Physiology 435 team

PHOTO TRANSDUCTION IN LIGHT & THE DARK

Objectives:

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

Done by:

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Color index: Important - Further explanation - Doctors Notes - Numbers.

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*Please check out this link before viewing the file to know if there are any additions or changes.

Visual Receptors / photoreceptors (Rods and Cones)

Rods	Cones
abundant in the **periphery** of the retina	abundant in & around **fovea**
best for **low light** (dim light) conditions (night vision/scotopic vision)	best for **bright light** conditions (photopic vision)
see **black/white and shades of gray**	see **all colors**

طريقة للحفظ .. اول شي لما نقول Cone نشوف اول حرف فيها اللي هو (C) نتذكر
- Color واكيد ماراح نشوف الالوان الا اذا كان فيه ضوء
- Centre (fovea centralis)

Shape of rods & cones (receptors of vision)

❖ Outer segment (modified cilia)

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

In cones it is conical, small and contain 3 types of rhodopsin in small amount.

In rods it is big, rod like and contain one type of rhodopsin, which composes 90% of rods' protein.

* Rhodopsin is a protein "opsin" which binds to the aldehyde form of vit A "retinal". Vit A is obtained from dietary beta-carotene and stored in pigment cell layer of retina.

2. There are Na channels in the outer segment, which allow Na to enter the photoreceptors.

الريسيبتور منقسمة الى جزئين (outer) و (inner) وفيه جزء يربط الاوتر بالانر اسمه **ciliary stalk** .. لما نتكلم عن الاوتر فهي تتكون من صبغات حساسه للضوء اللي هي rhodopsin << الاسم مرره مهم . على ان الكونز اصغر حجم الا انها تحتوي ع ٣ انواع من الرودوبسين .

❖ Inner segment

a. full of **mitochondria** (source of energy for Na-K pump), it is thick in cones.
b. There is **Na-K pump** in inner segment

The inner and outer segments are connected by a ciliary stalk through which the **photosensitive compounds "rhodopsin" travel from the inner segment (where they are manufactured) to the outer segment of the rods and cones (where they are used)** .

Convergence

low convergence	high convergence
in cones	In rods
each foveal cone synapse with →**one** bipolar cell →**one** ganglion cell →**single** optic nerve fiber	several rods about 300 synapse with **one** bipolar cell & one ganglion cell & one optic nerve fiber
Value of low convergence "advantage" increases **visual acuity** → integrated information from **small** area of retina	**Value of high convergence** "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** decreases **visual acuity, acuity** = integrated information from large area of retina
3- 120 million rod & 6 million cone converge on 1.2 million optic nerve fibers , (126 million receptor on 1.2 million nerve fiber) so convergence is 105 receptor : 1 fiber. ترا هذا قالت الدكتوره مو معنا بس حطته للتوضيح	

Genesis of photoreceptor potential

- **Rods & cones** potentials are **graded, local potential (generator potential)** (summated potential, just like any receptor in the body) propagated as A.P in ganglion cells.
  الجينيراتور بوتنشال هذي زي اللي البداية AP بس ماراح يبدأ AP الا اذا وصل الى threshold
- **Ganglion cell** action potential **(all or none A.P/ not graded)** 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 .

Photosensitive compound (rhodopsin)

Rhodopsin = Opsin protein + retinal [retinene 1 = aldehyde form of Vit A]

المعادله مرره مهمه : الريدوبسين يتكون من:
1- بروتين اسمه في الكونز Opsin ، بالرودز يتغير اسمه الى scotopsin ، البروتين نفسه بس التسميه غير.
2- الشي الثاني اللي يتكون منه هو فايتامين اي بس بصورة الدهايد اسمه ريتينال

cones	Rods

In cones rhodopsin (iodopsine) formed of 1. **Opsin protein** 2. **retinal** (retinene 1 = aldehyde form of Vit A)	In Rods, rhodopsin, is formed of 1. **Scotopsin protein (opsin)** 2. **retinal** (retinene 1 = aldhyde form of Vit A) = **visual purple** (Rhodopsin of the rods most strongly absorbs **green-blue light** and, therefore, appears reddish-purple, so called "visual purple")
There are 3 types of rhodopsin in cones (**photopsine I,II,III**) each respond to a certain **wavelength** of light for color vision	• It forms 90% of rods protein, stored in **disks** of rods at outer segment • **At dark** rhodopsin is in **11-cisretinal form (inactive,** but light sensitive form) which increase sensitivity of rods to light.

Asrar

ELECTROPHYSIOLOGY OF VISION (PHOTOTRANSDUCTION[1])

Visual Phototransduction (Duration 0:51)

طيب قبل ما نتعمق في الفوتوترانزدكشن خل نوضح بعض المعلومات:

- الحين عندنا في الريتنا نوعين من الفوتوريسبتورز اللي هم الرودز والكونز وكل واحد فيهم عنده ١- جزء خارجي يحتوي على membranous disk containing light sensitive photopigment و جزء داخلي يحتوي على cell nucleus and give rise to synaptic terminals that contact bipolar and horizontal cells
- الفوتوترانزدكشن هو العملية اللي تقوم فيها الخلية بامتصاص الضوء وتكَوّن له استجابة، غالبا الاستجابة تكون تغير في كمية الترانميترز التي أُطلقت إلى ال target neuron
- يوجد photopigment تغطي الجزء الخارجي من ال membranous disk . في الرودز (rods)، الفوتوبيقمنت اسمها rhodopsin . ال opsin يشكل تجويف خلاله منطقة امتصاص الضوء من الفوتوبيقمنت تقع * المنطقة اسمها *retinal
- ال retinal هنا توجد في تركيب يسمى cisretinal-11 ، سيس تعني ذرتين هيدروجين توجد في الجانب نفسه في رابطة ثنائية ، عندما تقوم الريتنال بامتصاص فوتون من الضوء عنصر من الرابطة الثنائية ينفصل مؤديا الى دوران حول الرابطة فتتحول السيس الى ترانز ! (طبعا ال 11- cis- retinal هي الاناكتف فورم من الرودوبسين)
- التغير في ال rhodopsin يؤدي الى حدوث سلسة من الاحداث في الخلية ـ> المكون التالي من السلسة هو ال trimeric G protein الذي يرتبط ب GDP عندما يكون inactive state

- then the altered rhodopsin molecular activates transducin , allowing it to exchange its GDP for GTP → alpha subunit of transducin activates phosphodiesterase in the disk membrane → phosphodiesterase hydrolyzed cGMP →وبكذا راح يقل التركيز لل cGMP في الجزء الخارجي

- وكل ما قل تركيز ال cGMP هالمركب يرتبط ب رابطة ايونية مفتوحة في غشاء القسم الخارجي

- OFF-center bipolar cell for Rods cells (يعني OFF CENTER يرتبط ب RODS, which are on the periphery)
- ON-center bipolar cell for cones (و ON CENTER يرتبط ب CONES which are in fovea centralis)
- So in the dark, stimulation of photoreceptor (Rods) will Depolarize the OFF Center and Hyperpolarize (Inhibit)[2] the ON Center
  And in the light, stimulation of photoreceptor (cones) will depolarize the ON Center an Hyperpolarize (Inhibit) the OFF Center

الحين راح نقارن تفاعل قنوات الايونات في اللايت والدارك

A-At Dark (scotopic vision[3], dim-light vision):

In dark, sodium channels are open and the influx of positively charged sodium and calcium ions has a depolarizing effect on the cell and The inward

[1] Visual phototransduction is the sensory transduction of the visual system. It is a process by which light is converted into electrical signals in the rod cells, cone cells and photosensitive ganglion cells of the retina of the eye.

[2] This Inhibition is called lateral inhibition and it's for the focus of the vision (contrast)
based on our doctor he said that the mechanism is uncertain .

[3] relating to or denoting vision in dim light, believed to involve chiefly the rods of the retina. الرؤية الظلامية = dim light vision هي نفسها

current in the dark is opposed by positively charged potassium ions flowing out through potassium channels * a hyperpolarizing influence* ⟶ the combined result of these ion flows is depolarization of photoreceptors in the dark.
The depolarized state of the membrane triggers continual transmitter release from the synaptic terminals of the photoreceptor cells.
Absorption of light reduces the concentration of cGMP in the outer segment, leading to the closure of the cGMP- gated channels. As a result, positive charge (carried by K+) flows out of the cell more rapidly than positive charge (carried by NA+ and Ca2+) flows in. The cell becomes hyperpolarized and decrease its release of transmitter.

1-Rhodopsin in 11-cis-retinal:

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

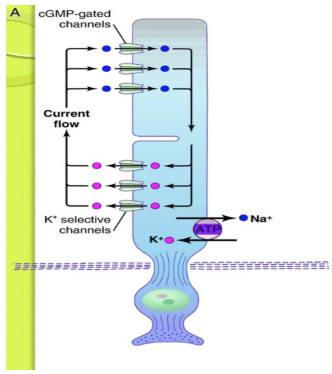
* highly sensitive to the light عشان كذا الرودز * الرودوبسين لما يكون في الاناكتف فورم التي هو ١١-سيسريتنال راح يزود تفاعل الرودز مع الضوء : بكل بساطة

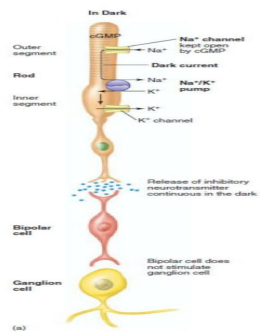
2- (5 –GMP)[4] in the c-GMP[5] form:

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

3- Dark current (Na current):

- At the inner segment, Na is 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 in response (off-center bipolar cells) ⟶ depolarize 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 in dark.
  - its inactivation keeps Na channels open by keeping cGMP & Na current occurs

YouTube **Phototransduction: Dark Phase**(Duration 04:55)

B- Incident light (PHOTOPIC VISION[6]) :

- Light- ⟶ Conformational change of photopigment retinene-1 in rhodopsin, a process

[4] 5-Guanosine MonoPhosphate
[5] Cyclic Guanosine MonoPhosphate
[6] Photopic vision is the vision of the eye under well-lit conditions (luminance level 10 to 108 cd/m²). In humans and many other animals, photopic vision allows color perception, mediated by cone cells, and a significantly higher visual acuity and temporal resolution than available with scotopic vision.

known as bleaching (11-cis-retinal form changed to ⟶ metarhodopsin I ⟶ all-trans isomer called metarhodopsin II which is an active rhodopsin) ⟶ Activation of G-protein (transducin) ⟶ activation of phosphodiesterase enzyme ⟶ conversion of c-GMP to 5-GMP ⟶

زي ما ذكرنا سابقا ان ال سيس تعني ذرتين هيدروجين توجد في الجانب نفسه في رابطة ثنائية ، عندما تقوم الريتنال بامتصاص فوتون من الضوء ـ> عنصر من الرابطة الثنائية ينفصل مؤديا الى دوران حول الرابطة فتتحول السيس الى ترانز ،، عندما تصبح ترانز يصبح اسمها metarhodopsin II والذي يعتبر النموذج النشط من ال رودوبسين بالتالي سيقوم بتنشيط ال جي بروتين او ما يسمى بالترانزدوسين الذي بدوره سينشط انزيم الفوسفوديستراز phosphodiesterase واخيرا سيتحول ال cGMP الى 5GMP منتجًا :

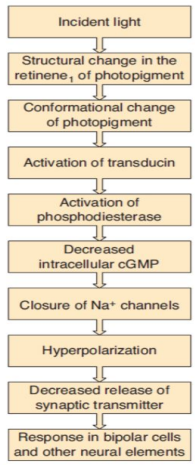


FIGURE 12–15 Sequence of events involved in phototransduction in rods and cones.

1. Decreased intracellular c-GMP ⟶ closure of Na channels in outer segment .

2. 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.
3. Hyperpolarization ⟶ Decreased release of synaptic transmitter ⟶ Response in bipolar cells (hyperpolarization) (off-center bipolar cells get hyperpolarized) ⟶ this causes decreased release of glutamate ⟶ Generator potential "ضئيل" in amacrine cells[7] and ganglion cells (depolarize) ⟶ AP ⟶ optic nerve ⟶ optic pathway.

- **NB:**

- these reactions occur in both rods & cones but in rods they occur at low illumination as in dim-light & in cones at high illumination.
- in cones 4 times faster

❖ In The Light[8] :

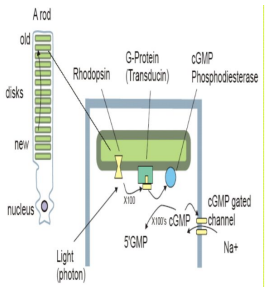
★ Additional reading from (Guyton 12th edition Page 613)

When light hits the photoreceptor (e.g., rod cell), the light-absorbing retinal portion of rhodopsin is activated. This stimulates transducin, a G-protein, which then activates cGMP phosphodiesterase. This enzyme catalyzes the degradation of cGMP into 5 -GMP. The reduction in cGMP then causes closure of the sodium channels, which, in turn, causes hyperpolarization of the photoreceptor. inside the membrane, and the greater the amount of light energy striking the rod, the greater the electronegativity becomes—that is, the greater is the degree of hyperpolarization. At maximum light intensity, the membrane potential approaches −70 to −80 millivolts, which is near the equilibrium potential for potassium ions across the membrane.

[7] The amacrine cells receive input from different combinations of on-center and off-center bipolar cells. Thus, the receptive fields of the amacrine cells are mixtures of on-center and off-center patterns.

[8] Here the light is just the same as the incidence light don't worry

- Light exposure will lead to closure of the cGMP gated NA+ channels
- However, the inner segment still is continually pumping sodium from inside the rod to the outside
- Despite potassium ions being pumped to the inside of the cell
- Potassium ions still leak out of the cell through non gated potassium channels in the inner segment of the rod (selective permeability of K along its concentration gradient)
- Therefore with loss of positively charged NA+ and K+ this creates a negative potential on the inside of the entire cell of about -70 to -80 MV ➞with the cell hyperpolarized at about -70 to -80 MV glutamate release is greatly inhibited.



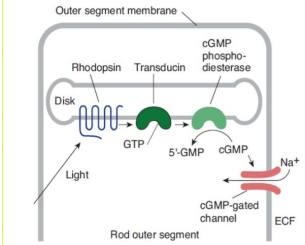
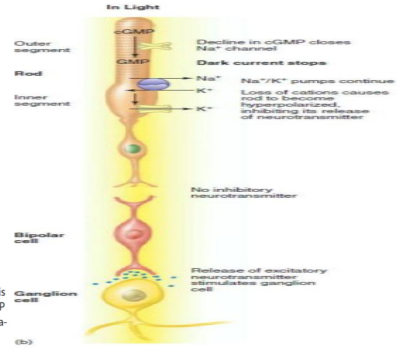
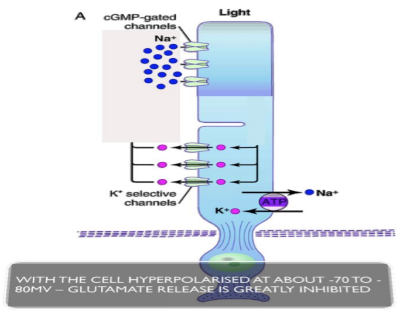


FIGURE 12–14 Initial steps in phototransduction in rods. Light activates rhodopsin, which activates transducin to bind GTP. This activates phosphodiesterase, which catalyzes the conversion of cGMP to 5'-GMP. The resulting decrease in the cytoplasmic cGMP concentration causes cGMP-gated ion channels to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



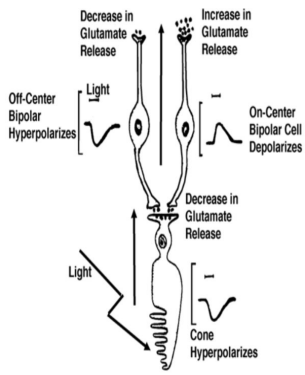


[Phototransduction: Light Phase](#) (Duration 3:17)

❖ We have 10 types of cones bipolar cells & one type of rod bipolar cell

In dark	In light
depolarize receptors ➞ increase glutamate at photoreceptor ends ➞ 1-hyperpolarize ON-center bipolar cells 2-depolarize OFF-center bipolar cells (active)	hyperpolarize the receptors ➞ decrease glutamate release at photoreceptor ends ➞ 1- depolarize ON-center bipolar cells 2- hyperpolarize OFF-center bipolar cells (inactive)

- **N.B:**
  - (ON) center bipolar (synaptic connection with center photoreceptors = cones, so light depolarize them to see in bright light)
  - (OFF) center bipolar (synaptic connection with peripheral photoreceptors= rods , so dark depolarize them to see in dark)
  - All these help to sharpen signal from rods in dark and from cones in light.



Synaptic mediators in retina:

Various types of synaptic transmitters found in retina are: Acetylcholine (secreted only by amacrine cells of retina), glutamate, GABA, serotonin, dopamine, glycine, substance P, TRH, GnRH, somatomedin, enkephalins, beta endorphin, CCK, VIP, glucagons and neurotensin.

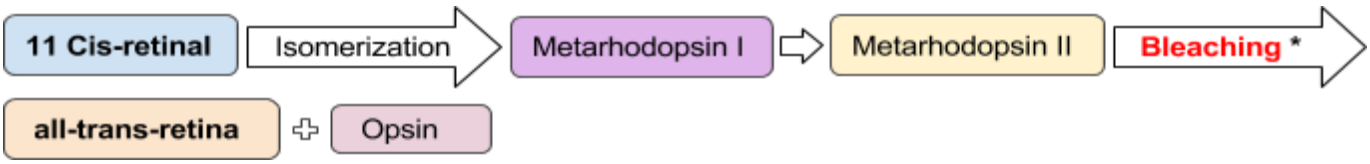
- Ach, glutamate (the main neurotransmitter) , dopamine, serotonin,GABA, substance P, somatomedin, VIP, enkephalins, glucagons & neurotensin.

In dark	In light
depolarization of receptors ⟶ glutamate is continuously (steadily) released by depolarization of rods depolarize bipolar cell (OFF-center) ⟶ generator potential ⟶ AP in ganglion cells	hyperpolarization of the receptors ⟶ decrease glutamate release ⟶ hyperpolarize bipolar cells (OFF-center) & gradual depolarize (on –center cells) ⟶ depolarize amacrine cell ⟶ generator potential ⟶ AP in ganglion cells.

VISUAL CYCLE (bleaching & regeneration)

Retinal is produced in the retina from Vitamin A, from dietary beta-carotene.

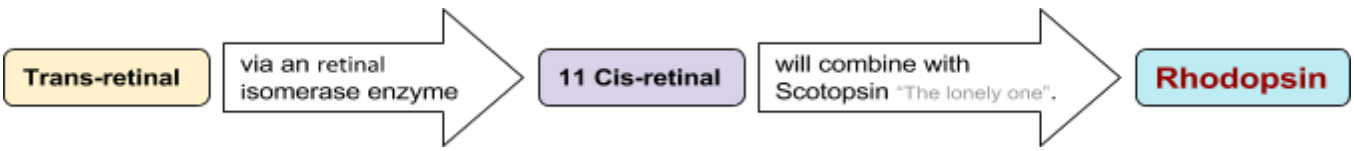
❖ At light:



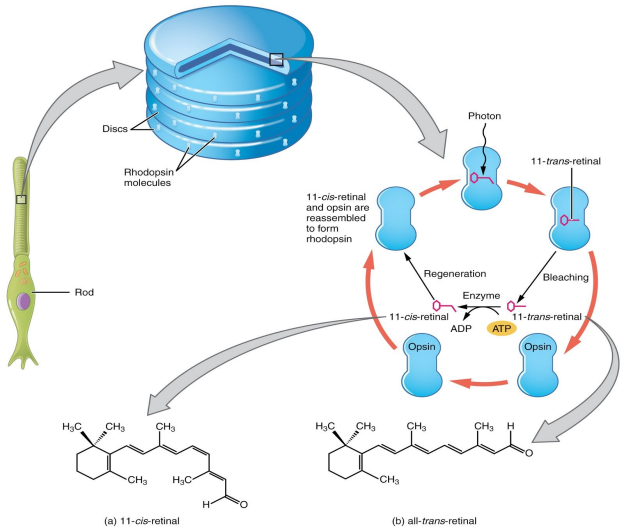
* conformational change.

- All trans-retinal separate from **opsin** by light and opsin remains alone "lonely".
- Isomerization induced by **light**.

❖ At dark:

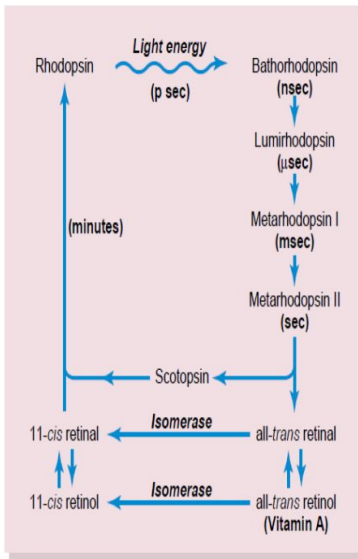


- Trans-retinal is enzymatically re-converted to the 11 cis-Retinal form via retinal isomerase enzyme.
- Remember that scotopsin (other name of opsin) is present alone having been removed PREVIOUSLY from rhodopsin at light, it immediately will combine again with 11 cis-Retinal to "regenerate" (form) new Rhodopsin.
- At dark: 11 cis-Retinal in rods + scotopsin ⟶ **rhodopsin Regeneration**
- rhodopsin is Stored in the desks of rods for time of need



RHODOPSIN IN THE DARK AND LIGHT (DURATION 0:33)

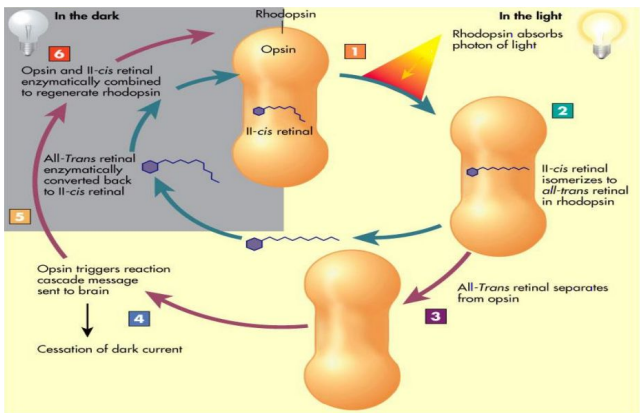
Scotopsin retinal visual cycle:



- The amount of Rhodopsin in the receptors therefore varies **inversely** with the incident light level. (decreases with light, regenerate in dark)
  الرودوبسين يتناسب عكسيًا مع كمية الضوء المتوفرة لأنه مع وجود الضوء سيتكسر (degenerate).
- 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. It is then stored in the pigment cell layer of the retina.

Photochemistry of Color Vision by the Cones : •Photopsins Retinal Visual Cycle

- The cones are about 30 to 300 times less sensitive than rods to light.



❖ NYCTALOPIA[9]: (night blindness)

- **What is it ?**

9 العشى الليلي.

Vitamin A deficiency cause rods, cones and retinal degeneration and loss of rods, which are responsible for night vision. Vitamin A is the **main source** of retinal of rhodopsin.

اذا أهمل و لم يعالج سوف يتسبب في تدمر شبكية العين و مستقبلات الضوء, ويعجز المريض عن الرؤية في الظلام ثم حتى في النور مع تقدم الحالة.

- **Treatment :** Intravenous vitamin A if receptors are well. It is not given orally because it breaks down in the GIT. IV also induces a faster effect.

Adaption

Dark adaptation

When a person **moves from lighted** environment **to a dimly**[10] **lighted** environment, the retina becomes more sensitive to light (Increased sensitivity of the photoreceptors when vision shifts from bright to dim light)
and the person will see at dark (accustomed to dark) in about **20 min**. (only gross features but no details or colors).

- Rhodopsin in darkness is essential for depolarization of rods to see in dark & for dark adaptation.
- The mechanism of dark adaptation: **increase Rhodopsin regeneration** .

#Dark adaptation has 2 components:

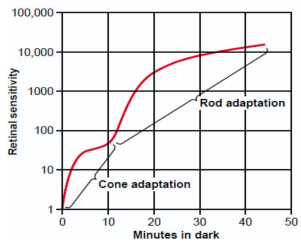
1. Rapid: (about **5 min**)

- Drop in visual threshold.
- Fast dark adaptation of cones, only in fovea
- Half of the cone rhodopsin regenerate in only 90 seconds.

2. Less rapid: (till **20 min**)

- drop in visual threshold stimulates dark adaptation of rods in the peripheral retina.
- sensitivity of rods to light increase 10 folds in 1 min.
- rods increase their sensitivity to light by convergence 300:1 ganglion cell , so summation at ganglion cells potential will increase sensitivity to light.

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



Light adaptation

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

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

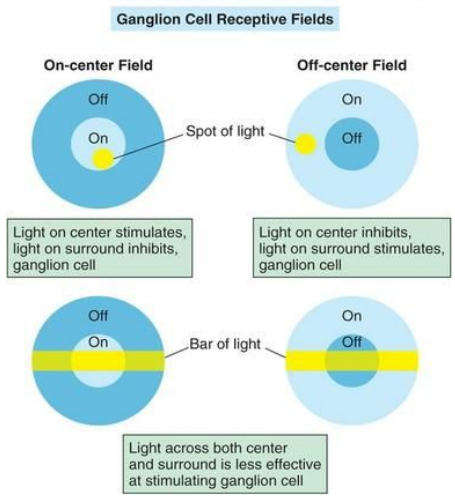
A Light wavelength of the red stimulate the cones & stimulates rods to some extent, so red goggles for rods act as dim light, so with it rods start adapting to darkness & form large amounts of rhodopsin while the person in bright light & when person enter dark places he can see well & not remain 20 minutes.

Retinal Ganglion Cells and Their Respective Fields

W-cells	X-cells	Y-cells
Sensitive for **detecting directional movement in the field of vision**, (important for much of our rod vision under dark conditions)	Transmission of the Visual Image and color → **Color Vision** (probably important for cones)	Transmit instantaneous & rapid Changes in the Visual Image , **either rapid movement or rapid change in light intensity** - للتحركات السريعة

❖ 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. "التجميع"



❖ types of retinal ganglion cells:

★ On-center cells:

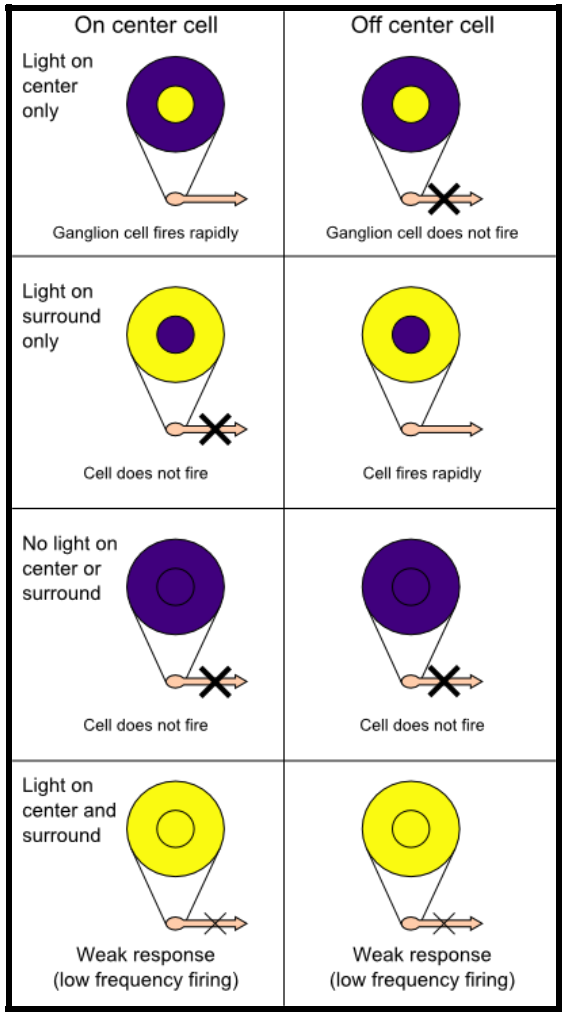
Is stimulated when the **center** of its receptive field is exposed to light, and is inhibited when the **surround** is exposed to light.

- Stimulation of on-center cell's receptive field produces **depolarization** and an increase in the firing of the ganglion cell.
- stimulation of the surround produces a **Hyperpolarization** of on-center and a decrease in the firing of the ganglion cell.

★ Off-center cells:

Is stimulated by activation of the surround and inhibited by stimulation of the center

- stimulation of both the center and surround produces only a mild response (due to mutual inhibition of center and surround).



★ References:

- 435 girls slides and notes.

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