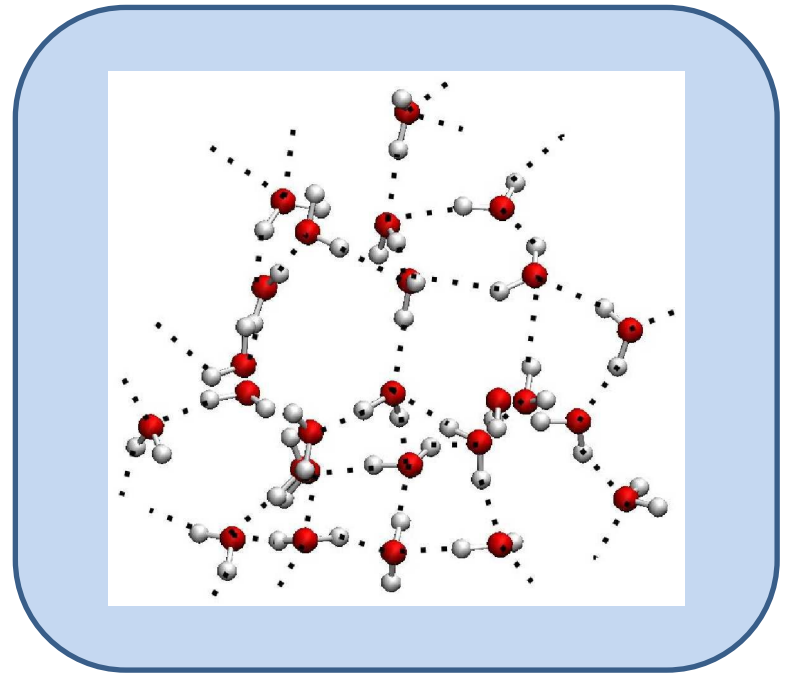


Topic: Force fields

Objective

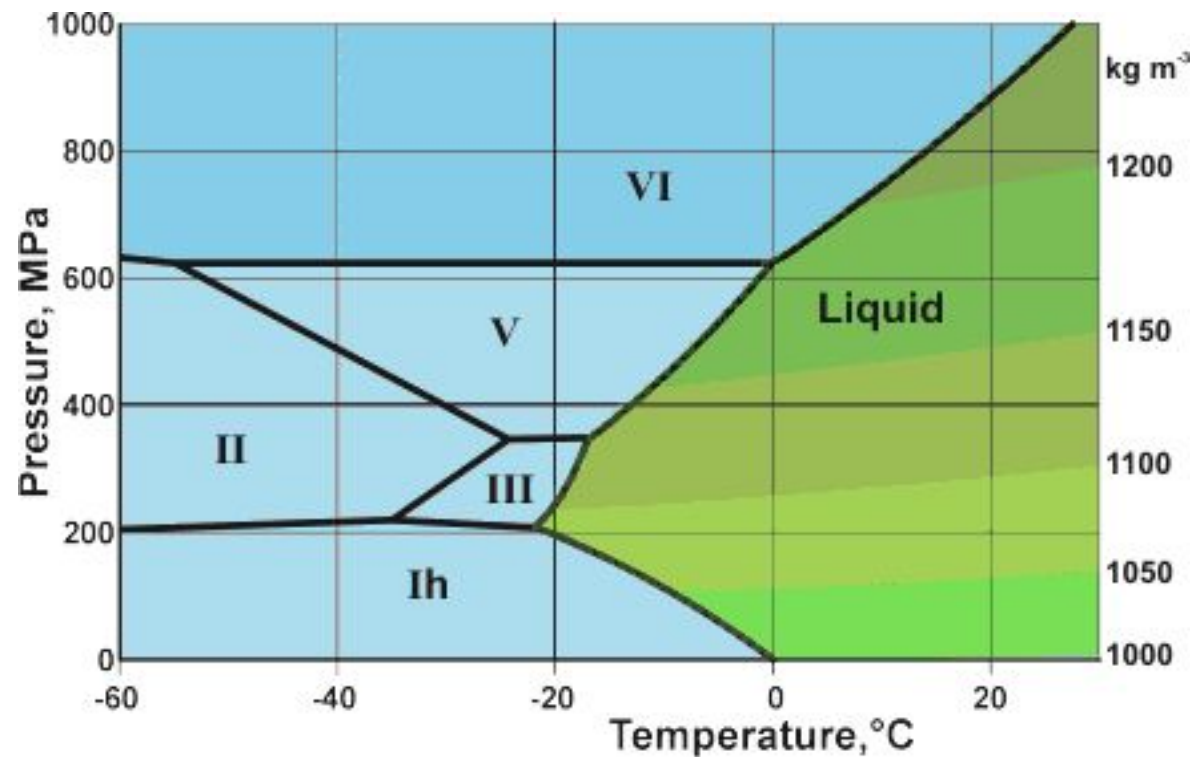
- How do you model a molecule and compute its properties
- Potential energy surfaces
- Bonded and non-bonded interactions
- Analytic expressions for bonded terms
- z-matrix or cartesian coordinates
- VMD

How do you model a molecular system and compute its properties



Phase diagram of water

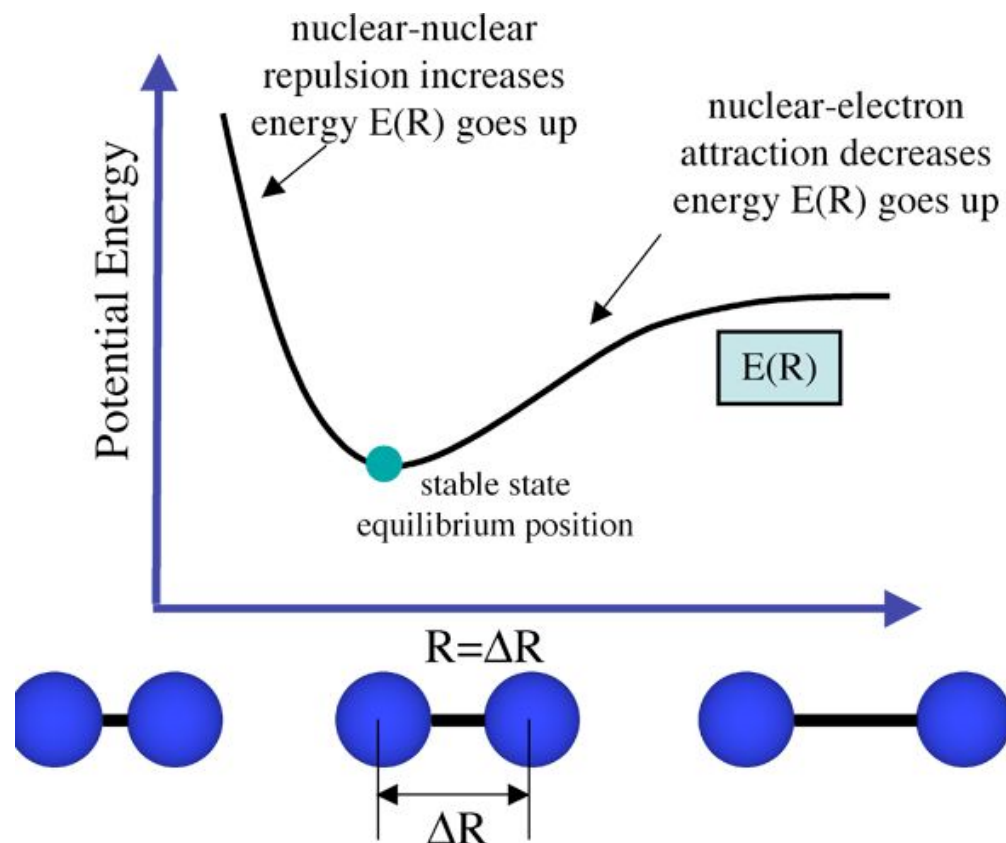
20 Ice phases
till now



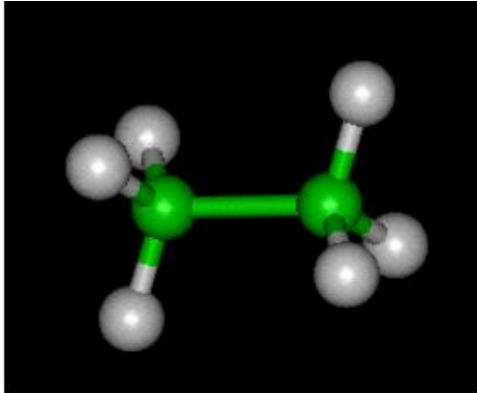
Potential energy surface (PES)

- Consequence of Born Oppenheimer approximation: energy of a molecule in ground electronic state can be considered as a function of nuclear coordinates only.
- PES: Mathematical function that describes the energy of molecules as a function of the geometry/coordinates of molecules.
- Coordinates can be internal coordinates, collective variables, etc.

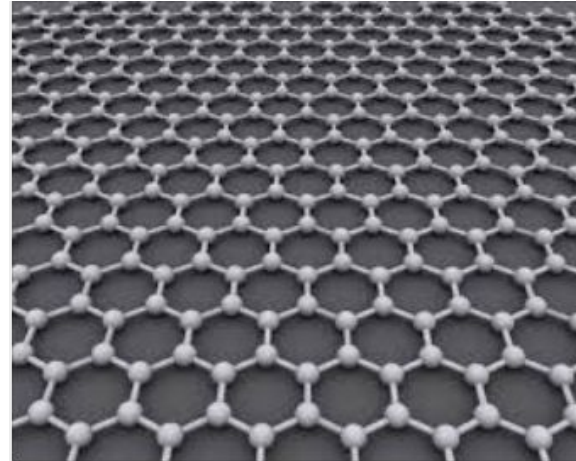
PES of diatomic molecule



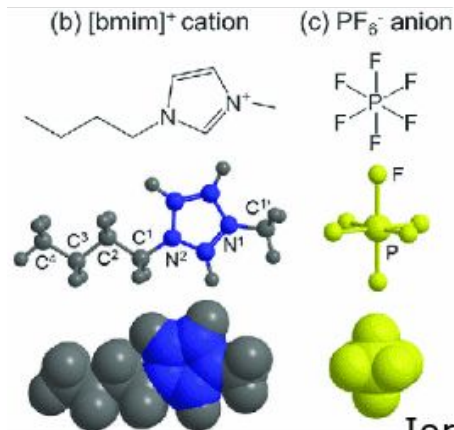
Polyatomic molecule



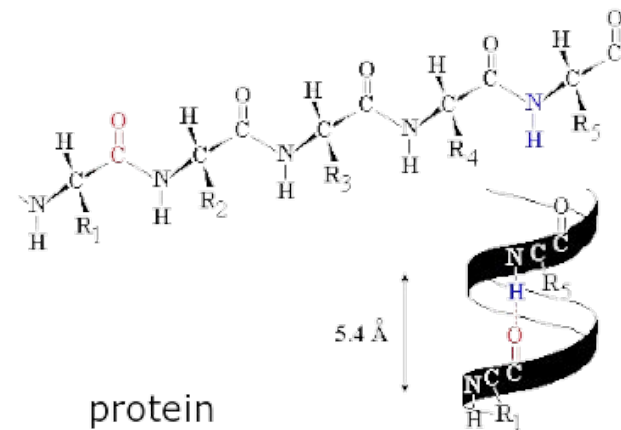
Alkanes



graphene

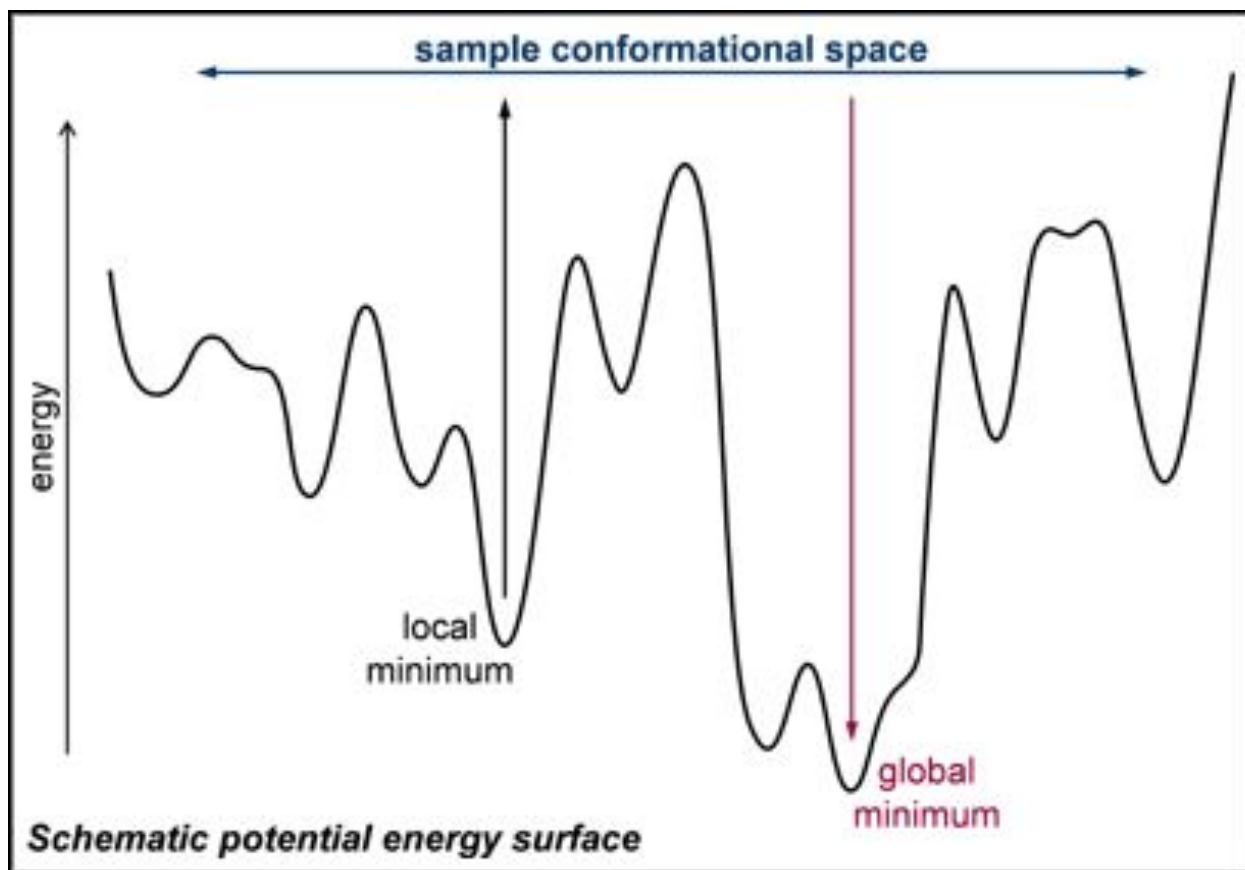


Ionic liquid



protein

PES of a large molecules



Force fields

- Force field is a collection of equations used to reproduce the structure of molecules and their target properties.
- Provides the energy and forces of a system as a function of nuclear positions
- Perform calculations on systems containing significant number of atoms
- Transferability: set of parameters developed for small number of systems or small molecules can be applied to wider range of problems and larger molecules
- E.g., biomolecular force fields: CHARMM, AMBER, GROMOS, alkanes: OPLS-AA

Force fields

- Many problems to be handled by molecular modelling are too large for quantum mechanics
- Molecular mechanics works, but several assumptions have been made

$$U_{\text{bond}} = \frac{1}{2}k_b(r_{ij} - r_0)^2$$

$$U_{\text{angle}} = \frac{1}{2}k_\theta(\theta_{ijk} - \theta_0)^2$$

$$U_{\text{dihedral}} = \sum_{n=1}^N V_n \cos(n\phi - \delta_n)$$

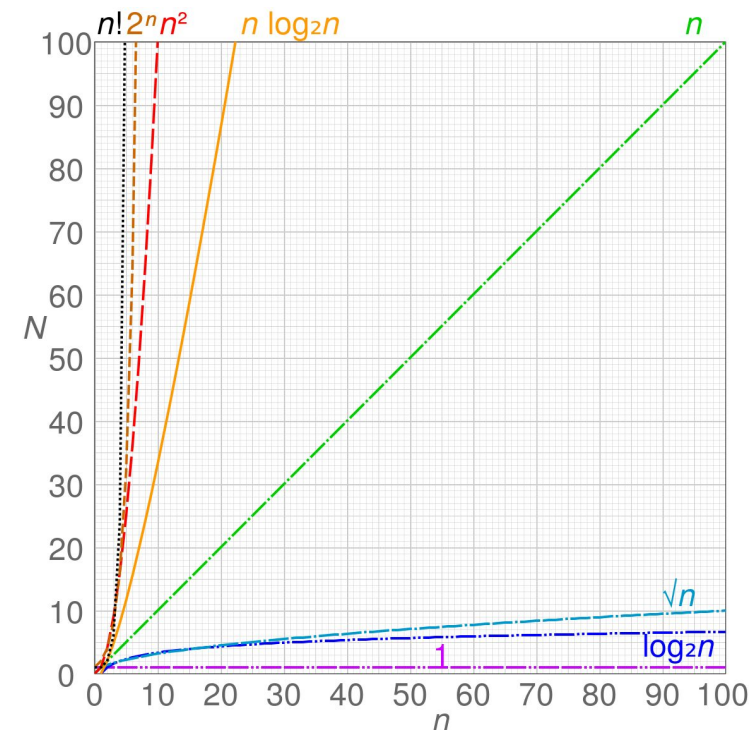
$$U_{\text{nonbonded}} = U_{\text{LJ}} + U_{\text{coulomb}}$$

$$U_{\text{LJ}} = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right]$$

$$U_{\text{coulomb}} = \frac{q_i q_j}{4\pi\epsilon_0 r}$$

Why force fields

- Take an example: benzene -- chemical formula – C_6H_6 .
- The number of electrons – 42 ; number of nuclei – 12
- Total number of variables: $(42+12)*3=162$
- Computational complexity 162^2

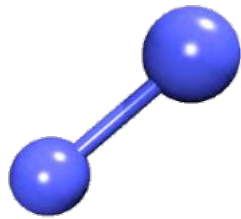


Molecular Mechanics

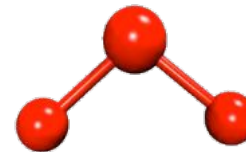
- Uses classical mechanics to study molecules/liquids/solids with the help of force fields
- Compute the properties of molecular systems of any complexity with many thousand to millions thousands of atoms.
- Atoms are modelled as single point particle, assigned the mass and charge. Interactions between them are modelled with spring-like interactions and van der Waals interactions
- Force fields = bonded terms + non-bonded terms

Types of bonded interactions

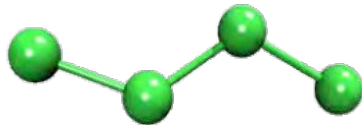
Interactions between atoms separated by one, two and three covalent bonds



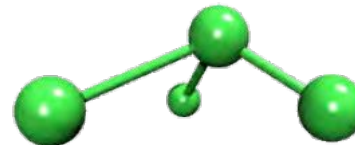
Bond



Angle



Dihedral



Improper

Bond stretching (1-2 interactions)

- Morse potential

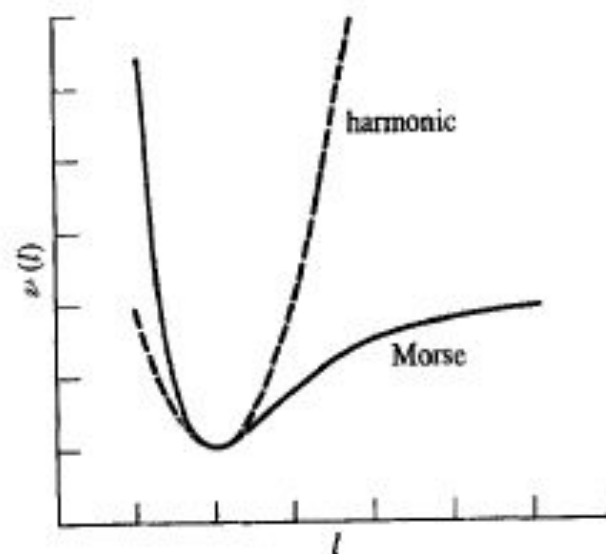
$$v(l) = D_e \{1 - \exp[-a(l - l_0)]\}^2$$

- Harmonic potential

$$v(l) = \frac{k}{2} (l - l_0)^2$$

Bond	l_0 (Å)	k (kcal mol ⁻¹ Å ⁻²)
Csp ³ –Csp ³	1.523	317
Csp ³ –Csp ²	1.497	317
Csp ² =Csp ²	1.337	690
Csp ² =O	1.208	777
Csp ³ –Nsp ³	1.438	367
C–N (amide)	1.345	719

Table 4.1 Force constants and reference bond lengths for selected bonds [Allinger 1977]



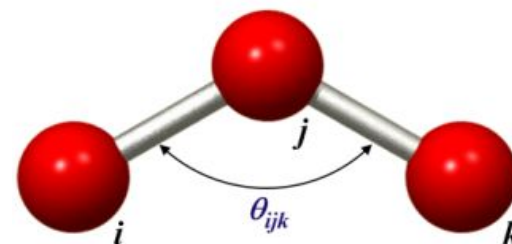
Angle bending (1-3 interactions)

- Harmonic potential

$$v(\theta) = \frac{k}{2}(\theta - \theta_0)^2$$

Angle	θ_0	k (kcal mol ⁻¹ deg ⁻¹)
Csp ³ –Csp ³ –Csp ³	109.47	0.0099
Csp ³ –Csp ³ –H	109.47	0.0079
H–Csp ³ –H	109.47	0.0070
Csp ³ –Csp ² –Csp ³	117.2	0.0099
Csp ³ –Csp ² =Csp ²	121.4	0.0121
Csp ³ –Csp ² =O	122.5	0.0101

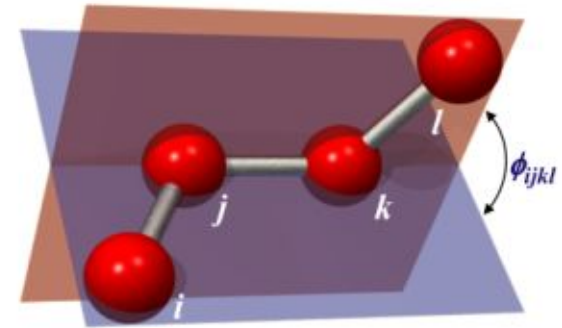
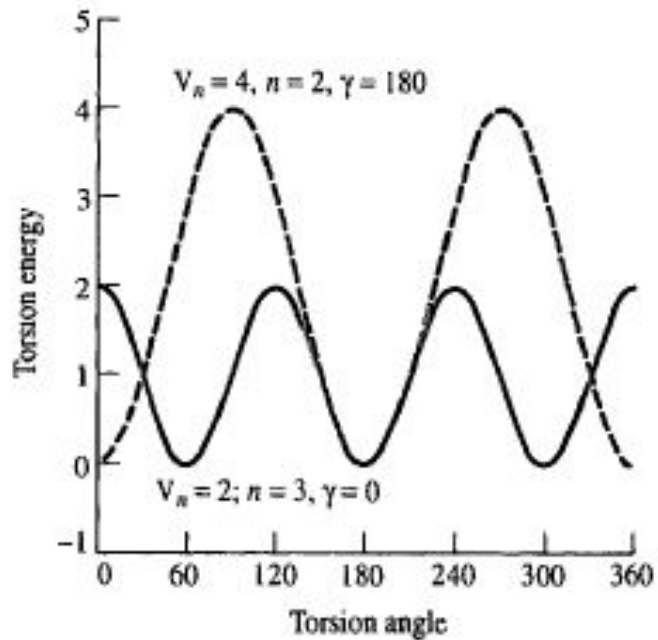
Table 4.2 Force constants and reference angles for selected angles
[Allinger 1977].



Torsions (1-4 interactions)

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

$$v(\omega) = \sum_{n=0}^N C_n \cos(\omega)^n$$

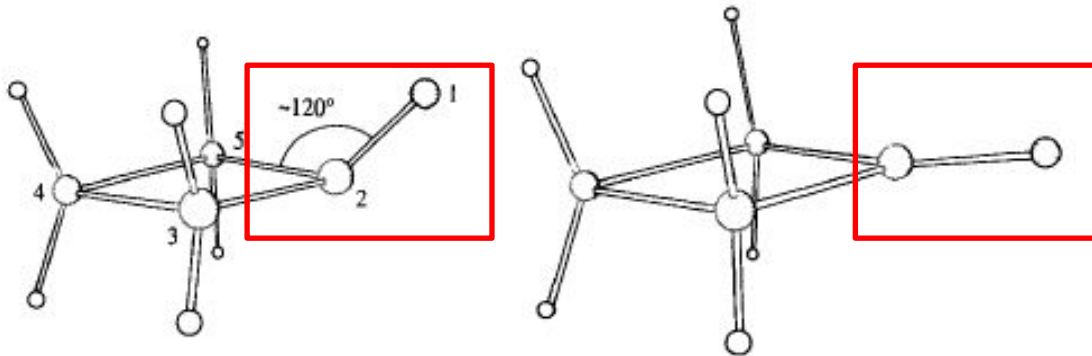
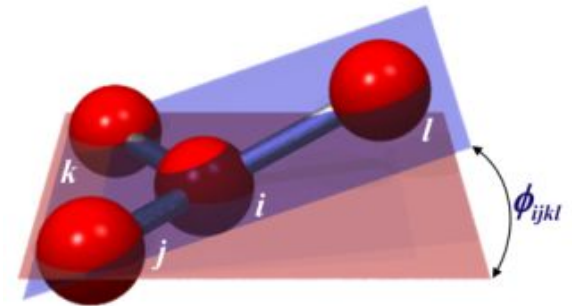


Dihedral (proper torsion)

Improper torsions (1-4 interactions)

Maintains the planarity of the molecule

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



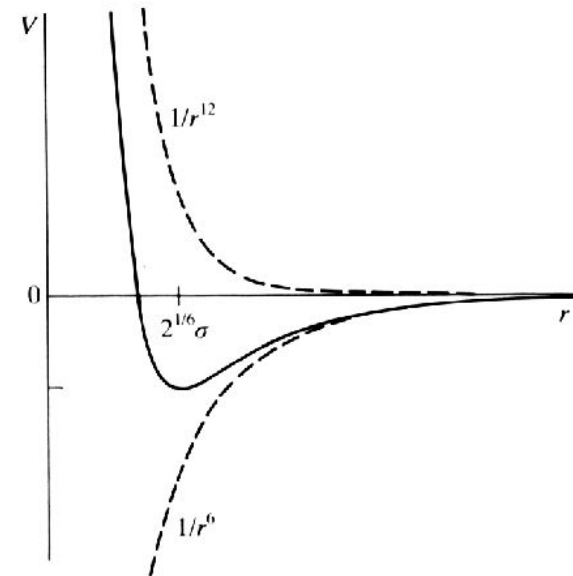
Non-bonded terms

- Between the atoms of two different molecules or atom pairs separated by more than (or equal to) three covalent bonds

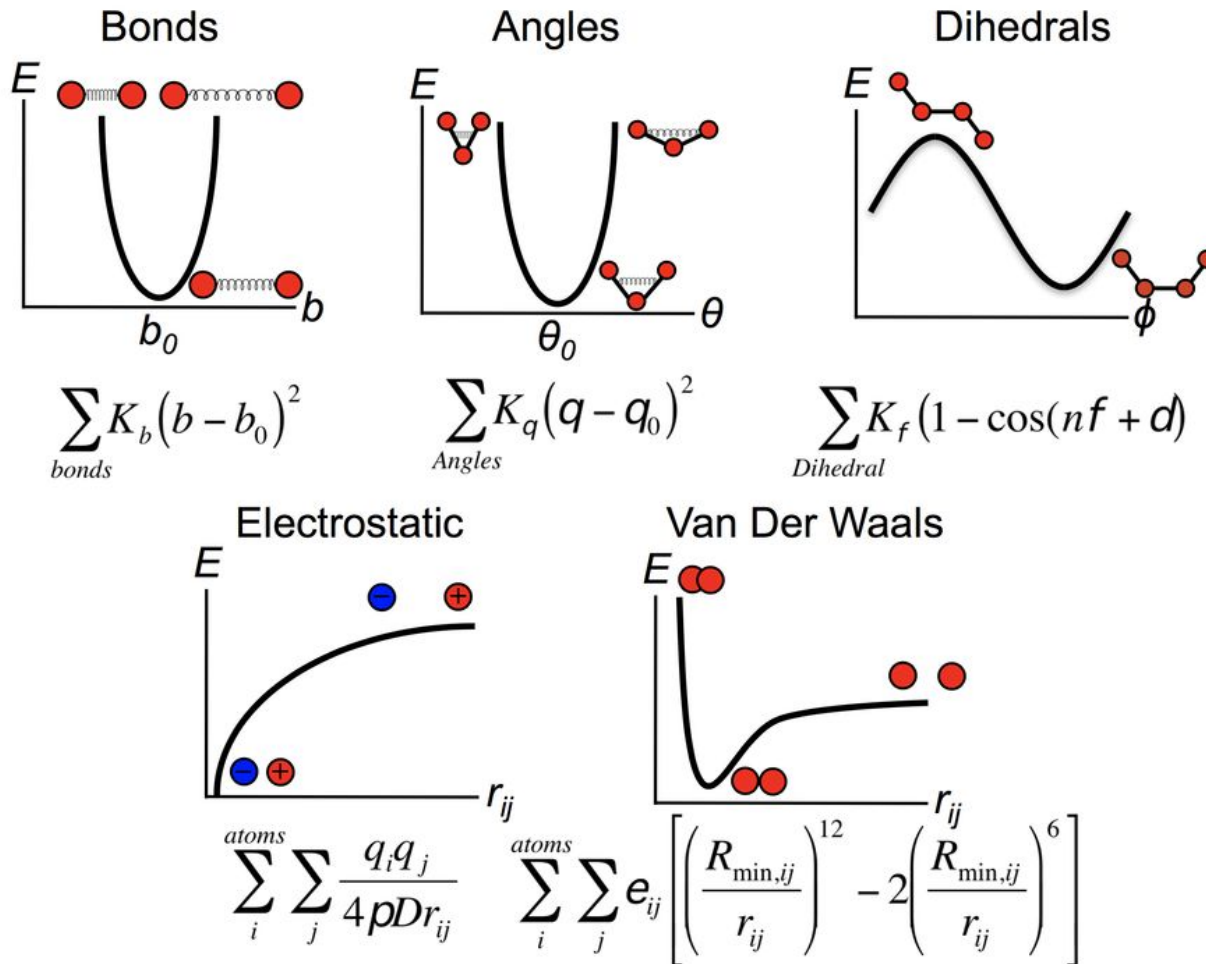
$$V(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right]$$

Lorentz Berthelot rules: polyatomic systems

$$V_E = \frac{q_i q_j}{4\pi\epsilon_0\epsilon_R r_{ij}}$$



All bonded and non-bonded terms



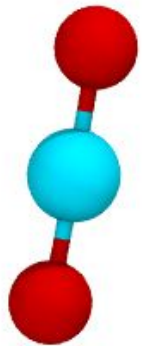
Parametrization of force fields

- Non-bonded and torsional terms most sensitive
- Vibrational frequencies
- Atomic coordinates: X-ray diffraction, neutron scattering
- Inter-atomic distance: NMR
- Quantum mechanics calculations provide data for parameterization

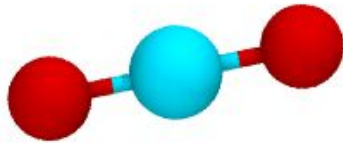
force fields for water

- https://docs.lammps.org/Howto_tip3p.html

Step by step procedure



CO₂ dimer



- Cartesian coordinates of the molecules/system
- The list of bonded and non-bonded atom pairs
- Bond types, angle types, dihedral types and improper types
- For bonded terms, figure out the parameters such as bond force constants, equilibrium distance, and angle force constants.
- Mass and charges of the atoms
- For non-bonded terms, sigma and epsilon of LJ potential
- Prepare the parameter file – file format depends on the software using this force field

Hands-on

- <https://traken.chem.yale.edu/ligpargen/moleculeDraw.html>
- Take any organic molecule
- Obtain Force field parameters. (click Gromacs Top option)
- Inspect charges on atoms
- Check eps, sigma parameters for LJ potential
- Check bond, angle, dihedral potential, etc
- Plot dihedral potential in the desmos graph calculator.

For eg: butane

<https://manual.gromacs.org/current/reference-manual/topologies/parameter-files.html>

<https://manual.gromacs.org/current/reference-manual/functions/bonded-interactions.html>

<https://manual.gromacs.org/current/reference-manual/topologies/topology-file-formats.html#tab-to-pfile2::~text=Table%2014%20Details%20of%20%5B%20moleculetype%20%5D%20directives>

Hands-on

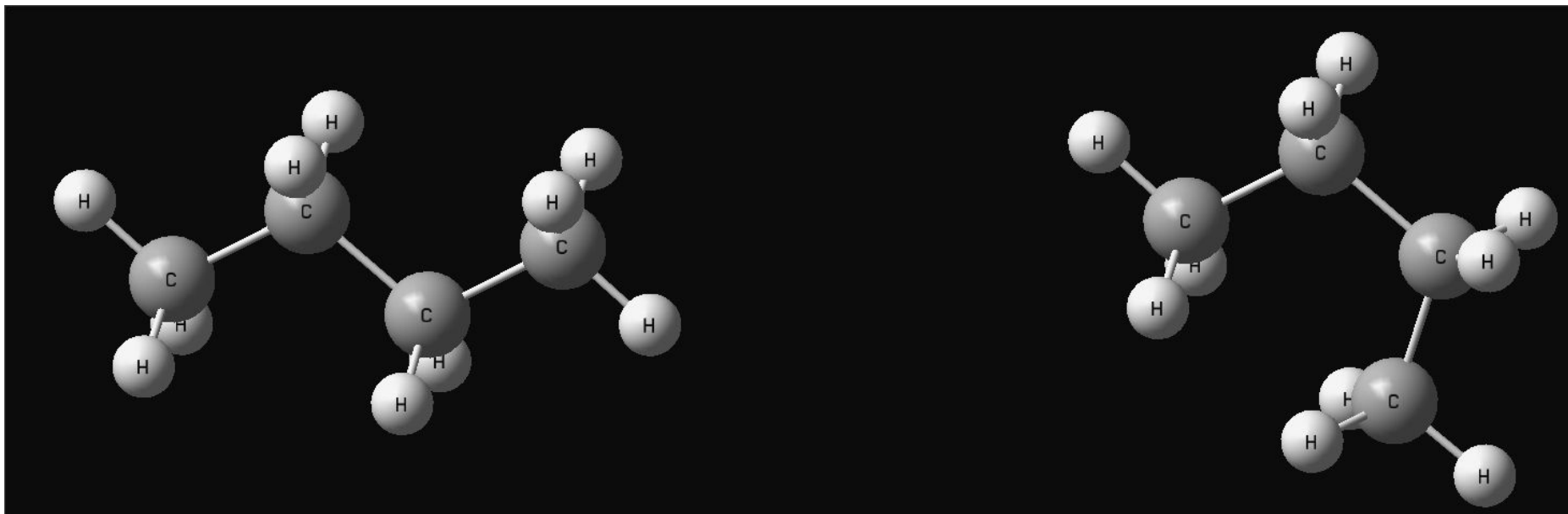
- <https://traken.chem.yale.edu/ligpargen/moleculeDraw.html>
- Take A. ethane (C₂H₆) B. ethene (C₂H₄) and C. benzene (C₆H₆) molecules and calculate their energy based on force field parameters. Use the above link to get force field files (gro and top files)
 - For electrostatic term, the conversion factor ($1/4\pi\epsilon_0$) is 138.935 kJ·mol⁻¹·nm·e⁻².

<https://manual.gromacs.org/current/reference-manual/topologies/parameter-files.html>

<https://manual.gromacs.org/current/reference-manual/functions/bonded-interactions.html>

<https://manual.gromacs.org/current/reference-manual/topologies/topology-file-formats.html#tab-to-pfile2~:text=Table%2014%20Details%20of%20%5B%20molecule%20type%20%5D%20directives>

Conformers - Butane



Topic: Force fields

Reading material

- A. R. Leach, Molecular Modelling - Principles and Applications, 2nd edition, Prentice Hall, Harlow, England (2001).

Hands-on

- Using VMD software, load the given molecules. Define the potential energy surfaces (write all pairs of atoms contributing to each component in the force field).
 - Ethanol ($\text{C}_2\text{H}_5\text{OH}$)
 - Benzene (C_6H_6)
- Calculate the _____ for both molecules
 - Number of bonds _____
 - Number of angles _____
 - Number of Dihedrals _____
 - Number of Improper torsions _____
 - Number of non-bonded atom pairs _____