Introduction to Semiempirical Methods

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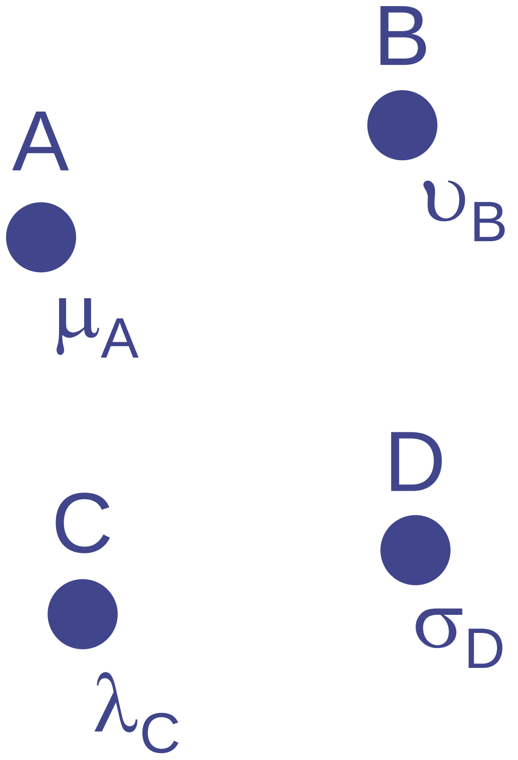
Semiempirical Methods

- Approximate version of Hartree-Fock
- Some two-electron and sometimes one-electron integrals are neglected to speed up the computation
- Some empirical parameters are inserted to make up for the neglected integrals

Eliminating Integrals

- Hartree-Fock formally scales as $O(N^4)$ because of the two-electron integrals (although this approaches $O(N^2)$ with Schwarz screening, and ultimately $O(N)$ for large molecules with multipole methods)
- Semiempirical methods reduce cost by eliminating many integrals



Atomic orbital μ_A is centered on atom A, etc.

Approximations in Semiempirical Methods

- Only valence electrons considered: core is treated by reducing nuclear charge or by adding special core functions
- Only a minimum basis is used (one AO basis function per real AO in atom): usually Slater functions are used!
- Various approximations for one- and two-electron integrals

Zero Differential Overlap (ZDO)

- ZDO is a common approximation to many semi-empirical methods
- Set the product $\mu_A(r)\upsilon_B(r)=0$ for μ, υ on different atoms ($A \neq B$)
- For $(\mu\upsilon|\lambda\sigma)$ this means all 3 & 4 center 2-electron integrals (most numerous ones) are neglected
- Get away with this by introducing parameters into (some of the) remaining integrals

Neglect of Diatomic Differential Overlap (NDDO)

- Semiempirical method based on ZDO
- Nuclear charge reduced by # of core electrons
- For two-electron integrals, $(\mu_A \upsilon_B | \lambda_C \sigma_D) = \delta_{AB}\delta_{CD}(\mu_A \upsilon_B | \lambda_C \sigma_D)$ (i.e., ZDO)
- For one-electron integrals, neglect those involving 3 centers (see next page)

Neglect of 3-center 1-electron Integrals in NDDO

$$\hat{h} = -\frac{1}{2}\nabla^2 - \sum_A \frac{Z'_A}{|\vec{R}_A - \vec{r}|} = -\frac{1}{2}\nabla^2 - \sum_A V_A$$

$$\begin{aligned}
\langle \mu_A|\hat{h}|\nu_A\rangle &= \langle \mu_A| -\frac{1}{2}\nabla^2 - V_A|\nu_A\rangle - \sum_{B\neq A}\langle \mu_A|V_B|\nu_A\rangle \\
\langle \mu_A|\hat{h}|\nu_B\rangle &= \langle \mu_A| -\frac{1}{2}\nabla^2 - V_A - V_B|\nu_B\rangle \\
\langle \mu_A|V_C|\nu_B\rangle &= 0
\end{aligned}$$

Intermediate Neglect of Differential Overlap (INDO)

- Similar to NDDO, but also neglect two-center integrals in which the AO's on an atom are different; only keep $(\mu_A\mu_A|\upsilon_B\upsilon_B)$ 2-center ints and $(\mu_A\upsilon_A|\lambda_A\sigma_A)$ 1-center ints
- Same approximations for 1-electron integrals as NDDO

Complete Neglect of Differential Overlap (CNDO)

- Most drastic of the NDDO, INDO, CNDO series
- Only keep two-electron integrals of the type
  $(\mu_A\mu_A|\upsilon_B\upsilon_B)$ 2-center ints and
  $(\mu_A\mu_A|\upsilon_A\upsilon_A)$ 1-center ints

Parameterization of Semiempirical Methods

For integrals that are kept, some of them are computed exactly, and others are computed using parameters from experiment (semi-empirical)

Modified Intermediate Neglect of Differential Overlap (MINDO)

$$\begin{aligned}\langle \mu_A|\hat{h}|\nu_B\rangle &= \langle \mu_A| -\frac{1}{2}\nabla^2 - V_A - V_B|\nu_B\rangle \\ &= \langle \mu_A|\nu_B\rangle \beta_{AB}(I_\mu + I_\nu)\end{aligned}$$

- I_μ is the ionization potential of an electron in atomic orbital μ
- β_{AB} is a fitted “diatomic” parameter

NDDO Models using Atomic Parameters

MINDO has been largely superseded by NDDO models based on *atomic parameters,* such as MNDO, AM1, PM3, which differ only in their treatment of core and how parameters are assigned

$$\begin{aligned}\langle \mu_A|\hat{h}|\nu_B\rangle &= \langle \mu_A| -\frac{1}{2}\nabla^2 - V_A - V_B|\nu_B\rangle \\ &= \langle \mu_A|\nu_B\rangle \frac{1}{2}(\beta_\mu + \beta_\nu)\end{aligned}$$

Modified Neglect of Diatomic Overlap (MNDO)

- Atomic parameterization, modified NDDO type model
- Largely superseded by AM1, PM3, etc.
- Some limitations:
    - Steric crowding exaggerated
    - H-bonds not reliable
    - Hypervalent molecules too unstable
    - Bond breaking/forming TS’s too high in energy

Austin Model 1 (AM1)

- Changed core functions relative to MNDO, reparameterized
- Improved over MNDO:
  - Alkyl groups too stable by ~2 kcal/mol per CH_2
  - Peroxide compounds not described well

M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, J. J. P. Stewart, *J. Am. Chem. Soc.* **107**, 3902-3909 (1985)

MNDO Parametric Method 3 (PM3)

- Reoptimized parameters automatically (previously done by hand) and changed core terms again
- Quite a few atoms available
- Performance:
  - H-bonds too short by ~0.1 Å
  - N atom charges often unreasonable

J. J. P. Stewart, *J. Comput. Chem.* **10**, 209-220 (1989)

Common Problems for MNDO, AM1, PM3

- Rotations about partial double bonds give barriers that are too low
- Parameters for metals based on only a few data points
- Weak interactions unreliable (like Hartree-Fock, semiempirical methods do not describe electron correlation effects that give rise to London dispersion forces, unless some special correction is added like a "-D" dispersion correction)

MNDO/d

- Adds d functions to MNDO
- For metals, these are essential
- For 2nd row atoms, these are helpful in describing polarization
- Can offer significant improvements over MNDO, AM1, PM3

Parameterized Model 6 (PM6)

- NDDO Method with improved parameters and improved core-core interaction term (diatomic parameters like original MINDO)
- 70 elements parameterized
- Corrects some problems with AM1, PM3
- Includes d functions for metals like MNDO/d

J. J. P. Stewart, *J. Mol. Model* **13**, 1173-1123 (2007)

Semiempirical Total Energies

- Like the Hartree-Fock model they’re derived from, semiempirical methods yield total electronic energies (relative to infinitely separated nuclei and valence electrons)
- Unlike HF, we don’t need to add zero-point vibrational energy (ZPVE) when computing enthalpy differences; it’s included *implicitly* in the parameters

Average ΔH_f error in kcal/mol

Compounds	**MNDO**	**AM1**	**PM3**
All normal valent (607 compounds)	24.3	14.8	11.2
Hypervalent (106 compounds)	104.5	62.3	17.3
All (713 compounds)	46.2	27.6	11.6

Data from Frank Jensen, *Introduction to Computational Chemistry* (Wiley, New York, 1999)

Average ΔH_f error in kcal/mol

Compounds	MNDO	AM1	PM3	MNDO/d
Al, Si, P, S, Cl, Br, I, Zn, Hg (488 compounds)	29.2	15.3	10.0	4.9
Si, P, S, Cl, Br, I (404 compounds)	31.4	16.1	9.5	5.1

Data from Frank Jensen, *Introduction to Computational Chemistry* (Wiley, New York, 1999)

Average ΔH_f error in kcal/mol

Compounds	**AM1**	**PM3**	**PM6**
H, C, N, O (1157 compounds)	9.4	5.7	4.6
Main group (3188 compounds)	22.3	17.8	6.2

Compounds	**PM6**	**B3LYP/ 6-31G***	**HF/ 6-31G***
1373 compounds	4.4	5.2	7.4

J. J. P. Stewart, *J. Mol. Model* **13**, 1173-1123 (2007)

Average errors in bond lengths (Å)

Bonds to	**AM1**	**PM3**	**PM6**
H, C, N, O (413 compounds)	0.031	0.021	0.025
H, C, N, O, F, P, S, Cl, Br, I (712 compounds)	0.046	0.037	0.031
Main group (2636 compounds)	0.131	0.104	0.085

J. J. P. Stewart, *J. Mol. Model* **13**, 1173-1123 (2007)

Typical semiempirical accuracy for other properties

Property	Accuracy
Bond angles	± 4°
Ionization potentials	± 0.5-1.0 eV
Dipole moments	± 0.4 D
Relative energies (ΔH_f)	± 5-10 kcal/mol (not as systematic as ab initio energy errors)

Improvements to PM6 (etc.) for Noncovalent Interactions: PM6-DH, PM6-DH2, PM6-D3H4X

- Add term for dispersion: damped $C_{6,AB}/R_{AB}^6$ terms with same form as in popular –D dispersion corrections to DFT and analogous to London dispersion terms in force fields
- Add term for hydrogen bonding

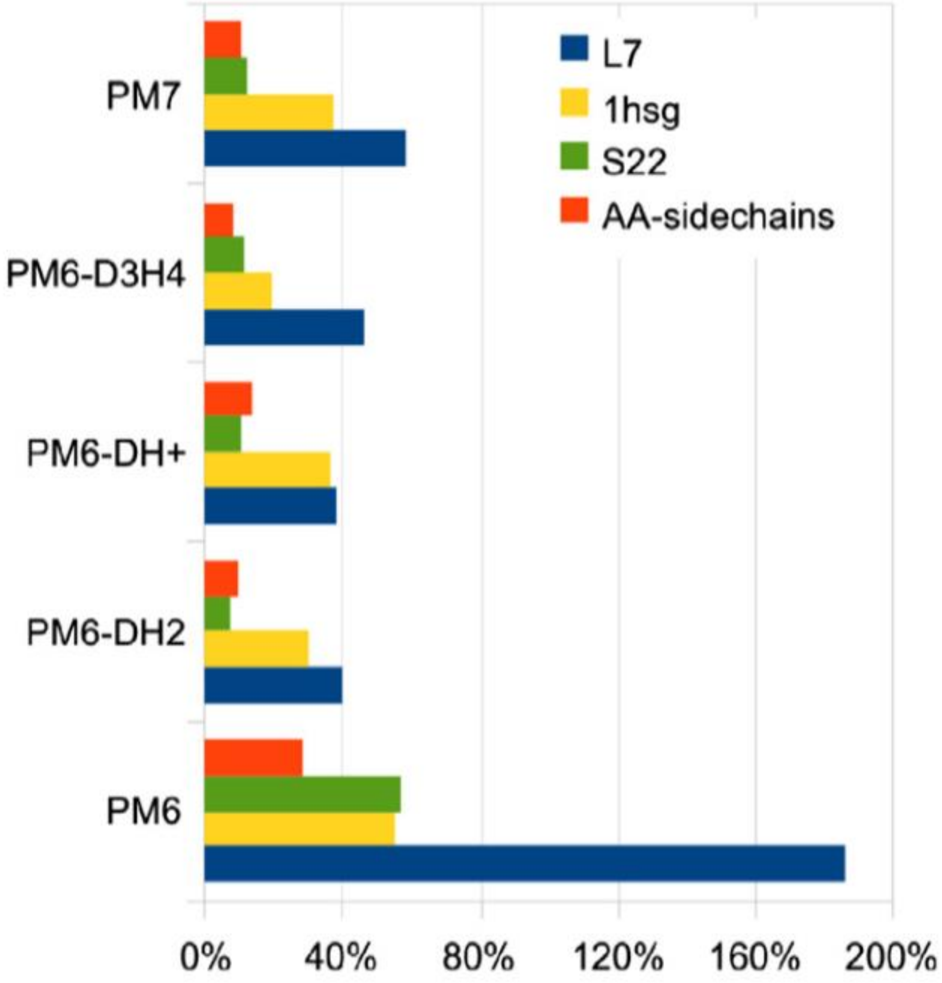
PM6-DH: J. Rezac, J. Fanfrlik, D. Salahub, and P. Hobza, *J. Chem. Theory Comput.* **5**, 1749-1760 (2009)
PM6-DH2: M. Korth, M. Pitonak, J. Rezac, and P. Hobza, *J. Chem. Theory Comput.* **6**, 344 (2010)
D3H4X correction: J. Rezac and P. Hobza, *J. Chem. Theory Comput.* **8**, 141 (2012)

Parameterized Model 7 (PM7)

- Further improvements upon PM6
- Added explicit terms to describe non-covalent interactions, based on ideas in the –DH2, -DH+, and –D3H4 corrections to PM6 by Hobza and co-workers
- Aimed at giving better results for molecules different than those in the training set
- Corrects two minor errors in the NDDO formalism
- MUE in bond lengths decreased by about 5% and in ΔH_f by about 10% relative to PM6 (for organic solids, improvement of 60% in ΔH_f)

J. J. P. Stewart, *J. Mol. Model* **19**, 1-32 (2013)

Modern Semiempirical Methods for Non-Covalent Interactions



RMS %error in intermolecular interaction energies, from J. Hostas, J. Rezac, and P. Hobza, *Chem. Phys. Lett.* **568**, 161 (2013)

Extended Hückel Theory

- Parameterizes the Fock matrix, not the integrals
- $F_{\mu\mu} = -I_{\mu}$
- $F_{\mu\upsilon} = -k\, S_{\mu\upsilon}(I_{\mu}+I_{\upsilon})/2$ (k=1.75)
- Very approximate method, but can be useful for getting trends or generating guess MO's for Hartree-Fock

Summary of Semiempirical Methods

- Neglect of all 3 and 4 center integrals makes formal scaling go from O(N^4) to O(N^2) for construction of Fock matrix
- Diagonalization of F scales as O(N^3) and therefore becomes formal rate-determining step (there are tricks to avoid explicit diagonalization)
- Share advantages/disadvantages of force fields: perform well for systems where experimental data available, not reliable otherwise
- Somewhat more robust than force fields because at least based on QM