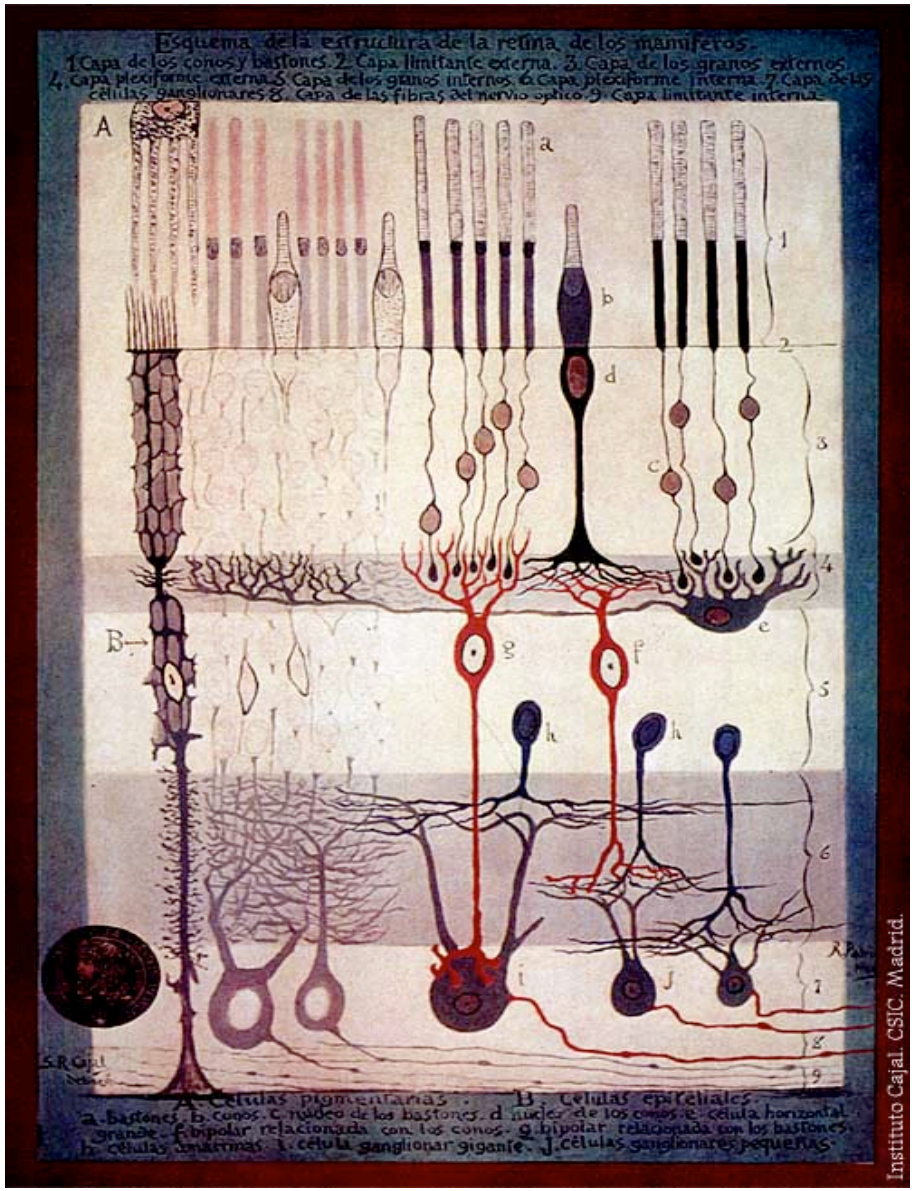
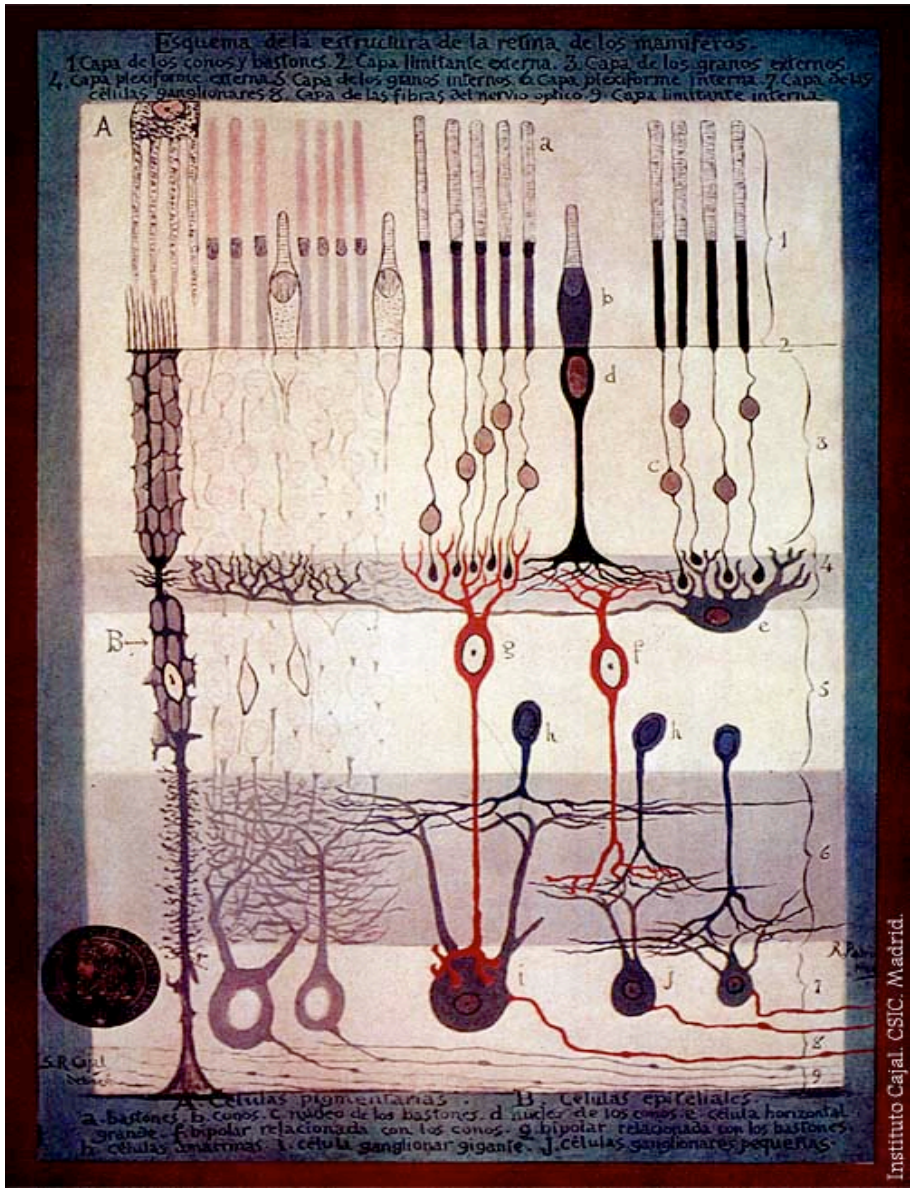
Retina

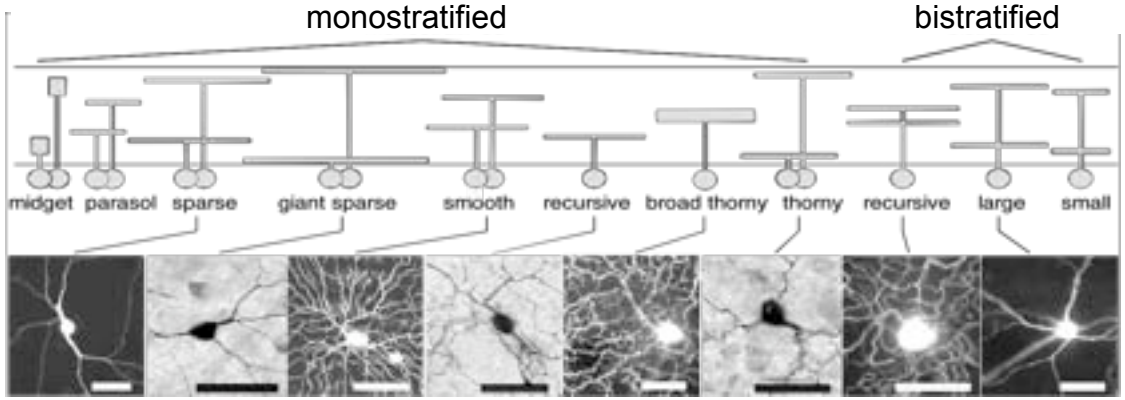


Cajal, 1900

Retina



Cajal, 1900



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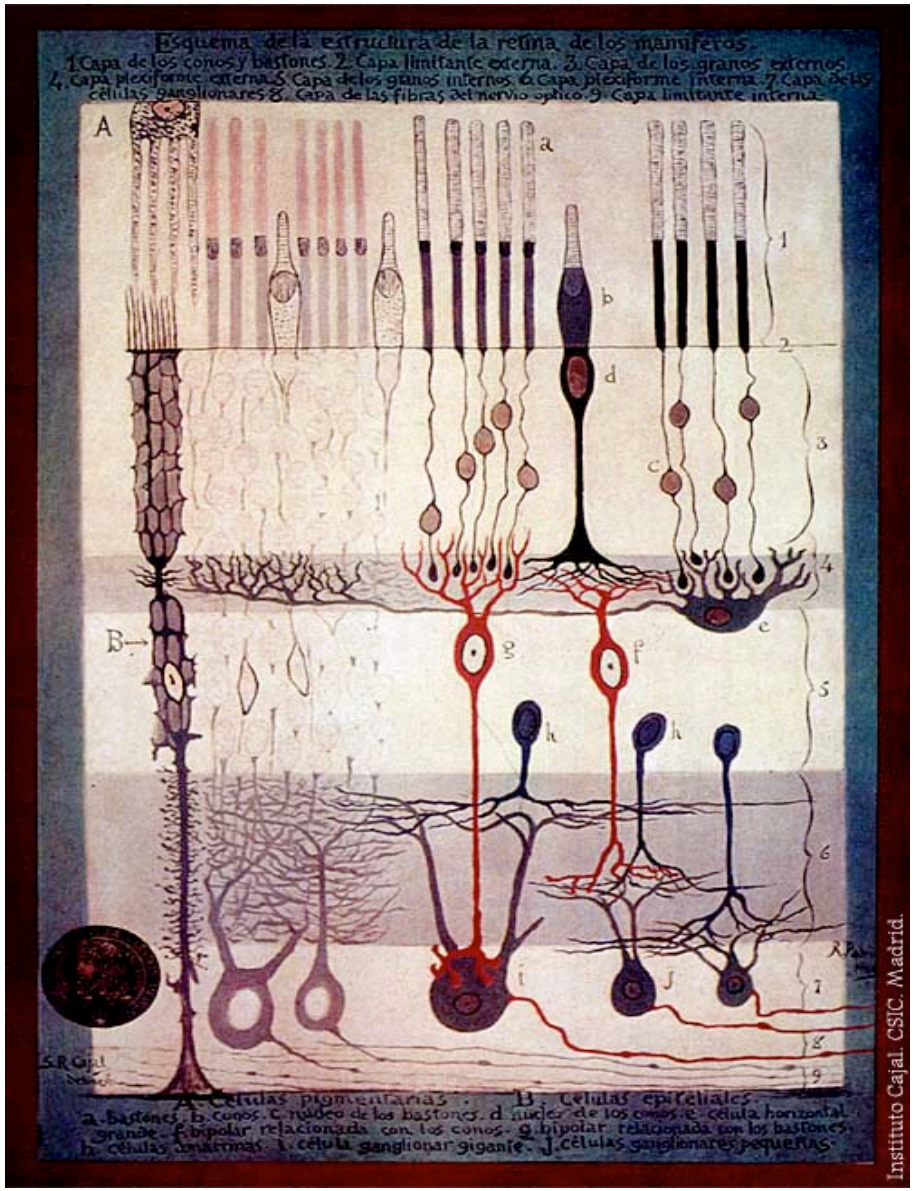
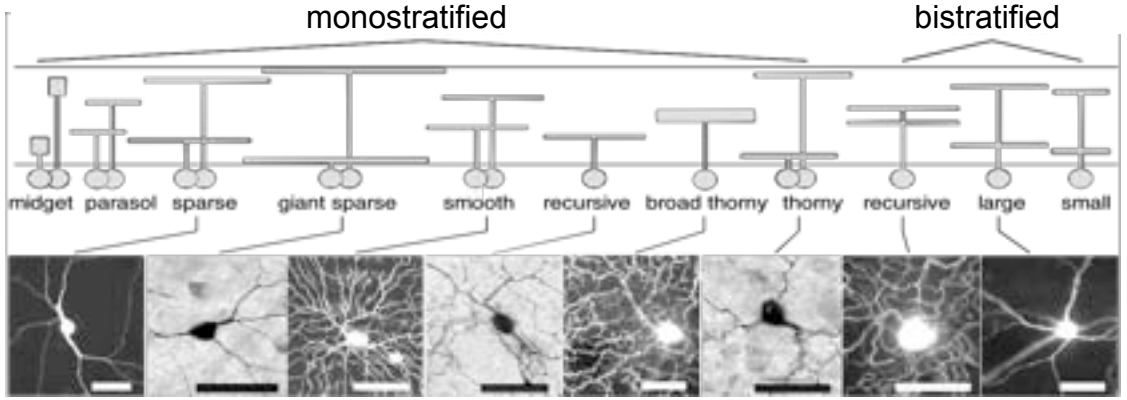
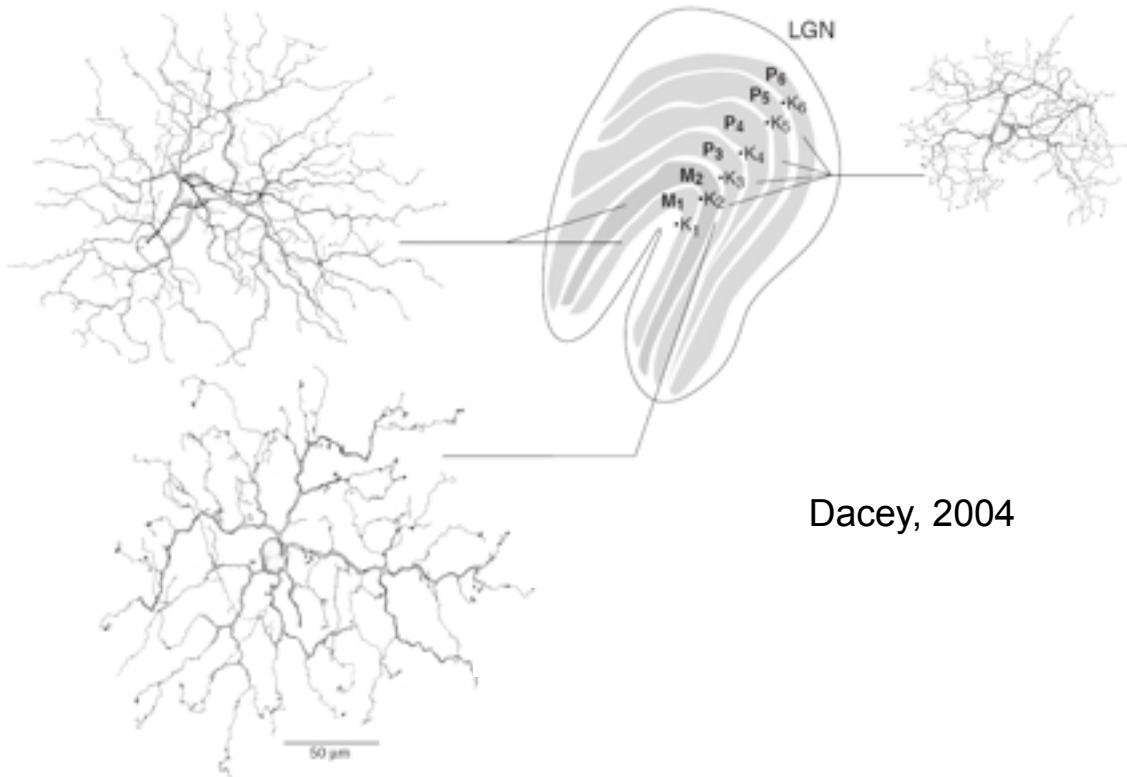


Cajal, 1900



parasol

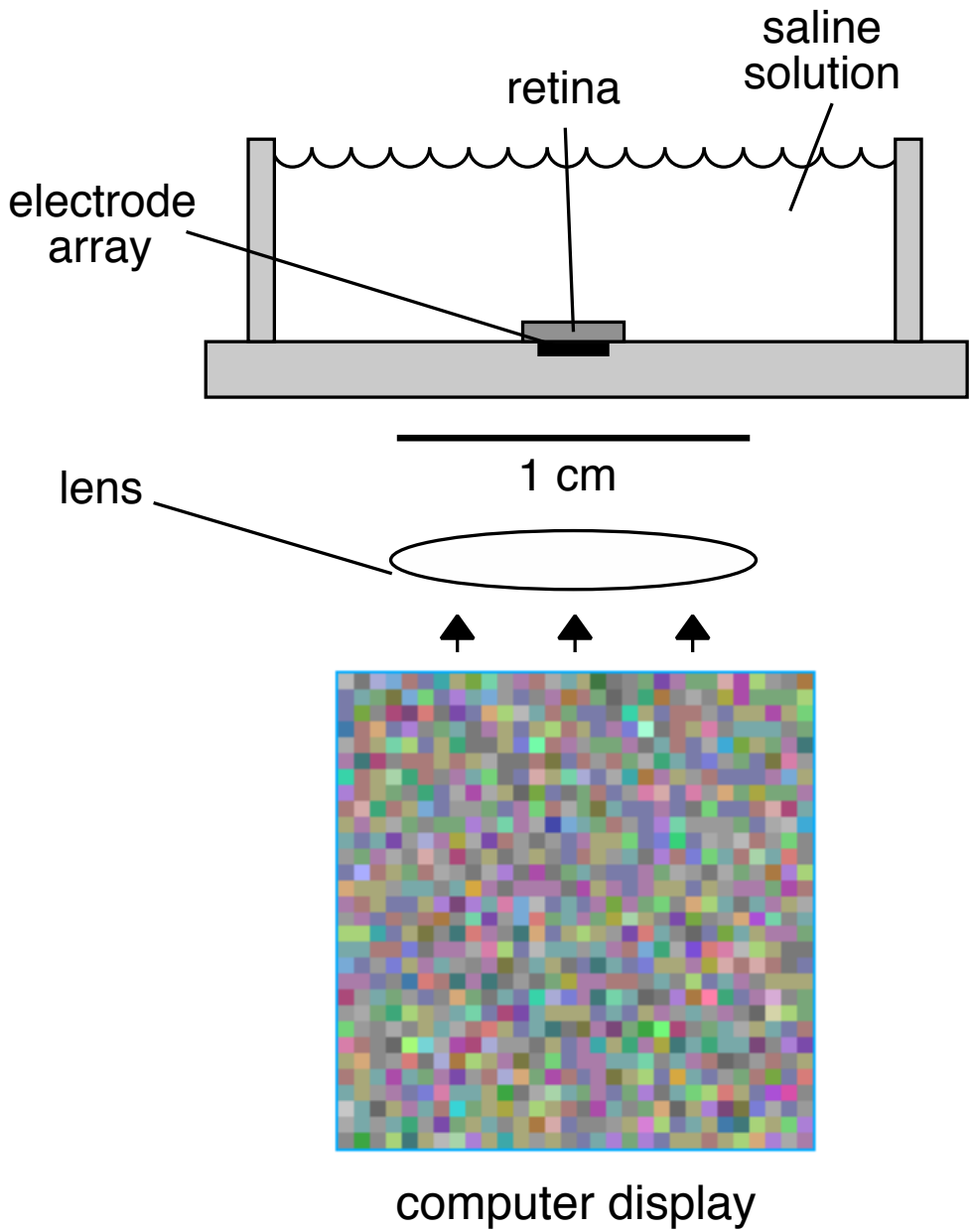
midget



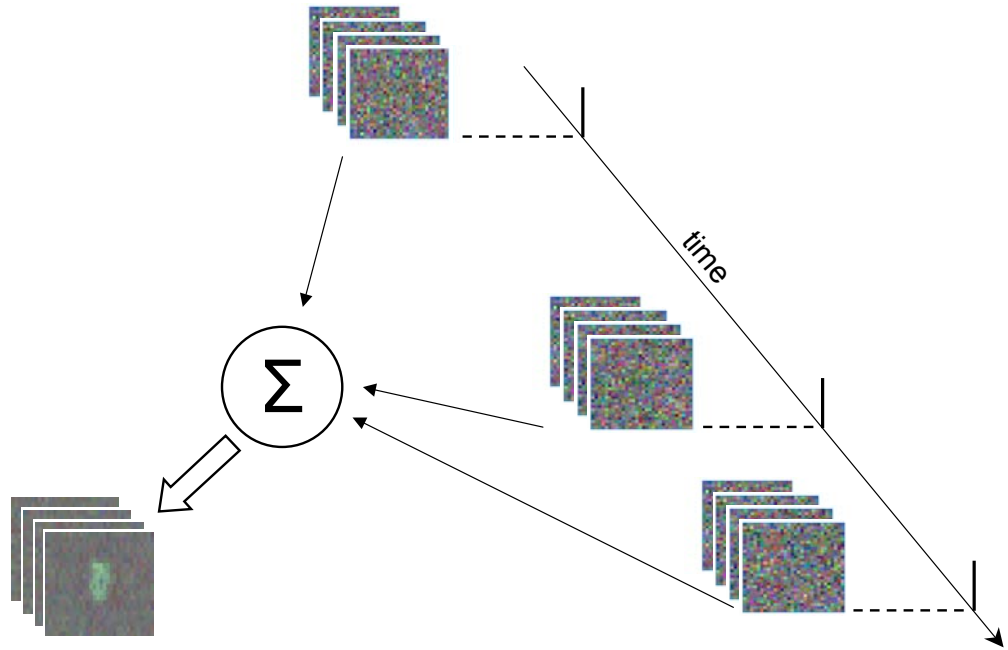
Dacey, 2004

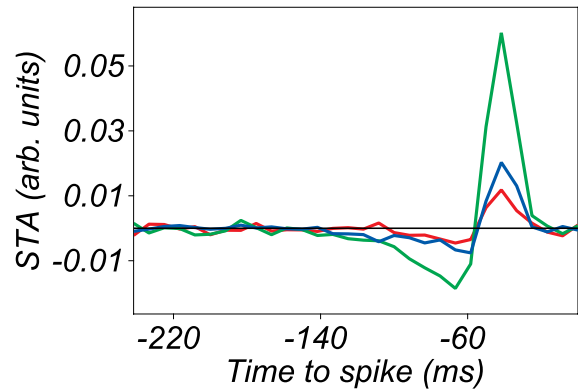
small bistratified

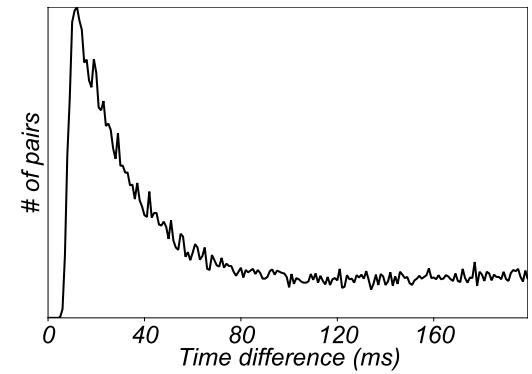
Physiology Recordings



Physiology Recordings





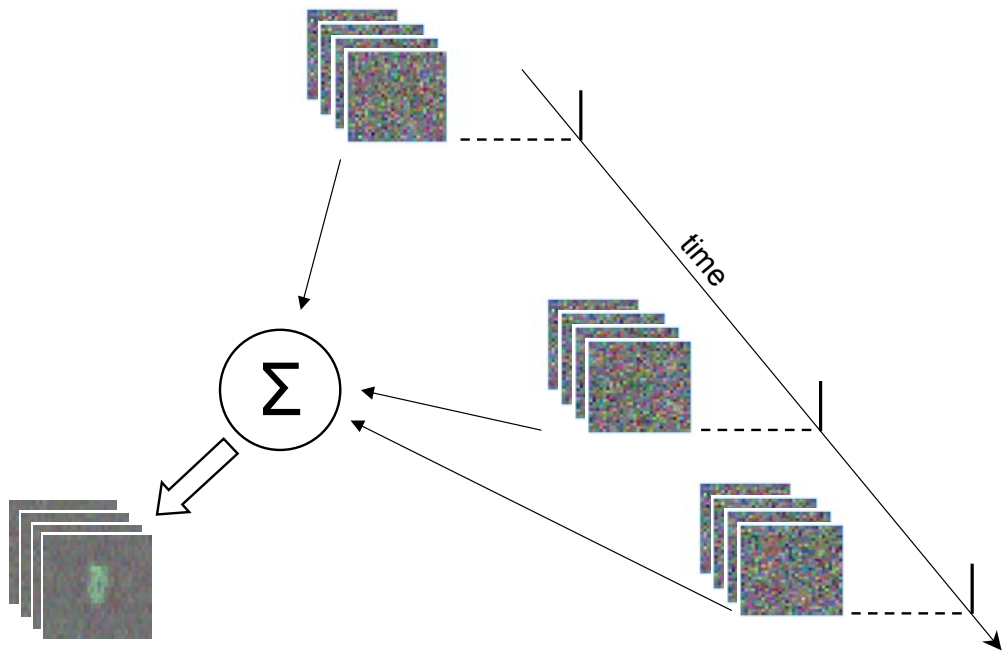


spatial filter
(receptive field)

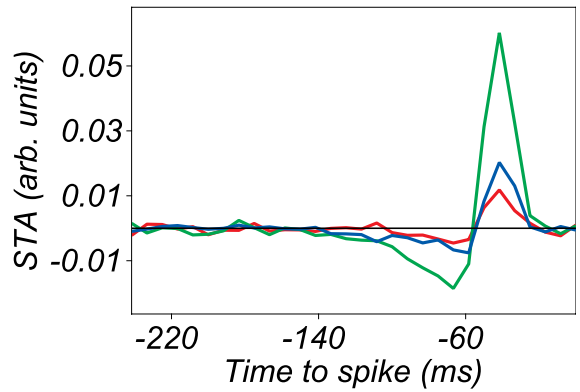
temporal filter
(time-course)

inter-spike time distribution
(autocorrelation function)

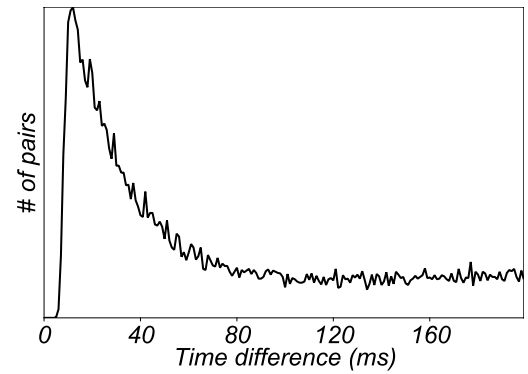
Physiology Recordings



spatial filter
(receptive field)

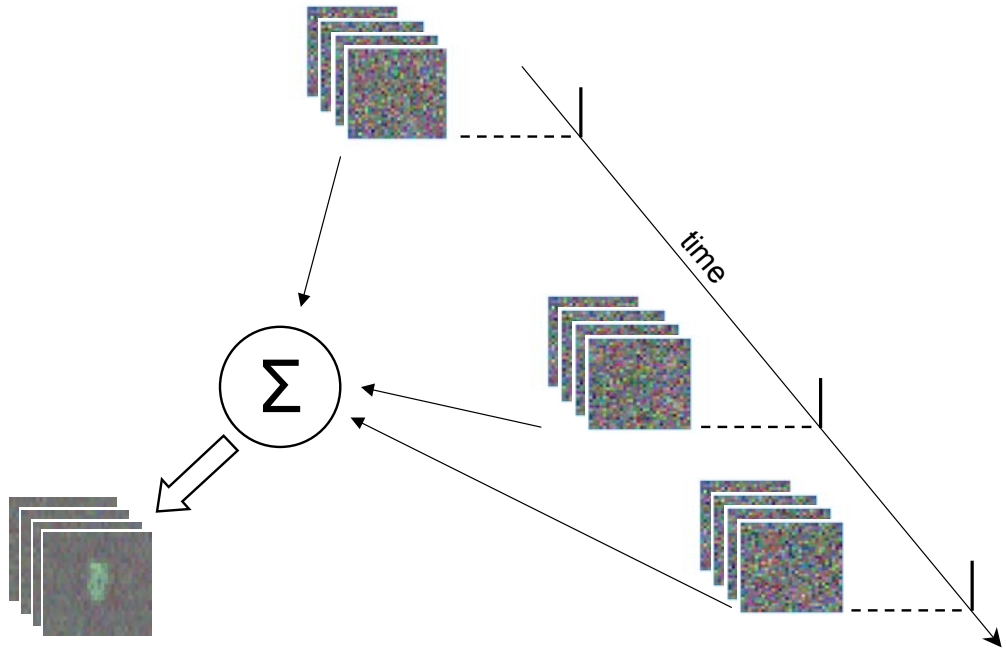


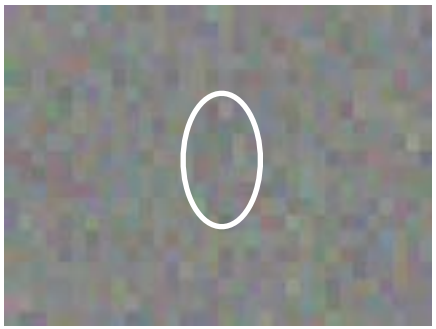
temporal filter
(time-course)



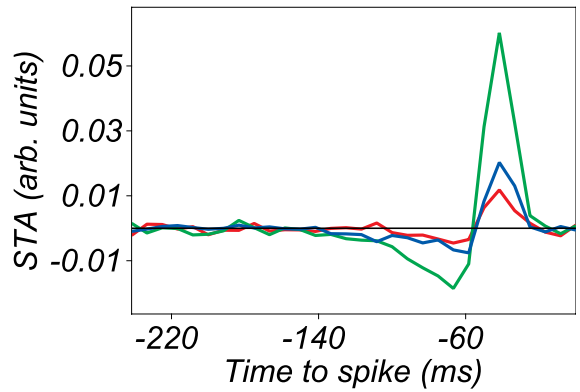
inter-spike time distribution
(autocorrelation function)

Physiology Recordings

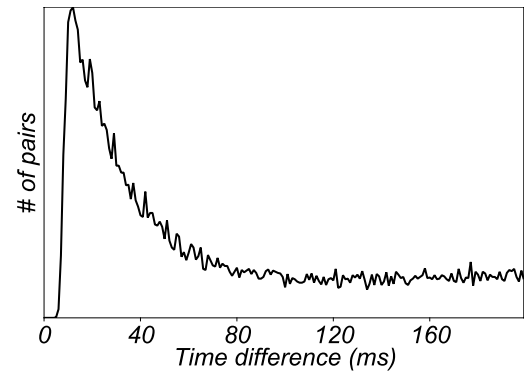




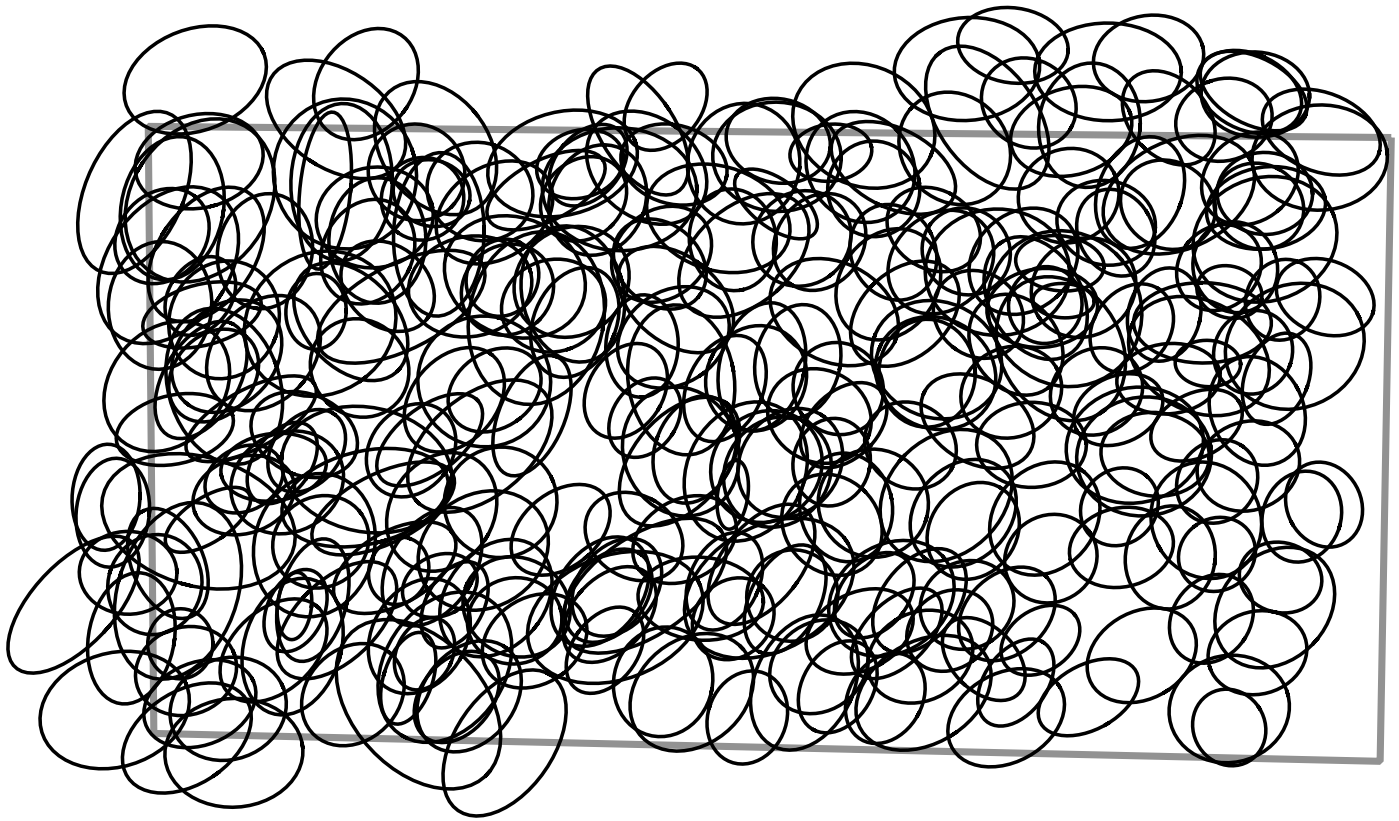
spatial filter
(receptive field)



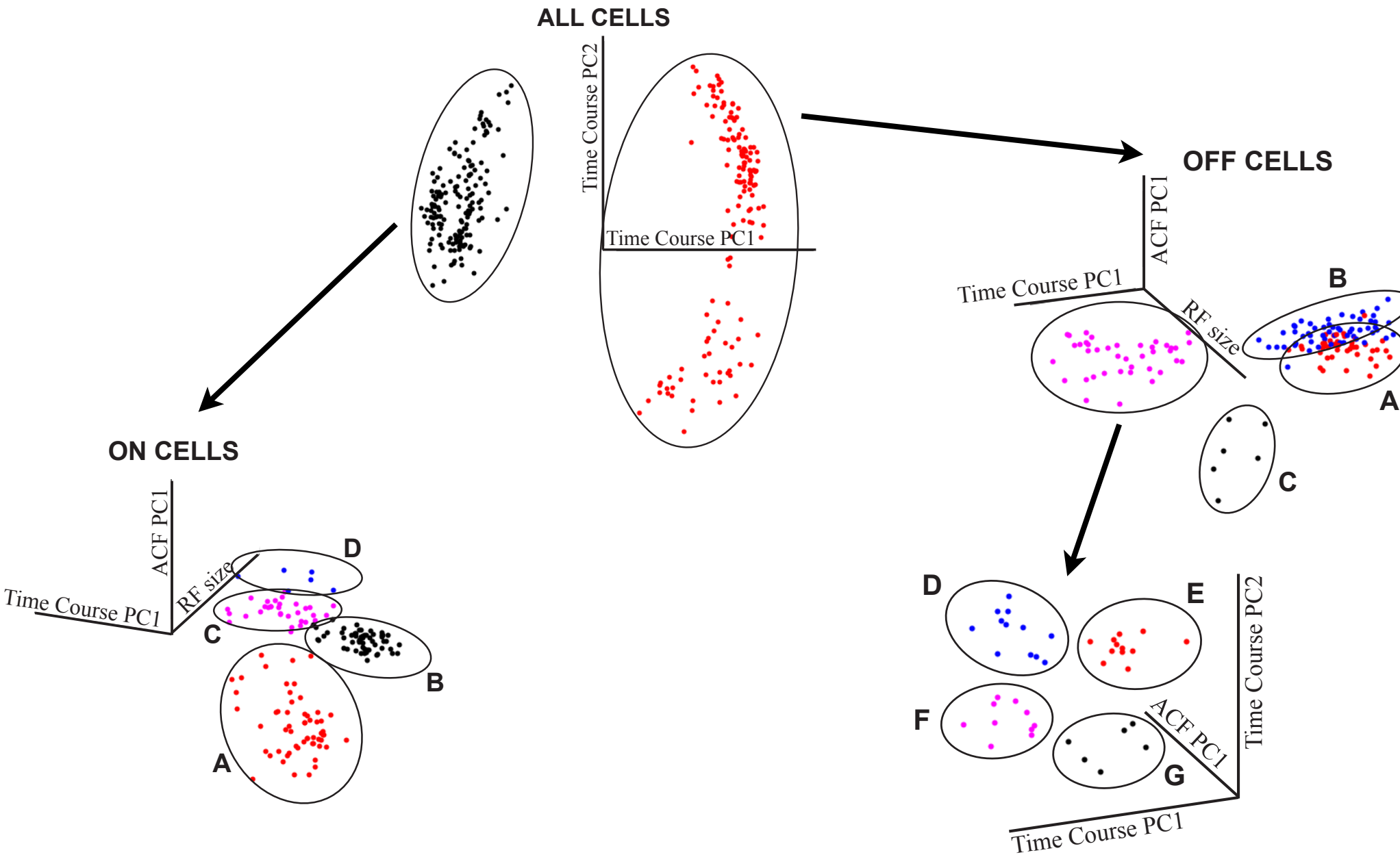
temporal filter
(time-course)



inter-spike time distribution
(autocorrelation function)

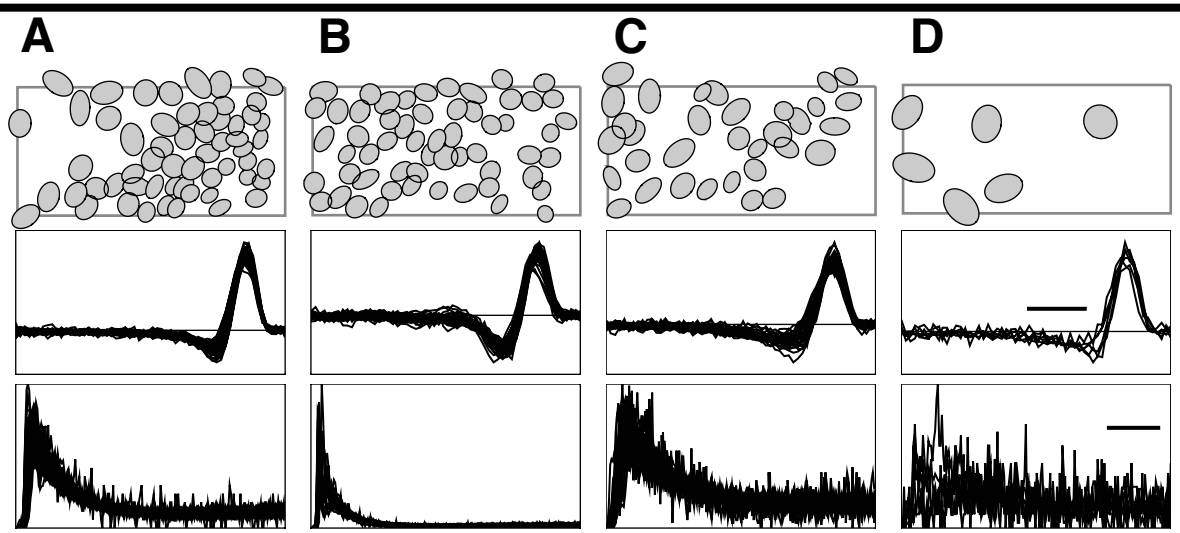


Functional Classification

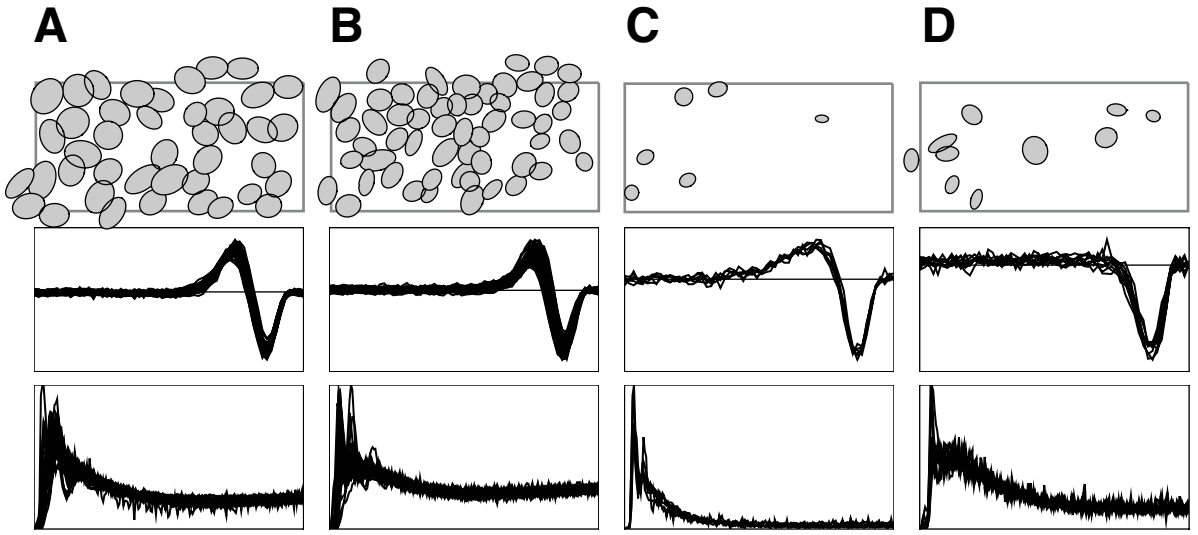


Functional Classification

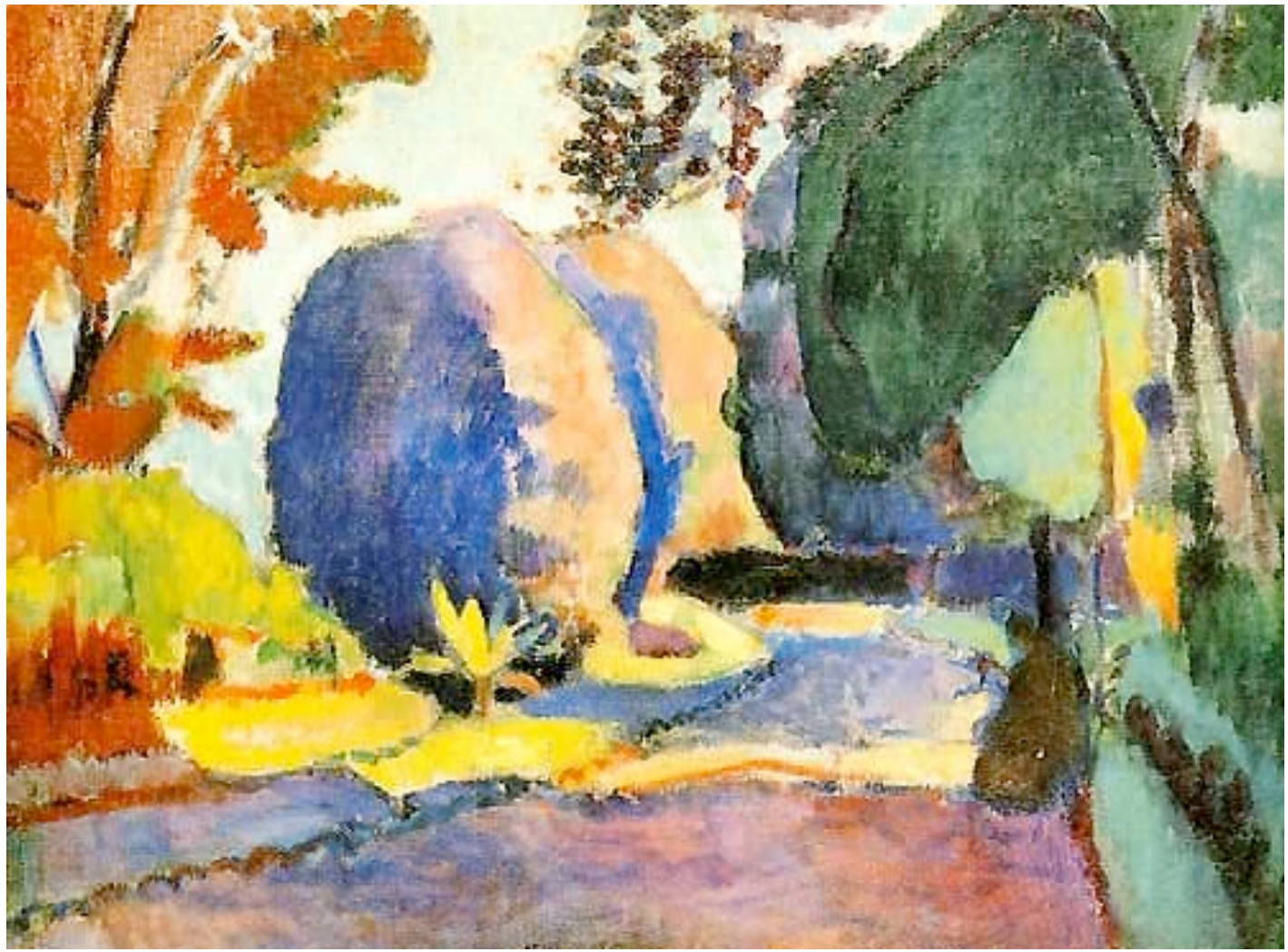
ON



OFF

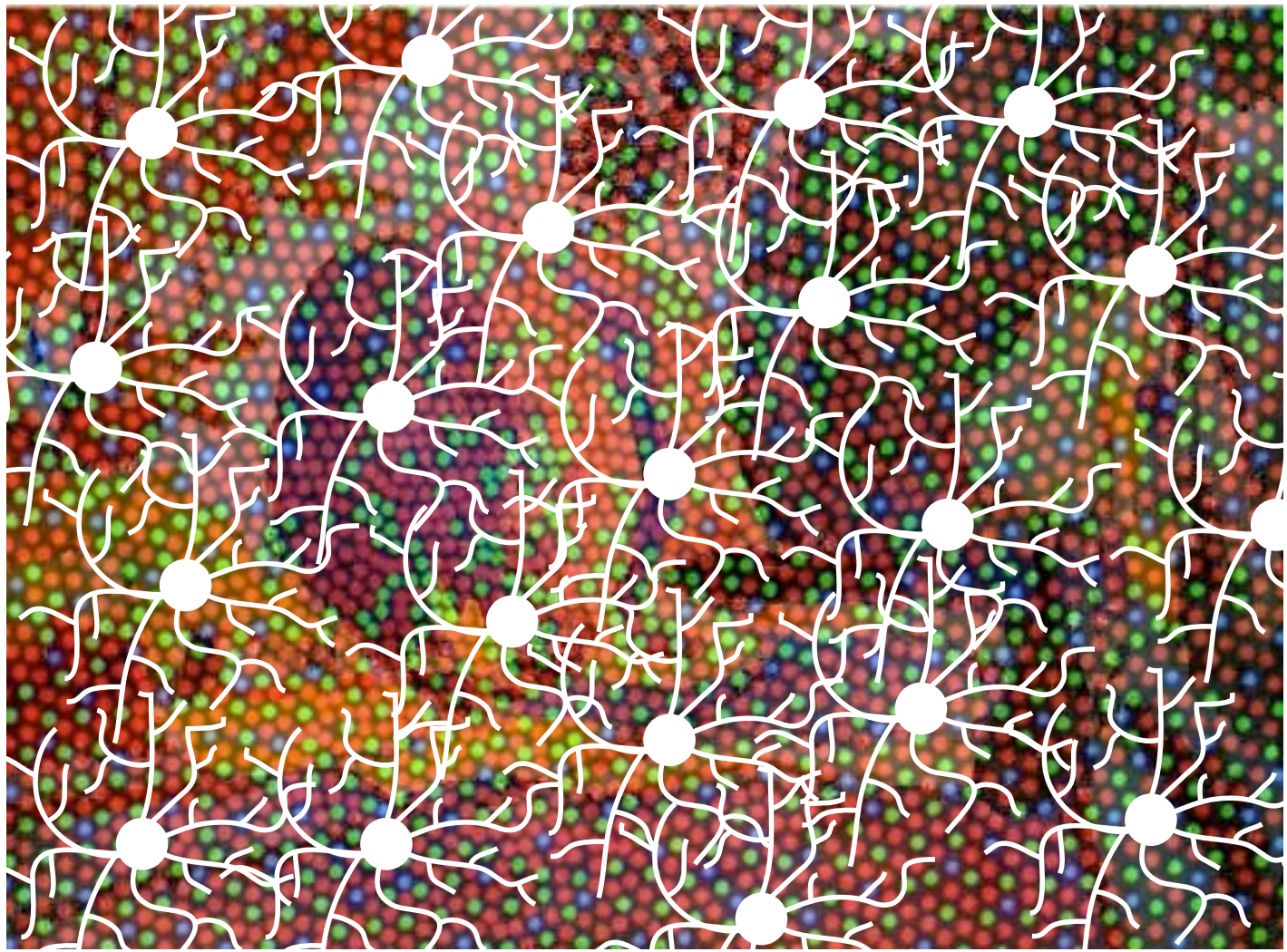


Cone connectivity to RGCs



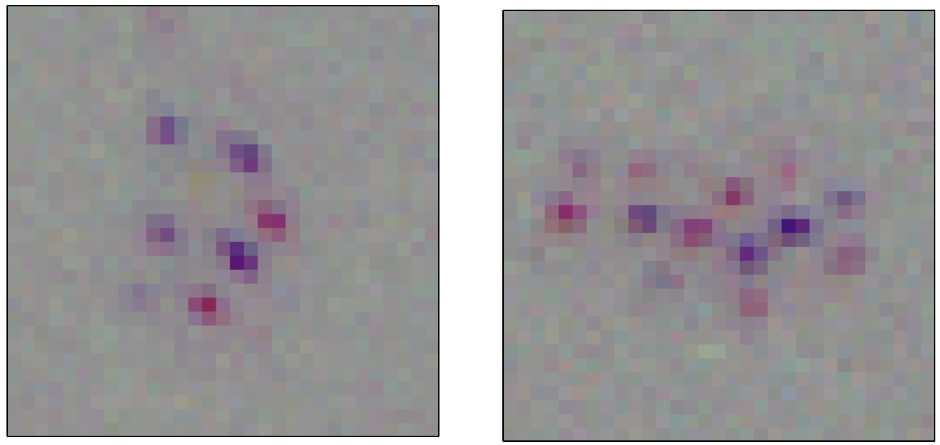
Henri Matisse, The Luxembourg Garden. 1901-1902

Cone connectivity to RGCs

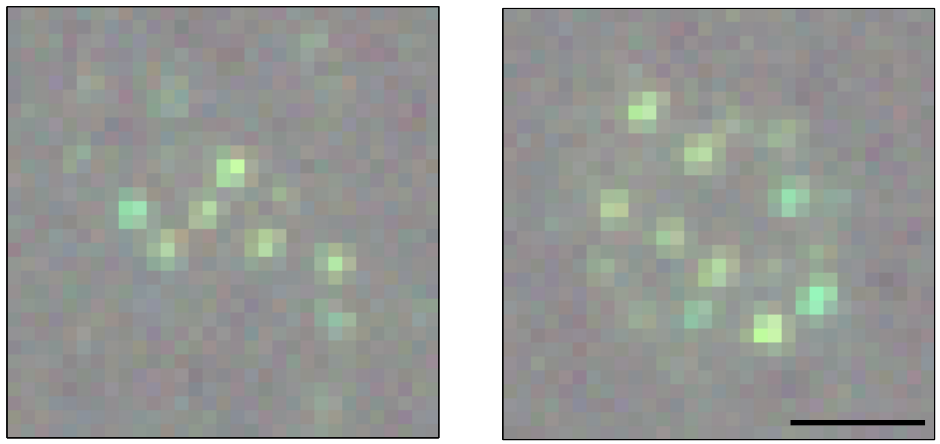


Cone connectivity to RGCs

off-midget

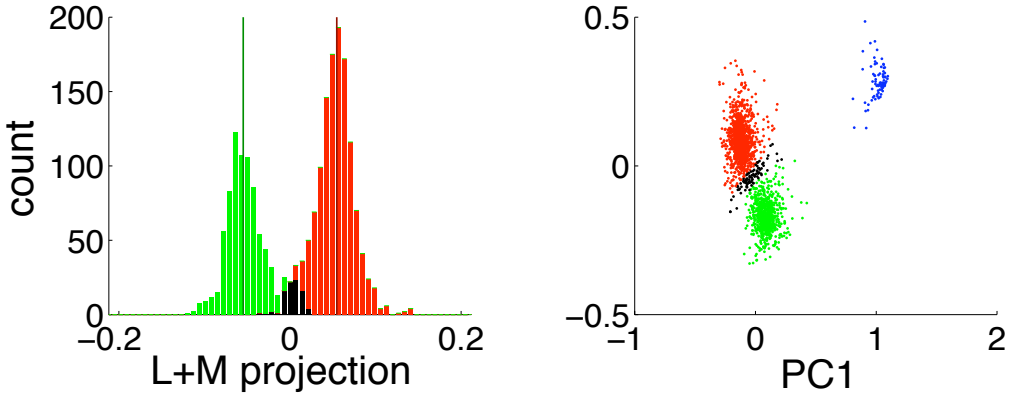


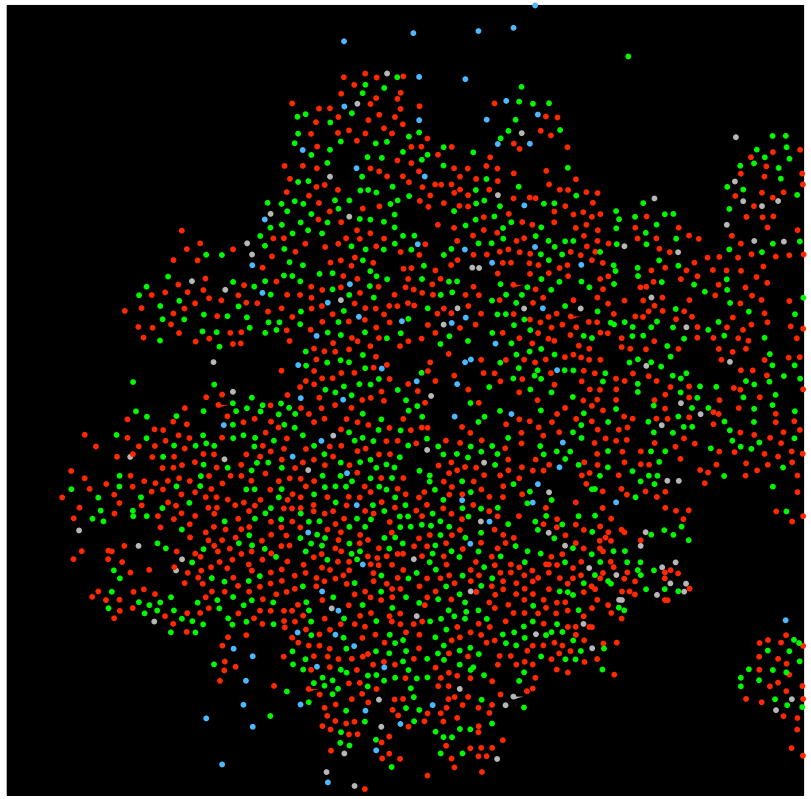
on-midget



Spatio-spectral sensitivity profiles of four midget cells

Cone connectivity to RGCs

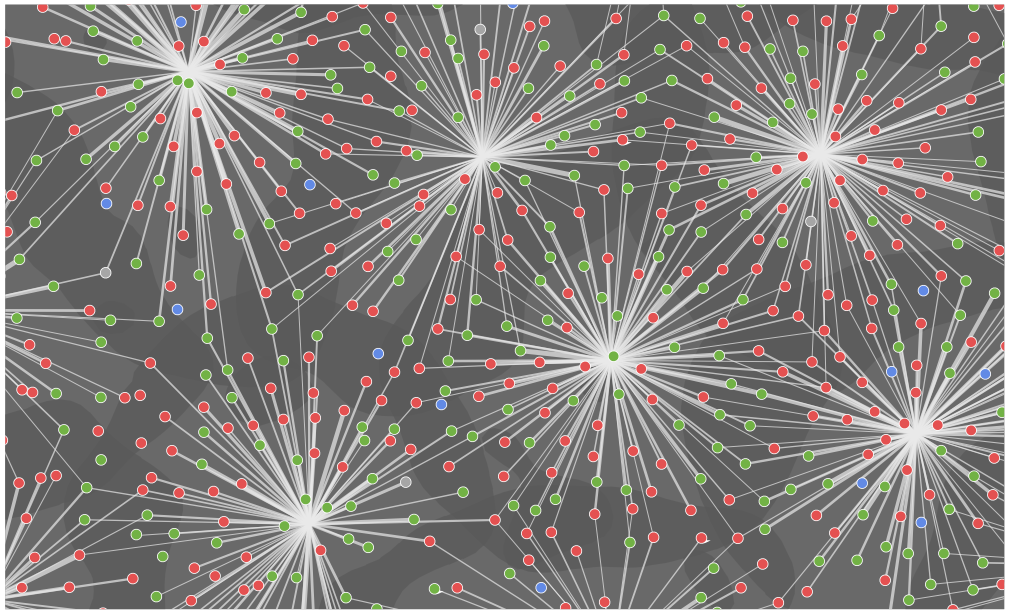




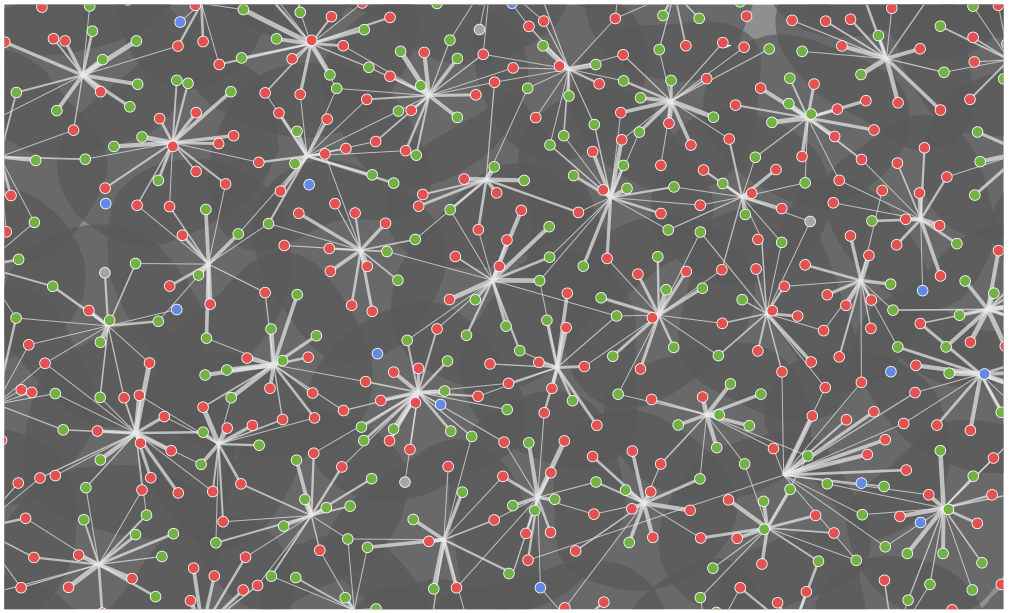
Classification of the three cone types based on their spectral response properties

Connection between cone and ganglion cell mosaics

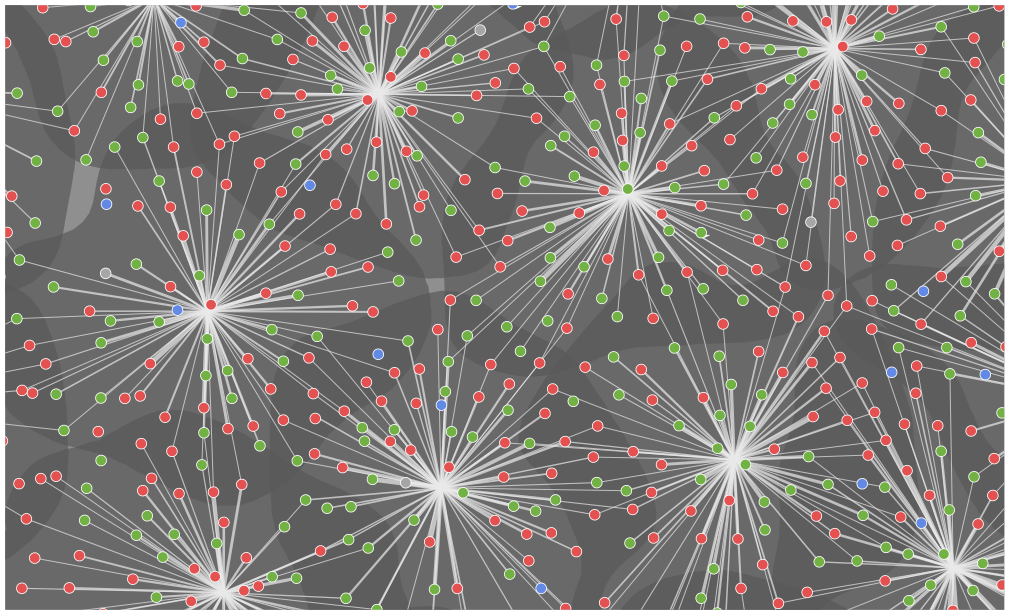
ON parasol



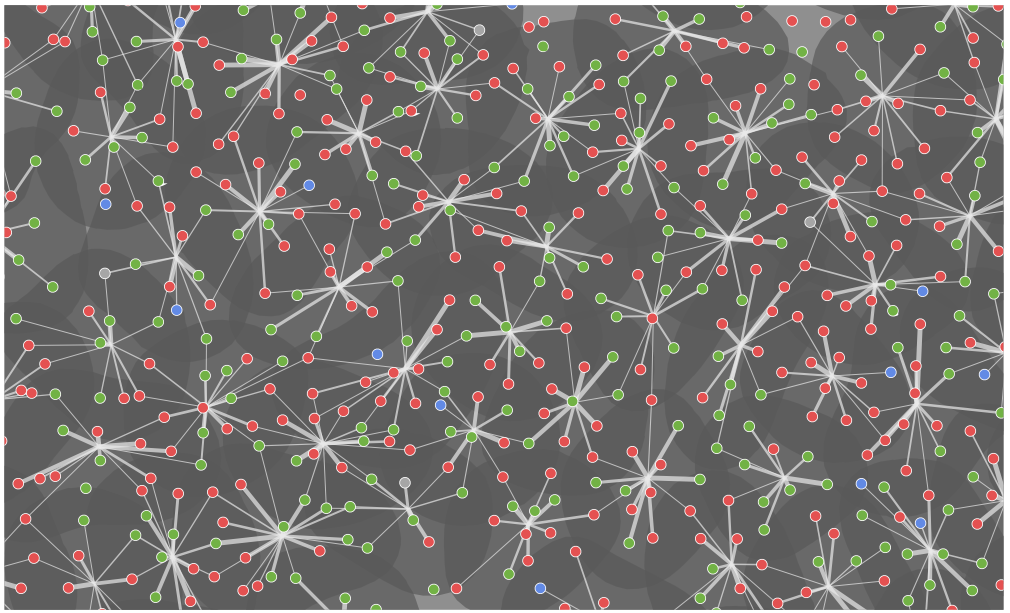
ON midget



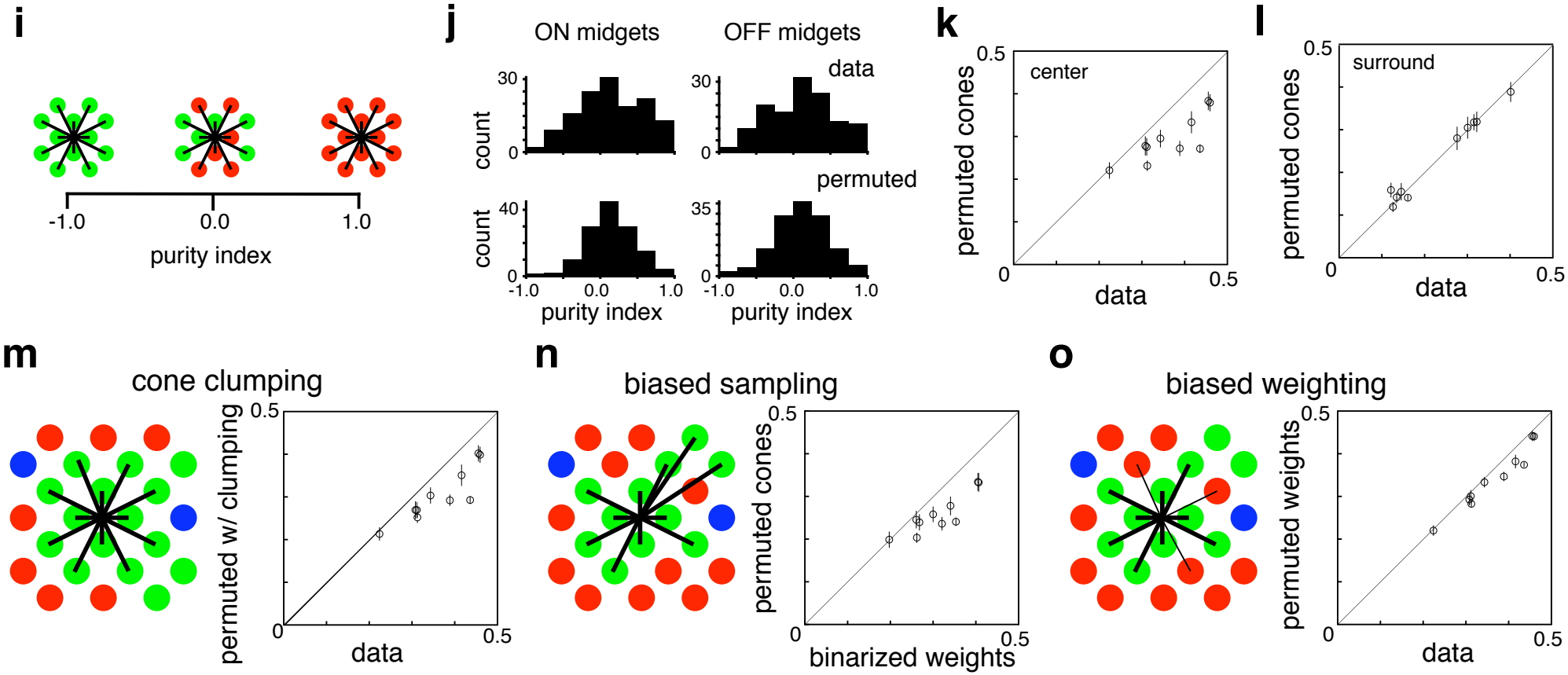
OFF parasol



OFF midget



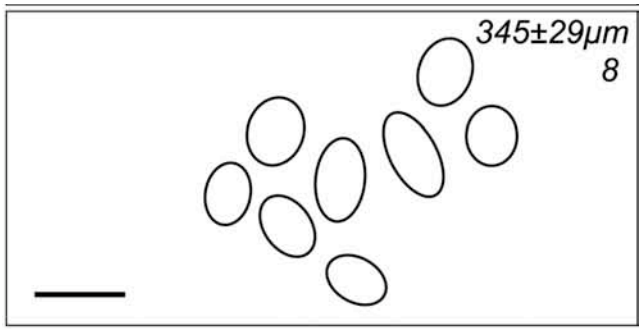
L and M cones are sampled in non-random fashion

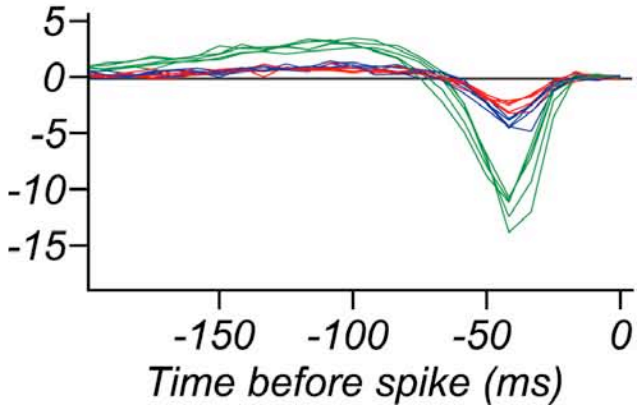


Large cells

Upsilon OFF RGC

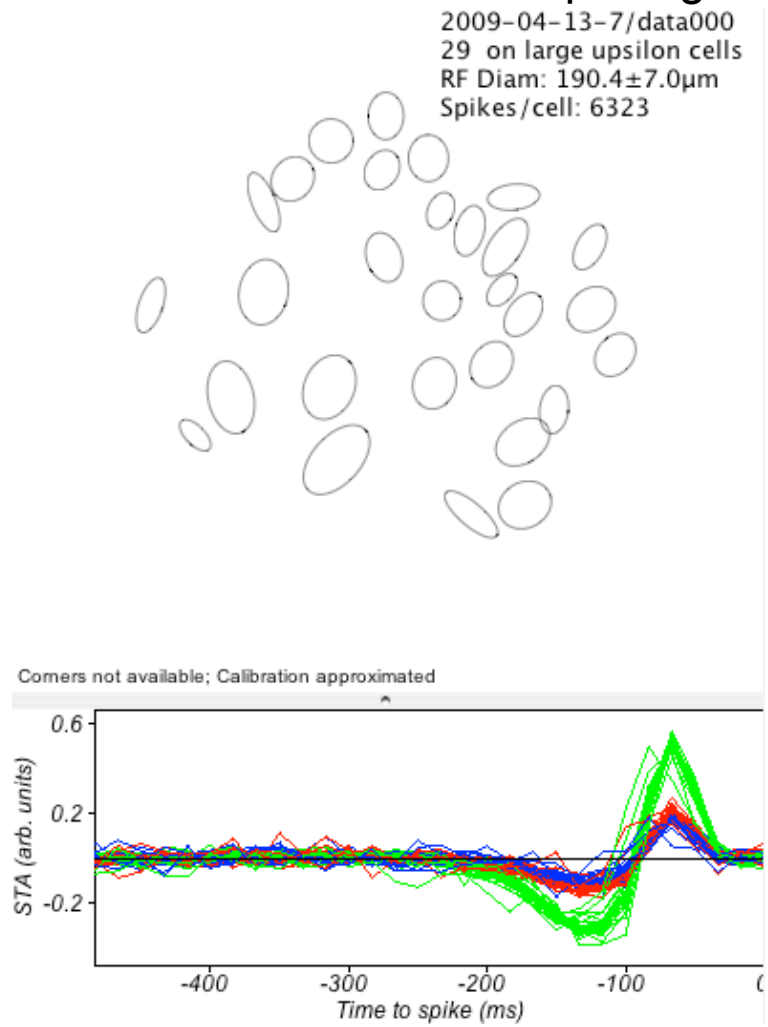
60 micron electrode spacing





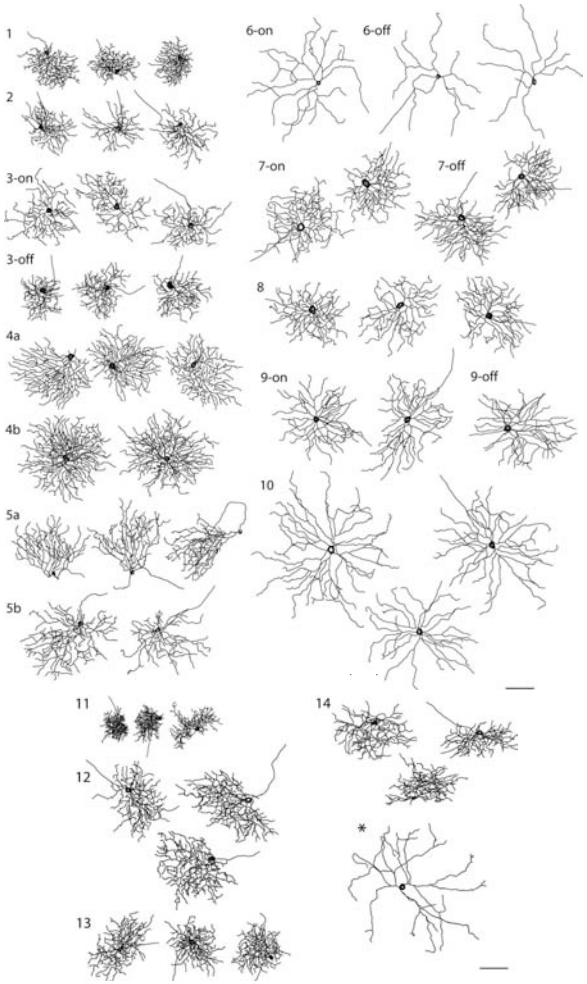
Upsilon ON RGC?

120 micron electrode spacing



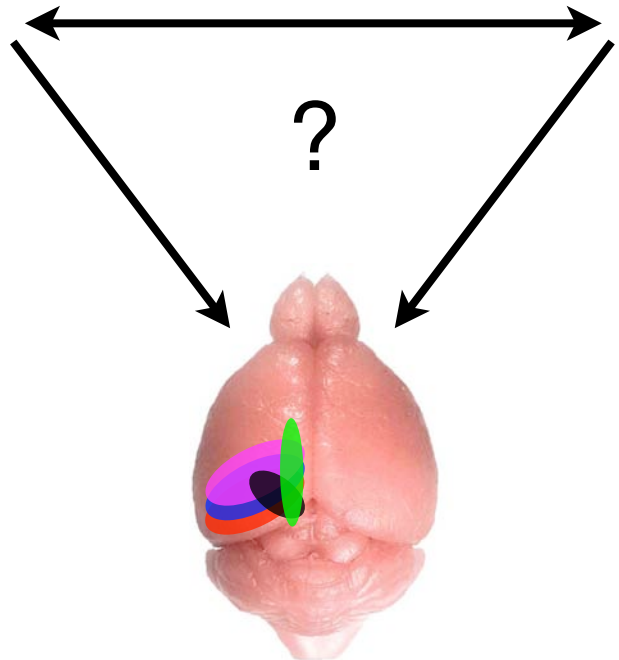
Connecting anatomy and function

anatomy

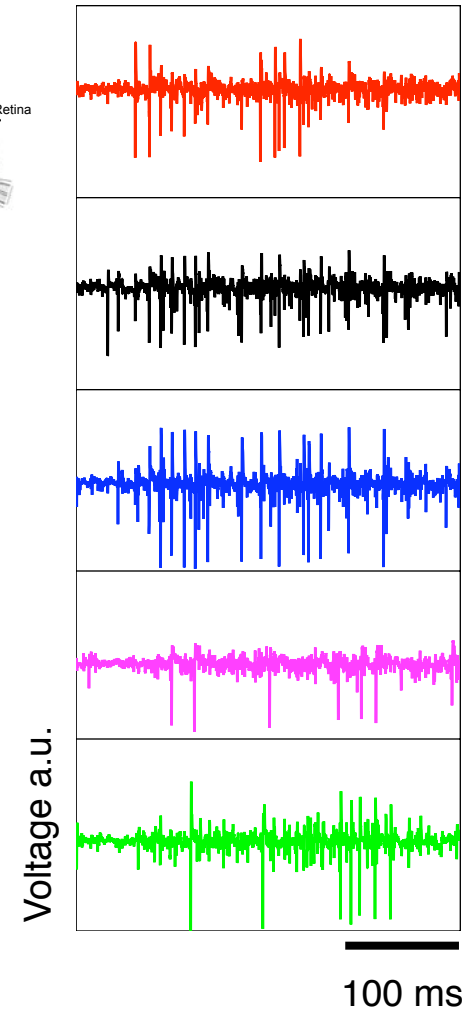


Coombs et al., 2006

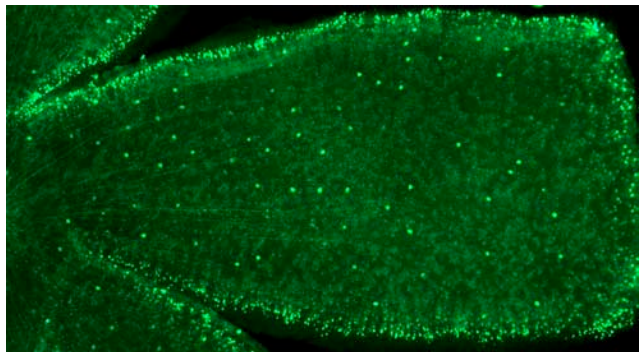
function



brain targets

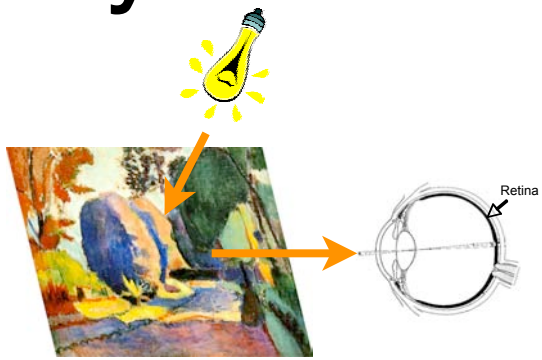


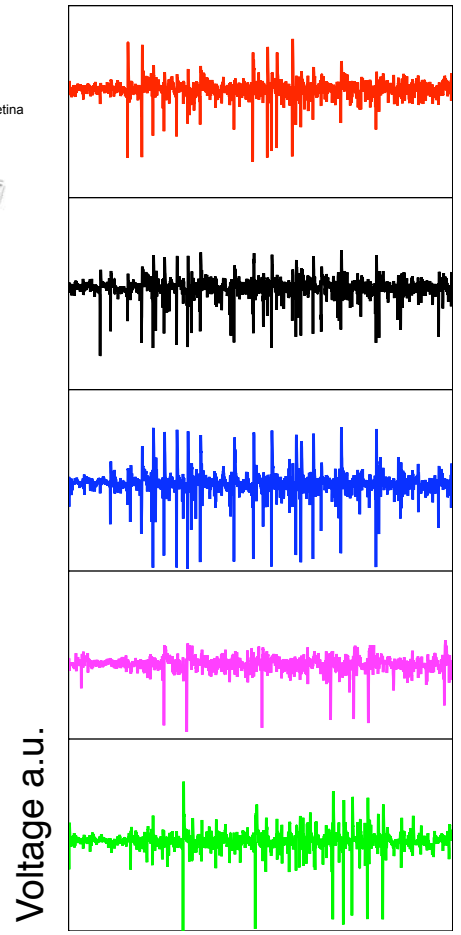
Connecting anatomy and function

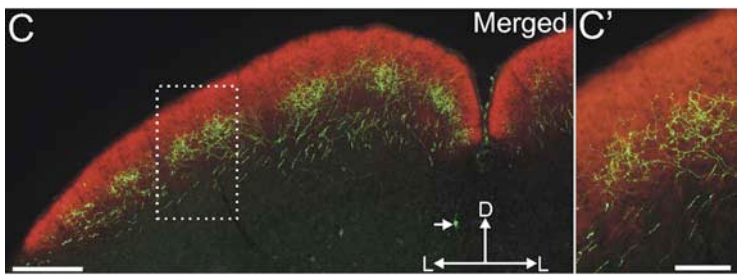


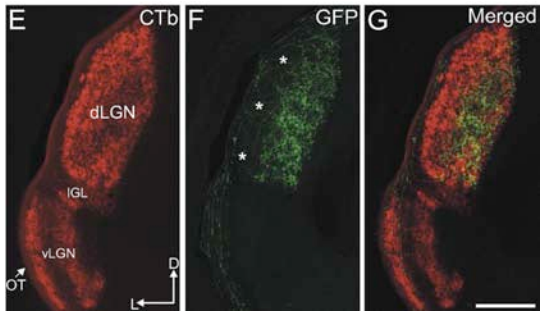
CB2-GFP mouse retina (Huberman, et al., 2008)

?

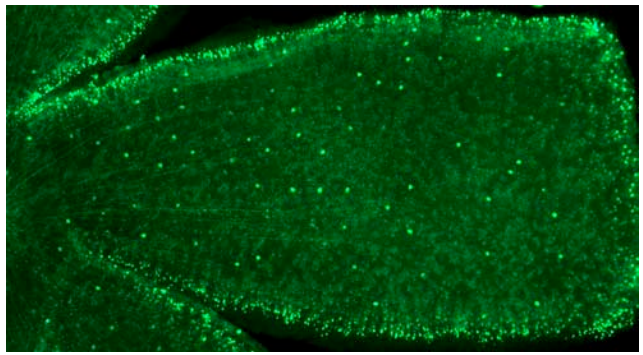




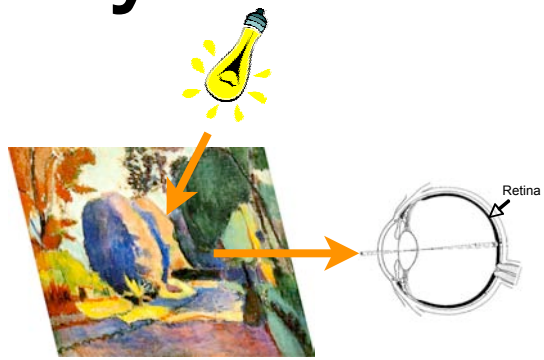


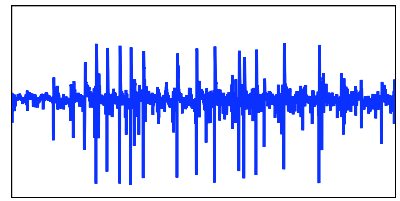


Connecting anatomy and function



?

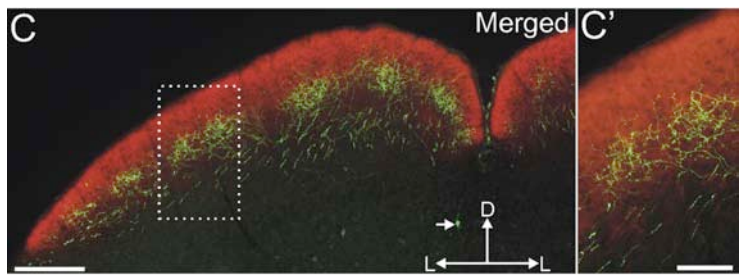


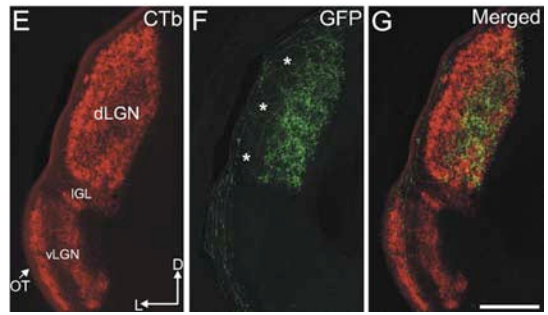


CB2-GFP mouse retina (Huberman, et al., 2008)

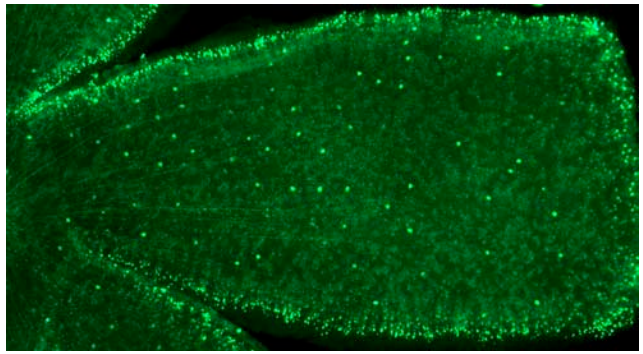
Voltage a.u.

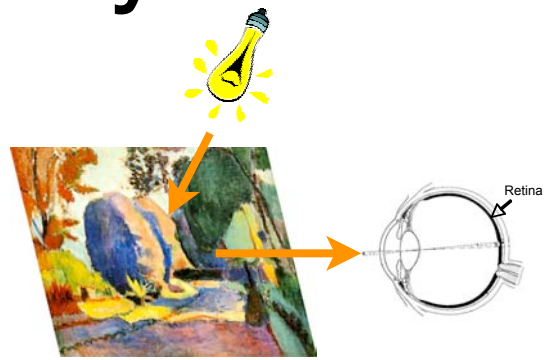
100 ms



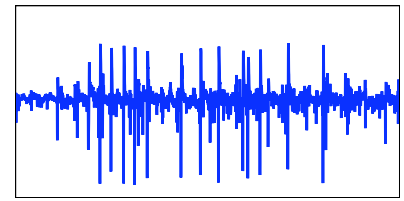


Connecting anatomy and function



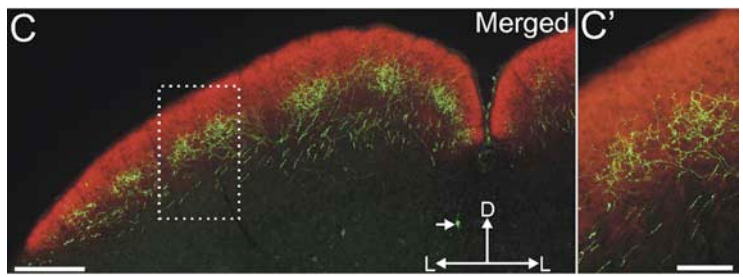


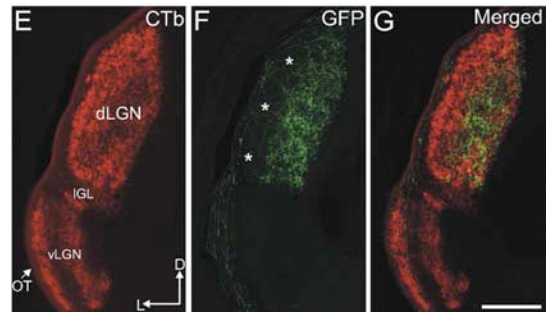
CB2-GFP mouse retina (Huberman, et al., 2008)



Voltage a.u.

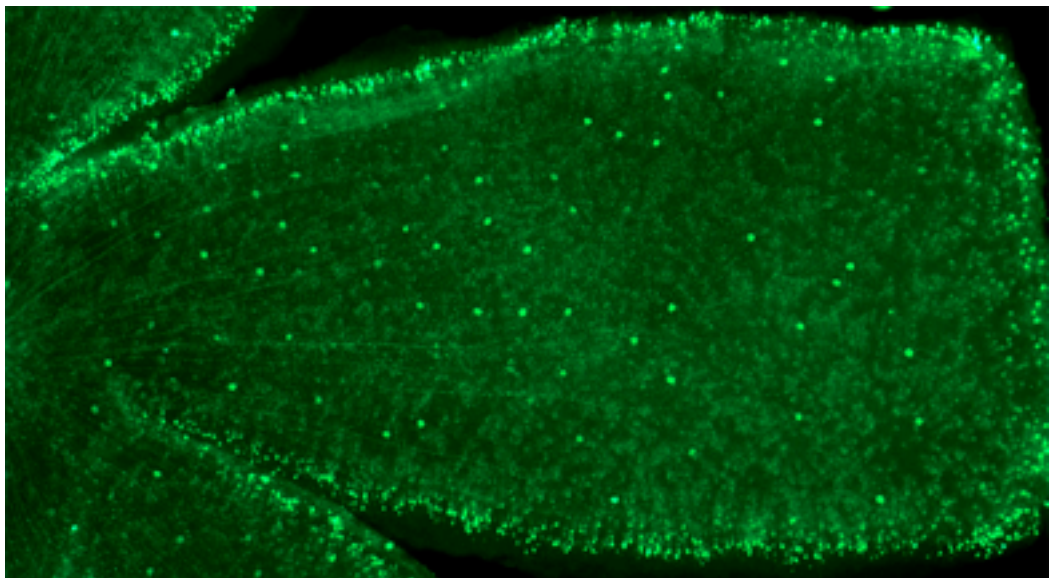
100 ms





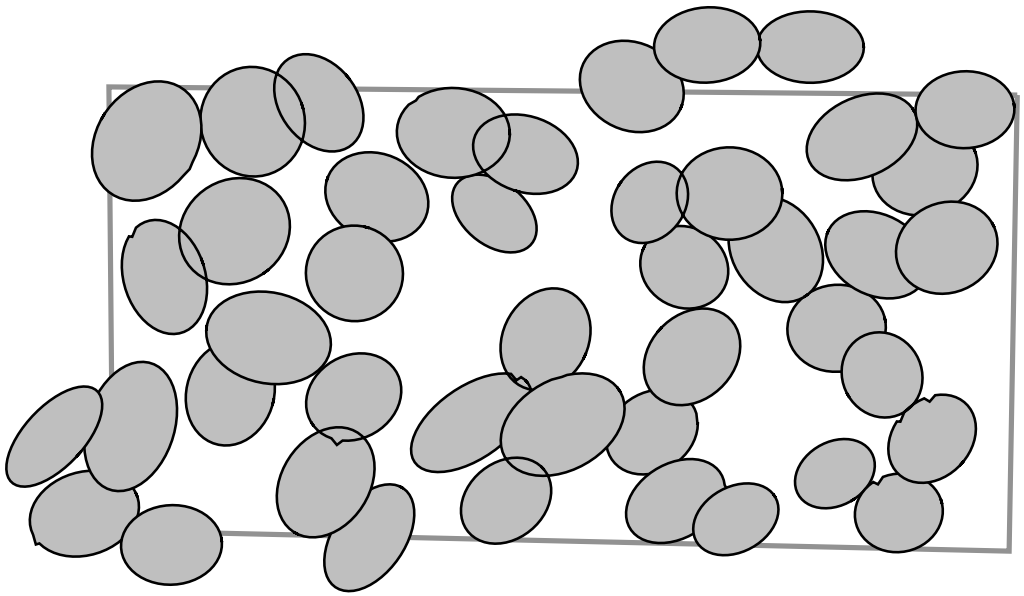
Correlating neural function and structure

Image anatomical mosaic



CB2-GFP mouse retina (Huberman, et al., 2008)

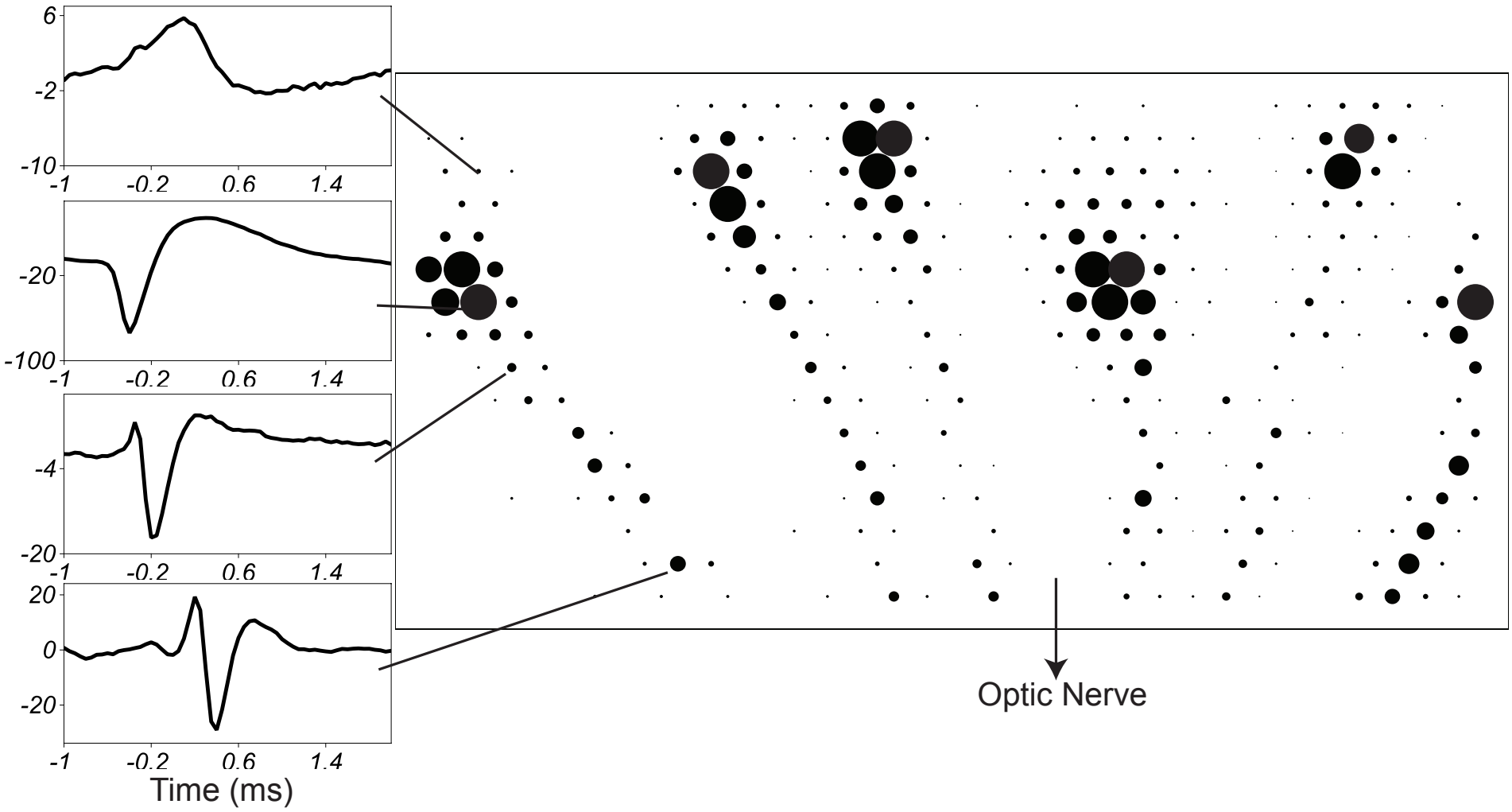
Image functional mosaic



receptive fields of one mouse RGC type

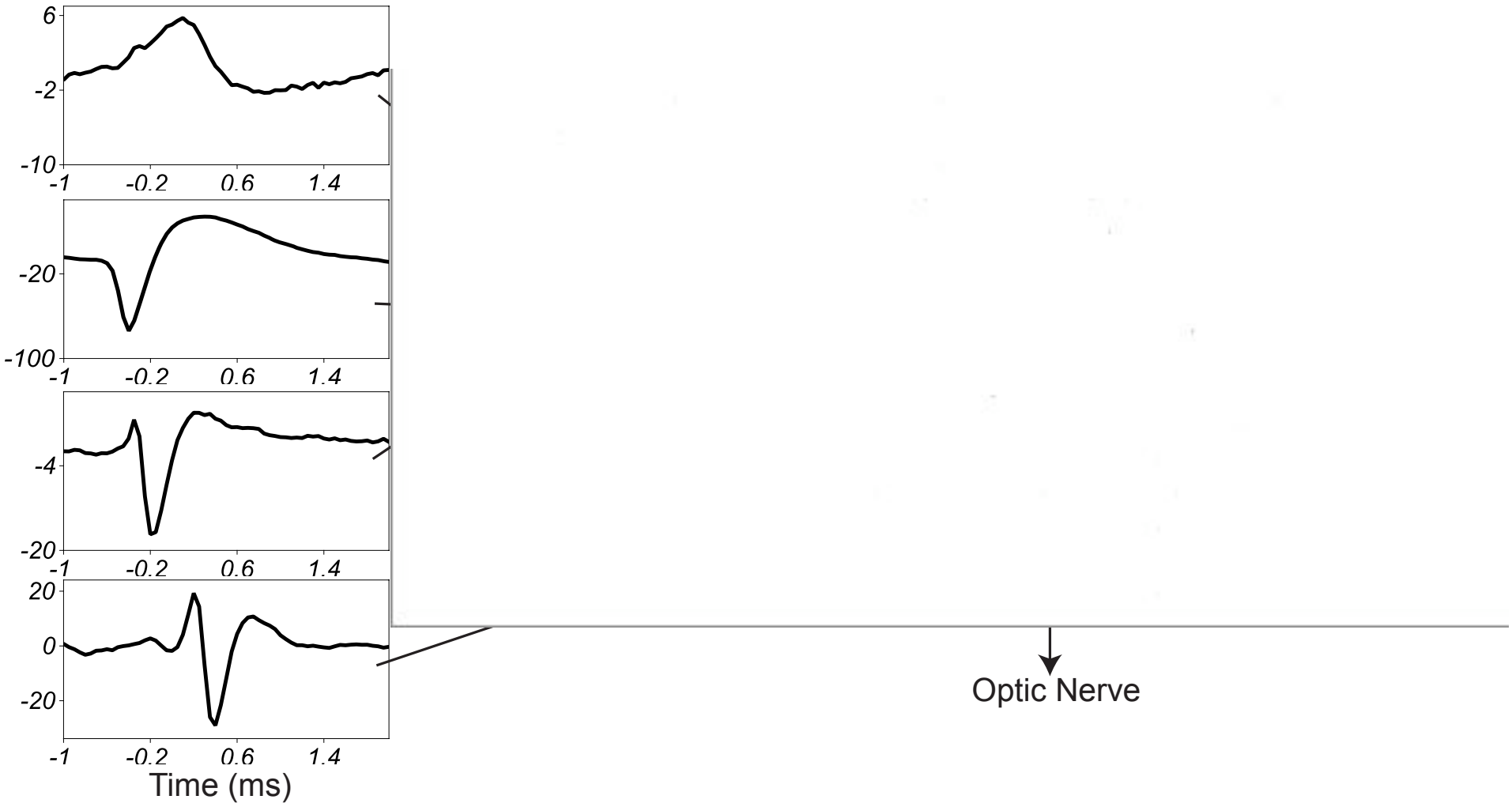
Electrophysiological images

Electrical “footprint” of a spiking neuron



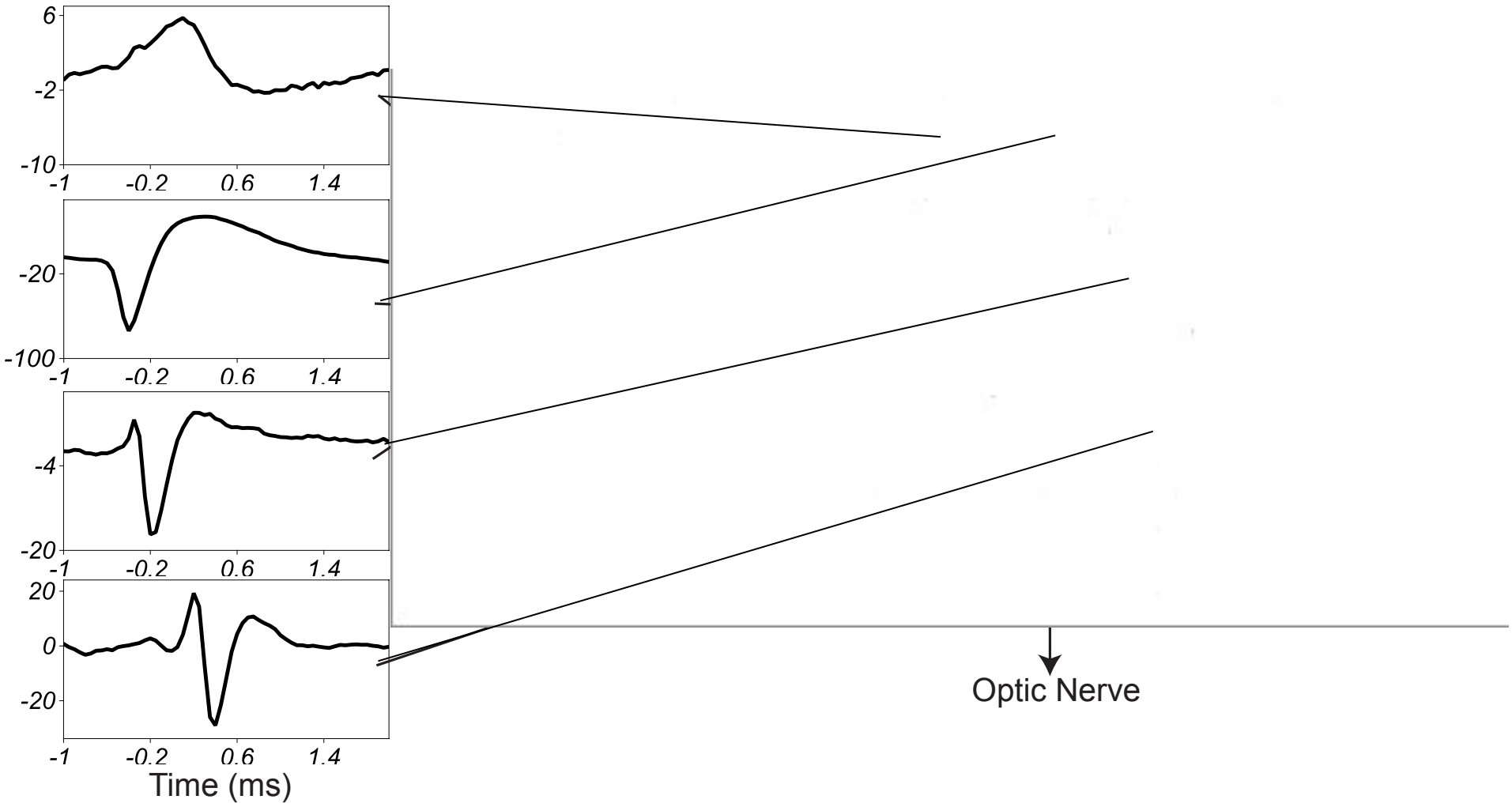
Electrophysiological images

Electrical “footprint” of a spiking neuron

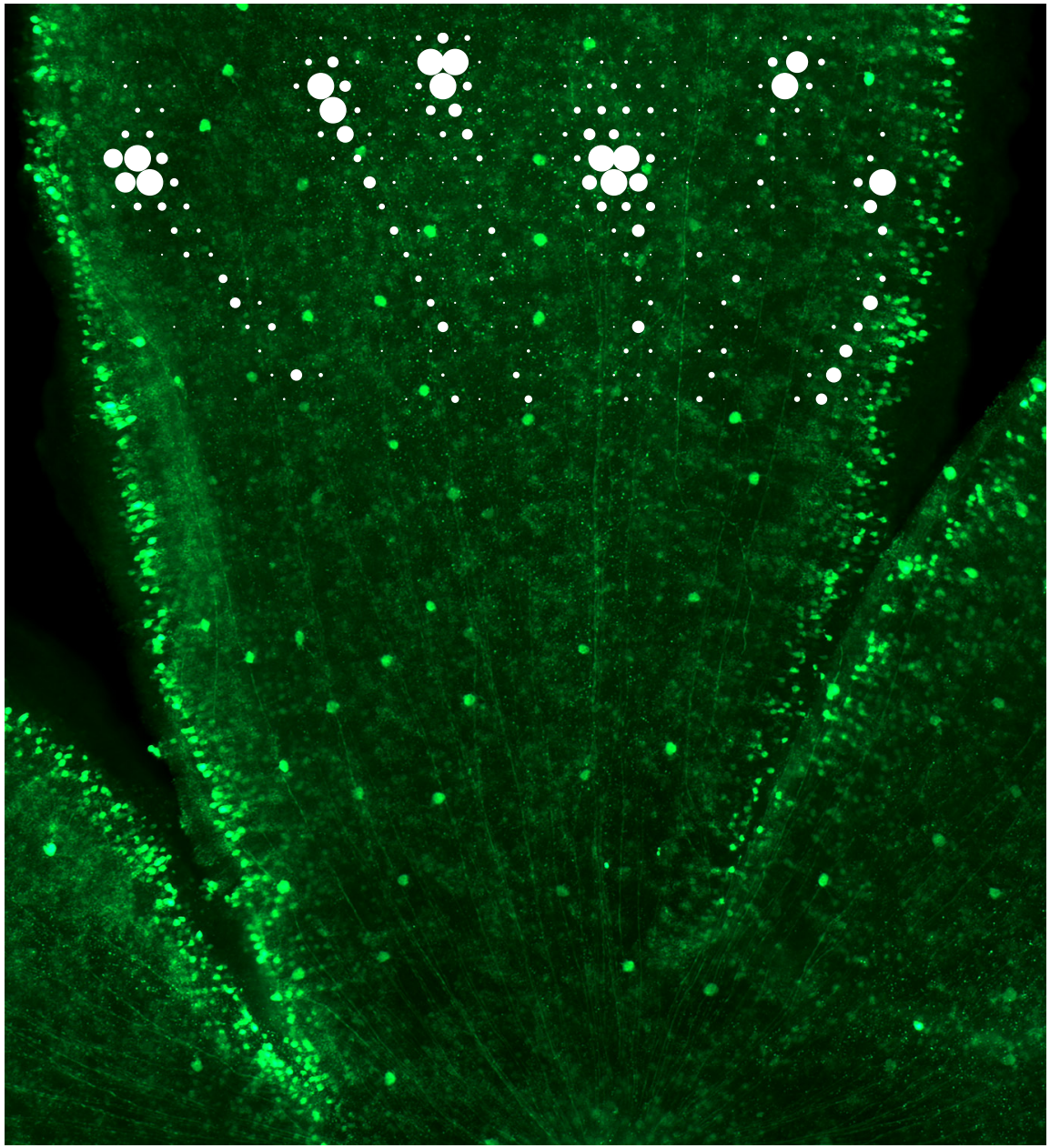


Electrophysiological images

Electrical “footprint” of a spiking neuron



Merge of the two images



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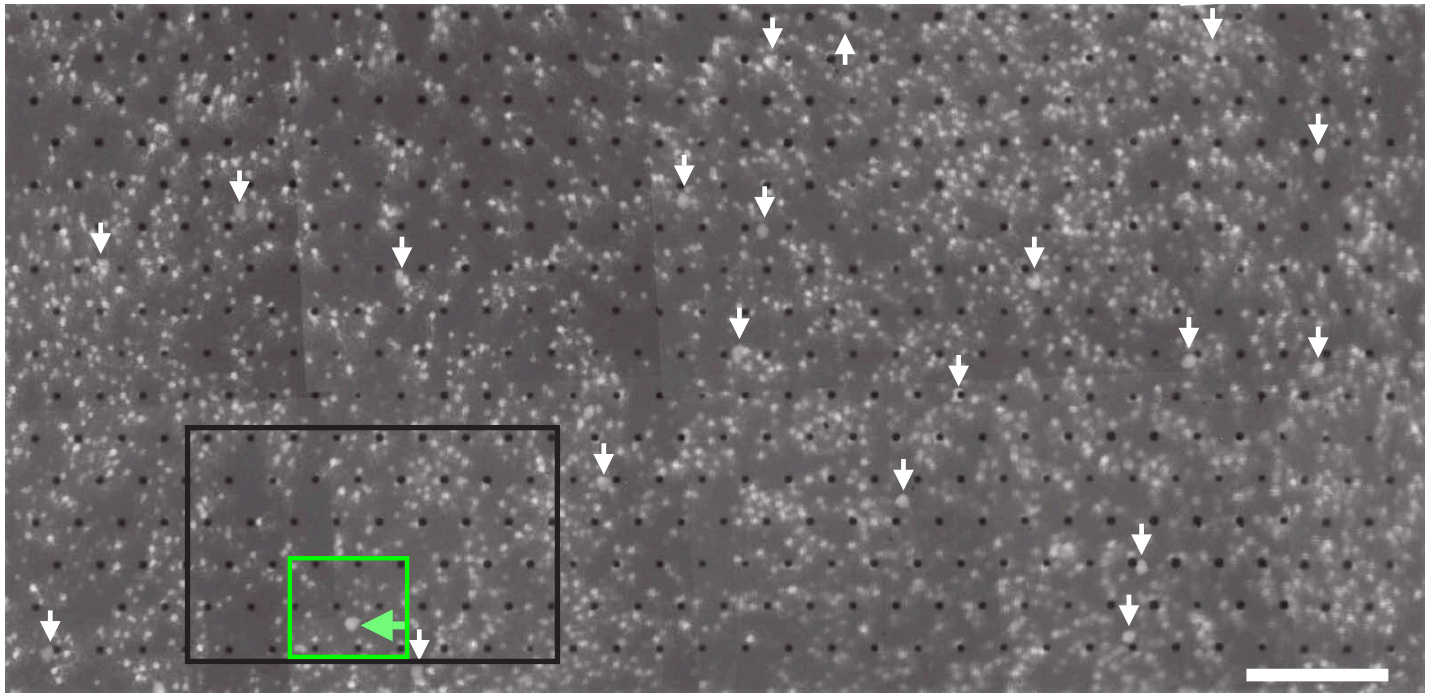
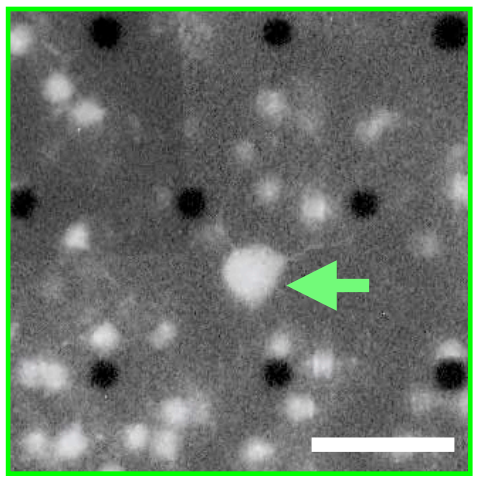
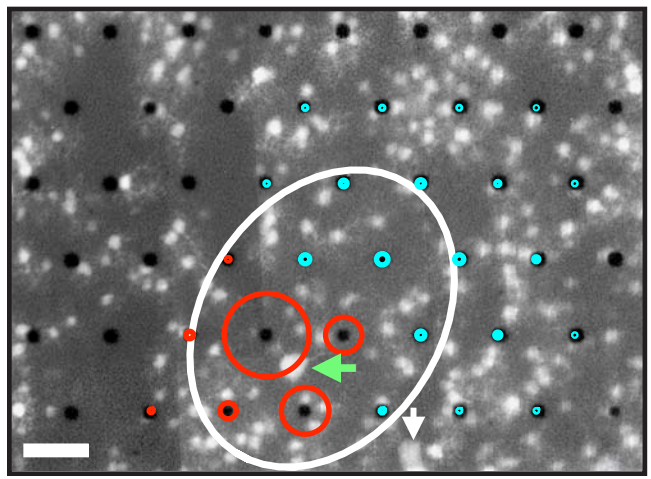
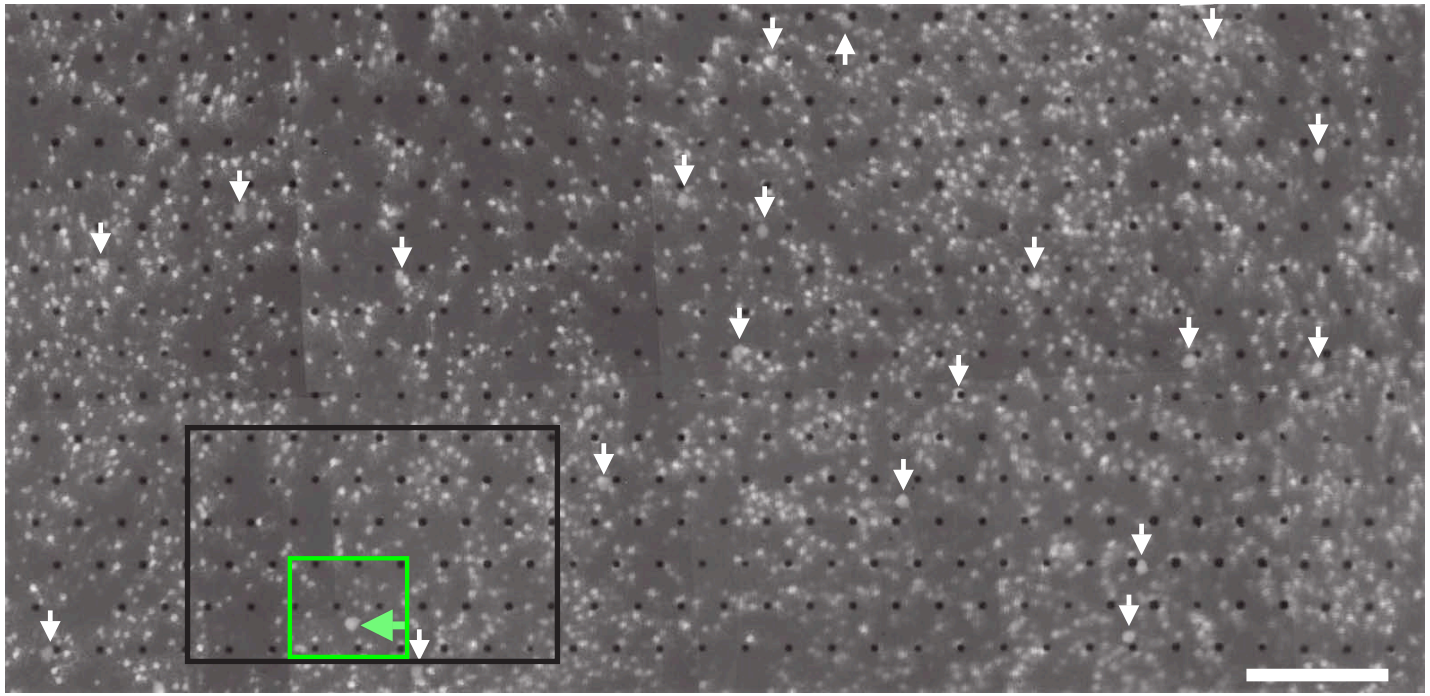
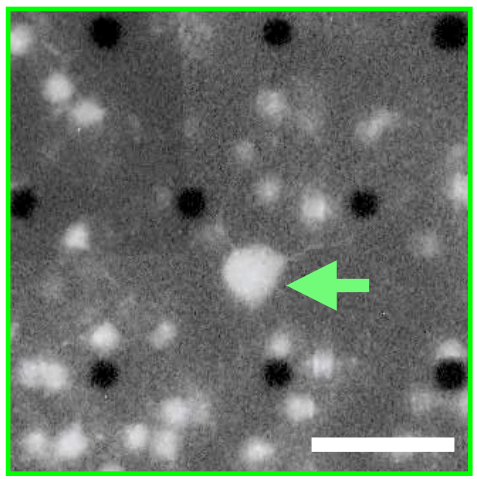


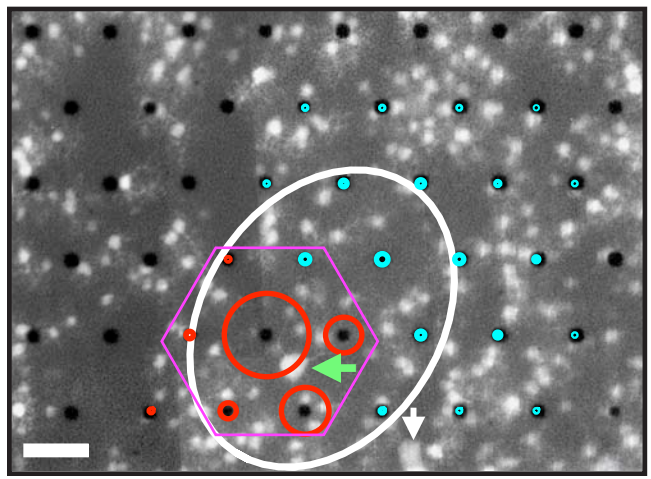




Merge of the two images







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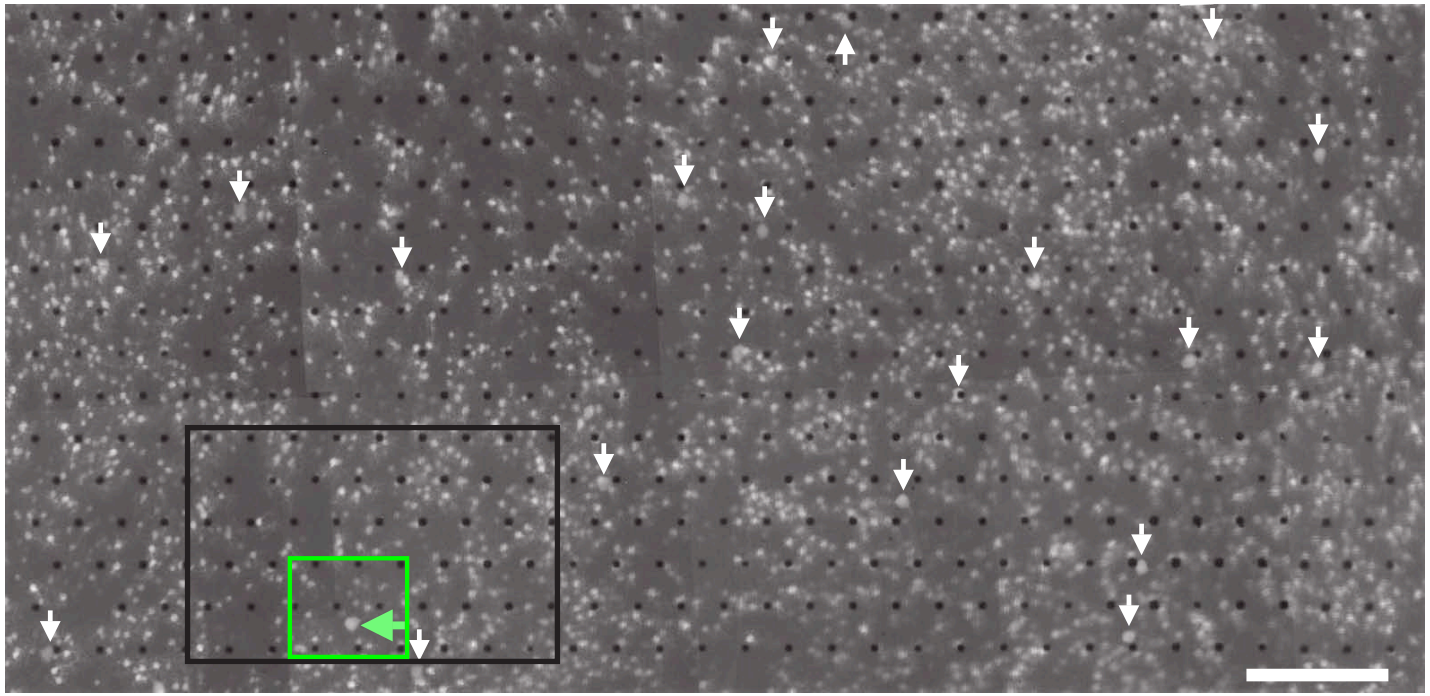
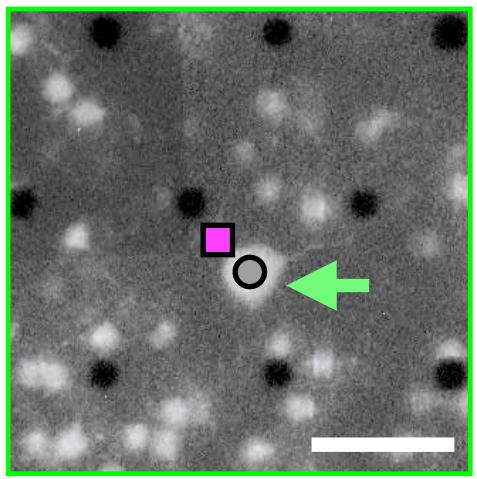
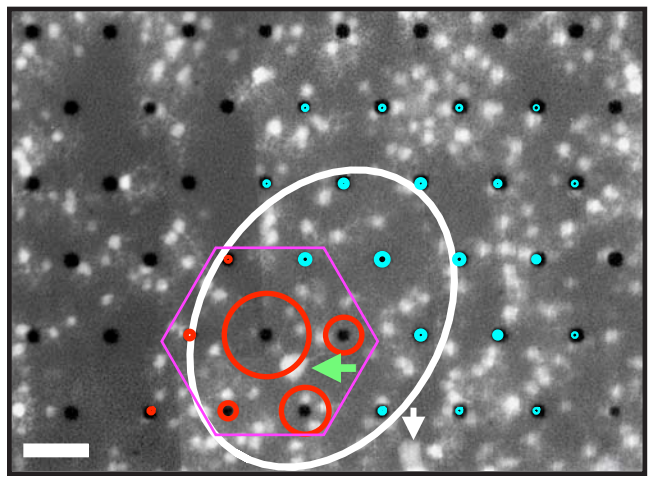
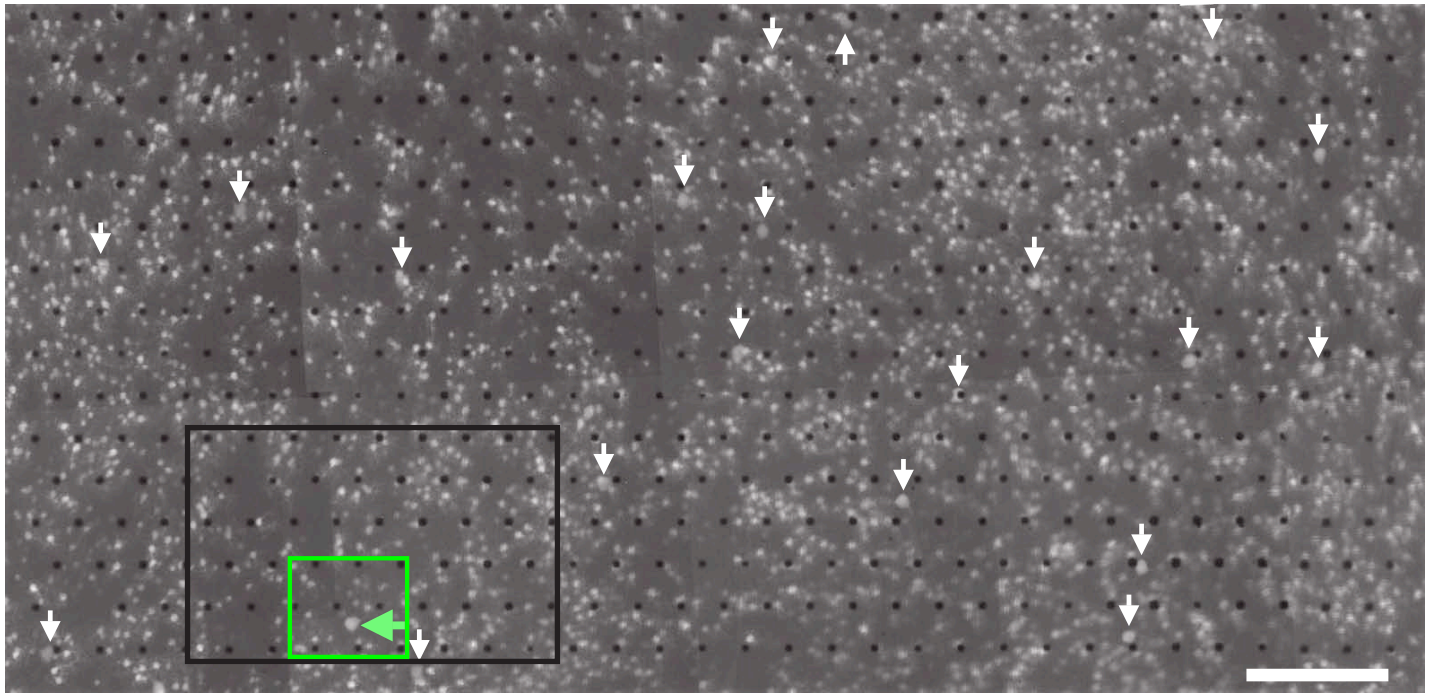
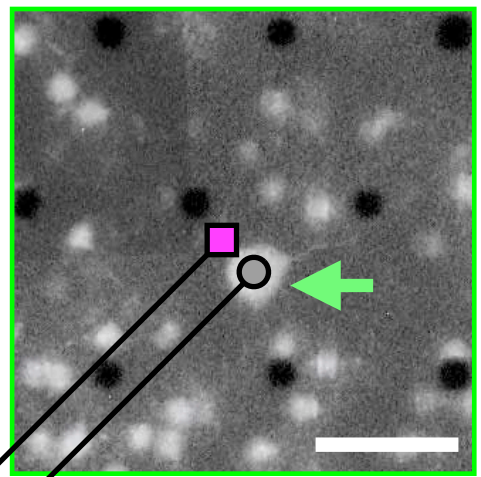




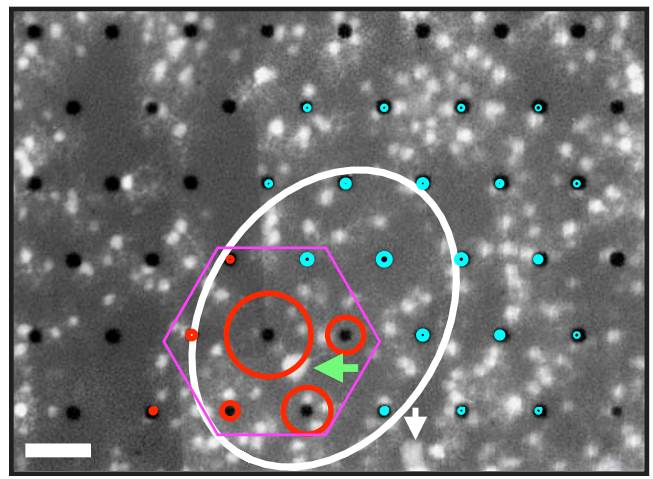


Merge of the two images

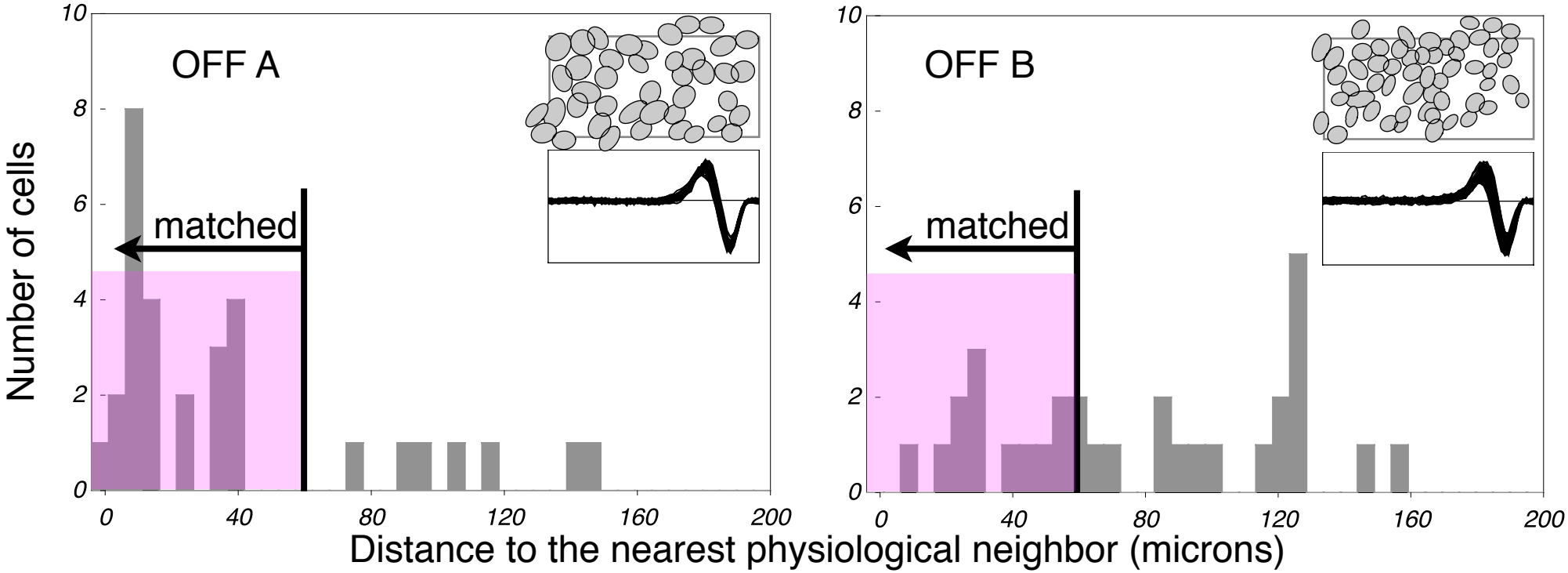


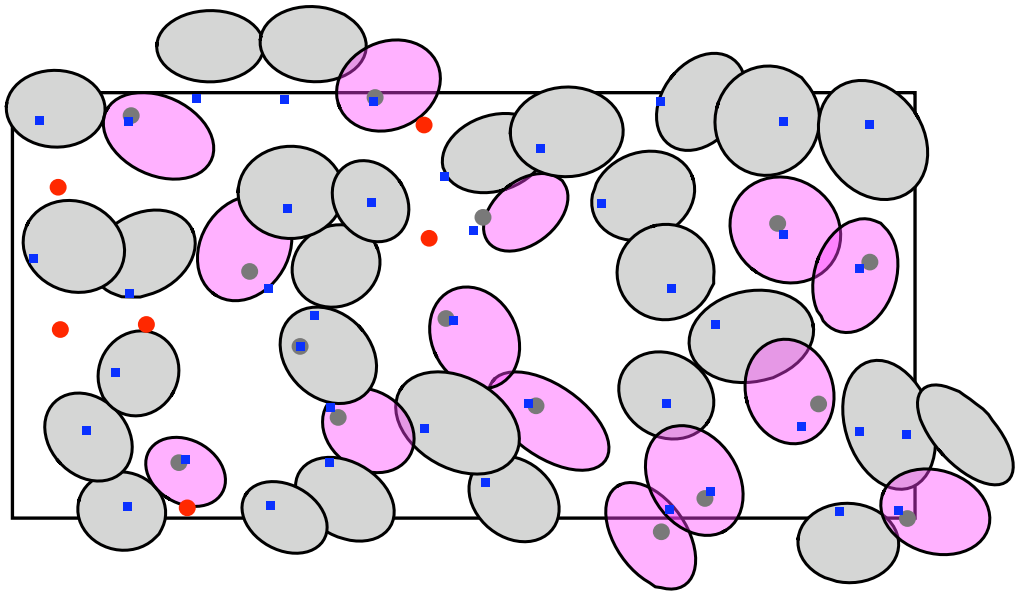


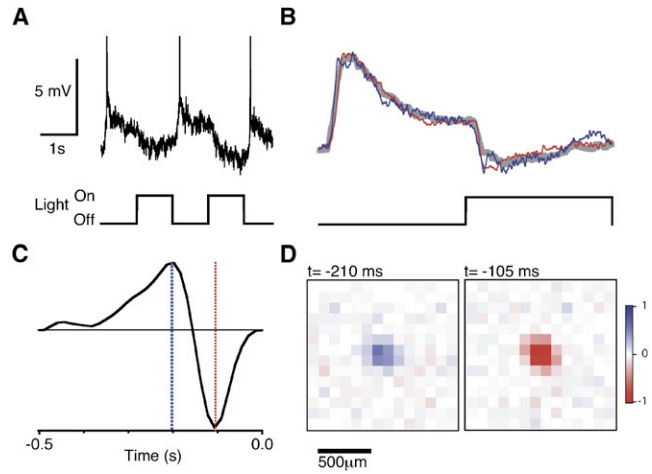
nearest physiological neighbor distance



OFF cell type matches CB2-GFP cells

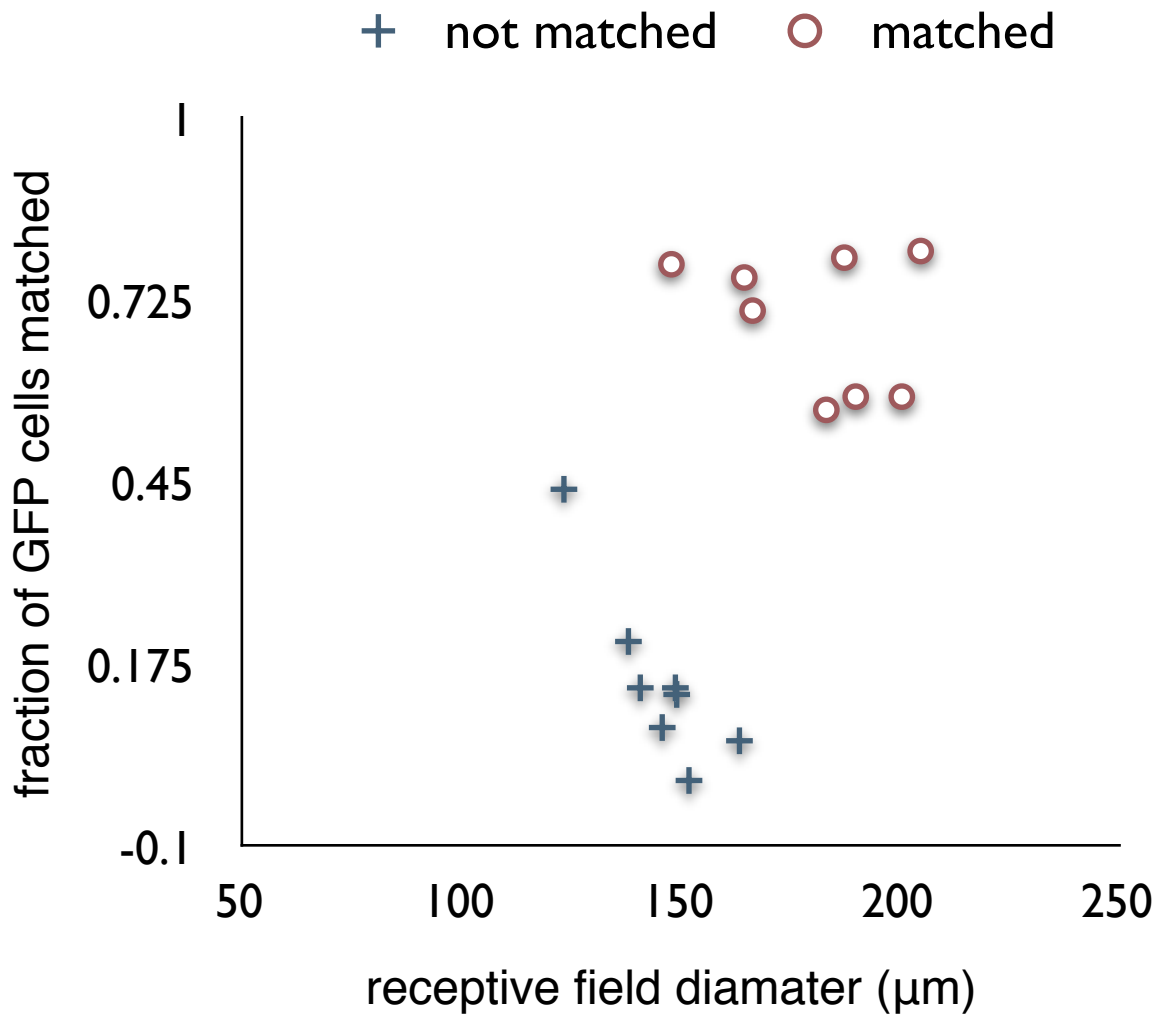




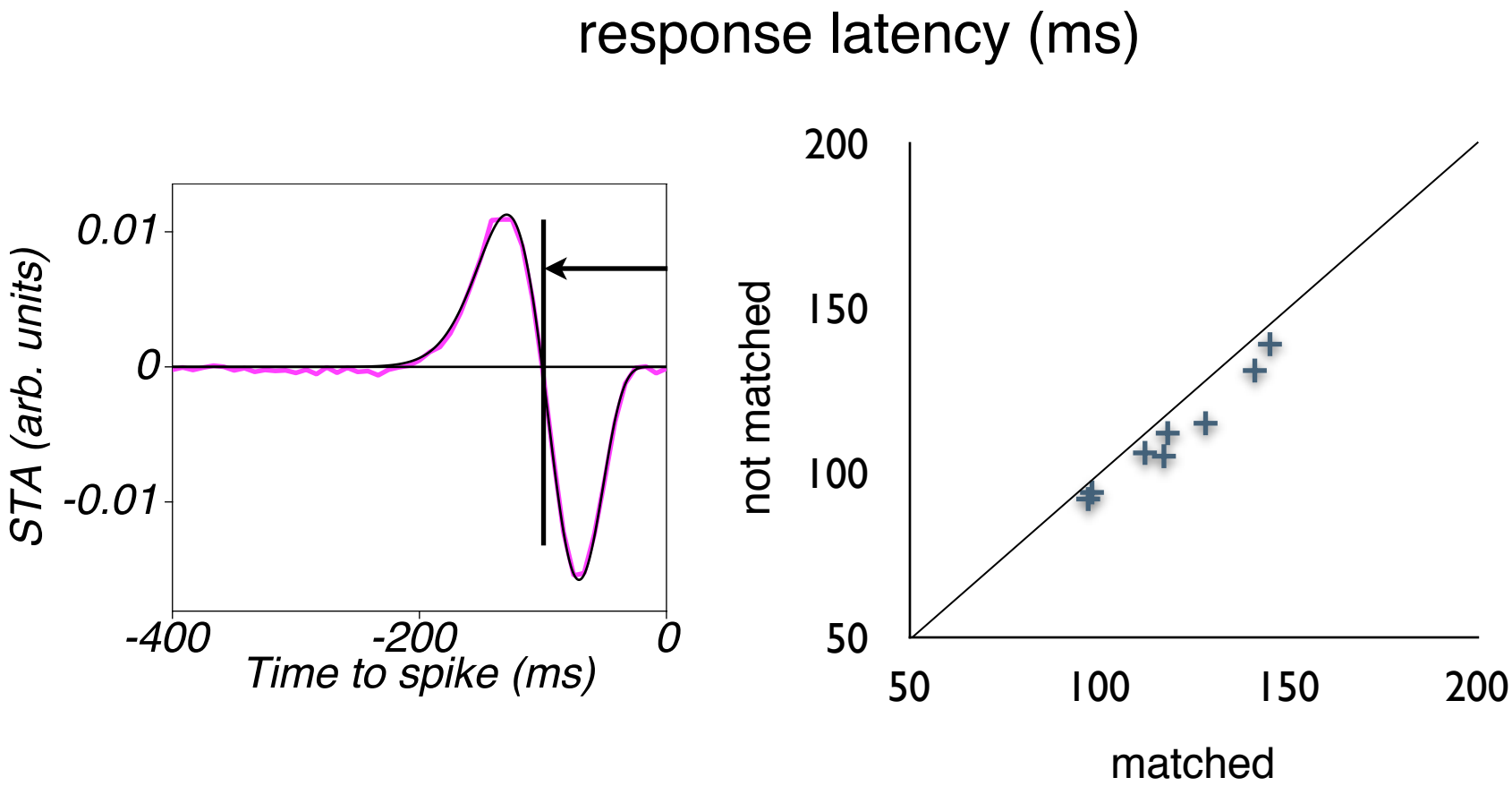


(Huberman, et al., 2008)

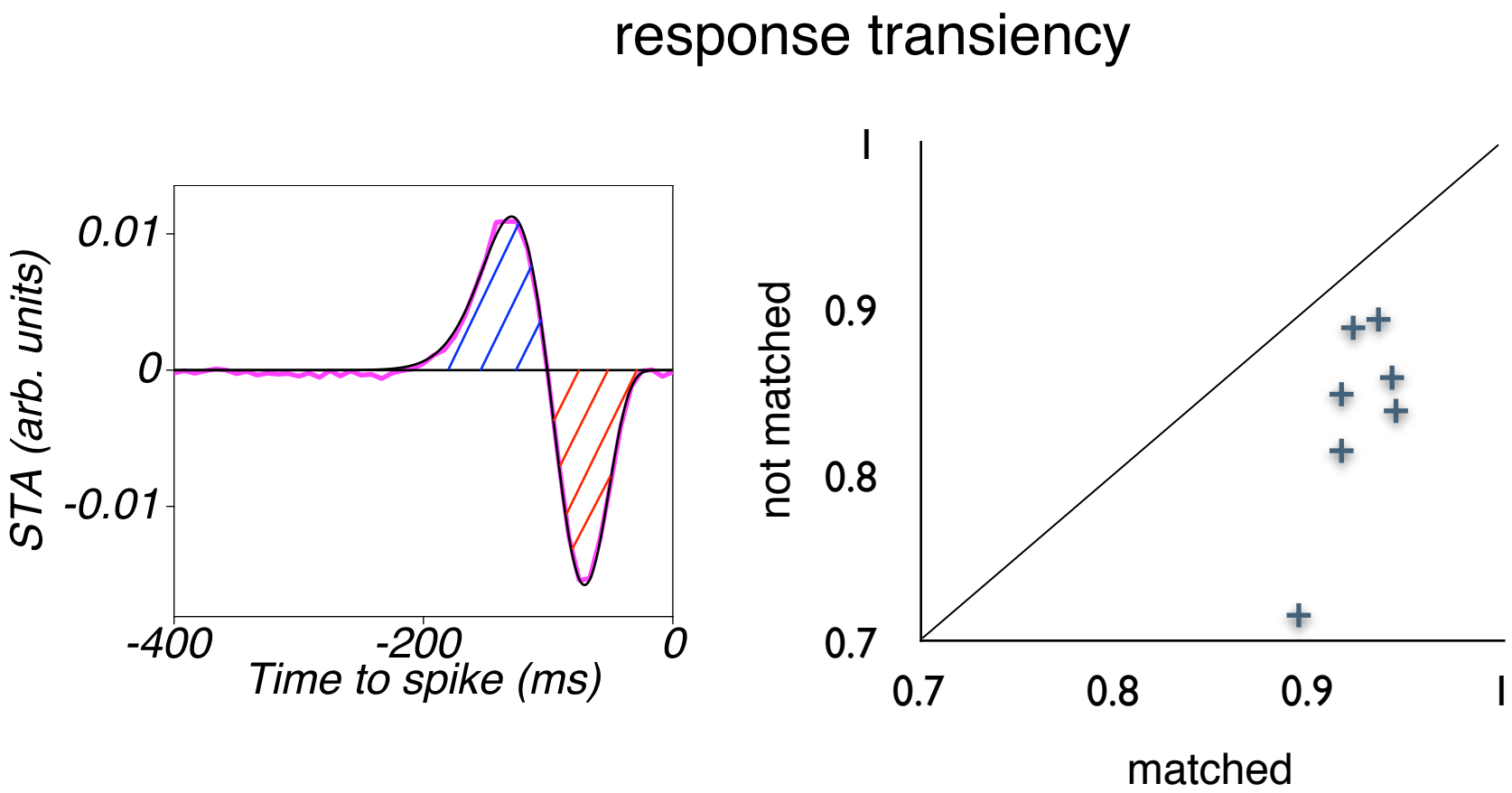
OFF Large cells



OFF Large Brisk cells

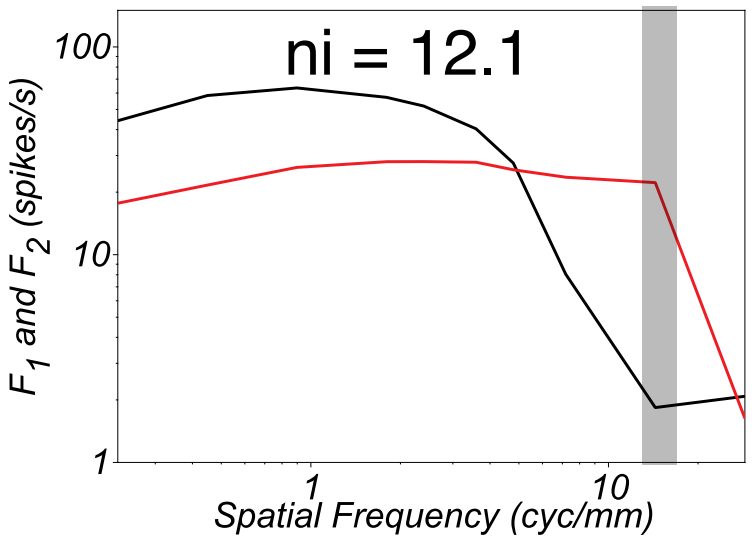


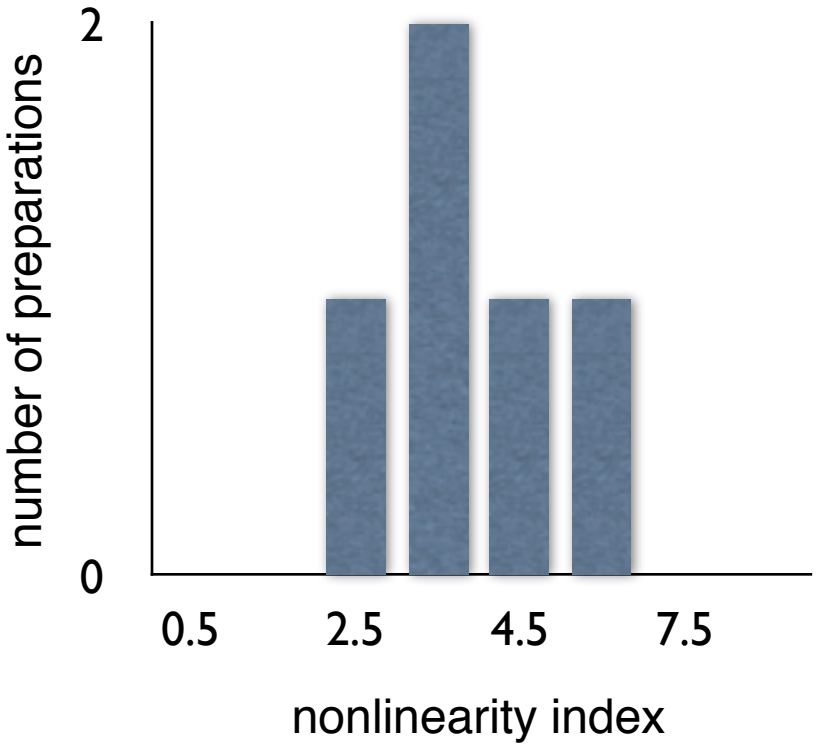
OFF Large Brisk Transient cells



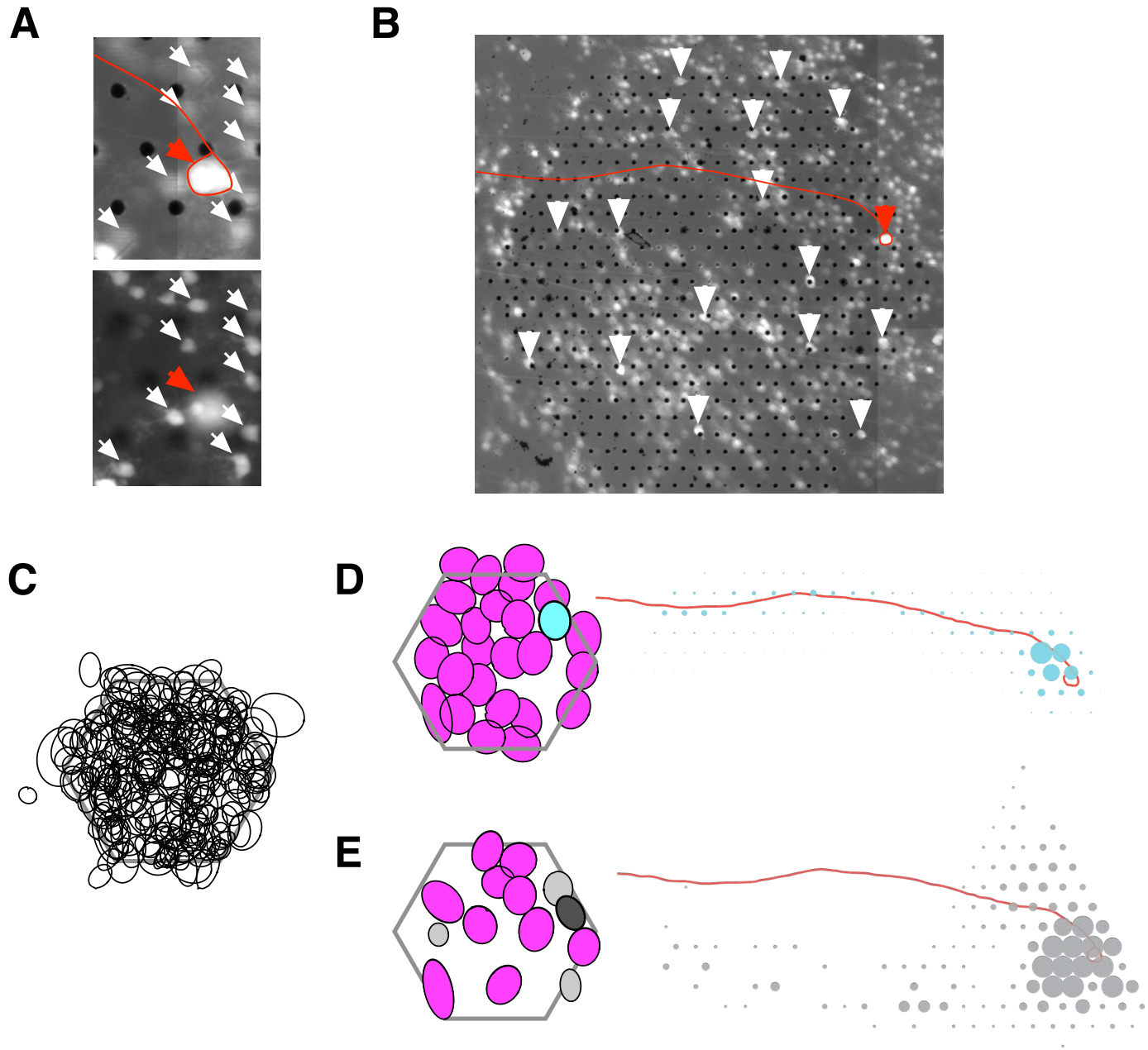
OFF Large Brisk Transient nonlinear cells

non-linearity index

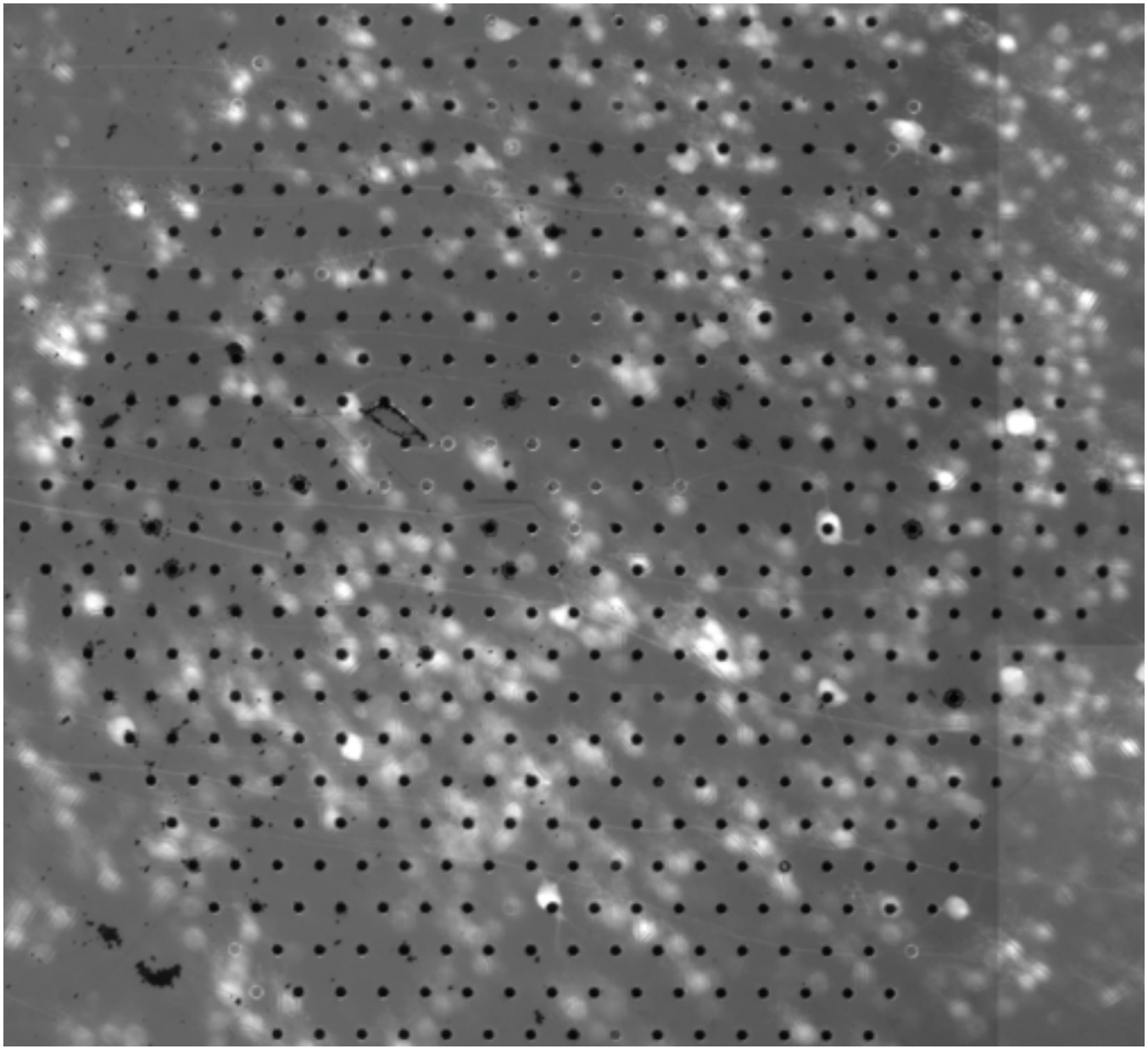




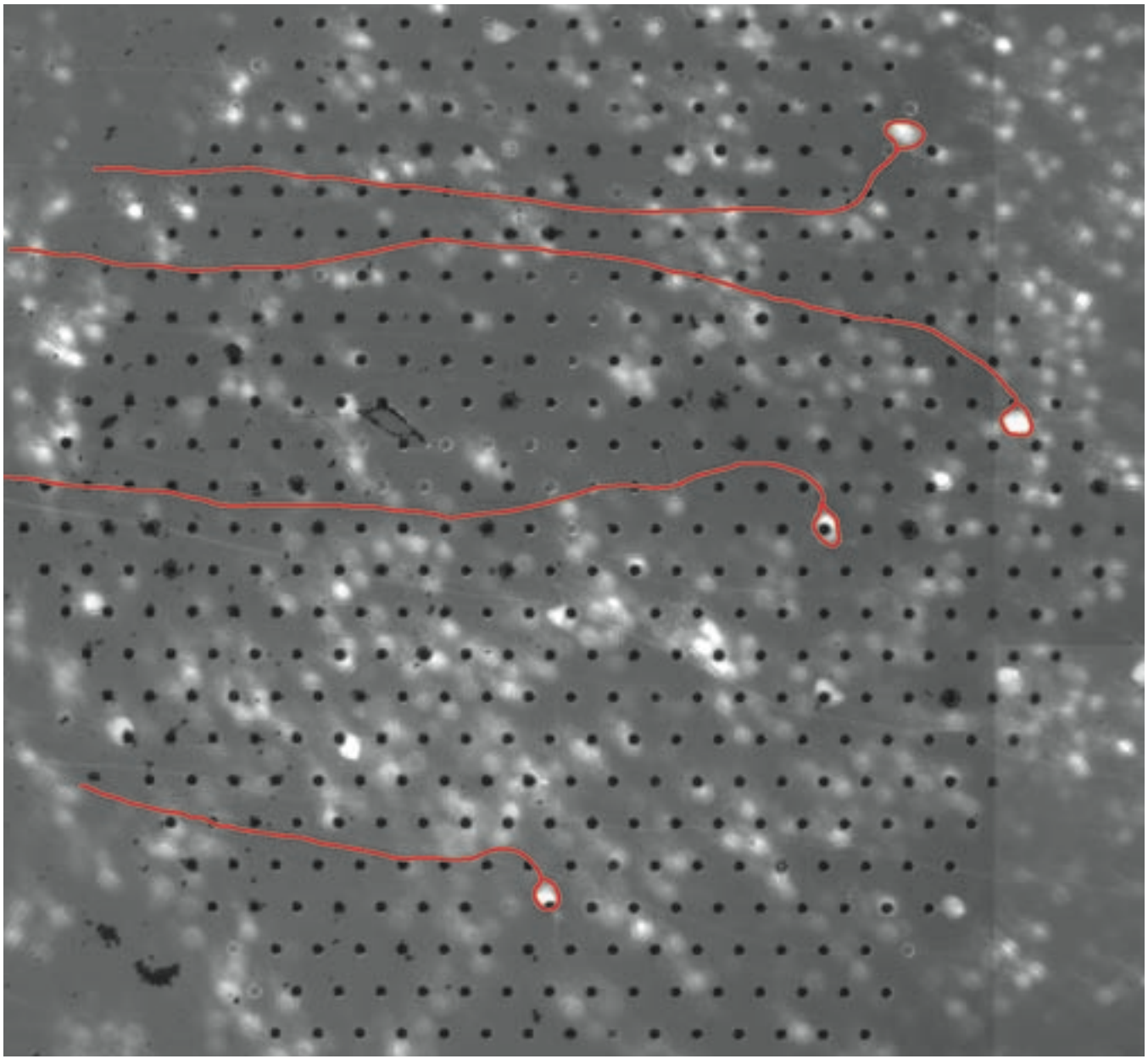
somas and axons



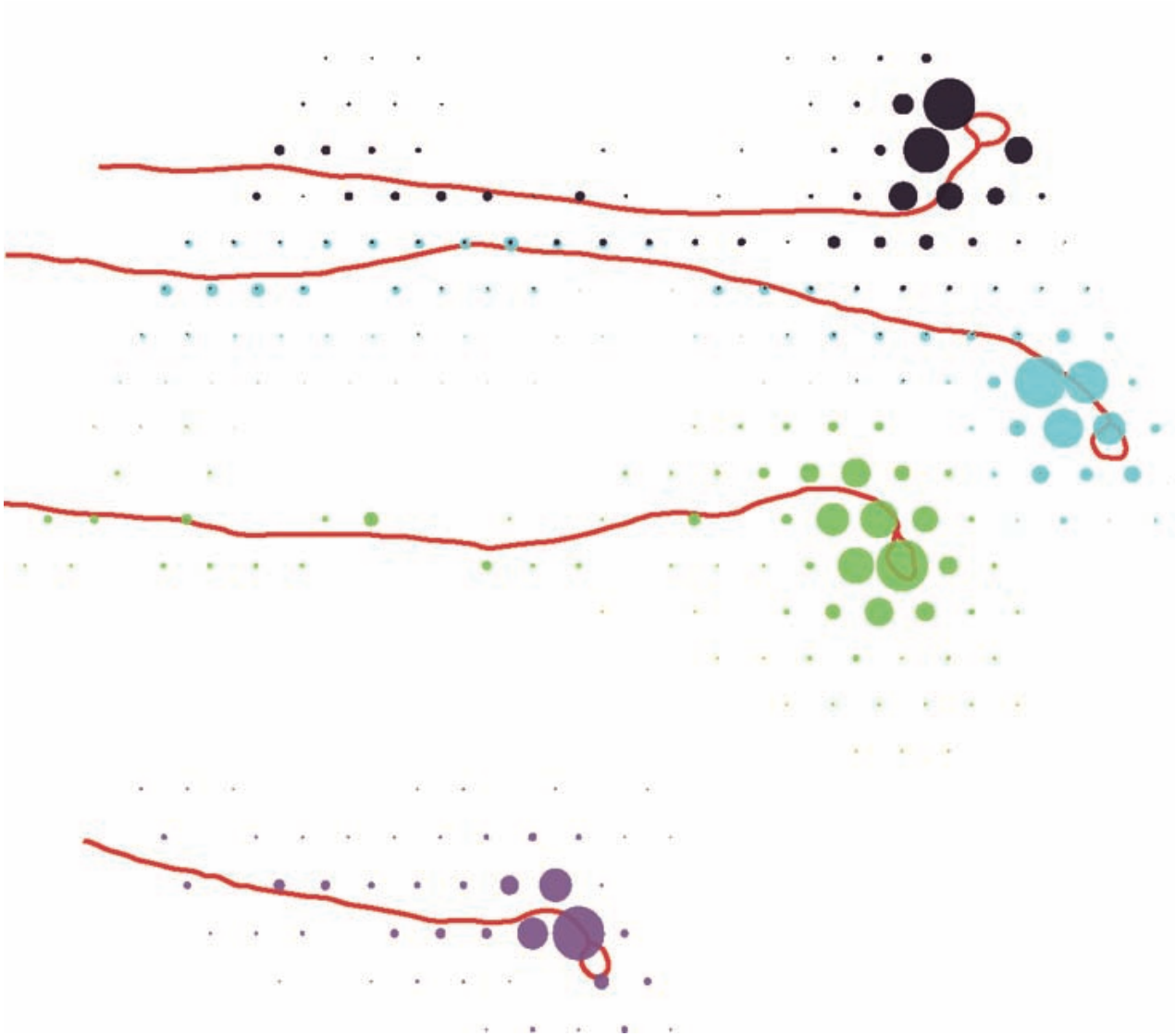
somas and axons



somas and axons

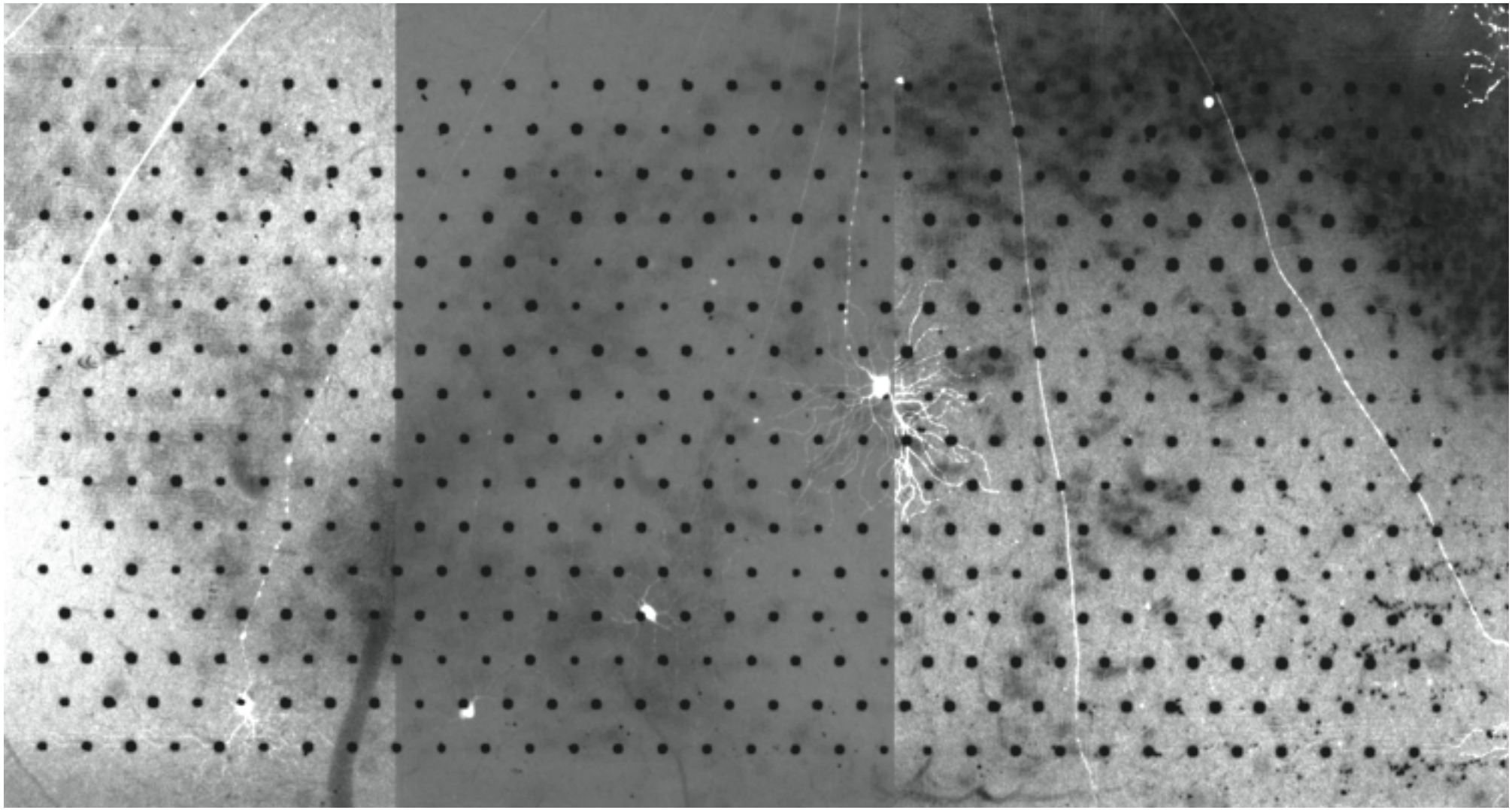


somas and axons



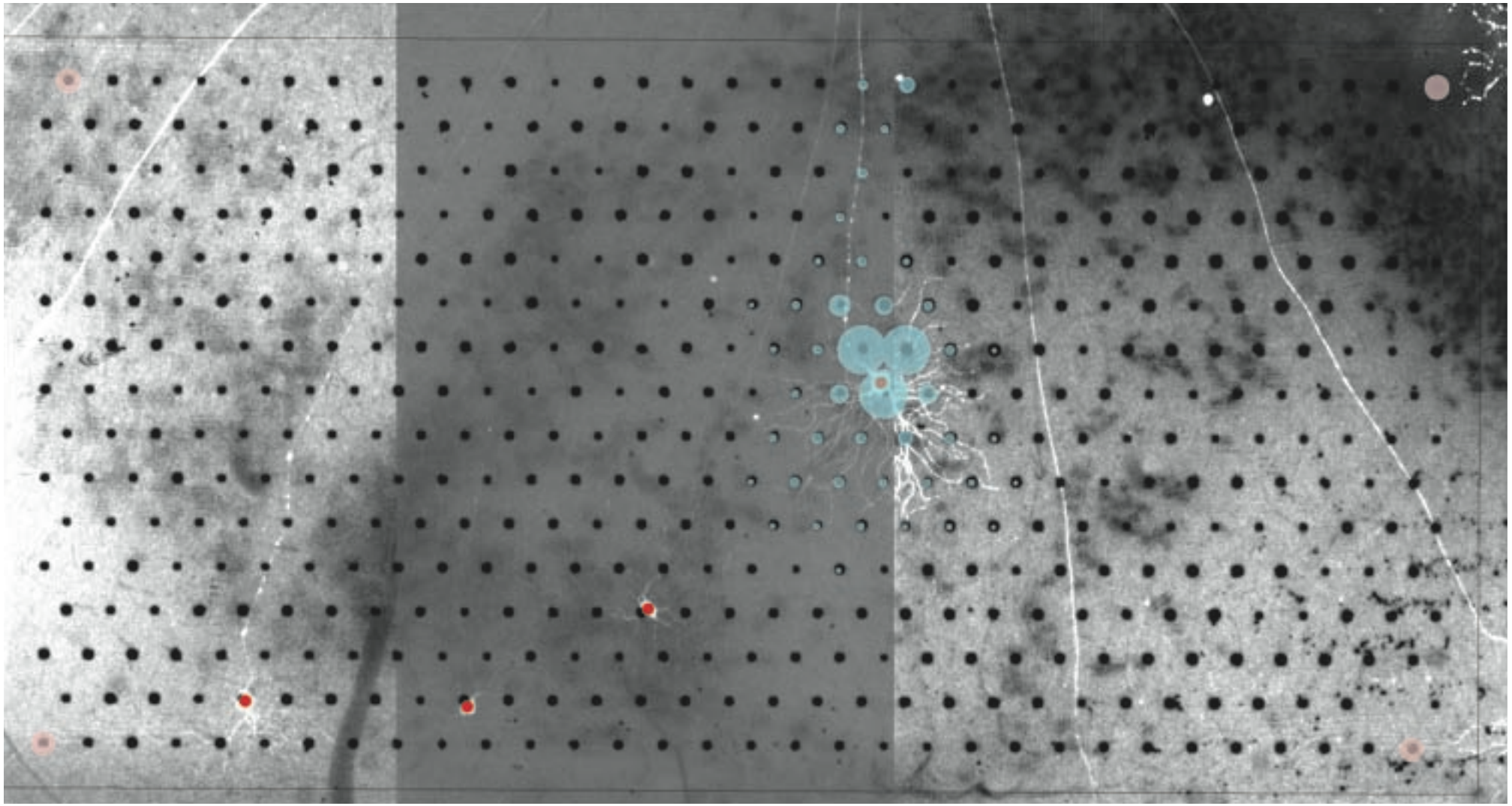
non specific labeling

YFP retina



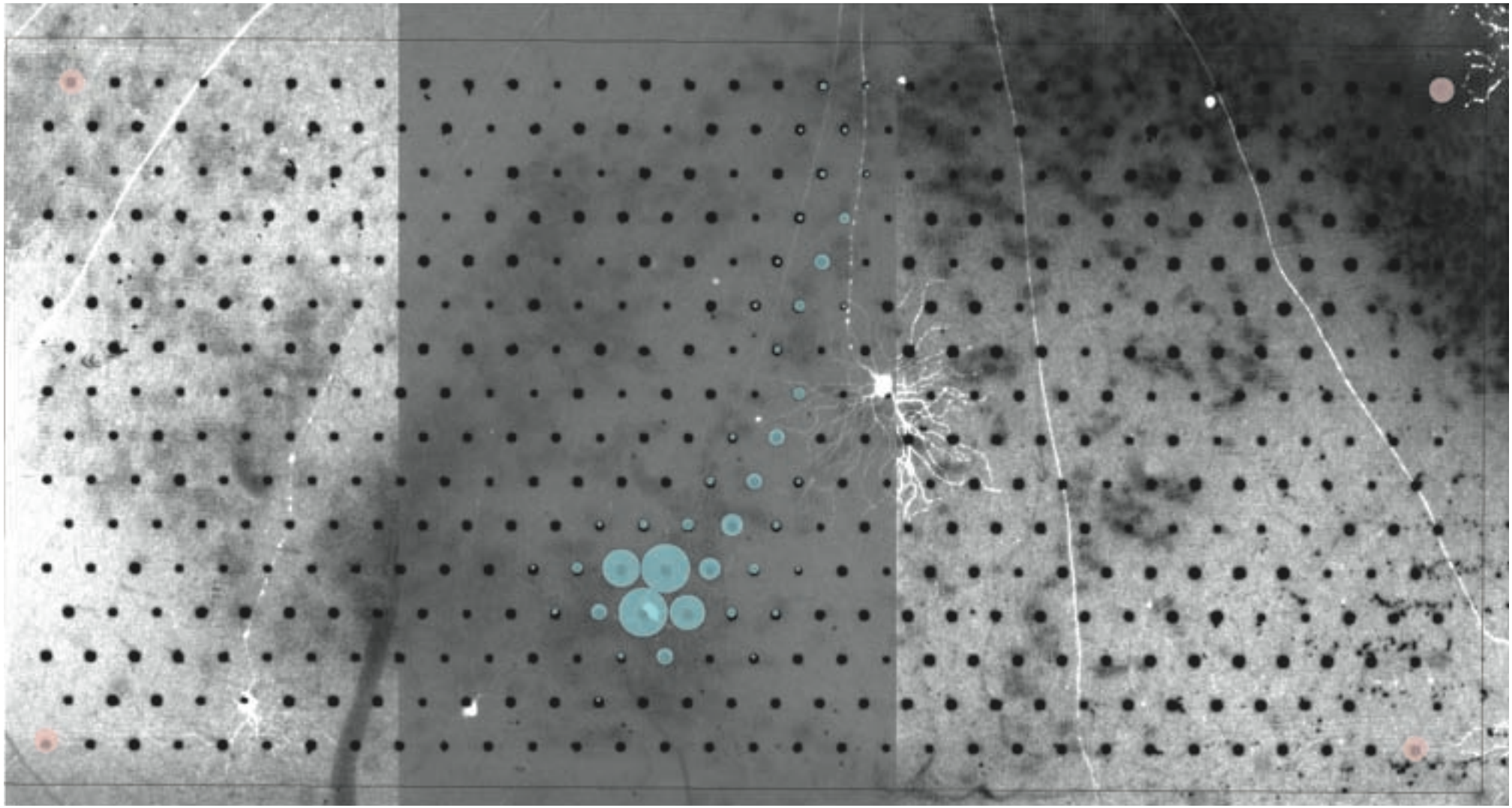
non specific labeling

good cell #1



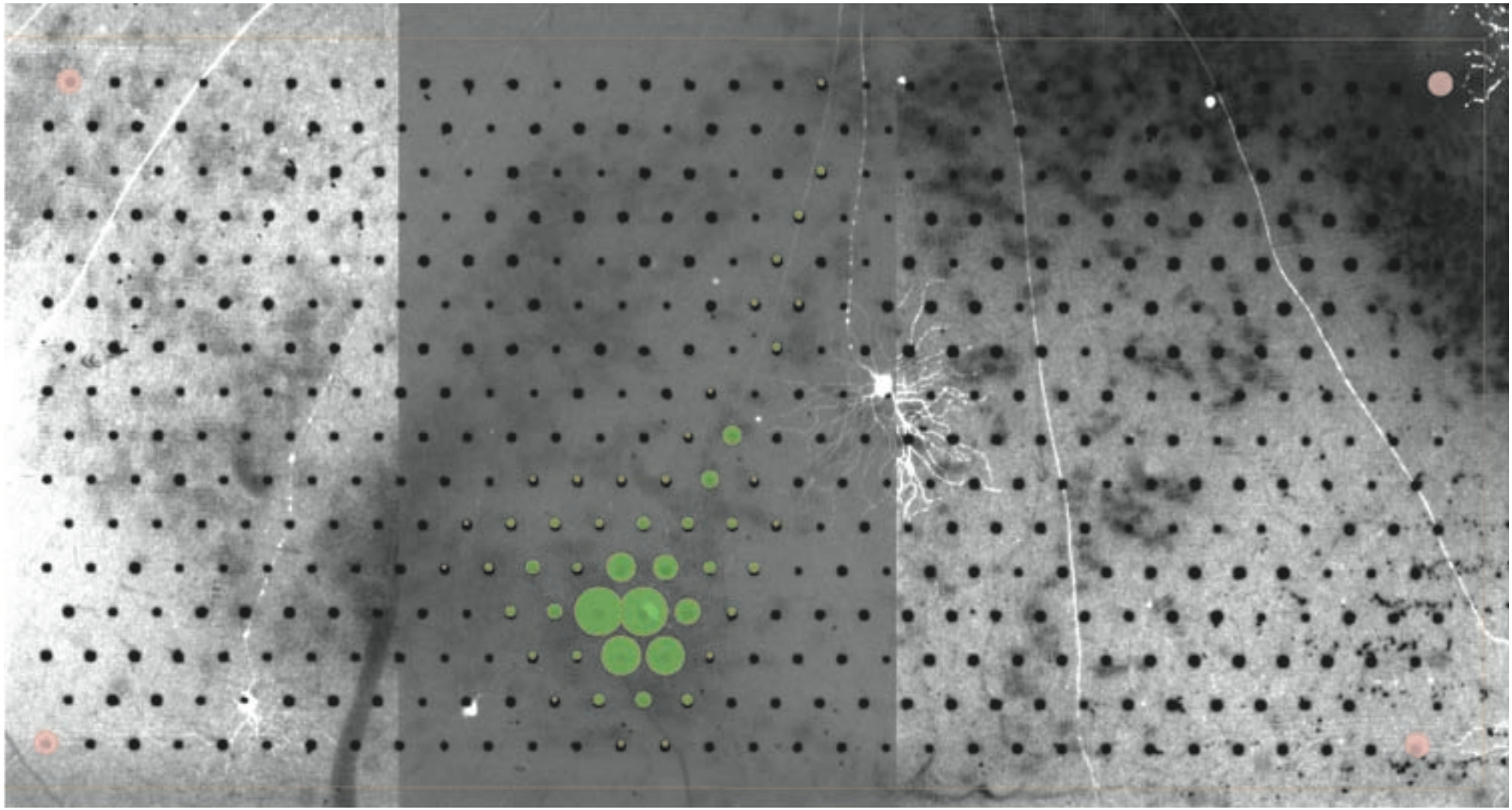
non specific labeling

good cell body but not so good axon match

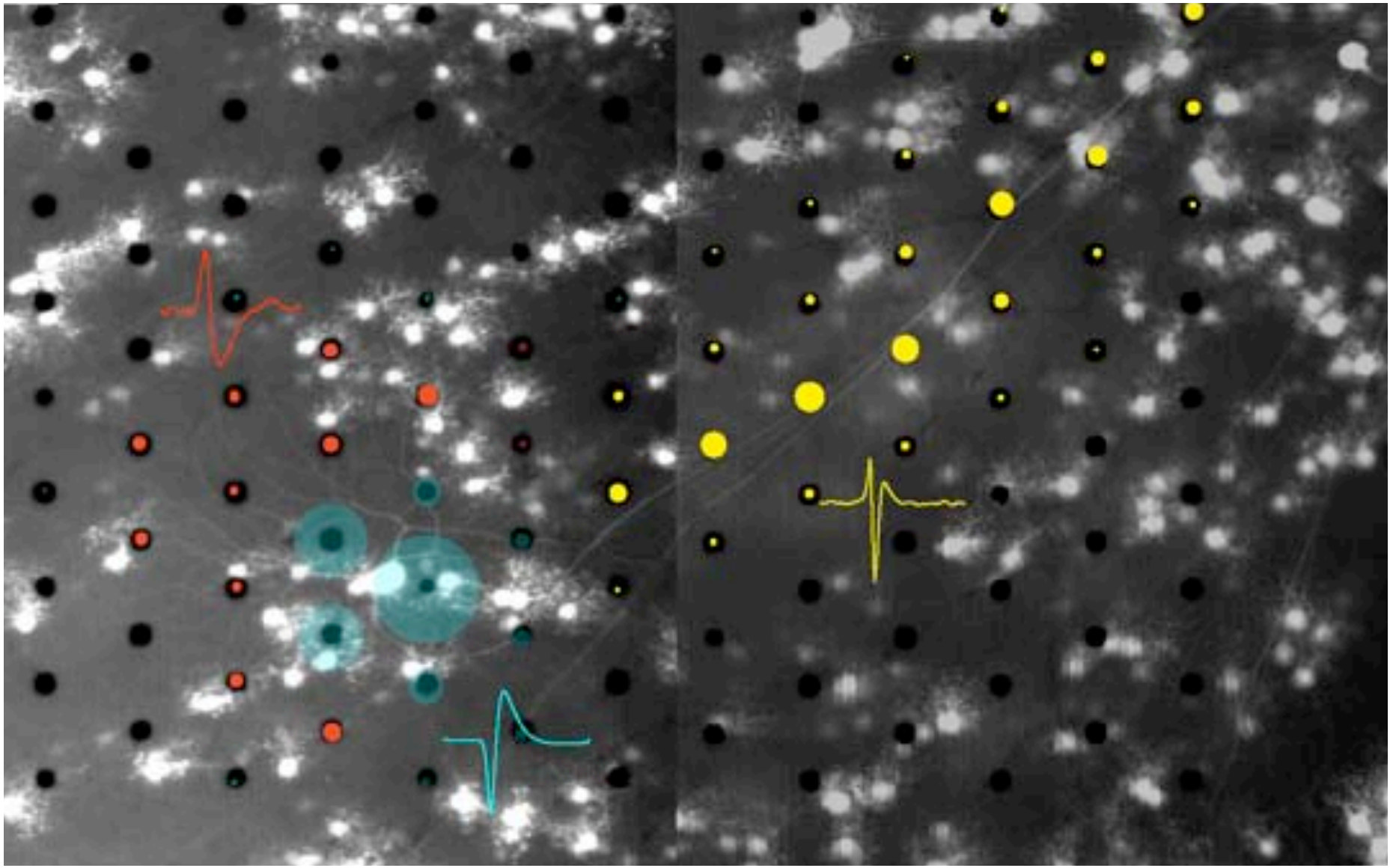


non specific labeling

good cell body and axon match



Connecting anatomy and function



Retinal Photocoagulation

Diabetic retinopathy is the leading cause of blindness among adults aged 20-74

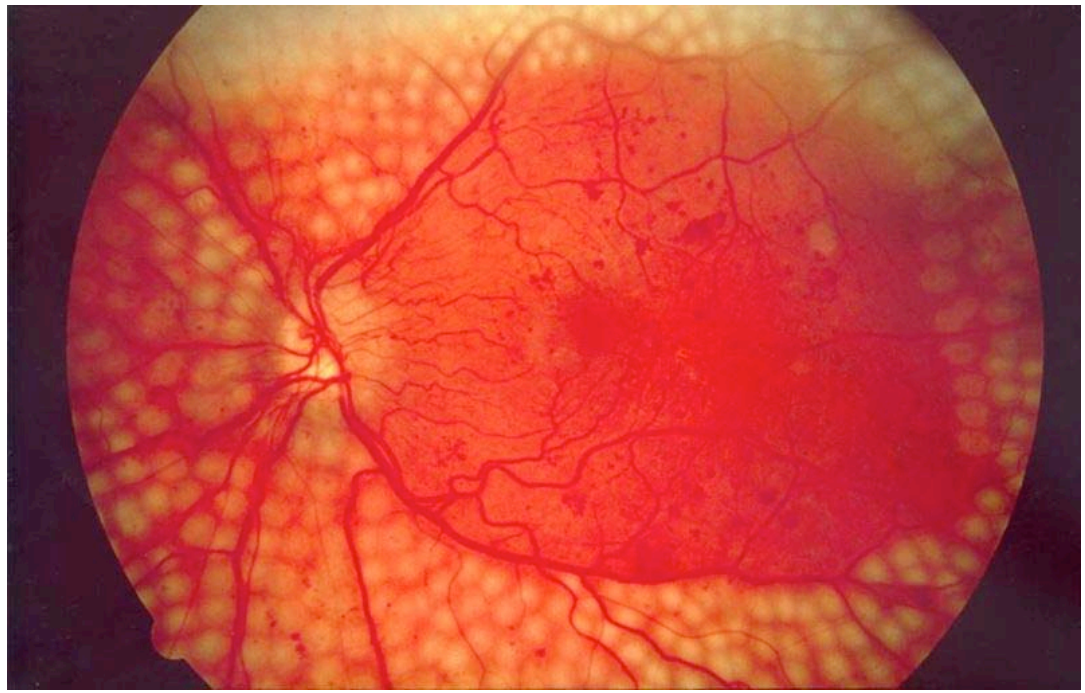
Pan-retinal photocoagulation (PRP) is the long-standing standard of care for diabetic retinopathy

Pulse duration of 100 - 200 ms results in significant heat diffusion and associated collateral damage

>1000 retinal burns individually placed with green laser

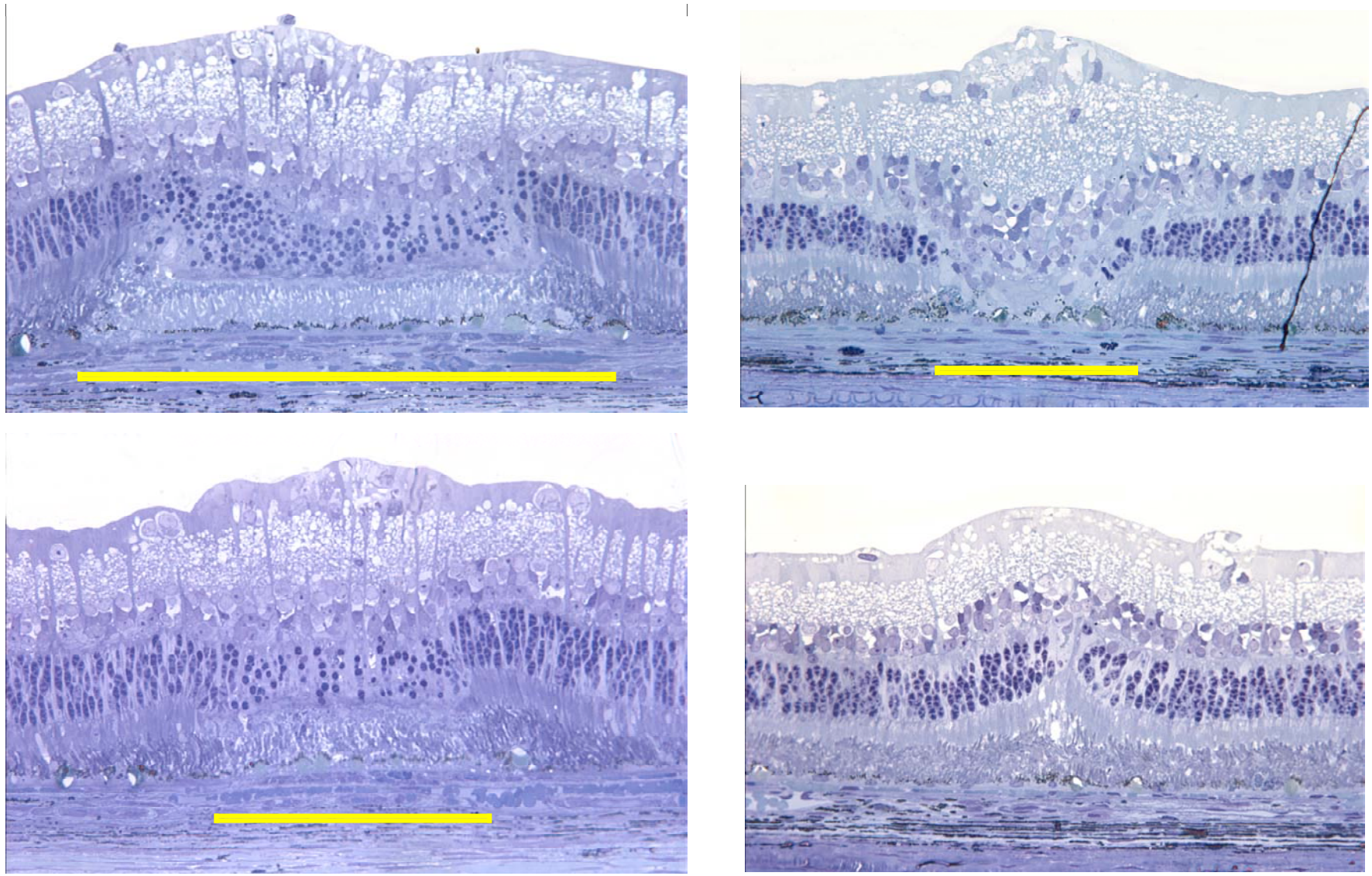
Fatiguing, painful and time consuming

Detrimental side effects: retinal scarring, loss of visual field, reduced night vision.



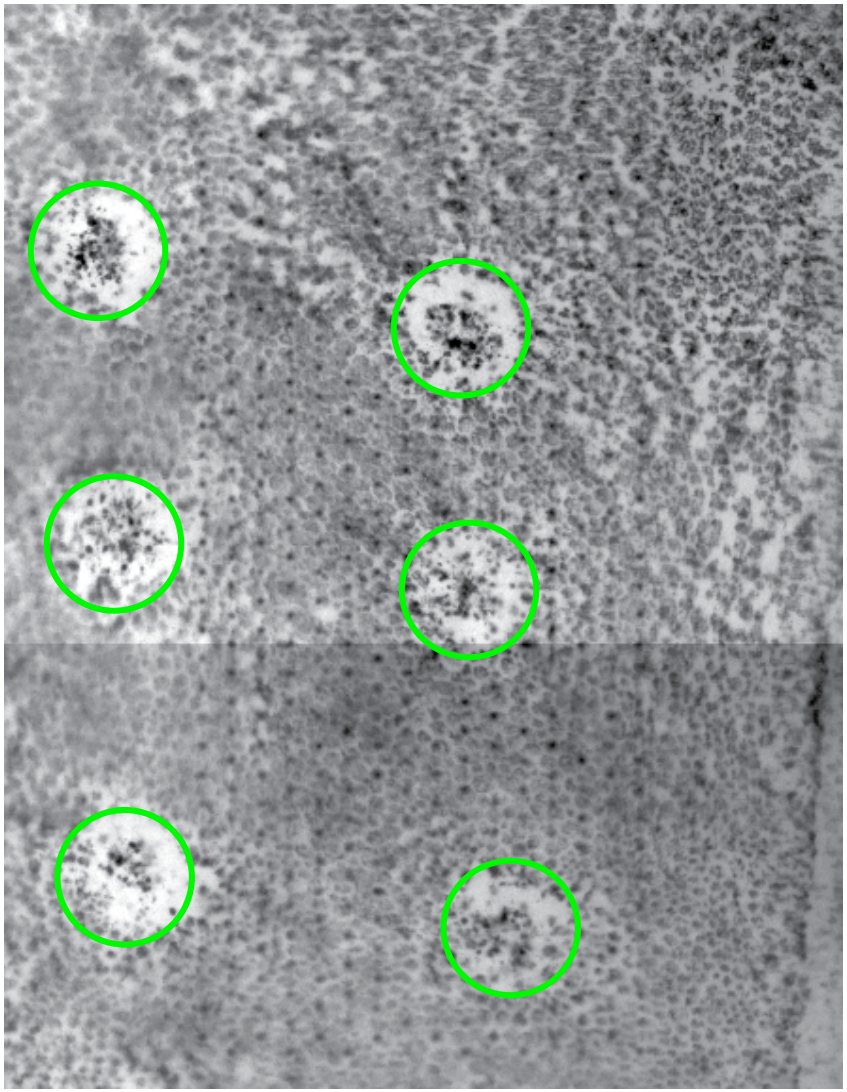
Conventional pan-retinal photocoagulation

Smaller (less power) lesions seem to “recover” the blind spot after some time

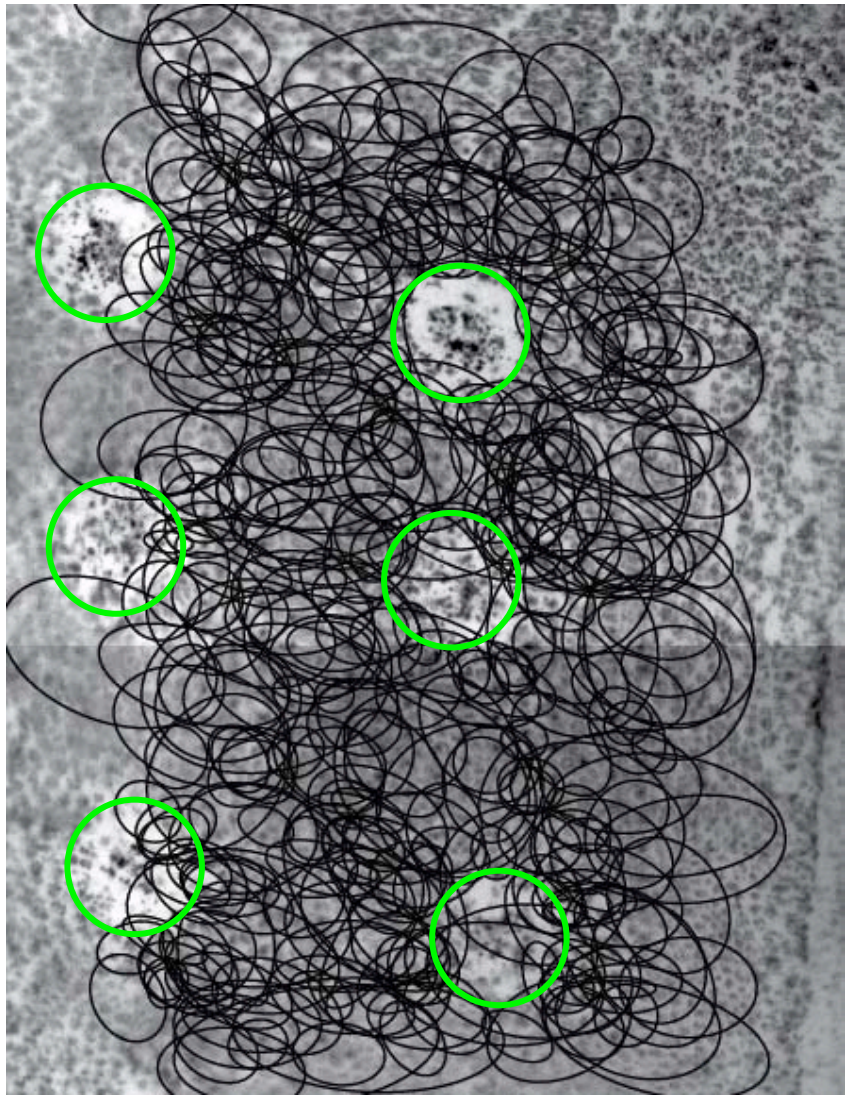


Preliminary Results

control: barely visible lesions 1 day



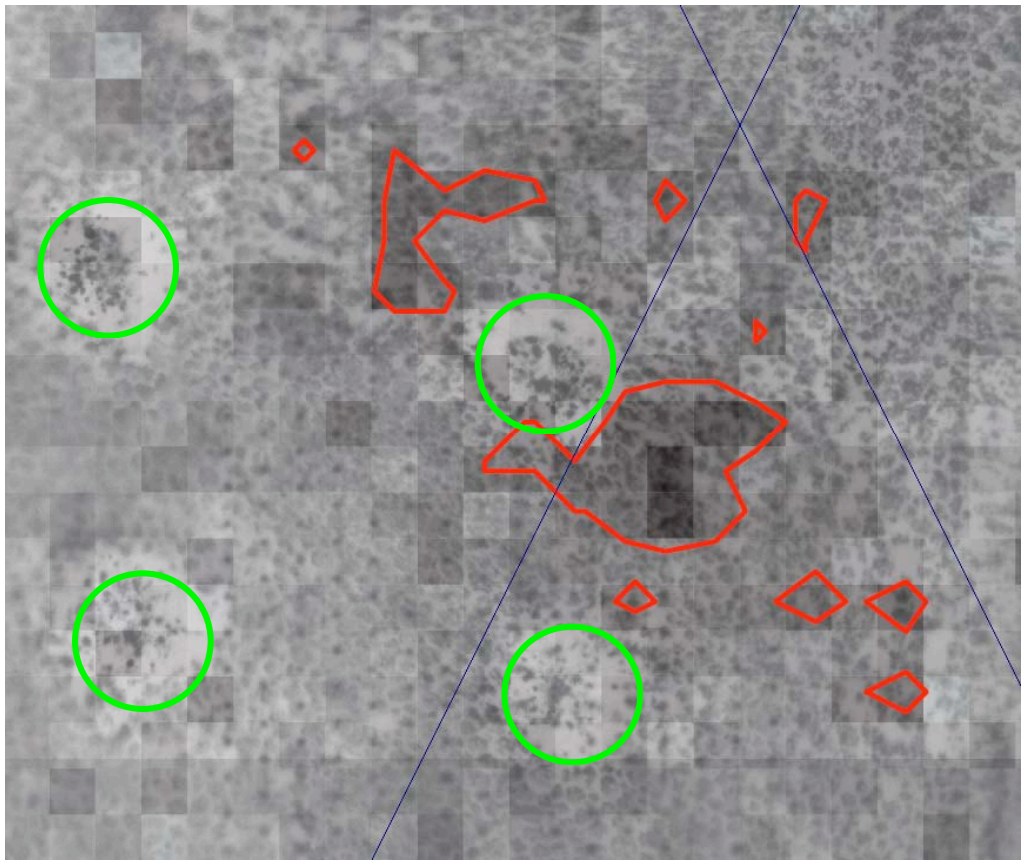
array and RPE

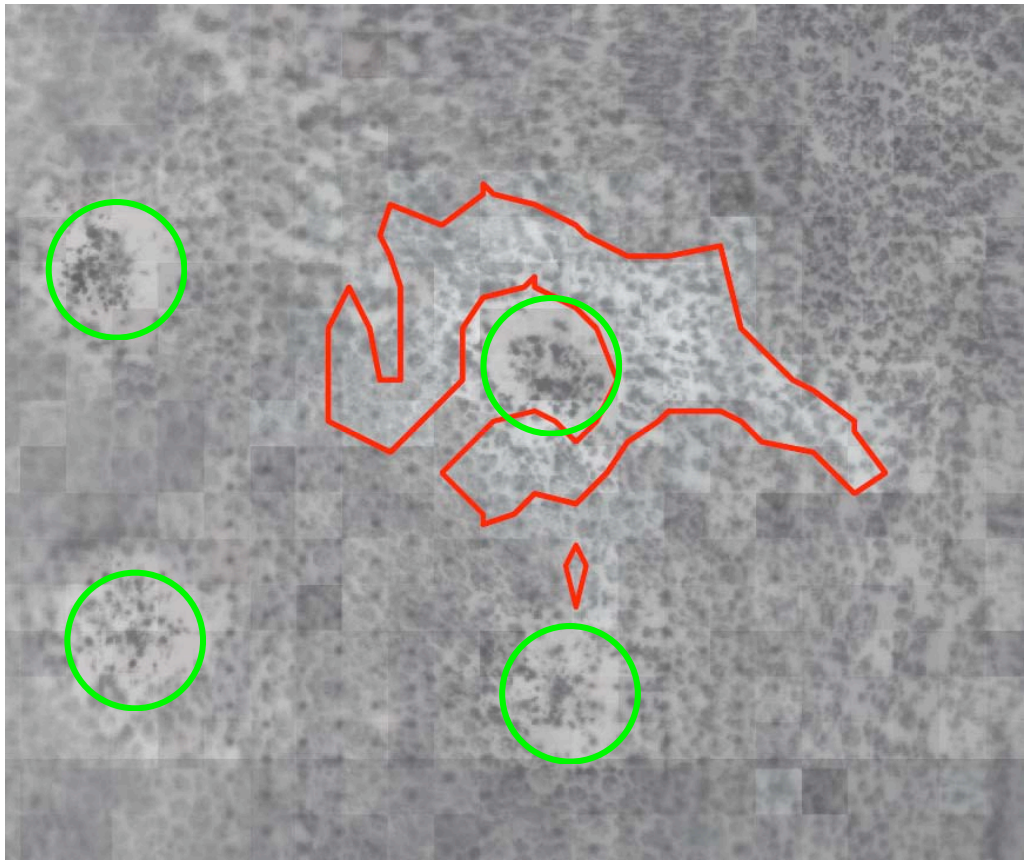


receptive fields

Preliminary Results

control: barely visible lesions 1 day

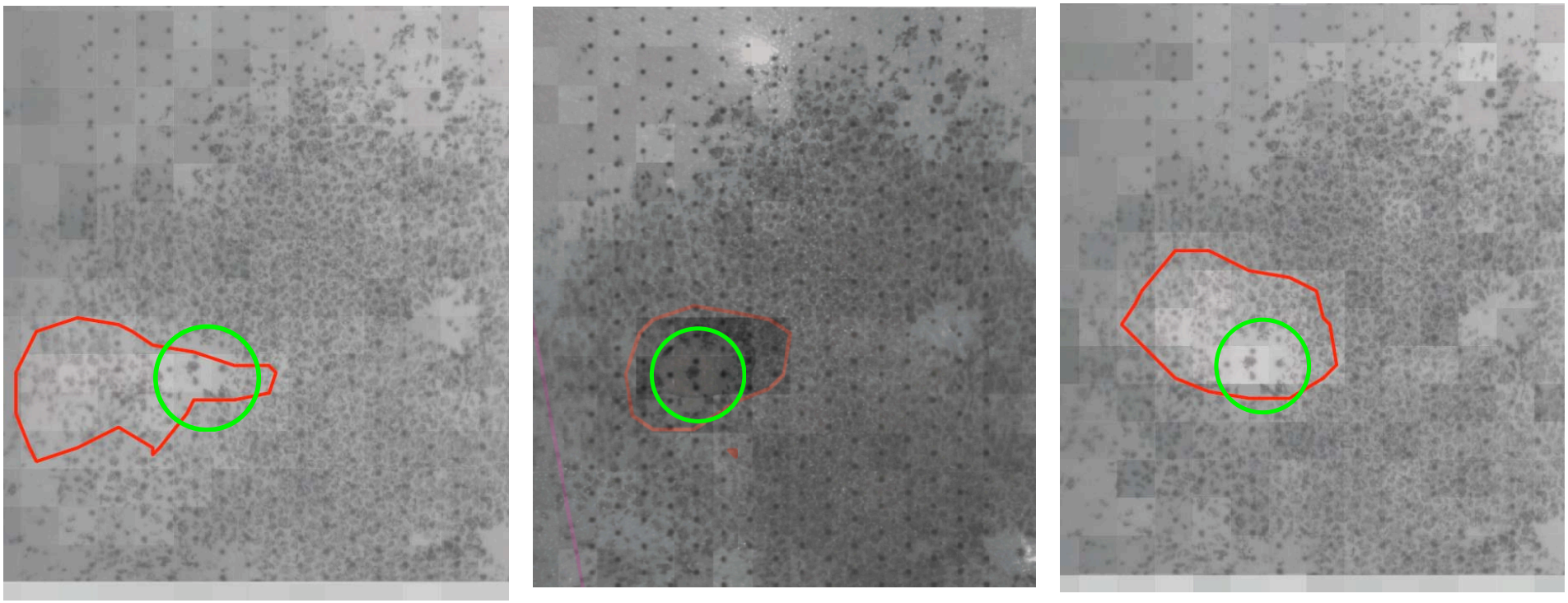




no sensitivity at all in the lesion areas

Preliminary Results

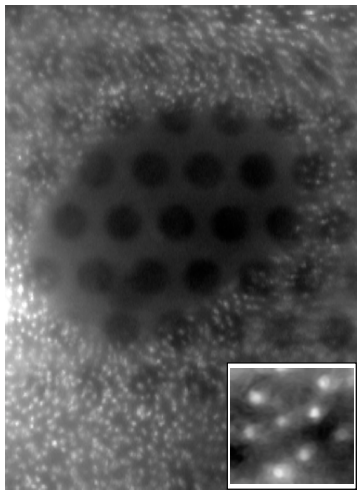
barely visible lesions

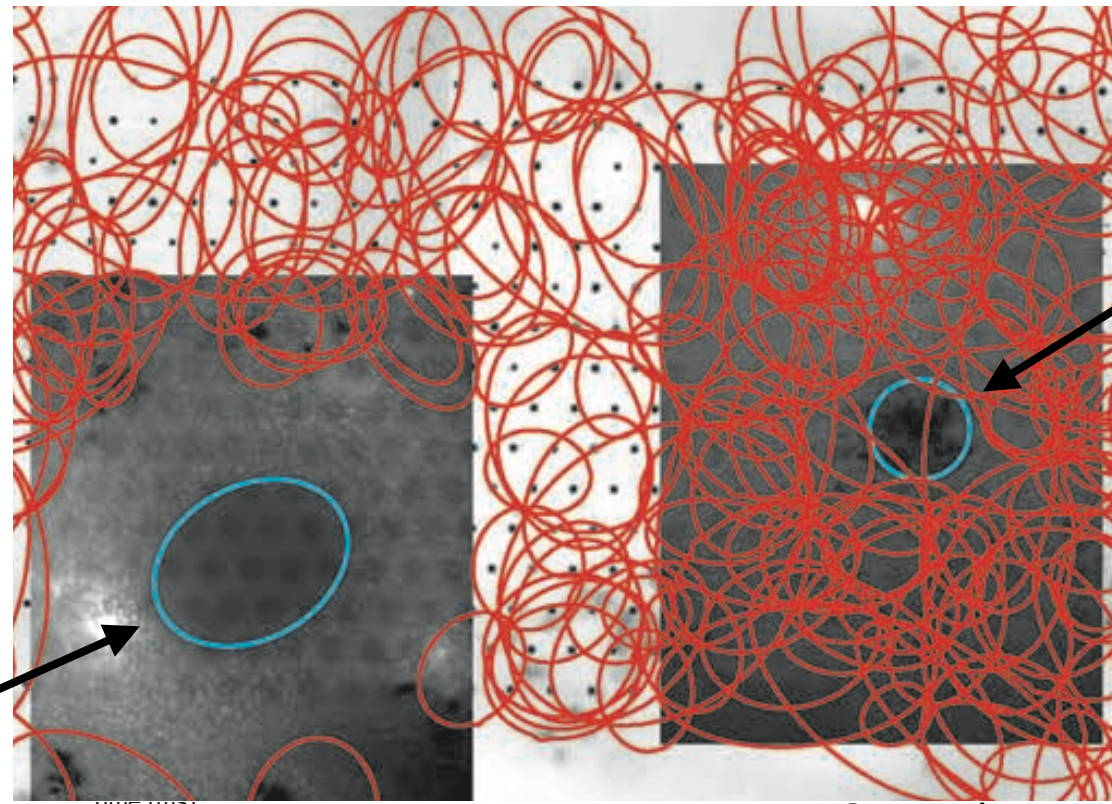


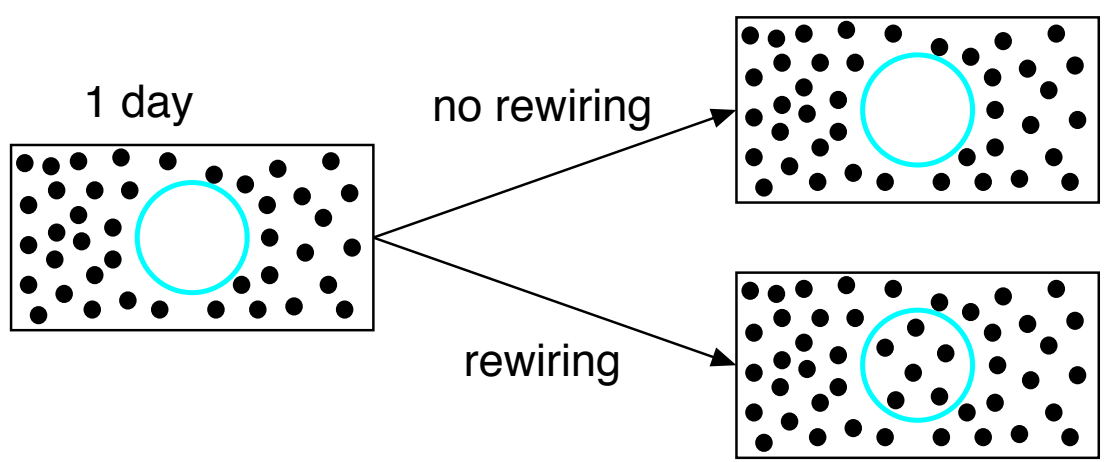
1 month

Preliminary Results

shift or shift plus rewiring?

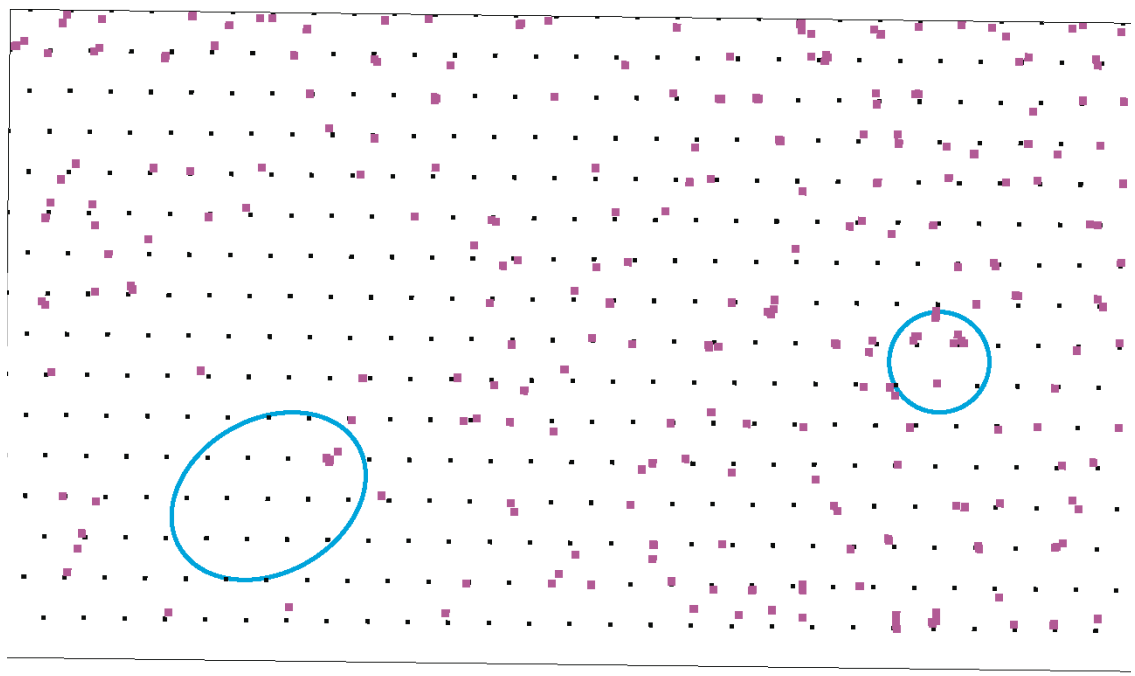


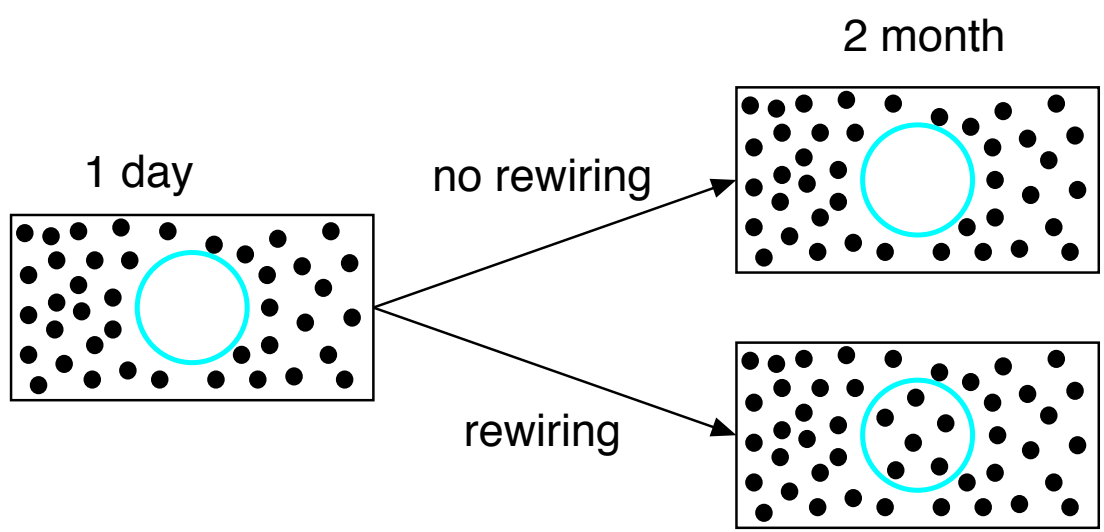




Preliminary Results

looks like rewiring!

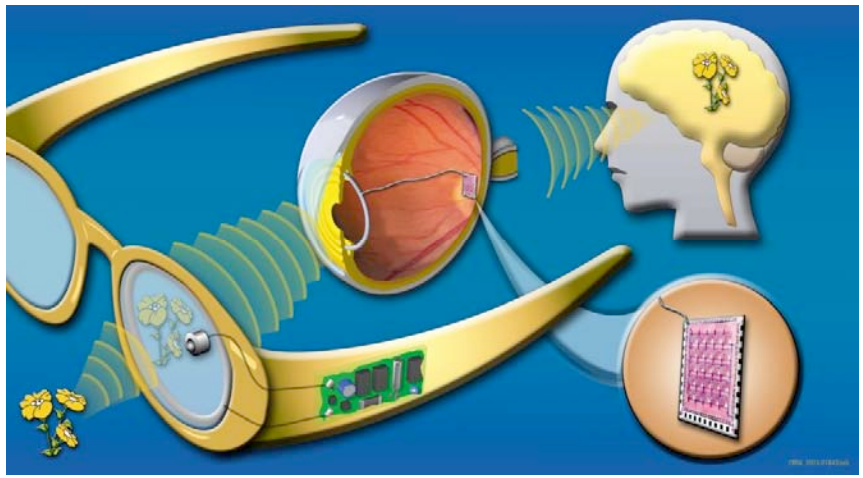




Medical Applications

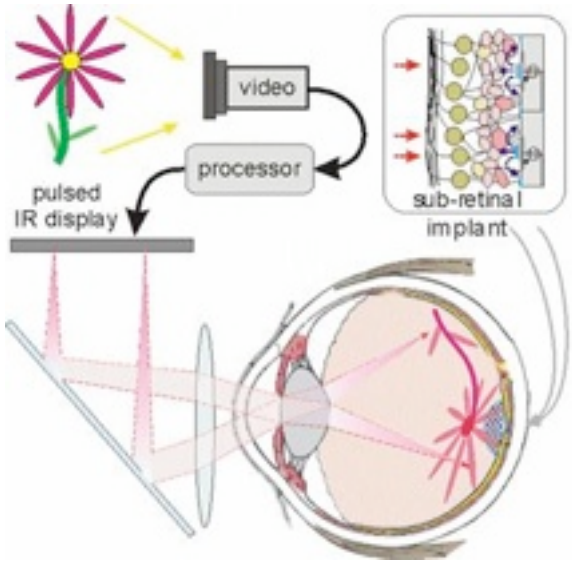
Retinal Prosthesis

Epiretinal



Custom circuitry for simultaneous stimulation and recording

Subretinal



Recording of responses to stimulation with photovoltaic implants

Subretinal Photovoltaic Implant

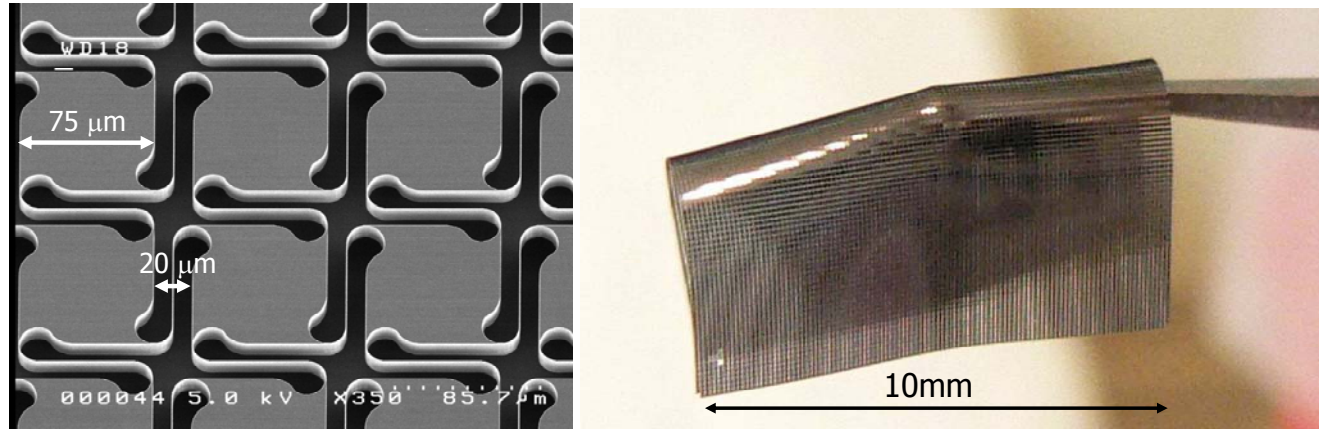


Figure C11. Flexible silicon array of 30 μm in thickness with 75μm islands connected by arms of 0.4 μm in width.

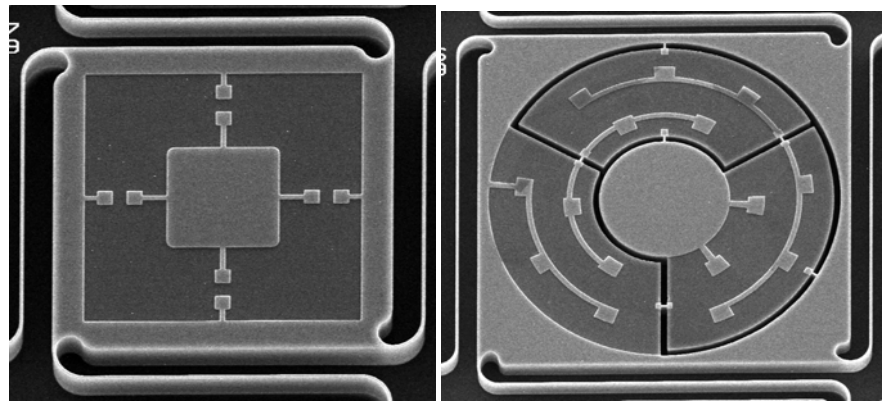
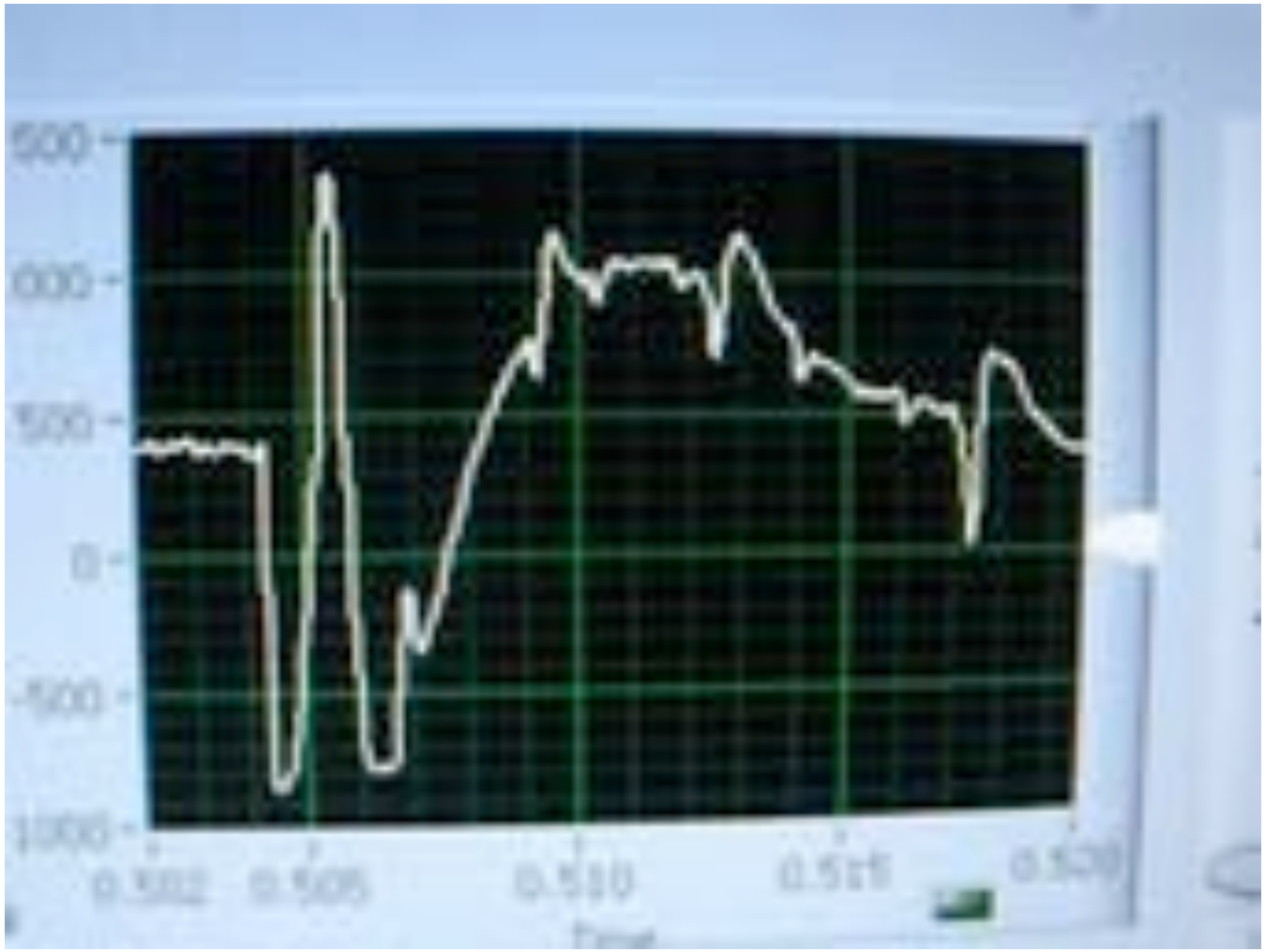


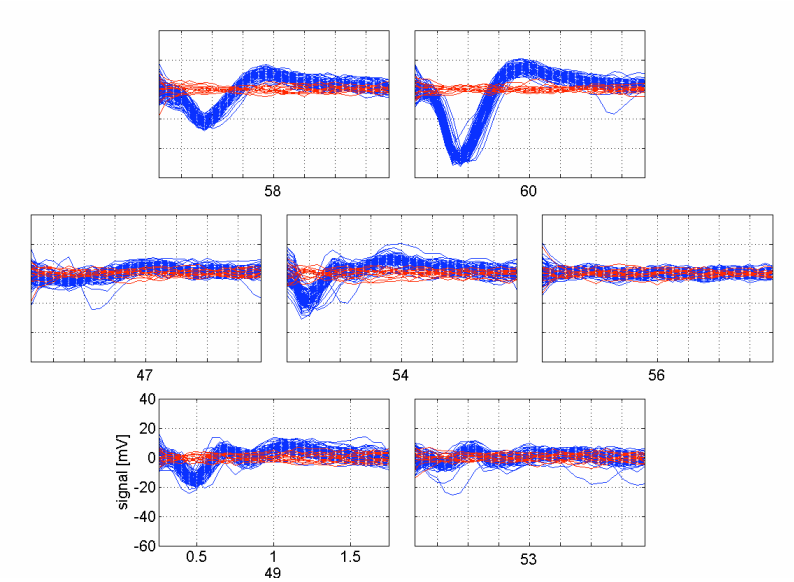
Figure D1. Two examples of the photodiode pixels in the flexible array: Left – a single diode pixel of 115 μm in size with 40 μm central electrode. Right – a 3-diode pixel of 230 μm in size with 80 μm active electrode. Active electrode is in the center, and return - in the periphery (lighter gray).

Subretinal Photovoltaic Implant



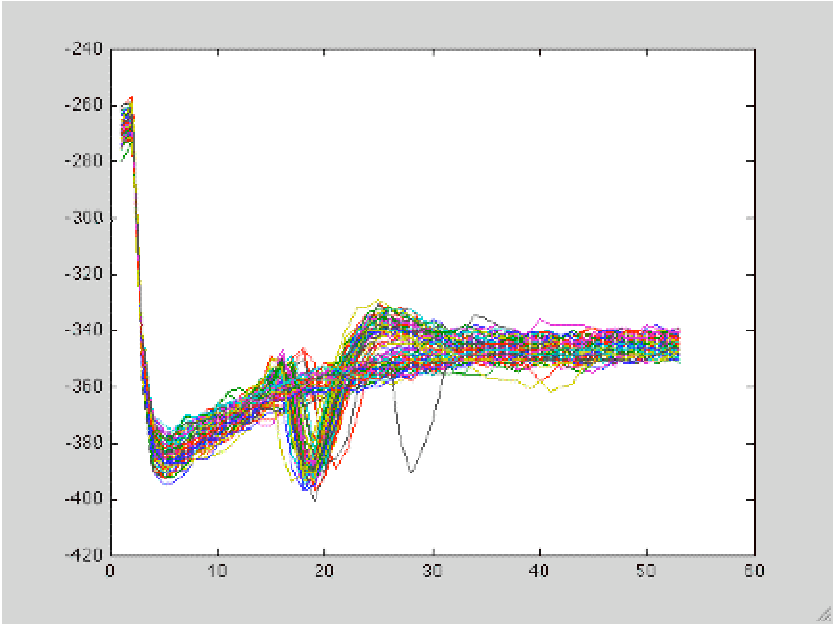
Electrical stimulation in other systems

Brain Slices



cultures rat cortex
(stimulation artifact already subtracted)

Living brain



mouse visual cortex