

THE EYE AND THE RETINA

REQUIRED READINGS: Blumenfeld Chapter 11, pp. 460 - 467, the Power Point Presentation and these notes

LEARNING OBJECTIVES: after studying this chapter, students should be able to:

1. Describe the 3 concentric layers of the eye.
2. Know the names, composition and function of the principal retinal cells and layers
3. Describe how light enters the eye and is transformed into action potentials at the photoreceptor level
4. Explain the retinal basis of color perception
5. Explain how visual information is transmitted inside the eye and to the visual pathways

OVERVIEW

Of all the senses, sight is probably the most important for humans; it provides information about the world in which we live as no other sense does. More than 40% of the neurons in the brain process some vision related information.

In this chapter, we will learn about the anatomy of the eye and the retina, the visual transduction and processing of visual information by retinal cells.

Objective # 1

Slide 3 – The eye consists of a central cavity surrounded by 3 concentric layers:

- A dense collagenous connective tissue layer: the fibrous layer or **Corneoscleral layer**
- A loose connective tissue layer very vascularized and containing melanocytes: the vascular layer or **Uvea**
- The neural layer: the **Retina**



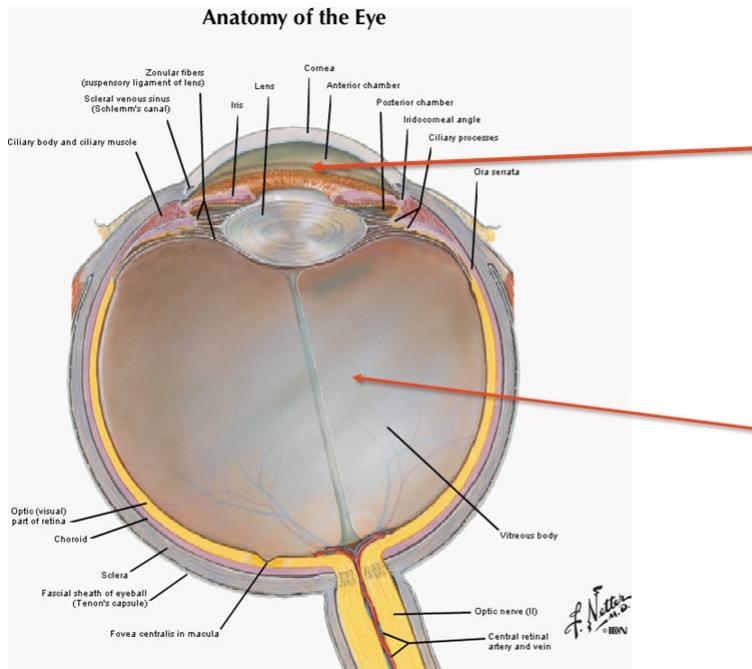
OBJ. # 1

The Eye

The eye consists of 3 complete layers surrounding a central space



Slide 4 – Diagram of the eye showing the eye anatomy. The central cavity is divided in 2 by the presence of the lens, which is suspended by radiating connective tissue fibers known as the **suspensory ligaments of the lens or zonule fibers of Zinn**. Anterior to the lens, the cavity is incompletely divided by the presence of the iris into the anterior chamber and posterior chamber, anteriorly and posteriorly to the iris respectively. Posterior to the lens, the vitreous body contains a gelatinous structure: the **vitreous humor**.



OBJ. # 1

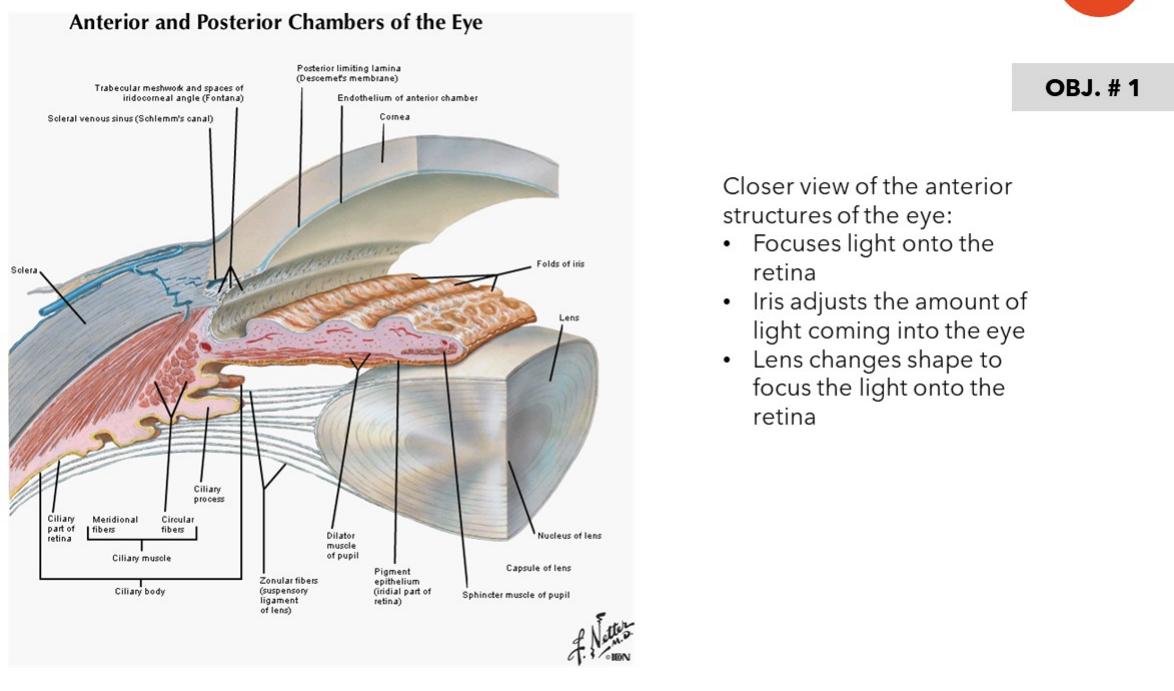
Anterior Chamber – covered in detail by Dr. Feinberg

Posterior Chamber:

- Everything behind the lens
- Filled with **vitreous humor**, a gelatinous structure



Slide 5 – A detailed view of the anterior and posterior chambers. Notice the presence of the constrictor and dilator pupillary muscles (smooth muscles) contained inside the iris and the ciliary muscles contained in the ciliary body - an anterior extension of the uveal layer. This detailed view allows us to see the posterior chamber where the aqueous humor is formed and the anterior chamber where it is reabsorbed and returns to the venous blood through the canal of Schlemm in the irido-corneal angle.



Objective # 2

Slide 6 – An image of a normal retina viewed through an ophthalmoscope. The centrally located **fovea centralis** is visible; this is the point of maximal visual acuity. The visual axis of the eye passes through the fovea. About 2.5 mm medial to it, the **optic disc** or **optic papilla** is visible; it is called the blind spot because there are no photoreceptors there, only axons of the retinal ganglion cells. Arteries and veins go through this place to enter/exit the eye.

OBJ. # 2

Macula and Fovea Centralis:

- Central vision - point of maximal visual acuity.
- Area of highest density of photo receptors

Optic Disc or Papilla:

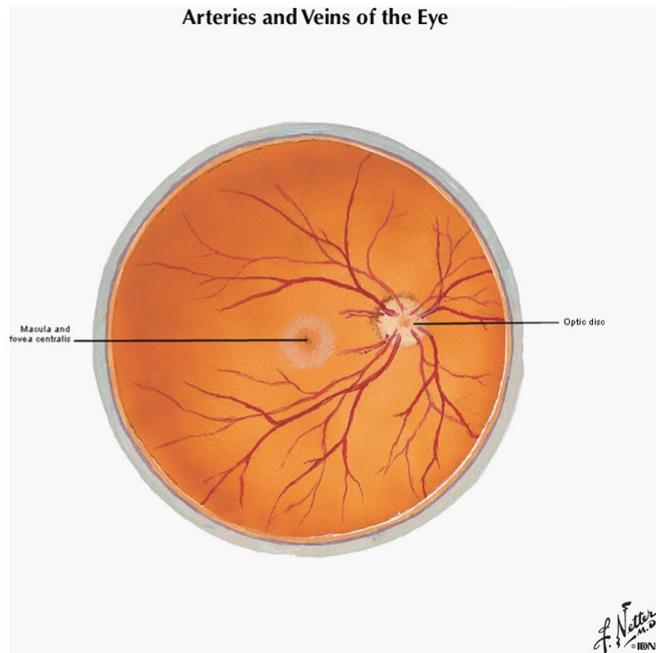
- Structure through which the axons of the retinal ganglion cells and vasculature of the retina enter the eye
- **Continuous with the CNS**



Clinical Pearl:

- **Increased intracranial pressure** in the CNS is transmitted to the eye via the optic nerve and is observed as a swelling of the optic disc called **papilledema**

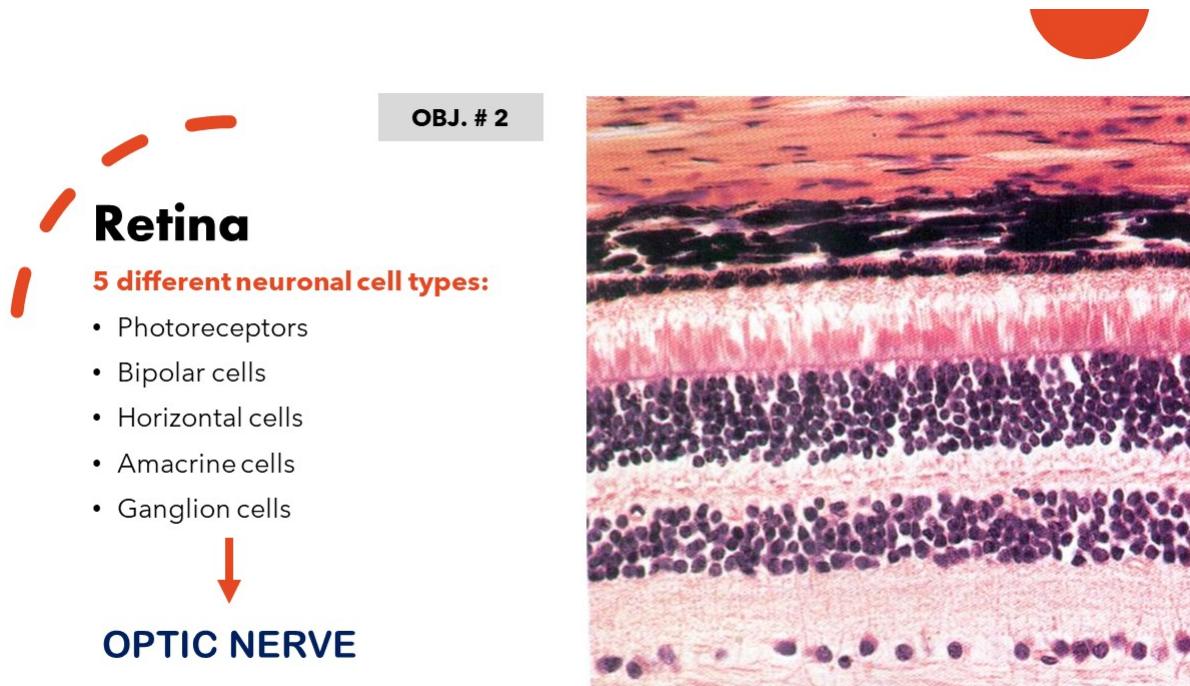
Arteries and Veins of the Eye



Slide 7 - Histological section of the retina that includes all the cells and retinal layers. The retina contains 5 different cell types. The main retinal neurons are: **the photoreceptor cells, the bipolar cells and the ganglion cells.** **Horizontal and amacrine cells** are inhibitory interneurons. The ganglion cells form the optic nerve which takes the final retinal output to the brain.

Slide 8 & 9 – The retinal cells are organized in several layers. From outer to inner these layers are:

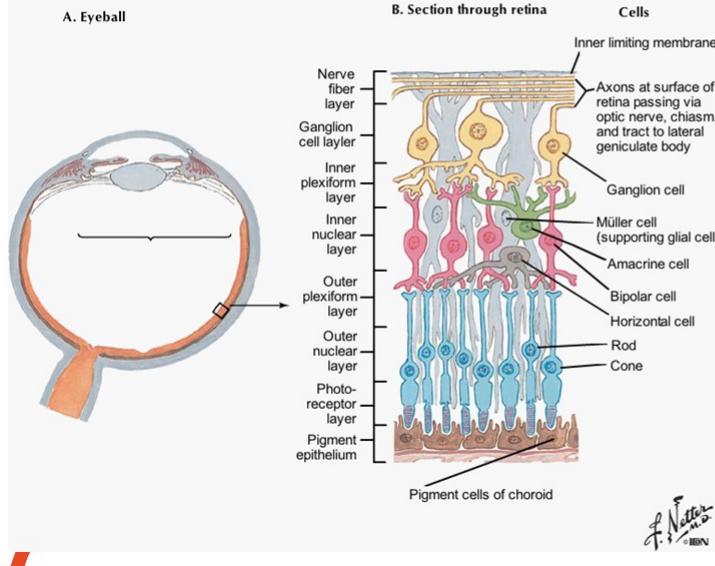
- **The photoreceptor layer** – comprises the outer and inner segment of the photoreceptors. The outer segment contains the pigment molecules that capture light and the inner segment contains the mitochondria that provide energy for the phototransduction process to occur.
- **The outer nuclear layer** – contains the nuclei of the photoreceptor cells
- **The outer plexiform layer** – a synaptic layer where the axons of photoreceptors synapse with dendrites of a bipolar neuron. The horizontal cells in this layer provide lateral inhibition to these synapses
- **The inner nuclear layer** – In this layer, we find the cell bodies of bipolar cells, amacrine and horizontal cells.
- **The inner plexiform layer** – This is a synaptic layer. The axons of bipolar cells synapse with dendrites of ganglion cells. The amacrine cells in this layer have an inhibitory effect on these synapses
- **The ganglion cell layer** – Ganglion cells are located here
- **Optic nerve layer** – The ganglion cell axons join together at the optic disc as the optic nerve



The **retinal pigment epithelium (RPE)** is the dark epithelial layer located outer to the photoreceptor layer. It performs very important functions related to the survival of the photoreceptor cells. Among these functions are: providing nutritional and mechanical support to the photoreceptor layer. In fact the tips of the photoreceptors are embedded in these pigmented cells. These cells have phagocytic activity; they phagocytose the old membranous disks that shed off of the photoreceptor cells. They absorb scattered light that is not captured by the photoreceptors, avoiding glare inside the eye. They also recycle the photopigment molecule. The retinal pigment epithelium is sometimes considered a part of the retina but embryologically it derives from the outer layer of the primitive optic cup, while the retina itself derives from the inner layer of the optic cup.

The Retina and the Photoreceptors

OBJ. # 2

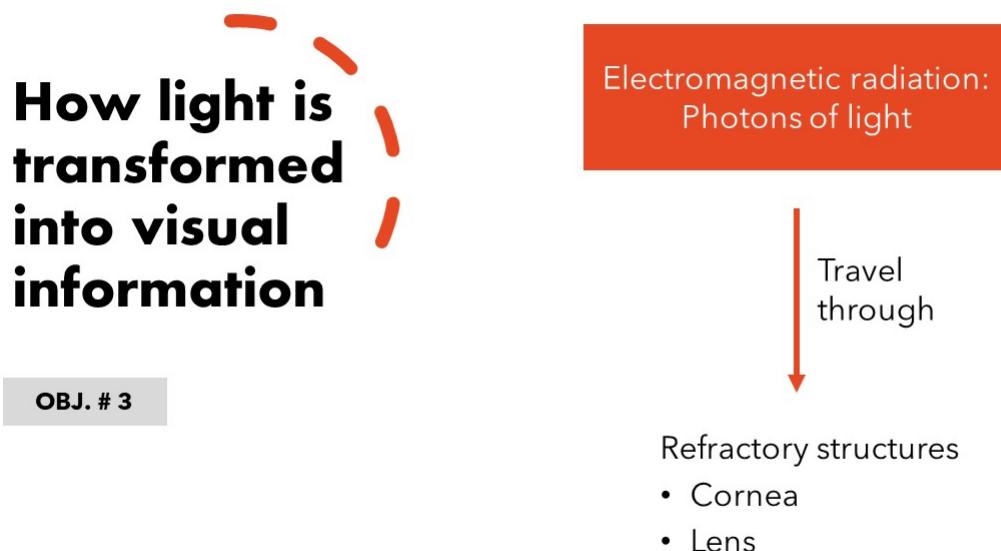


May seem a little backwards:

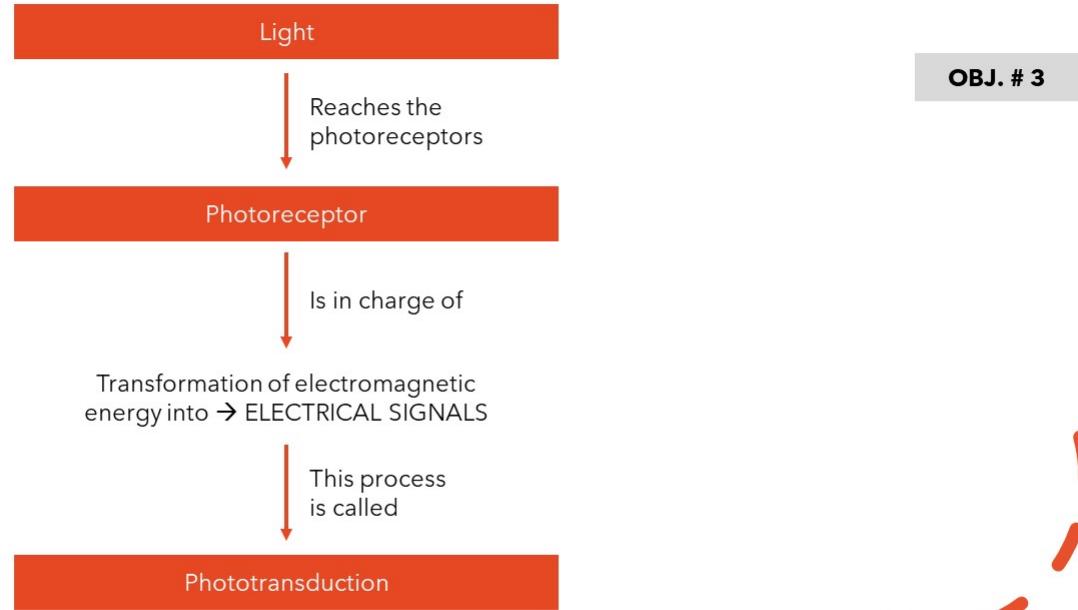
- The photo receptor cells are buried in the most posterior part of the retinal layer in the pigment cells of the choroid.
- **Light physically travels through the cells of the retinal layers but does not interact with any of them until it reaches the photoreceptor layer.**

Objective # 3

Slide 10 – Let's see now how electromagnetic radiation in the form of photons of light will finally produce a visual perception in the visual cortex. The electromagnetic radiation that hits the objects in our environment could be either absorbed by these objects or reflected by them. The reflected light enters our eyes going through the eye refractory structures. The ones with more refractory power are the cornea and the lens.



Slide 11 – Light travels across the retinal cells to get to the photoreceptor layer, the most outer retinal layer, where it is captured by the outer photoreceptor segments where light is transformed into electrical signals, the only language the brain can understand. This process is known as **phototransduction**.



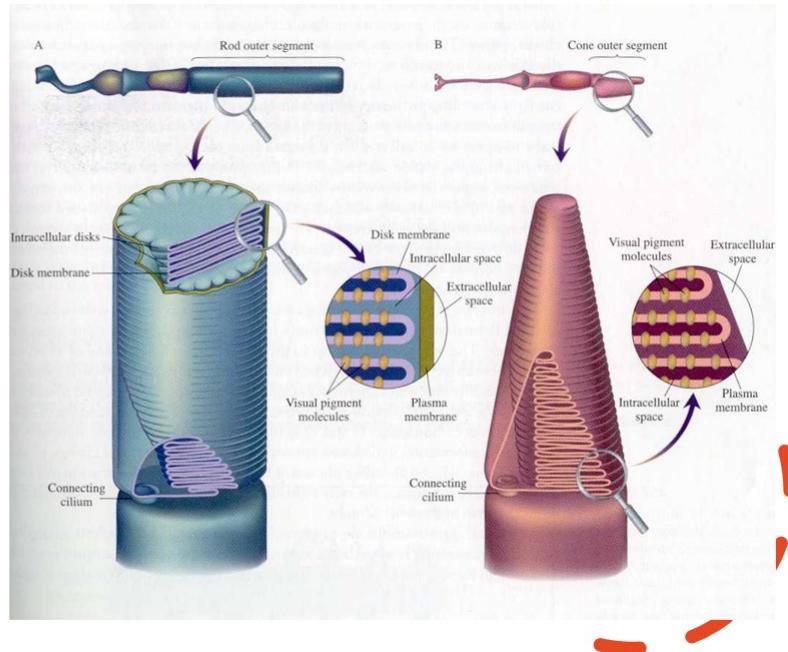
Slide 12 – There are 2 types of photoreceptor cells in the retina: rods and cones. The image shows the shape of the outer photoreceptor segments, what give these neurons their name. The outer segments are formed by stacks of membranous discs. Attached to the discs membranes there are many transmembrane proteins. These proteins are the photopigment that will be used for the capture of photons of light. These photopigment molecules are call rhodopsin. We will come back to them soon.

OBJ. # 3

2 Types:

- Rods
- Cones

Photoreceptors



Slide 13 – There are profound differences between the rods and cones. As you can see in the diagram of slide 12, rods have much longer outer segments than cones and for this reason they have many more photopigment molecules attached and then more opportunity to capture light. Because of this, rods are much more sensitive to light than cones. It means that when exposed to bright light they saturate easily, and they are better adapted for night conditions or scotopic conditions. Cones are less sensitive to light; they are better adapted for day light conditions and visual acuity. There are 3 different types of cones which capture 3 different wavelengths of light. This allows us to see in color.

OBJ. # 3

Photoreceptors – Functional differences

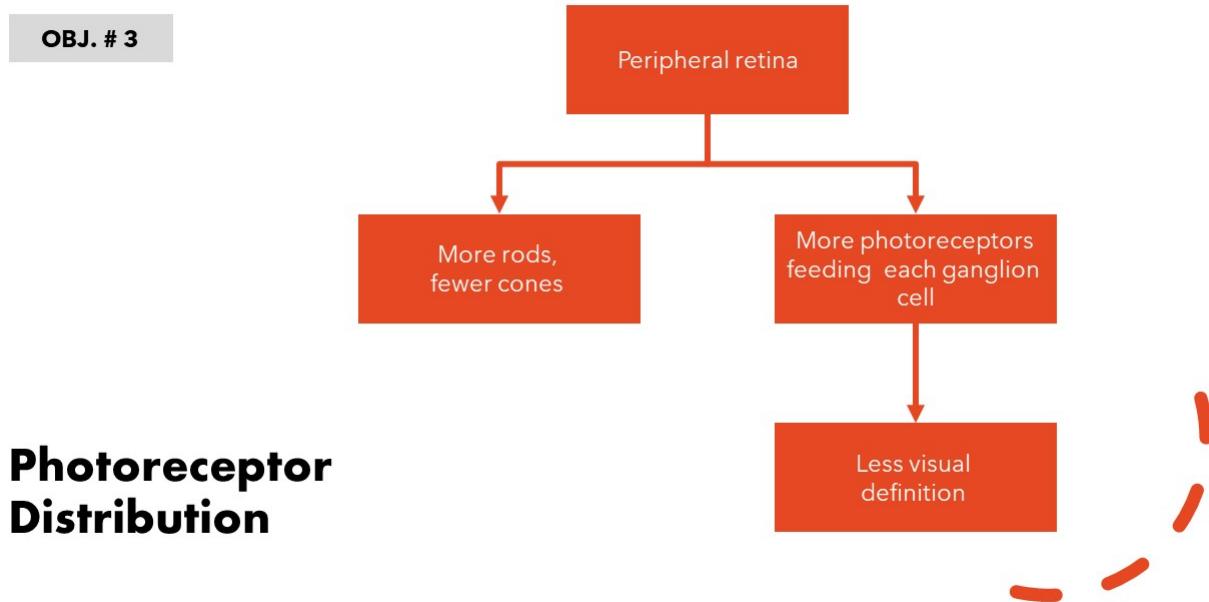
Rods

- Longer outer segment
- 30 times more sensitive to light
- Adapted for night time light conditions - Scotopic conditions

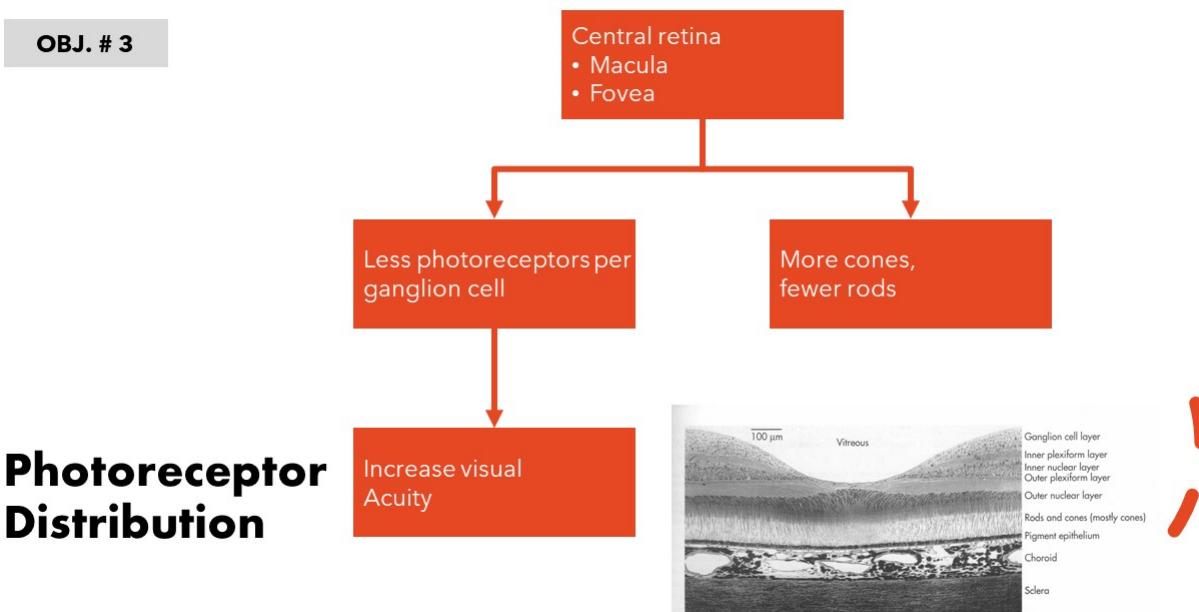
Cones

- Adapted for visual acuity
- Adapted for color vision
- Day time light conditions - PHOTOPIC CONDITIONS

Slide 14 – As we said before, the central retinal area, the fovea is the place for maximal visual acuity. The periphery of the retina provides less visual definition. Rods and cones are not equally represented in the central/peripheral retinal areas. The periphery of the retina has much more rods than cones, so it is better for night vision where color is not that relevant. The relationship between rods and ganglion cells is also important. In the peripheral retina there are many rods projecting information into one ganglion cell. This means large parts of the visual space processed by one ganglion cell which produces less image definition.



Slide 15 - Cones are more abundant in the central retina, particularly at the fovea. The center of the fovea, called the foveola contains almost exclusively cones and this is the place in the retina with maximal visual acuity because there is one to one cone – ganglion cell relationship. The inset image shows how at the foveola the layers of the retina are reclined laterally, increasing the photoreceptor exposure to light which contributes to the increased visual acuity.



Slide 16 – Phototransduction occurs in the outer photoreceptor segment. A photopigment called rhodopsin is attached to the plasma membrane of the membranous disks that form the outer segment. The membranous disks are stacks of plasma membrane as it is shown in the picture. The photopigment consists of a transmembrane protein: the opsin and a chromophore molecule called **retinal**.

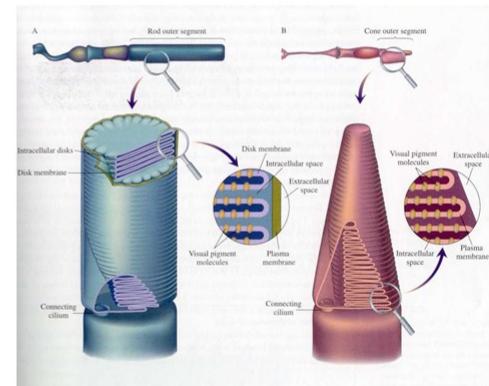
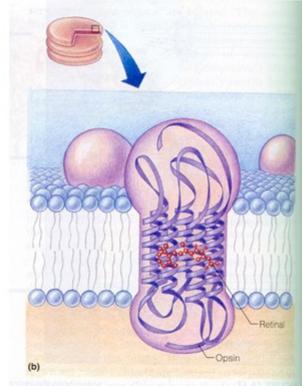


OBJ. # 3

Phototransduction

Occurs in the outer photoreceptor segment

The photopigment involved is called Rhodopsin: It is composed of a protein molecule: the Opsin and a Chromophore molecule: the Retinal



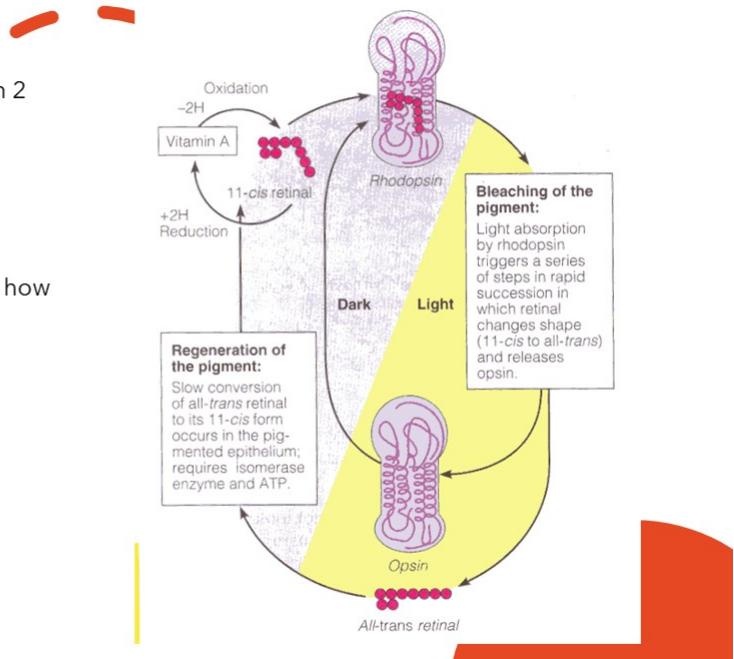
Slide 17 – The retinal molecule, a vitamin A derivative, exists as 2 isoforms in nature: **11-cis** and **all-trans retinal**. In the dark retinal is in its 11-cis isoform and is attached to the opsin molecule as you see in the picture. When 11-cis retinal captures a photon of light, it suffers a conformational change to become all-trans retinal and detaches from the opsin molecule. The all-trans retinal is then captured by the cells of the retinal pigment epithelium and converted back into 11-cis retinal to reenter the cycle.

The Retinal pigment Molecule could be in 2 isoforms:

- 11 -Cis
- All Trans

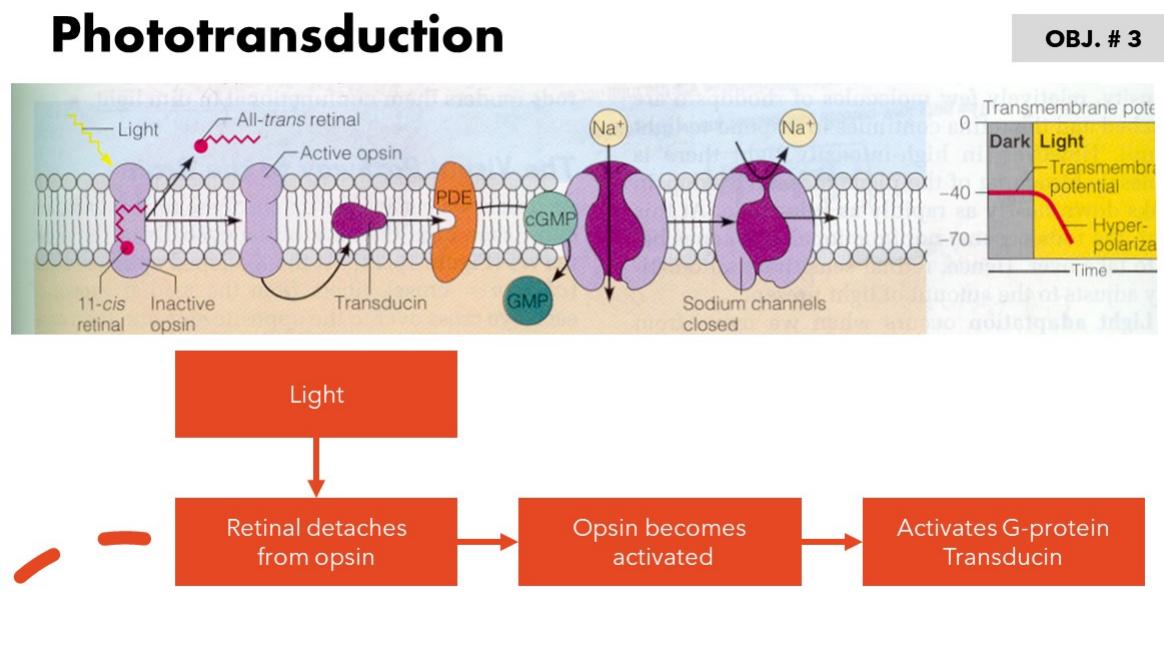
Here is the cycle of light vs. darkness and how Retinal suffers a conformational change

OBJ. # 3



Slide 18 – First, pay close attention to the inset at the top on the right. This small graph represents a recording of the transmembrane potential when the photoreceptor cell goes from being in the dark to suddenly being exposed to light. You see how the membrane potential in the dark was -40 mv and when the cell is exposed to light, the membrane potential becomes -70 mv. This means that photoreceptors are depolarized in the dark while light produces hyperpolarization of these cells. The preferred stimulus for the photoreceptors is not light but darkness!! Let's see if we can explain why.

The upper part of the slide shows a diagram of the plasma membrane of a photoreceptor disk initially in the dark with the rhodopsin molecule attached. When light hits the molecule, 11-cis retinal absorbs the photon of light, goes into the all-trans retinal isoform, and detaches from the opsin. Opson becomes activated and in turn activates a receptor coupled- G protein named transducin.

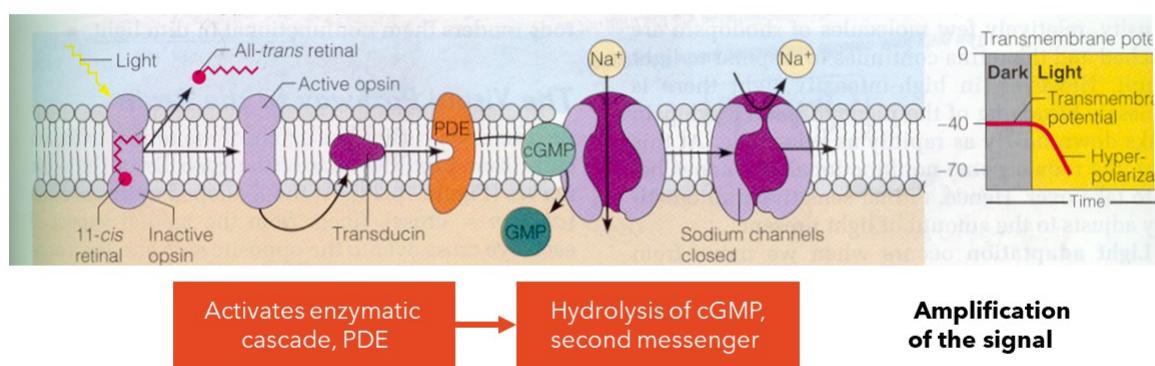


Slide 19 - Transducin activation triggers a sequence of PDE (phosphodiesterase) enzymatic activation. PDE hydrolyzes the second messenger c-GMP which is in the cytosol of the photoreceptor. In the dark c-GMP are attached to Na channels in the disk plasma membrane. When the c-GMP is attached to the Na channel, the channel is open and Na can get inside the cell which accounts for the depolarization of the photoreceptor in the dark. When light comes in and activation of PDE occur, hydrolysis of the cytosolic c-GMP triggers the detachment of the c-GMP from the Na channel. When this happens, the Na channel closes and precludes Na from going into the cell and the cell hyperpolarizes.

This complex process of signal transduction is a mechanism for signal amplification where one single photon of light that is absorbed produces the activation of a large number of G-proteins, an even larger number of PDE activation and the closing of even larger numbers of Na channels leading to hyperpolarization of the photoreceptor.

Phototransduction

OBJ. # 3



Slide 20 – Photoreceptors depolarize in the dark because the Na channels are open and there is a current of Na entering the cell. This is called the dark current of Na. When the receptors depolarize, they release glutamate which triggers the depolarization or hyperpolarization of the next retinal cell: the bipolar cell. There are 2 different types of bipolar cells: some of them depolarize in the presence of glutamate while others hyperpolarize in the presence of glutamate. Remember that this occurs in the dark.



Phototransduction

OBJ. # 3

Dark current



Opening of Na channels

Darkness



Photoreceptor depolarizes



Glutamate is released



Membrane potential - 30 mv

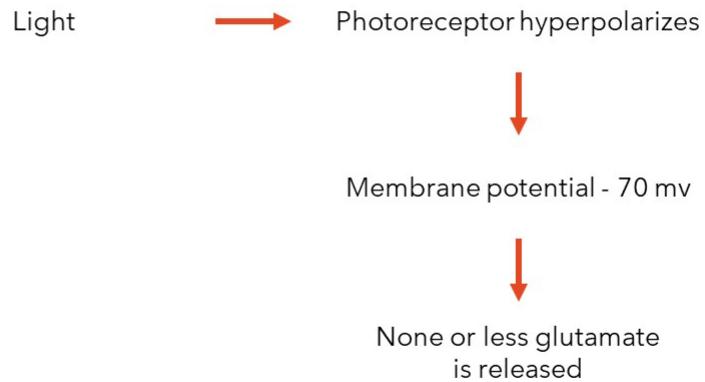


Slide 21 – When a photon of light is absorbed by the pigment molecule, the Na channels close, the photoreceptor hyperpolarizes and no glutamate or less glutamate is released to the bipolar cells. Photoreceptors don't fire action potentials, nor do the other retinal cells except for the ganglion cells. They use receptor potentials to communicate with nearby cells. The amplitude of a receptor potential depends on the amount of neurotransmitter released, which in turn depends on the relative amount of light or darkness that the cell is exposed to at any particular time. This allows for modulation of the signal according to the different lighting environments.



Phototransduction

OBJ. # 3



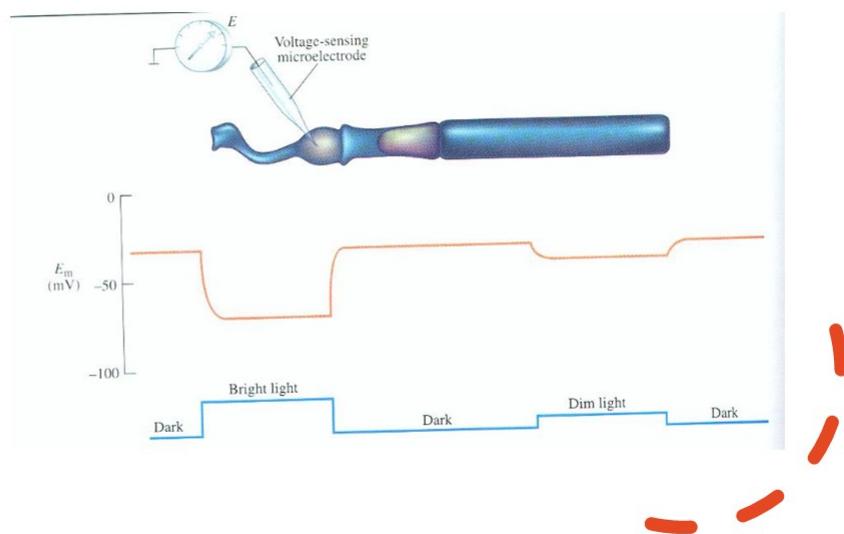
Modulation of the signal



Slide 22 – This slide shows the recording of receptor potentials when a photoreceptor is in the dark or when it is exposed to different light intensities. We see how the hyperpolarization varies with the intensity of light.

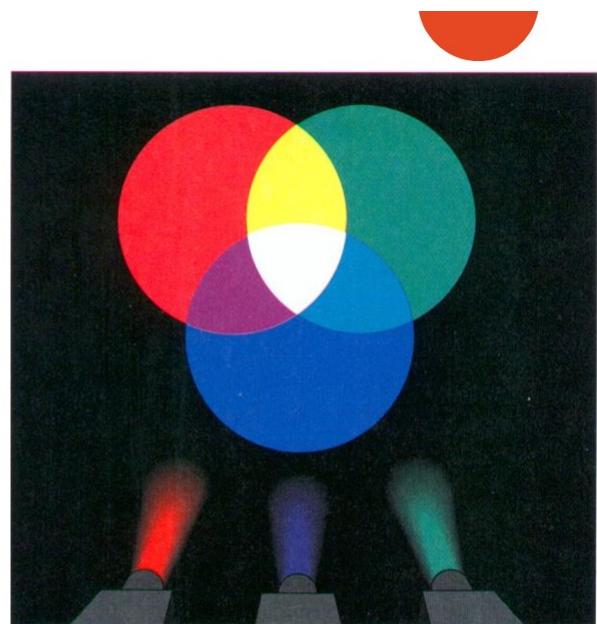
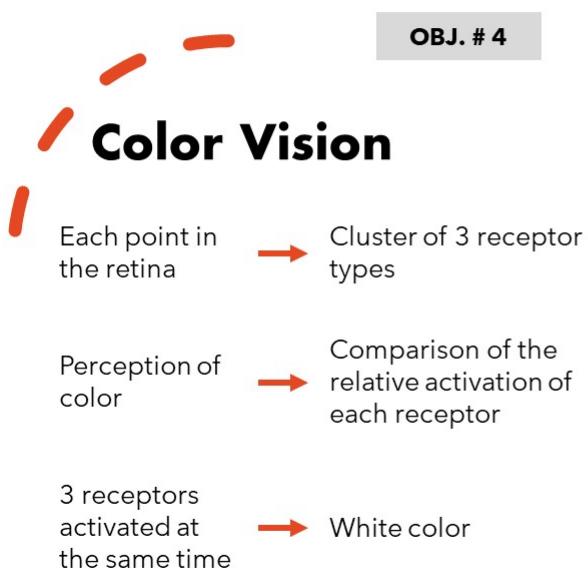
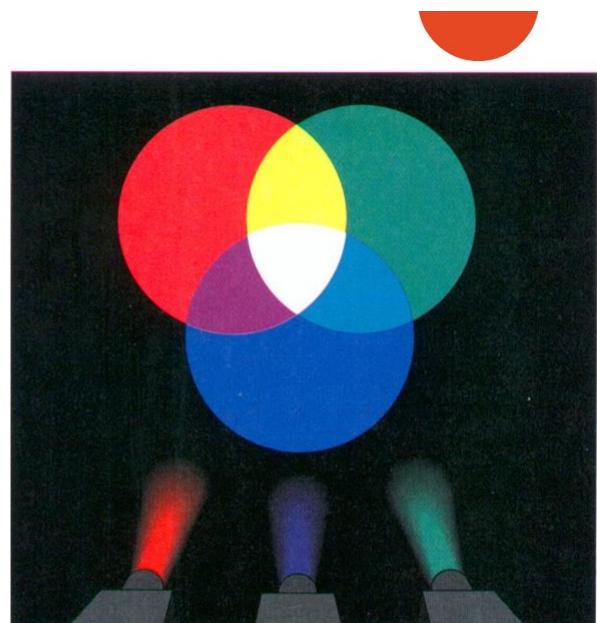
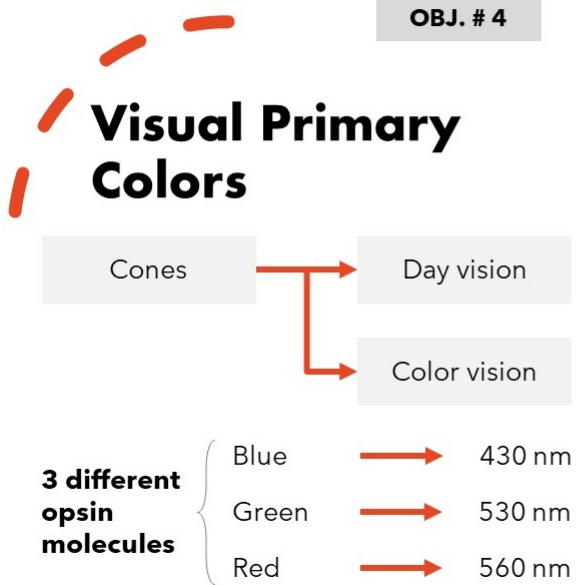
OBJ. # 3

Recording of a photoreceptor firing under different light intensities



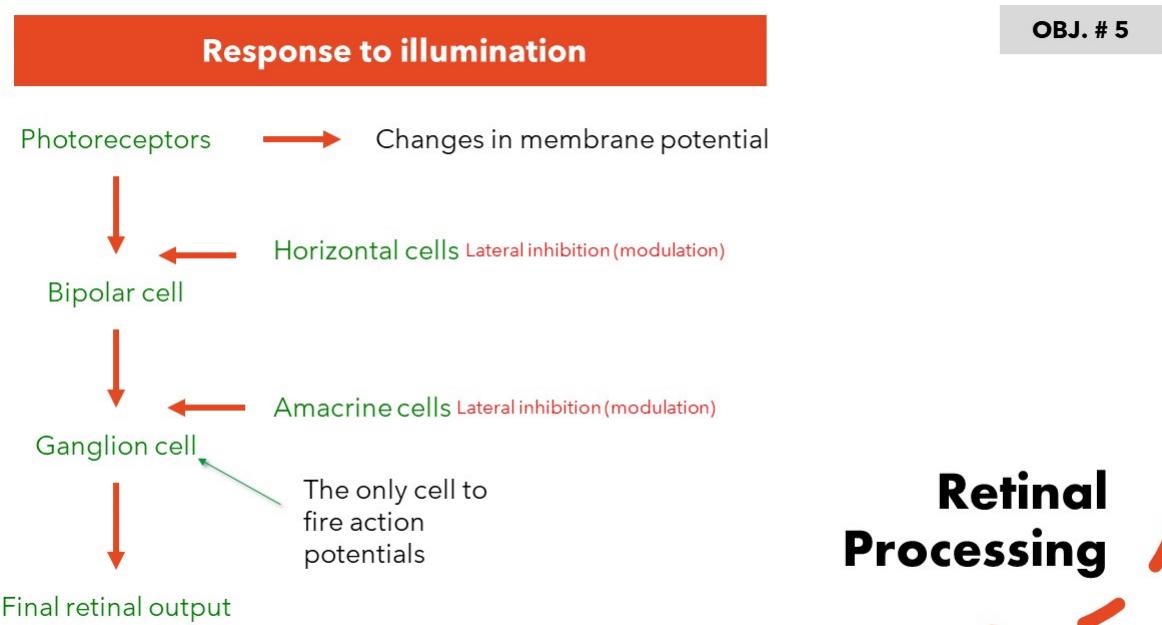
Objective # 4

Slide 23 & 24 – We see in color thanks to the properties of the 3 different types of cones that absorb light at 3 different wavelengths. The theory of color vision says that at each point in the retina (the central retina) we have a cluster of blue, green and red cone photoreceptors. Color is perceived by the cortex according to the information transmitted from the retina related to the differential activation of each one of these cells.



Objective # 5

Slide 25 – This slide shows the transfer of information in the retina from cell to cell. The photoreceptor cells transmit the captured visual information to the bipolar cell in the outer plexiform layer. The horizontal cells provide lateral inhibition to this synapse. The bipolar cell transmits this information to the ganglion cell in the inner plexiform layer. The amacrine cell provides lateral inhibition in this synapse. The ganglion cell is the only cell in the retina to fire action potentials and is the cell that sends visual information from the retina to higher brain centers.



Slide 26 – There are at least three types of ganglion cells in the retina. Some ganglion cells inform the brain about overall light intensity. Some other ganglion cells inform the brain about object movement in space. These ganglion cells are called M-ganglion cells (slide 27). There are other ganglion cells that specialize in color and shape of objects in their visual fields. These are P-ganglion cells.

OBJ. # 5

Retinal Output

Some ganglion cells → Inform the brain about light intensity

Some ganglion cells → Inform the brain about moving objects within their receptive fields

Some ganglion cells → Inform the brain about object shape and color vision

Slide 27 – M or magnocellular ganglion cells are located mostly in the peripheral retina and receive information mostly from rod photoreceptors and peripheral bipolar cells. The P or parvocellular ganglion cells are located mostly in the central retina and receive information mostly from cone photoreceptors and centrally located bipolar cells. Intermediate ganglion cells share characteristics from both M and P – ganglion cells.

Types Of Ganglion Cells

OBJ. # 5

Parasol cells:

- Seem to detect stimulus movement
- Large cell bodies, large dendritic field
- Project to the Magnocellular layer of the LGN

P cells, (midget cells):

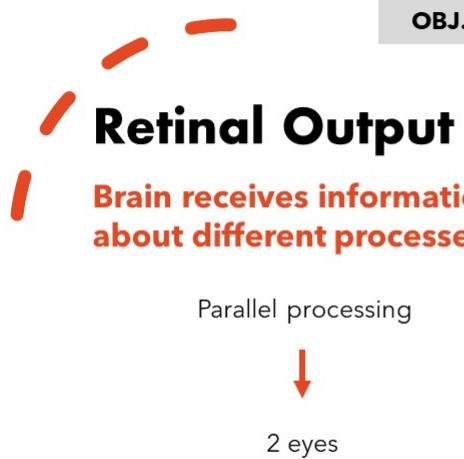
- Information about shape and fine details
- Sensitive to differences in wavelength - color
- Small cell bodies, smaller dendritic field
- Project to the parvocellular layer of the LGN



Slide 28 – The final output from the retina is transmitted through different parallel pathways. To start, we have 2 eyes that see the world around us with a slightly different perspective. Each point in our visual environment is captured by each one of our eyes and the M and P- ganglion cells in our retinas send their individual pathways of information. In this way, visual information starts to get segregated very early on in the visual pathways. We will see how this segregation continues as visual information reaches the thalamus and then the cortex.



OBJ. # 5



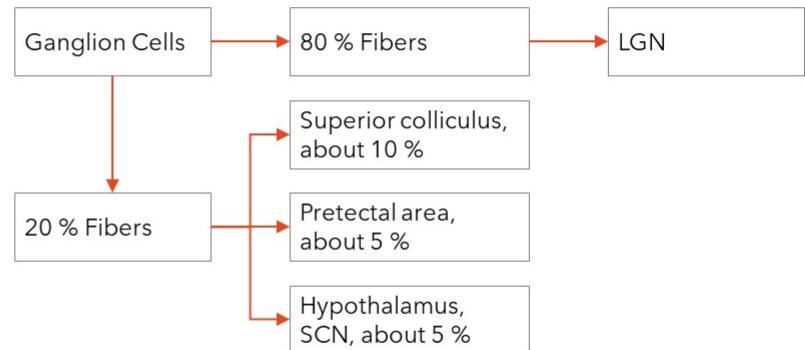
Each point in space is viewed by

- Magnocellular ganglion cells
- Parvocellular ganglion cells
- Intermediate ganglion cells

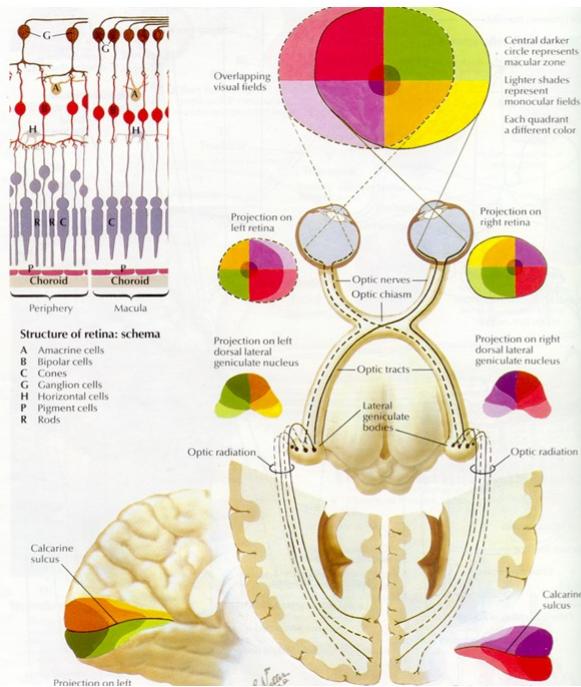
Slide 29 – The retinal output is distributed to different brain structures. Eighty percent of the retinal fibers terminate in the lateral geniculate nucleus of the thalamus. M and P-ganglion cells contribute to this pathway. Twenty percent of the retinal fibers terminate in the superior colliculus, the pre-tectal area and the hypothalamus in the percentages indicated in the slide. These fibers come from M-ganglion cells only.

Retinal Output

OBJ. # 5



Slide 30 –The entire visual pathway which we will study in the following lecture.



OBJ. # 5