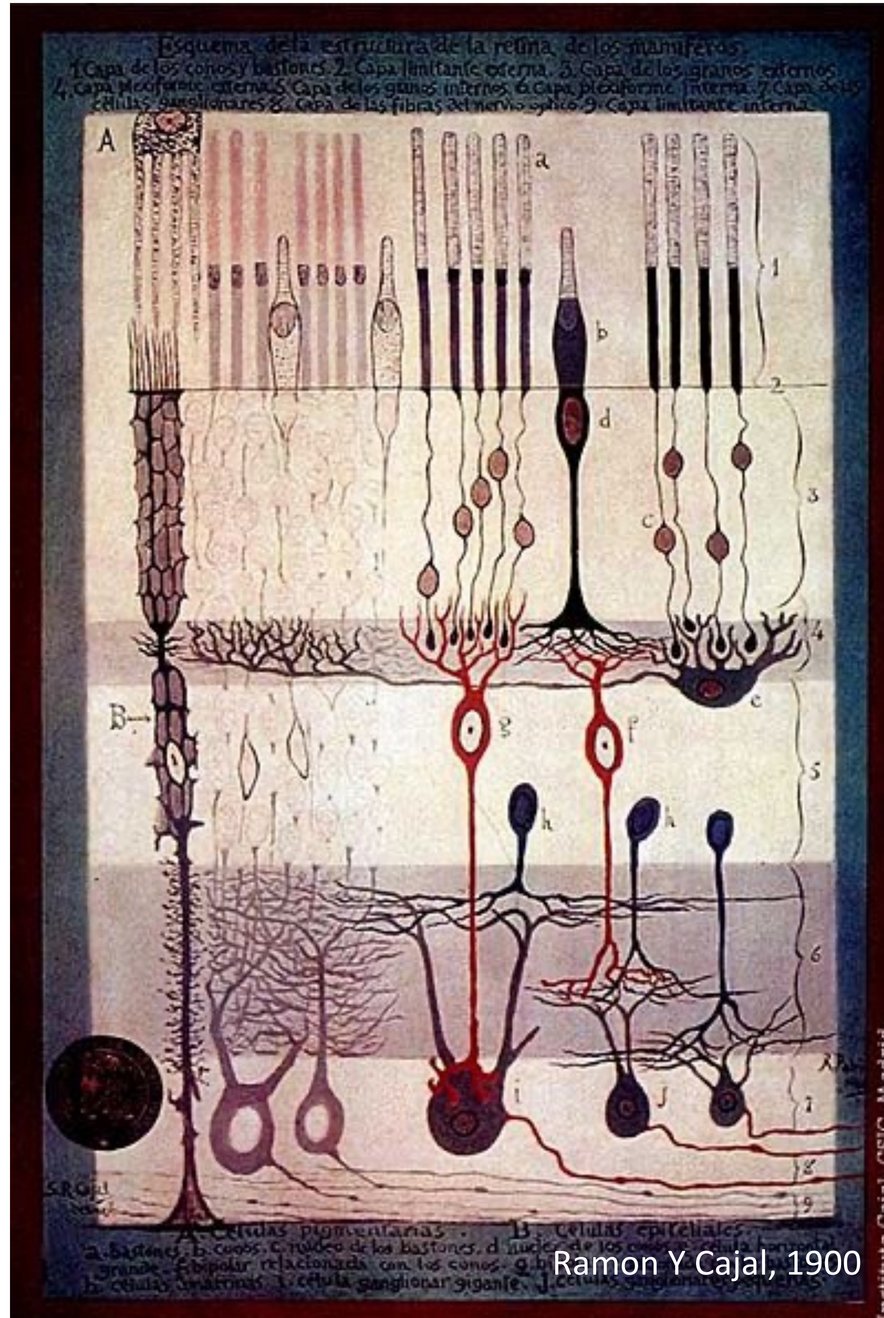
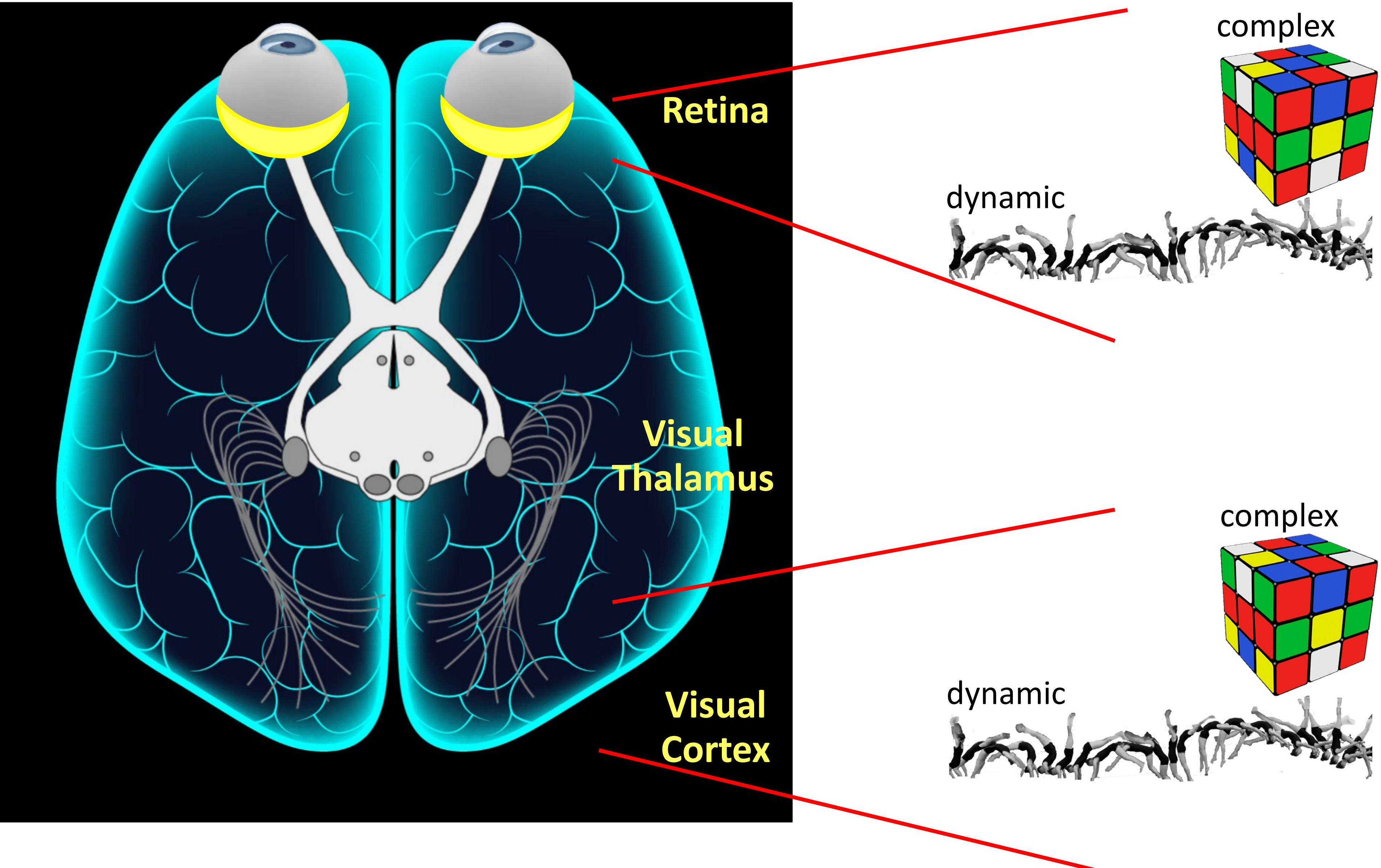
Introduction to Neuroscience:
Visual Processing by the Retina

Michal Rivlin

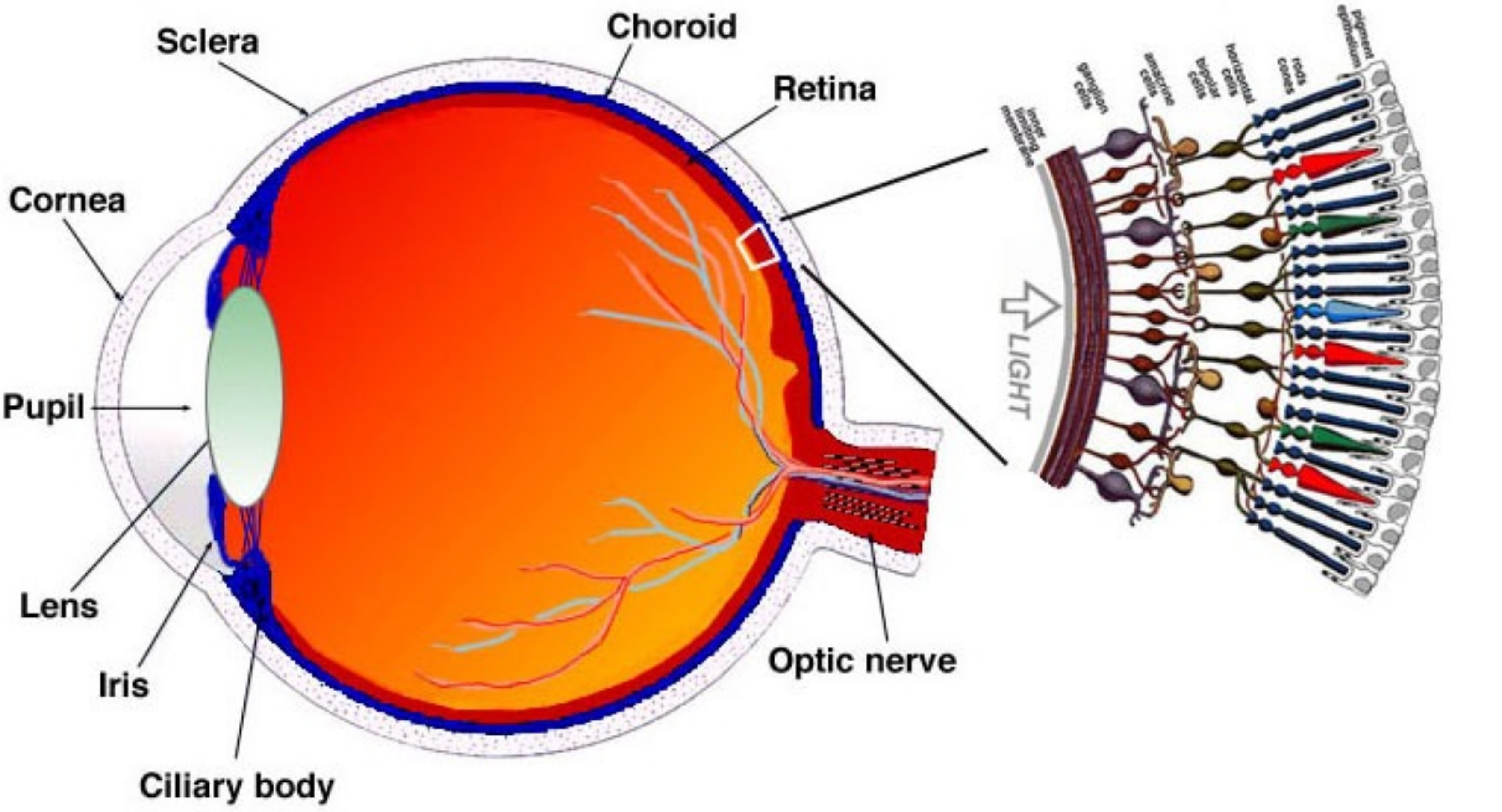


Ramon Y Cajal, 1900

Retinal processing: more than a simple camera

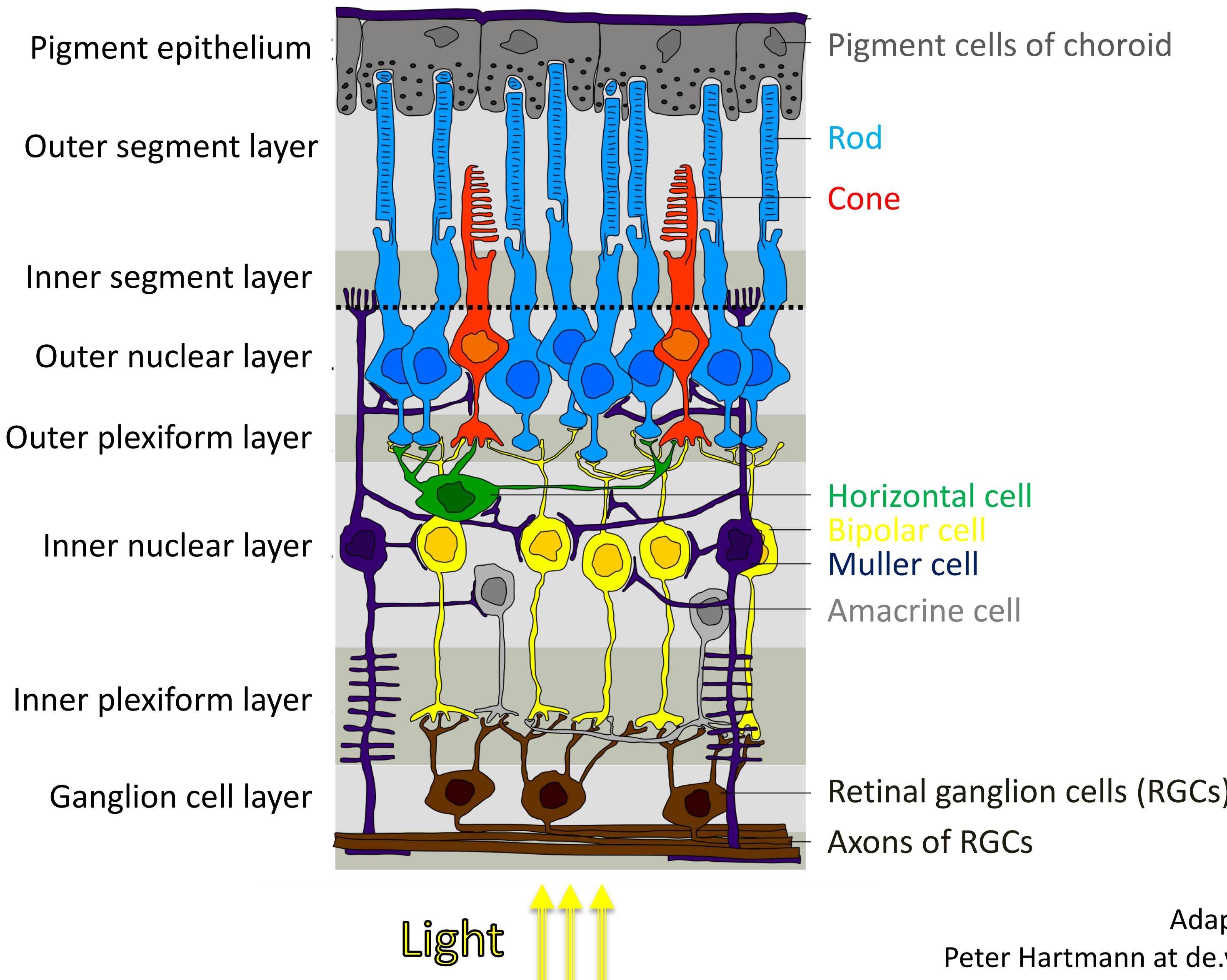


The human Eye



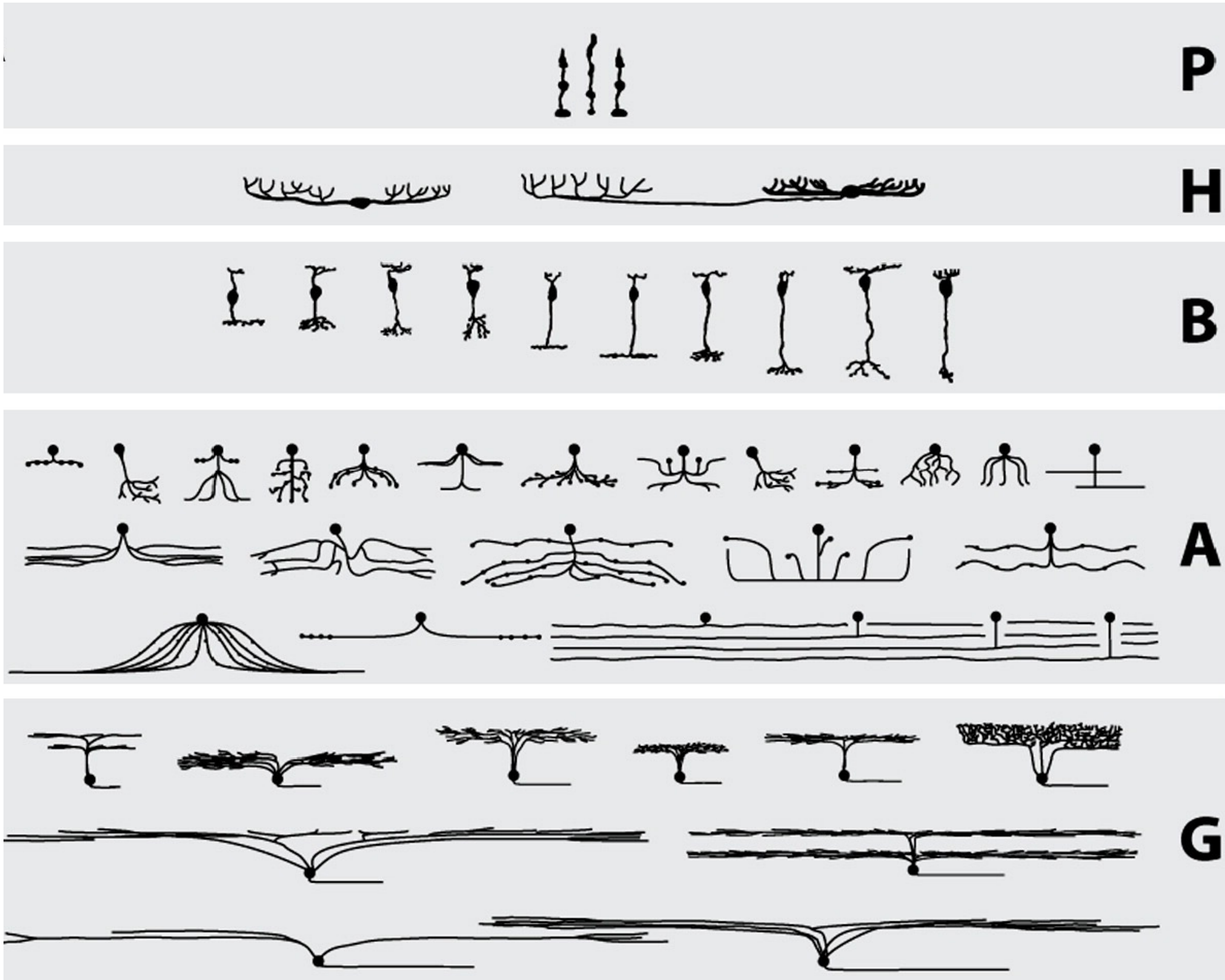
http://webvision.med.utah.edu/

An introduction to the cell types of the retina



Adapted from
Peter Hartmann at de.wikipedia
edited by Marc Gabriel Schmid

Each class is composed of multiple subtypes



Adapted from
Gollisch and Meister 2010
Based on Masland 2001

Photoreceptors: Rods and Cones

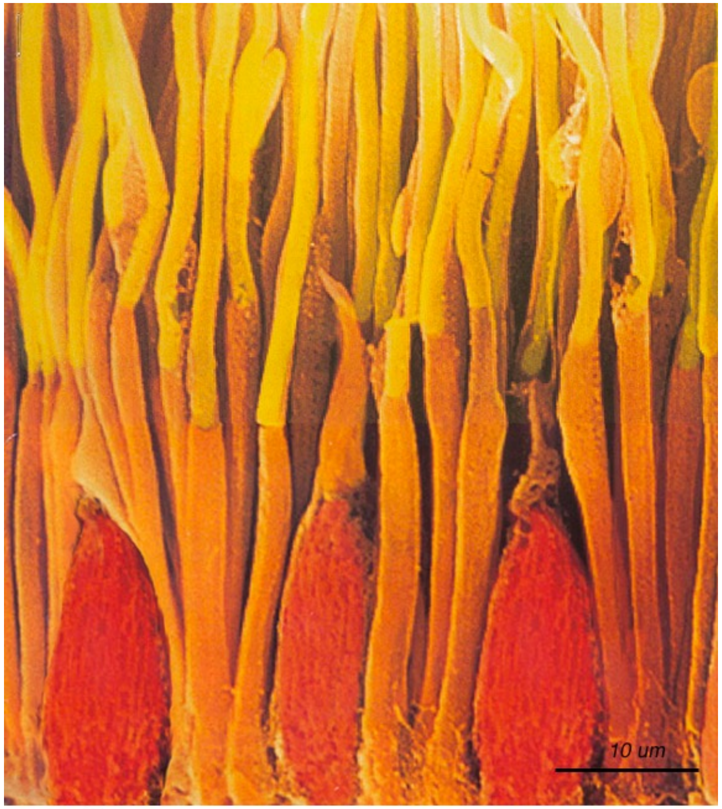
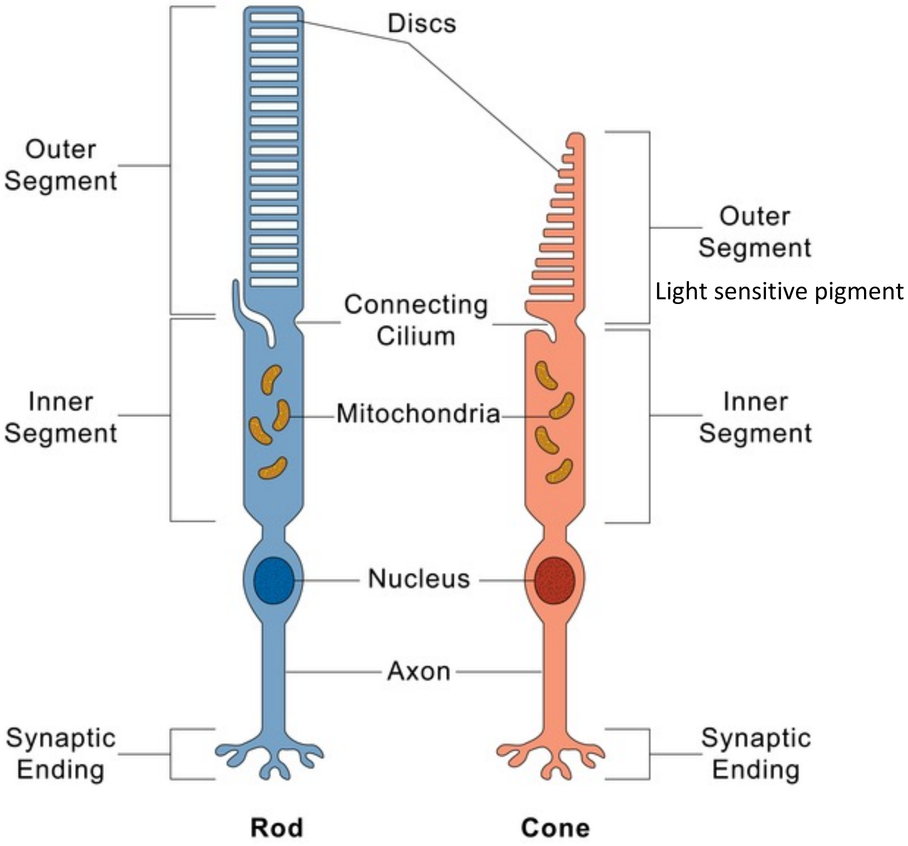
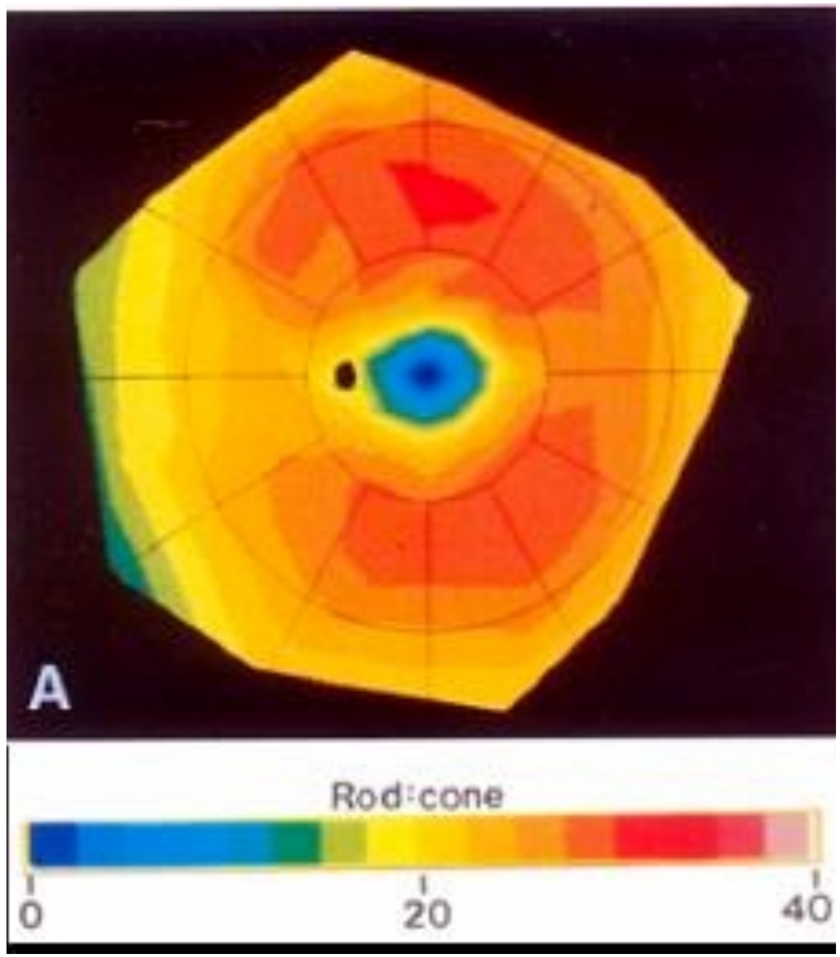


Fig1b. Scanning electron micrograph of the rods and cones of the primate retina. Image adapted from one by Ralph C. Eagle/Photo Researchers, Inc.



125 million photoreceptors in the retina
Rods: dim night vision.
Cones: bright day vision & color vision

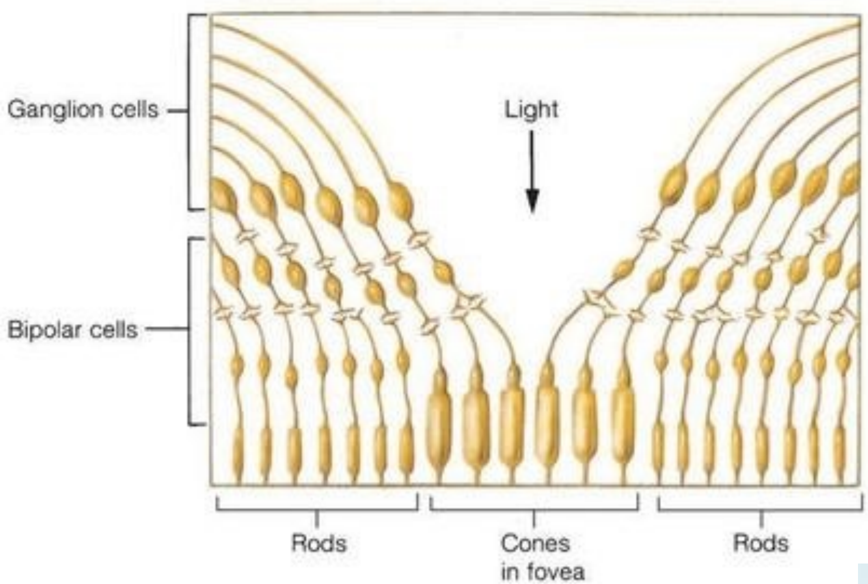
Distribution of Rods and Cones in human retina

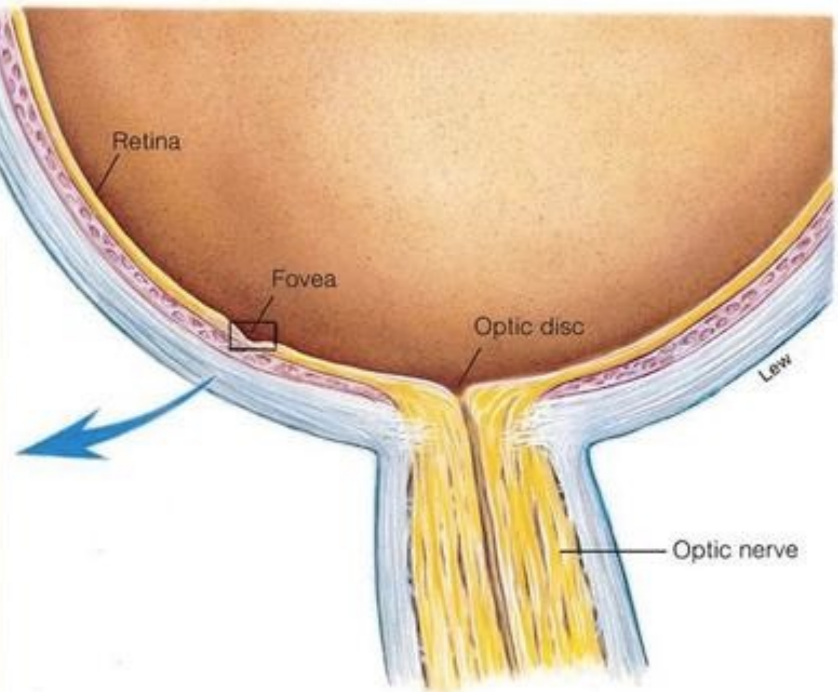


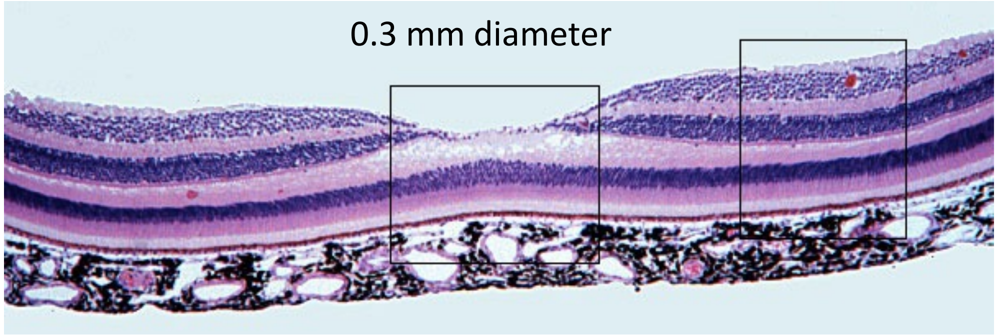
Curcio et al., 1990

Fovea

Note: not all retinas have a fovea!
Primates do.
Some species have area centralis.

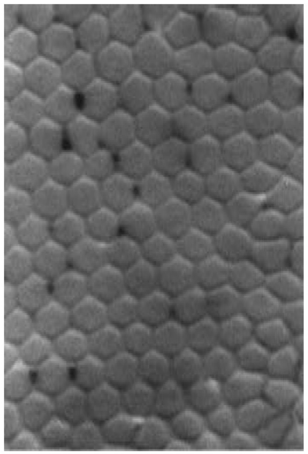




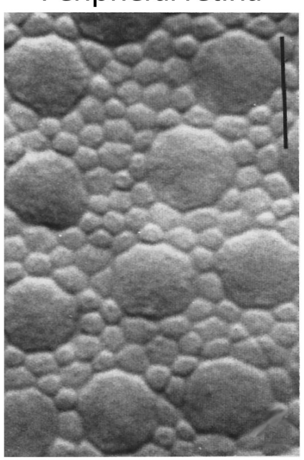


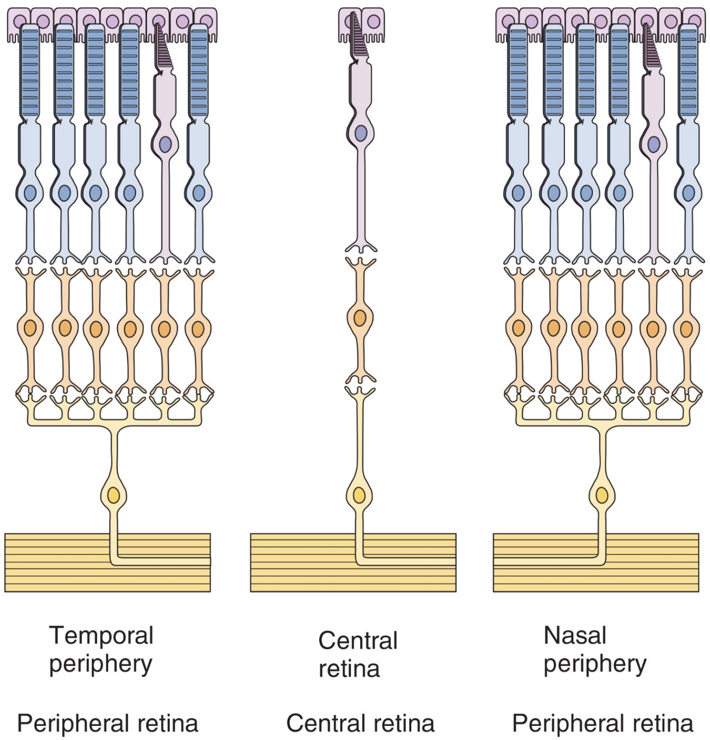
Topographic Variations in Retinal Encoding of Visual Space

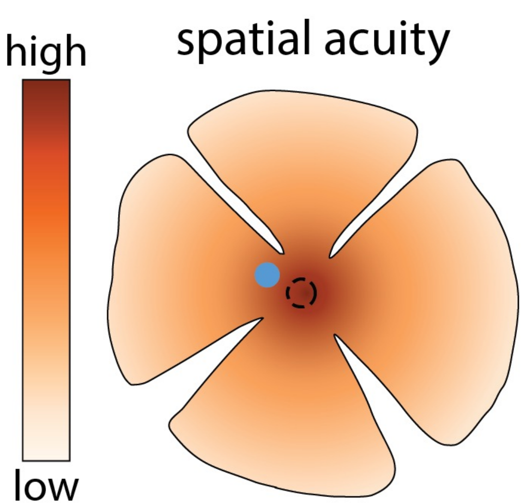
Central retina



Peripheral retina

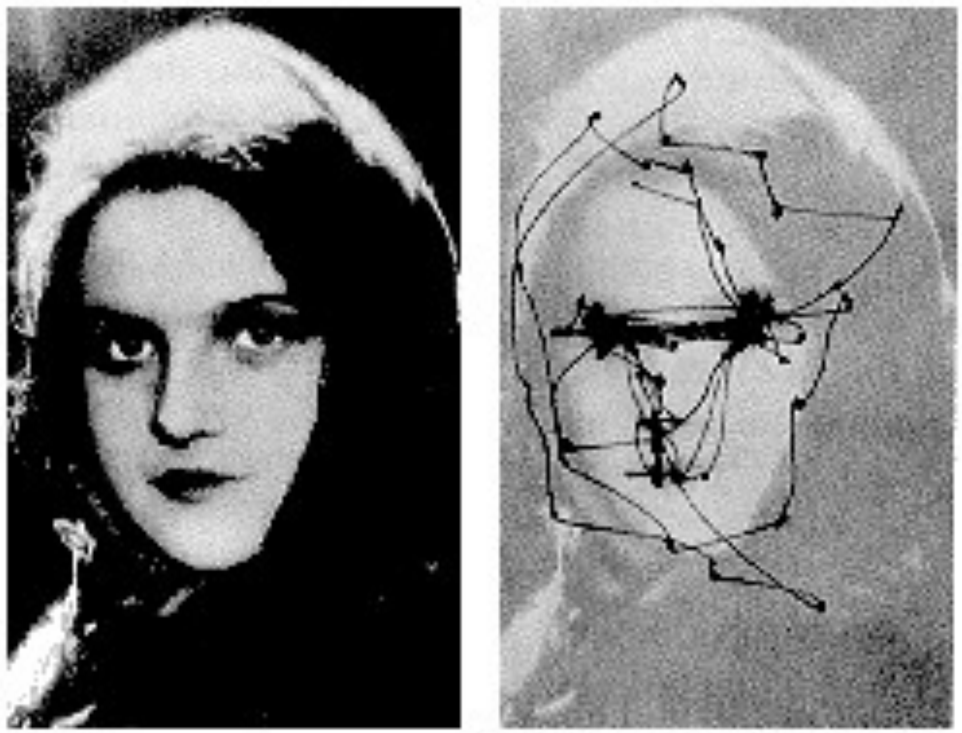






Heukamp et al., 2020

The visual image is not stable on the retina



saccades

The Blind Spot

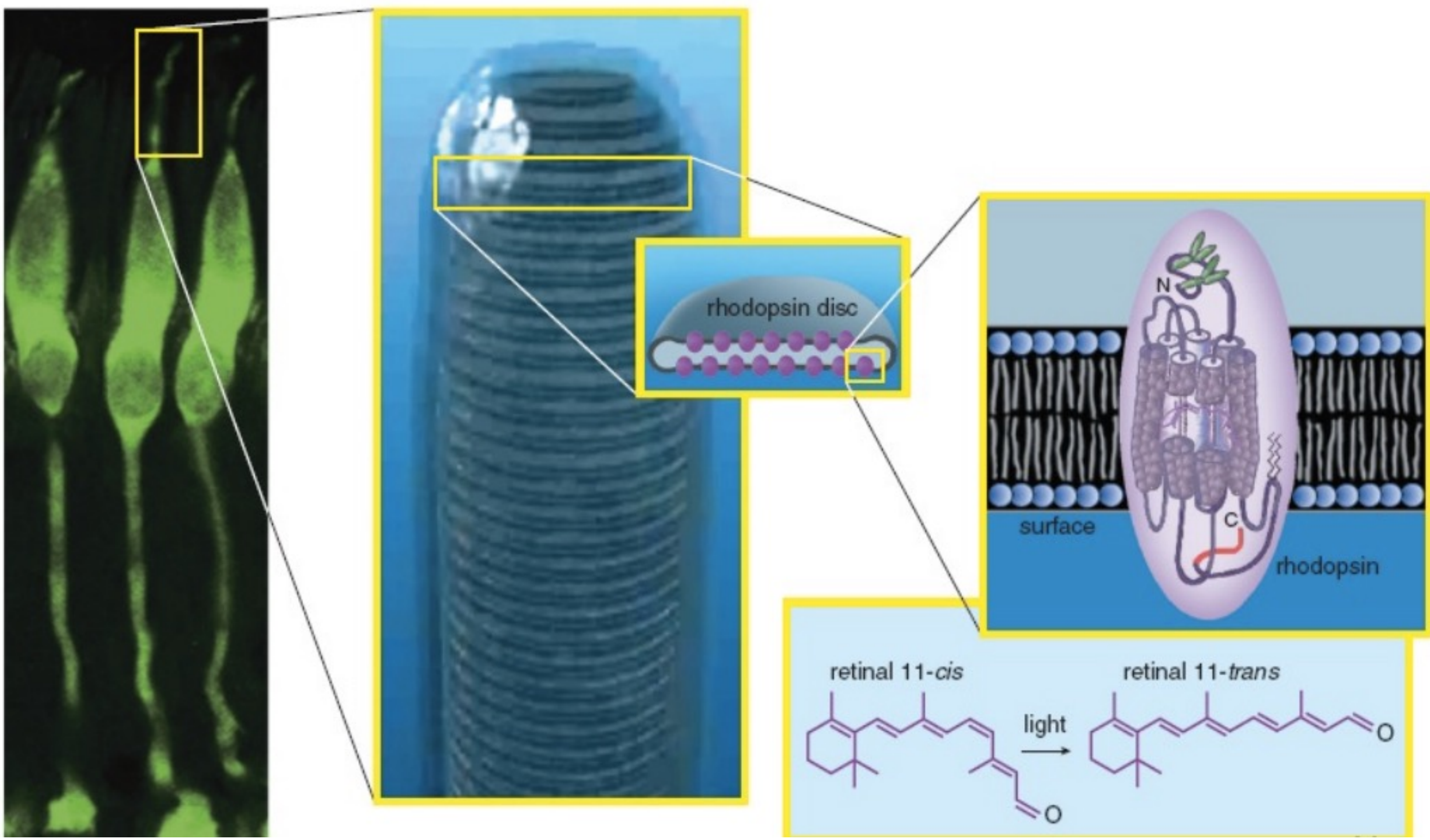
(located at the optic disc)

Close your right eye

Fixate on the spot with your left eye

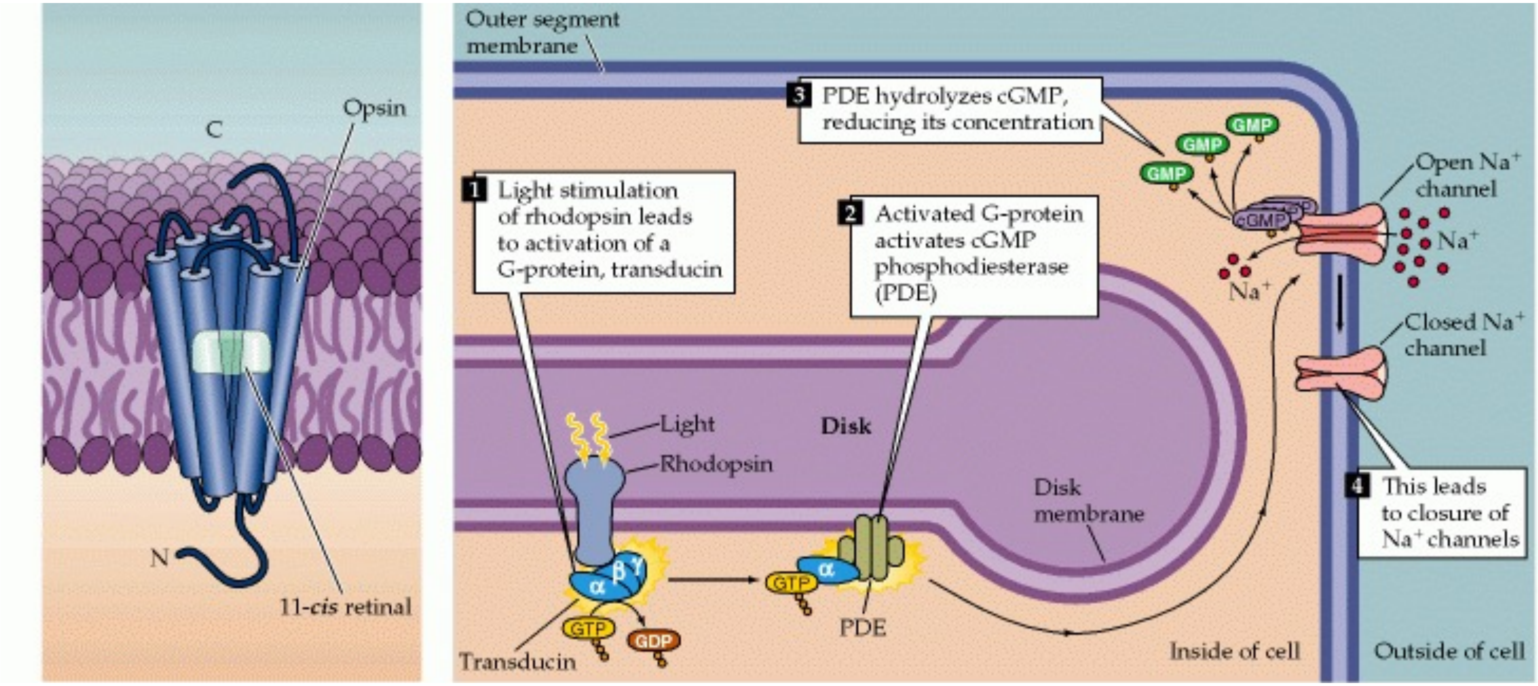
Move paper until cross disappears

Rhodopsin molecules are rod photopigments activated by photon absorption



Rhodopsin constitutes a G-protein-coupled receptor called opsin, and a chromophore called *11-cis retinal*. The conformational change in the chromophore retinal is called photoisomerization

Phototransduction in rods: converting light into electrical signal



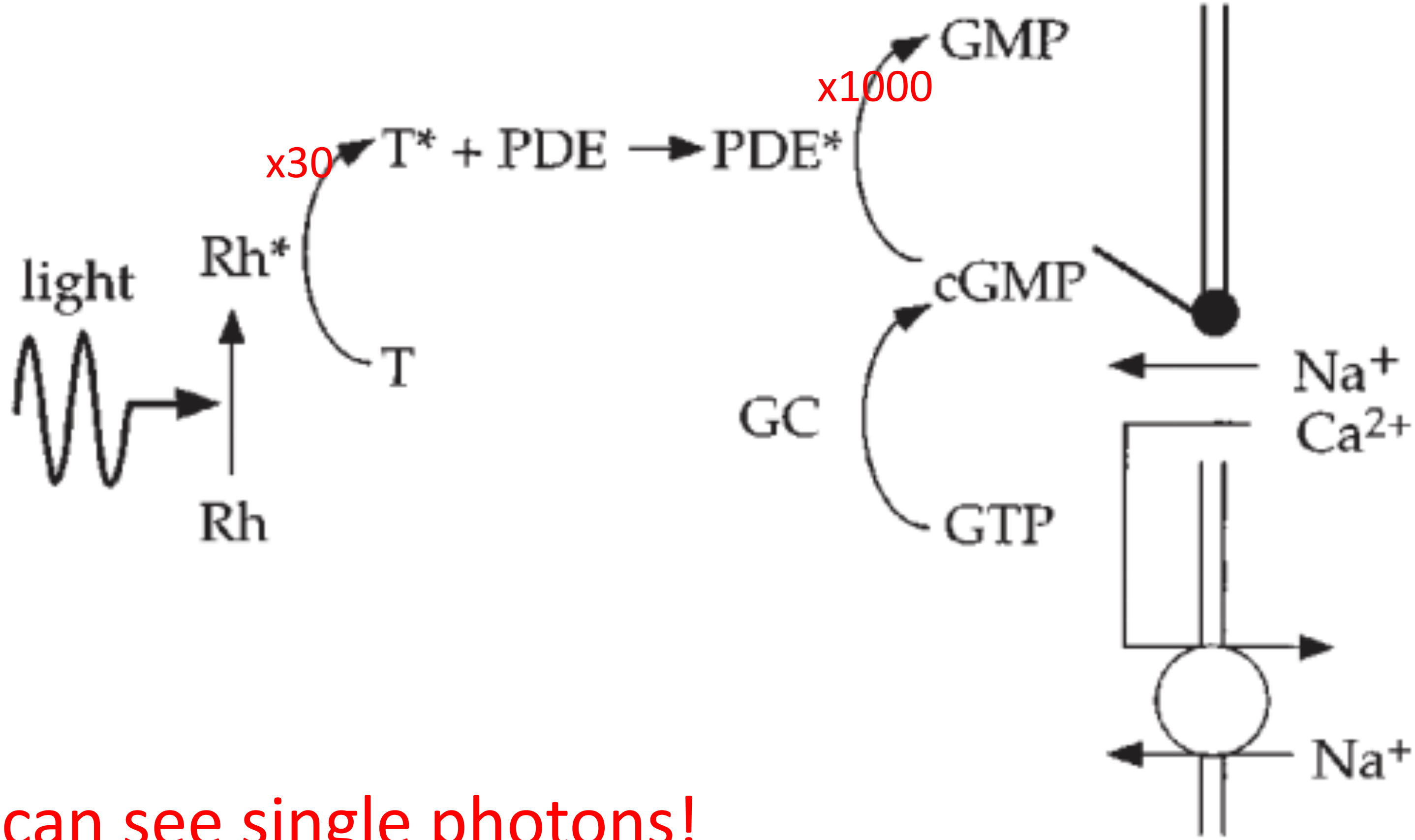
In the dark, Na^+ channels are open by cyclic guanosine monophosphate (**cGMP**).

With photon absorption, 11-cis retinal undergoes a conformational change (photoisomerization) to all-trans retinal leading to signal transduction cascades:

1) The activated rhodopsin stimulates the G protein **transducin**
2) Transducin activates phosphodiesterase (**PDE**), which breaks down cGMP
3) Closure of cGMP-gated channels & hyperpolarization

Purves, 2001

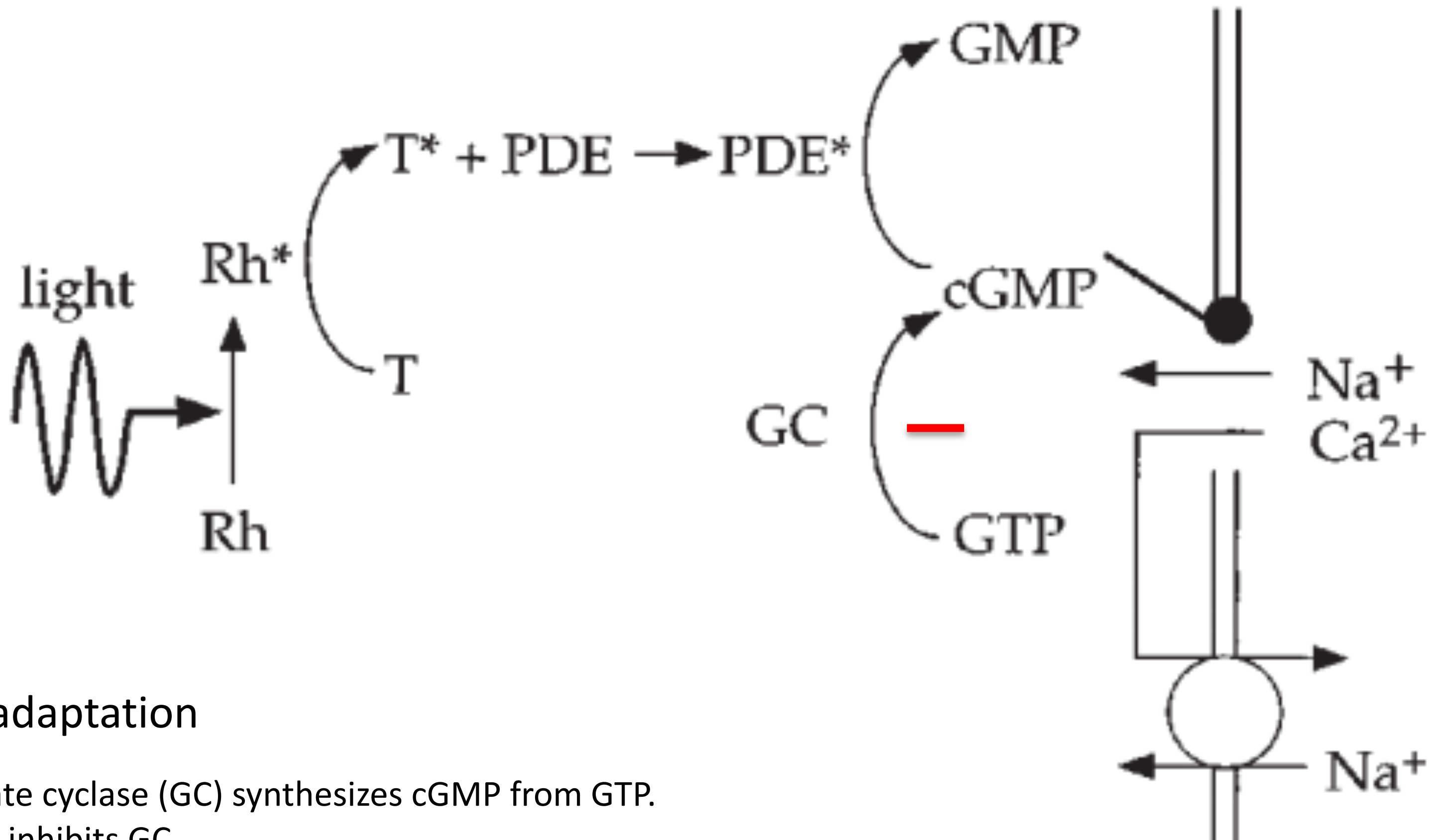
Amplifying the visual signal



We can see single photons!

Rieke & Baylor, 1998

Recovery

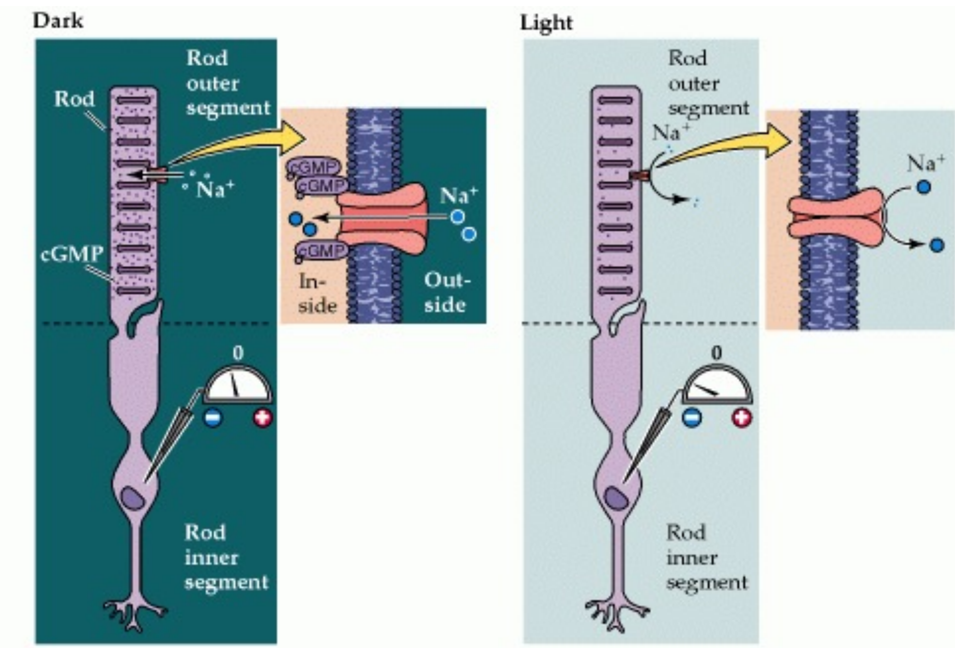


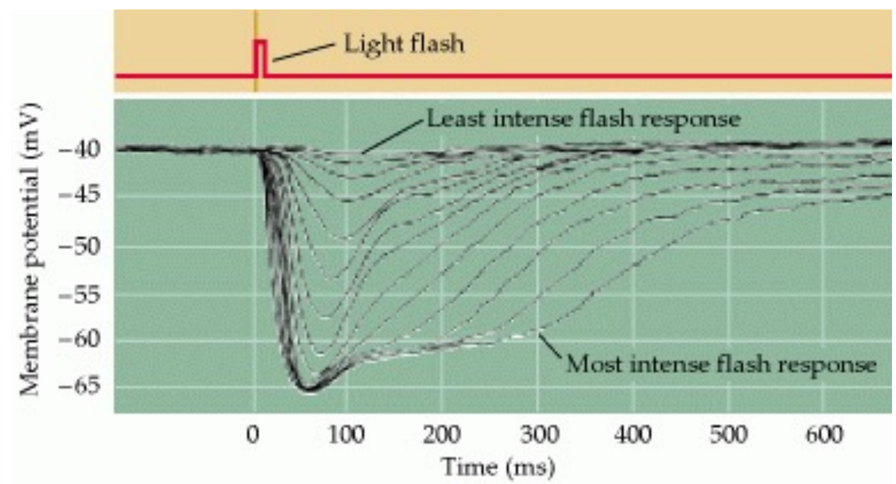
Light adaptation

Guanylate cyclase (GC) synthesizes cGMP from GTP.
Calcium inhibits GC.
Upon closure of channels (light), Ca concentration decreases -> cGMP level increases.

Rieke & Baylor, 1998

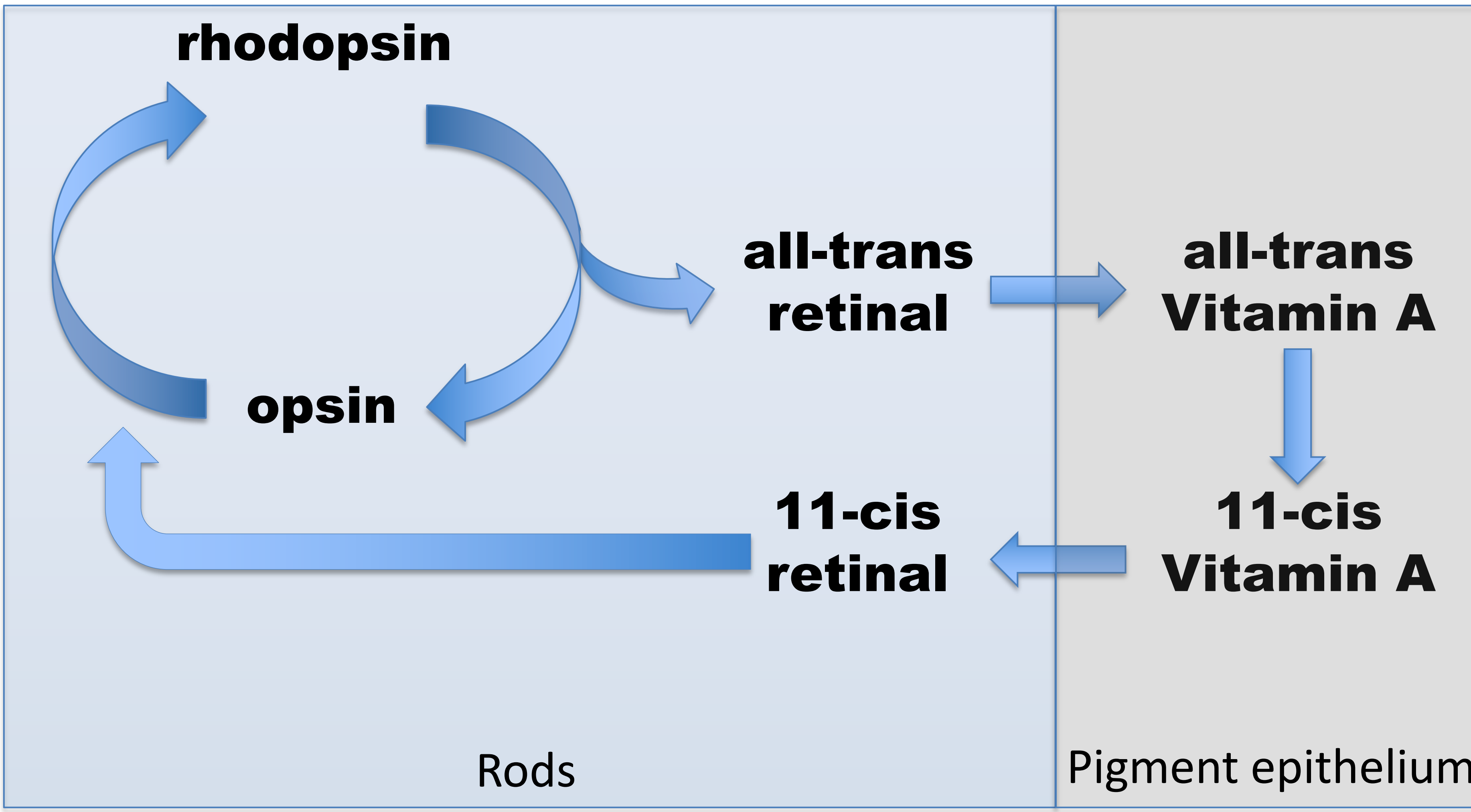
The dark current

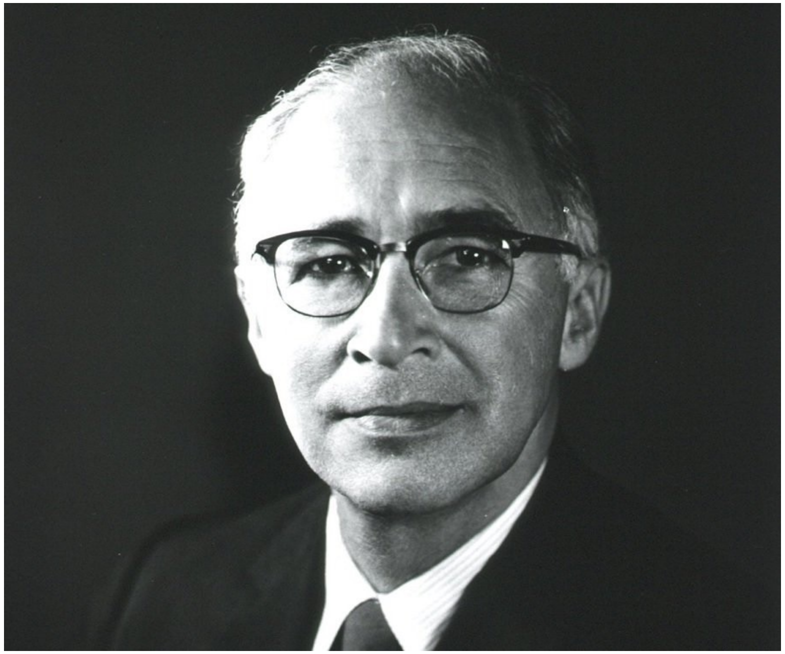




Purves et al., 2001

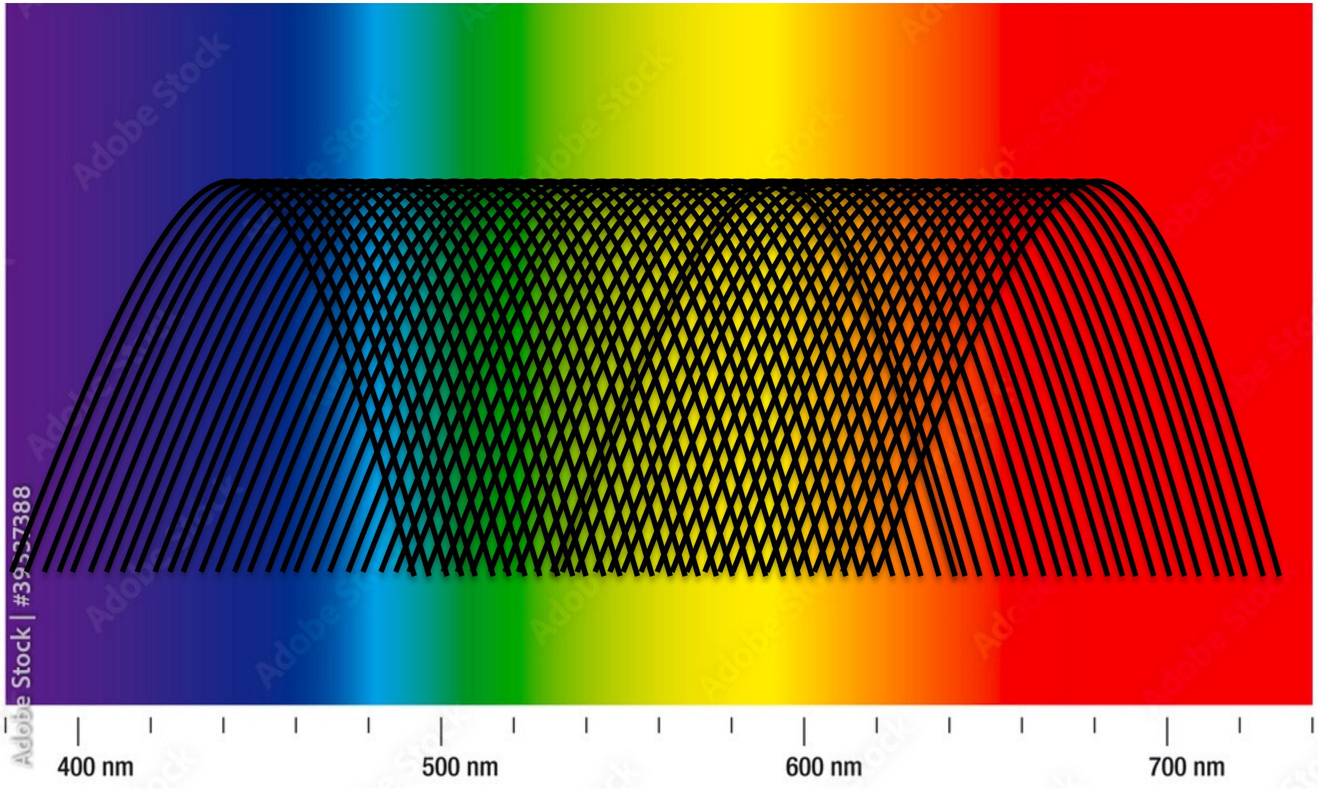
The rhodopsin cycle





George Wald
Nobel prize in Physiology and medicine, 1967

Cones mediate color vision

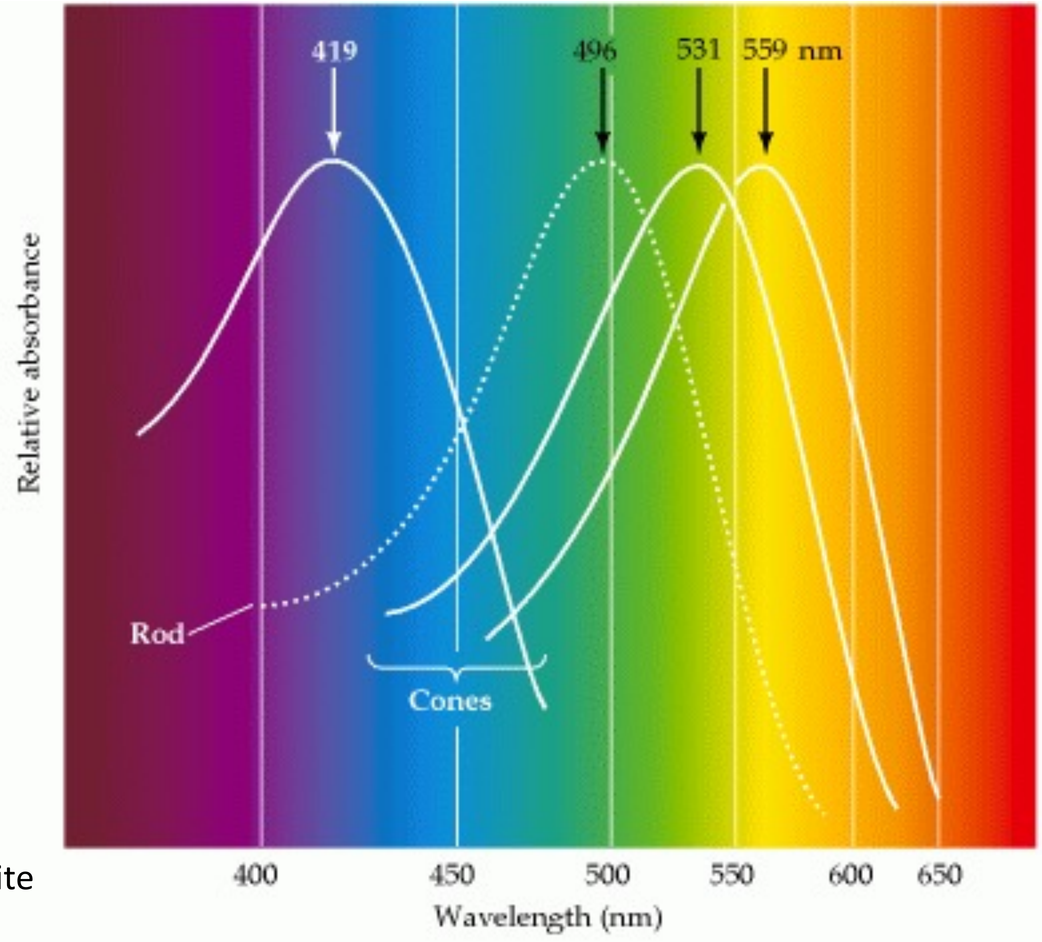


Cones mediate color vision

Color vision is based on two or more photoreceptors that bare different photopigments

- Red (L)
- Green (M)
- Blue (S)

"As it is almost impossible to conceive each sensitive point of the retina to contain an infinite number of particles…, it becomes necessary to suppose the number limited, for instance to the three principal colors."
Thomas Young, 1802



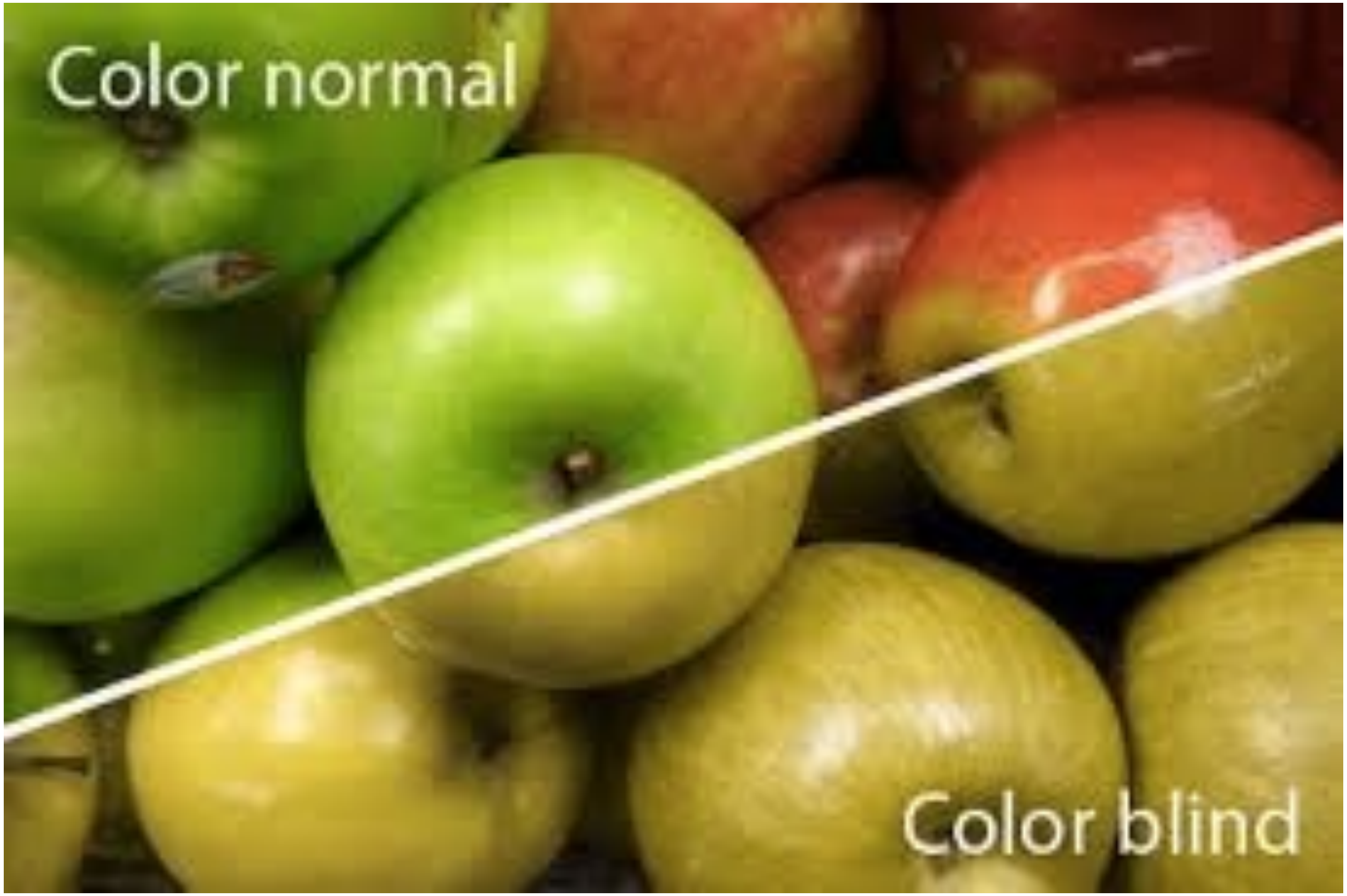
Purves 2001

Monochromatic vision at night

Some animals have 15 cone types

Some animals normally have monochromatic vision

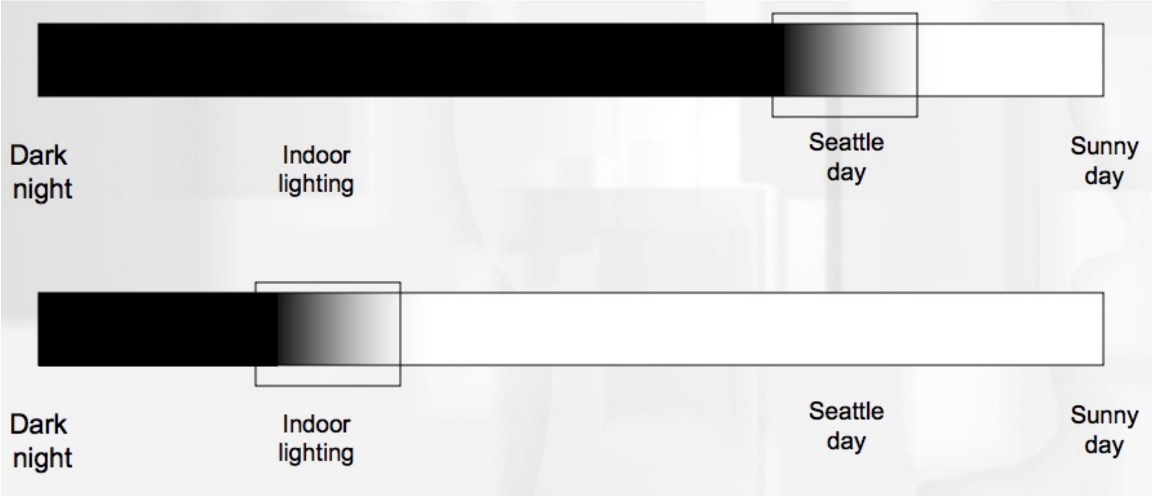
Color blindness



Visual adaptation

- Light intensities range across ~9 orders of magnitude.
  - A piece of white paper can be 1,000,000,000 times brighter in outdoor sunlight than in a moonless night.
  - If we were sensitive to this whole range all the time, we wouldn't be able to discriminate light levels in a typical scene.

  - The visual system solves this problem by restricting the 'dynamic range' of its response to match the current overall or 'ambient' light level.

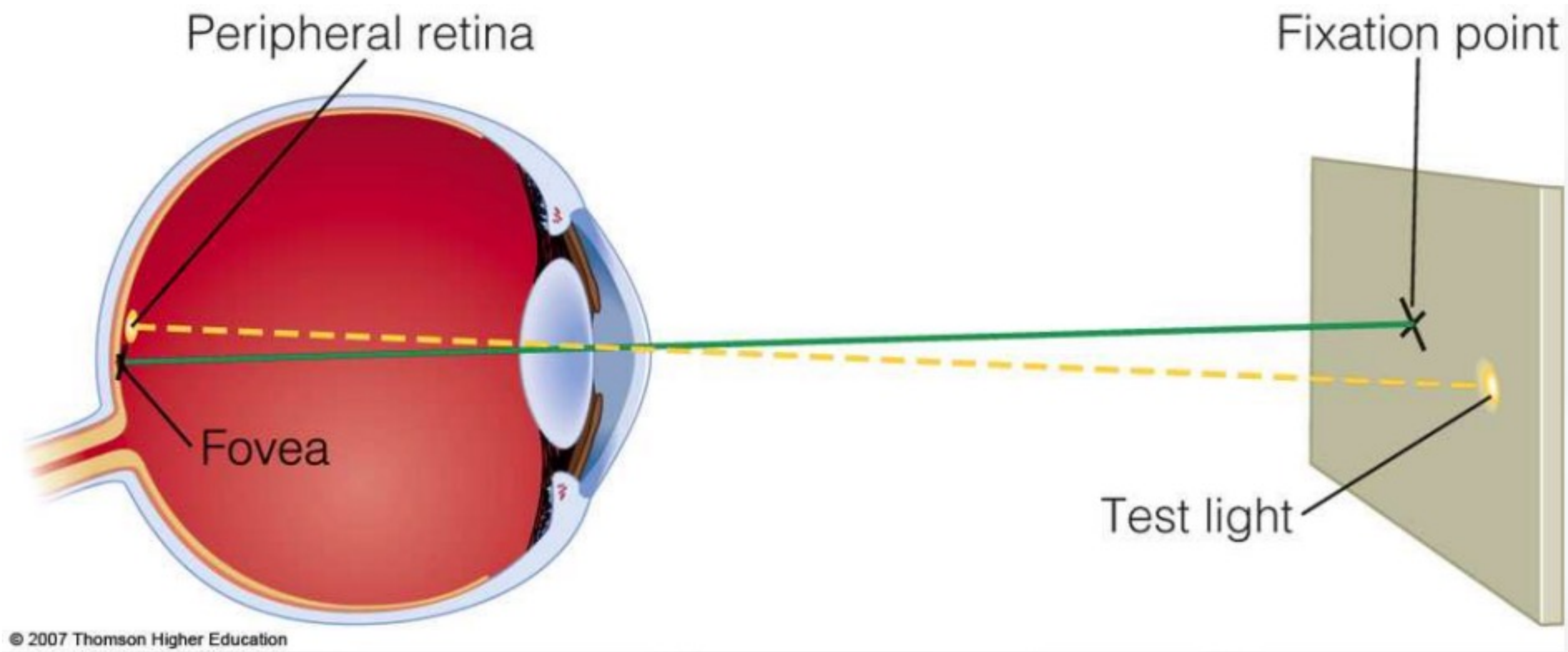


Visual adaptation

- Already at the retina!
  - Pupil's diameter: 2-8 mm.
  - Rods and cones – two visual systems.
  - Both rods and cones adapt – become less sensitive as light levels increase.
  - Further adaptation in retinal circuitry.

Craik & Vernon, 1941:
Pressure blind experiments.

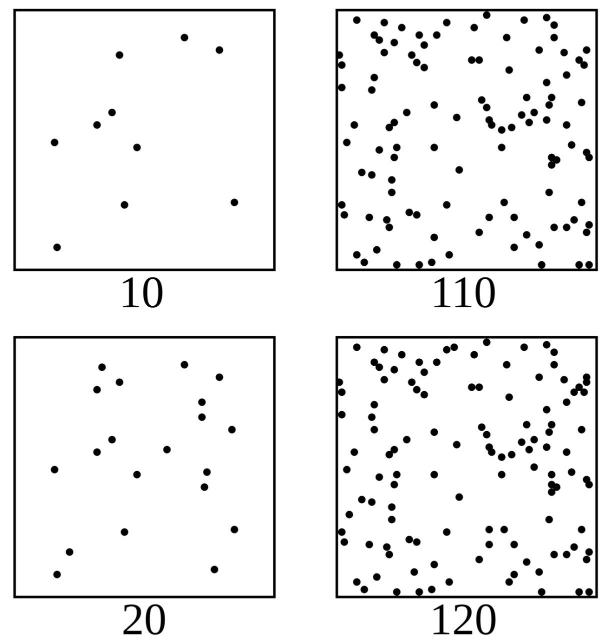
Psychophysical Measurement of Light/Dark Adaptation



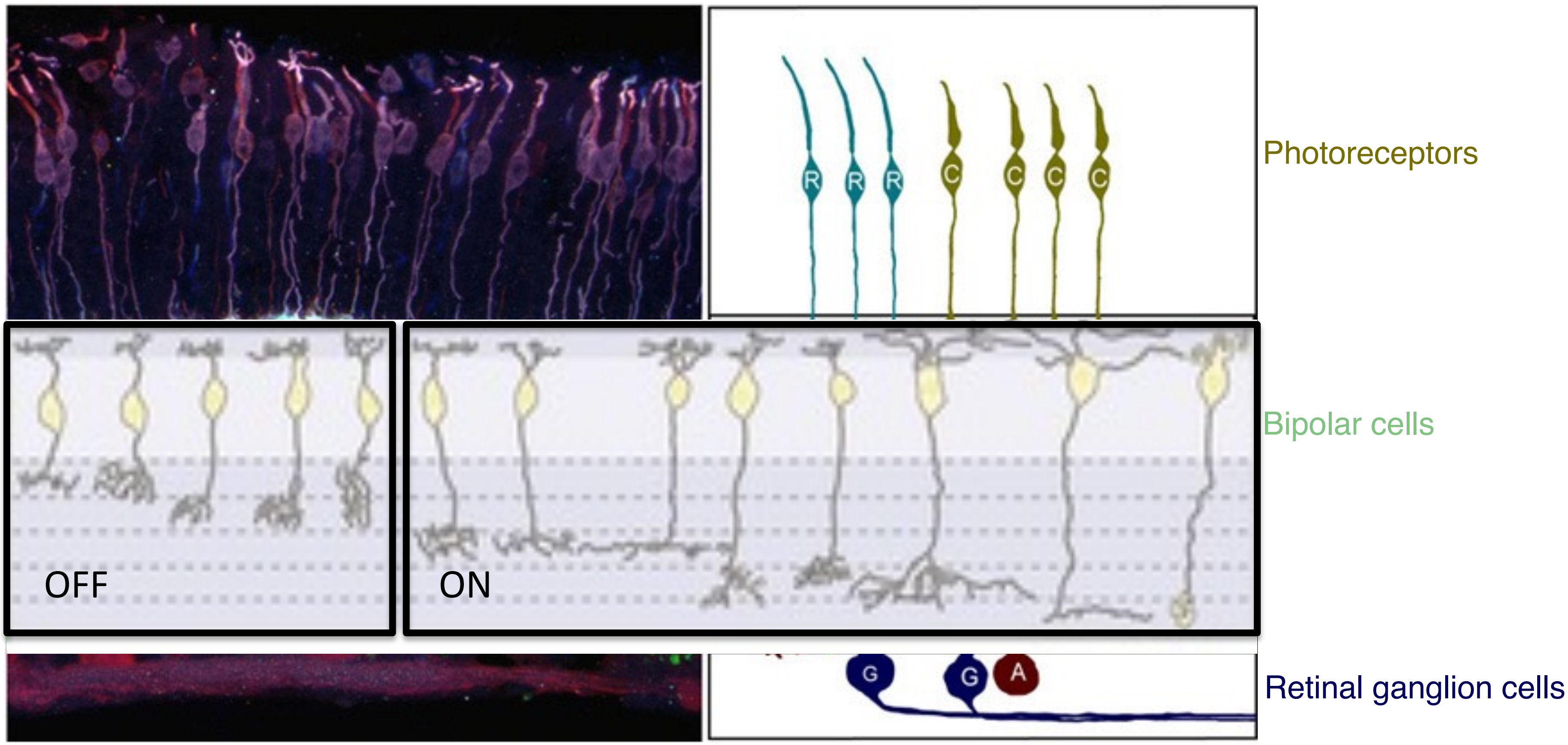
Weber–Fechner law and Weber contrast

- Visual response depends on contrast rather than absolute light levels

$$C = \frac{\Delta I}{I}$$



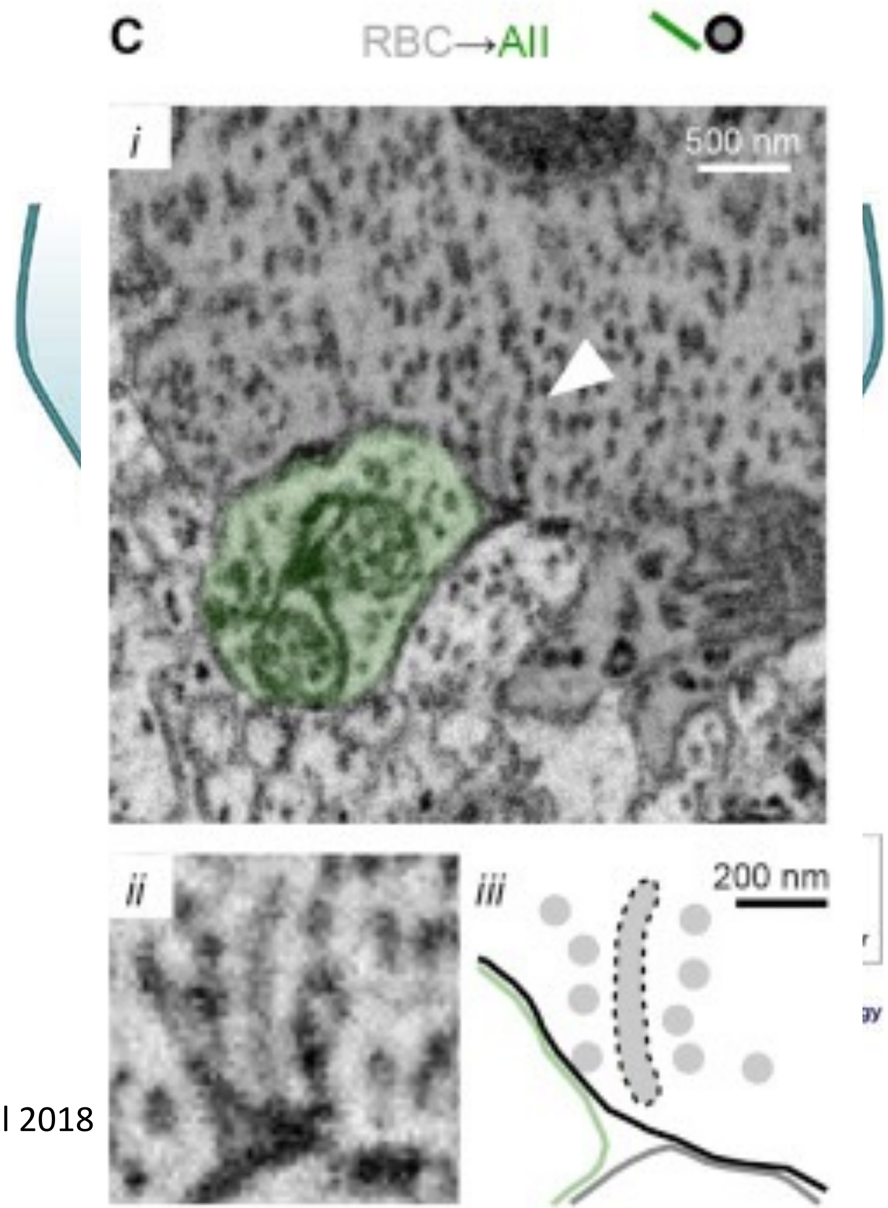
Bipolar Cells



Adapted from Morgan and Wong http://webvision.med.utah.edu
And from Euler et al. 2014 Nature reviews Neuroscience

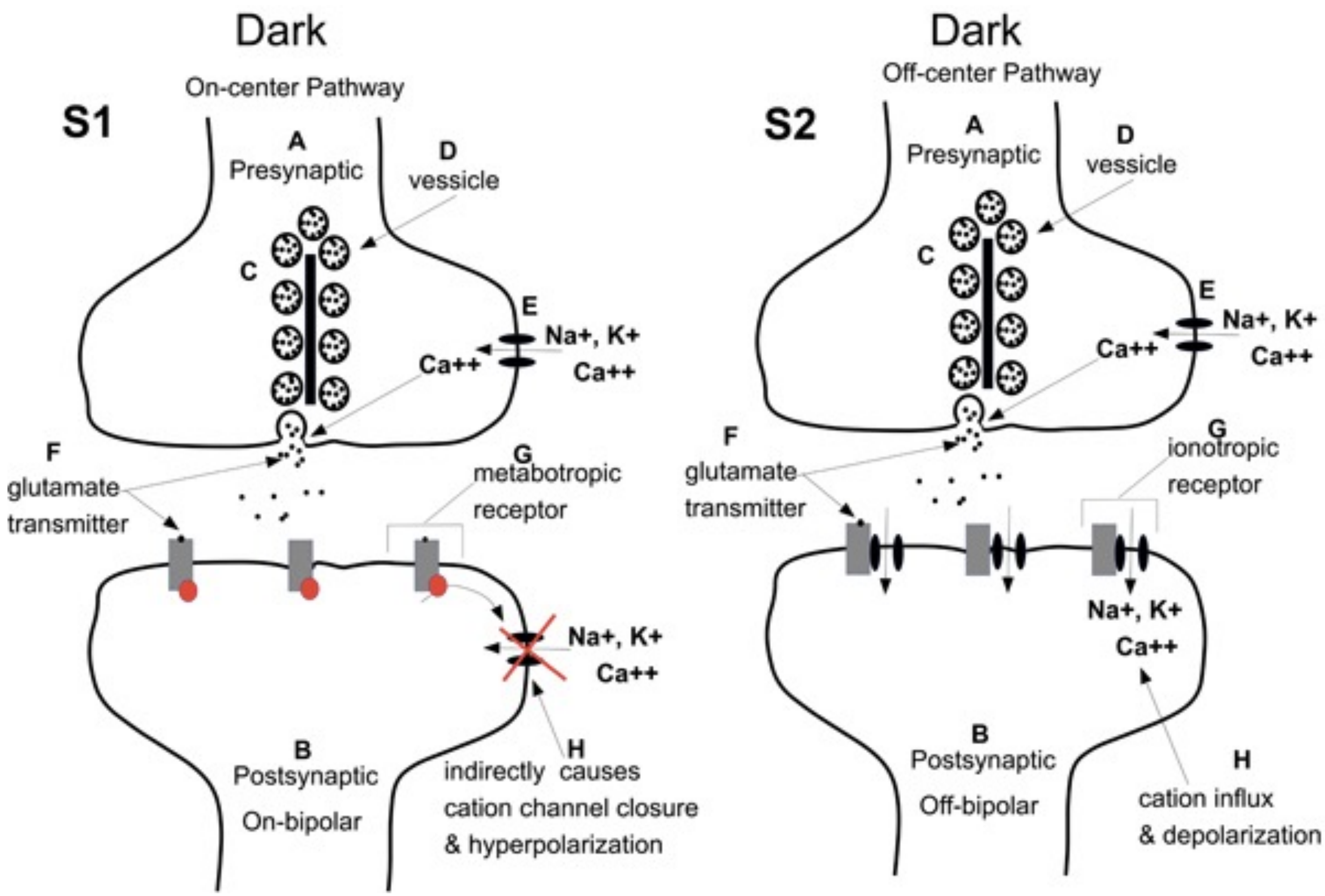
Ribbon synapse

- Graded neurotransmitter release. Precise, sustained, and rapid.
- The synaptic ribbon releases 100s-1000s vesicles per second.
- Each pre-synaptic cell has 10-100 ribbons.
- Requires a large pool of readily releasable vesicles.

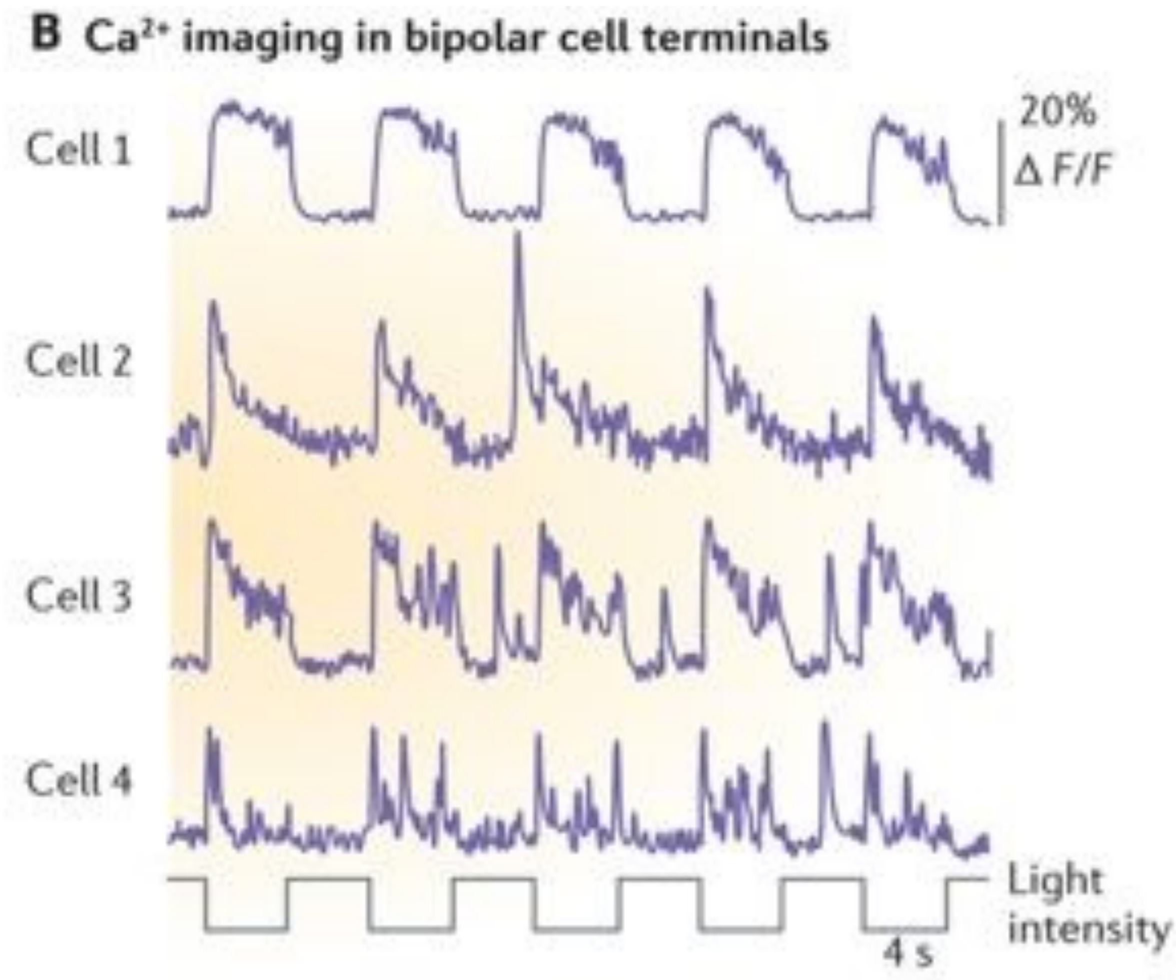


Graydon et al., Cur Biol 2018

On- and Off-bipolar cells

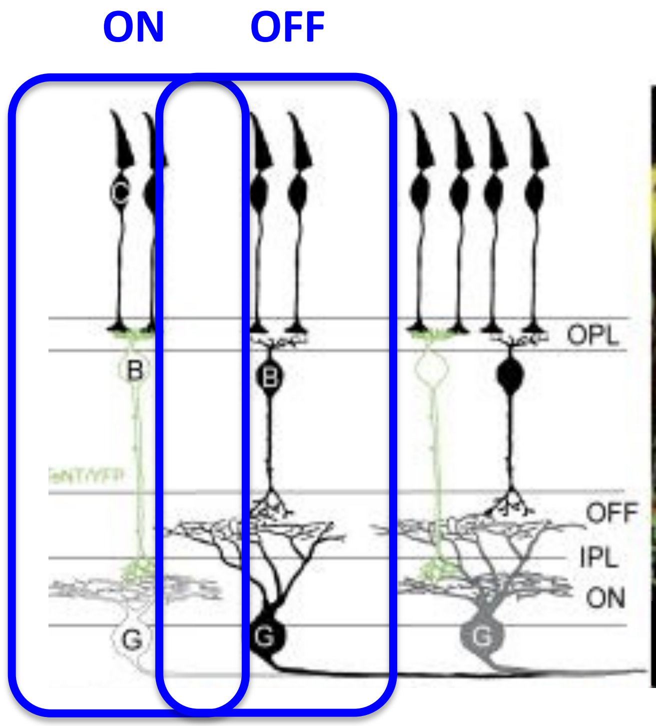


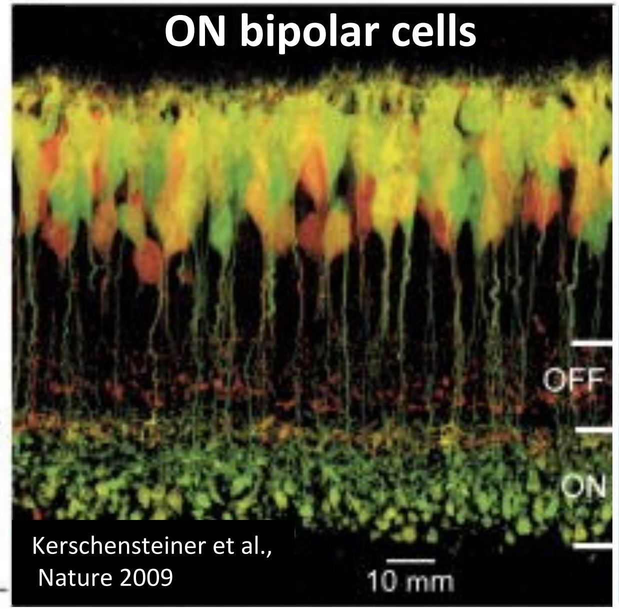
Sustained and transient bipolar cells

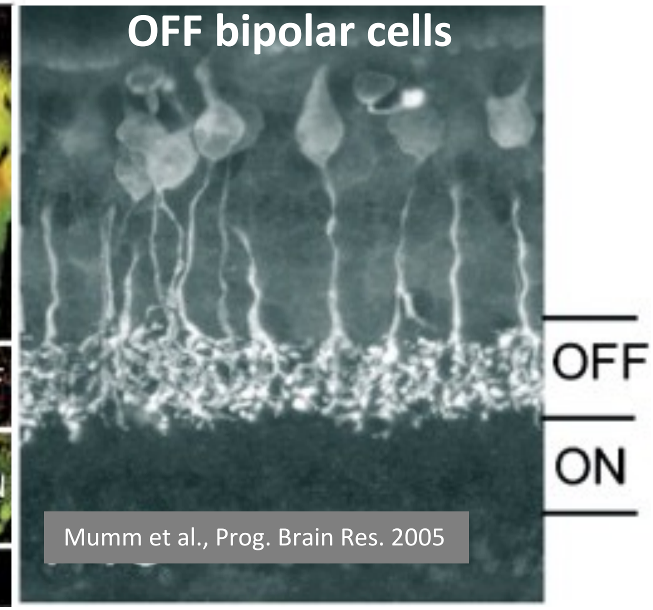


Euler et al., 2014

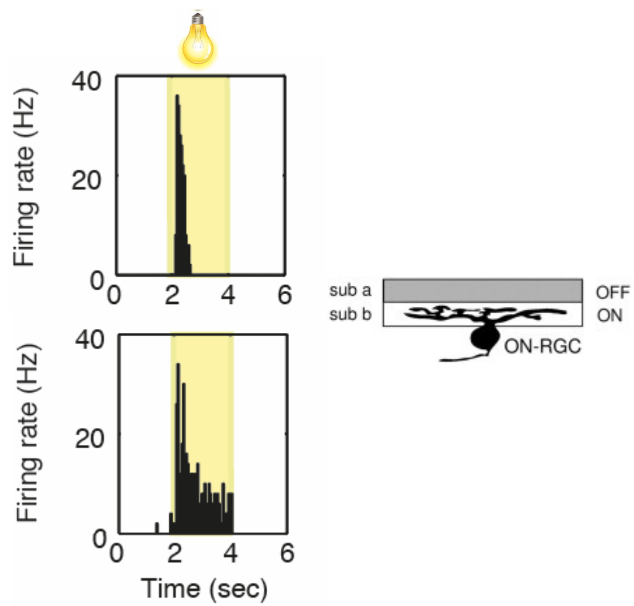
On and Off retinal pathways

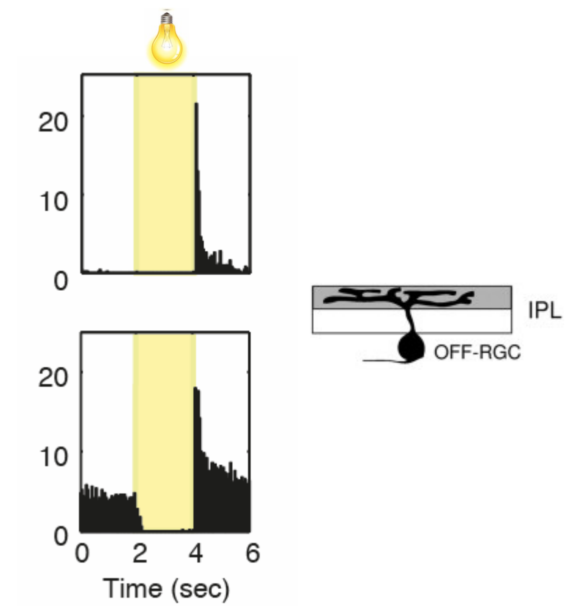




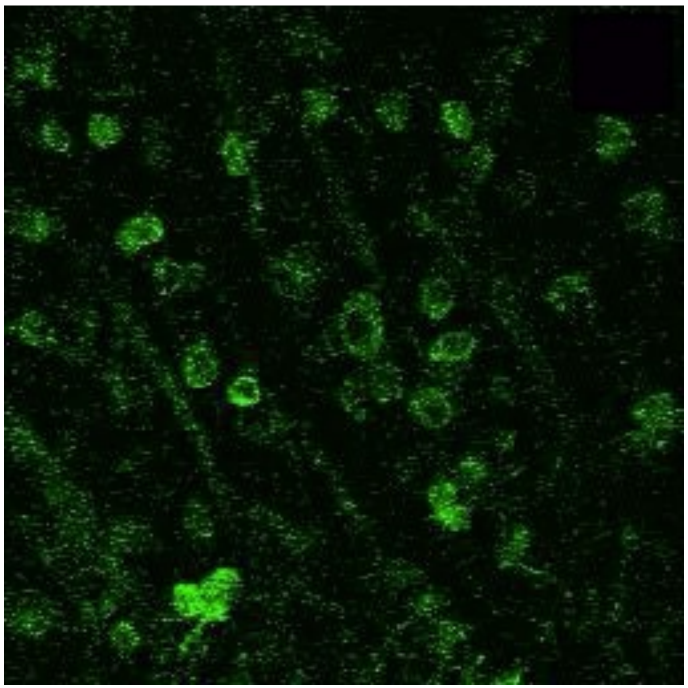


Retinal ganglion cells (RGC):

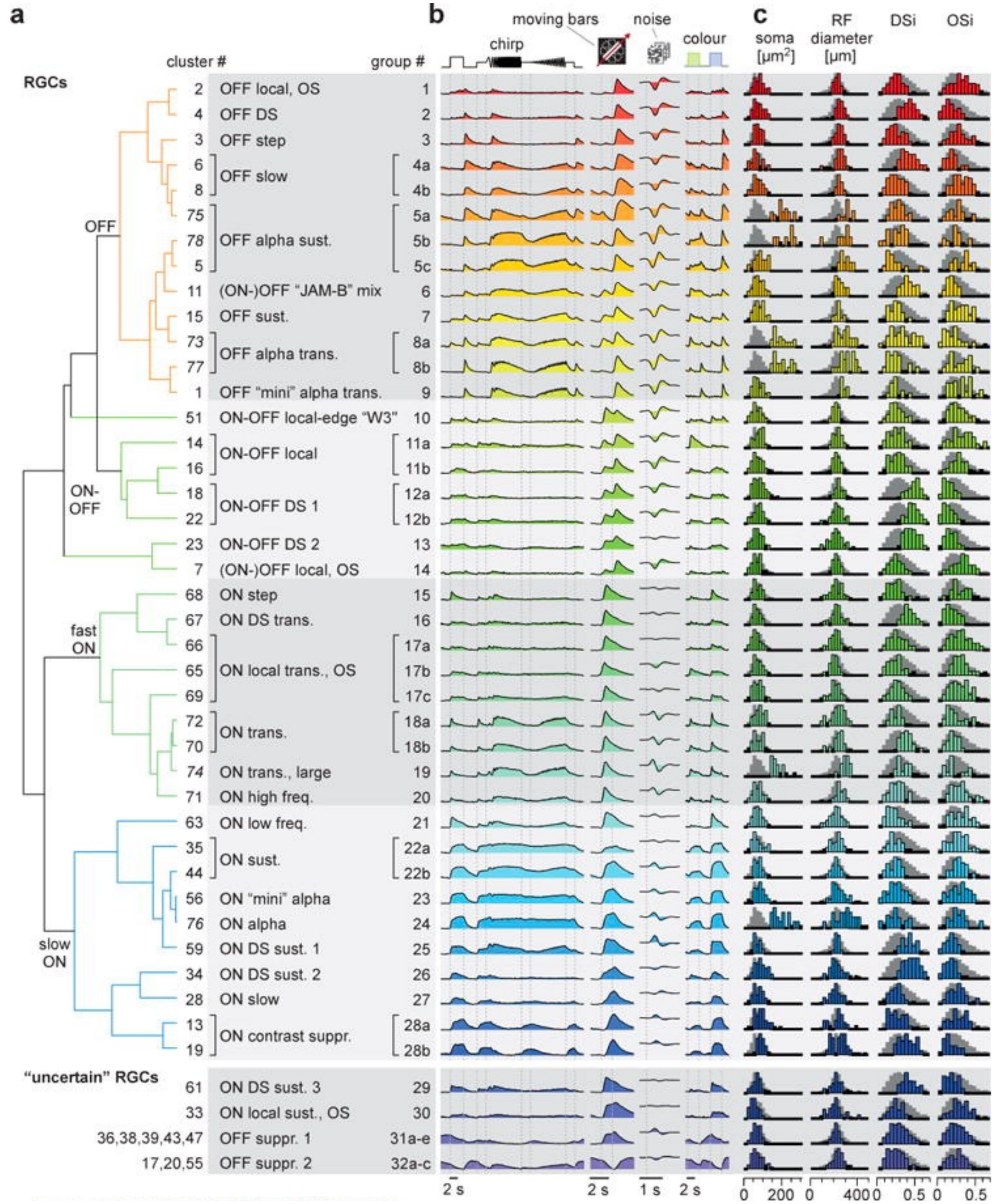




>30 different subtypes of retinal ganglion cells (RGCs)



Lior Pinkus

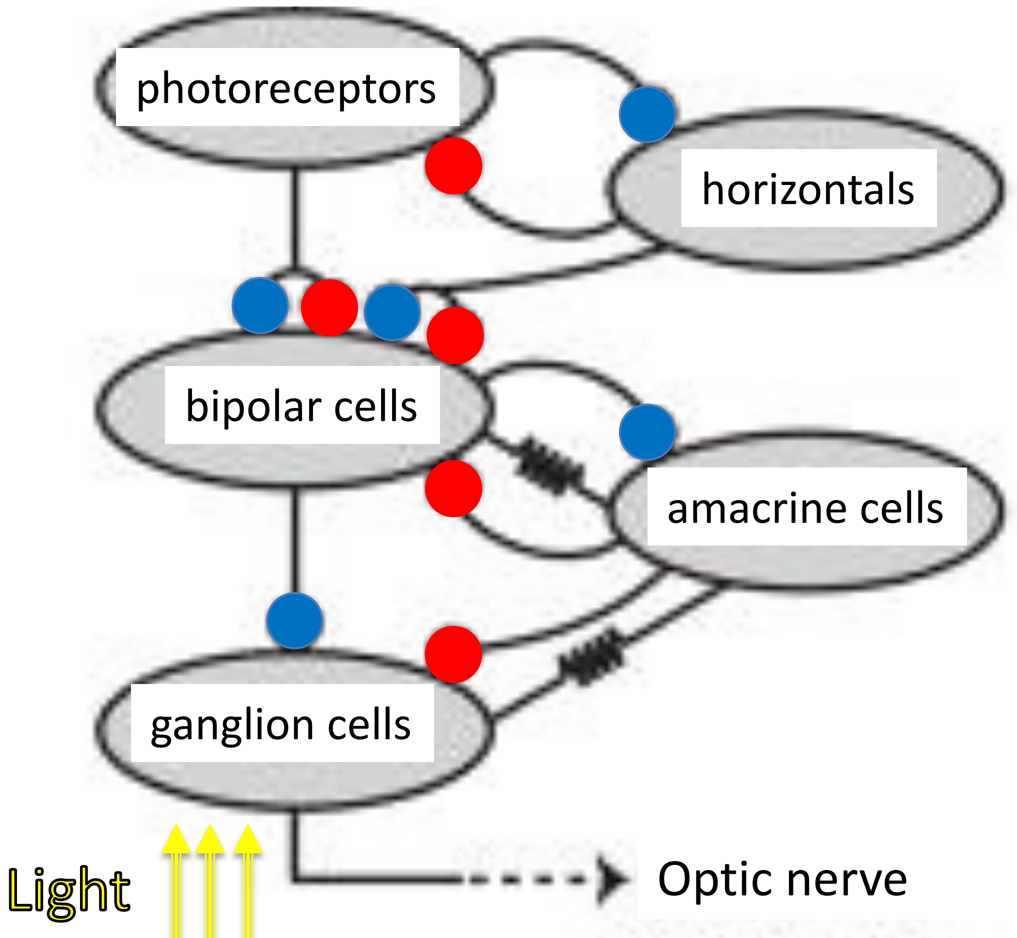


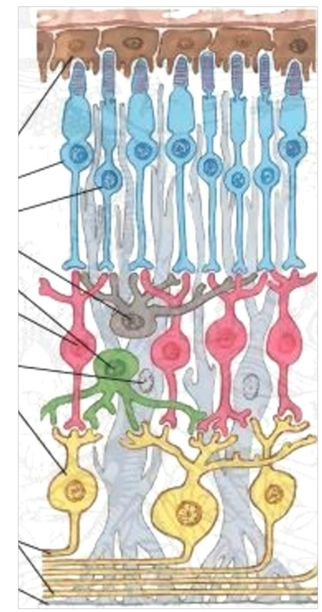
Baden et al., Nature 2016

Straight through pathway + lateral connections

Excitation

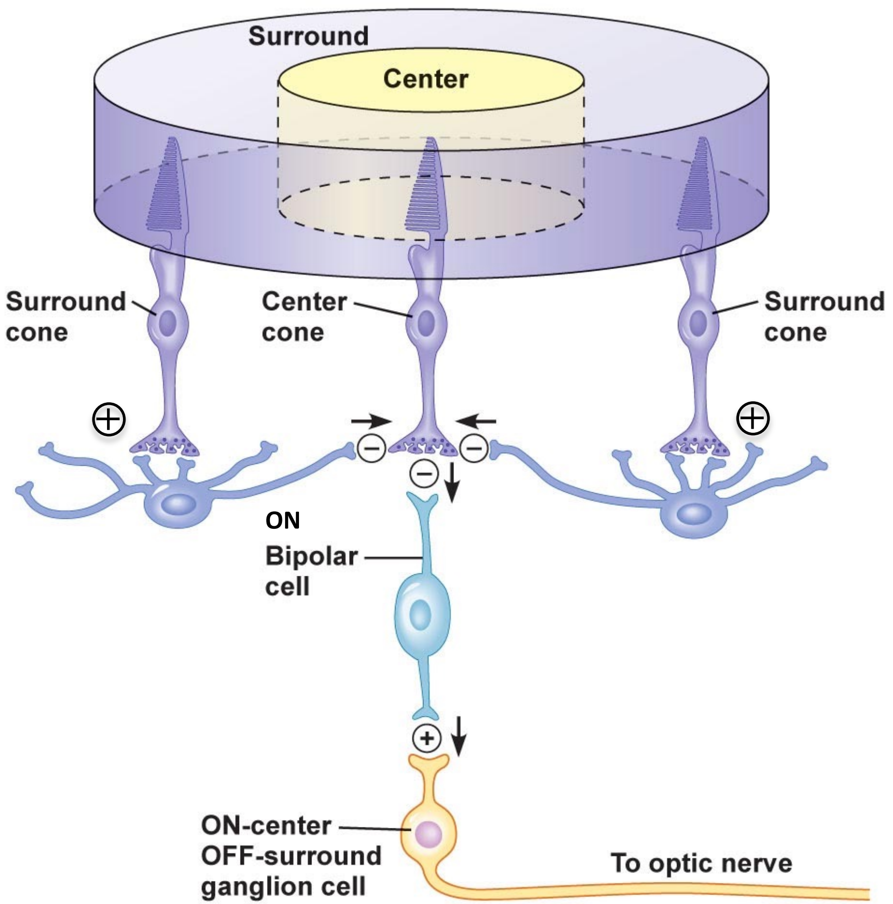
Inhibition





Golisch & Meister 2010

Horizontal Cells



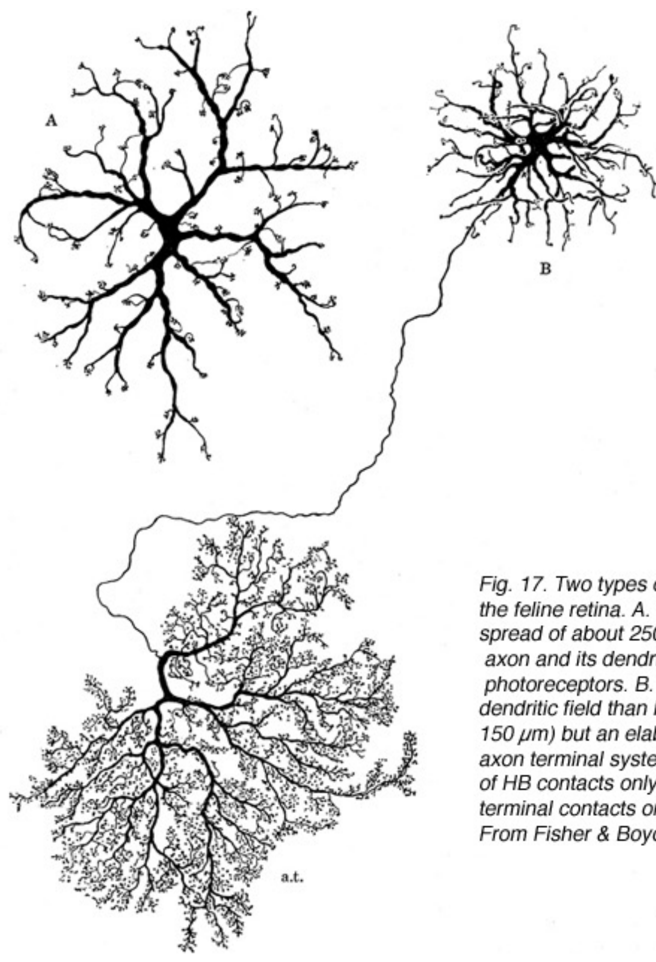
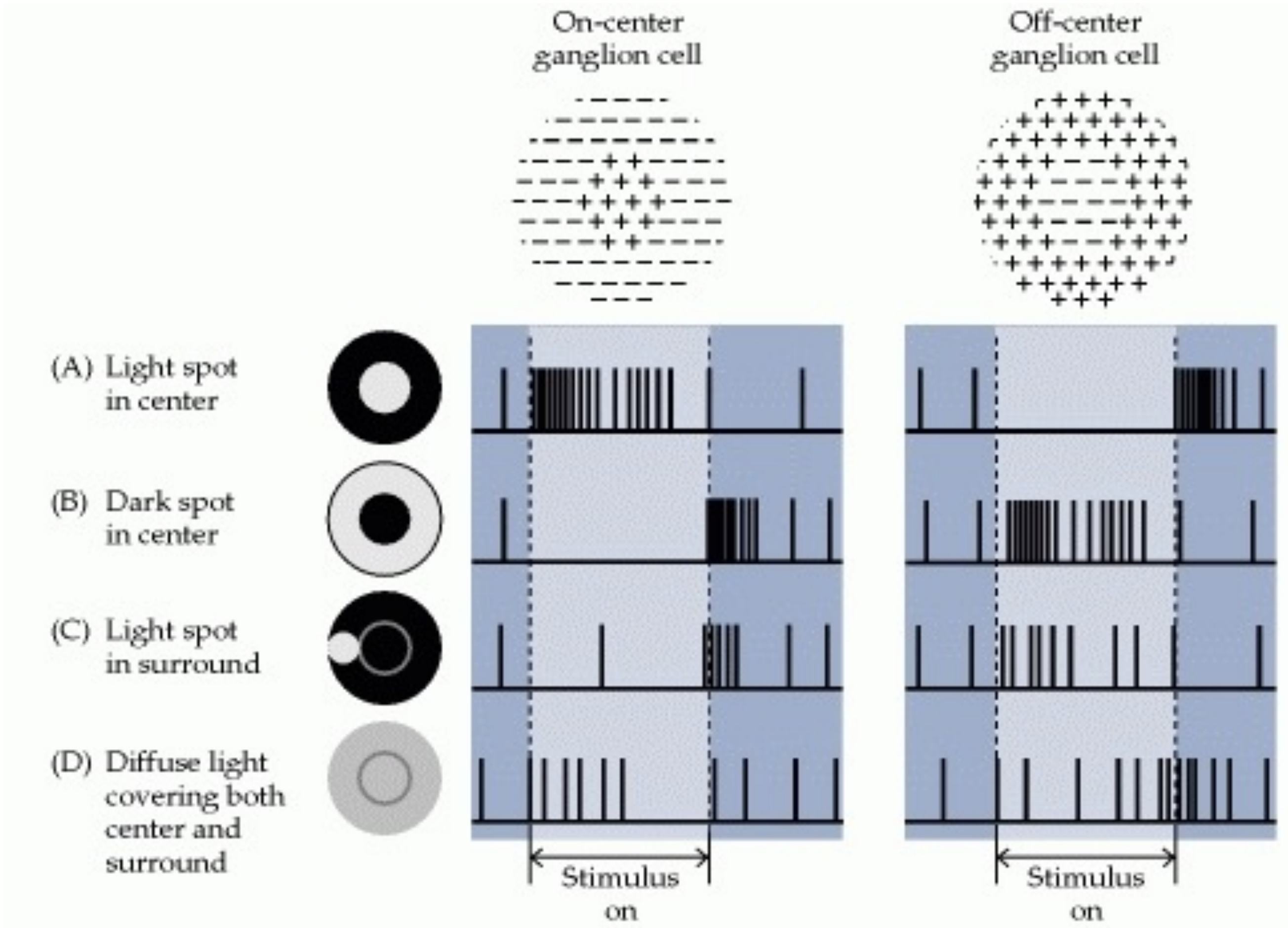
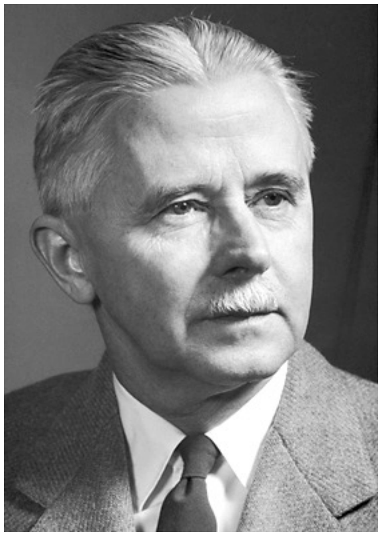
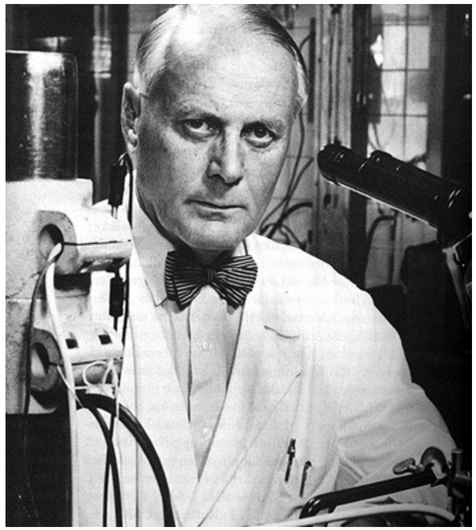


Fig. 17. Two types of horizontal cells in the feline retina. A. HA with a dendritic spread of about 250 μm x 250 μm has no axon and its dendrites contact only cone photoreceptors. B. HB has a smaller dendritic field than HA (about 150 μm x 150 μm) but an elaborately branched axon terminal system (a.t.). The dendrites of HB contacts only cones, while the axon terminal contacts only rods. From Fisher & Boycott, 1974.

Center-surround organization of receptive fields







Haldan Keffer Hartline
1938

Ragnar Arthur Granit
1947

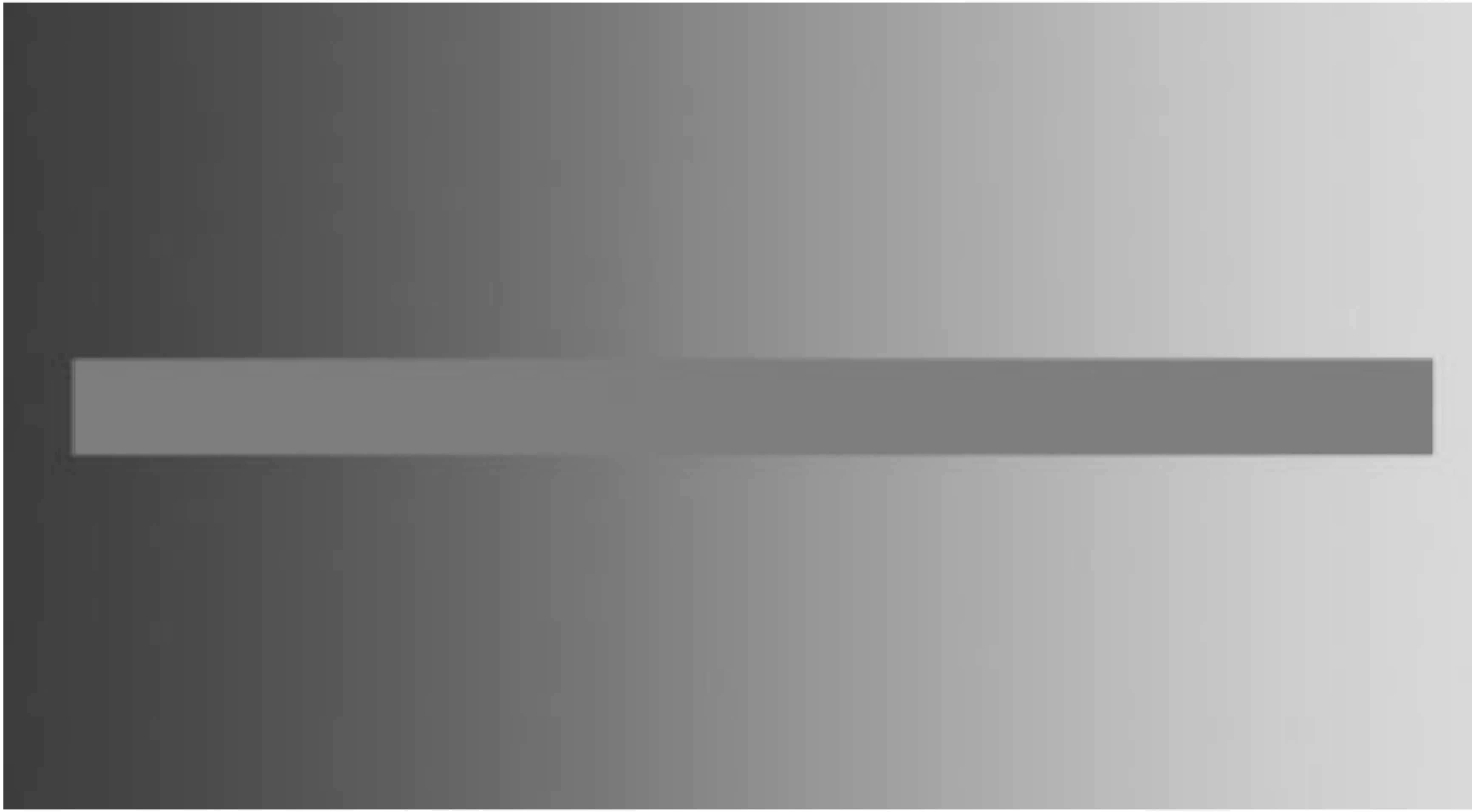
Record activity of single RGCs.
Finds On, Off, and On-Off cells.
Nobel prize in Physiology and medicine, 1967

Horace Barlow

Stephen Kuffler

1950
Find the antagonistic center-surround organization in RGCs

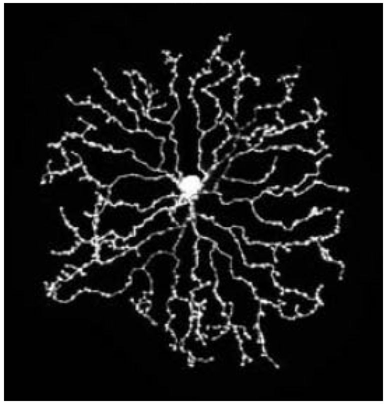
Retinal neurons signal relative intensity of stimulation



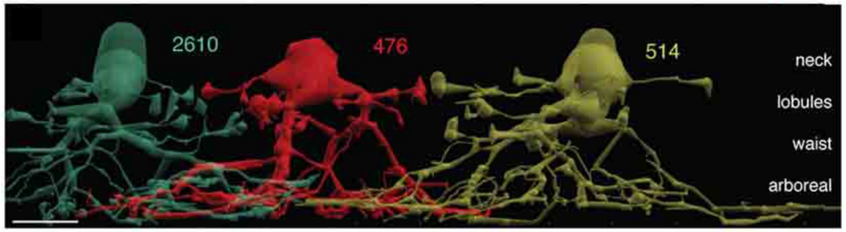
Retinal neurons signal relative intensity of stimulation

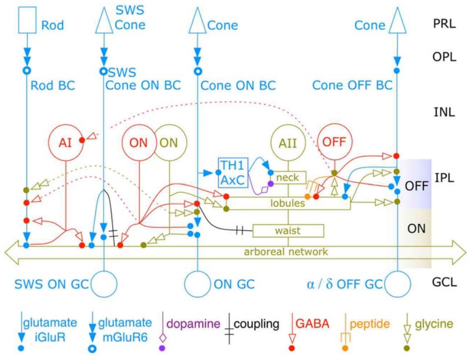
Narrow-field amacrine cells

Starburst amacrine cell



AII amacrine cell



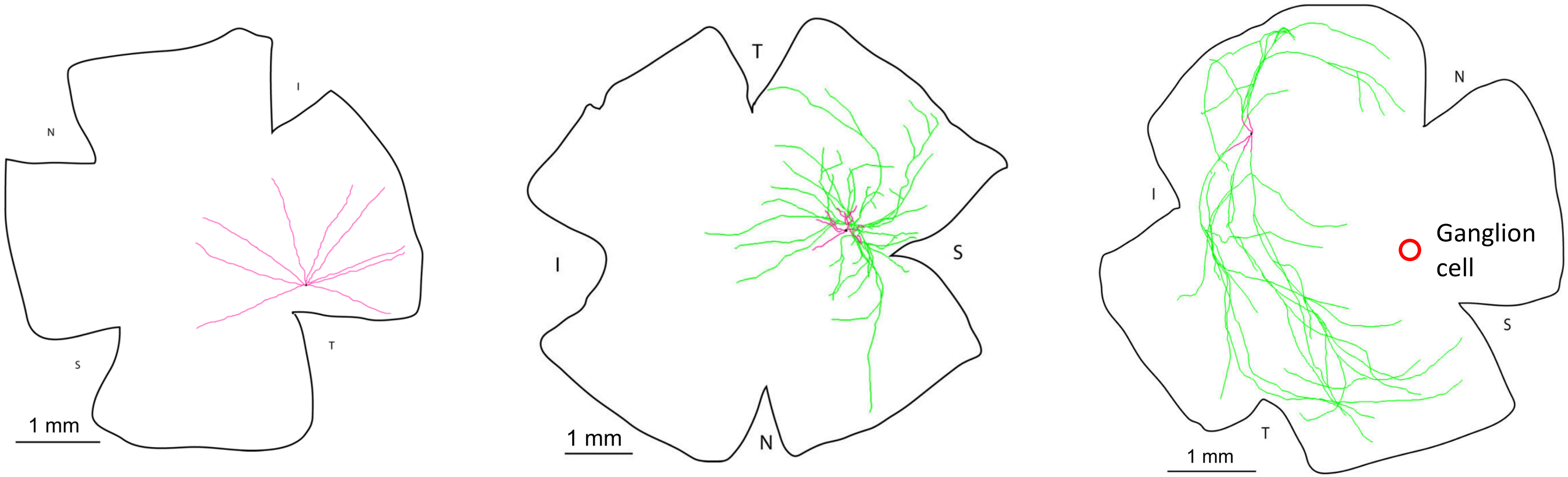


Marc et al., 2014 (*Front. Neural Circuits*)

Different neurotransmitters:

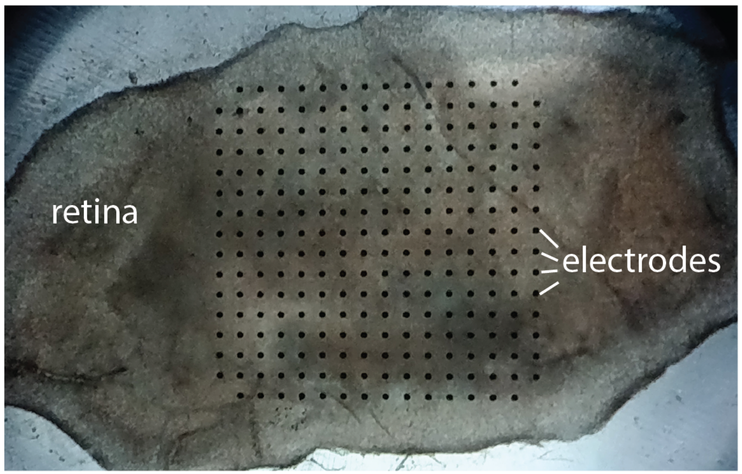
- GABA
- Glycine
- Dopamine
- Acetylcholine
- Glutamate (new!)

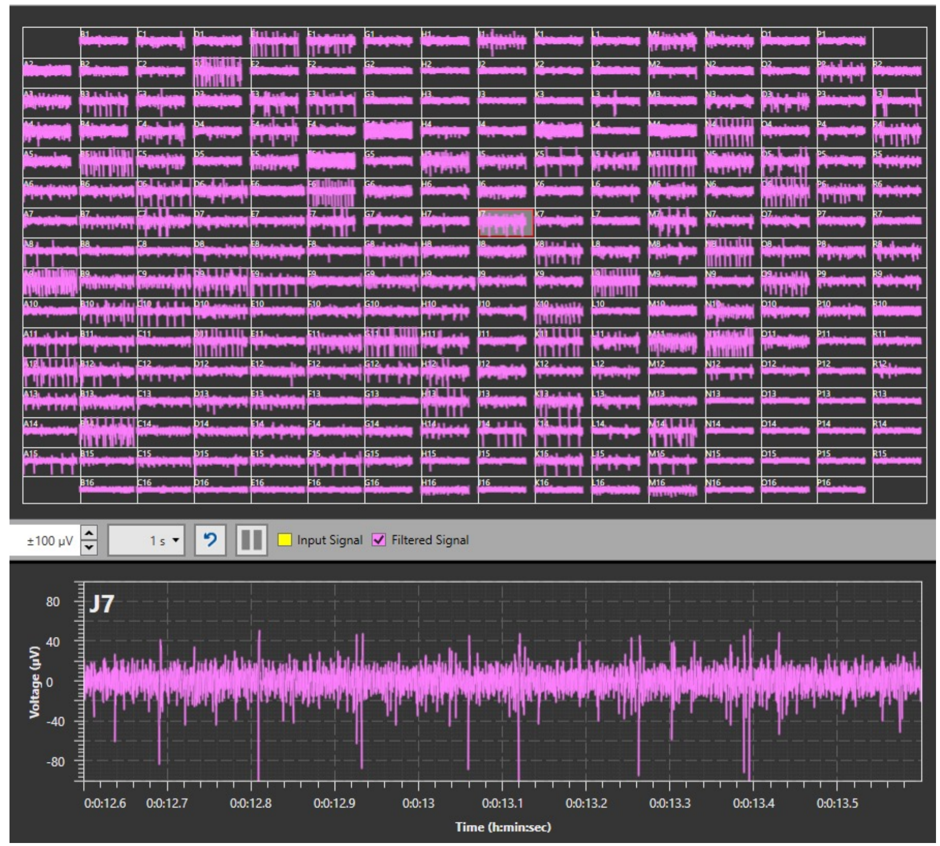
Wide-field amacrine cells



Lin and Masland, 2006 (*J. Comp. Neurol.*)

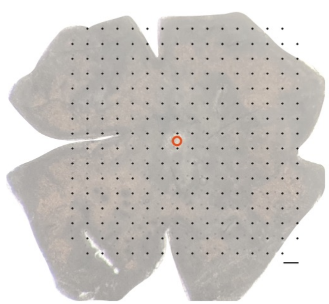
Identifying receptive fields of retinal ganglion cells using multi-electrode array recordings



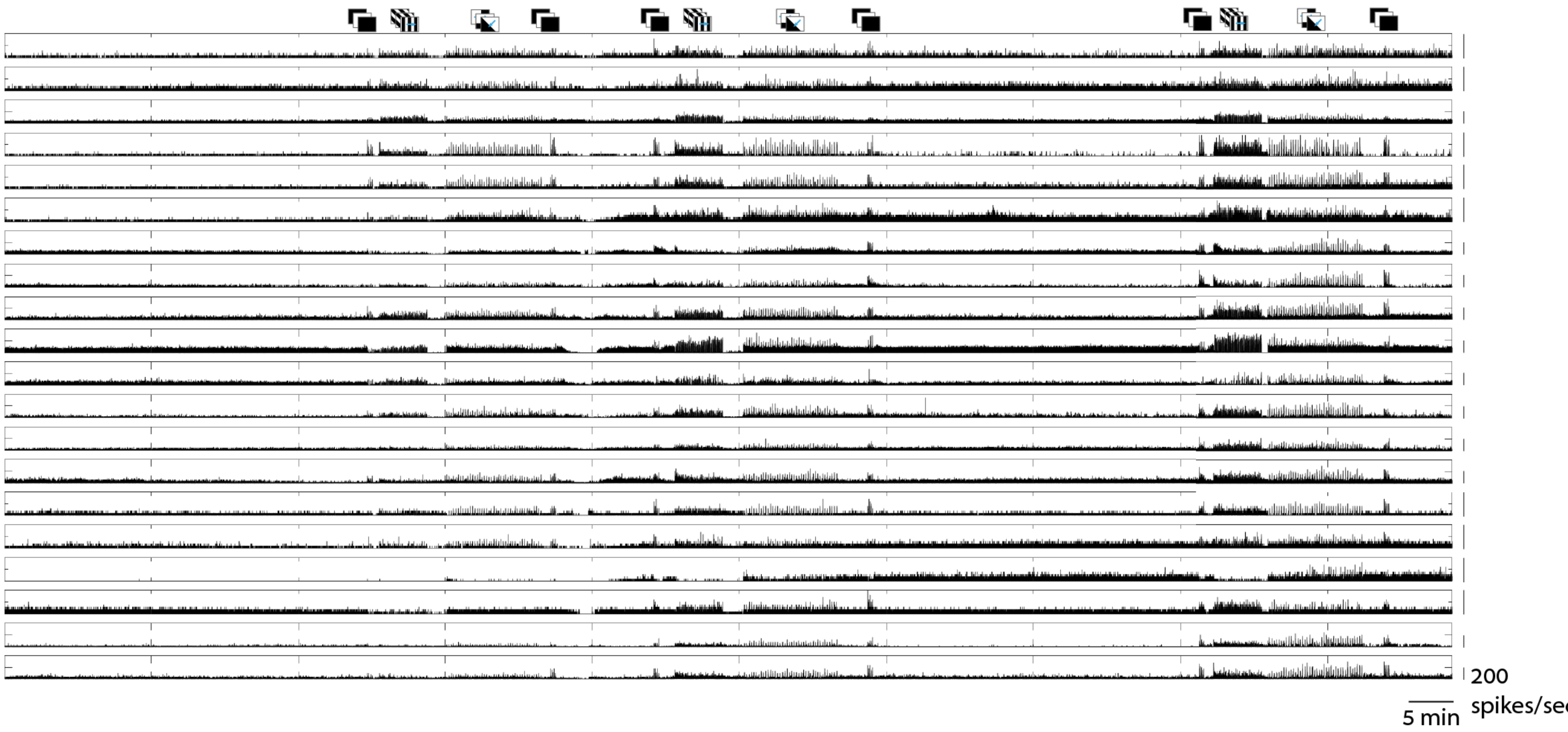


Serena Riccitelli

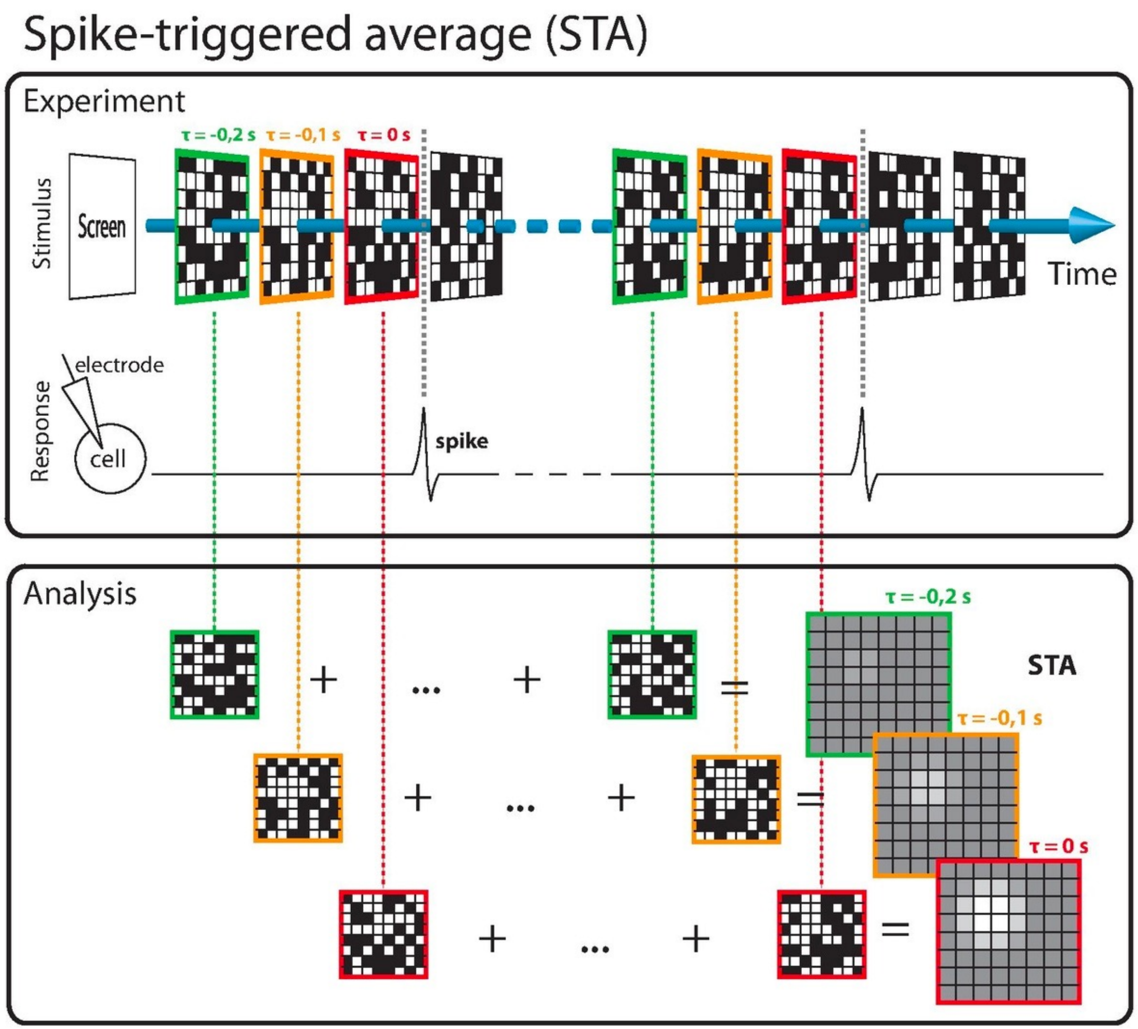
Alina Heukamp



Identifying receptive fields of retinal ganglion cells using multi-electrode array recordings

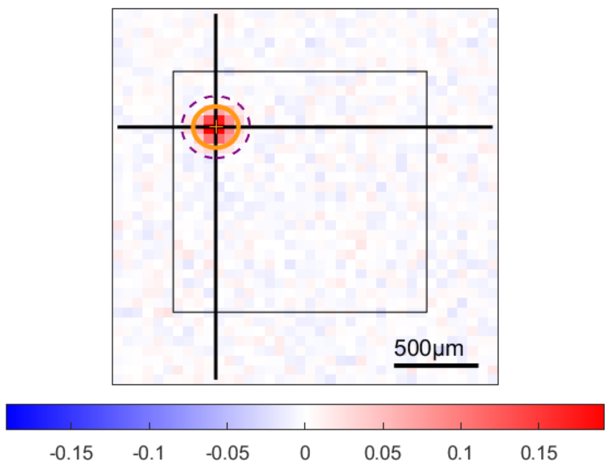


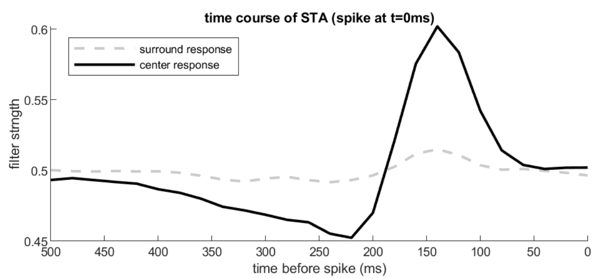
Receptive field of RGCs can be measured using the spike-triggered average of a spatio-temporal white noise stimulus



From Wikipedia

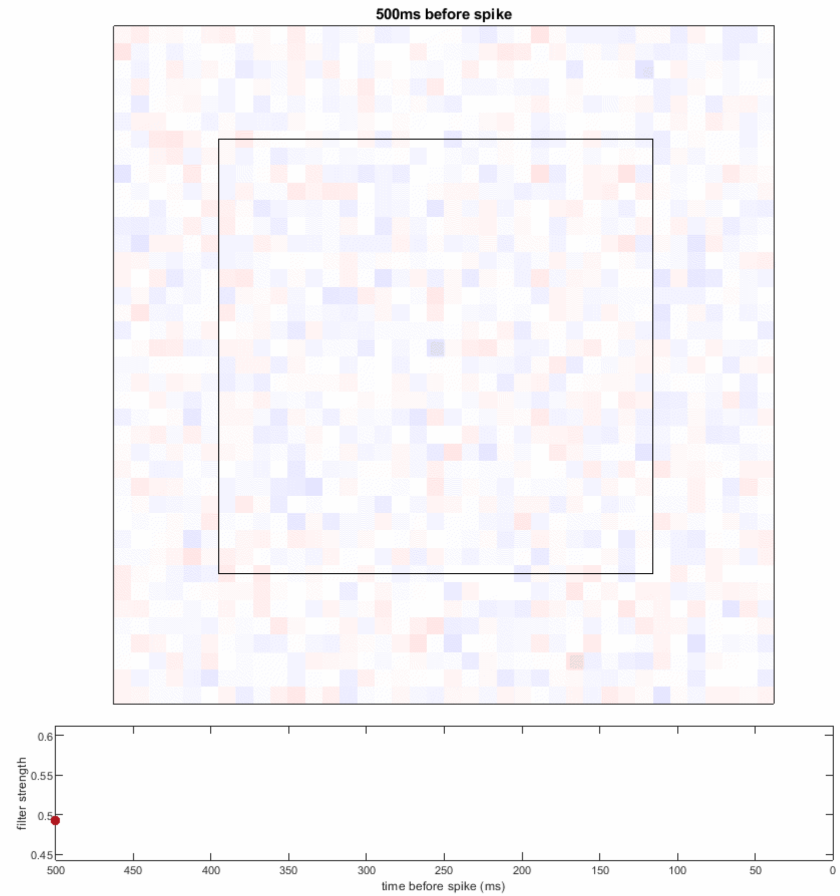
Receptive field of RGCs can be measured using the spike-triggered average of a spatio-temporal white noise stimulus



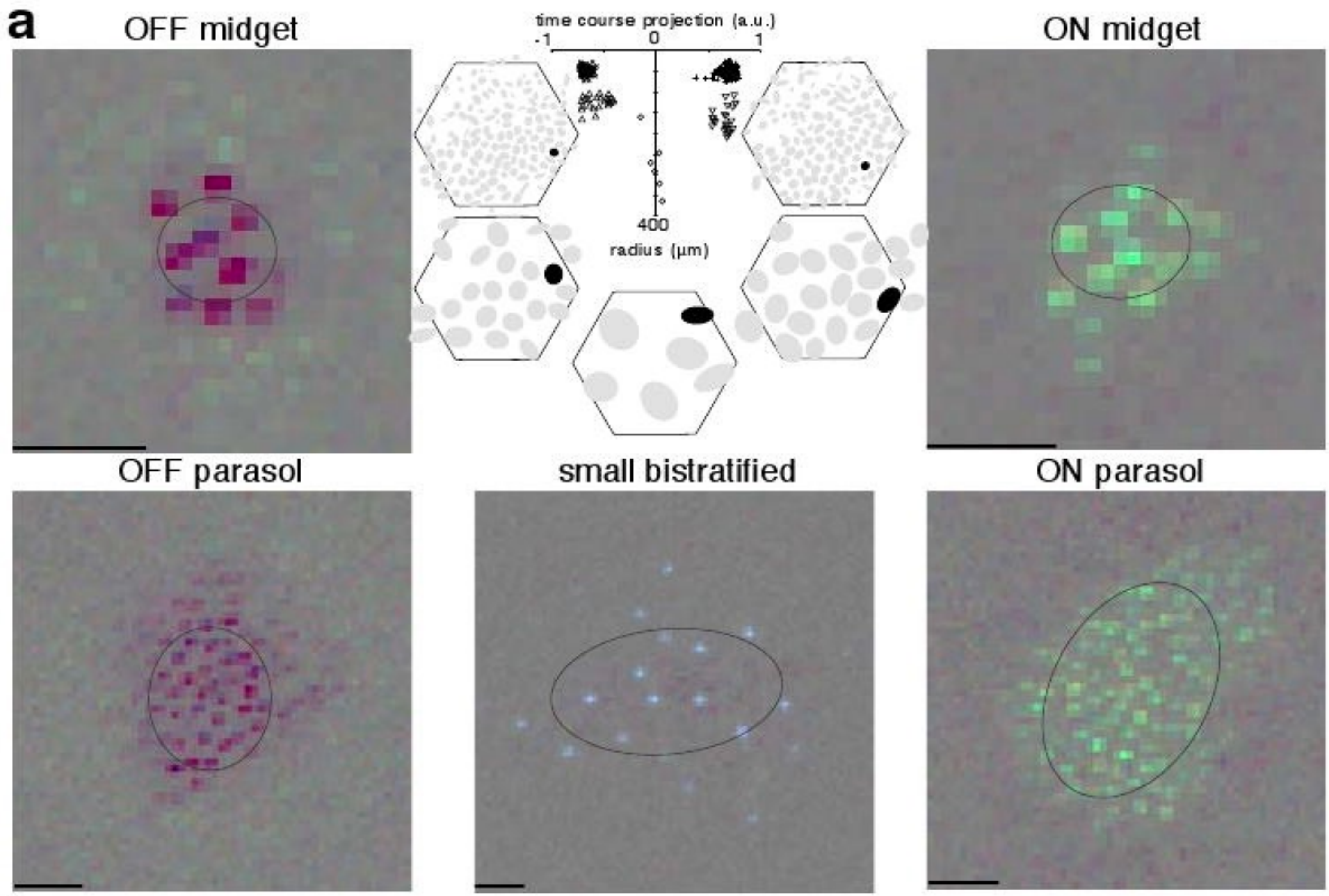


RF diameter:
in x direction: 150.0um
in y direction: 137.8um

maximum response: 140.0ms before spike
(positive response = ON cell)

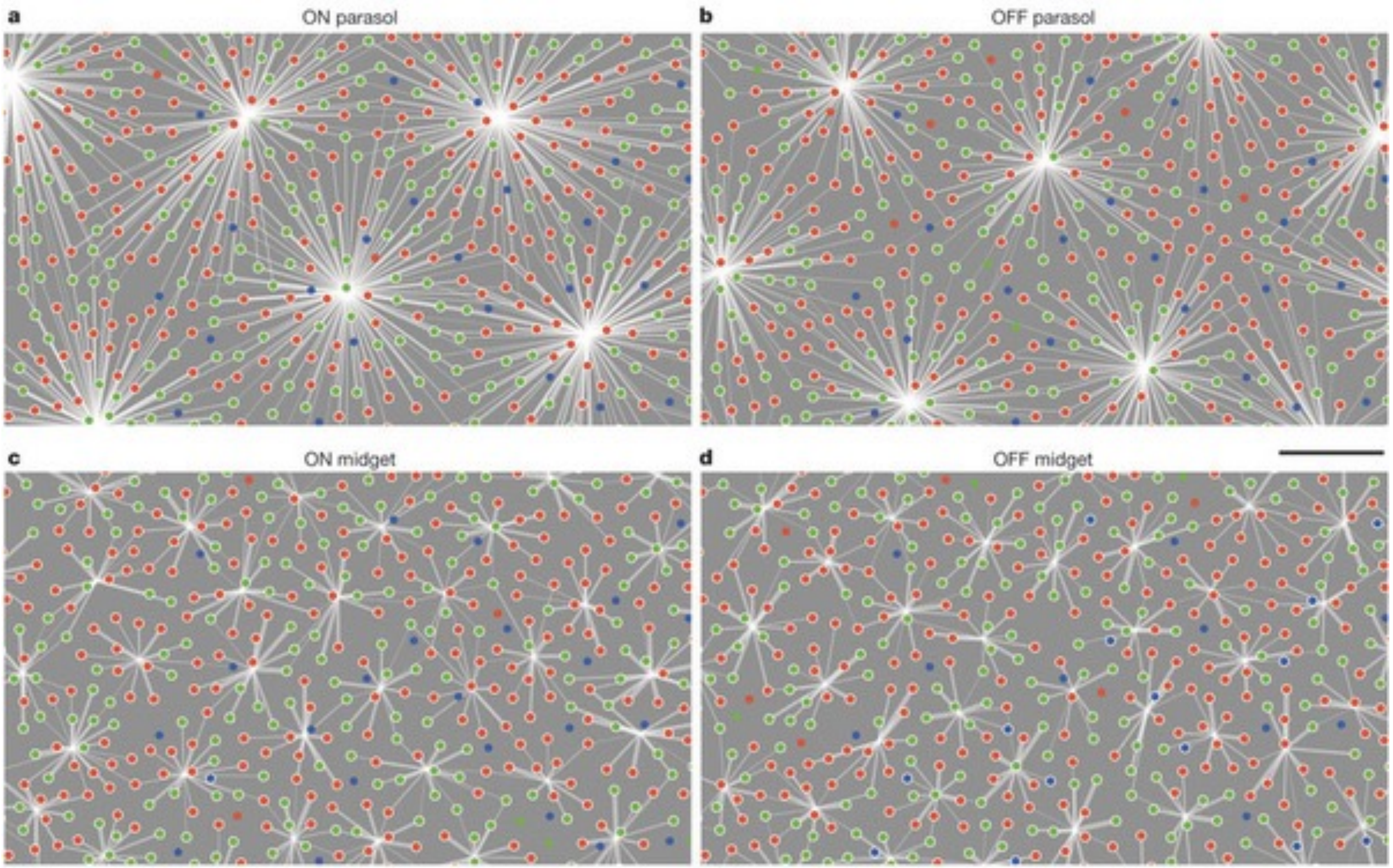


Receptive field of RGCs can be measured using the spike-triggered average of a spatio-temporal white noise stimulus



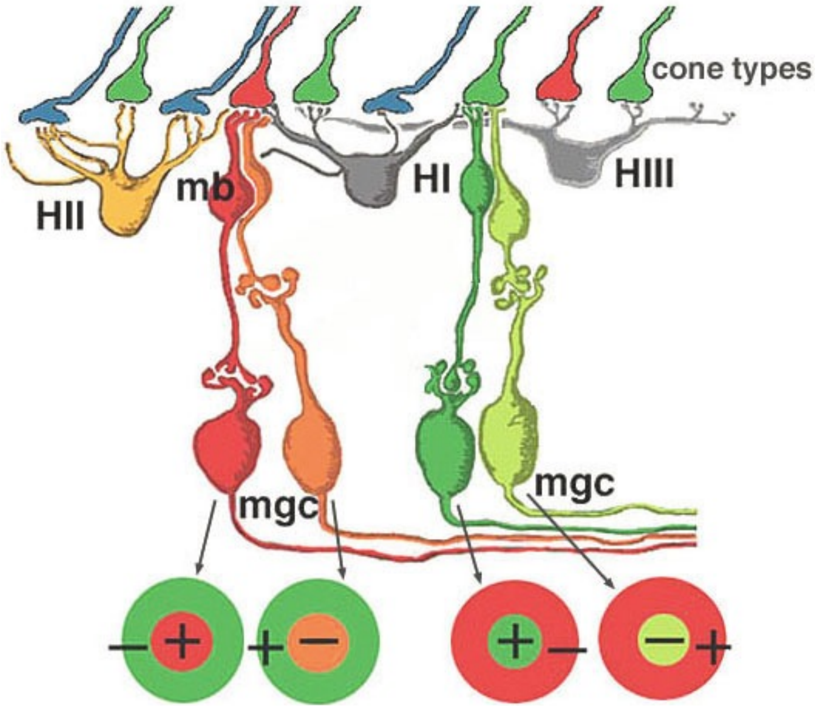
Field et al., Nature 2010

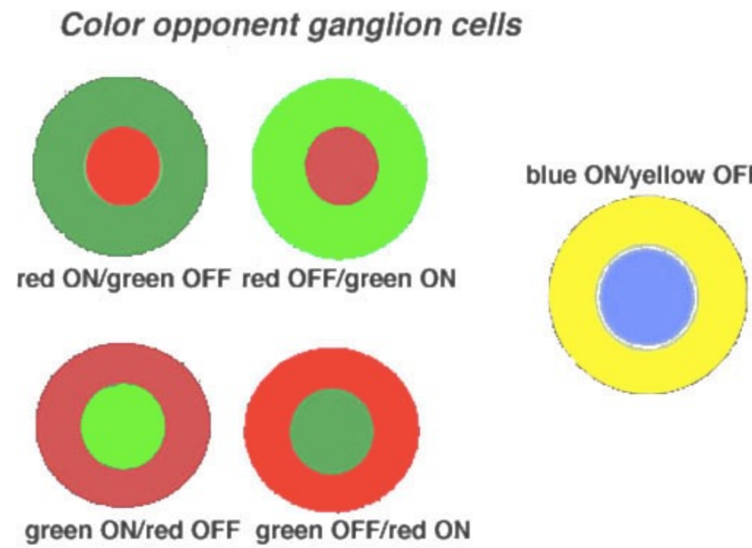
Functional sampling of cone lattice by RGCs



Field et al., Nature 2010

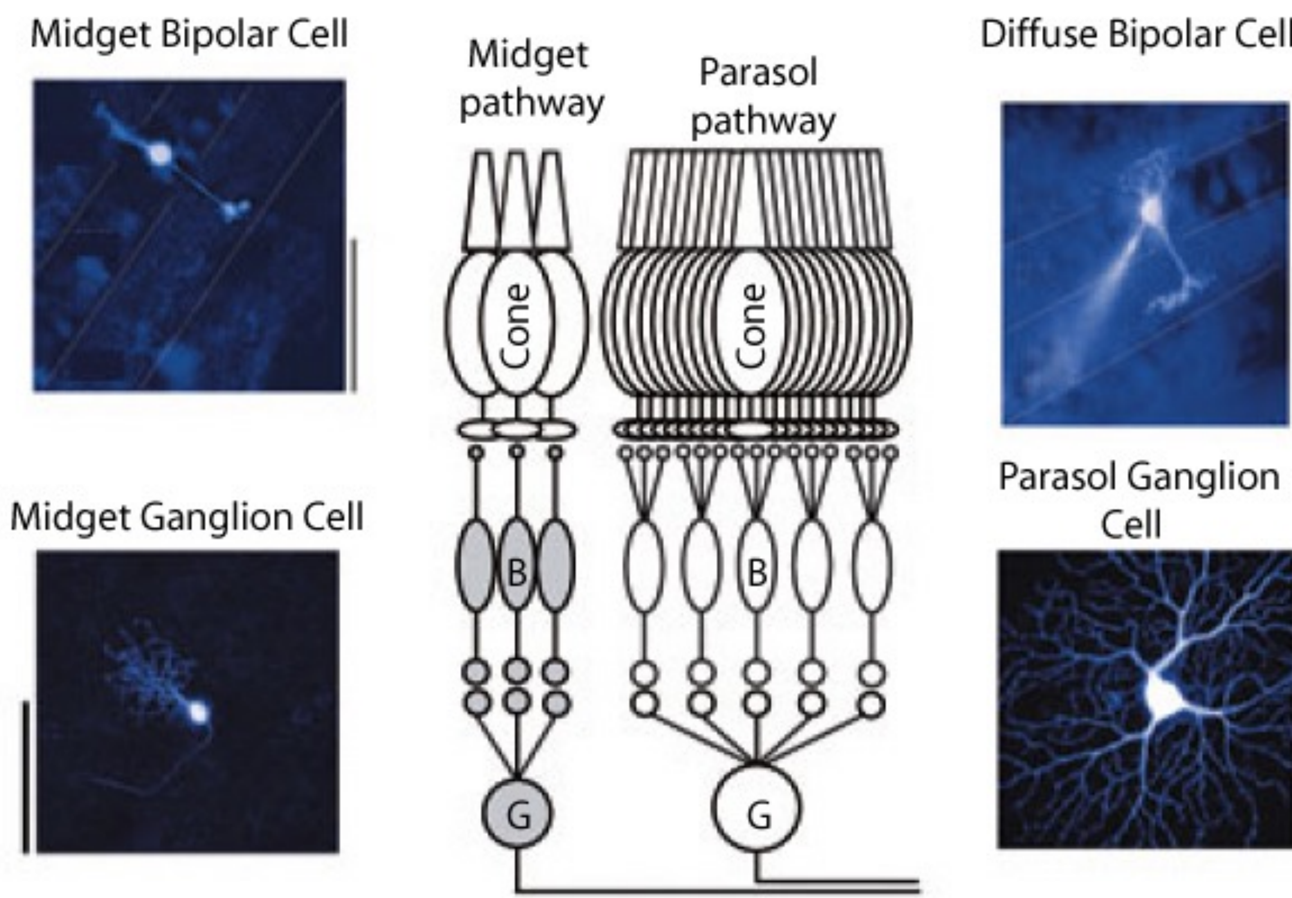
Retinal ganglion cells: midget cells





- Small cells responsible for our red/green color vision
- Comprise about 80% of our RGCs.
- High density in the fovea.
- Center-surround of opposite polarity and of opponent colors.
- The blue On/yellow Off is less dense and probably a different circuit is involved.

Retinal ganglion cells: midget vs. parasol cells
Convergence and acuity

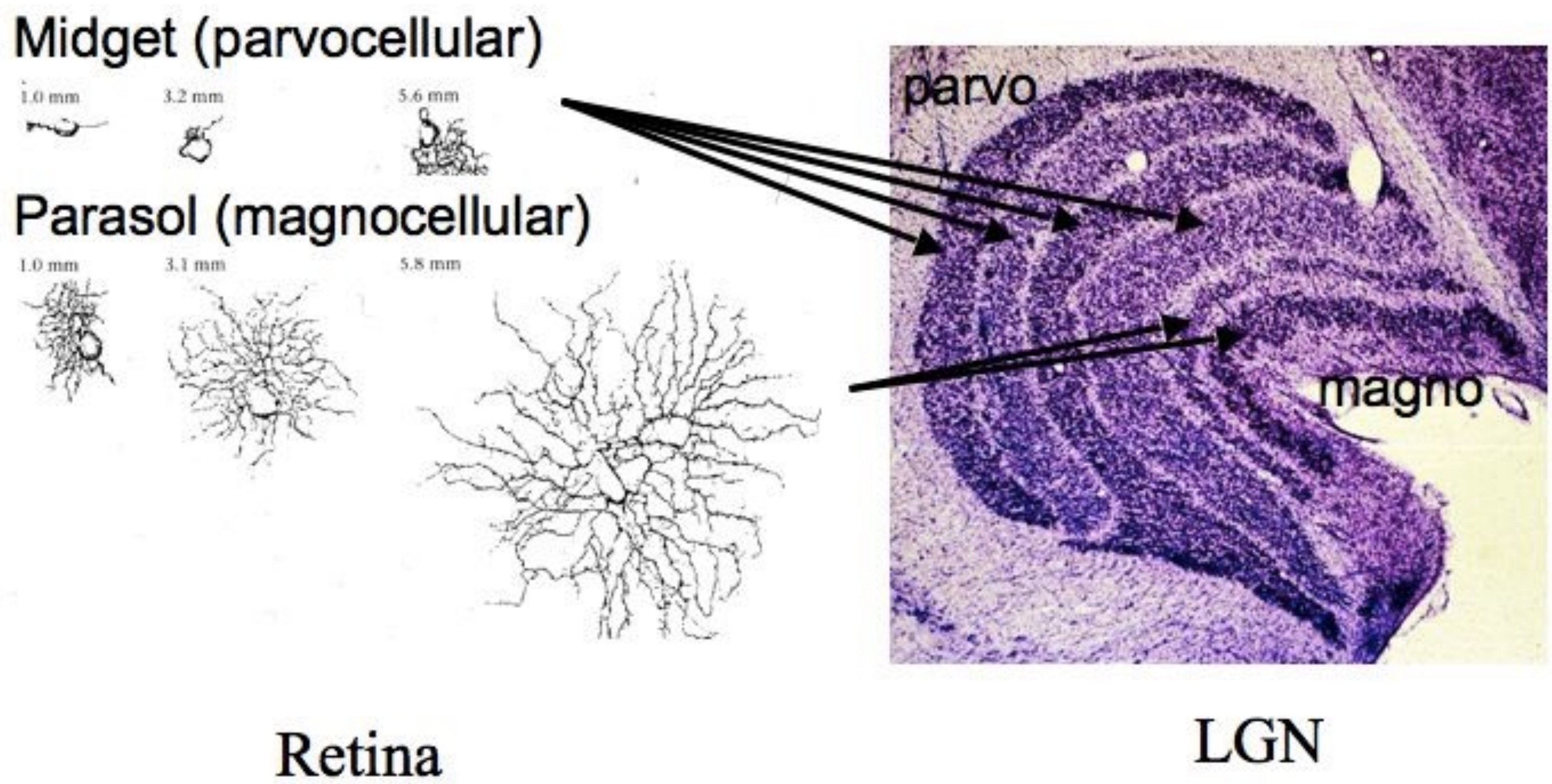


= not selective for color

- Small dendritic arbors
- Small receptive fields
- ~80% of ganglion cell
- chromatic
- Form and color
- Fine details

- Large dendritic arbors
- Large receptive fields
- ~10% of ganglion cells
- Non-chromatic
- Gross features of stimulus
- movement

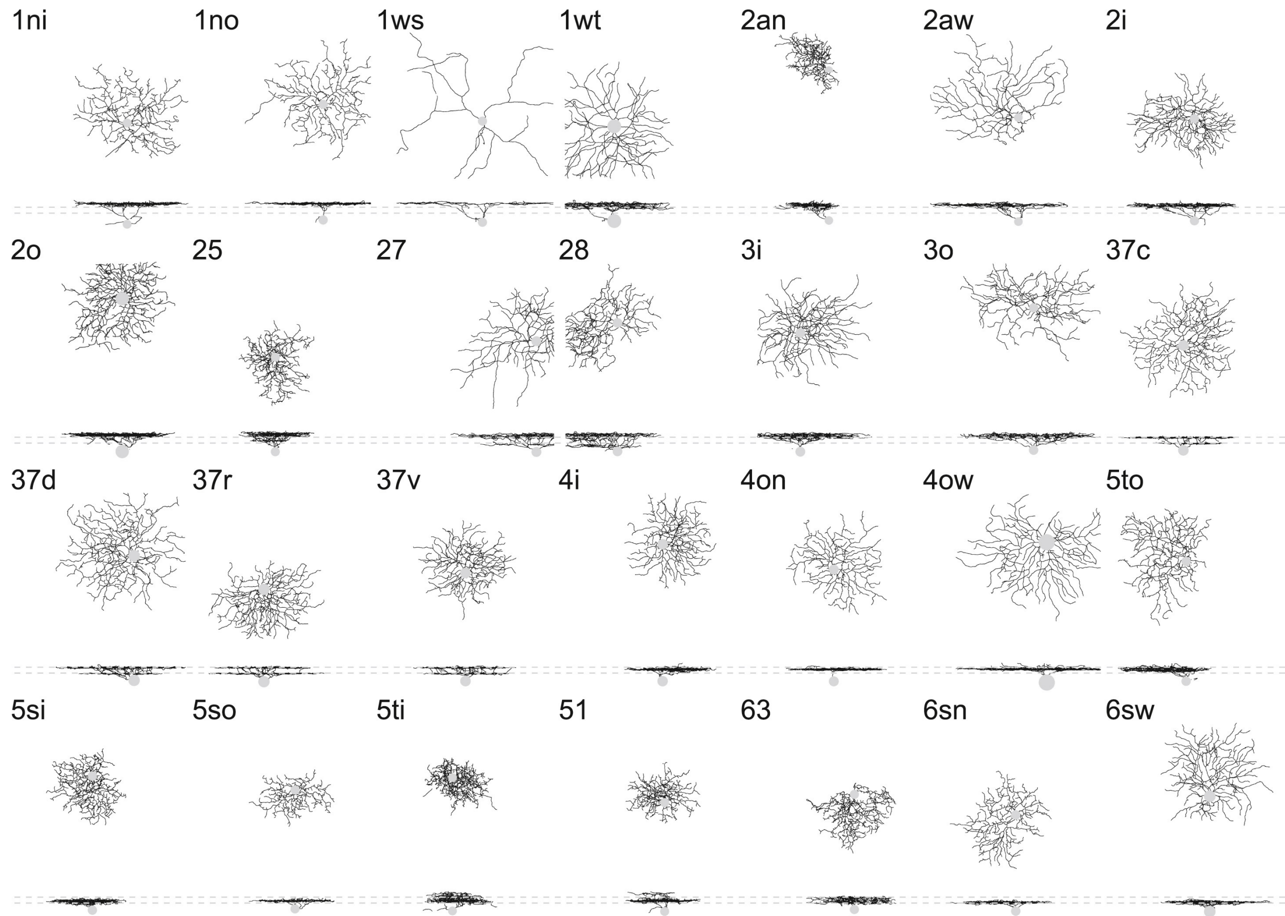
Magno and Parvo pathways



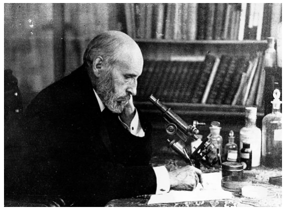
Retinal ganglion cells

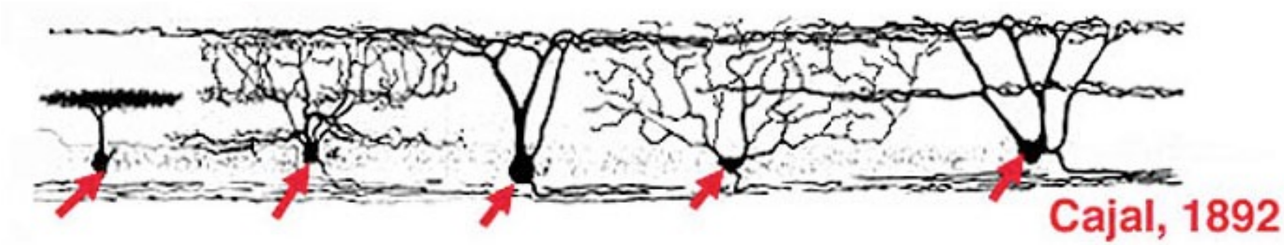
What defines a neuron subtype in the retina?

- Morphology (including input & output)
- Physiology (=light responses)
- Form mosaic/tile the retina

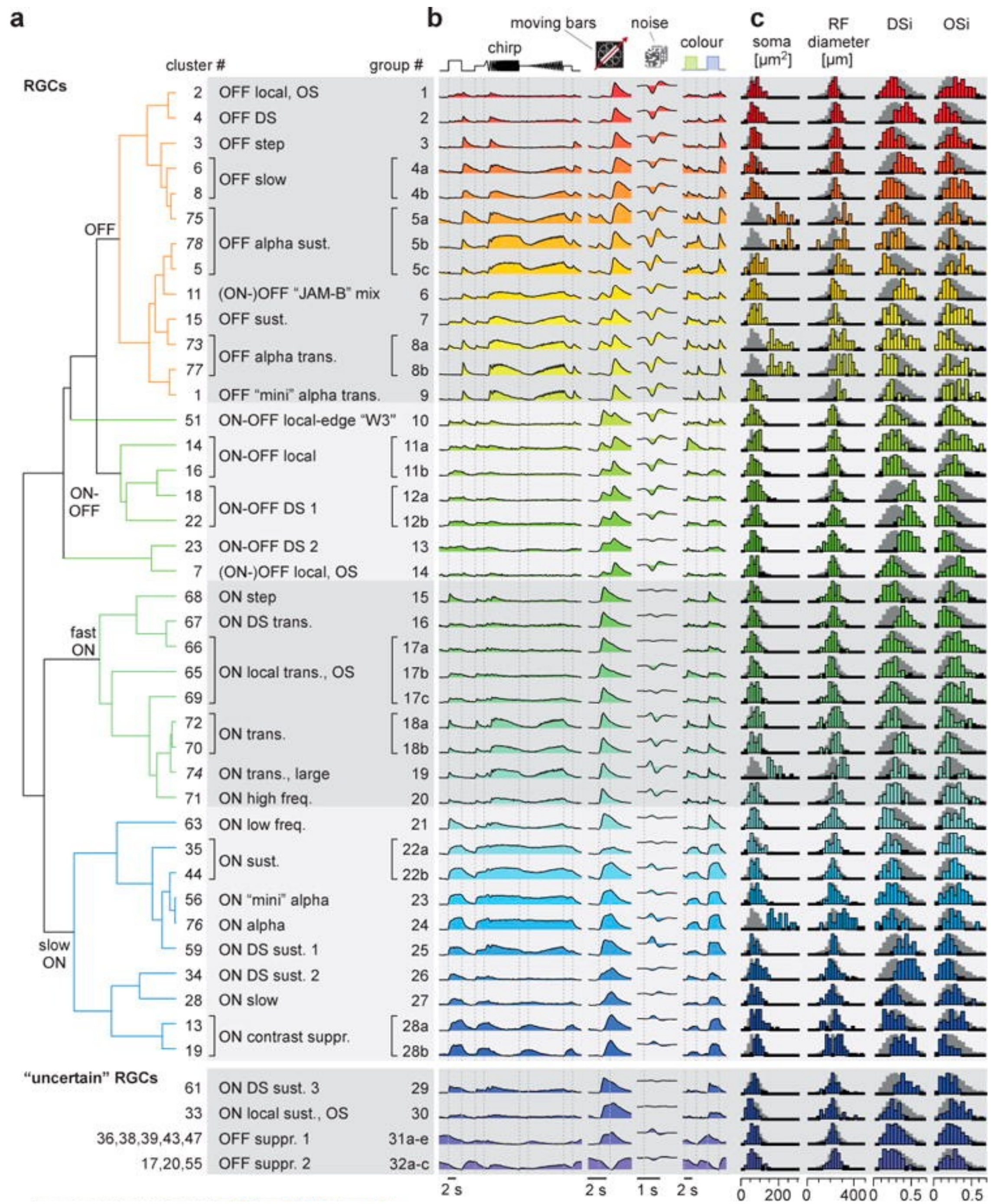


Bae et al., 2018 (*Cell*)



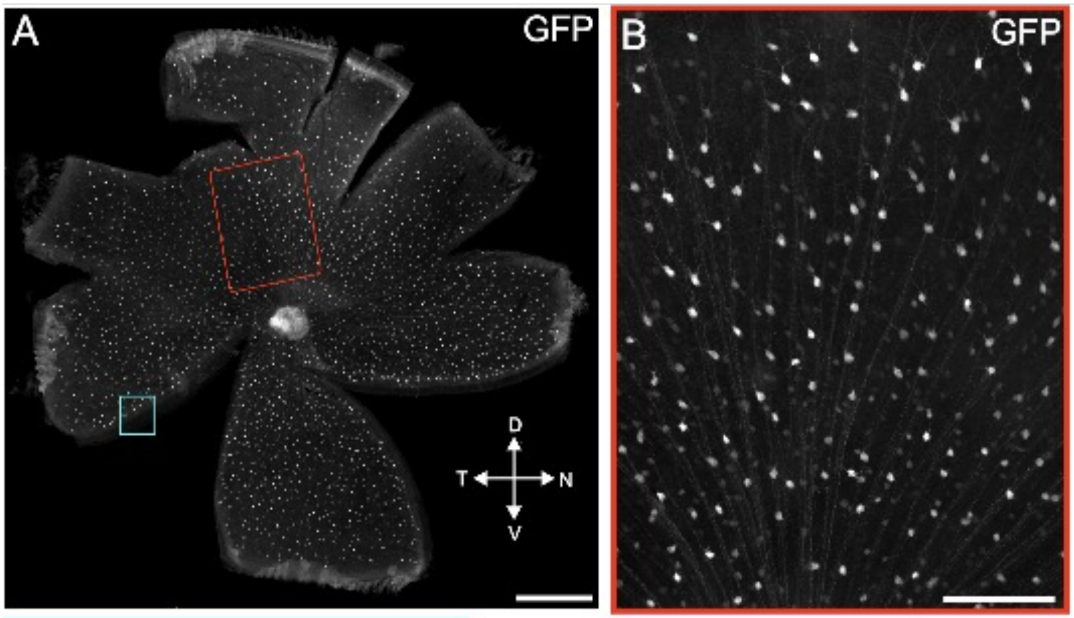


>30 different subtypes of retinal ganglion cells (RGCs)

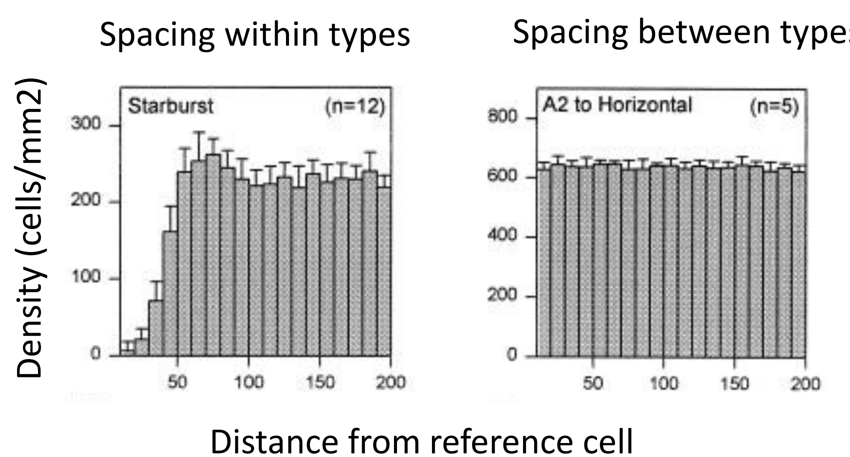


Baden et al., Nature 2016

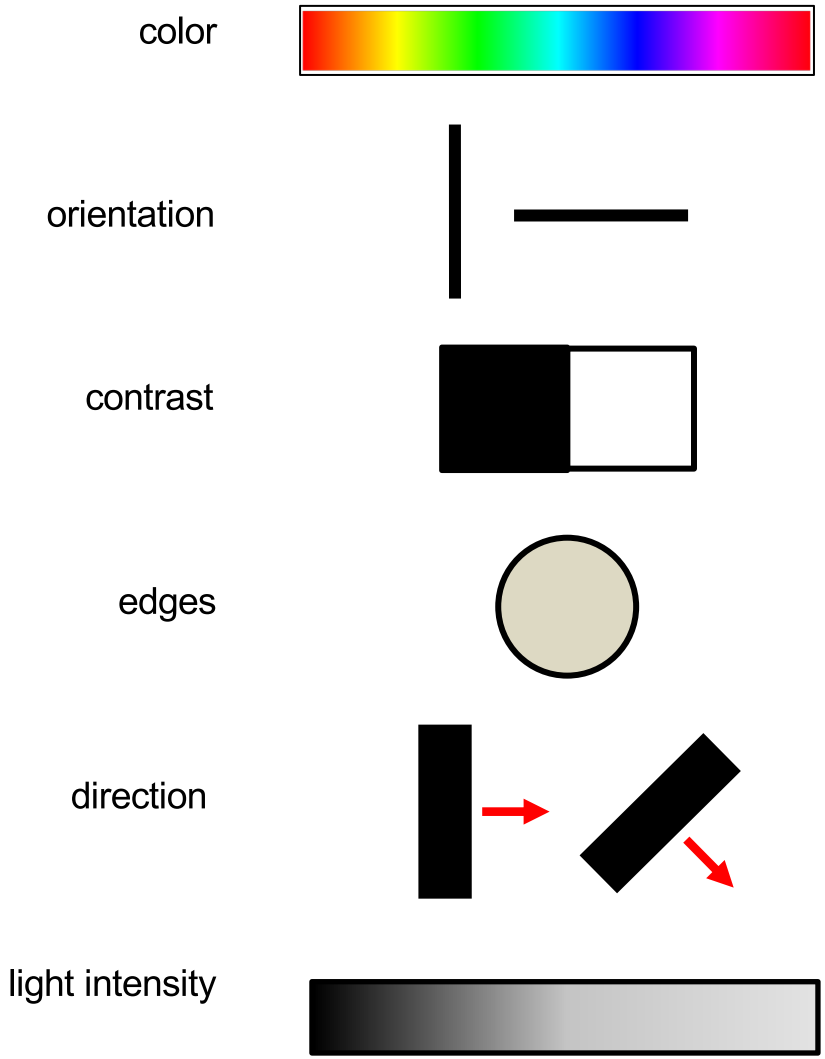
Mosaic organization



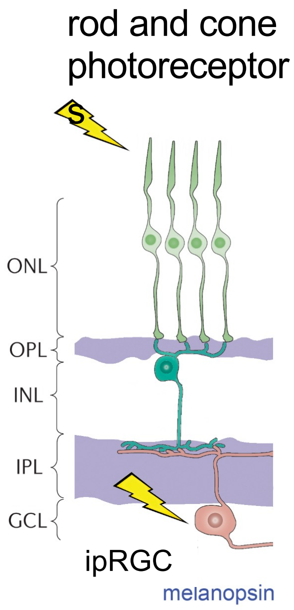
- Cover the entire visual field
- Exclusion zone for same cell type

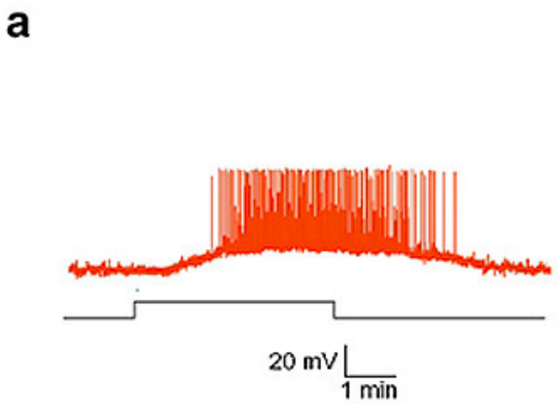


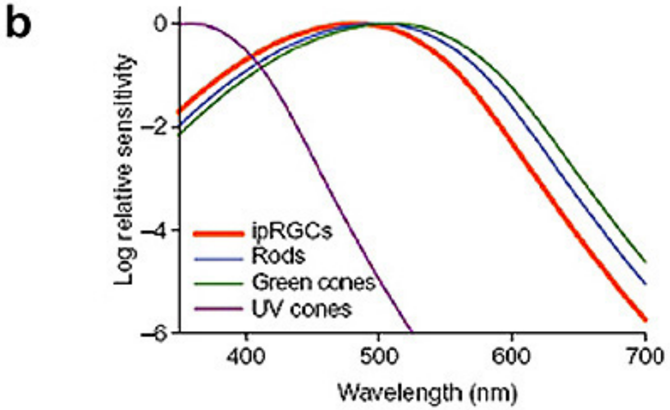
Diversity of ganglion cell receptive fields



Intrinsically photosensitive retinal ganglion cells (ipRGCs)

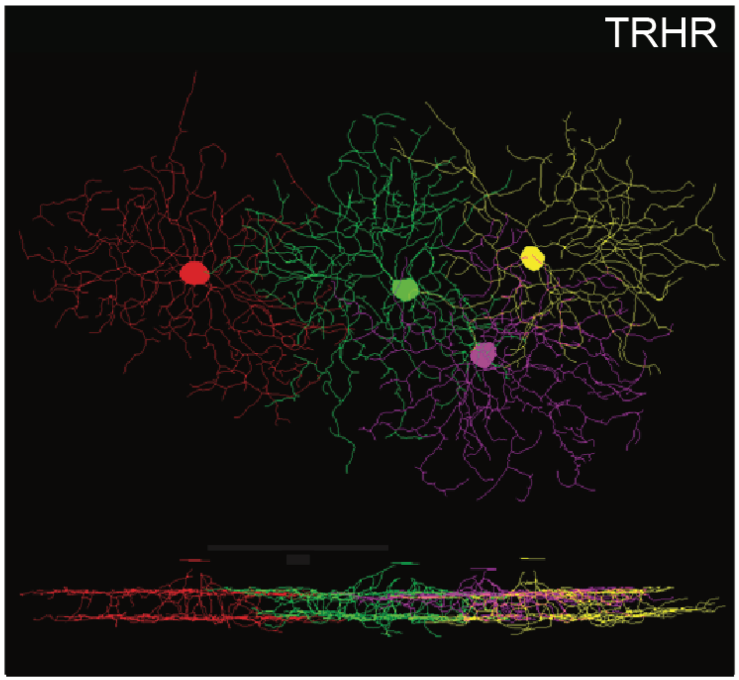


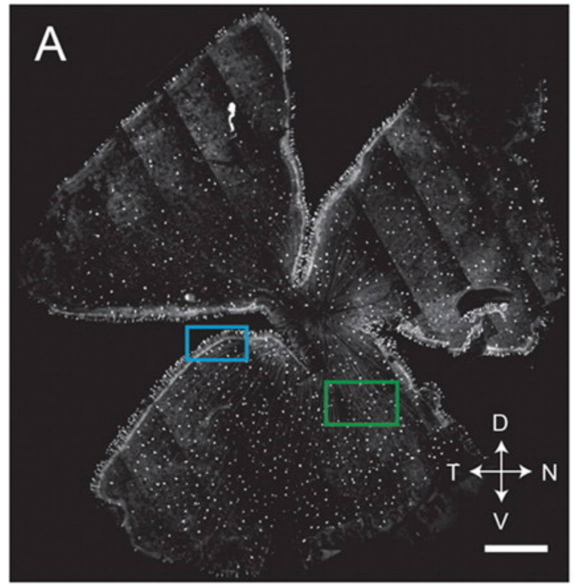


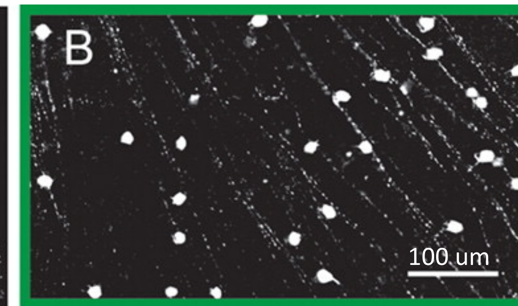


Adapted from Berson et al. 2003

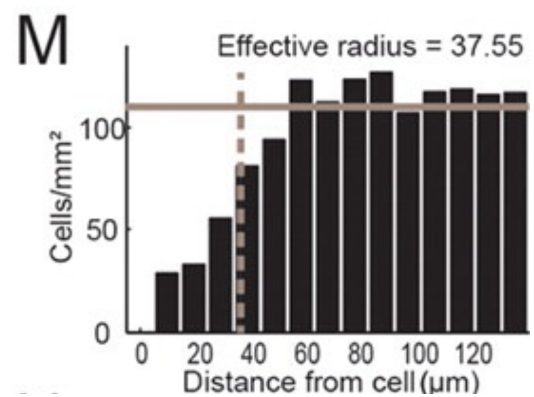
Two-photon targeted recordings from transgenic mouse lines





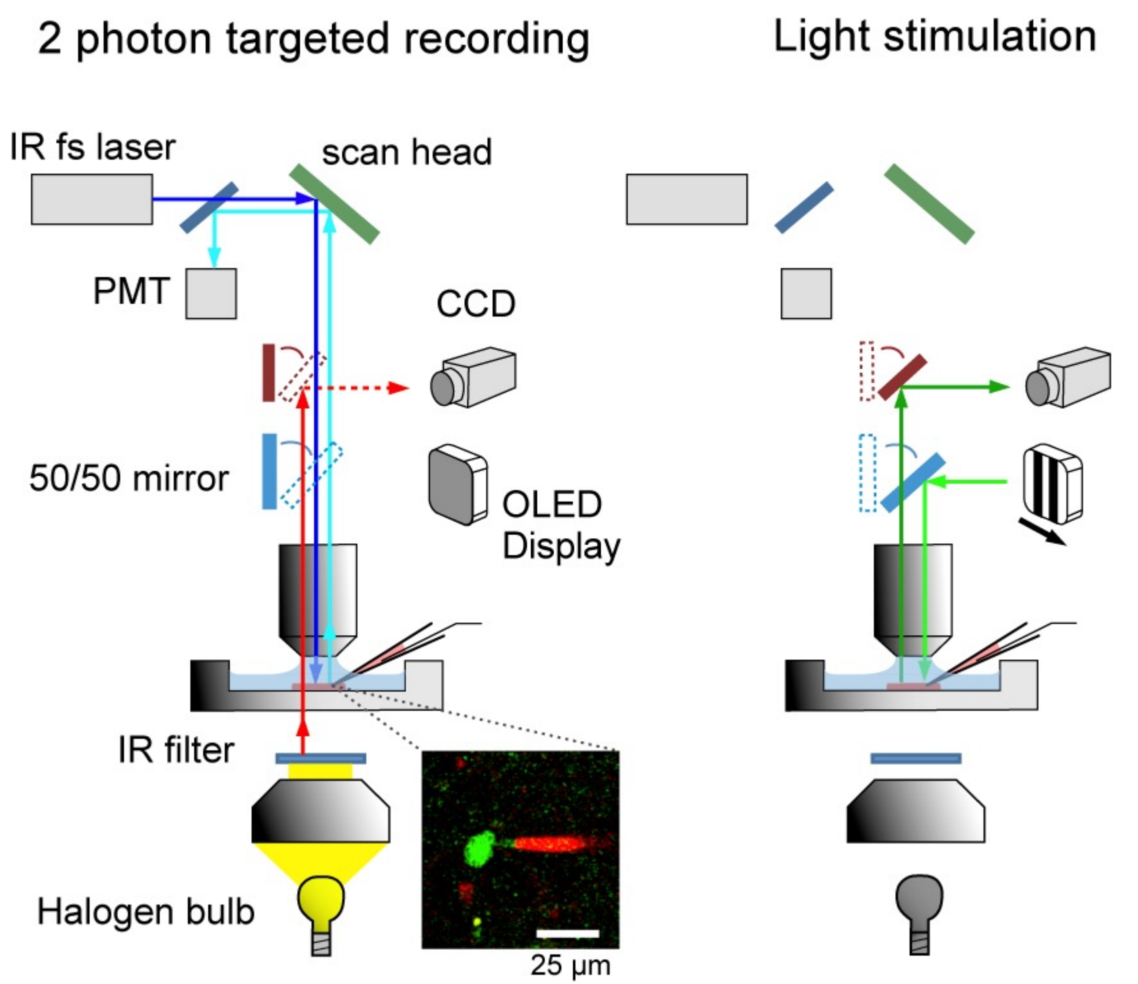


TRHR mouse line



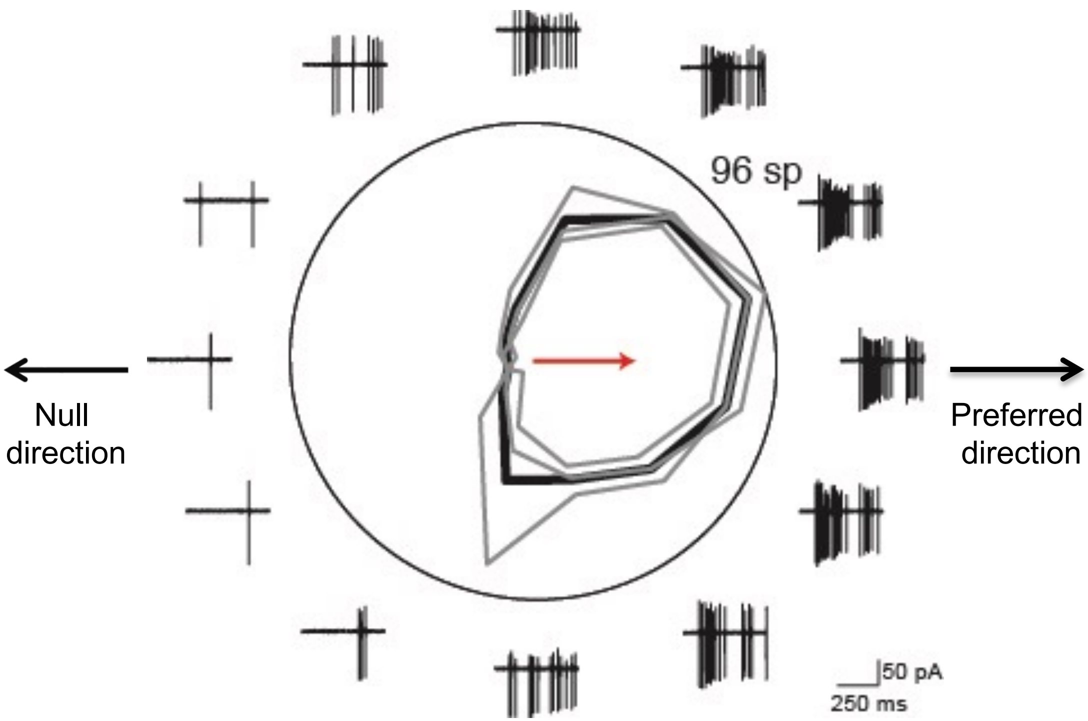
Rivlin-Etzion et al., 2011

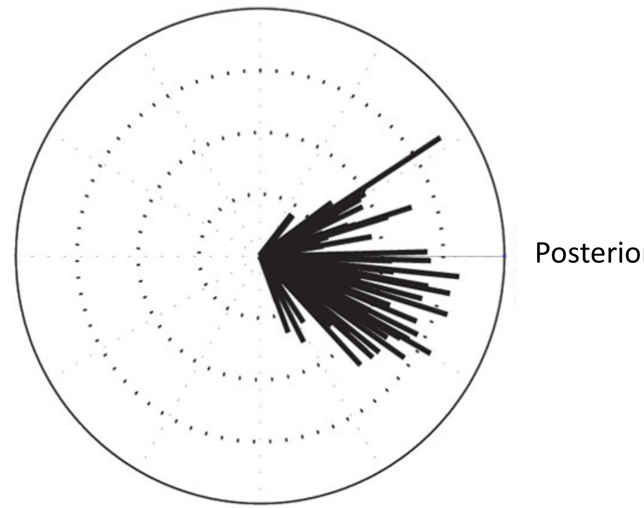
Two-photon targeting of GFP+ cells prevents bleaching of light response

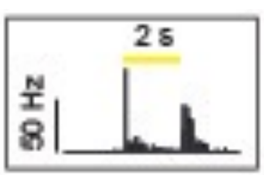


Wei et al., Nature protocols, 2010

TRHR line labels On-Off direction selective retinal ganglion cells (DSGCs)





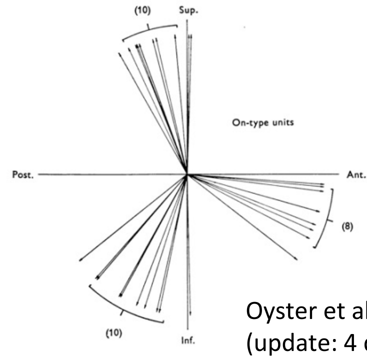


Rivlin-Etzion et al., 2011

Direction selective retinal ganglion cell (DSGC) subtypes

Type | **Function**

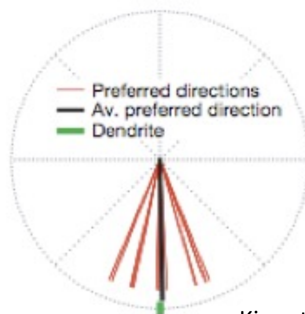
On DS cells



Oyster et al 1968
(update: 4 directions aligned with the gravitational and body axes
Sabbah et al., 2017)

Optokinetic reflex

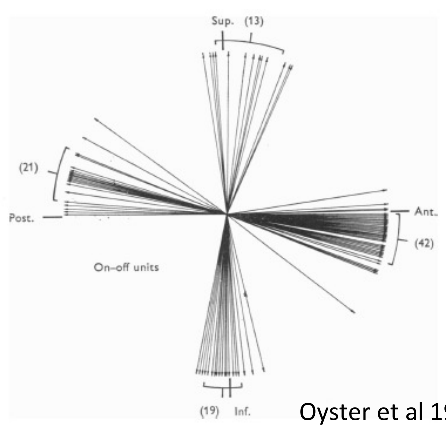
Off DS cells



Kim et al 2008

?

On-Off DS cells



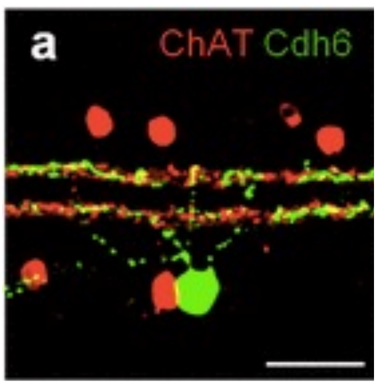
Oyster et al 1968

?

On starburst amacrine cells costratify with direction selective retinal ganglion cells

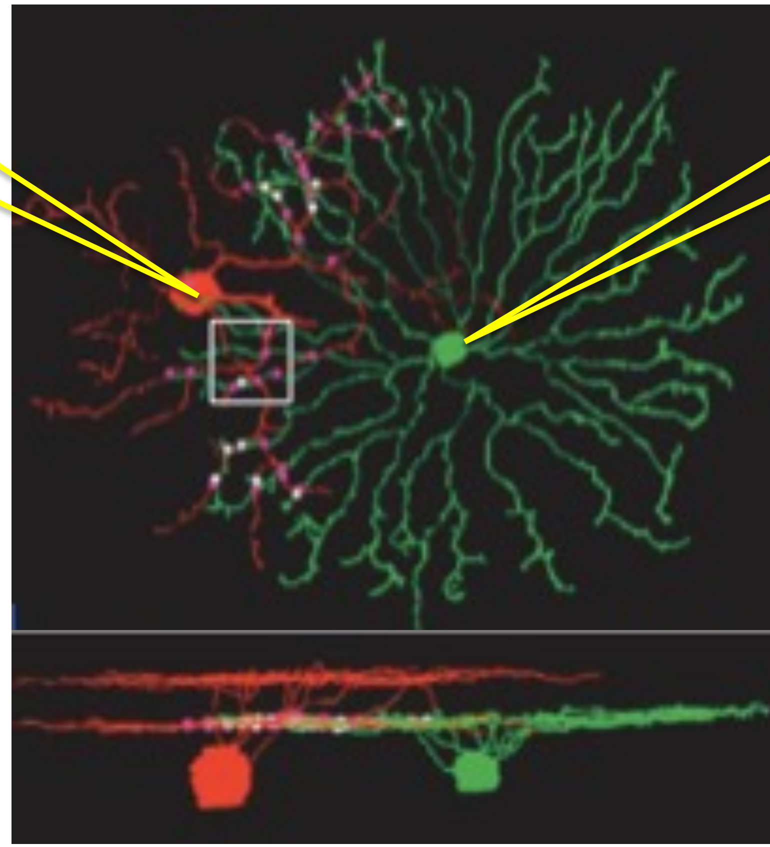
Direction selective ganglion cell

ON starburst Amacrine cell



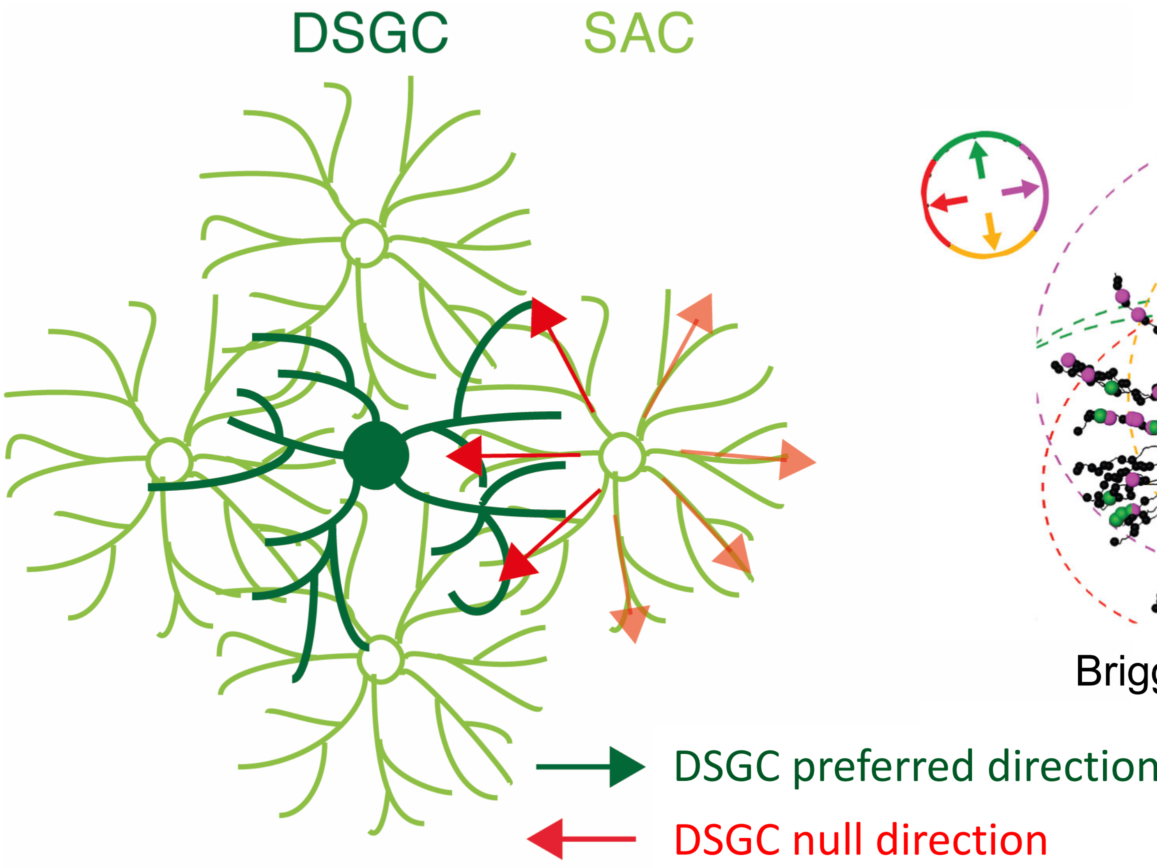
OFF

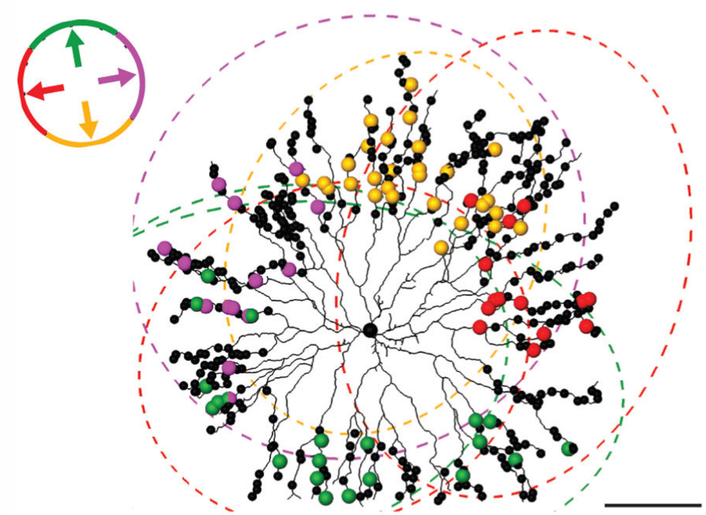
ON



Wei et al., 2011 (*Nature*)

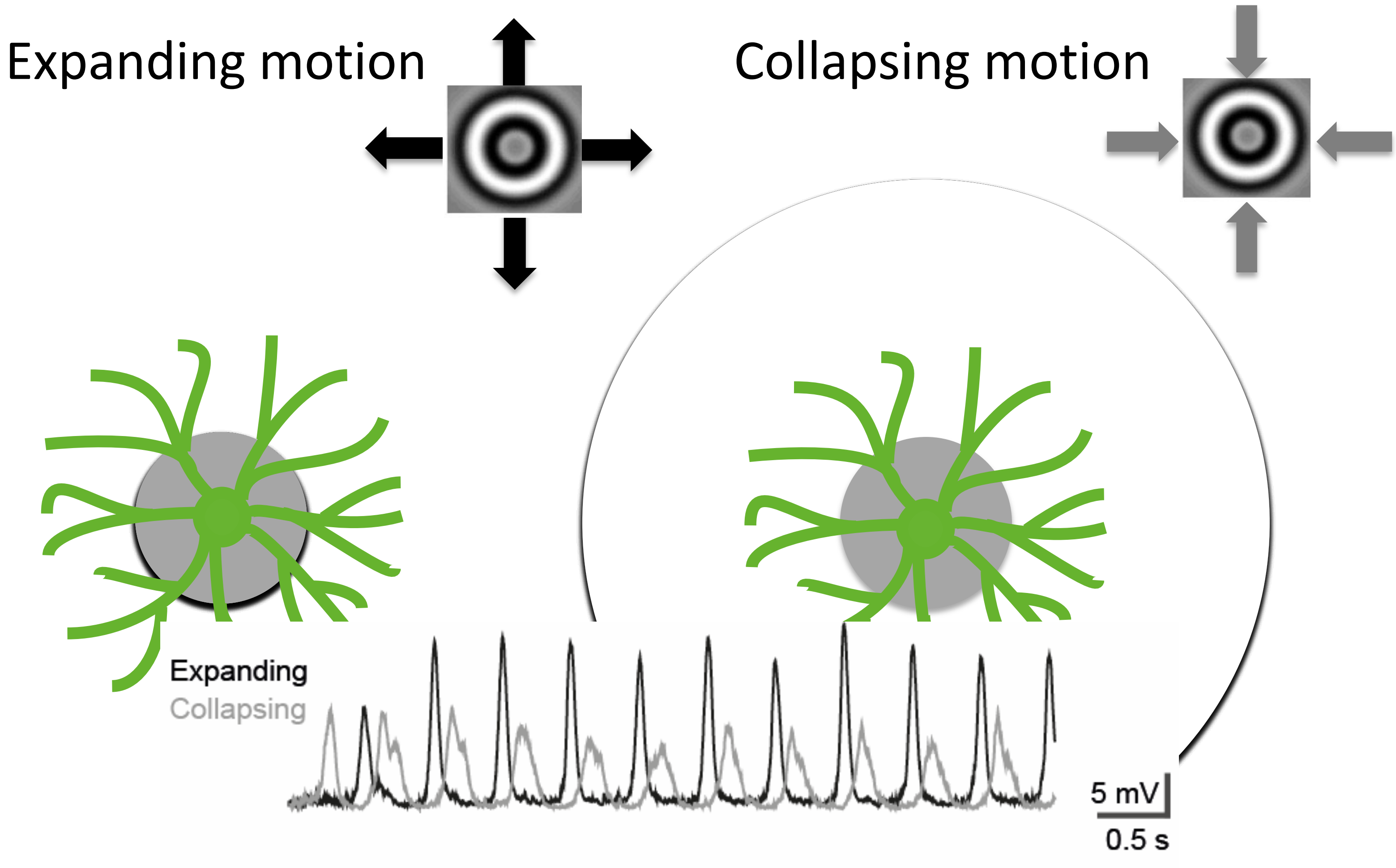
Directional responses are mediated by asymmetric inhibition from starburst amacrine cells





Briggman et al., 2011 (*Nature*)

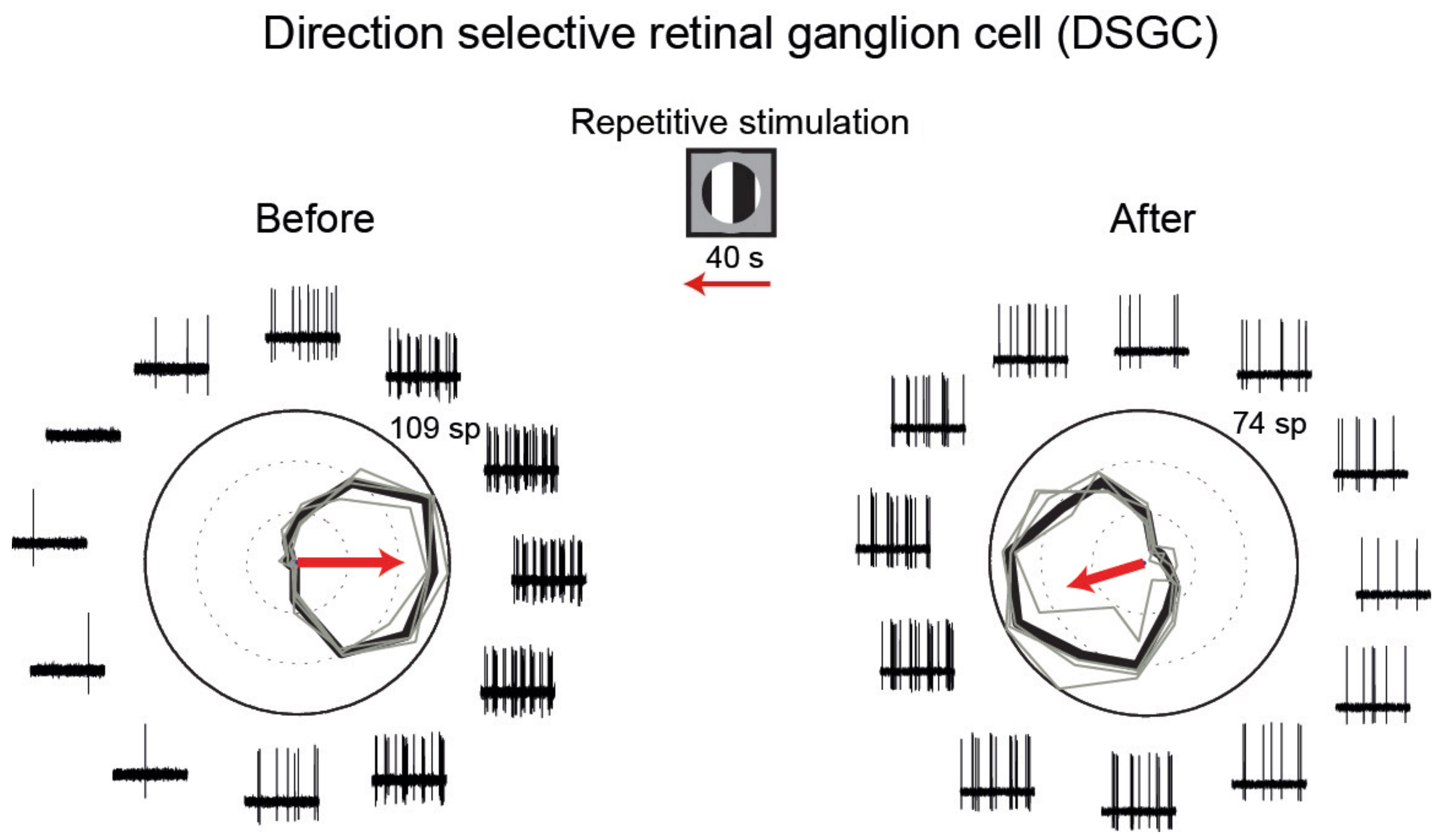
SAC processes prefer centrifugal motion



Lea Ankri

Ankri et al., Cell Reports 2020

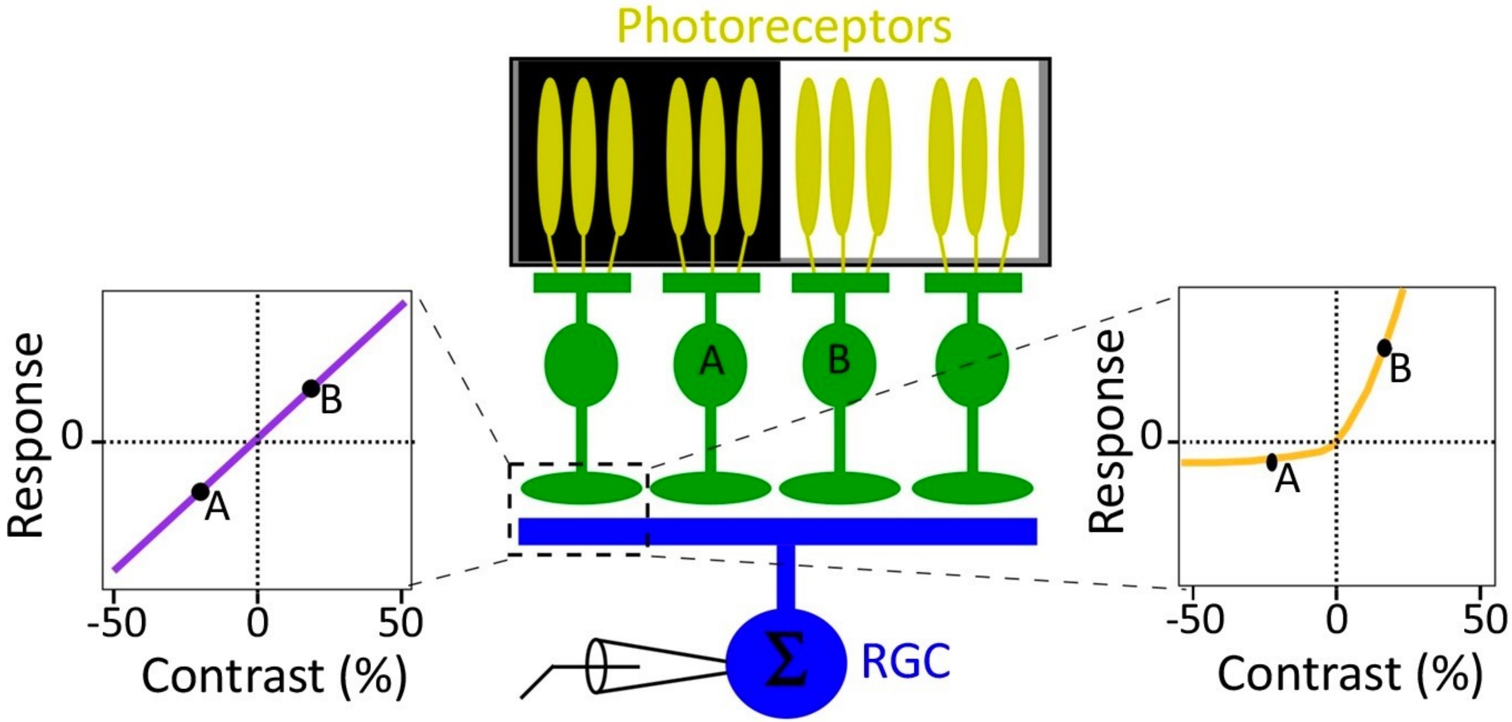
Retinal neurons can change the modality they encode



Rivlin-Etzion et al., Neuron 2012

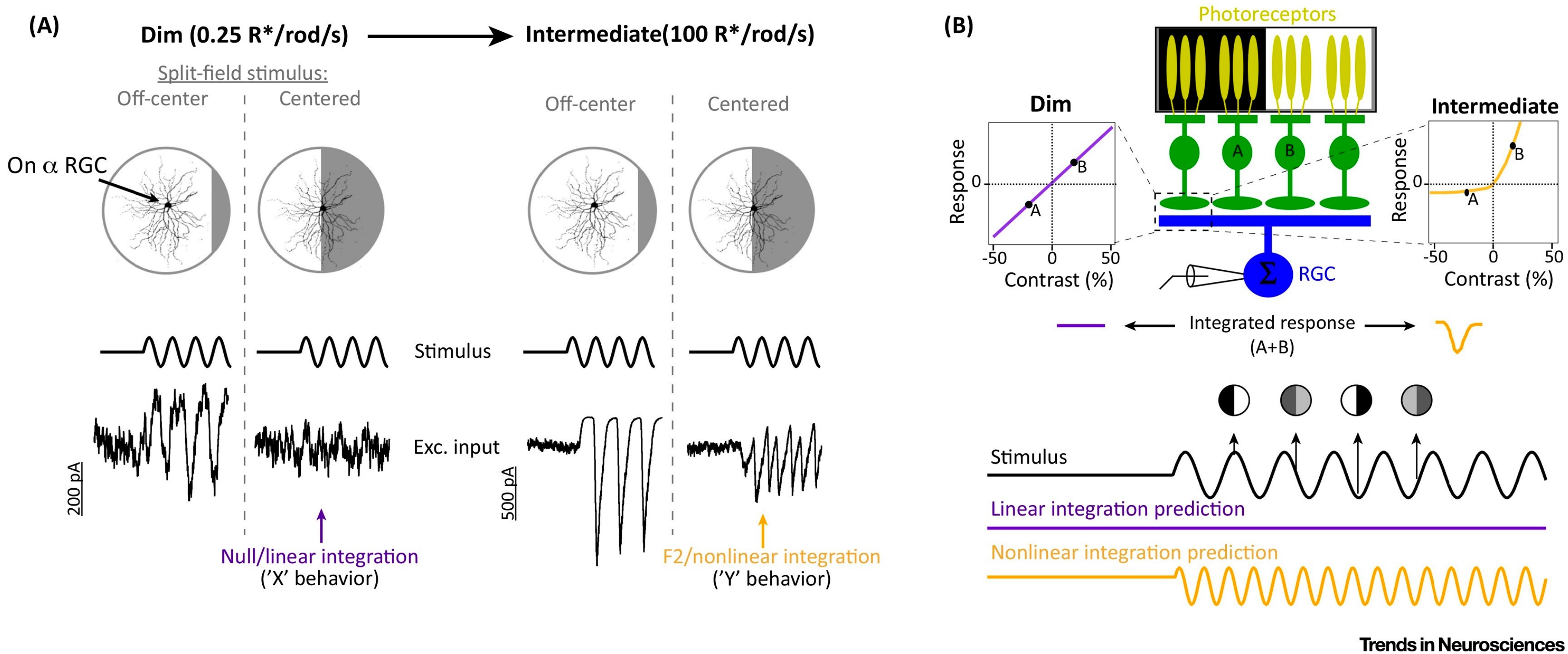
Ankri et al., Cell Reports 2020

Spatial integration properties of On Alpha RGCs depend on mean luminance



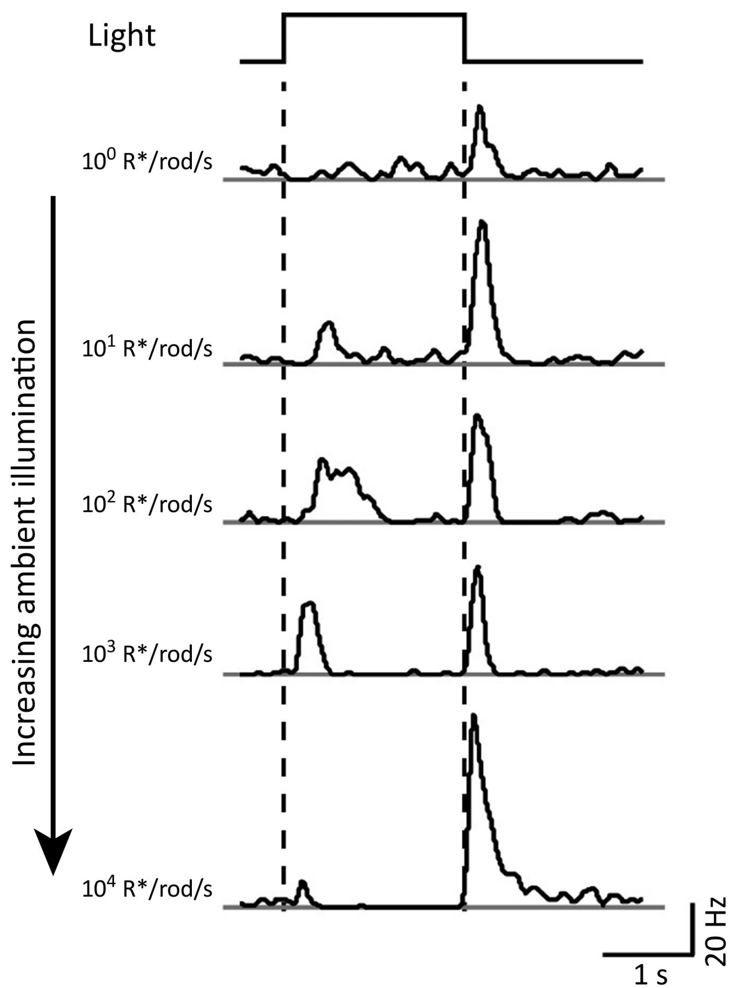
Grimes et al., 2014

Spatial integration properties of On Alpha RGCs depend on mean luminance



Grimes et al., 2014

RGCs change polarity preference with mean light level



Tikidji-Hamburyan et al., 2015

Thank you!

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