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.

The Potential Energy Function

$$U(\vec{R}) = \underbrace{\sum_{bonds} k_i^{bond}(r_i - r_0)^2}_{U_{bond}} + \underbrace{\sum_{angles} k_i^{angle}(\theta_i - \theta_0)^2}_{U_{angle}} +$$

$$\underbrace{\sum_{dihedrals} k_i^{dihe}[1 + \cos(n_i\phi_i + \delta_i)]}_{U_{dihedral}} +$$

$$\underbrace{\sum_i \sum_{j \neq i} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^6\right] + \sum_i \sum_{j \neq i} \frac{q_i q_j}{\epsilon r_{ij}}}_{U_{nonbond}}$$

U_{bond} = oscillations about the equilibrium bond length
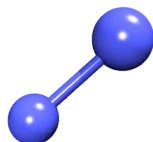U_{angle} = oscillations of 3 atoms about an equilibrium bond angle
$U_{dihedral}$ = torsional rotation of 4 atoms about a central bond
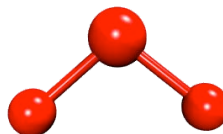$U_{nonbond}$ = non-bonded energy terms (electrostatics and Lenard-Jones)

Energy Terms Described in the CHARMm Force Field

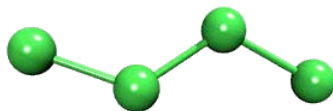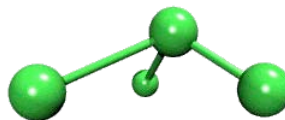Bond   Angle

Dihedral   Improper

Classical Molecular Dynamics

$$r(t + \delta t) = r(t) + v(t)\delta t$$

$$v(t + \delta t) = v(t) + a(t)\delta t$$

$$a(t) = F(t) / m$$

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

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
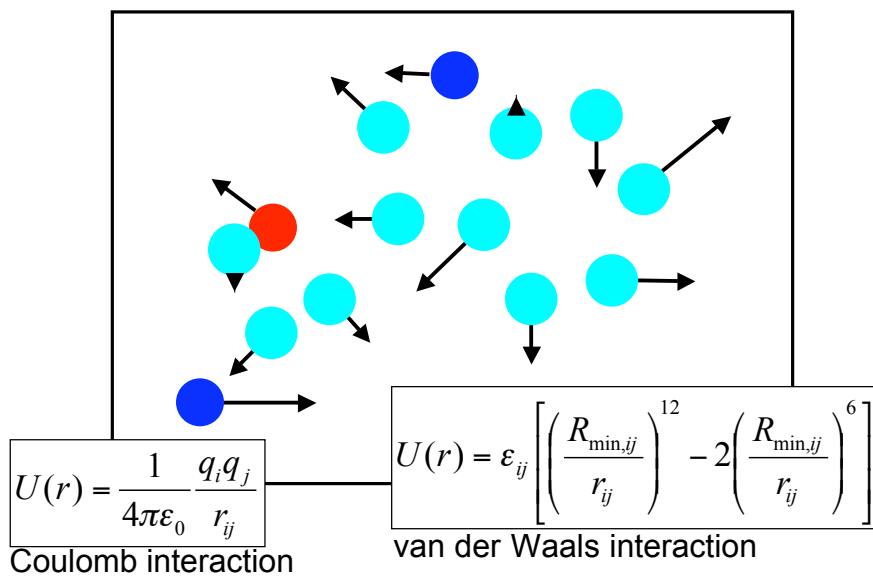
Classical Molecular Dynamics
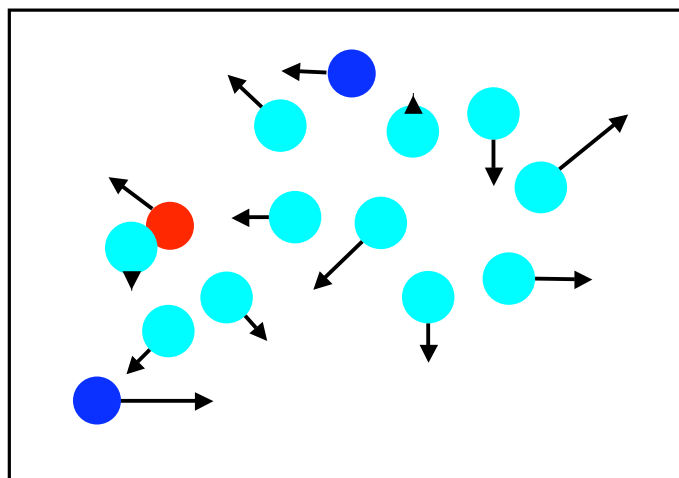
Classical Molecular Dynamics
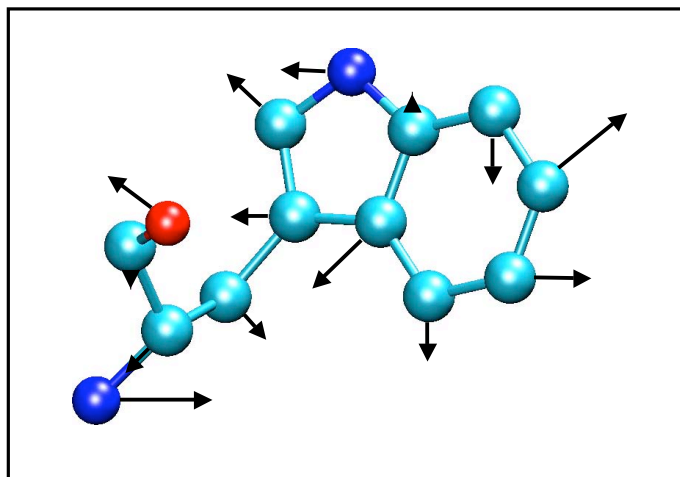
Bond definitions, atom types, atom names, parameters, ….

What is a Force Field?

In molecular dynamics a molecule is described as a series of charged points (atoms) linked by springs (bonds).
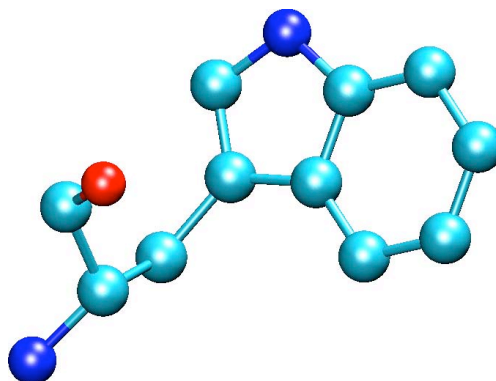
To describe the time evolution of bond lengths, bond angles and torsions, also the non-bonding van der Waals and elecrostatic interactions between atoms, one uses a force field.
The force field is a collection of equations and associated constants designed to reproduce molecular geometry and selected properties of tested structures.

Energy Functions

$$U(\vec{R}) = \underbrace{\sum_{bonds} k_i^{bond}(r_i - r_0)^2}_{U_{bond}} + \underbrace{\sum_{angles} k_i^{angle}(\theta_i - \theta_0)^2}_{U_{angle}} +$$

$$\underbrace{\sum_{dihedrals} k_i^{dihe}[1 + \cos(n_i\phi_i + \delta_i)]}_{U_{dihedral}} +$$

$$\underbrace{\sum_i \sum_{j\neq i} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^6\right] + \sum_i \sum_{j\neq i} \frac{q_i q_j}{\epsilon r_{ij}}}_{U_{nonbond}}$$

U_{bond} = oscillations about the equilibrium bond length
U_{angle} = oscillations of 3 atoms about an equilibrium bond angle
$U_{dihedral}$ = torsional rotation of 4 atoms about a central bond
$U_{nonbond}$ = non-bonded energy terms (electrostatics and Lenard-Jones)

Parameter optimization of the CHARMM Force Field

Based on the protocol established by

Alexander D. MacKerell, Jr , U. Maryland

See references: www.pharmacy.umaryland.edu/faculty/amackere/force_fields.htm

Especially Sanibel Conference 2003, JCC v21, 86,105 (2000)

Interactions between bonded atoms

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

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

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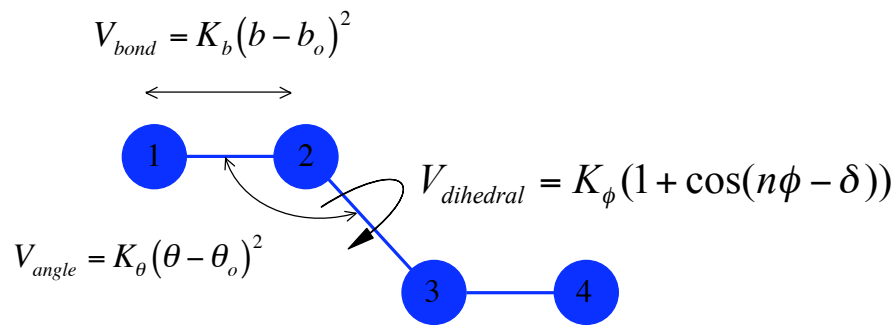
From MacKerell

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

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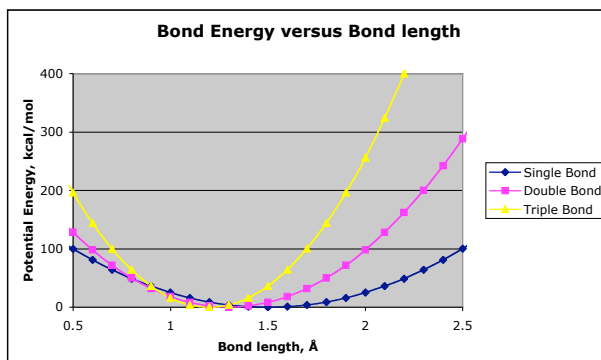
Bond angles and *improper* terms have similar quadratic forms, but with softer spring constants. The force constants can be obtained from vibrational analysis of the molecule (experimentally or theoretically).

Dihedral Potential

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

Dihedral energy versus dihedral angle
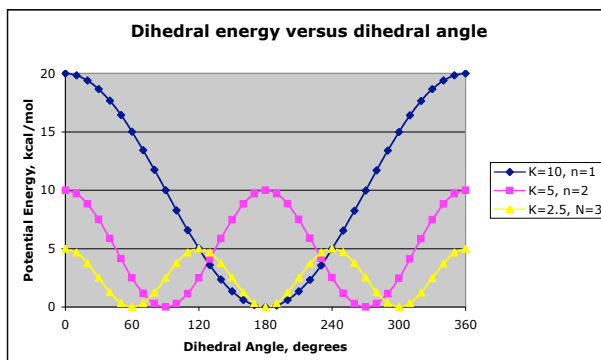
$$d = 0°$$

From MacKerell

Nonbonded Parameters

$$\sum_{nonbonded} \frac{q_i q_j}{4\pi D r_{ij}} + \varepsilon_{ij} \left[\left(\frac{R_{\min,ij}}{r_{ij}} \right)^{12} - 2 \left(\frac{R_{\min,ij}}{r_{ij}} \right)^6 \right]$$

q_i: partial atomic charge
D: dielectric constant
ε: Lennard-Jones (LJ, vdW) well-depth
R_{min}:   LJ radius (R_{min}/2 in CHARMM)
Combining rules (CHARMM, Amber)
$\quad R_{\min\ i,j} = R_{\min\ i} + R_{\min\ j}$
$\quad \varepsilon_{i,j} = SQRT(\varepsilon_i * \varepsilon_j)$

From MacKerell
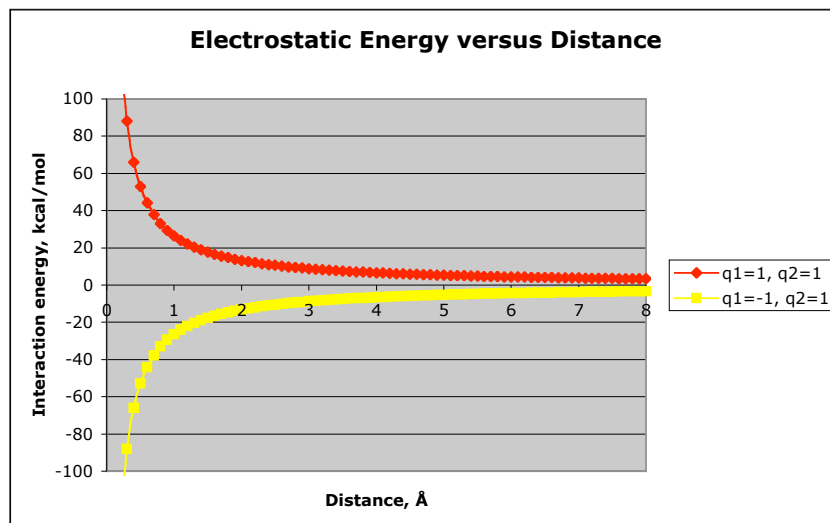
Note that the effect is long range.

From MacKerell

Charge Fitting Strategy

CHARMM- Mulliken*   AMBER(ESP/RESP)

Partial atomic charges
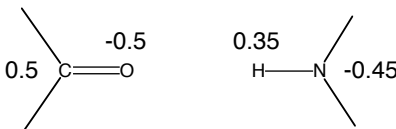
*Modifications based on interactions with TIP3 water

van der Waals interaction

Lennard-Jones Energy versus Distance
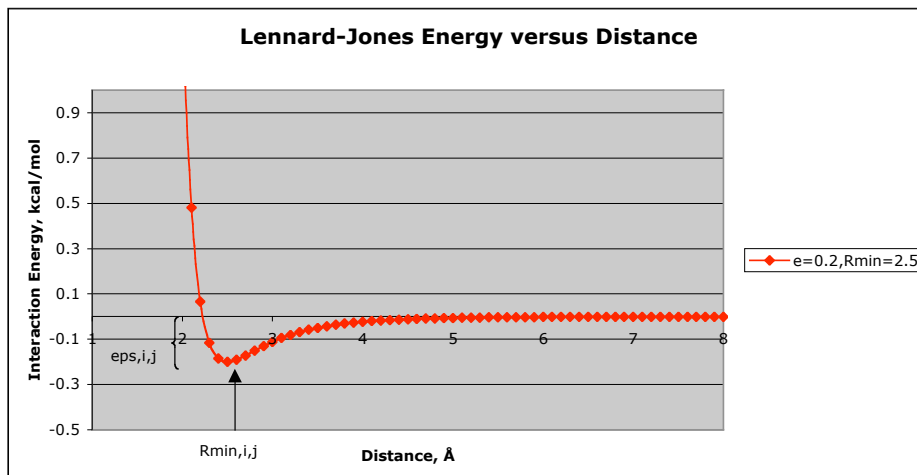
From MacKerell

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

Short range

CHARMM Potential Function

$$U(\vec{R}) = \sum_{bonds} k_i^{bond}(r_i - r_0)^2 + \sum_{angles} k_i^{angle}(\theta_i - \theta_0)^2 +$$

$$\underbrace{\phantom{\sum_{bonds} k_i^{bond}(r_i - r_0)^2}}_{U_{bond}} \quad \underbrace{\phantom{\sum_{angles} k_i^{angle}(\theta_i-\theta_0)^2}}_{U_{angle}}$$

PDB file → geometry

$$\underbrace{\sum_{dihedrals} k_i^{dihe}[1 + \cos(n_i\phi_i + \delta_i)]}_{U_{dihedral}} +$$

Topology

PSF file

$$\underbrace{\sum_i \sum_{j\neq i} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \sum_i \sum_{j\neq i} \frac{q_i q_j}{\epsilon r_{ij}}}_{U_{nonbond}}$$

parameters ← Parameter file

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

```
index      resname          resid      x     y     z          segname
      name            chain

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
00000000000000000000000000000000000000000000000000000000000000000000000000
         10        20        30        40        50        60        70
```

>>> It is an ascii, fixed-format file <<<   "No connectivity information"

VMD Atom Selection Commands

```
index        resname       resid        x      y      z         segname
      name            chain

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

Parameter Optimization Strategies

Check if it has been parameterized by somebody else

Literature

Google

Minimal optimization
By analogy (i.e. direct transfer of known parameters)
Quick, starting point - dihedrals??

Maximal optimization
Time-consuming
Requires appropriate experimental and target data

Choice based on goal of the calculations
Minimal
  database screening
  NMR/X-ray structure determination
Maximal
  free energy calculations, mechanistic studies,
  subtle environmental effects

Roadmap Charmm27 Optimization*

Exp. Data
IR,X-ray,…
Stat.Var.

QM/MP2/6-31G*
Barriers, bonds,…

Initial Geometries Model Compounds?

Partial Atomic Charges

VDW Parameters

HF/6-31G* hydrated groups, TIP3W

Bonds, Angles, Torsions, Impropers

Self-consistent iteration

Condensed Phase MD Simulations

Parameterization Complete
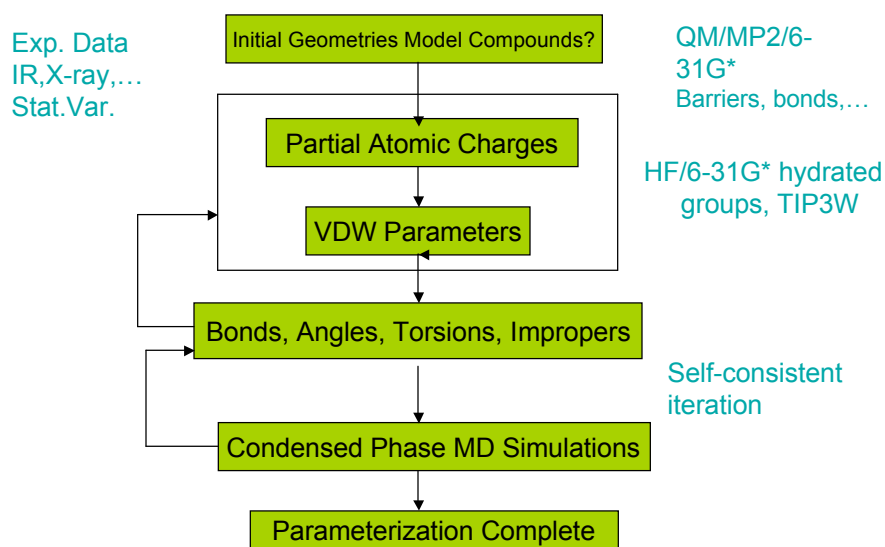
*based on MacKerell, JCC v21, 86,105 (2000)

Getting Started

- Identify previously parameterized compounds
- Access topology information – assign atom types, connectivity, and charges – annotate changes

CHARMM topology (parameter files)

top_all22_model.inp (par_all22_prot.inp)
top_all22_prot.inp (par_all22_prot.inp)
top_all22_sugar.inp (par_all22_sugar.inp)
top_all27_lipid.rtf (par_all27_lipid.prm)
top_all27_na.rtf (par_all27_na.prm)
top_all27_na_lipid.rtf (par_all27_na_lipid.prm)
top_all27_prot_lipid.rtf (par_all27_prot_lipid.prm)
top_all27_prot_na.rtf (par_all27_prot_na.prm)
toph19.inp (param19.inp)

NA and lipid force fields have new LJ parameters for the alkanes, representing increased optimization of the protein alkane parameters. Tests have shown that these are compatible (e.g. in protein-nucleic acid simulations). For new systems is suggested that the new LJ parameters be used. Note that only the LJ parameters were changed; the internal parameters are identical

www.pharmacy.umaryland.edu/faculty/amackere/force_fields.htm

Break Desired Compound into 3 Smaller Ones

A   B   C

Indole   Hydrazine   Phenol
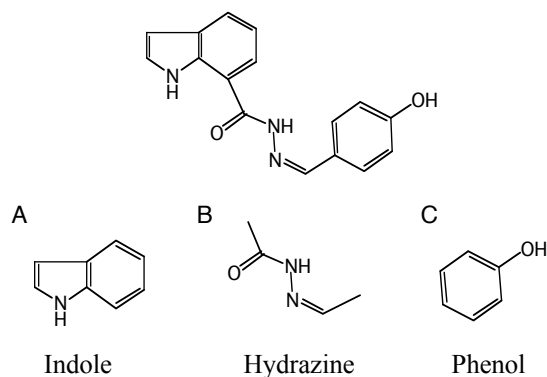
When creating a covalent link between model compounds move the charge on the deleted H into the carbon to maintain integer charge (i.e. methyl (q_C=-0.27, q_H=0.09) to methylene (q_C=-0.18, q_H=0.09)

From MacKerell

From top_all22_model.inp

```
RESI PHEN          0.00    ! phenol, adm jr.
GROUP
ATOM CG    CA    -0.115   !
ATOM HG    HP     0.115   !            HD1   HE1
GROUP                     !             |     |
ATOM CD1   CA    -0.115   !           CD1--CE1
ATOM HD1   HP     0.115   !           //      \\
GROUP                     !      HG--CG        CZ--OH
ATOM CD2   CA    -0.115   !            \     /     \
ATOM HD2   HP     0.115   !           CD2==CE2     HH
GROUP                     !             |     |
ATOM CE1   CA    -0.115   !           HD2   HE2
ATOM HE1   HP     0.115
GROUP
ATOM CE2   CA    -0.115
ATOM HE2   HP     0.115
GROUP
ATOM CZ    CA     0.110
ATOM OH    OH1   -0.540
ATOM HH    H      0.430
BOND CD2 CG CE1 CD1 CZ CE2 CG HG CD1 HD1
BOND CD2 HD2 CE1 HE1 CE2 HE2 CZ OH OH HH
DOUBLE CD1 CG CE2 CD2  CZ CE1
```

From MacKerell

Top_all22_model.inp contains all protein model compounds. Lipid, nucleic acid and carbohydate model compounds are in the full topology files.

HG will ultimately be deleted. Therefore, move HG (hydrogen) charge into CG, such that the CG charge becomes 0.00 in the final compound.

Use remaining charges/atom types without any changes.

Do the same with indole

Comparison of atom names (upper) and atom types (lower)
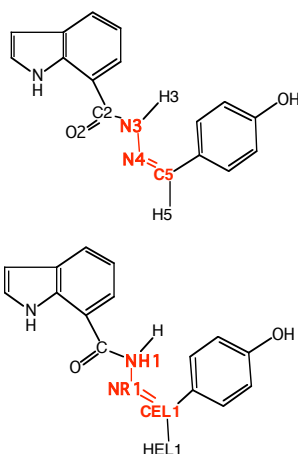
From MacKerell

Creation of topology for central model compound

```
RESI  Mod1 ! Model compound 1
Group
ATOM C1   CT3   -0.27
ATOM H11  HA3    0.09
ATOM H12  HA3    0.09
ATOM H13  HA3    0.09
GROUP
ATOM C2   C      0.51
ATOM O2   O     -0.51
GROUP
ATOM N3   NH1   -0.47
ATOM H3   H      0.31
ATOM N4   NR1    0.16    !new atom
ATOM C5   CEL1  -0.15
ATOM H51  HEL1   0.15
ATOM C6   CT3   -0.27
ATOM H61  HA     0.09
ATOM H62  HA     0.09
ATOM H63  HA     0.09
BOND C1 H11 C1 H12 C1 H13 C1 C2 C2 O2 C2 N3 N3
H3
BOND N3 N4 C5 H51 C5 C6 C6 H61 C6 H62 C6 H63
DOUBLE N4 C5 (DOUBLE only required for MMFF)
```
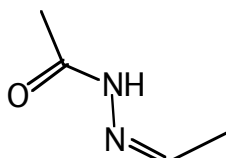
Start with alanine dipeptide. Note use of new aliphatic LJ parameters and, importantly, atom types.

NR1 from histidine unprotonated ring nitrogen. Charge (very bad) initially set to yield unit charge for the group.

Note use of large group to allow flexibility in charge optimization.

From MacKerell

```
RESI CYG 0.00
GROUP
ATOM N    NH1   -0.47 !        |
ATOM HN   H      0.31 ! HN-N
ATOM CA   CT1    0.07 !        |        HB1
ATOM HA   HB     0.09 !        |    |
GROUP                 ! HA-CA--CB--SG
ATOM CB   CT2   -0.11 !        |    |    |
ATOM HB1  HA     0.09 !        |    HB2 |
ATOM HB2  HA     0.09 ! O=C         |
ATOM SG   S     -0.07 !        |
!ATOM HG1 HS      0.16 !
GROUP                 !
ATOM CDG  CC     0.55 !
ATOM OE1  O     -0.55 !
GROUP                 !        HN2G
ATOM CGG  CT2   -0.18 !         \
ATOM HG1G HA     0.09 ! HN1G-NG    HB1G HG1G\
ATOM HG2G HA     0.09 !    |    |    |    |
GROUP                 ! HAG-CAG--CBG--CGG--CDG=OE1
ATOM CBG  CT2   -0.18 !    |    |    |
ATOM HB1G HA     0.09 !    |    HB2G HG2G
ATOM HB2G HA     0.09 ! O1G=CG
GROUP                 !    |
ATOM CG   CD     0.75 !    O2G-HO2G
ATOM O1G  OB    -0.55
ATOM O2G  OH1   -0.61
ATOM HO2G H      0.44
ATOM CAG  CT1   -0.12
ATOM HAG  HB     0.09
ATOM NG   NH3   -0.62
ATOM HN1G HC     0.31
ATOM HN2G HC     0.31
GROUP
ATOM C    C      0.51
ATOM O    O     -0.51
```

Protein-backbone
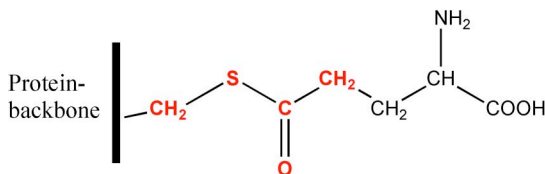
HG1 deleted from CYS and the charge was moved to SG (-0.23 +0.16=0.07) so that the SG charge becomes 0.07 in final compound and the group remains neutral
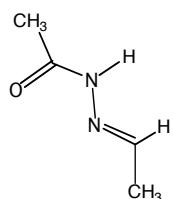
Changes annotated!

Partial Atomic Charge Determination
Method Dependent Choices

1. RESP: HF/6-31G overestimates dipole
   moments (AMBER)

2. Interaction based optimization (CHARMM)

For a particular force field do NOT change the
QM level of theory. This is necessary to maintain
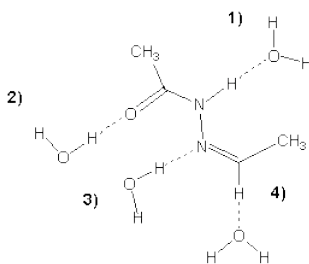consistency with the remainder of the force field.

From MacKerell

Starting charges??
Mulliken population analysis
Analogy comparison

peptide bond
methyl
imidazole (N-N=C)?

Final charges (methyl, vary q_C to maintain integer charge, $q_H = 0.09$)
  interactions with water (HF/6-31G*, monohydrates!)

From MacKerell

Model compound 1-water interaction energies/geometries

	Interaction Energies (kcal/mole)			Interaction Distances (A)		
	Ab initio	Analogy	Optimized	*Ab initio*	Analogy	Optimized
1) O2...HOH	-6.12	-6.56	-6.04	2.06	1.76	1.78
2) N3-H..OHH	-7.27	-7.19	-7.19	2.12	1.91	1.89
3) N4...HOH	-5.22	-1.16	-5.30	2.33	2.30	2.06
4) C5-H..OHH	-3.86	-3.04	-3.69	2.46	2.51	2.44
Energetic statistical analysis						
Ave. Difference		1.13	0.06			
RMS Difference		1.75	0.09			
Dipole Moments (debeye)						
	5.69	4.89	6.00			

Ab initio interaction energies scaled by 1.16.
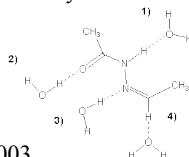
MacKerell: Sanibel Conference 2003

Comparison of analogy and optimized charges

Name	Type	Analogy	Optimized
C1	CT3	-0.27	-0.27
H11	HA3	0.09	0.09
H12	HA3	0.09	0.09
H13	HA3	0.09	0.09
C2	C	0.51	0.58
O2	O	-0.51	-0.50
N3	NH1	-0.47	-0.32
H3	H	0.31	0.33
N4	NR1	0.16	-0.31
C5	CEL1	-0.15	-0.25
H51	HEL1	0.15	0.29
C6	CT3	-0.27	-0.09
H61	HA	0.09	0.09
H62	HA	0.09	0.09
H63	HA	0.09	0.09
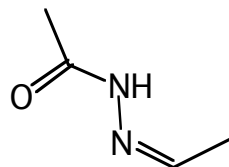
Summary of Parameterization

1. LJ (VDW) parameters – normally direct transfer from available parameters is adequate, but should be tested by comparison to heats of vaporization, density, partial molar volumes, crystal simulations,.... (MacKerell JCC 2002).

2. Bond, angle, dihedral, UB and improper force constants

Vibrational spectra- Frequencies
Conformational Energetics -
      Relative energies
      Potential energy surfaces

Vibrations are generally used to optimize the bond, angle, UB and improper FCs while conformational energies are used for the dihedral FCs.

Vibrational Spectra of Model Compound 1 from MP2/6-31G* QM calculations

#	Freq	Assign	%	Assign	%	Assign	%	#	Freq	Assign	%	Assign	%
1	62	tC2N	64	tN3N	46			21	1446	rNH	35		
2	133	tC1H3	50	tN3N	18	tC2N	17	22	1447	rC5H	47	sC-N	18
3	148	tC1H3	46	tC6H3	25			23	1527	dCH3	77		
4	154	dC2NN	44	dN3NC	28	dN4CC	16	24	1532	dCH3	88		
5	205	tC6H3	59	tN4C	22	tN3N	21	25	1599	dCH3a'	50	dCH3a	17
6	333	tN4C	73	tC2N	22			26	1610	dCH3a	71	dCH3a'	24
7	361	dC1CN	45	dN4CC	21	dN3NC	16	27	1612	dCH3a'	30		
8	446	rC=O	32	dN4CC	20			28	1613	dCH3a	70	dCH3a'	23
9	568	wNH	77					29	1622	dCH3a'	57	dCH3a	19
10	586	dC1CN	21	dC2NN	20	rC=O	18	30	1782	sN=C	71		
11	618	wC=O	83	wNH	28	tC2N	-26	31	1901	sC=O	78		
12	649	rC=O	27	dN4CC	19			32	3250	sCH3	76	sC5-H	21
13	922	sC1-C	62					33	3258	sC5-H	78	sCH3	21
14	940	wC5H	80					34	3280	sCH3	99		
15	1031	rCH3'	33	sC5-C	31			35	3330	sCH3a	75	sCH3a'	25
16	1114	rCH3	66					36	3372	sCH3a'	100		
17	1139	rCH3'	76	wC=O	20			37	3377	sCH3a'	73	sCH3a	24
18	1157	rCH3	61	wC5H	21			38	3403	sCH3a	99		
19	1234	sC5-C	33	sN-N	32			39	3688	sN-H	100		
20	1269	sN-N	36	rCH3'	18								

Frequencies in cm^{-1}. Assignments and % are the modes and there respective percents contributing to each vibration.
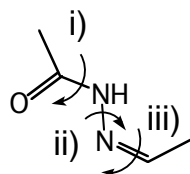
From MacKerell

Dihedral optimization based on QM potential
energy surfaces (HF/6-31G* or MP2/6-31G*).
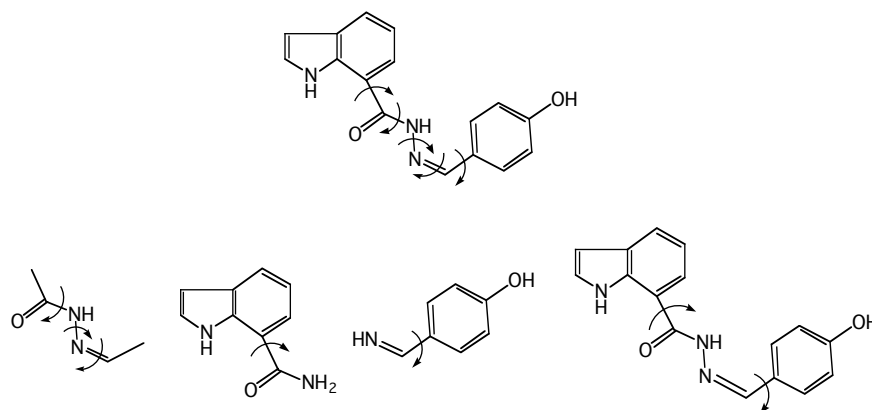
From MacKerell

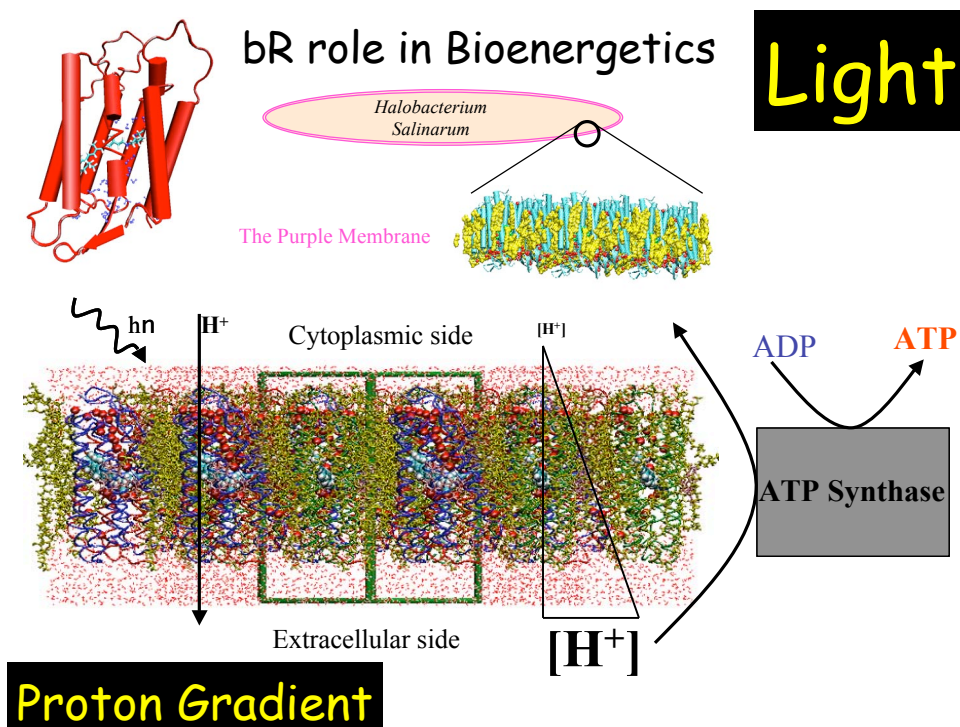Potential energy surfaces on
compounds with multiple
rotatable bonds

1) Full geometry optimization
2) Constrain n-1 dihedrals to minimum energy values or trans
   conformation
3) Sample selected dihedral surface
4) Repeat for all rotatable bonds dihedrals
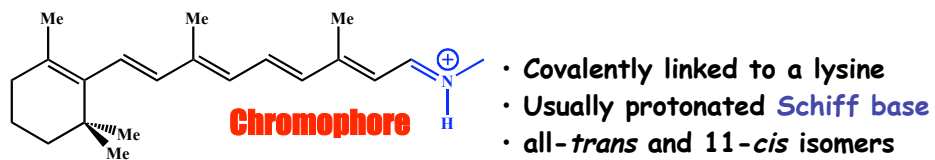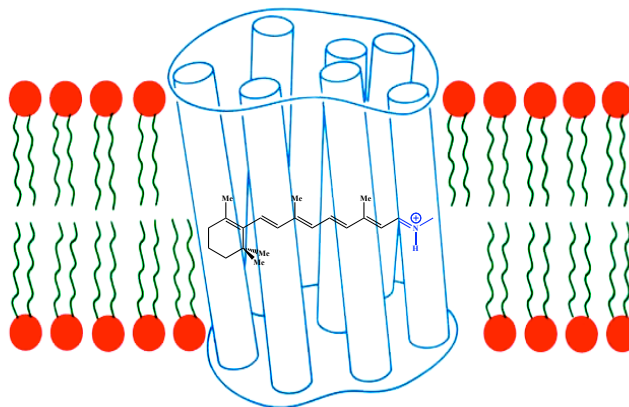5) Repeat 2-5 using alternate minima if deemed appropriate
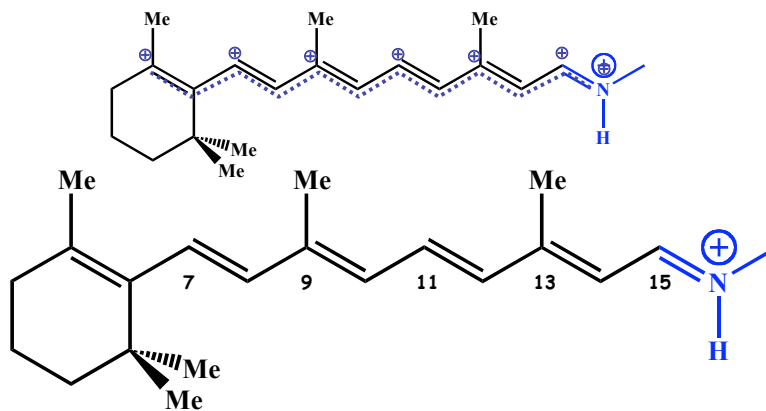
From MacKerell

QM development of force field parameters for retinal

Used for rhodopsin and bacteriorhodopsin simulations

Retinal Proteins -- Rhodopsins

Chromophore

- Covalently linked to a lysine
- Usually protonated Schiff base
- all-*trans* and 11-*cis* isomers

Unconventioanl chemistry

Photocycle

Photo-induced

5 ms → BR₅₇₀

BR_{570}

3 ps

O_{630} K_{610}

5 ms   1 ms

N_{560} L_{550}

5 ms M_{410} 40 ms
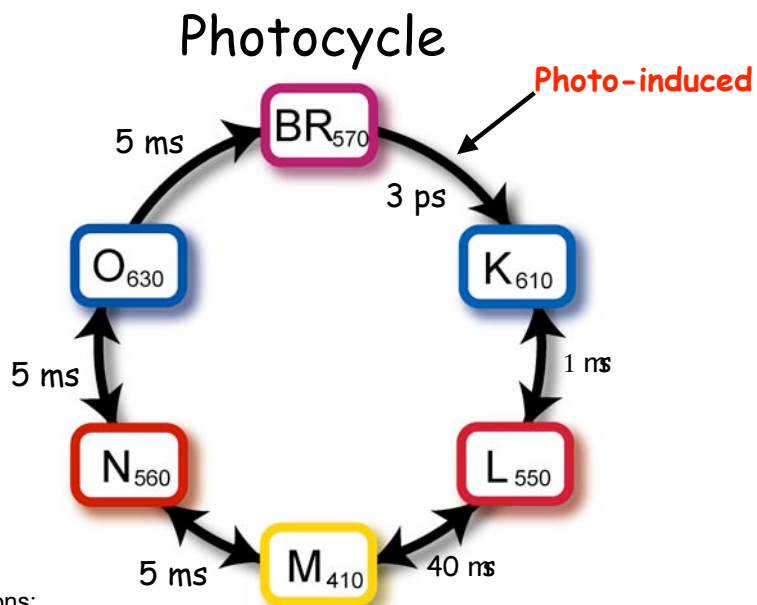
Two questions:
    The structure of the ground state
    What happens after the isomerization

Coupling of electronic excitation and conformational change in bR

S_1

S_0

BR

K

$C_{13}=C_{14}$-*trans* $C_{13}=C_{14}$-*cis*
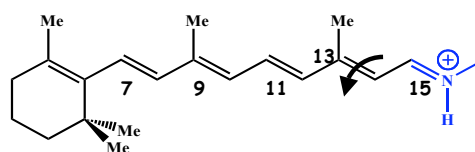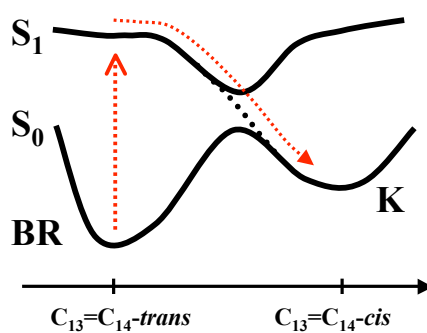
What is the structure of retinal in its binding pocket?
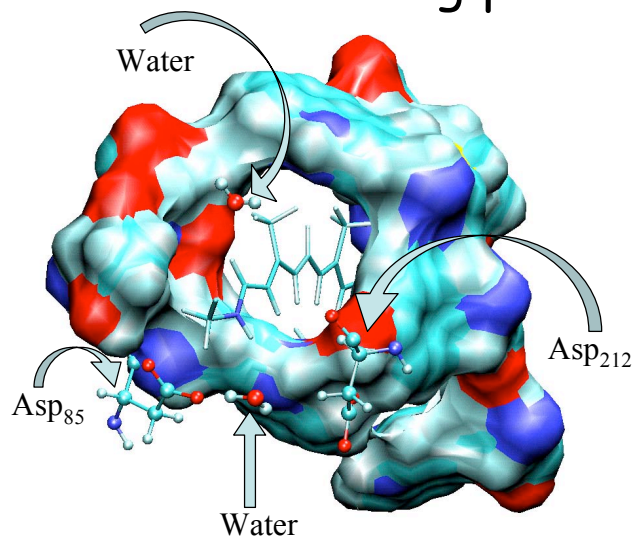
Isomerization Barriers in retinal

DFT/6-31G**
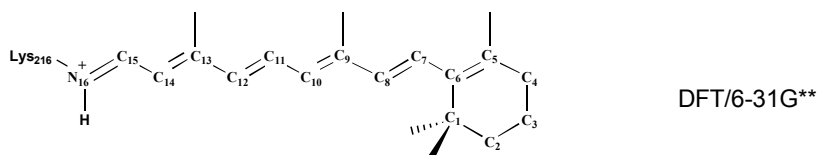
TABLE 2 The parameter set B used for the torsional
potentials of the main polyene chain of the retinal Schiff base

ϕ_i	k_i (kcal/mol)*	n_i	δ_i (deg)
$C_5{=}C_6{-}C_7{=}C_8$	11.24	2.0	180.00
$C_6{-}C_7{=}C_8{-}C_9$	39.98	2.0	180.00
$C_7{=}C_8{-}C_9{=}C_{10}$	17.03	2.0	180.00
$C_8{-}C_9{=}C_{10}{-}C_{11}$	37.28	2.0	180.00
$C_9{=}C_{10}{-}C_{11}{=}C_{12}$	22.50	2.0	180.00
$C_{10}{-}C_{11}{=}C_{12}{-}C_{13}$	35.08	2.0	180.00
$C_{11}{=}C_{12}{-}C_{13}{=}C_{14}$	28.30	2.0	180.00
$C_{12}{-}C_{13}{=}C_{14}{-}C_{15}$	29.46	2.0	180.00
$C_{13}{=}C_{14}{-}C_{15}{=}N_{16}$	30.43	2.0	180.00
$C_{14}{-}C_{15}{=}N_{16}{-}C_\varepsilon$	28.76	2.0	180.00

Tajkhorshid et al., 1999.

*$E_i^{\text{dihedral}} = (1/2)k_i[1 + \cos(n_i\varphi_i - \delta_i)]$.

A twisted chromophore in bR?
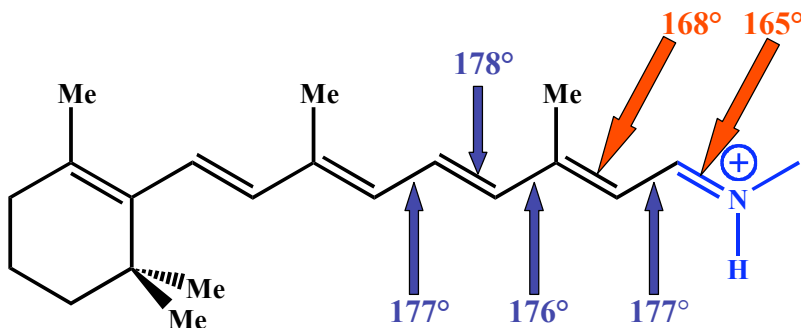
- A twisted chromophore is also experimentally reported.
- X-ray structures of bR report the twisted form of chromophore
- The twist is found around the terminal double bonds
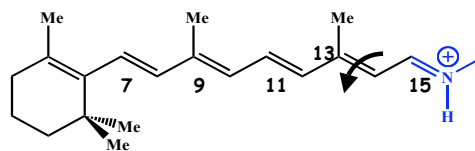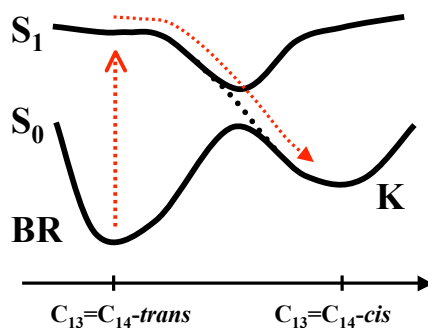- It may influence pK_a of the chromophore
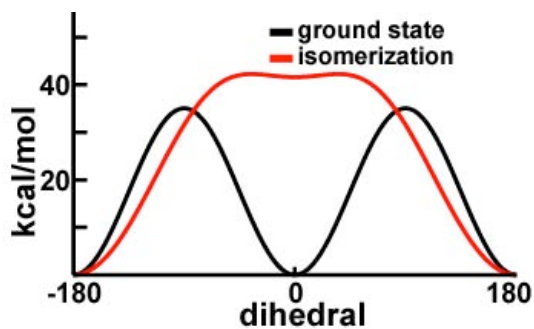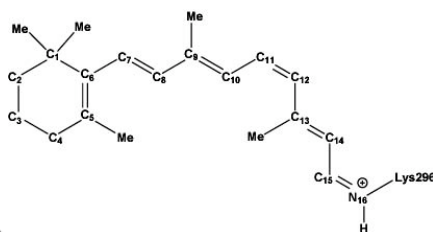
Ab Initio QM/MM Excited State MD Simulation
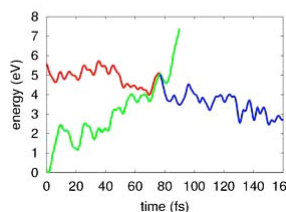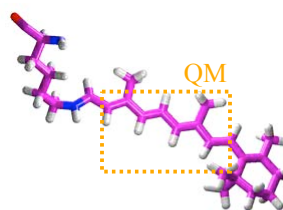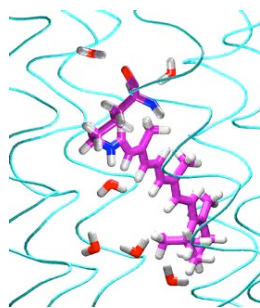
Quantum mechanical (QM) treatment of the chromophore, and force field (MM) treatment of the embedding protein

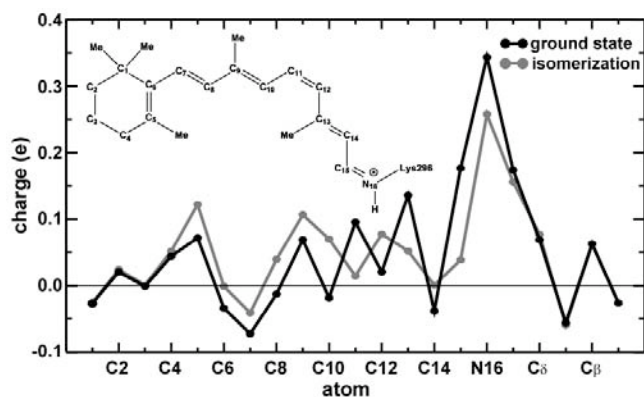# Coupling of electronic excitation and conformational change in bR
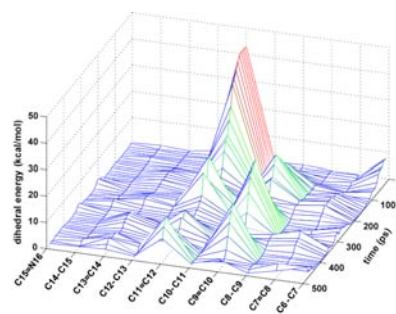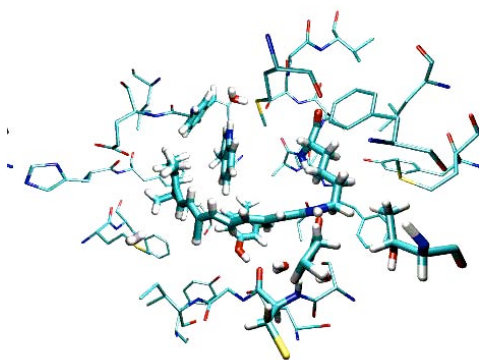

Inducing isomerization

500 nm
~50 kcal/mole

Retinal Charge Distribution

QM/MM derived partial atomic charges
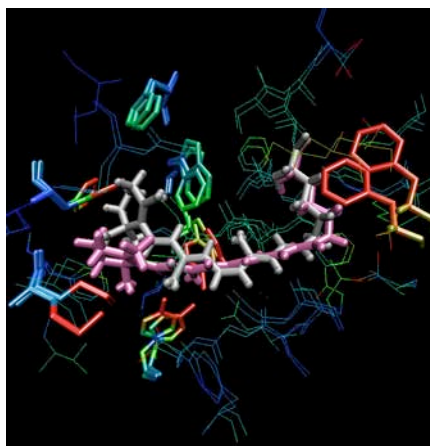
Classical Retinal
Isomerization in Rhodopsin
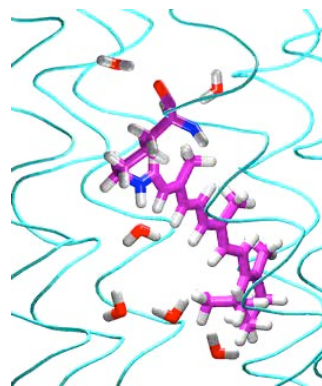

Twist Propagation

11-*cis*-Retinal   Light →   All-*trans*-retinal   5 Å
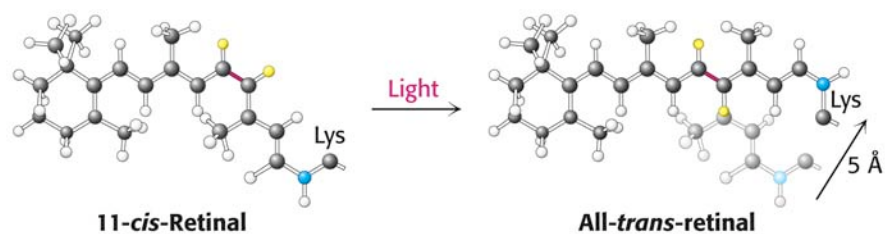
Text book figures not quite right!

Rhodopsin   Bacteriorhodopsin

Isomerization 11-cis → all-trans   Isomerization: all-trans → 13-cis

QM/MM calculations

Lys216-RET

MM   QM

dummy atom

Asp85, 212

MM   QM

$$\hat{H} = \sum_i \frac{1}{2} p_i^2 + \sum_i \sum_A \frac{Z_A}{r_{iA}} + \sum_{i>j} \frac{1}{r_{ij}} + \sum_{A>B} \frac{Z_A Z_B}{r_{AB}}$$

$$+ \sum_i \sum_p \frac{q_p}{r_{ip}} + \sum_A \sum_p \frac{Z_A q_p}{r_{Ap}}$$

$$+ V_{QM-MM}^{MM} + V_{MM}^{MM}$$

QM/MM calculation of ATP hydrolysis

WAT4   βARG189

ATPa

WAT1

WAT3   WAT5

WAT2

βLYS162   βGLU188

Initial configuration

Transition state

Intermediate structure

Intermediate structure

Product
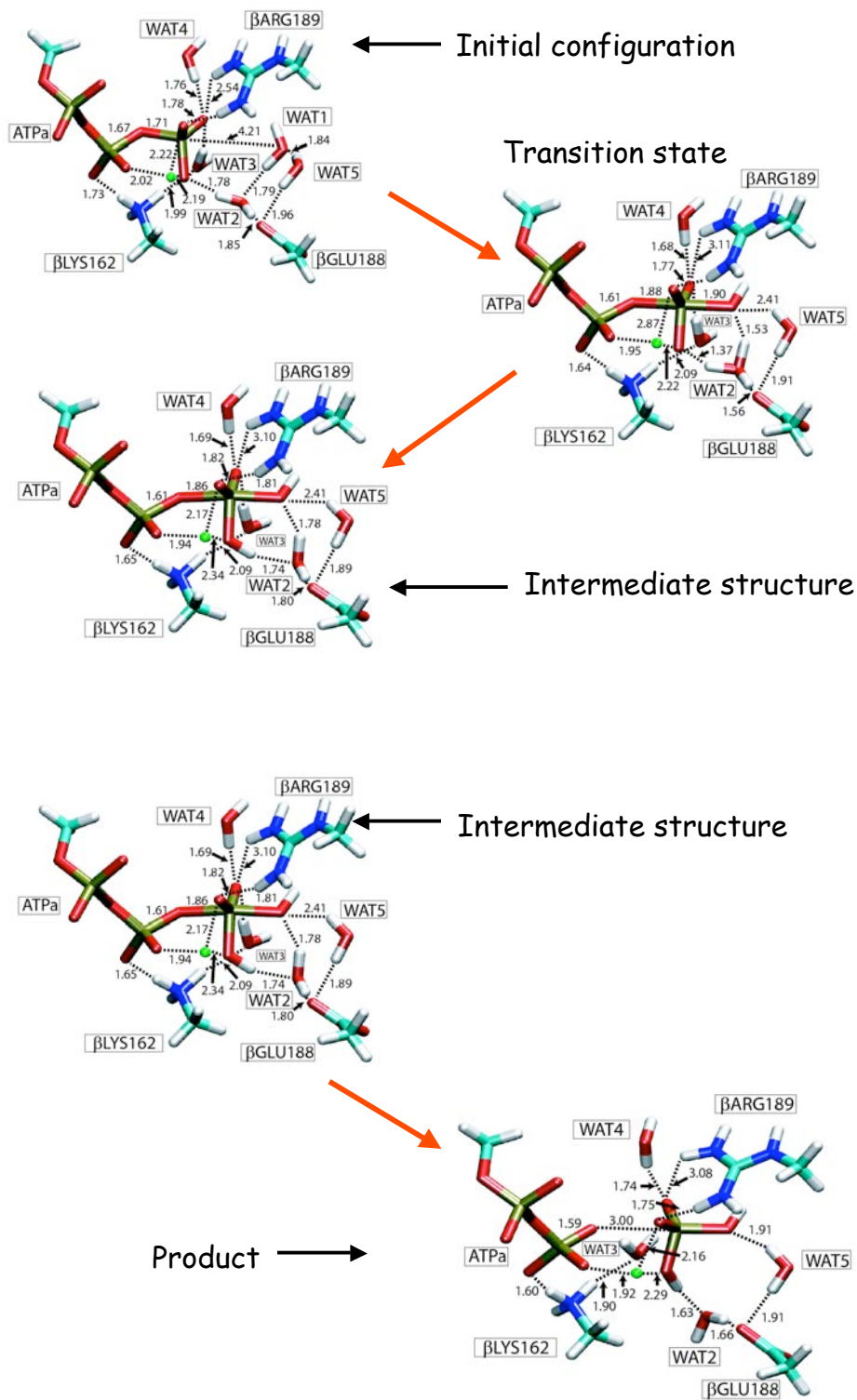
ATP hydrolysis in b$_{TP}$
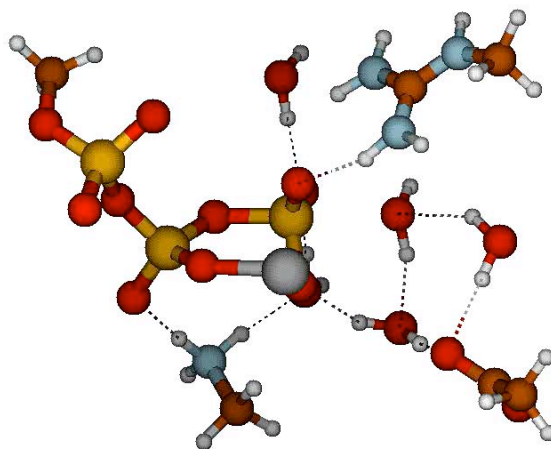
Coarse grain modeling of lipids

150 particles

9 particles!