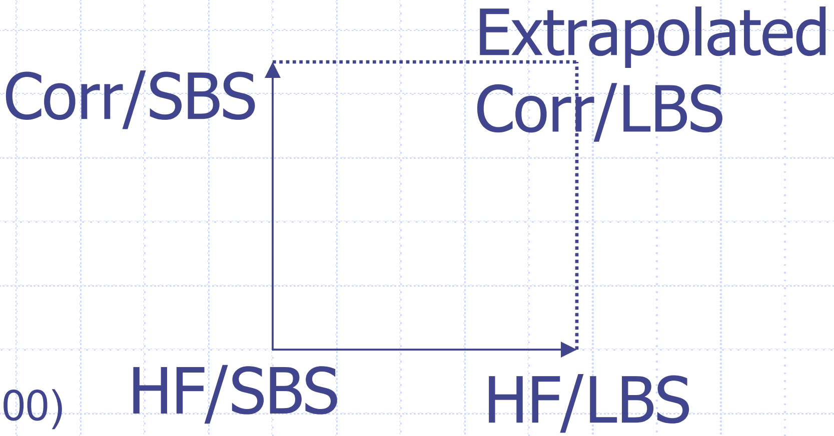
Implies that electron correlation and the flexibility of the electronic wfn are independent – cannot be true…

Examples: Gaussian-2 (G2); Complete Basis Set (CBS)

$$E_{extrapolated} = E_{HF/SBS} + \left(E_{Corr/SBS} - E_{HF/SBS}\right) + \left(E_{HF/LBS} - E_{HF/SBS}\right)$$

$$= E_{Corr/SBS} + E_{HF/LBS} - E_{HF/SBS}$$

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

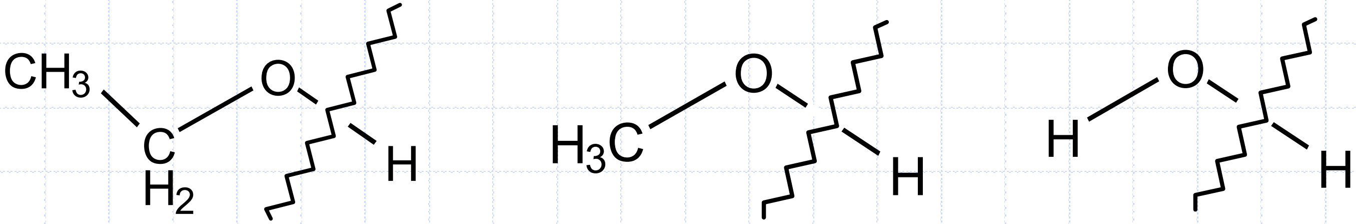


G2/G3 – Curtiss, et al. J. Phys. Chem. **105** 227 (2001)
CBS – Montgomery, et al. J. Chem. Phys. **112** 6532 (2000)

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:

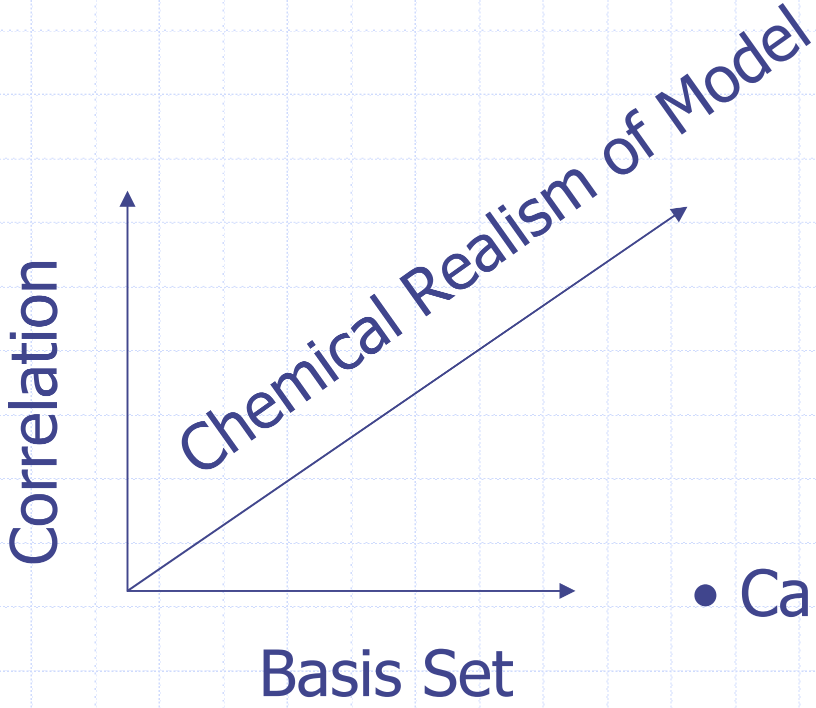


Should not ask about *total* energy, but rather about energy differences, e.g. D_e(OH) in the above examples.

Always looking for ΔE anyway – total energies are not experimentally observable for molecules.

Extending the Canon - IMOMO

Canon is now a cube…



- Again, assume additivity:

$$E_{real/LBS/Corr} \approx E_{small/SBS/HF} + (E_{small/LBS/HF} - E_{smal/SBS/HF}) + (E_{small/SBS/Corr} - E_{small/SBS/HF}) + (E_{real/SBS/HF} - E_{small/SBS/HF})$$

- Can be very sensitive to choice of small model…
- Test thoroughly for your problem!

Vreven, et al. J. Comp. Chem. **21** 1419 (2000)

IMOMO Simplified

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

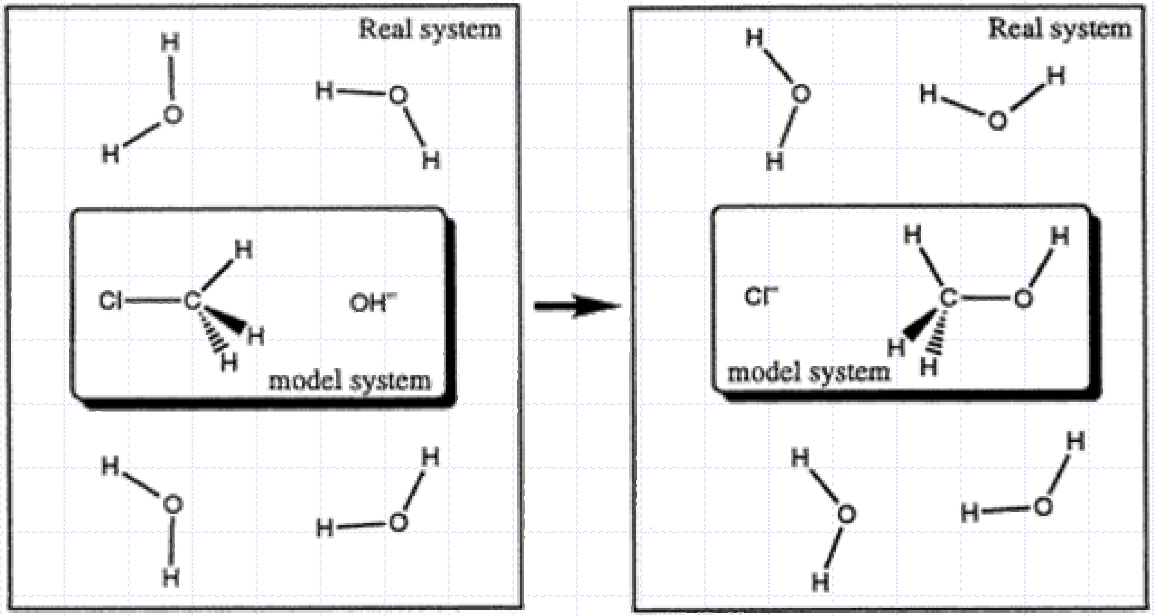
$$E_{high,real} \approx E_{low,real} + E_{high,\mathrm{model}} - E_{low,\mathrm{model}}$$

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

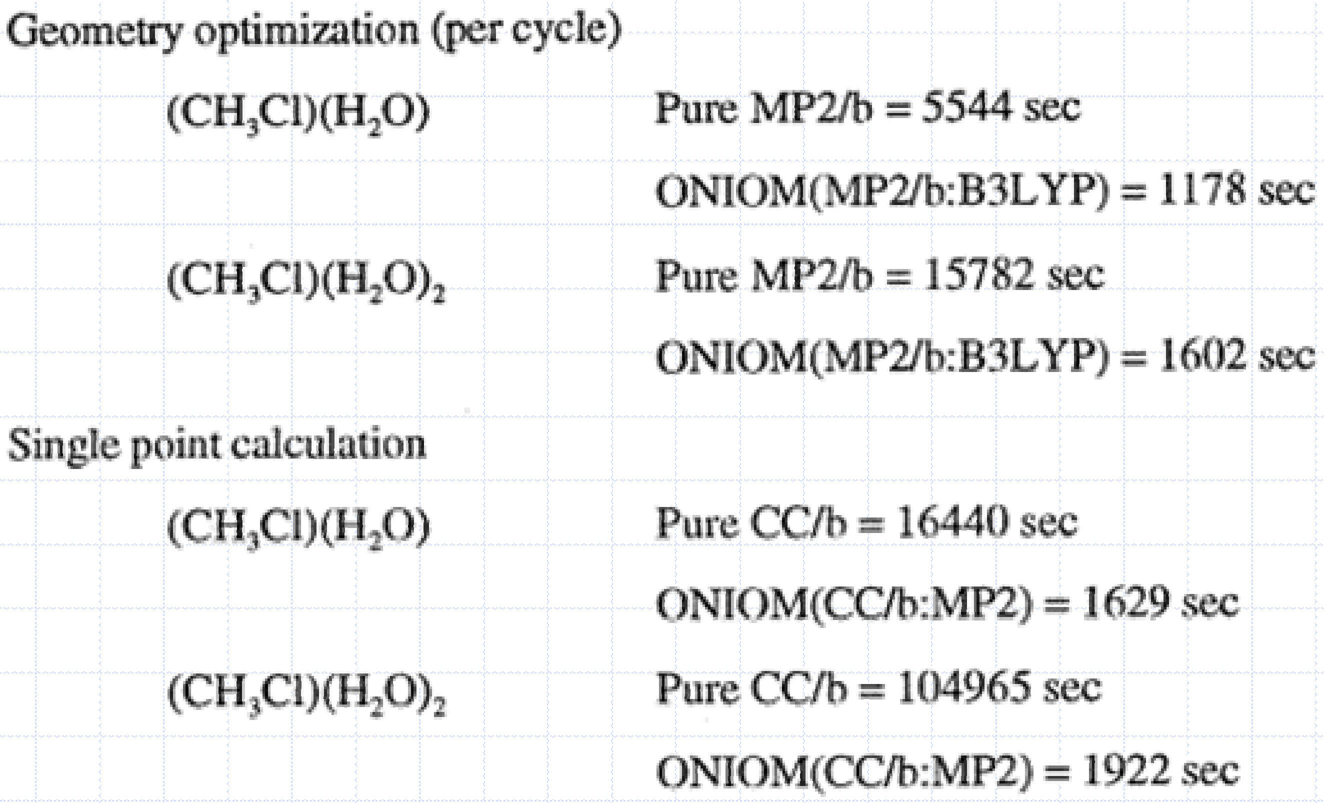
IMOMO Example

S_N2 Reaction Energy



Re, et al. J. Phys. Chem. 105A, 7185 (2001)

IMOMO Example



Geometry optimization (per cycle)	
$(CH_3Cl)(H_2O)$	Pure MP2/b = 5544 sec
	ONIOM(MP2/b:B3LYP) = 1178 sec
$(CH_3Cl)(H_2O)_2$	Pure MP2/b = 15782 sec
	ONIOM(MP2/b:B3LYP) = 1602 sec
Single point calculation	
$(CH_3Cl)(H_2O)$	Pure CC/b = 16440 sec
	ONIOM(CC/b:MP2) = 1629 sec
$(CH_3Cl)(H_2O)_2$	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

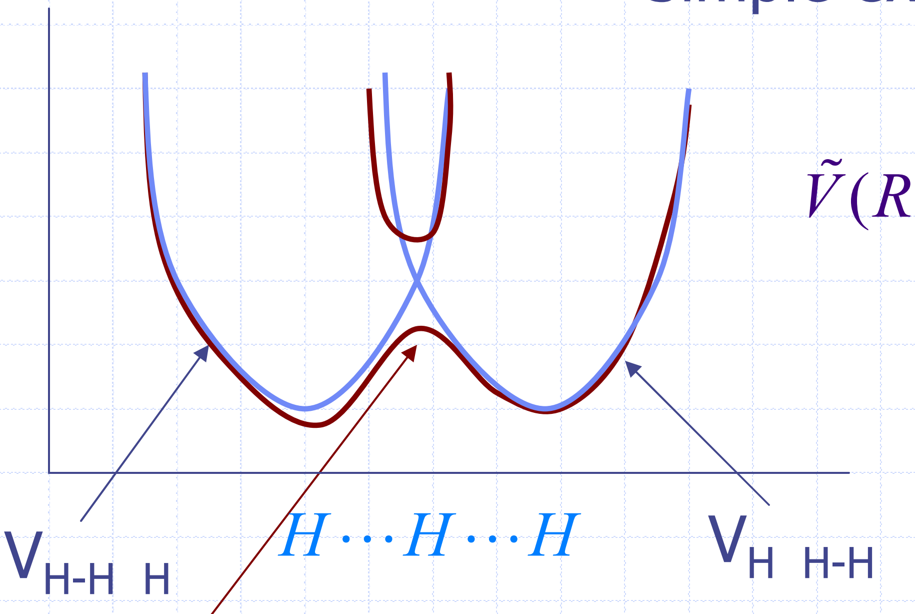
Multi-Level for Transition States?

- 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: $H_2 + H \rightarrow H + H_2$



Adiabatic PES – w/barrier

$$\tilde{V}(R) = \begin{pmatrix} V_{H\,H-H}(R) & V_{12}(R) \\ V_{12}(R) & V_{H-H\,H}(R) \end{pmatrix}$$

"diabats," often reasonably approximated as harmonic

$$V_{H\,H-H}(R) = \left\langle \psi_{H\,H-H} \middle| \hat{H}_{el} \middle| \psi_{H\,H-H} \right\rangle$$

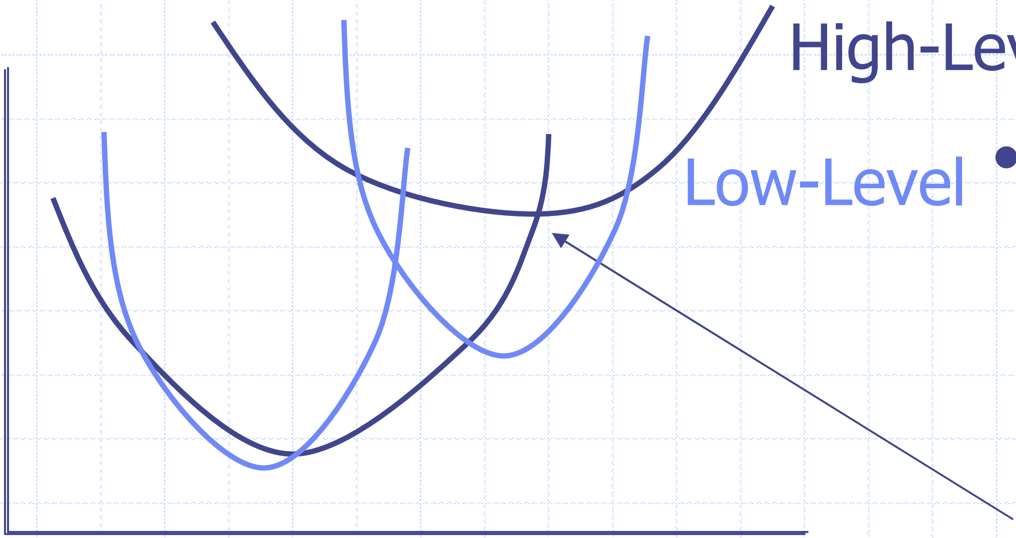
Crudely approx'd as constant →

$$V_{12}(R) = \left\langle \psi_{H\,H-H} \middle| \hat{H}_{el} \middle| \psi_{H-H\,H} \right\rangle$$

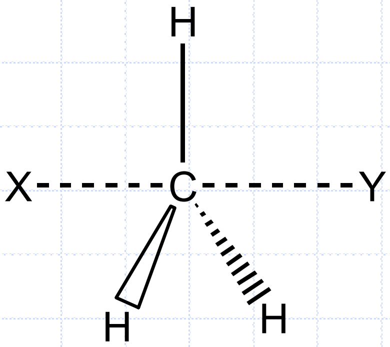
Shift and Distort…

To see the point, we need to complicate things…

Consider $XCH_3 + Y^- \rightarrow X^- + H_3CY$

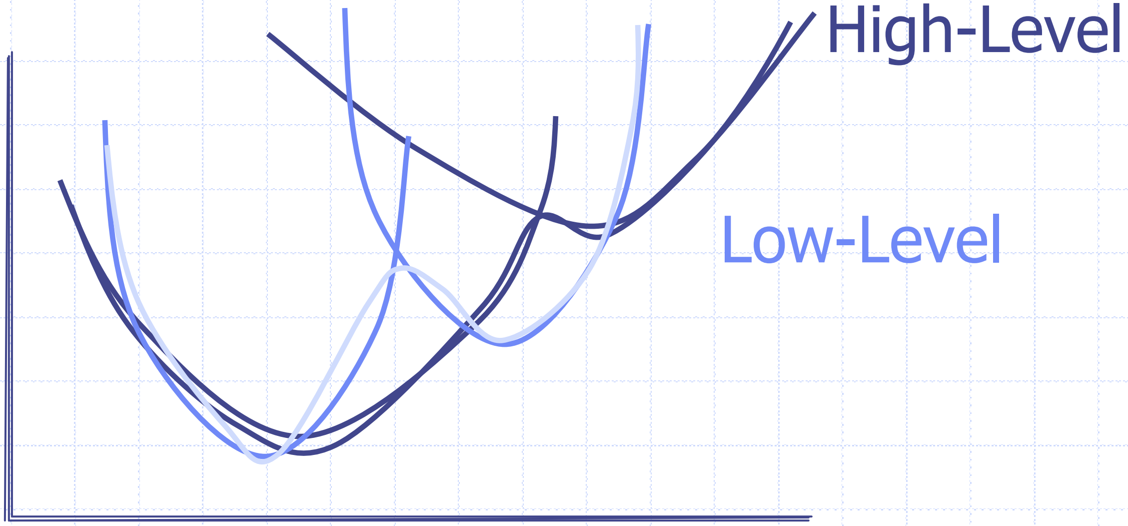


- Correlation and basis set affect frequency and relative energy of diabatic states



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"



Malick, Petersson, and Montgomery, J. Chem. Phys. ***108*** *5704 (1998)*

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

Warshel, et al. – J. Amer. Chem. Soc. **102** 6218 (1980)
Cuma, et al. J. Phys. Chem. **105** 2814 (2001)

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

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

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

N^4 work!

Try a numerical grid…

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

$$= \sum_{g} R_{pg} R_{qg} \left(\sum_{rs} P_{rs} A_{rsg} \right)$$

$2N^3$ work!

$$A_{rsg} = \int \frac{\chi_r(r_1)\chi_s(r_1)}{|r_1 - r_g|} dr_1$$

$$R_{pg} = \chi_p(r_g)$$

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

$R\psi_{\text{spectral}}=\psi_{\text{physical}}$ $Q\psi_{\text{physical}}=\psi_{\text{spectral}}$

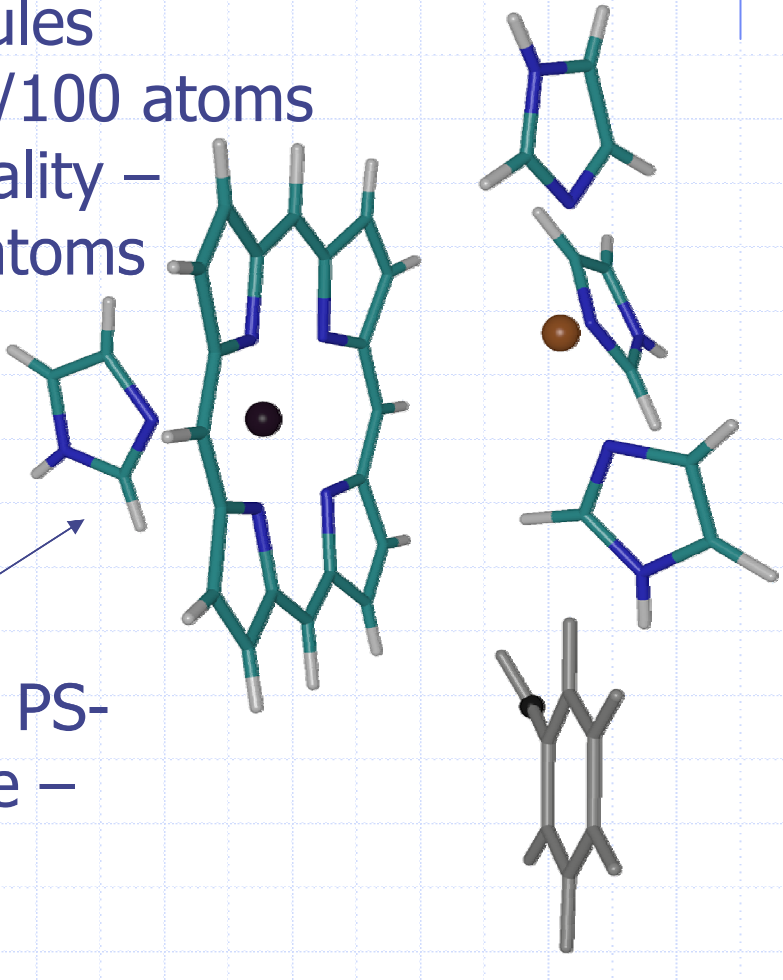
$$\psi_{spectral} = \begin{pmatrix} c_1^{MO} \\ \vdots \\ c_N^{MO} \end{pmatrix} \qquad \psi_{physical} = \begin{pmatrix} \psi\left(r_{g1}\right) \\ \vdots \\ \psi\left(r_{gM}\right) \end{pmatrix} \qquad R_{pg} = \chi_p\left(r_g\right)$$

Q must be R^{-1}…

$$Q = S(R^t wR)^{-1} R^t w \longleftarrow$$ 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, ≈10x faster/100 atoms
- Advantage partly additive w/locality – local MP2≈30x faster/100 atoms
- Only available in commercial code – Jaguar (Schrödinger) (accessible at NCSA)

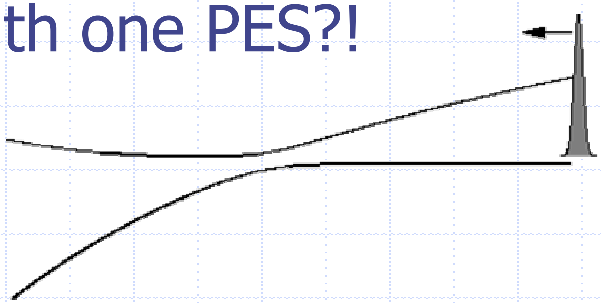


Eg where PS-B3LYP optimization and PS-LMP2 energy calculations are possible – active site of cytochrome *c* oxidase

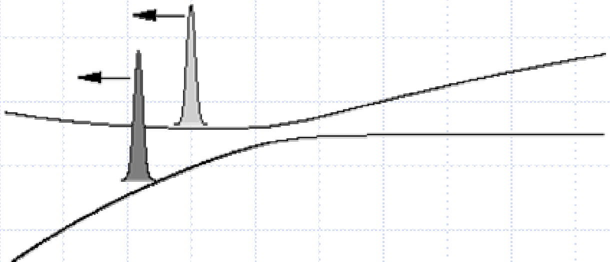
Moore and Martínez, J. Phys. Chem. **104,** 2367 (2000)

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



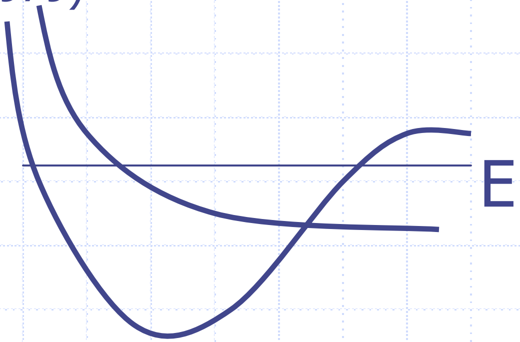
Traditional Methods

Need to solve TDSE for nuclear wavefunction:

$$\frac{i}{\hbar}\frac{\partial}{\partial t}\psi\left(R,t\right)=\hat{H}\psi\left(R,t\right)$$

- 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

$$V_{ave}(R,t)=\sum_{i\in electronic\ states} n_i(t)V_i(R)$$



Spawning Methods

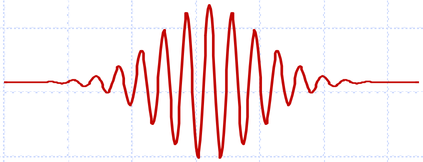
- Classical mechanics guides basis set
- Adaptively increase basis set when quantum effects occur
- Best for t-localized quantum effects
- Effort ≈ N Classical Trajectories,
  size of N controls accuracy

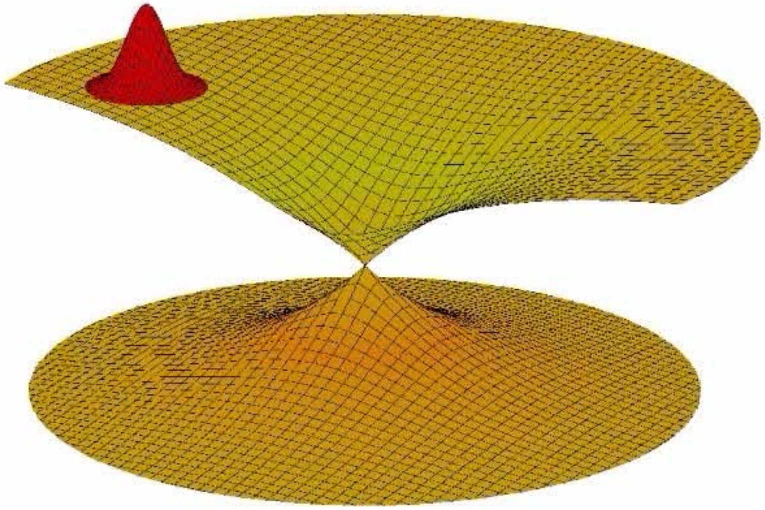
$$\Psi(\mathbf{R};t)=\sum_I\sum_j C_j^I(t)\,\chi_j^I(\mathbf{R};t)\,|I\rangle$$

Nuclear wavefunction

Electronic state

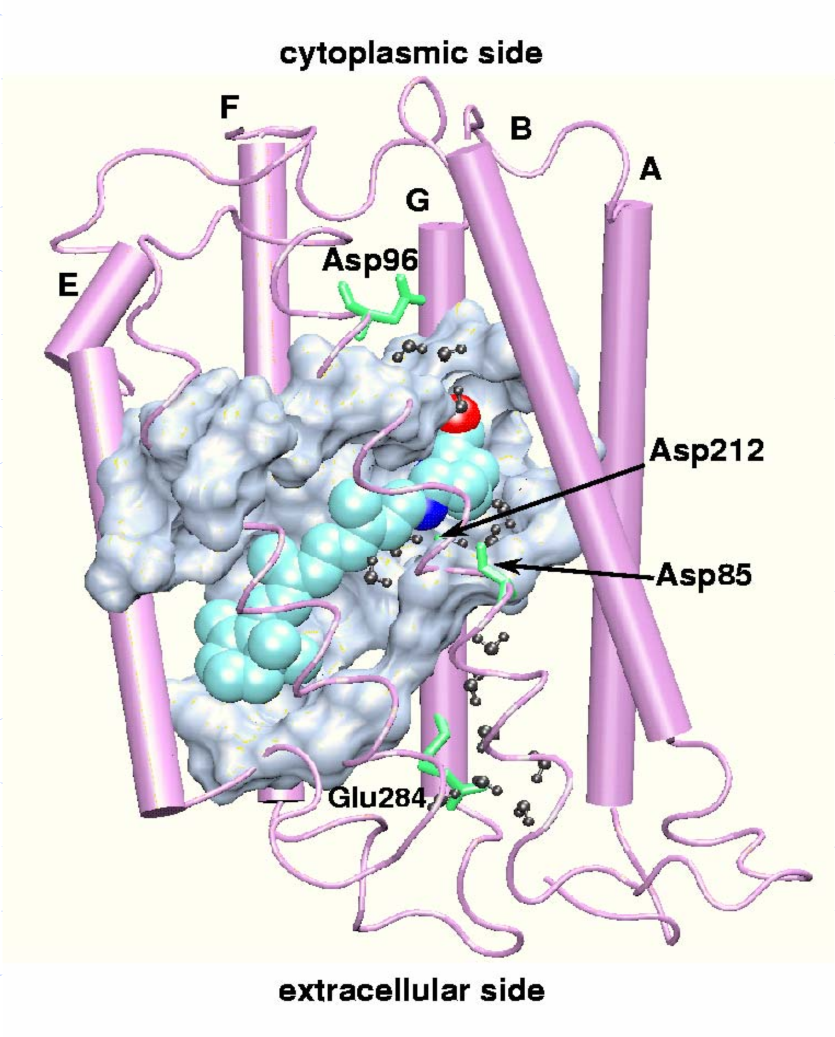
$$\chi_j^I(\mathbf{R};t)=$$





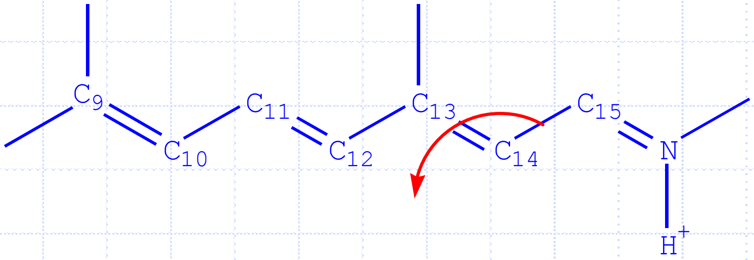
M. Ben-Nun and T. J. Martínez, Adv. Chem. Phys. **121**, 439 (2002)

Spawning Application



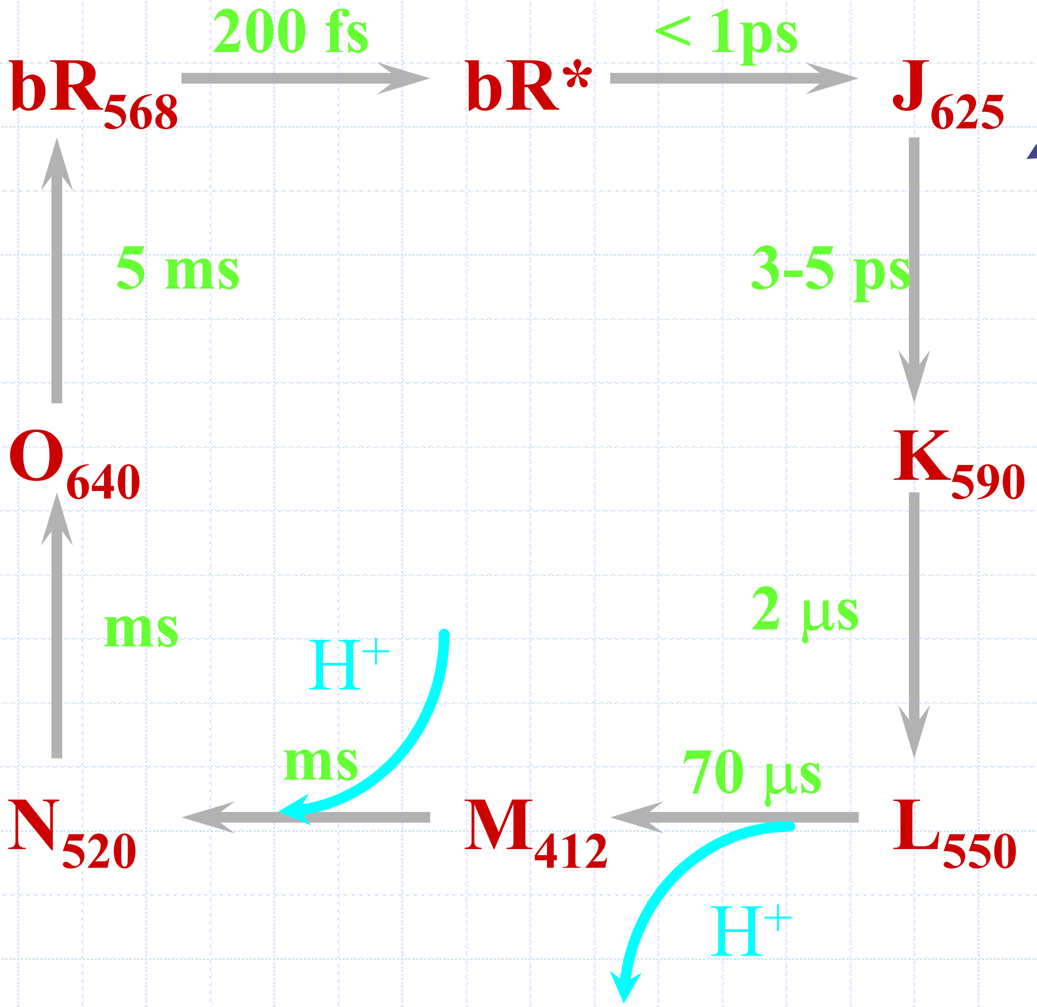
- Transmembrane protein
- 248 AA/7 helices
- Chromophore: all-*trans* retinal
- 3762 atoms = 11,286 DOF
- **Light-driven proton pump**

Light-induced isomerization:



bR Photocycle

Can simulate first steps directly



bR_{568} → 200 fs → bR^* → < 1ps → J_{625}

J_{625} → 3-5 ps → K_{590}

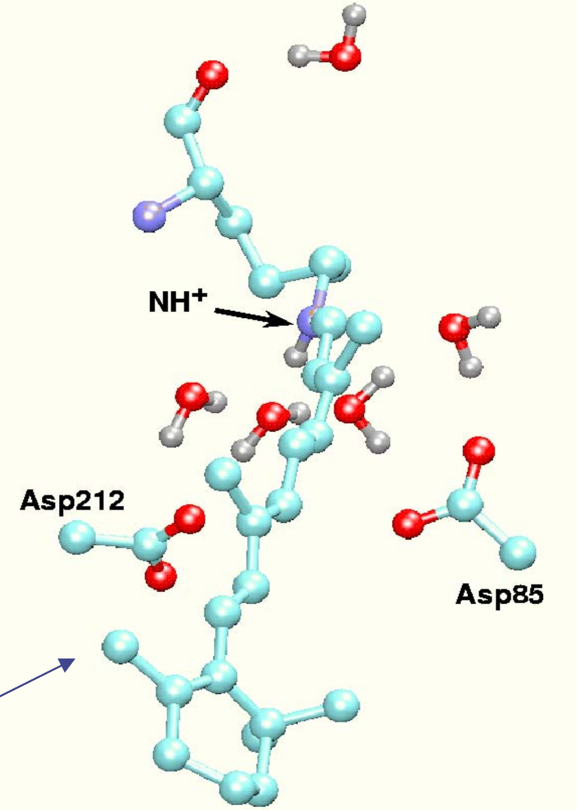
K_{590} → 2 μs → L_{550}

L_{550} → 70 μs → M_{412} (H^+)

M_{412} → ms → N_{520} (H^+)

N_{520} → ms → O_{640}

O_{640} → 5 ms → bR_{568}



Initial Geometry of RPSB

Sample Results