Microsystem technology in the brain: what can we offer and what can be expected?

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The fundamental question

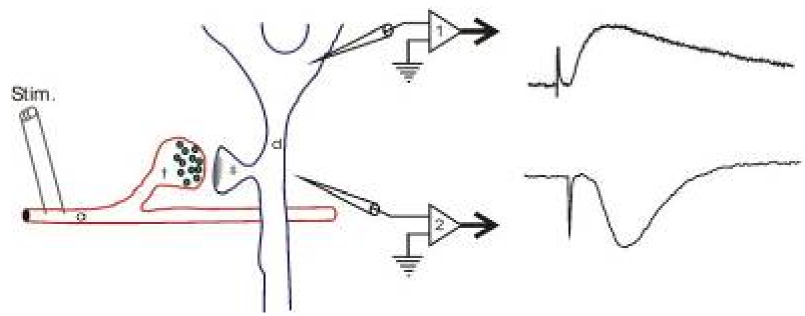
How do we correlate actions, perceptions and thoughts with the activities of individual neurons?

Our tools

- There is a long successful history of electrically interacting with biological tissue.
- Monitoring chemical activity – especially over long periods of time – is a much more demanding task.
- Optical monitoring of neural network activity is a complex endeavour, requiring techniques such as two-photon laser scanning microscopy.

Neural recording

- It is the only possibility for investigating the link between neural ensemble activity and subject behaviour.
- In-vivo studies aim to observe single-unit activity by measuring extracellular potentials.



- Extracellular recordings collect signals from all the nearby neurons (field potential). This usually has to be resolved into single units (action potentials).
- For this reason, electrodes have to be sufficiently close to neurons (typically less than 100 µm).
- Potential application: man-machine interface

Recording in neuroprosthesis

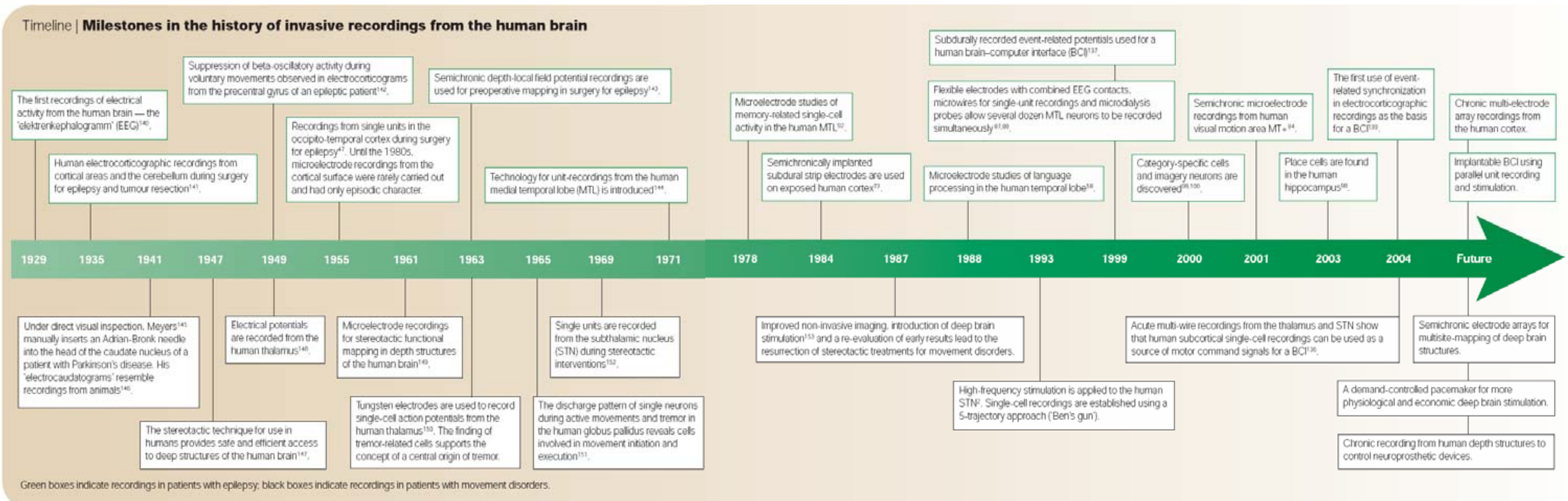
Although at first glance neuroprosthesis has to do exclusively with stimulation, recording is also of paramount importance in the characterisation and mapping of the areas of interest.

- Perhaps the most relevant neuroprosthetic device to date is the cochlear implant. Its success has to do with the tonotopic organisation of the cochlea, which was first investigated using extracellular recordings.
- What we know today about the mapping of the primary visual cortex is also owed to extracellular recordings.

Neural recording is also important in closed-loop prosthesis; for instance, the recording of signals in the motor cortex can be used for controlling robotic devices.

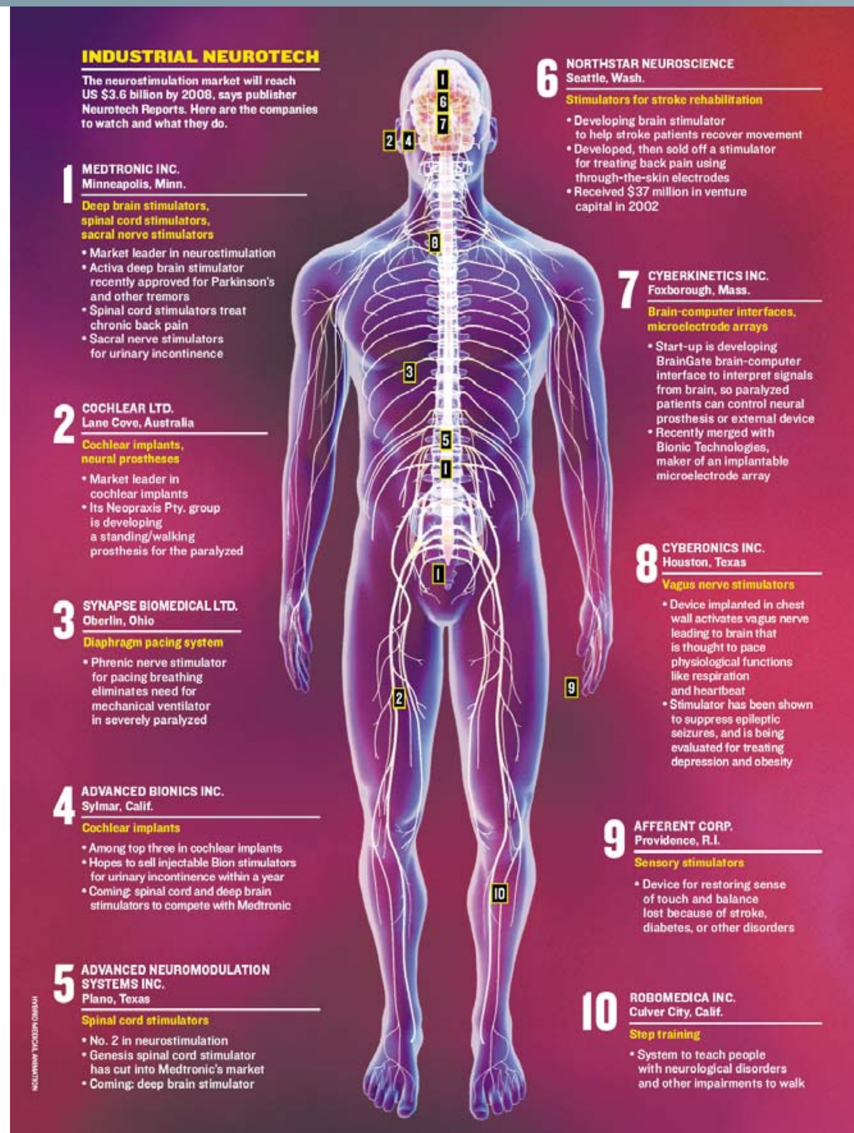
Clinical relevance

- Modern non-invasive techniques such as fMRI cannot provide information on physiological processes in the brain at the cellular level. Clinical use of brain recording is used mainly in two areas:
  - Management of movement disorders resulting from pathologies affecting deep brain structures (thalamus, basal ganglia);
  - Localisation of pathological activity foci for surgical excision in intractable epilepsy.



Source: Nature Reviews Neuroscience (© Nature Publishing Group)

Neural stimulation



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Social relevance

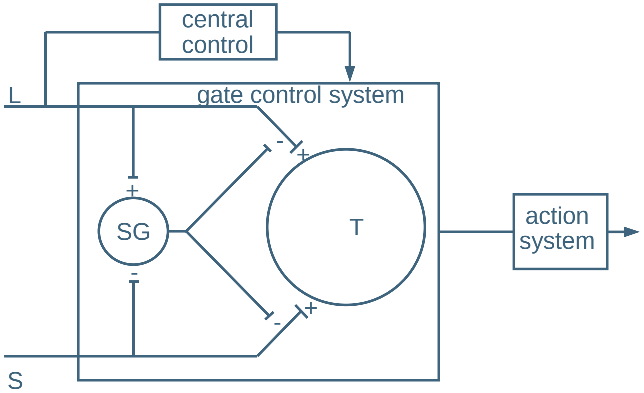
- Disease management leading to improved quality of life
- Opportunity to address rare diseases, the limbo of healthcare
- Fundamental research still much needed to understand mechanisms so far implicated in important disorders
  - Link between glutamate function and schizophrenia
  - Link between acetylcholine and cognitive decline in Alzheimer's disease

Pain management

"*Physicians have the obligation to relieve pain and suffering and to promote the dignity and autonomy of dying patients in their care. This includes providing effective palliative treatment……adequate pain control may decrease dramatically the demand for euthanasia and assisted suicide*".

Council on Ethical and Judicial Affairs, American Medical Association

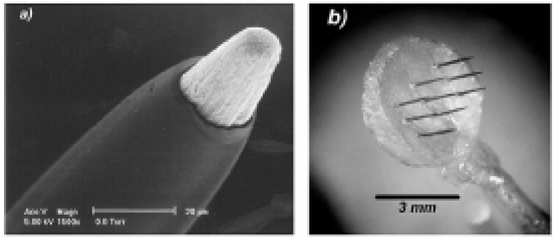
After René Descartes, 1664.



Melzack's Gate Control Theory

Medtronic's neurostimulator

State of the art in cortical interfacing



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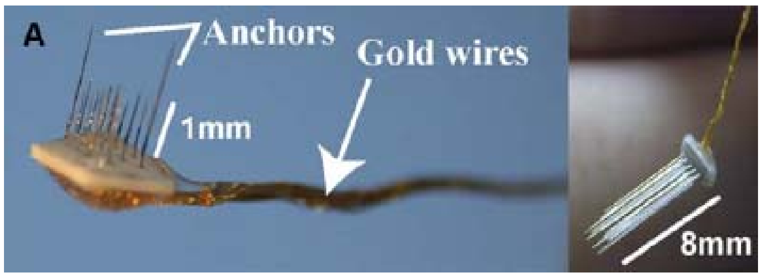

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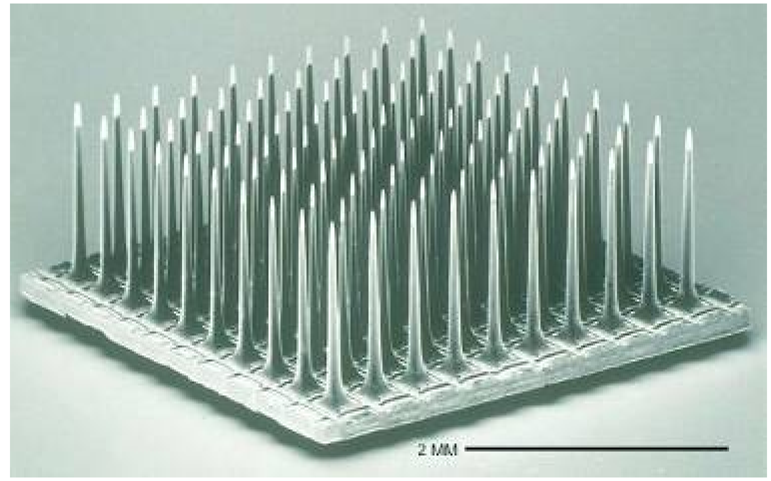

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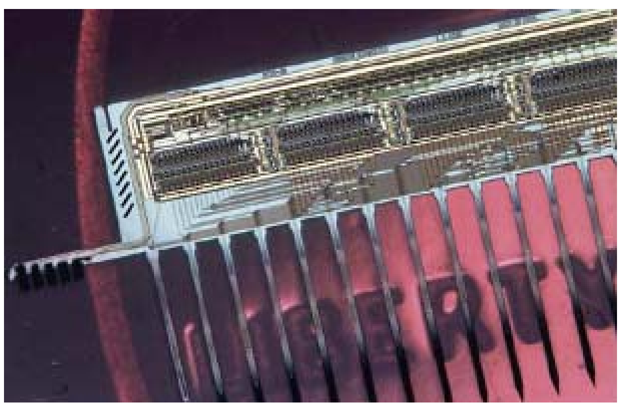

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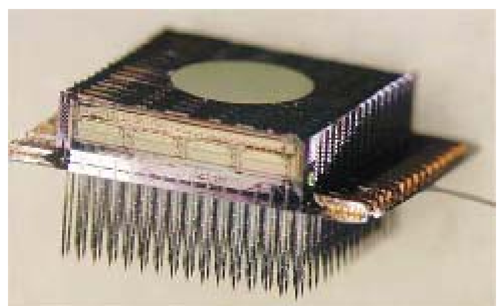
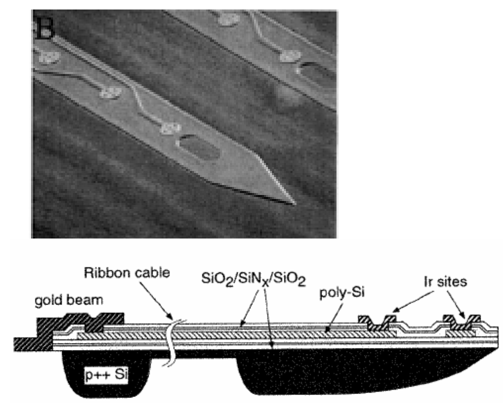




Challenges if in-vivo extracellular recording

- According to J.C. Lilly, in "Correlations between neuro-physiological activity in the cortex and short-term behavior in monkey", *Biochemical Bases of Behavior (1940)*,

> *"… one of the large difficulties in correlating structure, behavior, and CNS activity is the spatial problem of getting enough electrodes, and small enough electrodes, in there with minimal injury. Still another difficulty is the temporal problem of getting enough samples from each electrode per unit of time, over a long enough time, to begin to see what goes on during conditioning or learning, especially when a monkey can learn with one exposure to a situation, as we see repeatedly. As for the problem of the investigator's absorbing the data – if he has adequate recording techniques, he has a lot of time to work on a very short recorded part of a given monkey's life."*

The problem from a microsystem perspective

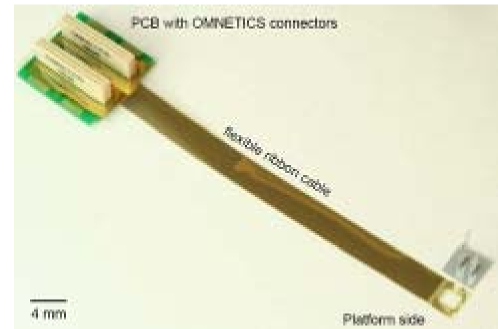
- Microsystems largely confined to two dimensions – 3D integration
- Most solutions limited to hybrid system-in-package
- Full solution needed
- Diversity of environment needs customisable solutions
- Interactions with tissue largely seen as a “black & white problem”
  - Biocompatibility, biostability
  - Passive materials
  - True opportunity for nano
- Dynamic biological systems vs. static microsystems
- The dark art of electrode technology
  - Factors influencing electrode performance are thought to be well known
  - Actual interface with biological medium far more complex

The NeuroProbes Integrated Project

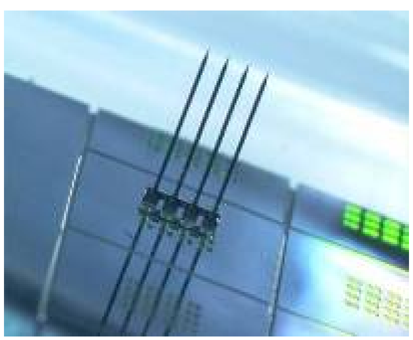
Objective

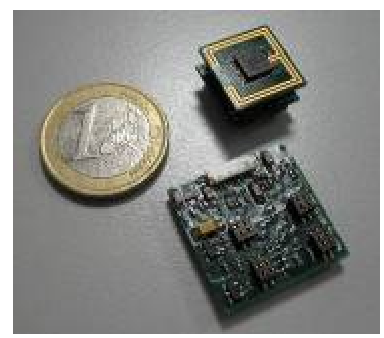
Development of arrays of multifunctional microprobes for high temporal and spatial resolution brain studies that include freely moving subjects, with recording **and** stimulation done both electrically and chemically.

Features

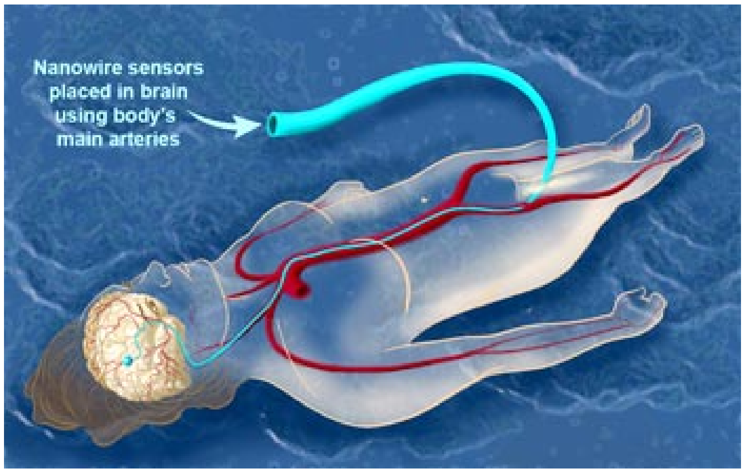


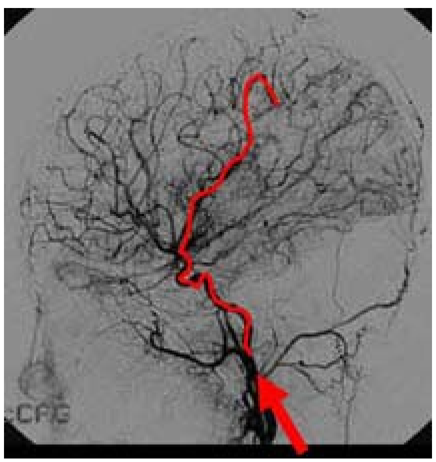
- Dense 3-D microelectrode arrays for recording
- Modular technology
- Microfluidics for inactivation studies
- Individual and independent control of electrode position
- Attachment and insertion technologies
- Conformation to convoluted surfaces such as *sulci* of highly folded cortices
- Integrated biosensor probes
- Telemetry





Future of cerebral interfacing





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Challenges

- Invasiveness
- Tackling a 3D problem with a 2D solution
- Using static devices in a dynamic environment
- Chemical interfacing
- Electronics
- Energy

Possible solutions

- Departure from traditional designs (e.g. function splitting)
- Microsystem integration (incl. electronics)
- Materials investigation

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