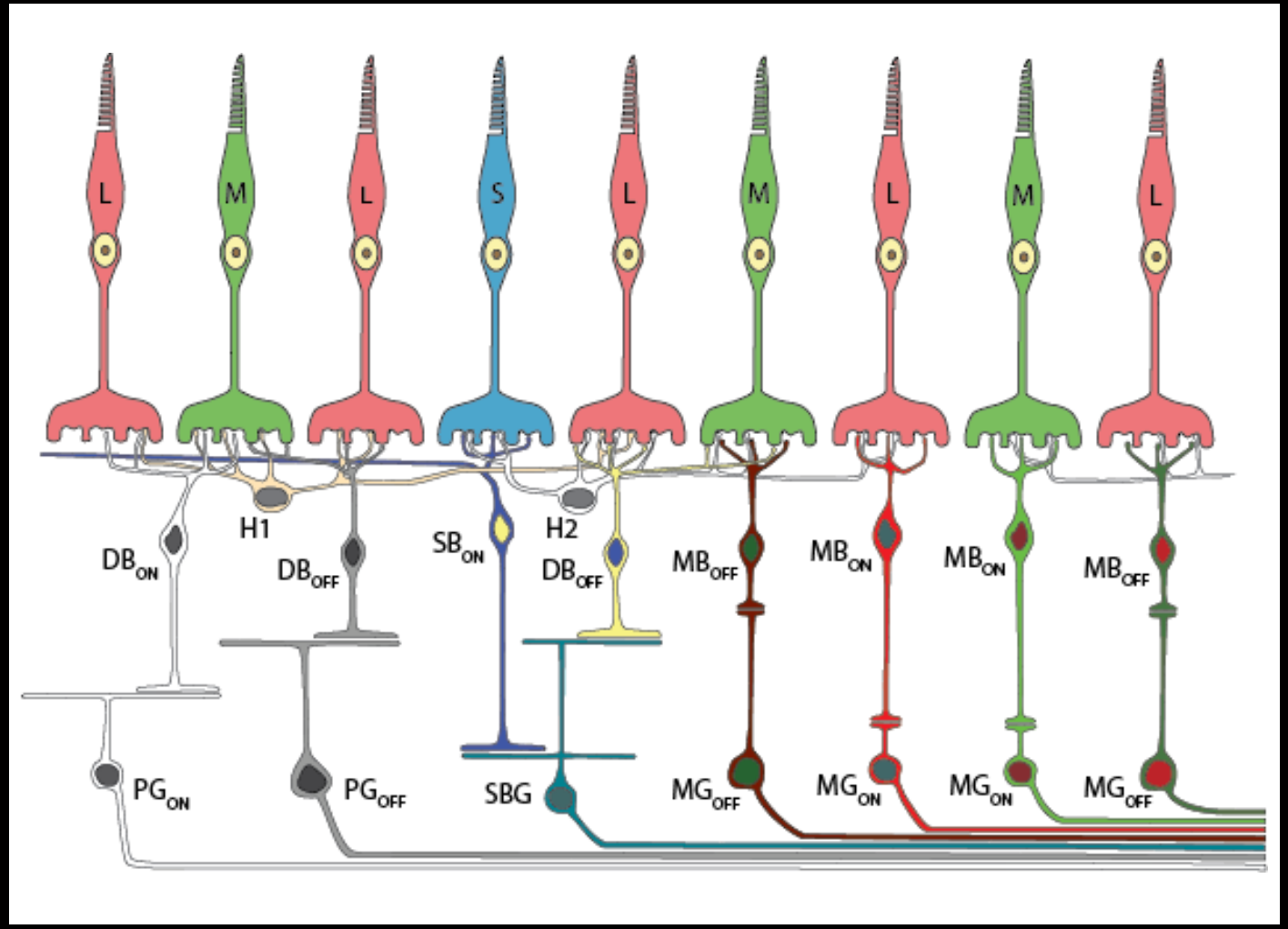
Introduction to the Retina

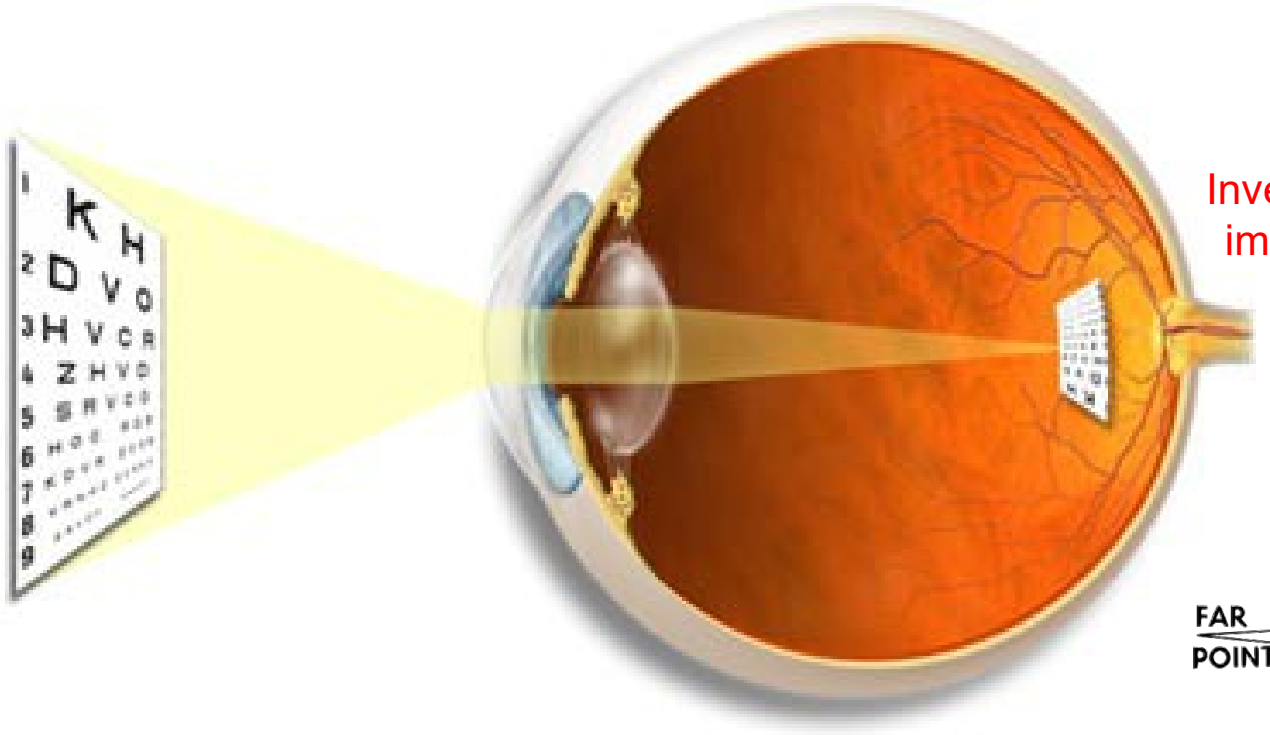
Andrew Stockman

NEUR 0017
Visual Neuroscience

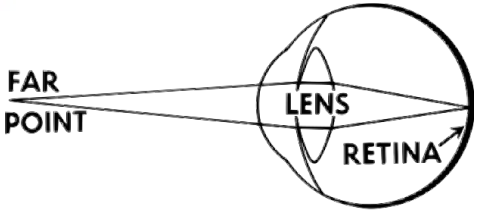


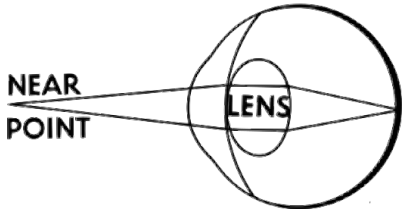
Optics

An image of an object is focused by the cornea and lens onto the rear surface of the eye: the retina.



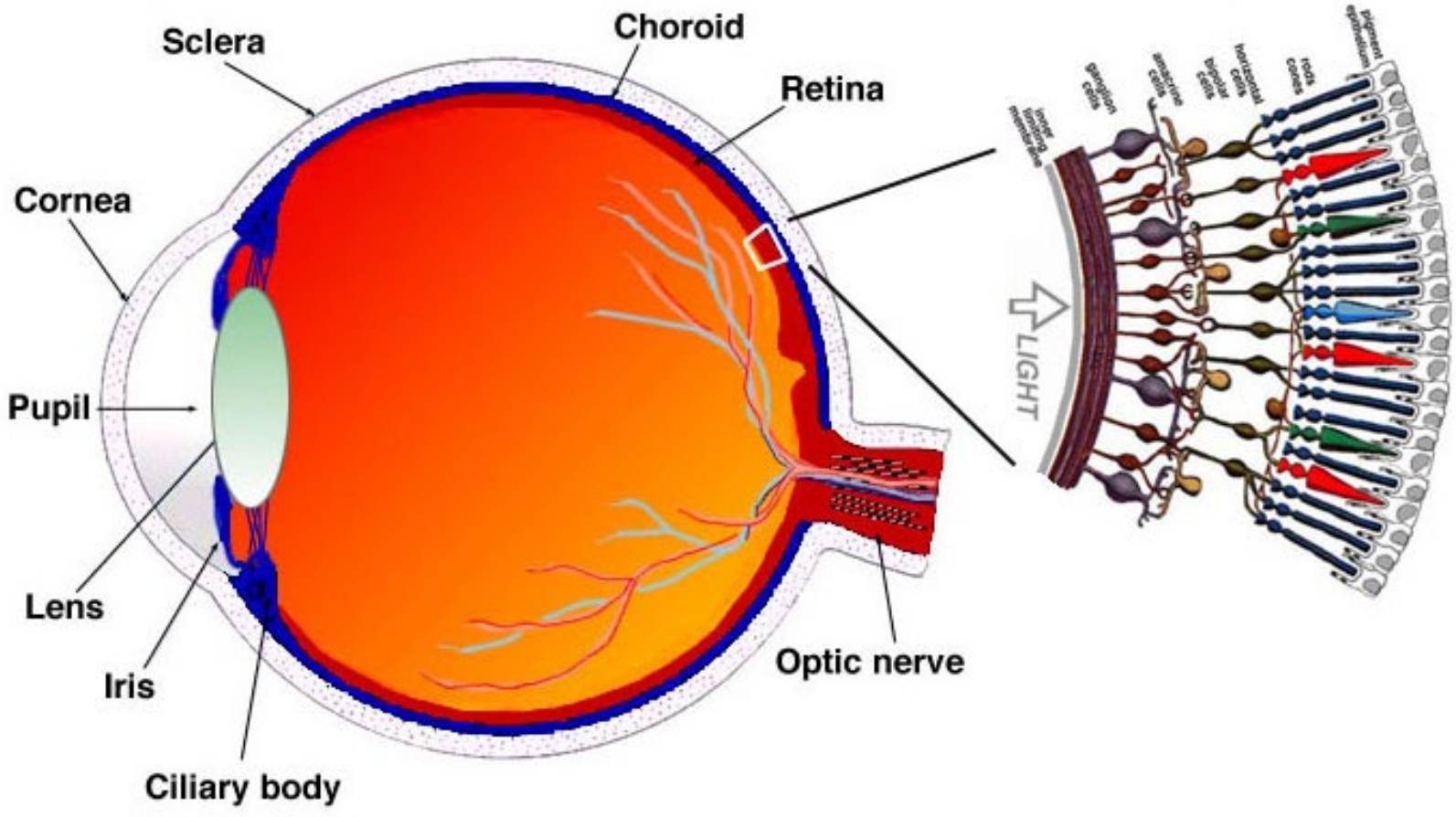
Inverted image





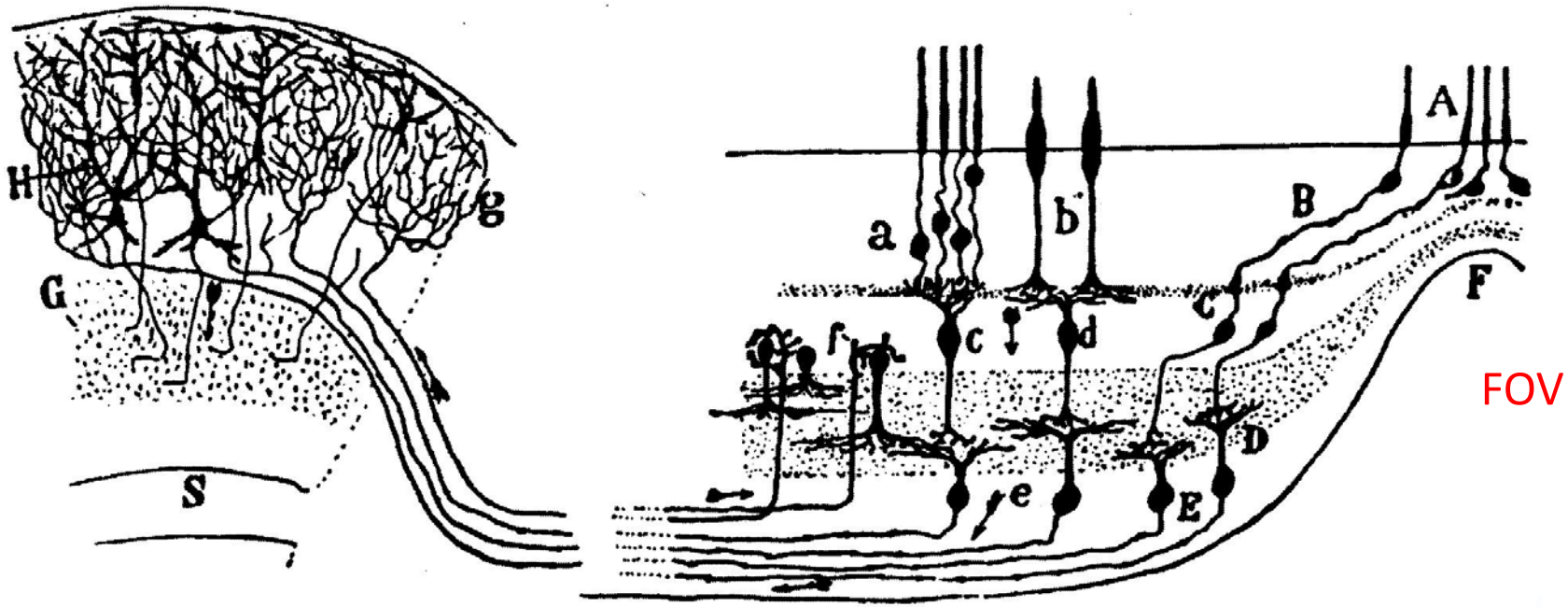
Accommodation: Focus on near objects by contracting Ciliary muscle and changing shape of lens.

Eye and retina



Retinal cells

Cajal's (1909-1911) neural architecture drawing based on the Golgi method.



Optic Tectum
(superior colliculus)

FOVEAL PIT

- Ramon y Cajal noted that neurons have anatomical polarity.
- No myelination in the retina
- Myelination of axons in the optic nerve

Retina: a light sensitive part of the CNS

Light microscopic vertical section

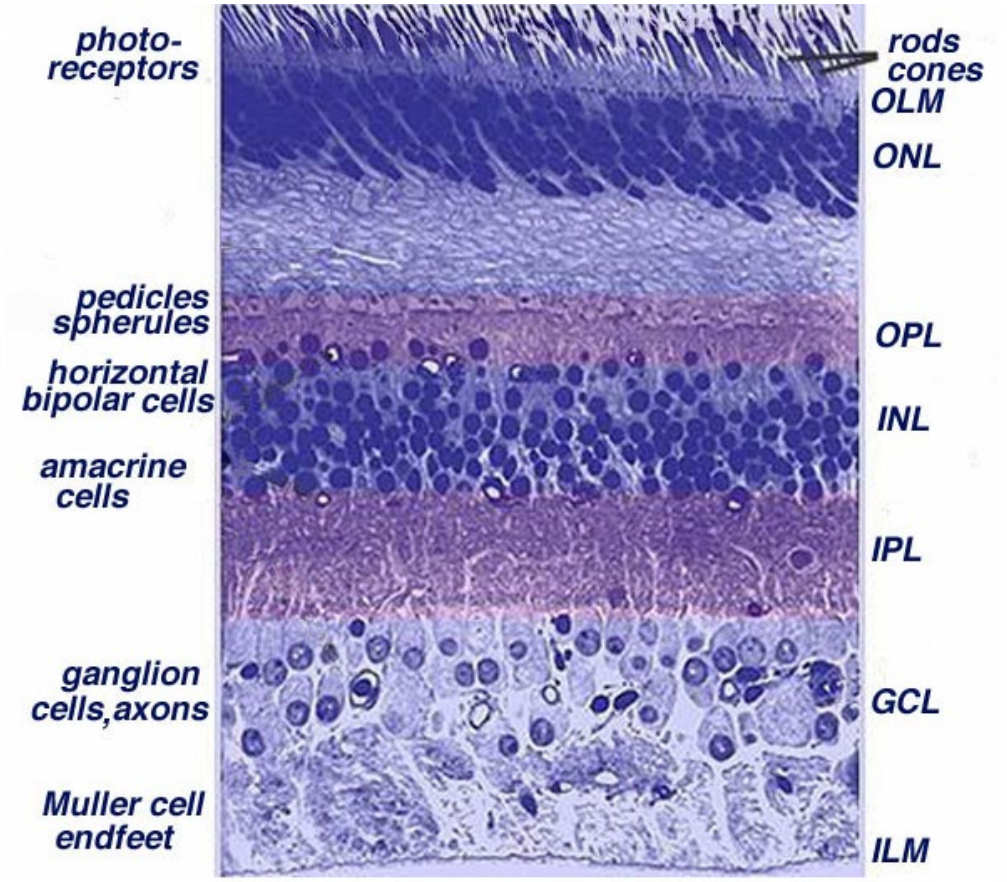


Fig. 3. Light micrograph of a vertical section through central human retina.

OUTER LIMITING MEMBRANE
OUTER NUCLEAR LAYER

OUTER PLEXIFORM LAYER

INNER NUCLEAR LAYER

INNER PLEXIFORM LAYER

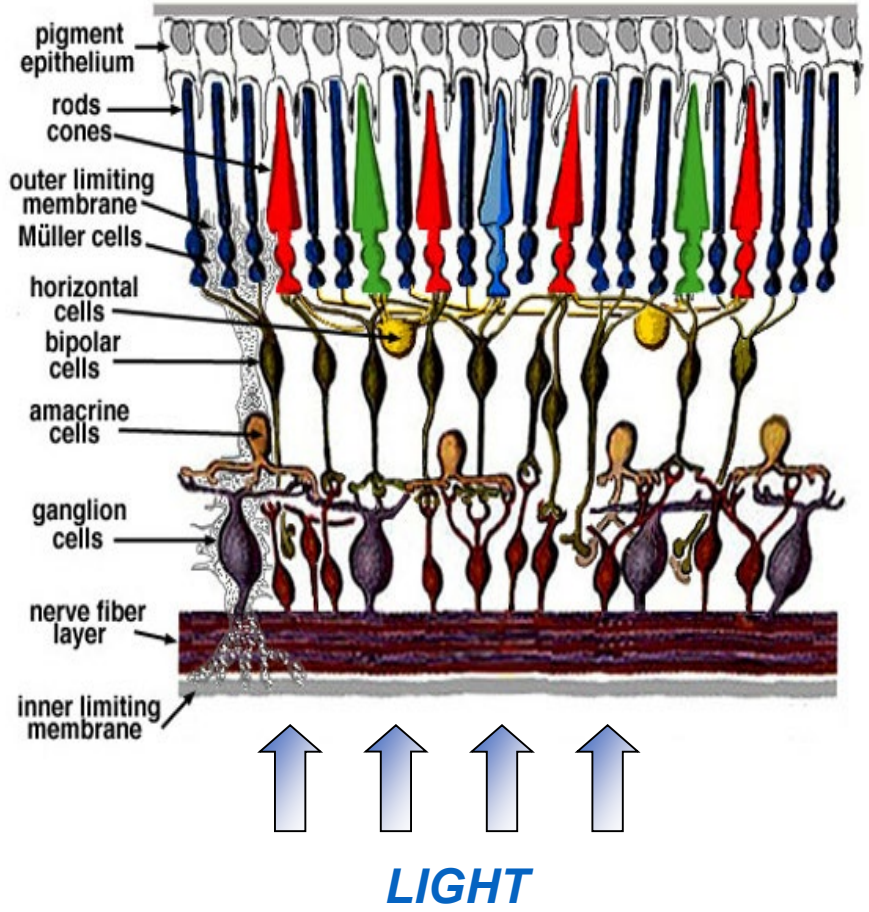
GANGLION CELL LAYER

INNER LIMITING MEMBRANE

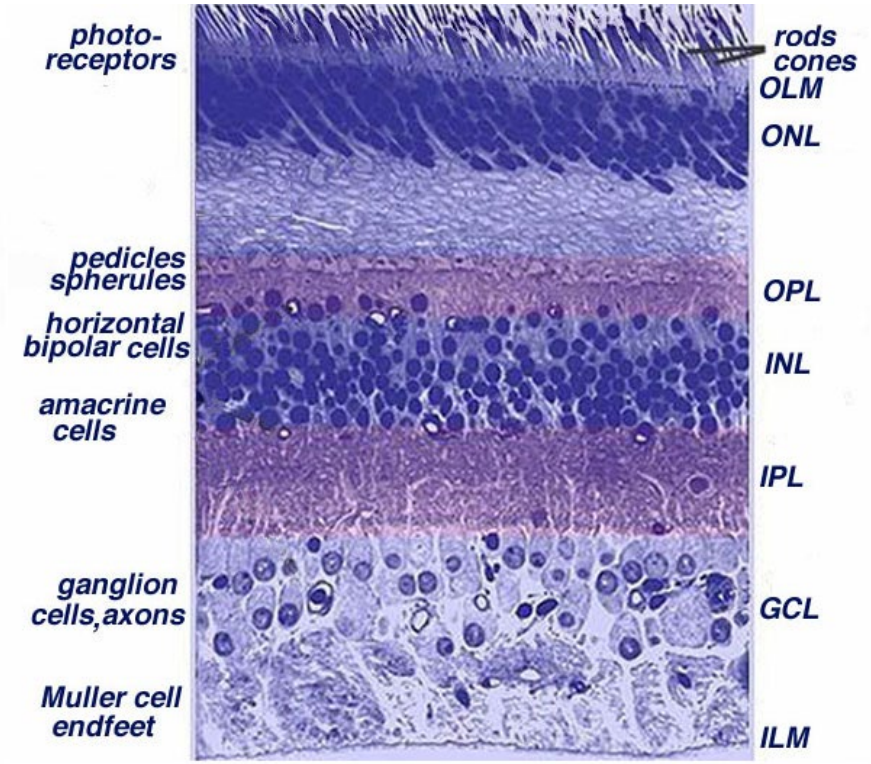
"Plexiform": weblike or complex

Retina: a light sensitive part of the CNS

Schematic vertical section

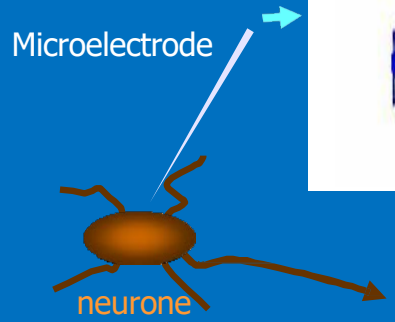


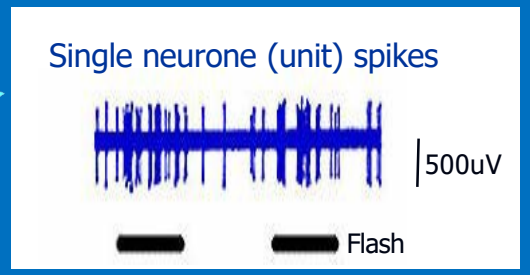
Light microscopic vertical section

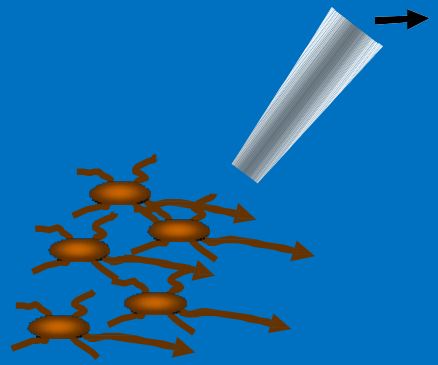


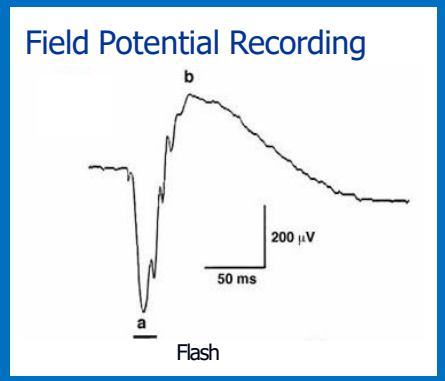
Electrophysiological recording methods

Extracellular recordings



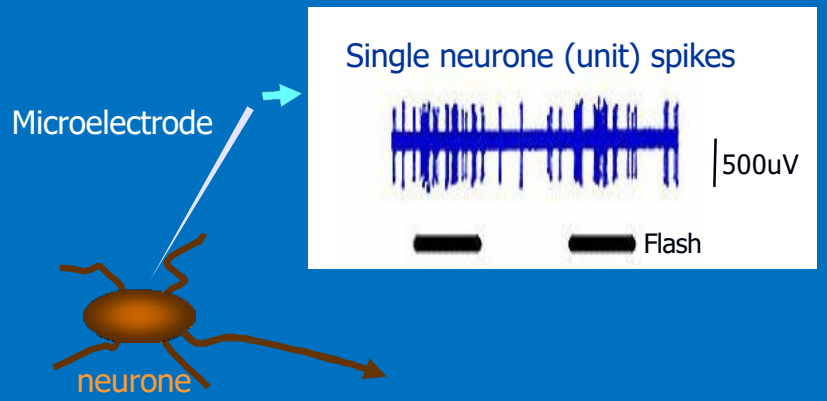


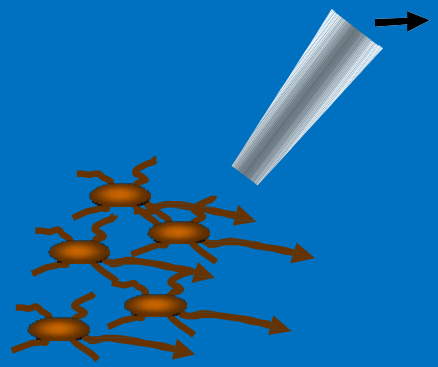


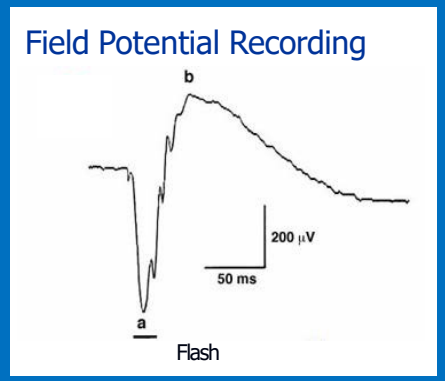


Electrophysiological recording methods

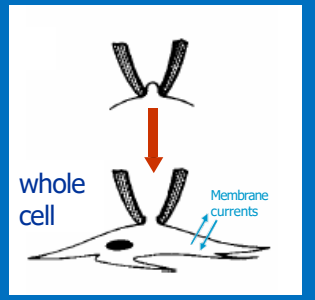
Extracellular recordings

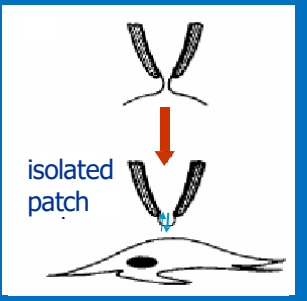






Whole cell (Patch clamp) recordings





Patch clamping can use:

(1) **Voltage clamp** technique in which the voltage across the cell membrane is controlled by the experimenter and the resulting currents are recorded.

(2) **Current clamp** technique in which the current passing across the membrane is controlled by the experimenter and the resulting changes in voltage are recorded, generally as action potentials.

Start at the retinal output:

RETINAL GANGLION CELLS

Common primate retinal ganglion cells

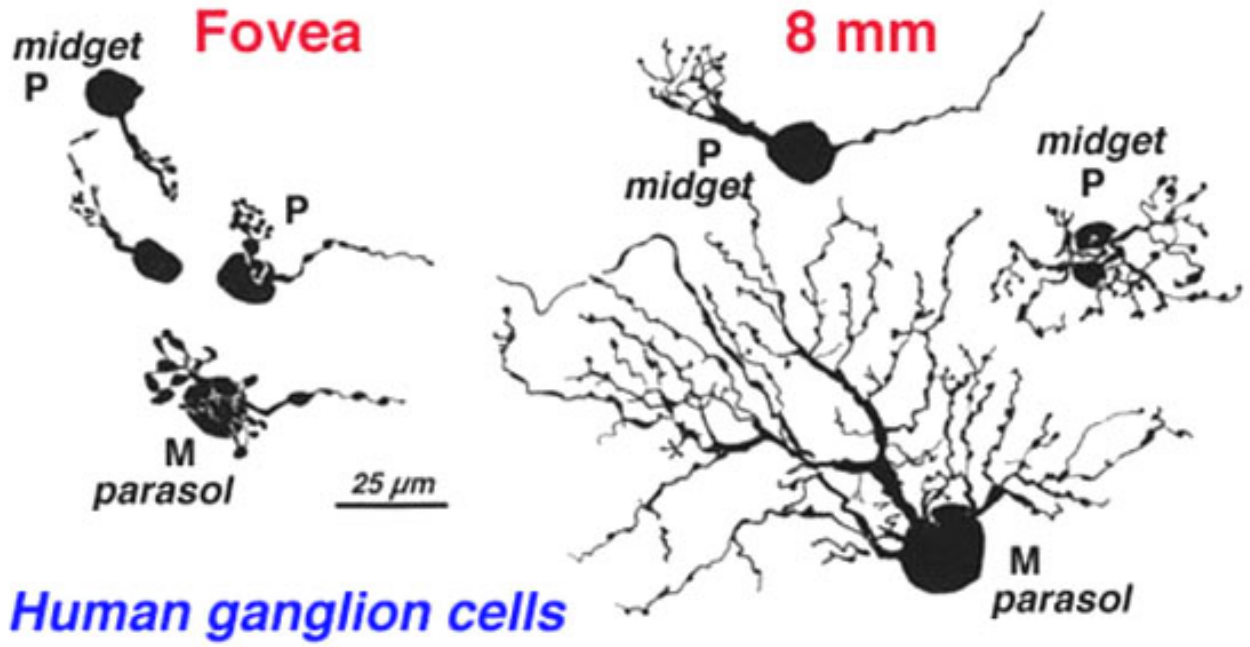
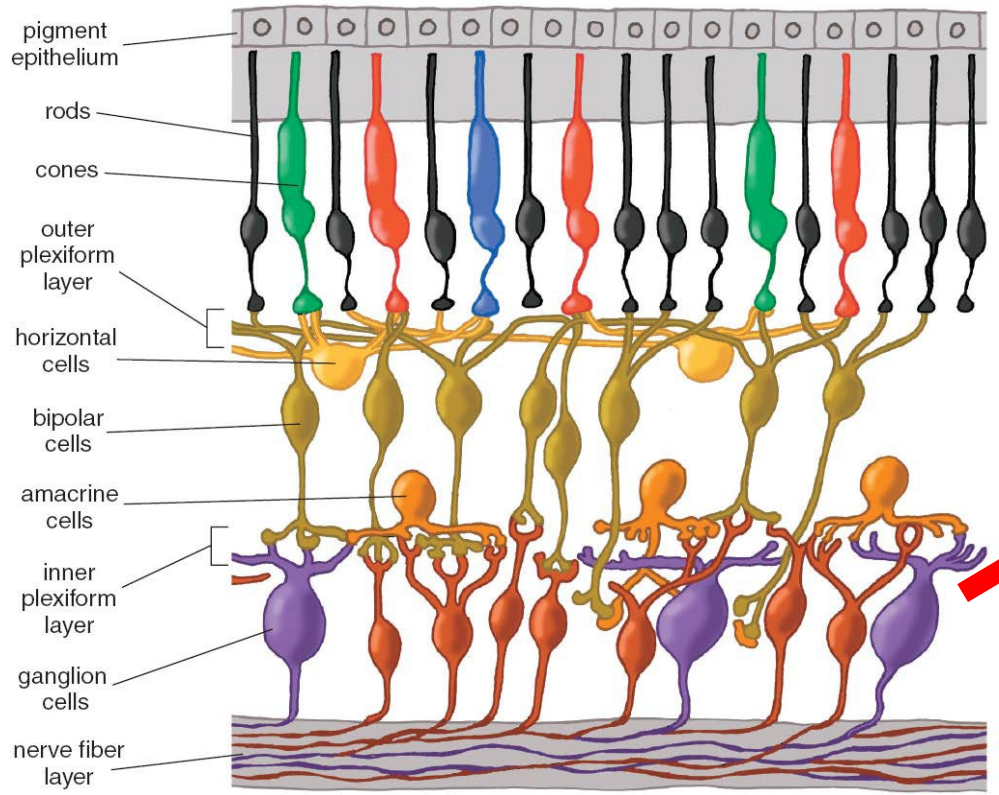
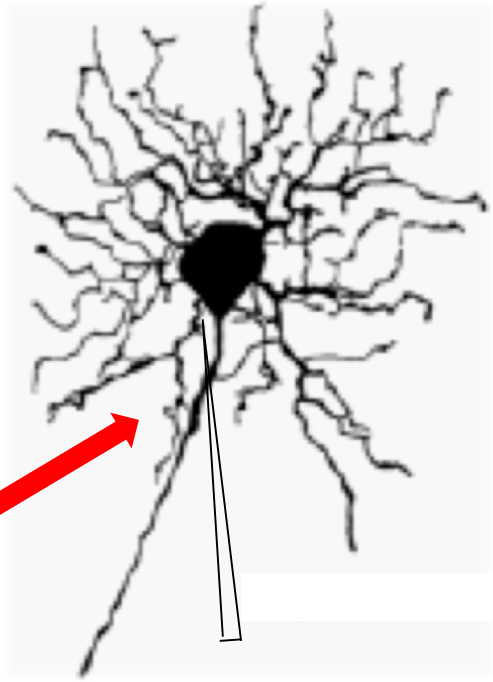


Fig. 19. Ganglion cell types involved in geniculate-striate pathways of primate retina.

Recording from retinal ganglion cells

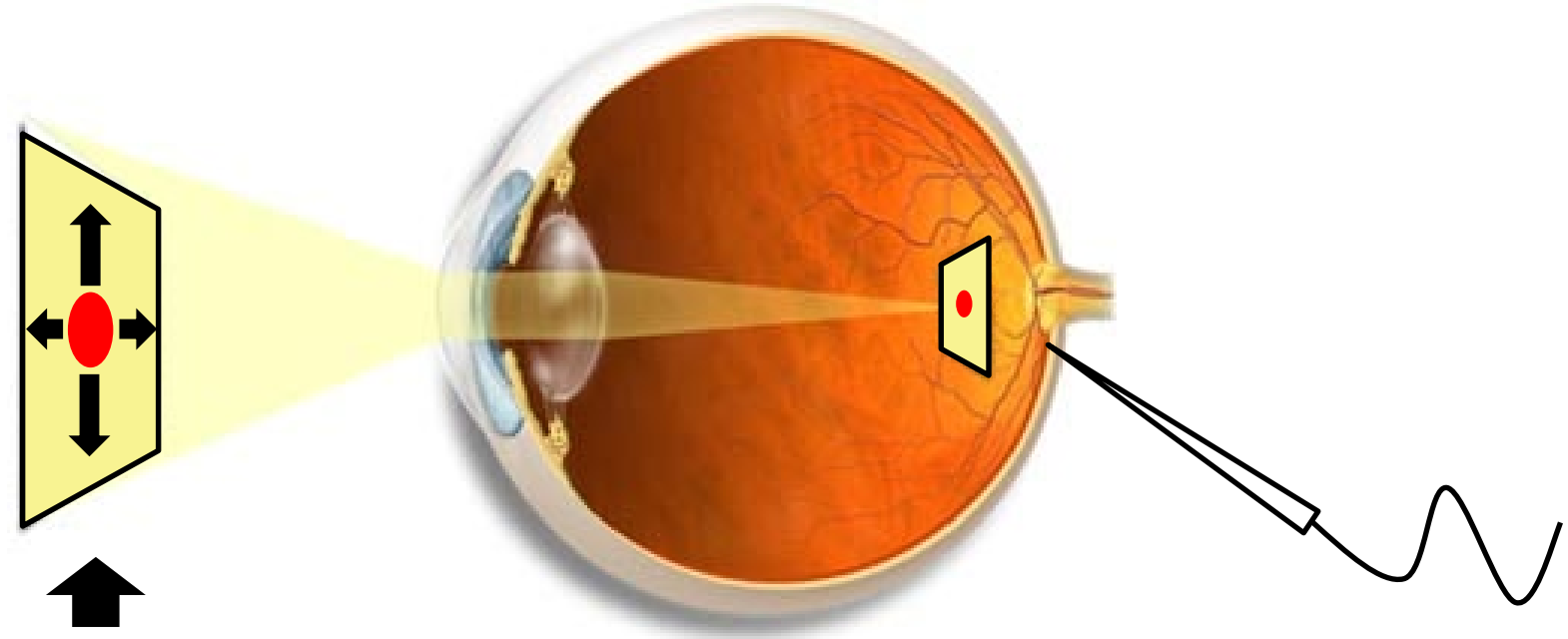




Stephen Kuffler 1950

Retinal ganglion cells: retinal output and relatively easy to record from

We can investigate what a cell encodes by recording its response to visual stimulation and so “map” its receptive field

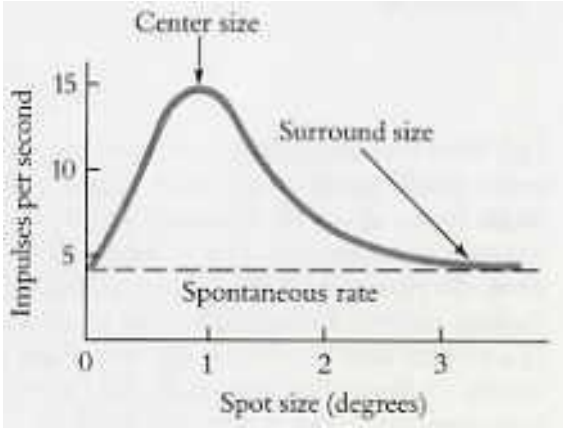


Find the area in visual space to which the cell responds.

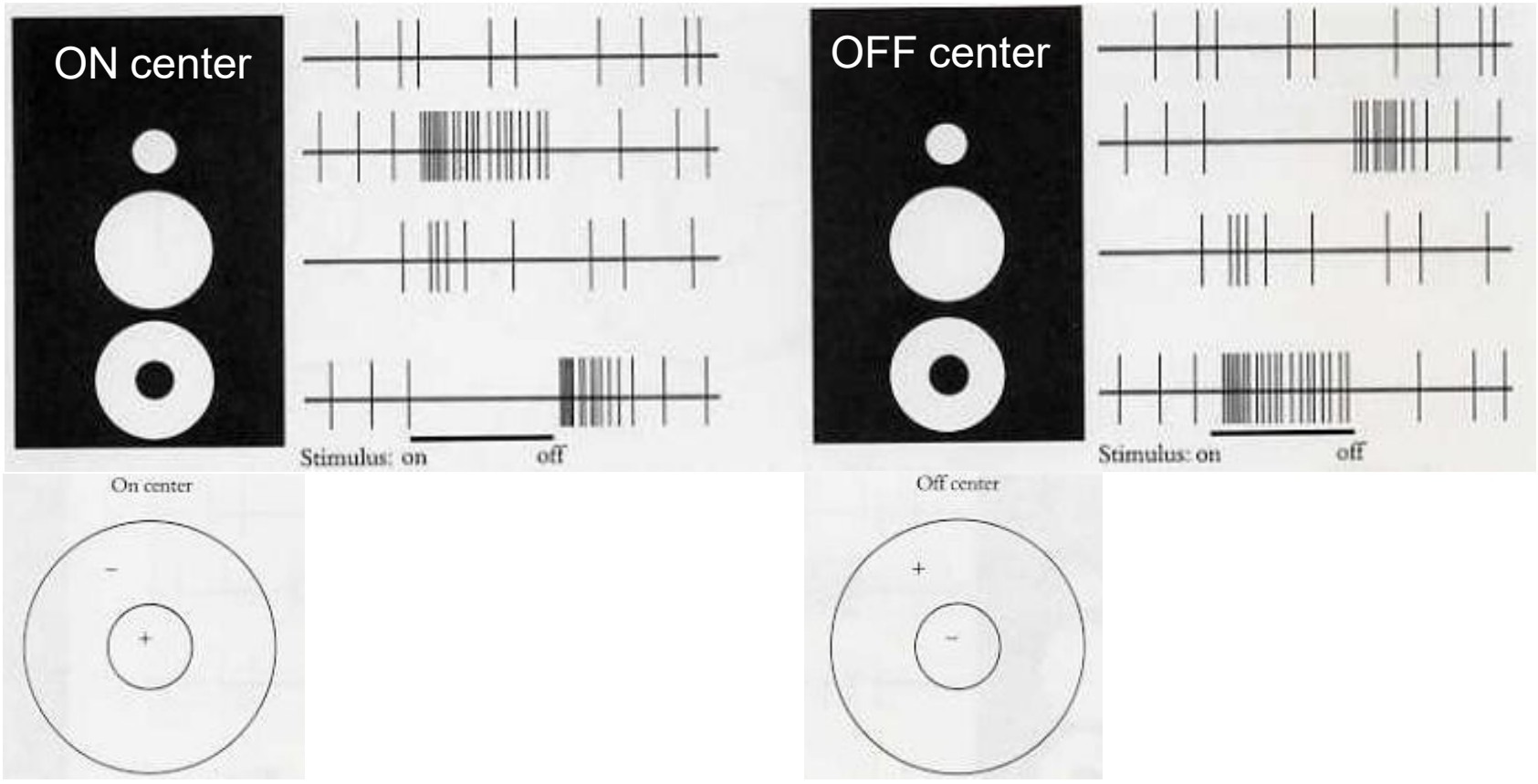
And then find what type of stimuli elicit a response in the cell.

Recordings

Spots and annuli.

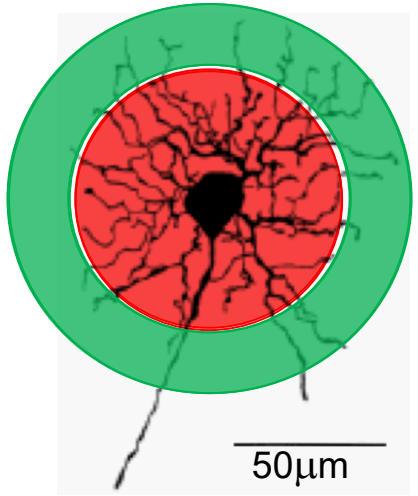


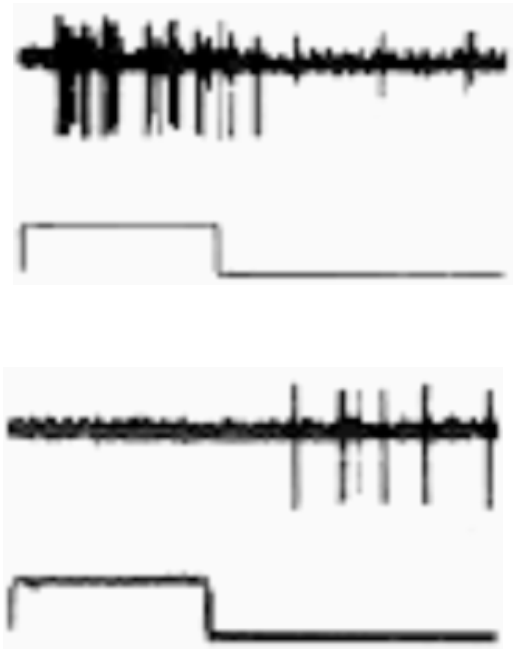
Stephen Kuffler 1950



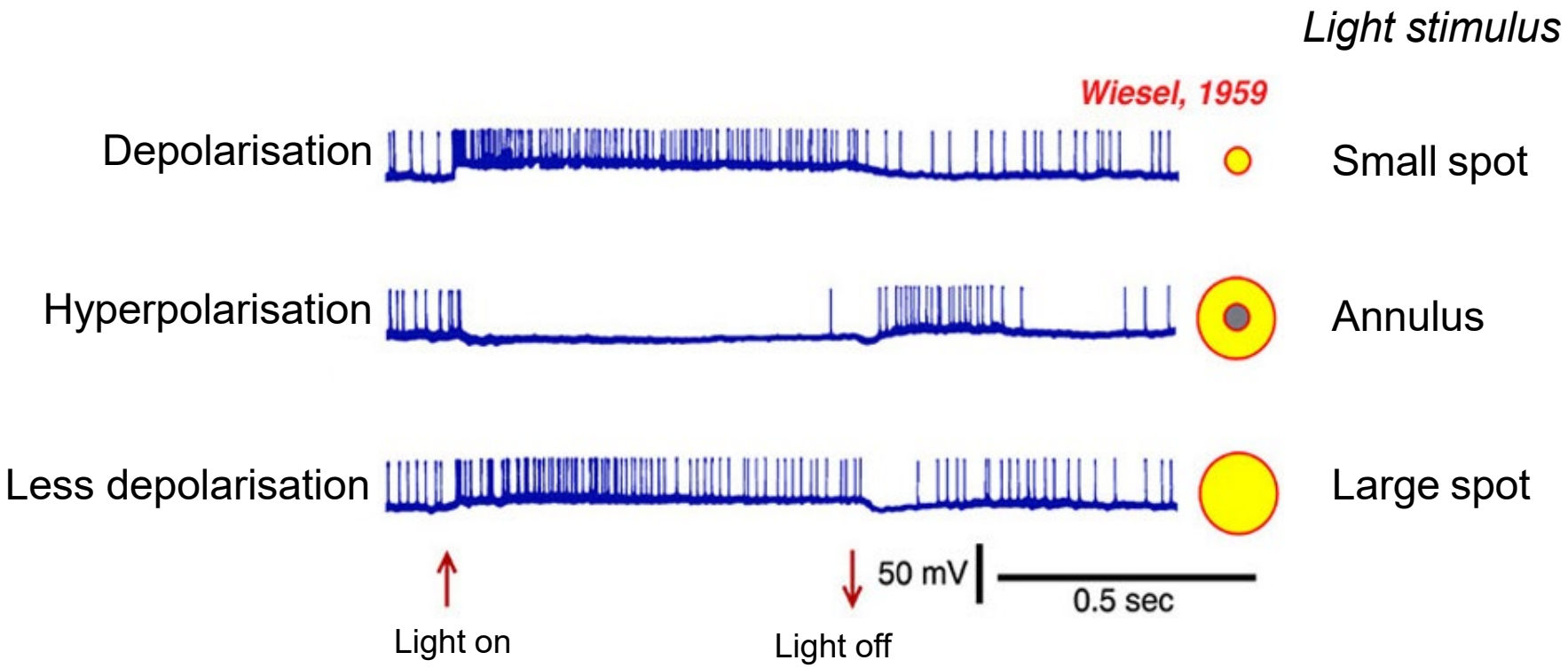
RGC receptive field

- **ON centre**
- **OFF surround**





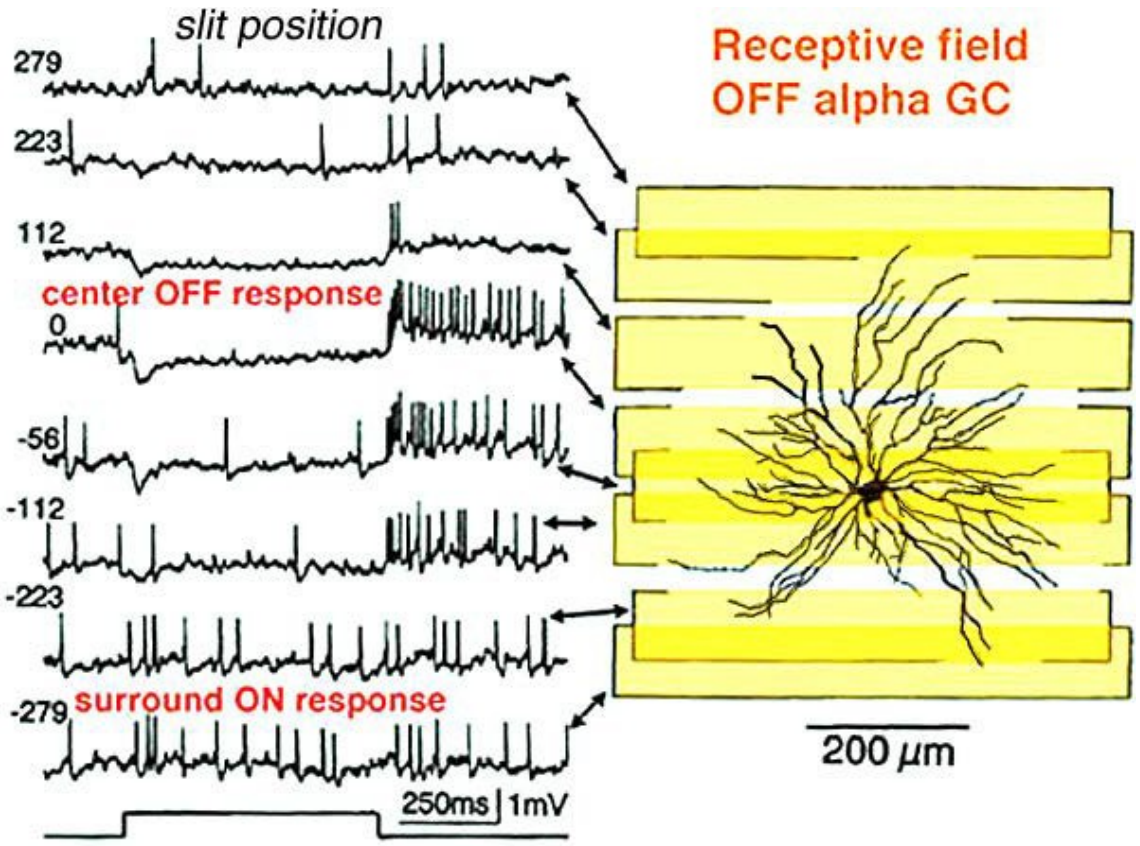
RGC receptive field



Retinal Ganglion Cell (RGC) output is a train of action potentials whose rate and pattern depends on the position and properties of the light stimulus.

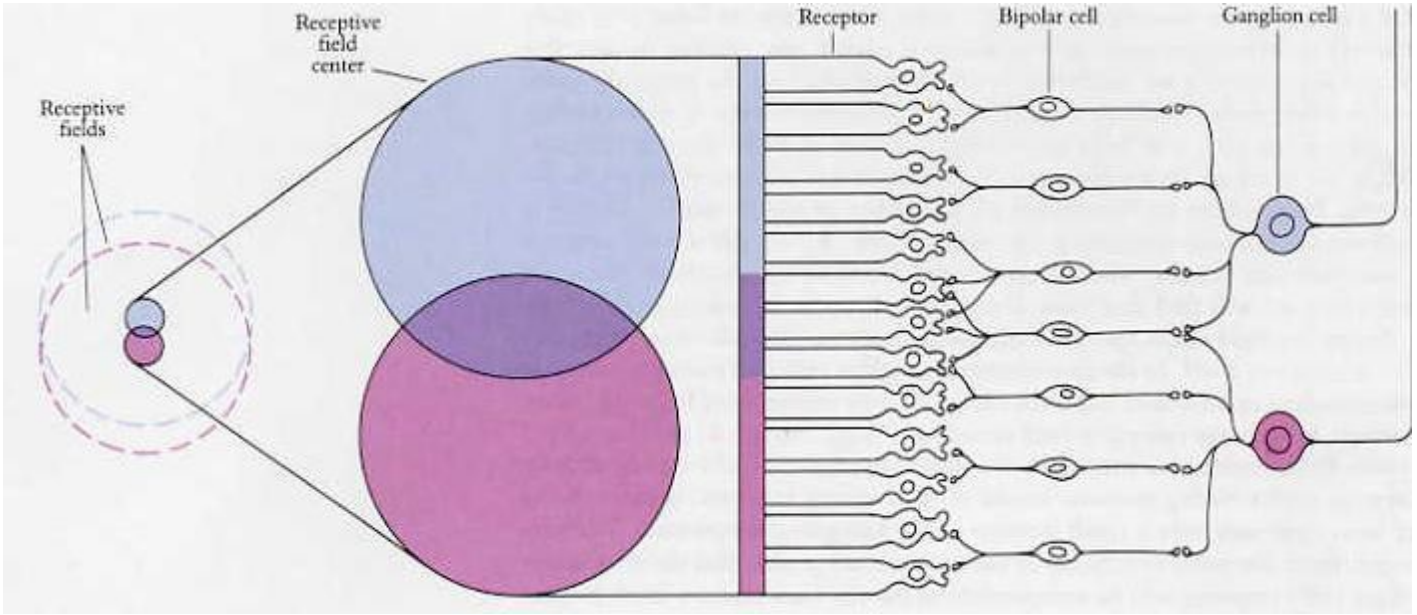
Center-surround inhibition prevents the lateral spread of activation. As a consequence, RGCs respond best to small spots of light.

RGC receptive field



Ganglion cell responses can also be elicited by bars of light

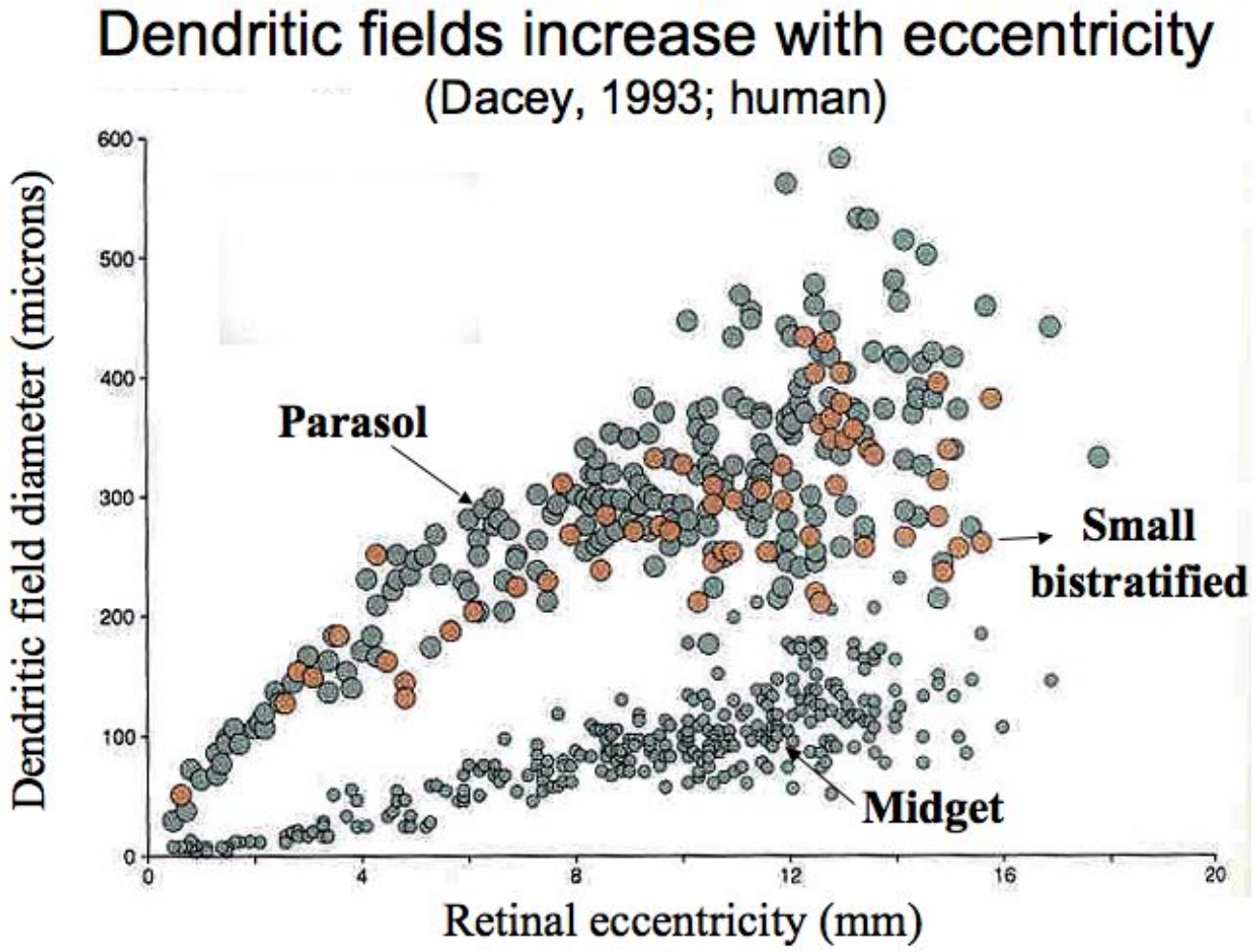
Overlapping RGC receptive fields



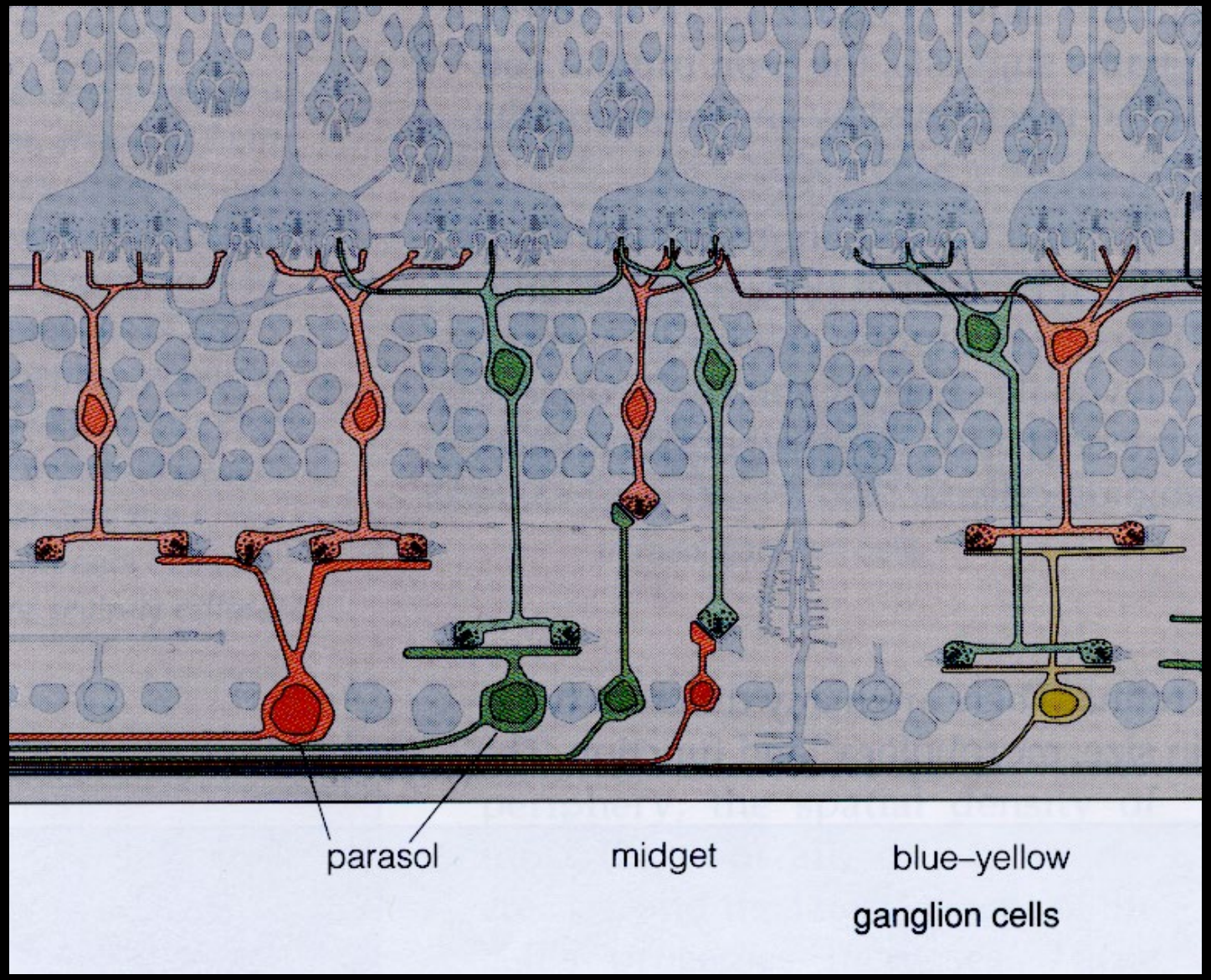
David Hubel

The size of receptive field differs from RGC to RGC. The RGCs in fovea have smallest centers for highest acuity. Larger receptive fields in the retinal periphery result in lower acuity. The size also depends on the type of ganglion cell.

Retinal eccentricity

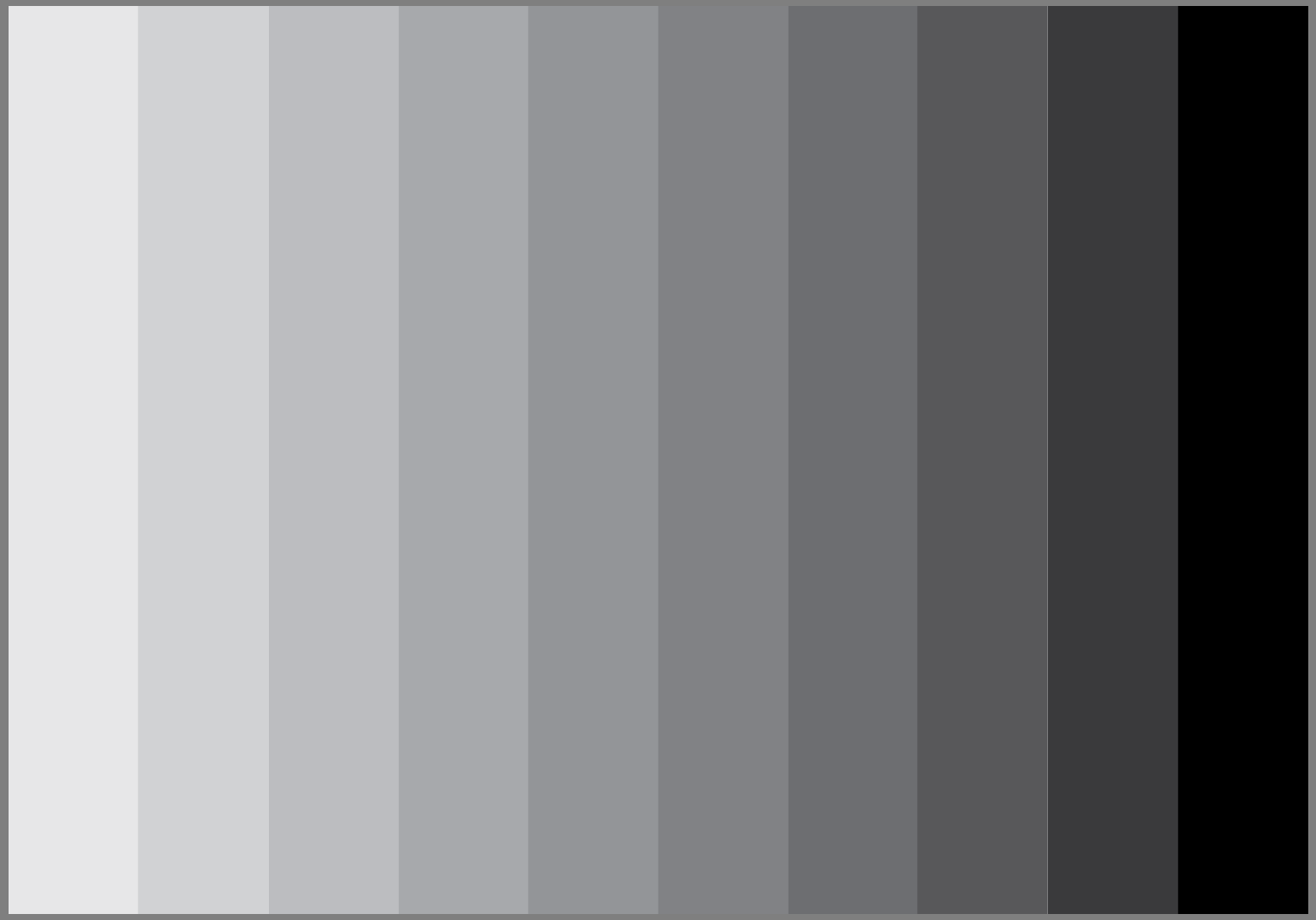


Ganglion cells

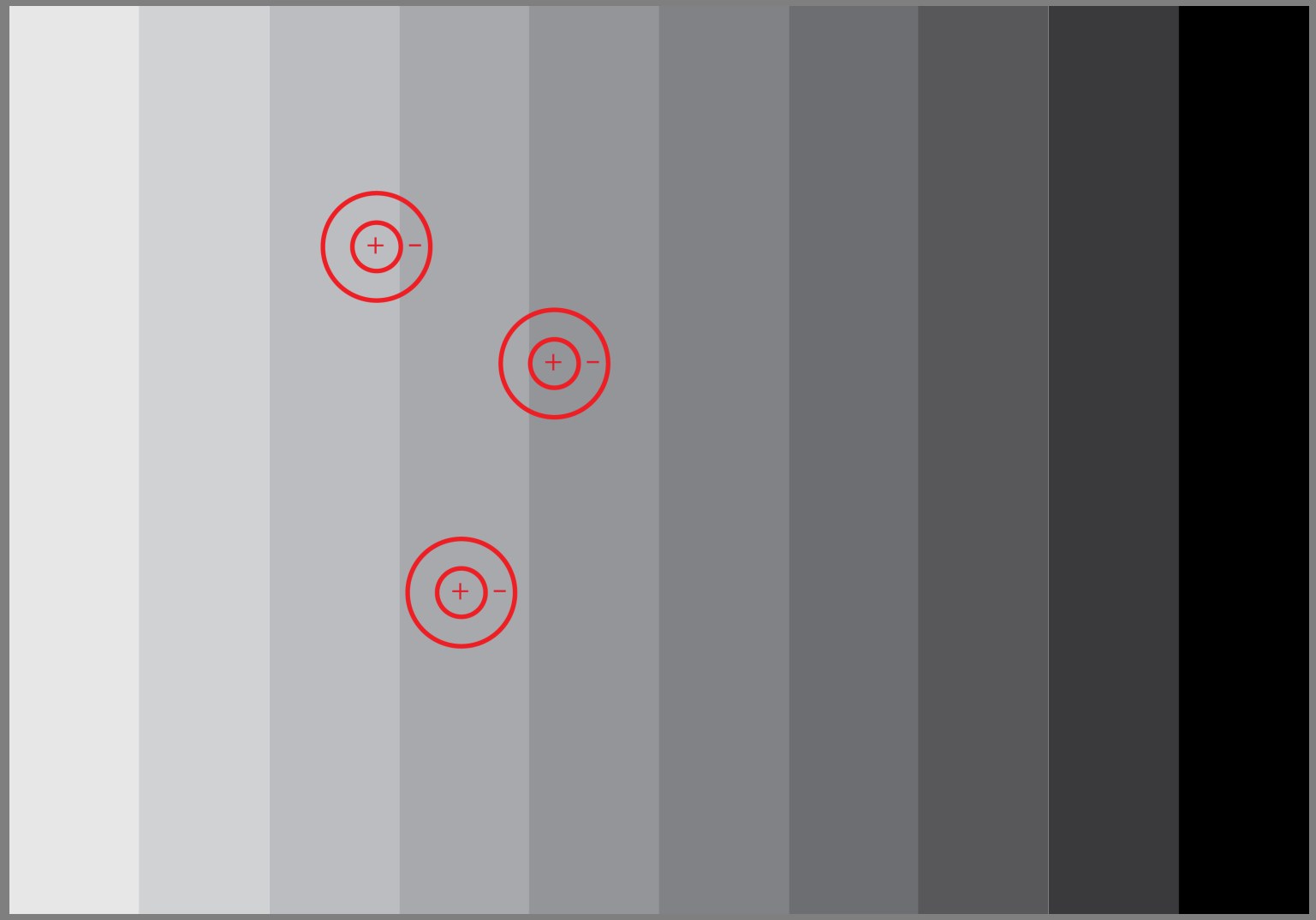


From Rodieck (1998)

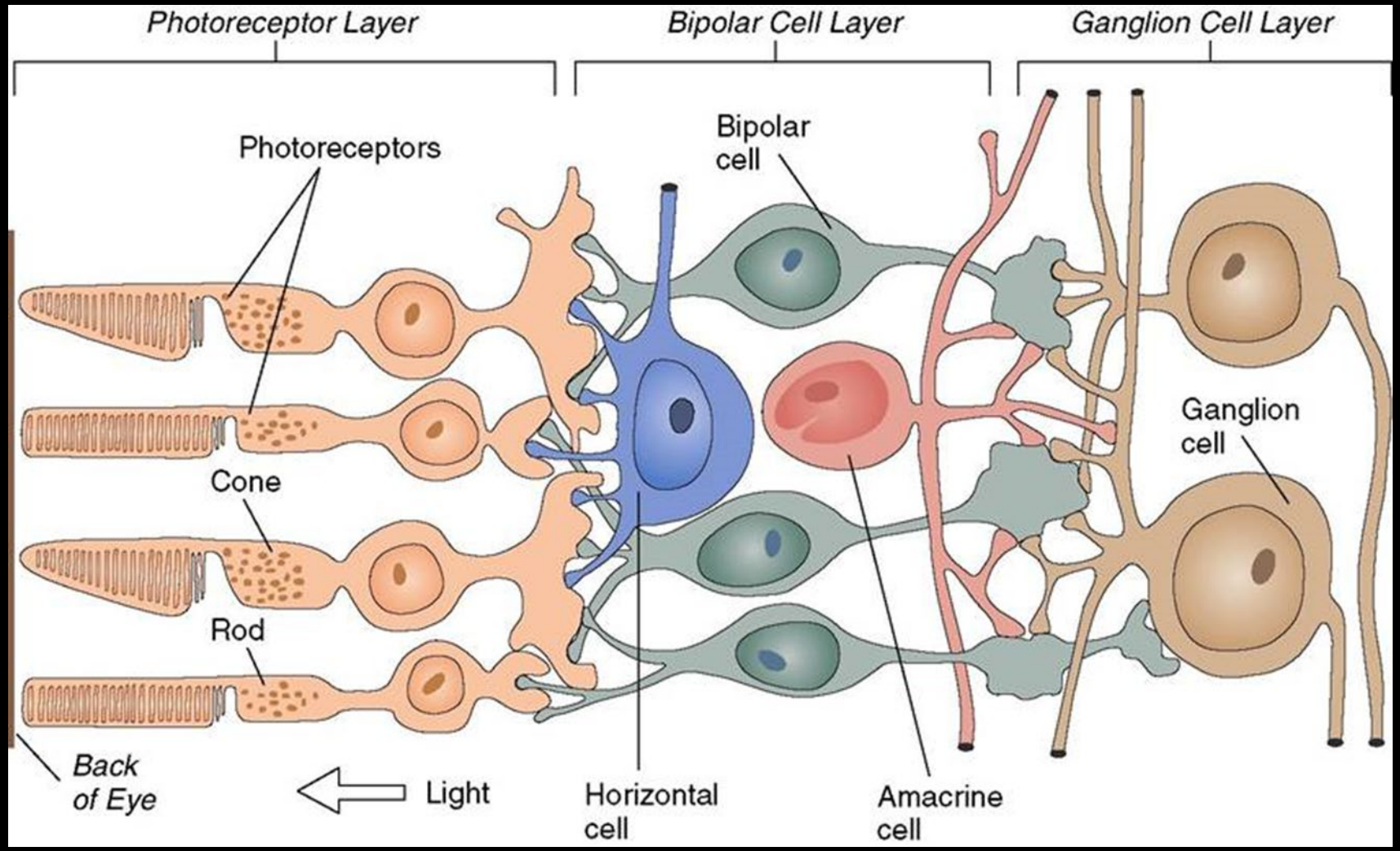
Mach band steps

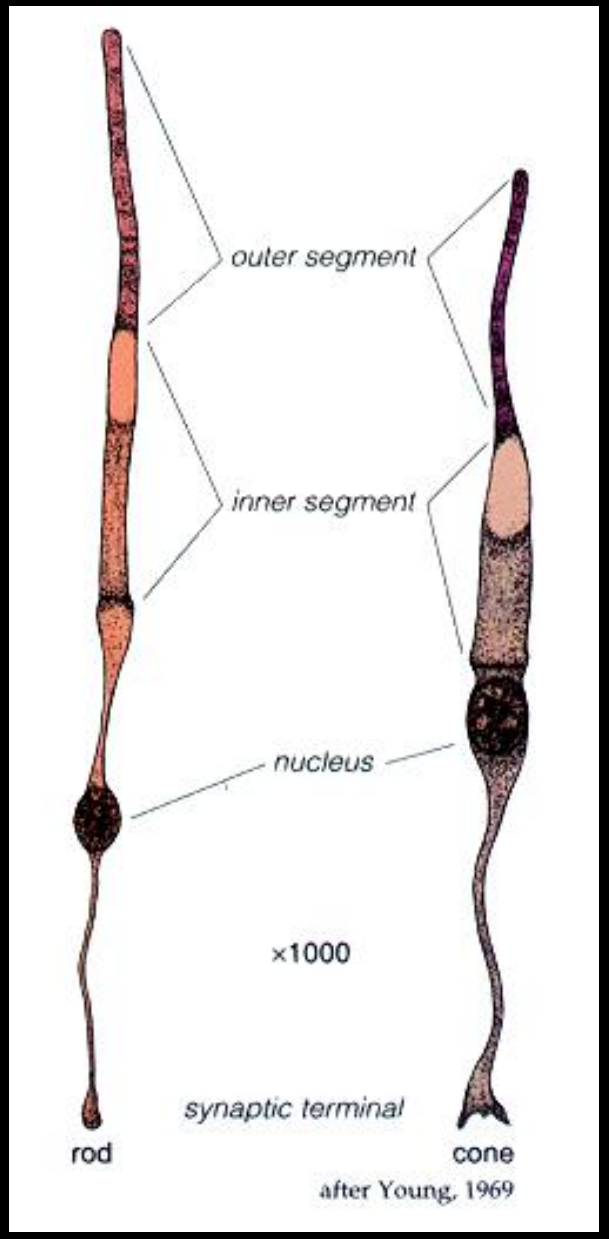


Mach band steps



How do signals from the photoreceptors produce the characteristic retinal ganglion cell responses?





PHOTORECEPTORS

- Rods
  - Achromatic night vision
  - 1 type
- Cones
  - Daytime, achromatic *and* chromatic vision
  - 3 types

Rod

Long-wavelength-sensitive (L) or "red" cone

Middle-wavelength-sensitive (M) or "green" cone

Short-wavelength-sensitive (S) or "blue" cone

Phototransduction

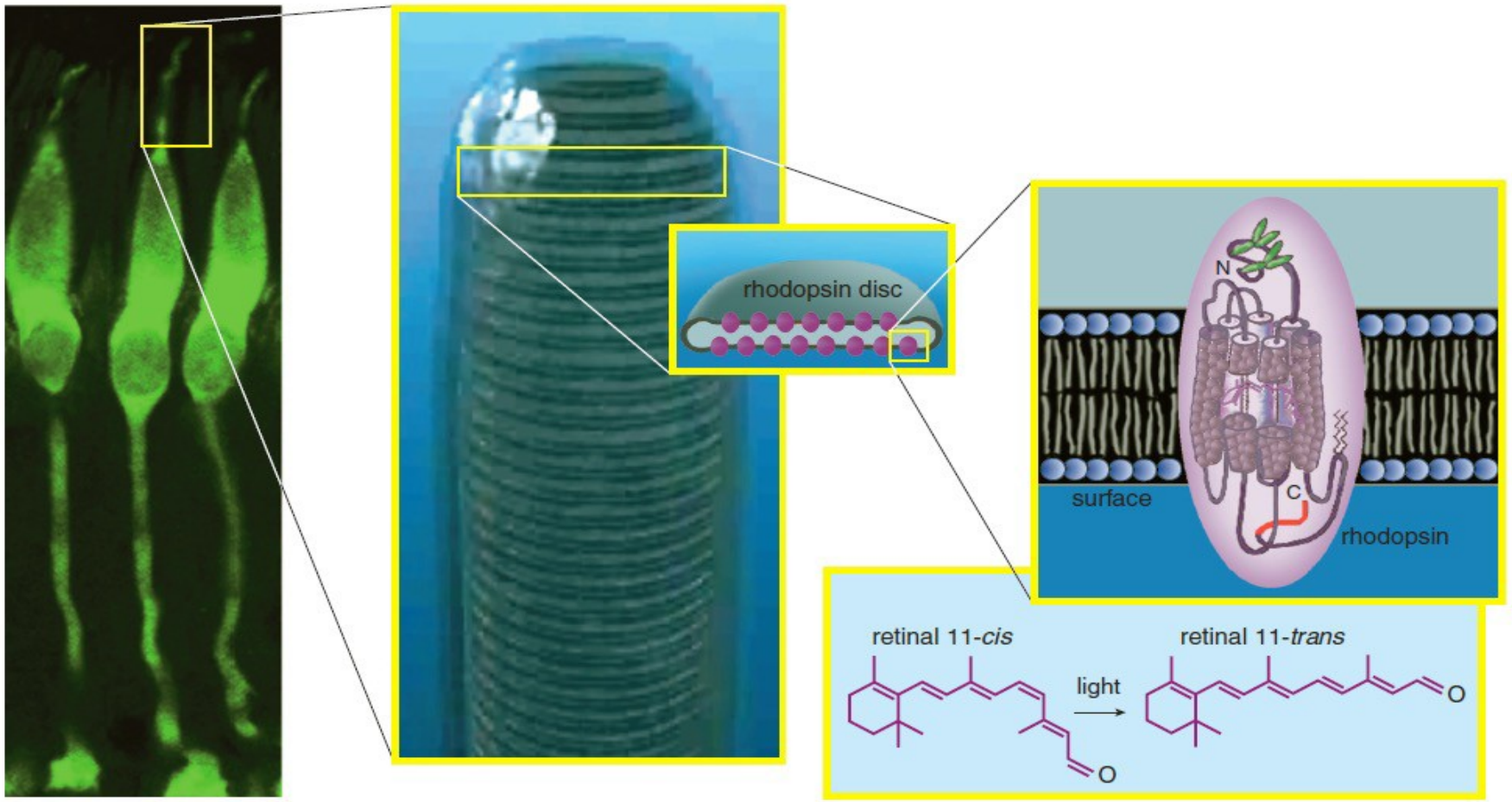
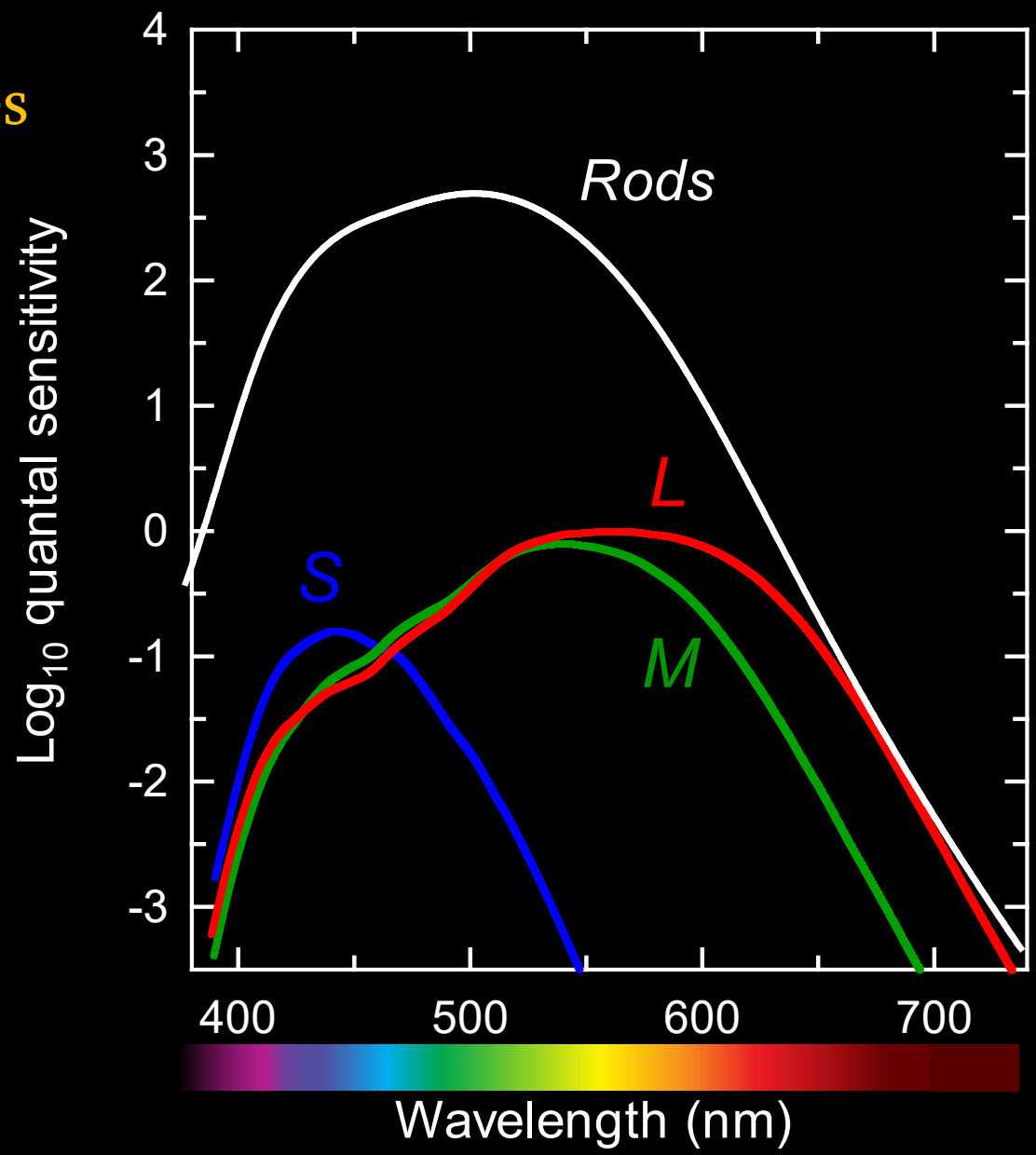


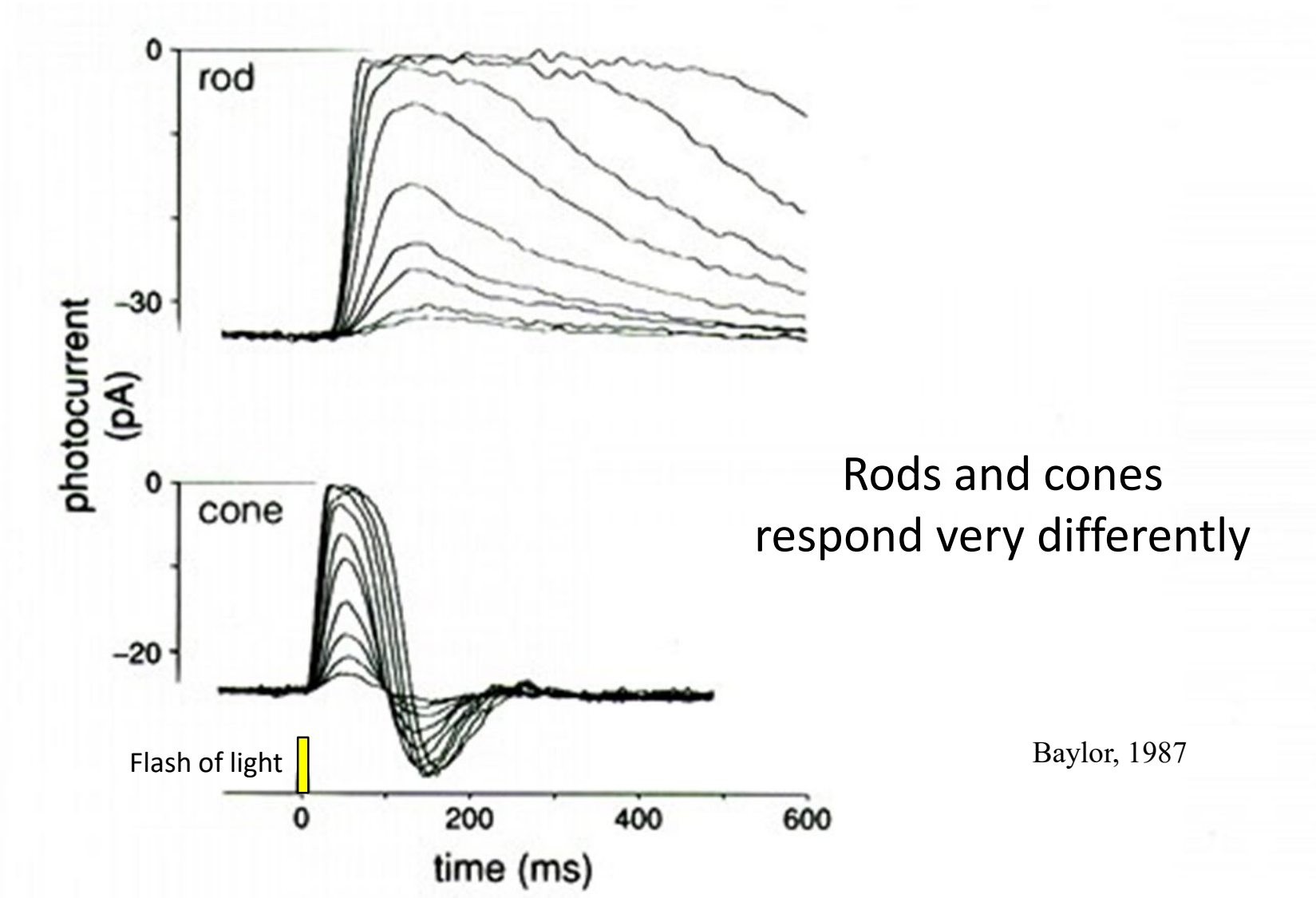
Figure 4. Cone photoreceptors from a monkey are stained with a fluorescent green dye *(left)*. When the outer segments of cones or rods are magnified further, stacked membrane disks are visible inside *(middle)*. The disks are studded with thousands of rhodopsin complexes. Each rhodopsin consists of a membrane-traversing protein with a retinal molecule embedded in its core *(right)*. When exposed to light, one of the bonds in the retinal molecule rotates, changing the shape of the protein *(lower right)*. (Middle photograph courtesy of Carlos Rozas.)

From: Kolb, H., *American Scientist*, 91 (2003)

Photoreceptor spectral sensitivities



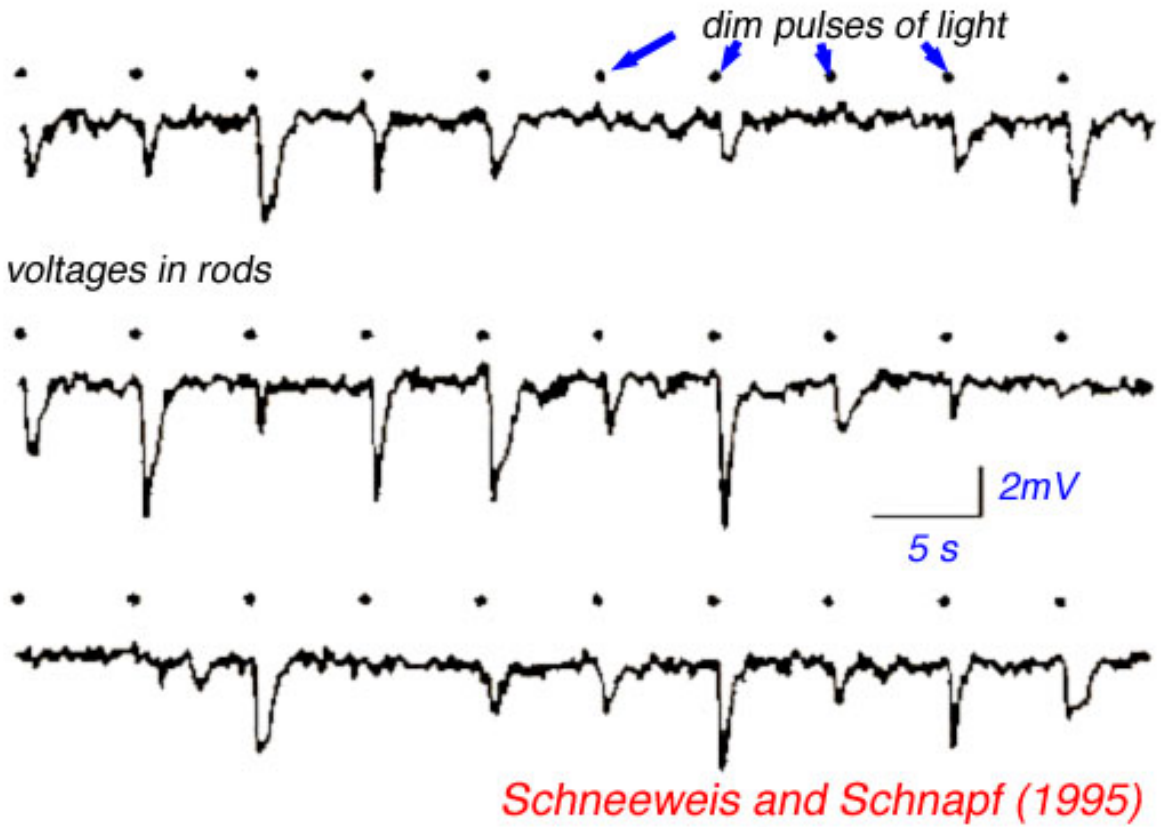
Photoreceptor current responses



Rods and cones
respond very differently

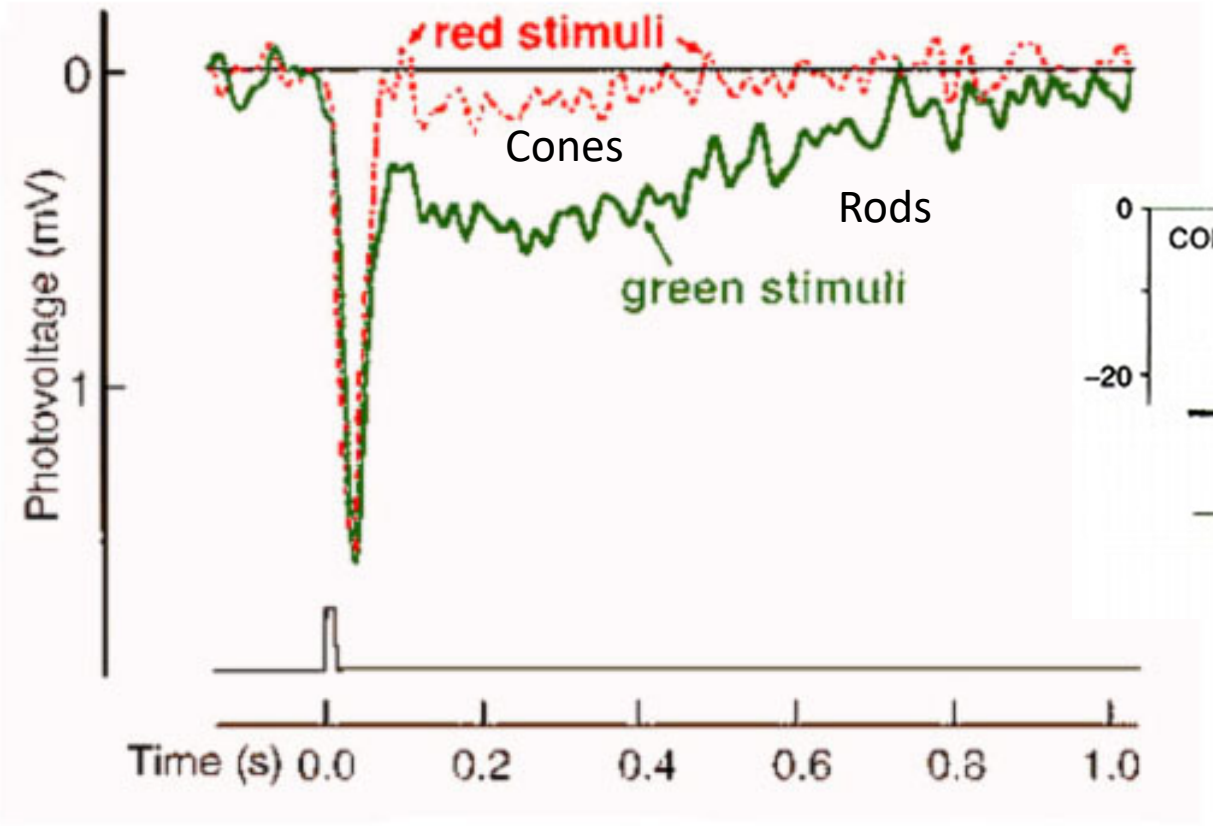
Baylor, 1987

Rod photoreceptor voltage responses



Photovoltages recorded in monkey rods with suction electrodes.
The granularity of response to dim light stimuli is evident.

Cone photoreceptor voltage responses (red stimuli)



Photocurrent response much slower

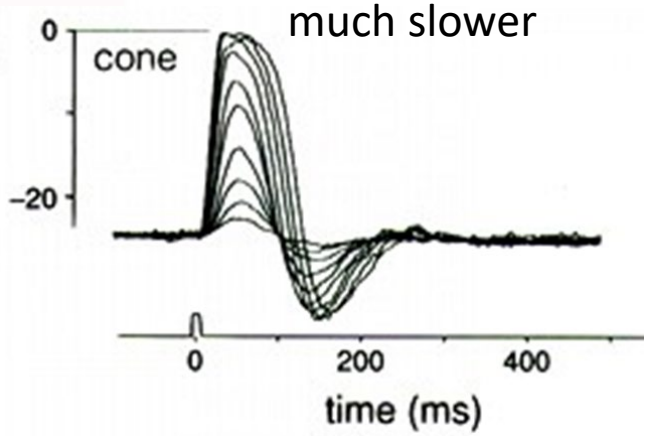
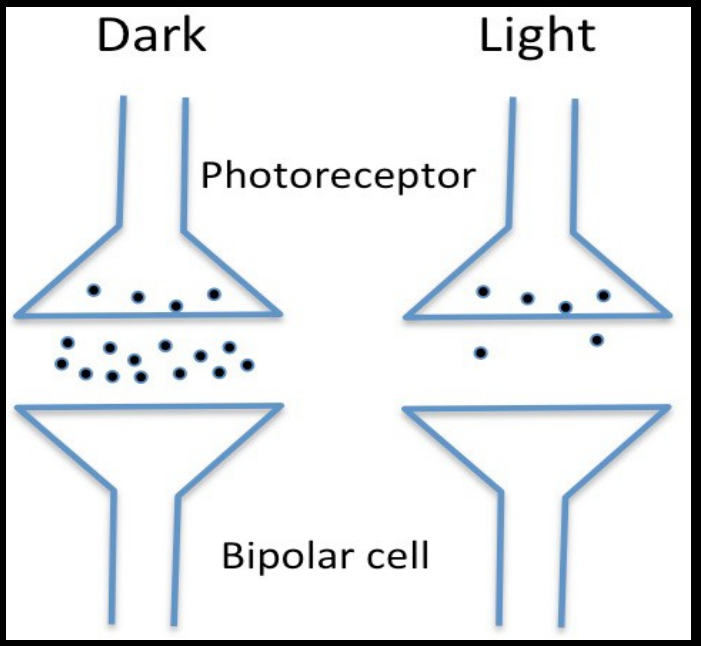


Fig. 30. Voltage recording from monkey cone with balanced red and green stiimuli. The green stimulus (solid trace) also evokes a slower hyperpolarizing phase after the initial response which the red stimulus (dotted trace) does not. This latter electrical wave has the characteristics of a rod signal. Schneeweis and Schnapf, 1995.

Photoreceptor response to light



- In the dark (*i.e.* absence of light), photoreceptors have a depolarised cell membrane potential and are releasing their neurotransmitter (L-glutamate) continuously.

- Photoreceptors always respond to light **ON** with membrane potential hyperpolarisation: this results in a reduction of neurotransmitter release, which can be thought of as an "**OFF“** response

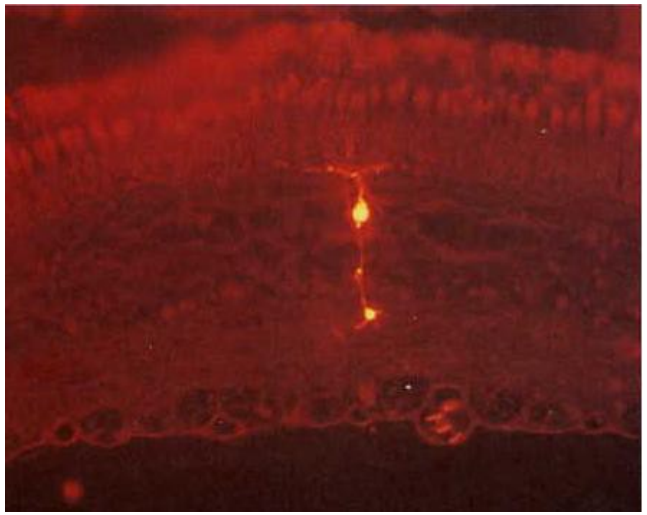
- Photoreceptors synapse onto bipolar cells and horizontal cells…

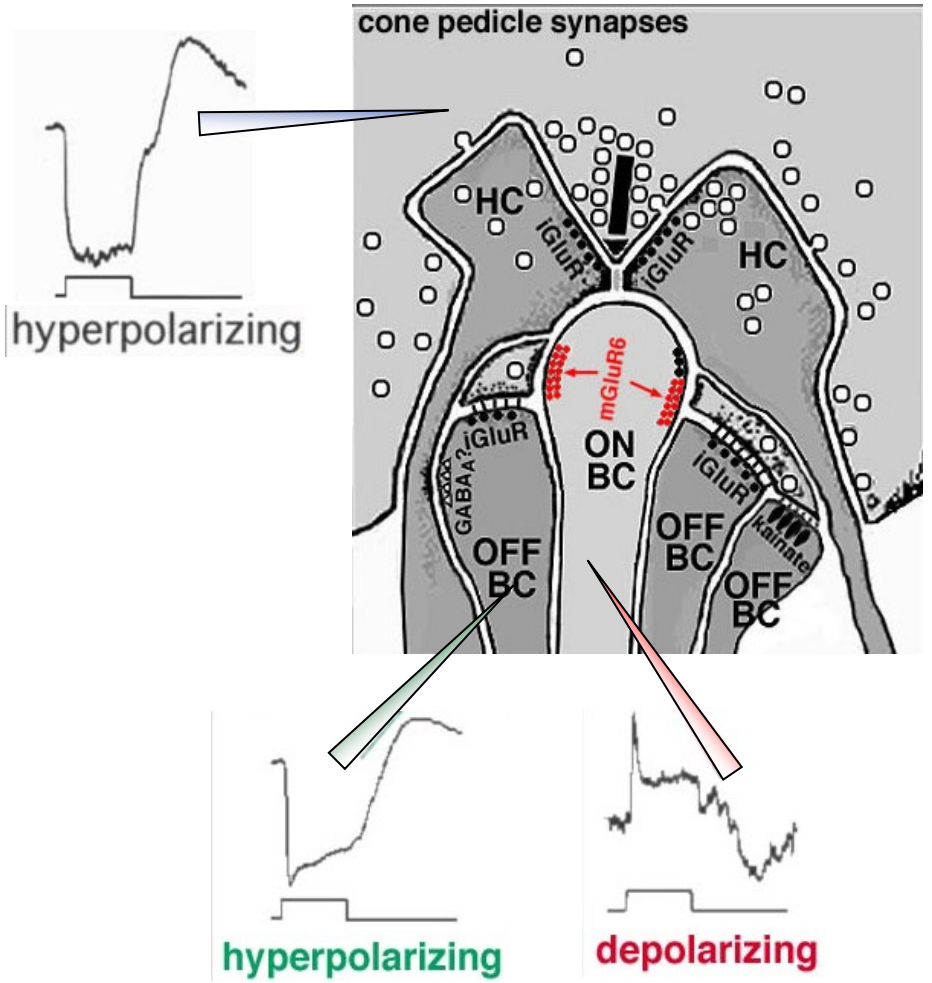
BIPOLAR CELLS

ON and OFF signals in response to light are produced at cone-cone bipolar synapses to produce both ON- and OFF-bipolar cell types.

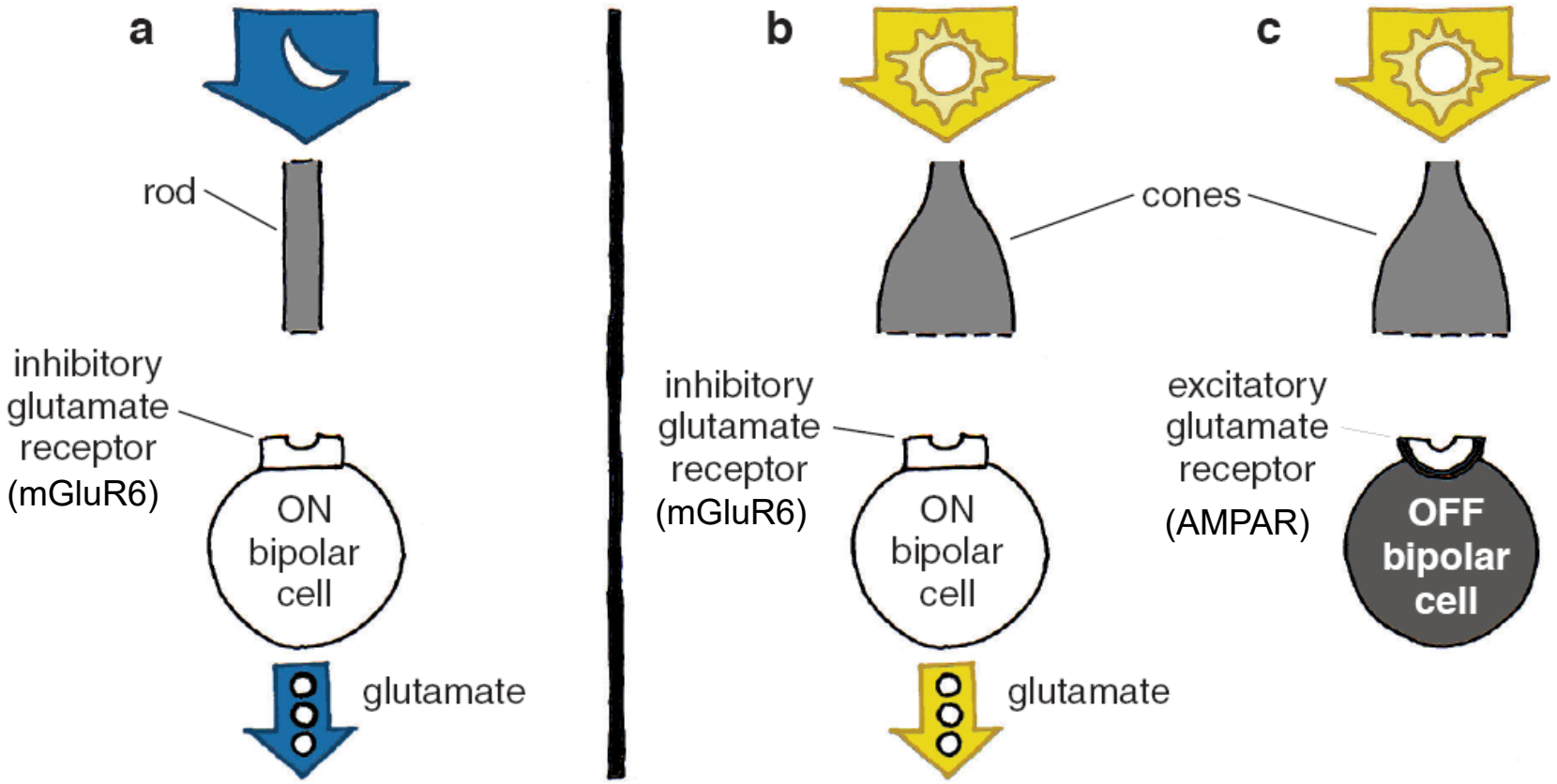
Cone bipolar cells

Connections of cone photoreceptors to ON- and OFF-cone bipolar Cells





ON and OFF bipolar cells

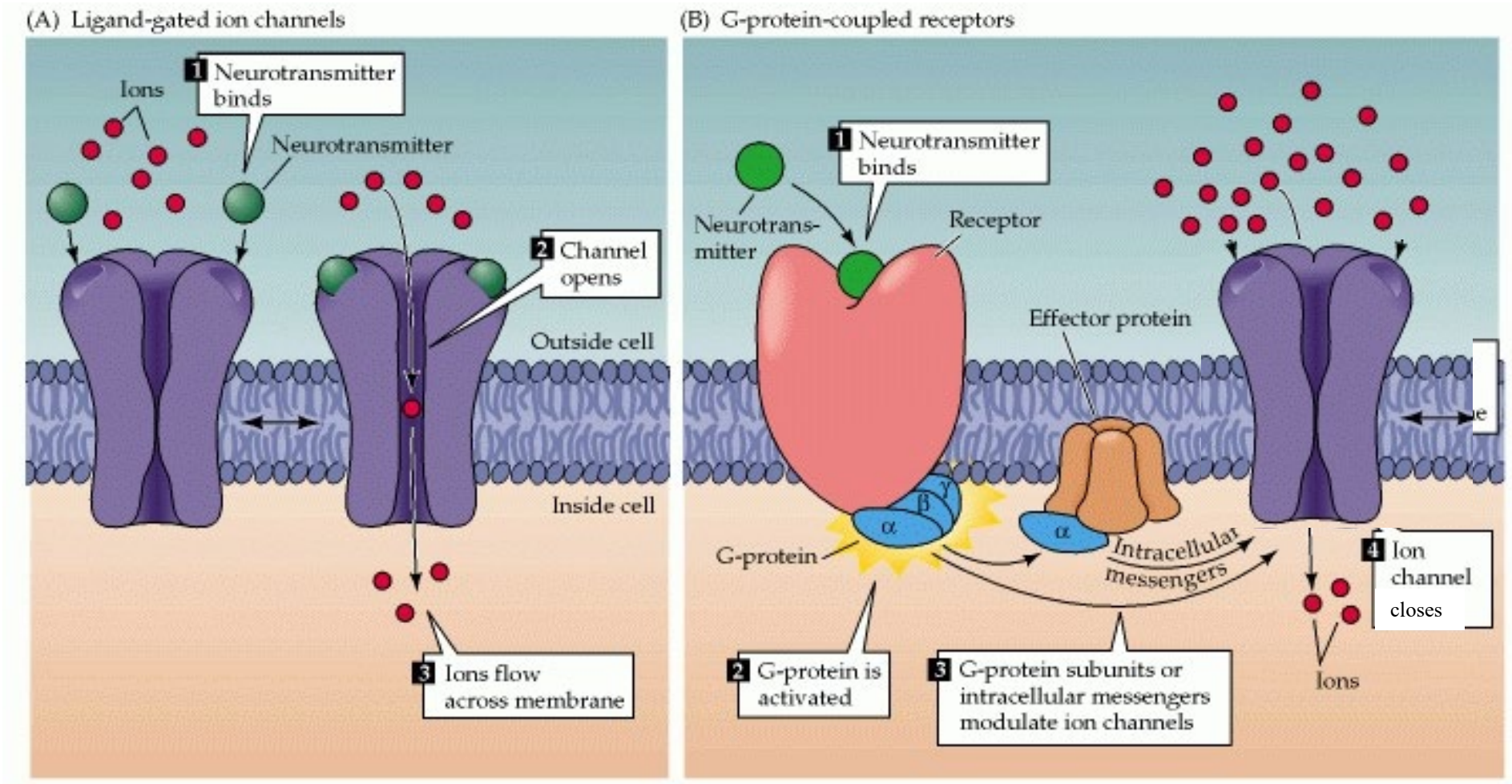


Photoreceptors release the transmitter glutamate in the dark, and stop releasing glutamate when stimulated by light.

Different bipolar cells respond differently to glutamate, depending on their type of glutamate receptor:

- ON bipolar cells have a depolarising receptive field (a, b)
- OFF bipolar cells have a hyperpolarising receptive field (c).

ON and OFF cone-cone bipolar synapses



(AMPAR)

α-amino-3-hydroxy-5-methyl-4-isoxazole propionate

(mGluR6)

Image: Purves *et al.*, 2001

Bipolar cell types

L- and M-cone centres (red and green), and S-cone (blue).

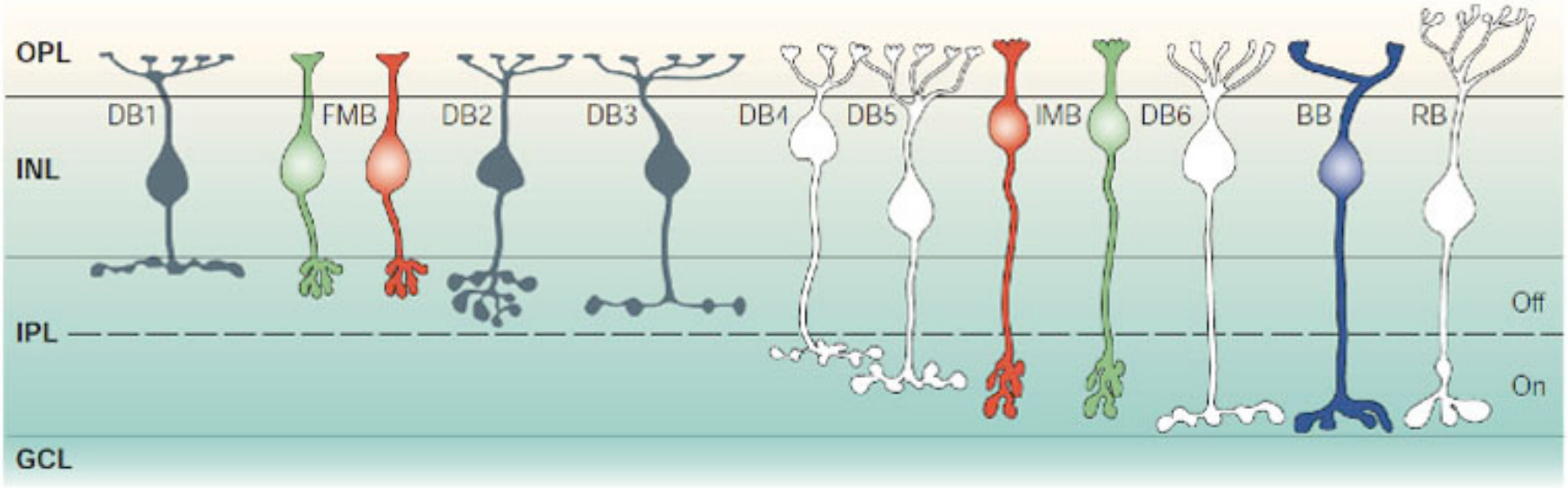


Figure 1: The major subtypes of bipolar cells of primate retina (Adapted from Wassle, 2004). Similar ones have been observed in the rats (Euler and Wassle, 1995), rabbit, cat (Kolb et al., 1981; Cohen and Sterling, 1990), monkey (Boycott and Wassle, 1991) and human (Kolb et al., 1992).

Credit: Webvision, Wässle, 2004

Macaque OFF bipolar cell types

Credit: Tsukamoto & Omi (2015)
Frontiers in Neuroanatomy

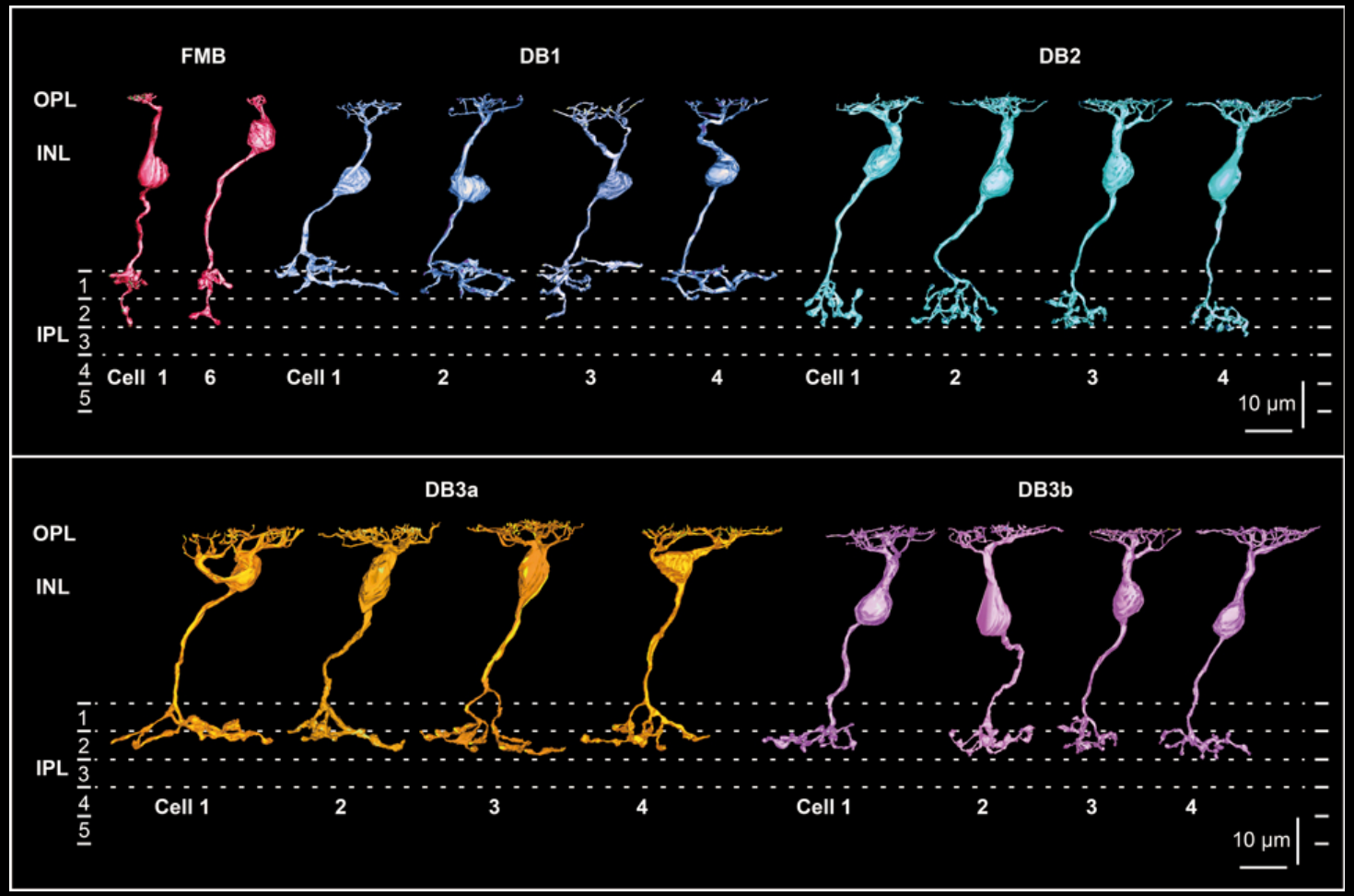
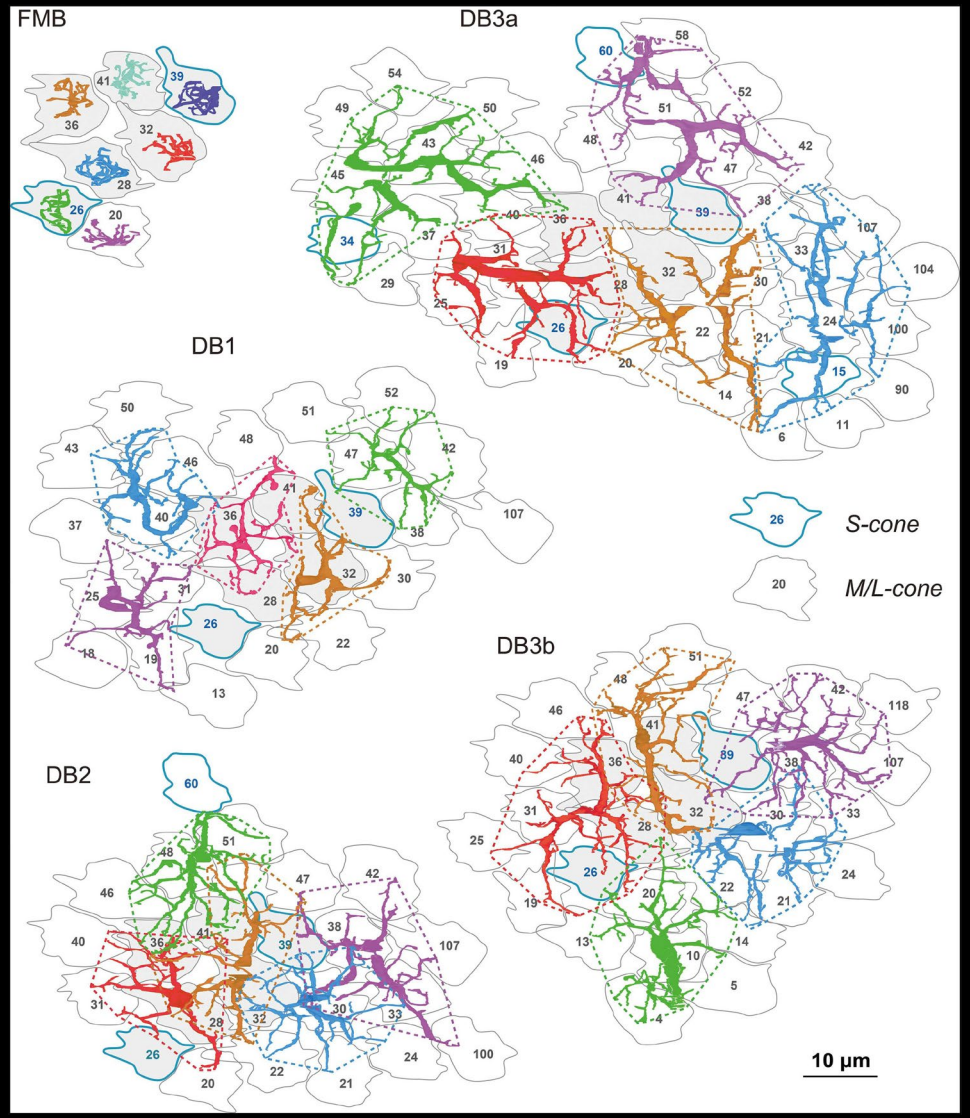


FIGURE 1 Morphology and stratification of FMB, DB1, DB2, DB3a, and DB3b types of OFF bipolar cells. FMB cell-1 and cell-6 (FMB-1 and FMB-6) are connected to M/L and S cones, respectively. Four cells (1-4) are displayed for each DB type. Each stratum of the IPL (1-5) is 6µm thick. Strata 1-2 comprise the OFF sublamina.

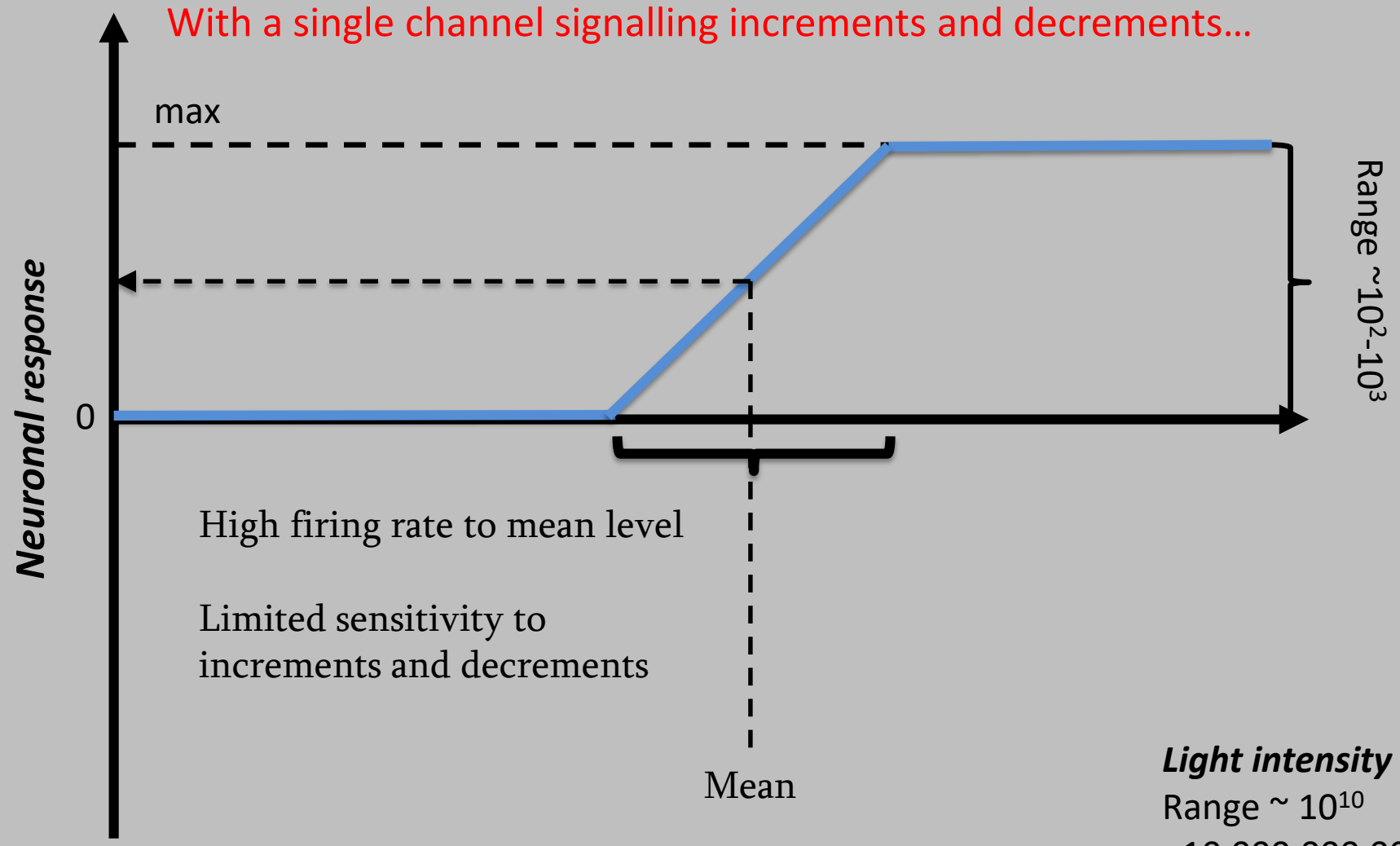
Macaque OFF bipolar cell types

Credit: Tsukamoto & Omi (2015)
Frontiers in Neuroanatomy

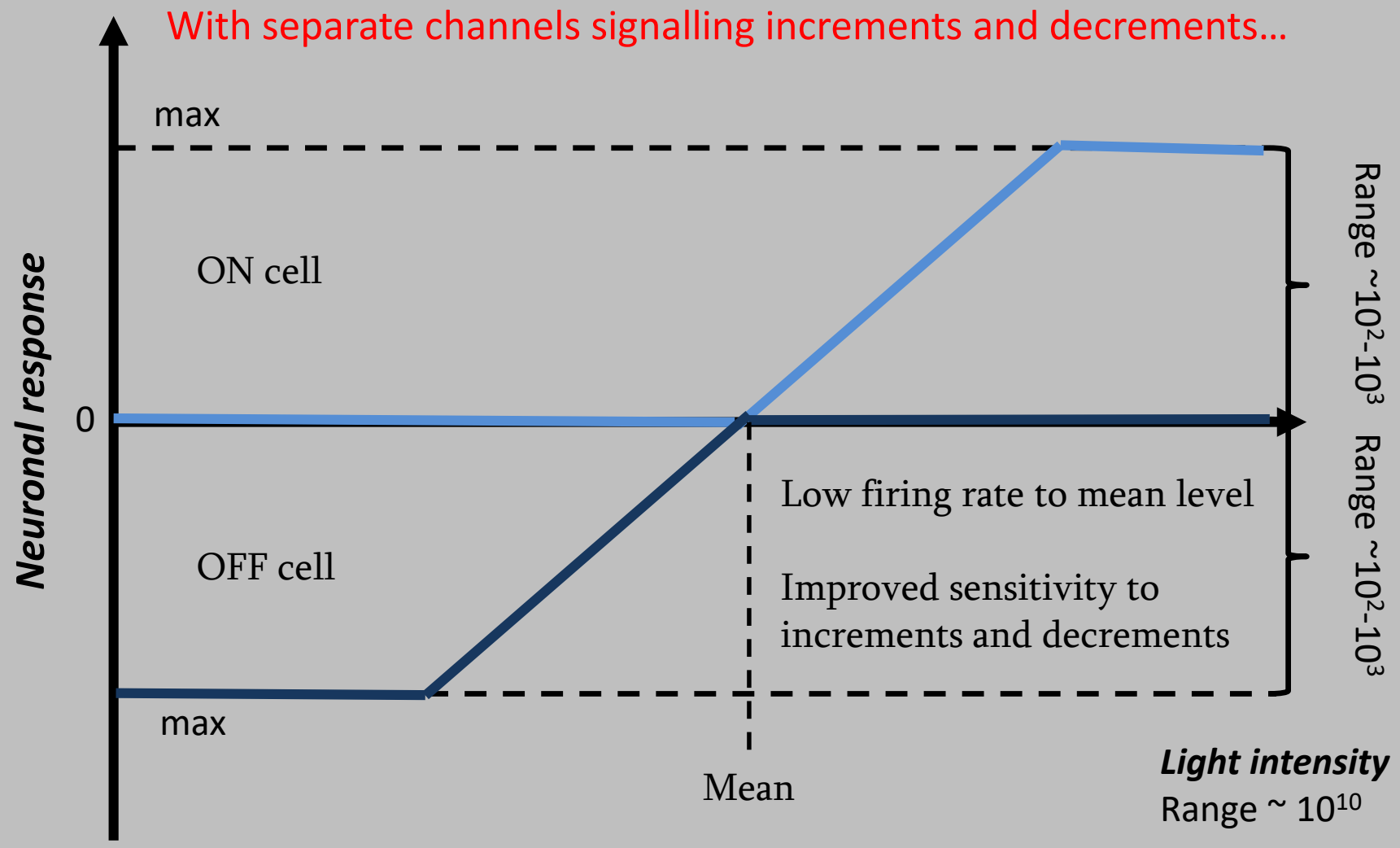
FIGURE 2 : Dendrites of each OFF bipolar cell type covering arrays of cone photoreceptor pedicles. The dendrites of seven (FMB) or five (DB) cells in each subgroup are shown in different colors for clarity. Cone pedicles are labelled by serial numbers and accordingly in the following figures. M/L-cones are labelled with black letters and S cones with blue letters and contours. Each type tiles an area of cone pedicles and most of each cone area is innervated by the dendrites of the five types of OFF bipolar cells. Six central pedicles (26, 28, 32, 36, 39, and 41) are designated in gray for reference.



Why have ON and OFF channels?

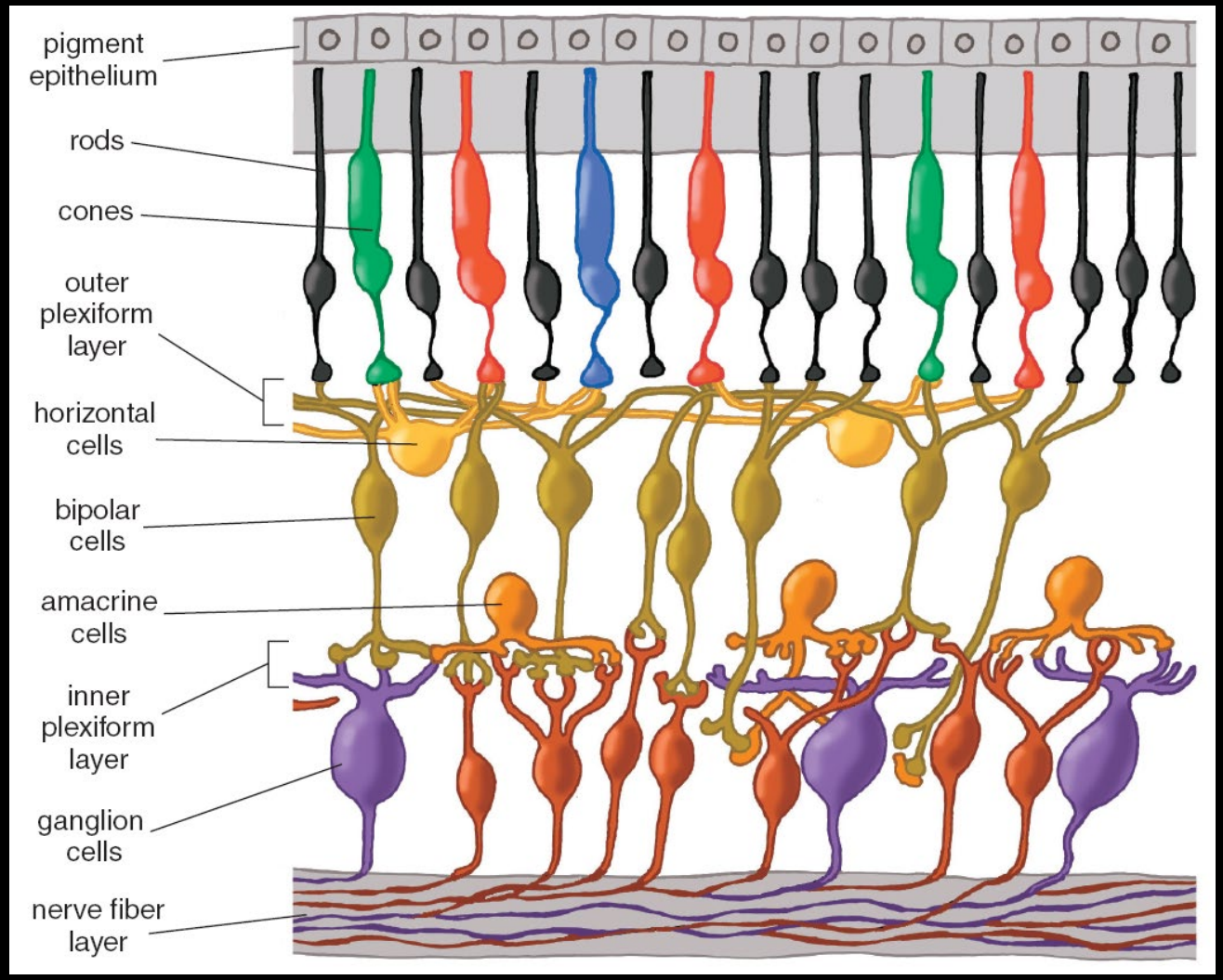


Why have ON and OFF channels?

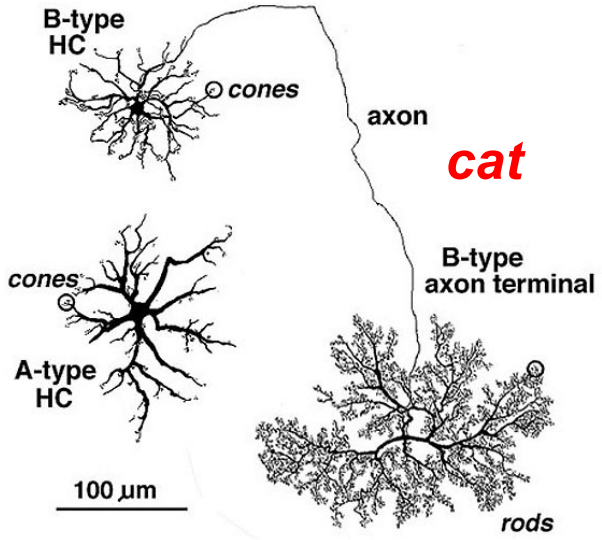


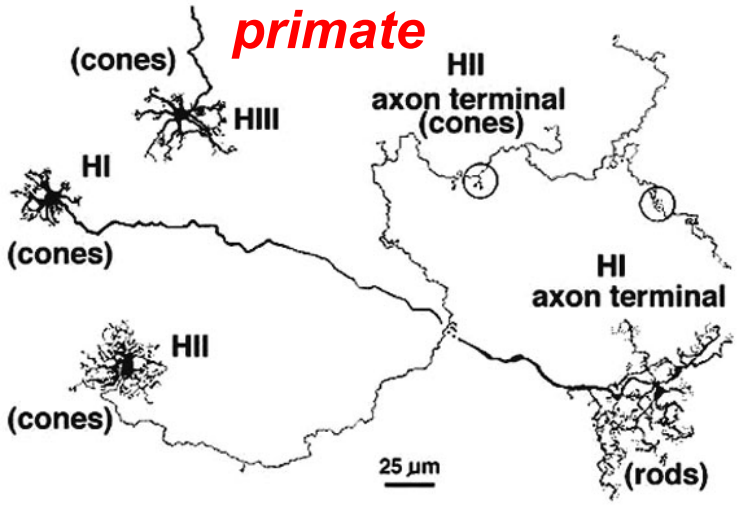
HORIZONTAL CELLS

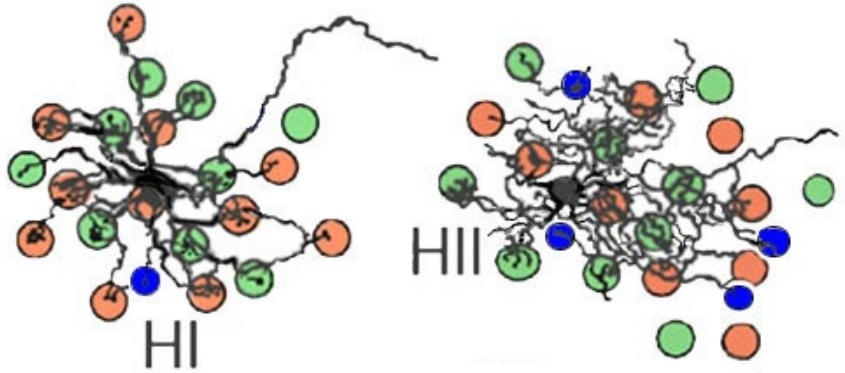
Lateral inhibition



Horizontal cell types





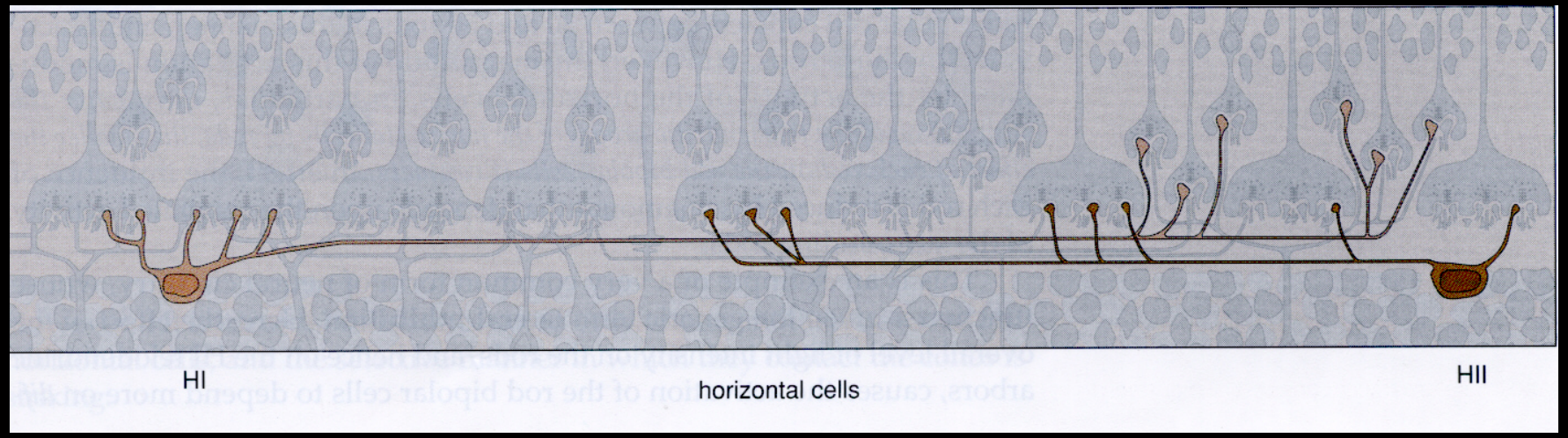


S-cones
L-cones
M-cones

human

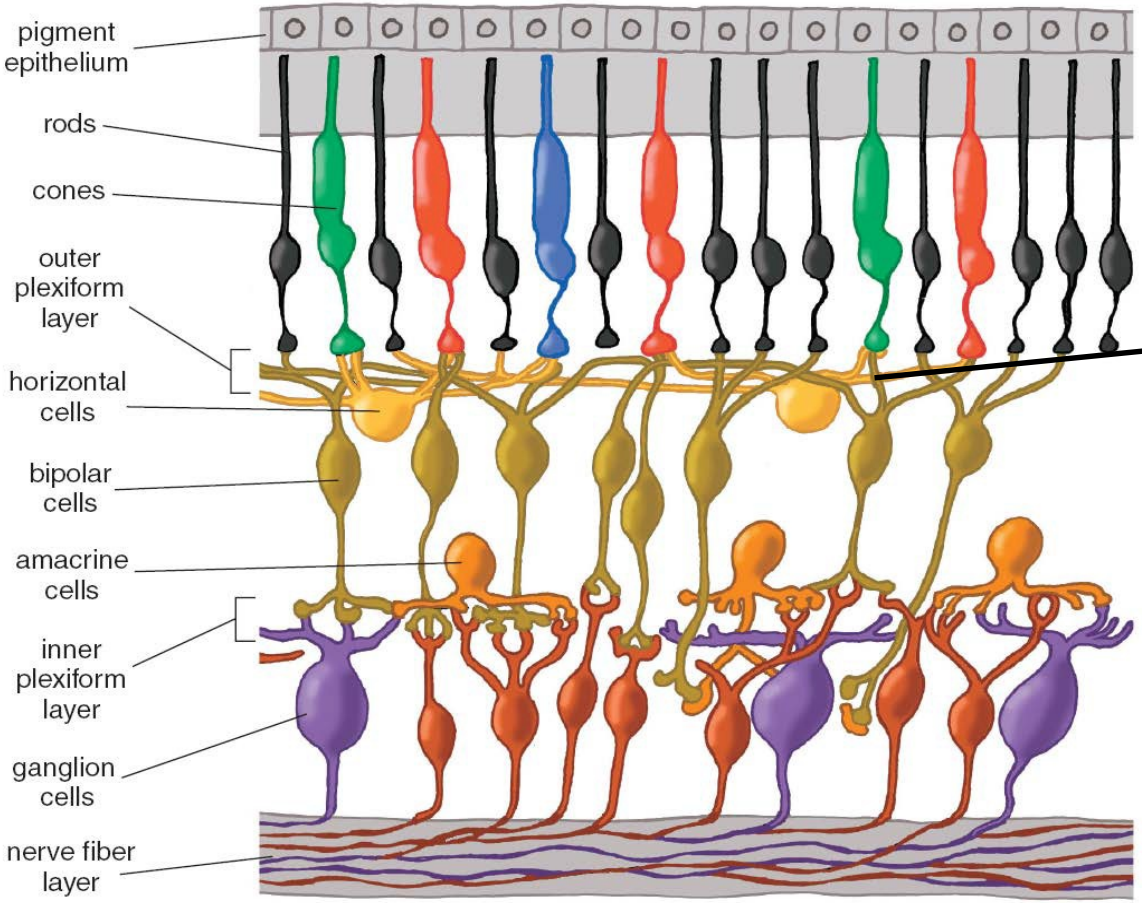
Horizontal cells

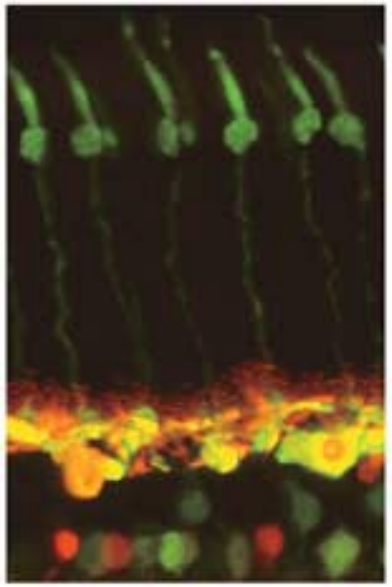
Lateral interactions

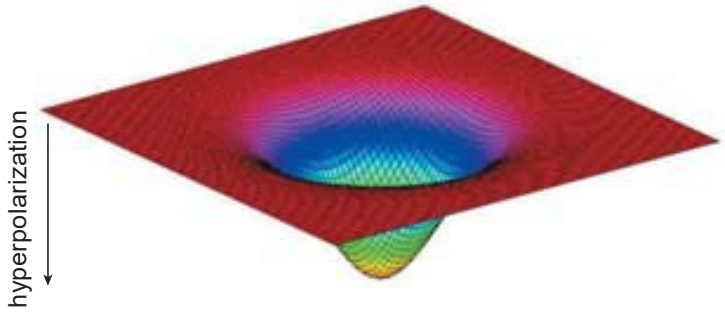


From Rodieck (1998)

Horizontal cell responses



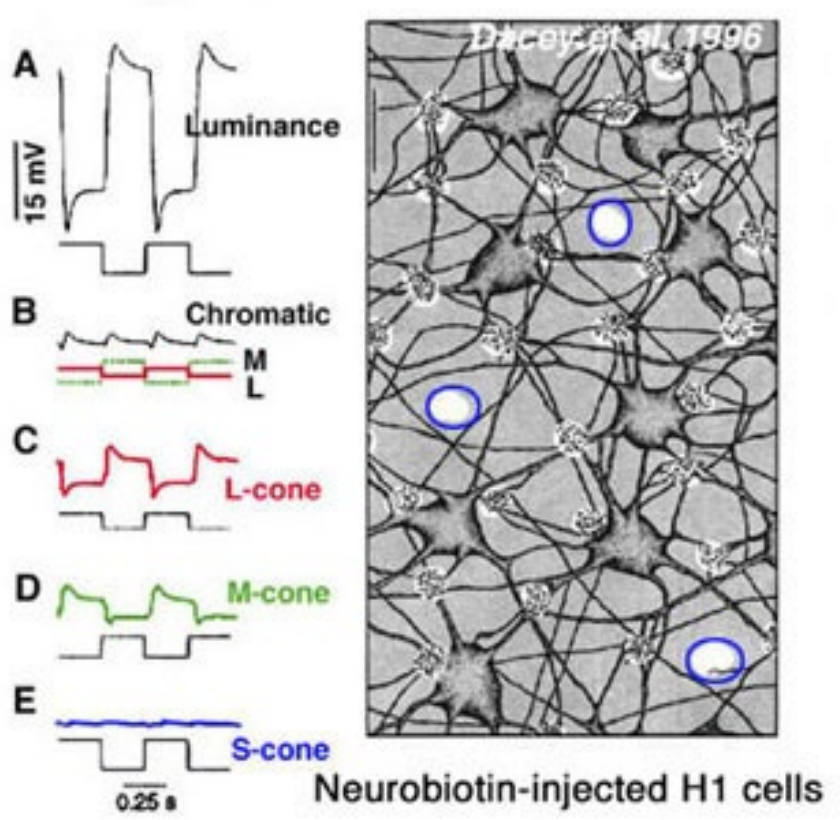




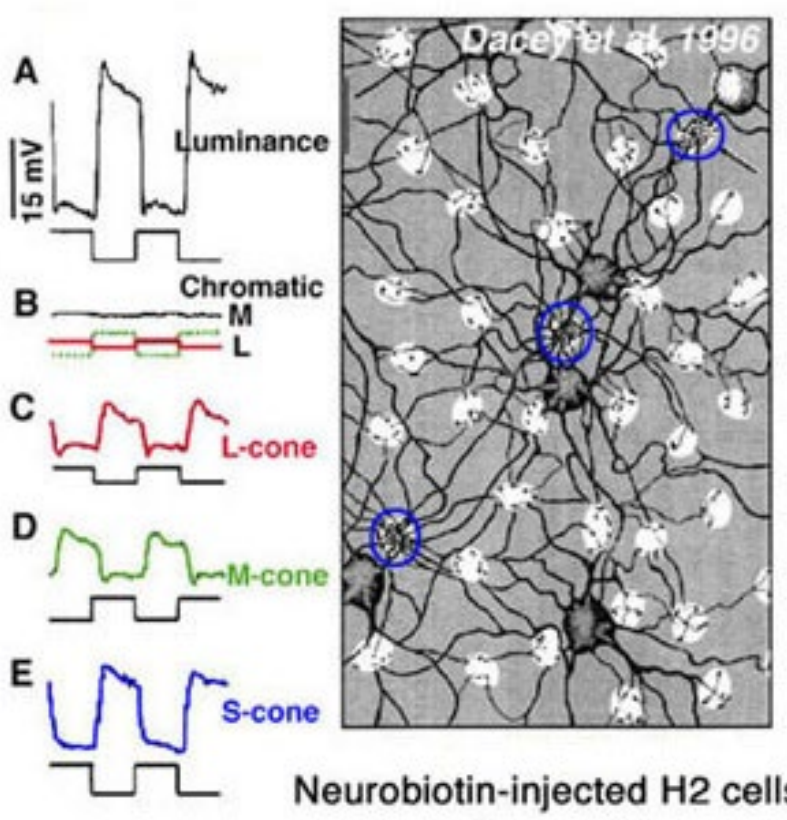
Horizontal cells hyperpolarize in response to light

Primate horizontal cell responses

Responses to L, M and S-cone and luminance signals all have the same sign.



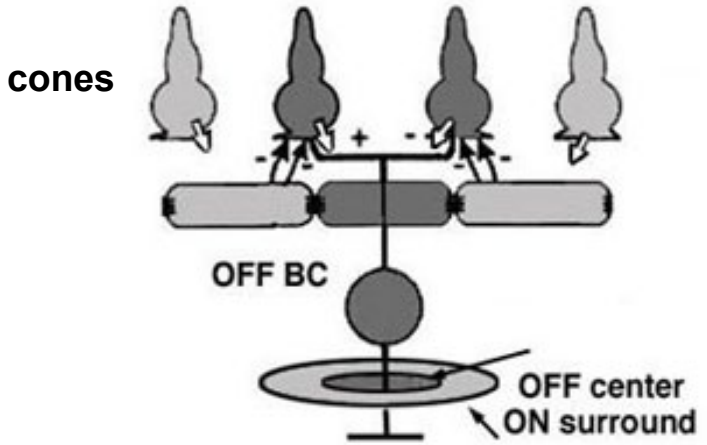
Neurobiotin-injected H1 cells



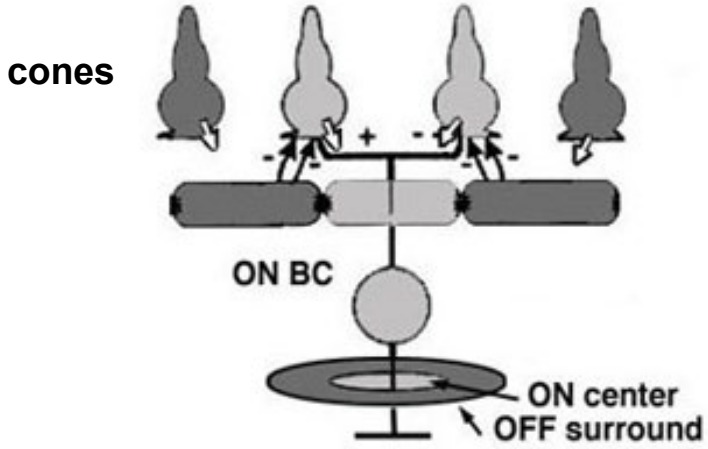
Neurobiotin-injected H2 cells

Horizontal cell function

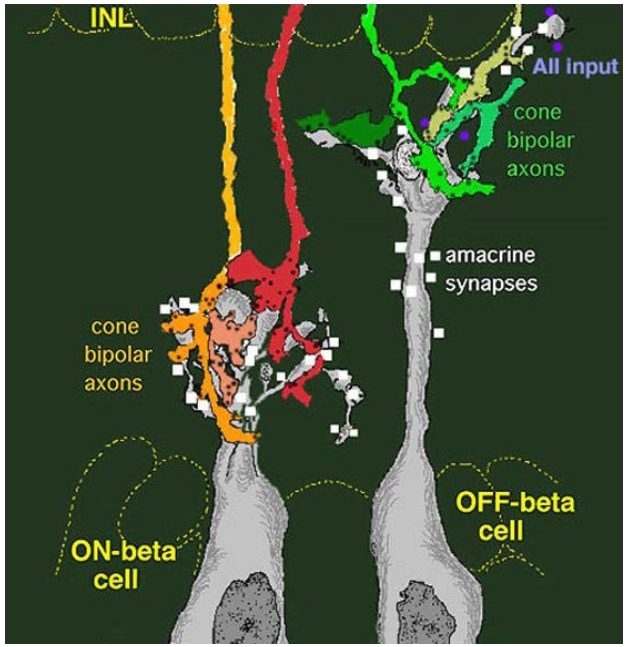
Produce spatially-opponent surrounds of both ON and OFF bipolar cells.

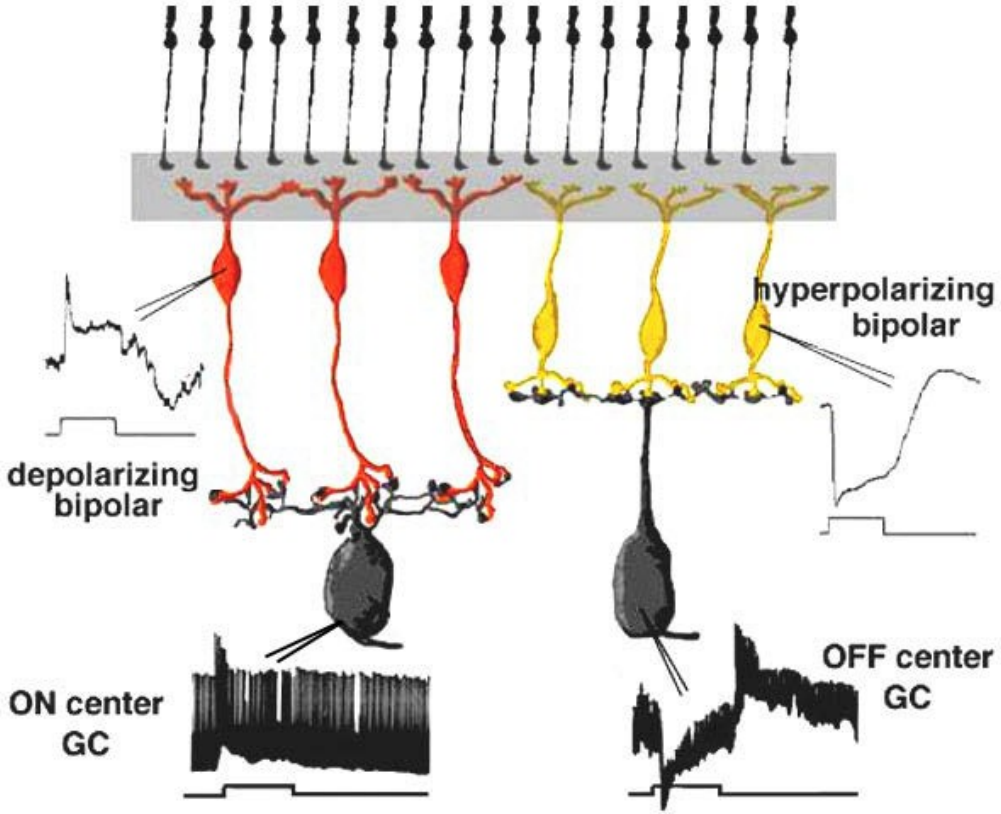


By inhibiting the cones they produce the inhibitory surrounds of both ON and OFF bipolars.

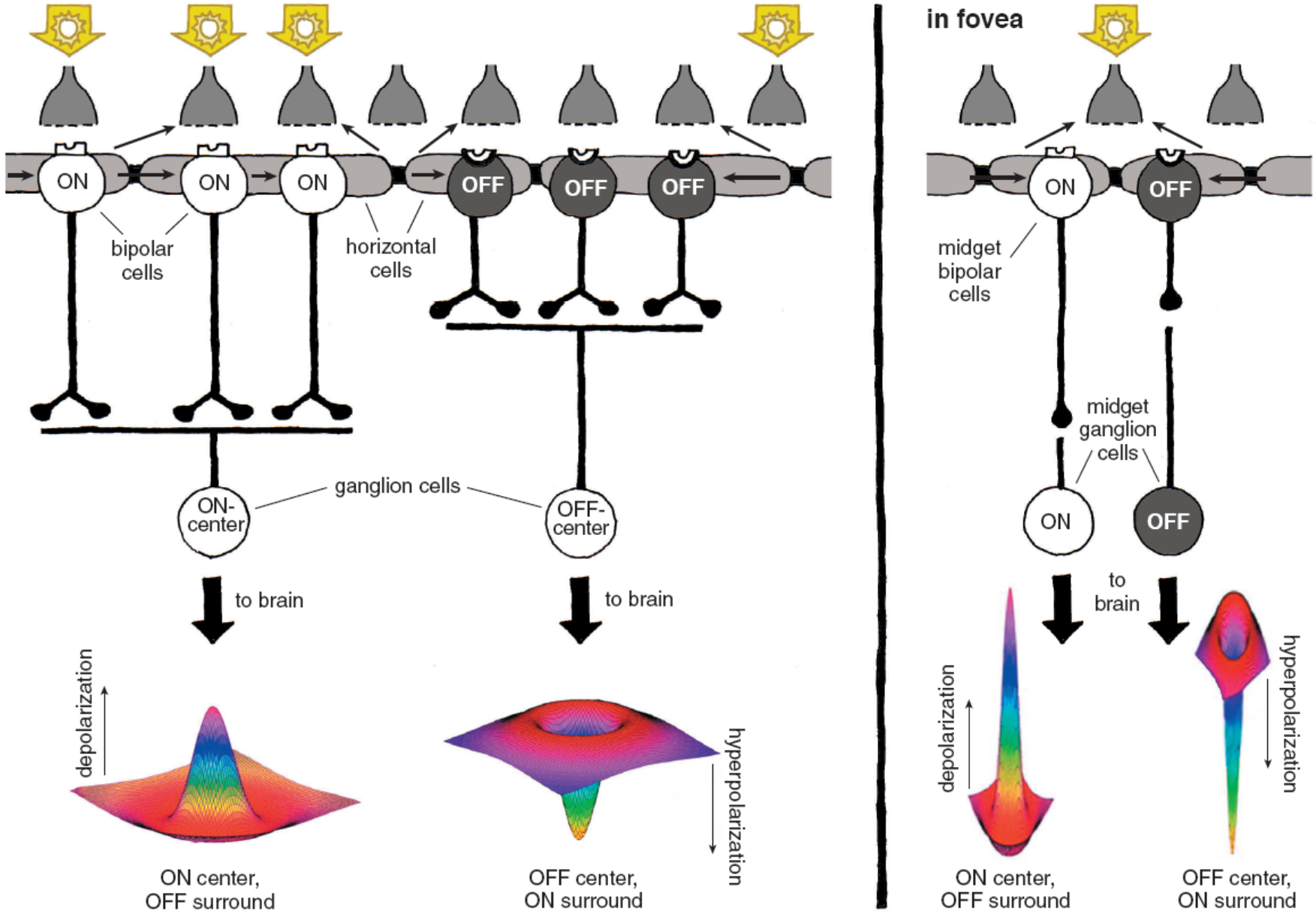


Cone bipolar termination on RGCs





ON and OFF cone paths to ganglion cells



Summary of pathways through the retina

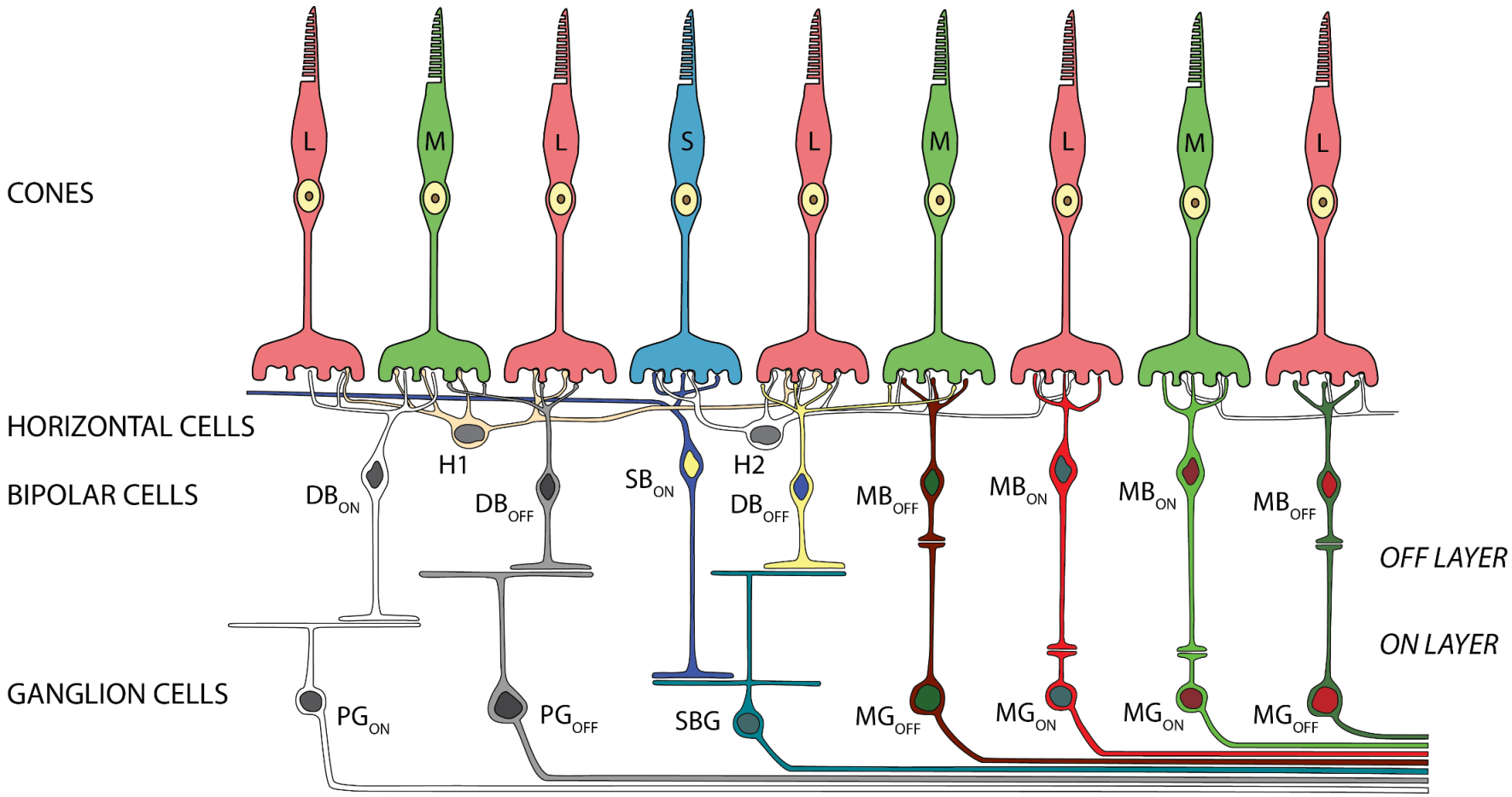
- Photoreceptors always respond to light ON with membrane potential hyperpolarisation, resulting in a reduction of neurotransmitter (glutamate) release onto bipolar cells.

- Bipolar cells respond to light with either **ON** or **OFF** responses. This is due to the expression of different Glutamate receptor types at the photoreceptor-bipolar cell synapse.

- Bipolar cells utilise glutamate to synapse onto retinal ganglion cells, conferring them with either **ON** or **OFF** responses.

- Retinal ganglion cells (RGCs) generate action potentials in response to graded synaptic input potentials. Action potentials are conducted to the brain along the axons of RGCs running in the optic nerve.

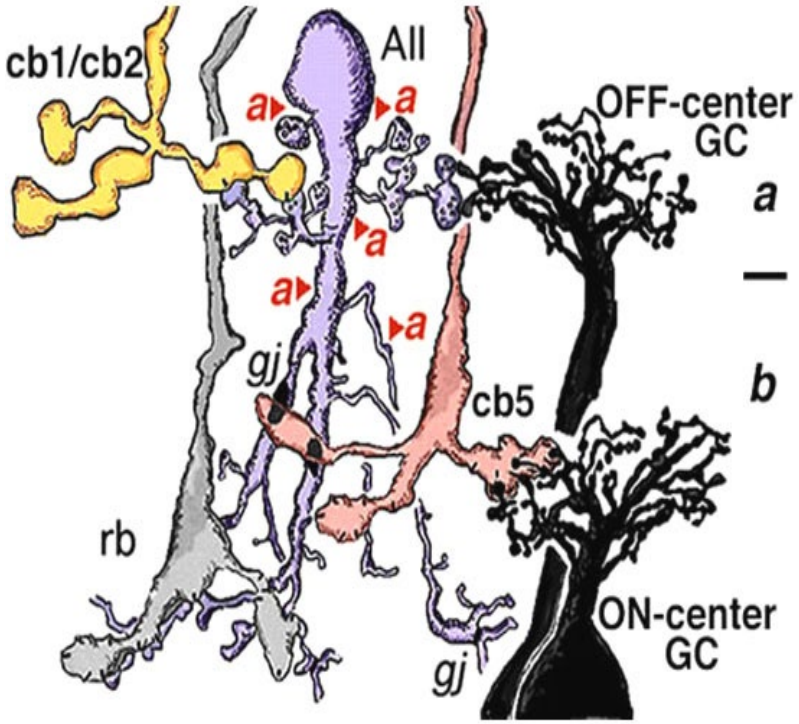
Summary


CONES
HORIZONTAL CELLS
BIPOLAR CELLS
GANGLION CELLS
L
M
L
S
L
M
L
M
L
H1
H2
DB$_{ON}$
DB$_{OFF}$
SB$_{ON}$
DB$_{OFF}$
MB$_{OFF}$
MB$_{ON}$
MB$_{ON}$
MB$_{OFF}$
PG$_{ON}$
PG$_{OFF}$
SBG
MG$_{OFF}$
MG$_{ON}$
MG$_{ON}$
MG$_{OFF}$
OFF LAYER
ON LAYER

AMACRINE CELLS

Amacrine cells are interneurons that interact at the second synaptic level of the vertically direct pathways consisting of the photoreceptor-bipolar-ganglion cell chain. They are synaptically active in the inner plexiform layer (IPL) and serve to integrate, modulate, and interpose a temporal domain to the visual message presented to the ganglion cell.

Amacrine AII cells



Drawing to show the circuitry of the AII amacrine cell with pre and post synaptic neurons. Sublaminas a and b are indicated.

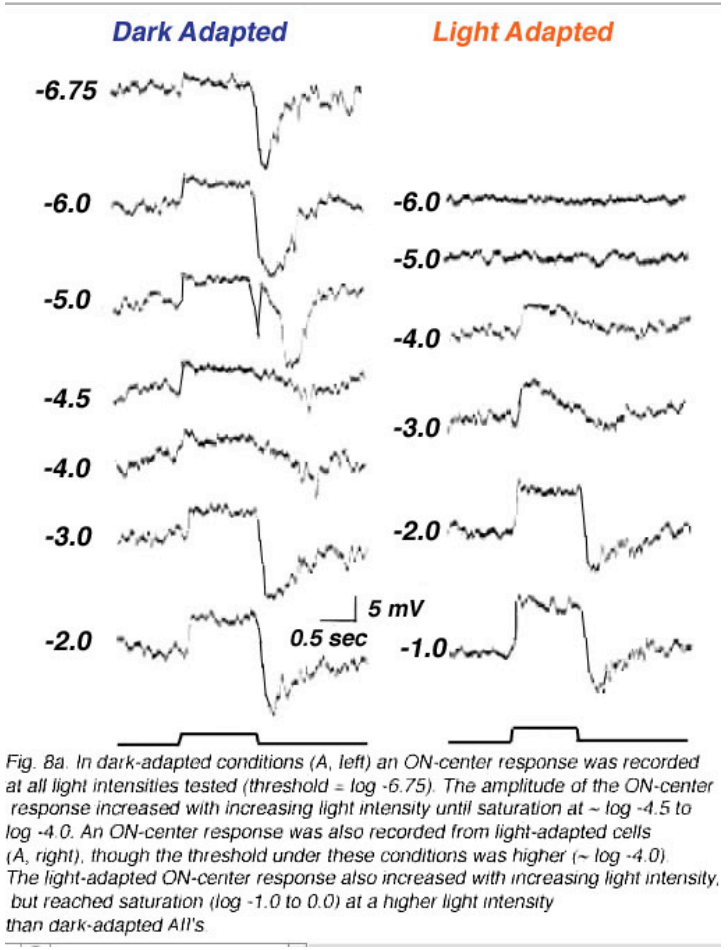
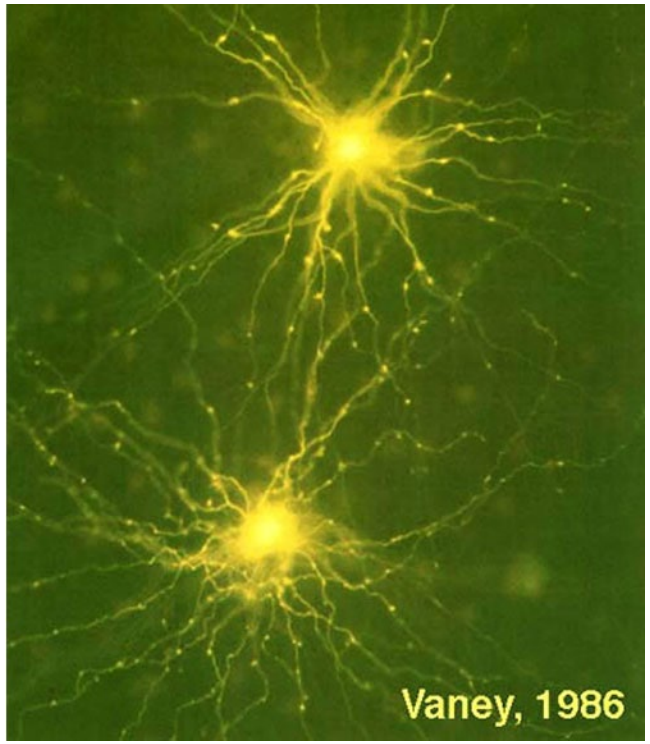


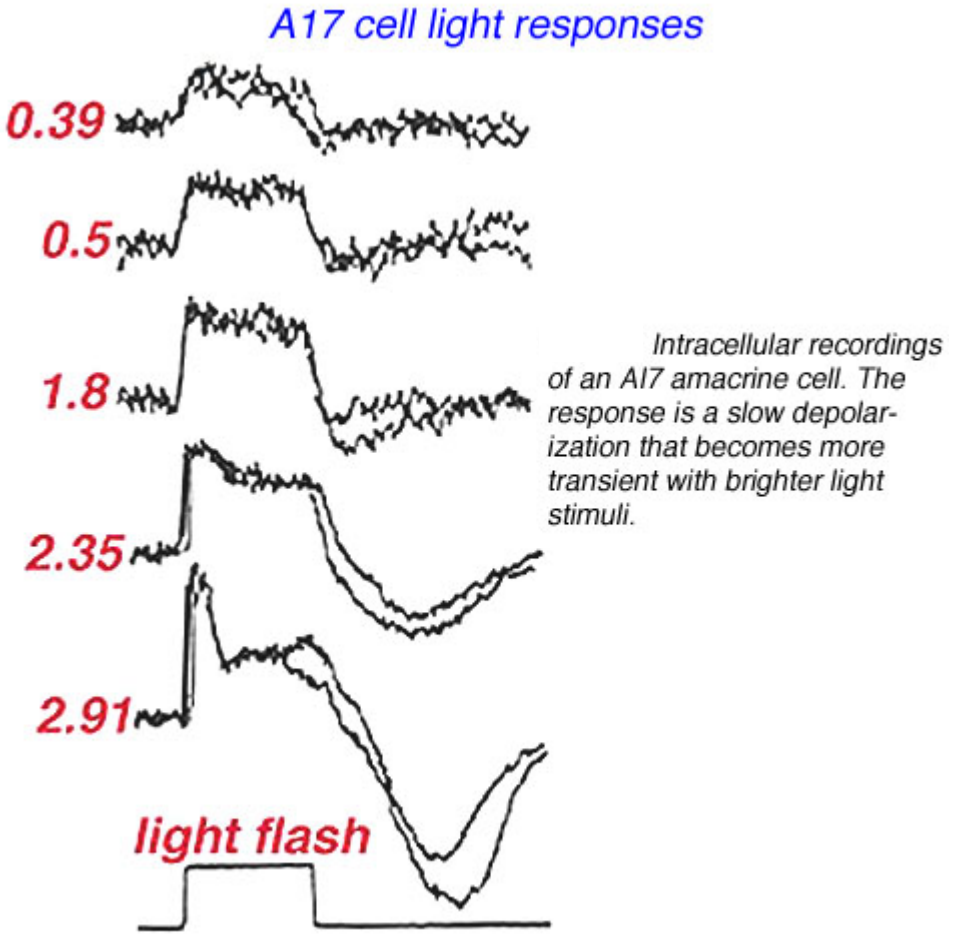
Fig. 8a. In dark-adapted conditions (A, left) an ON-center response was recorded at all light intensities tested (threshold = log -6.75). The amplitude of the ON-center response increased with increasing light intensity until saturation at ~ log -4.5 to log -4.0. An ON-center response was also recorded from light-adapted cells (A, right), though the threshold under these conditions was higher (~ log -4.0). The light-adapted ON-center response also increased with increasing light intensity, but reached saturation (log -1.0 to 0.0) at a higher light intensity than dark-adapted AII's.

Webvision

ADVANCED LECTURE

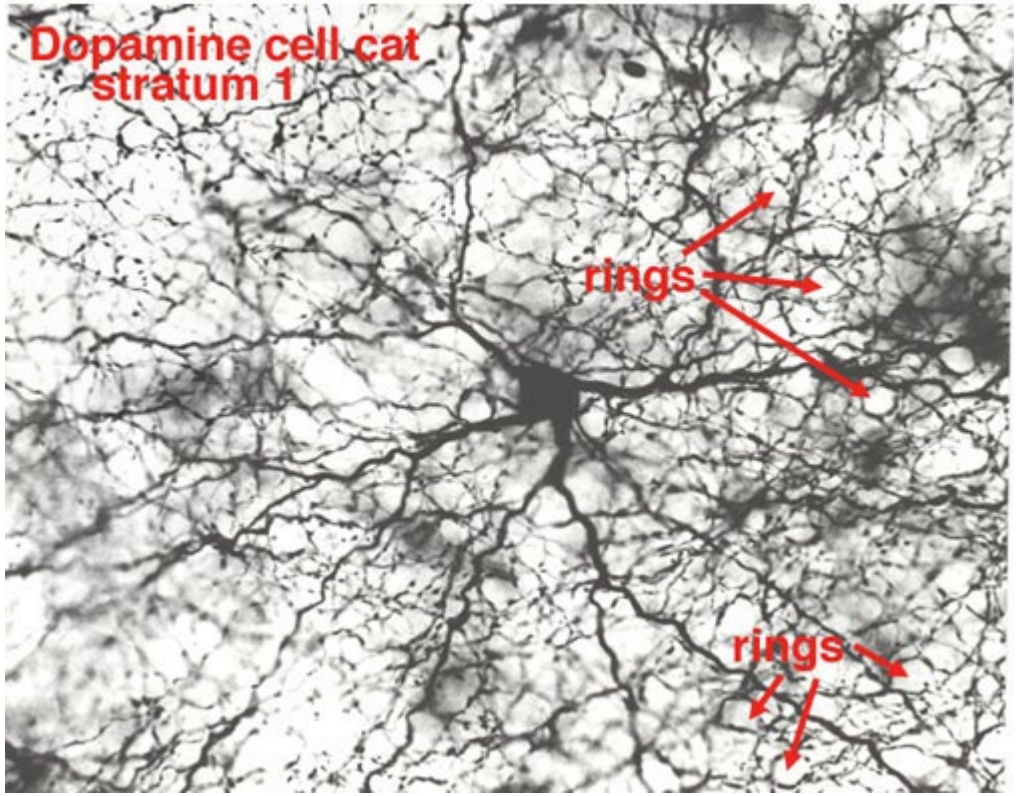
Amacrine A17 cells





Wide-field *diffuse* amacrine. Large coverage allows it to collect scotopic rod signals from several thousand rod bipolar axons. Its high sensitivity to scotopic conditions (rod driven light intensities) suggests that this amacrine plays a role in converging rod signals from huge areas of retina and to amplify them at very low light intensities (Webvision).

Amacrine A18 cells



Wide-field diffuse amacrine cells that are dopaminergic. Dopamine affects AII coupling.

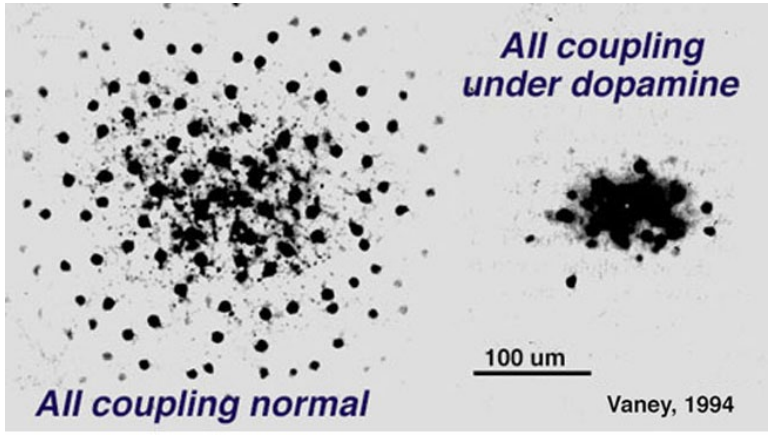
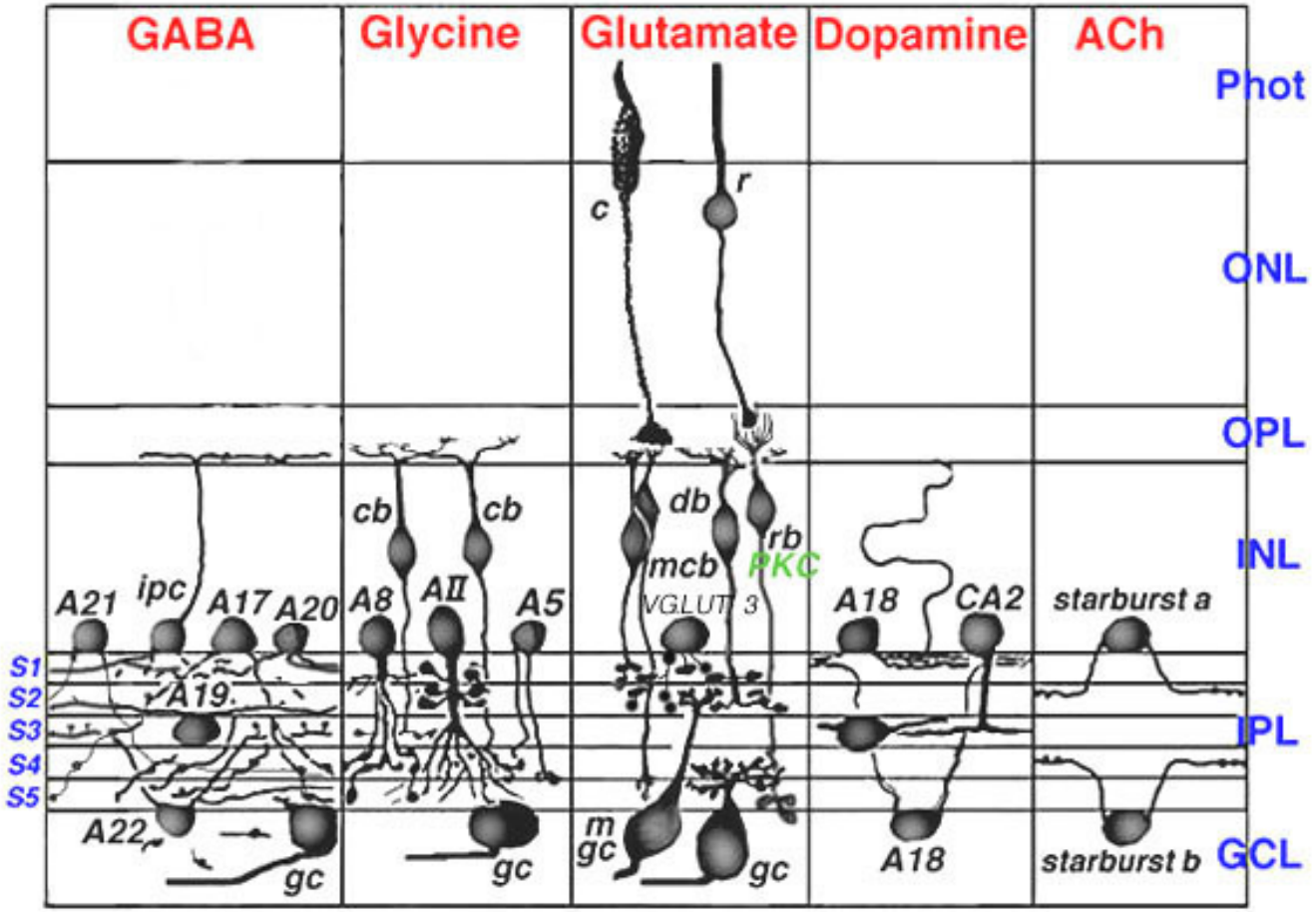


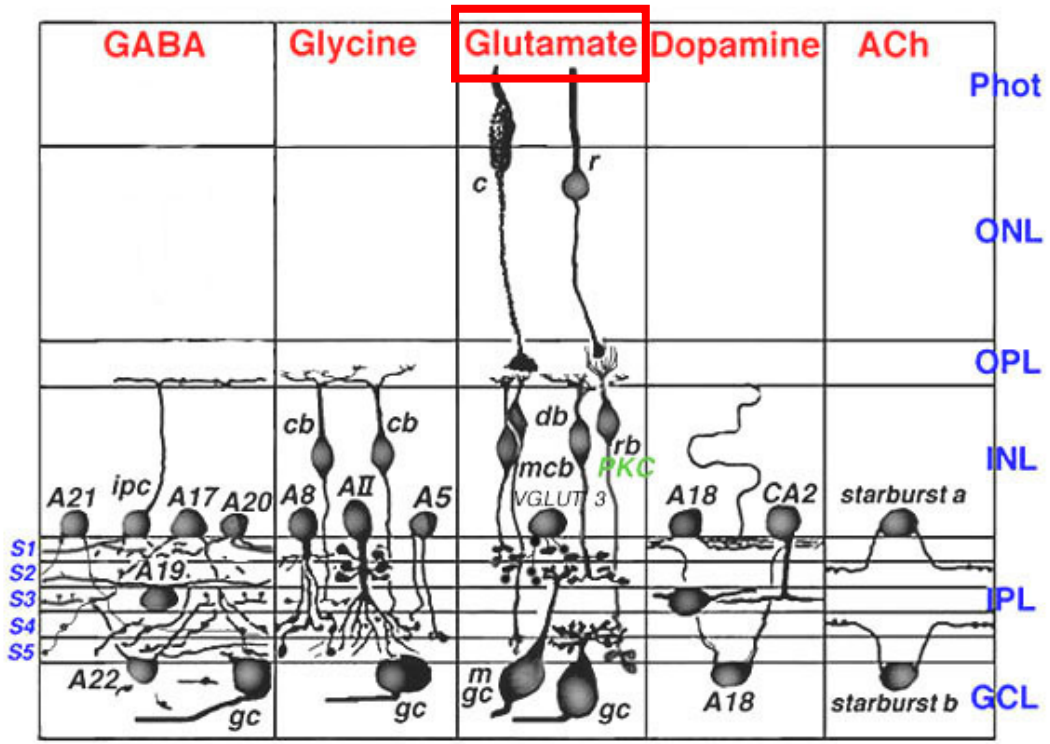
Fig. 34. Effects of dopamine on AII amacrine cell coupling. AII cells are normally coupled extensively, but under the influence of dopamine release, AII cells uncouple.

Immunostaining for tyrosine hydroxylase. A18 Amacrine cells have overlapping dendrites that form into rings.

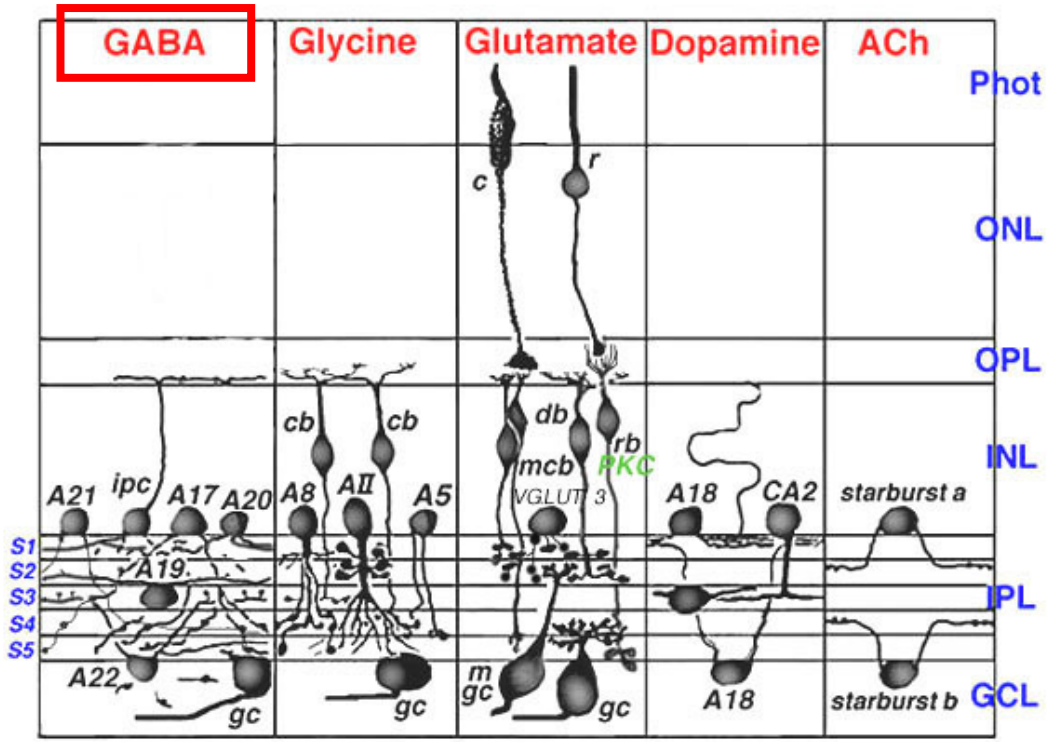
Neurotransmitters in Retina



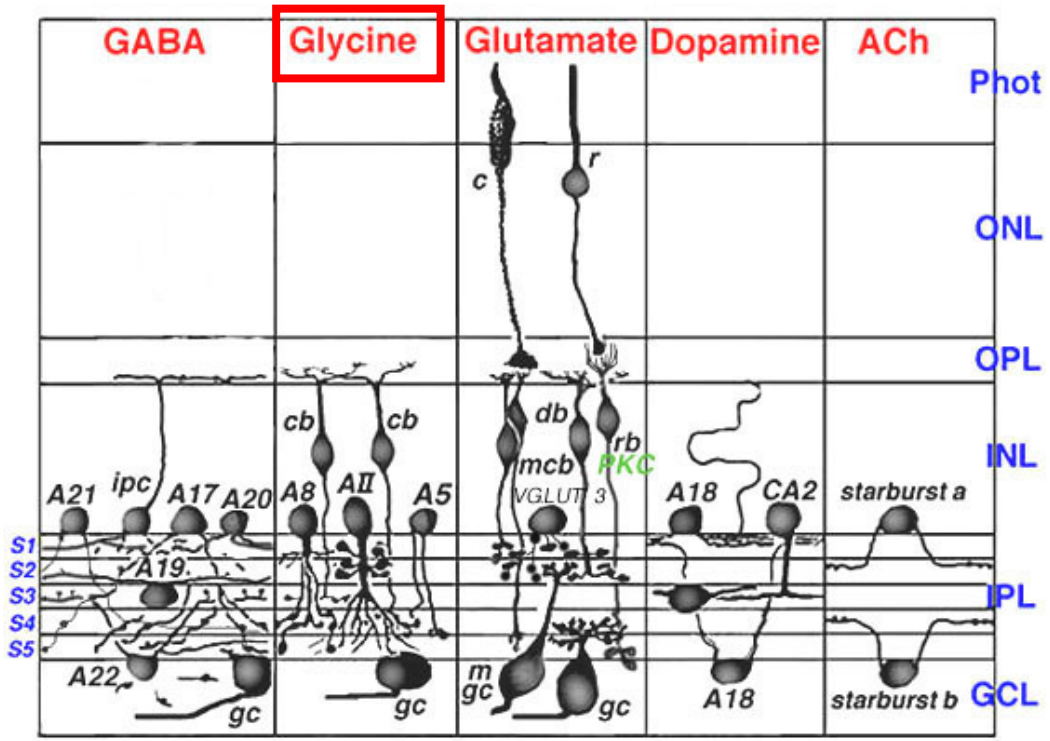
Organisation of neurotransmitters according to cell type in mammalian retina.



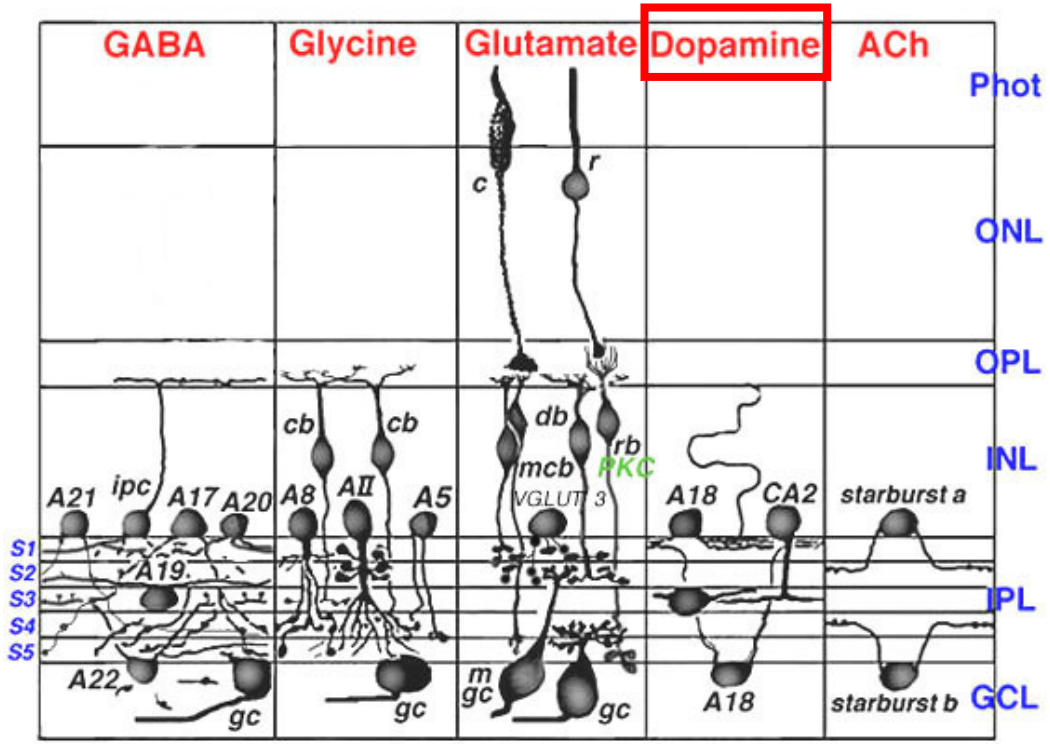
Glutamate is the neurotransmitter of the neurons of the vertical pathways through the retina. All photoreceptor types, rods and cones, use the excitatory amino acid glutamate to transmit signals to the next order neuron in the chain.



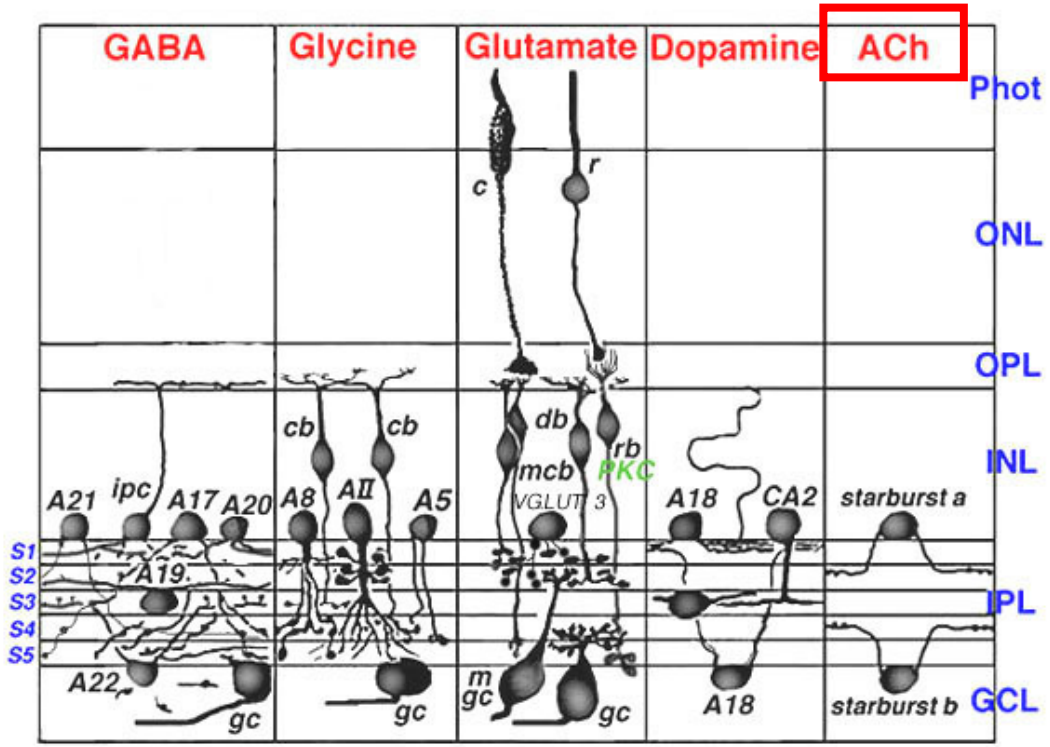
The classical inhibitory neurotransmitter gamma aminobutyric acid (GABA) occurs in many different varieties of amacrine cells, and in one or more classes of horizontal cell in most vertebrate retinas. There is still some controversy over whether GABA is contained within horizontal cells in monkey and human retina.



The other classic inhibitory neurotransmitter glycine, accounts for most of the small-field types of amacrine cell. All amacrine cells in the vertebrate retina can be accounted for by the two inhibitory neurotransmitters GABA and glycine. In addition one or more types of bipolar cell are also thought to contain glycine in mammalian retinas including monkey and human.



The neuromodulator dopamine is found in one or more types of amacrine cell in the mammalian retina.



The classic fast excitatory neurotransmitter of the peripheral nervous system, acetylcholine (ACh), is found in a mirror symmetric pair of amacrine cells in the vertebrate retina.