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

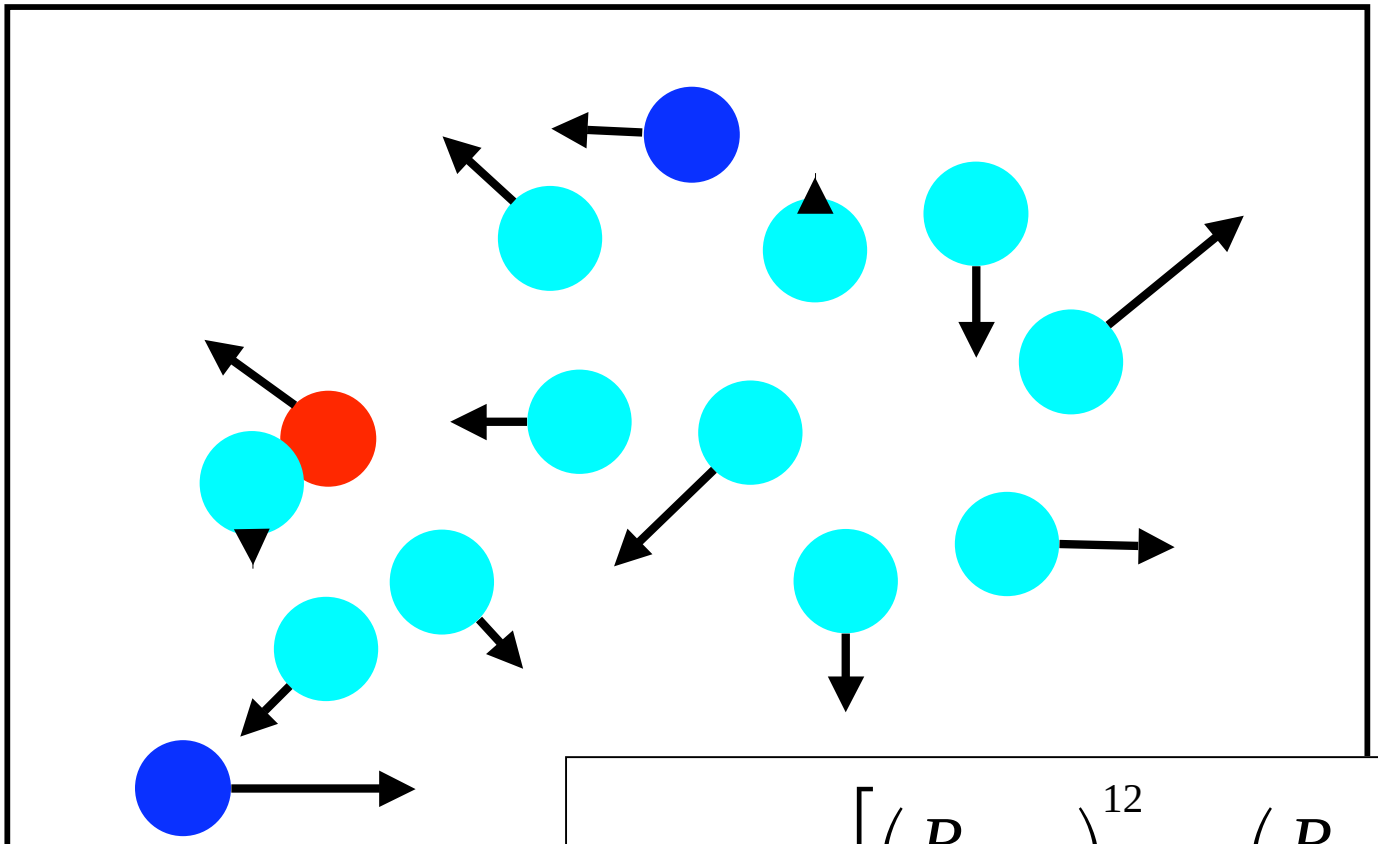
$$\boldsymbol{r}(t+\delta t) = \boldsymbol{r}(t) + \boldsymbol{v}(t)\delta t$$

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

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

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

Classical Molecular Dynamics



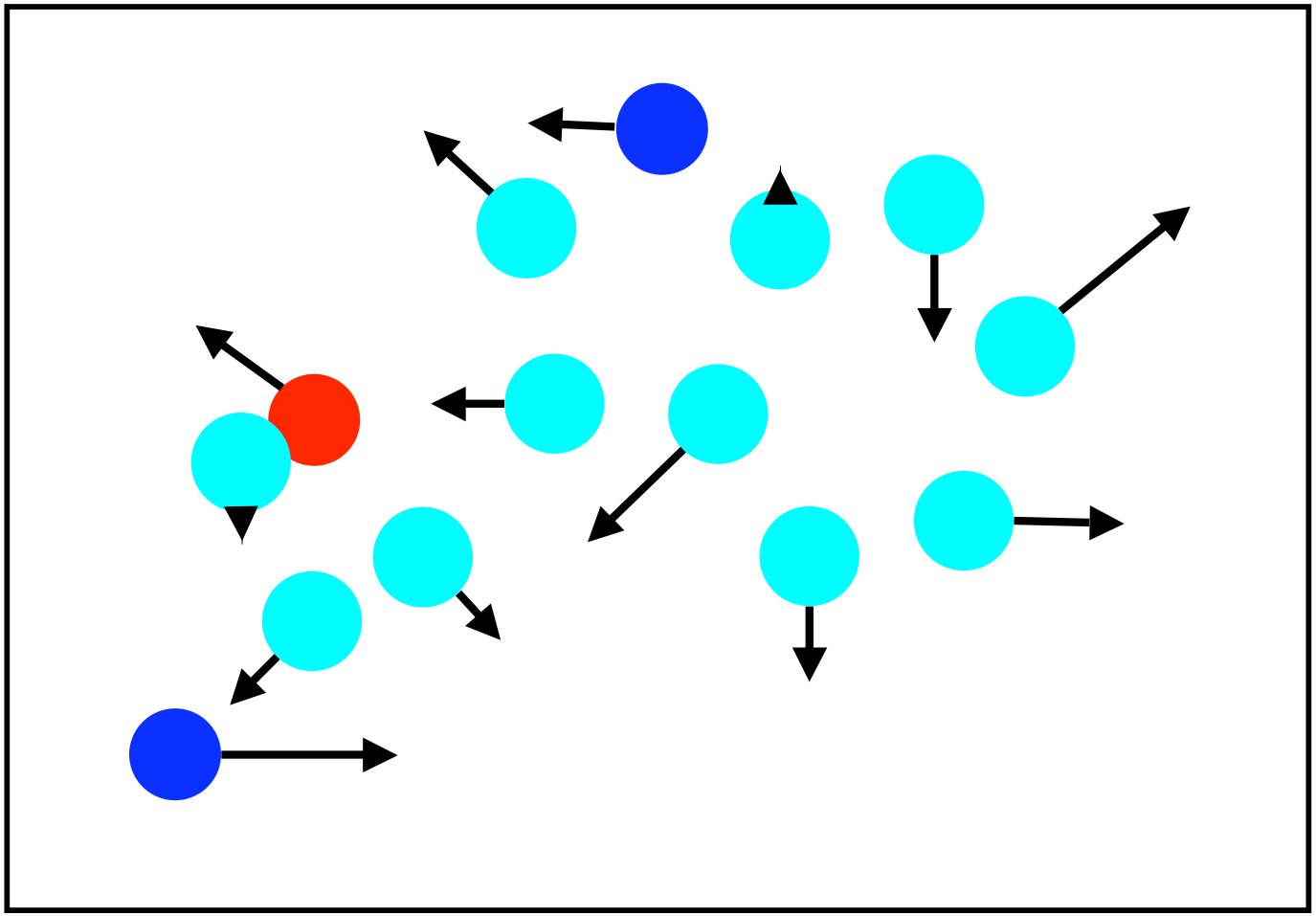
$$U(r) = \frac{1}{4\pi\varepsilon_0}\frac{q_i q_j}{r_{ij}}$$

Coulomb interaction

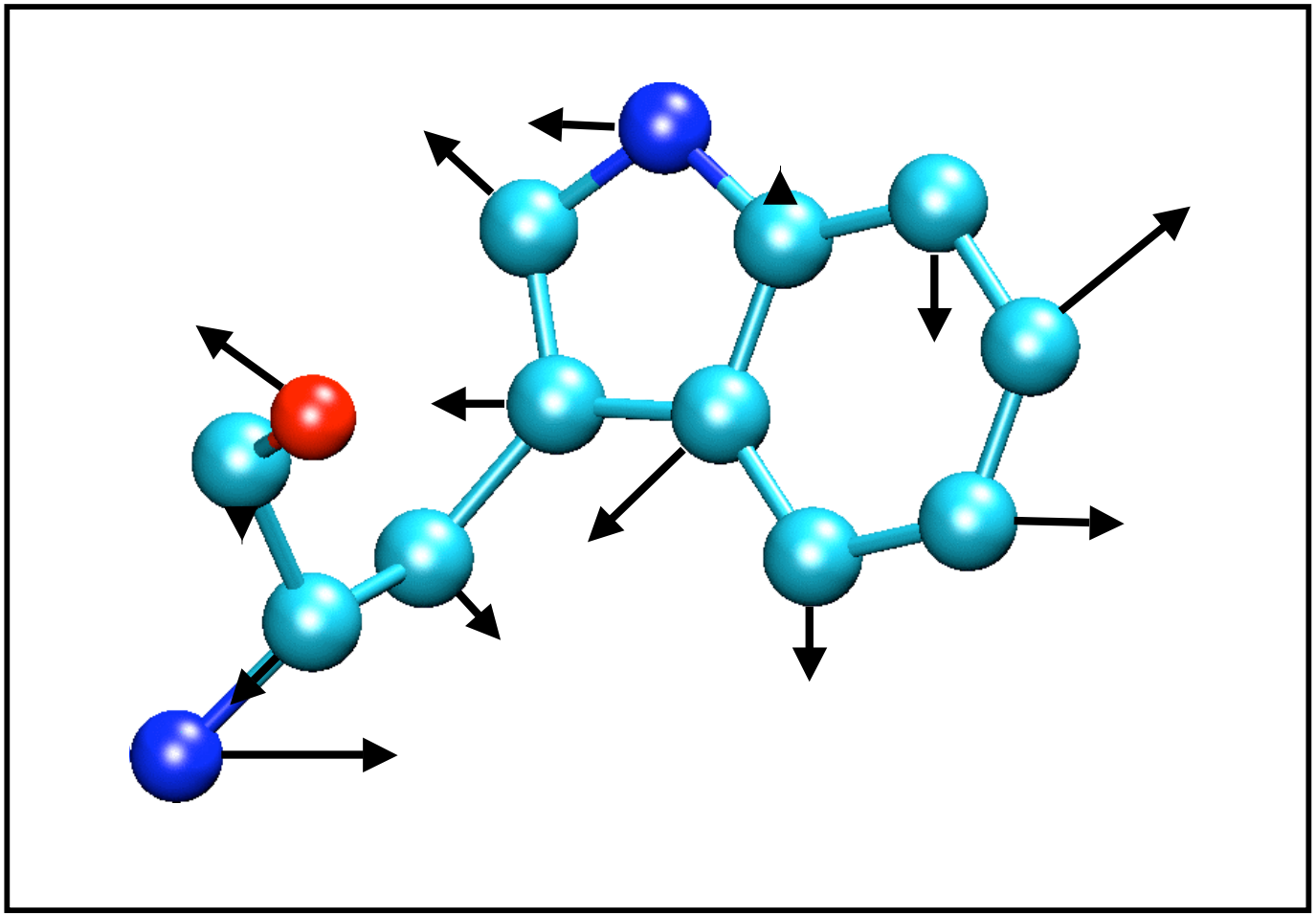
$$U(r) = \varepsilon_{ij}\left[\left(\frac{R_{\min,ij}}{r_{ij}}\right)^{12} - 2\left(\frac{R_{\min,ij}}{r_{ij}}\right)^{6}\right]$$

van der Waals interaction

Classical Molecular Dynamics



Classical Molecular Dynamics

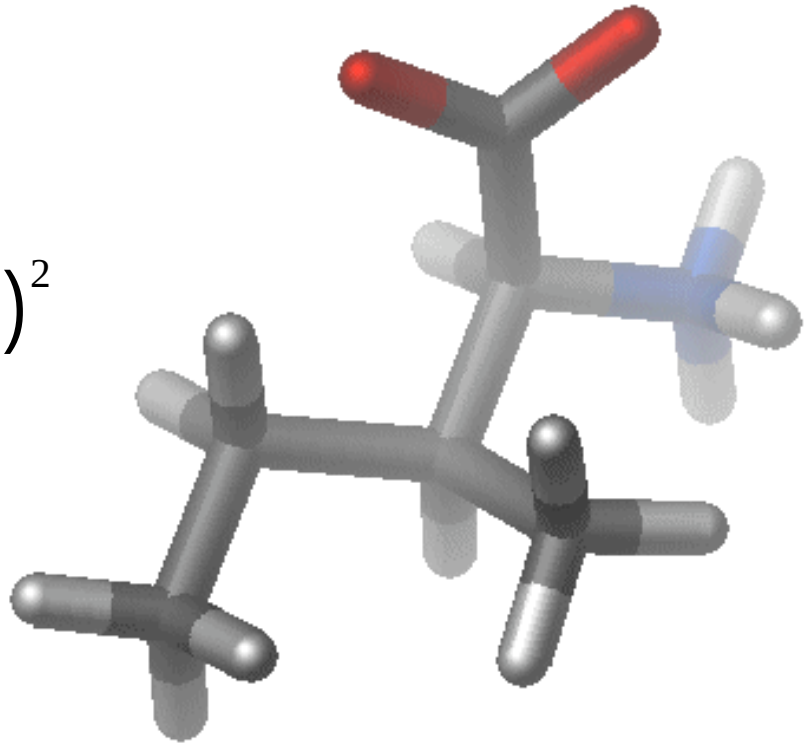


Bond definitions, atom types, atom names, parameters, ….

Interactions between bonded atoms

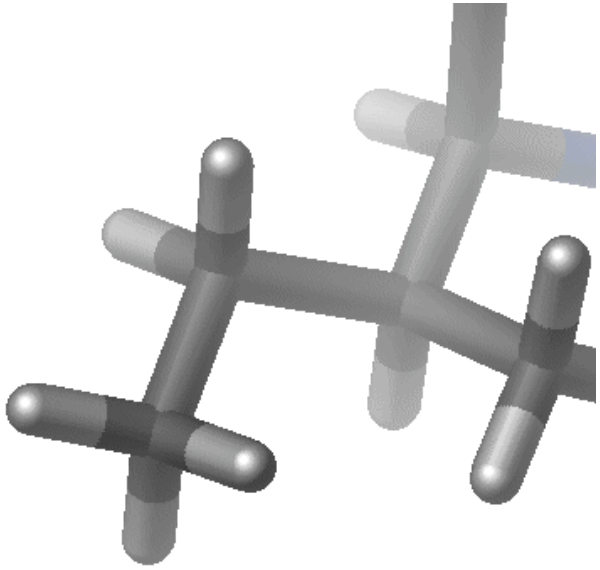
$$V_{angle} = K_\theta \left(\theta - \theta_o\right)^2$$

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

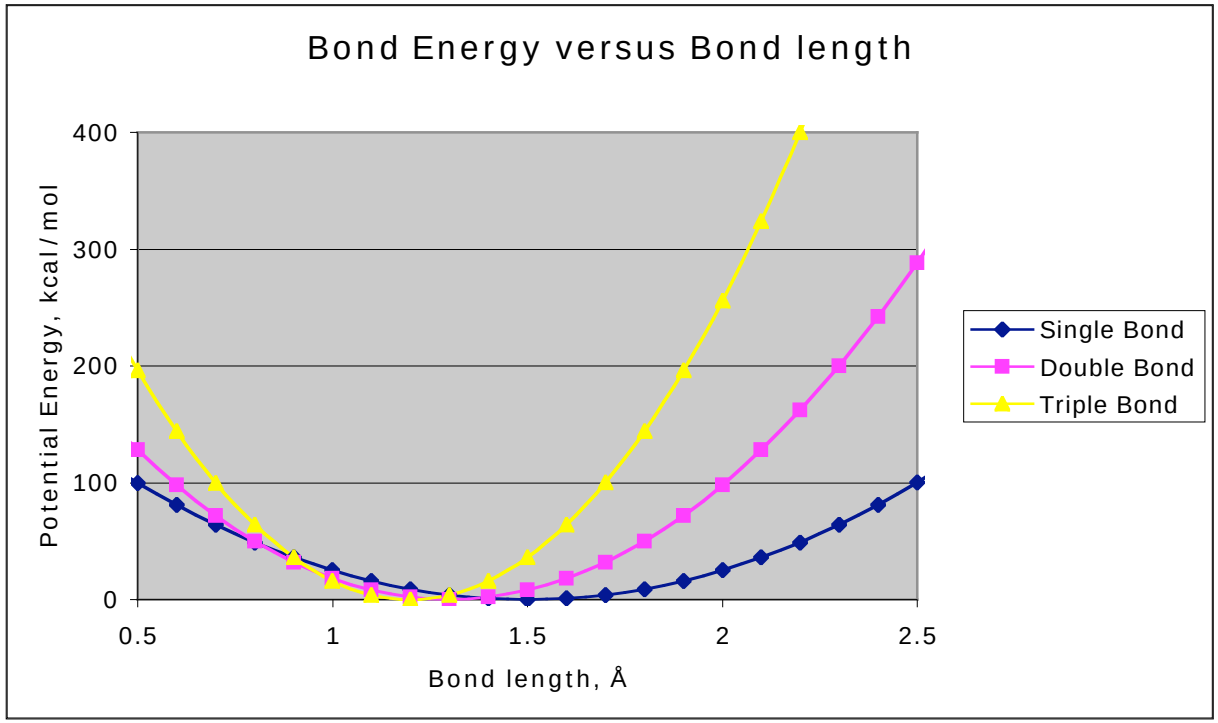


$$V_{dihedral} = K_\phi (1 + \cos(n\phi - \delta))$$

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



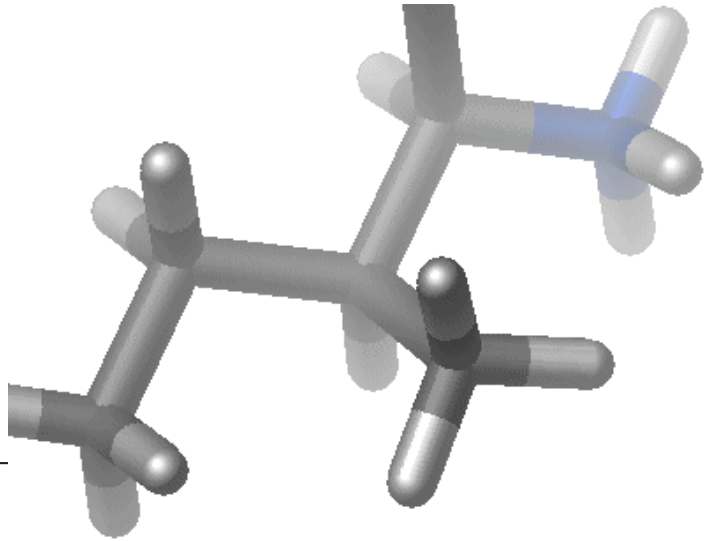
Chemical type	K_{bond}	b_o
C-C	100 kcal/mole/Å ^{2}	1.5 Å
C=C	200 kcal/mole/Å ^{2}	1.3 Å
C≡C	400 kcal/mole/Å ^{2}	1.2 Å

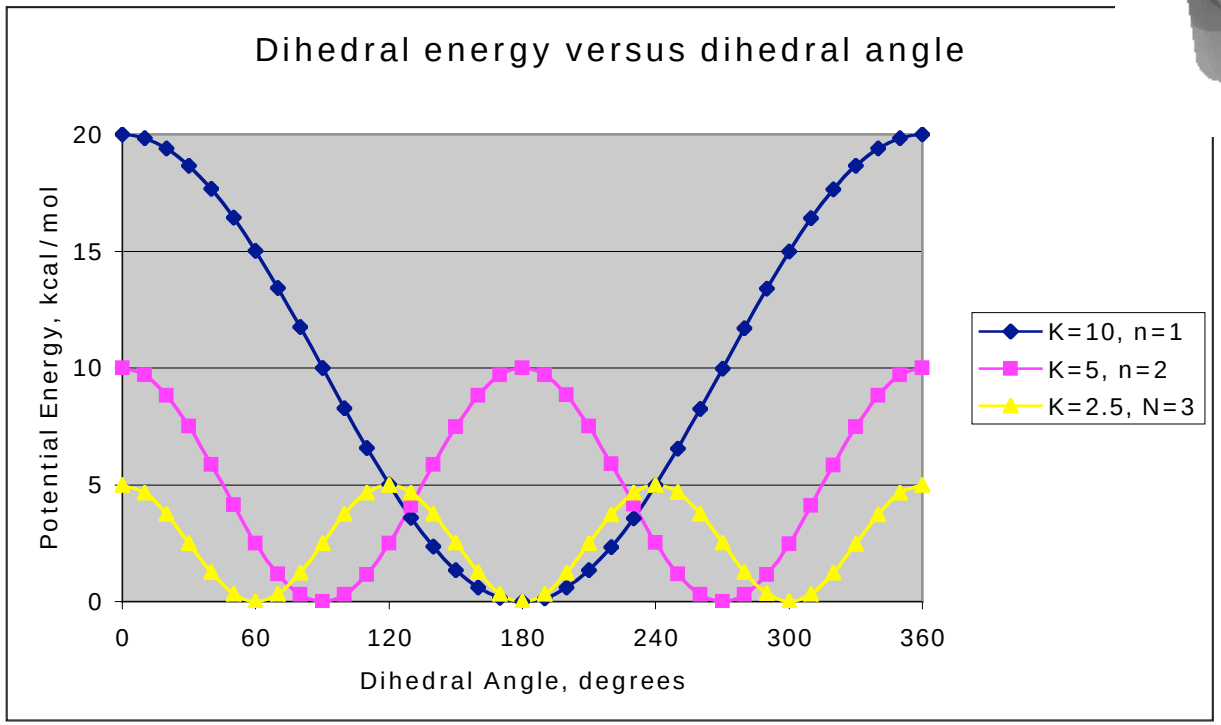


Bond angles and *improper* terms have similar quadratic forms, but with softer spring constants. The force constants can be obtained from vibrational analysis of the molecule (experimentally or theoretically).

Dihedral Potential

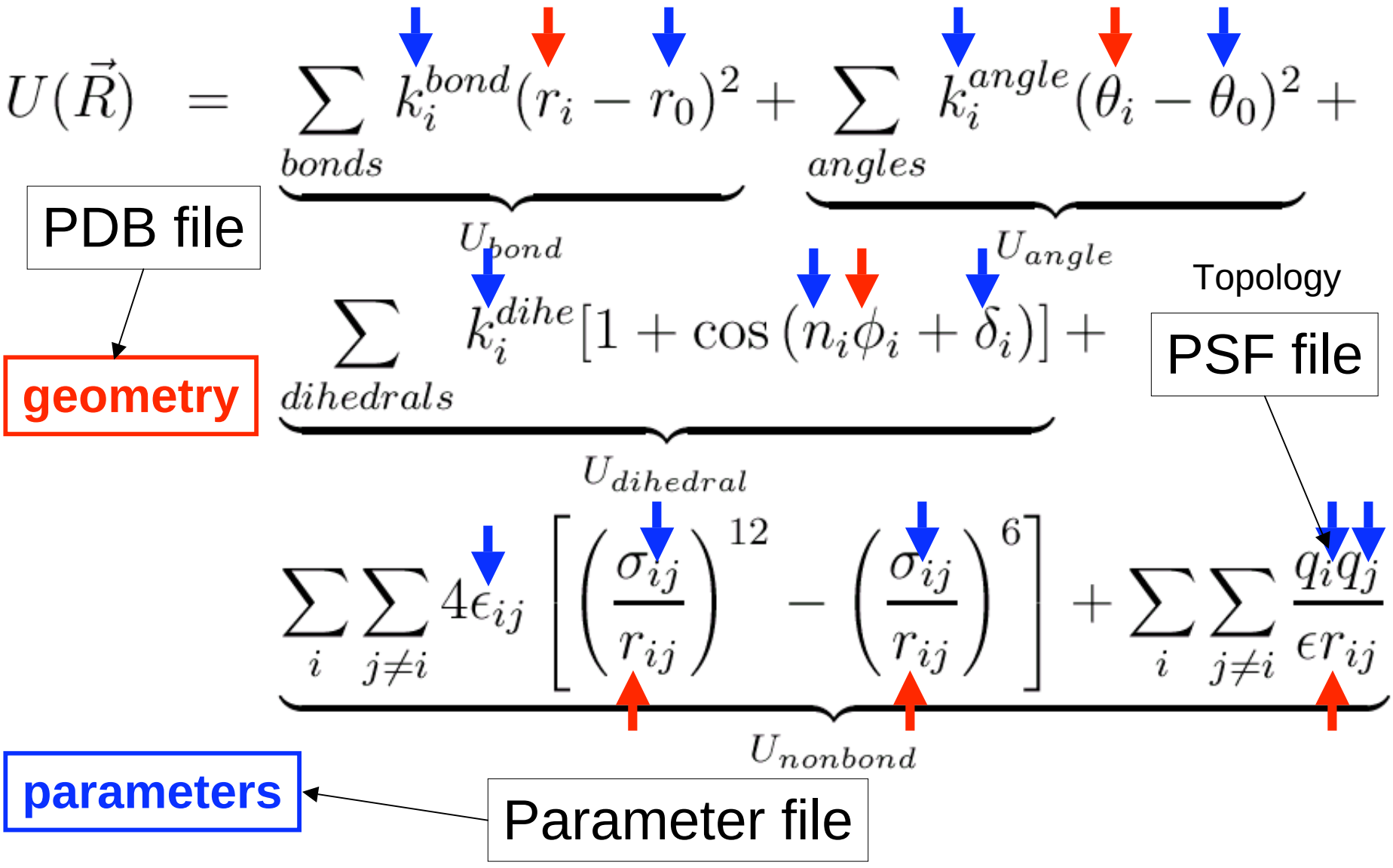
$$V_{dihedral} = K_{\phi}(1+\cos(n\phi - \delta))$$





$\delta = 0^{\circ}$

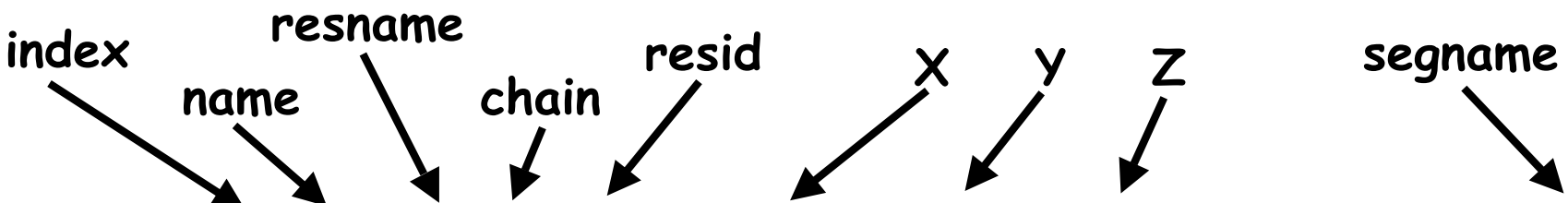
CHARMM Potential Function



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

Structure of a PDB file

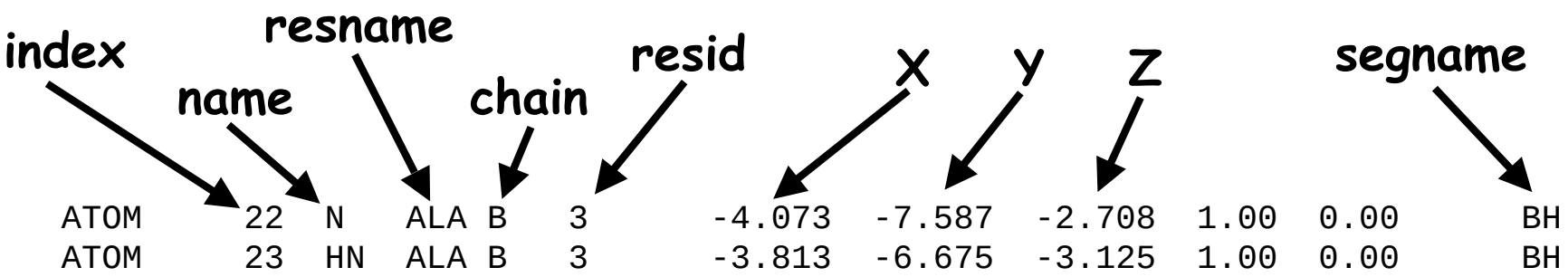



```
ATOM     22  N   ALA B   3      -4.073  -7.587  -2.708  1.00  0.00      BH
ATOM     23  HN  ALA B   3      -3.813  -6.675  -3.125  1.00  0.00      BH
ATOM     24  CA  ALA B   3      -4.615  -7.557  -1.309  1.00  0.00      BH
ATOM     25  HA  ALA B   3      -4.323  -8.453  -0.704  1.00  0.00      BH
ATOM     26  CB  ALA B   3      -4.137  -6.277  -0.676  1.00  0.00      BH
ATOM     27  HB1 ALA B   3      -3.128  -5.950  -0.907  1.00  0.00      BH
ATOM     28  HB2 ALA B   3      -4.724  -5.439  -1.015  1.00  0.00      BH
ATOM     29  HB3 ALA B   3      -4.360  -6.338   0.393  1.00  0.00      BH
ATOM     30  C   ALA B   3      -6.187  -7.538  -1.357  1.00  0.00      BH
ATOM     31  O   ALA B   3      -6.854  -6.553  -1.264  1.00  0.00      BH
ATOM     32  N   ALA B   4      -6.697  -8.715  -1.643  1.00  0.00      BH
ATOM     33  HN  ALA B   4      -6.023  -9.463  -1.751  1.00  0.00      BH
ATOM     34  CA  ALA B   4      -8.105  -9.096  -1.934  1.00  0.00      BH
ATOM     35  HA  ALA B   4      -8.287  -8.878  -3.003  1.00  0.00      BH
ATOM     36  CB  ALA B   4      -8.214 -10.604  -1.704  1.00  0.00      BH
ATOM     37  HB1 ALA B   4      -7.493 -11.205  -2.379  1.00  0.00      BH
ATOM     38  HB2 ALA B   4      -8.016 -10.861  -0.665  1.00  0.00      BH
ATOM     39  HB3 ALA B   4      -9.245 -10.914  -1.986  1.00  0.00      BH
ATOM     40  C   ALA B   4      -9.226  -8.438  -1.091  1.00  0.00      BH
ATOM     41  O   ALA B   4     -10.207  -7.958  -1.667  1.00  0.00      BH
00000000000000000000000000000000000000000000000000000000000000000000000000000
         10        20        30        40        50        60        70
```

>>> It is an ascii, fixed-format file <<<

"No connectivity information"

VMD Atom Selection Commands



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

protein and resname LYS ARG GLU ASP

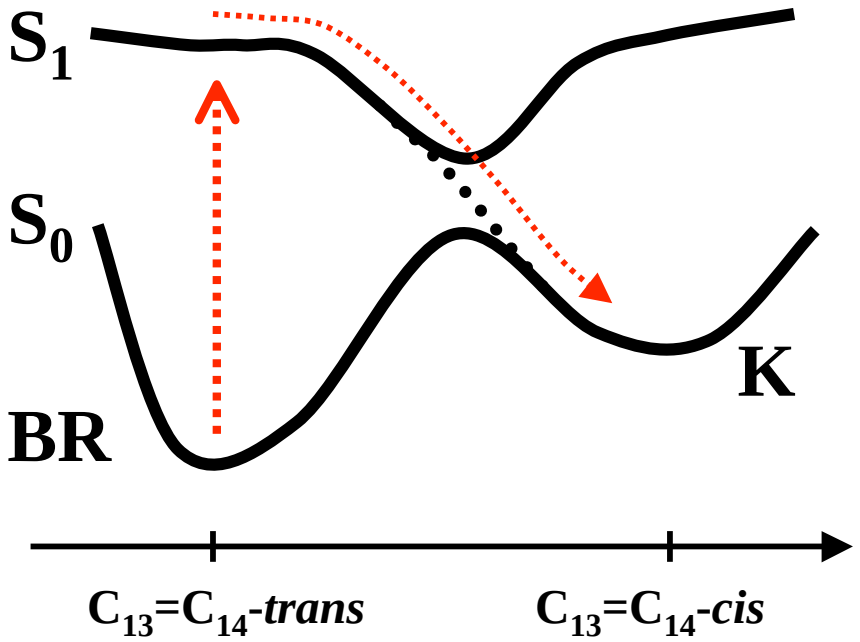
water and within 5 of (protein and resid 62 and name CA)

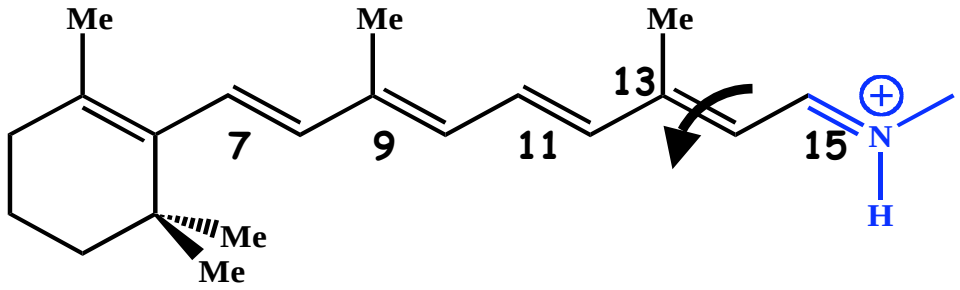
water and within 3 of (protein and name O and z < 10)

Checking file structures

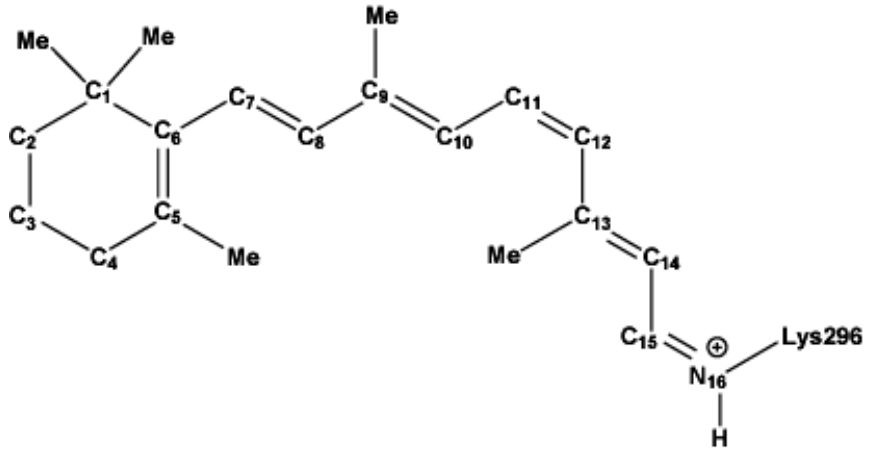
- PDB file
- Topology file
- PSF file
- Parameter file

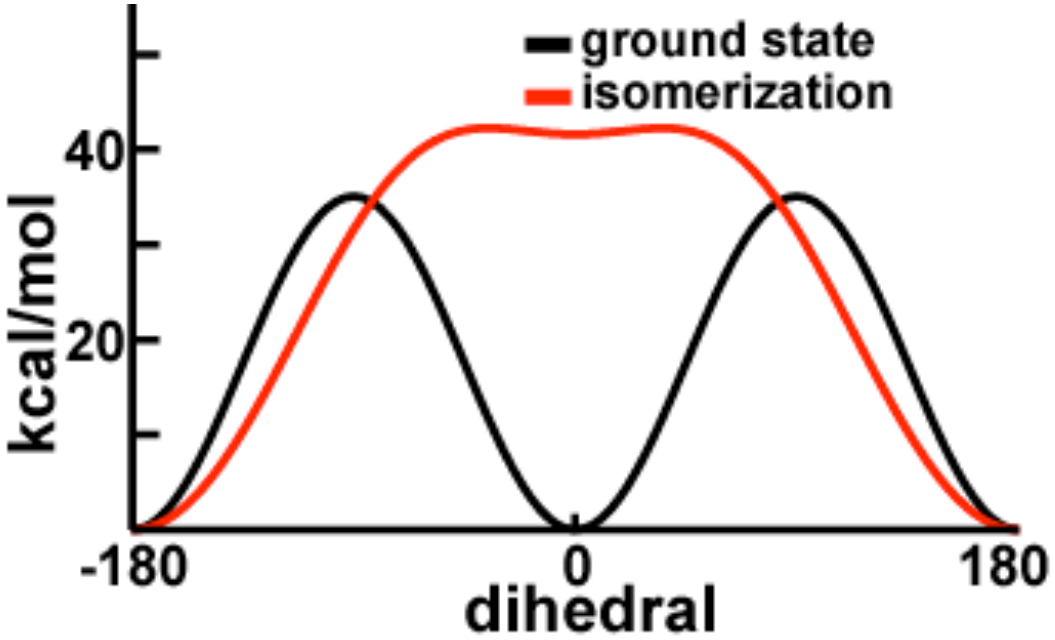
Coupling of electronic excitation and conformational change in bR





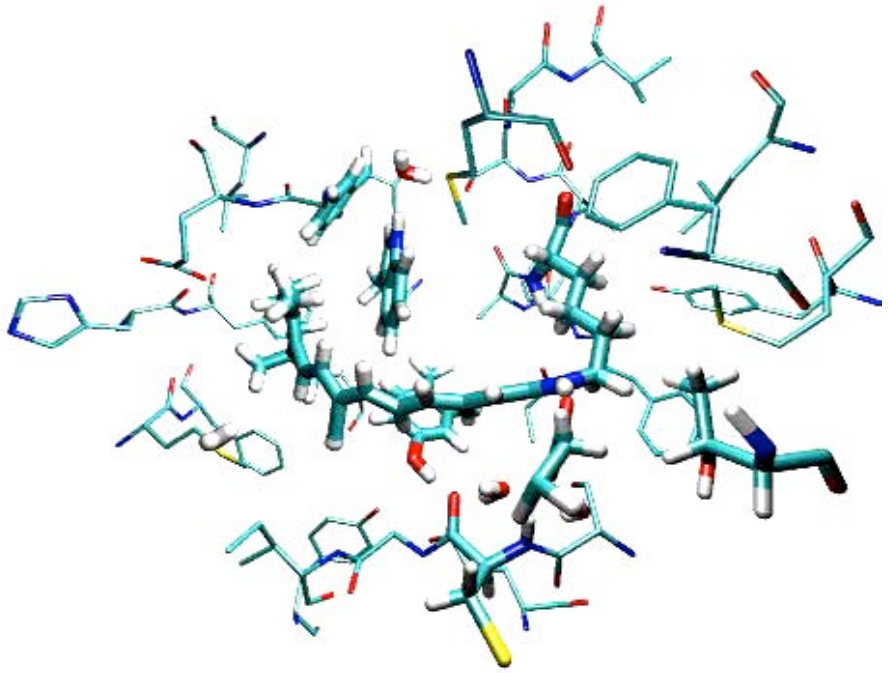
Inducing isomerization

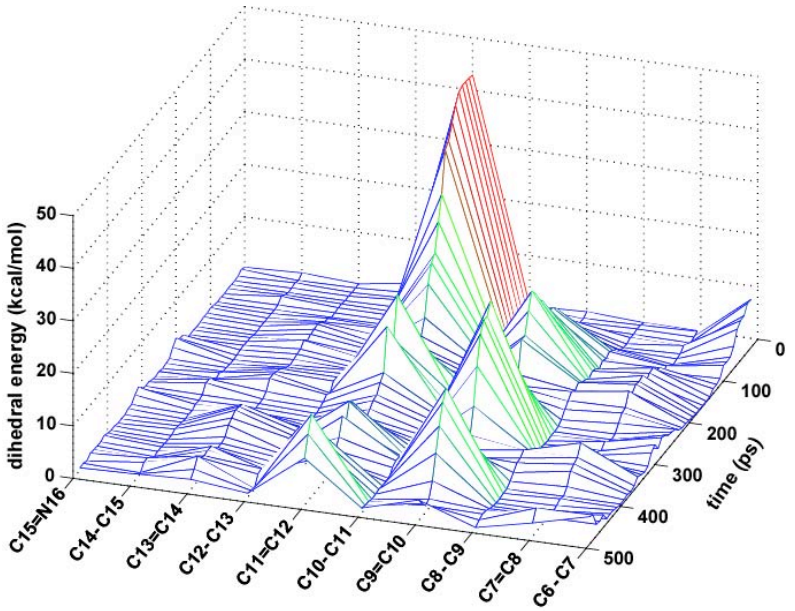




500 nm
~50 kcal/mole

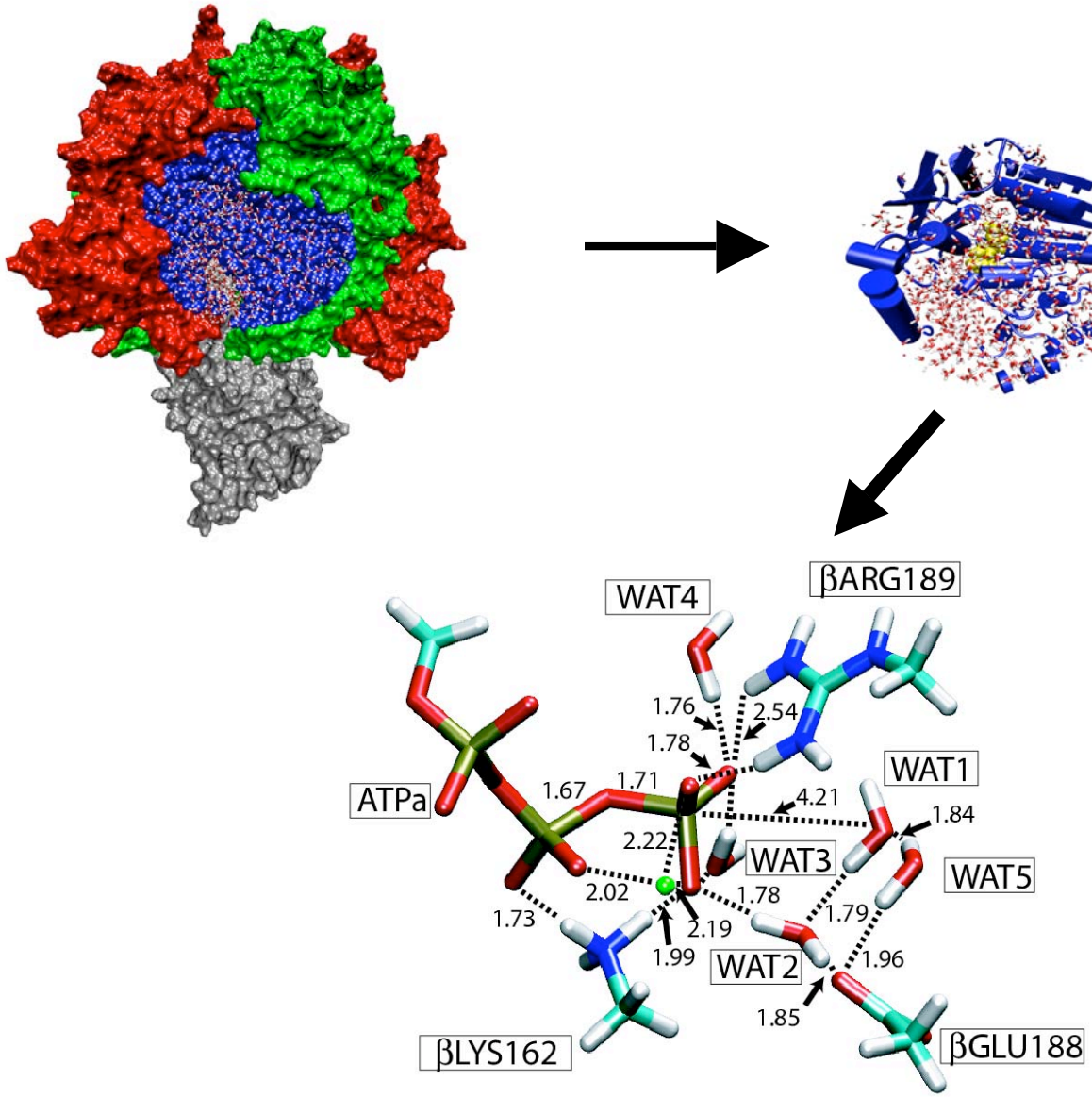
Classical Retinal Isomerization in Rhodopsin

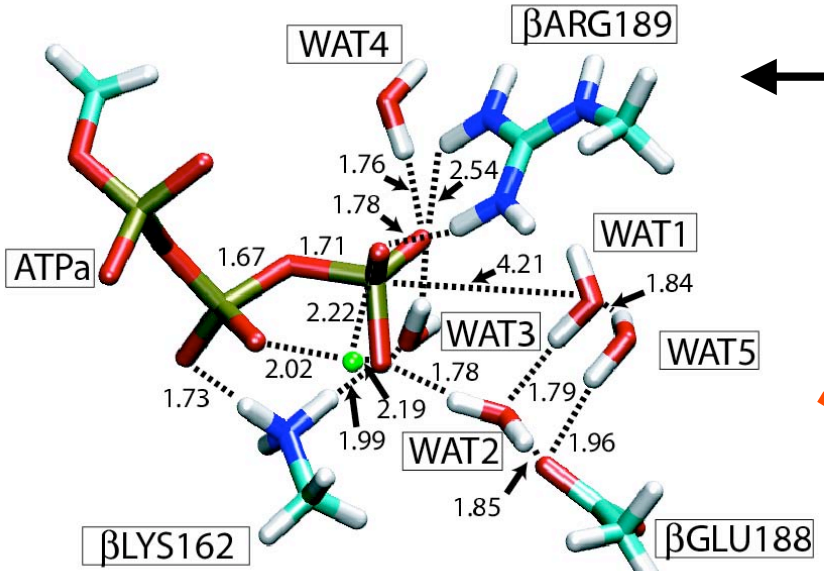




Twist Propagation

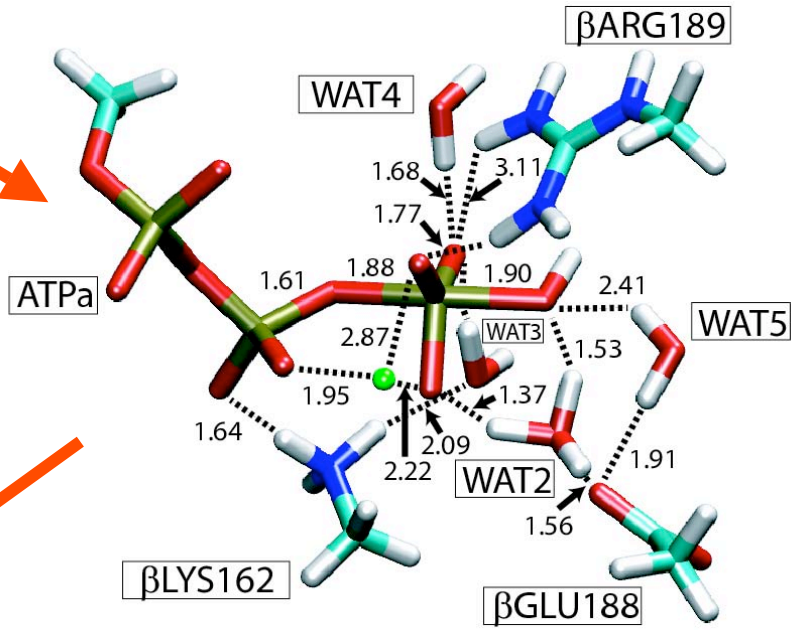
QM/MM calculation of ATP hydrolysis

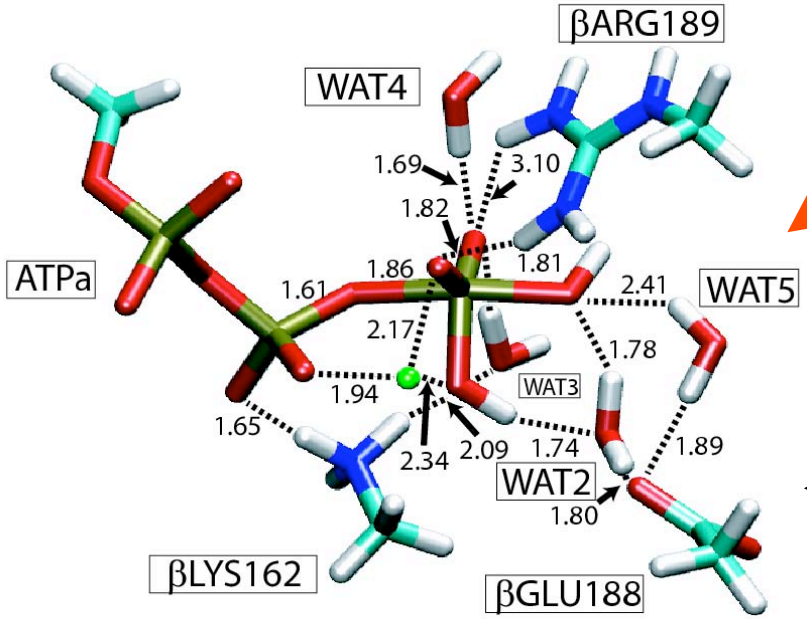




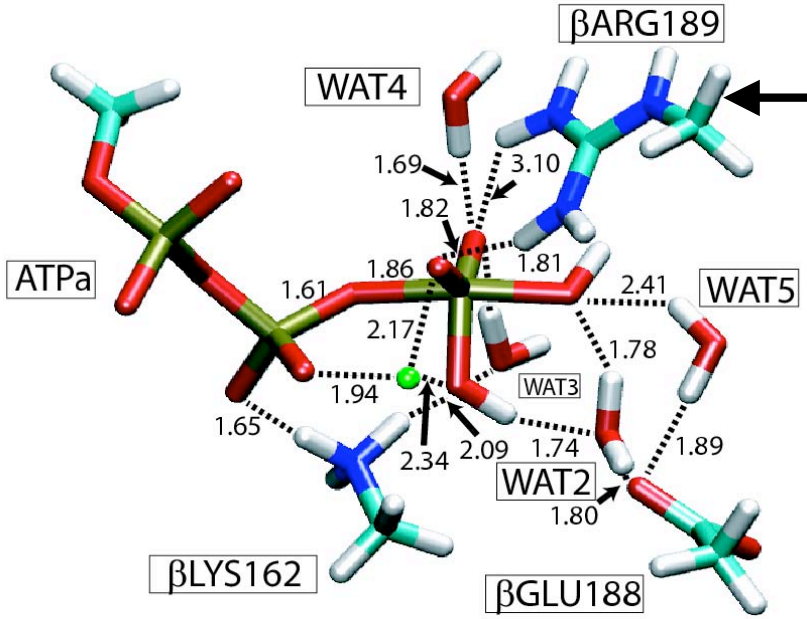
Initial configuration

Transition state



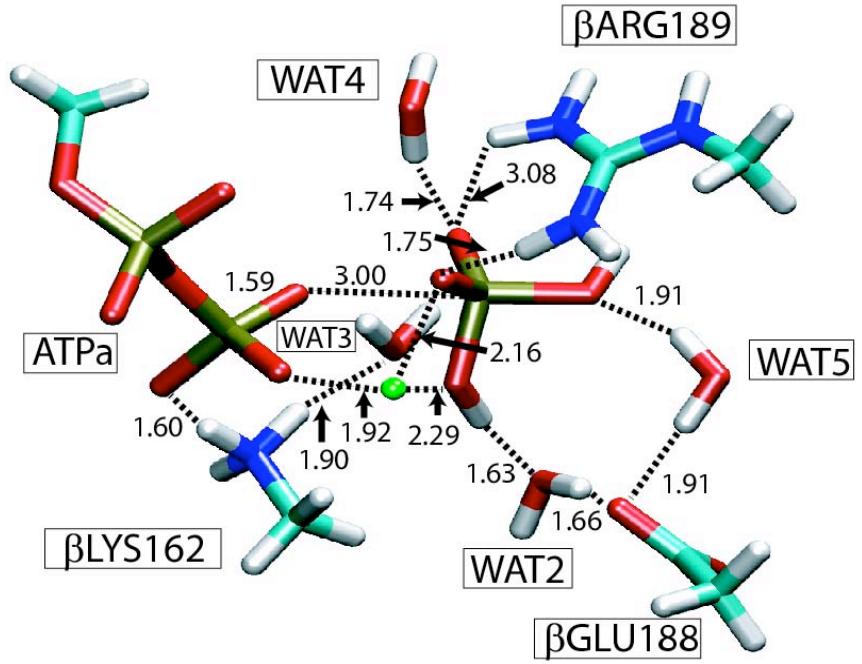


Intermediate structure

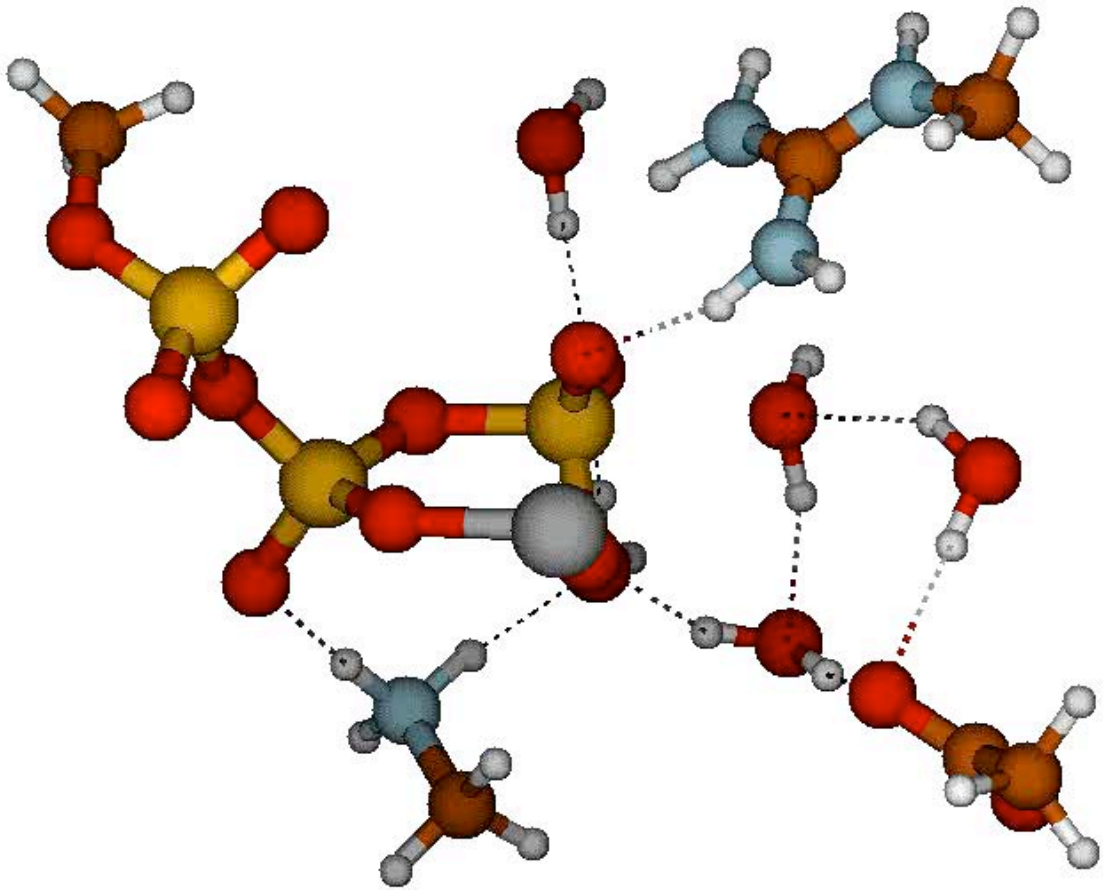


Intermediate structure

Product



ATP hydrolysis in β_{TP}



Coarse grain modeling of lipids

150 particles

9 particles!