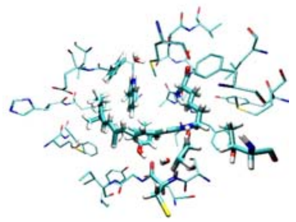
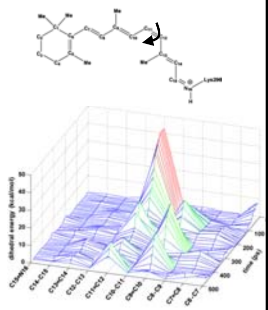
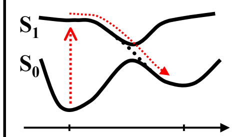
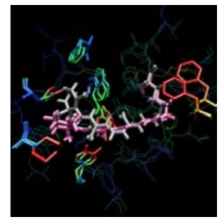
Retinal isomerization in rhodopsin moves the β-ionone ring

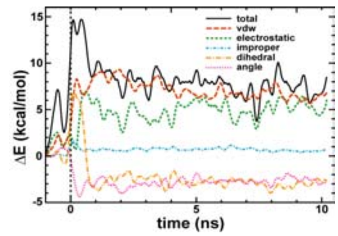




How does photon energy is stored in rhodopsin?

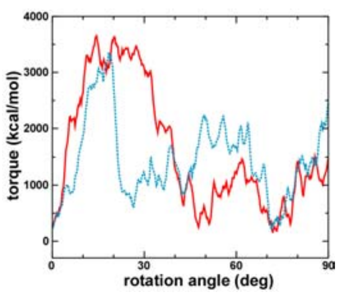


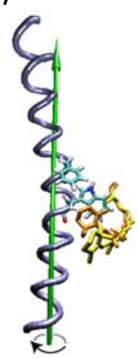




Internal (bonded) and interaction energy of retinal with its surrounding

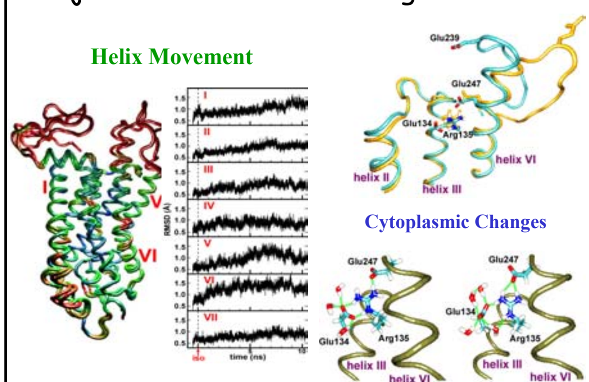
Isomerization of retinal allows helix VI to rotate freely



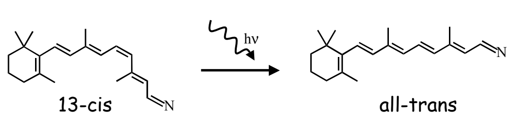


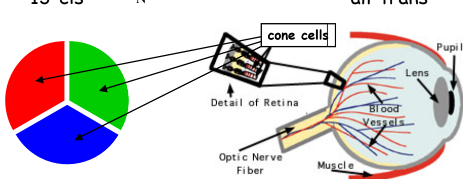
Torque applied to rotate helix VI before (red) and 5 ns after isomerization (blue)

Major conformational Changes in 10 ns



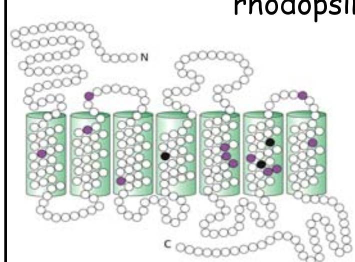
Color Vision





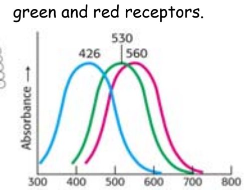
Visual receptors of rhodopsin family are classified based on their color sensitivity

Comparison of color visual receptors and rhodopsin



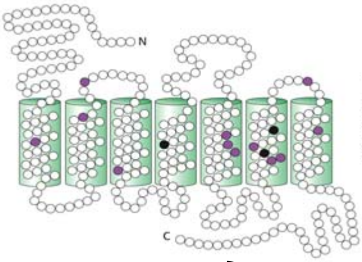
Each of the human cone receptors is only 40% identical with human rhodopsin.

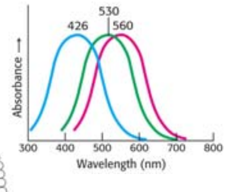
The human blue color receptor is only 40% identical with the human green and red receptors.



Only 15 out of 364 residues of human green and red cone receptors are different.

Green to red





Green → Red
Ala180 → Serine
Phe277 → Tyrosine
Ala285 → Threonine

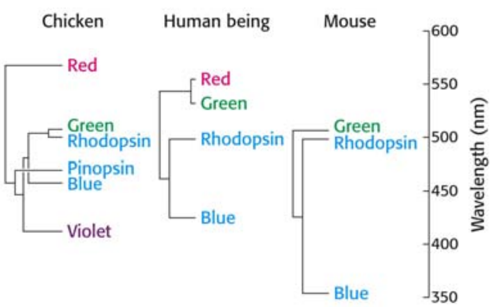
Electrostatic interaction of retinal and the binding pocket, in favor of excited state or in disfavor of the ground state.

Too bad we do not have the structures, but we could use Rh.

VMD examination of rhodopsin and color visual receptors

Sequence alignment of color receptors

Color vision in other mammals



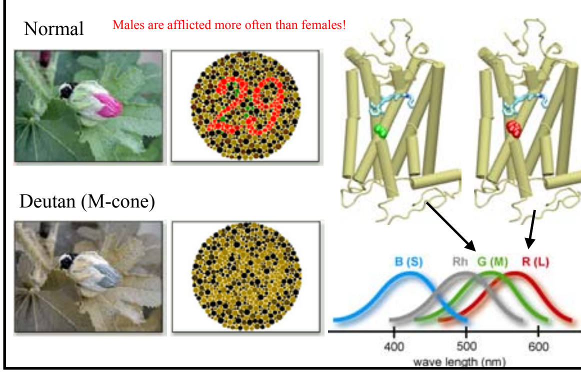
Sequences are all available and one could mutate them in rhodopsin, and try to explain the effect of amino acid exchange on the spectral properties.

Physics of Color Deficiency

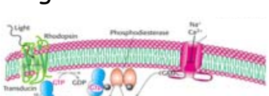
Normal

Males are afflicted more often than females!

Deutan (M-cone)



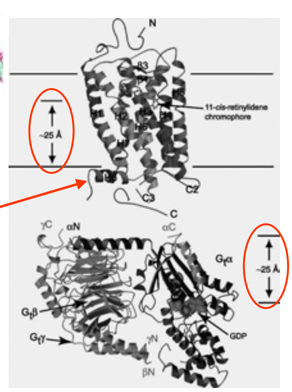
Signal transduction over a 5 nm distance



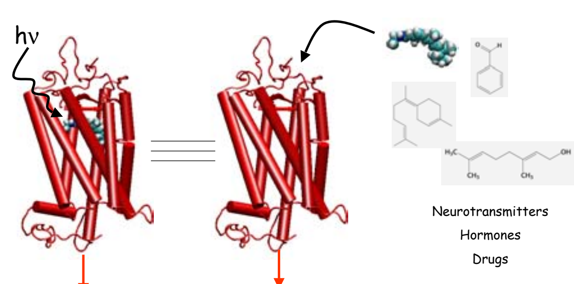
Retinal-rhodopsin complex

Amphiphilic H8

Trimeric G-protein (Transducin)



Photoinduced isomerization = Ligand binding



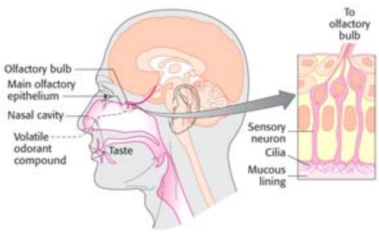
Neurotransmitters
Hormones
Drugs
...

G-protein activation

G-protein activation

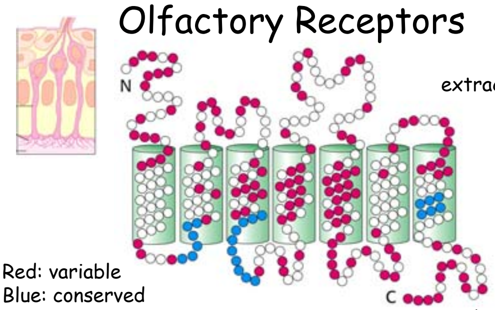
Ligand induced conformational changes is the main mechanism of activation of GPCRs

Olfaction



The organization and components are very similar to vision.
So we expect similar receptor architecture for olfaction.

Olfactory Receptors

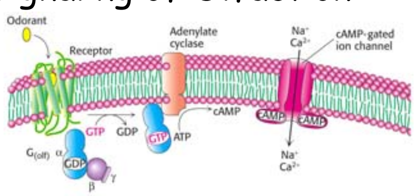


Red: variable
Blue: conserved

A few hundred types of ORs are present in human beings.
Each neuron has only one type of OR.

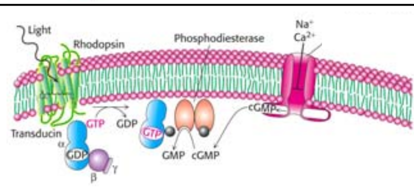
Cell Signaling of Olfaction

cAMP ↑

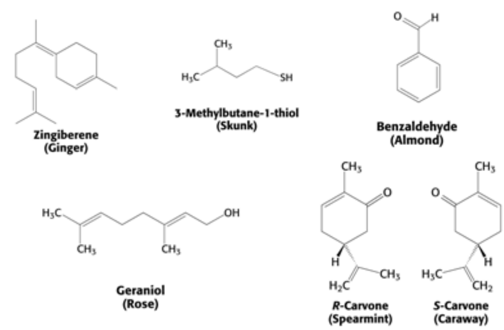


Signaling in vision

cGMP ↓



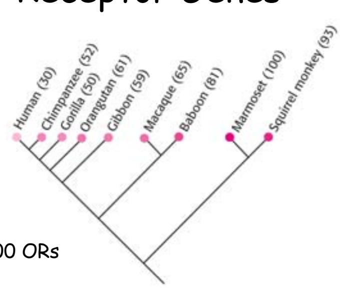
Ligands for Olfactory Receptors



Small molecules – Stereoselecitve binding

Olfactory Receptor Genes

Fraction of OR pseudogenes in different species



Rat gene: more than 1000 ORs
All functional

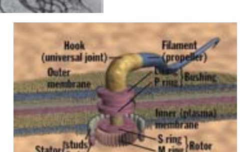
Human genome: 500-750 Ors (One of the largest gene family in human beings)
More than half are pseudogenes

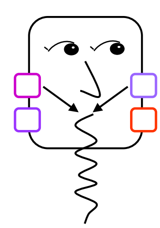
Single cells too can smell and see!

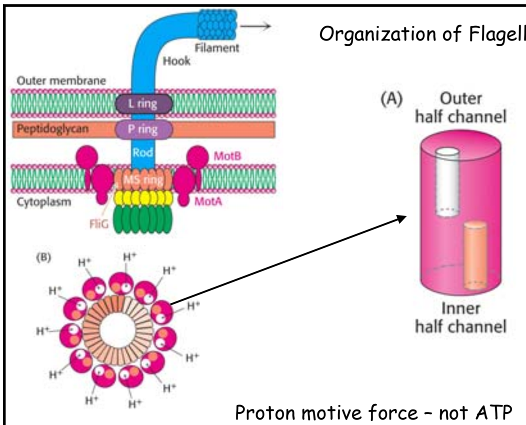
The response of bacterium is moving toward or away from the signal

chemotaxis

phototaxis

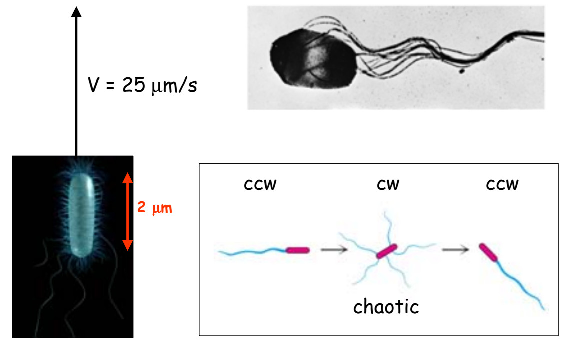






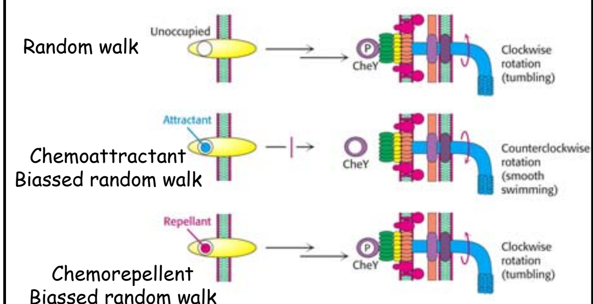
Proton motive force – not ATP

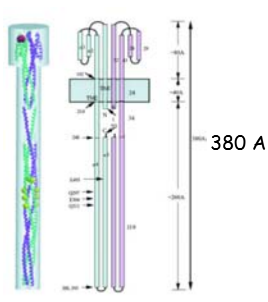
Chemotaxis and Phototaxis



A motile bacterium can move 10 times its body length in one second.

Effective motion of the bacterium in the absence of any signal:
R A N D O M W A L K



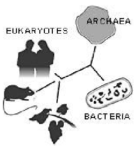


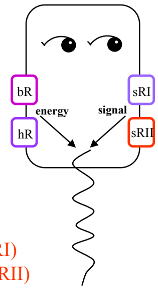
Animations:

Chemotaxis

Archaeal Sensory Rhodopsins

Prof. Carl Woese (UIUC) wins the Crafoord Prize in Biosciences
http://www.news.uiuc.edu/news/03/0213crafoord.html





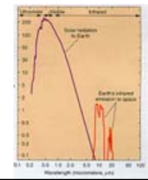
- Bacteriorhodopsin (bR)
- Halorhodopsin (hR)
- Sensory rhodopsin I (sRI)
- Sensory rhodopsin II (sRII)

Oxygen and light together could be very harmful for the cell

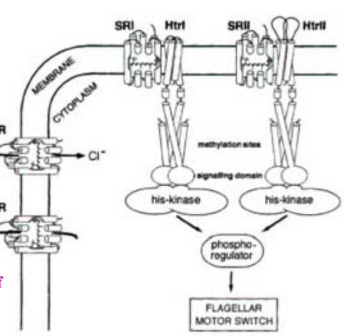
In aerobic condition: electrogenic pumps are not needed (bR/hR)
Attractant response is not needed (sR-I)

These proteins are repressed; sR-II (repellent sensory rhodopsin) is expressed to help find the dark and avoid oxidative damage to the cell.
Maximal absorption of sR-II (498 nm) matches the highest intensity wavelength of sunlight at the surface of the Earth.

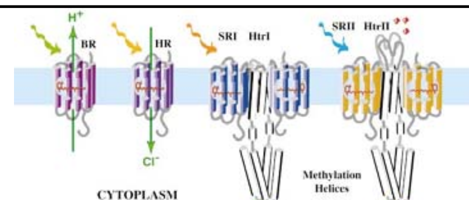
In anaerobic condition: bR/hR/sR-I are expressed; and sR-II is suppressed.



Bacterial Rhodopsins



Single protien of PM (568nm)



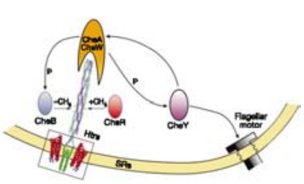
Slower cycle in sR-I and sR-II

sR-I: Attracted to light at > 520 nm; repelled by to UV – anoxic condition

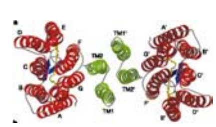
sR-II: Repelled by < 500 nm – (490nm) constitutively produced – phoborhodopsin

Htr – similar to chemo-receptors

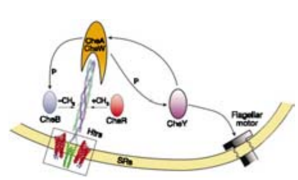
Structure of the Sensory rhodopsin II/transducer complex: a molecular basis for transmembrane signalling

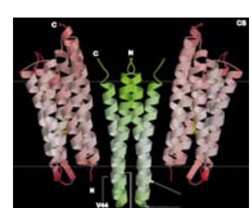


Cytoplasmic view



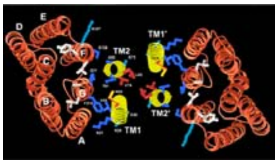
Activation is based on the interaction of Helix F and TM2

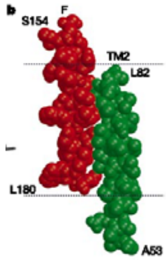




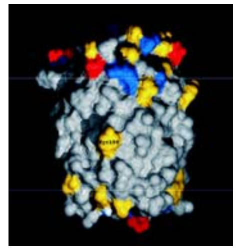
Dark color: high B factor, mobile

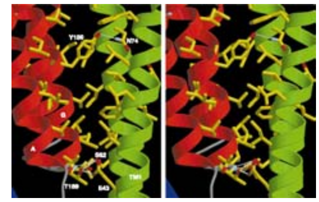
Inherent proton pump activity of sR-II is blocked after complex formation with HtrII





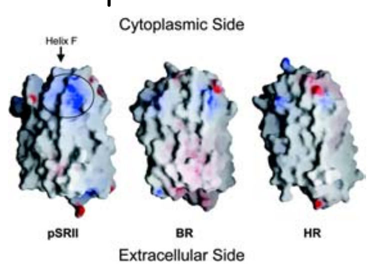
Receptor-transducer interface

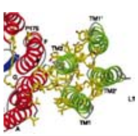


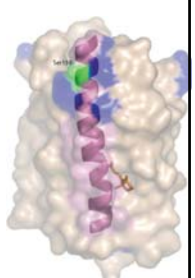


Structure is strikingly very similar to Np-sR-II alone; only Tyr199 is different (90 degree rotated)
Interface mainly vdW, only a few H-bonds

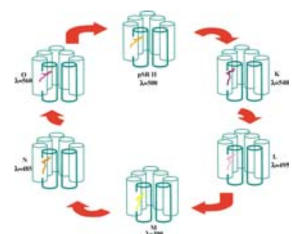
Receptor-transducer interface

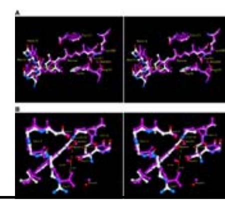






Remarkable similarity between bR and sR-II why different functions?

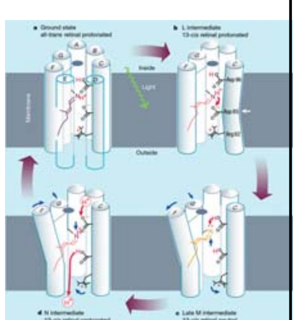




If you decouple it from Htr-II, it functions as a proton pump!!

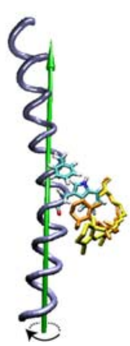
Similarities of conformational changes in retinal proteins

Displacement of helices F and G in bR is responsible for the opening of the cytoplasmic half channel and entrance for water molecules necessary for reprotonation of retinal Schiff base.

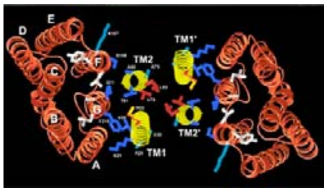


Similarities of conformational changes in retinal proteins

Rotation of helix VI (F) in Rh is one of the major conformational changes triggering the activation of transducin (G-protein).



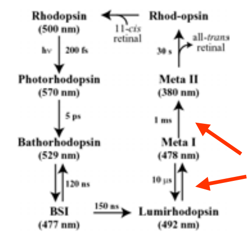
Similarities of conformational changes in retinal proteins



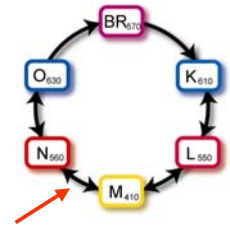
Outward motion of helix F in sR-II causes the rotation of one of the two helices in the transmembrane region of the transducer and its further conformational change.

Importance of protein-lipid interaction

Kinetic of Rh photocycle



Kinetic of bR photocycle



… and probably also the kinetics of sR-II photocycle, can be influenced by the lipid composition of the membrane

Next week

Membrane channels:

Aquaporins