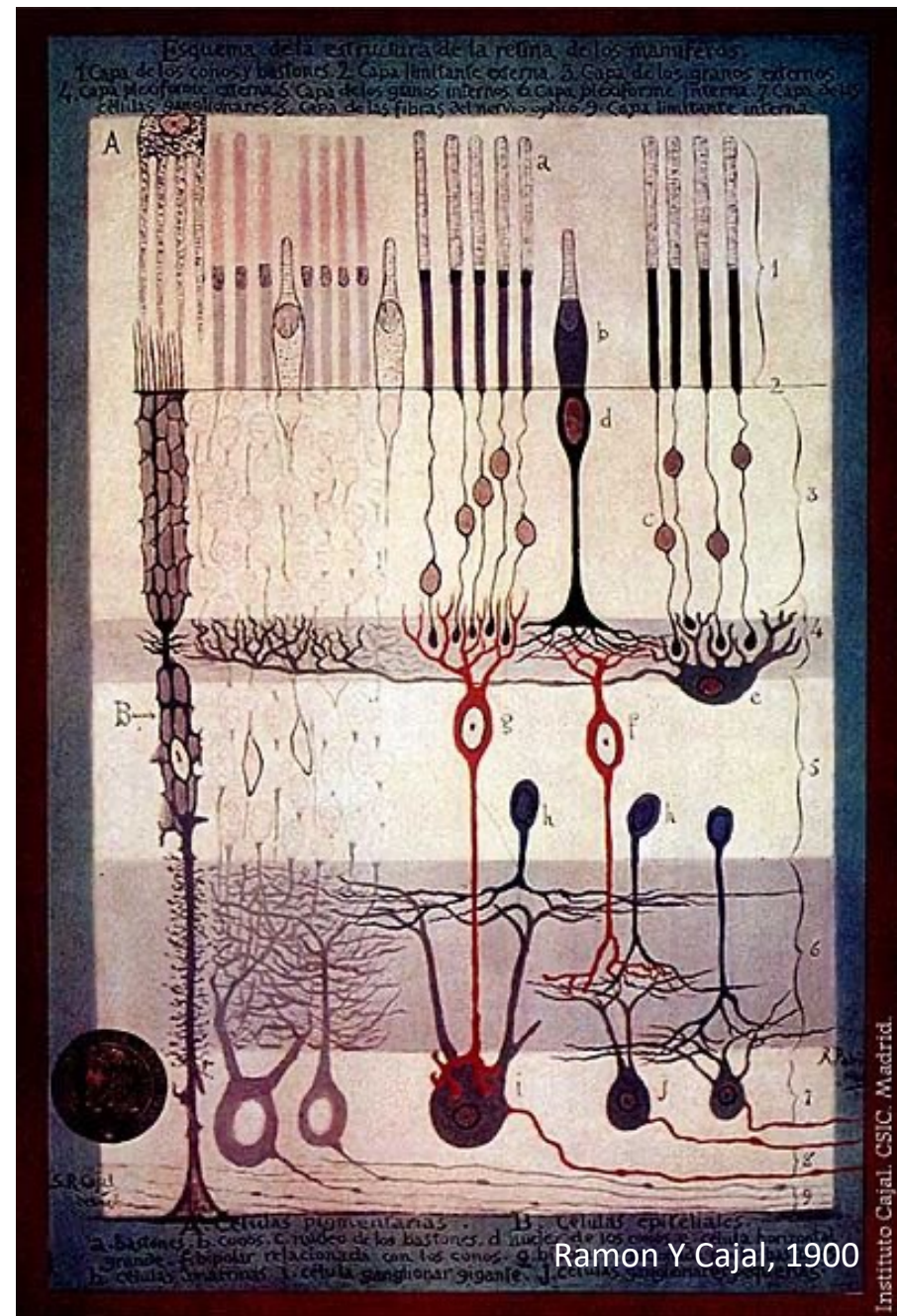
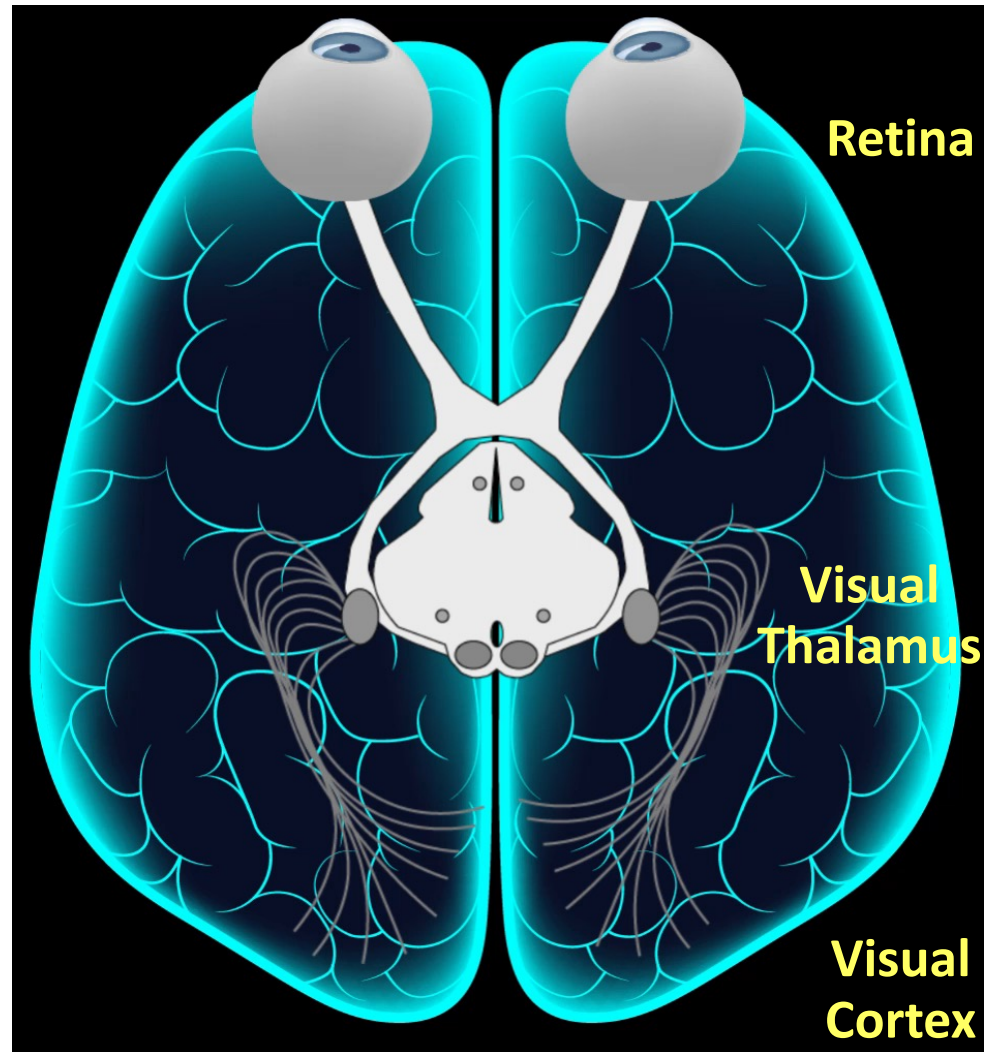


Introduction to Neuroscience: Visual Processing in the Retina

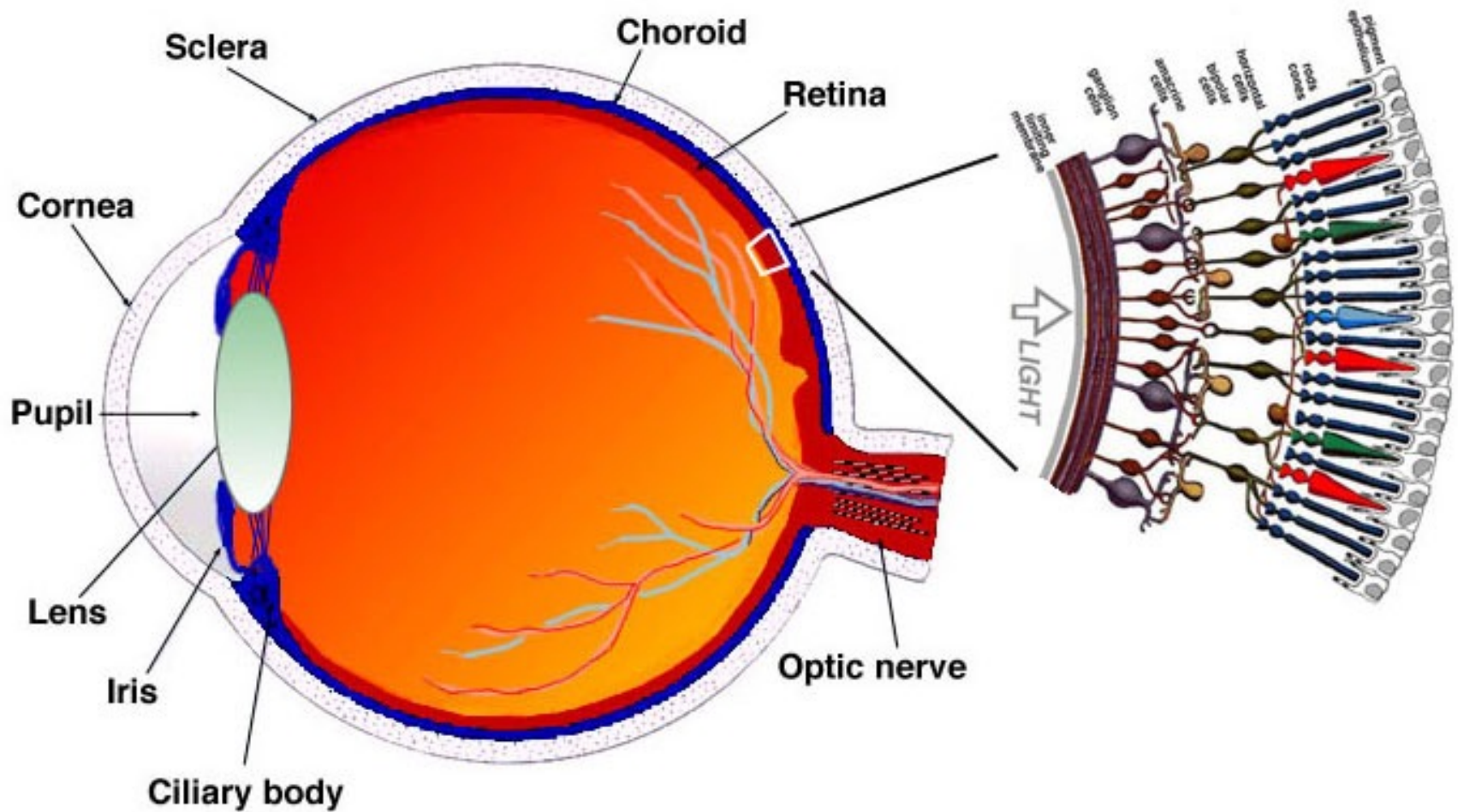
Michal Rivlin



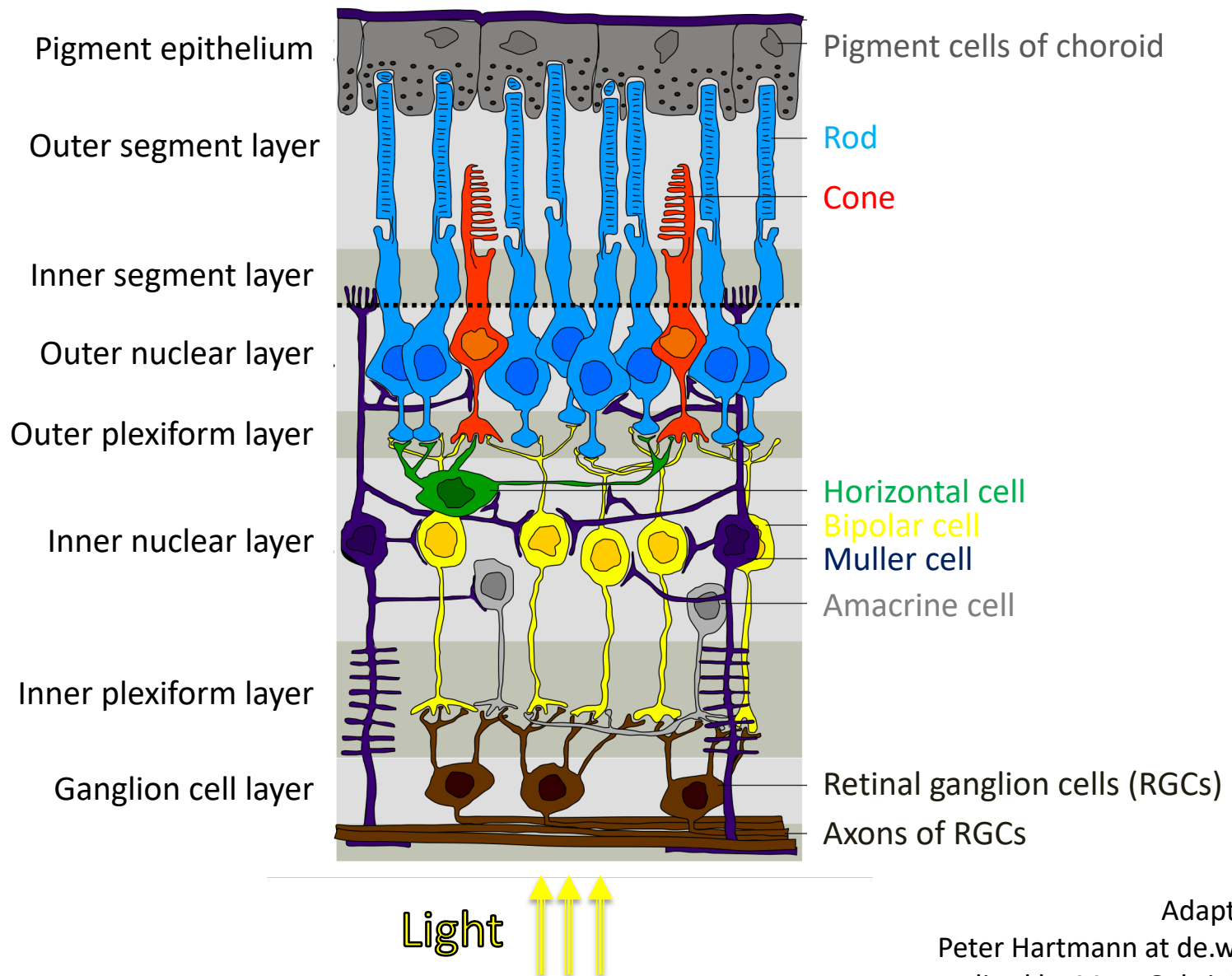
Retinal processing: more than a simple camera



The human Eye

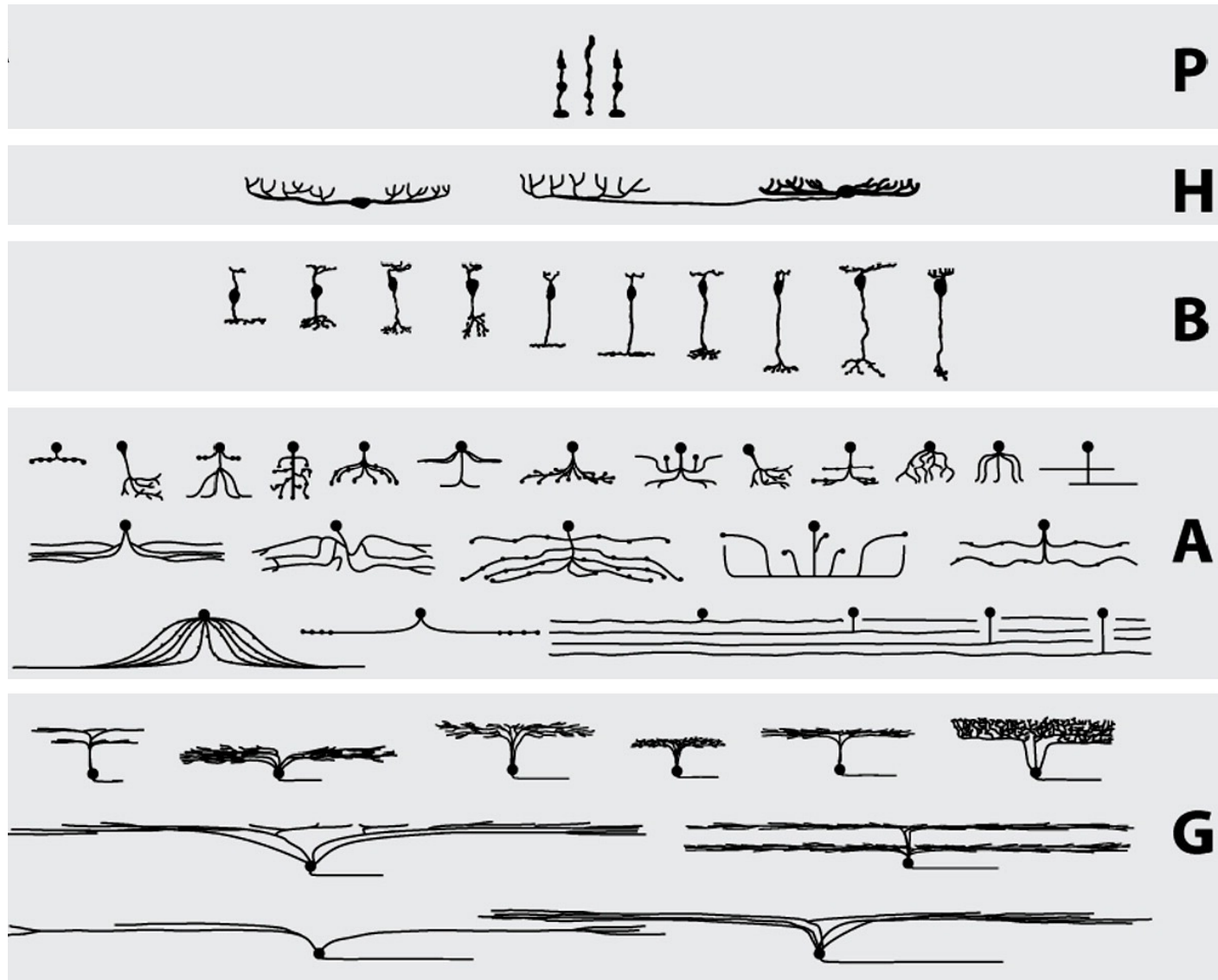


An introduction to the cell types of the retina



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

Each class is composed of multiple subtypes

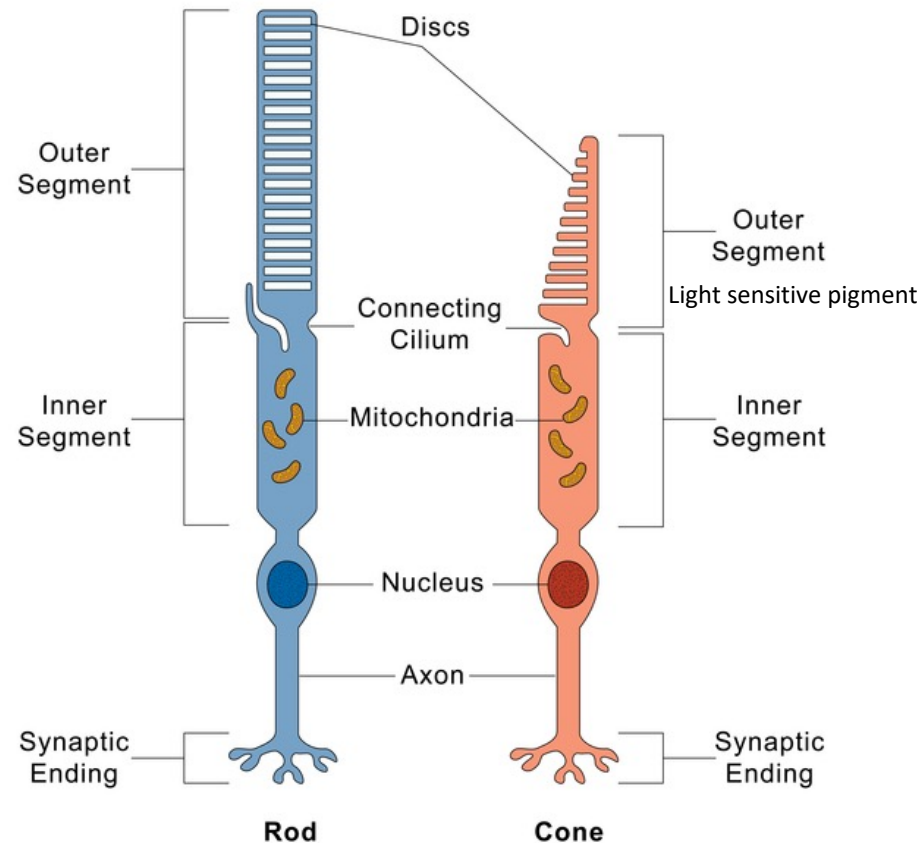


Adapted from
Gollisch and Meister 2010
Based on Masland 2001

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.

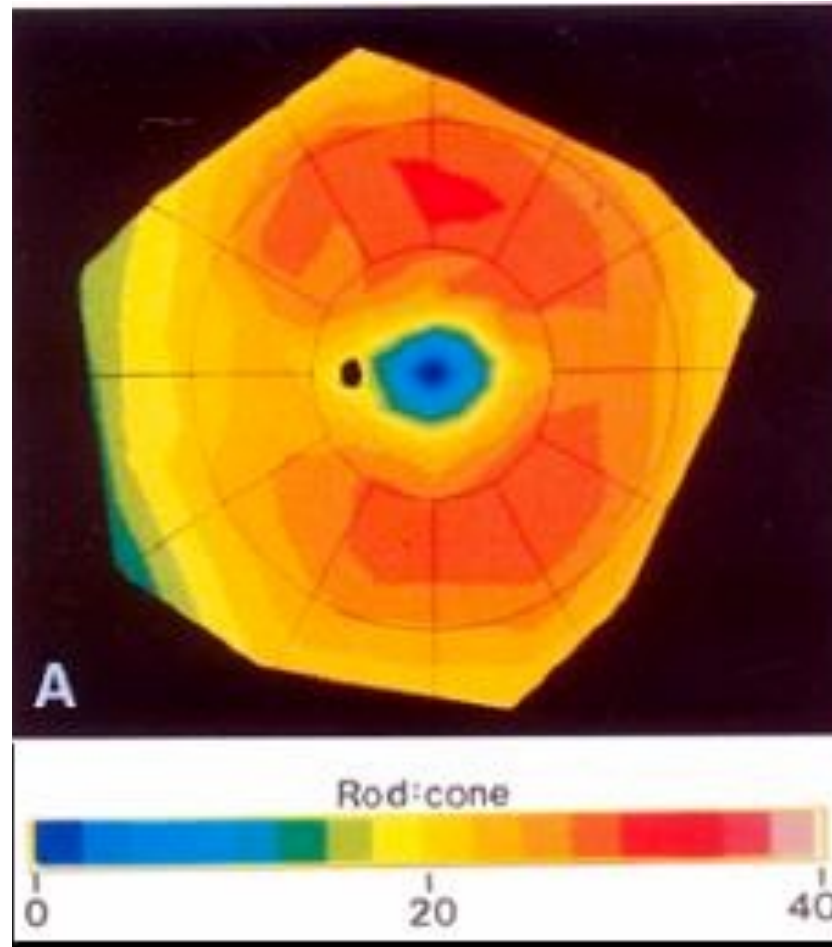


125 million photoreceptors in the retina

Rods: dim night vision.

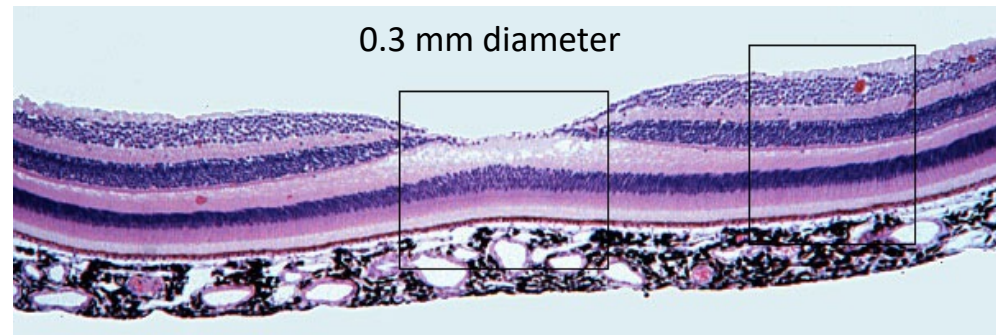
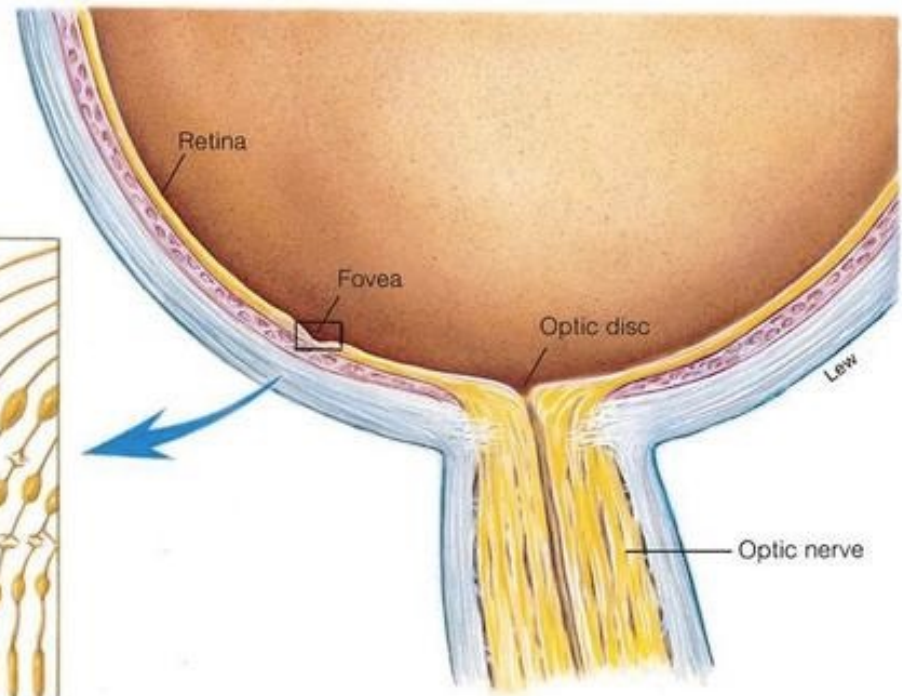
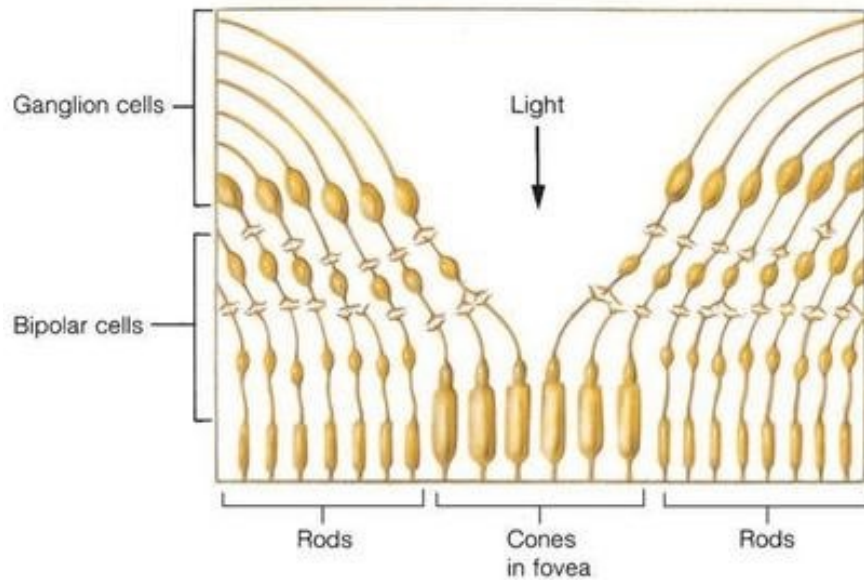
Cones: bright day vision & color vision

Distribution of Rods and Cones in human retina



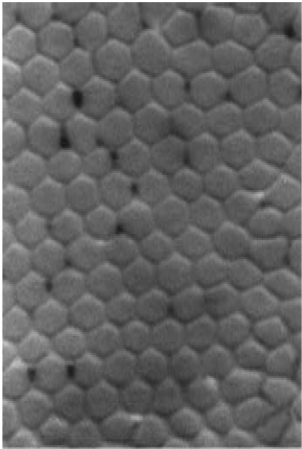
Fovea

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

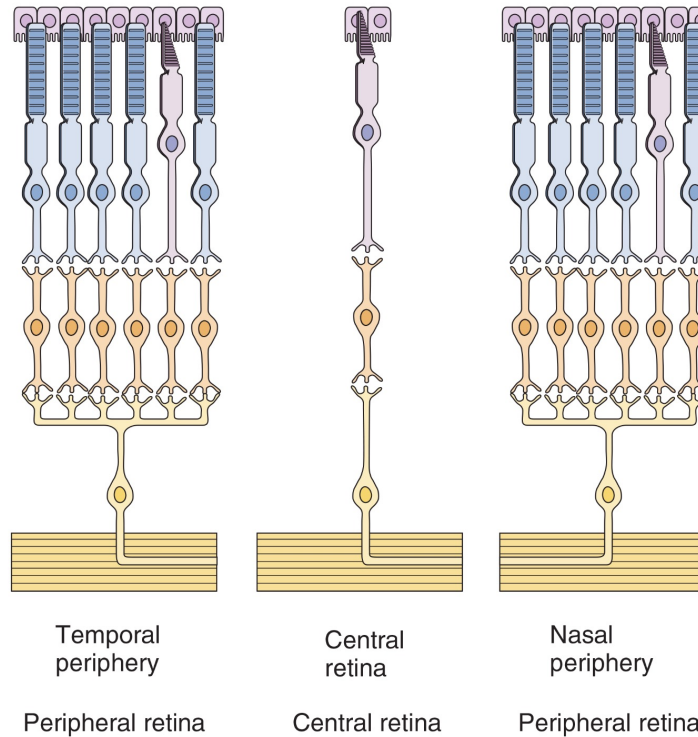
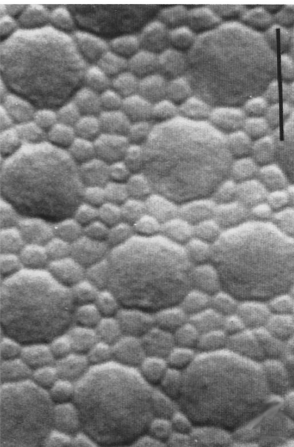


Topographic Variations in Retinal Encoding of Visual Space

Central retina



Peripheral retina

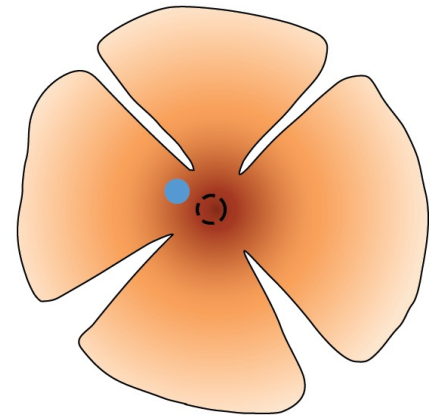


high



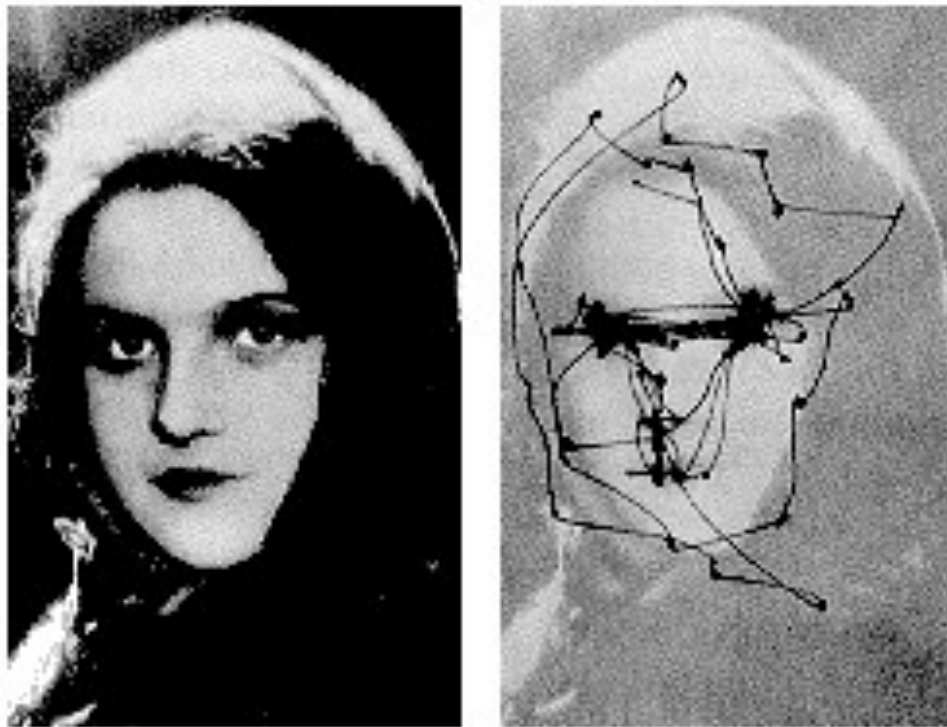
low

spatial acuity



Heukamp et al., 2020

The visual image is not stable on the retina



saccades

The Blind Spot

(located at the optic disc)

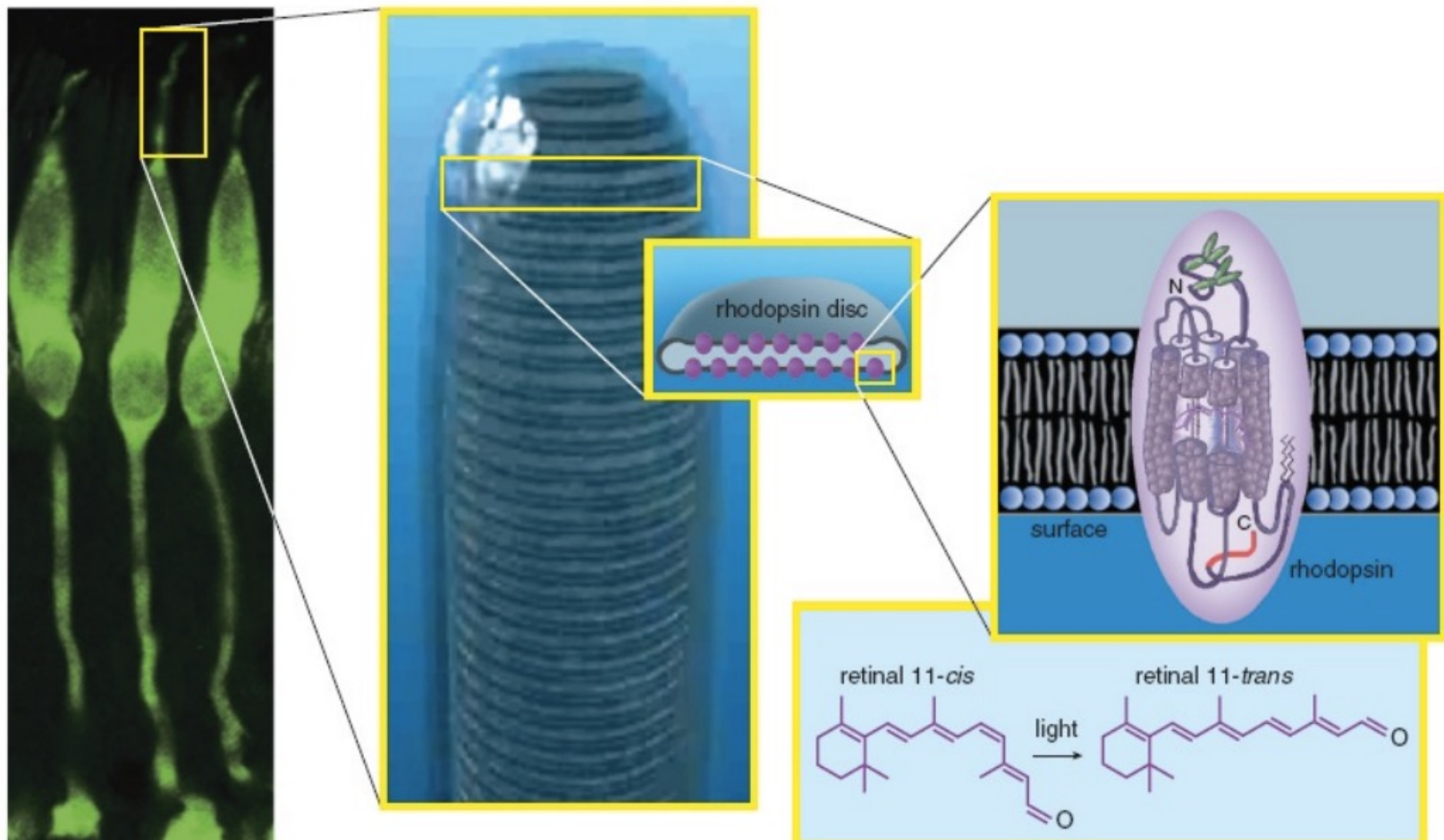


Close your right eye

Fixate on the spot with your left eye

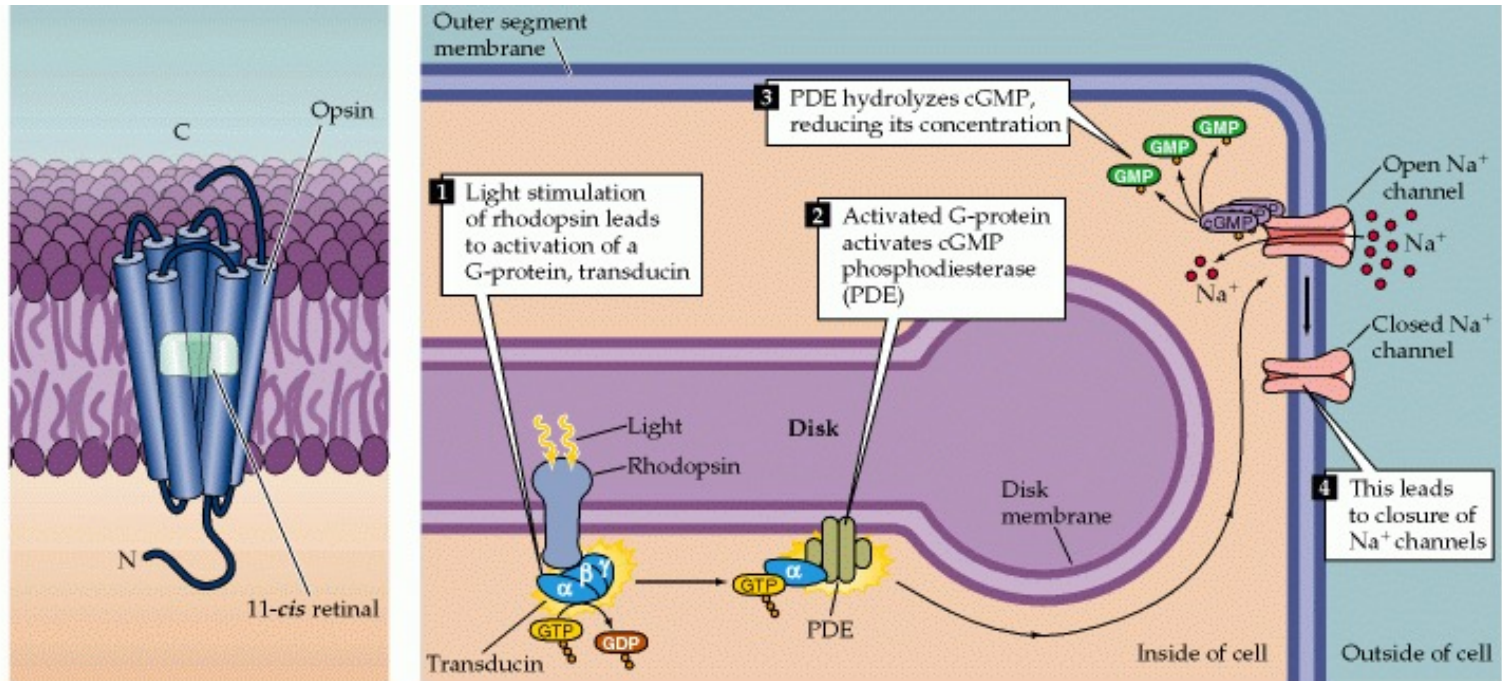
Move paper until cross disappears

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

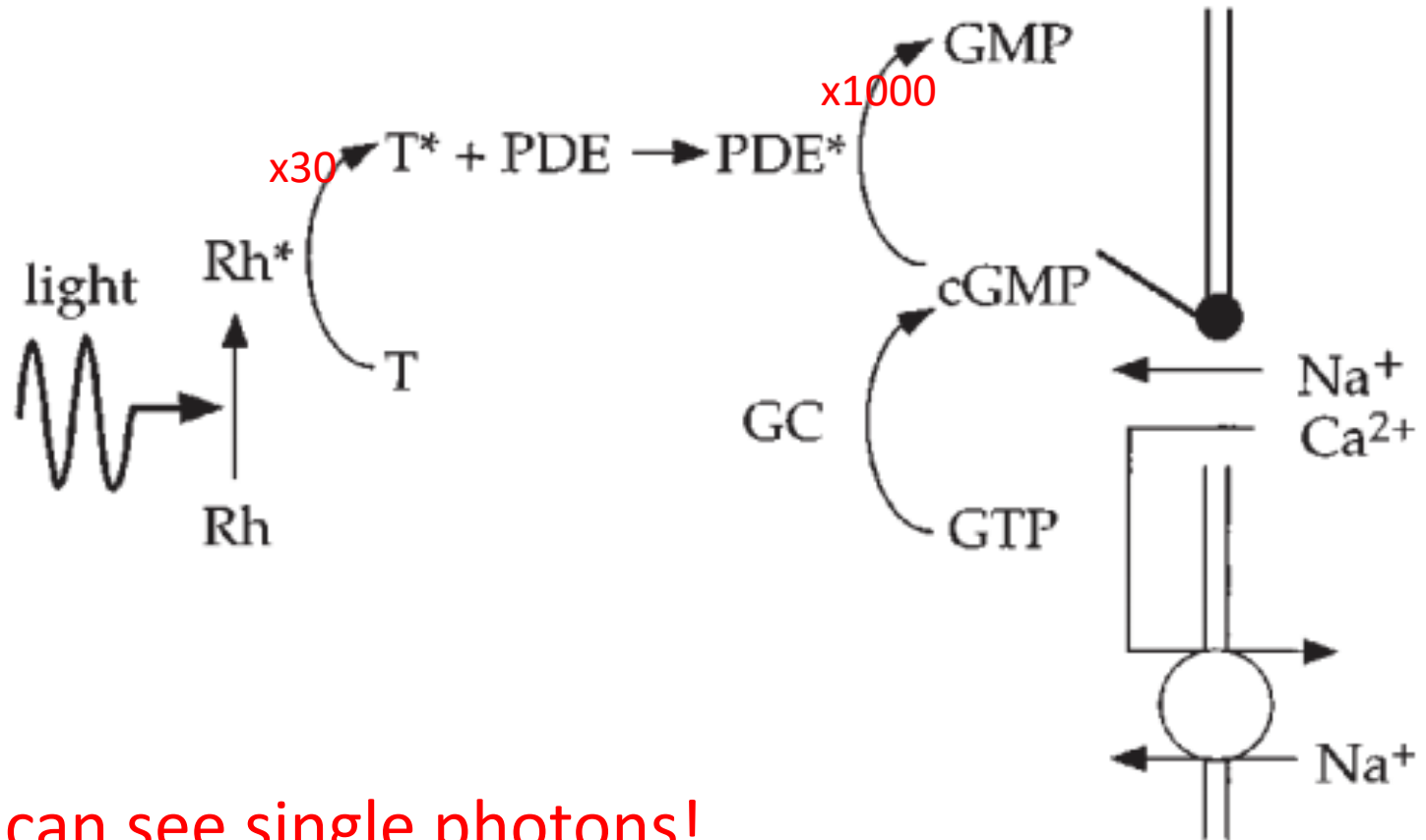


In the dark, Na^+ channels are open by cyclic guanosine monophosphate (**cGMP**).

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

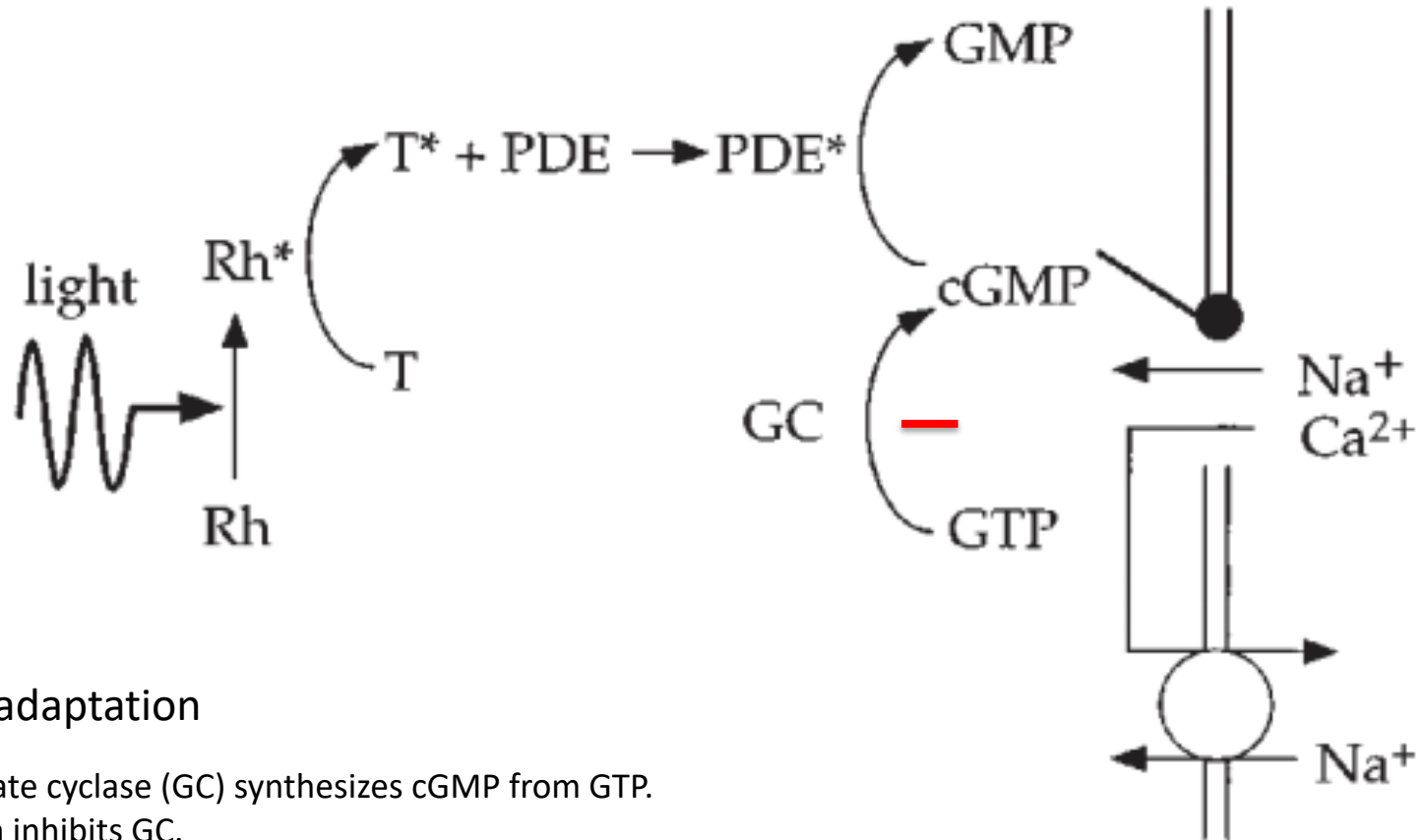
- 1) The activated rhodopsin stimulates the G protein **transducin**
- 2) Transducin activates phosphodiesterase (**PDE**), which breaks down cGMP
- 3) Closure of cGMP-gated channels & hyperpolarization

Amplifying the visual signal



We can see single photons!

Recovery



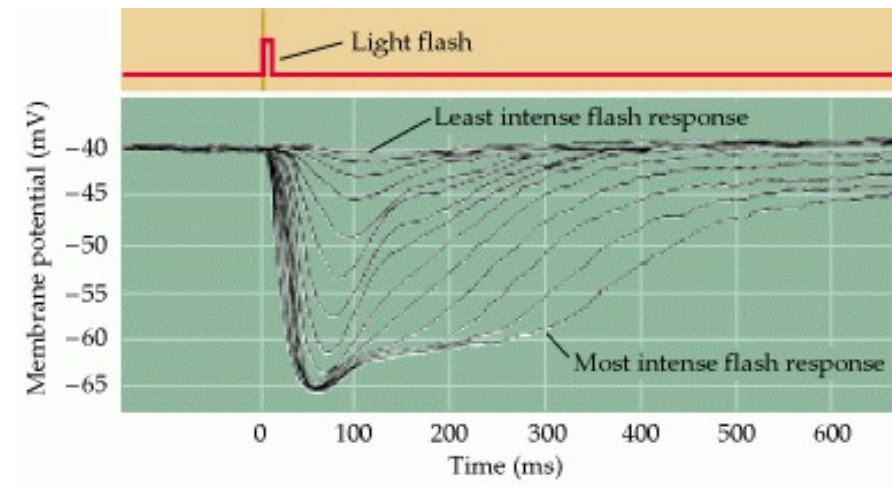
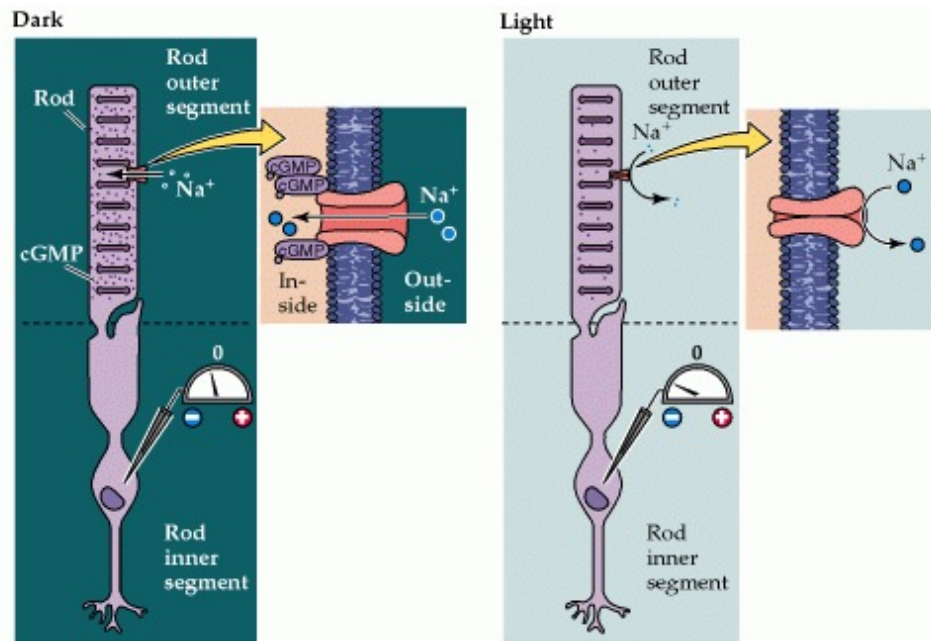
Light adaptation

Guanylate cyclase (GC) synthesizes cGMP from GTP.

Calcium inhibits GC.

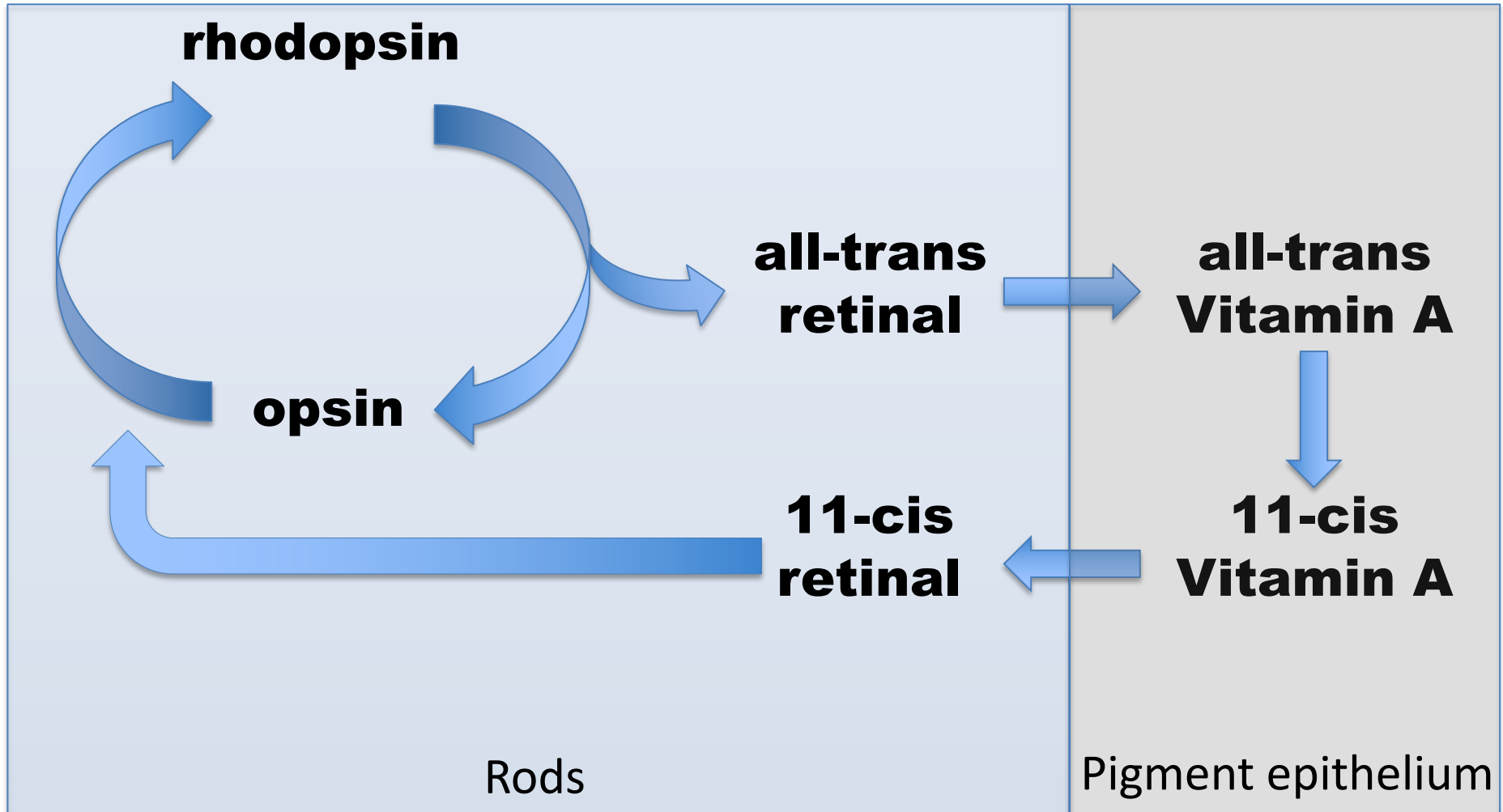
Upon closure of channels (light), Ca concentration decreases -> cGMP level increases.

The dark current



Purves et al., 2001

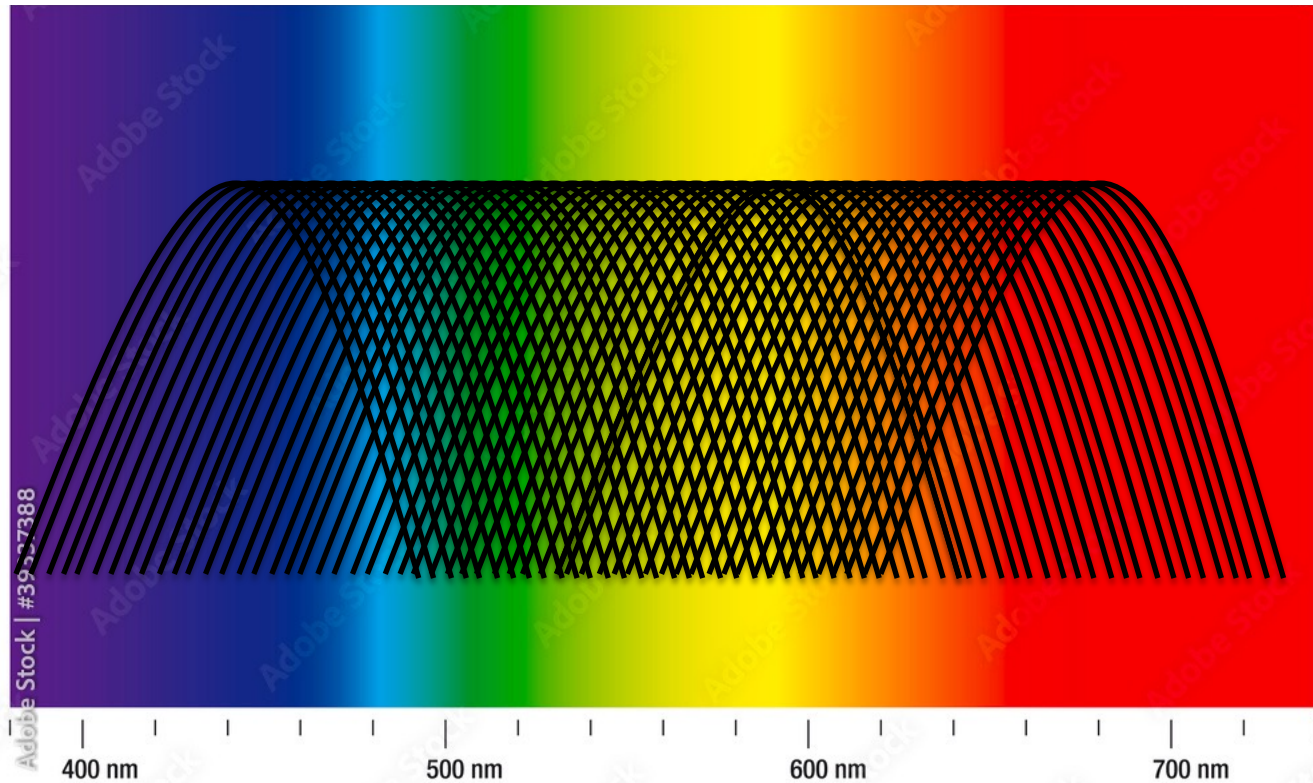
The rhodopsin cycle





George Wald
Nobel prize in Physiology and medicine, 1967

Cones mediate color vision



Cones mediate color vision

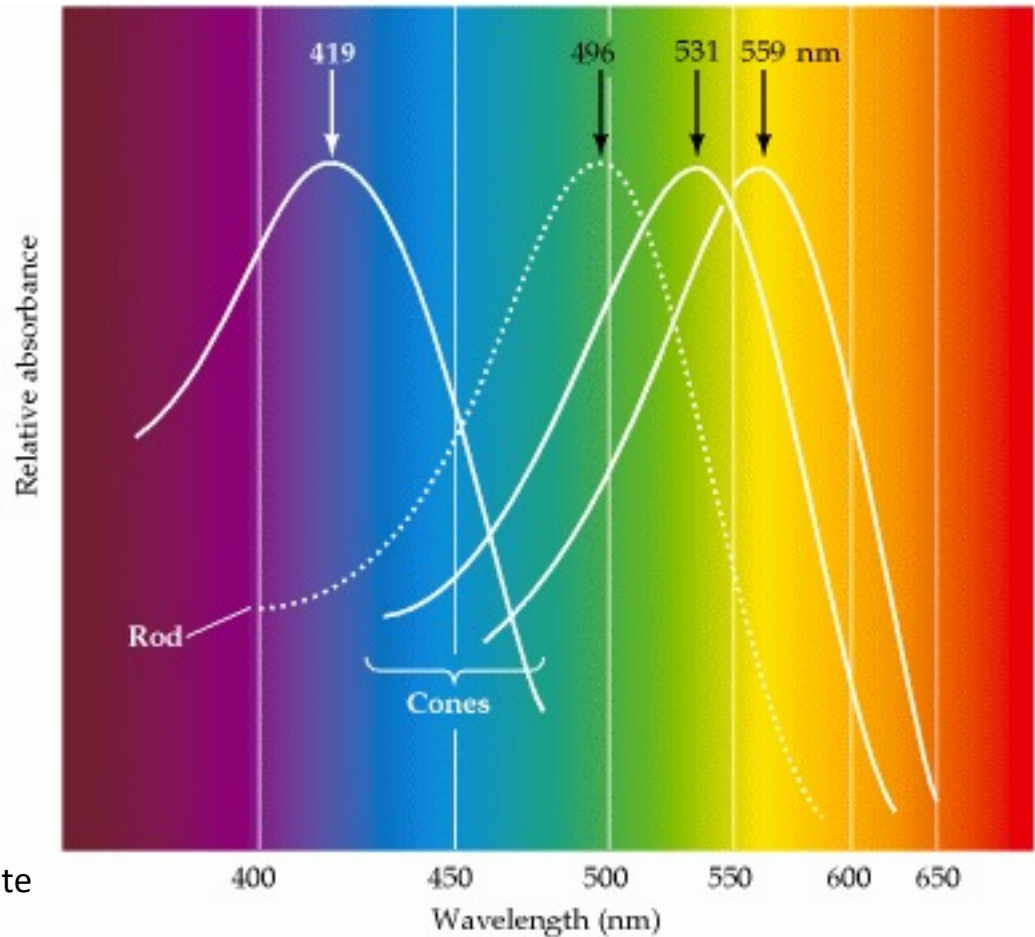
Color vision is based on two or more photoreceptors that have different photopigments

- 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

Cone vision (day)



Rod vision (night)

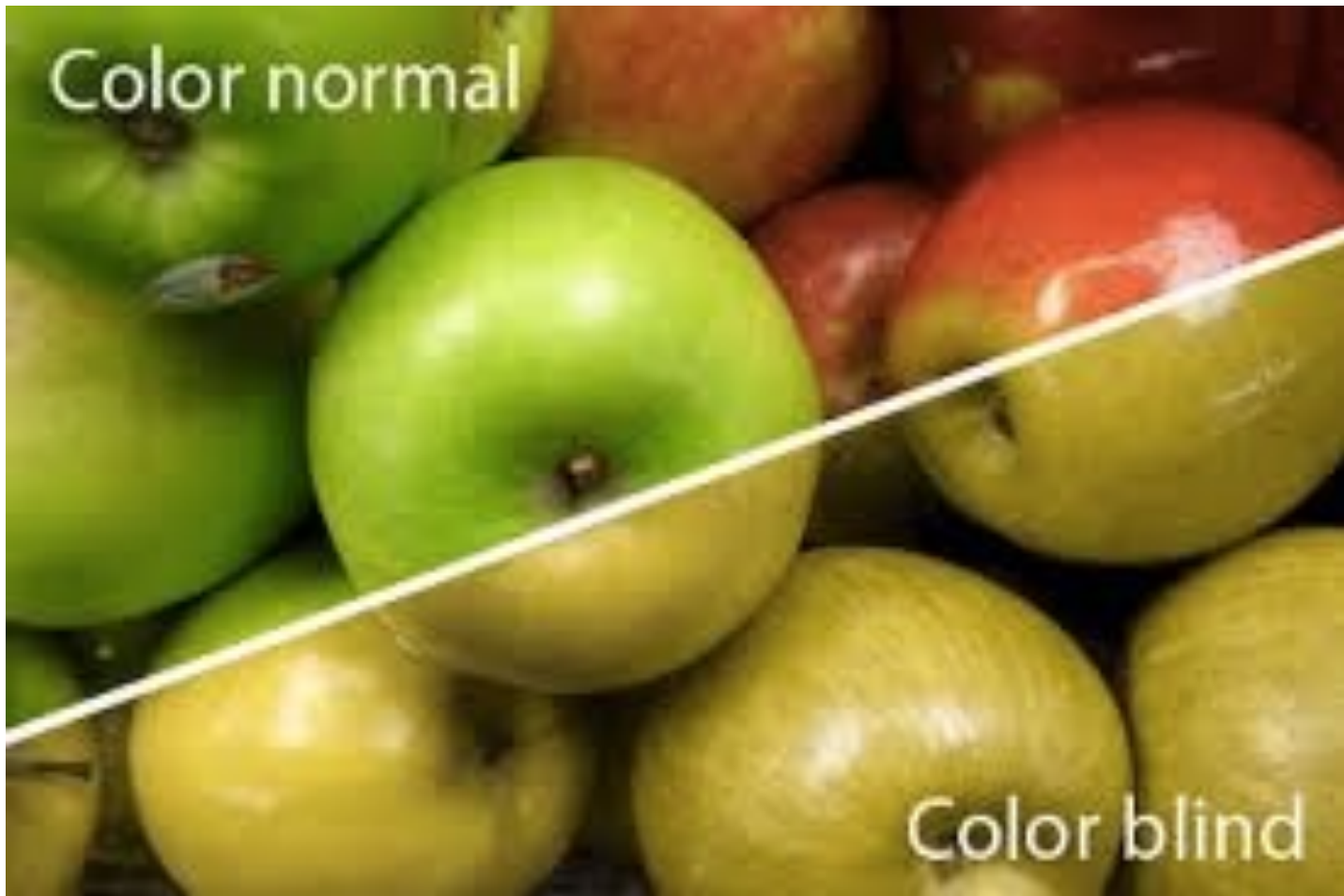


Some animals have 15 cone types

Some animals normally have monochromatic vision



Color blindness

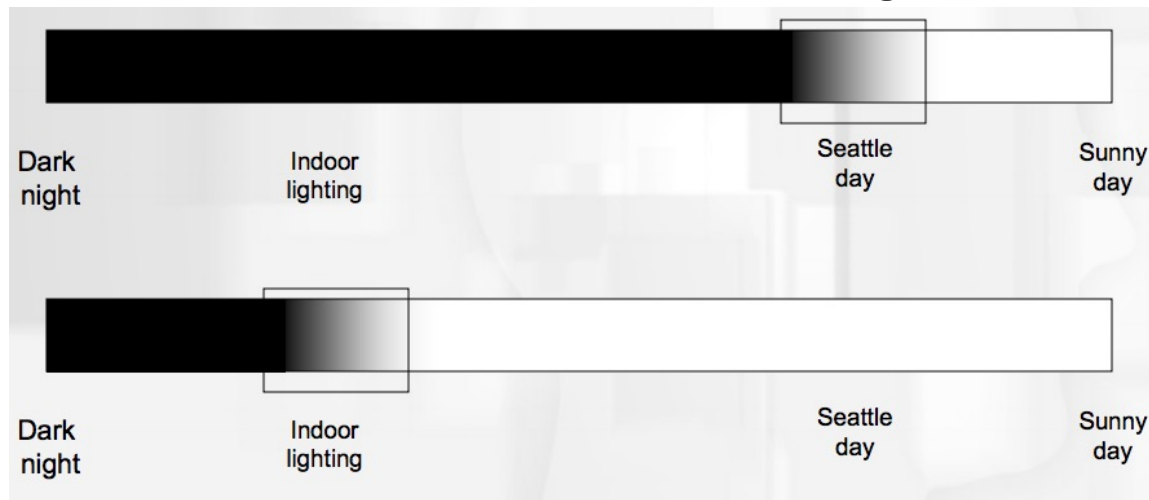


Visual adaptation

- 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.



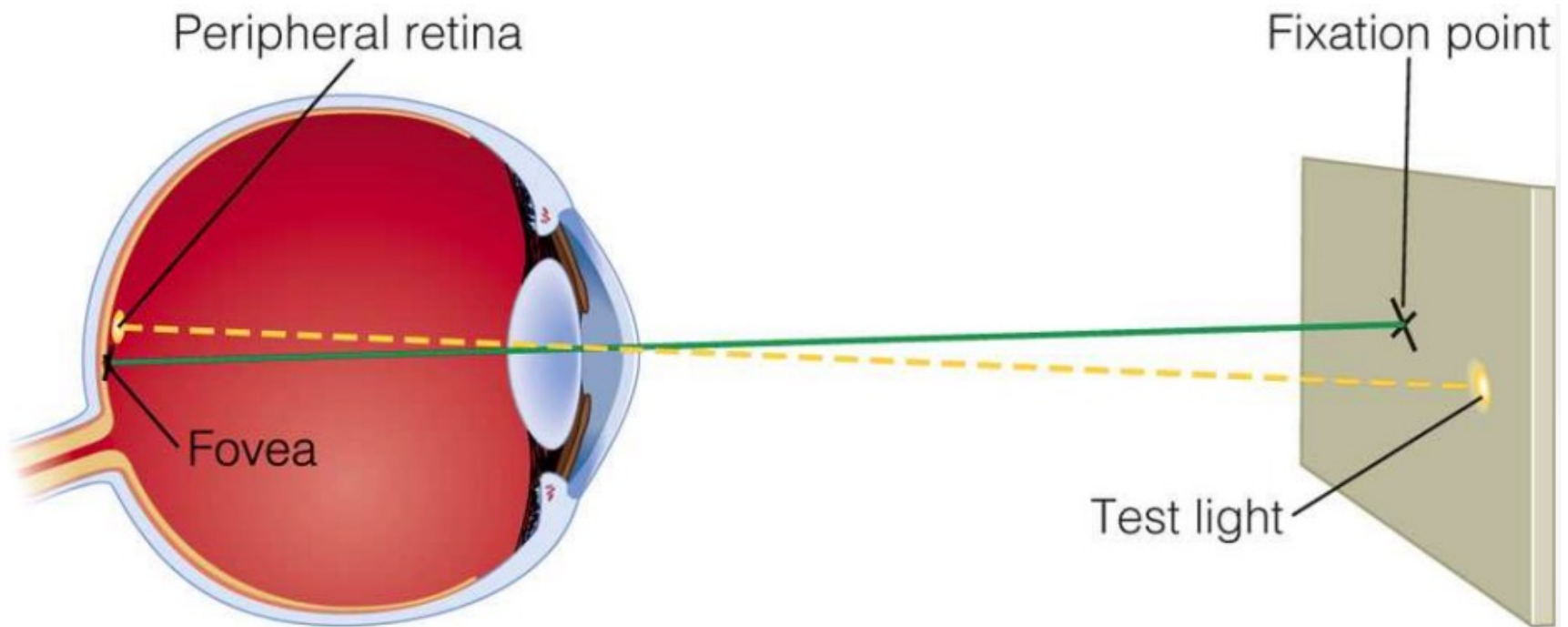
Visual adaptation

- 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.

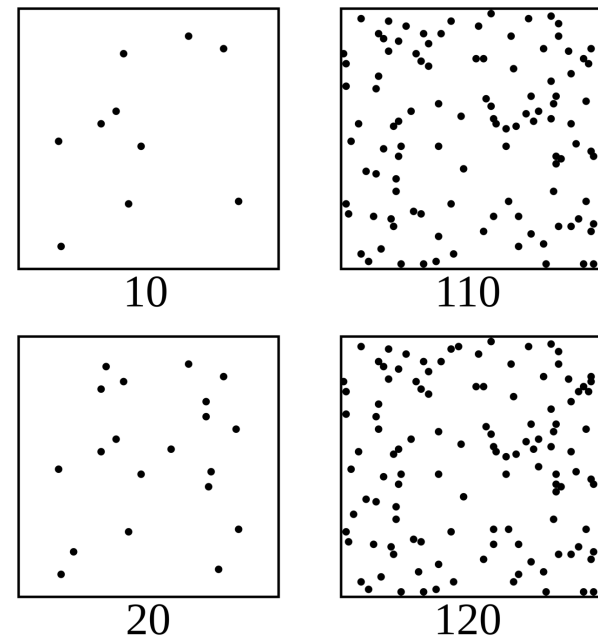
Psychophysical Measurement of Light/Dark Adaptation



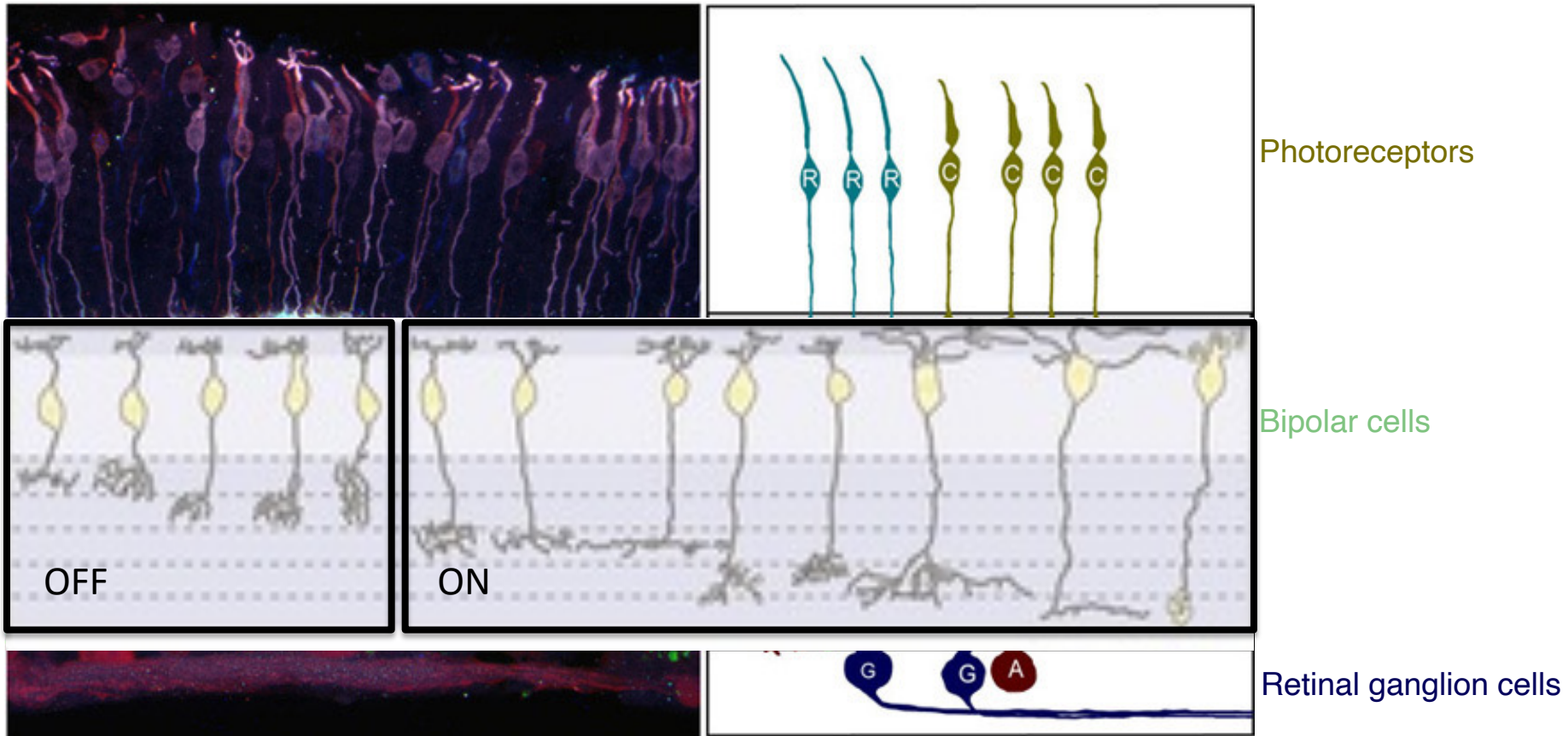
Weber–Fechner law and Weber contrast

- Visual response depends on contrast rather than absolute light levels

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



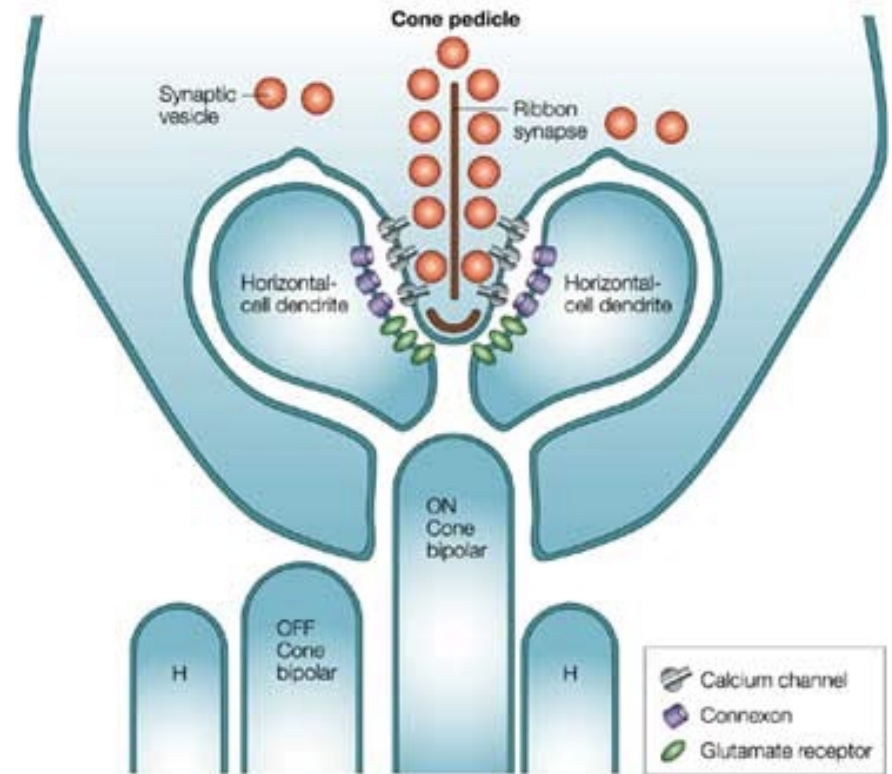
Bipolar Cells



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

Ribbon synapse

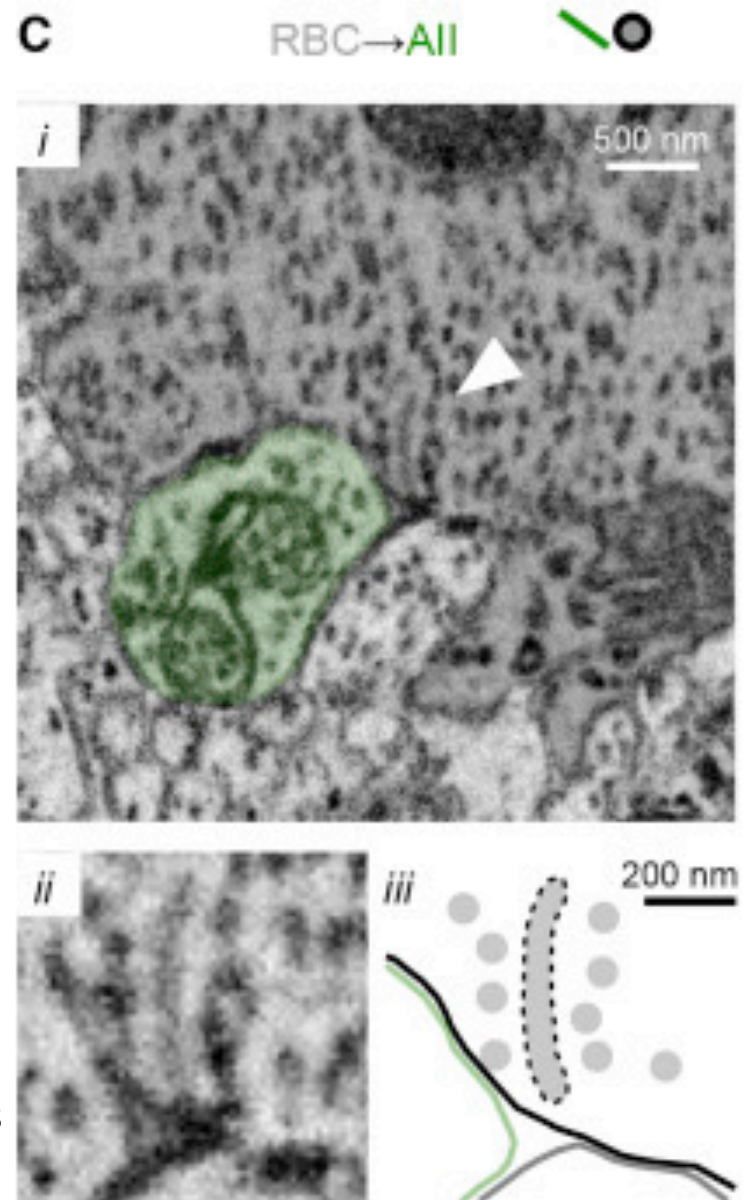
- Graded neurotransmitter release. Precise, sustained, and rapid.
- The synaptic ribbon releases 100s-1000s vesicles per second.
- Each pre-synaptic cell has 10-100 ribbons.
- Requires a large pool of readily releasable vesicles.



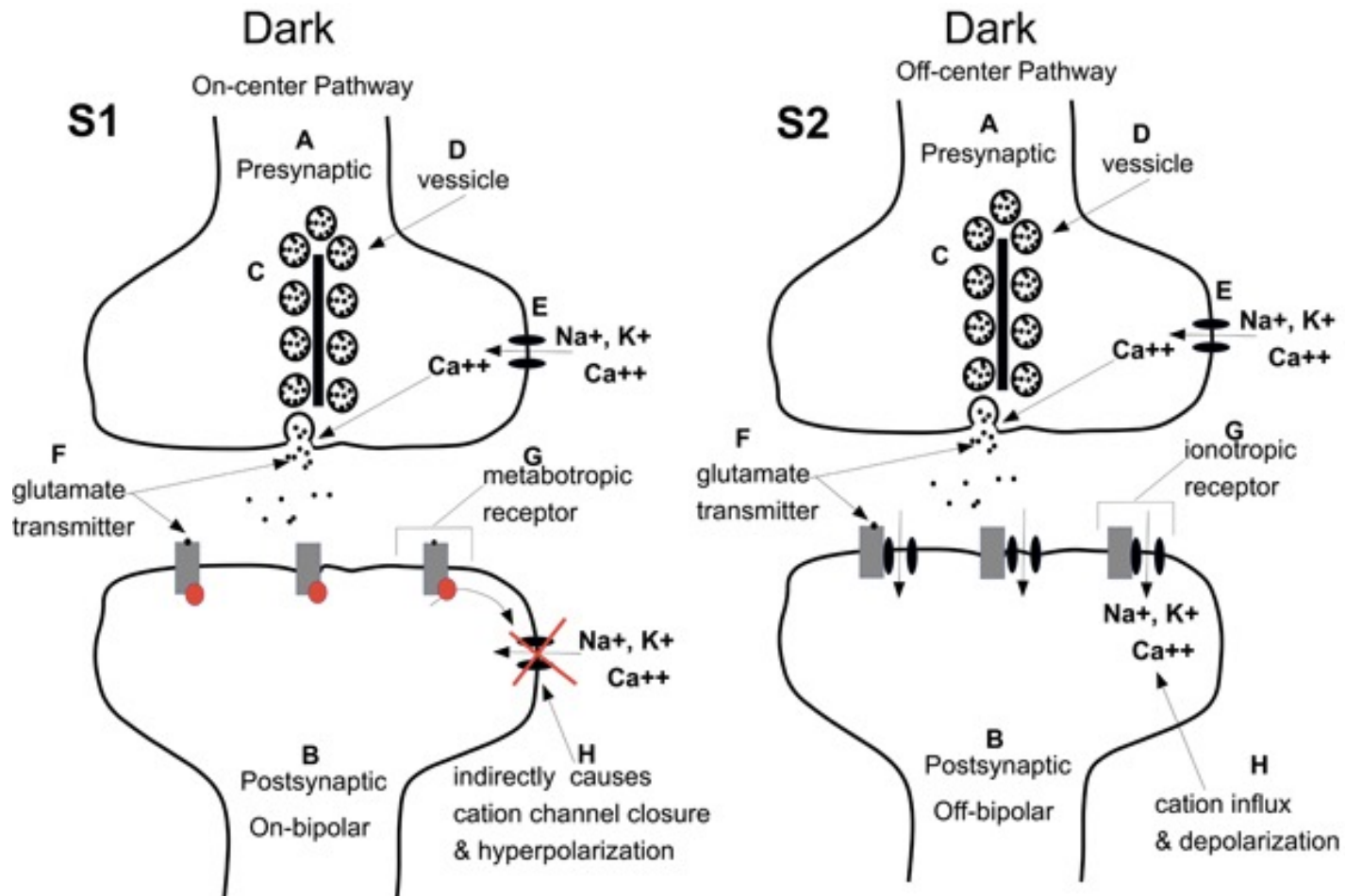
Nature Reviews | Molecular Cell Biology

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.

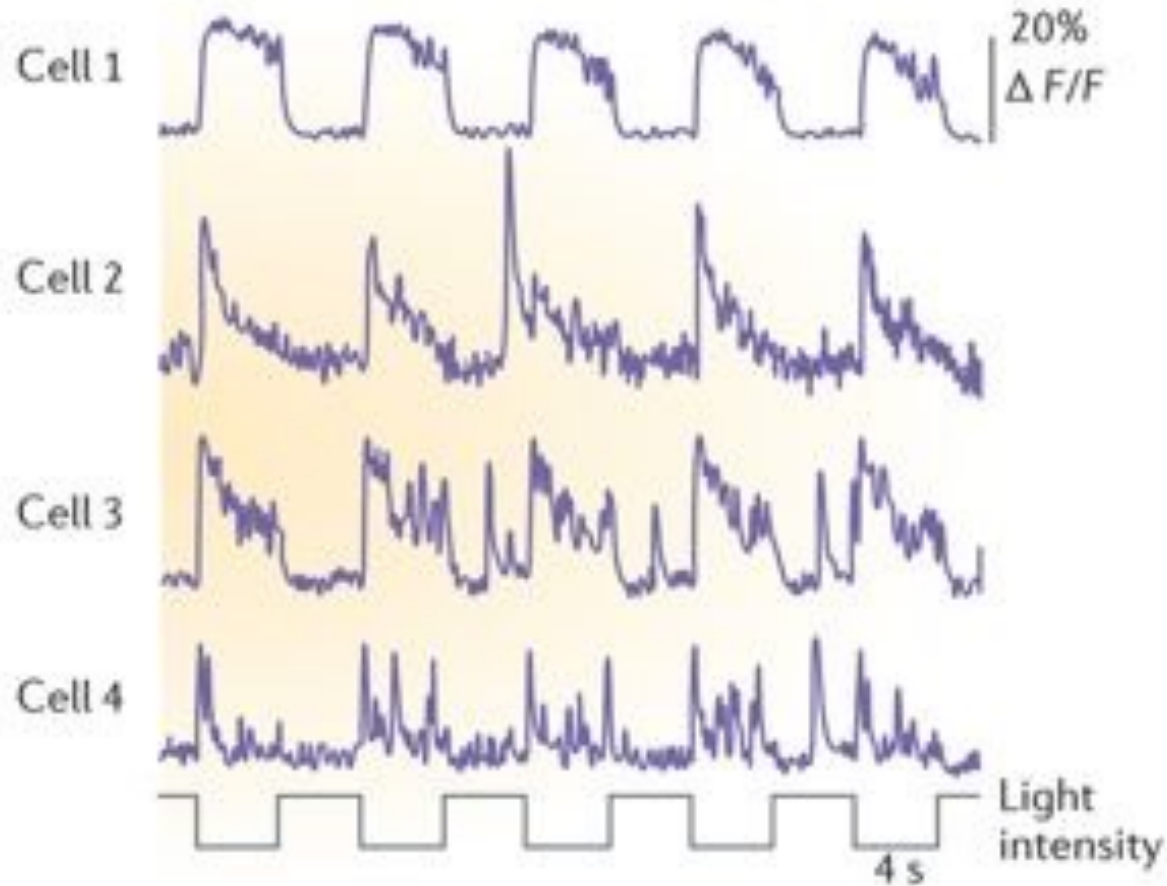


On- and Off-bipolar cells



Sustained and transient bipolar cells

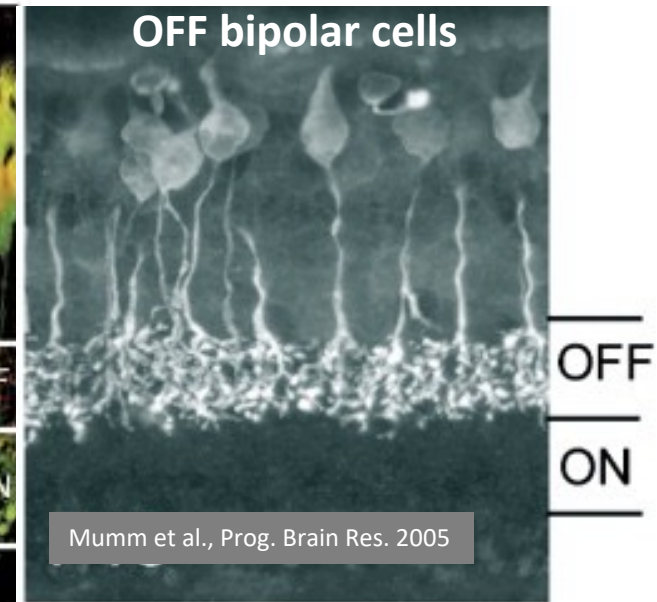
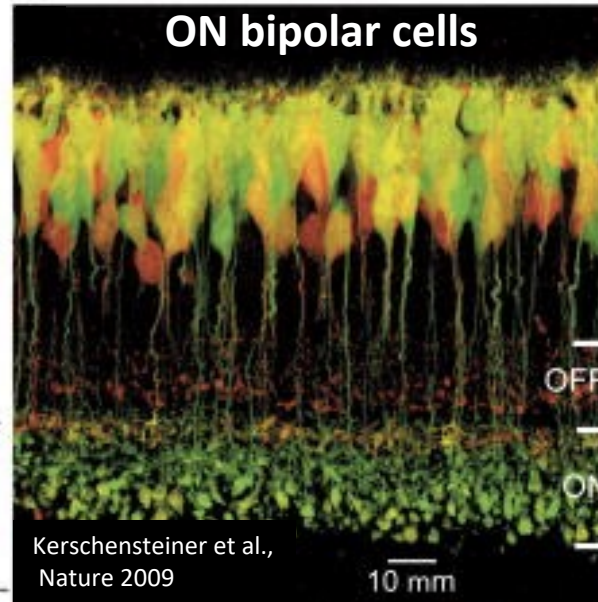
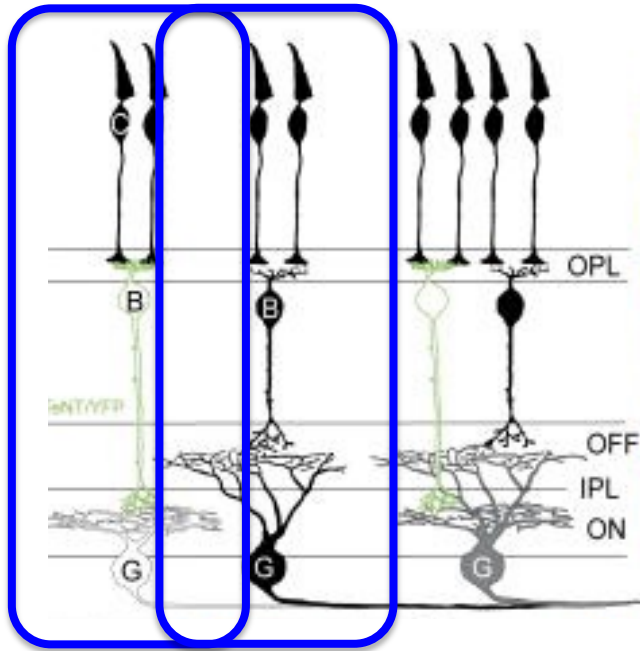
B Ca^{2+} imaging in bipolar cell terminals



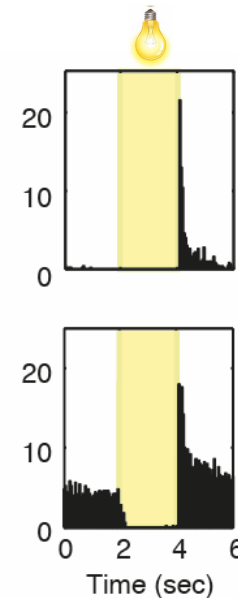
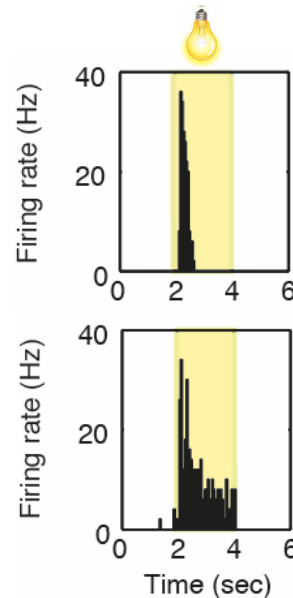
Euler et al., 2014

On and Off retinal pathways

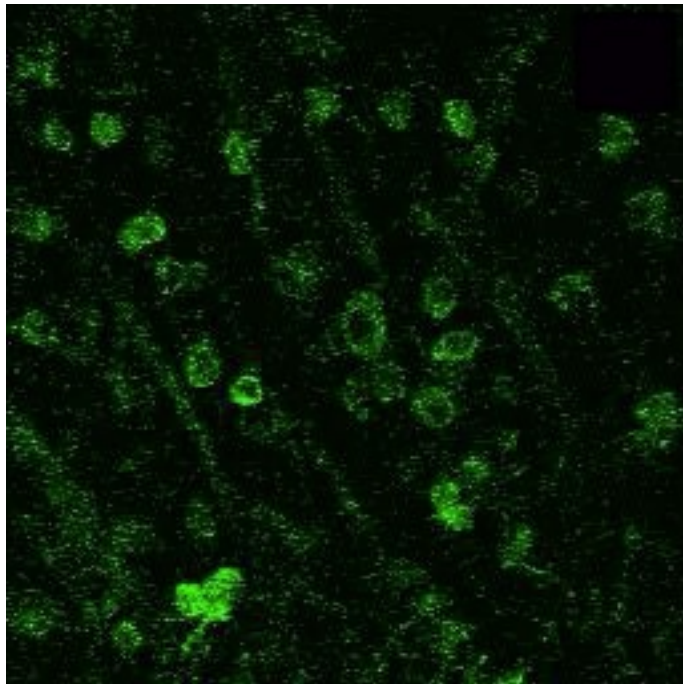
ON OFF



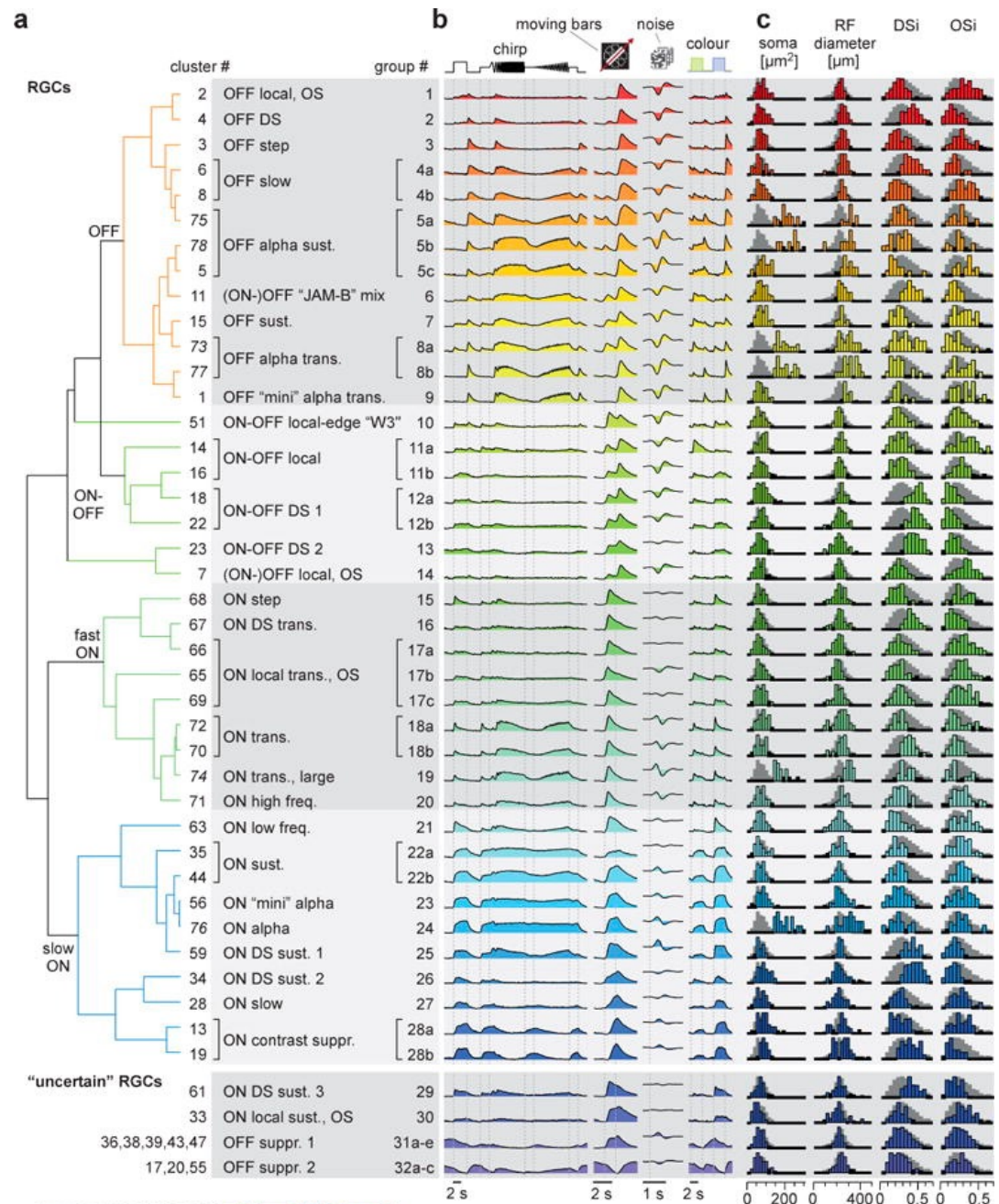
Retinal ganglion cells (RGC):



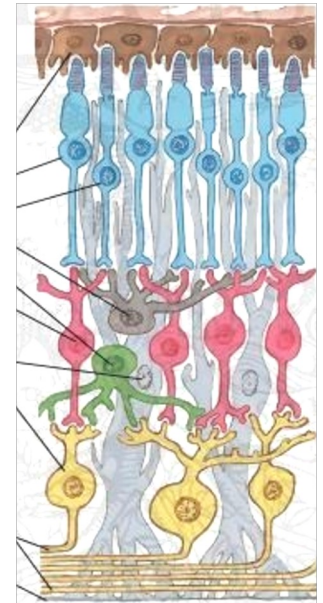
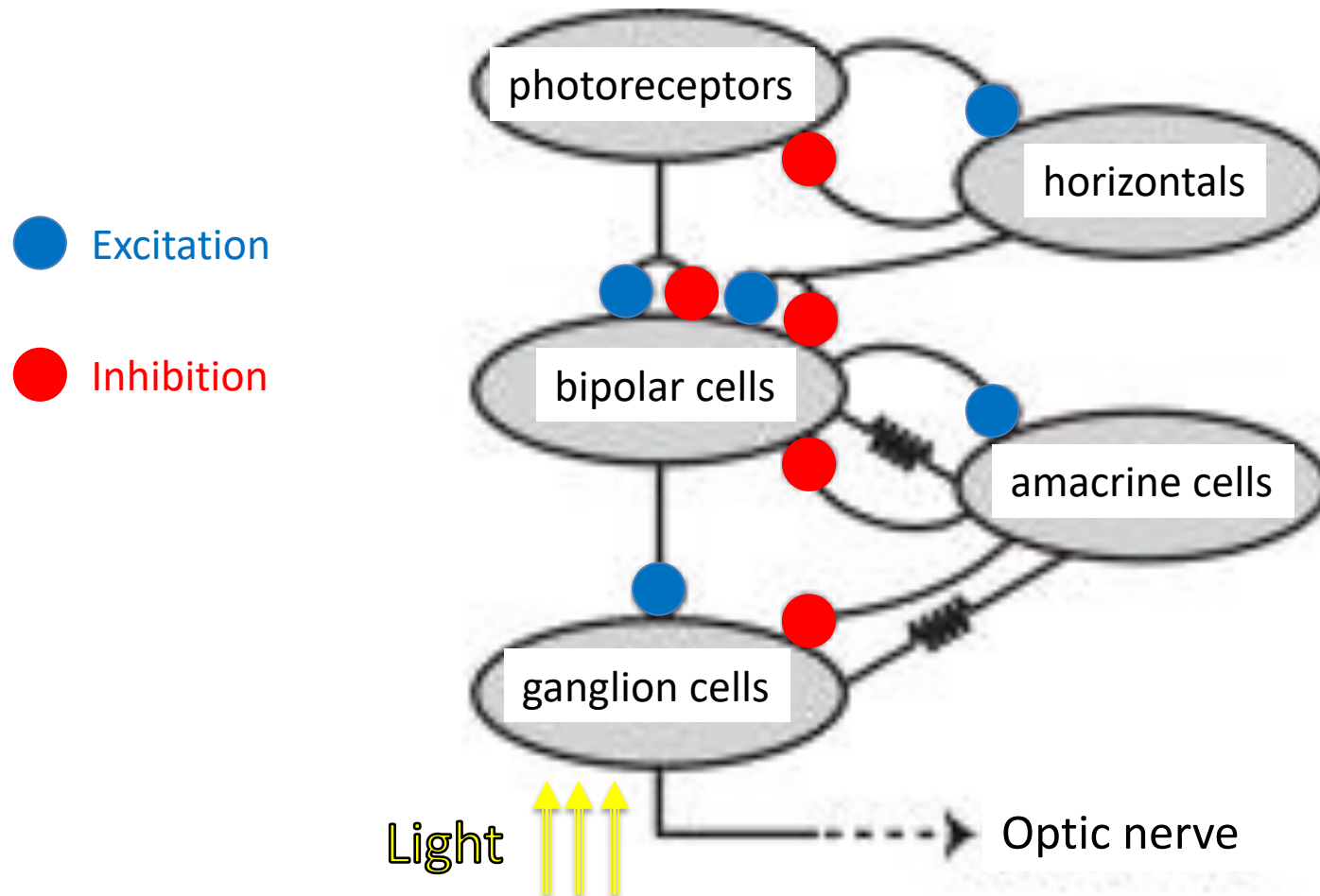
>30 different subtypes of retinal ganglion cells (RGCs)



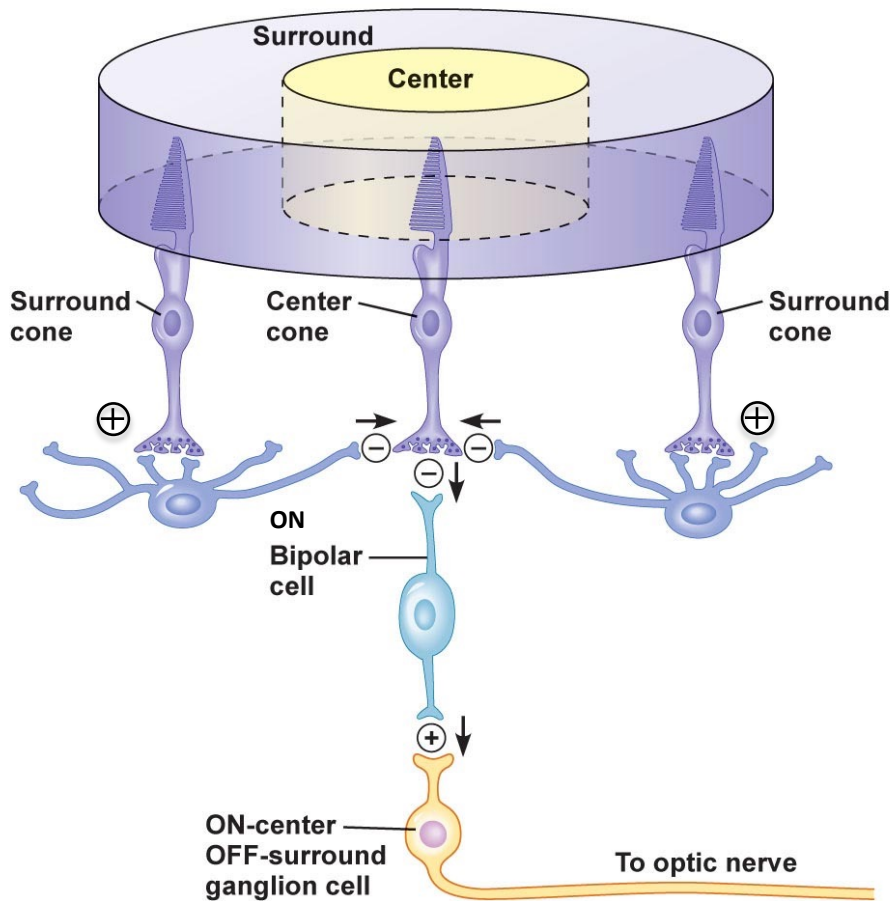
Lior Pinkus



Straight through pathway + lateral connections



Horizontal Cells



© 2011 Pearson Education, Inc.

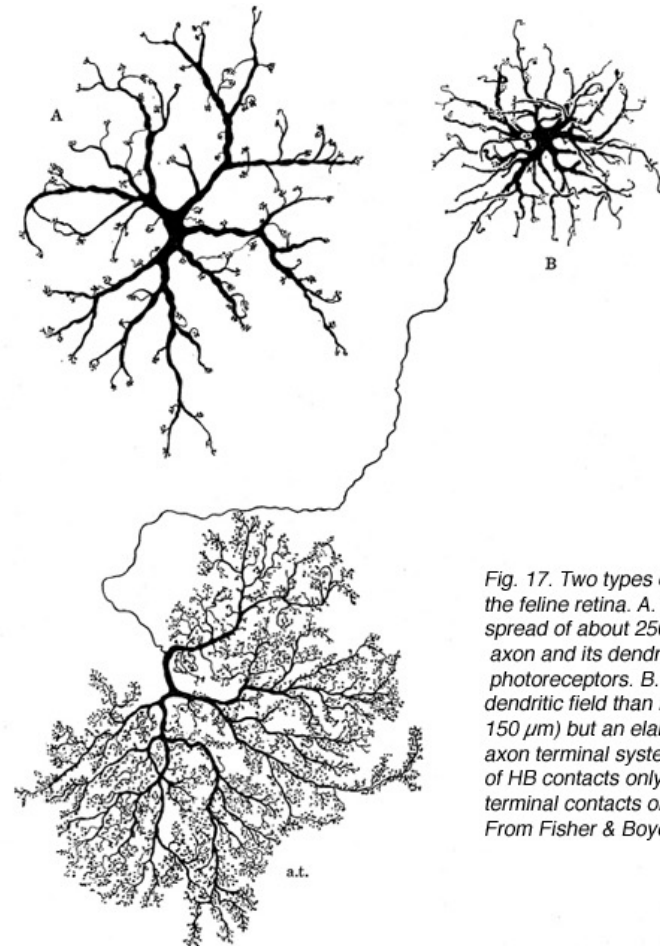
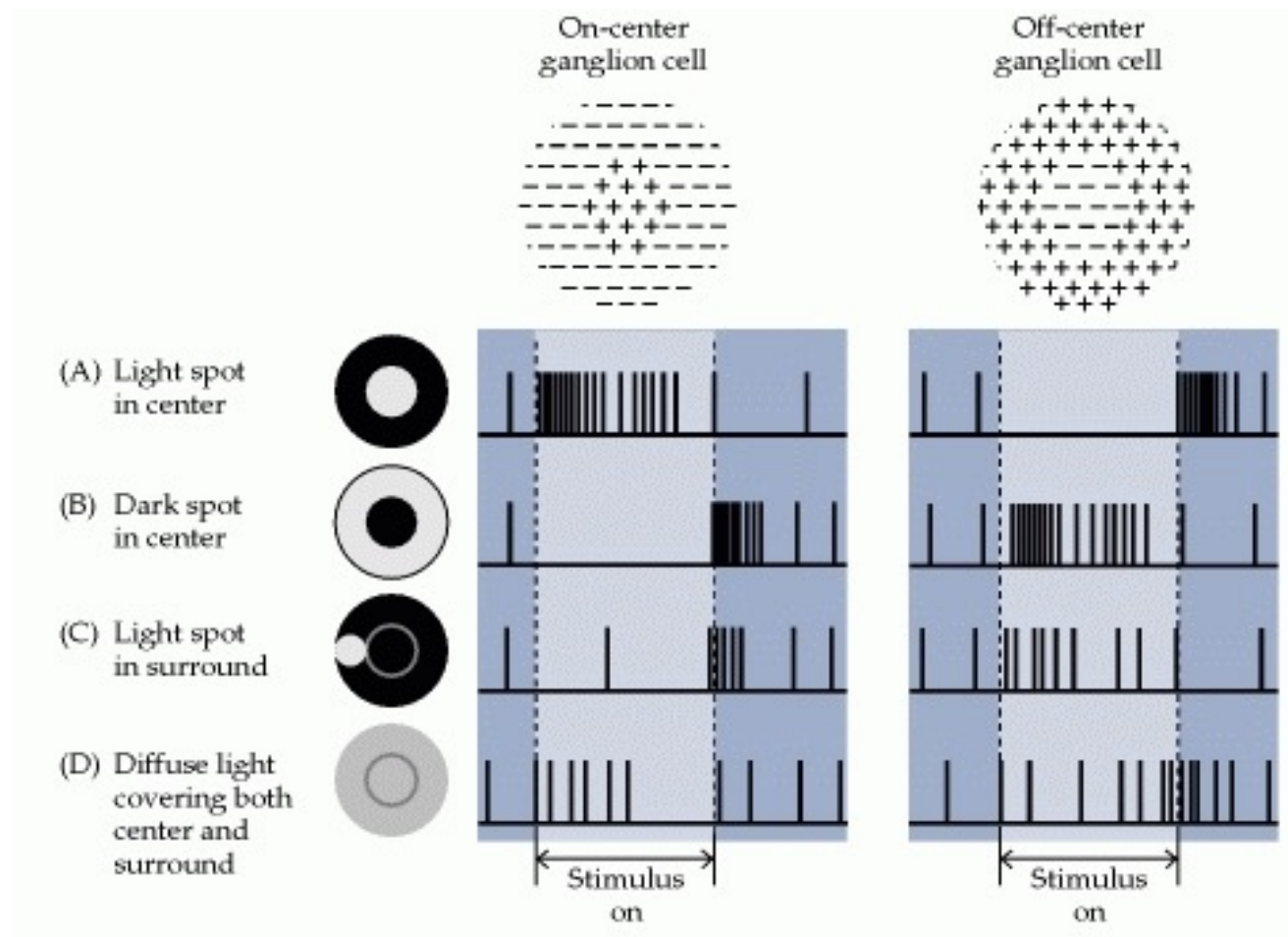
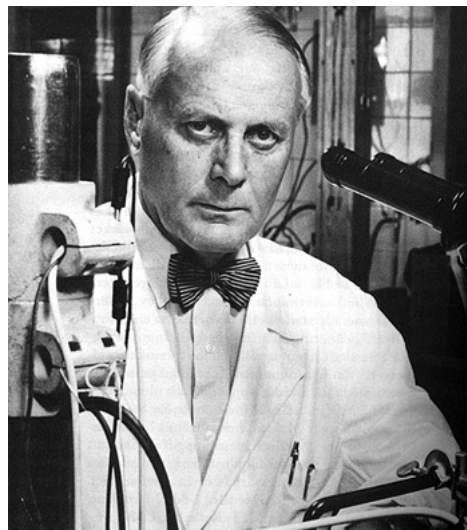


Fig. 17. Two types of horizontal cells in the feline retina. A. HA with a dendritic spread of about $250\ \mu\text{m} \times 250\ \mu\text{m}$ has no axon and its dendrites contact only cone photoreceptors. B. HB has a smaller dendritic field than HA (about $150\ \mu\text{m} \times 150\ \mu\text{m}$) 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

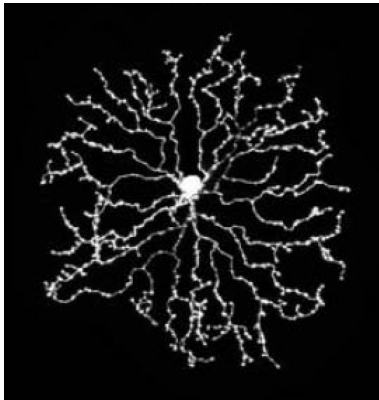
Stephen Kuffler

1950

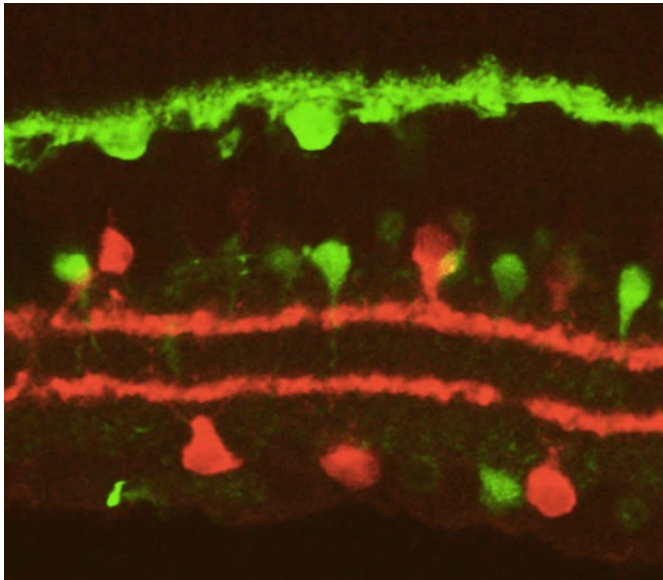
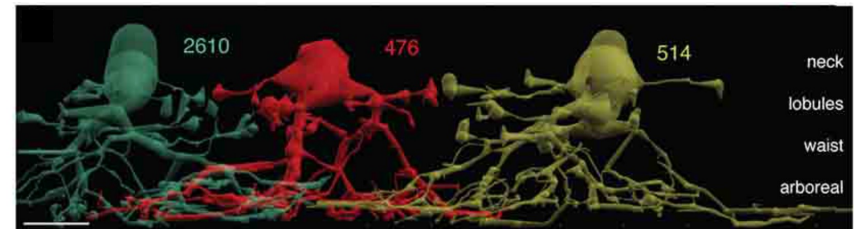
Find the antagonistic center-surround
organization in RGCs

Narrow-field amacrine cells

Starburst amacrine cell

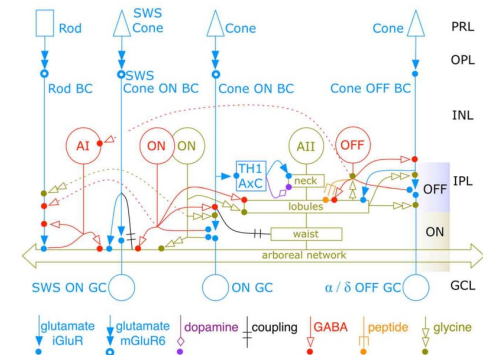


All amacrine cell



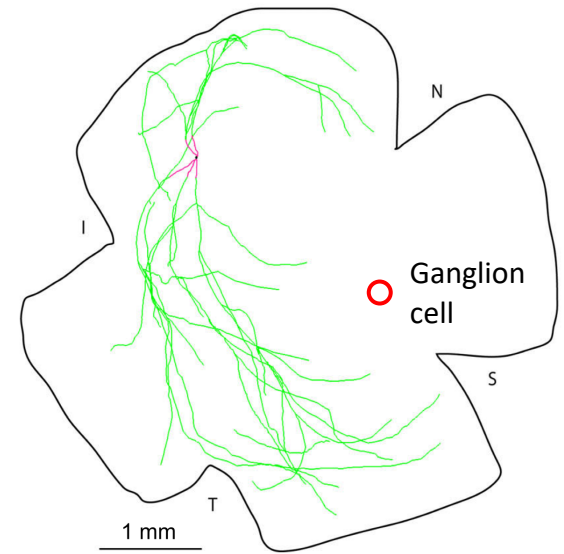
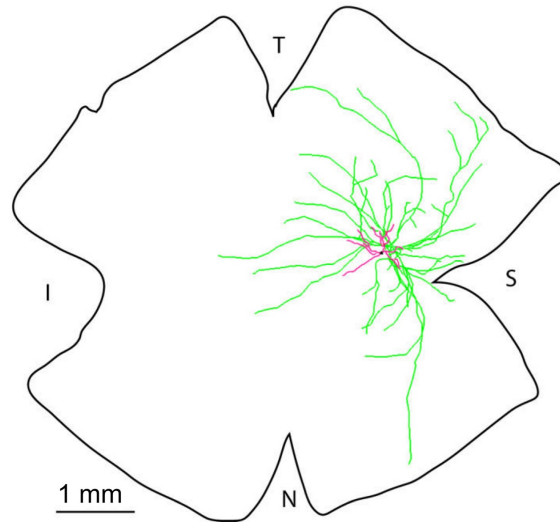
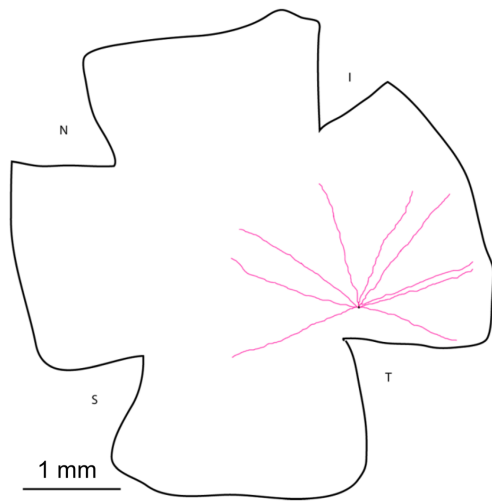
rotransmitters:

Off ChAT band
On ChAT band
(new!)



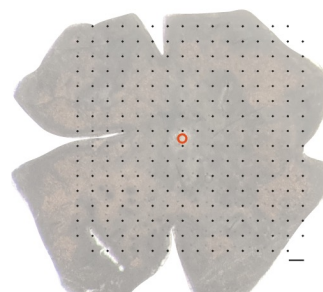
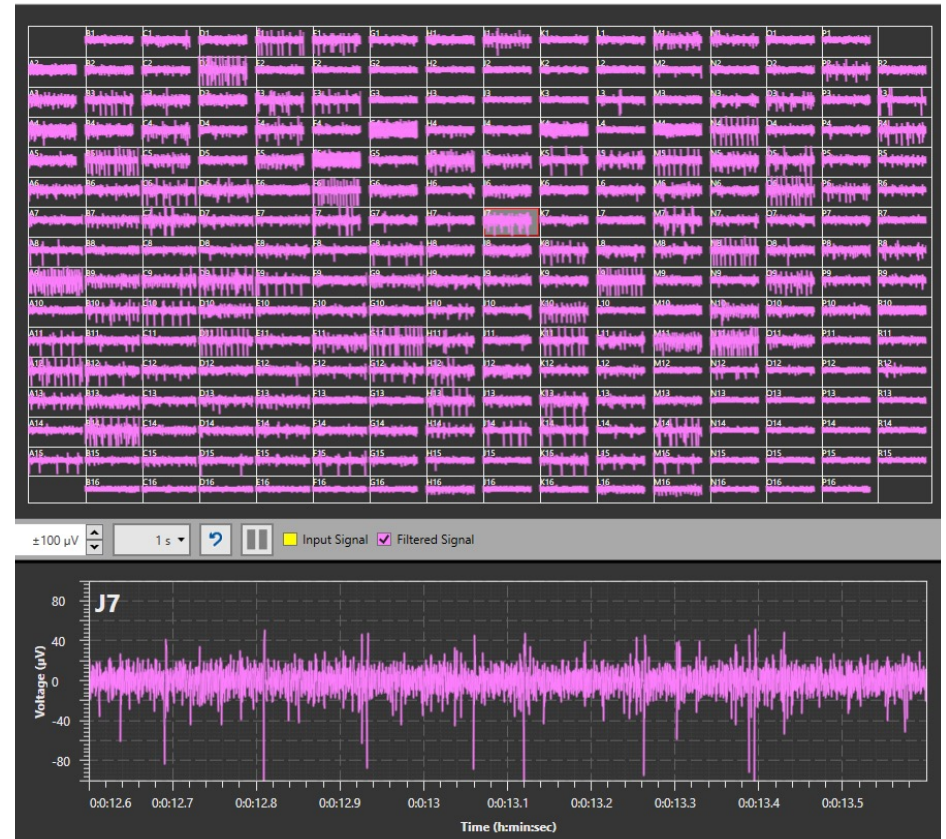
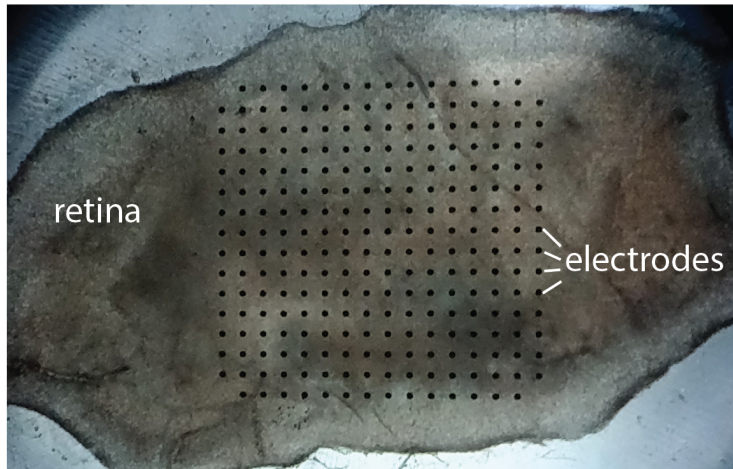
Marc et al., 2014 (*Front. Neural Circuits*)

Wide-field amacrine cells



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

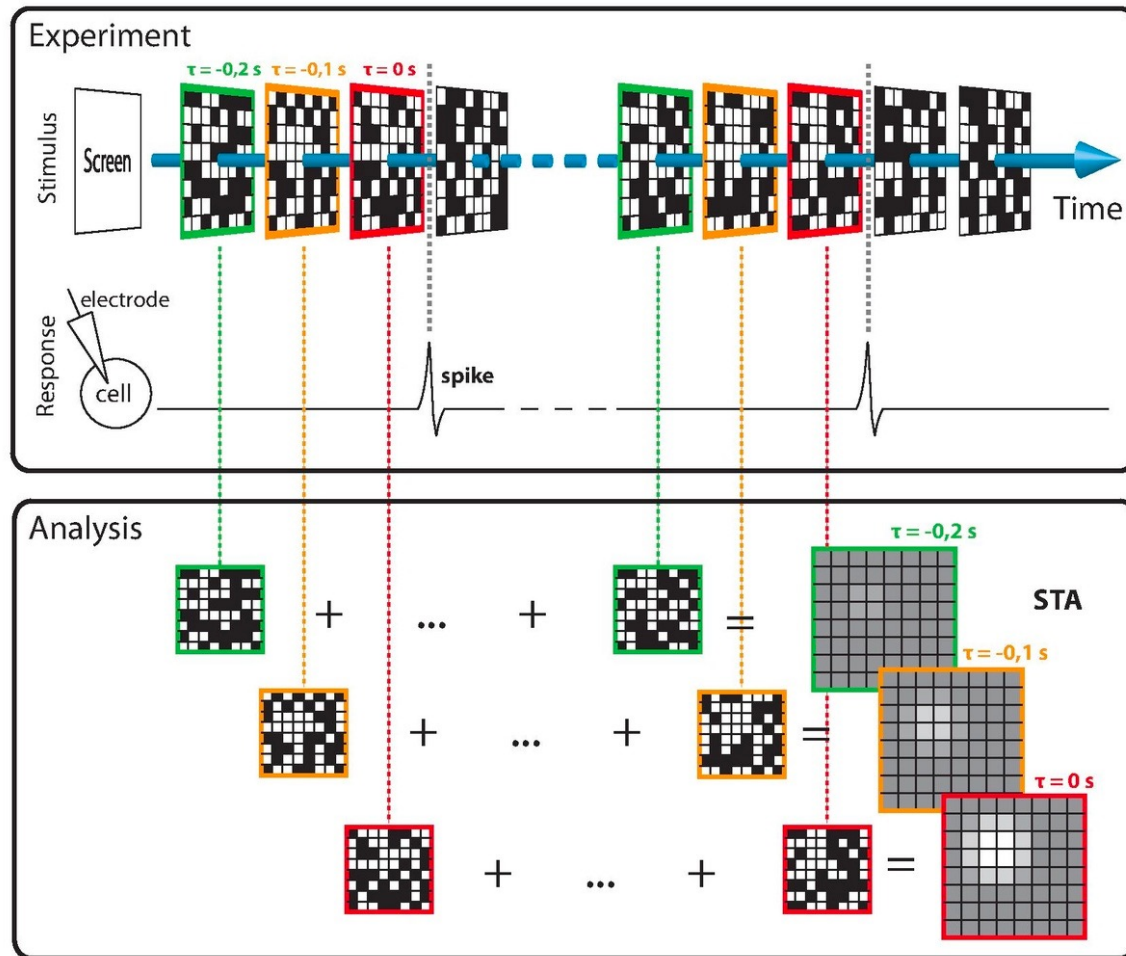
Identifying receptive fields of retinal ganglion cells using multi-electrode array recordings



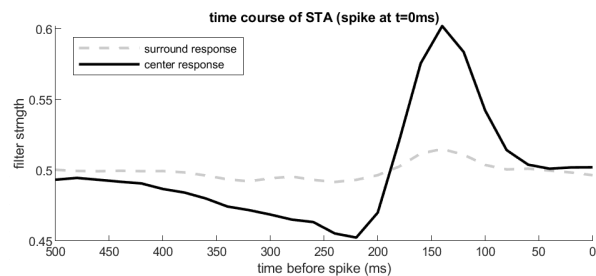
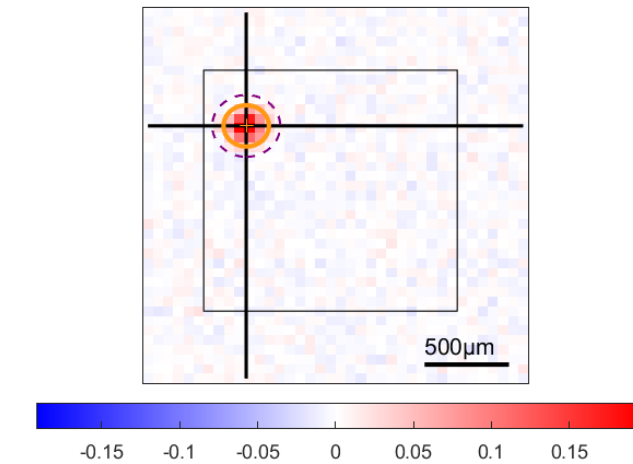
Serena Riccitelli Alina Heukamp

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

Spike-triggered average (STA)

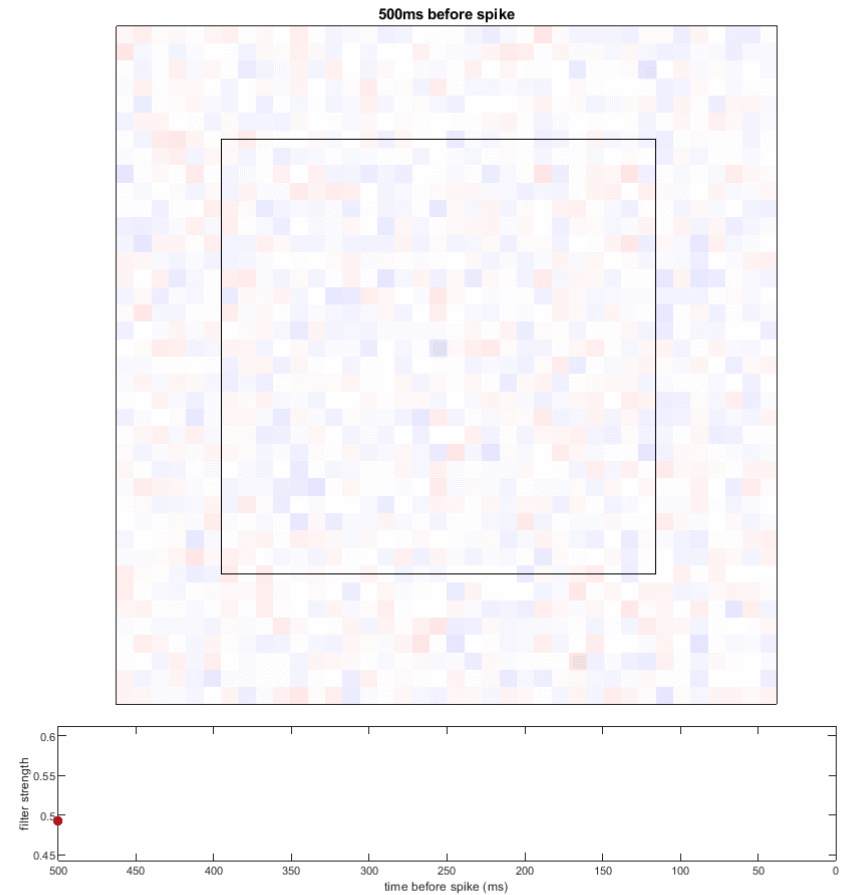


Receptive field of RGCs can be measured using the spike-triggered average of a spatio-temporal white noise stimulus

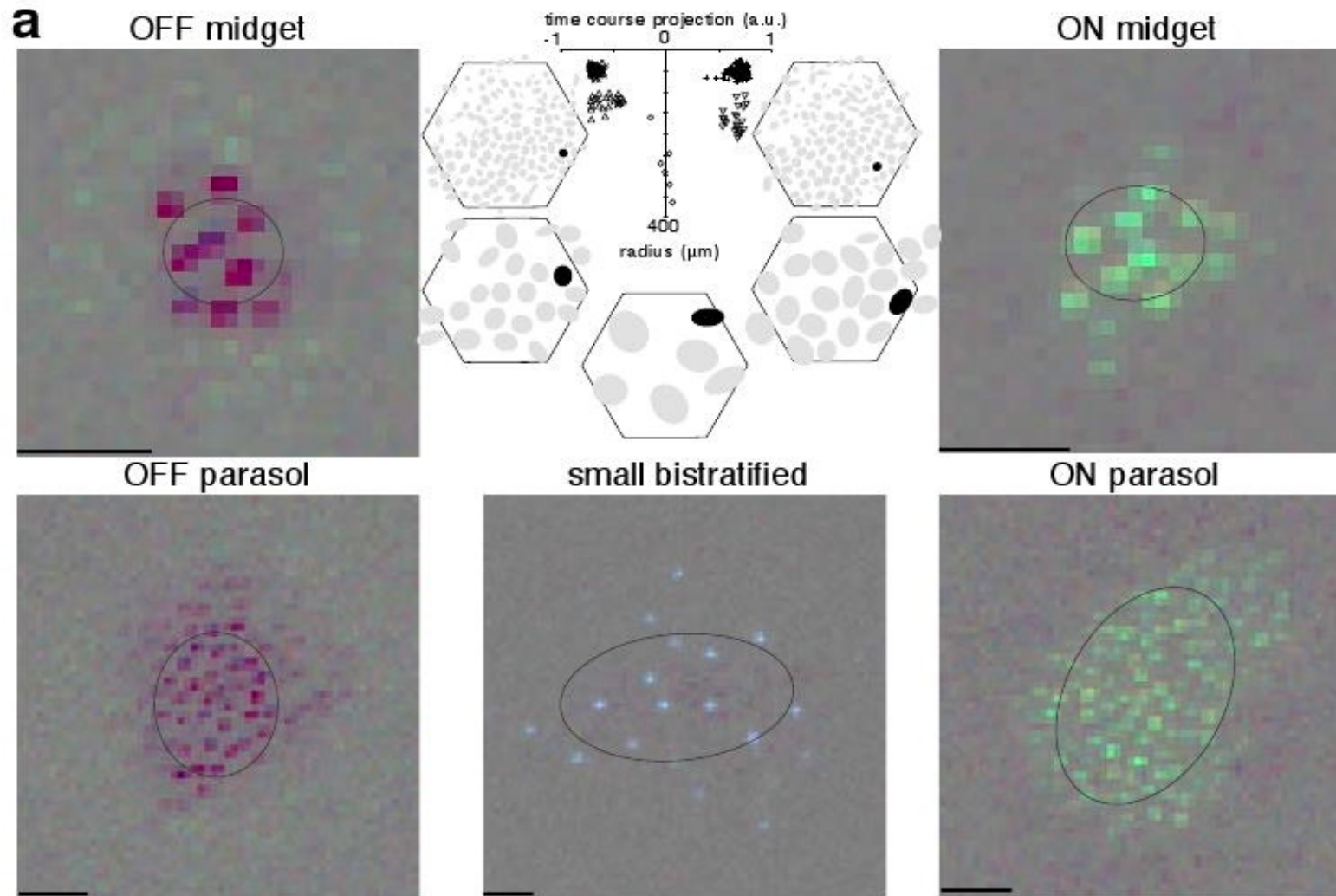


RF diameter:
in x direction: 150.0 μm
in y direction: 137.8 μm

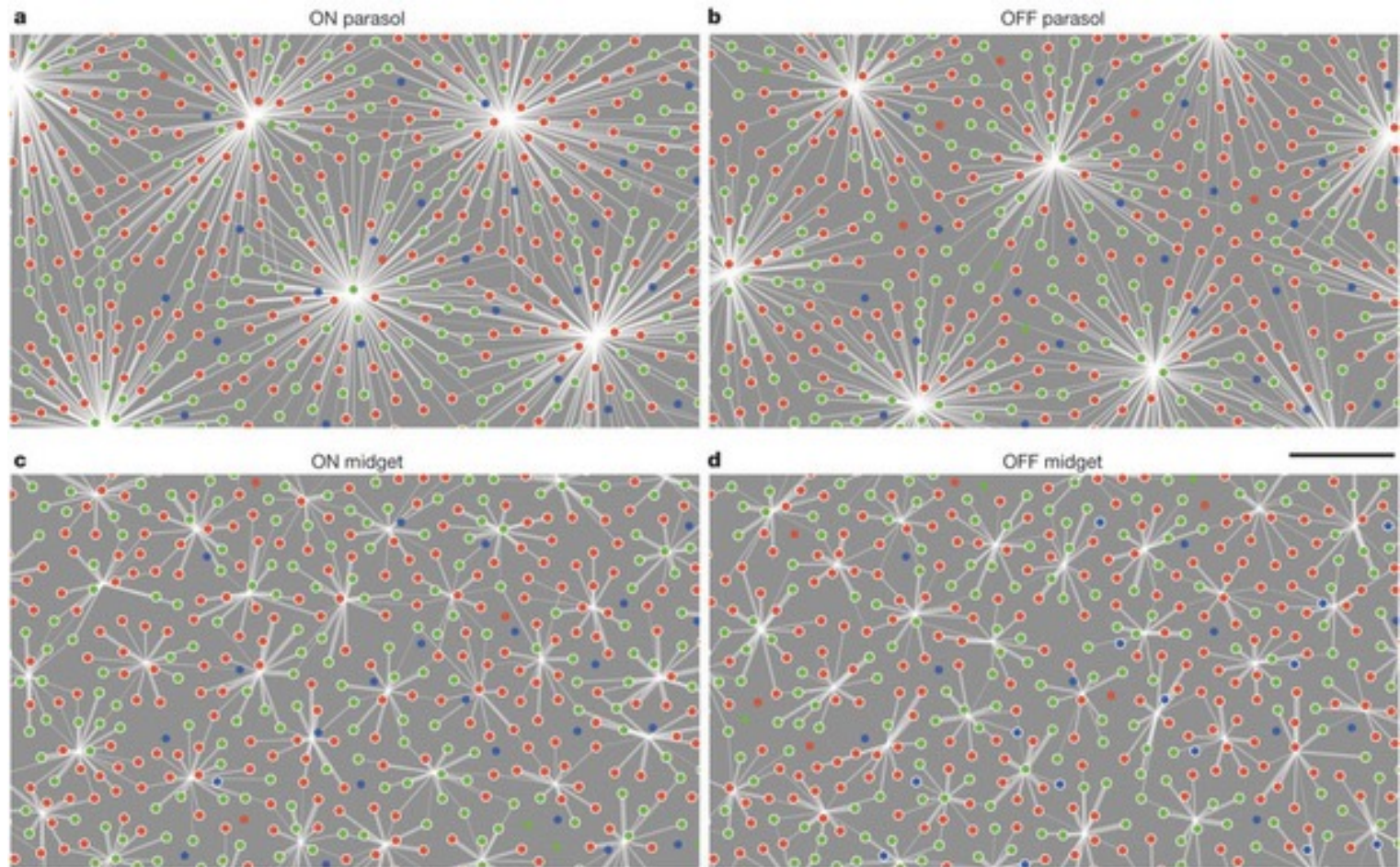
maximum response: 140.0ms before spike
(positive response = ON cell)



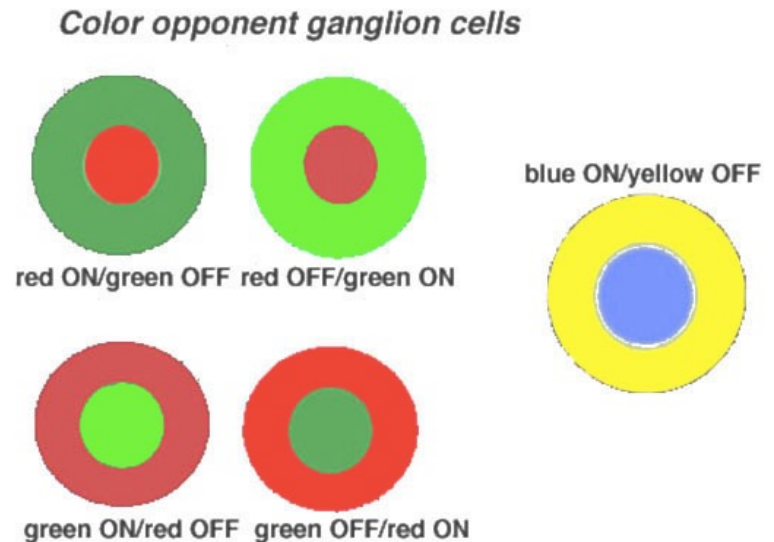
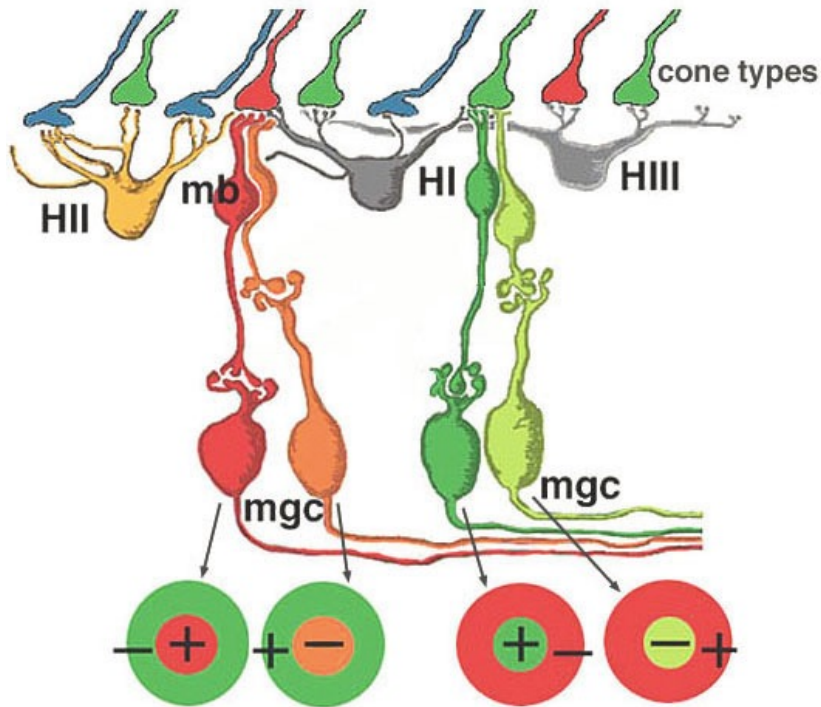
Receptive field of RGCs can be measured using the spike-triggered average of a spatio-temporal white noise stimulus



Functional sampling of cone lattice by RGCs



Retinal ganglion cells: midget cells

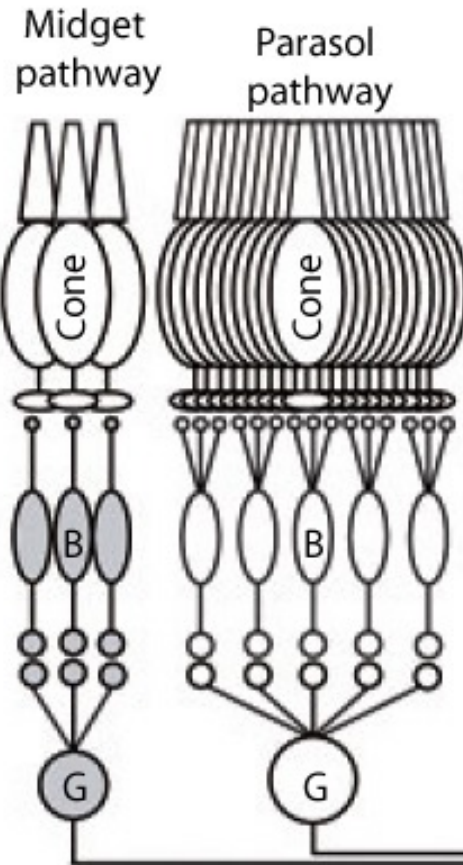
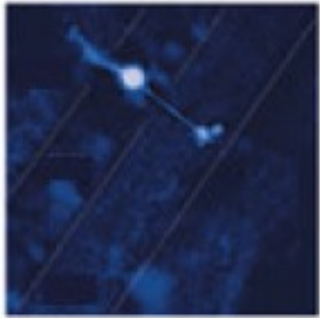


- Small cells responsible for our red/green color vision
- Comprise about 80% of our RGCs.
- High density in the fovea.
- Center-surround of opposite polarity and of opponent colors.
- The blue On/yellow Off is less dense and probably a different circuit is involved.

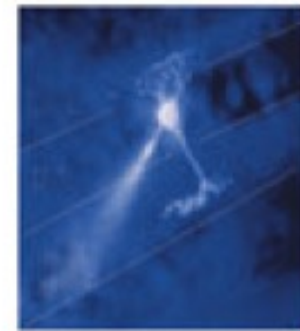
Retinal ganglion cells: midget vs. parasol cells

Convergence and acuity

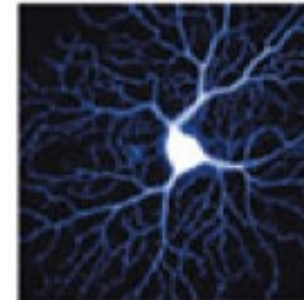
Midget Bipolar Cell



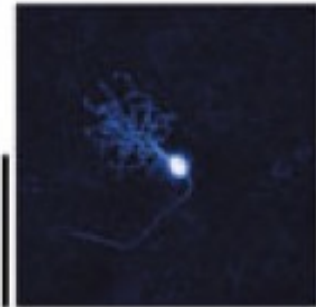
Diffuse Bipolar Cell = not selective for color



Parasol Ganglion Cell



Midget Ganglion Cell

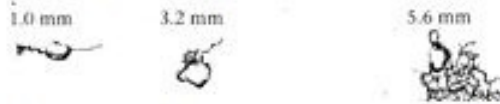


- Small dendritic arbors
- Small receptive fields
- ~80% of ganglion cell
- chromatic
- Form and color
- Fine details

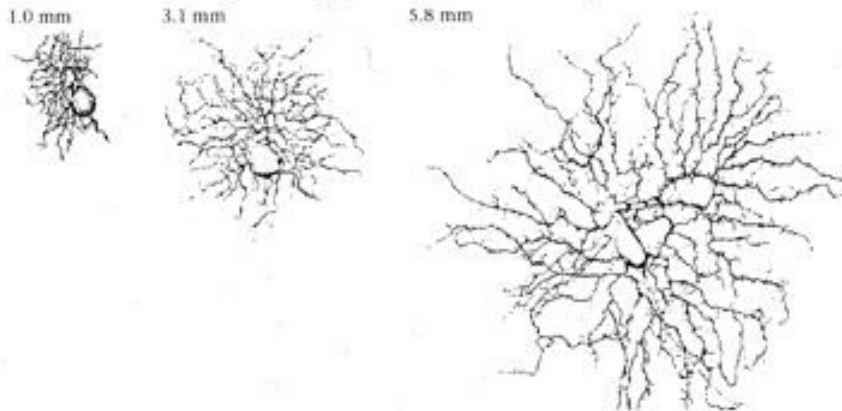
- Large dendritic arbors
- Large receptive fields
- ~10% of ganglion cells
- Non-chromatic
- Gross features of stimulus
- movement

Magno and Parvo pathways

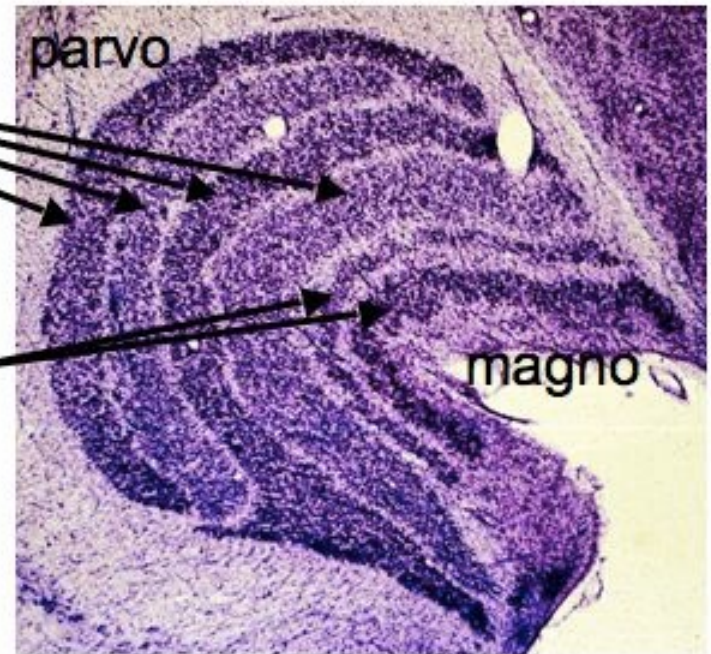
Midget (parvocellular)



Parasol (magnocellular)



Retina

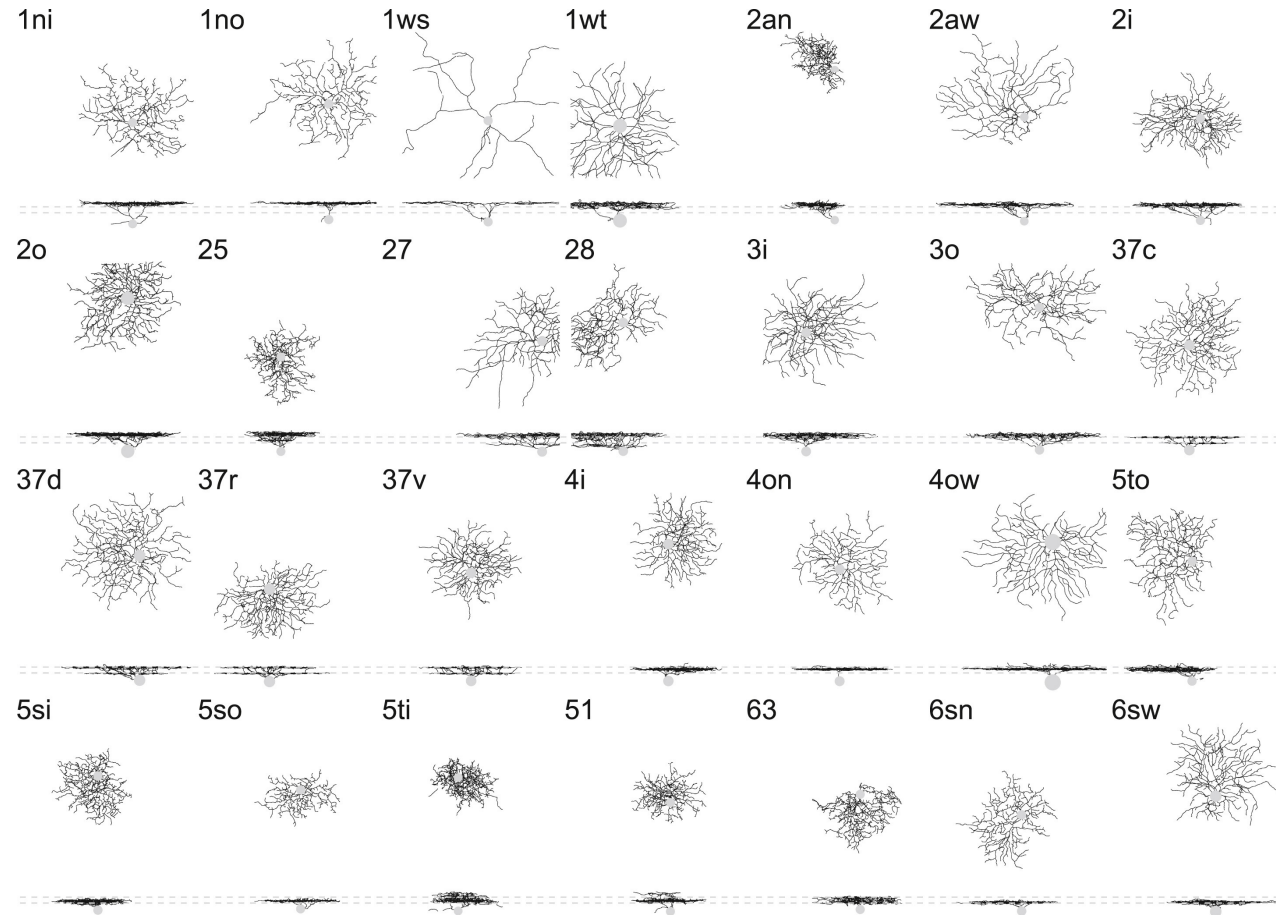


LGN

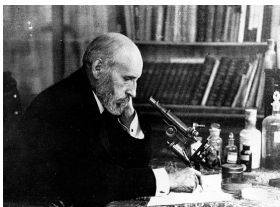
Retinal ganglion cells

What defines a neuron subtype in the retina?

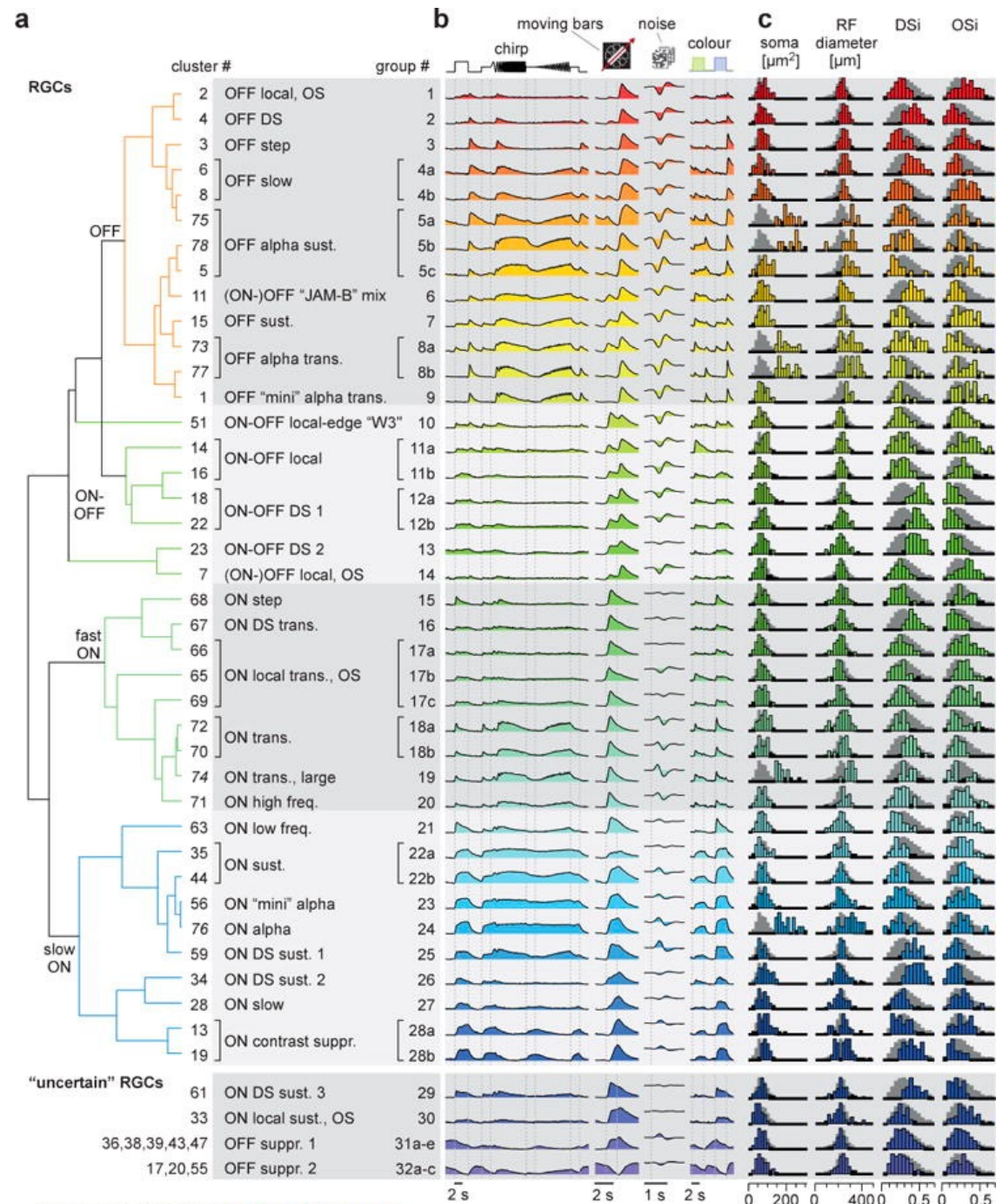
- Morphology (including input & output)
- Physiology (=light responses)
- Form mosaic/tile the retina



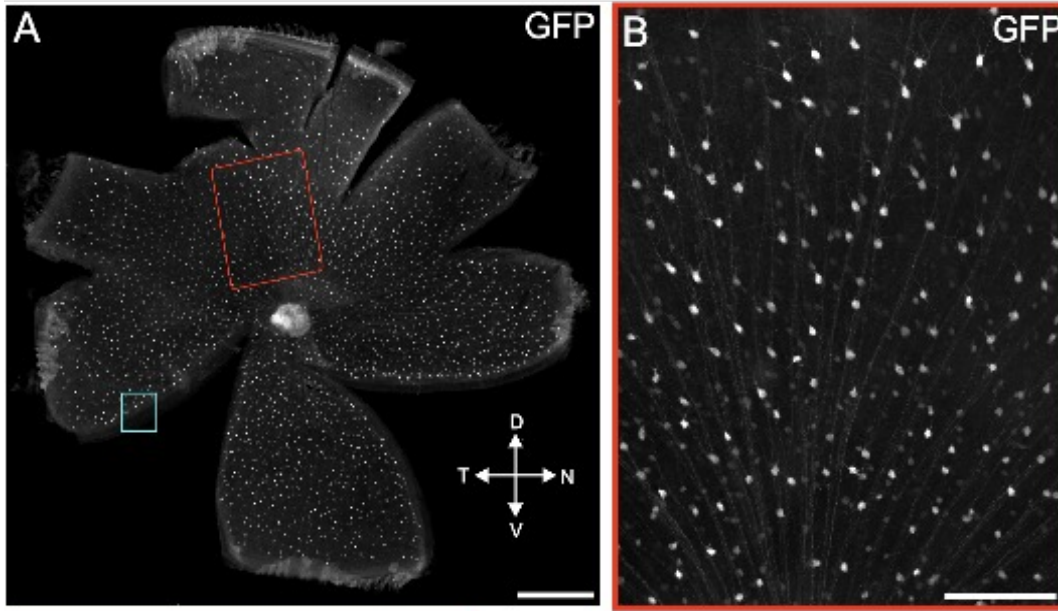
Bae et al., 2018 (*Cell*)



>30 different subtypes of retinal ganglion cells (RGCs)

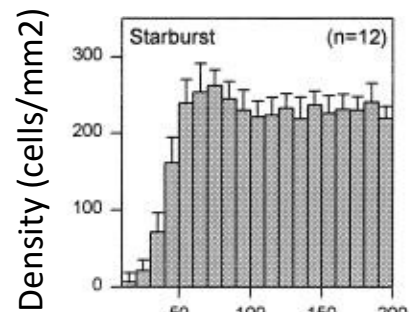


Mosaic organization

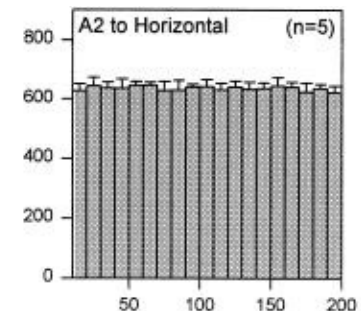


- Cover the entire visual field
- Exclusion zone for same cell type

Spacing within types

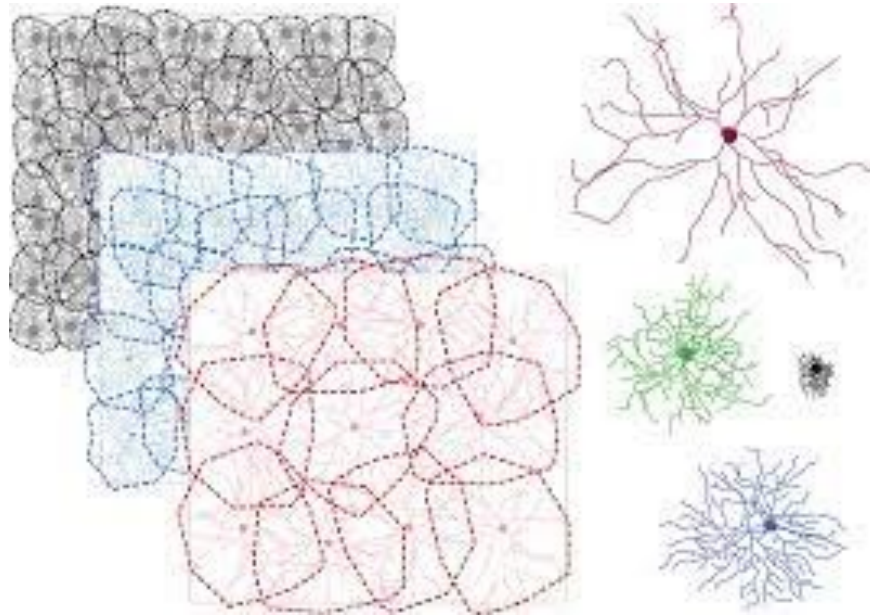


Spacing between types



Distance from reference cell

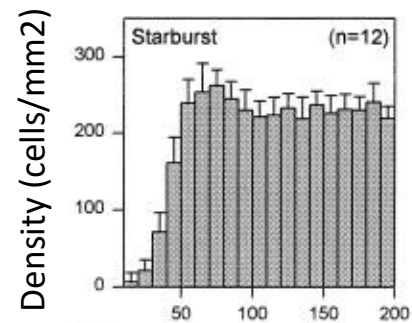
Mosaic organization



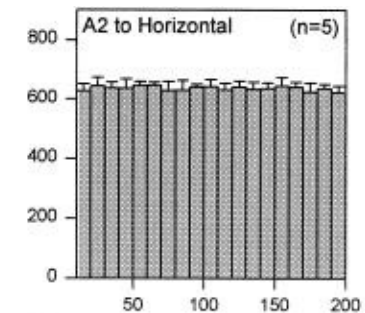
Dhande et al., 2015

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

Spacing within types

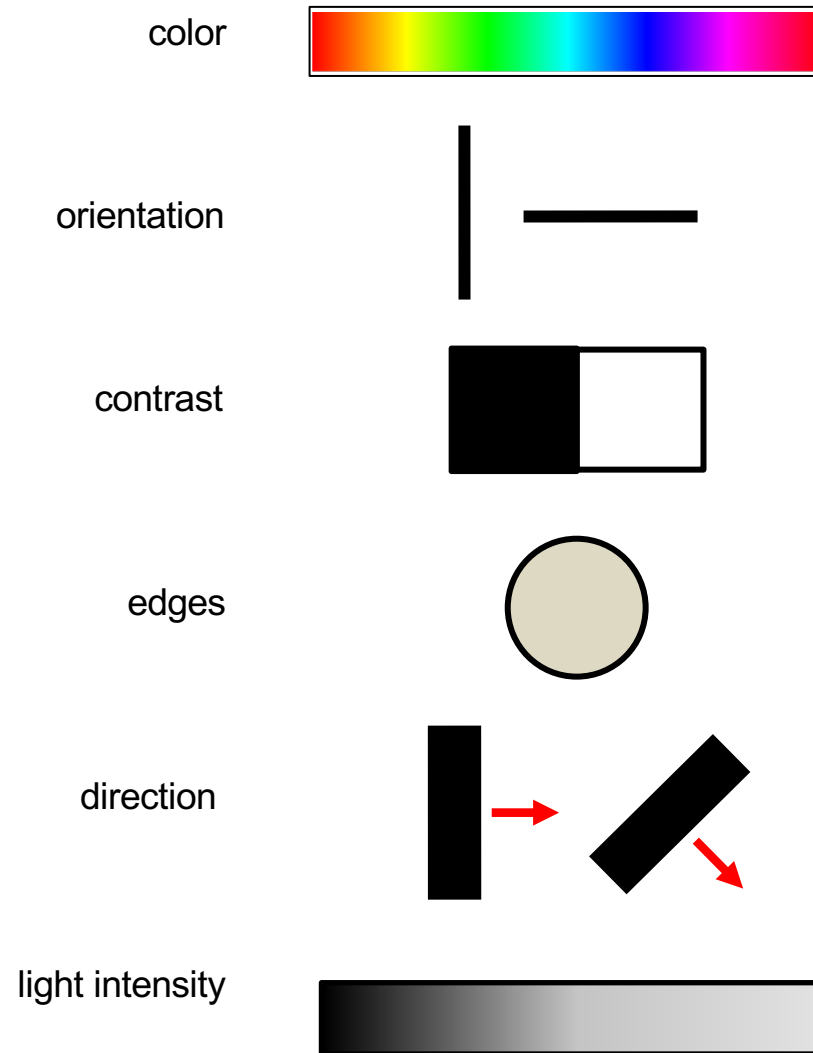


Spacing between types

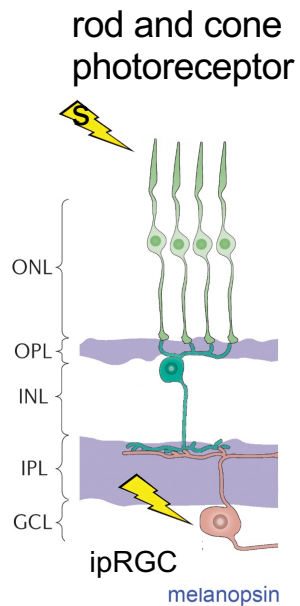


Distance from reference cell

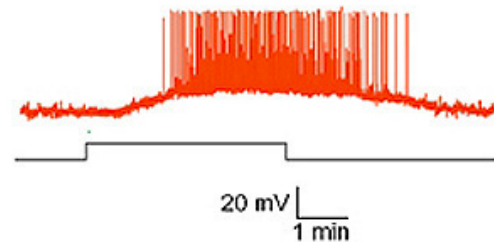
Diversity of ganglion cell receptive fields



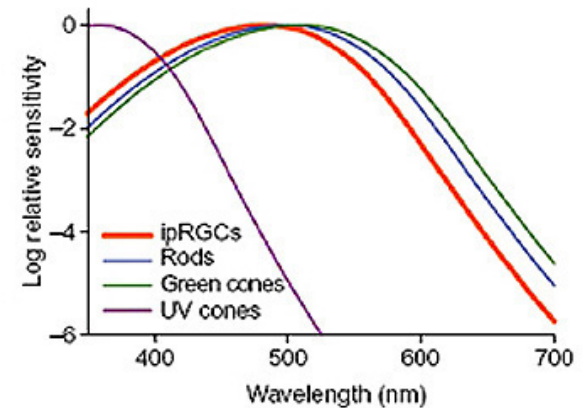
Intrinsically photosensitive retinal ganglion cells (ipRGCs)



a

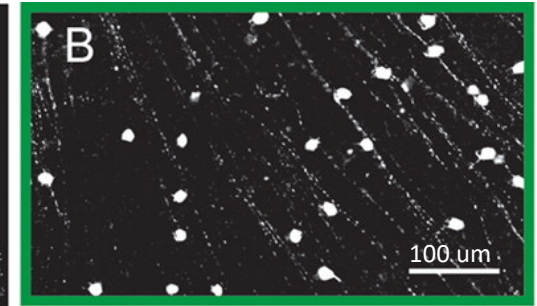
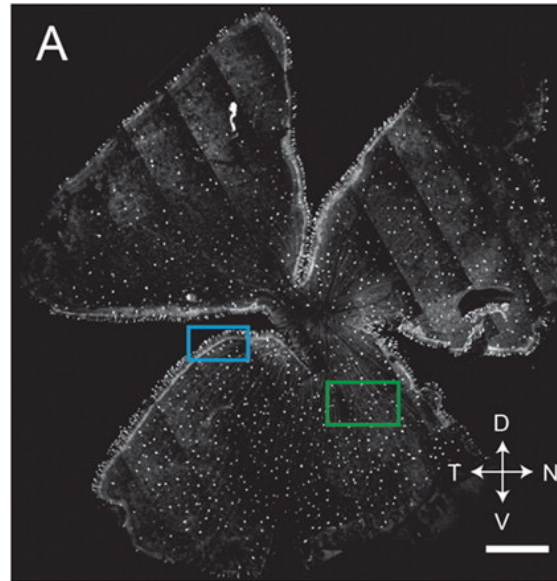
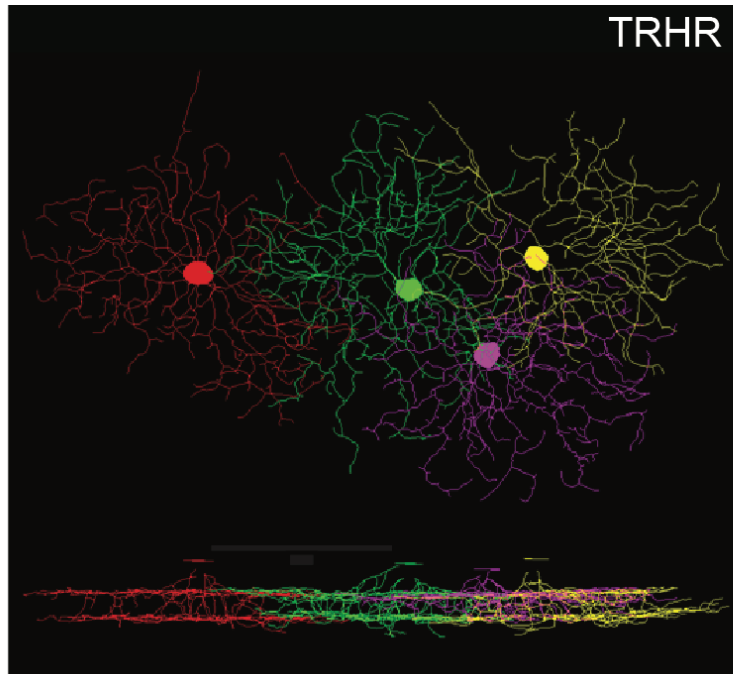


b

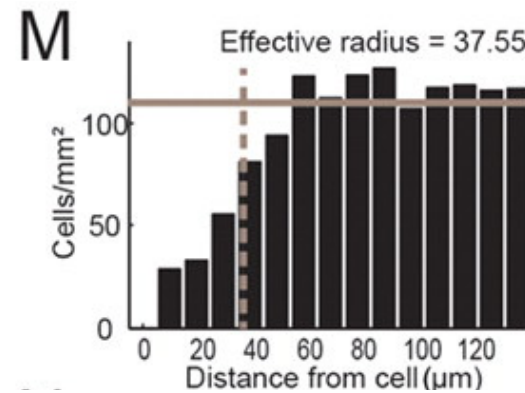


Adapted from Berson et al. 2003

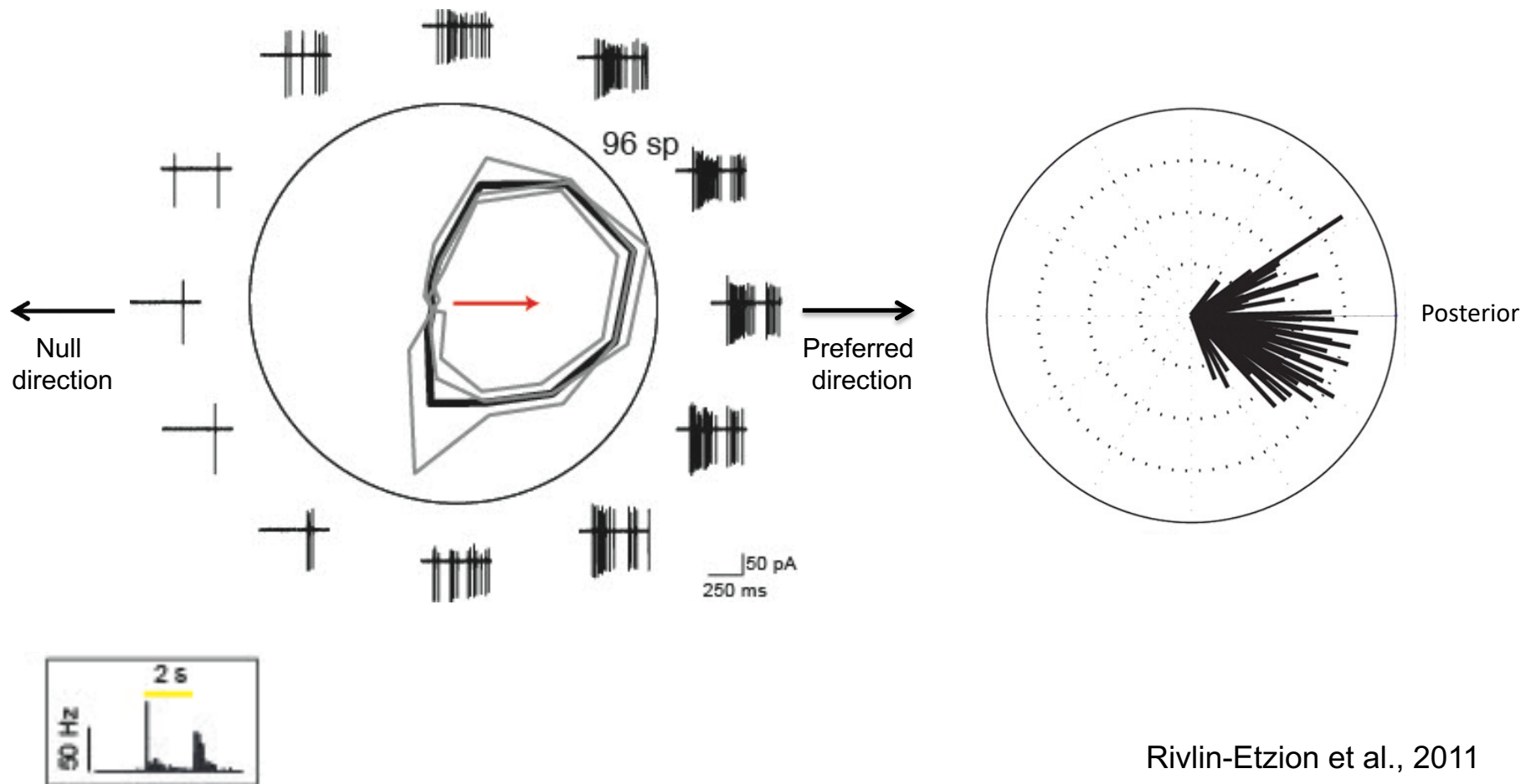
Two-photon targeted recordings from transgenic mouse lines



TRHR mouse line



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

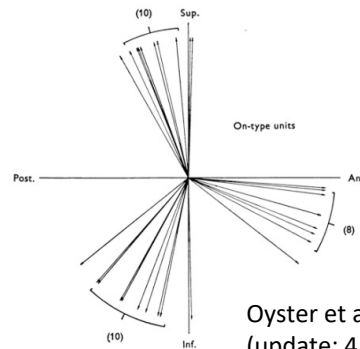


Direction selective retinal ganglion cell (DSGC) subtypes

Type

Function

On DS cells

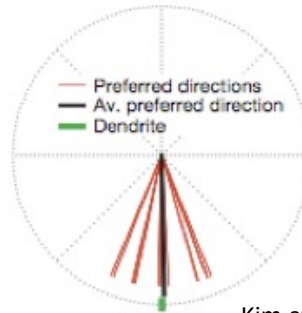


Oyster et al 1968

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

Optokinetic
reflex

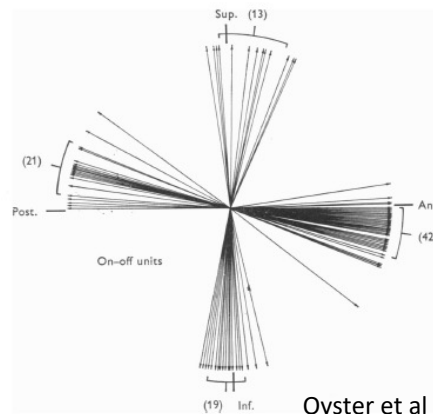
Off DS cells



Kim et al 2008

?

On-Off DS cells



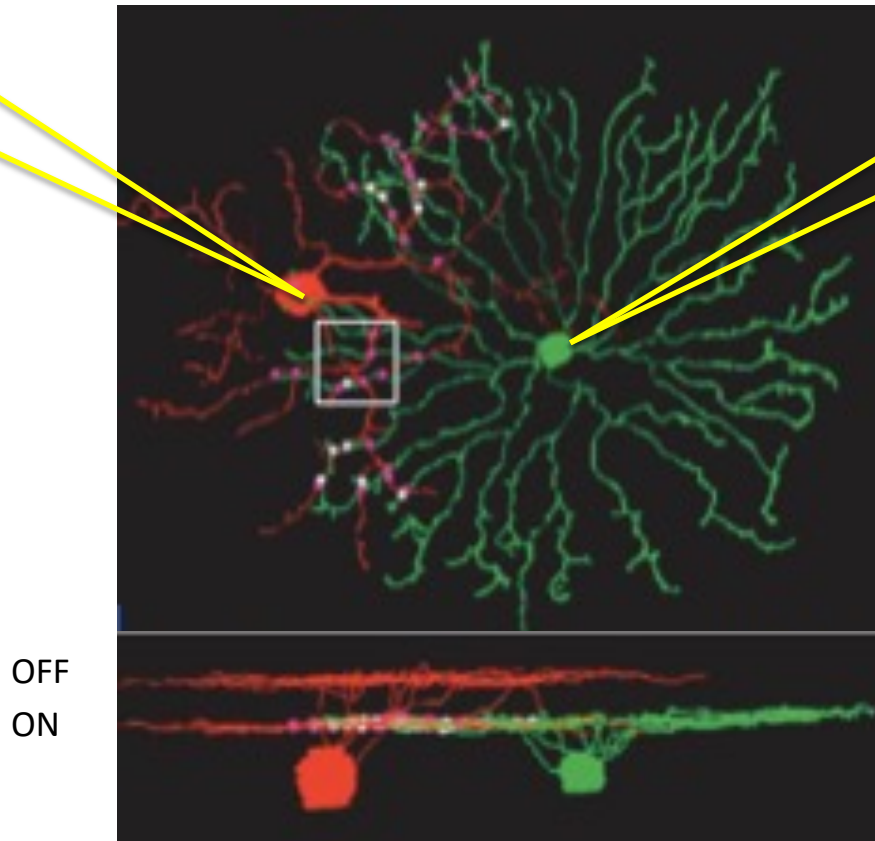
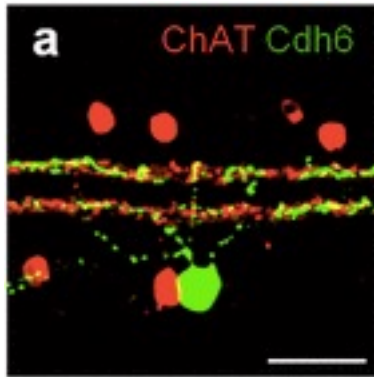
Oyster et al 1968

?

Starburst amacrine cells co-stratify with direction selective retinal ganglion cells

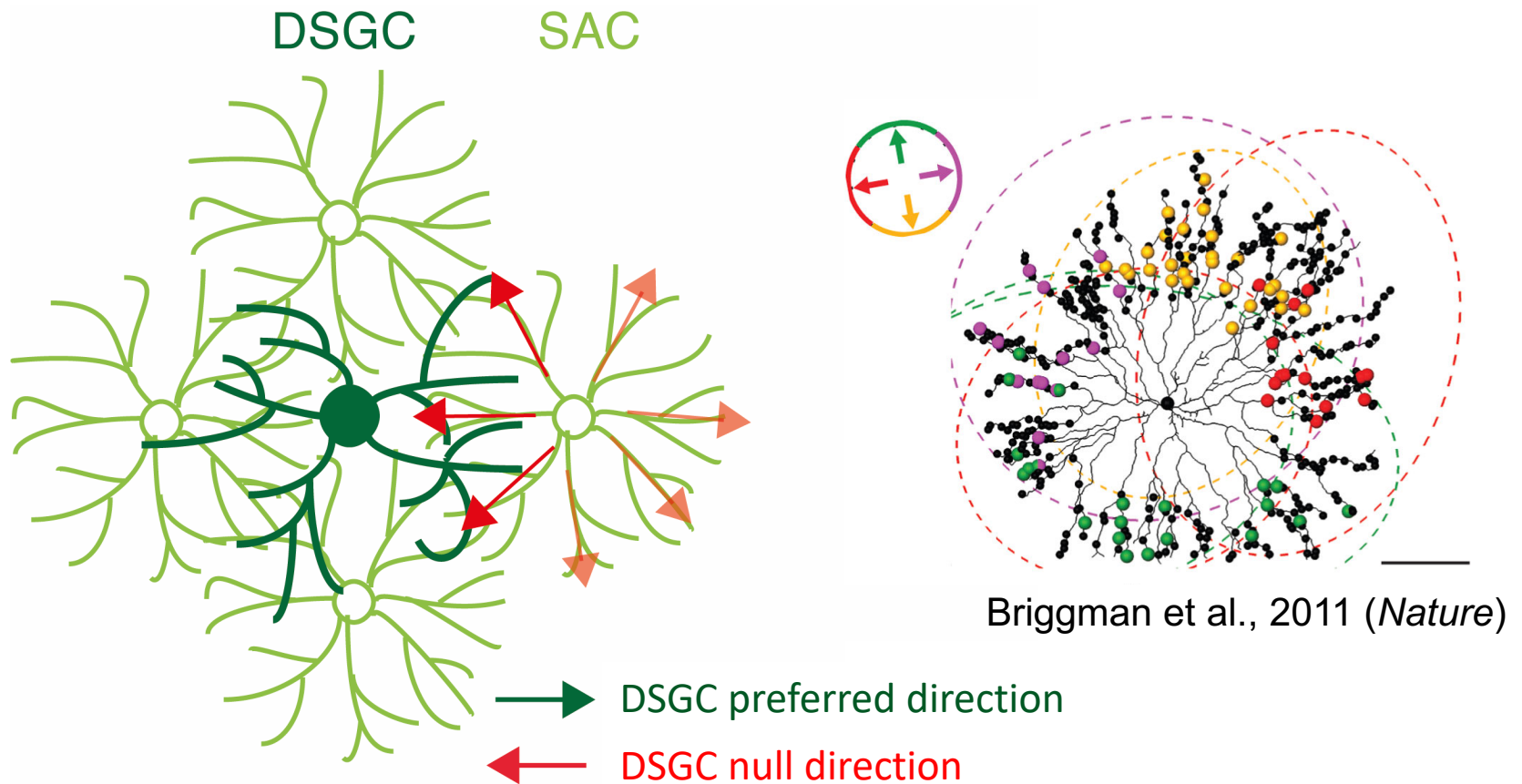
Direction selective
ganglion cell

ON starburst
Amacrine cell

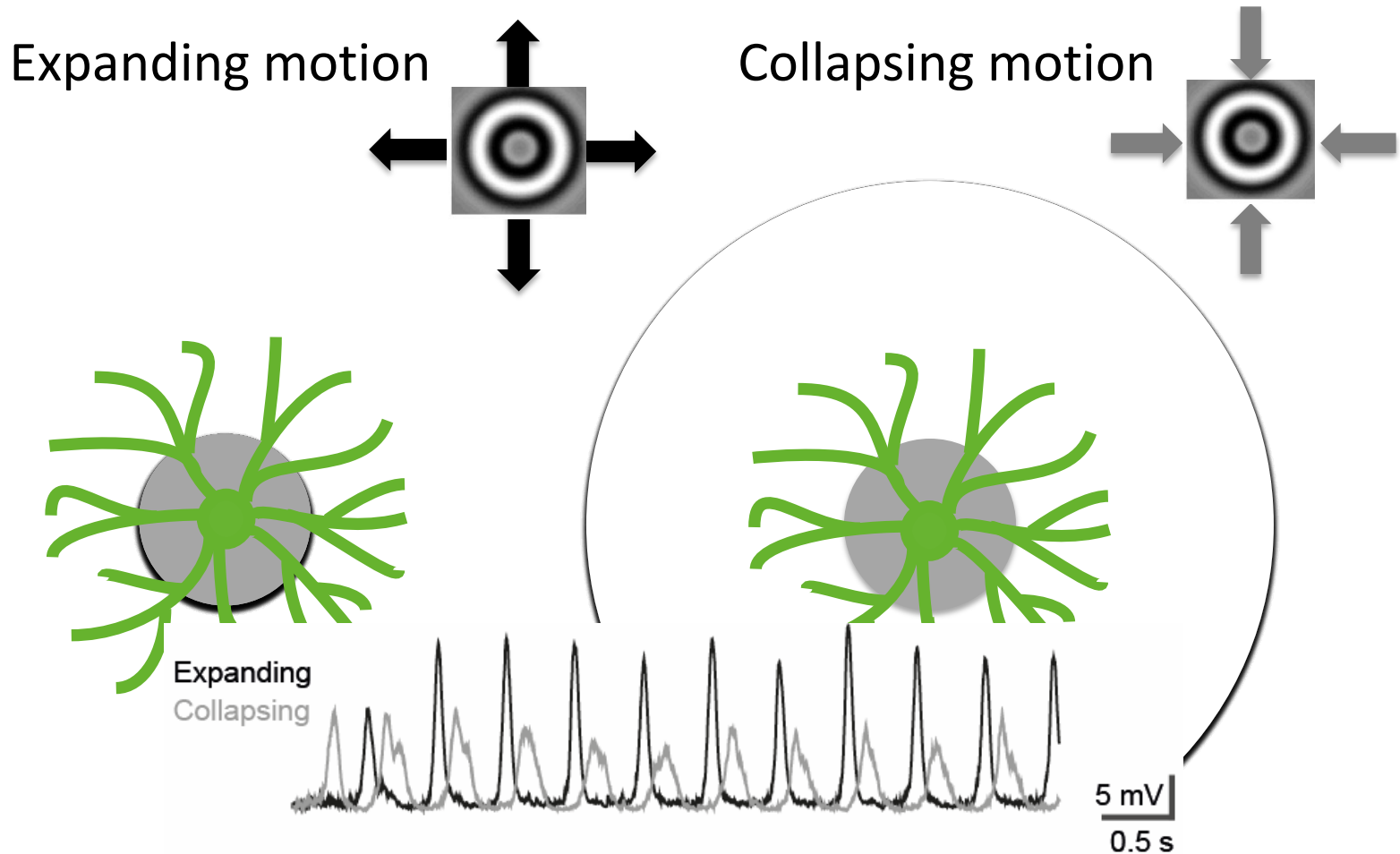


Wei et al., 2011 (*Nature*)

Directional responses are mediated by asymmetric inhibition from starburst amacrine cells



SAC processes prefer centrifugal motion

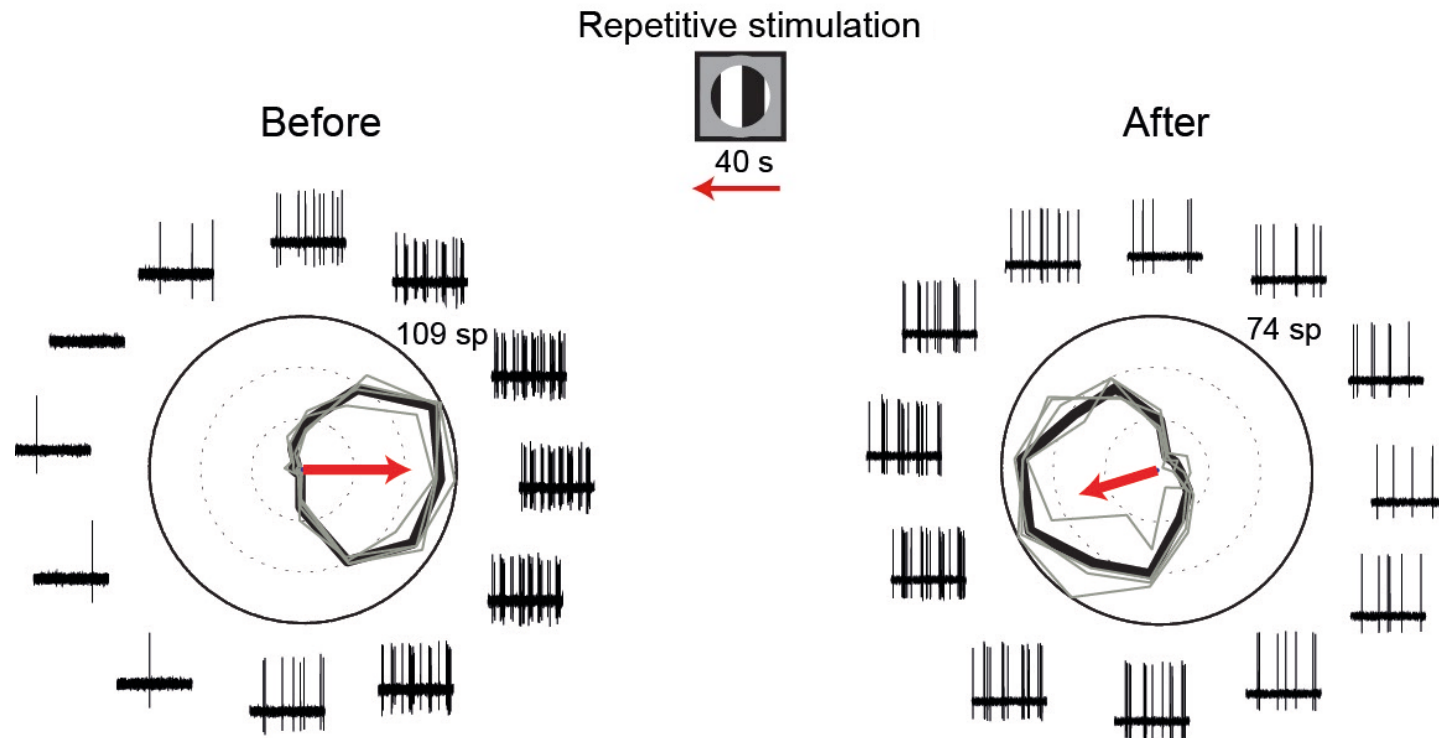


Lea Ankri

Ankri et al., Cell Reports 2020

Retinal neurons can change the modality they encode

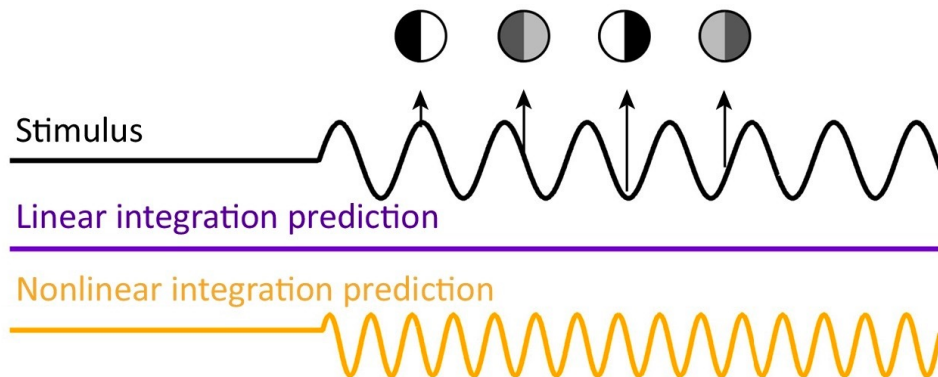
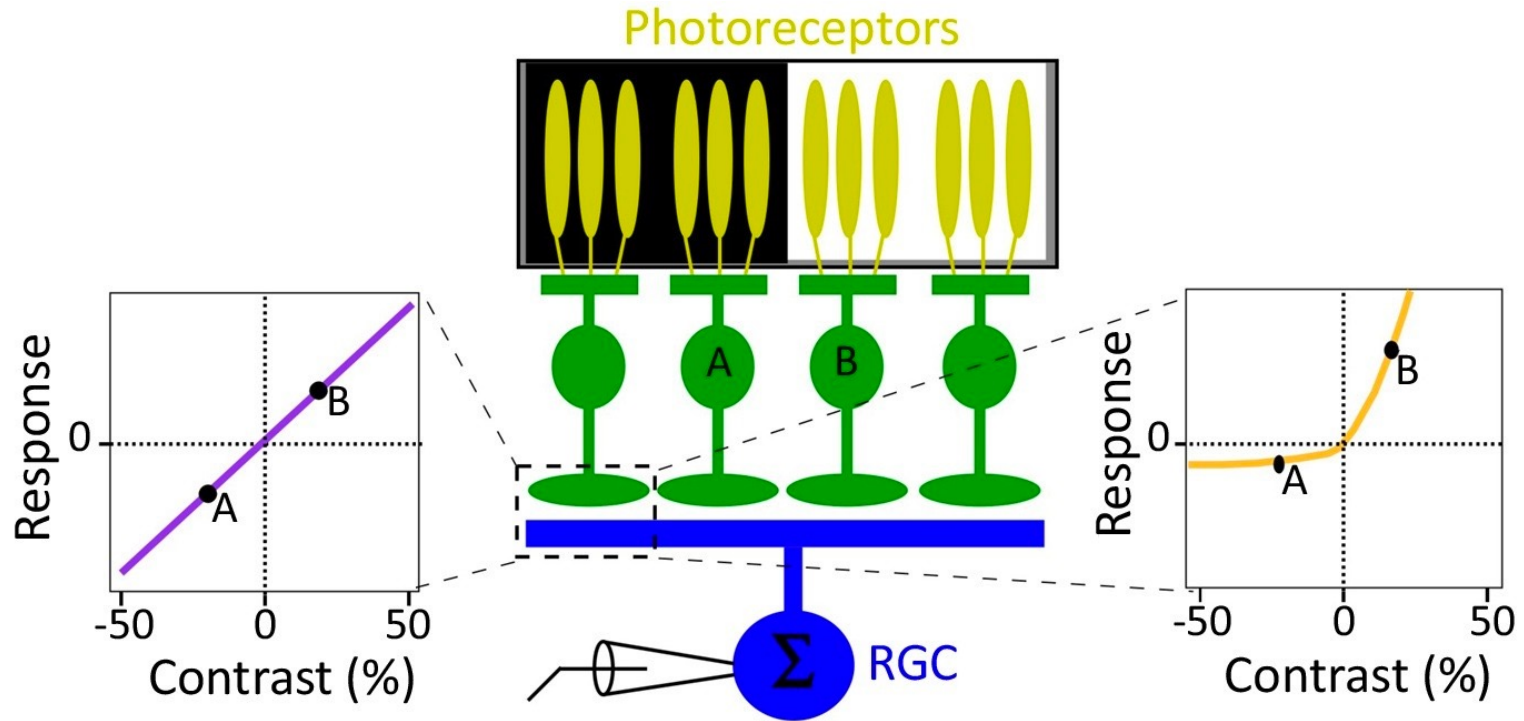
Direction selective retinal ganglion cell (DSGC)



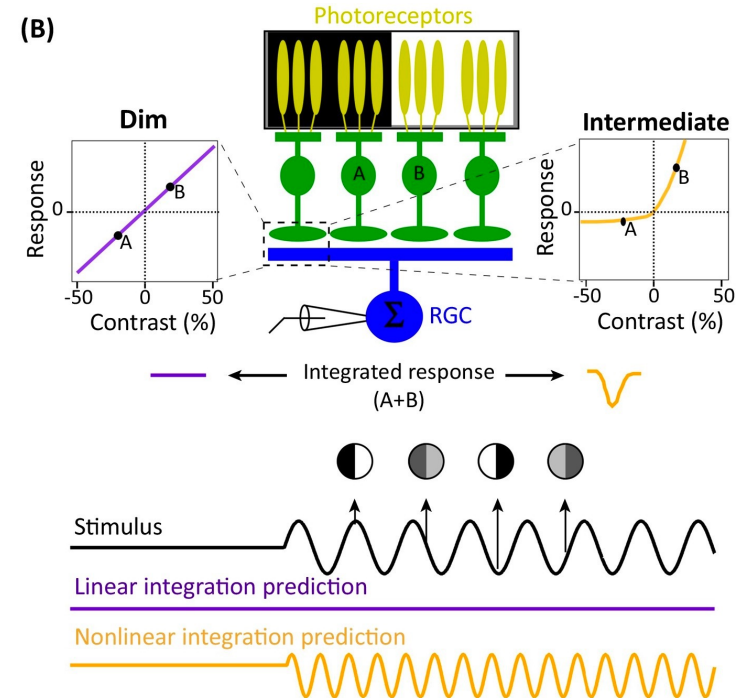
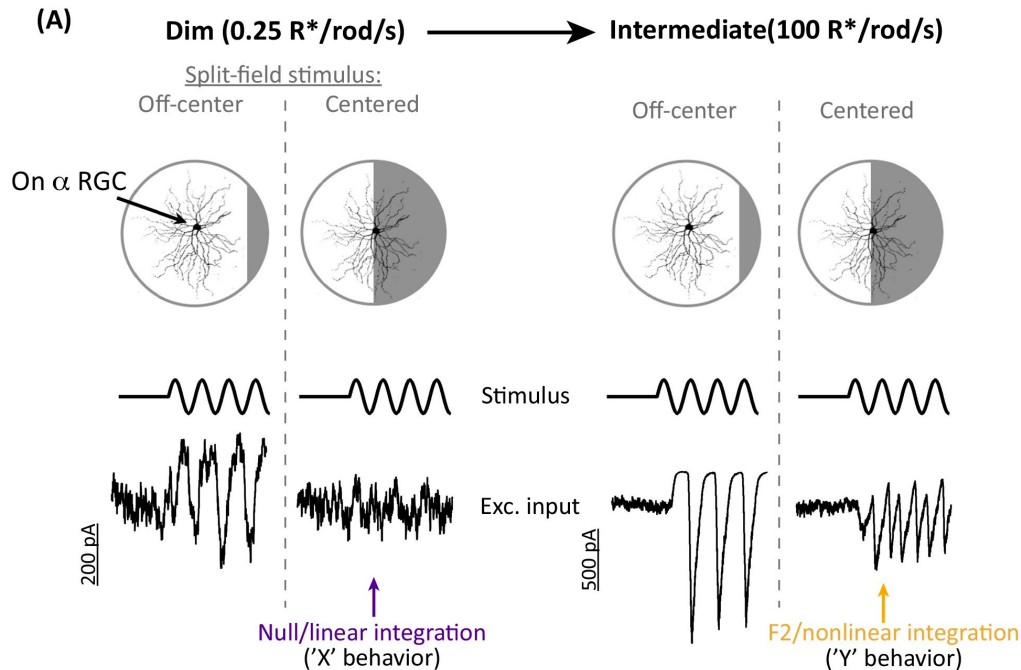
Rivlin-Etzion et al., 2012, 2014

Ankri et al., 2020, 2024

Spatial integration properties of On Alpha RGCs depend on mean luminance

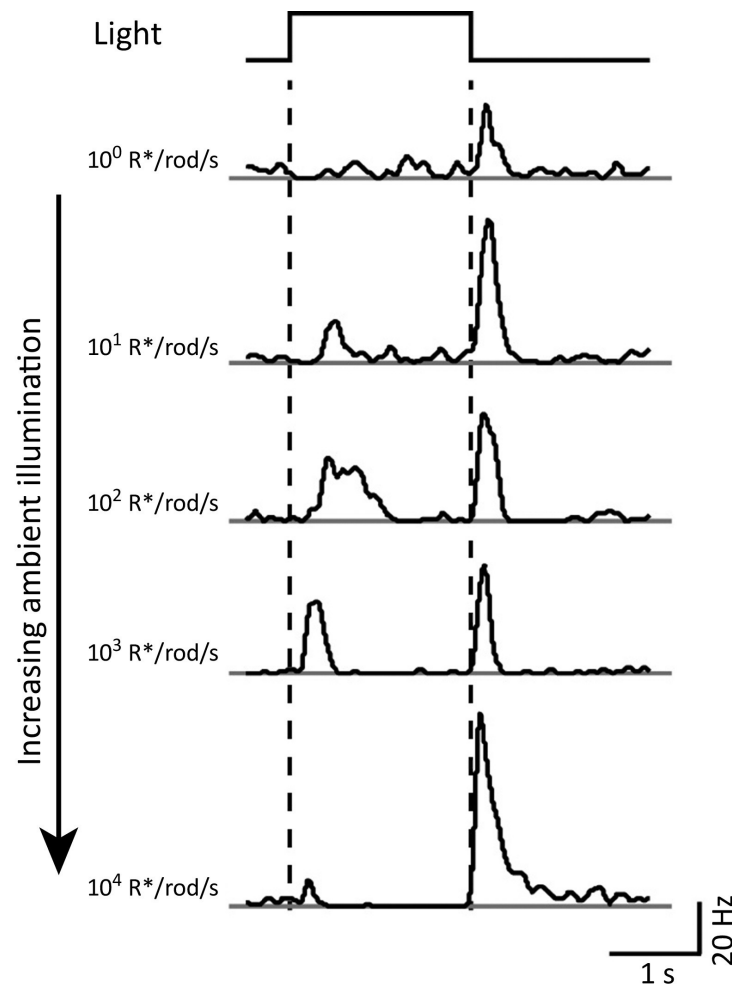


Spatial integration properties of On Alpha RGCs depend on mean luminance



Trends in Neurosciences

RGCs change polarity preference with mean light level



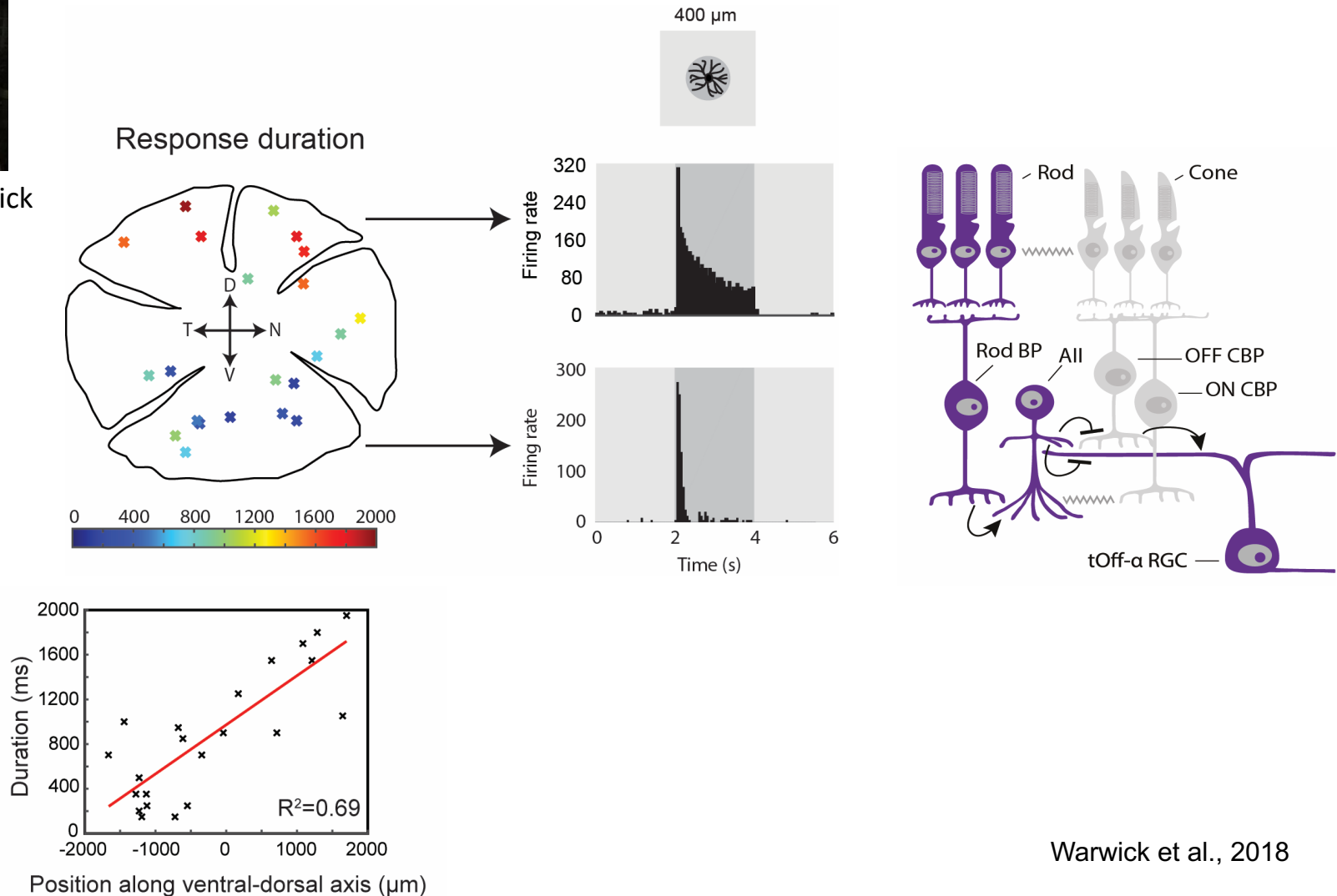
Each subtype of retinal ganglion cell encodes
a specific visual property;
Each visual property is represented in the entire visual field



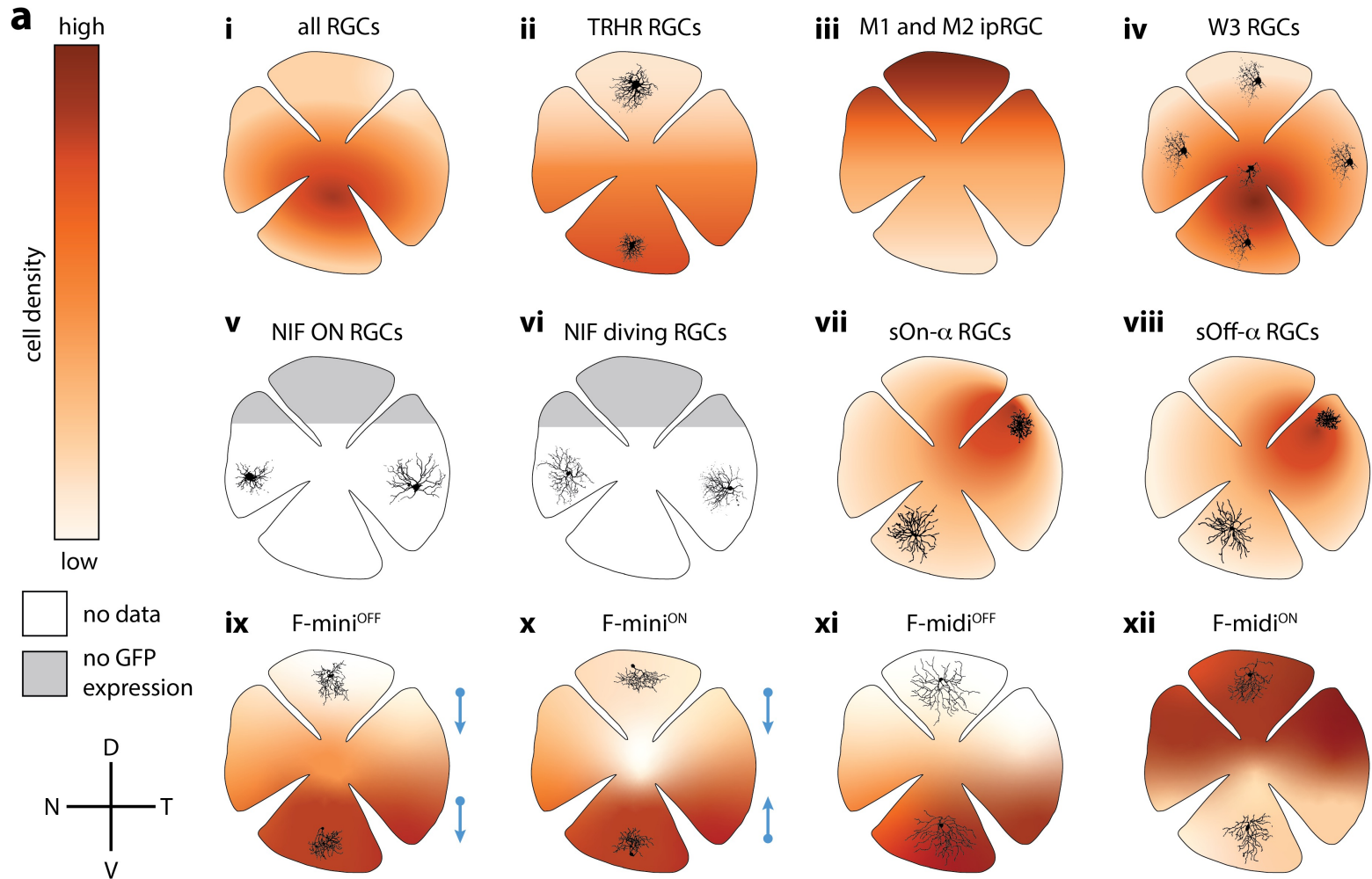
Visual responses of transient-Off- α RGCs gradually change along the dorsal-ventral axis



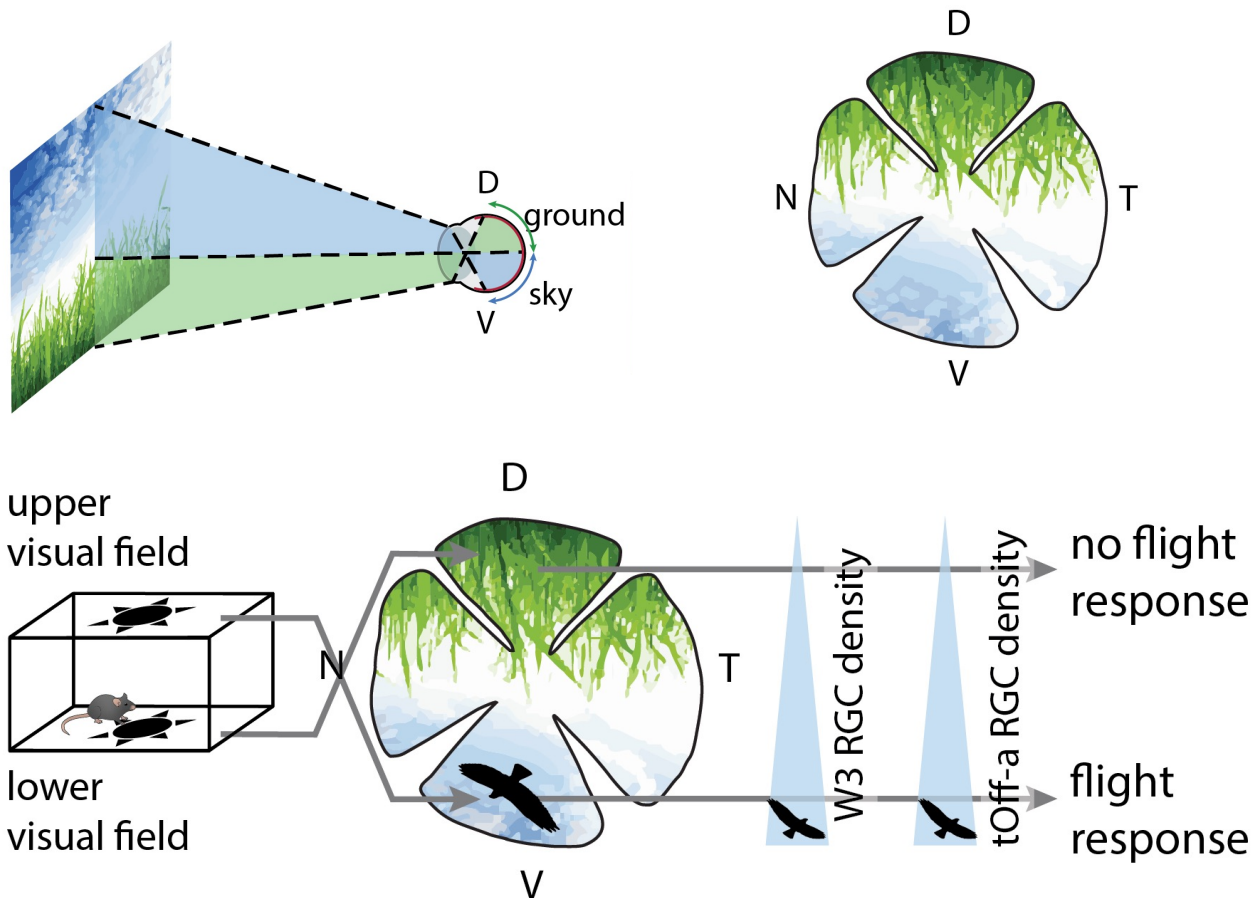
Rebekah Warwick



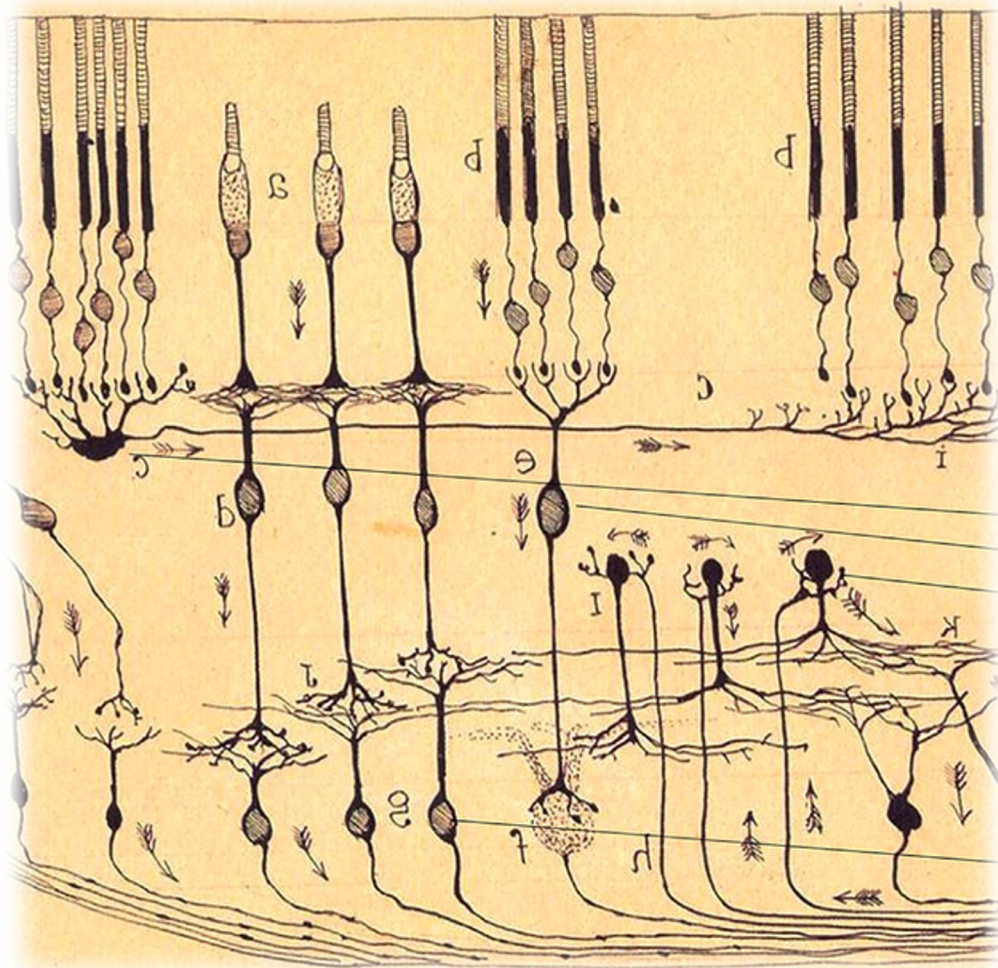
Topographic Variations in Mouse Retinal Ganglion Cells



Functional Requirements of different retinal areas

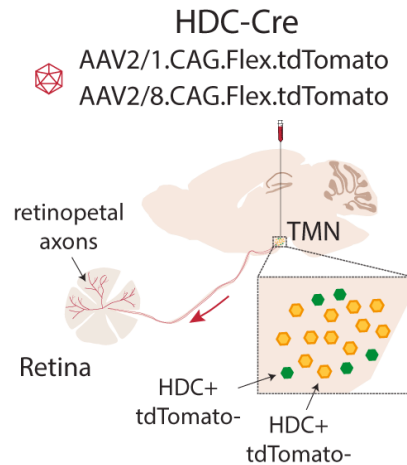


Can the brain affect visual processing in the retina?

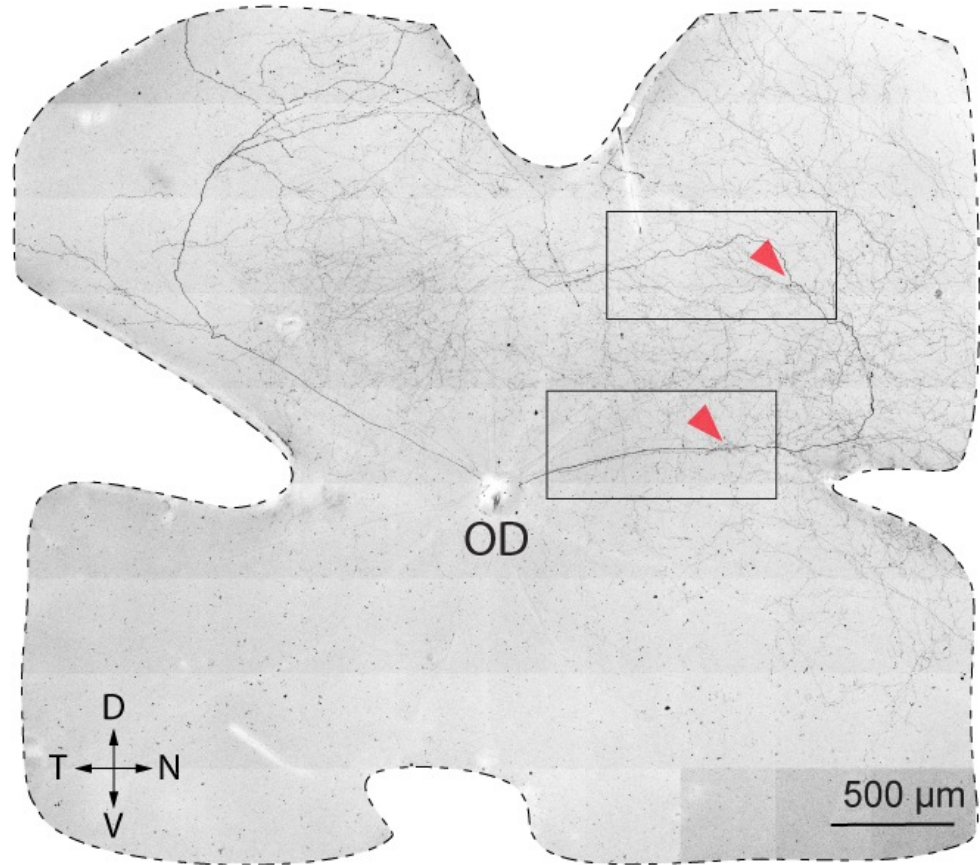


Ramon y Cajal, 1891

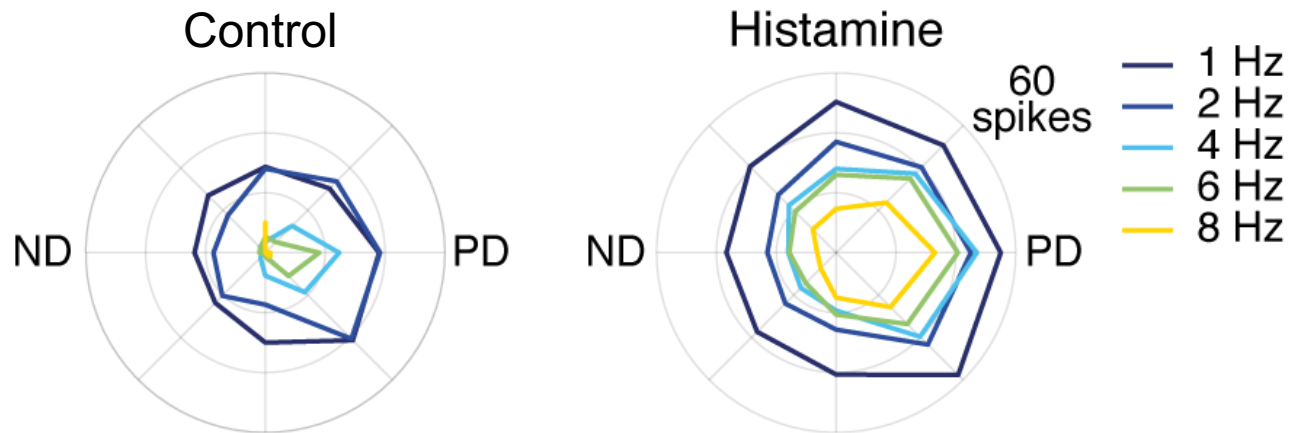
Top-down modulation of the retinal code via histaminergic neurons of the hypothalamus



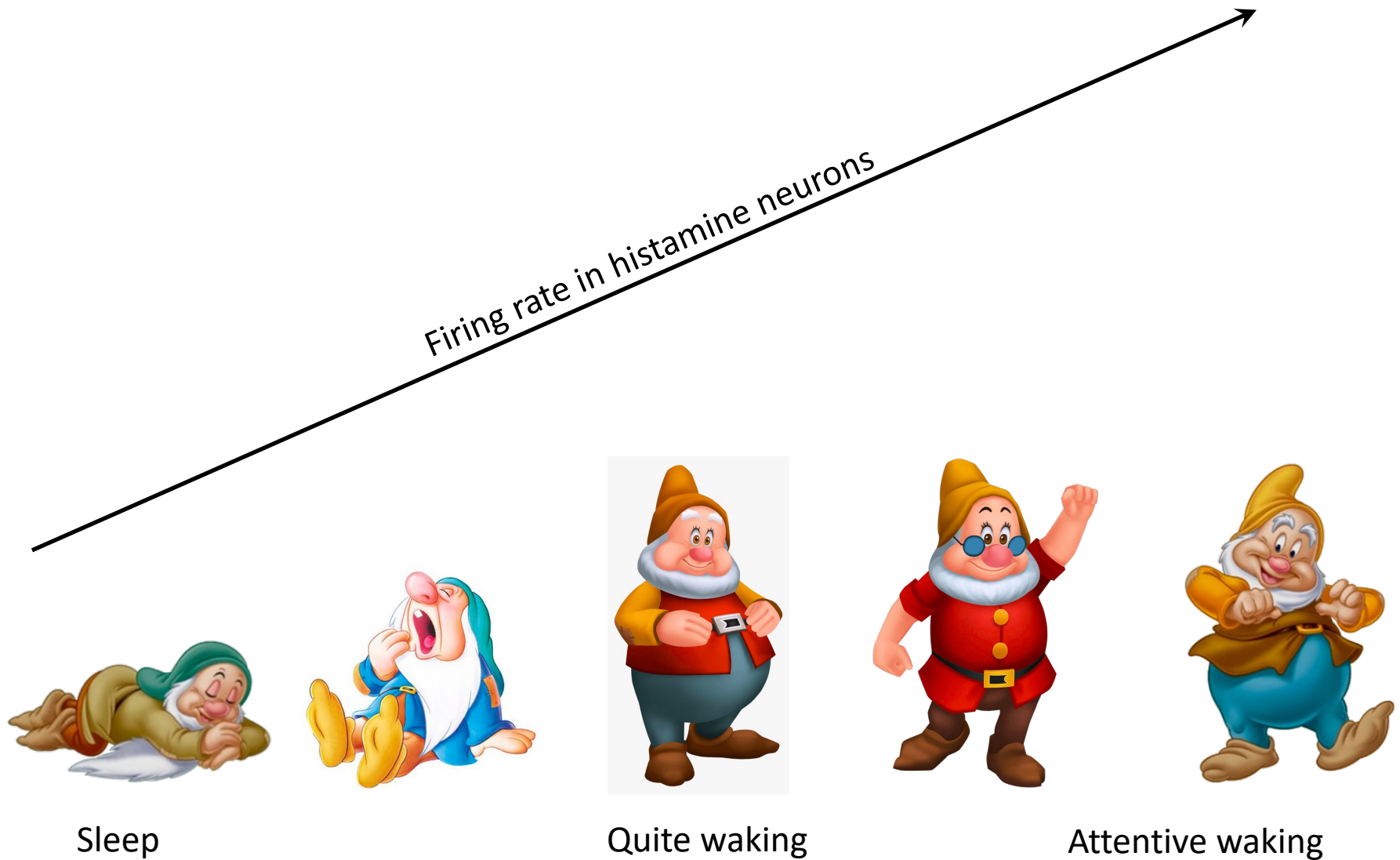
Retinopetal histaminergic projections in mouse



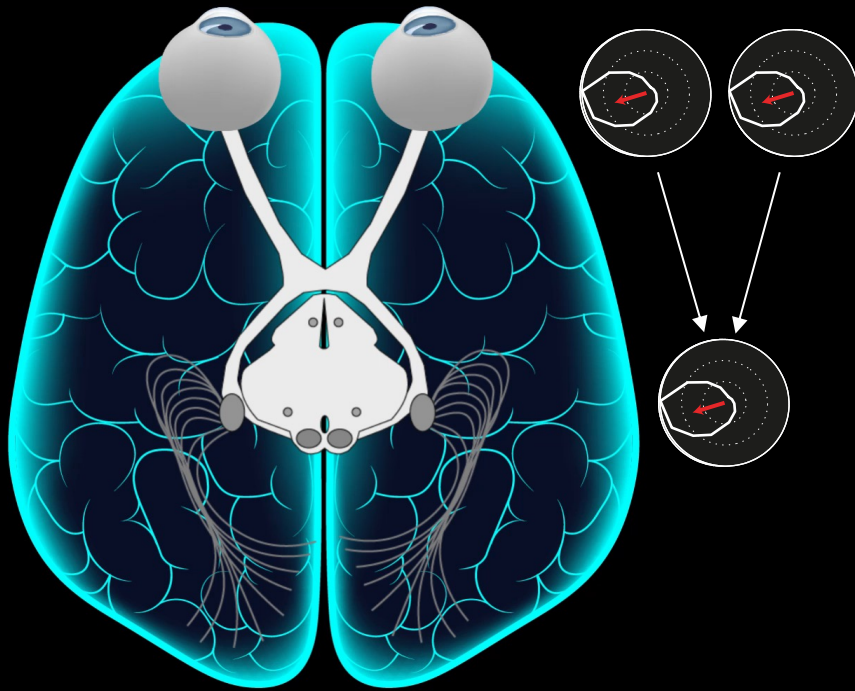
Histamine enhances responses of DSGCs to high velocity stimuli



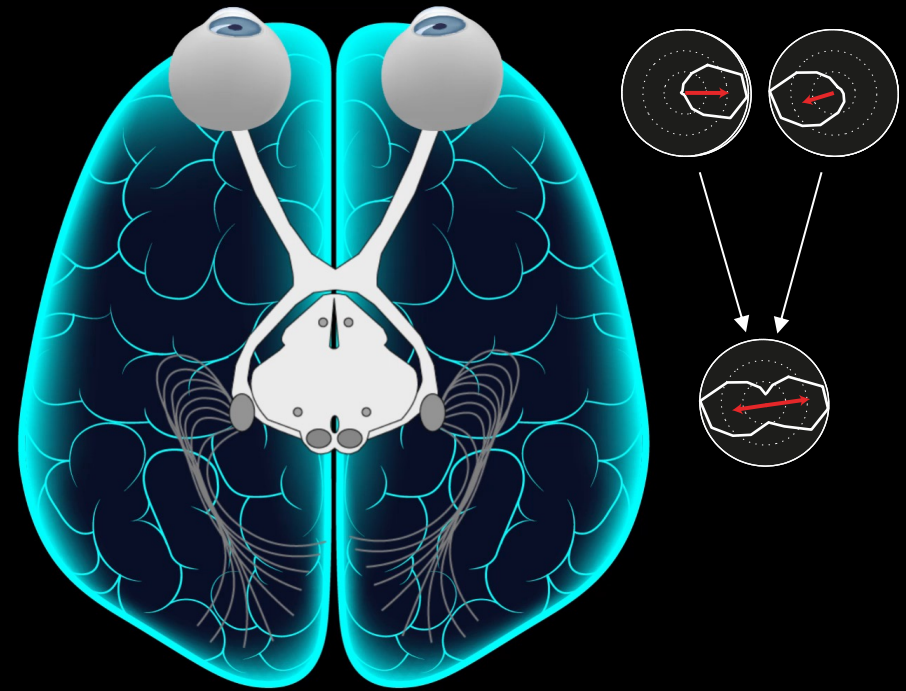
The histaminergic system: “wake-on, sleep-off”



Resolve the transfer function from the retina to the visual thalamus and beyond



Textbook:
relay station



New hypothesis:
convergence station

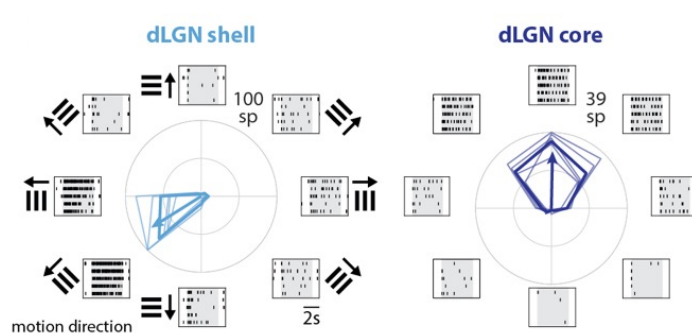
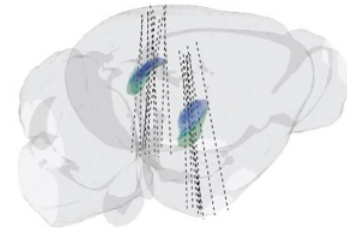
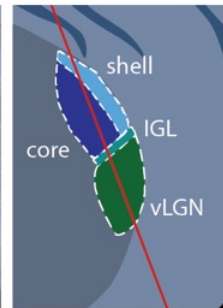
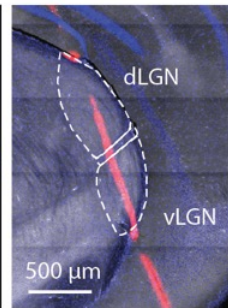
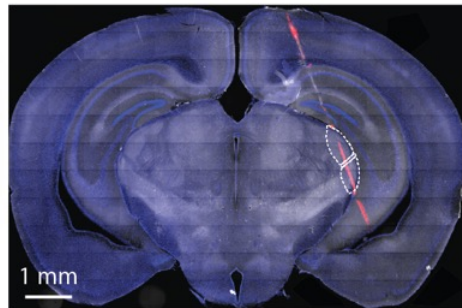
Resolve the transfer function from the retina to the visual thalamus and beyond



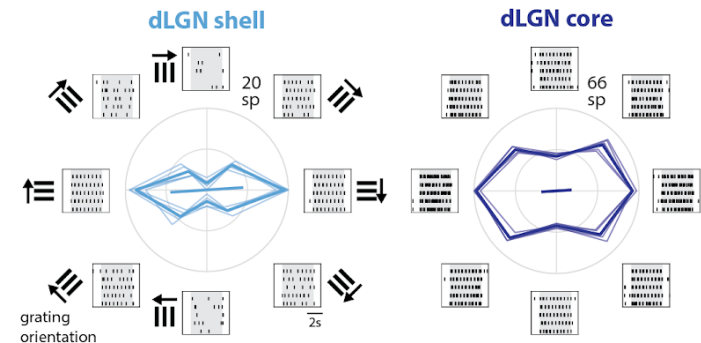
Hadar Yaakov



Alina Heukamp

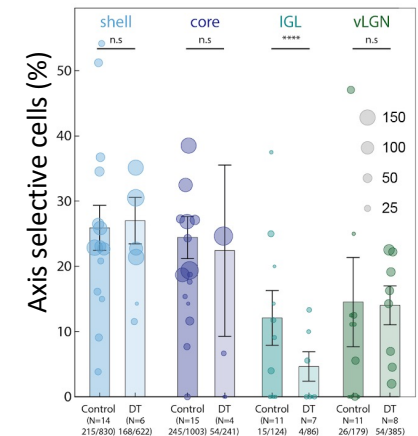
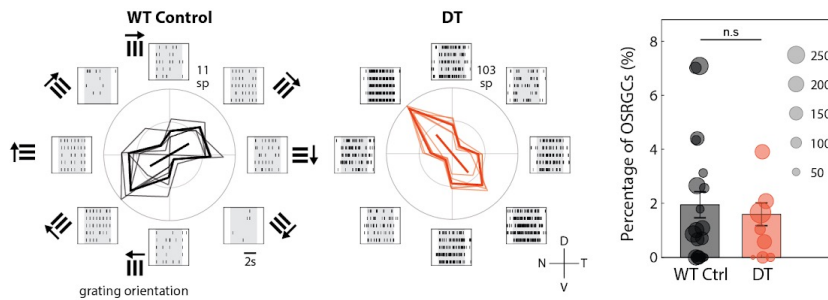
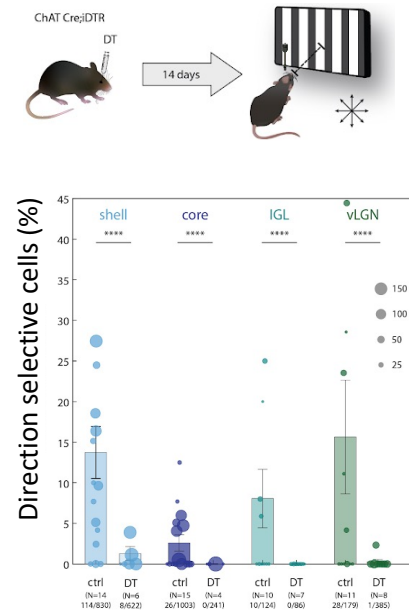
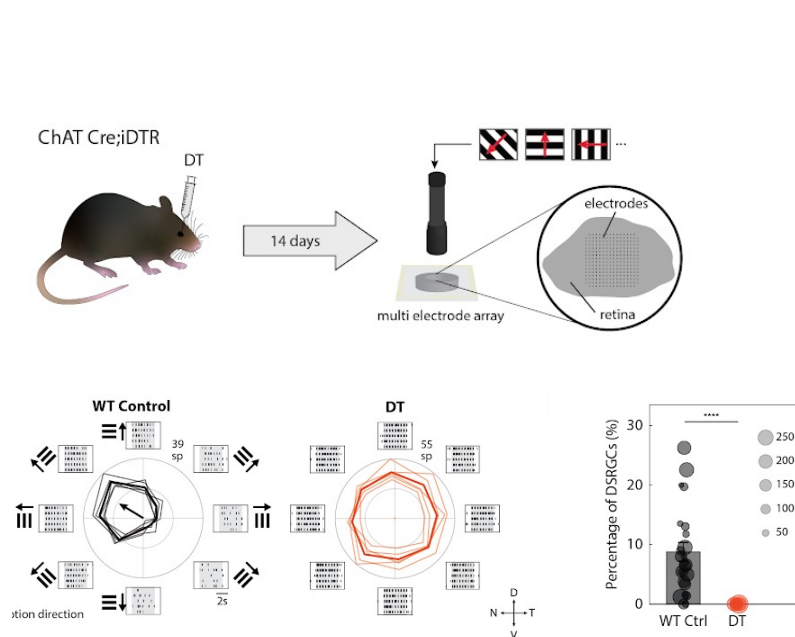


Direction selective cells

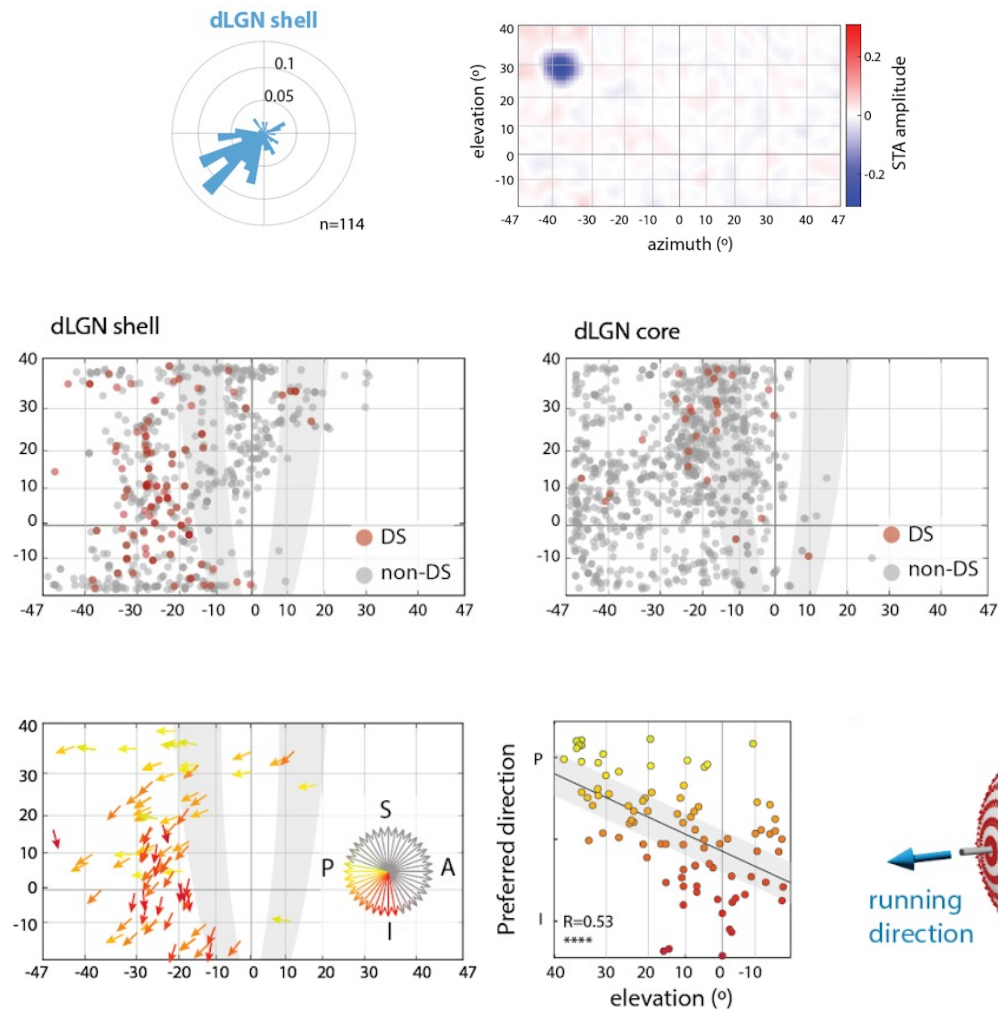


Axis selective cells

DS, but not AS responses in the LGN depend on retinal DS



Direction-selective responses in the dLGN are topography dependent, representing optic flow dynamics





Thank you!

