CNS PHYSIOLOGY

5

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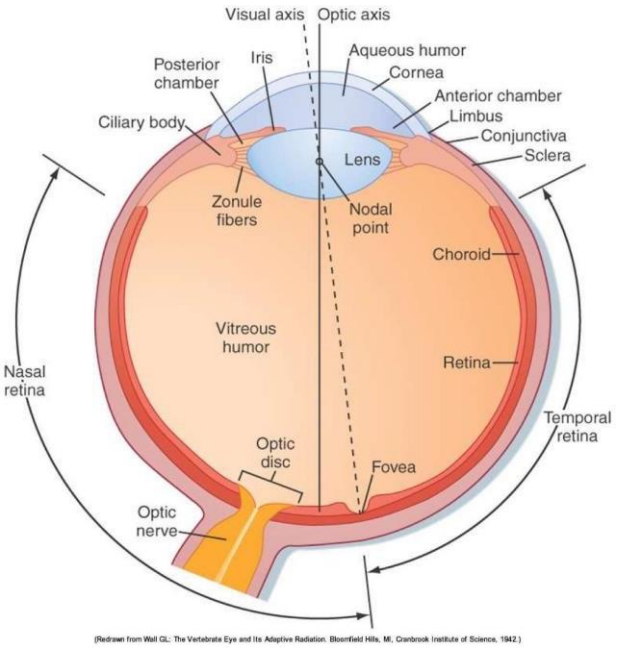
We know from the previous lecture that the eye contains three layers:

1- **Outer layer:** sclera that continues as cornea in front.
2- **Middle layer:** choroid [vascular layer] that continues as ciliary body and iris (the colored part of the eye) in front.
3- **Inner layer:** retina [neural layer]

In this lecture we will focus on the retina which is the light sensitive portion of the eye. Retina contains the neural architecture so light must pass through the neural elements to strike the light sensitive rods and cones.



Before we continue talking about the structure of the retina, we must mention two important areas found in the eye:

- **Macula lutea**: a small area at the center of the retina about 1 sq mm. the center of this area is **the central fovea** or **fovea centralis** which, as we will study later, contains cones only and that's what makes it responsible for sharp and discriminative vision. [for a picture to be seen clear and colorful it must come into fovea]
- **Optic disc:** it is the area where optic nerve exits, and central retinal vessels enter or leave. This area lacks visual receptor; therefore, it is called **blind spot**.

Ophthalmologists examine the optic disc area looking at **the central retinal artery** because it is the most superficial artery in the body to diagnose atherosclerosis or bleeding especially in hypertensive patients.

Structure of the retina:

Please notice that the layers are arranged from outside to inside that is from the outer region of the retina to the vitreous body inside the posterior cavity.

A. Pigmented layer

- ✓ Pigment layer of the retina is very important.
- ✓ Layer of cells that produce the black pigment (**melanin**)
- ✓ **Absorbs extra light = prevents light reflection in the globe of the eye**
- ✓ Without the pigment there would be diffuse scattering of light rather than the normal contrast between dark and light = if this layer is absent, light will reflect, and the picture will be hazy because this extra light will stimulate many receptors

This what happens in albinos (genetic absence/ deficiency in melanocyte activity = melanocytes are normal in structure and number, but they don't produce melanin). They have poor visual acuity because of scattering of light and when they try to read, they get the book close to them to control the amount of light coming to their eye.

✓ Vitamin A derivatives are stored in **alcoholic form** [cis- / trans- retin**ol**] inside this layer and in the rods and cones also.

B. Neural retina

1- Photoreceptor layer (the rods and cones layer): contains the outer segment of these cells (photoreceptors).

Notice that the receptors are in a very deep layer except in the fovea centralis receptors are superficial

2- Outer nuclear layer: contains cell bodies of photoreceptors

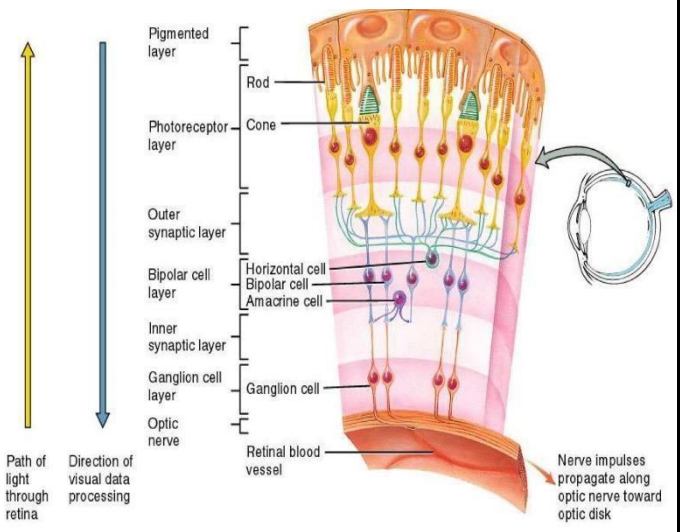
3- Outer plexiform layer (outer synaptic layer): contains synapses between axons of the rods and cones and the dendrites of the bipolar cells.

4- Inner nuclear layer (bipolar cell layer): contains nuclei of the bipolar cells, amacrine cells and horizontal cells.
**horizontal cells: are inhibitory interneurons (lateral inhibition)

5- Inner plexiform layer (inner synaptic layer): contains synapses between axons of bipolar cells and dendrites of ganglion cells

6- The ganglionic layer: contains ganglion cells with long axons

7- Nerve fiber layer (optic nerve): ganglionic axons that converge at the optic disc and form the optic nerve [these axons converge and go back to exit out from the retina as optic nerve]



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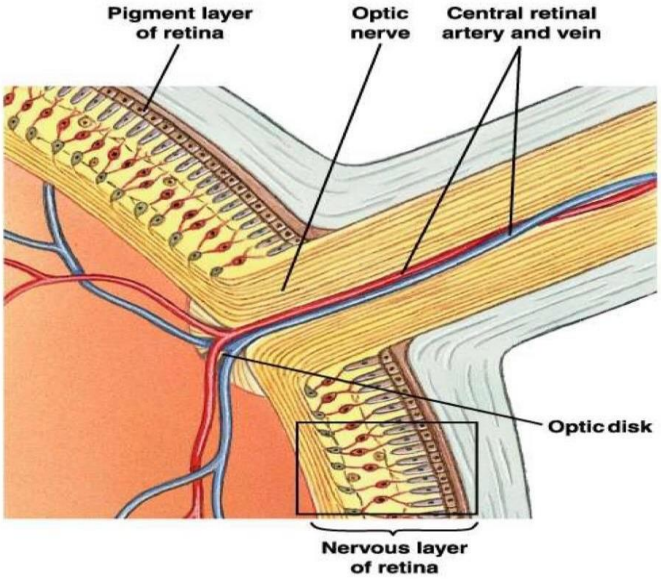
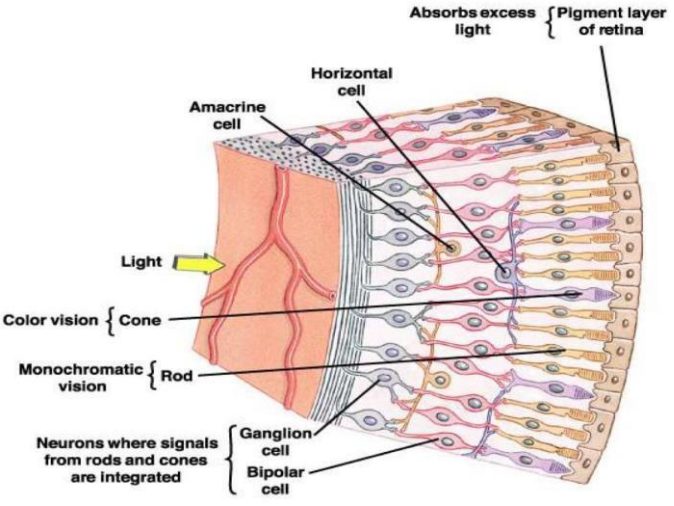


Layers of the retina, the light-sensitive layer lining the posterior chamber of the eye



Notes:

- path of light through retina is from layer 7 back to the pigmented layer, while the direction of visual data processing is the opposite.
- In the central fovea the neuronal cells and blood vessels are displaced to each side so that the light can strike the cones directly and that's the cause of the depression or groove seen in this area and the cause of the very sharp vision [because light doesn't pass through all the layers so it doesn't refract, and the picture willnot be hazy]

Comparison between rods and cones:

	Rods + very dim light	**Cones** + bright light
Vision	Night vision (no color discrimination)	Day Color vision Sharp (aid in detecting details)
Number	100 million for each retina	3 million for each retina
Sites	Periphery (laterally)	Center (fovea centralis contains cones only)
Types / pigment	One type (produce white or black color only) – achromatic	Three types each with a different pigment that is sensitive to a different part of the visible spectrum (red, blue, green) – trichromatic Any other color is a mixture of stimulation of the three types
Convergence	Every 60 rods converge into one ganglion cell (leads to loss of sharpness)	Every 2 cones converge into one ganglion cell (at the central fovea there are no rods and the ratio of cones to ganglion cells is 1:1 / sharp)
Light sensitivity	High sensitivity (small amount of light can stimulate it producing receptor potential that is going to summate because of the high number of convergences) More sensitive to scattered light	Lower sensitivity More sensitive to direct axial rays
Amplification	High – can detect single point	Low – less convergence (1:1 is more)
Photopigment	More	Less
Visual acuity	Low (highly convergent retinal pathways)	High (less convergent retinal pathways)
Response and integration time	Slow response, long integration time	Fast response, short integration time
Saturate in	In day light	With intense light

- The number of ganglionic cells is 1.6 million for each retina
- Visual acuity (two-point discrimination) is greatest in cones. These cones have a special conical structure with a diameter of 1µm. for the image to go into fovea centralis (cones only) and hit two cones, the distance between the two points must be 2µm. and as we know the distance between the retina and the center of the lens is 17mm so the angle will be 1 minute .

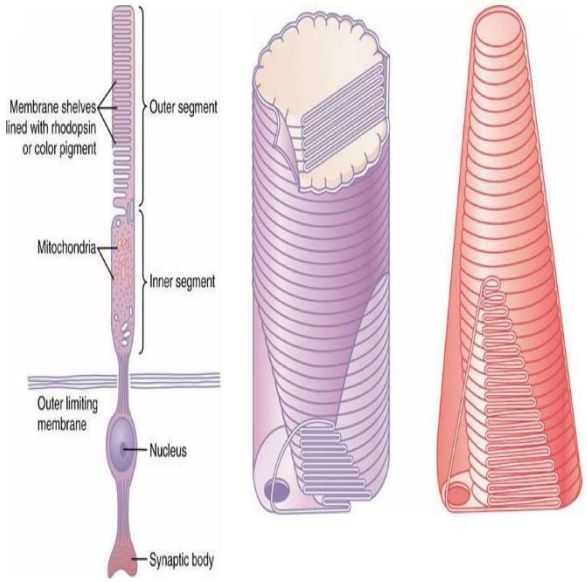
Structure of the rods and cones:

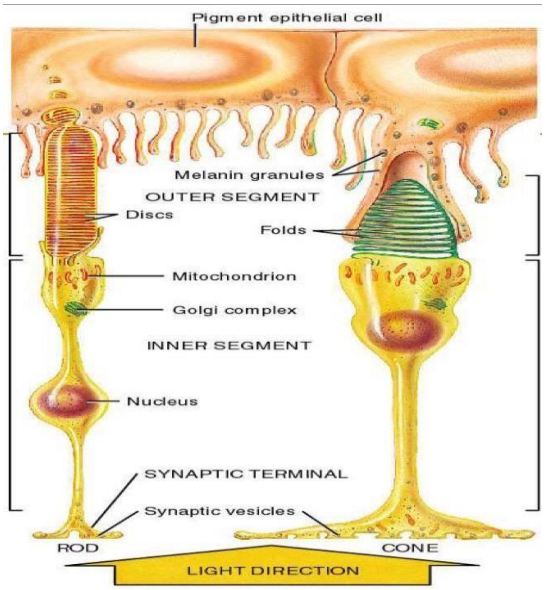
1- Outer segment:
- ✓ Membranes of cells stacked together. 40% of the membrane constitutes of the **opsin** protein and 11-cis retin**al** (vitamin A derivative,aldehyde form) forming **rhodopsin** which is the color pigment.
- ✓ There are 1 type of opsin in rods and 3 types of opsin in cones.
- ✓ Vitamin A derivatives are formed in the pigmented layer and in the rods and cones.
- ✓ this segment is embedded in the pigmented layer.

2- Inner segment: contains mitochondria (for energy).

3- Nucleus.

4- Synaptic body: like axon terminal containing the neurotransmitter glutamate.





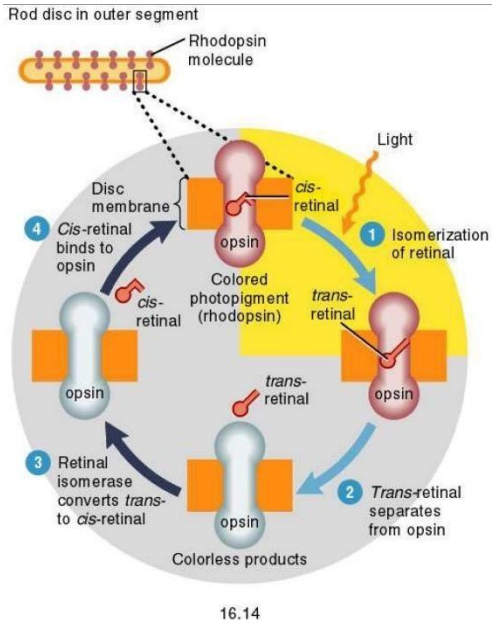
Photochemistry of vision:

A. As we know, in the rods or cons discs present in the outer segments there are rhodopsin molecules [**visual purple** in rods called scotopsin **scoto =dark , opsin = responsible for the sensitivity in dark)** and **photopsin** in cones]. Rhodopsin is composed of a protein called **opsin** and a pigment **retinal.** Retinal has two forms:

1- **Cis-retinal**: which is bound to opsin forming the colored photopigment rhodopsin. → opsin is inactivated

2- **Trans-retinal**: which is separated from opsin. → opsin is activated

- **Light** converts retinal from the **cis** form to the **trans** form [isomerization of retinal] leading to decomposition of rhodopsin and activation of opsin.
- **Retinal isomerase** converts **trans**- to **cis**-retinal leading to deactivation of opsin (dark)



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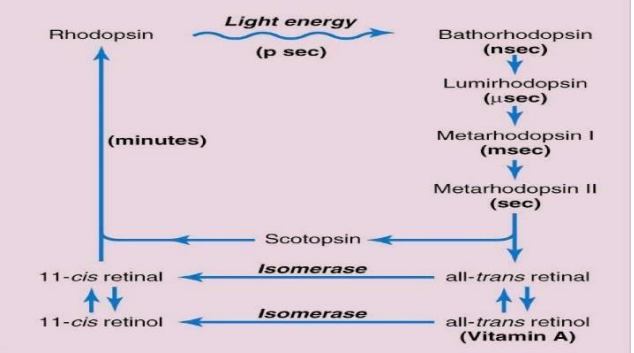
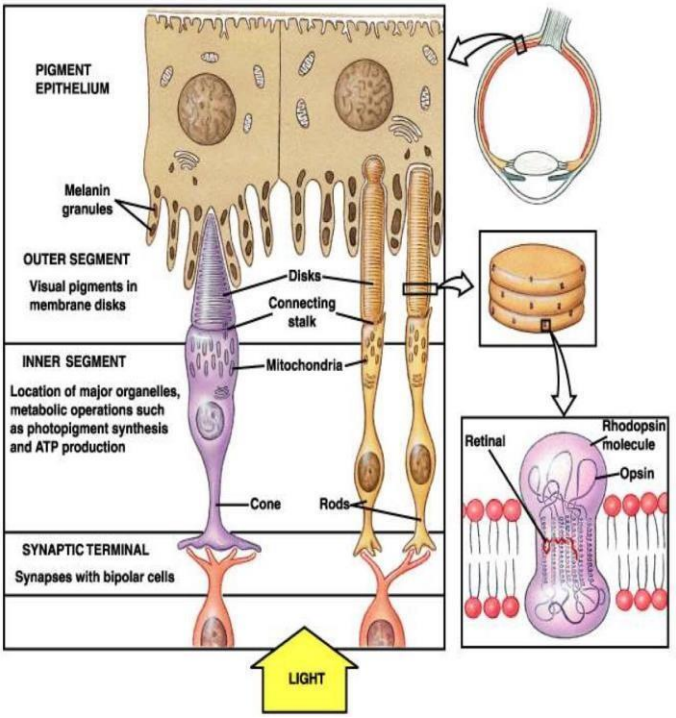


- Trans retinal has the same chemical structure but is a straight molecule rather than an angulated molecule.
- Trans configuration doesn't fit with the binding site on the scotopsin and the retinal begins to split away (decomposition).
- In the process of splitting away a number of intermediary compounds are formed.

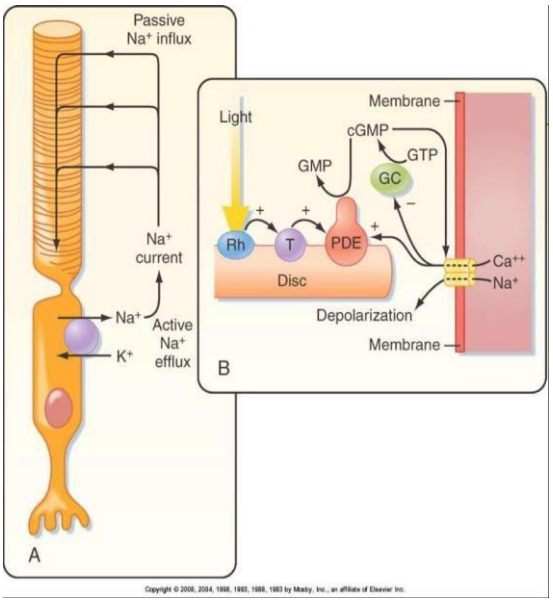


B. Light activates **opsin** -> opsin activates membrane protein called **transducin** (G- protein) -> transducin activates **cGMP phosphodiesterase** -> cGMP phosphodiesterase will **break down cGMP** into GMP.

In the outer segment of rods and cones there are cGMP gated Na-channels (which open whenever there is cGMP). Those channels are ligand-gated channels and not voltage-gated channels, so they don't cause action potential.

In the previous sequence cGMP is broken down by cGMP phosphodiesterase, meaning that **cGMP is becoming less**, and those **cGMP dependent Na-channels are closing**.

Thus, Na isn't getting into the outer segment of the rods and cones, no more Na influx, causing **hyperpolarization** of these receptors.

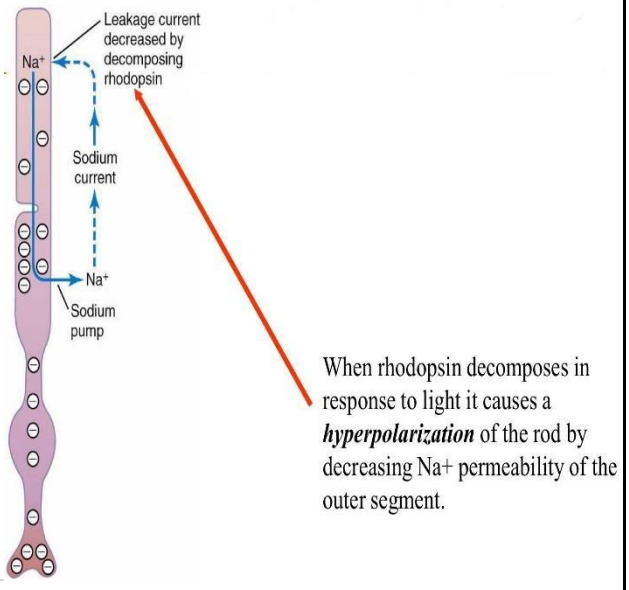


<u>To summarize: light leads to hyperpolarization of photoreceptors.</u>

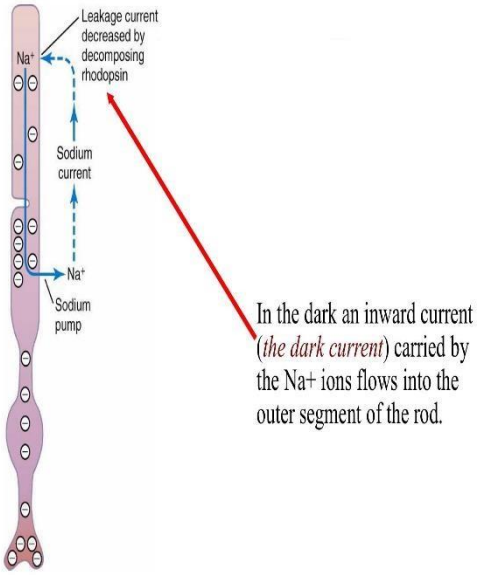
Hyperpolarization stops the secretion of neurotransmitters.

- *Photoreceptor potential (when exposed to the stimulus/light) is hyperpolarizing potential*
- **Rhodopsin kinase** deactivates the activated rhodopsin (which began the cascade) and cGMP is regenerated re-opening the Na+ channels.

Dark



C. The opposite occurs during night (in the Dark), retinal isn't converted from cis to trans form, thus, it stays attached to opsin deactivating it. This leads to the deactivation of cGMP phosphodiesterase, cGMP won't be broken down, we have a lot of cGMP **opening the cGMP dependent Na-channels**, **Na will influx** into the outer segment of the rods and cones causing **Depolarization**.



To summarize: Dark leads to Depolarization of photoreceptors.

Depolarization leads to secretion of neurotransmitters.

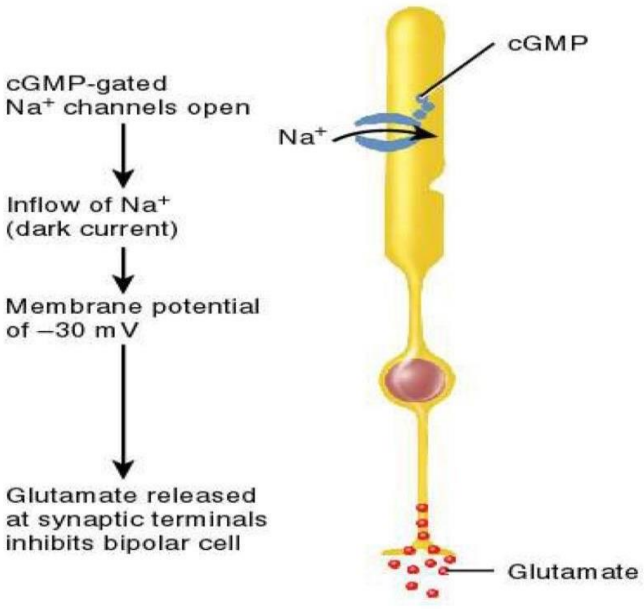
- The question here is that light which is the stimulus of photoreceptors leads to hyperpolarization decreasing the neurotransmitters release, while dark leads to depolarization increasing the neurotransmitters release and that's opposing what we always thought about the stimulus and the depolarization and hyperpolarization states, so how can we explain that?

The answer is that the neurotransmitter here is **glutamate** which is considered **inhibitory** in the visual receptors.

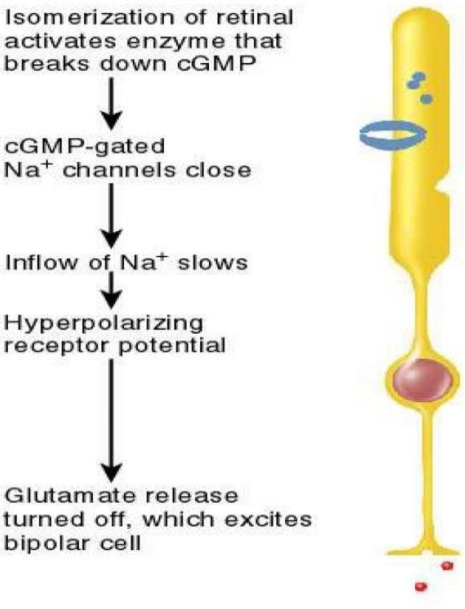
Meaning that when light leads to hyperpolarization and decrease of glutamate, **in fact light excites the rest of cells (bipolar cells and ganglionic cells)**.

On the other hand, dark leads to depolarization and increase of glutamate release, **in fact darkinhibits the rest of cells (bipolar cells and ganglionic cells)**.

Extra notes: 1- there is Na+ pump in the inner segment that keeps pumping Na+ out of the cell. 2- The greater the amount of light the greater the decomposition of the pigment and the greater the electronegativity (hyperpolarization).



(a) In darkness



(b) In light

D. Receptor cells and bipolar cells respond by **local potentials** (receptor potential) either **EPSP** or **IPSP** not action potential.
The only type of cells that respond by action potential in the eye is **the ganglionic cells**. (and **some** amacrine cells)
for revision: The rod receptor potential: Normally about -40 mV. Normally the outer segment of the rod is very permeable to Na+ ions. In the dark an inward current (the dark current) carried by Na+ ions flow into the outer segment of the rod. The current flows out of the cell, through the efflux of K+ ions in the inner segment of the rod.

Duration and sensitivity of the receptor potential:

- ✓ A single pulse of light causes activation of **the rod receptor potential** for more than on second. [slow response, long integration time]
- ✓ **In the cones** these changes occur 4 times faster. [fast response, short integration time]

Synaptic after potential:- when you look at light and close your eyes, you will see spotlights. That's because receptor potential continues more than the time for action potential/ receptor potential continues to activate ganglionic cells for more time than the time for a single pulse light.

- ✓ Receptor potential is proportional to the logarithm of the light intensity and this is very important for discrimination of the light intensity.

When we are using the logarithmic scale, we will have bigger numbers and therefore bigger differences between the degrees of light intensity (1, 10, 100, 1000, …) increasing the sensitivity of the retina.

Role of vitamin A:

- It is the precursor of all-trans-retinal, the pigment portion of rhodopsin.
- it is stored in the pigmented layer, rods and cones.
- Vitamin A is lipid soluble. It is stored in fat and liver. Therefore, **vitamin A deficiency (lack of vitamin A) occurs if there is no intake of vitamin A for more than 6 months.** (nutritional disease)
- Lack of vitamin A causes a decrease in retinal. This result in a decreased production of rhodopsin and a lower sensitivity of the retina to light or what's called **night blindness**.
  Explanation: rods will be affected more because of their huge number and they are responsible of vision during night so there will be an abnormality in seeing things during night. But during the day, there is too much intense light that can easily stimulate cones and rods even with the lack of vitamin A.

[sensitivity is directly proportional to amount of pigment]

Dark and light adaptation

	Dark adaptation	Light adaptation
Sensitivity of the retinal automatically adjusts to the light level	In dark conditions retinal is converted back to rhodopsin. (increasing formation of the pigment -> increasing the sensitivity)	In light conditions most of the rhodopsin has been reduced to retinal so the level of photosensitive chemicals is low. (decreasing the sensitivity)
Explanation	When you enter a dark area, the 1st pigment that starts to form is in the cones (they have fast response but low number). When cones finish the synthesis, rods start (they have slow response but high number) and the synthesis peaks after 30-40 minutes. Therefore, after 30-40 minutes you start seeing clearly.	When you enter a lighted area where the stimulus (light) is very strong, all the pigment is decomposed, decreasing the sensitivity of the retina starting with the cones (low number) then the rods (high number).
Opening and closing of the pupil also contributes to adaptation because it can adjust the amount entering the eye	Mydriasis	Miosis

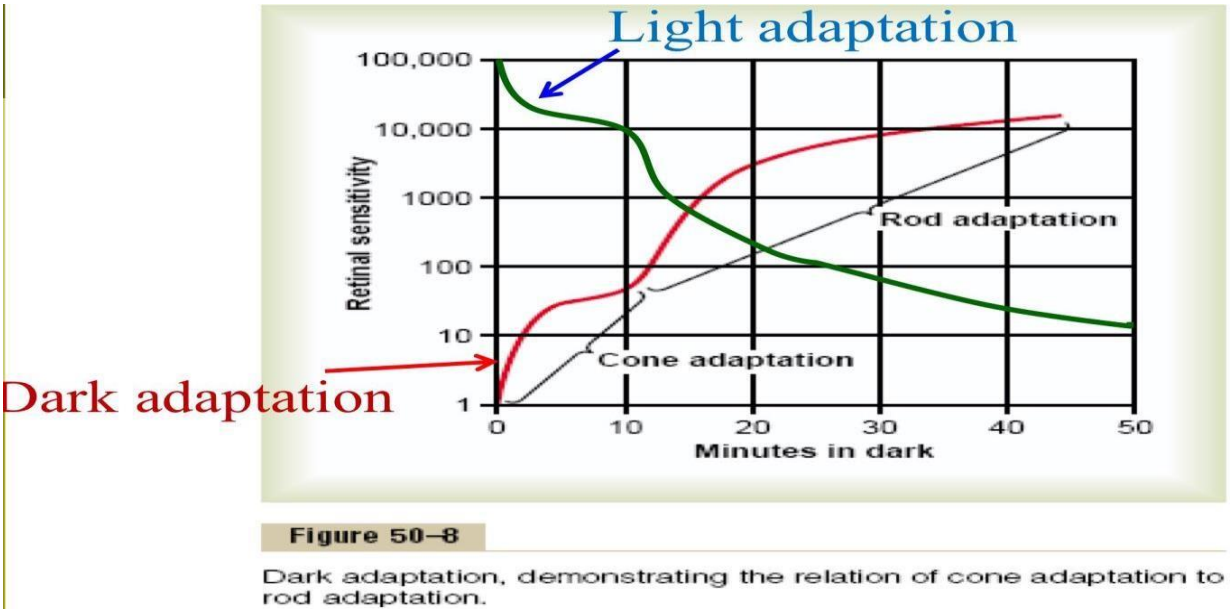


Figure 50–8

Dark adaptation, demonstrating the relation of cone adaptation to rod adaptation.