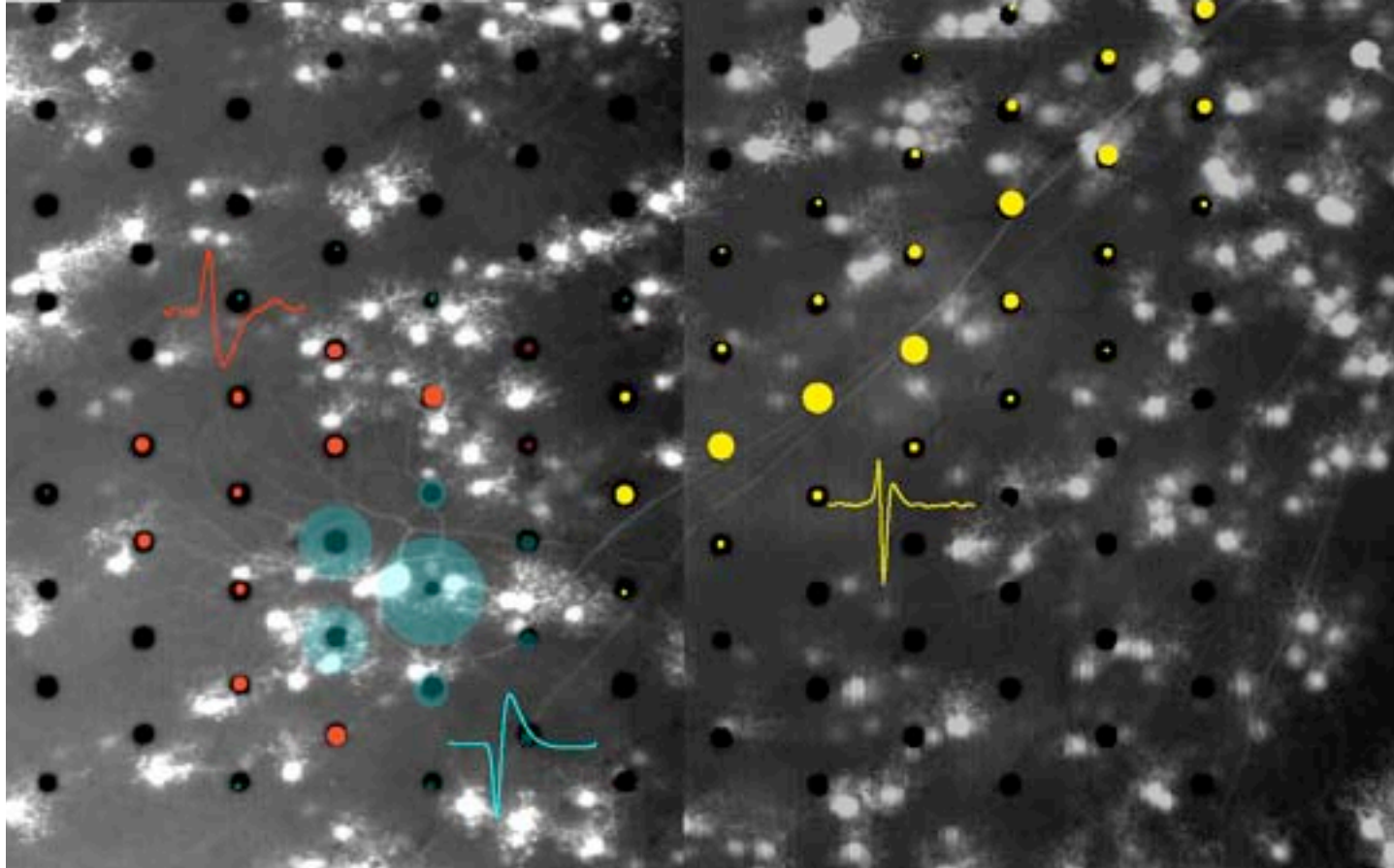
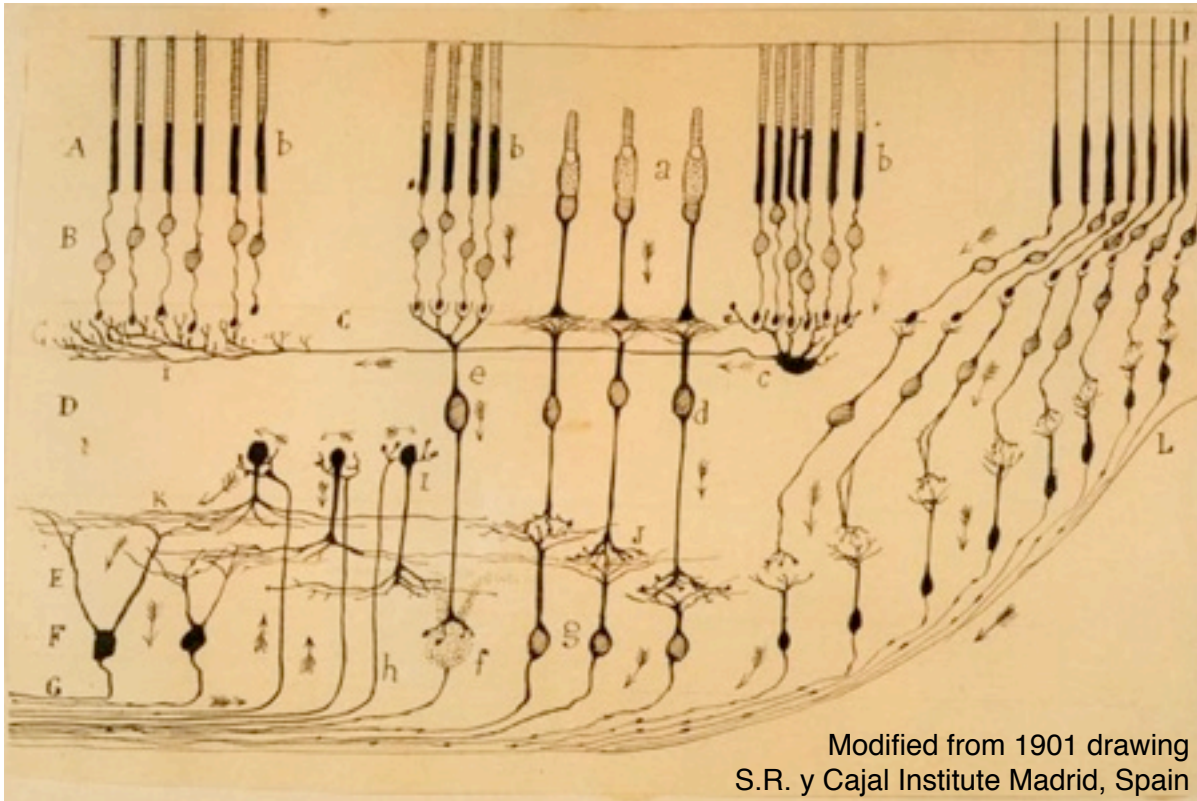


# Exploring neural function, structure, and development



Alexander Sher  
Santa Cruz Institute for Particle Physics

# Brain circuitry



How does it work?

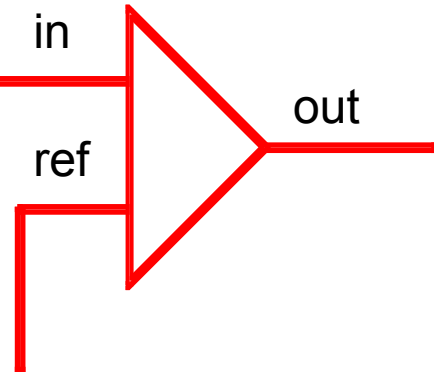
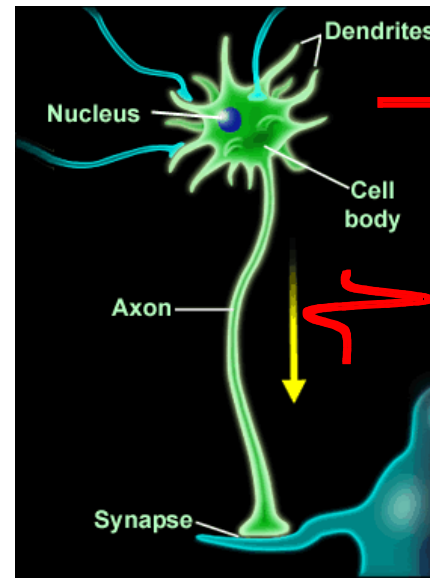
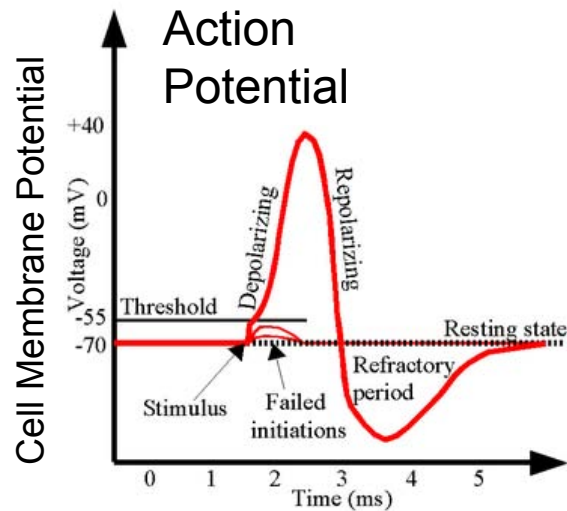
How does it develop?

How can we fix it if it breaks?

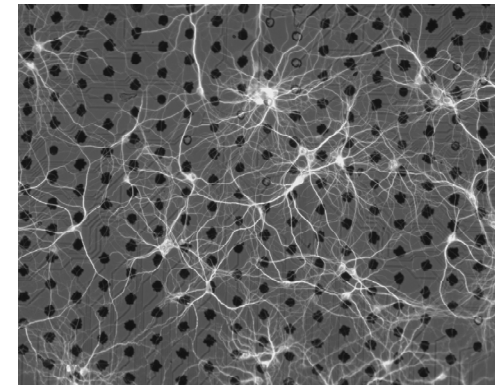
# Outline

- 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



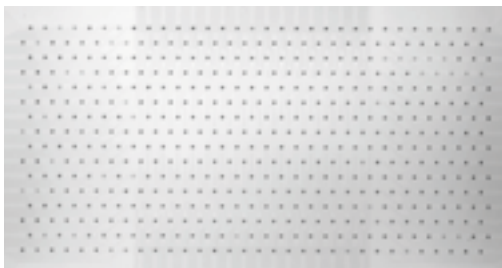
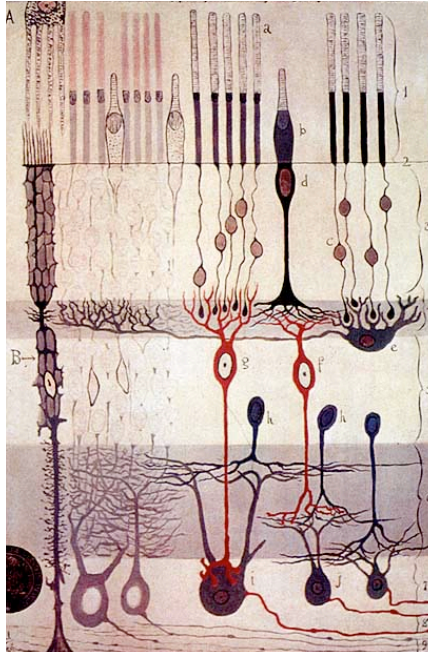
=> network of ~100 billion neurons



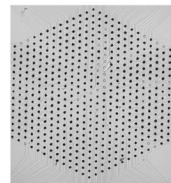
Extracellular Multielectrode recording of neural activity

- Simultaneous activity of many neurons
- Best spatial resolution: single neuron
- Best time resolution: single action potential

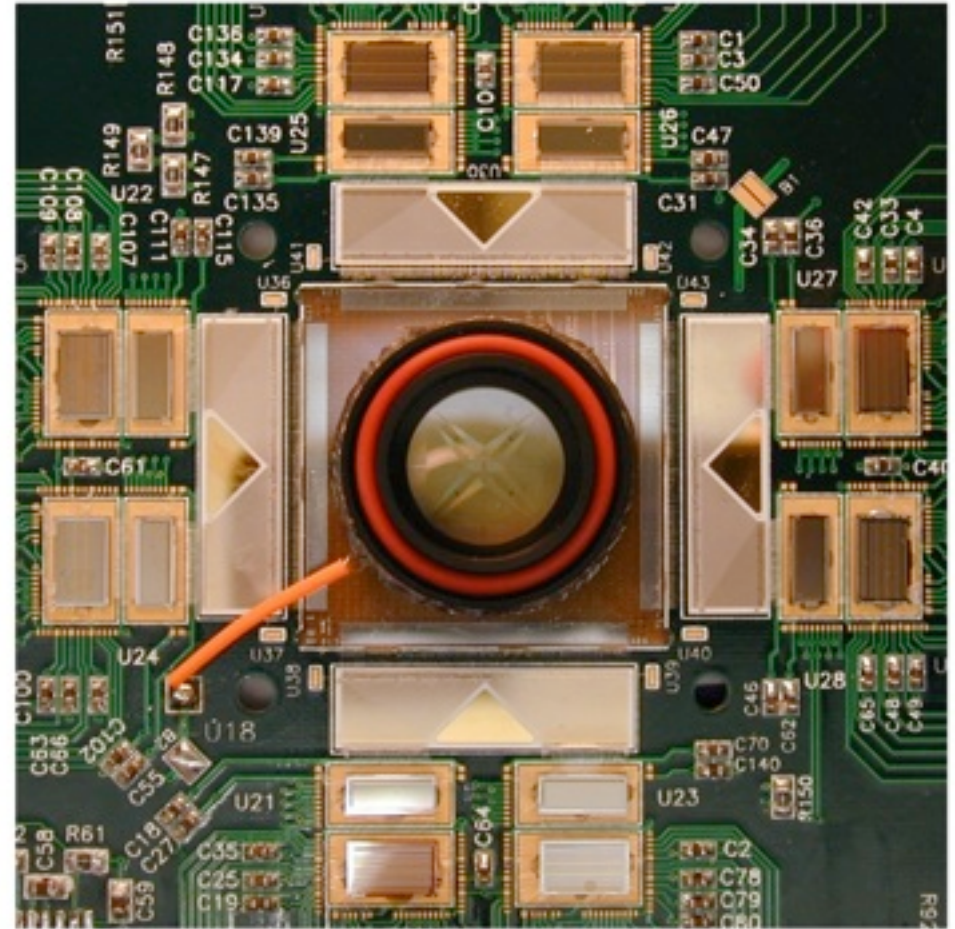
# Technology



1 mm

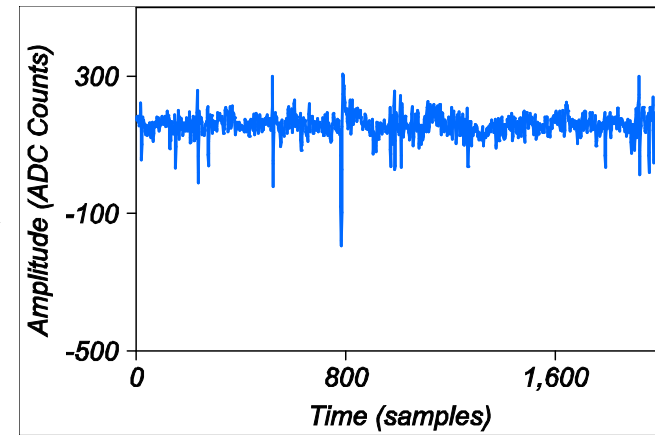
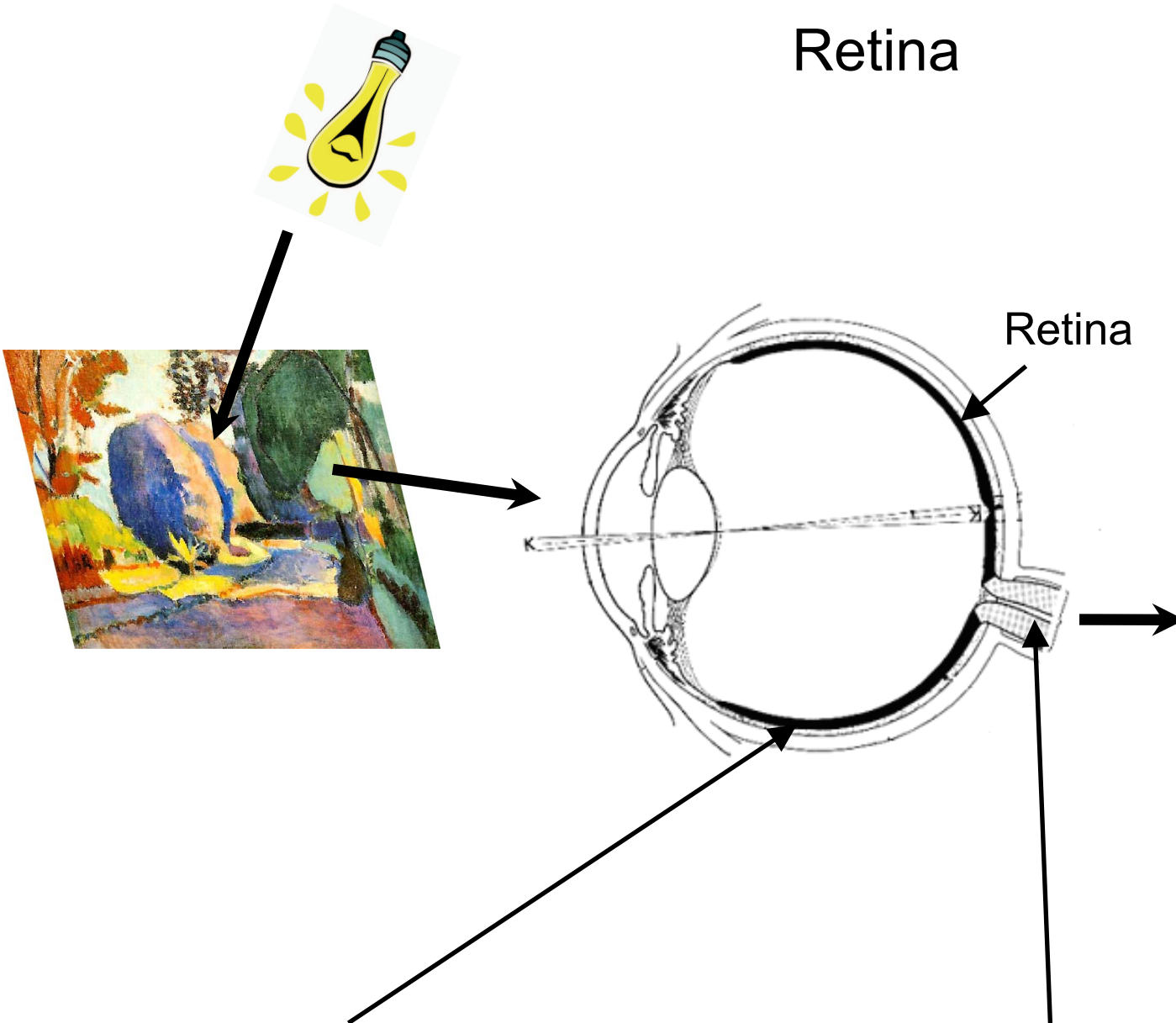


512 electrodes with 60 and 30 micron spacing



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

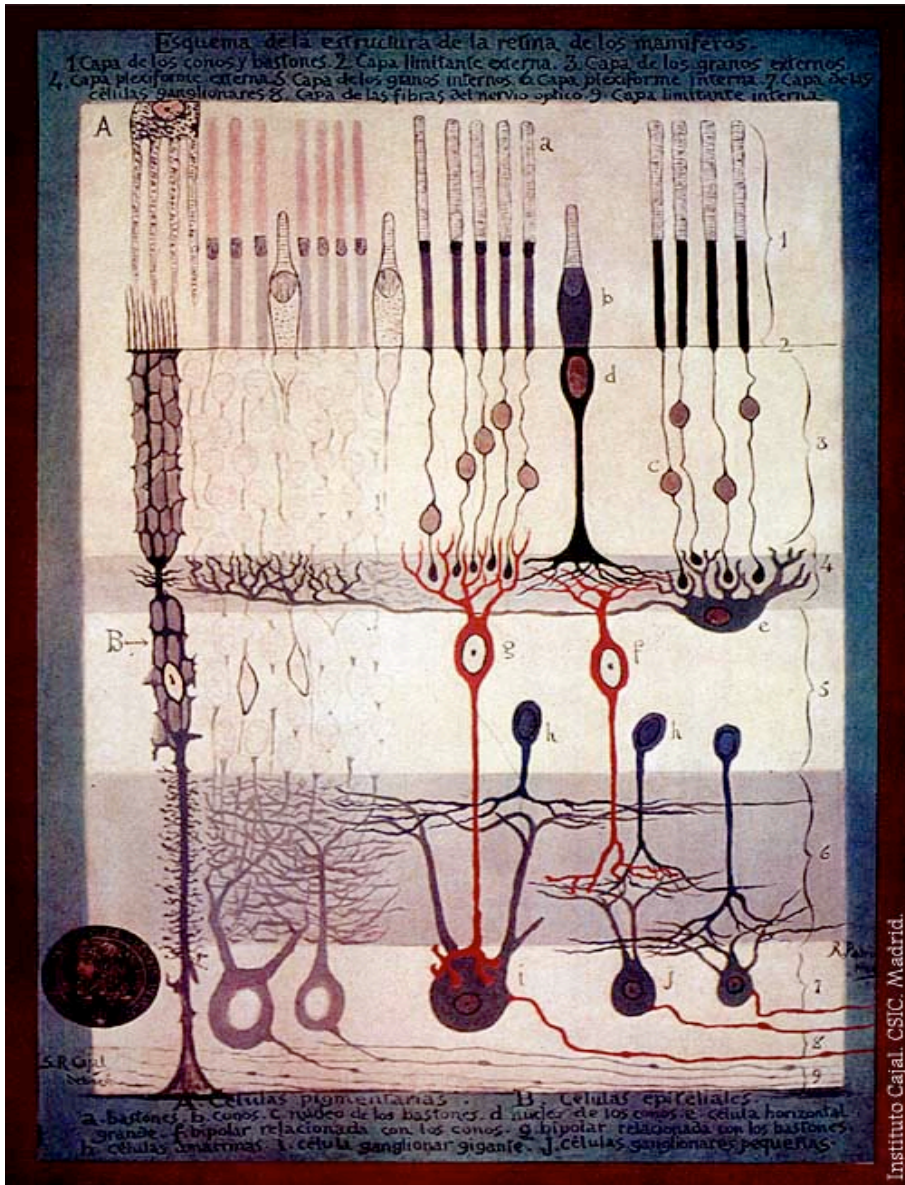
# Retina



~100 million photoreceptors

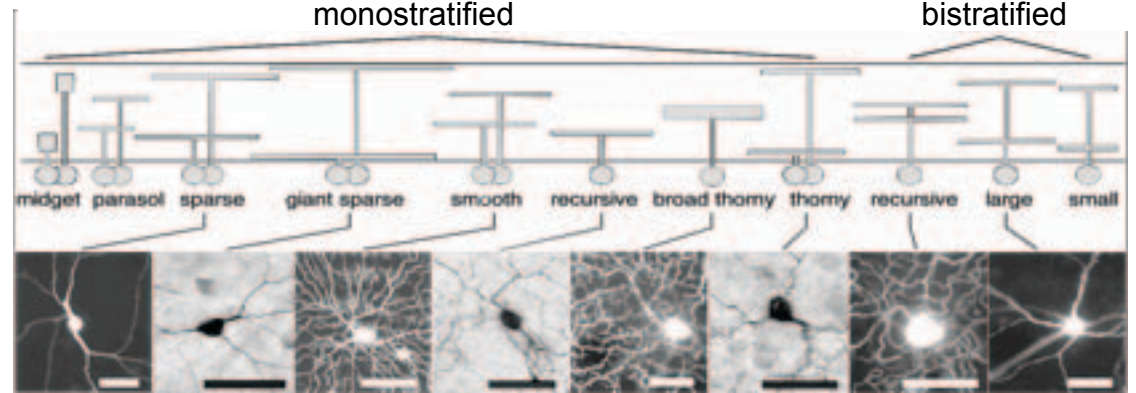
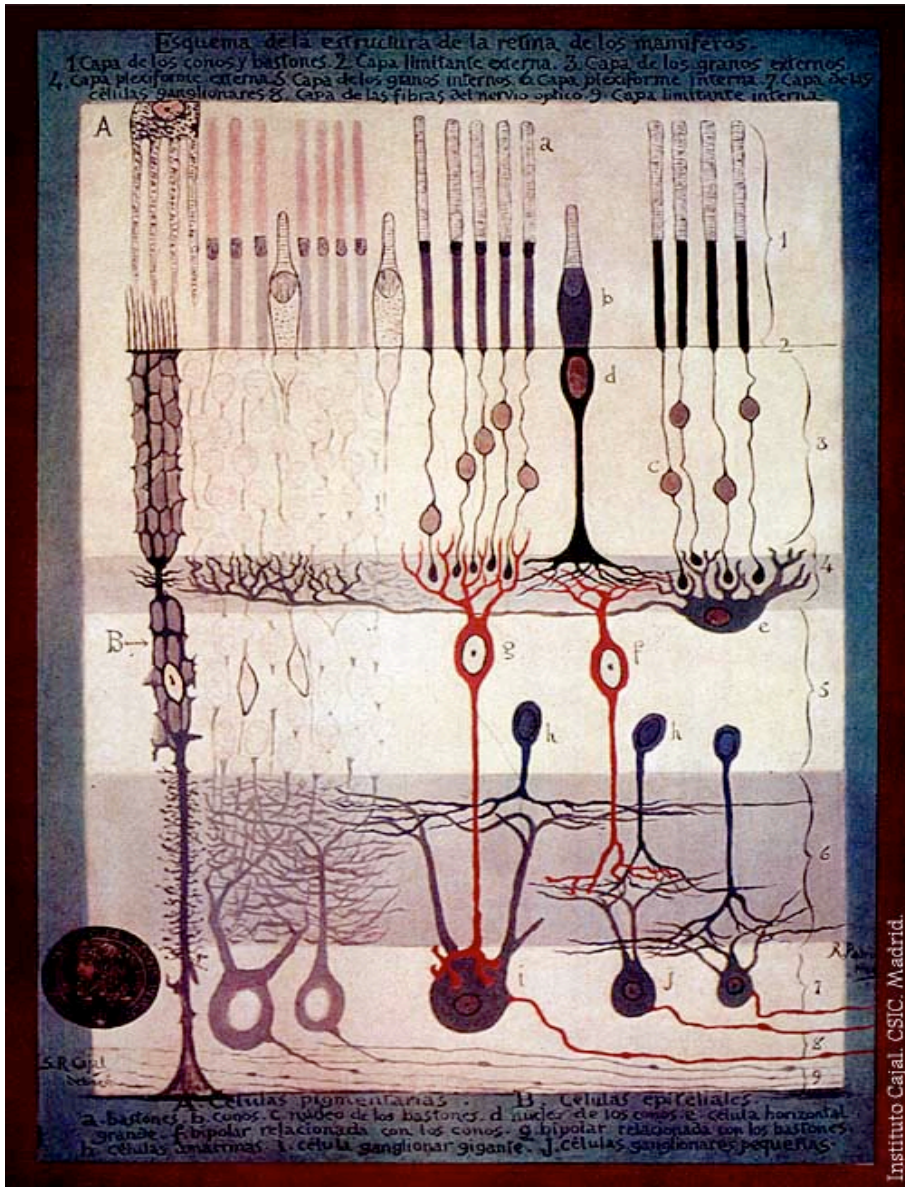
~1 million axons

# Retina



Cajal, 1900

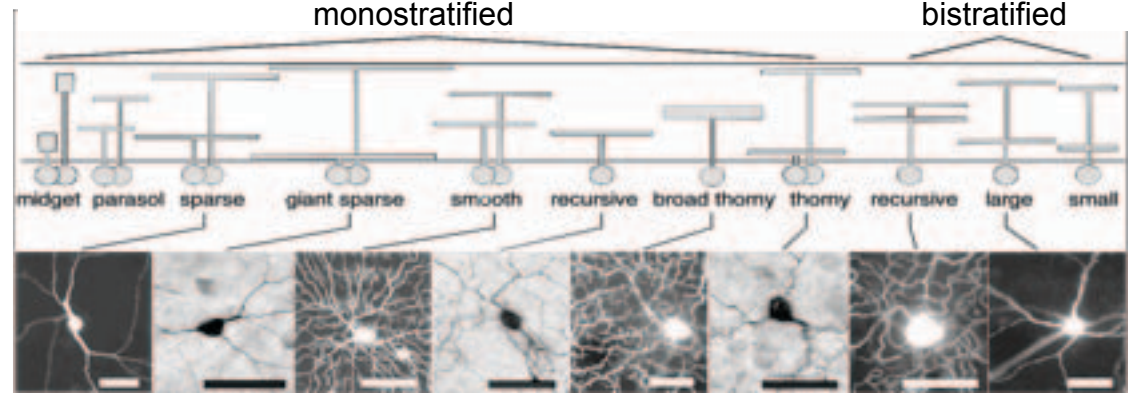
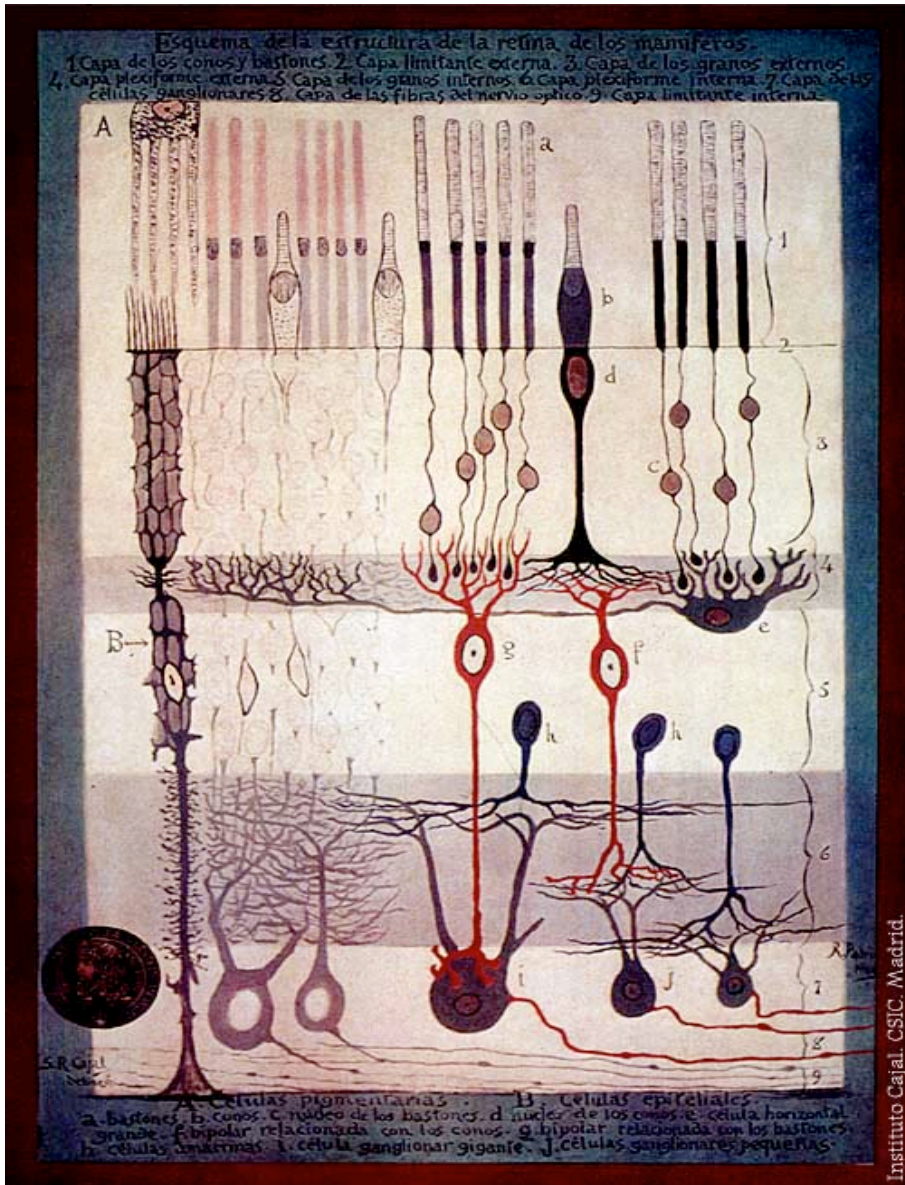
# Retina



Cajal, 1900

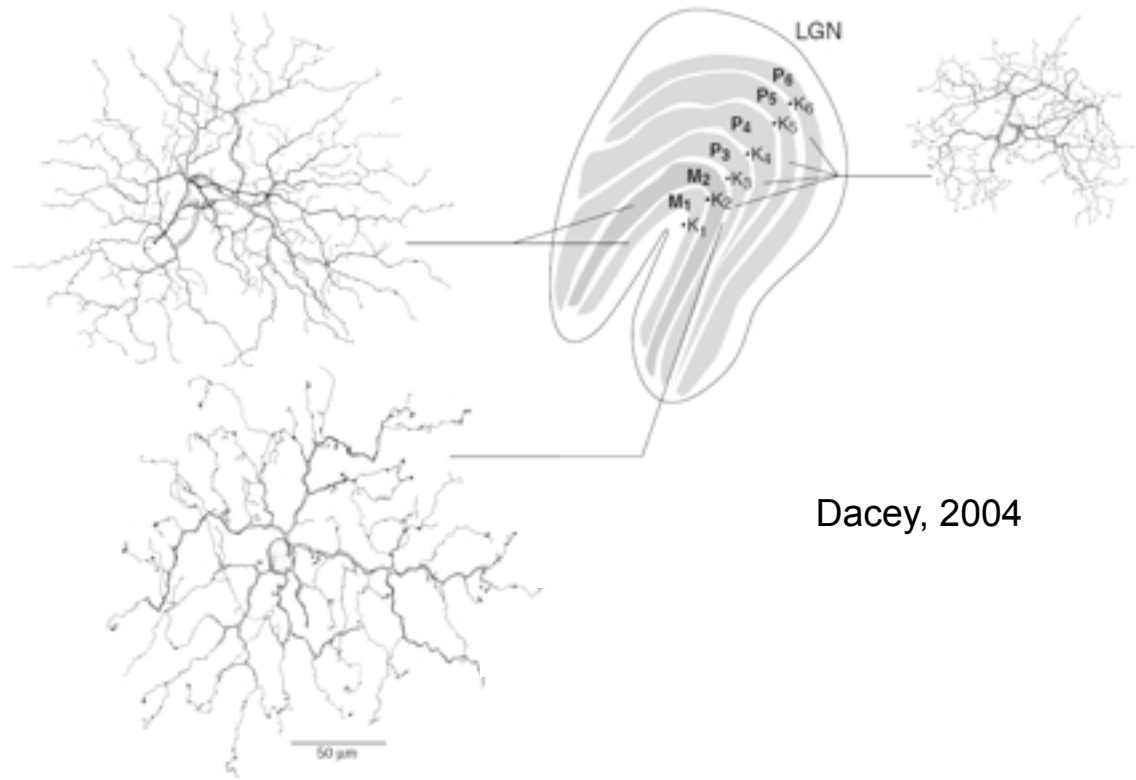


# Retina



parasol

midget



Dacey, 2004

small  
bistratified

Instituto Cajal, CSIC, Madrid.

Cajal, 1900

# Color vision

Brain's interpretation of the wavelength composition of light



Henri Matisse, The Luxembourg Garden. 1901-1902

# Color vision

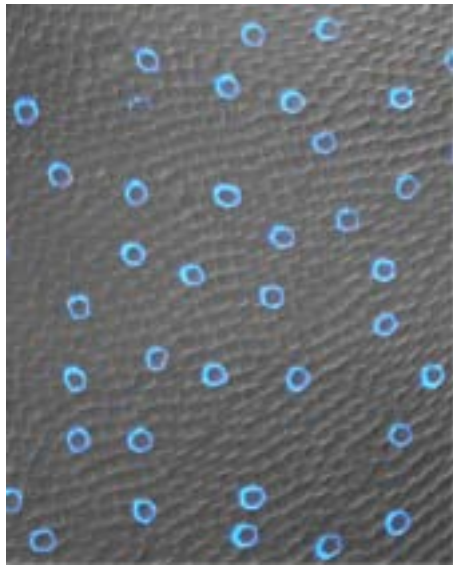
Brain's interpretation of the wavelength composition of light



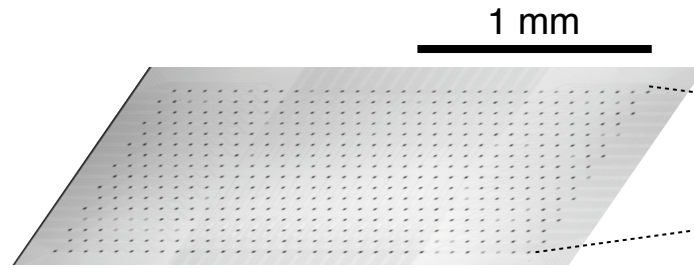
Henri Matisse, The Luxembourg Garden. 1901-1902

# Methods

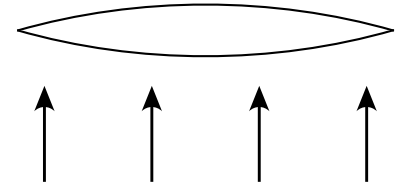
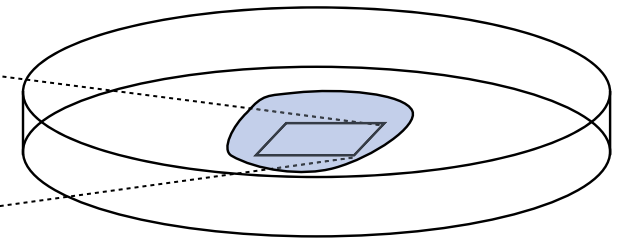
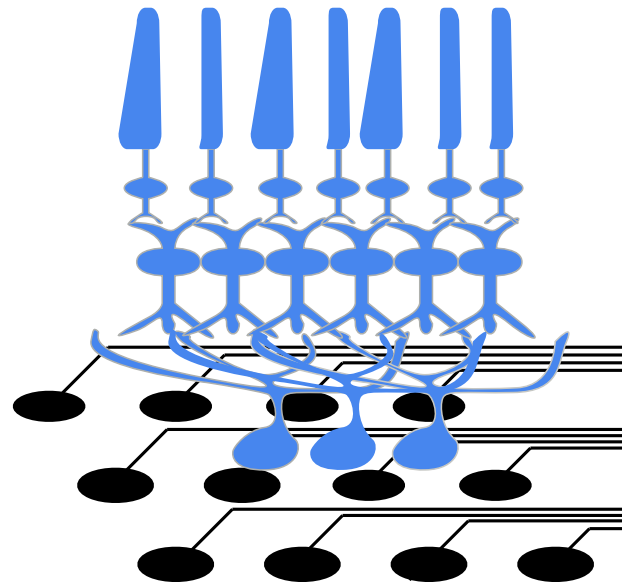
## Physiology Recording



50 μm



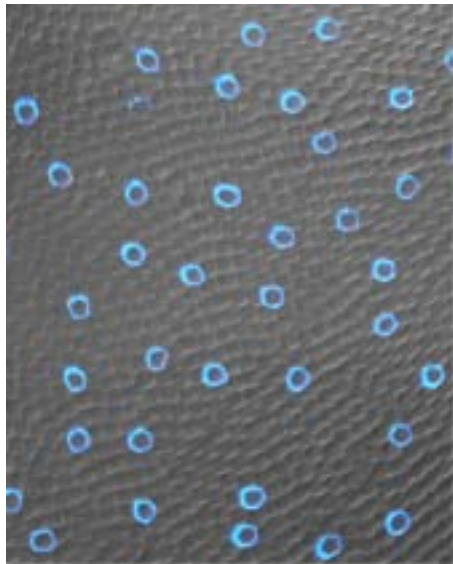
512 electrodes spaced at 60 μm



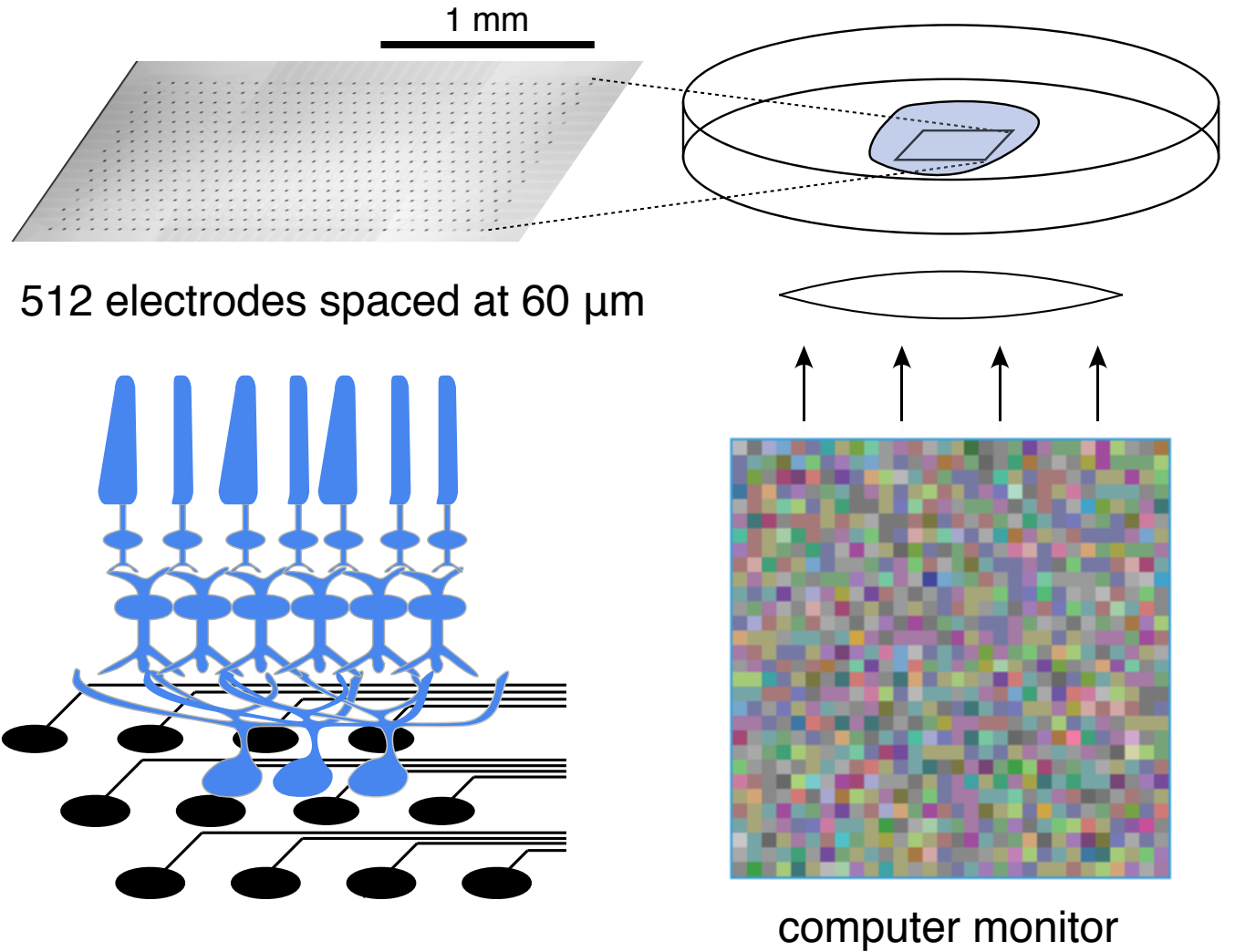
computer monitor

# Methods

## Physiology Recording

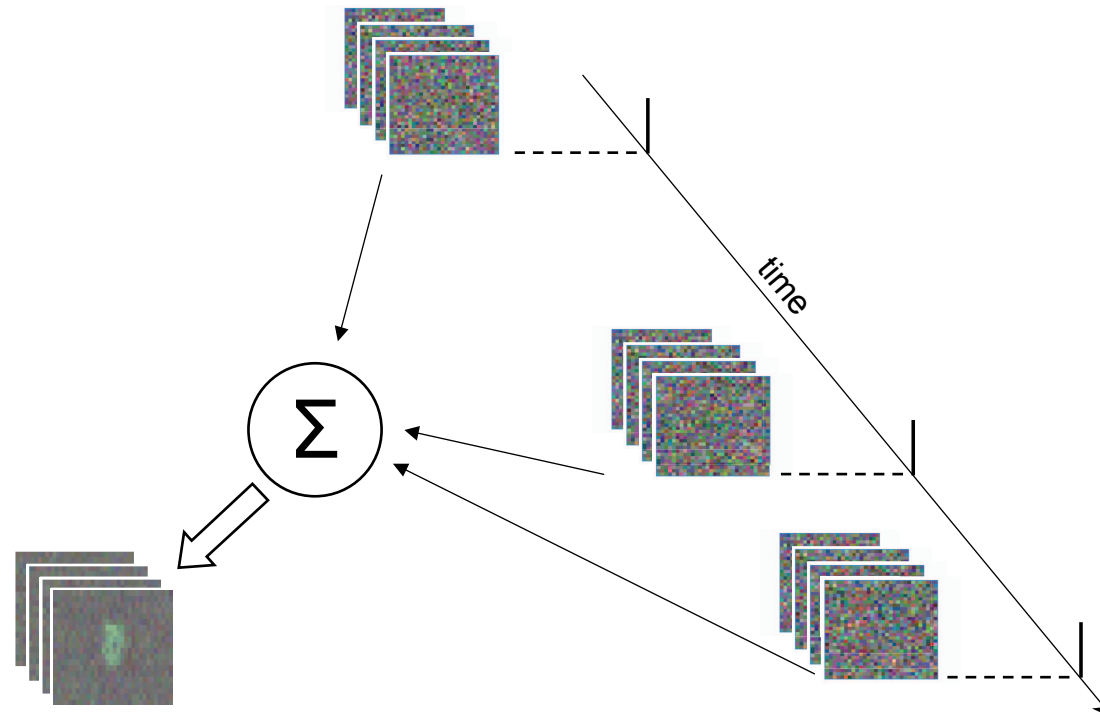


50  $\mu\text{m}$



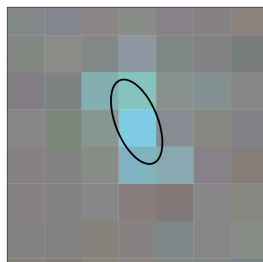
# Methods

## Response properties



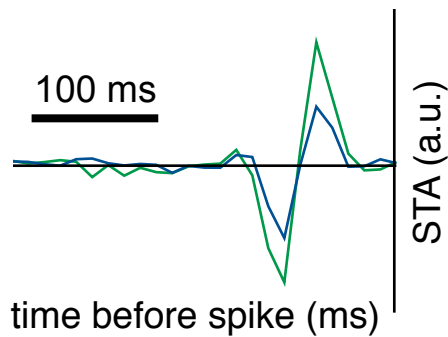
M-ON

M-OFF

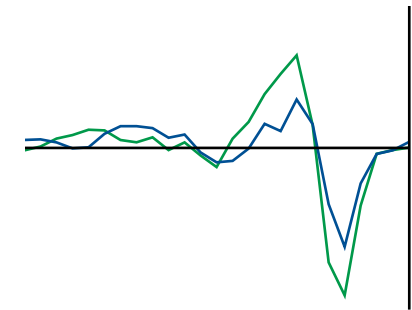
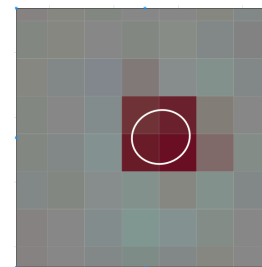


200  $\mu\text{m}$

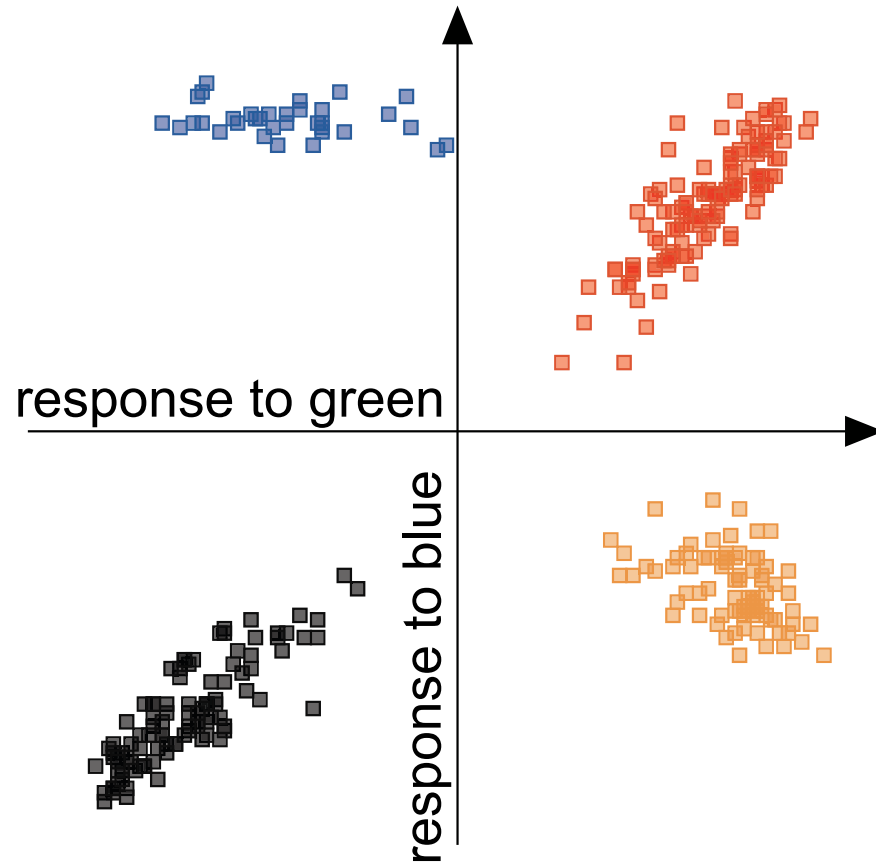
spatial filter  
(receptive field)



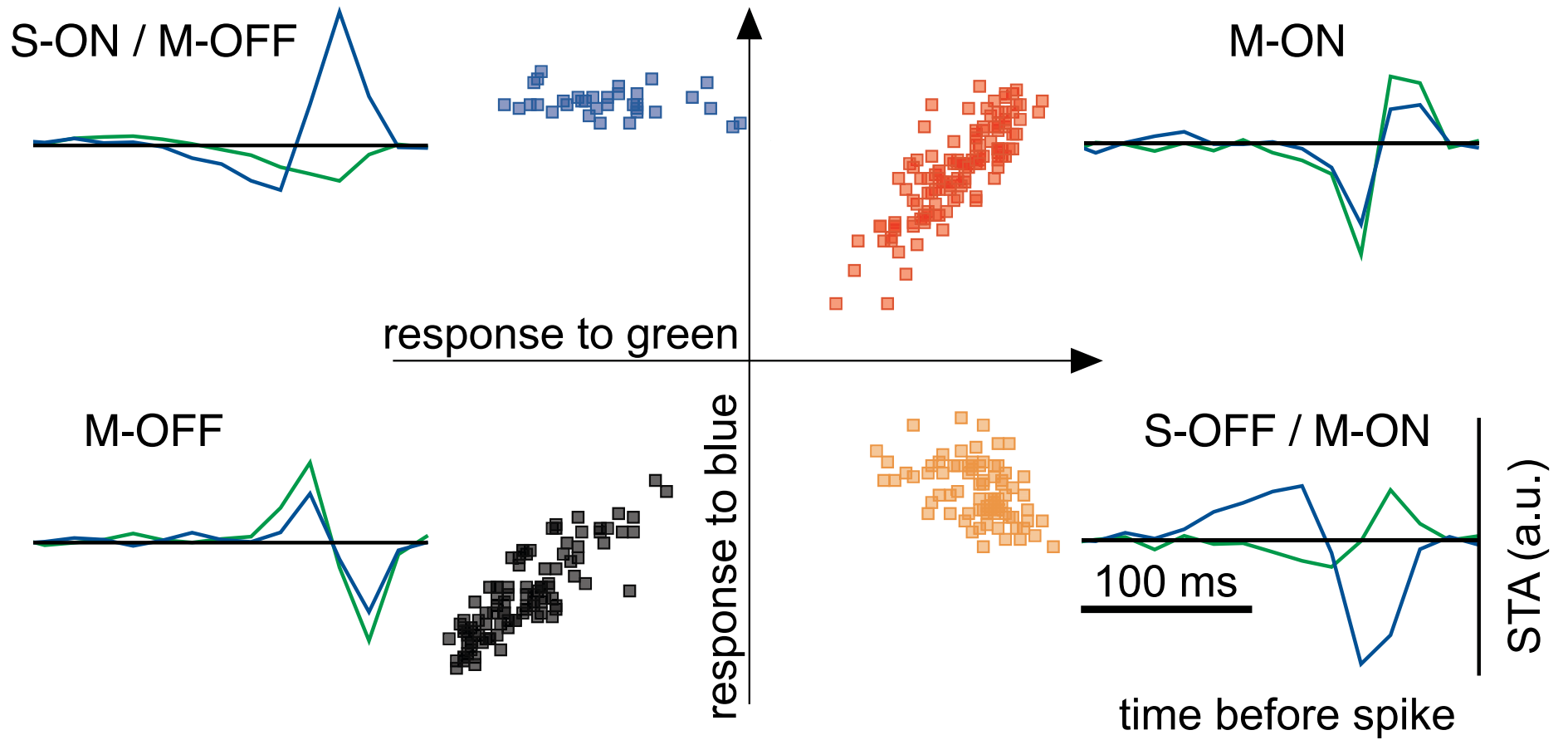
temporal filter  
(time-course)



# Functional classification



# Functional classification

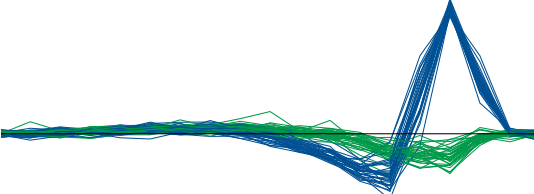
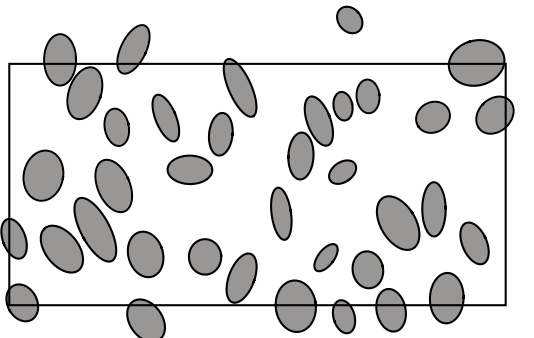




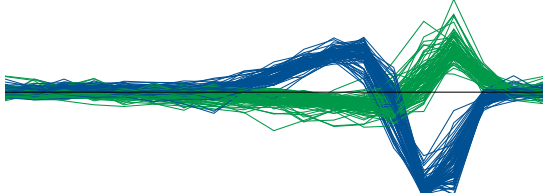
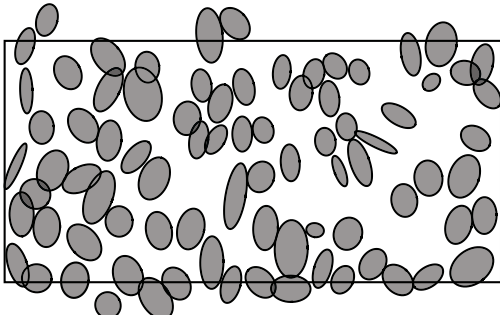
# S-OFF / M-ON fields tile visual space

retina 1

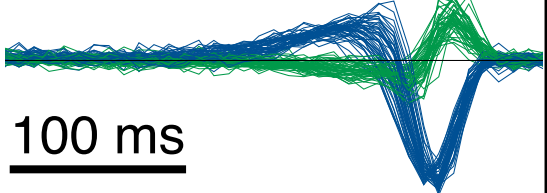
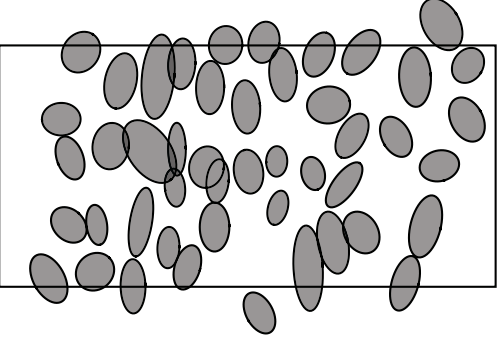
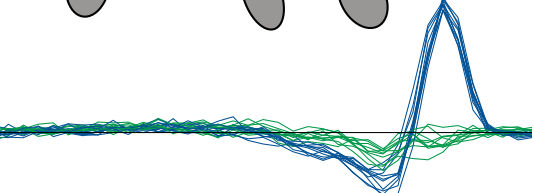
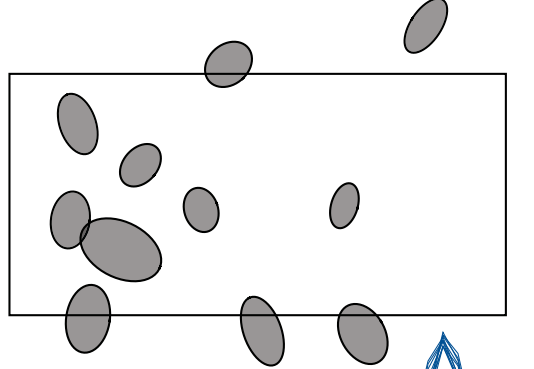
S-ON / M-OFF



S-OFF / M-ON



retina 2

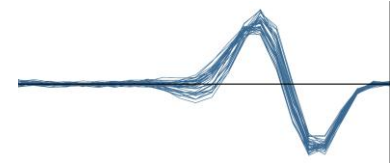
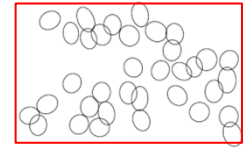
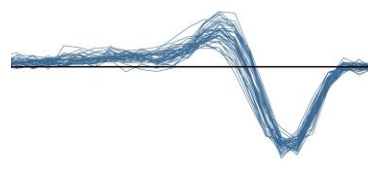
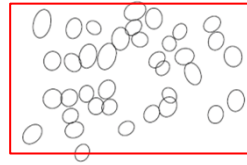
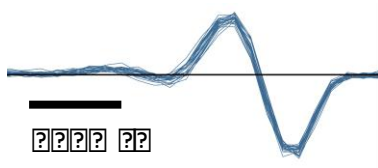
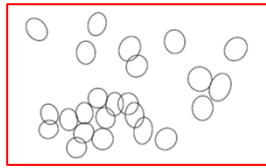


100 ms

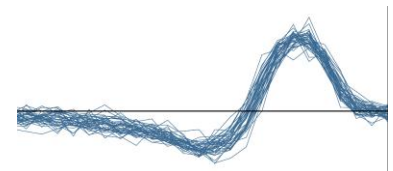
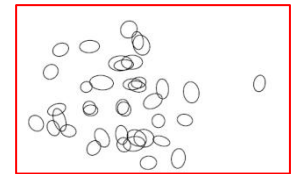
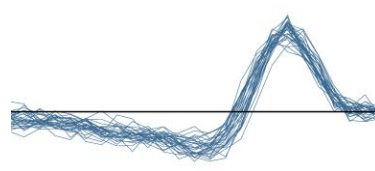
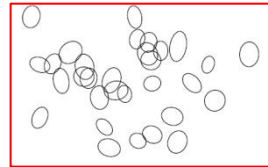
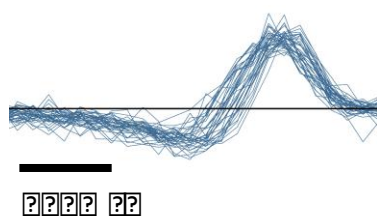
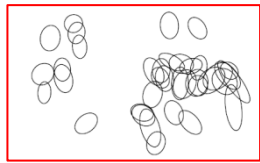
STA (a.u.)

# 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.**

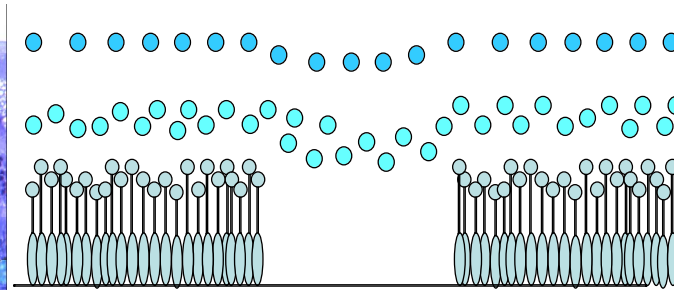
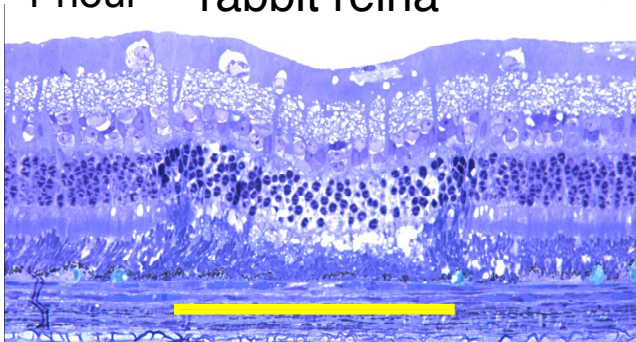


**Conventional pan-retinal photocoagulation**

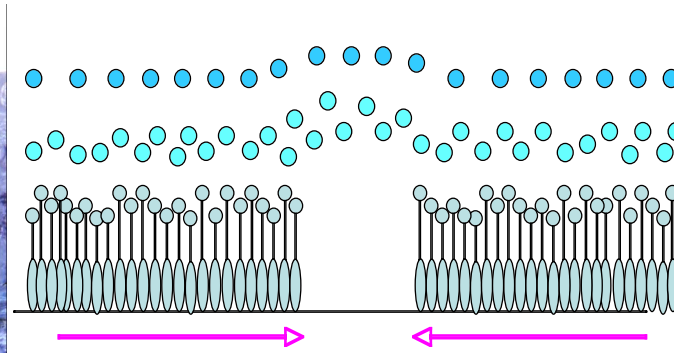
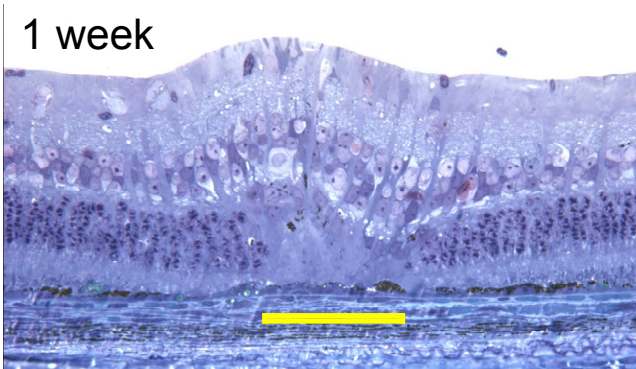
# Photocoagulation

barely visible lesion

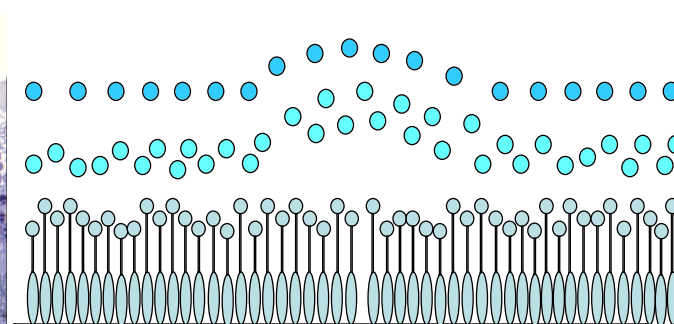
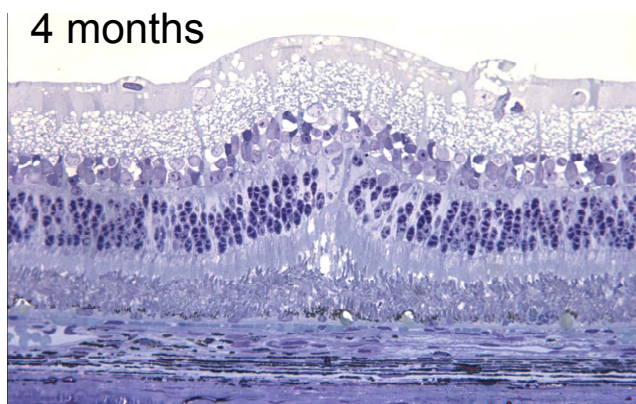
1 hour rabbit retina



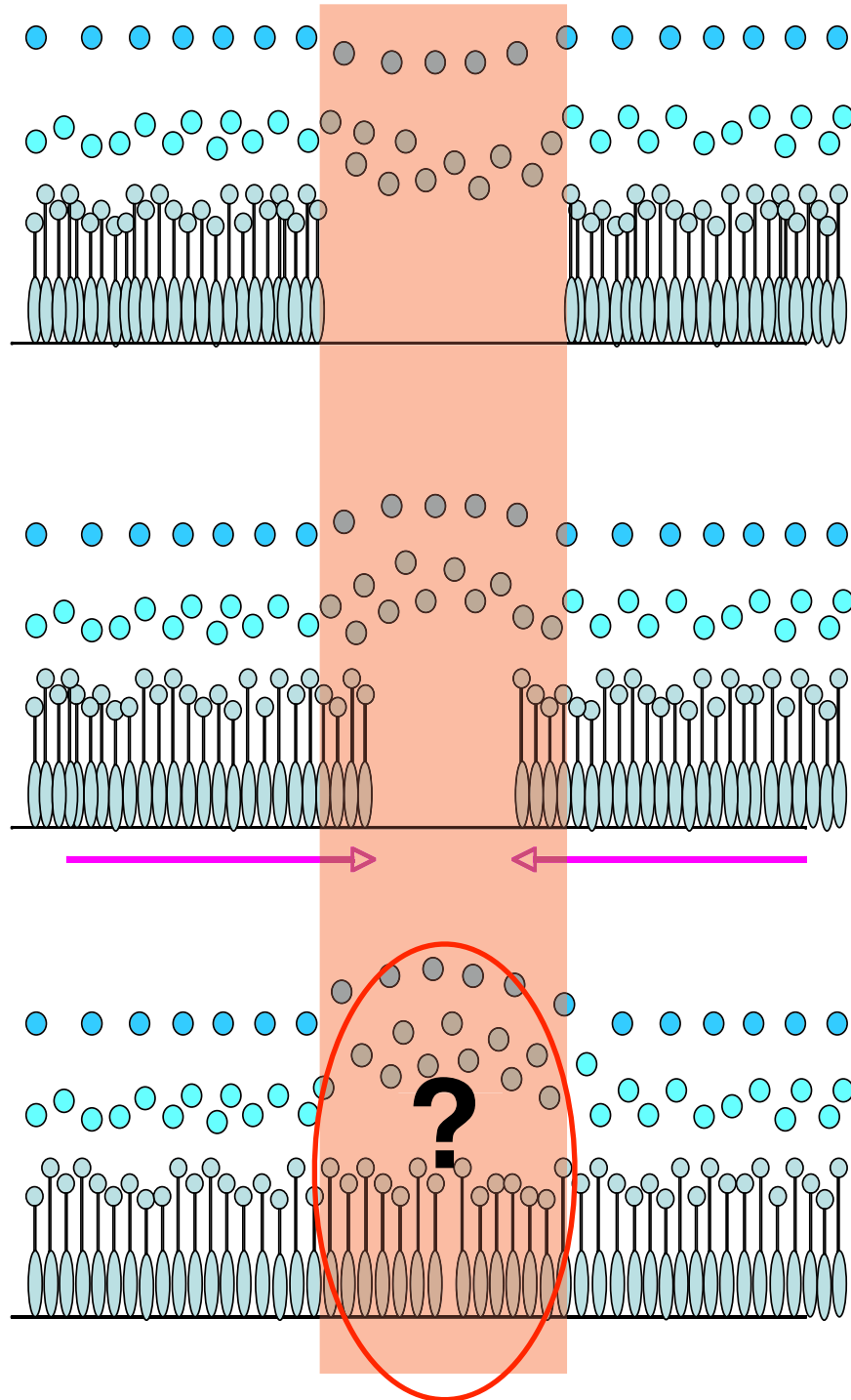
1 week



4 months



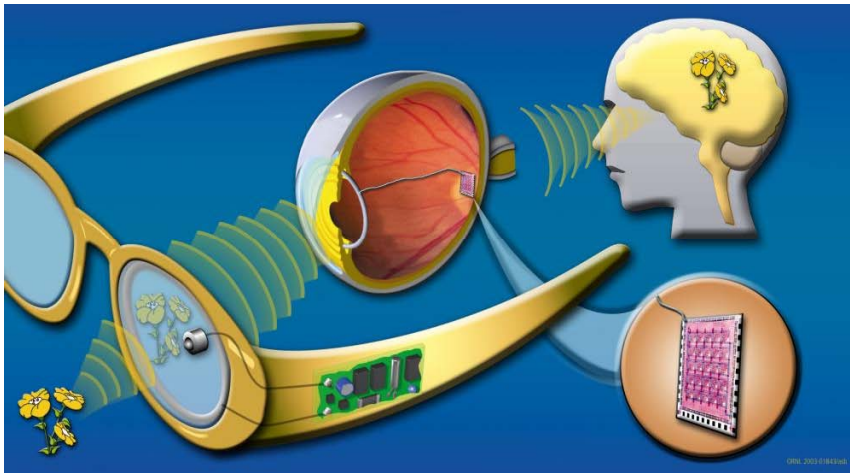
# Photocoagulation



# Medical Applications

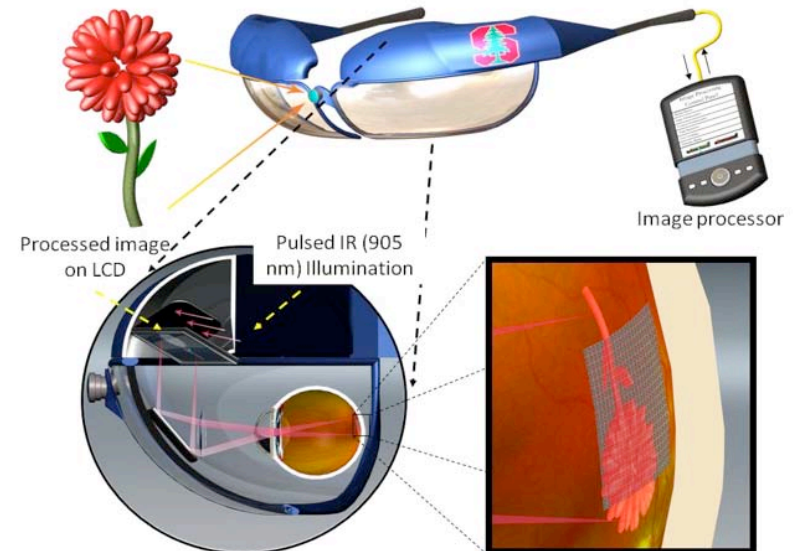
## Retinal Prosthesis

### Epiretinal



Custom circuitry for simultaneous stimulation and recording

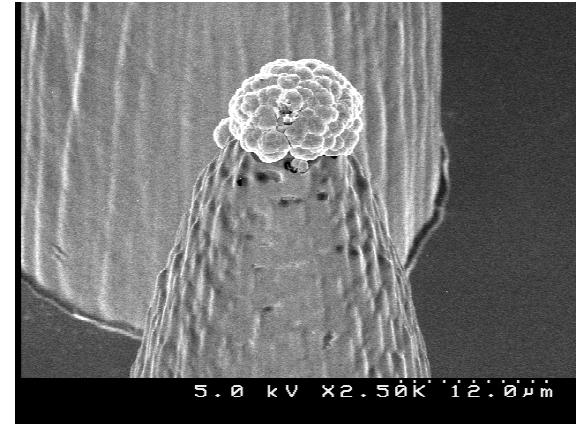
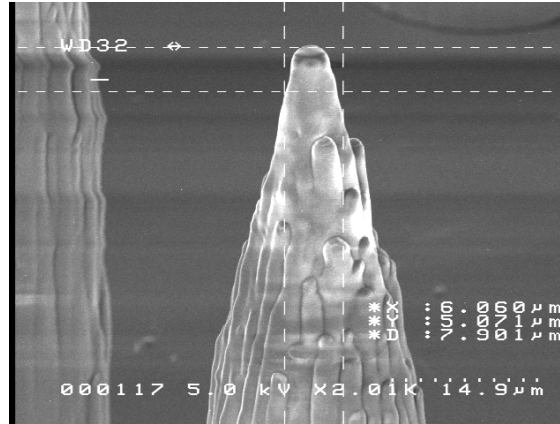
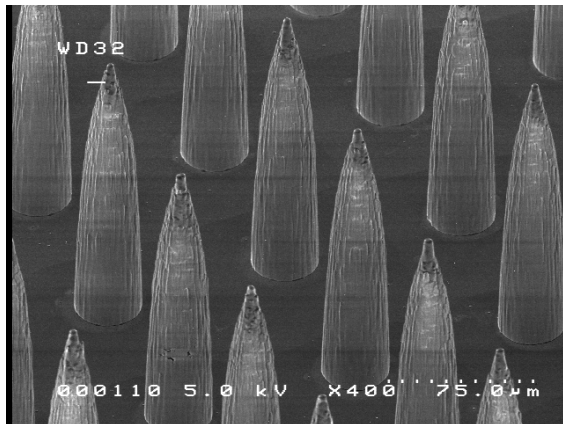
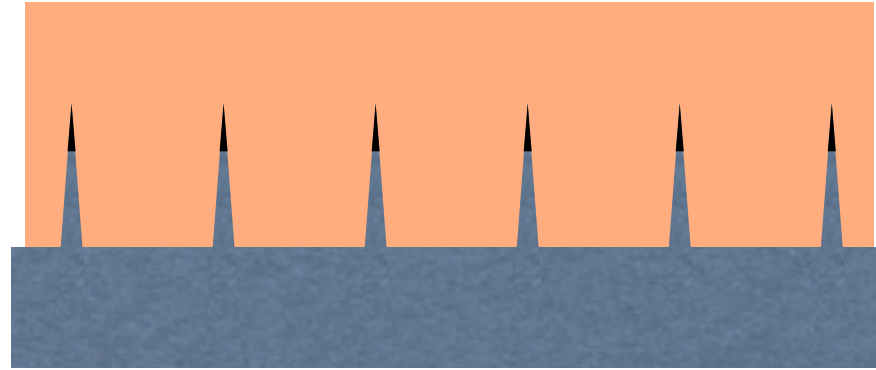
### Subretinal



Recording of responses to stimulation with photovoltaic implants

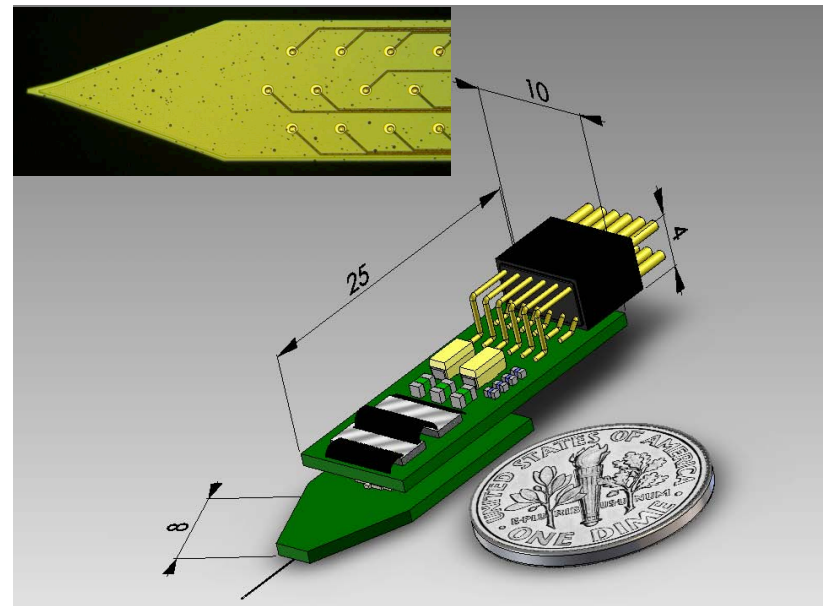
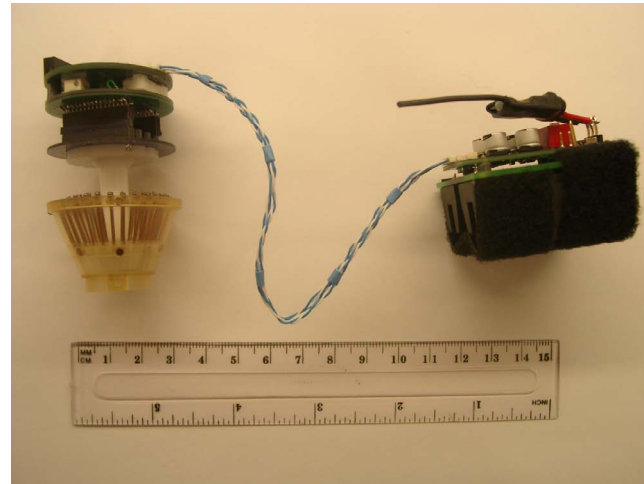
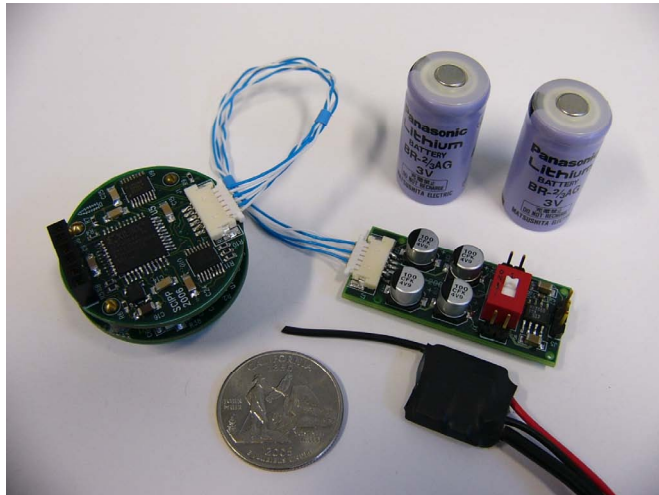
# Brain Activity Recording in-vitro

Bed of Nails electrode array for penetrating inside the tissue

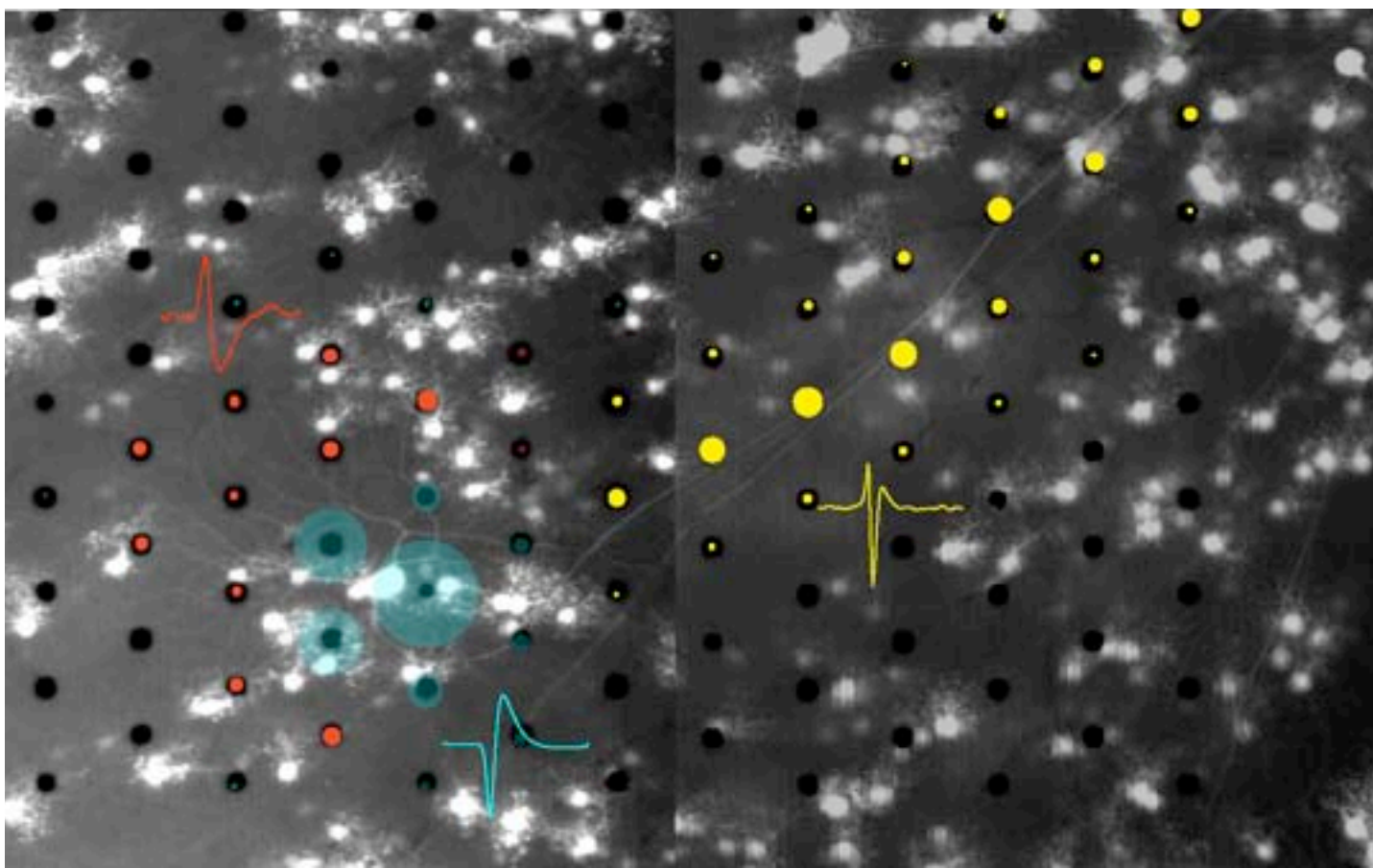


Debbie Gunning

# Brain Activity Recording in-vivo







Salk Institute



AGH USTK. Poland



UCSC MCD Biology



Applied Physics  
Ophthalmology

Alexander Sher  
[sasha@scipp.ucsc.edu](mailto:sasha@scipp.ucsc.edu)  
Alan Litke  
[Alan.Litke@cern.ch](mailto:Alan.Litke@cern.ch)

- 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.