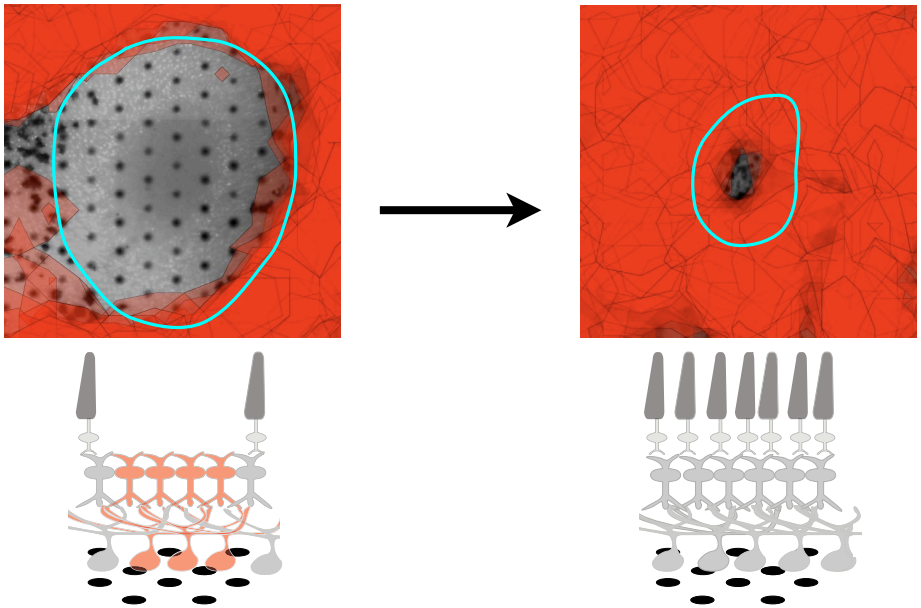
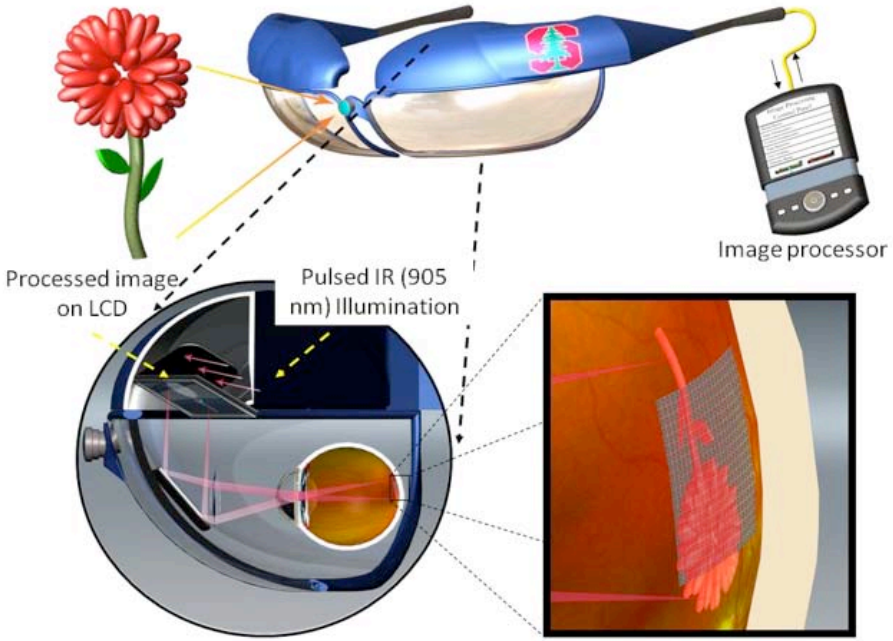
The retina: What can go wrong and how can we make it better?

Sasha Sher
Santa Cruz Institute for Particle Physics, University of California, Santa Cruz





Two leading causes of blindness/vision loss

Diabetic Retinopathy

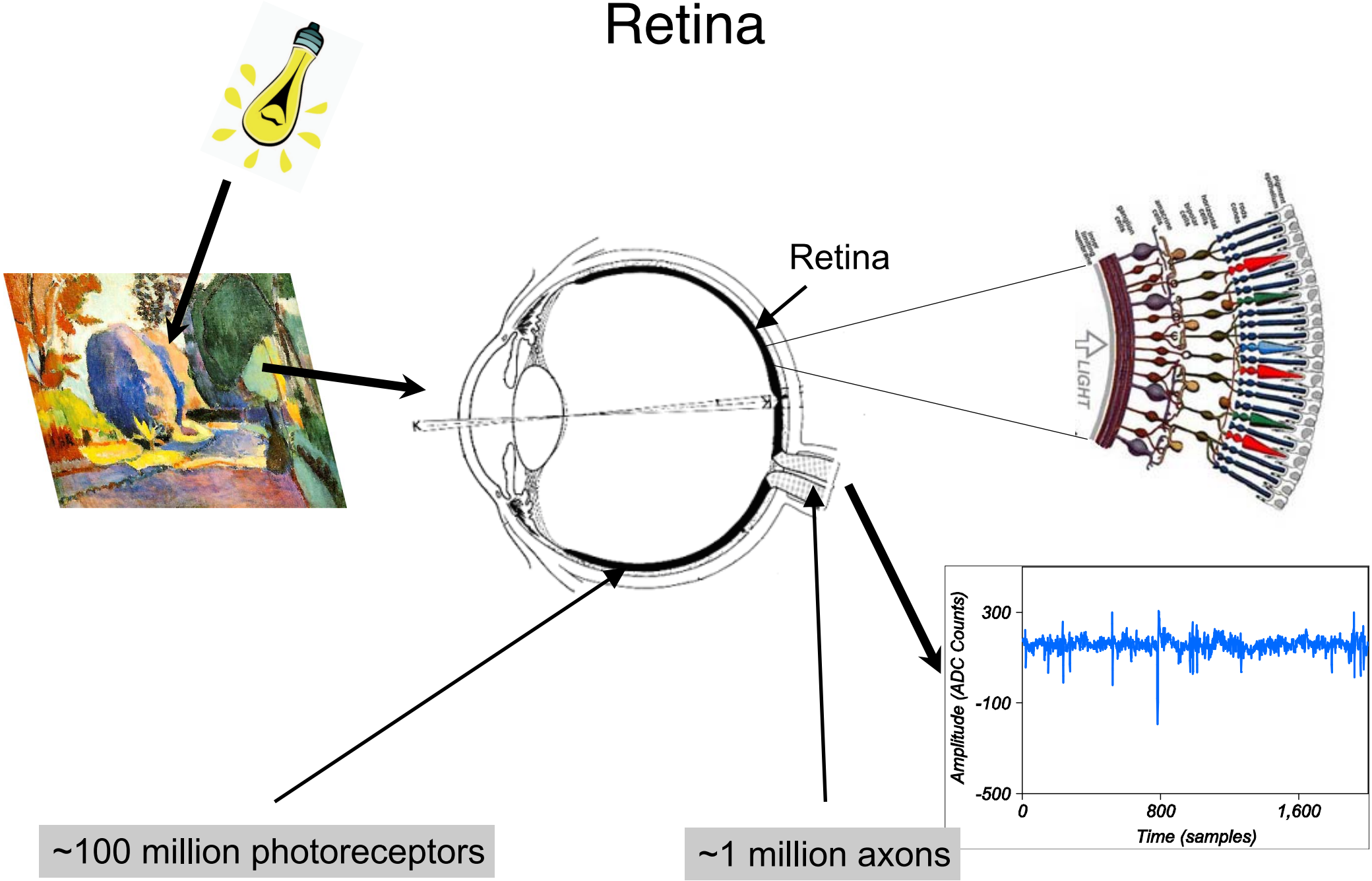
rises from 2% to 8% between 40 and 74 years

Age Related Macular Degeneration

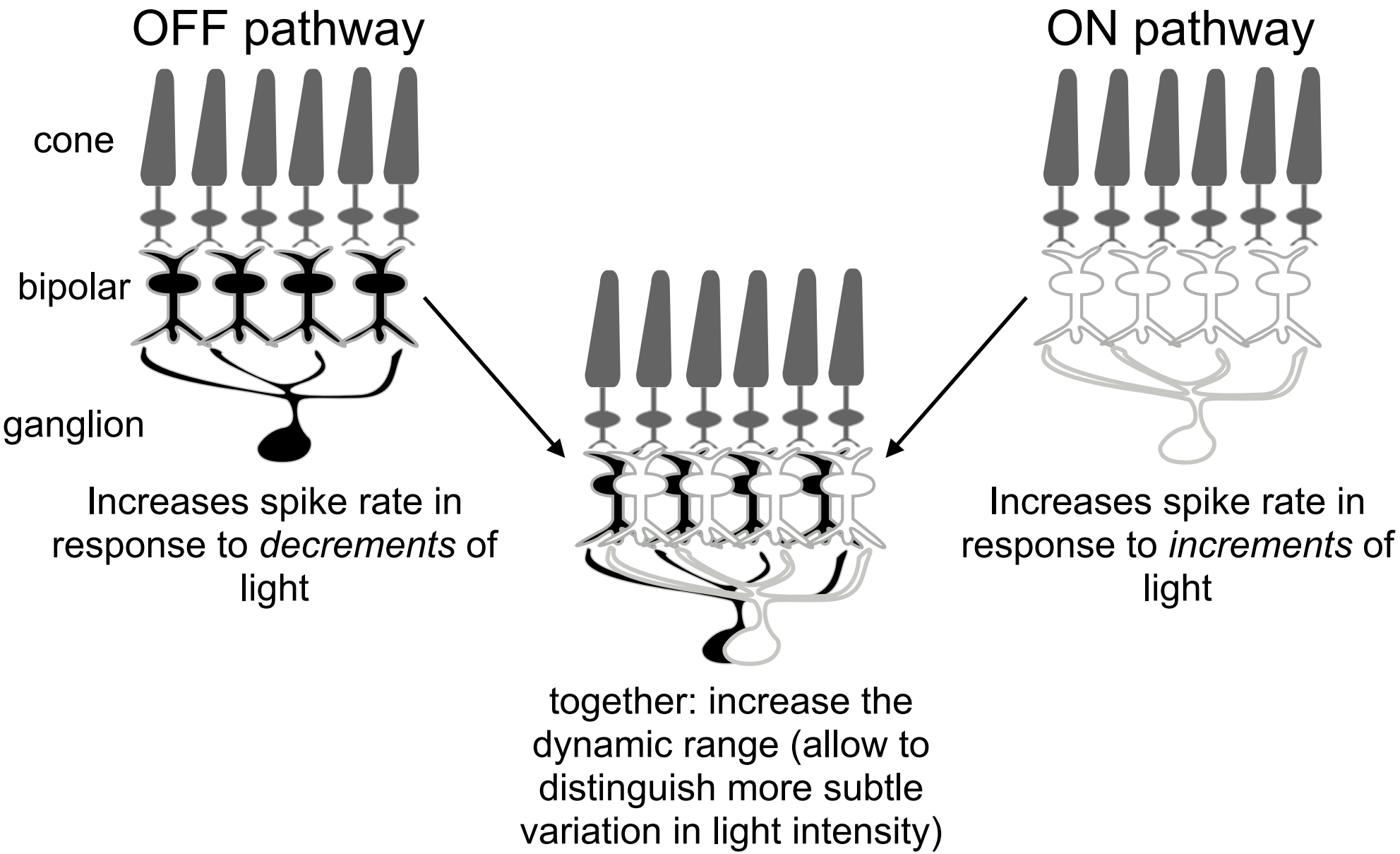
rises from 3% to 11% between 75 and 80 years

images from the National Eye Institute of NIH

Retina


Retina
LIGHT
Amplitude (ADC Counts)
300
-100
-500
0
800
1,600
Time (samples)
~100 million photoreceptors
~1 million axons

Parallel pathways in the retina



Diabetic Reinopathy

diabetes causes blockage of retinal blood vessels

deprived retinal neurons ask for more nutrients

new, abnormal, blood vessels grow

new blood vessels leak

leakage kills retinal neurons

Diabetic Reinopathy

retinal blood vessels
are blocked

~~deprived retinal neurons~~
~~ask for more nutrients~~

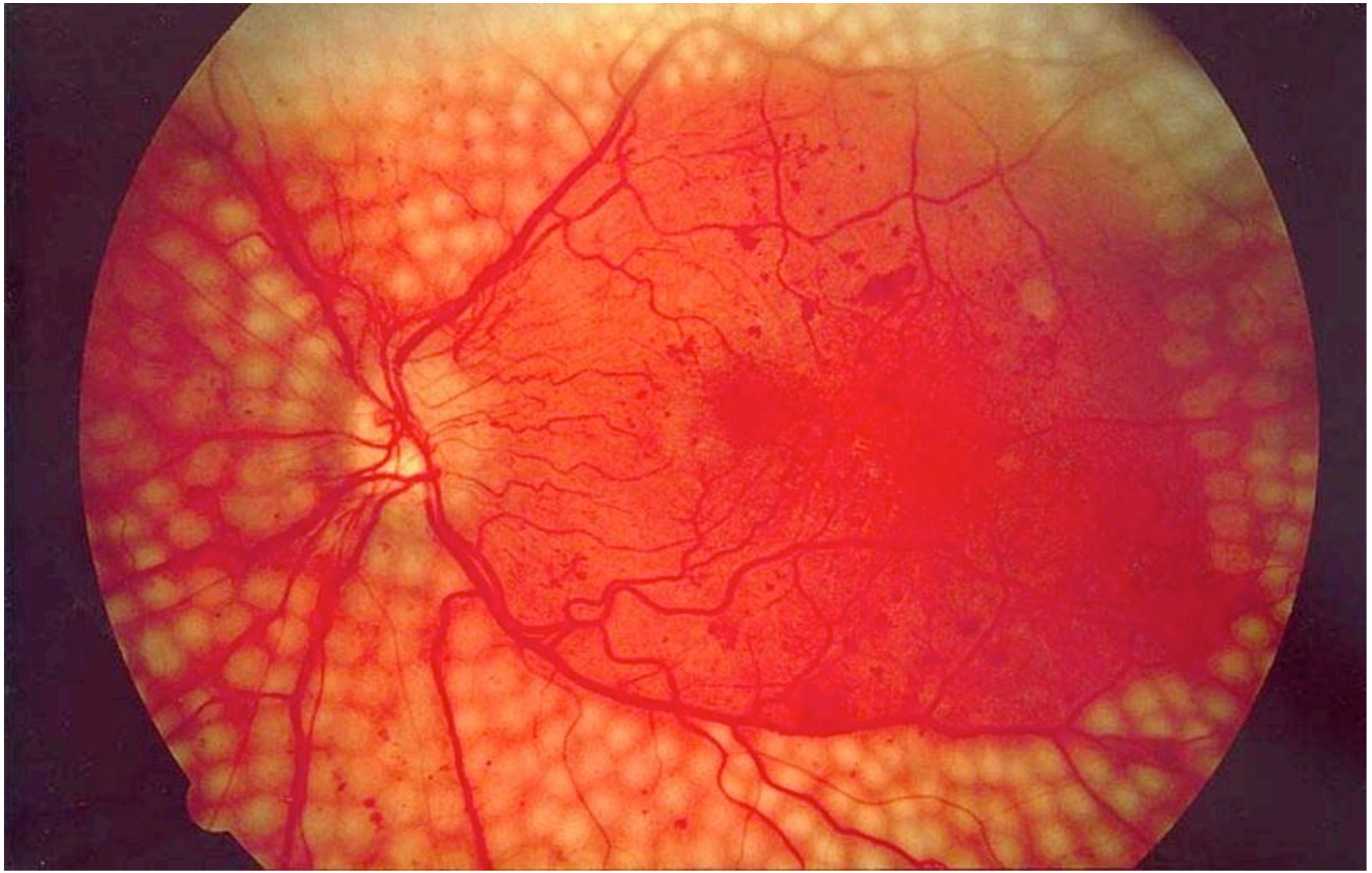
kill some retinal neurons to delay the distress signal

new, abnormal, blood
vessels grow

new blood vessels leak

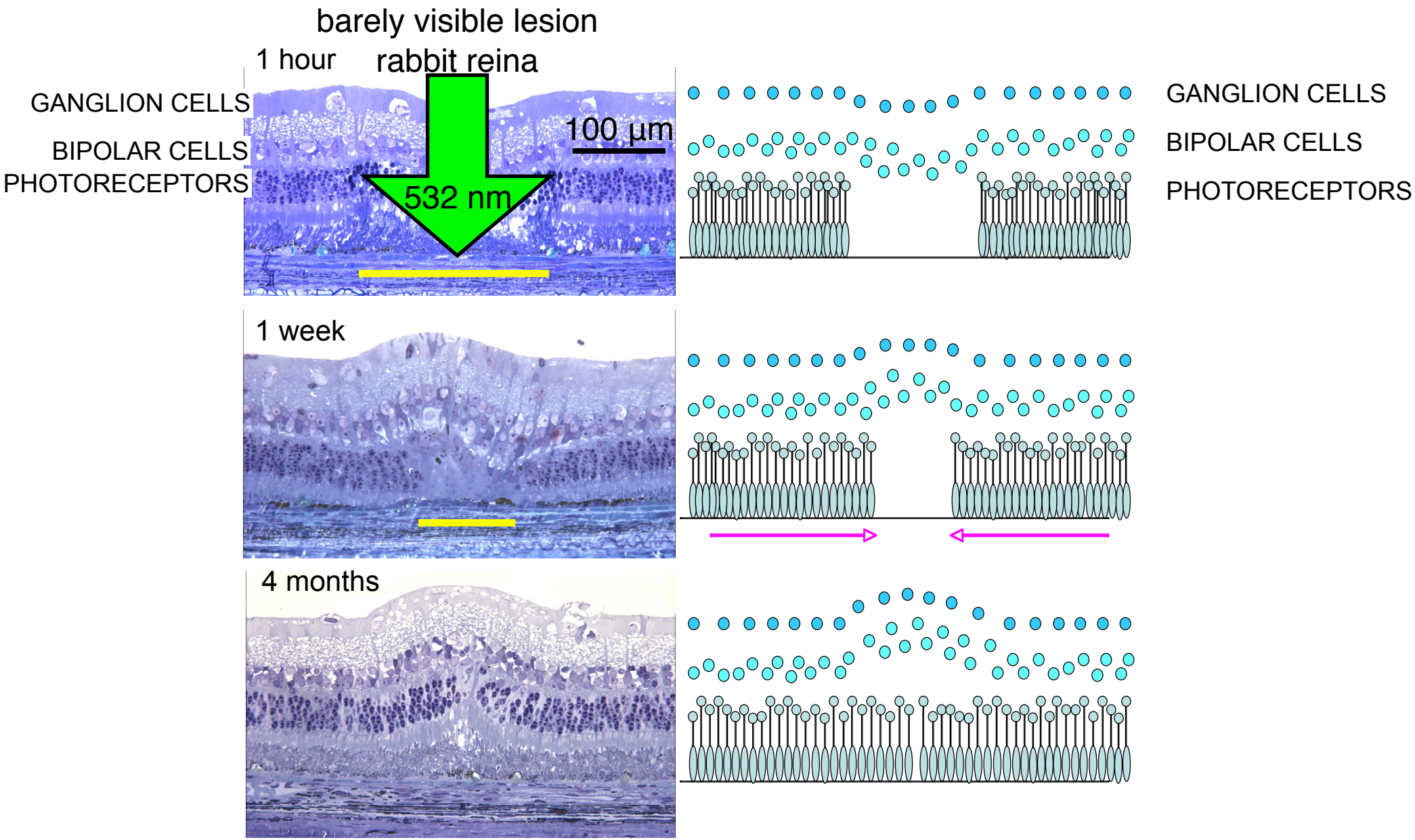
leakage kills retinal
neurons

Photocoagulation



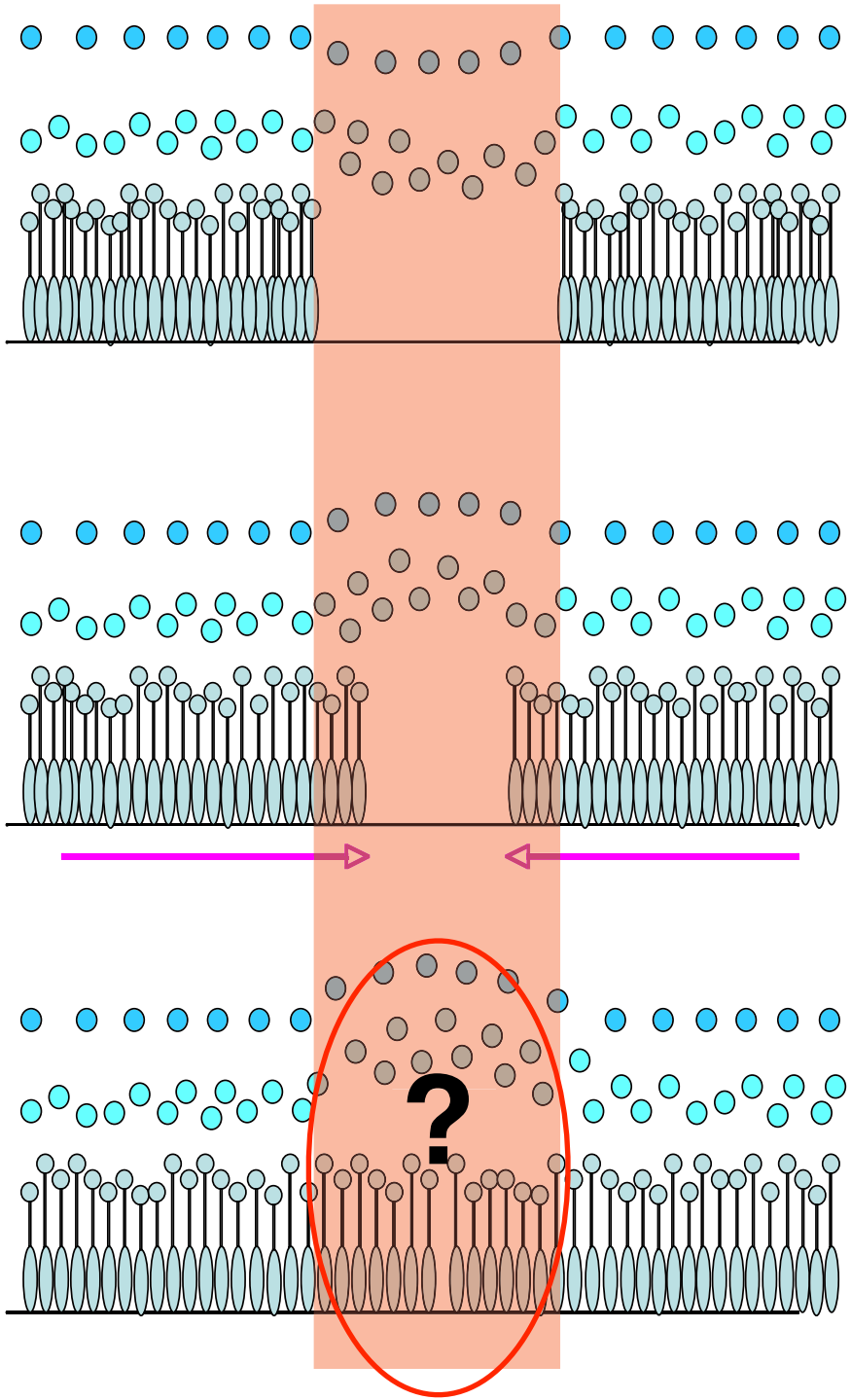
human retina after photocoagulation

Selective photoreceptor photocoagulation



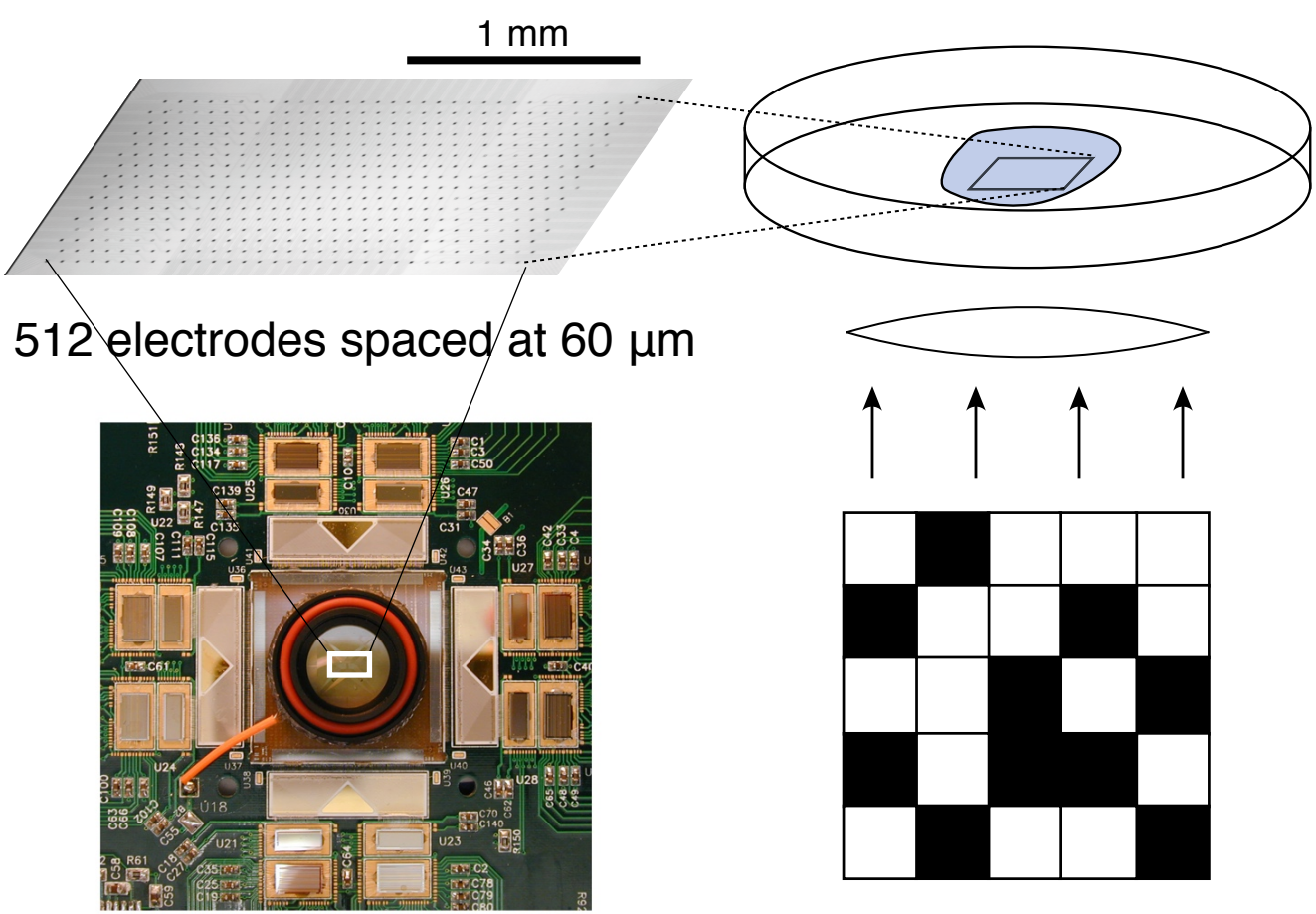
Paulus Y.M., et al, Invest. Ophthalmol. Vis. Sci., 2008

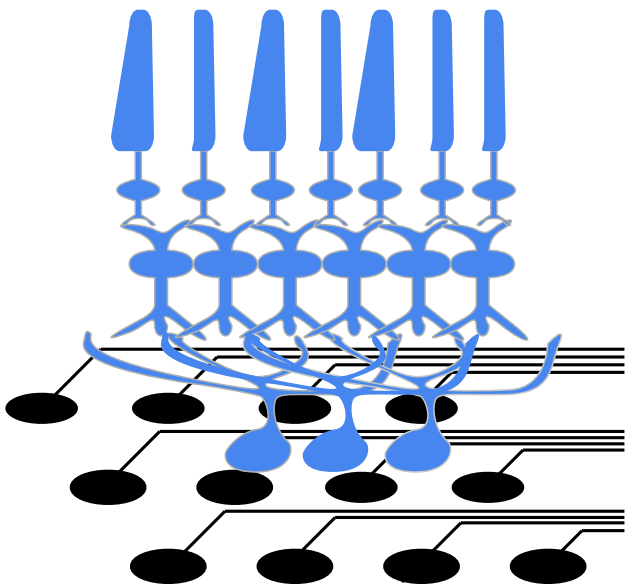
Selective photoreceptor photocoagulation



Methods

multielectrode array recording





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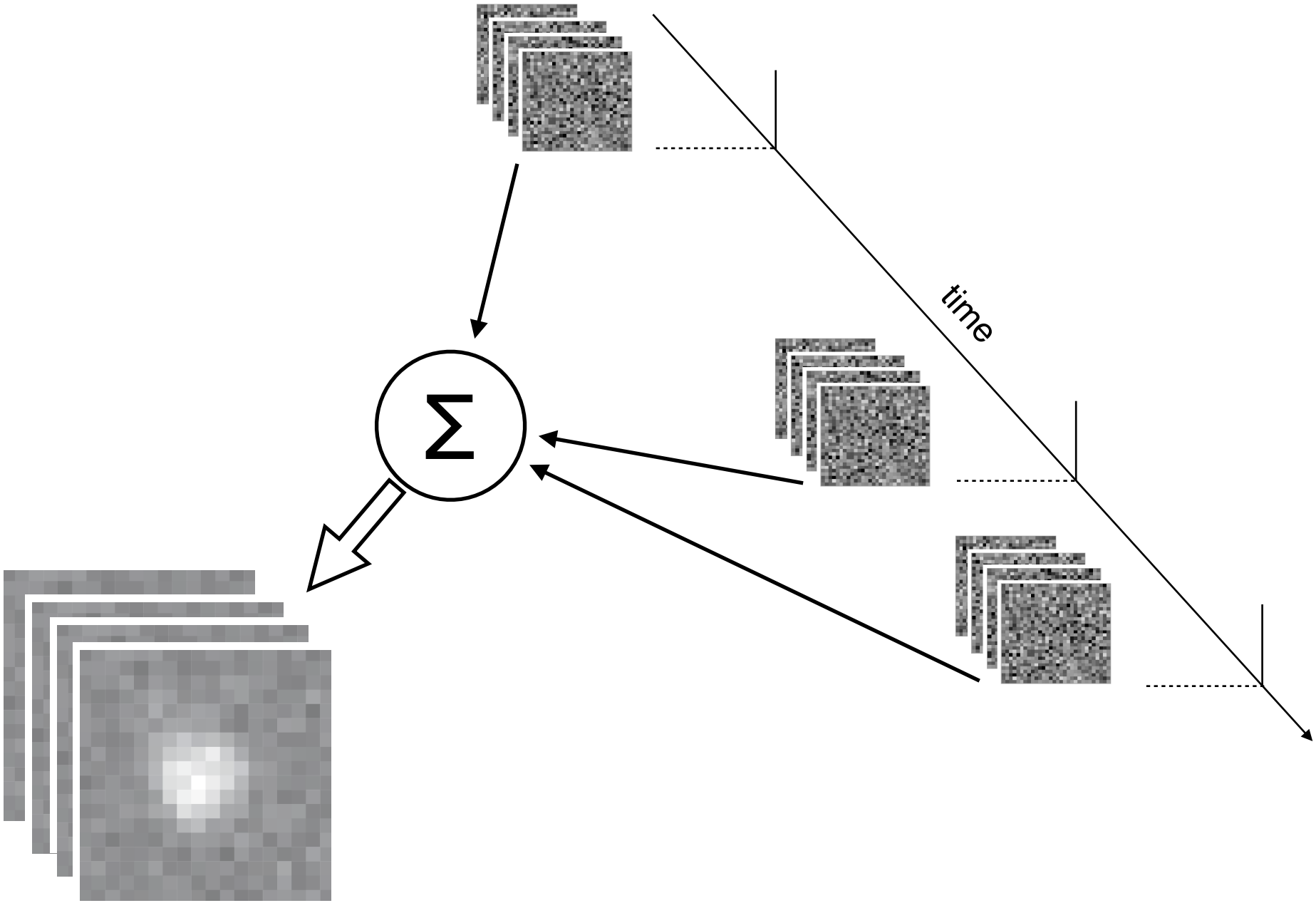
AGH UST, Krakow, Poland
Salk Institute
Starthclyde U., Scotland

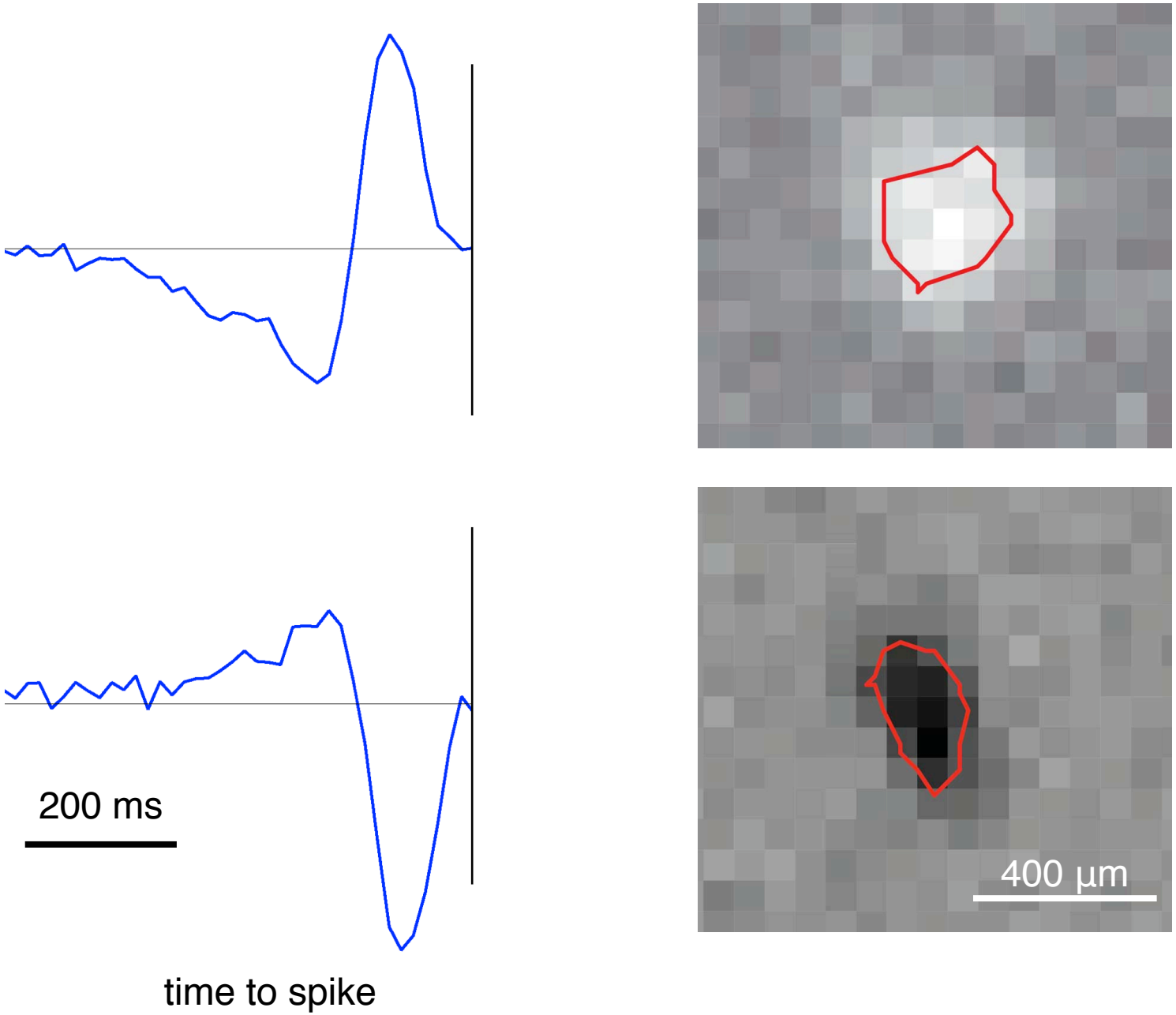
Methods

spike triggered average response of the detected cells



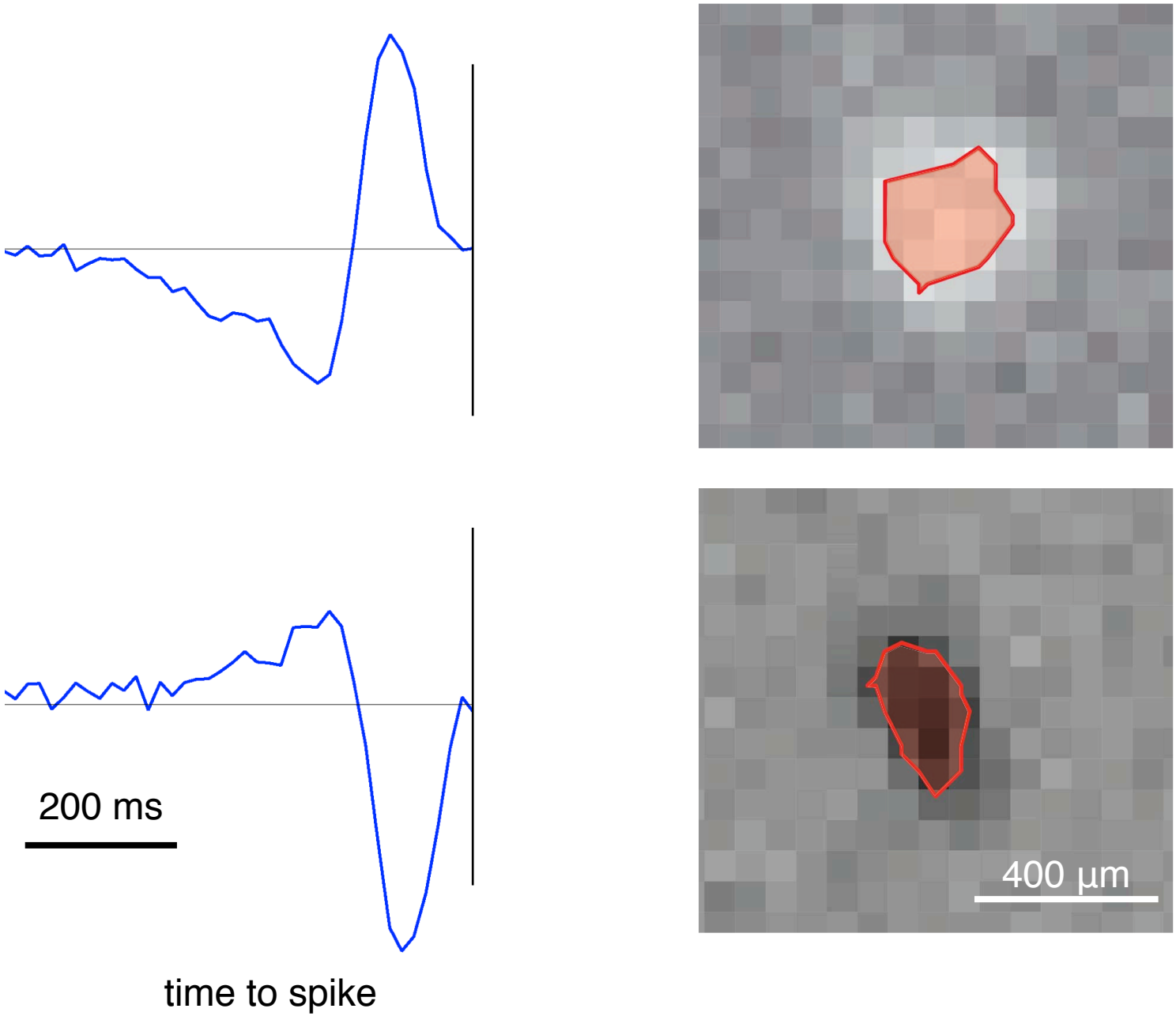
Methods

ON and OFF retinal ganglion cells



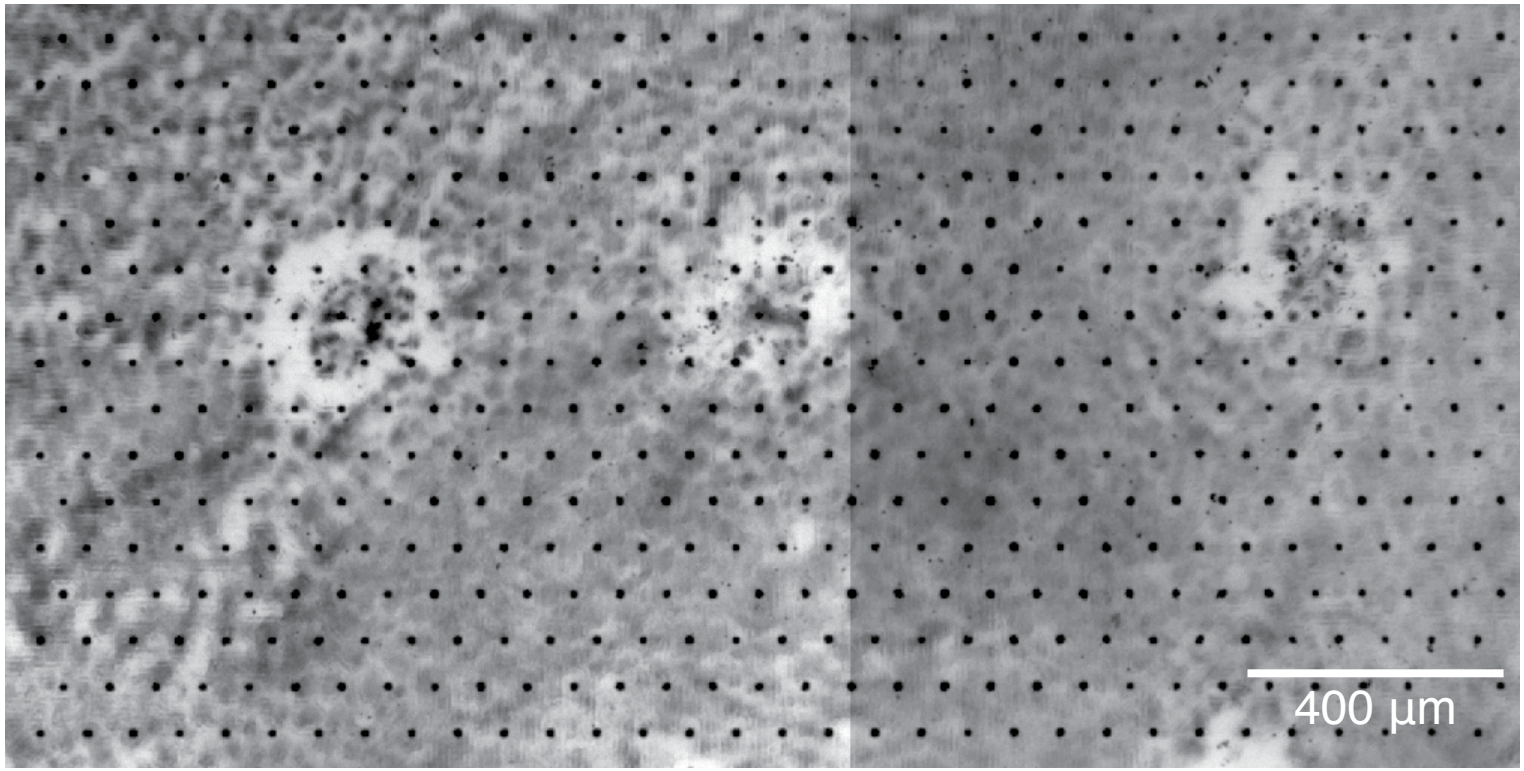
Methods

ON and OFF retinal ganglion cells



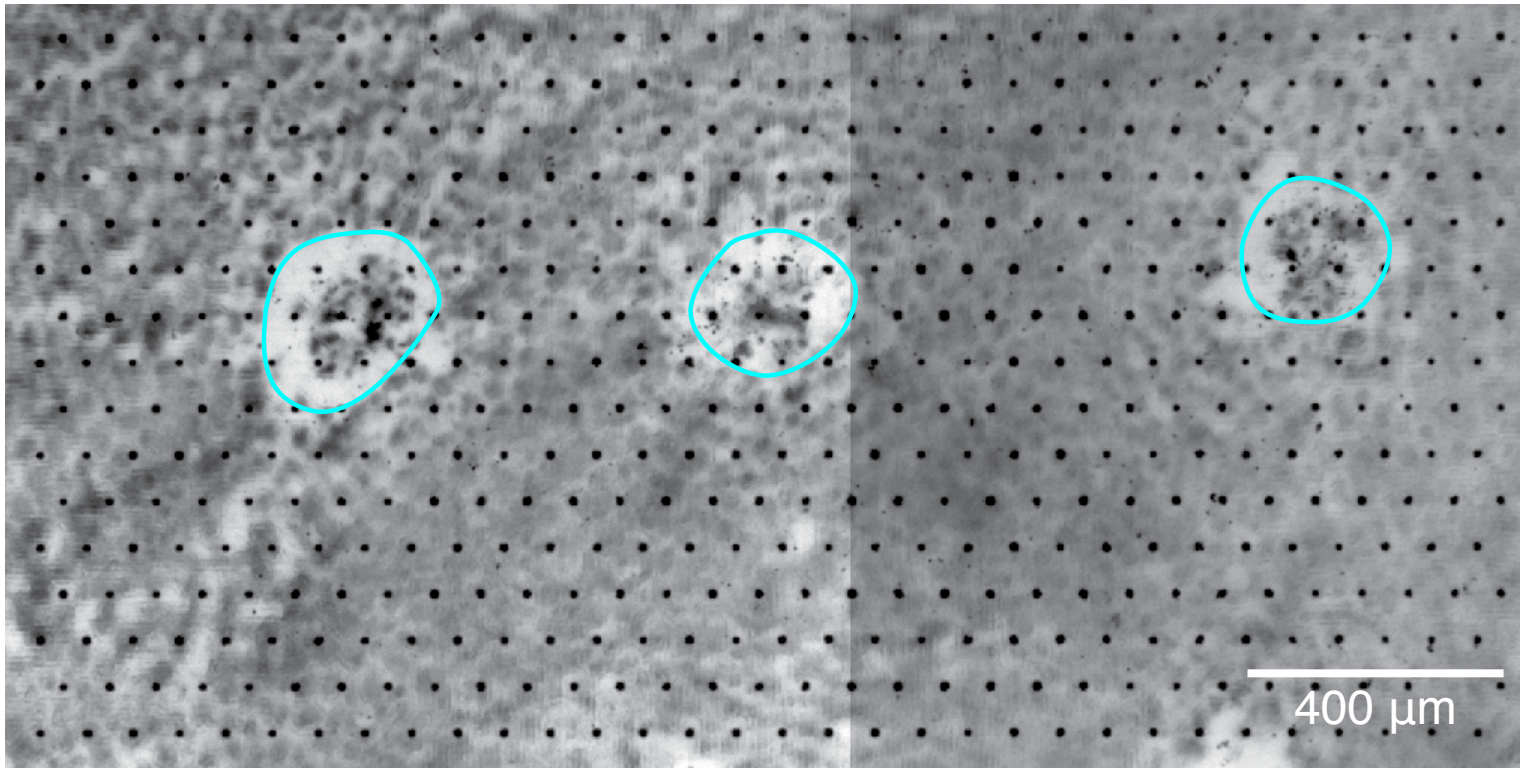
Methods

retina on the electrode array



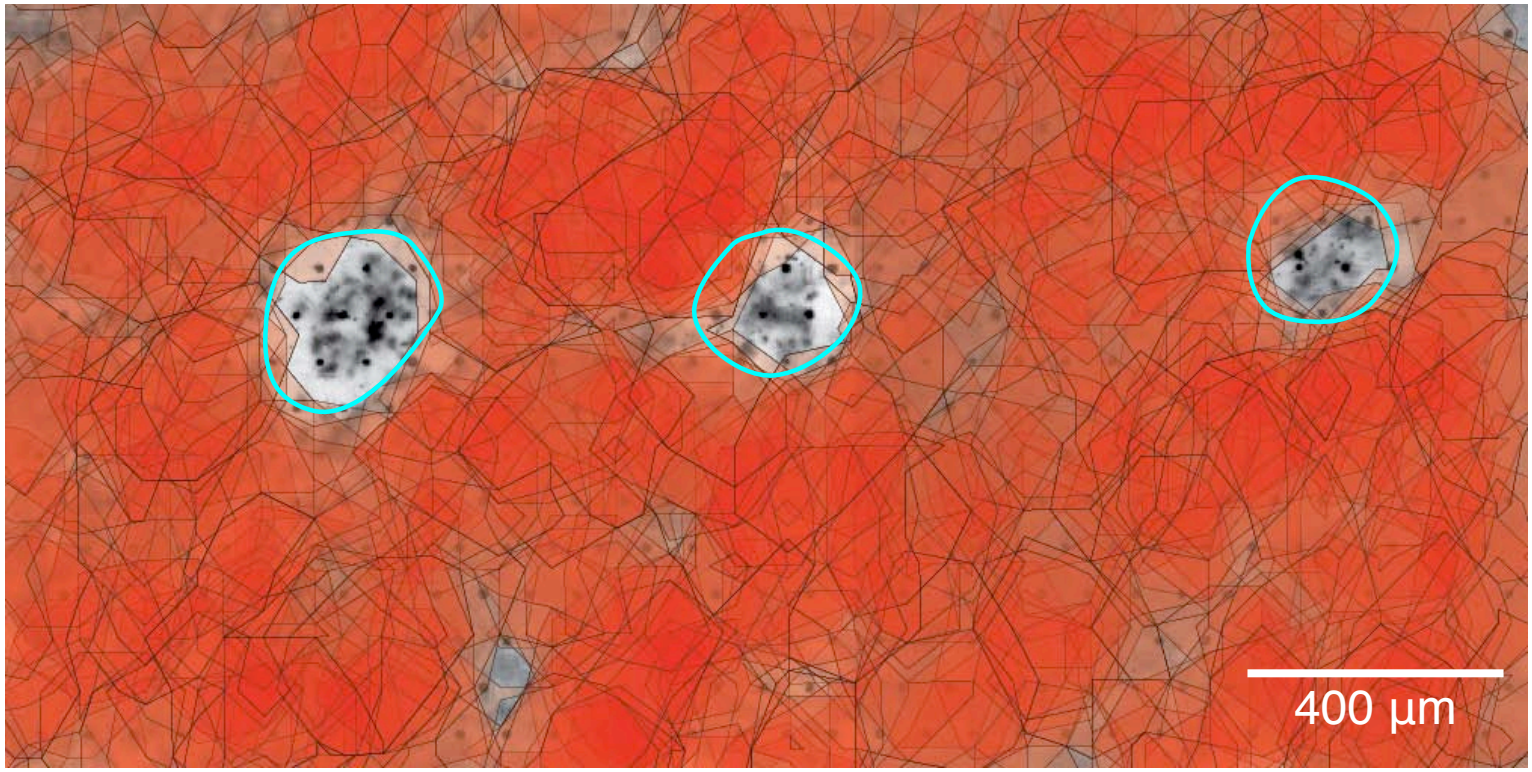
Methods

RPE abnormality zones

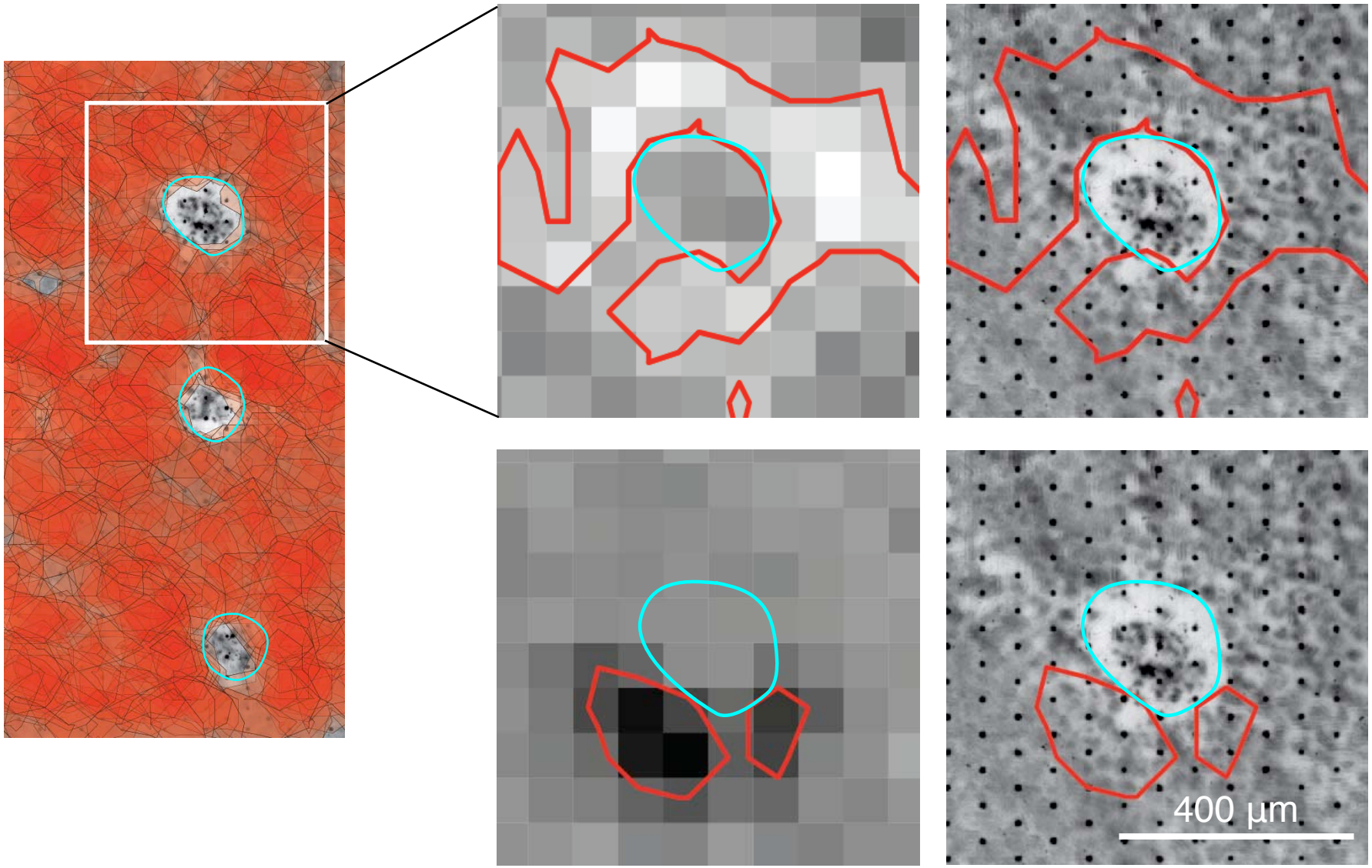


Methods

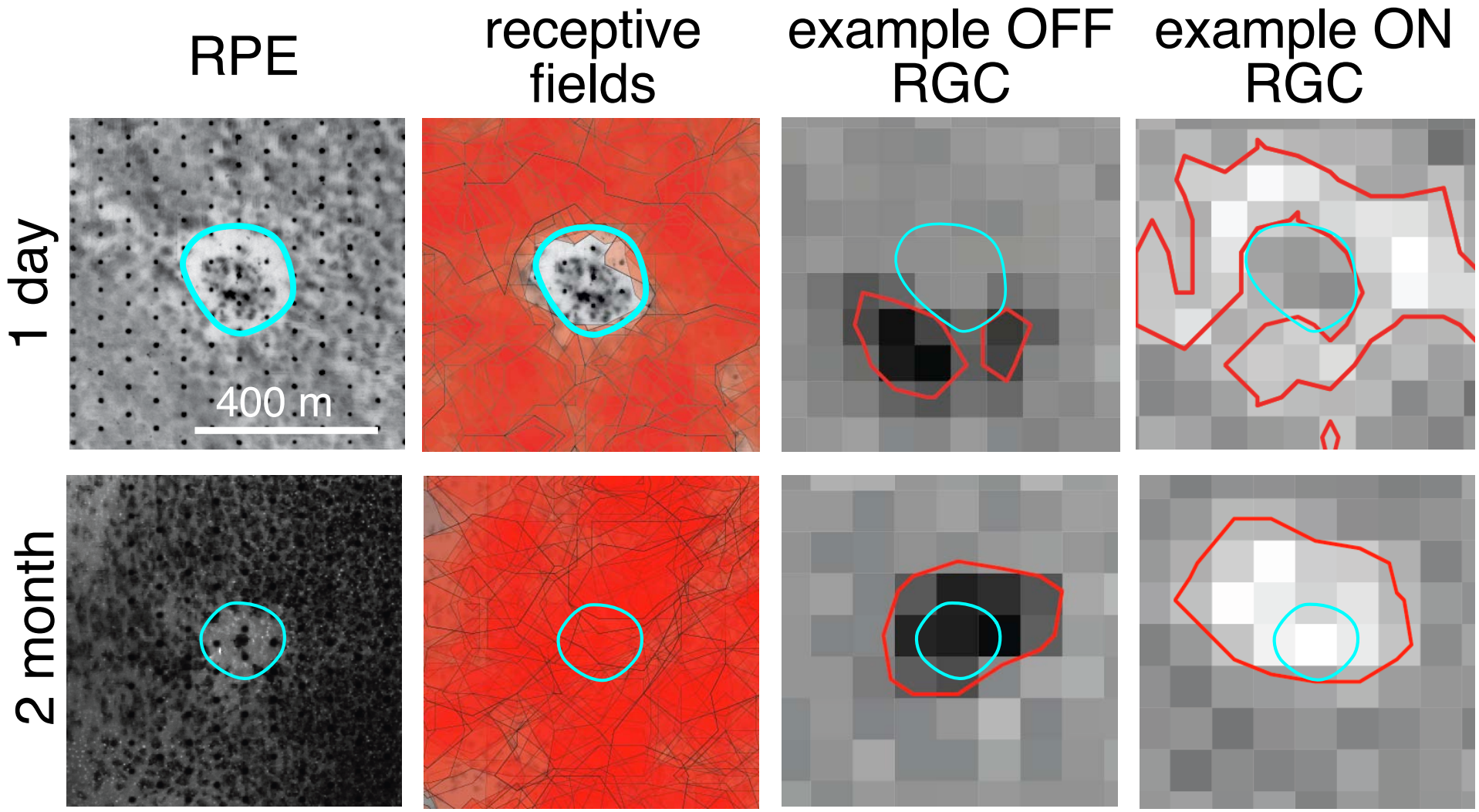
receptive fields of recorded RGCs



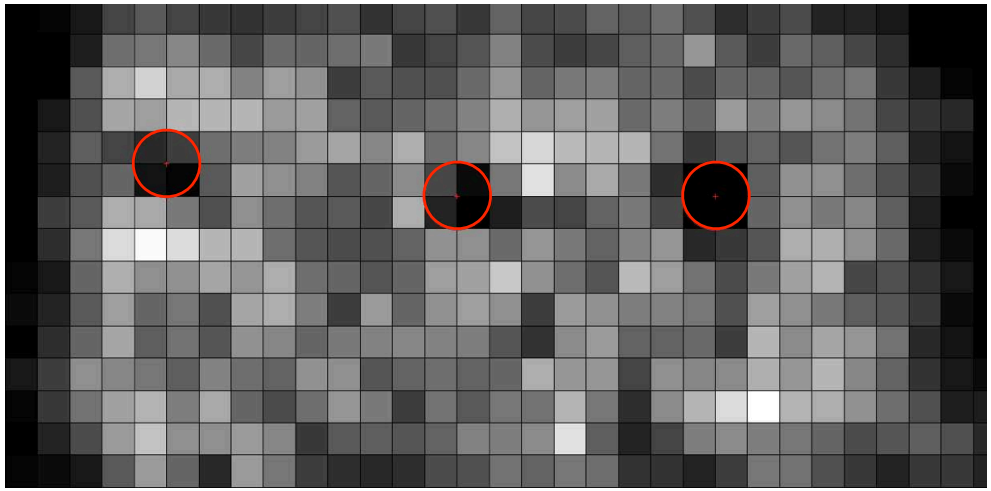
Methods

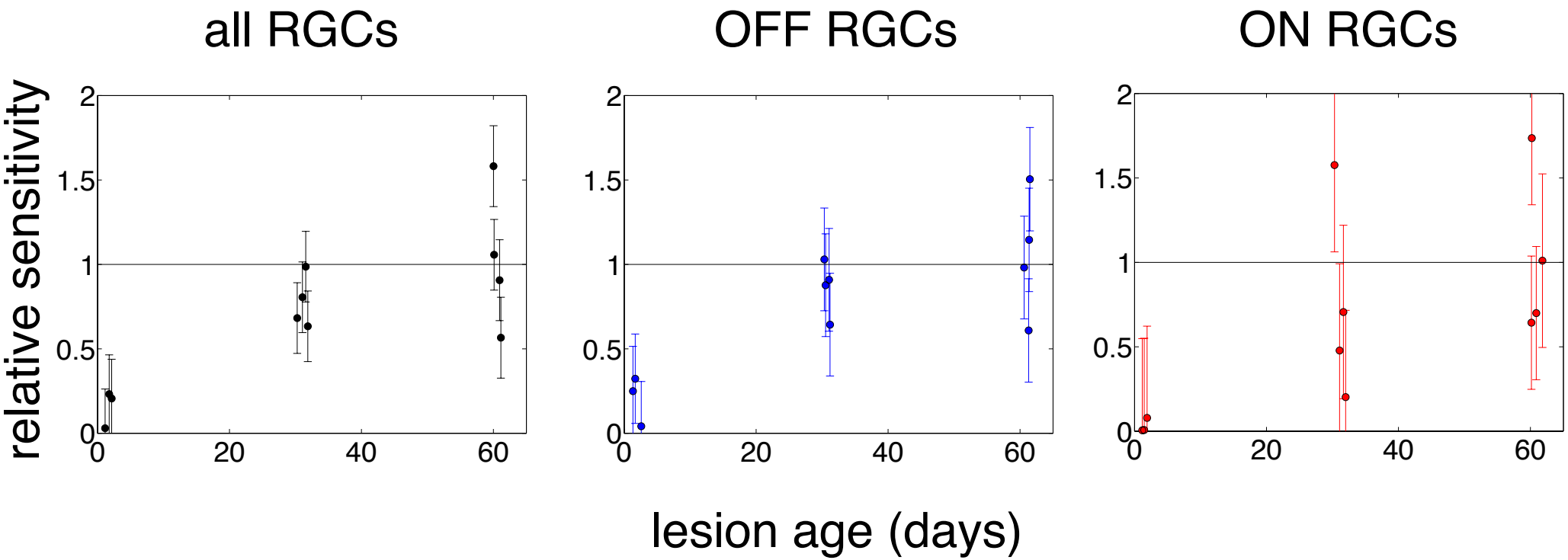


Visual sensitivity is restored

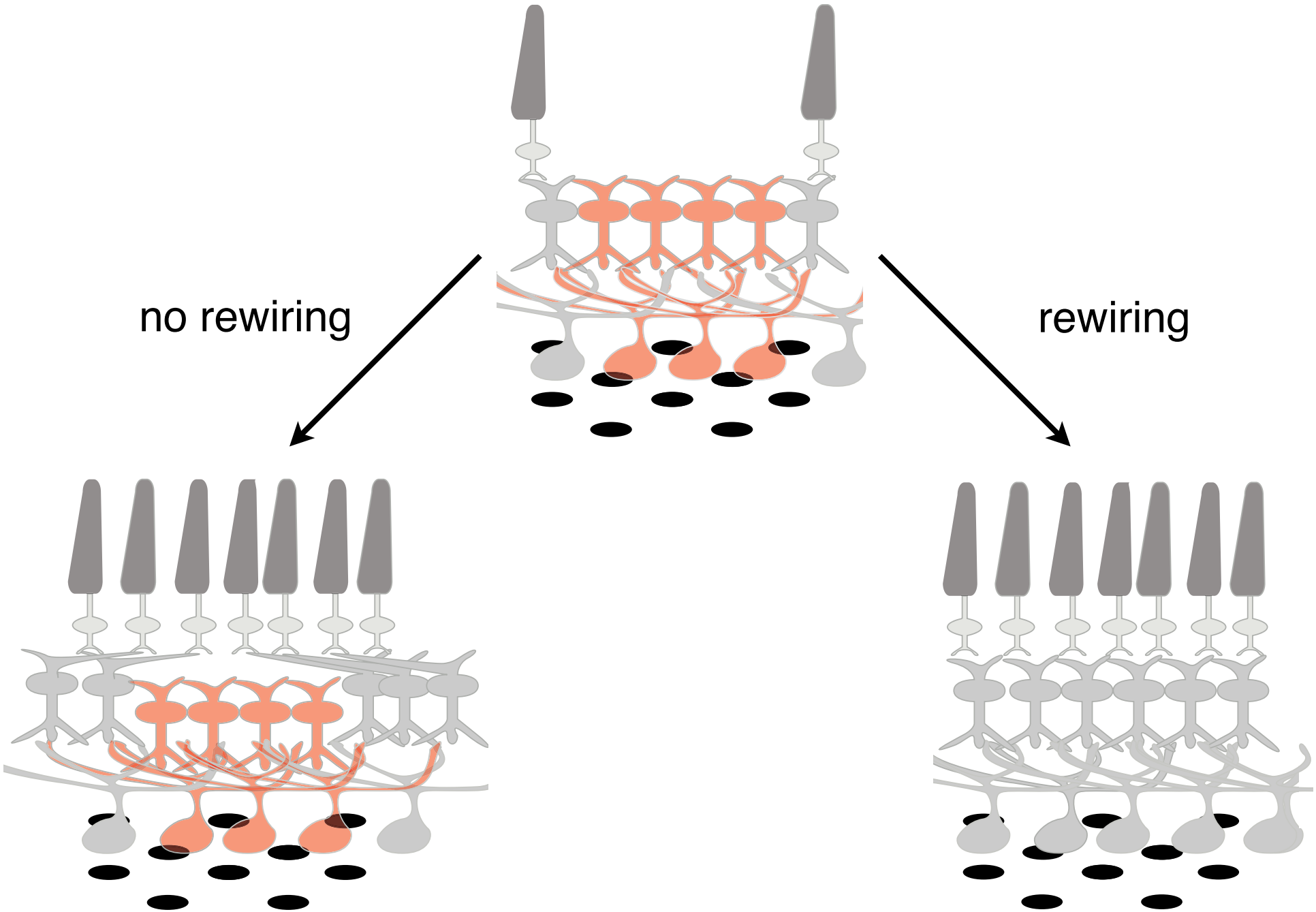


Visual sensitivity is restored

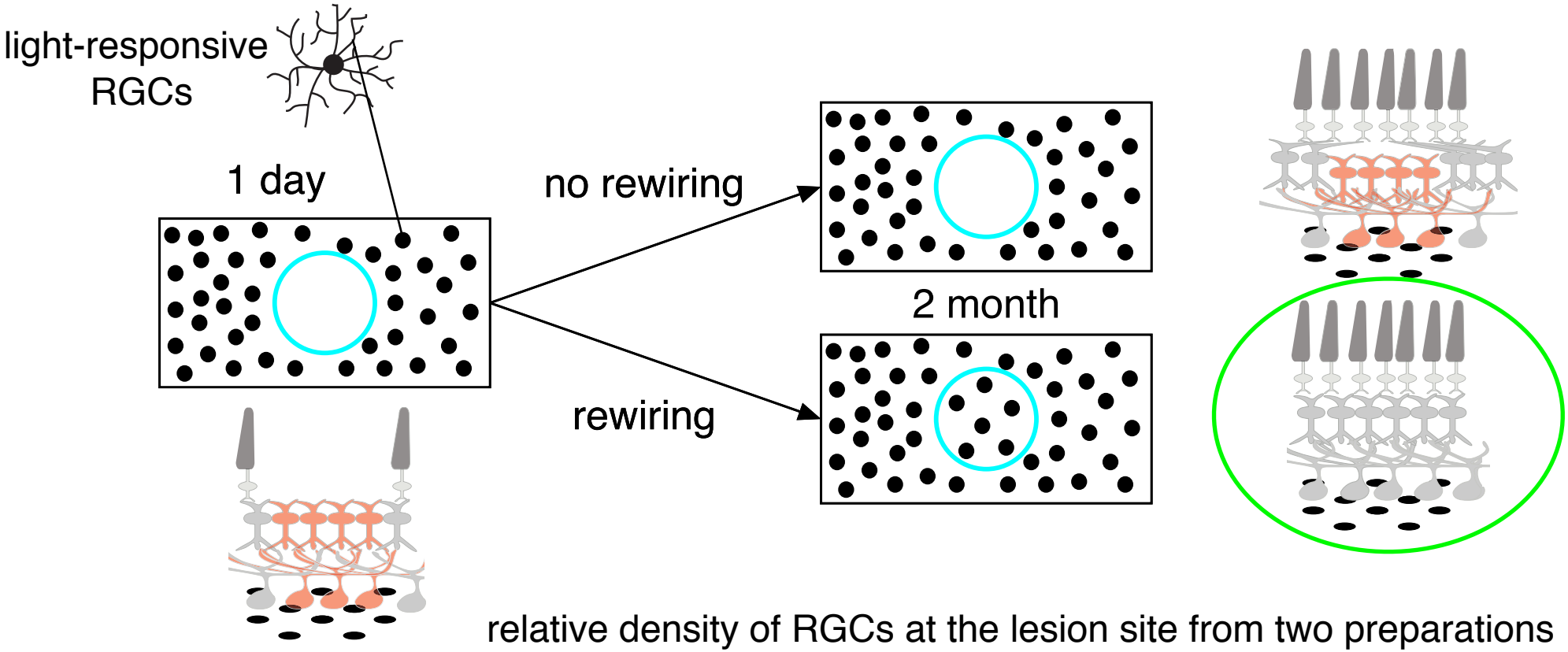




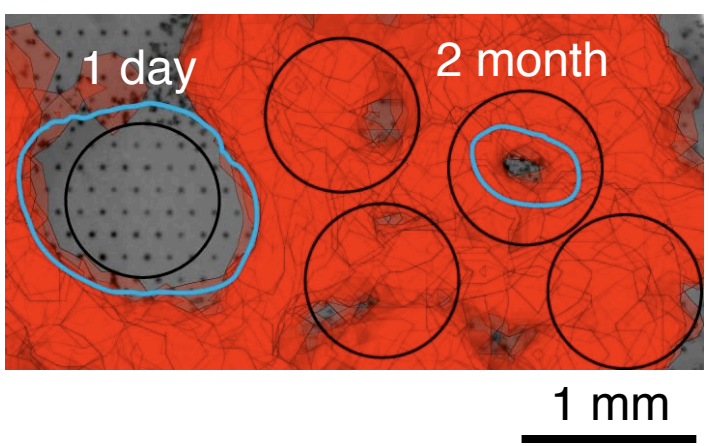
Rewiring

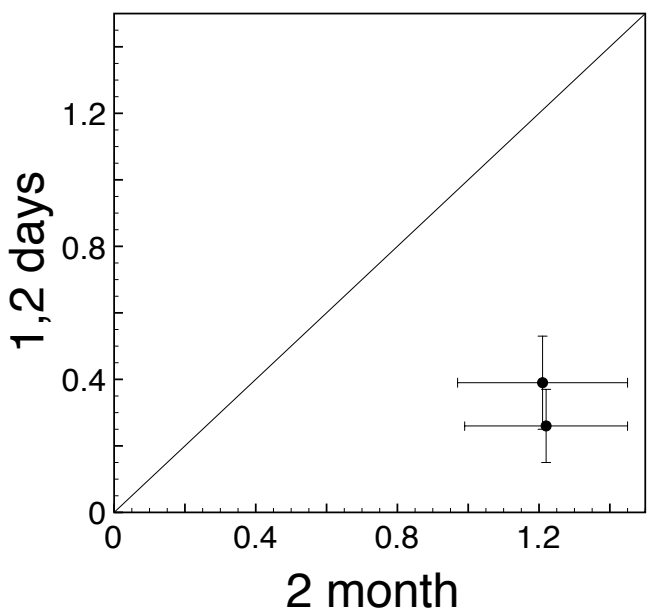


Rewiring



relative density of RGCs at the lesion site from two preparations





Conclusions

- Visual sensitivity restoration occurs both in ON and OFF retinal pathways.
- Migrating photoreceptors rewire to deafferented bipolar cells, bringing retinal circuitry closer to normal and demonstrating restorative plasticity.
- Selective ablation of photoreceptors avoids side effects that accompany conventional (more severe) burns, while reducing the metabolic load by killing photoreceptors. It also allows for *repeated* treatment.

Sher, et al, Journal of Neuroscience, 2013

Age related macular degeneration

photoreceptors in the central retina (macula) start to break down causing blurring and potentially blind spots

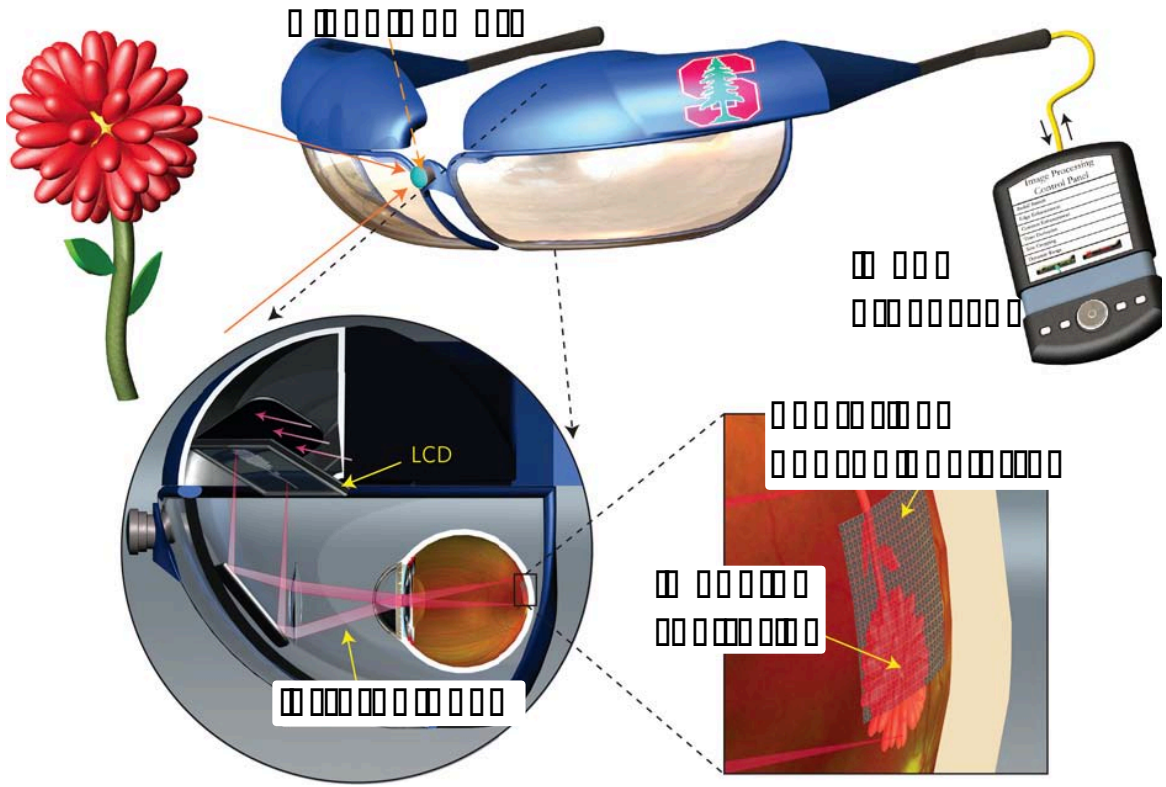
Age related macular degeneration

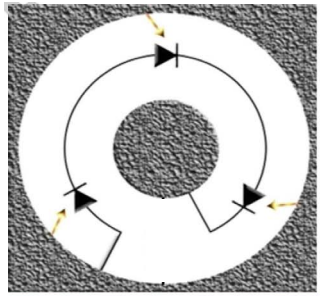
photoreceptors in the central retina (macula) start to break down causing blurring and potentially blind spots

But the processing and output retinal neurons are still there!

Activate them using electrical currents

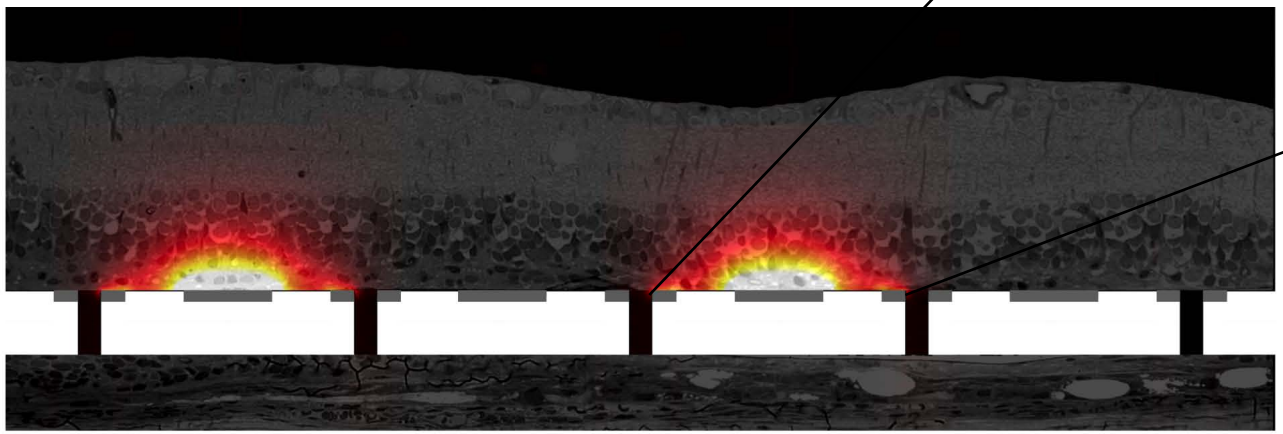
Subretinal photovoltaic prosthesis



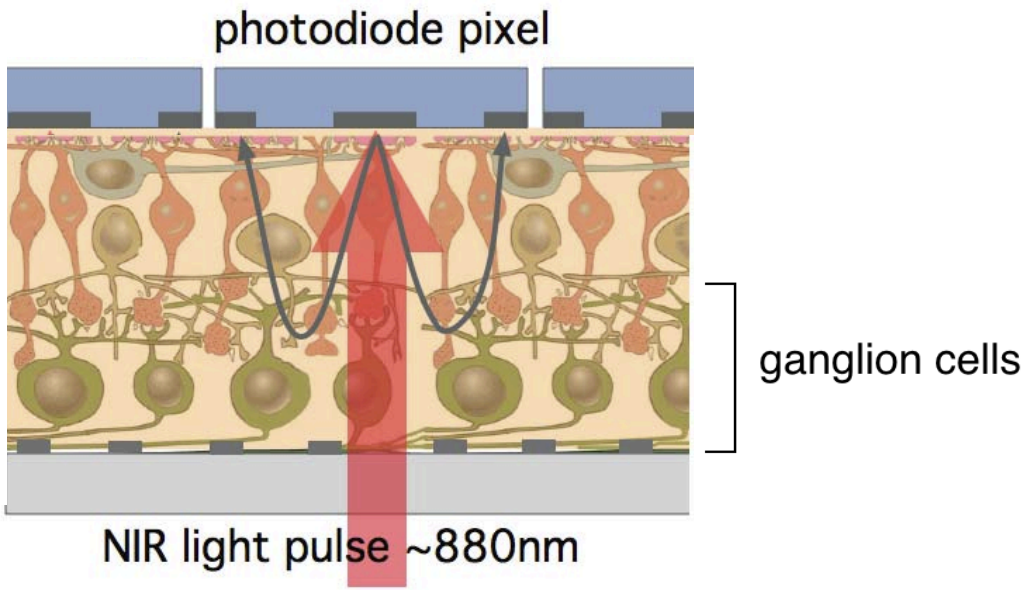


50 µm

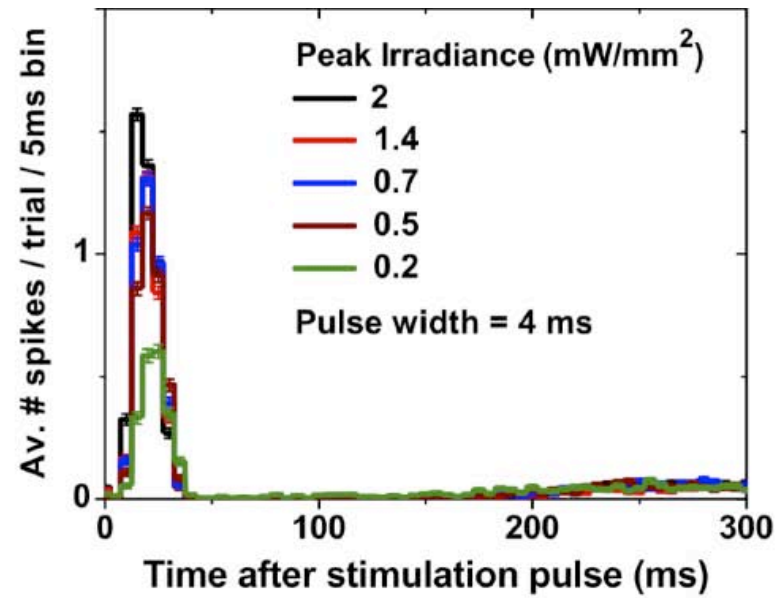
each photodiode pixel consists of 3 diodes in series:



Photovoltaic prosthesis activates ganglion cells



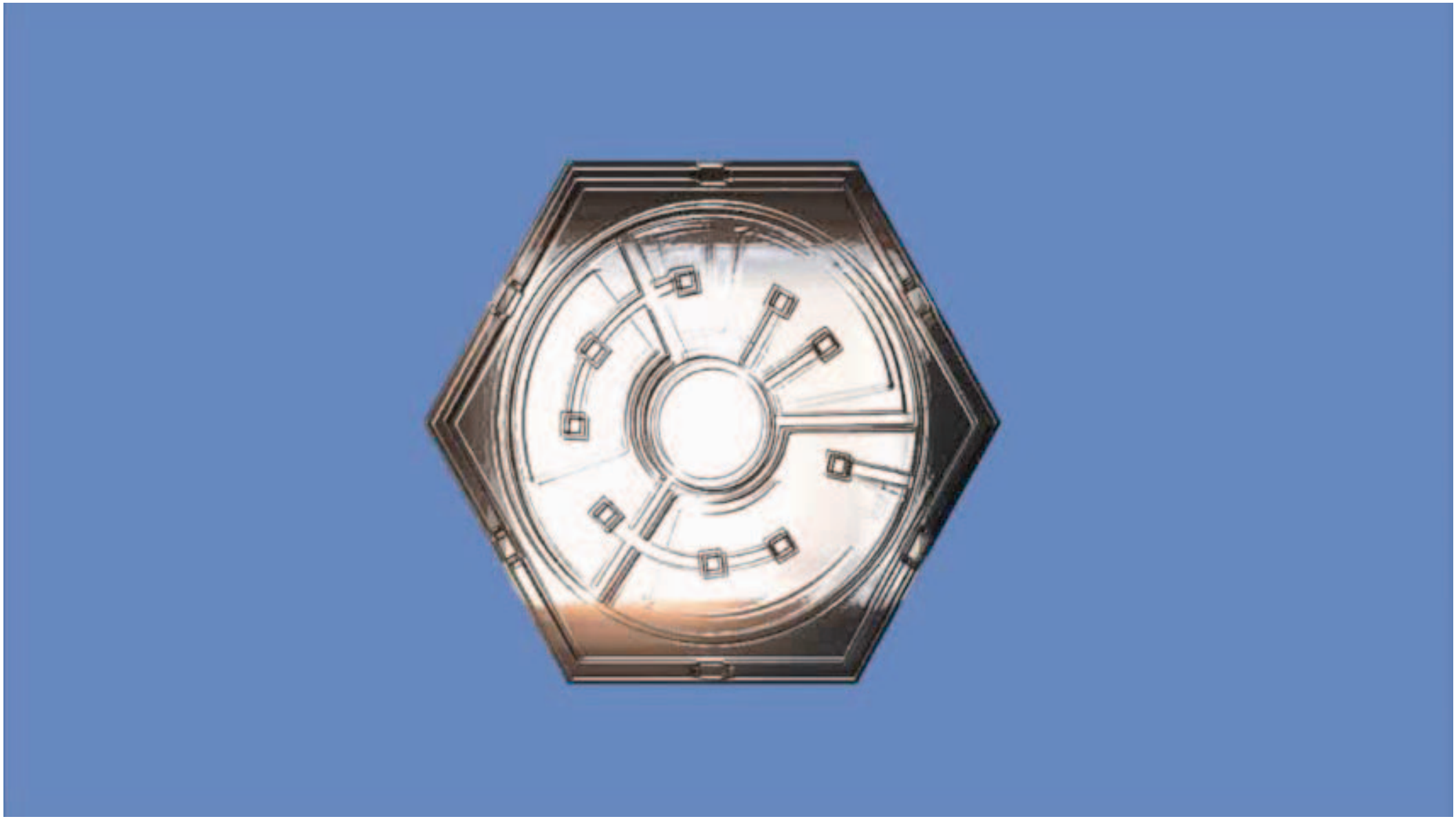
Response of a ganglion cell to photovoltaic stimulation



- Ganglion cells can be activated with safe amount of infrared light.
- Activation occurs not directly, but through the bipolar cells.

Matheison, et al, Nature Photonics, 2012

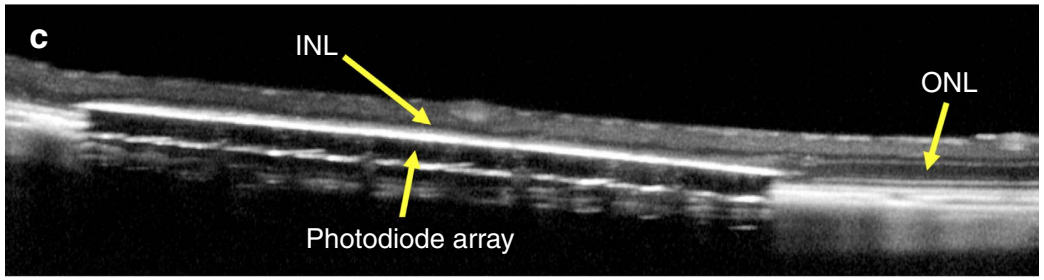
Implantation procedure



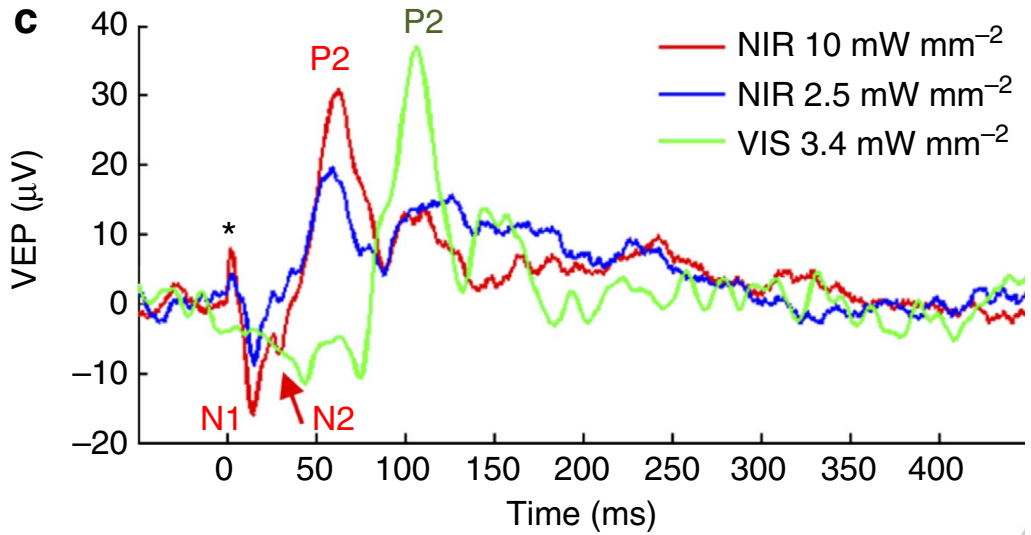
video curtesy of D. Palanker

Brain visual areas get activated through the prosthesis

Optical Coherence Tomography image of the photodiode array chronically implanted under the rat retina.



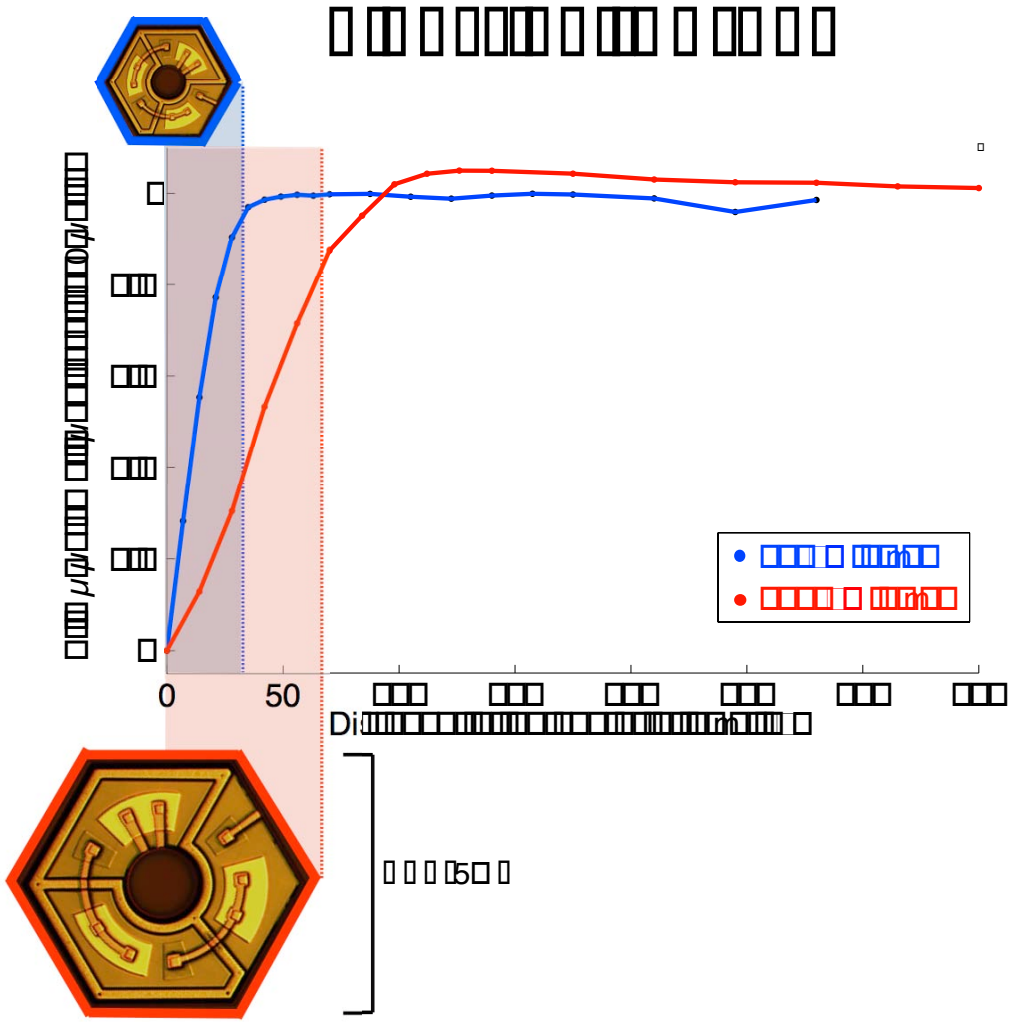
Visually Evoked Potentials recorded from the rat implanted with the photodiode array.

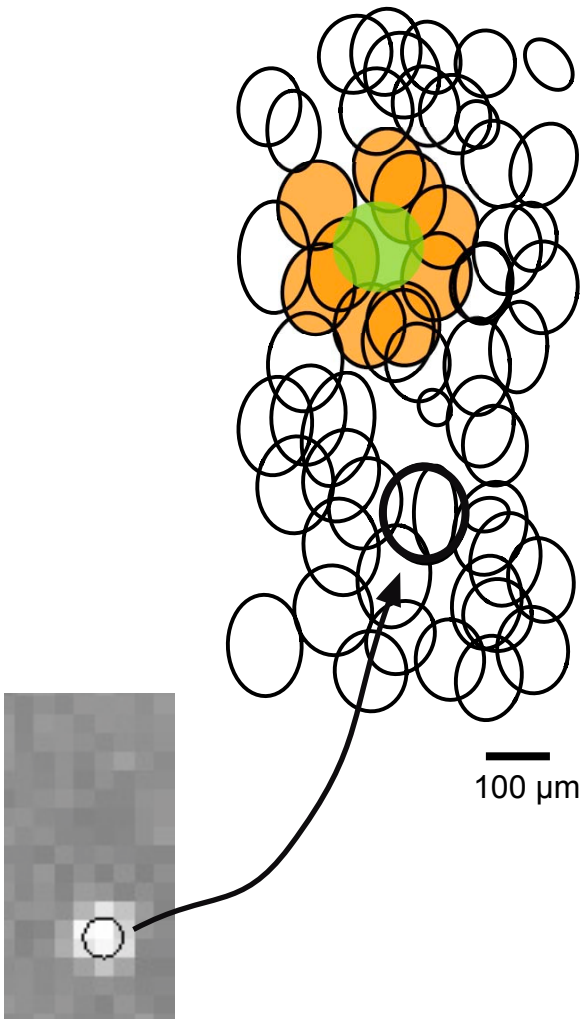


Mandel, et al, Nature Communications, 2013

What is the spatial resolution?

Stimulus Spread: Electrical and Retinal

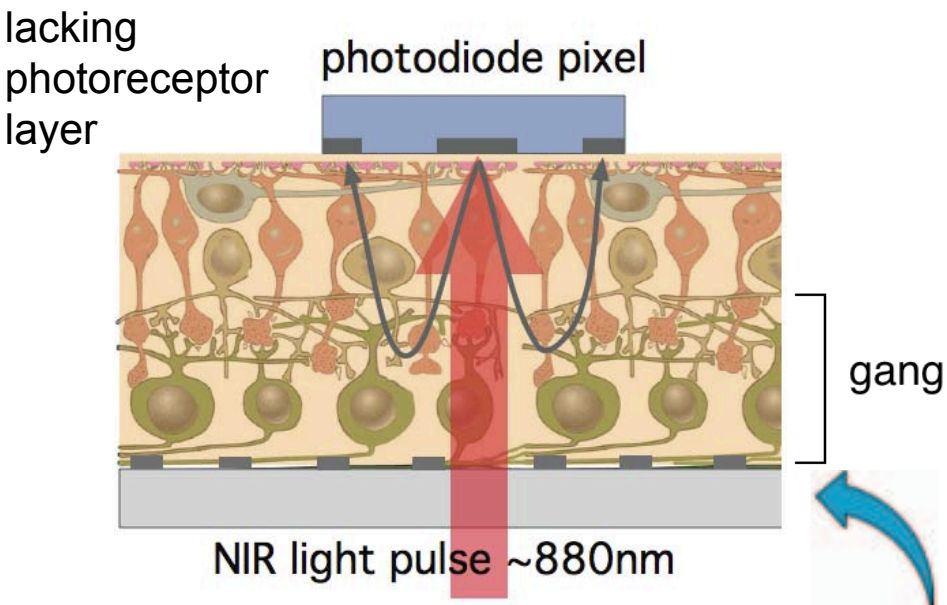


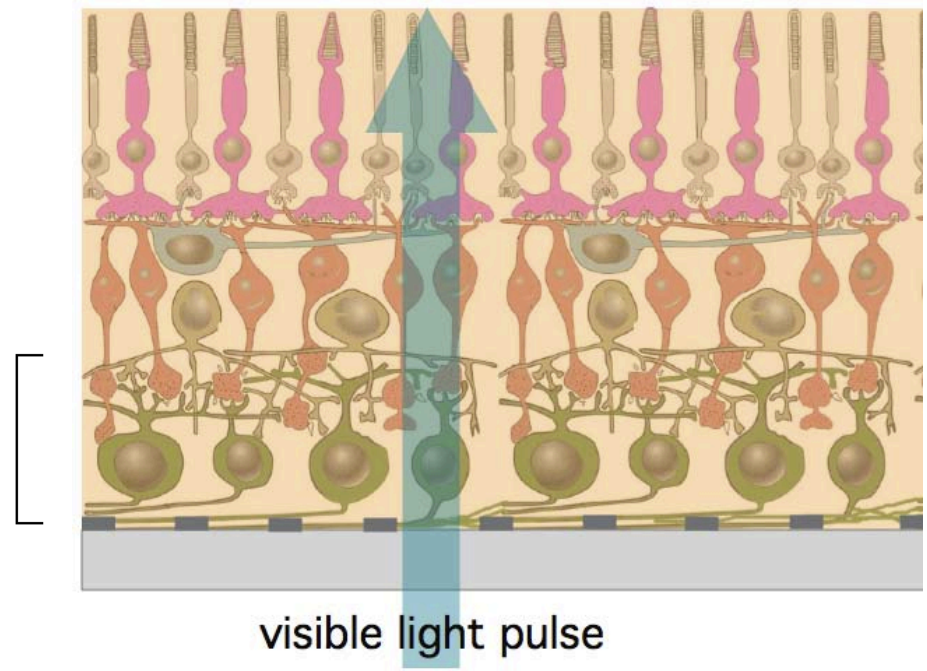


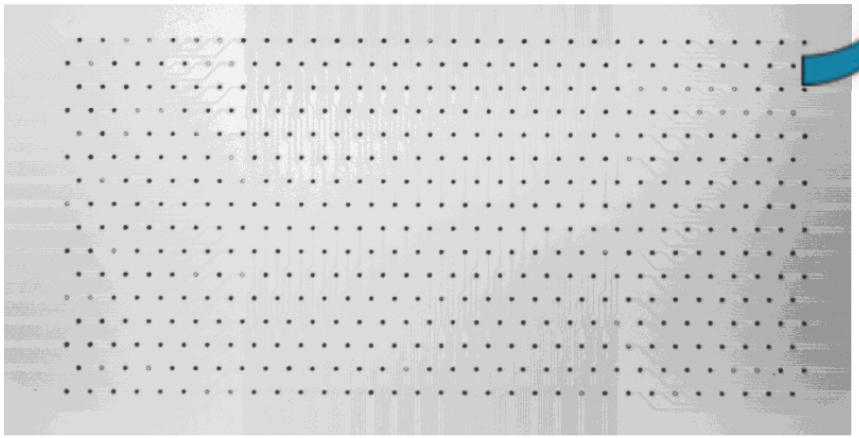
Methods

photodiode stimulation
of RCS degenerate retina:

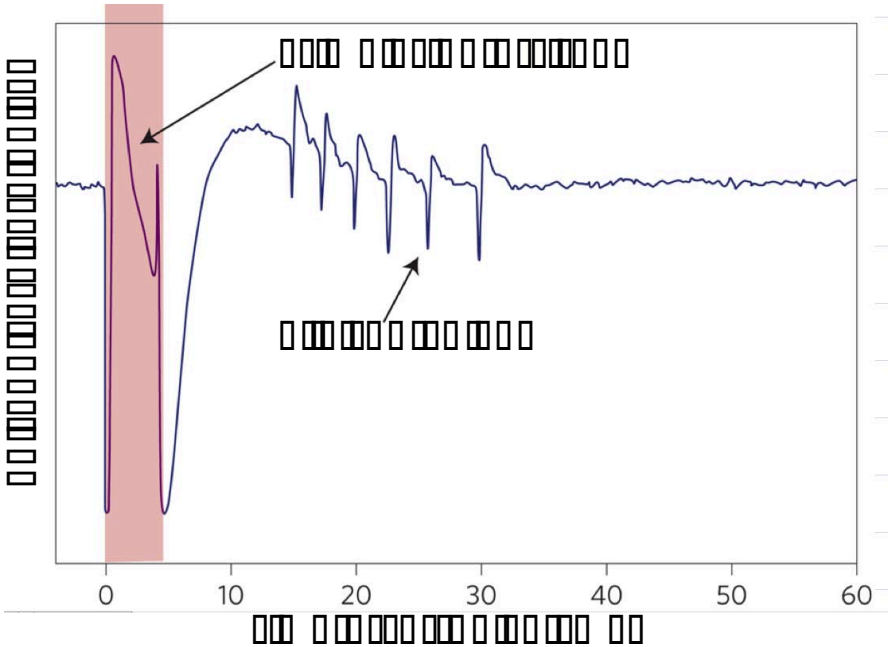
Visible light stimulation
of wild-type rat retina:



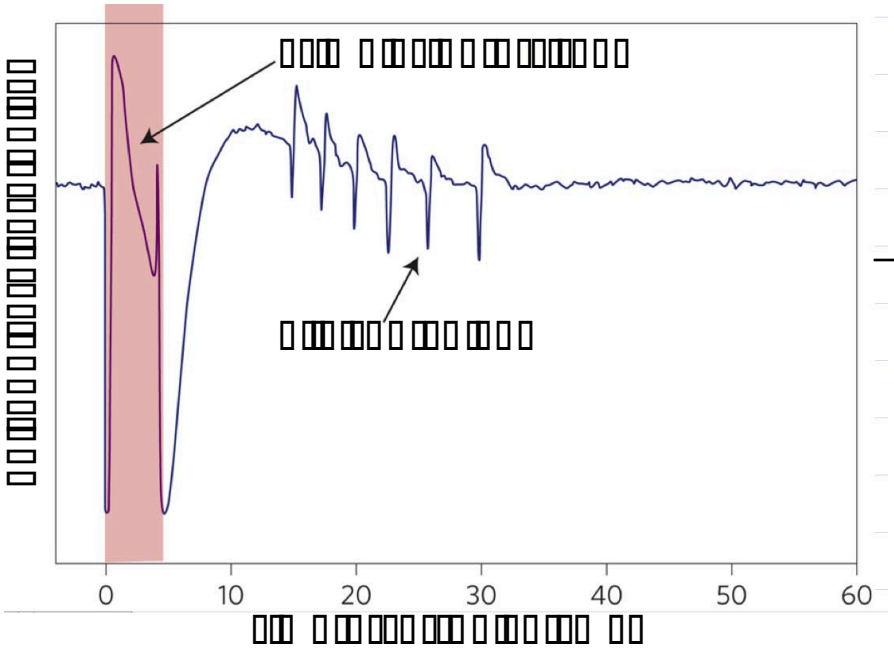


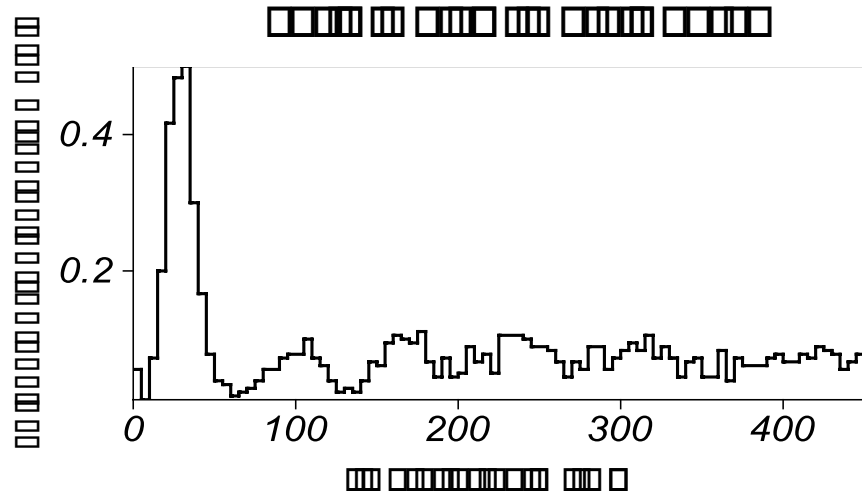


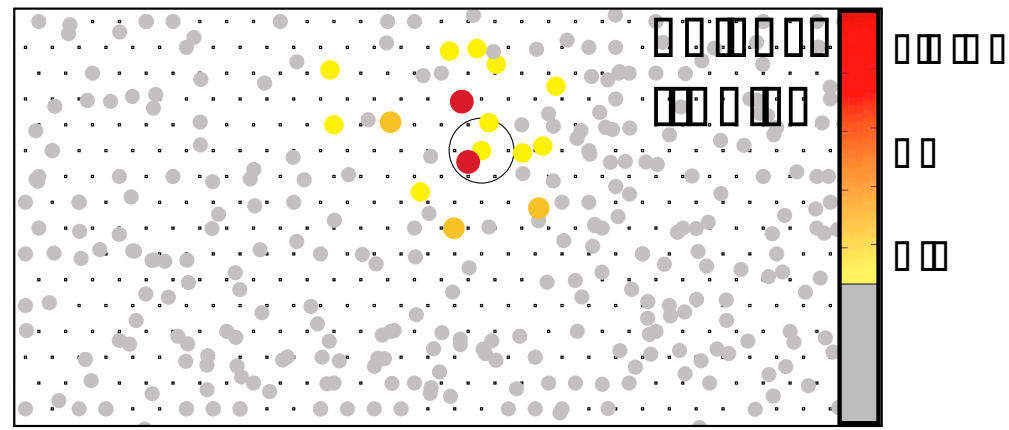
multielectrode recording
array with 512 electrodes,
spaced at 60 microns

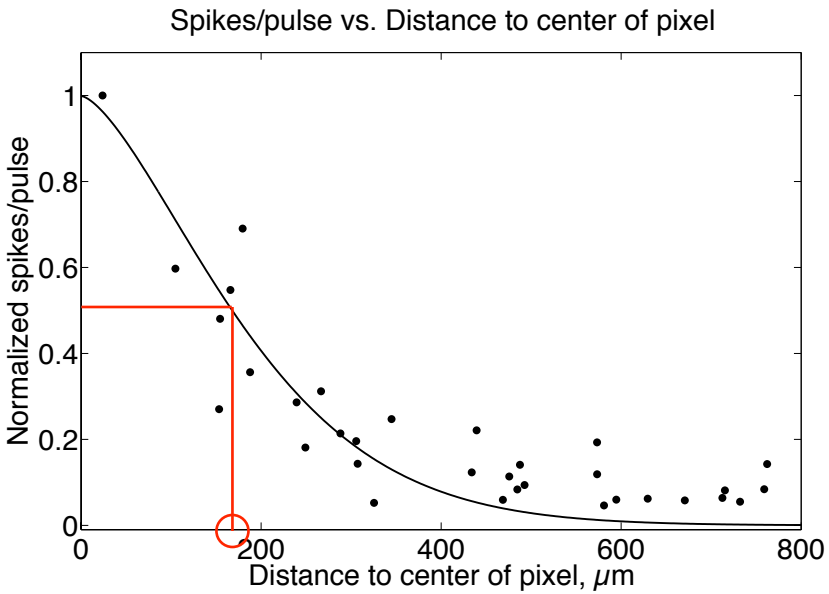


Mapping the Spread of Stimulation



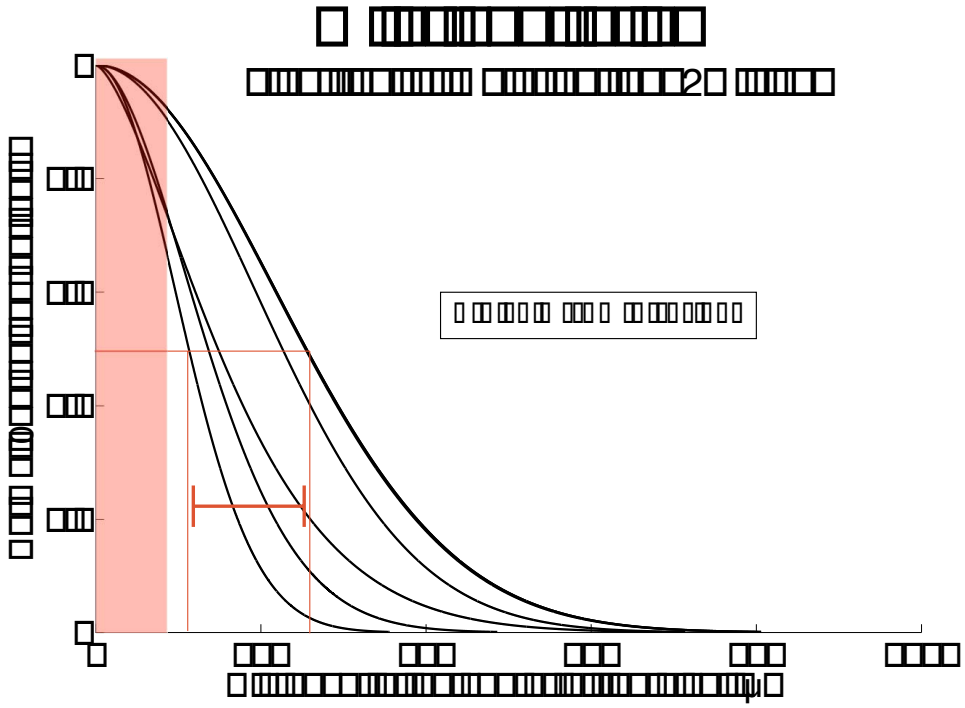


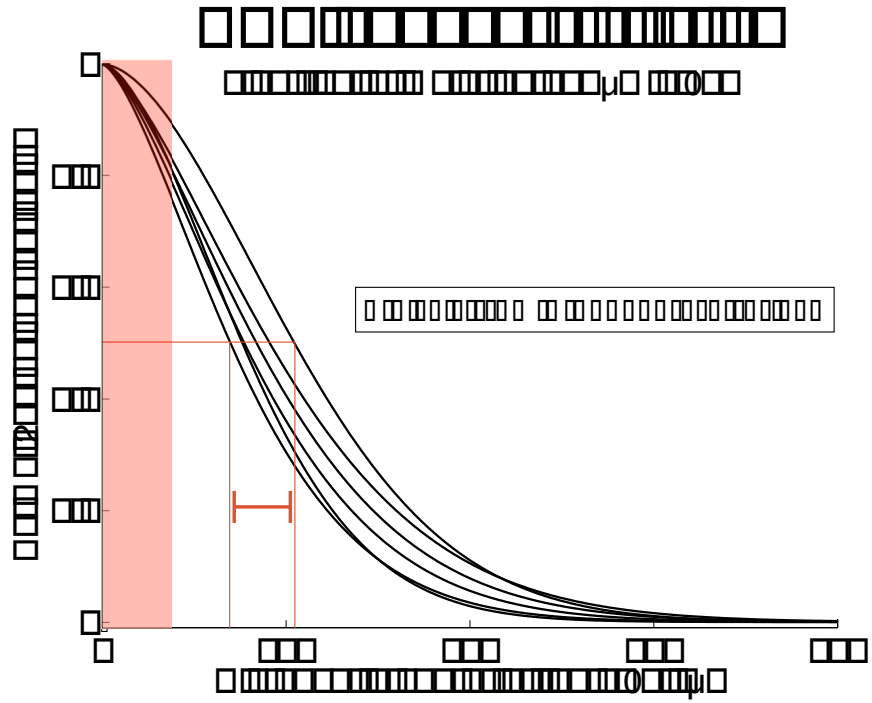


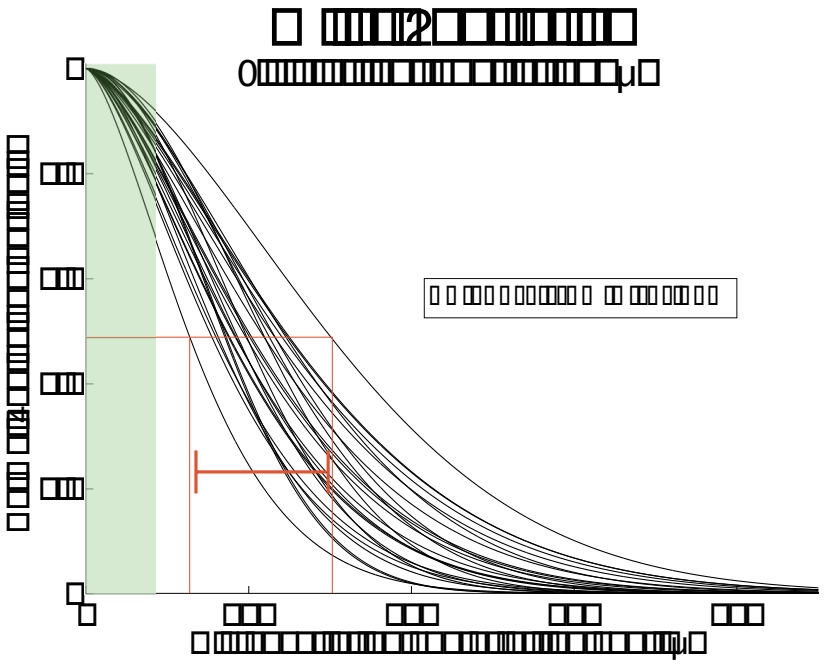


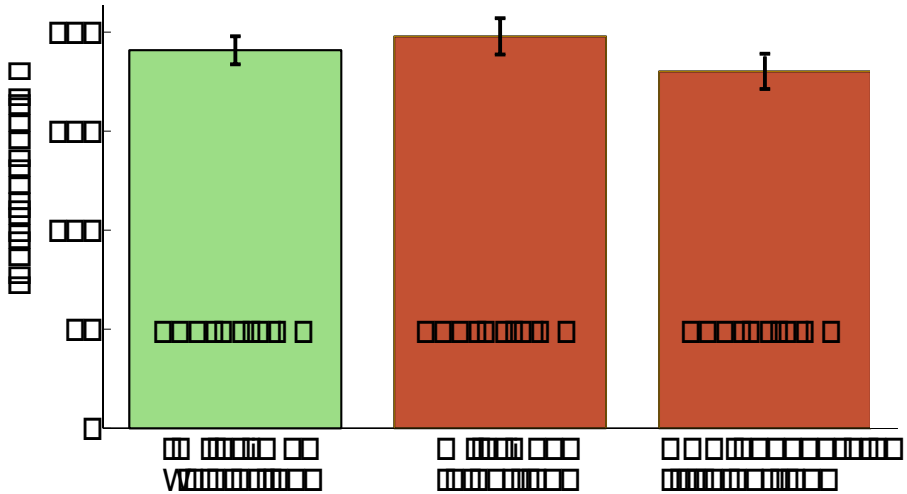
Radial spread: defined as distance at which stimulation drops to 50% of it's maximum

Stimulation Spread









Conclusions

- Photovoltaic retinal prosthesis provides for safe stimulation of the retina that is relayed to the brain.
- Measured spatial spread of photovoltaic stimulation is comparable to the spread of visual stimulation measured in the healthy rat retina.
- It remains to be seen if this prosthesis design can provide spatial resolution needed by ARMD patients.

Thank you!

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