

CORTIVIS
QLK6-CT-2001-00279



Designing a Brain- Machine Interface for Direct Communication with Visual Cortex Neurons

Neuro-IT.net Workshop

July 8, 2003
Alicante, Spain

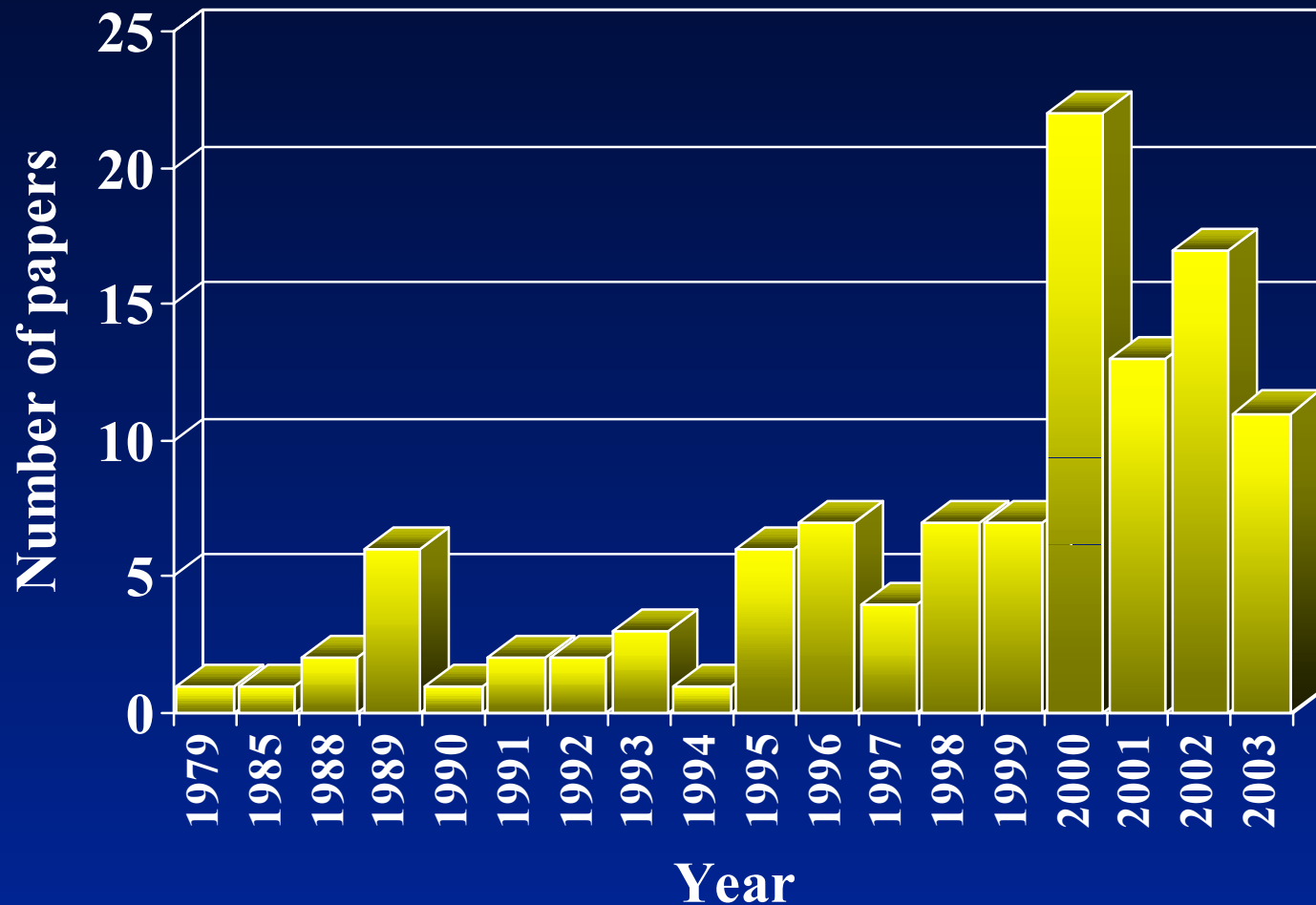
E. Fernández, MD, Ph.D.



Instituto de Bioingeniería
Universidad Miguel Hernández



PubMed: Papers referring to “brain-machine interfaces”, “brain-computer interfaces” or “neuroprostheses”



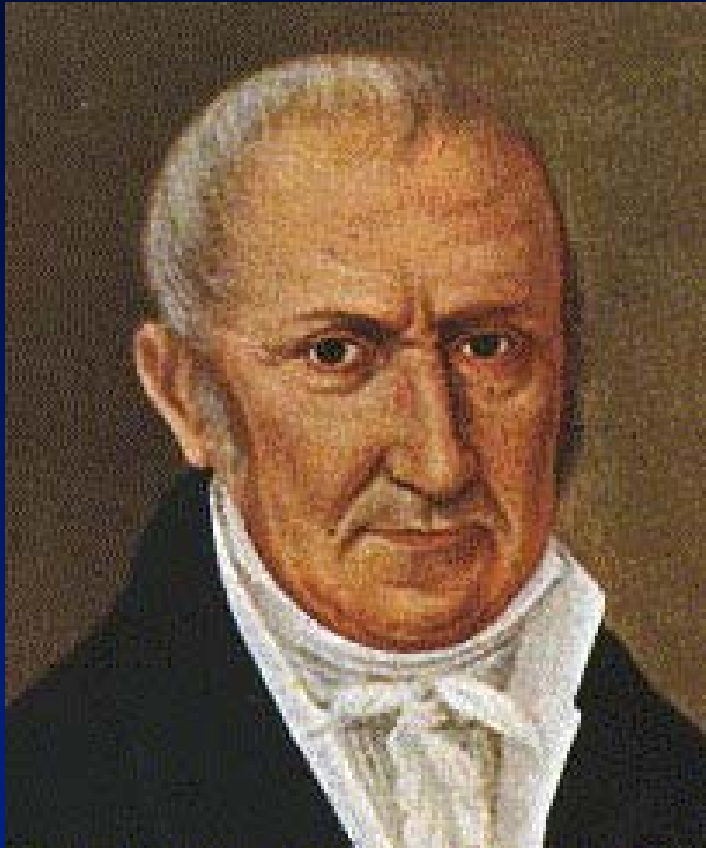
5/7/2003

EIGHTEENTH CENTURY



Fig. 331. — Larrey provoque, par le galvanisme, des contractions musculaires, sur un membre récemment amputé (page 643).

NINETEENTH CENTURY

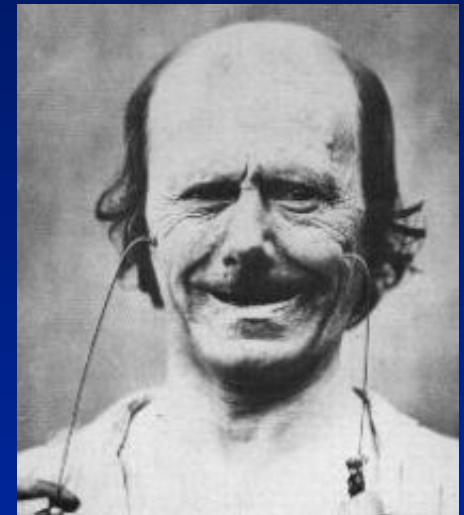
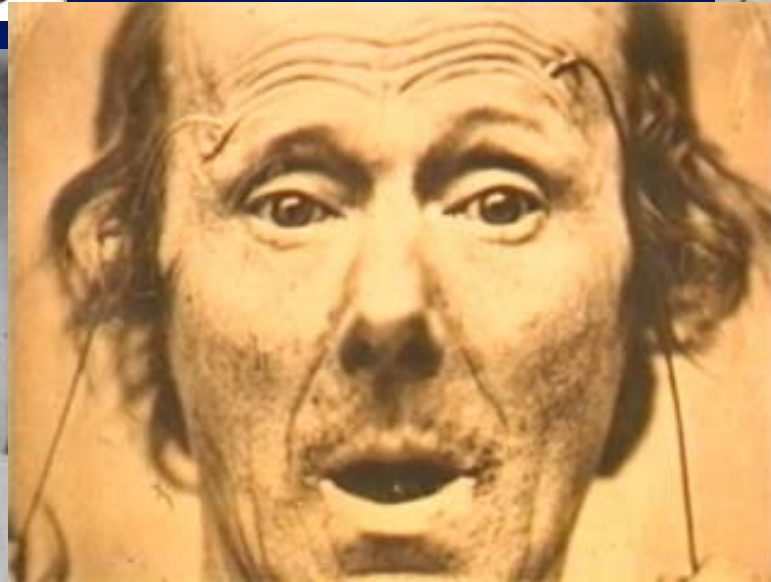
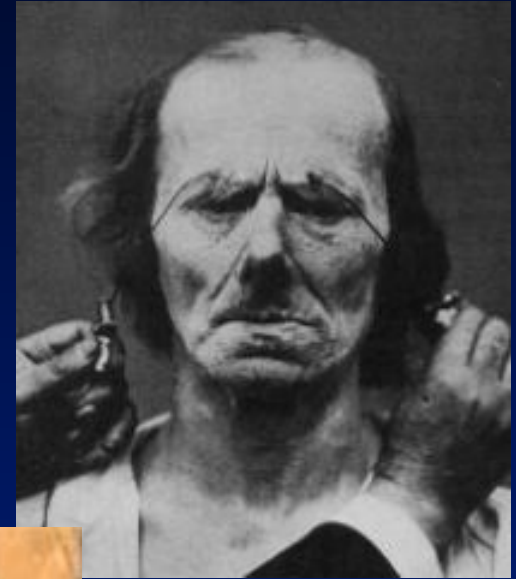


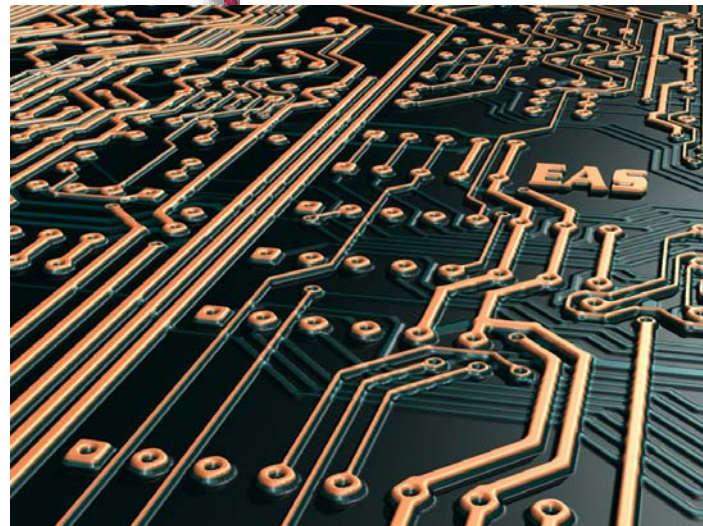
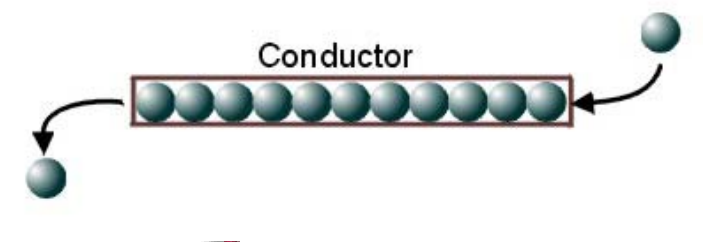
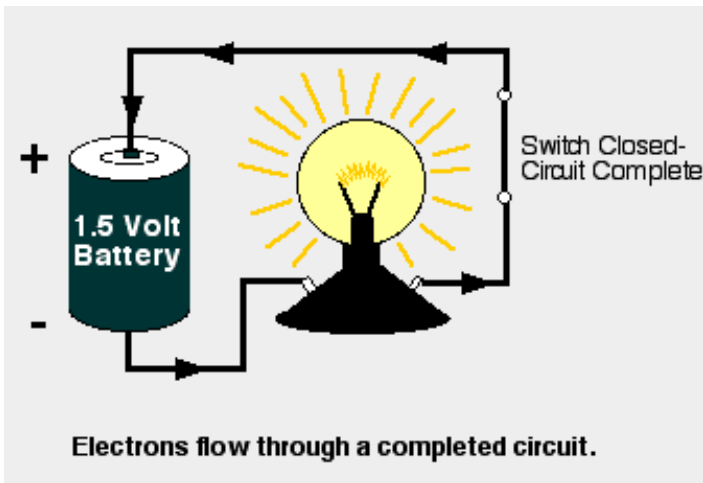
Alessandro Volta 1745-1827

I have only one work to say about hearing. I had tried without success to excite this sense with two single metallic plates, although they were the most active among all the movers of electricity, namely, one of silver or gold and the other of zinc, but I finally managed to affect it with my new apparatus, made up of 30 or 40 couples of these metals. I introduced two probes of metallic rods with rounded ends quite forward into the two ears, and I immediately connected them to the two ends of the apparatus. At the moment the circuit was completed in this way, I received a shock in the head, and a few moments later (the circuit operating continuously without any interruption), I began to be conscious of a sound, or rather a noise, in my ears that I cannot define clearly; it was a kind of jerky crackling or bubbling, as though some paste or tenacious matter was boiling. This noise continued without stopping and without increasing all the time the circuit was complete. Because of the disagreeable, and I feared, dangerous sensation of the jolt in the brain, I did not repeat this experiment several times.

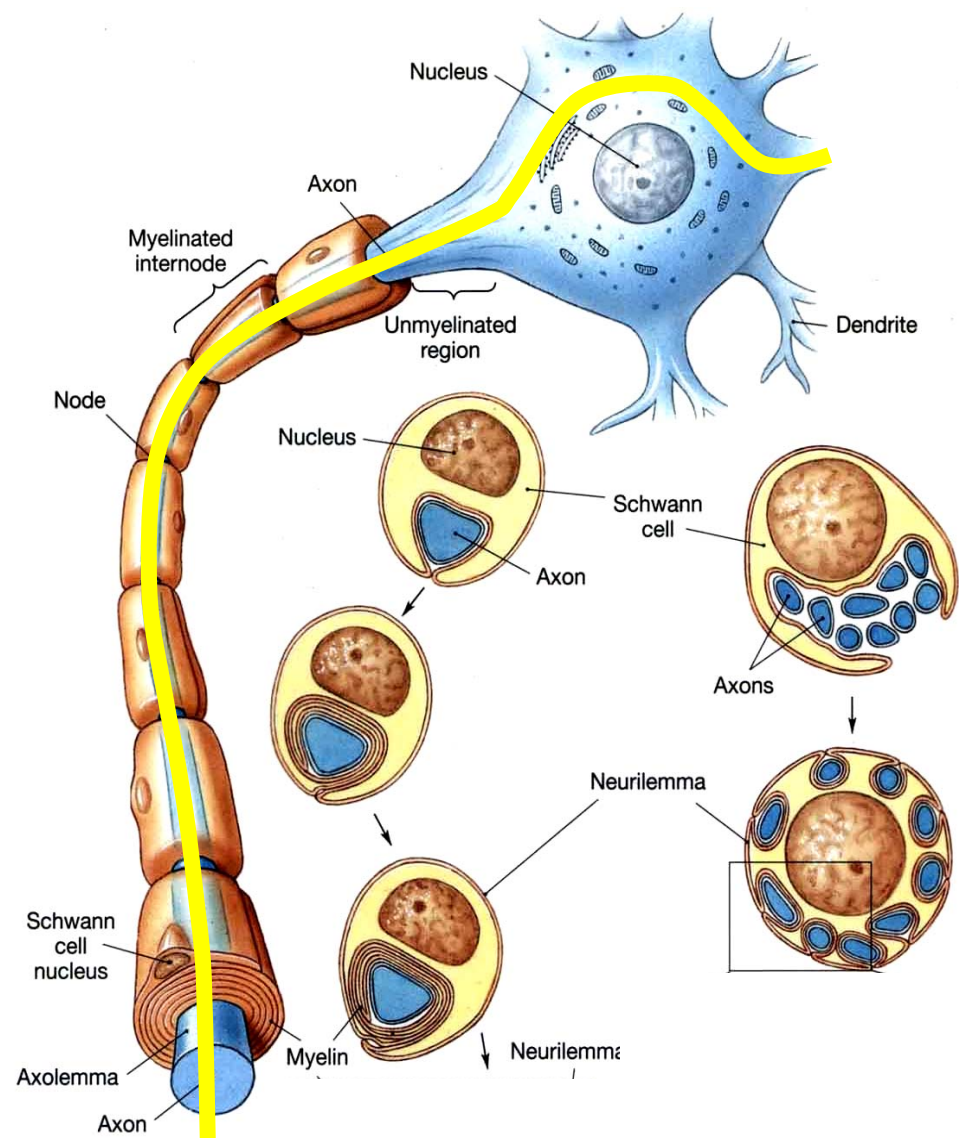
Mechanism of Human Facial Expression

Guillaume Duchenne, 1862

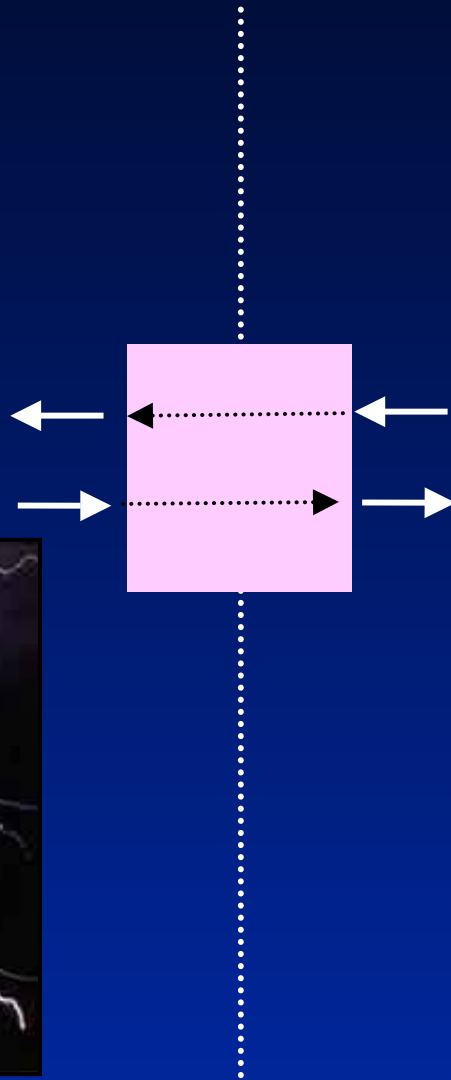
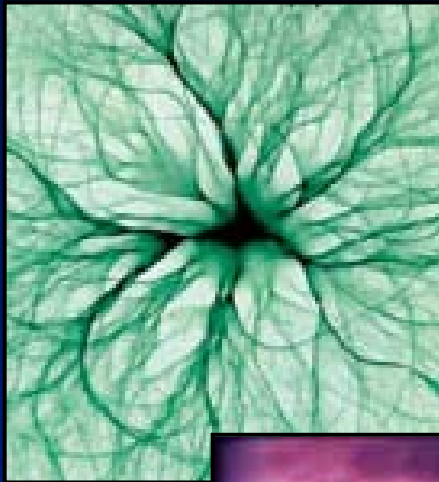




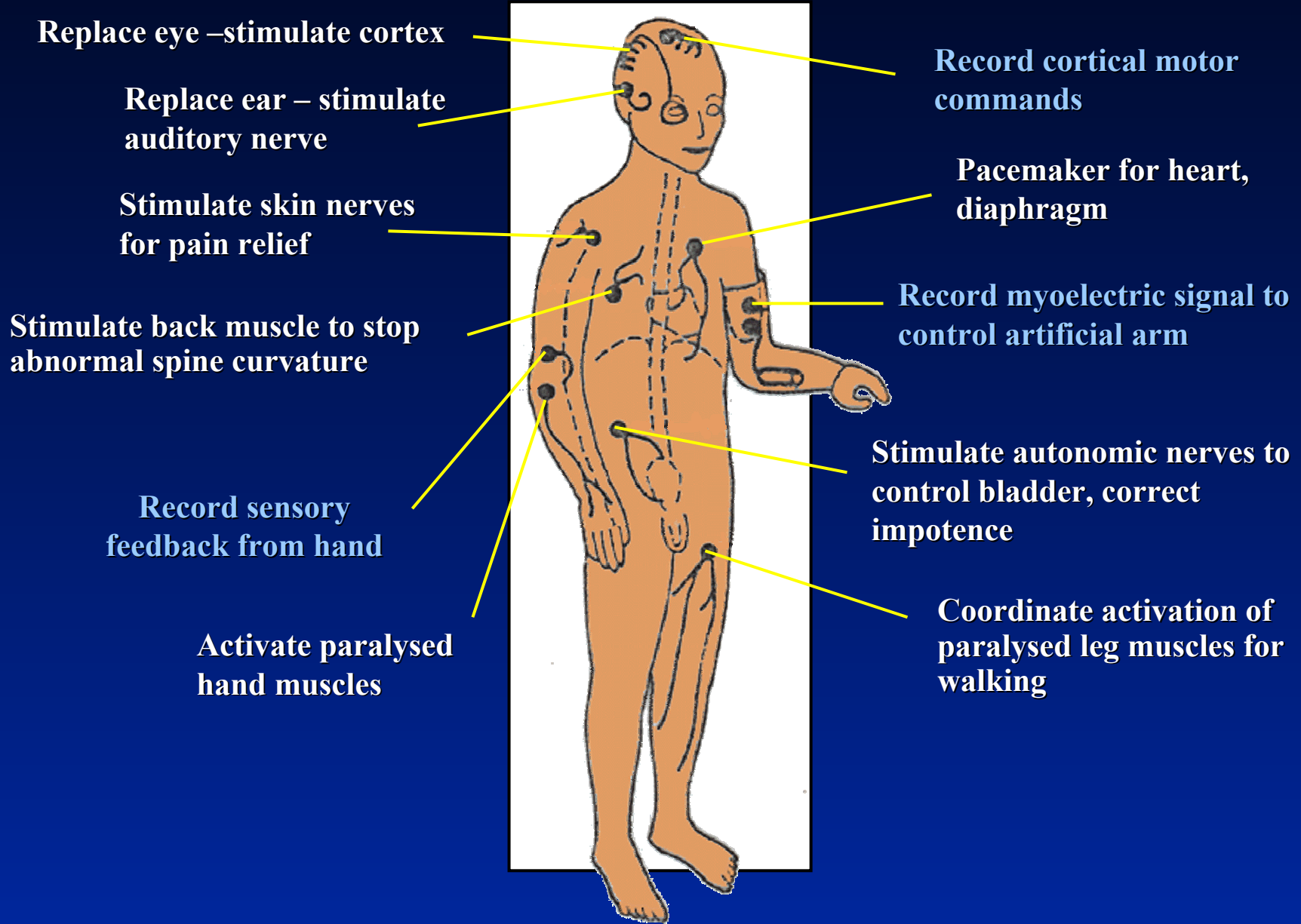
Stimulus



The goals of Neural Interfaces are to obtain control signals directly from the electrical activity of neurons and convey sensory information and/or motor commands directly to the nervous system.



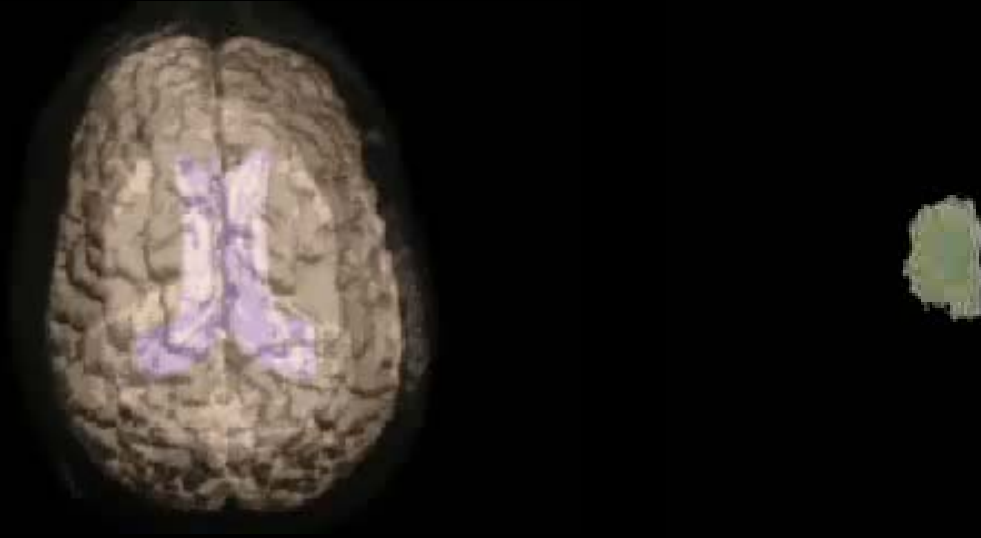
Neuroprosthetic interfaces with the nervous system



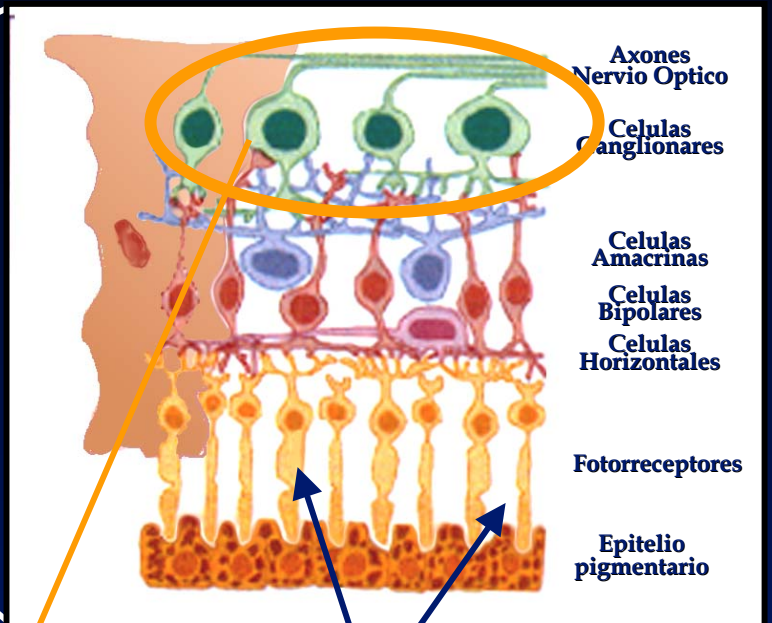
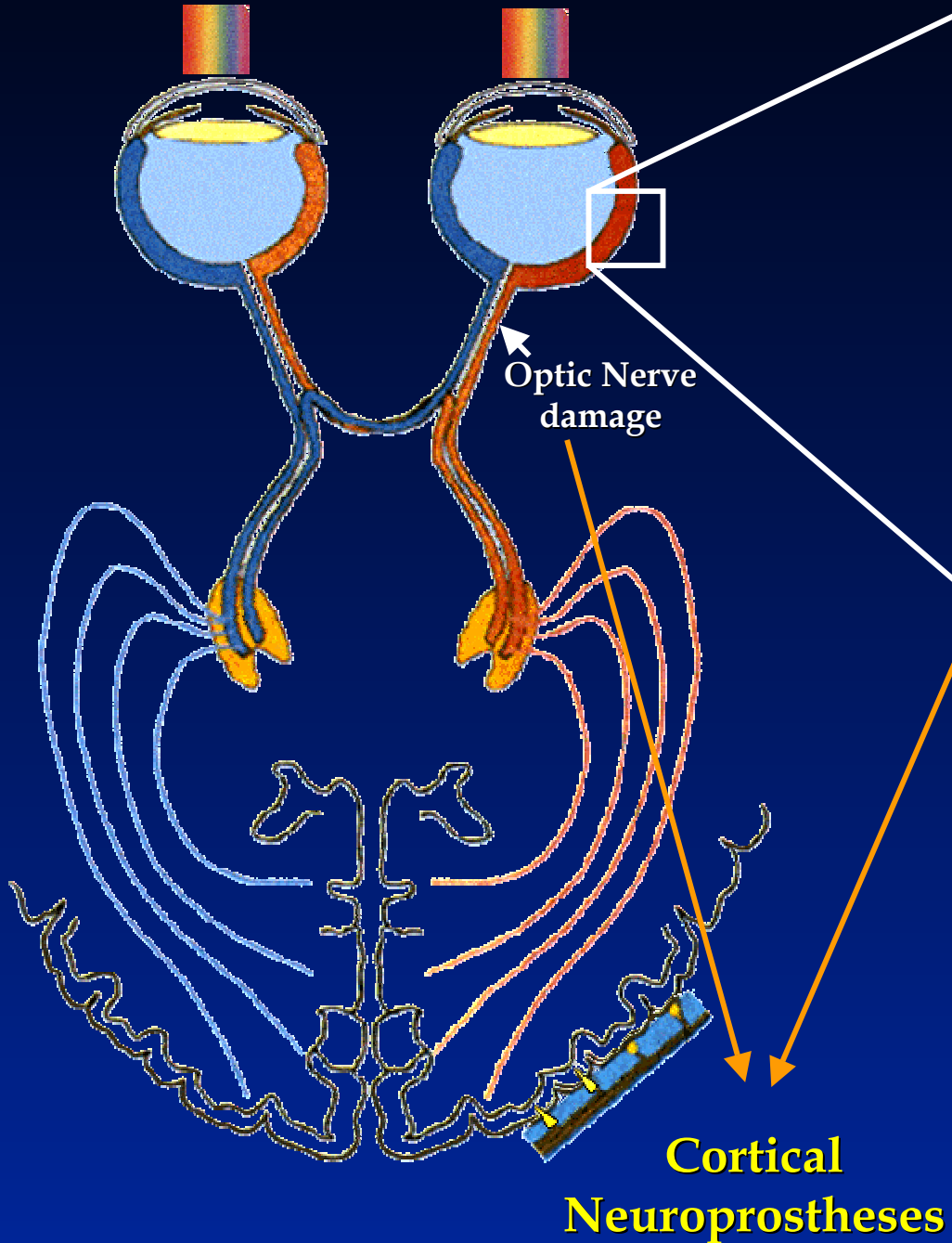
The Problem:

- **Damage to Peripheral Nervous System**
- **Injury to Spinal Cord**
- **Disorders of Sensory Organs**

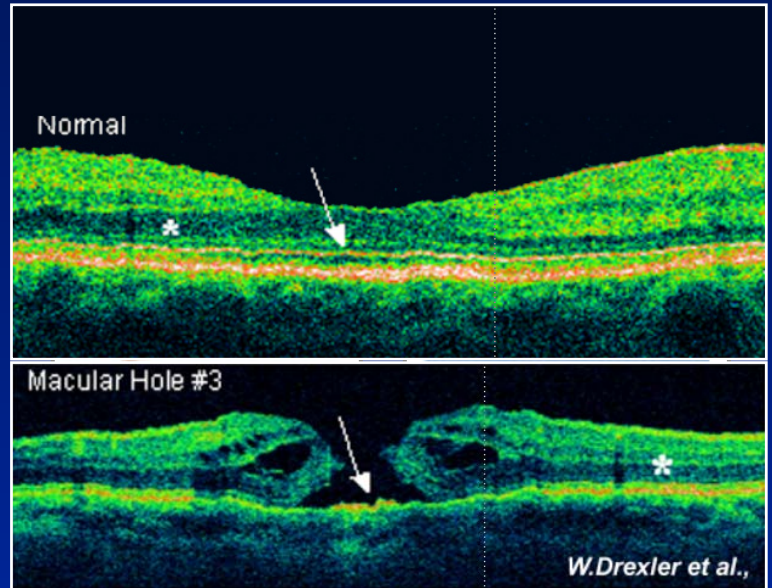
...However, the brain is usually perfectly functional in spite of these injuries.

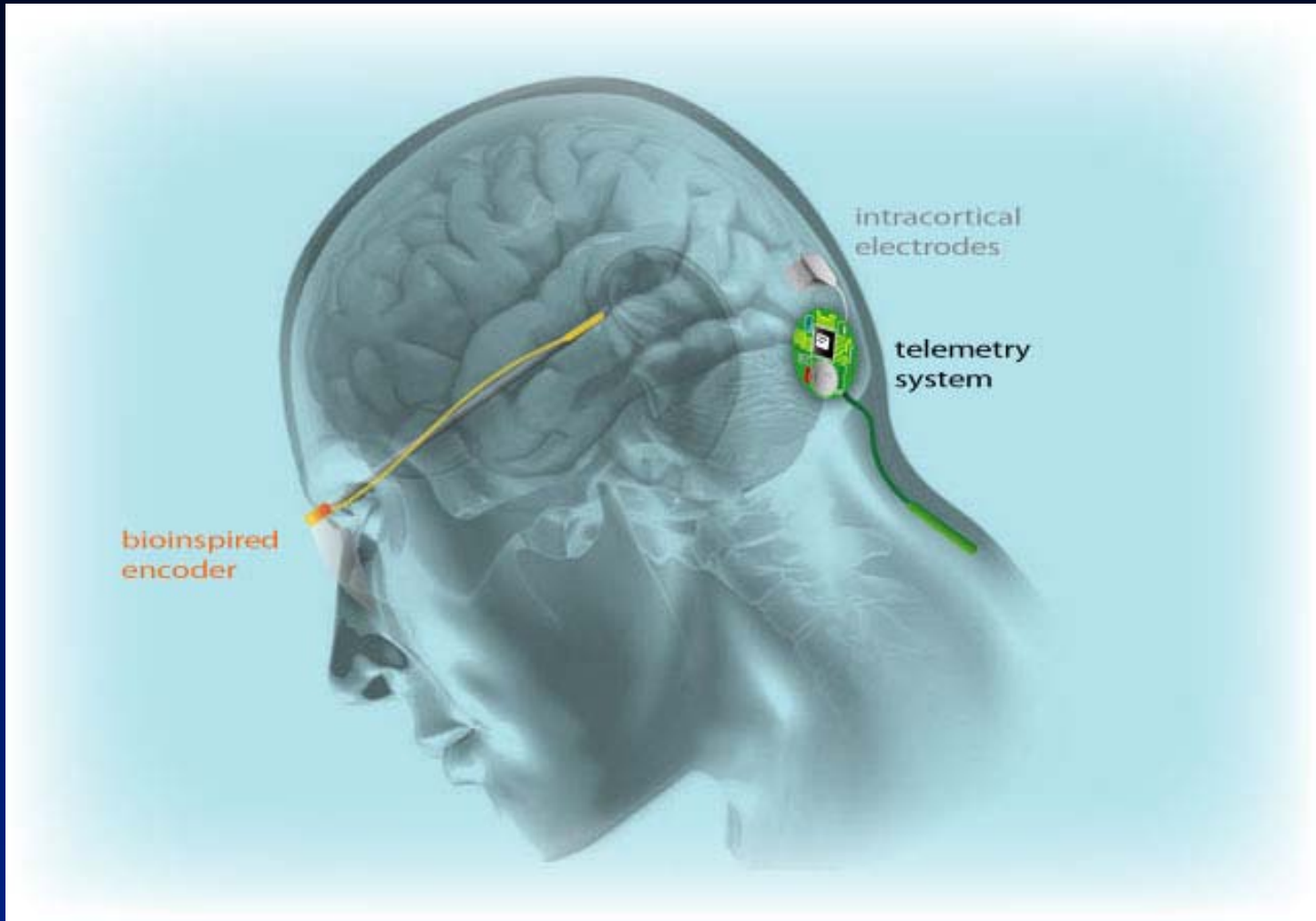


... the solution: Communicate directly with the brain



Degeneration (RP, DM)



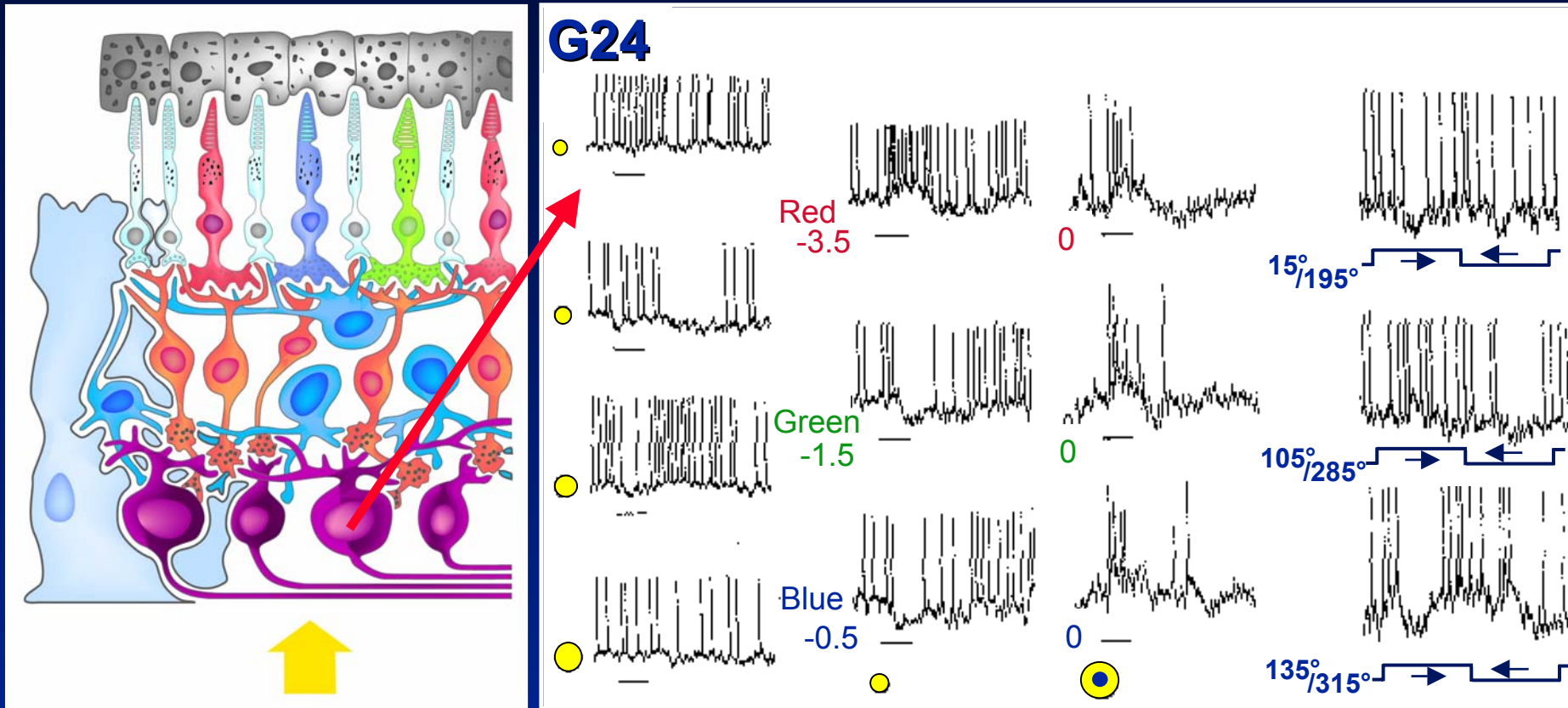


External processing

The problem is not to transmit a image with a high resolution, but to send useful information to the right locations inside the SNC.

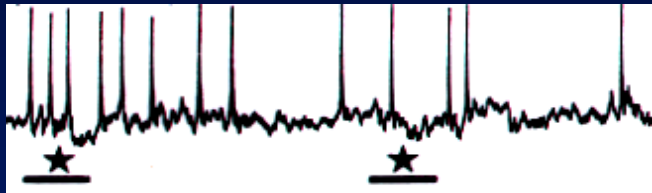
- ✓ **It is important to know how the visual information is encoded in the retina.**

Ganglion cell spike trains are the result of extensive signal processing in the retinal network

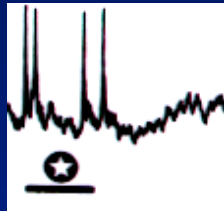
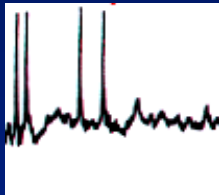


Individual ganglion cells are unreliable stimulus encoders due to response variability and ambiguity

Variability

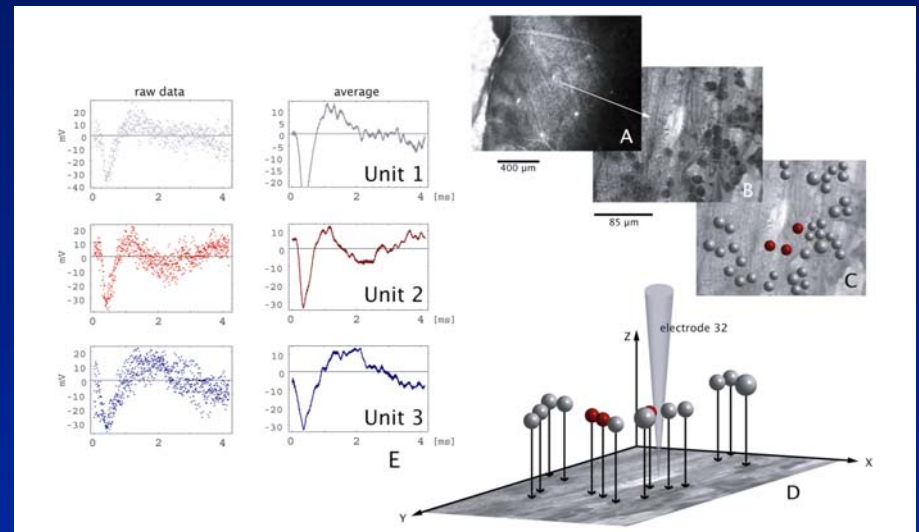
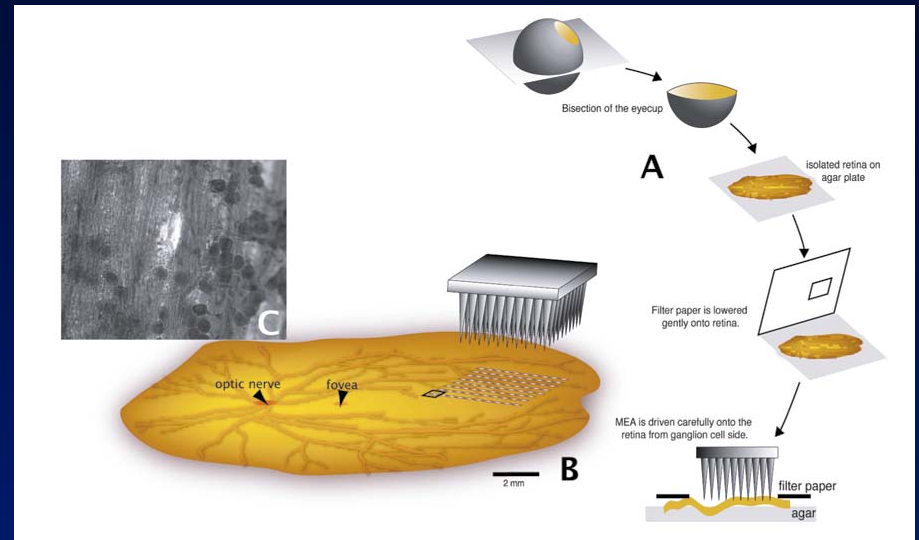


Ambiguity



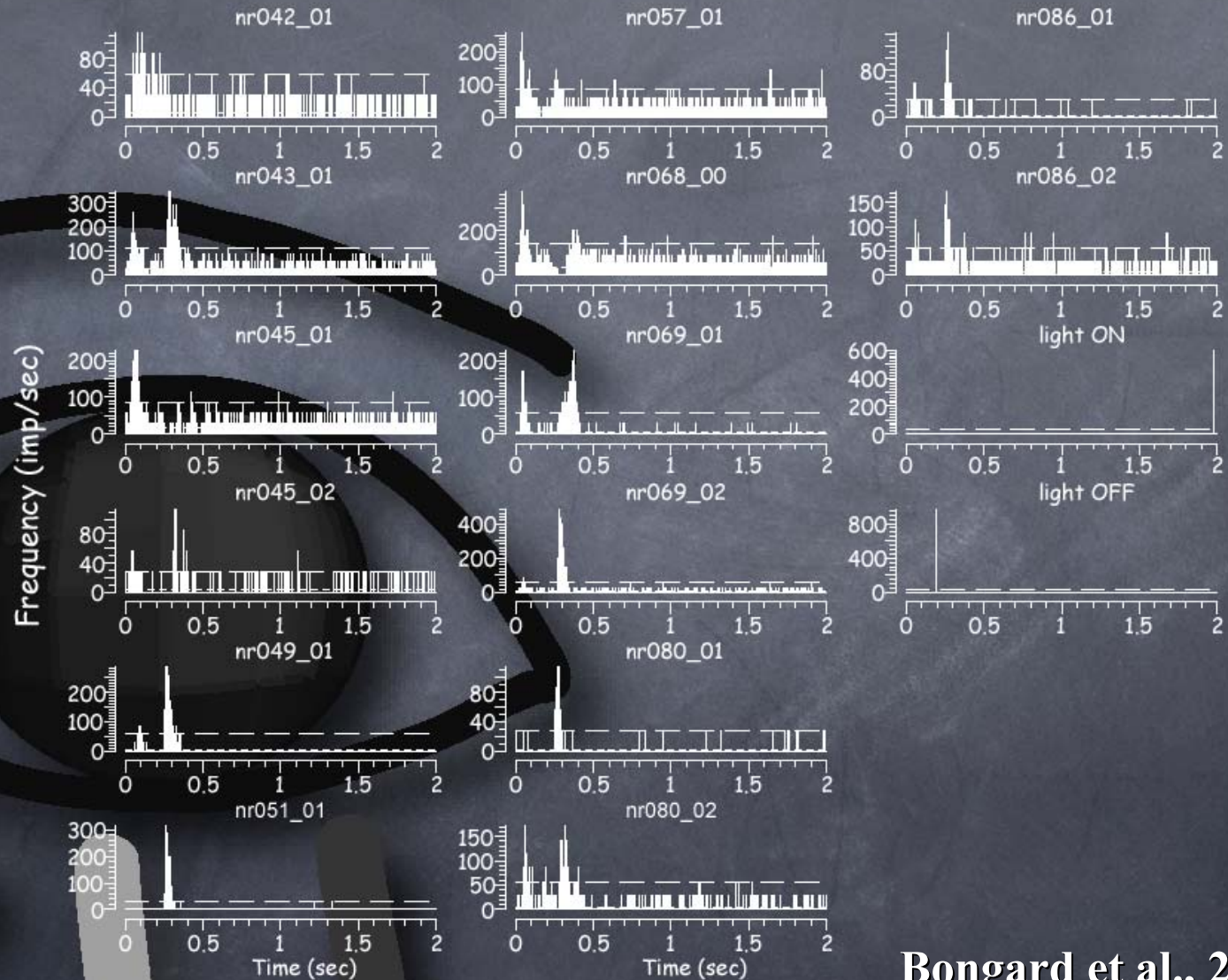
Ratecode?
Timecode?

local versus distributed representation

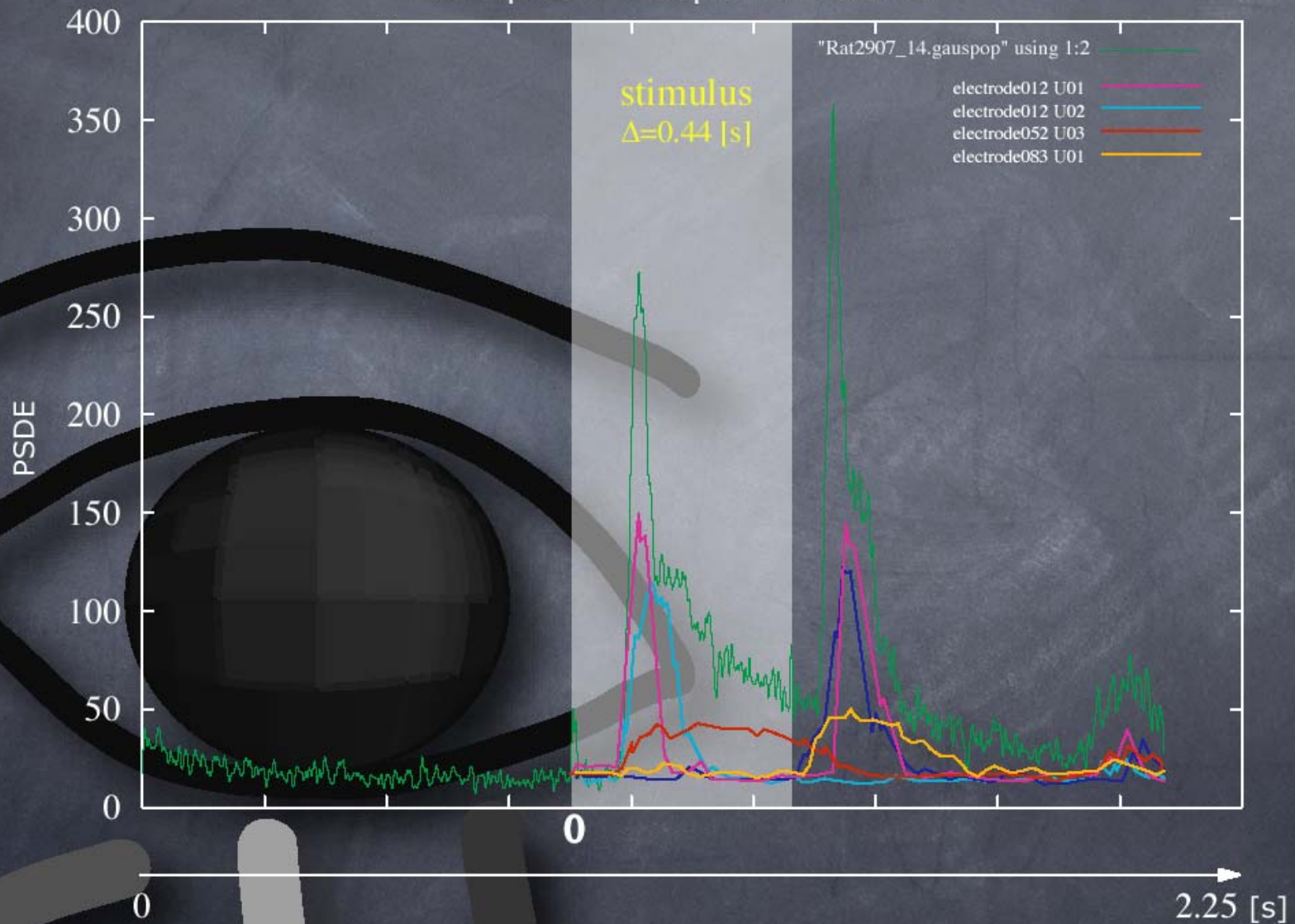


in vivo recordings of retinal ganglion cells
Oryctolagus cuniculus

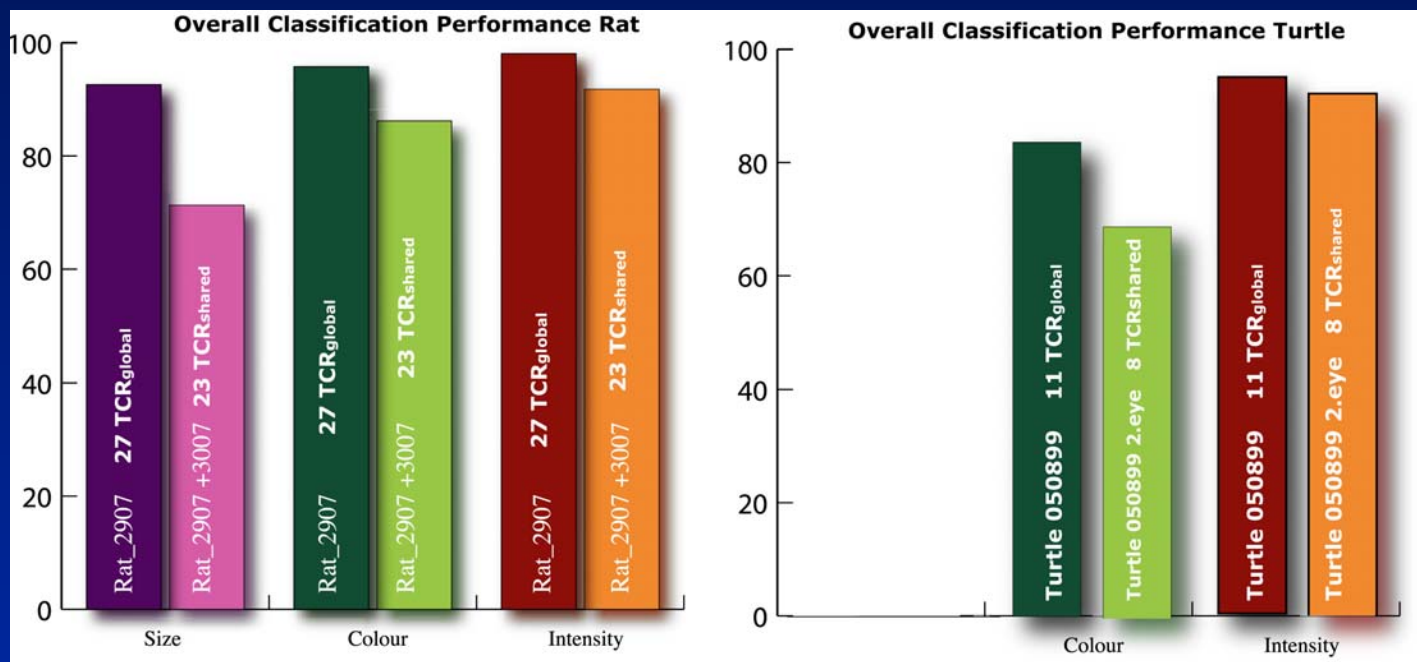
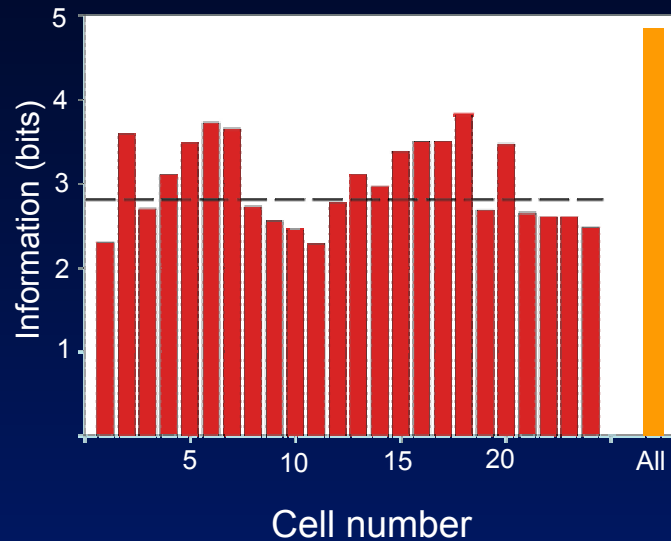
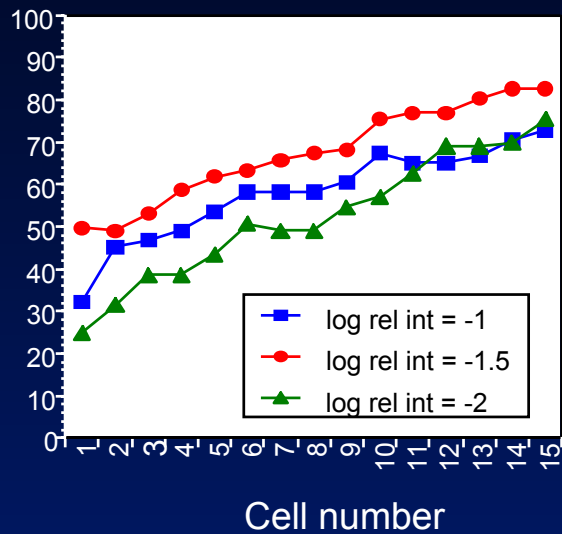
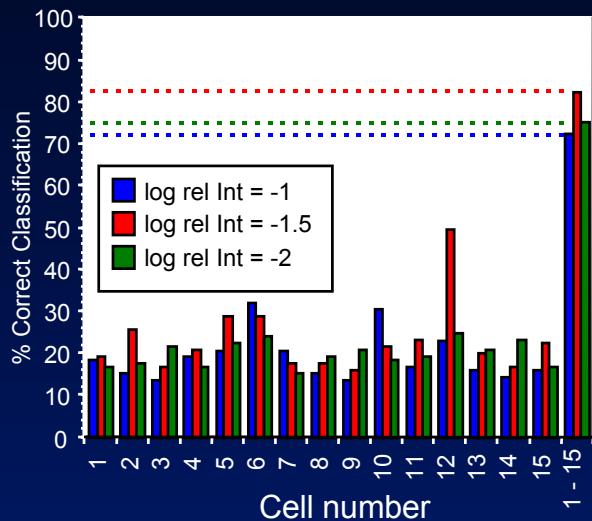
Experiment 06.03.2003, rabbit
Perievent Histograms, reference = light ON, bin = 1 ms



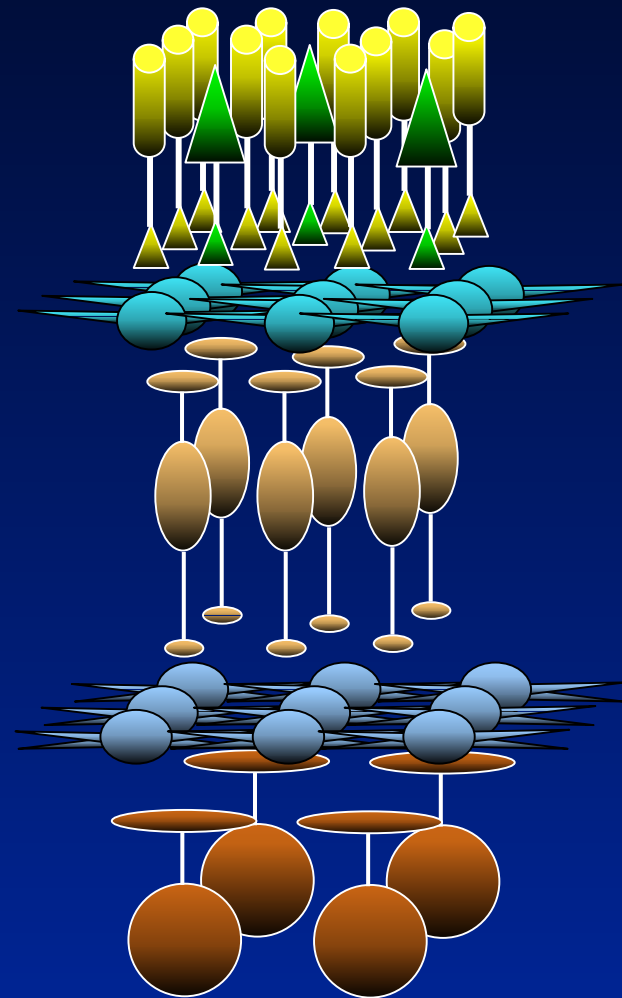
PSDE modulo period
Examples of Response Classes



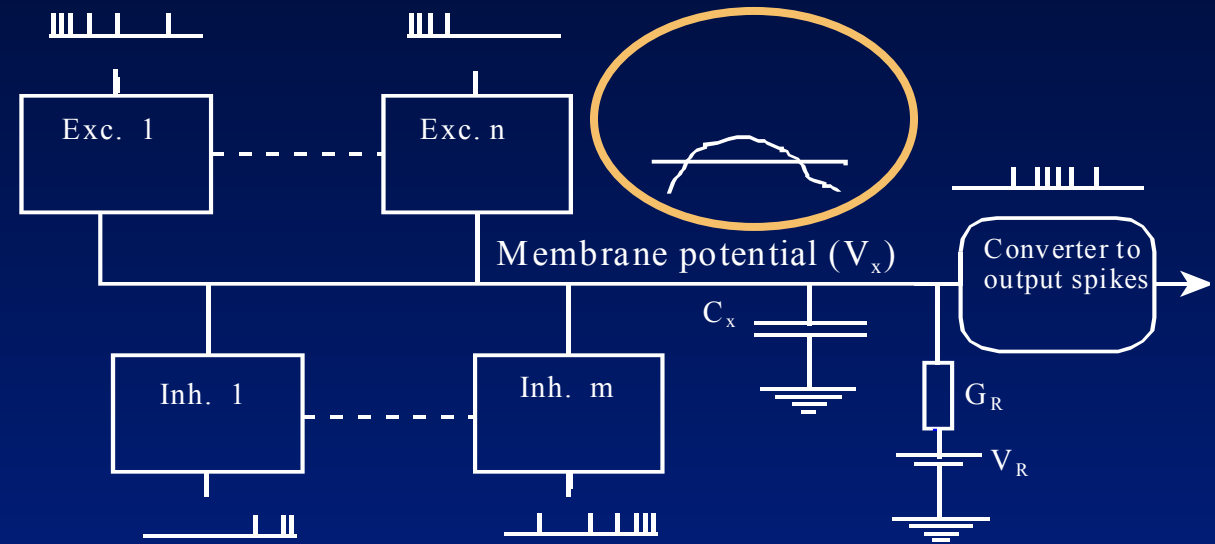
The brain can potentially deduce reliable information about stimulus features from response patterns of retinal ganglion cell populations



Development of a reconfigurable bioinspired visual processing front-end (artificial retina)



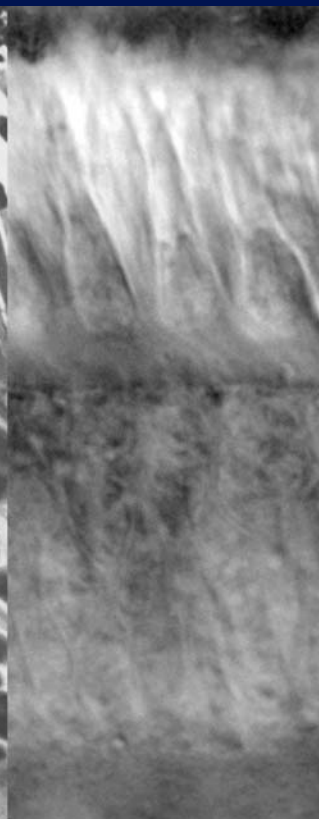
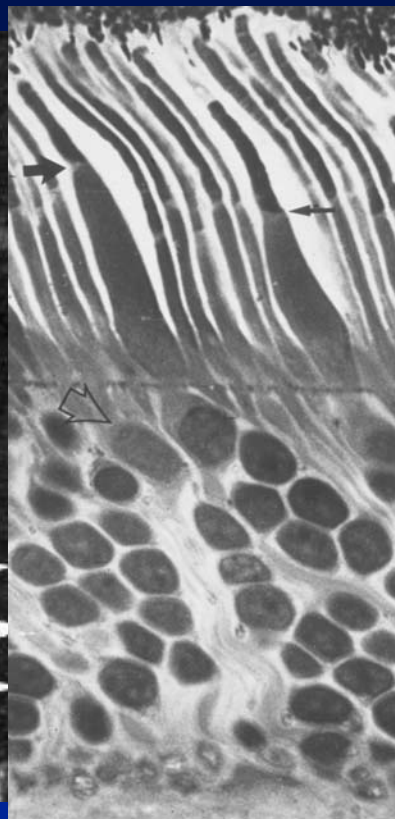
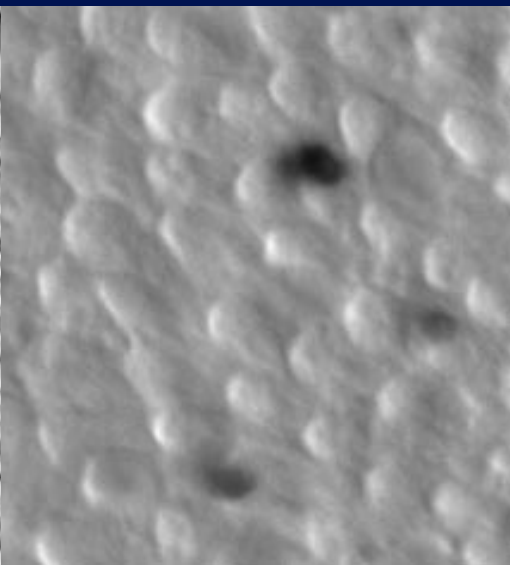
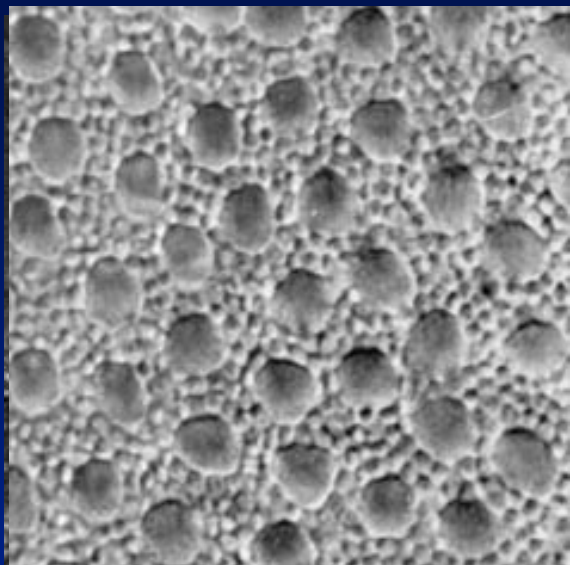
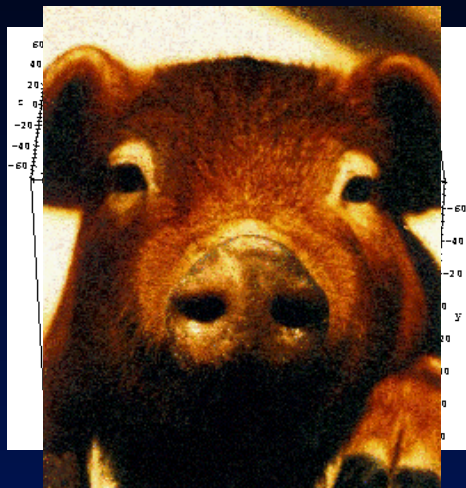
Generation of output spikes



Different approaches:

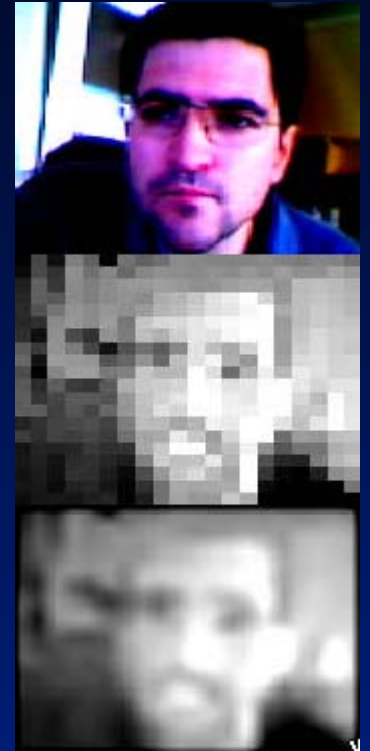
- Phase coding (firing-time): $t_d(V_x)$
- Spike frequency coding (firing-rate): $F(V_x)$

What animal model?

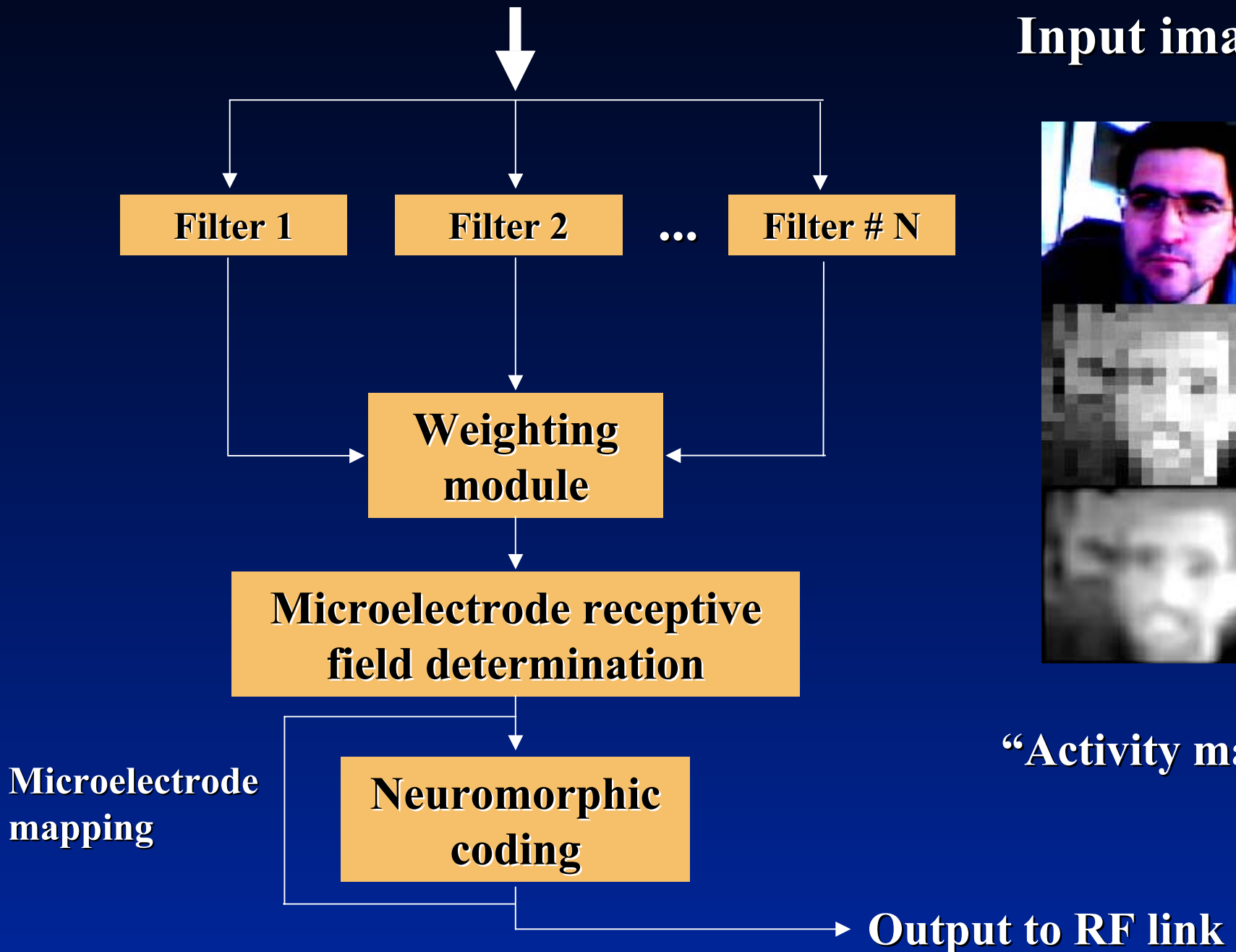


- Mammals have 2 - 4 photoreceptor types, ca. 50 retinal cell types

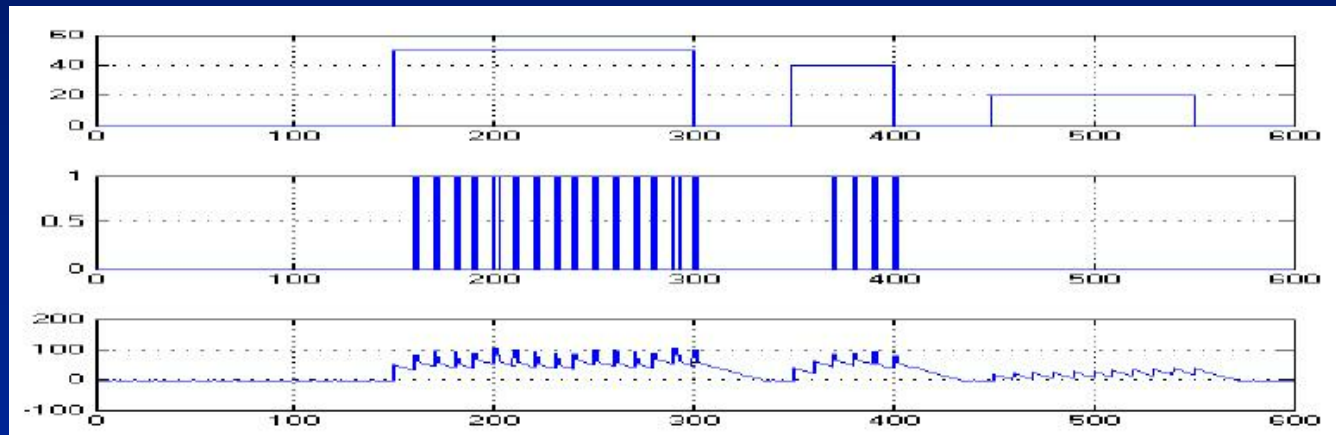
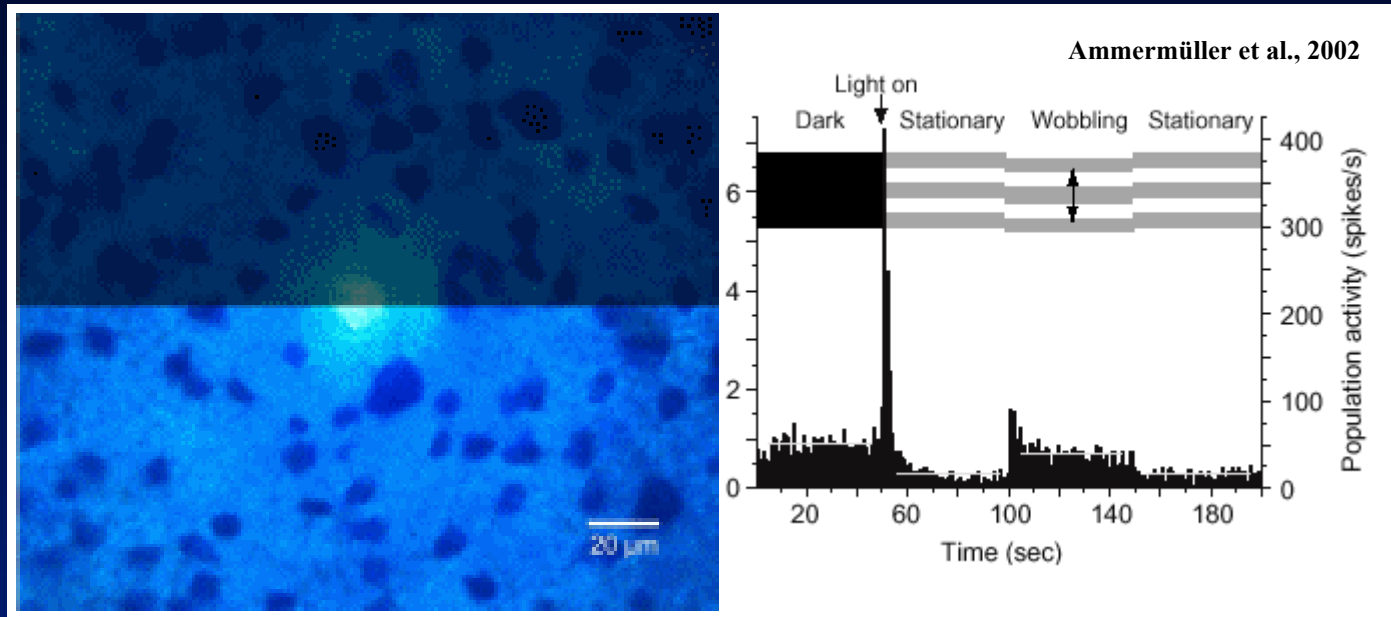
Input image

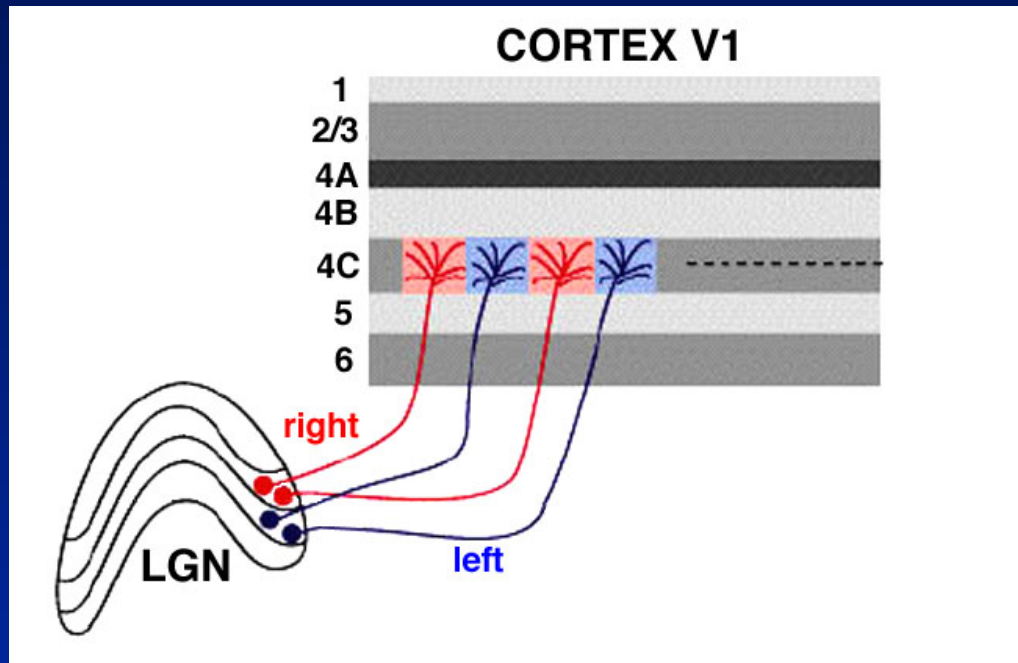
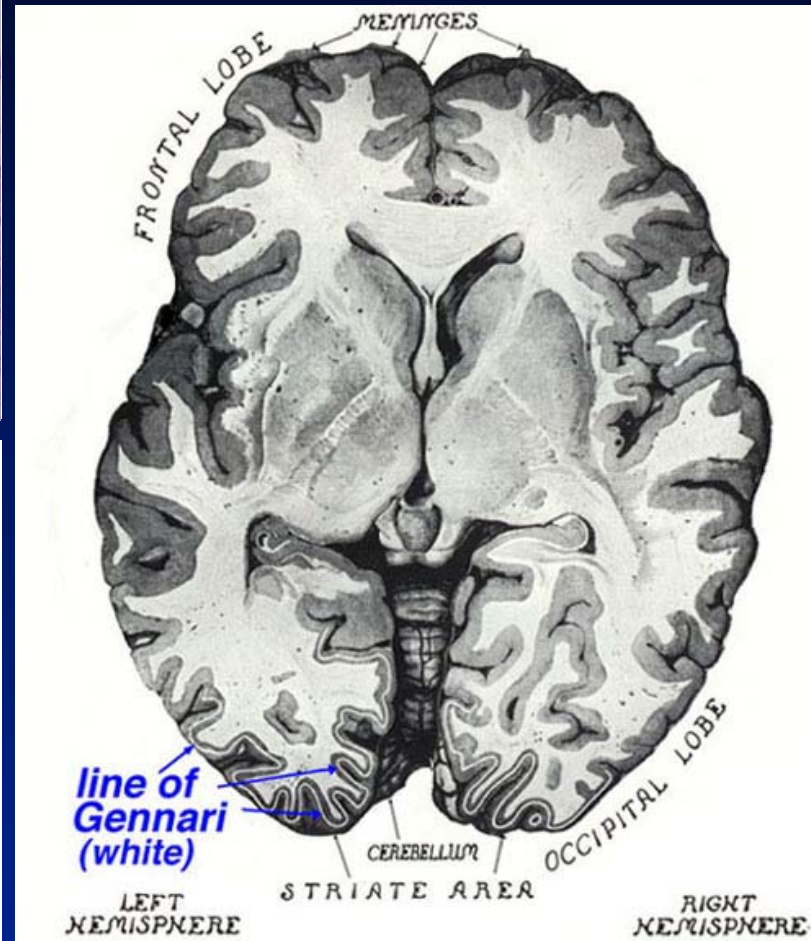
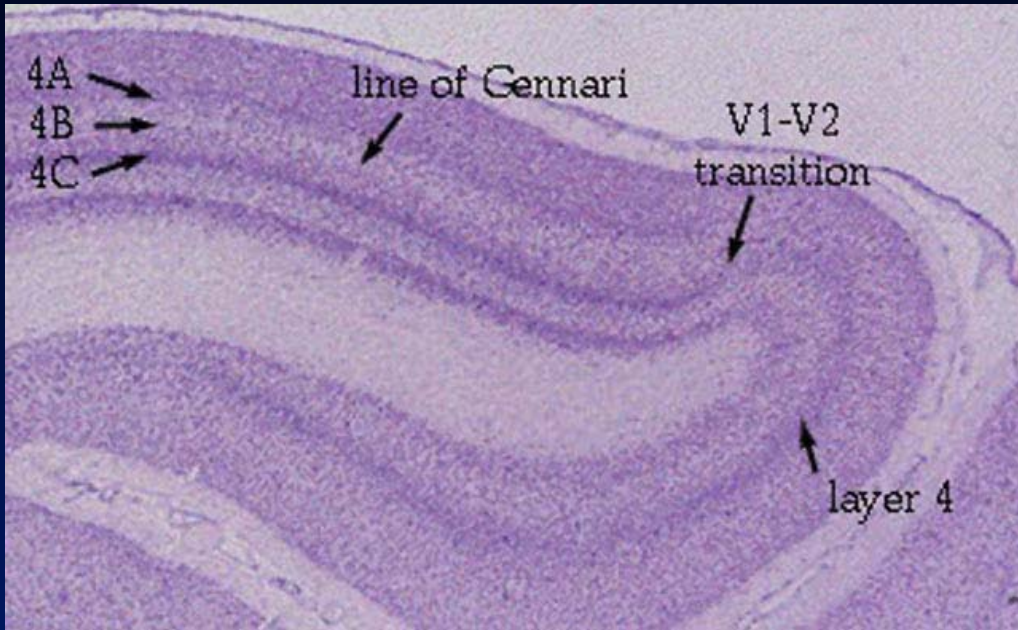


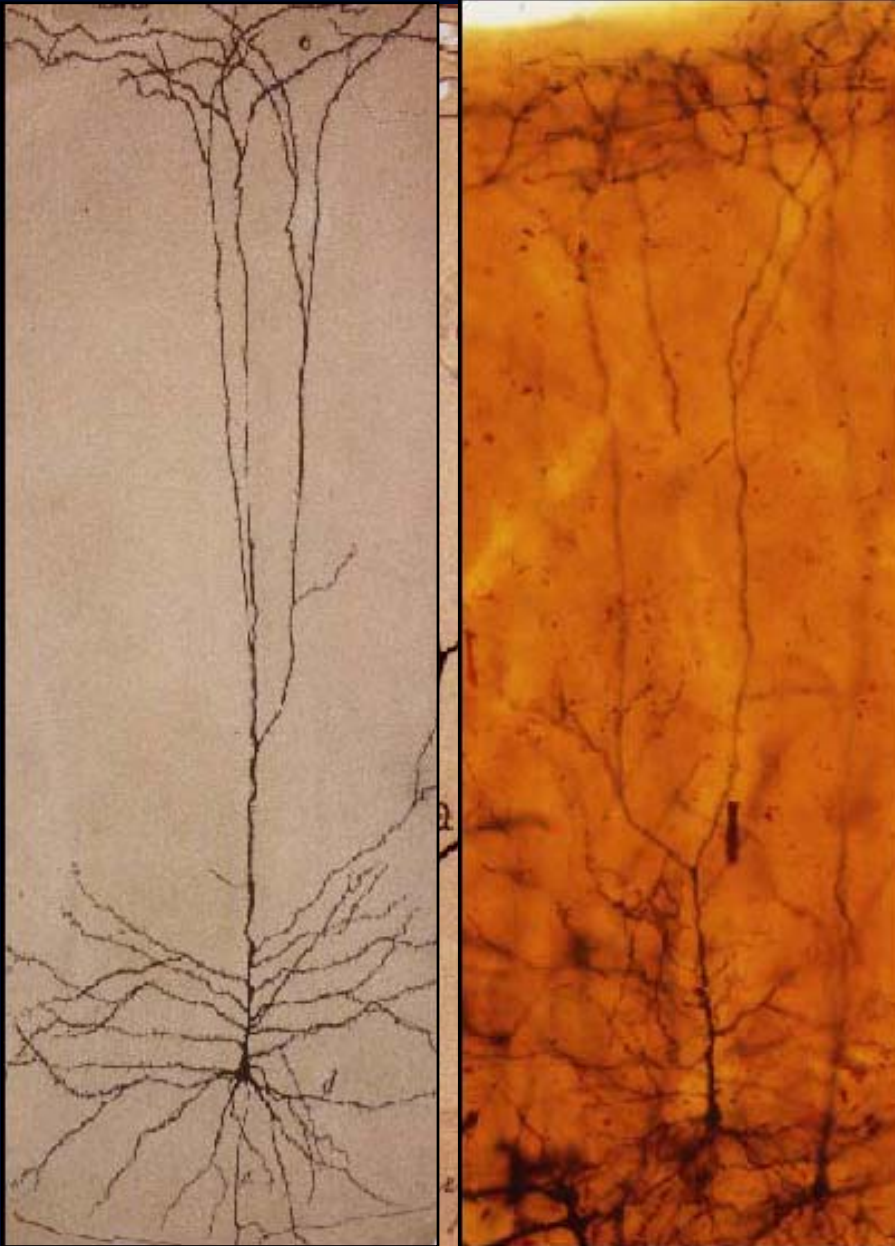
“Activity matrix”



Single spike neuron (Xilinx block set for Simulink) and simulation results for flashes of different duration and intensity







“ . . . the cerebral cortex is similar to a garden filled with trees, the pyramidal cells, which,

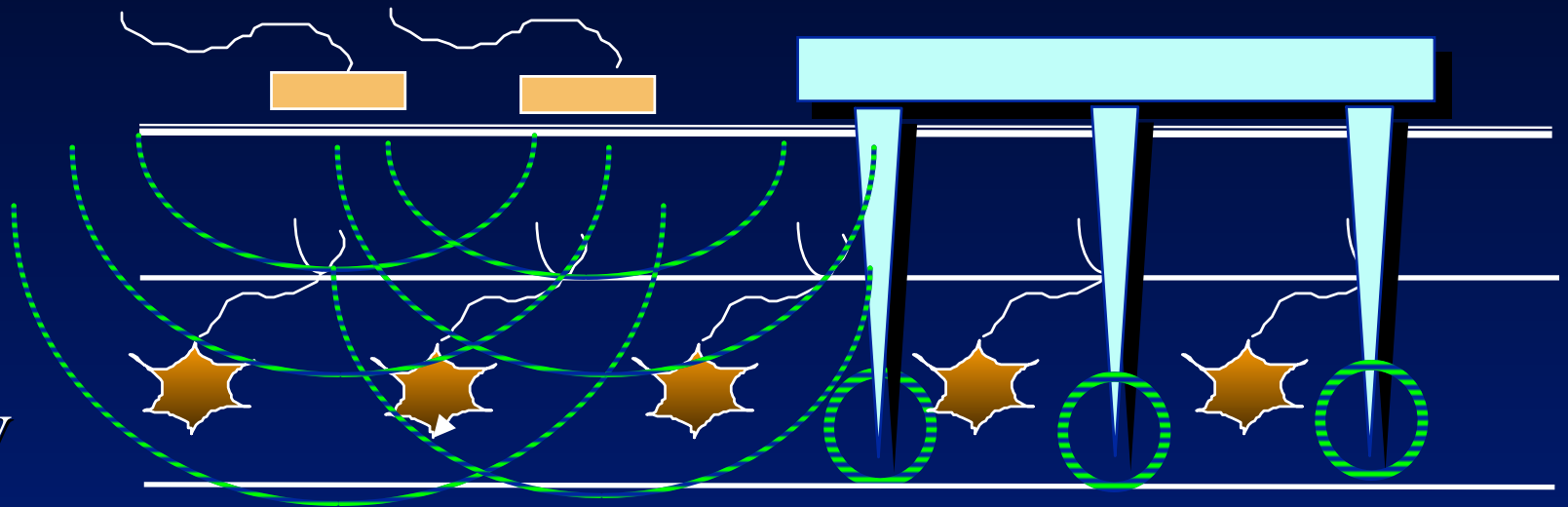
thanks to intelligent culture, can multiply their branches, sending their roots deeper and

producing more and more varied and exquisite flowers and fruits.”

Santiago Ramon y Cajal

Surface macrostimulation

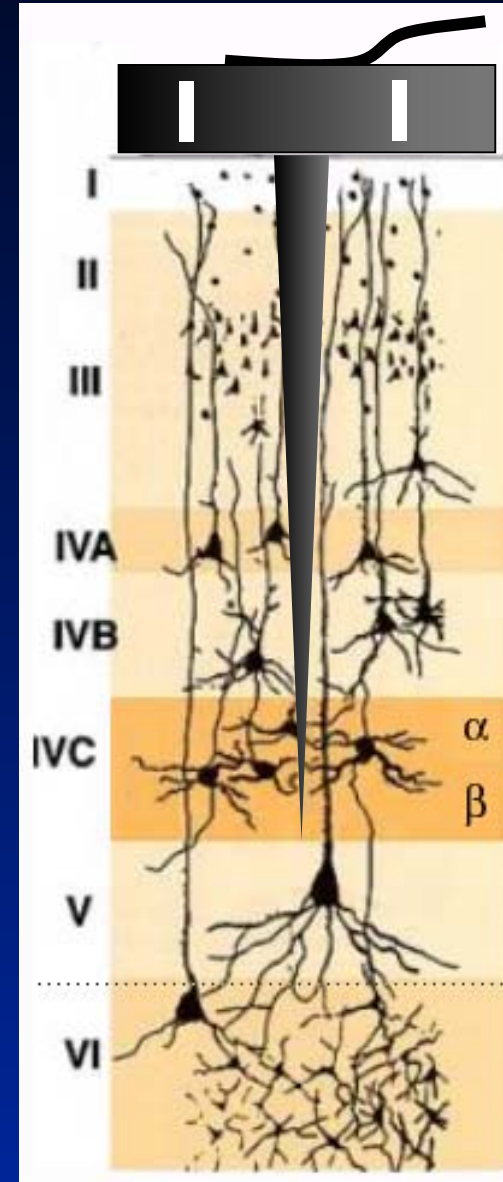
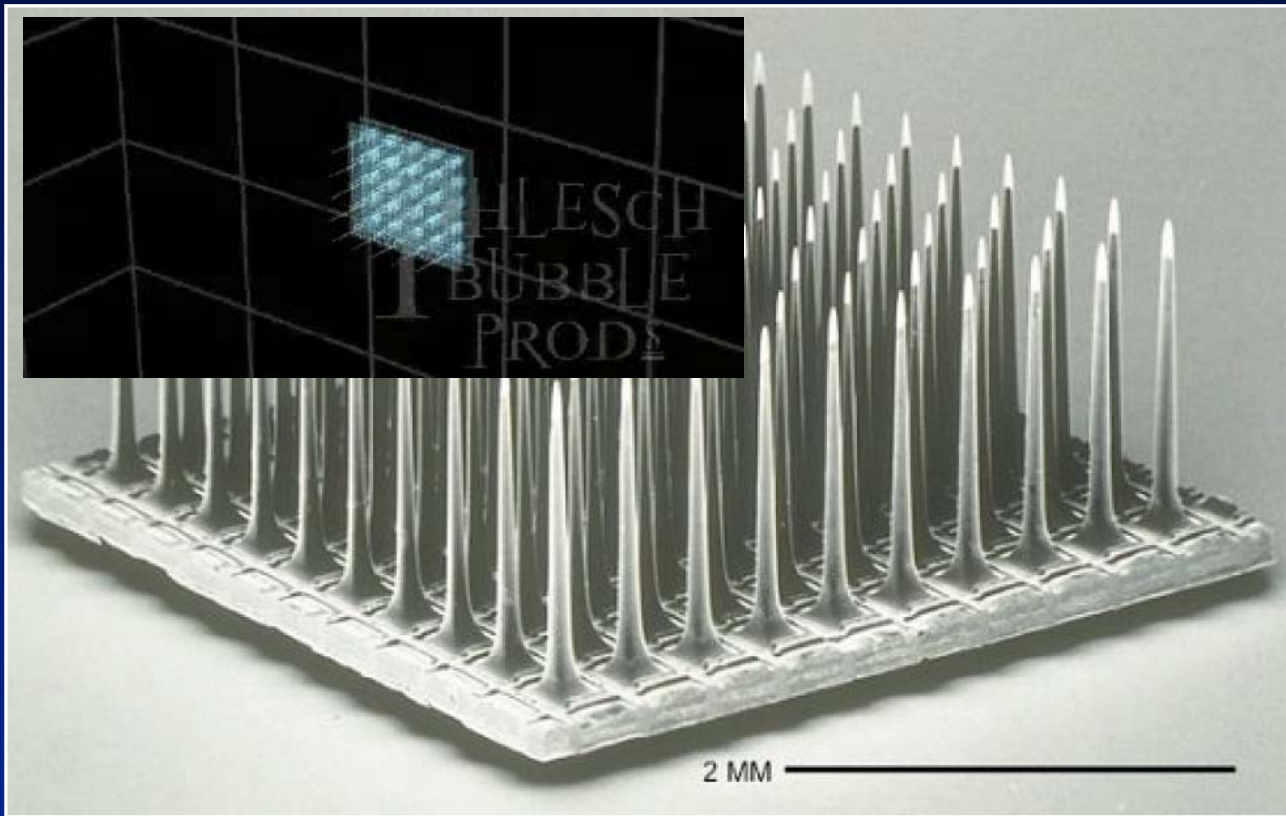
Intracortical microstimulation

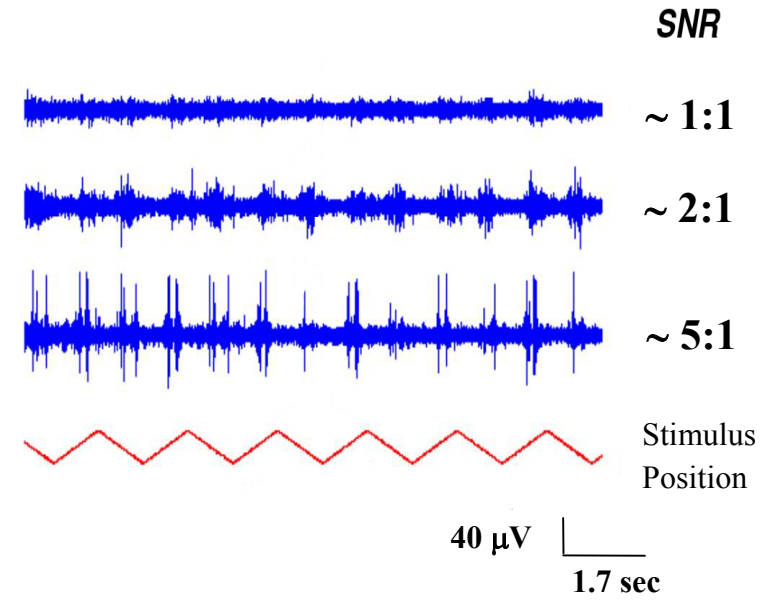
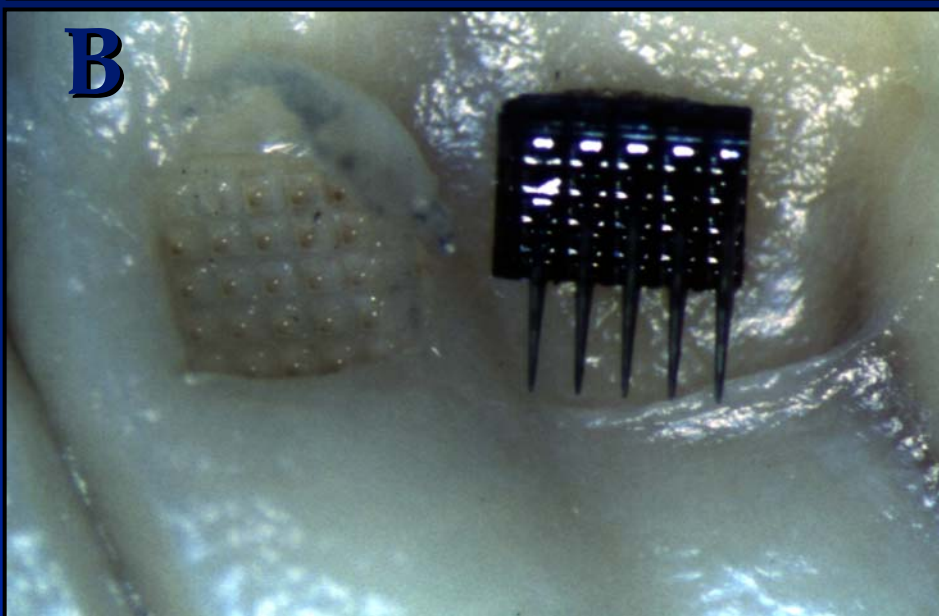
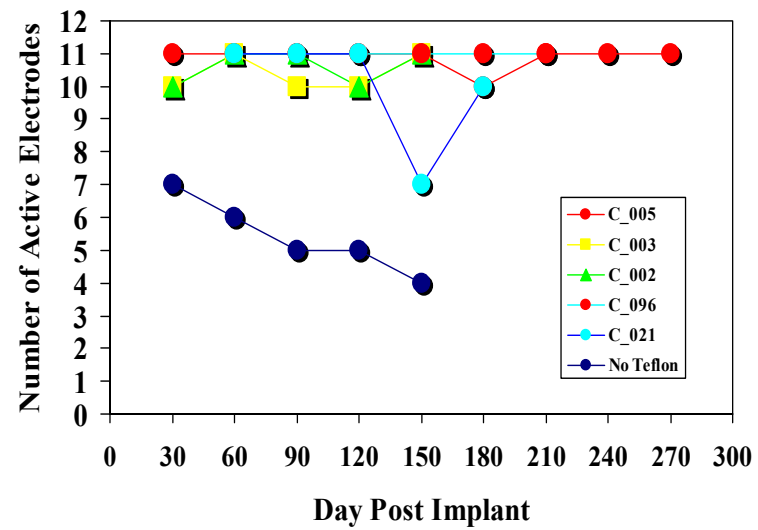
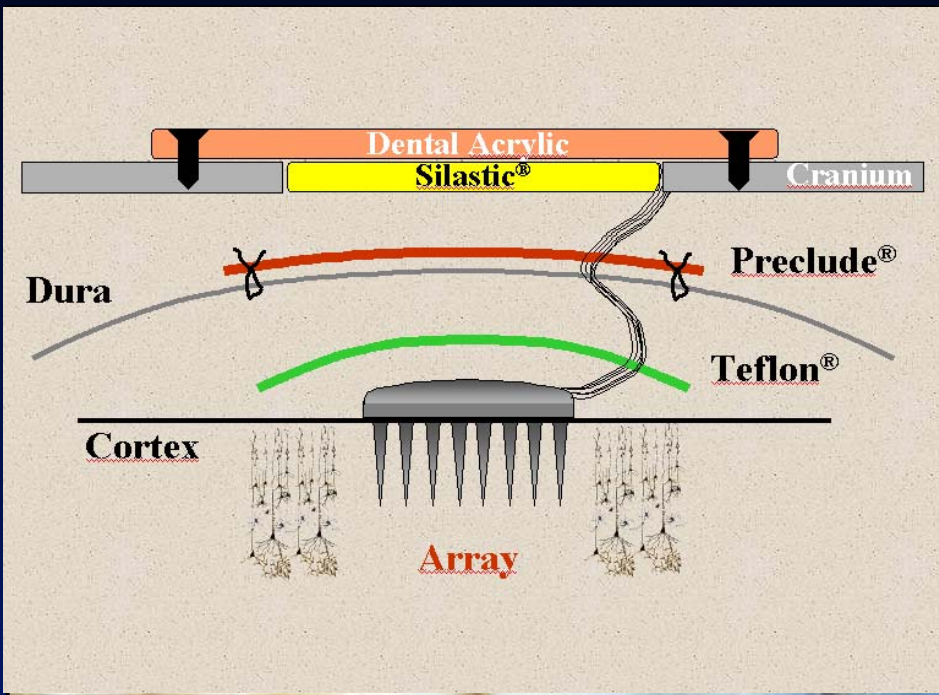


Layer IV

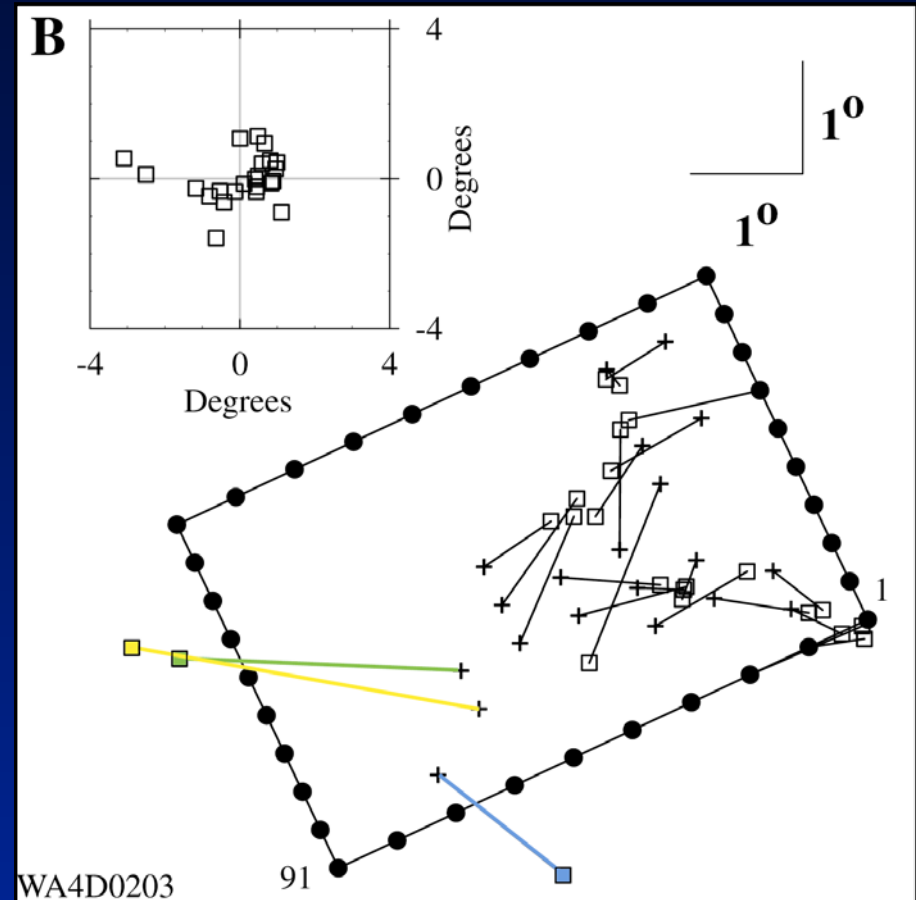
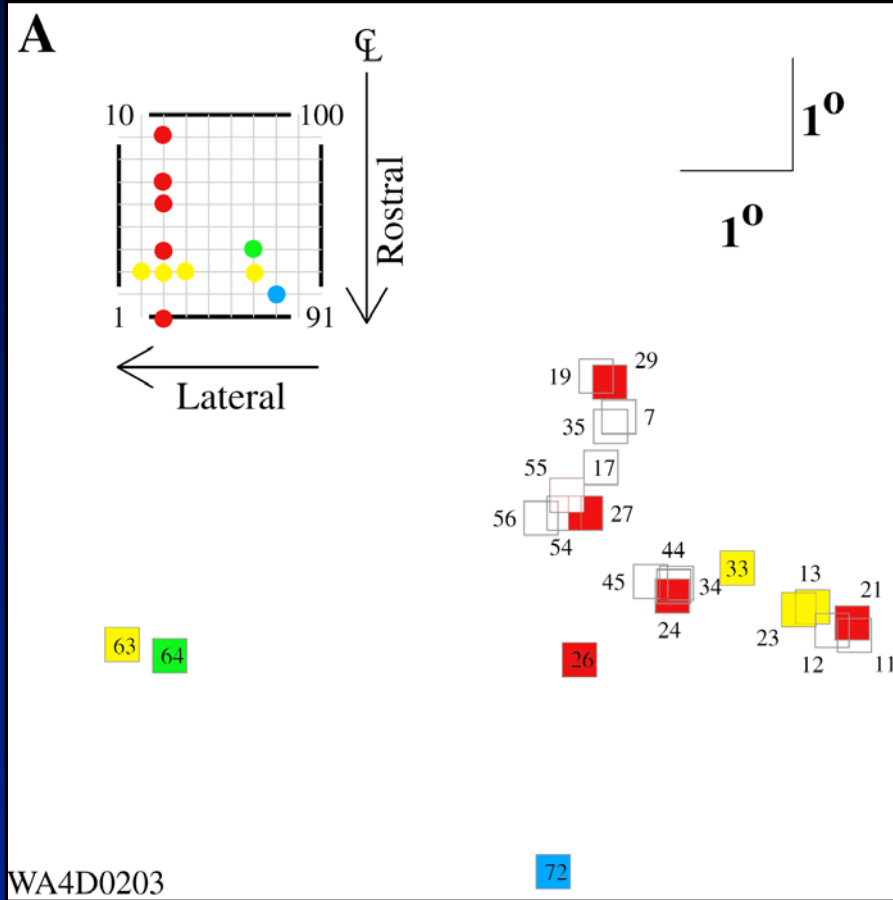
Contact area	1 mm ²	0.001 mm ²
Impedance	10 kΩ	100 kΩ
Current	1 mA	0.01 mA
Charge density	10 μC/cm ²	100 μC/cm ²
Mean power	20 μW/channel	0.02 μW/channel

Design of electrodes for cortical stimulation



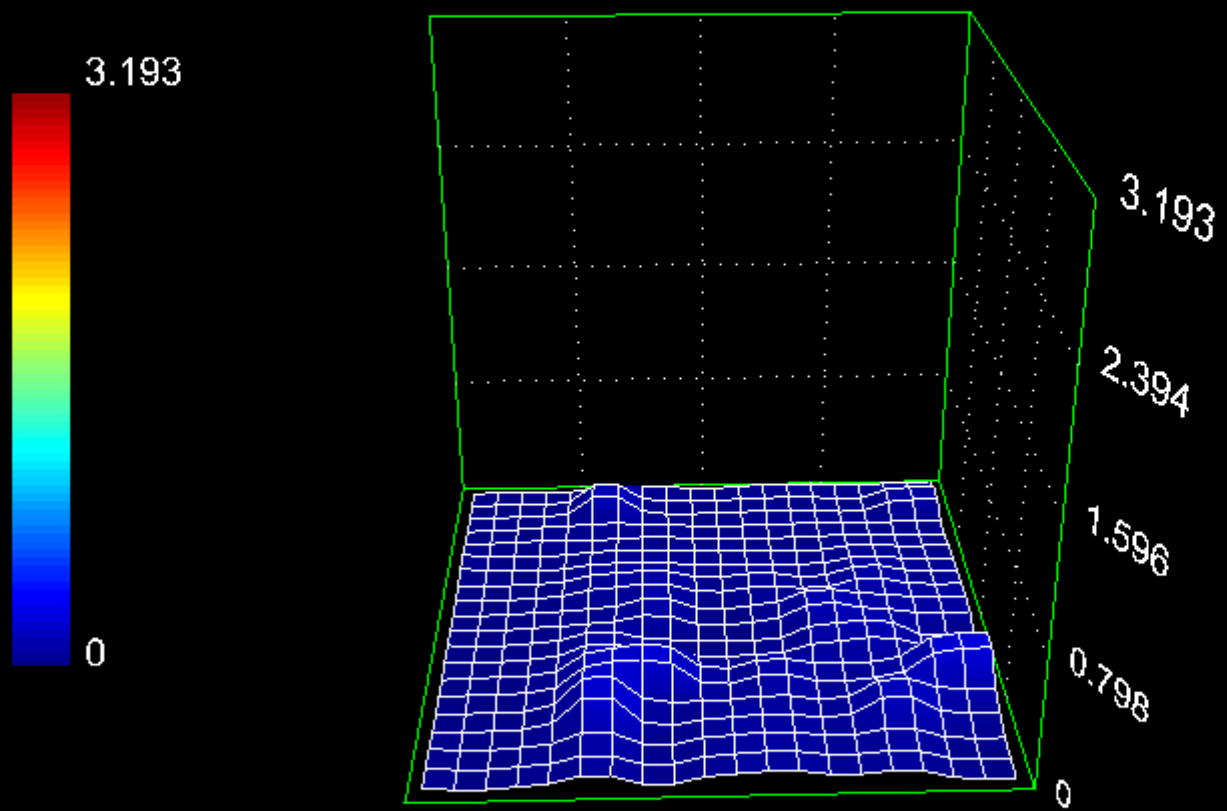


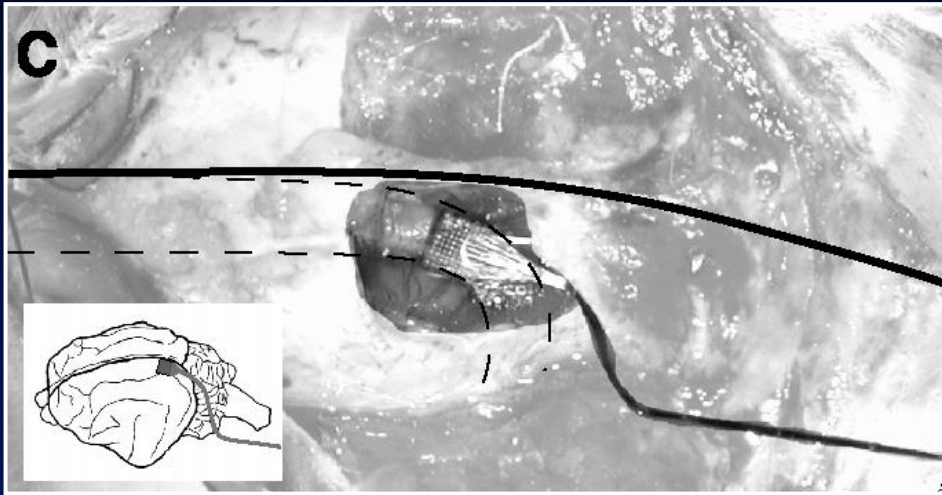
Receptive field map of cat visual cortex obtained with simultaneous recordings using intracortical microelectrodes



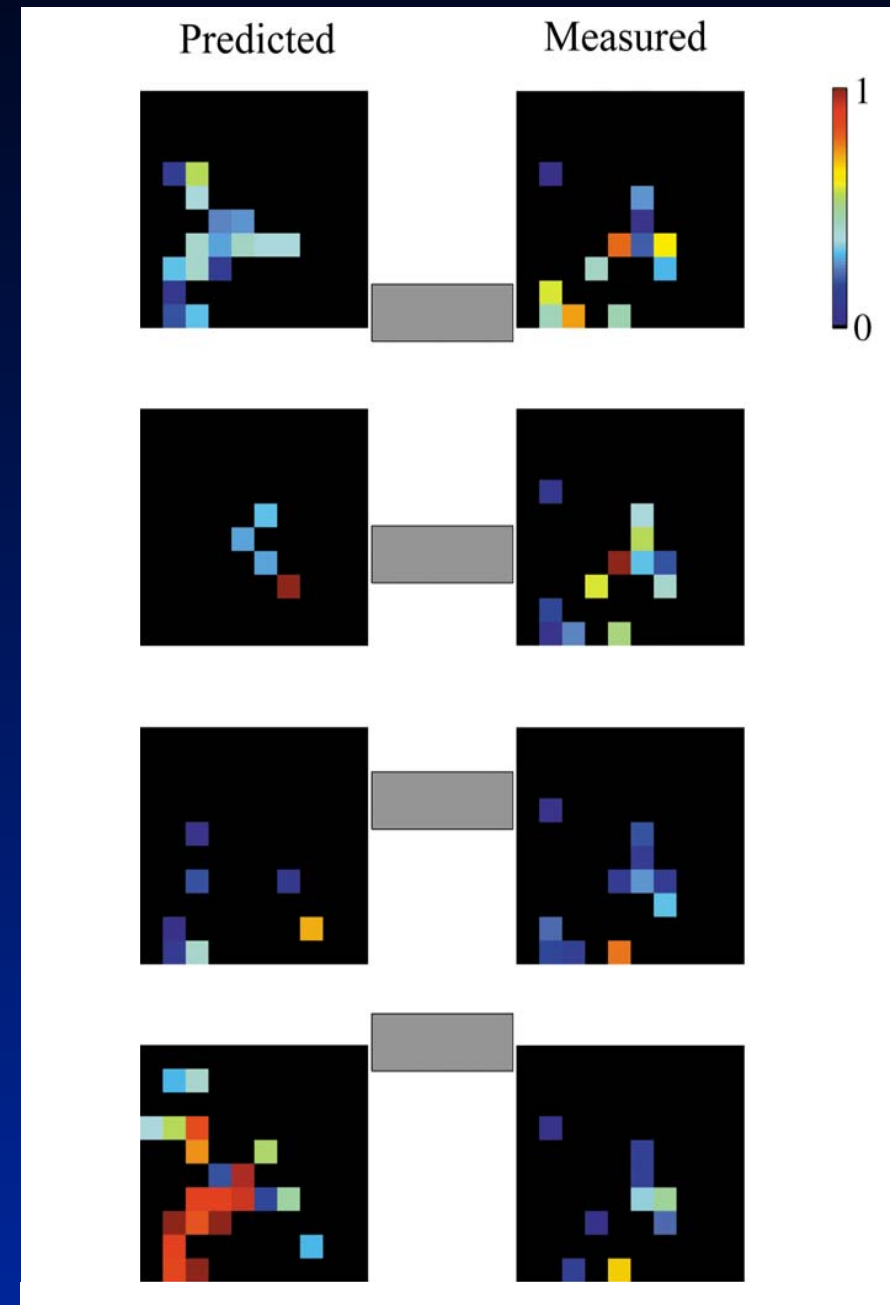
Neuronal Activity, Ack1543g.nex

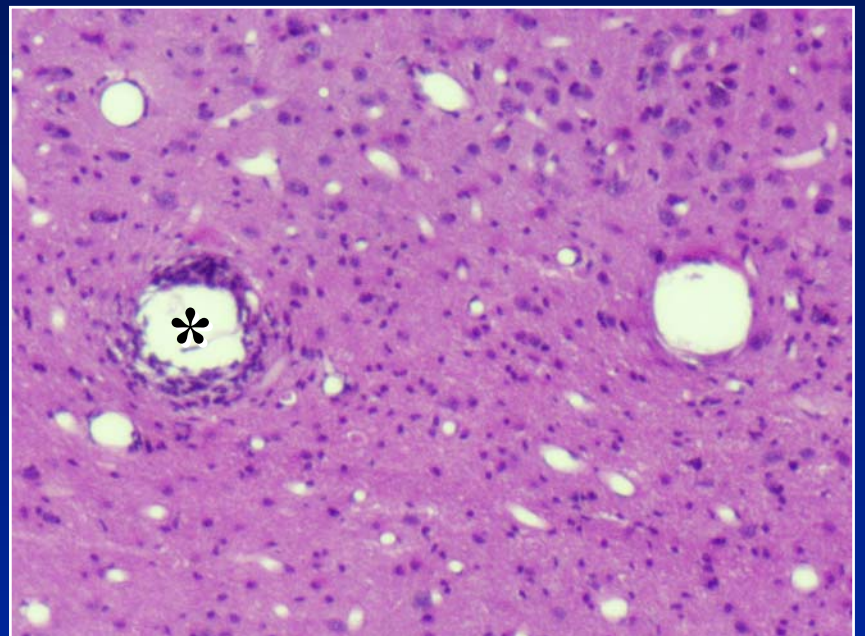
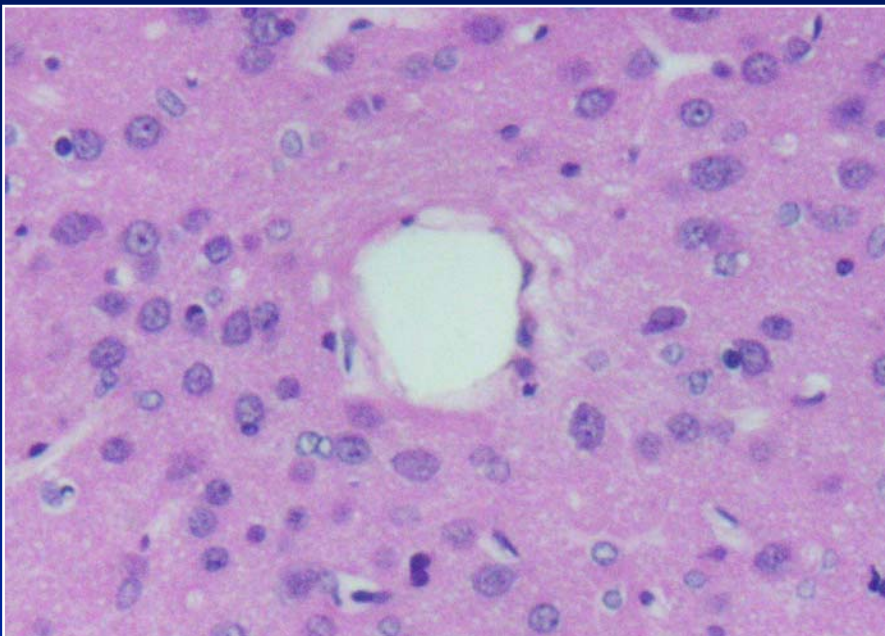
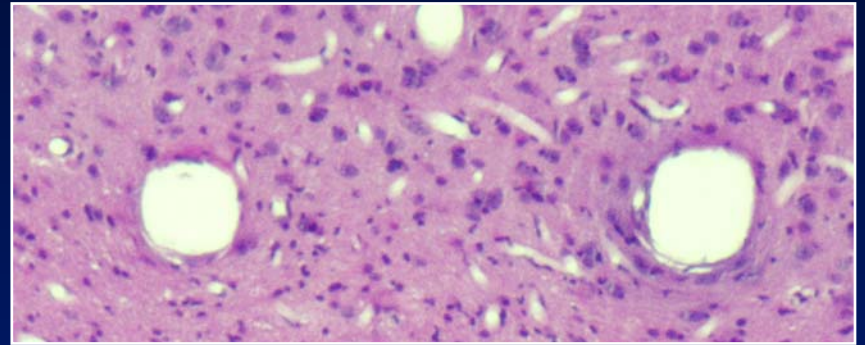
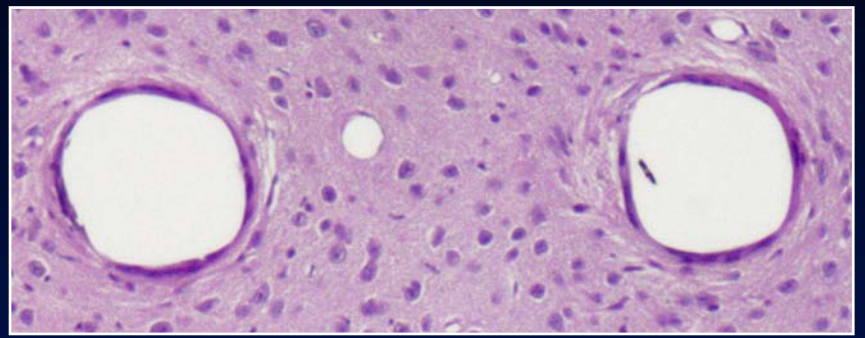
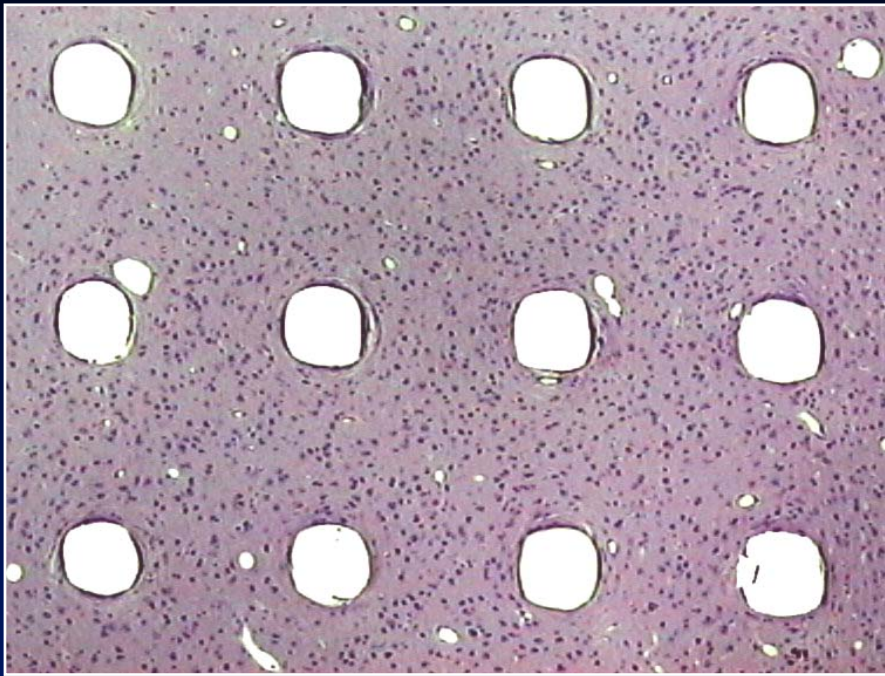
0.545 sec



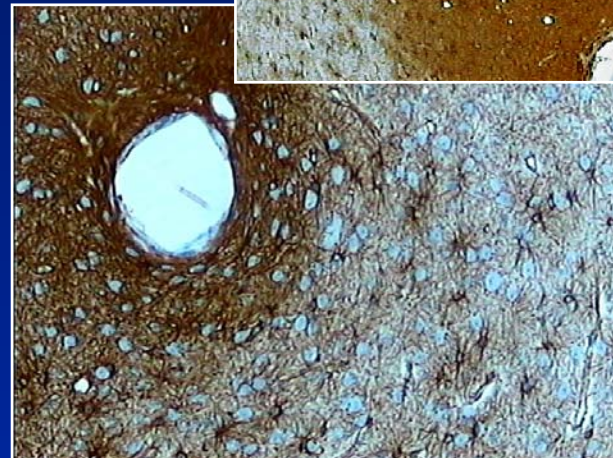
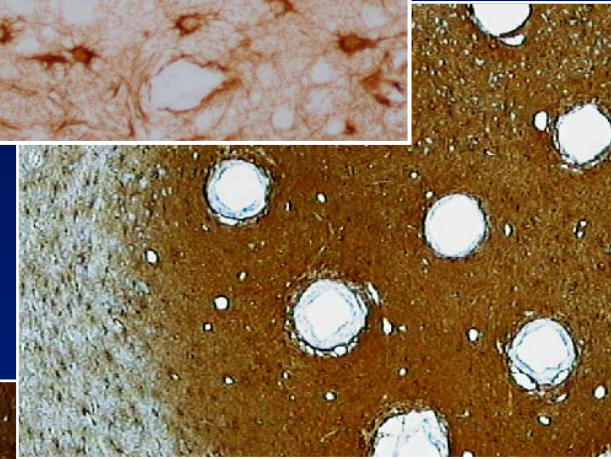
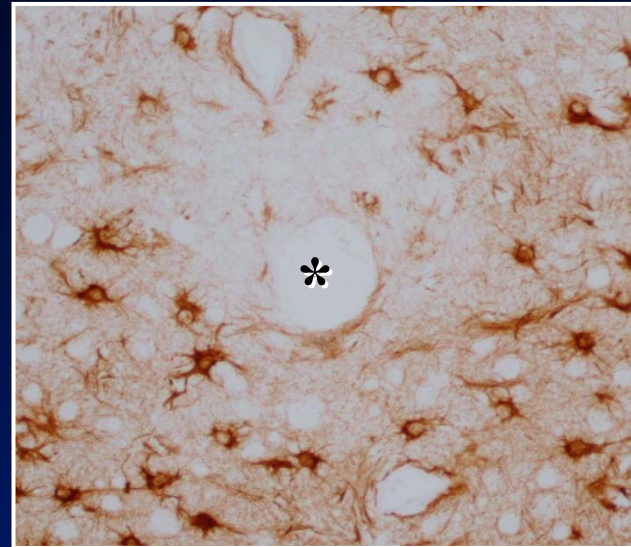
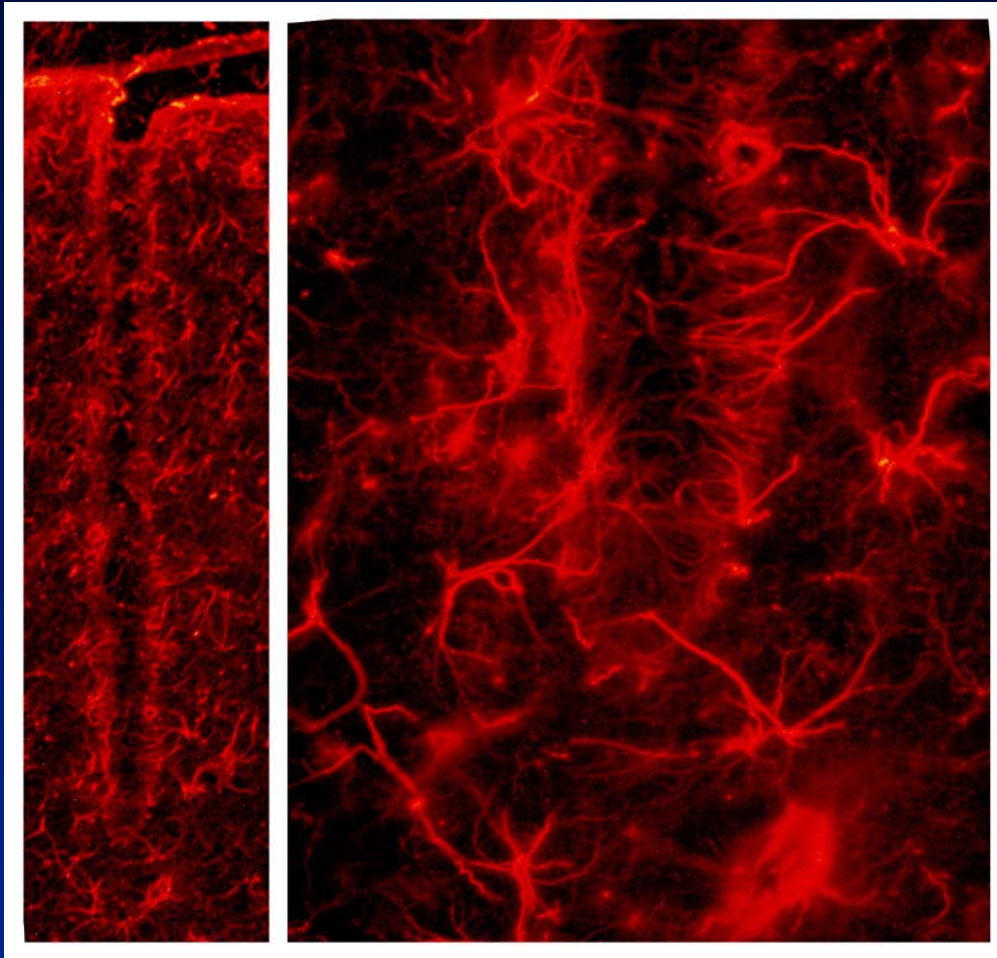


Predicted and measured responses of cat area 17 cell ensemble to upwardly moving horizontal bar

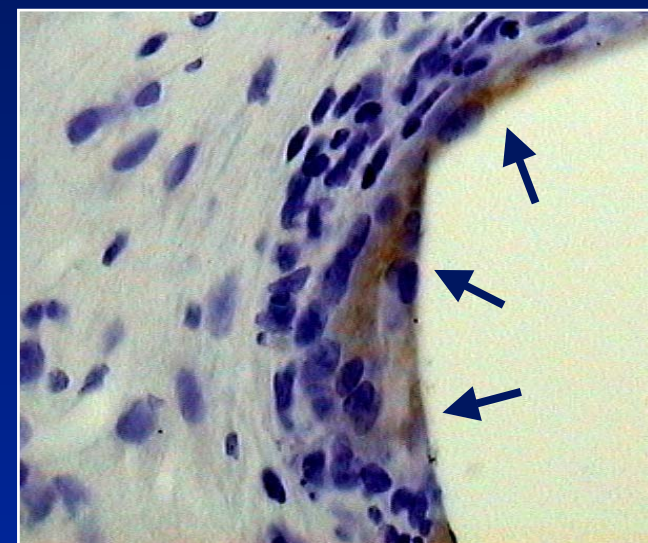
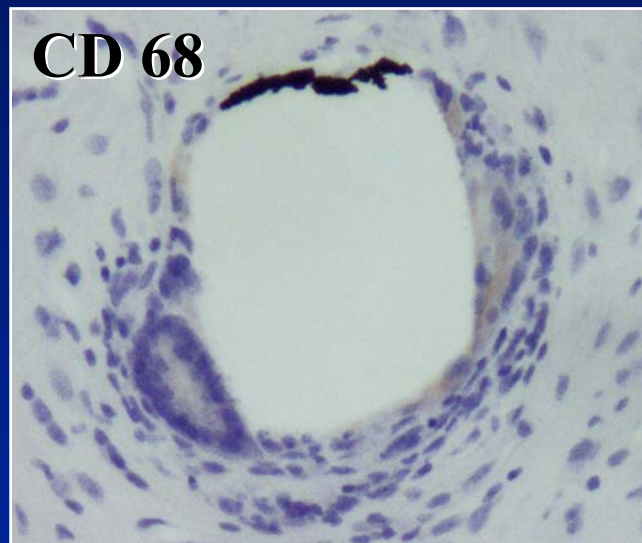
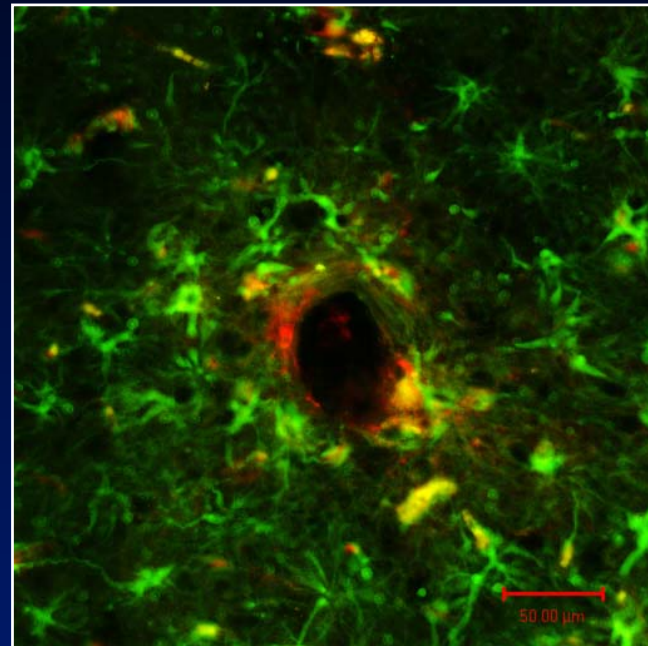
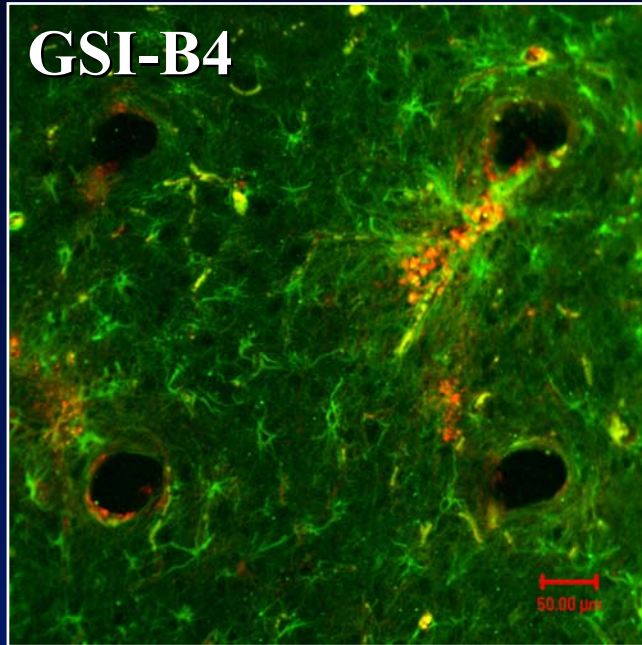


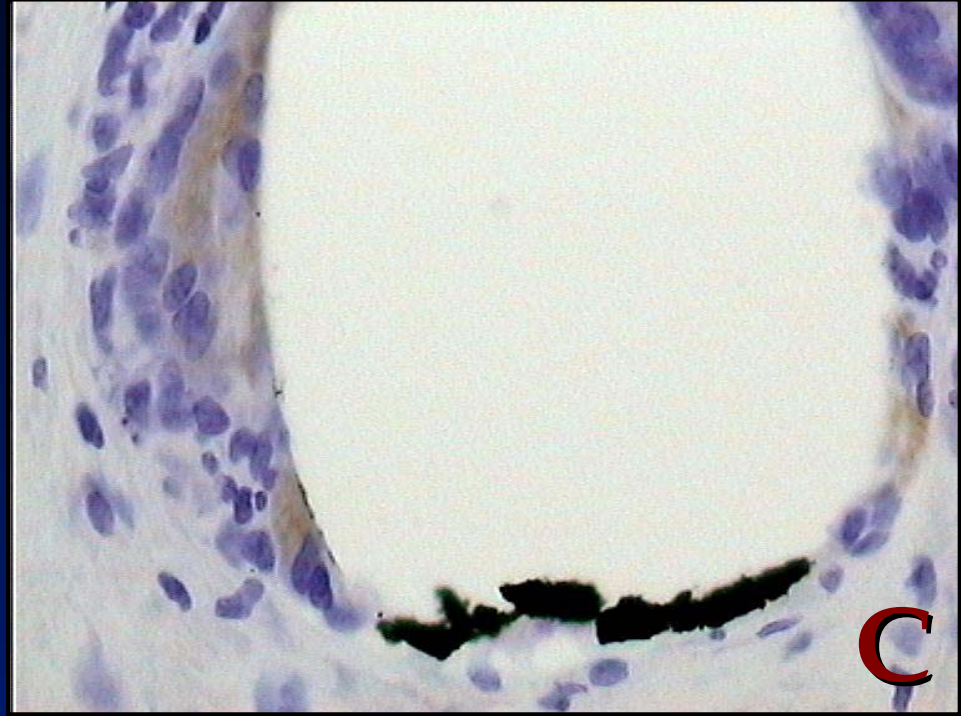
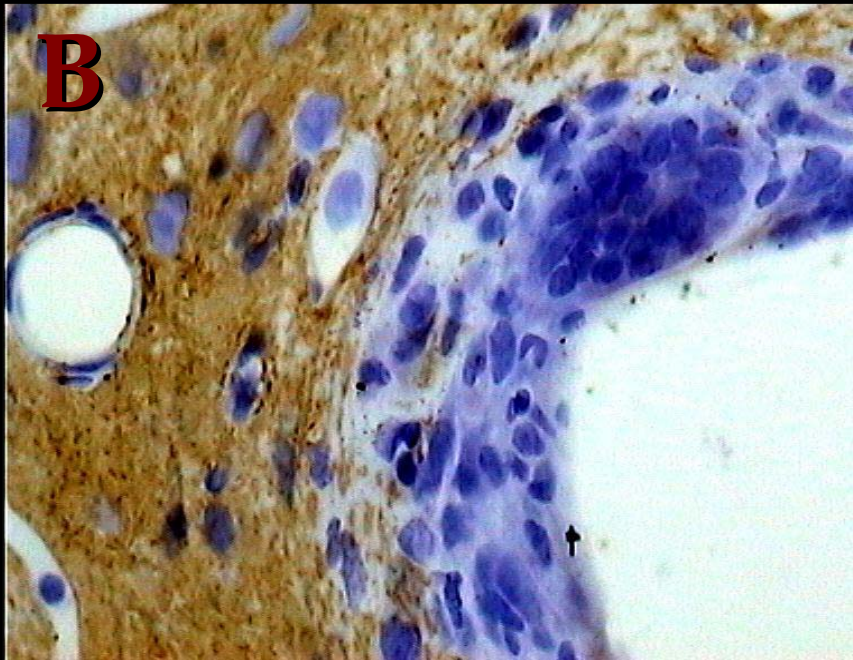
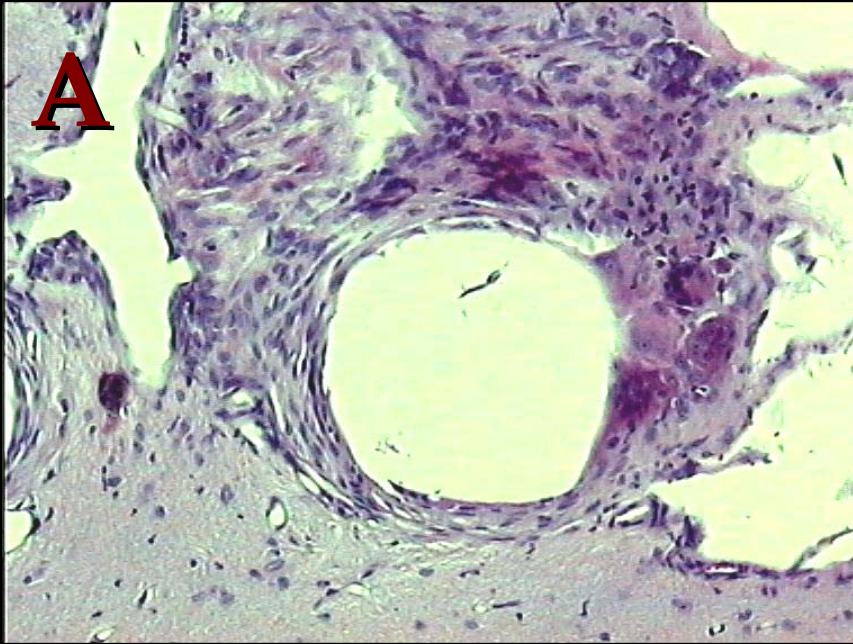


Proliferation of reactive astrocytes (GFAP stain)



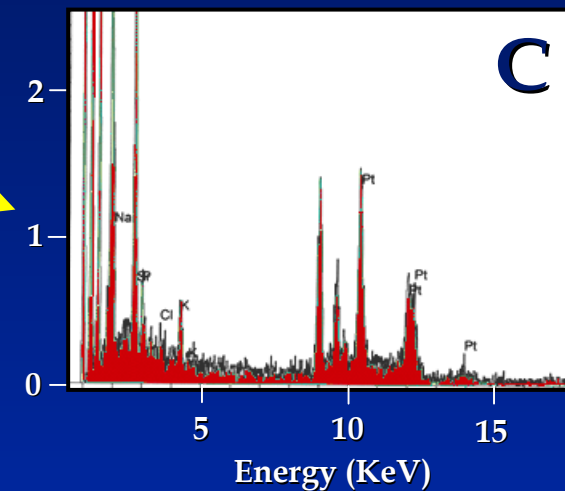
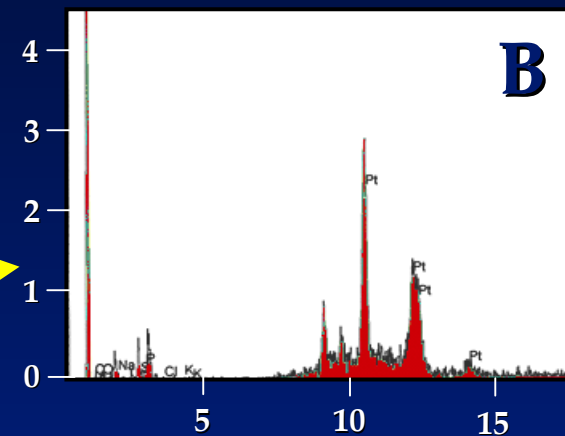
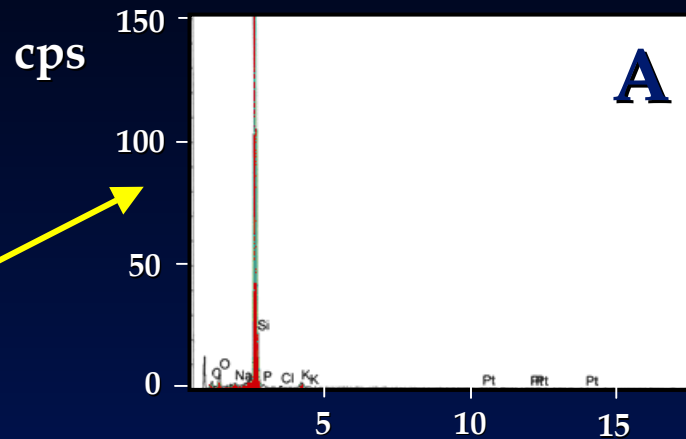
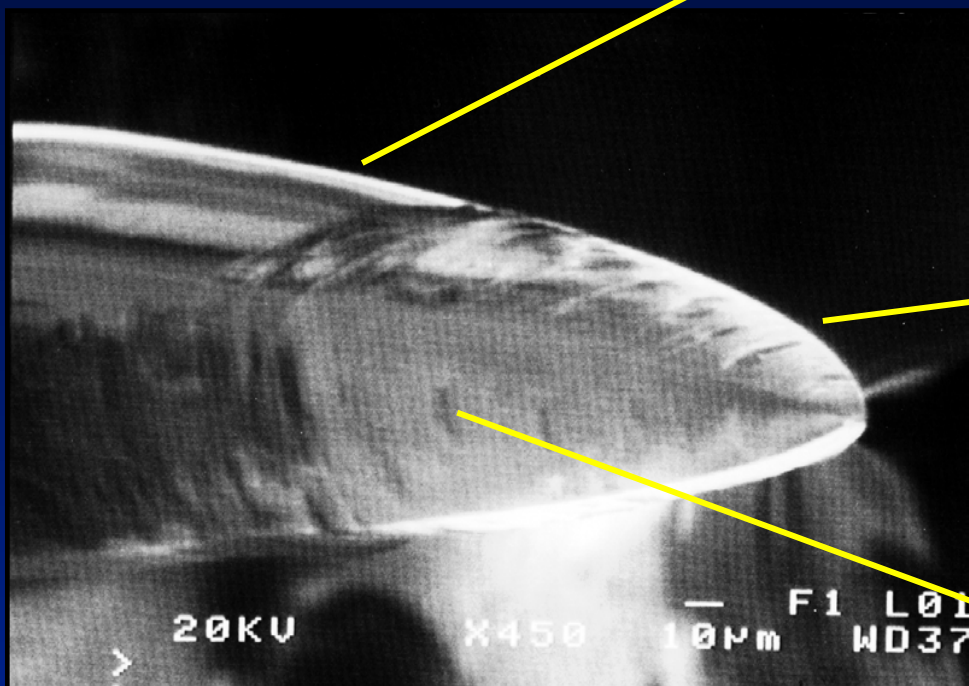
Proliferation of microglia and macrophages





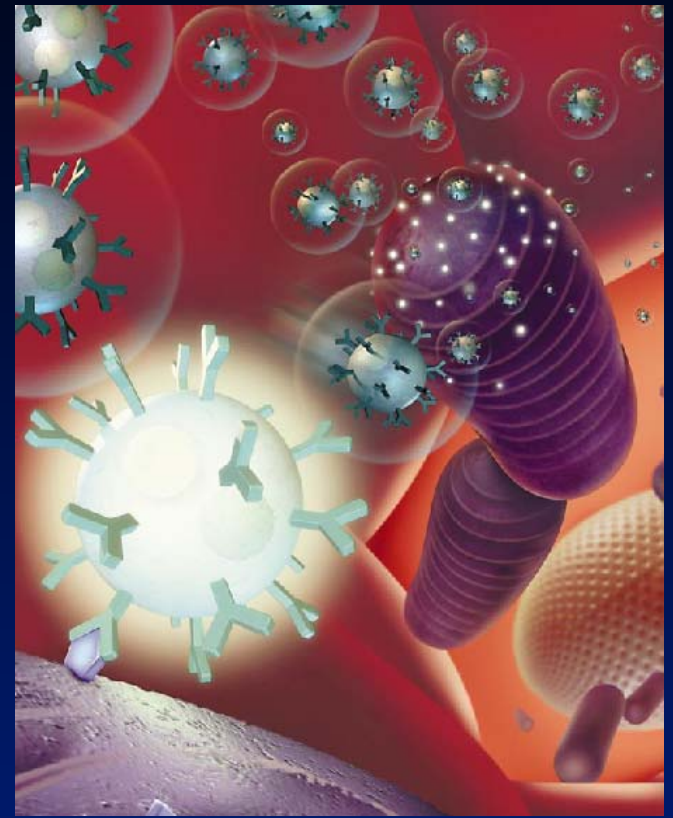
**Deposit of metallic-matter
in some of the
microelectrode tracks**

Microanalysis



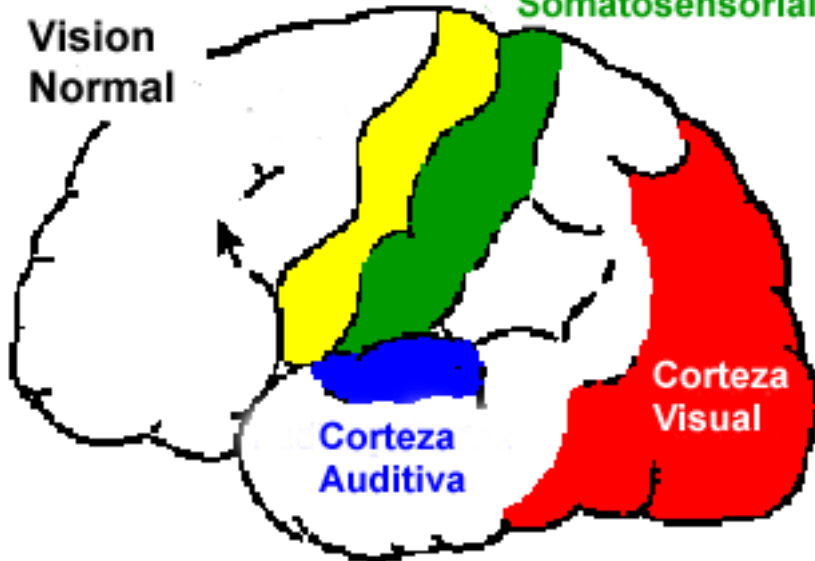
Because the initial response is stereotypic across a wide variety of injuries, it may be possible to understand the signals that lead to the neuroglial activation and ...

- **To control the response.**
- **Reduce the adverse nature of the response.**
- **Maintain an ideal environment for the brain-electrode interface.**



Corteza Somatosensorial

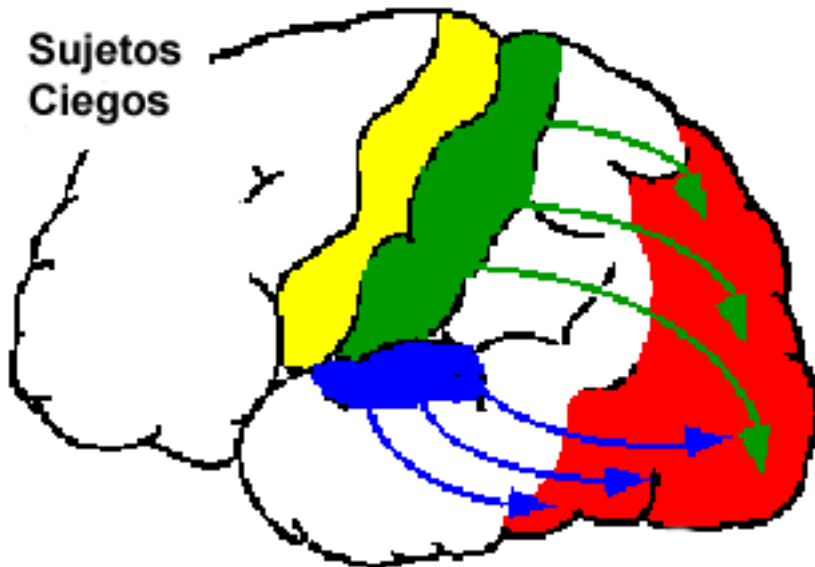
Vision Normal



Corteza Visual

Corteza Auditiva

Sujetos Ciegos



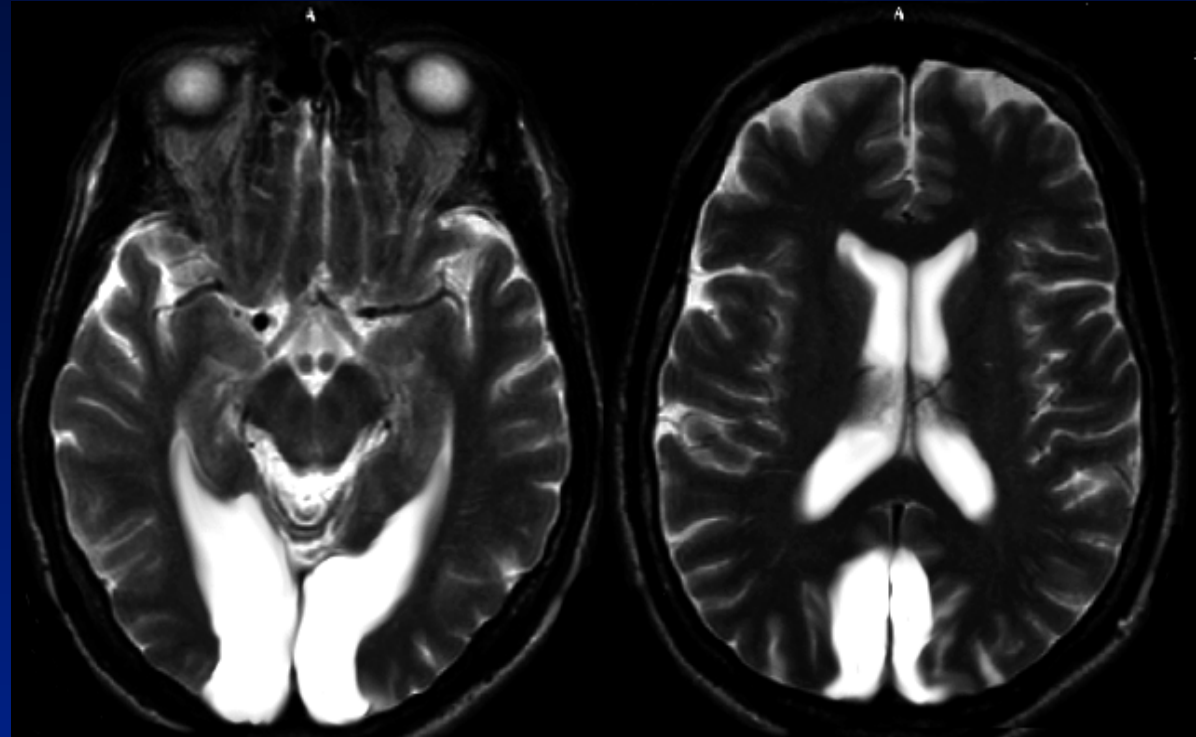
Plasticidad Transmodal

Is the occipital cortex of blind subjects able to process visual information?

Braille alexia

Lesion study

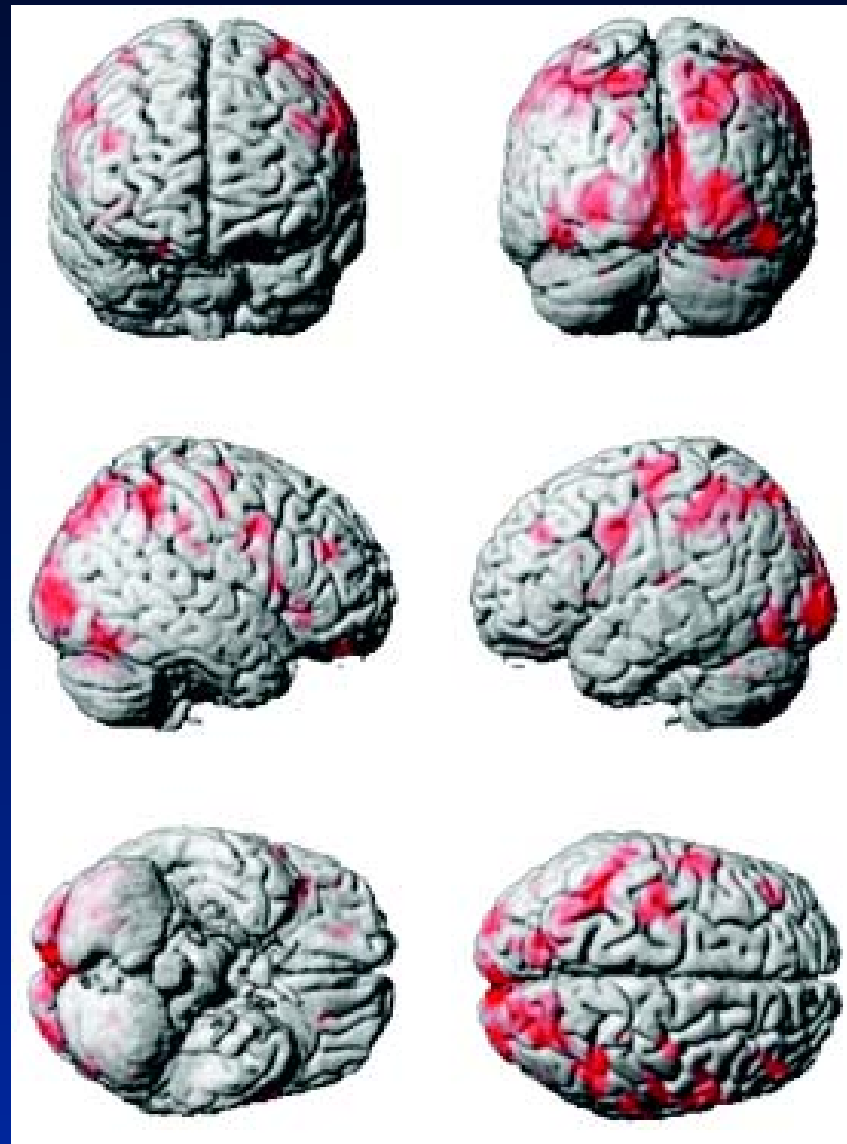
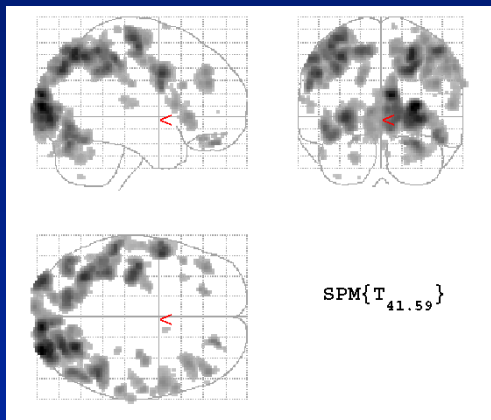
- 54 y/o woman
- Blind “since birth”
- Braille since age 7
- Braille 4-6 h/d
- Unable to read Braille after transient coma
- Normal neurological exam



Pascual Leone et al. 1999

Braille reading in blind subjects

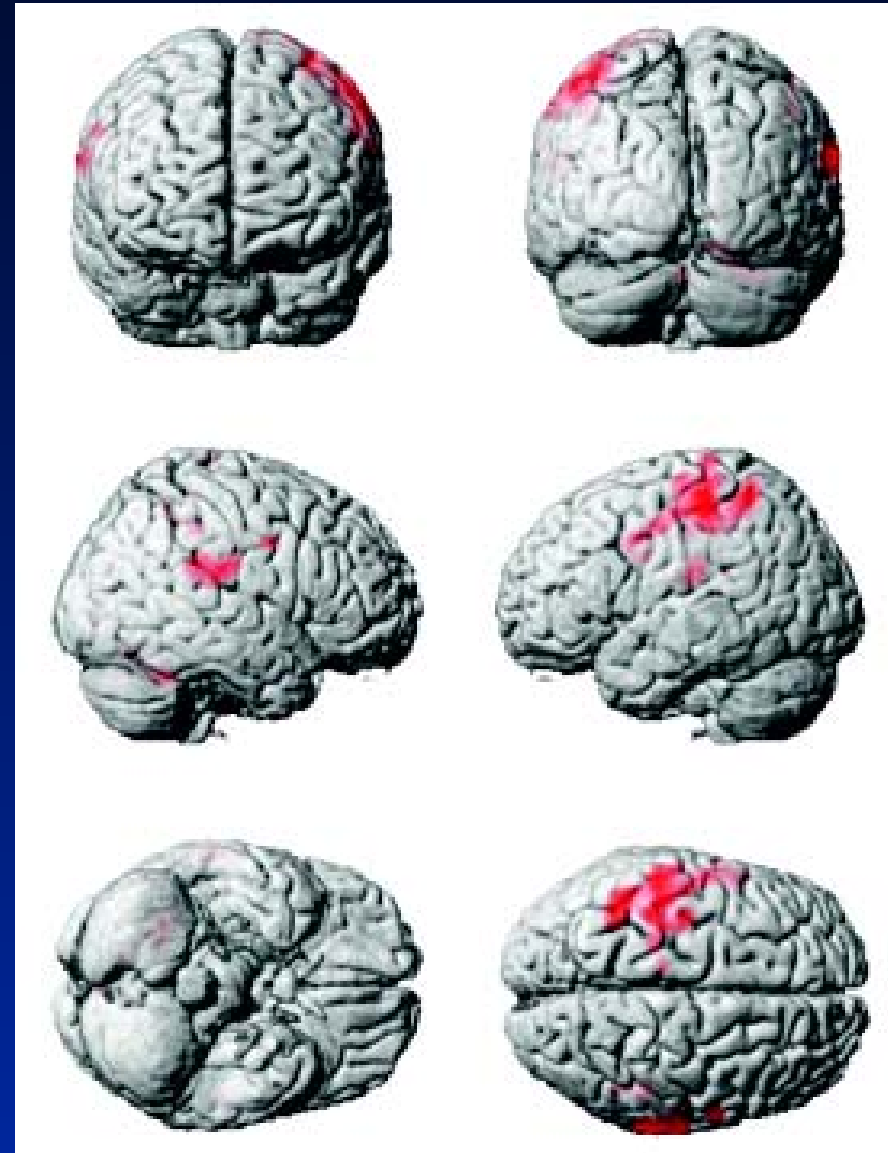
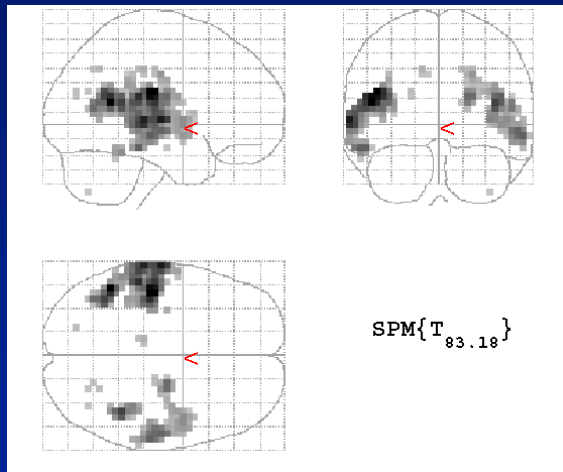
- **Main activation areas:**
 - Somatosensory cortex (contralateral to the side of stimulation)
 - Primary and associative visual cortex (mainly contralateral to the side of stimulation) ($p < 0.05$)
- **Less significant activation:**
 - Motor areas
 - Left prefrontal cortex



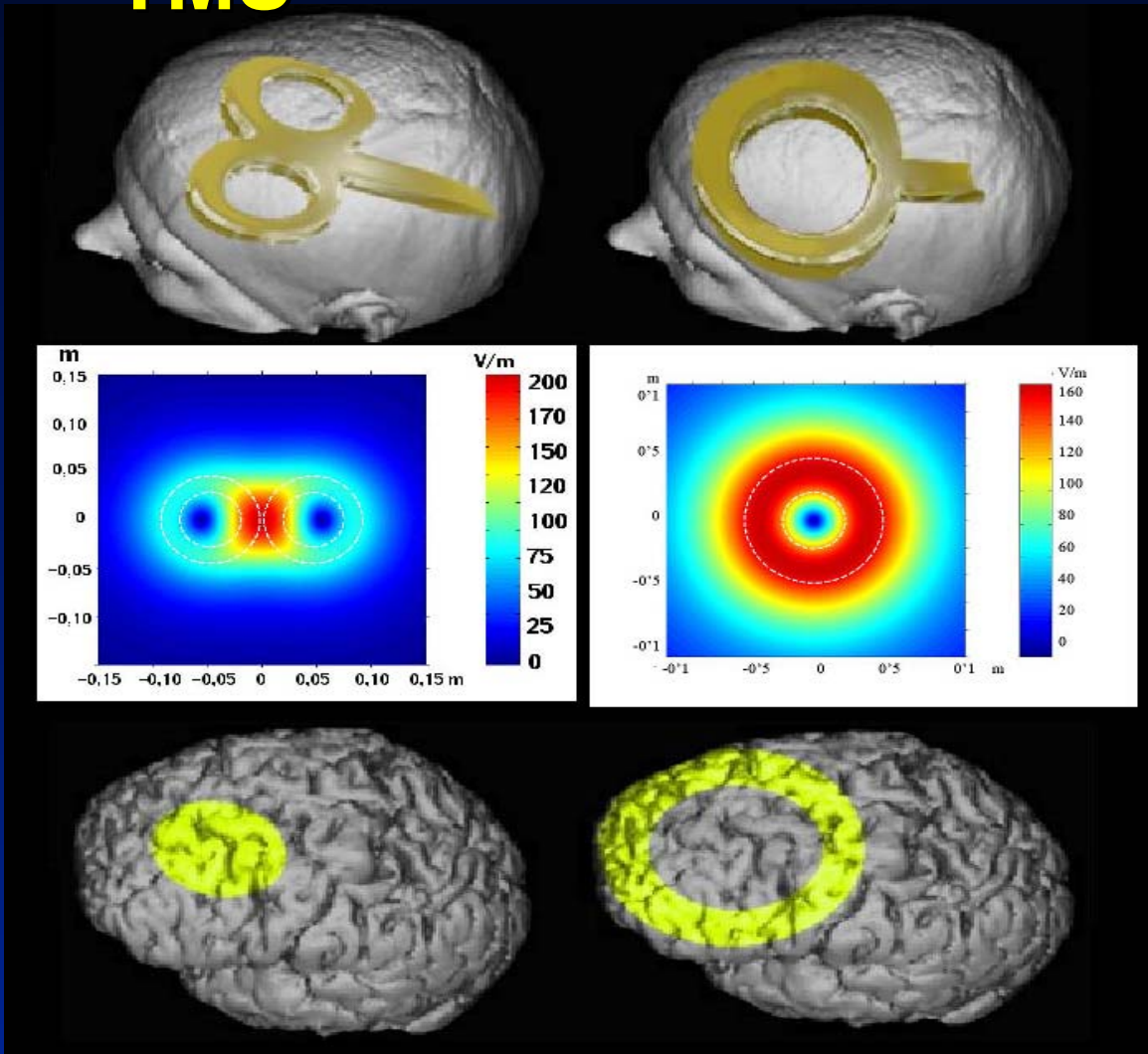
Sensory discrimination of Braille characters by sighted subjects

- **Postero-central sulcus (contralateral to the side of stimulation)**

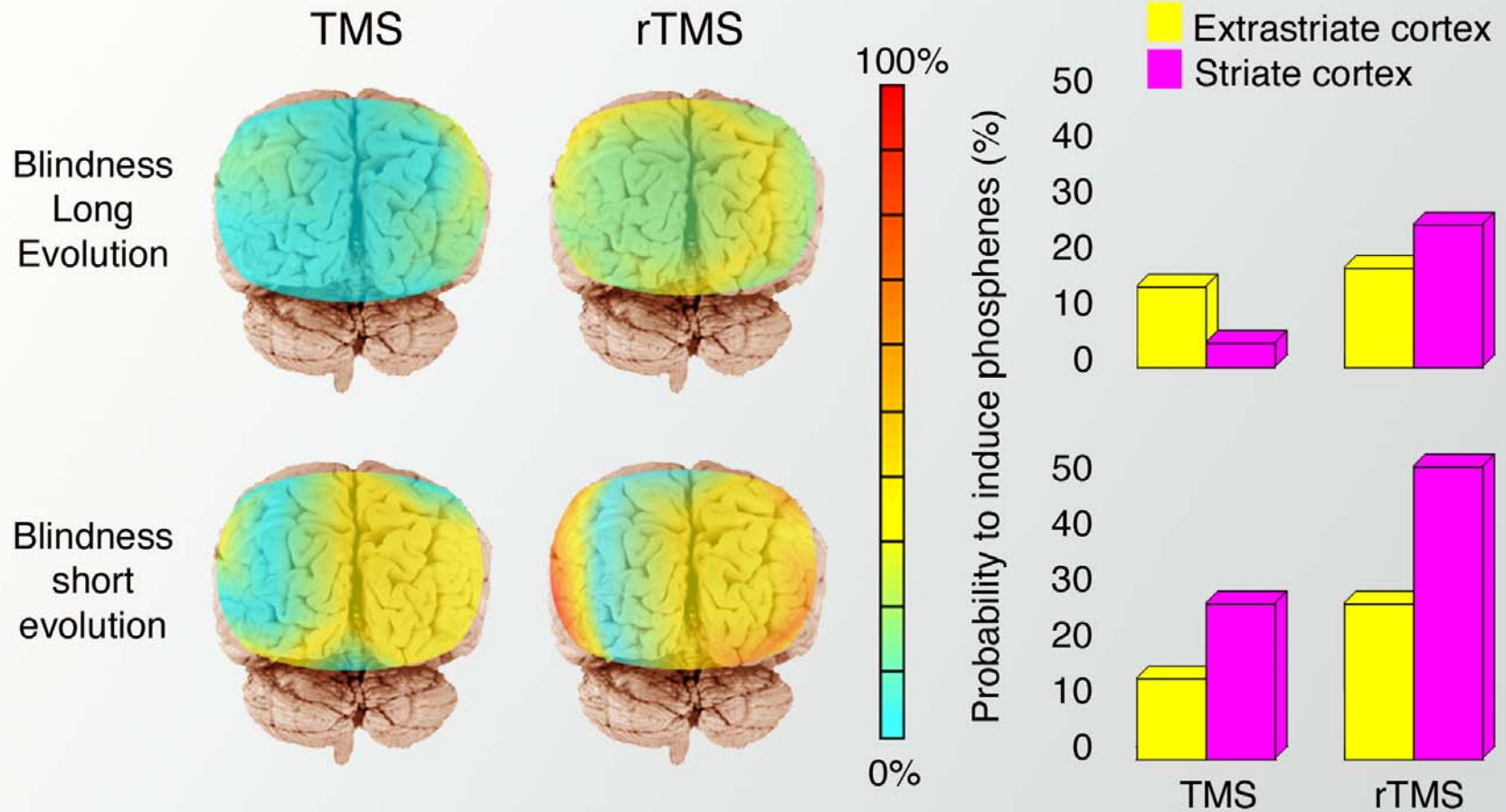
($p < 0.05$)



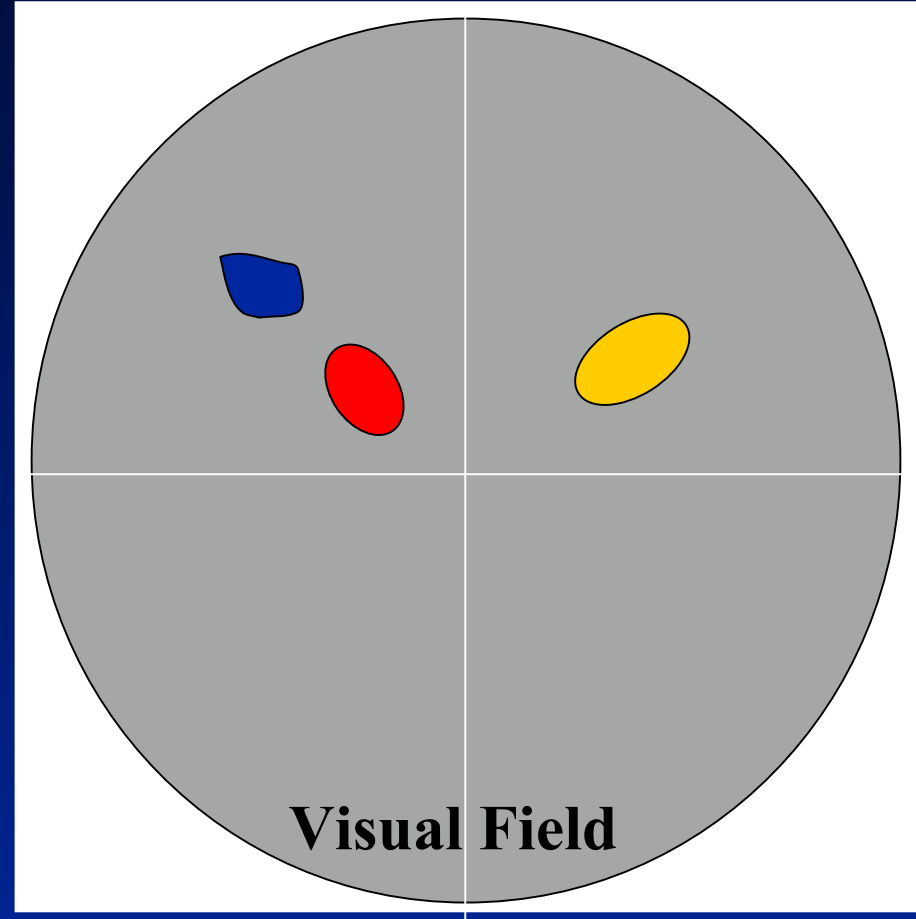
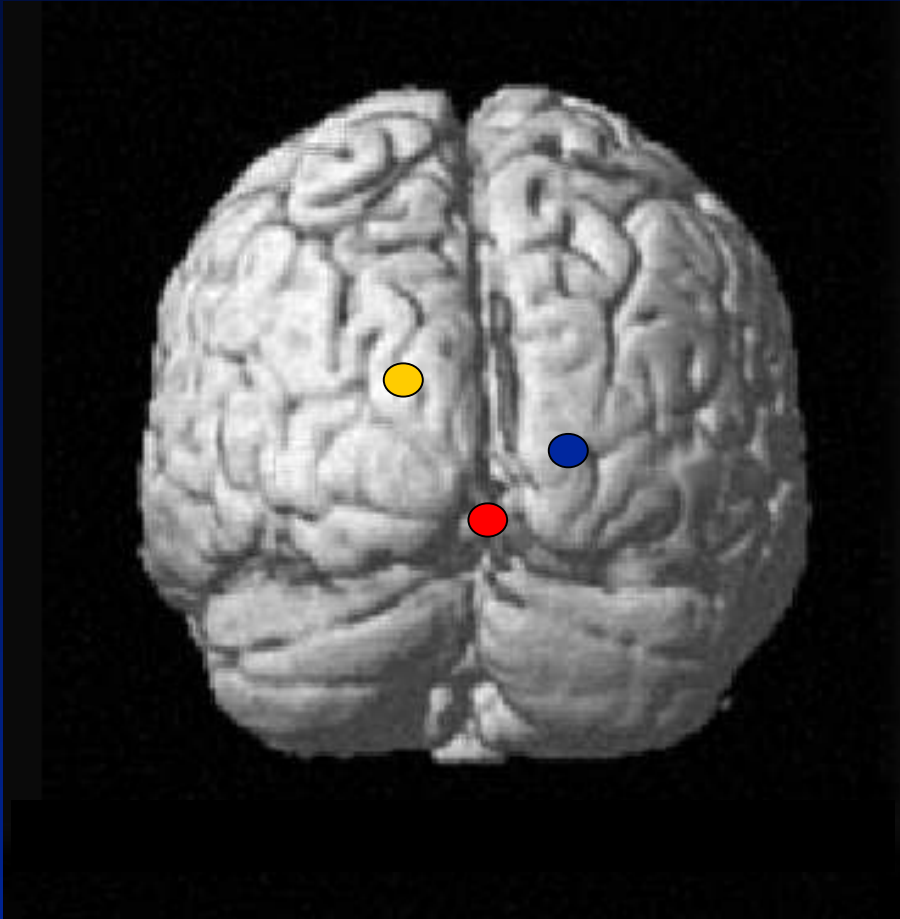
Mapping the human visual cortex using TMS



Perception of phosphenes in blind subjects



Examples of retinotopic mapping of TMS induced phosphenes in blind subject #8



- **How many electrodes are required to produce a useful visual sense?**
- **How stable are the phosphene thresholds on a day by day basis?**
- **How far apart can a pair of electrodes be positioned and still produced contiguous phosphenes?**
- **Does patterned stimulation produce patterned percepts?**

Conclusions:

- ✓ If we can understand more about the fundamental mechanism of neuronal coding, and to safely stimulate nervous system, there will real potential to apply this knowledge clinically.
- ✓ Our results show that intracortical microelectrodes could be safely used in long-term applications, although more studies regarding safety and preservation of neuronal tissues as well as optimizations of stimulating parameters are needed preceding any clinical trial.

Never in the history have been so many new findings concerning neural prosthesis as have been achieved in the recent 10 years. Still there may be a long way to application of such findings in patients. However, it can be expected that, at least for some patients, effective therapies will be developed during the upcoming years.

University of Oldenburg

- Josef Ammermüller

Universidad de Granada

- F. Pelayo

University of Montpellier

- Pierre Rabischong

University of Vienna

- Peter Ahnelt

CNRS (Paris)

- Lyle Graham

INESC-ID (Portugal)

- M. Piedade

University of Utah

- R.A. Normann

Universidad de Harvard

- Alvaro Pascual-Leone

Hospital General Universitario de Alicante

- Carlos Botella

Biomedical Technologies

- Fco Garcia de Quirós

Universidad Miguel Hernández

- Eduardo Fernández
- Jose Manuel Ferrandez
- M. Bongard
- Marcelino Avilés
- Jose M^a Tormos
- Raquel Climent
- Arantxa Alfaro
- Paula Bonomini
- Cristina Marin
- Paqui Leyva

