

## Biomedical Technologies in Diagnostic and Therapy

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### Devices and methods in clinical neurophysiology

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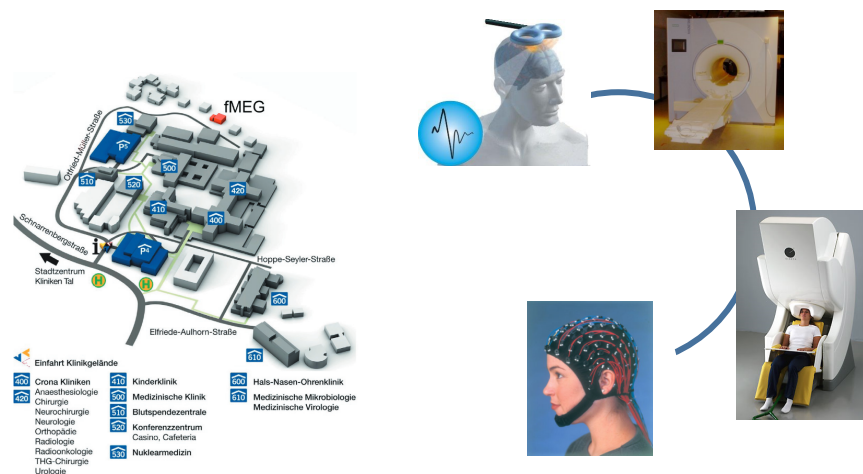
MEG-Zentrum  
Universität Tübingen

### Overview

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- Introduction
- Clinical Neurophysiology
- Basics
  - Neurons
  - Physical Laws
  - Brain anatomy and histology, brain function
- Functional imaging methods
  - biochemical activity
  - neurometabolic activity
  - neuroelectrical activity

## MEG-Zentrum



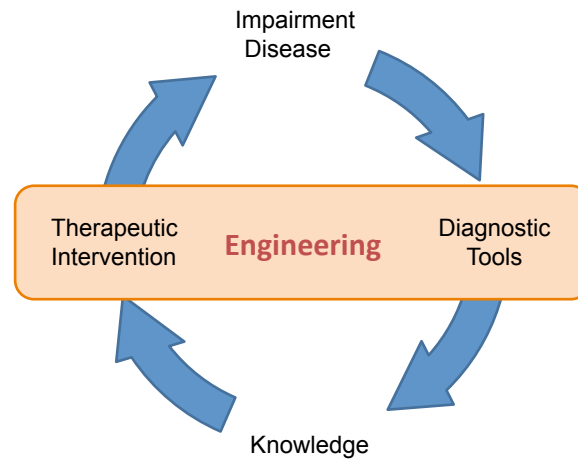
## MEG-Zentrum





## Clinical Neurophysiology

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## Devices and Methods in Clinical Neurophysiology

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**Clinical neurophysiology** is a medical specialty that studies the **central and peripheral nervous systems** through the **recording of bioelectrical activity**, whether spontaneous or stimulated.

It encompasses both **research regarding the pathophysiology** along with **clinical methods used to diagnose diseases** involving both central and peripheral nervous systems.

*Wikipedia: [http://en.wikipedia.org/wiki/Clinical\\_neurophysiology](http://en.wikipedia.org/wiki/Clinical_neurophysiology)*

Furthermore, it involves **therapeutic approaches** that **alter the neurophysiological activity** by **adequate stimulation** of the nervous system (electrical stimulation, magnetic stimulation, neurofeedback)

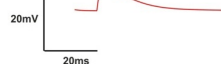
## Neurobiological Basics

### Neuron

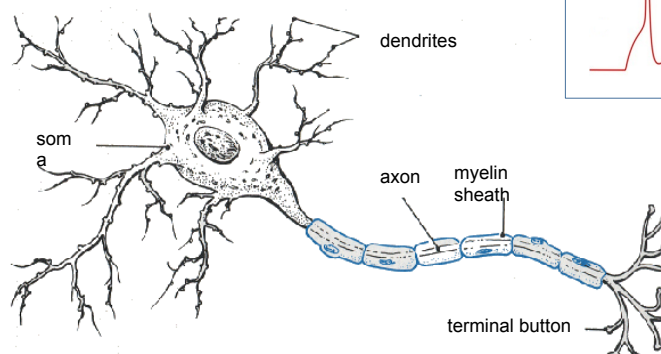
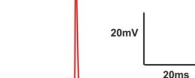
- Dendrite
- Soma
- Axon
- Synapse
- Excitatory and inhibitory postsynaptic potential
- Action potential
- Nervous system

## Electrical Phenomena in Neurons

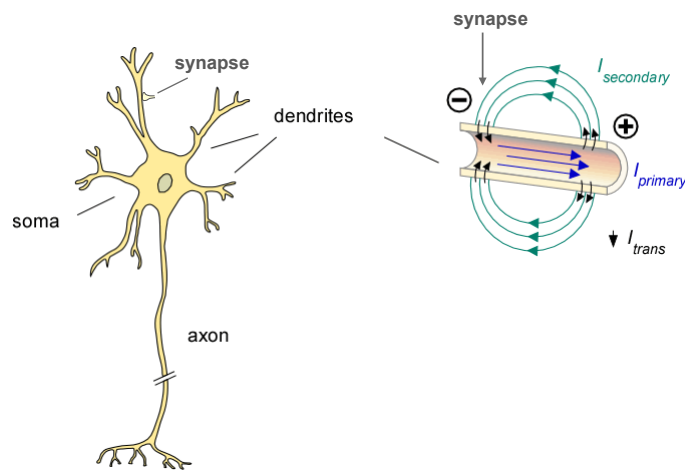
### EPSP



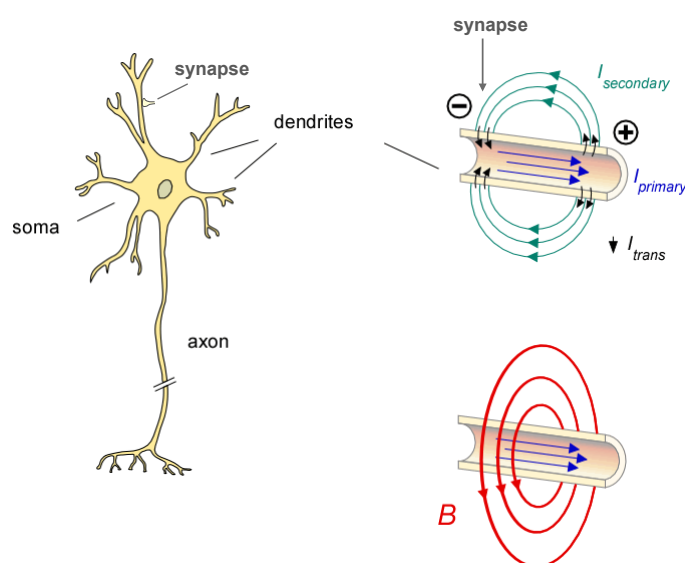
### action potential



### Electrical Phenomena in Neurons



### Electrical Phenomena in Neurons



## Clinical Neurophysiology

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### Methods

- EEG and MEG
- EMG and TMS
- tDCS and tACS
- MRI and fMRI
- NIRS

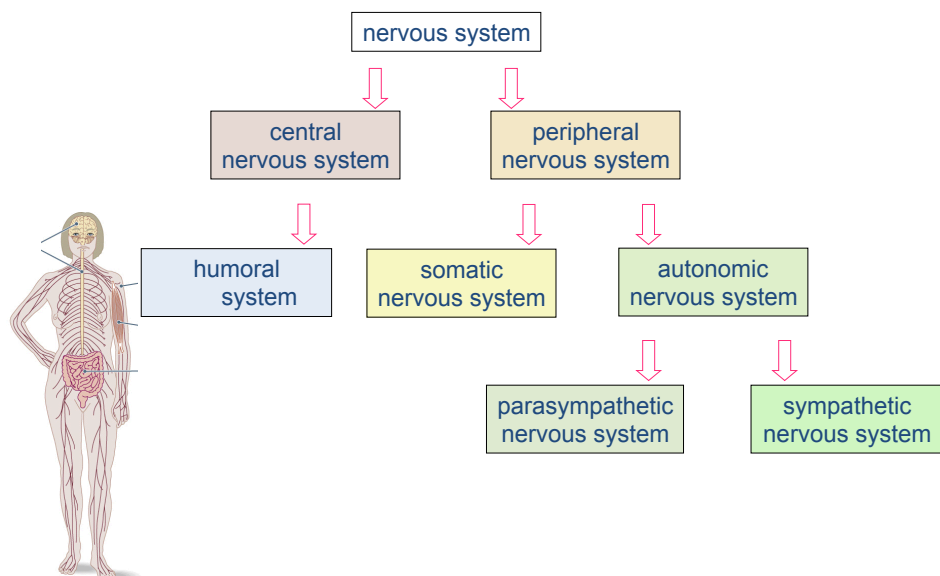
### Diseases

- Sensory and motor functions
- Chronic pain
- Neuropathy (Diabetes)
- Stroke and paralysis
- Amyotrophic lateral sklerosis
- Parkinson's disease
- Epilepsy
- Brain tumors
- Alzheimer's disease
- Cognitive disorders

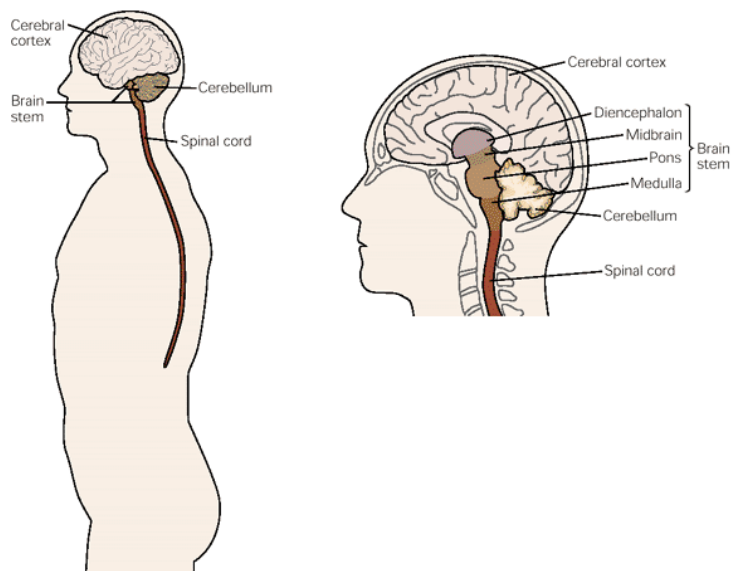
Wikipedia: [http://en.wikipedia.org/wiki/Clinical\\_neurophysiology](http://en.wikipedia.org/wiki/Clinical_neurophysiology)

## Organisation of the Nervous System

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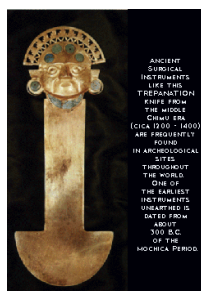
## Central Nervous System



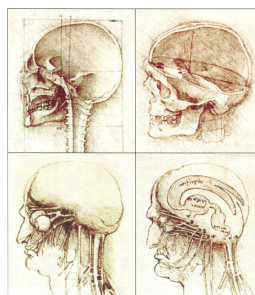
## History



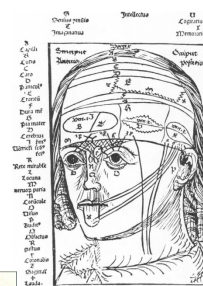
Egypt ~3000 BC



South America  
~300 BC



Leonardo da Vinci ~1490



1501 by Magnus Hundt



## Organisation of the Brain

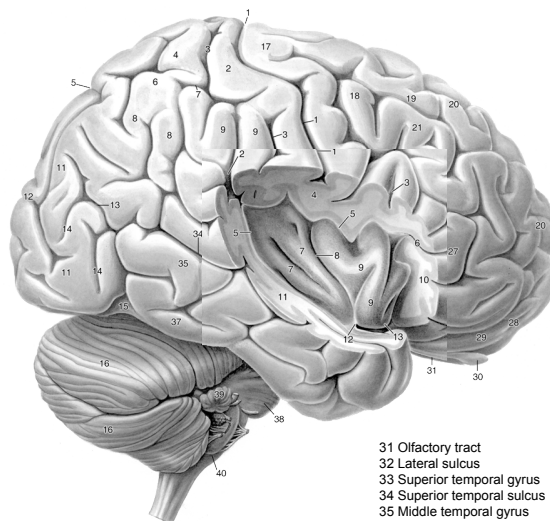
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A lateral view of the human brain with color-coded regions. The brain is divided into four main lobes: Occipital (blue), Parietal (green), Temporal (orange), and Frontal (red). The poles are the Occipital pole (1) and Frontal pole (10). The opercula are the Frontoparietal operculum (5) and Temporal operculum (6). The limbic lobe (11) is shown as a small region on the medial surface. A dashed line indicates the boundary between the temporal and frontal lobes. A small arrow points to the top of the brain.

- 1 Occipital pole
- 2 Occipital lobe
- 3 Parietal lobe
- 4 Temporal lobe
- 5 Frontoparietal operculum
- 6 Temporal operculum
- 7 Frontal operculum
- 8 Temporal pole
- 9 Frontal lobe
- 10 Frontal pole
- 11 Limbic lobe

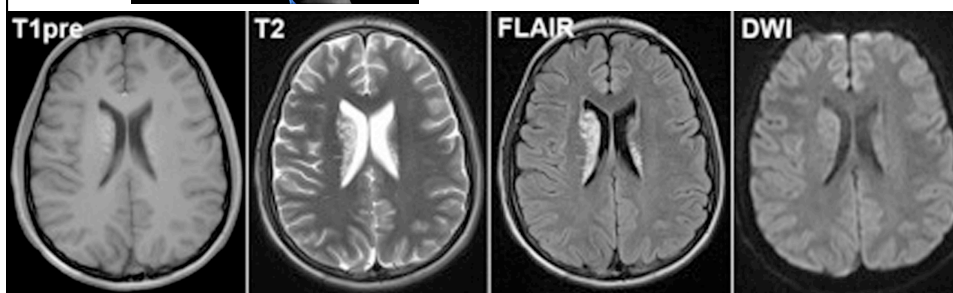
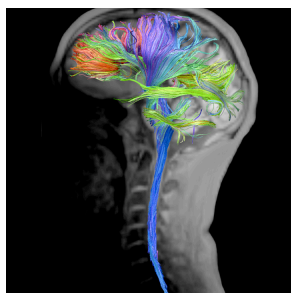
## Organisation of the Brain

- 1 Central sulcus
- 2 Postcentral gyrus
- 3 Postcentral sulcus
- 4 Superior parietal lobule
- 5 Parieto-occipital sulcus
- 6 Inferior parietal lobule
- 7 Intraparietal sulcus
- 8 Angular gyrus
- 9 Supramarginal gyrus
- 10 Lateral sulcus, posterior branch
- 11 Occipital gyri
- 12 Lunate sulcus
- 13 Anterior occipital sulcus
- 14 Occipital sulci
- 15 Preoccipital notch
- 16 Cerebellar hemisphere
- 17 Precentral gyrus
- 18 Precentral sulcus
- 19 Superior frontal sulcus
- 20 Superior frontal gyrus
- 21 Middle frontal gyrus
- 22 Inferior frontal gyrus
- 23 Opercular part of inferior frontal gyrus
- 24 Triangular part of inferior frontal gyrus
- 25 Orbital part of inferior frontal gyrus
- 26 Lateral sulcus, ascending branch
- 27 Lateral sulcus, anterior branch
- 28 Orbital sulci
- 29 Orbital gyri
- 30 Olfactory bulb

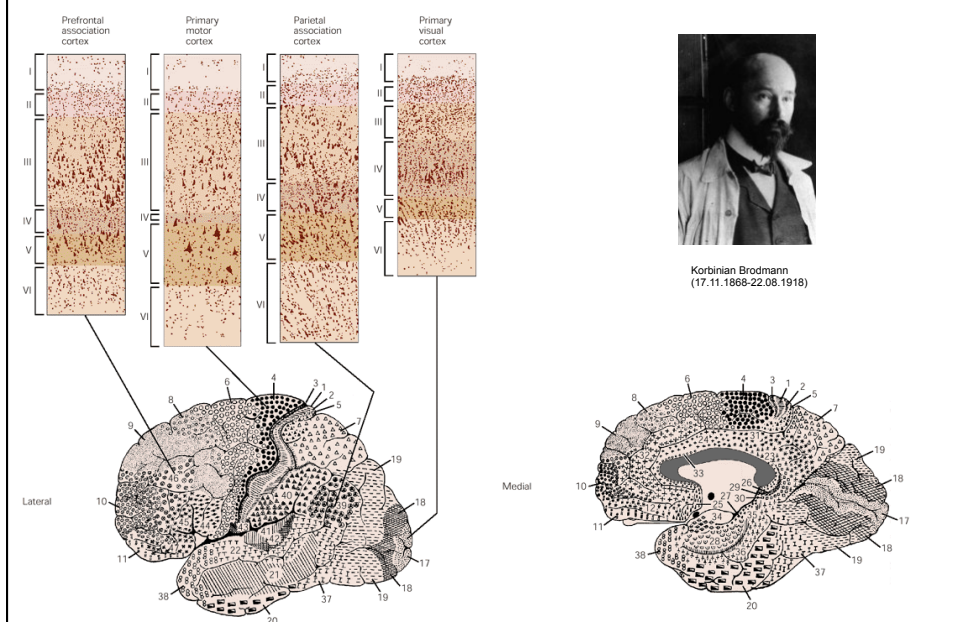


- 31 Olfactory tract
- 32 Lateral sulcus
- 33 Superior temporal gyrus
- 34 Superior temporal sulcus
- 35 Middle temporal gyrus
- 36 Inferior temporal sulcus
- 37 Inferior temporal gyrus
- 38 Pons
- 39 Flocculus
- 40 Medulla oblongata

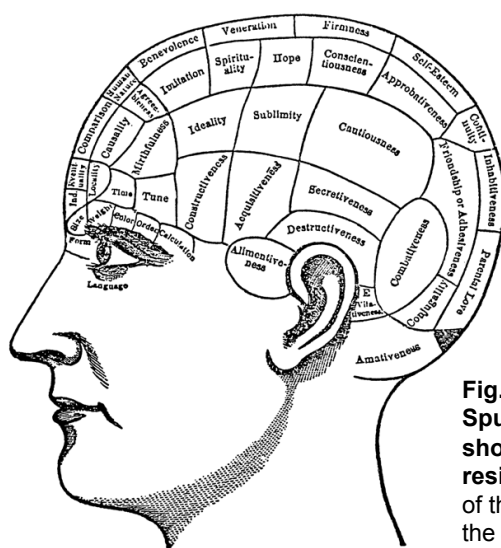
## Brain Anatomy: Structural MRI



### Brain histology: Brodman areas

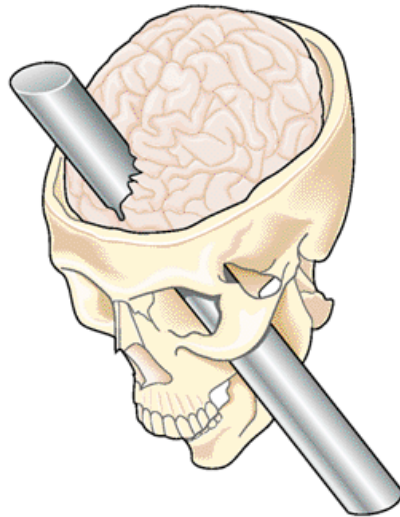


### Phrenology: Gall and Spurzheim



**Fig. 15.16. Gall and Spurzheim's "phrenological head", showing 35 mental faculties, residing in specific organs of the cerebral cortex, projected upon the surface of the skull**

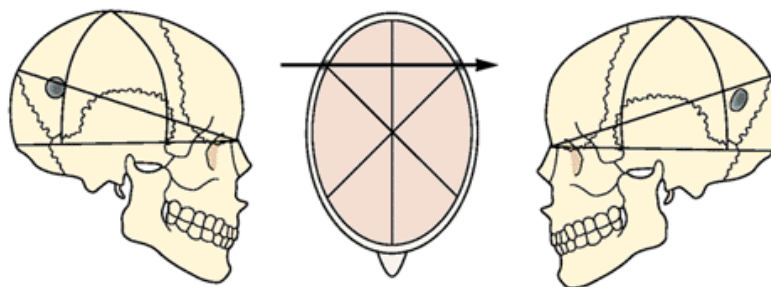
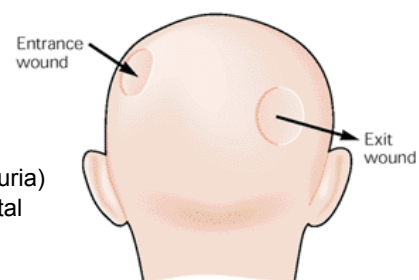
### Brain functions Inferred from Injuries



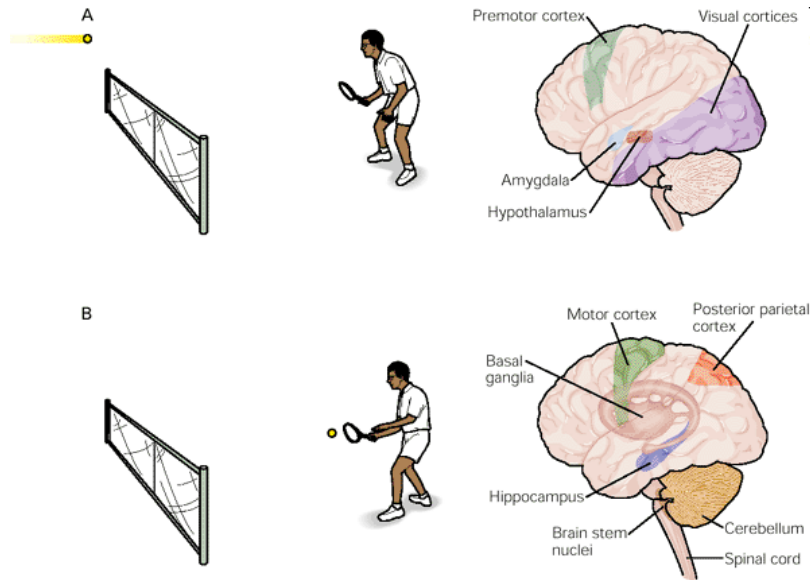
Phineas Gage  
severe personality changes  
after frontal lobe damage

### Brain Functions Inferred from Injuries

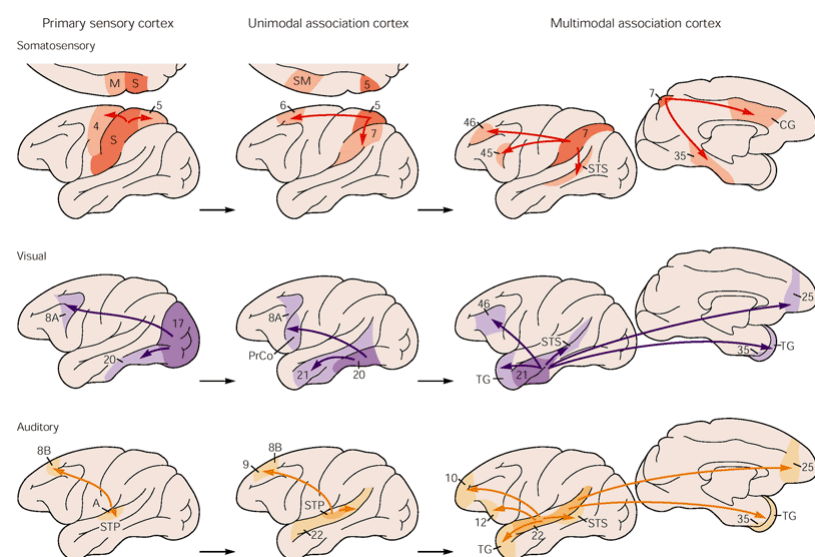
Studies in wounded soldiers  
in world war I (Holmes) and II (Luria)  
revealed the critical role of parietal  
cortex in spatial integration



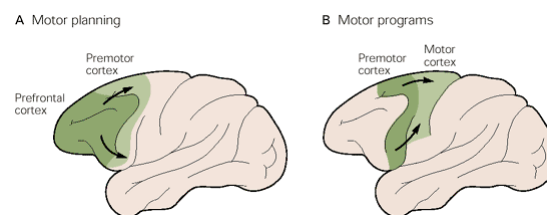
## Sensory and motor functions



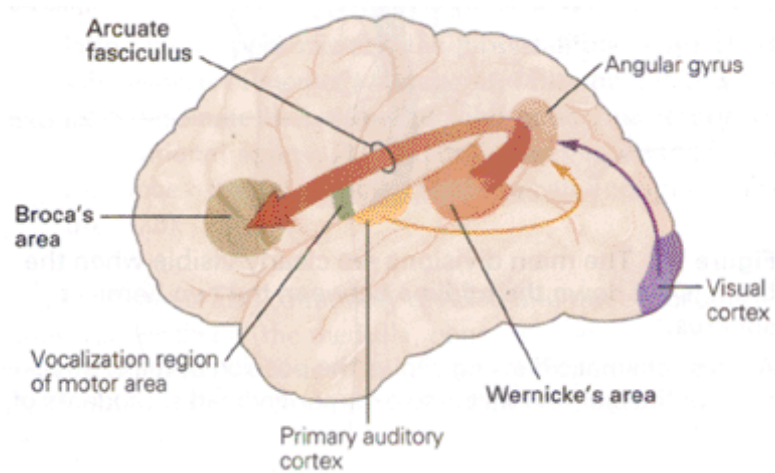
## Sensory systems



## Motor system

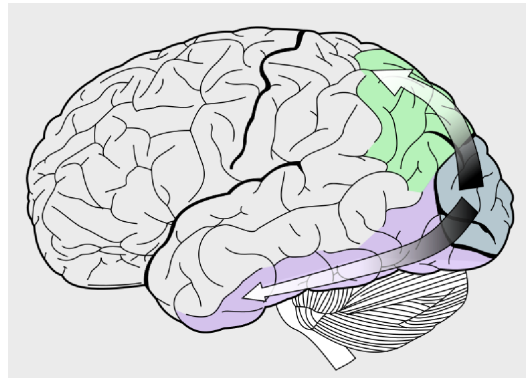


## Language



### Visual processing

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where

what

### Physical Basics of Neuroimaging

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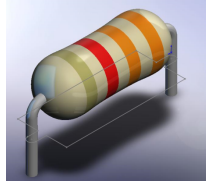
#### Electricity and Magnetism

- Ohm's Law
- Biot-Savarts Law
- Faraday's Law
- Superconductivity
- Josephson Conjunction, SQUID



## Ohm's Law

## EEG

Georg Simon Ohm  
(1789 - 1854)

Ohm's Law

$$\mathbf{E} = \int_V \left( \frac{\rho}{\epsilon_0} \frac{\vec{r} - \vec{r}'}{|\vec{r} - \vec{r}'|^3} \right) dV' + \frac{1}{\sigma} \mathbf{J}$$

$$\nabla \mathbf{E} = \frac{\rho}{\epsilon_0} + \frac{1}{\sigma} \mathbf{Q} = 0$$

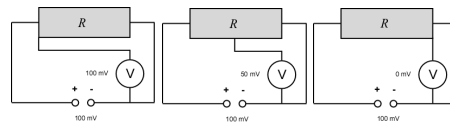
$$\mathbf{E} = \nabla U$$

$$\Delta U = 0$$

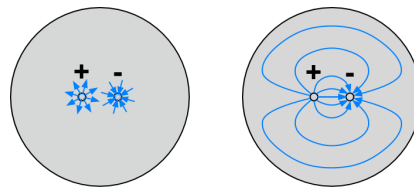
Ohm's law

$$U = RI$$

Voltage drop across a resistor

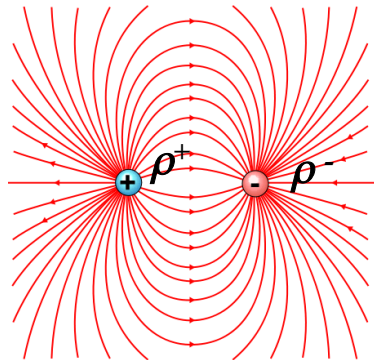


Current in a spherical conductor



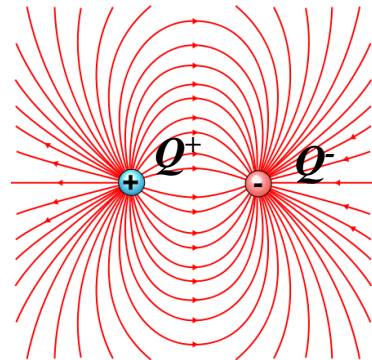
## Dipole field

## Electrostatics



$$\Delta U = \nabla \mathbf{E} = \frac{\rho}{\epsilon_0}$$

## Electrodynamics



$$\Delta U = \nabla \mathbf{E} = \frac{1}{\sigma} \mathbf{Q}$$



## Physical background of EEG and MEG

## MEG

Jean-Baptiste Biot  
(1774 - 1862)

Biot-Savart's Law

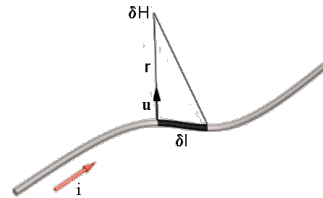
right hand rule

Félix Savart  
(1791 - 1841)

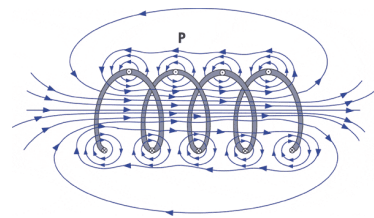
$$d\mathbf{B}(r) = \frac{\mu_0}{4\pi} I d\mathbf{l} \times \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^3}$$

$$\mathbf{B}(r) = \frac{\mu_0}{4\pi} \int_V \mathbf{J}(\mathbf{r}') \times \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^3} dV'$$

Biot-Savart's law: magnetic fields generated by electrical current



Magnetic field generated by a current flow coil



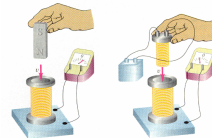
## Magnetic induction: Faraday's law

Michael Faraday  
(1791 - 1867)

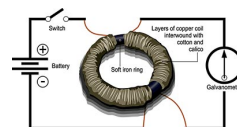
$$U = \frac{d\Phi}{dt}$$

Changing magnetic  
field induces voltage

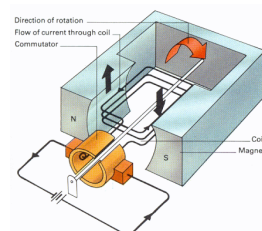
- 1) Moving magnet: increase and decrease of magnetic field



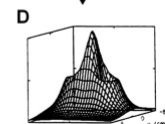
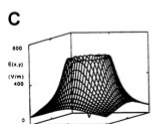
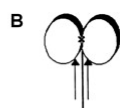
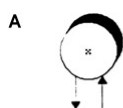
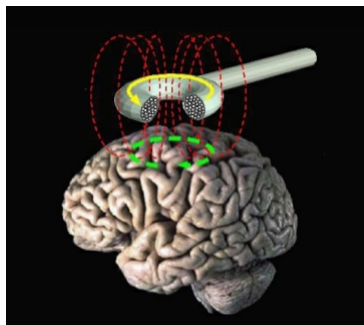
- 2) Switch magnetic field (electromagnet) on and off



- 3) Rotating coil: the coil area "sees" changing magnetic field



## Transcranial magnetic stimulation

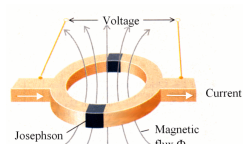
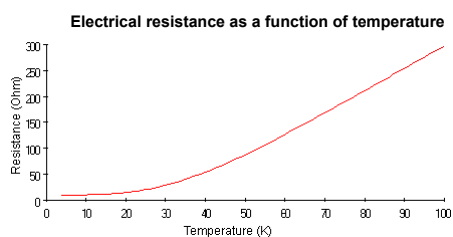
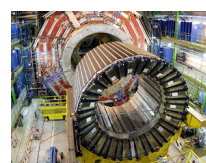
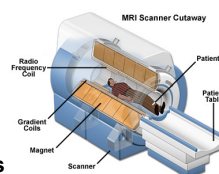


## Superconductivity

Cooling down electrical conductors close to 0 K

- any resistance vanishes
- strong magnets
- magnetic field sensors
- magnetic shielding

**strong magnets**



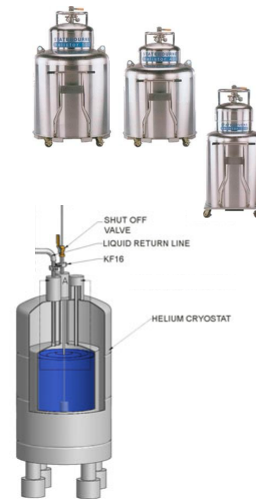
**magnetic field sensors**  
**SQUIDS**

**shielding**



## Superconductivity

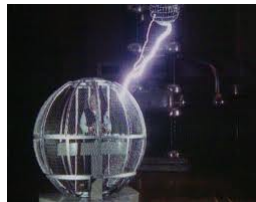
Strong magnetic fields can be generated by cooling them until they become superconducting



## Superconductivity

### Shielding of electrical fields:

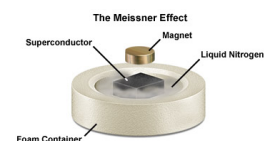
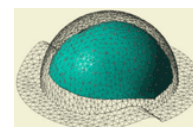
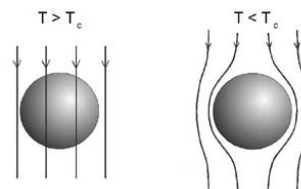
- Faraday cage



### Shielding of magnetic fields:

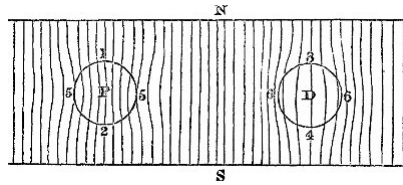
- Meissner effect
- Mu-Metal
- Eddy currents (Lenz rule)

Meissner Effect



## Alternative shielding of magnetic fields

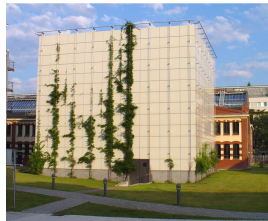
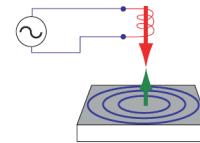
Mu Metal: Alloy of iron and nickel



paramagnetic >>  
ferromagnetic  
Mu-Metal  
deoxyhemoglobin

diamagnetic  
copper  
oxyhemoglobin

Eddy currents



## Brain imaging methods

### Type of methods

- functional imaging methods
- biochemical activity
  - neurometabolic activity
  - neuroelectrical activity

## Functional imaging methods

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### Type of methods

functional imaging methods

- biochemical activity
- neurometabolic activity
- neuroelectrical activity



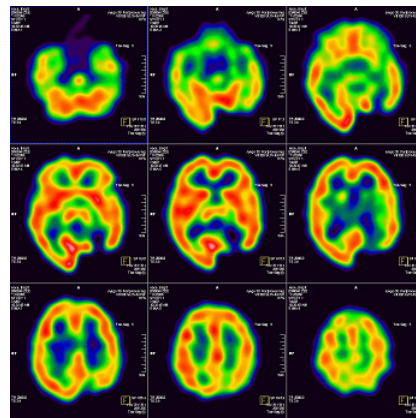
nuclear magnetic resonance tomography  
(NMR, MRT, MRI)



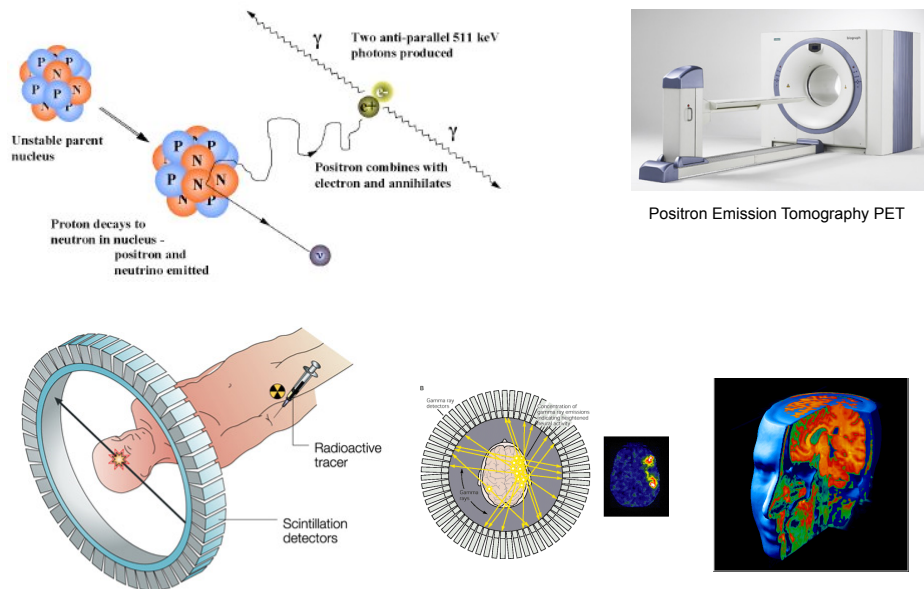
Positron Emission Tomography  
(PET)

## Single photon emission tomography SPECT

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## Positron emission tomography PET



## Positron emission tomography PET

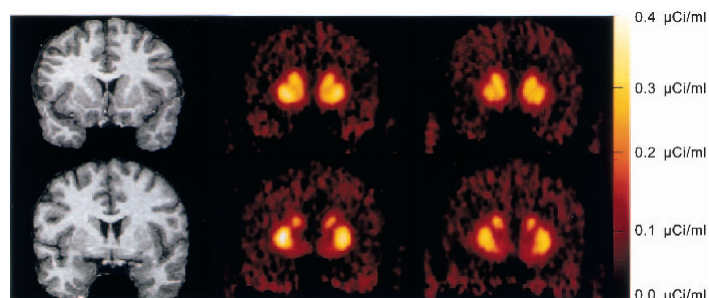
*Journal of Cerebral Blood Flow & Metabolism*  
29:285-300 © 2009 The International Society for Cerebral Blood Flow and Metabolism  
Published by Lippincott Williams & Wilkins, Inc., Philadelphia

### Imaging Human Mesolimbic Dopamine Transmission With Positron Emission Tomography. Part II: Amphetamine-Induced Dopamine Release in the Functional Subdivisions of the Striatum

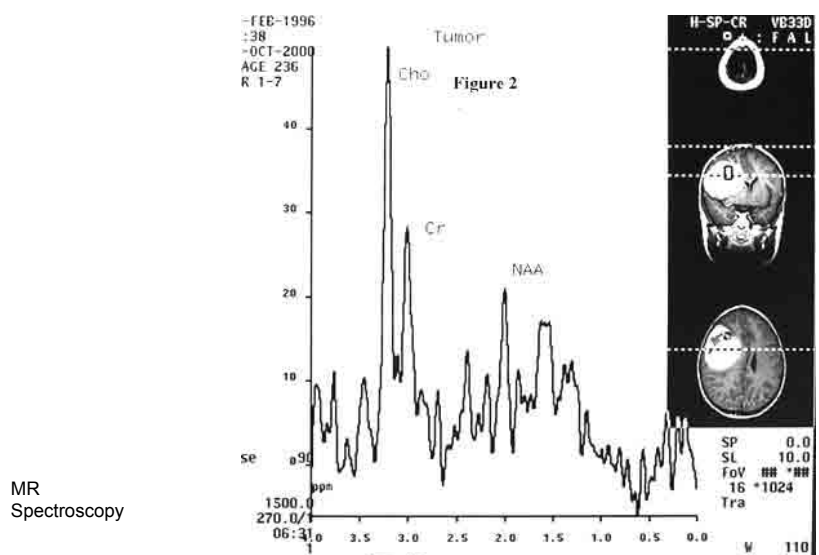
\*Diana Martinez, \*Mark Slifstein, \*Allegra Broft, \*†Osama Mawlawi, \*Dah-Ren Hwang, \*†Yiyun Huang, \*Thomas Cooper, \*Lawrence Kegeles, \*Eric Zarahn, \*†Anissa Abi-Dargham, ‡§Suzanne N. Haber, and \*†Marc Laruelle

Departments of \*Psychiatry and †Radiology, Columbia University College of Physicians and Surgeons, New York, New York, and Departments of ‡Neurobiology and §Anatomy, University of Rochester School of Medicine, Rochester, New York, U.S.A.

PET



## Magnetic resonance spectroscopy

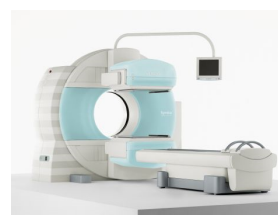


## Functional imaging methods

### Type of methods

functional imaging methods

- biochemical activity
- neurometabolic activity
- neuroelectrical activity



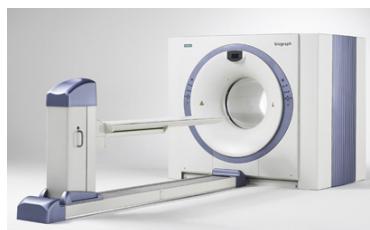
Single Photon Emission Tomography (SPECT)



near infrared spectroscopy (NIRS)



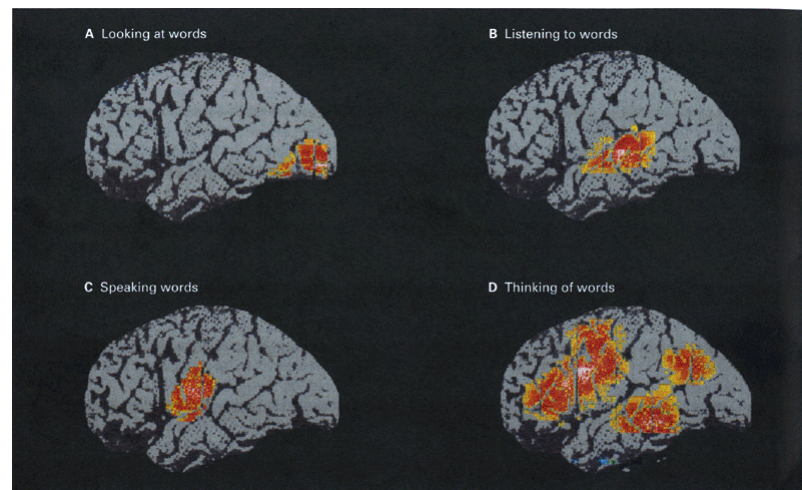
nuclear magnetic resonance tomography (NMR, MRI)



Positron Emission Tomography (PET)



## Positron emission tomography PET



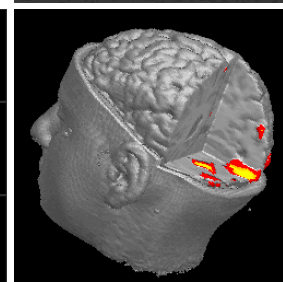
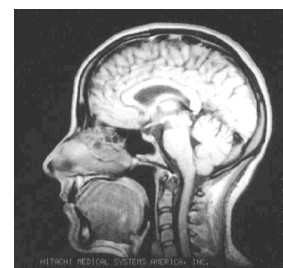
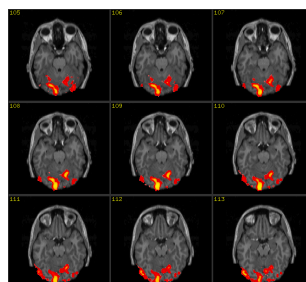
*Cathy Price*

## Magnetic resonance imaging MRI

also  
nuclear magnetic resonance NMR



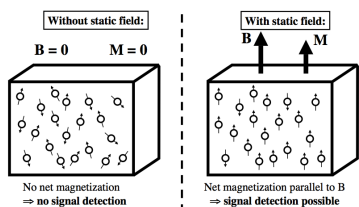
nuclear magnetic resonance  
tomography  
(NMR, MRT, MRI)



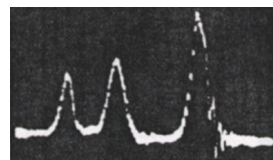


## Magnetic resonance imaging MRI

How to get a macroscopic magnetization  
(using a static magnetic field  $B$ )

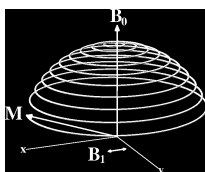
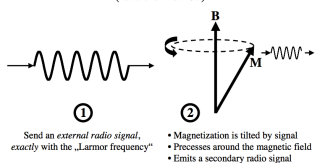


One of the first spectra of Ethanol  
(CH<sub>3</sub>---CH<sub>2</sub>---OH)

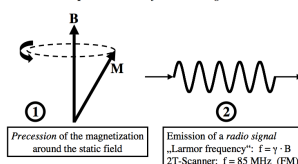


Resonance frequency of H<sub>1</sub> ± a few ppm

Tilt of the magnetization  
(feasible method)



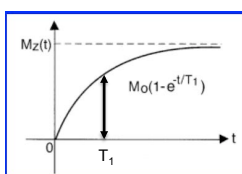
How to get a signal from the magnetization M  
Step 2: Behaviour of the tilted magnetization



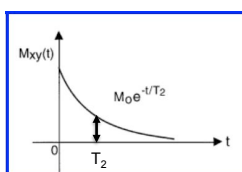
The emitted signal can be measured with a detector similar to an FM radio

## Magnetic resonance imaging MRI

T<sub>1</sub>:  $M_z/M_0 = (1 - 1/e) = 63\%$



T<sub>2</sub>:  $M_{xy}/M_0 = 1/e = 37\%$



## Relaxation types

T<sub>1</sub>: longitudinal relaxation  
spin-lattice interaction  
exchange of energy with the  
near environment (molecules)

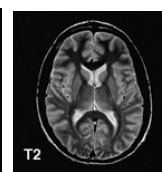
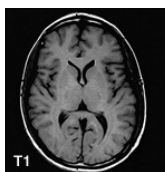
T<sub>2</sub>: transversal relaxation  
spin-spin interaction

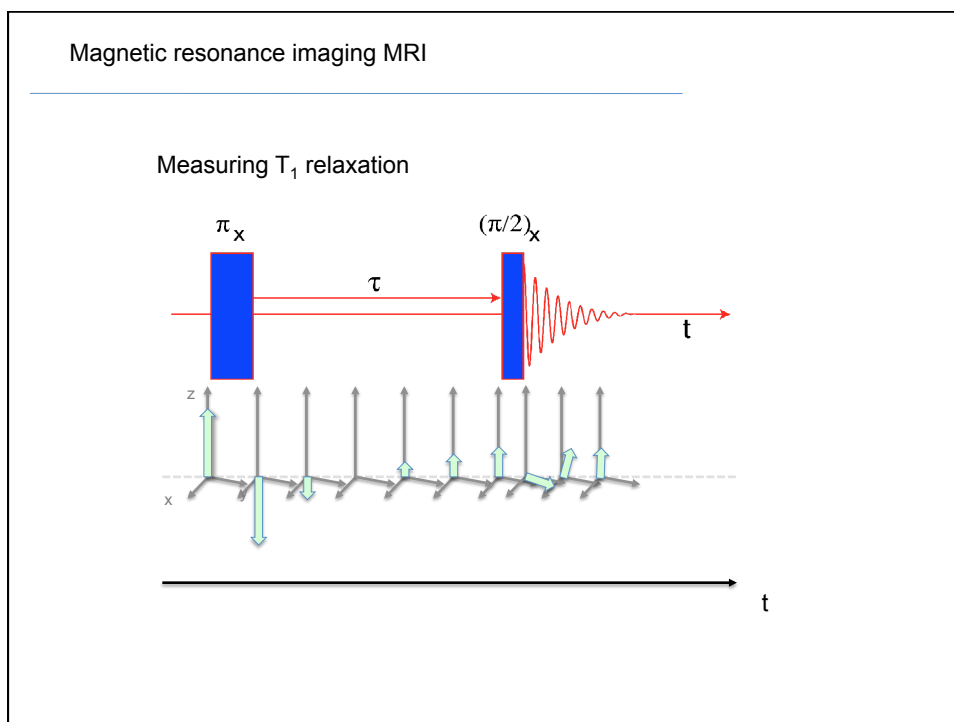
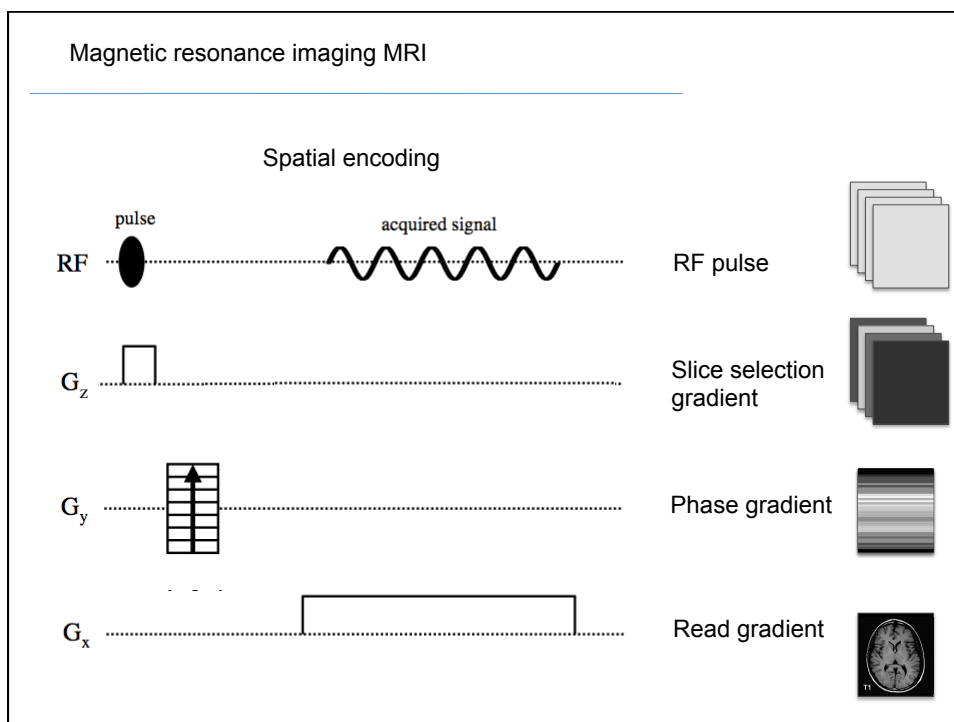
always:

$$T_2 < 2T_1$$

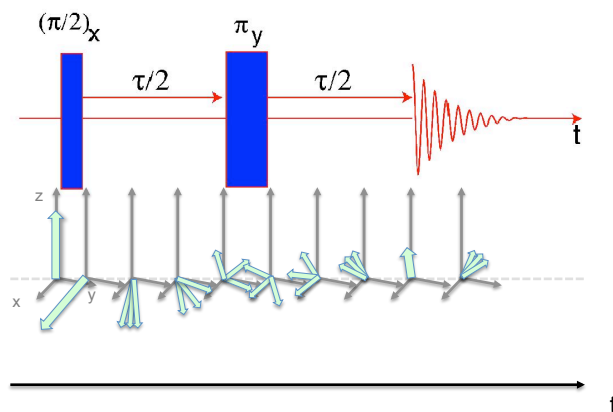
mostly:

$$T_2 < T_1$$



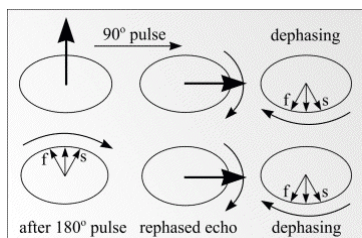
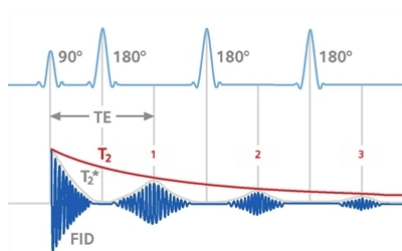


## Magnetic resonance imaging MRI

Measuring  $T_1$  relaxation

## Magnetic resonance imaging MRI

## Relaxation types



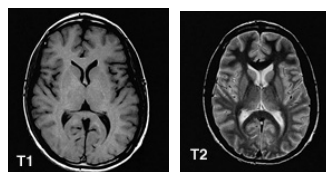
$T_1$ : longitudinal relaxation  
spin-lattice interaction  
exchange of energy with the  
near environment (molecules)

$T_2$ : transversal relaxation  
spin-spin interaction

$T_2^*$ : inhomogeneities of local magnetic field  
Fe-atoms in hemoglobin

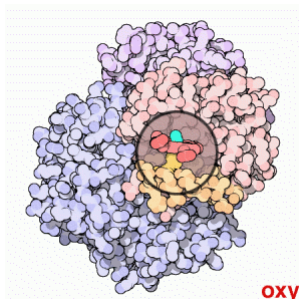
mostly:

$$T_2^* < T_2 < T_1$$

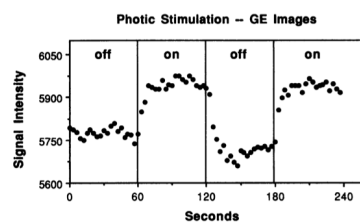
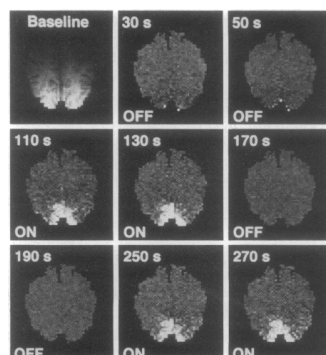


## Functional Magnetic resonance imaging fMRI

Blood oxygen level dependent response: BOLD



Oxy-hemoglobin: diamagnetic  
(i.e. not magnetic, no effect on  $T2^*$ )  
Deoxy-hemoglobin: paramagnetic  
(i.e. magnetic, affects  $T2^*$ )

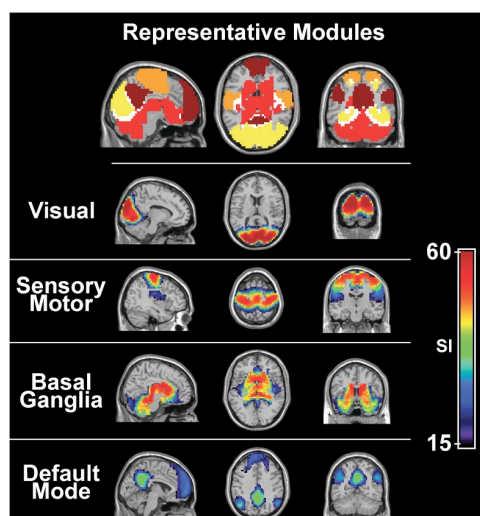


## Functional Magnetic resonance imaging fMRI

Correlation between the activity of voxels:

→ functional connectivity

→ resting state networks

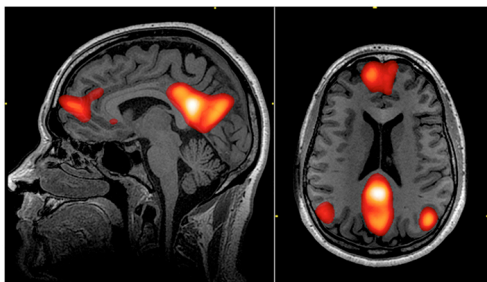


## Functional Magnetic resonance imaging fMRI

Correlation between the activity of voxels:

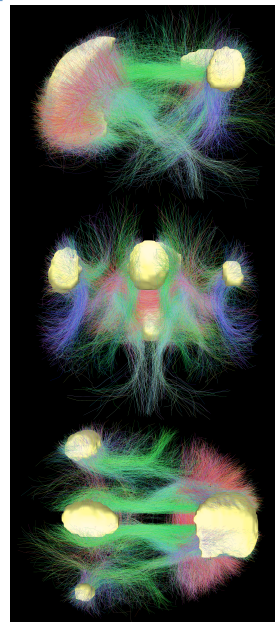
→ functional connectivity

→ Default mode network



Default mode network

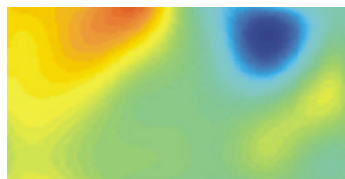
- Posterior cingulate cortex (PCC) & precuneus: Combines bottom-up attention
- Medial prefrontal cortex (mPFC): decision making
- Angular gyrus: Connects perception, attention, spatial cognition, action, and recall of episodic memories



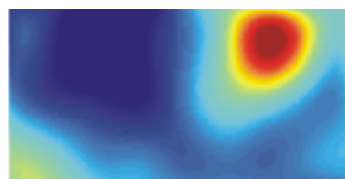
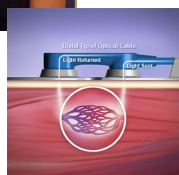
## Near infrared spectroscopy NIRS



Stimulation of the left and right hemifield by an alternating black and white checkerboard. The difference between the two conditions is mapped. The red and blue spot show the maximum difference and correspond to the primary visual areas of the subject.

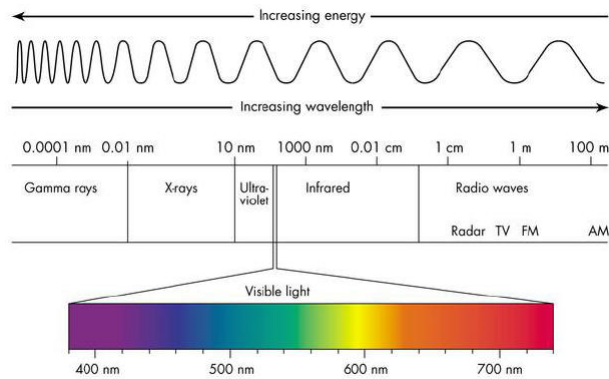


The image corresponds to the changes in the concentration of deoxygenated haemoglobin [ deoxy-Hb ]



The image shows the corresponding changes in oxygenated haemoglobin [ oxy-Hb ].

## NIRS

**Bio-optical window:**

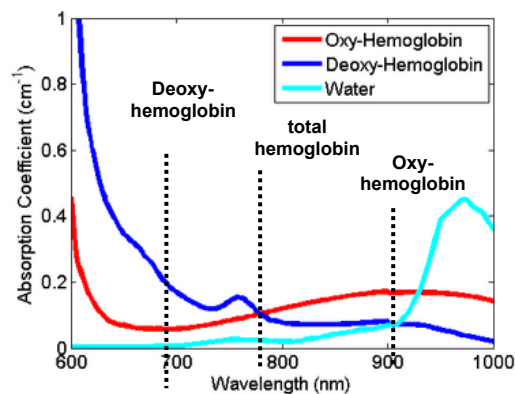
from 700 nm  
to 900 nm

Relationship between wavelength  $\lambda$  and frequency  $\nu$  :

$$c = \lambda \nu$$

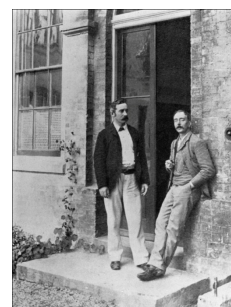
$c$ : speed of light

## NIRS: Absorption



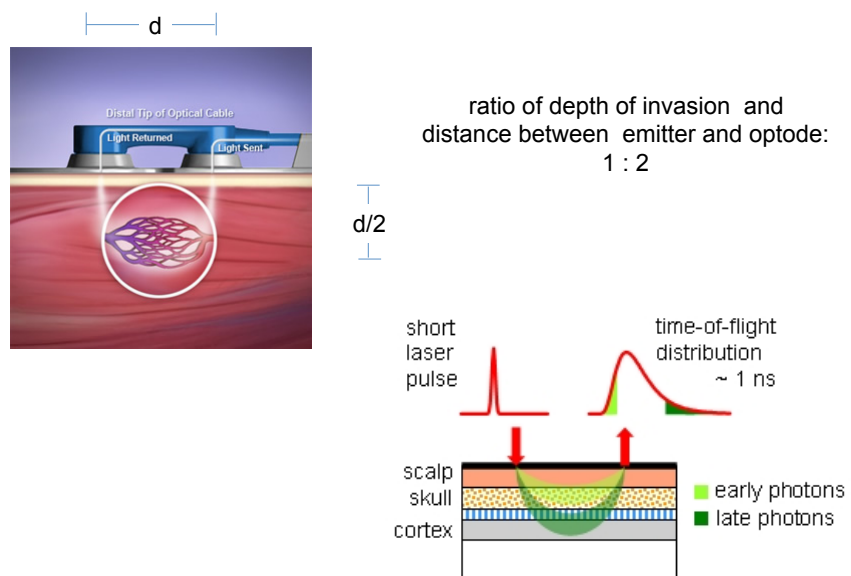
- near infrared light can invade tissue several centimeters
- skin and bone are basically transparent for near infrared light

absorption depends on concentration:  
regional cerebral blood volume (rcbv)  
regional cerebral blood flow (rcbf)  
oxygenation

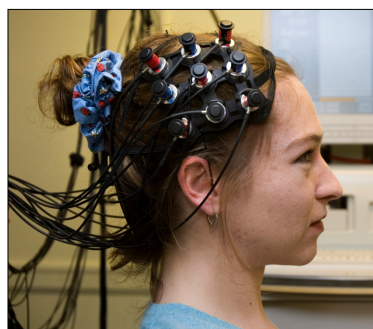


⇒ **neurovascular coupling**  
(Roy and Sherrington 1890)

## NIRS



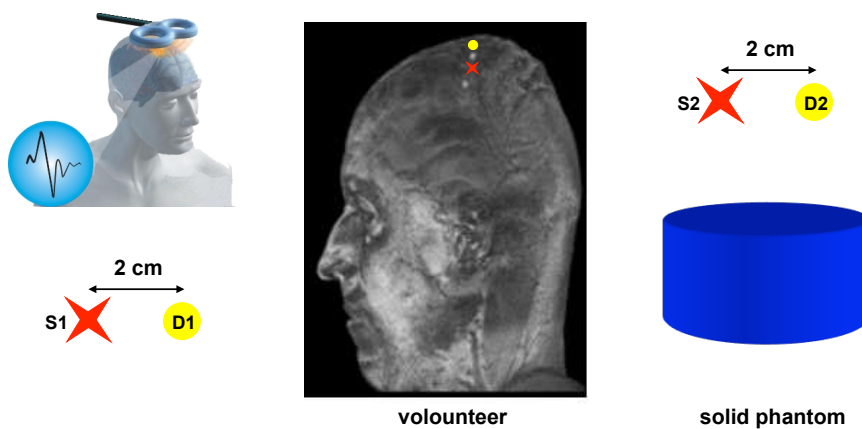
## NIRS





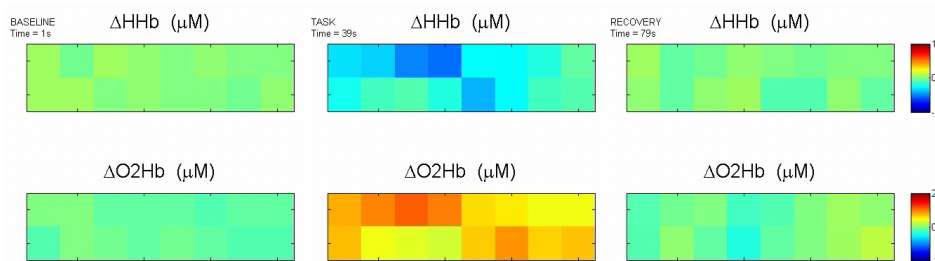
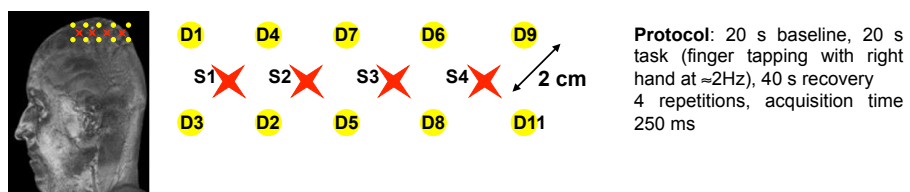
## NIRS

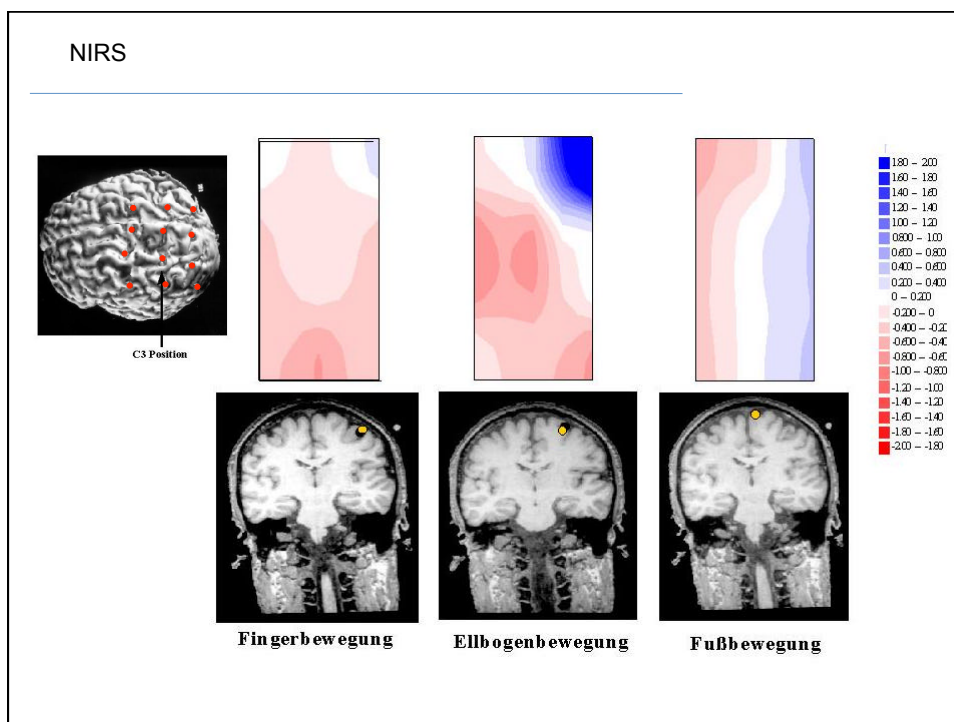
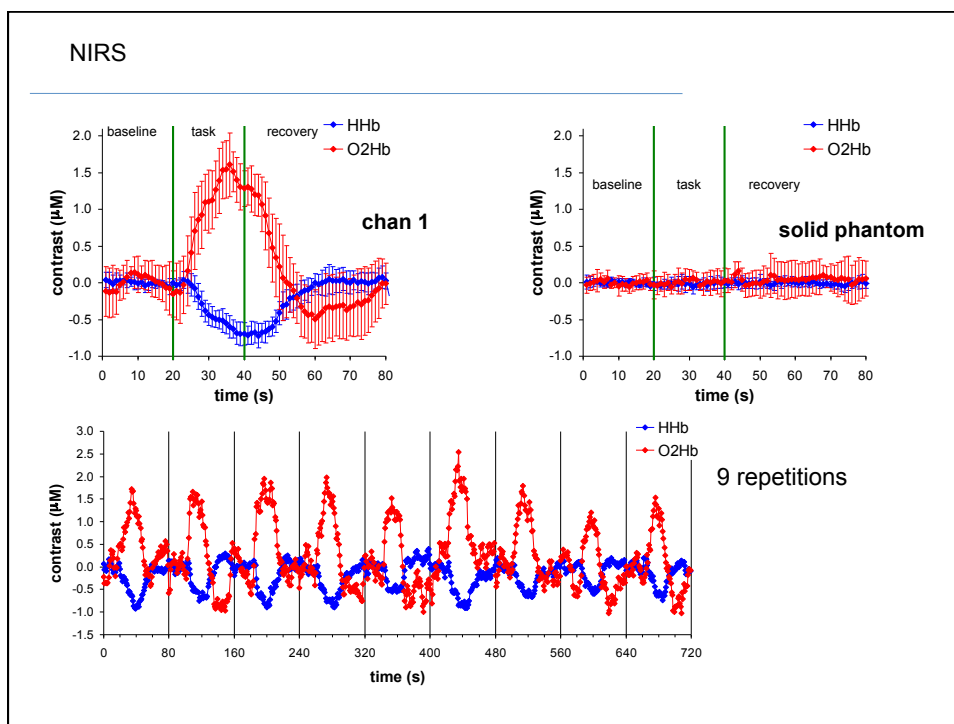
Motor area for right hand identified by Transcranial Magnetic Stimulation (TMS)



**Protocol:** 20 s baseline, 20 s task (finger tapping with right hand at  $\approx 2\text{Hz}$ ), 40 s recovery  
9 repetitions, acquisition time 1 s

## NIRS





## Functional Imaging Methods

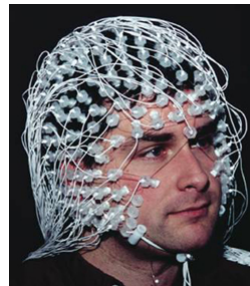
### Type of methods

functional imaging methods

- biochemical activity
- neurometabolic activity
- neuroelectrical activity



Transcranial Magnetic Stimulation  
TMS



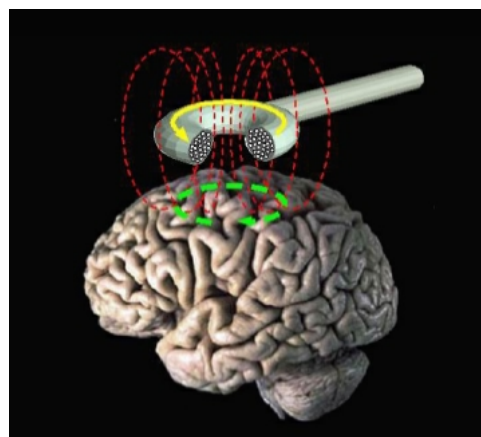
Electroencephalography  
EEG



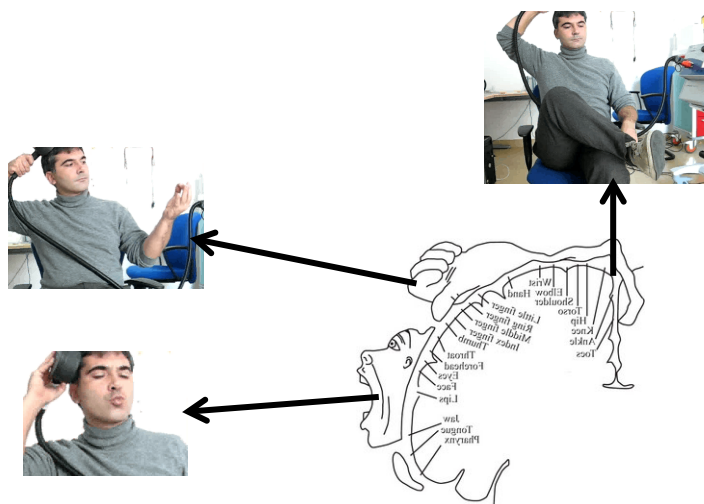
Magnetoencephalography  
MEG

## Physical Principle of TMS

Conductor 1 is the magnetic coil;  
Conductor 2 is the extracellular fluid  
of the cerebral cortex.



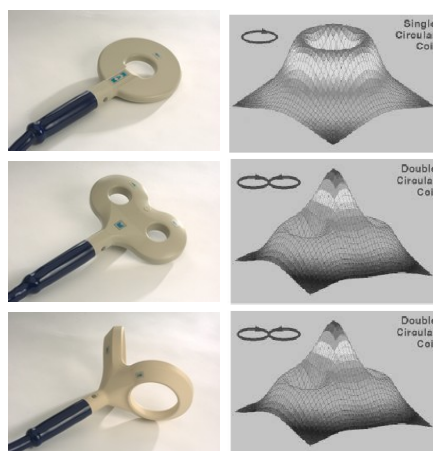
## TMS: Stimulating the Motor Cortex



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## TMS: Types of Coils

The shape of the coil “shapes” the magnetic field and hence the electrical field and ultimately it determines the way you stimulate the brain tissue



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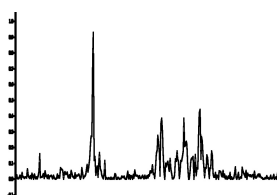
## Interpretation of MEP Recordings

### Tongue recordings

Raw MEP

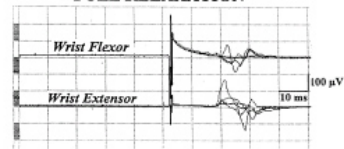


Rectified MEP

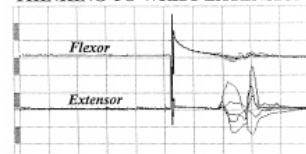


### Motor imagery

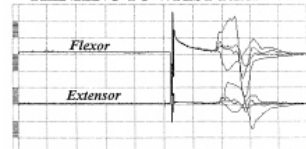
#### FULL RELAXATION



#### THINKING TO WRIST EXTENSION

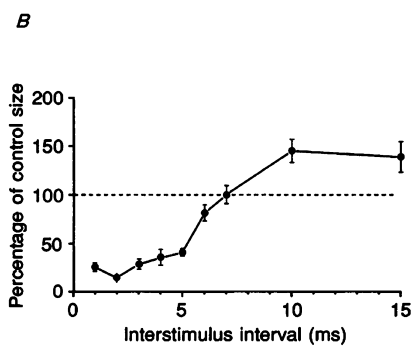
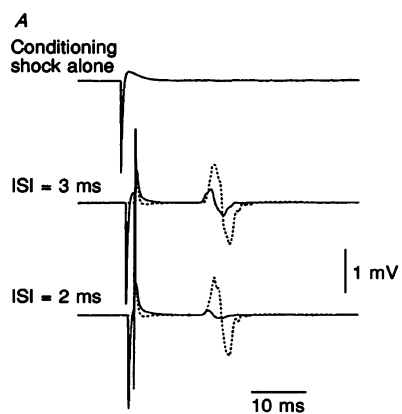


#### THINKING TO WRIST FLEXION



## Paradigms: 1 - Conditioned TMS

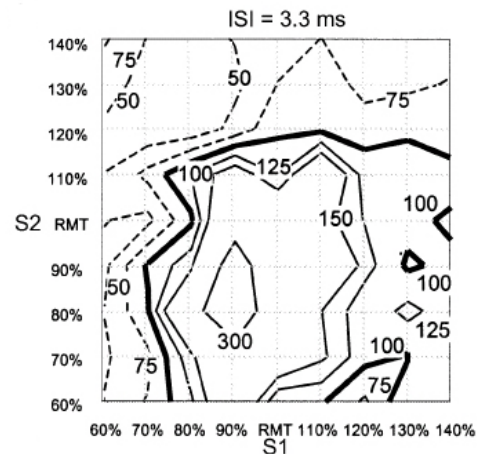
Classical paired pulse paradigm (Kujirai):



### Paradigms: 1 - Conditioned TMS

It is not as simple as it looks: the interaction between conditioning and test stimulus is defined in a 3-dimensional space taking into account

- 1) the intensity of conditioning stimulus;
- 2) the intensity of the test stimulus and
- 3) the ISI



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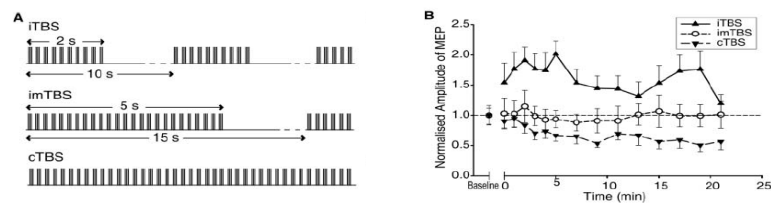
### Paradigms: 2 - Shaping the Excitability of Cerebral Cortex

#### rTMS

A train of transcranial magnetic stimuli produces effects that outlast the train of stimuli.

We distinguish:

1. Low frequency rTMS: 0.2 Hz and 1 Hz produce inhibitory effects over the motor cortex
2. High frequency rTMS: > 5 Hz. Facilitatory effects
3. Patterned TMS: Theta-burst stimulation (TBS)
  - iTBS: intermittent TBS, cTBS: continuous TBS, imTBS: intermediate TBS

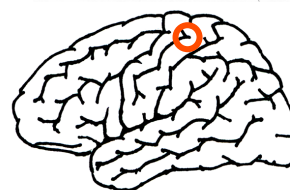
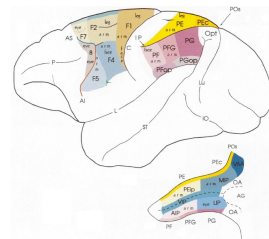


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## Paradigms: 3 – Online Virtual Lesion

**Virtual lesions of the anterior intraparietal area disrupt goal-dependent on-line adjustments of grasp**Eugene Tunik<sup>1</sup>, Scott H Frey<sup>2</sup> & Scott T Grafton<sup>1</sup>

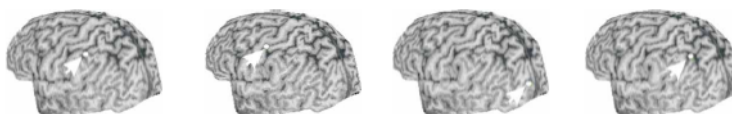
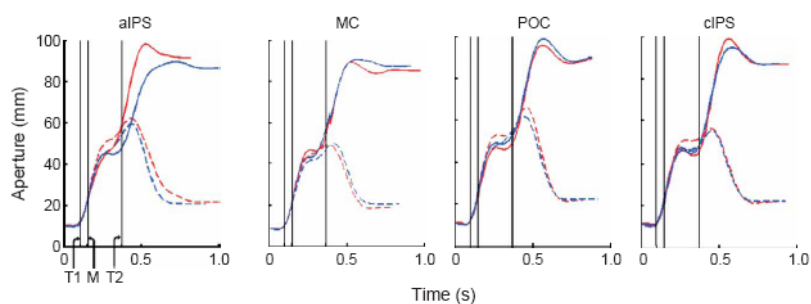
- Hypothesis: the anteriormost part of the IPS in humans in the homologue of monkey AIP and mediates visually guided grasping
- Conditioning stimulus: TMS applied over the rostral IPS at various intervals from the test stimulus.
- Test stimulus: target object perturbations during reaching, requiring online adjustments.
- Measurement: finger kinematics of grasping. Control conditions: TMS over posterior areas or over M1.



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## Paradigms: 3 – Online Virtual Lesion

- Results: only TMS over the rostral IPS in the time window around 65 ms from object perturbation reduces the capacity of online adjustment of grasping

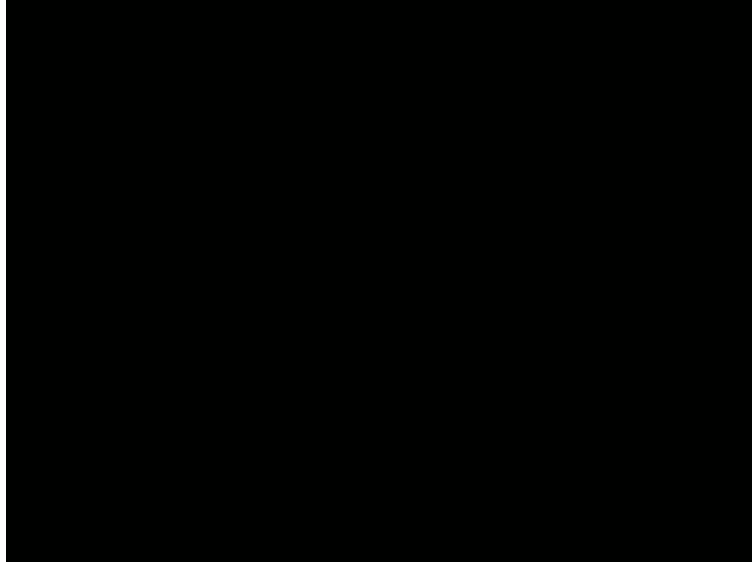


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### Deep Brain Stimulation in Parkinson

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### Techniques – Transcranial Direct Current Stimulation: tDCS

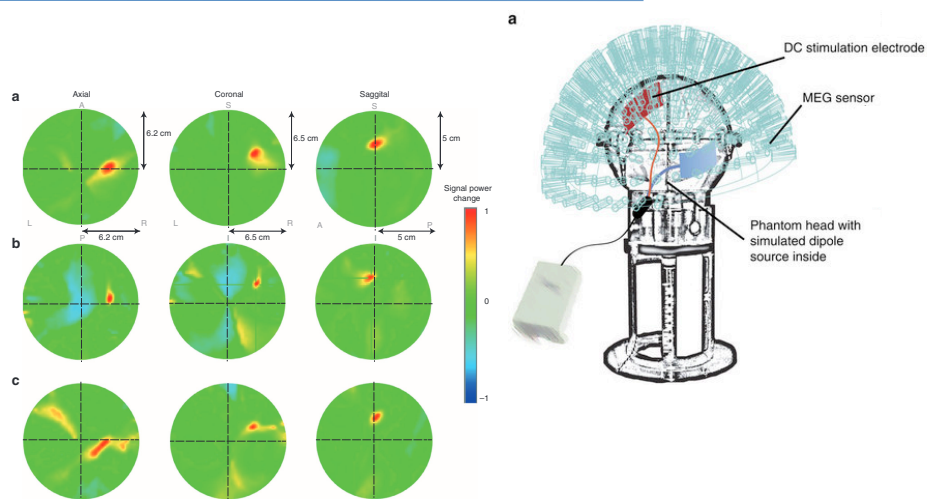
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tDCS is delivered with a pair of soaked sponges applied to the scalp



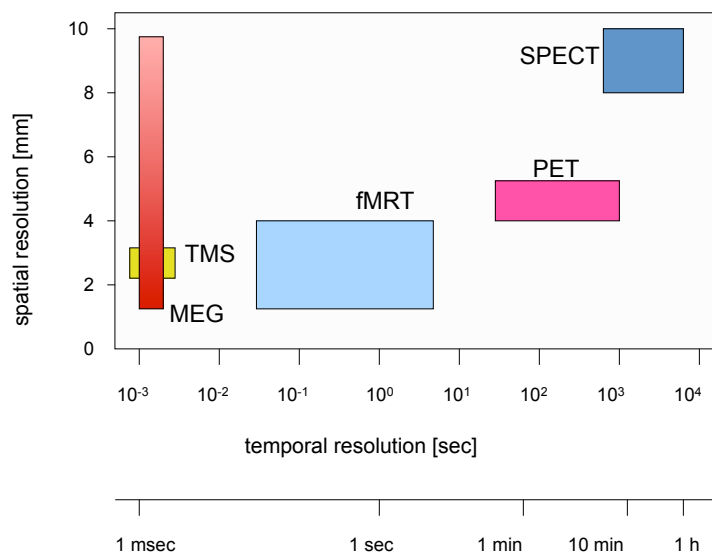
76

## Techniques – Transcranial Direct Current Stimulation: tDCS



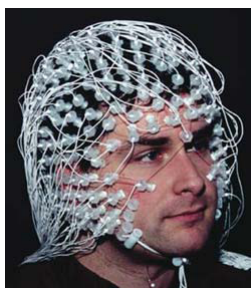
77

## Neuroimaging Methods



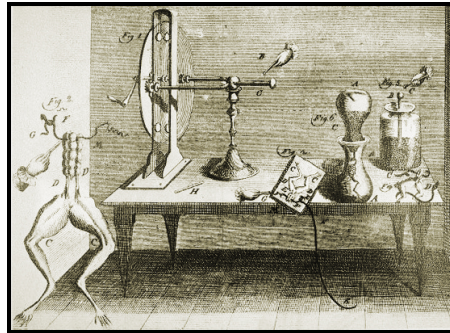
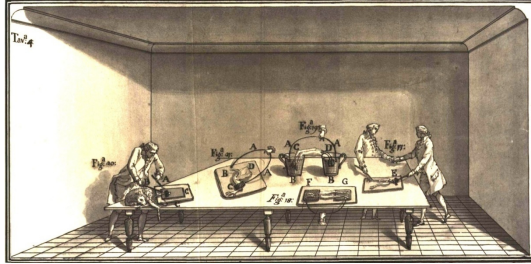
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## EEG



Electroencephalography  
EEG

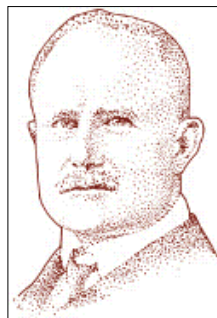
### Luigi Galvani: Animal electricity



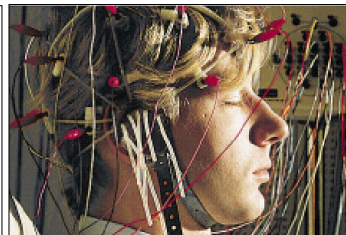
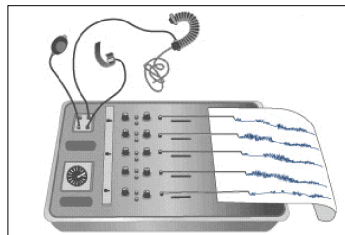
Luigi Galvani  
1737 - 1798

late 18<sup>th</sup> century

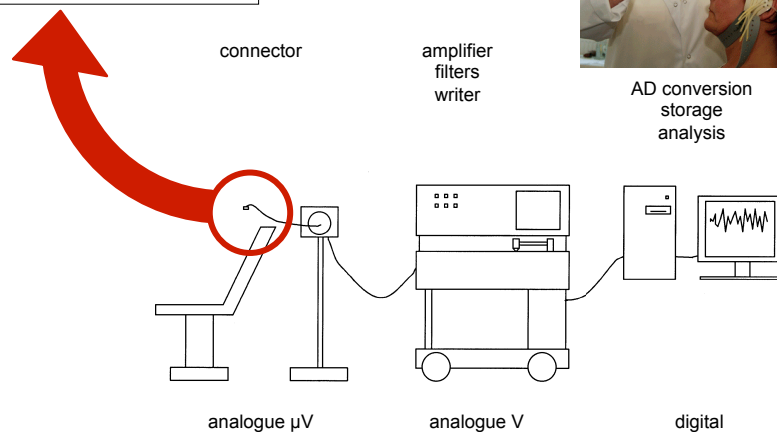
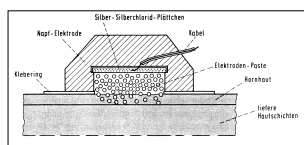
### Electroencephalography (EEG)



Hans Berger  
1873-1941



## Electroencephalography



## History



32 channel amplifier



Miniaturisation

high density  
high efficiency

256 channels



wireless electrodes

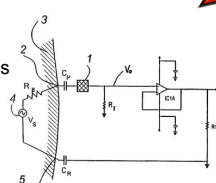


flexibility

easy to use

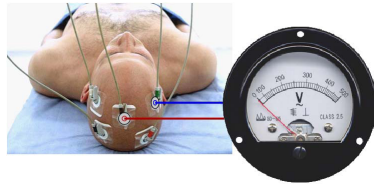
lower sensitivity to noise

dry electrodes



active electrodes

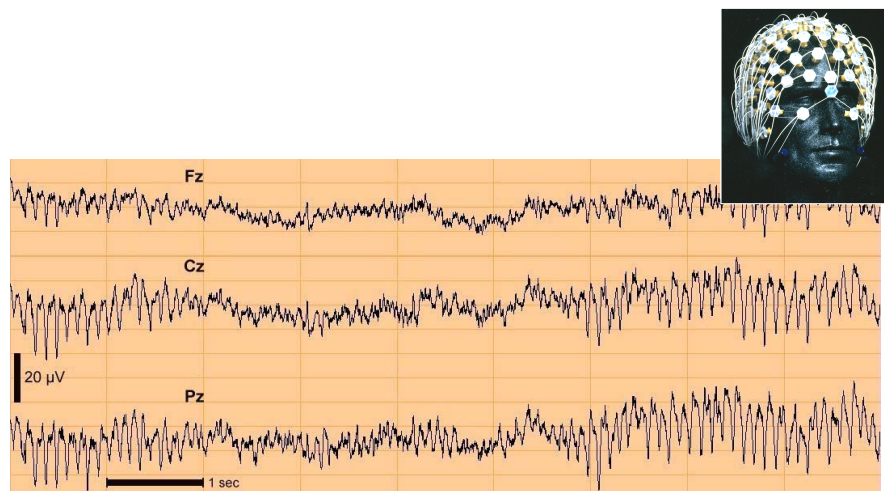
## EEG Measurement



How to do an EEG recording

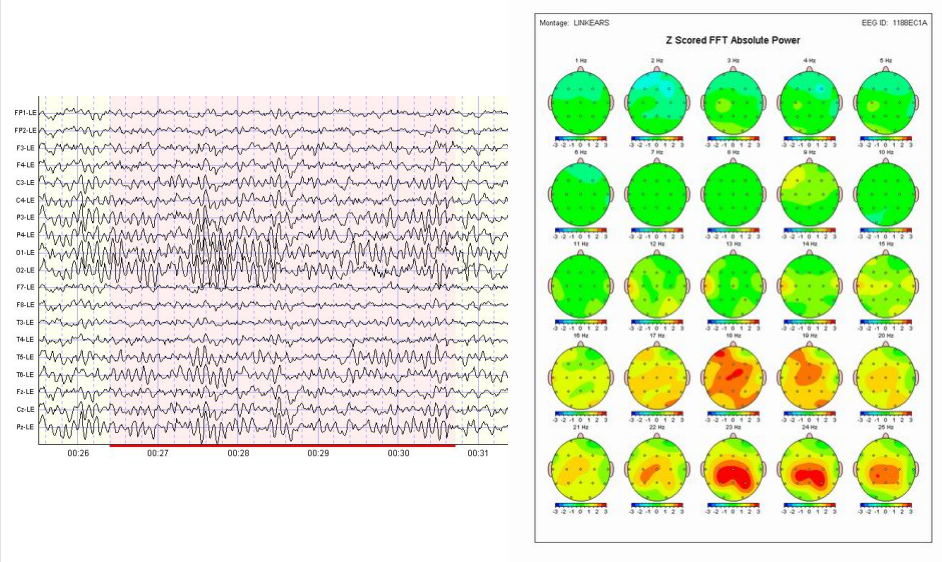
- What is the ground electrode?
- What is the reference electrode?
- What is rereferencing?
- What are clinical applications of EEG?
- What is the 10-20 systems
- Which brain rhythms do you know?

## EEG Recording

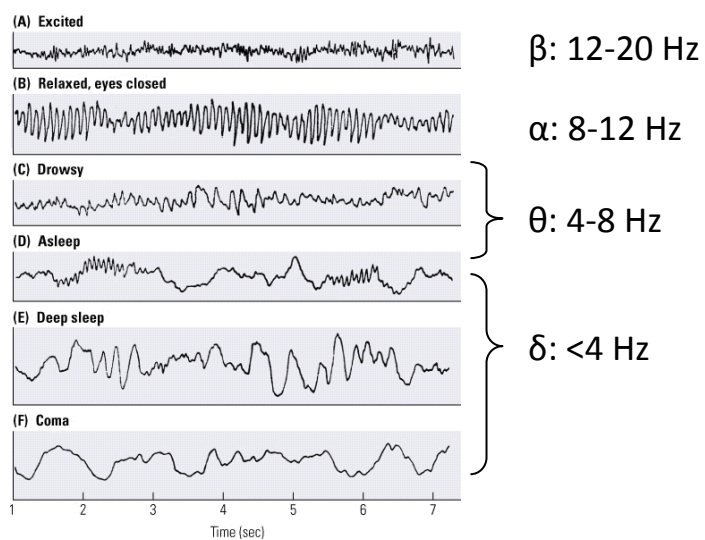


EEG-traces recorded from 3 electrodes

## Electroencephalograph EEG

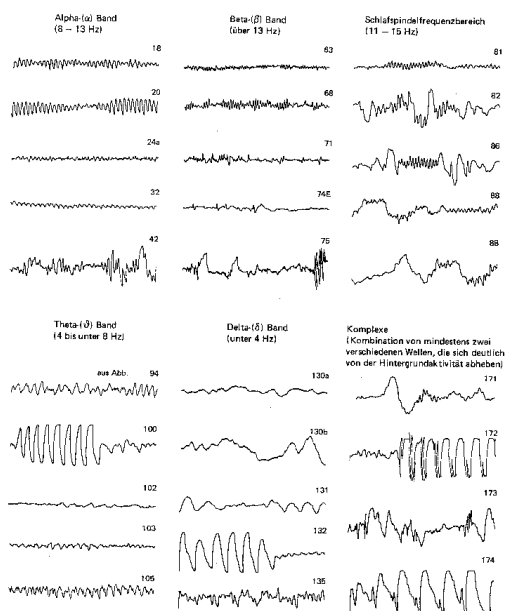


## Spontaneous EEG

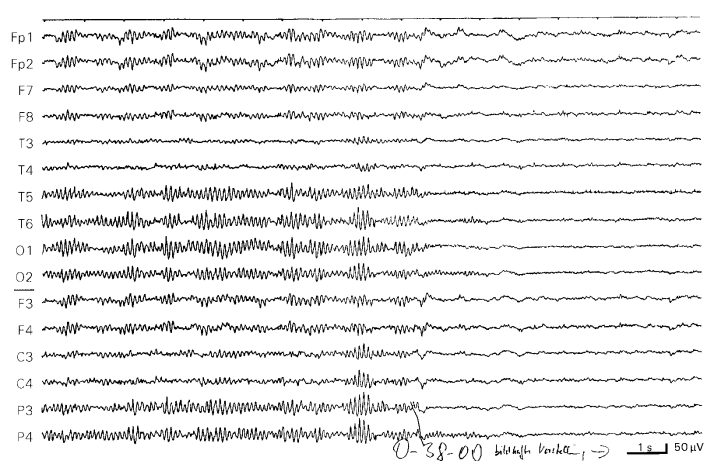




## Individual Variability



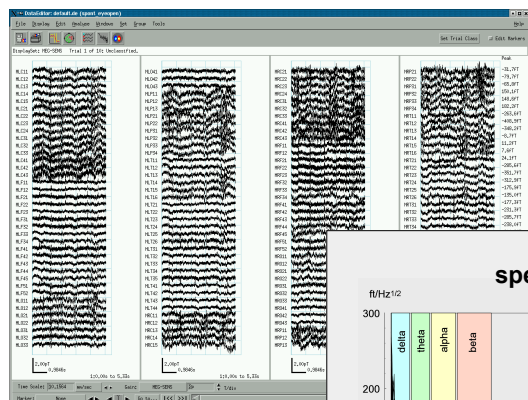
## Spontaneous EEG: Alpha Block



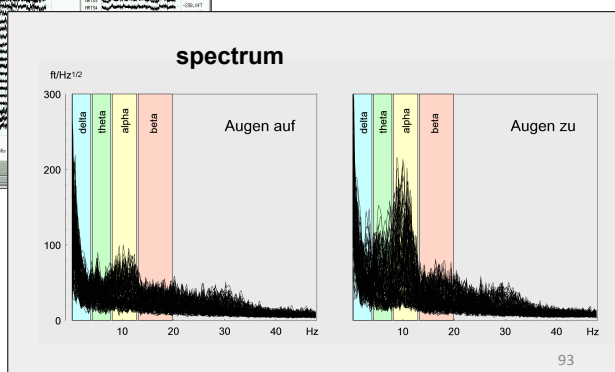
eyes closed

eyes open

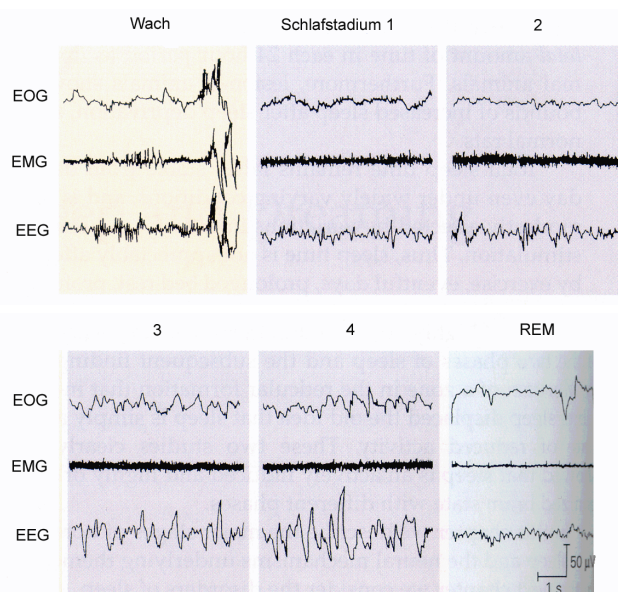
## Spontaneous MEG



spontaneous-activity

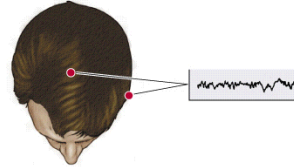


## Spontaneous EEG: Sleep Stages

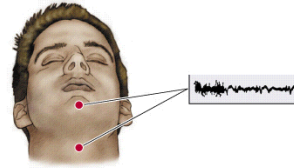


## Spontaneous EEG: Sleep Stages

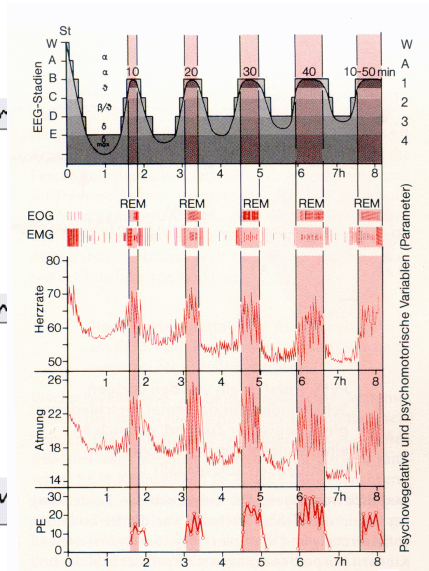
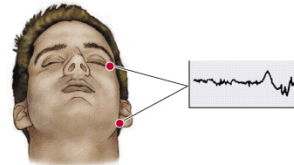
(A) Electroencephalogram (EEG)



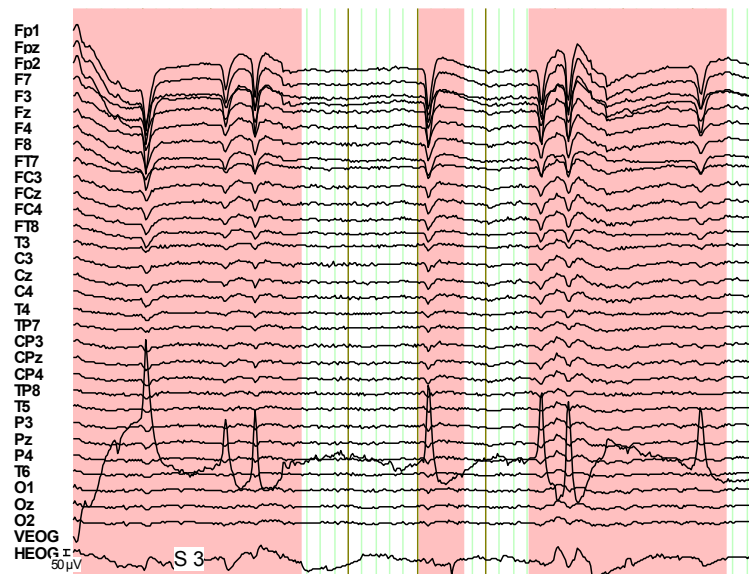
(B) Electromyogram (EMG)



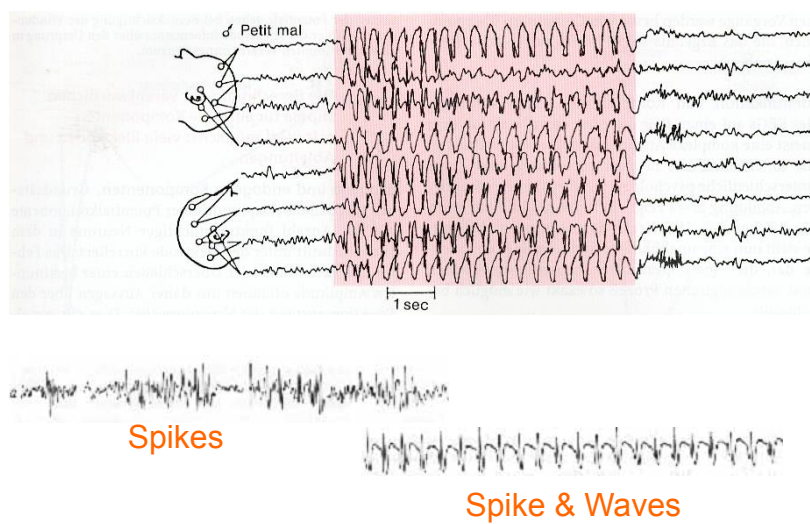
(C) Electrooculogram (EOG)



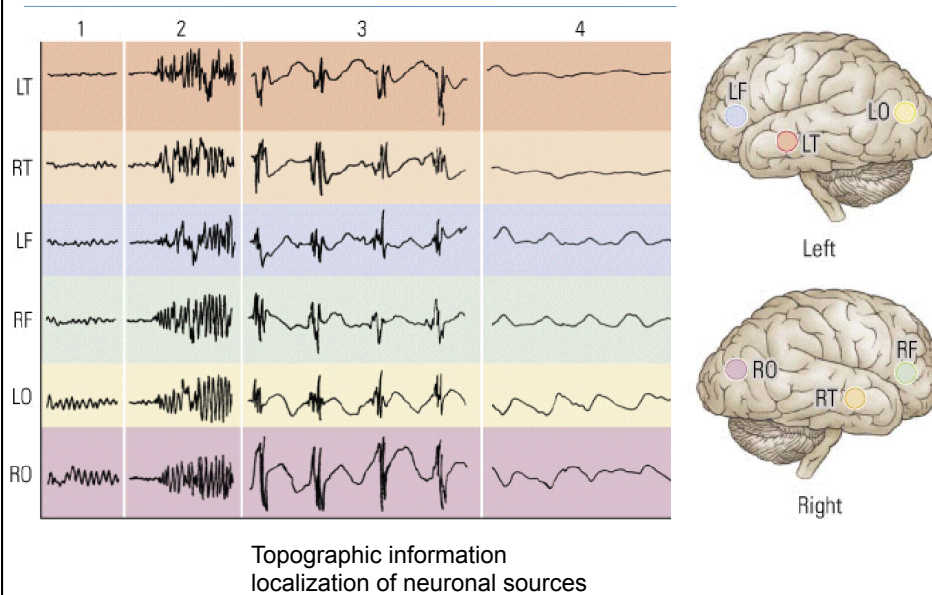
## Artifacts: Eye Blinks and Eye Movements



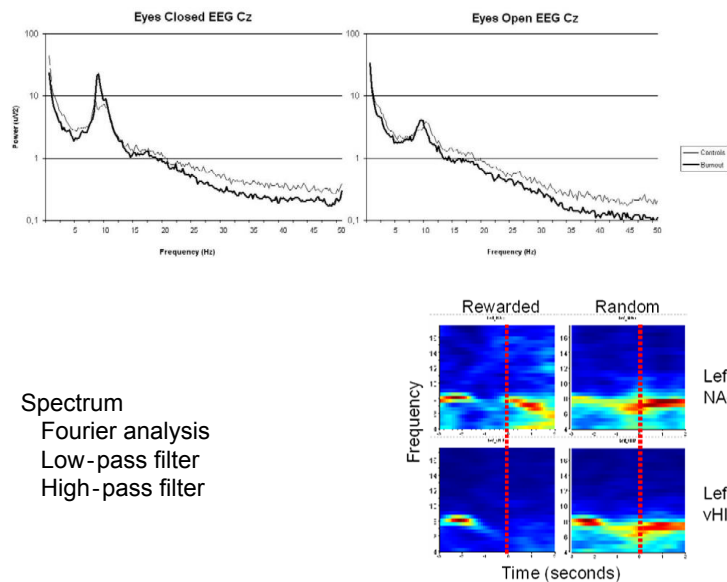
### Clinical Applications: Epilepsy



### Spontaneous EEG: Epilepsy

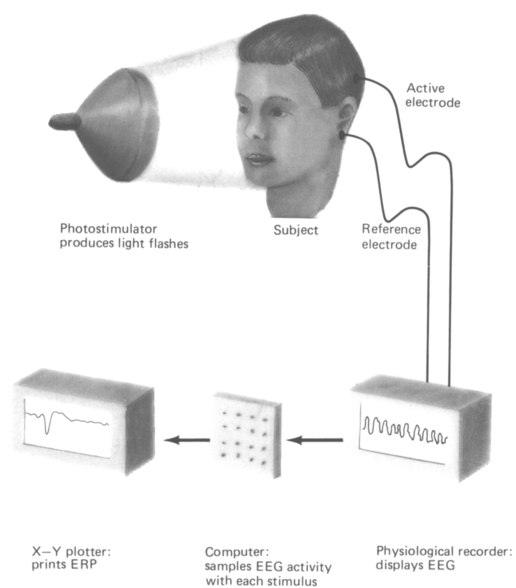


## Spontaneous EEG

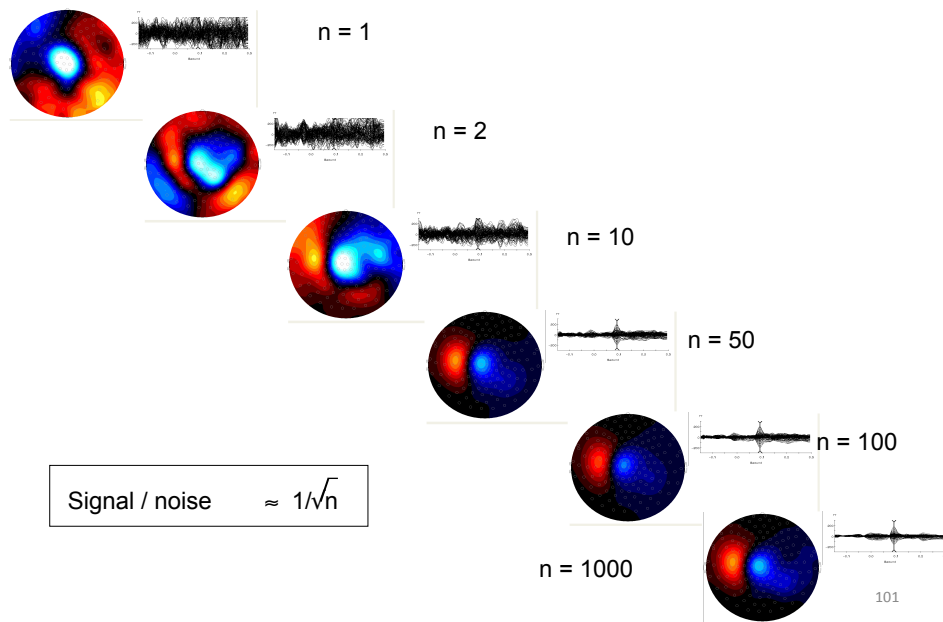


Spectrum  
Fourier analysis  
Low-pass filter  
High-pass filter

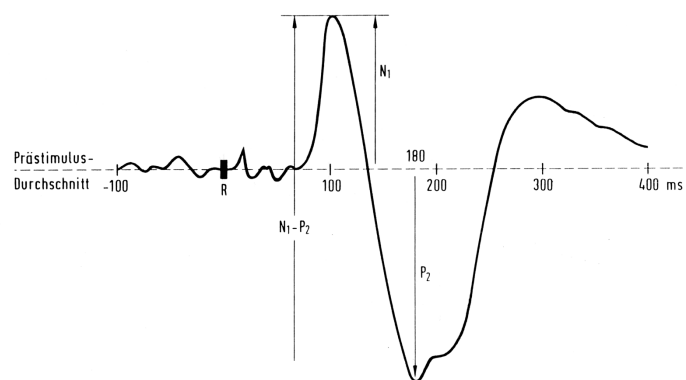
## EEG: Event-Related Potentials



### Evoked Brain Responses - Averaging

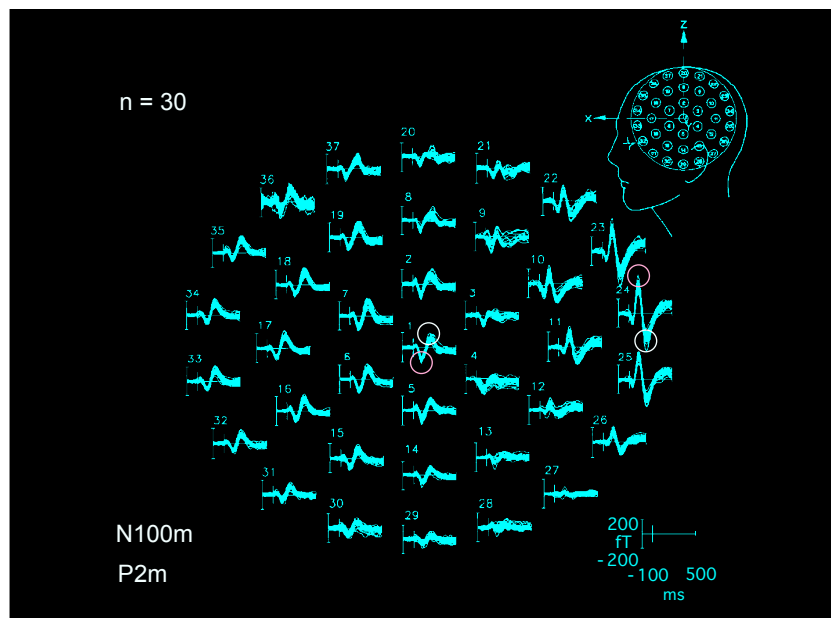


### EEG: Event-Related Potentials

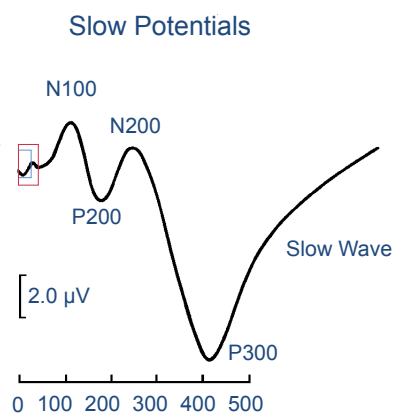
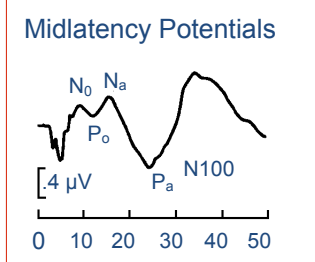
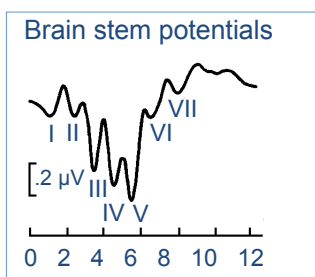


somatosensory evoked potential

### Reproducibility of MEG-Responses

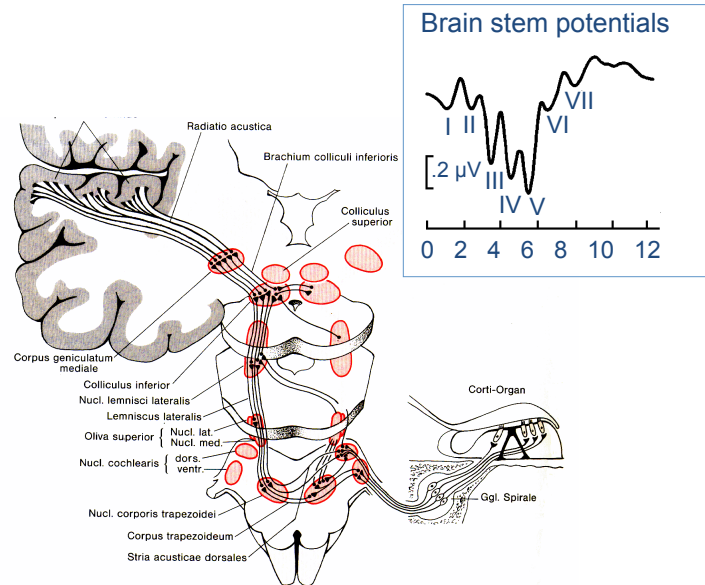


### EEG: Types of Event-Related Potentials

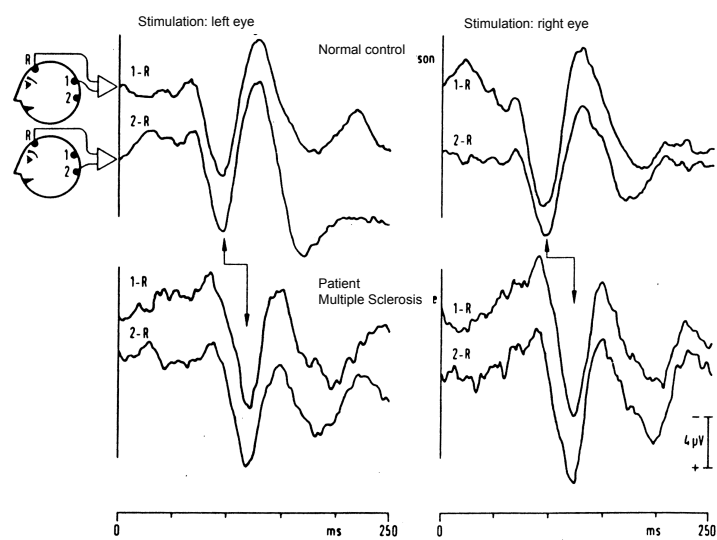




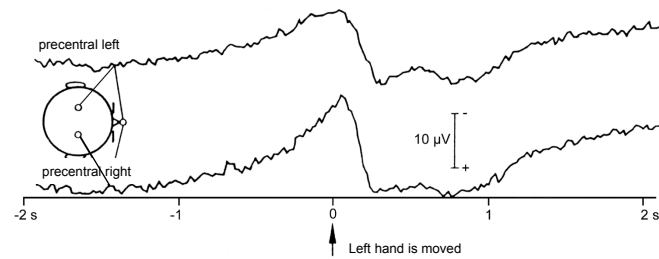
## Brainstem Potentials



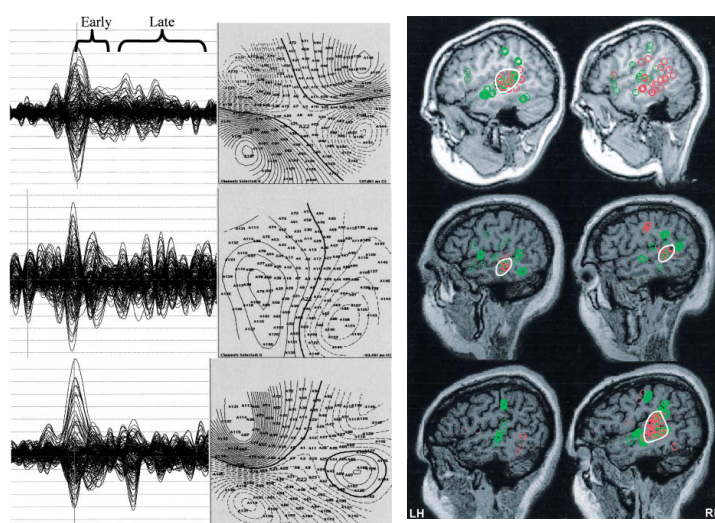
## EEG Application: Multiple sclerosis (MS)



## EEG: Bereitschafts-Potential



## Magnetoencephalography



Papanicolaou, 2004, J.  
Neurosurg

## Magnetoencephalography (MEG)



## Franz Anton Mesmer: Animal Magnetism

### curative effects of magnetism on humans

- As a consequence of Galvani's experiments on animal electricity, also the existence of an **animal magnetism** was hypothesised by F. A. Mesmer, who tried to associate "mysterious" magnetic fields with a deep influence on human behaviour
- Mesmer theories were examined by a committee of scientists - including Benjamin Franklin - nominated by King Louis XVI, and were declared totally absurd. Nevertheless, mesmerism continued to be widespread across Europe and to be practiced in the so-called Mesmer "saloons" for at least other 50 years
- Only when the deep connections existing between electric currents and magnetic field were fully understood – thanks to the exceptional synthesis operated by Maxwell – mesmerism definitively disappeared



Franz Anton Mesmer  
1734 -1815



### Physiological Electro-Magnetic Signals

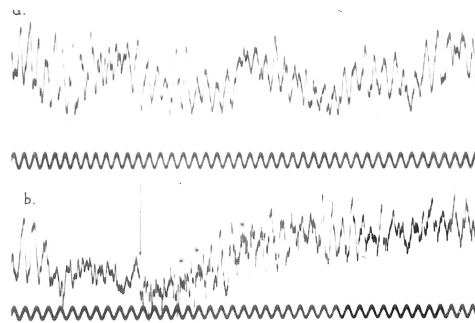
At the beginning of the 20<sup>th</sup> century electric signals associated with cardiac and cerebral activity were recorded for the first time:

- electrocardiogram (ECG) - (**Einthoven, 1903**)
- electroencephalogram (EEG) - (**Berger, 1929**)

Willem Einthoven  
1860-1927



Hans Berger  
1873-1941



### Physiological Electro-Magnetic Signals

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Willem Einthoven  
1860-1927



Hans Berger  
1873-1941



Only at the beginning of the sixties, the magnetic signals associated with cardiac currents were first described (magnetocardiogram (MCG) recorded by resistive coils, **Baule & McFee, 1963**)

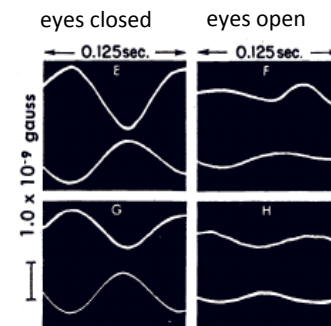
Finally, a MCG was measured for the first time using the rfSQUID developed by Edelsack, Cohen, and Zimmerman at MIT (**David Cohen et al., 1970**)



## Magnetoencephalography

The magnetic field due to electric currents flowing inside the brain was first recorded in 1968 by **David Cohen** using resistive coils

*Cohen, Science 1968*



In 1971 David Cohen measured the spontaneous alpha rhythm using a SQUID, and the expression magnetoencephalography (MEG) was introduced



*Cohen, Science 1972*

## Progress in Magnetoencephalography



**In the eighties**  
the single channel...



**In the nineties**  
from 37 to 150 channels...



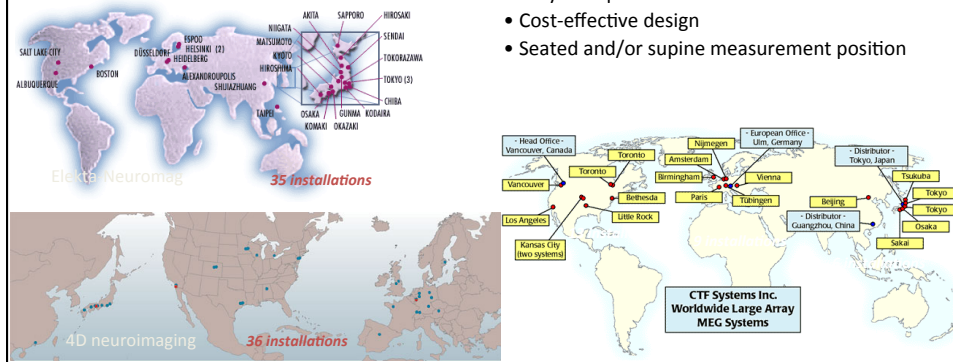
**In the current millennium**  
the channel number is increased up to some hundreds



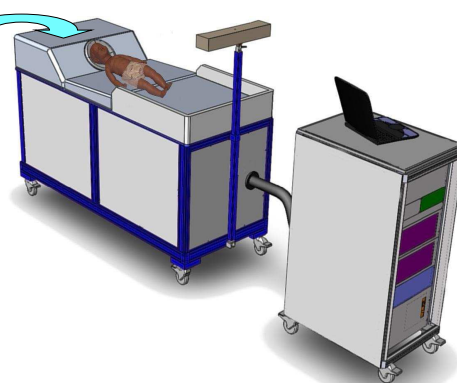
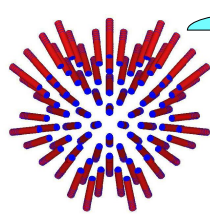
## MEG-Systems World Wide

Presently there are about 100 MEG systems installed worldwide. Major companies selling whole head MEG equipment are: 4D neuroimaging, Elekta-Neuromag, Yokogawa.

- Whole head coverage
- 100+300 detection points consisting of one to three channels
- Stable and reliable LTS SQUIDS
- Easy and friendly operation
- Easy set-up and maintenance
- Cost-effective design
- Seated and/or supine measurement position



## BabySQUID® Neonatal Biomagnetometer by Tristan Technologies, Inc.

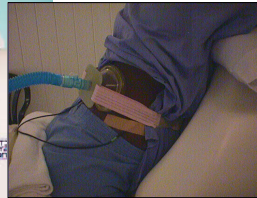


- 76 first-order axial gradiometers with baseline of 30 mm and pickup coil diameter of 6 mm
- spacing among channels is about 12 mm

- The gradiometers are connected by thermal conductors to the liquid helium bath
  - the distance between the signal coils and the headrest is about 6 mm
  - the magnetic field noise ~ 17 fT/VHz



## Fetal Magnetoencephalography



Control condition

- 6 x two minutes recording without any stimulus

### Stimulation

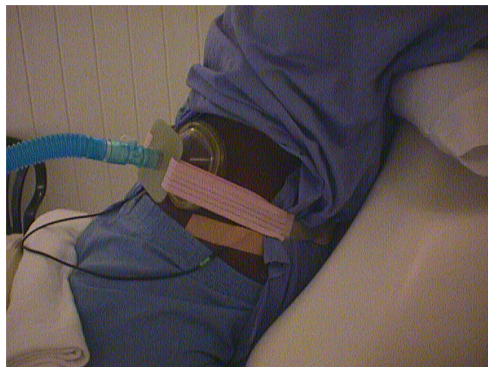
- 1000 Hz tones, 100 ms duration
- Interstimulus interval 2.0 sec
- presentation via tube
- phone: ca 120dB
- continuous recording 250 Hz: 2 x 6 min

## Fetal Magnetoencephalography (fMEG)





## Fetal Magnetoencephalography (fMEG)



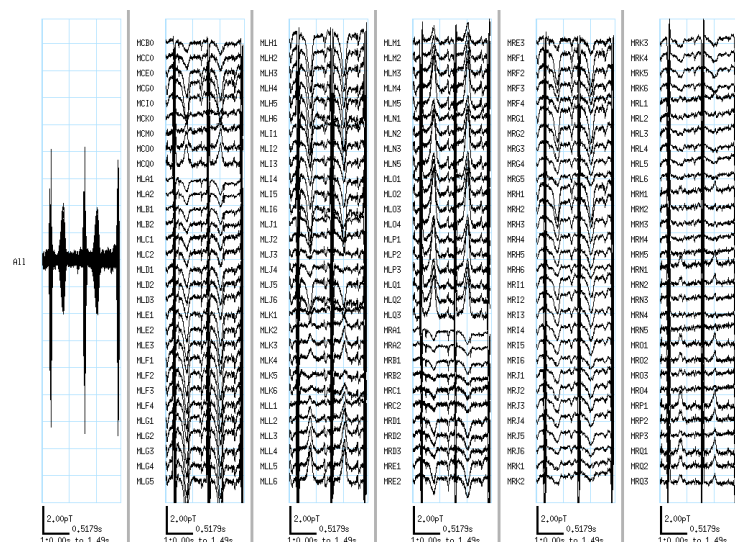
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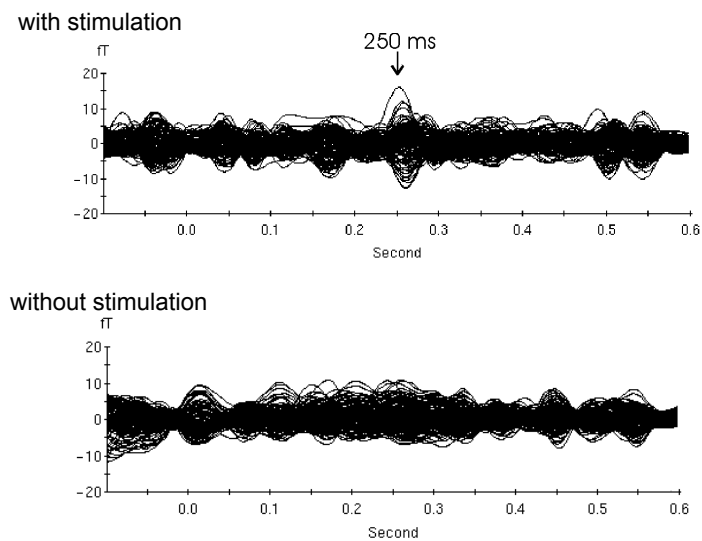
### Control condition

- 6 x two minutes recording without any stimulus

## Fetal Magnetoencephalography (fMEG)



## Fetal Magnetoencephalography (fMEG)



## New Developments: Atomic Magnetometers

### Magnetoencephalography



Measuring neuro magnetic fields of the brain by means of SQUID technology

- expensive
- no flexible configurations

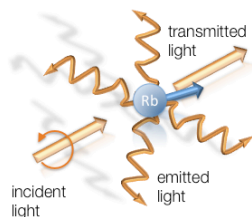
### Atomic magnetometers



## New Developments: Atomic Magnetometers

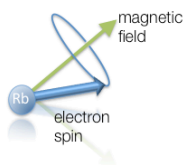
### Working principle of CSAMs

1. The spins of atoms in a gas can be aligned with resonant light



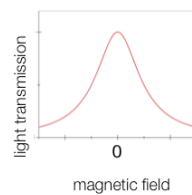
Optical  
pumping

2. Atoms with spin and magnetic moment precess in a magnetic field



Precession

3. The absorption of resonant light depends on the orientation of the atomic spins

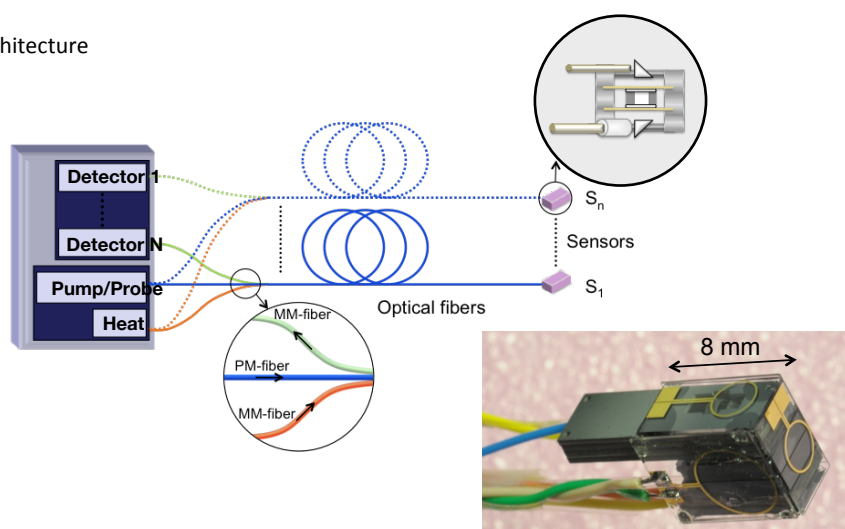


Optical  
probing

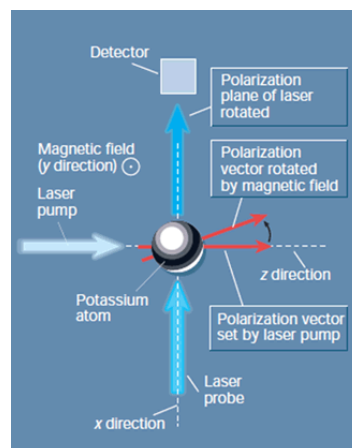
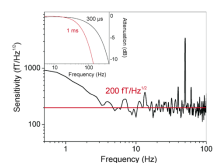
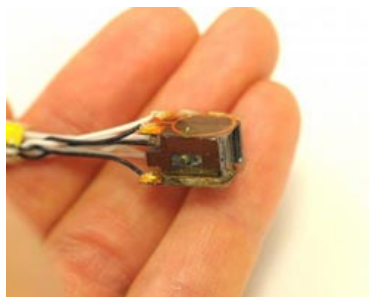
## New Developments: Atomic Magnetometers

### Working principle of CSAMs

Architecture

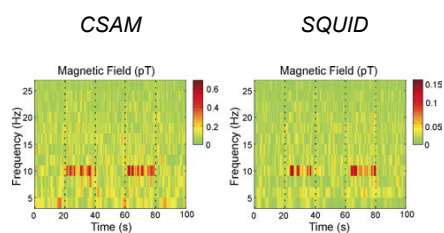


## Atomic Magnetometers: Is this the Future?

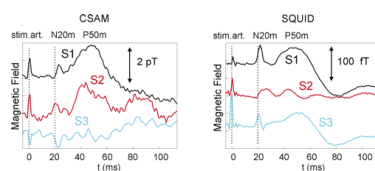


## Atomic Magnetometers: Is this the future?

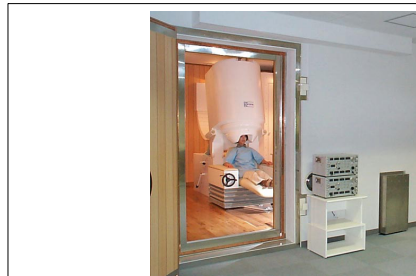
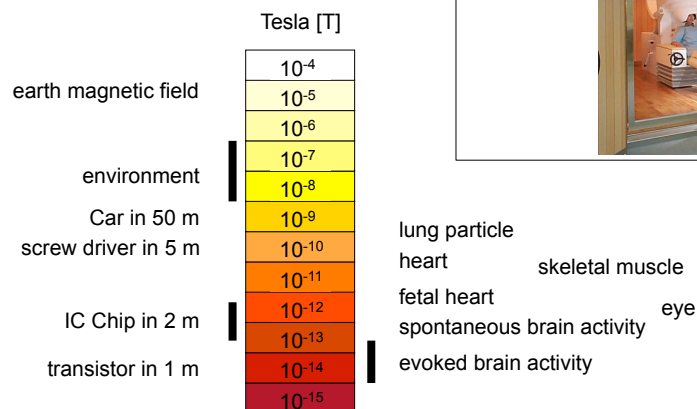
noise



somatosensory  
evoked field  
(SEF)



## Strength of Magnetic Fields

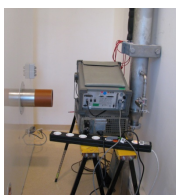


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## Noise Suppression: Shielding



the basis of the magnetic shielded room is an aluminium frame

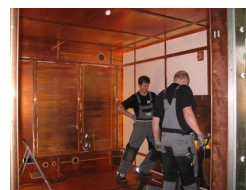


demagnetisation



finish

inner layer  
copper coated  
aluminium



middle layer  
mu metal with  
high magnetic  
susceptibility



outer layer  
aluminum

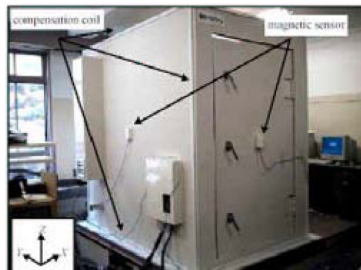


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## Noise Suppression: Shielding



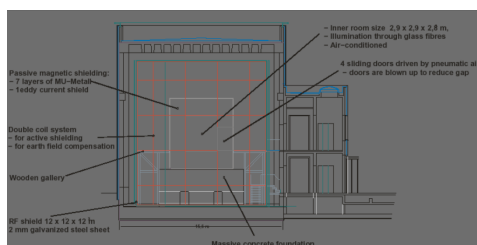
AK3B Vakuumschmelze:  
3 Layer shielding



active compensation



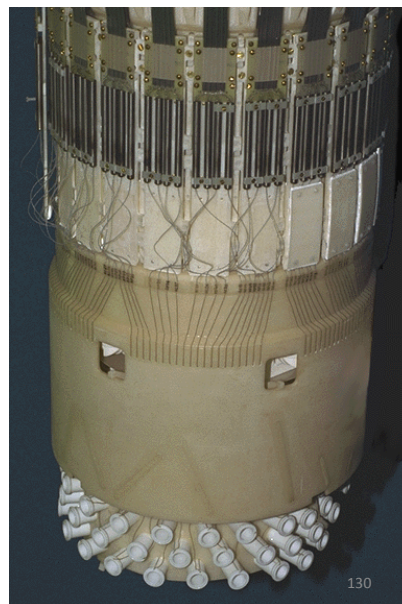
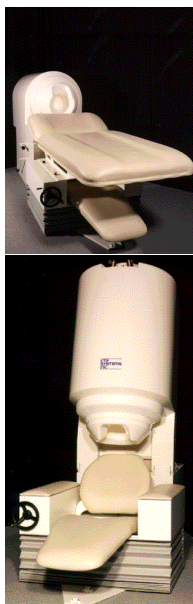
Superconductive Shielding :  
Shielding factor: 10 000 bei 0.05 Hz



passive 7 layer shielding  
double coil system for  
- active shielding  
- earth field compensation  
RF-shield

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## MagnetoEncephaloGraphy

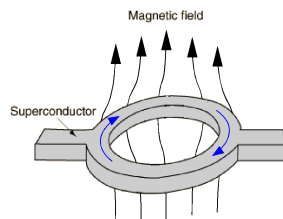


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## SQUID: Superconducting Quantum Interference Device

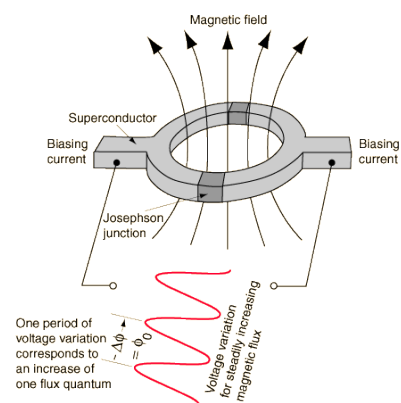
### superconducting ring

- an external magnetic field creates a current in the coil
- current creates magnetic field opposite to the original field
- no magnetic field inside the ring



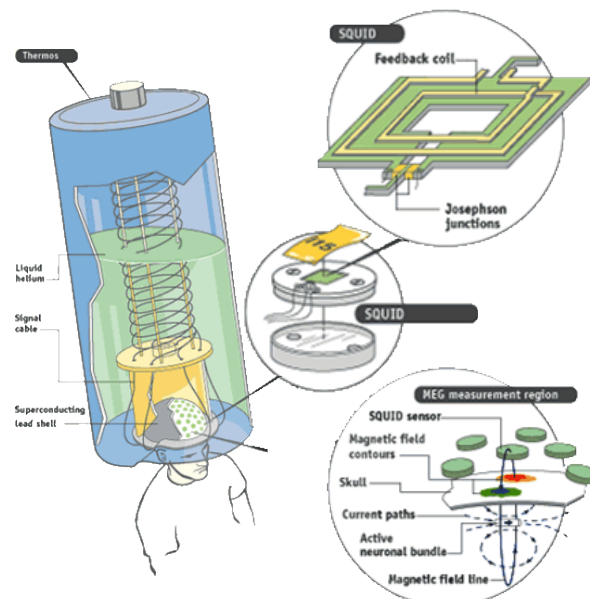
### superconducting ring with Josephson junction

- differences between multiples of flux quanta
- only multiples of flux quanta can pass generate a current
- the current causes a voltage drop at the Josephson junction



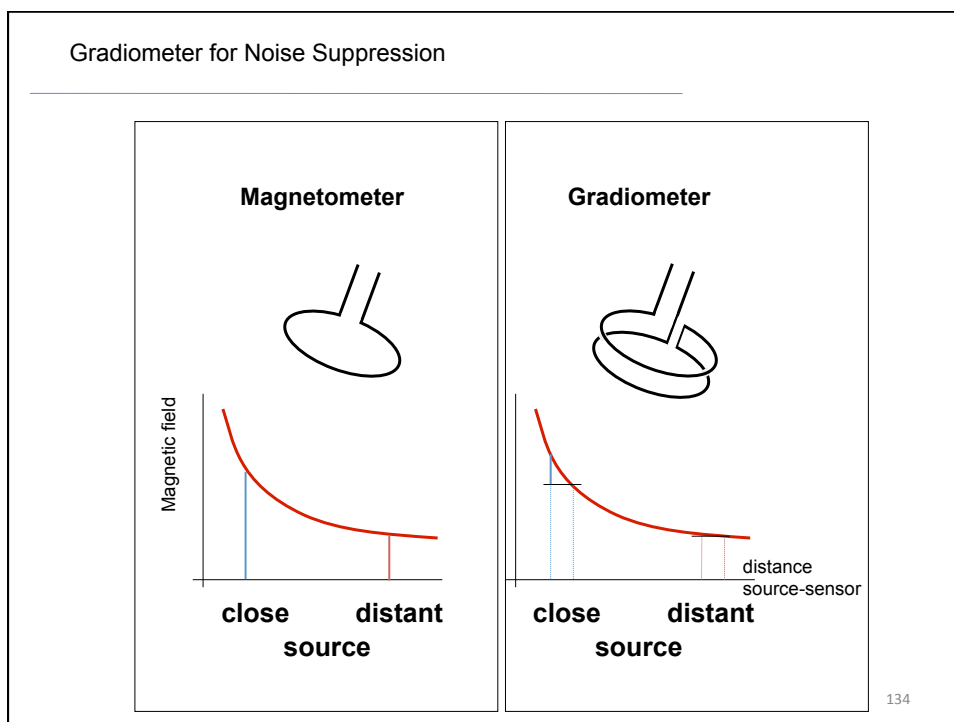
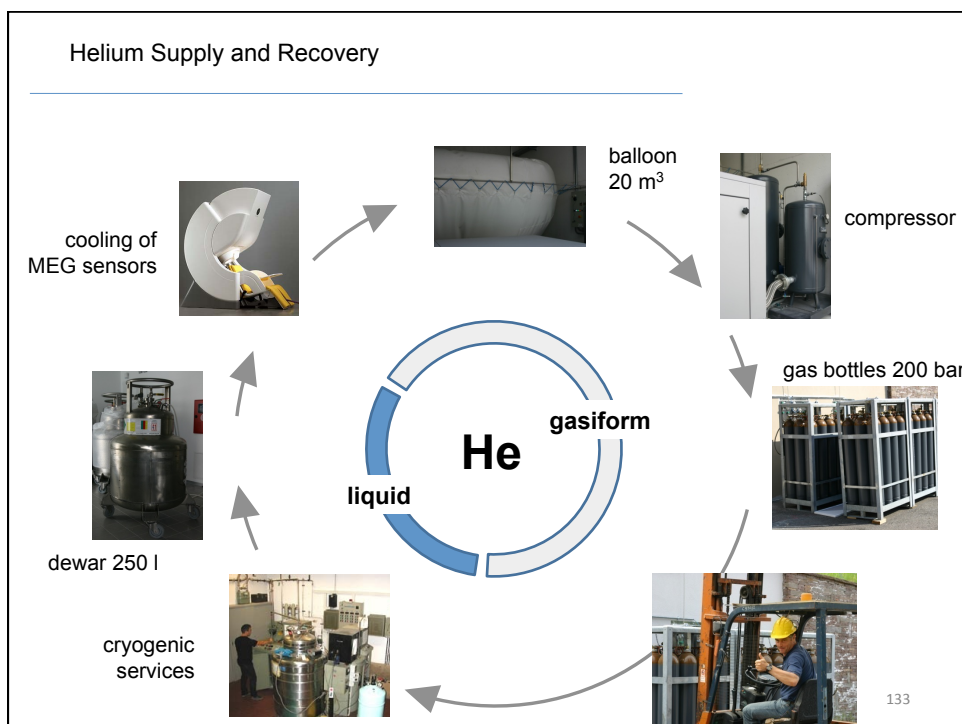
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## Principle of Magnetoencephalography

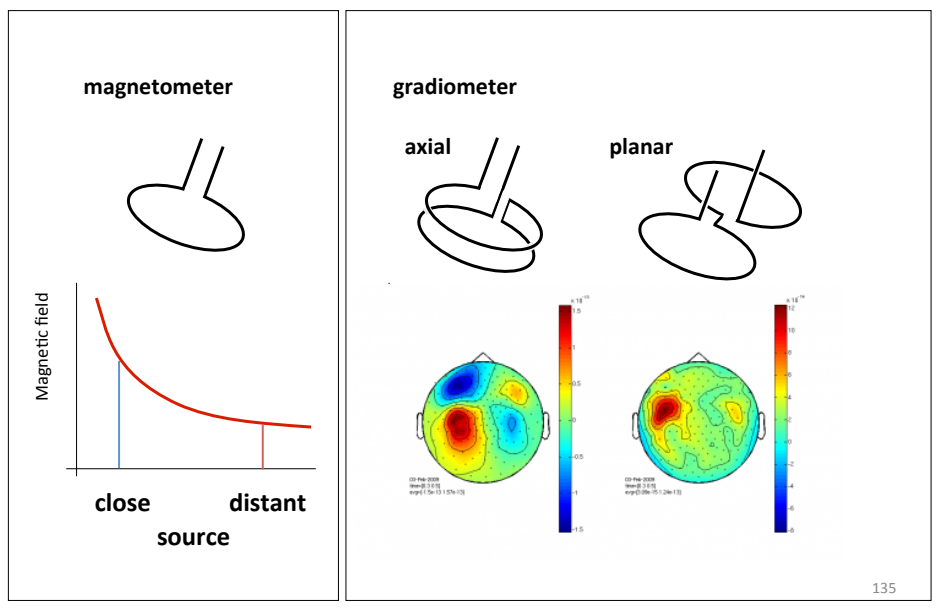


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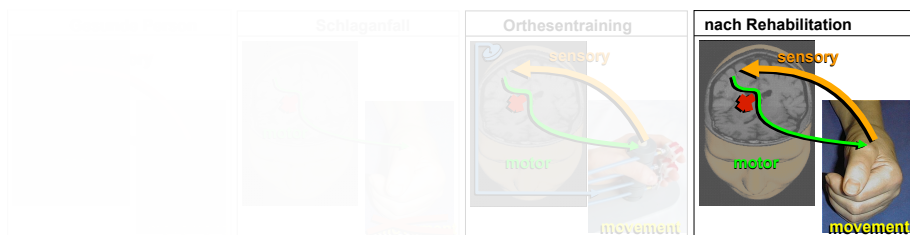


### Noise Suppression: Magnetometers and Gradiometers



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### Brain Controlled Neuroprosthesis



Brain-Computer-Interface for  
the control of „Orthosis-training“:

Feedback of  $\mu$ -rhythm activity

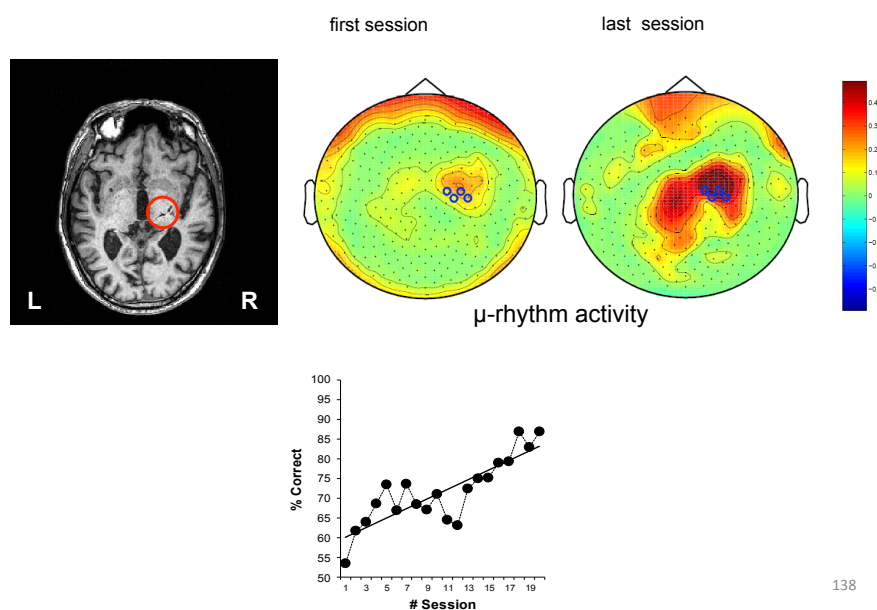
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## Brain Controlled Neuroprosthesis



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## Brain Controlled Neuroprosthesis



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