

Retina - a perfect model for studies of the central nervous system

Olivia [Dumitrescu] Auferkorte

Max-Planck-Institut
for Brain Research

-Neuroanatomy-

Frankfurt/ Main, Germany



Talk overview

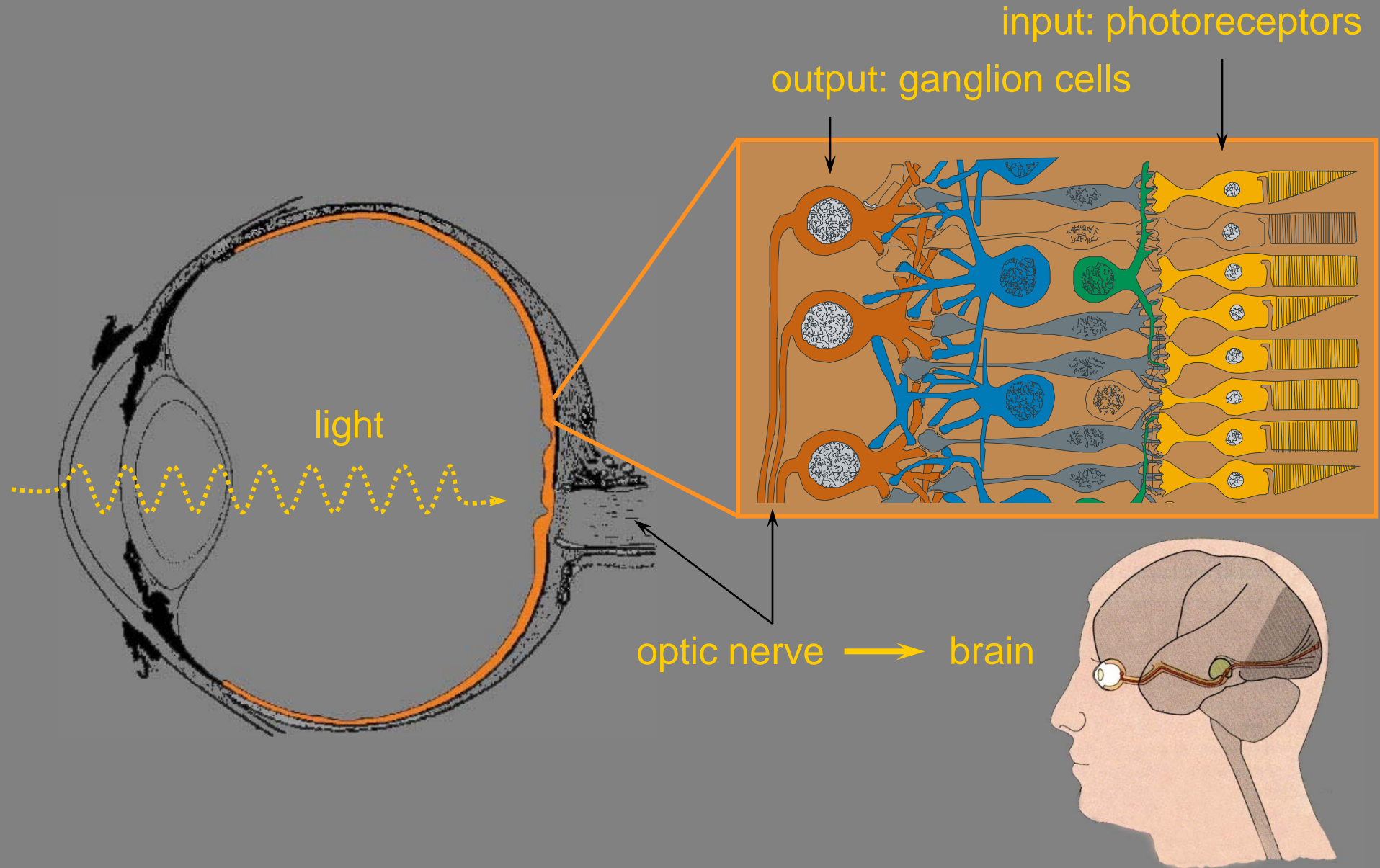
Anatomy of the mammalian retina

- gross anatomy
- whole-mount retina and retinal slices
- retinal cell types and neurotransmitters

Physiology of the retina & methods for investigating it

- glutamate receptors of inhibitory amacrine interneurons
- melanopsin-containing ganglion cell photoreceptors
- direction selectivity of motion

Brief anatomy of vision



Neural computations in the retina

Cell
PRESS

Neuron
Review

Eye Smarter than Scientists Believed: Neural Computations in Circuits of the Retina

Tim Gollisch^{1,2} and Markus Meister^{3,*}

¹Max Planck Institute of Neurobiology, Visual Coding Group, Am Klopferspitz 18, 82152 Martinsried, Germany

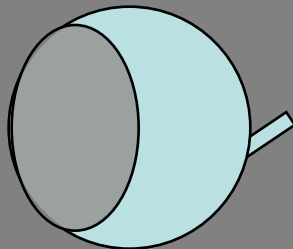
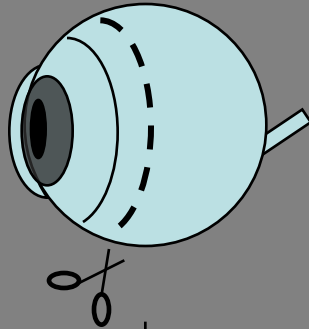
²Bernstein Center for Computational Neuroscience, Munich, Germany

³Harvard University, Department of Molecular and Cellular Biology and Center for Brain Science, 52 Oxford Street, Cambridge, MA 02138, USA

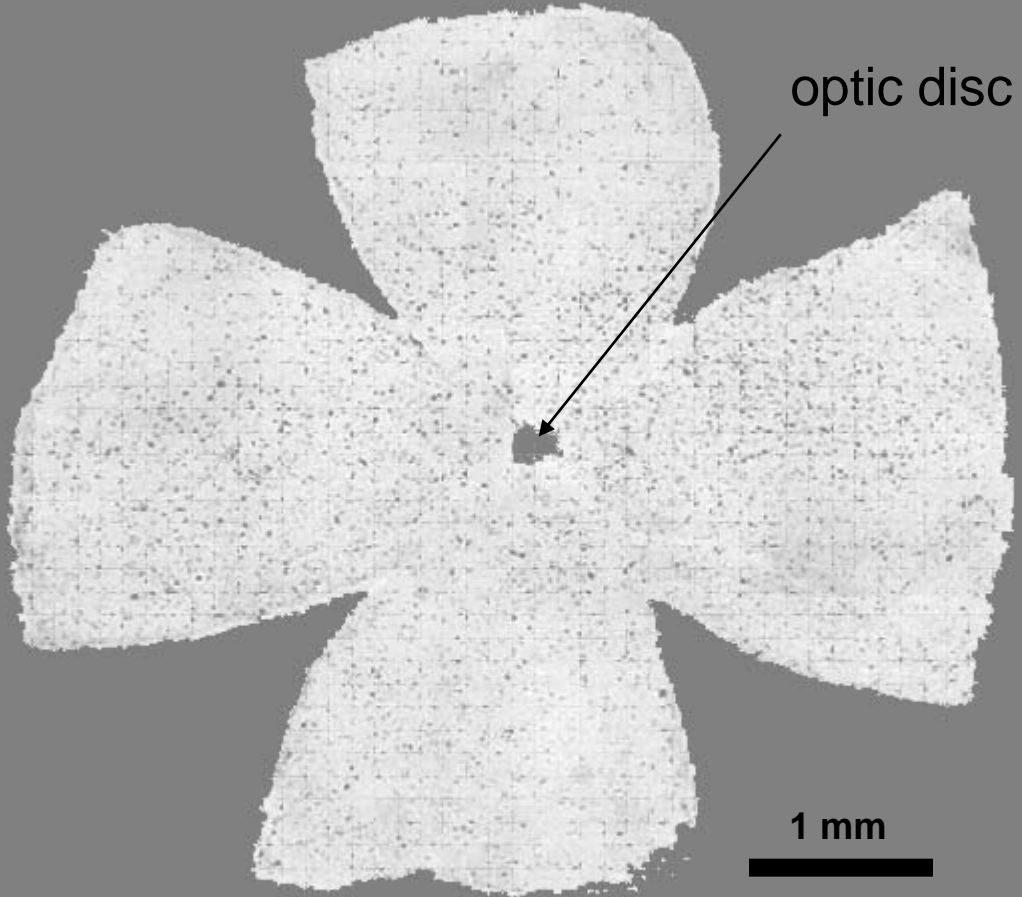
*Correspondence: meister@fas.harvard.edu

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Whole flat mount of rodent retina



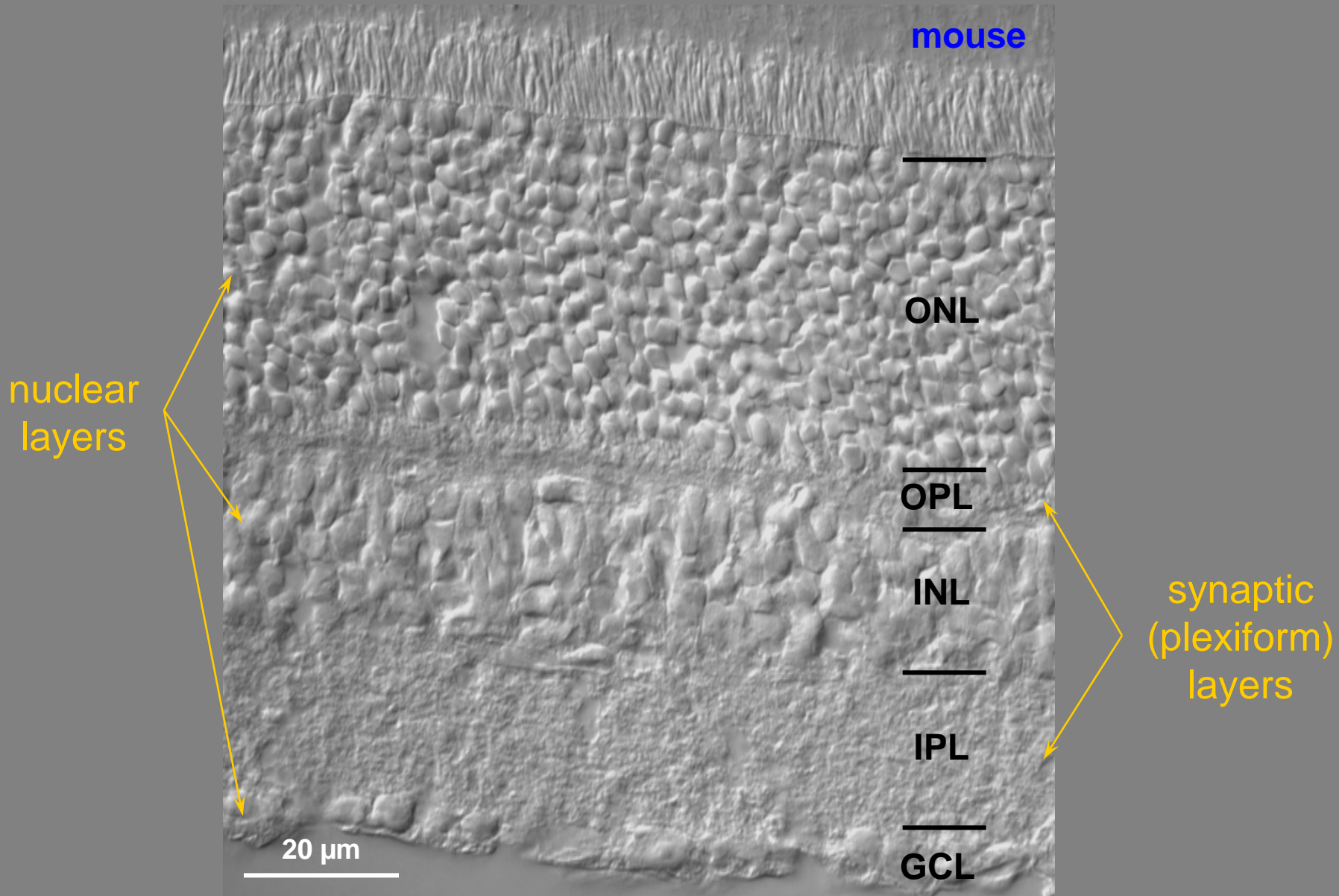
eyecup



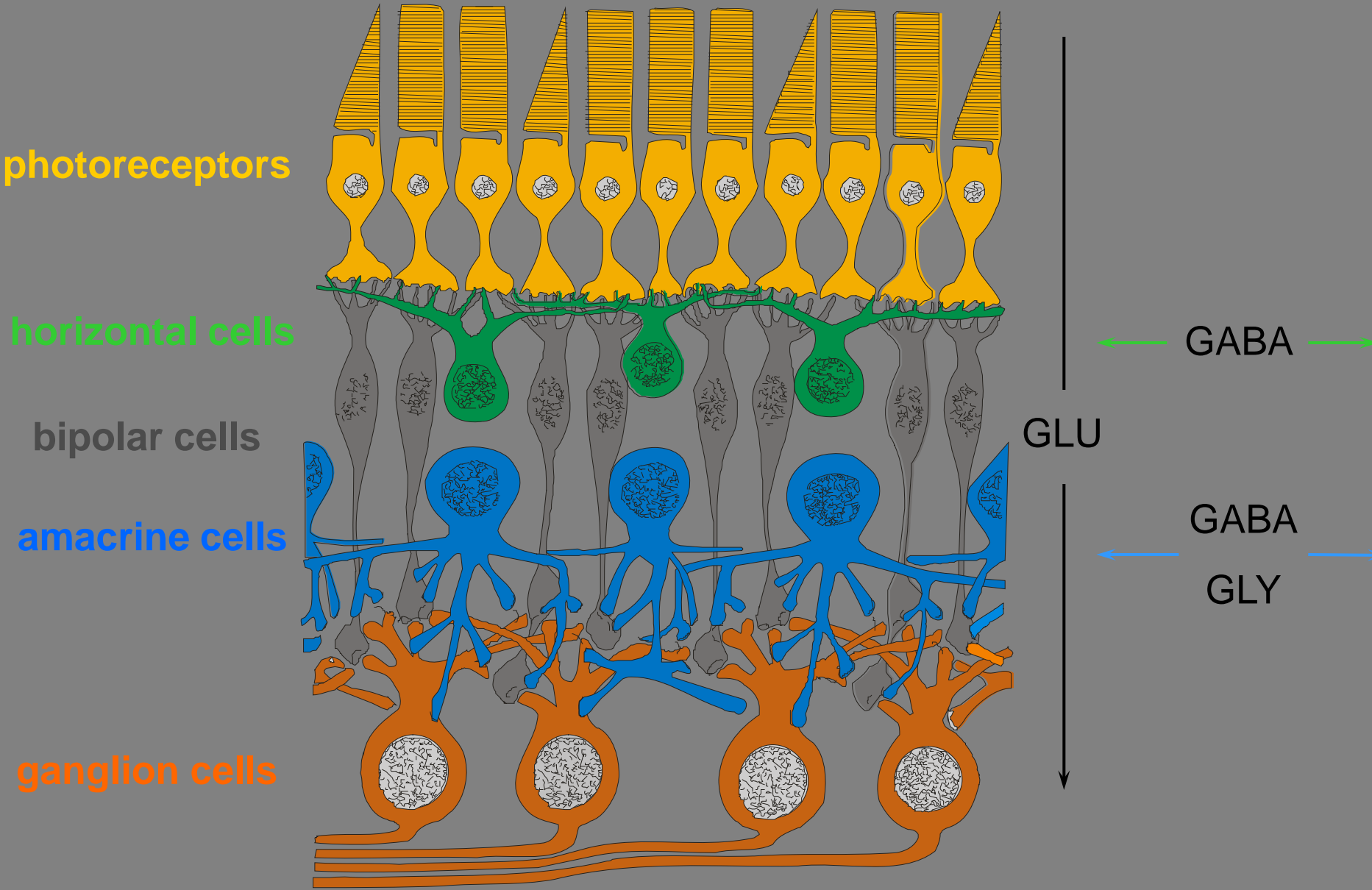
optic disc

1 mm

Mammalian retina in cross-section



Excitatory and inhibitory pathways in the retina



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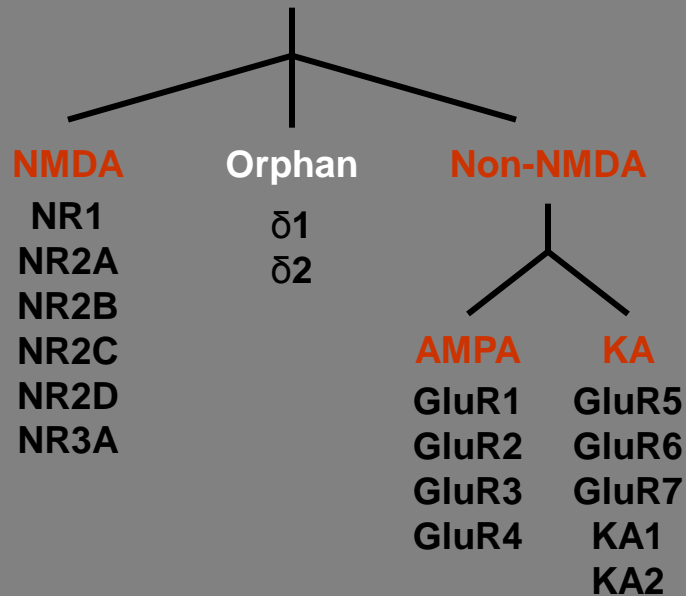
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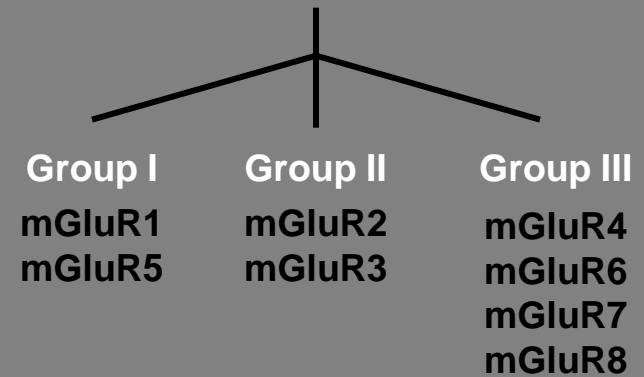
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Glutamate receptors (GluRs)

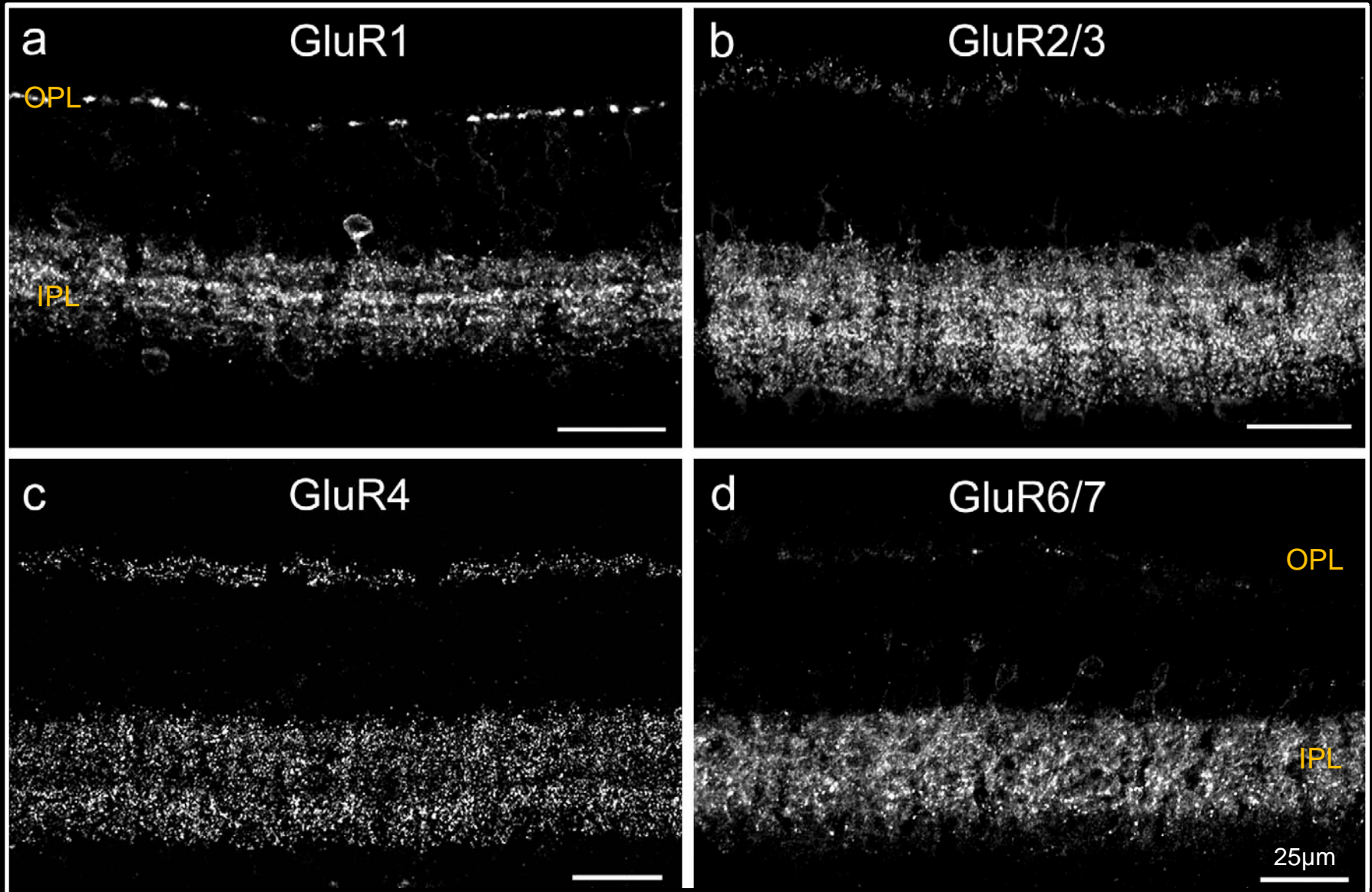
Ionotropic GluRs (iGluRs)



Metabotropic GluRs (mGluRs)



Synaptic localization of iGluR subunits in the retina



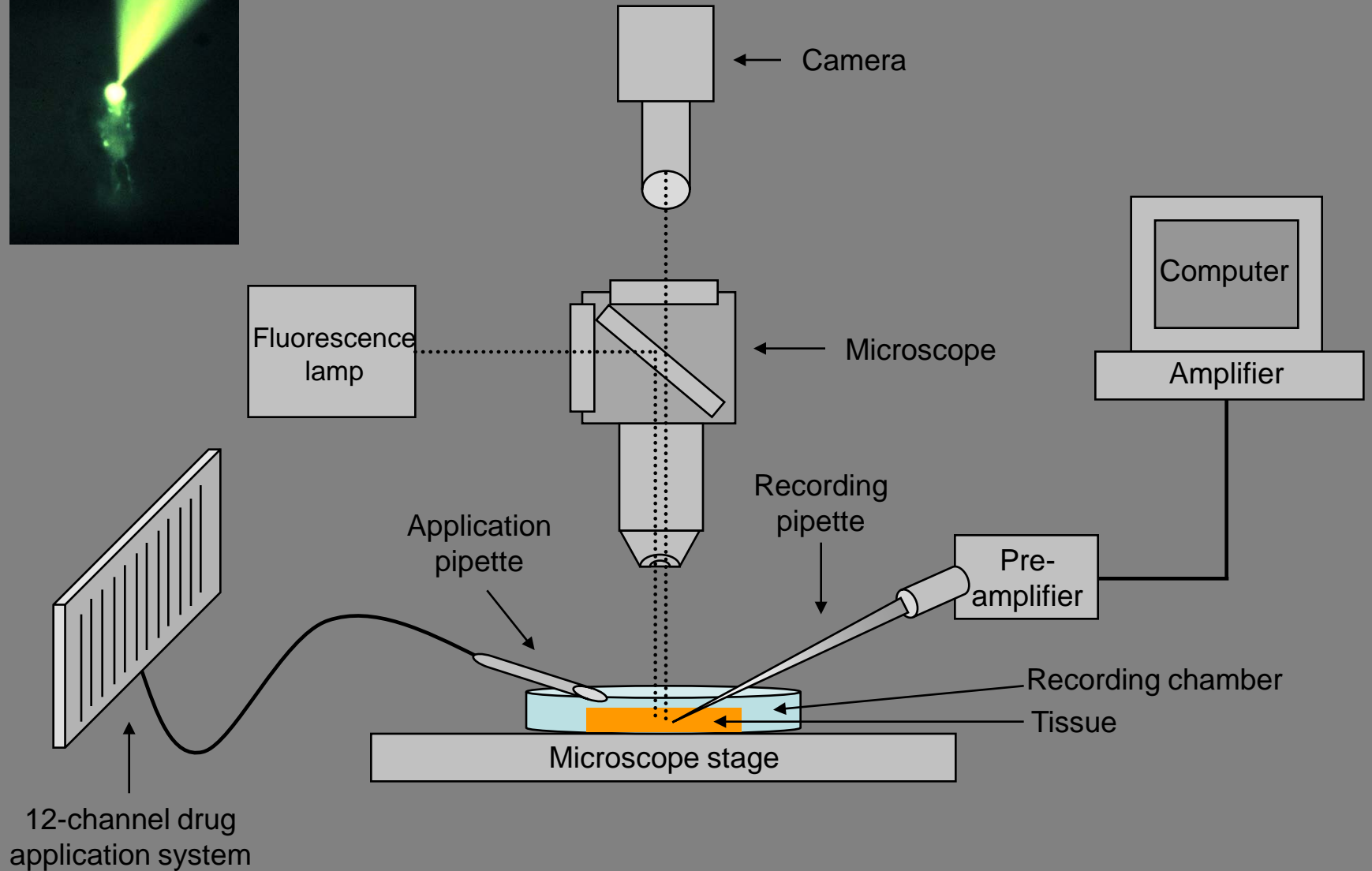
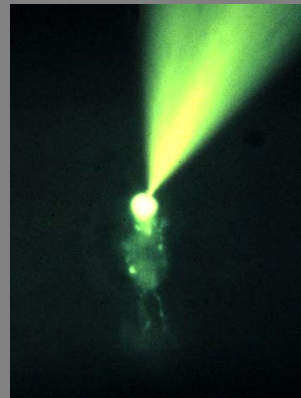
Functional diversity of iGluRs

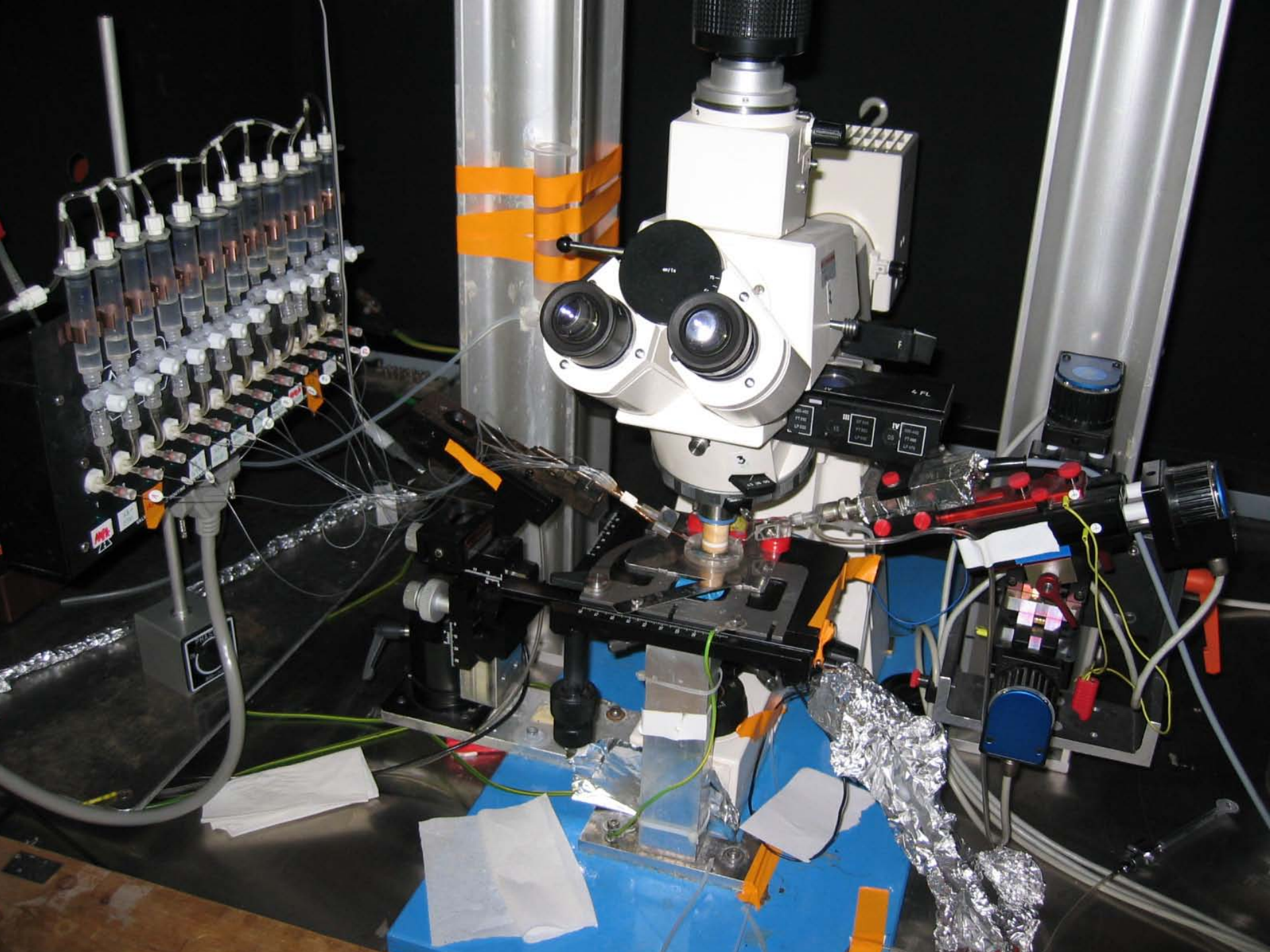
- Kinetics
- Pharmacology

	NMDA	Non-NMDA	
		AMPA	KAINATE
NONSELECTIVE AGONISTS	L-GLUTAMATE		
		AMPA, KAINATE	
SELECTIVE AGONISTS	NMDA, L-ASPARTATE	CYCLOTHIAZIDE, ACPA, (S)APPA	SYM 2081 ATPA, DZKA, CONCANAVALIN A
NONSELECTIVE ANTAGONISTS		QUINOXALINES (NBQX, CNQX, DNQX)	
SELECTIVE ANTAGONISTS	AP5, AP7, CPP; IFENPRODIL*	GYKI 52466, GYKI 53655, ATPO	LY293558*, LY294486*

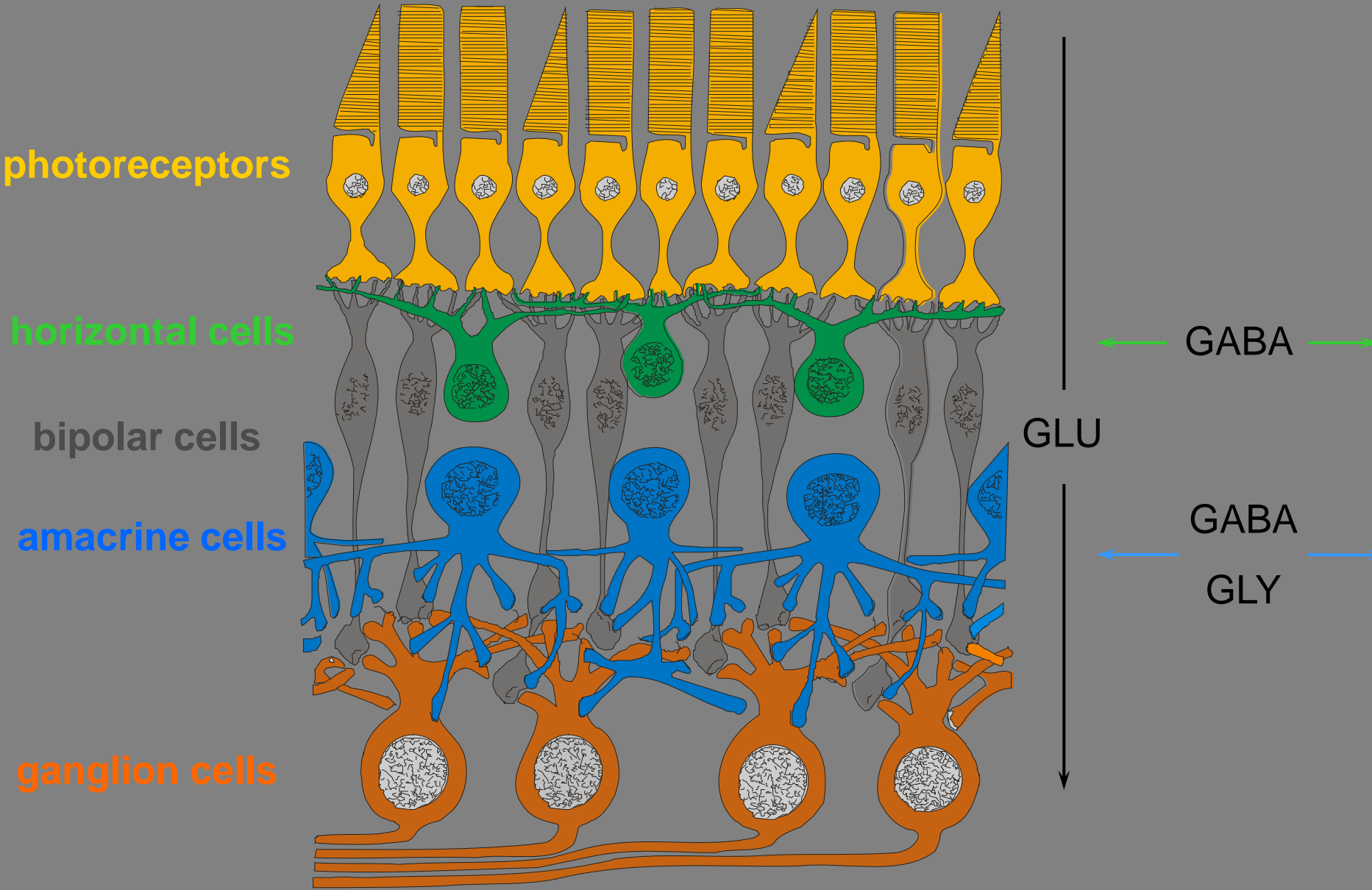
* subunit specific

Method: patch-clamp set-up

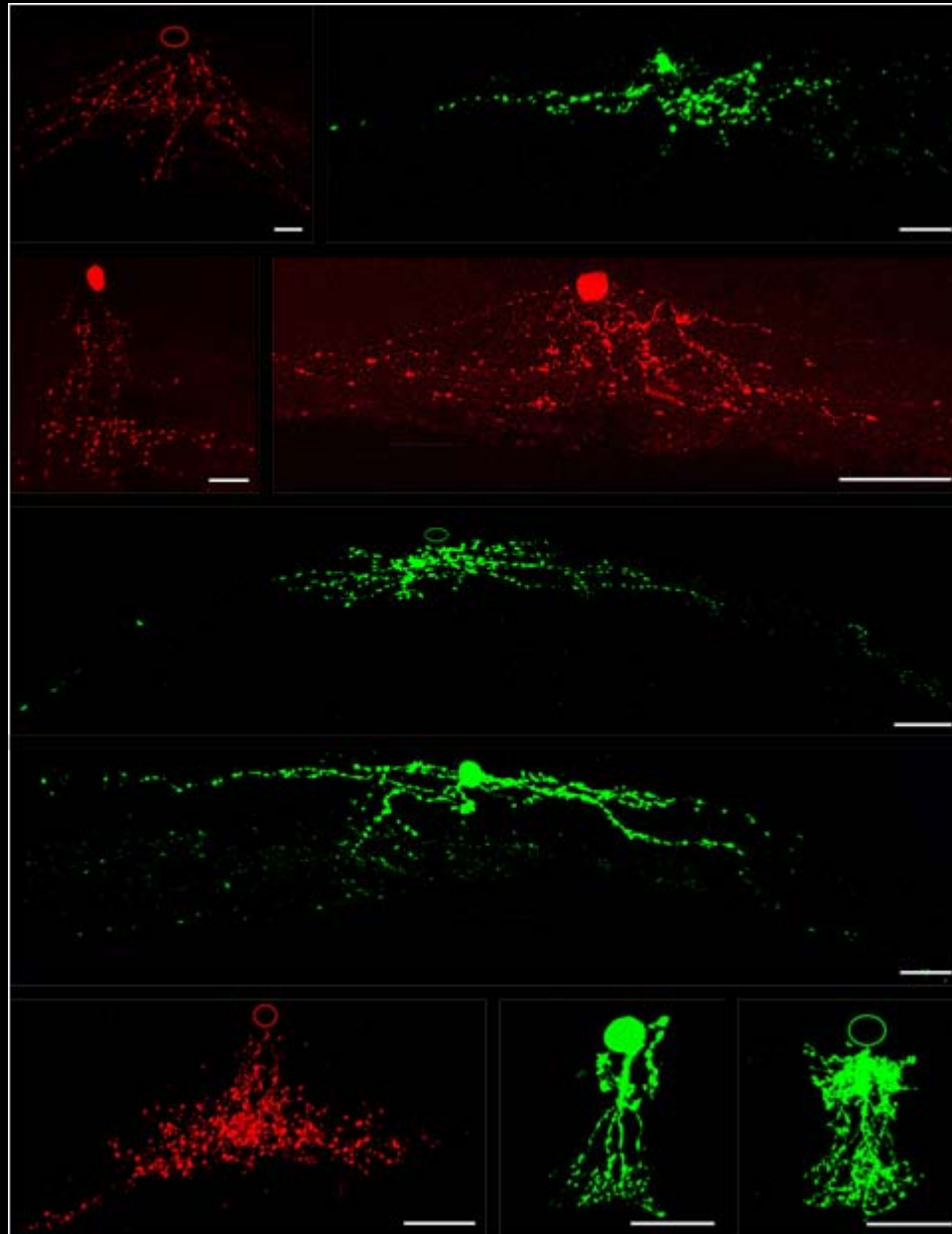




Excitatory and inhibitory pathways in the retina

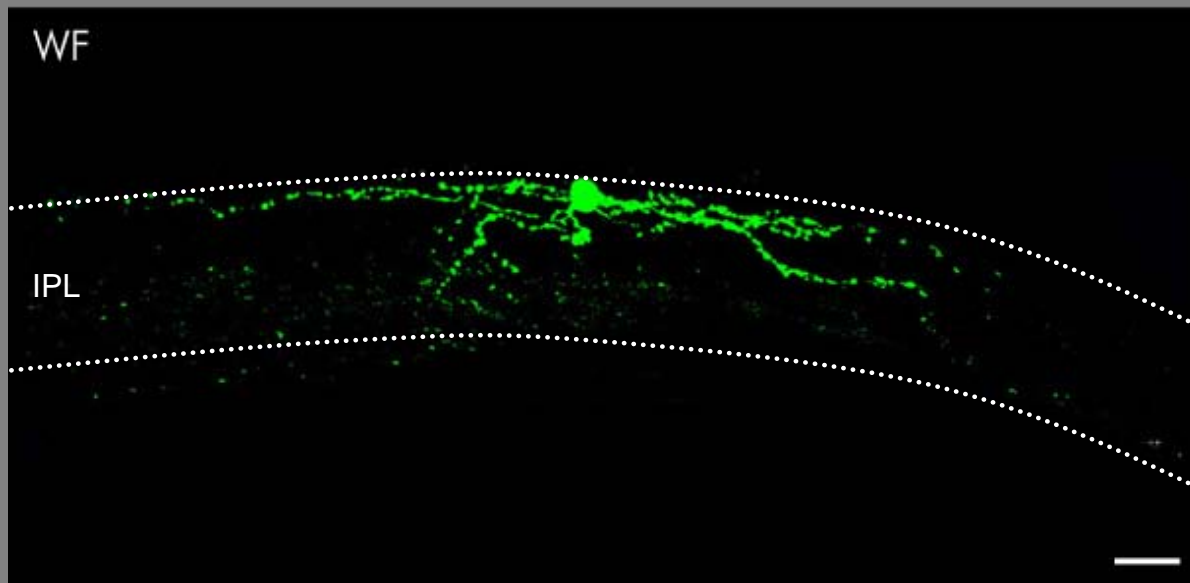
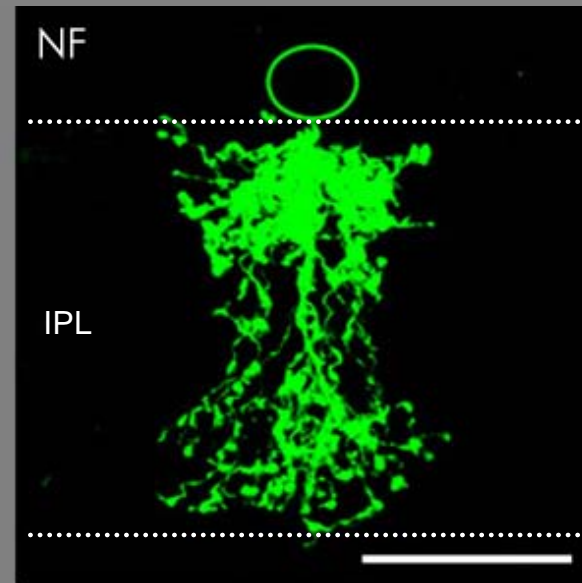
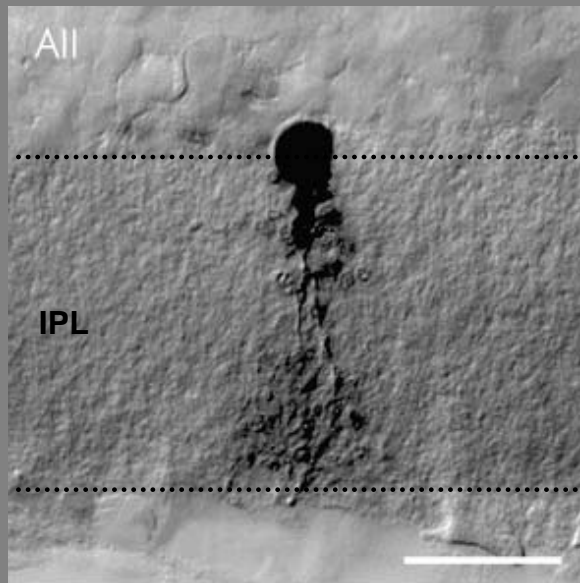


Diversity of retinal amacrine cells



all scale bars 20 μ m

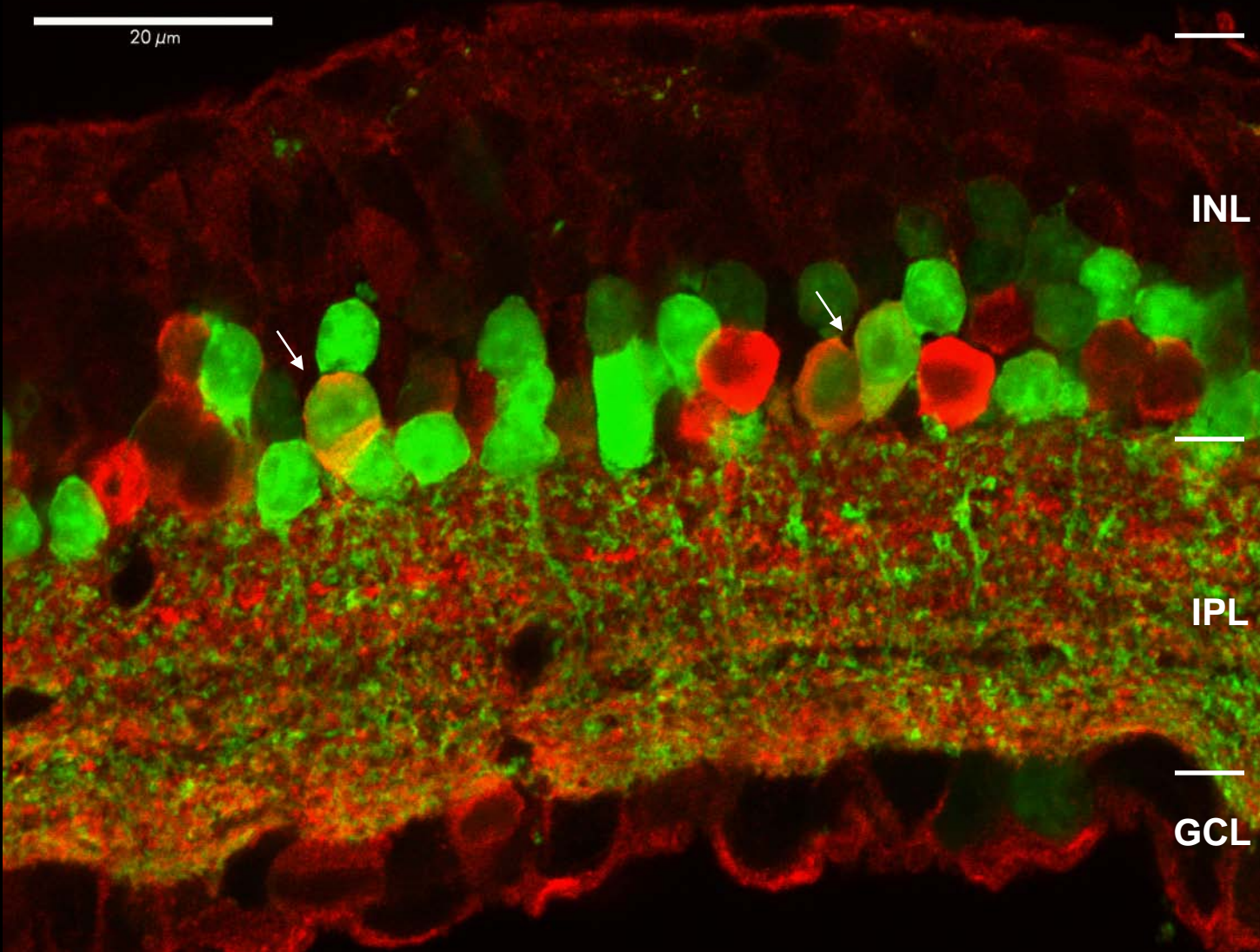
Amacrine cell classification by dendritic field size



Scale bars 20 μ m

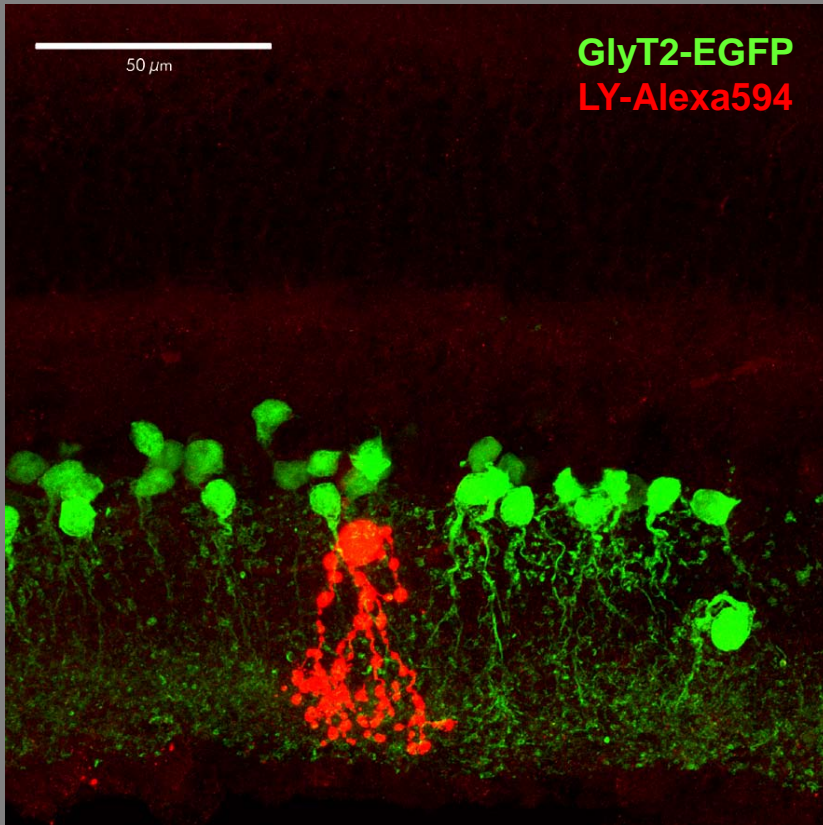
Amacrine cell classification by neurotransmitter

GlyT2-EGFP GABA



courtesy of Silke Haverkamp

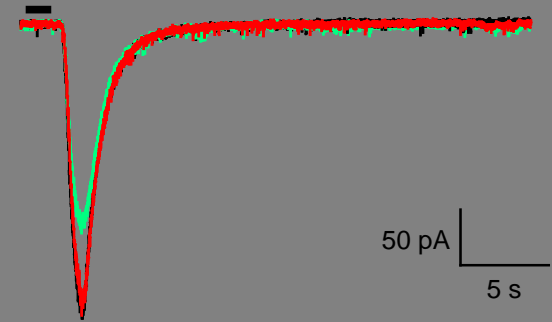
Responses of a narrow-field amacrine cell



KA 100 μM

KA 100 μM + GYKI 20 μM

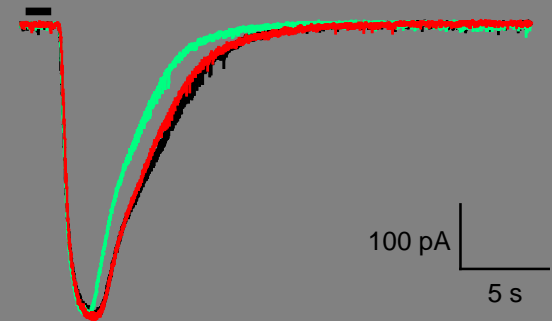
KA 100 μM (recovery)



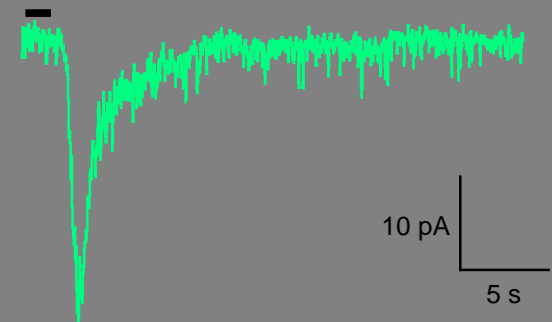
KA 100 μM

KA 100 μM + SYM 20 μM

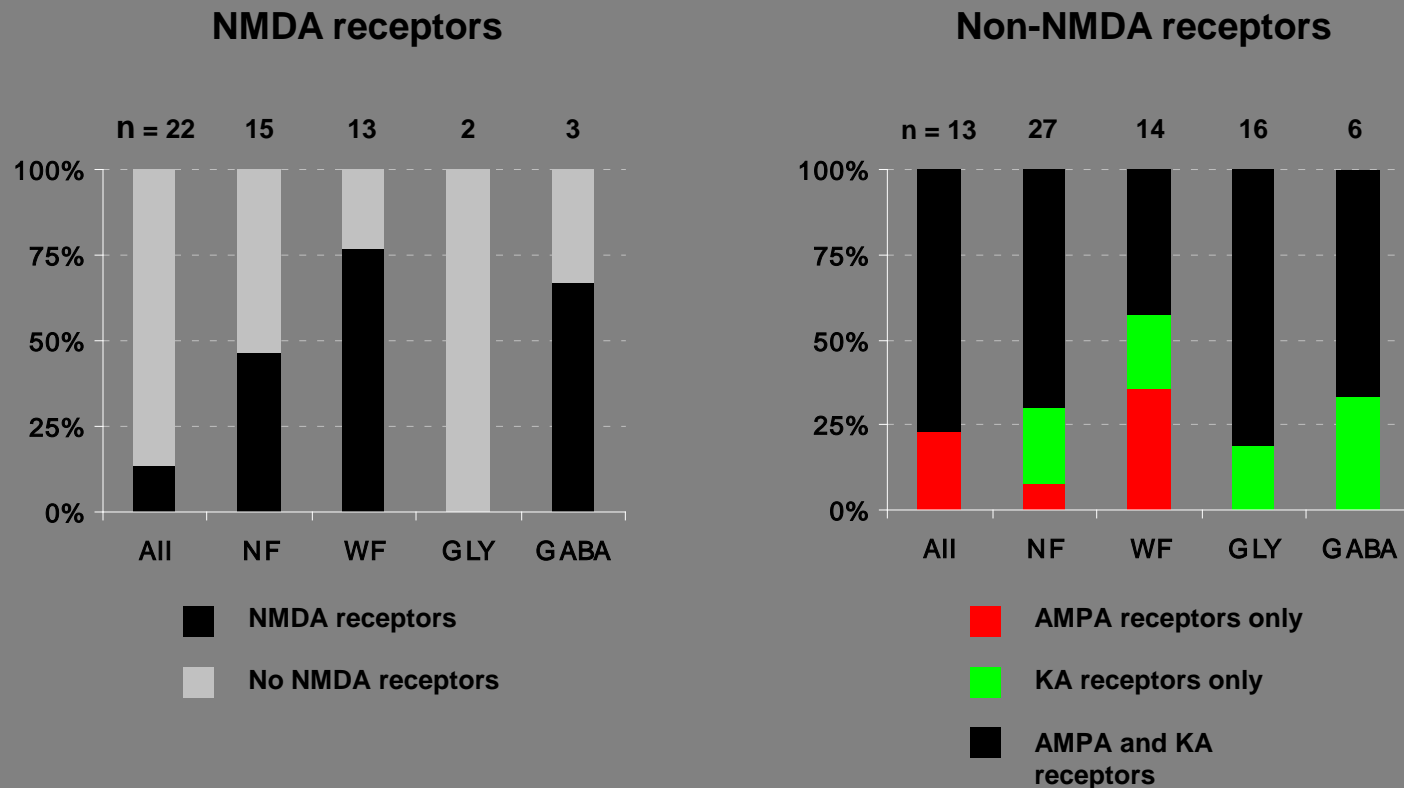
KA 100 μM (recovery)



SYM 50 μM



GluR statistics among amacrine cells



- **Dendritic field size and neurotransmitter content do not correlate with a specific GluR expression among amacrine cells.**
- **Individual cell types may have different patterns of ionotropic GluR expression.**
- **Different GluRs may be involved with different synapses within a single cell.**

Talk overview

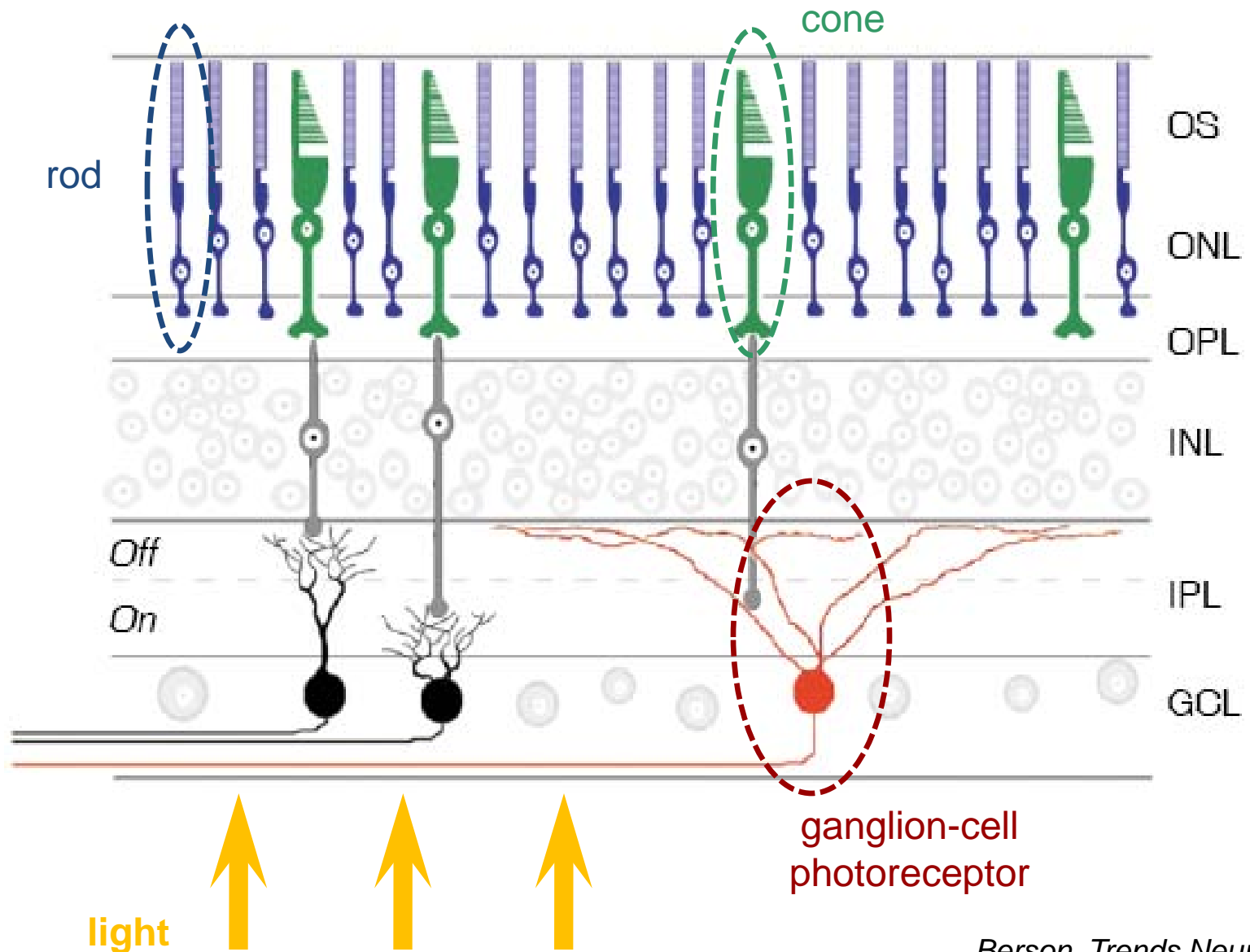
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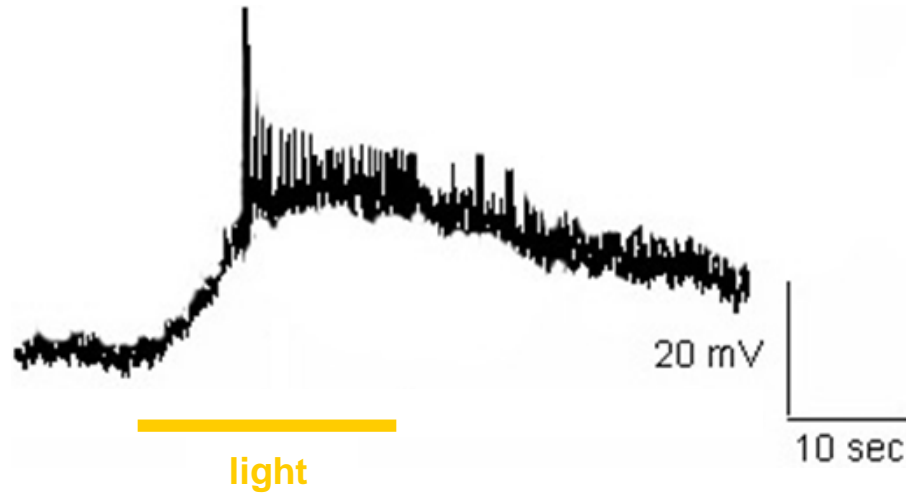
Three classes of photoreceptors in the mammalian retina



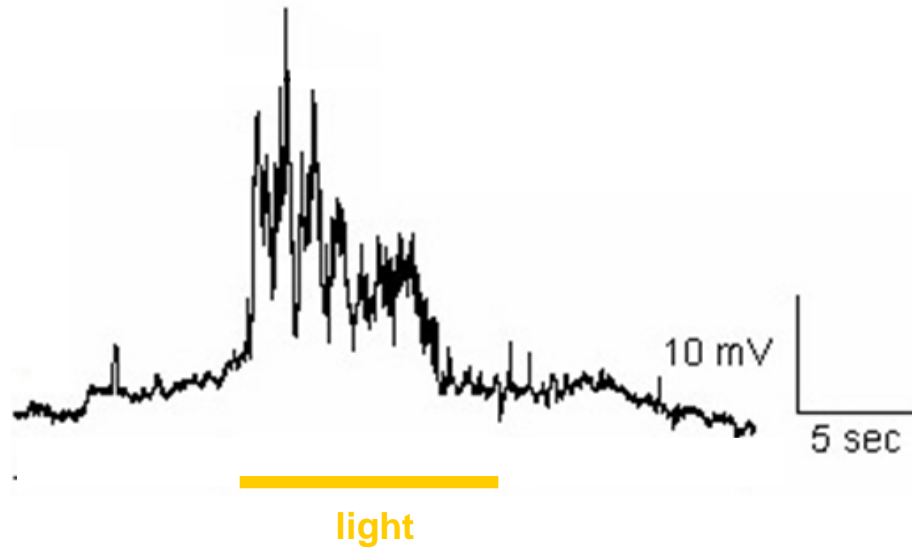
Melanopsin-containing,

intrinsically photosensitive retinal ganglion cells (ipRGCs)

Synaptic input blocked
with drugs:



Cell body
mechanically
isolated:

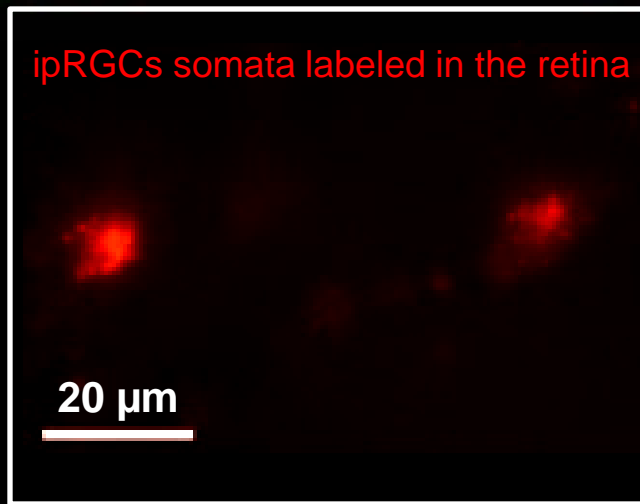
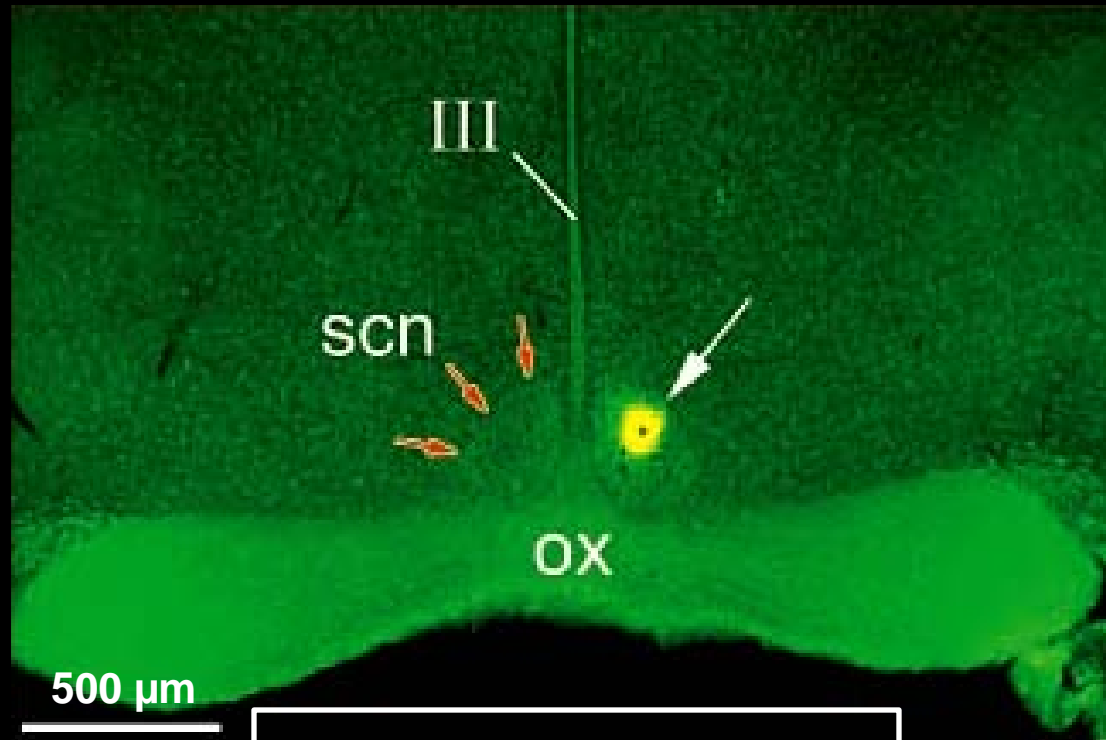


Intrinsically photosensitive retinal ganglion cells (ipRGCs)

mediate non-image-forming vision

- **Synchronization of circadian rhythms to the solar cycle (“photoentrainment”)**
- **Pupil constriction**
- **Regulation of pineal melatonin release**
- **Acute suppression of locomotor activity of nocturnal animals (“masking”)**

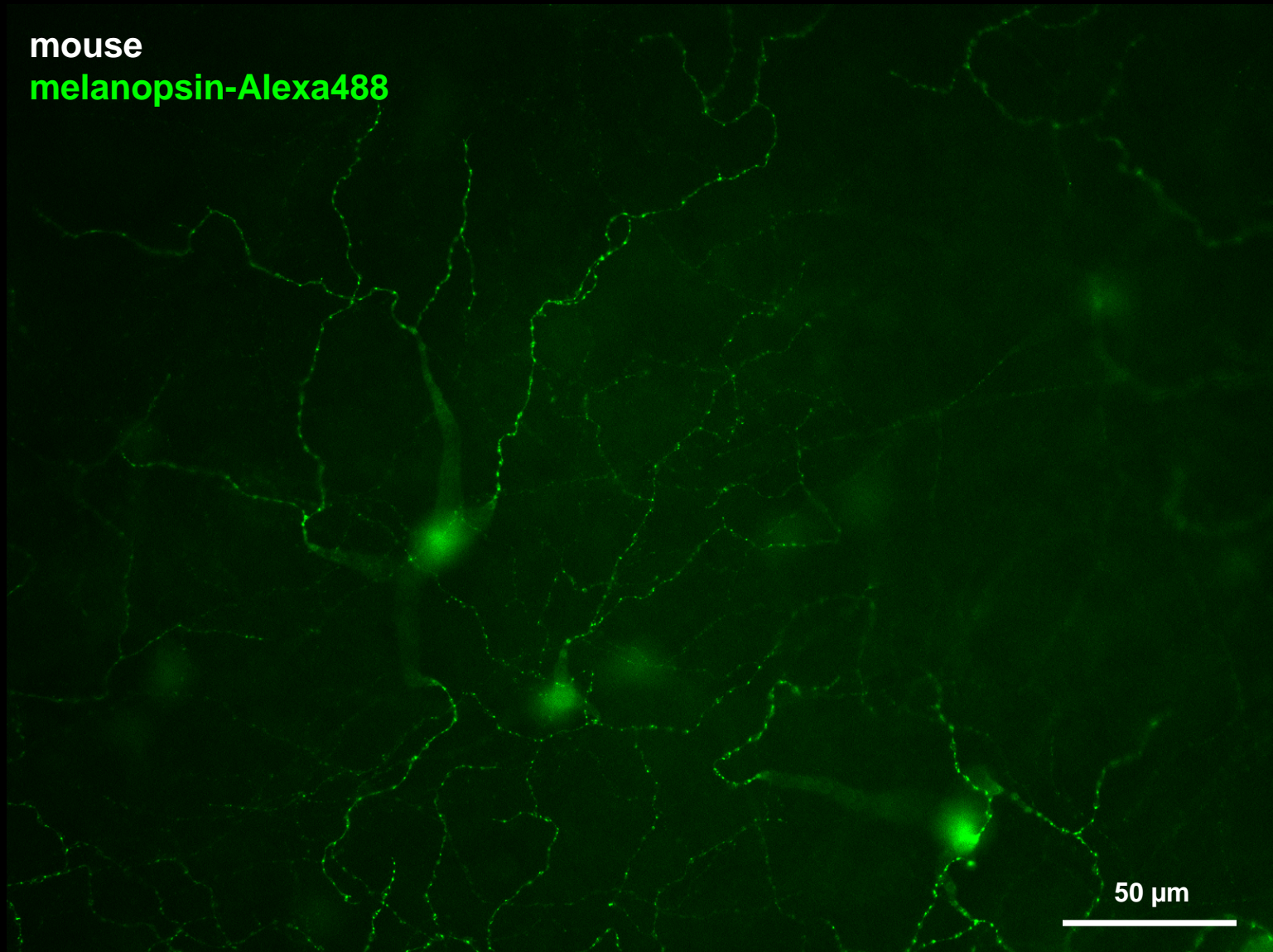
IpRGCs were identified by retrograde labeling from the SCN



Melanopsin immunofluorescence reveals two distinct cell types

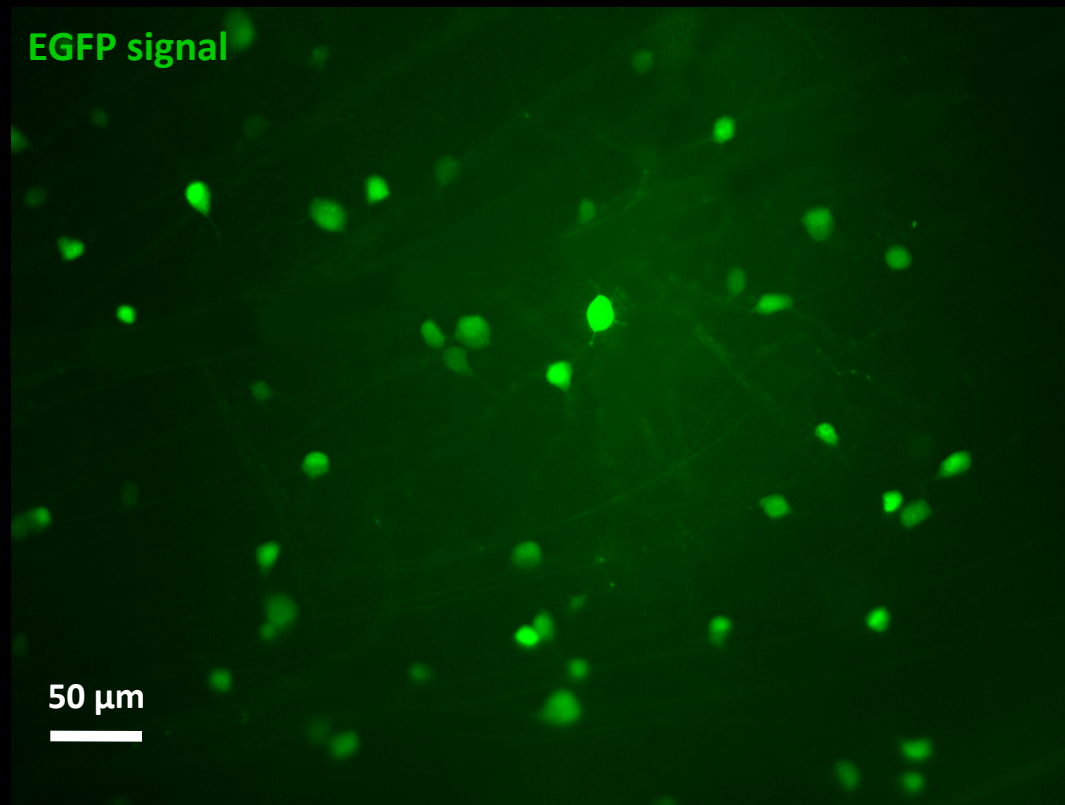
mouse

melanopsin-Alexa488

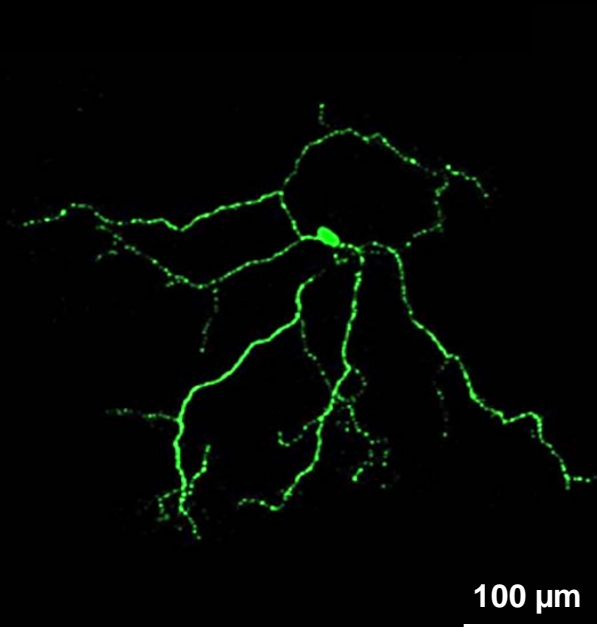


50 μm

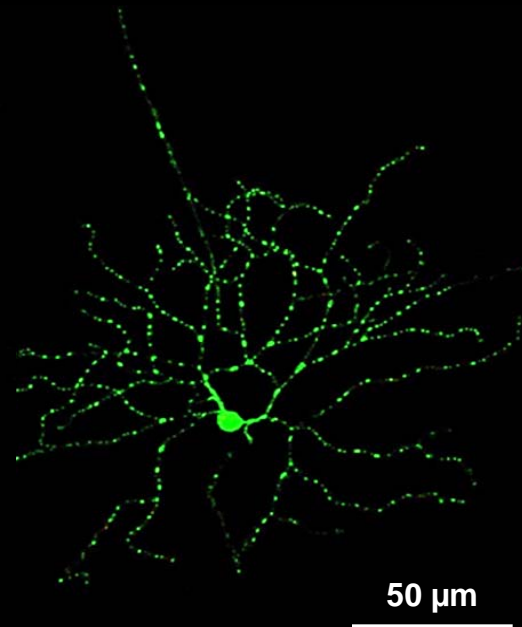
A transgenic mouse line using the Cre-lox system labels all melanopsin-expressing cells with EGFP



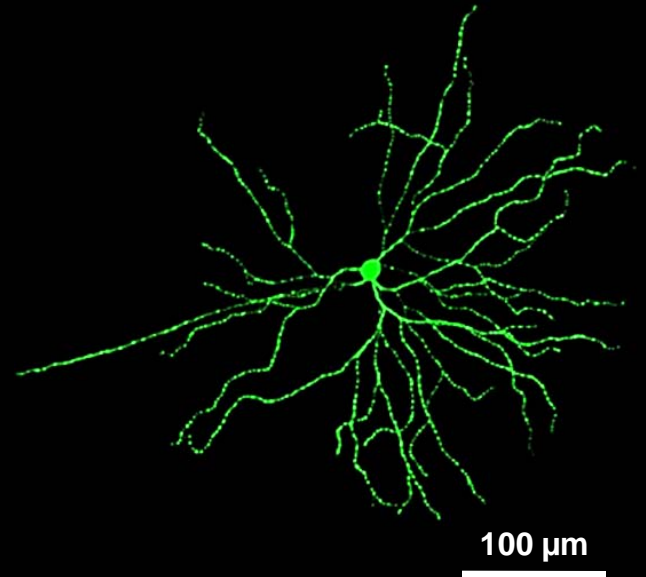
3 morphological types of EGFP-labeled RGCs



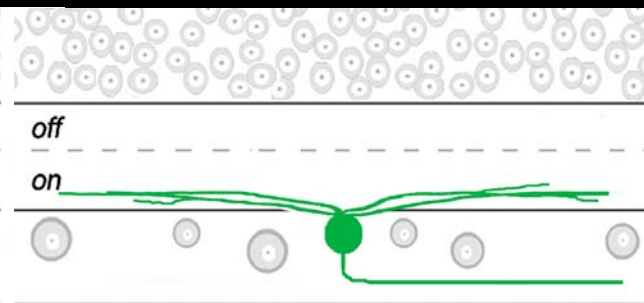
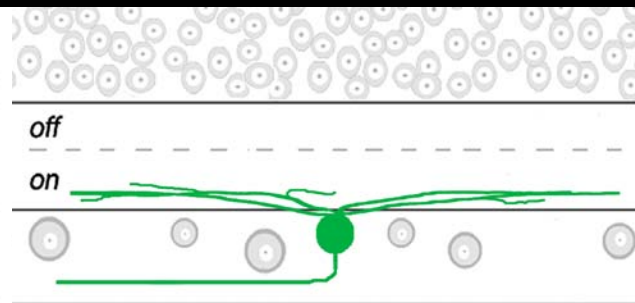
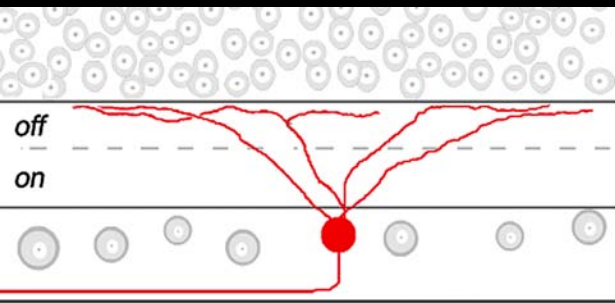
M1



M2

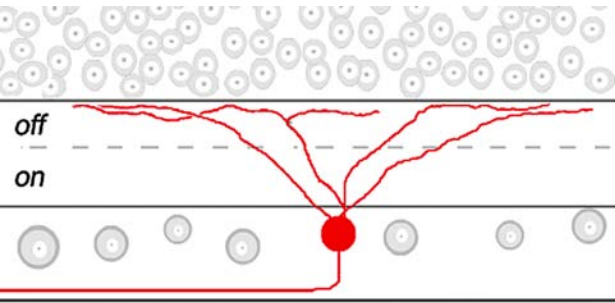


alpha-like

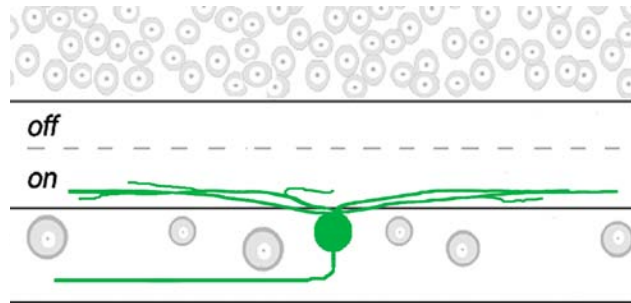


M2 and alpha-like cells have dendrites in the ON sublamina and generate weaker light responses

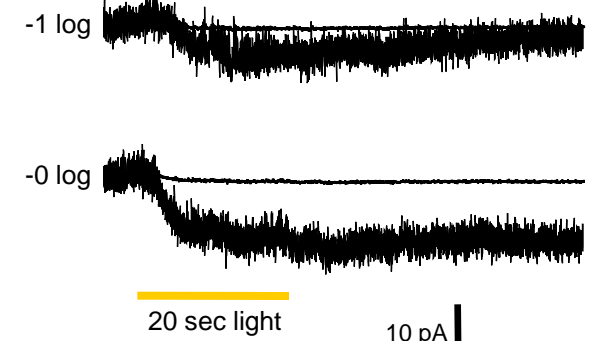
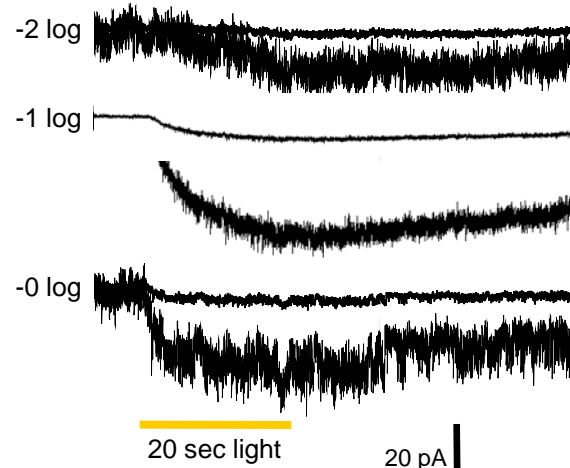
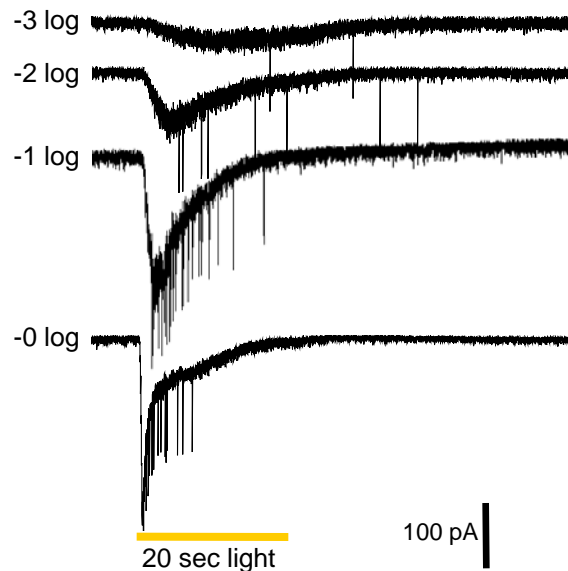
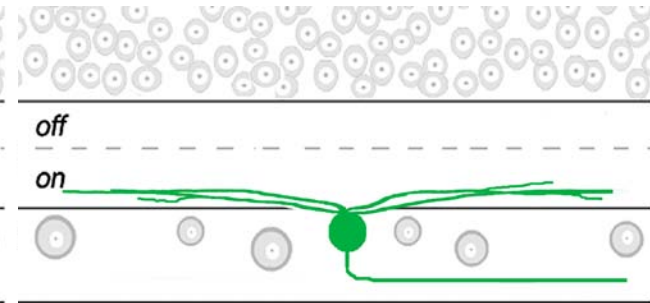
M1 (*OFF* sublamina):



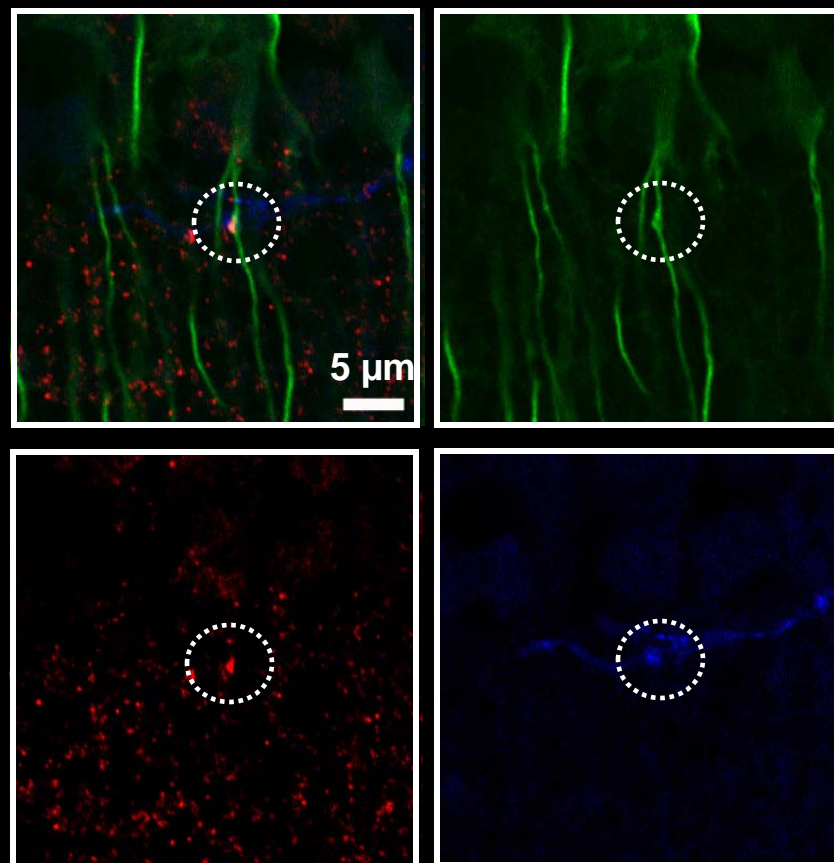
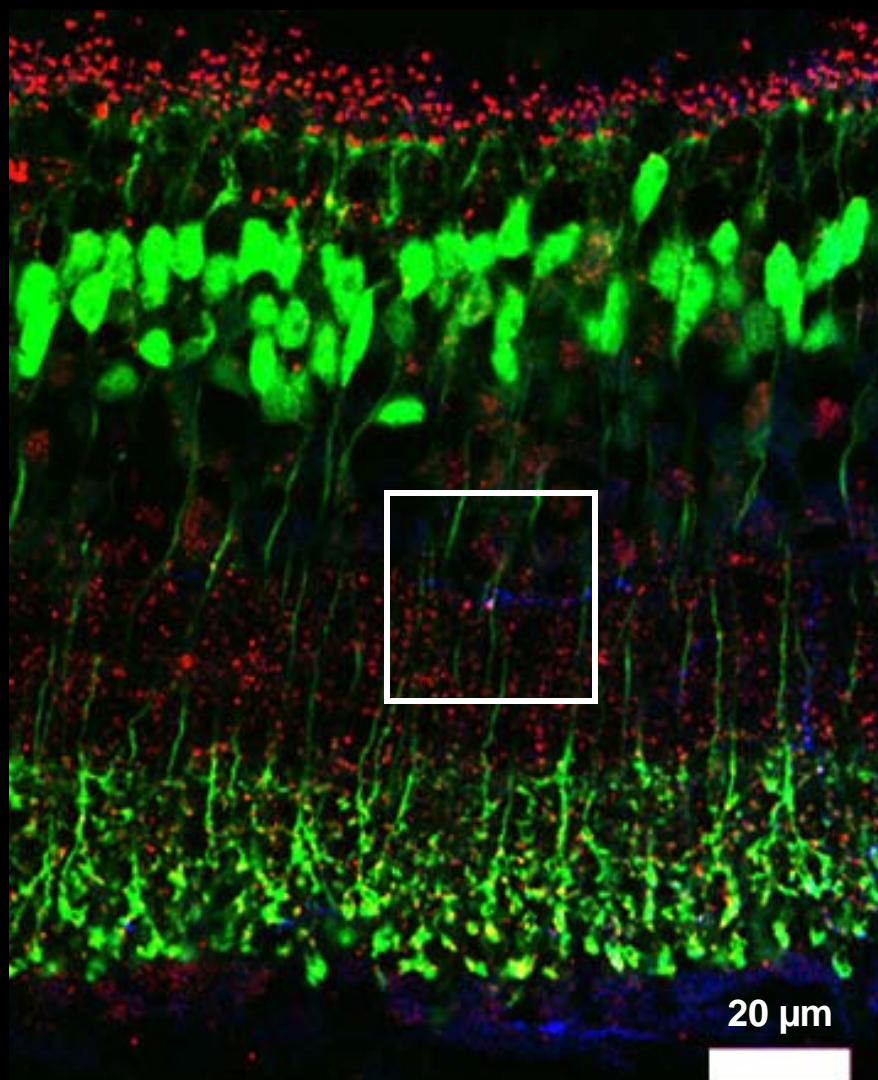
M2 (*ON* sublamina):



Alpha-like (*ON* sublamina):

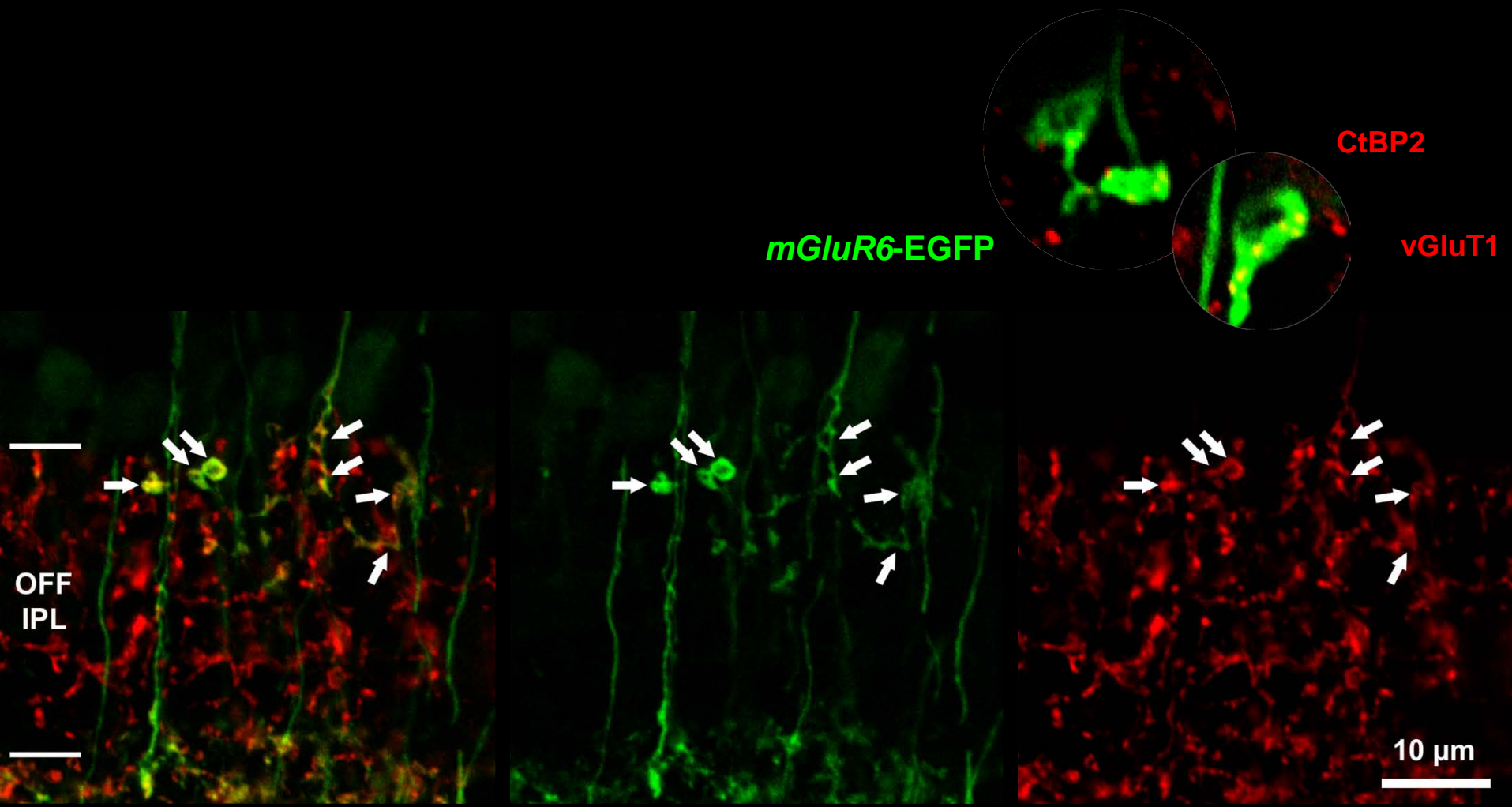


Ectopic ON bipolar cell ribbon synapses are significantly associated with melanopsin-positive dendrites

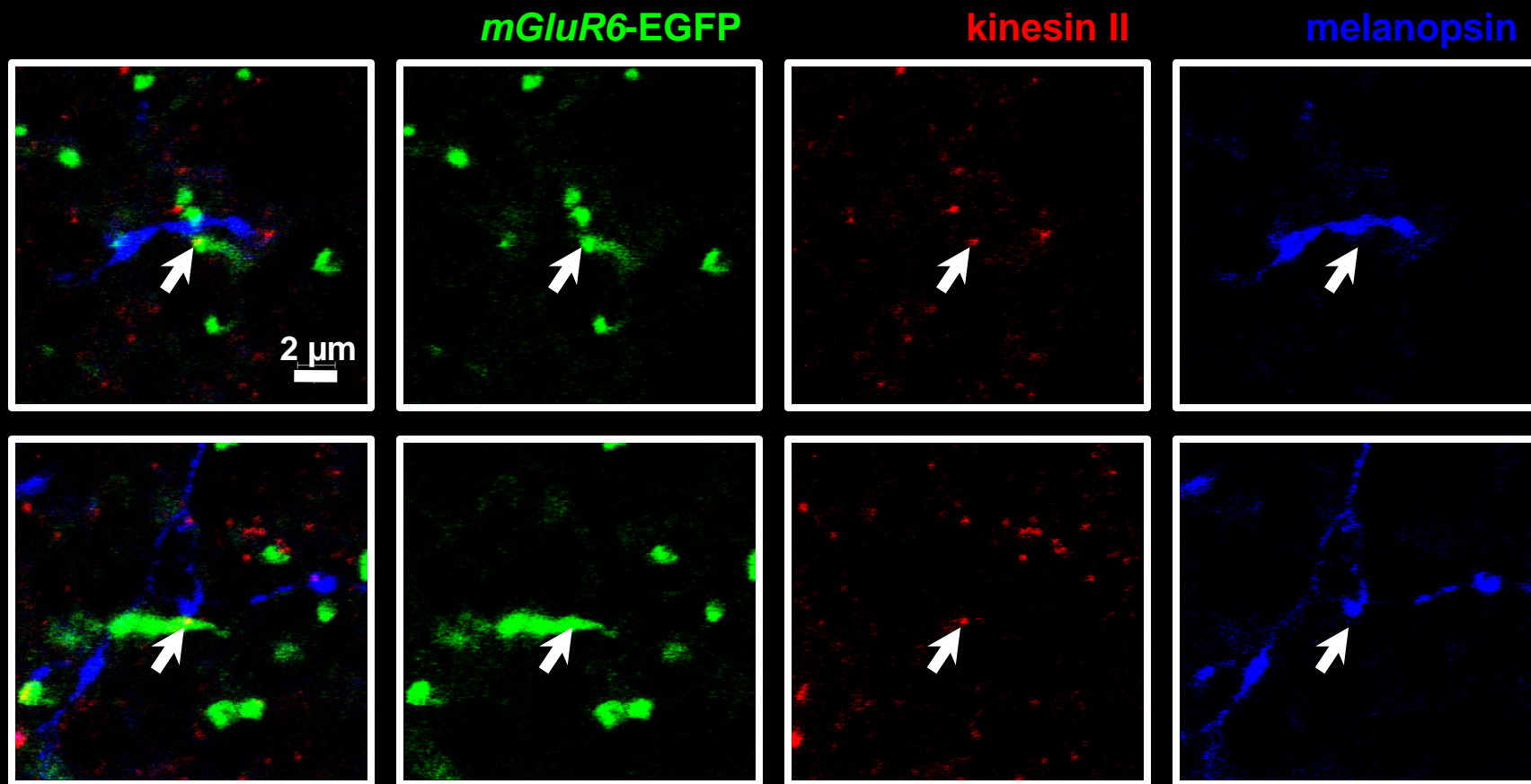


mGluR6-EGFP **kinesin II** **melanopsin**

The ectopic ON bipolar cell terminals contain vesicular glutamate transporter 1 (vGluT1)



The ectopic ON bipolar cell ribbon synapses are significantly associated with melanopsin-positive dendrites



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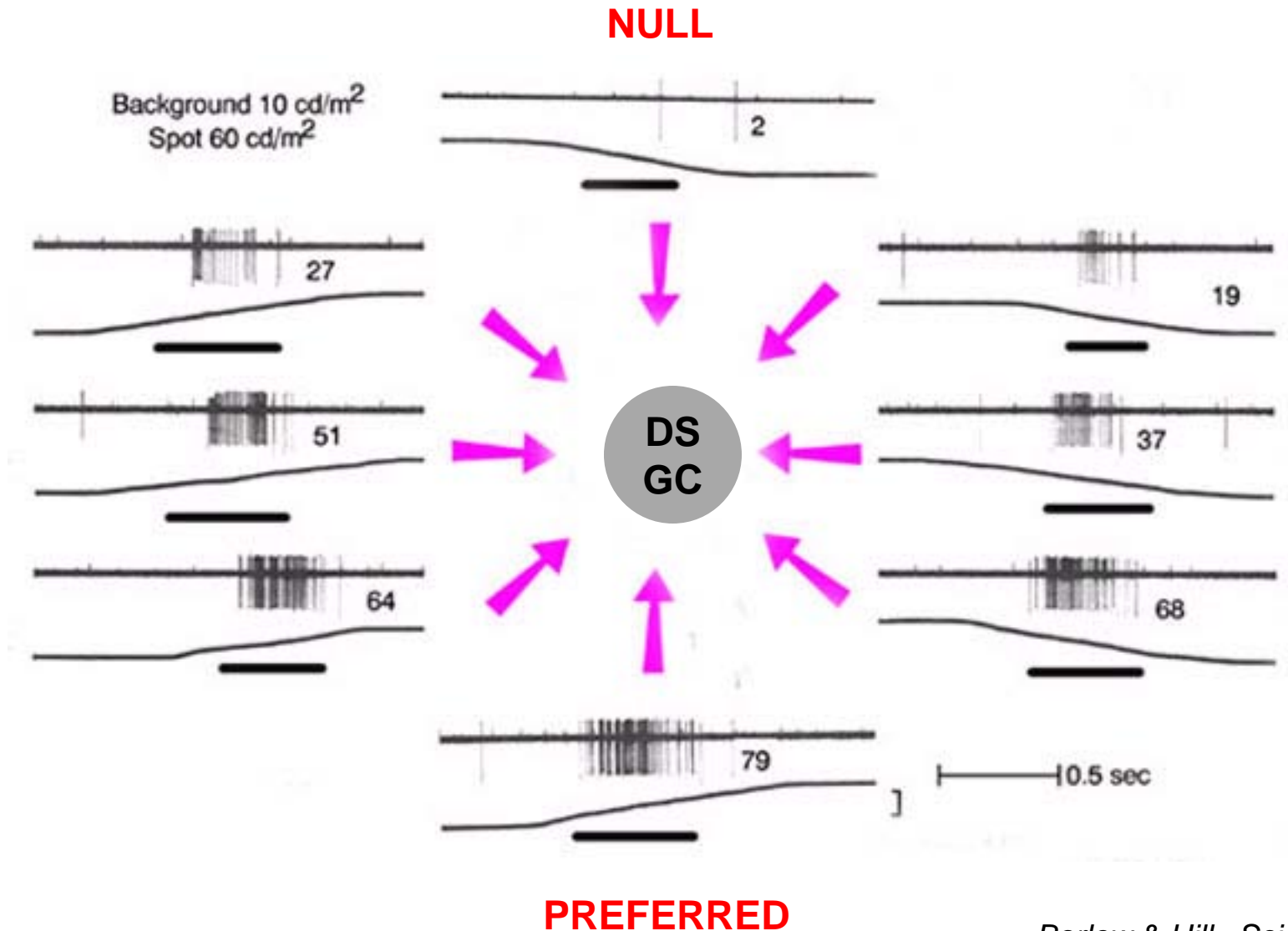
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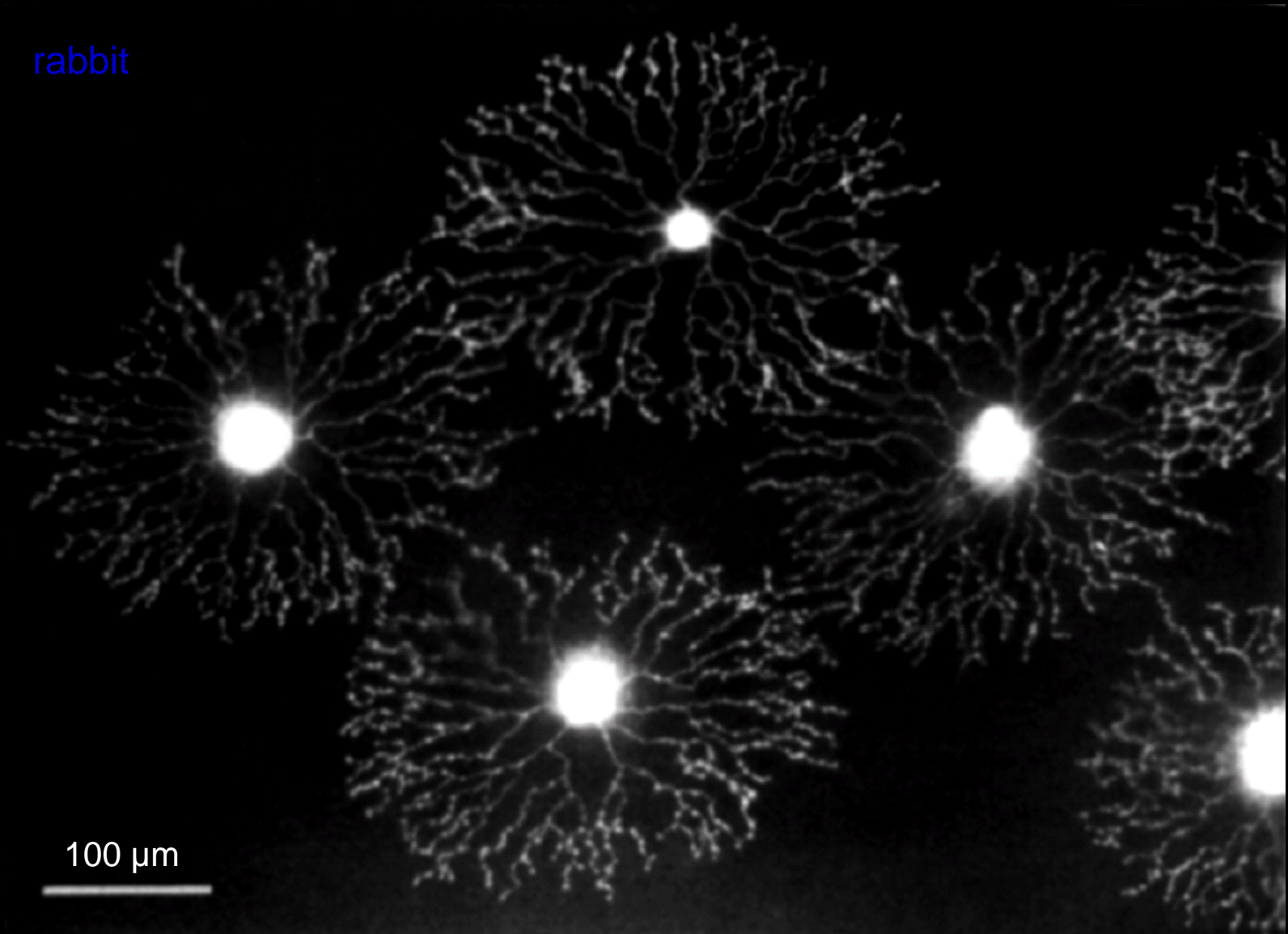
Direction selectivity (DS) in the retina

Direction selective ganglion cells (DSGCs) were first described in the rabbit retina

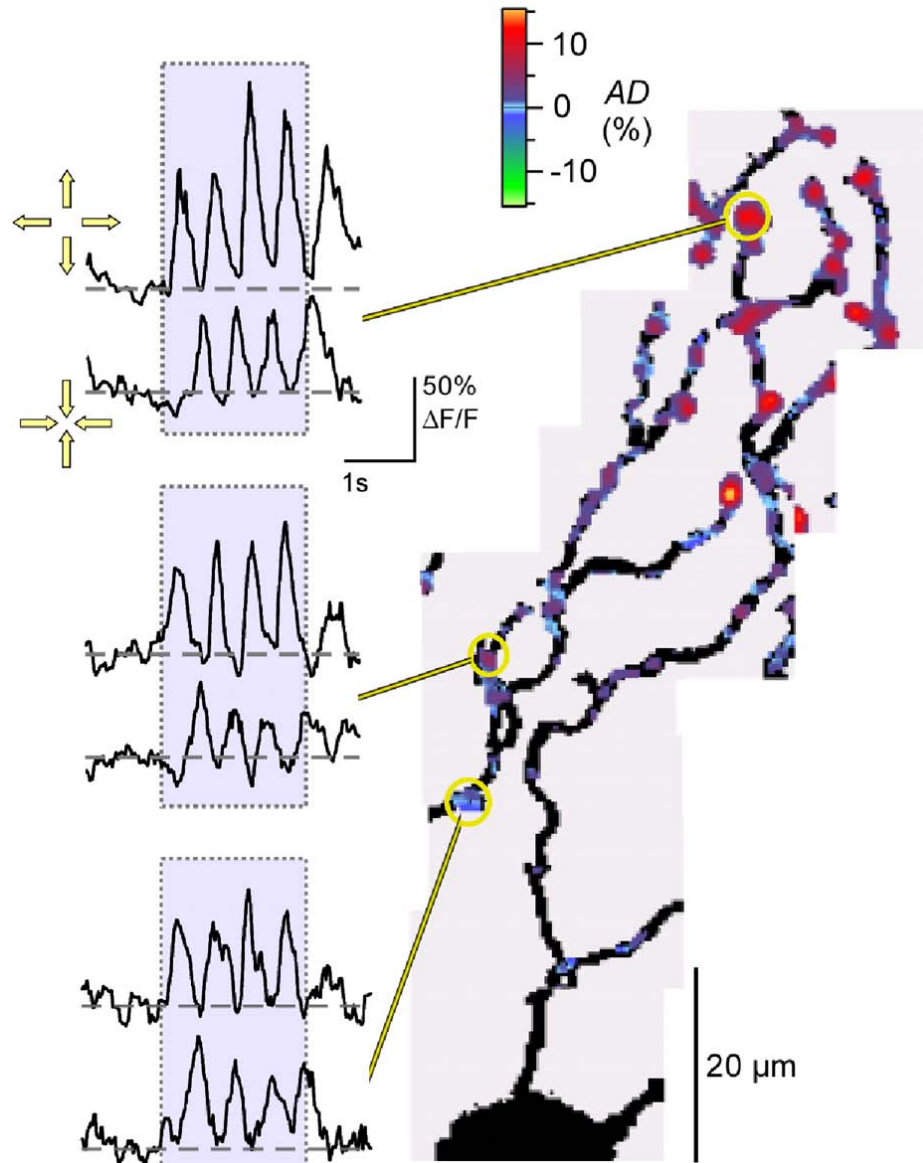


A key element of the DS circuitry: starburst amacrine cells (SACs)

rabbit



Light-evoked dendritic Ca^{2+} signals in ON-SAC dendrites





Acknowledgements



Leo Peichl & Heinz Wässle
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Neuroscience, Brown University