Phototransduction and retinal adaptation

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Learning outcomes:

- **At the end of the lecture, you will be able to:**

1. Explain the functions of the pigmented epithelium.
2. Explain the structure of rods and cones
3. Compare rods and cones
4. Describe the special areas of retina (optic disc and fovea centralis).
5. Explain the duplicity theory of vision
6. Explain the mechanisms of phototransduction.
7. Define retinal adaptation and explain its types.

Retina

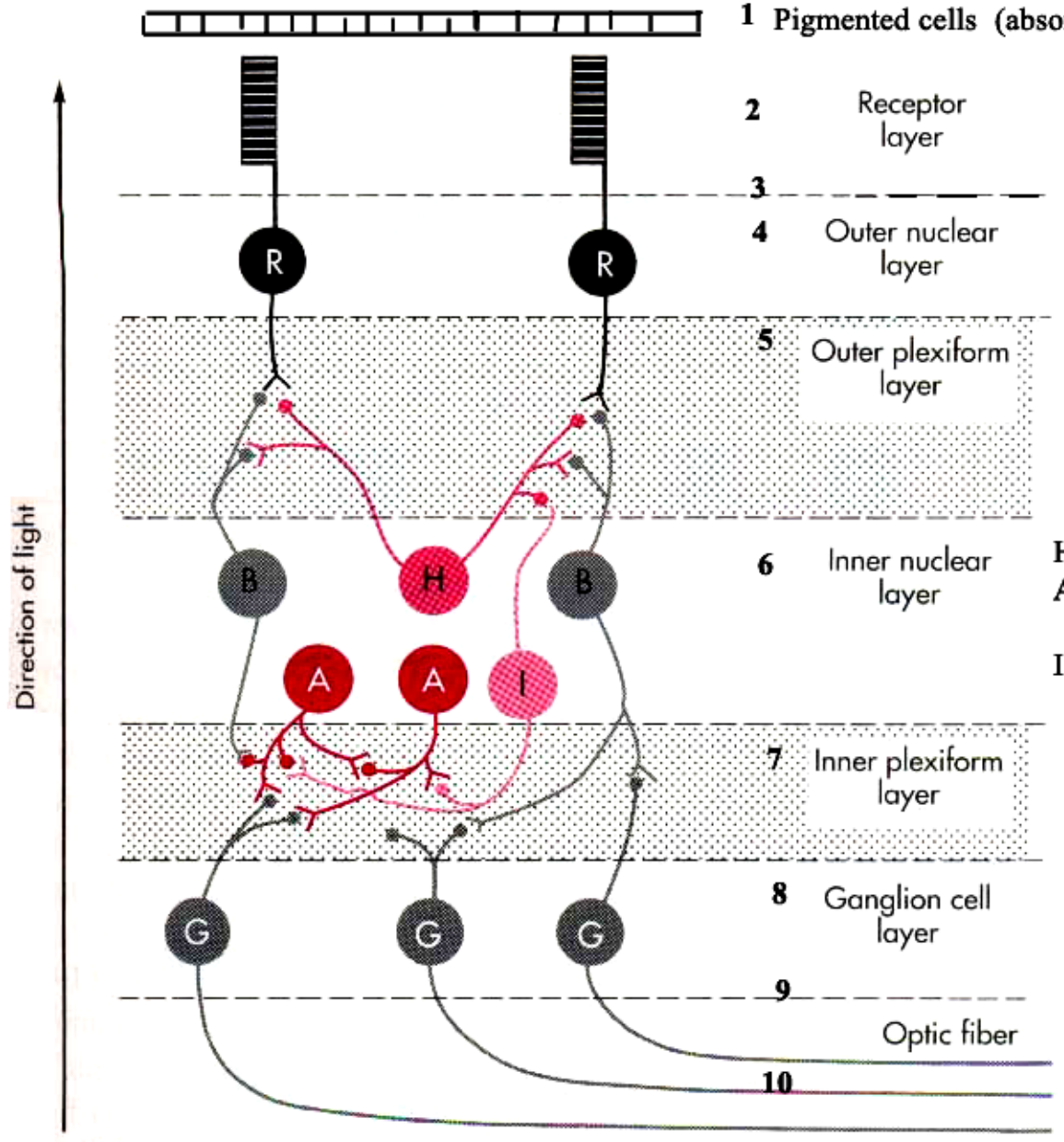
- The retina is the **innermost photosensitive layer** of the eyeball.
- **Histologically,** it is formed of **10 layers**
- **Physiologically, 4 layers** have special importance

  a. Layer of pigmented epithelium.

  b. Layer of rods and cones.

  c. Layer of bipolar cells.

  d. Layer of ganglion cells.



Lateral cells (have feedback & feedforward signals)

H; Horizontal cells :transmit signals from R to B cells.
A; Amacrine cells : connections with B, G & A. ~30 types, primary analysis of visual signals.
I; Interplexiform cells : interconnecting outer & inner plexiform layers; all inhibitory preventing lat.spread of visual signals.

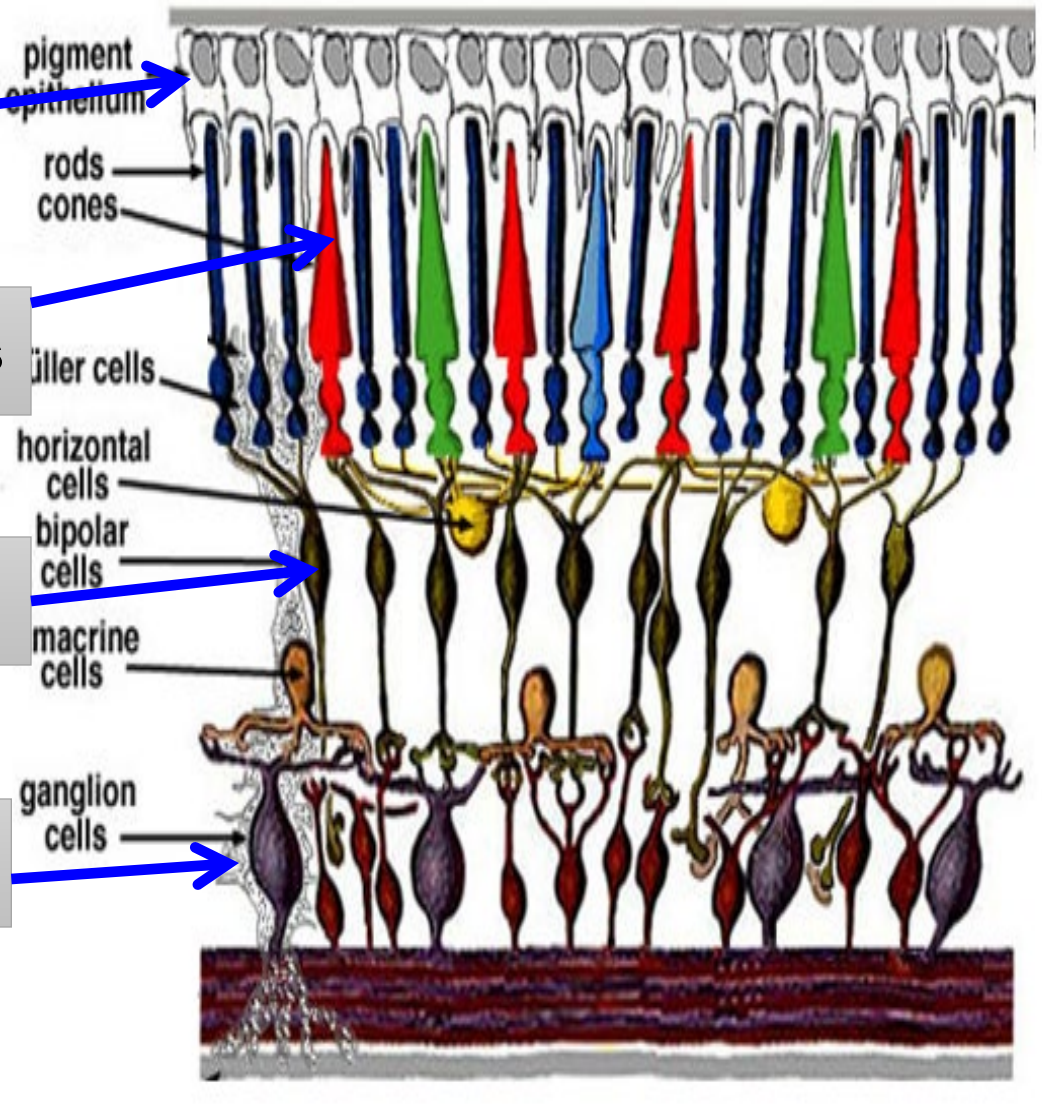
Functional Layers

Pigmented Epithelium

Photoreceptors

Bipolar cells

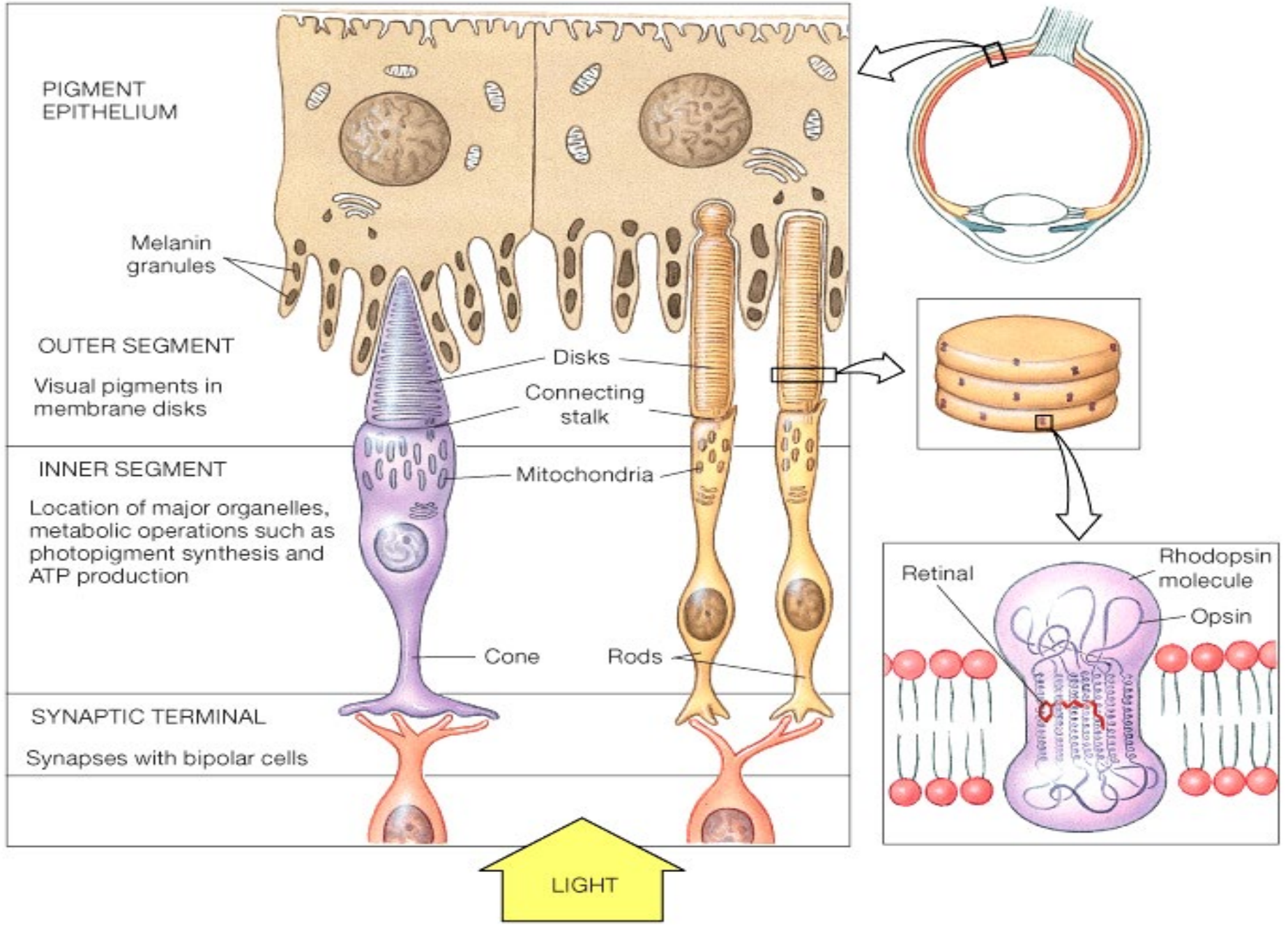
Ganglion cells



(I) Retinal Pigmented Epithelium (RPE)

- It is a monolayer of **pigmented epithelial cells**; its outer side is in contact with the **choroid** and its inner side with the **rods and cones**.
- Functions:

1. It contains large amounts of **melanin pigments which absorb light** and prevent its reflection inside the eyeball which cause glare.


PIGMENT EPITHELIUM
Melanin granules
OUTER SEGMENT
Visual pigments in membrane disks
Disks
Connecting stalk
INNER SEGMENT
Location of major organelles, metabolic operations such as photopigment synthesis and ATP production
Mitochondria
Cone
Rods
SYNAPTIC TERMINAL
Synapses with bipolar cells
LIGHT
Retinal
Rhodopsin molecule
Opsin

2. It produces a **sticky extracellular matrix material** that keeps the outer segments of rods and cones straight and aligned.
3. It participates in the **breakdown and resynthesis of the photopigments**.
4. It helps the **continual renewal of the outer segment** by ingesting the old outermost tips of the rods and cones.
5. It stores large amount of **vit. A** needed for **photopigments recycling**.

(II) Photoreceptors (rods and cones)

➢ **Structure of photoreceptors:** Each rod or cone is formed of:

(i) An outer segment:

- They are **modified cilia** which are **long cylindrical** in rods and **short conical** in cones.
- They contain a great number of **disc-shaped shelves** which are composed of folds of the cell membrane.

- **<u>The disc membrane contains</u>**:

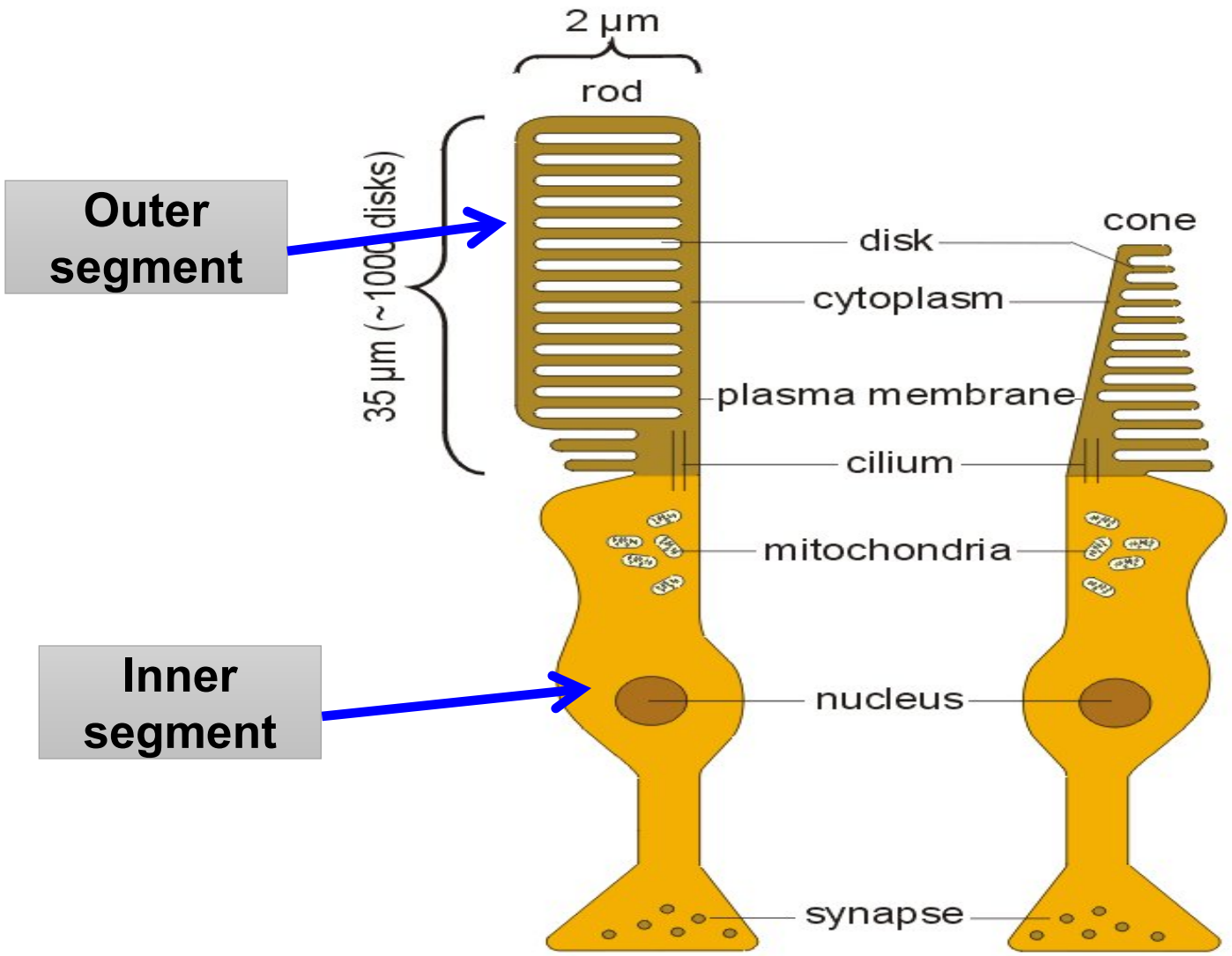
  - Photosensitive pigments e.g. rhodopsin.

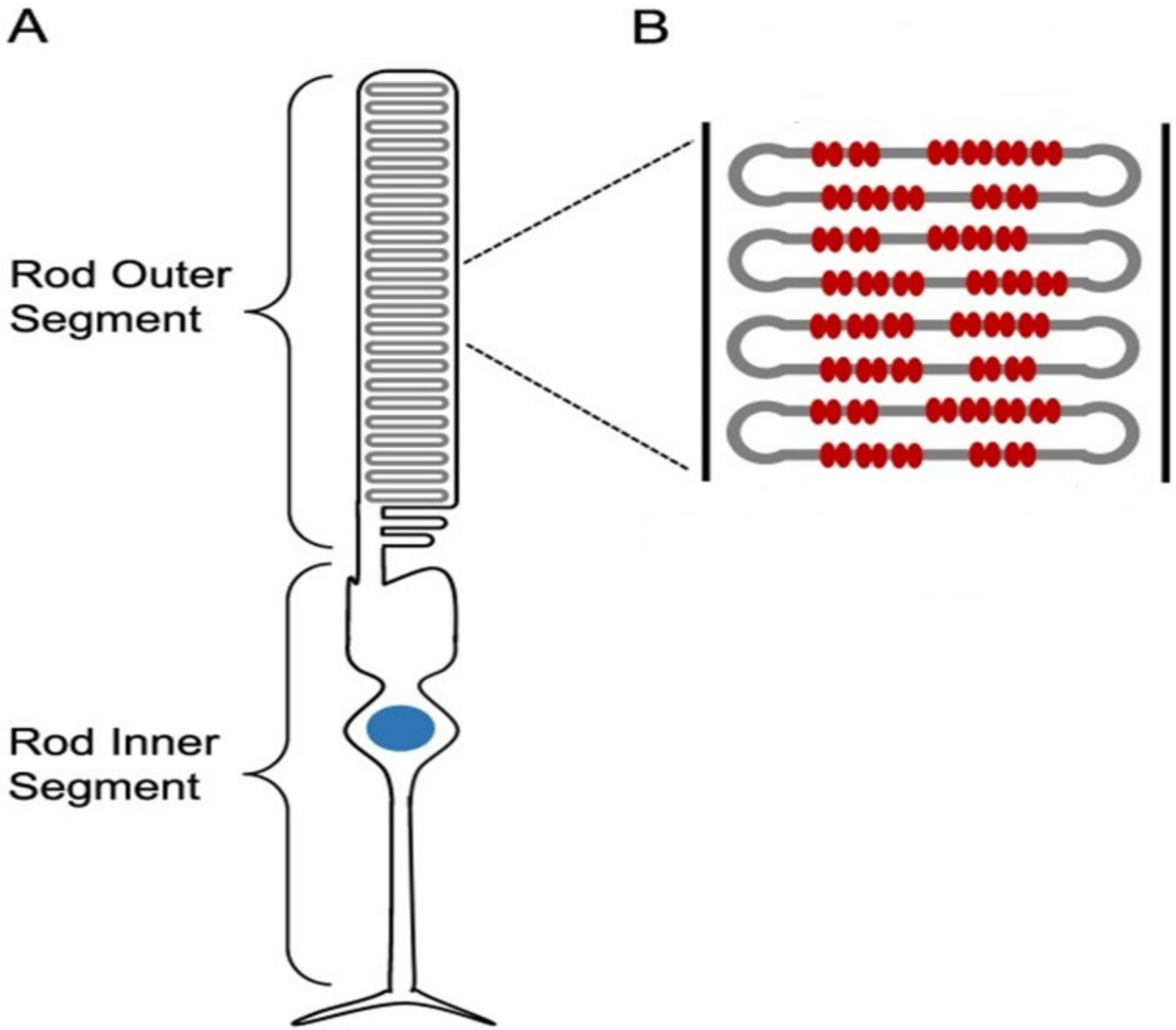
  - G protein called transducin.

  - c GMP phosphodiestrase (PDE).

- **<u>The membrane of the outer segment of rods and cones</u>** contains ***<u>cGMP-gated ion channels</u>*** selective for Na^{+}, Ca^{++} and Mg^{++}.

Structure of rods and cones



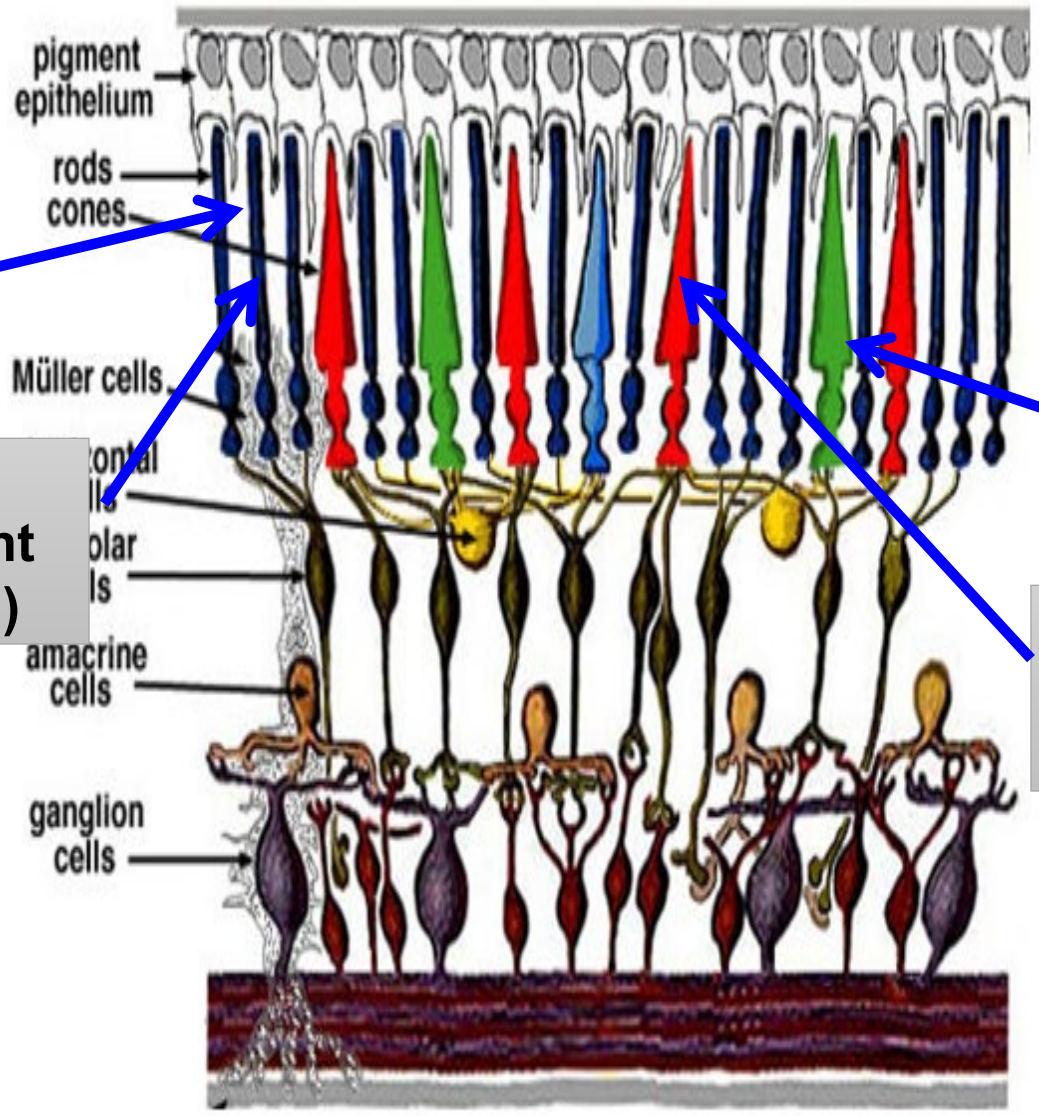

A
B
Rod Outer Segment
Rod Inner Segment

(ii) An inner segment:

- They contain **nucleus and mitochondria**.
- The membrane of inner segment contains an **active Na^+-K^+ pump and K+ channels**.
- They have **synaptic body** that synapses with bipolar cells (contains transmitter **glutamate**).

	Rods	Cones
Number:	120 millions	6-7 millions
Shape	Cylindrical	Conical
Distribution	-**Mainly** in peripheral part of retina -**Less** in the middle part -**Absent** in fovea centralis & optic disc	-**Mainly** in fovea centralis. -**Less** in the middle part.
Photosensitive pigments	Rhodopsin (visual purple)	Iodopsin (3 types)

Number of Rods and Cones



Rod
120 millions

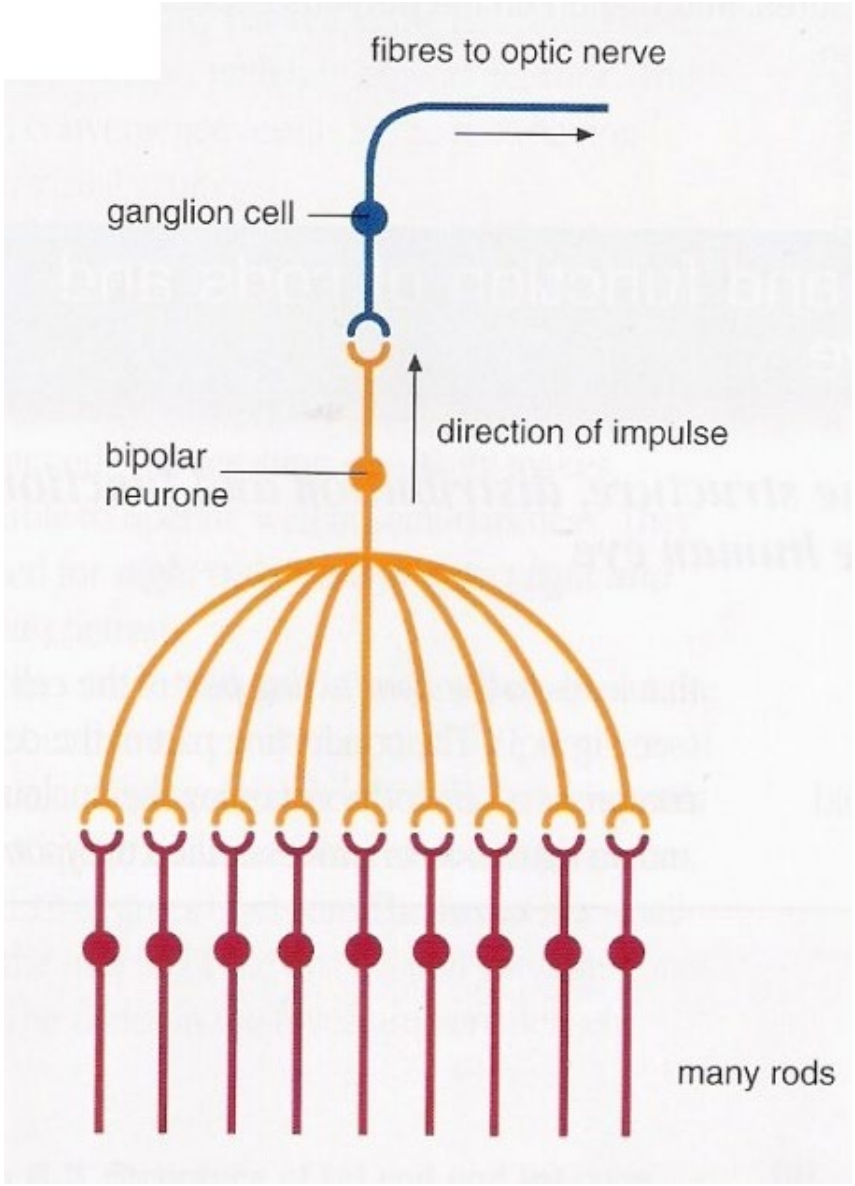
Rod
One pigment
(rhodopsin)

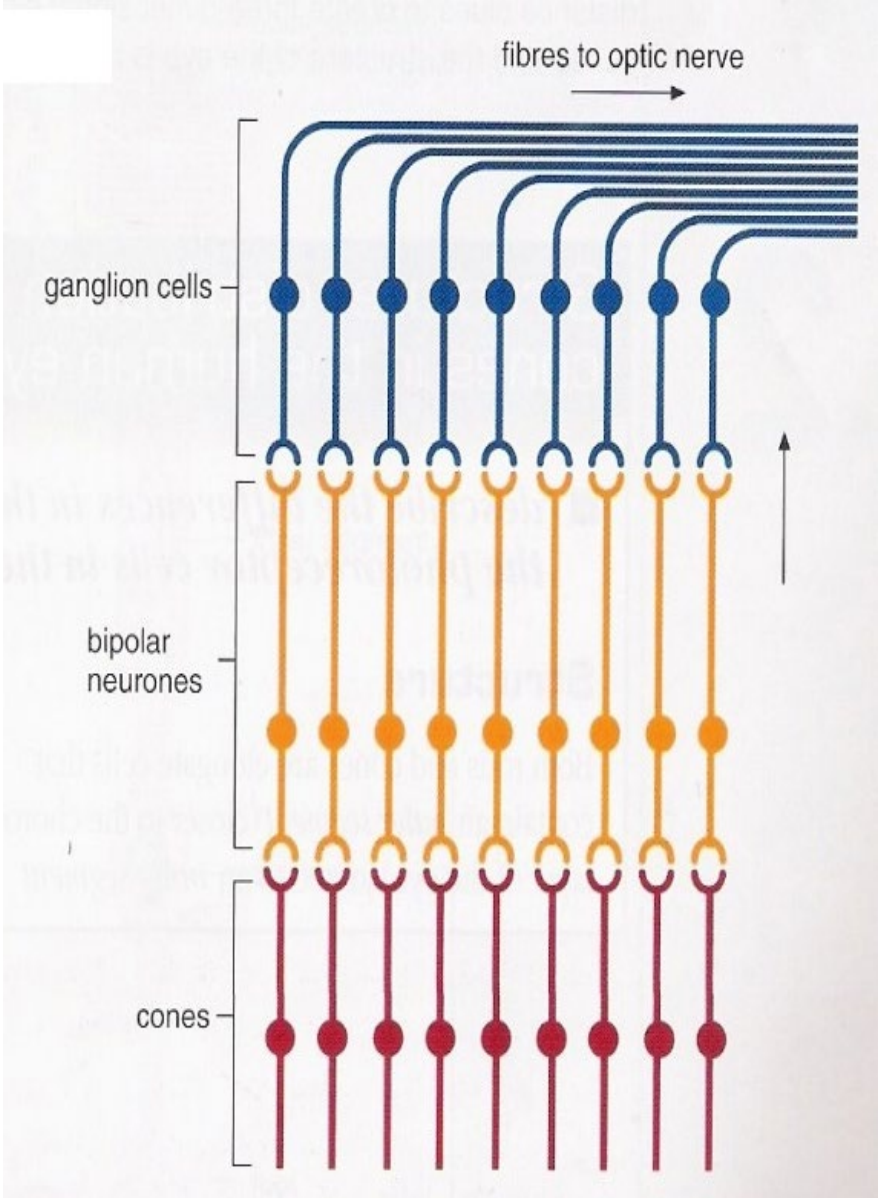
Cones
7 millions

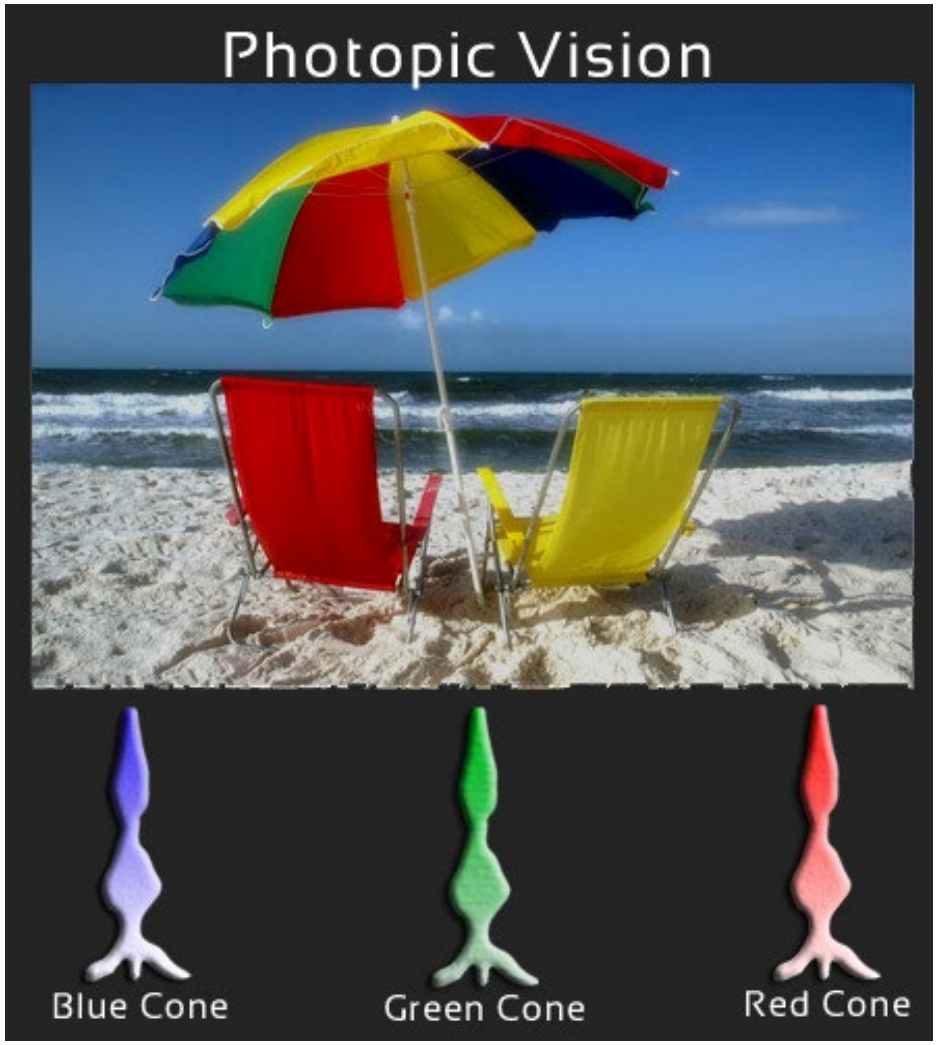
Cond
3 pigments
(iodopsin)

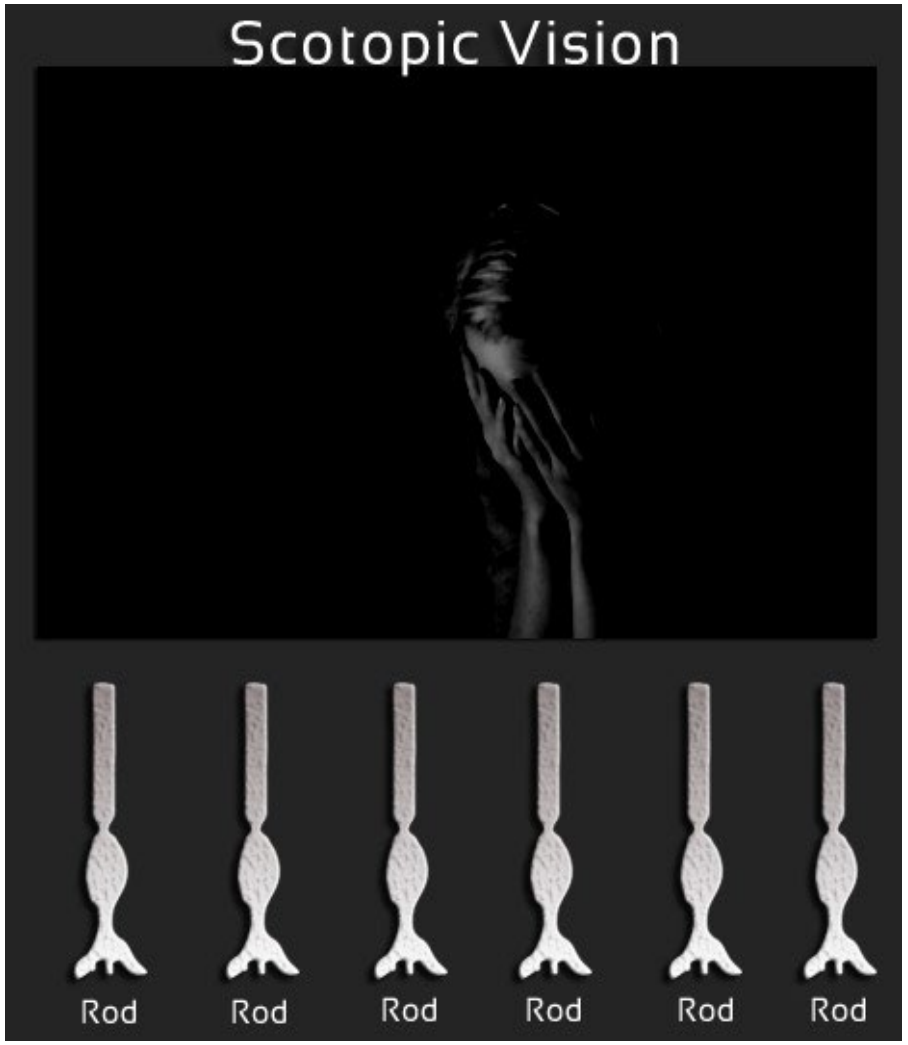
	Rods	Cones
Connection	Many rods converge to one bipolar cell Many bipolar cell converge to one ganglion cell (300:1)	One cone to one bipolar cell that can be connected to one ganglion cell (1:1:1)
Functions	- more sensitive to light - less accurate vision i.e. can not perceive the details of the subject - can not differentiate colours - responsible for night vision	- less sensitive to light - more accurate i.e. can perceive fine details of subject - can differentiate colours - responsible for day vision

Convergence of Rods and Cones





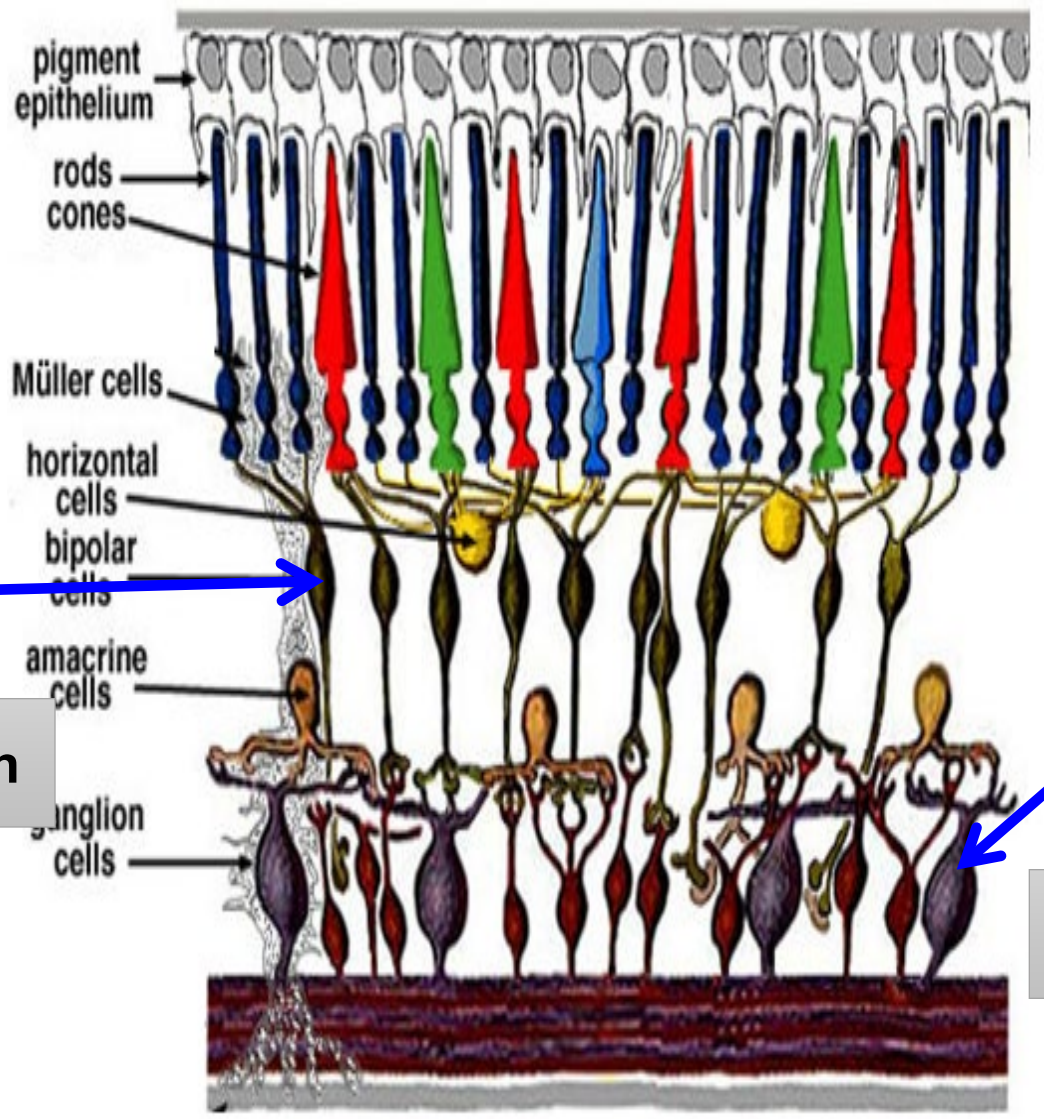

Photopic Vision
Blue Cone
Green Cone
Red Cone


Scotopic Vision
Rod
Rod
Rod
Rod
Rod
Rod

(III) Layer of bipolar and ganglion cells

- They constitute **1st and 2nd order neurons** in visual pathway.
- **Bipolar cells** transmit signals from **photoreceptors** to **ganglion** cells, while **ganglion cells** transmit signals from **bipolar** cells to **brain** through the optic nerve.

Ganglion and Bipolar cells



Bipolar cells

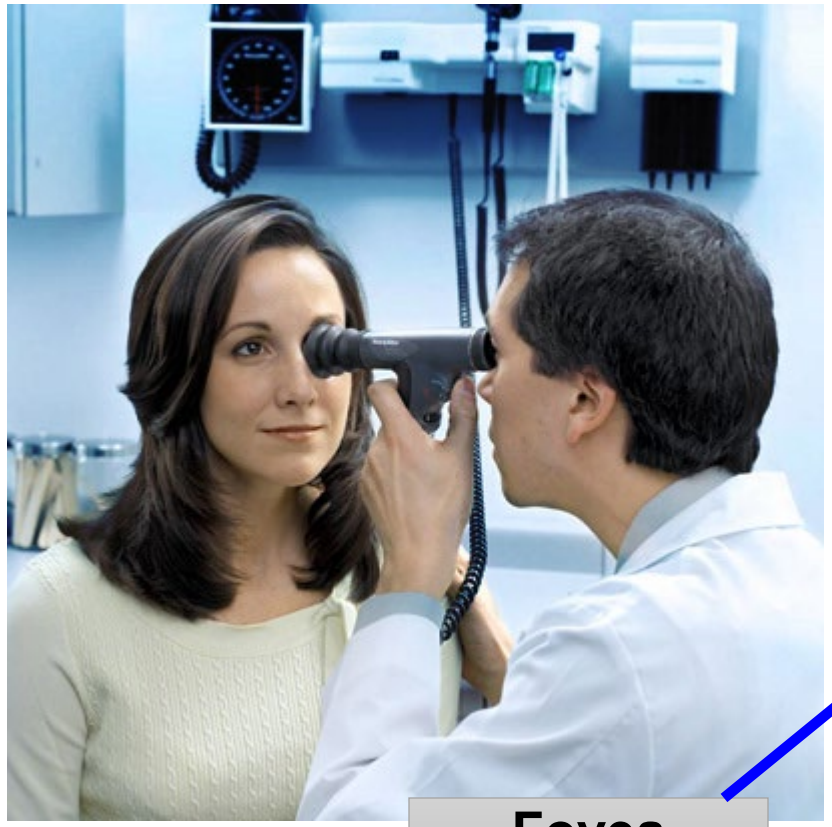
1st order neuron

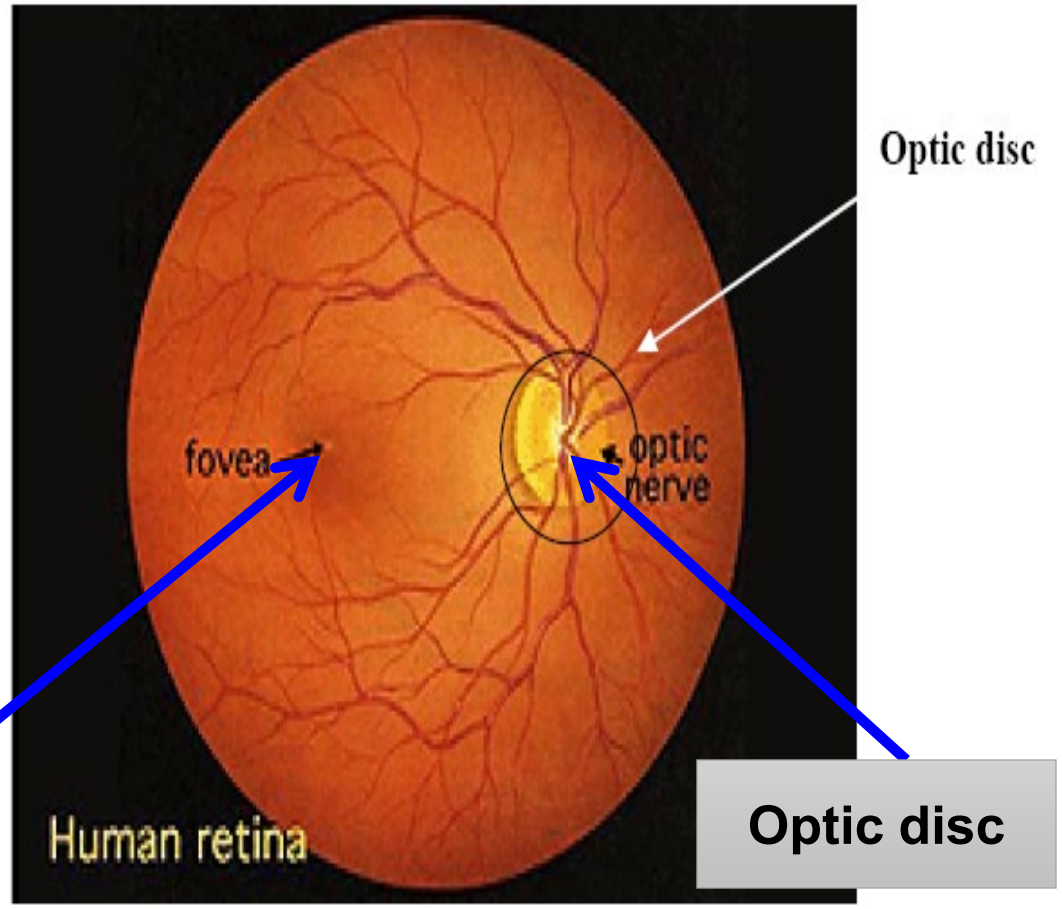
Ganglion cells

2nd order neuron

Fundus oculi

- Fundus oculi is the part of the retina which can be seen by ophthalmoscope.



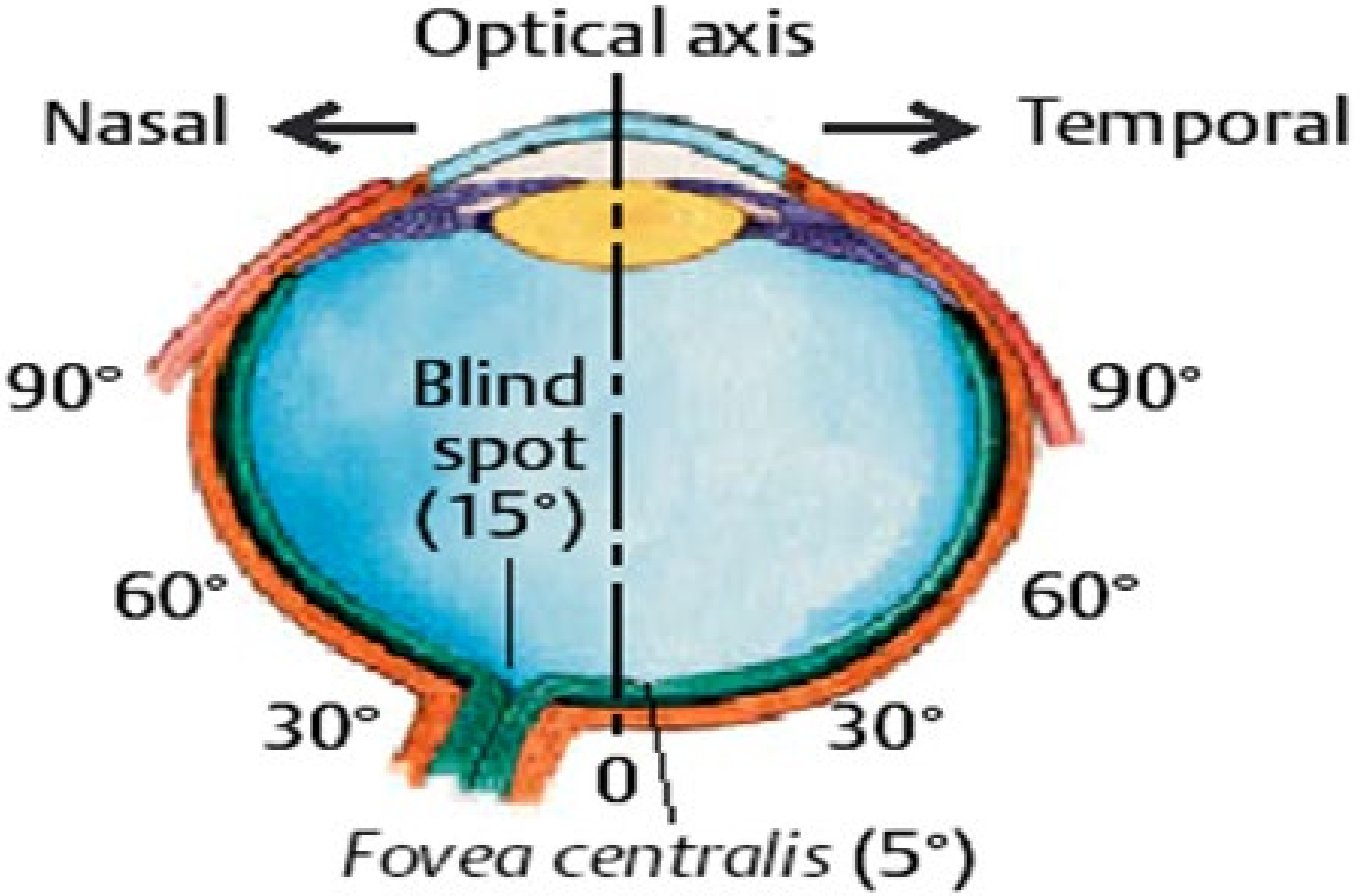


Fovea centralis

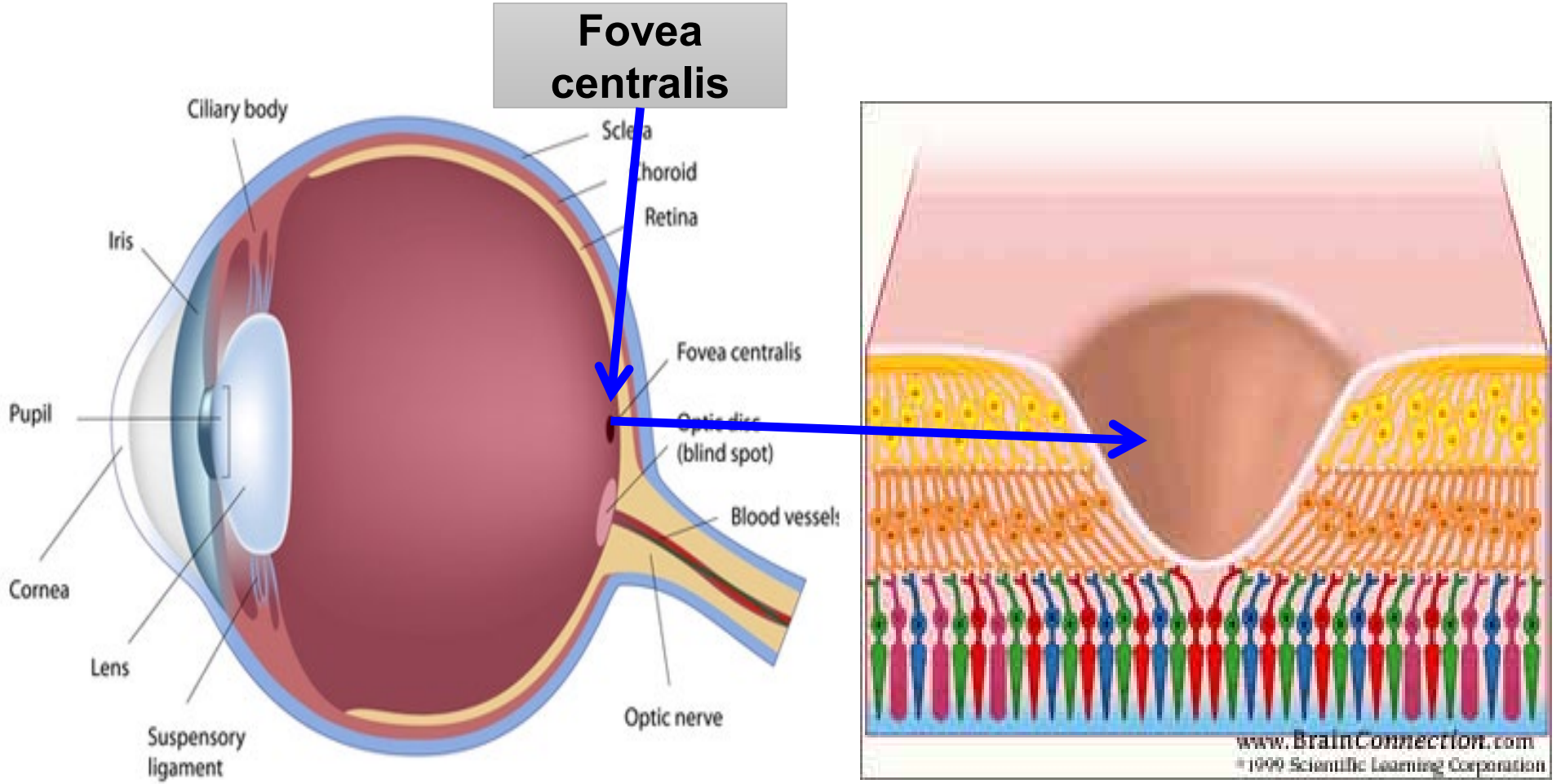
Optic disc

Special areas of the retina (fundus oculi)

	Fovea centralis (Macula Lutea)	*Optic Disc (blind spot)*
Site	At the posterior pole of the eye 4 mm lateral to optic disc	It is located 4 mm medial to fovea centralis
Size	- The macula is a small yellow area (4.5 mm in diameter). - It contains in its center, an oval depression called the fovea centralis.	It is 1.5 mm in diameter
Structure	The fovea cones are very thin and densely packed	It contains no photoreceptors, so it is a blind spot


Optical axis
Nasal
Temporal
90°
90°
Blind
spot
(15°)
60°
60°
30°
30°
0
Fovea centralis (5°)

Fovea Centralis



	Fovea centralis (Macula Lutea)	*Optic Disc (blind spot)*
Functions	-It is the area of acute vision and it contains only cones	It is the site of exit and entry of blood vessels and optic nerves to the retina.
	-Fovea is the most sensitive spot in retina because; 1- All layers are shifted aside leaving outer segments of photoreceptors to be hit directly by light 2- High density of cones 3- 1:1 convergence (cone-bipolar cell –ganglion cell) 4- Wide presentation in occipital primary visual area	**N.B.** Changes in the appearance of the optic disc are important **clinically**, the depression may be **exaggerated** due to loss of ganglion cell axons **(optic atrophy)** or may be **protruded** because of **edema (papilledema)** caused by an increase in the intracranial pressure.

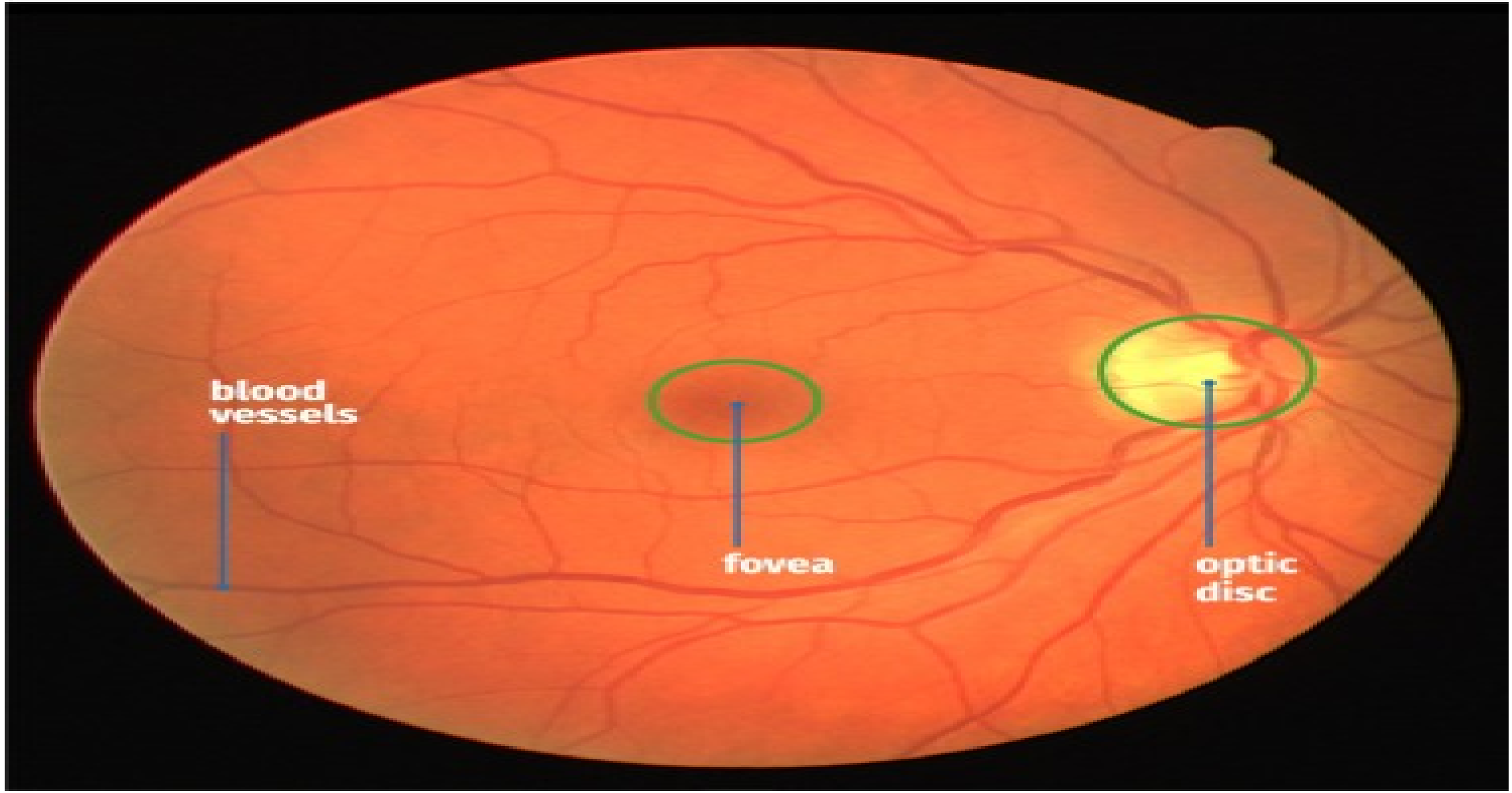
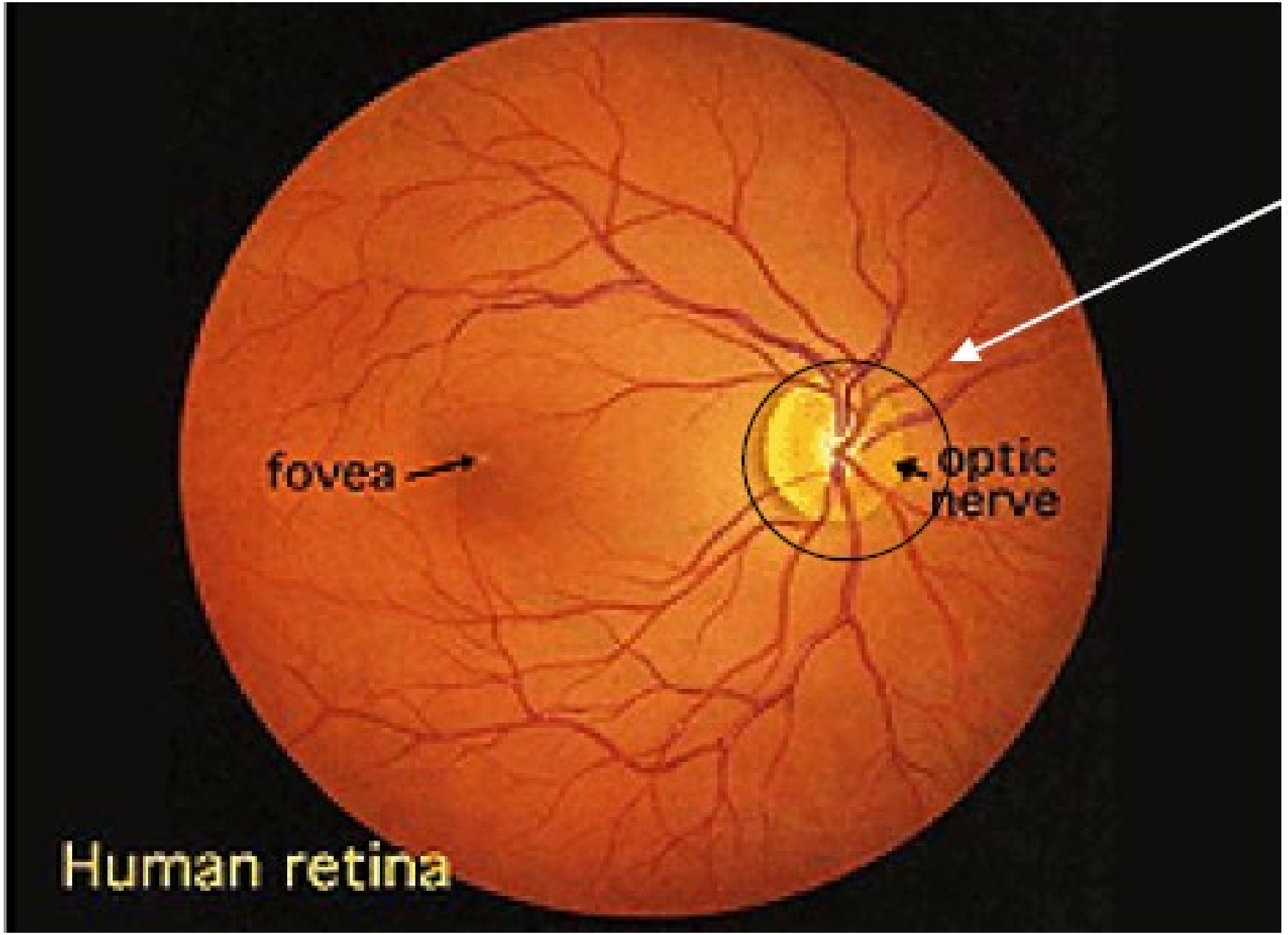


Figure: Special Parts of the Retina

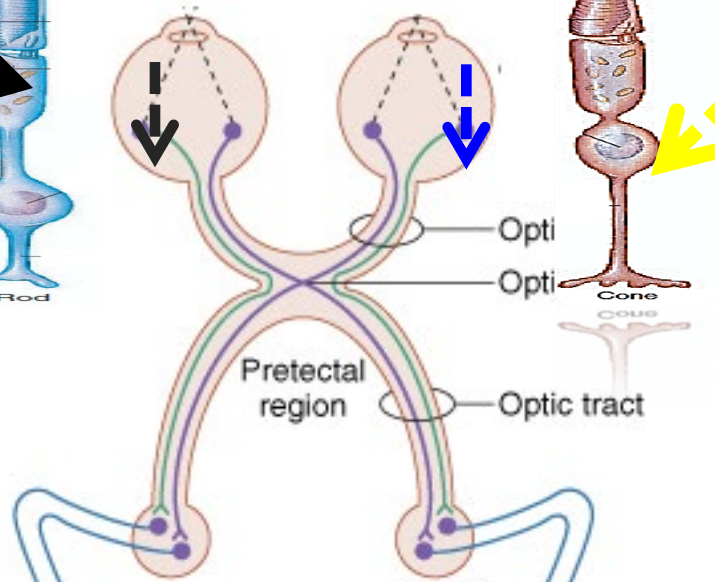


Optic disc

Duplicity theory of retinal function

- This theory states that **retinal function is double in nature depending on the properties of its 2 photoreceptors**.
- It assumes the existence of **2 different inputs from the retina** (one from rods & the other from the cones) to the CNS, each input works maximally under a different condition of illumination.
- Cones are used for bright day light (**photopic vision**) while rods are used for dim night light (**scotopic vision**).

Duplicity Theory of Retinal Function



Scotopic Vision

Photopic Vision

Duplicity theory of retinal function

	Photopic Vision	Scotopic Vision
Receptors	**Cones.**	**Rodes**
Site	**Central part** of the retina	**Peripheral part** of retina
Threshold	Is **high**.	Is **low**.
Sensitivity to light	**low**	**high**
Accuracy	**High** (can perceive the fine details of the object)	**Less** (cannot perceive the fine details of the object)
Colour vision	**Can perceive colours**	**Cannot perceive colours**
Adaptation	**rapid**	**slow**

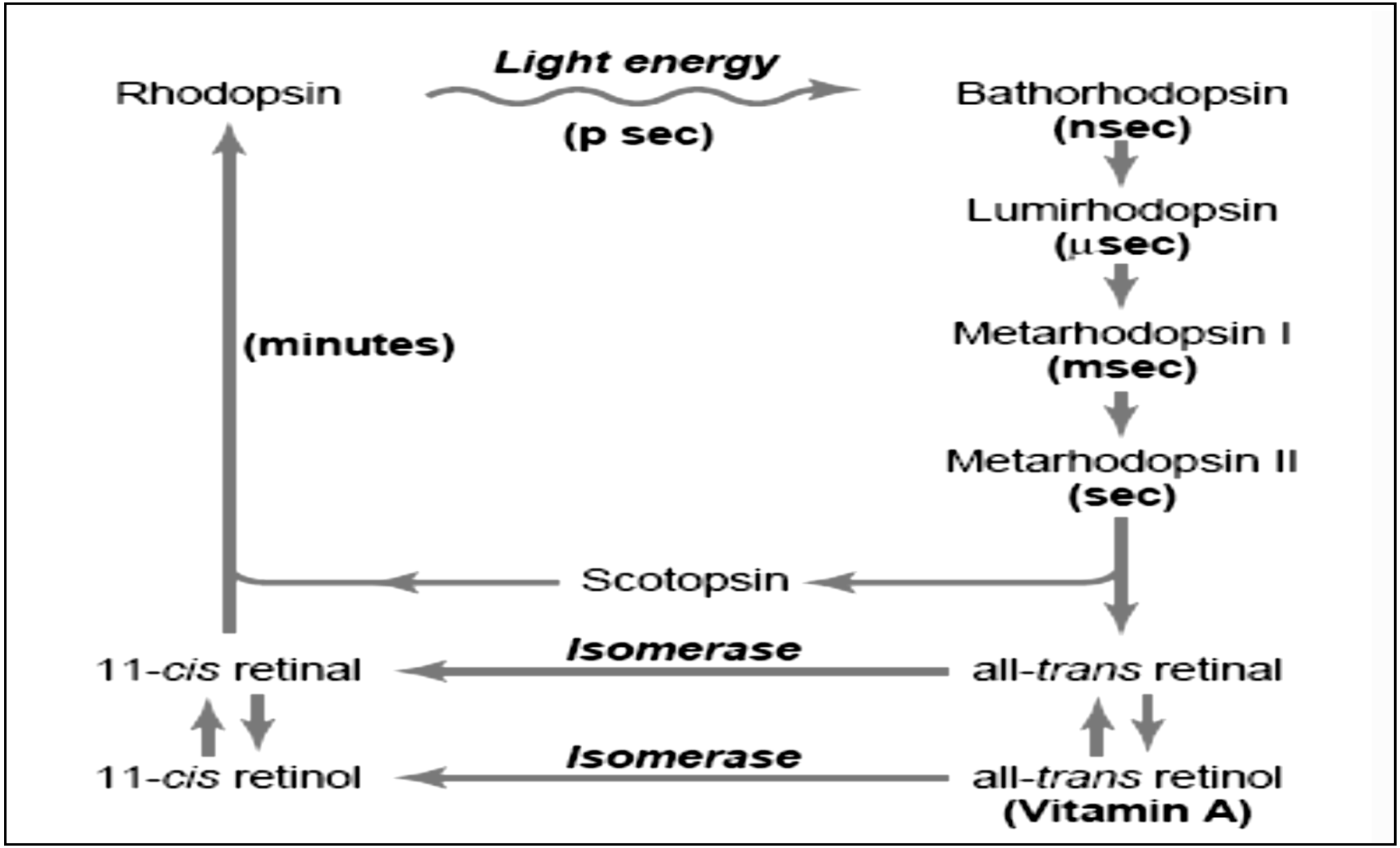
Phototransduction (mechanism of vision)

- **Def:** It is a process by which light is converted into signals in the rods & cone cells and photosensitive ganglion cells of the retina of the eye.
- **It consists of 4 steps:**

1. Decomposition of photosensitive pigment in rods & cones
2. Excitation of the photoreceptors by activated rhodopsin and generation of photoreceptor potential
3. Termination of excitation
4. Regeneration of photopigments

a) Decomposition of photosensitive pigment

- **Rhodopsin** consists of protein (**scotopsin**) and pigment (**11-cis retinal**).
- **Light** coverts the **angulated 11-cis retinal** to **straight all-trans retinal** → enhance splitting between scotopsin & all-trans retinal, thus rhodopsin is converted to **bathorhodopsin** → **lumirhodopsin** → **metarhodopsin I** → **metarhodopsin II (activated rhodopsin)**.
- **Metarhodopsin II** splits slowly (in seconds) into scotopsin and all-trans retinal by rhodopsin kinase enzyme.


Light energy
Rhodopsin
(p sec)
Bathorhodopsin
(nsec)
Lumirhodopsin
(μsec)
Metarhodopsin I
(msec)
Metarhodopsin II
(sec)
(minutes)
Scotopsin
Isomerase
11-cis retinal
all-trans retinal
Isomerase
11-cis retinol
all-trans retinol
(Vitamin A)

b) Generation (ionic basis) of photoreceptor potential

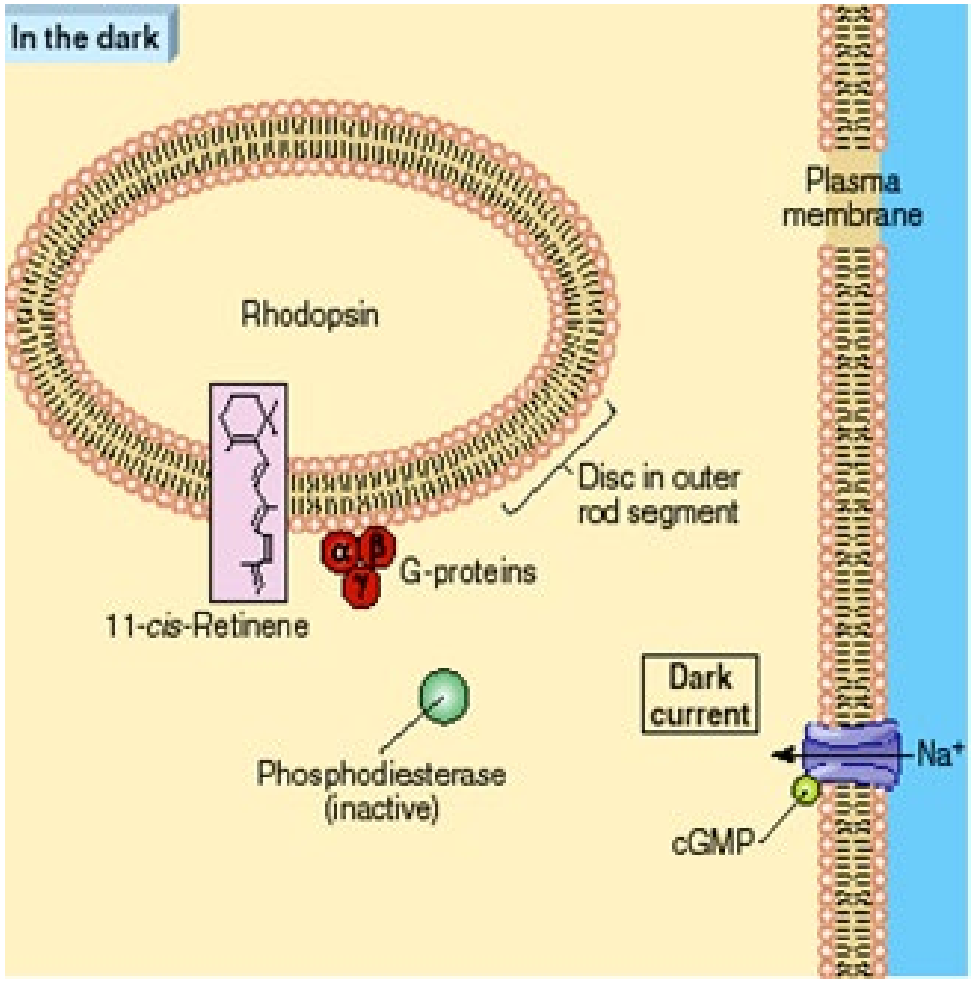
❑In Dark:

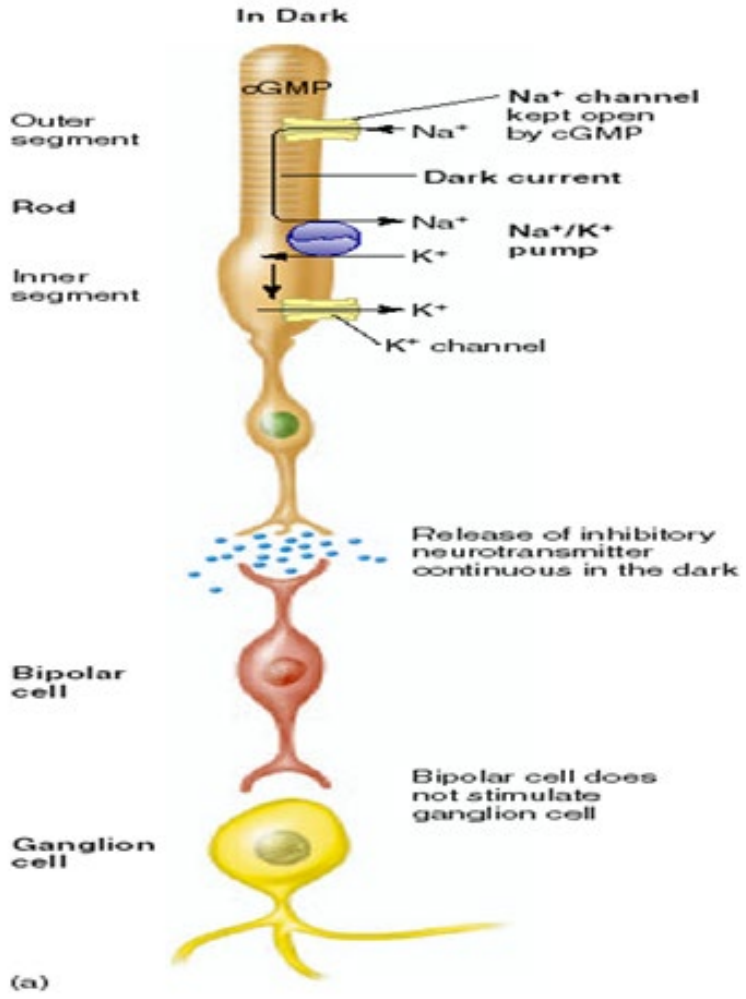
- In dark, the intracellular concentration of cGMP is high → open **cGMP dependent cation channels** in the outer segment of the photoreceptor cells.
- **Na^+ ions** enter the outer segment & diffuse into the inner segment where it is pumped out.

- The flow of Na^+ between outer and inner segments forms a current flow called **dark current** of about **– 40 mV (depolarization)** → continuous release of synaptic transmitter (**glutamate**) from the synaptic terminals → **hyper polarization (inhibition) of bipolar cells** by opening of **Cl- channels** → ↓ release of excitatory transmitter from bipolar cells → **disfacilitation (inhibition) of ganglion cells** → no action potentials in optic nerve.

Photoreceptor Potential

In Dark



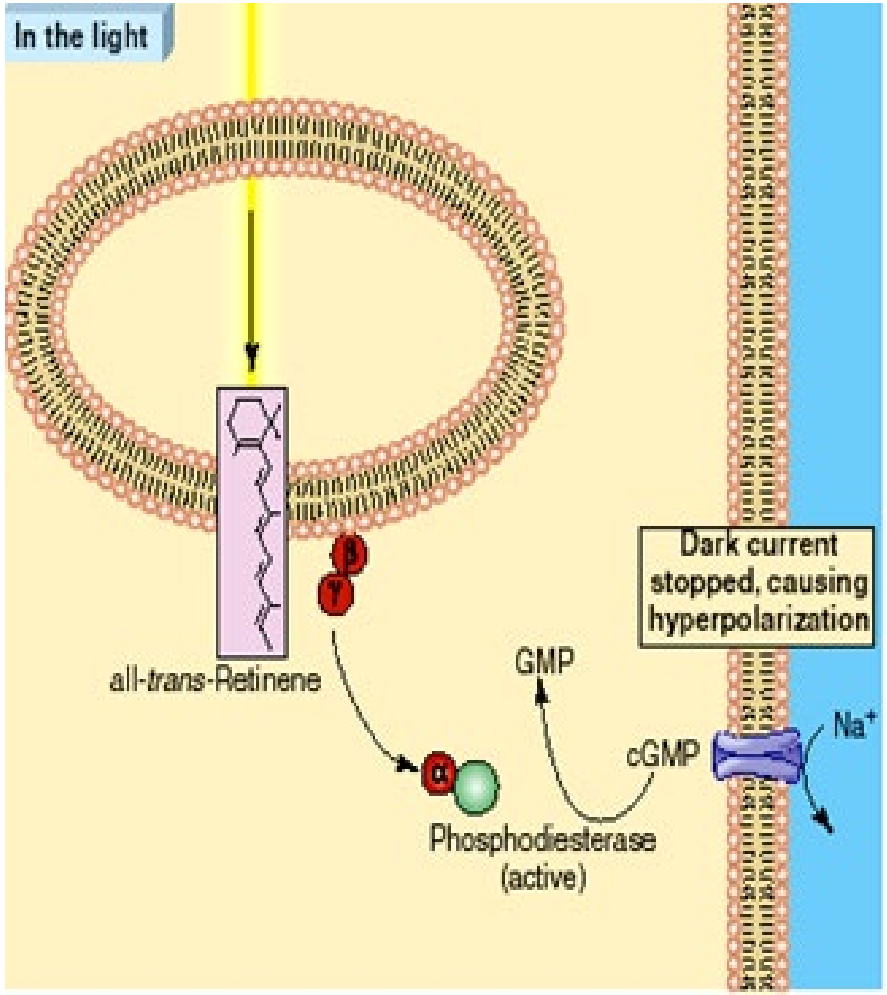


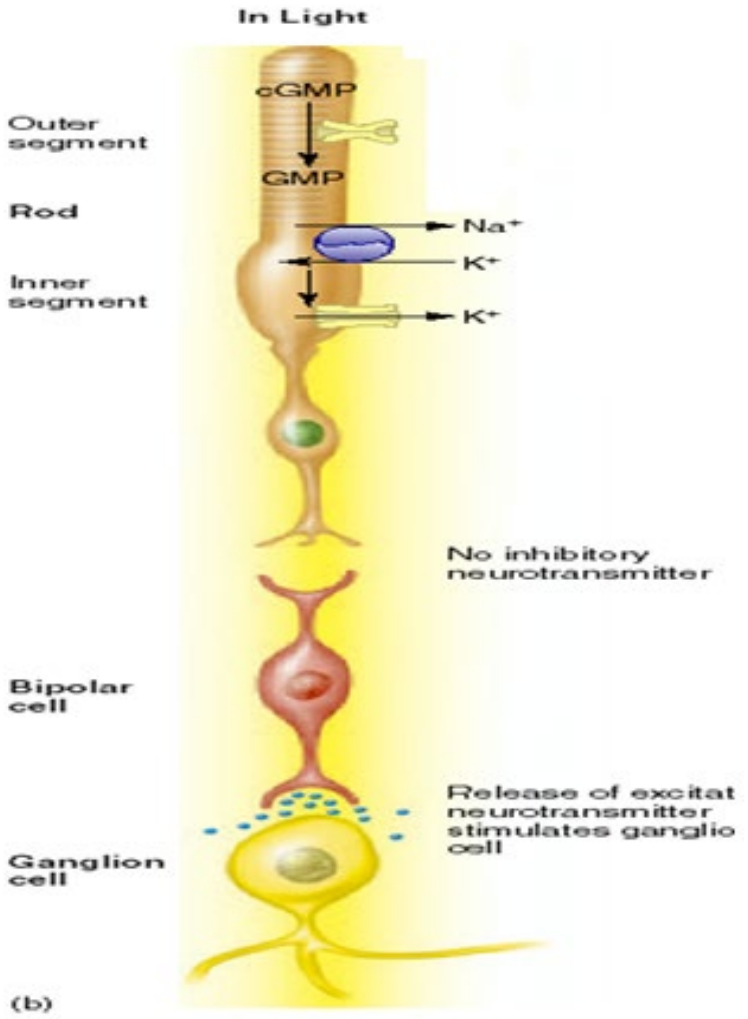
❑In Light:

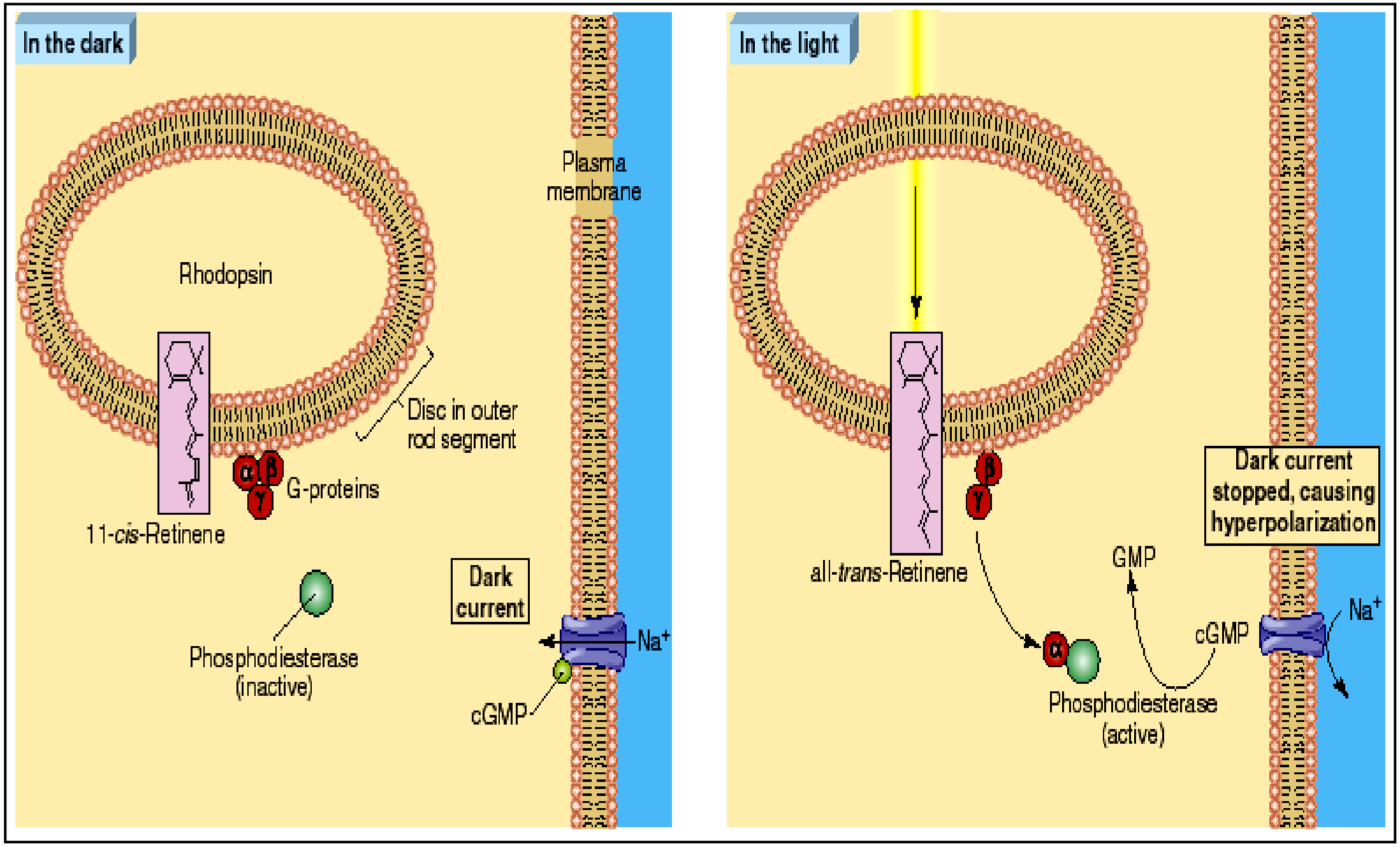
The **activated rhodopsin** activates **G- protein transducin** which in turn activates **phosphodiestrase** enzyme→ breakdown of cGMP → closure of **cGMP dependent Na^+ channels** → ↓ Na entry to outer segment (with Na^+ still pumped out of inner segment) → **hyperpolarization** of rod to **-80 mv** → ↓ transmitter (**glutamate**) release in synaptic terminal → **stimulation of bipolar cells** → **excitation of ganglion cells** that respond by generation of action potential in optic nerve → visual pathway

Photoreceptor Potential

In Light






In the dark
Plasma membrane
Rhodopsin
Disc in outer rod segment
α
β
γ
G-proteins
11-cis-Retinene
Phosphodiesterase (inactive)
Dark current
Na+
cGMP
In the light
all-trans-Retinene
β
γ
α
Phosphodiesterase (active)
GMP
cGMP
Dark current stopped, causing hyperpolarization
Na+

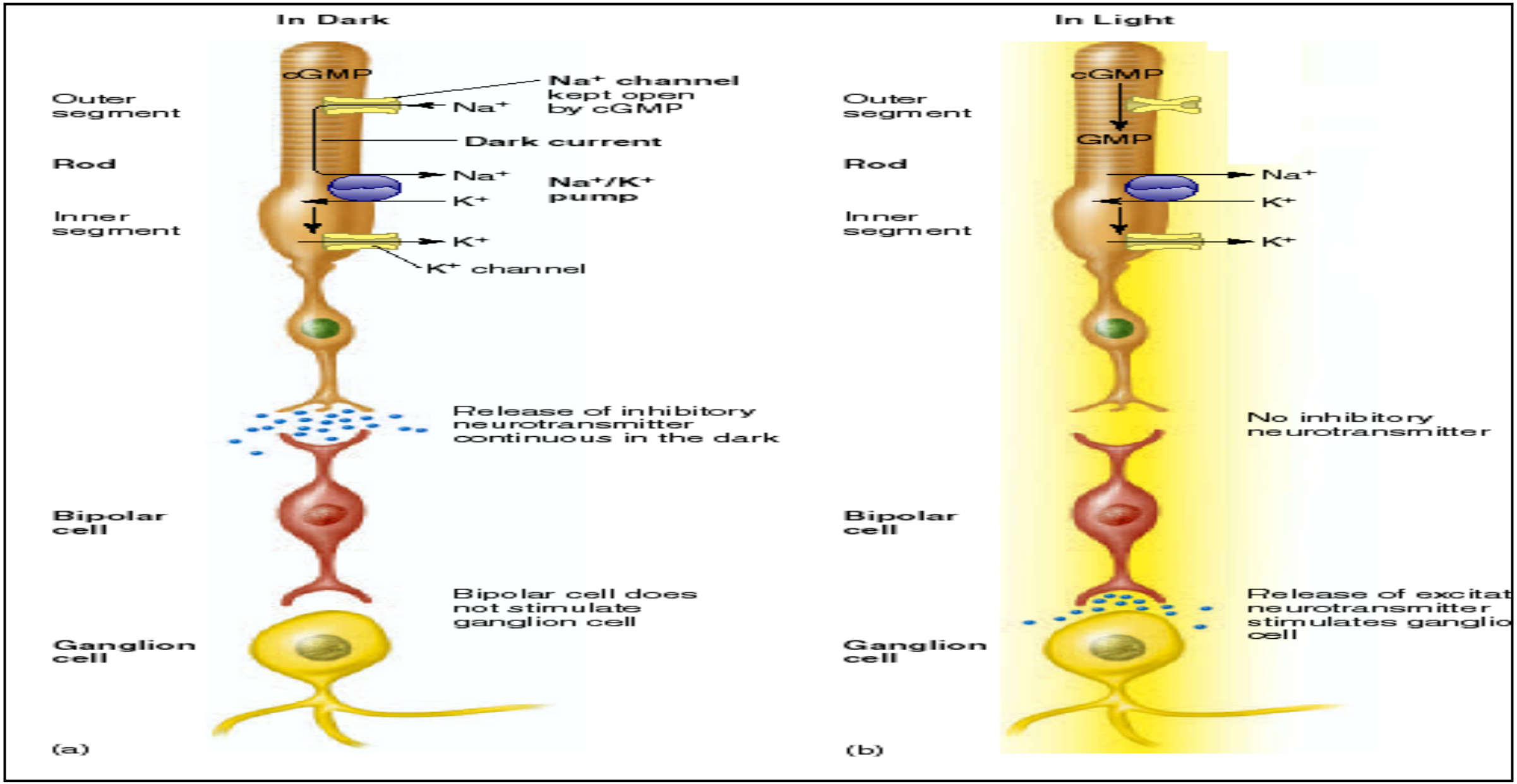
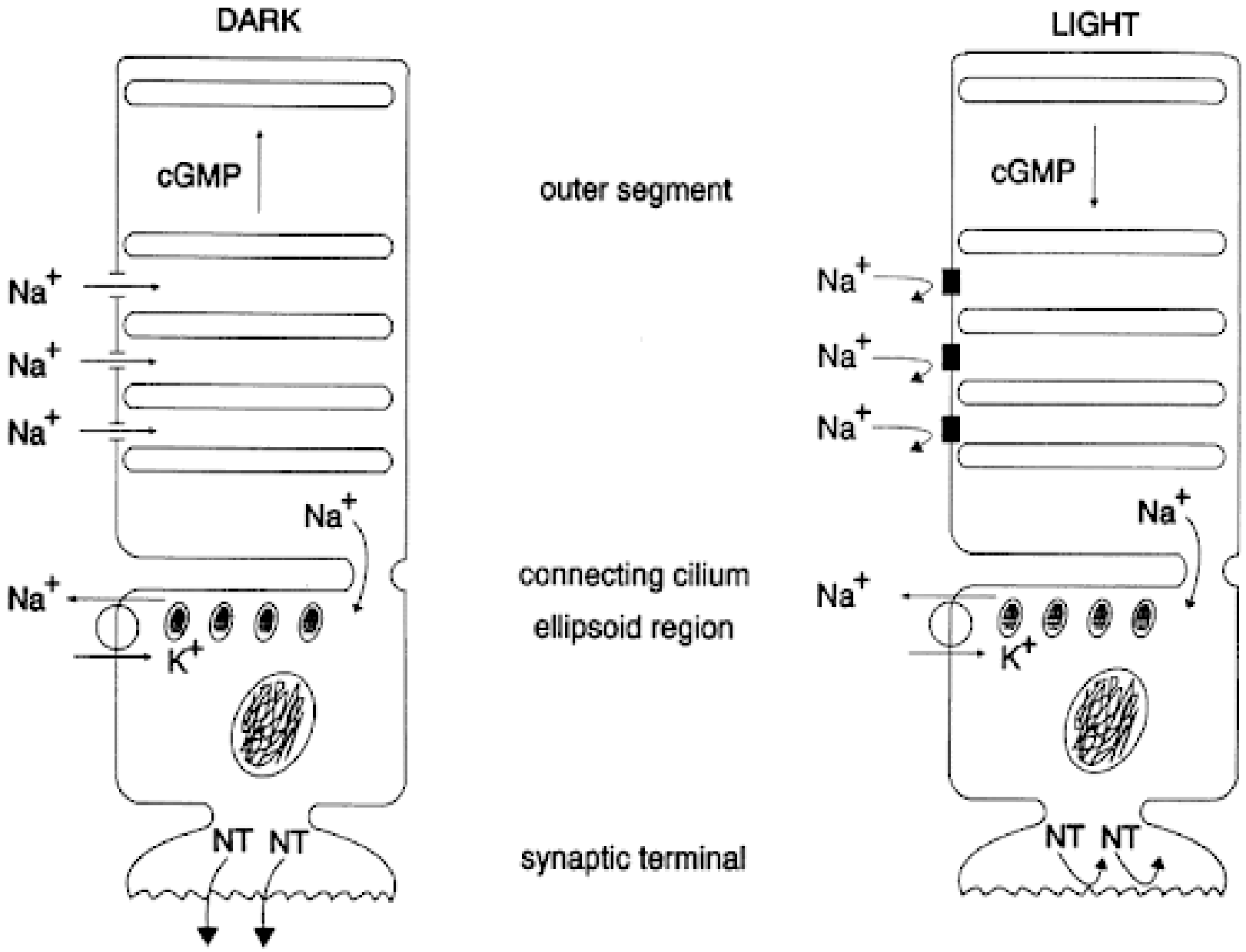


Fig: Mechanism of phototransduction. In the dark, Na^+ channels in the outer segment are held open by cGMP. Light leads to increased conversion of cGMP to 5′-GMP, and some of the channels close. This produces hyperpolarization of the synaptic terminal of the photoreceptor and decrease in release of inhibitory chemical transmitters.


DARK
LIGHT
cGMP
cGMP
outer segment
Na+
Na+
Na+
Na+
Na+
Na+
Na+
Na+
connecting cilium
ellipsoid region
K+
K+
NT NT
NT NT
synaptic terminal

c) Termination of excitation

- Within a second the activated rhodopsin is inactivated by the enzyme **rhodopsin kinase** → reversal of all reactions → regeneration of cGMP → reopening of Na^+ channels → termination of excitation.

d) Regeneration of the photopigment

- **All-trans retinal** is taken up by **pigmented epithelium** where it is converted to **11-cis retinal** by **isomeraze** enzyme then sent back to rods to recombine with **opsin.**

Retinal adaptation

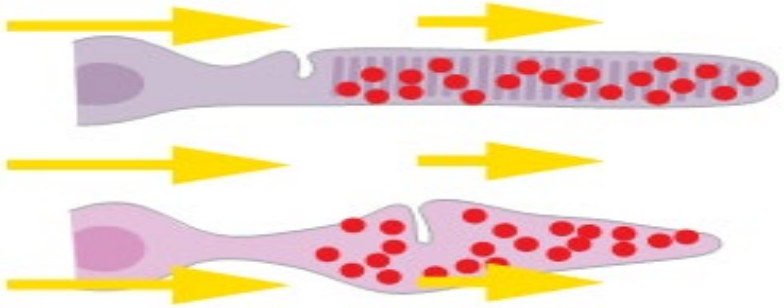
- **Def: Change in the sensitivity of** the retina according to the **intensity of light**. So, **retinal sensitivity increases** in **dark** and **decreases in light**.
- **Types:**

	Dark Adaptation	Light adaptation
1) Def	The ability of the retina to becomes **more sensitive** to **faint light.**	A **decrease in the retinal sensitivity** which occurs in bright light.
2) Mechanism	Due to **regeneration of photosensitive pigments** (rhodopsin& iodopsin).	Due to **degeneration of the photosensitive pigments** (rhodopsin & iodopsin).

Mechanism of Dark adaptation

Regeneration of the photosensitive pigments in the rods and the cones (rhodopsin and iodopsin).

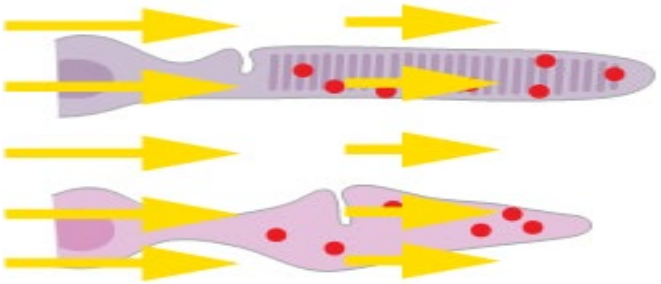
Dim light



Mechanism of Light adaptation

Degeneration of the photosensitive pigments in the rods and cones (rhodopsin and iodopsin).

Bright light



	Dark Adaptation	Light adaptation
3) Example	***When a person enters a dark room** after being previously exposed to bright light, he cannot see anything at the start in spite of the rapid pupillary dilatation. ***After a few minutes**, he becomes accustomed to the dark and can see well, i.e. the retina become more sensitive to light. The sensitivity of the retina ↑ by 10,000 - 100,000 times.	***When a person moves from a dark place to bright light**, at the start even moderate light seems to be very intense and uncomfortable. ***After about 5 minutes**, this sensation disappears due to the decrease in the retinal sensitivity,

Dark adaptation

Example

After 5 minutes

After 30 minutes

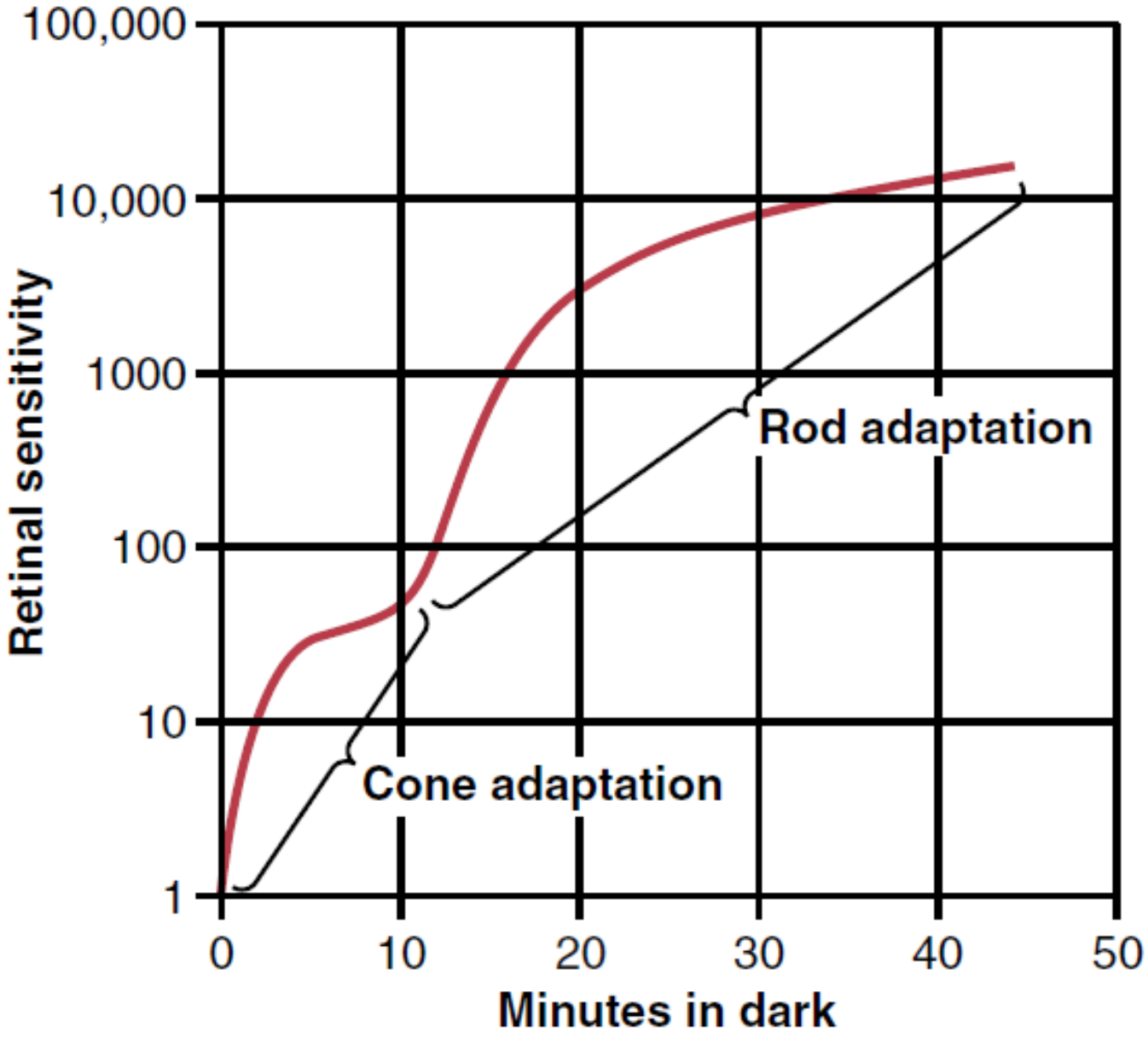
Light adaptation

Example

On entry of room

After 5 minutes

	Dark Adaptation	Light adaptation
4) Duration	becomes completed **after 30 minutes (Slow process)**	**About 5 minutes**,
5) Phases	**Dark adaptation occurs in 2 phases:** ***A) Cone adaptation:*** due to regeneration of **iodopsin** → a slight ↑ in the retinal sensitivity and completed within **5 minutes**. ***B) Rod adaptation:*** due to regeneration of **rhodopsin** → a marked ↑ in the retinal sensitivity and completed within **30 minutes**.	

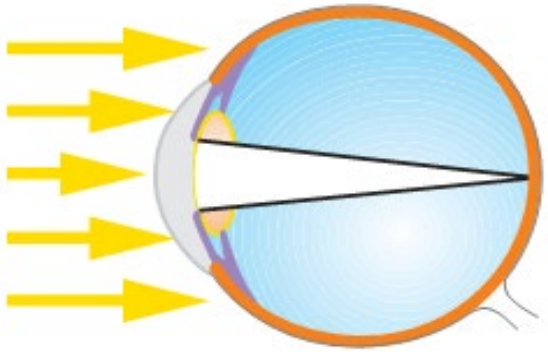

100,000
10,000
1000
100
10
1
Retinal sensitivity
Rod adaptation
Cone adaptation
0
10
20
30
40
50
Minutes in dark

	Dark Adaptation	Light adaptation
4) Changes in the eye	**1. Dilatation of the pupils** which allows more light to enter the eye and stimulates more rods. **2. Regeneration of the pigments** in the rods and the cones which ↑ retinal sensitivity to dim light. **3.↑ in the retinal sensitivity** due to regeneration of the photosensitive pigments of the rods and cones. **4. ↓ visual acuity** so that the fine details and colours of the object cannot be seen	**1. Constriction of the pupils (miosis)** to ↓ the amount of light entering the eye. **2. Breakdown of the pigments** in the rods and cones, so photopigments are decreased. **3. ↓ in the retinal sensitivity** due to degeneration of the photosensitive pigments of the rods and cones. **4. ↑ visual acuity** so that the fine details and colours of the object cannot be seen

Changes in the eye at dark adaptation

Dilatation of the pupils which allows more light to enter the eye and stimulates more rods

Dim light

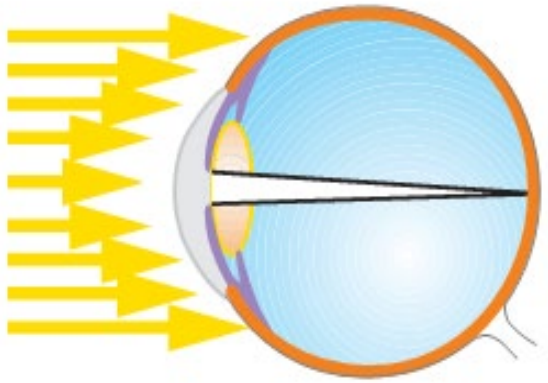


Wide pupil

Changes in the eye at light adaptation

Constriction of the pupils (miosis) to reduce the amount of light entering the eye

Bright light



References

1. Costanzo, Linda S. "BRS Physiology (Board Review Series)." (2018).

2. Ganong, William F. "Review of medical physiology." (2020).