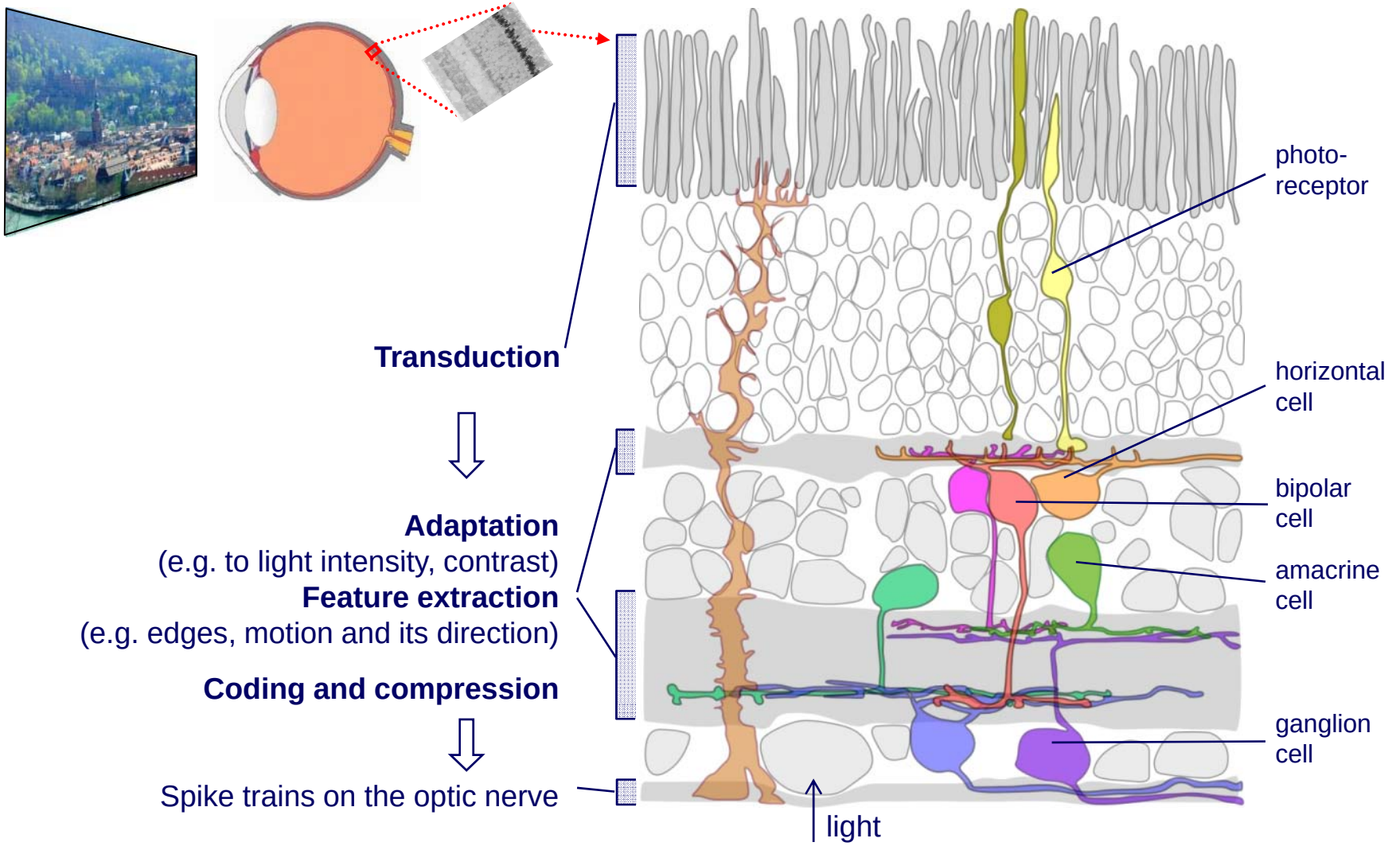
Outline

- Why having a retina in the first place?
- Retina structure; main cell classes and their basic properties
- Morphological variety in retinal cell types
- Synapses in the outer plexiform layer (OPL)
- Horizontal cells
  - Feed-back and feed-forward pathways/mechanisms
- Bipolar cells
  - ON/OFF pathways and their molecular basis
  - Rod pathway
  - Modulation of bipolar cell signals
  - Chromatic pathways
- Synapses in the inner plexiform layer (IPL)
- Amacrine cells
  - Narrow field vs. wide-field
  - Distinct functional roles for different types?
- Ganglion cells

The retina is a sophisticated image processor



Transduction

⇩

Adaptation
(e.g. to light intensity, contrast)
Feature extraction
(e.g. edges, motion and its direction)

Coding and compression

⇩

Spike trains on the optic nerve

Some facts about the (human) retina

~ 0.2 g of nervous tissue, 100-200 µm thick, somewhat larger than a 2 € coin

Analog image processor with ~ 70 different types of neurons

125 million photoreceptors (rods & cones)

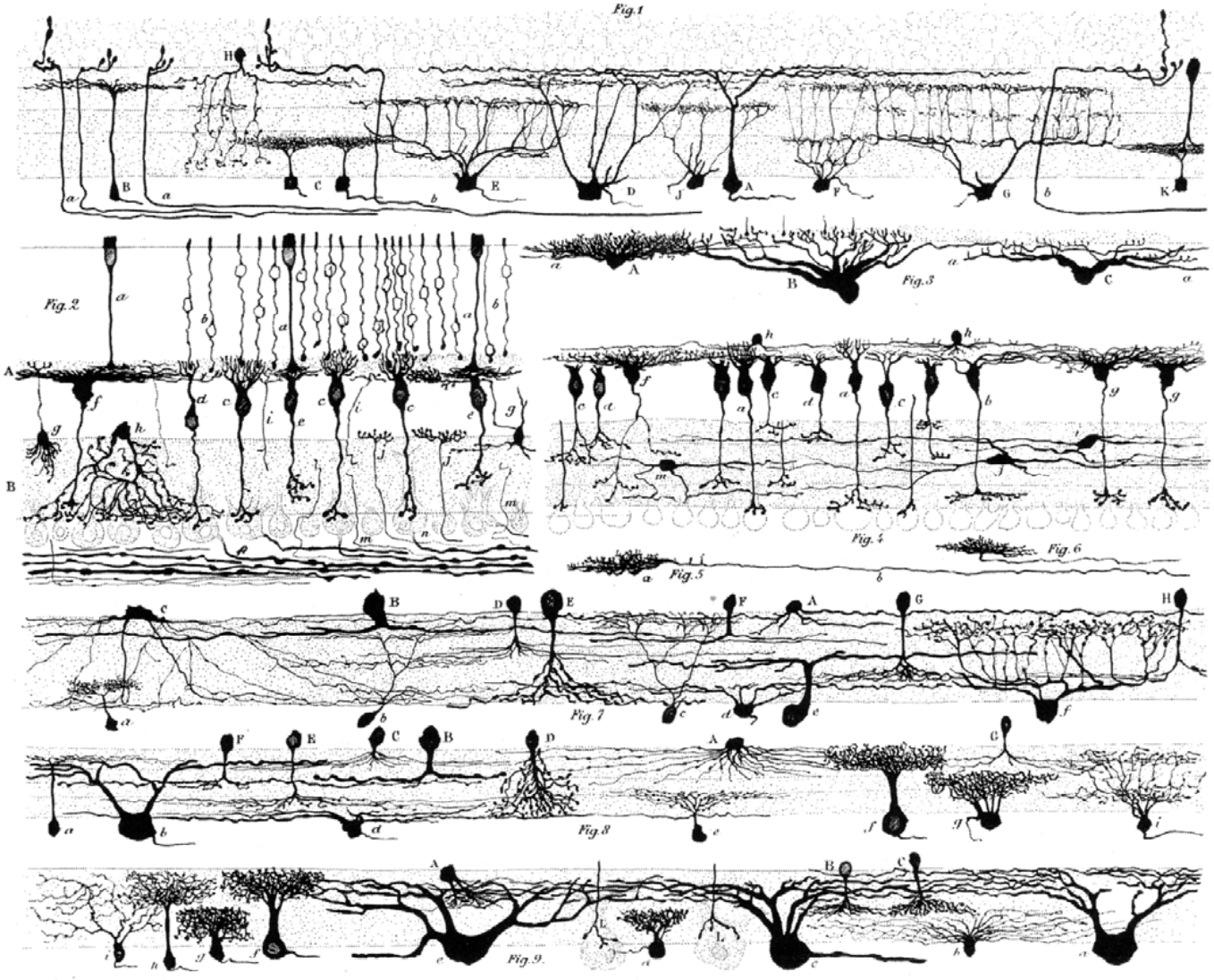
1.3 million fibers (optic nerve)
(Analysis of the information occupies app. 50% of the cerebral cortex)

Intensity range covered 10^6
Responds to contrasts as low as 1%
Integration time ~ 100 ms (cones)

daylight: > 100 photons /cone /100 ms needed
(graded signals)

starlight: 200 ms integration time
very low noise: 1 photoisomerization /10,000 rods /200ms
50fold higher gains than cones
('binary' signals)
=> single photons are detected and signaled

Diversity of cell types in the retina



Golgi's method

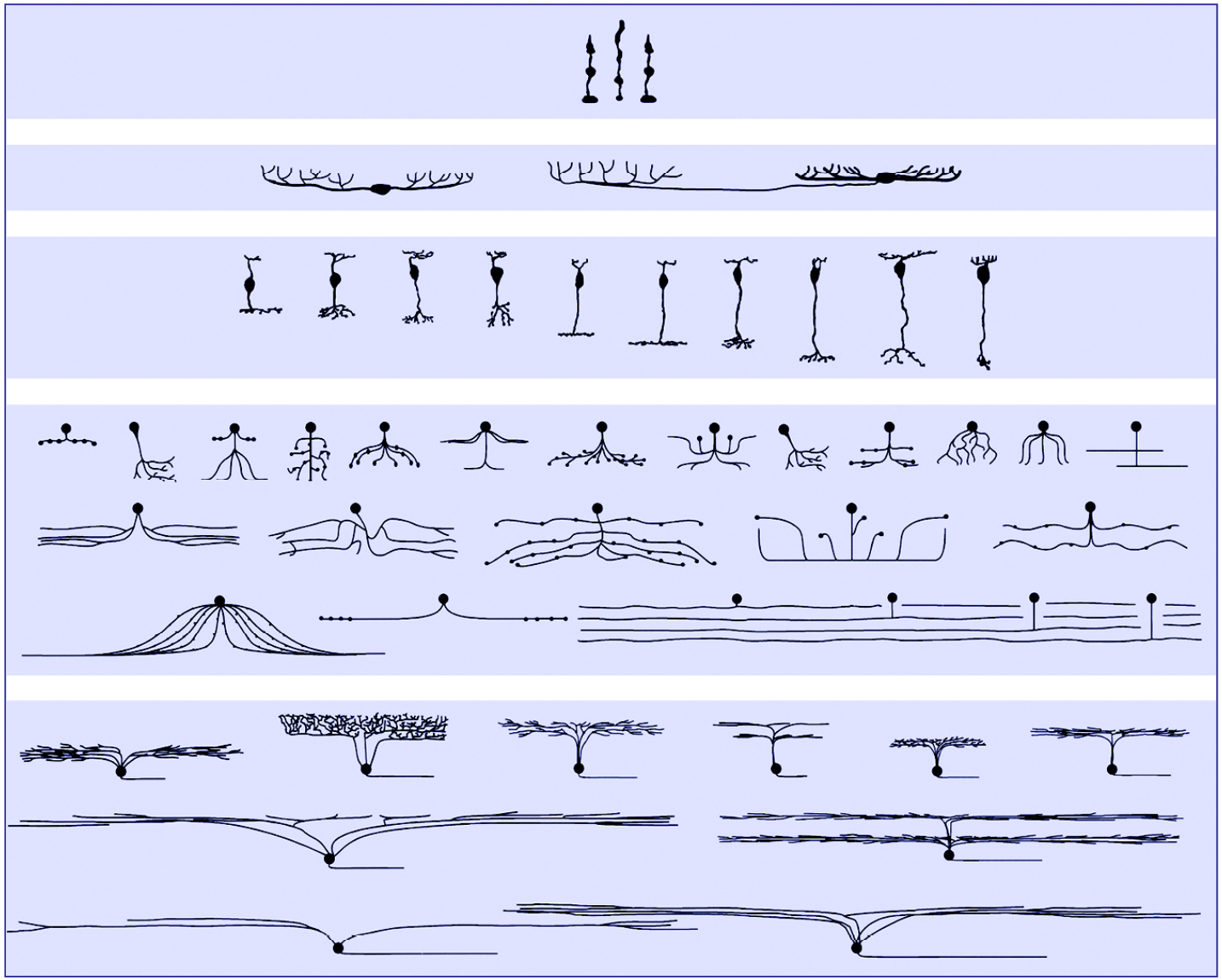
Neurons are units
(the nervous system
is not a continuum)

Cell classes & types

Suggested circuitry
from morphology

Santiago Ramon y Cajal,1892-

Diversity of cell types in the retina



3..4

2..3

10..13

20..30

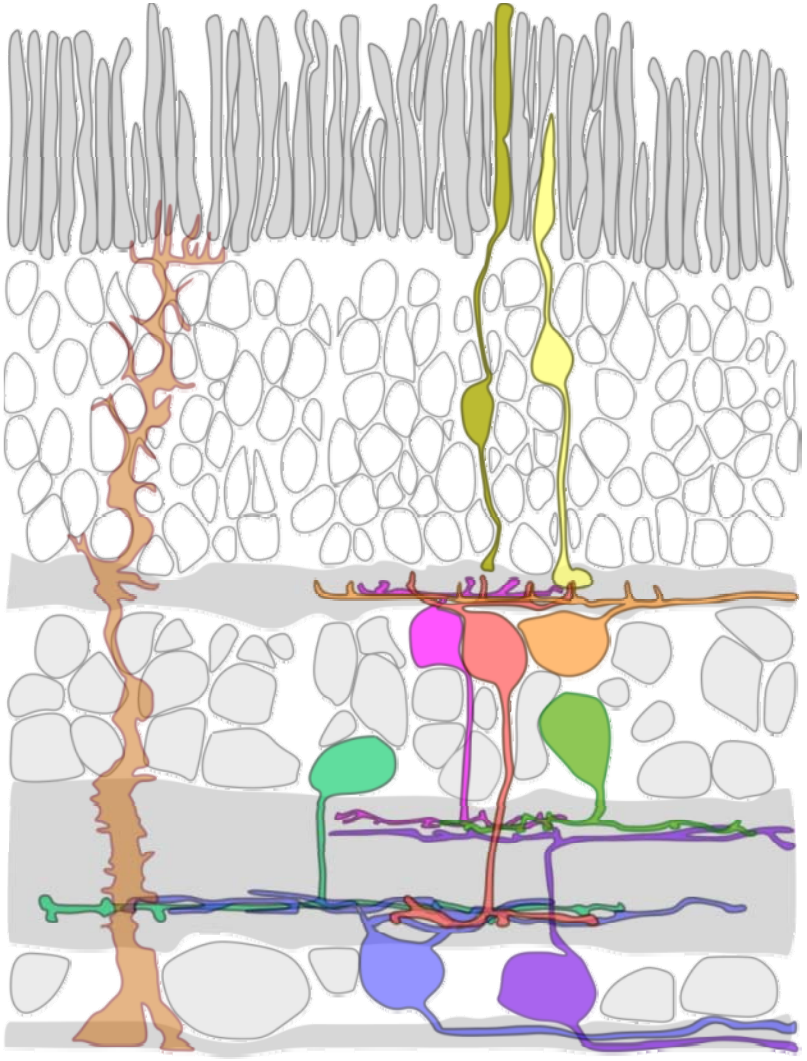
20..25

55..75

Masland, 2001

Retinal cell classes

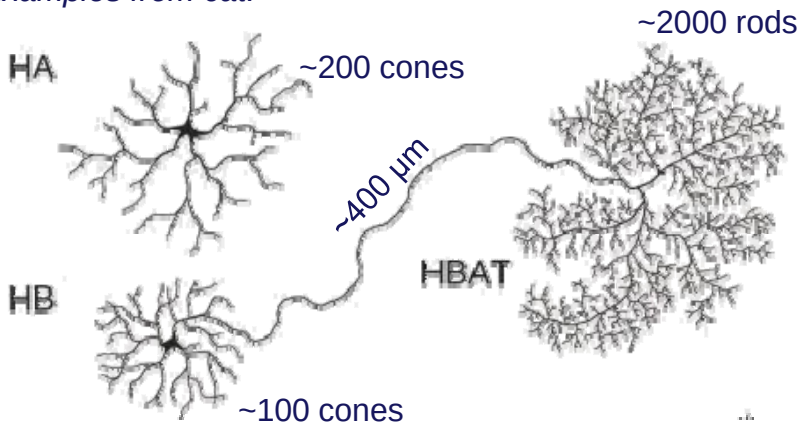
Focus on inner retina neurons
(horizontal, bipolar and amacrine cells)

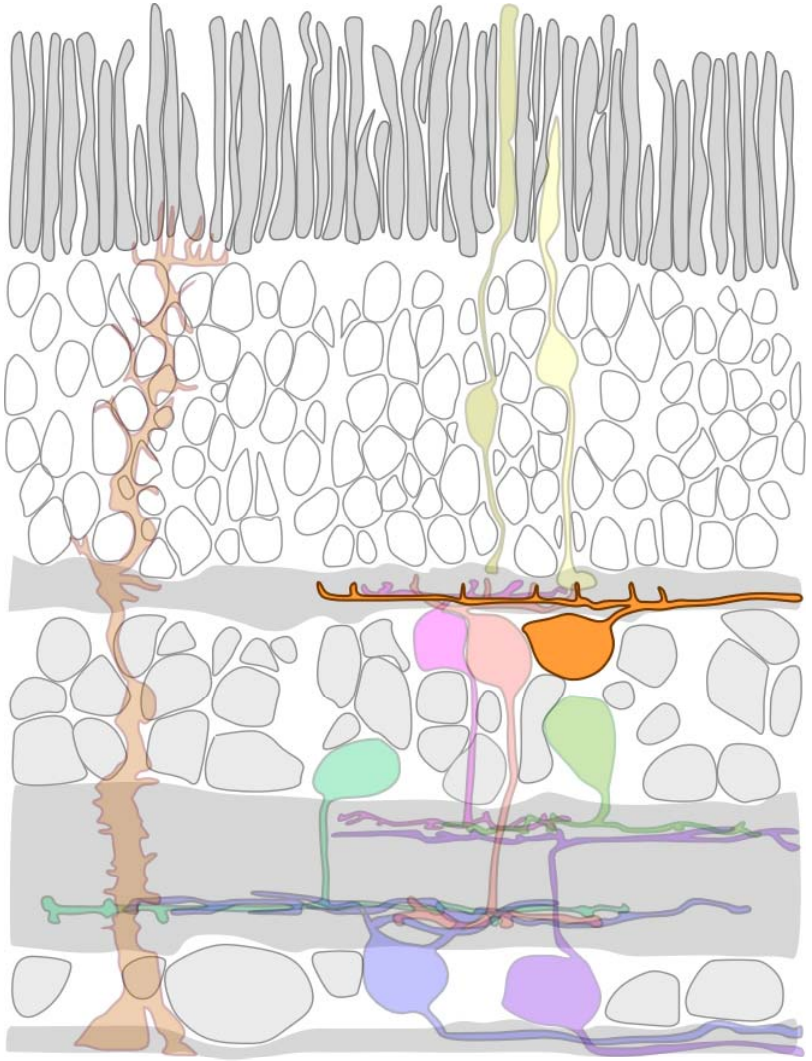


Retinal cell classes – Horizontal cells

- Two types in most retina
  (but e.g. 1 in mouse, 3 in horses)
- **a-type** (= axon-lacking):
  sparse, larger, contacts only cones (cat: ~200),
  b-type (= axon bearing):
  denser, smaller, contacts cones with “dendrites” (cat: ~100) and rods with “axon terminal” (cat: ~2000)
- OFF cells, GABAergic, graded neurons
- feed-back to photoreceptors
  three different feed-back mechanism suggested:
  1) ephaptic, 2) pH-mediated, 3) GABA

Examples from cat:





Adapted from Boycott et al. 1978, Kolb et al., 1992

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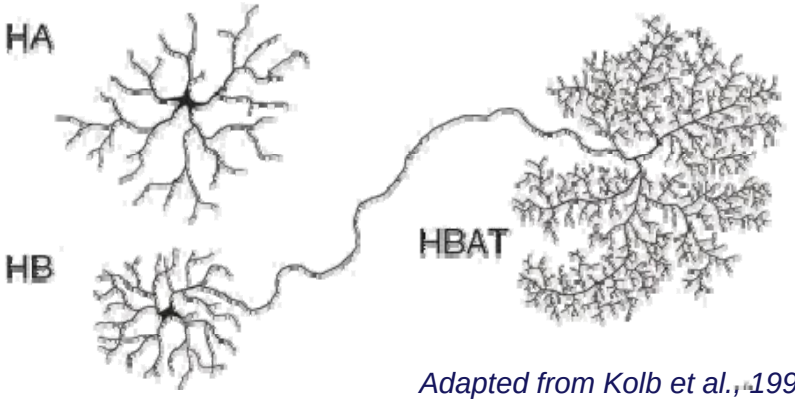
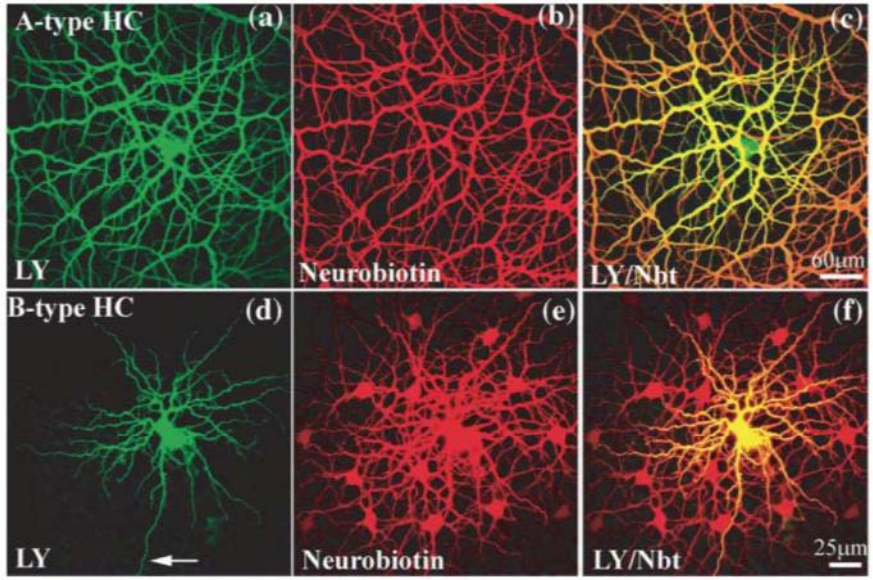
  three different feed-back mechanism suggested:
  1) ephaptic, 2) pH-mediated, 3) GABA
- each type is coupled via gap-junctions (controlled by dopamine)
- involved in: gain control, adjustment of photoreceptor integration time, generation of receptive fields



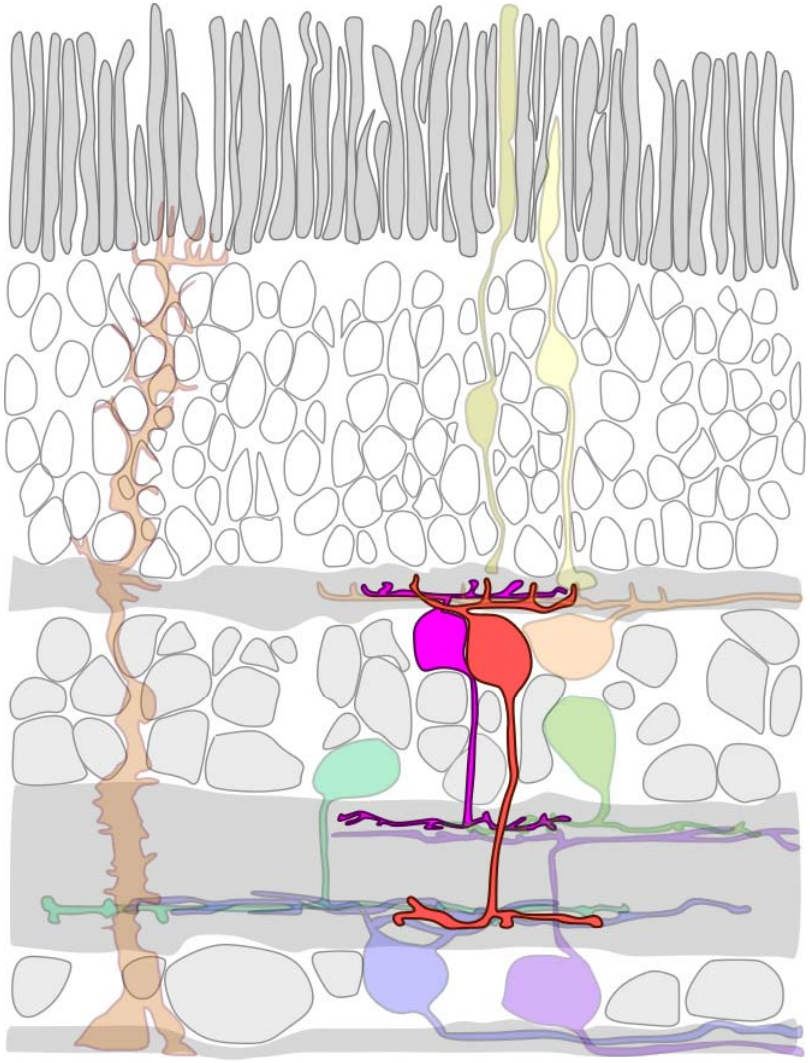
Adapted from Kolb et al., 1992



O‘Brien at al., 2006

Retinal cell classes – Bipolar cells

- 10-12 types, stratifying at different levels of the inner plexiform layer (IPL)
- relaying photoreceptor signals to the circuits in the inner retina (parallel signal pathways)



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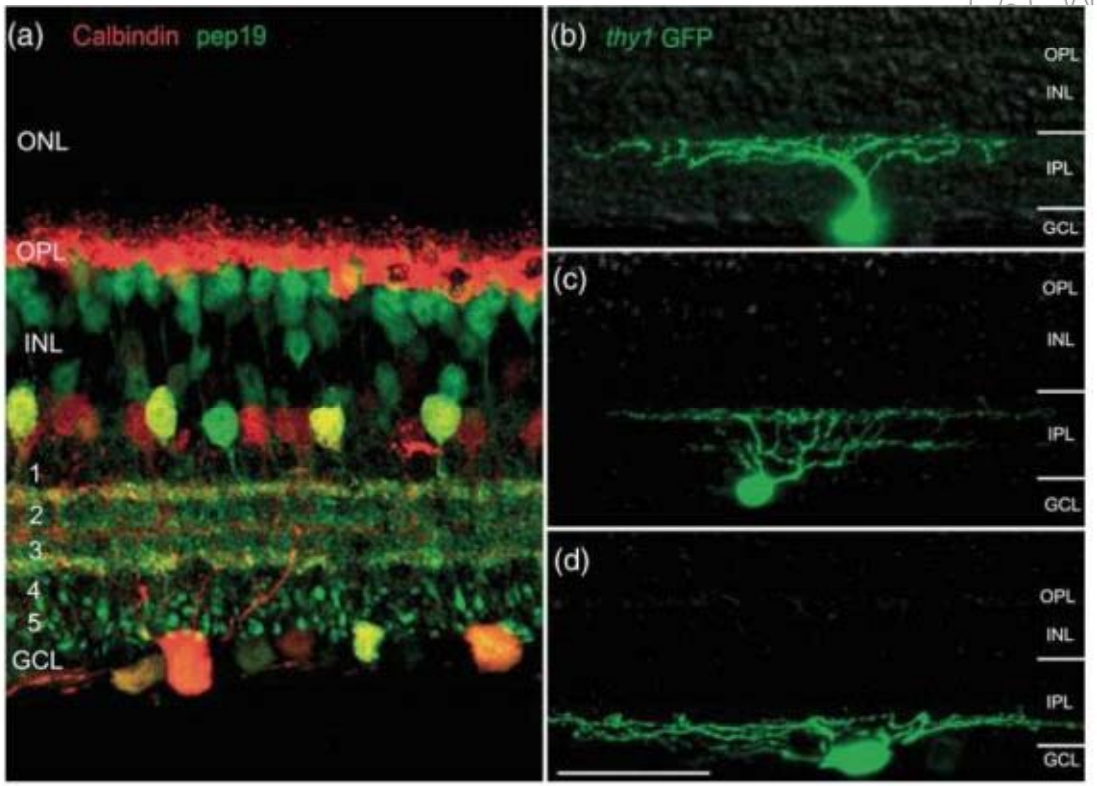
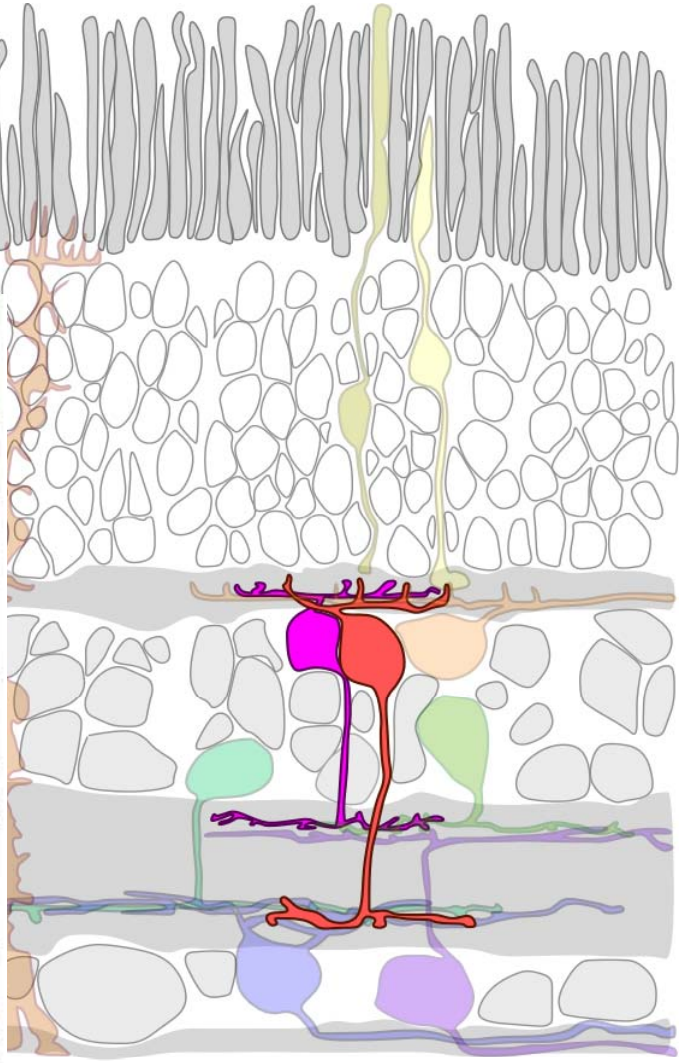
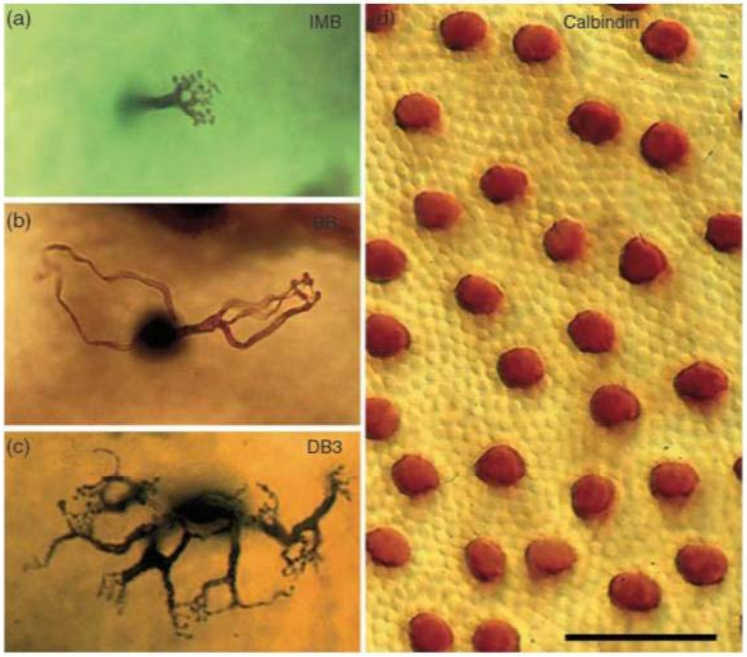


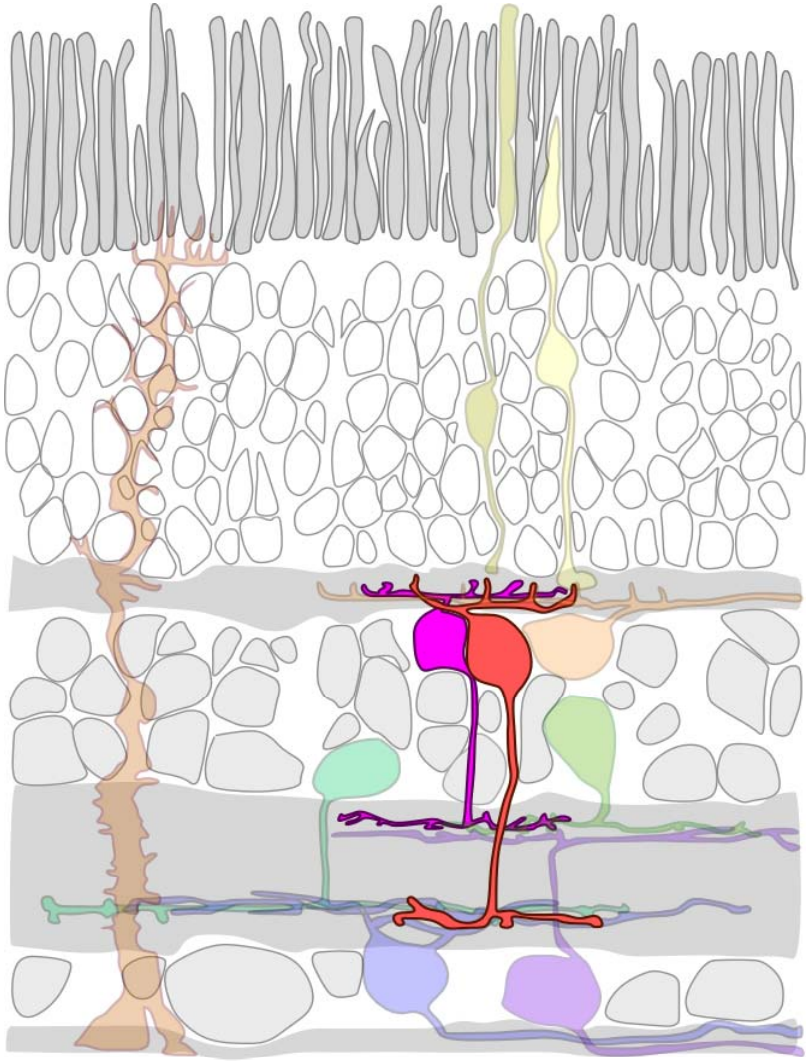


Adapted from Wässle, In: The Senses, Elsevier 2008, p313-340

Retinal cell classes – Bipolar cells

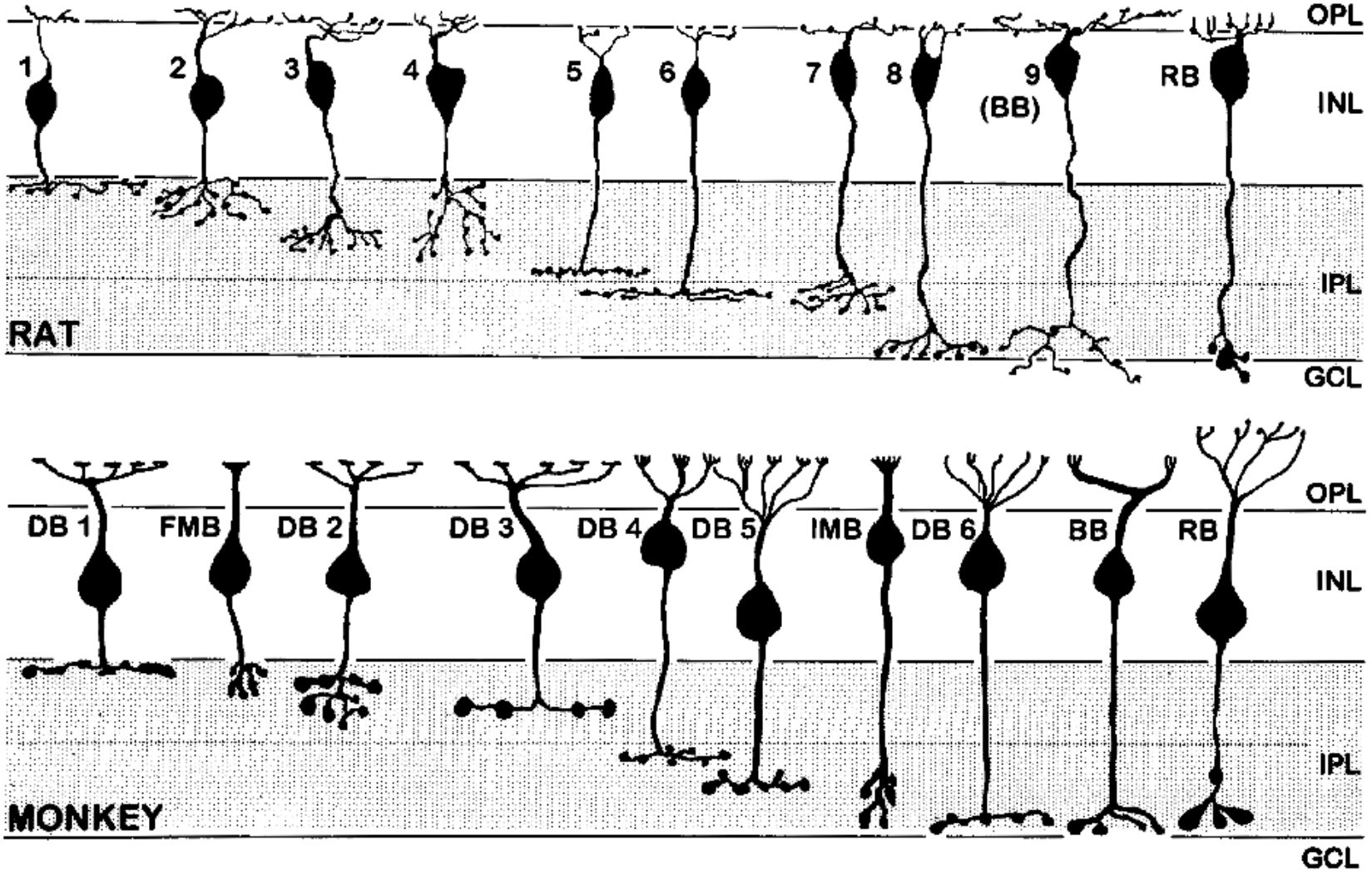
- 10-12 types, stratifying at different levels of the inner plexiform layer (IPL)
- relaying photoreceptor signals to the circuits in the inner retina (parallel signal pathways)
- graded neurons
- rough classification: ON vs. OFF, transient vs. sustained, rod vs. cone, etc.





Adapted from Wässle, In: The Senses, Elsevier 2008, p313-340

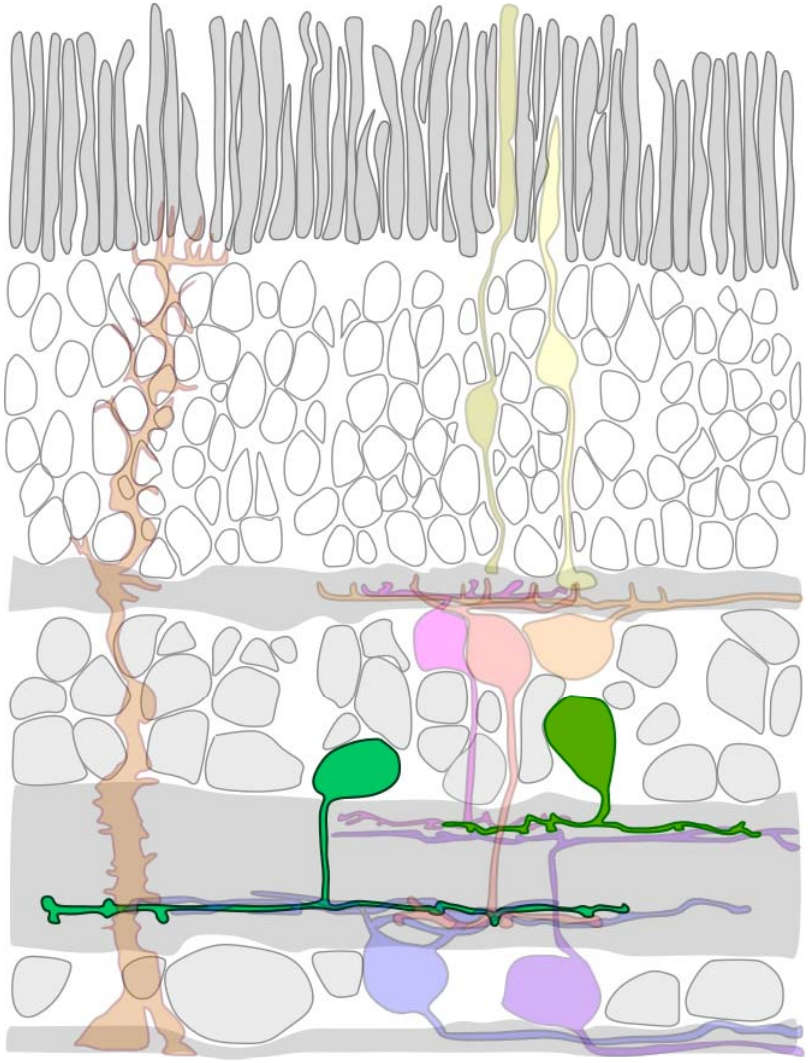
Bipolar cell types in two mammalian retinas



Boycott & Wässle (1999)

Retinal cell classes – Amacrine cells

- 20-30 types of amacrine cells (or more)
- amacrine = “no axon” (Greek: a = “no” or “none”, makrós = “large” and ís (genitive of inós) = “fibre”)
- neuronal “hardware” in the inner retina
- graded, dual transmitter neurons
- most use dendrites for synaptic input and output (dendritic processing)
- only few types functionally well understood (A2, A17, dopaminergic ACs, polyaxonal ACs, starburst ACs)



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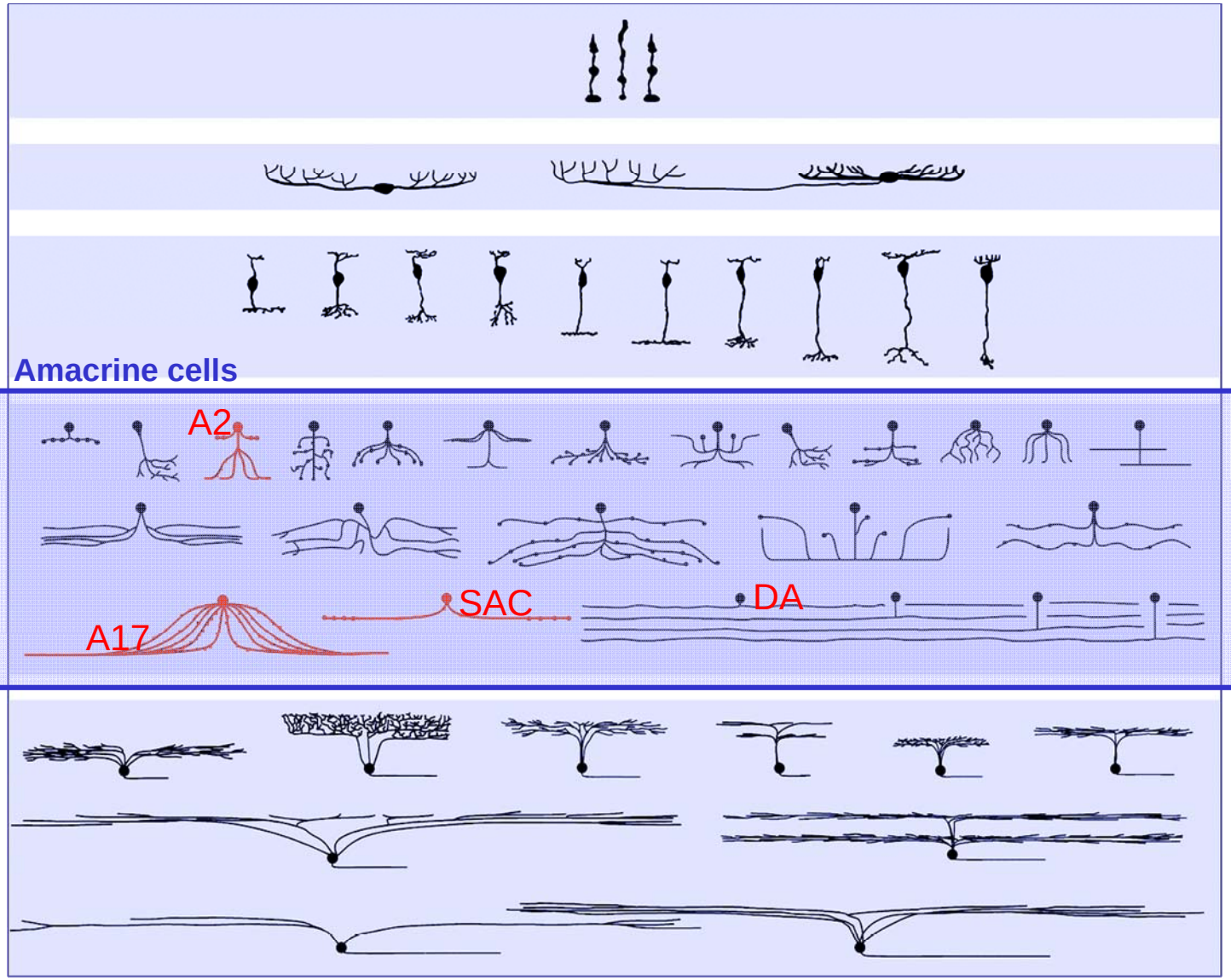

Masland, 2001

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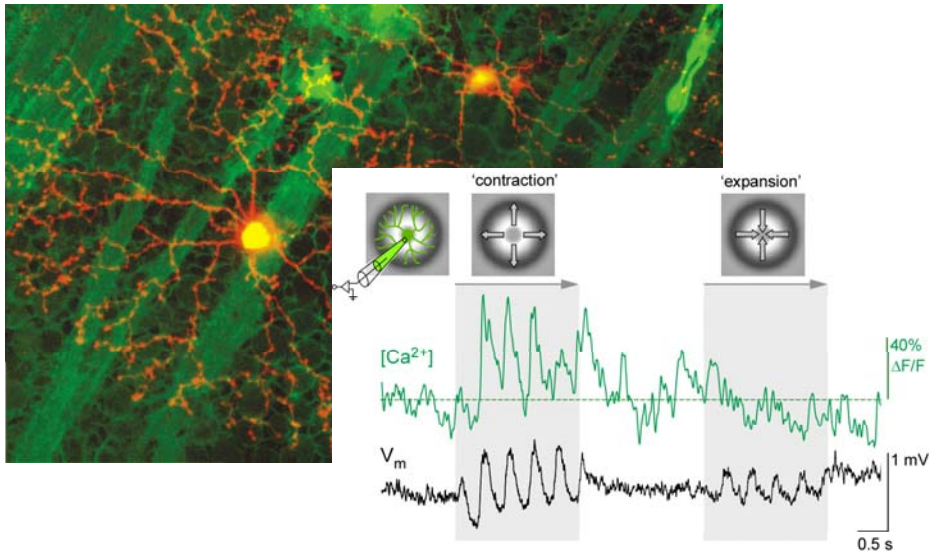
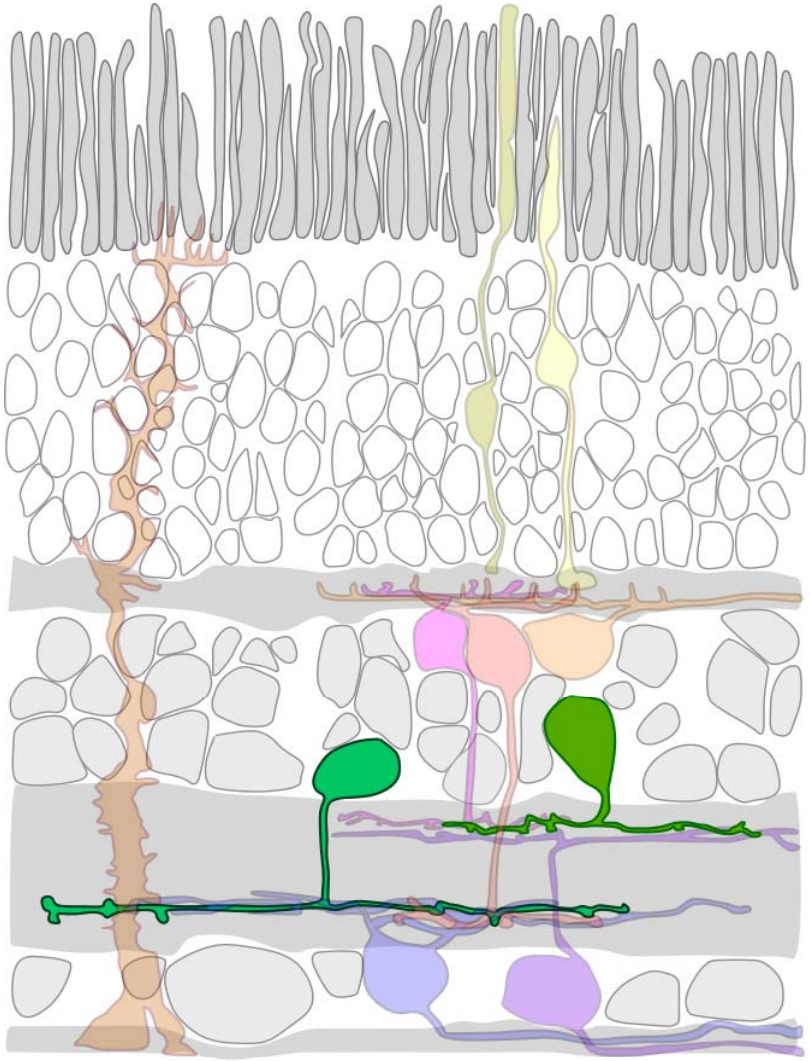
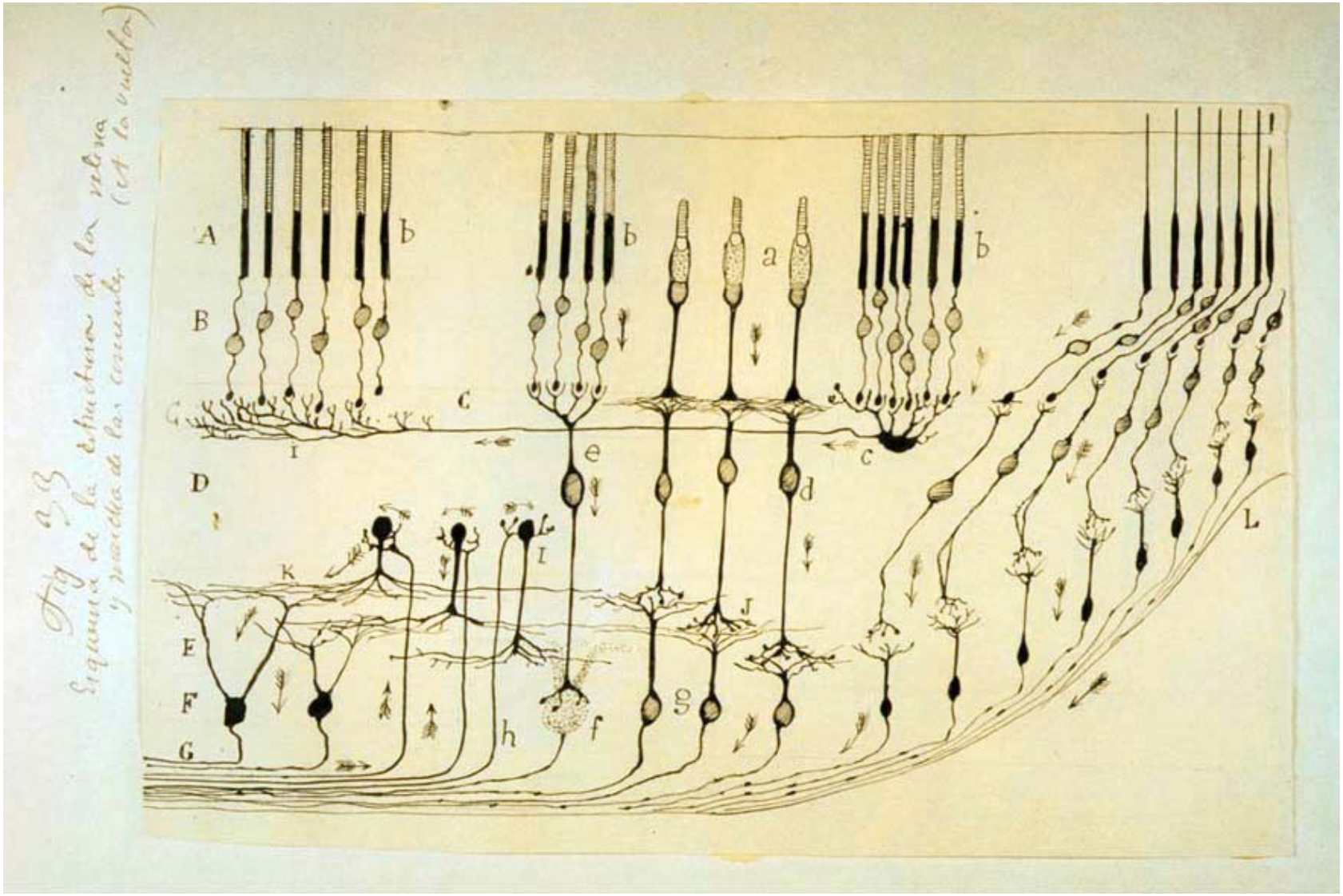




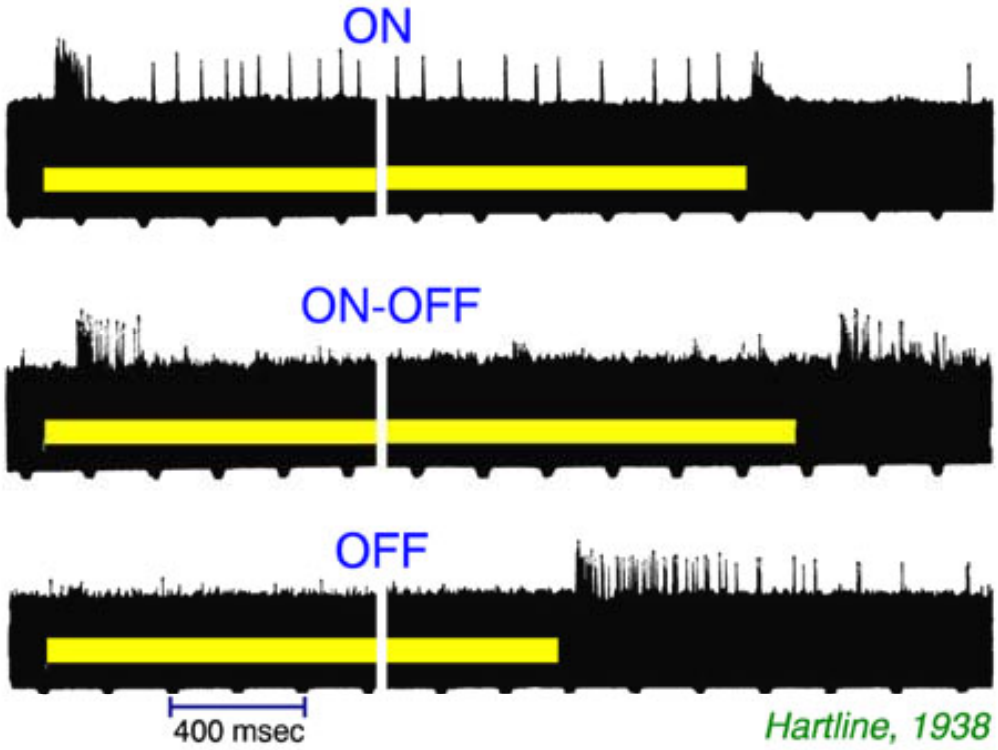
Euler et al., 2002, Hausselt et al., 2007

Retinal signal flow

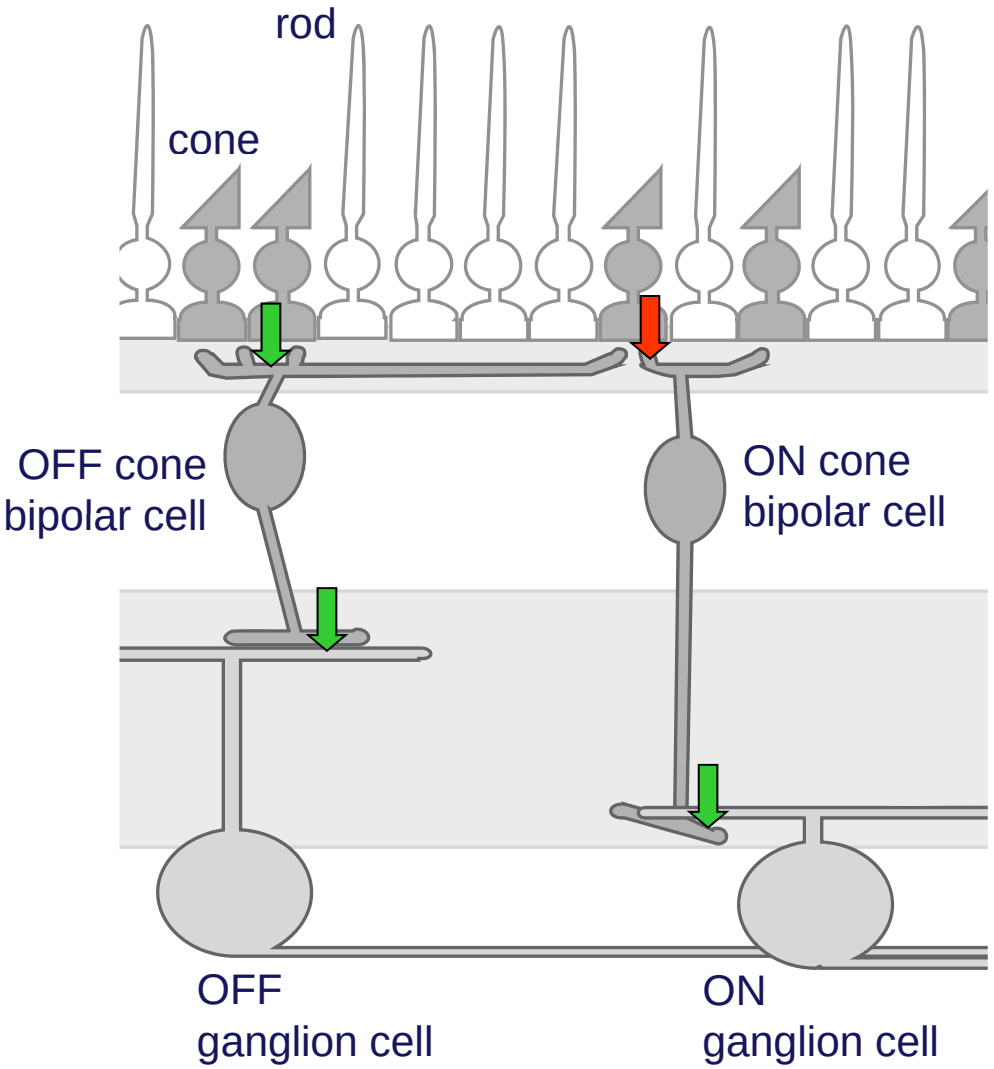


Santiago Ramon y Cajal,1901 (http://www.psu.edu/nasa/cajal2.htm)

ON/OFF pathways



ON/OFF pathways – Standard or “day-light” version



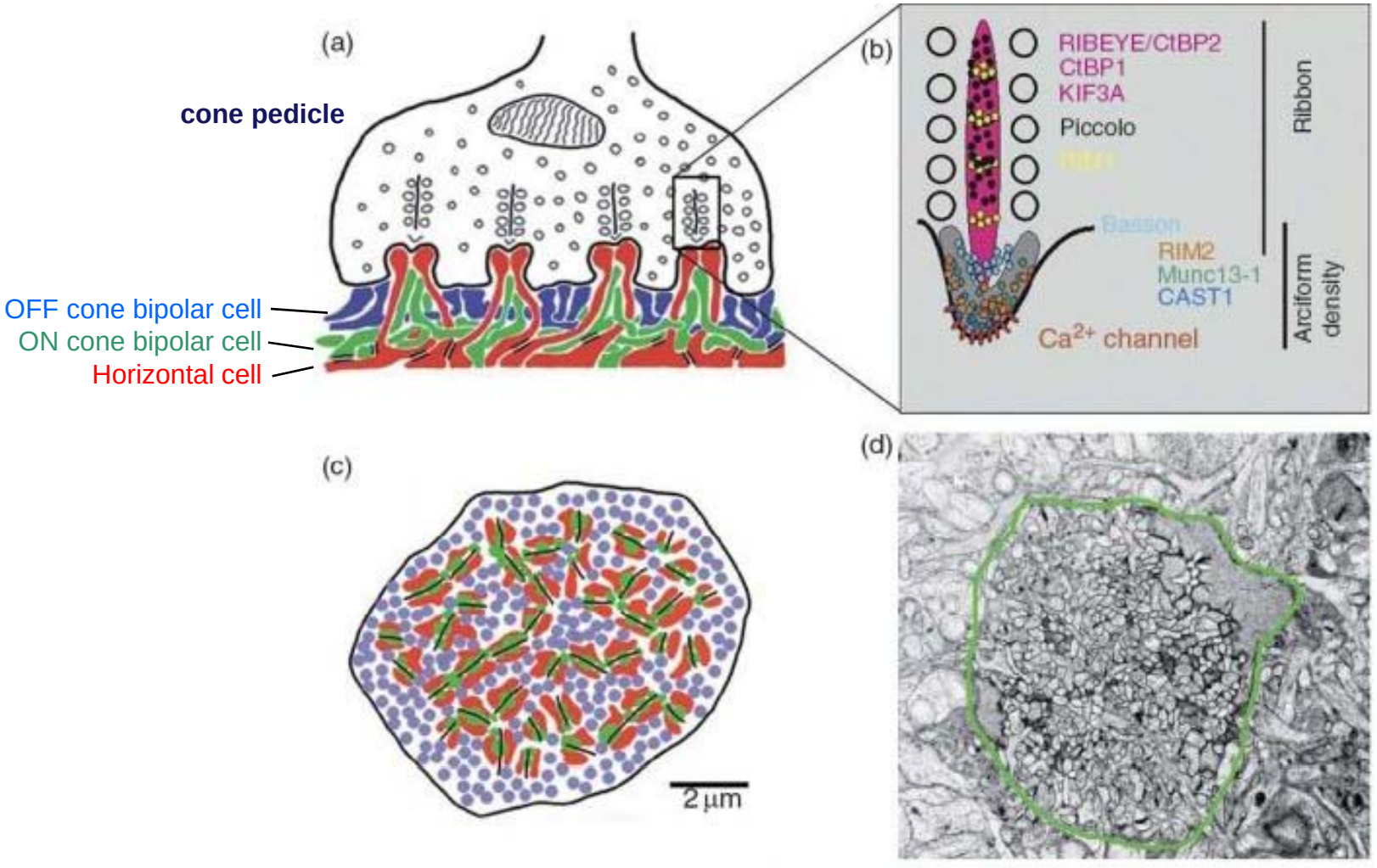
sign conserving synapse
(AMPA/KA receptors)

sign inverting synapse
(metabotropic GluRs)

gap junction
(electrical synapse)

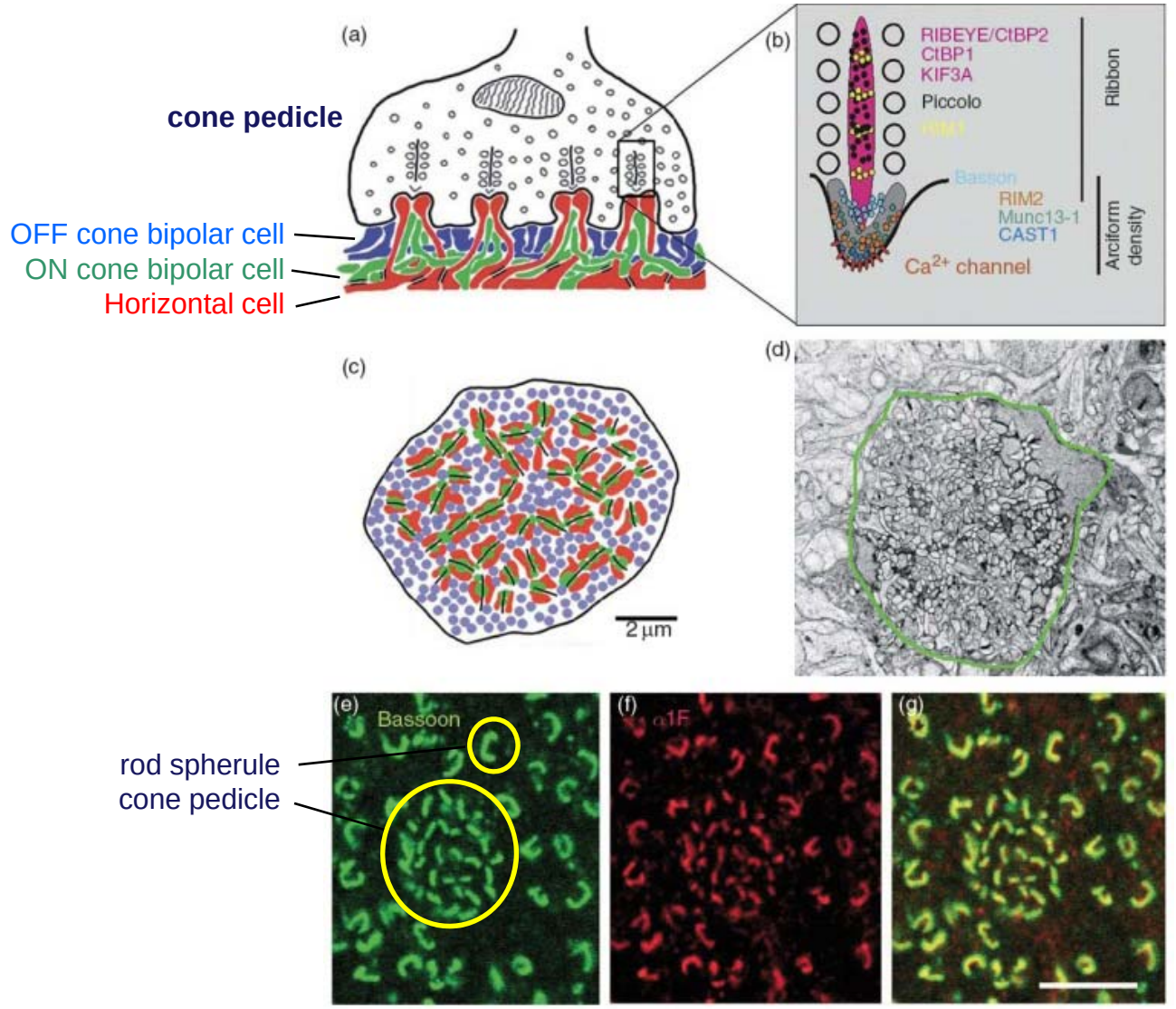
photopic range
“day light”
(luminance)

First synapse in the visual system



Adapted from Wässle, In: The Senses, Elsevier 2008, p313-340

First synapse in the visual system – Cone pedicles



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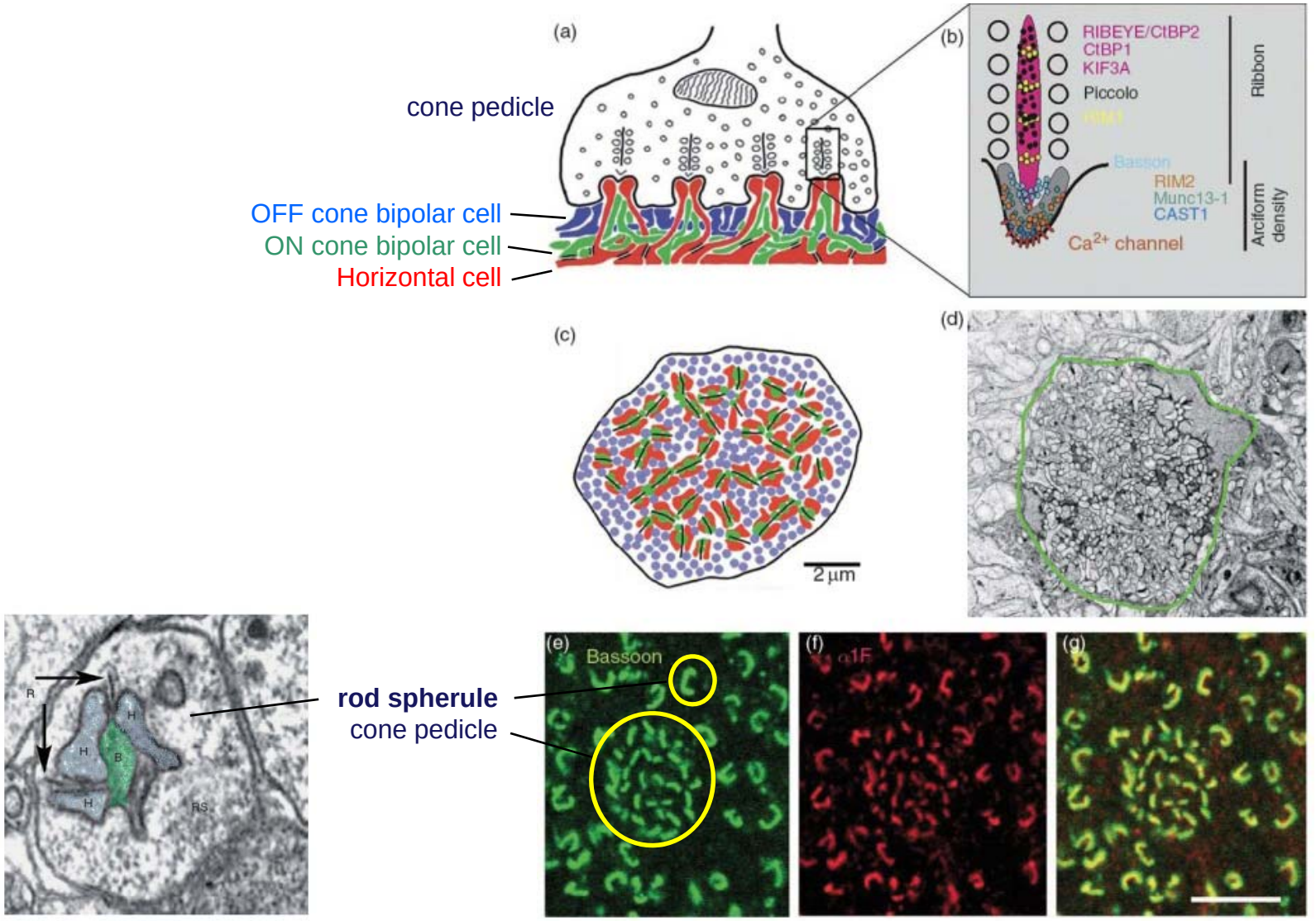
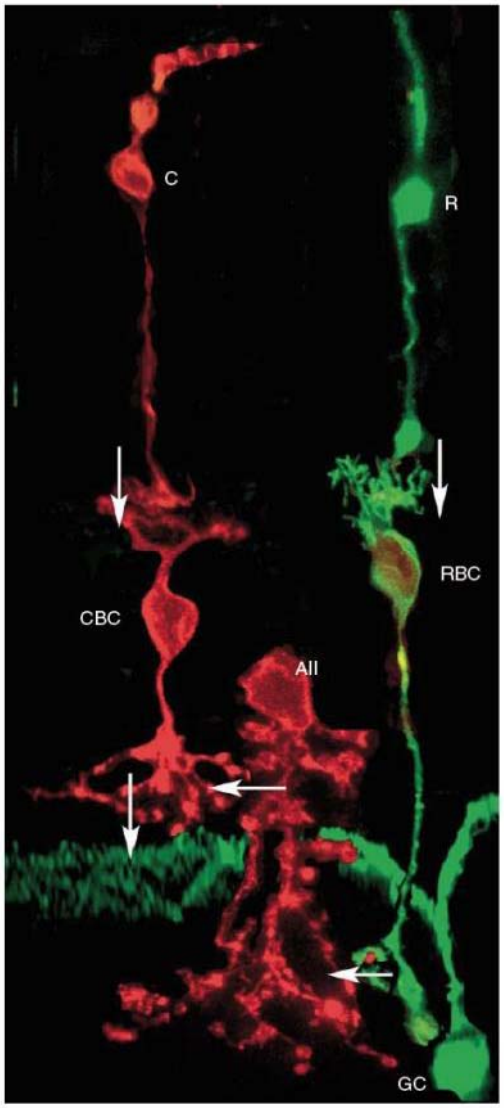
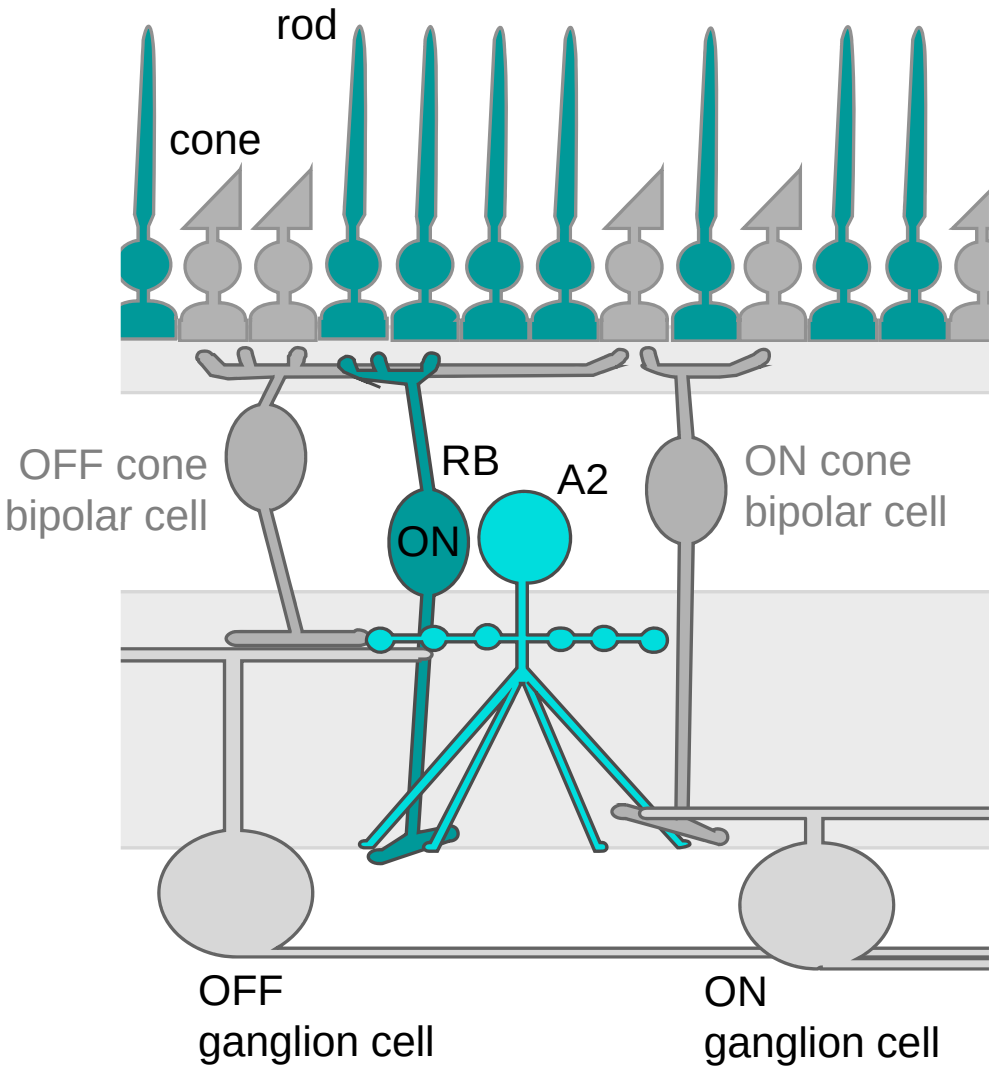


Adapted from Wässle, In: The Senses, Elsevier 2008, p313-340
EM: Adapted from Strettoi, In: The Senses, Elsevier 2008, p303-312

Rod pathway(s)





Adapted from Strettoi, In: The Senses, Elsevier 2008, p303-312

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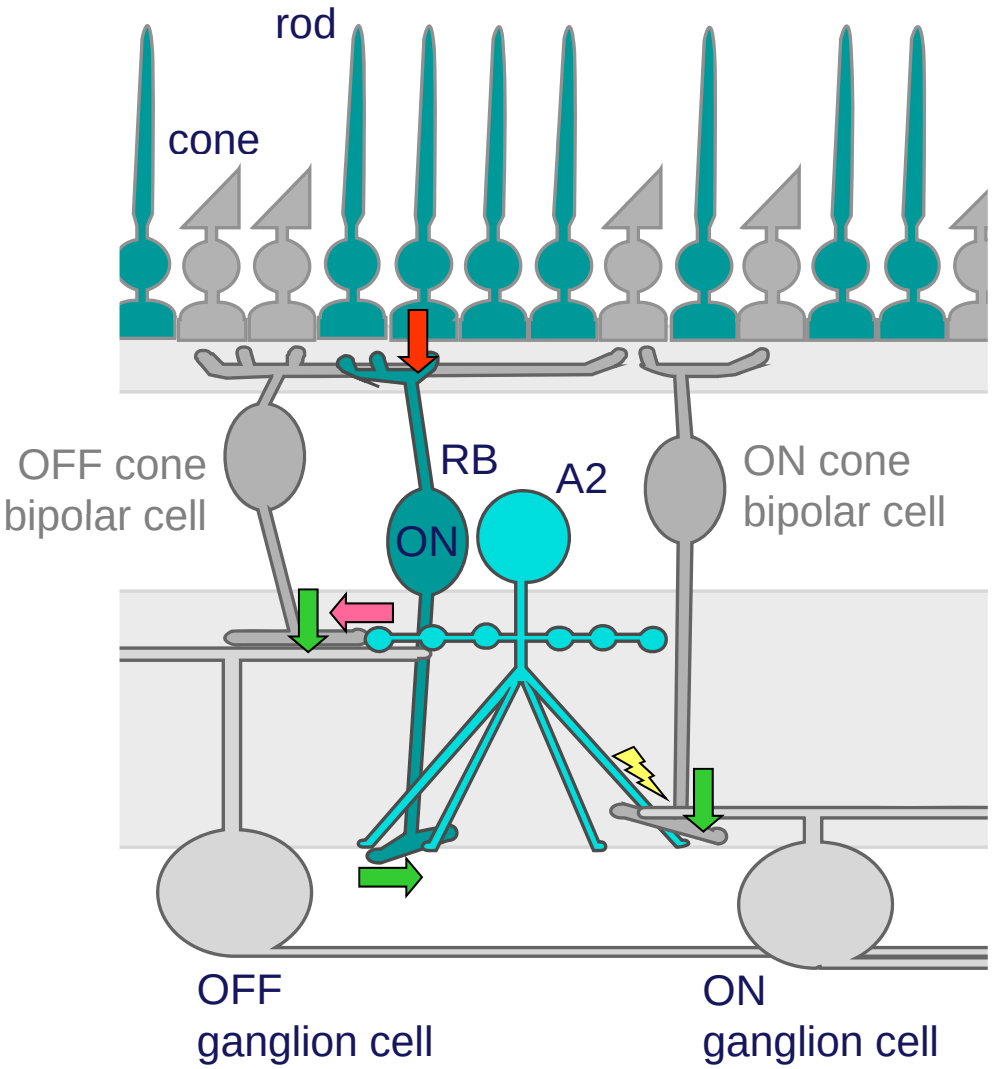


sign conserving synapse
(AMPA/KA receptors)

sign inverting synapse
(metabotropic GluRs)

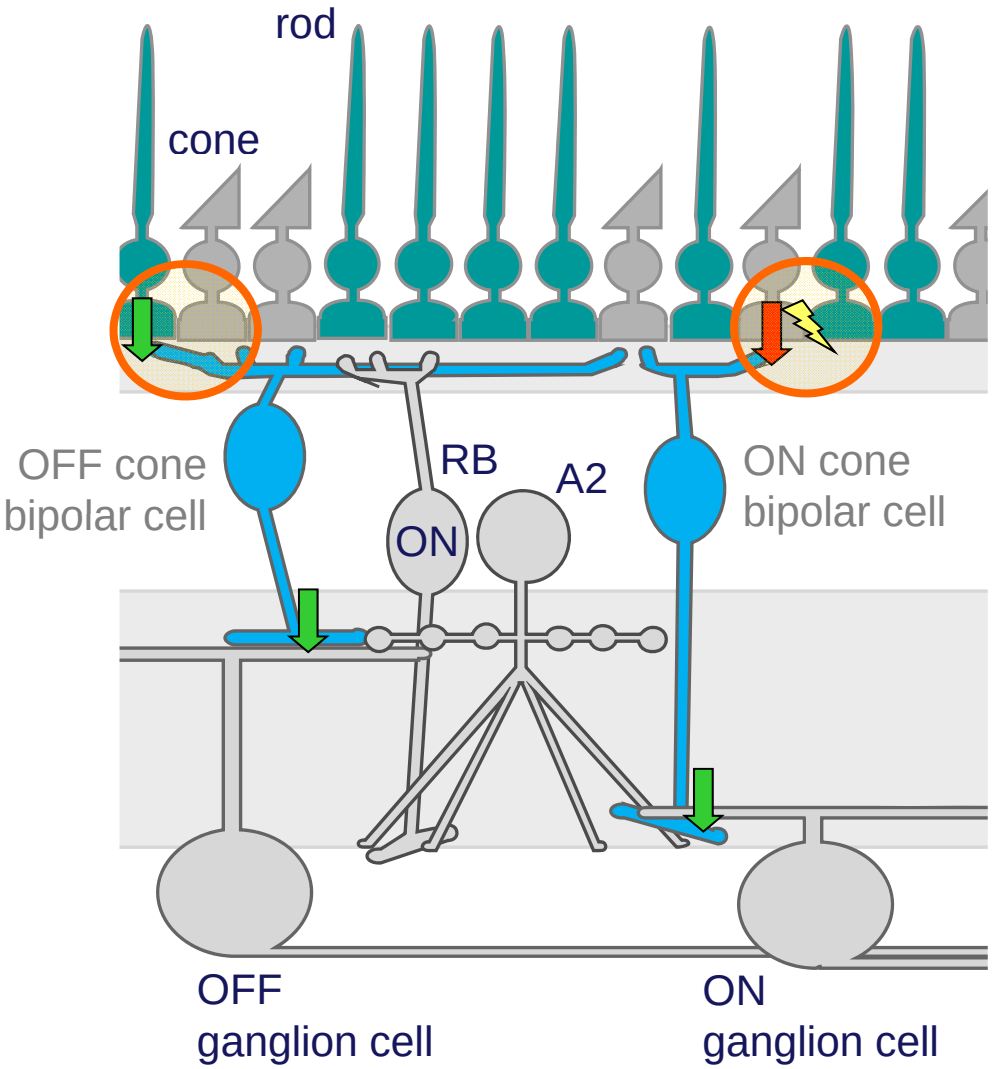
sign inverting synapse
(Glycine receptors)

gap junction
(electrical synapse)

RB = rod bipolar cell
A2 amacrine cell

scotopic range
“star light”

Rod pathway(s)



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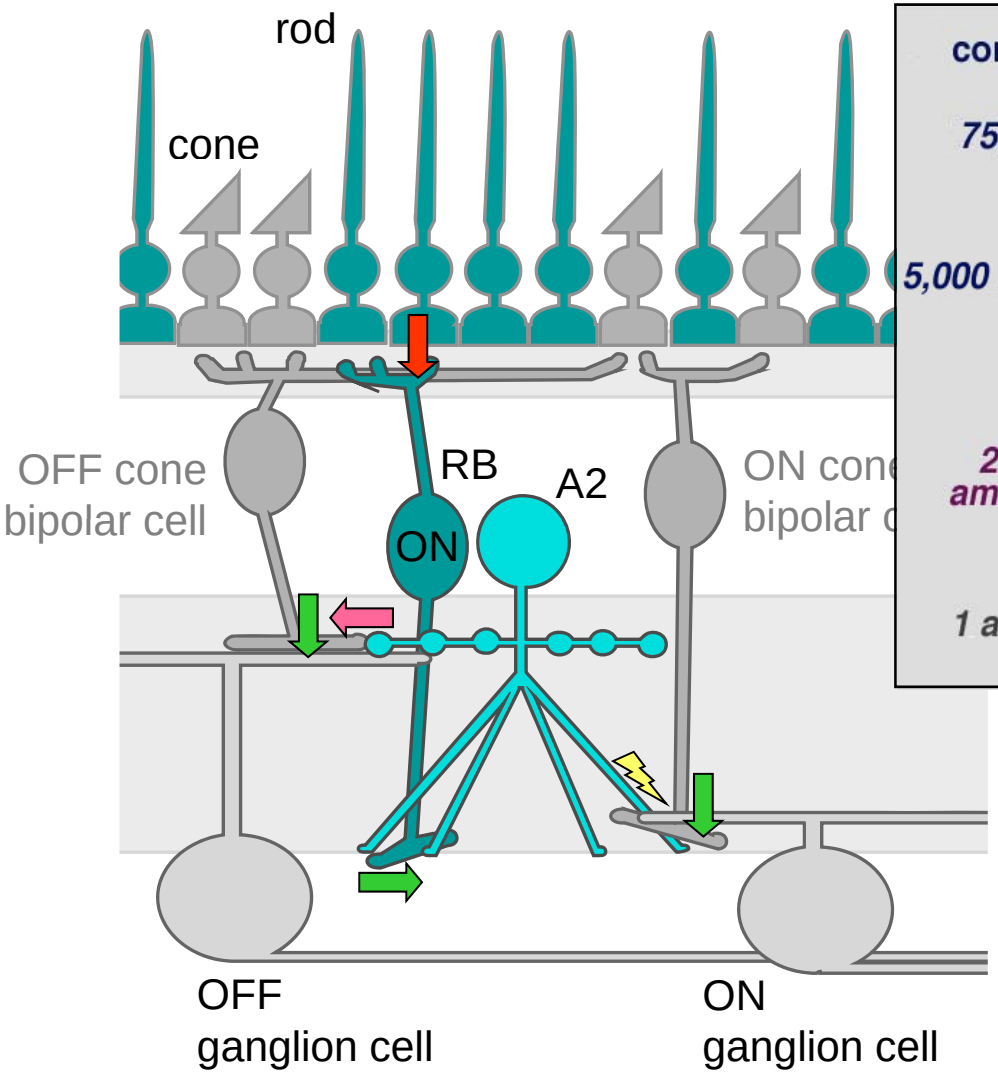
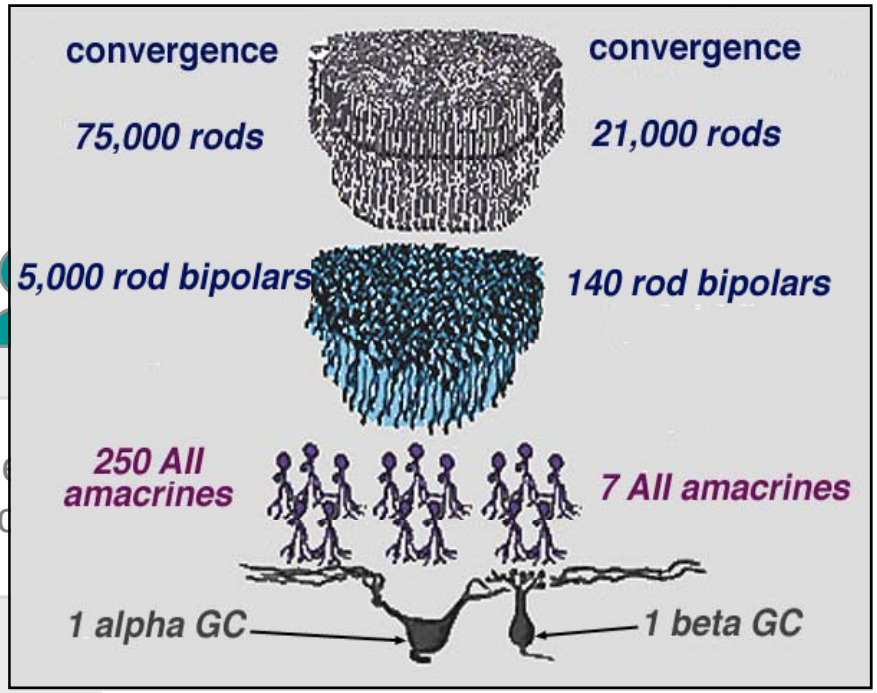
ON/OFF pathways – Rod system





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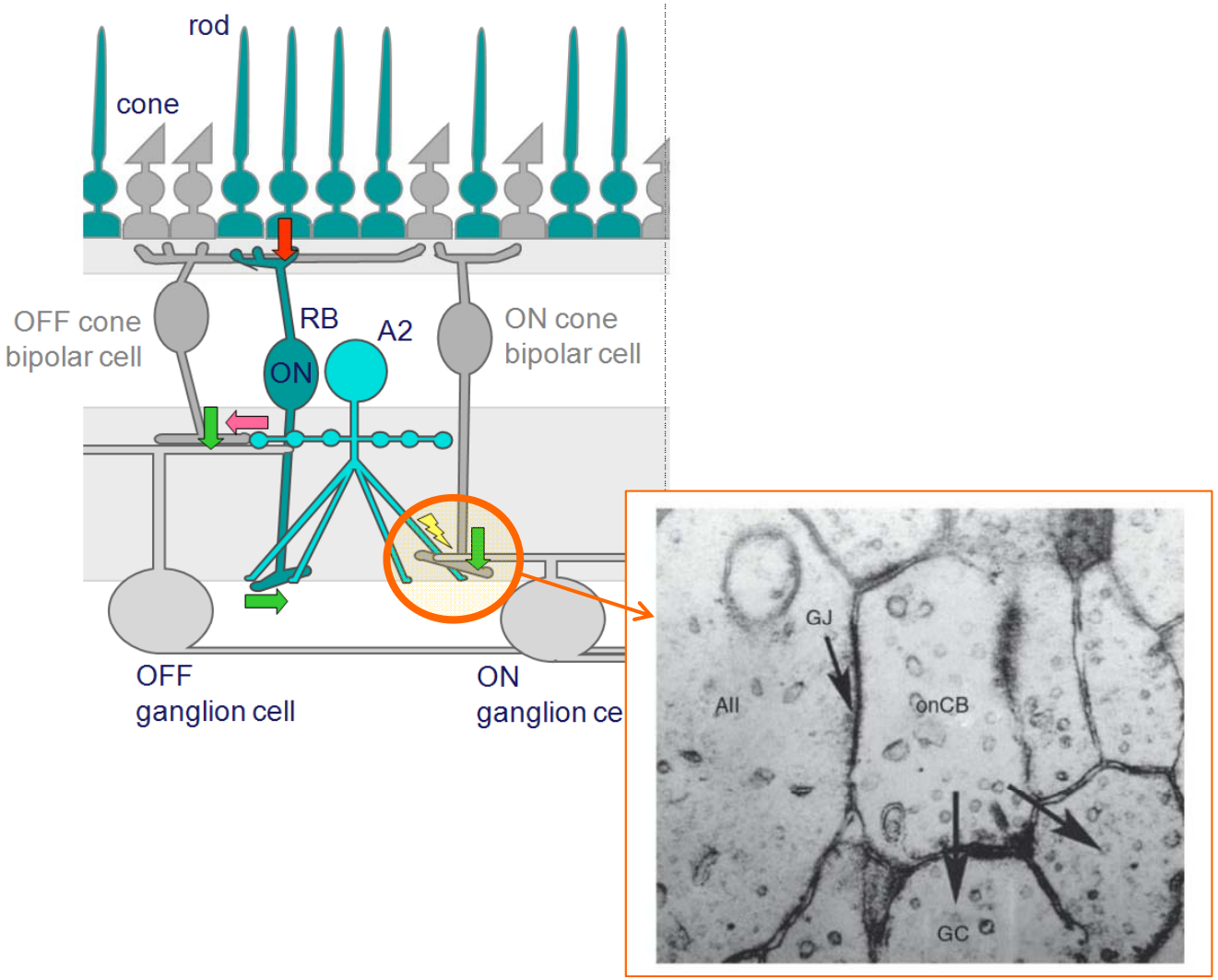
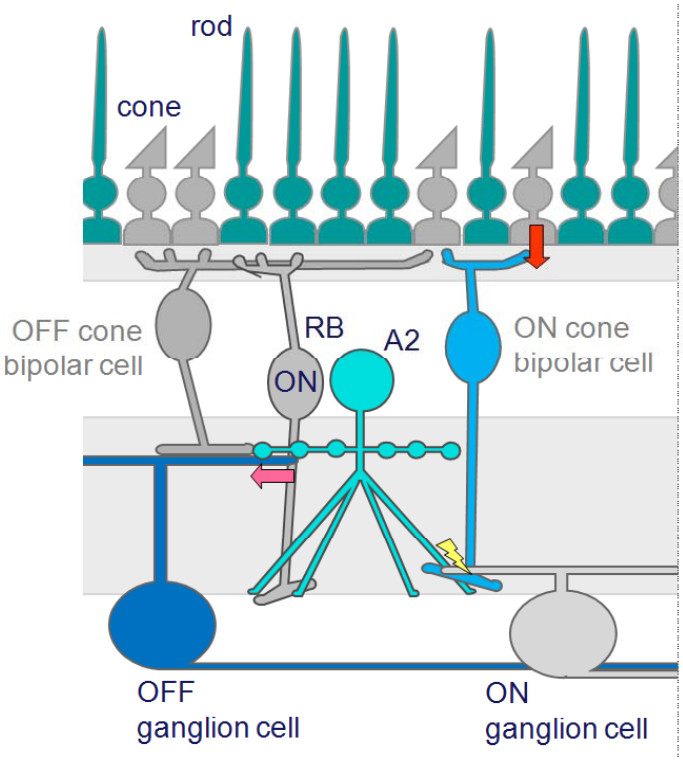
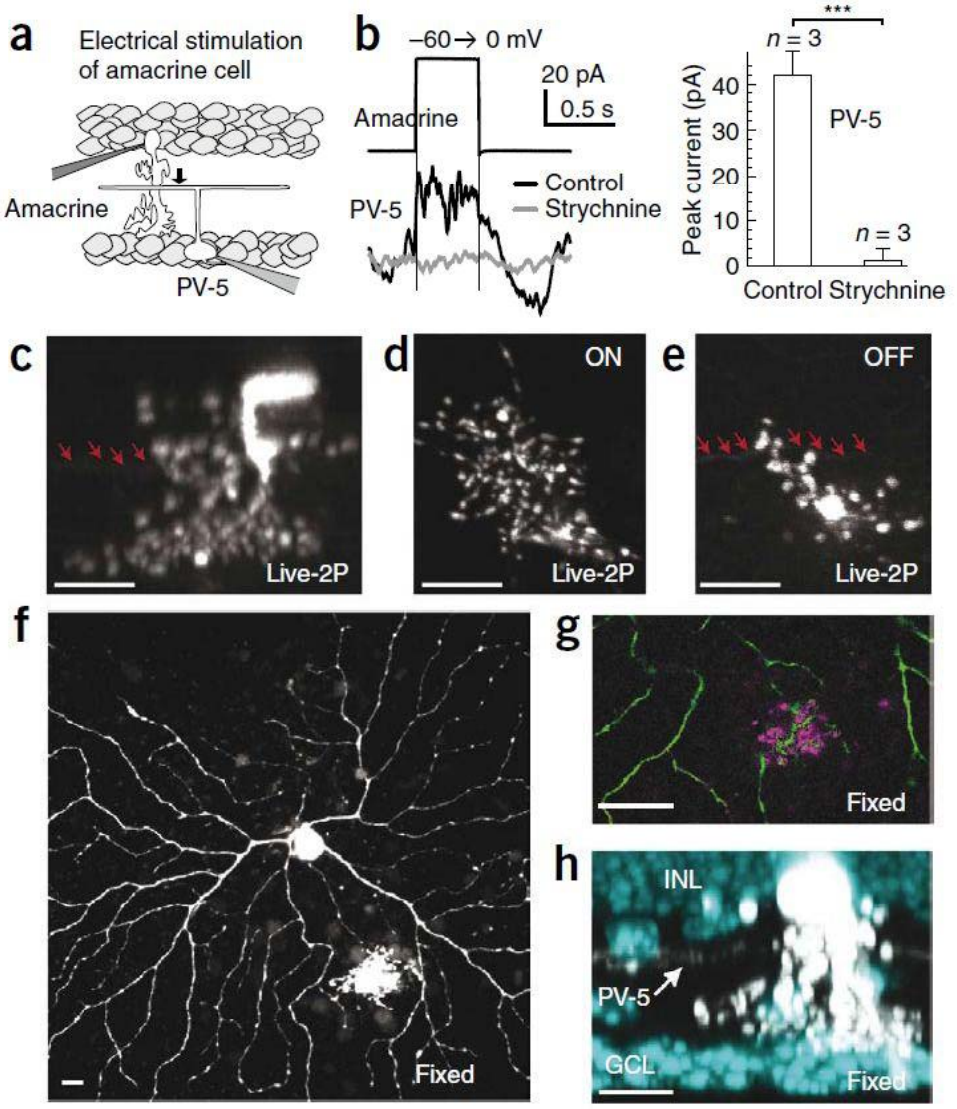


EM: Adapted from Strettoi, In: The Senses, Elsevier 2008, p303-312

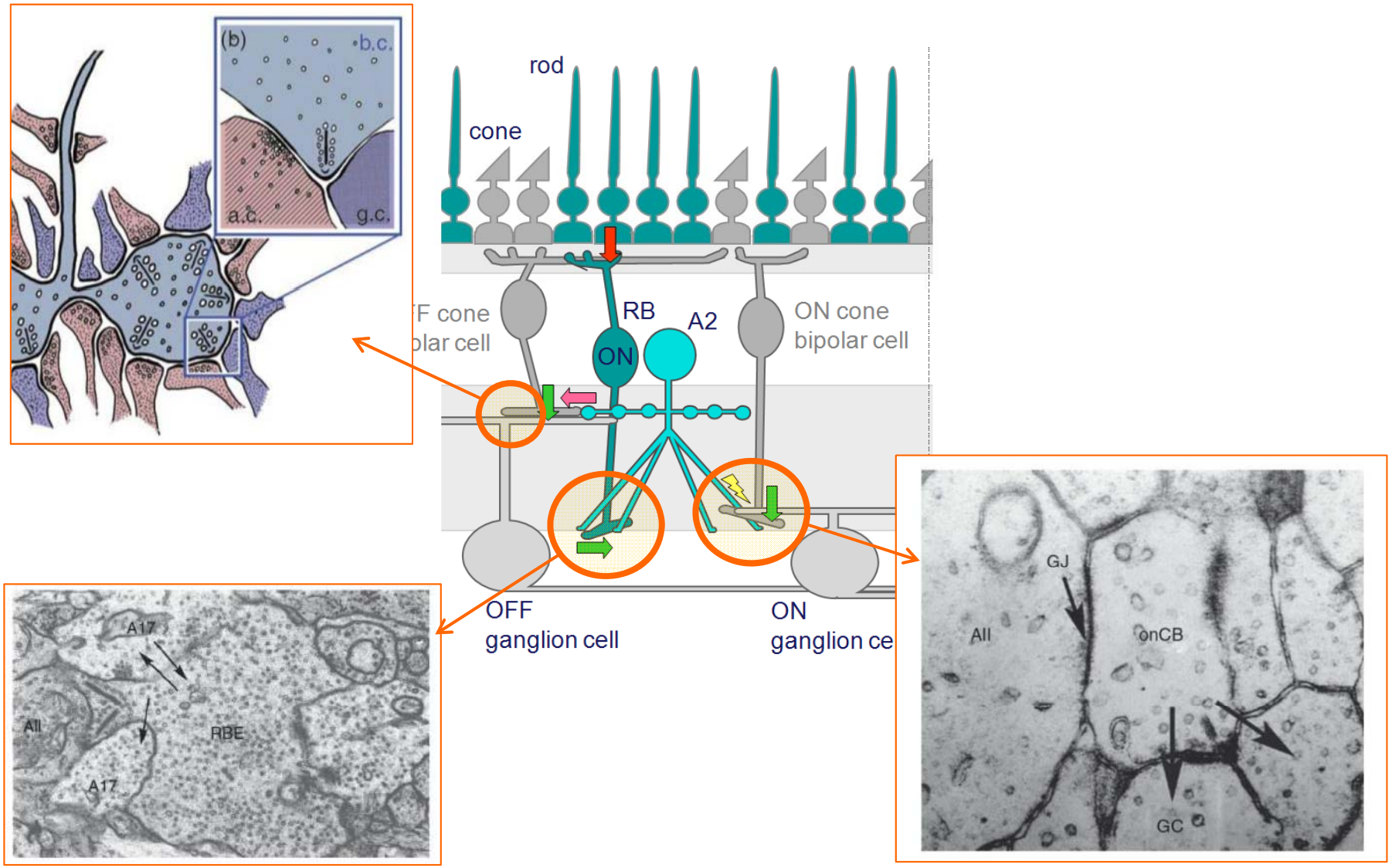
Rod pathway(s) – Multiple roles for A2 amacrine cells?





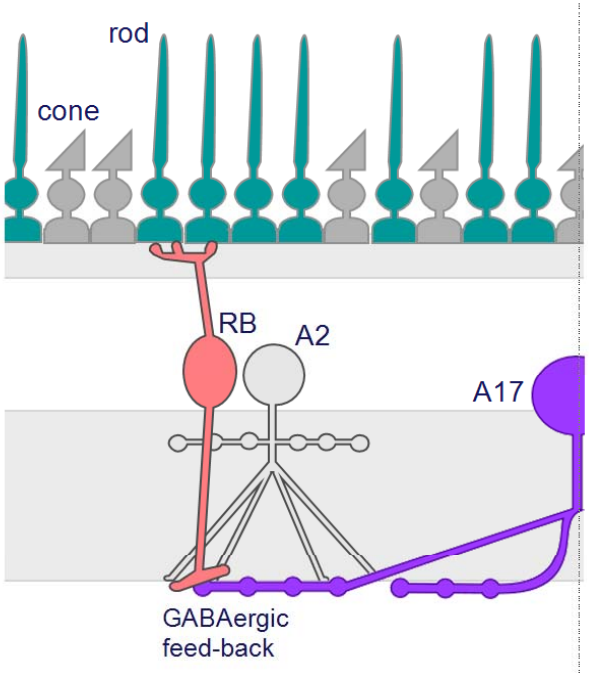
Münch et al., 2009

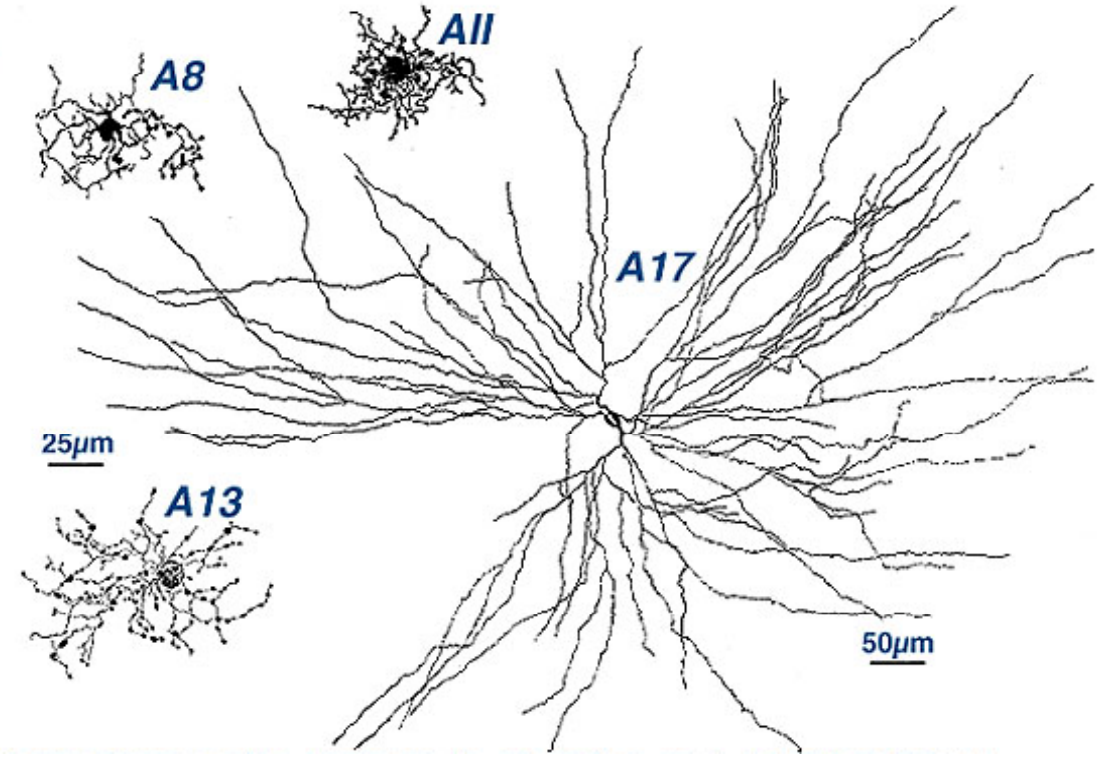
Rod pathway(s)



EM: Adapted from Strettoi, In: The Senses, Elsevier 2008, p303-312

Rod pathway - Local feed-back from A17 cells





Kolb &Famiglietti, 1974

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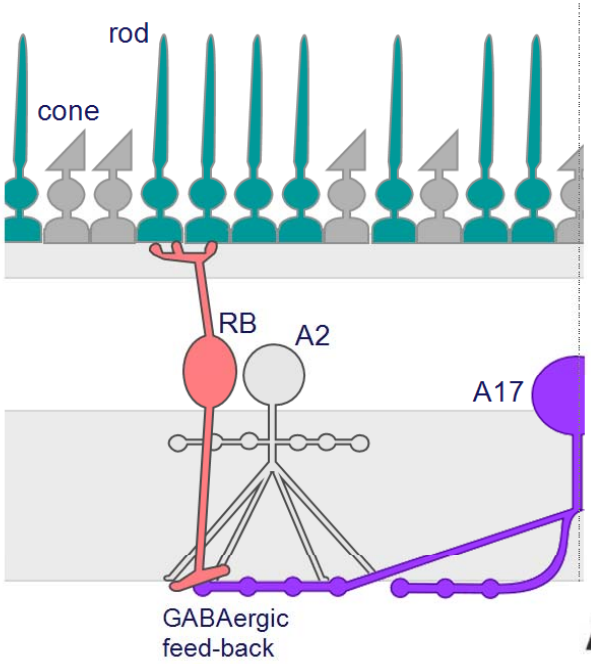
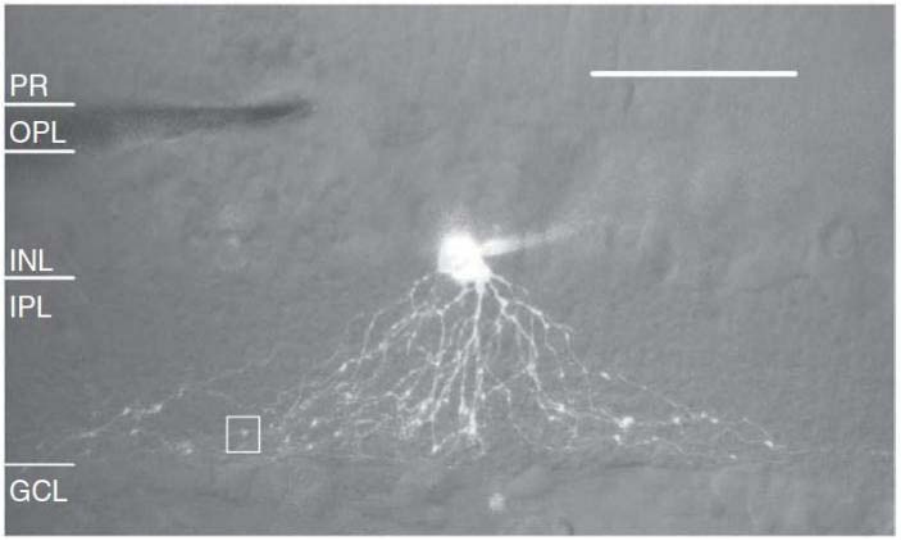
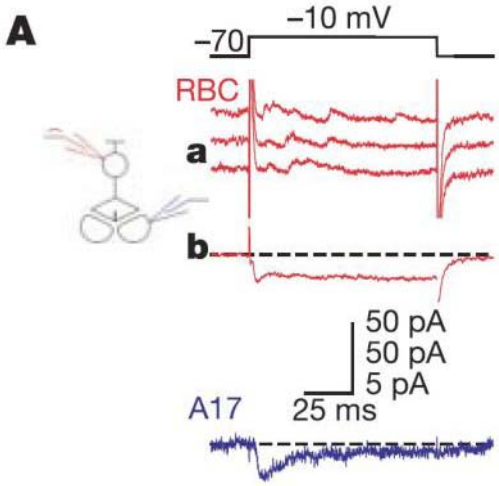
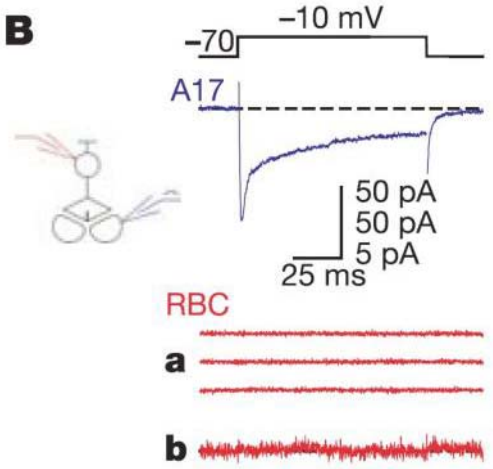


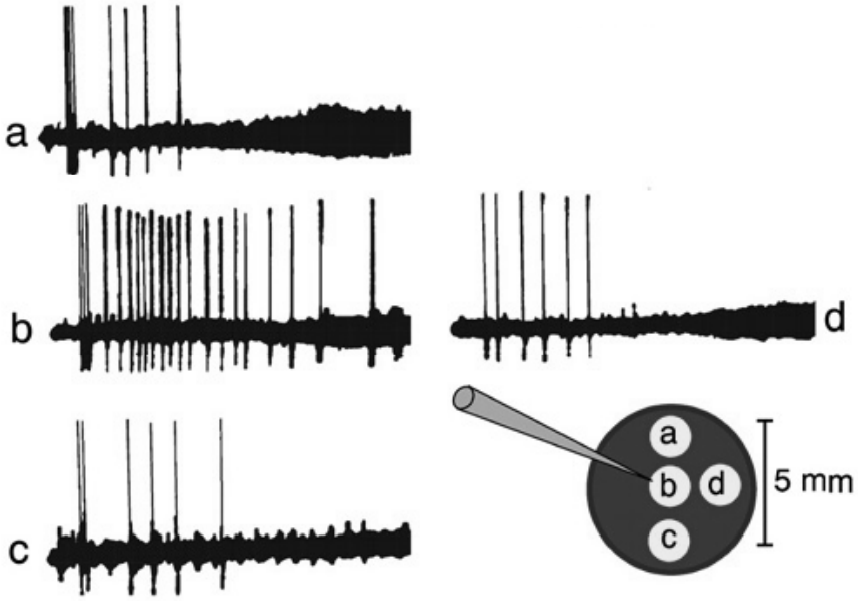


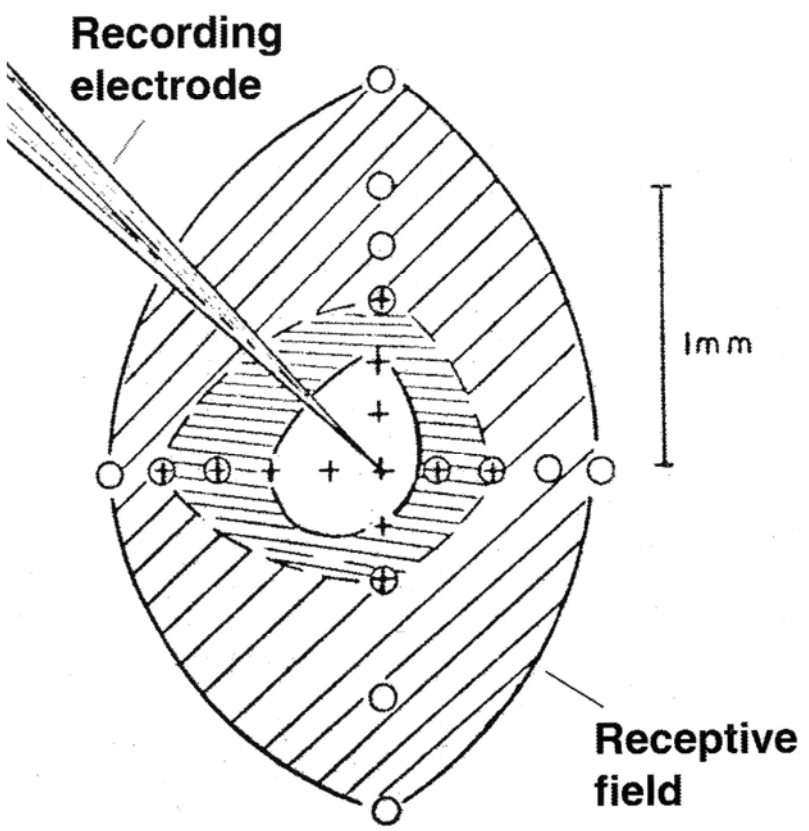




Grimes et al., 2009, Chavéz et al., 2006

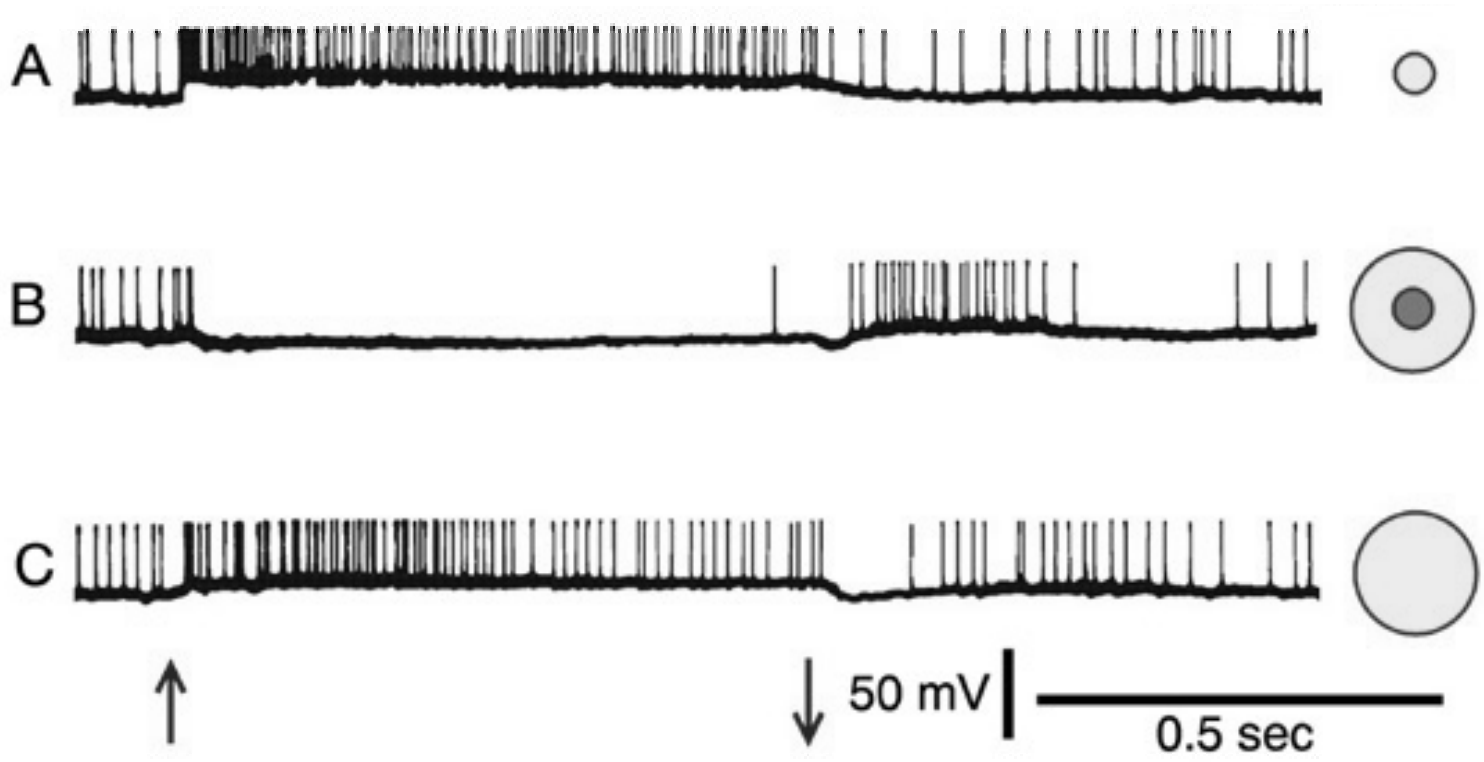
Classical receptive field (RF)





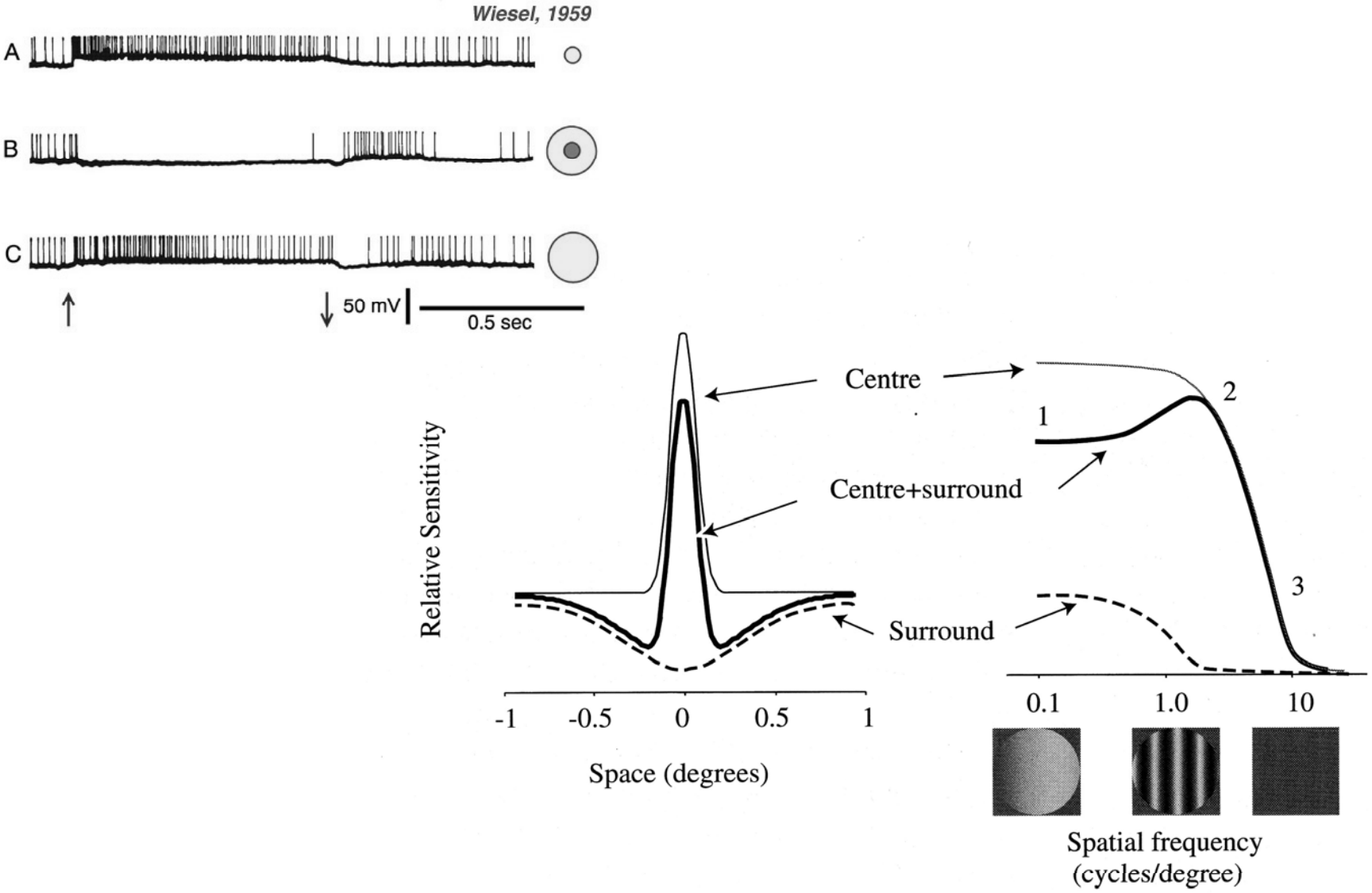
modified from Kuffler (1953), Fig. 6

Classical receptive field (RF) – Center/surround

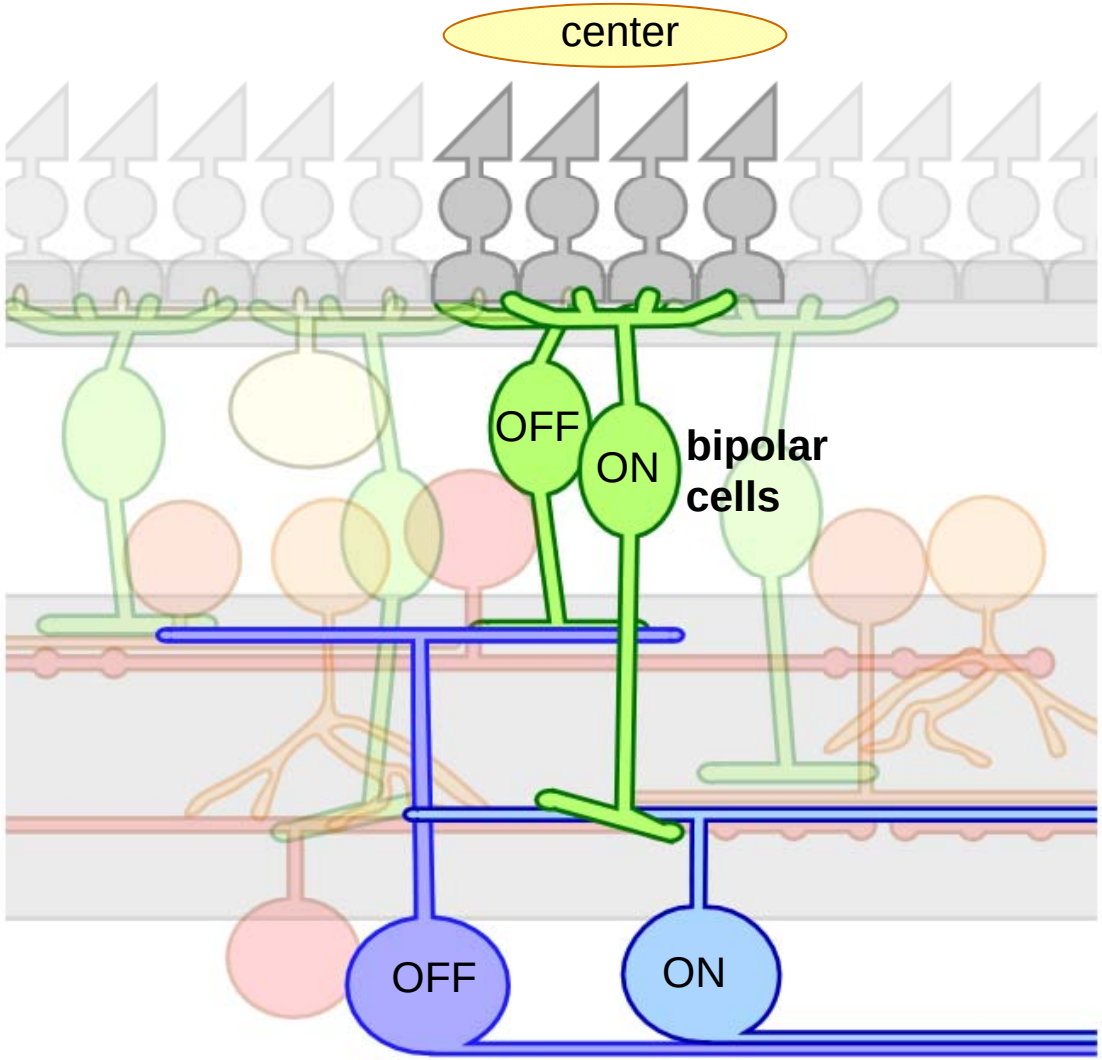


Wiesel (1959)

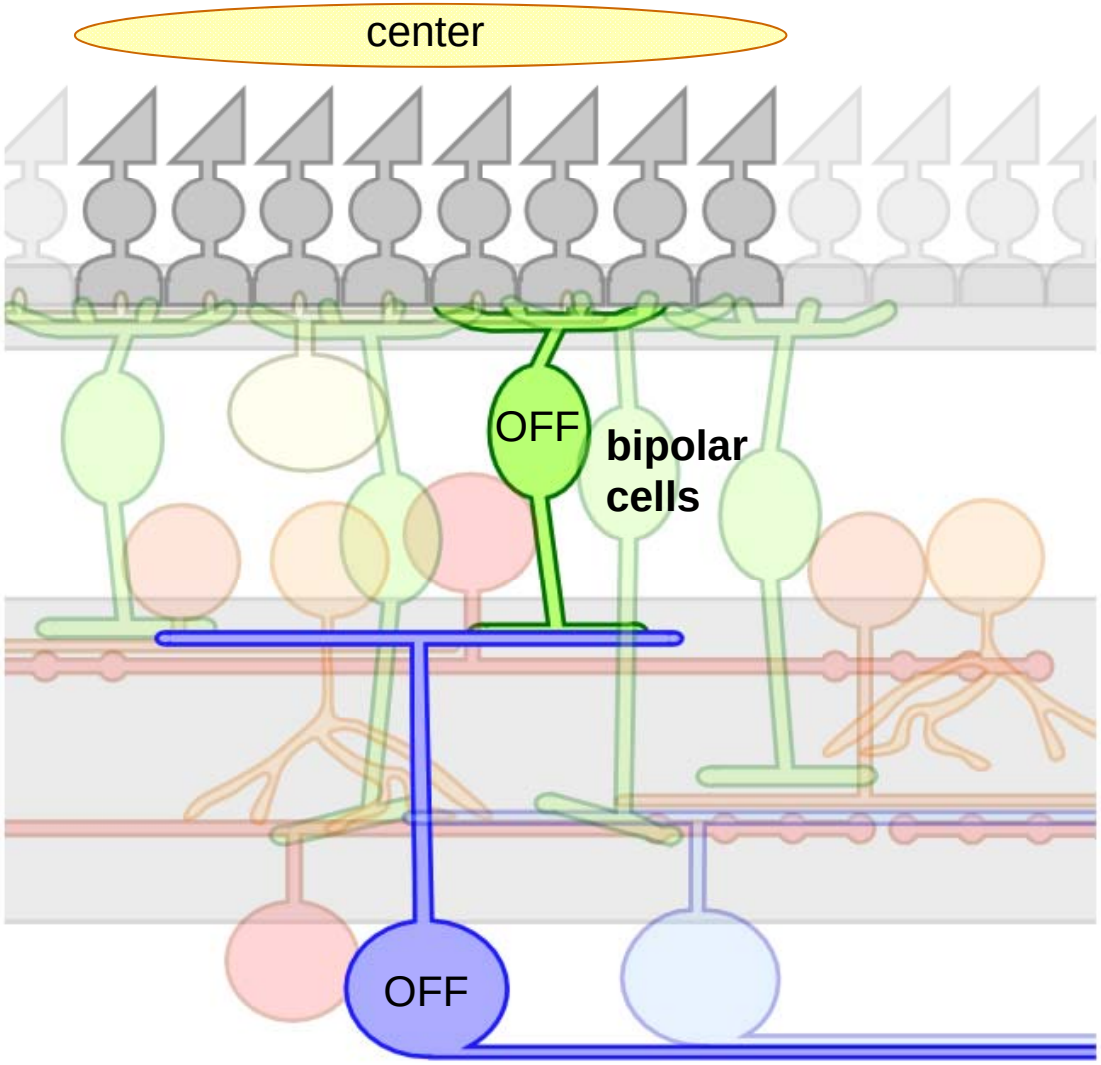
Classical receptive field (RF) – Center/surround



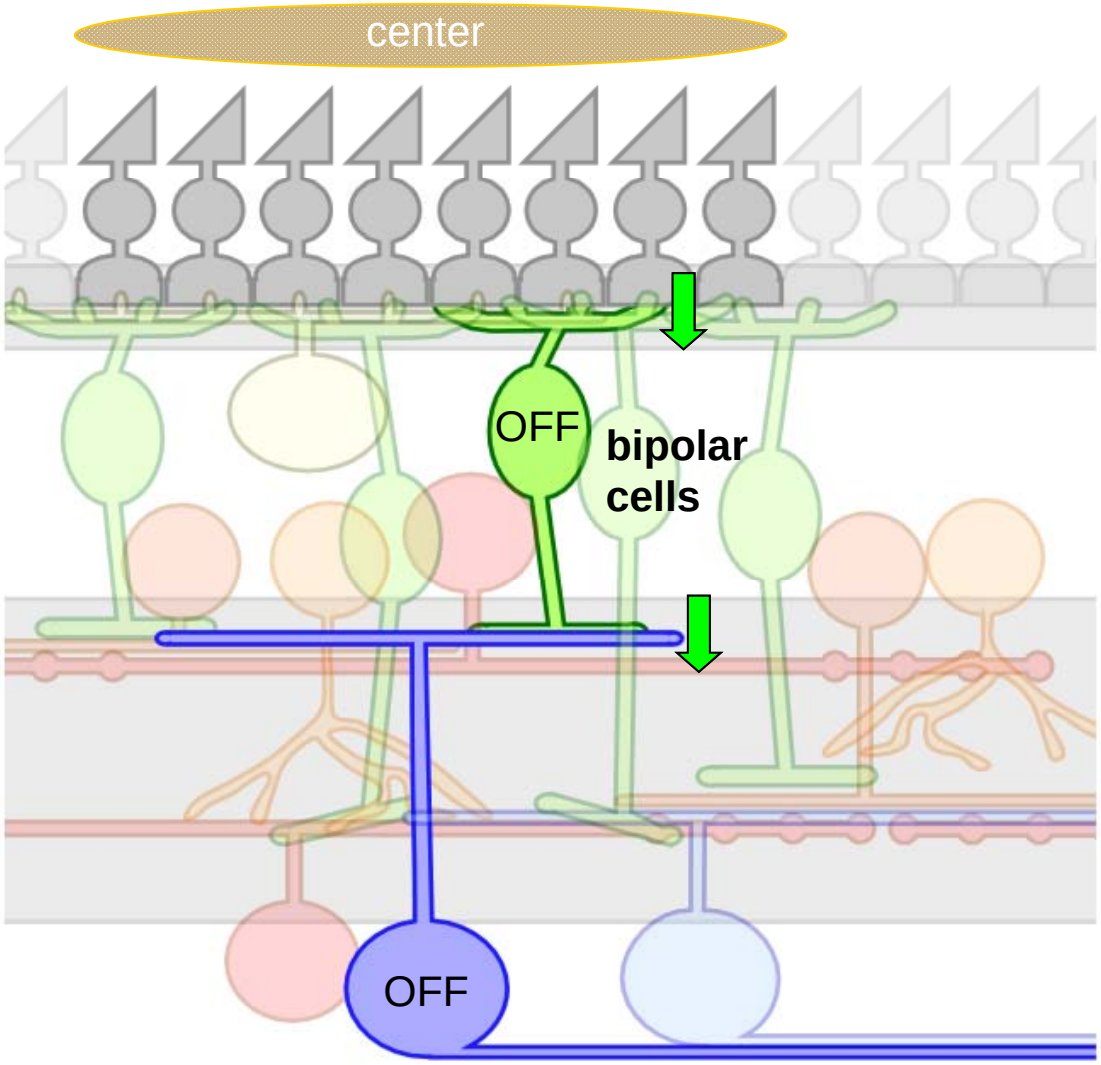
(Excitatory) vertical pathways …



(Excitatory) vertical pathways …



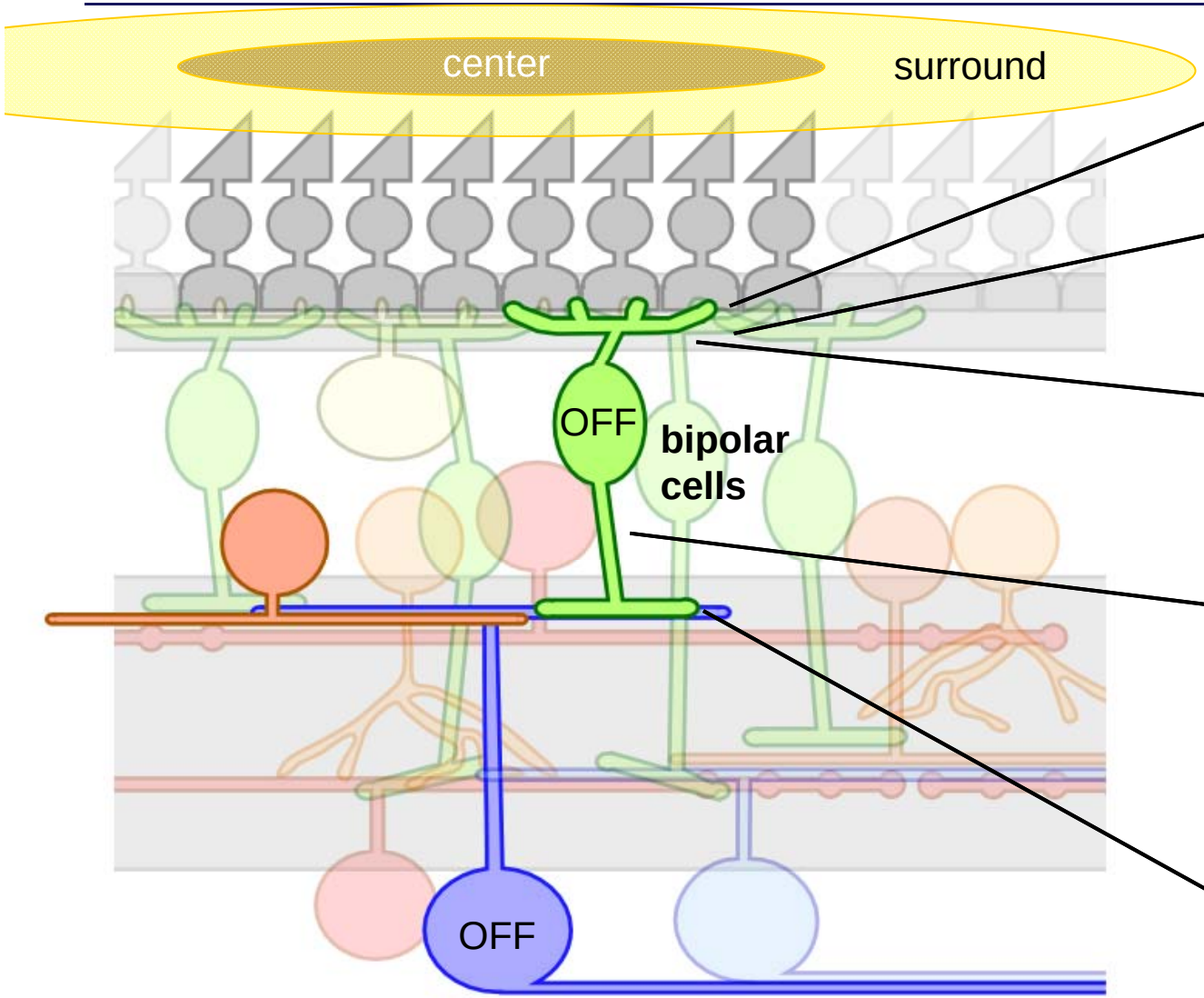
(Excitatory) vertical pathways …



excitation

inhibition

Modulation of bipolar cell signals



Dendritic glutamate receptor types

Inhibitory input in the OPL (feedback from horizontal cells)

Intracellular signaling (e.g. mGluR6 / G-protein cascade in ON bipolar cells)

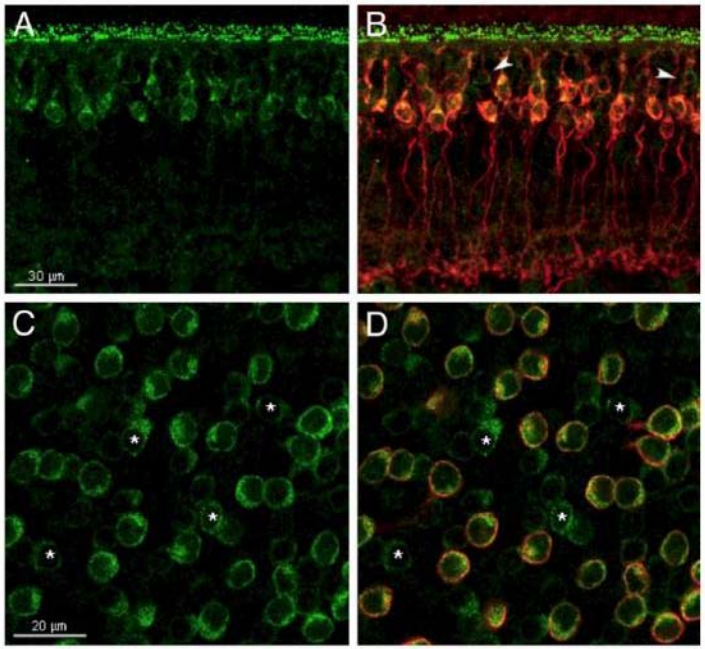
Intrinsic membrane properties (e.g. voltage-gated channels)

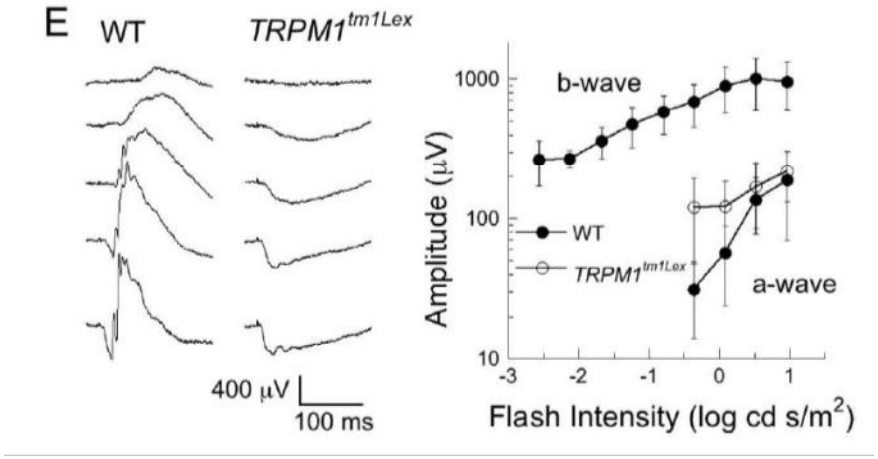
Inhibitory input in the IPL (feedback from amacrine cells)

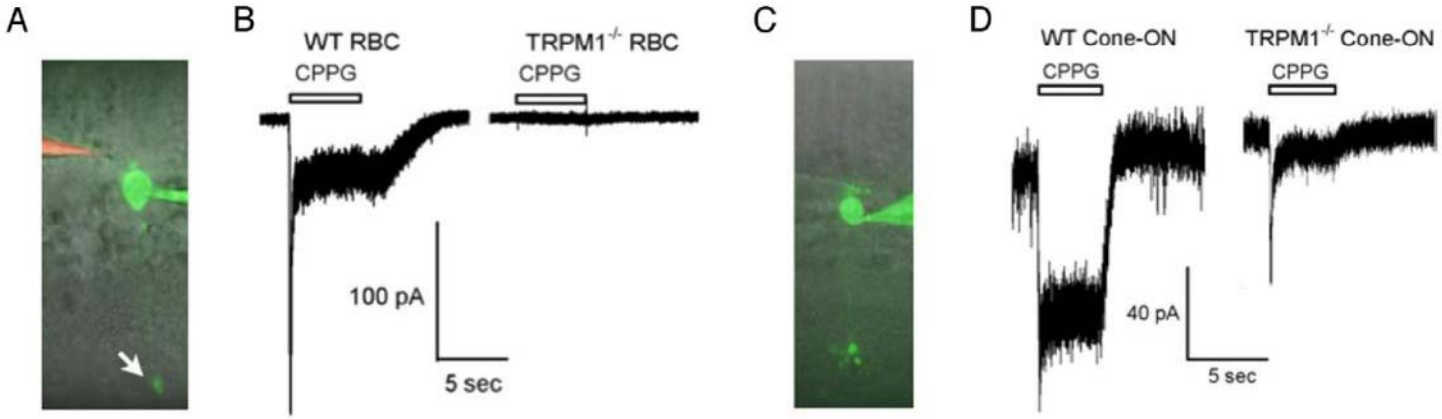
excitation

inhibition

Modulation of bipolar cell signals – TRP channels

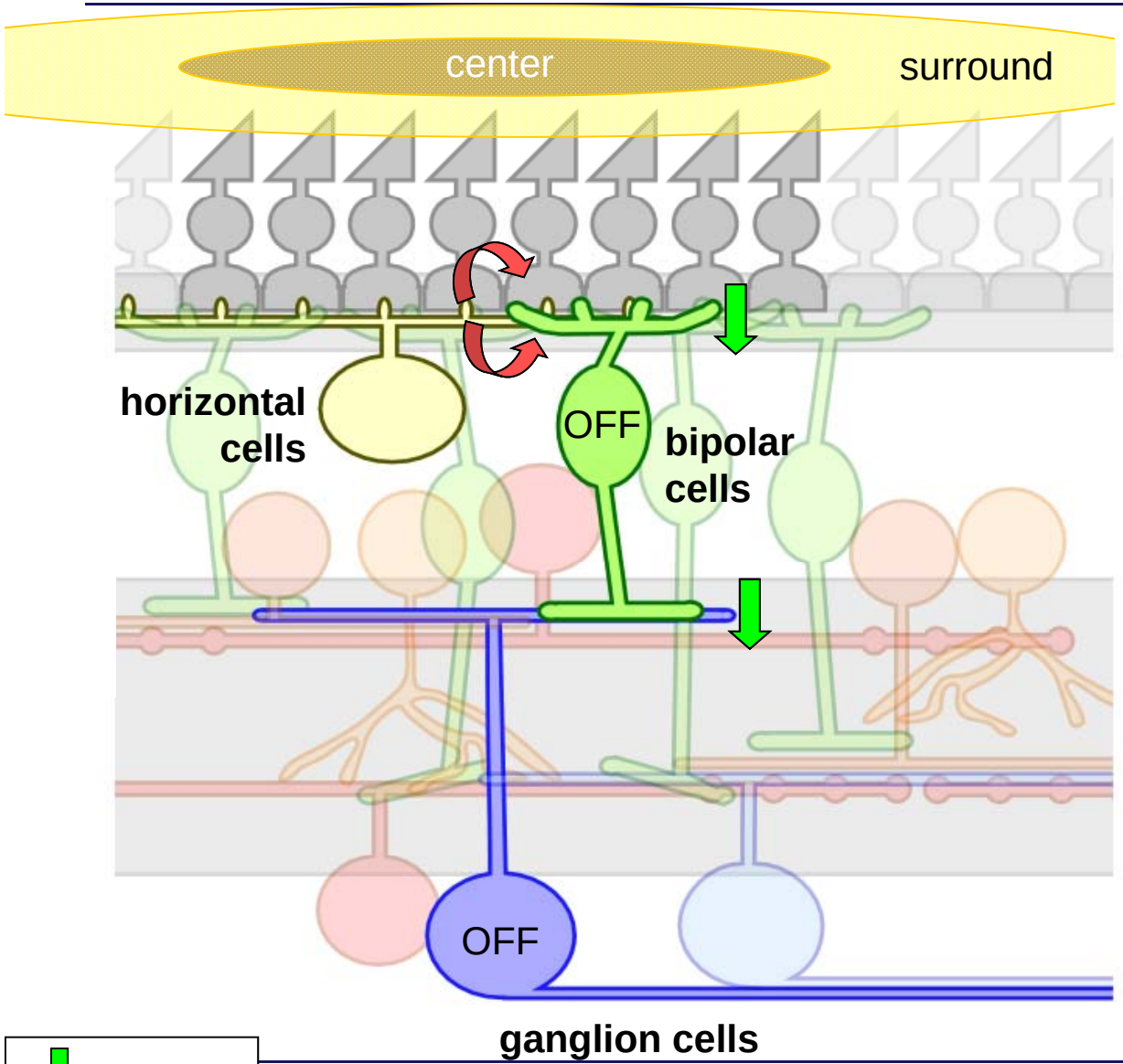






Shen et al., 2009, Morgans et al., 2009

(Inhibitory) lateral pathways – Interactions in the OPL



Horizontal cell function

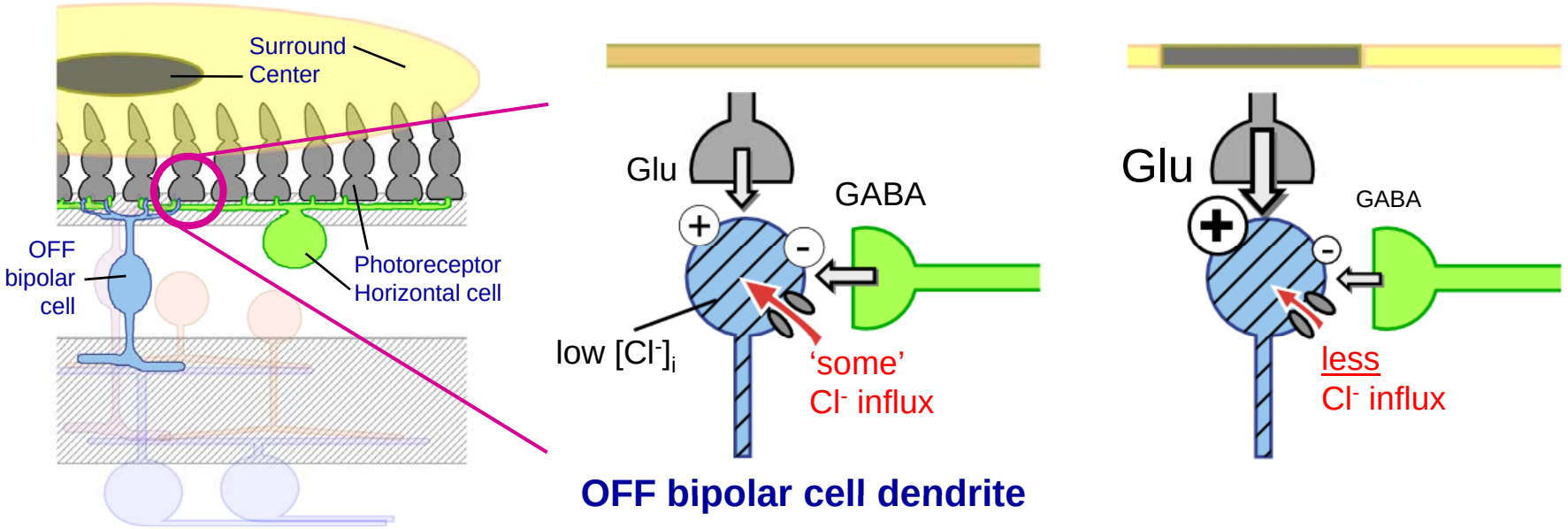
- measure background intensity (also: color opponancy in non-mammals)

- feedback to photoreceptors (GABA and/or ephatic)
- feedforward to bipolar cells (GABA, differential [Cl^-])

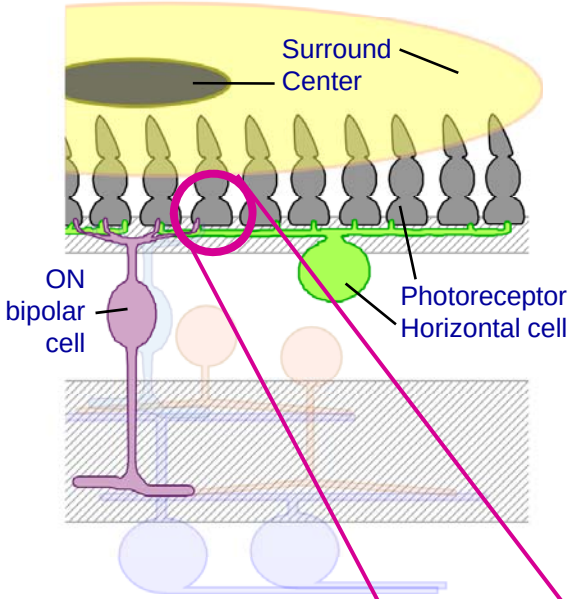
=> Surround

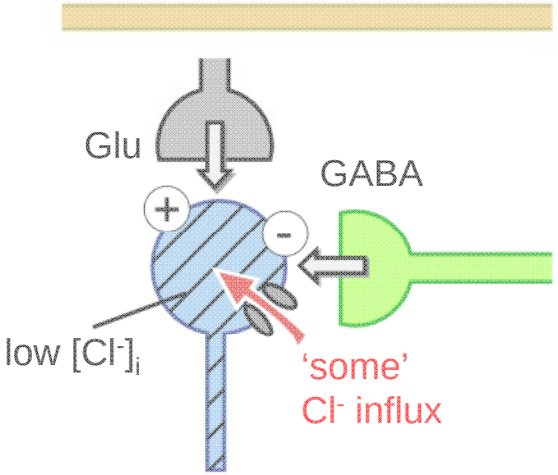
- coupled via gap junctions ... (modulated by retinoic acid, dopamine ...)

(Inhibitory) lateral pathways - Center-surround in bipolar cells

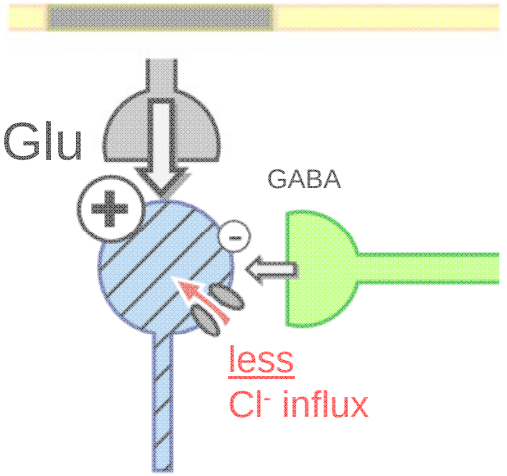


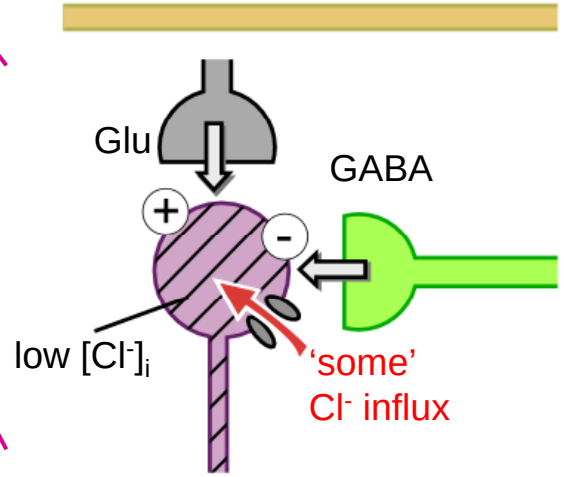
(Inhibitory) lateral pathways - Center-surround in bipolar cells



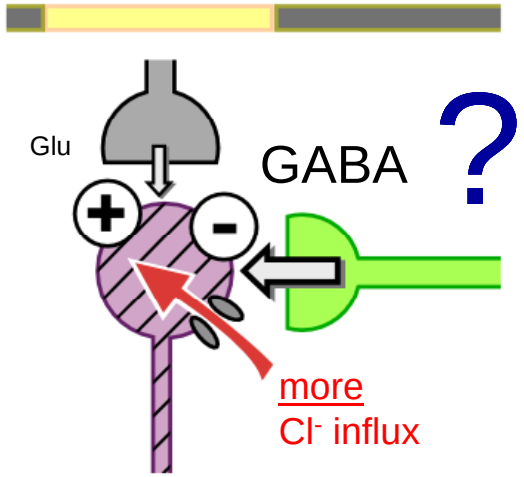


OFF bipolar cell dendrite

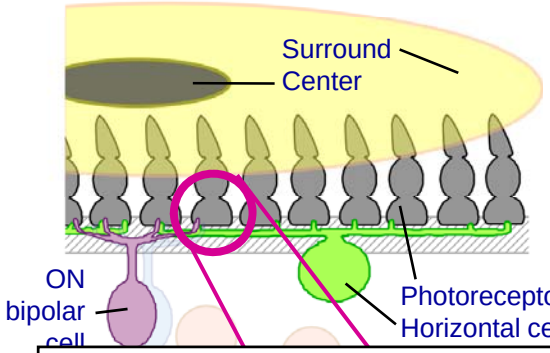


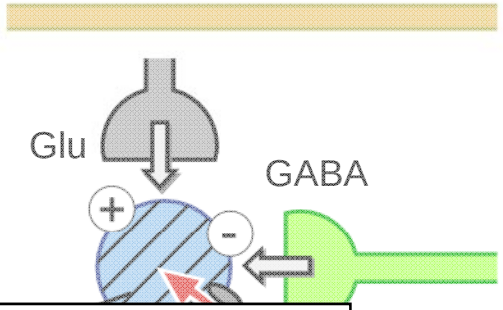


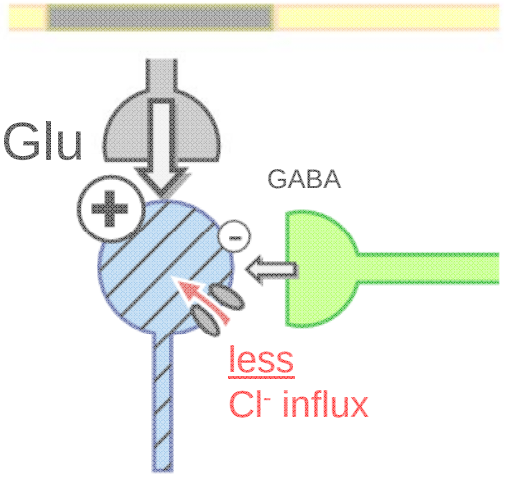
ON bipolar cell dendrite

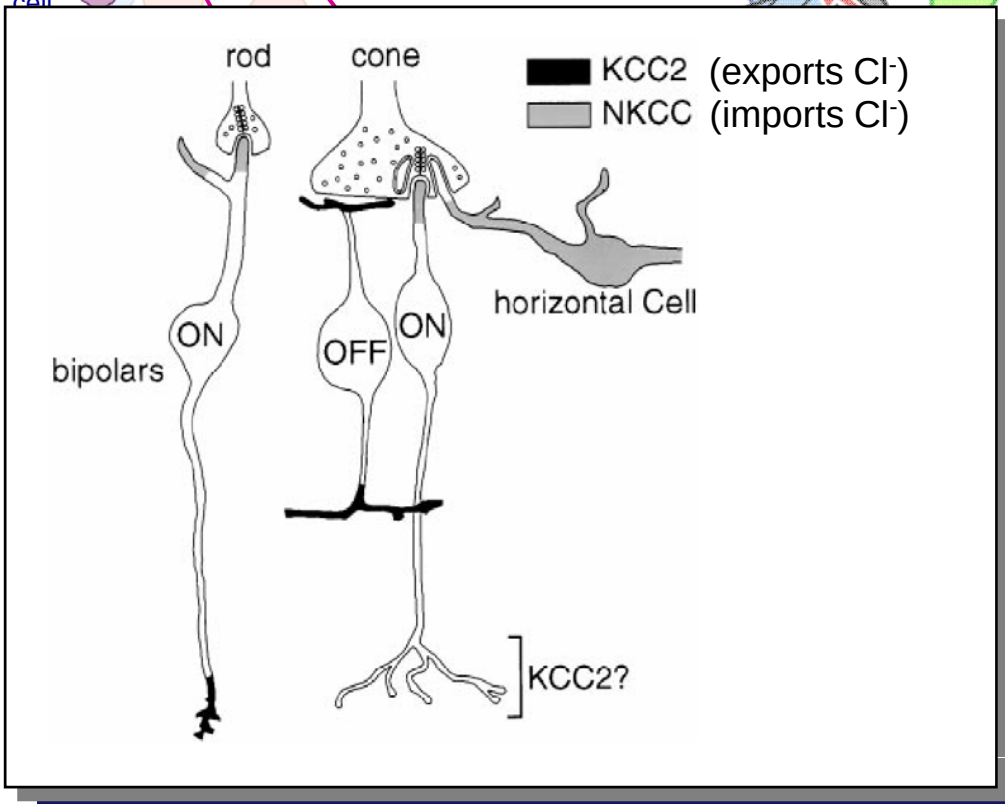


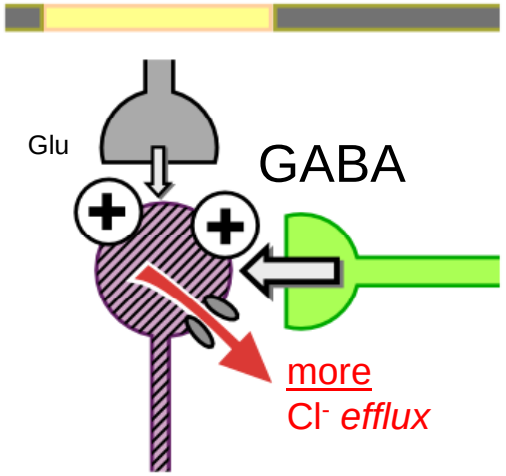
(Inhibitory) lateral pathways - Center-surround in bipolar cells





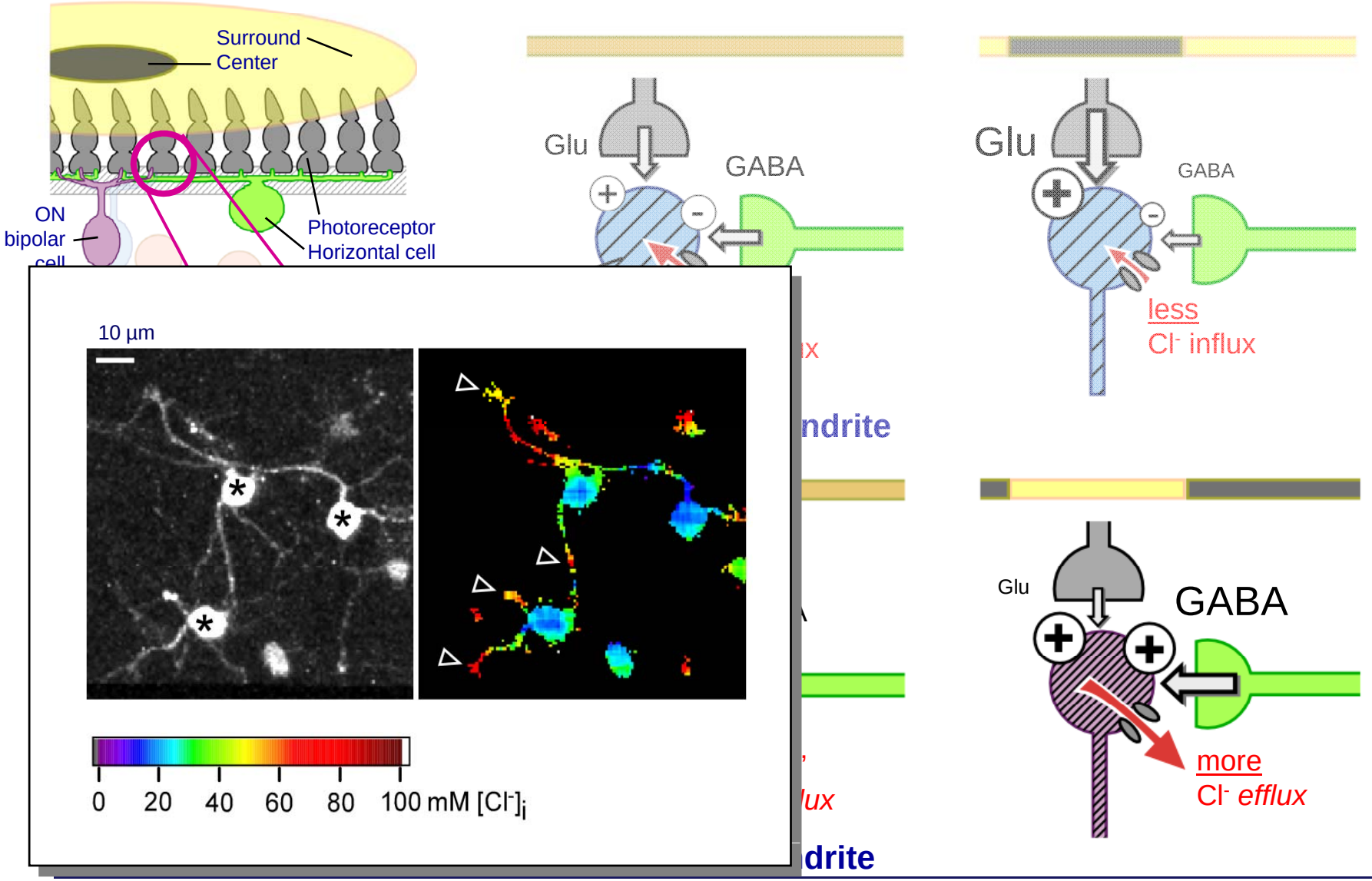






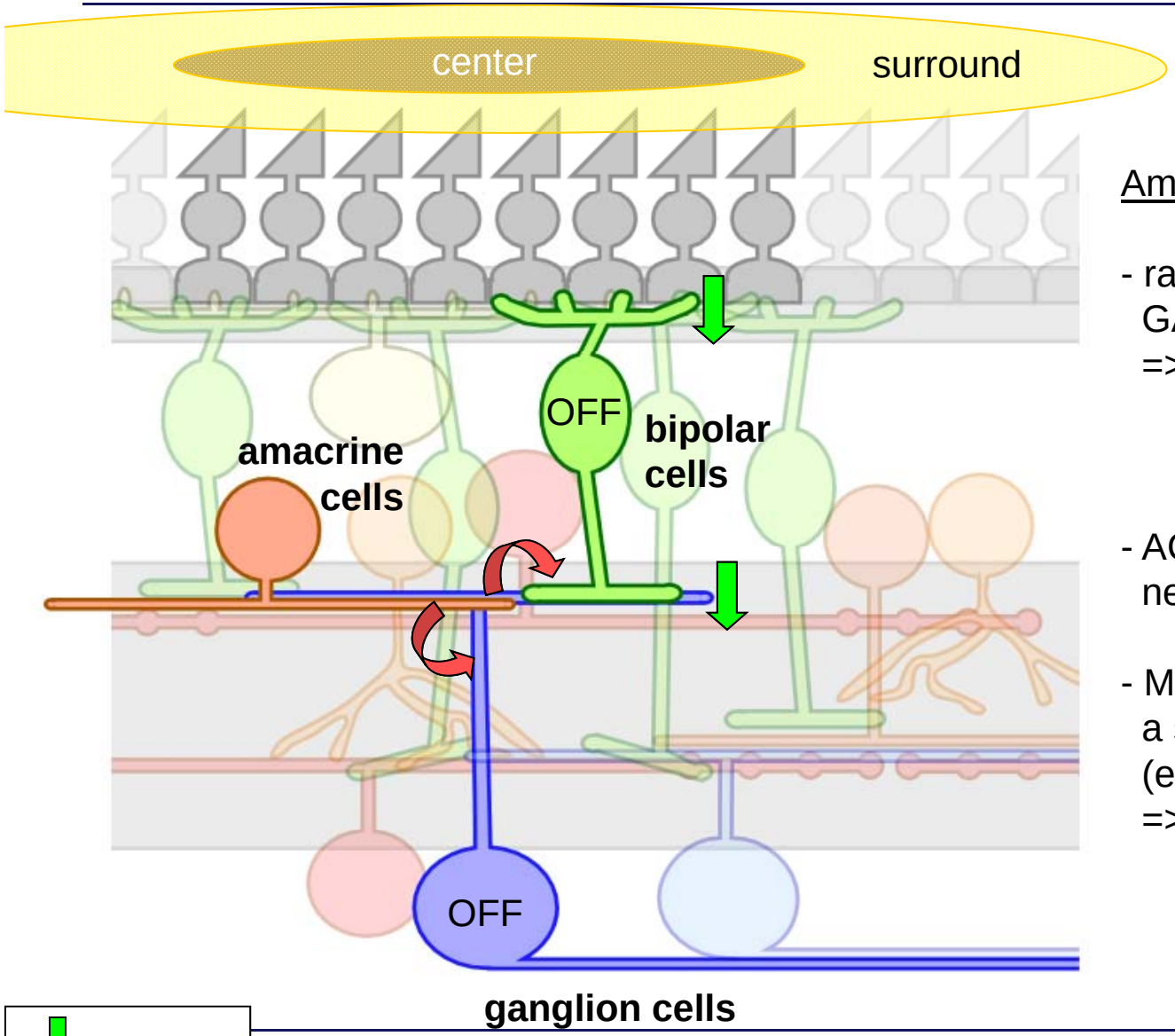
Vardi et al. (2000)

(Inhibitory) lateral pathways - Center-surround in bipolar cells



Dübel et al. (2006)

(Inhibitory) lateral pathways – Interactions in the IPL



Amacrine cell function

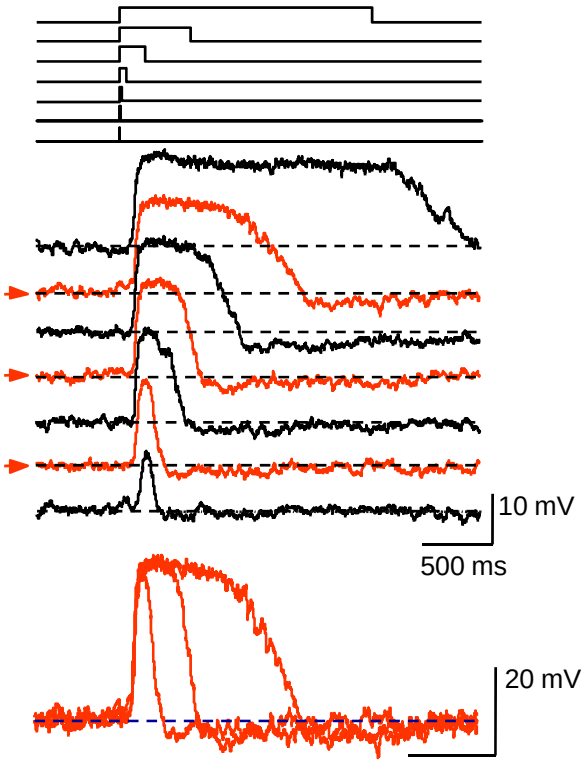
- rapid feedback/-forward via GABA and glycine
  => contribute to surround, temporal response shape
  …

- ACs form complex (serial) networks

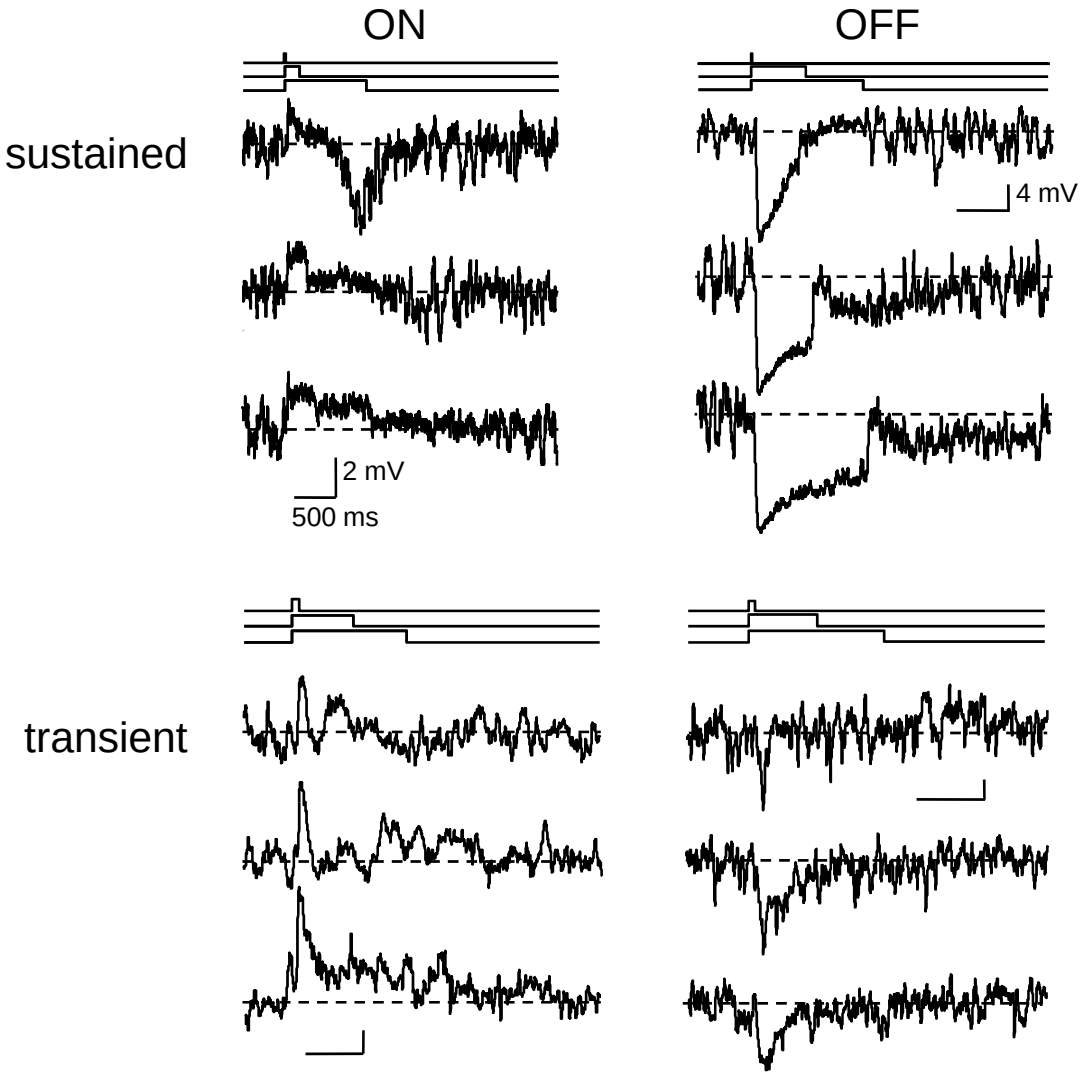
- Many ACs co-release a second transmitter (e.g. peptides, dopamine, etc)
  => modulatory effects

Bipolar cells – Voltage responses to light

Rod bipolar cell

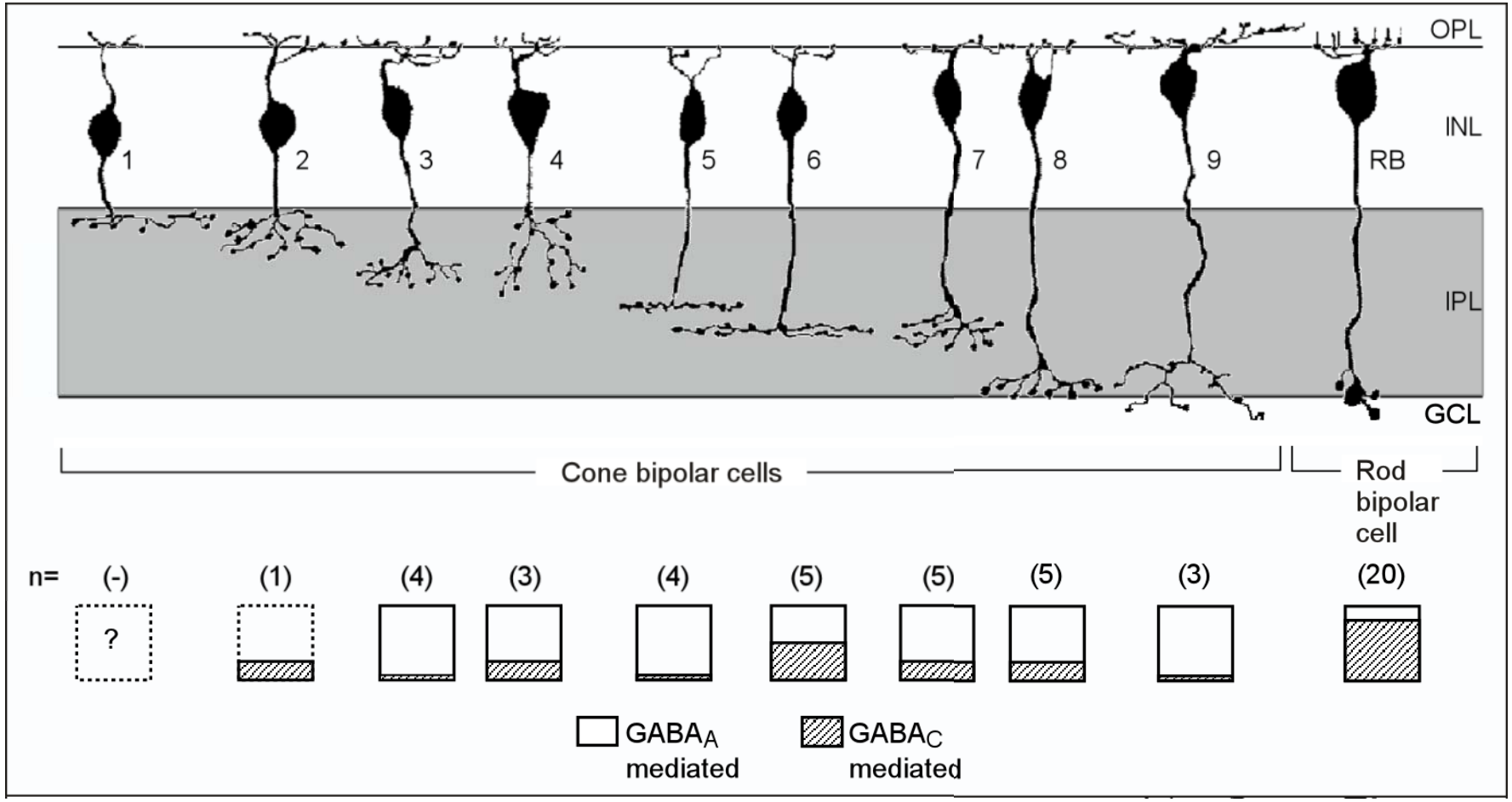


Cone bipolar cells



Euler & Masland (2000)

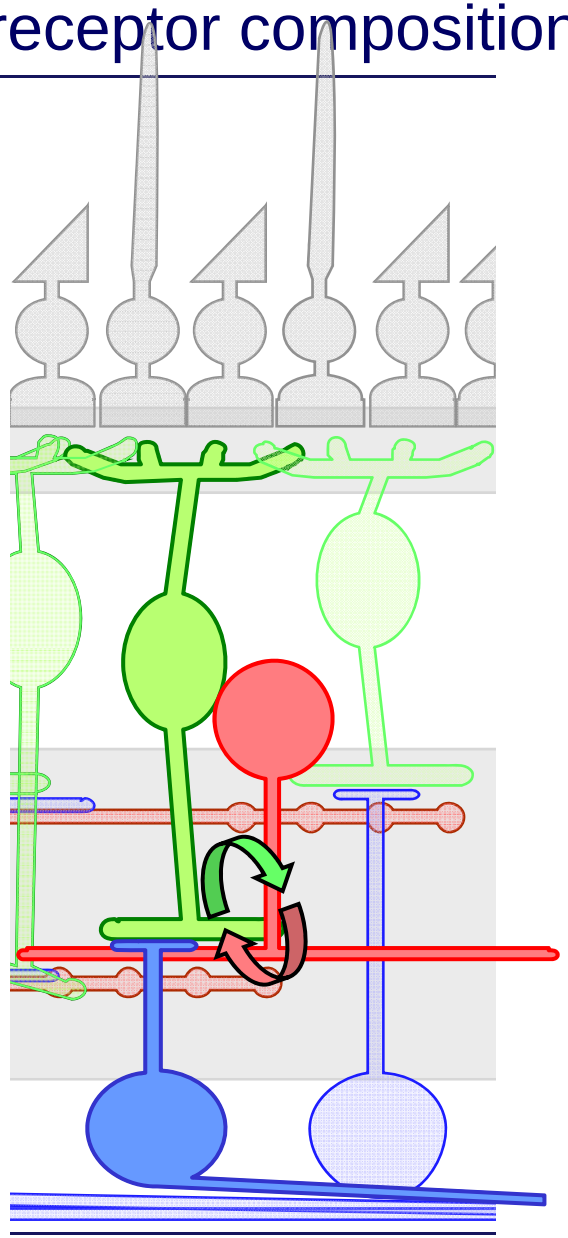
GABA receptor contribution in rat bipolar cells

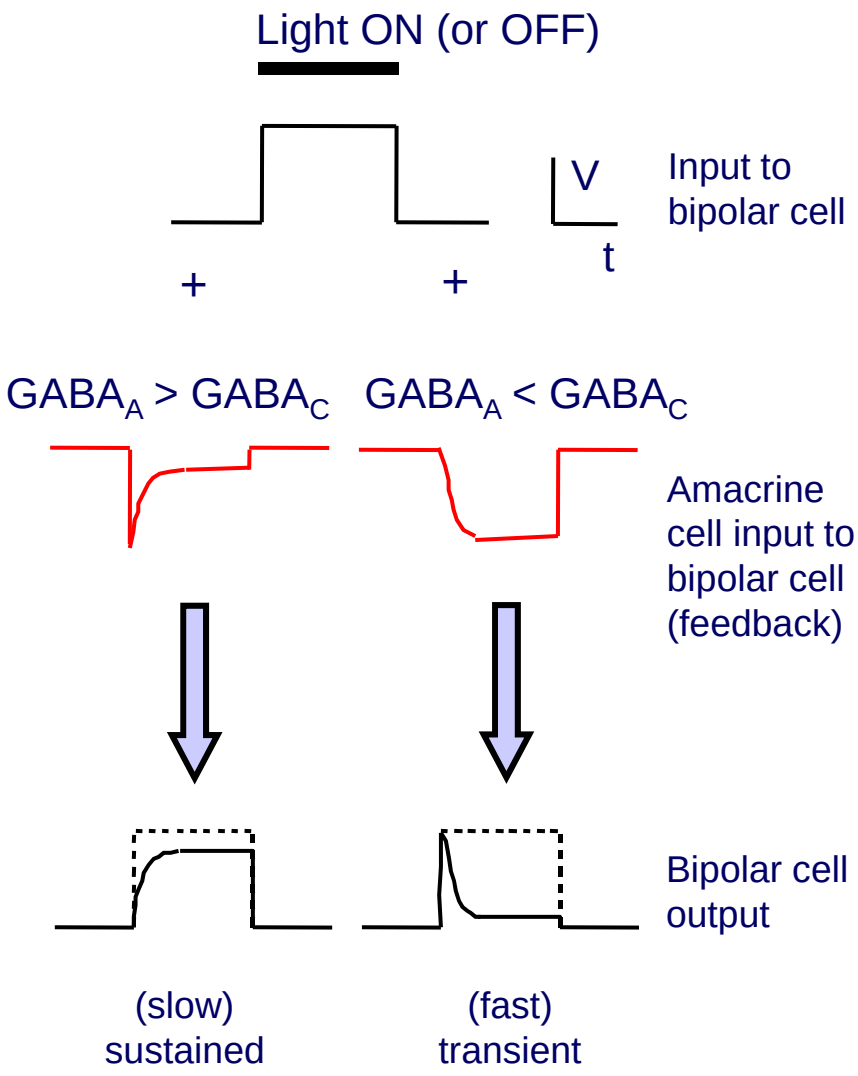


Euler & Wässle (1998)

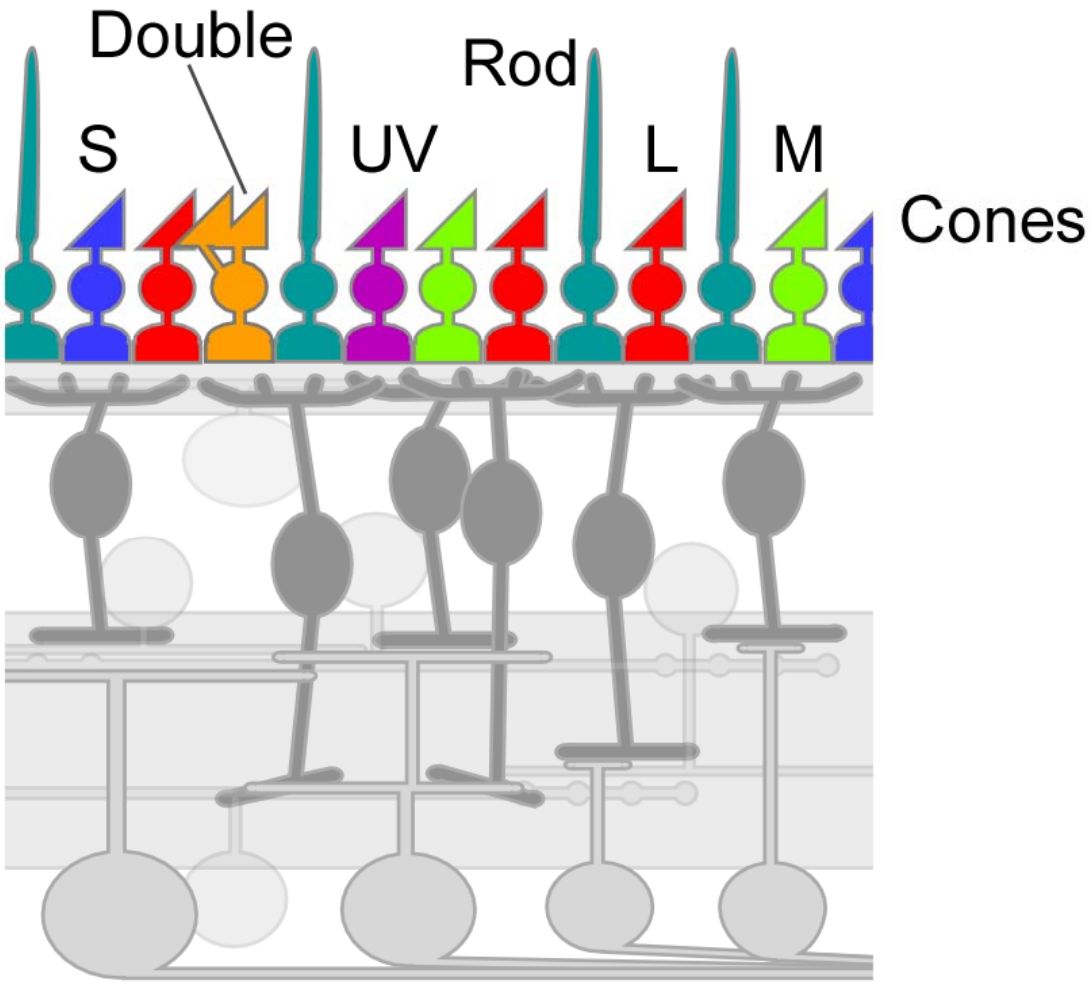
GABA receptor composition shapes the responses

feed-back inhibition





Photoreceptor types in “ancient” retina...



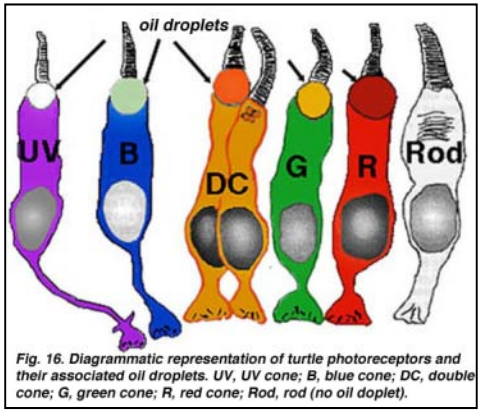
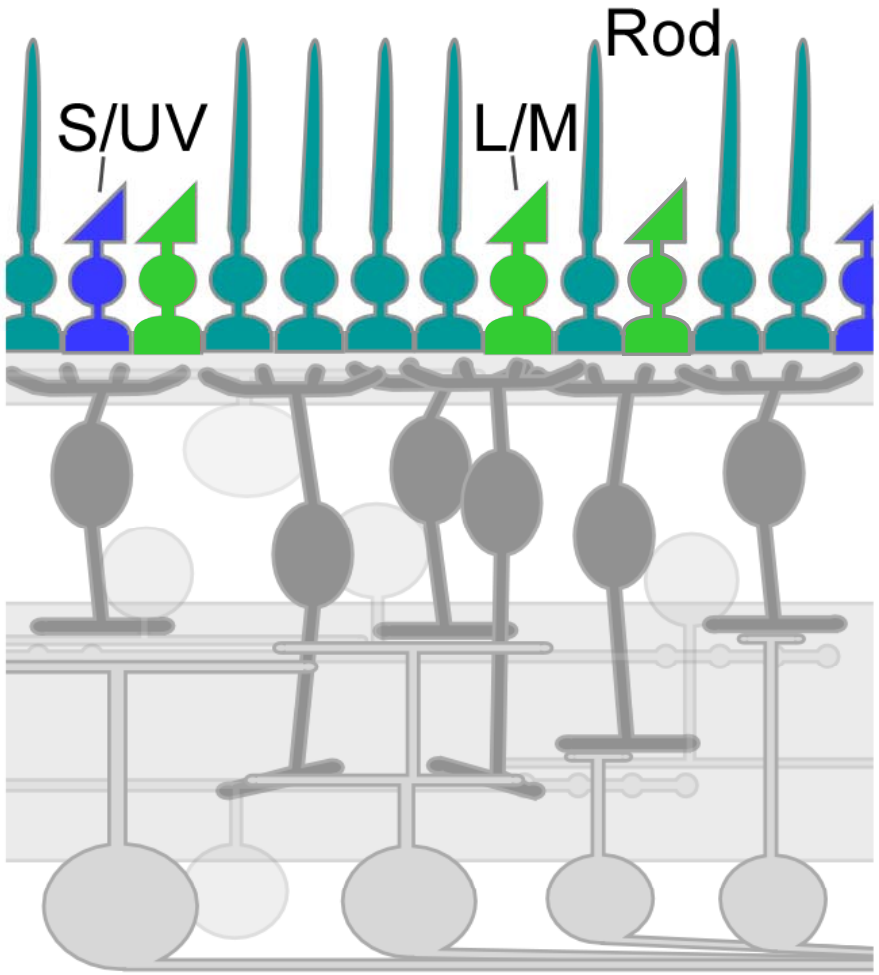
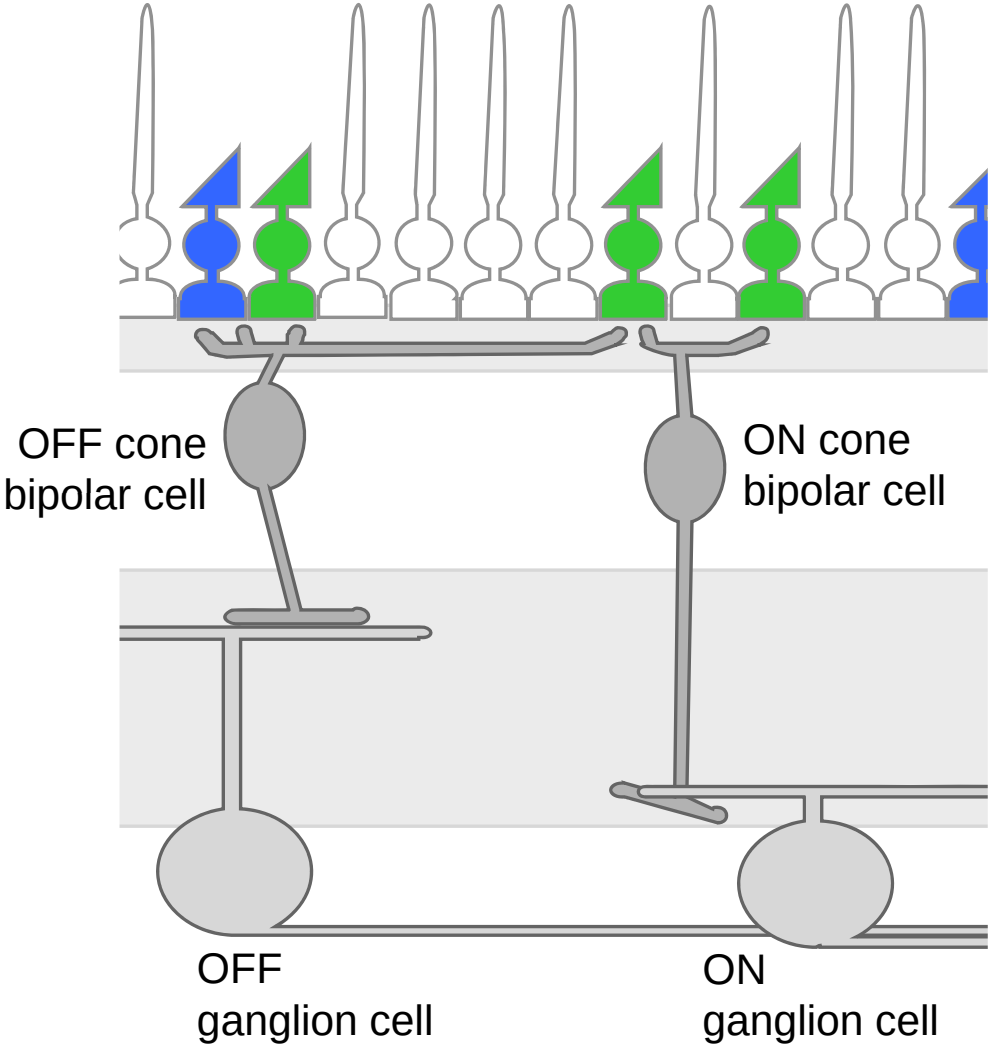


Fig. 16. Diagrammatic representation of turtle photoreceptors and their associated oil droplets. UV, UV cone; B, blue cone; DC, double cone; G, green cone; R, red cone; Rod, rod (no oil doplet).

Photoreceptors in a ‘standard’ mammal (= dichromatic)

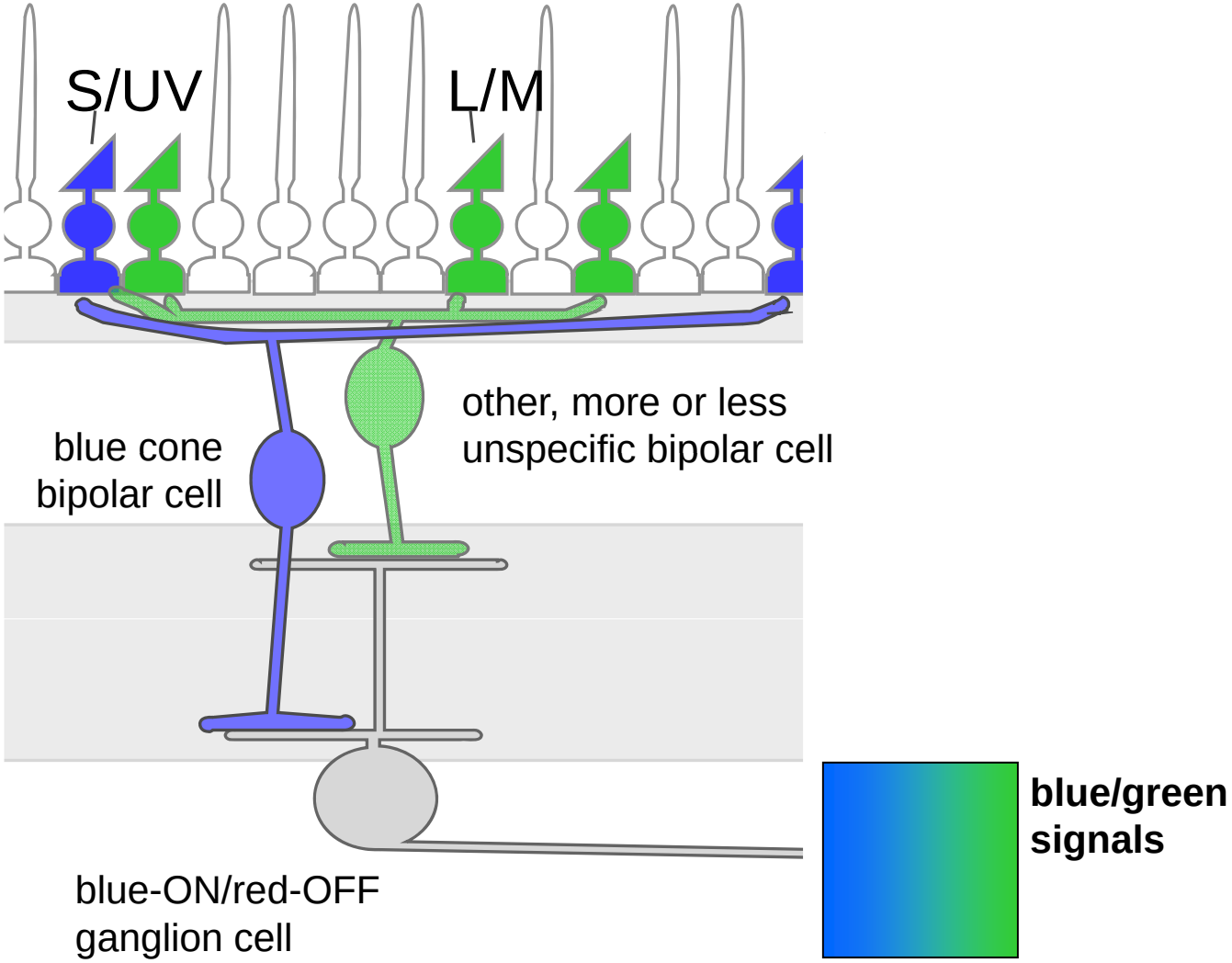


ON/OFF pathways – Standard version or “day light”

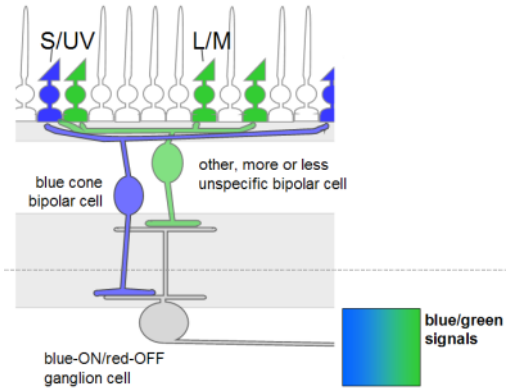


Luminance (“daylight; photopic range)

Color vision in dichromatic mammals (**blue/green pathway**)



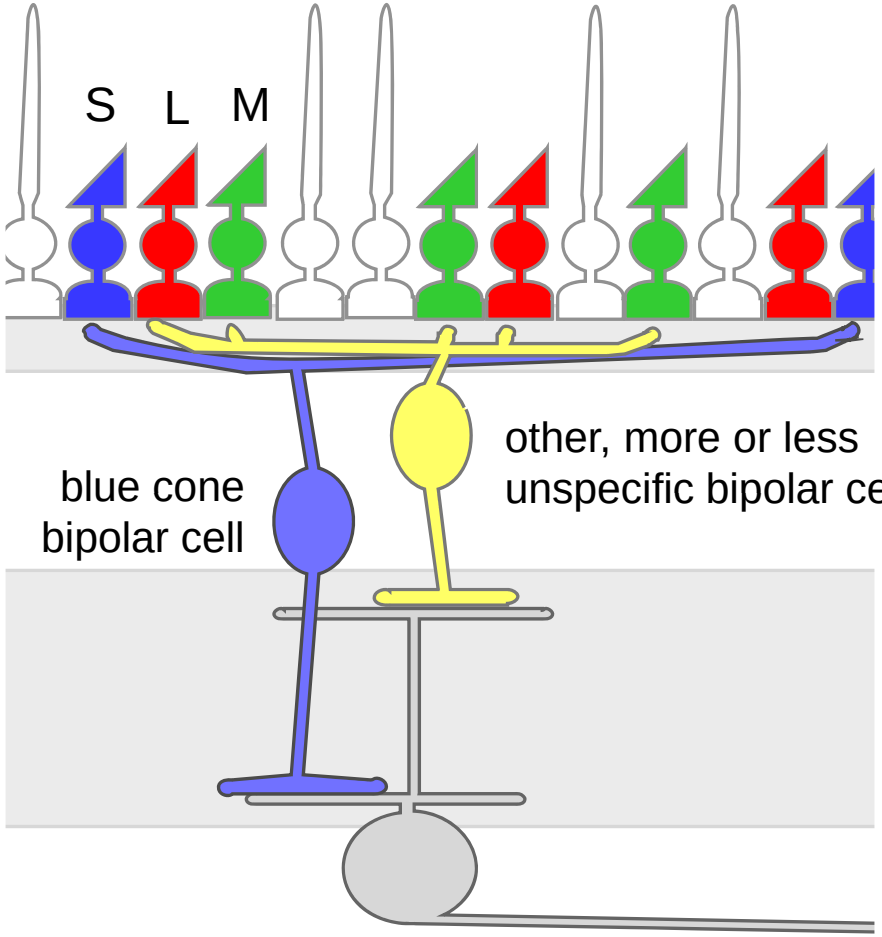
Color vision in dichromatic mammals (**blue/green pathway**)

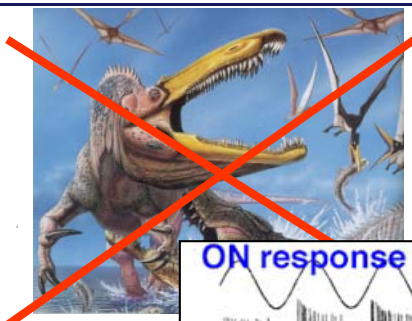


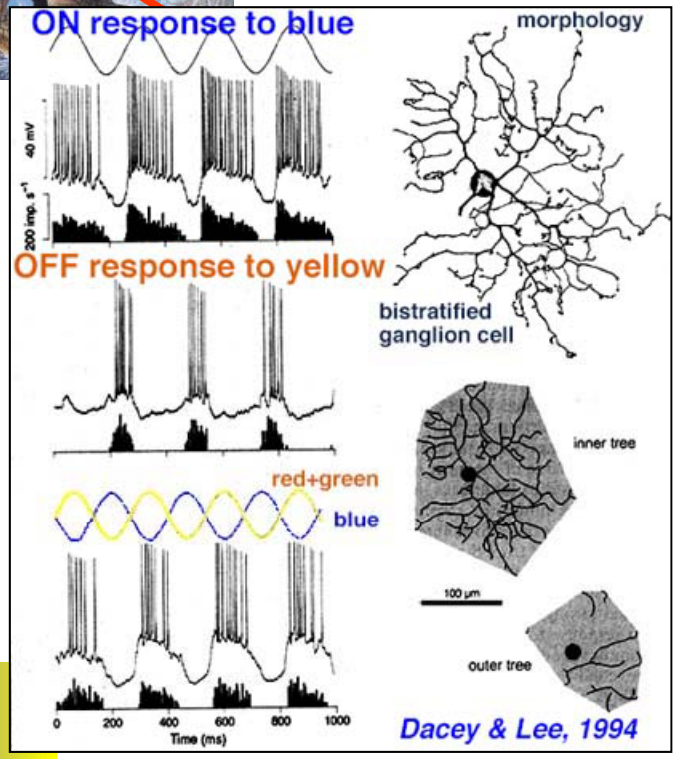
Carrol, Neitz & Neitz (unpublished)

Trichromatic mammals (=old-world primates)

Blue/yellow pathway



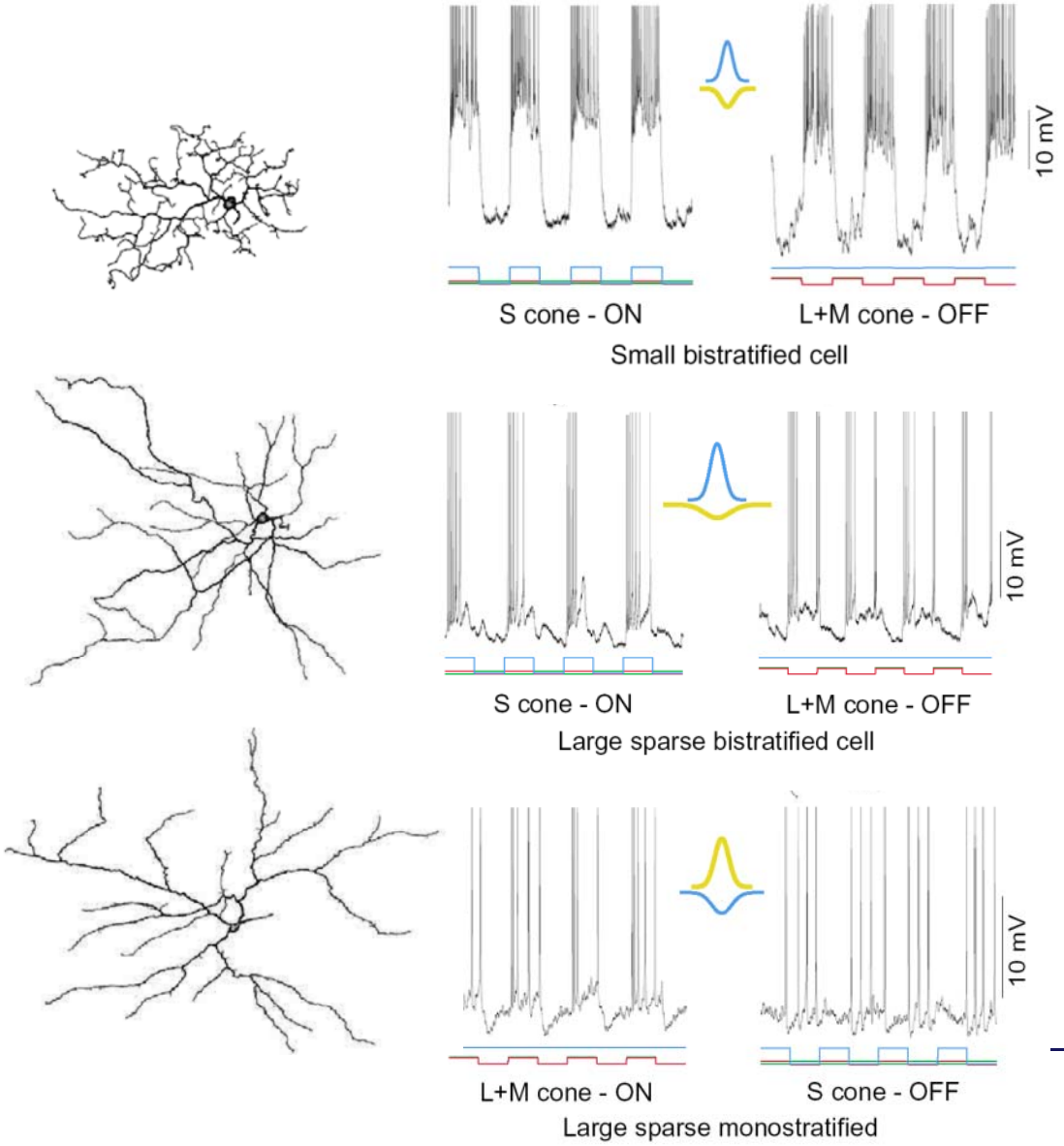




blue/yellow signals

Trichromatic mammals (=old-world primates)

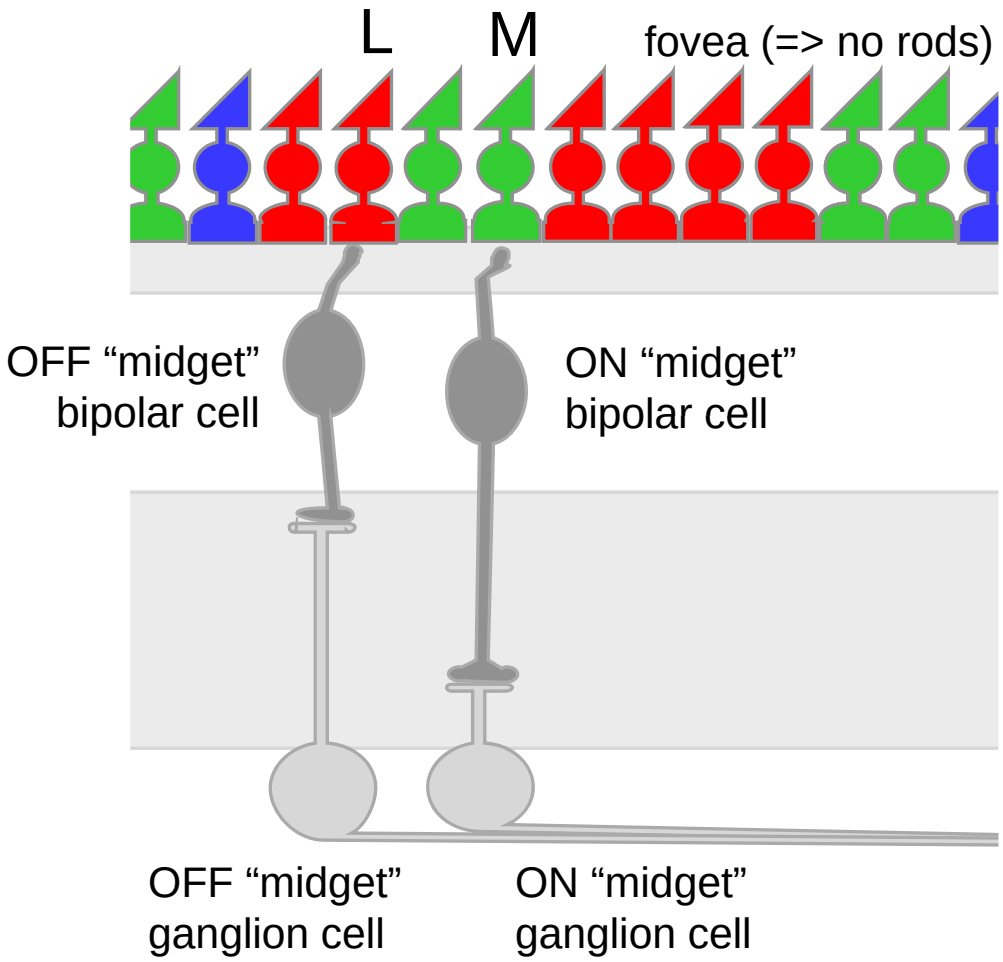
Blue/yellow pathway



(Dacey & Packer, 1993)

Trichromatic mammals (=old-world primates)

Red/Green pathway (='midget' hypotheses)



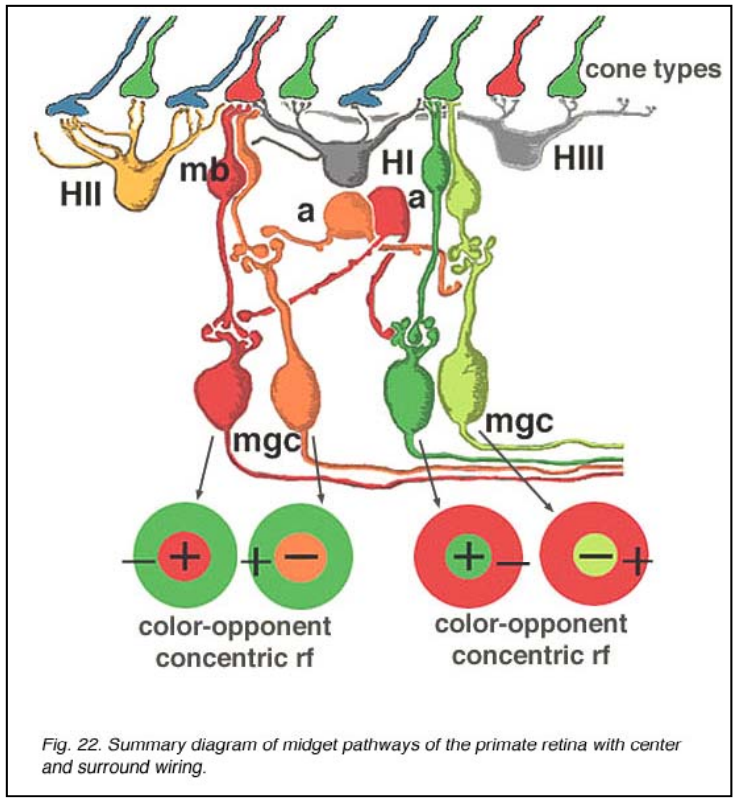
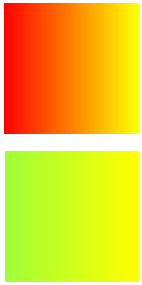


Fig. 22. Summary diagram of midget pathways of the primate retina with center and surround wiring.



red/yellow and green/yellow signals

Some conclusions

Parallel channels	(using limited coding capacity, separation of extracted features => divergence of signals)
ON/OFF	(as example for channels, to widen sensitivity range, allows coding of intensity relative to mean)
Rod/cone system	(‘new inventions’ piggy-back on older systems, different ‘hardware’ for different tasks/conditions convergence)
Receptive fields	(antagonistic center/surround organization or more complex features, e.g. “local edge detector”, direction- or orientation selective; extra-classical RFs