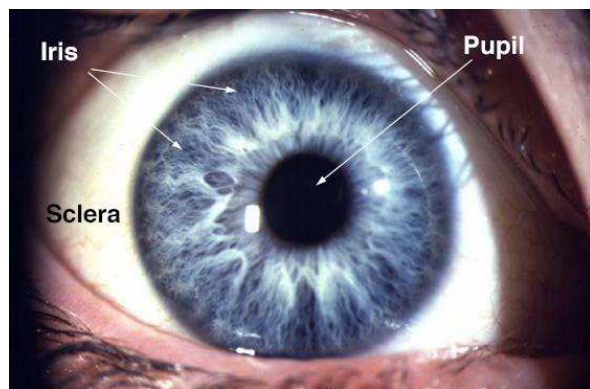


# Vision

- A glance at an object lets us know where it is, its size, shape, color, texture, direction and speed of movement
- We can do this at many different intensities of light from faint light to bright sunlight
- Two main components of the CNS are responsible for this: the retina in the eye and the visual centers of the brain



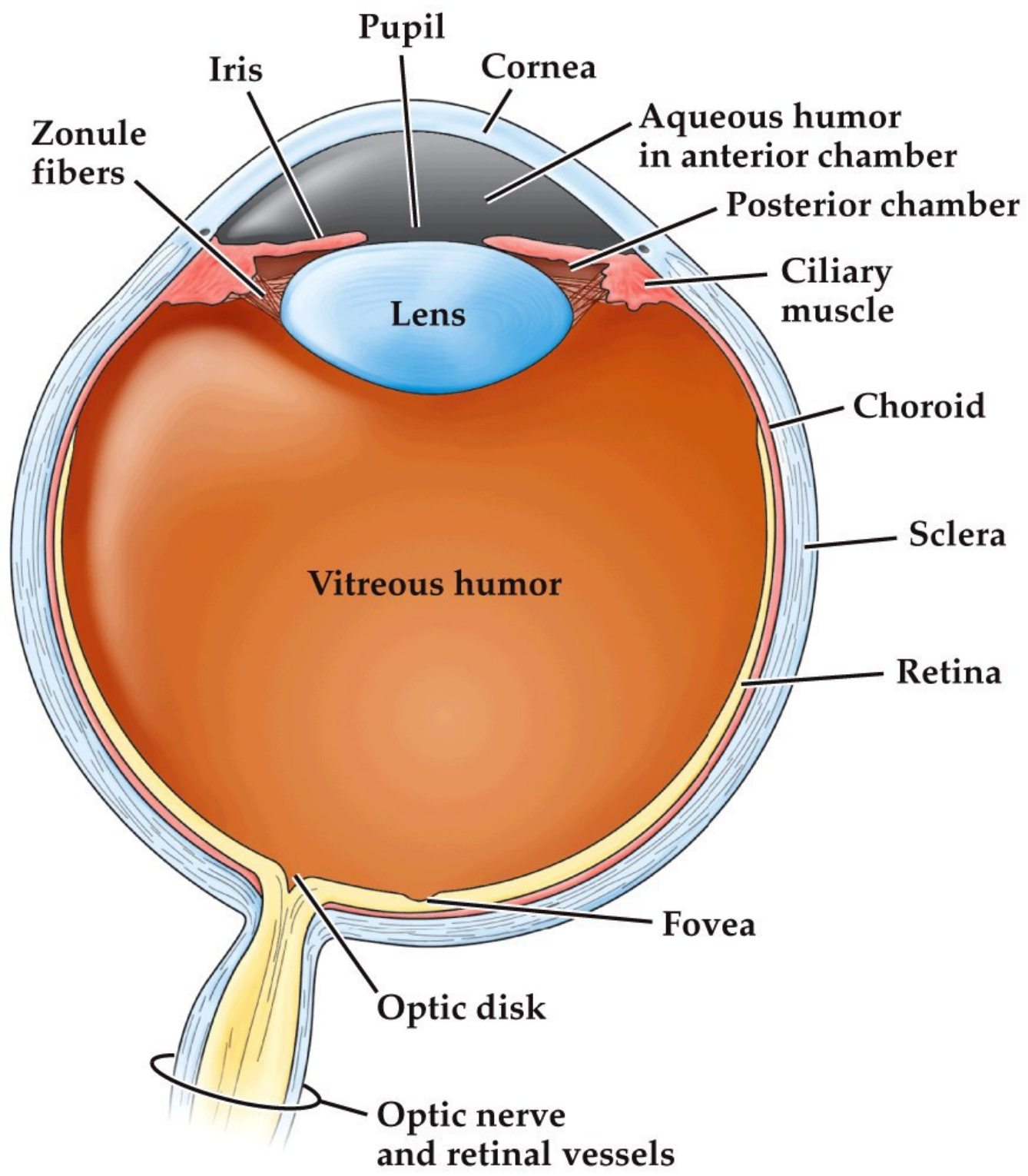
[H. Kolb Webvision, med.utah.edu](http://H.KolbWebvision.med.utah.edu)

Speaker notes

Learning goals:

- Identify the major parts of eye and retinal anatomy and their functions
- Become aware of the main proteins involved in the signal transduction pathway that lead to changes in membrane potential, calcium flux, and ultimately changes in amount of neurotransmitter released by photoreceptive cells in response to light
- Learn the neural pathway that takes information from photoreceptors to the brain
- Understand the concept of the receptive field

# Anatomy of the human eye



Neuroscience 5e Fig. 11.1

# Anatomy of the human eye video



Neuroscience 5e Animation 11.1

# Parts of the eye

- Outside:
  - **Sclera**– outer layer composed of white fibrous tissue
  - **Cornea**– front part of eye, transparent, provides 80% refractive power of the eye
- Middle:
  - **Iris**– colored portion of the eye, contains muscles that adjust the pupil size under neural control. Open during dim light, closed during bright light
  - **Ciliary body**– ring of tissue that encircles the lens and includes both a muscle component and a vascular component
  - **Choroid**– composed of a rich capillary bed that serves as the main blood supply for the photoreceptors and contains melanin containing cells
- Inside:
  - **Retina**– neural part of the eye, detects light, processes information, and sends it to the brain
  - **Lens**– transparent structure that and change shape to allow fine focus
  - **Aqueous humor**– in anterior chamber, supplies nutrients to anterior eye
  - **Vitreous humor**– gelatinous substance in posterior chamber, provides shape, contains macrophages that removes debris

Increased curvature in an optical lens increases the refraction of light, allowing closer focal distance.

Lens held in place by zonule fibers (connective tissue bands). Two opposing forces-- tension of lens tends to keep it rounded up (into a sphere if removed) and tension of zonule fibers which tend to flatten it.

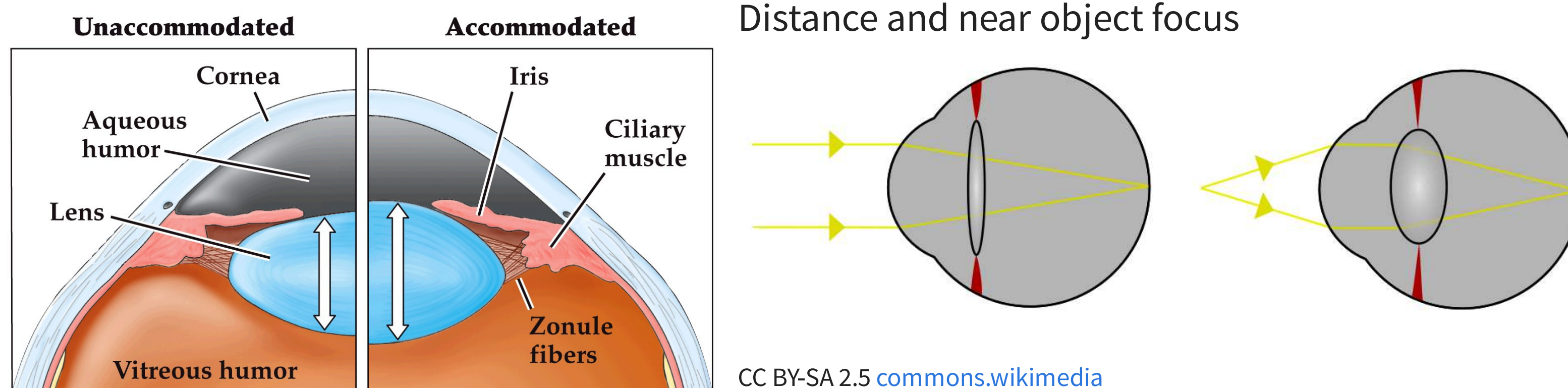
Contraction of ciliary muscle as a ring around the lens causes zonule fibers to reduce tension on lens allowing lens to increase curvature.

Pupil has circular muscles that contract when pupil closes, and radial bands of muscles that contract when pupil dilates.

- Efferent pathway controlling the iris and ciliary muscle are via the Edinger-Westphal nucleus --> ciliary ganglion (parasympathetic, cranial nerve III, oculomotor nerve) --> ciliary muscle
  - more on this in vision2

# Anterior of the human eye in the unaccommodated and accommodated state

Accommodation to focusing on near objects involves the contraction of the ciliary muscle, which reduces tension of the Zonule fibers and the lens is allowed to increase its curvature



Neuroscience 5e Fig. 11.2

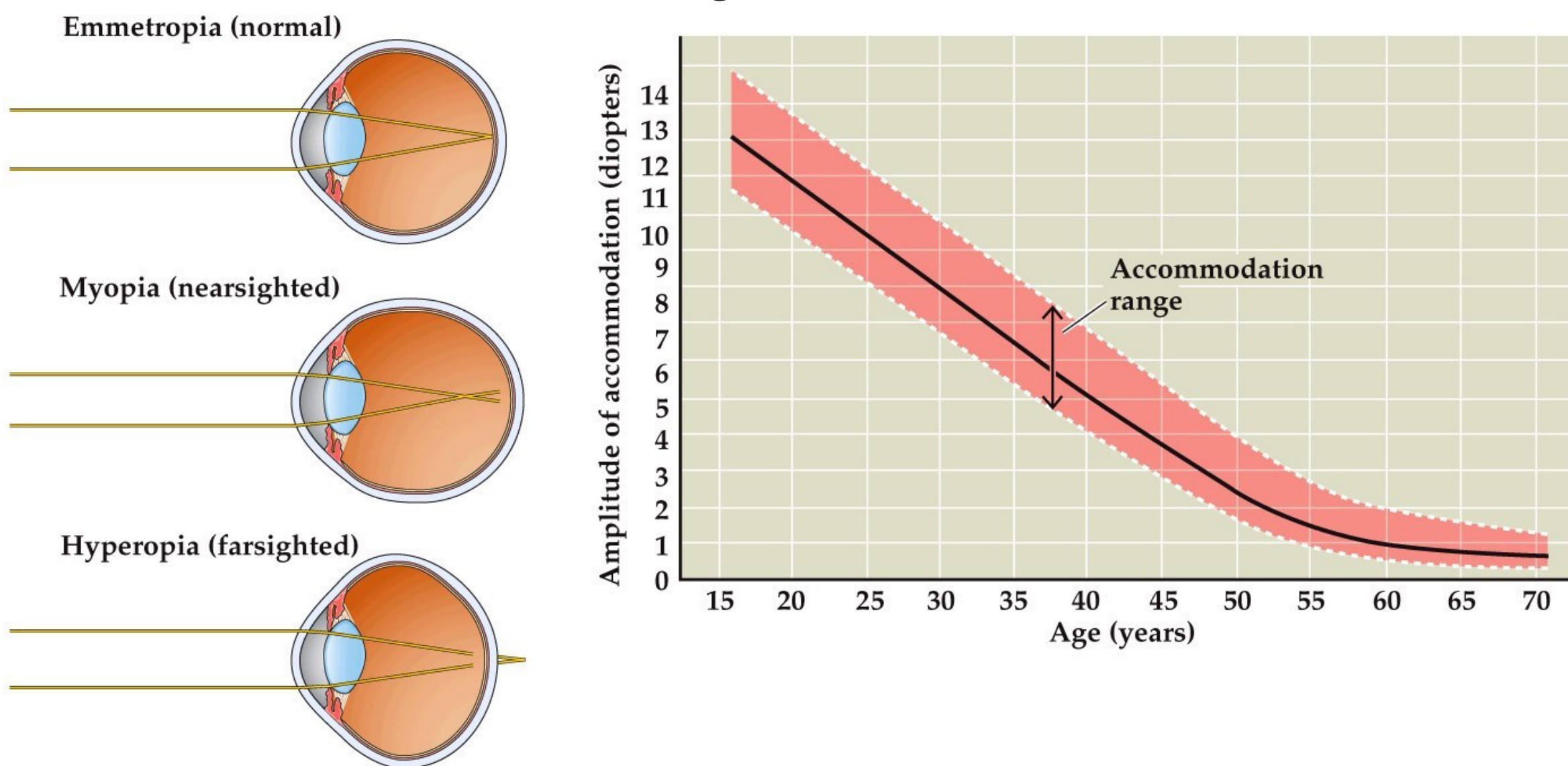
The lens loses elasticity with age (trouble focusing on near objects).

diopter is a unit of measurement of the optical power of a lens or curved mirror, which is equal to the reciprocal of the focal length measured in metres (that is,  $1/\text{metres}$ )

# Myopia & Hyperopia

- Myopia: eyeball too long or cornea too curved while lens is as flat as can be. Image focuses in front. Near sightedness
- Hyperopia: eyeball too short or refracting system too weak. Image focuses behind eye. Far sightedness

Reduced accommodation with age



Neuroscience 5e Box 11A

# Diseases of the anterior eye

- Cataracts– clouding of the lens
- Floaters– happens when the vitreous slowly shrinks, it becomes stringy and the strands cast a shadow on the retina
- Refractive errors, near and far sightedness



cataracts, Mayo Clinic

## Speaker notes

Lens proteins denature and degrade over time, and this process is accelerated by diseases.

genetic disorder, diabetes, surgery, long term steroid use, UV light

from: [https://en.wikipedia.org/wiki/Lens\\_\(anatomy\)](https://en.wikipedia.org/wiki/Lens_(anatomy))

*Crystallins are water-soluble proteins that compose over 90% of the protein within the lens*

*The three main crystallin types found in the human eye are  $\alpha$ -,  $\beta$ -, and  $\gamma$ -crystallins.*

*The refractive index of human lens varies from approximately 1.406 in the central layers down to 1.386 in less dense layers of the lens.[10] This index gradient enhances the optical power of the lens*

*Crystallins tend to form soluble, high-molecular weight aggregates that pack tightly in lens fibers*

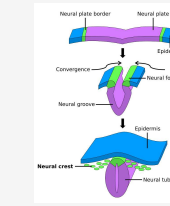
*lens capsule is a smooth, transparent basement membrane that completely surrounds the lens. The capsule is elastic and is composed of collagen. It is synthesized by the lens epithelium and its main components are Type IV collagen and sulfated glycosaminoglycans (GAGs)*

*cells of the lens epithelium also serve as the progenitors for new lens fibers. It constantly lays down fibers in the embryo, fetus, infant, and adult, and continues to lay down fibers for lifelong growth*

*lens fibers form the bulk of the lens. They are long, thin, transparent cells, firmly packed, with diameters typically 4–7 micrometres and lengths of up to 12 mm long*

neural crest—&gt; PNS

neural tube—&gt; CNS (and retina)

Public domain [commons.wikimedia.org/wiki/Neural\_crest#/media/File:Neural\_crest.svg]

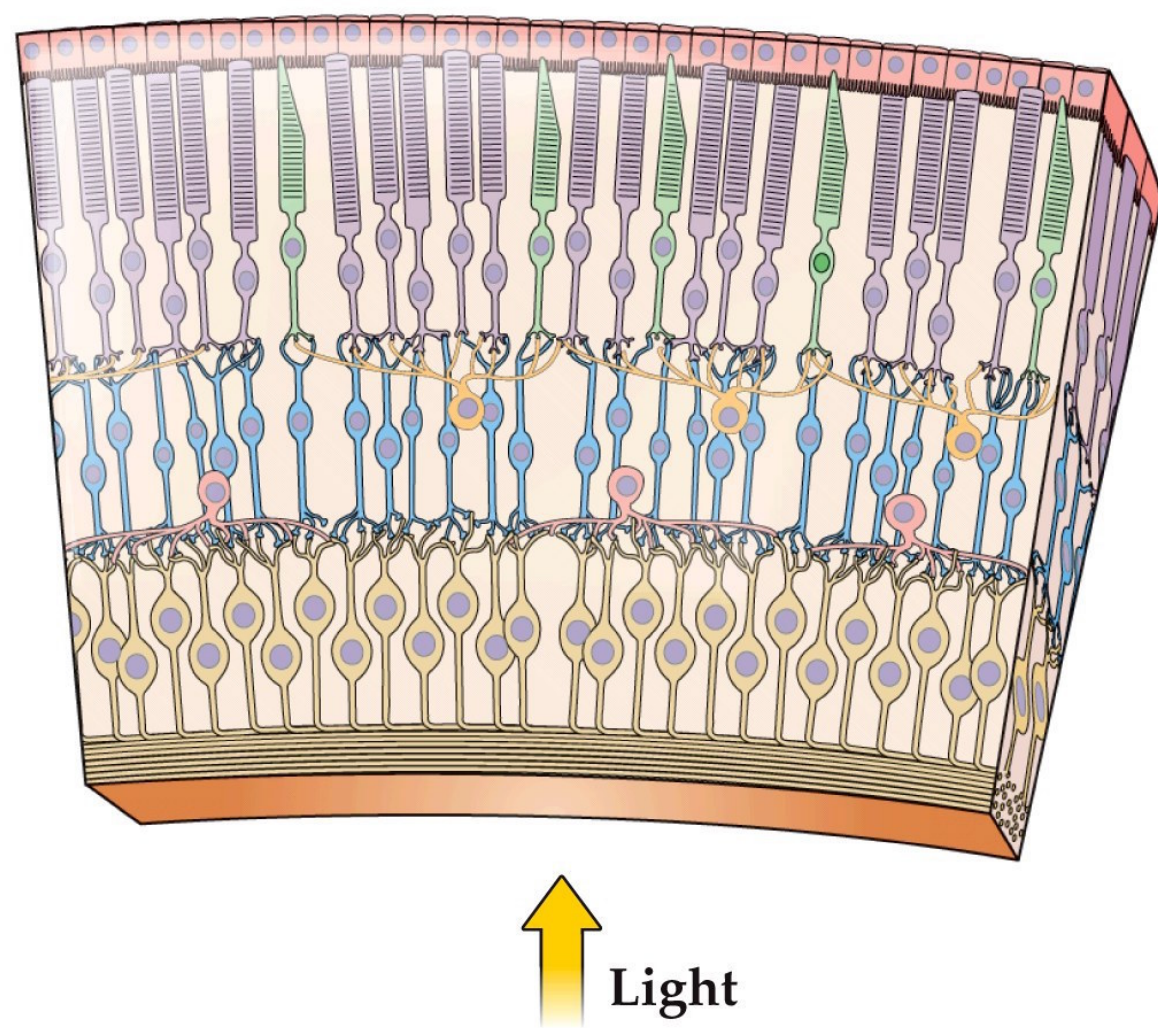
- olfactory bulb mitral neurons (primary afferent neurons of olfactory system) are from neural tube (telencephalon)
- retinal ganglion neurons in retina (first order afferent neurons of visual system) are from neural tube (diencephalon)
- spiral ganglion neurons in cochlea (first order afferent neurons of auditory system) are also from neural tube

# The retina

- The retina is part of the central nervous system!
- Contains neural circuitry that converts photon energy into action potentials that travel out of the eye within the optic nerve into the brain
- Is a layered structure, relatively simple for a CNS structure
- Surrounded on one side by pigmented epithelium which contains melanin that helps reduce backscattering of light. Also plays a key role in maintenance of photoreceptors
- 5 types of neurons in the retina: photoreceptors, bipolar cells, retinal ganglion cells, horizontal cells, and amacrine cells
- A direct 3 neuron chain is the basic unit of transmission. Photoreceptor to bipolar cell to ganglion cell

# Anatomy of the retina

Light travels through the retina to hit the photoreceptors in the photoreceptor layer



Neuroscience 5e Fig. 11.5

*Because the rods and cones are at the back of the retina, the incoming light has to go through the other two layers in order to stimulate them. We do not fully understand why the retina develops in this curious backward fashion. One possible reason is the location behind the receptors of a row of cells containing a black pigment, melanin (also found in skin)*

number of rods and cones vary across the retina. In the center where vision is best (fovea) there are only cones. This area is about 0.5mm in diameter.

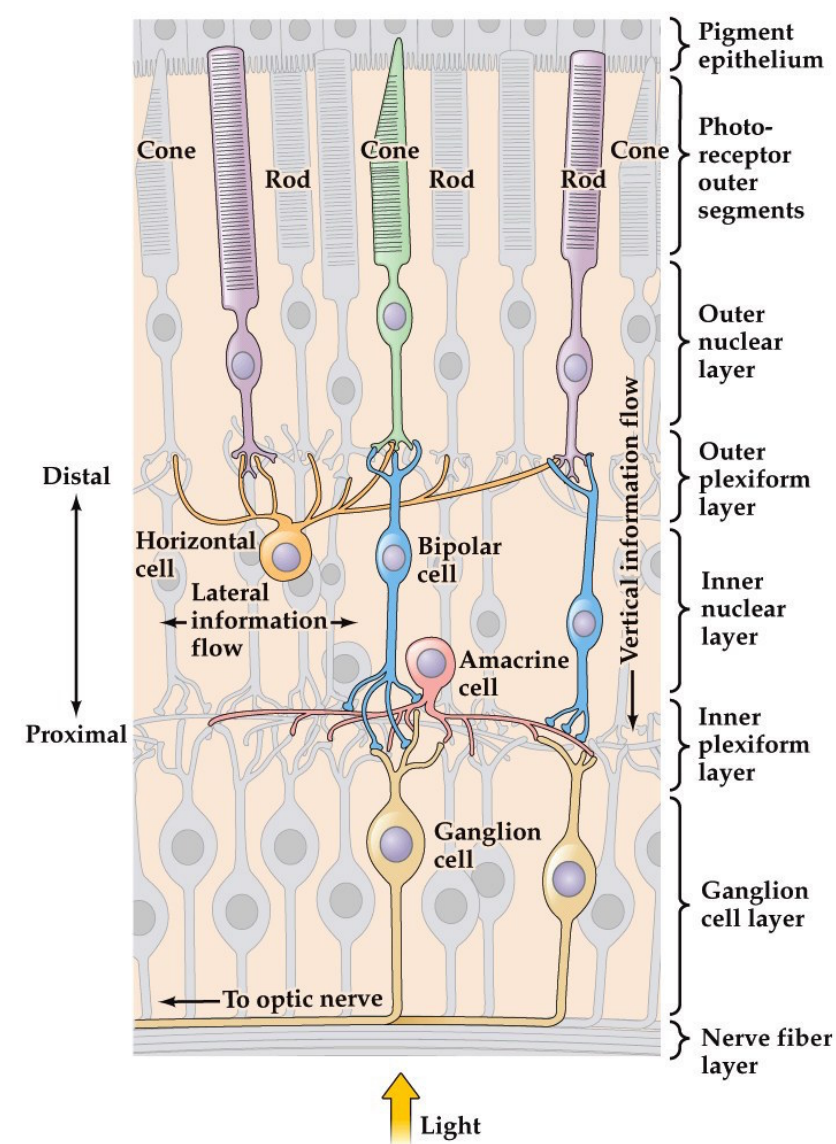
125 million rods and cones in each eye. But only 1 million ganglion cells. How is visual information then preserved. Think of two paths: the direct path and an indirect path involving lateral interactions mediated by horizontal cells between receptors and bipolars and amacrine cells between bipolars and ganglion cells.

*The total area occupied by the receptors in the back layer that feed one ganglion cell in the front layer, directly and indirectly, is only about one millimeter*

high degree of convergence, together with more direct path in and near fovea (one cone—>one bipolar—>one ganglion cell) can explain the 125:1 ratio of receptors to optic nerve fibers without having really bad vision.

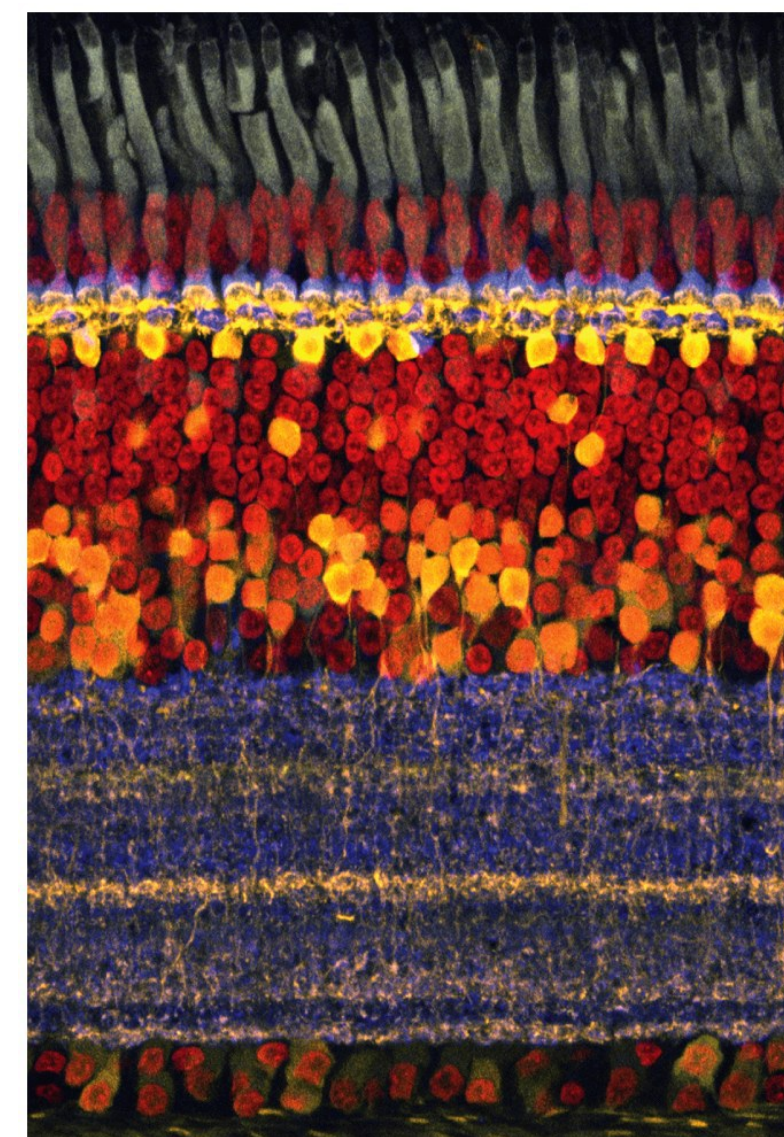
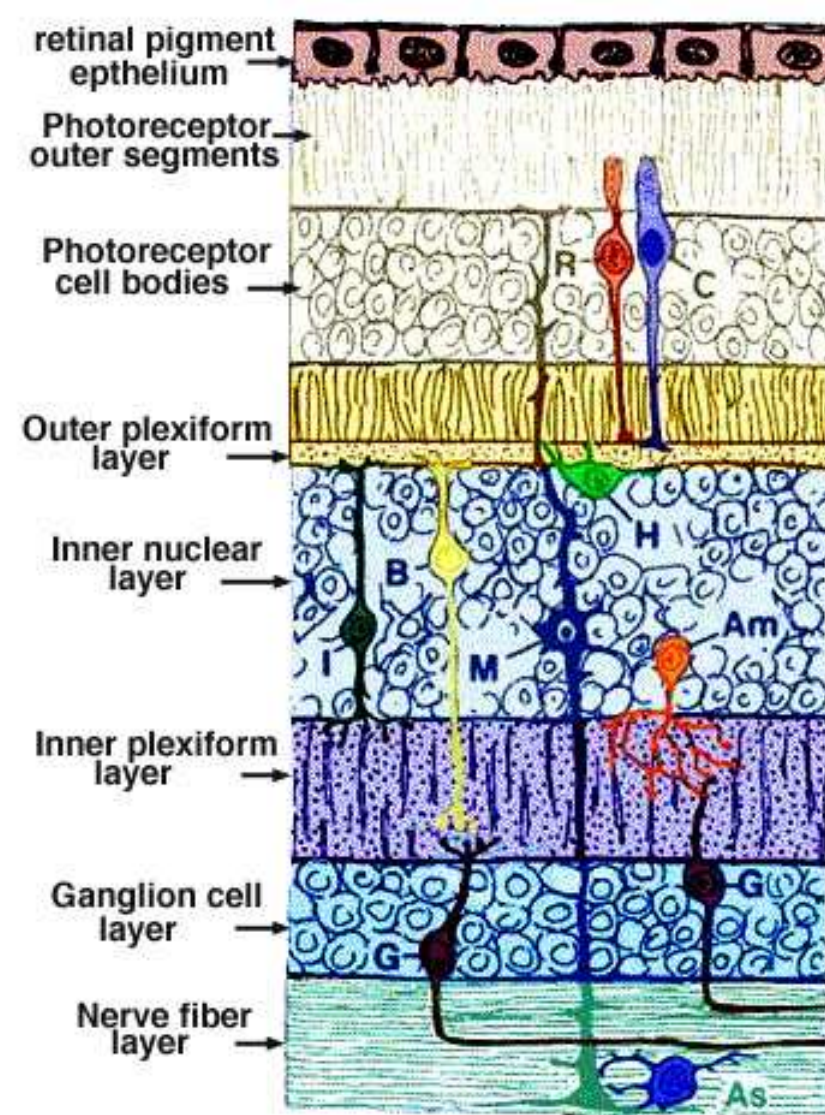
# Layers of the retina

- Three main cell body layers (photoreceptor cell bodies, inner nuclear layer, and ganglion cell layer)
- Two main synaptic transmission layers (outer plexiform and inner plexiform)



Neuroscience 5e Fig. 11.5

[H. Kolb Webvision, med.utah.edu](http://H.KolbWebvision.med.utah.edu)

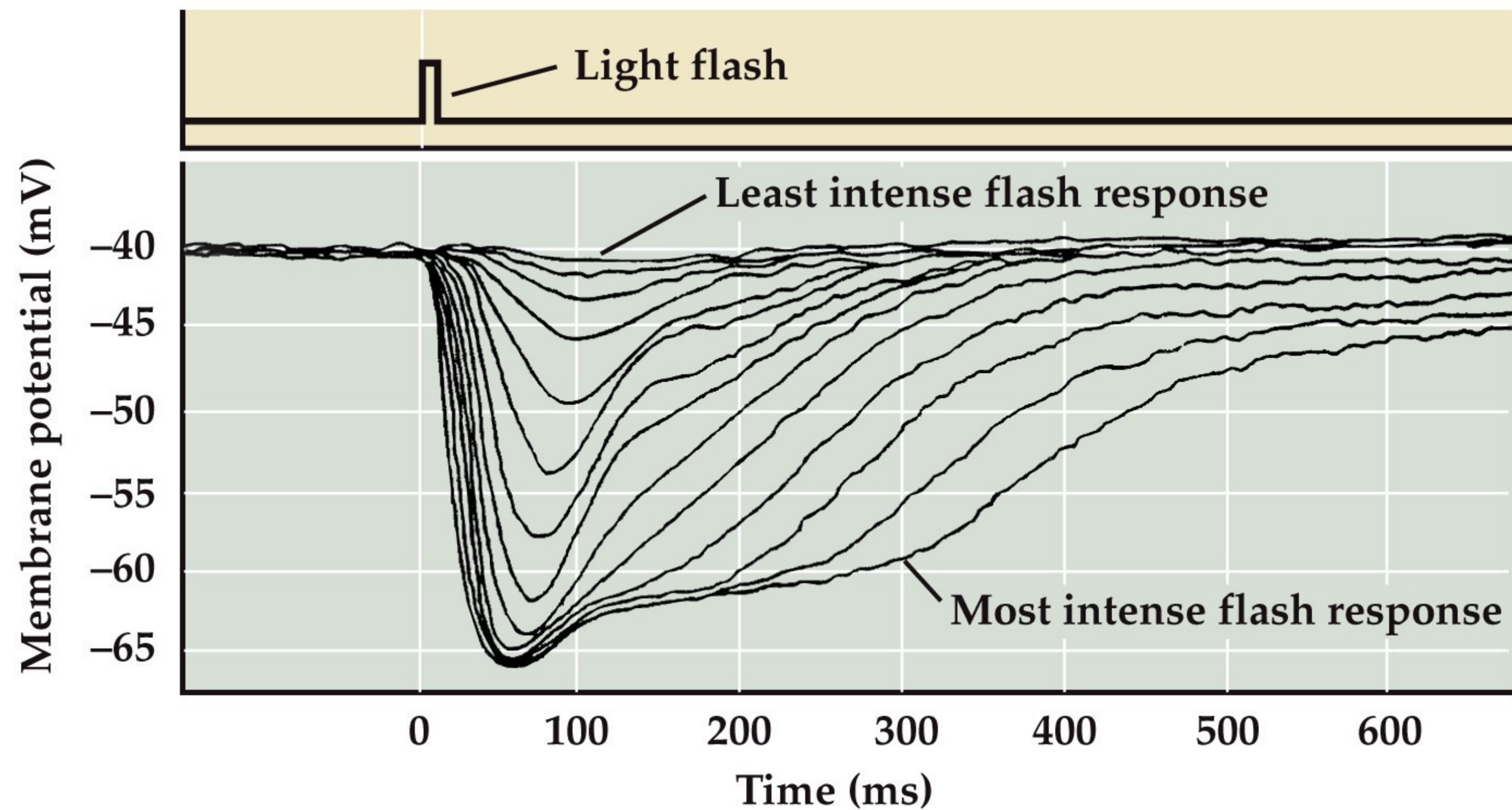


Neuroscience 5e Ch. 11

# Phototransduction

- Photoreceptors do not exhibit action potentials– light causes a graded change in membrane potential that changes the rate at which neurotransmitter is released
- Within the retina projections are rather short– do not need action potentials
- Light absorption leads to **hyperpolarization** of the photoreceptor. This leads to less release of neurotransmitter to the post-synaptic cell

# Cones and rods hyperpolarize in response to light



# What does light energy do?

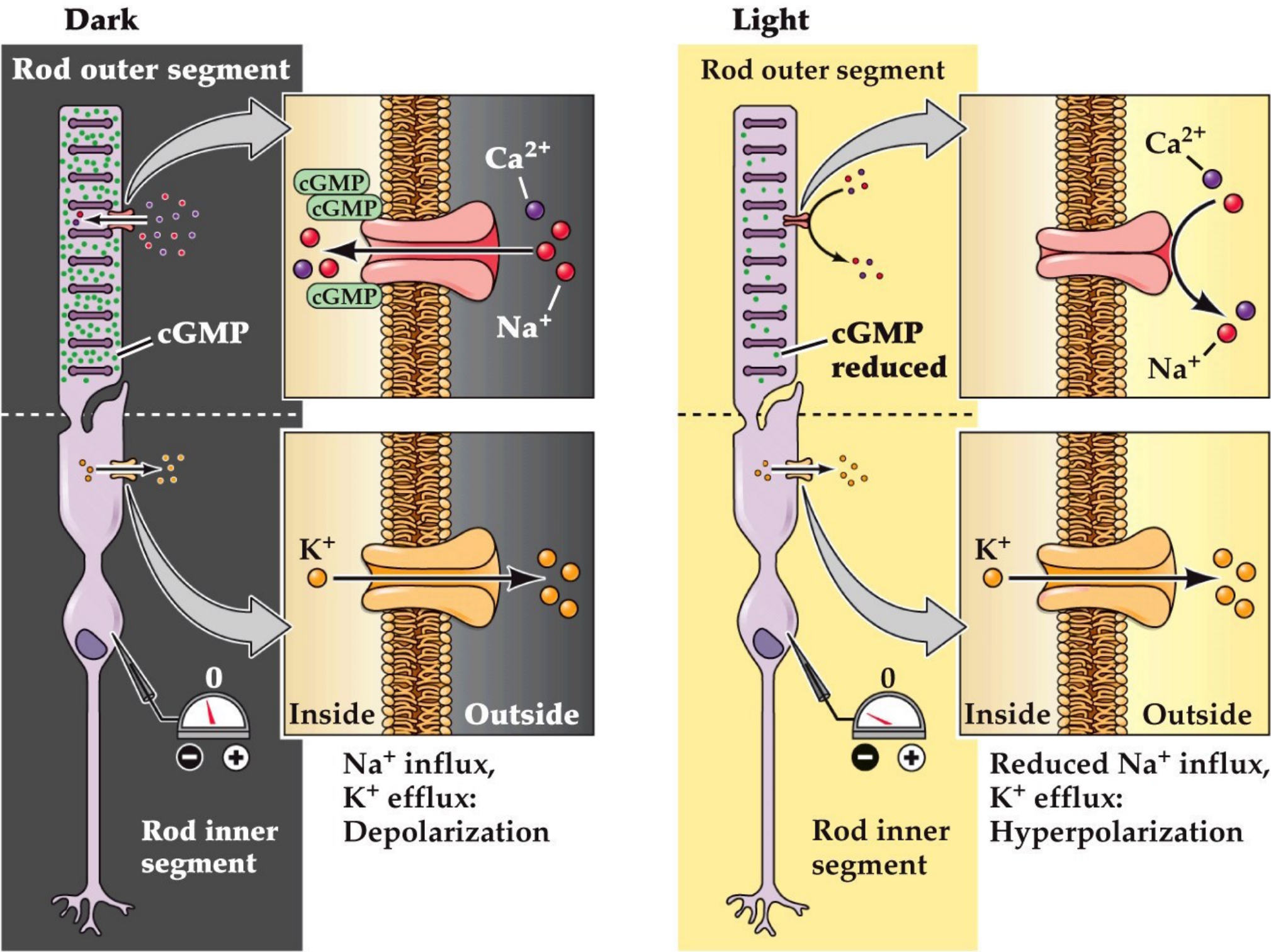
- In the dark, the resting potential of the photoreceptor is -40 mV
- Light shining onto outer segment leads to the **hyperpolarization** of the photoreceptor and reduction of neurotransmitter released
- In the dark the number of voltage-gated Ca<sup>2+</sup> channels open at the synaptic terminal is relatively high, and therefore the rate of neurotransmitter release is high. In the light the number of open voltage-gated Ca<sup>2+</sup> channels is reduced and rate of neurotransmitter release is reduced

# In the dark

- cGMP gated cation channels in outer segment are open allowing ions to flow inside the cell. This leads to a resting potential of -40 mV or so
- The probability of these channels being open is regulated by the levels of cGMP
- In the dark, high levels of cGMP keep the channels open

# cGMP gated cation channels are key

In the dark channels open due to cGMP binding.  $\text{Na}^+$  and  $\text{Ca}^{2+}$  rushes in and cell is depolarized



Neuroscience 5e Fig. 11.8

Speaker notes

cyclic nucleotide gated cation channels in the outer membrane segment of the photoreceptors

the nucleotide cyclic guanosine monophosphate

these cGMP gated channels are permeable to both  $\text{Na}^+$  and  $\text{Ca}^{2+}$  actually

Balanced by  $\text{K}^+$  selective channels in the inner segment of the photoreceptor cell

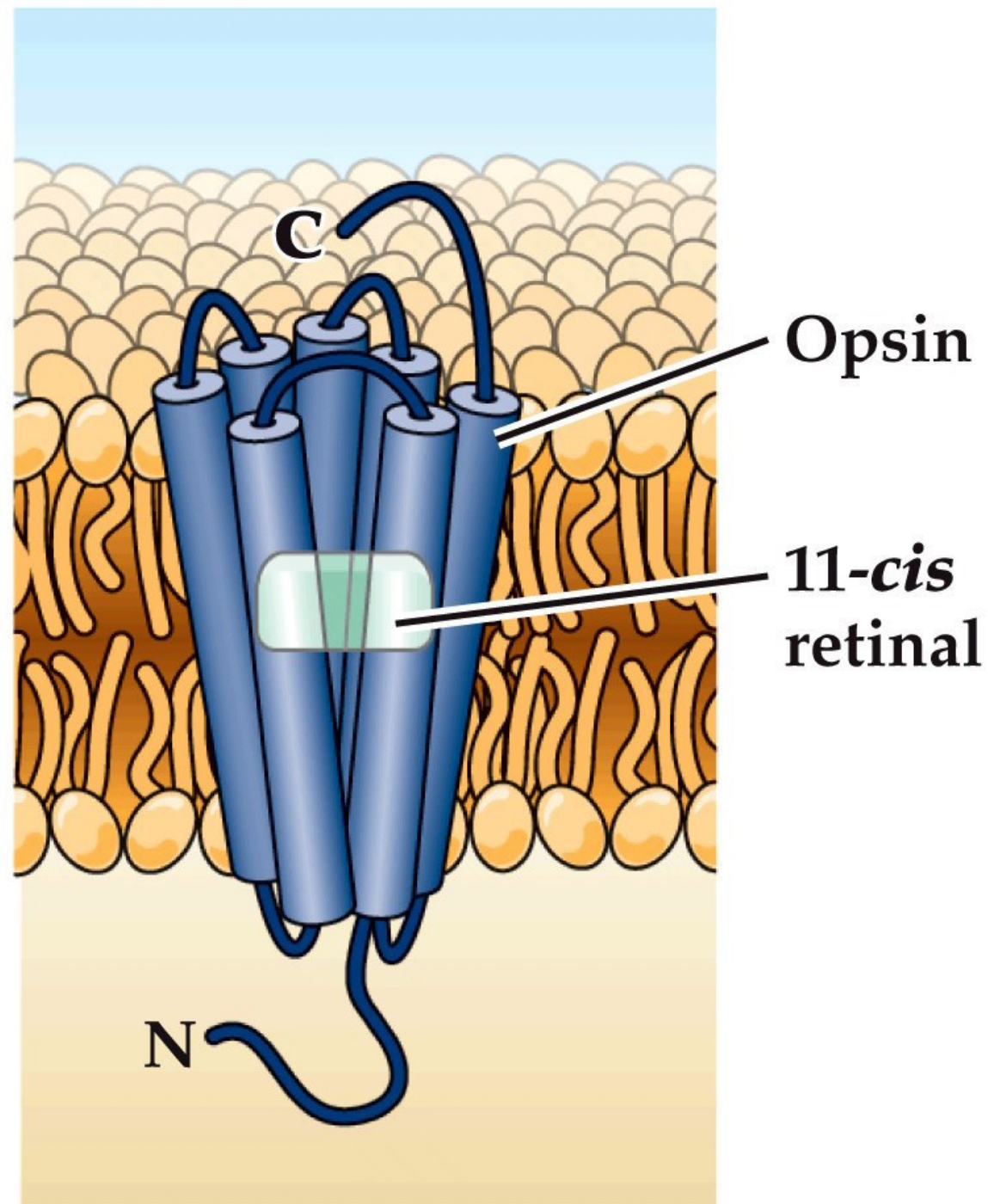
Light transduction results in a **decrease in cGMP levels** thus closing the cGMP cation channels.  $\text{K}^+$  efflux becomes dominant and hyperpolarization ensues. Then less  $\text{Ca}^{2+}$  dependent transmitter release at synapse with bipolar cells

# In the light

- A photon of light is absorbed by photopigment (retinal or retinaldehyde, an aldehyde of Vitamin A) that is coupled to a protein in the outer segment called opsin. Absorption causes a change in conformation of retinal (photon absorption breaks a carbon double bond and switching from cis to trans configuration) that in turn changes the conformation of opsin
- The opsin then can activate the trimeric G-protein **transducin**
- Transducin in turn activates a cGMP phosphodiesterase. The phosphodiesterase then hydrolyzes cGMP to GMP. Channel opening probability decreases, cell gets hyperpolarized

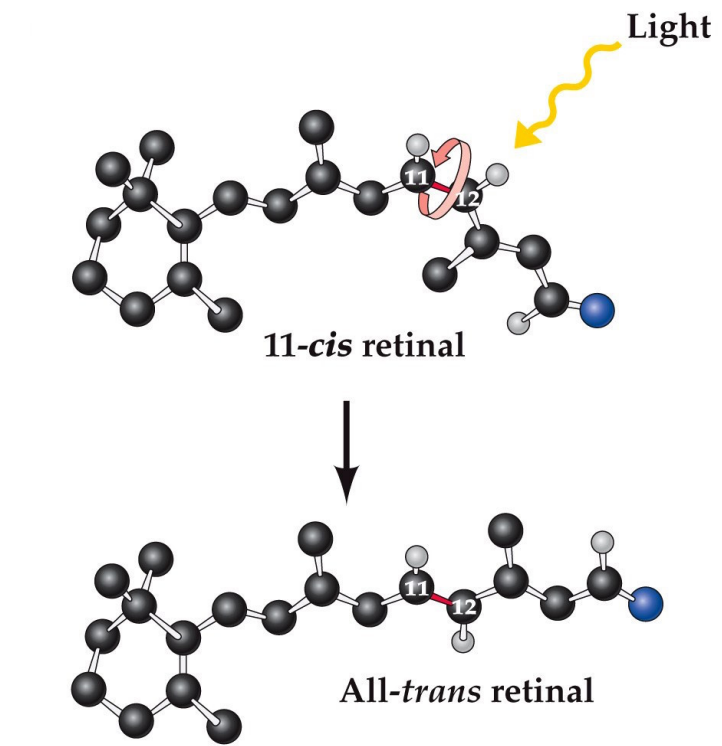
# Phototransduction in rod photoreceptors

rhodopsin



Neuroscience 5e Fig. 11.9

retinaldehyde



Neuroscience 5e Fig. 11.9

Speaker notes

Four types of cone opsins in vertebrates (LWS, SWS1, SWS2, and Rh2)

from: <https://en.wikipedia.org/wiki/Opsin>

name	abbr	type	bandwidth	color	human gene
long-wave sensitive	LWS	cone	500–570 nm	green, yellow, red	OPN1LW "red" / OPN1MW "green"
short-wave sensitive 1	SWS1	cone	355–445 nm	ultraviolet, violet	OPN1SW "blue"
short-wave sensitive 2	SWS2	cone	400–470 nm	violet, blue (extinct in therian mammals)	
rhodopsin-like 2	Rh2	cone	480–530 nm	green (extinct in mammals)	
rhodopsin-like 1 (vertebrate rhodopsin)	Rh1	rod	~500 nm	blue-green	OPN2 = Rho = human rhodopsin

Melanopsin OPN4

: circadian rhythms, pupillary reflex, and color correction in high-brightness situations

: expressed in a small fraction of retinal ganglion neurons distributed across retina

therian mammals

: giving birth to live young

: eutherians (placental mammals) and metatherians (marsupials)

: not egg laying monotremes

Interesting table, [Opsins in the human eye, brain, and skin](#)

*Like type II opsins, type I opsins have a seven transmembrane domain structure similar to that found in eukaryotic G-protein coupled receptors.*

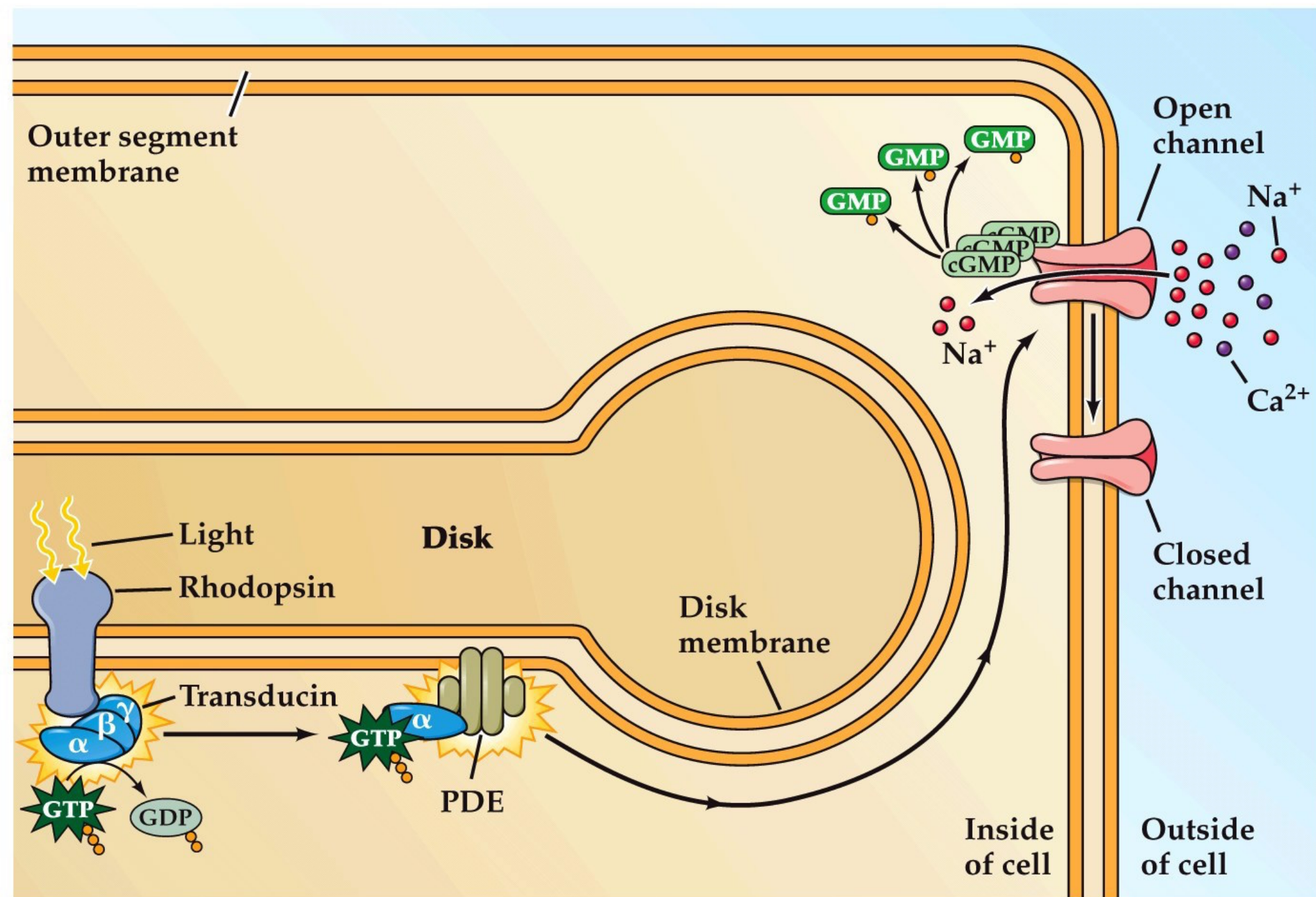
# Phototransduction in rod photoreceptors

Speaker notes

PDE phosphodiesterase catalyses breakdown of cGMP to GMP

cGMP, cyclic nucleotide gated channel

more info: <http://webvision.med.utah.edu/book/part-ii-anatomy-and-physiology-of-the-retina/photoreceptors/>



# Phototransduction summary video



Neuroscience 5e Animation 11.2

Tremendous amplification. Single photon hitting rhodopsin is estimated to activate 800 transducin molecules, about 8% of transducin molecules on disk surface. Each transducin molecule activates a single phosphodiesterase molecule and ea PDE can catalyze the breakdown of 6 cGMP molecules. Results in closure of 200 ion channels or ~2% of n channels in ea rod open in dark, resulting in net change in membrane potential of 1 mV.

*~30 mV working (dynamic) range for photoreceptors. But adaptation scales this to work for different background light levels.*

# Signal amplification

- One photon of light can activate 800 transducin molecules. This leads to about 800 phosphodiesterases activated. Each phosphodiesterase cleaves 300 or so cGMPs/second. This can result in the closing of about 200 ion channels (2% of total).  $10^6 - 10^7$   $\text{Na}^+$  ions per second are prevented from entering the cell for a period of ~1 second
- Changes membrane potential about 1 mV

Rhodopsin is a seven-transmembrane g protein coupled receptor.

*Rhodopsin kinase/arrestin– activated rhodopsin is phosphorylated by rhodopsin kinase and intracellular Ser/Thr residues.*

Retinoid cycle one important part of light adaptation (other being horizontal cell-photoreceptor interactions). Rate of retinal regeneration sufficient even under bright illumination.

# After photon absorption, opsin signaling is inactivated and cis-retinal gets regenerated

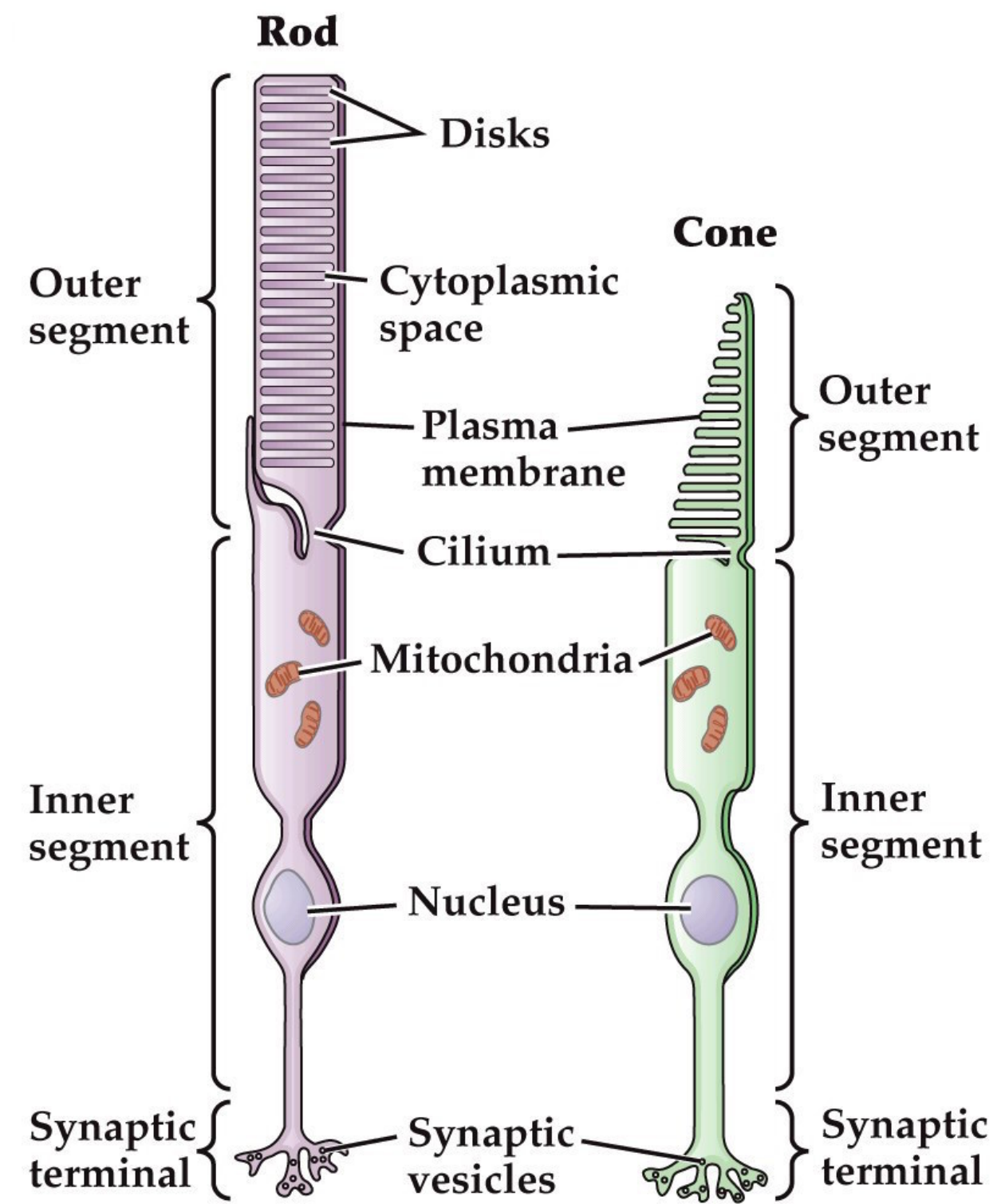
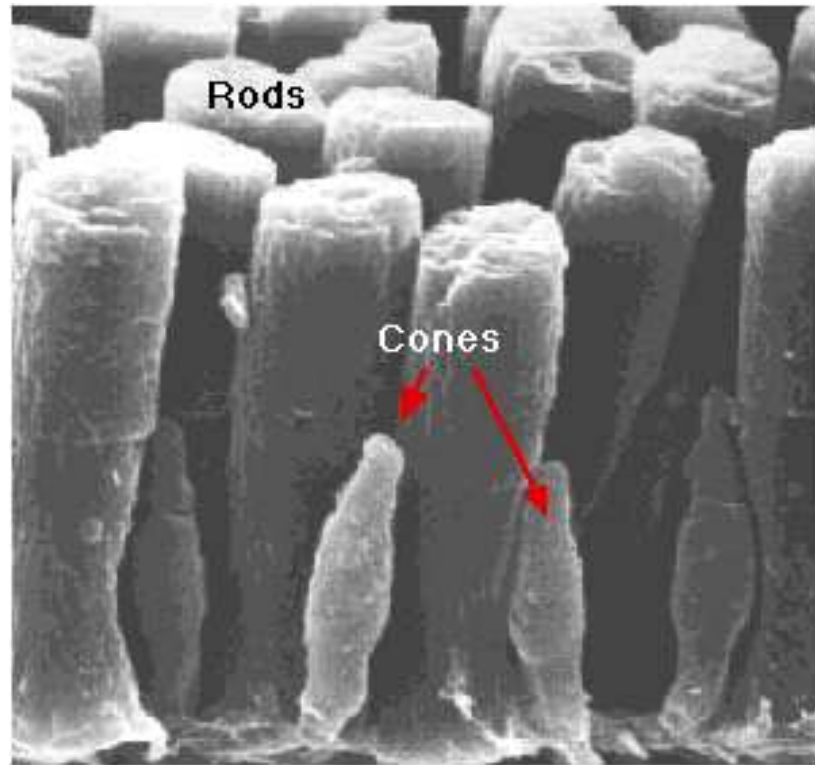
- Rhodopsin kinase/arrestin– activated rhodopsin is phosphorylated by rhodopsin kinase, permitting the protein arrestin to bind to rhodopsin. **Prevents further activation of transducin**, thus ending the phototransduction cascade
- All-trans retinal gets shed, transported to pigment epithelium cells, changed to cis-retinal and then reincorporated into opsin

# Cell types of the retina: photoreceptors

- Rods and cones– have an outer segment comprised of membranous disks that contain photopigment and an inner segment that contains the cell nucleus and synaptic terminals
- The absorption of light by photopigment in outer segment initiates a signal transduction cascade that changes the membrane potential of the cell, and therefore the amount of neurotransmitter released plus or minus light energy
- Photoreceptors synapse with bipolar cells and horizontal cells in the outer plexiform layer

# Structural Differences Between Rods and Cones

Why the cone shape? Shape of cone preferentially accepts light directed straight into the eye through the pupil instead of off axis. Known as the Stiles–Crawford effect.



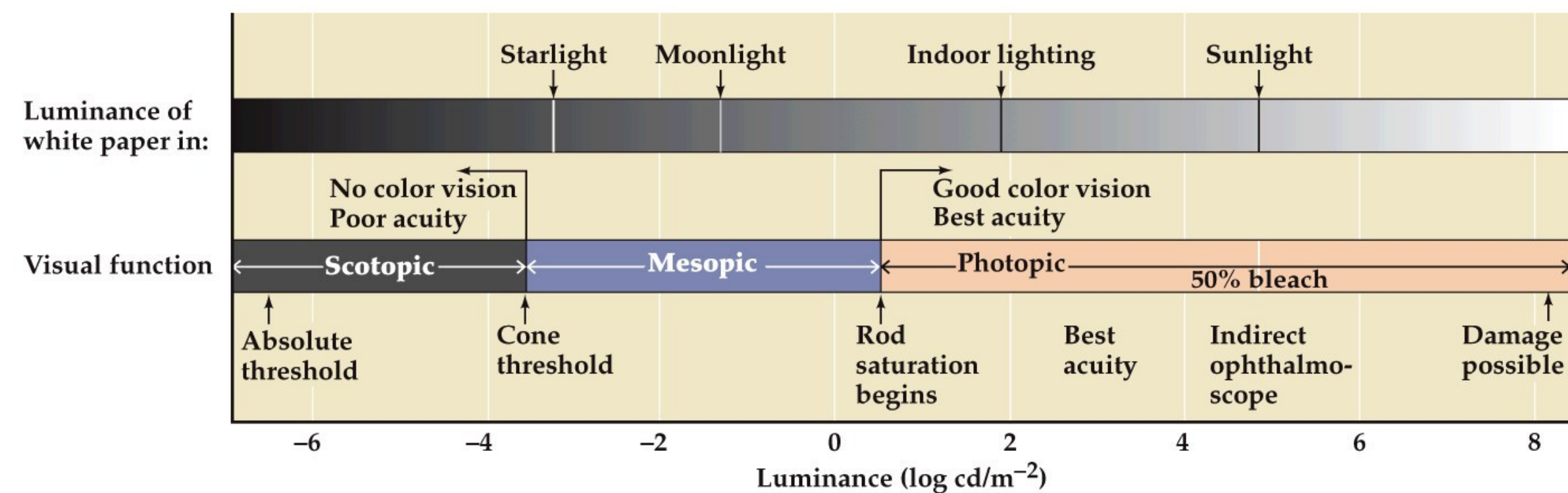
Neuroscience 5e Fig. 11.5

# Rods and cones are distinguished by:

- shape
- type of photopigment they contain
- distribution across the retina
- pattern of synaptic connections
- specialized for different aspects of vision
- Rod system– low spatial resolution but extremely sensitive to light
- Cone system– high spatial resolution but is less sensitive to light

# Range of luminance values over which the visual system operates

- Rods– used mostly for dim light to almost indoor lighting
- When only rods are used called scotopic vision. Not very good
- Cones dominant in visible light. Called photopic
- Twilight uses both called mesopic vision



Neuroscience 5e Fig. 11.11

# More factoids

- Rods produce a reliable response to a single photon of light, it takes over a 100 photons to produce a comparable response in a cone
- Cones adapt better than do rods– about 200 ms for a cone, 800 ms for a rod
- Rods synapse onto specific bipolar cells (rod bipolars) that synapse onto amacrine cells which contact both cone bipolars and ganglion cells. Cones go bipolar to RGC directly
- Rods exhibit convergence– many rods synapse onto a single bipolar cell, many bipolars onto a single amacrine cell
- Cones can be 1 cone - 1 bipolar - 1 ganglion cell

# Differential properties of primate rods and cones

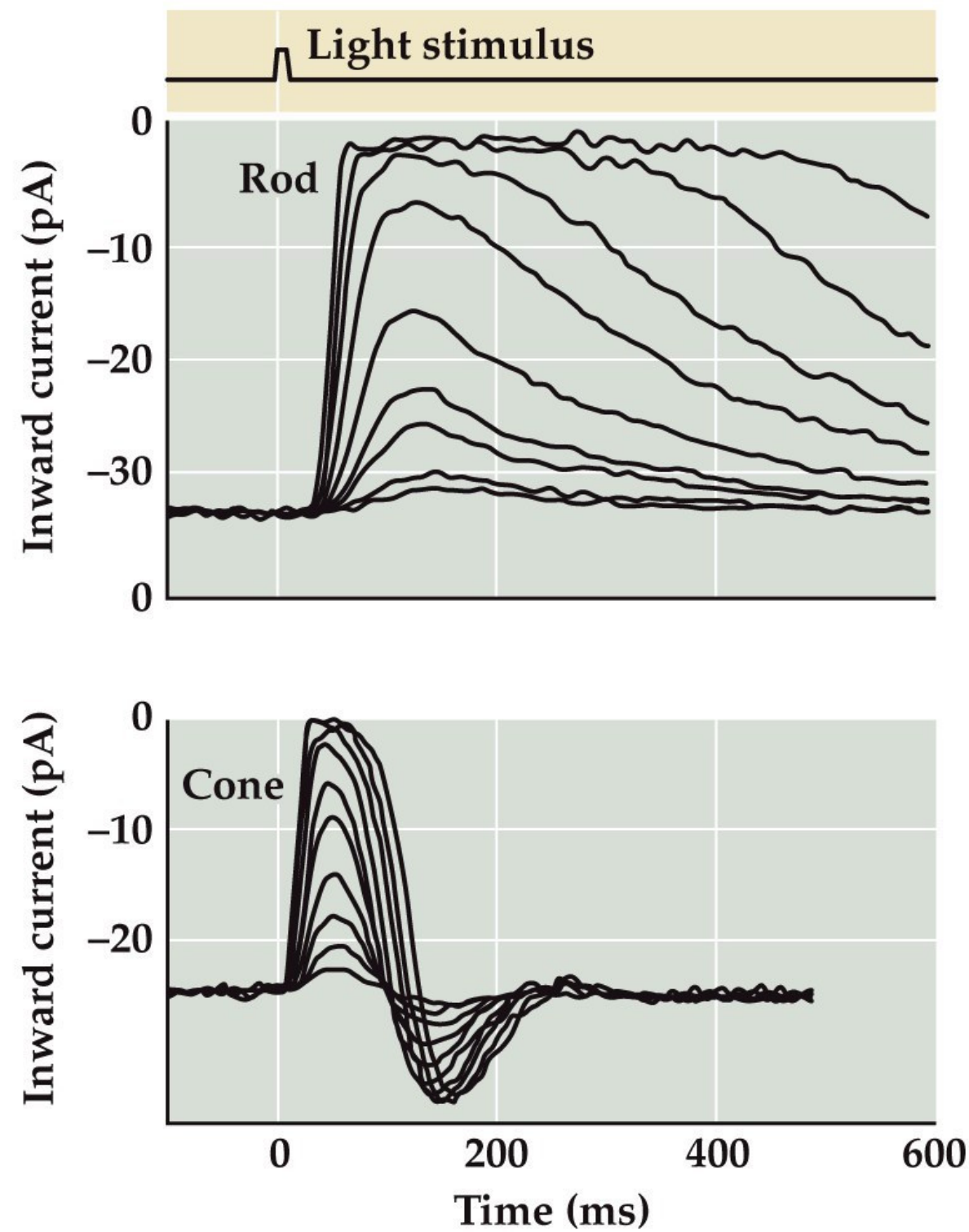
Figure show electrical recordings (suction electrodes) of the current flowing across the photoreceptor membranes of primate (*Macaca fascicularis* / cynomolgus monkeys/crab-eating macaque) rods and cones for high flashes of successive higher intensity.

Cone response over in about 200 ms (with an overshoot of inward current), whereas the rod response can continue for more than 600 ms. Both rods and cones adapt to operate over a range of luminance values, but the adaptation mechanisms of cones are more effective.

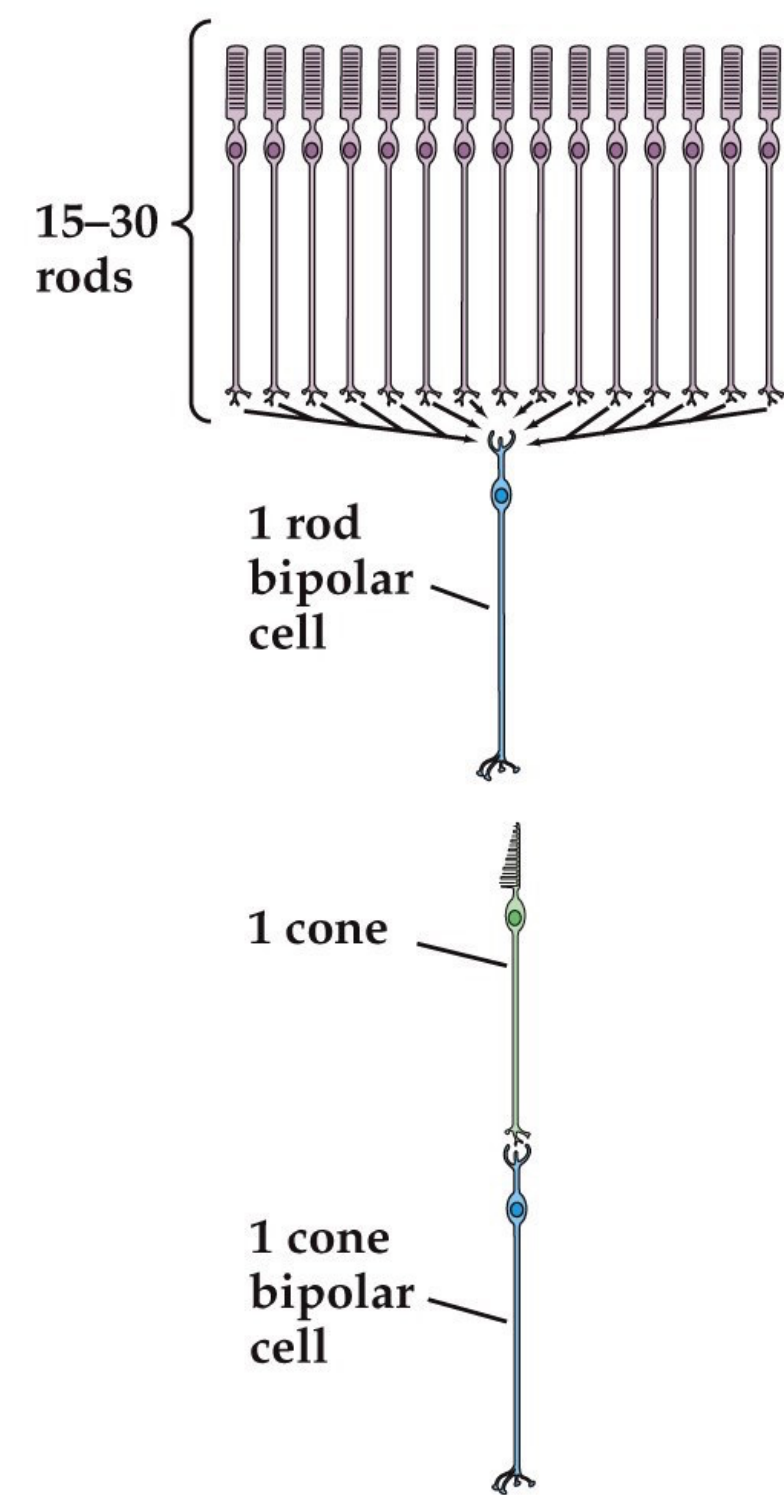
[Ca<sup>2+</sup>] in outer segment plays key role in light adaptation (light induced modulation of photoreceptor sensitivity). More light leads to less [Ca<sup>2+</sup>] leading to more guanylate cyclase activity and more cGMP production and higher [cGMP]. Less [Ca<sup>2+</sup>] also leads to incr activity of rhodopsin kinase and more arrestin binding to rhodopsin so that rhodopsin is inactivated quicker. This is the basis of the enhanced cone light adaptation and the briefer cone response and the outward current overshoot compared with rods.

*15-30 rod to bipolar cell convergence, reduces spatial resolution of rod system but increases light detection*

outward currents after light flashes



convergence in rod pathway



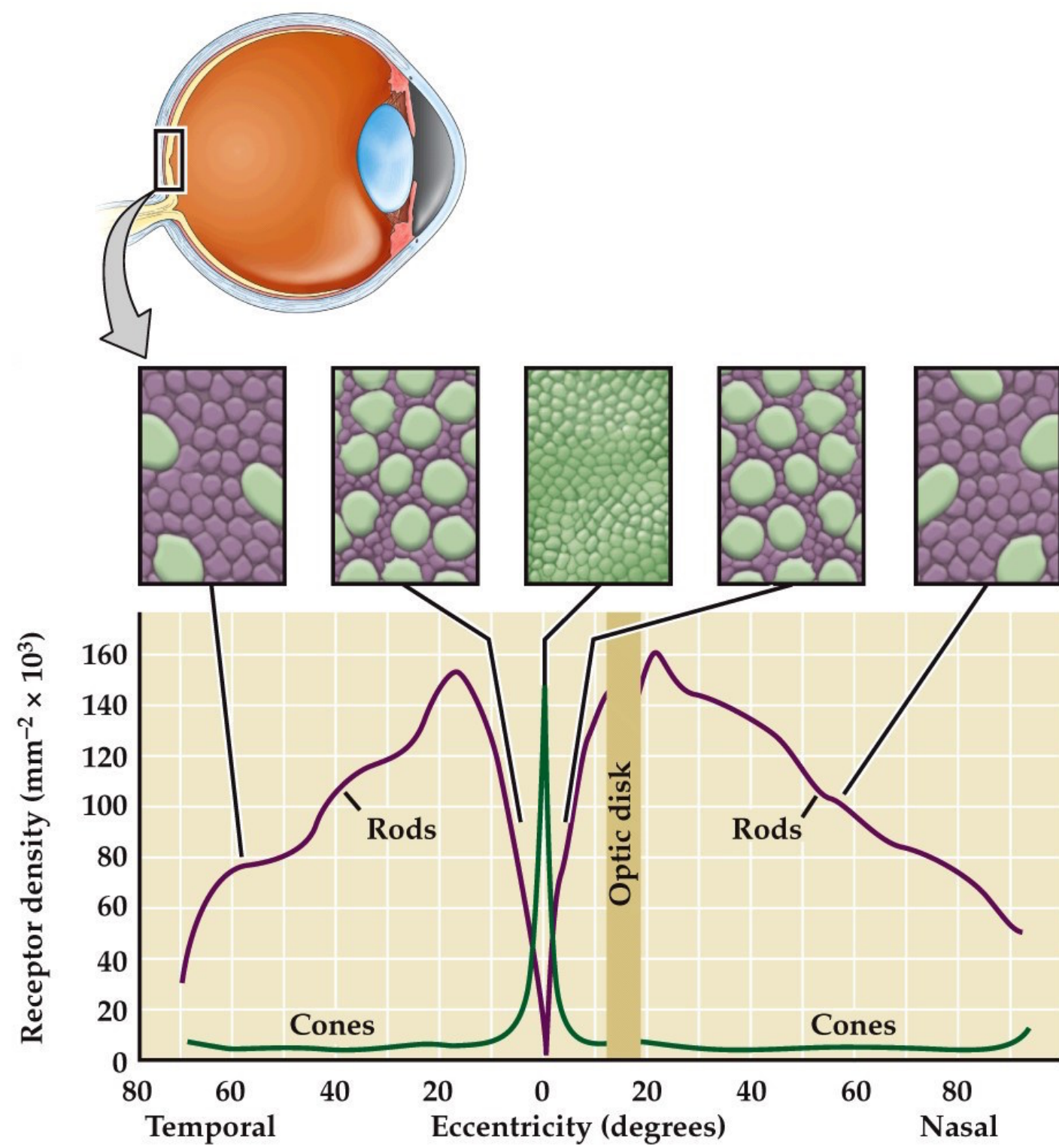
Neuroscience 5e Fig. 11.12, Baylor J Physiol 1984, 1987

Neuroscience 5e Fig. 11.12

# Rods and cones are not distributed equally in the retina

- Human retina– 91 million rods, 4.5 million cones
- In most places the density of rods exceeds that of cones
- Changes dramatically in the fovea, central retina (1.2 mm in diameter)
- Cones increase in density 200 fold, become highly packed. Center of the fovea, called foveola is totally rod free
- Gives high visual acuity, which decreases rapidly away from the fovea
- Reason why we are constantly moving our heads to center our eyes toward what we want to look at
- Reason why it is best to see a dim object by looking away from it

# Distribution of rods and cones in the human retina

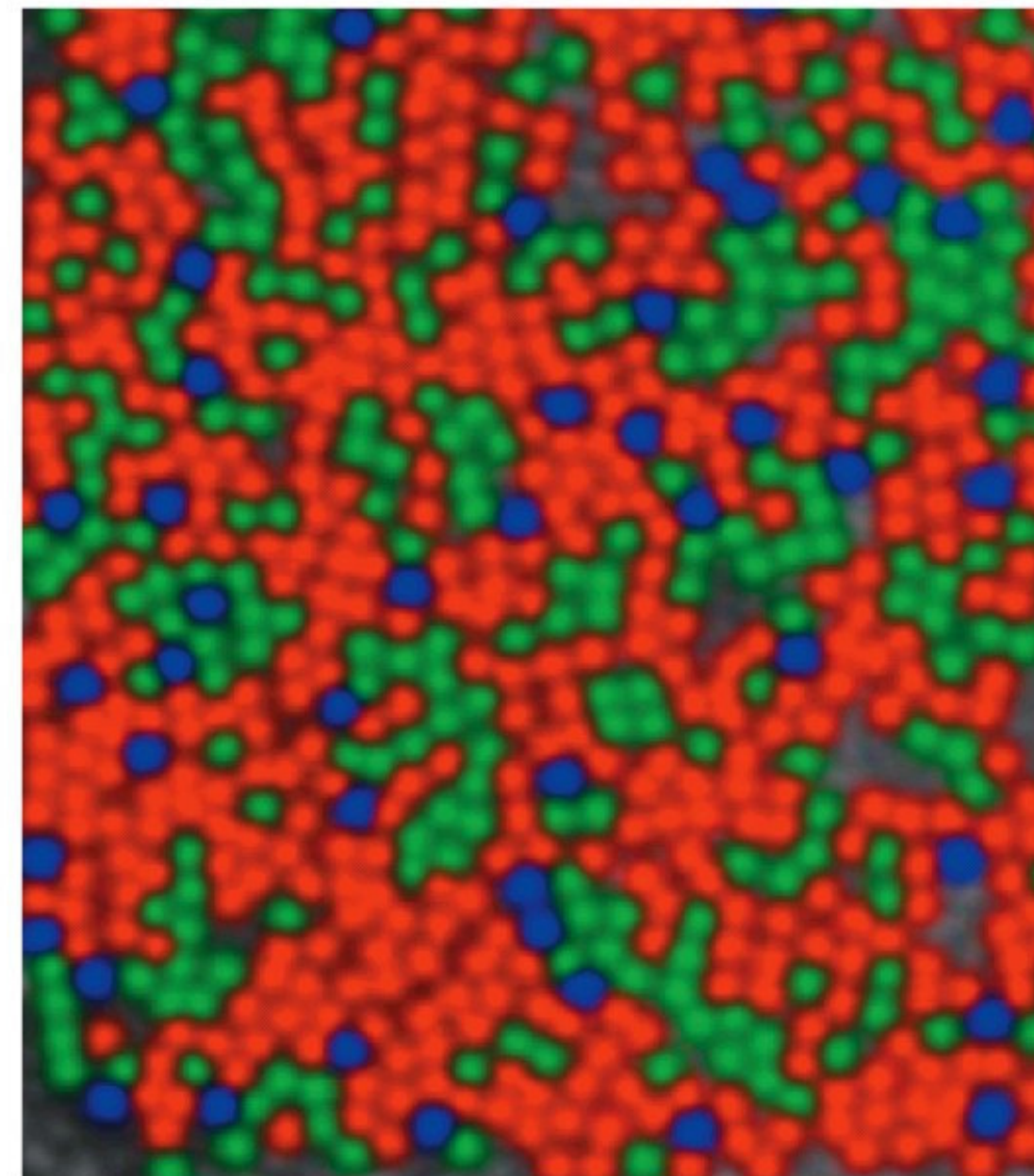
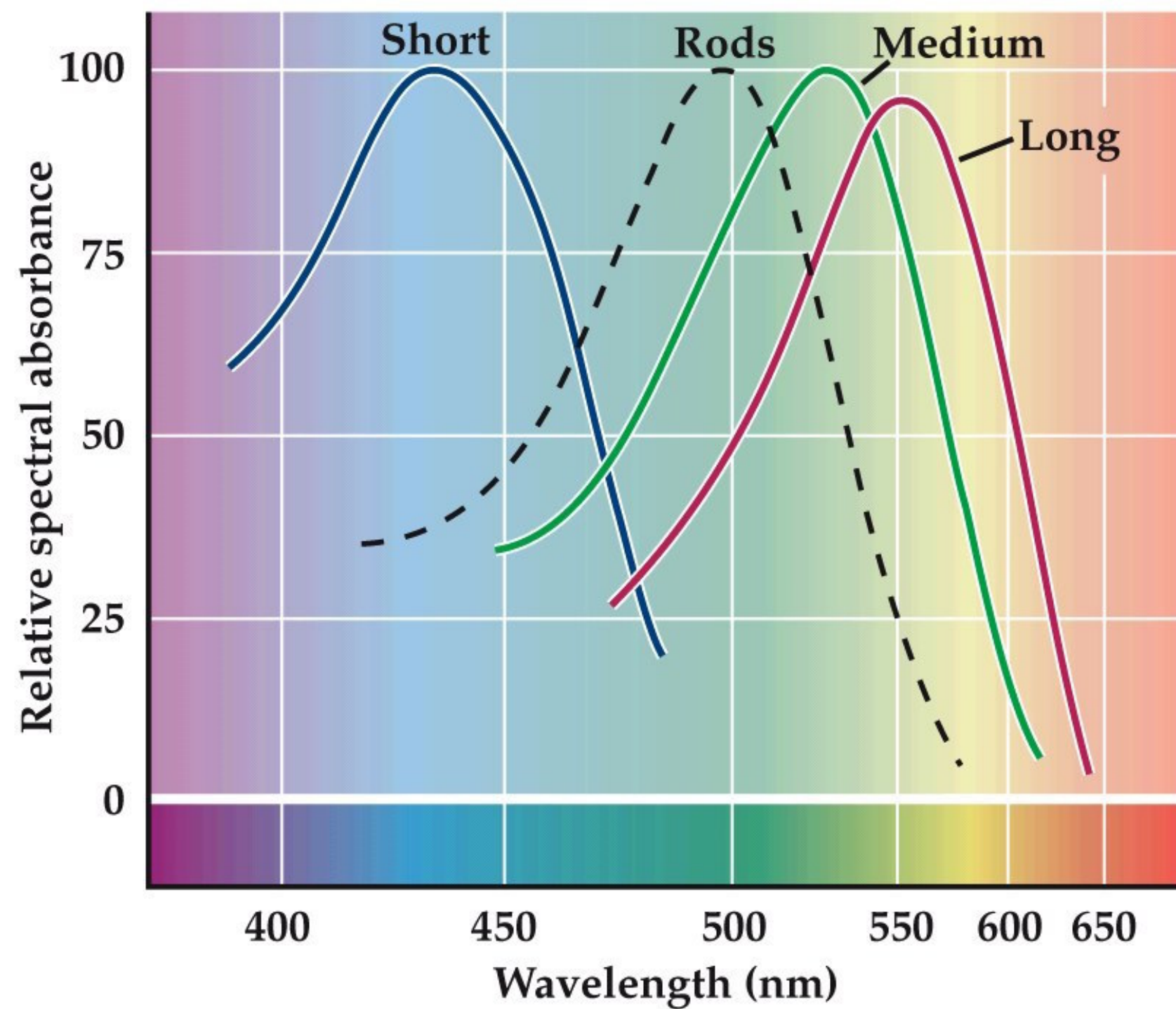


Neuroscience 5e Fig. 11.13

# Cones and color vision

- 3 types of cones, each having different absorption spectra- called blue (S-cones), green (M-cones), and red (L-cones) opsin
- Most people can match any color by changing the intensities of these three colors (RGB)
- 5-6% of males are color blind- due to mutations in the red or green opsins. They are X-linked and near each other

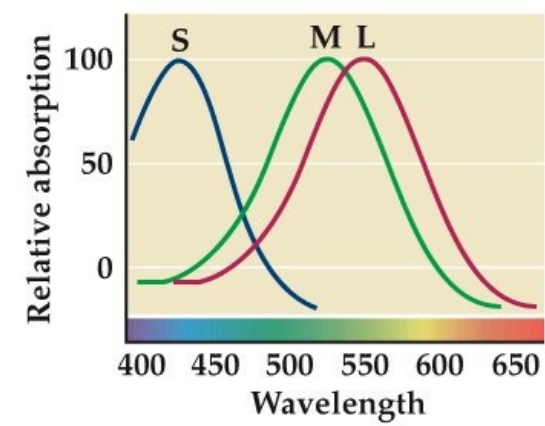
# Cone absorption spectra and distribution in the retina



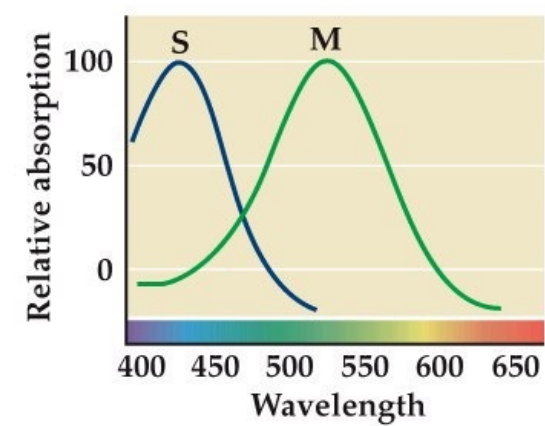
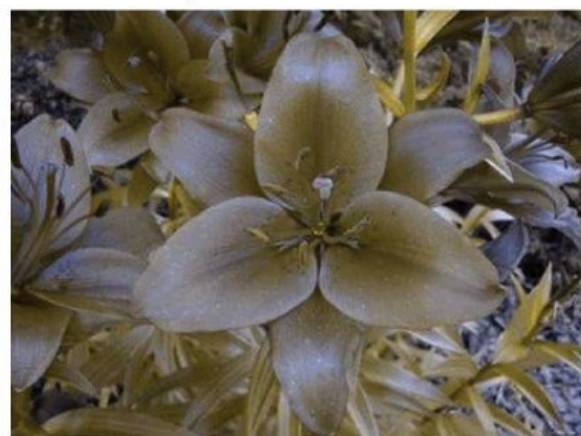
Neuroscience 5e Fig. 11.14, Hofer 2005

# Many deficiencies of color vision are the result of genetic alterations in the red or green cone pigments

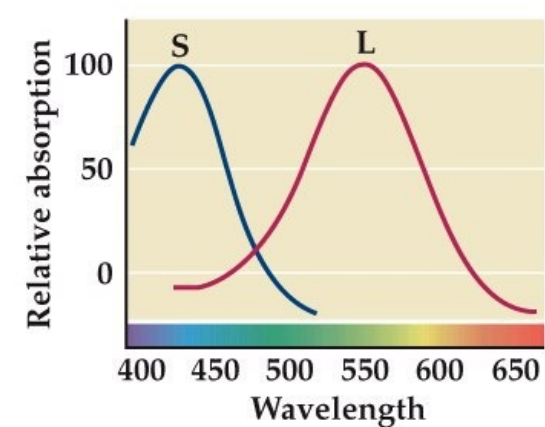
Normal (trichomat)



Protanopia



Deuteranopia



Neuroscience 5e Fig. 11.15

# Rods and cones summary

## Rods

- 90 – 120 million
- Peripheral vision
- Located everywhere except fovea
- Very sensitive to light
- Used in low light situations
- One type
- Highly convergent
- Black and White

## Cones

- 4-6 million
- Central vision
- High density in the macula and fovea
- Less sensitive to light
- Most normal lighting conditions
- Three types
- Nonconvergent
- Color vision

# Other cell types of the retina

- Bipolar cells– cell bodies in the inner nuclear layer. Gets info from photoreceptors in outer plexiform layer and transmits it to ganglion cells and amacrine cells in inner plexiform layer. Rods and cones use specific types of bipolars
- Ganglion cells– cell bodies in ganglion cell layer. Output neurons of the retina. Receives info from bipolar and amacrine cells and sends it out through the optic nerve
- Horizontal cells– cell bodies in inner nuclear layer. Makes multiple contacts with photoreceptors and bipolar cells. Largely responsible for luminance contrast
- Amacrine cells– cell bodies in inner nuclear layer. Makes contact in the inner plexiform layer with bipolar cells and ganglion cells. Several distinct subclasses. Coordinate ganglion cell activity. e.g. motion

# Retinal ganglion cells (RGC)

- RGCs are the cell that sends action potentials to the brain
- Much of the information in vision has to do with changes in light intensity. Example black and white movies
- In order to understand how the brain makes sense of the differences in light intensity that the eye sees, it is important to know what makes RGCs fire
- Record from an RGC and shine light onto different photoreceptors. Find:
  - Even in the dark RGCs are spontaneously active
  - Receptive fields of RGCs are circular. Smaller in the center of the retina and bigger in the periphery
  - Find two classes of RGCs. Those that have receptive field profiles that are ON center and those that are OFF center
  - The receptive fields of RGCs overlap so that multiple RGCs see each point of space

# Stephen Kuffler 1950s

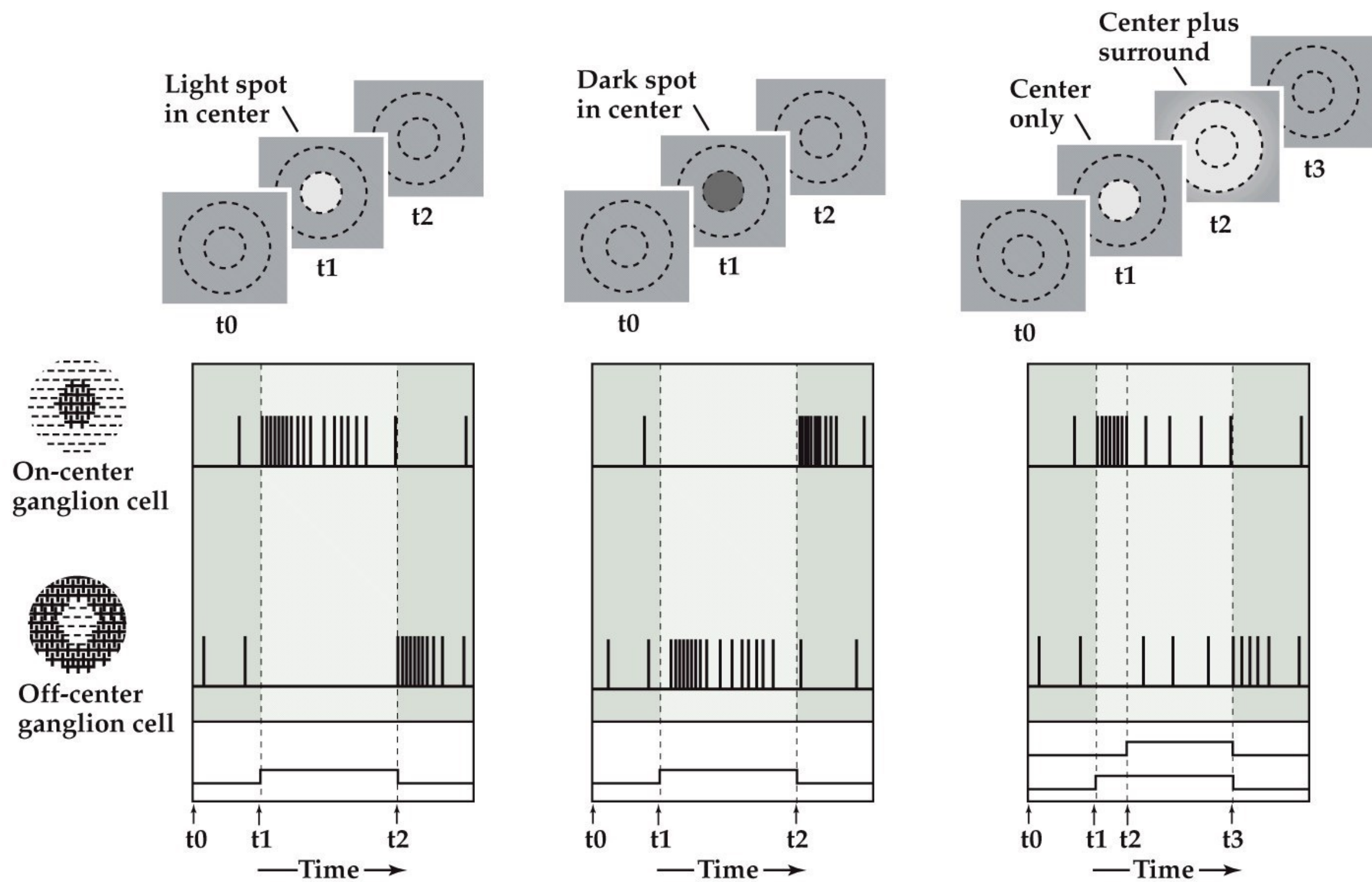
- Measured the action potentials from specific RGCs after shining light on the retina
- Determined that RGCs have receptive fields. Found that a receptive field can be divided into center and a surround
- Ganglion cells come in two types- ON-center/OFF surround and OFF-center/ON surround, in roughly equal proportions
- ON center RGCs fire more when light that hits the center is brighter than that of the surround and fire less when it is darker in the center than in the surround. OFF center fire less when it is brighter in center and more when it is darker in the center
- Acts like having separate luminance channels. **Changes in intensity** (increases or decreases), are conveyed by action potentials. **RGCs are not photodetectors but are detecting the contrast** between areas

# On- and off-center retinal ganglion cell responses to stimulation of different regions of their receptive fields

Speaker notes

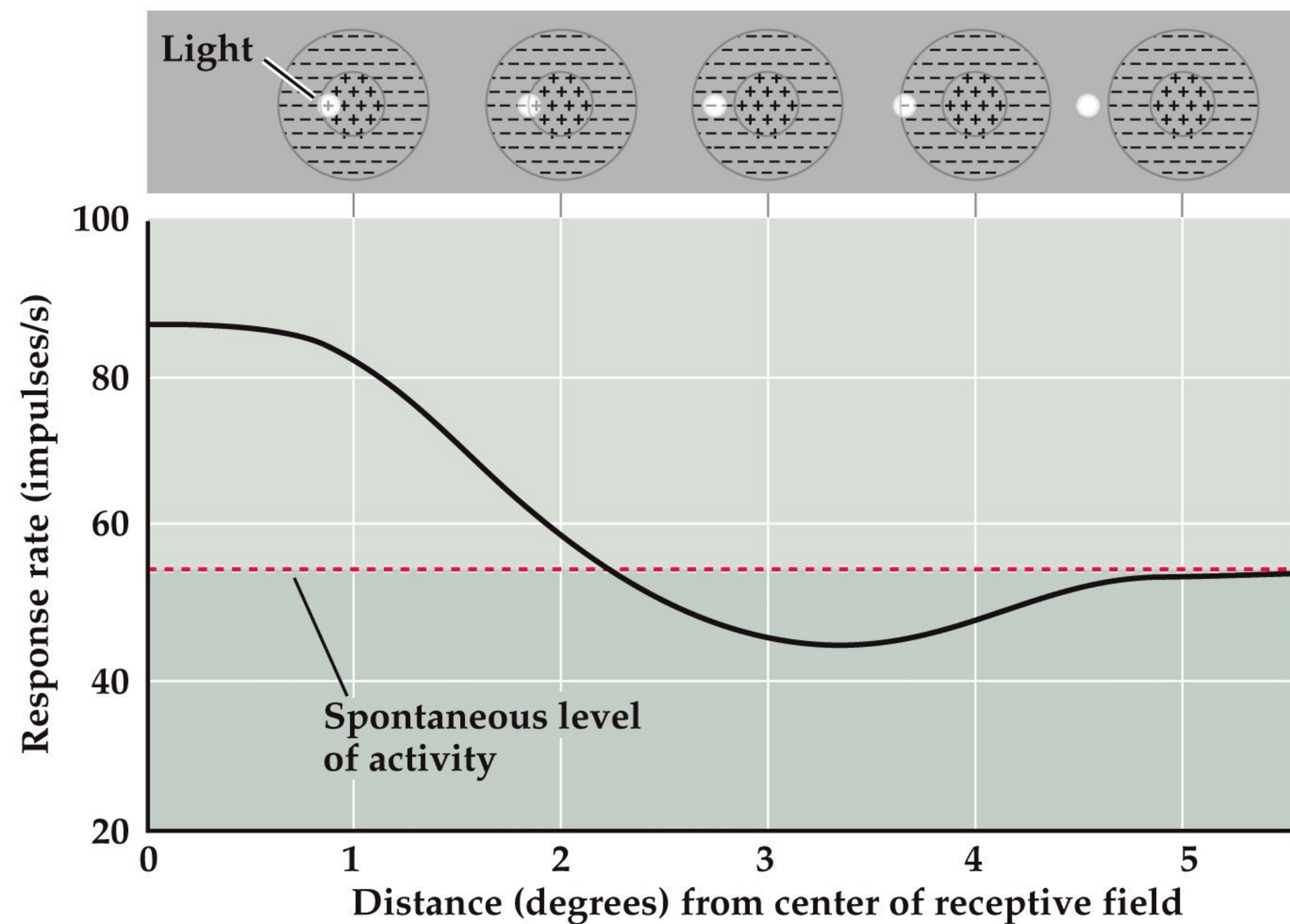
luminance increment in receptive field center vs luminance decrements in receptive field center

Contrast. luminance change, increments or decrements, carried by separate channels to brain by increased spike rate



Neuroscience 5e Fig. 11.17

# Responses of On-center ganglion cells whose receptive fields are distributed across a small spot

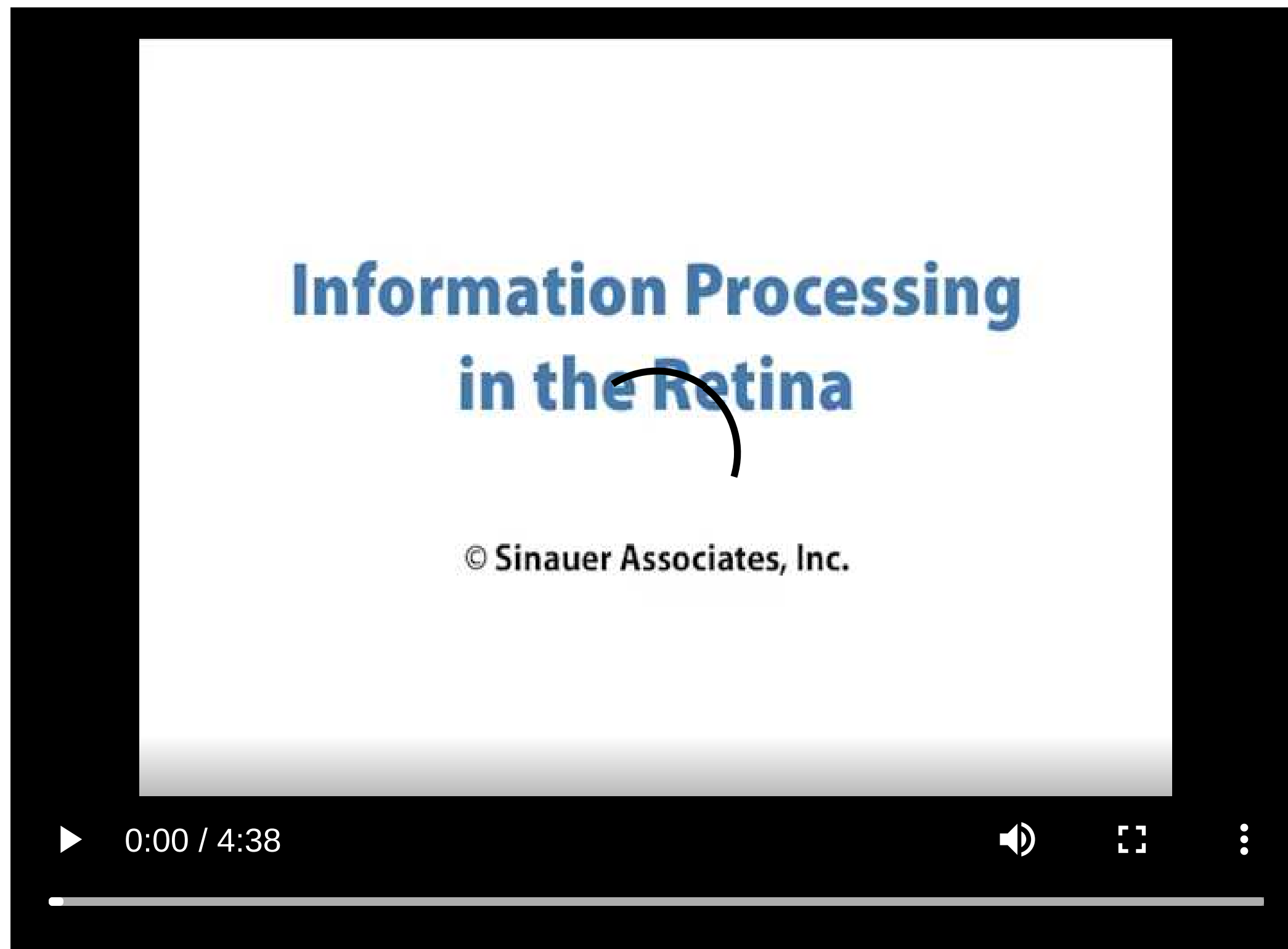


Neuroscience 5e Fig. 11.19, 6e Fig. 11.20

# ON center RGC receptive field summary

- For an ON- center/OFF-surround RGC, a point of light that fills the entire center but not in the surround will give maximal stimulation (increased action potentials). i.e. brighter in center than in surround
- A point of light in surround but not in the center will hyperpolarize the RGC (reduce baseline spike rate)
- Light that crosses into both will be in the middle depending on the relative amounts
- Both center and surround illuminated is basically the same as being in the dark (background levels)
- RGCs fire depending on contrast, not by absolute light intensity

# Information flow in the retina video summary



Neuroscience 5e Animation 11.3

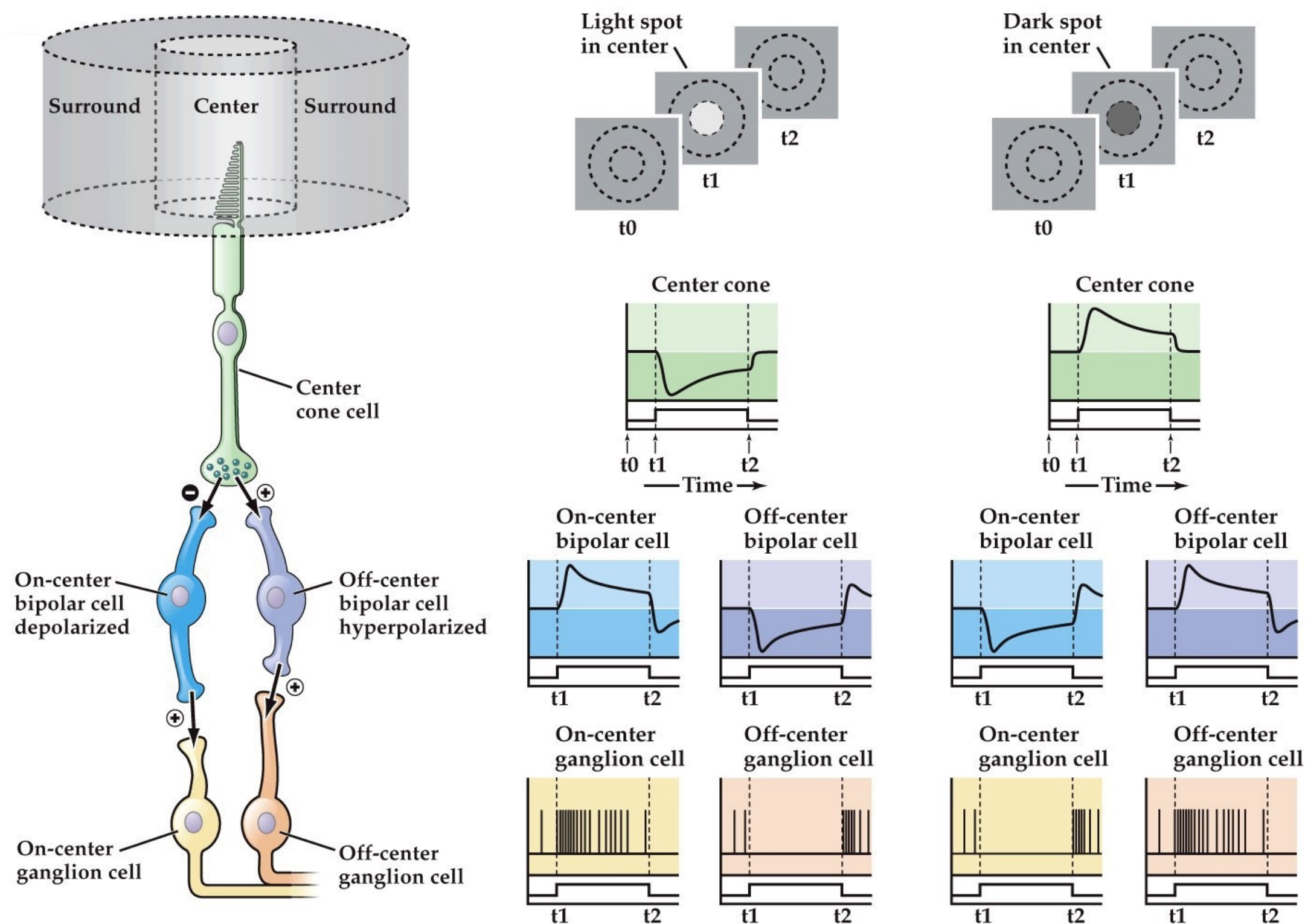
# ON and OFF bipolar cells

- RGC dendrites terminate in separate strata of the inner plexiform layer, forming selective synapses with different types of bipolar cells
- Bipolar cells do not use action potentials, but use graded (passive/electrotonic) potentials to release neurotransmitter
- There are two types of bipolar cells– ON center and OFF center. OFF center uses AMPA receptors (ionotropic) that cause the cell to depolarize in response to glutamate released by photoreceptors. ON center use metabotropic glutamate receptors that lead to the closing of  $\text{Na}^+$  channels and hyperpolarize the cell

# Circuit that shapes the RGC response to light hitting the receptive field center includes two types of bipolar cells

- Light hits cone causes hyperpolarization of cone, leads to less release of glutamate
- Two bipolar cells synapse with cone, an on-center and off center bipolar cell
- **On center bipolars are normally inhibited by glutamate**, less glutamate, less inhibition, more release of neurotransmitter onto RGCs which increases of on-center RGC firing
- **Off center bipolars are normally activated by glutamate**, become hyperpolarized, decrease transmitter release, which leads to a decrease in firing rate of Off-center RGCs

# Light in center causes ON ganglion cells to increase firing rate and OFF ganglion cells to decrease their firing rate



Neuroscience 5e Fig. 11.18

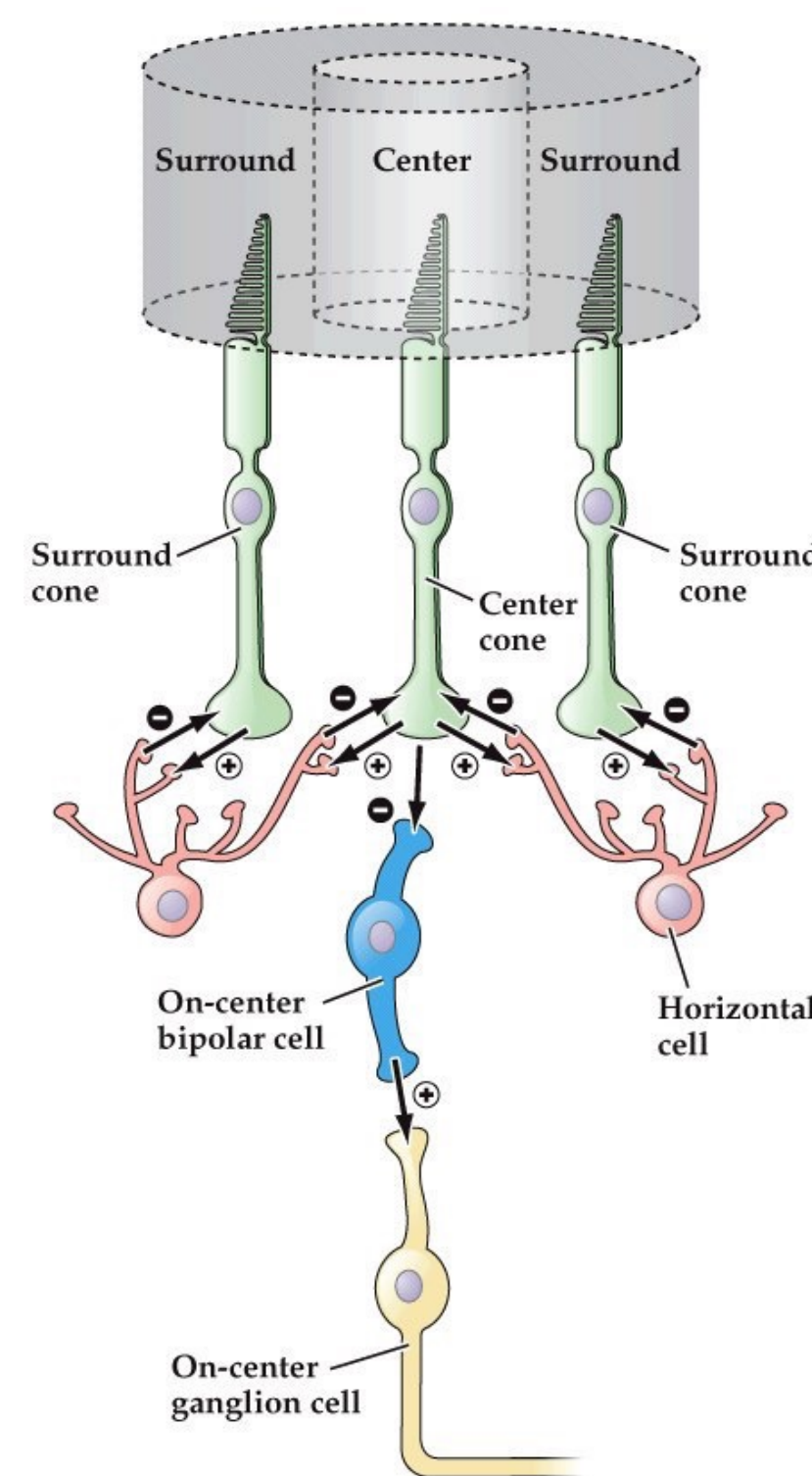
Neuroscience 5e Fig. 11.18; y-axis is voltage

# Horizontal cells create circuitry that is responsible for generating the antagonistic surrounds of RGCs

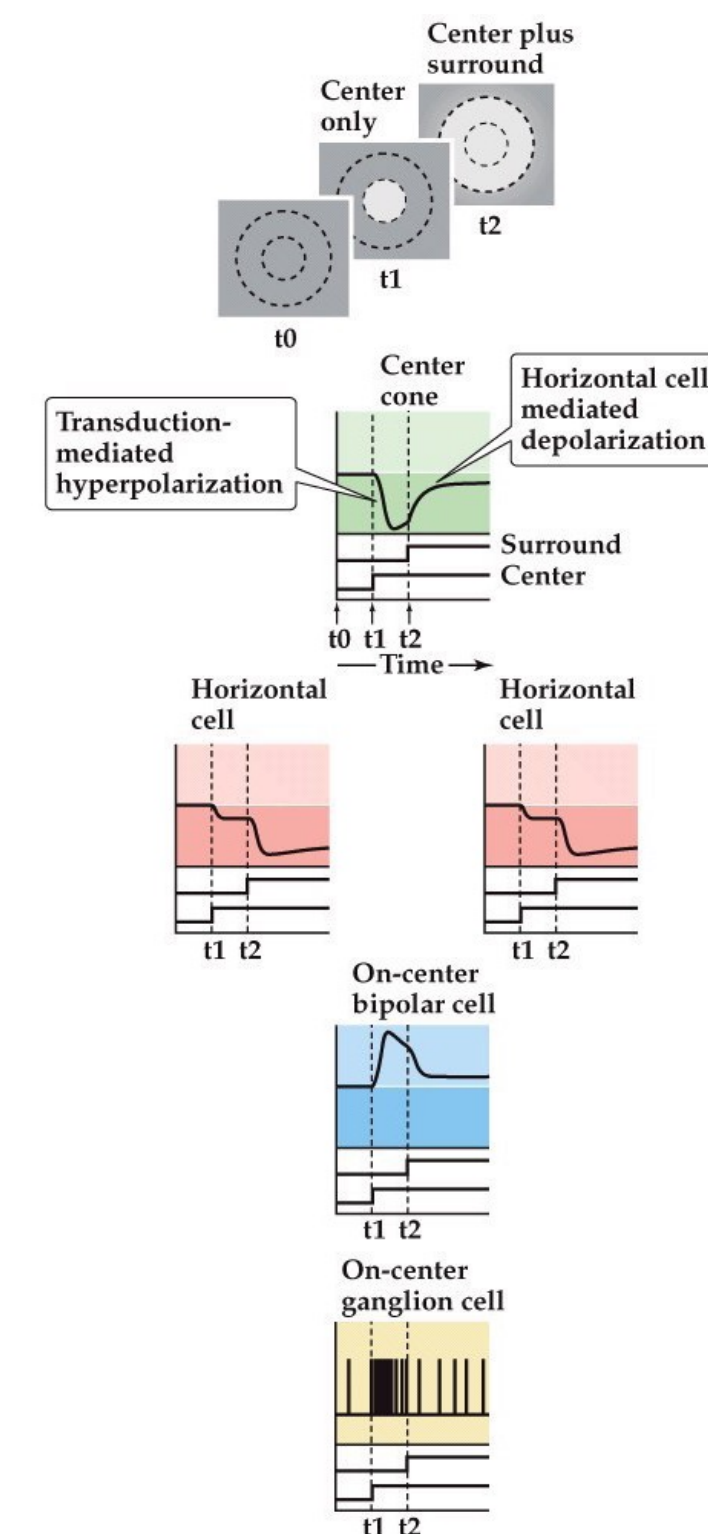
- Light hitting surround cones hyperpolarizes causing less glutamate to be released onto horizontal cell dendrites
- Horizontal cells hyperpolarize because of less glutamate (have AMPA receptors) and decrease their rate of transmitter release (GABA) onto the synaptic terminals of the nearby photoreceptors
- Horizontal cells normally inhibit cones (use GABA), thus now cones are less inhibited (depolarized), and release more glutamate than without surround
- This leads to a depolarization of off-center RGCs, causing them to increase their firing rate
- And hyperpolarizes on-center RGCs, causing them to decrease their firing rate

# Circuitry that generates the antagonistic surrounds of retinal ganglion cell receptive fields

- Light hits cone in surround
- Less glutamate released on horizontal cell
- Horizontal cell is hyperpolarized, releases less GABA onto cone in center. This depolarizes center cone relative to before light
- More glutamate released by center cone to ON and OFF bipolars
- Off-center depolarized, on-center hyperpolarized
- Off-center ganglion cell fires more
- On-center fires less



Neuroscience 5e Fig. 11.21



Neuroscience 5e Fig. 11.21

# Summary

- Light falls on photopigment, that is transformed to action potentials that ganglion cells convey to the brain
- Phototransduction occurs in rods and cones that have different properties that meet the conflicting demands of sensitivity and acuity
- RGCs have a center-surround arrangement of receptive fields that makes them good at contrast detection and relatively insensitive to background illumination