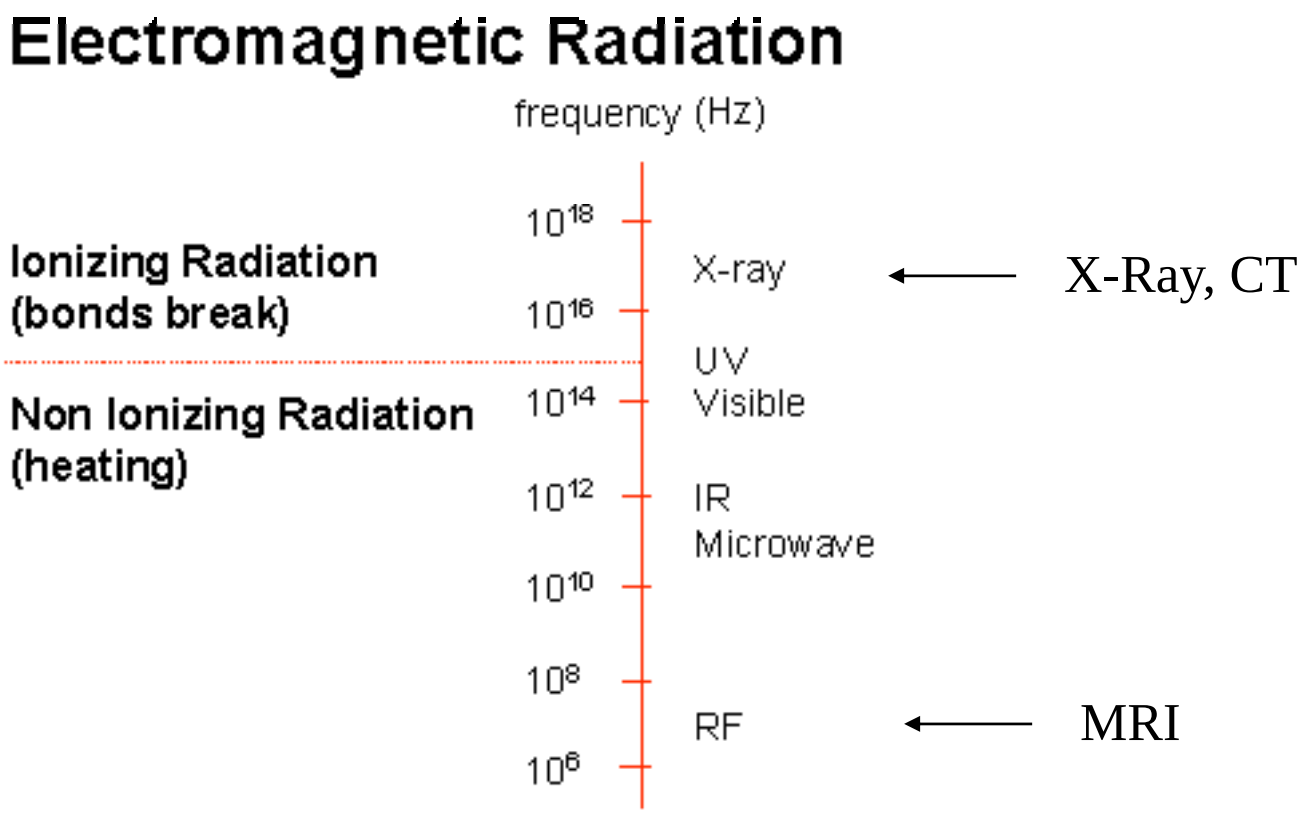
New diagnostic tools

Studying human brain

- Structural (static)
  - Histology
  - X-ray
  - Computed tomography (CT or CAT)
  - Magnetic Resonance Imaging (MRI)

- Functional (active): particular task at particular times
  - PET (Positron Emission Tomography, 양전자방출단층촬영)
  - fMRI (functional MRI, 기능성 자기공명영상)
  - MEG (Magnetoencephalography)
  - EEG (Electroencephalography)

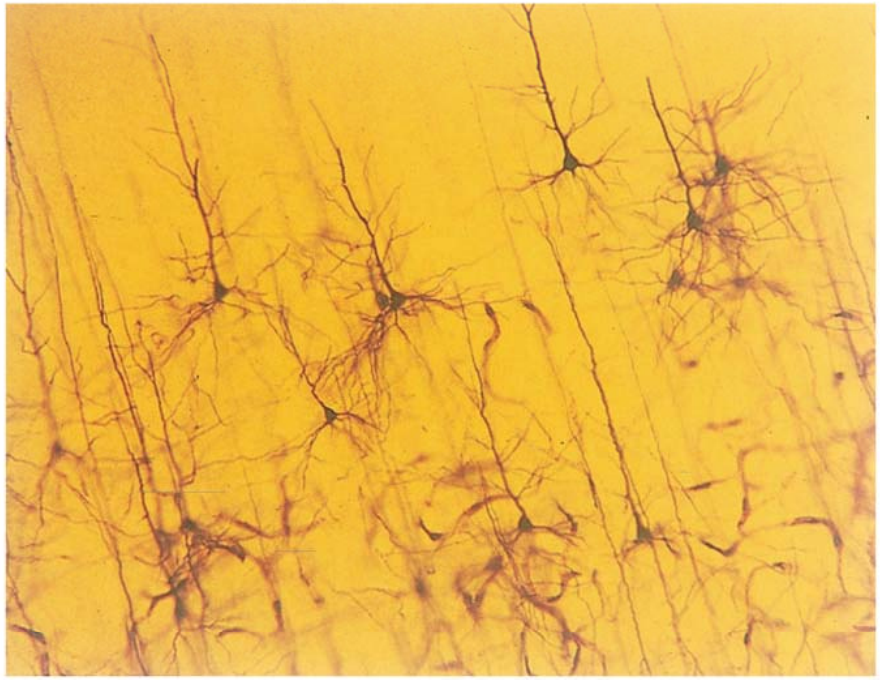
Electromagnetic Radiation Energy

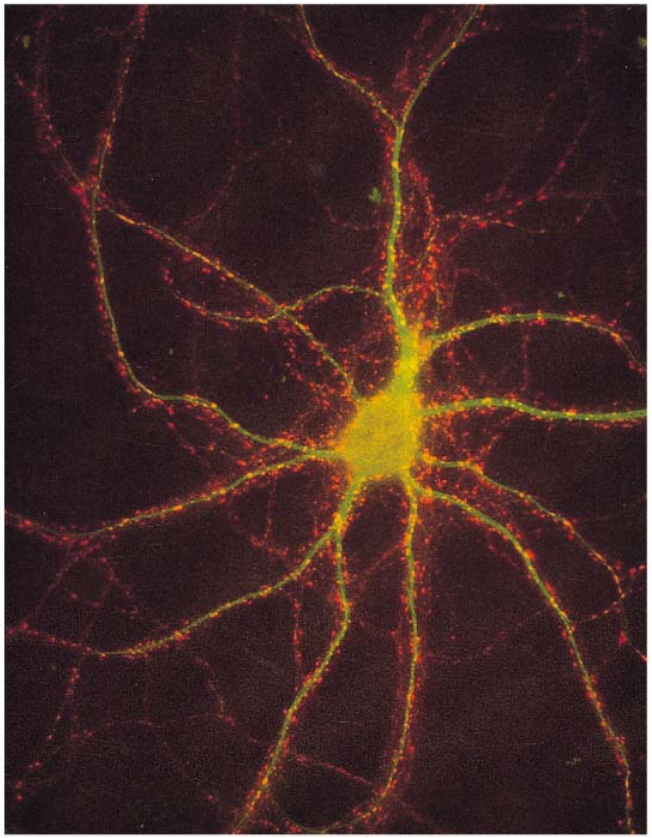


Structural investigation

Histological Analyses

Figure 2.3
Golgi-stained neurons. (Source: Hubel, 1988, p. 126.)

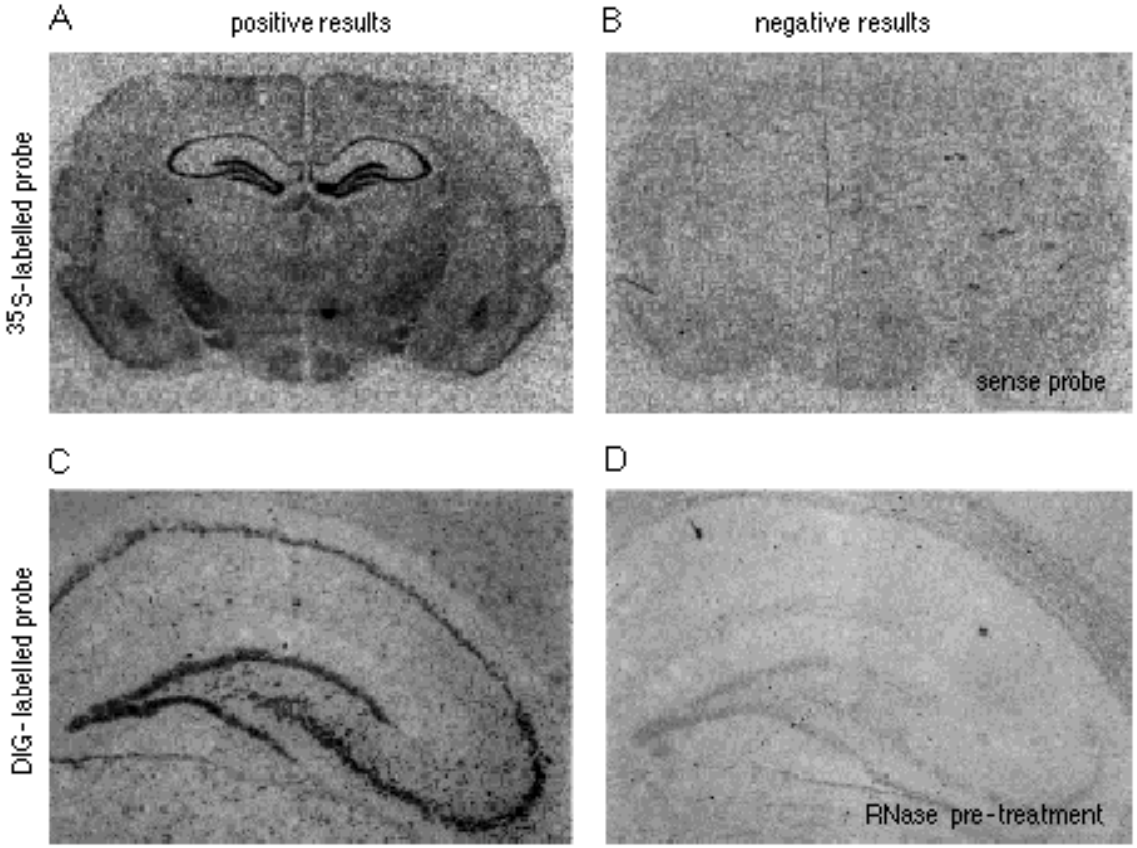




<u>Direct manipulation and staining of tissue</u>
-cellular and molecular analyses
-can only be done post-mortem

Radioisotope injection and tracking

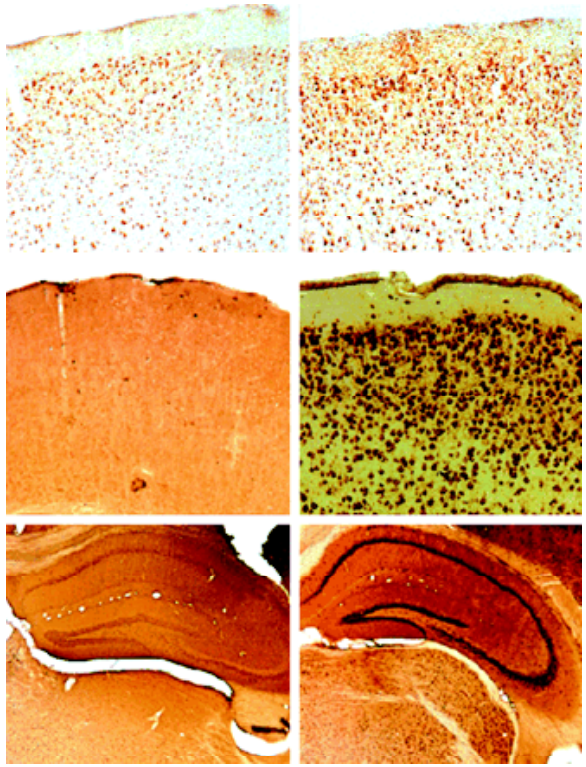
In situ hybridization

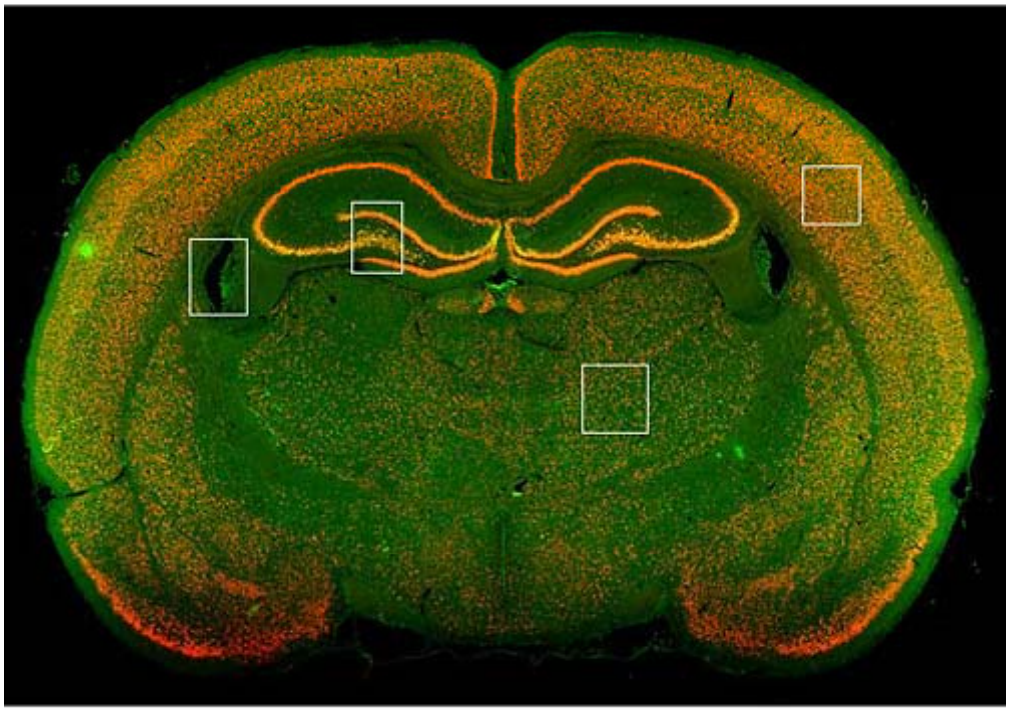


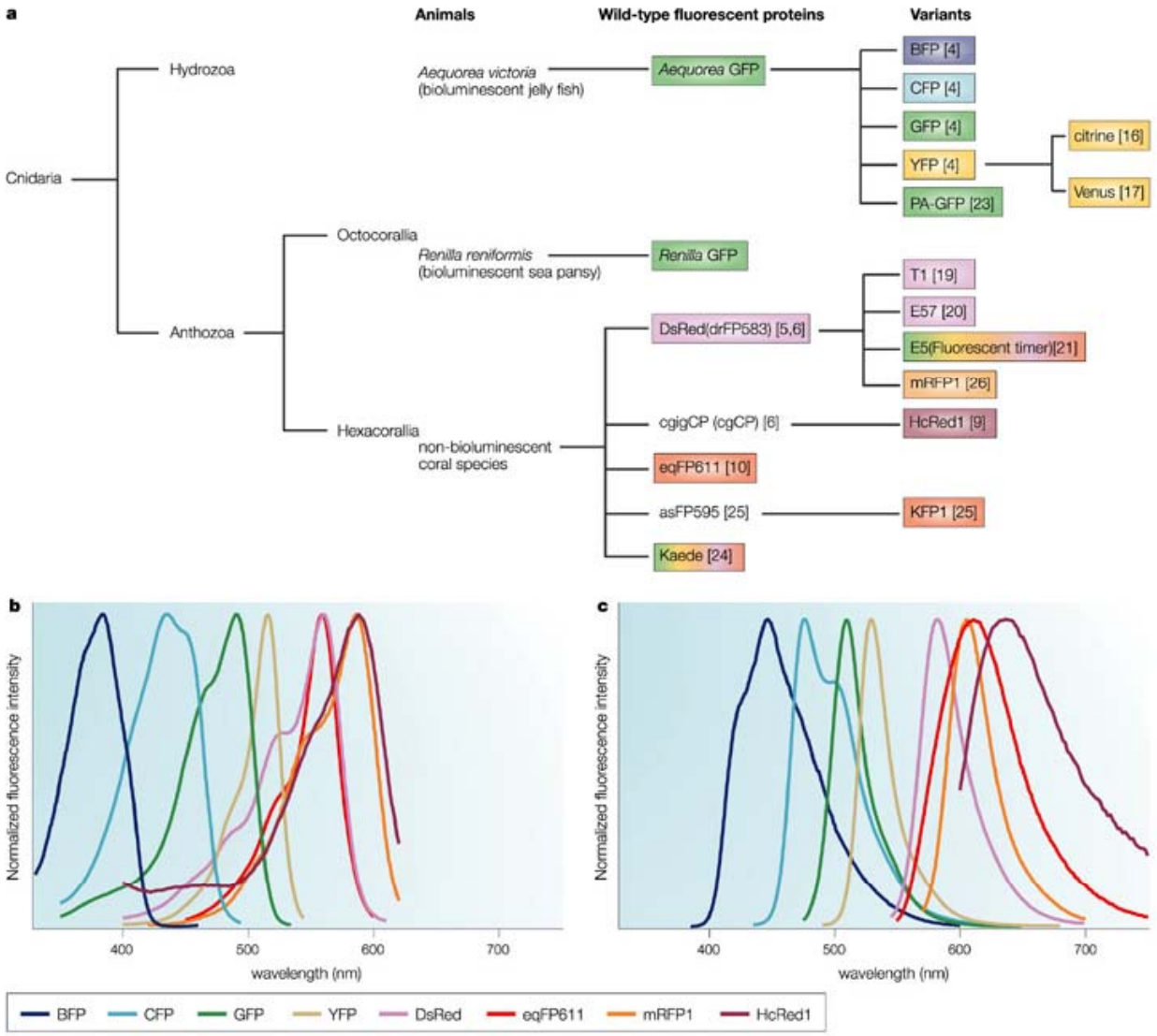
Color visualization

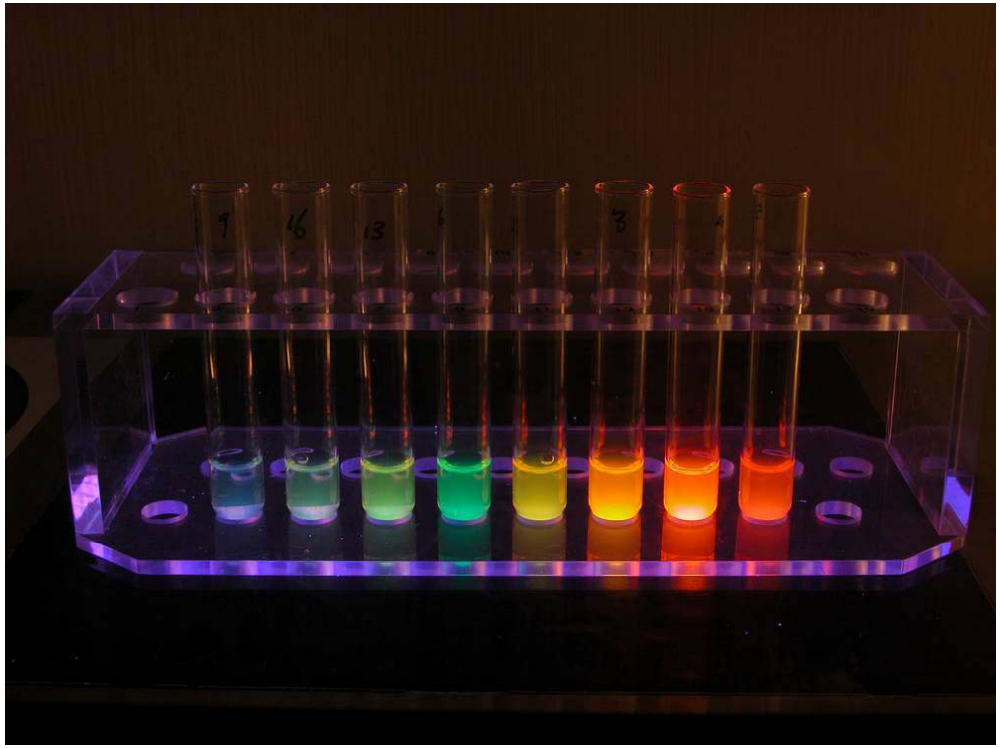
enzyme reaction: immunohistochemistry

fluorescent protein expression

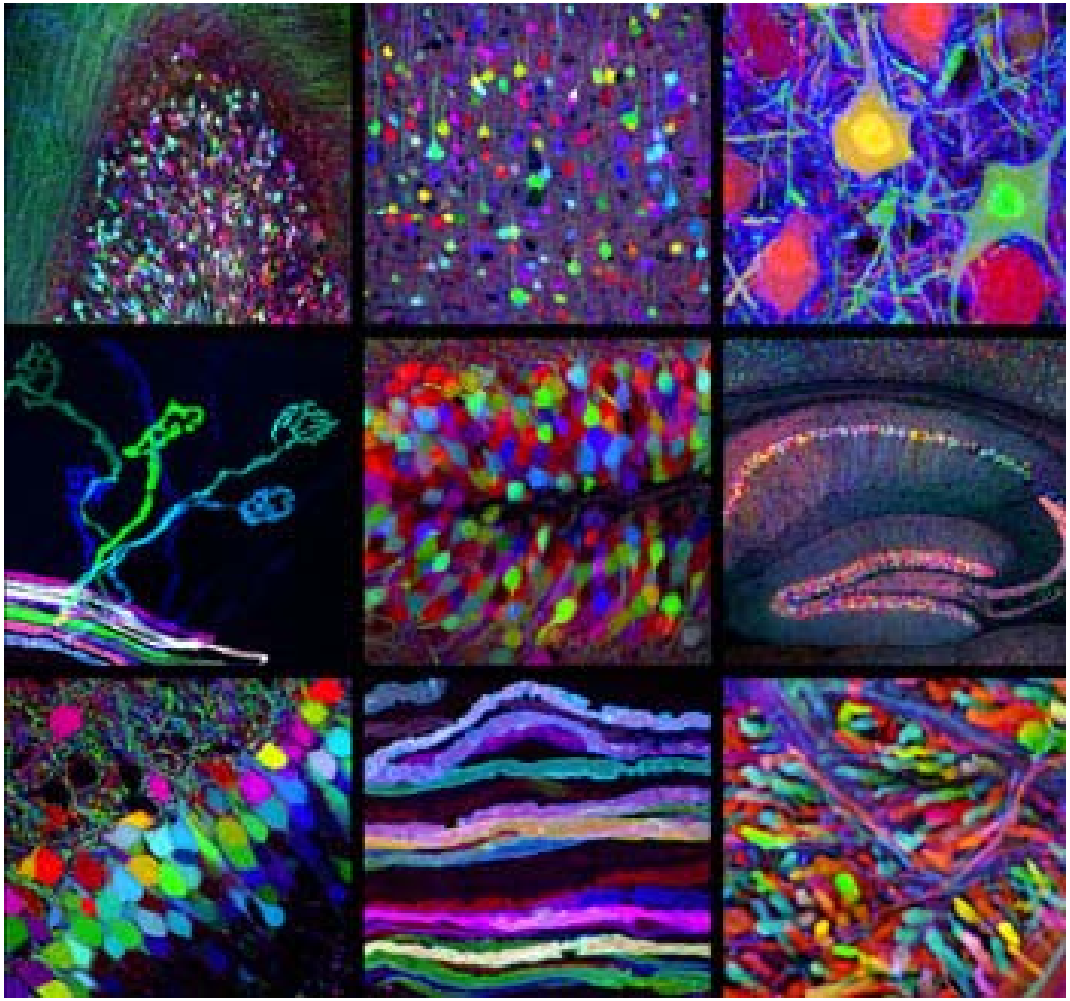





a
Animals
Wild-type fluorescent proteins
Variants
Cnidaria
Hydrozoa
Anthozoa
Octocorallia
Hexacorallia
Aequorea victoria
(bioluminescent jelly fish)
Aequorea GFP
BFP [4]
CFP [4]
GFP [4]
YFP [4]
PA-GFP [23]
citrine [16]
Venus [17]
Renilla reniformis
(bioluminescent sea pansy)
Renilla GFP
non-bioluminescent
coral species
DsRed(drFP583) [5,6]
T1 [19]
E57 [20]
E5(Fluorescent timer)[21]
mRFP1 [26]
cgigCP (cgCP) [6]
HcRed1 [9]
eqFP611 [10]
asFP595 [25]
KFP1 [25]
Kaede [24]
b
c
Normalized fluorescence intensity
400
500
600
700
wavelength (nm)
BFP
CFP
GFP
YFP
DsRed
eqFP611
mRFP1
HcRed1



Fluorescent protein expression



The researchers inserted into mice a construct targeted (Cre/Lox system) to the central nervous system, with **genes coding for 4 fluorescent protein emmiting 'primary' colours** (red, yellow, cyan and orange) organized so that, randomly, only one of the genes are expressed per insertion. **Depending on the number and 'color' of insertions (combinatorial expression), distinct cells will show distinct hues.** Colours show how cells intertwine.

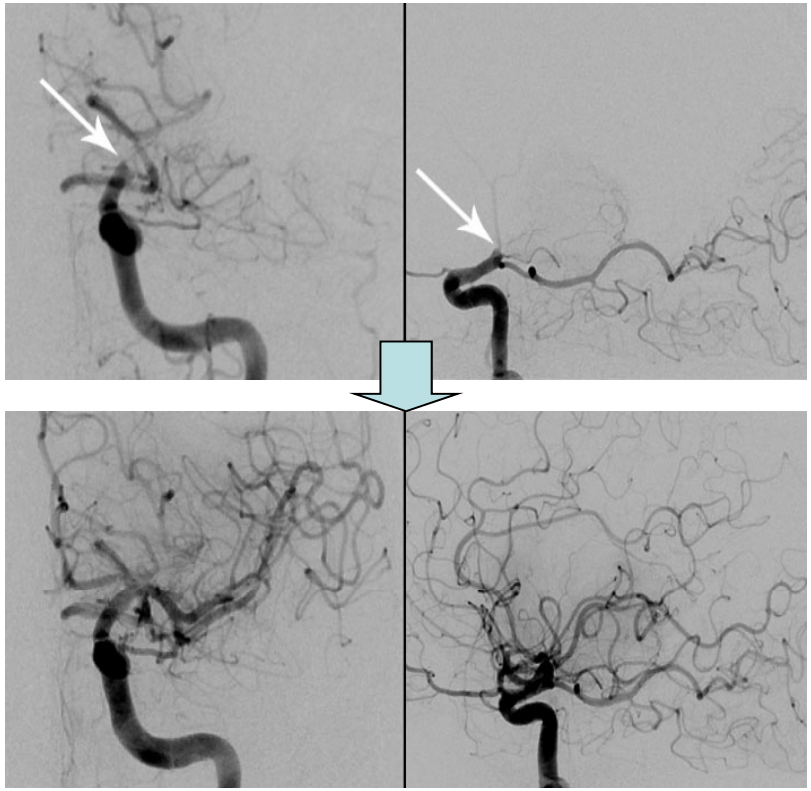
The research is showing the brain as we have never seen it before. This technique **will allow neurobiologist to track changes in the neural circuitry up to the individual cell level**; it could be also used to monitor the effects of therapies on the neural wiring, and more generally to (more precisely and easily) track tissue organisation changes in model organisms.

X-rays

Brain has little difference in the density

Angiograms (혈관조형술)

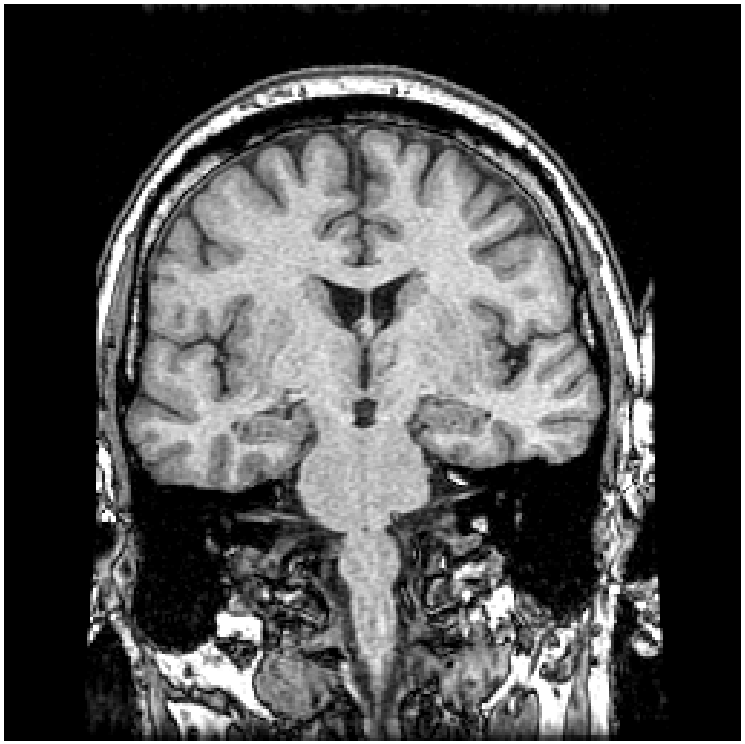
detect blood vessel problems by chemical injection



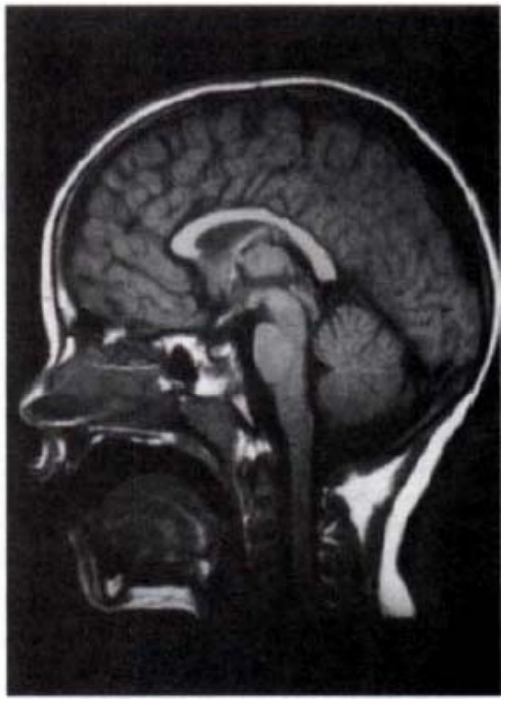
http://www.mghradrounds.org/index.php?src=gendocs&link=2008_march

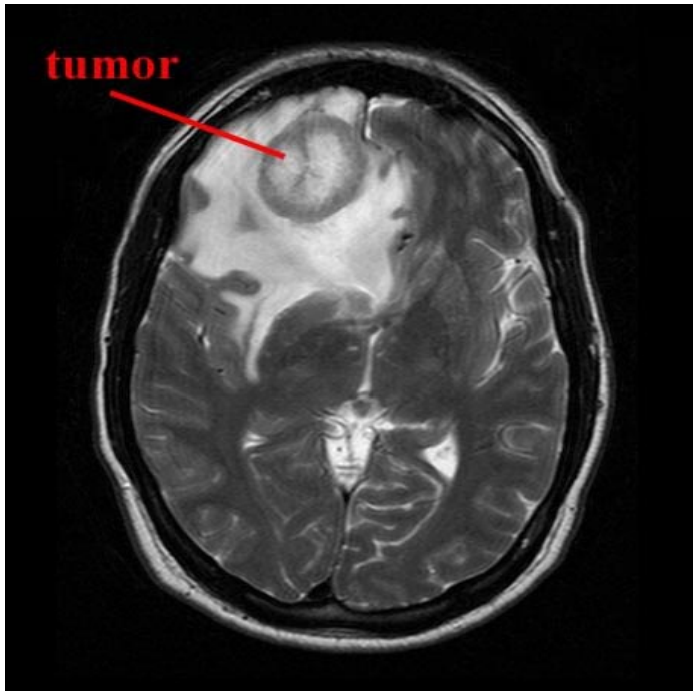
Computerized axial tomography (CAT)

Amplification of X-ray signal using a sensor connected to a computer
Series of x-ray images
- Scan living brain
- Localization of brain tissue problems
- Low resolution
- Exposure to radiation



Magnetic Resonance Imaging (MRI)





Use electromagnetic fields to image atom (hydrogen) density

- Scan living brain
- High resolution
- Expensive

Hydrogen atoms are best for MRI

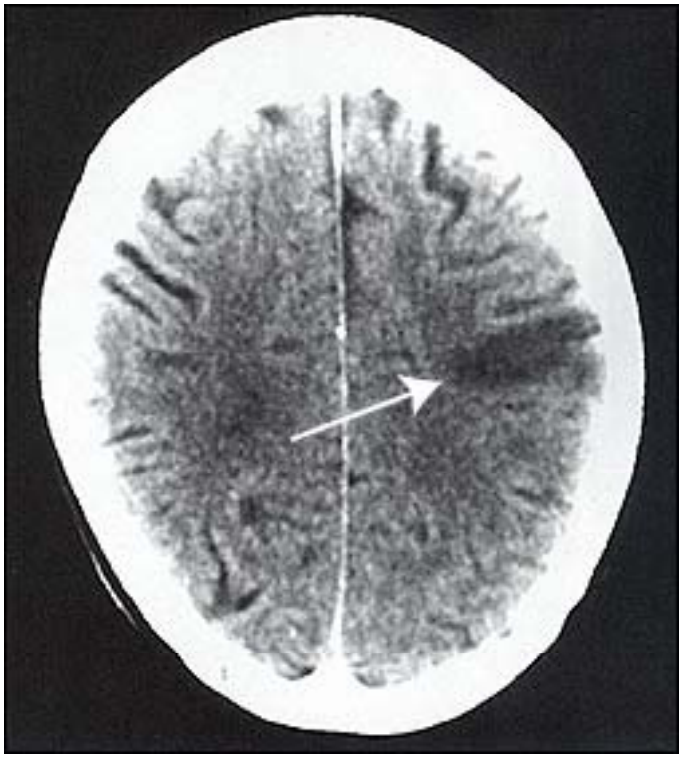
Biological tissues are predominantly 12C, 16O, 1H, and 14N

Hydrogen atom is the only major species that is MR sensitive

Hydrogen is the most abundant atom in the body

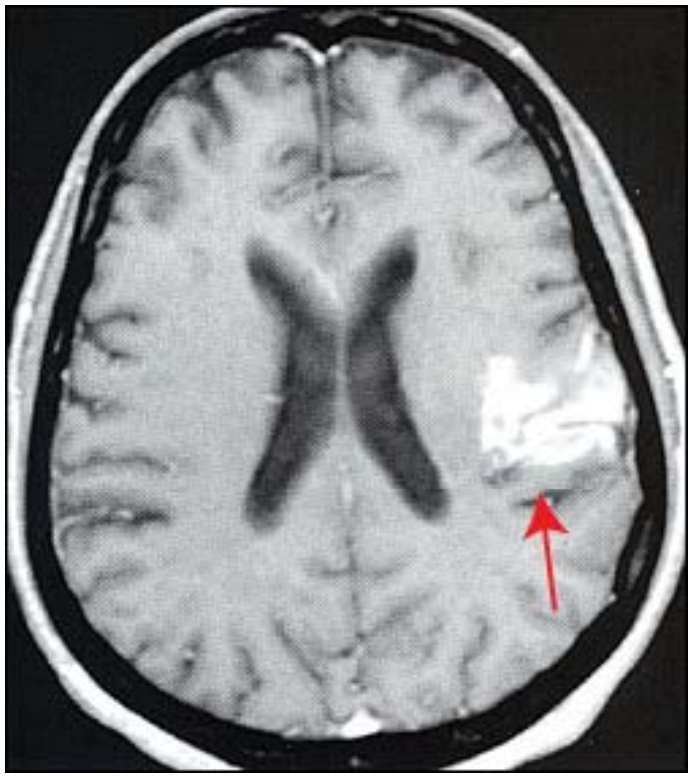
The majority of hydrogen is in water (H2O)
Essentially all MRI is hydrogen (proton) imaging

CAT



CT scan of a patient who has had a left middle cerebral artery stroke. The arrow indicates the location of the stroke.

MRI



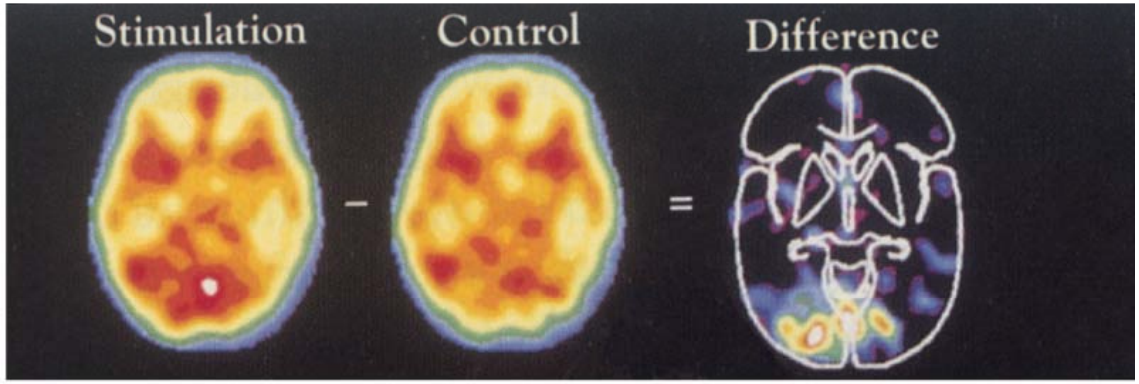
MRI of a patient who has had a stroke of the left hemisphere of the brain. The arrow indicates the area that was affected.

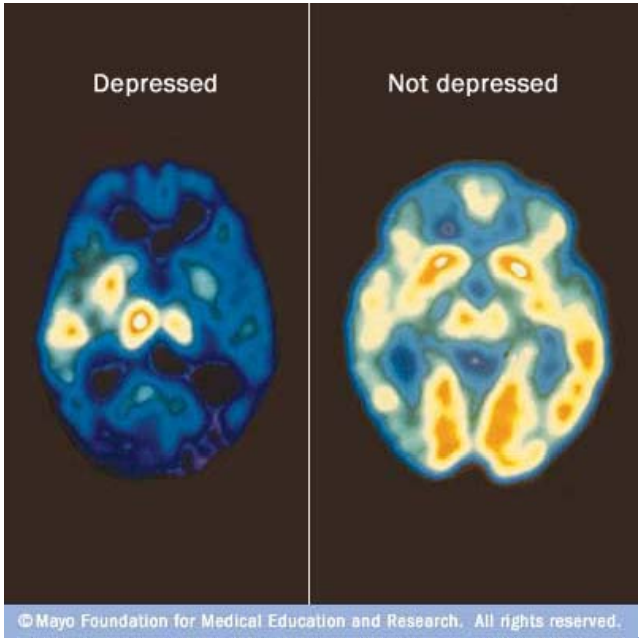
http://www.theuniversityhospital.com/stroke/inhospital.htm

Functional investigation

Positron Emission Tomography (PET)

Box 7.3B
A PET image. (Source: Posner and Raichle, 1994, p. 65.)





<u>Detect decay of injected radioactive substance (18-fluorodeoxyglucose)</u>

-unstable isotope emits positrons which collide with electrons in other molecules and ultimately emits high energy gamma rays

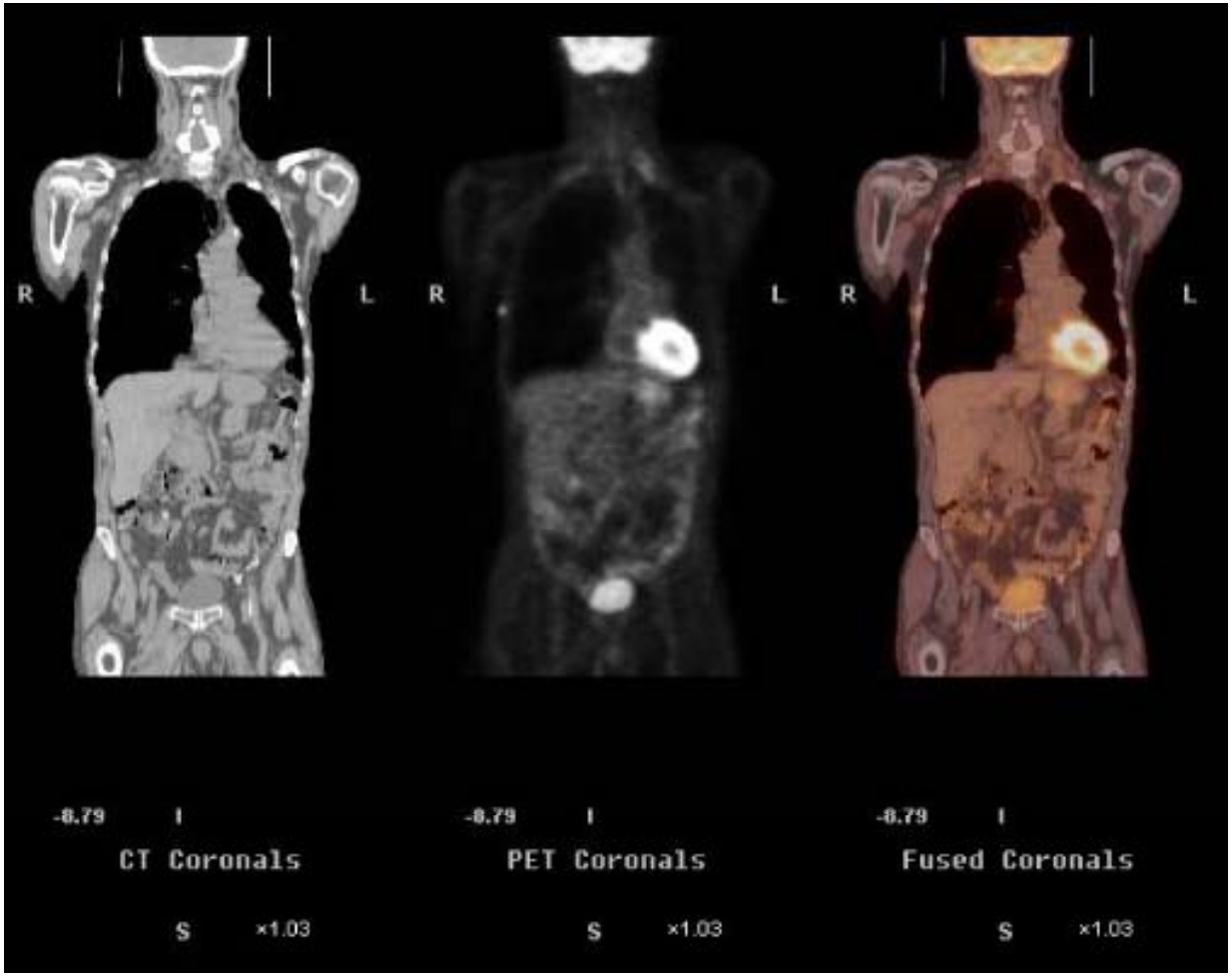
-Scan metabolic/chemical changes in living brain (tens of seconds)

-Can be mapped onto MRI

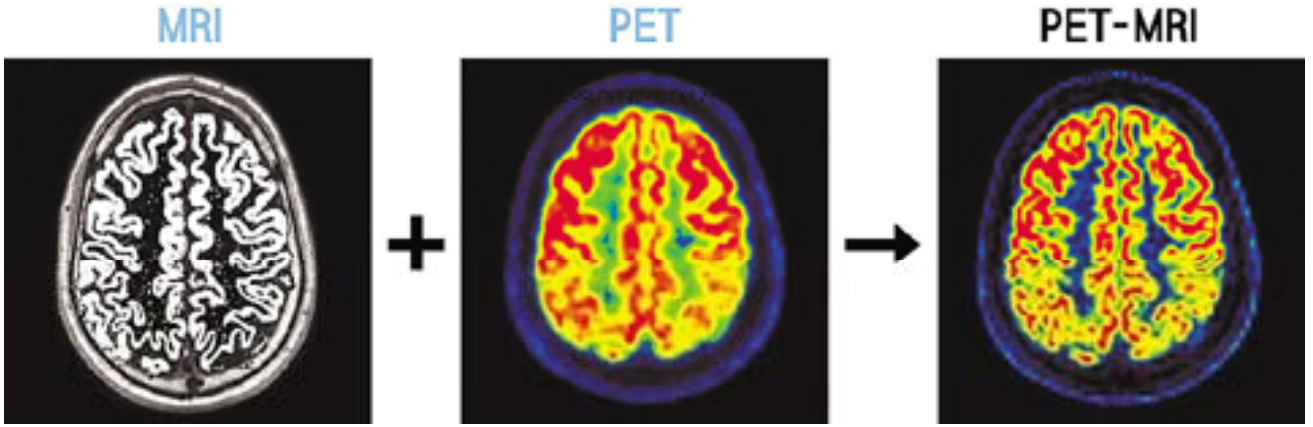
-Low resolution

-Exposure to radioactive substance

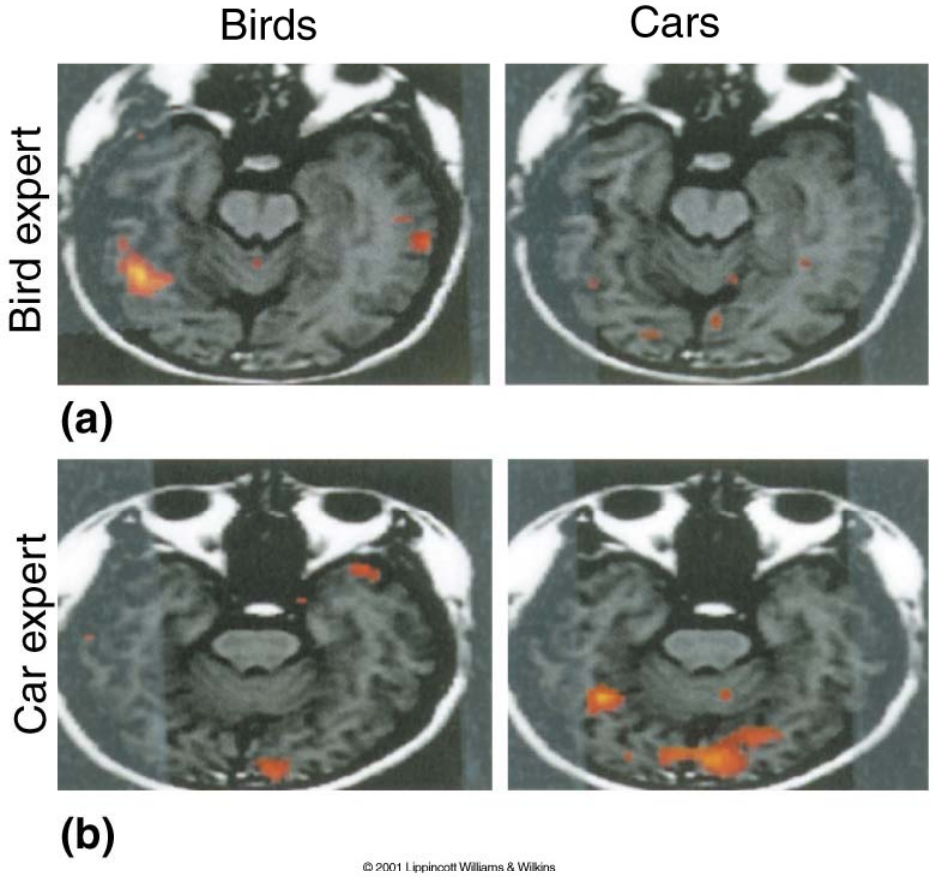
PET-CT


R
L
R
L
R
L
-8.79
I
CT Coronals
S
×1.03
-8.79
I
PET Coronals
S
×1.03
-8.79
I
Fused Coronals
S
×1.03

PET-MRI



Functional MRI (fMRI)



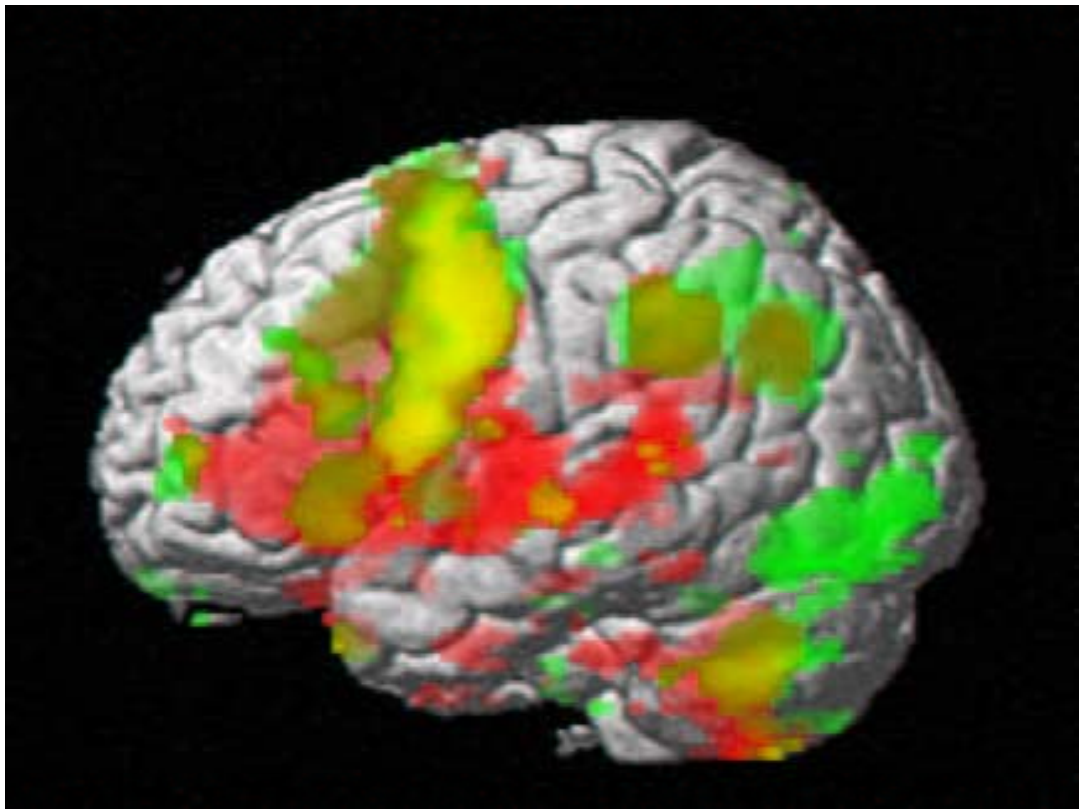
Use electromagnetic fields to image hemoglobin

-Detect metabolic needs of living brain (50-100 ms)

-High resolution

-Very expensive

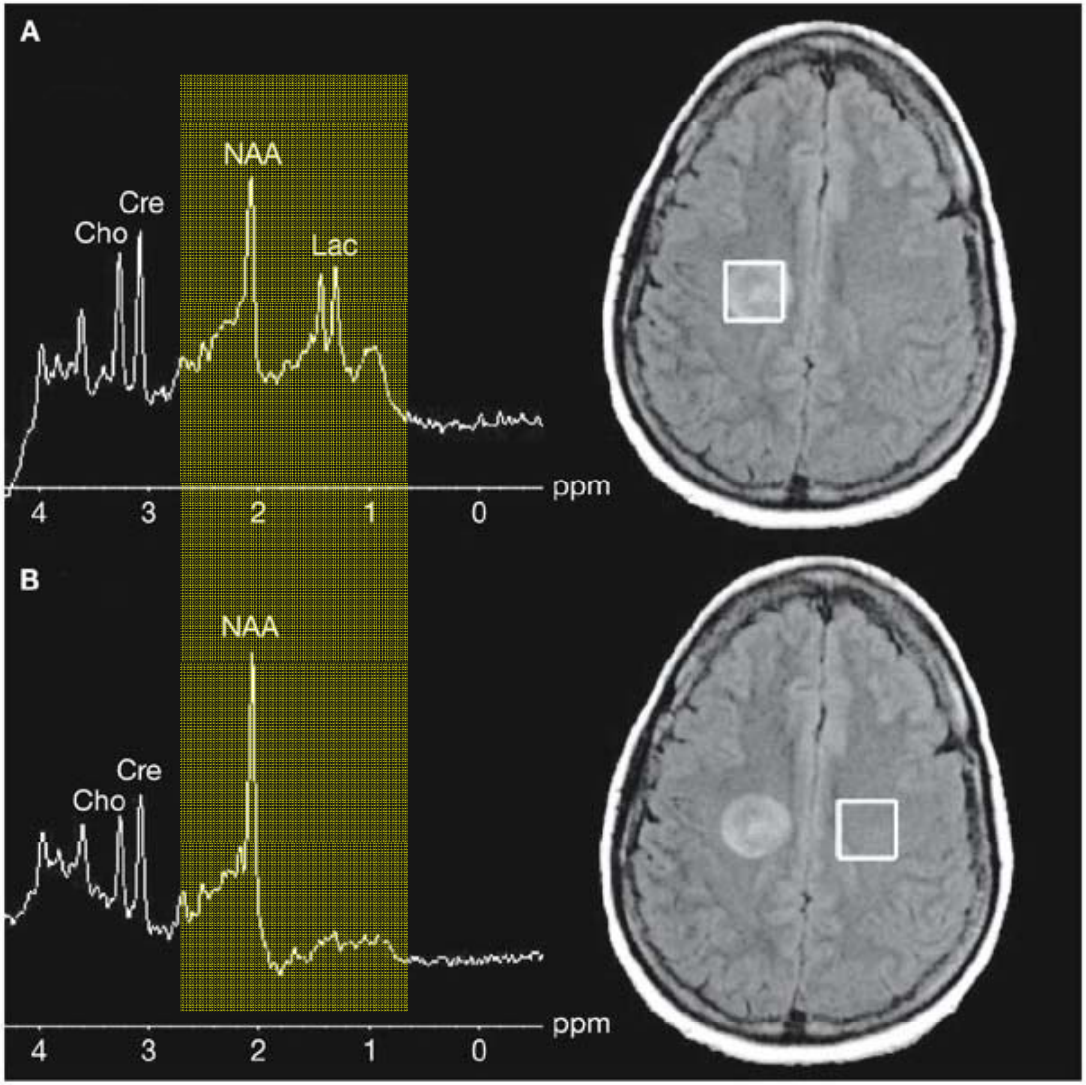
fMRI for studying of mental activities



An fMRI of the brain. Green areas were active while subjects remembered information presented visually. Red areas were active while they remembered information presented aurally. Yellow areas were active for both types.
http://stanmed.stanford.edu/2005fall/brain-main.html

Magnetic resonance spectroscopy (MSR)

Detect molecular and metabolic changes



Nature Clinical Practice Neurology (2007) 3, 349-354

Optical imaging techniques (Near Infrared Imaging)

Noninvasive functional mapping of the human cortex
Detecting changes in blood hemoglobin concentrations associated with neural activity
NIRS is much more portable than fMRI machines, even wireless instrumentation is available
However, NIRS cannot fully replace fMRI because it can only be used to scan cortical tissue

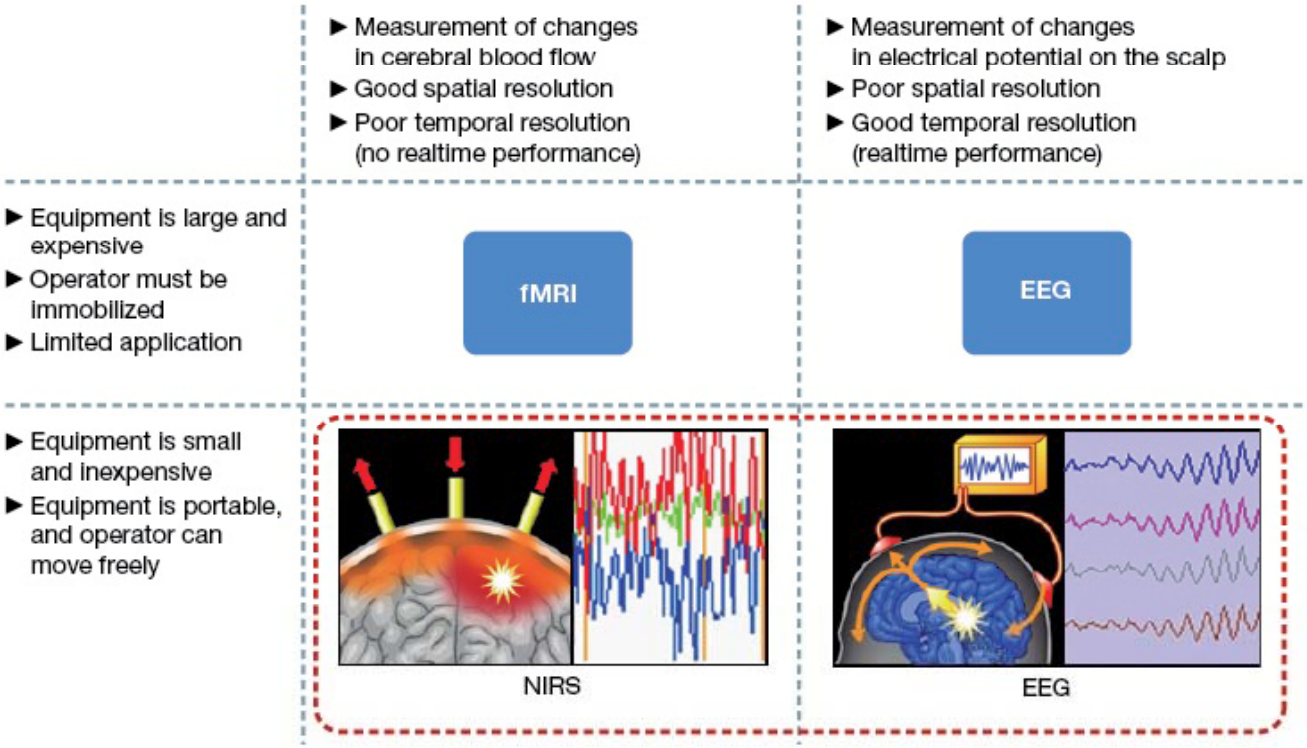


Fig 2 Combining Two Measurement Methods Researchers combined NIRS (high spatial resolution) with EEG (high temporal resolution) to improve judgment precision (portion in red frame). Diagram from ATR material.

http://techon.nikkeibp.co.jp/article/HONSHI/20090527/170831/

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ASIA EDITION / 台灣版 / 나케이 일렉트로닉스

Nikkei Electronics Asia -- June 2009

Features

ASIMO Responds to Brain Activity with 90% Accuracy

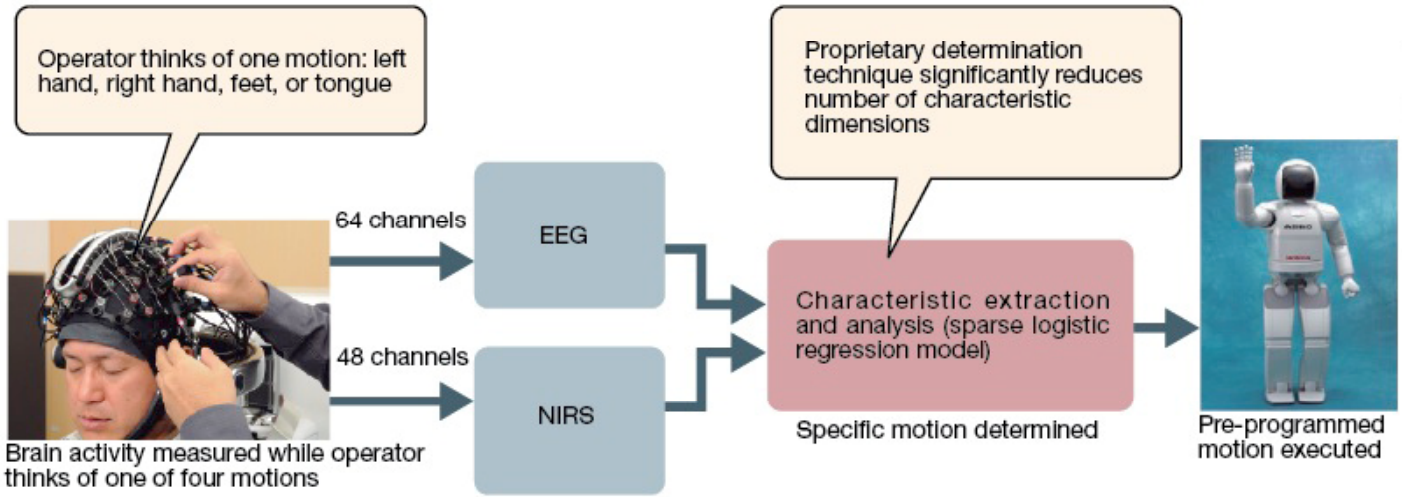
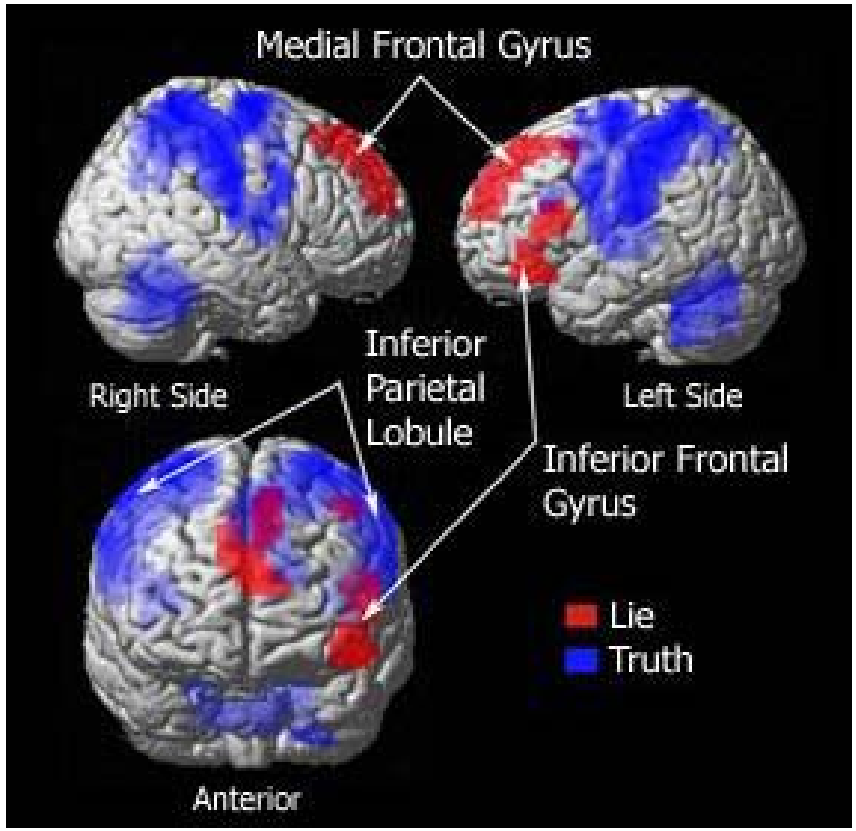


Fig 1 Precision Improved with Proprietary Determination Technique When the operator thinks of one of four possible motions, the corresponding brain activity is detected, and the new technique used to identify which motion.

EEG: electroencephalography
NIRS: near-infrared spectroscopy

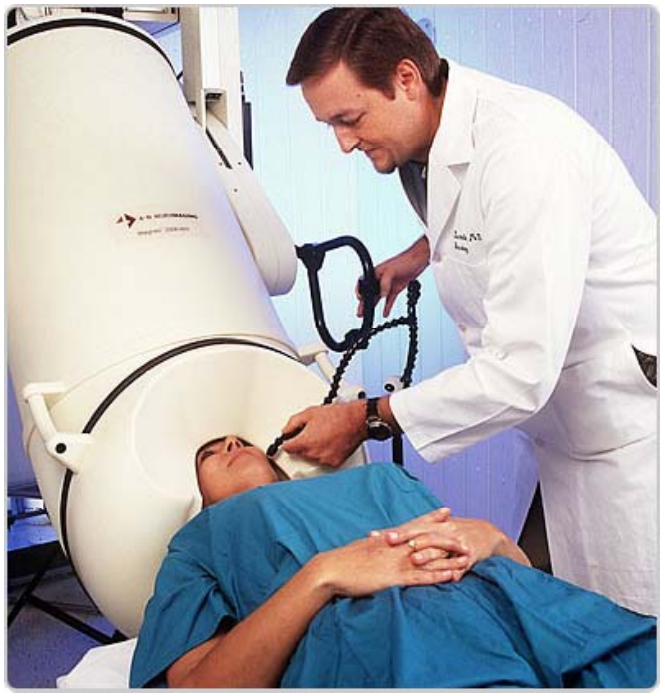
fMRI lie detection technology



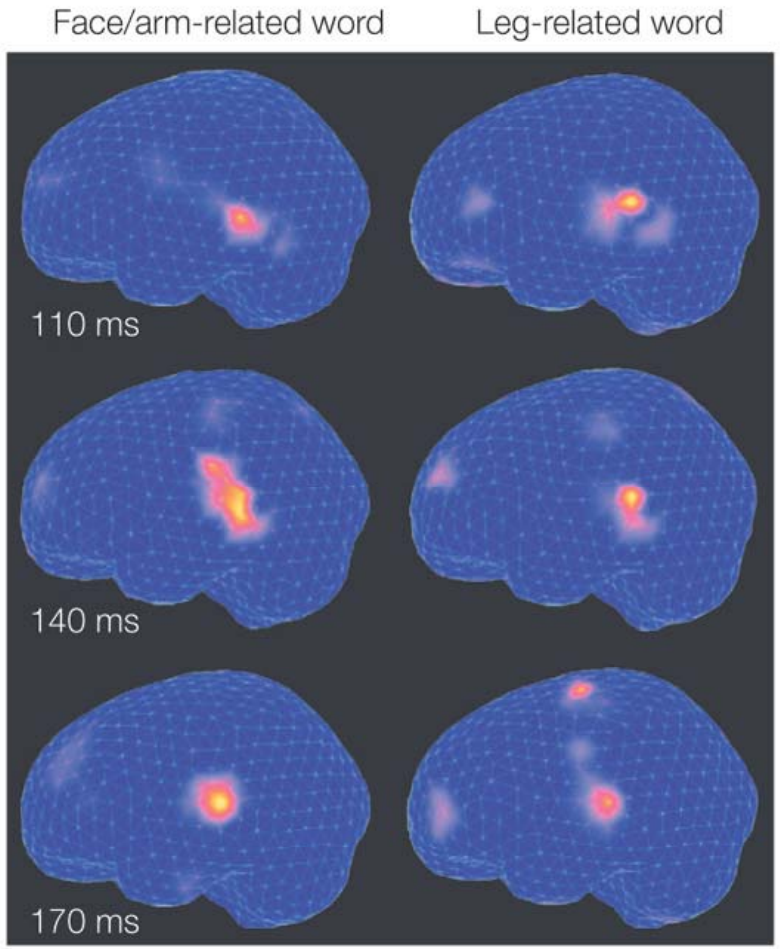
Magnetoencephalography (MEG)

Measure magnetic fields produced by electrical activity in the brain

-high temporal resolution (1 ms)
-low spatial resolution (2 mm)



http://www.horizons-2000.org/2.%20Ideas%20and%20Meaning/Topics/NeuroPsychology.htm



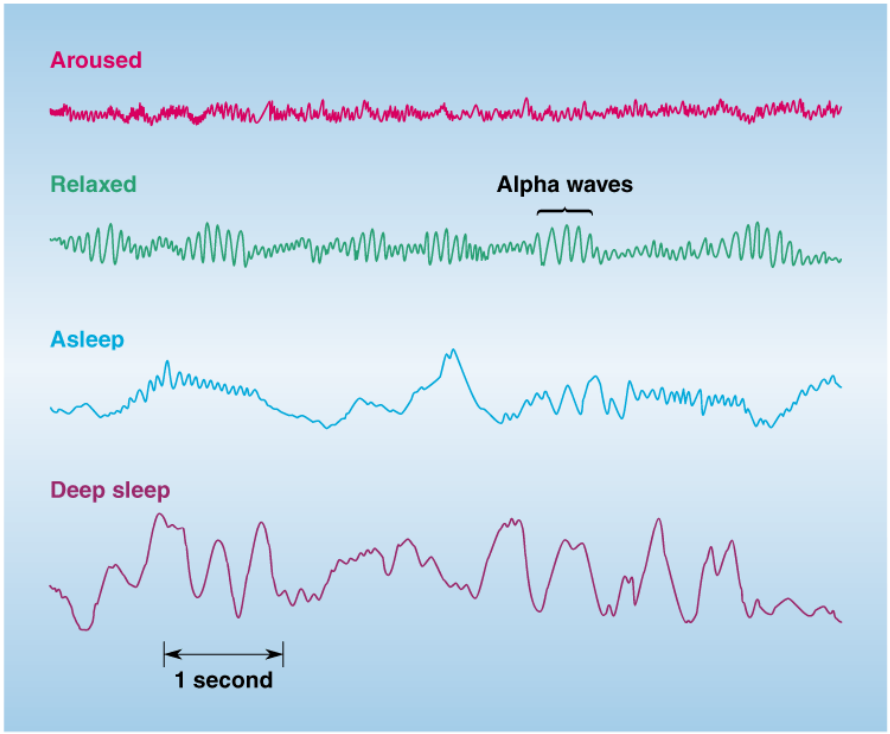
Magnetoencephalography (***n*** = 16) was used to measure the activation elicited at different times after spoken action words could be uniquely recognized. Note the slight upward movement of the inferior central source for the face/arm-related word and the delayed appearance of the superior central source for the leg-related word. These activation time courses might reflect the movement of neuronal activity in distributed neuronal assemblies that represent and process words with different action-related meanings. ***Nature Reviews Neuroscience*** **6**, **576-582 (July 2005)**

Electroencephalography

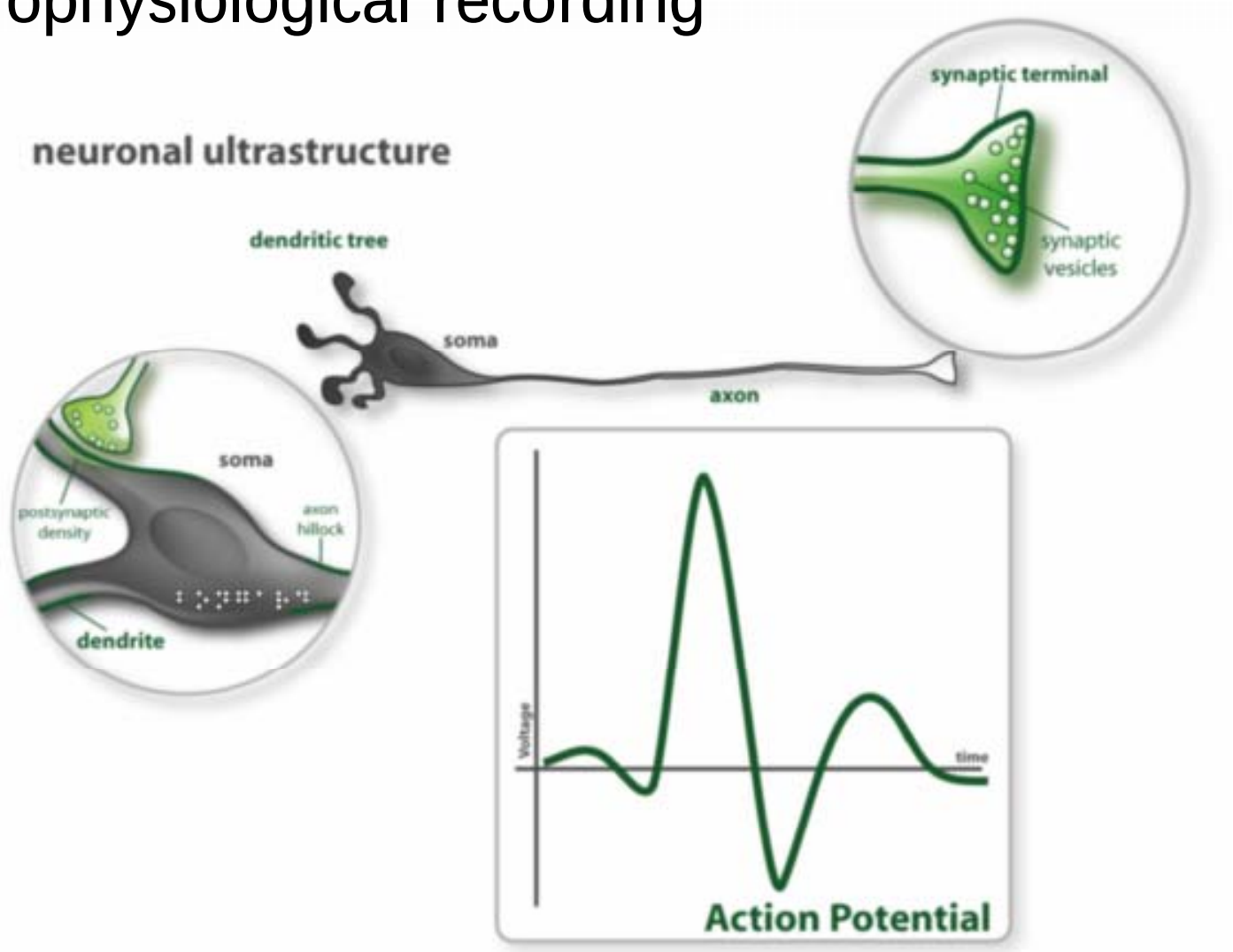
<u>electrical potentials amplified from scalp</u>
-high temporal resolution
-low spatial resolution
-cortical tissue only

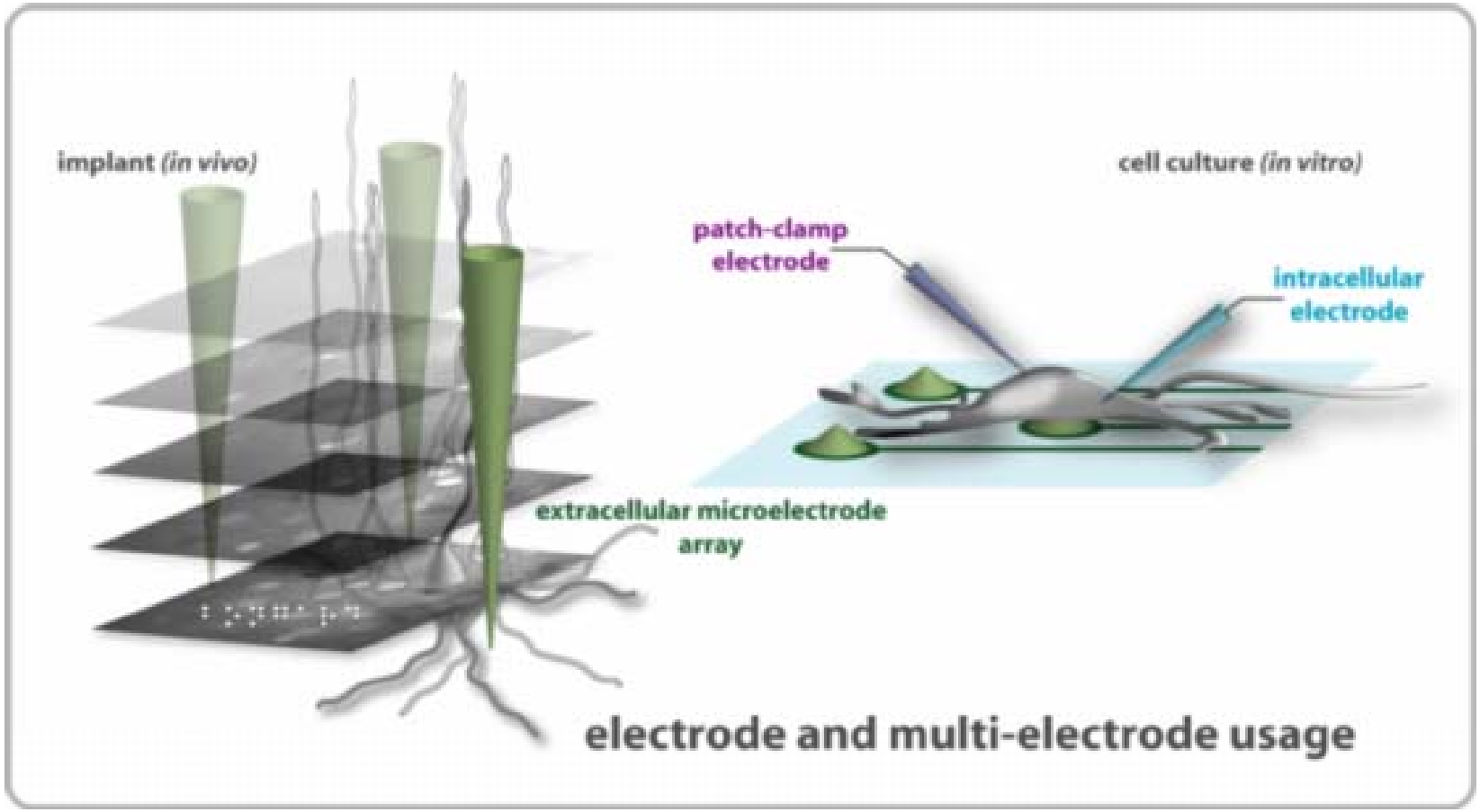
Electroencephalograghy (EEG) recording

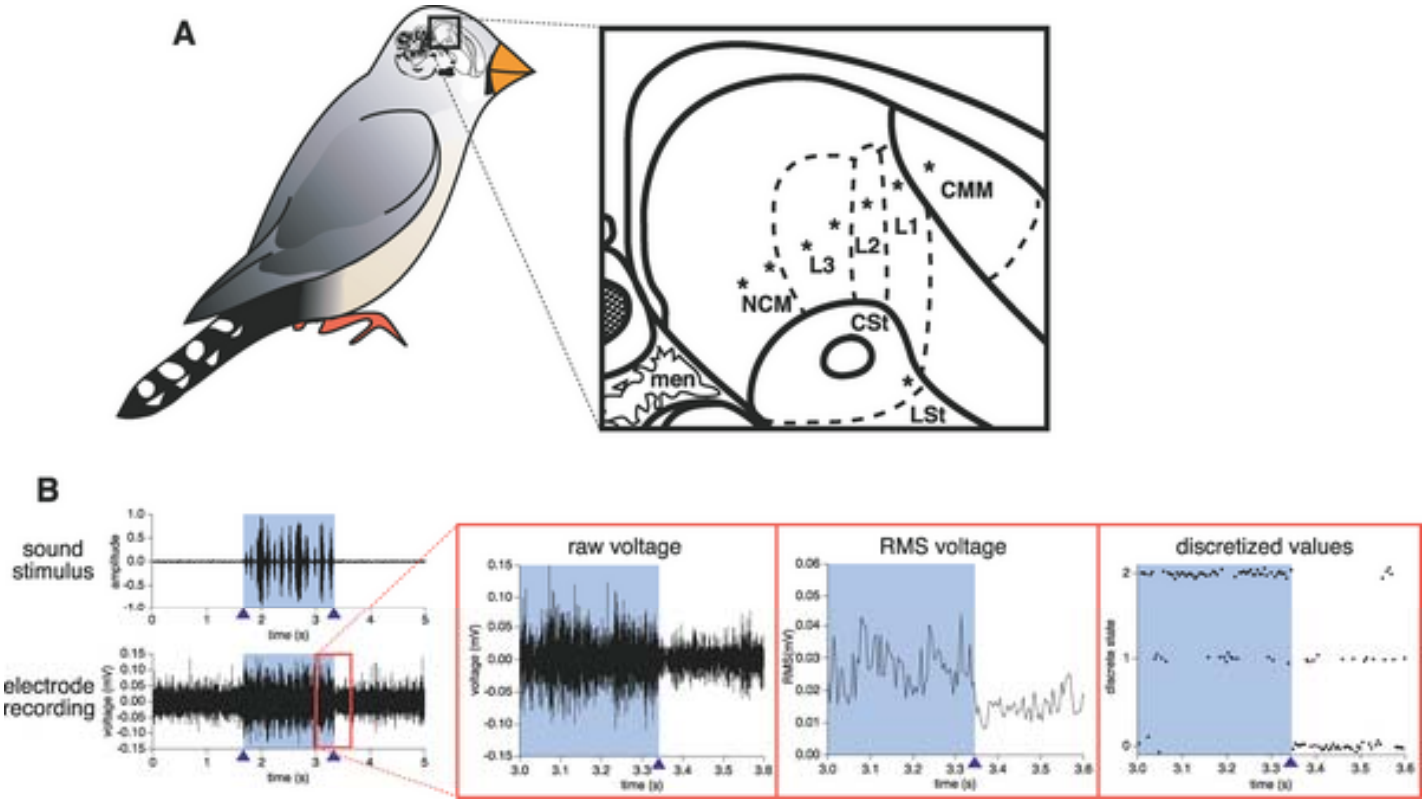
► Typical EEGs



Electrophysiological recording

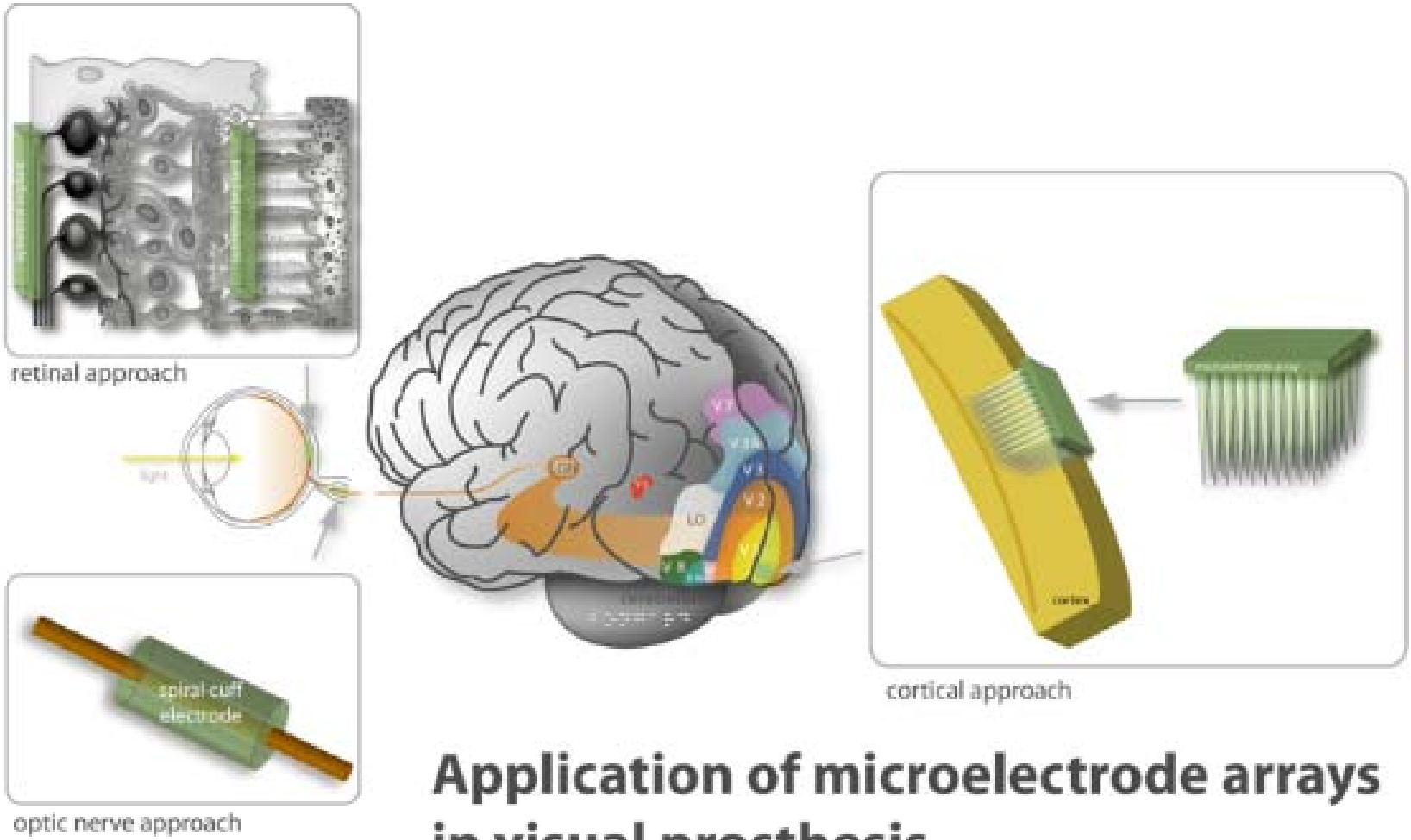



implant (in vivo)
cell culture (in vitro)
patch-clamp electrode
intracellular electrode
extracellular microelectrode array
electrode and multi-electrode usage



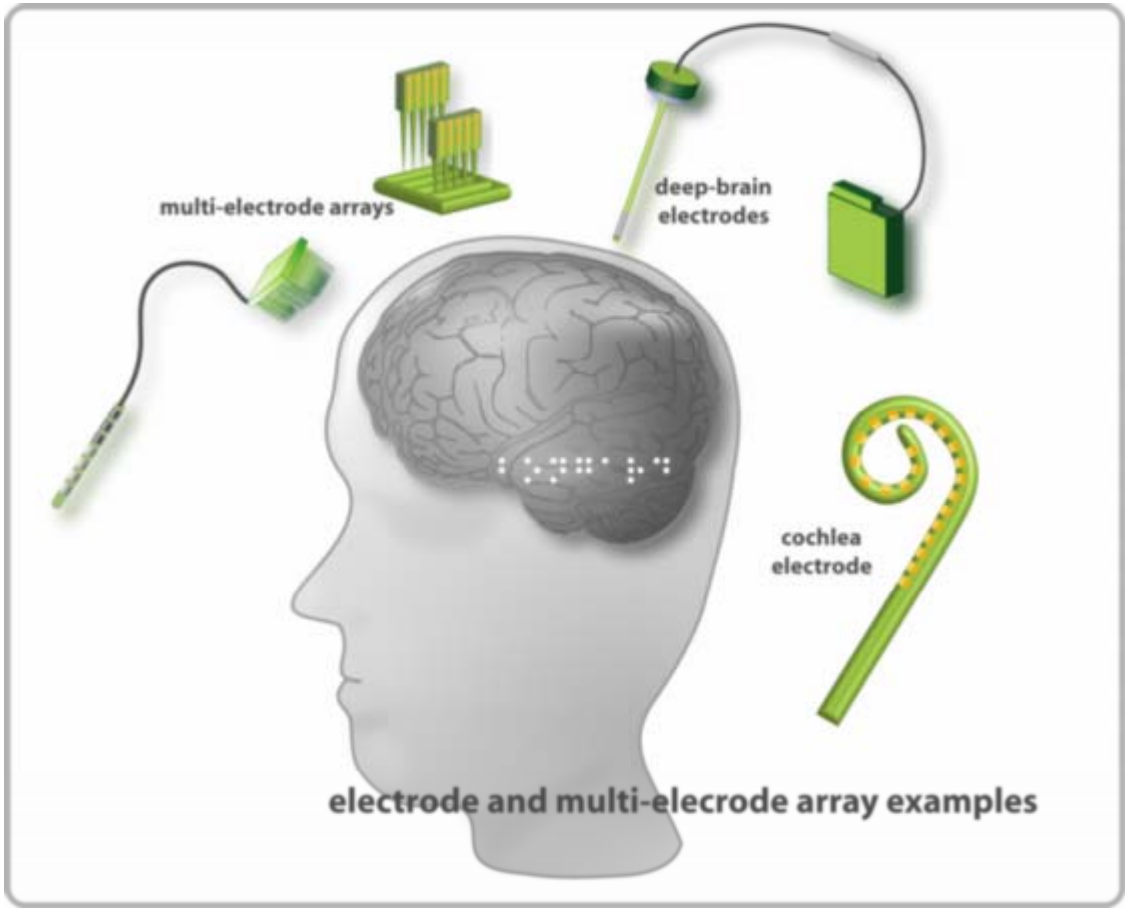
Electrophysiological Recording from Songbird Auditory Forebrain

http://www.ploscompbiol.org/article/slideshow.action?uri=info:doi/10.1371/journal.pcbi.0020161&imageURI=info:doi/10.1371/journal.pcbi.0020161.g001#



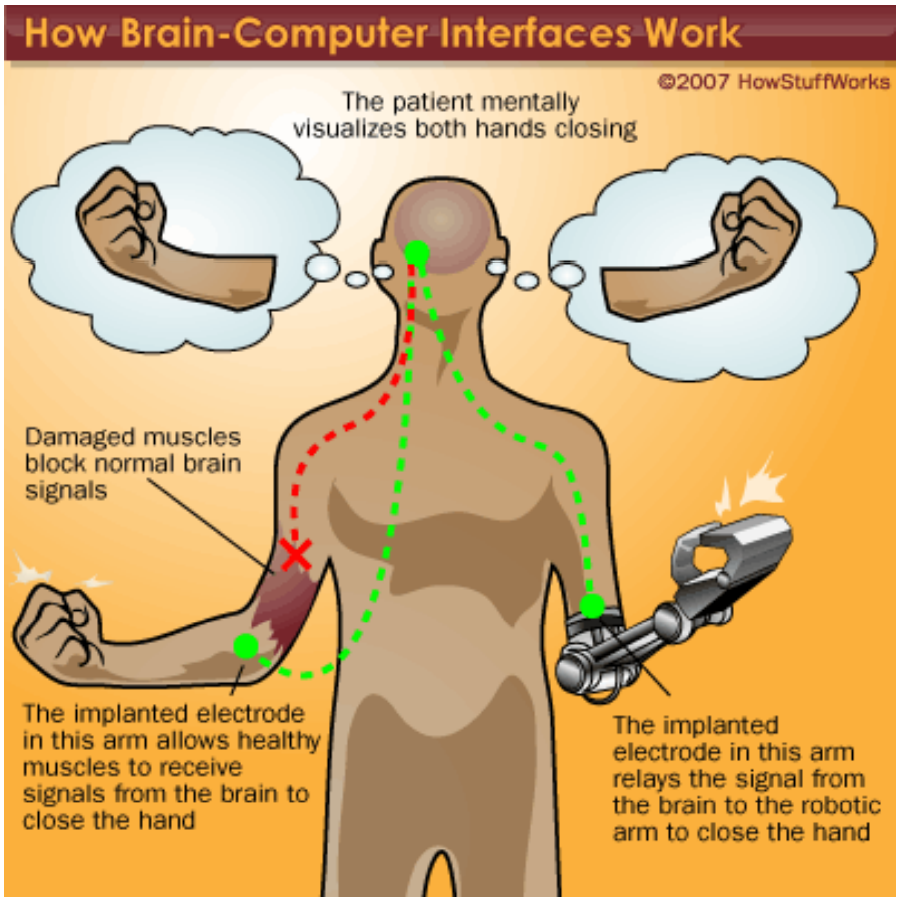
Application of microelectrode arrays in visual prosthesis

http://naranja.umh.es/~np/index.php?option=com_content&task=view&id=14&Itemid=29

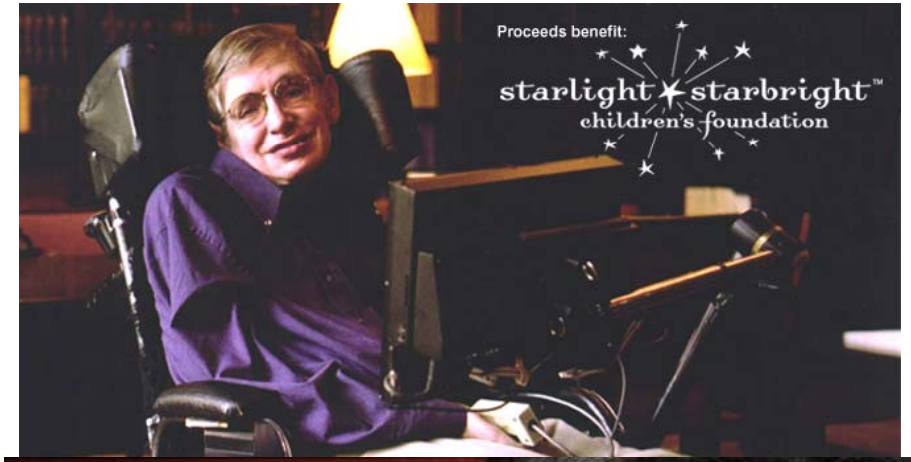

multi-electrode arrays
deep-brain electrodes
cochlea electrode
electrode and multi-elecrode array examples

Cyborg

A cybernetic organism (i.e., an organism that has both artificial and natural systems).



Cyborg Steven Hawking

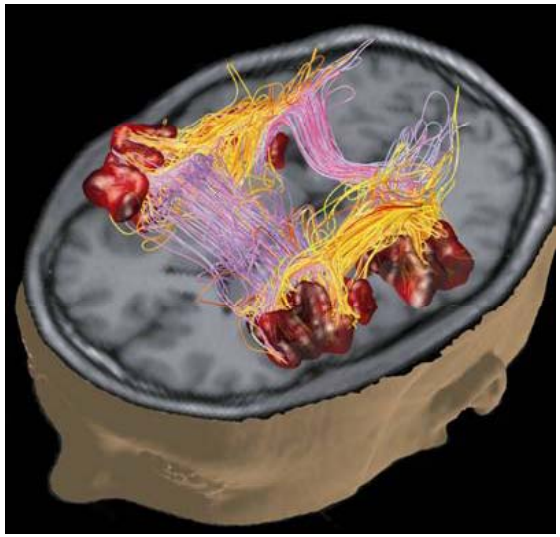


http://igargoyle.com/archives/2006/04/steven_hawkings.html

Human Connectome Project (HCP)

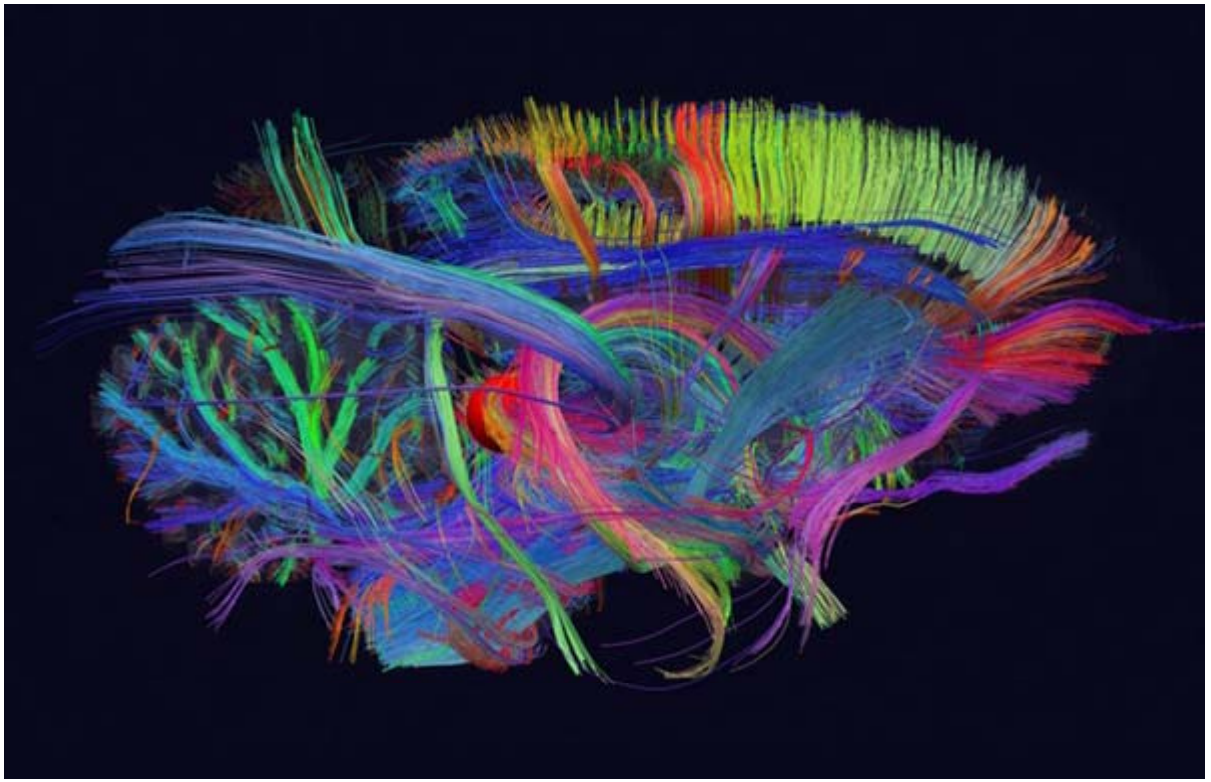
Three imaging techniques that will be used to carry out the HCP may include:

(1)High angular resolution diffusion imaging with magnetic resonance (HARDI), which detects the diffusion of water along fibrous tissue, and can be used to visualize axon bundles.



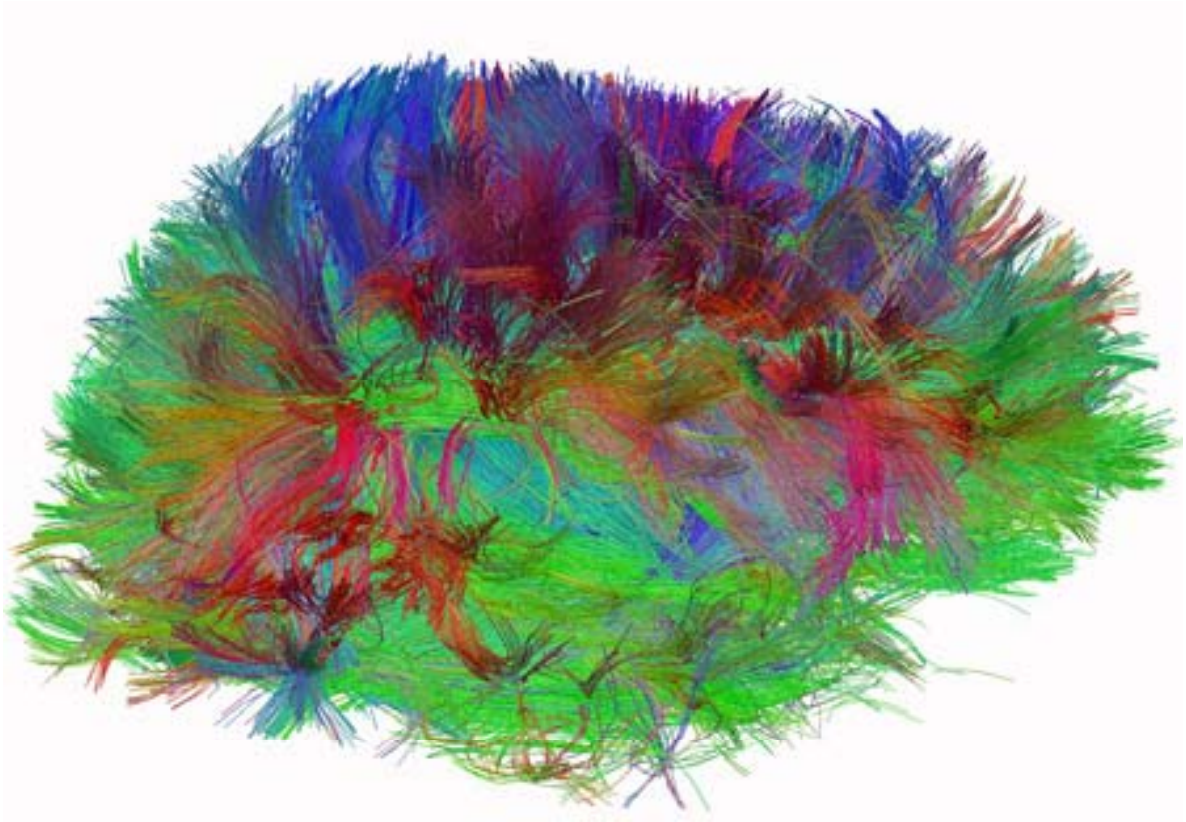
(2) Resting state fMRI (R-fMRI), which detects fluctuations in brain activity while a person is at rest, and can be used to look for coordinated networks within the brain.

(3) Electrophysiology and magnetoencephalography (MEG) combined with fMRI (E/M fMRI), which adds information about the brain's electrical activity to the fMRI signal. In this procedure, the person performs a task so that the brain regions associated with that task become active. Since this is the first time that researchers will combine these brain imaging technologies to systematically map the brain's connections, the HCP will support development of new data models, informatics and analytic tools to help researchers make the most of the data.
http://brainwaves.corante.com/archives/2009/07/24/human_connectome_project_launched_to_reveal_brain_connectivity.php



3D image of an owl-monkey’s brain

The three-dimensional map of all its neurons. They call this circuit diagram the “connectome”, and it could help us better understand everything from imagination and language to the miswirings that cause mental illness.



Diffusion spectrum image shows brain wiring in a healthy human adult. The thread-like structures are nerve bundles, each containing hundreds of thousands of nerve fibers.
http://www.nimh.nih.gov/science-news/2010/40-million-awarded-to-trace-human-brains-connections.shtml

Homework: Brain 관련 동영상 제출

http://www.google.co.kr/search?hl=ko&rlz=&q=fmri&um=1&ie=UTF-8&tbo=u&tbs=vid:1&source=og&sa=N&tab=wv