From the Microplex to Neural Systems

Alan Litke

Parker Symposium

31 March 2012

It All Started with Sherwood!!

DEVELOPMENT OF HIGH DENSITY READOUT FOR SILICON STRIP DETECTORS

James T. WALKER

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Sherwood PARKER

University of Hawaii, Hawaii, USA

Bernard HYAMS

CERN, Geneva, Switzerland

Stephen L. SHAPIRO

Stanford Linear Accelerator Center, Stanford, CA, USA

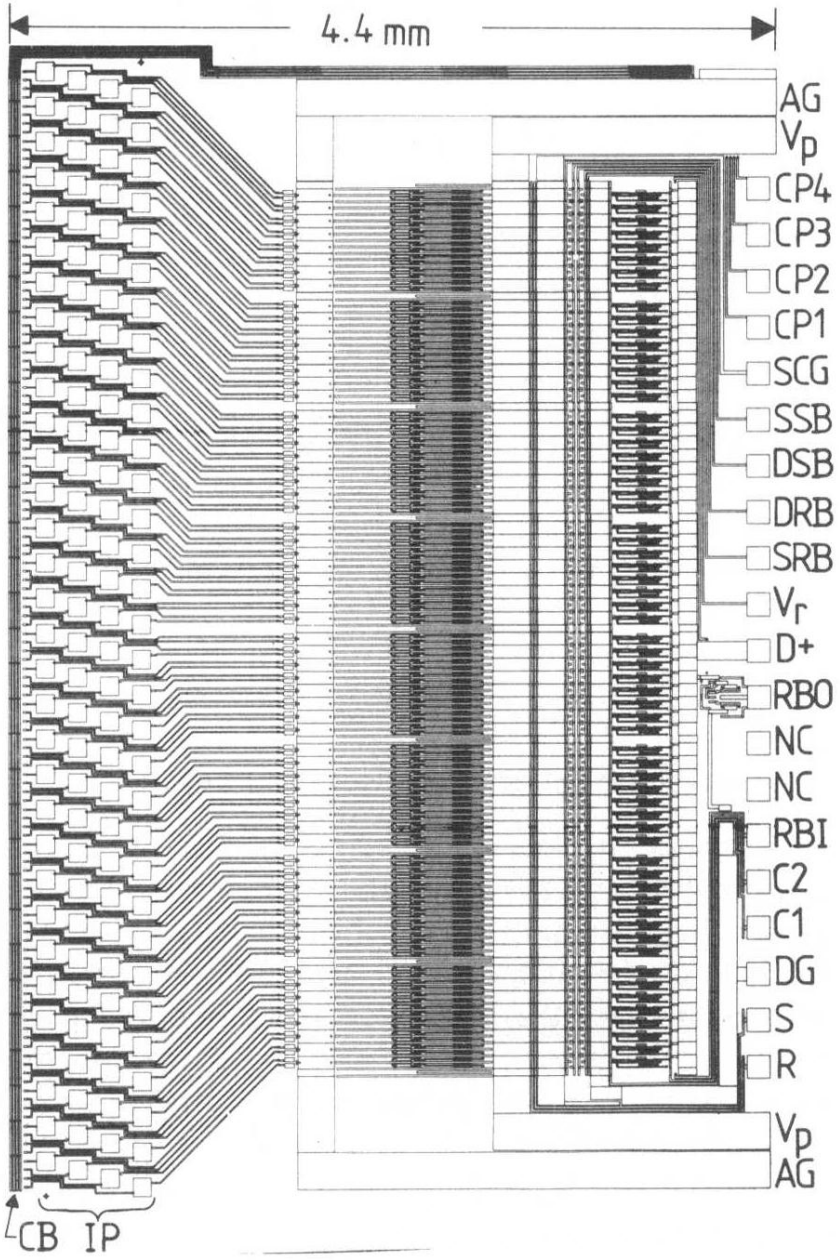
Microplex Chip

NIM **226** (1984) 200-203.

A compact readout for silicon strip detectors is being developed. It employs an nMOS circuit with 128 channels of charge sensitive amplifiers and multiplexed output.

Microplex Layout

- 128 low-noise amplifier channels
- Multiplexed output
- High Density Wire Bonding



Application to Other Scientific Fields

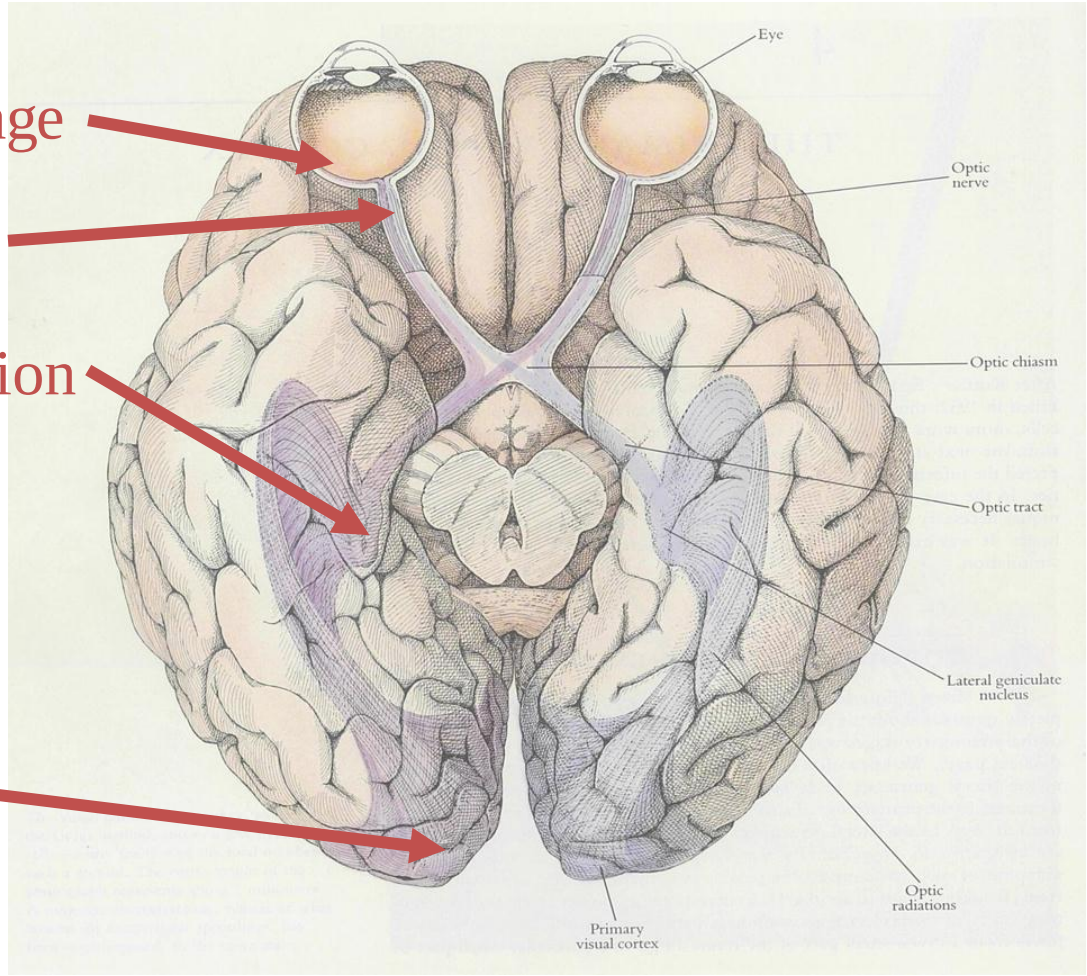
Pixel detector +
first processing stage

cable

relay station

The Visual System

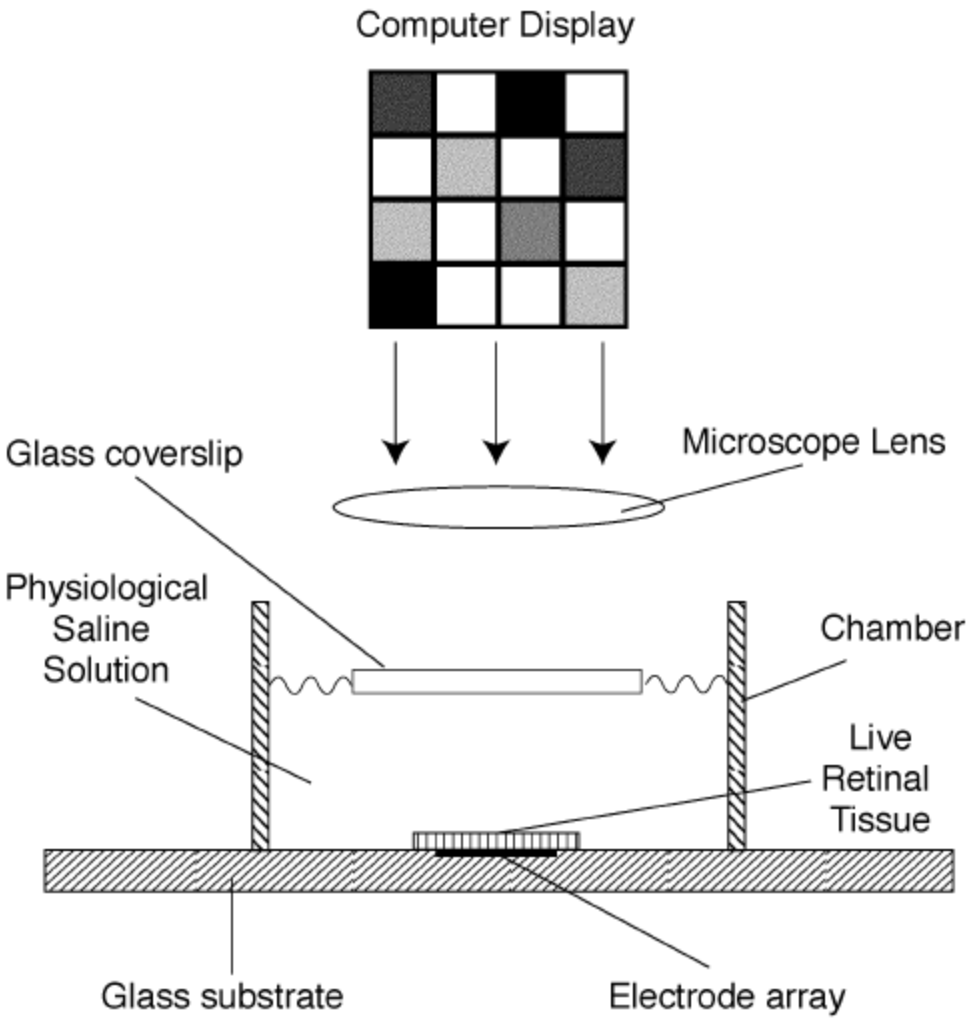
more
processing

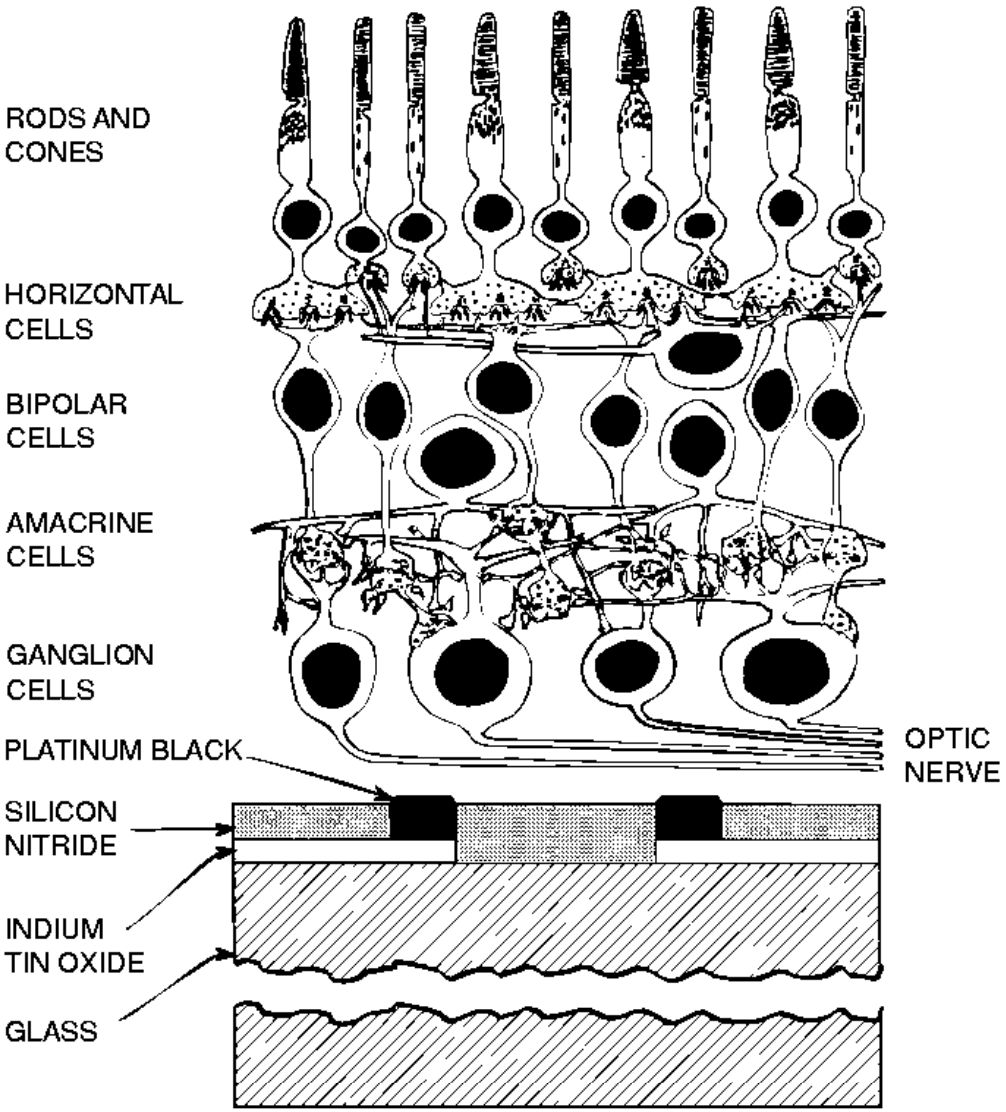


How do neural systems develop (get wired up)?
How do neural systems process information?
How can neural systems be repaired when something goes wrong (due to injury or disease)?

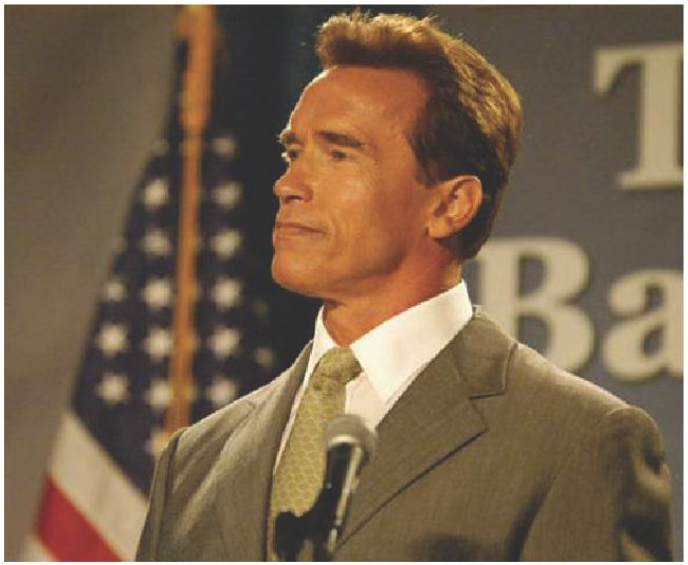
Functional Properties of the Retina

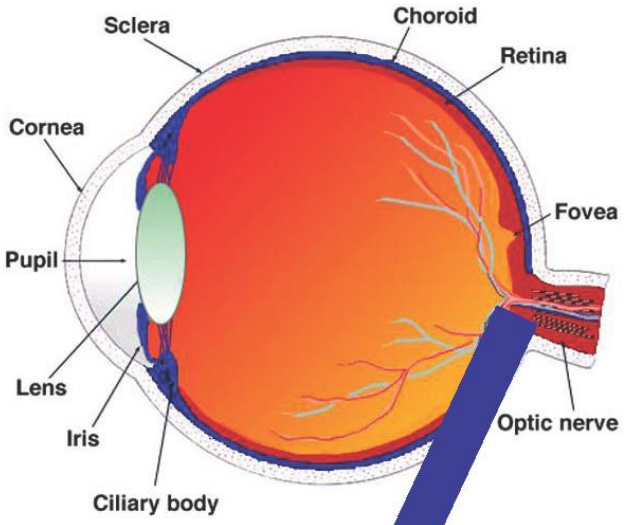
M. Meister, J. Pine, D. A. Baylor,
J. Neuroscience Meth. 51 (1994) 95.

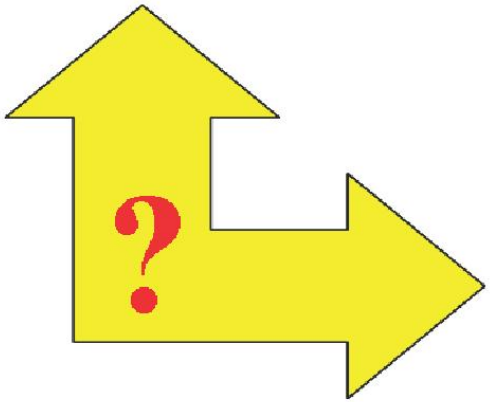


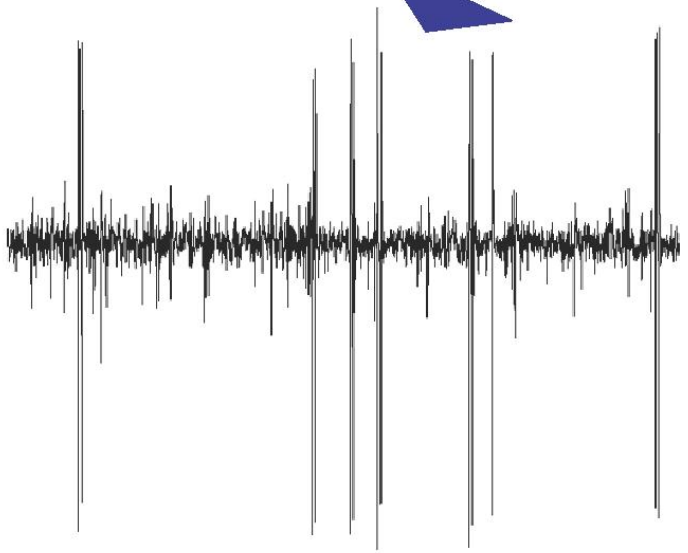

RODS AND
CONES
HORIZONTAL
CELLS
BIPOLAR
CELLS
AMACRINE
CELLS
GANGLION
CELLS
PLATINUM BLACK
OPTIC
NERVE
SILICON
NITRIDE
INDIUM
TIN OXIDE
GLASS

Recording Neural Activity: Retina

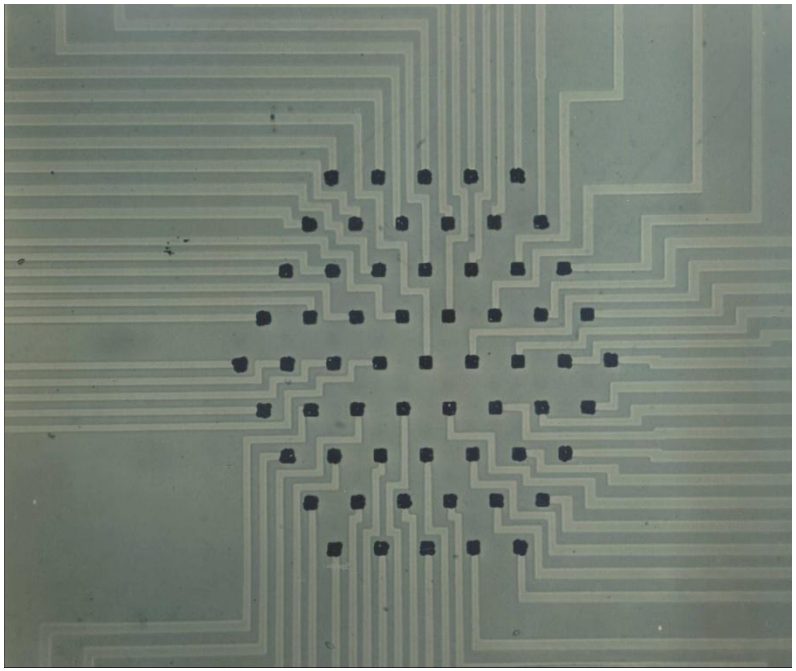








State-of-the-Art Multielectrode Array (1990)



- 61 electrodes,
- 60 µm electrode spacing,
- conventional electronics
- Mechanical "zebra" interconnect,
- tens of retinal ganglion cells simultaneously detected

How do we increase, by an order of magnitude, the number of neurons simultaneously detected –
from tens of neurons to hundreds of neurons?

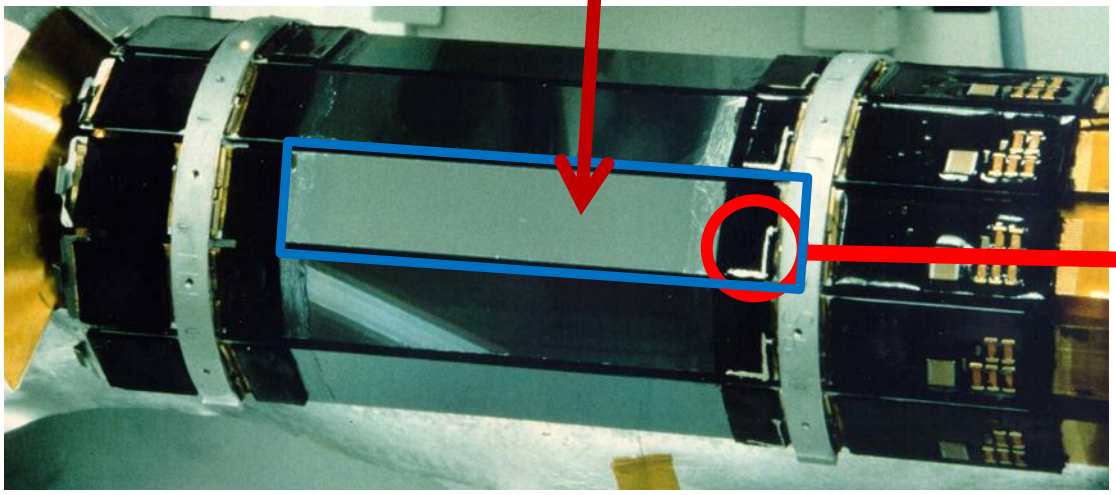
Number of Neurons: one→tens→hundreds→???
Number of Electrodes: 1→61→512→???

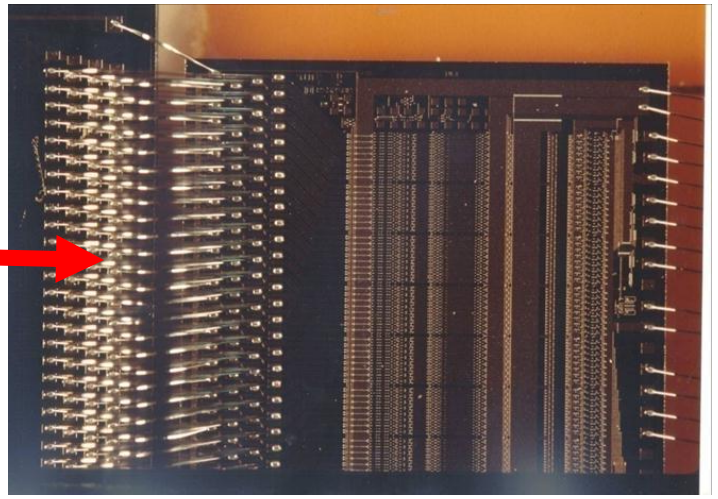
Sherwood, with the SSVD project, had shown the way:

- Silicon nanofabrication technology
- Multichannel low-noise analog amplifier integrated circuits
- Time multiplexing
- High-density wire bonding for interconnect

→ Make a Neural Recording (&Stimulation) Module
look like an SSVD Module

Turn a 61-electrode multielectrode array into something like a 512-channel Silicon Strip Detector Module





Silicon Strip Vertex Detector:
512 channels/module (18K channels total)

Microplex readout chip
(128 channels, 47.5 µm pitch)

Electrode Array Geometries

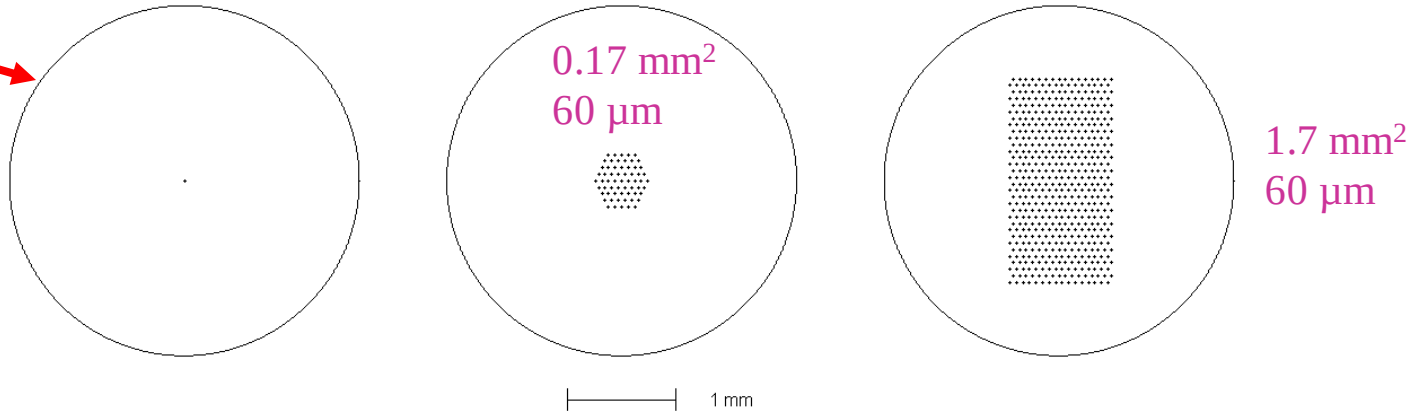
(Electrode diameters = 5 µm; area and electrode spacing given below.)

Input region for monkey MT neuron

1 electrode:
"traditional"

61 electrodes:
previous state-of-the-art

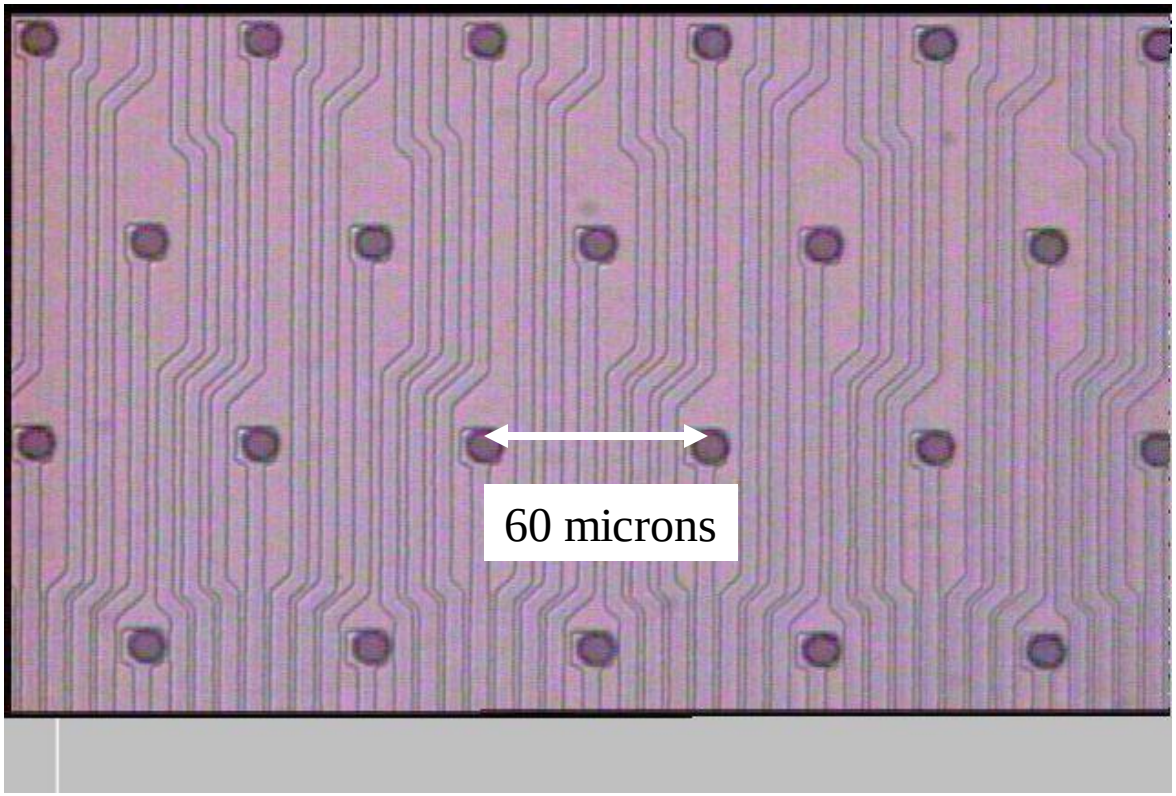
512 electrodes (32x16):
standard system



519 electrodes:
high density
(developed by U. Glasgow)

519 electrodes:
large area

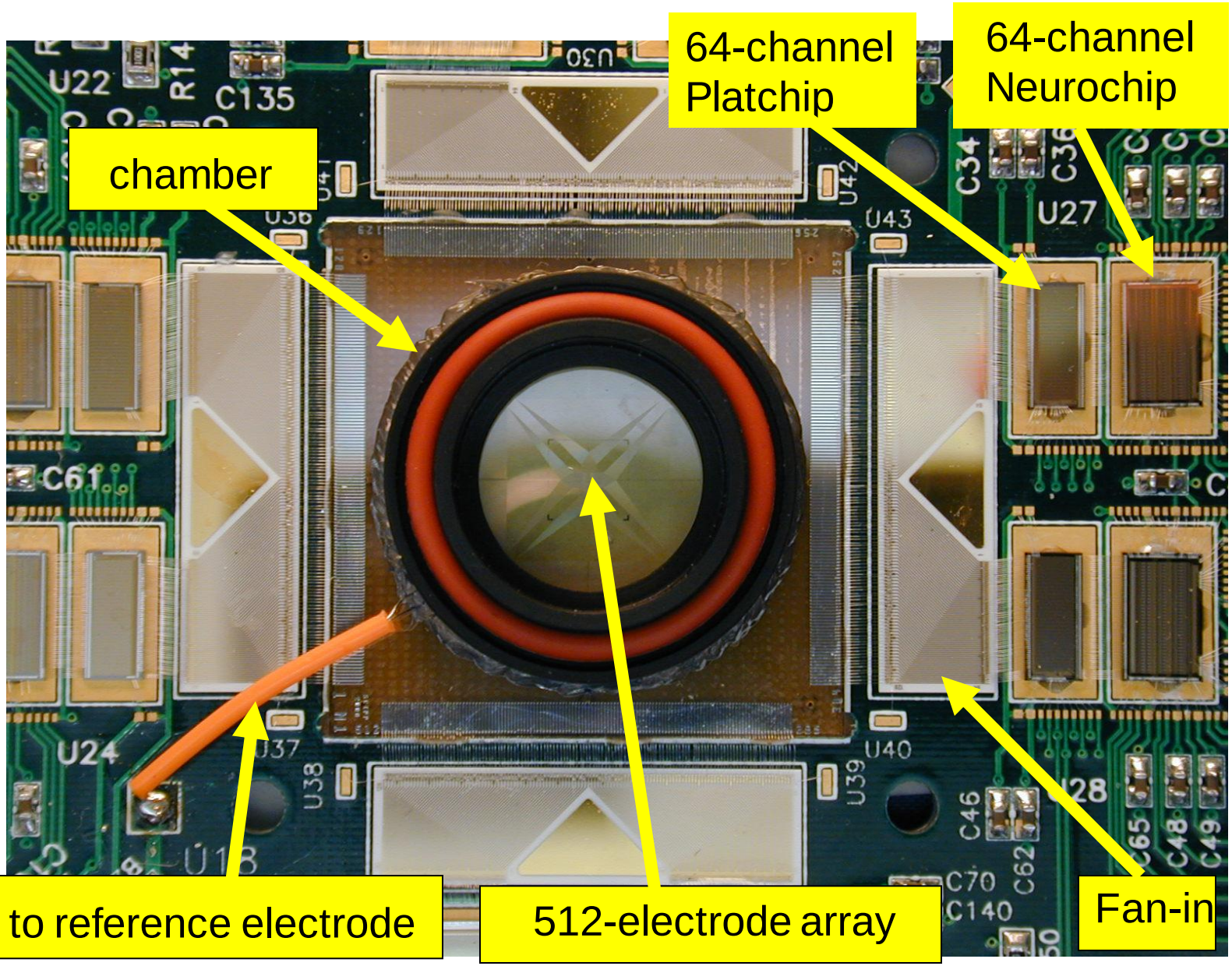
Section of
512-electrode Array (32x16)



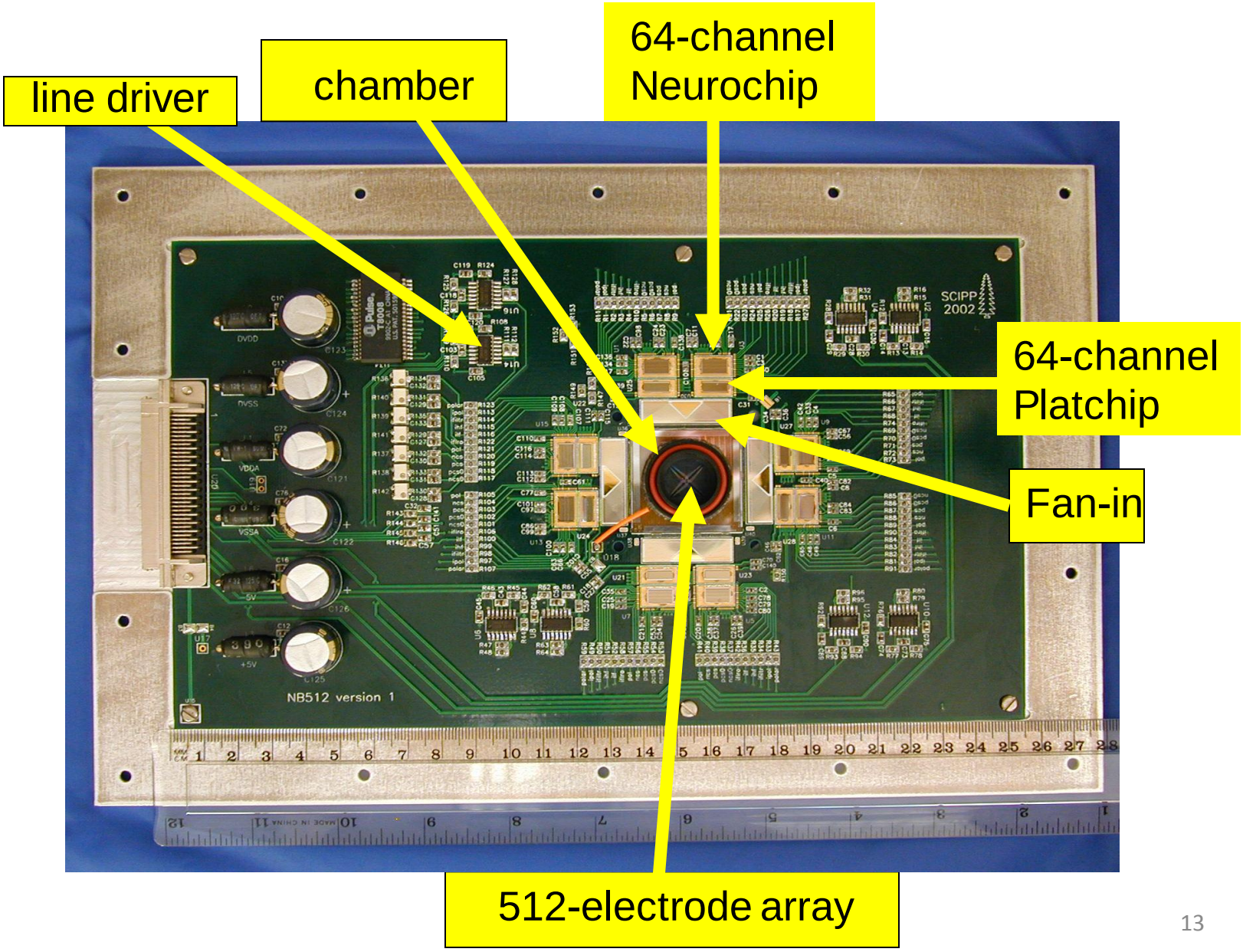
Electrode diameter = 5 μm

(Litke et al., IEEE Trans. Nucl. Sci. (2004) 1434)

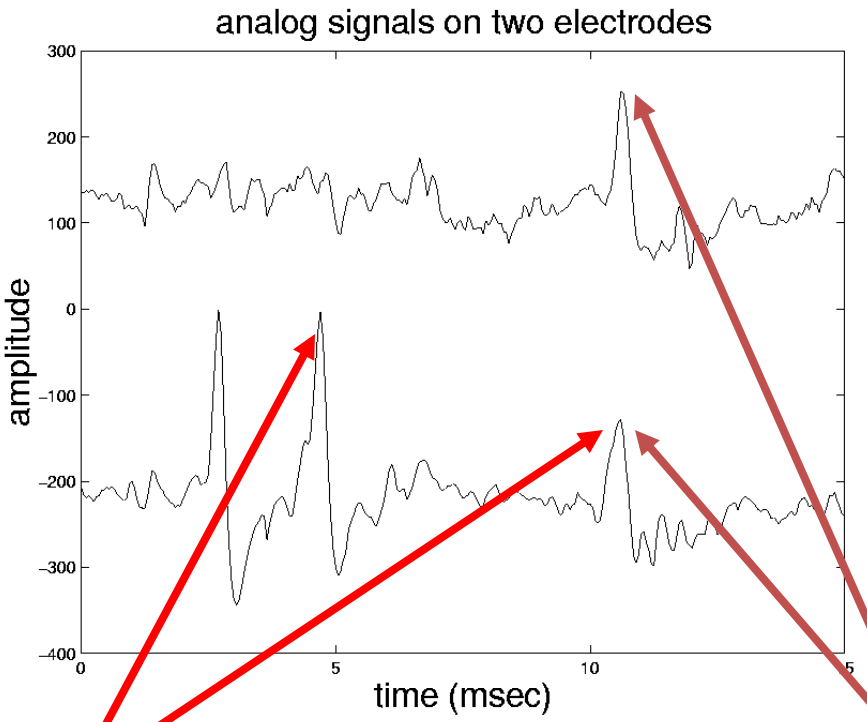
Section of 512-electrode “Neuroboard”



512-electrode “Neuroboard”



Spikes on electrodes ⇒ spikes from identified neurons



2 separate cells recorded on same electrode

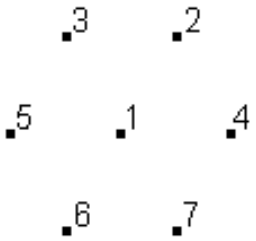
Same cell recorded on 2 electrodes

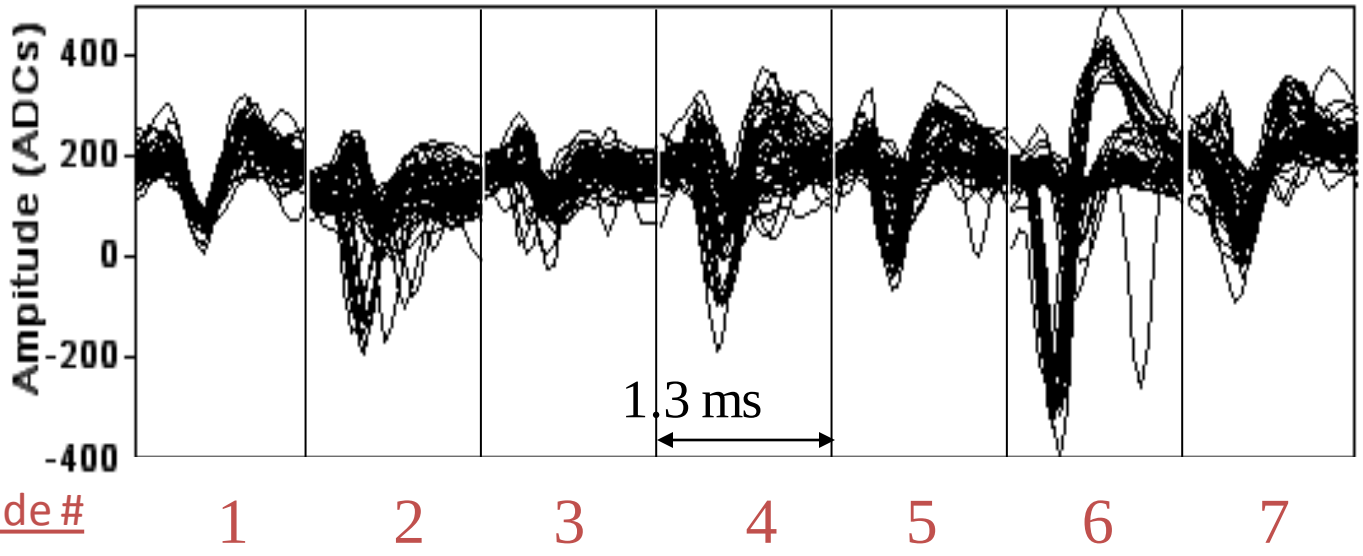
Neuron Identification

(signals on electrodes ⇒ spikes from identified neurons)

7x26=182 measurements

Multiple electrodes



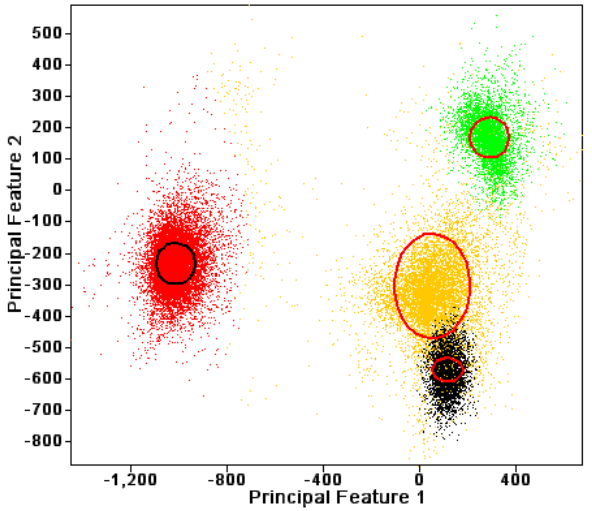


- Principal Components Analysis

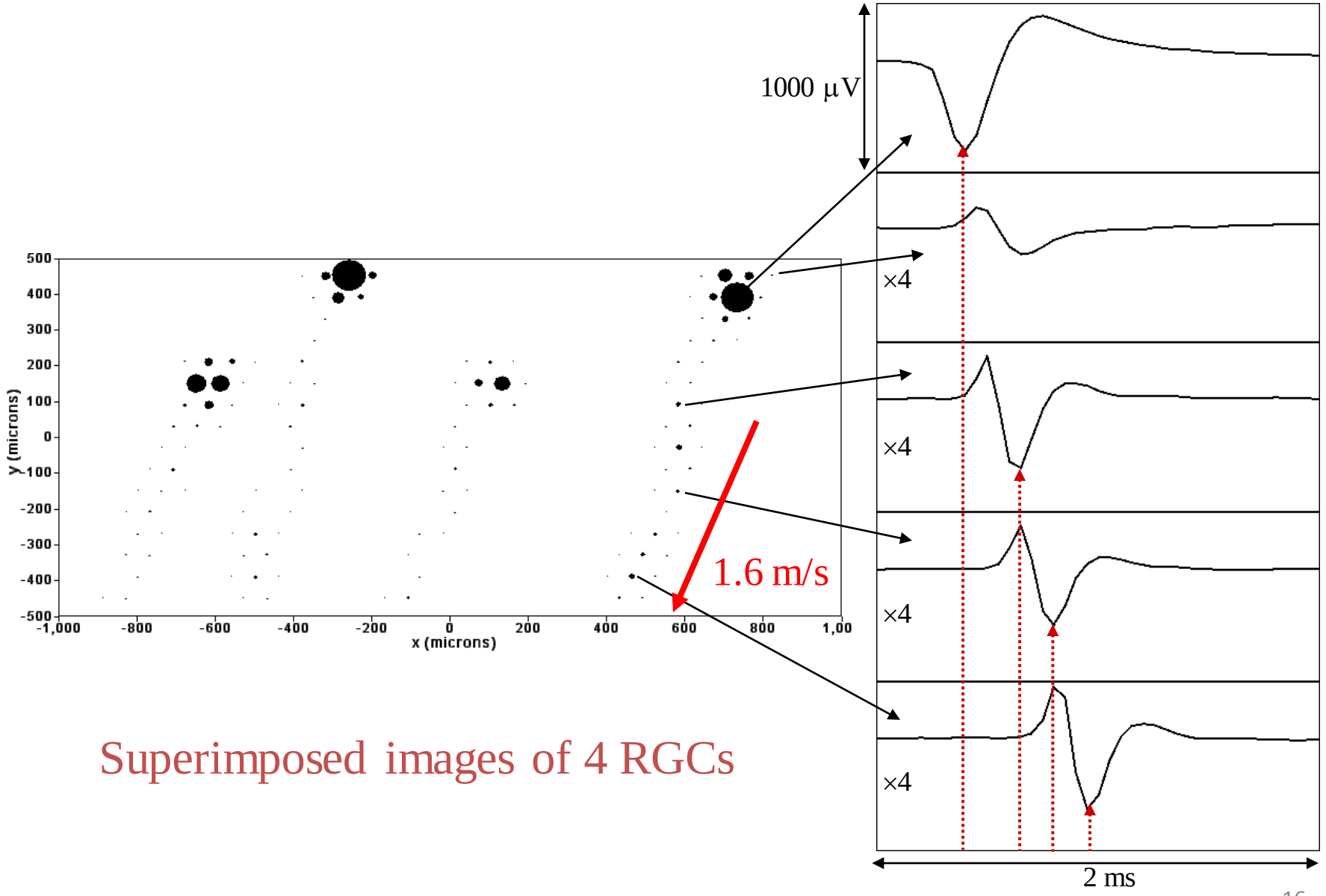
Find ~5 most significant variables that are linear combinations of the 182 measurements

- Multidimensional Clustering

⇒ Identified Neurons



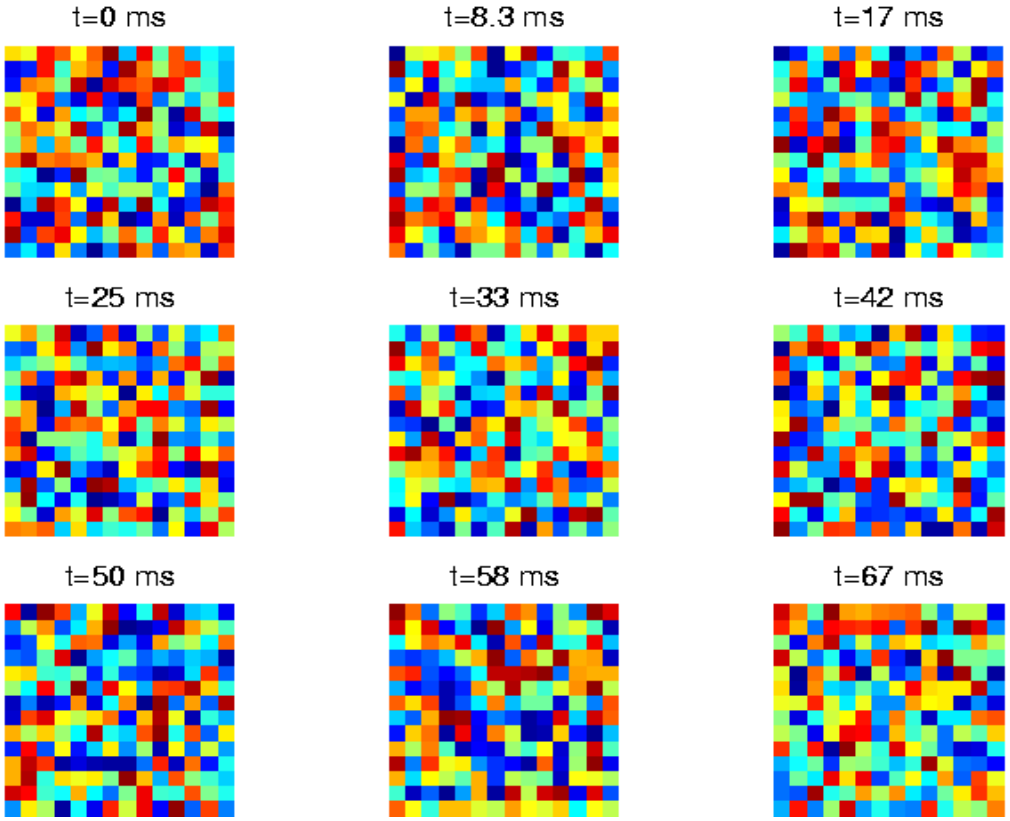
Electrophysiological Imaging

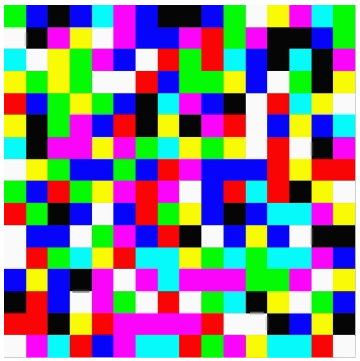


Superimposed images of 4 RGCs

Measure the visual response properties of identified neurons

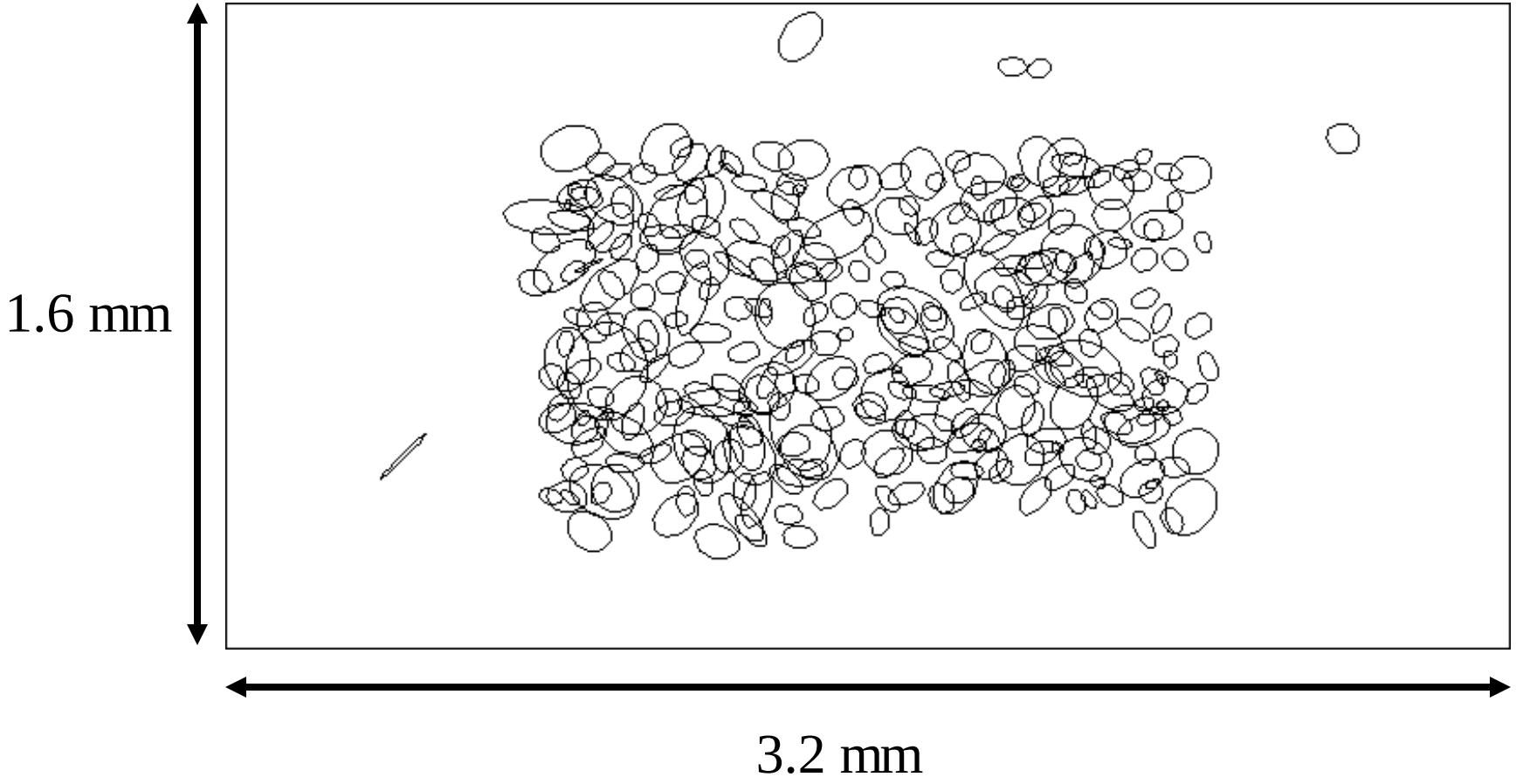
⇒ white noise analysis: use time sequence of random checkerboard images

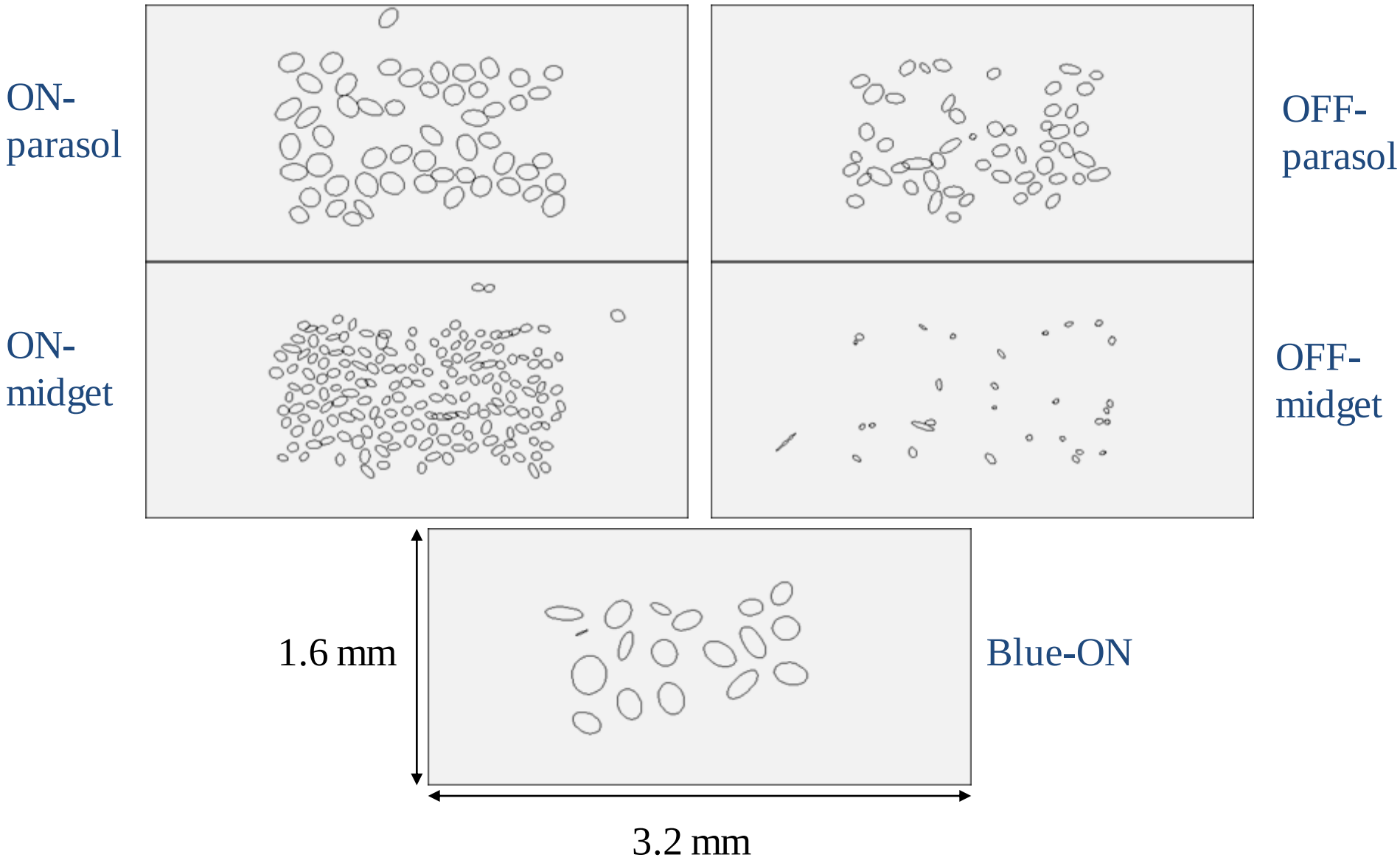




⇒ measure the "spike-triggered average" (sta) response for each neuron

Light-sensitive regions ("receptive fields") on the retina for 338 identified retinal ganglion cells (RGCs)



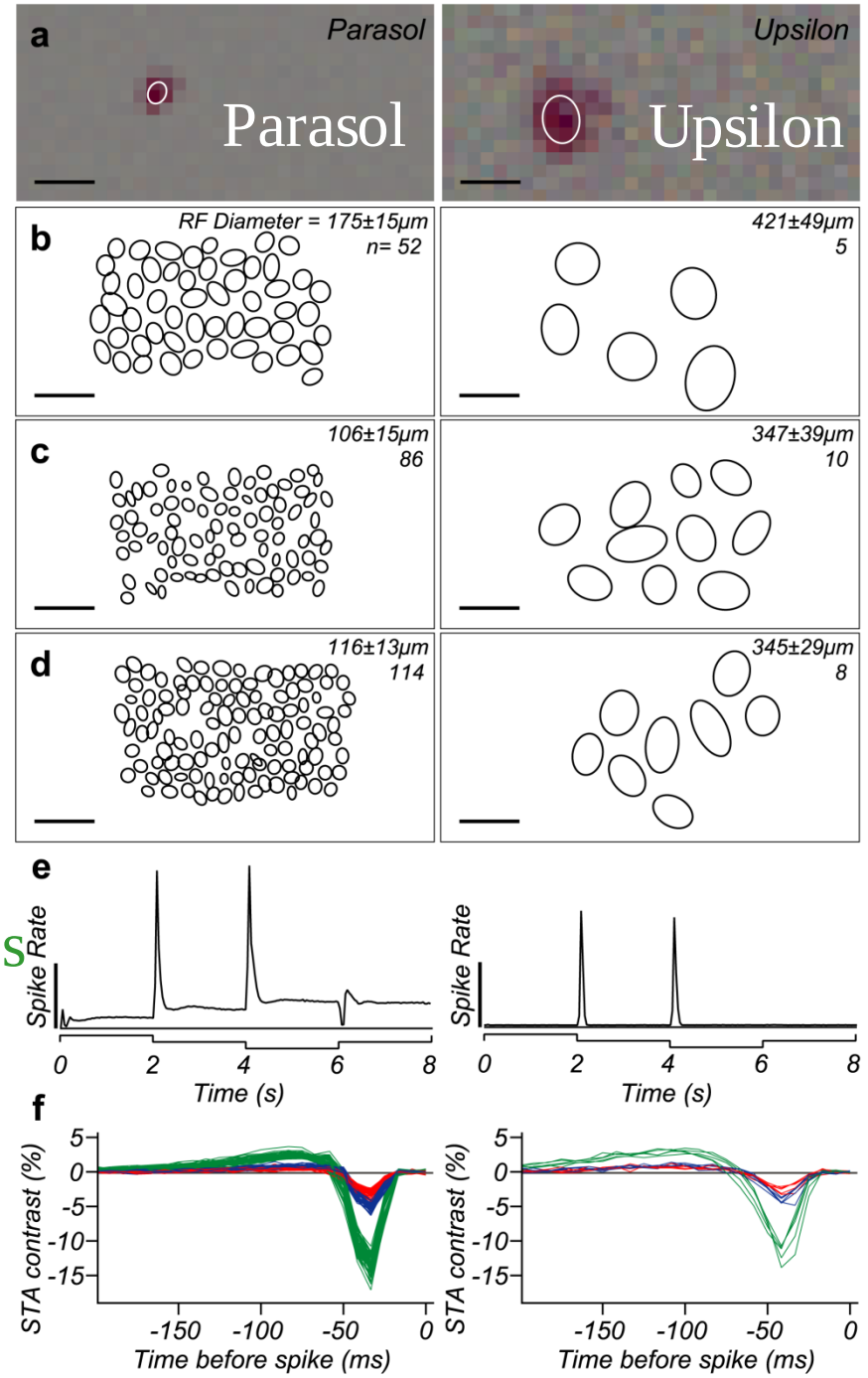

ON-parasol
OFF-parasol
ON-midget
OFF-midget
1.6 mm
Blue-ON
3.2 mm

Receptive field

Mosaics in 3 preparations

Response to diffuse light steps

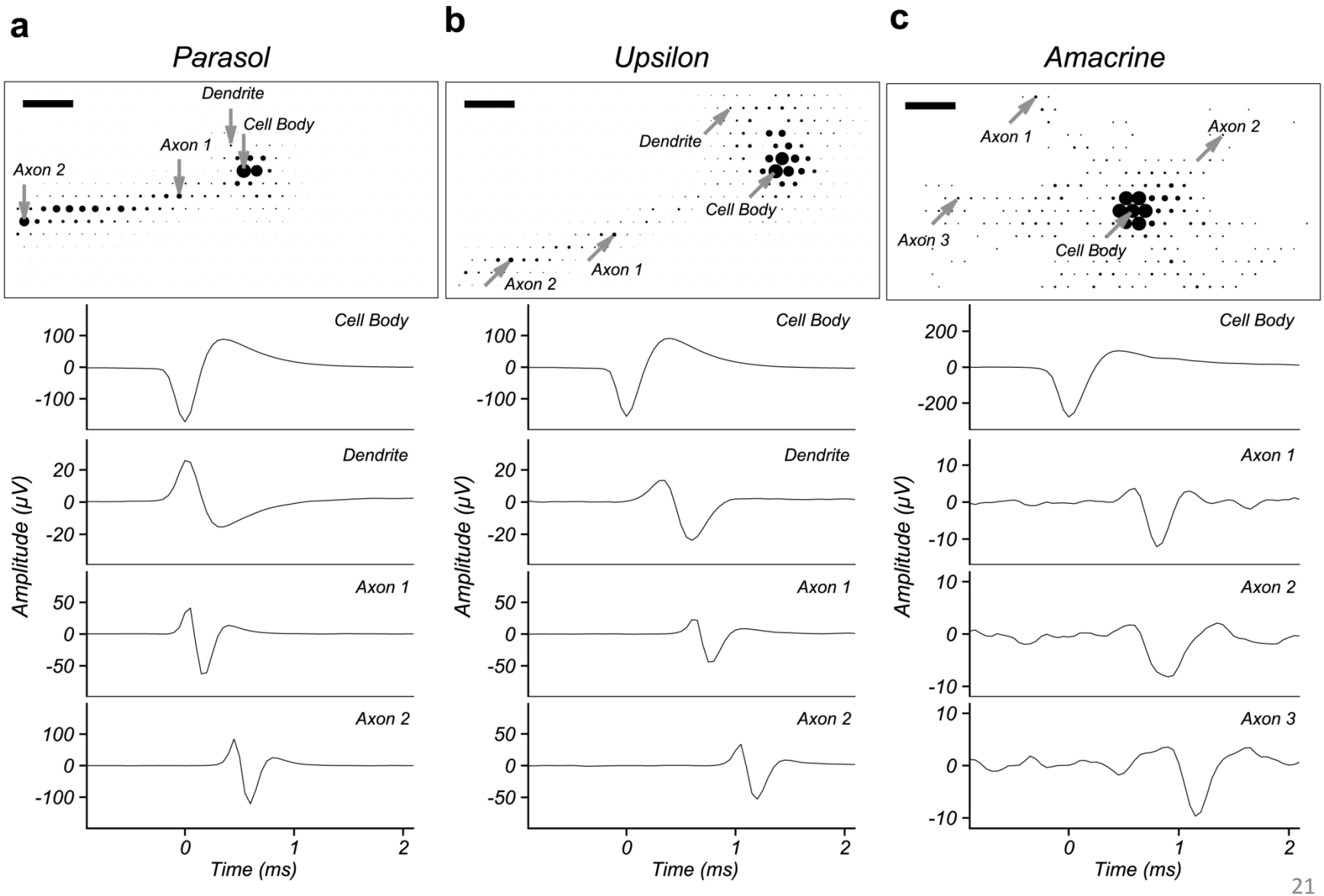
Sta time filter



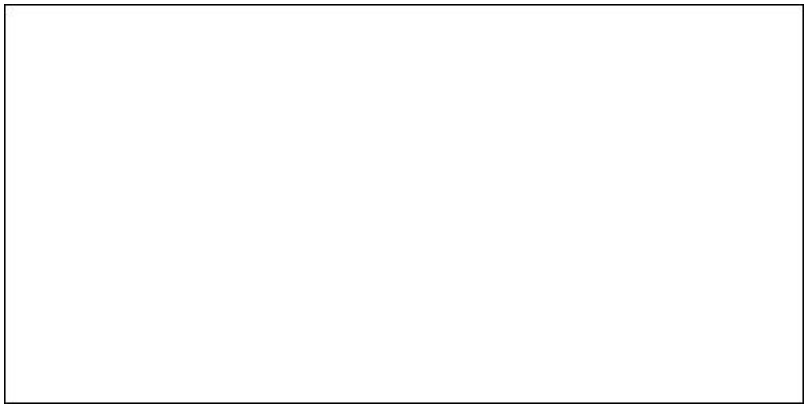
Parasol

Upsilon

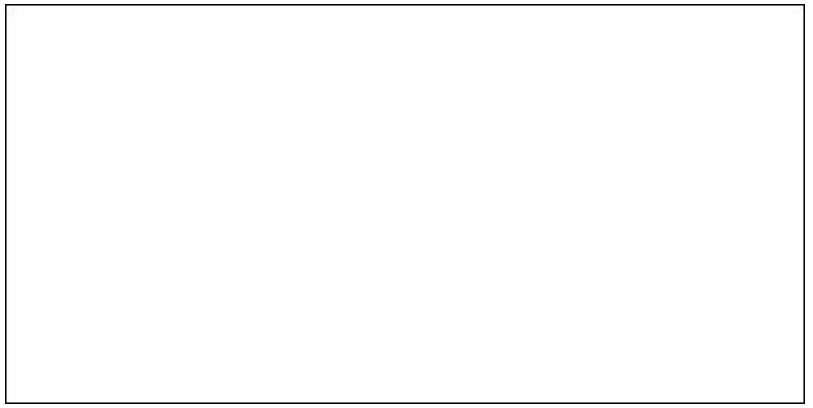
Amacrine



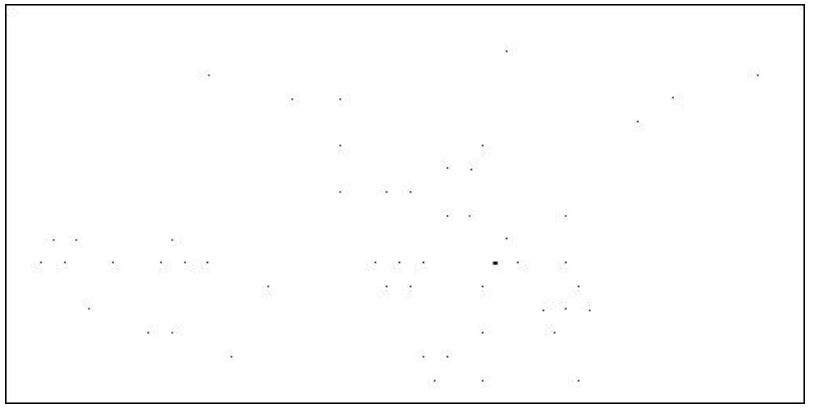
OFF Parasol



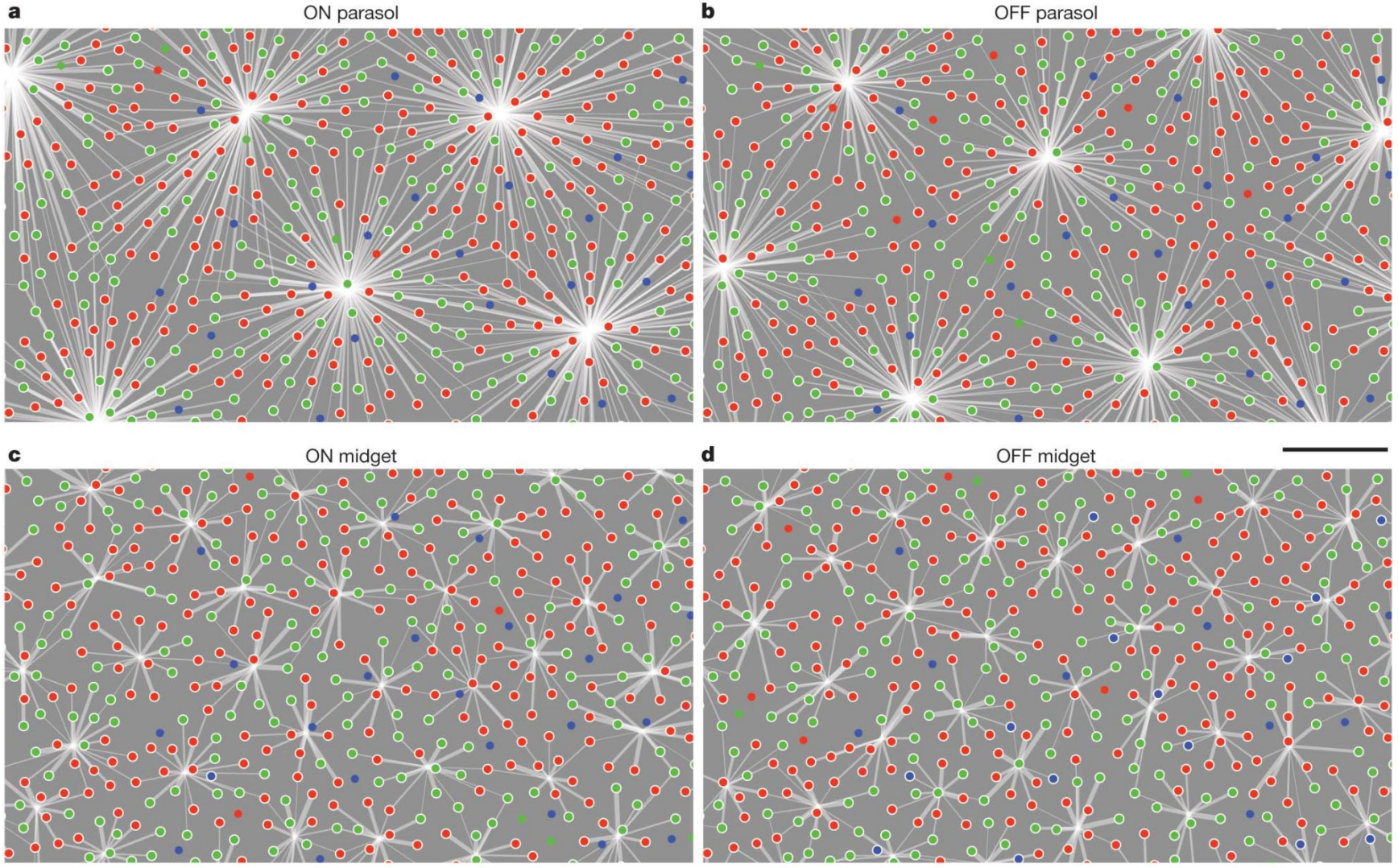
Upsilon



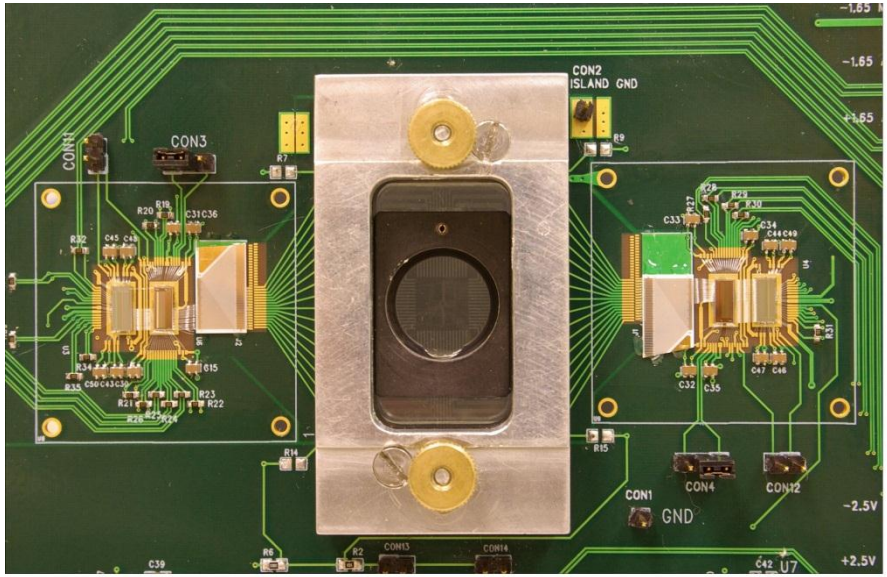
Polyaxonal Spiking Amacrine

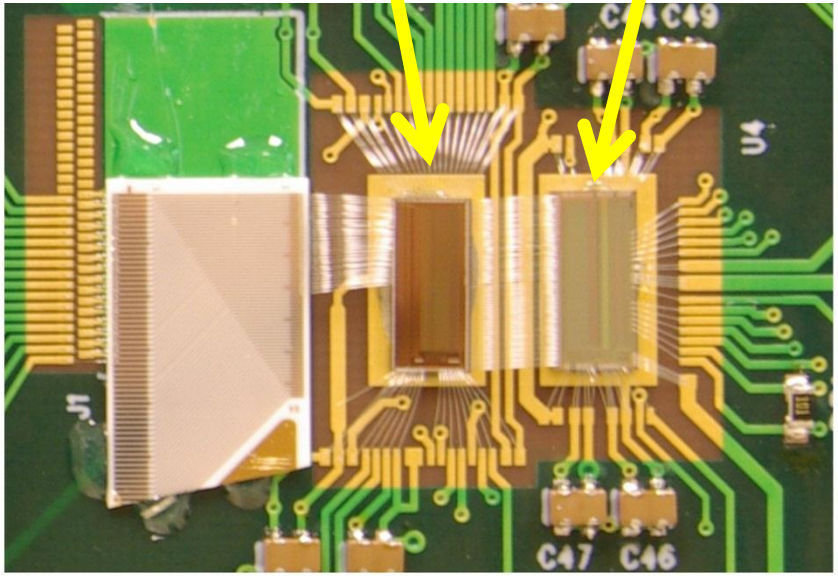


Functional connectivity in the retina at the resolution of individual photoreceptors and individual retinal ganglion cells (Field et al., Nature 2010)



61 Electrode Neural Stimulation/Recording System



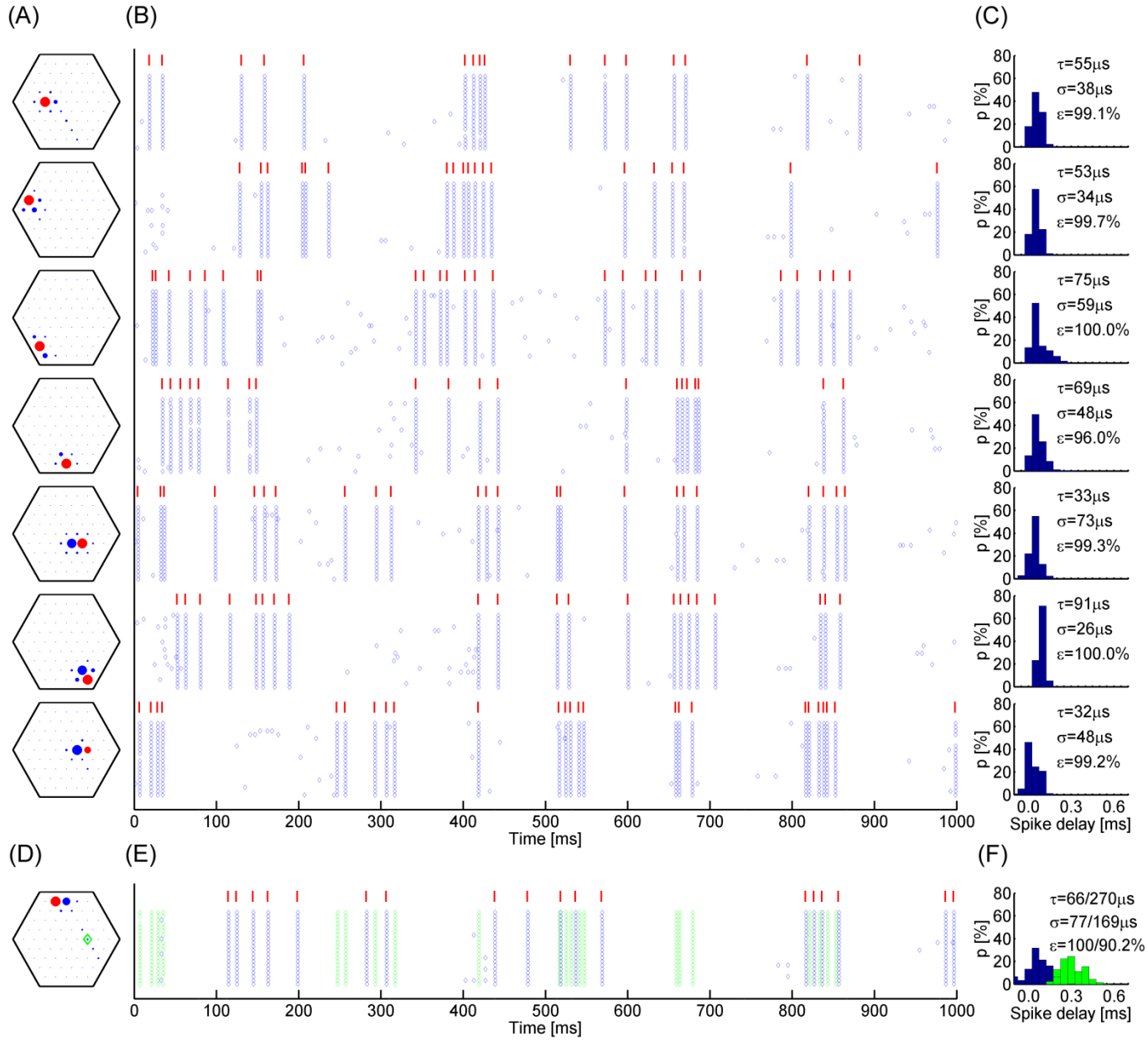


Stimchip

- 64 channels
- ability to generate arbitrary, independent stimulation pulses on each channel, under software control
- → spatio-temporal patterned stimulation

(P. Hottowy et al., Analog ICs and Sig. Processing **55** (2008) 239)

Spatio-Temporal Patterned Stimulation of Multiple Neurons with Multiple Electrodes
(Application to Retinal Prosthesis Studies)



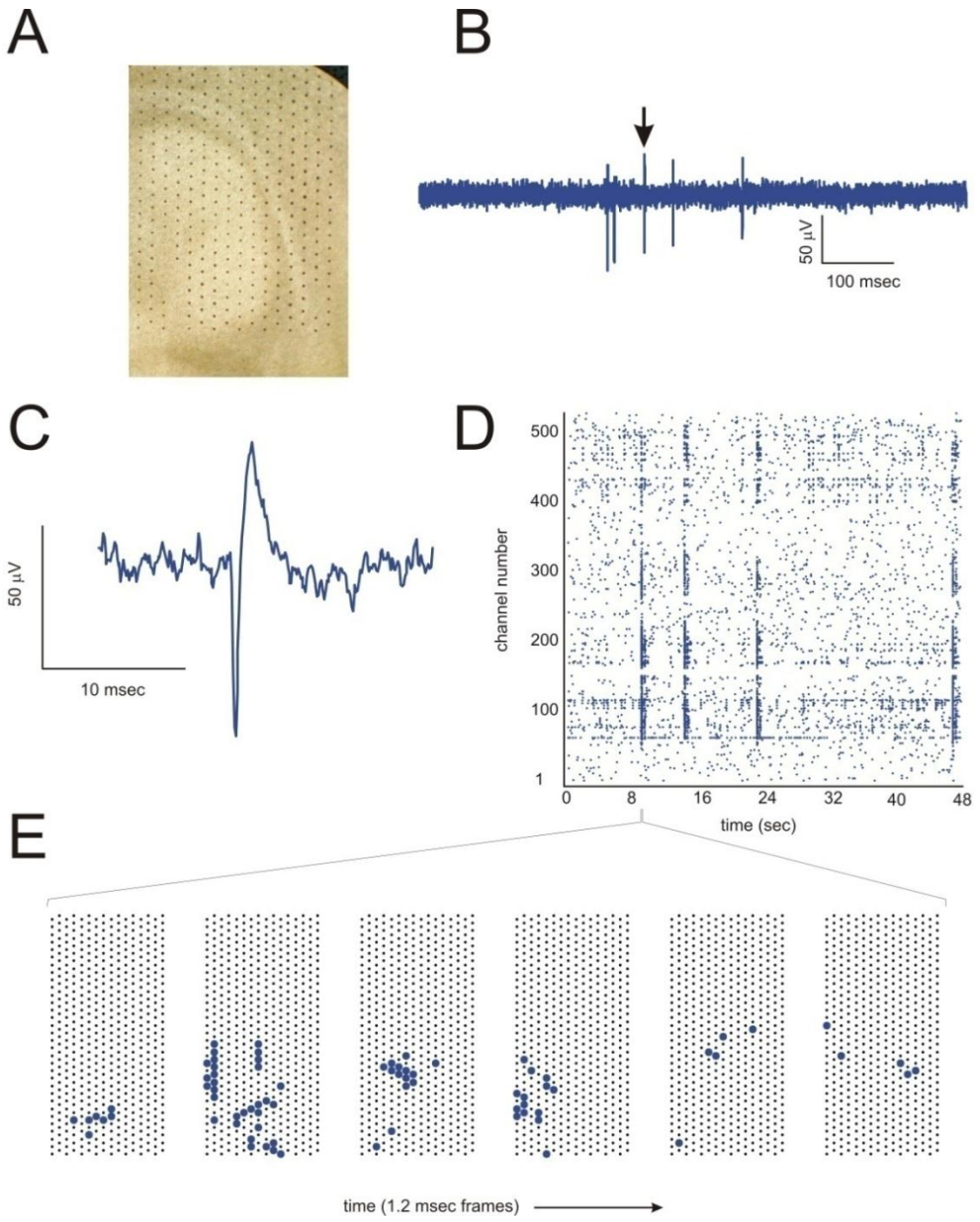
Technology Development and Applications to Other Neural Systems:

Cultured Brain Slices
(with John Beggs, Shinya Ito, Frances Yeh)

- Neural Connectivity and Neural Circuitry
- Neurological Disorders (with transgenic mice)
- Neurotoxicity

Stimulating & Recording Neural Activity: Cultured Brain Slices

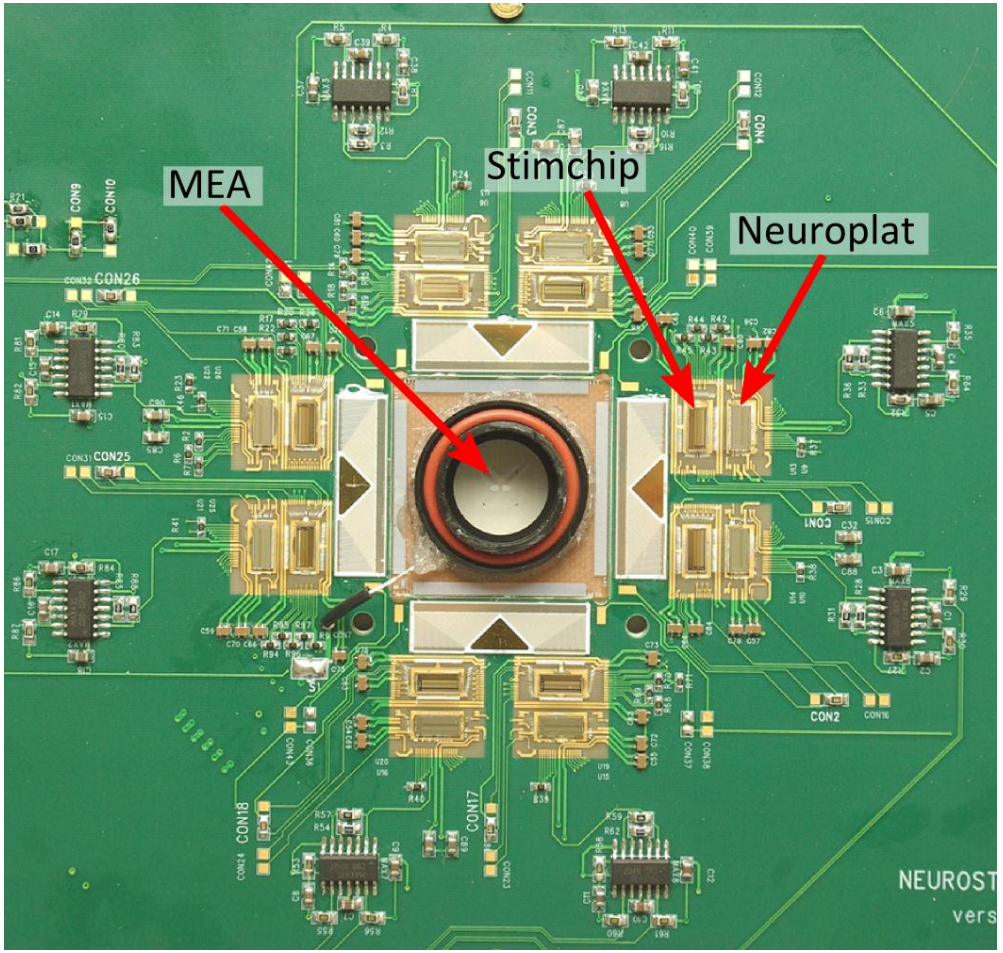
Rat cultured cortical slice on 512-electrode array



512 Electrode System for Stimulating and Recording Neural Activity

write information into a cortical network and then record its response

$\Rightarrow$ use multielectrode electrical stimulation combined with multielectrode recording (as with retinal prosthesis studies)

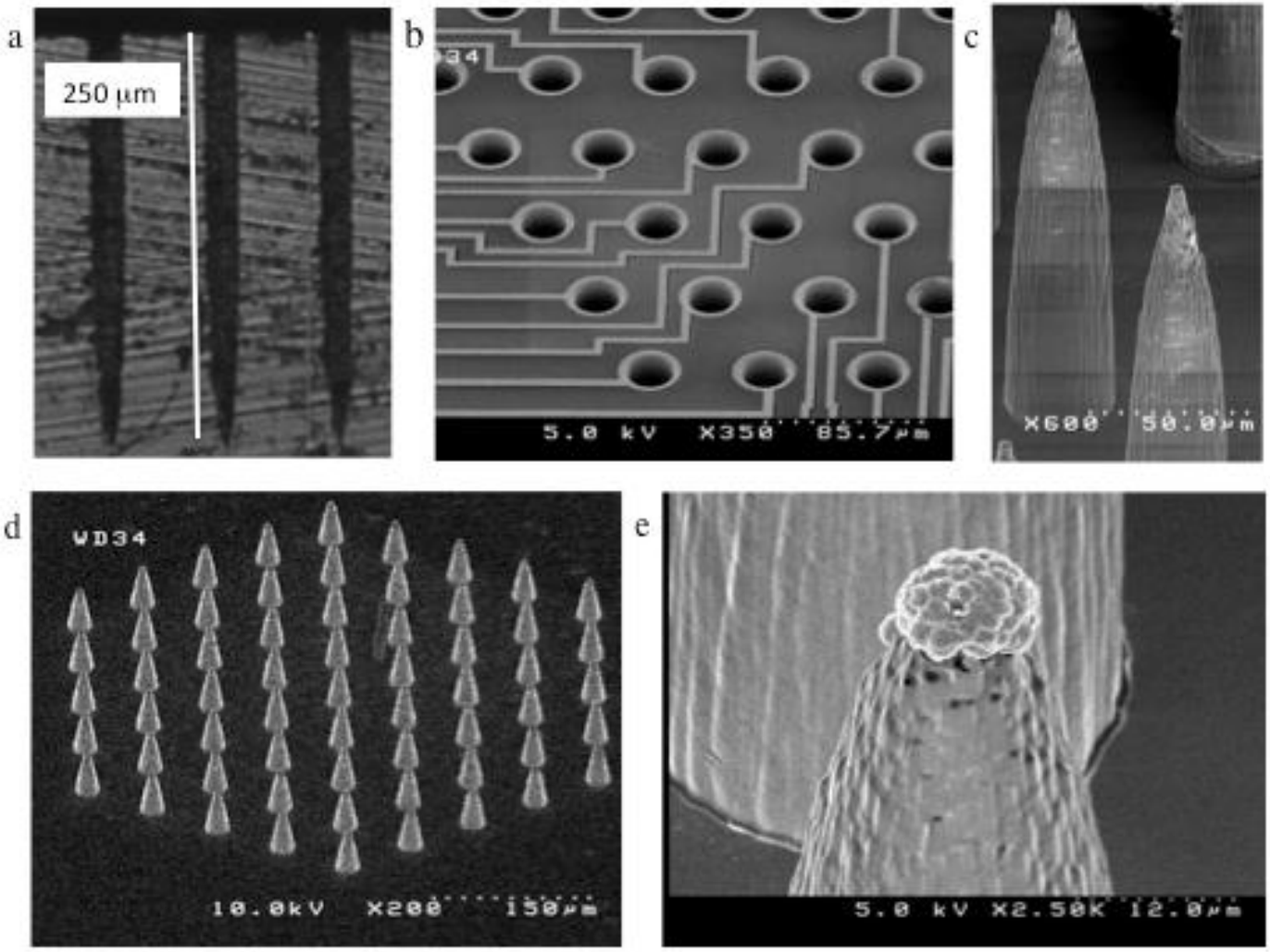


Acute Brain Slices

Bed-of-Nails electrode arrays:
can penetrate through ~50 microns of dead tissue due to cut

- Based on 3D Detector Technology from Sherwood
- First Mechanical prototypes fabricated by Chris Kenney
- Electrically Active Bed-of-Nails Arrays Implemented by Debbie Gunning

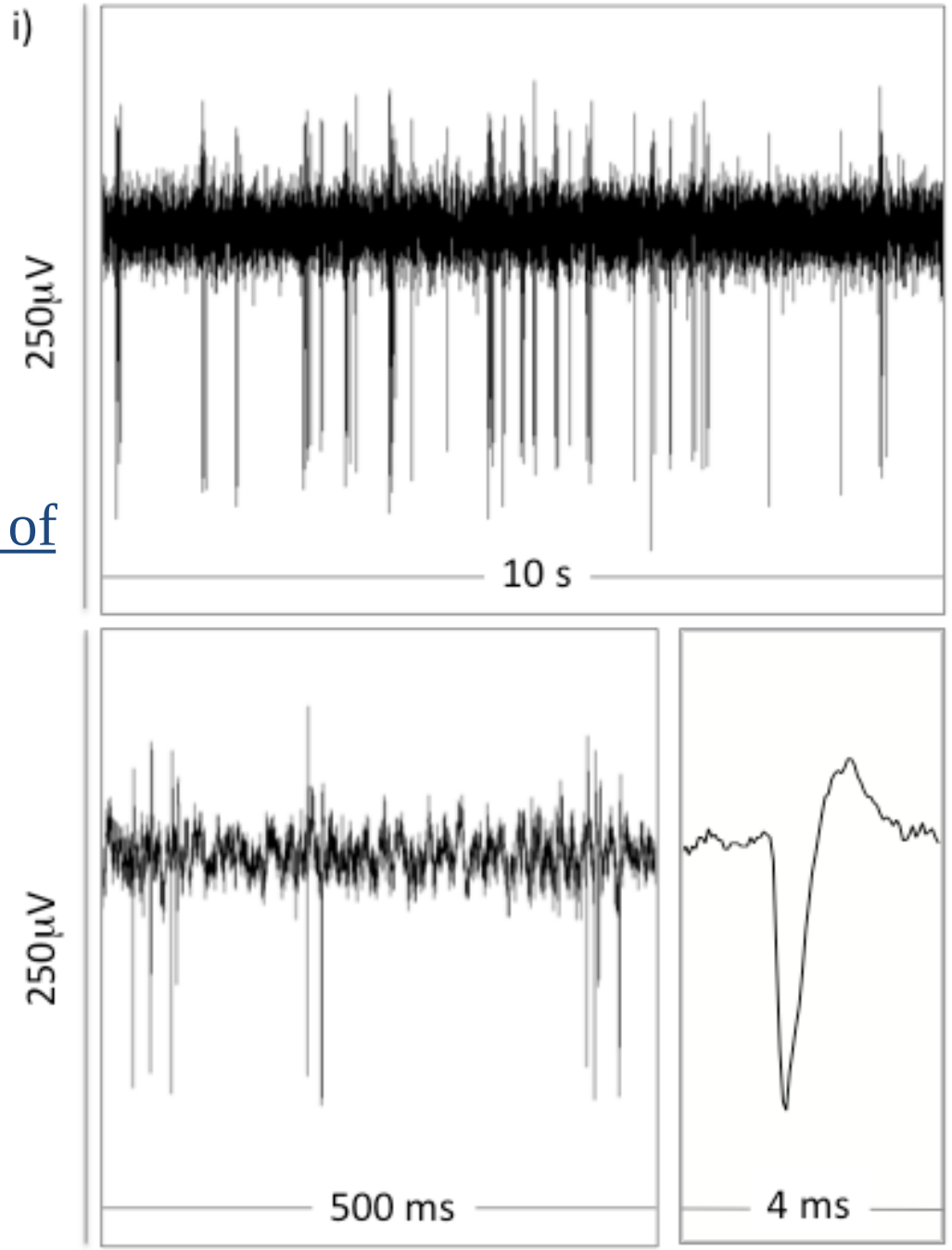
Bed-of-Nails Electrode Array:
(Fabricated by Debbie Gunning)



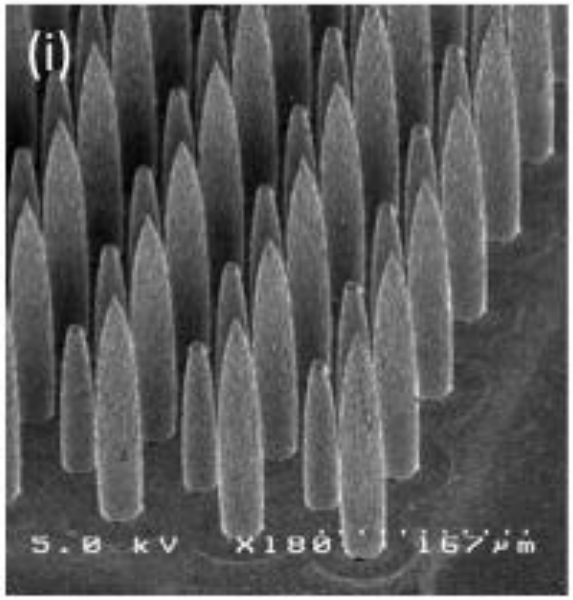
Height=150 microns; Diameter at base=30 microns

61 electrodes; 60 micron spacing; height=50 microns

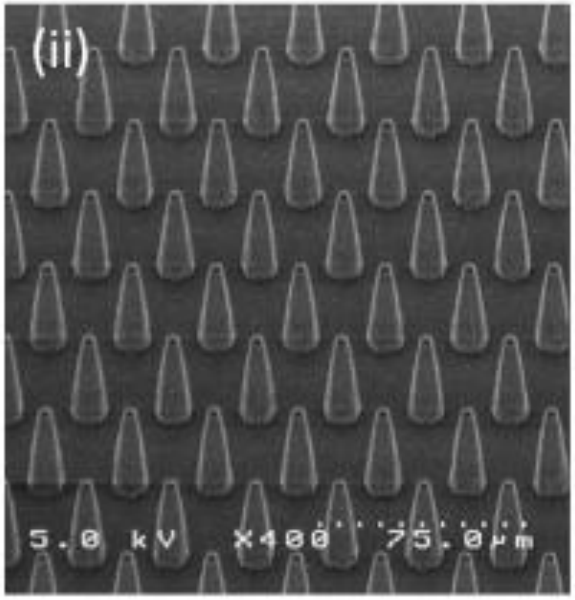
Bed-of-Nails Recording of Neural Activity in a Rat Acute Brain Slice



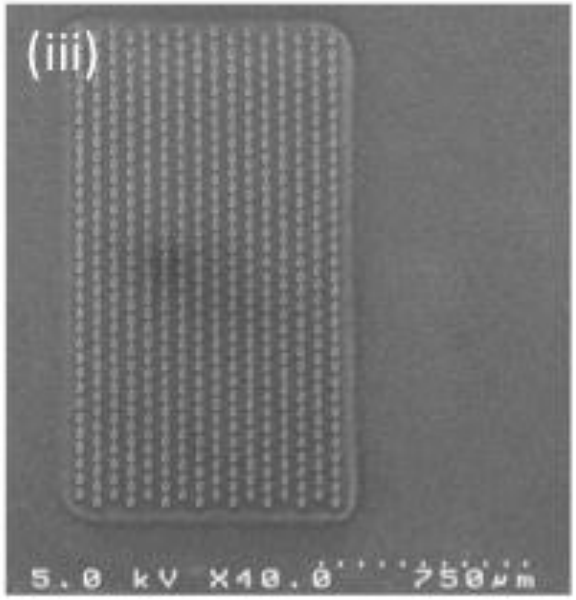
Mechanical prototypes
(fabricated by Debbie Gunning)



Multi-length needles



High density :
30 micron spacing



512 electrodes;
60 micron spacing

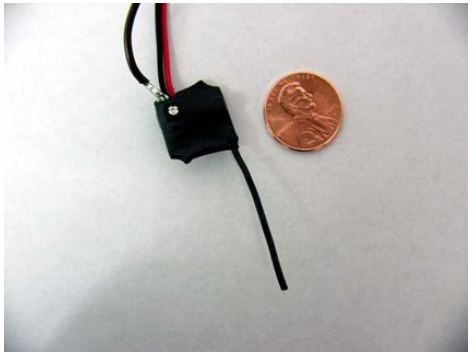
Wireless In-Vivo Brain Activity Recording System

Study the brain activity of awake, naturally-behaving animals (e.g. burrowing, climbing, flying)

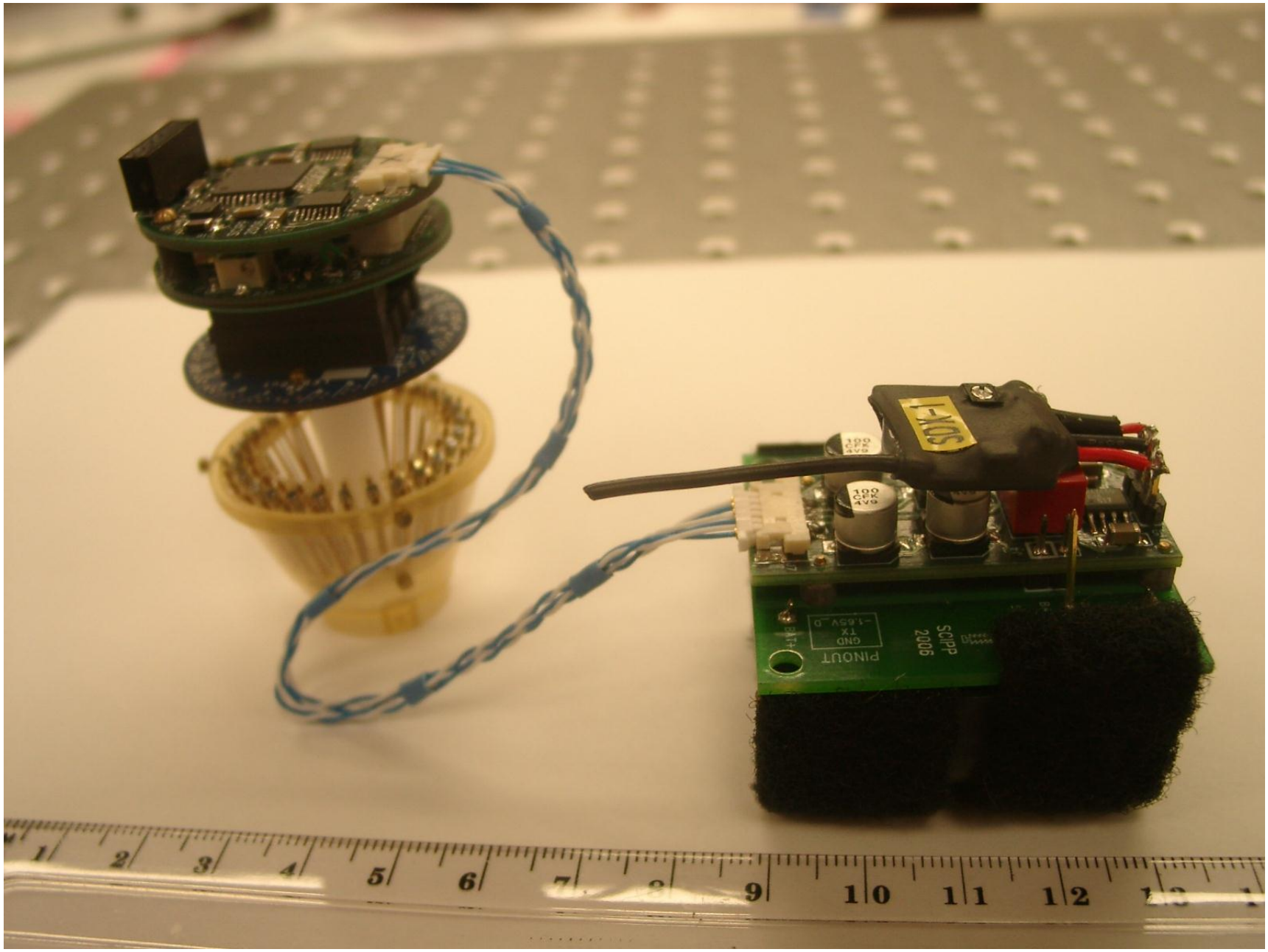
- Record brain activity on multiple (~64) electrodes (or ~16 tetrodes) with portable, battery-operated system that can be carried by a freely moving rat or a flying barn owl
- Neurochip-based system with wireless telemetry

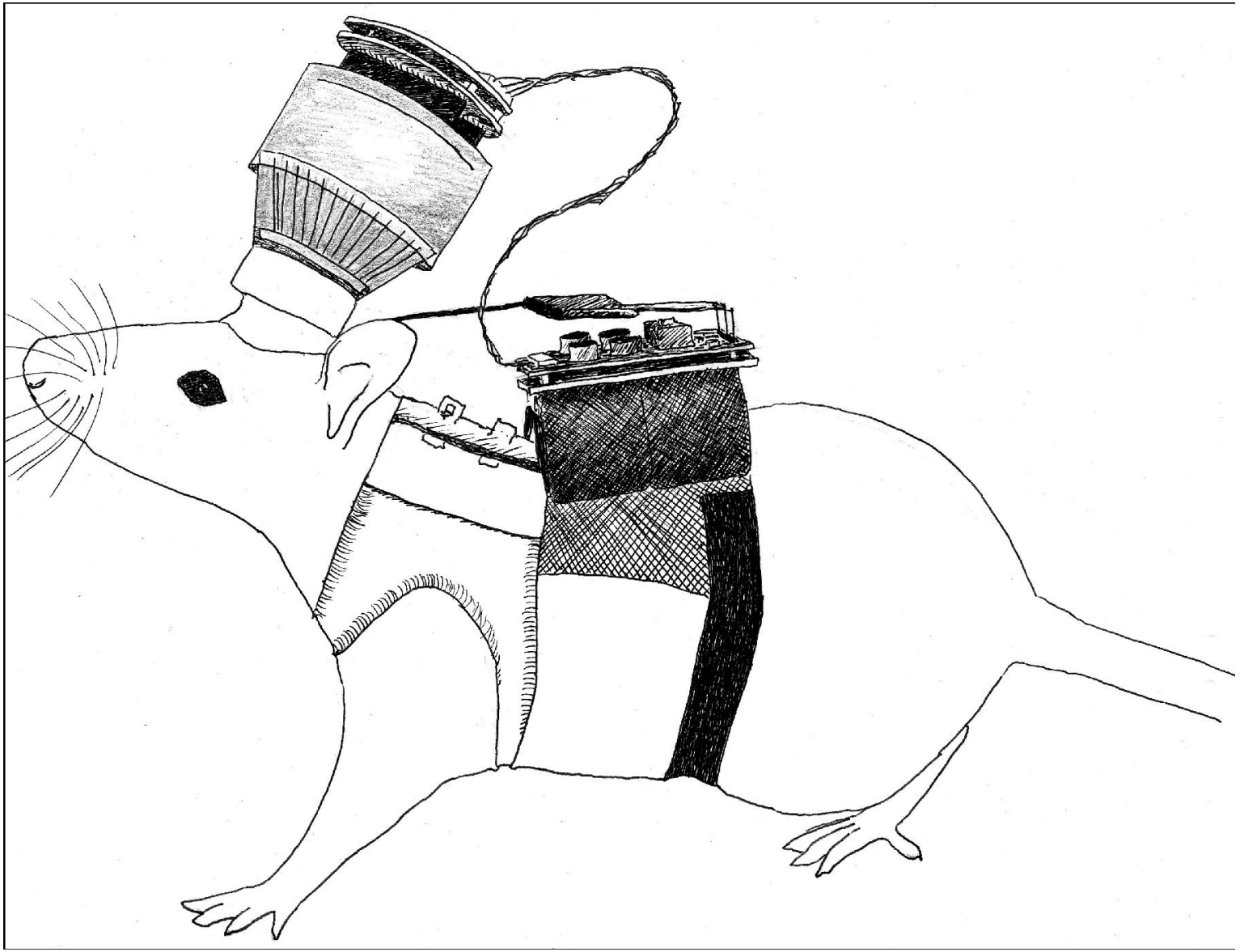
28 tetrodes
with microdrives
(Neuralynx)

Neurochip
(Dabrowski)

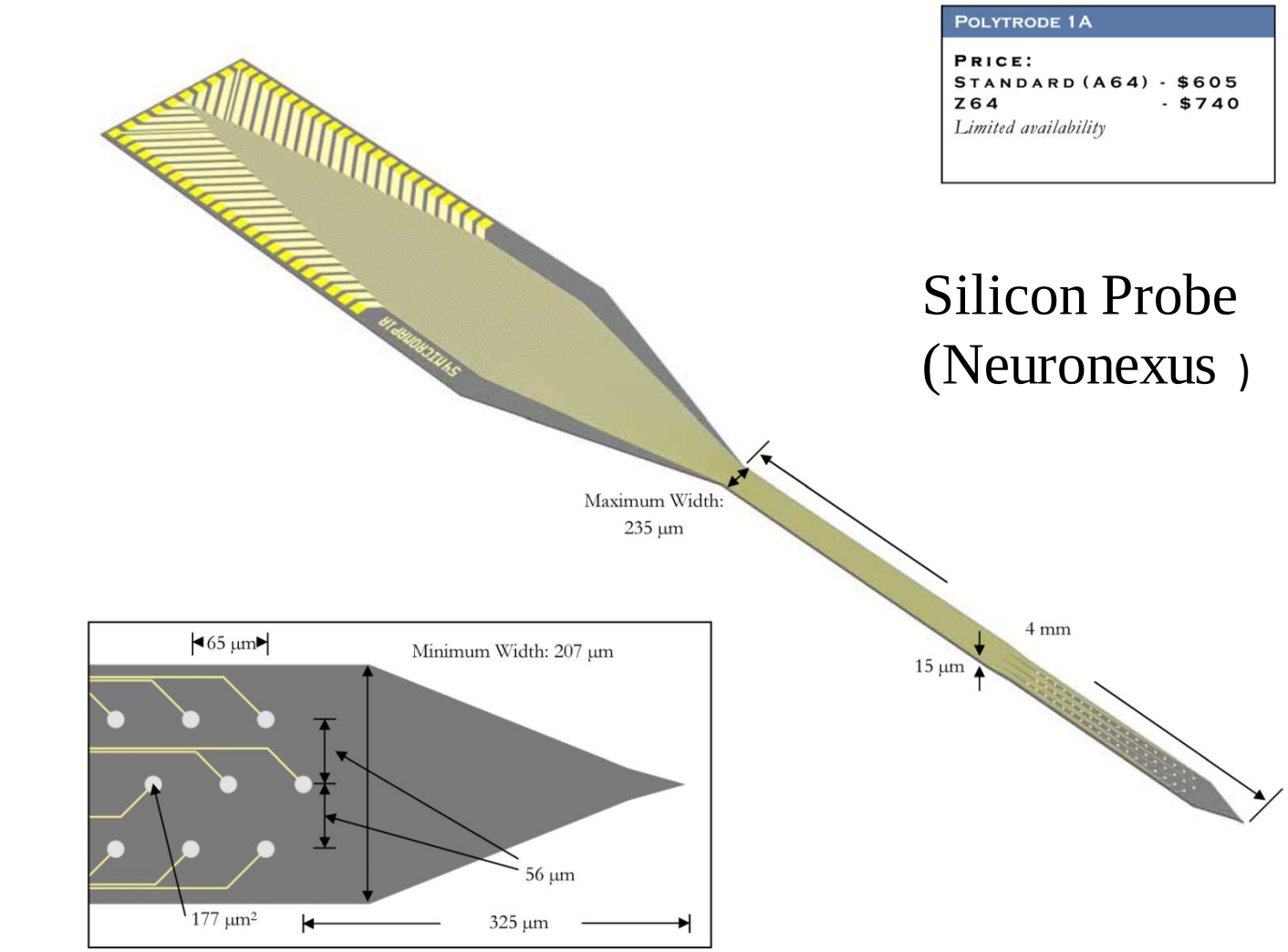


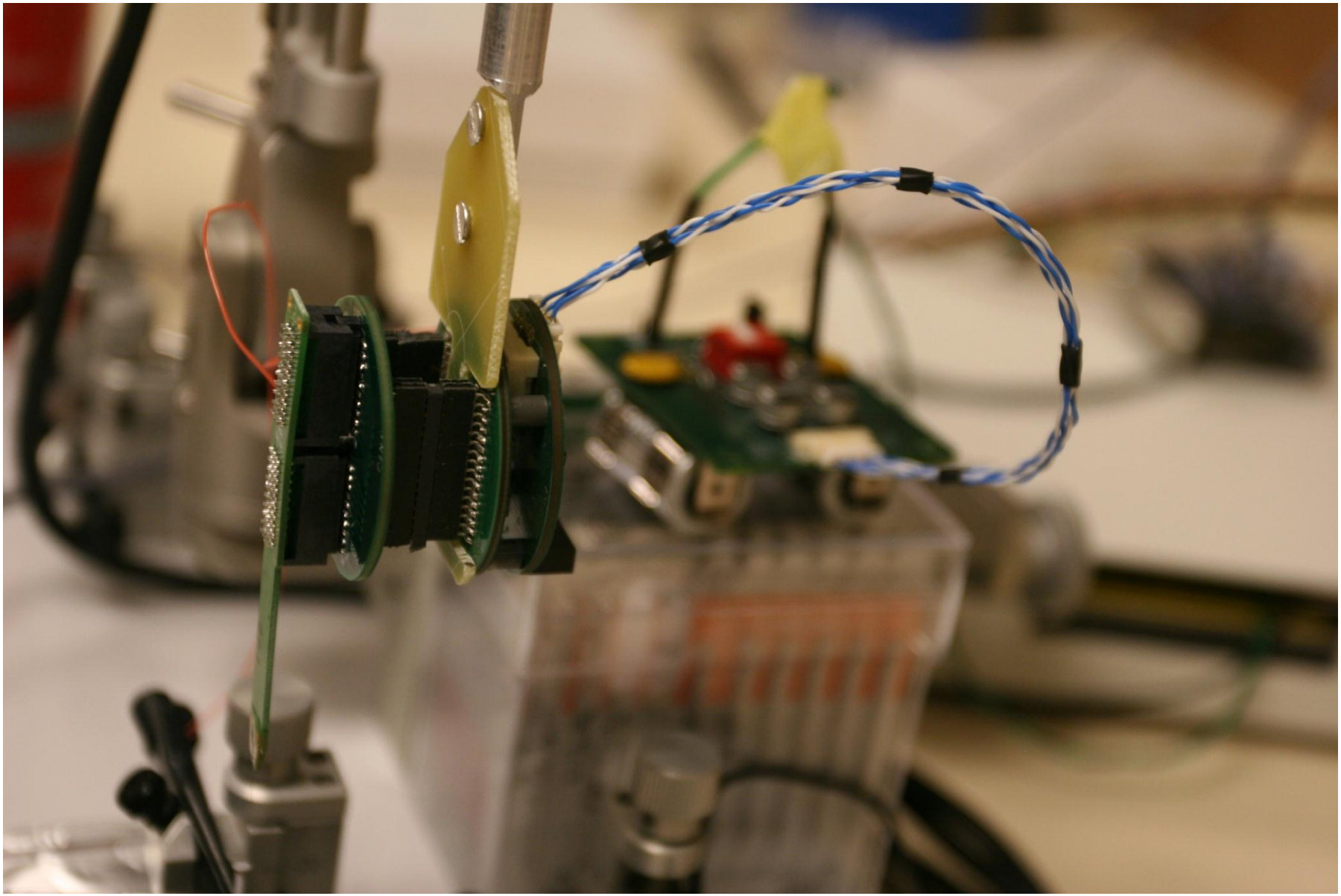
Spy Transmitter
(Meister)


SOI-1
SCIPP
2006
PINOUT
GND
TX
-1.65V_D



Wired System for Recording Brain Activity In Vivo with Silicon Probes (with Yi Zuo)





Thank you, Sherwood, for starting me off on this amazing journey.

You are one of my heroes. I have learned so much from you, sometimes much more than I realized I needed to know.

Decades before Google or Wikipedia or Scholarpedia, when I desperately needed information, I could depend on you for accurate and patient answers.

You are a National, even International, Resource. Keep it up!!

My Very Best wishes to you on your 80th birthday.