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

=> network of ~100 billion neurons
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

Cajal, 1900

Dacey, 2004

monostratified
bistratified

parasol
midget

small
bistratified
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

512 electrodes spaced at 60 μm

computer monitor
Methods
Physiology Recording

512 electrodes spaced at 60 μm

computer monitor
How do we study retinal encoding?

Characterization of each neuron's encoding properties:

- **Spike Triggered Average (STA)**

Methods

**Response properties**

1. **M-ON**
   - Spatial filter (receptive field)
   - Temporal filter (time-course)
   - Time before spike (ms)
   - STA (a.u.)

2. **M-OFF**
Functional classification
Functional classification

- **S-ON / M-OFF**
- **M-OFF**
- **M-ON**
- **S-OFF / M-ON**

- response to green
- response to blue
- time before spike

STA (a.u.)
S-OFF / M-ON fields tile visual space

S-ON / M-OFF

S-OFF / M-ON

retina 1

retina 2

STA (a.u.)

100 ms
DSCAM is necessary for functional mosaics
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

1 week

4 months

Photocoagulation

[Diagram of Photocoagulation process]
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

- 15 um thick. ~55 micron separation. 15 um diameter sites.
- Original site impedance ~1.2 MOhm. We do platinize them.
- Used two types of probes: 54- and 16-channel. There are others…
• 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.