CNS
Doctor 2021

Physiology

Modified (8)

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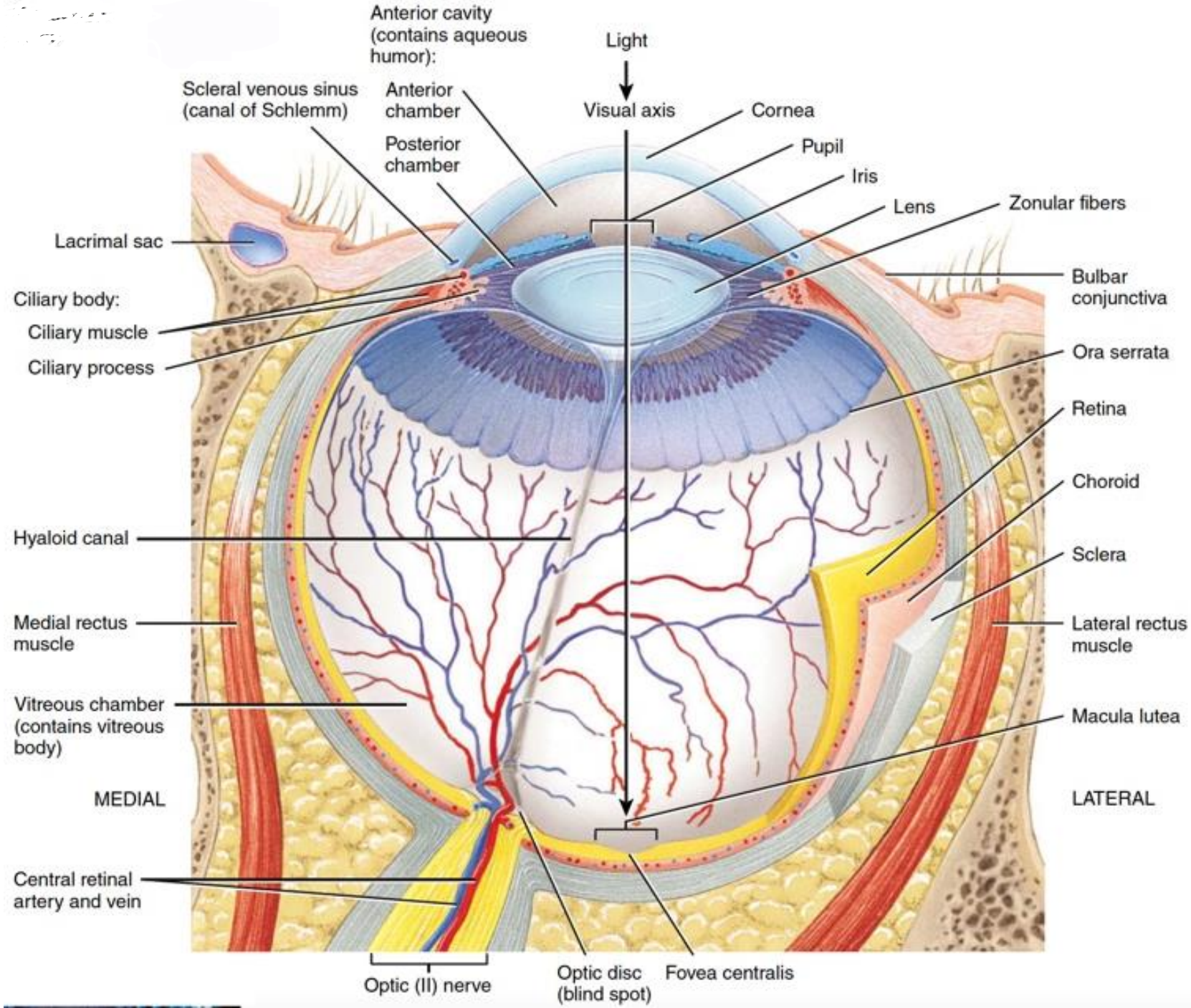
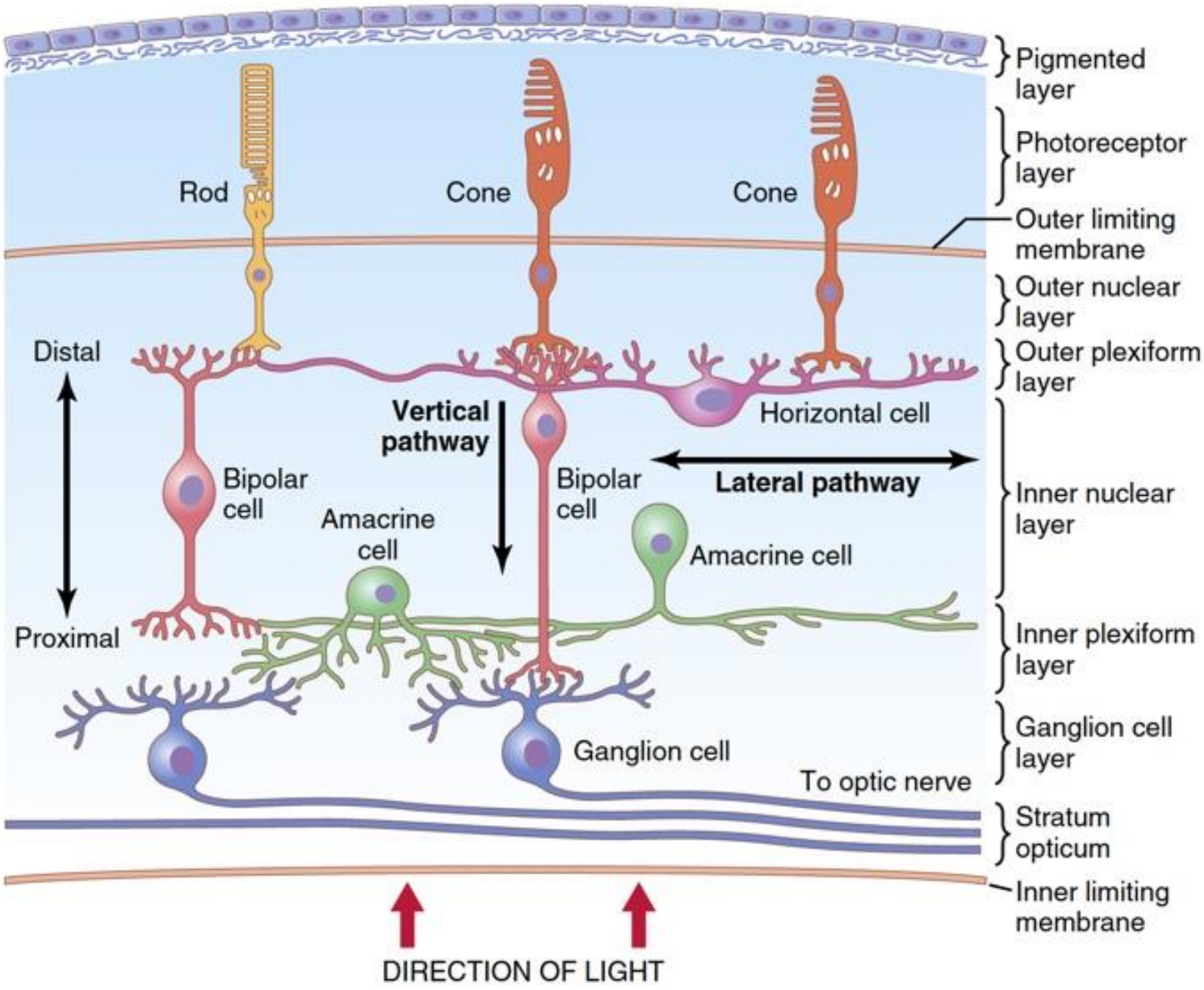
Physiology for medical students

Vision-II

Fatima Ryalat, MD, PhD

- As discussed earlier , the electromagnetic rays of visible light pass all through transparent components of eyeball (and undergo 4 stages of refraction, till being precisely converged and concentrated at retina , to excite the photoreceptors there , and consequently phototransduction gonna take place and image gets detected in the CNS


Anterior cavity (contains aqueous humor):
Light
Scleral venous sinus (canal of Schlemm)
Anterior chamber
Visual axis
Cornea
Posterior chamber
Pupil
Iris
Lens
Zonular fibers
Lacrimal sac
Bulbar conjunctiva
Ciliary body:
Ciliary muscle
Ciliary process
Ora serrata
Retina
Choroid
Hyaloid canal
Sclera
Medial rectus muscle
Lateral rectus muscle
Vitreous chamber (contains vitreous body)
Macula lutea
MEDIAL
LATERAL
Central retinal artery and vein
Optic (II) nerve
Optic disc (blind spot)
Fovea centralis



Retina can be mainly devided into 2 segment :
1-The outer – closer to sclera – contains the photoreceptors (cones and and rods) represented in the adjacent figure as the part above .
2-The inner-closer to vitreous humor- the initial to recieve light rays – the neural layer .
Each segment is further divided into sub layers
Represented in the adjacent figure as the part bellow

- After getting refracted by the cornea , lens , etc ,when the light first reaches the retina , is passes by the inner layer toward the pigmented layer – the outer most in the outer segment -, where it gets absorbed rather than scattered, generating signals upon the excitement of photoreceptore located there , the resultant signal propagates in the opposite direction toward the inner neural layer closer to the vitreous humor ; the direction of by which the light rays reaches the retina is opposite to the direction of signals they propagate

- The previous case is generally true in all parts of retina , except for two parts : The optic disc and fovea centralis .

- The optic disc is a photoreceptor -free retinal spot , it does not participate in the process of vision even though light rays reach this blind area .

- We see objects simply by the light rays reflecting against their outer surface , if the object is oriented in such a way that it reflects light rays in the direction of being converged at the blind spot only , the object is out of our vision zone.

- However , having retinal spot free of photoreceptors does not affect the picture captured by the brain for the scene , because central processes of photoreceptors in remaining retinal zones fill the missing part

- The fovea spot on contrast is a point of the sharpest and most accurate vision , light rays are not distracted there , this is partially because light doesn't pass by the inner neural layer before propagating the signal in the opposite direction , in fovea , light simply encounters the photoreceptors at first because the neural layer is displaced from the top of photoreceptors in fovea at the center of retina .
- Another advantage adding to the sharp foveal retinal vision is that it's entirely covered only by cones -the photoreceptors of acute discriminate , bright light vision- .

- Cones are present in their highest concentration in foveal retina
- The objects oriented to reflect light rays toward foveal retina are the best to be visualized .

- Foveal cones are thinner and more cylindrical than cones in remaining peripheral parts of the retina , this structural property allows more content of the color pigment packed in, and therefore providing sharper and sharper vision by processing greater amount of absorbed photons.

- Recall that rods predominate as retinal photo receptors by 20 folds greater than cones .
- Retina usually contains 120 million rod (photons of night vision) scattered all over the peripheral retina , in contrast to 8 million cones mostly concentrated in fovea .

- The sharpness and acuity of vision decreases as light rays are absorbed by surrounding more peripheral photoreceptors .
- Fovea is responsible for the most discriminative vision , followed by the area directly surrounding fovea ; called macula lutea and subsequently the more peripheral retinal zones provide weaker vision .

- Macular degeneration is the most common cause of blindness in elderlies , in western countries , it manifests as loss of the central spot in the captured image of the scene , due to the cellular destruction in the retinal spot (macula lutea) responsible for processing this lost central part of image .However the remaining peripheral vision and retinal processing is preserved

Optic disc

- The point on the retina at which the optic nerve leaves and through which blood vessels pass is the optic disc.
- This region is often called the blind spot; no image can be detected in this area because it has no rods and cones.
- We are normally not aware of the blind spot because central processing somehow “fills in” the missing spot.

Fovea

- Light must pass through the ganglion and bipolar layers before reaching the photoreceptors in all areas of the retina except the fovea, located in the center of the retina.

- Because of this feature, and because only cones (which have greater acuity or discriminative ability than the rods) are found here, the fovea is the point of most distinct vision.

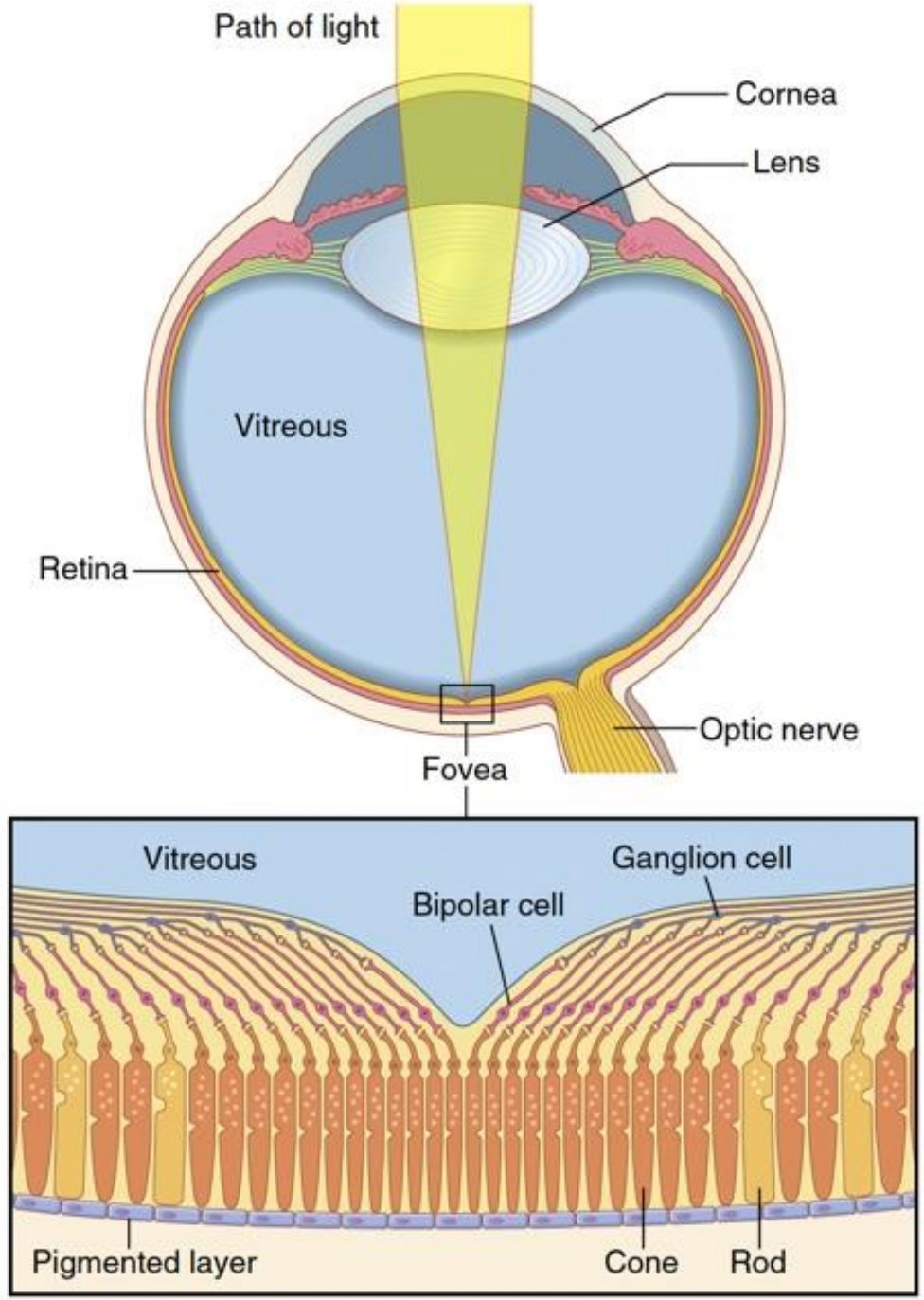
Fovea

- The fovea is a minute area in the center of the retina, especially capable of acute and detailed vision.

- The central fovea is composed almost entirely of cones. These cones have a special structure that aids their detection of detail in the visual image—that is, the foveal cones have especially long and slender bodies, in contradistinction to the much fatter cones located more peripherally in the retina.

Fovea

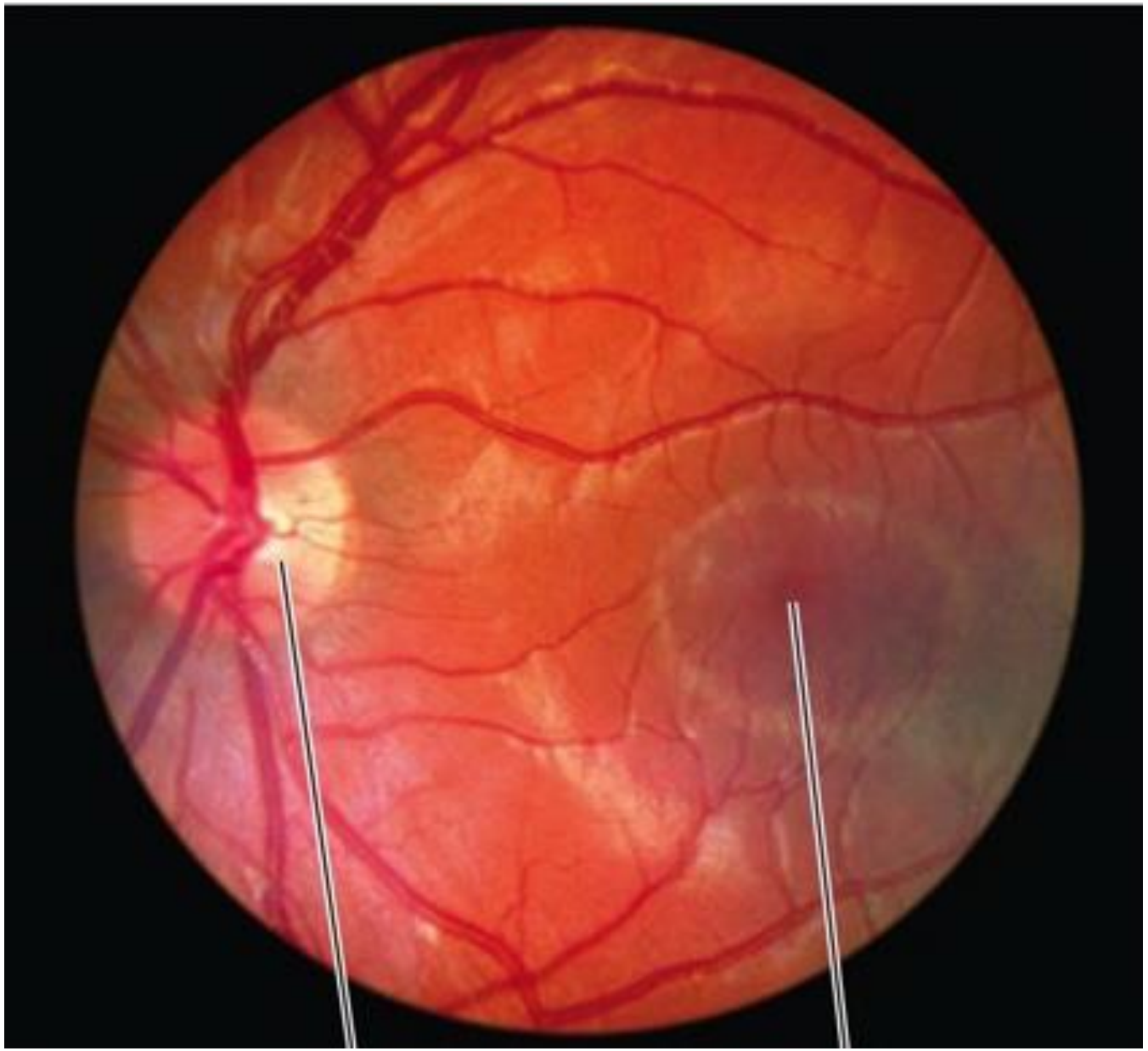
- Also, in the foveal region, the blood vessels, ganglion cells, inner nuclear layer of cells, and plexiform layers are all displaced to one side rather than resting directly on top of the cones, which allows light to pass unimpeded to the cones.


Path of light
Cornea
Lens
Vitreous
Retina
Optic nerve
Fovea
Vitreous
Ganglion cell
Bipolar cell
Pigmented layer
Cone
Rod

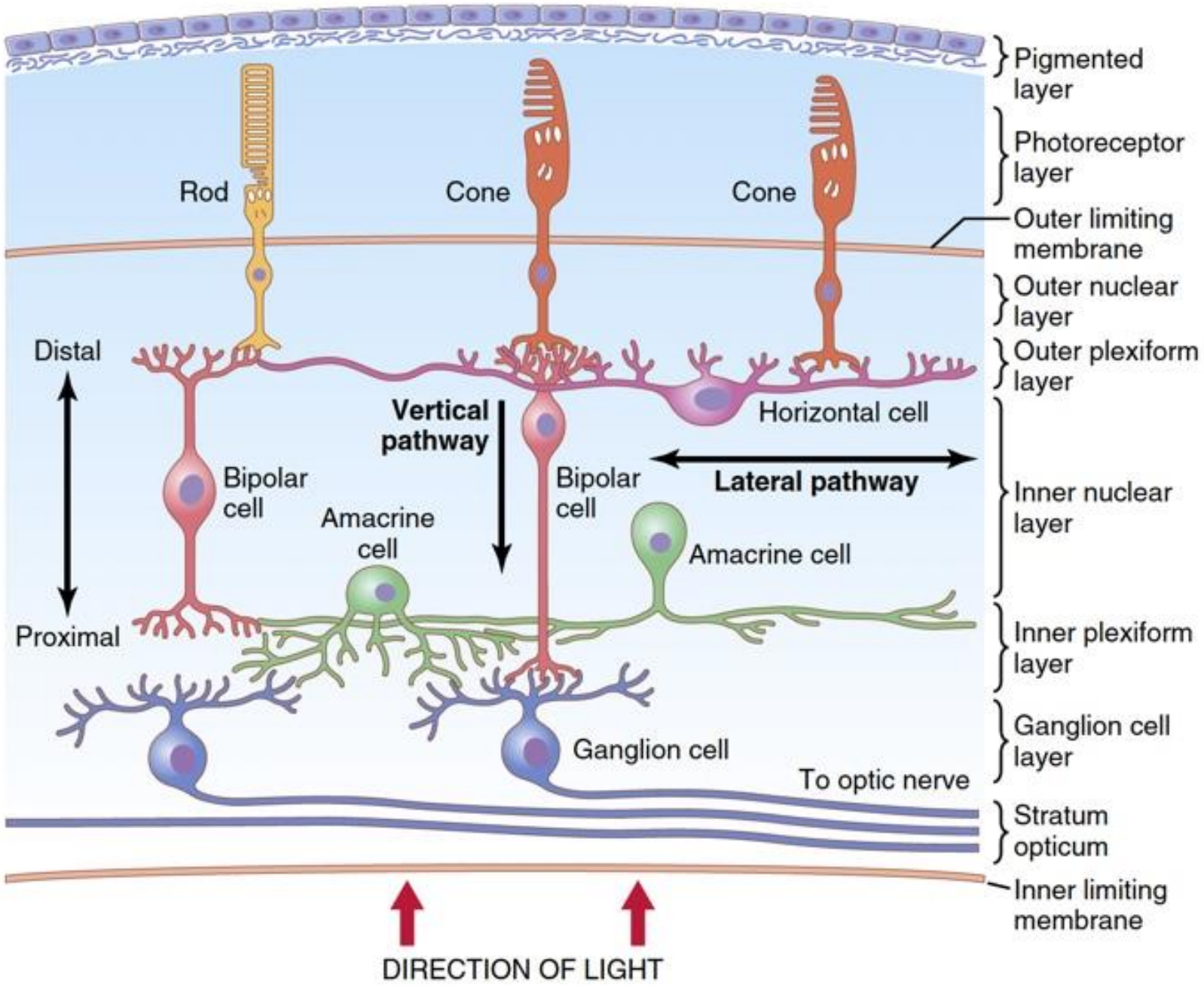
Macula

- The area immediately surrounding the fovea is called the macula lutea, has a high concentration of cones and fairly high acuity.
- Macular acuity is less than that of the fovea because of the overlying ganglion and bipolar cells in the macula.
- Macular degeneration.

Through the ophthalmoscope we can visiuilize two spots
1) optic blind disc (with vascular bundle passing through) (on the left side of the graph)
2)macula lutea with fovea centralis in the center (on the right side of the graph)



Macular degeneration



Recall : outer means toward sclera
Inner means toward vitreous humor

Refer to the adjacent neural segment with its layers of :
1-photoreceptors (cones and cones)
2-outer limiting membrane
3- outer nuclear layer .
4- outer plexiform layer : horizontal cell; interneuron form a network there .

Between bipolar and ganglion cells are the amachrine cells, processing of visual information before reaching the CNS is very complicated and not well understood

Pigment

- The black pigment melanin in the pigment layer prevents light reflection throughout the eye ball, which is extremely important for clear vision.

- Albinism

Due to insufficiency of melanin pigment in albino patients , light gets scattered and reflected throughout the eyeball after encountering with the the outer segment, rather than being absorbed, this in turn leads to random signaling of multiple pathways , therefore albino patients are photophobic , and avoid direct contact with bright light by means of sun glasses.
Other ophthalmologic symptoms and signs are further present in albino patients .

Vitamin A

- The pigment layer also stores large quantities of vitamin A. That is exchanged back and forth through the cell membranes of the outer segments of the rods and cones, which are embedded in the pigment.

- vitamin A is an important precursor of the photosensitive chemicals –(photo pigment) -of the rods and cones (photoreceptors present in the outer segment) .

-By-side note : a photo receptor (rod or cone) contributes to the visual process by means of excitement of its light sensitive photo chemical pigment .

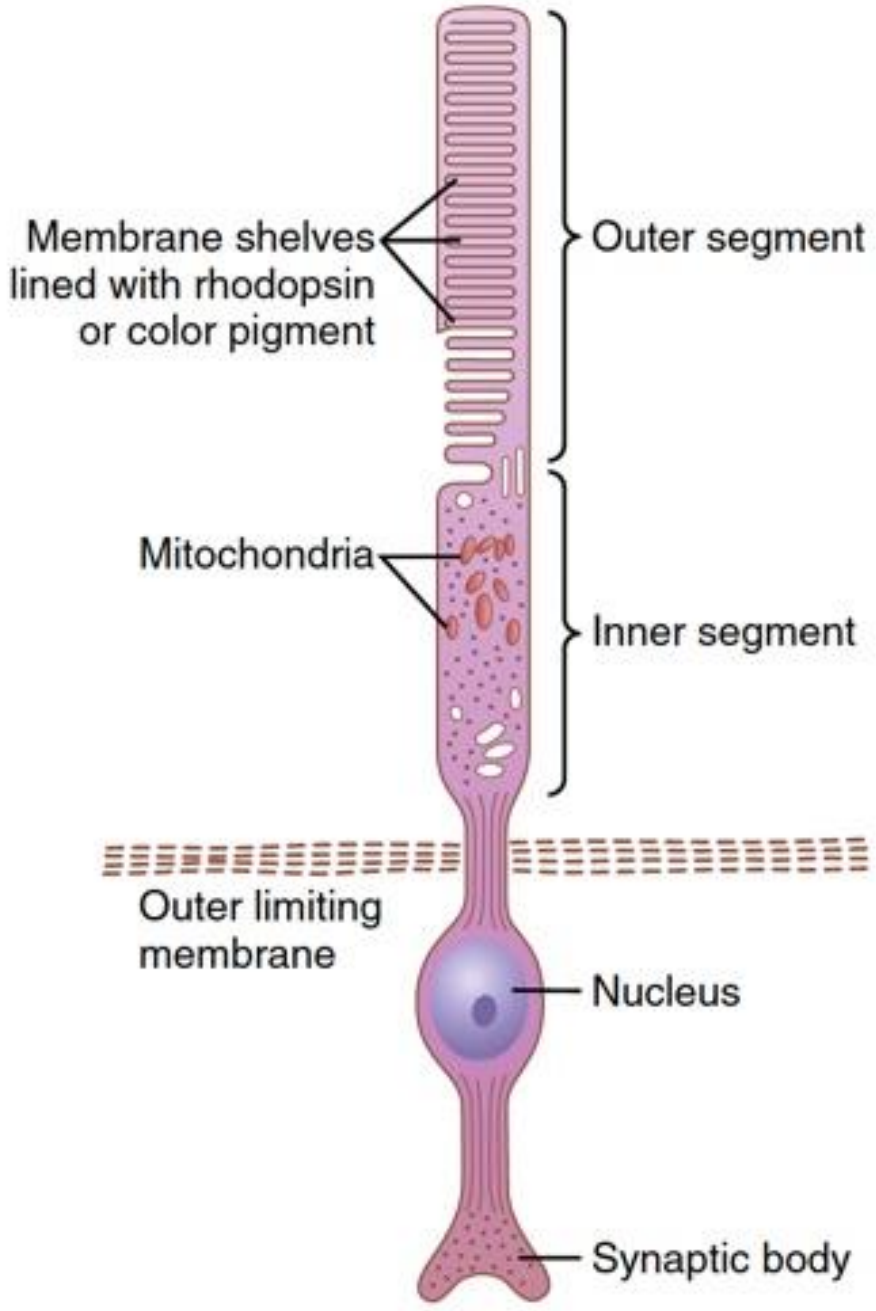
The pigment is a holoprotein, whose nonprotein part called retinal.

The protein part of the pigment is called opsin .

In rods Opsin is referred to as scotopsin , in cones is photopsin ,differences between the two is what distinguish cones from rods in terms of absorbable spectrum☺

- Significant Vitamin A deficiency is very unlikely , as it's stored sufficiently in liver, however if deficit the subsequent retinal disorder causes Night blindness.

Notice the molecular structure of rods :
1)Outer segment :a stack of membranous discs, the exact site of phototransduction, and contains photopigments involved in the process as transmembrane proteins .
Numerous photopigments are anchored to the membranous discs in the outer segment of rod , this collectively increases the sensitivity of the whole photoreceptor (the rod) making it sensitive to dim light and responsive to smaller amount of light photons present there .
2)Inner segment : contains organelles, mainly mitochondria to provide the energy essential for intracellular metabolic reactions of synthesizing and regenerating photopigment all the time.
3)Synaptic body : where neurotransmitters initiate connection with the following component of neural pathway.



How does phototransduction take place, and how does the brain become aware of the captured image ?

Photoreceptors

- The major functional segments of either a rod or cone are:
- (1) the outer segment; (2) the inner segment; (3) the nucleus; and (4) the synaptic body.
- The light-sensitive photochemical is found in the outer segment. In the case of the rods, this photochemical is rhodopsin; in the cones, it is one of three “color” photochemicals, usually called simply color pigments, that function almost exactly the same as rhodopsin except for differences in spectral sensitivity.
- In the outer segments of the rods and cones, note the large numbers of discs. Each disc is actually an infolded shelf of cell membrane. There are as many as 1000 discs in each rod or cone.

Photoreceptors

- The inner segment of the rod or cone contains the usual cytoplasm, with cytoplasmic organelles. Especially important are the mitochondria, which play the important role of providing energy for function of the photoreceptors.

- The synaptic body is the portion of the rod or cone that connects with subsequent neuronal cells, the horizontal and bipolar cells, which represent the next stages in the vision chain.

Photoreceptors

- Both rhodopsin and the color pigments are conjugated proteins. They are incorporated into the membranes of the discs in the form of transmembrane proteins.

- The concentrations of these photosensitive pigments in the discs are so great that the pigments themselves constitute about 40% of the entire mass of the outer segment.

Biochemical cascade of phototransduction in dark (resting state) (applies to both types of photoreceptors):

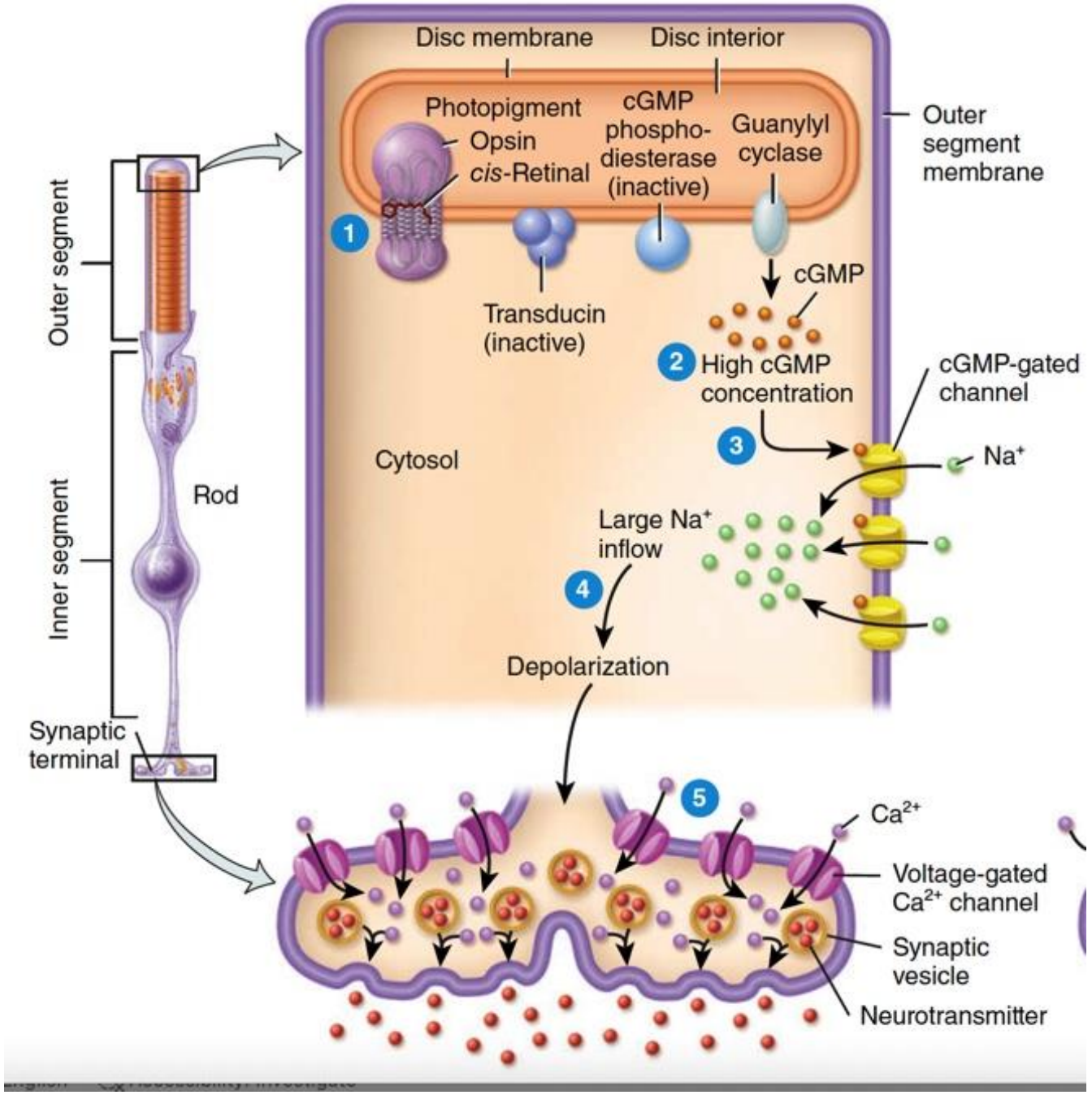
-Photopigments anchored to the membranous disc of rod is called rhodopsin .

- Conformational state of Retinal then is 11-cis (recall retinal is nonprotein portion of photopigment).

- protein part of photopigment in rods is called scotopsin And in cones is photopins .

- during rest in the background of high intracellular Ca concentration ,guanylyl cyclase gets activated to provide adequate cGMP that insures Na influx though cGMP ligand gated channels , the resultant depolarization opens voltage gated Ca channels at the synaptic body , and glutamate consequently is exocytosed .

Glutamate maintains the resting state via its inhibitory effect on bipolar cells



When the photopigment (rhodopsin in rods) gets excited by photons , conformational alternation of retinal occurs , from cis to all-trans , resulting in instability and dissociation of the photopigment
(opsin gets released from the all trans retinal).
Stimulated photopigment activates Transducin , a G protein whose alpha subunit gets released upon replacement of bound GDP with GTP .
The GTP -bound alpha subunit switches on the cGMP phosphodiesterase converting cGMP into GMP.
A subsequent decrease in intracellular cGMP hyperpolarizes the membrane potential , and prevents the Ca influx and the resultant exocytotic release of glutamate .
The inhibitory action of glutamate is no longer there , signals are processes to photocenters in the brain , and the individual becomes aware of the image .
By the light stimulus , hyperpolarizing receptor potential along photoreceptor is generated .

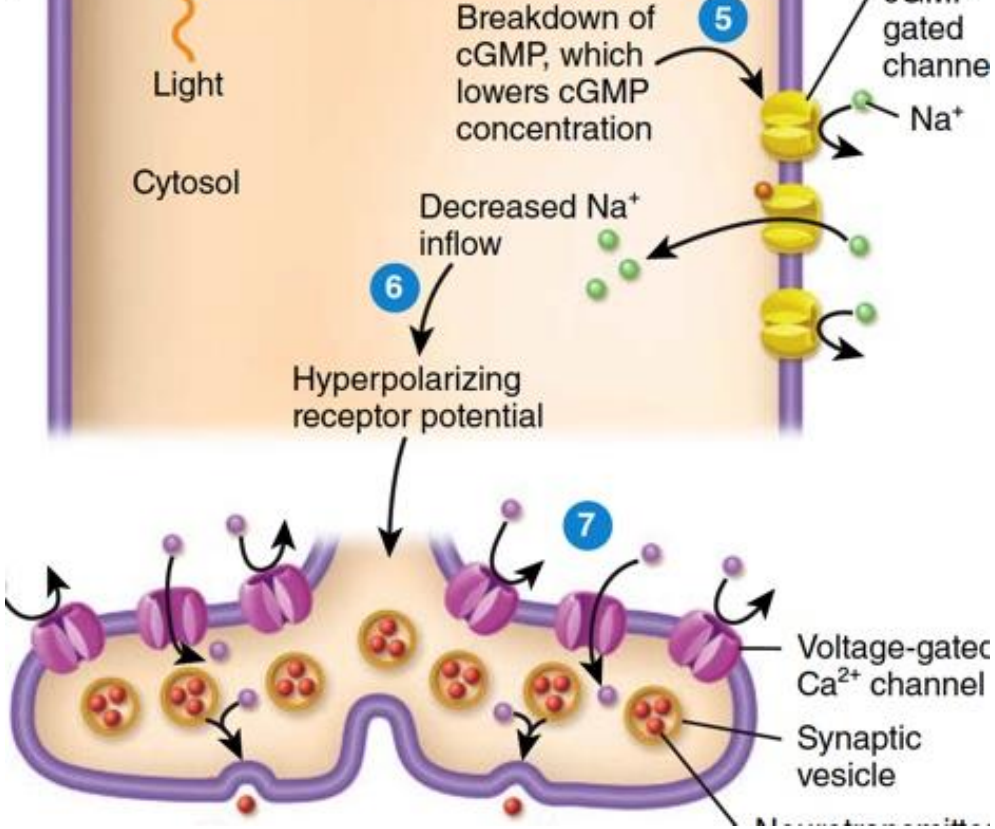


Photo-transduction

- The outer segment of the rod that projects into the pigment layer of the retina has light-sensitive pigment called rhodopsin.
- This substance is a combination of the protein scotopsin and the carotenoid pigment retinal.
- Furthermore, the retinal is a particular type called 11-cis retinal. This cis form of retinal is important because only this form can bind with scotopsin to synthesize rhodopsin.

- all-trans retinal no longer fits with the orientation of the reactive sites on the protein scotopsin, the all-trans retinal begins to pull away from the scotopsin.

- Several changes lead to the formation of metarhodopsin II, also called activated rhodopsin, that excites electrical changes in the rods.

- When light energy is absorbed by rhodopsin, the rhodopsin begins to decompose within a very small fraction of a second.

Re-formation

- The first stage in re-formation of rhodopsin is to reconvert the all-trans retinal into 11-cis retinal.
- This process requires metabolic energy and is catalyzed by the enzyme retinal isomerase.
- Once the 11-cis retinal is formed, it automatically recombines with the scotopsin to re-form rhodopsin, which then remains stable until its decomposition is again triggered by absorption of light energy.

Cones

- photochemicals in the cones have almost exactly the same chemical composition as that of rhodopsin in the rods.

- The only difference is that the protein portions, or the opsins—called photopsins in the cones—are slightly different from the scotopsin of the rods.

- The retinal portion of all the visual pigments is exactly the same in the cones and rods.

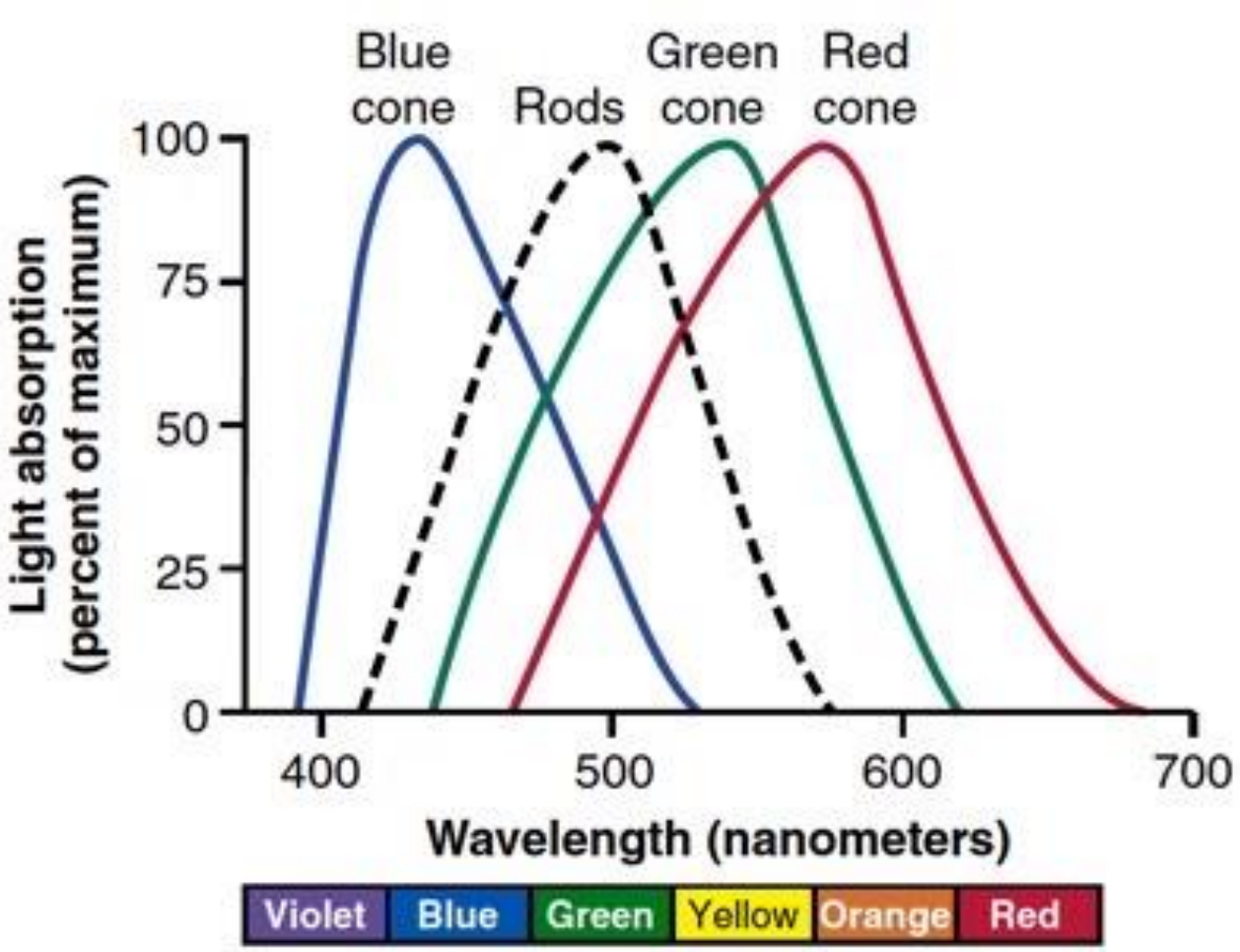
Color vision

- Each photopigment maximally absorbs a particular wavelength but also absorbs a range of wavelengths shorter and longer than this peak absorption.

- The farther a wavelength is from the peak wavelength absorbed, the less strongly the photopigment responds.

- The absorption curves for the three cone types overlap so that two or three cones may respond to a given wavelength but to a different extent.

Color vision



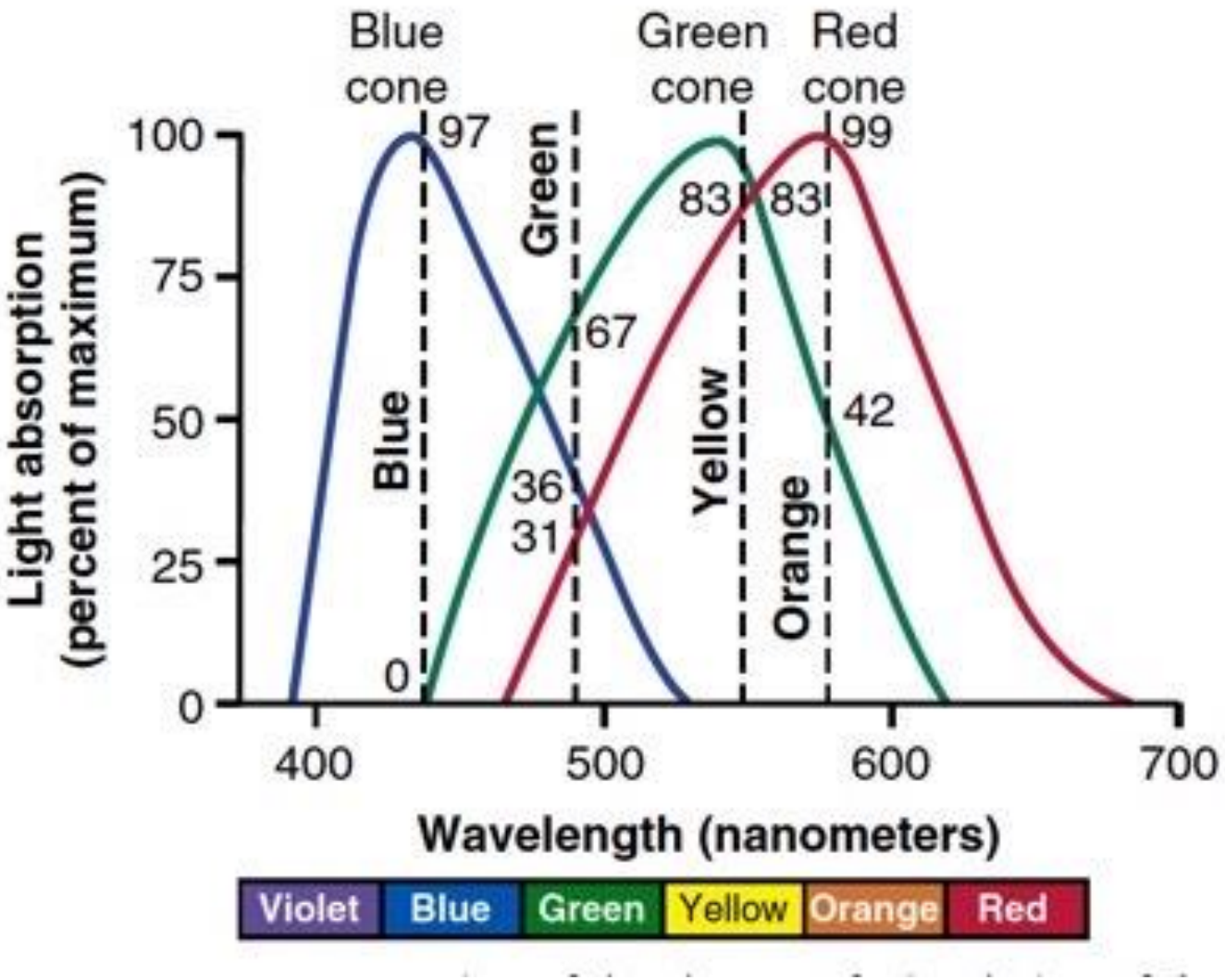
Absorbable spectrum of photopigment is related to its opsin .
The S-pigment in the blue cone absorbs short wavelengths around the visible blue .
The M-pigment in green cones absorbs medium wavelengths around green .

And same is for L-pigment in red cones for long wavelengths around red.

And this is how all the visible wavelength spectrum of electromagnetic rays is covered ☺

Color vision

- Each cone type is most effectively activated by a particular wavelength of light in the range of color indicated by its name.
- cones also respond in varying degrees to other wavelengths.
- According to the trichromatic theory of color vision, the perception of the many colors of the world depends on the three cone types' various ratios of stimulation in response to different wavelengths.

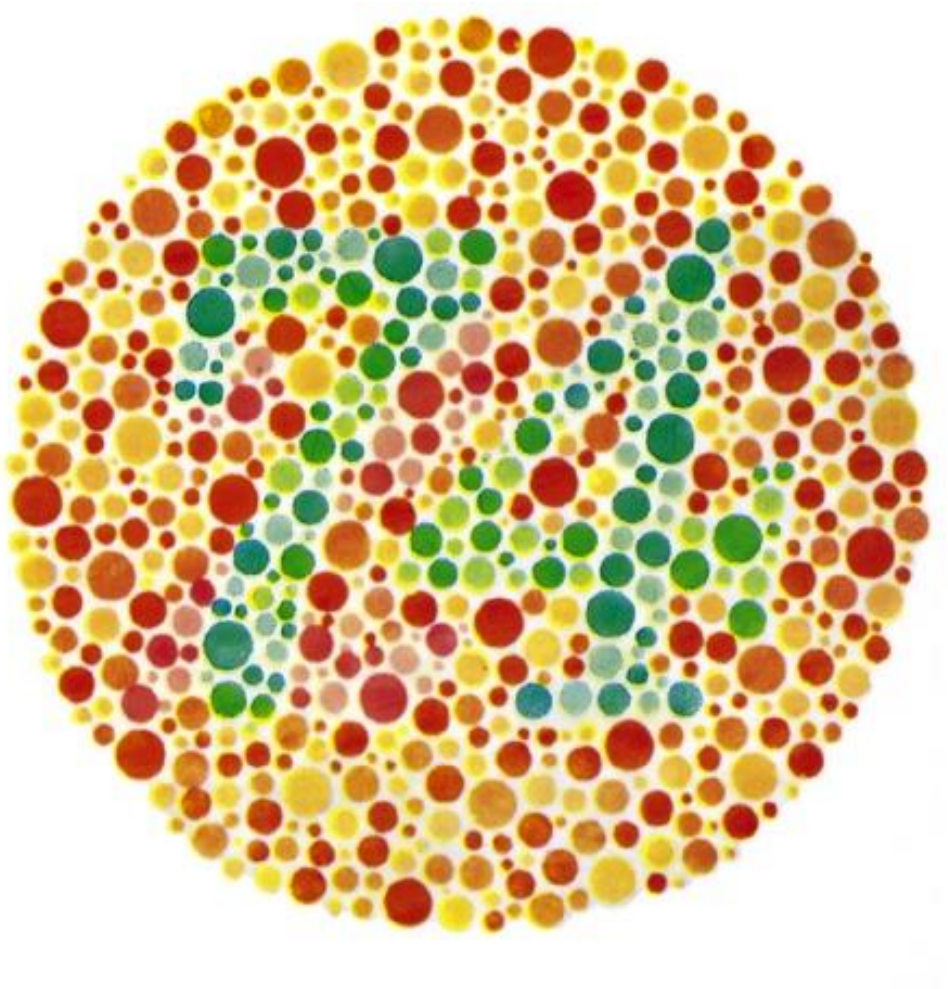


the ratios of stimulation of the three types of cones.

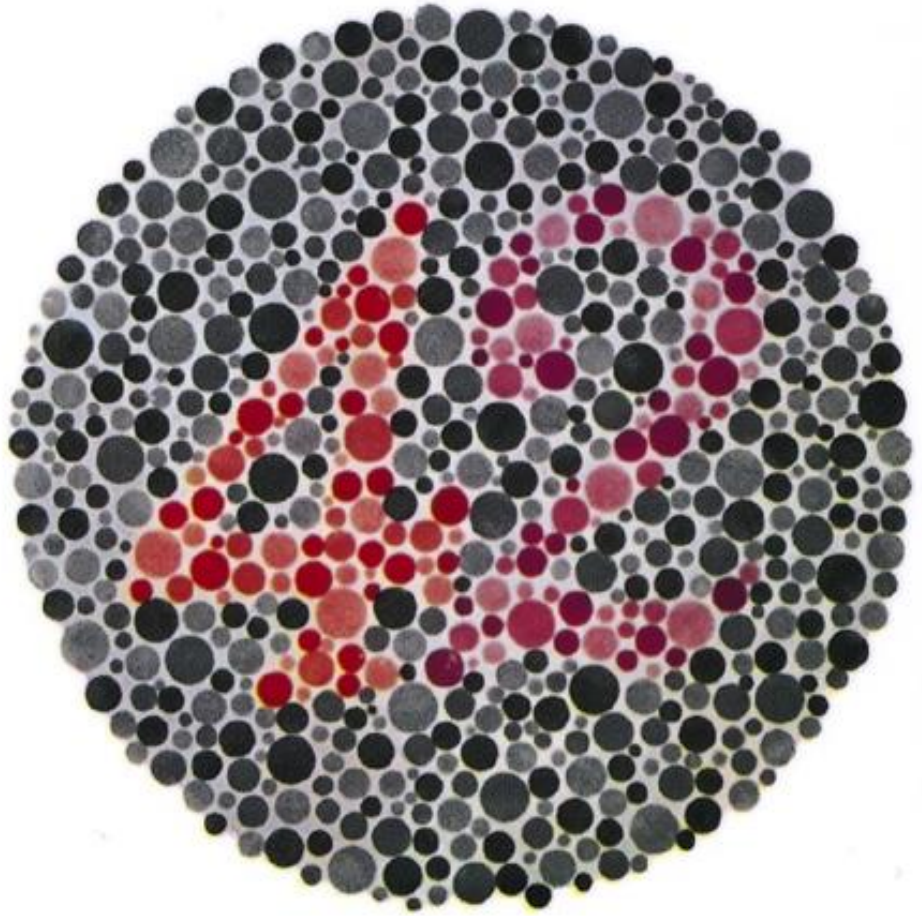
Yellow is perceived by activation of 83% or L-pigment cones , 83% of M-pigment cones but no S-pigment cone is activated .. Thus yellow is coded 83%-83%-0%.

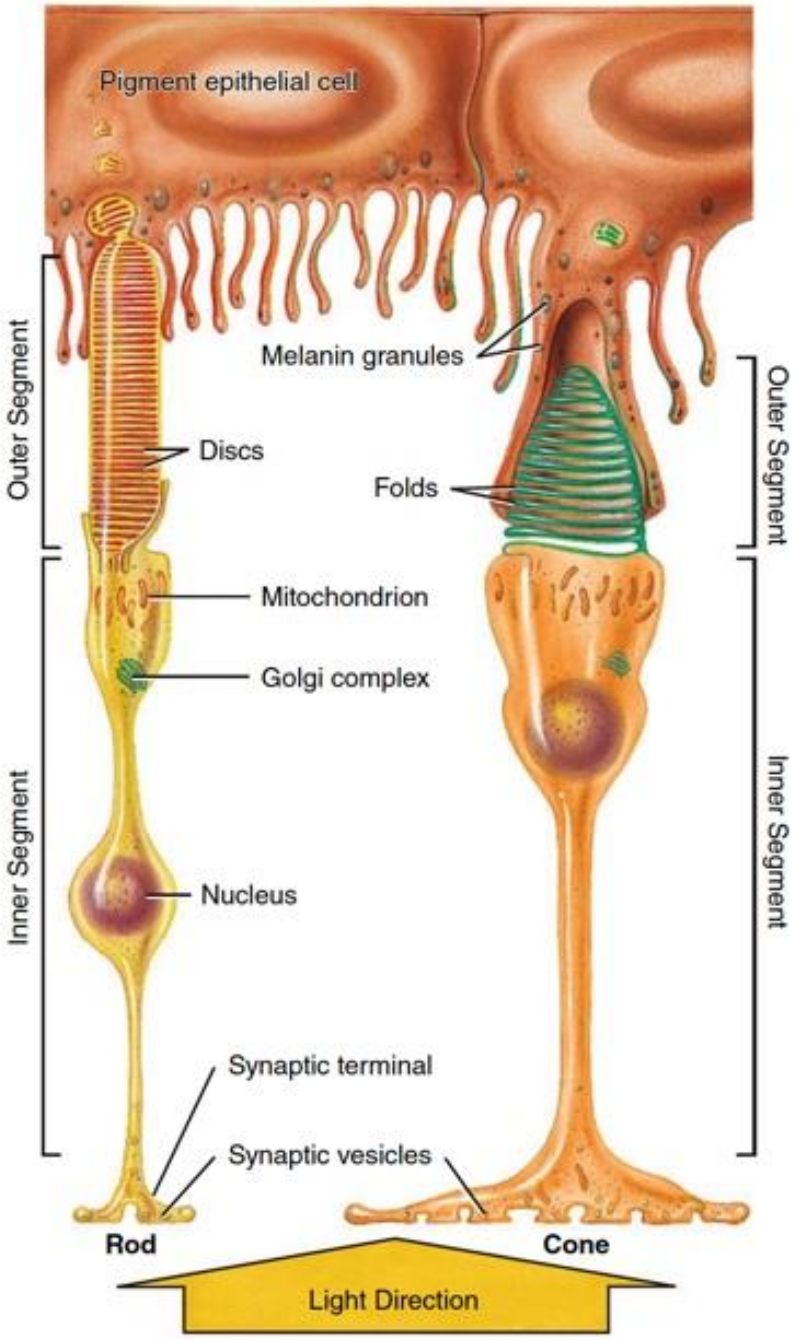
Orange (you are perceiving at this moment by reading the sentence)is perceived by activation of 42% of M-pigment cones and 99%of L-pigment cones , but no S-pigment cone is activated .

About equal stimulation of
all the red, green, and blue cones gives one the sensation
of seeing white.



Green-red color blindness is X-linked disorder and commoner in males.
Blue color blindness on contrast is somatic -linked
It manifests as abnormal perception of specific lengths-corresponding to the exact mutational defect-as pale shade of the color-responsibility of the remaining preserved types of cones ...
Patients simply define this pale shade as the color they are not capable to perceive
..
For example .. Patients with red blindness perceive an apple as a shade of pale green , and this is their definition of red despite being totally different than what a healthy individual perceives .





Rods vs cones:

shape : rods are cylindrical and distinguishable from cones in peripheral retina ,elongated and cylindrical foveal cones somehow mimic rods .

location : cones are central (in fovea) ,rods are peripheral.

Number : rods are much more numerous .

sensitivity to light :scattered all through the retina, the more numerous rods, with more transmembrane photopigments are more efficiently responsive to dim light.

visual acuity : cones provide more distinst vision

color vision : perceived by cones

- Photon of bright light , absorbed by a cone is intense enough to propagate a signal of action potential alone , that's why it is sufficient for each cone to synapse alone with one bipolar cell , and this adds further more to the sharpness of acute and discriminative image perceived by the brain though cones .
- Cone:bipolar synapse ratio is 1:1 .
- However , the dim light photon with the subsequent receptor potential at the level of rods isn't intense enough to reach threshold and establish an impulse of action potential at the level of ganglion cells -despite generating hyperpolarizing receptor potential- on its own membrane , therefore , convergence of multiple rods into single bipolar cell takes place ,so that a stronger summation of multiple receptor potentials is stronger and enough to propagate action potential at the level of ganglion cells, this collectively contributes to the less accurate image that is perceived in dark , brain can't precisely detect the photoreceptor which has detected the point.
- That's why rods collectively by their high numbers and convergence on bipolar cells are said to be sensitive and responsive to small photons of dim light , whereas photons are not

Photoreceptor	Sensitivity to Light	Acuity	Dark Adaptation	Color Vision
Rods	Low threshold Sensitive to low-intensity light Night vision	Low acuity Not present on fovea	Adapt late	No
Cones	High threshold Sensitive to high-intensity light Day vision	High acuity Present on fovea	Adapt early	Yes

Dark and light adaptation

- Photoreceptors must regenerate to re-perceive its zone of absorption once again .
- When getting suddenly (after being in bright light) Into the dark, the photopigments are initially broken down(consumed) as were all previously busy in perceiving the image of the scene during light exposure , little photoreceptors are available initially to detect this new scene of darkness ,that's why vision is kind of lost until phtoreceptors are gradually regenerated to detect the new scene .

- As a result, the sensitivity of your eyes gradually increases so that you begin to see in the darkened surroundings.

Dark and light adaptation

- Conversely, when you move from the dark to the light, at first a general sudden stimulation of photoreceptors takes place , producing this irritating vision, your eyes are suddenly very sensitive to the dazzling light.

- As some of the photopigments are rapidly broken down by the intense light, the sensitivity of the eyes decreases and normal contrasts can again be detected, softer signals by less photoreceptors is carried then after consumption , a process known as light adaptation.

Night blindness

- Our eyes' sensitivity can change as much as 1 million times as they adjust to various levels of illumination through dark and light adaptation.

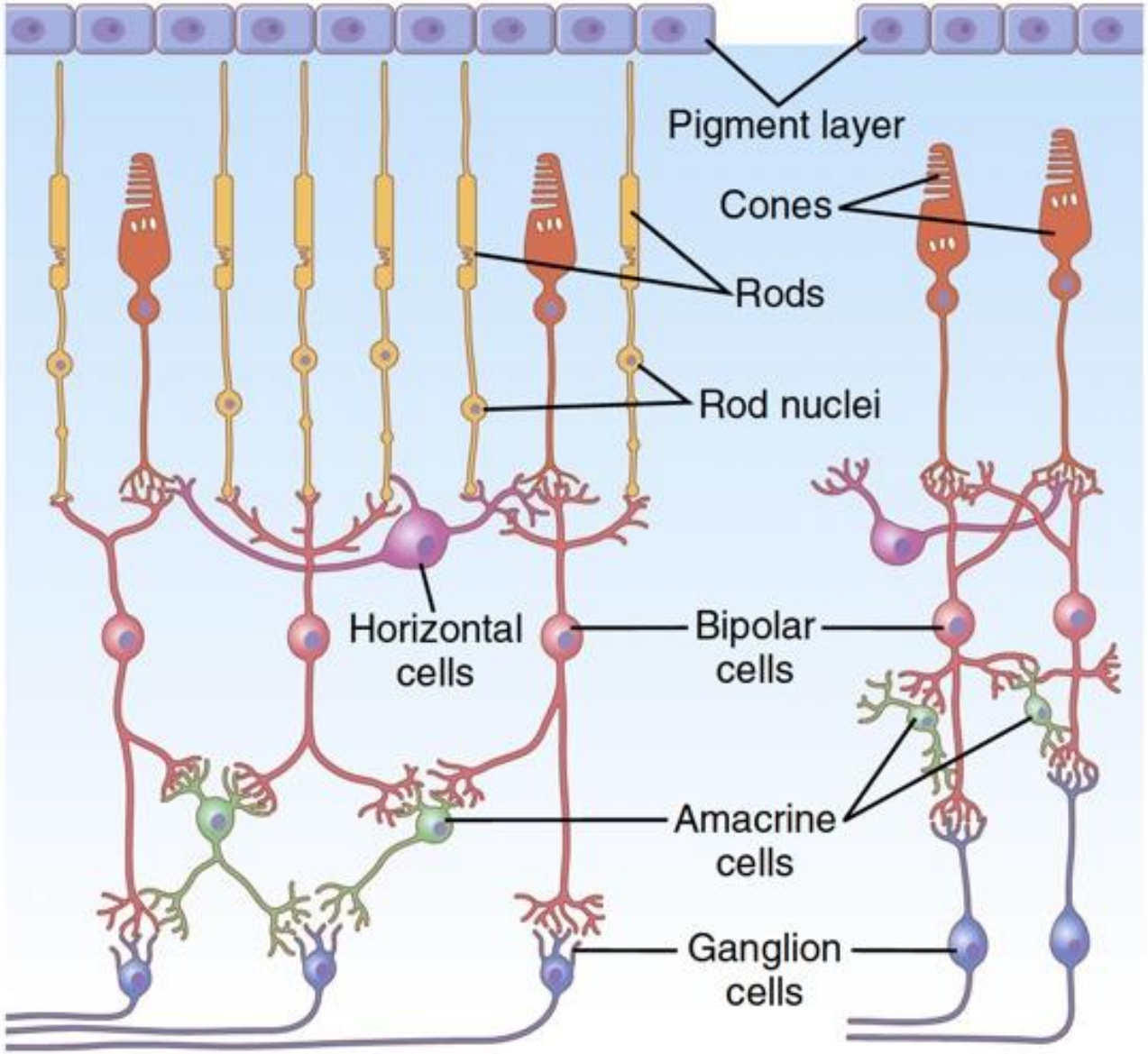
- Because retinal is a derivative of vitamin A, adequate amounts of this nutrient must be available for synthesis of photopigments.

- Night blindness occurs as a result of dietary deficiencies of vitamin A.

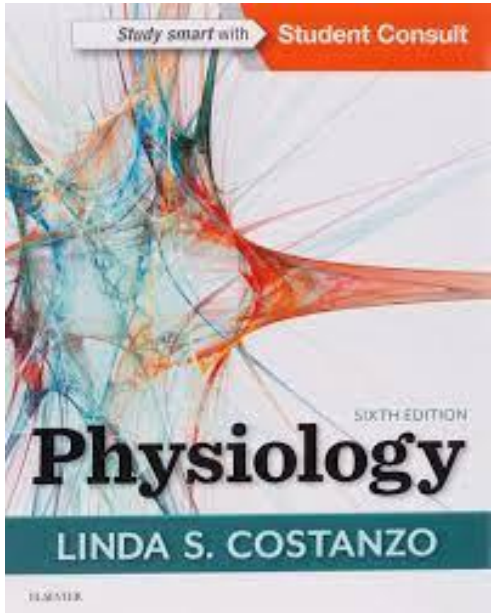
Adaptation

- These adaptive measures are also enhanced by pupillary reflexes that adjust the amount of available light permitted to enter the eye.
- Dilation allows a more general perceptive photo.

- The other mechanism is neural adaptation, involving the neurons in the successive stages of the visual chain in the retina and in the brain.


Pigment layer
Cones
Rods
Rod nuclei
Horizontal cells
Bipolar cells
Amacrine cells
Ganglion cells

References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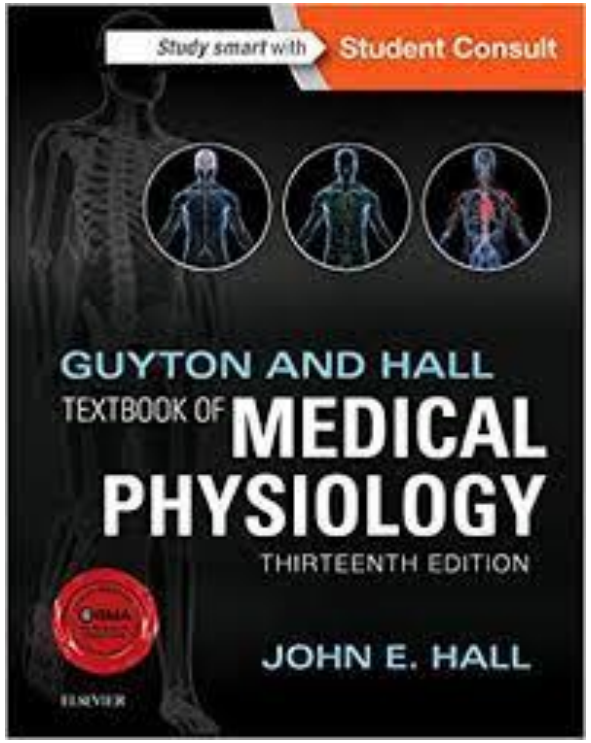
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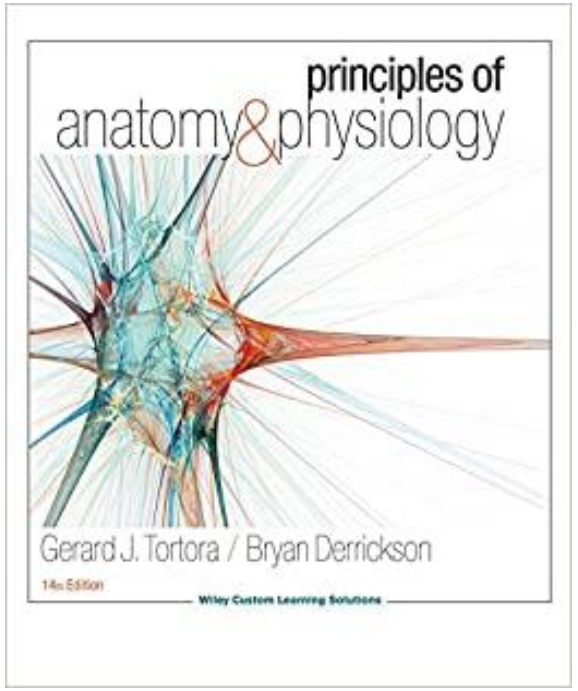
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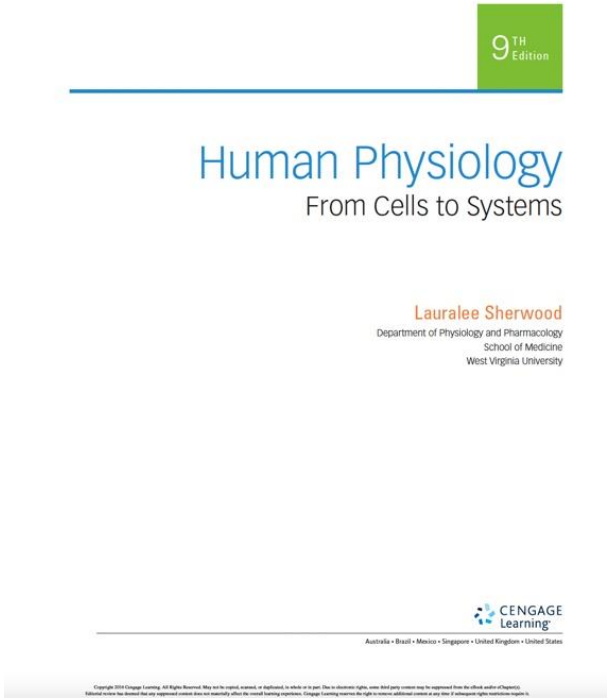
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Thank you

يارب ها هم أهل غزة وقفوا ببابك ، لم تمنعهم الحربُ ولا القصفُ ولا الموتُ من القيامِ بين يديك ، و لم يحل بينهم و بين استقامة صفوفهم دمارُ بيتِك ولا تهدّم مساجدِك ، يتضرعون إليك و يتوسلون بكَ و و يصلّونَ لك و يصومون و هم جياع ولم تدفعهم أقدارُك لسخط ولا نقمة و لا يبتغون سوى مرضاتك و لو كان بمصرعهم ولا يمنون عليك بإيمانهم و ثباتهم ، فاللهم اجعل فيهم فرجَك و فرحهم و نصرَك و عزتَهم و انقشاعَ الكرب و نزولَ الغيث و النجاةَ من البلاء 💕

رمضان كريم 💕