Neuroscience II
Spring 2024
Lecture 2
Neurophysiology of Retina

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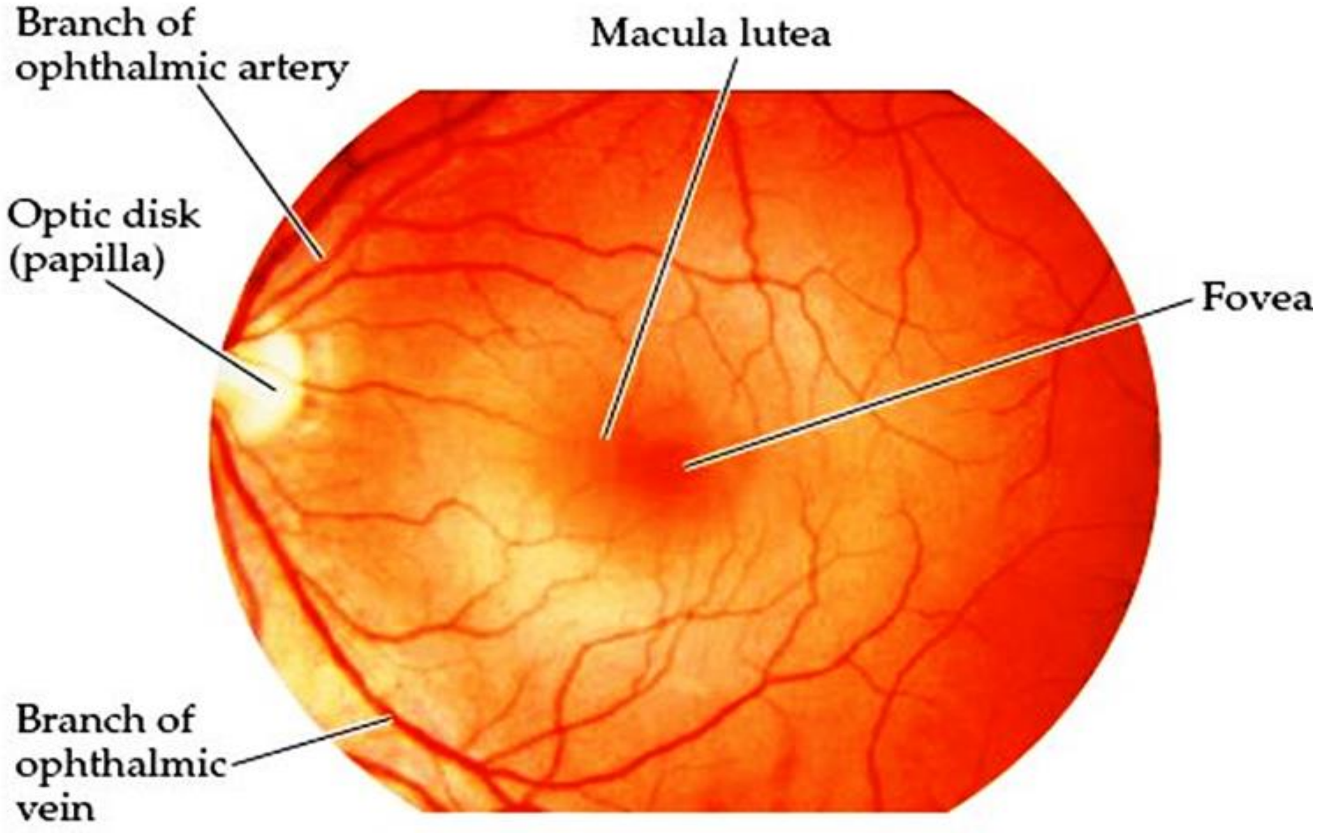
Learning objectives

- Describe the main features of the fundus in health individuals as visualized by the ophthalmoscope. (ophthalmoscopy)
- Describe the functional organization of the retina
- Describe the function of different neurons in the retina
- Describe properties of electrical responses produced by bipolar cells, horizontal cells, amacrine cells, and ganglion cells.
- Identify the anatomical component of rods and cones and list their functions
- Describe the chemical structure of photo pigments in rods and cones
- Explain the visual abnormalities (night blindness) caused by vitamin A deficiency
- List the sequence of events involved in photo transduction and the ionic basis of phototransduction.
- Explain visual transduction mechanism and the ionic basis of photo transduction .
- Define and outline the mechanism of light and dark adaptation
- Explain role of cones in color vision neuronal basis of color vision (Will be discussed during Lab session)
- List the main types of color vision abnormality vision (Will be discussed during Lab session)

The Inner surface of the retina, viewed with an ophthalmoscope.



Fundus of the eye and ophthalmoscopy

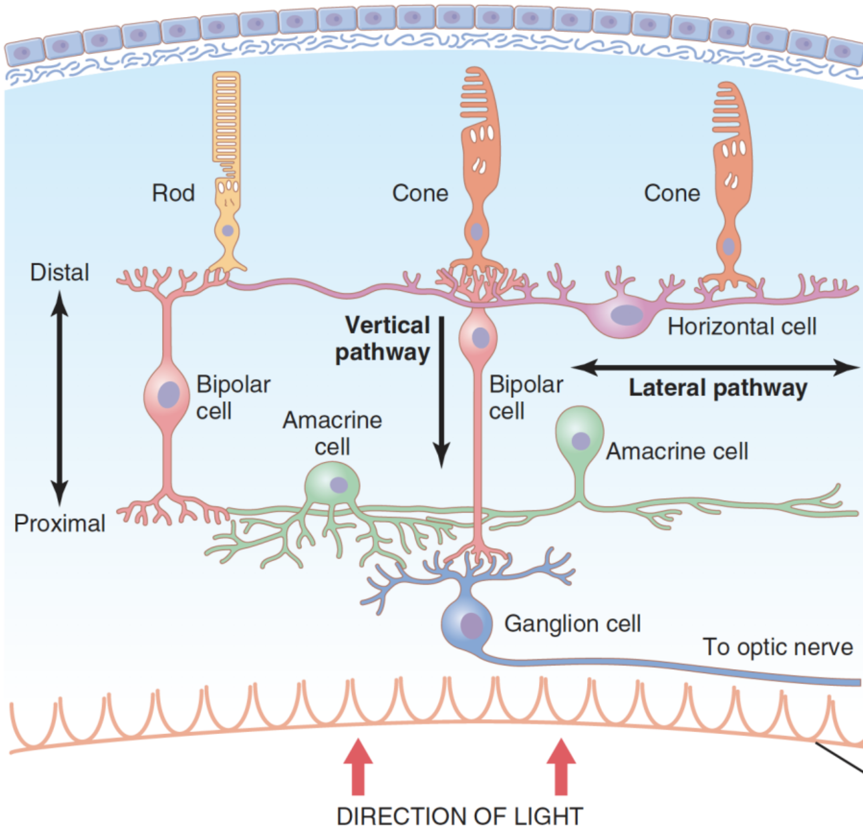
- The fundus of the eye refers to the interior surface of the eye.
- Includes the retina, optic disk, macula and fovea, and posterior pole.
- The retina is the innermost layer in the eye that is responsible for the visual processing that turns light energy from photons into images.[
- Located in the posterior portion of the eyeball
- the retina is the only extension of the brain that can be viewed from the outside world and gives ophthalmologists a rare window into real-time pathology affecting the retina
- Ganglion cells fibers (Optic nerve fibers) leave the eyeball at the optic disk to form the optic nerve.
- The point at which the optic nerve exits the eye is the optic disc (which corresponds to blind spot in the visual field). Optic nerve fibers composed of ganglion cells axons leave the eyeball at the optic disk to form the optic nerve This area has no photorecptors

Macula and fovea

- **Macula lutea** (Yellowish spot) is an area in the center of retina
- **Fovea centralis** Depression in centre of macula lutea (0.5 mm in diameter) a total area of fovea a little more than 1 square millimeter in this region retinal layers are thin.
- It is the rea of highest and most acute visual acuity and it is important for detailed colored visions.
- Fovea is the region of most **acute vision** because it contains **only cones**.
- The arteries, arterioles, and veins in the superficial layers of the retina near its vitreous surface can also be seen through the ophthalmoscope

Layers of retina

outer layers of the retina → utrition from choroid→ retinal detachment→ damage



- **Pigmented layer**: melanin called fuscin→ absorbs light & prevents reflection of light rays back from retina
  Albinos-poor visual acuity because of the scattering of light.
  stores vitamin A (precursor of the photosensitive chemicals)
- **Outer nuclear layer**: cell bodies of rods and cones
- **Outer plexiform layer**: synapses between dendrites of horizontal cells, bipolar cells & and photoreceptor cell
- **Inner nuclear layer**: bipolar cells, horizontal cells & amacrine cells.
- **Inner plexiform layer**: synapses between dendrites of ganglionic cells & axons of bipolar cells+ processes from amacrine cells.
- **Ganglion cell layer**: giant & midget ganglion cells → axons form the optic nerve
  Retinal blood vessels
- **Stratum opticum**: horizontal non-myelinated axons of ganglionic cells converge → optic disk
- **Inner limiting membrane**: separates retina from the vitreous body formed by Müller fibers

Inner layers of the retina → nutrition from central retinal artery

Physiological anatomy of the retina

- The **retina** is derived from the neural tube and is, therefore, part of central nervous system.
- It consists of two parts, the retinal pigment epithelium, which separates the middle, choroid coat of the eyeball from the other innermost component and the neural retina
- The RPE is a single layer of **cuboidal epithelial cells** and located in the outermost layer of the retina.
- The neuronal retina consists of different layers The innermost layers are located nearest the vitreous chamber, whereas the outermost layers are located adjacent to the retinal pigment epithelium and choroid.
- Types of cells in retina :
  - Photo (Visual)receptor cells (the rods and cones)
  - Horizontal cells
  - Bipolar cells
  - amacrine cells
  - ganglion cells.

Retinal layers and their function

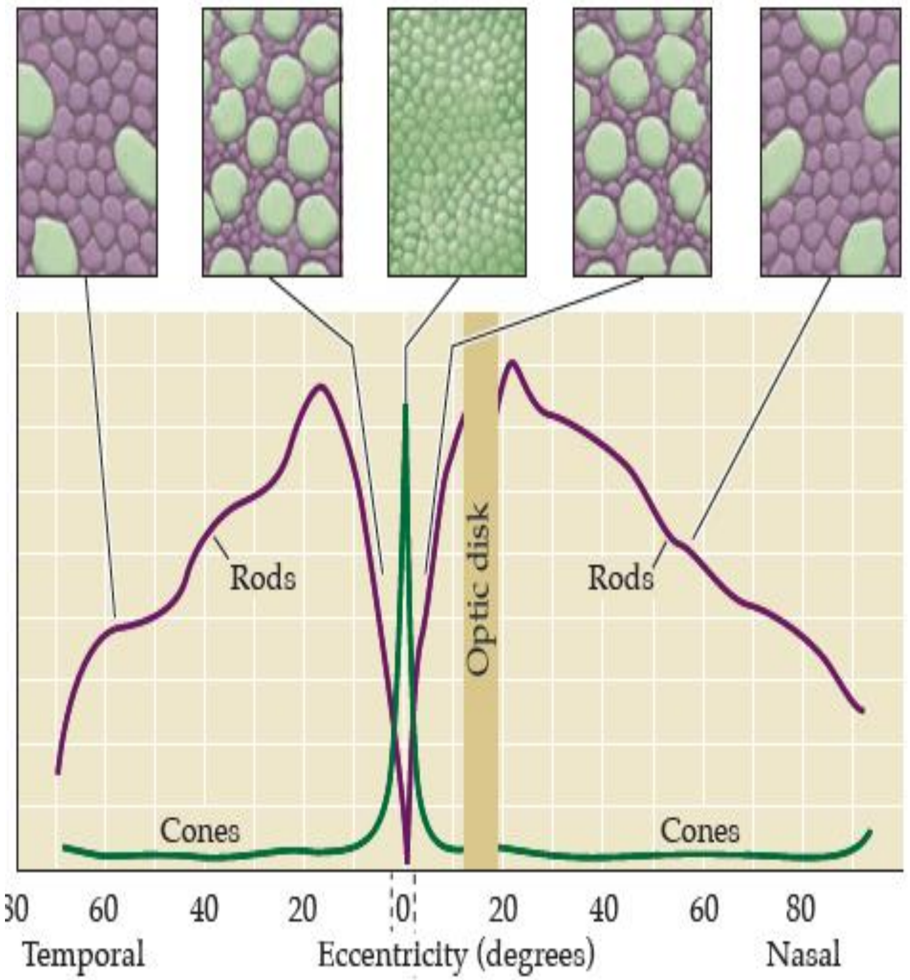
- **Pigment epithelium:**
  - provides critical metabolic and supportive functions to the photoreceptors
  - Prevents light refraction and diffuse illumination of the eye
  - Contains melanin
  - Store vitamin A. Thus , the RPE is also involved in a visual cycle as it regenerates photosensitive pigments
  - The tight junctions between the RPE cells form part of the **blood-retinal barrier**, which helps to prevent molecules passing from the choroid into the retina.
- absence of melanin in people with *albinism* (congenital absence of melanin pigment in all parts of their bodies).

Albinism and visual acuity

- When a person with albinism enters a bright room, light that impinges on the retina is reflected in all directions inside the eyeball by the unpigmented surfaces of the retina , so a single discrete spot of light that would normally excite only a few rods or cones is reflected everywhere and excites many receptors.
- Therefore, the visual acuity of people with albinism is severely impaired

Distribution of rods and cones in retina

Rod and cone distribution in the human retina.
In eccentricity 0, the cones are closely packed.
Moving away from the fovea, the cones become separated by rods; the distance between cones increases farther with greater eccentricity
Note the absence of rerectors at the optic disc site

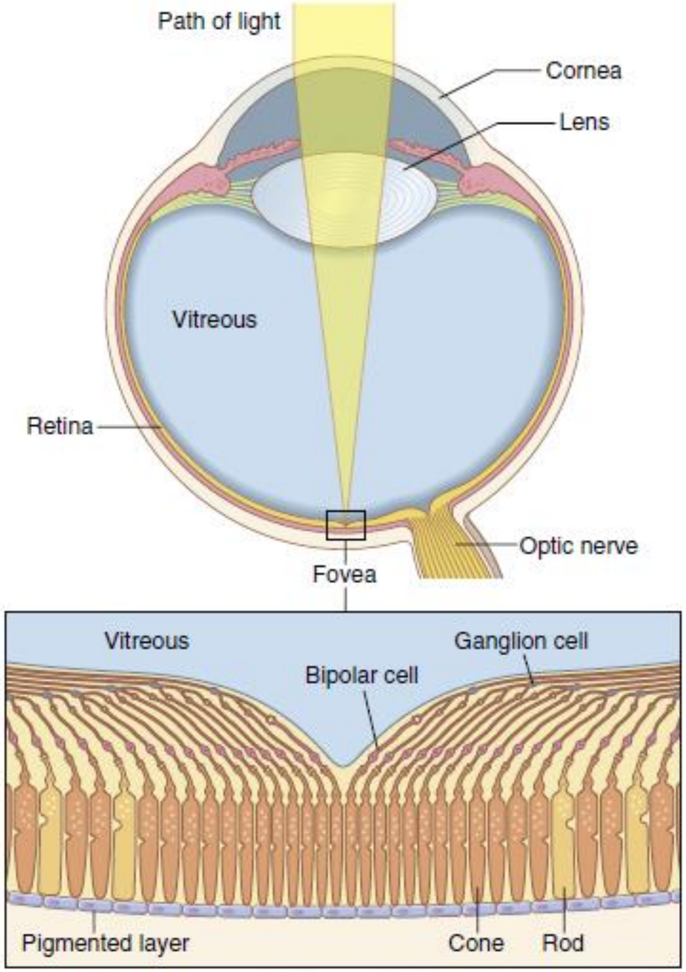


Characteristics of cons and other cell layers distribution in the fovea.

In the foveal region, the blood vessels, ganglion cells, inner nuclear layer of cells, and plexiform layers are all displaced to one side rather than resting directly on top of the cones,
which allows light to pass unimpeded to the cones.

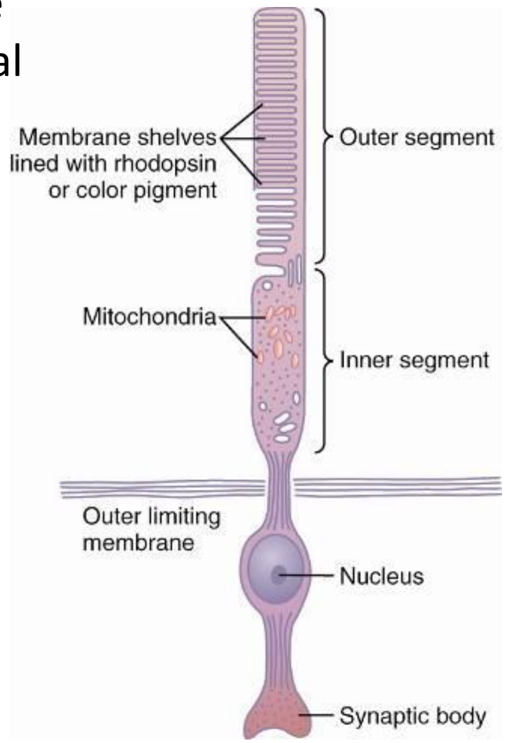
Visual acuity is decreased by light passage through nonhomogeneous tissue so lateral displacement increases visual

Note that visual acuity is decreased by light passage through nonhomogeneous tissue



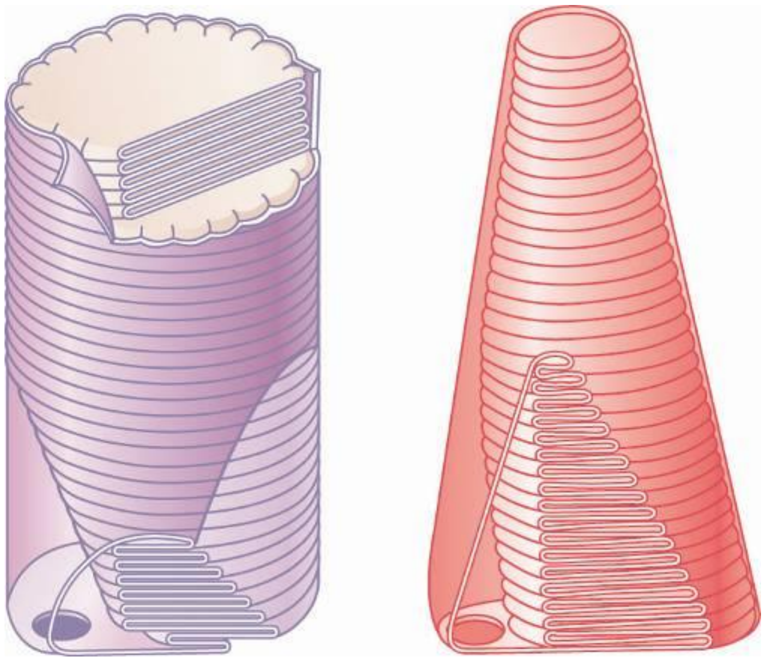
Structure of the Rods and Cones

light-sensitive
photochemical
40% of outer
seg. mass



rhodopsin

photopsin
Color/cone pigments



connects with horizontal and bipolar cells

The anatomical segments of a rod or a cone and their function

- *Outer segment*
  - Contains light-sensitive photochemical *rhodopsin in rods and* one of three "color" photochemical (*color pigments)*
  - light-sensitive chemicals found in rods and cones , absorb light , play a crucial role in the process of phototransduction (the conversion of light signals into electrical signals
  - Contain large numbers of *discs*. Each disc is an infolded shelf of cell membrane.
  - Both rhodopsin and the color pigments are conjugated proteins. They are incorporated into the membranes of the discs in the form of transmembrane proteins
- *Inner segment:* The *inner segment* of the rod or cone contains the usual cytoplasm, with cytoplasmic organelles and the mitochondria, which, play the important role of providing energy for function of the photoreceptors. *Including r metabolic and biosynthetic functions.*
- *Connecting cilium links inner and outer segments, enabling protein transport*
- *Nucleus*
- *Synaptic body:* which makes synapses with bipolar cells and horizontal cells .

Visual pigments

- **Photopigments:** light-sensitive chemicals found in rods and cones play a crucial role in the process of phototransduction (the conversion of light signals into electrical signals within photoreceptor cells).

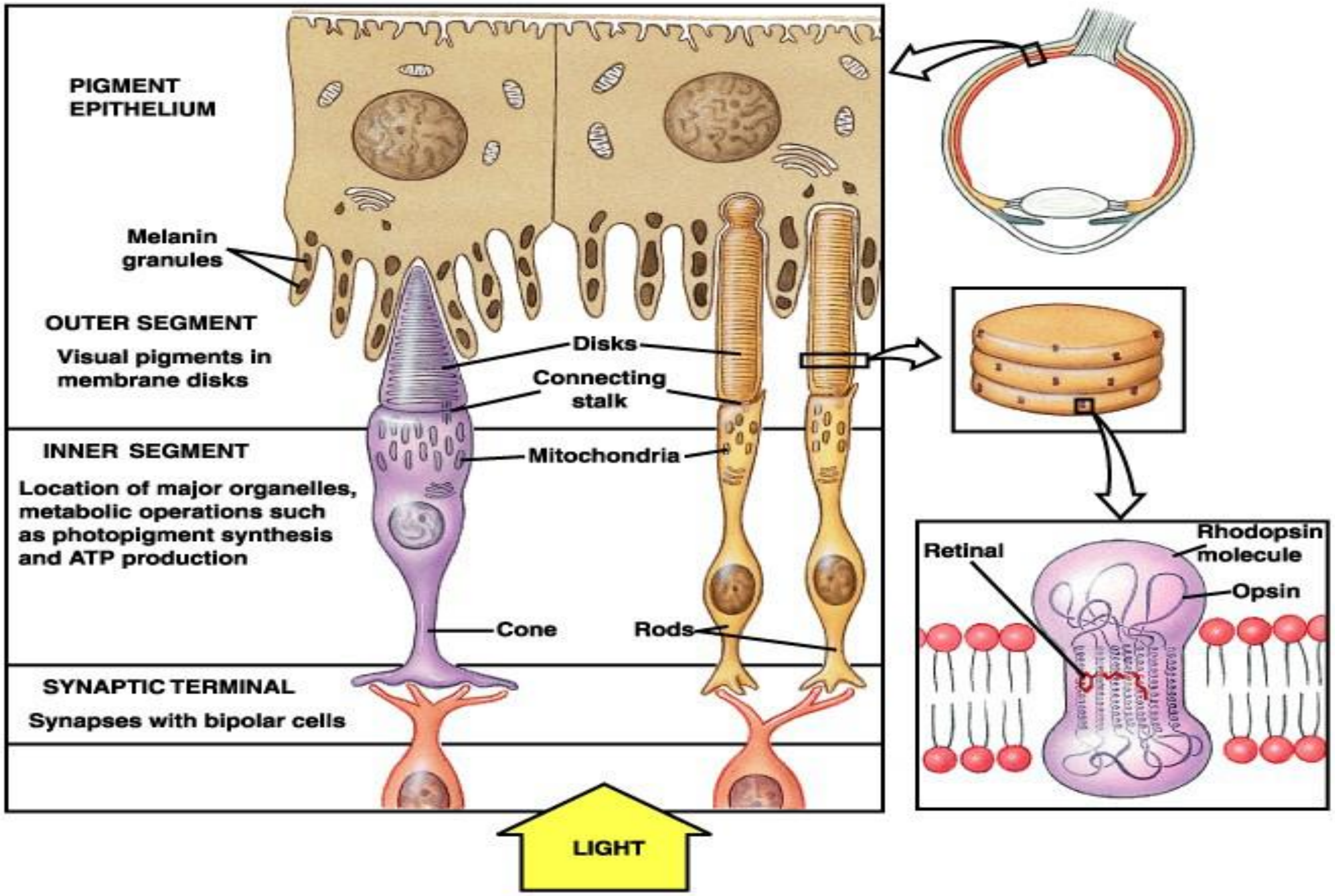
- Captures and absorbs light. This Initiates biochemical reactions for generating electrical signals.

- Rods photopigment= Rhodopsin, Cones photopigment= Colour pigment.
- These photopigments consist of two primary components:

1. A protein: The type of protein differs between rods and cones.
    1. Rods: Contain scotopsin
    2. Cones: Contain photopsin
2. An aldehyde form of Vitamin A (retinal): Vitamin A is the same in both rods and cones.

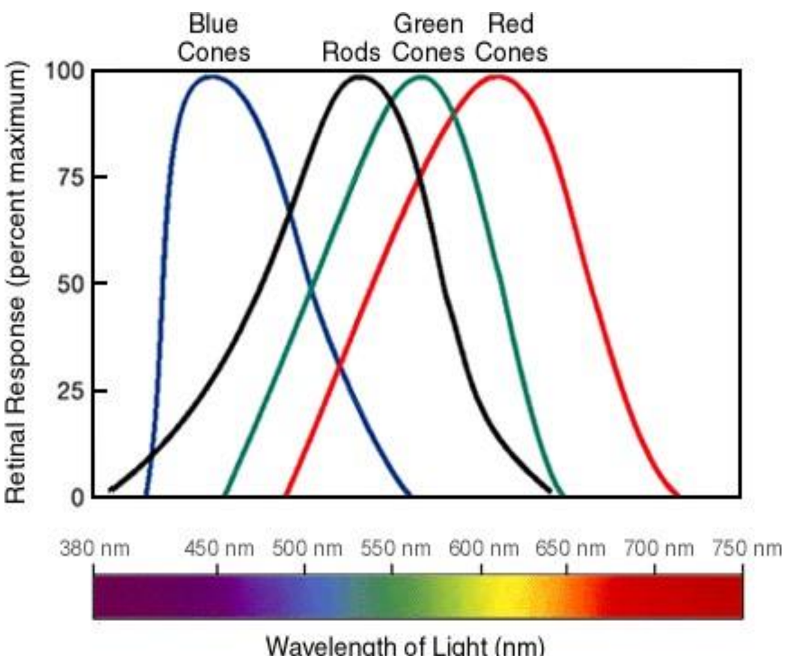
- The structural difference in photopigments between rods and cones lies in the protein type.

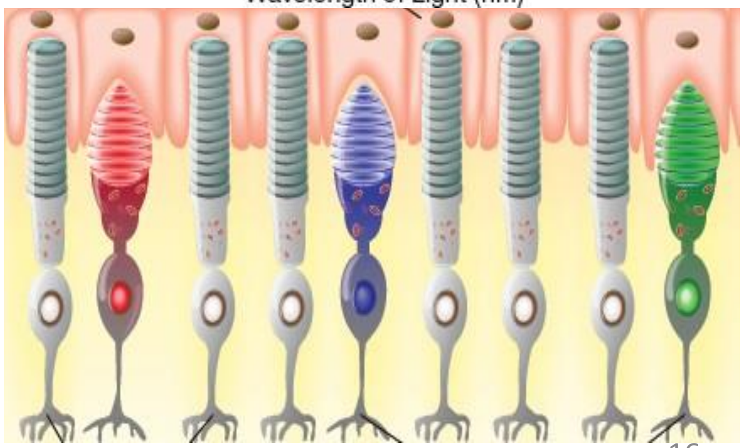
Visual pigments



Cones photopigment and Light absorption by the pigment of the rods and by the pigments of the three color-receptive cones of the human retina.

- Know as Photopsin
- Combinations of retinal and photopsins
- Stored in photoreceptors discs
- The cones in our retinas contain one three opsins that give the photopigments different spectral sensitivities.
- S cone (Blue cone) short-wavelength cones that are maximally activated by light with a wavelength of about 430 nm,
- M cone (Green cones) that are maximally activated by light with a wavelength of about 530 nm
- L cone (Red cones) that are maximally activated by light with a wavelength of about 560 nm

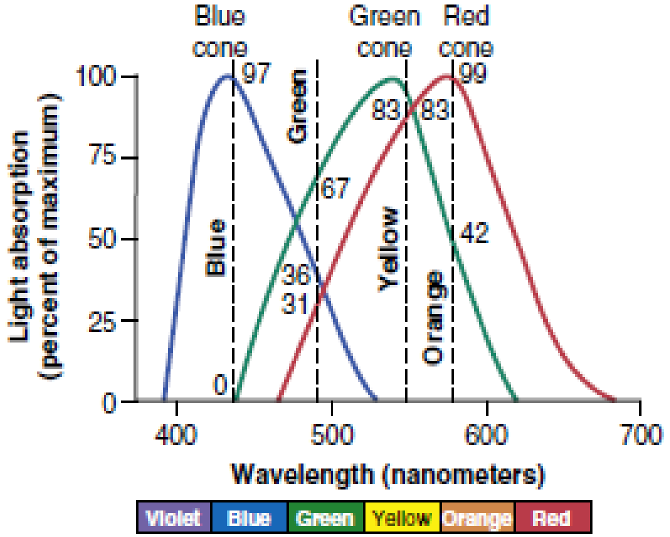




Demonstration of the degree of stimulation of the different color-sensitive cones by monochromatic lights of four colors—blue, green, yellow, and orange.

Interpretation of Color in the Nervous System

An orange monochromatic
light with a wavelength of 580 nanometers stimulates the red cones to a value of about 99 (99% of the peak stimulation at optimum wavelength); it stimulates the green cones to a value of about 42, but the blue cones are not Thus, the ratios of stimulation of the three type of cones in this case are 99:42:0. The nervous system interprets this set of ratios as the sensation of orange.
a monochromatic blue light with Conversely, a monochromatic blue light with a wavelength of 450 nanometers stimulates mainly blue cone 97 So the set of rations 97 0 0 is intercepted by the brain as blue



Role of Vitamin A

- Vitamin A is the precursor of all-transretinal, the pigment portion of rhodopsin.
- Decrease vitamin reduced production of rhodopsin and a lower sensitivity of the retina to light or night blindness (nyctalopia).
- Vitamin A deficiency also contributes to blindness by causing the eye to become very dry, which damages the cornea (xerophthalmia) and retina.
- Vitamin A deficiency first alters rod function, but concomitant cone degeneration occurs as vitamin A deficiency develops.
- Prolonged deficiency is associated with anatomic changes in the rods and cones followed by degeneration of the neural layers of the retina

Comparison of rods and cones

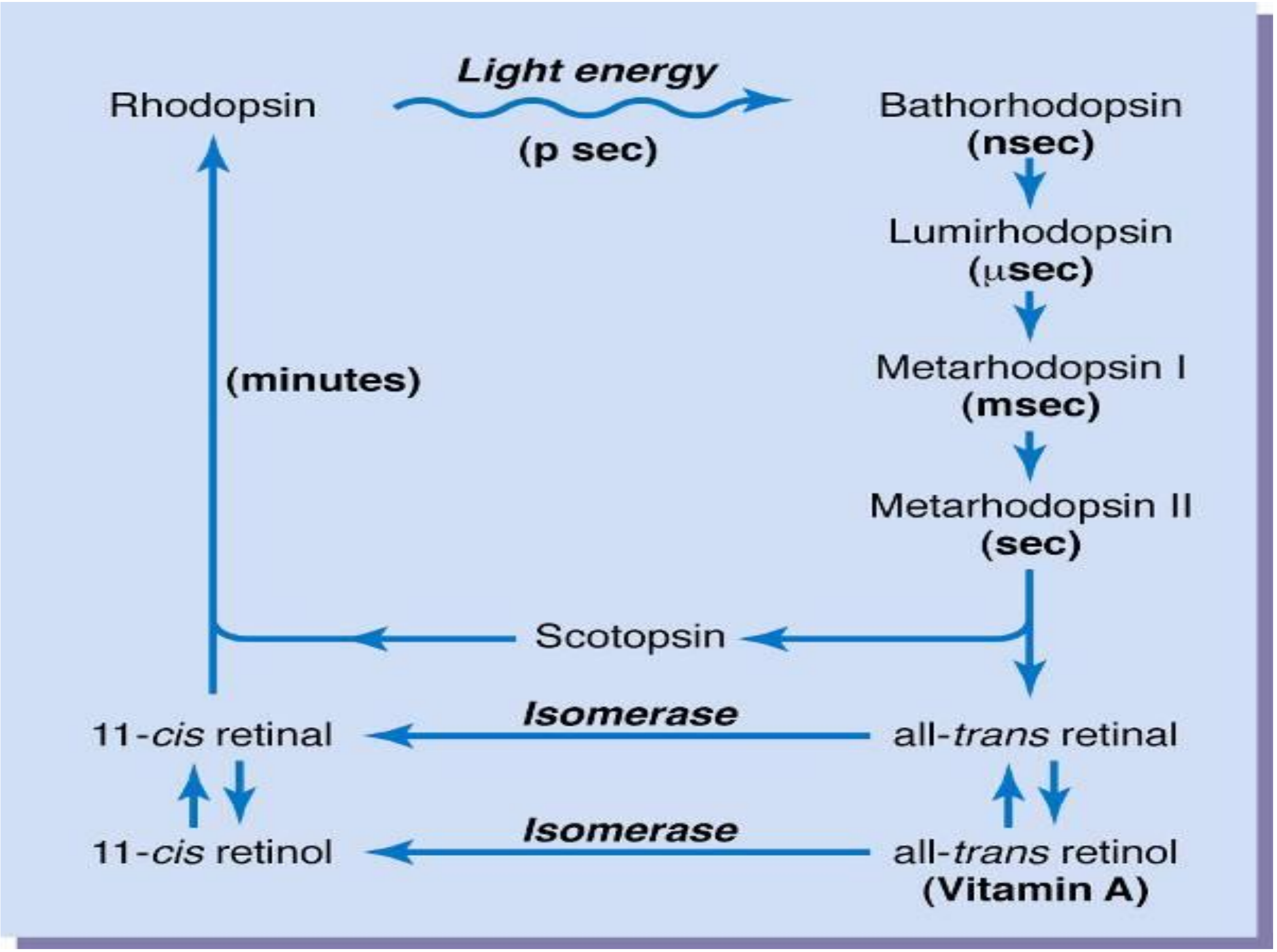
Rods	Rods Vs Cones:	Cones
120 millions	No. (In one eye)	6 Millions
None in fovea centralis (found mostly in peripheral retina)	Distribution	Highly concentrated in fovea
Scotopsin	Protein in photopigment	Photopsin
Low	Acuity	High
Very sensitive (excited by little amount of light) Specialized for scotopic vision Night Vision	Sensitivity to light	Less sensitive , have high (needs more light for excitation)Less photopigment so lower Day light vision (Photopic vision) and colored vision
500 nm (colour blind)	Peak of wave length sensitivity	Depends on the type of cones (colour sensitive)
Slow	Adaptation to dark	Fast (the metabolic processes are fast)
Need more time	Excitation time	Need less time
One	Types	Three
High level of convergence Less area of cortical presentation	Receptors/ganglion ratio	Low level (or no) convergence High cortical area presentation high visual acuity

Rhodopsin Or *Visual Purple*

- The outer segment of the rod that projects into the pigment layer of the retina has a concentration of about 40% of the light-sensitive pigment called *rhodopsin*, or *visual purple.*
- This substance is a combination of the protein *scotopsin* and the carotenoid pigment *retinal* (also called "retinene").
- Furthermore, the retinal is a particular type called 11-*cis* retinal. This *cis* form of retinal is important because only this form can bind with scotopsin to synthesize rhodopsin

RHODOPSIN-RETINAL VISUAL CYCLE AND EXCITATION OF THE ROD

Rhodopsin and Its Decomposition by Light Energy



RHODOPSIN-RETINAL VISUAL CYCLE AND EXCITATION OF THE ROD

Rhodopsin and Its Decomposition by Light Energy.

- When light energy is absorbed by rhodopsin, the rhodopsin begins to decompose within a very small fraction of a second, as shown at the top
- The causeof this rapid decomposition is photoactivation of electrons in the retinal portion of the rhodopsin, which leads to instantaneous change of the *cis* form of retinal into an all-*trans* form that has the same chemical structure as the *cis* form but a different physical structure—it is a straight molecule rather than an angulated molecule the all-*trans* retinal begins to pull away from the scotopsin.
- Serval intermediates and finally the formation of *metarhodopsin II*, and finally, much more slowly (in seconds),into the completely split products *scotopsin* and all-*trans* retinal.
- It is the metarhodopsin II, also called *activated rhodopsin*, that excites electrical changes in the rods, and the rods then transmit the visual image into the central nervous system in the form of optic nerve action potentials,

Re-Formation of Rhodopsin

- The first stage in re-formation of rhodopsin, is to reconvert the all-*trans*
- retinal into 11-*cis* retinal. This process requires metabolic energy and is catalyzed by the enzyme
- *retinal isomerase.* Once the 11-*cis* retinal is formed, it automatically recombines with the scotopsin to re-form rhodopsin, which then remains stable until its decomposition is again triggered by absorption of light energy
- **Role of Vitamin A for Formation of Rhodopsin**
- This second route is by conversion of the all-*trans* retinal first into all-*trans* retinol, which is one form of vitamin A. Then, the all-*trans* retinol is converted into 11-*cis* retinol under the influence of the enzyme isomerase.
- Finally, the 11-*cis* retinol is converted into 11-*cis* retinal, which combines with scotopsin to form new rhodopsin

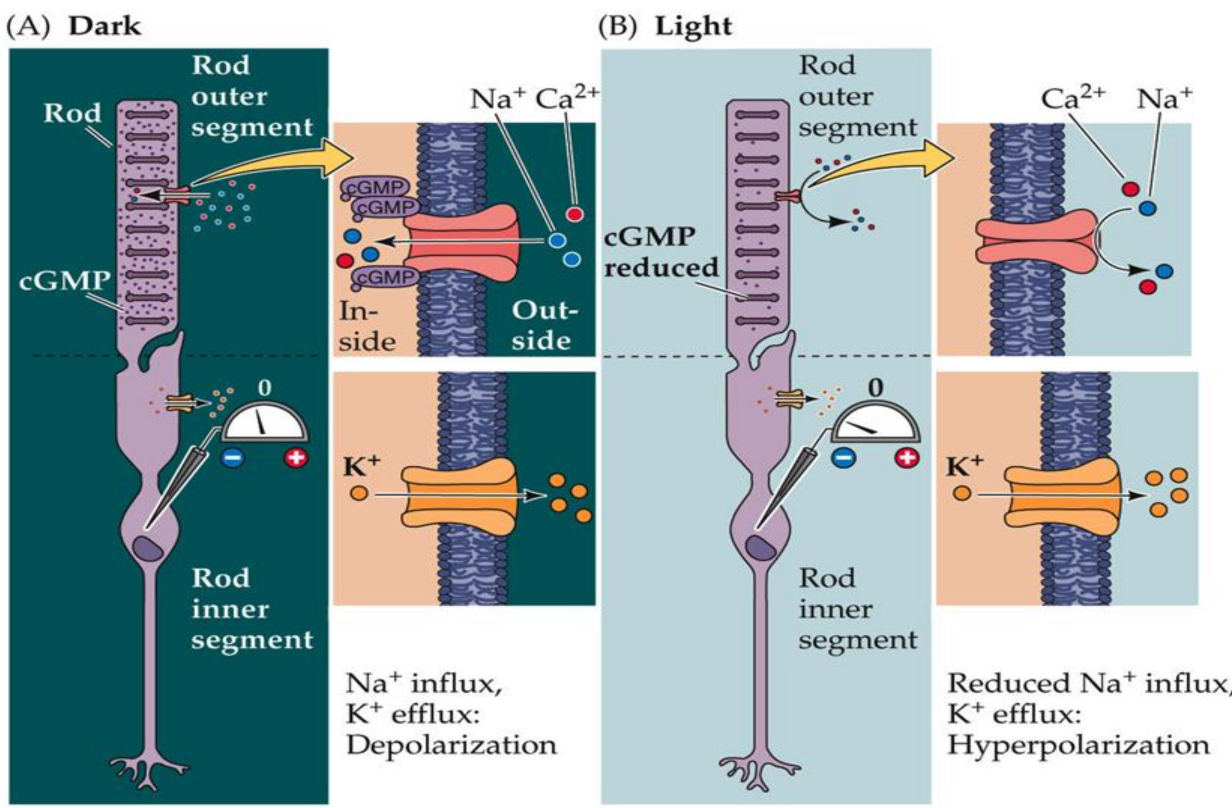
Electrical properties of receptors : The Rod Receptor Potential in the dark

- Normally about -40 mV in the dark (depolarized)
- Normally the outer segment of the rod is very permeable to Na^+ ions during darkness
- In the dark an inward current (the dark current) carried by the Na^+ ions flows into the outer segment of the rod , the opening of channels depends on the level of intracellular cGMP
- The current flows out of the cell, through the efflux of K^+, ions in the inner segment of the rod.
- The photoreceptors exhibit a fairly high basal release of glutamate during darkness

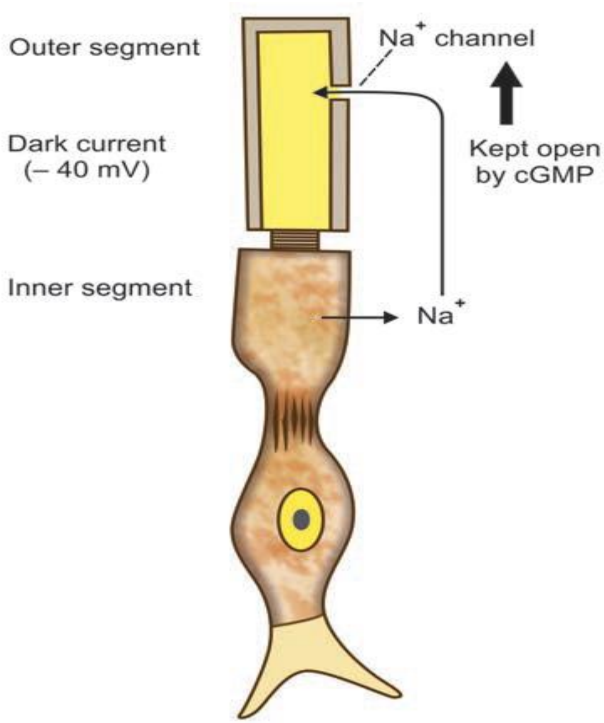
Properties of rods and cones receptor potentials

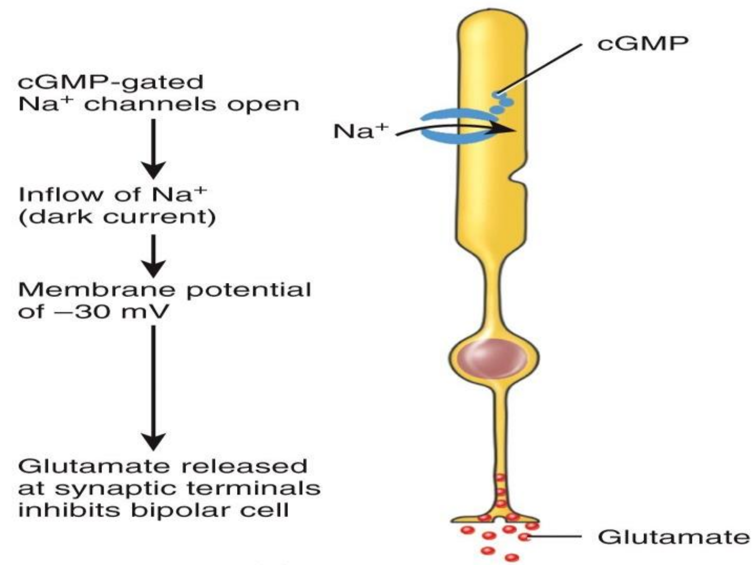
- Depolarization in darkness and hyperpolarization upon light exposure
- The cone receptor potential has a sharp onset and offset.
- The rod receptor potential has a sharp onset and slow offset.
- Receptor potential is **a graded response** to a stimulus that may be depolarizing or hyperpolarizing.
- Electronic conduction ie no action potential
- Graded means the amplitude of the receptor potential is proportional to the size of the stimulus/ log of light intensity →allows eye to discriminate light intensities

Electrical changes in rods when phototransduction is initiated by light



Electrical activity of photoreceptors in darkness





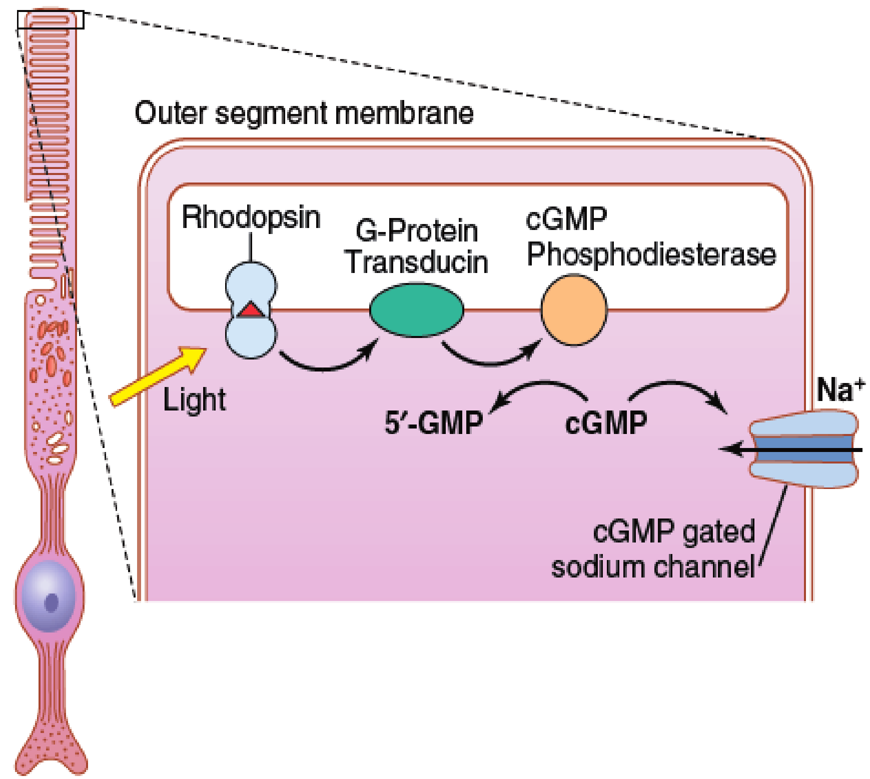
(a) In darkness

In darkness, when phosphodiesterase activity is low, cGMP-gated Na+ channels are maintained in an open state so both Na+ and Ca2+ enter the photoreceptor; the cell is depolarized, and glutamate is released. Glutamate release change the response off bipolar cells and ganglion cells.

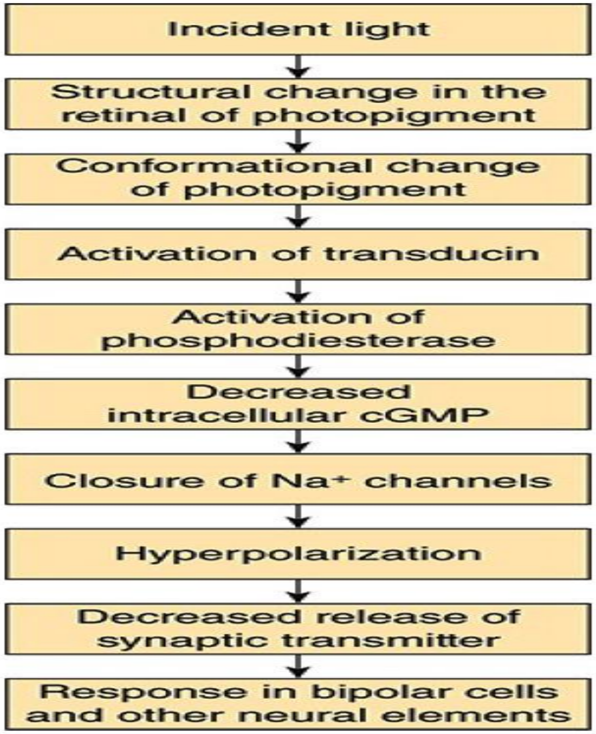
Note that there is basal release of glutamic during darkness

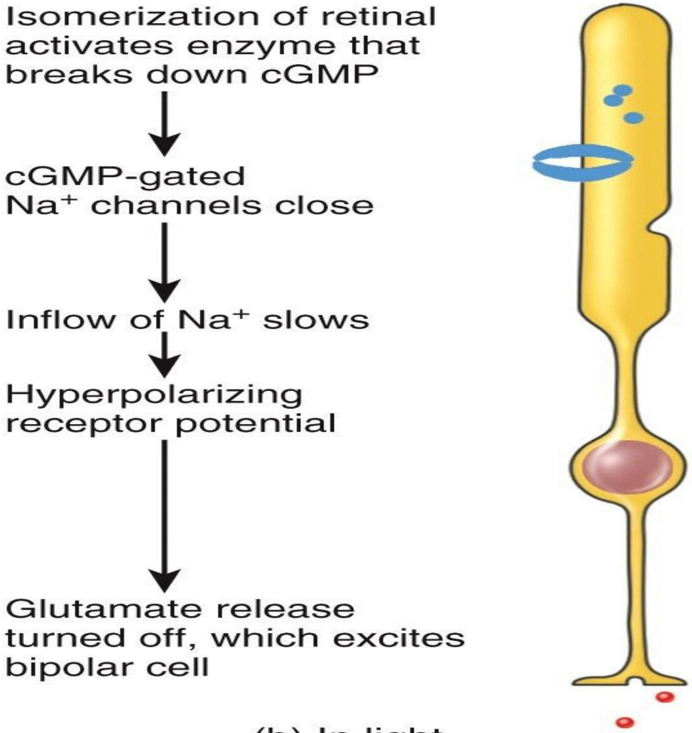
Phototransduction in the outer segment of the photoreceptor (rod or cone) membrane.

When light hits the photoreceptor (e.g., a rod cell), the light-absorbing retinal portion of rhodopsin is activated.
This activation stimulates transducin, a G protein, which then activates cyclic guanosine monophosphate (cGMP) phosphodiesterase.
This enzyme catalyzes the degradation of cGMP into 5′-GMP.
The reduction in cGMP then causes closure of the sodium channels, which, in turn, causes hyperpolarization of the photoreceptor
Within about 1 second, another enzyme, *rhodopsin kinase*, which is always present in the rod, inactivates the activated rhodopsin (metarhodopsin II), and the entire cascade reverses back to the normal state with open sodium channels



Phototransduction and change in electrical activity of photoreceptors





(b) In light

The light induced decline in the cytoplasmic cGMP concentration causes some cGMP gated Na+ channels to close, reducing the entry of Na+ and Ca2+ and producing the hyperpolarizing potential. This cascade of reactions occurs very rapidly and amplifies the light signal. The amplification helps explain the remarkable sensitivity of rod photoreceptors; these receptors can produce a detectable response to as little as one photon of light.

light adaptation

- If a person has been in bright light for hours, large portions of the photochemicals in both the rods and the cones will have been reduced to retinal and opsins. Furthermore, much of the retinal of both the rods and the cones will have been converted into vitamin A.
- Because of these two effects, the concentrations of the photosensitive chemicals remaining in the rods and cones are considerably reduced, and the sensitivity of the eye to light is correspondingly reduced.
- This type of adaptation also occurs when a person passes suddenly from a dim to a brightly lighted environment
- This adaptation occurs over a period of about 5 min and is called light adaptation
  - constriction of the pupil helps a bit in reducing the light entering the eye
  - Neuronal adaption in the visual path ways ??

dark adaptation

- if a person remains in darkness for a long time, the retinal and opsins in the rods and cones are converted back into the light-sensitive pigments.
- Furthermore, vitamin A is converted back into retinal to increase light-sensitivepigments, the final limit being determined by the amount of opsins in the rods and cones to combine with the retinal.
- Also , a decline in visual threshold and gradual increase in photoreceptor sensitivity when moving from bright light to dim environment or a dark room is also known as dark adaption
- It is nearly maximal in about 20 min, although some further decline occurs over longer periods.
- The dark adaptation response has two components
  - The first drop in visual threshold, rapid but small in magnitude, is due to dark adaptation of the cones
  - Further drop in visual threshold occurs because of adaptation of the rods in peripheral retina
  - Increased rhodopsin in rods produces greater increase in sensitivity , 100,00-fold increase in light sensitivity in rods