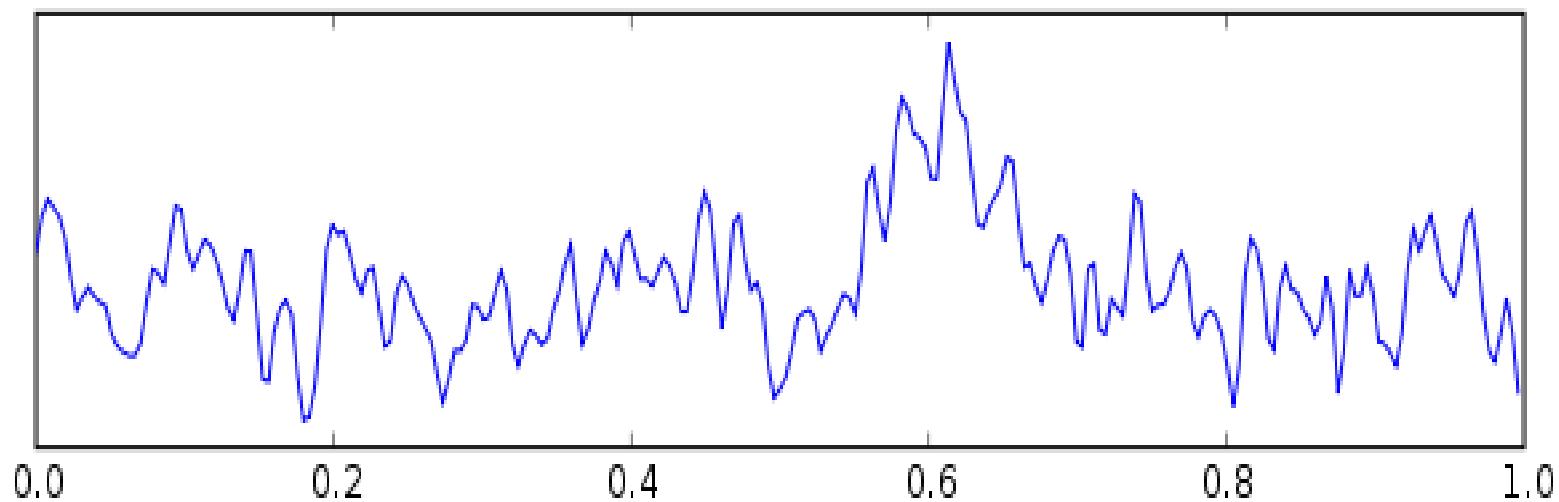




Basis of the EEG/MEG signal





History

- Richard Caton (1842-1926) from Liverpool published findings about electrical phenomena of the exposed cerebral hemispheres of rabbits and monkeys in the British Medical Journal in 1875.
- In 1890 Adolf Beck published findings of spontaneous electrical activity and rhythmic oscillations in response to light in the brains of rabbits and dogs.
- In 1912 Vladimir Vladimirovich Pravdich-Neminsky published the first animal EEG study described evoked potential in the mammalian brain.
- In 1914 Napoleon Cybulski and Jelenska-Macieszyna photographed EEG recordings of experimentally induced seizures.



History

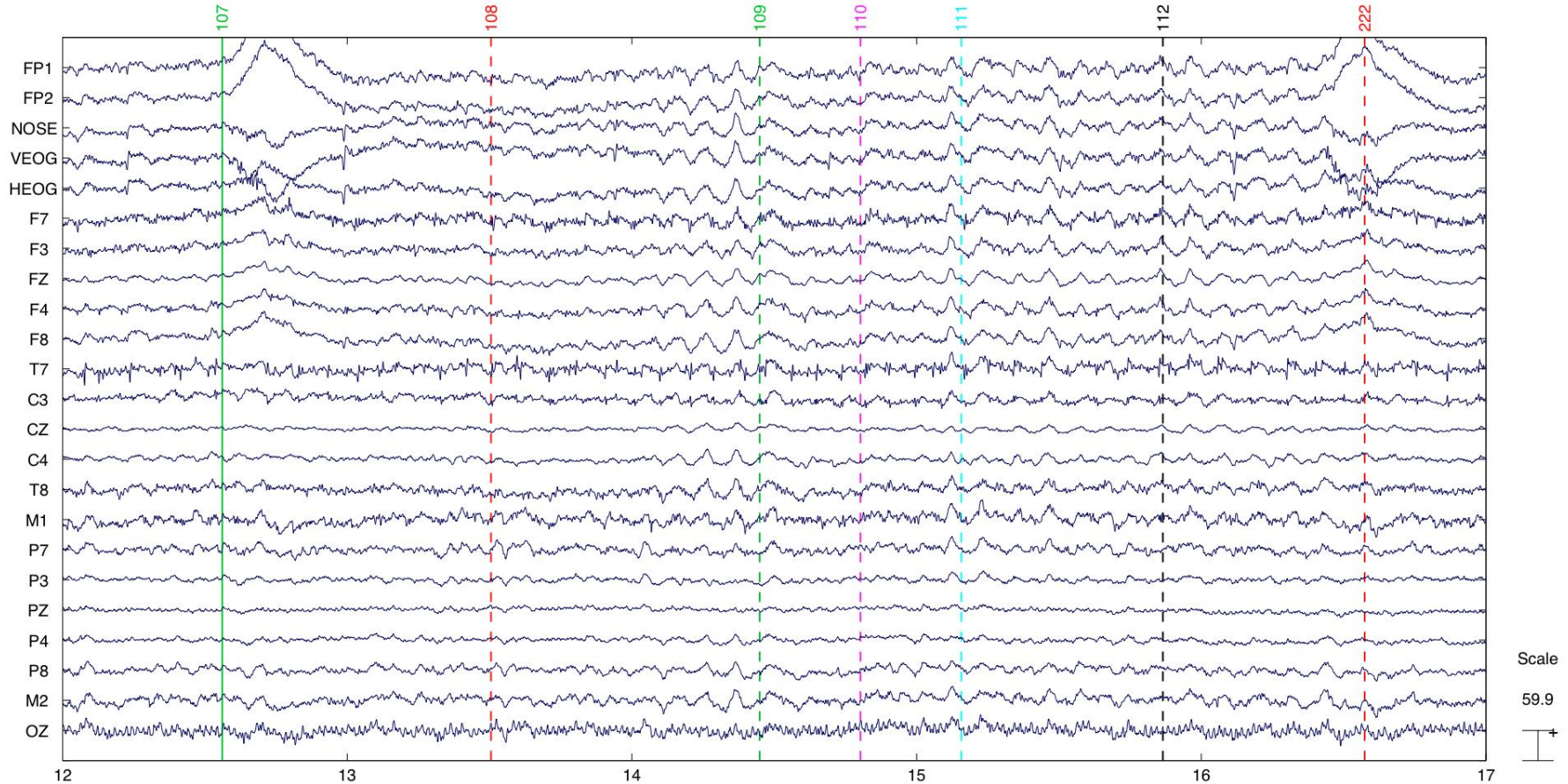


1929: Hans Berger developed electroencephalography, the graphic representation of the difference in voltage between two different cerebral locations plotted over time

He described the human alpha and beta rhythms



Continuous EEG recording



F = frontal, T = temporal, C = central, etc

Even number = right side of head, Odd number = left side

International 10-20 system – ensures consistency

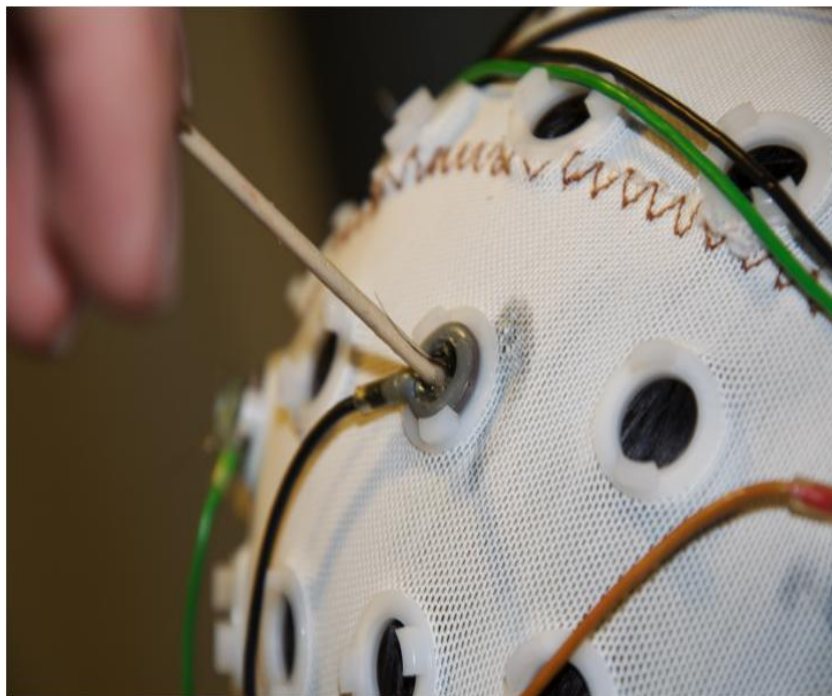


Digital vs. Analogue

- Conventional analogue instruments consist of an amplifier, a galvanometer (a coil of wire inside a magnetic field) and a writing device. The output signal from the amplifier passes through the wire causing the coil to oscillate, and a pen mounted on the galvanometer moves up and down in sync with the coil, drawing traces onto paper.
- Digital EEG systems convert the waveform into a series of numerical values, a process known as Analogue-to-Digital conversion. The rate at which waveform data is sampled is known as the *sampling rate*, and as a rule should be at least 2.5 times greater than the highest frequency of interest. Most digital EEG systems will sample at 240Hz.
- The accuracy of digital EEG waveforms can be affected by *sampling skew* – a small time lag that occurs when each channel is sampled sequentially. This can be reduced using *burst mode* – reduced the time lag between successive channel sampling.
- Be aware of the relationship between sampling rate, screen resolution and the EEG display. If there are more data samples than there are pixels then this will have the effect of reducing the sampling rate and the data displayed will appear incomplete. However, most modern digital EEG systems will draw two data samples per screen pixel.



EEG Acquisition



Electrodes: Usually made of silver (or stainless steel) – active electrodes placed on the scalp using a conductive gel or paste. Signal-to-noise ratio (impedance) reduced by light abrasion. Can have 32, 64, 128, 256 electrodes. More electrodes = richer data set. Reference electrodes (arbitrarily chosen “zero level”, analogous to sea level when measuring mountain heights) commonly placed on the midline, ear lobes, nose, etc.

Amplification: one pair of electrodes make up one channel on the differential amplifier, i.e. there is one amplifier per pair of electrodes. The amplifier amplifies the difference in voltage between these two electrodes, or signals (usually between 1000 and 100 000 times). This is usually the difference between an active electrode and the designated reference electrode.



EEG records differences in voltage: the way in which the signal is viewed can be set up in a variety of ways called *montages*

Bipolar montage: Each waveform in the EEG represents the difference in voltage between two adjacent electrodes, e.g. 'F3-C3' represents the difference in voltage between channel F3 and neighbouring channel C3. This is repeated across the whole scalp through the entire array of electrodes.

Reference montage: Each waveform in the EEG represents the difference in voltage between a specific active electrode and a designated reference electrode. There is no standard position for the reference, but usually a midline electrode is chosen so as not to bias the signal in any one hemisphere. Other popular reference signals include an average signal from electrodes placed on each ear lobe or mastoid.

Average Reference montage: Activity from all electrodes is measured, summed and then averaged. The resulting signal is then used as a reference electrode and acts as input 2 of the amplifier. The user can specify which electrodes are to be included in this calculation.

Laplacian montage: Similar to average reference, but this time the common reference is a weighted average of all the electrodes, and each channel is the difference between the given electrode and this common reference.



Montages (continued)

- In digital EEG setups, the data is usually stored onto computer memory in reference mode, regardless of the montage used to display the data when it is being recorded.
- This means that “remontaging”, i.e. changing the montage either ‘on-line’ or ‘off-line’, can be done via a simple subtraction which cancels out the common reference.

$$\begin{aligned} \text{E.g. } & \boxed{\text{F3 - Reference}} - \boxed{\text{F4 - Reference}} \\ & = \text{F3} - \text{F4} \end{aligned}$$

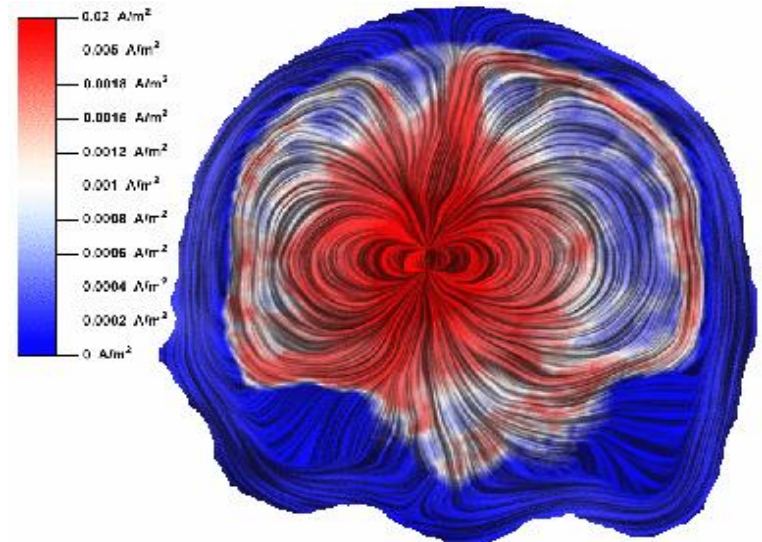


What does the EEG record?

Volume conduction

Ions are constantly flowing in and out of neurons to maintain resting potential and propagate action potentials. Movement of like-charged ions out of numerous neighbouring neurons can create waves of electrical charge, which can push or pull electrons on scalp electrodes, creating voltage differences.

In summary, the EEG signal represents the deflection of electrons on the scalp electrodes, caused by cortical “dipoles” (the summed activity within a specific area of cortex that creates a current flow).





Neural basis of the EEG (1)

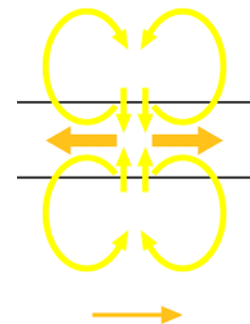
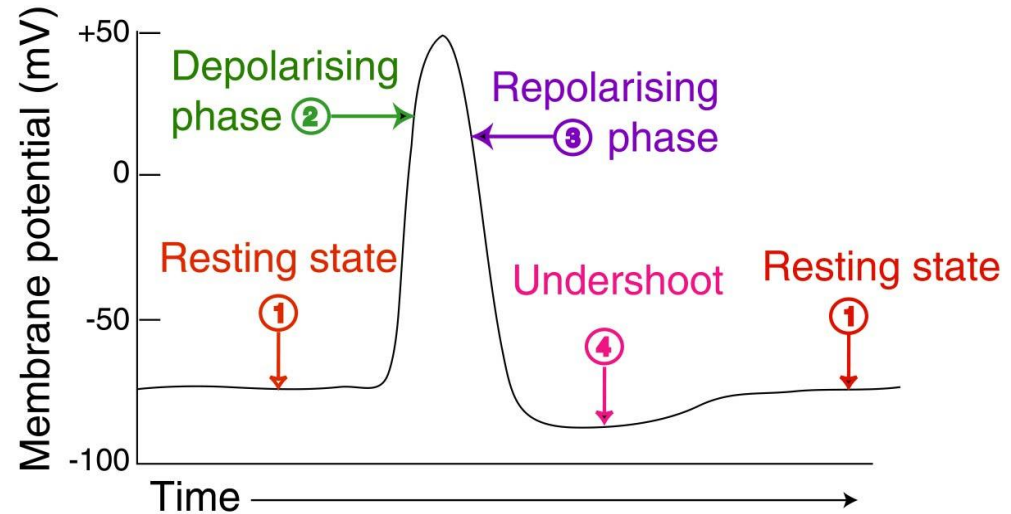
Action Potentials

Rapid, transient, all-or-none nerve impulses that flow from the body to the axon terminal of a neuron.

They are generally too short in duration (a few ms) and too “deep” to contribute significantly to the EEG signal.

In addition they create 2 dipoles = *quadrupole*

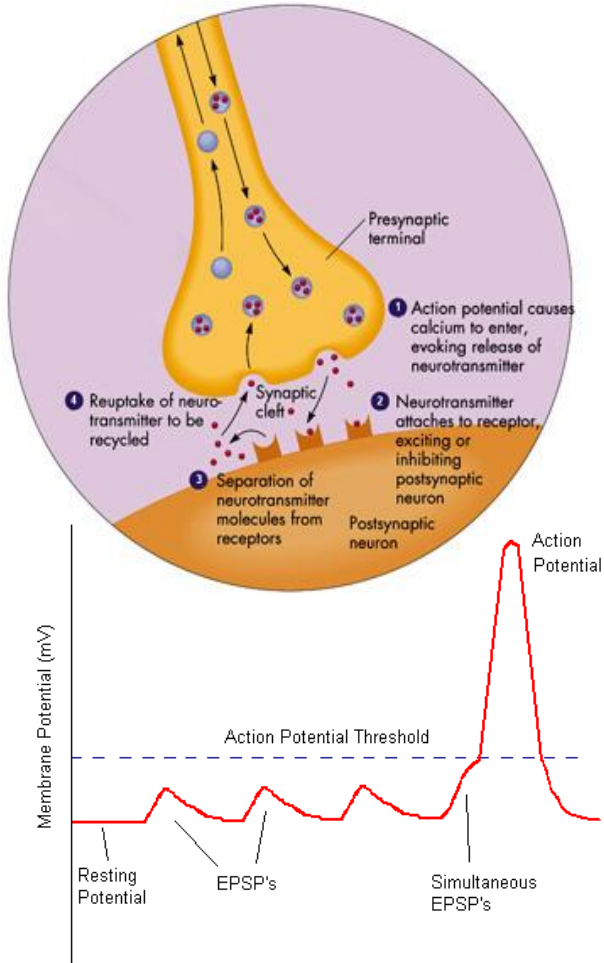
Finally, synchronous firing is unlikely preventing the summation of potentials





Neural basis of the EEG (2)

Post-synaptic potentials



Scalp EEG is a summation of non-propagating dendritic and somatic post-synaptic potentials which arise relatively slower than action potentials (approx 10ms).

EPSPs – Excitatory Post Synaptic Potentials

IPSPs – Inhibitory Post Synaptic Potentials

Post synaptic potentials summate spatially and temporally – A single pyramidal cell may have more than 10^4 synapses distributed over its soma and dendritic surface.



Neural basis of the EEG (3)

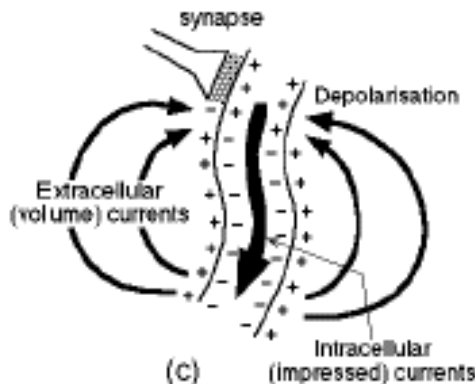
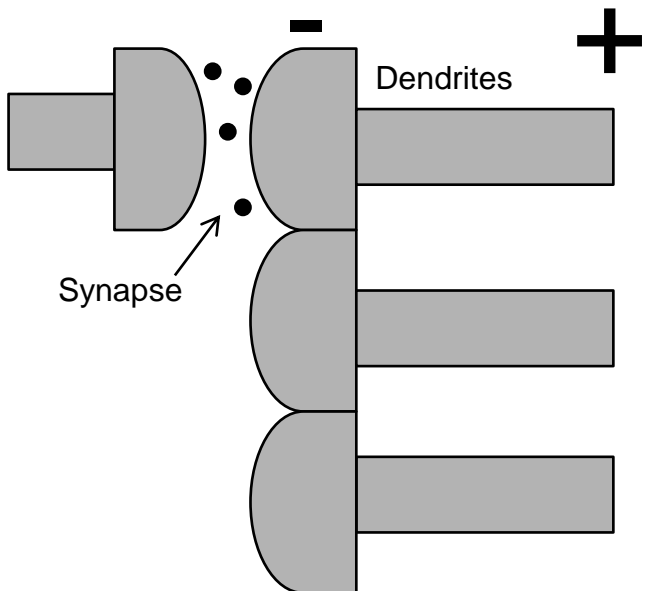
When an EPSP is generated in the dendrites of a neuron, Na^+ flow inside the neuron's cytoplasm creating a current sink.

The current completes a loop creating a dipole further away from the excitatory input (where Na^+ flows outside the cell as passive return current), which can be recorded as a positive voltage difference by an extracellular electrode.

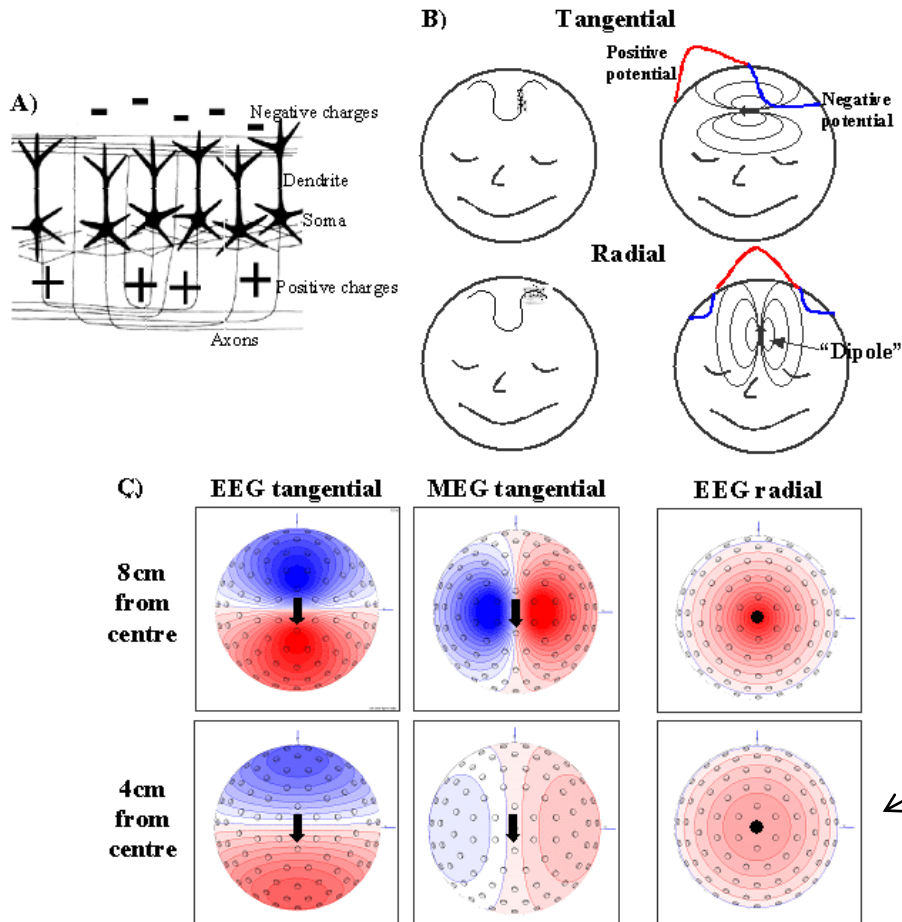
Large numbers of vertically oriented, neighbouring pyramidal neurons create these field potentials.

Thus, EEG detects summed synchronous activity (PSPs) from many thousands of apical dendrites of neighbouring pyramidal cells (mainly).

“It takes a combined synchronous electrical activity of approximately 108 neurons in a minimal cortical area of 6cm^2 to create visible EEG”... *Olejniczak, J. Clinical Neurophysiology, 2006.*



Neural basis of the EEG (4)



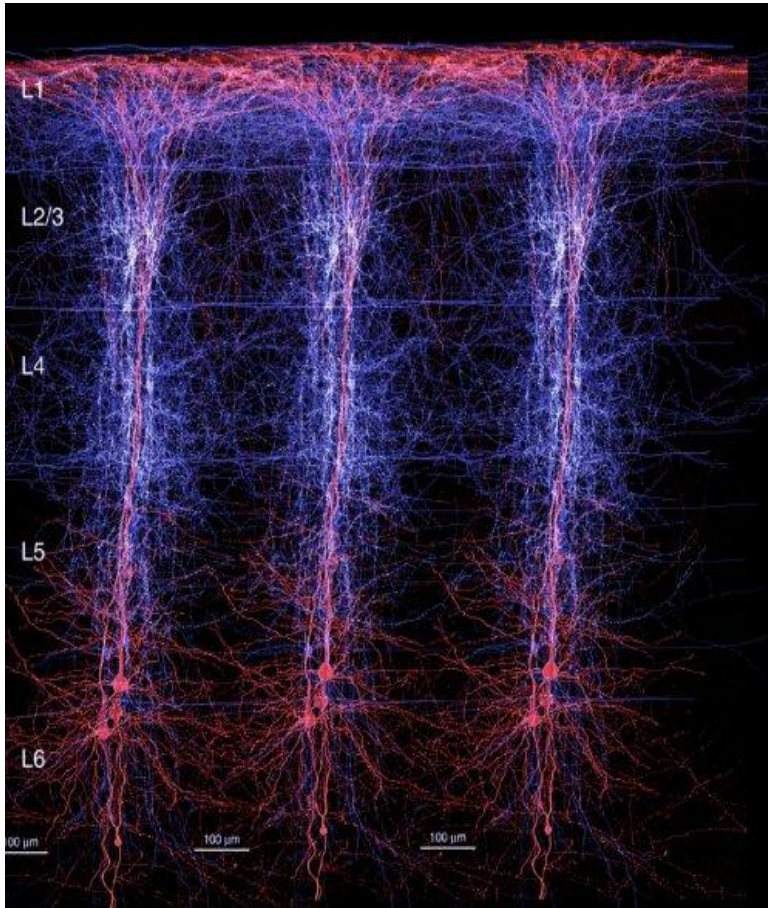
“The closer a dipole is to the centre of the head, the broader the distribution and the lower the amplitude”

Figure 1: Illustration of the physiological basis of the EEG.

- A) The main generators of the EEG (and MEG) signals are voltage gradients along dendrites in upper cortical layers. This, in turn, causes a current flow in the conducting medium surrounding it. Several thousands of parallel oriented neighbouring dendrites have to be active synchronously to produce a measurable signal.
- B) The summed activity within a small area of cortex can be described by a so-called “dipole”. This dipole describes the strength and direction of the current flow within this area. A “tangential dipole” is oriented parallel to the scalp surface, whereas a “radial dipole” points towards or away from it. Each dipole produces a positive scalp potential in the direction it points to, and a negative potential in the opposite direction. Each current also produces a magnetic field. The magnetic field of a tangential dipole is roughly perpendicular to its potential distribution (not illustrated, but see item C).
- C) Simulation of the scalp potential (EEG) and magnetic field (MEG) distributions for dipoles with different orientations and different distances from the centre of the head. Because MEG is very insensitive to radial compared with tangential dipoles, only distributions for the latter are shown. Note that the closer a dipole is to the centre of the head, the broader the distribution and the lower the amplitude. The amplitude decrease with depth is more pronounced for the MEG.



Neural basis of the EEG (5)



Pyramidal neurons, the major projection neurons in the cortex, make up the majority of the EEG signal (particularly layers III, V and VI), because they are uniformly orientated with dendrites perpendicular to the surface, long enough to form dipoles. We can assume that the EEG signal reflects activity of cortical neurons in close proximity to the given electrode.

The thalamus acts as the pacemaker ensuring synchronous rhythmic firing of pyramidal cells.

Activity from deep sources is harder to detect as voltage fields fall off as a function of the square of distance.



EEG Rhythms:

can characteristically be broken down into different frequency bands



Attenuated during movement

Seen during alertness,
active concentration

Beta (β) 13-30 Hz

Parietally and
frontally

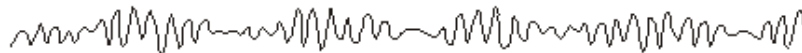


Relaxation, closing of the
eyes

Control of inhibition

Alpha (α) 8-13 Hz

Occipitally



Drowsiness, meditation,
action inhibition

Theta (θ) 4-8 Hz

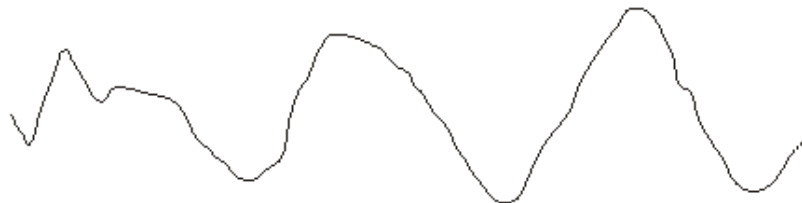
Children,
sleeping adults



Continuous attention, slow
wave sleep

Delta (δ) 0.5-4 Hz

Infants,
sleeping adults

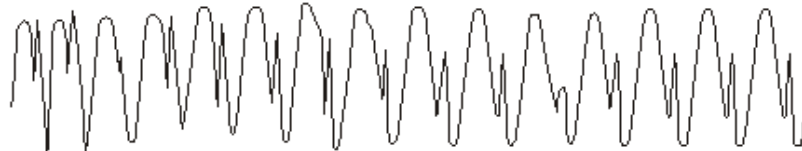


• Mu (8 – 13 Hz):

Rest state motor neurons

Spikes 3 Hz

Epilepsy -
petit mal



Cross-modal sensory
processing, short-term
perceptual memory

200
100
0

0 1 2 3 4 Time [s]



EEG Analysis (1)

Evoked Potentials stereotyped *early* responses time and phase-locked to the presentation of a physical stimulus

Event-related Potentials stereotyped *late* (?) responses time and phase-locked to stimuli, but often associated with “higher” cognitive processes, e.g. attention, expectation, memory, or top-down control

Both require averaging the same event over multiple trials (typically 100+), in order to average out noise/random activity, but preserve the signal of interest.

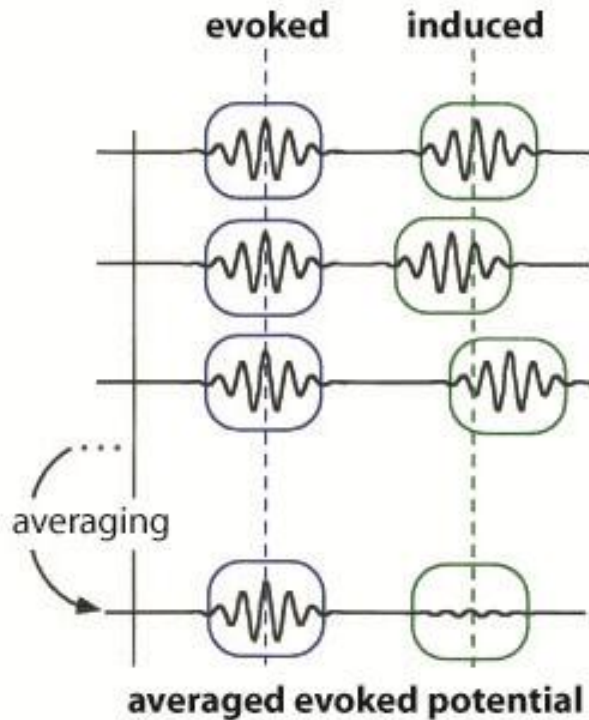
If the signal of interest is roughly known a priori then **filters** can be applied to suppress noise in frequency ranges where the amplitude is low or are of no interest. E.g. High-pass, low-pass, band-pass...



EEG Analysis (2)

Induced Activity

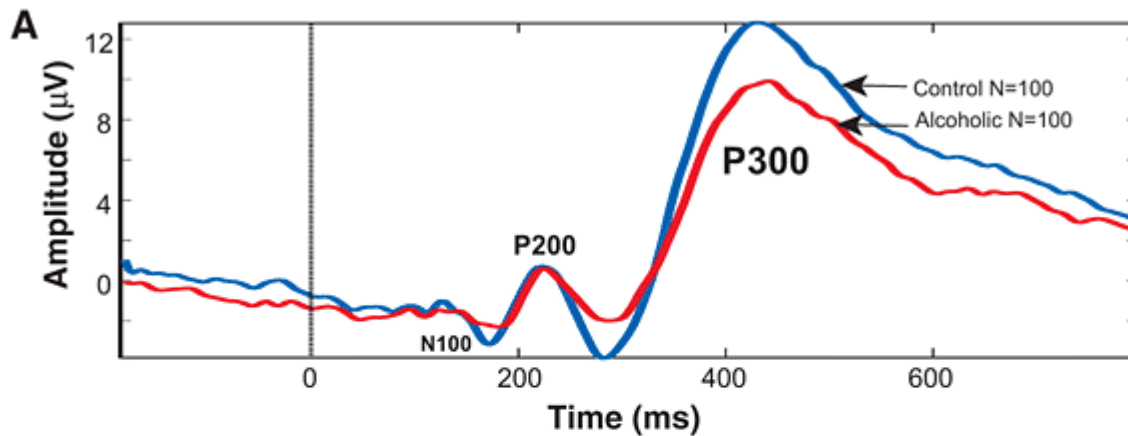
stereotyped responses time but not phase-locked to the presentation of a physical stimulus, i.e. there is some jitter in the response between epochs. Averaging over trials would not be appropriate. Instead, the signal amplitude for different frequency bands is computed for every epoch. This type of analysis only considers frequency amplitude and not phase.



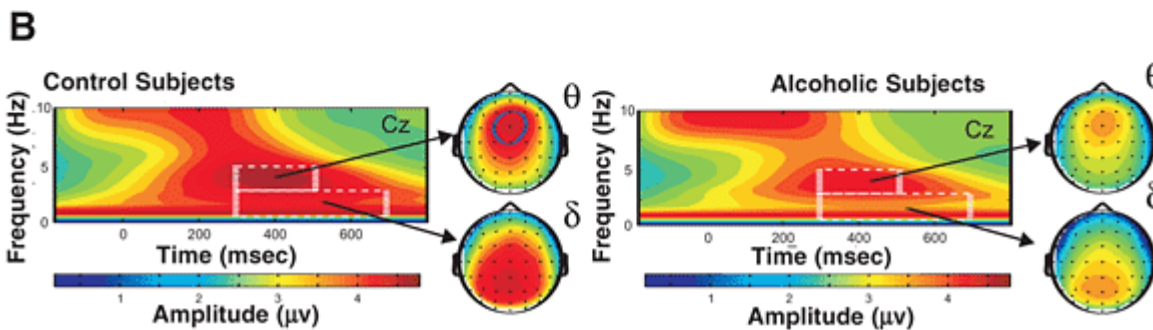


EEG Analysis (3)

Evoked Response / Event – related potential



Grand mean ERP in response to visual oddball paradigm – subjects are asked to react when they see a rare occurrence amongst a series of common stimuli, e.g. rotating arms of a clock



It produces a stereotyped evoked response over parieto-central electrodes at around 300ms (termed P300 component) that is largest after seeing the rare target stimulus



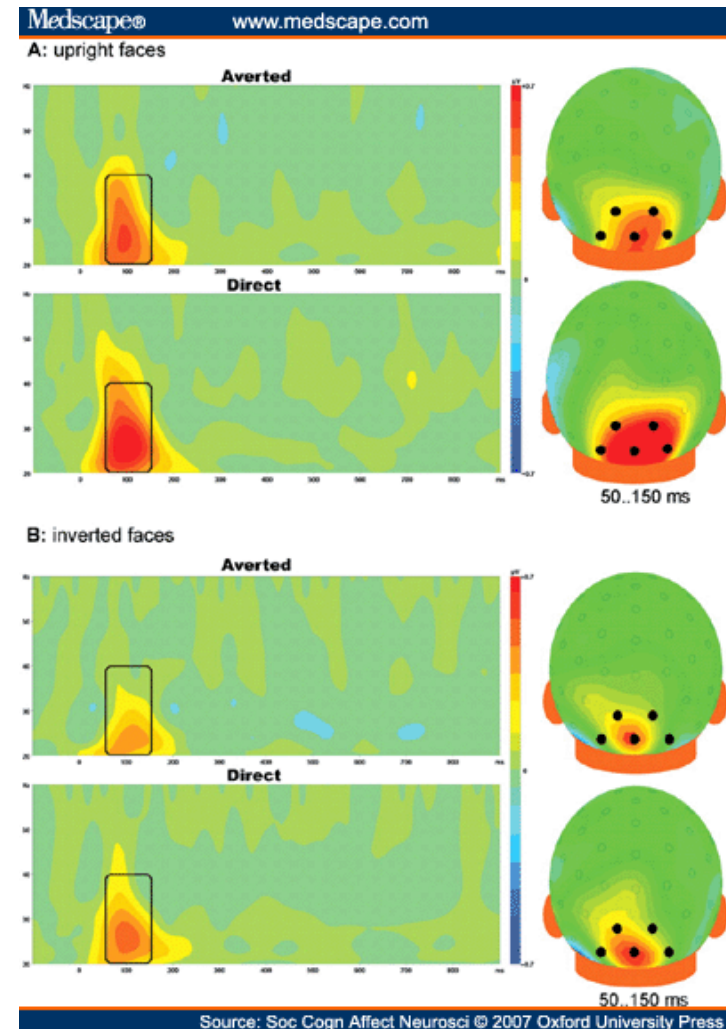
EEG Analysis (4)

Time-Frequency Analysis

Tells you which frequencies are present/dominant in the signal over a given time. Can be for one single electrode or the average across multiple electrodes.

Useful for:

- Analysing *induced* activity that isn't phase-locked, i.e. that would be averaged out with conventional event-related analysis
- Characterising and understanding typical responses to specific events – e.g. significant increase in gamma band activity 20-60 ms following an auditory stimulus





EEG Analysis (3)

Artifacts

Physiological

Eye blinks and eye movements

Muscle artifacts

Heart artifacts

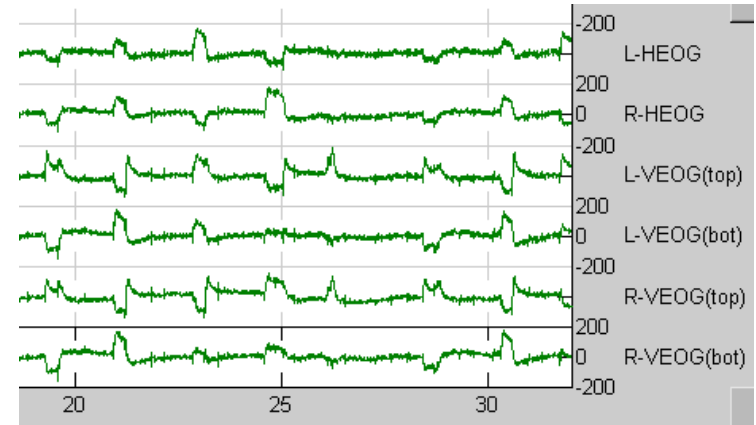
Environmental

Momentary changes in electrode impedance

Dried electrode gel

Electrode wire contact

Poor grounding can give a 50/60 Hz signal



Baseline Correction

the EEG signal can undergo small baseline shifts away from zero due to sweating, muscle tension, or other sources of noise.

Removal of artifacts can be done manually, e.g. epoching the signal and manually removing contaminated trials; OR through automated artifact rejection techniques build into the software.



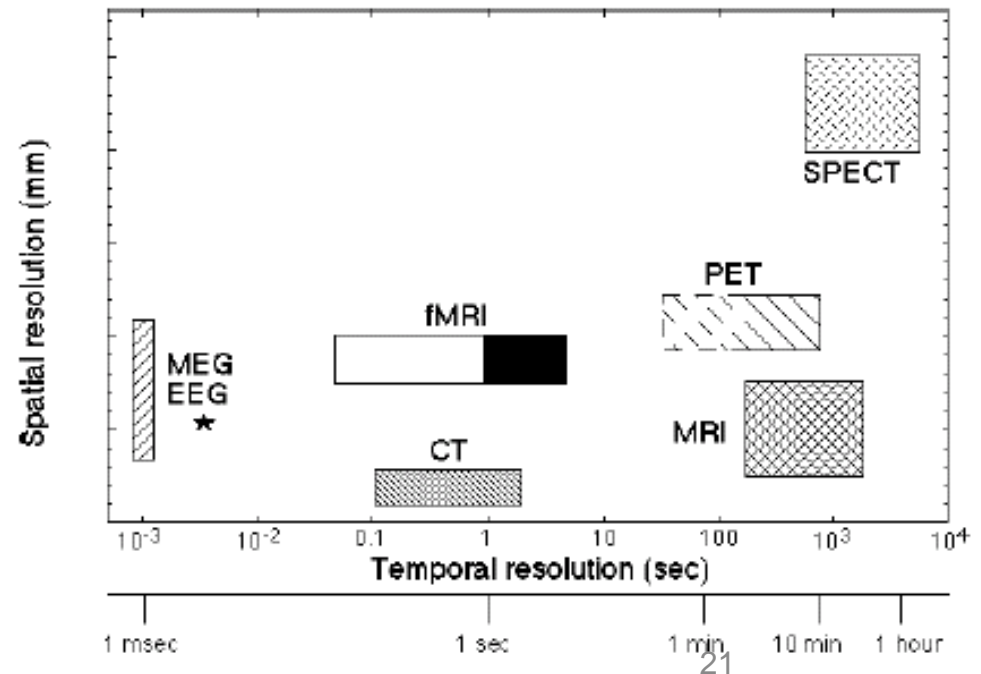
EEG

Pros

- Good time resolution, ms compared to s with fMRI
- Portable and affordable
- More tolerant to subject movement than fMRI
- EEG is silent and so useful for studying auditory processing
- Can be combined with fMRI or TMS

Cons

- Low spatial resolution
- Artifacts / Noise

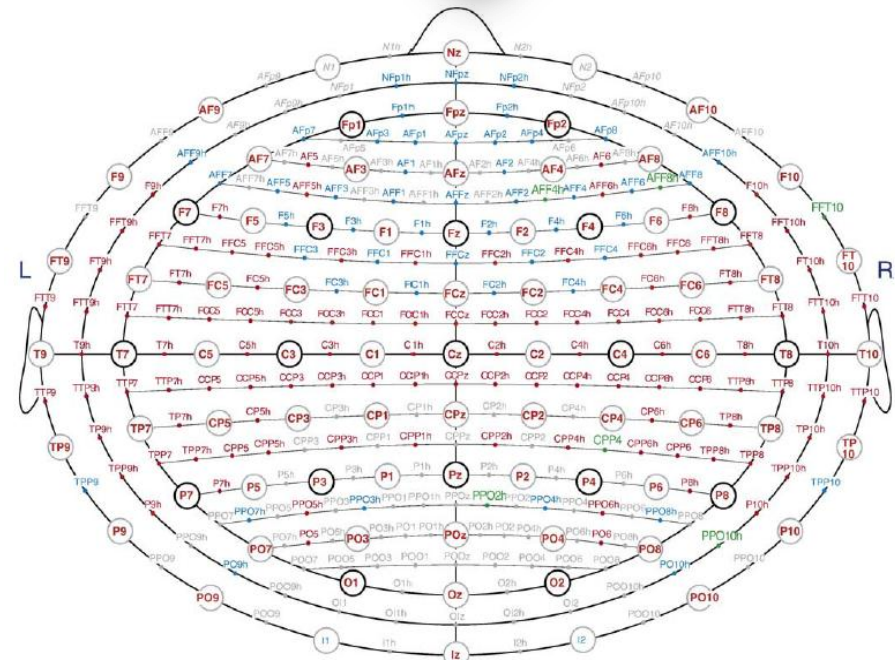




Signal Transduction

329 positions are defined as potential electrode locations:

- 24 to 36 channels are commonly used; 64 and 128-channel EEGs are used in research
- **10/20 configuration (black):** yields 19 channels plus several reference channels (typically the ears and forehead)
- **10/10 configuration (gray):** typically doubles the number of channels
- Differential voltages are typically measured between a sensor and an ear (e.g., F3-T9)
- Common reference points include the ears (T9 and T10), the nose (e.g., ???) and the heart/respiratory system (e.g., EKG1 and EKG2)





Common Diseases Diagnosed With An EEG



- **Epilepsy:** a neurological disorder marked by sudden recurrent episodes of sensory disturbance, loss of consciousness, or convulsions.
- **Stroke:** a sudden disabling attack or loss of consciousness caused by an interruption in the flow of blood to the brain.
- **Posterior Reversible Encephalopathy Syndrome (PRES):** characterized by headache, confusion, seizures and visual loss. It may occur due to a number of causes, predominantly malignant hypertension, eclampsia and some medical treatments.
- **Middle Cerebral Artery (MCA) Infarct:** obstruction of one of the three major paired arteries that supply blood to the cerebrum.
- Other uses of EEGs include diagnosis of Alzheimer's disease, certain psychoses, and sleep disorders (narcolepsy).
- The EEG may also be used to determine the overall electrical activity of the brain, which is used to evaluate trauma, drug intoxication, or brain damage.
- The EEG may also be used to monitor blood flow in the brain during surgical procedures.
- The EEG cannot be used to measure intelligence 😊



Most Significant Primitives



- **Spike and Wave:** ... describe.....

.....

- **GPED Triphasic:** ... describe

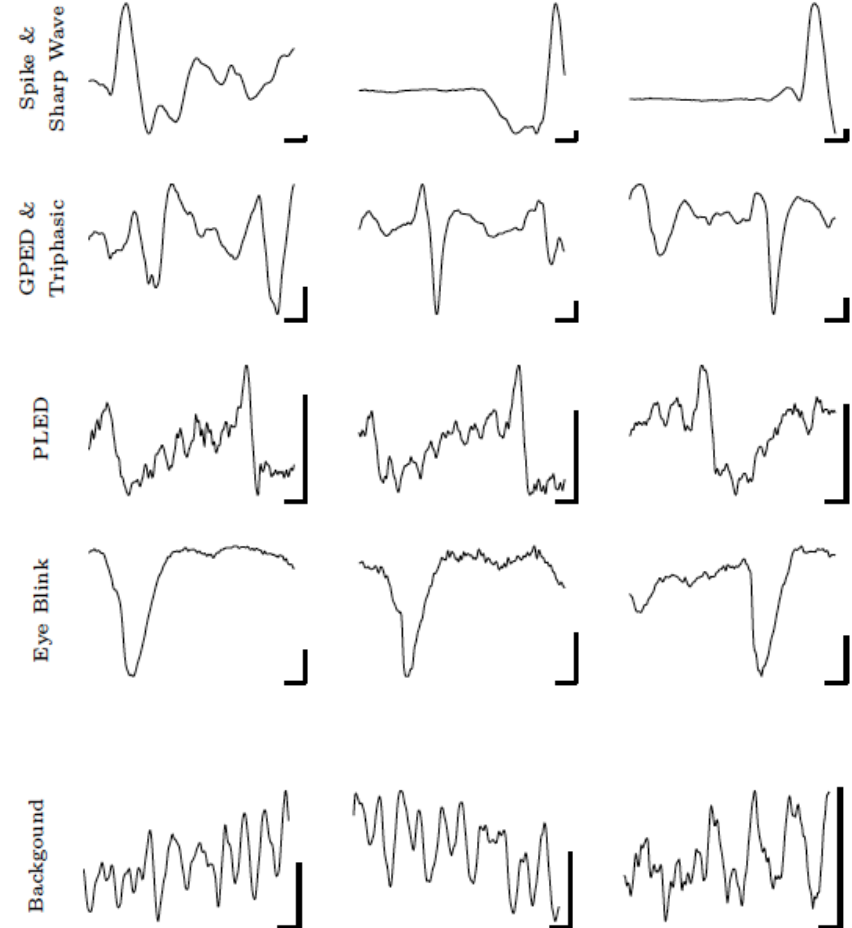
.....

- **PLED:** ... describe

.....

- **Eye Blink:** ... describe why

.....



- **Background:** models all other artifacts not included in the above categories.

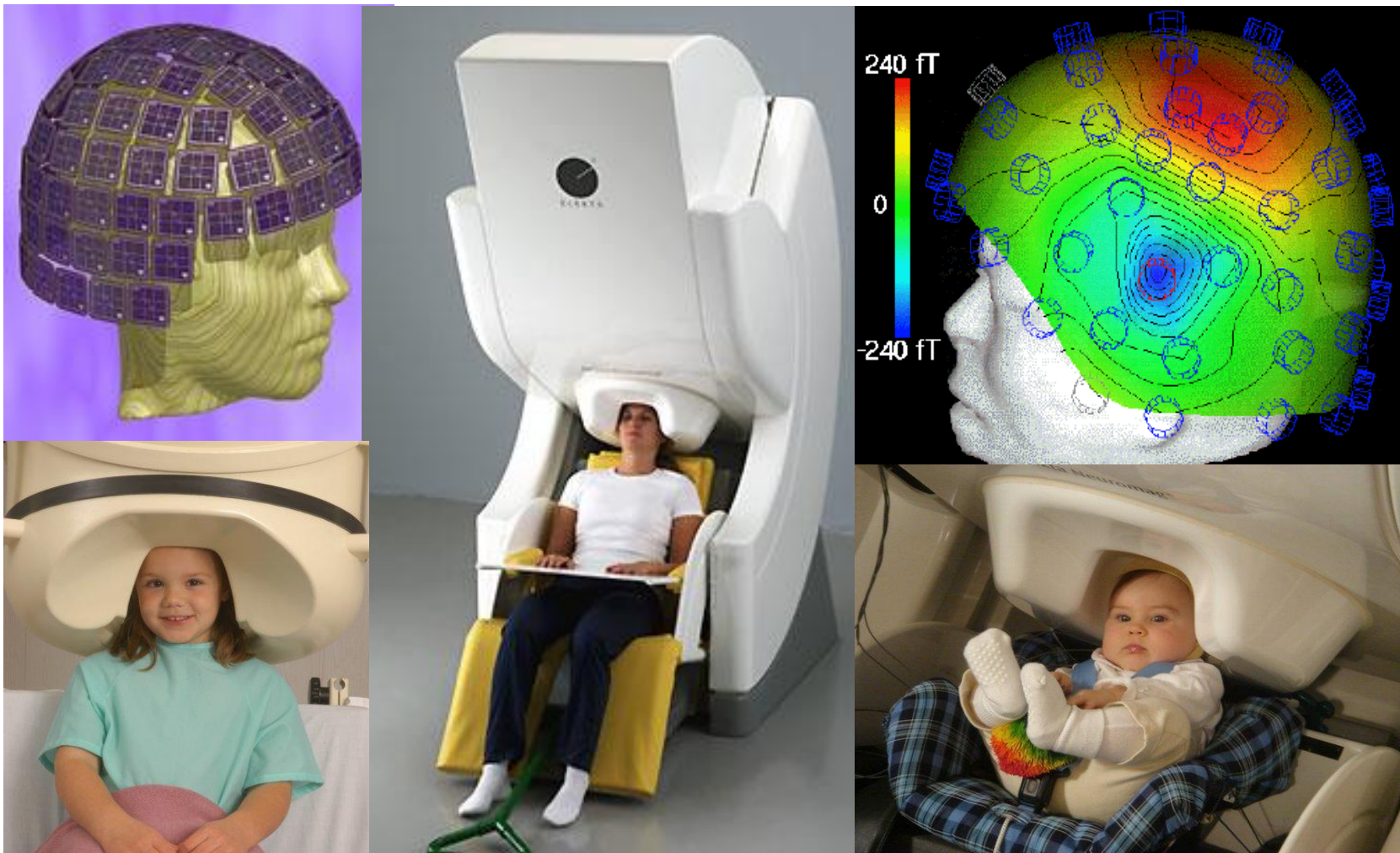
- Though there are some variations in these signals for infants whose brains are not fully developed, the basic composition of these signals is relatively age and subject invariant.



Other Primitives



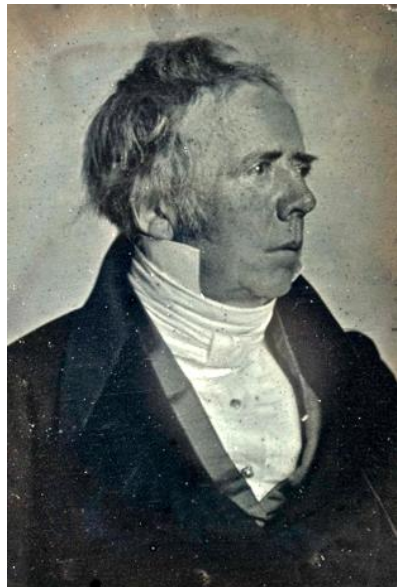
Name	Acronym	Definition
Electrographic Seizure	N/A	Rhythmic discharge or spike and wave pattern with definite evolution in frequency, location or morphology lasting at least 10 sec
Periodic Epileptiform discharges	PED	Repetitive sharp waves, spikes, or sharply contoured waves at regular or nearly regular intervals and without clear evolution in frequency or location
Periodic Lateralized Epileptiform discharges	PLED	Consistently lateralized PED
Generalized PED	GPED	Bilateral and synchronous PED with no consistent lateralization
Bilateral PLED	BiPLED	PLED occurring bilaterally, but independently and synchronously
Triphasic Waves	N/A	Generalized periodic sharp waves or sharply contoured delta waves with triphasic morphology, at 1-3 Hz, with/without anterior-posterior or posterior-anterior lag
Frontal Intermittent Rhythmic Delta Activity	FIRDA	Moderate- to high-voltage monorhythmic and sinusoidal 1-3 Hz activity seen bilaterally, maximal in anterior leads, no evolution



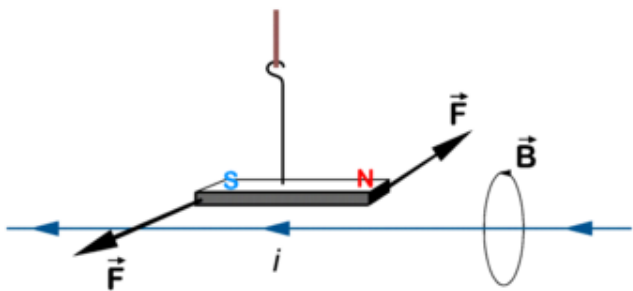
Magnetoencephalography (MEG)



Electromagnetism



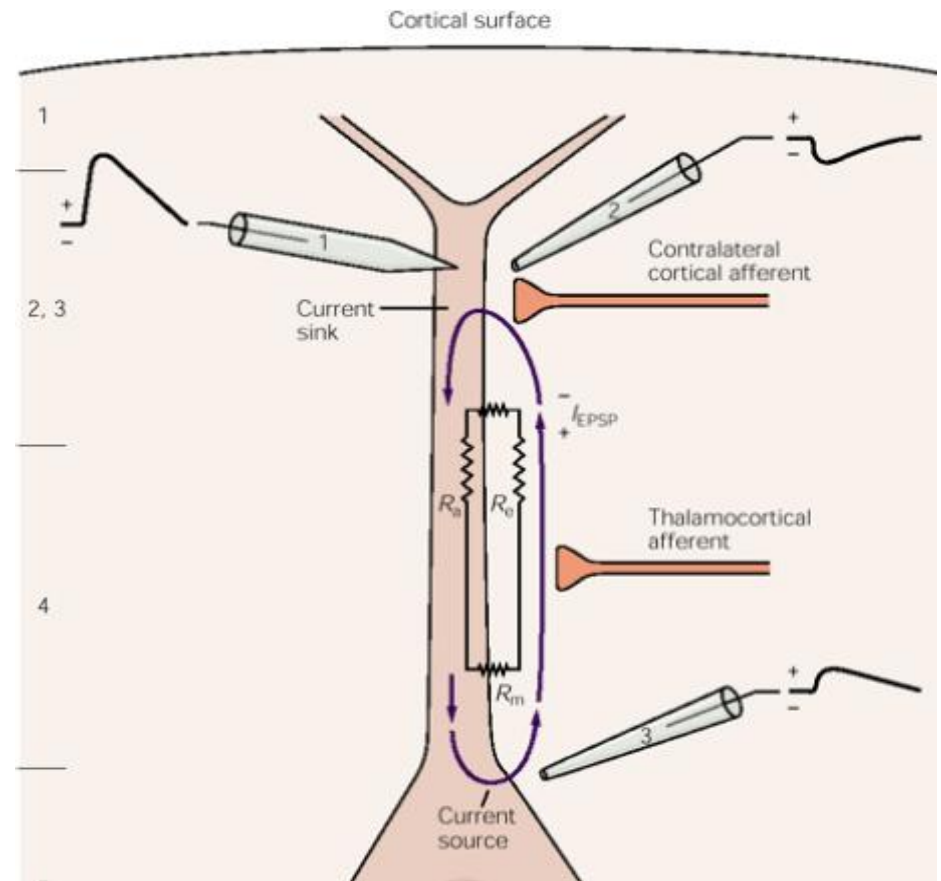
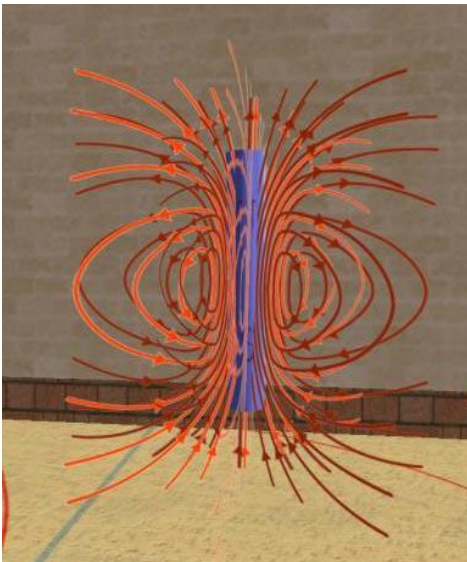
- Hans Christian Orsted (1777 – 1851)
- Current passing through a circuit affects a magnetic compass needle (1819)





Electromagnetism (2)

- An electrical dipole is always surrounded by a corresponding magnetic field
- The polarity of the field is determined by the direction of the current



- Apical dendrites of pyramidal cells also act as dipoles (more of this later...)

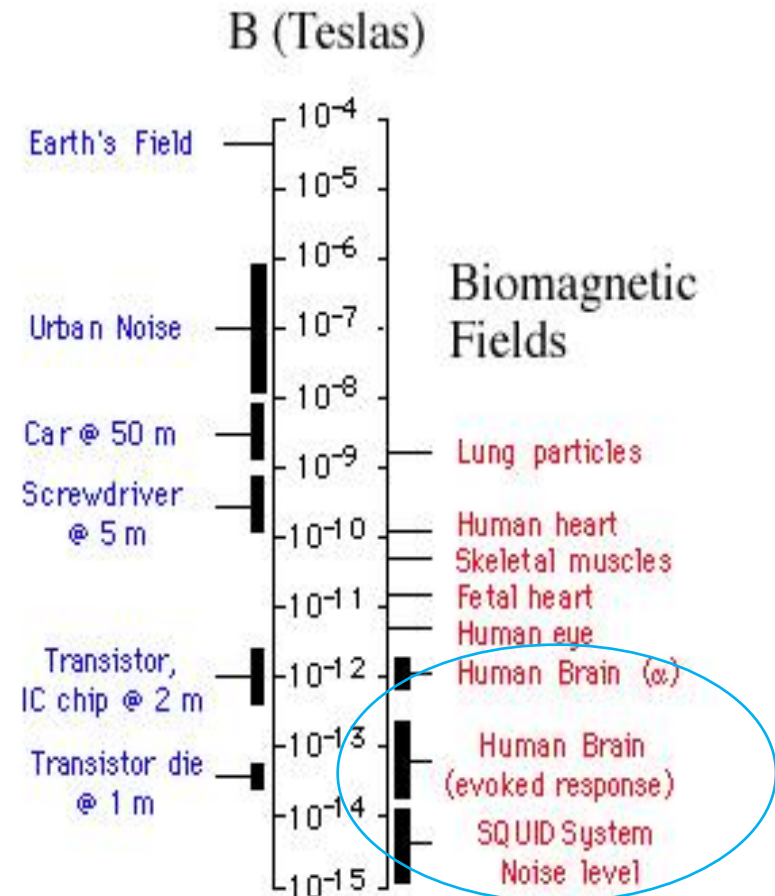


Biomagnetic Fields



But...

- The magnetic fields generated by the brain are minute: 100 million times weaker than the earth's magnetic field, one million times weaker than the magnetic fields generated by the urban environment.
- By way of contrast, MRI scanners generate a magnetic field of between 3 to 3.5 tesla.





Early Recordings of Biomagnetic Fields

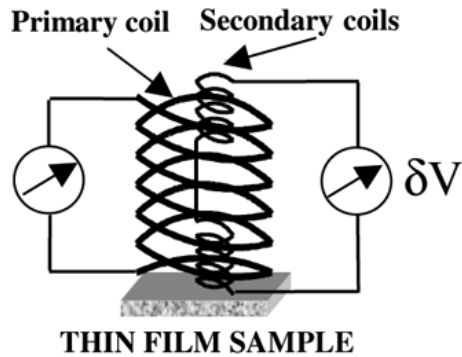
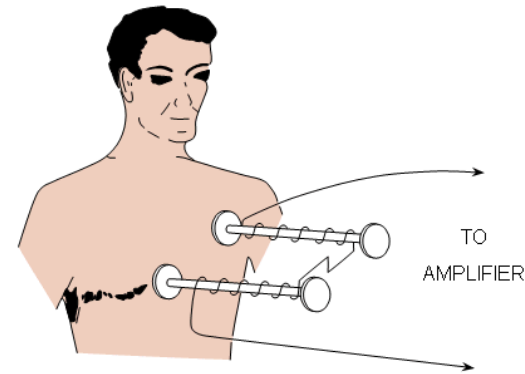


Figure 3. Screening method in the reflection technique, where an excitation coil (primary) coaxially surrounds a pair of counter-wound pick up coils (secondaries).



- First recording of biomagnetic field generated by the human heart (Gerhard Baule and Richard Mcfee, 1963)
- Two copper pick-up coils twisted round a ferrite core with 2 million turns.
- The two coils were connected in opposite directions so as to cancel out the background fluctuations. Never the less, they had to conduct their experiment in the middle of a field because the signal was still very noisy.
- A group working in the Soviet Union (Safonev et al, 1967) produced similar results but in a shielded room: reduced background noise by a factor of 10.
- Thermal noise was limiting in the use of copper.



1968

- David Cohen and colleagues make measurements using a copper induction coil in a magnetically shielded room in University of Illinois.
- Measurements were too noisy for useful analysis

Two key problems:

1. Sensors sensitive enough to record tiny changes in magnetic flux
2. Eliminate 'noise' from other environmental fluctuations in flux



Superconductivity

- When cooled to -269°C , solid mercury suddenly lost all resistance to the flow of electric current (Heike Onnes, 1911) .

“Superconductivity”

- Later found in other materials, such as tin and metal alloys.

- When two superconducting materials are separated by a thin insulating layer a ‘tunnel effect’ is produced which enables the flow of electrons - even in the absence of any external voltage. This is a Josephson Junction (Brian Josephson 1962).





Recording a Weak Signal: SQUIDS

Create a superconducting loop and measure changes in interference of quantum-mechanical electron waves circulating in this loop as magnetic flux in loop changes

Invented at Ford Research Labs in 1964/1965 by Jaklevic, Lambe, Silver, Mercerau and Zimmerman

Two types: DC and RF SQUIDS. RF squids generally used to make measurements of biomagnetism (less sensitive but much cheaper).

Niobium or lead alloy cooled to near absolute zero with liquid helium

Can measure magnetic fields as small as 1 femtotesla (10^{-15})





1972

- David Cohen, now at MIT, used one of the first SQUIDs to record a cleaner MEG signal.
- By now they had designed a better magnetically shielded room.
- Used one SQUID only, which was moved around to different positions

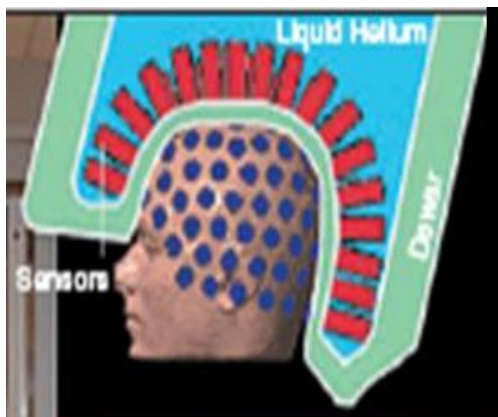
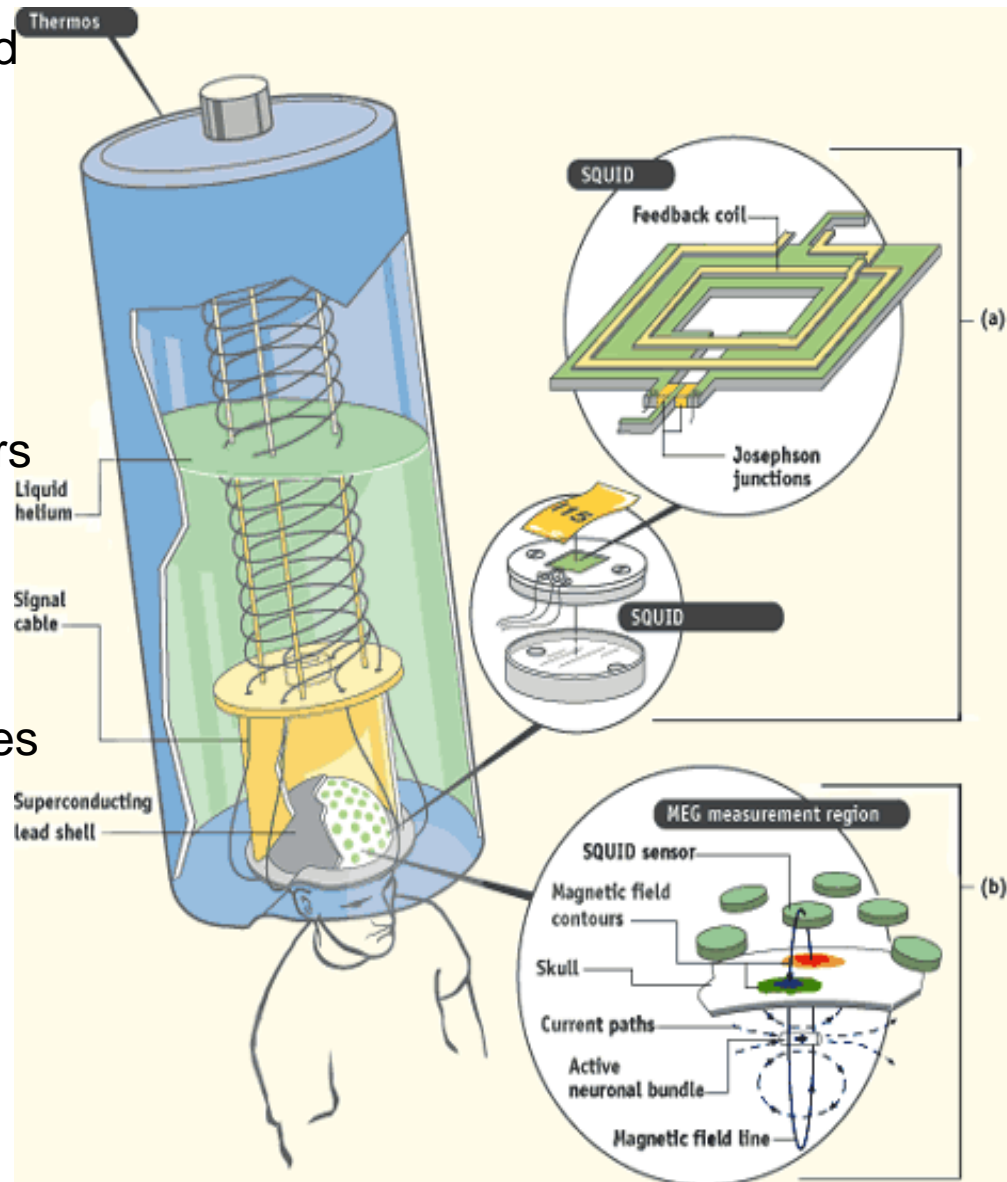


Modern MEG

Since 1980s – multiple SQUIDS arranged in arrays to allow measurement over the whole scalp surface

The helmet-shaped *dewar* of current systems typically contains around 300 sensors (connected to SQUIDS) and contains liquid helium to keep the sensors cooled enough to superconduct.

Carefully designed and constructed magnetically shielded rooms. Different metals used to shield different frequencies of magnetic interference.





Minimising Noise

Flux Transformers

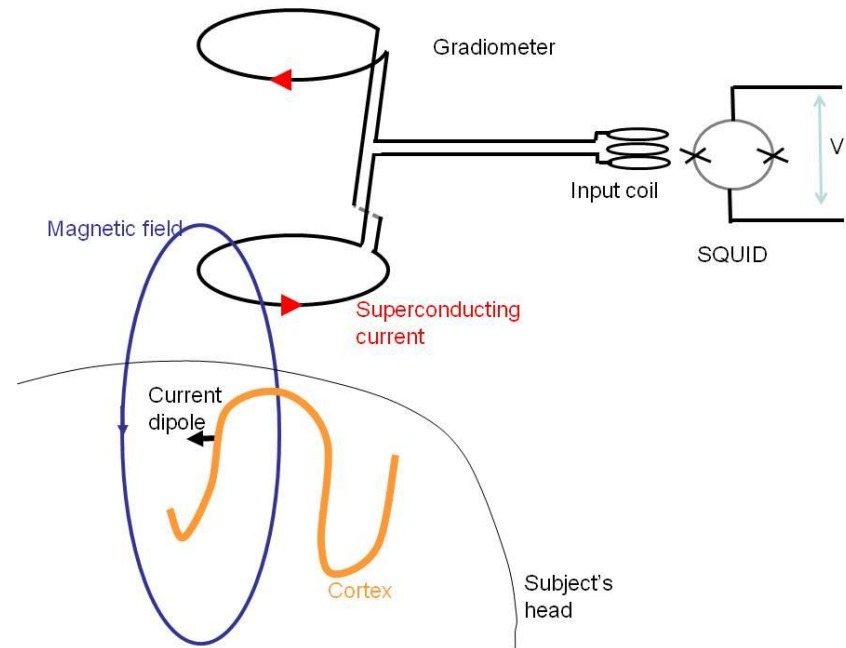
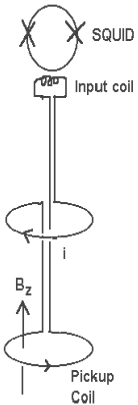
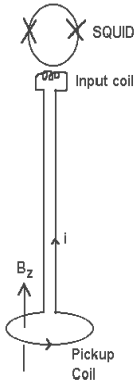
Convert changes in magnetic flux to changes in current.

Magnetometers: pick up environmental 'noise'

Gradiometers: two or more coils – magnetic interference from distant sources uniform across them while interference from close by isn't

Changes in output from gradiometer to SQUID are caused mainly by changes in flux close-by (in subject's brain).

Only a small percentage of the external noise arrives at the SQUID.



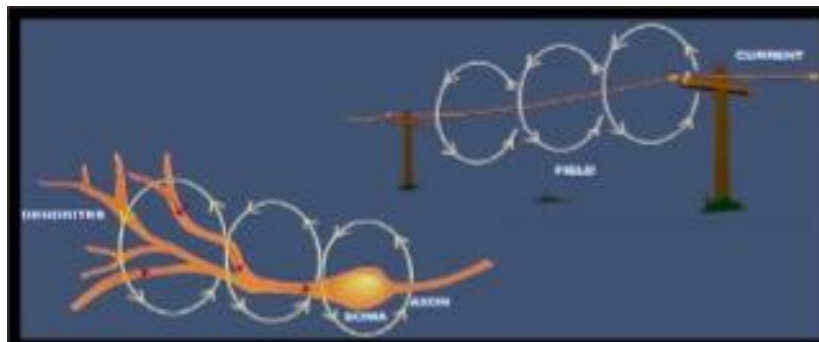
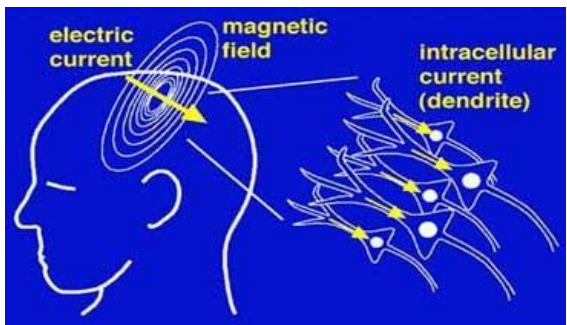


Neural Basis of the MEG Signal

Magnetic fields are produced by same electrical changes recorded by EEG
Again, the main source is post-synaptic currents flowing across pyramidal neurones... as previously described

However, there are some key differences:

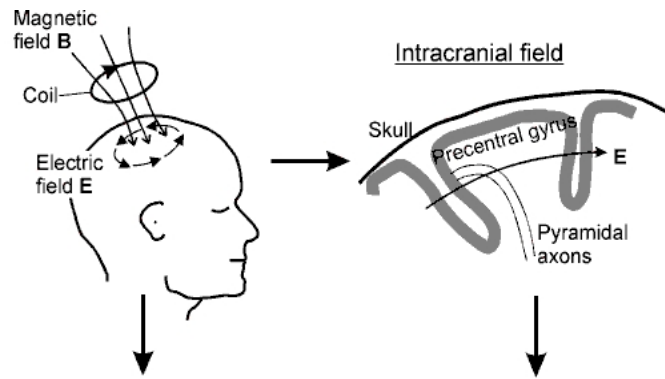
1. Magnetic field is perpendicular to current



- If the current is running parallel to the scalp the magnetic field exits the head from one side of the dipole and re-enters on the other side and so can be measured.
- But if the current is perpendicular to the scalp the magnetic field does not leave the scalp and cannot be measured.



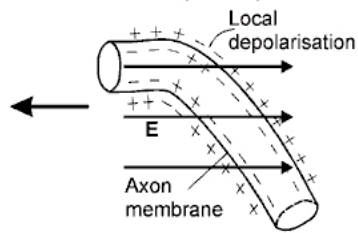
2. Differential sensitivity by brain region



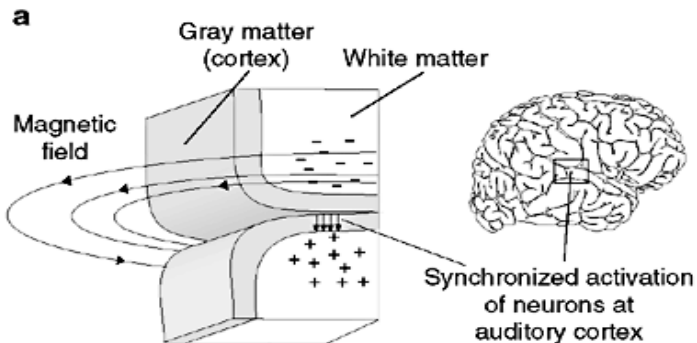
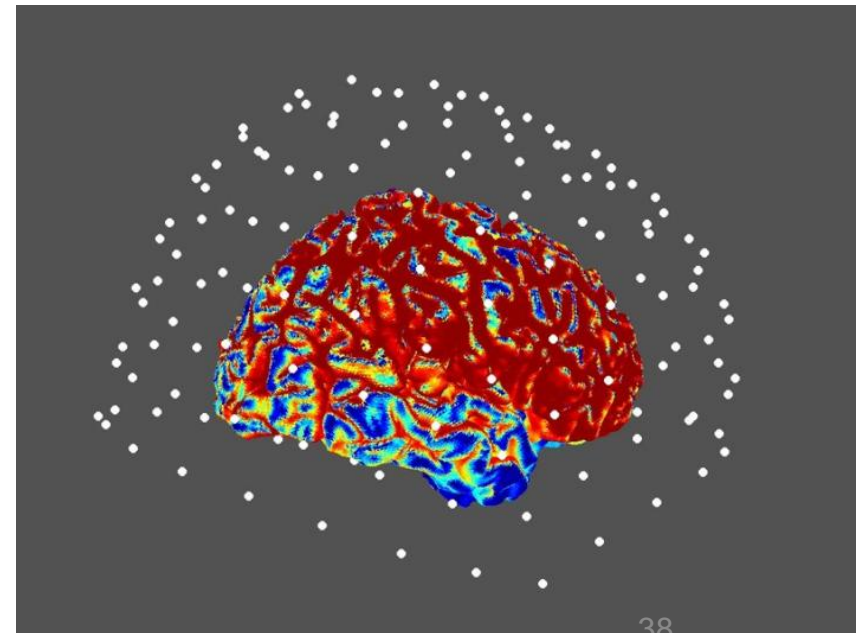
Macroscopic response

- evoked neuronal activity (EEG)
- changes in blood flow and metabolism (PET, fMRI, NIRS, SPECT)
- muscle twitches (EMG)
- changes in behaviour

Microscopic response

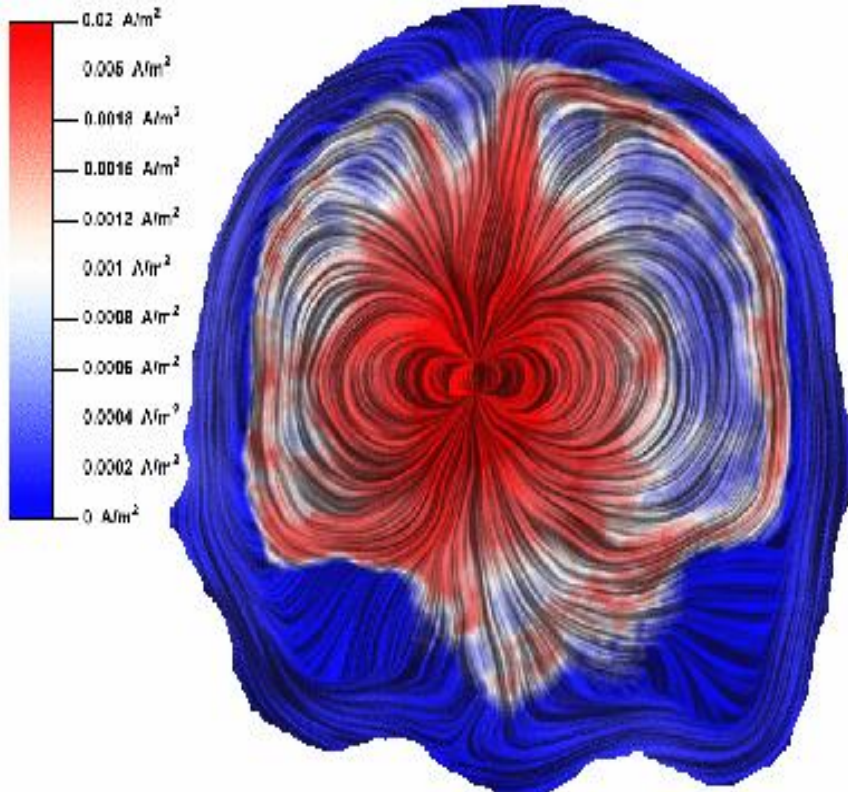


- MEG is more sensitive to activity of pyramidal cells in the walls of the sulci.
- MEG registers no information from radially aligned axons (unlike EEG)
- MEG signal decays more quickly with distance (in proportion to distance²) so problems recording deep (subcortical) areas





3. MEG signal is less distorted by skull/scalp anatomy



Bone is transparent to magnetism and magnetic fields are not smeared by the resistance of the skull.

Accurate reconstruction of the neuronal activity that produced the external magnetic fields therefore requires simpler models than with EEG

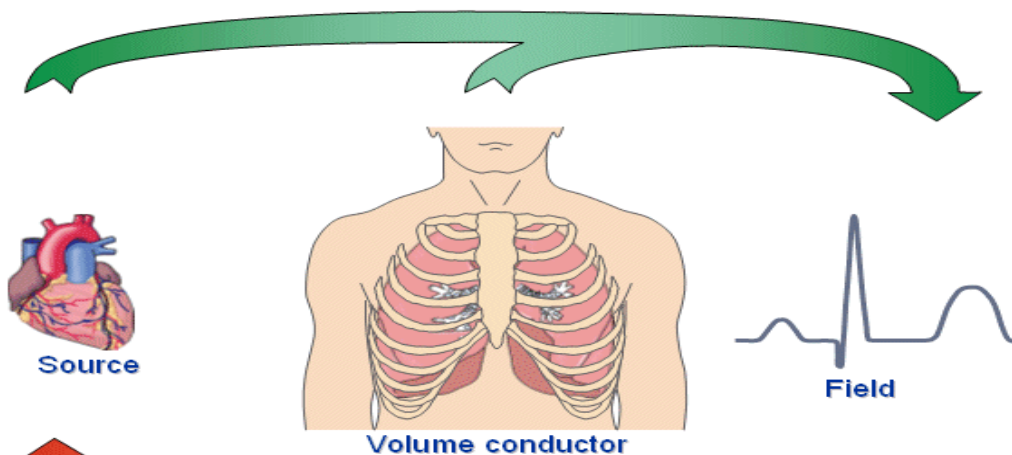


4. Different problems of source localisation

Differences discussed in last slide mean that we can make stronger inferences about the origin of the signals in MEG.

The Forward and Inverse Problems

To determine the **FIELD** from the known source and conductor is called the **FORWARD PROBLEM**



To determine the **SOURCE** from the known field and conductor is called the **INVERSE PROBLEM**



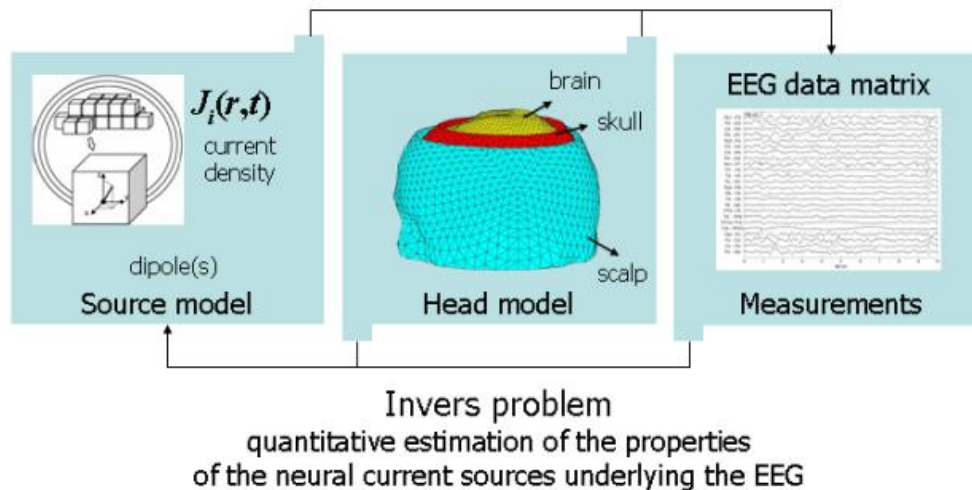
The Forward and Inverse Problems



EEG source analysis: forward and inverse problem

Forward problem

computation of the scalp potentials for a set of neural current sources



1. Forward modelling generates expected signal
2. Compare model to actual recorded signal
3. Use difference between the two to work backwards and refine understanding of where signal comes from

Forward Modelling:

1. Dipolar source models – can explain many configurations of electrical current caused by groups of neurones and measured at ~ 2cm
2. Volume conductor models – modelling effects of cranial anatomy (simpler for MEG).



The Inverse Problem

A given magnetic field recorded outside head could have been created by an enormous number of possible electrical current distributions

→ Theoretically ill-posed as there are many possible solutions

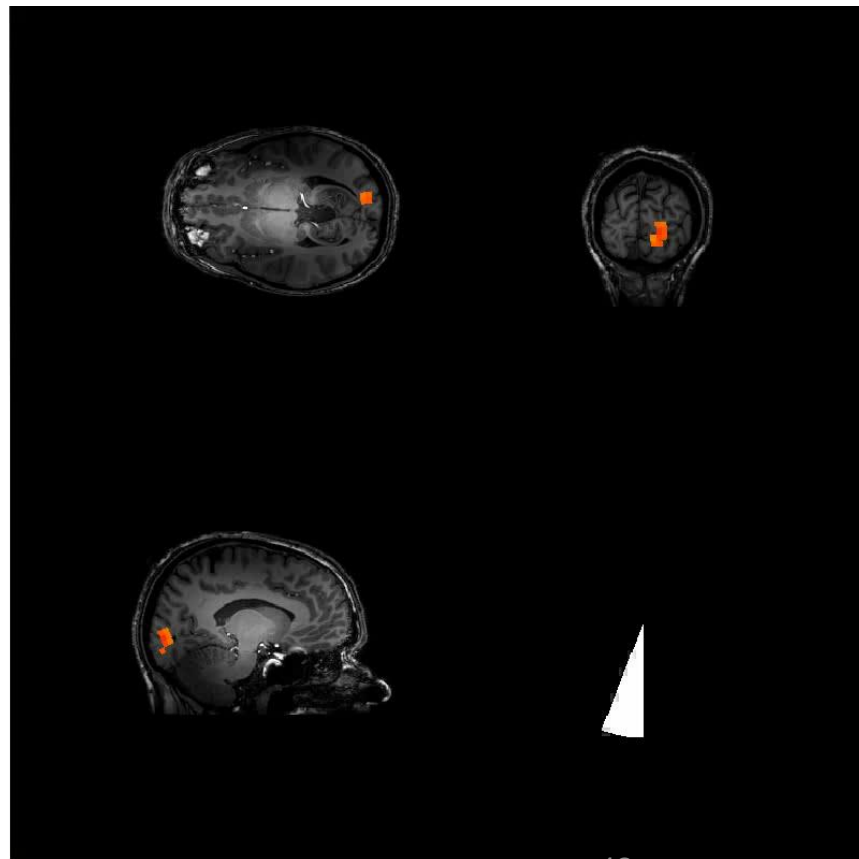
Source localisation models require assumptions about brain physiology to make the problem soluble

Many algorithms of source reconstruction exist. This will be covered in a future talk...

Dipole Fitting

Minimum norm approaches

Beamforming



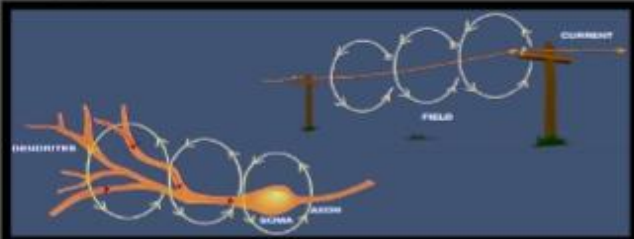


MEG: Overview

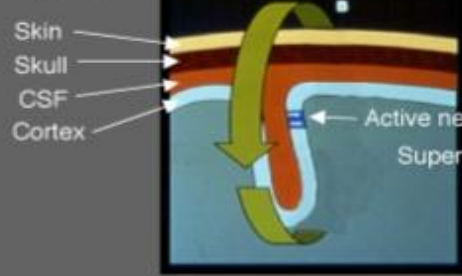


Basic Principles of MEG

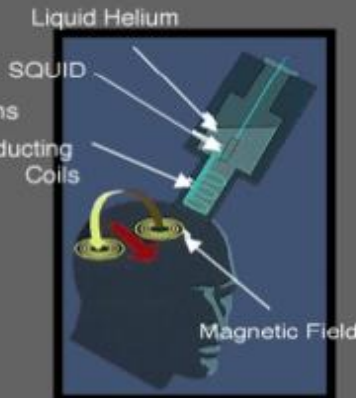
Sources of Magnetic Fields



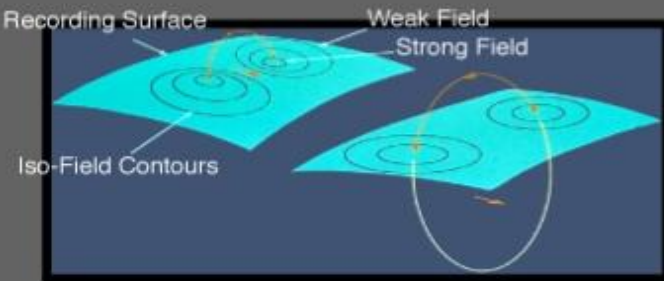
Orientation of Neurons



Detection Device



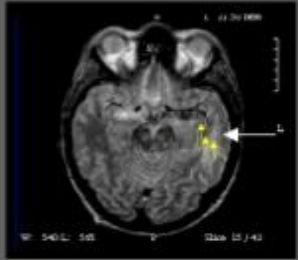
Magnetic Field Pattern



Model



Result



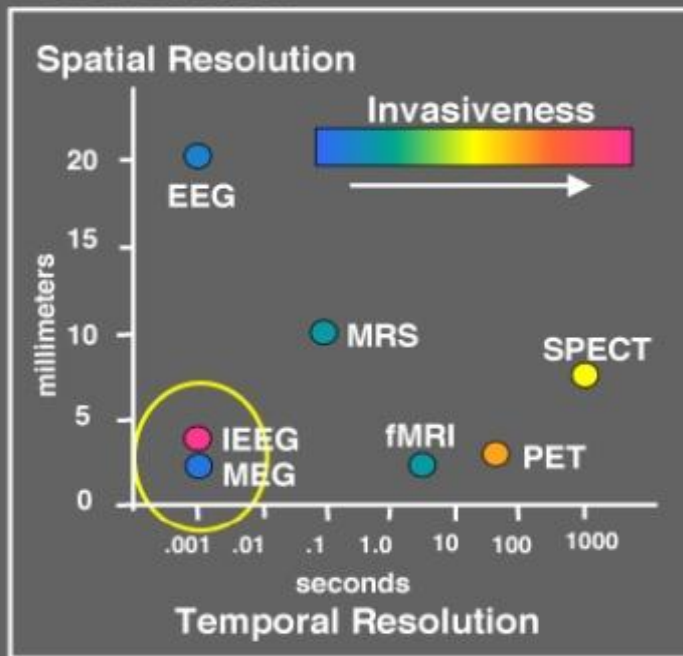


Advantages/Disadvantages of MEG

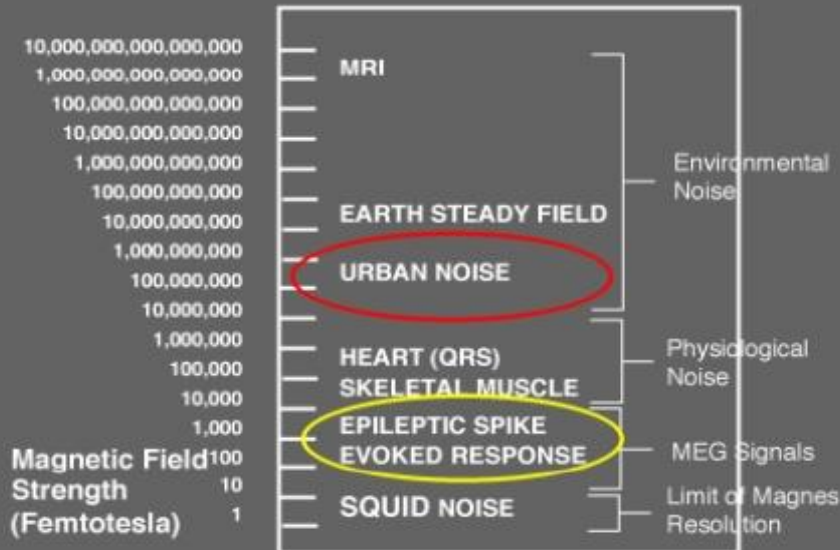


Properties of MEG

MEG Provides High Spatial and High Temporal Resolution



Strengths of Biological and Environmental Magnetic Fields





EEG vs. MEG

EEG

- Cheap
- Large Signal (10 mV)
 - Signal distorted by skull/scalp
- Spatial localization ~1cm
- Sensitive mostly to radial dipoles (neurones on gyri)
 - Allows subjects to move
- Sensors attached to head
 - Can be done anywhere

MEG

- Expensive
- Tiny Signal (10 fT)
- Signal unaffected by skull/scalp
- Spatial localization ~1 mm
- Sensitive mostly to tangential dipoles (neurons in sulci)
- Subjects must remain still
- Sensors in helmet
- Requires special laboratory with magnetic shielding

- Good temporal resolution (~1 ms)
- Problematic spatial resolution (forward & inverse problems)
- No structural or anatomical information



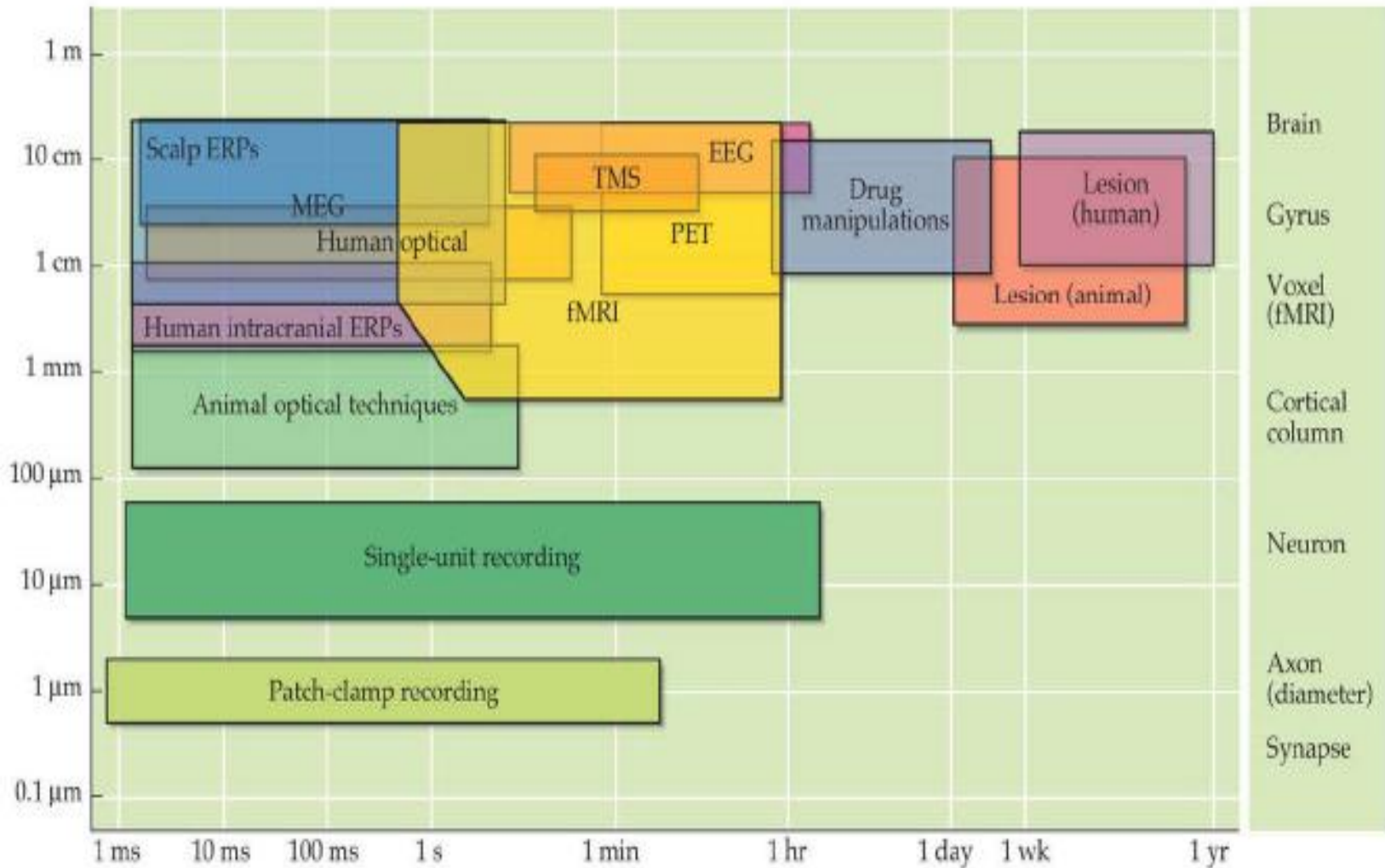
EEG vs. MEG



- The sensors do not need to come into direct contact with the scalp. Unlike EEG, MEG does not mess up your hair!
- Less preparation time, more child-friendly.



MEG/EEG and Other Experimental Approaches





ADVANTAGES OF M/EEG

- Non-invasive (records electromagnetic activity, does not modify it).
- More direct measure of neuronal function than metabolism-dependent measures like BOLD signal in fMRI
- Can be used with adults, children, clinical population.
- High temporal resolution (up to 1 millisecond or less, around 1000x better than fMRI) => ERPs study dynamic aspects of cognition.
- Allow quiet environments.
- Subjects can perform tasks sitting up- more natural than in MRI scanner

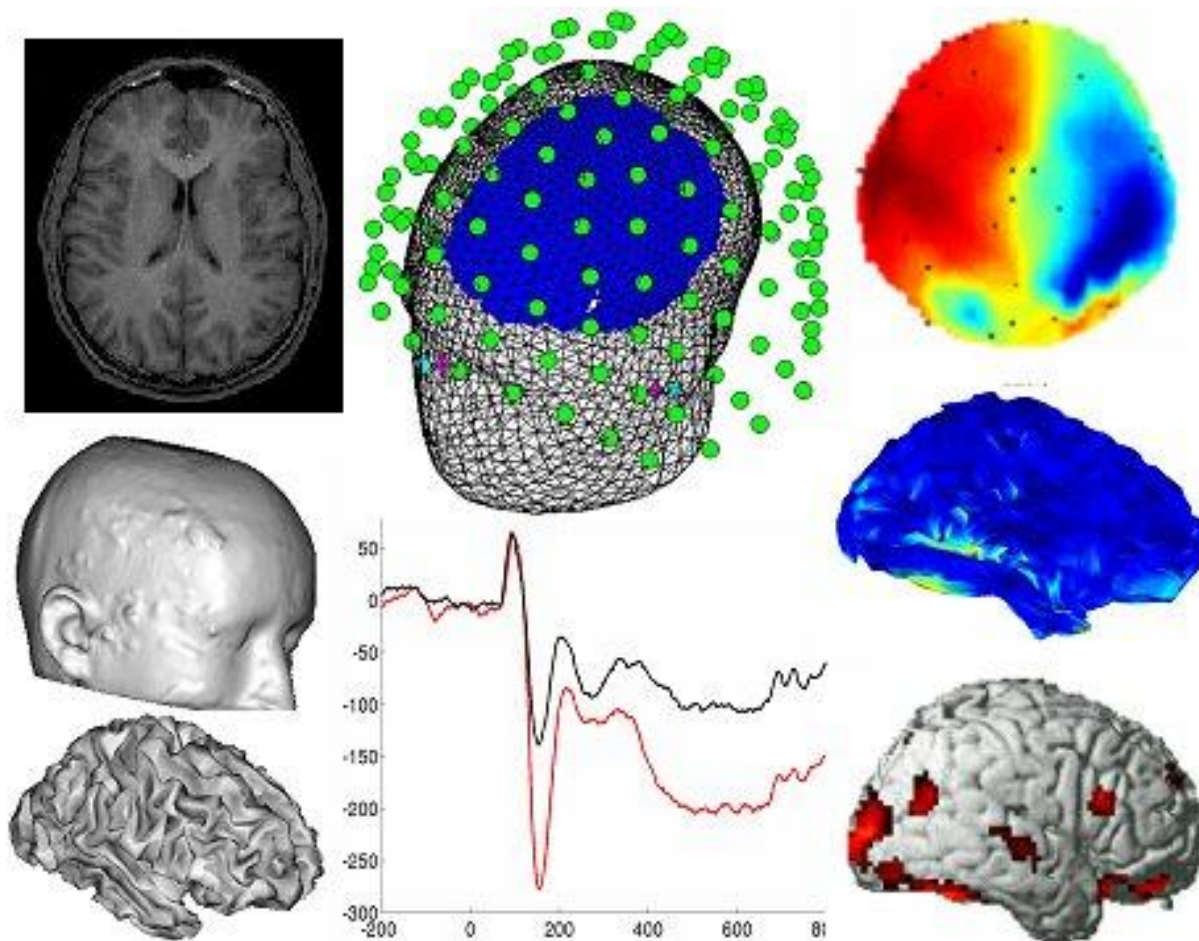
DISADVANTAGES OF M/EEG

- Problematic source localisation (forward & inverse problems)
- Limited spatial resolution (especially EEG)
- Anatomical information not provided





Multimodal Imaging





References/suggested reading

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- http://www.psych.nmsu.edu/~jkroger/lab/EEG_Introduction.html