

Molecular Mechanics

Outline

Definition of the force field

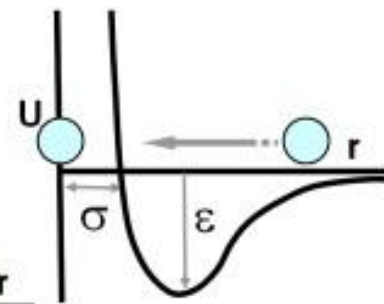
Bonding terms

Non-bonded terms

Parametrization

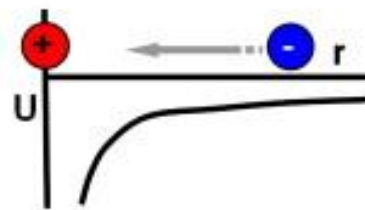
Force Field = Potential Energy of Molecular System

$$U = \sum_{i < j} \sum 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]$$

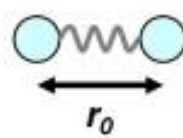


Non-Bonding terms

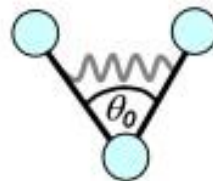
$$+ \sum_{i < j} \sum \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$



$$+ \sum_{bonds} \frac{1}{2} k_b (r - r_0)^2$$

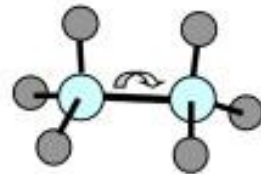


$$+ \sum_{angles} \frac{1}{2} k_a (\theta - \theta_0)^2$$



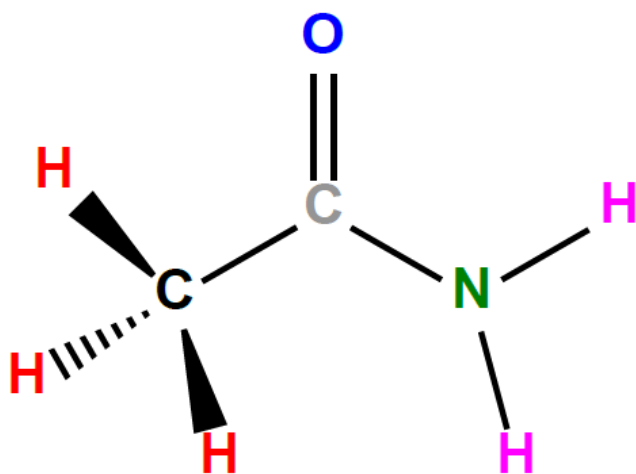
Bonding terms

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



Force Field = Functional Form + Parametrization

Example: acetamide



acetamide

$3N-6 = 21$ internal coordinates

vs. redundant internals

8 bonds

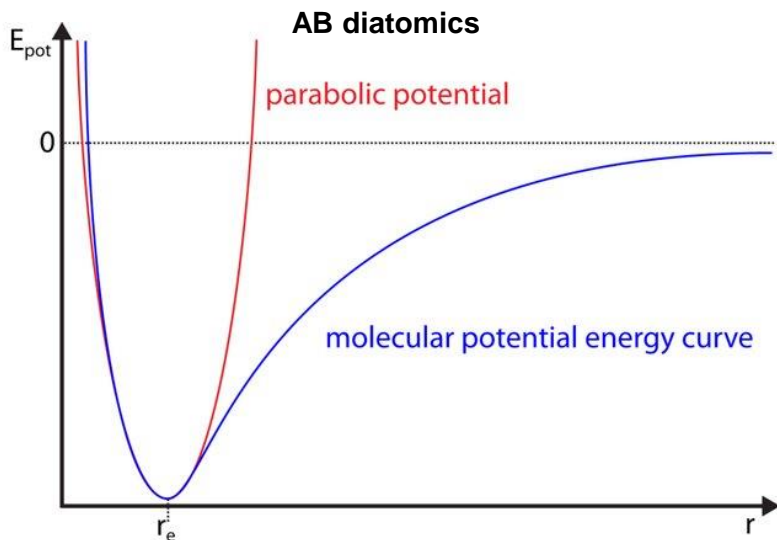
12 valence angles

10 torsions

Simplicity vs. complexity
universal parametrization
derivatives

Bonding Terms

Bond stretching



$$U(r) = U(r_{\text{eq}}) + \left. \frac{dU}{dr} \right|_{r=r_{\text{eq}}} (r - r_{\text{eq}}) + \frac{1}{2!} \left. \frac{d^2U}{dr^2} \right|_{r=r_{\text{eq}}} (r - r_{\text{eq}})^2 + \frac{1}{3!} \left. \frac{d^3U}{dr^3} \right|_{r=r_{\text{eq}}} (r - r_{\text{eq}})^3 + \dots$$



$$U(r_{\text{AB}}) = \frac{1}{2} k_{\text{AB}} (r_{\text{AB}} - r_{\text{AB,eq}})^2$$

(inclusion of quadratic terms)
[used in MM for biopolymers]



$$U(r_{\text{AB}}) = \frac{1}{2} [k_{\text{AB}} + k_{\text{AB}}^{(3)} (r_{\text{AB}} - r_{\text{AB,eq}})] (r_{\text{AB}} - r_{\text{AB,eq}})^2$$

(inclusion of cubic terms)



$$U(r_{\text{AB}}) = \frac{1}{2} [k_{\text{AB}} + k_{\text{AB}}^{(3)} (r_{\text{AB}} - r_{\text{AB,eq}}) + k_{\text{AB}}^{(4)} (r_{\text{AB}} - r_{\text{AB,eq}})^2] (r_{\text{AB}} - r_{\text{AB,eq}})^2$$

(inclusion of quartic terms)

[used in MM3 force-field fororganic chemistry]

$$U(r_{AB}) = \frac{1}{2}k_{AB}(r_{AB} - r_{AB,eq})^2$$

Typical values of k (in $kcal.mol^{-1}.\text{\AA}^{-2}$)

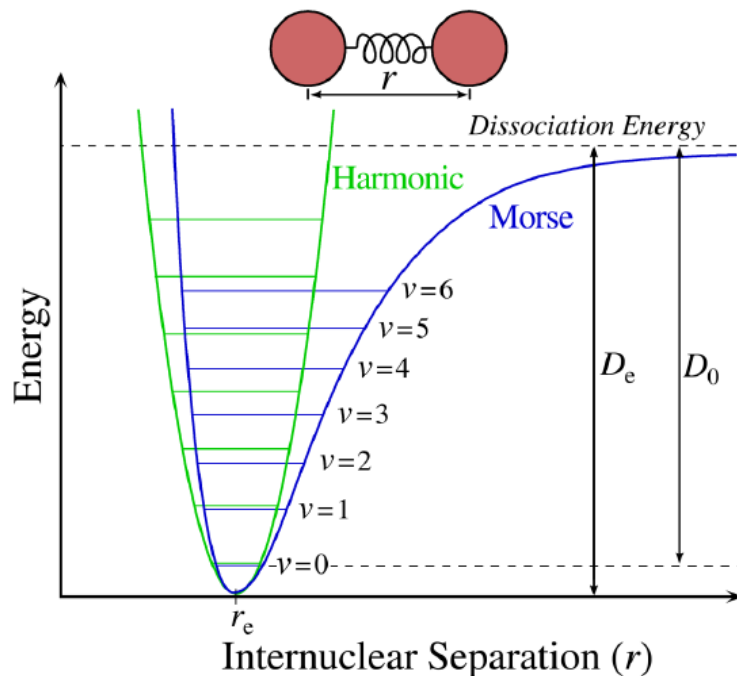
C-C ~300

C=C ~650

C=O ~780

Bond Stretching

Morse potential $V(r) = D_e(1 - e^{-a(r-r_e)^2})$



$$a = \omega \sqrt{\mu / 2D_e}$$

Good description of chemical bond

3 parameters
NOT efficient computation

Harmonic potential

$$V(r) = k/2 (r - r_e)^2$$

Angle Bending

$$V(\Theta) = k/2 (\Theta - \Theta_e)^2$$

Typical values of k (in $kcal.mol^{-1}.deg^{-2}$)

C-C-C ~ 0.01

Higher-order terms can be used (cubic, quartic)

Torsions

$$V(\omega) = \sum_{n=0}^N \frac{V_n}{2} [1 + \cos(n\omega - \gamma)]$$

Amplitudes (parameter)

AMBER

One or two terms

MM2

Mostly 3 terms

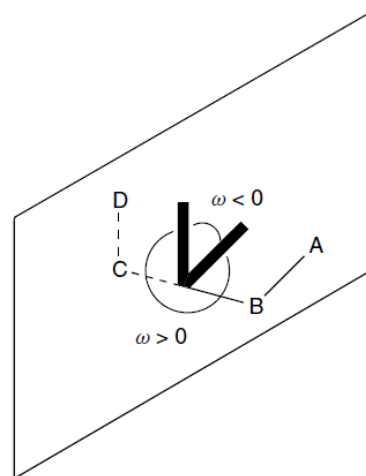


Figure 2.2 Definition and sign convention for dihedral angle ω . The bold lines are the projections of the AB and CD bonds into the bisecting plane. Note that the sign of ω is independent of whether one chooses to view the bisecting plane from the AB side or the CD side

Improper Torsions or Out-of-Plane Bending

For cyclic or conjugated systems

To keep atoms in plane (e.g. cyclobutanone)

(oop = out-of-plane)

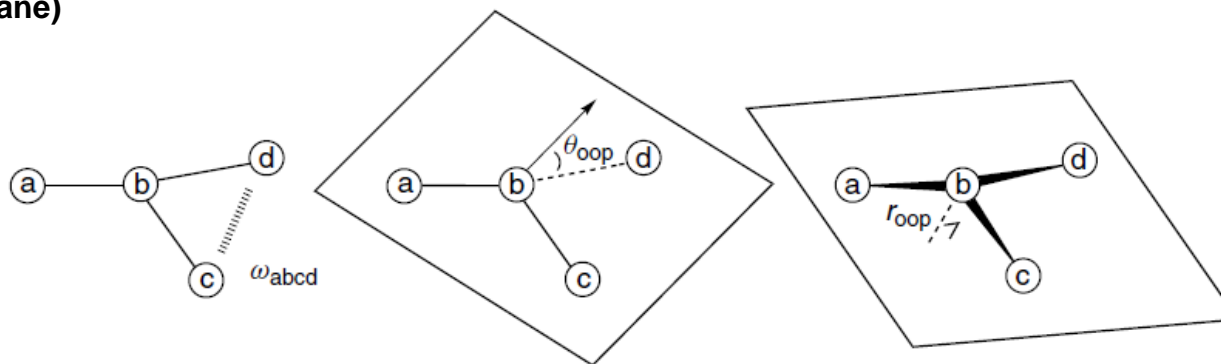


Figure 2.5 Alternative molecular coordinates that can be used to compute the energetics of distortions from planarity about a triply substituted central atom

Cross-terms in force fields

Bond-bond, bond-stretch, bend-bend-torsion, ...

e.g.

$$V(r_1, r_2, \Theta) = \frac{k_{r_1, r_2, \Theta}}{2} [(r_1 - r_{1,e}) + (r_2 - r_{2,e})](\Theta - \Theta_e)$$

Non-Bonding Terms

Van der Waals interactions

Dispersive interactions (London force, 1930)

Two Drude Oscillators

$$V(r) = -\frac{\alpha^4 \hbar \omega}{2(4\pi\epsilon_0)^2 r^6}$$

Drude particles are model oscillators used to simulate the effects of electronic polarizability in the context of a classical molecular mechanics force field. They are inspired by the Drude model of mobile electrons and are used in the computational study of proteins, nucleic acids, and other biomolecules.

Lennard-Jones potential

$$V(r_{AB}) = 4\epsilon_{AB} \left[\left(\frac{\sigma_{AB}}{r_{AB}} \right)^{12} - \left(\frac{\sigma_{AB}}{r_{AB}} \right)^6 \right]$$

\downarrow repulsive term \downarrow attractive term

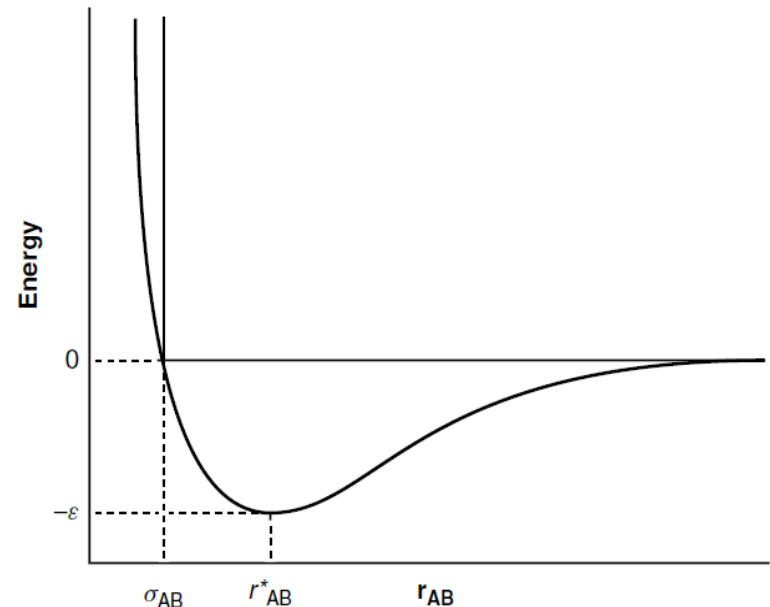


Figure 2.6 Non-attractive hard-sphere potential (straight lines) and Lennard-Jones potential (curve). Key points on the energy and bond length axes are labeled

Electrostatic Interactions

Coulomb's law

$$V_{el} = \sum_{i < j} \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

Central multipole expansion

Charge-charge

Charge-dipole

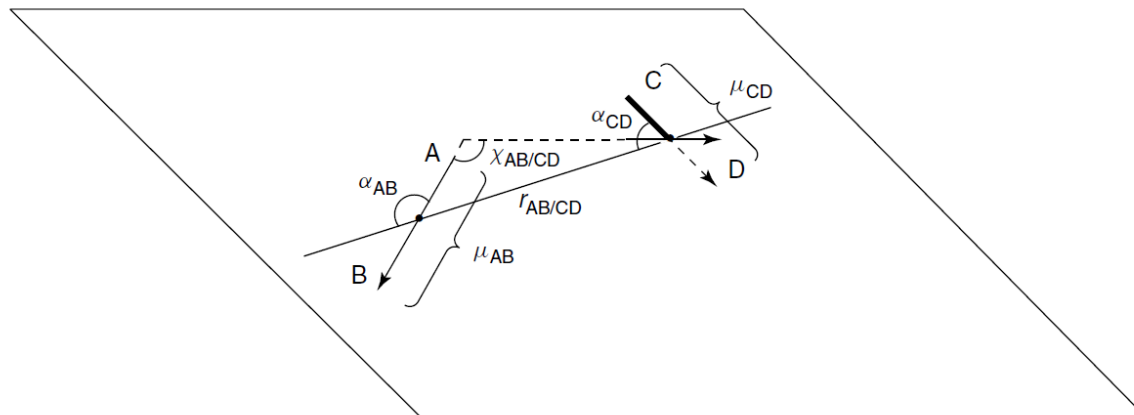
Dipole-dipole



$$U_{AB/CD} = \frac{\mu_{AB}\mu_{CD}}{\epsilon_{AB/CD}r_{AB/CD}^3} (\cos \chi_{AB/CD} - 3 \cos \alpha_{AB} \cos \alpha_{CD})$$

Charge-quadrupole

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Methods for deriving partial atomic charges

Atomic charge ... not observable!

QM: Mulliken, Lowdin, Bader AIM, ESP

Rapid Methods: partial equalisation of orbital electronegativity

ESP: Electrostatic Potential Fits

Solvent dielectric models

Solvent Effects

Water Models

Polarized FFs

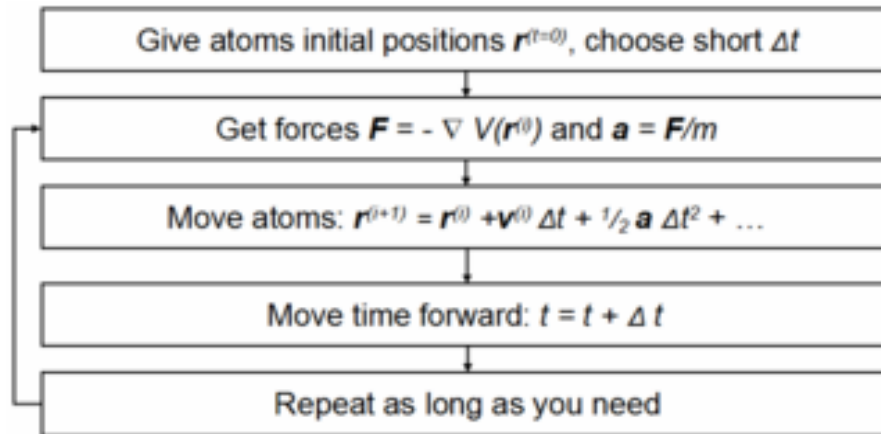
United Atoms Force Field (Coarse-Grained Models)

Force Field Parametrization (Transferability, Heterocompounds, Inorganic Molecules)

MM/MD (force field) methods: molecular simulations

Molecular mechanics (MM): optimization of molecular geometry

Molecular dynamics (MD): dynamical trajectory (t , T , ... p , V , PBC)



(Dis)advantages: universal parametrization

Systems: 100.000 atoms can be studied conveniently (more on the coarse-grained level)

Limitations: *standard* force fields are not able to describe chemical reactions; heterocompounds poorly described