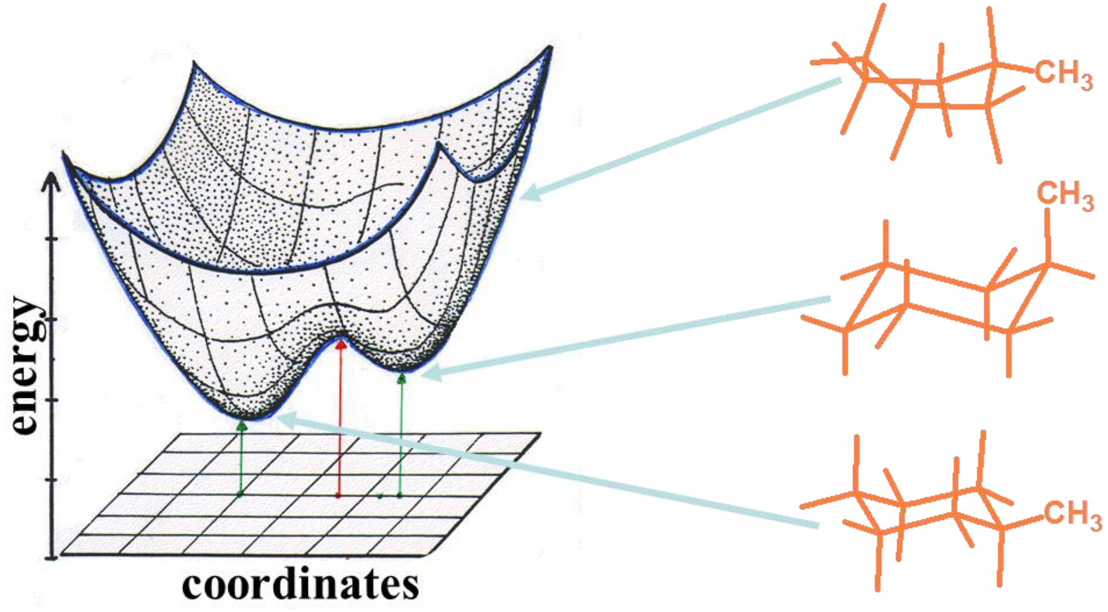
CHEM-E4115
Computational Chemistry I (5op)
2nd part: molecular modelling

Book Chapter 4.1-4.12

Empirical Force Field Models:
Molecular Mechanics

Introduction to force-fields

- Revision
  - Potential energy surface: defined by force-field for each molecule or molecule system
  - Each point represents a molecular conformation



Revision: From quantum mechanics to molecular mechanics

- Many molecular systems in chemistry unfortunately too large to be considered by quantum mechanics
- Force-field methods (molecular mechanics) ignore electronic motion and calculate **the energy of the system as a function of nuclei positions** (molecular subunit positions in coarse-grained force-fields)
  - Enables treating large number of atoms (up to ~10^6-10^7)
  - Looses most electron based characteristics (conductivity, i.e., band-gaps, most often also reaction kinetics*, all chemical reactions* and charge re-distribution*)

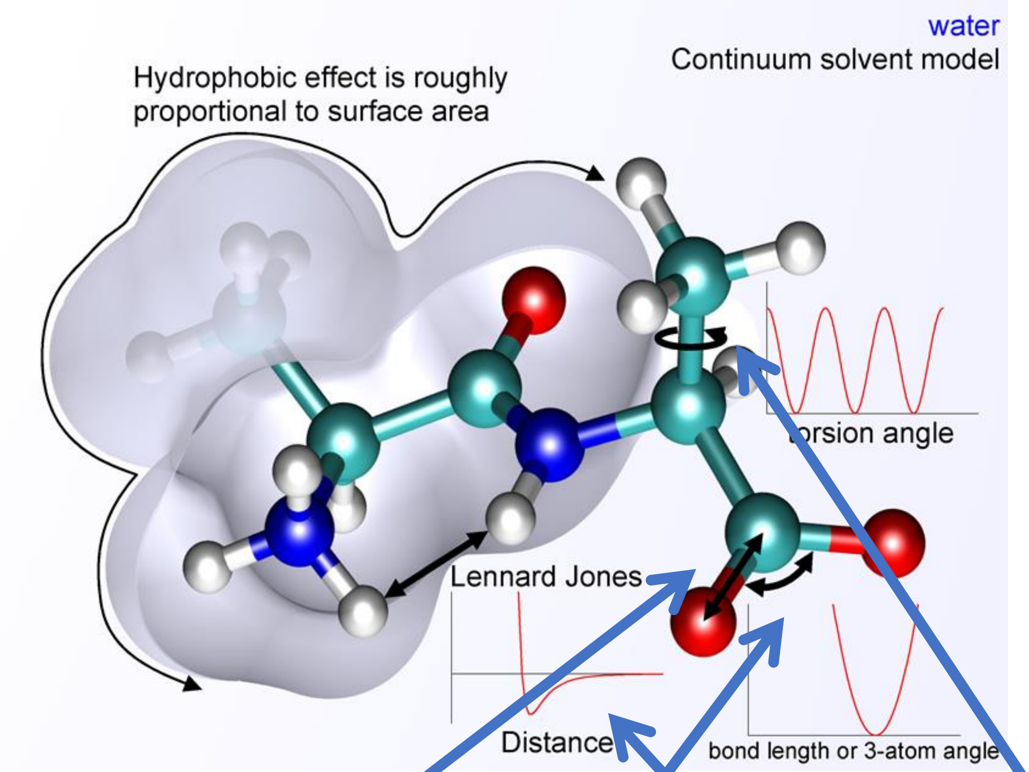
* Typically. That is, some specific force-fields are designed to reproduce also reaction barriers and limited reactions (typically bond-order type advanced force fields) and some enable charge re-distribution (polarization) to some extent

Why do force-field methods work, or do they?

- Assumptions to obtain a functional force-field
  - Born-Oppenheimer approximation (electron motion can be treated separately from nuclei motion due to different time scales)
    - Energy can be written as a function of nuclear coordinates
    - Nuclei follow classical mechanics
  - Force-field terms can be written as separate, simple expressions with separated contributions due different molecular conformation and coordinate changes
    - Typically: Bond stretching, angle between two bonds, twisting (dihedrals), van der Waals, and electrostatic interaction terms
    - Force-field needs to be transferable! (tested on a small number of cases -> must be usable to a much wider set of molecules and problems)

Revision: Typical representation of a force-field (Potential energy surface)

Dialanine peptide in implicit (continuum) solvent



$$E_{bonded} = E_{bond} + E_{angle} + E_{dihedral}$$

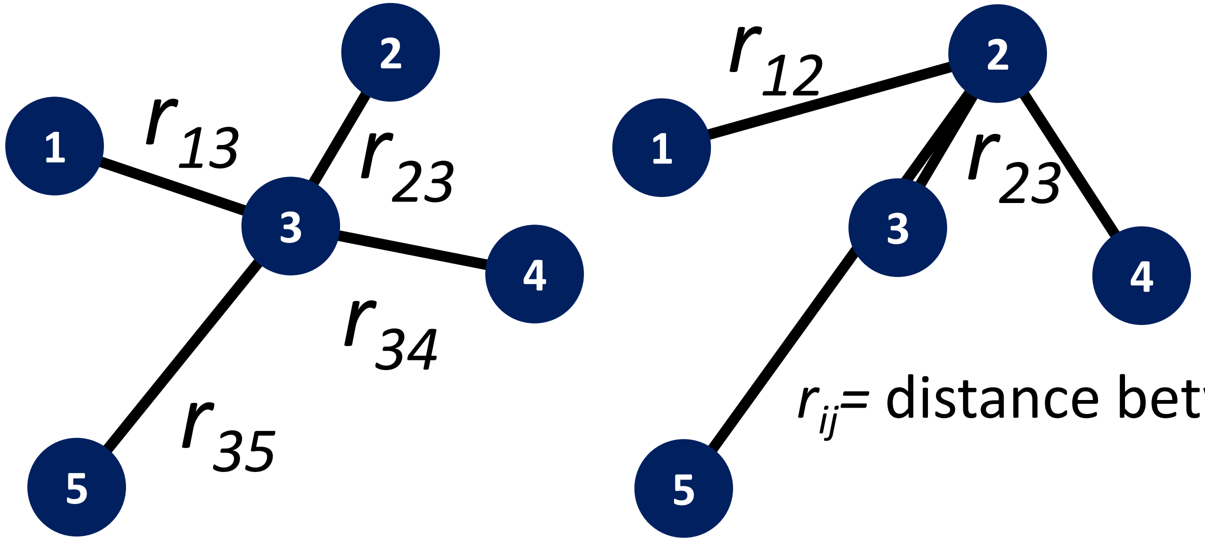
$$E_{nonbonded} = E_{electrostatic} + E_{van\ der\ Waals}$$

Force-fields: A diverse family

- Two-body force-fields (pair potentials)
  - Simple, extremely fast
  - Liquids, gases, solids
  - Lennard-Jones, Morse, ...
- **Many-body chemically non-reactive force-fields**
  - **Many different atom types and molecules covered**
  - **Typically: a wide variety of organic molecules such as proteins, hydrocarbons, lipids, polymers, ...**
  - **Non-reactive!**
- Many-body (reactive) force-fields
  - A wide variety of typically inorganic materials and compounds including also metals (structural & mechanical properties). Organic molecules tend to be too complex.
  - Some are **reactive!**

Pair potentials (two-body force-fields)

- Total potential energy calculated as sum over pairs of interacting objects

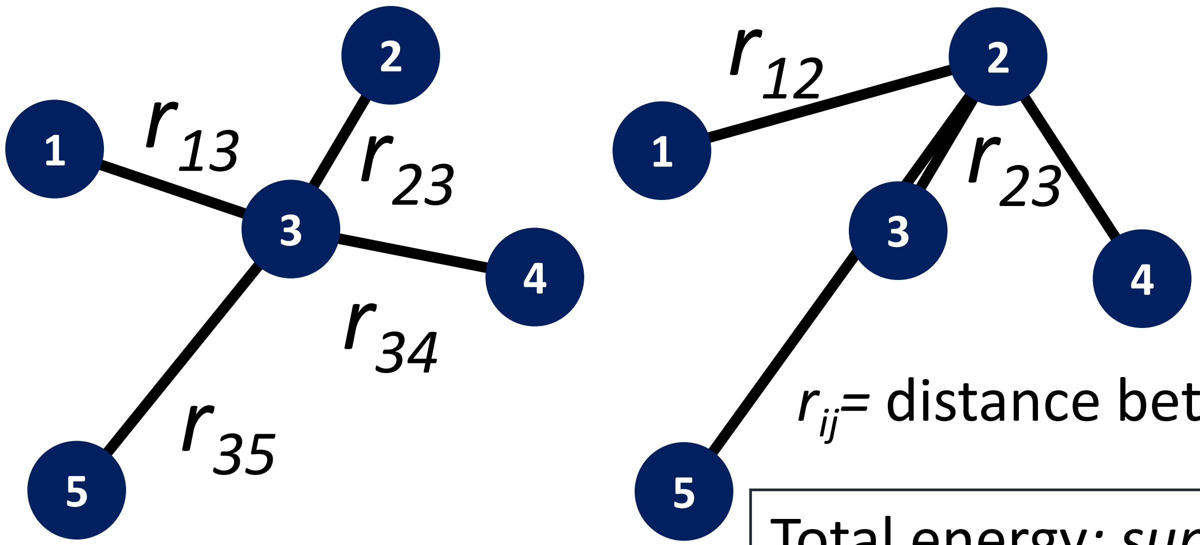


r_{ij}= distance between *i* and *j*

Energy of atom *i* $$V_i = \sum_{j}^{N} V_{ij}\left(r_{ij}\right)$$

Pair potentials (two-body force-fields)

- Total potential energy calculated as sum over pairs of interacting objects



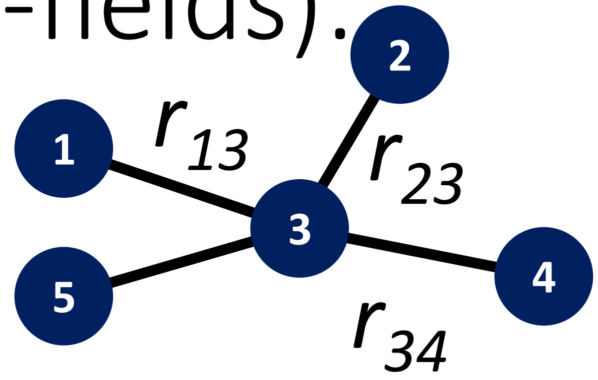
r_{ij}= distance between *i* and *j*

Total energy: *sum of all pairs*

Energy of atom *i* $$V_i = \sum_{j}^{N} V_{ij}(r_{ij}) \quad V_{tot} = \frac{1}{2} \sum_{i \neq j} \sum_{j}^{N} V_{ij}(r_{ij})$$

Avoid double counting

Pair potentials (two-body force-fields): examples



$$V(r_{ij}) = De^{\left(-2\alpha(r_{ij}-r_0)\right)} - 2De^{\left(-\alpha(r_{ij}-r_0)\right)}$$

Morse potential

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

Lennard-Jones 12-6 potential

$$V(r_{ij}) = Ae^{\left(-\frac{r_{ij}}{\sigma}\right)} - C\left(\frac{\sigma}{r_{ij}}\right)^{6}$$

Buckingham potential

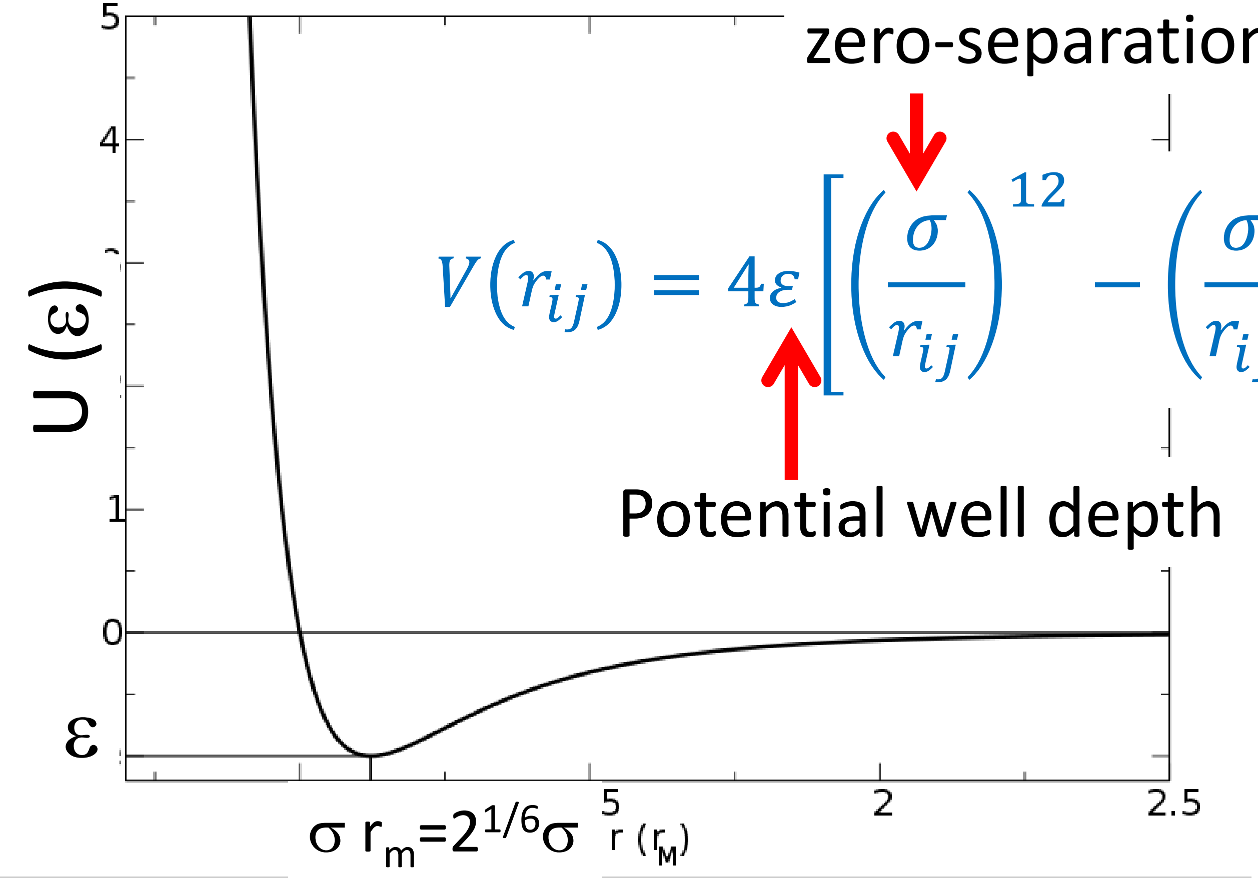
$$V(r_{ij}) = a_0 + \frac{1}{2}k(r_{ij} - r_0)^2$$

Harmonic approximation (spring potential)

Outside molecular modeling: Newton’s law of gravity, Coulomb’s law, …

Pair potentials: Lennard-Jones 12-6

~interaction between a pair of neutral atoms or molecules



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Pair potentials: Lennard-Jones 12-6

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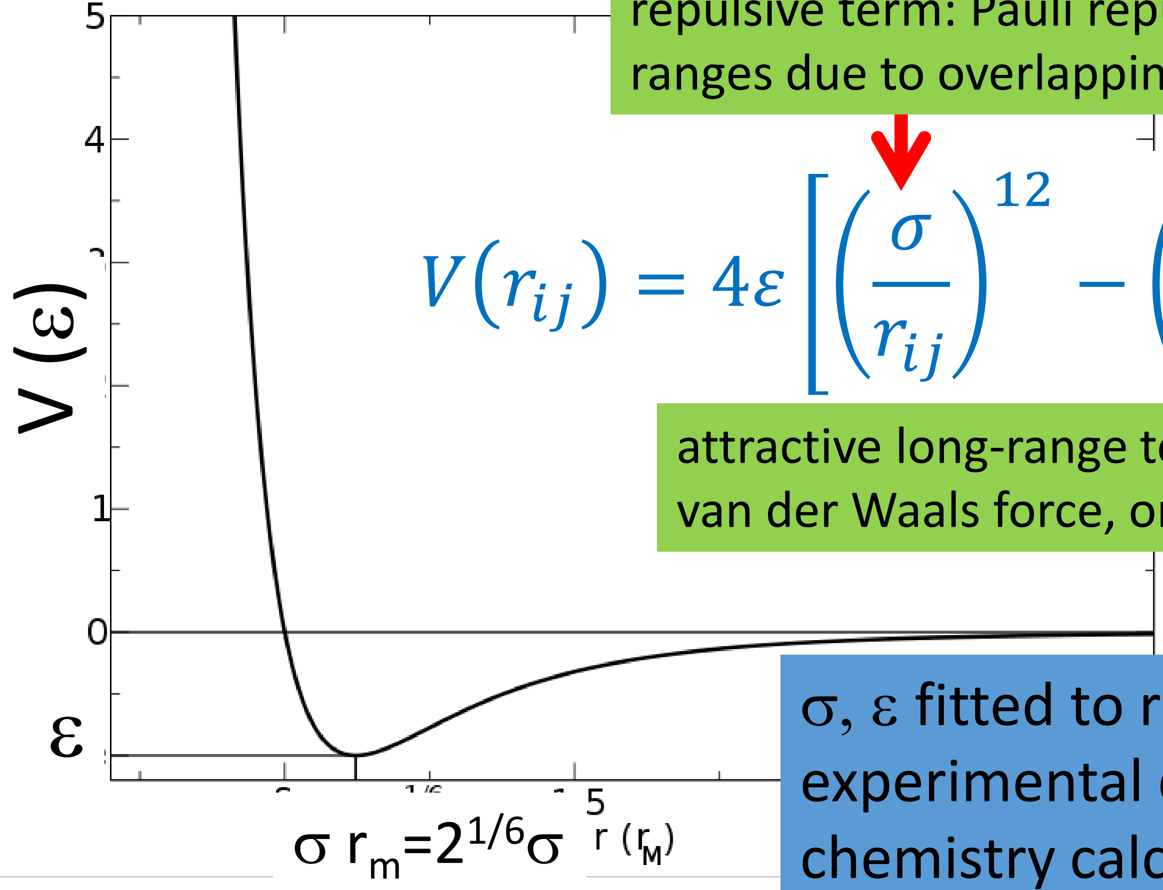


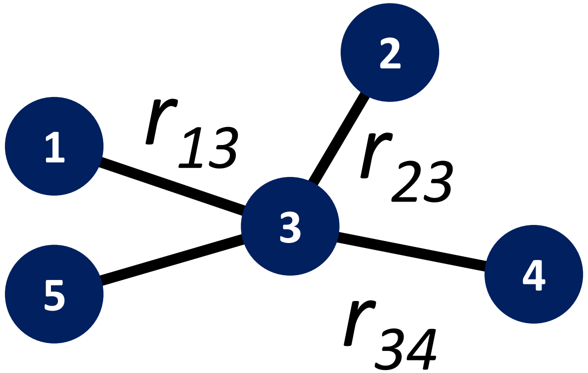
repulsive term: Pauli repulsion at short ranges due to overlapping electron orbitals

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

attractive long-range term:
van der Waals force, or dispersion force

σ, ε fitted to reproduce experimental data or quantum chemistry calculations.

Pair-potentials: summary



Total energy: *sum of all pairs*

Energy of atom *i* $V_i = \sum_{j}^{N} V_{ij}(r_{ij})$ $\quad V_{tot} = \frac{1}{2} \sum_{i \neq j} \sum_{j}^{N} V_{ij}(r_{ij})$

Avoid double counting

- Interaction based on just pair-wise distance
- Good for: noble gases, non-directed bonding
- Simple, fast!

Failures of pair potentials

- bond strength explicitly independent of environment
- Vacancy formation energy in lattice fundamentally overestimated
- Only close-packed lattice structures
- Elastic moduli C12=C44 (not true!)

Force-fields: A diverse family

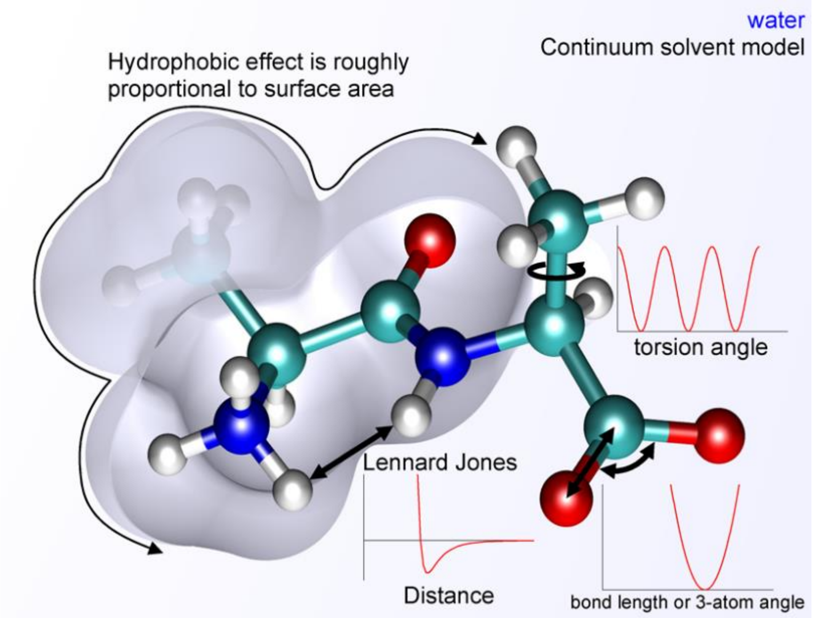
- Two-body force-fields (pair potentials)
  - Simple, extremely fast
  - Liquids, gases, solids
  - Lennard-Jones, Morse, ...
- **Many-body chemically non-reactive force-fields**
  - **Many different atom types and molecules covered**
  - **Typically: a wide variety of organic molecules such as proteins, hydrocarbons, lipids, polymers, ...**
  - **Non-reactive!**

In the following: Force-field = Many-body chemically non-reactive force-field

- Many-body (reactive) force-fields
  - A wide variety of typically inorganic materials and compounds including also metals (structural & mechanical properties). Organic molecules tend to be too complex.
  - Some are **reactive!**

Typical approach for many-body chemically non-reactive force-fields:

Division of interactions into analytical expression that has separate terms each corresponding to physical interactions of different origin/magnitude -> force-field (Potential energy surface)



Dialanine peptide in implicit (continuum) solvent

$$E_{bonded} = E_{bond} + E_{angle} + E_{dihedral}$$

$$E_{nonbonded} = E_{electrostatic} + E_{van\ der\ Waals}$$

Many-body chemically non-reactive force-fields classification

- **Class 1 force fields.**
  - Dynamics of bond stretching and angle bending is described by simple harmonic motion (quadratic approximation)
  - Correlations between bond stretching and angle bending are omitted.
  - Examples: AMBER, CHARMM, GROMOS, OPLS
- **Class 2 force fields.**
  - Add anharmonic cubic and/or quartic terms to the potential energy for bonds and angles.
  - Contain cross-terms describing the coupling between adjacent bonds, angles and dihedrals.
  - Examples: MMFF94, UFF
- **Class 3 force fields.**
  - Explicitly add special effects of organic chemistry such as polarization, stereoelectronic effects, electronegativity effect, Jahn–Teller effect, etc.
  - Examples of class 3 force fields are: AMOEBA, DRUDE

https://computecanada.github.io/molmodsim-md-theory-lesson-novice/aio/index.html

Class 1 force-field typical functional form (Leach's notation)

$$V = V_{bonded} + V_{nonbonded}$$
$$V_{bonded} = V_{bonds} + V_{angles} + V_{dihedrals}$$
$$V_{nonbonded} = V_{van\ der\ Waals} + V_{electrostatic}$$

$$V(\vec{r}^N) = \frac{1}{2}\sum_{bonds} k_i(l_i - l_{i,0})^2 + \frac{1}{2}\sum_{angles} k'_i(\theta_i - \theta_{i,0})^2$$
$$+ \sum_{torsions} \frac{V_N}{2} k''_i(1 + cos(n\omega - \gamma))$$
$$+ \sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(4\varepsilon_{ij}\left[\left(\frac{\sigma_{ii}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ii}}{r_{ij}}\right)^{6}\right] + \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}\right)$$

For example, AMBER force-field has this form

Class 1 force-field typical functional form (Leach's notation)

Potential energy

Bond i length

Bond i reference length

Angle i

Angle i reference

$$V(\vec{r}^N) = \frac{1}{2}\sum_{bonds} k_i (l_i - l_{i,0})^2 + \frac{1}{2}\sum_{angles} k'_i (\theta_i - \theta_{i,0})^2$$

$$+ \sum_{torsions} \frac{V_N}{2} k''_i (1 + cos(n\omega - \gamma))$$

Bond rotation energy
n=multiplicity
γ shift

$$+\sum_{i=1}^{N} \sum_{j=i+1}^{N} \left(4\varepsilon_{ij} \left[\left(\frac{\sigma_{ii}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ii}}{r_{ij}}\right)^{6} \right] + \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}} \right)$$

Summation over all particle pairs

Lennard-Jones 12-6 potential van der Waals (dispersion) interaction)

Coulomb energy charge-charge interaction

For example, AMBER force-field has this form

Dialanine peptide in implicit (continuum) solvent

$$V(\vec{r}^N)=\frac{1}{2}\sum_{bonds} k_i(l_i - l_{i,0})^2 + \frac{1}{2}\sum_{angles} k'_i(\theta_i - \theta_{i,0})^2$$

$$+ \sum_{torsions} \frac{V_N}{2} k''_i(1 + cos(n\omega - \gamma))$$

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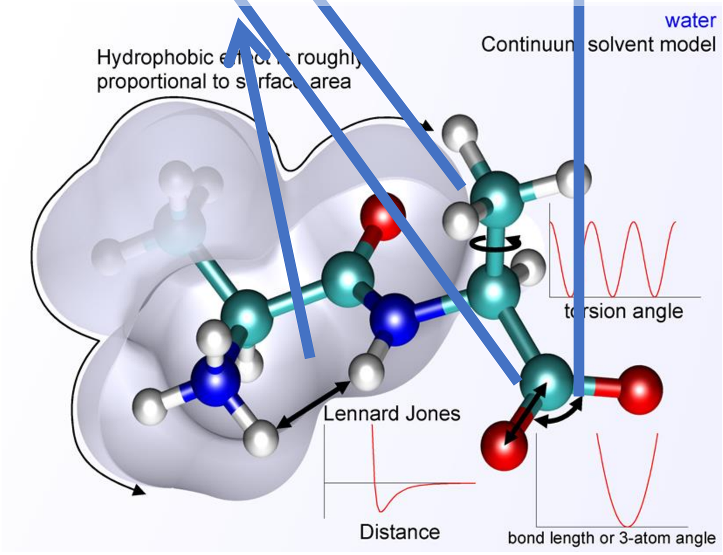
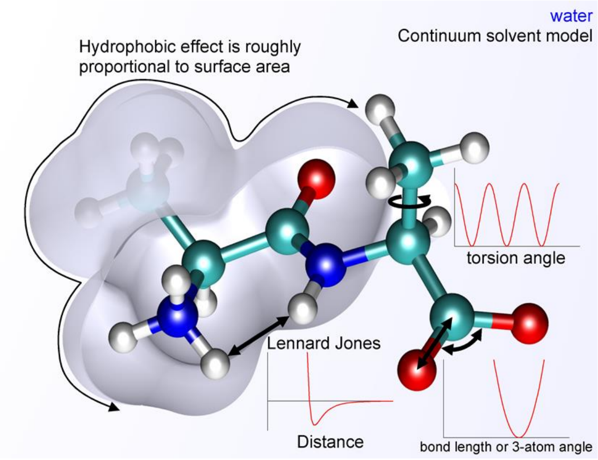


Force-field terms have different magnitudes (compare with thermal energy $k_B T$)

Energy scale of potential terms

$k_B T$ at 298 K	~ 0.593	$\frac{kcal}{mol}$
Bond vibrations	~ 100 - 500	$\frac{kcal}{mol \cdot Å^2}$
Bond angle bending	~ 10 - 50	$\frac{kcal}{mol \cdot deg^2}$
Dihedral rotations	~ 0 - 2.5	$\frac{kcal}{mol \cdot deg^2}$
van der Waals	~ 0.5	$\frac{kcal}{mol}$
Hydrogen bonds	~ 0.5 - 1.0	$\frac{kcal}{mol}$
Salt bridges	~ 1.2 - 2.5	$\frac{kcal}{mol}$



Keep in mind thermodynamics: state probability $\sim e^{\Delta \mathrm{Energy}/k_B T}$ (Boltzmann)

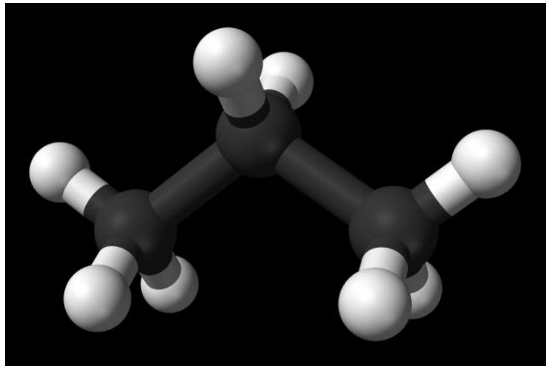
->Bond vibrations, angle bending involve much larger energy cost than the others listed

https://computecanada.github.io/molmodsim-md-theory-lesson-novice/aio/index.html

Force-field parameters

$$V(\vec{r}^N) = \frac{1}{2}\sum_{bonds} k_i (l_i - l_{i,0})^2 + \frac{1}{2}\sum_{angles} k'_i (\theta_i - \theta_{i,0})^2$$
$$+ \sum_{torsions} \frac{V_N}{2} k''_i (1 + cos(n\omega - \gamma))$$
$$+ \sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}\right)$$

- Inherently huge number of parameters
- Grouping of similar / same -> reduces complexity, more generally usable force fields, but may cause problems going outside original parametrization regime
- Sources: Reproducing experimental data and ab initio (quantum chemical calculations)



Propane C_3H_8

Force-fields and parameters

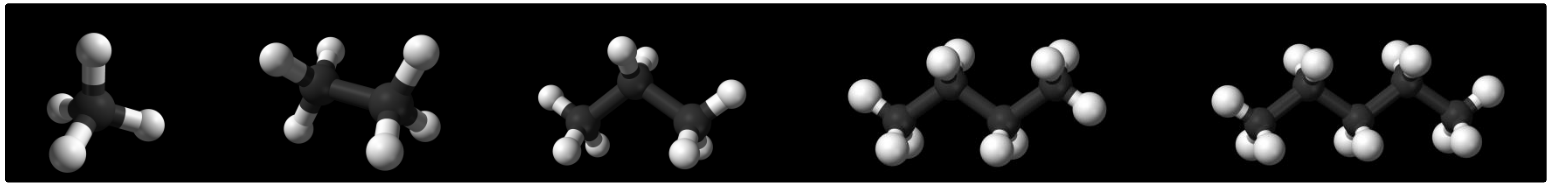
- Force-field requires: Both functional form and parameter values
- Two force fields may have
  - Same functional form but different parameter values
  - Different functional form but same accuracy on same problem
- Force-field should be considered as an entity, not as divided into individual components
  - Parameters from one force-field are not transferable to another even though functional forms may be same!
  - Bond length and angle form an exception (some cases)

Force-field parameters

- Typically designed to reproduce structural properties, can also be designed to reproduce spectra (vibrations)
  - A force-field may predict other quantities outside the parametrization regime but if it does not, it is not a failure!
- Important to know what each force-field has been parameterized to reproduce
- Examples: Liquid properties (density, heat of vaporization) (OPLS), condensed phase properties of alkenes (GROMOS) partition properties between two different solvents (MARTINI), model peptide structure formation accuracy, ...
- Examples for pair potentials & inorganic potentials (typically): Lattice structures, phase behavior, mechanical properties, bond dissociation, ...

Force-fields and parameters

- Transferability important
  - Same set can be used to model related molecules



- Computational efficiency important
  - Compromise between accuracy and computational efficiency
- Calculation methods such as energy minimization or molecular dynamics require first and second derivatives, preferably in simple analytic form

Common features in force-fields

- Atom type
  - Contains information about hybridization and local environment
  - For example: sp, sp^2, sp^3 carbon are different atom types (in a non-reactive force-field)
  - Force-fields for specific class of molecules (for example, protein force-fields) have more atom types than general force-fields
- Partial charge (in non-polarizable force-fields)
  - Electron localization described by assigning each nucleus a fraction charge

Example from course book: Fig. 4.3 AMBER atom types for histidine, tryptophan, and phenylalanine

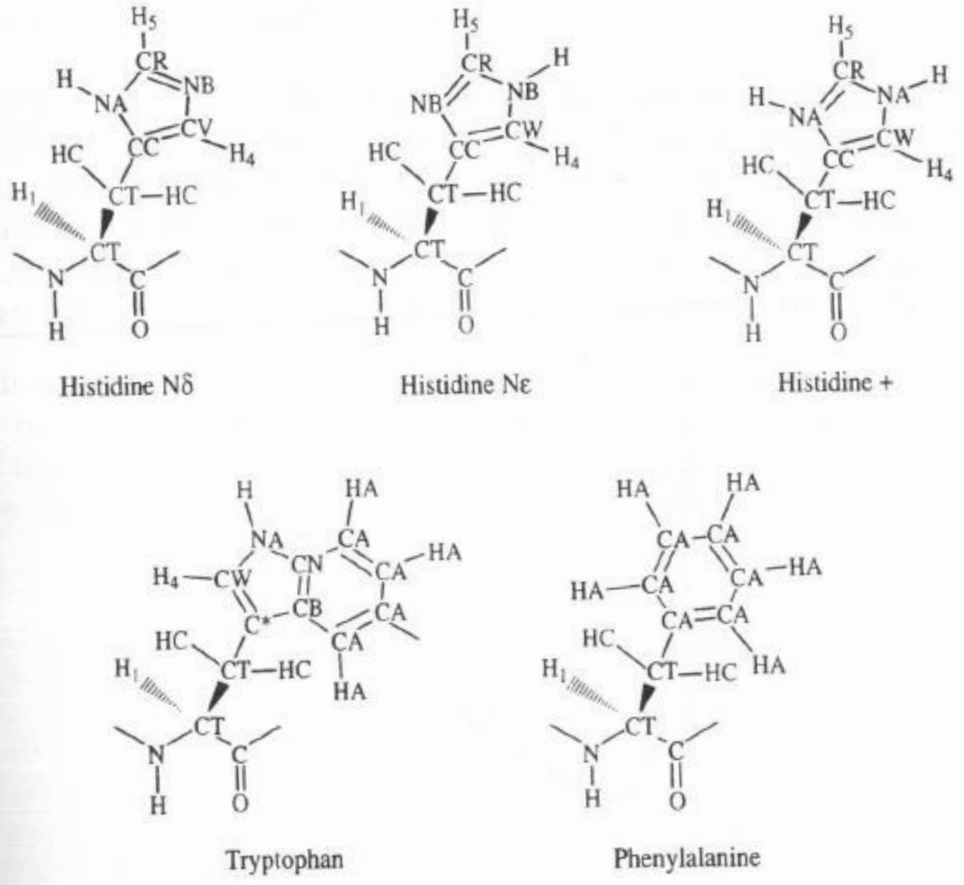


Fig. 4.3: AMBER atom types for the amino acids histidine, tryptophan and phenylalanine. There are three possible protonation states of histidine.

Andrew Leach ”Molecular Modelling: Principles and Applications”, 2nd Edition

Many-body chemically non-reactive force-fields: terms

$$V = V_{bonded} + V_{nonbonded}$$
$$V_{bonded} = V_{bonds} + V_{angles} + V_{dihedrals}$$
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$$+ \sum_{i=1}^{N} \sum_{j=i+1}^{N} \left(4\varepsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6} \right] + \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}} \right)$$

Next: 1) Bonds, 2) Angles, 3) Torsions (dihedrals), 4) van der Waals (dispersion) forces, and 5) Electrostatics

Bonds vs. Angles vs. Torsions (dihedrals) vs van der Waals (dispersion) forces vs Electrostatics in force-fields

- Most variation in molecular structure in molecular modelling due to interplay between torsional and non-bonded contributions
  - Bonds and angles require higher energies for significant deviations
- Electrostatics is a long-range interaction. Molecular modelling typically sensitive to long-range electrostatics (computationally heavy)

Bond stretching in force-field

$$V(l_i) = \frac{1}{2}k\left(l_i - l_{i,0}\right)^2$$

Most common: Hookean spring harmonic approximation behavior close to reference bond length $l_{i,0}$ only

Requires 2 parameters:

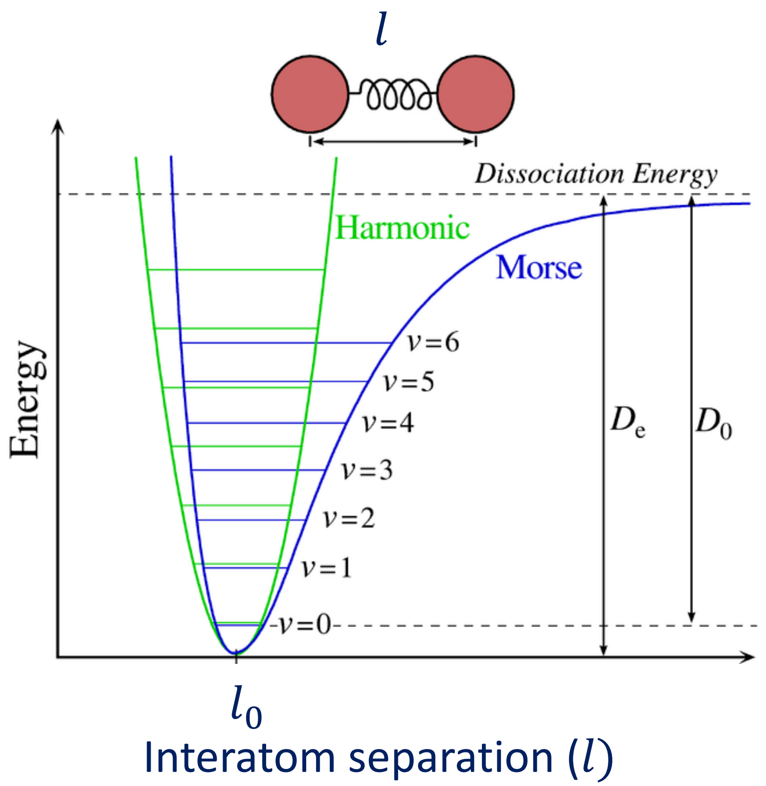
k (spring) force constant, $l_{i,0}$

$$V(l_i) = D_e\left(1 - e^{\left(-\alpha\left(l-l_{i,o}\right)\right)}\right)^2$$
$$= D_e e^{\left(-2\alpha\left(l_i-l_{i,0}\right)\right)} - 2D_e e^{\left(-\alpha\left(l_i-l_{i,0}\right)\right)} + C$$

Less common but more realistic: Morse potential

Describes wider range of behavior (also bond dissociation), vibration anharmonicity

Requires 3 parameters



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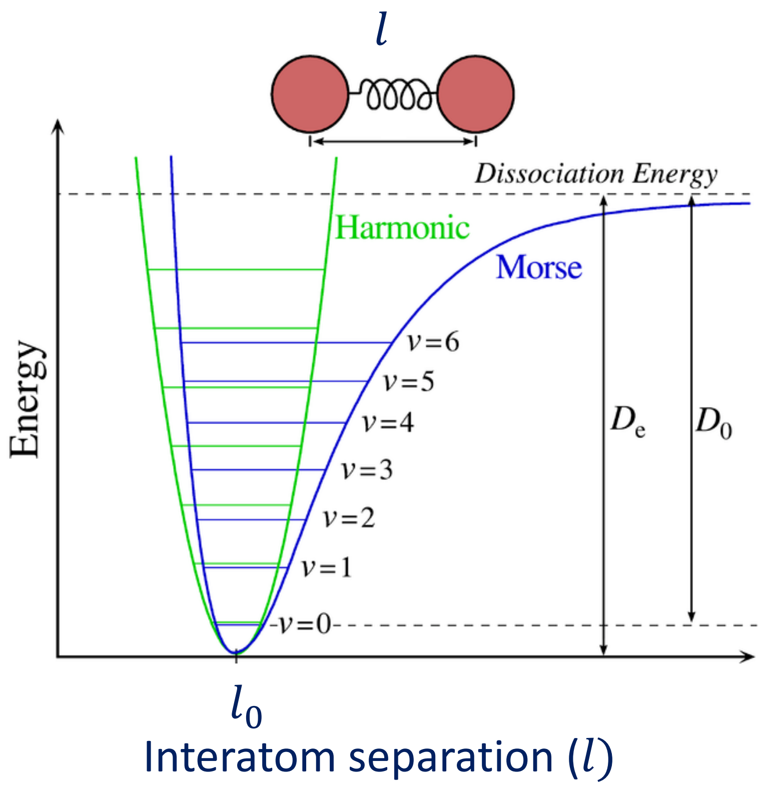


Why harmonic approximation:

Bonds are ”stiff”, i.e., force constants relatively large and typically small deviations from reference! Exception: high temperature, dissociation and association. Special case: irradiation simulations

Bond stretching in force-field

$$V(l_i) = \frac{1}{2}k\left(l_i - l_{i,0}\right)^2$$

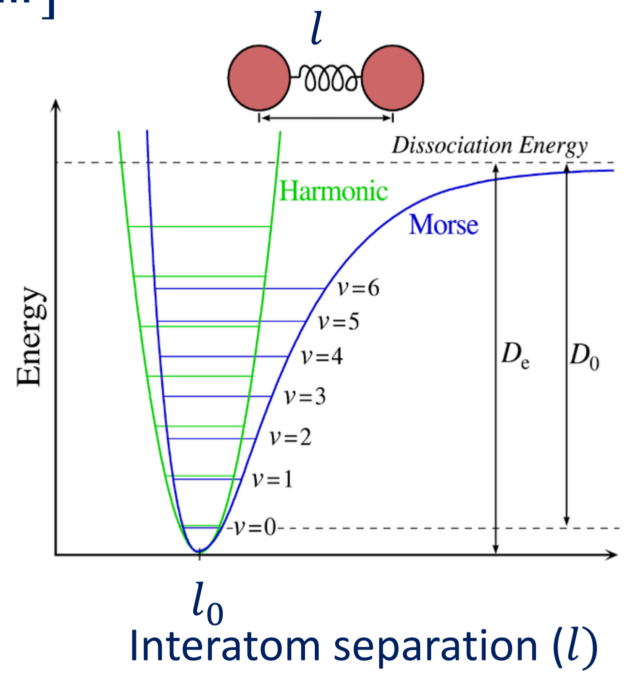
Most common: Hookean spring

harmonic approximation

$$V(l_i) = \frac{1}{2}k\left(l_i - l_{i,0}\right)^2\left[1 - k'\left(l_i - l_{i,0}\right) - k''\left(l_i - l_{i,0}\right)^2 - k'''\left(l_i - l_{i,0}\right)^3 \ldots\right]$$

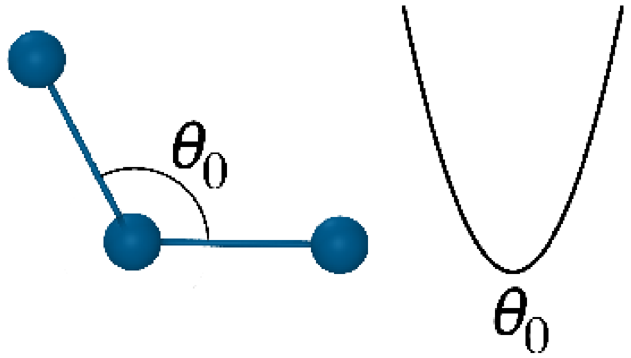
Taylor expansion of any potential energy functional (with analytic derivatives) around reference bond length $l_{i,0}$.

Higher order expansion terms also sometimes used. Note: higher order terms may pass through maxima -> catastrophic lengthening of bonds.



Angle bending in force-field

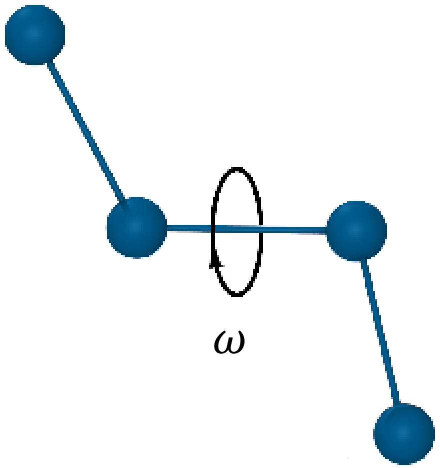
$$V(\theta)=\frac{1}{2}\sum_{\text{angles}} k'_i\left(\theta_i-\theta_{i,0}\right)^2$$



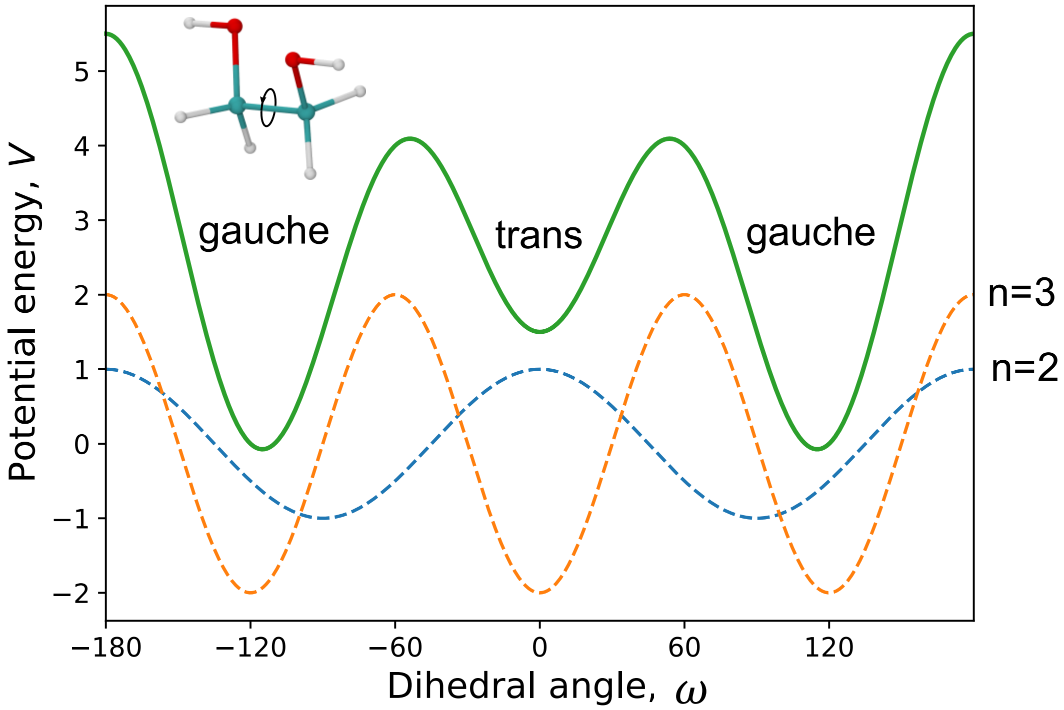
- Most common: Hooke's law (harmonic potential)
- As with bonds, force constant and reference angle
- Angle bending force constants significantly smaller than bond stretching!
- Like with bonds, higher order terms (of Taylor's expansion) can be used to improve accuracy but at computational cost (quadratic term is sometimes used)

Torsion (dihedral) angle potential in force-field

Defined for every 4 sequentially bonded atoms.
Sum of any number of periodic functions, n - periodicity, γ phase shift angle.



$$+\sum_{torsions}\frac{V_N}{2}k''_i\left(1+cos(n\omega-\gamma)\right)$$



n is the number of potential maxima or minima in a 360° rotation.

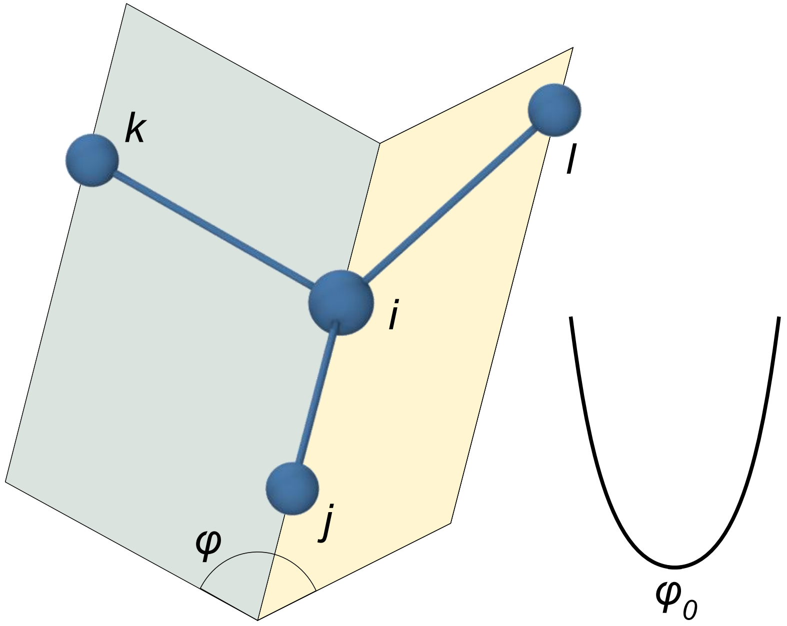
Improper torsion potential in force-field

Also known as 'out-of-plane bending'
Defined for a group of 4 bonded atoms where the central atom *i* is connected to 3 peripheral atoms *j*, *k*, and *l*.
Enforces planarity. Not necessary for all atom quadruplets

$$V_{\text{Improper}} = k_{\varphi}\left(\varphi_i - \varphi_{i,0}\right)^2$$

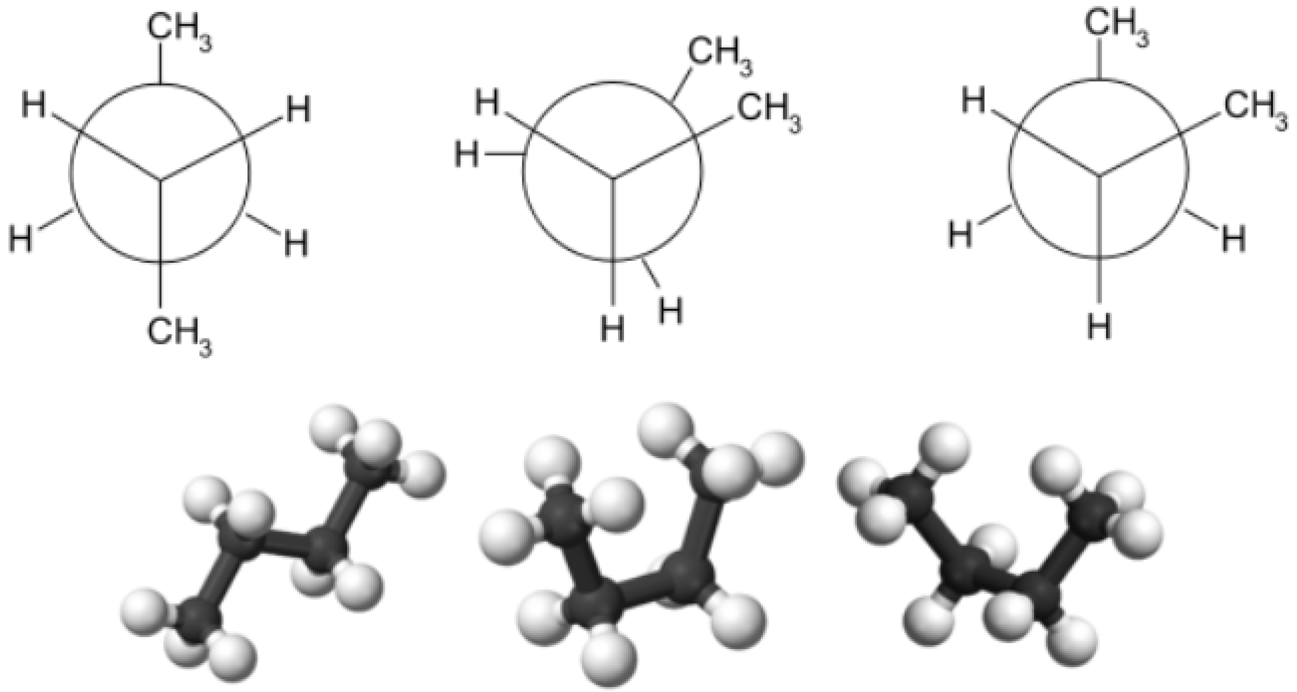
Harmonic potential.

The dihedral angle ϕ is the angle between planes *ijk* and *ijl*.



Proper dihedrals: Let's rotate a butane

In butane, the two staggered conformations are no longer equivalent and represent two distinct conformers:the **anti-conformation** (left-most, below) and the **gauche conformation** (right-most, below).



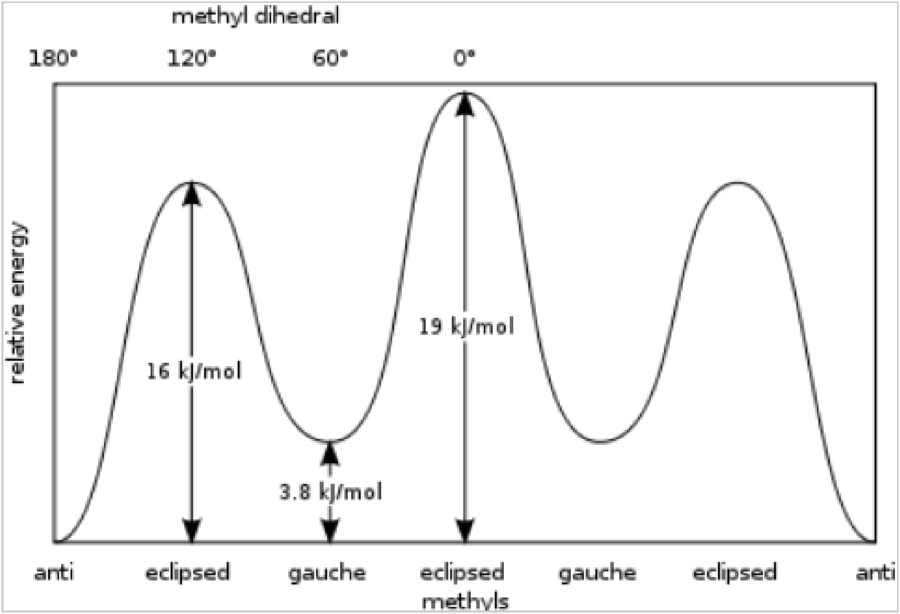
Both conformations are free of torsional strain, but, in the gauche conformation, the two methyl groups are in closer proximity than the sum of their van der Waals radii. The interaction between the two methyl groups is repulsive (van der Waals strain), and an energy barrier results.

http://en.wikipedia.org/wiki/Alkane_stereochemistry

Proper dihedrals : Let’s rotate a butane

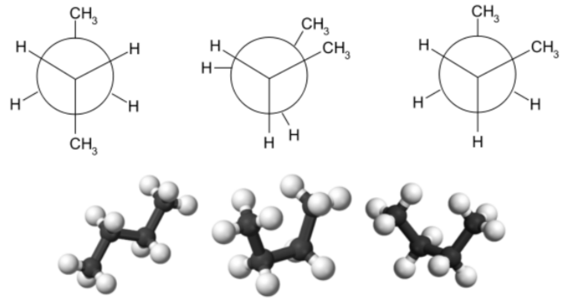
- Gauche, conformer - 3.8 kJ/mol
- Eclipsed H and CH_3 - 16 kJ/mol
- Eclipsed CH_3 and CH_3 - 19 kJ/mol.

The eclipsed methyl groups exert a greater steric strain because of their greater electron density compared to lone hydrogen atoms.



Relative energies of conformations of butane with respect to rotation of the central C-C bond.

In butane, the two staggered conformations are no longer equivalent and represent two distinct conformers:the **anti-conformation** (left-most, below) and the **gauche conformation** (right-most, below).



Both conformations are free of torsional strain, but, in the gauche conformation, the two methyl groups are in closer proximity than the sum of their van der Waals radii. The interaction between the two methyl groups is repulsive (van der Waals strain), and an energy barrier results.

(Proper) dihedrals in force-fields

- Barriers for rotation necessary for reproducing basic chemical structure
- Torsion potentials can be defined either for (all) 4 atom sets or as general torsions around central bond
- 1-fold dihedral: bond dipoles (difference in electronegativity); 2-fold dihedral: double bond character; 3-fold and higher: steric interactions
  - parameterization becomes complex and molecule-specific with high-order dihedrals

Improper dihedrals

- Example: cyclobutanone C_4H_6O (course book Fig 4.9)
  - Experimentally known the oxygen remains in the plane of the carbon atoms; To achieve this a out-of-plane bending term added

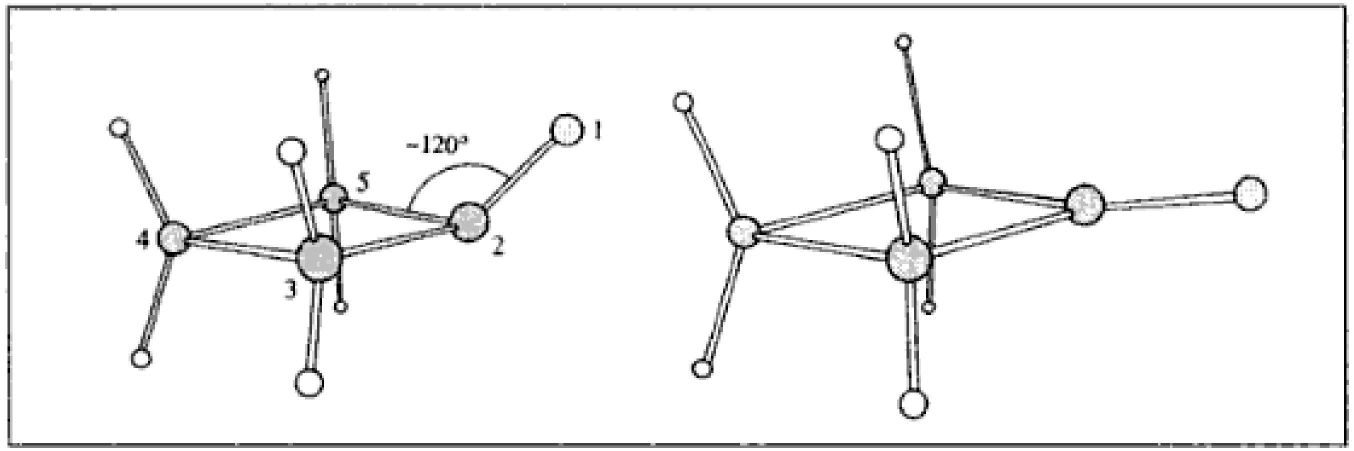


Fig. 4.9: Without an out-of-plane term, the oxygen atom in cyclobutane is predicted to lie out of the plane of the ring (left) rather than in the plane.

A torsional potential of the following form is then used to maintain the improper torsion angle at 0° or 180°:

$$v(\omega) = k(1 - \cos 2\omega) \quad (4.11)$$

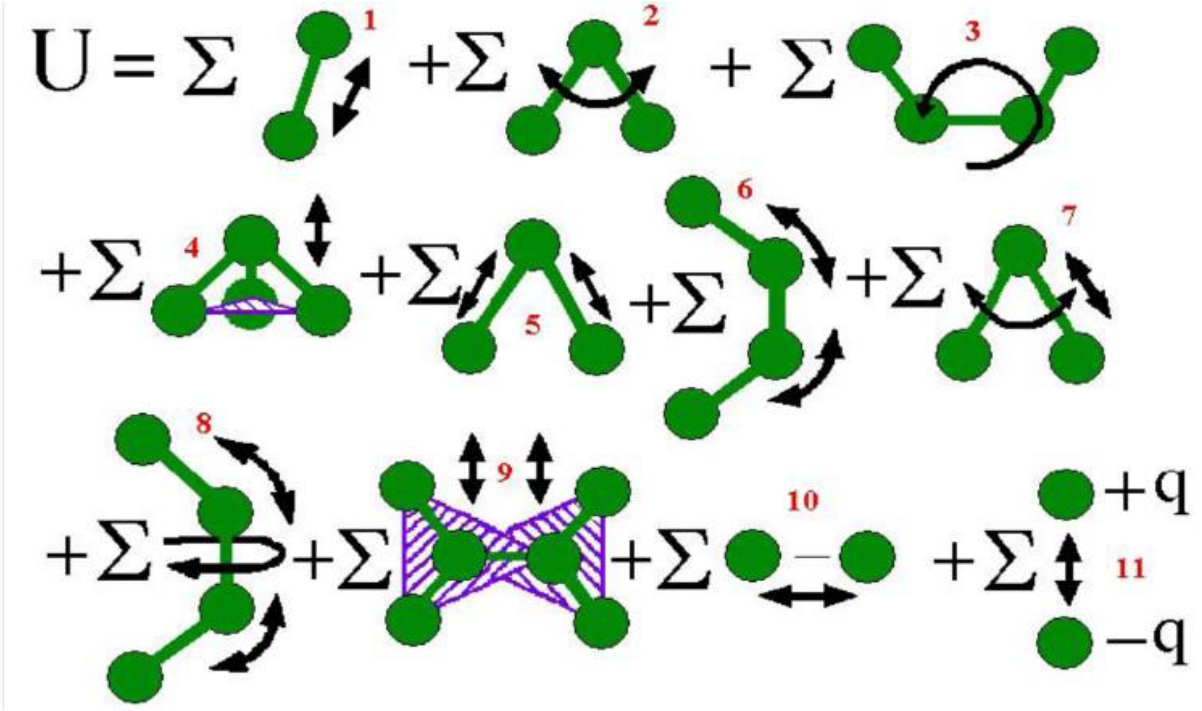
Improper dihedrals

- Necessary for (for example)
  - aromatic rings (planar)
  - stereochemistry in united-atom force-fields (force-fields which combine non-polar hydrogens with adjanced heavy atom)
- Quite often omitted in force-fields because
  - Necessary only for some molecular configurations (when necessary, cannot be omitted)
  - Including out-of-plane terms often has bad effect on force-field behaviour
  - Vibration frequencies sensitive

Examples of less common bonded interaction terms

- Cross-terms
  - Cross-interaction of 2 bonds stretching
  - Cross-interaction of bond stretching and angle
- Relating 2nd neighbor distance with angle (=1-3 distance energy term instead of angle energy term)
- Including bond stretching into dihedrals
- Including angle bending into dihedrals

Many-body chemically non-reactive force-fields: functional form



1.Bond stretching term;
2. Angle term;
3. Torsion term;
4. Out of plane term;

5. Bond -Bond term;
6. Angle - Angle term;
7. Bond - Angle term;
8. Angle - Angle - Torsion term;

9. Out of plane - Out of plane term;
10. Non bonded term;
11. Electrostatic term; etc..

Force-field terms have different magnitudes (compare with thermal energy $k_B T$)

Energy scale of potential terms

$k_B T$ at 298 K	~ 0.593	$\frac{kcal}{mol}$
Bond vibrations	~ 100 - 500	$\frac{kcal}{mol \cdot \text{Å}^2}$
Bond angle bending	~ 10 - 50	$\frac{kcal}{mol \cdot deg^2}$
Dihedral rotations	~ 0 - 2.5	$\frac{kcal}{mol \cdot deg^2}$
van der Waals	~ 0.5	$\frac{kcal}{mol}$
Hydrogen bonds	~ 0.5 - 1.0	$\frac{kcal}{mol}$
Salt bridges	~ 1.2 - 2.5	$\frac{kcal}{mol}$

Keep in mind thermodynamics:
state probability $\sim e^{\Delta \text{Energy}/k_B T}$
(Boltzmann)

->Bond vibrations, angle bending involve much larger energy cost than the others listed

https://computecanada.github.io/molmodsim-md-theory-lesson-novice/aio/index.html

Force-fields: A diverse family

- Two-body force-fields (pair potentials)
  - Simple, extremely fast
  - Liquids, gases, solids
  - Lennard-Jones, Morse, ...
- **Many-body chemically non-reactive force-fields**
  - **Many different atom types and molecules covered**
  - **Typically: a wide variety of organic molecules such as proteins, hydrocarbons, lipids, polymers, ...**
  - **Non-reactive!**

- Many-body (reactive) force-fields
  - A wide variety of typically inorganic materials and compounds including also metals (structural & mechanical properties). Organic molecules tend to be too complex.
  - Some are **reactive!**

Revision: Many-body chemically non-reactive force-fields: terms

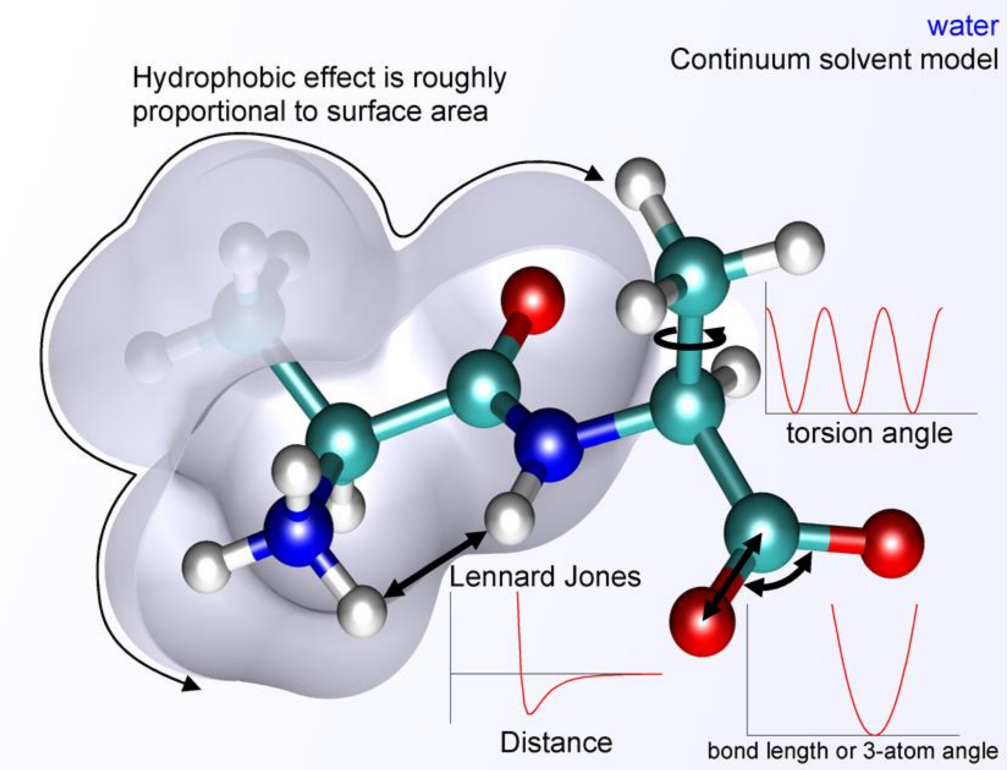
$$V = V_{bonded} + V_{nonbonded}$$
$$V_{bonded} = V_{bonds} + V_{angles} + V_{dihedrals}$$
$$V_{nonbonded} = V_{van\ der\ Waals} + V_{electrostatic}$$

$$V(\vec{r}^N) = \frac{1}{2}\sum_{bonds} k_i(l_i - l_{i,0})^2 + \frac{1}{2}\sum_{angles} k'_i(\theta_i - \theta_{i,0})^2$$
$$+ \sum_{torsions} \frac{V_N}{2} k''_i(1 + cos(n\omega - \gamma))$$
$$+ \sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(4\varepsilon_{ij}\left[\left(\frac{\sigma_{ii}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ii}}{r_{ij}}\right)^{6}\right] + \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}\right)$$

Last time: 1) Bonds, 2) Angles, 3) Torsions (dihedrals),
Next: 4) van der Waals (dispersion) forces, and 5) Electrostatics

Revision: Typical representation of a force-field (Potential energy surface)

Dialanine peptide in implicit (continuum) solvent



$$E_{bonded} = E_{bond} + E_{angle} + E_{dihedral}$$

$$E_{nonbonded} = E_{electrostatic} + E_{van\ der\ Waals}$$

Many-body chemically non-reactive force-fields: Now moving on to non-bonded terms

$$V = V_{bonded} + V_{nonbonded}$$
$$V_{bonded} = V_{bonds} + V_{angles} + V_{dihedrals}$$
$$V_{nonbonded} = V_{van\ der\ Waals} + V_{electrostatic}$$

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For example, AMBER force-field has this form

Many-body chemically non-reactive force-fields: Now moving on to non-bonded terms

Potential energy

Bond i length

Bond i reference length

Angle i

Angle i reference

$$V(\vec{r}^N)=\frac{1}{2}\sum_{bonds} k_i\left(l_i - l_{i,0}\right)^2 + \frac{1}{2}\sum_{angles} k'_i\left(\theta_i - \theta_{i,0}\right)^2$$

$$+\sum_{torsions}\frac{V_N}{2}k''_i\left(1+cos(n\omega-\gamma)\right)$$

Bond rotation energy
n=multiplicity
γ shift

$$+\sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(4\varepsilon_{ij}\left[\left(\frac{\sigma_{ii}}{r_{ij}}\right)^{12}-\left(\frac{\sigma_{ii}}{r_{ij}}\right)^{6}\right]+\frac{q_iq_j}{4\pi\varepsilon_0 r_{ij}}\right)$$

Summation over all particle pairs

Lennard-Jones 12-6 potential van der Waals (dispersion) interaction)

Coulomb energy charge-charge interaction

For example, AMBER force-field has this form

Non-bonded interactions

- Long range
- Not dictated by ”bonds”
- Both within molecules and between different molecules
- Long-range nature introduces a need for either cut-off distance in computation or long-range calculation scheme

Non-bonded interactions

On this course:
(nomenclature varies in different books)

- Typically 4 components
  - **Repulsive component resulting from the Pauli exclusion principle** (prevents the collapse of molecules) — van der Waals
  - Attractive or repulsive **electrostatic interactions between permanent charges, dipoles, multipoles** — electrostatic
  - **Polarization** (induced electrostatic interactions) (Debye forces) — electrostatic
  - **Dispersion** arising from the interactions of instantaneous multipoles (London forces) — van der Waals
- Most common in molecular modelling to divide these into van der Waals and electrostatic interactions

Non-bonded interactions

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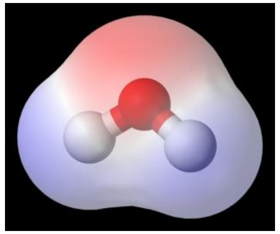
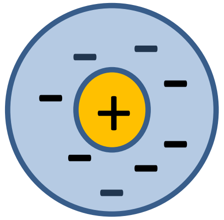
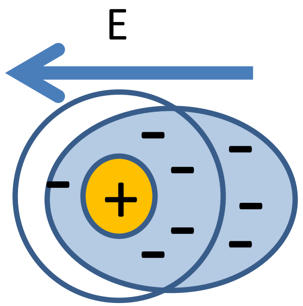
Electrostatic interactions: basics

- Electronegative elements attract electrons more than less electronegative elements
  - Unequal charge distribution in molecule
  - Electric field changes this distribution (polarization)
    - Can be external field or caused by molecular environment
  - Most commonly, polarization not taken into account in force-fields but instead fixed charge distribution used
  - Polarizable force-fields an important method development direction in molecular modelling







Electrostatics by fractional point charges

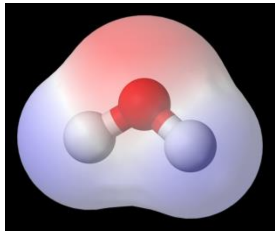
- One common approach in molecular modelling to assign fractional point charges throughout the molecule
  - Point charges designed to reproduce electrostatic properties of the molecule
  - Do not need to be at same locations as nuclei
  - If located at nuclei positions: partial atomic charges

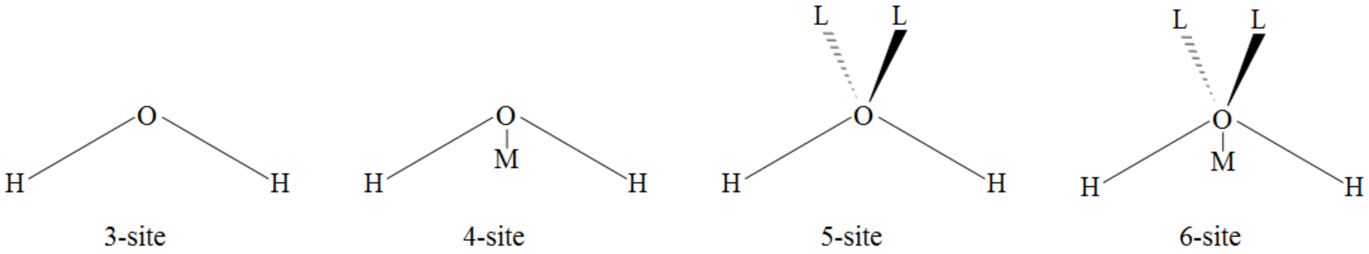
$$V=\sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(\frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}\right)$$

- Downsides of using fractional point charges
  - No dynamical charge redistribution due to changes in electric field (due to changes in molecular environment)

Electrostatics by fractional point charges

- Electrostatics can be represented by multipole expansion of the electrostatic interaction energy
- Sufficient number of fractional point charges reproduce all electric moments of the multipole expansion
  - This may require charges at other positions besides nuclei locations
  - Example: Water molecule



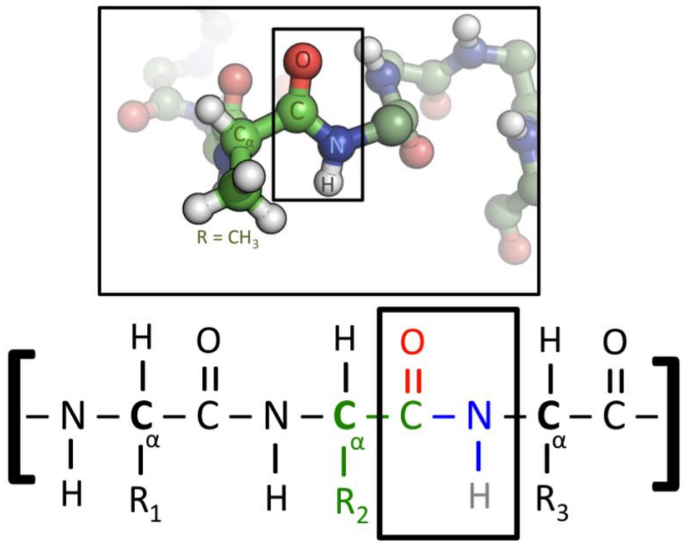


Fractional point charges: where do the numbers come from?

- For simple molecules, can be calculated exactly based on experimental multipole moments
- Sometimes chosen to reproduce thermodynamic properties (large number of simulations required)
- Ab initio simulations: several ways to determine partial charges
- Charge distribution validified by ability to reproduce experimental multipole moments, electrostatic potential, or thermodynamic quantities

Fractional point charges of large molecules

- Look at a small fraction of the larger system
  - Proteins: dipeptide, tripeptide
  - Polymers: oligomers
- Charge distribution will depend on conformation
  - Possible to average over a number of conformations, can be problematic for large molecules

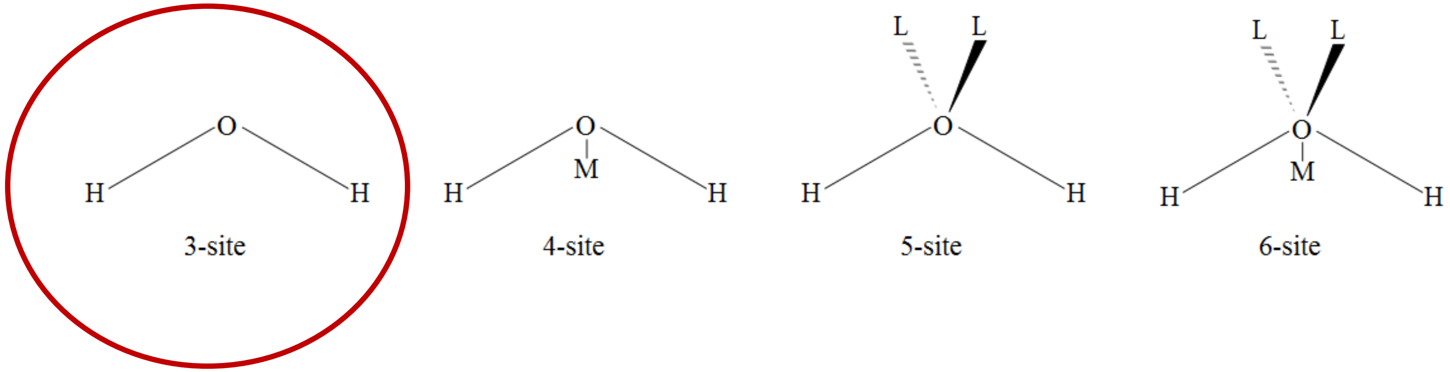


Fractional point charges

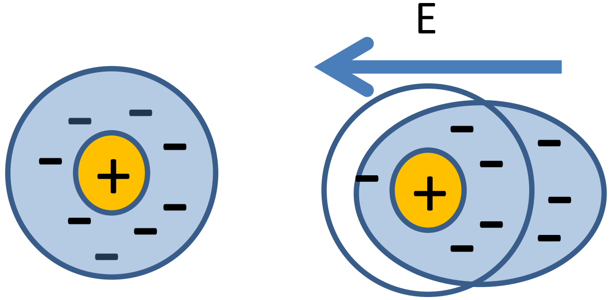
- Charges determined from ab initio calculations depend on
  - Basis set (larger does not necessary improve charges, or force-field performance)
  - Molecular conformation
- In parameterizing new molecules, must be consistent with existing parameterization

Fractional point charges at atom positions (partial atomic charge)

- Electrostatic forces act directly on nuclei
  - Makes things more simple computationally
- Assume charge distribution spherically symmetric
- Incapability to reproduce some higher multipole moments



Polarization



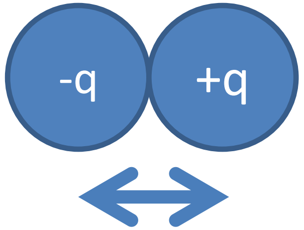
Induced dipole moment

$$\vec{\mu}_{ind} = \alpha \vec{E}$$

electric field

polarizability

Dipole moment



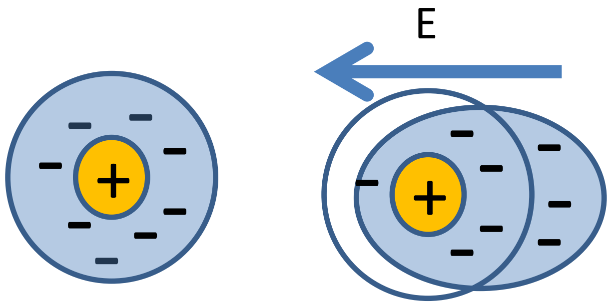
$$\vec{\mu} = q\vec{r}$$

$$v(\alpha, E) = -\int_0^E d\vec{E}\,\vec{\mu}_{ind} = \int_0^E d\vec{E}\,\alpha\vec{E} = -\frac{1}{2}\alpha E^2$$

Energy of interaction for each dipole calculated by work done when charging field from zero to E

At high electric fields also higher order terms may be important (typically quadrupole moment).

Polarization



- Polarization of one molecule will affect electric field observed by another molecule; other molecules influence the effect: A collective (cooperative) effect
  - Modeled by coupled equations
  - Typically iterative solution methods
    - Dipoles get an initial value
    - Value updated
    - Iterated until dipoles do not change significantly
  - Computationally costly

Electrostatic interactions in medium

Vacuum

$$V=\frac{1}{4\pi\boldsymbol{\varepsilon_0}}\frac{q_i q_j}{r_{ij}}$$

Permittivity of vacuum

In medium

$$V=\frac{1}{4\pi\boldsymbol{\varepsilon_0}\boldsymbol{\varepsilon_r}}\frac{q_i q_j}{r_{ij}}$$

Relative permittivity of medium

Permittivity of vacuum

- Medium, for example, solvent, can be modelled by explicit molecules
- In addition, dielectric screening of electrostatic interactions can be taken into account without explicit solvent molecules (implicit solvent)

Electrostatic interactions in medium

Vacuum

$$V=\frac{1}{4\pi\boldsymbol{\varepsilon_0}}\frac{q_i q_j}{r_{ij}}$$

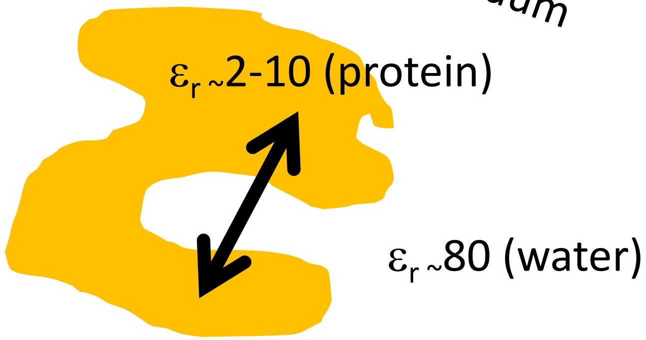
Permittivity of vacuum

In medium

$$V=\frac{1}{4\pi\boldsymbol{\varepsilon_0}\boldsymbol{\varepsilon_r}}\frac{q_i q_j}{r_{ij}}$$

Relative permittivity of medium

Permittivity of vacuum



- Choosing appropriate value for bulk dielectric may be difficult, solvent is not present everywhere especially with large molecules

Vacuum ε_r =1
Ar gas ε_r ~1.0005 (~1)
Ar liquid ε_r ~1.5 (van der Waals)
NaCl crystal ε_r ~1.0005 Ar gas (~1)
Water ε_r ~80
PVC ε_r ~7
Lipid bilayer ε_r ~2-4
Protein ε_r ~2-10

Non-bonded interactions

On this course:
(nomenclature varies in different books)

- Typically 4 components
  - Now → **Repulsive component resulting from the Pauli exclusion principle** (prevents the collapse of molecules) ← van der Waals
  - Attractive or repulsive **electrostatic interactions between permanent charges, dipoles, multipoles** ← electrostatic
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- Most common in molecular modelling to divide these into van der Waals and electrostatic interactions

What is left?

- A repulsive component resulting from the Pauli exclusion principle
- Dispersion: attractive interaction between any pair of molecules due to interactions of instantaneous multipoles
  - Relatively weak (compared to other molecular interactions)
  - Highly relevant in molecular self-assembly, supramolecular chemistry, structural biology (proteins etc.), surface science (surface interactions), ...

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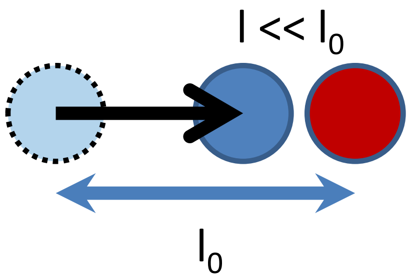
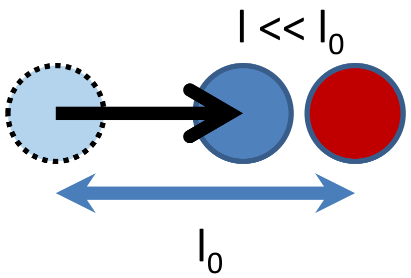
Repulsive Contribution



- Pauli principle: no two fermions (here electrons) in a system can have exactly the same quantum numbers
- Forbids electrons to occupy the same region of space (internuclear region at short separations) -> reduced electron density between nuclei -> repulsion between incompletely shielded nuclei
- Also called: exchange forces, overlap forces

Repulsive Contribution



- Pauli principle: no two fermions (here electrons) in a system can have exactly the same quantum numbers
- Functional form

$$\propto \frac{1}{r}, \text{at very short distances}$$

$\propto e^{-2r/a_0}$, at larger separations, a_0 Bohr radius

What is left?

1

- A repulsive component resulting from the Pauli exclusion principle

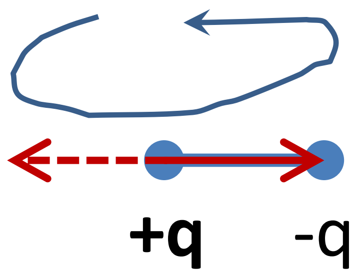
2

- Dispersion: attractive interaction between any pair of molecules due to interactions of instantaneous multipoles
  - Relatively weak (compared to other molecular interactions)
  - Highly relevant in molecular self-assembly, supramolecular chemistry, structural biology (proteins etc.), surface science (surface interactions), ...

Attractive contribution (dispersion)

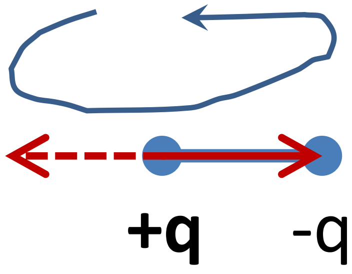
- Long range (opposed to very short range repulsive)
- Due to dispersive forces induced by instantaneous dipoles arising from fluctuations in the electron clouds
  - (instantaneous) dipole can induce a dipole in neighboring atoms -> attractive effect
- Also called: London forces

Drude model for dispersive interaction (a simple model): Isolated molecule



Molecule with two charges, +q and –q
-q: Harmonic motion around +q, angular frequency ω

Drude model for dispersive interaction (a simple model): Isolated molecule



Molecule with two charges, +q and –q

-q: Harmonic motion around +q, angular frequency ω

Potential energy (z separation, $\omega^2=k/m$, k force constant)

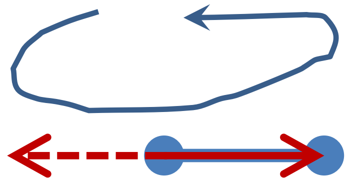
$$V = \frac{1}{2}kz^2$$

Schrödinger equation

$$\left(-\frac{\hbar}{2m}\frac{\partial}{\partial z^2} + V\right)\psi = E\,\psi$$

$$-\frac{\hbar}{2m}\frac{\partial\psi}{\partial z^2} + \frac{1}{2}kz^2\psi = E\,\psi$$

Drude model for dispersive interaction (a simple model): Isolated molecule



Simple harmonic oscillator

Energies: $E_\nu = (\nu + \frac{1}{2}) \times \hbar\omega$

$$E_0 = \frac{1}{2}\hbar\omega$$

Molecule with two charges, +q and –q

-q: Harmonic motion around +q, angular frequency ω

Potential energy (z separation, ω^2=k/m, k force constant)

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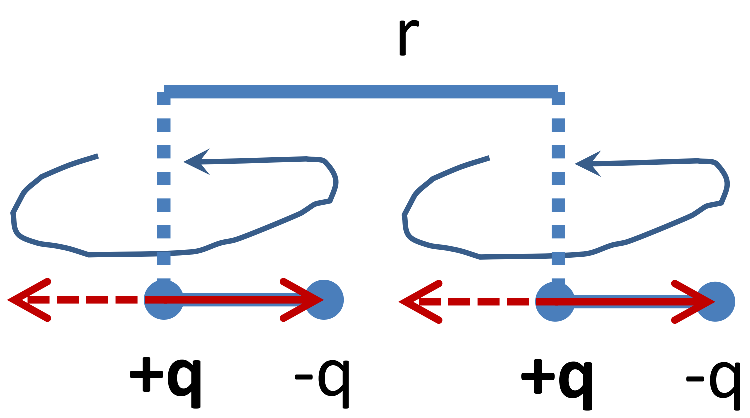
Drude model for dispersive interaction (a simple model): Interacting molecules



Simple harmonic oscillator
When separated, energy
2 x isolated Drude molecule energy $E_0 = \frac{1}{2}\hbar\omega$

Molecules with two charges, +q and –q
-q: Harmonic motion around +q, angular frequency ω

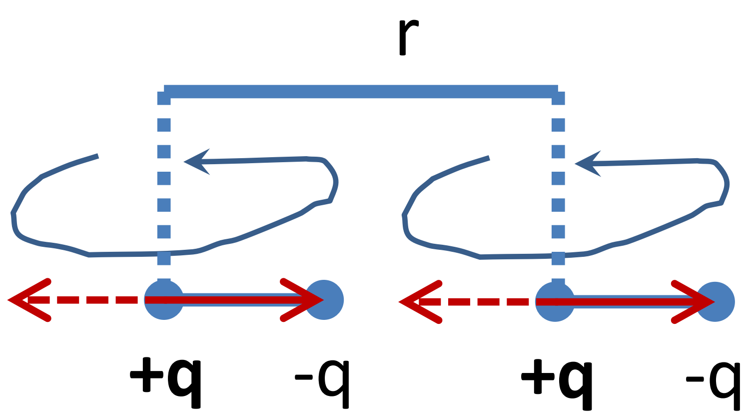
When interacting, energy

$$1D:\ v(r) = -\frac{\alpha^4\hbar\omega}{2(4\pi\varepsilon_0)^2 r^6}$$

$$3D:\ v(r) = -\frac{3\alpha^4\hbar\omega}{2(4\pi\varepsilon_0)^2 r^6}$$

$$-\frac{\hbar}{2m}\frac{\partial\psi}{\partial z^2} + \frac{1}{2}kz^2\psi = E\ \psi$$

Drude model for dispersive interaction (a simple model): Summary



Interaction proportional to

$$\propto \frac{1}{r^6}$$

Molecules with two charges, +q and –q

-q: Harmonic motion around +q, angular frequency ω

When interacting, energy

$$1D:\ v(r) = -\frac{\alpha^4 \hbar\omega}{2(4\pi\varepsilon_0)^2 r^6}$$

$$3D:\ v(r) = -\frac{3\alpha^4 \hbar\omega}{2(4\pi\varepsilon_0)^2 r^6}$$

Interaction always attractive (also with higher order multipoles)

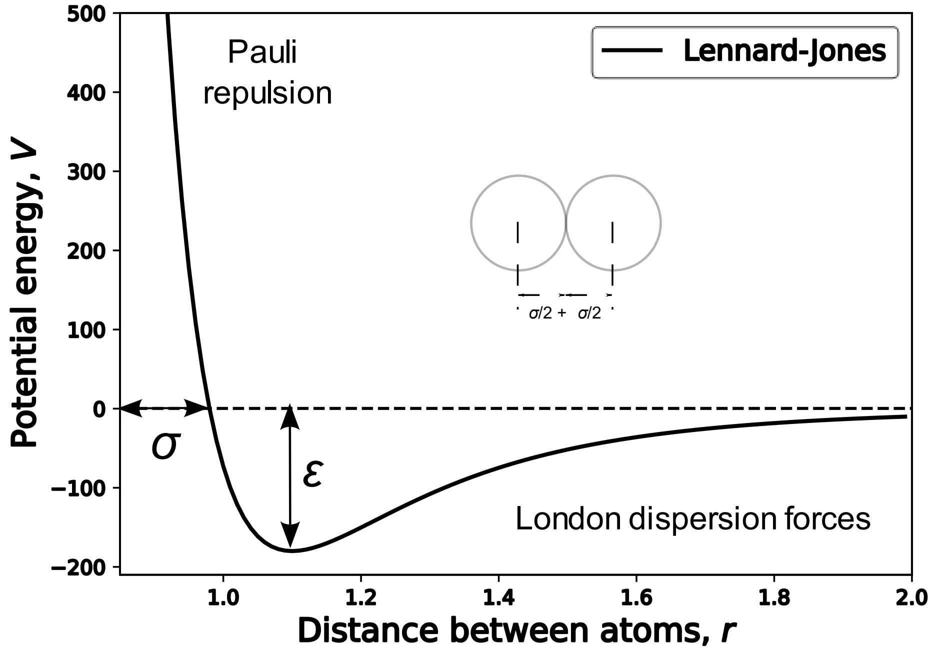
Summary of Pauli exclusion repulsion and dispersion attraction (van der Waals interactions)

- A repulsive short range component resulting from the Pauli exclusion principle
  - $\propto \frac{1}{r}$, at very short distances
  - $\propto e^{-2r/a_0}$, at larger separations, a_0 Bohr radius
- Dispersion: attractive interaction between any pair of molecules due to interactions of instantaneous multipoles
  – proportional to $1/r^6$
  – Long-range

Modeling van der Waals interactions

- Most common model: Lennard-Jones

$$v(r) = 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]$$



- No solid theoretical arguments for repulsive part, attractive is the dispersion term (Drude model)
- 12^{th} power reasonable for noble gases, too steep for most other systems, also 9^{th} or 10^{th} power used sometimes. The too steep repulsive part often leads to overestimation of the pressure in the system
- More general: n-m Lennard-Jones (12-6 a special case)

$$v(r) = k\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{n} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{m}\right]$$

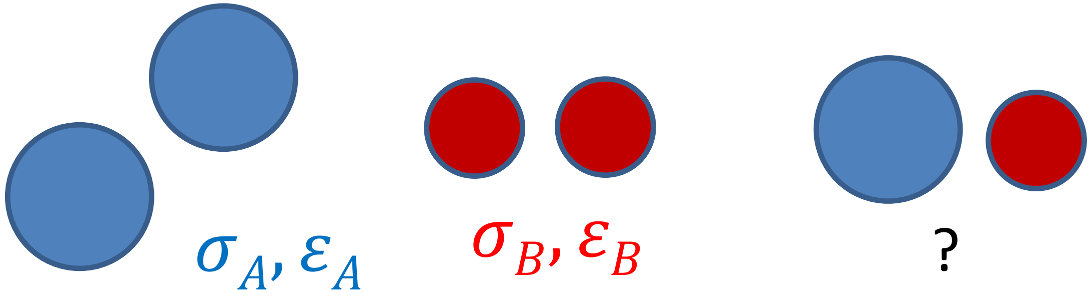
Modeling van der Waals interactions

- Theoretically more realistic alternative to Lennard-Jones: Buckingham potential

$$v(r_{ij}) = \varepsilon\left[\frac{6}{\alpha-6}e^{\left(-\alpha\left(\frac{r_{ij}}{r_m}-1\right)\right)} - \frac{6}{\alpha-6}\left(\frac{r_m}{r_{ij}}\right)^6\right]$$

- α approx 14 or 15 corresponds to Lennard-Jones 12-6 close to minimum
- Collapses at very short distances!!!
  - must check
- Morse potential is also sometimes used for van der Waals interactions

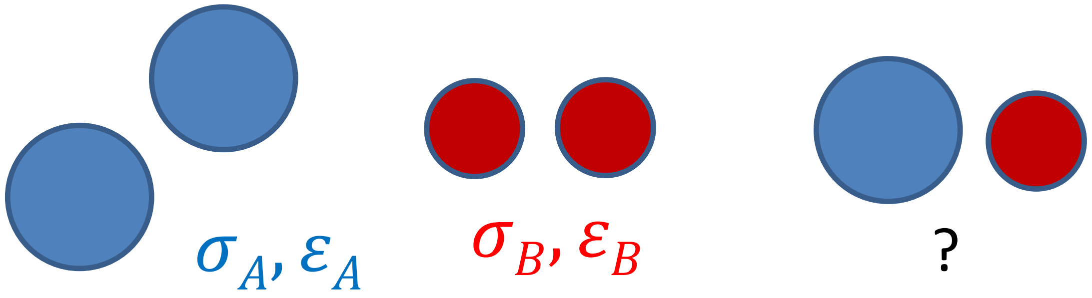
Modelling van der Waals interactions: Systems of many atoms / molecules



$$v(r) = 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]$$

- van der Waals interactions usually parametrized for one atom / molecule type for one orientation / conformation

Modelling van der Waals interactions: Systems of many atoms / molecules



$$v(r) = 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]$$

- van der Waals interactions usually parametrized for one atom / molecule type for one orientation / conformation
- Mixing rules used for calculating cross-interaction between different atoms A and B

Geometric mean:

$$C12_{ij} = \sqrt{C12_{ii} \times C12_{jj}} \qquad C6_{ij} = \sqrt{C6_{ii} \times C6_{jj}} \qquad \text{(GROMOS)}$$

$$\sigma_{ij} = \sqrt{\sigma_{ii} \times \sigma_{jj}} \qquad \epsilon_{ij} = \sqrt{\epsilon_{ii} \times \epsilon_{jj}} \qquad \text{(OPLS)}$$

The geometric mean (Berthelot) does not have proper physical origin

Lorentz–Berthelot:

$$\sigma_{ij} = \frac{\sigma_{ii}+\sigma_{jj}}{2}, \qquad \epsilon_{ij} = \sqrt{\epsilon_{ii} \times \epsilon_{jj}} \qquad \text{(CHARM, AMBER).}$$

The arithmetic mean (Lorentz) is motivated by collision of hard spheres
Known issue: overestimates the well depth

Many body terms in non-bonded interactions

$$V=\sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12}-\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]+\frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}\right)+\sum_{i=1}^{N}\sum_{j=i+1}^{N}\sum_{k=j+1}^{N}V_3$$

Until now, two-body interactions

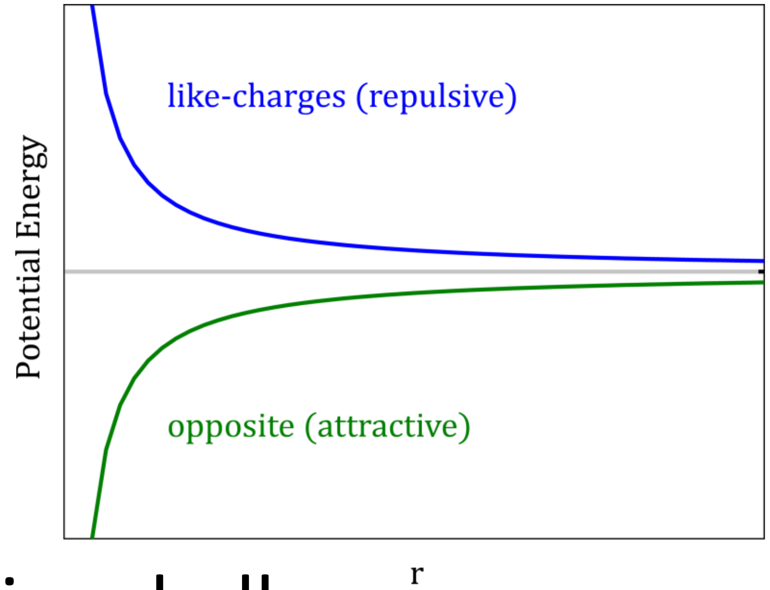
Here, three-body interactions

- Lennard-Jones terms can be affected 10% by 3-body interactions
- 2-body: ~N^2 interactions (N number of particles); 3-body: ~N^3 interactions
- Axilrod-Teller terms

van der Waals summary

- Obtaining van der Waals parameter values
  - Sources: Experimental lattice packing, density, sublimation energy, enthalpy of vaporization, vapor pressure
  - Computationally long-range

Electrostatics

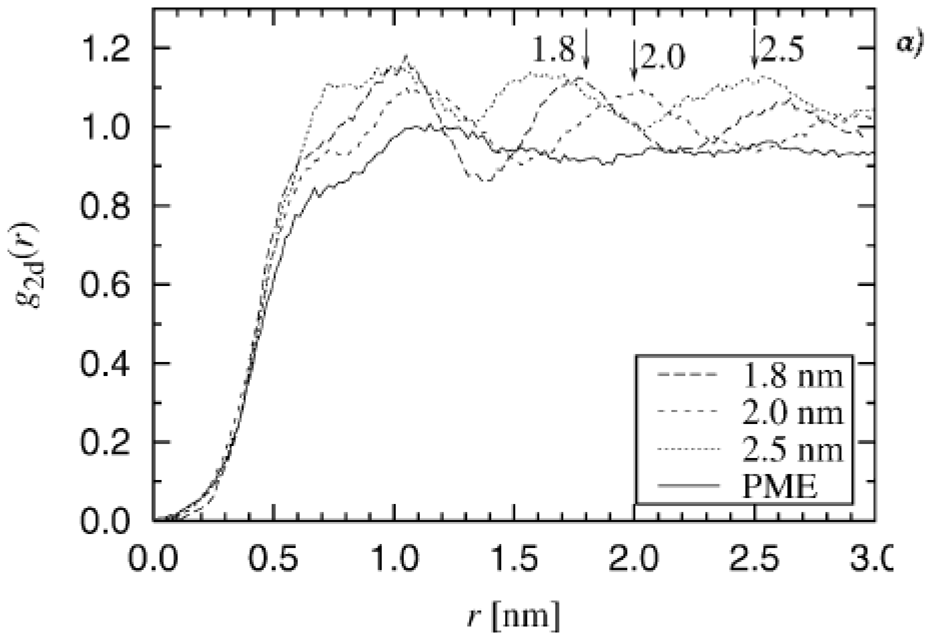


$$V_{\text{electrostatic}} = \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}$$ (Coulomb's law)

- Computationally, electrostatics poses a major challenge
  - long-ranged and decays as $1/r$
  - In general, we define a long-range interaction as one for which $V(r) \sim 1/r^a$, where $a < d$, and d is the dimension of space
- Cut-off, reaction-field, Ewald-type methods, multipole expansions, …

Effect of truncating electrostatic interactions in lipid bilayer: radial distribution function

Bare truncation of Coulomb interactions is likely to cause major error



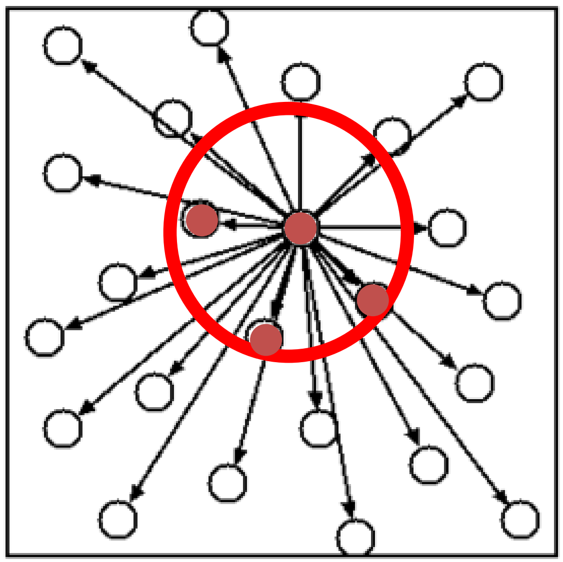


FIGURE 2 Radial distribution function $g_{2d}(r)$ for the center of mass positions of the DPPC molecules (Patra *et al.*, 2003).

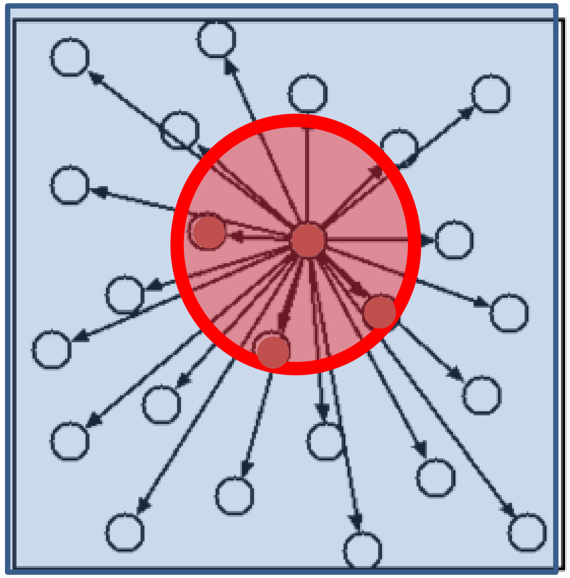
M. Patra et al., Biophys. J., 84:3636-3645, 2003

Reaction field electrostatics

- Explicit electrostatics with $r<r_{cut}$.
- For $r > r_{cut}$ the system is treated on a mean-field level and is thus completely described by its dielectric constant ε .

$$\mathcal{V}(r) = \frac{q_i q_j}{4\pi\epsilon_0 r}\left[1 + \frac{\epsilon - 1}{2\epsilon + 1}\left(\frac{r}{r_{\mathrm{cut}}}\right)^3\right] - \frac{q_i q_j}{4\pi\epsilon_0 r_{\mathrm{cut}}}\frac{3\epsilon}{2\epsilon + 1},$$

for $r \leqslant r_{\mathrm{cut}}$.



Ewald summation

- Ewald converted 1927 the slowly, conditionally convergent sum for the Coulomb potential in infinite lattice into two sums that converge rapidly and absolutely, one in real space another in reciprocal space

$$\frac{1}{r} = \frac{f(r)}{r} + \frac{1 - f(r)}{r}$$

Ewald sum: periodicity

A.Y. Toukmaji, J.A. Board Jr. / Computer Physics Communications 95 (1996) 73–92

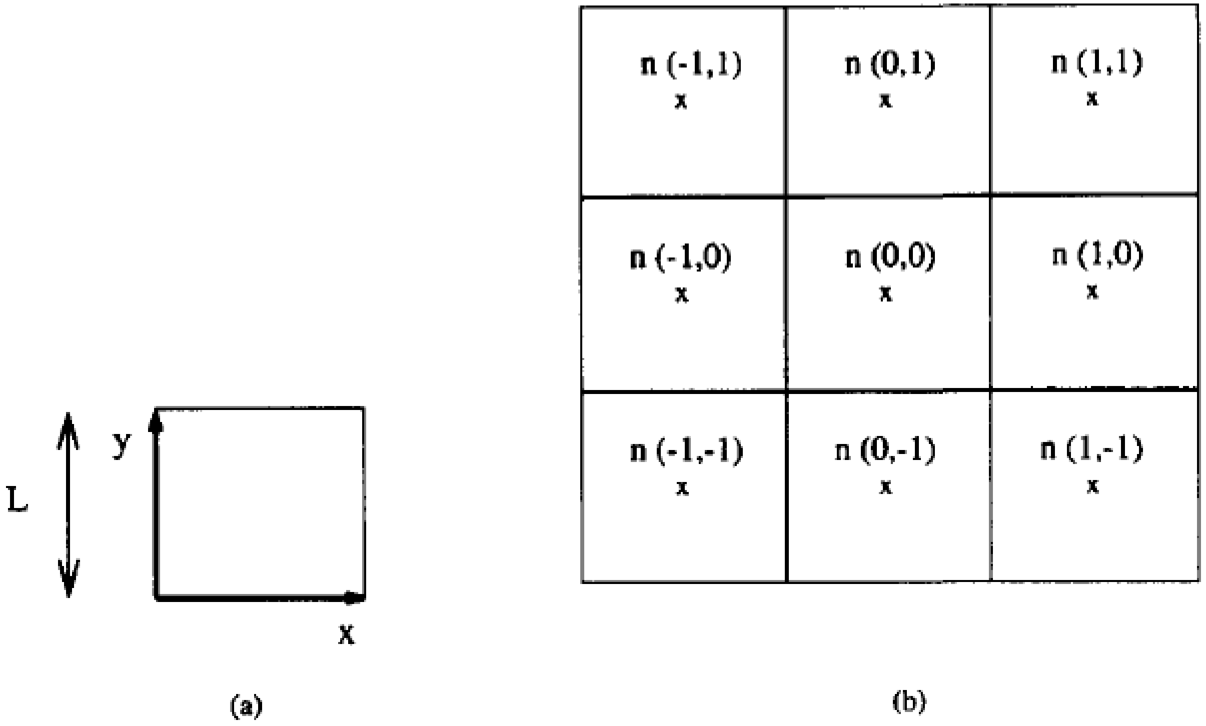
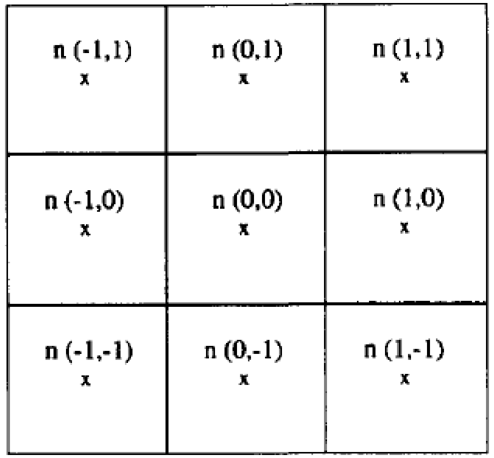


Fig. 1. In a 2D system (a) the unit cell coordinates and (b) a 3 × 3 periodic lattice built from unit cells.

Ewald sum



$$U = \frac{1}{2} \sum_{n}^{\prime} \sum_{i=1}^{N} \sum_{j=1}^{N} \frac{q_i q_j}{r_{ij,\boldsymbol{n}}} ,$$

- $U_{Ewald} = U^r + U^m + U^0$
  - U^r Real space sum
  - U^m Reciprocal space sum
  - U^0 Constant term

$$U^r = \frac{1}{2} \sum_{i,j}^{N'} \sum_{\boldsymbol{n}} q_i q_j \frac{\operatorname{erfc}(\alpha r_{ij,\boldsymbol{n}})}{r_{ij,\boldsymbol{n}}} ,$$

$$U^m = \frac{1}{2\pi V} \sum_{i,j}^{N} q_i q_j \sum_{\boldsymbol{m} \neq 0} \frac{\exp(-(\pi \boldsymbol{m}/\alpha)^2 + 2\pi \mathrm{i} \boldsymbol{m} \cdot (\boldsymbol{r}_i - \boldsymbol{r}_j))}{\boldsymbol{m}^2} ,$$

$$U^o = \frac{-\alpha}{\sqrt{\pi}} \sum_{i=1}^{N} q_i^2 .$$

V is the volume of the simulation box, $\boldsymbol{m} = (l, j, k)$ is a reciprocal-space vector, and $\boldsymbol{n}$ was defined earlier. The self-term U^o is a correction term that cancels out the interaction of each of the introduced artificial counter-charges with itself as will be explained in Section 2.2. The complimentary error function decreases monotonically as x increases and is defined by $\operatorname{erfc}(x) = 1 - \operatorname{erf}(x) = 1 - (2/\sqrt{\pi}) \int_0^x e^{-u^2} du$. The theory of Ewald summation is described in more detail by Kittel [33] and Tosi [51].

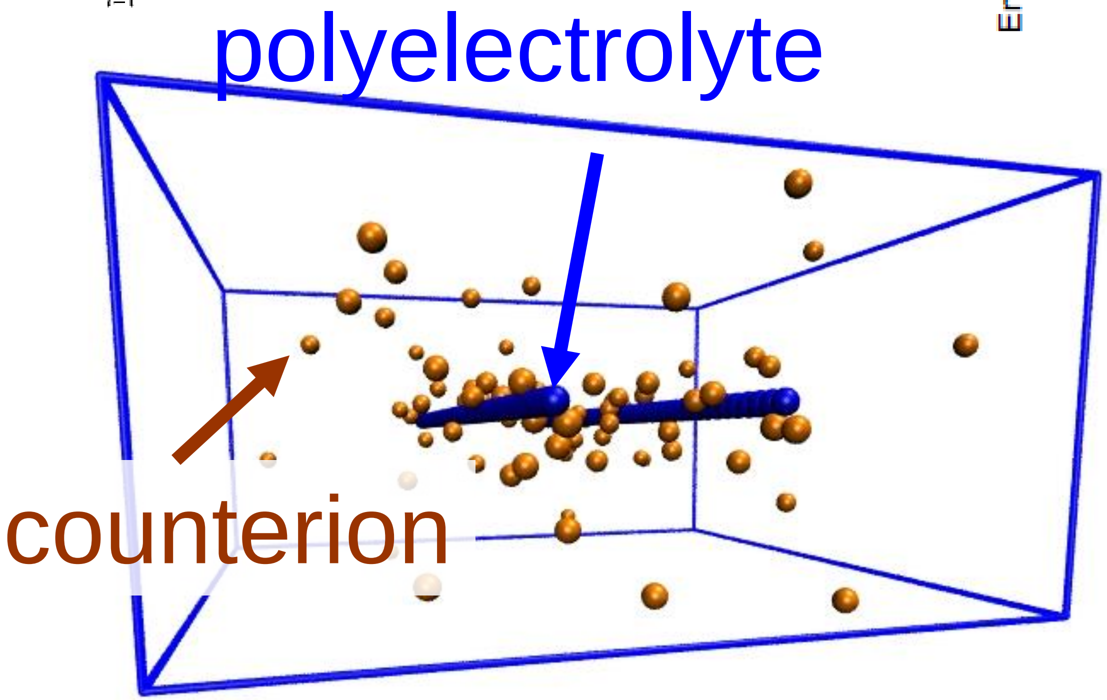
A.Y. Toukmaji, J.A. Board Jr./Computer Physics Communications 95 (1996) 73-92

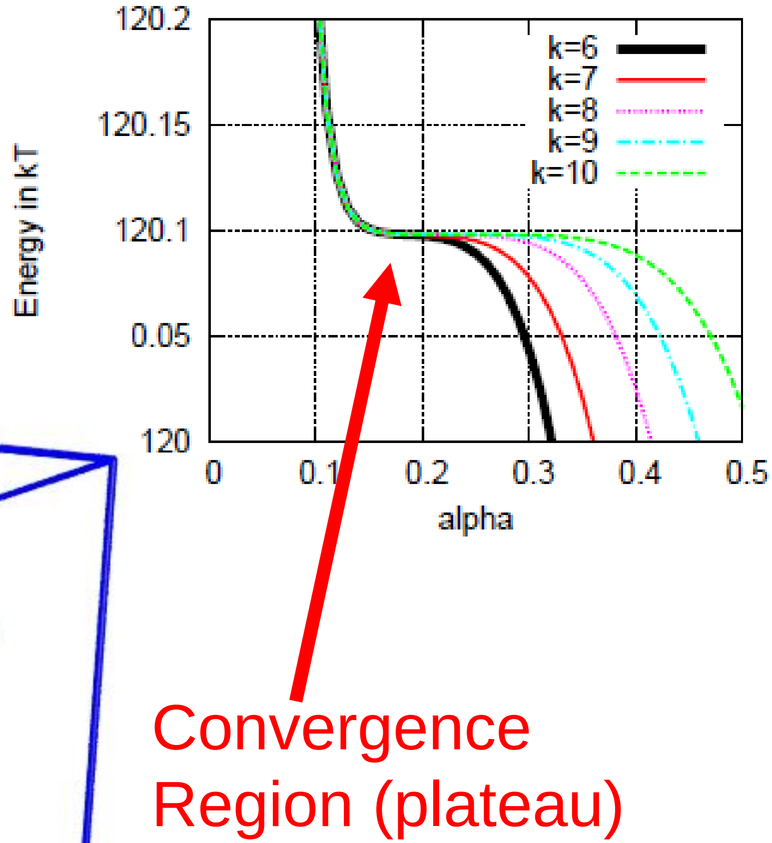
Ewald summation convergence: Example

$$U^{r} = \frac{1}{2}\sum_{i,j}^{N'}\sum_{\boldsymbol{n}} q_i q_j \frac{\operatorname{erfc}(\alpha r_{ij,\boldsymbol{n}})}{r_{ij,\boldsymbol{n}}},$$

$$U^{m} = \frac{1}{2\pi V}\sum_{i,j}^{N} q_i q_j \sum_{\boldsymbol{m}\neq 0} \frac{\exp(-(\pi \boldsymbol{m}/\alpha)^2 + 2\pi i \boldsymbol{m}\cdot(\boldsymbol{r}_i - \boldsymbol{r}_j))}{\boldsymbol{m}^2},$$

$$U^{o} = \frac{-\alpha}{\sqrt{\pi}}\sum_{i=1}^{N} q_i^2 .$$





Force-fields: A diverse family

- Two-body force-fields (pair potentials)
  - Simple, extremely fast
  - Liquids, gases, solids
  - Lennard-Jones, Morse, ...
- **Many-body chemically non-reactive force-fields**
  - **Many different atom types and molecules covered**
  - **Typically: a wide variety of organic molecules such as proteins, hydrocarbons, lipids, polymers, ...**
  - **Non-reactive!**
- Many-body (reactive) force-fields
  - A wide variety of typically inorganic materials and compounds including also metals (structural & mechanical properties). Organic molecules tend to be too complex.
  - Some are **reactive!**

Intro

Main

Briefly

Modelling inorganic molecules

- Inorganic molecules have a wider range of geometries and highly delocalized bonds
  - Model needs to capture also these properties
  - More complex / different than organic molecular models (often)
  - Coordination numbers vary
- More specialized force-fields than for organic compounds, quite often capture also bond reorganization (changes in bond order)

Empirical potentials for semiconductors and metals

- Bond-order potentials
  - Examples: Finnis-Sinclair; Tersoff; Brenner; Stillinger-Weber; Sutton; Pettifor (several models)
  - Physical basis: relating quantum mechanical electronic density of states and its moments to classical bond order (bond strength)
  - Binding energy strongly correlated with square root of the second moment of the electronic density of states
    - In practice, local density of states is used
    - Second moment approximation for binding energy $E_i^{el} \propto \sqrt{Z_i}$, Z_i number of neighbors

Bond-order potentials

- Can describe several different bonding states of an atom with the same parameters
- May be able to describe chemical reactions (correctly)
- strength of a chemical bond depends on the bonding environment

Bond-order potentials

- Two alternative ways to write potential energy expression (equivalent)
  - $V_{ij} = V_{repulsive}(r_{ij})$+b$_{ijk}V_{attractive}(r_{ij})$
  - $V_{ij} = V_{pair}(r_{ij}) + A\sqrt{\rho_i}$, ρ_i local electron density

  - $\rho_i = \sum_{j=1,j\neq 1}^{N} \varphi_{ij}(rij)$
- Relies on number of neighbors which is not always straightforward to define (disordered materials, bond reorganization, ...)
- Continuous transition between different numbers of neighbors

Example: Brenner bond-order potential for hydrocarbons

$$E_b=\sum_i \sum_{j(>i)} [V_R(r_{ij})-\bar{B}_{ij}V_A(r_{ij})] , \qquad \bar{B}_{ij}=(B_{ij}+B_{ji})/2+F_{ij}(N_i^{(t)},N_j^{(t)},N_{ij}^{\mathrm{conj}}) ,$$

where the repulsive and attractive pair terms are given by

$$V_R(r_{ij})=f_{ij}(r_{ij})D_{ij}^{(e)}/(S_{ij}-1)e^{-\sqrt{2S_{ij}}\beta_{ij}(r-R_{ij}^{(e)})} \quad (7)$$

and

$$V_A(r_{ij})=f_{ij}(r_{ij})D_{ij}^{(e)}S_{ij}/(S_{ij}-1)e^{-\sqrt{2/S_{ij}}\beta_{ij}(r-R_{ij}^{(e)})} , \quad (8)$$

respectively. The function $f_{ij}(r)$, which restricts the pair potential to nearest neighbors, is given by

$$f_{ij}(r)=\begin{cases} 1, & r<R_{ij}^{(1)} \\ \left[1+\cos\left[\frac{\pi(r-R_{ij}^{(1)})}{(R_{ij}^{(2)}-R_{ij}^{(1)})}\right]\right]\Big/2, & R_{ij}^{(1)}<r<R_{ij}^{(2)} \\ 0, & r>R_{ij}^{(2)} . \end{cases}$$

$$N_{ij}^{\mathrm{conj}}=1+\sum_{\text{carbons } k(\neq i,j)} f_{ik}(r_{ik})F(x_{ik}) + \sum_{\text{carbons } l(\neq i,j)} f_{jl}(r_{jl})F(x_{jl}) \quad (15)$$

where

$$F(x_{ik})=\begin{cases} 1, & x_{ik}\le 2 \\ \{1+\cos[\pi(x_{ik}-2)]\}/2, & 2<x_{ik}<3 \\ 0, & x_{ik}\ge 3 \end{cases} \quad (16)$$

and

$$x_{ik}=N_k^{\mathrm{tot}}-f_{ik}(r_{ik}) . \quad (17)$$

$$B_{ij}=\left[1+\sum_{k(\neq i,j)} G_i(\theta_{ijk})f_{ik}(r_{ik})e^{\alpha_{ijk}[(r_{ij}-R_{ij}^{(e)})-(r_{ik}-R_{ik}^{(e)})]}+H_{ij}(N_i^{(\mathrm{H})},N_i^{(\mathrm{C})})\right]^{-\delta_i}$$

$$G_{\mathrm{C}}(\theta)=a_0\{1+c_0^2/d_0^2-c_0^2/[d_0^2+(1+\cos\theta)^2]\} \quad (18)$$

Example: Brenner bond-order potential

TABLE VI. Predicted energetics and intramolecular carbon-carbon bond lengths for various single molecules chemisorbed on terrace sites on a hydrogen-terminated diamond {111} surface.

Molecule	Potential I Potential energy (eV)	Potential I Bond length (Å)	Potential II Potential energy (eV)	Potential II Bond length (Å)
Hydrogen atom	−4.1[a]		−4.2[a]	
Methyl radical	−3.7[a]		−4.0[a]	
Acetyl radical	−3.9[a]	1.20	−4.1[a]	1.29
Hydrogen molecule	−3.6[b]		−3.6[b]	
Acetylene	−5.0[b]	1.33	−4.9[b]	1.39
Ethylene	−4.3[b]	1.59	−4.3[b]	1.57

[a]Relative to a hydrogen-terminated surface with one radical site and the gas-phase molecule.
[b]Relative to a hydrogen-terminated surface with two adjacent radical sites and the gas-phase molecule.

TABLE VII. Predicted energetics and intramolecular carbon-carbon bond lengths for a monolayer of various molecules chemisorbed on the diamond {111} surface. The energies are relative to a relaxed clean surface and the gas-phase molecules.

Molecule	Potential I Potential energy	Potential I Bond length (Å)	Potential II Potential energy	Potential II Bond length (Å)
Hydrogen atom	−4.2 eV/atom[a]		−4.3 eV/atom[a]	
Methyl radical	−3.2 eV/molecule[a]		−3.0 eV/molecule[a]	
Acetyl radical	−4.2 eV/molecule[a]	1.20	−4.3 eV/molecule[a]	1.29
Hydrogen molecule	−3.7 eV/molecule[b]		−3.9 eV/molecule[b]	
Acetylene	−5.2 eV/molecule[b]	1.33	−5.2 eV/molecule[b]	1.39
Ethylene	−4.0 ev/molecule[b]	1.58	−3.9 eV/molecule[b]	1.57

[a]One surface atom per chemisorbed molecule.
[b]Two surface atoms per chemisorbed molecule.

Stillinger-Weber bond-order potential

$$U = \sum_i \sum_{j>i} \phi_2(r_{ij}) + \sum_i \sum_{j\neq i} \sum_{k>j} \phi_3(r_{ij}, r_{ik}, \theta_{ijk})$$

$$\phi_2(r_{ij}) = A_{ij}\epsilon_{ij}\left[B_{ij}\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{p_{ij}} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{q_{ij}}\right] exp\left(\frac{\sigma_{ij}}{r_{ij} - a_{ij}\sigma_{ij}}\right)$$

$$\phi_3(r_{ij}, r_{ik}, \theta_{ijk}) = \lambda_{ijk}\epsilon_{ijk}\left[cos\theta_{ijk} - cos\theta_{0ijk}\right]^2 exp\left(\frac{\gamma_{ij}\sigma_{ij}}{r_{ij} - a_{ij}\sigma_{ij}}\right) exp\left(\frac{\gamma_{ik}\sigma_{ik}}{r_{ik} - a_{ik}\sigma_{ik}}\right)$$

Effective Medium Theory (EMT)

- approximation in which models based on density-functional theory are used to describe the properties of solids, usually metals
- Environment around each atom replaced by ”jellium”,
  - corresponds to homogeneous electron gas (a constant positive background density (metal ions)
  - Atoms embedded into this jellium (Daw and Baskes: Embedded atom method EAM)

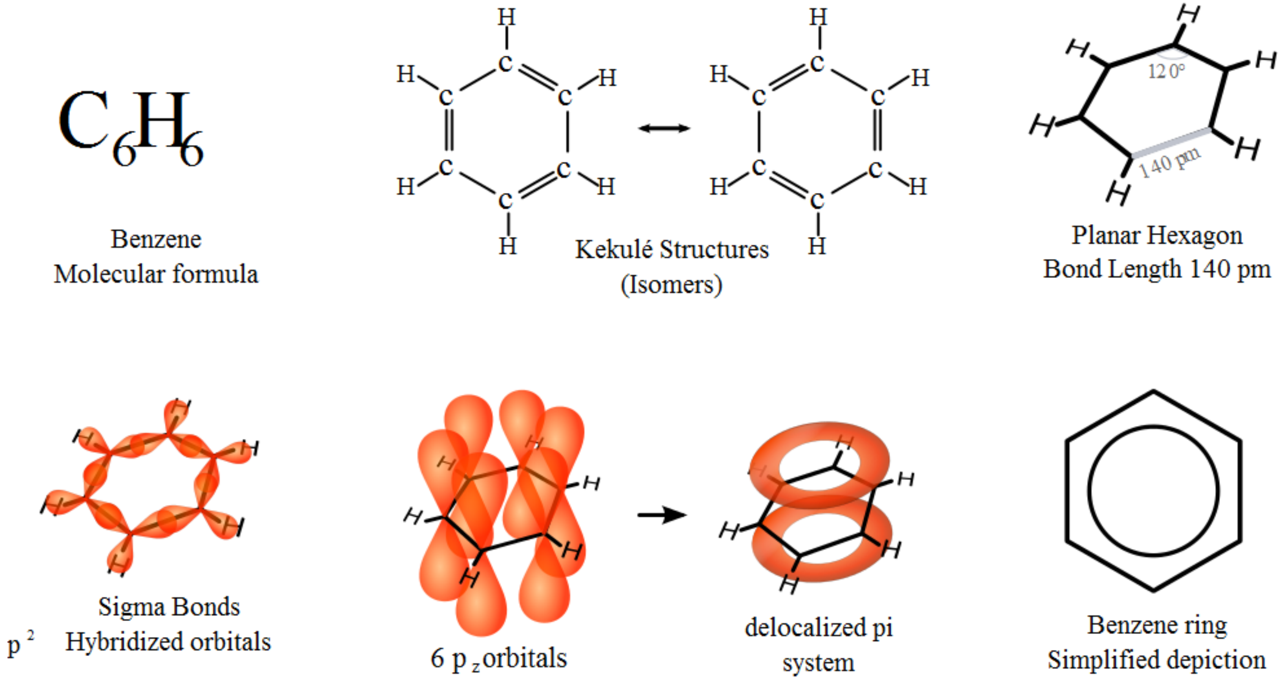
Summary: Empirical bond-order and effective medium potentials

- Can be quite accurate (and fast) within their parametrization regime
- Increased computational speed: Modern tight binding simulations compete
- Can be reactive, can allow for bond-reorganization and can describe non-localized bonds
- Structural properties, not electronic properties!

Movies for visualizing molecular modelling

- Materials simulations (metals, surfaces, shear flows, liquids, some molecular materials...)
  - http://lammps.sandia.gov/movies.html
- Biomolecules
  - http://www.ks.uiuc.edu/Gallery/Movies/

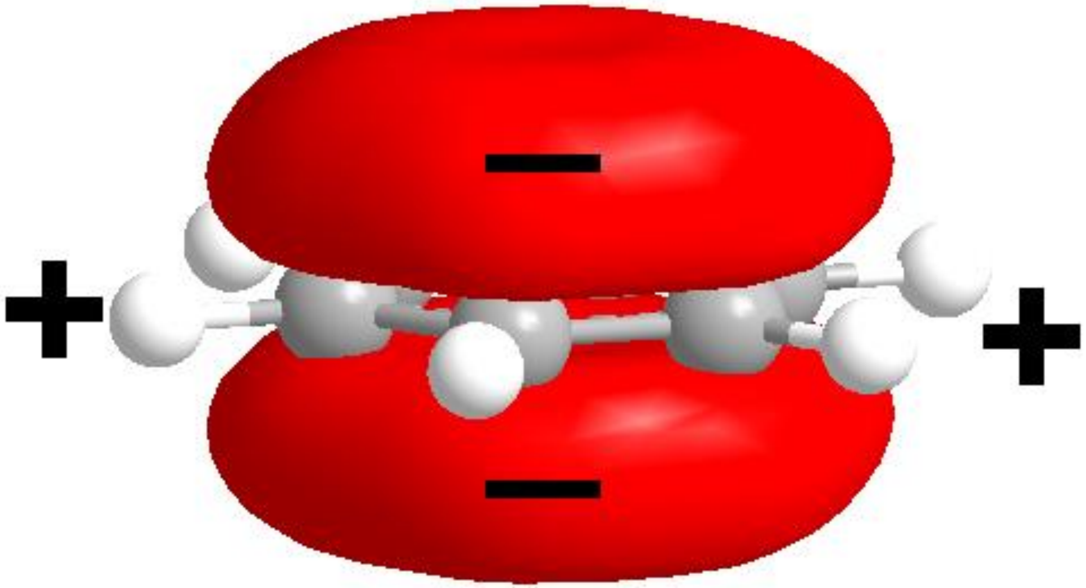
Benzene



- Question: How should the partial charges be distributed? Why?

http://upload.wikimedia.org/wikipedia/commons/9/9a/Benzene_Representations.svg

Benzene



- Question: How should the partial charges be distributed? Why?

http://upload.wikimedia.org/wikipedia/commons/9/9a/Benzene_Representations.svg

Example of aromatic-aromatic interactions

- P-stacking difficult to model (nucleic acids, benzene, ring-like molecules)

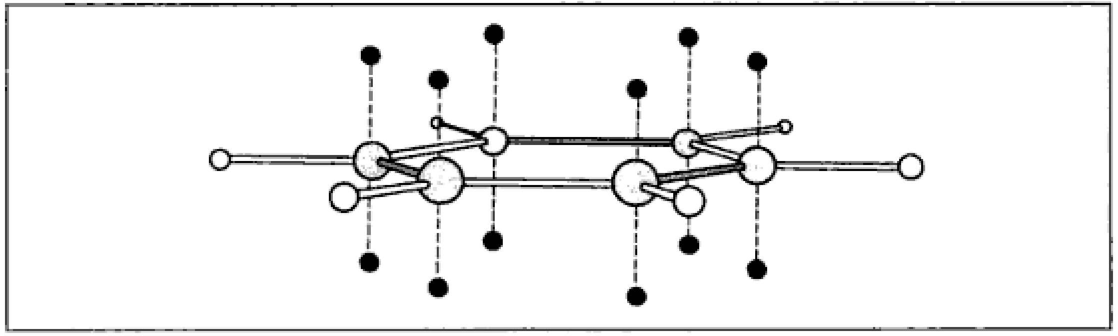


Fig. 4.25: Anisotropic model of benzene developed by Hunter and Saunders [Hunter and Saunders 1990].

- Hunter-Saunders: Carbons have +1 charge on plane, -1/2 above and below plane of ring
- Classical force-fields can be tuned to a wide variety of behavior . Most typical force-fields do not have this benzene property.

Leach: Molecular Modelling, Figure 4.25