

# Force Fields for MD simulations

- Topology/parameter files
- Where do the numbers an MD code uses come from?
- How to make topology files for ligands, cofactors, special amino acids, ...
- How to obtain/develop missing parameters.
  
- QM and QM/MM force fields/potential energy descriptions used for molecular simulations.

# Classical Molecular Dynamics

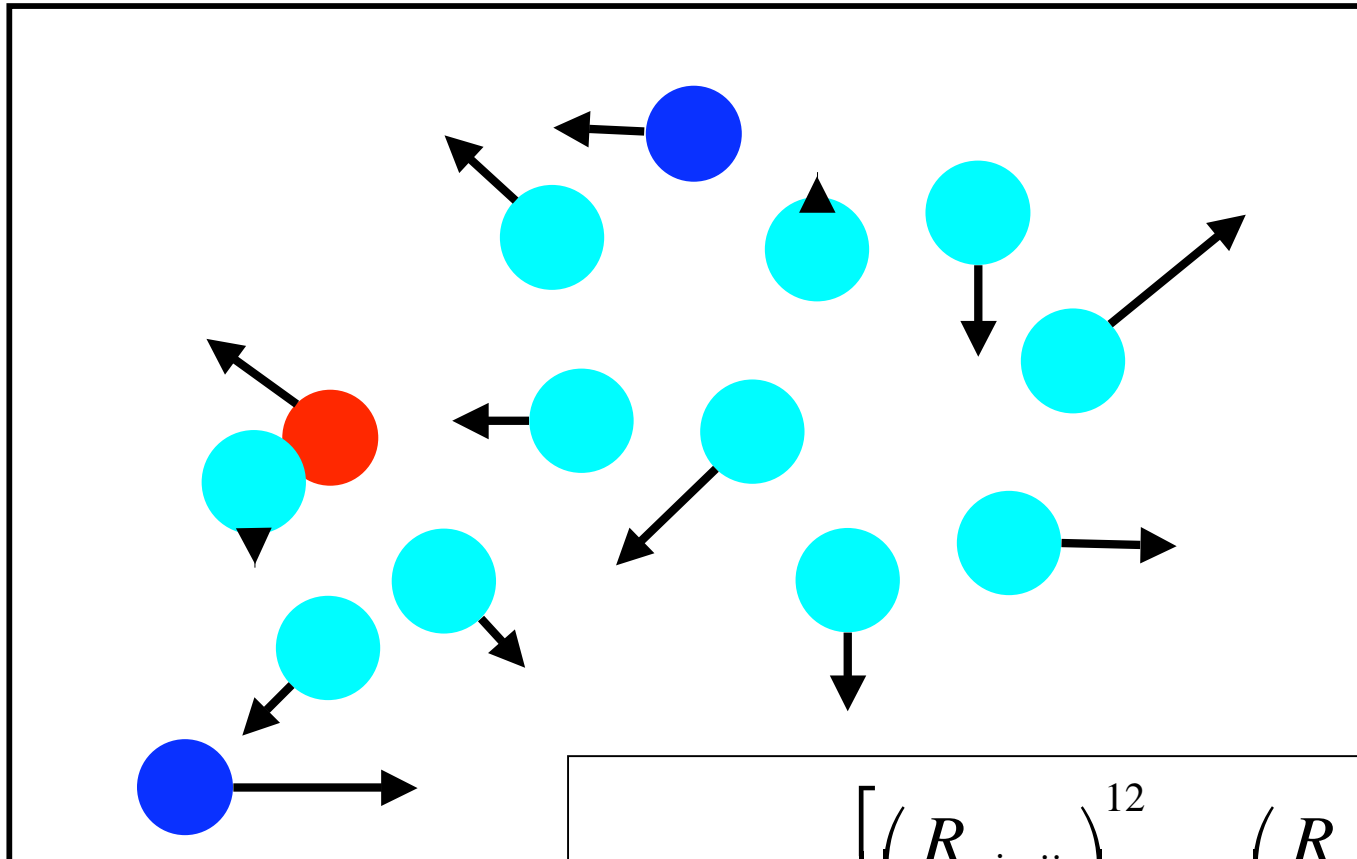
$$\mathbf{r}(t + \delta t) = \mathbf{r}(t) + \mathbf{v}(t)\delta t$$

$$\mathbf{v}(t + \delta t) = \mathbf{v}(t) + \mathbf{a}(t)\delta t$$

$$\mathbf{a}(t) = \mathbf{F}(t) / m$$

$$\mathbf{F} = -\frac{d}{dr}U(\mathbf{r})$$

# Classical Molecular Dynamics



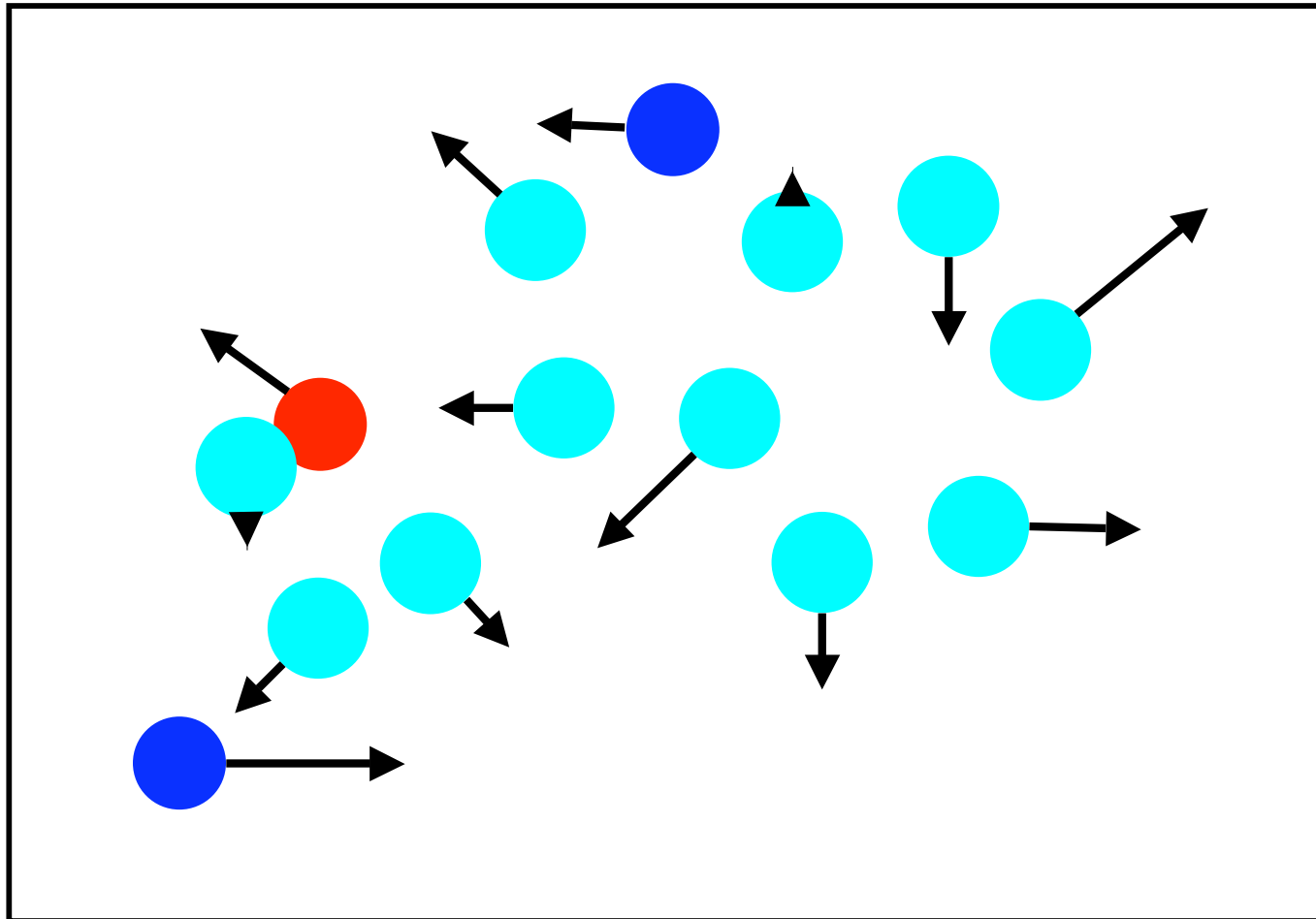
$$U(r) = \frac{1}{4\pi\epsilon_0} \frac{q_i q_j}{r_{ij}}$$

Coulomb interaction

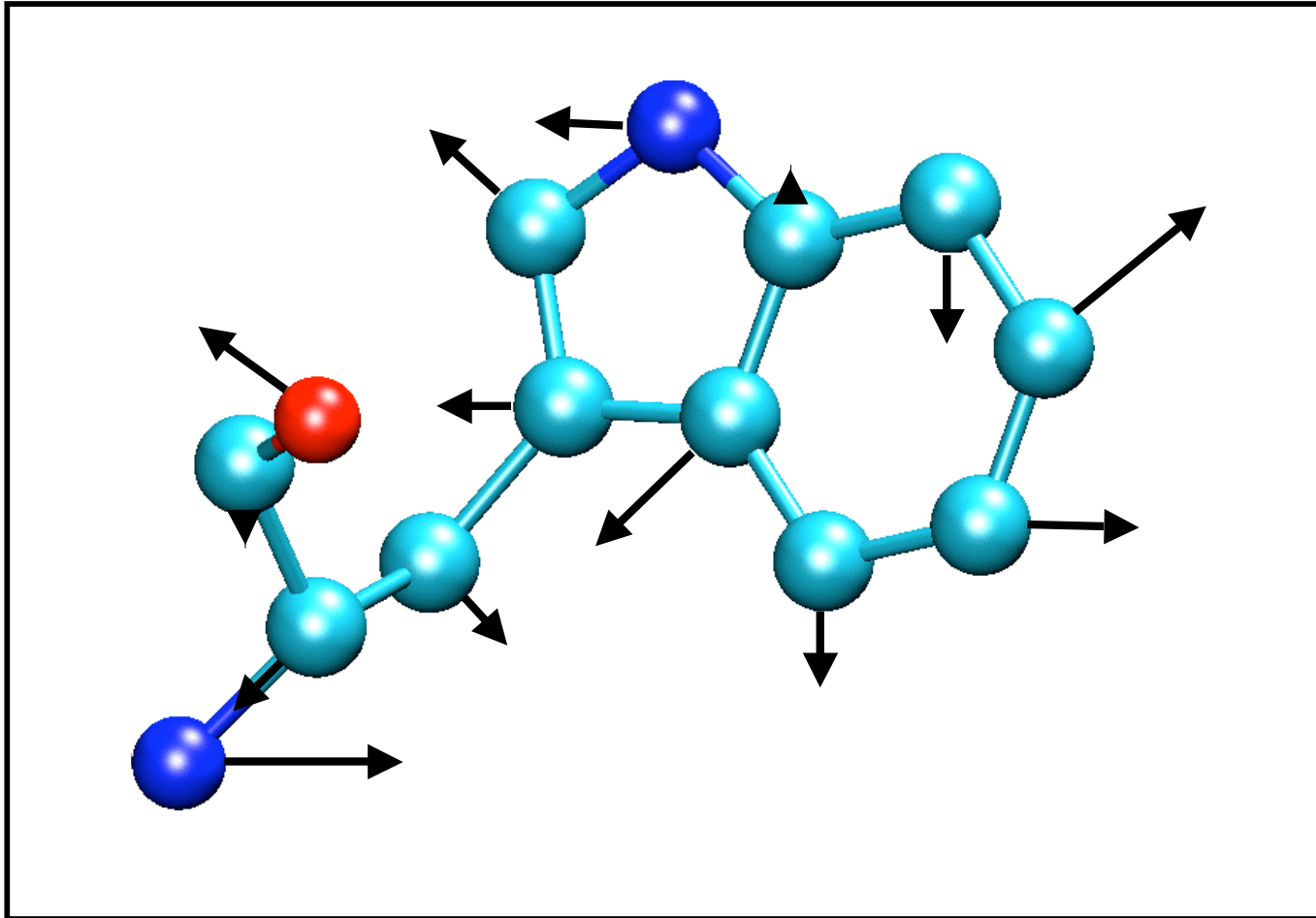
$$U(r) = \epsilon_{ij} \left[ \left( \frac{R_{\min,ij}}{r_{ij}} \right)^{12} - 2 \left( \frac{R_{\min,ij}}{r_{ij}} \right)^6 \right]$$

van der Waals interaction

# Classical Molecular Dynamics



# Classical Molecular Dynamics

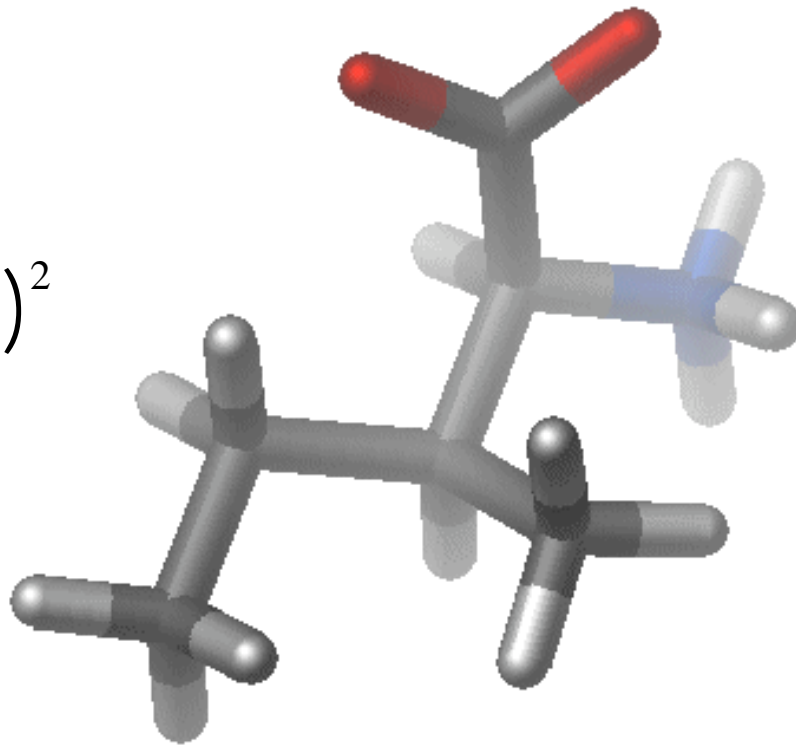


Bond definitions, atom types, atom names, parameters, ....

# Interactions between bonded atoms

$$V_{angle} = K_{\theta} (\theta - \theta_o)^2$$

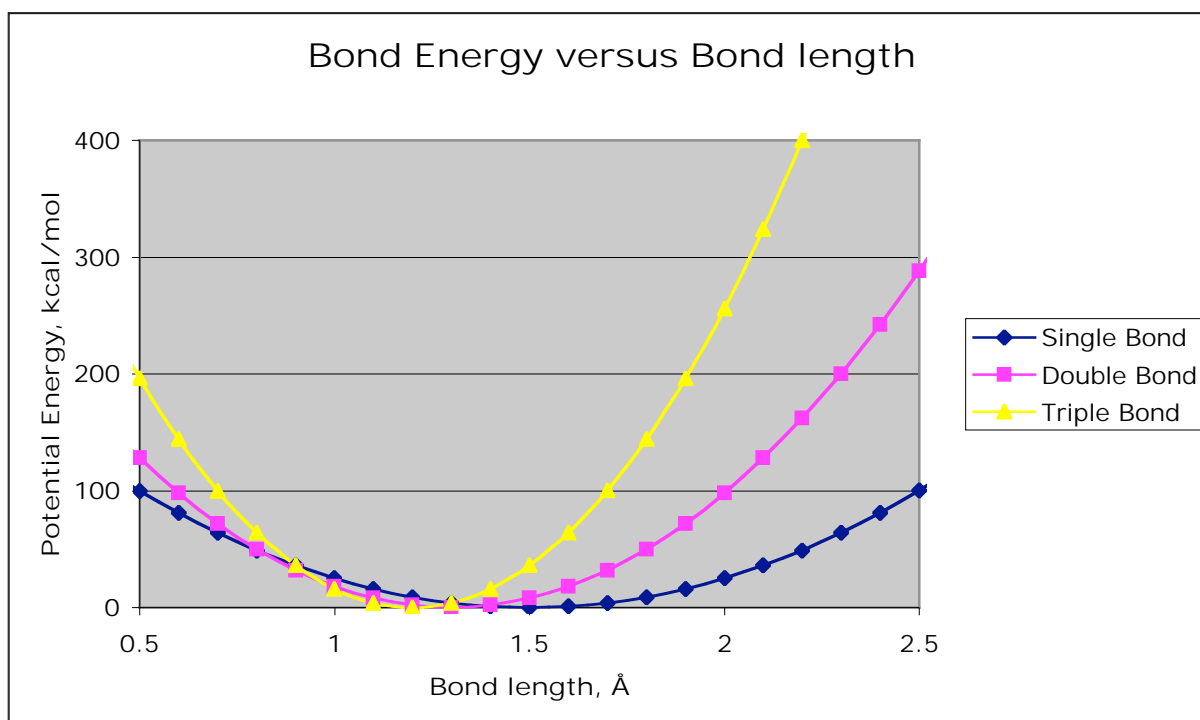
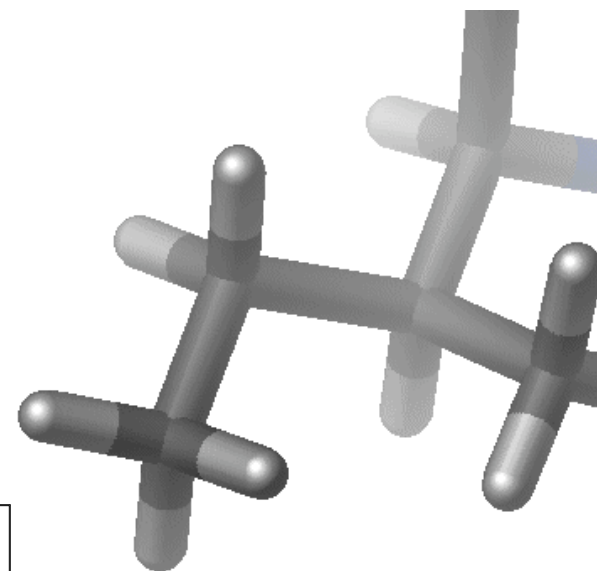
$$V_{bond} = K_b (b - b_o)^2$$



$$V_{dihedral} = K_{\phi} (1 + \cos(n\phi - \delta))$$

$$V_{bond} = K_b (b - b_o)^2$$

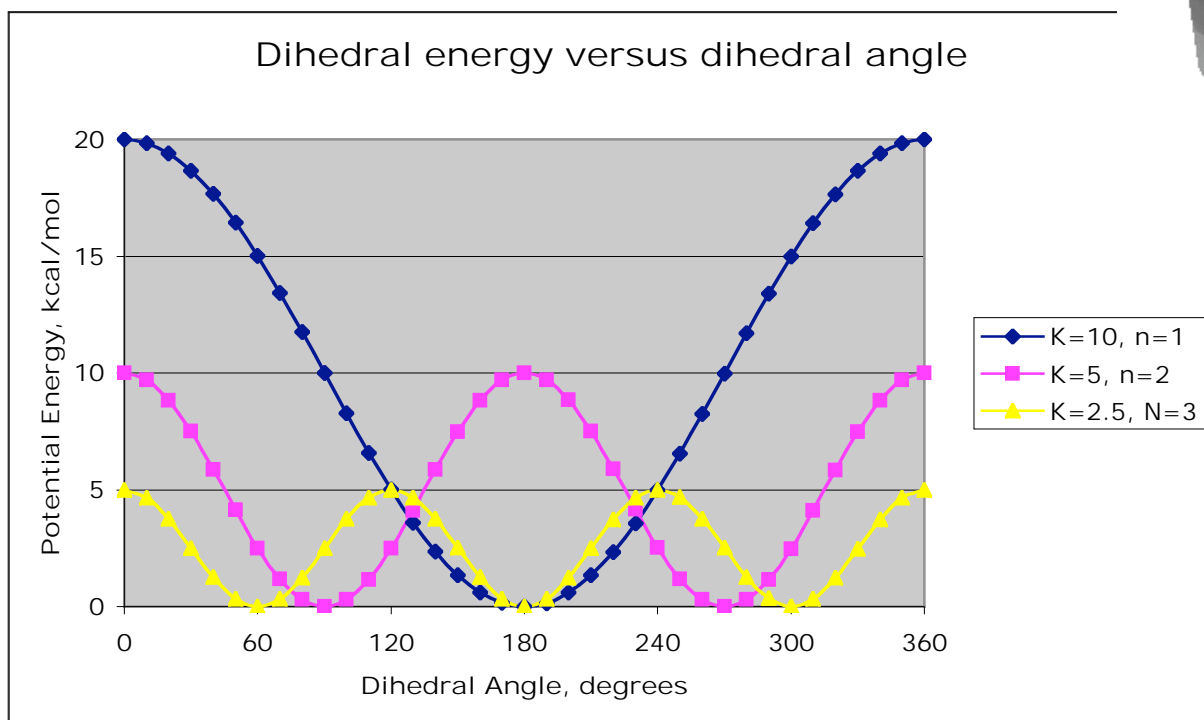
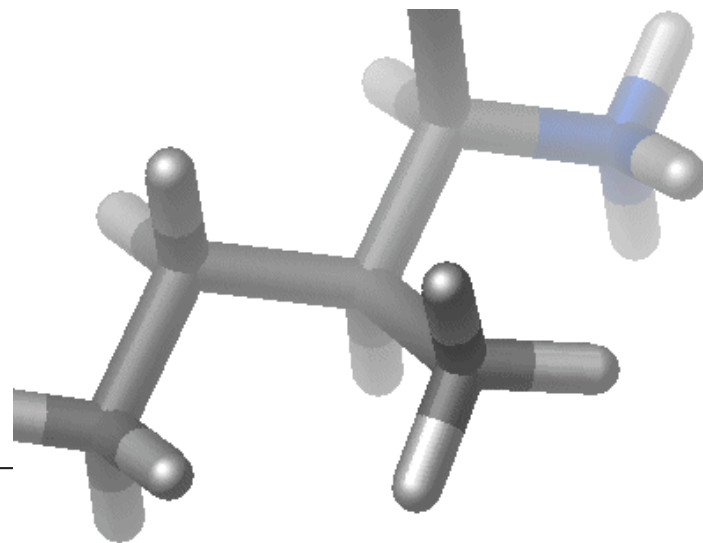
Chemical type	$K_{bond}$	$b_o$
C-C	100 kcal/mole/Å <sup>2</sup>	1.5 Å
C=C	200 kcal/mole/Å <sup>2</sup>	1.3 Å
C≡C	400 kcal/mole/Å <sup>2</sup>	1.2 Å



*Bond angles* and *improper* terms have similar quadratic forms, but with softer spring constants. The force constants can be obtained from vibrational analysis of the molecule (experimentally or theoretically).

# Dihedral Potential

$$V_{dihedral} = K_{\phi} (1 + \cos(n\phi - \delta))$$



$$\delta = 0^\circ$$



# CHARMM Potential Function

$$\begin{aligned}
 U(\vec{R}) = & \underbrace{\sum_{\text{bonds}} k_i^{\text{bond}} (r_i - r_0)^2}_{U_{\text{bond}}} + \underbrace{\sum_{\text{angles}} k_i^{\text{angle}} (\theta_i - \theta_0)^2}_{U_{\text{angle}}} + \\
 & \underbrace{\sum_{\text{dihedrals}} k_i^{\text{dihe}} [1 + \cos(n_i \phi_i + \delta_i)]}_{U_{\text{dihedral}}} + \underbrace{\sum_i \sum_{j \neq i} 4 \epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]}_{U_{\text{nonbond}}} + \sum_i \sum_{j \neq i} \frac{q_i q_j}{\epsilon r_{ij}}
 \end{aligned}$$

PDB file → **geometry** (points to  $k_i^{\text{bond}}$ ,  $k_i^{\text{angle}}$ ,  $k_i^{\text{dihe}}$ )  
 Topology PSF file (points to  $n_i$ ,  $\phi_i$ ,  $\delta_i$ )  
 Parameter file → **parameters** (points to  $\epsilon_{ij}$ ,  $\sigma_{ij}$ ,  $q_i$ )

# File Format/Structure

- The structure of a pdb file
- The structure of a psf file
- The topology file
- The parameter file
- Connection to potential energy terms



# VMD Atom Selection Commands

The diagram shows a table of atom data with arrows pointing from labels above to specific columns. The labels are: 'index' points to the first column; 'name' points to the second column; 'resname' points to the third column; 'chain' points to the fourth column; 'resid' points to the fifth column; 'x' points to the sixth column; 'y' points to the seventh column; 'z' points to the eighth column; and 'segname' points to the tenth column.

ATOM	22	N	ALA	B	3	-4.073	-7.587	-2.708	1.00	0.00	BH
ATOM	23	HN	ALA	B	3	-3.813	-6.675	-3.125	1.00	0.00	BH

(name CA CB) and (resid 1 to 4) and (segname BH)

protein and resname LYS ARG GLU ASP

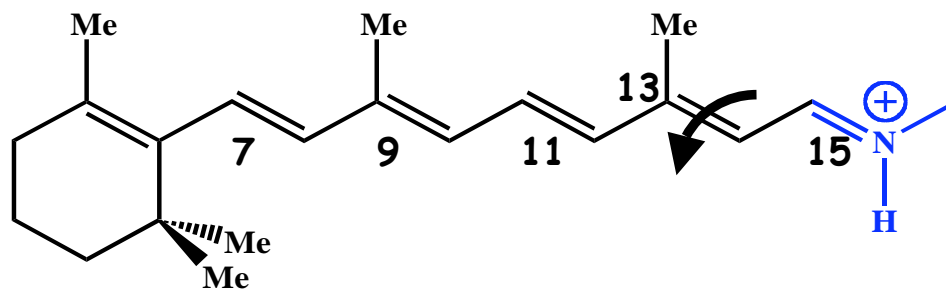
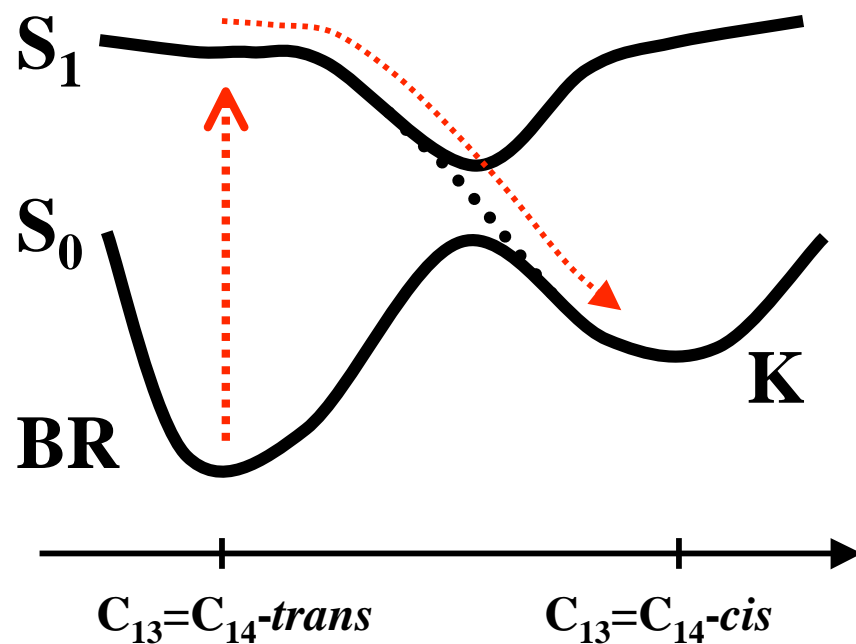
water and within 5 of (protein and resid 62 and name CA)

water and within 3 of (protein and name O and z < 10)

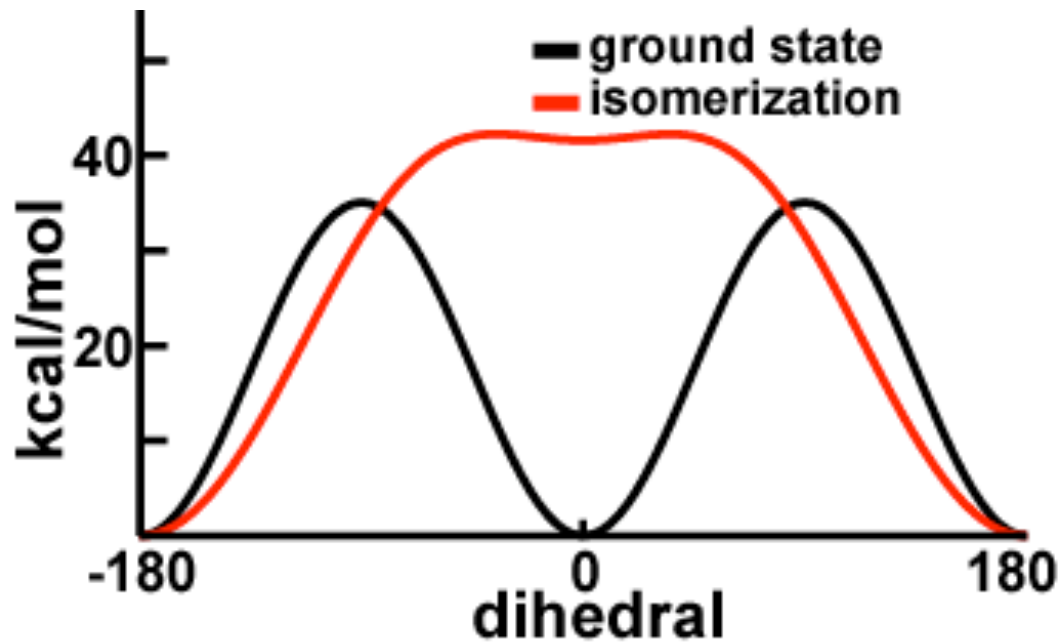
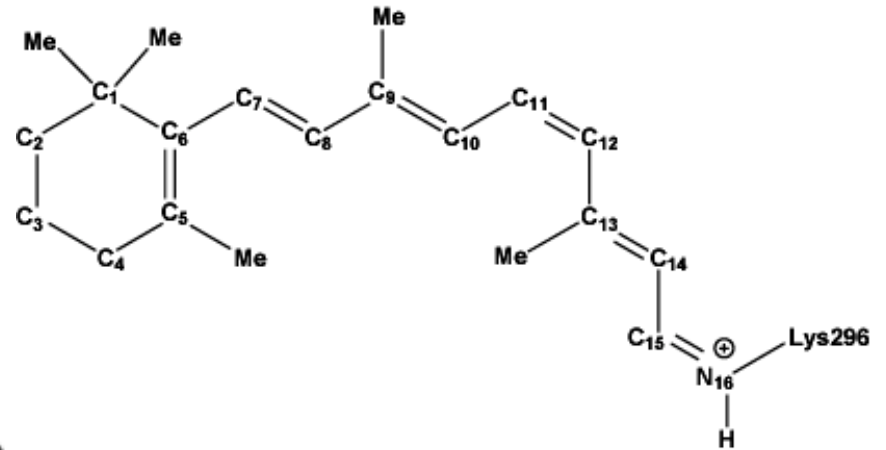
# Checking file structures

- PDB file
- Topology file
- PSF file
- Parameter file

# Coupling of electronic excitation and conformational change in bR

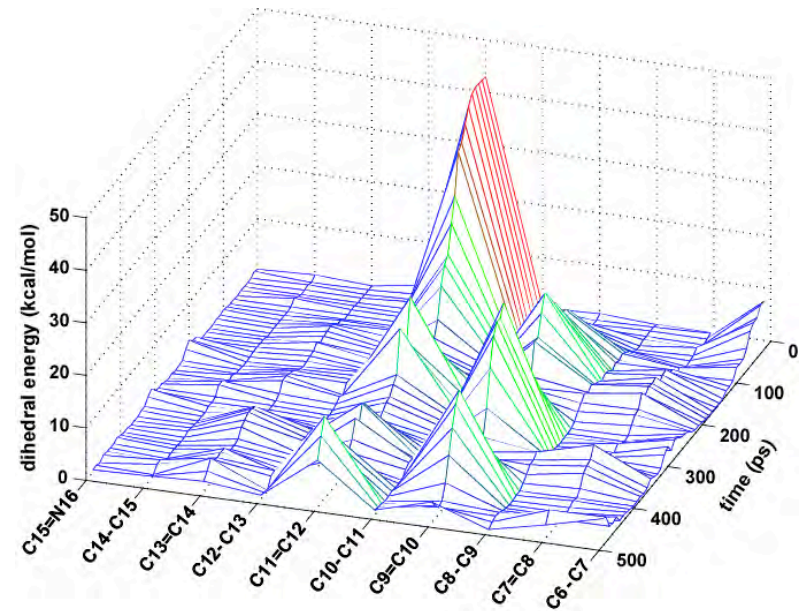
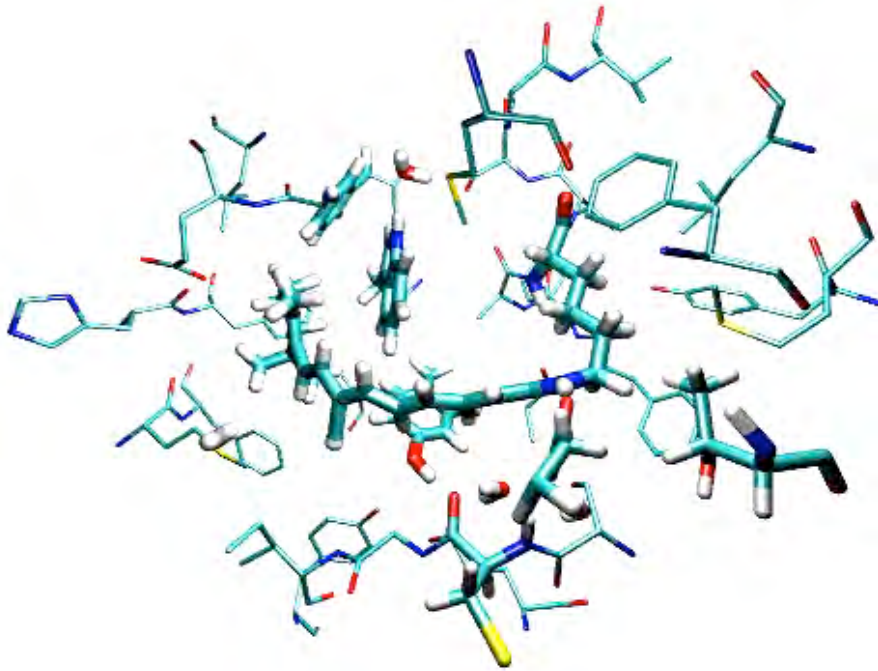


# Inducing isomerization



500 nm  
~50 kcal/mole

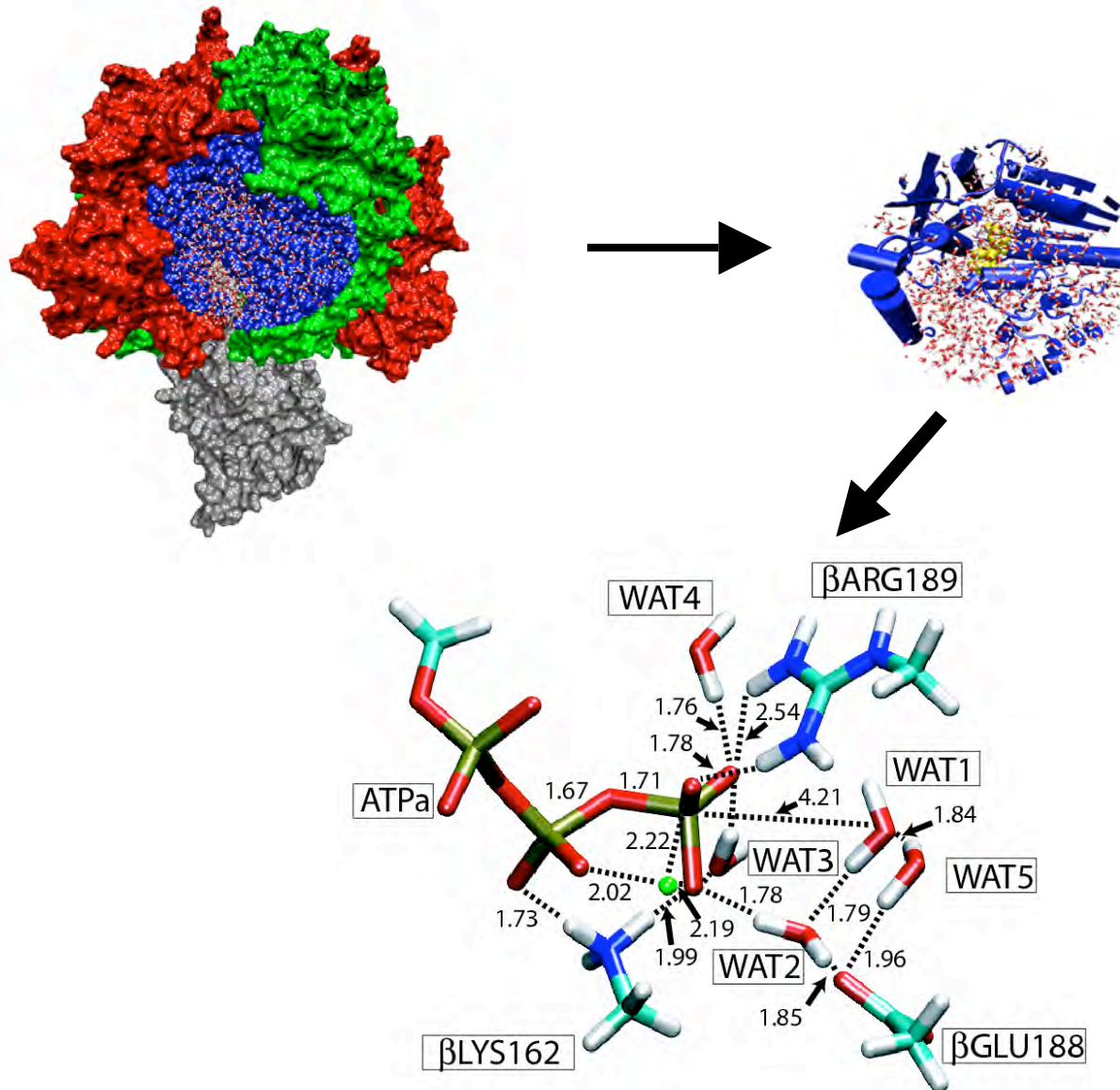
# Classical Retinal Isomerization in Rhodopsin



**Twist Propagation**



# QM/MM calculation of ATP hydrolysis



# Coarse grain modeling of lipids

150 particles



9 particles!

(A)

