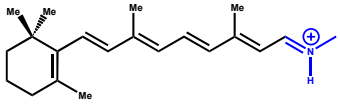
## Same chromophore – different absorption maximum



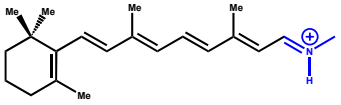
Length of the conjugation

Electrostatic interaction with the binding pocket

Steric interaction with the protein

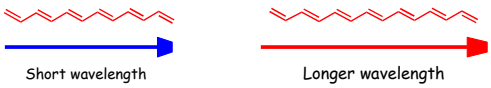
Protonation / deprotonation

## Same chromophore – different absorption maximum



Length of the conjugation

Shorter chain (blue shift) Longer chain (red shift)

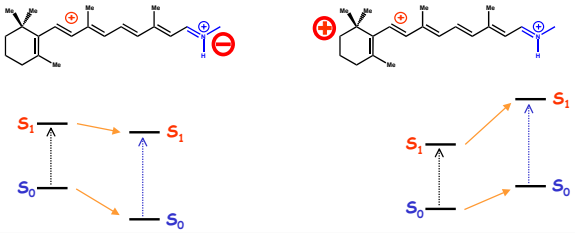



## Same chromophore – different absorption maximum

**Electrostatic interaction with the binding pocket**

BLUE SHIFT (shorter wavelengths):

- Ground state stabilization
- Excited state destabilization

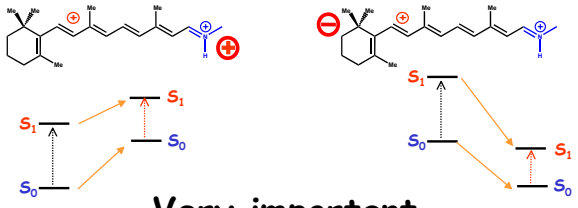



## Same chromophore – different absorption maximum

Electrostatic interaction with the binding pocket

RED SHIFT (longer wavelengths):

- Ground state destabilization
- Excited state stabilization



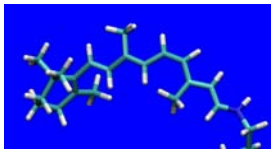

**Very important**

## Same chromophore – different absorption maximum

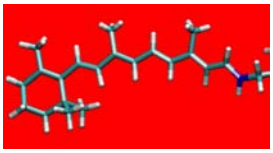
Steric interaction with the protein

Twisting the bonds in the backbone (blue shift)

Straightening the backbone (red shift)



Rhodopsin (500 nm)

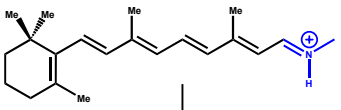


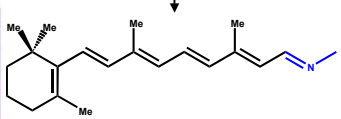
Bacteriorhodopsin (568 nm)

## Same chromophore – different absorption maximum

Protonation / deprotonation

UV vision
birds, honeybee

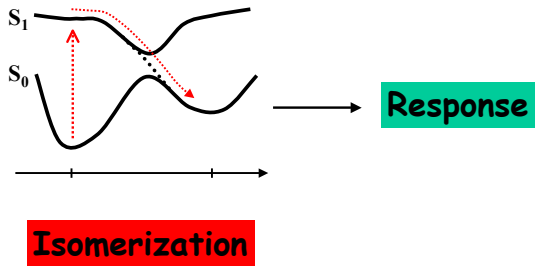




**Strong blue shift**

## Isomerization triggers the biological response

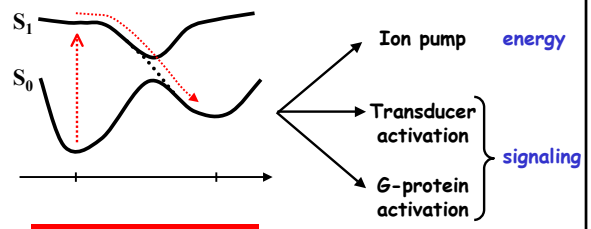
Light




Isomerization

## Isomerization triggers different cellular responses

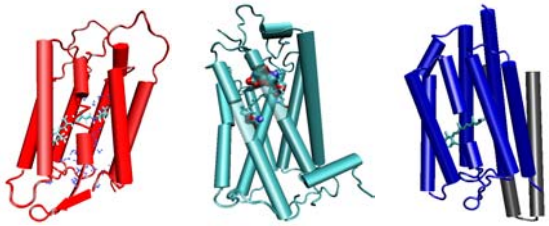
Light




Isomerization

## Variety of responses to retinal isomerization

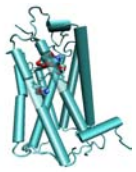
bacteriorhodopsin | Rhodopsin | Sensory rhodopsin



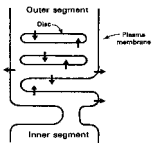
ion pump | G-protein activation | transducer activation

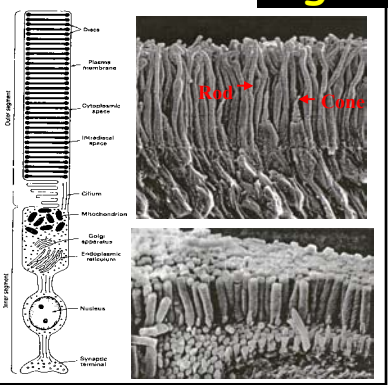
## Rhodopsin

Light

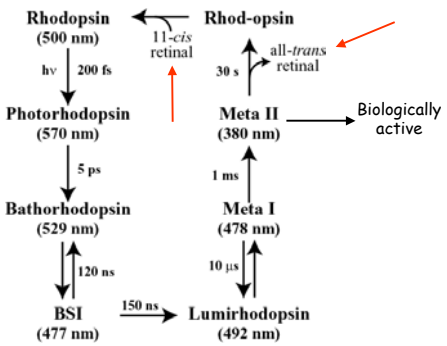


G-protein signaling pathway

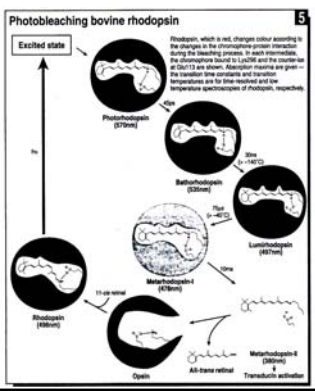


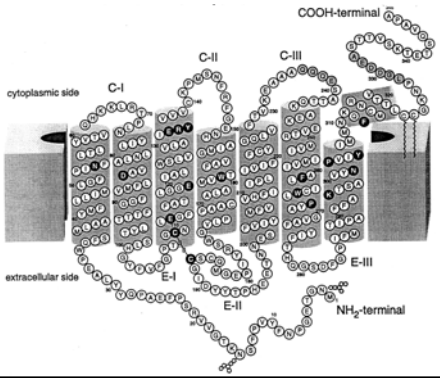

## Rhodopsin Photocycle



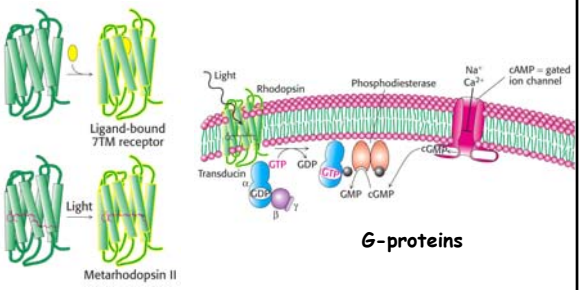

## Rhodopsin Photocycle



## Rhodopsin Architecture




## Signaling pathway of rhodopsin




Rhodopsin: $D = 0.4\mu m^2 \cdot s^{-1}$ (effective signaling)

Lipid molecules: $D = 1\mu m^2 \cdot s^{-1}$

## G-protein coupled receptors

More than 1000 types of receptor specific for:

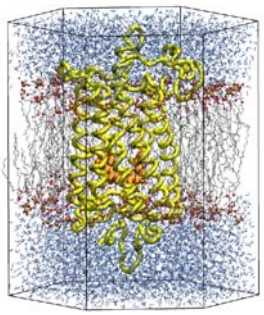
- odorants
- Photon
- Neurotransmitter
- Hormones
- Calcium
- Peptides
- ...

50% of drugs in the market act on GPCRs, which are very difficult to crystallize ☹

↓

Importance of rhodopsin structure

## Simulation of rhodopsin in membrane



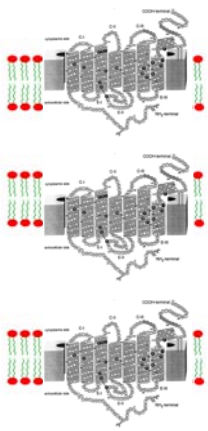
Protein: pdb file, 1HZX

Lipids: POPC bilayer (artificial)

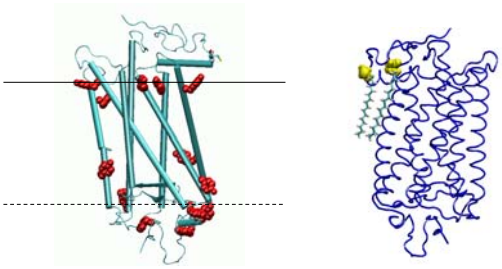
Total: ~40,000 atoms

NAMD2, CHARMm27, PME

1 ns equilibration,
10 ns relaxation after isomerization



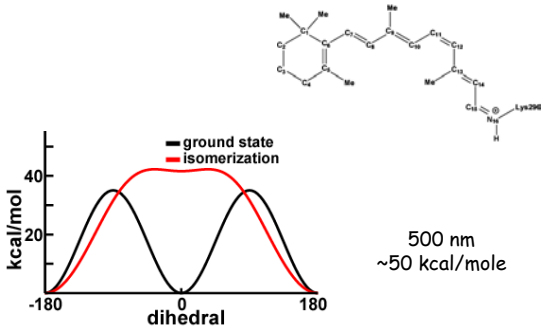
## Embedding the protein in membrane



1. Tyrosine residues

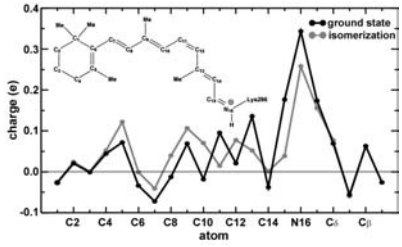
2. Palmitoyls connected to Cys322 and Cys323

## Inducing isomerization



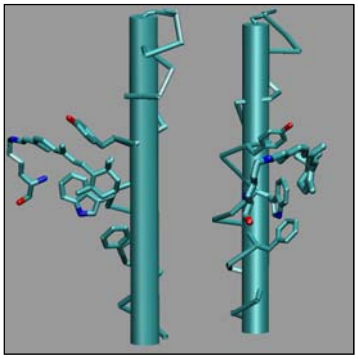

500 nm
~50 kcal/mole

## Retinal Charge Distribution

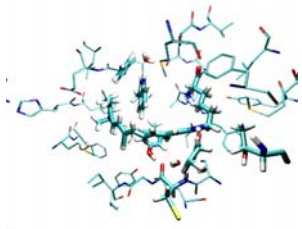


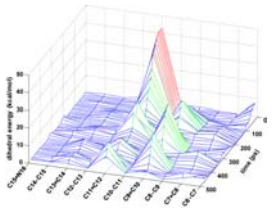

QM/MM derived partial atomic charges

**In the ground state, the ring of the chromophore blocks the rotation of helix VI**



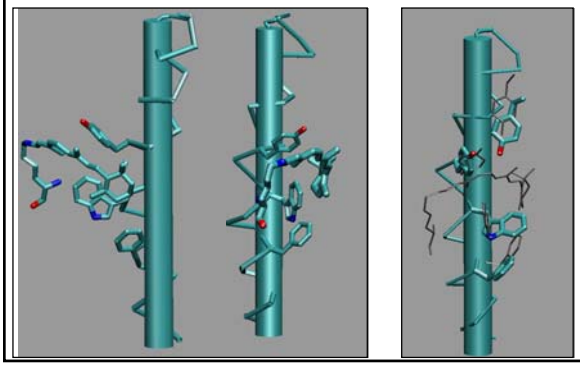
## Retinal Isomerization

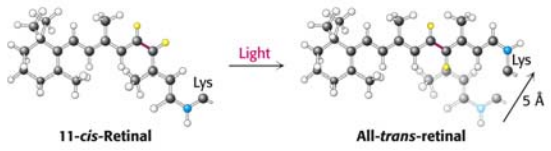




Twist Propagation

**In the ground state, the ring of the chromophore blocks the rotation of helix VI**

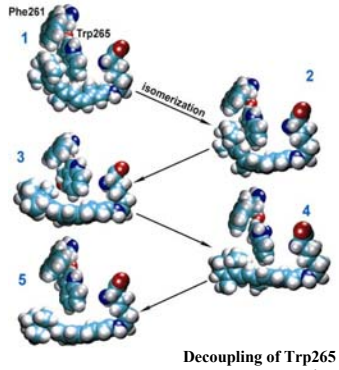





11-*cis*-Retinal All-*trans*-retinal

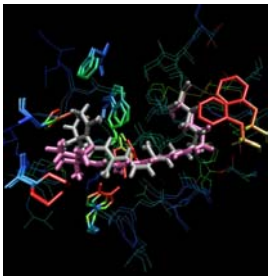
Text book figures not quite right!

# Retinal Isomerization



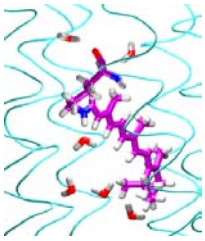

Decoupling of Trp265 and the β-ionone ring

## Rhodopsin



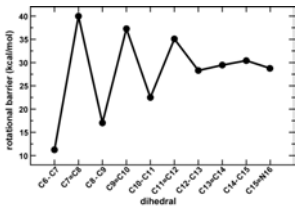
Isomerization 11-cis → all-trans

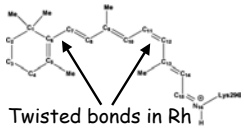
## Bacteriorhodopsin



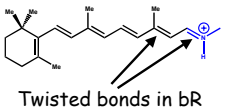
Isomerization: all-trans → 13-cis

## Isomerization Barriers and bond selectivity



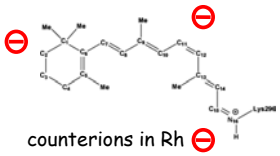



Twisted bonds in Rh

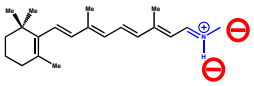


Twisted bonds in bR

## Counterion and bond selectivity



counterions in Rh ⊖



counterions in bR