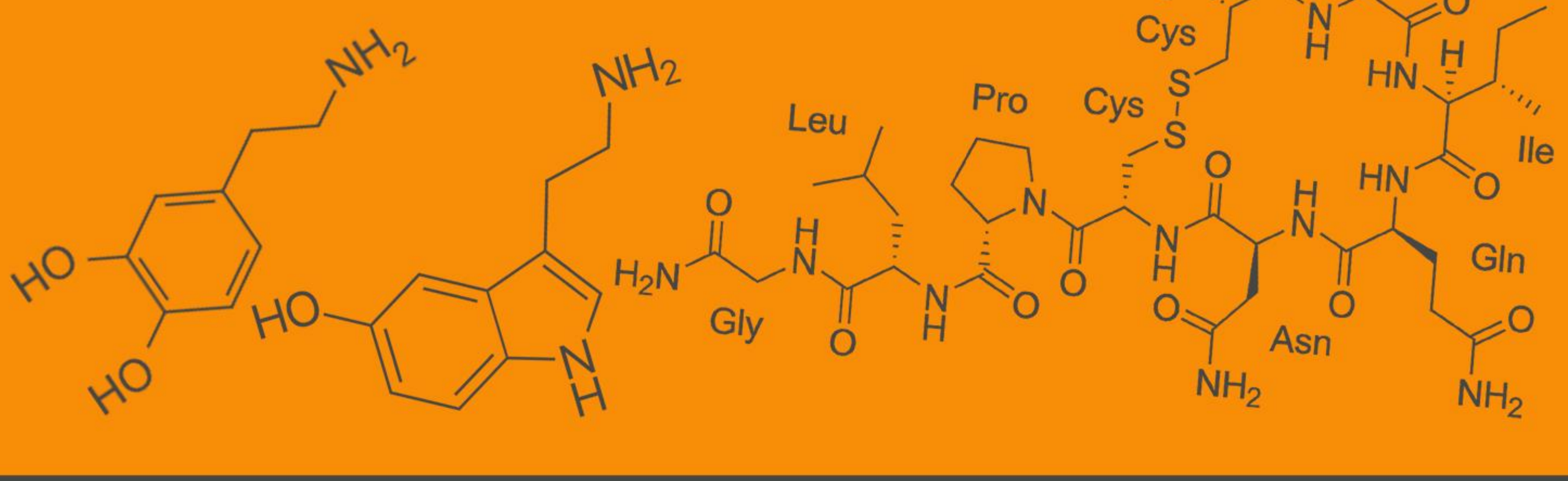
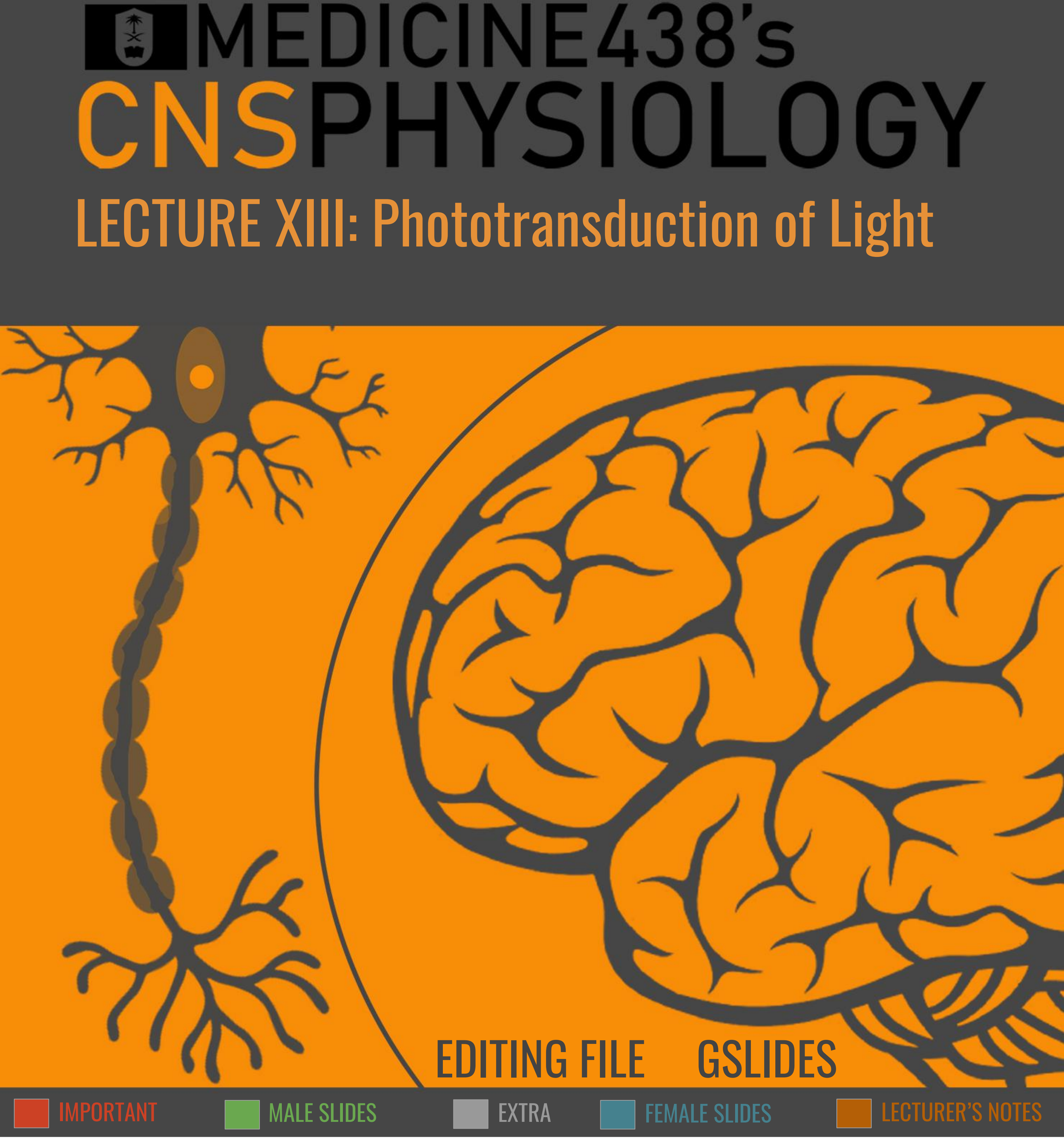


MEDICINE438's CNS PHYSIOLOGY

LECTURE XIII: Phototransduction of Light



EDITING FILE GSLIDES

IMPORTANT | MALE SLIDES | EXTRA | FEMALE SLIDES | LECTURER'S NOTES

1 Phototransduction of light

Lecture Thirteen

OBJECTIVES

- List and compare functional properties of rods and cones in scotopic and photopic vision
- To know the convergence and its value
- To describe the photosensitive compounds
- To Contrast the phototransduction process for rods and cones in light and dark and the ionic basis of these responses
- To know the process of rhodopsin regeneration
- To know the meaning of nyctalopia
- Contrast the dark and light adaptation
- To know the visual cycle and rhodopsin regeneration
- To recognize types of ganglion cells

Visible light spectrum:

- Extends from 397 to 723nm
- Eye functions under two 2 conditions of illumination

Duplicity theory of vision

- Bright light (Photopic vision)...Cones
- Dim light (Scotopic vision) ..Rods

Physiology of vision:

Stimulus:light. Receptor:retina(photoreceptors)

Definition of light:electromagnetic radiation that. Is capable of exciting the human eye(extremely fast)

Visible receptors:Rods and Cones

RODS	CONS
Abundant in the periphery of the retina	Abundant in & around fovea
Best for low light(dimlight) conditions (Night vision/scotopic vision)	Best for bright high light conditions (Photopic vision)
See black/white and shades of gray Monochromatic	See all colors
100,000,000,12,000,000 (Poor acuity)	5,000,000,600,000,000 (Good acuity)

Table 13-1

Shape of rods & cones (receptors of vision):

-Outer segment(modified cilia)

A has disks full of photosensitive pigment (rhodopsin) react with light to initiate action potential

B In cones is conical, small and contain 3 types of rhodopsin / photopsin (in small amount) photopsin is more precise cause rhodopsin moves in segments

C In rods it is big,rod-like and contain <u>one</u> type of rhodopsin

D There are Na channels in the outer segment which allow Na to enter the photoreceptors

-Inner segment

A There is Na-K pump In inner segment

B Full of mitochondria (source of energy for Na-K pump), it is thick in cons

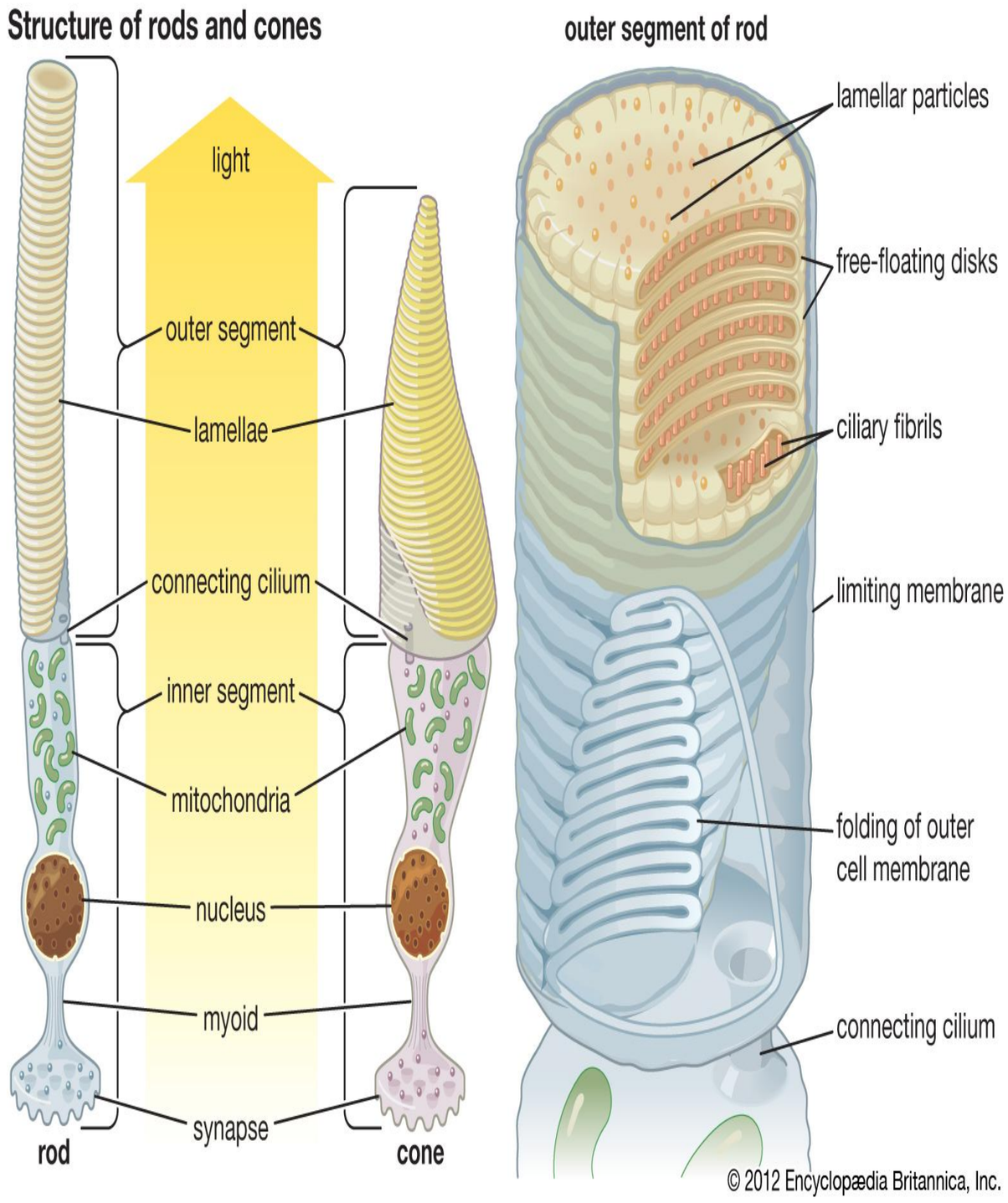


Figure 13-1

The inner and outer segments are connected by a ciliary stalk through which the photosensitive compounds travel from the inner segment (where they are manufactured) to the outer segment of the rods and cones (where they are used).
(although the cones is small it has three types of photopsin /rhodopsin)

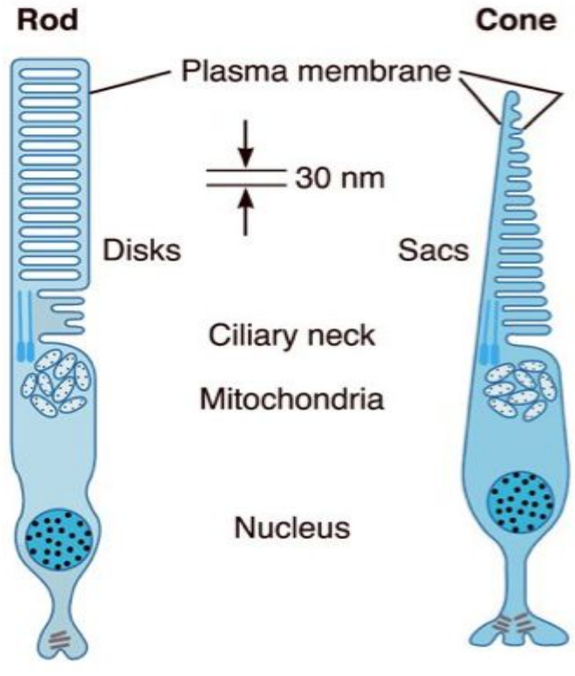


Figure 13-2

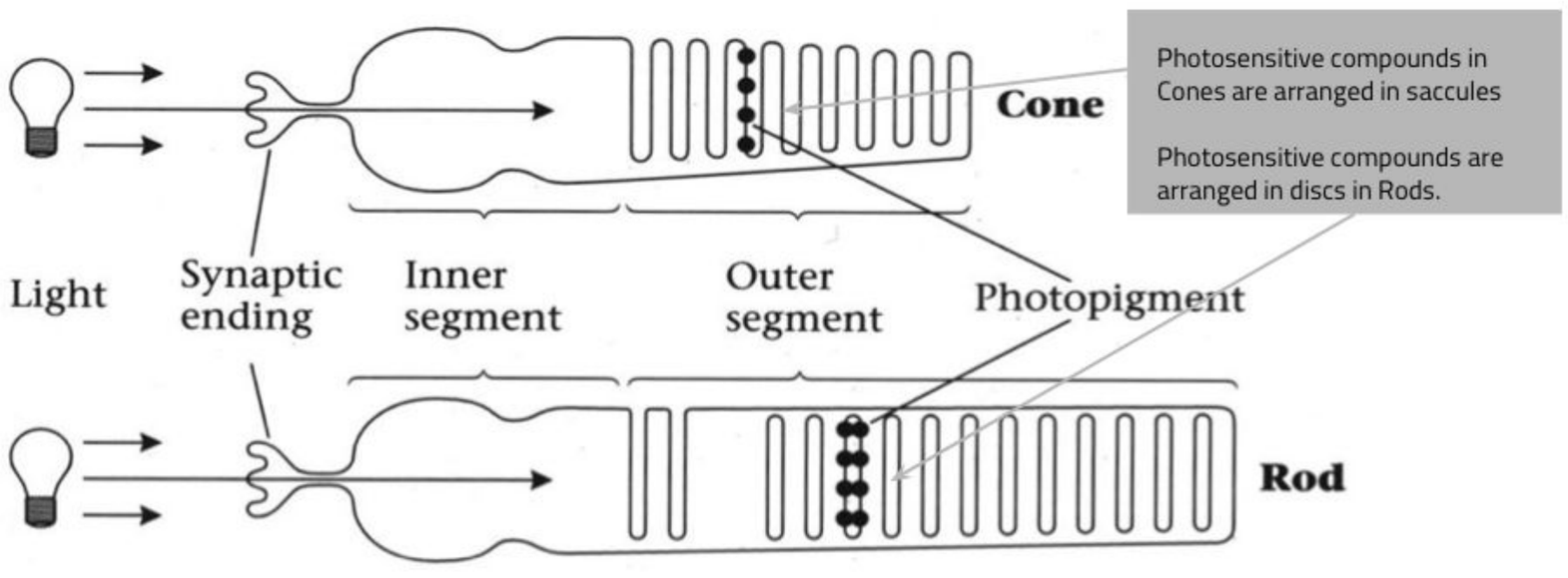
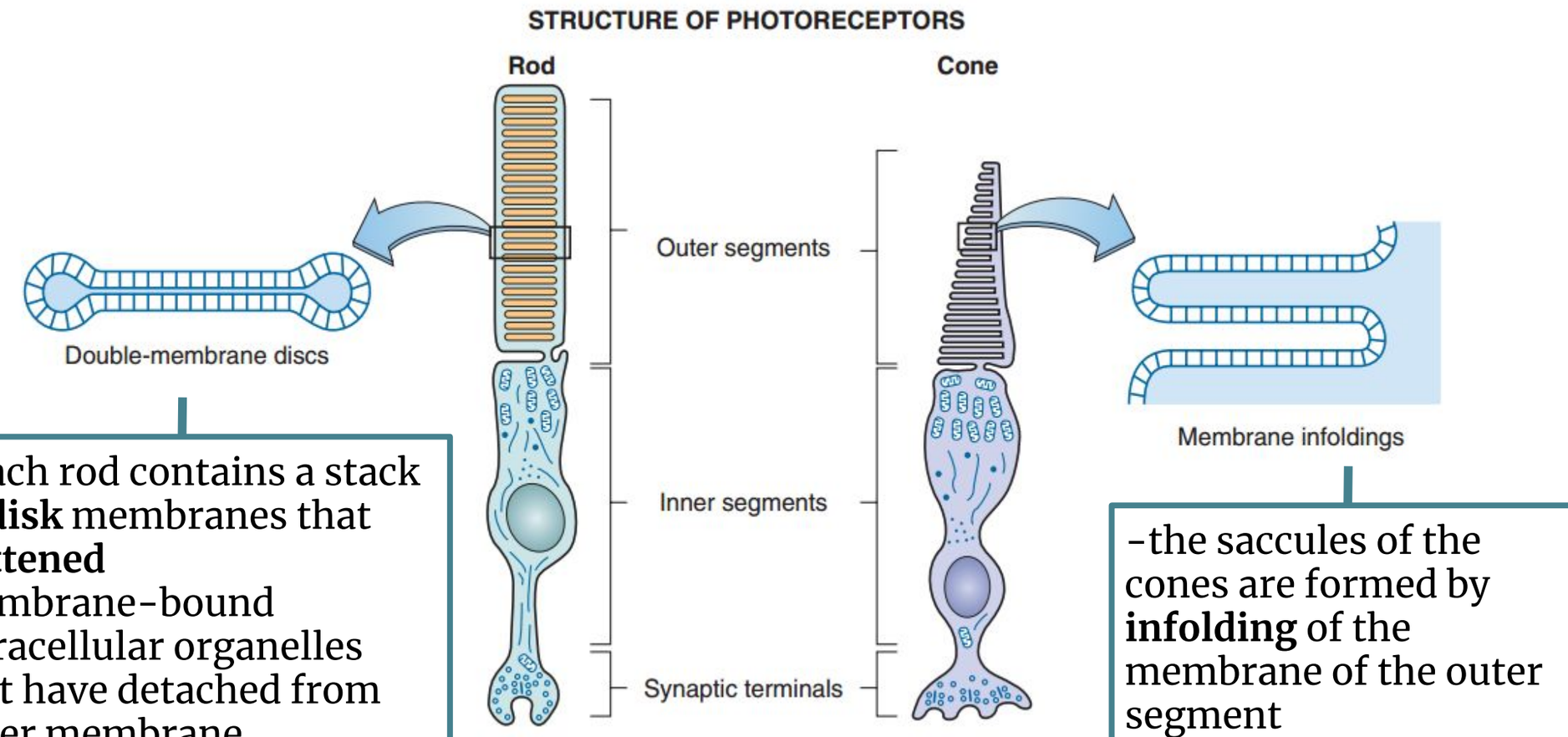


Figure 13-3



-Each rod contains a stack of **disk** membranes that **flattened** membrane-bound intracellular organelles that have detached from outer membrane
-Disks are free floating,

-the saccules of the cones are formed by **infolding** of the membrane of the outer segment

Figure 13-4

The saccules and disks contain the photosensitive compounds that react to light initiating action potentials in the post synaptic cells

Convergence:

Rule: Convergence increases sensitivity to light and decrease acuity

Low convergence	High convergence
In cones	In rods
Each foveal cone synapse with → one bipolar cell → one ganglion cell → single optic nerve fiber. peripheral 2-3 cones converge into one bipolar cell unlike foveal cones which transmit 1 to 1 approximately 3000 cones concentrated in fovea centralis	several rods (about 300) synapse with one bipolar cell & one ganglion cell
advantage (value of low convergence): increases visual acuity → integrated information from small area of retina	**advantage:** increases sensitivity to light i.e so low light threshold stimulate the rods
Disadvantage: decreases sensitivity to light i.e need high threshold of illumination to stimulate cones	**Disadvantage:** High convergence /decreases visual acuity= integrated information from large area of retina
120 million rods & 6 million cone converge on 1.2 million optic nerve fibers , (126 million reception on 1.2 million nerve fiber)so convergence is 105 receptor : 1 fiber Further explanation:if we divide 126 by 1,2 it will give us 105 **so** each 105 of the photoreceptors will be carried by 1 of the bipolar and the majority will be the rods cause their more than the cones	

Table 13-2

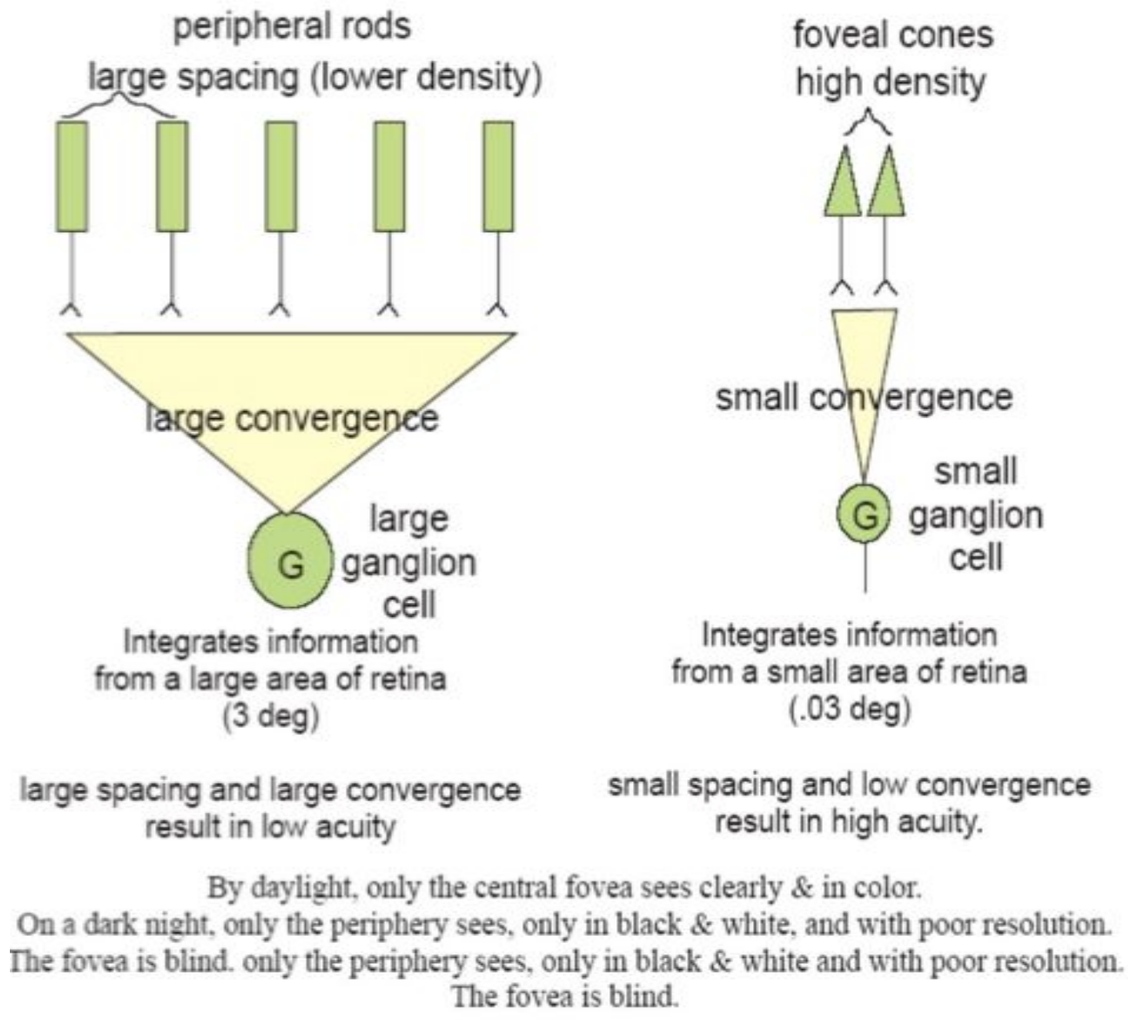


Figure 13-5

▸ Convergence of Cones and Rods

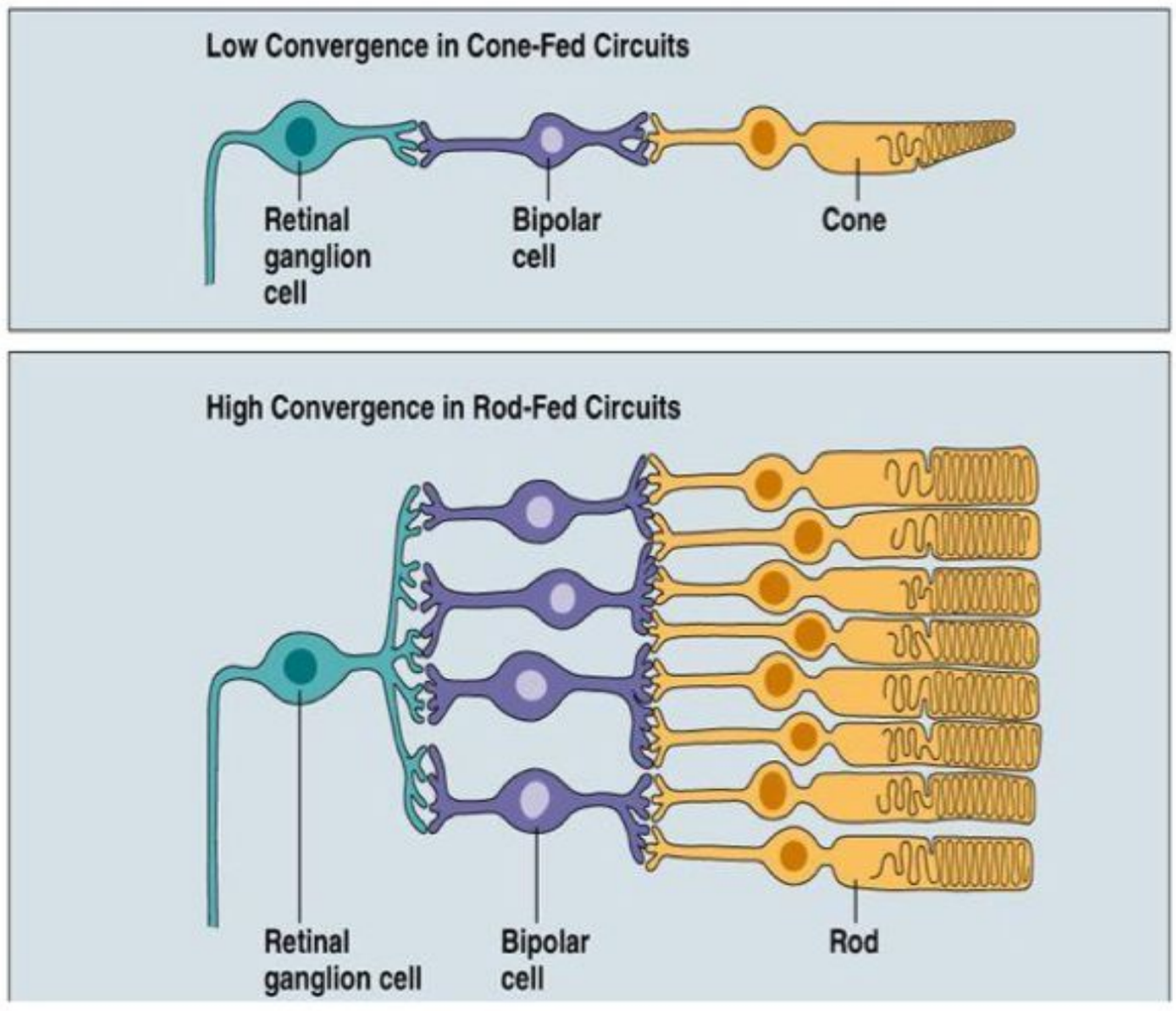


Figure 13-6

Photosensitive Compounds (rhodopsin)

Cones

In cones rhodopsin (iodopsine) formed of:
1. Opsin protein (photopsin)
2. Retinal (retinene 1 = aldehyde form of Vit A)

There are 3 types of rhodopsin in cones (photopsine I,II,III) each respond to a certain wavelength of light for color vision

Rods

In Rods, rhodopsin, is formed of:
1. Opsin protein (scotopsin)
2. Retinal (retinene 1 = aldehyde of Vit A) = visual purple

(Rhodopsin of the rods most strongly absorb green-blue light and, therefore, appears reddish-purple)
(this appearance is under the microscope)

- Rhodopsin forms 90% of rods protein, stored in disks of rods at outer segment
- At dark "no light at all" rhodopsin is in 11-cisretinal form (inactive, but light sensitive form) which increase sensitivity of rods to light.

Light>absorption by photosensitive substances>structural change in photosensitive substances>phototransduction>action potential in optic nerve

Photoreceptors pigments

Composition:

- Retinine1 (Aldehyde of vitamin A) , same in all pigments.
- Opsin (protein) , Different amino acid sequence in different pigments.
- Rhodopsin (Rod pigment): Retinine + scotopsin

Genesis of photoreceptor potential:

- Rods & cones potentials are graded, local potential (generator potential) propagated as A.P in ganglion cells.
- Ganglion cell action potential (all or none A.P) transmitted to optic nerve.
- Cones respond to high levels of light intensity (illumination)
- Rods respond to levels of light intensity (illumination) below threshold levels for cones, so rods are more sensitive.

- **Electric recording in Retinal cells:**

1- Rods & Cones are stimulated by hyperpolarization
2- Bipolar cells: Hyper- & Depolarization
3- Horizontal cells: Hyperpolarization
4- Amacrine cells: Depolarizing potential
5- Ganglion cells: Depolarizing potential

ELECTROPHYSIOLOGY OF VISION(PHOTOTRANSDUCTION)

A-at dark(scotopic vision,dim light vision)"no light at all"

1-Rhodopsin in 11-cisretinal

- (inactive form-light sensitive form which increase sensitivity of rods to light) in the outer segment.

Simply:when the rhodopsin is in its inactive form which is"11-cisretinal"it will increase the rods activity with light so that's why the rods are highly sensitive to light

2- 5 –GPM of the outer segment Na channels is in the c-GMP[1] form (c-GMP at c-GMP gated Na channels of the outer segment , it bound to proteins at Na channel membrane & keep them open) → opening of Na channels at outer segment → allow Na influx after its is pumped out from Na –K pump of the inner segment→ depolarization. (-40mvolt , instead of -80 mvolt in most receptors)

3-Dark current (Na current):

- At the inner segment Na pumped by Na- K Pump to outside & re-entered through Na channels (at outer segment) → Depolarization flow to synaptic endings → **steady increased release of glutamate** at synapses with bipolar cells → which get depolarization potential (off-center bipolar cells in the periphery=rods,so in-center will mean cones)→ depolarize ganglion cells

FOOTNOTES

1. cGMP is a common regulator of ion channel conductance, glycogenolysis, and cellular apoptosis. It also relaxes smooth muscle tissues. In blood vessels, relaxation of vascular smooth muscles lead to vasodilation and increased blood flow.

Synaptic mediators in retina:-

Ach, glutamate, dopamine, serotonine,GABA, substance P,somatomedin, VIP, enkephalins, glucagons,neurotensin.

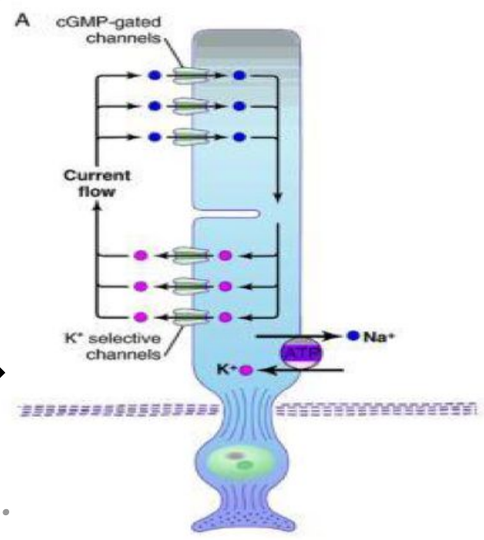


Figure 13-7

- Response in bipolar cells(OFF –center bipolar cells) (depolarization) → ganglion cells- → AP in optic nerve- → vision at dark. This Na current is continuous in dark, thus called "Dark current". it causes a wave of depolarization.

NB/

- at dark rhodopsin is inactive (11 cis-retinal needs light for its activation) / inactive rhodopsin is essential for depolarization
- its inactivation keeps Na channels open by keeping cGMP & Na current occurs

(So when this activation happens through light what will happen?)

Retinine1 in the 11-cis configuration[1] → (LIGHT) → All-trans isomer → Metarhodopsin II[2] → Closure of Na channels

B-incident light(photopic vision):

Light → Conformational change of photopigment retinine-1 in rhodopsin (a process known as bleaching) (11-cisretinal form changed to → metarhodopsin → all-trans isomer called metarhodopsin II which is an active rhodopsin) →Activation of G – protein (transducin) → activation of phosphodiestrase enzyme → conversion of c-GMP to 5- GMP → Decreased intracellular c-GMP → closure of Na channels in outer segment but still Na pump out of inner segment (Na-K pump) → Hyperpolarization of photoreceptors (-70 ~ -80 millivolts)
Hyperpolarization is caused by increased negativity, which is caused by the cations pumped out, accumulating in ECF and not re-entering through Na channels.

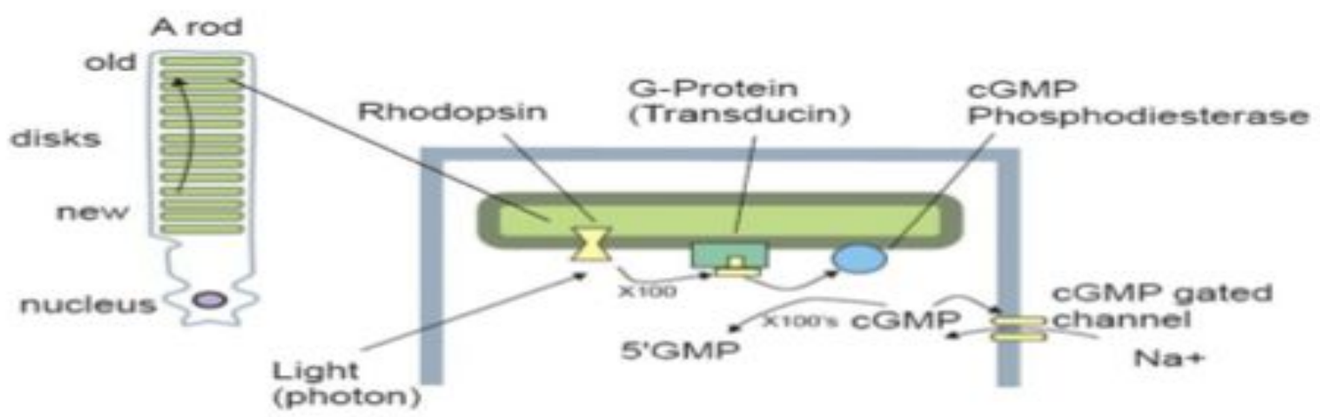


Figure 13-8

Hyperpolarization → Decreased release of synaptic transmitter "disinhibition concept which means you inhibit release of inhibitory neurotransmitter that results in stimulation of desired cell""→ Response in bipolar cells[3] (hyperpolarization) (off-center bipolar cells get hyperpolarized)(this cause decreased release of glutamate= gradual depolarization of on-center bipolar cells)→ Generator potential in amacrine cells & ganglion cells (depolarize) → AP→ optic nerve → optic pathway.

FOOTNOTES

1. A photon hits an electron in the cis portion of retinal, causing a gradual conformational change.
2. Metarhadobsin II acts as an enzyme after its formation to activate transducin.
3. It is thought that bipolar cells hyperpolarize when they are activated by a metobotropic receptor, and depolarize if it is ionotropic.

NB/ these reactions occur in both rods & cones

- but in rods occur at low illumination as in dim-light & in cones at high illumination.
- in cones 4 times faster. (We took here rhodopsin as an example of photosensitive pigment which is really similar to iodopsin "photosensitive pigment of cones" but iodopsin is 4 times faster than rhodopsin.)

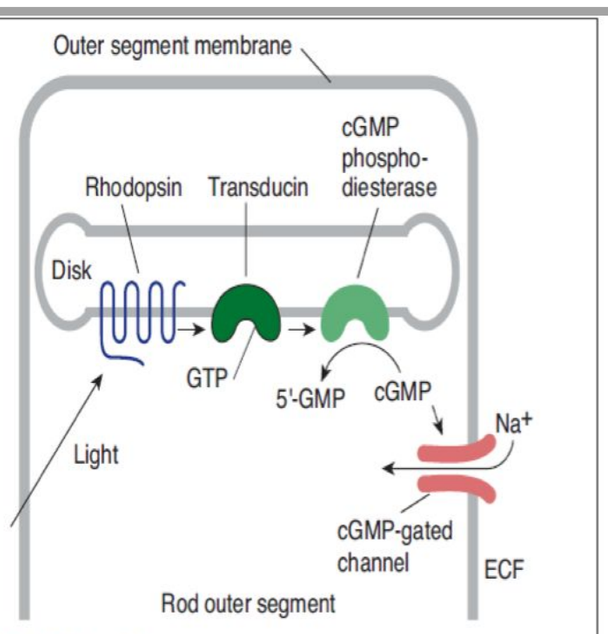


FIGURE 12–14 **Initial steps in phototransduction in rods.** Light activates rhodopsin, which activates transducin to bind GTP. This activates phosphodiesterase, which catalyzes the conversion of cGMP to 5'-GMP. The resulting decrease in the cytoplasmic cGMP concentration causes cGMP-gated ion channels to close.

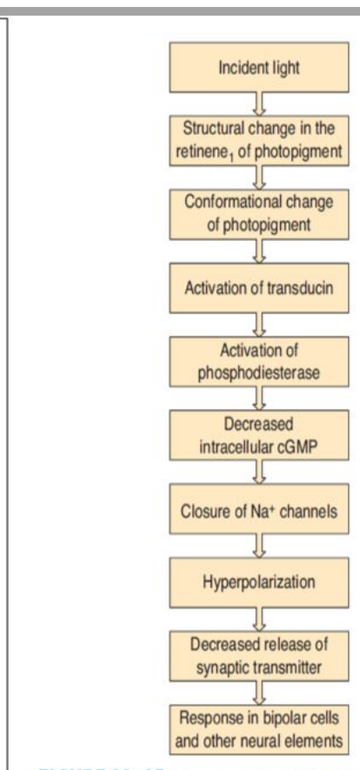


FIGURE 12–15 **Sequence of events involved in phototransduction in rods and cones.**

Figure 13-9

Figure 13-10

Change in photopigment
↓
Metarhodopsin II
↓
Activation of transducin
↓
Activation of phophodiesterase
↓
Decrease IC cyclic GMP
↓
Closure of Na channels
↓
Hyperpolarization of receptor
Decrease release of synaptic transmitter
Action potential in optic nerve fibres

PHOTOTRANSDUCTION PROCESS

OBJ OBJ OBJ OBJ OBJ

To contrast the phototransduction process for rods and cones in light and dark and the ionic basis of these responses we have 10 types of cones bipolar cells & one type of rod bipolar cell

Dark	Light
• depolarize receptors → **increase** glutamate at photoreceptor ends → 1. hyperpolarize ON- center[1] bipolar cells . 2. depolarize OFF-center[2] bipolar cells (active).	• hyperpolarize the receptors → **decrease** glutamate release at photoreceptor ends → 1. depolarize ON- center[1] bipolar cells 2. hyperpolarize OFF-center[2] bipolar cells (inactive).

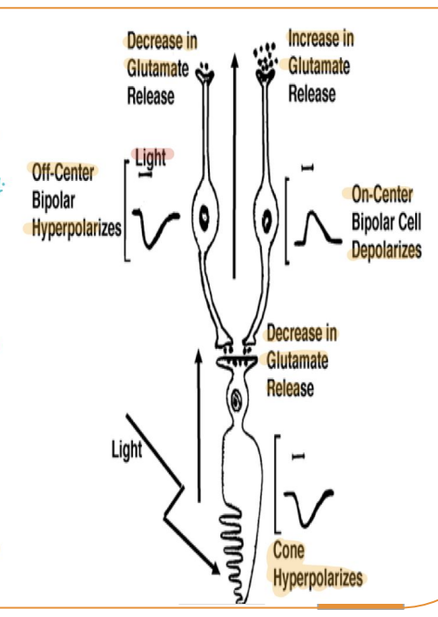
Table 13-3

- All these help to sharpen signal from rods in dark and from cones in light.

At depth [3]

At bipolar cells Hyperpolarization & depolarization occur depending on which environment it's being exposed to (light/dark) and which is effected, the rods or the cones.

Figure 13-11



FOOTNOTES

1. **ON**- center bipolar (synaptic connection with **center** photoreceptors= c**ON**es , so <u>light</u> depolarize them to see in <u>bright</u> light).
2. **OFF**- center bipolar (synaptic connection with **peripheral** photoreceptors= **rods** , so <u>dark</u> depolarize them to see in <u>dark</u>).
3. Video 14-1: Neuroscience: Phototransduction (https://www.youtube.com/watch?v=8Oclbrd06c8&feature=youtu.be)

LIGHT & DARK ADAPTATION

Dark(light → dim)

The retina becomes **more sensitive** to light & the person will be accustomed to dark in about **20 min** (gross features only with no details or colors) .

- Rhodopsin in darkness is essential for depolarization of rodes to see in dark, So it **increases** Rhodopsin regeneration .

•And it reaches max in 20 minutes
First 5 minutes → -threshold of cones.
5 to 20 mins → +Sensitivity of rods.

Rapid phase

Less rapid phase

Light

When light switched on again, the rods are knocked out of action (they stop sending AP at high levels of light) & cones start to function to adjust & adapt to the level of brightness **in 5 min** this is called Light adaptation.

- Photopsins Retinal Visual Cycle: The cones are about 30 to 300 times less sensitive than rods to light.

Rapid phase(5mins)	Less rapid phase(‘till 20 mins)
• Drop in Cones visual threshold. • Fast dark adaptation of cones, only in fovea • Half of the cone rhodopsin regenerate in only **90 seconds** This phase is rapid but the sensitivity of light increase partially in contrast to less rapid phase which the sensitive of light increases dramatically due to rhodopsin existence.	• Drop in visual threshold stimulates dark adaptation of rods in the peripheral retina. • Sensitivity of rods to light increase, in **1 min increase 10 folds.** (200 times in 20 mins) • Rods increase their sensitivity to light by convergence 300:1 ganglion cell , so summation at ganglion cells potential will increase sensitivity to light.

Table 13-4

in addition to adaptation caused by changes in concentrations of rhodopsin or colour photochemicals, the eye has two other mechanisms for light and dark adaptation:

A change in pupillary size	Neural adaptation:
This change can cause adaptation of approximately 30-fold within a fraction of a second because of changes in the amount of light allowed through the pupillary opening	Involving the neurons in the successive stages of the visual chain in the retina itself and in the brain. That is, when light intensity first increases, the signals transmitted by the bipolar cells, horizontal cells, amacrine cells, and ganglion cells are all intense. However, most of these signals decrease rapidly at different stages of transmission in the neural circuit

Table 13-5

DARK ADAPTATION

N.B (20 min for dark adaptation are for regeneration of rhodopsin → increase sensitivity of rods to light due to a drop in visual threshold)

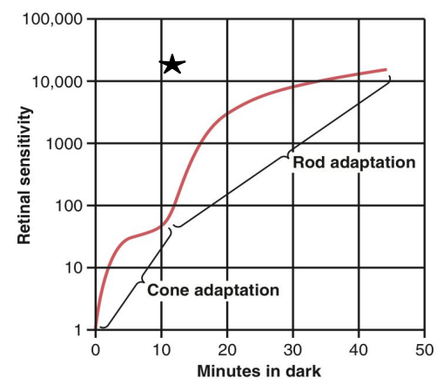


Figure 13-12

Why radiologists & aircraft pilots wear red goggles in bright light?

A- Light wavelength of the red stimulate the cones & stimulates rods to some extent, so red goggles for rods act as dimlight, so with it rods are adapted to darkness & form large amounts of rhodopsin while the person in bright light & when person enter dark places he can see well & not remain 20 minutes.

AT LIGHT

Retinal is produced in the retina from Vitamin A, from dietary **beta-carotene** (ex: carrots)
11-cis-retinal gets ISOMERISED into **Metarhodopsin I** which then converts to **Metarhodopsin II** transforms into **All-trans-retinal** & **Opsin** via BLEACHING (conformational change).

- Keep in mind that **All trans-retinal** separate from **opsin** by light and <u>opsin remains alone.</u>

AT DARK

All trans-retinal via RETINAL ISOMERASE ENZYME gets reconverted into **11-cis retinal** which will combine with **Scotopsin** to make up **Rhodopsin** (Regeneration)

- The amount of rhodopsin in the receptors therefore varies **inversely** with the incident light level [Light breaks it apart via Bleaching]
- when there is excess retinal in the retina, it is converted back into vitamin A, thus reducing the amount of light-sensitive pigment in the retina.

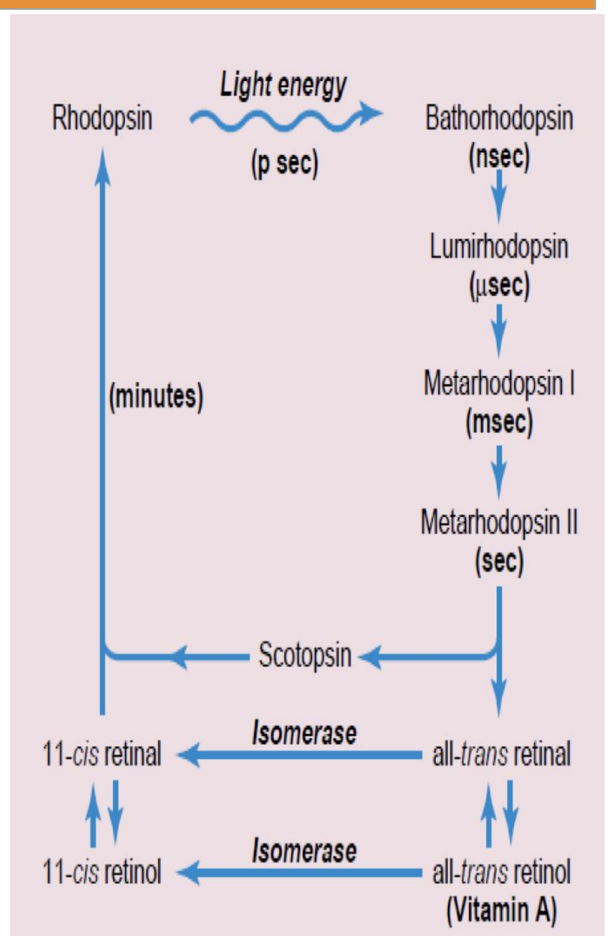


Figure 13-13

NYCTALOPIA (night blindness)

Vitamin A deficiency cause rods, cones & retinal degeneration & loss of rods, which are responsible for night vision.

CLINICAL RELEVANCE

Rx: Intravenous vit A (rapid effect) if receptors are well. It is not given orally because it breaks down in the GIT.

Convergence of ganglion cells

- The receptive field of a ganglion cell in the retina of the eye is composed of input from all of the photoreceptors which synapse with it
- A group of ganglion cells in turn forms the receptive field for a cell in the brain. This process is called convergence

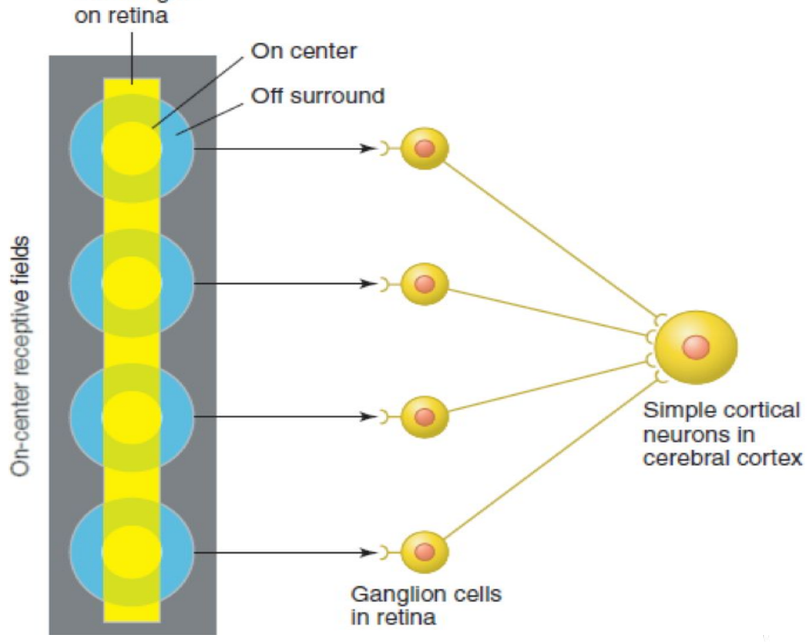


Figure 13-14

QUIZ

MEDICINE438's CNSPHYSIOLOGY

1. The Na /k pump is located in:
   A) Inner segment
   B) Outer segment
   C) Bipolar cells
   D) Ganglion cells

2. Under low or reduced light conditions, which chemical compound is responsible for the inward-directed sodium current in the outer segments of the photoreceptors?
A) Metarhodopsin II
B) cGMP
C) 11-cis retinal
D) cAMP
E) 11-trans retinal

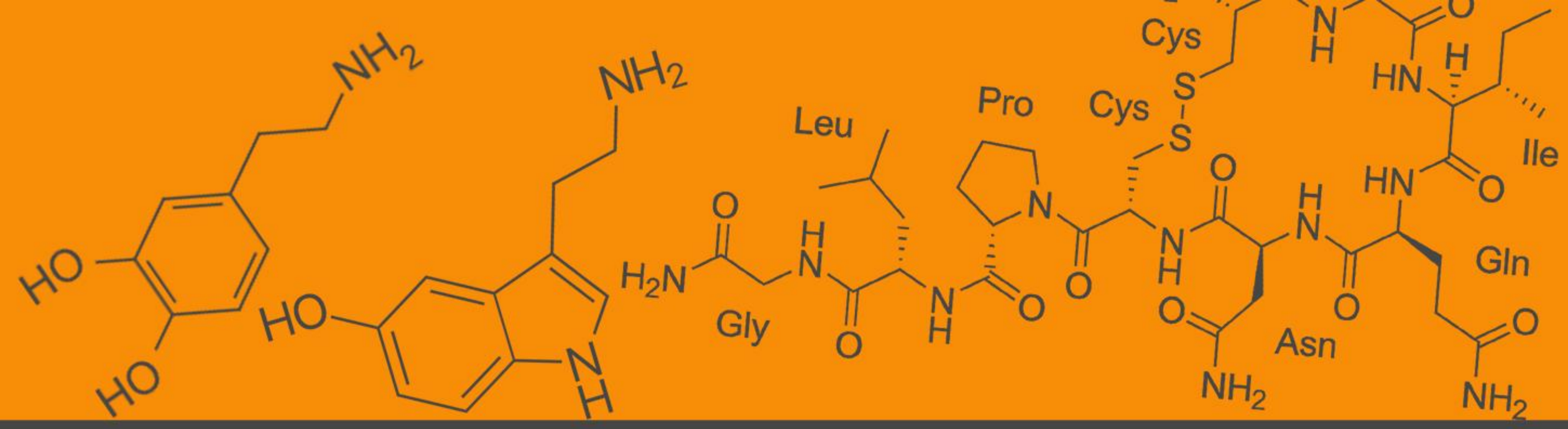
ANSWER:, In low light conditions, the level of cGMP is high. cGMP-dependent sodium channels in the outer portions of the rods and cones allow sodium ions to pass from the extracellular space to the intracellular space of the photoreceptor. This passage results in a membrane potential that is somewhat lower than the resting membrane potential of a typical neuron. The movement of the sodium ions and resulting electrical potential change as a result of this enhanced permeability is known as the *dark current.*

3. Mitochondria is found fully in:
A) inner segment and is thick in cones
B) outer segment and is thick in cones
C) inner segment and is thick in rods
D) outer segment and is thick in rods

4. The sacules of the cones are formed by?
A) the folding of the membrane of the outer segment
B) the flattening of the membrane of the outer segment
C) the unfolding of the membrane of the outer segment
D) the free floating disc of the membrane of the outer segment

5. Convergence....
A) increases sensitivity to light and increases acuity
B) decreases sensitivity to light and decreases acuity
C) increases sensitivity to light and decreases acuity
D) decreases sensitivity to light and decreases acuity

ANSWER KEY: A, B, A, C, C



THIS LECTURE WAS DONE BY

Leena Alnassar, Nujud Alabdullatif

FEMALE PHYSIOLOGY CO-LEADERS

Maha Alnahdi, Ghaliah Alnufaei

MALE PHYSIOLOGY CO-LEADERS

Nayef Alsaber, Hameed M. Humaid

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REFERENCES

- Guyton and Hall Textbook of Medical Physiology
- Ganong's Review of Medical Physiology