# *Cell-to-Cell Signaling*

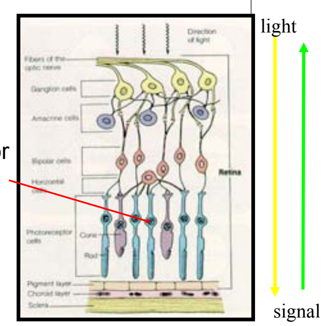
## *A little bit of neuroscience*

## Light "receptors"

- Rods and cones in retina (they are actual neurons)
- Transduce electromagnetic energy into action potentials
- Only limited part of the spectrum excites the photoreceptors
- In human eye the wavelengths are between 400 and 700 nm

## Retina

- Is a neural tissue
- Has layered structure
- Is built of 5 types of cells including two types of photoreceptor neurons
  - Rods and cones that contain special molecules that change in response to light

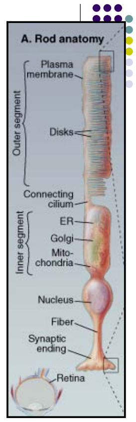



## Rods and cones

- Responsible for vision in different light conditions
- Rods provide black and white vision and are most important in low light intensities
- Cones provide sharpness but require greater intensities of light
- Both have similar signal transduction mechanisms (different photopigments)

## Rhodopsin

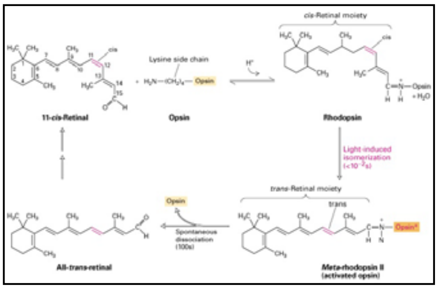
- Light sensitive transmembrane protein – **seven helix receptor**
- Light sensor (REAL RECEPTOR)
- Present both in rods and cones
- Located in membrane disks in the outer segment




## Rhodopsin

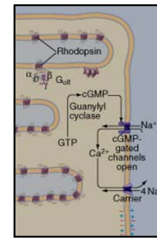
- Bound to the chromophore (retinal)
  - Molecule that changes when hit by photons
  - **Ligand for the receptor** (notice that ligand is permanently bound to the receptor)
- Light triggers isomerization of retinal and activation of rhodopsin (receptor)

## Light triggers isomerization of retinal and activation of rhodopsin




## Another necessary component – effector in the cascade

- Rods and cones are neurons so the only "language" they understand are changes in membrane potential
- Cell membrane of rods and cones contains cGMP gated $Na^+$ channels
- These channels are opened by cGMP

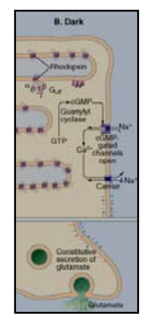



## In the DARK (yes, even when you're sleeping)

- In the dark there is lots of cGMP in rods and cones (phosphodiesterase is not active)
- cGMP gated cation channels are open = current flow ("dark current")
- A "dark" current keeps cells constantly depolarized
  - Membrane potential is -30mV

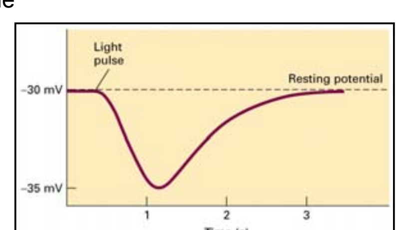
## In the DARK (yes, even when you're sleeping)

- Rods are depolarized and constantly secrete glutamate (inhibitory neurotransmitter) at the first synapse between rods and bipolar cells
- Bipolar cells are constantly inhibited



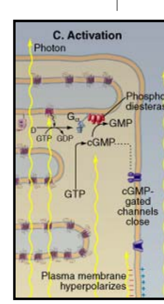

## Light!!!

- Light causes a slight hyperpolarization of the membrane




## Molecular mechanisms of light transduction

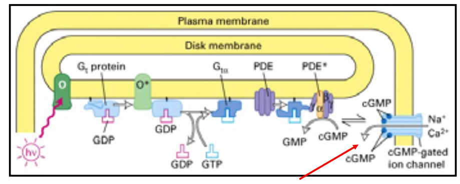
- A chromophore absorbs light and changes the conformation of seven helix receptor
- Activated receptor activates G protein transducin $G_t$



## Molecular mechanisms of light transduction

- $\alpha$ subunit of $G_t$ activates PDE (phosphodiesterase)
- Phosphodiesterase (enzyme) converts cGMP to GMP and lowers the level of cGMP
- Less cGMP causes dissociation of cGMP from nucleotide gated channel in the membrane
- Channel closes (hyperpolarization of rods) because there is too little cGMP to keep it open
- Lack of cGMP will close the channel

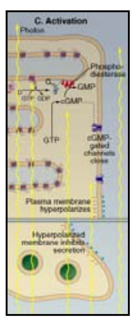
## Molecular mechanisms of light transduction – another view




dark current channel

## Molecular mechanisms of light transduction

- Hyperpolarization of rods
- Decrease in glutamate release
- "Uninhibition" of bipolar cells

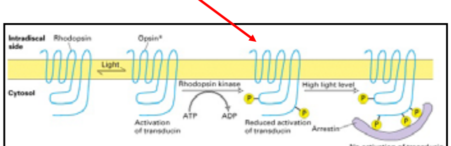



## The power of light

- A single photon hyperpolarizes the cell 1mv for 1-2 sec (we can detect 5 photons)
- One photon decreases $Na^+$ flow by $10^6$
- 30 - 50 photons are needed to cause half maximal hyperpolarization

## Rod cells adapt to varying levels of ambient light

- Rhodopsin has 7 phosphorylation sites
- Rhodopsin kinase phosphorylates activated receptor
- This reduces the ability of receptor to activate transducin ($G_t$)

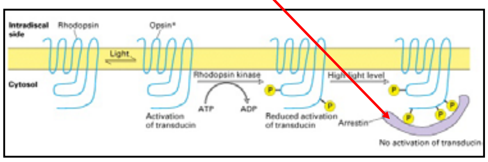



## Light adaptation

- The more light, the more activated rhodopsin, the more phosphorylation, the more light needed to create a visual signal
- When light levels drop rhodopsin becomes dephosphorylated

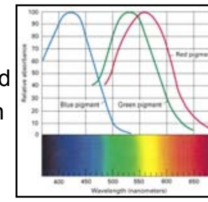
## Light adaptation

- At very high light levels phosphorylated rhodopsin binds arrestin and shuts down rod cell activity




## Color vision

- Utilizes three opsin pigments
- Different photopigments absorb different wavelengths
- Mutation in the pigment causes the change of wavelengths that are absorbed
- Color is a matter of perception




## Why are signaling systems so complex?

- Interaction of different signaling pathways permits fine-tuning of cellular activities (local logical network)
  - Redundancy
  - Reliability
  - Robustness
- Evolutionary convenience? (if parts are there, tweak them for new uses?)