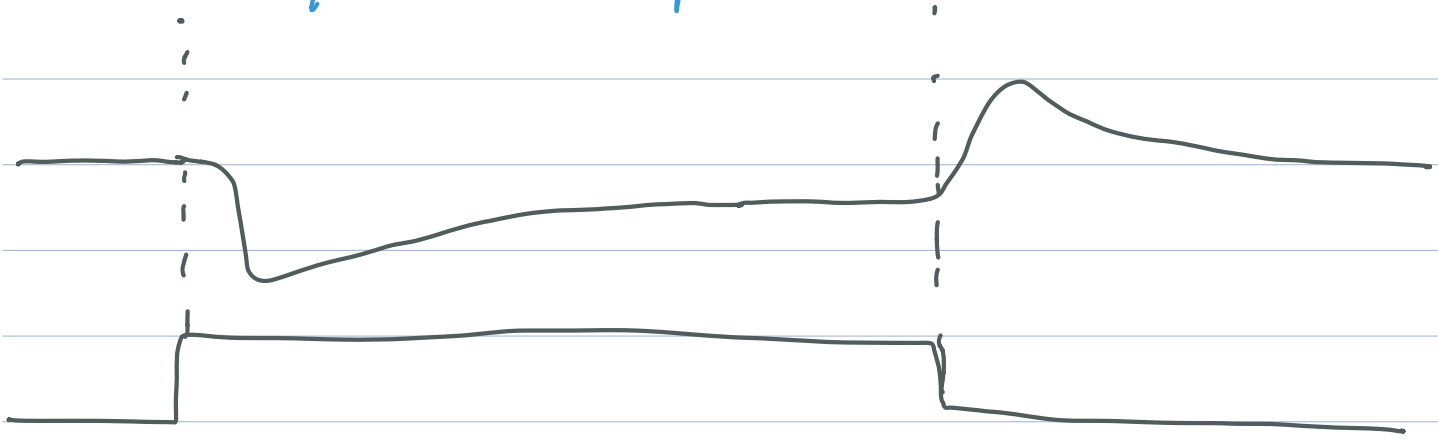
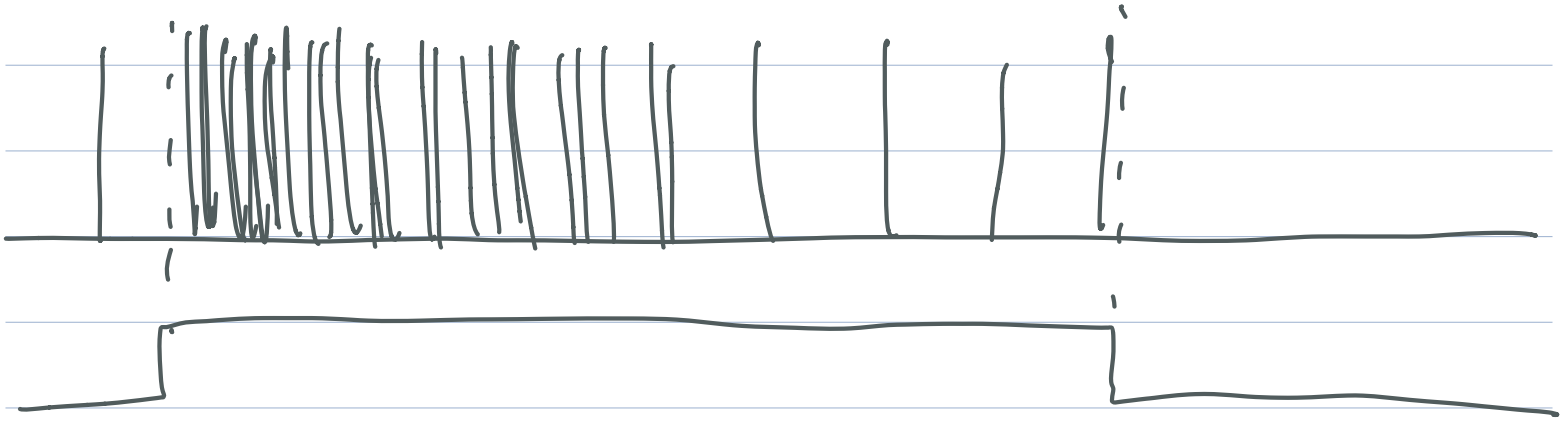
Neuro 80 Lecture 13 October 21st

Shine light on rod photoreceptor, what is response?

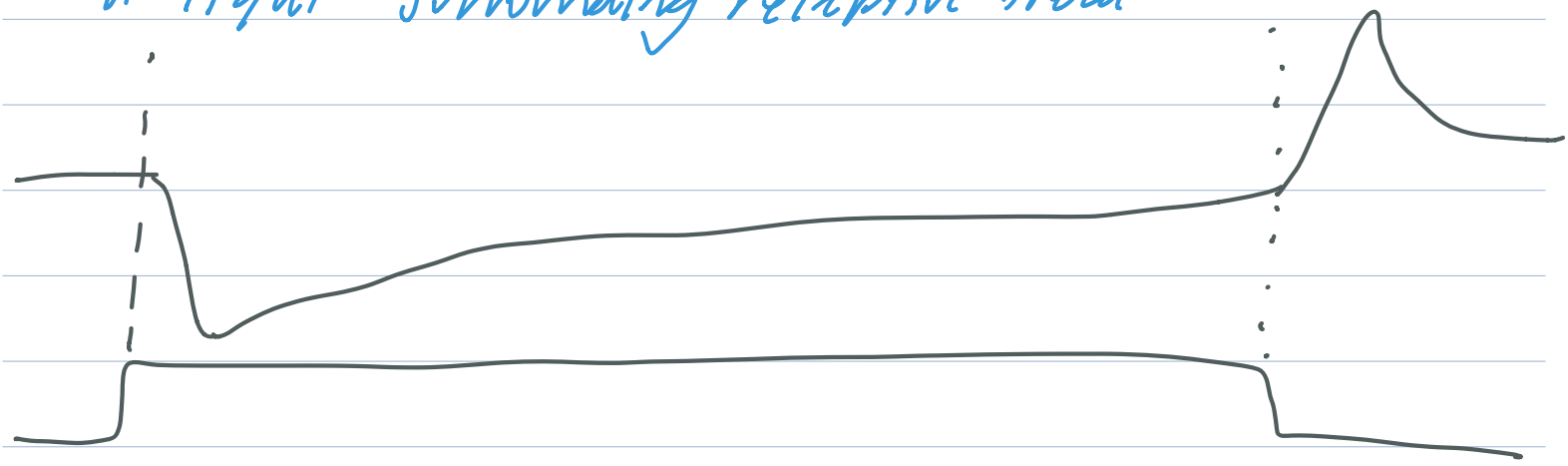


Membrane response of ON bipolar cell to a dark spot in the center of its receptive field

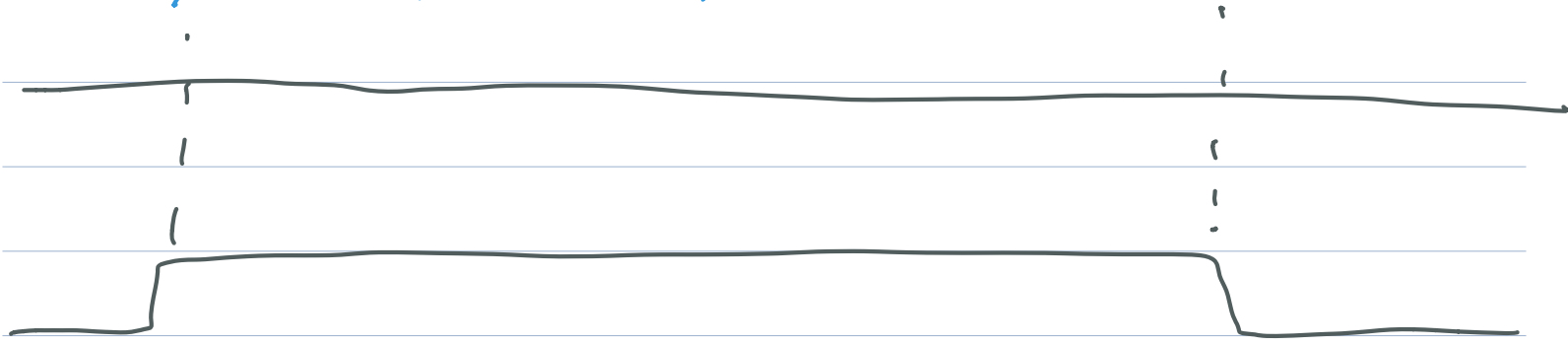
Membrane response of ON RGC to a spot of light



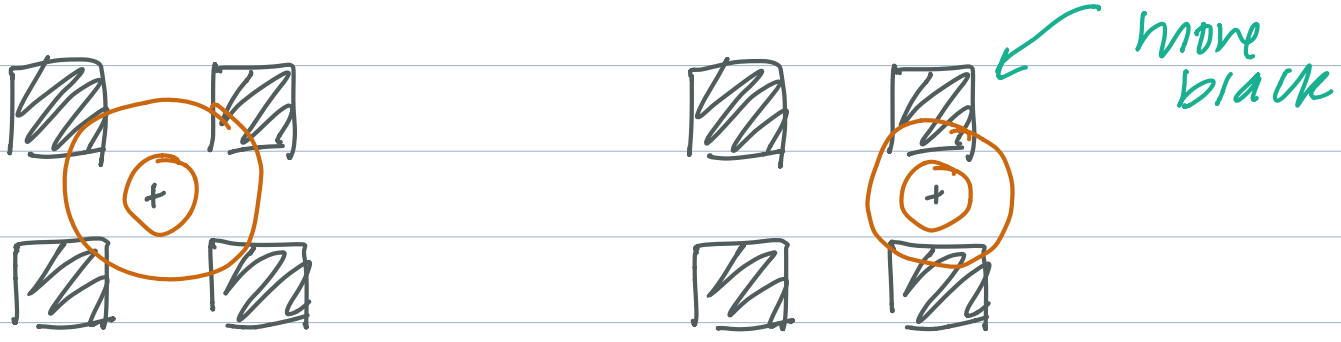
membrane response of ON bipolar cell to ring of light surrounding receptive field



membrane response of OFF bipolar cell to light on whole receptor field



Which ON-cell is more active



MCB/Neuro 80 - Neurobiology of Behavior

Today's Topic:

Vision 2 – Retinal circuits

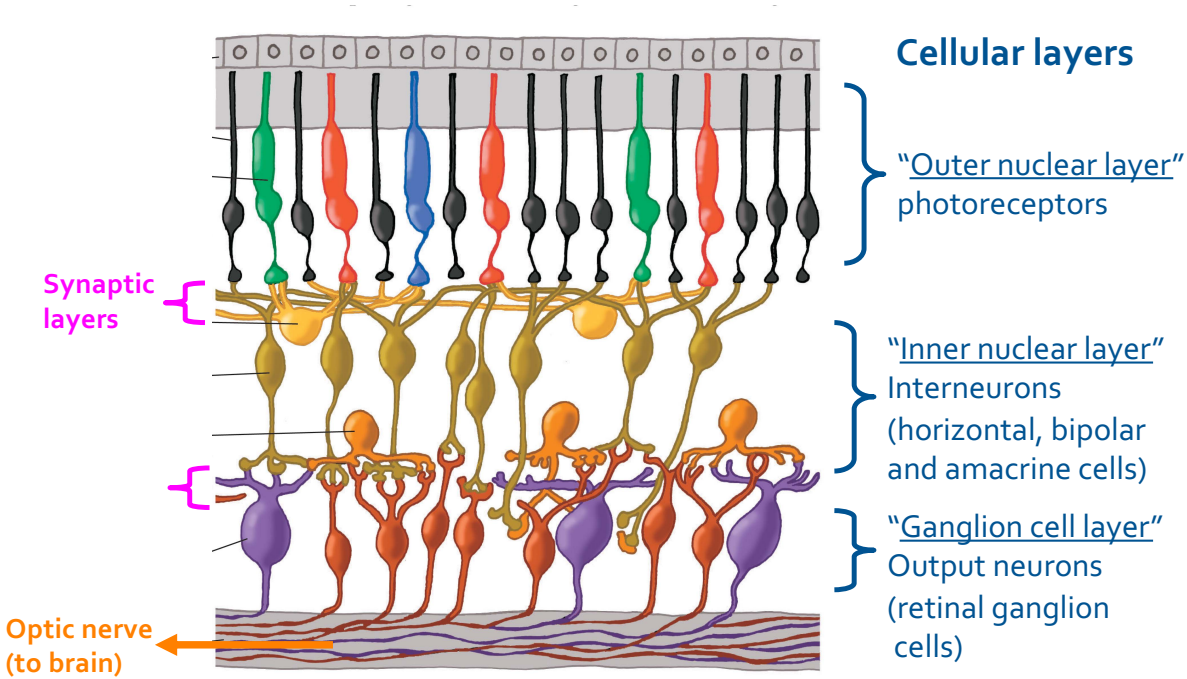
Lecture 13

Optional reading: Purves et al., Neuroscience 6th pages 251-258

Lecture notes, review questions, office hour times available at:

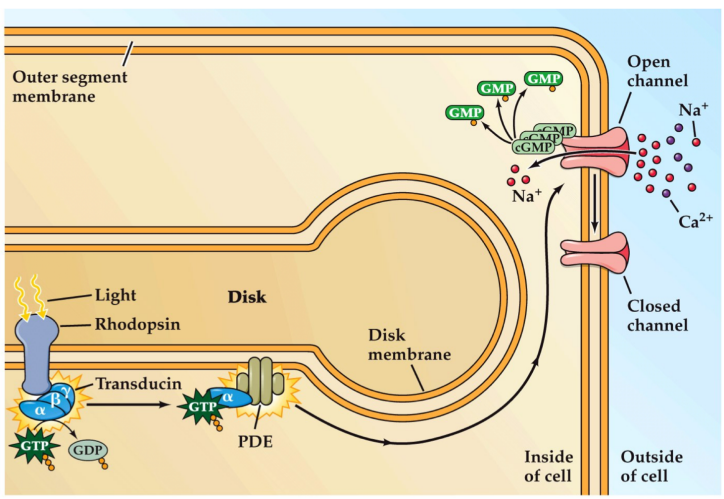
https://canvas.harvard.edu/courses/59120

Neurons of the retina



Phototransduction

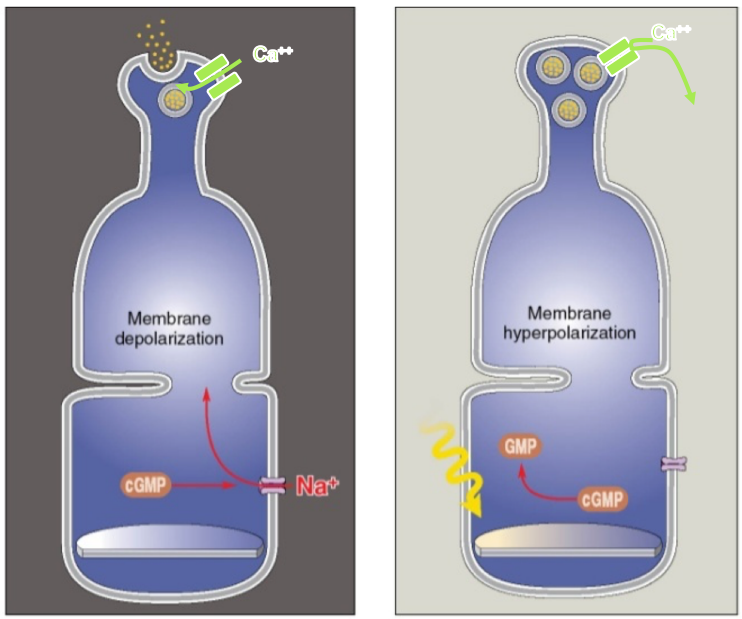
- Light-activated biochemical cascade in a photoreceptor



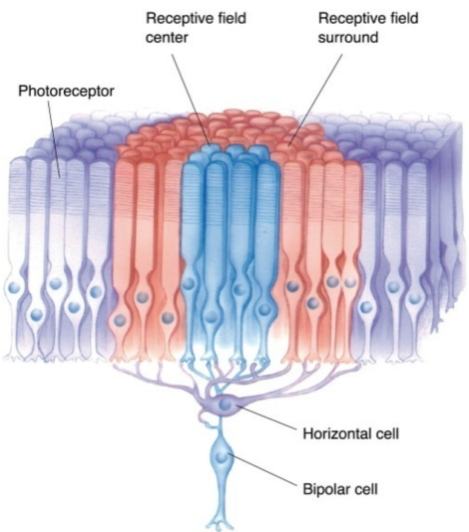
- Light causes conformational change that activates the rhodopsin GPCR
- Activated rhodopsin activates a G protein (Transducin)
- Transducin then activates phosphodiesterase, an enzyme that breaks down cyclic GMP (similar to cyclic AMP)
- Without cGMP, cGMP-gated channels close
- Photoreceptors hyperpolarize in response to light

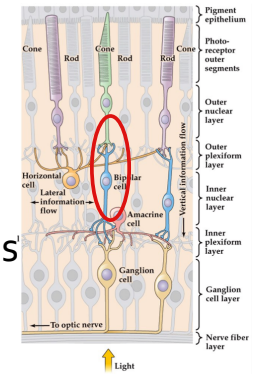
Rods and Cones have a high resting membrane potential

- At rest (in the dark), cyclic-GMP gated cation channels are open
  - Vm relatively high ~ -40 mV
  - Voltage-gated Ca^{++} channels in the terminal are open
  - Release synaptic vesicles continuously in the dark
- When light closes the cGMP channels, the cell hyperpolarizes
  - Voltage-gated Ca^{++} channels in the terminal close
  - Vesicle fusion stops



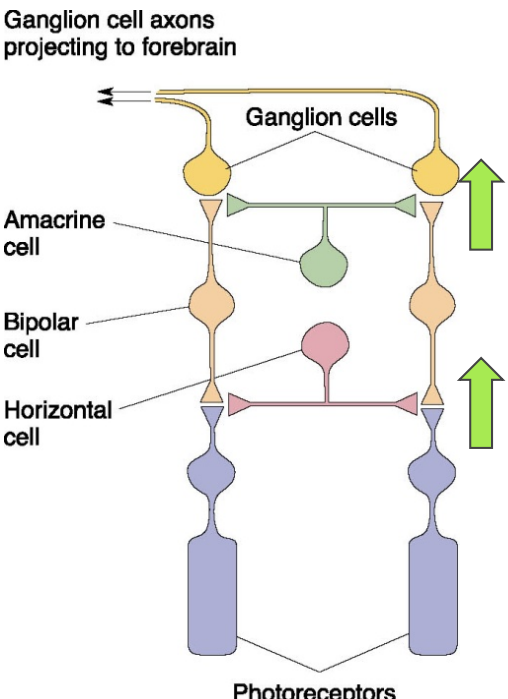
Bipolar Cells





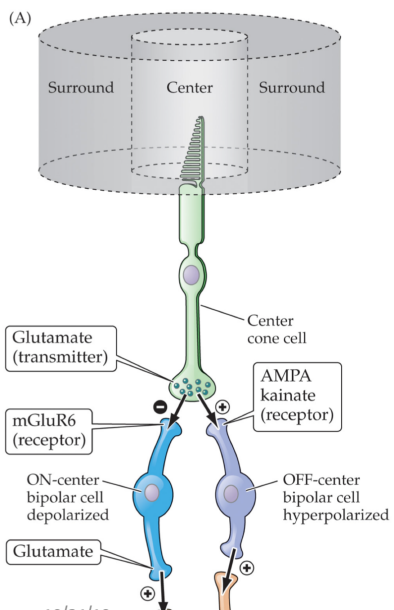
- Have graded electrical responses.
- Graded depolarization of a bipolar leads to an increase in transmitter release.
- Release glutamate.
- Two subtypes:
  - Off bipolar - dark activated, has "traditional" receptors that depolarize cell when NT binds
  - On bipolar - light activated, light activated, "sign switching" receptors that hyperpolarize when NT binds
- Receptive field:
  - Antagonistic center-surround receptive fields

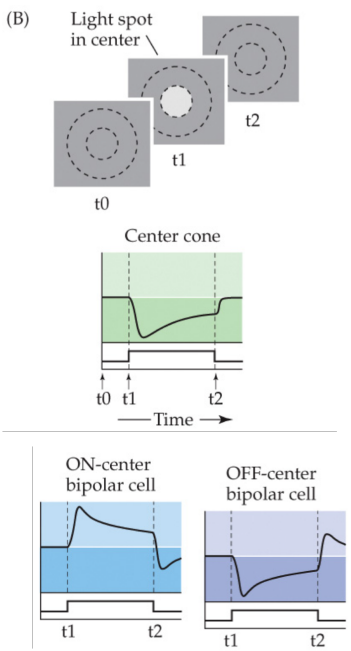
"Direct" pathway



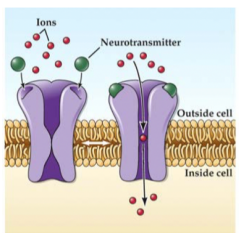
- Direct pathway: Photoreceptors connect to Bipolar cells which connect to Retinal Ganglion Cells
- Direct pathway responsible for the "center" of the receptive field
- Photoreceptors release glutamate
  - Need bipolar cells with the opposite response (excited vs inhibited) from same neurotransmitter (glutamate)

OFF-bipolar cells repeat photoreceptor signal while ON-bipolar receptors invert photoreceptor signal

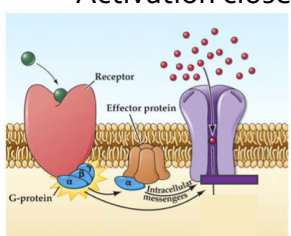




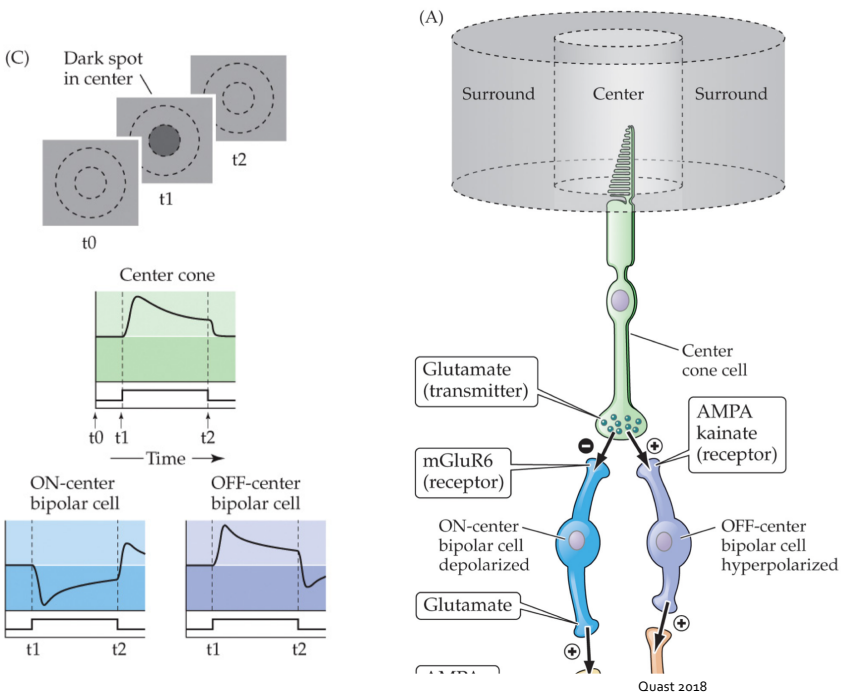
- OFF-Bipolar (excited by light➔off)
  - Express AMPA (ionotropic)
  - Depolarize from glutamate



- ON-Bipolar (excited by light➔on)
  - Express mGluR (metabotropic)
  - Activation closes cation channels
  - Hyperpolarize from glutamate



On and Off Bipolar Cells



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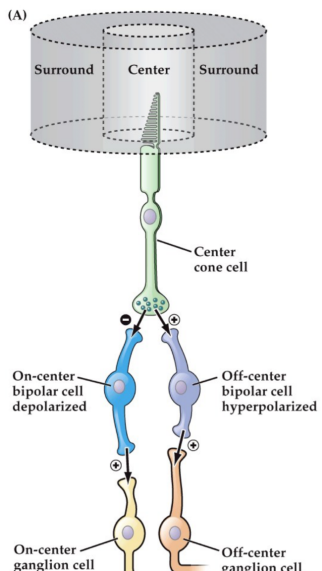
Ganglion Cells

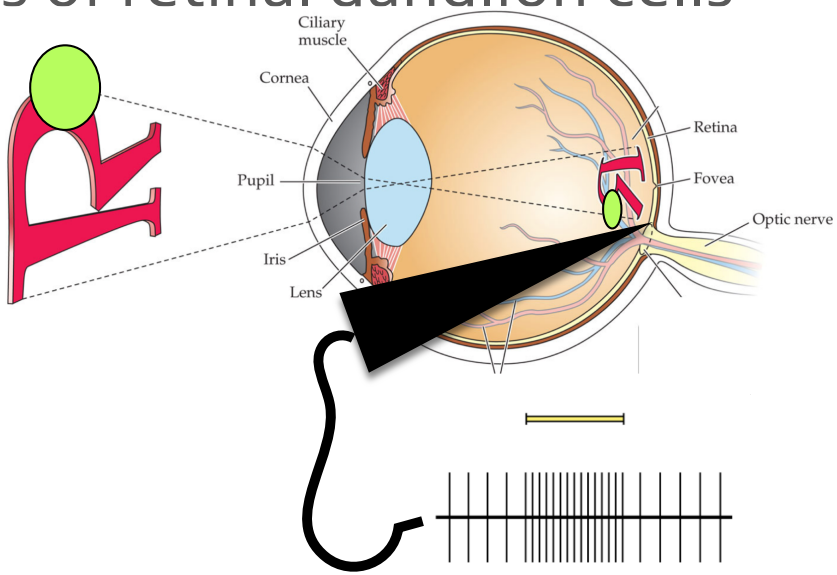


***NEUROSCIENCE 5e*, Figure 11.18 (Part 1)**

- Only cells in retina that fire true action potentials
- Like bipolar cells have a center/surround receptive field.
- On-center ganglion cells synapse with on-bipolar cells; off-center ganglion cells synapse with off-bipolar cells
- The different classes synapse in different layer of the inner plexiform layer

Recording responses of retinal ganglion cells

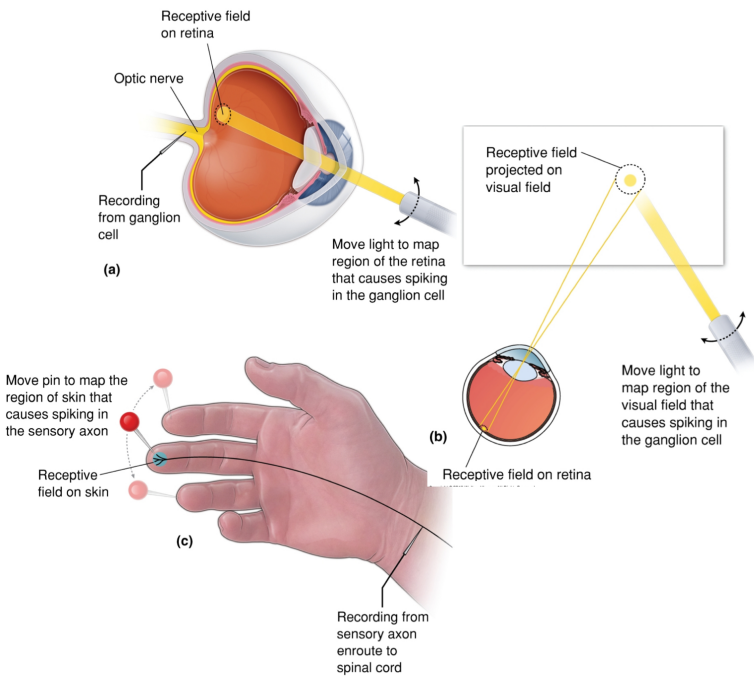
- Experimental animal is anesthetized and positioned facing a screen.
- Electrode positioned near a retinal ganglion cell to record action potentials
- Shine spots or other shapes on screen



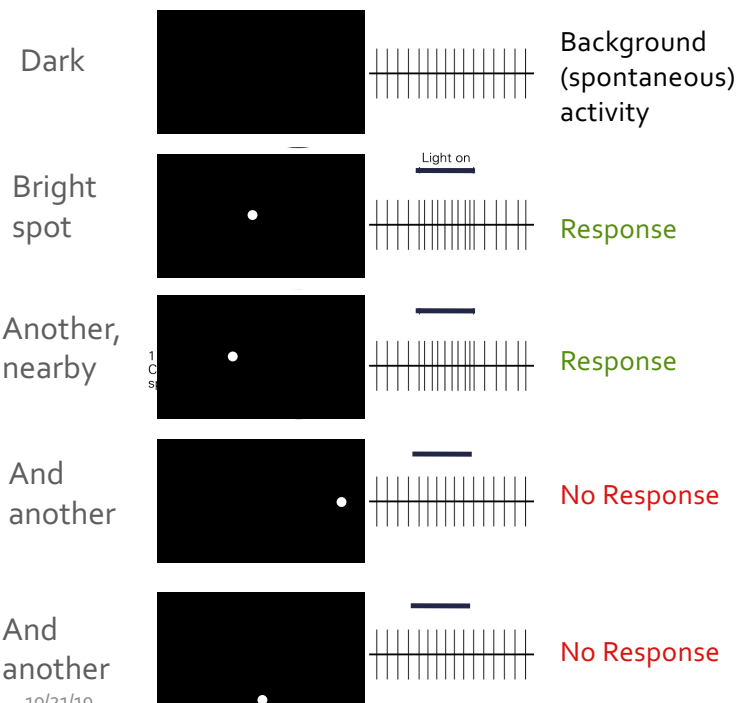
- Map the region of the world (the screen) that affects the activity of the neuron. This region is the cell's receptive field.

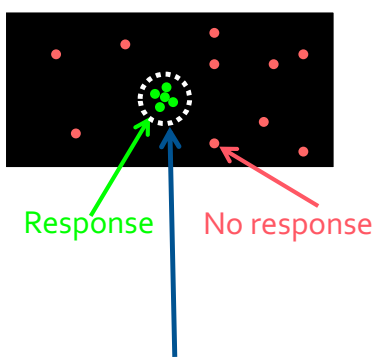
Receptive Fields

- A general term useful in describing the stimulus specificity of neurons across sensory systems
- Includes the particular region of sensory space that a stimulus will activate that neuron
- Receptive fields tend to enlarge and increase in complexity as information passes through the brain



The receptive field of retinal ganglion cells

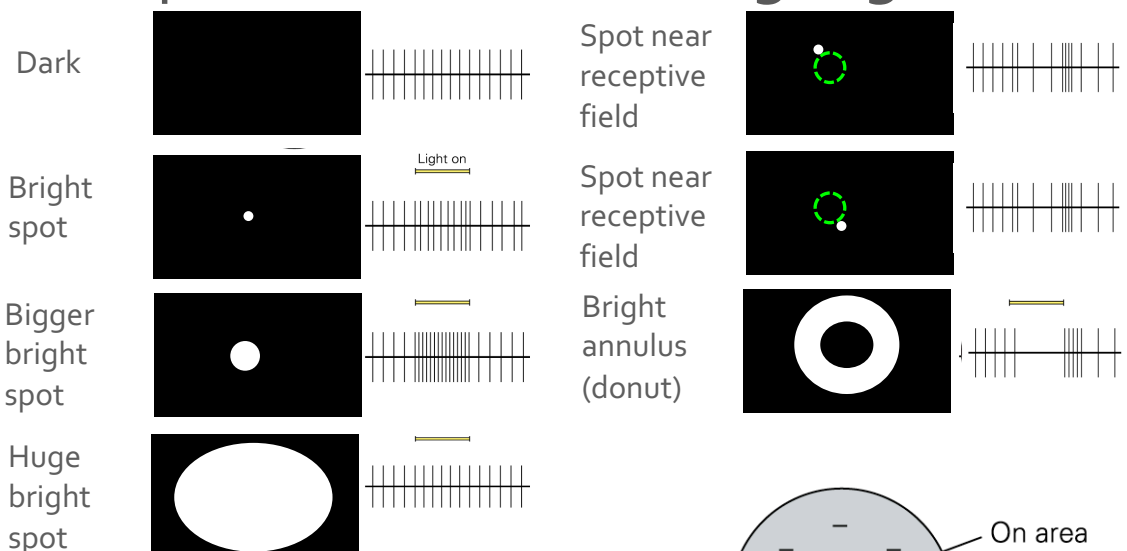


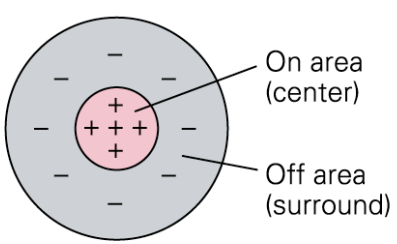


Receptive field: the area to which a cell is responsive

(but not the whole story)

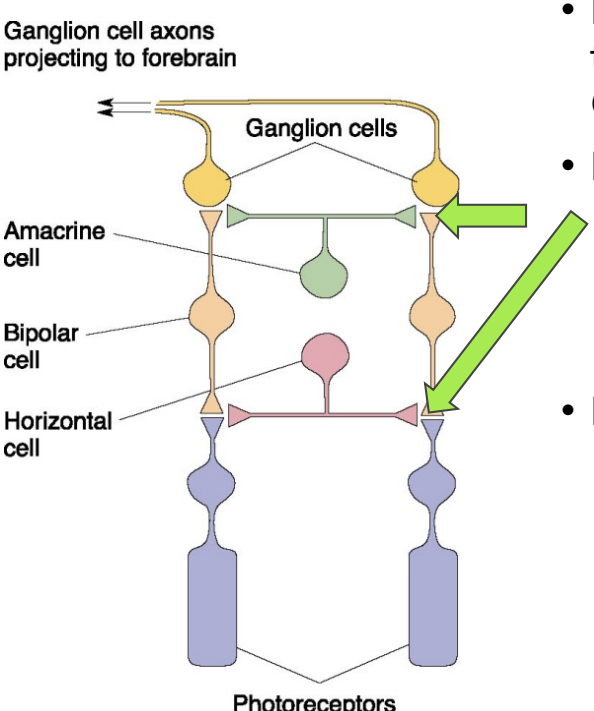
The receptive field of retinal ganglion cells





Center and surround parts of the receptive field

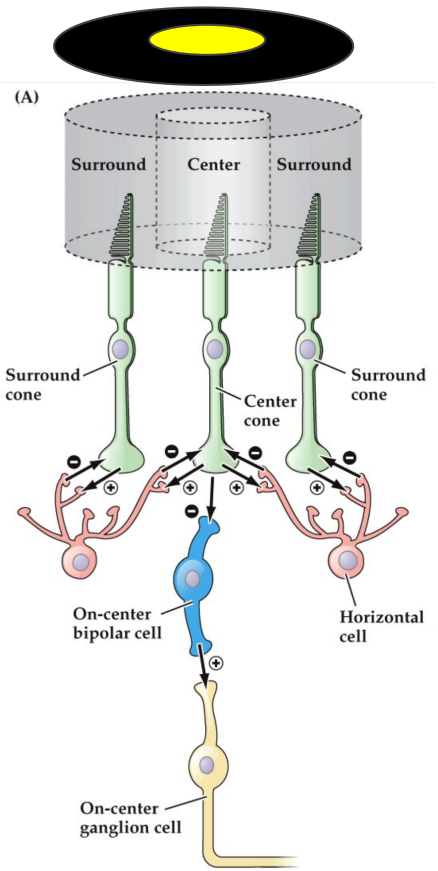
"Lateral" pathway



- Direct pathway: Photoreceptors connect to Bipolar cells which connect to Retinal Ganglion Cells
- Horizontal and amacrine cells
  - GABAergic (inhibitory)
  - Linked via gap junctions forming a network
  - Can help adjust the entire retinal circuit response to changing levels of illumination.
- Horizontal cells
  - Receive input from photoreceptor terminals
  - Depolarized by the glutamate released by photoreceptors (in the dark)
  - Release GABA which hyperpolarizes the photoreceptor terminals

Opposite surround – the "indirect pathway"

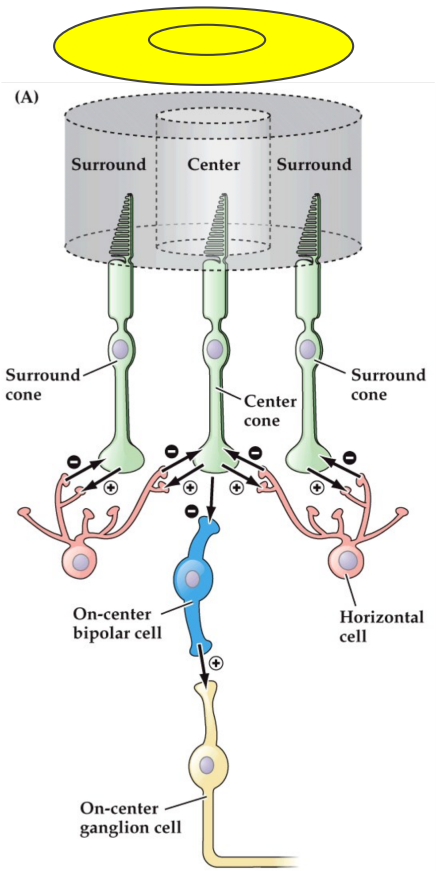
- Small, center spot:
  - Light inhibits center cone
  - Signal inverted for ON-Bipolar ➔ Active!
  - Surround cones excited
  - Activate Horizontal cell
  - Inhibits center cone further
  - Maximal activation of ON-Bipolar



Opposite surround – the "indirect pathway"

- Large spot:
  - Light inhibits center cone
  - Signal inverted for ON-Bipolar ➔ Active!

  - Surround cones inhibited (light)
  - Horizontal cell inactive
  - Reduced inhibition of center cone
  - Reduced activation of ON-Bipolar



The center is equally stimulated at both positions, but on the right, the inhibitory surround is also stimulated, so net excitation is less than on the left

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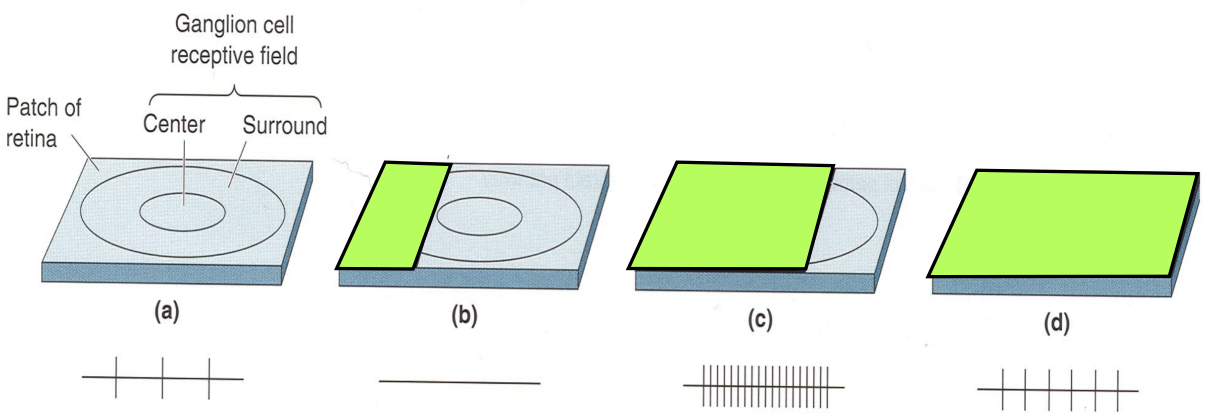
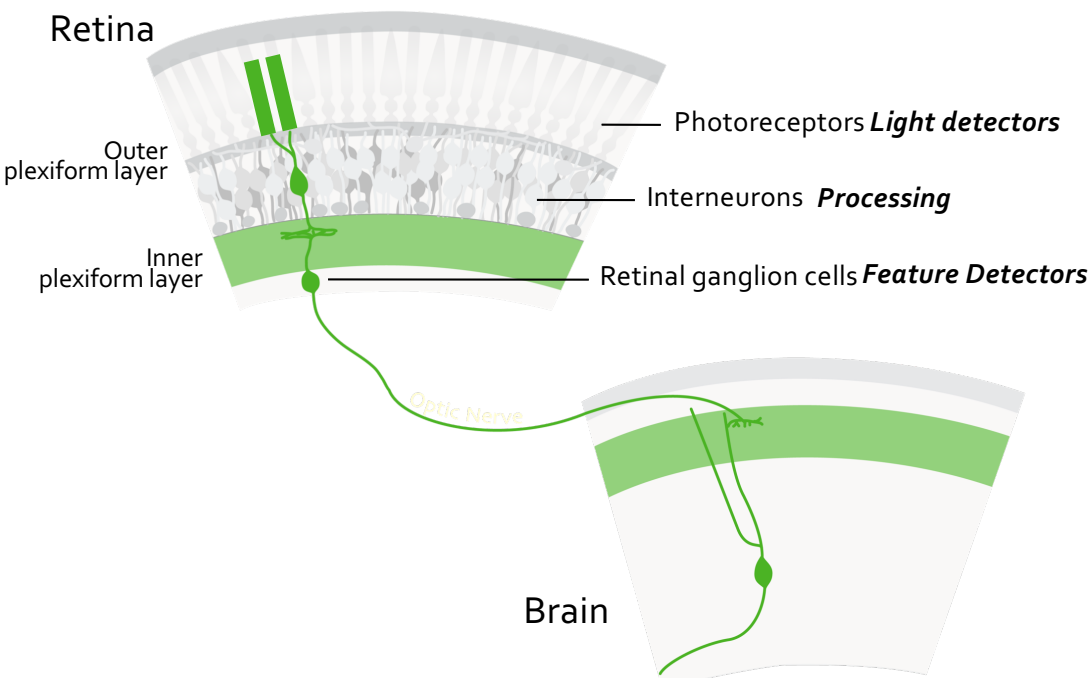
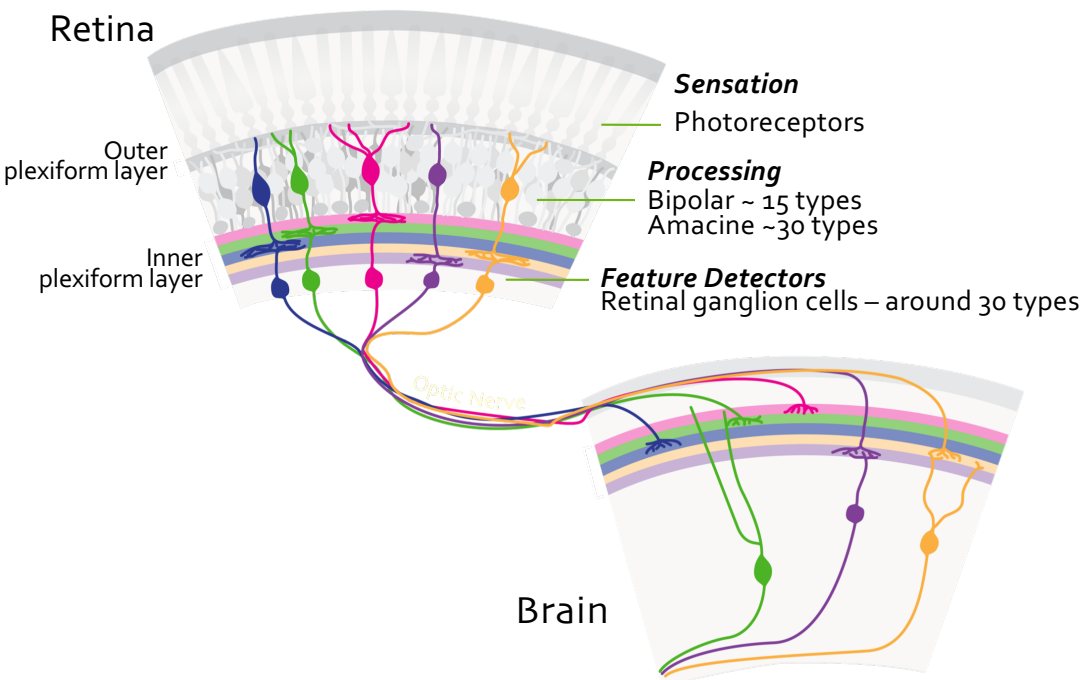
Center-surround organization enhances sensitivity to edges and contrast



Information processing in the retina

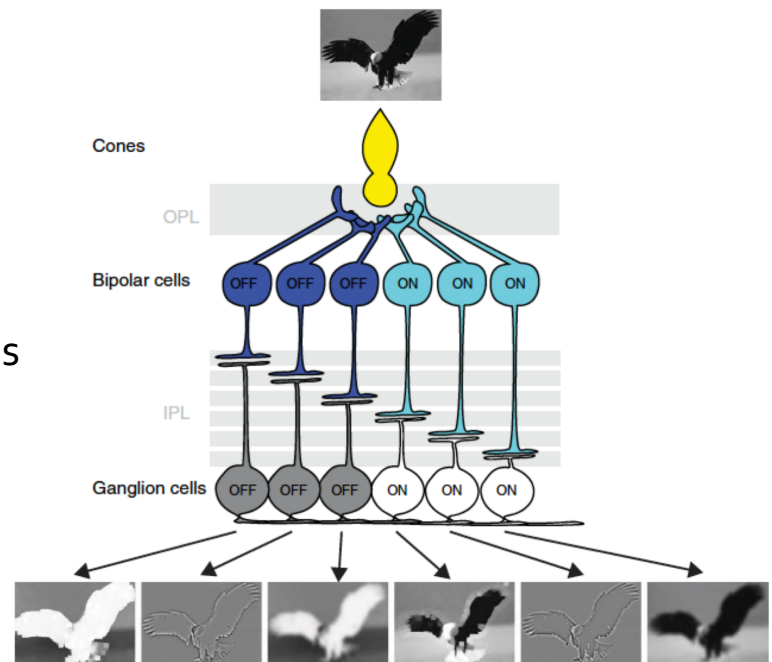


Information processing in the retina



Parallel output pathways from the retina

- Retina is not a camera
- Does not send point-by-point intensity and color information to the brain
- High processed; breaks up visual world in many different features
- Many (~30) different types of RGCs
  - Color center/surround
  - Prefer moving stimuli
  - Large or small RFs, etc.



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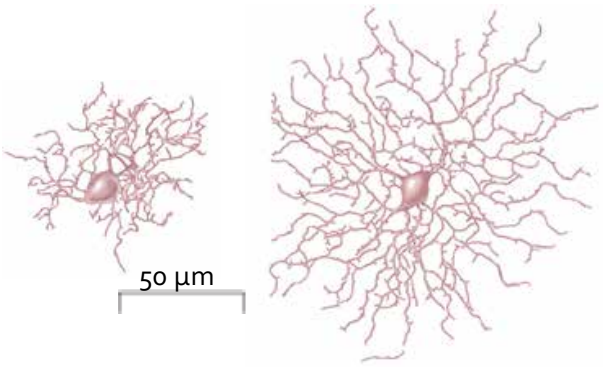
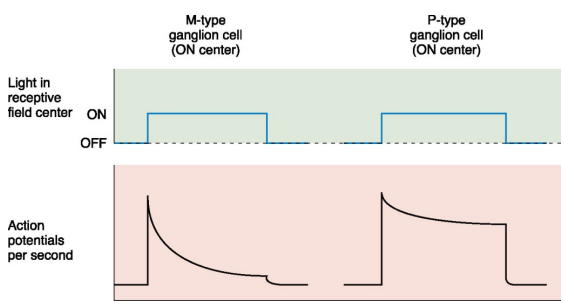
M-type and P-type RGCs

form, texture, outline

- P-type (parvocellular or midget)
  - Smaller, and smaller receptive fields
  - Large majority of RGCs
  - Often color specific receptive fields.
  - Respond to prolonged stimulation with sustained action potential rate.
- M-type (magnocellular or parasol)
  - Larger
  - Color insensitive, receptive fields.
  - Respond to stimulation with a burst of action potentials.





Learning Objectives – Lecture 13

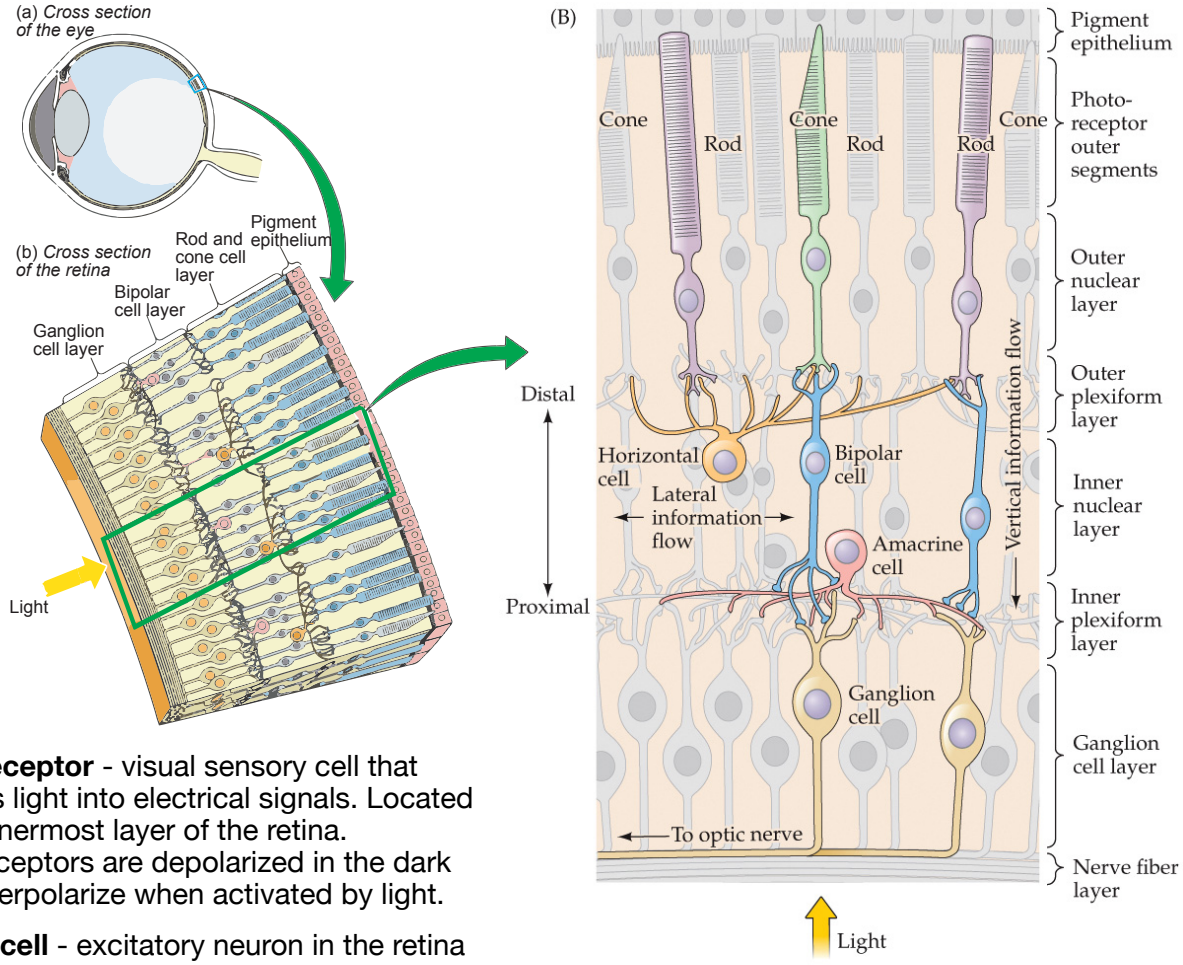
- Illustrate how the major cell types of the retina are connected to each other and the function of each.
- Explain how shining light on either the center or the surround of an on-center (or off-center) ganglion cell's receptive field differentially affects the cell's activity and how that response may differ from an on or off-center bipolar cell.
- Compare the pathways in the retina that lead to the formation of an on-center ganglion cell versus an off-center ganglion cell.
- Define receptive field and explain why a center-surround receptive field enhances sensitivity to contrast and edges

Lecture 14 - Vision 2: Circuits of the retina

Pre-class notes for October 21, 2019

Reading: *Neuroscience ed. 6* by Purves et al., pages **251-258**

The **retina** is the innermost layer of the eye and is Itself a layered structure that contains the visual sensory neurons, circuitry for the initial processing of visual information, as well as neurons that transmit that information to the brain. But the neurons of the retina do not simply detect light and pass that message on, a great deal of processing and filtering occurs in the retina, before the visual information reaches the brain.



NEUROSCIENCE 6e, Figure 11.5 (Part 2)

Photoreceptor - visual sensory cell that converts light into electrical signals. Located at the innermost layer of the retina. Photoreceptors are depolarized in the dark and hyperpolarize when activated by light.

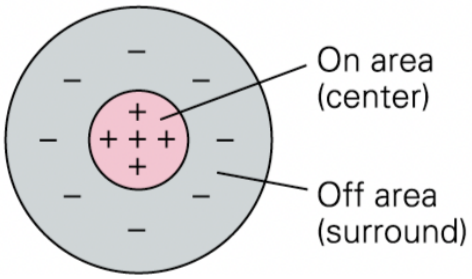
Bipolar cell - excitatory neuron in the retina that transmits information from the photoreceptors to the retinal ganglion cells and amacrine cells. Bipolar cells do <u>not</u> fire action potentials, but have a graded release of neurotransmitter.

Horizontal cell - inhibitory neuron in the retina whose actions influence the signals that are transmitted from the photoreceptors to the bipolar cells. They make inhibitory, GABAergic synapses on the synaptic terminals of photoreceptors.

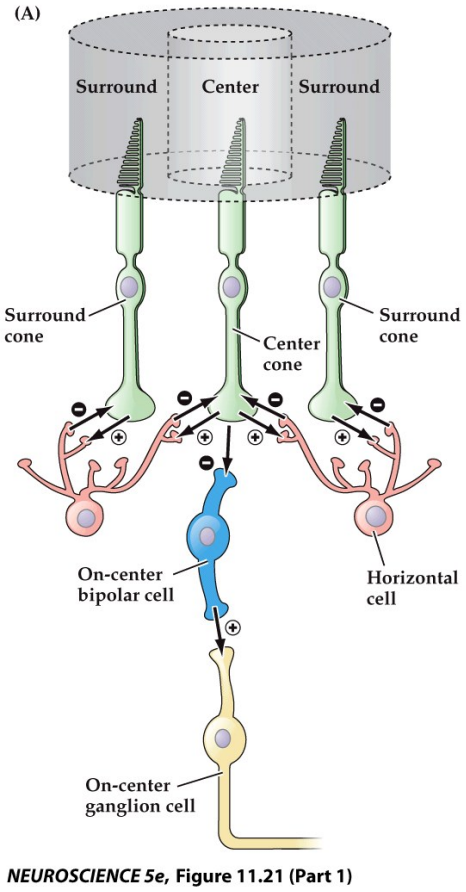
Amacrine cell - inhibitory/modulatory neuron whose actions influence the signals that are transmitted from the bipolar cells to the retinal ganglion cells.

Retinal ganglion cell (RGC) - Output cell of the retinal that transmits information from the eye to the brain. Only type of neuron in the retina that fires action potentials. There are both “on” and “off” that can be further divided into many different subtypes of RGCs based on specific *receptive field* properties (color, size of receptive field, etc.).

Receptive field - region or characteristics of the sensory space that elicits the greatest activity (action potentials or largest graded potentials in the retina) from either a sensory cell or neuron within the CNS. For neurons in the retina, receptive filed properties include the area of the visual field (location in space) where light (or dark) would hit the neuron.



Center/surround - In the retina, both bipolar cells and RGCs have center surround receptive fields. For an "ON cell", that means that the cell is excited by center stimulation (i.e. light/"on"), inhibited by light in the surround, and would be more optimally stimulated by dark in the surround. These receptive fields are very useful because they enable cells to detect more than the brightness of a spot of light, but rather detect *contrast* (edges or boundaries between light and dark).



***NEUROSCIENCE 5e*, Figure 11.21 (Part 1)**

In the visual system, center/surround receptive fields are first found in the bipolar cells of the retina. The center of the receptive field is formed by the direct synapses between photoreceptors and the bipolar cell while the surround is caused by the inhibitory actions of horizontal cells being activated by the surrounding photoreceptors. This circuit motif of inhibiting neighboring cells is common in the nervous system and is known as **lateral inhibition.**

OFF bipolar cell - bipolar cell that is inactivated by light (activated by dark). Their dendrites contain excitatory inotropic (AMPA type) glutamate receptors. Since photoreceptors release more glutamate in the dark, "OFF" cells also release more neurotransmitter in the dark and less neurotransmitter in the light.

ON bipolar cell - bipolar cell that is active by light. Their dendrites contains inhibitory mGluR6 type glutamate receptors, thus they invert the signal the photoreceptors send. Since photoreceptors release less glutamate in the light, "ON" cells invert that signal and release more NT in the light.

ON RGC - retinal ganglion cell that fires more action potentials when light is in the center. Receives excitatory synaptic input from ON-bipolar cells via AMAP type glutamate receptors.

OFF RGC - retinal ganglion cell that fires fewer action potentials when light is in the center. Receives excitatory synaptic input from OFF-bipolar cells via AMAP type glutamate receptors.

In addition to having a center-surround receptive field with either an ON or an OFF center, RGCs can be further characterized based on their size, appearance, connectivity and electrophysiological properties into 30 or more types. In primates, including humans, two major types of ganglion cells have been identified, large *M-type ganglion cells* (magno, from Latin meaning large) and smaller *P-type ganglion cells* (parvo, from Latin meaning small). These the different types of ganglion cells appear to play different roles in visual perception.

P-type RGCs - make up the large majority of RGCs, have smaller, often color specific receptive fields. P-type RGCs, respond to prolonged stimulation with sustained action potential rate.

M-type RGCs - make up a much smaller percentage of RGCs, have large, color insensitive, receptive fields. M-type RGCs transiently respond to stimulation with a burst of action potentials.

Learning Objectives: (By the end of Lecture 13 you should be able answer the following)

1. Illustrate how the major cell types of the retina are connected to each other and the function of each.
2. Explain how shining light on either the center or the surround of an on-center (or off-center) ganglion cell's receptive field differentially affects the cell's activity and how that response may differ from an on or off-center bipolar cell.
3. Compare the pathways in the retina that lead to the formation of an on-center ganglion cell versus an off-center ganglion cell.
4. Define receptive field and explain why a center-surround receptive field enhances sensitivity to contrast and edges