An active pixel sensor and microelectrode array for retinal stimulation

Detector Development Group
(Experimental Particle Physics)

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of
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Outline

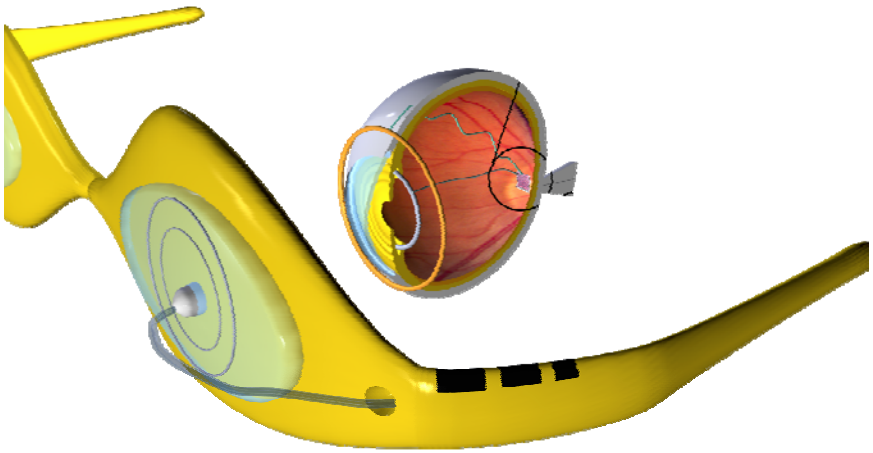
- Background
- The retina
- Causes of blindness -retinal diseases
- Implant design
- Prototype system
- CMOS retinal chip
- Microelectrode array development
- Retinal experiments

Cochlear implants/retinal implants

Electrode array stimulates auditory neurons

~ 60,000 patients worldwide with cochlear implants (2002)

Electrode array to stimulate retinal neurons



Worldwide research area
- USA, Germany, Japan, Australia

Leading causes of blindness in the western-world

Age-related macular degeneration(AMD)

–UK has an incidence of 8% above the age of 65 yr and is responsible for 39% of cases of registered blindness (almost 1 million people).

–Affects central region (fovea) of retina responsible for detailed vision.

–Light-sensitive cells (photoreceptors - cones) no longer function, rest of retina remains healthy.

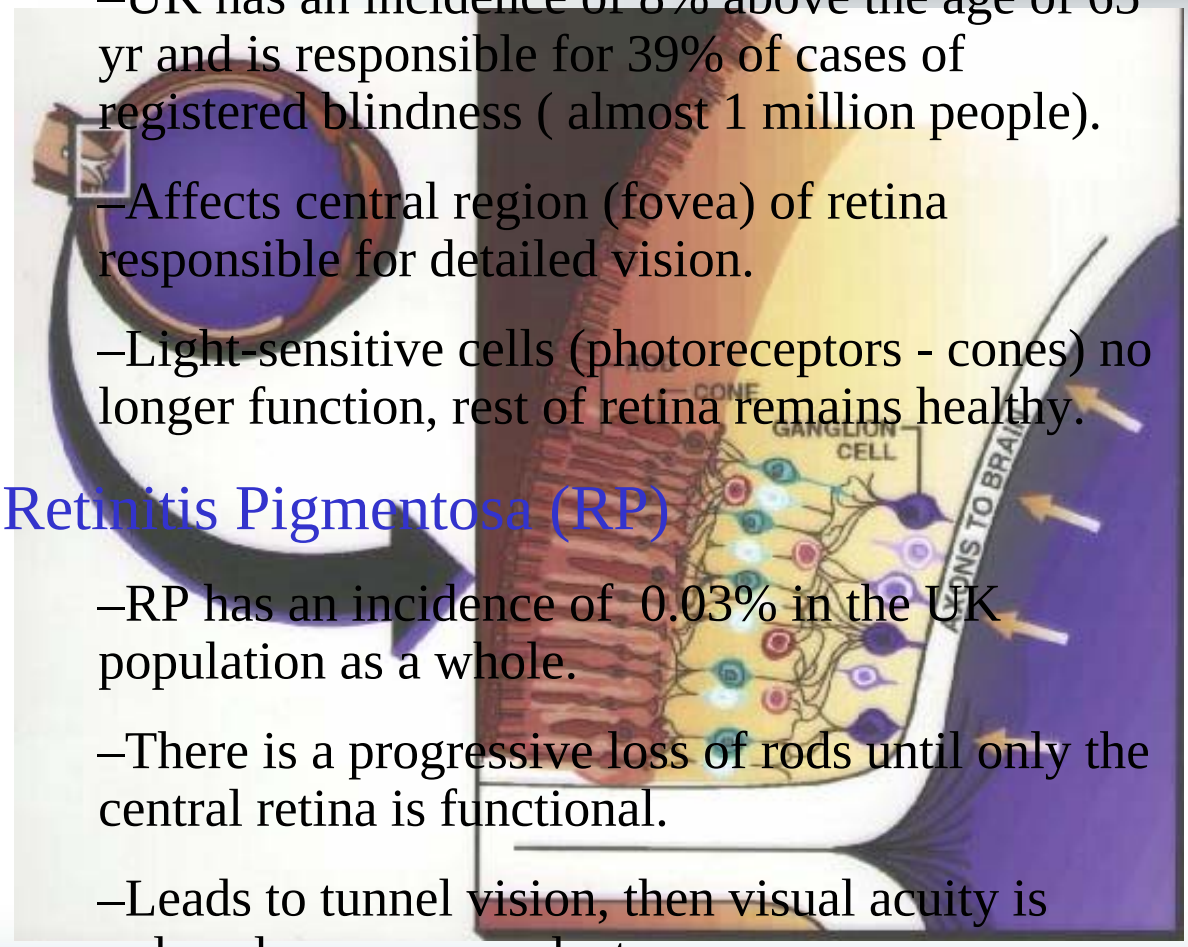
Retinitis Pigmentosa (RP)

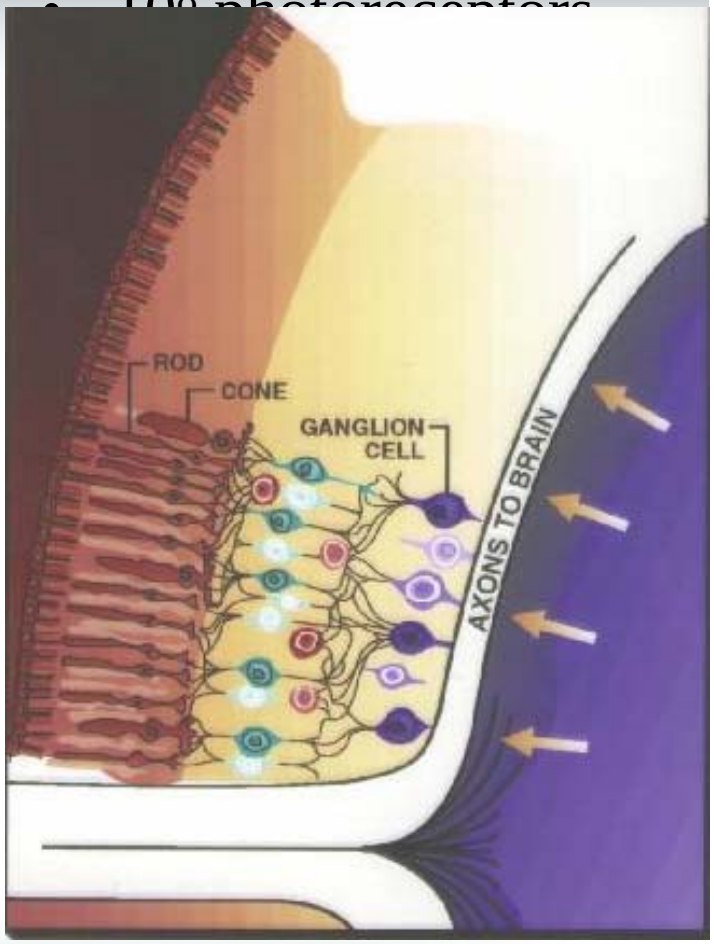
–RP has an incidence of 0.03% in the UK population as a whole.

–There is a progressive loss of rods until only the central retina is functional.

–Leads to tunnel vision, then visual acuity is reduced as cones are lost.

–Again retina healthy except photoreceptors.



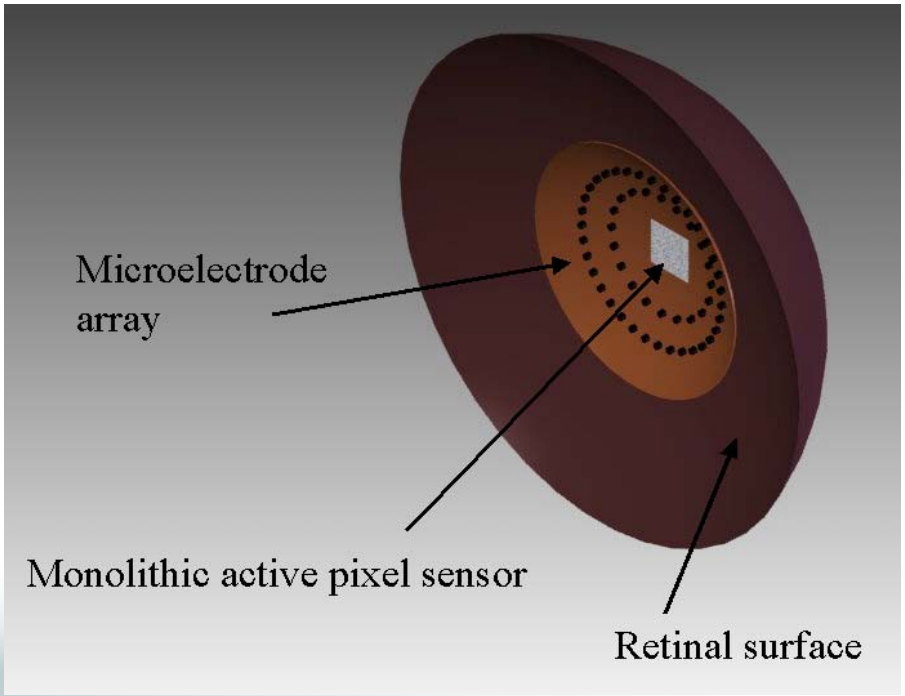


Design of implant

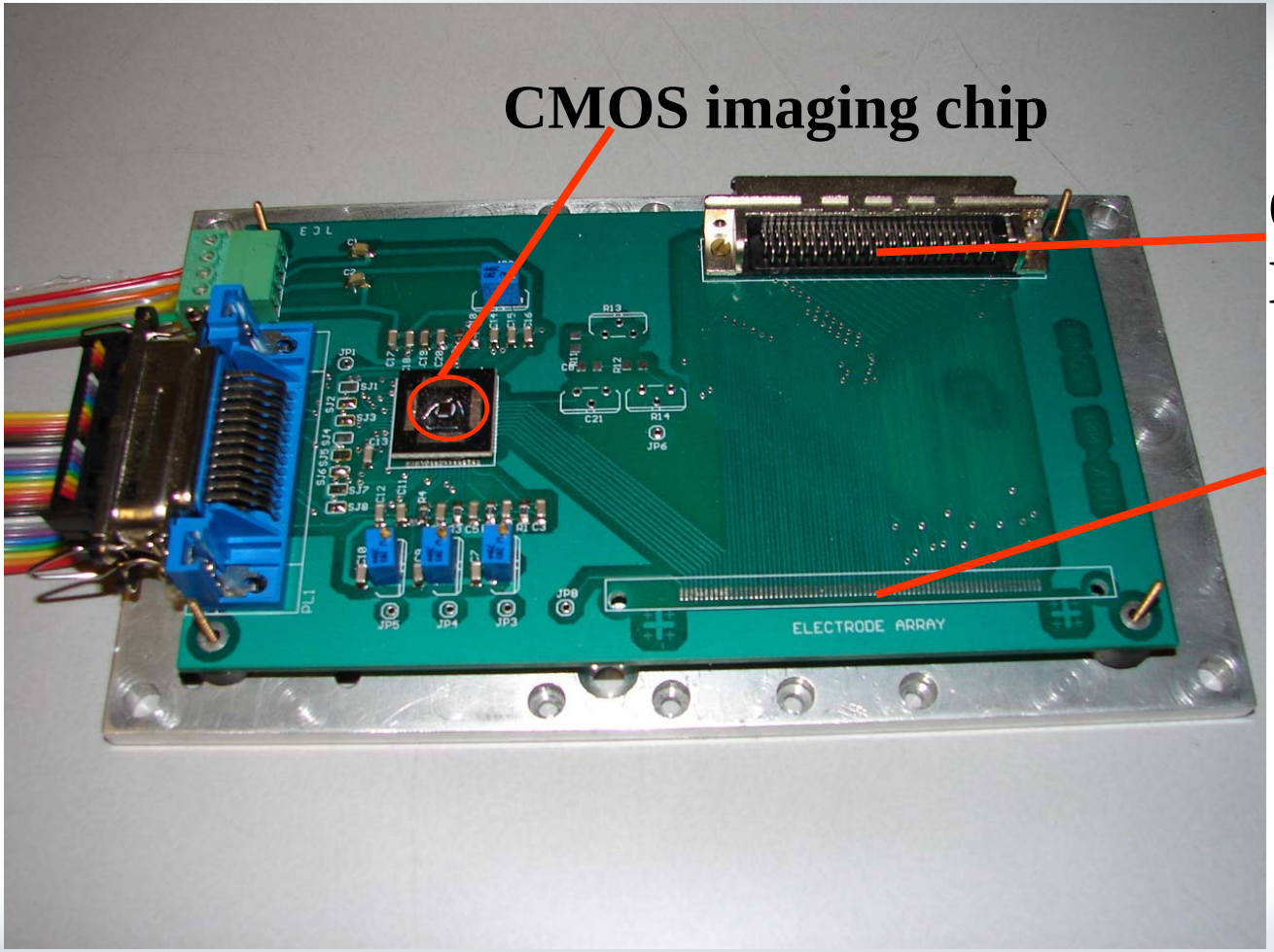
Collaboration involving neuroscientists, detector physicists and ASIC designers at the Council for the Central Laboratory of the Research Councils (CCLRC)

EPSRC funded, started Dec 2002

- CCLRC
  - Retinal chip
- Glasgow
  - Microelectrode arrays
  - System development
  - Physiological testing



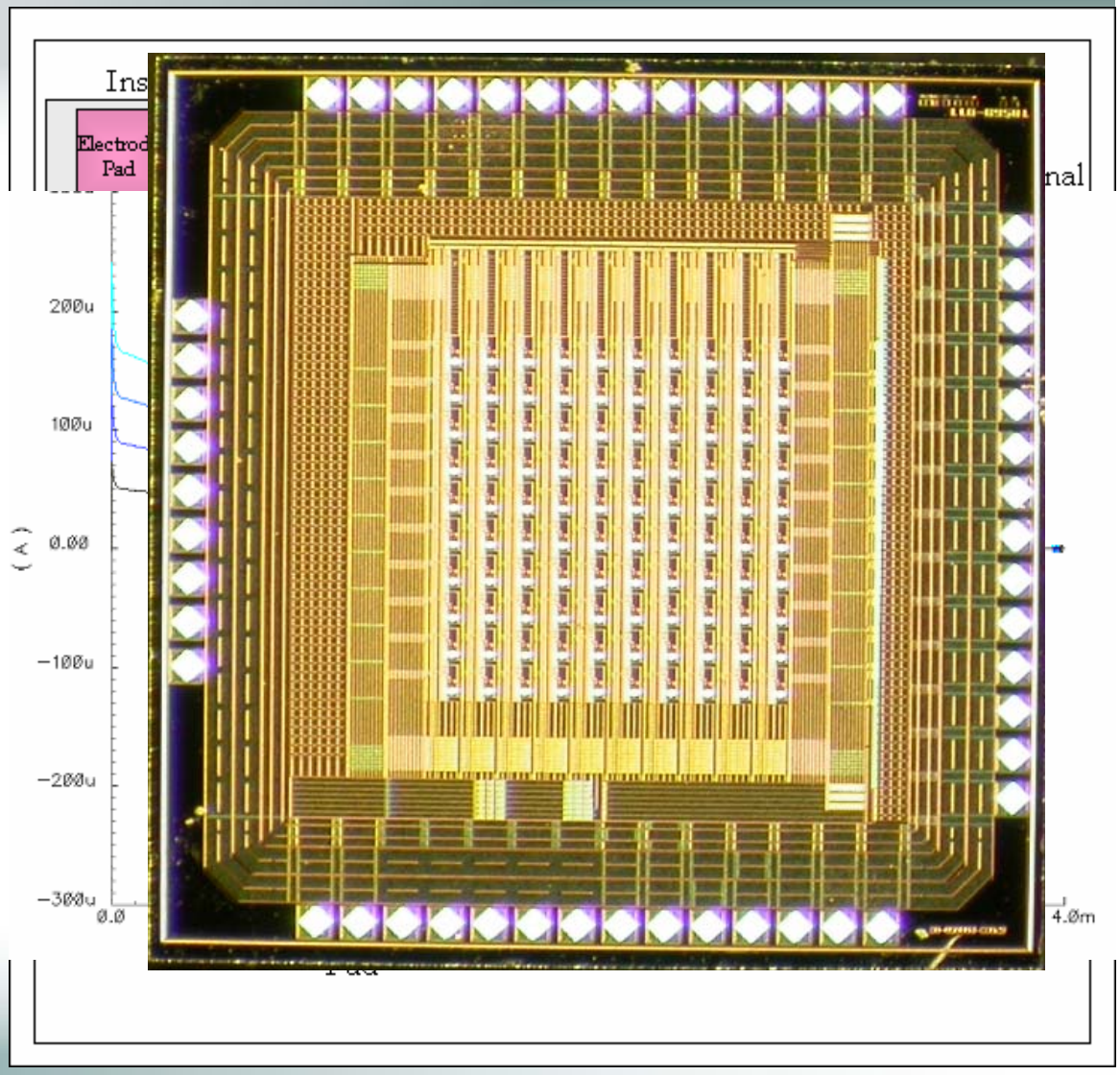
Prototype system



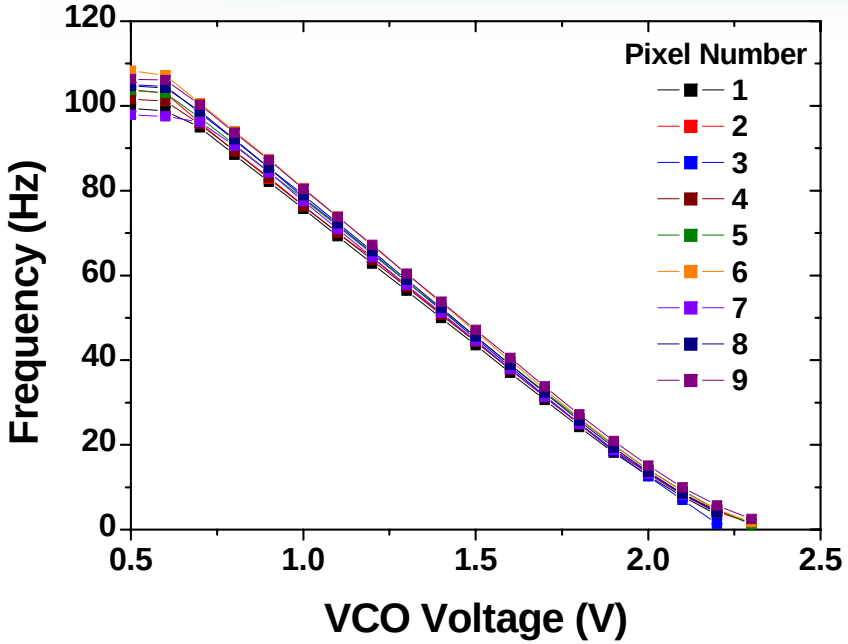
IPIX detector

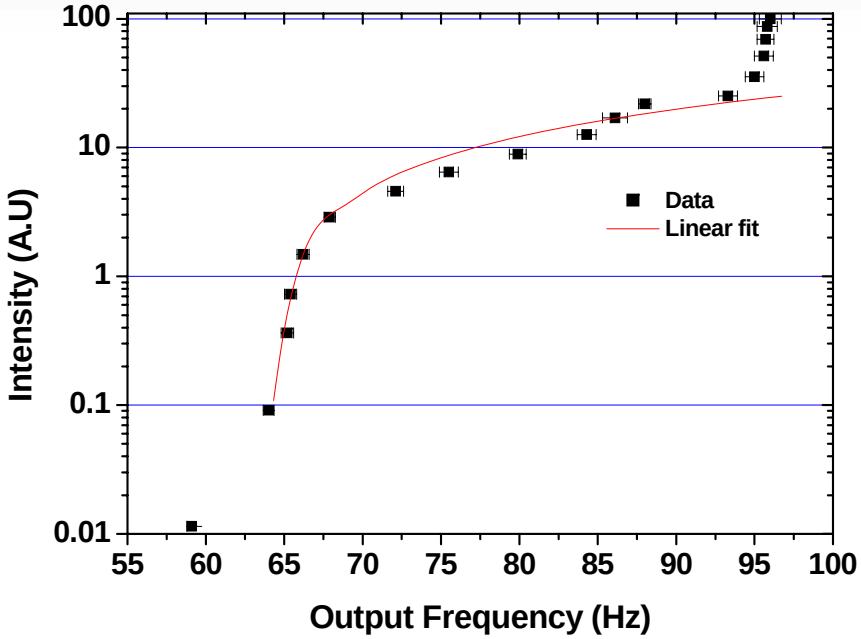
- 10x10 pixel matrix
- pixel pitch 100µm
- Each pixel contains
  - Photodiode
  - Voltage controlled oscillator (VCO)
  - Bi-phasic output driver
- Creates signals capable of stimulating retinal ganglion cells.
- Frequency of VCO depends on incident light.

Frequency range : 10Hz-100 Hz



IPIX characteristics

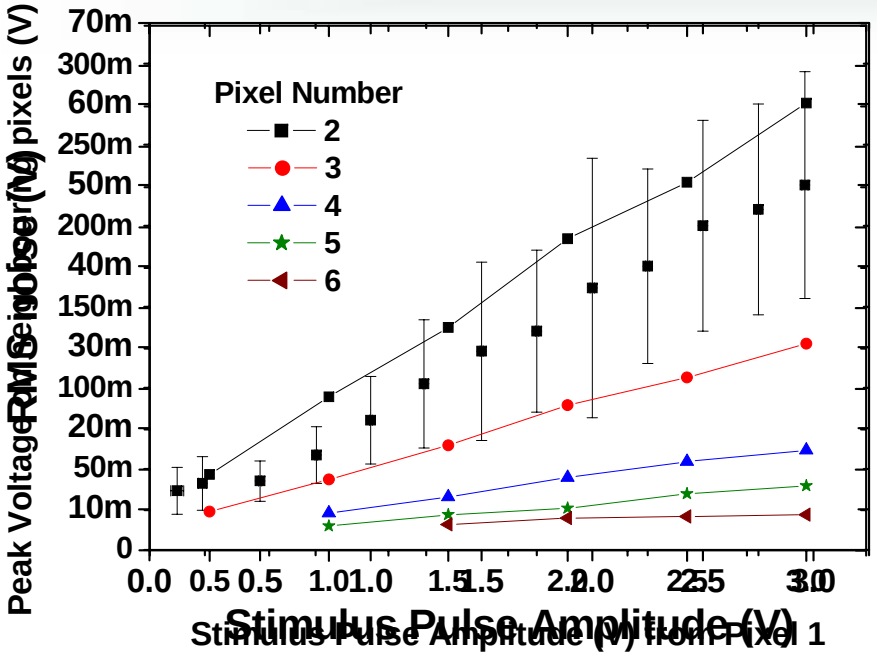




5-100 Hz output range
Good linearity
Pixel-pixel variation < 5%

Photodiode output range 65-100Hz
Good linearity

System Noise



Centre 9 pixels

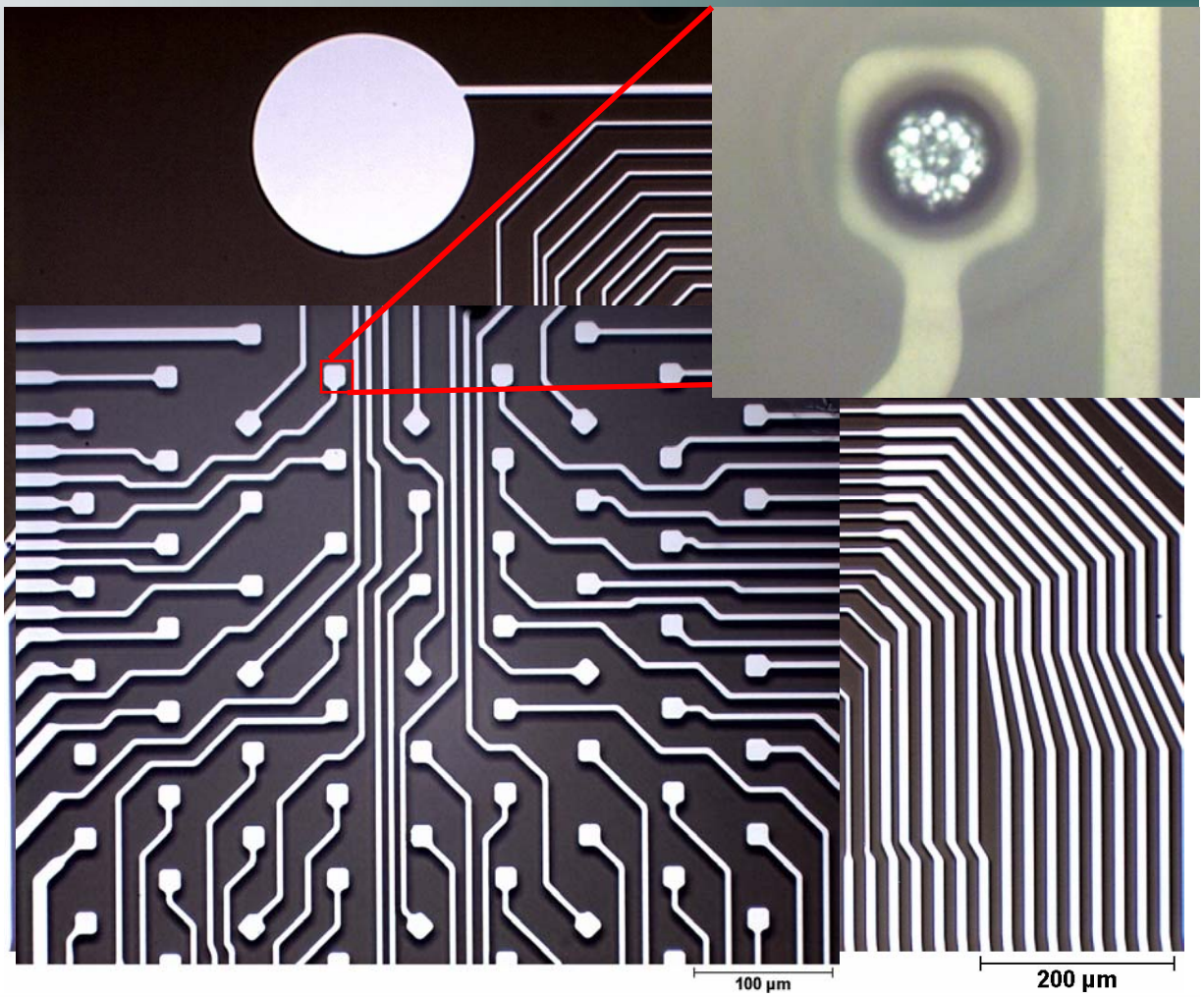
1	2	3
4	5	6
7	8	9

Crosstalk pixels 2, 3, 4, 5 and 6 from stimulating pixel 1

Retinal ganglion cells require a certain stimulation threshold to be exceeded in order to elicit a response. Noise is well below this threshold

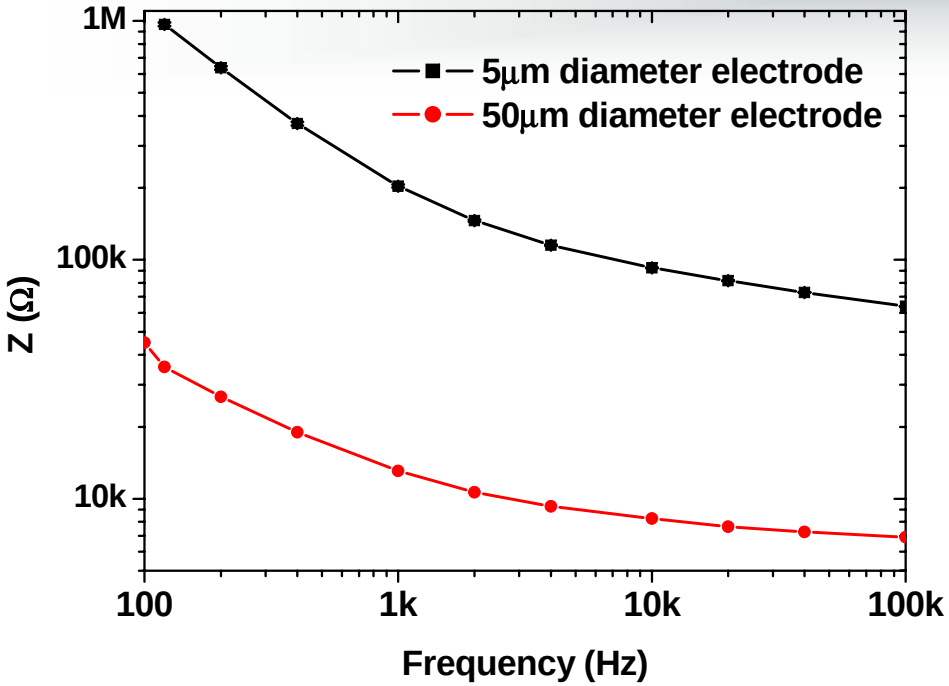
Current status: Electrode arrays

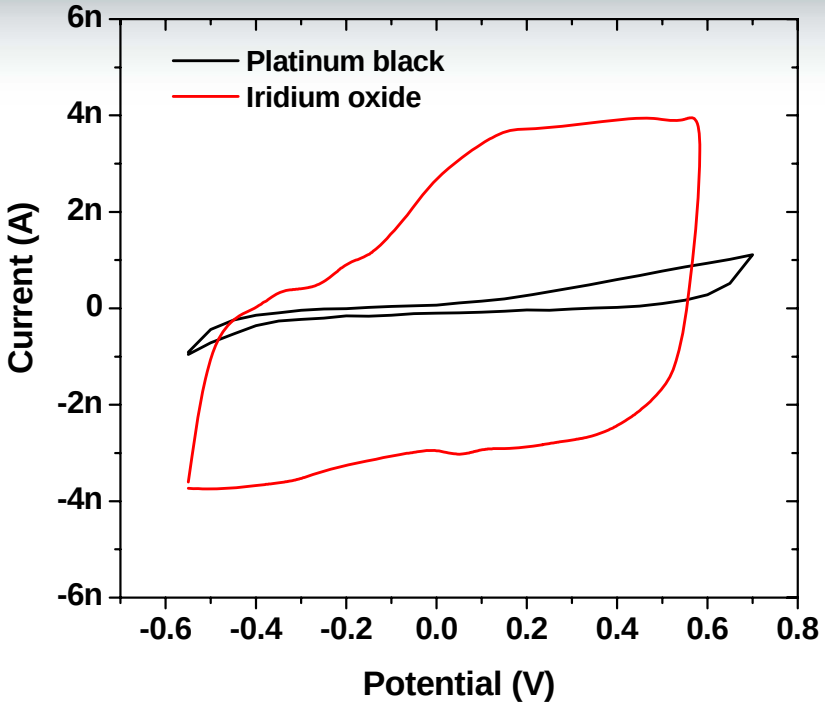
- Have fabricated flexible electrode arrays on a bio-compatible substrate (polyimide)
- Only 20 microns thick
- Extremely flexible and able to assume the contours of the eye
- Electrode spacing of 60 microns
- Numbers of electrodes:
  - **8 (in-situ recordings)**
  - **74 (9 stimulating, 64 recording)**



Array characteristics

Measurements taken in physiological saline solution





Impedance of electrodes at 1kHz
50 μm ~ 15-20kΩ
5 μm ~ 150-200kΩ

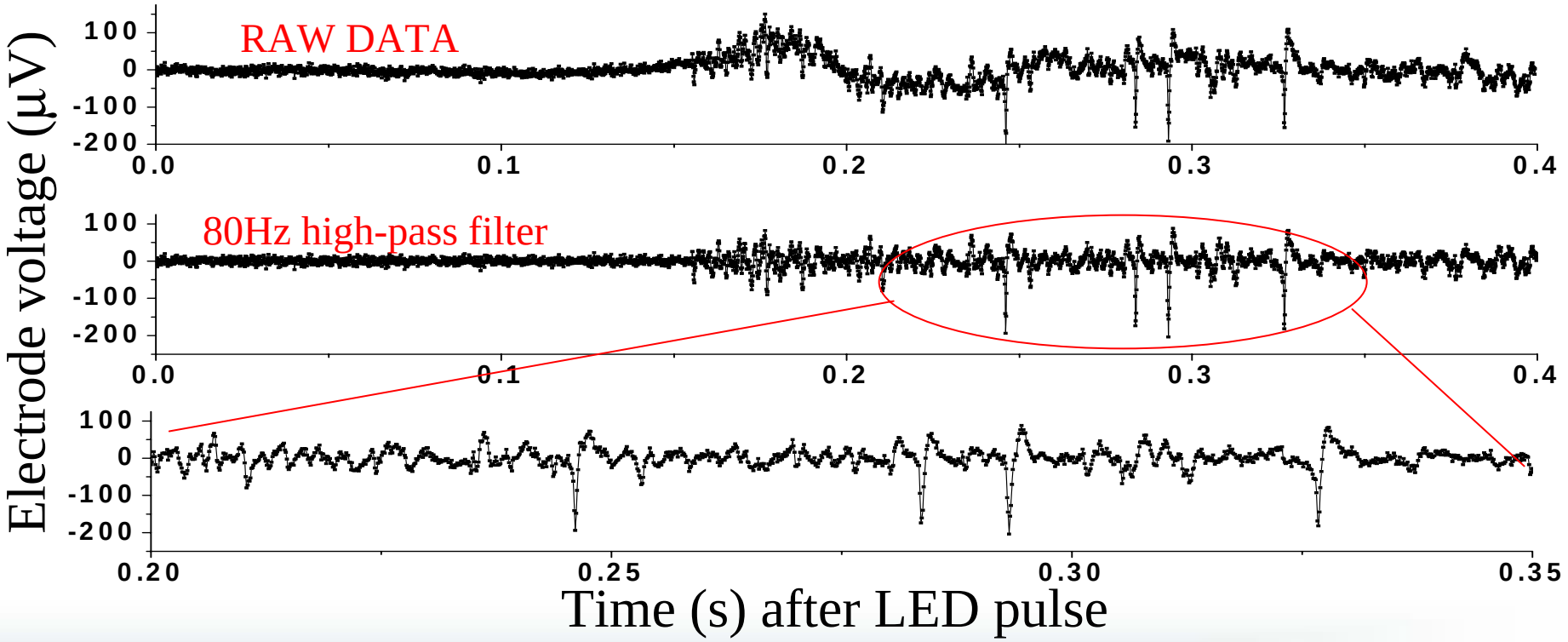
Charge capacity: How much charge the electrode can hold without degrading (undergoing a non-reversible reaction)

Platinum ~ 260μC/cm^2

Iridium oxide ~ 4mC/cm^2

Recording from small RGCs

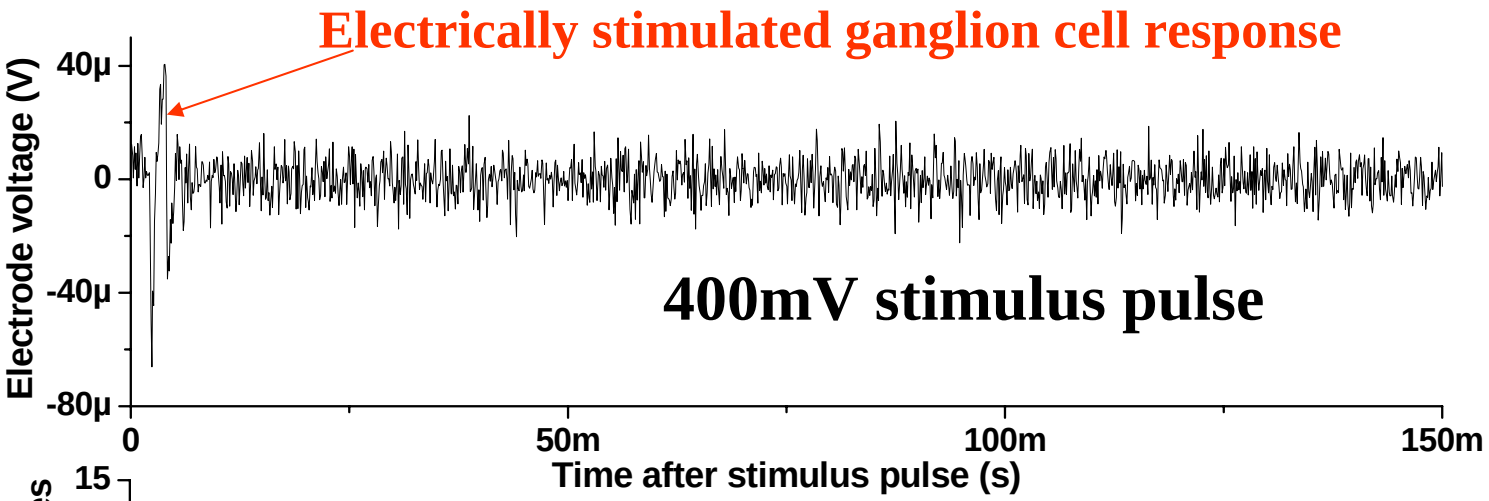
- Bio-compatible electrode array recording from frog retinal ganglion cells (RGCs)
- RGCs only ~10μm in diameter, good model for human fovea

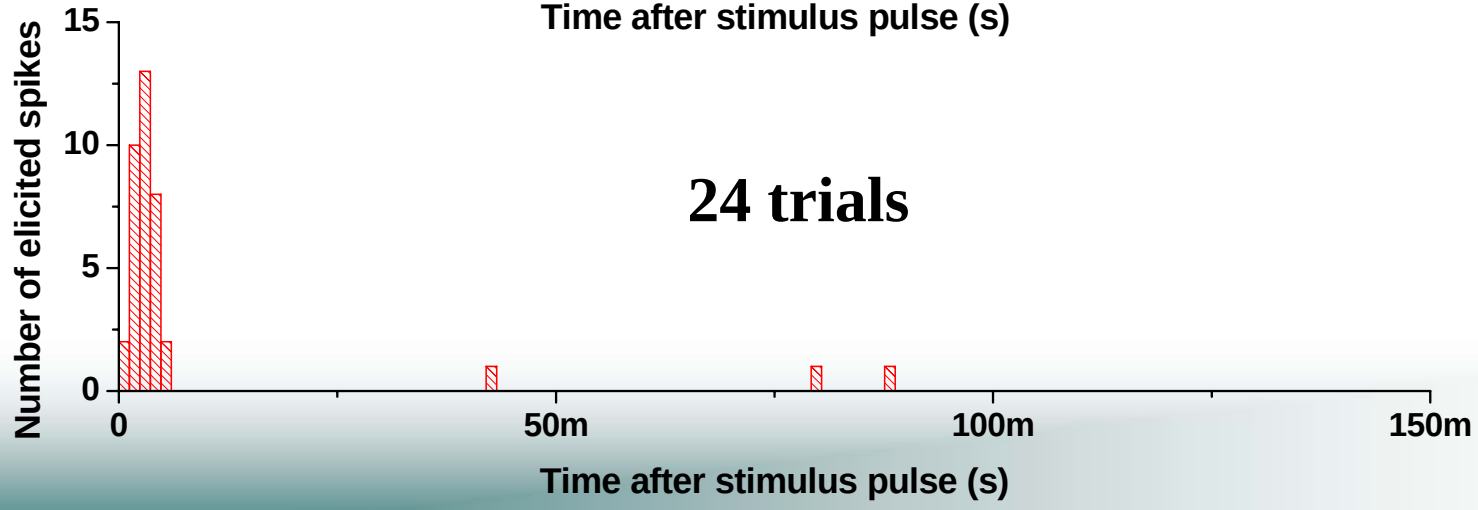


1 sec green LED stimulus: recording starts when LED is switched on

Stimulation Studies

Stimulate with one electrode whilst recording from surrounding electrodes





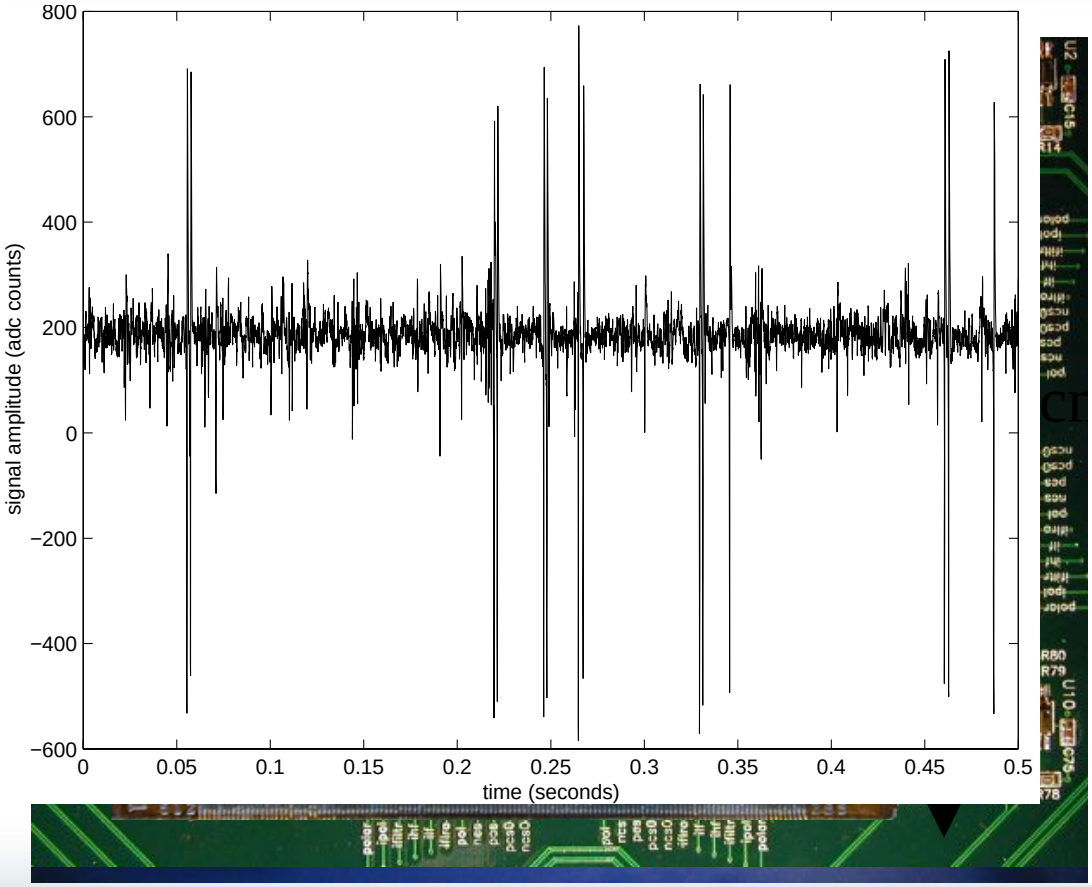
Conclusions

- IPIX cmos sensor delivering voltage pulses dependent upon light intensity.
- High-density microelectrode arrays fabricated with good electrical characteristics:
  - Impedance at 1kHz ~ 150kΩ
  - Charge capacity of
    - **Pt electrodes 260μC/cm^2**
    - **Iridium oxide 4mC/cm^2**
- Retinal experiments undertaken *in situ.*
  - Successful retinal recordings from very small RGCs
  - Voltage threshold of 400mV needed to elicit response from RGCs
  - Corresponds to ~ 130μC/cm^2 on the electrode
    - Permits electrodes as small as 5μm in diameter and high density electrode arrays
- Many issues still to be dealt with
  - Biocompatibility
  - Power requirements
  - Safe operating limits

Research background: Physics to retinal studies

How does the eye talk to the brain?

Record the patterns of electrical activity generated by hundreds of retinal output neurons in response to a movie focused on the input neurons



Electrode separation

=30μm - 60μm

Sensitive area

~ 0.45mm² ~ 2mm²

Electrode diameter

= 5μm

Requires electron-beam lithography

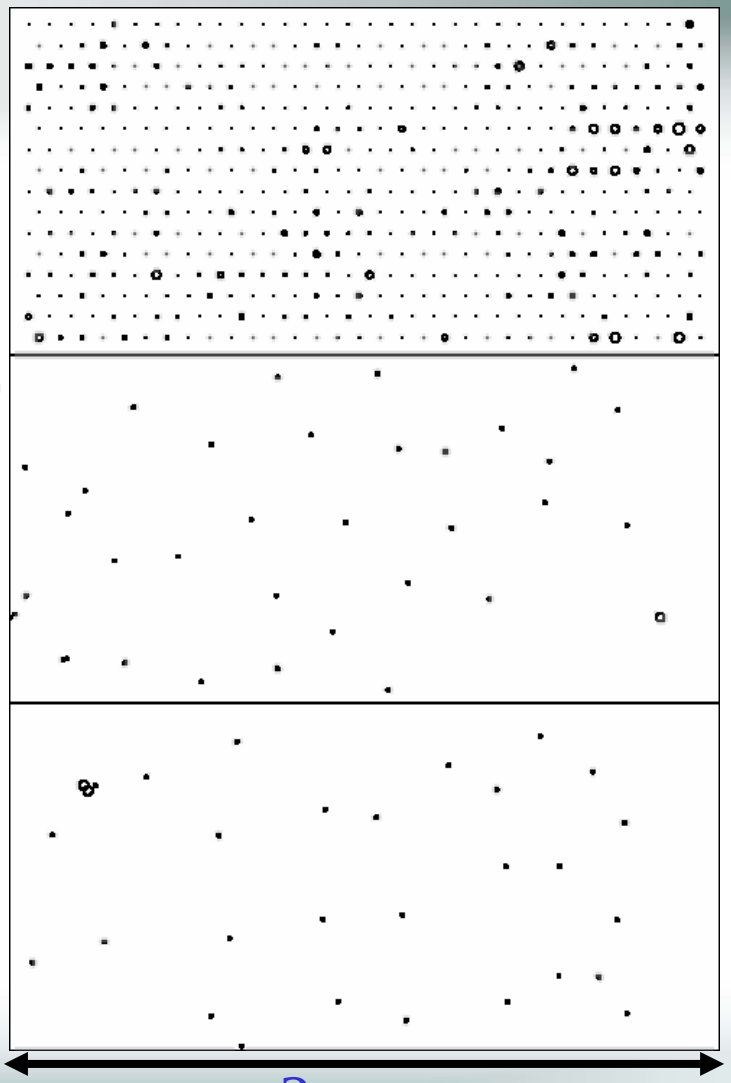
Results using microelectrode arrays

(Animation repeats after 2 sweeps)

Electrode spike-rate

Spike-rate for On-off DS neurons

Spike-rate for On-off DS neurons



2 mm

Image of vertical moving bar is focused on a section of guinea pig retina

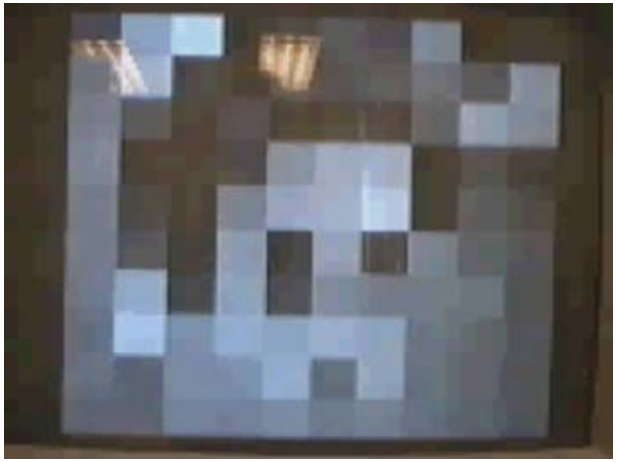
Conclusions

- Necessary expertise in place:
  - Semiconductor fabrication, detector technology
  - Electrophysiology (Dr. J.D. Morrison)
  - PhD students: C. Adams, D. Gunning, A. Moodie
- Validated electrode array in retinal experiments
- Imaging detector with stimulation capabilities complete and under characterisation
- Begun retinal stimulation studies with high-density electrode arrays

Fellowship work plan

- Move towards viable prosthesis by:
  - Scaling up electrode arrays (~ 600 electrodes)
  - Programmable imaging detector capable of reproducing retinal function
  - Implantation and testing in animal model

How many pixels are needed to represent an image?



10 x 10

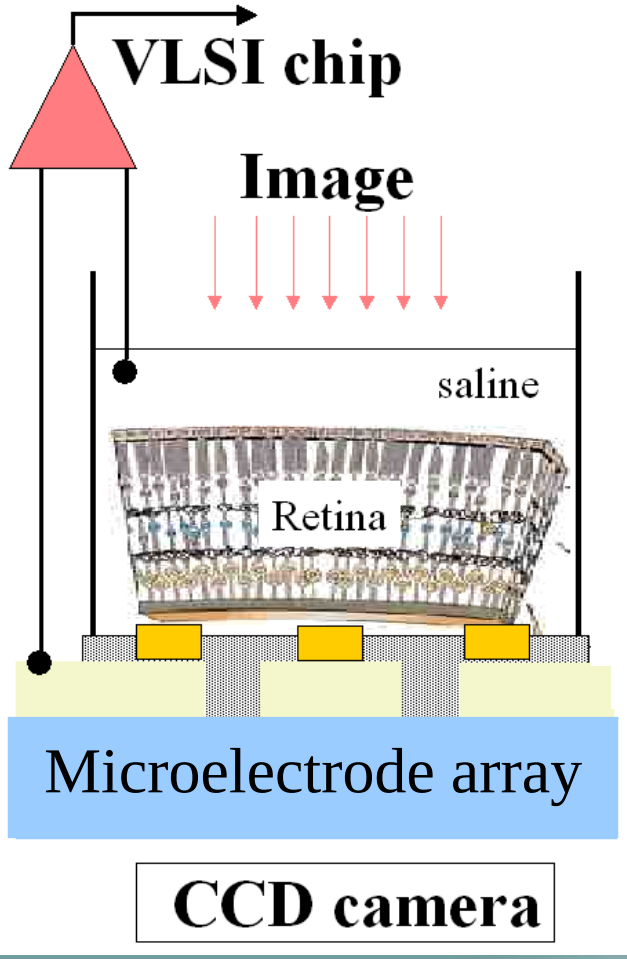
30 x 30

640 x 480

From : http://www.icat.ncsu.edu/projects/retina/archive.htm

Retinal project

How does the eye talk to the brain?



Biological studies

Salk Institute, San Diego

Readout system & data analysis

University of California

Santa Cruz (UCSC)

Microelectrode array development

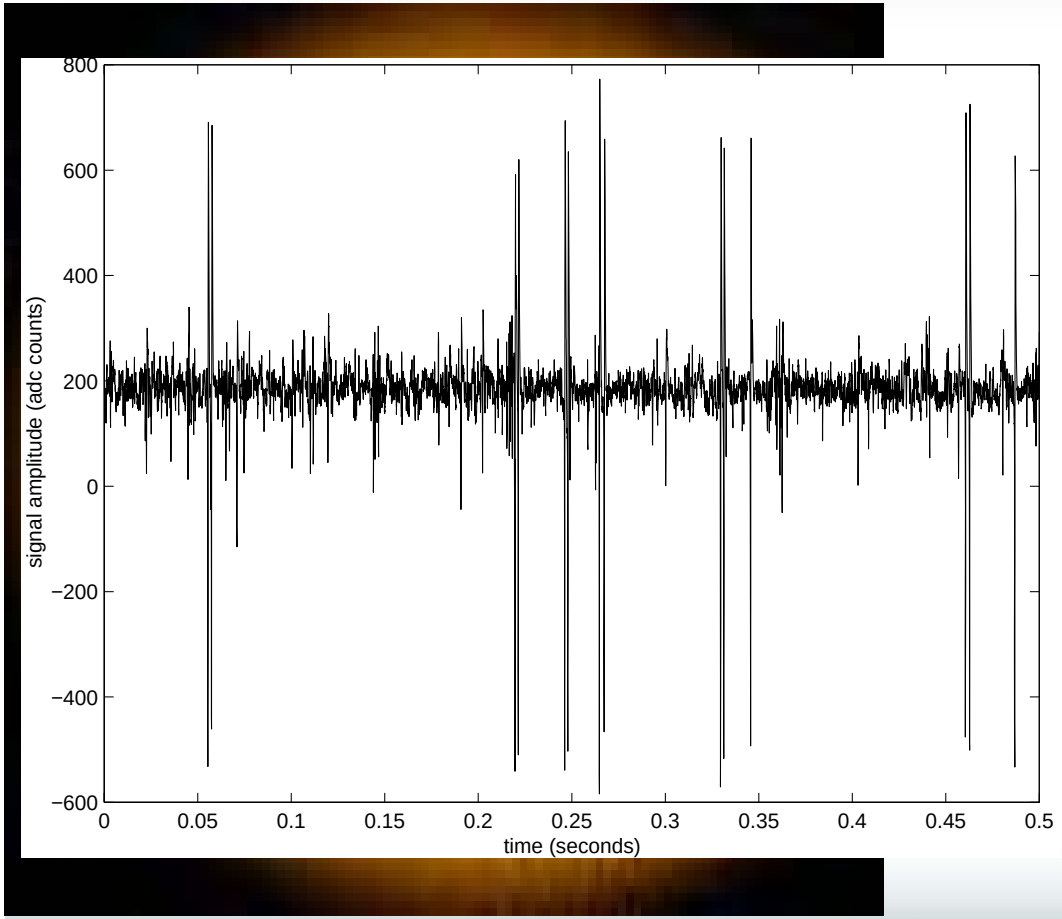
University of Glasgow

VLSI chip design

University of Krakow (CERN)

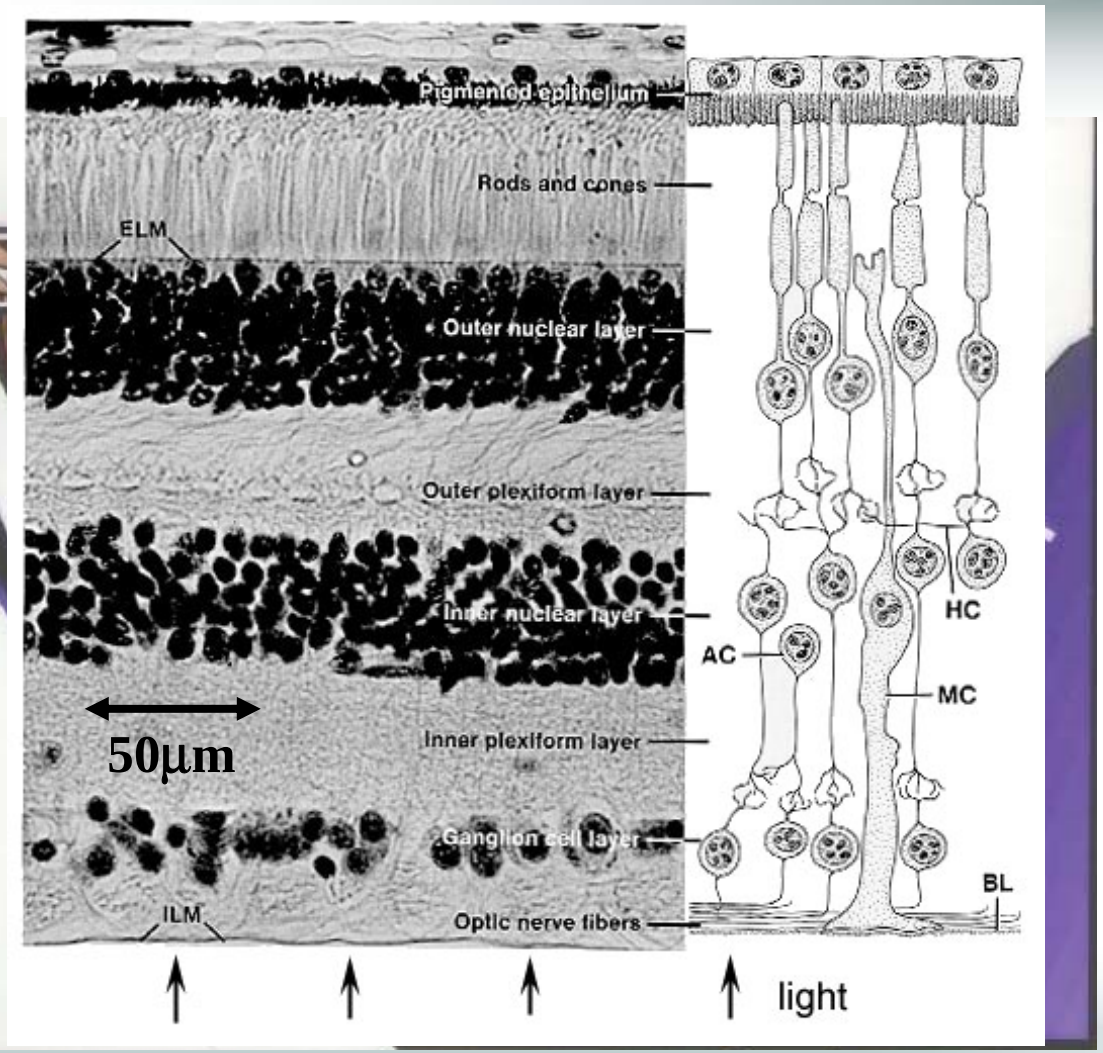
The retina project led by Prof Alan Litke (UCSC & CERN)

Signals from 512 array



- Able to make maps of neural activity as a dynamic image is focussed on to the photoreceptors
- Large data sets from recordings, ~ 8 hours gives 650Gb

The eye's pixel detector: The Retina



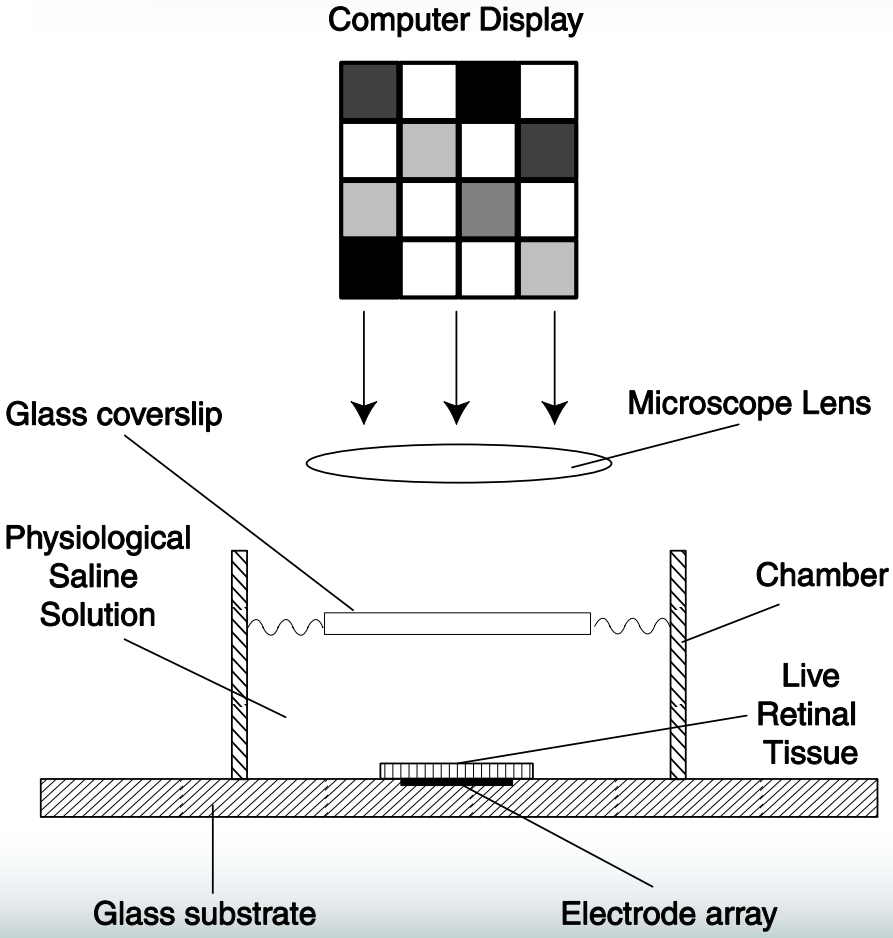
- 10^8 photoreceptors
  - rods and cones
- Parallel analogue processing layers of cells
  - horizontal, bipolar and amacrine cells
- Output from ganglion cell layer
- 10^6 optic nerve connections
- Area 10 cm^2

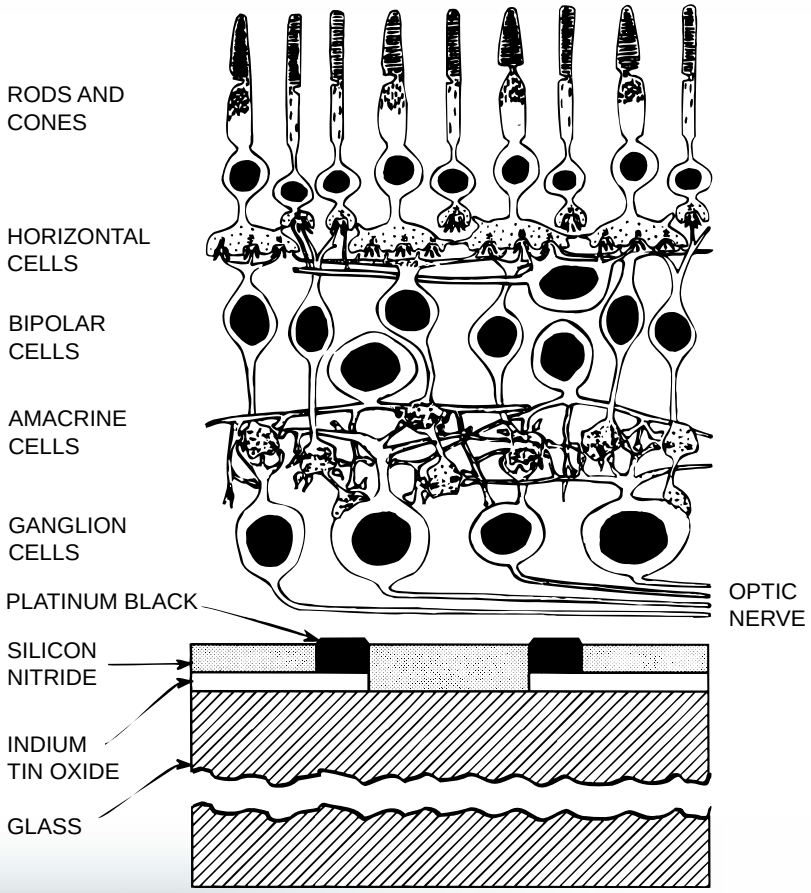
Research Aims

To improve quality of life by restoring some semblance of vision to blind patients through electrical stimulation of the retina

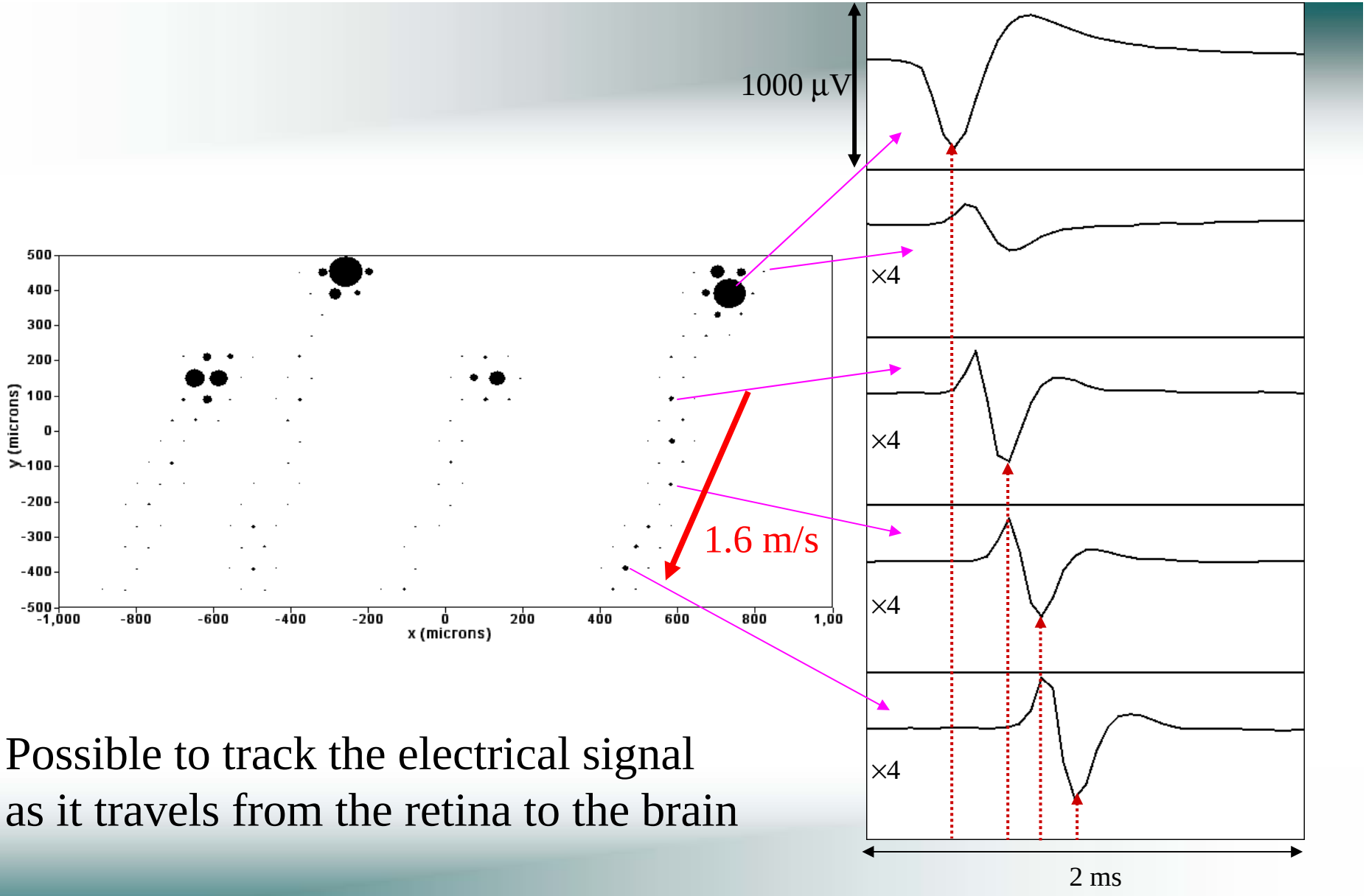
1. Develop high-density electrode arrays : Interface to retina
2. Imaging detector to detect visual scene and provide patterned stimulation to electrodes : Smart retina chip
3. Stimulation and recording of small retinal ganglion cells (frog) to determine optimal stimulus parameters
4. Develop physiological experiments in which a binocularly-activated visual cortex neuron is stimulated directly by a pattern of light and by equivalent patterned electrical stimulation of the companion retina

Retinal experiments





Electrophysiological Imaging



Possible to track the electrical signal
as it travels from the retina to the brain