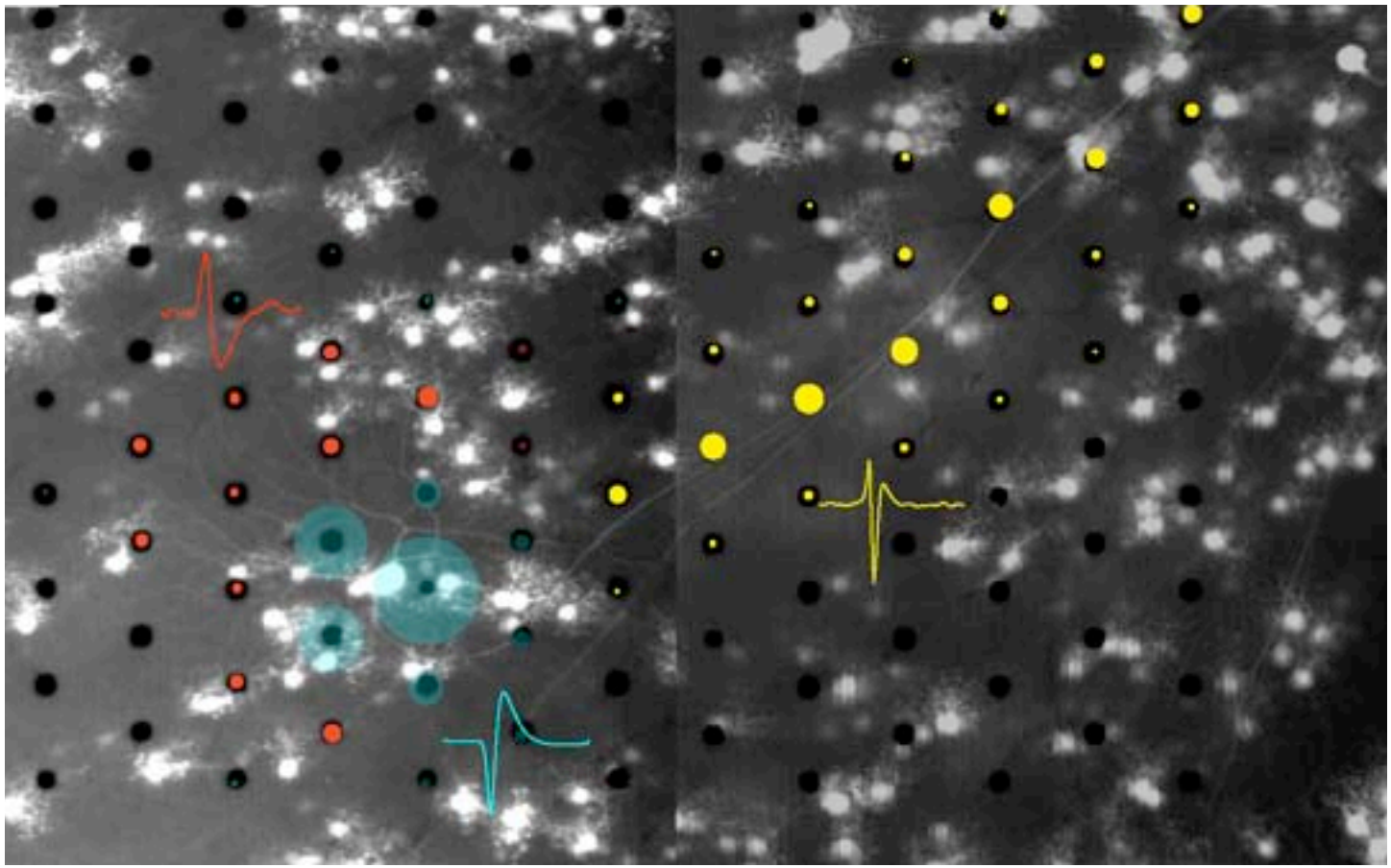
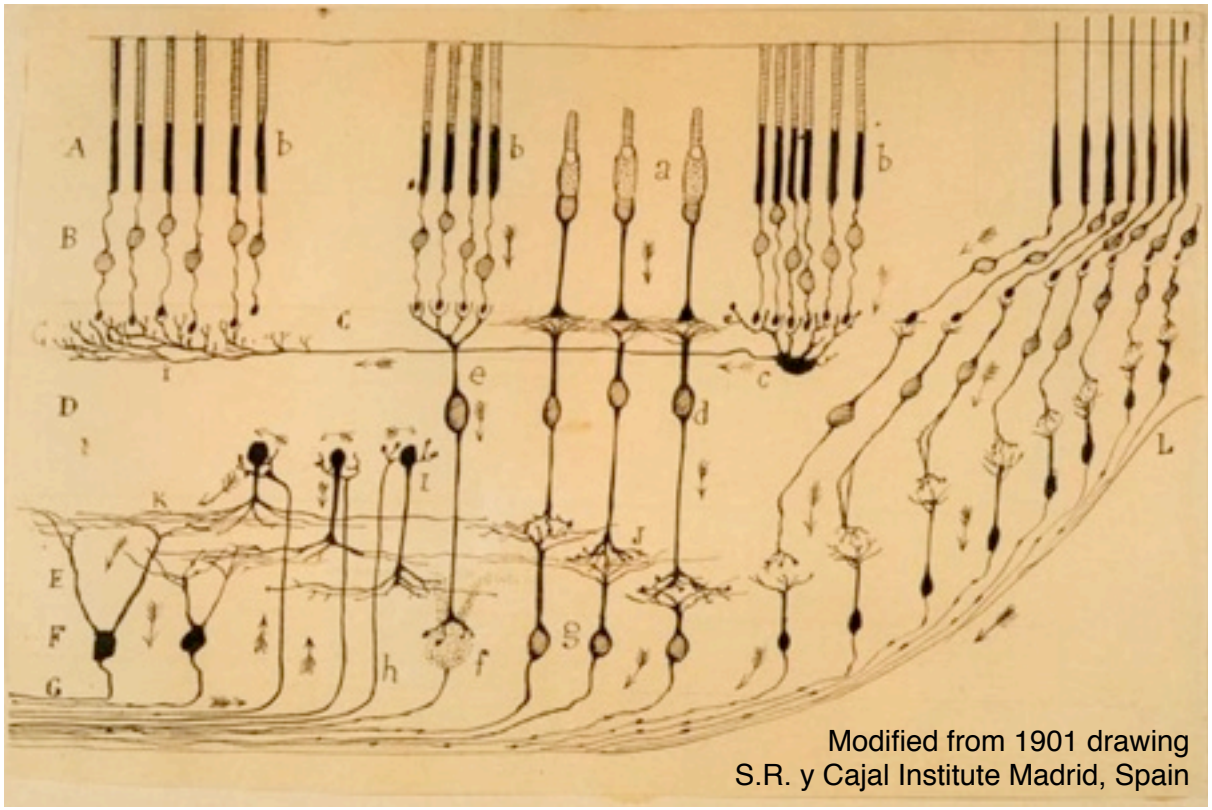
Exploring neural function, structure, and development



Alexander Sher
Santa Cruz Institute for Particle Physics

Science Frontiers

Very Small - Elementary Particle Physics
Very Large - Astrophysics
Very Complex - *Brain*



Modified from 1901 drawing
S.R. y Cajal Institute Madrid, Spain

How does it work?

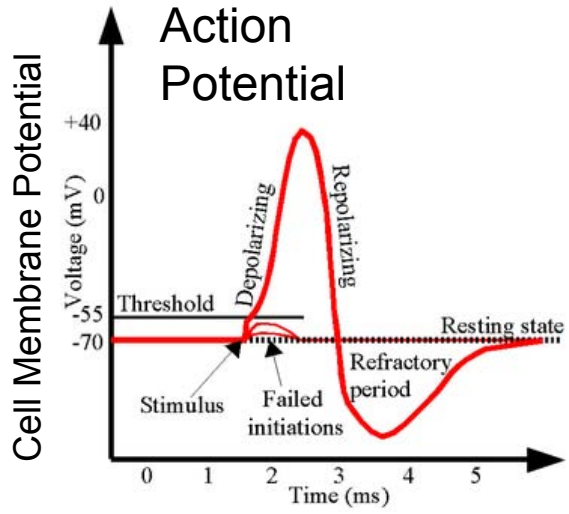
How does it develop?

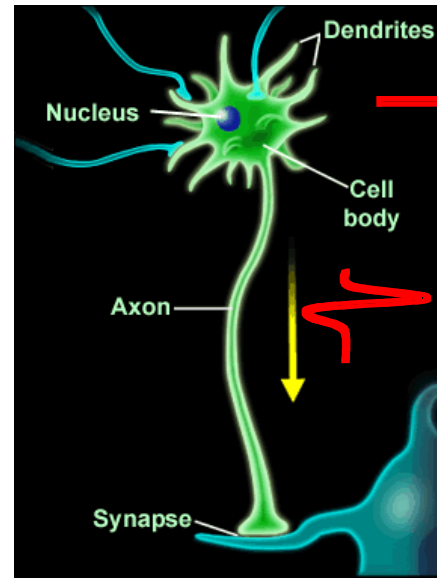
How can we fix it if it breaks?

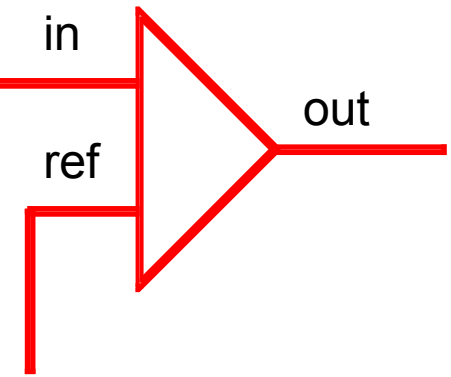
Outline

- Technology
- Retina
- How does it work?: color encoding in the retina
- How does it develop?: mouse retina
- How can we fix it?:
  - retinal healing after laser photocoagulation
  - photovoltaic retinal prosthesis
- Further technology development

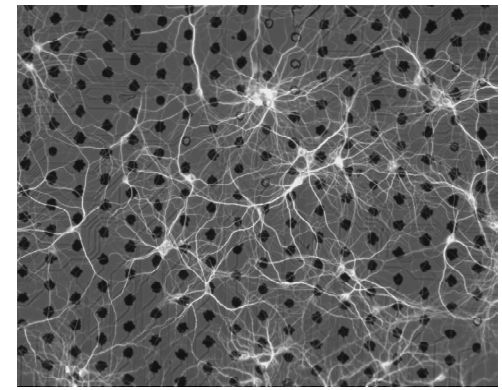
Technology





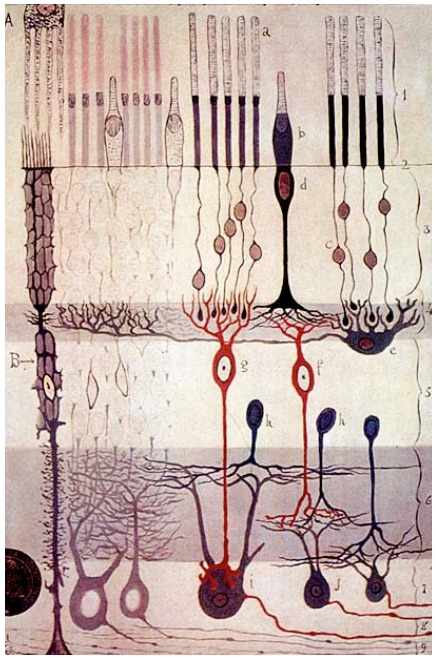


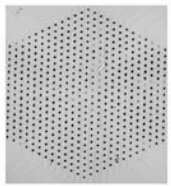
=> network of ~100 billion neurons



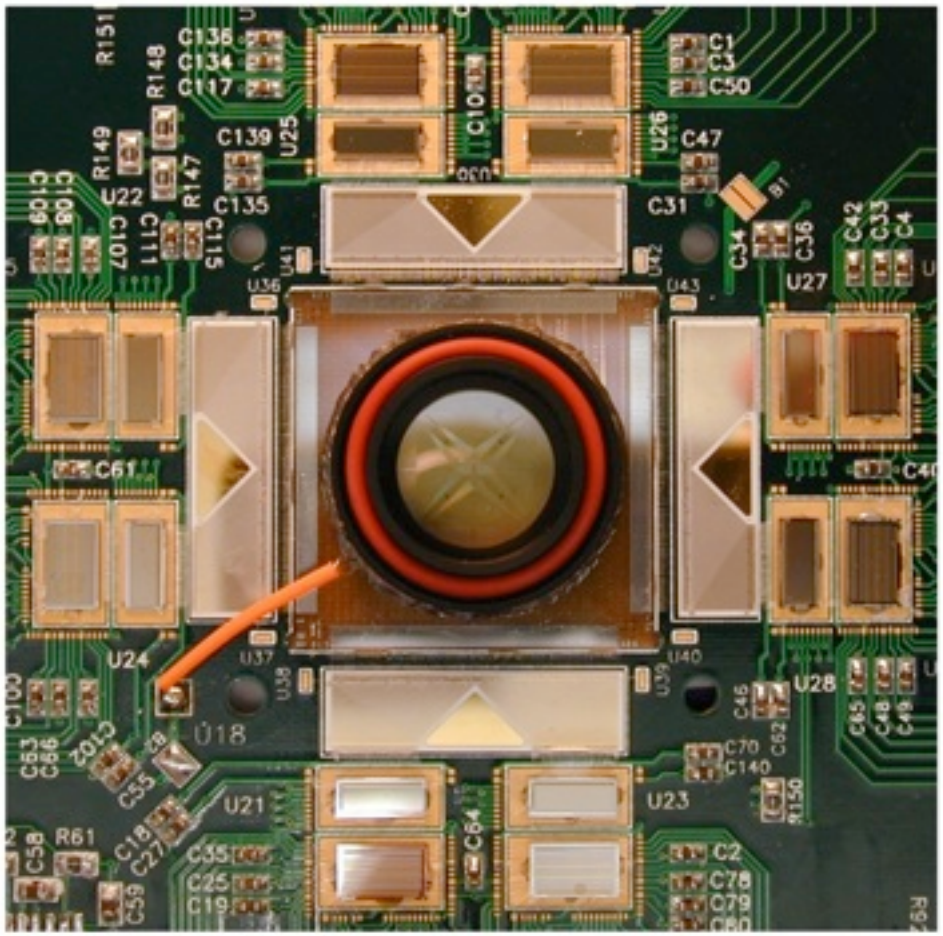
Extracellular Multielectrode recording of neural activity
- Simultaneous activity of many neurons
- Best spatial resolution: single neuron
- Best time resolution: single action potential

Technology



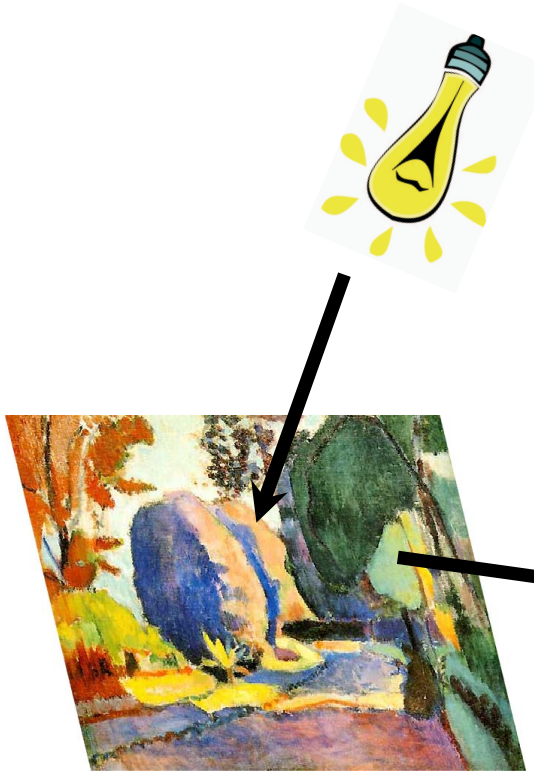


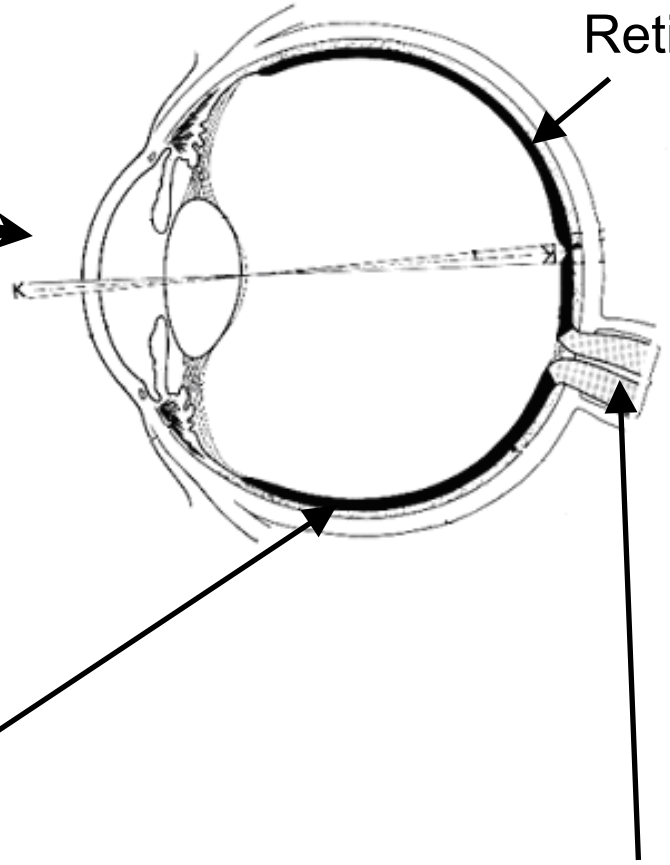
512 electrodes with 60 and 30 micron spacing

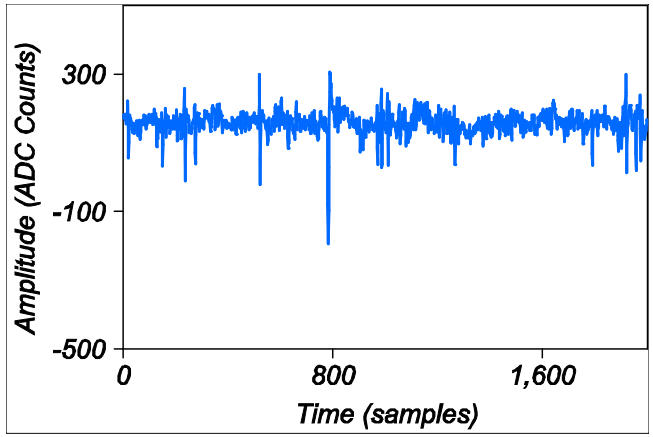


UCSC
AGH UST, Krakow, Poland
Salk Institute
U. of Glasgow, Scotland

Retina



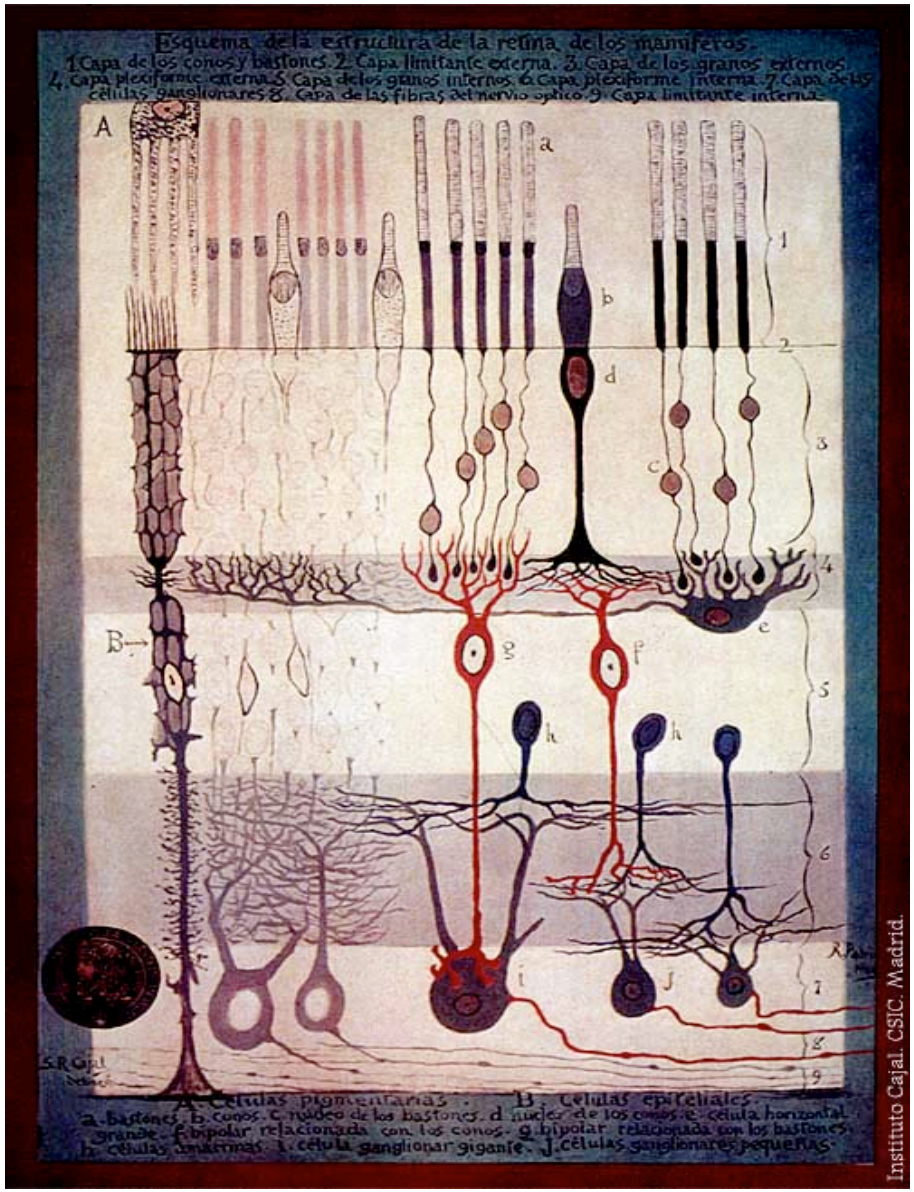




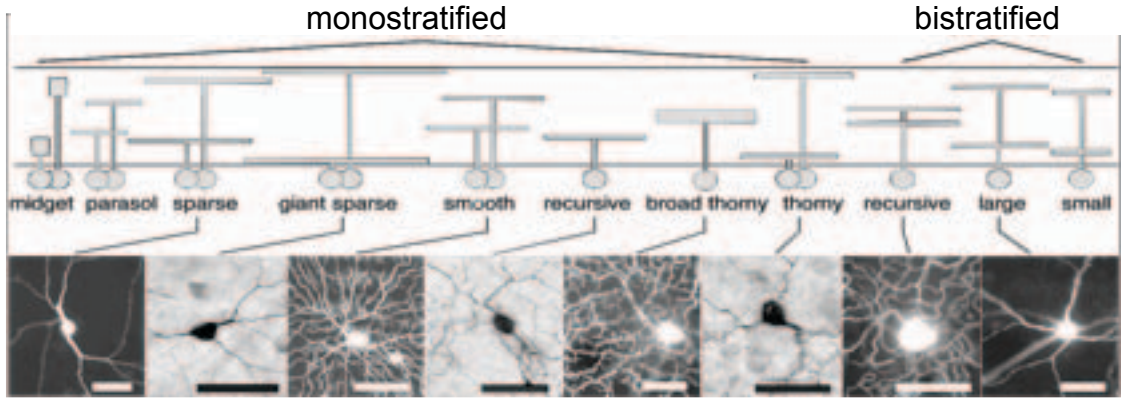
~100 million photoreceptors

~1 million axons

Retina

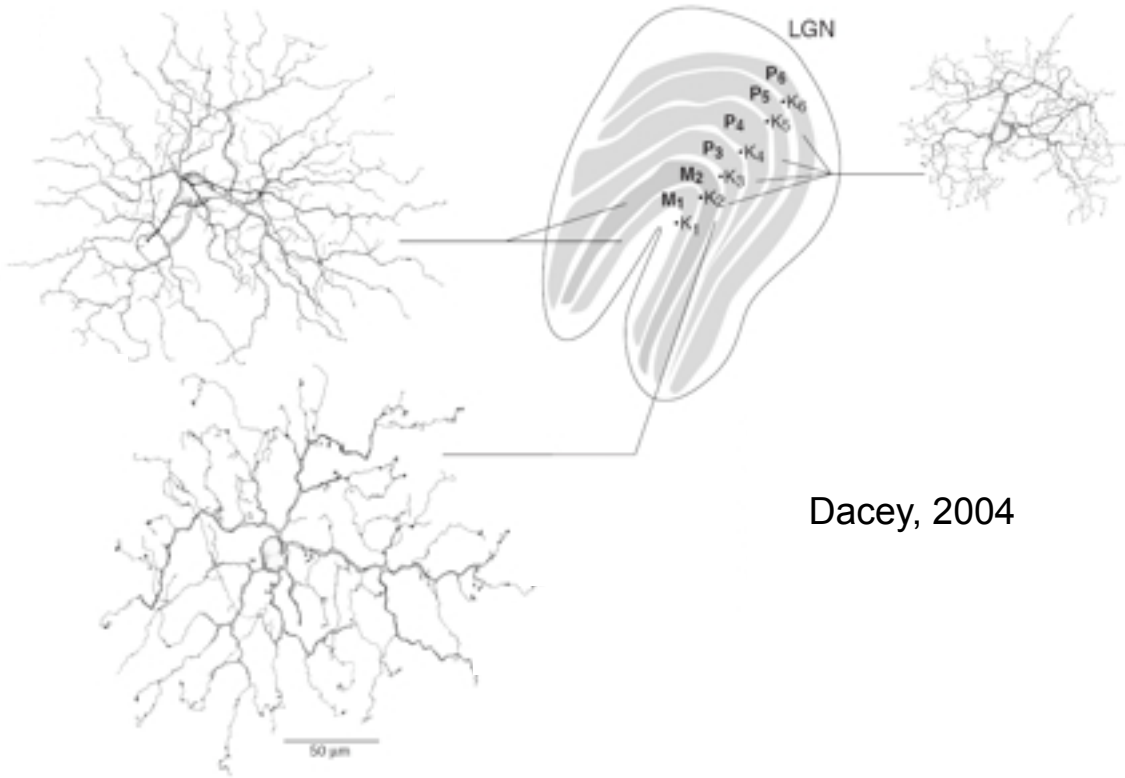


Cajal, 1900



parasol

midget



Dacey, 2004

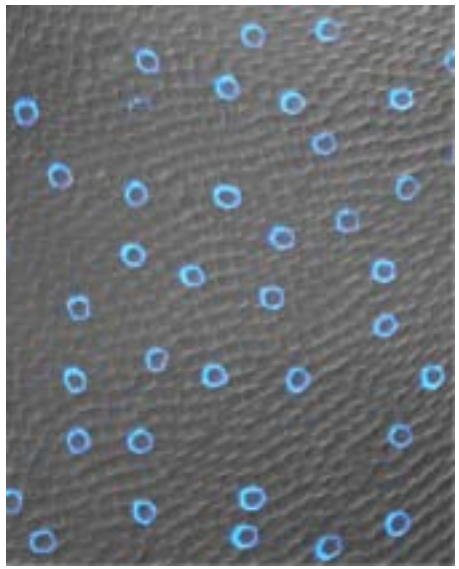
small bistratified

Color vision

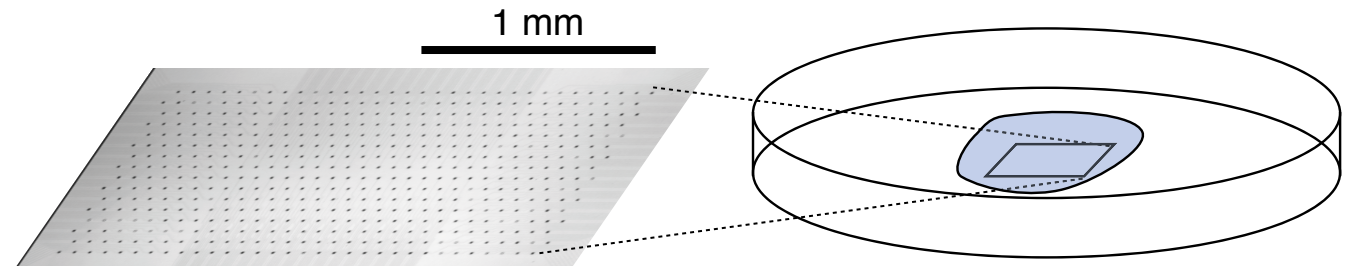
Brain’s interpretation of the wavelength composition of light

Henri Matisse, The Luxembourg Garden. 1901-1902

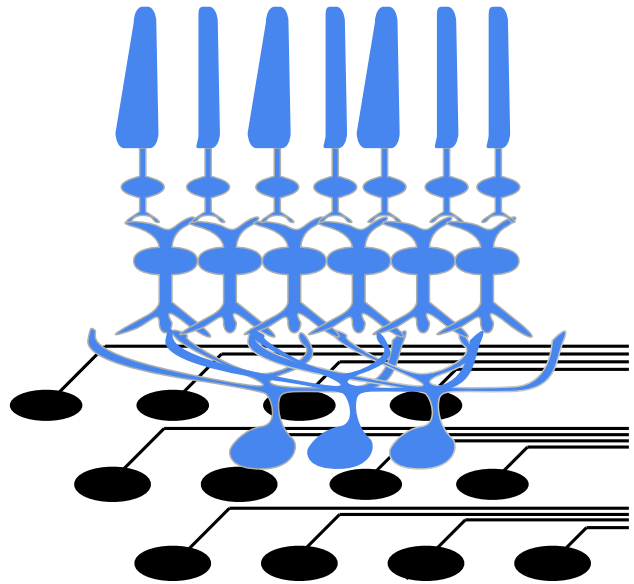
Methods
Physiology Recording

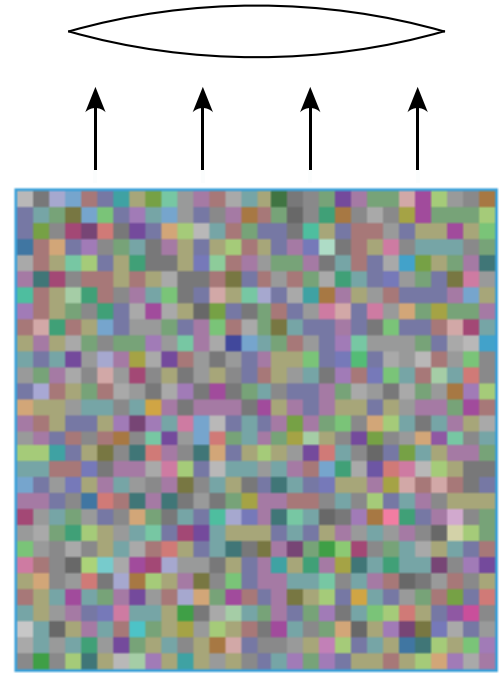


50 µm



512 electrodes spaced at 60 µm

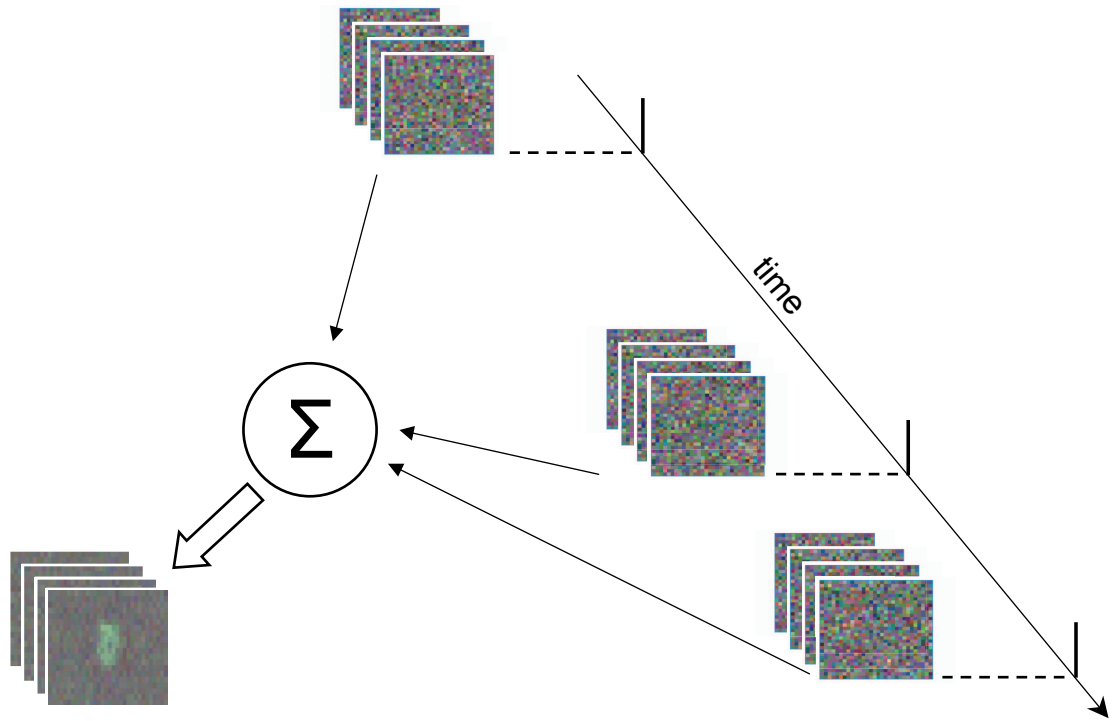




computer monitor

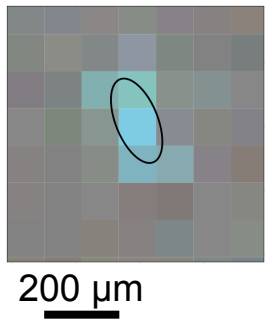
Methods

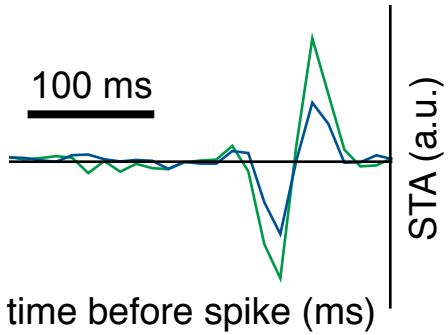
Response properties

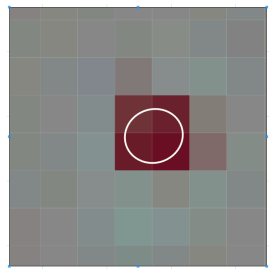


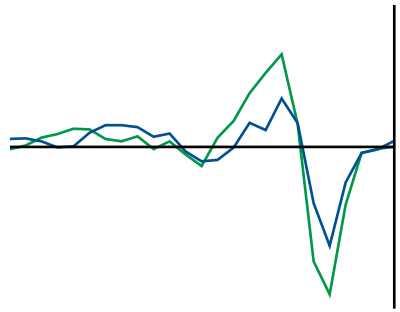
M-ON

M-OFF





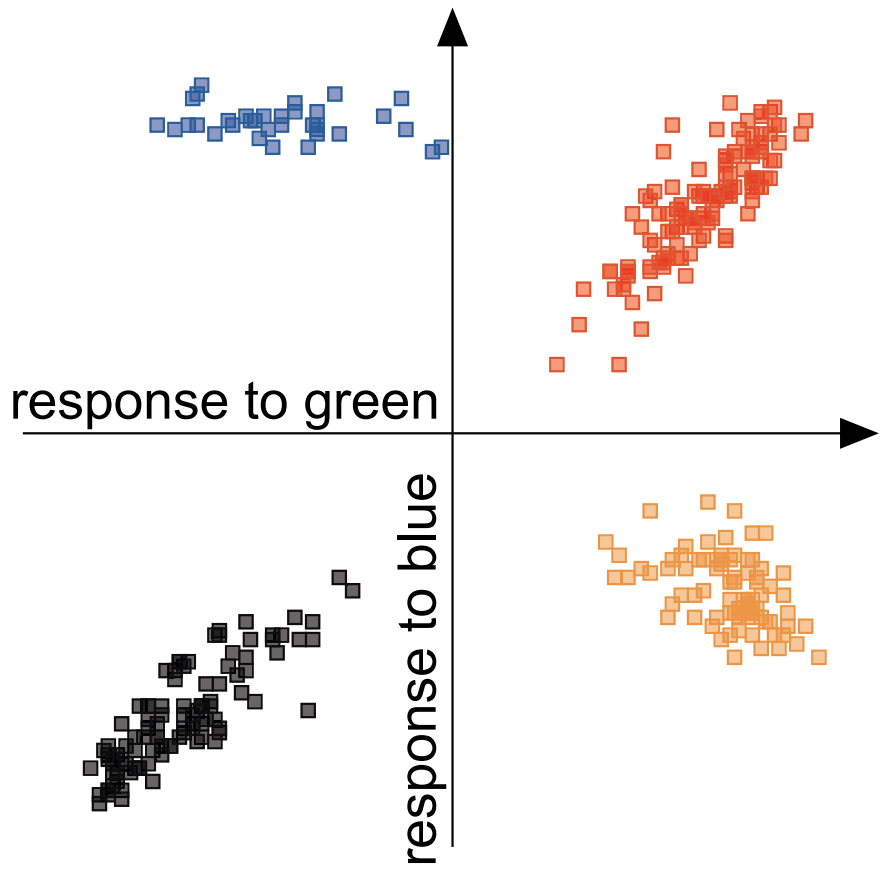




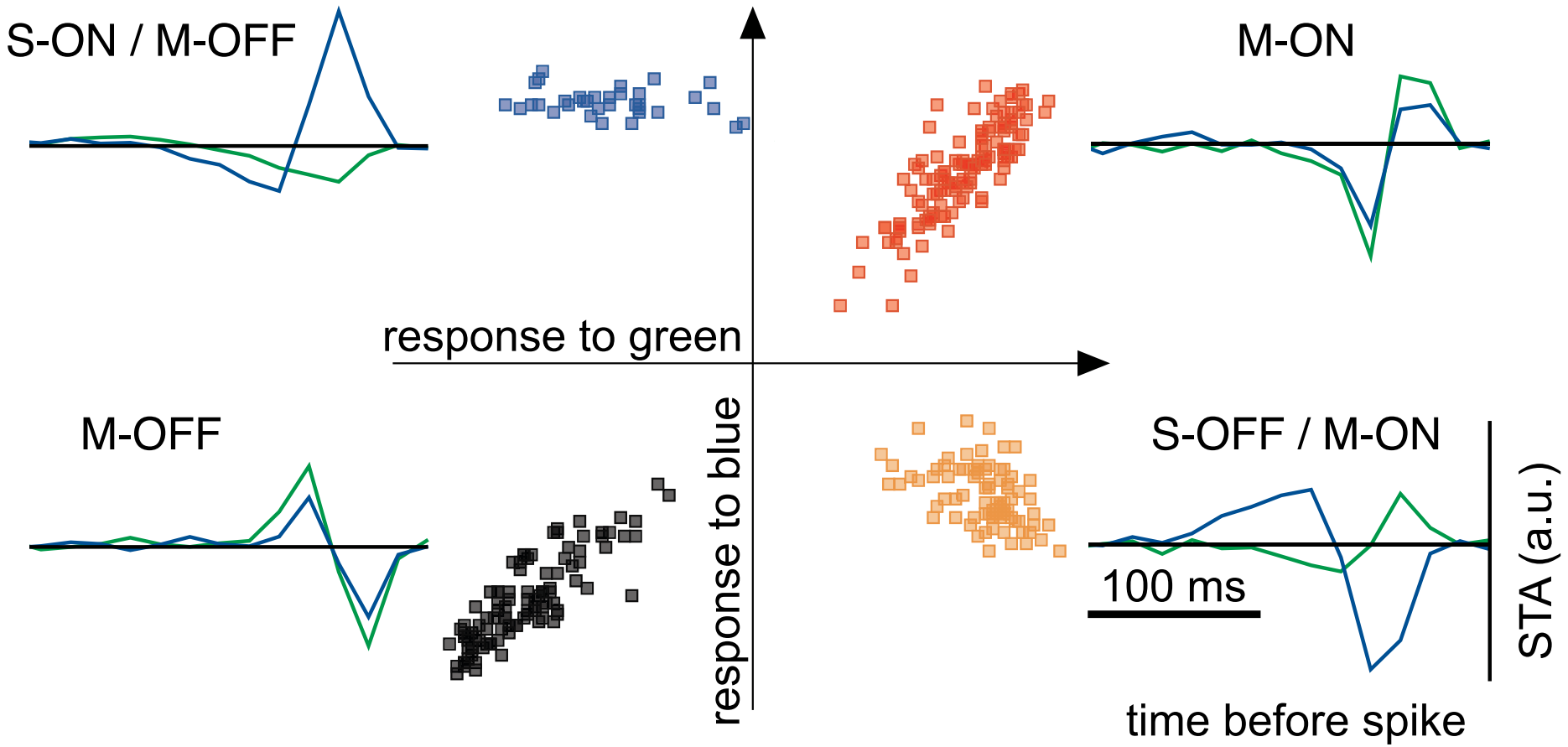
spatial filter
(receptive field)

temporal filter
(time-course)

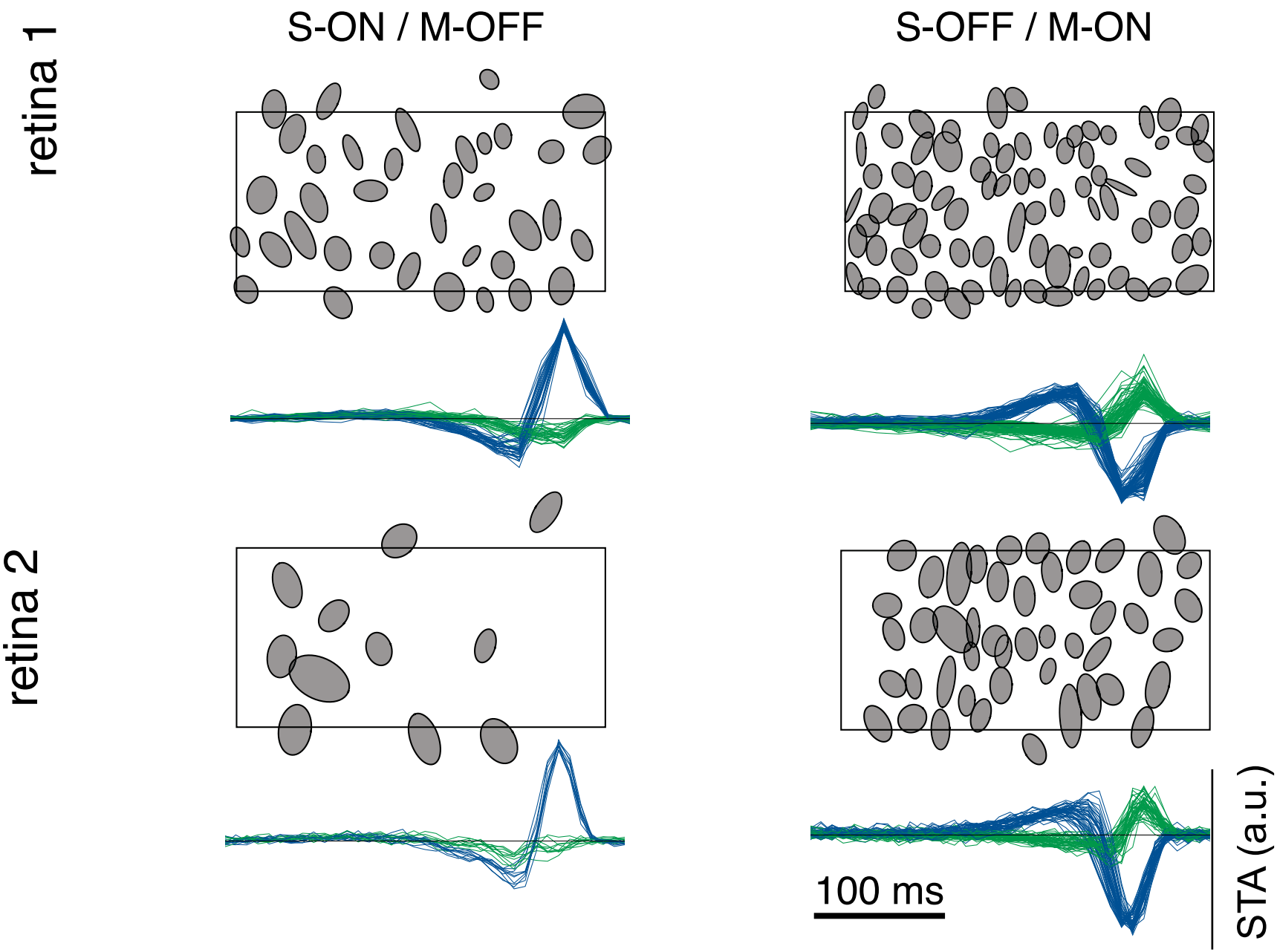
Functional classification



Functional classification

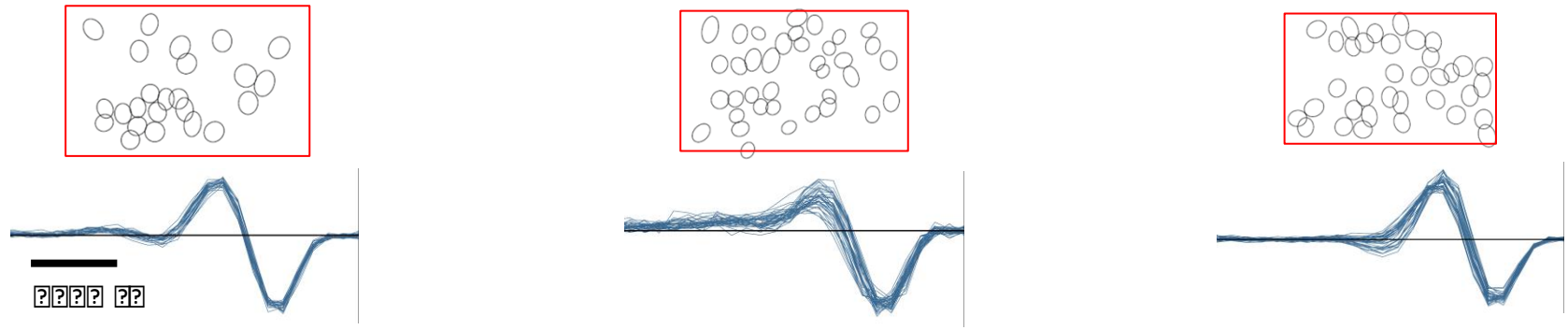


S-OFF / M-ON fields tile visual space

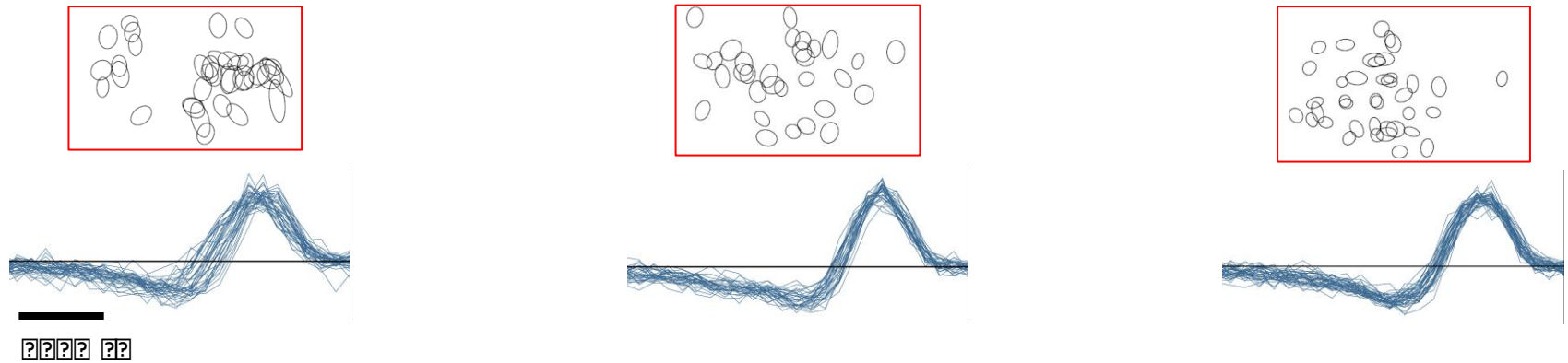


DSCAM is necessary for functional mosaics

wild type



DSCAM -/-



Medical Applications

Retinal Photocoagulation

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

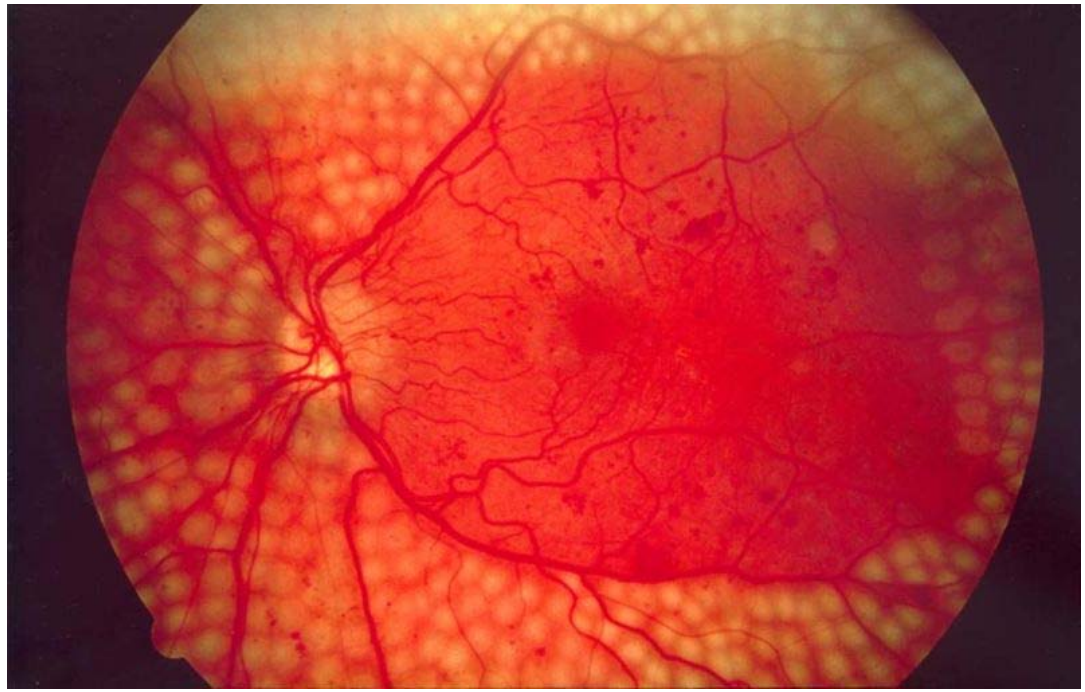
Pan-retinal photocoagulation (PRP) is the long-standing standard of care for diabetic retinopathy

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.

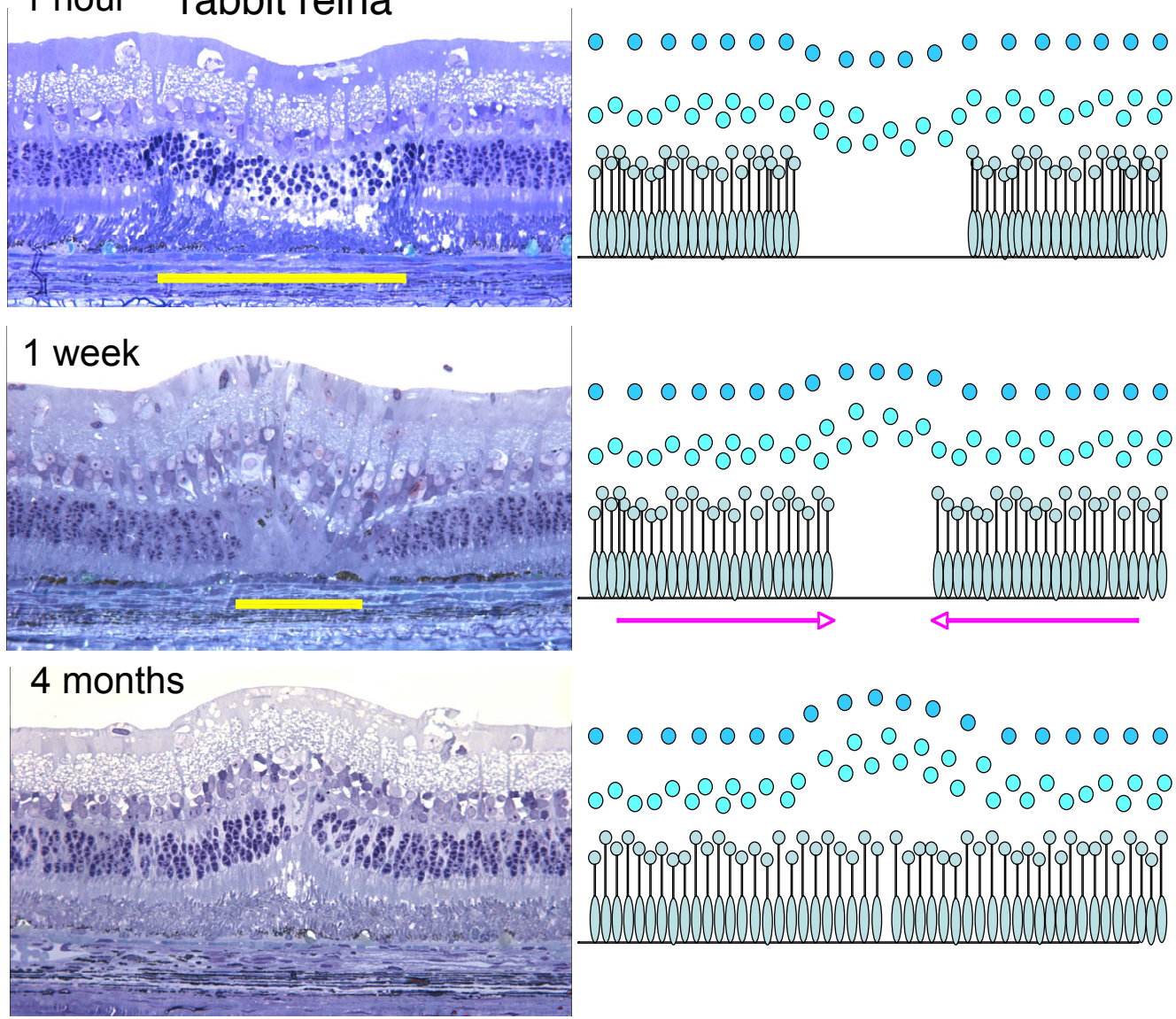


Conventional pan-retinal photocoagulation

Photocoagulation

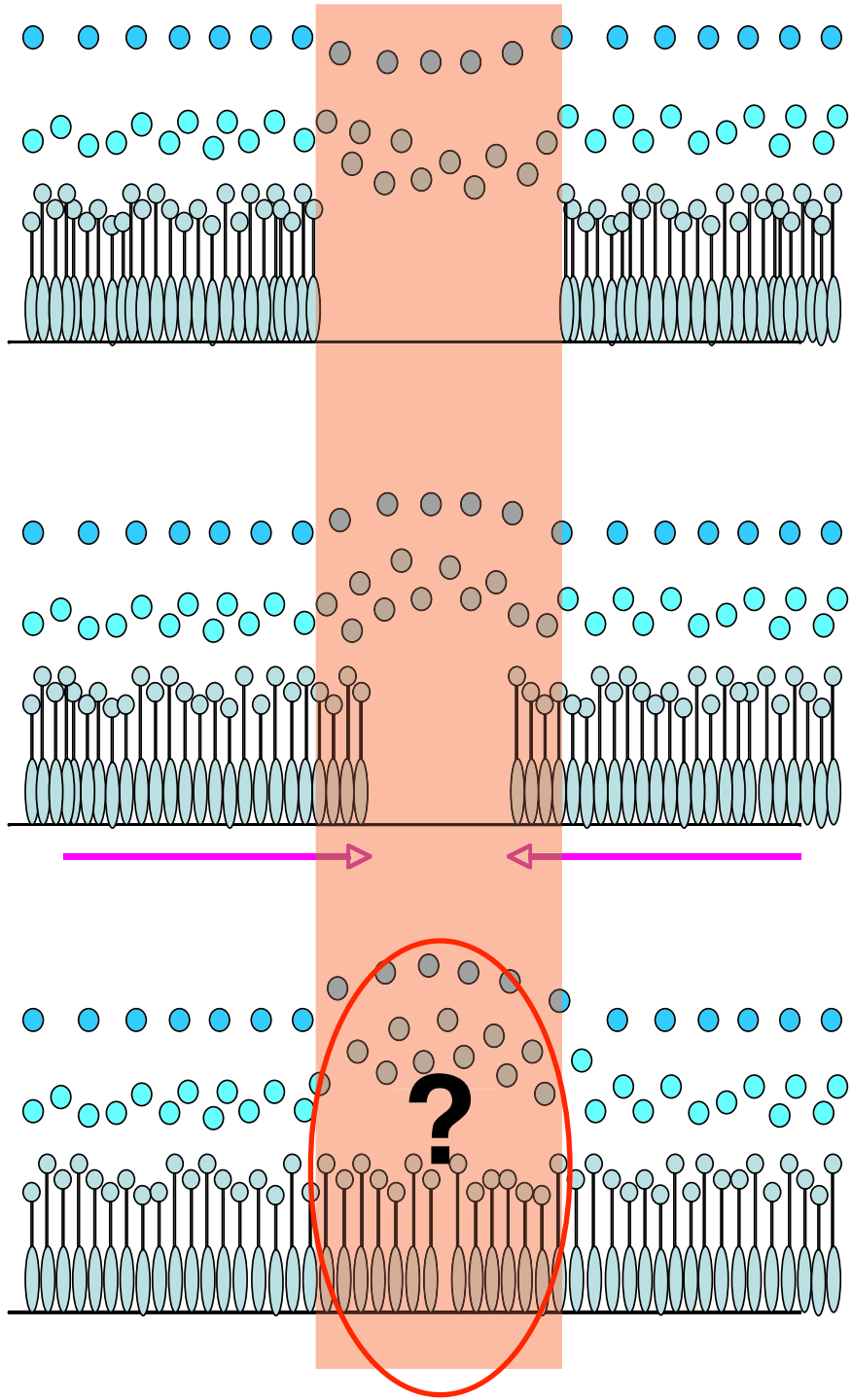
barely visible lesion

1 hour rabbit reina



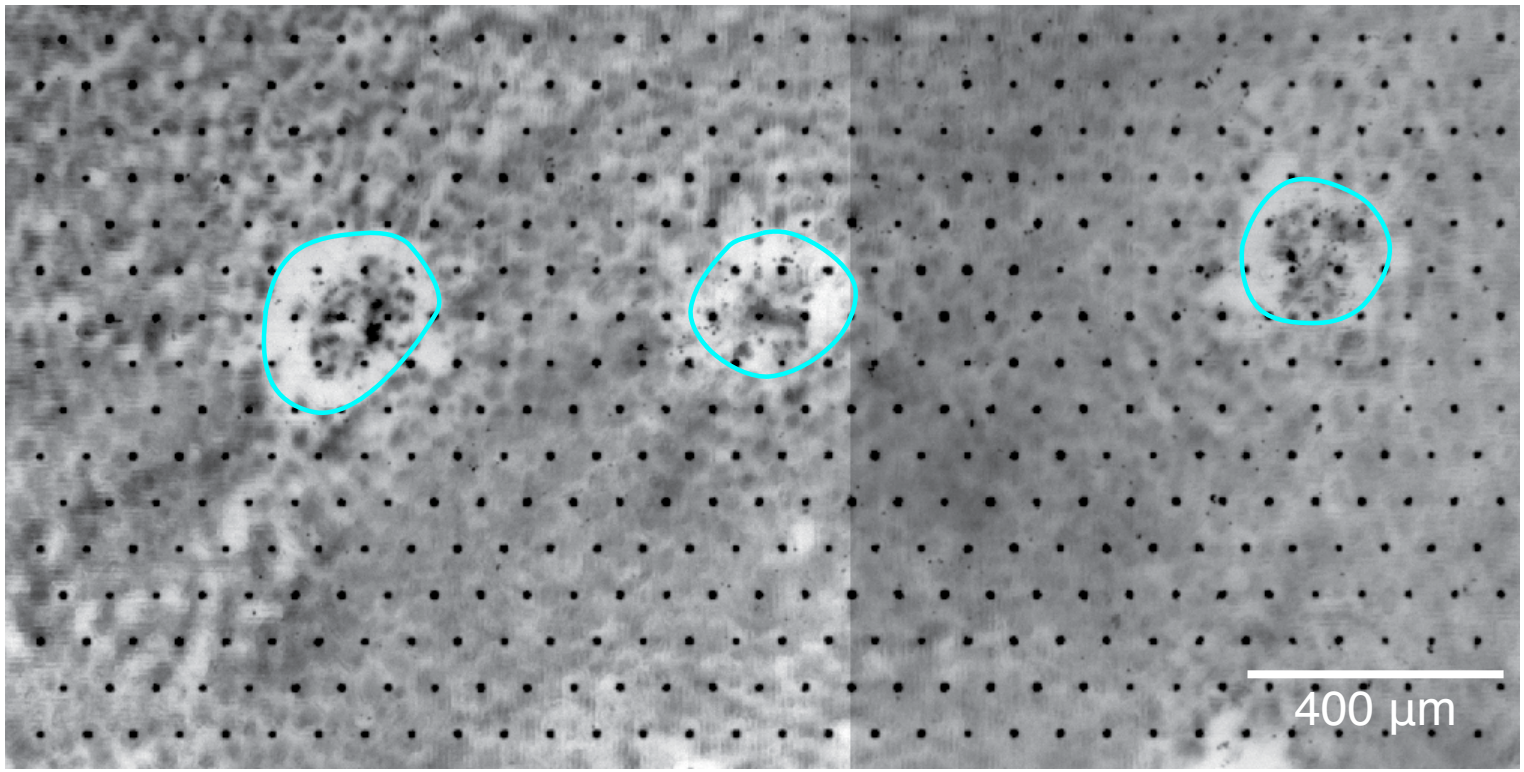
Paulus Y.M., et al, Invest. Ophthalmol. Vis. Sci., 2008

Photocoagulation



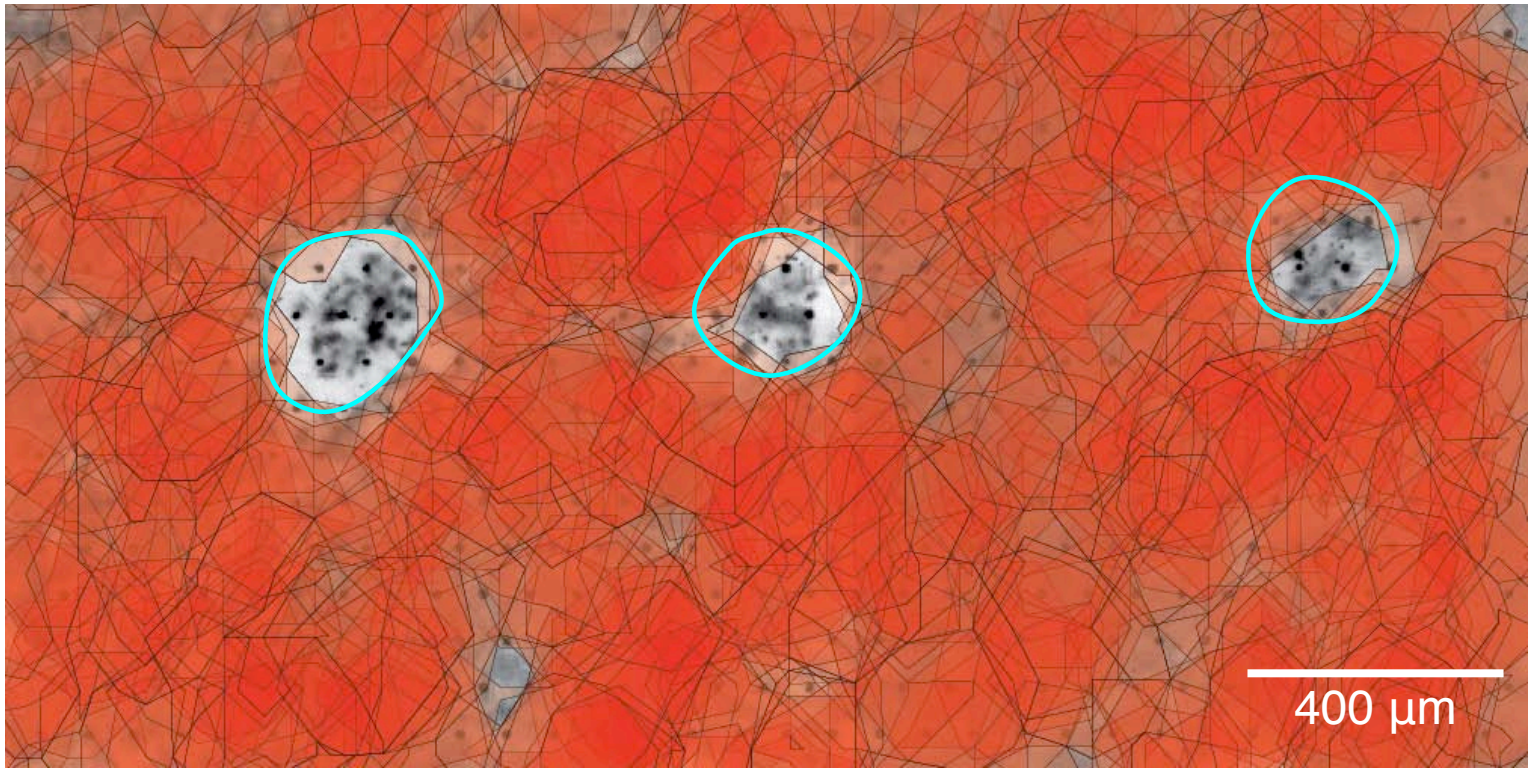
Methods

RPE abnormality zones

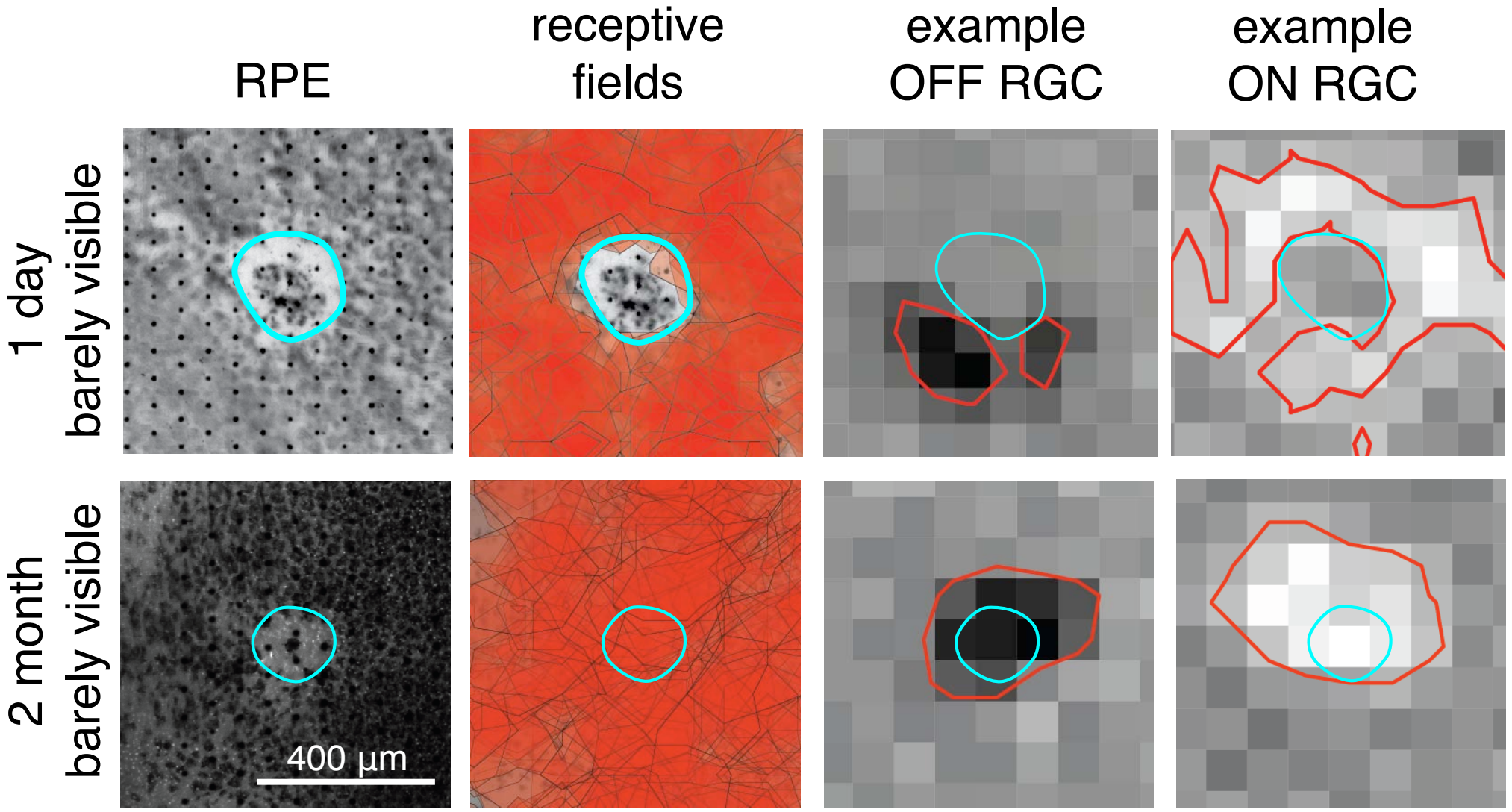


Methods

receptive fields of recorded RGCs



250 µm *barely visible* lesions

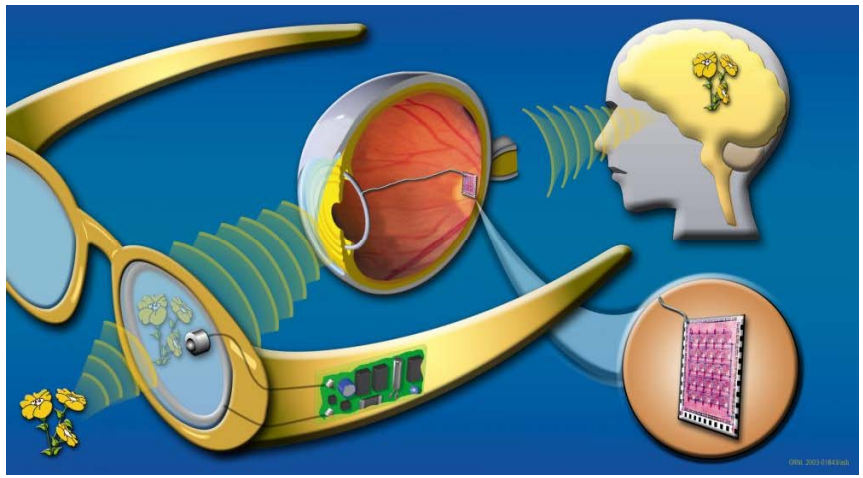


sensitivity is restored over 250 µ barely visible lesions
for both ON and OFF RGCs

Medical Applications

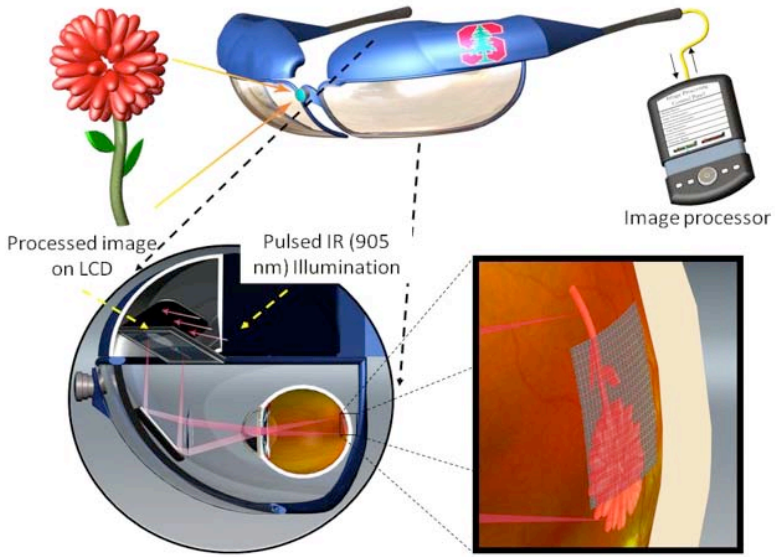
Retinal Prosthesis

Epiretinal



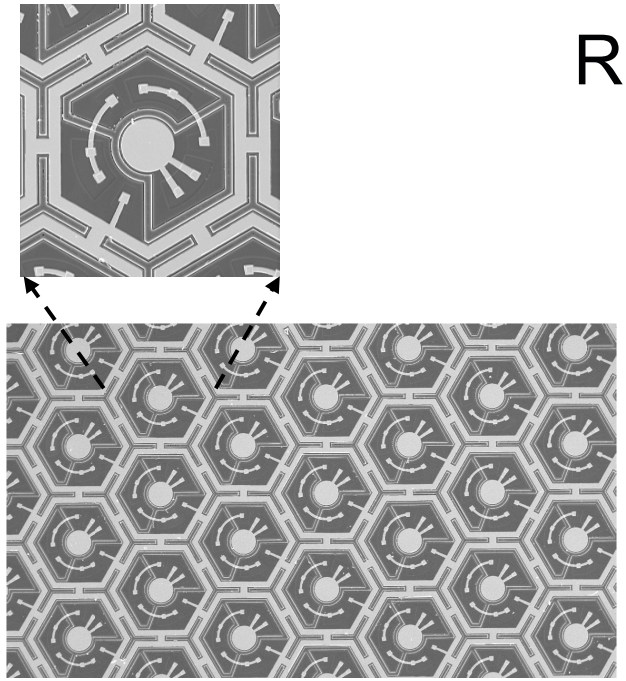
Custom circuitry for simultaneous stimulation and recording

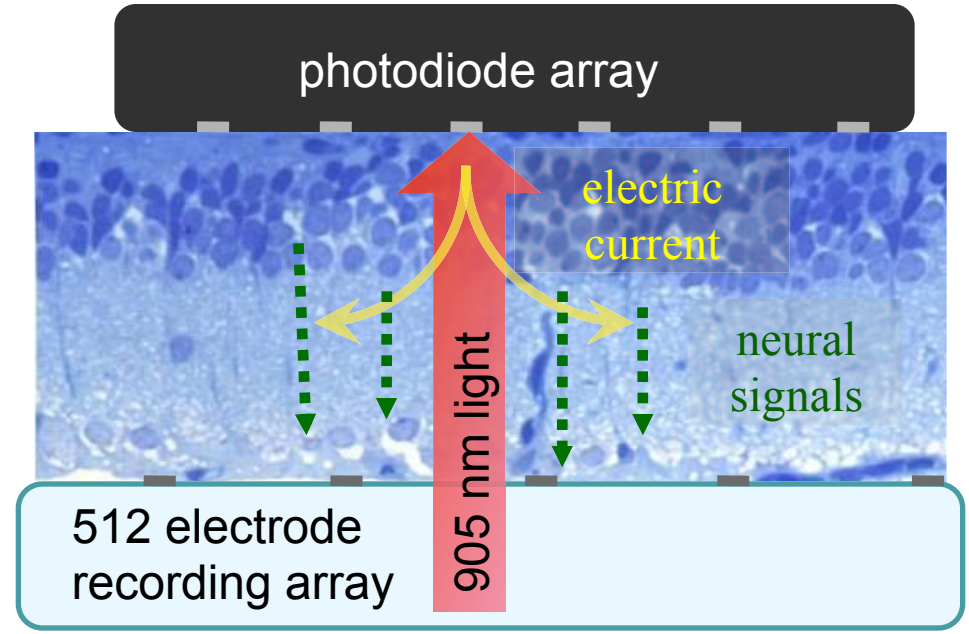
Subretinal

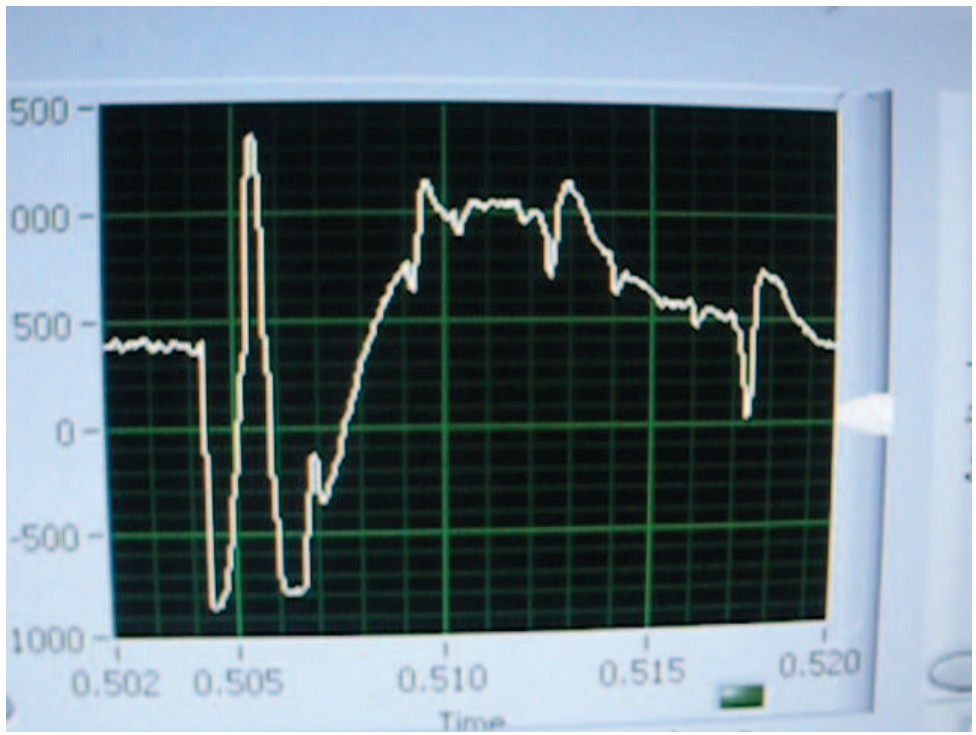


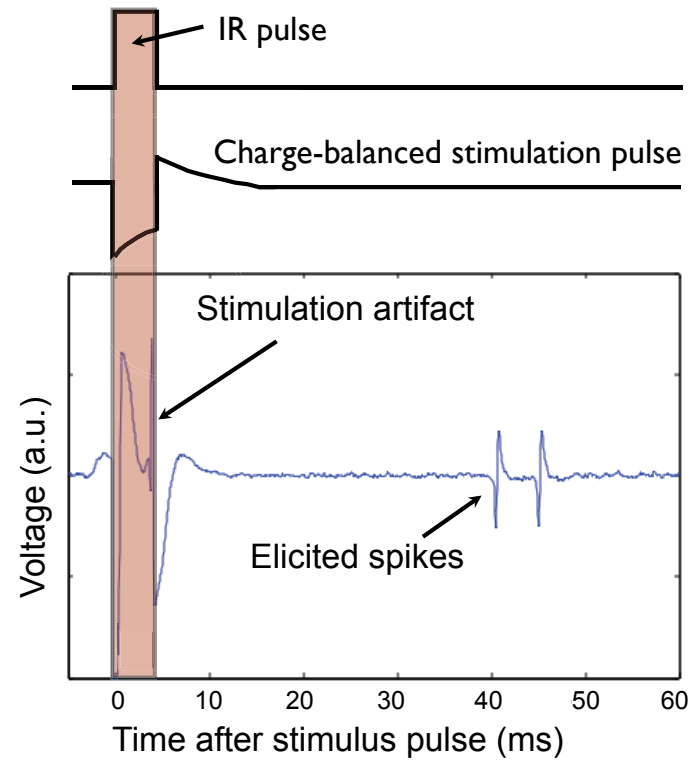
Recording of responses to stimulation with photovoltaic implants

Retinal Prosthesis



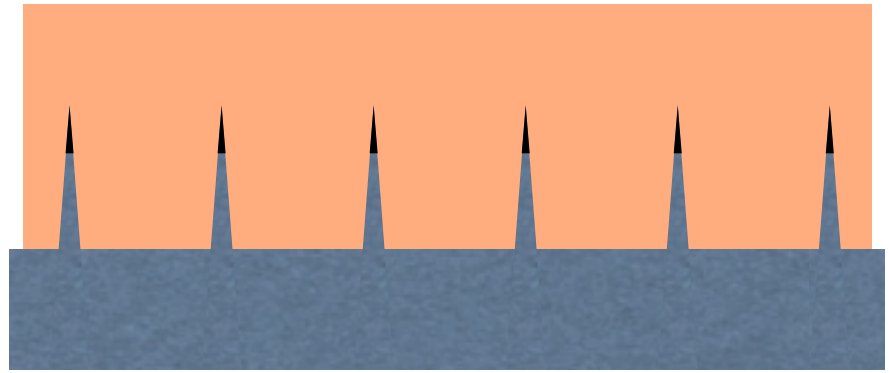


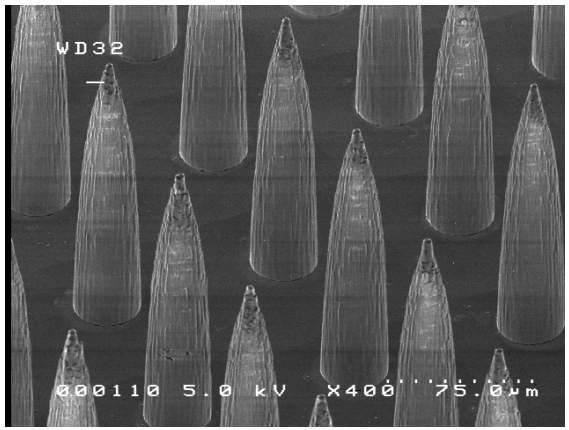


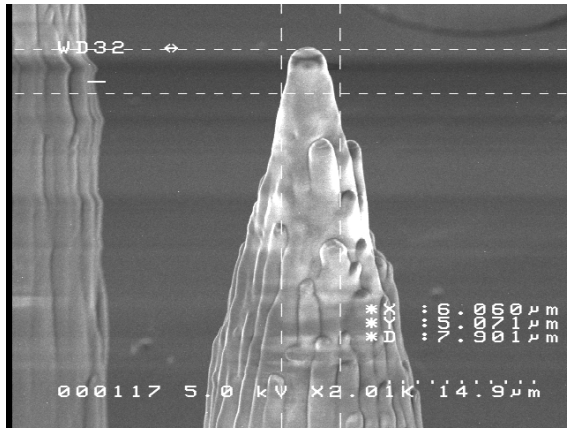


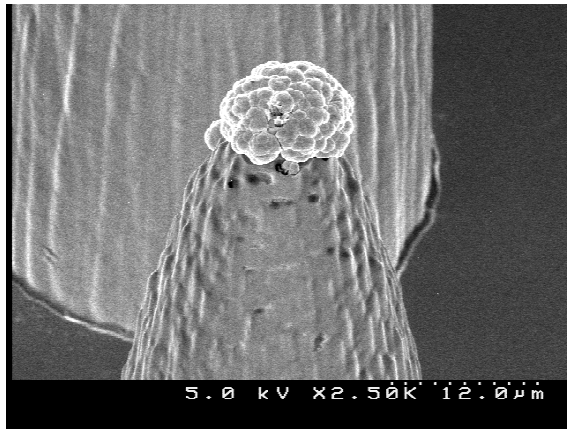
Brain Activity Recording in-vitro

Bed of Nails electrode array for penetrating inside the tissue

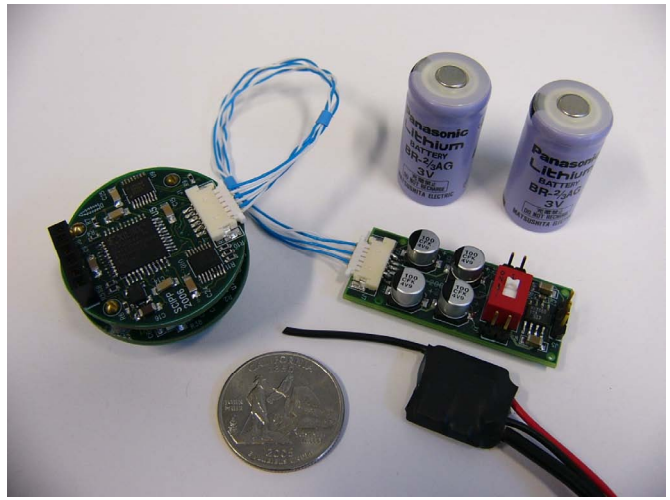


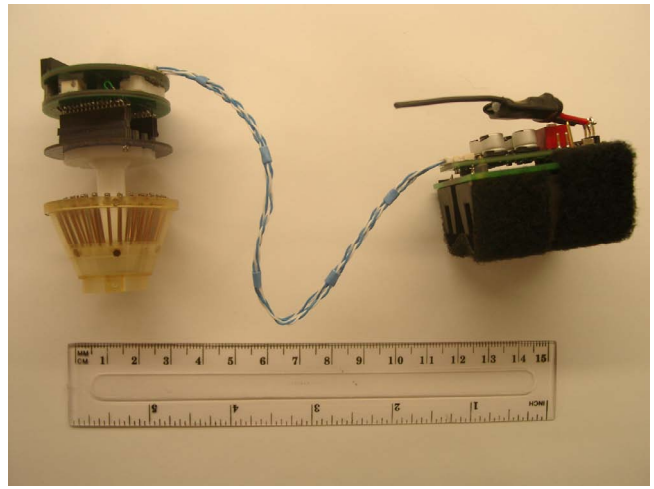


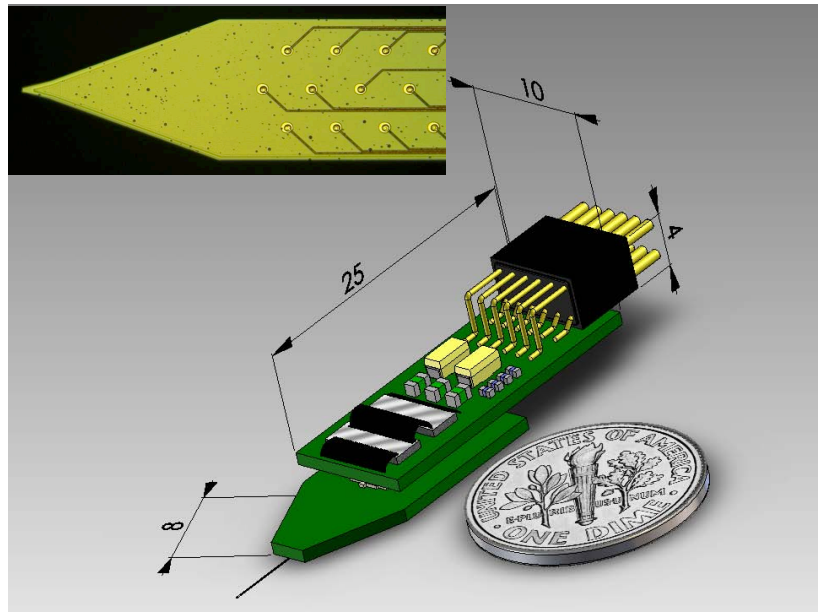


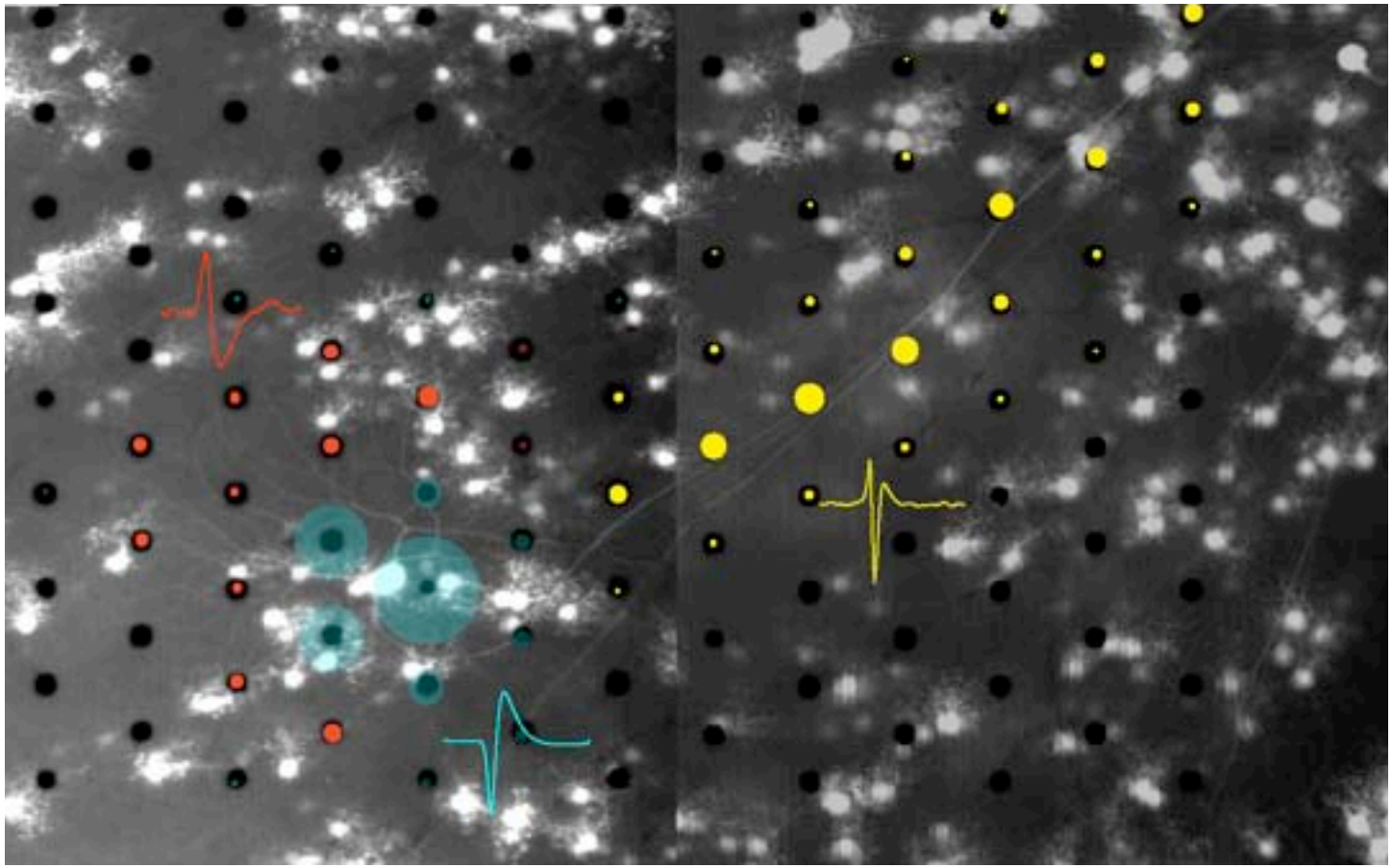


Brain Activity Recording in-vivo









SCIPP
Santa Cruz Institute for Particle Physics

Salk Institute

AGH

AGH USTK. Poland

University of Glasgow

Biological Sciences at UC Santa Cruz
Molecular Cell & Developmental Biology

UCSC MCD Biology

Stanford University

Applied Physics
Ophthalmology

- Development of novel tools for stimulation and recording of neural activity
- Application of the developed techniques to study neural function, development, and ways of ameliorating neural diseases.

Alexander Sher
sasha@scipp.ucsc.edu