Neuro Lecture 12

October 18 2019

Visual field seen by both eyes (binocular area) is

located primarily on the temporal portion of both eyes

What advantage would GPCR-type receptor add to phototransduction

signal amplification

If the result of the phototransduction cascade is that cGMP-gated channels close, then

the photoreceptor hyperpolarize in response to light

What part of retina would be able to detect a faint star at night

periphery (more rods)

MCB/Neuro 80 - Neurobiology of Behavior

Today's Topic:

Vision 1: The eye and Phototransduction

Lecture 12

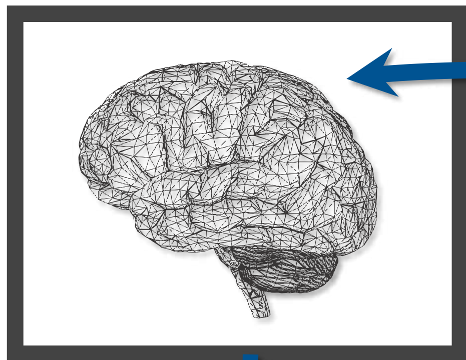
Optional reading: Purves et al., Neuroscience 6th pages 233-250

Lecture notes, review questions, office hour times available at:

https://canvas.harvard.edu/courses/59120

How will you study an unknown machine?

World



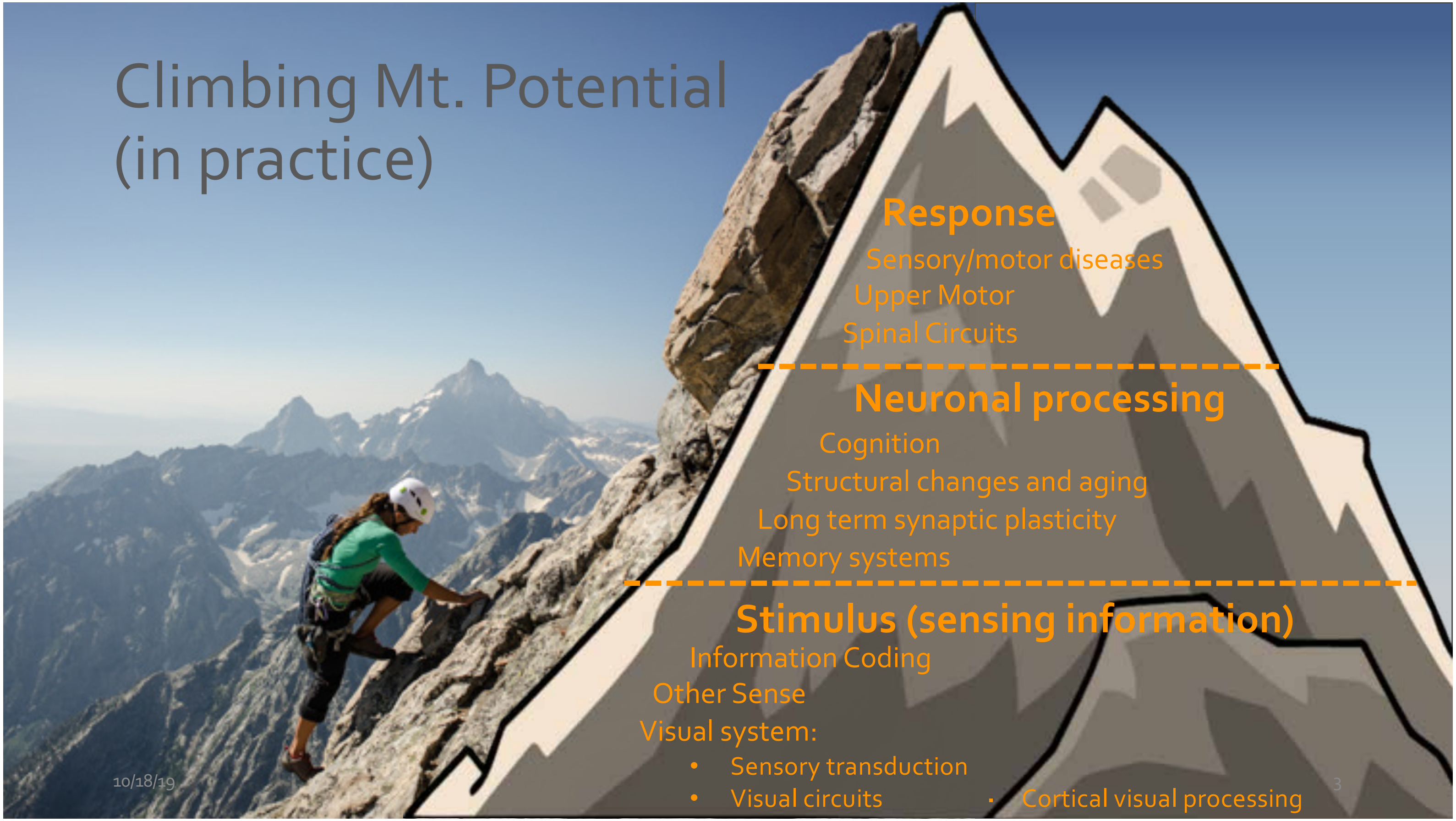
Behavior

Open the
“black box”

Signals in neurons
(Part 1)

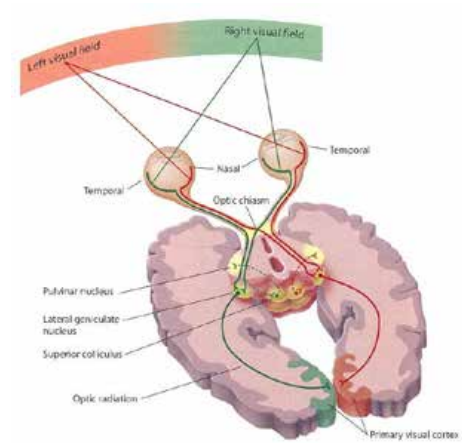
Real circuits
(Part 2)

Climbing Mt. Potential (in practice)



Sensory Systems

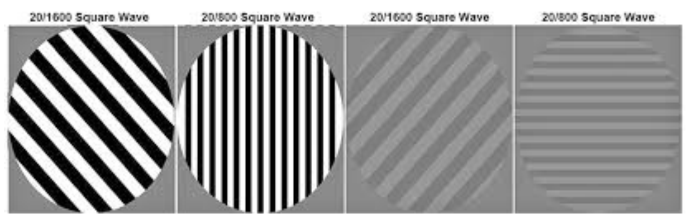
- Detect and convert information from the environment to a neuronal code
- Code is processed and interpreted by the brain
- Creates <u>perception</u> of the world around us
  - Visual
  - Auditory
  - Somatosensory
  - Olfactory
  - Gustatory
- Information detected by sensory receptors, conducted along neural pathways to dedicated sensory areas of the brain.



Visual System

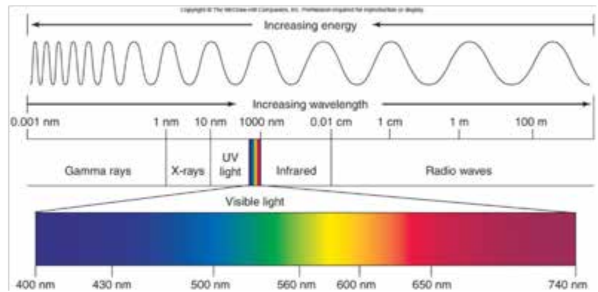
- Primates rely heavily on vision
  - ~40% of our cortex is devoted to visual processing
- Vision gives us information about:
  - Shape
  - Color
  - Texture
  - Direction
  - Speed
  - Location

- Arguably the most studied sensory system
  - Visual stimuli are easy to control
  - Acuity - ability to distinguish two nearby points

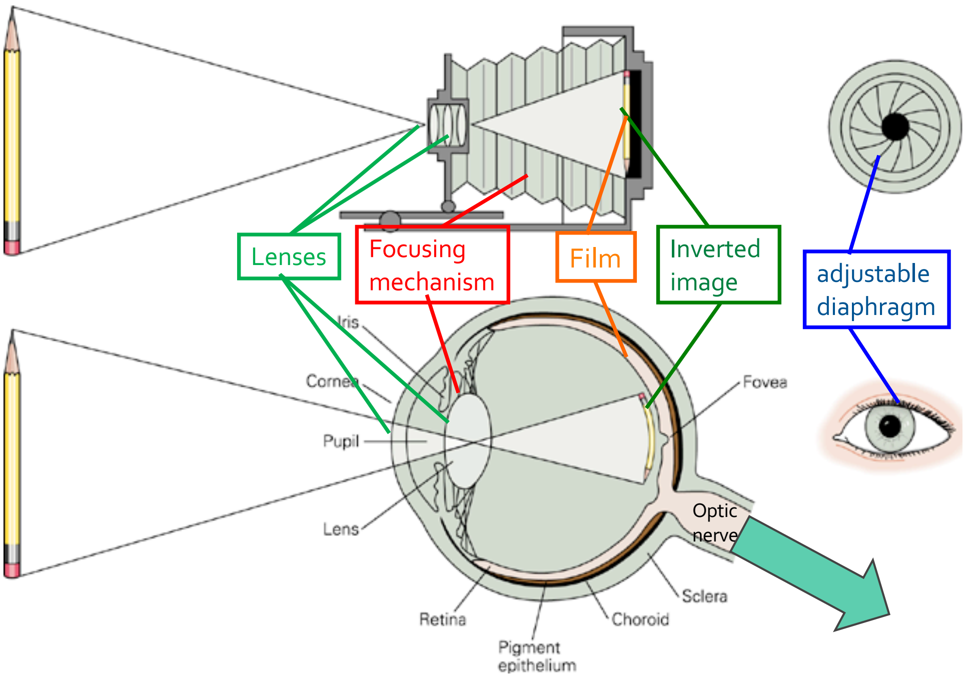


Light

- Light is a form of electromagnetic energy, also called electromagnetic radiation
  - It travels in rhythmic waves
  - Also behaves as though it consists of discrete particles, called <u>photons</u>
  - The wavelength is the distance between crests of waves determines the type of electromagnetic energy
- Light is bent when traveling from one medium to another *(refraction)*
- Vision is the detection of photons bouncing off objects and hitting our eyes



The eye as a camera



- Image passes through the lenses, causes an inversion
- Focus: contraction of lens by ciliary muscle
- Image sensor (Film) : photoreceptors in retina
- Apature/diaphragm: iris
- Optic nerve: USB port

Differences include:

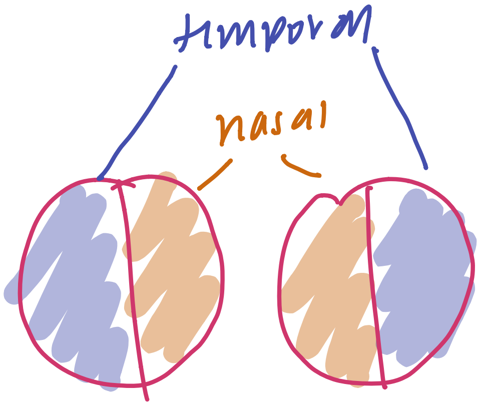
- Eye's image sensor does not have uniform sensitivity
- Dynamic sensitivity to light

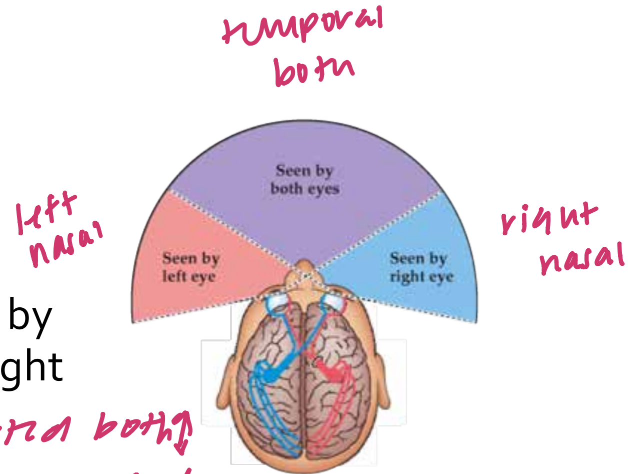
Visual field

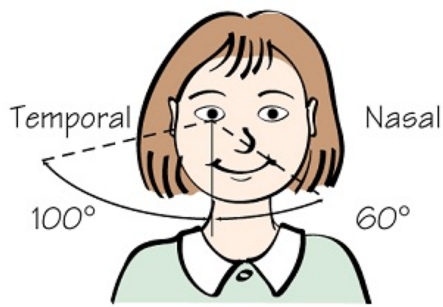
- The entire visual space viewed by retina when eye is fixated straight ahead

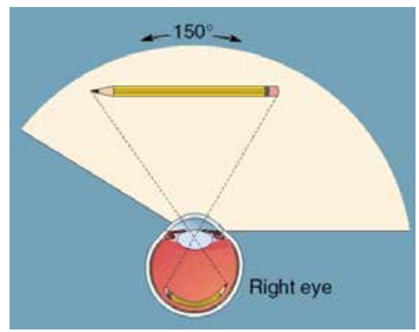
inverted both

- Since the image is inverted, neurons and on the nasal part of the retina detect light from the periphery



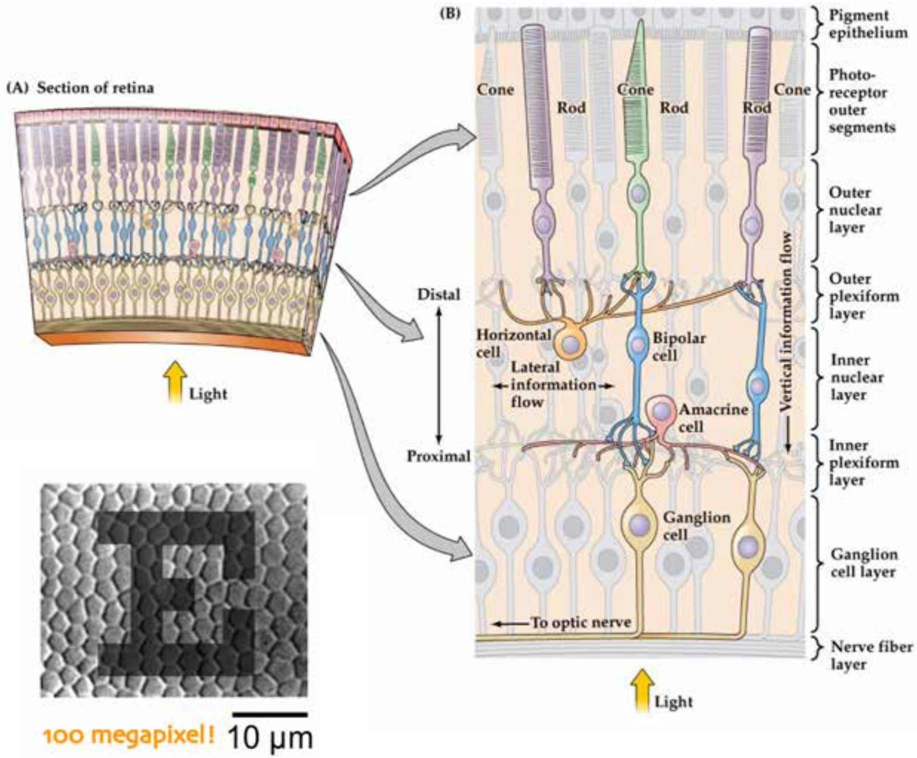






Retina

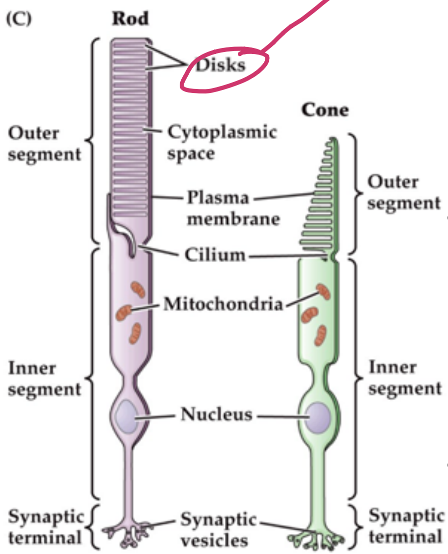
- Laminar organization
- Seemingly inside-out layers
- Light passes through ganglion cells and bipola
cells before reaching photoreceptors.
- Photoreceptors are like pixels



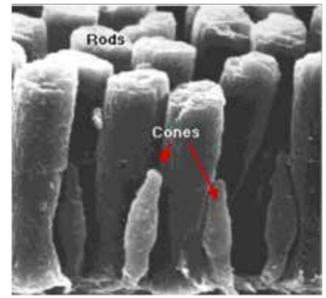
Photoreceptors convert light into neural signals

where detection of photons occur

- 2 types:
  - Rods: long, cylindrical outer segment with many disks
    - Low light (night vision)
  - Cones: shorter, tapering outer segment with fewer disks
    - Bright light (color vision)
- Three main regions
  - Outer segment
  - Inner segment/Cell body
  - Synaptic terminal Δ in Vmemb
    - but no action potential! (super short)
- Absorb light and convert to first a chemical signal, then electrical signal within the outer segment
- Then convert again into a chemical signal at the terminal



NEUROSCIENCE 5e, Figure 11.5 (Part 3)



light

· light energy sensed by GPCR

· Rhodopsin rods

· "ligand" retinal already bound

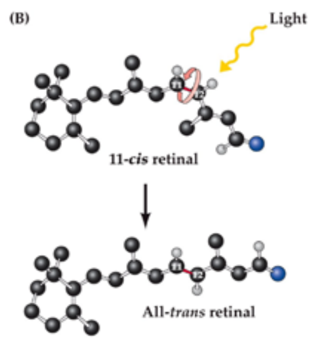
  · vitamin A derivative

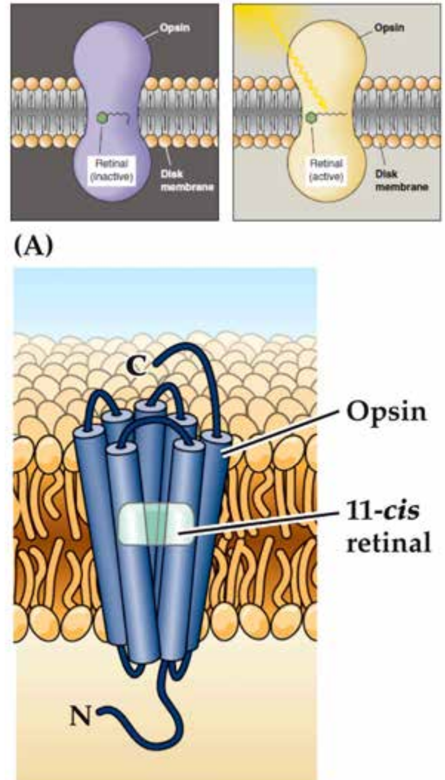
· 11-cis retinal → all-trans retinal → · activates rhodopsin

· Δ in Vmems

Phototransduction in rods

- Light energy interacts with photopigment.
  - Rhodopsin is the photopigment in rods
  - Located in the disk membrane of the outer segment
  - Light coverts 11-cis retinal to All-trans retinal
  - Produces a change in membrane potential
- Analogous to activity at G-protein-coupled neurotransmitter receptor





NEUROSCIENCE 5e, Figure 11.9 (Part 1)

Rods and Cones have a high resting membrane potential

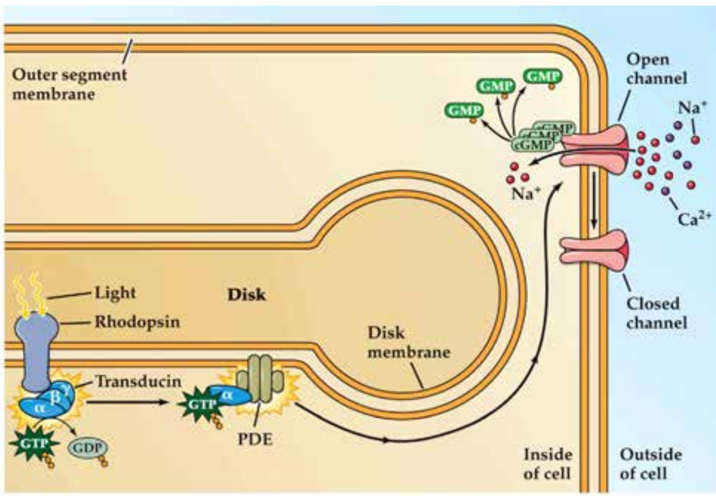
- At rest (in the dark), cyclic-GMP gated cation channels are open
  - Keep Vm relatively high ~ 40 mV
  - Open voltage-gated Ca^{++} channels in the terminal
  - Release synaptic vesicles continuously in the dark
  - "Dark currents"
  - Many Na/K pumps at work to maintain concentration gradients

continuous neurotransmitter release

more Na^{+} in than K^{+} out

Phototransduction

- Light-activated biochemical cascade in a photoreceptor
- The consequence of this biochemical cascade is signal amplification - sensitivity to small amounts of light

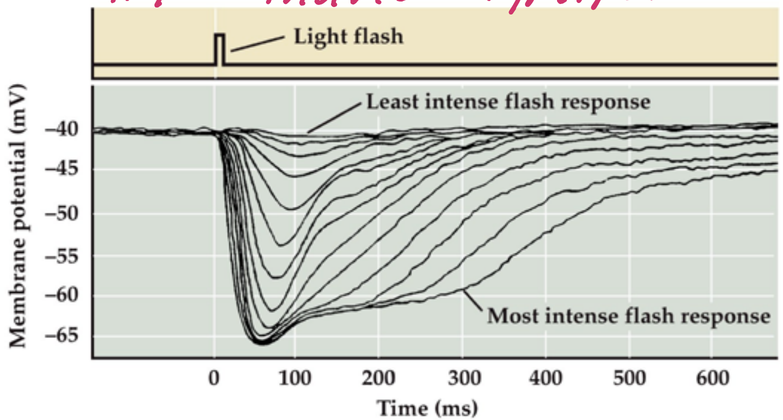


- Light causes conformational change that activates the rhodopsin GPCR
- Activated rhodopsin activates a G protein (Transducin)
- Transducin then activates phosphodiesterase, an enzyme that breaks down cyclic GMP (similar to cyclic AMP)
- Without cGMP, cGMP-gated channels close

Photoreceptors hyperpolarize in response to light

- V_{rest} depolarized
- Increased light intensity, causes changes hyper polarization magnitude and duration.
- Light induced hyperpolarization closes voltage-gated Ca^{++} channels
- Light leads to decreased neurotransmitter (glutamate) release

light-induced hyperpolarization

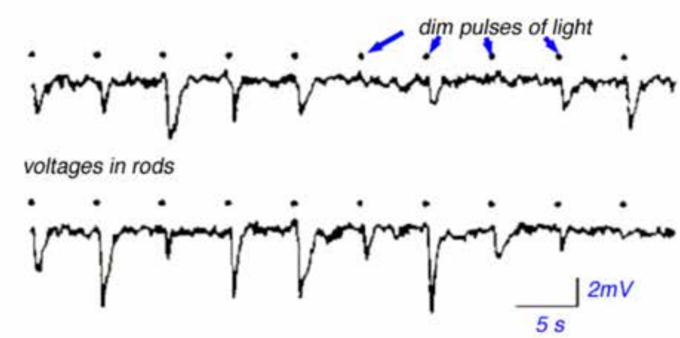


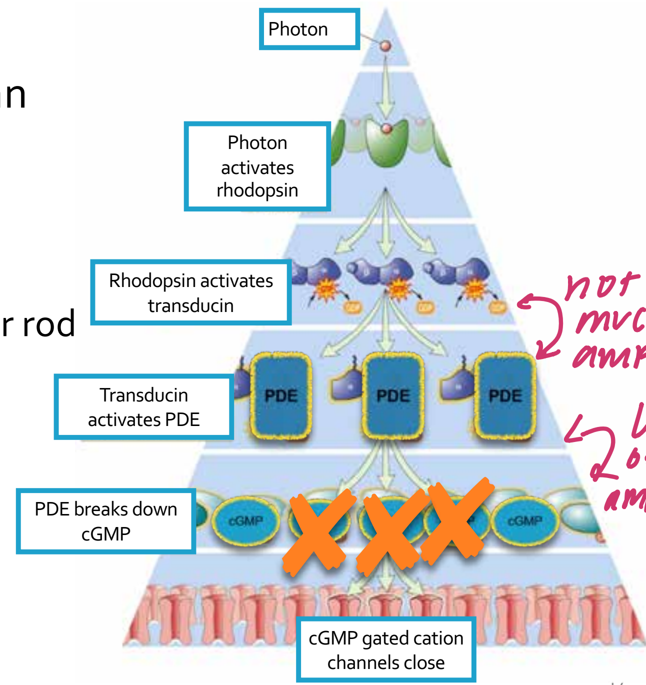
NEUROSCIENCE 5e, Figure 11.7

Amplification during phototransduction

- A single light-activated rhodopsin can result in the cleavage of 10,000$_s$ of cGMP molecules per second
- Humans can detect a single photon!

Dim pulses of light averaging one photon per rod





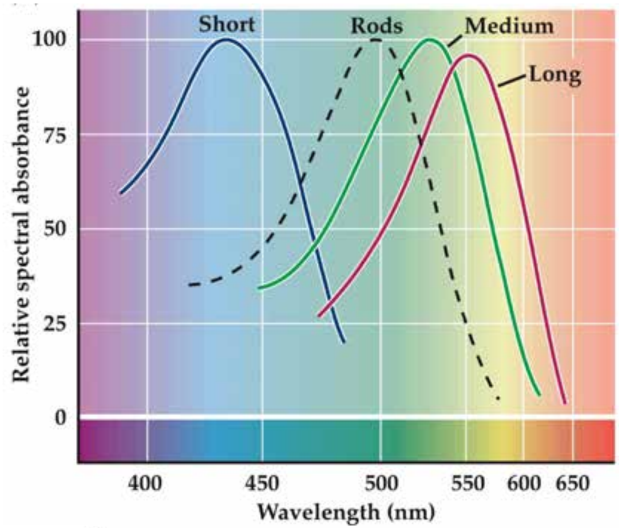
not much amplification

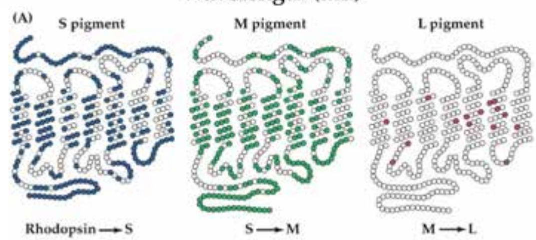
lots of amplification

increased refraction error w/ small wavelengths → more M/L → greater visual acuity

Color vision in cones

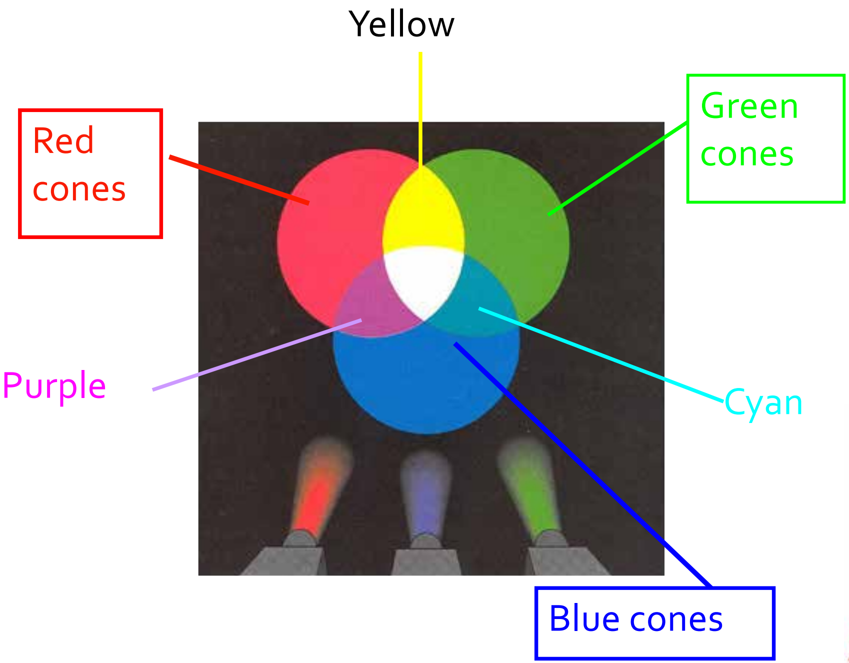
- Similar process to rod phototransduction
  - Different opsins
- Red (long wavelength), green (medium wavelength), blue (short wavelength)
- Color perception
  - Contributions of blue, green, and red cones to retinal signal
  - Mostly M & L (due to light bending)
  - Mixing of red, green, and blue light causes equal activation of the three types of cones.
  - The perception of "white" results





Subtle differences in opsin protein alter wavelength sensitivity

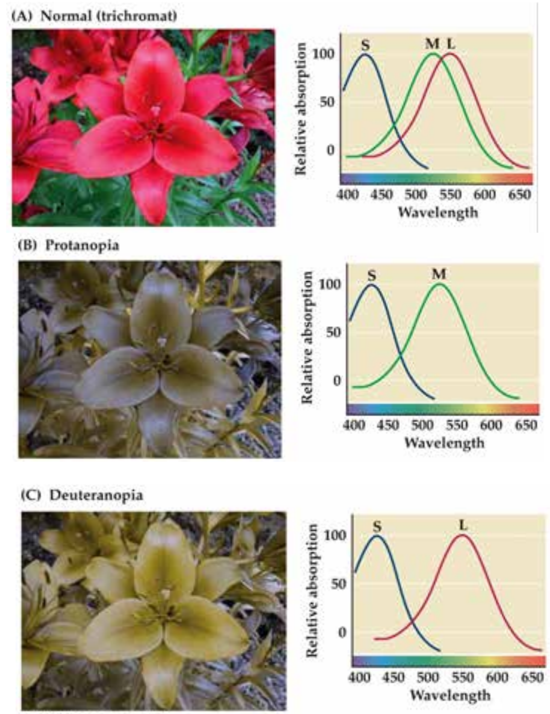
Trichromatic color vision



- Our brain produces the conscious sensation of color from differences in these three pigments

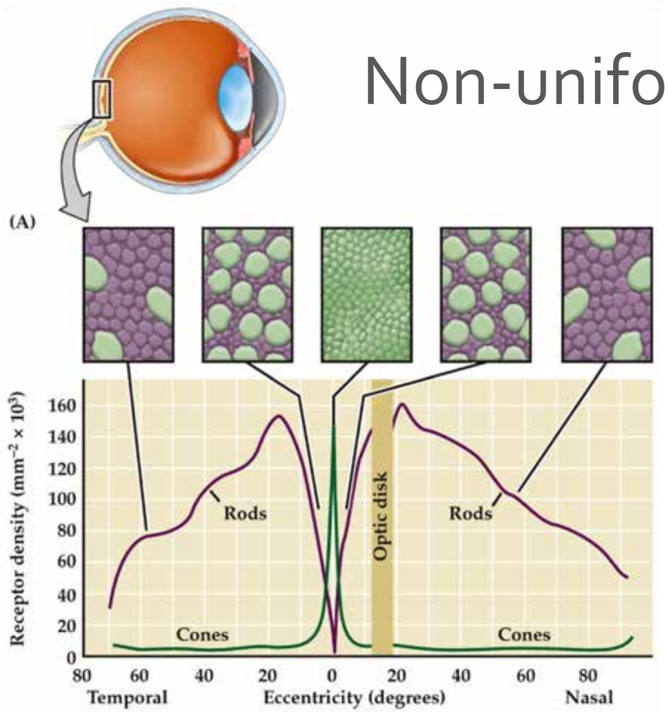
Trichromatic vision – color blindness

- Mutations in cone opsins cause color blindness
  - most commonly red or green opsins
- Rods are more sensitive than cones, thus color blind people have normal night vision
- Red-green color blindness
  - 75% caused by defect in green cone
  - Gene is on X chromosome (1 copy in males)
  - ~8% males and 0.4% females



NEUROSCIENCE 5e, Figure 11.15 (Part 3)

Non-uniform retina

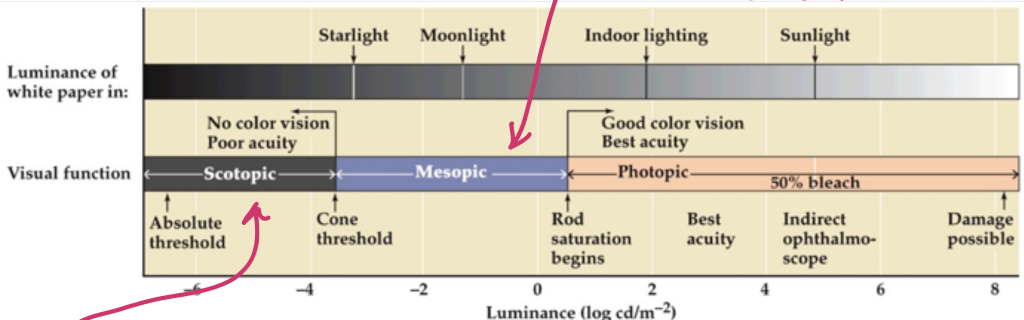


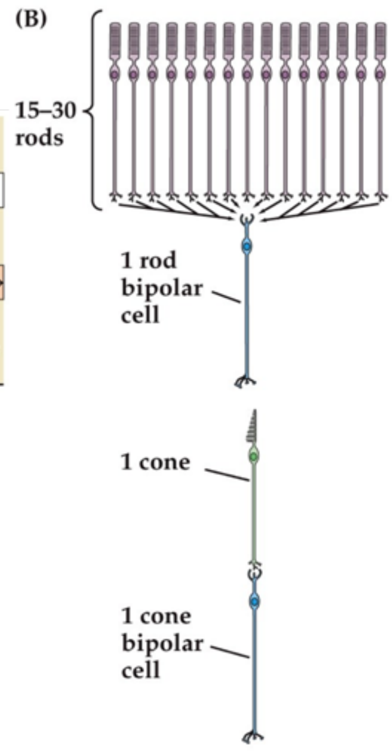
NEUROSCIENCE 5e, Figure 11.13 (Part 1)

- Structure varies from fovea to retinal periphery.
- Peripheral retina
  - Higher ratio of rods to cones
  - Higher ratio of photoreceptors to ganglion cells
  - More sensitive to low light (bleached in high light situations)
- Non-uniform field of view

Rods vs Cones

rod saturation (bleaching) occurs





***NEUROSCIENCE 5e*, Figure 11.12 (Part 2)**

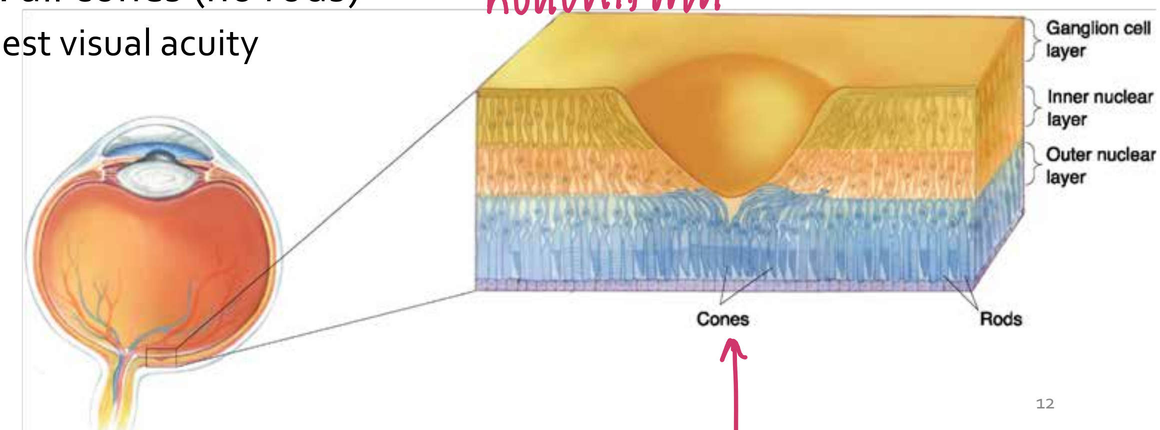
- Rod system has very low spatial resolution but extremely sensitive to light.
- Cones are less sensitive but faster than rods
- Cones dominate "normal seeing"
- Cone recovers from photobleaching faster

barely used in normal day-to-day life

Fovea: area of highest acuity

- Cross section of fovea: pit in retina where outer layers are pushed aside
  - Maximizes visual acuity
- Central fovea: all cones (no rods)
  - Area of highest visual acuity

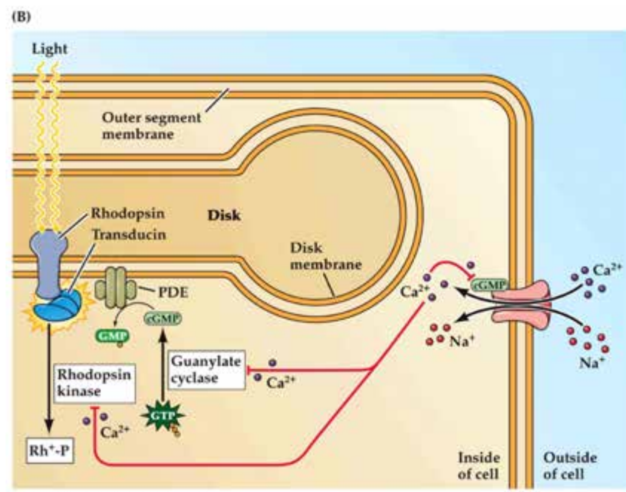
nonuniform



dominated by shorter cone cells

Recovery allows the visual system to respond to light continually

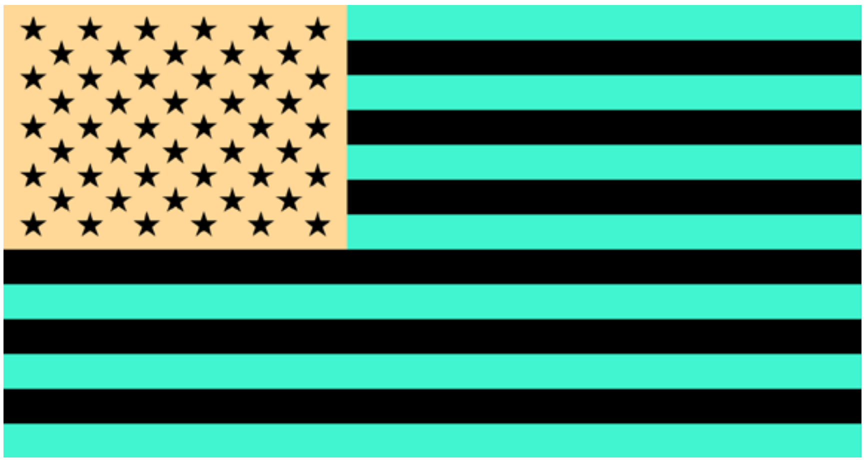
- The cGMP gated channels are permeable to both Na^{+} and Ca^{++}.
- Light induced closure causes a decrease in Ca^{++} concentration and reduces sensitivity of receptors to light
  - Low calcium increases cGMP production
  - Low calcium increases arrestin (rhodopsin kinase) binding
- Photobleaching of opsins reduces the amount of available opsins and contributes to adaptation as more light is needed to produce the same response



NEUROSCIENCE 5e, Figure 11.10 (Part 2)

Adaptation produces "after images"

↳ photoreceptors used to yellow → need yellow to activate



opposite of yellow is blue

Adaptation can also make images disappear

Visual image fades due to adaptation in the retina and the rest of the image is “filled in” by the brain

Lecture 12 - Learning Objectives:

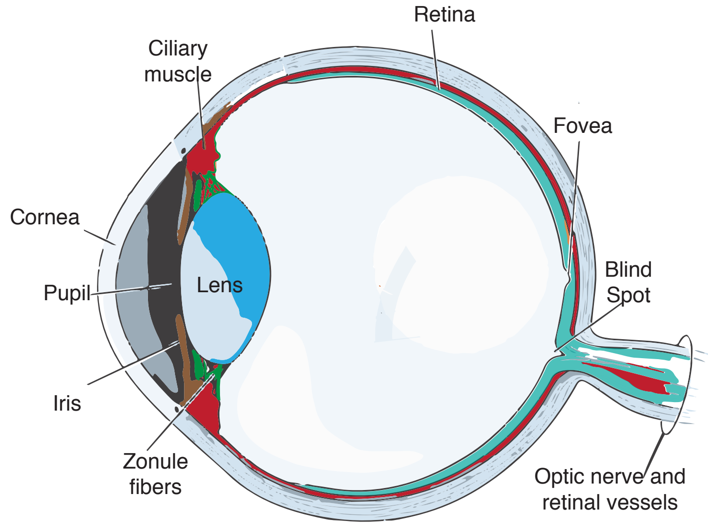
- Make a simple diagram of the structures light passes through before being detected by sensory neurons in the eye.
- List the steps in phototransduction including critical molecules and channels.
- Explain why phototransduction leads to photoreceptor hyperpolarization and reduction of neurotransmitter release upon light activation.
- Explain the advantages of having both rods and cones.

Lecture 13 - Vision 1: The eye and phototransduction

Pre-class notes for October 18, 2019
Reading: *Neuroscience ed. 6* by Purves et al., pages **233-250**

For the second half of the course, we will move beyond learning how an idealized single neuron or neuron pair sends signals, to learning about real circuits in the nervous system. We will start by thoroughly examining the visual system and how light information enters, is encoded, and eventually perceived by the nervous system. We will start with vision not just because visual is the sense that most humans rely on, as the saying *"seeing is believing"* indicates, but also because the visual system has been thoroughly studied and we have a good understanding on how visual information is processes and transmitted through the visual areas of the nervous system.

We feel that our visual perception is an exact representation of the world as it exists, but our nervous system filters, processes, and encodes visual information so objects can be readily identified and motion, or moving objects can be easily perceived in any environment or lighting. The eye itself plays a role in focusing the light and adjusting light levels. Light is first bent and focused by the *cornea*, and then enters the eye through the *pupil,* is further focused by the *lens*, before hitting the *retina,* the layers of neurons lining the back of the eye.



Cornea - specialized transparent tissue at the front of the eye. The curved surface of the cornea bends the light so that the light rays that hit the cornea at different angles are bent such that they converge on the back of the retina, to produce a crisp image. Thus, the cornea provides most of the *refractive power* of the eye.

Pupil - the opening in the *iris*, that allows light to enter the eye and eventually strike the retina on the back. The size of the pupil is determined by the **iris**, a thin circular structure.

Lens - another specialized transparent tissue that works in conjunctions with the cornea to focus light on the retina. Although the lens provides less refractive power than the cornea, it is adjustable so it plays a critical role in allowing the eye to bring objects at various distances into sharp focus. The *ciliary muscles* are attached to the lens by *zonule fibers.* When the ciliary muscles contract they reduce the tension on the zonule fibers, allowing the lens to become thicker and rounder, increasing the refractive power and improving the focus on near objects (*accomodation)*. When the ciliary muscles relax, the lens becomes flatter, which is better for distance vision.

Retina - innermost layer of the eye. Itself a layered structure that contains the visual sensory neurons, circuitry for the initial processing of visual information, as well as neurons that transmit that information to the brain.

Pigment epithelium - layer of cells just behind the retina that is heavily pigmented to absorb any scattered light that is not sensed by the sensory neurons. It also nourishes the sensory cells.

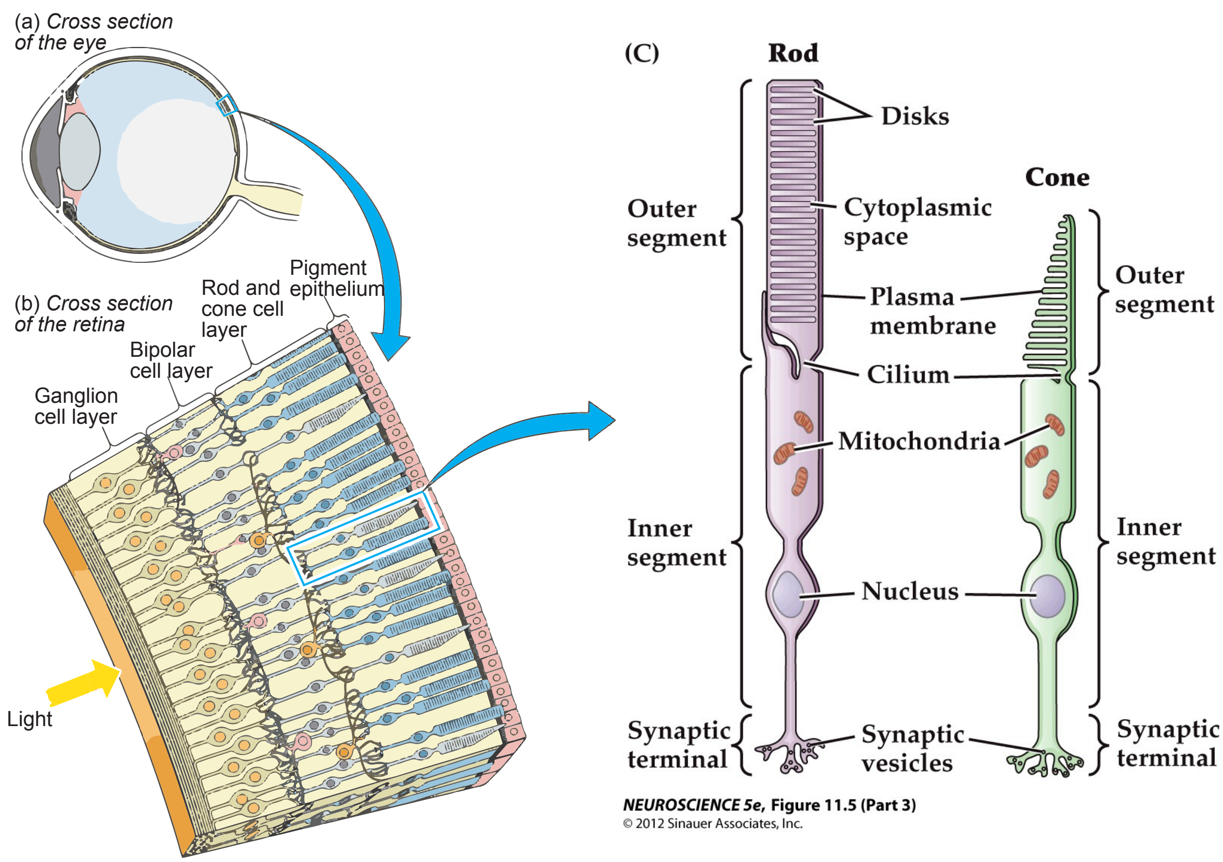
Fovea - Latin for pit, the fovea is the central, thinnest part of the retina that has a high density of cone photoreceptors, the least amount of *convergence* (multiple presynaptic neurons synapsing onto a single postsynaptic target), and the highest *acuity*.

Optic disk (blind spot) - the area on the back of the retina where the retinal blood vessels originate and where the axons carrying visual information exit the eye and carry visual information to the brain. There are no photoreceptors on the optic disk, which is why it creates a blind spot in the visual field for that eye.

Due to the limits of the structure of our eyes and anatomy, humans cannot see all of the world at one time. The **visual field**, is the extent of space seen by one eye. The ability of the eye to distinguish two points near each other is called visual **acuity**. Acuity depends on several factors but especially on the spacing of the sensory cells in the retina and the precision of the eye's refraction. The eye test we are familiar with at a doctor's office is a test of acuity, specifically the acuity of the fovea.

The retina is where light first encounters neurons, and light must actually pass by 4 other layers of neurons before reaching the *photoreceptors*, where special molecules absorb and detect light.

Photoreceptor - visual sensory cell that converts light into electrical signals. Located at the innermost layer of the retina next to the pigment epithelium. The *outer segment* of a photoreceptor cell contains membranous disks with light-sensitive photopigments, the *inner segment* contains the nucleus and the *synaptic terminal* releases glutamate onto bipolar and horizontal cells. Due to the presence of cGMP-gated cation channels, photoreceptors are relatively depolarized (V_{mem} ≈ 40 mV) in the dark. Photoreceptors do not fire action potentials as their axons are very short.



***NEUROSCIENCE 5e*, Figure 11.5 (Part 3)**

Rod cell - type of photoreceptor with very high sensitivity to light, but has very low spatial resolution and does not contribute to color vision. Rod cells are specialized for night vision and saturate in daylight.

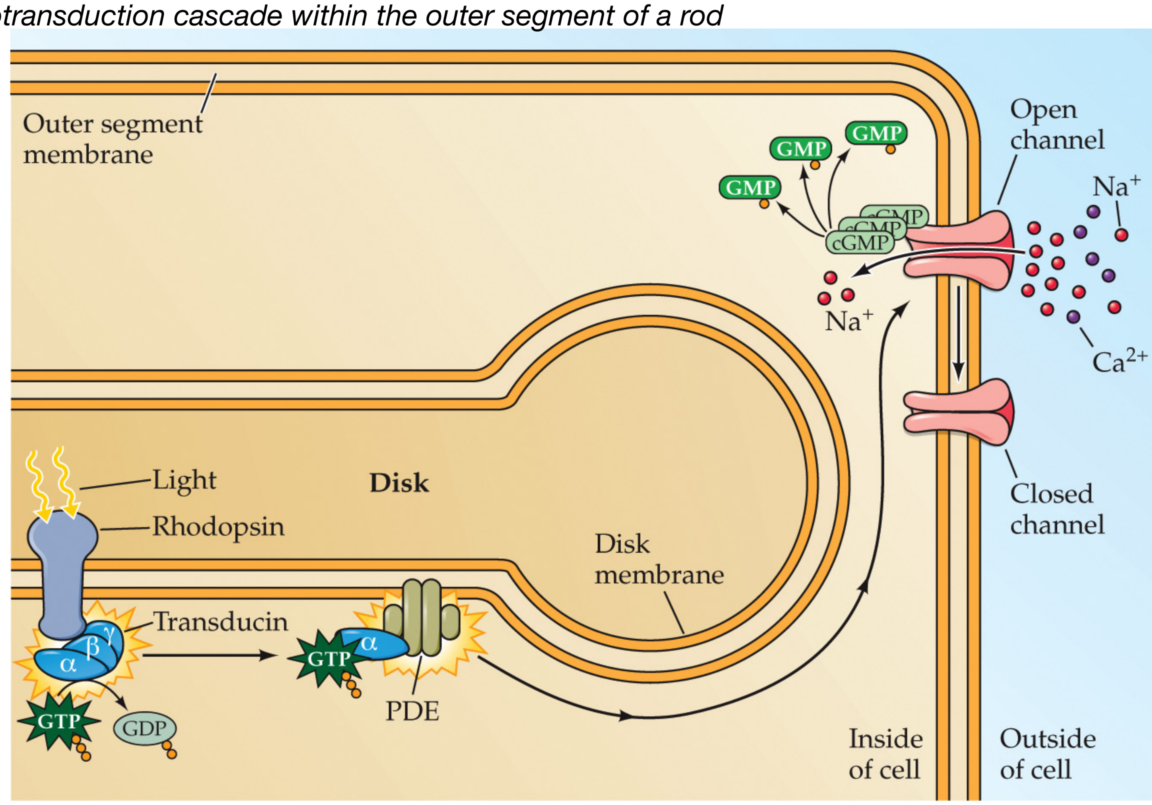
Cone cell - type of photoreceptor with very high spatial resolution, sensitivity to color and motion. It is relatively less sensitive to light than the rod cells and works best in daylight. In humans there are three different types of cones each detect different segments of the light spectrum: red (long wavelength), green (medium wavelength) and blue (short wavelength). Our brain then combines the signals of the different cone cells to give the perception of different colors.

Opsins - a family of g-protein couple receptors found in the membraneous disks of photoreceptors. In rods opsin is coupled with _retinal_ (a molecule derived from vitamin A) to form _rhodopsin_. Retinal can have 2 different isoforms. (*11-cis* and all-*trans* retinal). The colored opsins in cones are known by which colors (or wave length) they best detect (e.g. green/medium wavelength opsin).

Phototransduction is the biochemical process by which light is converted to an electrical signal within photoreceptor cells. Photoreceptors are strange, in the dark (or what we think of at rest) they are relatively depolarized, and light causes hyperpolarization. Although this seems counterintuitive, we will see that the retina is not just a photon detector, but senses the *change in light*, in which case detecting lights turning OFF (or getting dimmer) can be just as informative as detecting lights turning ON (or getting brighter).

In rods, when a photon converts the 11-*cis* retinal into all-*trans* retinal, the rhodopsin molecule also changes shape and activates the g-protein (*transducin*). Transducin activates another messenger (*phosphodiesterase)* which breaks down cGMP. Within the cell membrane of photoreceptor cells are cGMP-gated cation channels which allow the flow of Na^+ and Ca^{++} into the cell and K^+ out of the cell. Since light leads to a break down of cGMP, these cGMP-gated channels close causing the cell to hyperpolarize and release less neurotransmitter.

Phototransduction cascade within the outer segment of a rod



NEUROSCIENCE 6e, Figure 11.9 (Part 3)

Learning Objectives: (By the end of Lecture 13 you should be able answer the following)

1. Make a simple diagram of the structures light passes through before being detected by sensory neurons in the eye.
2. List the steps in phototransduction including critical molecules and channels.
3. Explain why phototransduction leads to photoreceptor hyperpolarization and reduction of neurotransmitter release upon light activation.
4. Explain the advantages of having both rods and cones.