Molecular Mechanics

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Learning Goals

- Transferability in Chemistry
- Empirical Chemical Bonding
- Non-Bonding Interactions
- Determining the Empirical Force Field
- Quantum Corrections
- Software

References

- Leach, A.R., *Molecular modelling : principles and applications.*

http://dasher.wustl.edu/tinker/
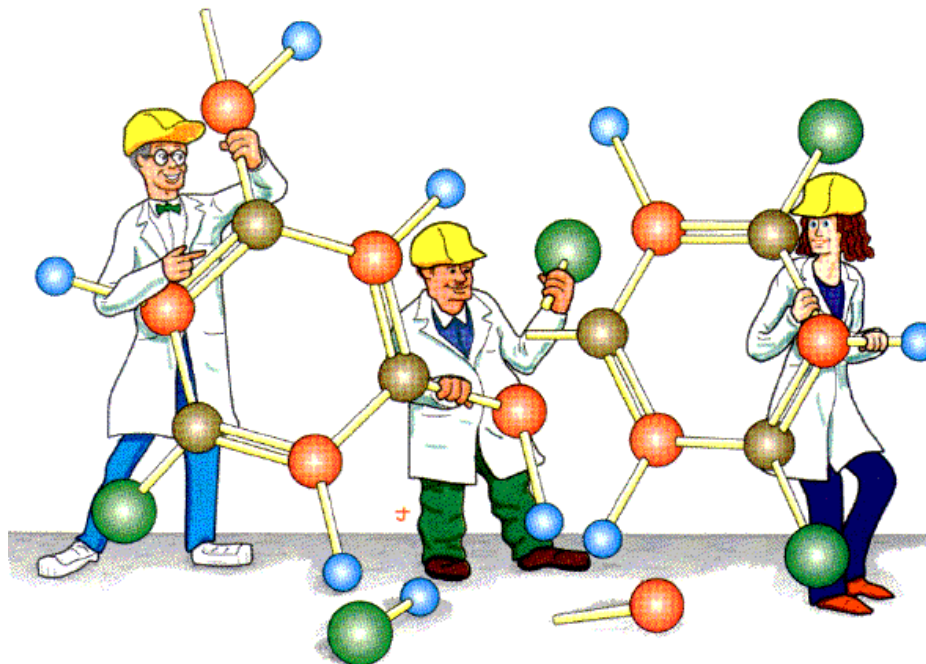
Tutorials

- *A Tour of the Foundations of Computational Chemistry And Material Science,* www.arl.hpc.mil/ PET/cta/ccm/training/courses/foundations/foundations.html

- *CMC modelling guide,* wwwcmc.pharm.uu.nl/webcmc/

- Adrian Parsegian, *Intermolecular Forces,* www.biophysics.org/btol/ intermol.html

- *Molecular Mechanics and Dynamics,* www.chem.swin.edu.au/ modules/mod6/

- Peter J. Steinbach, *Introduction to Macromolecular Simulation* cmm.cit.nih.gov/intro_simulation/ course_for_html.html

- *A molecular dynamics primer,* www.fisica.uniud.it/~ercolessi/md/md/ md.html

- *Introduction to Molecular Modeling,* mccammon.ucsd.edu/ ~chem215/lectures/lecture5/lecture5/ node1.html

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Transferability in Chemistry

- ◆ Searching the Atoms and Bonds within the Molecule

- ◆ Atom in Molecule

- ◆ Empirical Force Field

- ◆ Transferability of the Force Field
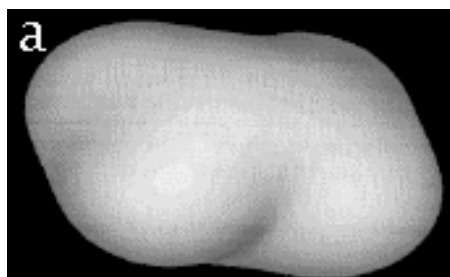
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Atoms and Bonds

- Demo: Molecular models of benzene
  - Lines, Balls and Sticks, CPK (Corey, Pauling, Koltun)

- Electron density

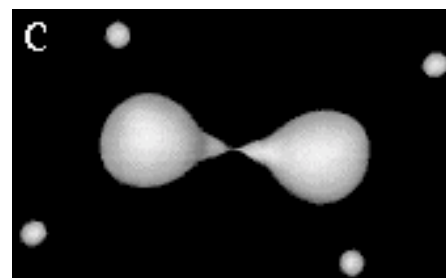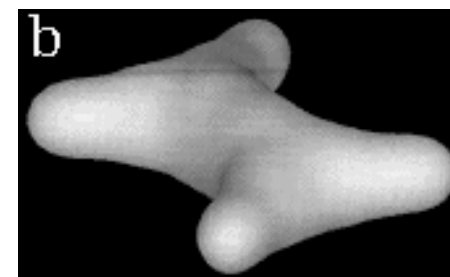$$\rho(r) = 2\sum\left|\psi_i(r)\right|^2$$

- Ethene, $H_2C=CH_2$

b - 0.20

a - 0.002

c - 0.36

Transferability in Chemistry

Atom in Molecule

- Partioning electron density between the nuclei.
  - Mulliken analysis: based on MO, very simple, often leads to unrealistic results.

- R.F.W. Bader - Gradient Vector Path: example of $H_2C=CH_2$.
- GAMESS can make output to AIMPAC to do it.
- www.chemistry.mcmaster.ca/faculty/bader/aim/

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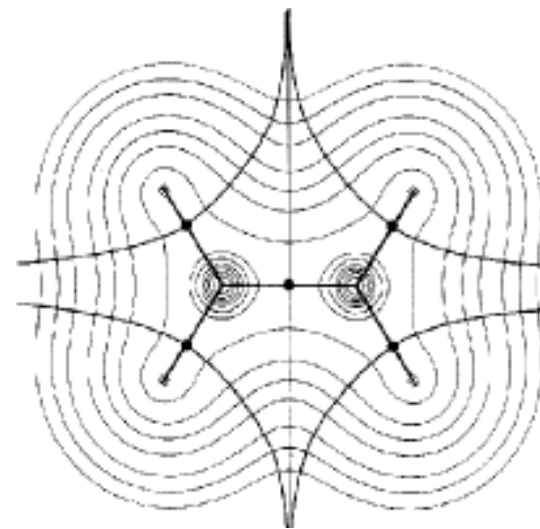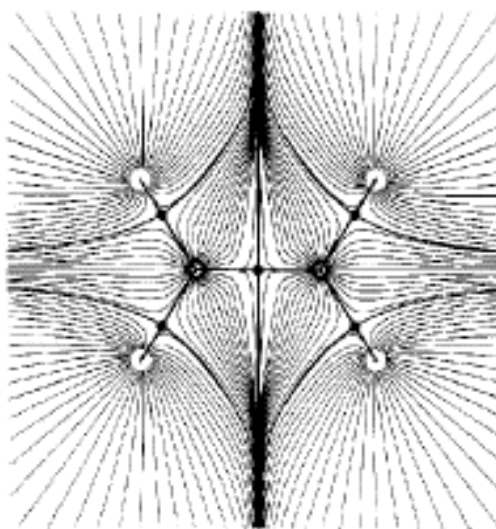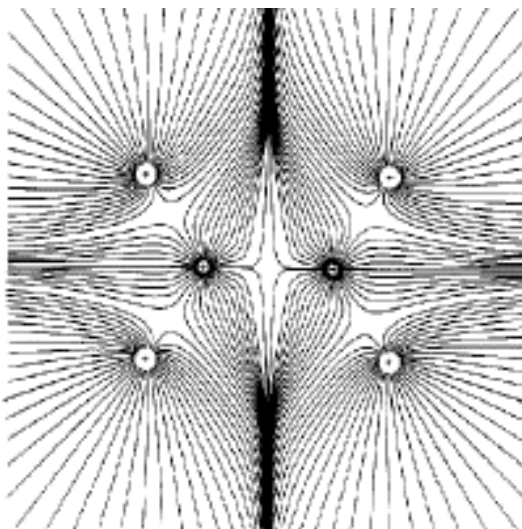
Empirical Force Field

♦ Quatum chemistry does not scale:

- ♦ Number of integrals is $O(K^4)$.
- ♦ Nonlinear eigenproblem is $O(K^3)$.
- ♦ Can be improved in some extent, but ...
  - ♦ Local orbitals.
  - ♦ Subspace methods based on Krylov subspaces.
  - ♦ Linear scaling QC: $O(K)$.

♦ Bonding and non-bonding interaction

- ♦ $E = E_{bond} + E_{non-bond}$.

♦ Bonding: streching, bending, torsion, cross-terms

$$E_{bond} = E_{str} + E_{bend} + E_{torsion} + E_{cross}$$

- ♦ Expressed in the internal coordinates.

♦ Non-bonding: van der Vaals, electrostatic, hydrogen, etc...

♦ Contains empirical parameters, specific for given atoms.

- ♦ Could be used (with great care) for different molecules.

Transferability of the Force Field

- Methane, ethane, propane, butane, ...
  - CH_4, CH_3-CH_3, CH_3-CH_2-CH_3, CH_3-CH_2-CH_2-CH_3, ...
  - Homological series - C_nH_{2n+2}
  - sp3 carbon
  - Roughly bonds C-C and C-H are the same.
- Ethene, $CH_2=CH_2$, sp2 carbon.
- Ethyne, $CH \equiv CH$, sp carbon.
- Propene, $CH_2=CH$-CH3, 2 sp2 and 1 sp3 carbon.

http://ull.chemistry.uakron.edu/genobc/
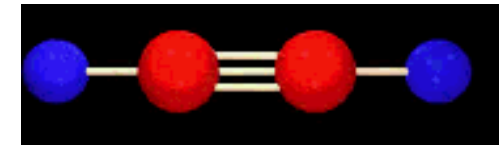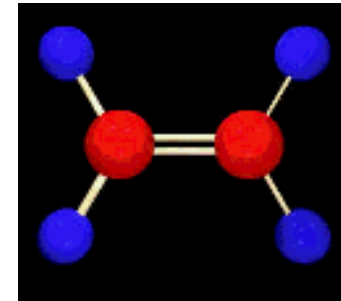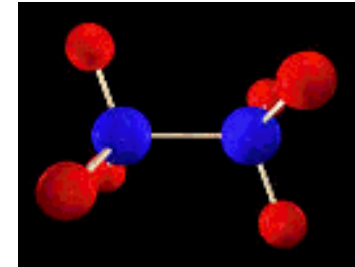
- There is no justification from quantum chemistry.

Empirical Chemical Bonding

- Bond Streching

- Angle Bending

- Torsional Terms

- Cross Terms

Pictures and demos from www-wilson.ucsd.edu/education/
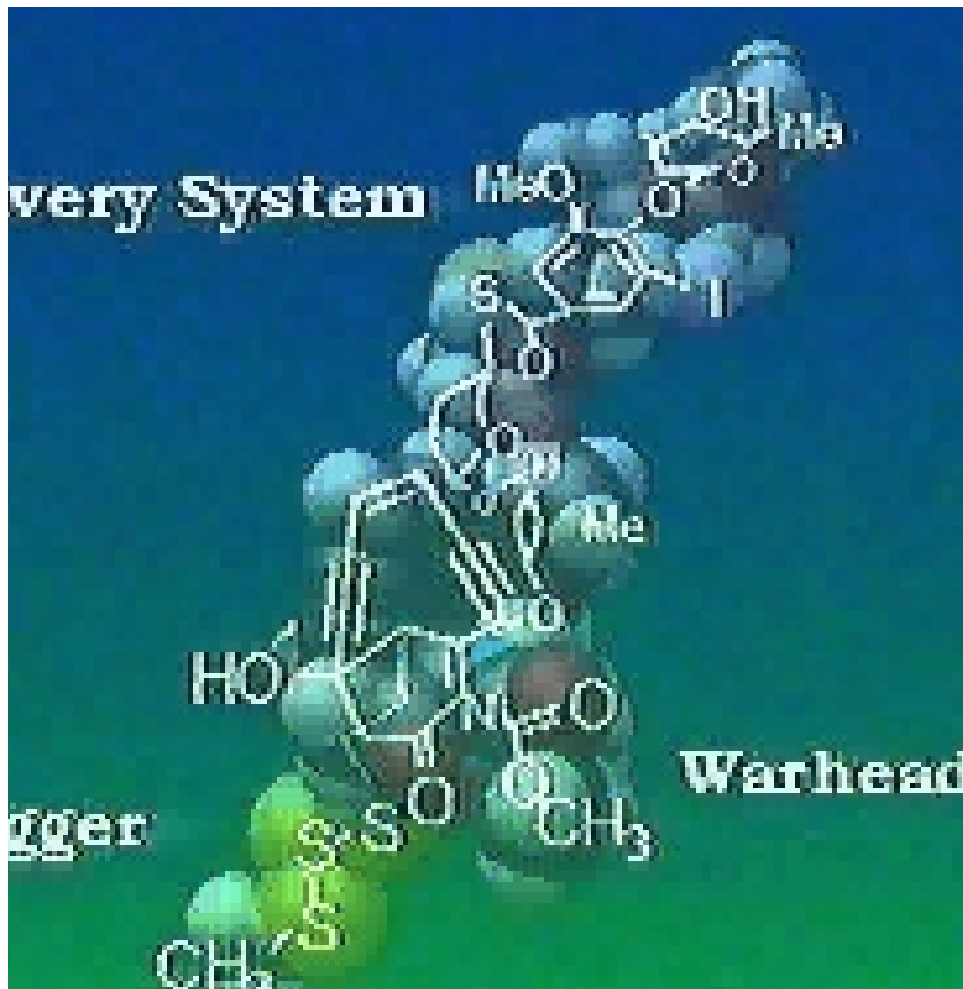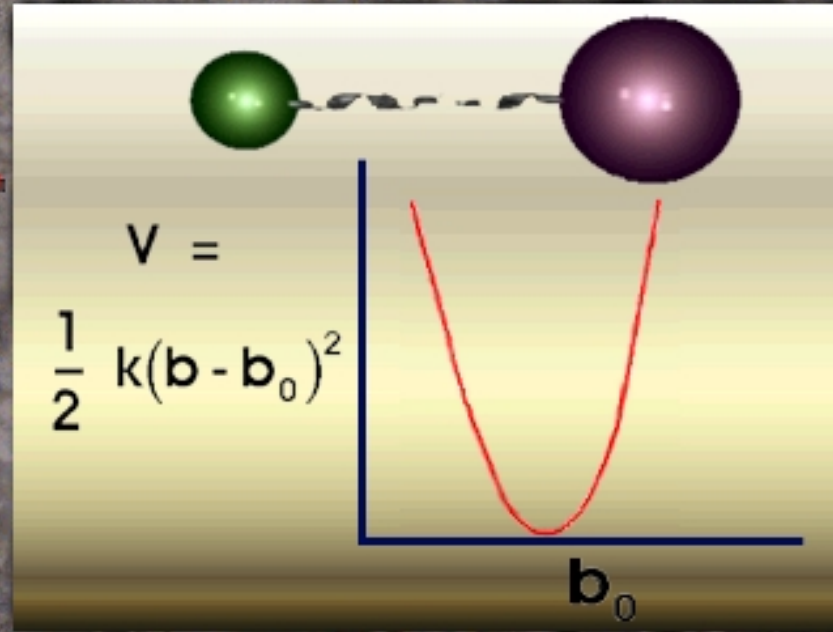
$$V = \frac{1}{2} k(b - b_0)^2$$

$$V_{bonded} = \sum_{bonded\ pair\ of} \frac{1}{2} k(b - b_0)^2$$

$k=1200$ $kJ/mol/A^2$

$b-b_0=0.2A$

$V=48$ kJ/mol

$kT \approx 2.4$ kJ/mol

Empirical Bonding: Angle bending
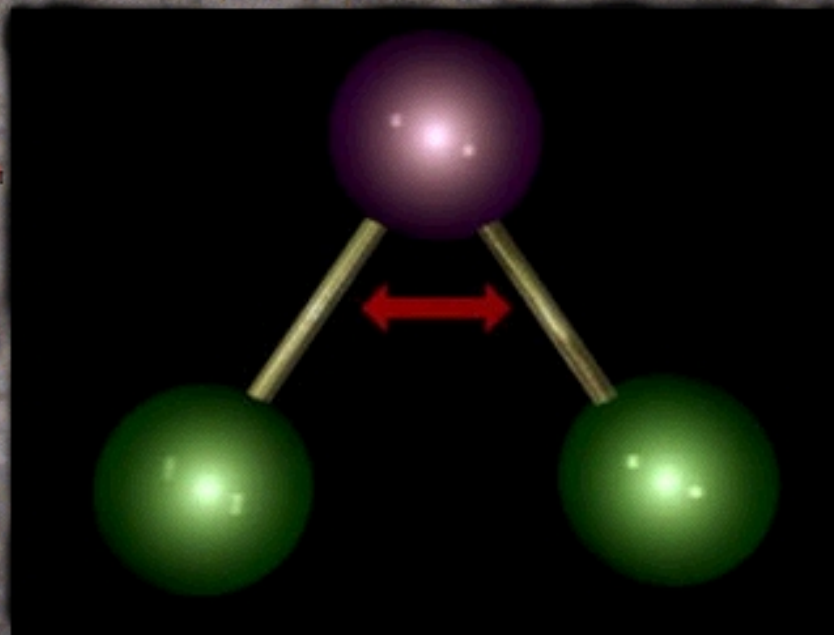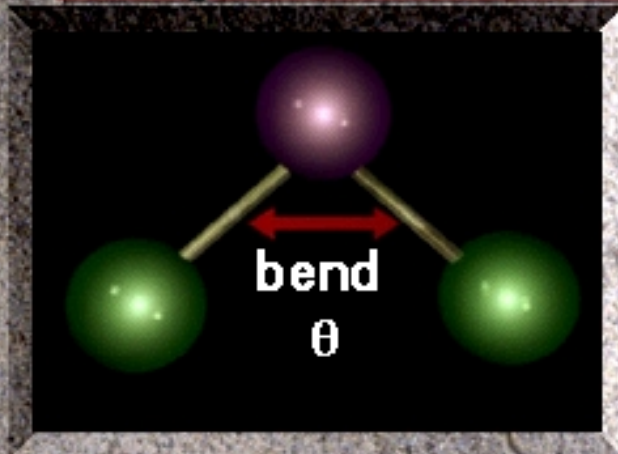
k=0.04 kJ/mol/deg

change
10 deg
4 kJ/mol

$kT \approx 2.4$ kJ/mol

$$V_{bend} = \sum_{bond} \frac{1}{2} k_\theta (\theta - \theta_0)^2$$

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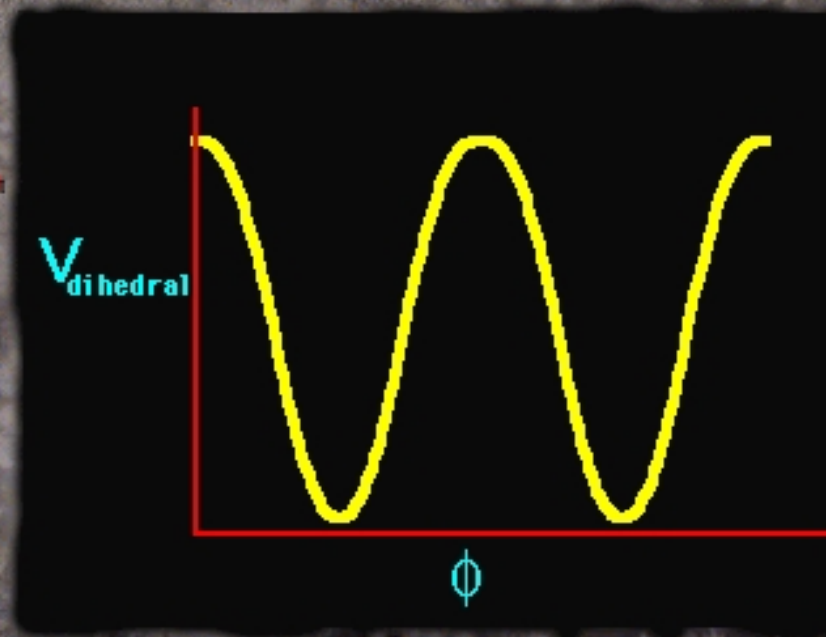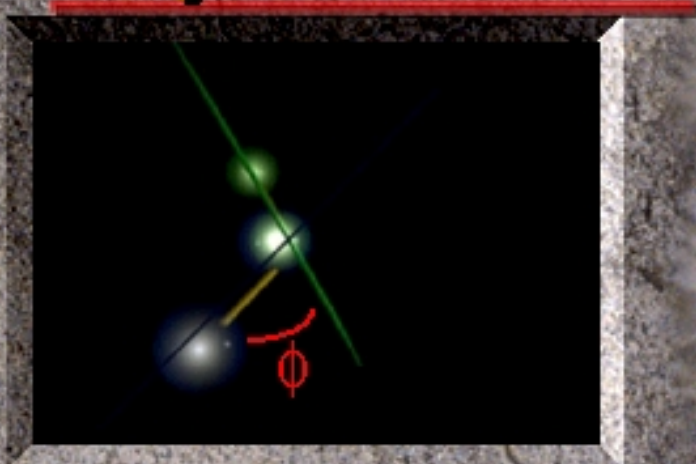
$$V_{dihedral} = \sum_{dihedral} k_\phi [1 + \cos(n\phi - \delta)]$$

strech-strech

- $v(l_1, l_2) = k_{l_1, l_2}(l_1 - l_{1,0})(l_2 - l_{2,0})$

strech-bond

- $v(l, \Theta) = k_{l, \Theta}(l - l_0)(\Theta - \Theta_0)$

strech-torsion

- $v(l, \omega) = k_{l, \omega}(l - l_0)(1 - \cos n\omega)$

...

- Chemical bonding scales almost linearily.

- Torsion
  - $kT >> U_o$: free rotation, otherwise hindered rotation or restricted rotation.

Non-Bonding Interactions

♦ van der Waals Interactions

♦ Electrostatic Interactions

♦ Special Chemical Interactions

♦ Common Approximations

♦ Demo: MD of $C_{10}H_{22}$

van der Waals interactions

♦ Lennard-Jones

$$V(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$$

♦ Mixing rules for the polyatomic molecules:

♦ Lorentz-Berthelot

$$\sigma_{AB} = (\sigma_A + \sigma_B)/2,$$

$$\varepsilon_{AB} = \sqrt{\varepsilon_A \cdot \varepsilon_B}$$

♦ van der Walls interaction betwee 1,4 atoms (at the end of the dihedral angles) is artificially reduced or ignored.

♦ It is necessary to have cut-off radius, to be computationally effective.

Electrostatic interactions

- Partial atomic charge :
  - From quantum chemistry.
  - From quantum chemistry of fragments.
  - Different empiric schemes based on ionisation potential and electron affinity.
- Distribute multipole models.
- Polarisation: dipole moment is proportional to the electric field - computationally demanding.

- It is necessary to have an efficient scheme to computed the electrostatic energy.

Electronic polarization

Field

resulting dipole moment

http://gilsonlab.umbi.umd.edu
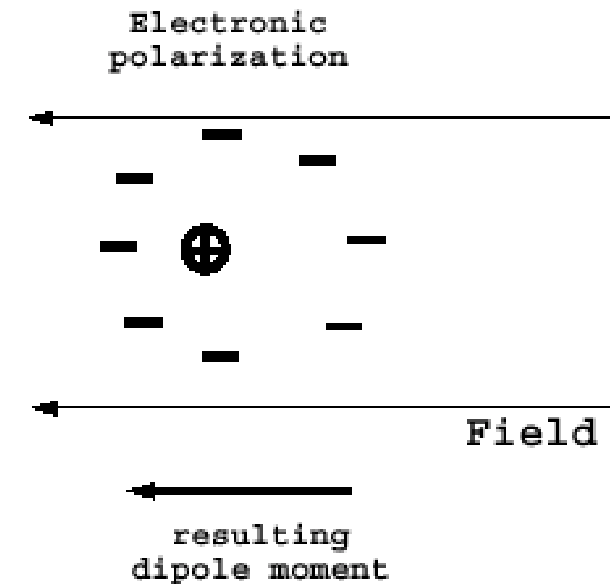
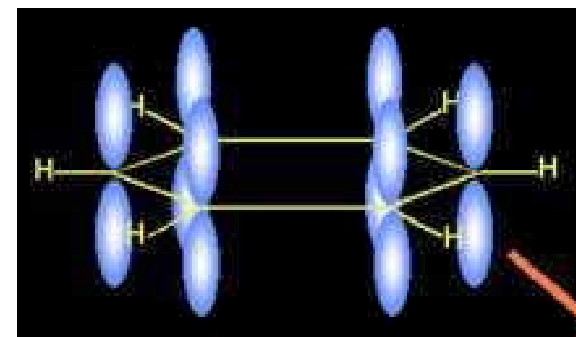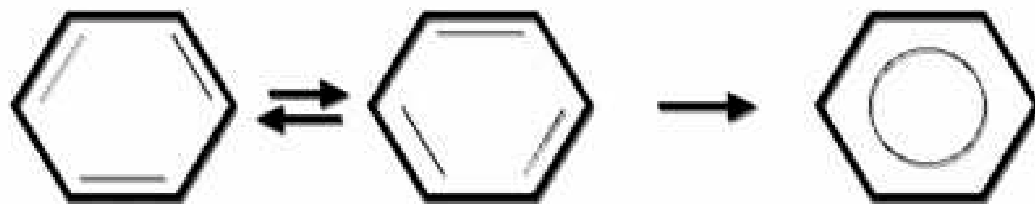# Special chemical interactions

Hydrogen bonding

Delocalised π-systems

♦ YETI:

$$\left(\frac{A}{r_{H\ldots Acc}^{12}} - \frac{B}{r_{H\ldots Acc}^{10}} \right) (\cos \Theta_{Don\ldots H\ldots Acc})^2 (\cos \omega_{H\ldots Acc\ldots LP})^4$$

http://ull.chemistry.uakron.edu/genobc/Chapter_12/

Common approximations

○ Rigid intramolecular degrees of freedom
  - *fast intramolecular motions slow down MD calculations*

○ Ignore hydrogen atoms
  - *united atom representation*

○ Ignore polarization
  - *expensive n-body effect*

○ Ignore electrostatics

○ Treat whole molecule as one big atom

  - *maybe anisotropic*

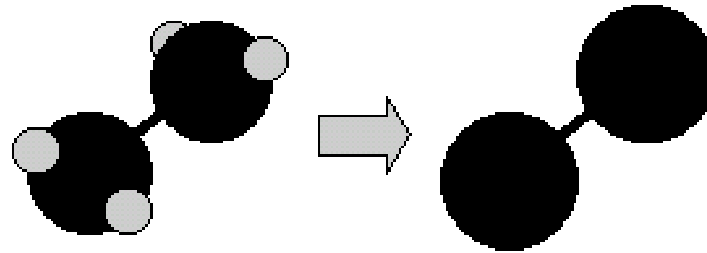○ Model vdW forces via discontinuous potentials

○ Ignore all attraction

○ Model space as a lattice

  - *especially useful for polymer molecules*

Qualitative models
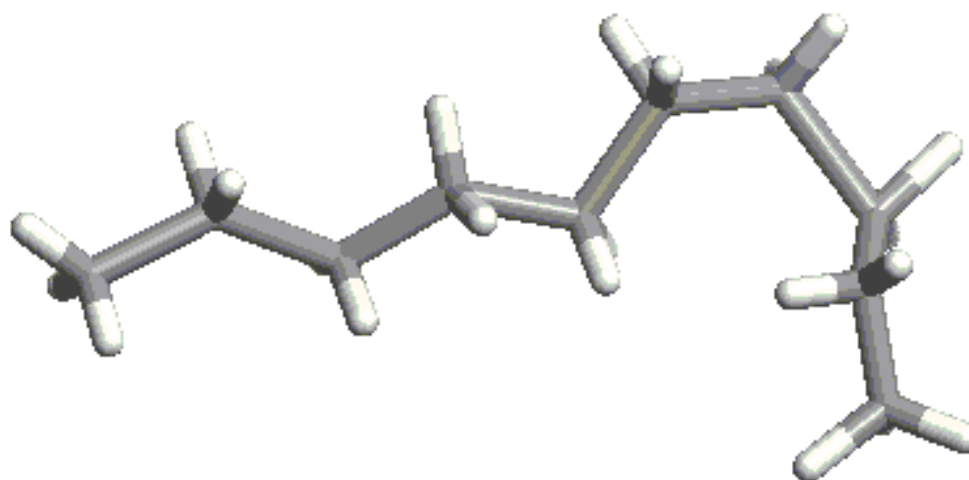
http://www.cheme.buffalo.edu/courses/ce530/

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Demo: MD of $C_{10}H_{22}$

♦ Made with MSI Materials Studio www.accelrys.com

- ◆ Definition

- ◆ Experimental Information

- ◆ Available Force Fields

Definition

- Empricial potential energy contains unknown parameters Θ.
- We choose a set of reliable experimental values $[y_i, x_i]$.
- Due to our model, we have
  $$y_i = f_i(x_i; \Theta) + \varepsilon_i.$$
- $f_i(x_i; \Theta)$ is a direct problem.
- Best fit of y_i produces uknown parameters: inverse problem.
- Weighted least squares,

$$SS = \Sigma_i(\varepsilon_i^2 w_i).$$

- The results depends on the weights.
  - Systematic errors: variance components.
- The same concerns semi-empirical quantum chemistry.
 - The difference is in the level of parametrization.

Experimental Information

- Potential energy points and its derivatives from quantum chemistry.
  - Caution: different zero energies.
- Experimental dissociation energies and conformational barriers.
- Vibrational frequencies
  - $\left| U - \omega^2 M \right| = 0$.
- Dipole moments.

- Macroscopic properties (diffusion coefficient, thermal conductivity, heat capacity).
  - Computationally expensive: the direct problem is a simulation.

Available force fields

- Allinger's MM2, MM3

  europa.chem.uga.edu/ccmsd/mm2mm3.html

- AMBER

  www.amber.ucsf.edu/amber/amber.html

- CHARMM

  yuri.harvard.edu/

- GROMOS

  igc.ethz.ch/gromos/

- COMPASS from MSI Materials Studio, www.accelrys.com

- Typically you can not borrow parameters from the different

fields.
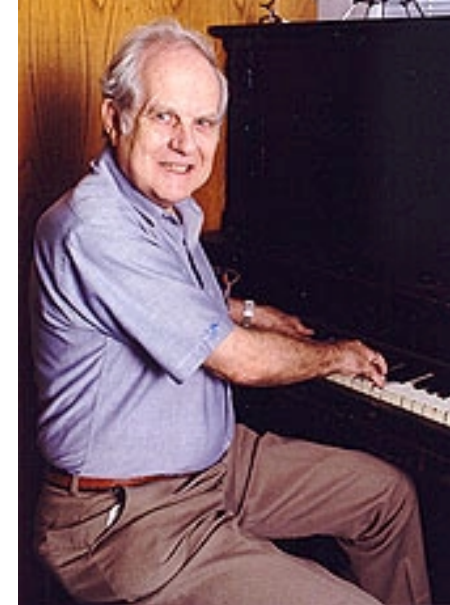
Prof. Allinger

- Your problem may require a new force field: an inverse problem.

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Quantum Molecular Dynamics

- The week side of all the empirical force fields is the breaking of bonds.
- The current state of the art: M. Parirnello "*Simulating Comlex Systems without Adjustable Parameters*", Comp. Sci. Eng, 2000, N 4, p. 22 - 27.
- Roughly: QMD is MD when forces are computed by QC.
- Real implementations are more intellegent.
- Several hunderd atoms for 10 picoseconds is routine.
- Can be combined: Quantum Chemistry/Molecular Mechanics (QC/MM).

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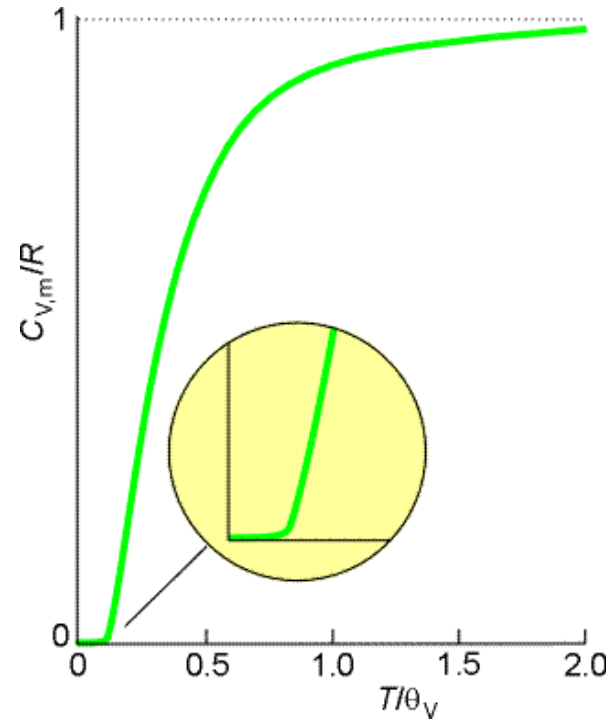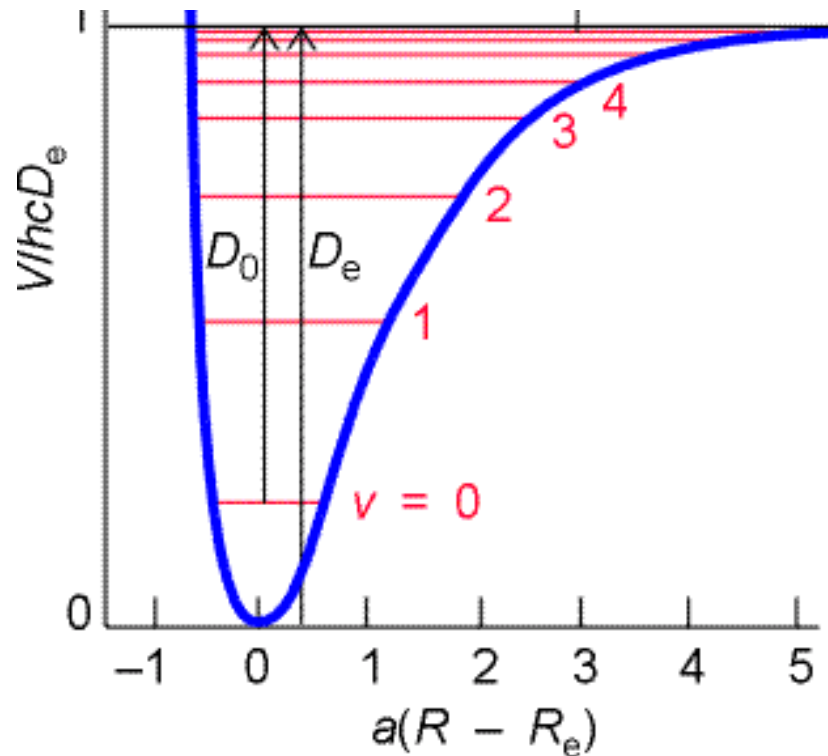
Non-adiabatic reactions

◆ Example: electron transfer $Fe^{2+} + Fe^{3+} = Fe^{3+} + Fe^{2+}$

from 98Chandler2

state A^-B state AB^-

$F = \frac{1}{2\alpha}\mathcal{E}^2 - \mathcal{E}$

$\mathcal{E} = 0$
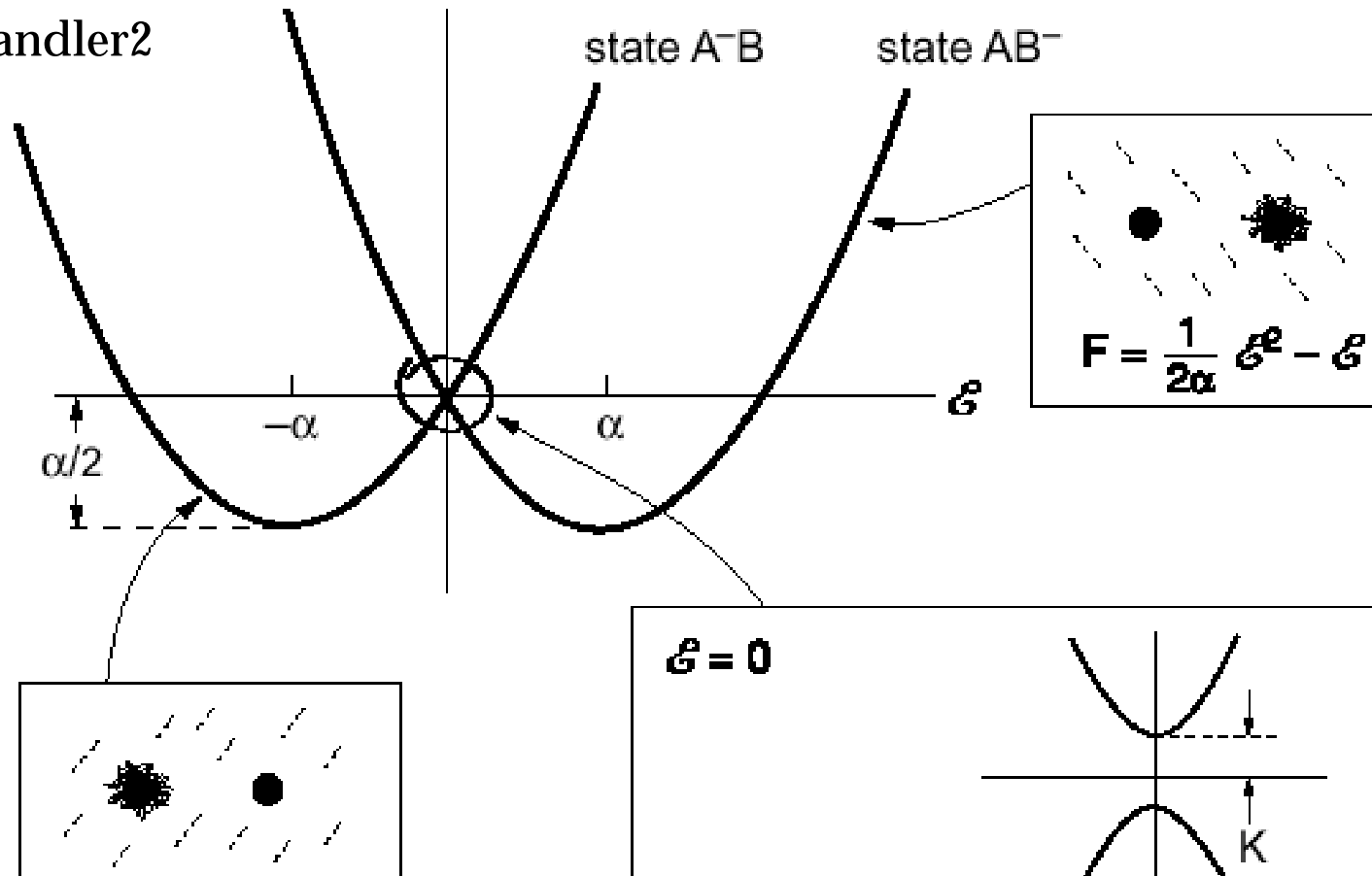
- ♦ Zero-point energy
  $$D_o = D_e - 0.5hc\omega.$$
- ♦ Frozen degree of freedom:
  $\Theta = hc\omega/k$, harmonic oscil-

lattor: classical $Q = 2\pi T/\Theta$, C_v = R, quantum

$$Q = (1 - \exp(-T/\Theta))^{-1}.$$

from Atkins

Commercial

- CACHE and Materials Explorer: www.cachesoftware.com
- Materials Studio: www.accelrys.com

Free

- GROMAX, Herman Berendsens group, department of Biophysical Chemistry of Groningen University, www.gromacs.org/
- TINKER, Jay Ponder Lab, Dept. of Biochemistry & Molecular

Biophysics, Washington University School of Medicine, St. Louis, Missouri, dasher.wustl.edu/tinker/
- GAMESS + TINKER can do QMD.

Lists

- www.ch.ic.ac.uk/local/organic/mod/software.html
- bogense.chem.ou.dk/~icc/software.html

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Summary

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