Large Scale Multielectrode Recording and Stimulation of Neural Activity

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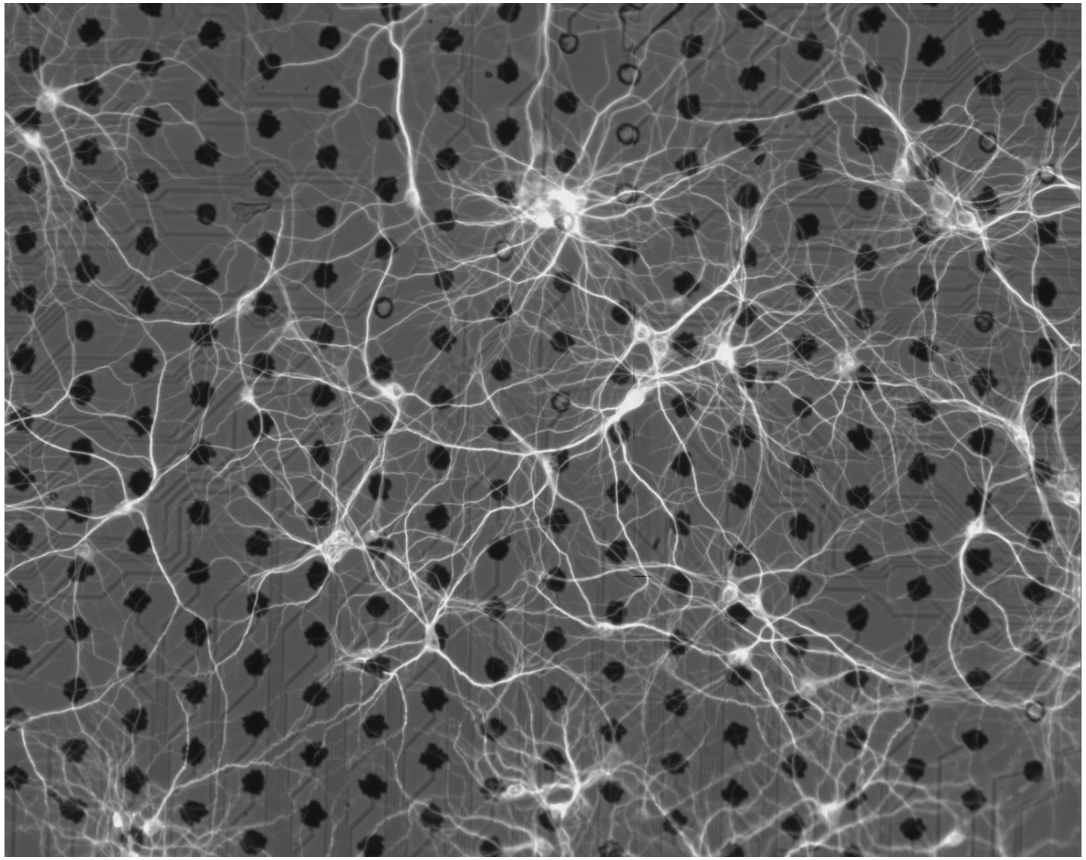
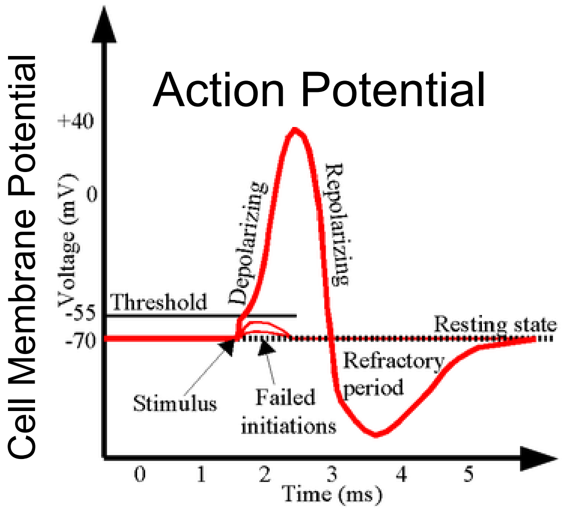
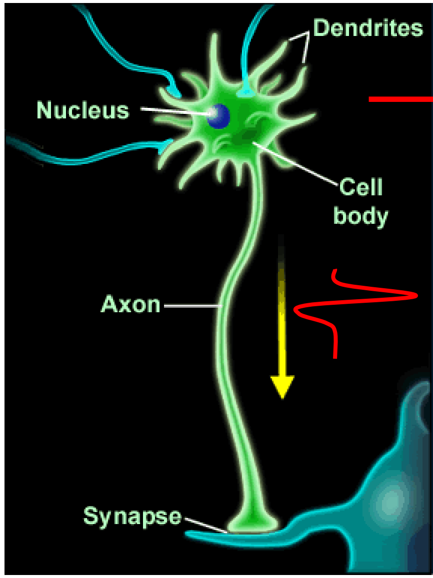
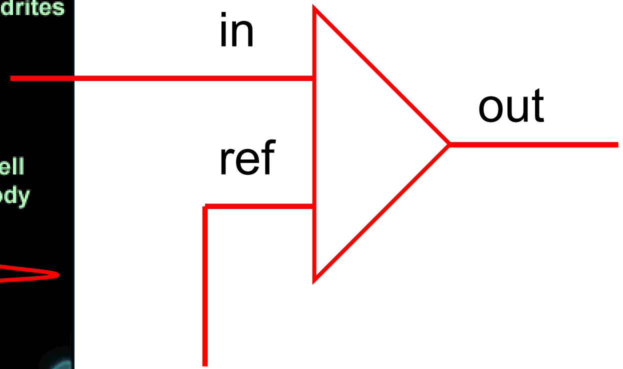
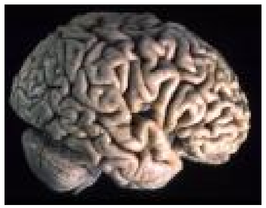
[2]Systems Neurobiology, Salk Institute, La Jolla, CA
[3]AGH University of Science and Technology, Kraków, Poland
[4]University of Glasgow, Glasgow, UK



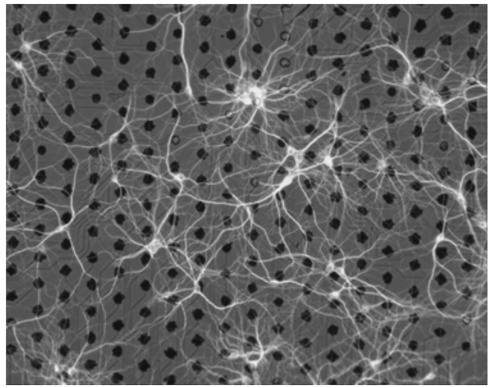








=> network of ~100 billion neurons



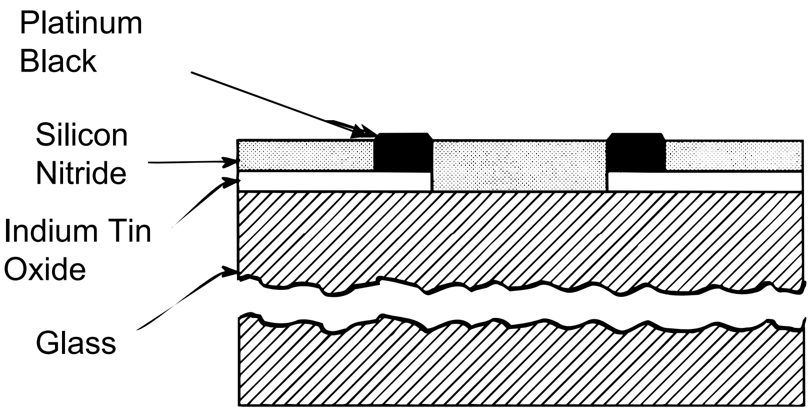
Extracellular Multielectrode recording of neural activity

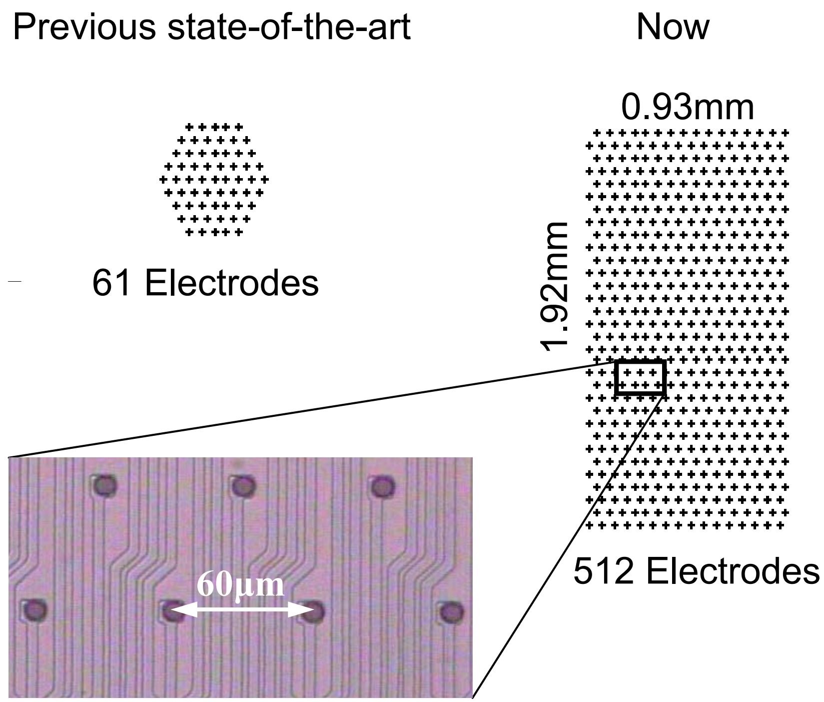
- Simultaneous activity of many neurons
- Best spatial resolution: single neuron
- Best time resolution: single action potential

System Overview

- Hundreds of electrodes and readout channels
- Interelectrode distance of tens of microns
- Signal amplification (input ~ hundreds of μV)
- Low noise
- DAQ system for digitizing and saving the data
- Data analysis

Electrode Array

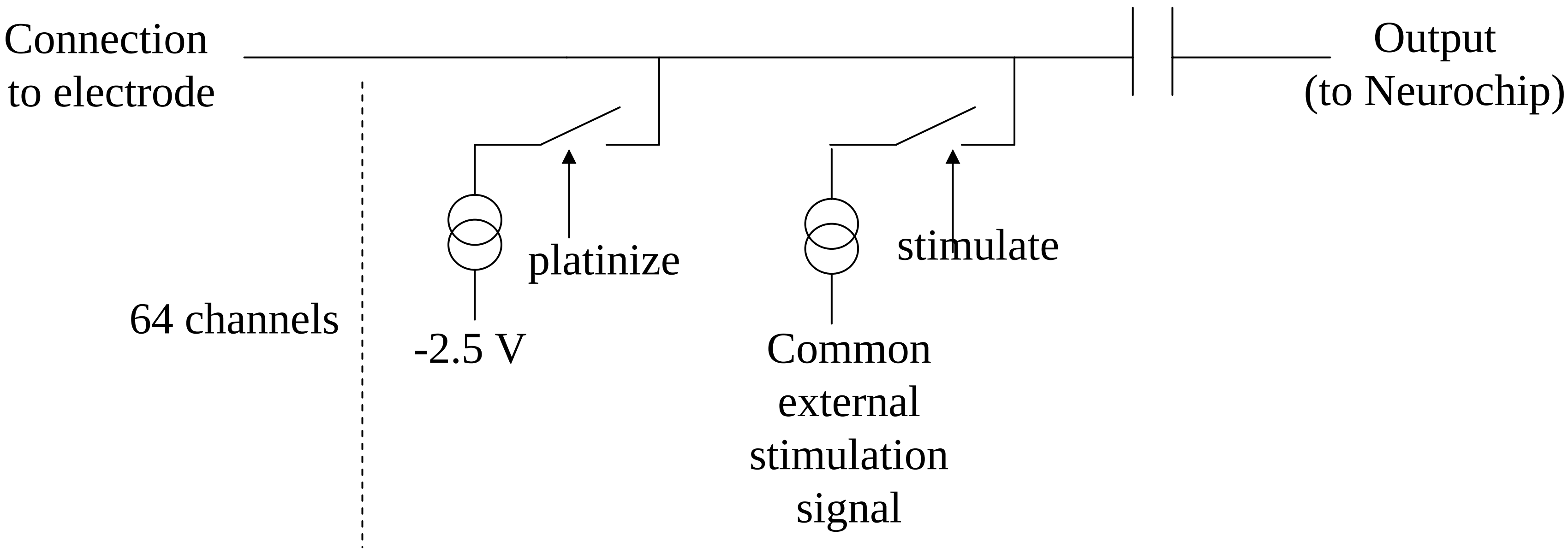




S. Kachiguine (SCIPP)

Platchip

- 64 channels; 120 µm pitch; die size = 3.3 x 7.8 mm^2
- AC coupling: 150 pF
- Platinization current: 0-1.2 µA (controlled by 5 bit DAC)
- Stimulation current: 0-150 µA (controlled by external analog signal with gain set by 5 bit DAC)



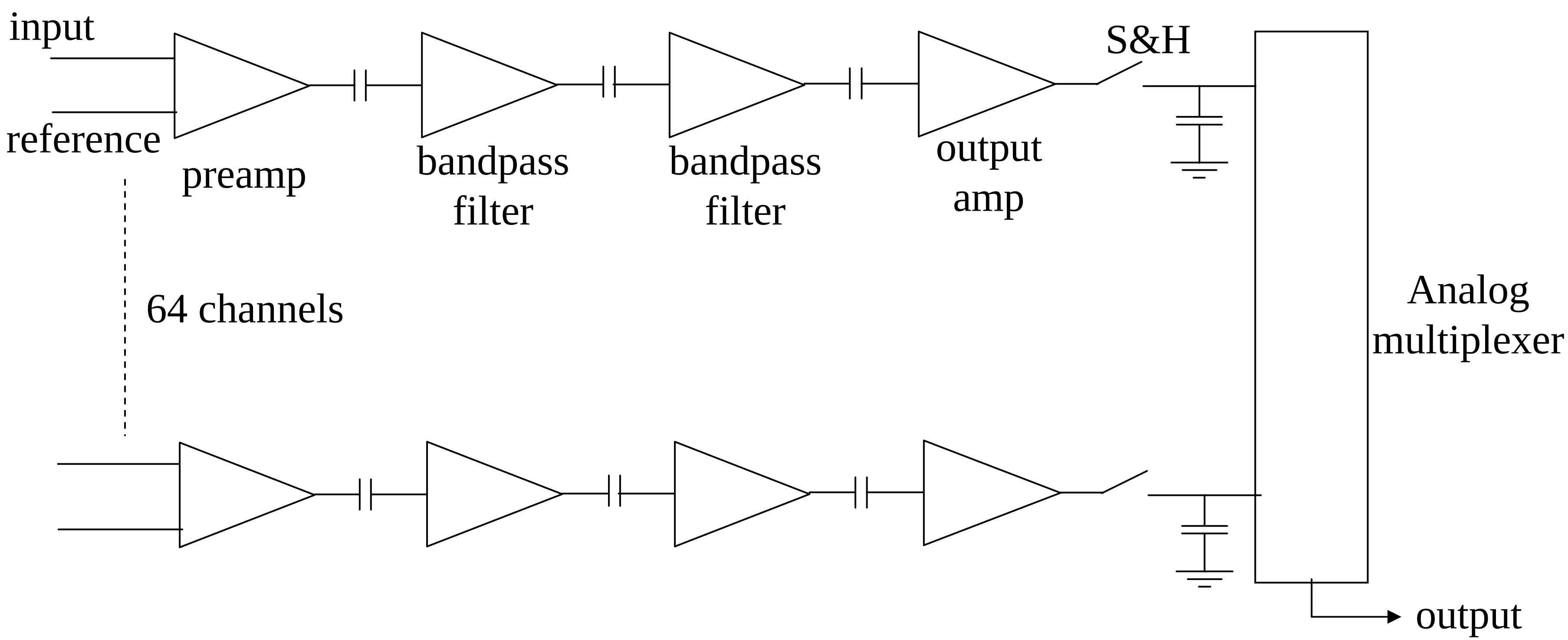
Design by W. Dabrowski et al., Krakow

Neurochip

•64 channels; 120 µm pitch; die size = 4.8 x 7.8 mm^2

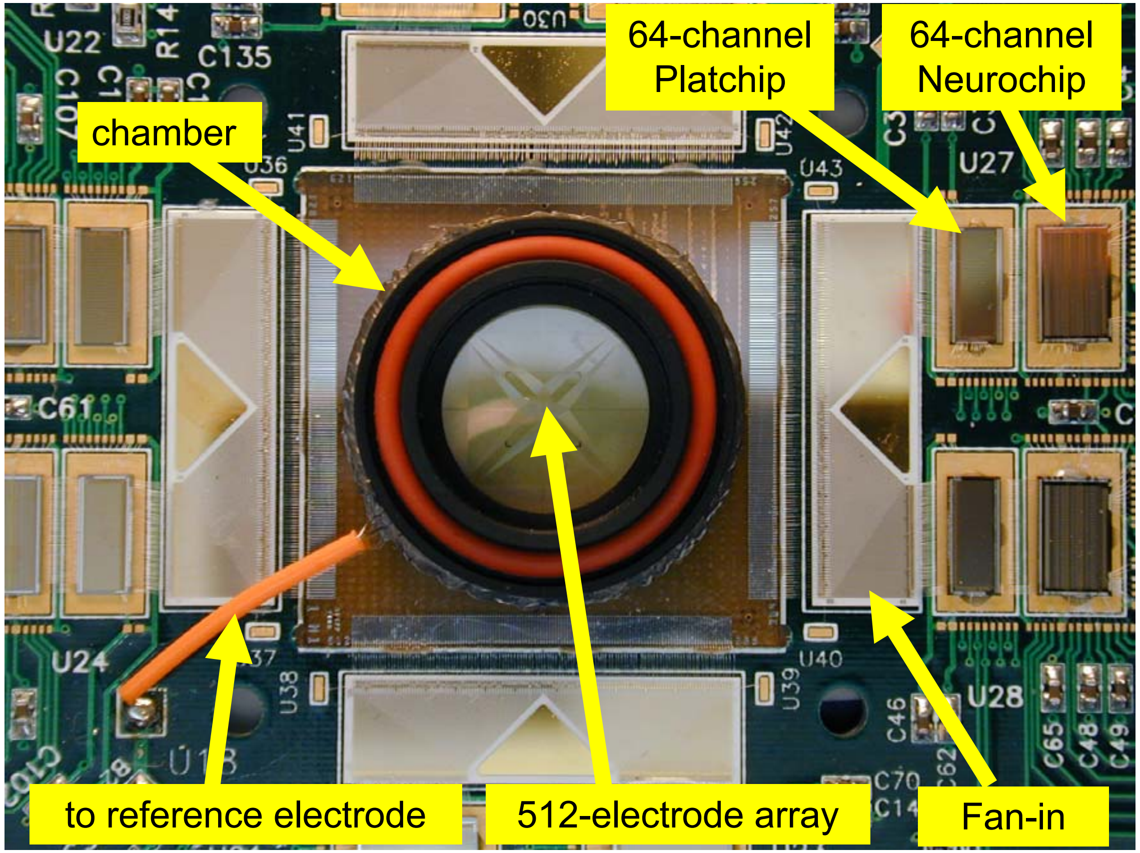
•bandpass filter: 80 - 2000 Hz (typical); equivalent rms input noise ~5 µV (~7 µV for complete system with saline; signal amplitude range = 50 – 800 µV)

• sampling rate/channel = 20 kHz (typical); multiplexer freq. = 1.3 MHz (typical)



Design by W. Dabrowski et al., Krakow

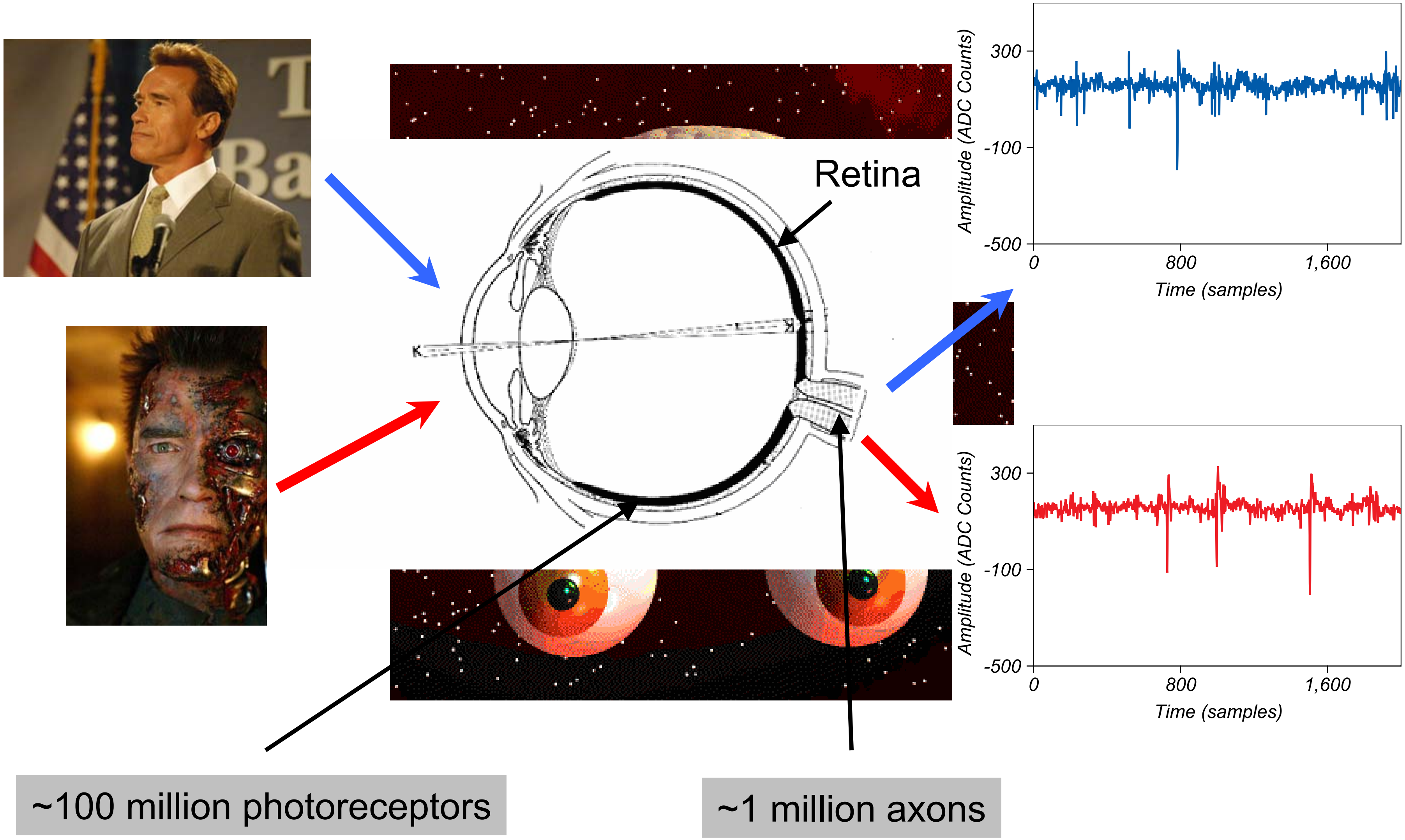
512 electrode Readout System



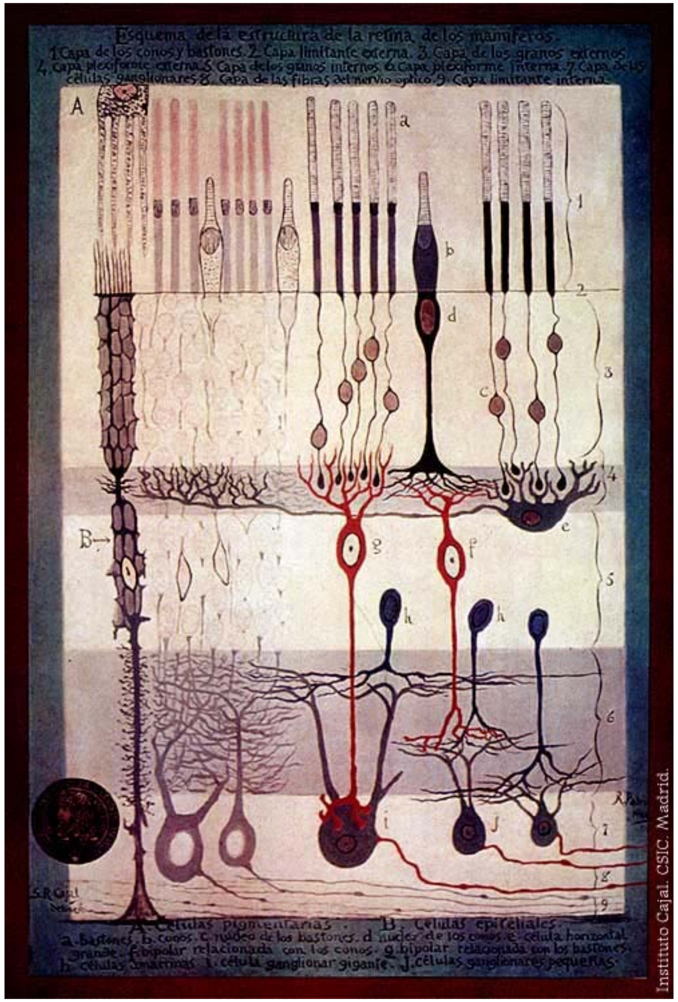
SCIPP

- 64:1 multiplexing.
- Gain: ~1000.
- Bandpass: 80Hz – 2kHz.
- Input noise: <10μV.
- DAQ: NI PCI ADC cards; 20kHz sampling of each channel; 15MB/s data rate.

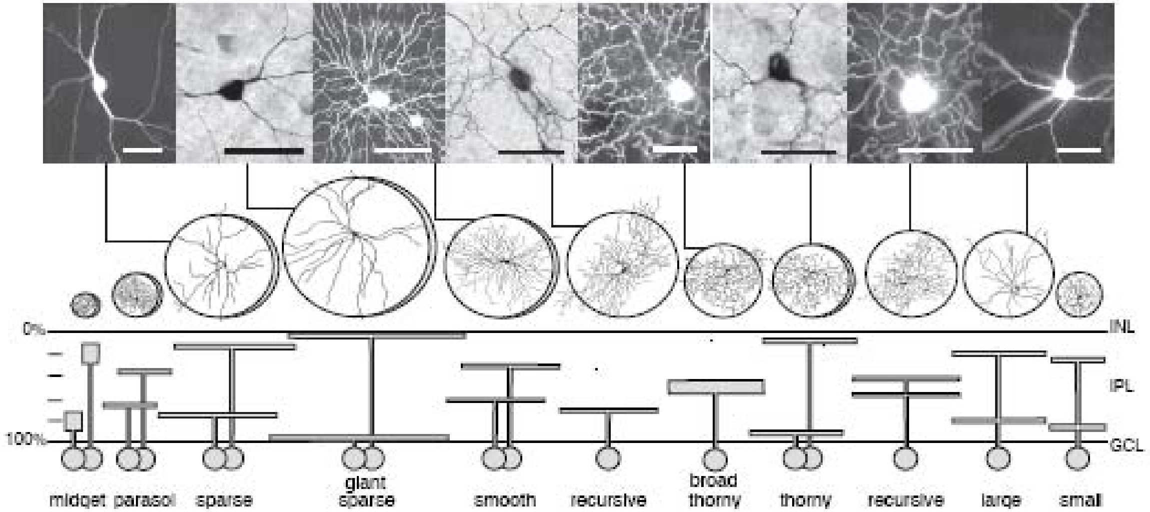
Retina


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

Retina

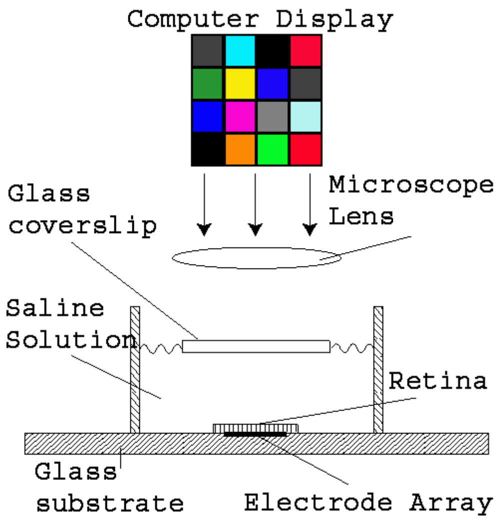


Cajal, 1900



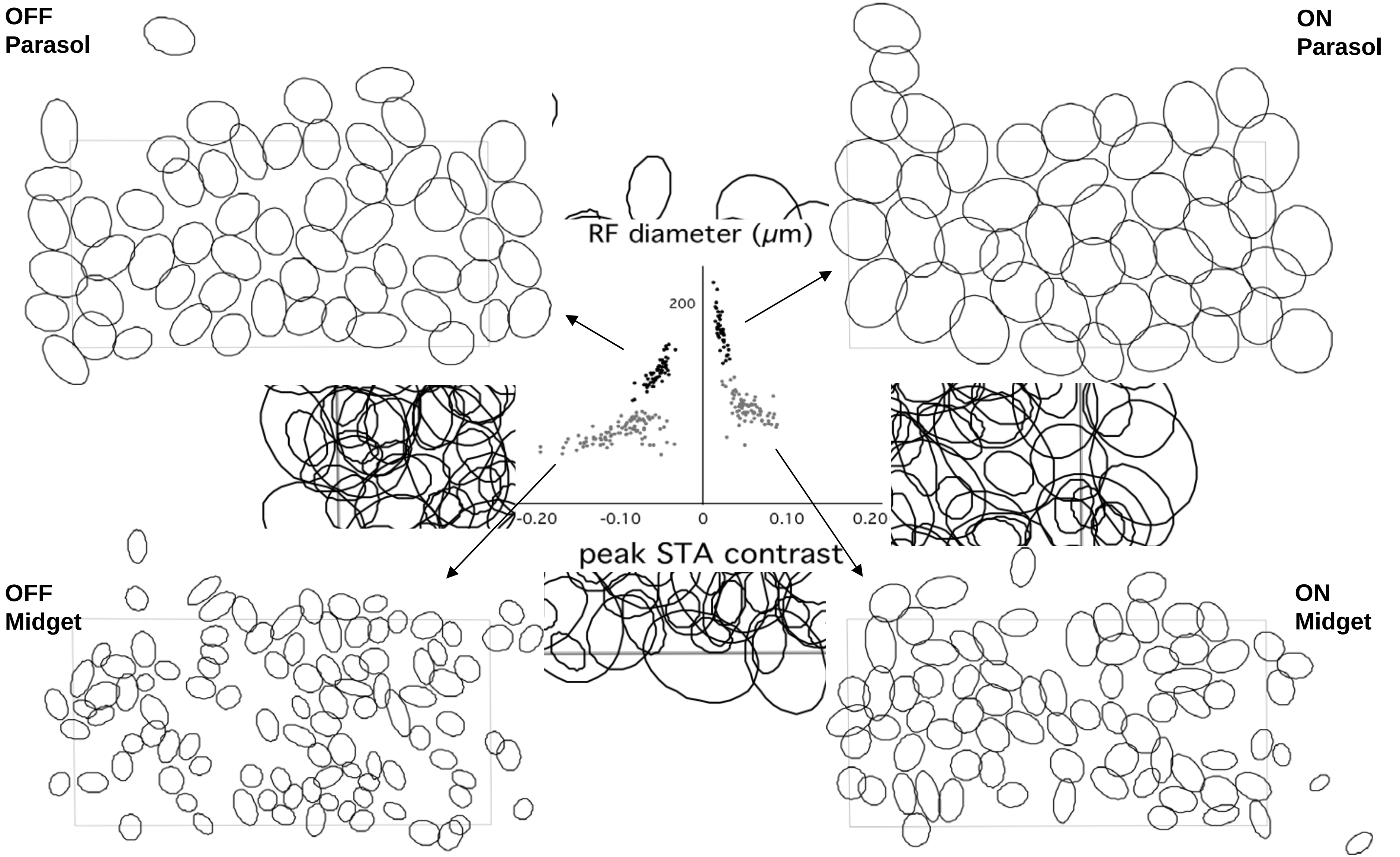
Dacey, 2004

How is visual information (patterns, color, motion) encoded by different ganglion cell classes?



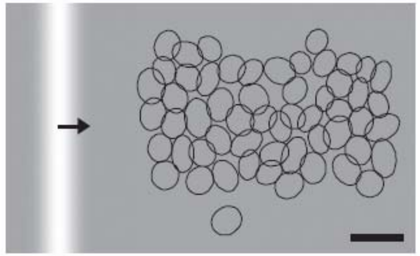
Collaboration with E.J. Chichilnisky (Salk Institute, San Diego)

Retina

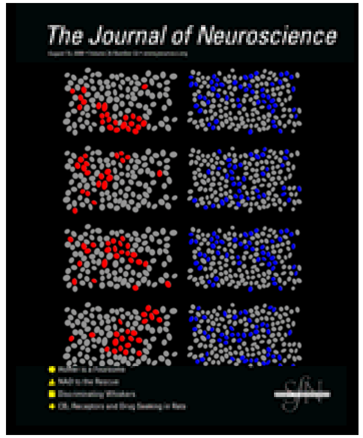

OFF
Parasol
ON
Parasol
OFF
Midget
ON
Midget
RF diameter (μm)
200
-0.20
-0.10
0
0.10
0.20
peak STA contrast

Retina

Results:



E.S. Frechette, A. Sher, M.I. Grivich, D. Petrusca, A.M. Litke,
E.J. Chichilnisky,
"Fidelity of the ensemble code for visual motion in primate retina,"
J Neurophysiol., 94(1), pp. 119-35, 2005



J. Shlens, G.D. Field, J.L. Gauthier, M.I. Grivich, D. Petrusca,
A. Sher, A.M. Litke, E.J. Chichilnisky,
"The structure of multi-neuron firing patterns in primate retina,"
J Neurosci., 26(32), pp. 8254-66, 2006

Ongoing work:

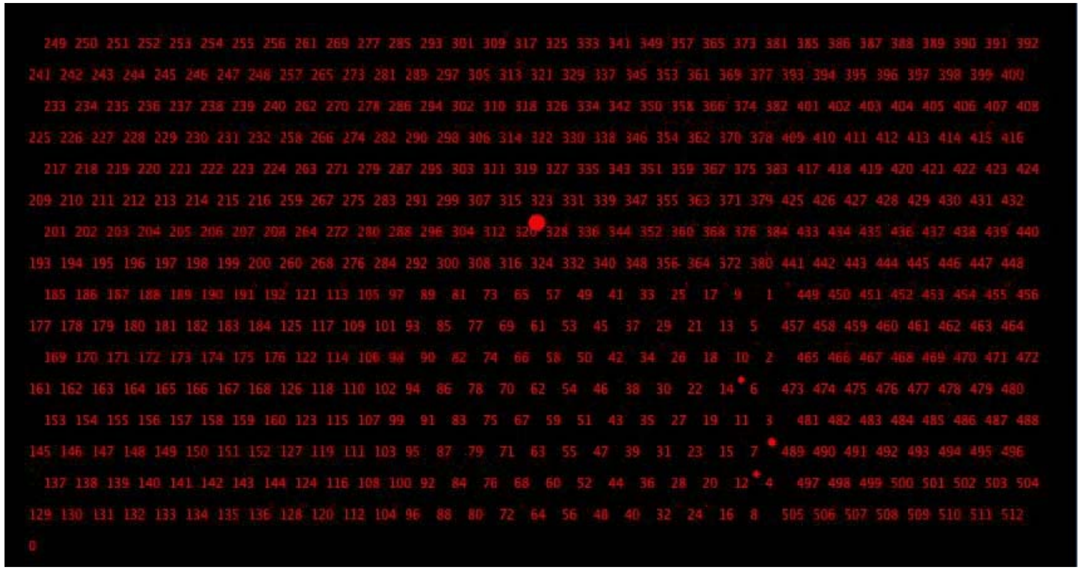
- Characterization of new cell types
- Color processing in the retina

Retinal Development

How is retinal architecture and its connectivity to the brain formed?
•Molecular cues
•Activity dependent “wiring”

512 electrode readout system: best tool to
•Characterize mouse retina functional properties
•Characterize changes of these properties in genetically modified mice

First step:
Spontaneous activity in the developing mouse retina (“retinal waves”)



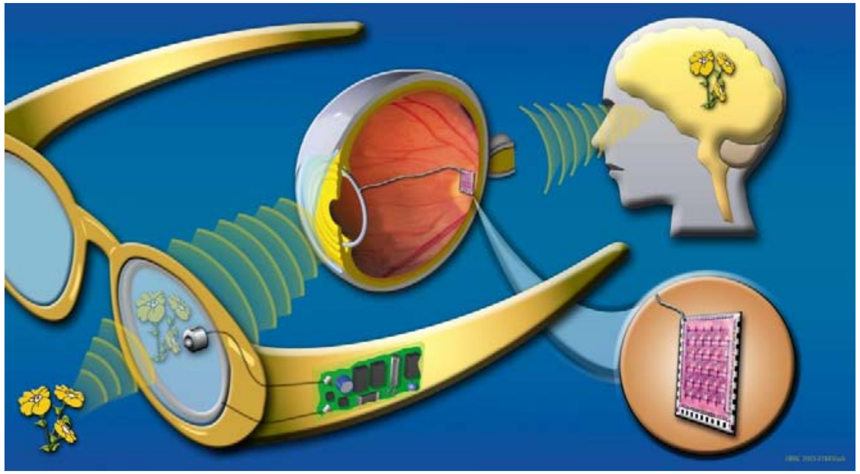
Collaboration with D. Feldheim (UC Santa Cruz)

Retinal Stimulation

Millions of people have photoreceptor degenerative diseases (Retinitis Pigmentosa, Macular Degeneration)

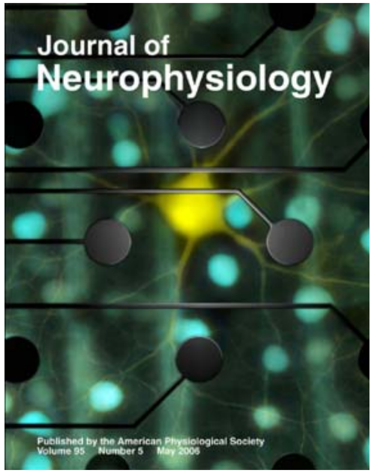
Possible solution: electrical stimulation of retinal ganglion cells.

Current state-of-the-art:
•Human trials
•Array of 16 electrodes of ~500μm diameter

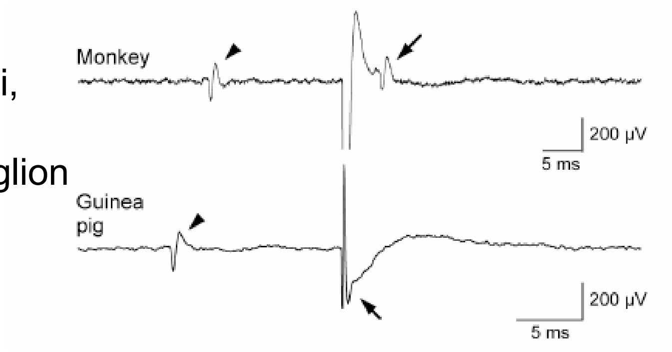


Credit: DOE

Dense electrode arrays + Simultaneous stimulation (Platchip) and recording (Neurochip):
•For the first time showed that safe and reliable stimulation with <10μm diameter electrodes is possible

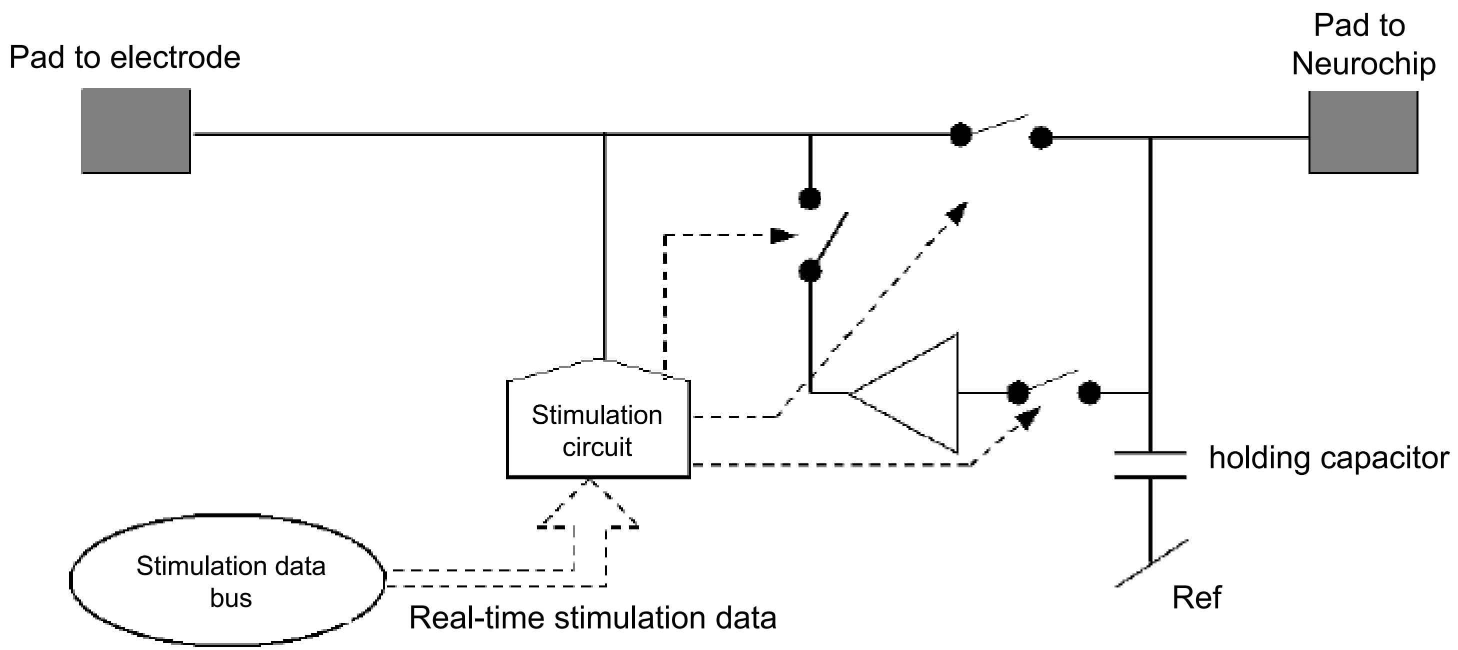


C. Sekirnjak, P. Hottowy, A. Sher, W. Dabrowski, A.M. Litke, E.J. Chichilnisky, “Electrical stimulation of mammalian retinal ganglion cells with multielectrode arrays,” *J Neurophysiol.*, 95(6), pp. 3311-27, 2006



New Stimulation Chip

- Arbitrary stimulation current patterns on all electrodes
- Stimulation artifact suppression



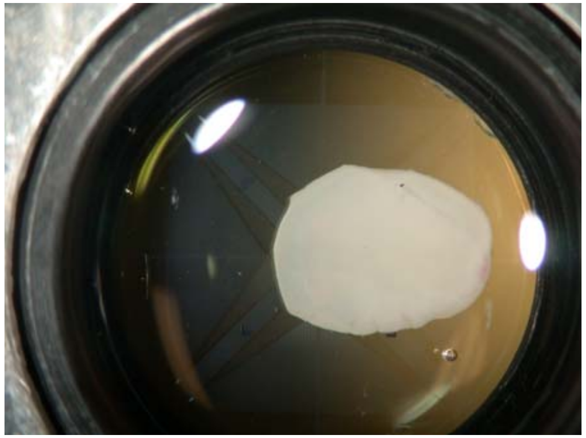
Design by P. Hottowy et al., Krakow

Neural network Activity in brain slices

Current 512 electrode readout and future 512 electrode Stimulation systems
=>

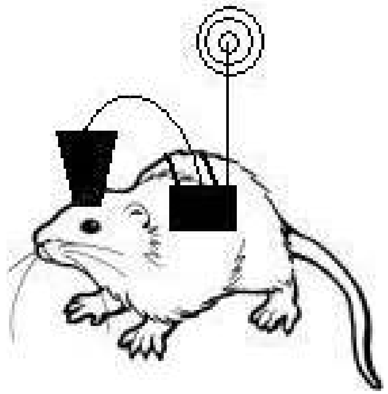
Recording of network activity on unprecedented scale:
•Detailed characterization of the neural network properties

Simultaneous Stimulation and Recording:
•Study of neural plasticity through active interaction with the neural network



Collaboration with J. Beggs (Indiana University)

Recording of brain neural activity of freely behaving animals



Current:
- New 64 channel NeuroPlat chip (built-in AC coupling, digitally controlled gain and bandpass)
- Digital logic circuitry to set gain and bandpass on power-up, and to provide continuous multiplexer commands
- Battery operated
- "Spy" FM transmitter and receiver

Future:
Addition of electrical stimulation with the new StimChip

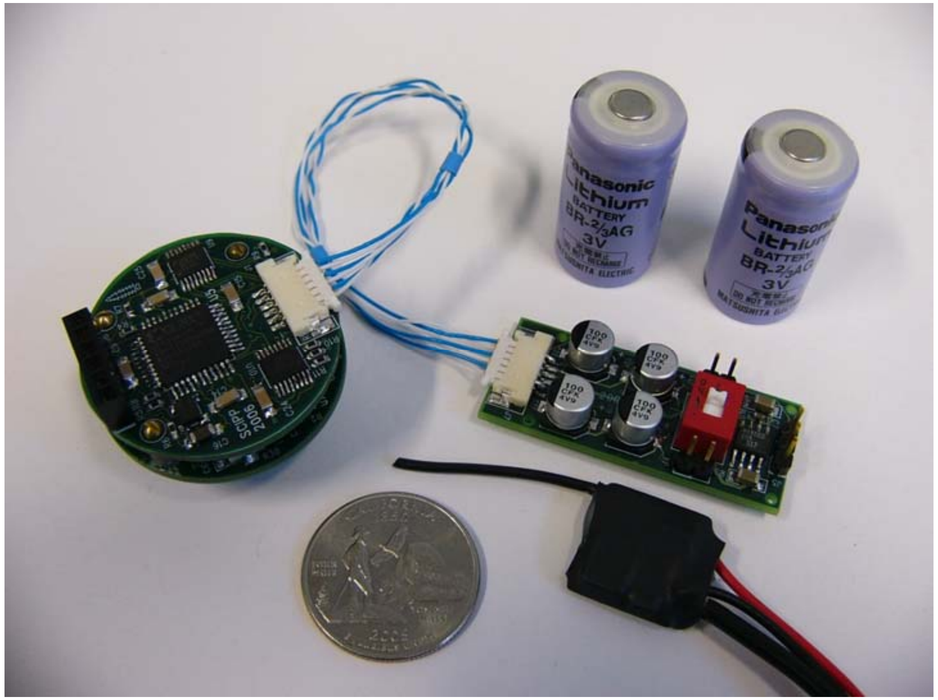
Some applications (and advantages over the existing wired systems):

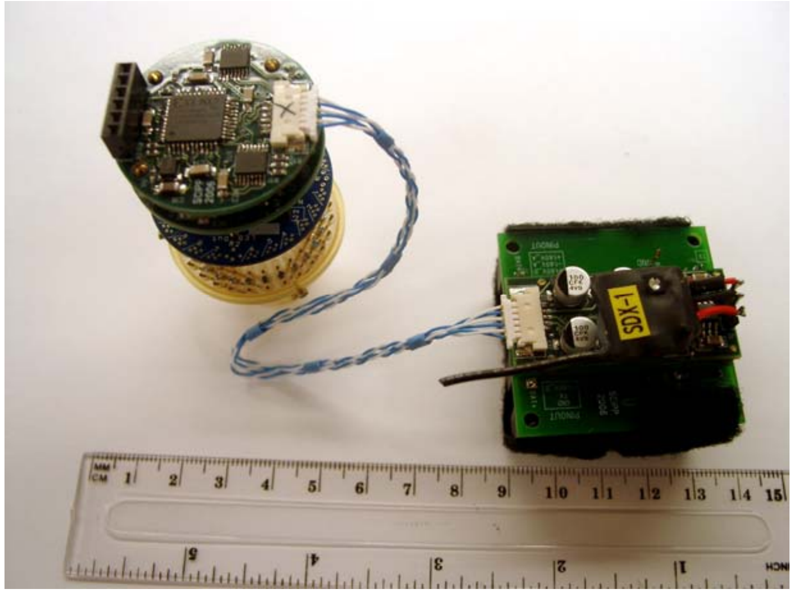
- Study of brain activity in rats (larger scale of movement; 3D; more natural environment; better scales to larger number of electrodes)

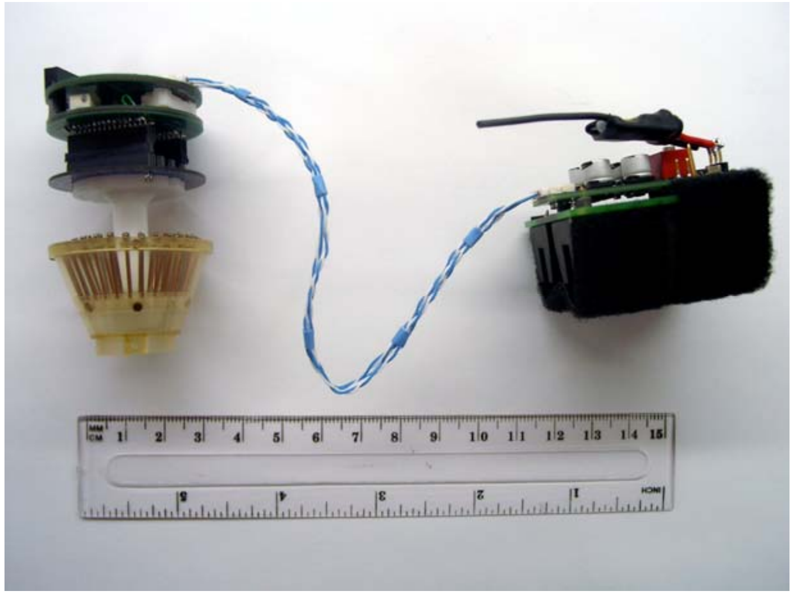
- Study of navigation system in barn owls (IN FLIGHT)

Collaboration with M. Meister (Harvard U.), T. Siapas (Caltech)

Recording of brain neural activity of freely behaving animals







Prototype system:
- 64 channels
- 20kHz per channel sampling rate
- Noise: <15μV
- FM signal transmission: up to 60m
- Weight: 80g
- Operation time: 10hours

Successfully tested on a rat two weeks ago!

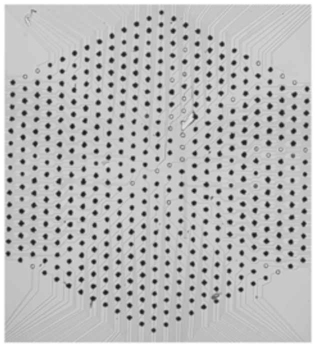
Future Directions: Technology

•Develop a stimulation system based on the new Stimchip. (retinal prosthesis, brain slices).

•Further develop the in-vivo system, increasing the number of readout channels and adding stimulation capabilities.

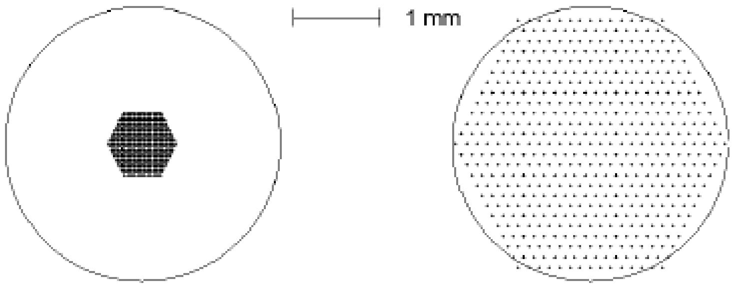
•519 electrode arrays with larger (120μm) spacing.

•Continue work on 30μm spacing 519 electrode array (K. Mathieson, *et al.,* University of Glasgow).



30μm prototype

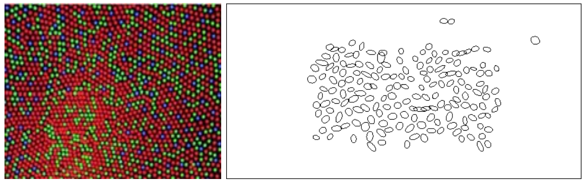
519 electrodes

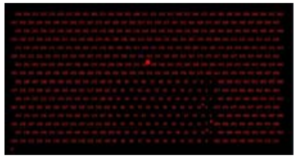


30μm 120μm

Future Directions: Biology and Medicine

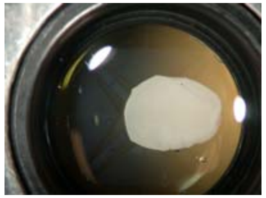
Ongoing:
•Study of new cell types and color processing in primate retina.



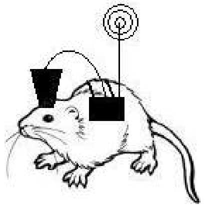


•Retinal development.

•Retinal prosthesis.



•Study of network activity in the brain slices.



•Study of brain activity in freely-behaving animals

Some of the potential:
•Wireless recording of brain activity in epilepsy patients

•Screening for neural toxicity