

Introduction to MEEG

Cyril Pernet, PhD
Brain Research Imaging Centre

Overview

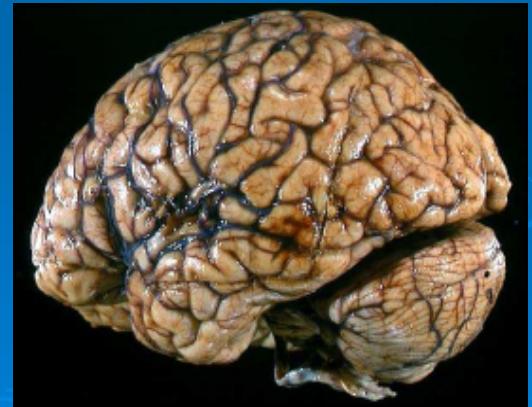
- Neurons and neuronal communication
- Various type of recordings
- MEEG: history and equipment
- Physiological principles
- Neural sources
- Data Processing

Back to basics

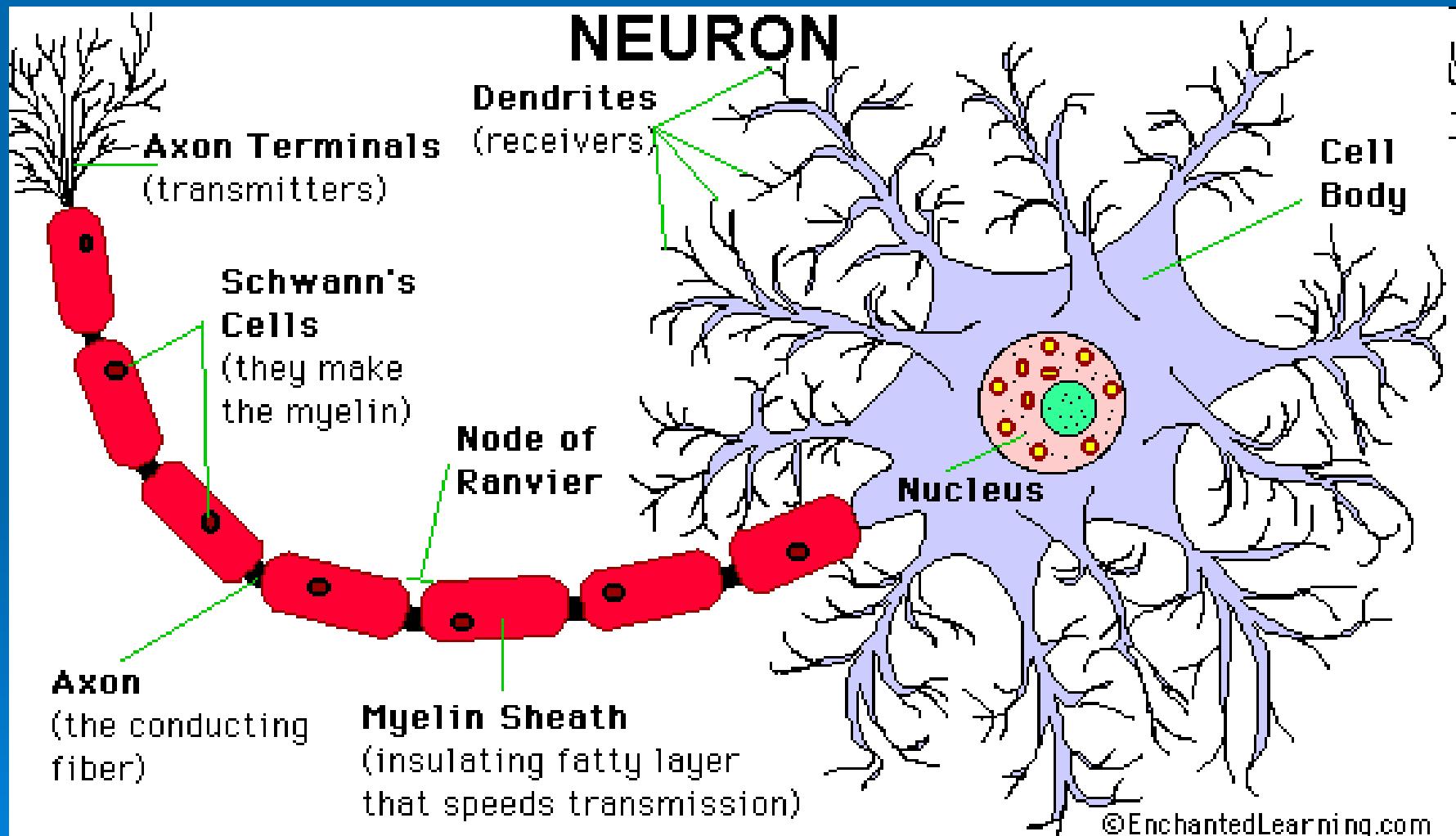
Neurons and neuronal
communication

What is the brain made of?

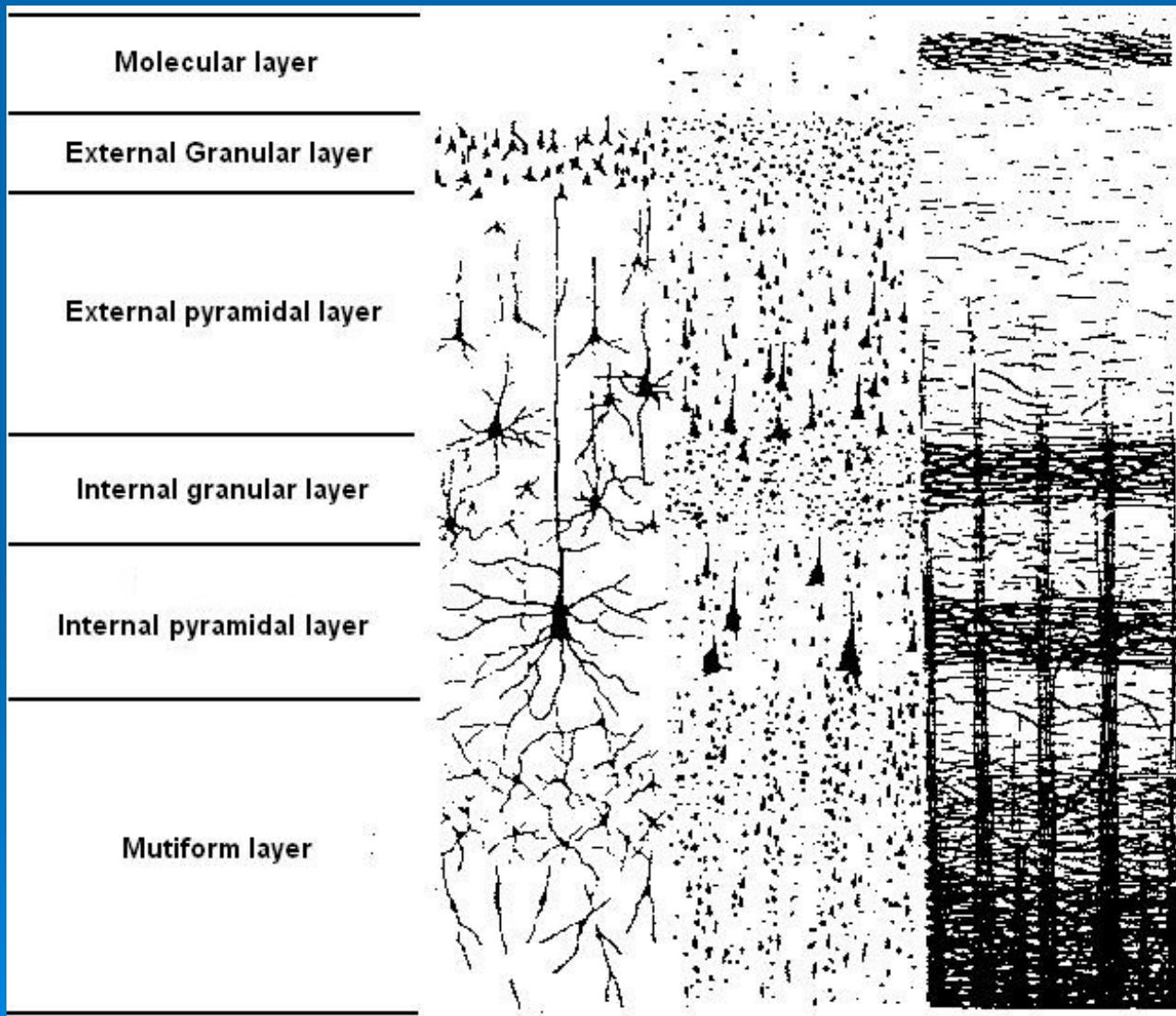
- The estimated number of neuron varies between 2.6×10^9 and 16×10^9 , with a density of 14-18 neurons in the agranular cortex to 40-100 neurons for 0.001mm^3 in the visual cortex. Despite this huge numbers, neurons make up only 10% of brain cells and about 90% of the cells are glial (microglia, astrocytes, oligodendrocytes).
- One neuron may have hundreds or thousands of synapses on its dendrites and soma and the estimated number of synapses is 100×10^{12} synapses for the human brain.



What is the brain made of?



What is the brain made of?



Neuronal communication

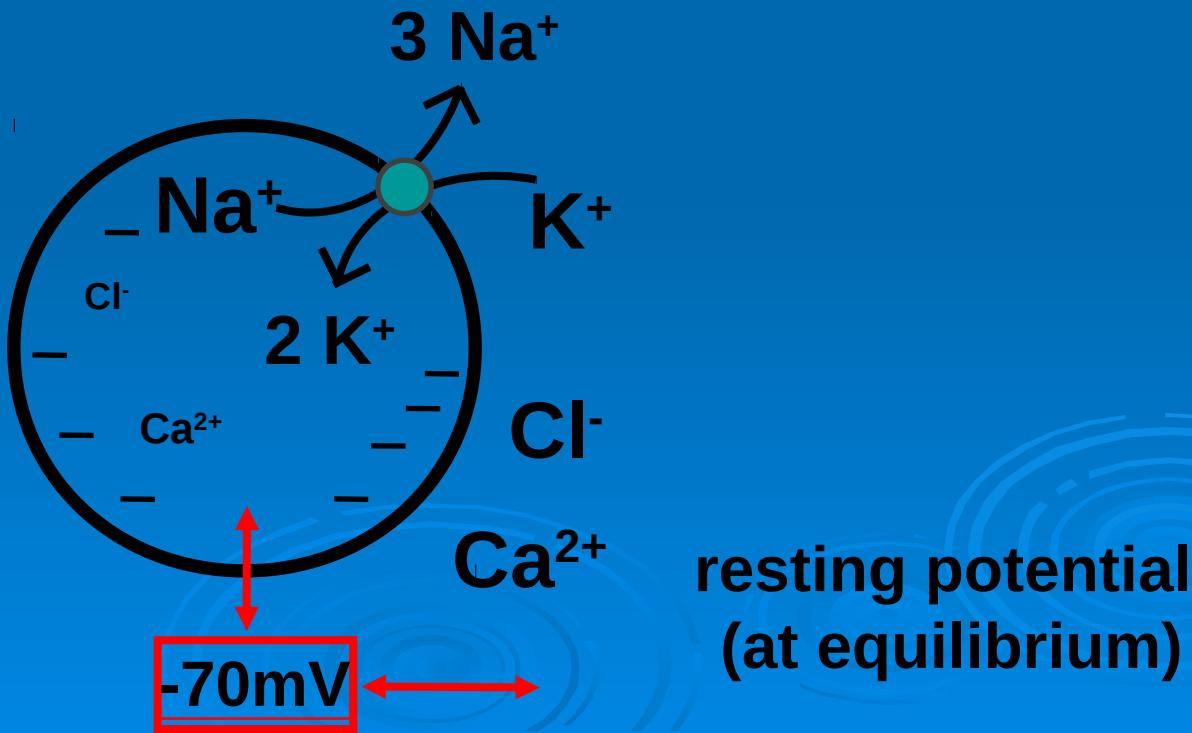
- Communication between neurons depends upon the properties of neuronal membranes.
- When substances are allowed to diffuse freely, they tend to diffuse from areas of high concentration to areas of low concentration (**osmosis law**). That is, they move along a concentration gradient until equilibrium is reached.
- Neuronal membranes are 10nm-thick liquid-crystal bilayer of phospholipids that preserve differences between the intra and extracellular environments, and thus preventing the freely diffusion of molecules.

Neuronal communication

- Neuronal membranes also have embedded proteins that form **ions channels** through which some ions, such as sodium (Na^+), chloride (Cl^-), potassium (K^+) and calcium (Ca^{2+}), can diffuse.
- To go against the concentration gradient, neuronal membranes use **selective pumps**. For example, the sodium-potassium pump uses transporter molecule that forces 3Na^+ out of the cell and picks up 2K^+ into the cell on the return trip. Due to these pumps, neurons at rest show greater concentration of K^+ inside the cell than outside and greater concentration of Na^+ , Cl^- and Ca^{2+} outside the cell than inside.
- Any transient change in the permeability of the membrane will cause an influx or an efflux of these ions as the system attempts to eliminate the **concentration gradient** and establish equilibrium.

Neuronal communication

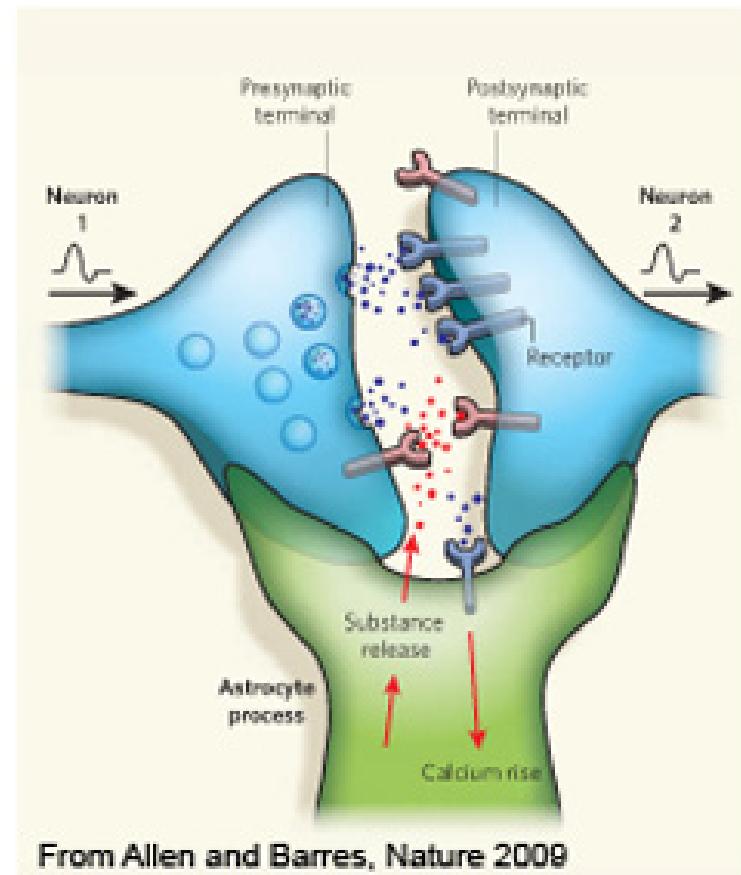
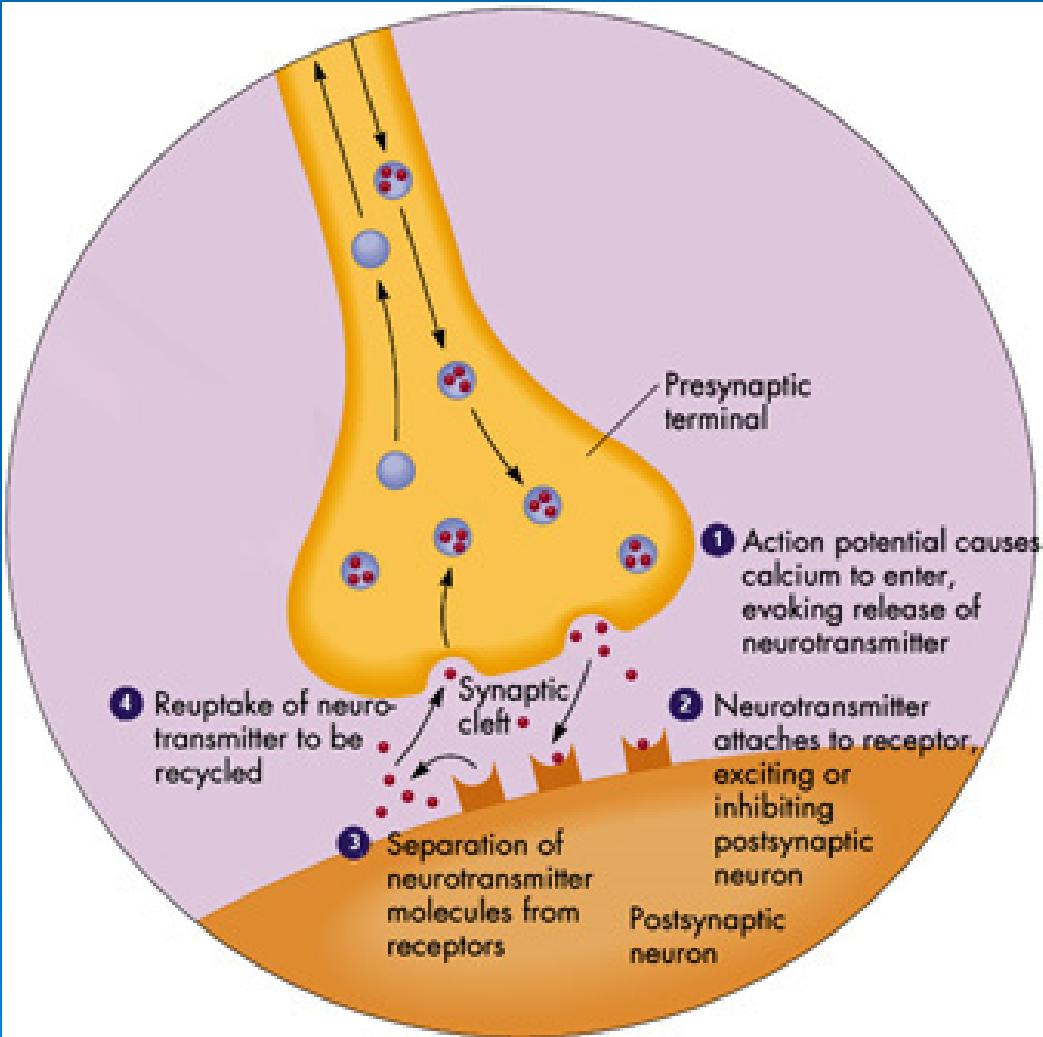
- Because ions have electrical charge, the concentration gradient creates an **electrical potential** (about -70 millivolt) between the inside and the outside of the cell. Movement of ions across the membrane are thus governed by both chemical and electrical gradients.



Neuronal communication

- The presynaptic process of the axon releases neurotransmitters in the synaptic left that interact with postsynaptic membrane receptors that gate ion channels.
- For example, the glutamate (the most common neurotransmitter ~90%) opens postsynaptic Na⁺ channels. The influx of Na⁺ decreases the electrical potential at the channels location. This local **depolarization** is referred to as an **excitatory postsynaptic potential (EPSP)**.
- Other neurotransmitters show, on the opposite, inhibitory effects. For example, the GABA (gamma aminobutyric acid) interacts with receptors to open Cl⁻ and K⁺ channels. The influx of Cl⁻ or exflux of K⁺ results in an increase in the resting potential at the channels location. This local **hyperpolarization** is referred to as an **inhibitory postsynaptic potential (IPSP)**.

Neuronal communication



From Allen and Barres, Nature 2009

Recordings of neural activity



What types of recordings?

- For intracellular recording, the electrical potential relies on the comparison between the membrane cell and the extracellular environment (~ sum EPSP*resistivity).
- For extracellular recording (close to cells), the variation of the electrical potential depends on the importance of EPSP and the resistance of the extracellular environment.
- Intracellular recording shows membrane depolarization and thus the amplitude is in millivolt, whereas for extracellular recording, the amplitude is in microvolt.
- More importantly, the intracellular recording signal is always positive whereas the extracellular recording shows **different polarities** according to the electrode position. If the electrode 'looks' at where current enters, the signal is negative, whereas if it looks at where the current leaves, the signal is positive.

What types of recordings?

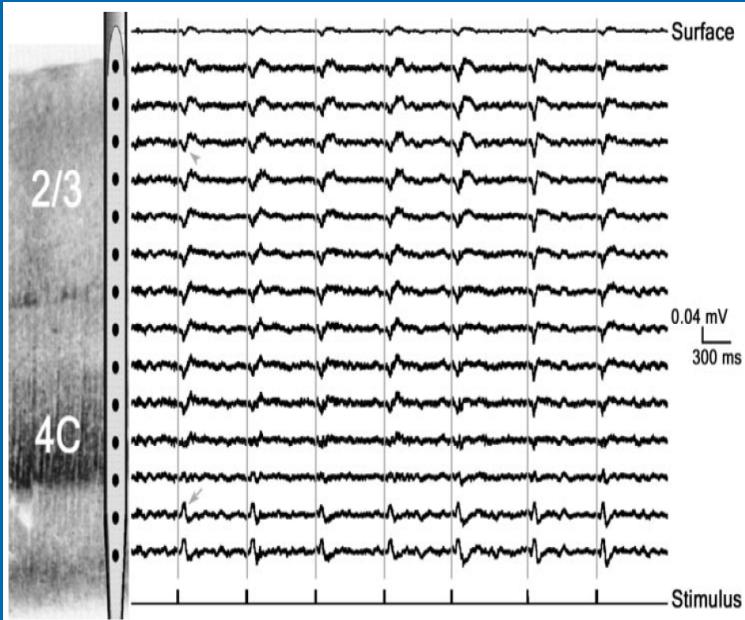
- A nanoelectrode located on the cortex record **field potentials**, i.e. the sum of extracellular potentials elicited by the synchronous firing of neurons.
- Field potential varies according to:
- The distance between the electrode and the neural population (amplitude decreases in $1/d^2$)
- The electrode position (when EPSPs arrive at the surface layers, the electrode sees positive charges 'leaving' and thus record a negative potential, whereas a deep electrode sees positive charges 'approaching' and thus record a positive potential and vice versa when EPSP arrive to the deep layers. Polarities are reversed for IPSP).

What types of recordings?

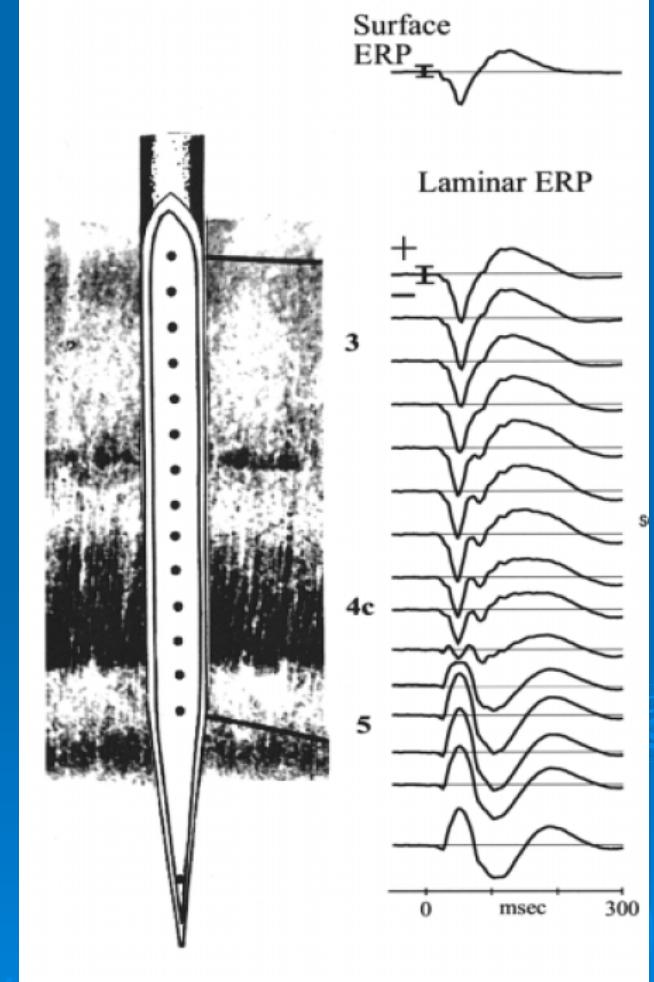
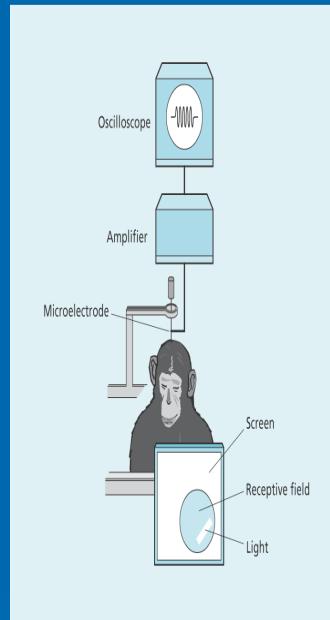
Magneto/Electro EncephaloGraphy

- The electrical activity of neuronal populations, and thus magnetic concurrent fields, can be recorded using macro-detectors on the scalp surface.
- One can distinguish primary currents (movement of ions), and volume currents (passive ohmic currents). EEG/MEG recordings correspond to the sum of ionic current in the extracellular space.
- Electric and magnetic fields provide large-scale, short-time measures of the modulations of synaptic potential fields around their background levels. They correspond directly to LFP.

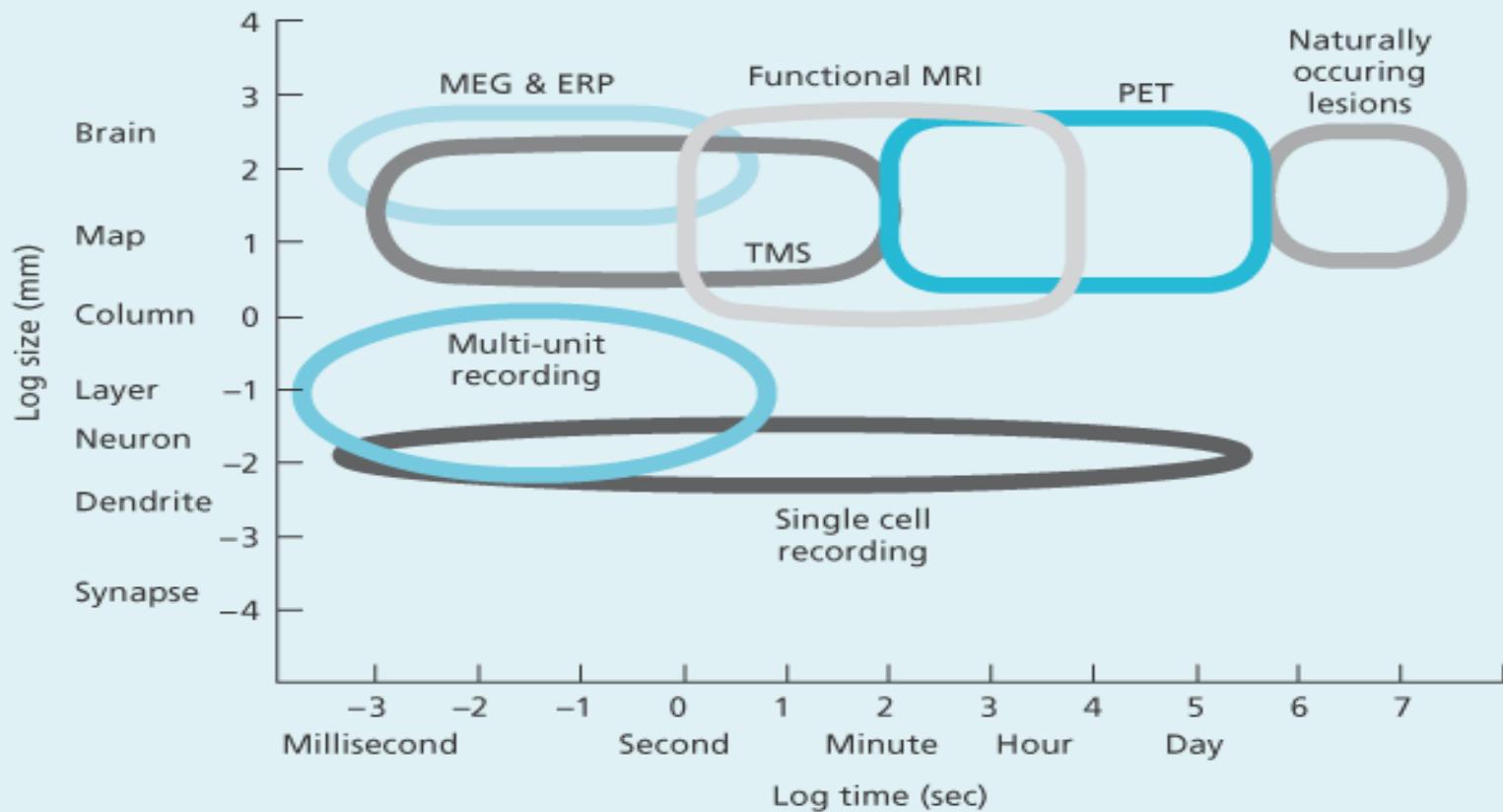
Spikes - LFP - EEG



Prominent single-trial stimulus-evoked response observed as a negative field potential above layer 4. (Hyp. 1)



Putting everything together



EEG-MEG

History and Equipment

EEG History



**neuro-psychiatrist
Hans Berger, 1929**

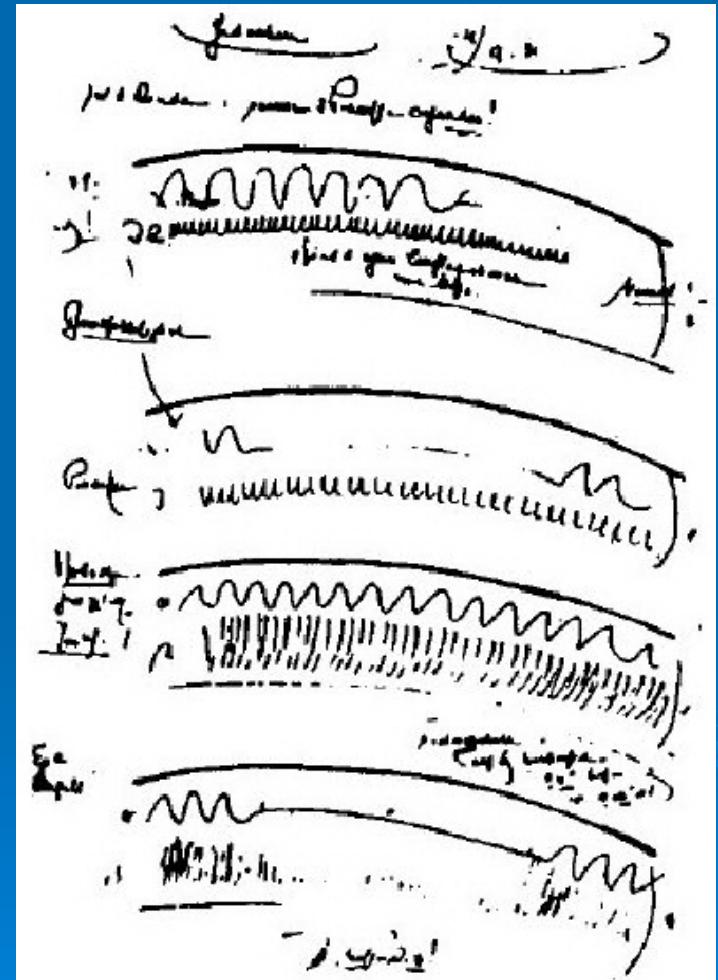


trepanned patient

subjects with eye closed:

**10 Hz => alpha waves
faster frequency => beta
waves**

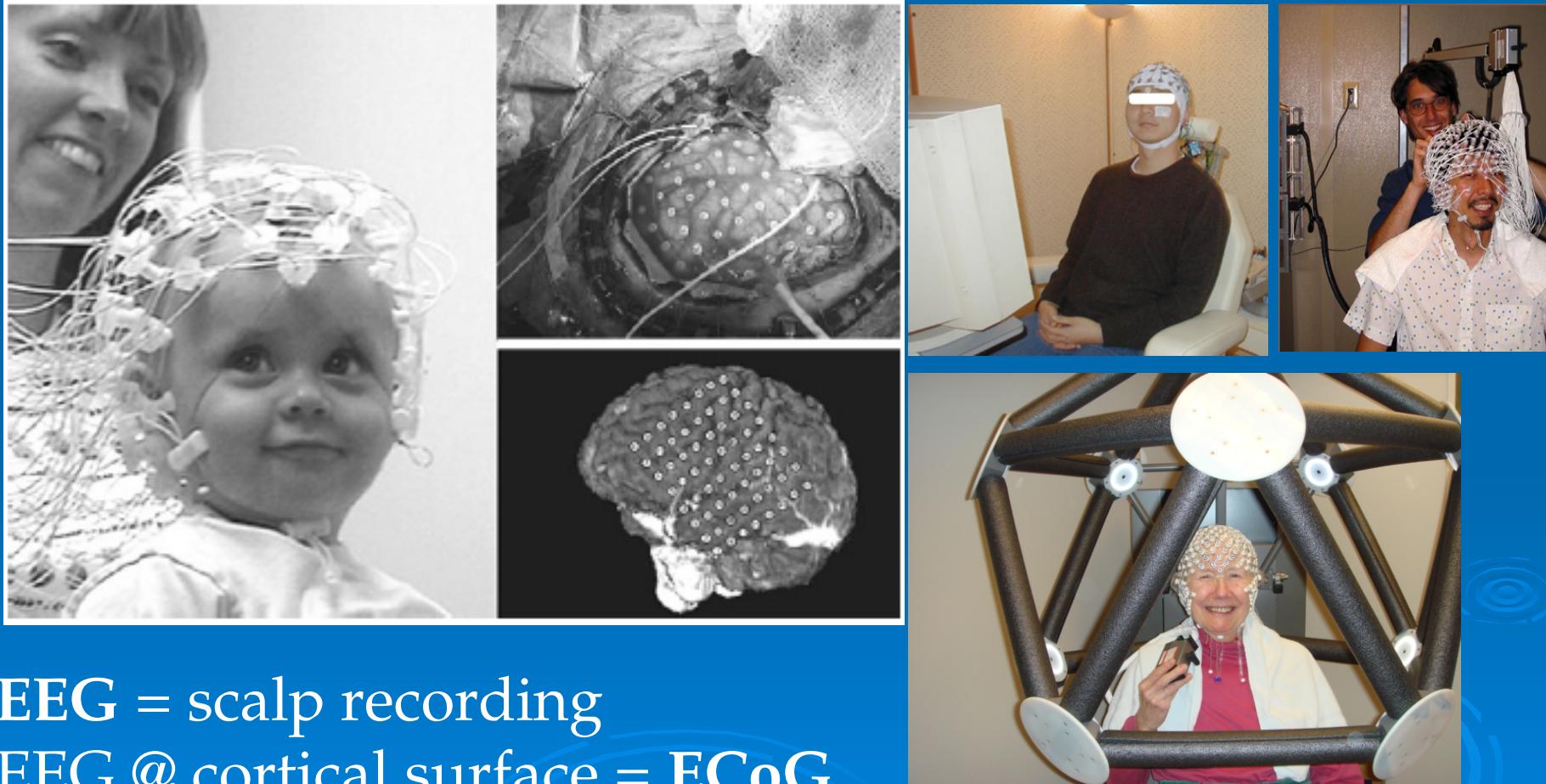
**termed the whole record:
'Elektrenkephalogram'
(EEG)**



EEG recordings

- The ElectroEncephalography method measures neuronal activity using several electrodes placed on the scalp.
- EEG recording corresponds to the electrical potential difference between two electrodes: either between one active electrode on the scalp and one reference electrode located far from the recording site, or between two active electrodes.
- EEG is correlated with arousal, sleep stages, depth of anesthesia, seizures, and other neurological disorders, cognitive processes associated with mental calculations, working memory, and selective attention

EEG systems



EEG = scalp recording
EEG @ cortical surface = ECoG
(ElectroCorticoGram)

MEG system



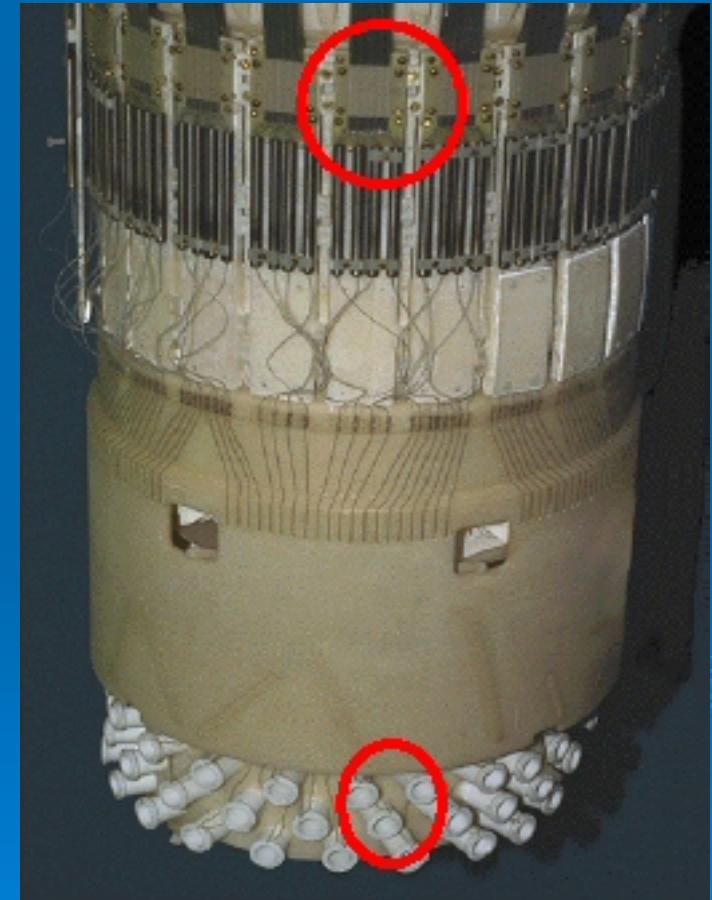
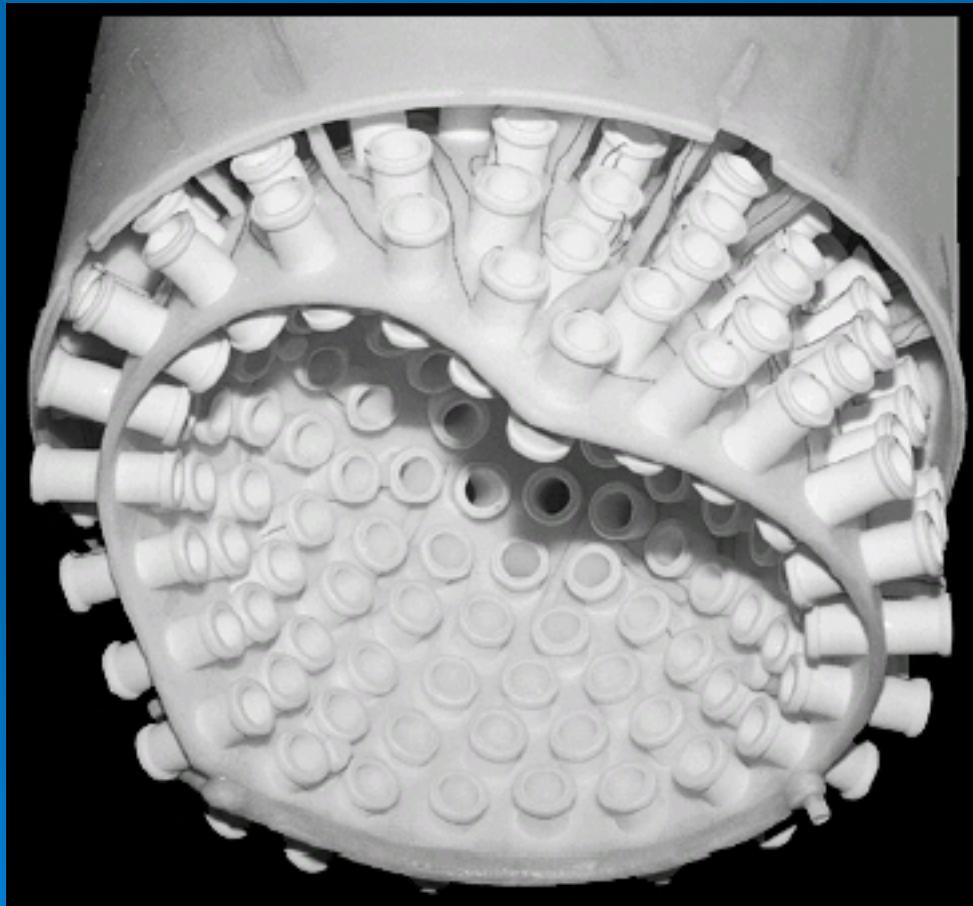
MEG measures magnetic field
signal $\sim 10^{-13}$ tesla (T)

"Brain magnetic field" = 10^9 Earth mag. field
Set of keys creates a magnetic perturbation 100-1000 > brain magnetic perturbation.

captors = SQUID coupled to magnets
(superconducting quantum interference device) - Very expensive systems

1st MEG in 1968 by Cohen, MIT

MEG system

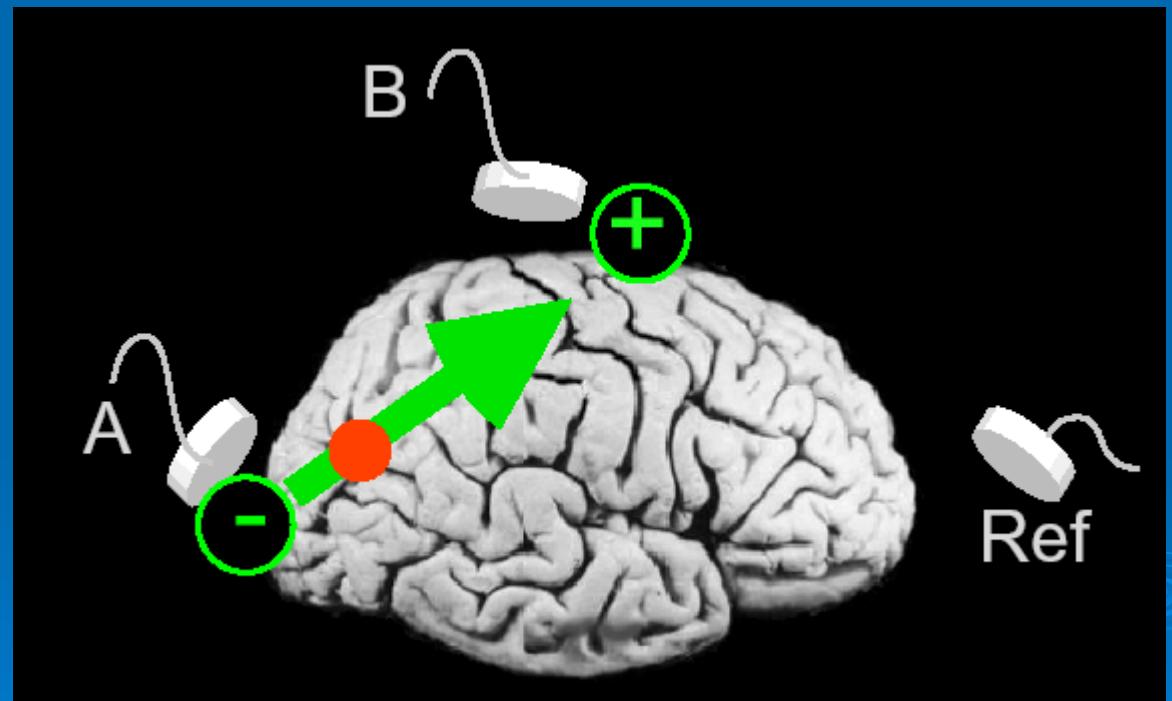


MEEG: physiological principles

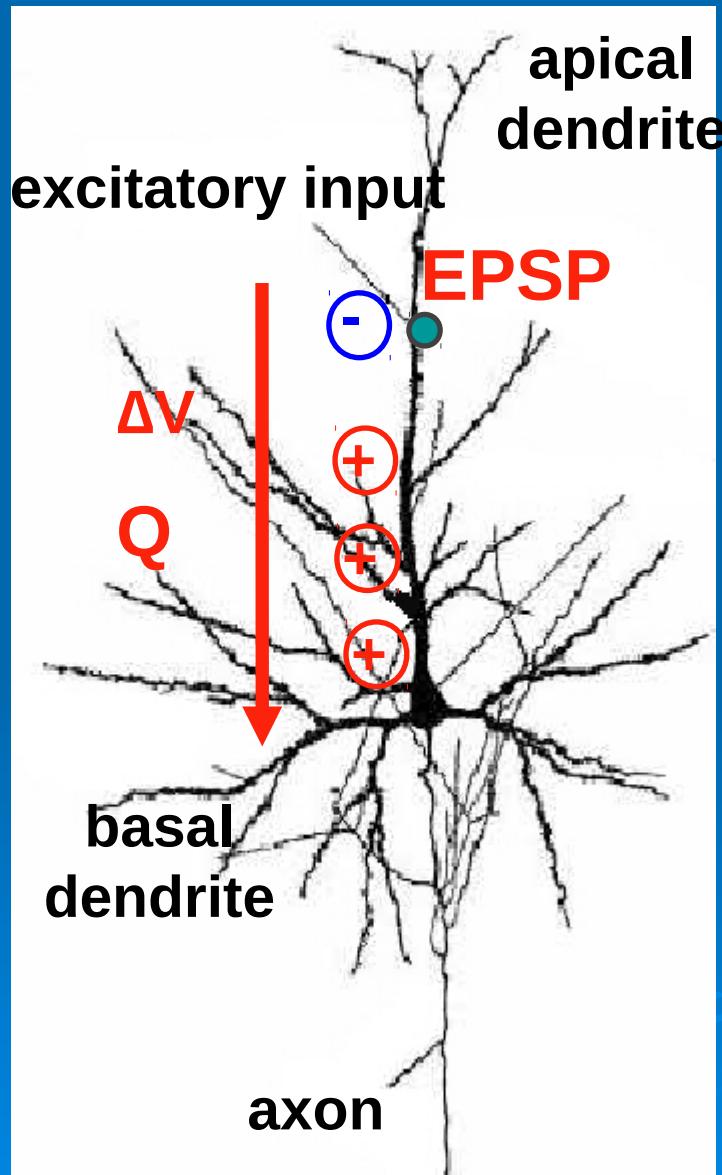
How is the signal generated?



Principle 1: The brain does not produce electricity!



Principle 2: Measure a difference



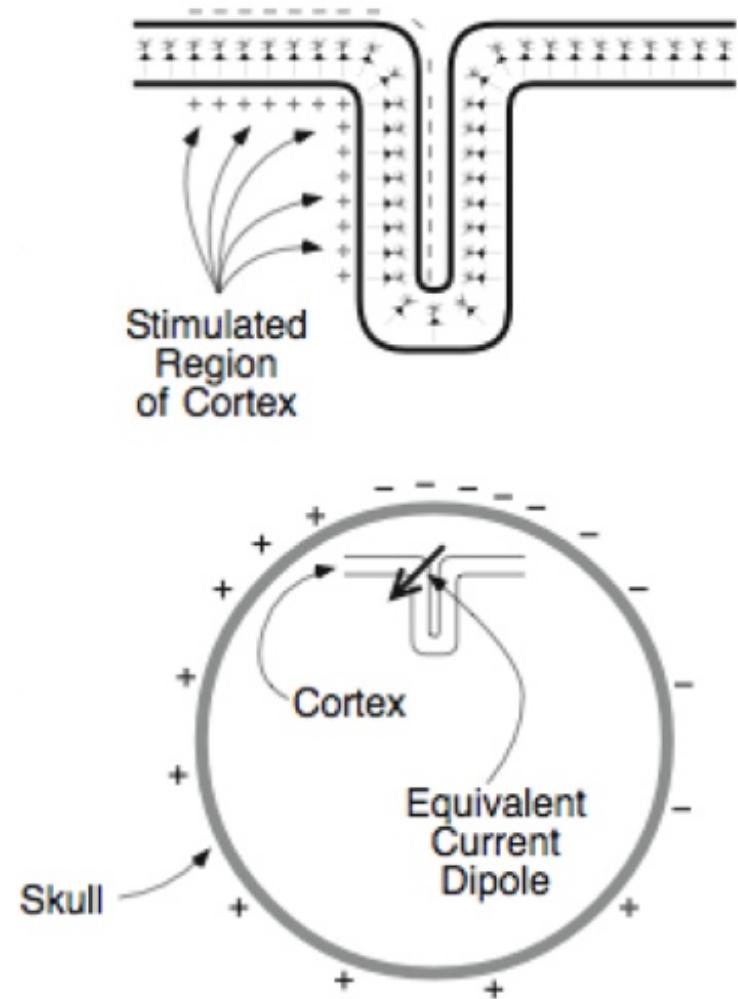
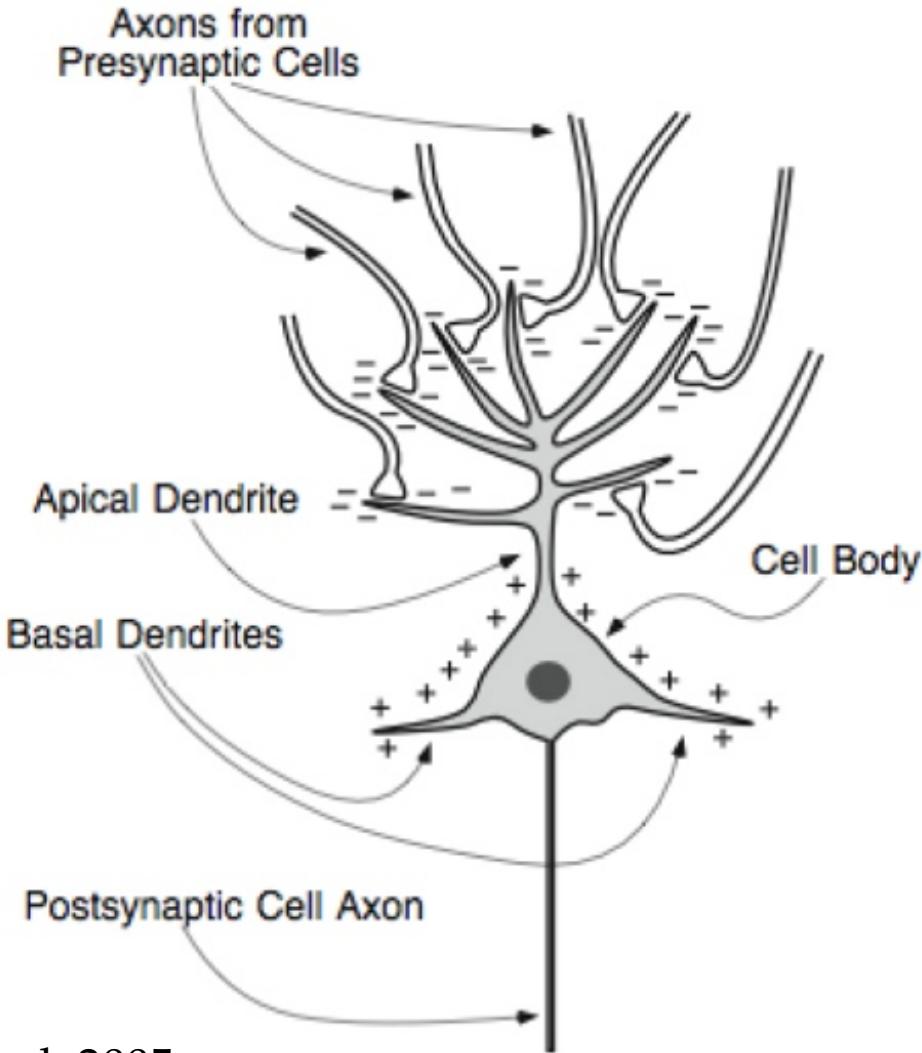
Na^+ enter the cell
= dipole with current Q

duration = 10 ms

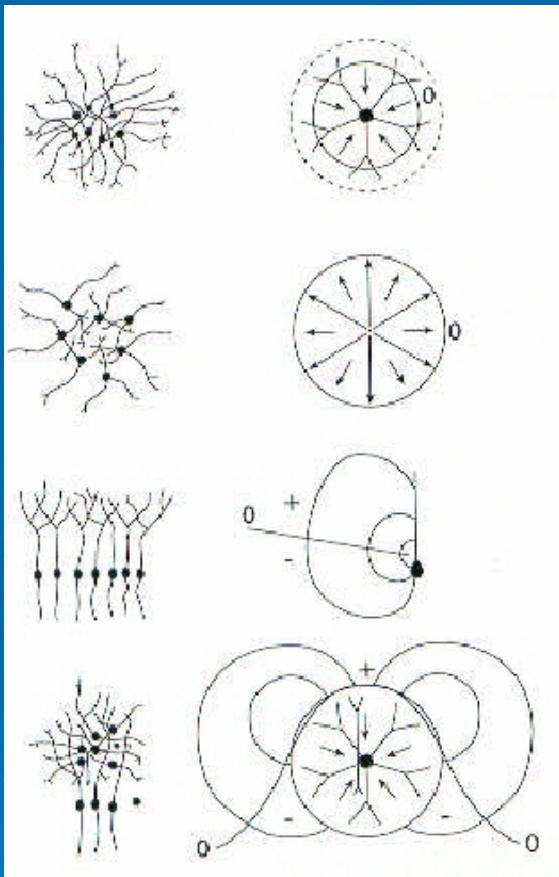
extra-cellular currents $100\text{-}1000 <$
intra-cellular currents

+ contribution from glial cells

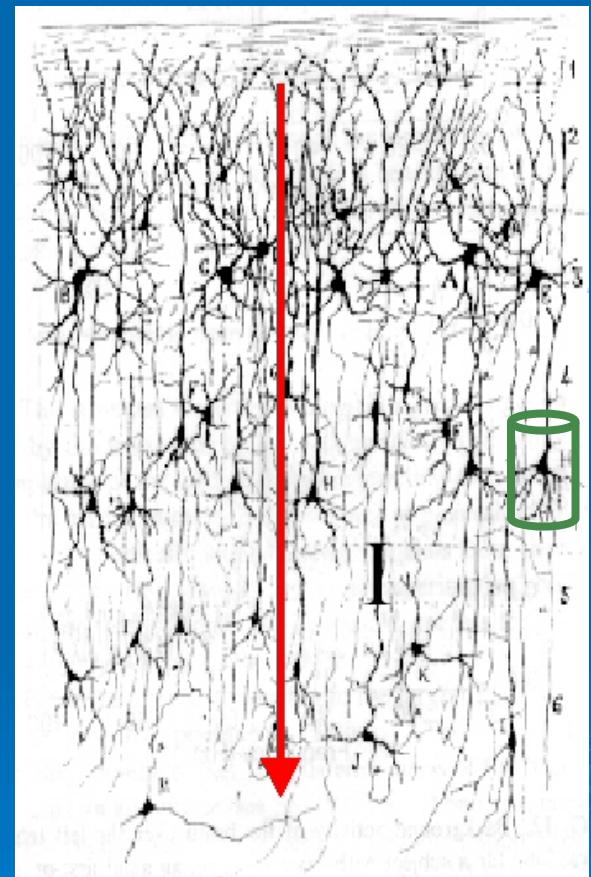
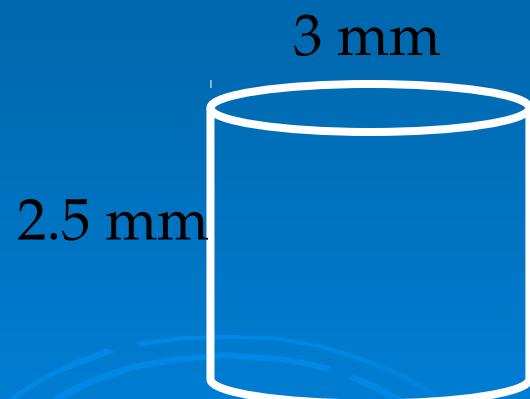
EEG = summed post-synaptic potentials (mainly)



Principle 4: Macroscopic currents

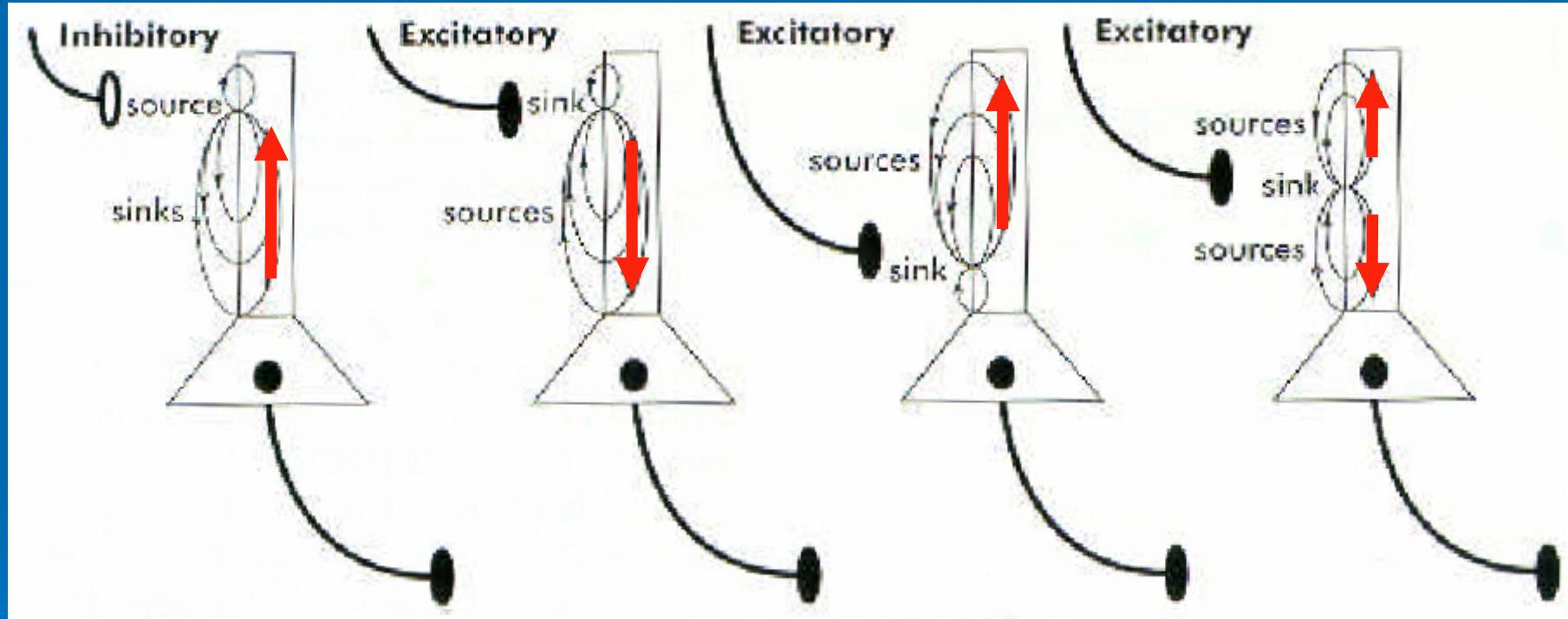


We can only record from specific anatomical organizations of neurons:
columns that form dipoles of activity.



dipole of current
cortical macro-column
 $10^5 - 10^6$ neurons
10 – 100 nAm

Principle 3: Polarity doesn't mean anything



very difficult to establish the participation of excitation
and inhibition from the sign of the dipole

MEEG ‘Sources’

Where is the signal coming from?

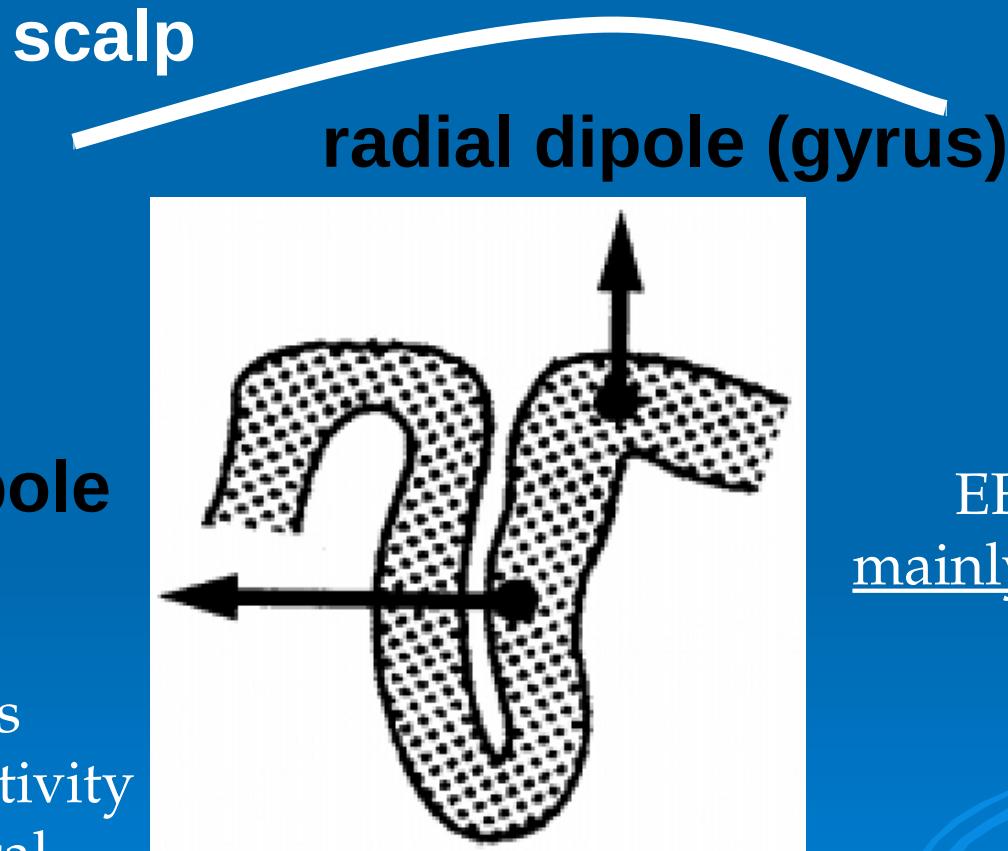


Neural Sources

- If the primary source and the surrounding conductivity distribution are known, the resulting electric potential and magnetic fields can be calculated from Maxwell's equations.
- Discovering the sources of EEG or MEG data is known as the electromagnetic inverse problem, i.e. dealing with the deduction of the source currents responsible for the measured field. Indeed, such problem has no unique solution (von Helmholtz, 1853) and source models are used to approximate the solution. The optimal solution is usually found by fitting (least-squares method) the theoretical and measured field patterns to get the equivalent current dipole (ECD).

Tangential vs. Radial dipoles

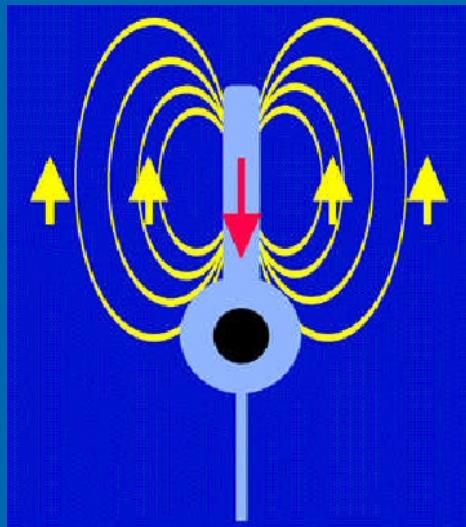
**tangential dipole
(sulcus)**
MEG captures
only tangential activity
(60-70% cerebral
surface)



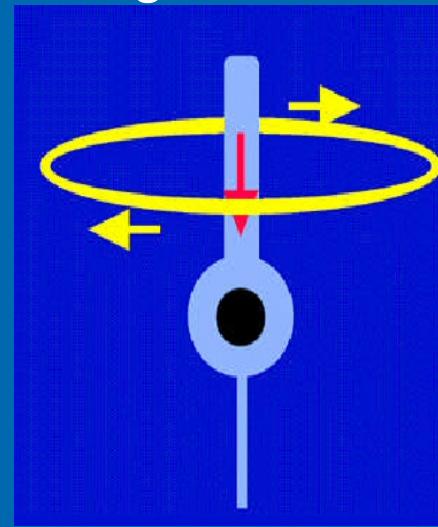
EEG captures
mainly radial activity

Electric and magnetic fields

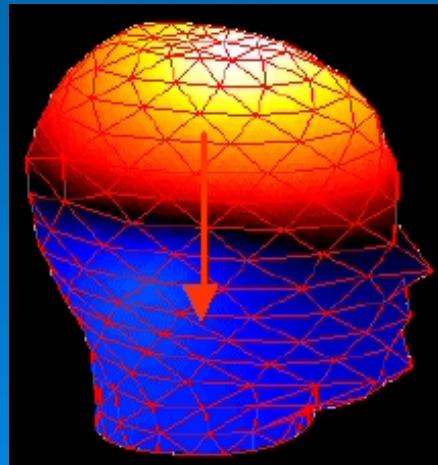
electric field



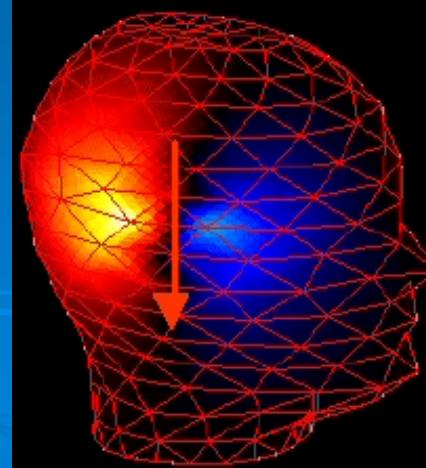
magnetic field



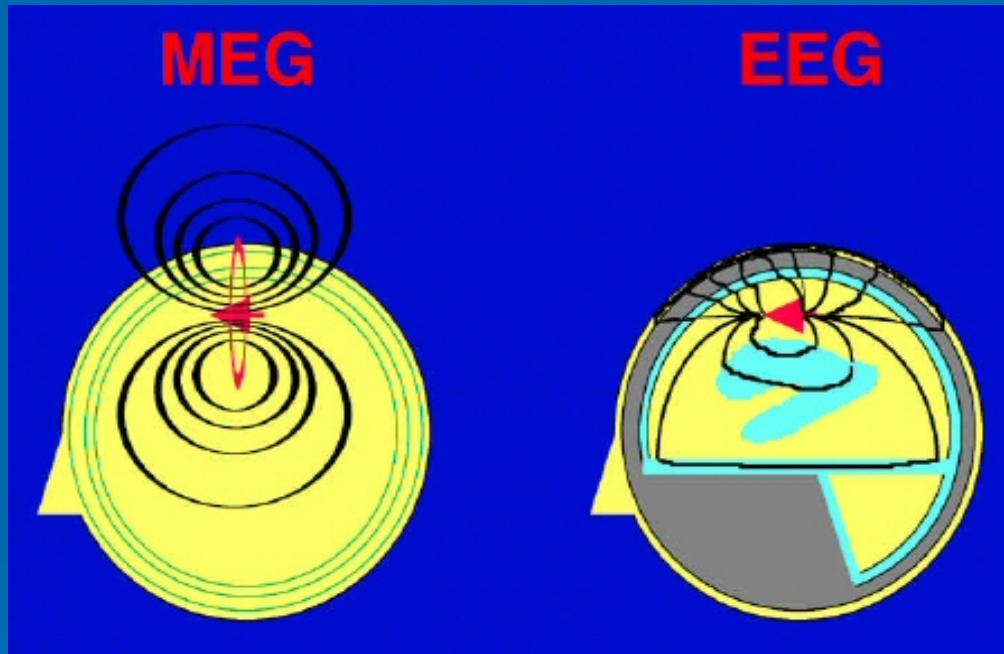
EEG



MEG



MEG / EEG : current sensitivity



Best approach:
Merge EEG & MEG data
to capture all dipoles
at all orientations.

MEG = primary, intra-cellular, currents (no diffusion => good source localization)

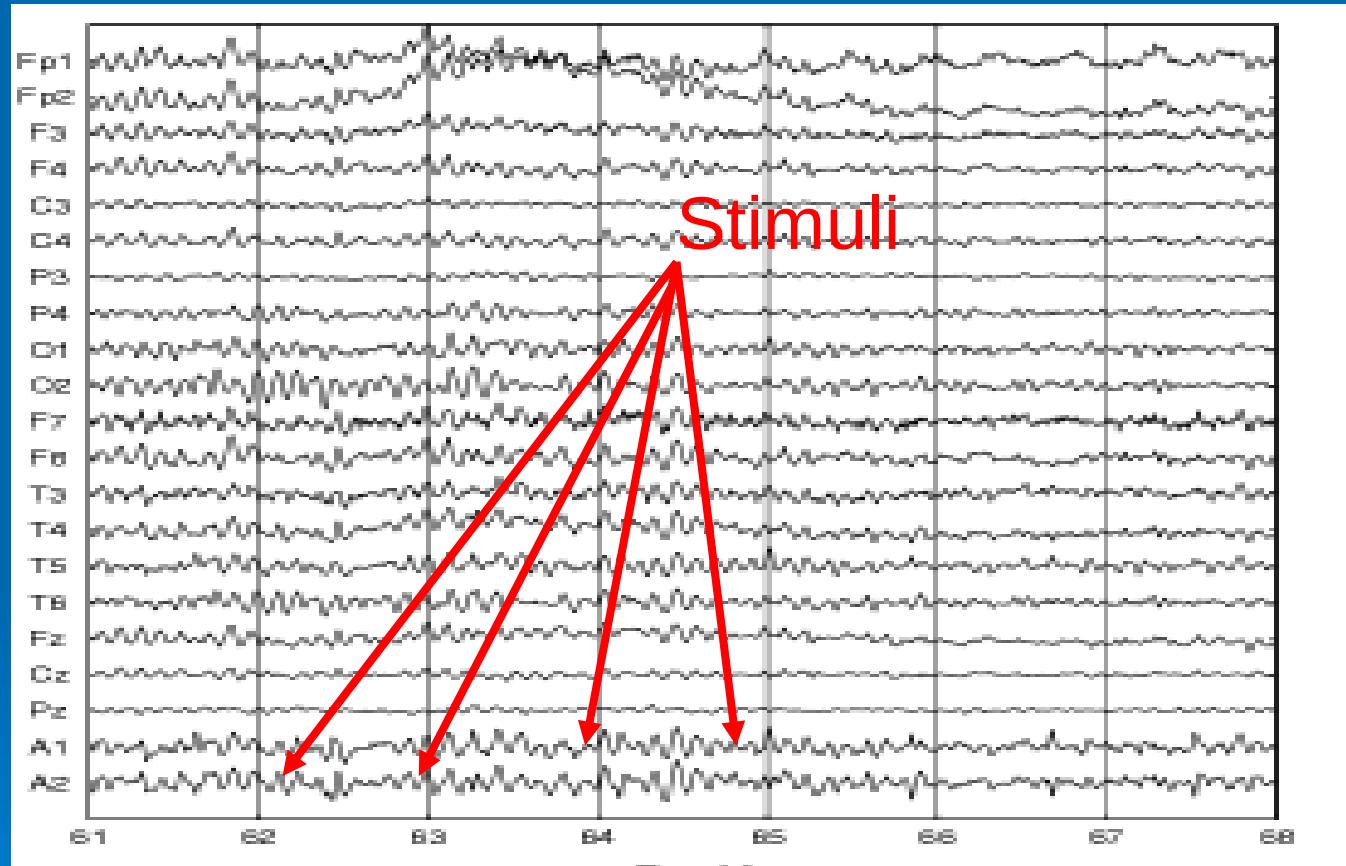
EEG = secondary, extra-cellular, currents (diffusion through meninges, bone & skin => difficult source localization, need complex models taking into account the properties of the layers electrical currents go through)

Data processing



What are the data?

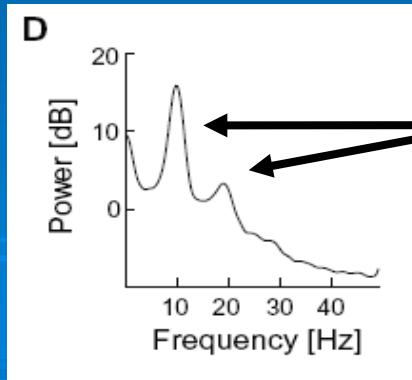
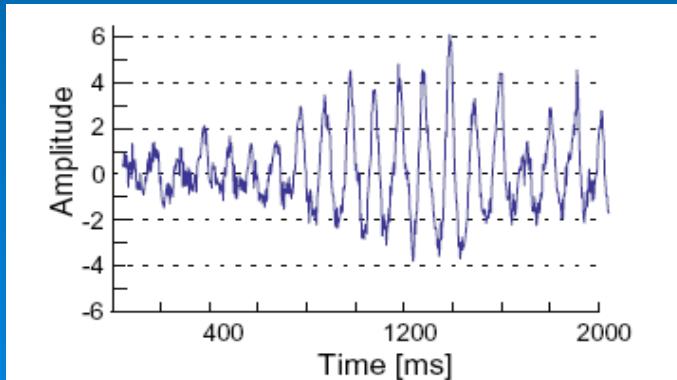
electrodes



Time

What can you do with the data?

- Look at the oscillation frequency (useful to differentiate clinical states: $\delta < 4\text{Hz}$, $\theta 4\text{-}7\text{Hz}$, $\alpha 8\text{-}12\text{Hz}$, $\beta 12\text{-}30\text{Hz}$, $\gamma >30\text{Hz}$)
- Compute the power spectrum: portion of a signal's power (energy per unit time) falling within given frequency bins; e.g. how much energy in the α range



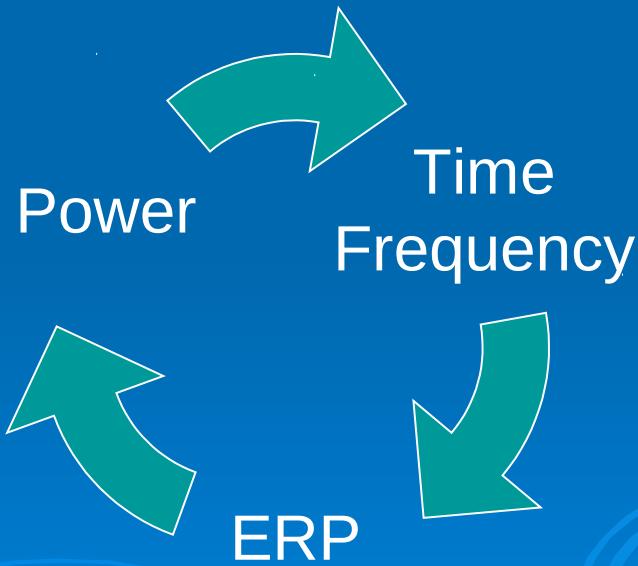
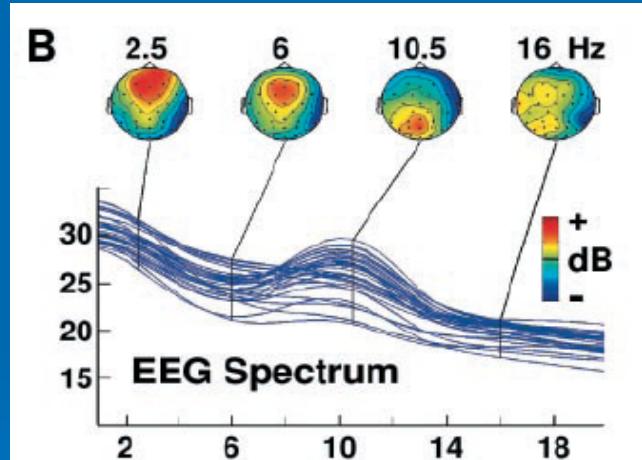
α and β components

What can you do with the data?

- Do the same as power spectrum but decomposing in time bins → time frequency analysis (of course you can't estimate low frequencies if your stimuli have short ISI and the sampling across frequencies will be different)
- Compute the evoked response, i.e. the response time locked with the stimulus

Processing EEG Data

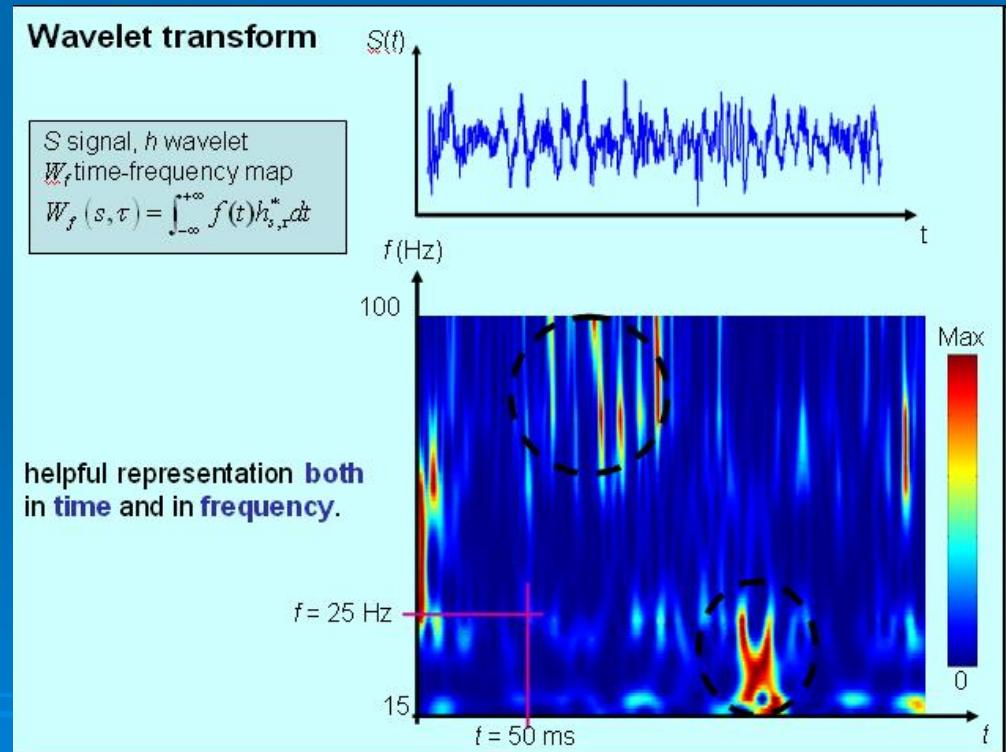
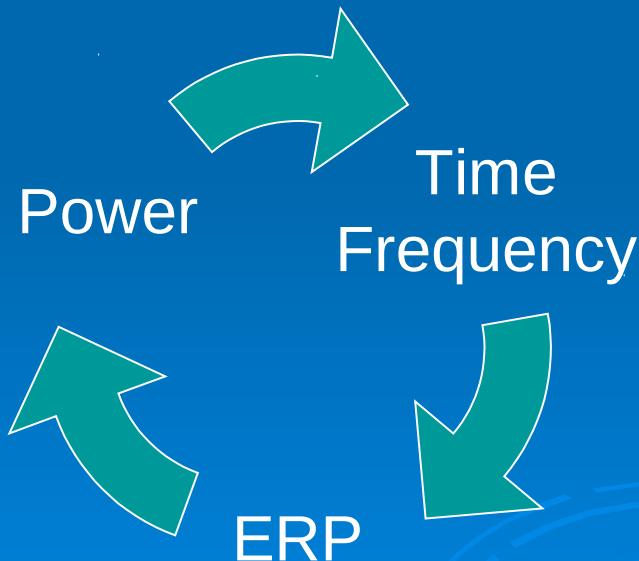
The oscillation speed and strength can also be computed to determine the main frequencies / power



Relating power to BOLD amplitude

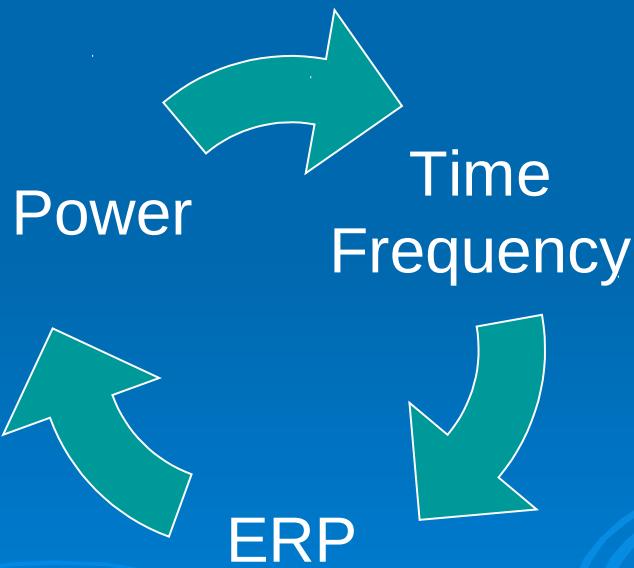
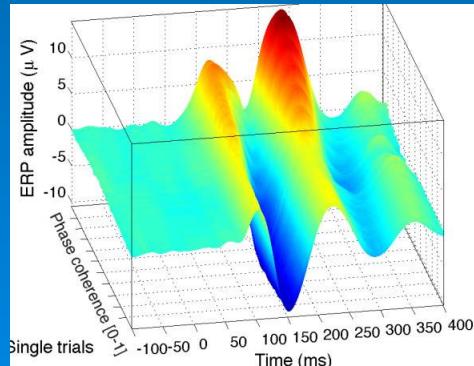
Processing EEG Data

And changes in frequencies can be observed at different time bins



Processing EEG Data

The EEG signal can be averaged to produce ERPs but also modelled (GLM) / decomposed (ICA) at the single subject levels (Rousselet, Pernet BMC Neuroscience 2008)



Relating components to BOLD
(getting the timing of fMRI events)

Evoked responses

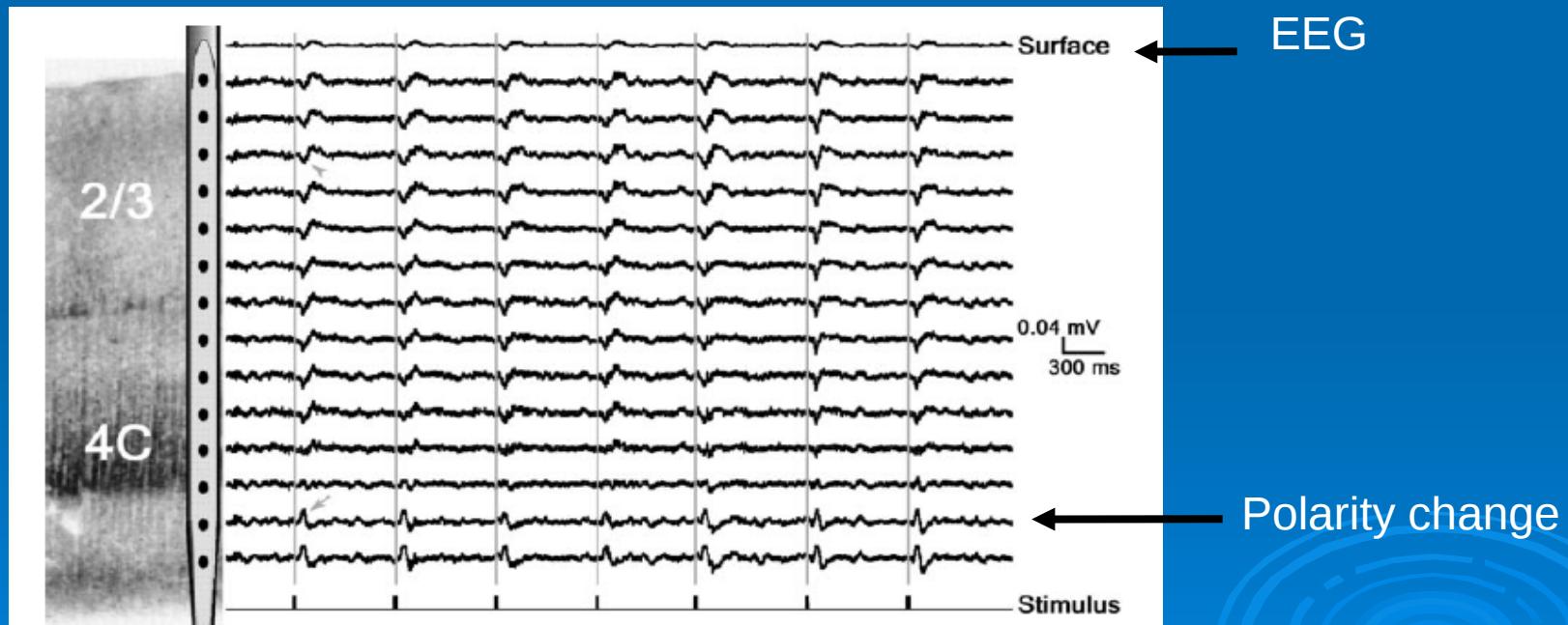
- Present multiple times the same stimulus and average data time locked (i.e. ‘cut’ before/after the stimulus and average all the bits) → makes an event-related potential (ERP) or event related field (ERF)
- The ER is a summary measure of the brain’s electric/magnetic activity. Underlying this averaging process is an assumption that the ER is generated from a set of stimulus-evoked, fixed-latency, brain events.

Evoked responses

- *Hypothesis 1 – Dawson 1950*: Signal plus noise (SPN) model → an ER is the result of a set of discrete stimulus-evoked brain events identical from trial to trial superimposed onto the ongoing EEG (Gaussian correlated noise).
- *Hypothesis 2 – Sayers 1974*: Phase-reset (PR) model → an ER corresponds to the phase resetting of alpha waves induced by the stimuli.
- *Hypothesis 3 – Nikulin 2007*: Baseline-shift (BS) model → alpha wave amplitudes are modulated asymmetrically by the stimulus (modulation of waves not centred on 0 create the ER).

ERP – SNP evidence

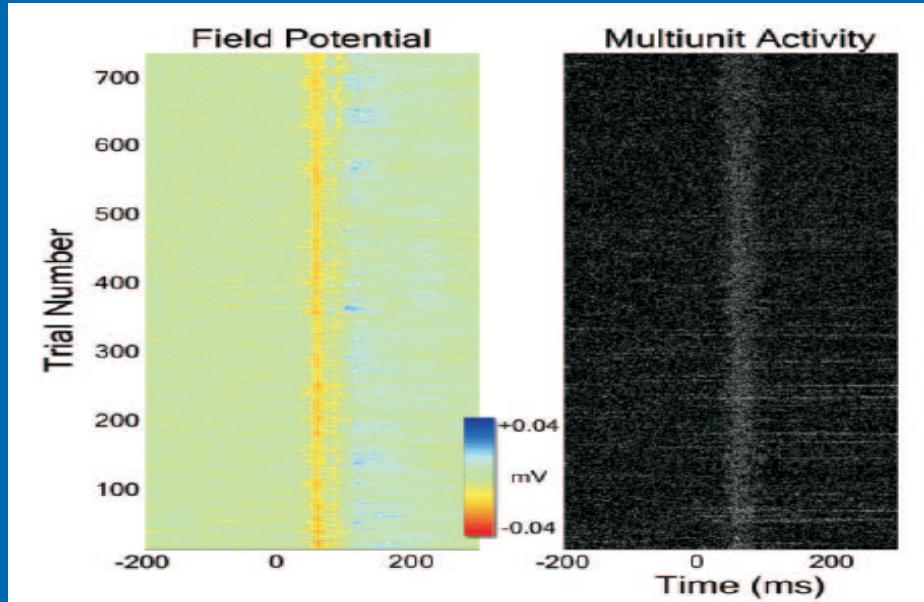
- Electrodes on the visual cortex of monkeys performing an oddball paradigm



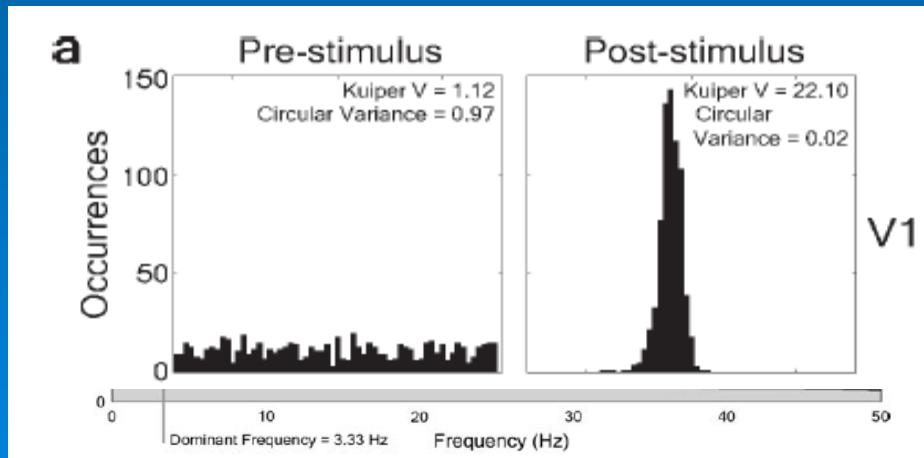
Not much oscillations pre-stimulus

Shah, Cereb Cortex 2004

ERP – SNP evidence



Recording from 1 electrode in the granular layer: again not much activation before the stimuli at the synaptic level (field potential) or neuronal level (multiunit activity)

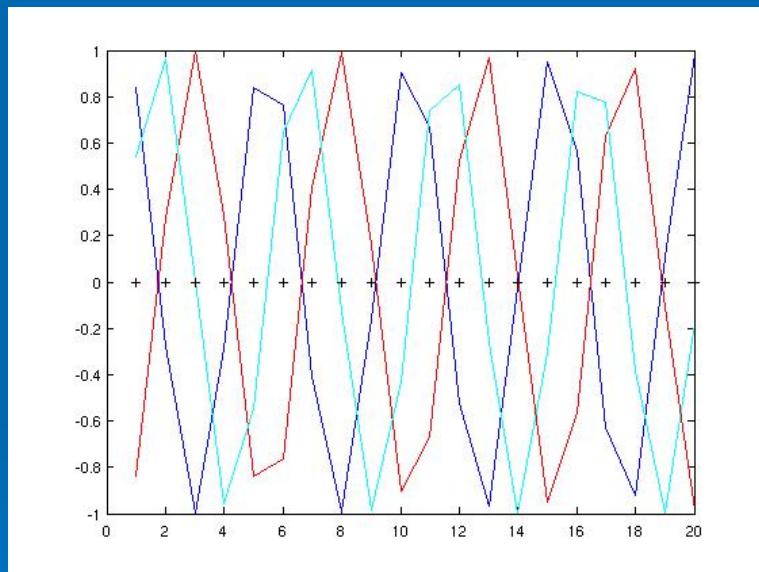


Signal power increases post-stimulus with a change in f0 and additional harmonics
BUT phase concentration also occurs

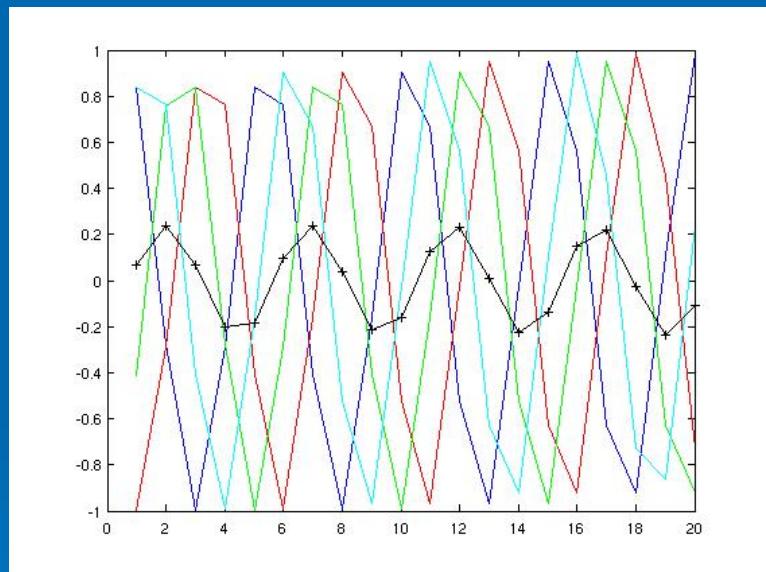
Shah, Cereb Cortex 2004

ERP – PS evidence

- If waves synchronize then you get an ERP

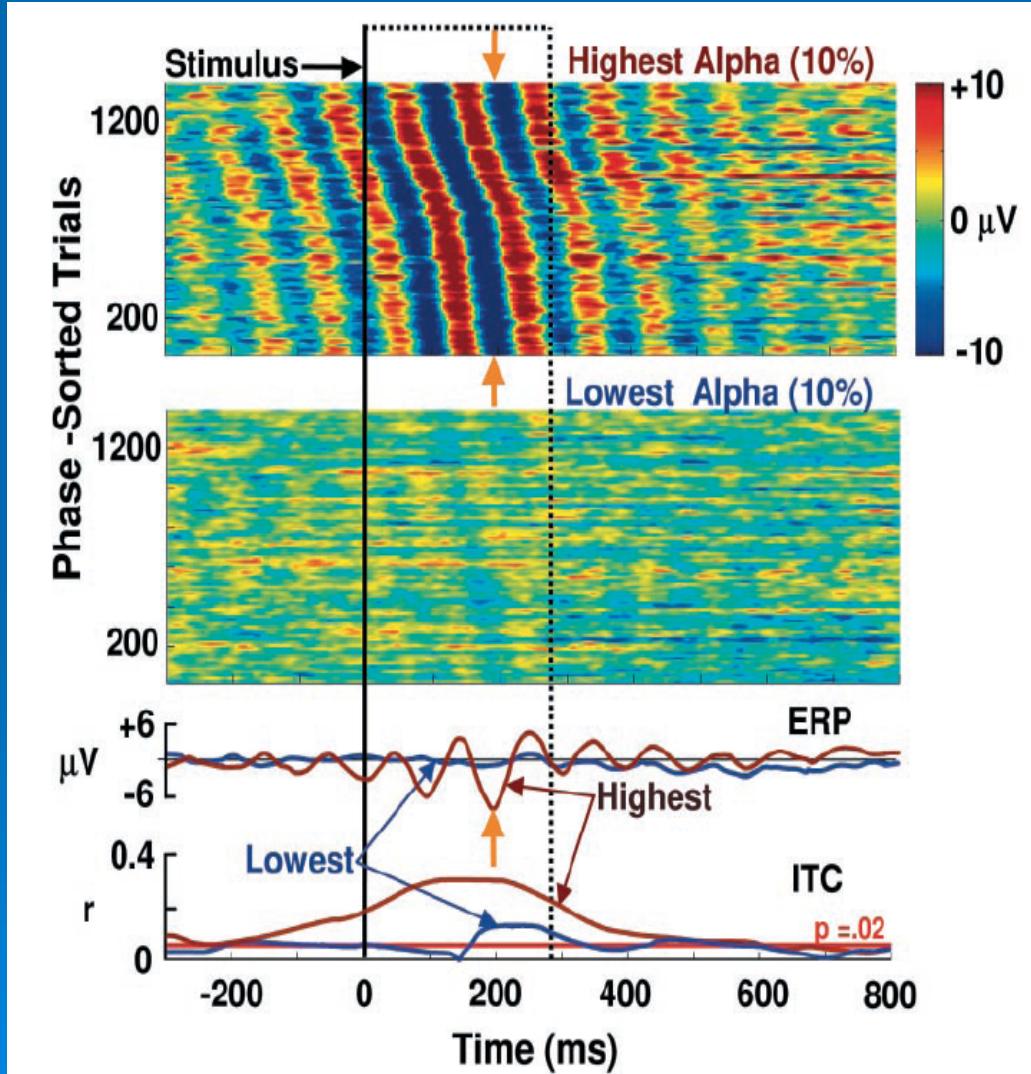


4 waves in antiphase → avg = 0



4 waves slightly in phase → avg = erp

ERP – PS evidence



From trial to trial, even for the same stimulus there is some variability.

If you take trials with low α power, the ERP is weak and ITC is low ; conversely trials where the α power is high give rise to a strong ER when averaged and the ITC is high.

It is believed that α oscillations emerge from the interactions thalamus/cortex reflecting rhythmic successions of EPSP in the cortex → role in information processing

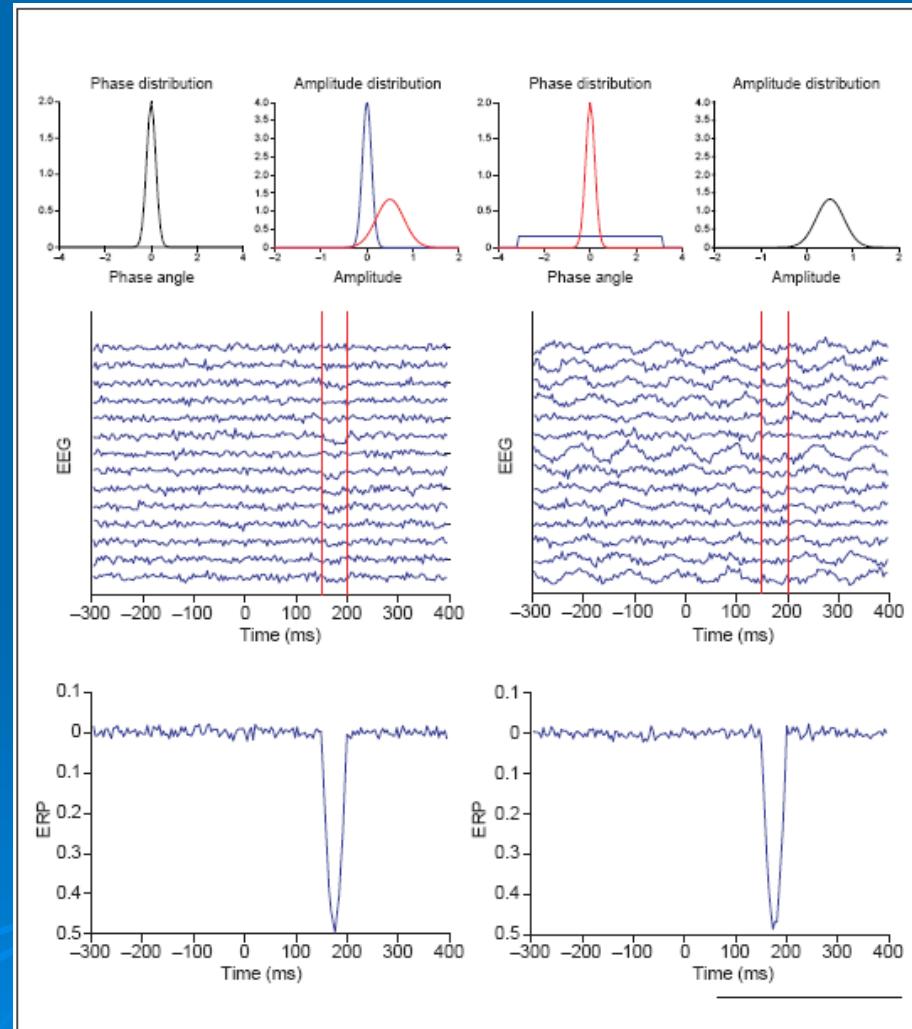
SNP or PR?

Hyp. 1

- No change in phase
- Change in amplitude
- Avg == ERP

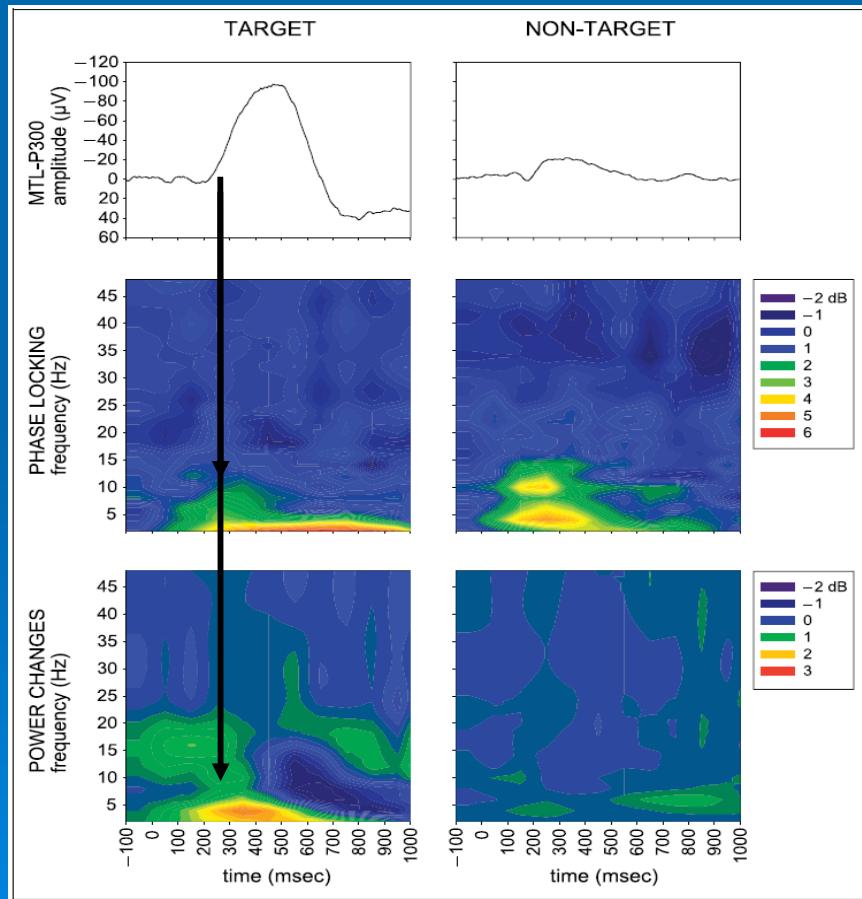
Hyp. 2

- Background activity gets in phase
- No change in amplitude
- Avg == ERP



SNP or PR?

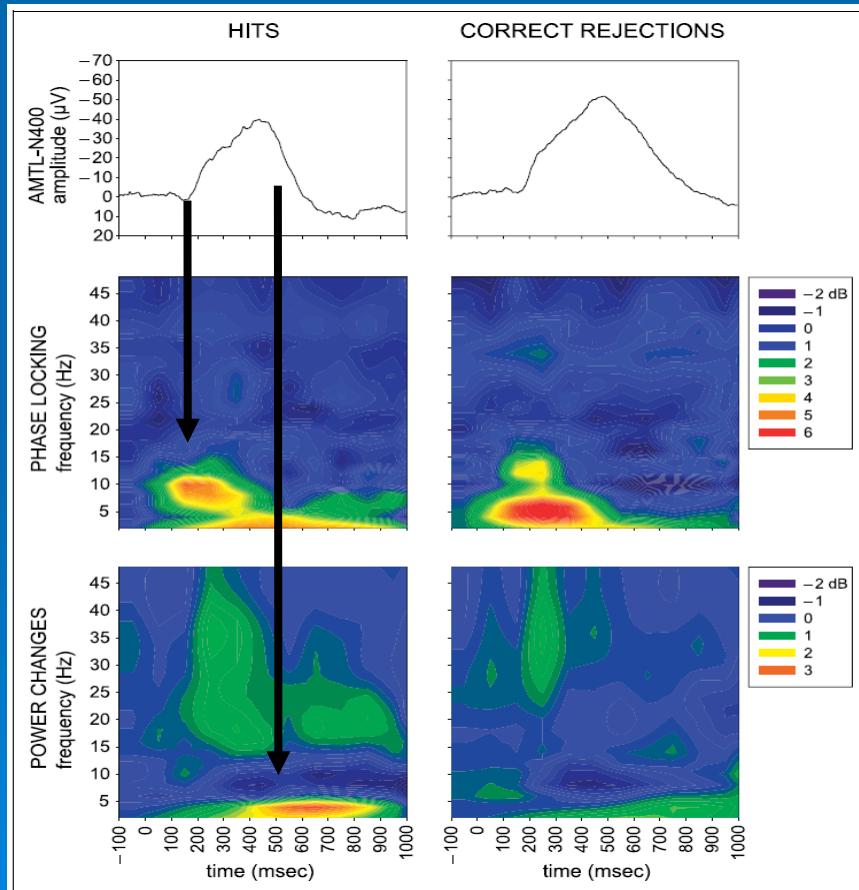
➤ Intracranial recording in epileptic patients



Medial temporal lobe P300
→ Phase reset and power increase

SNP or PR?

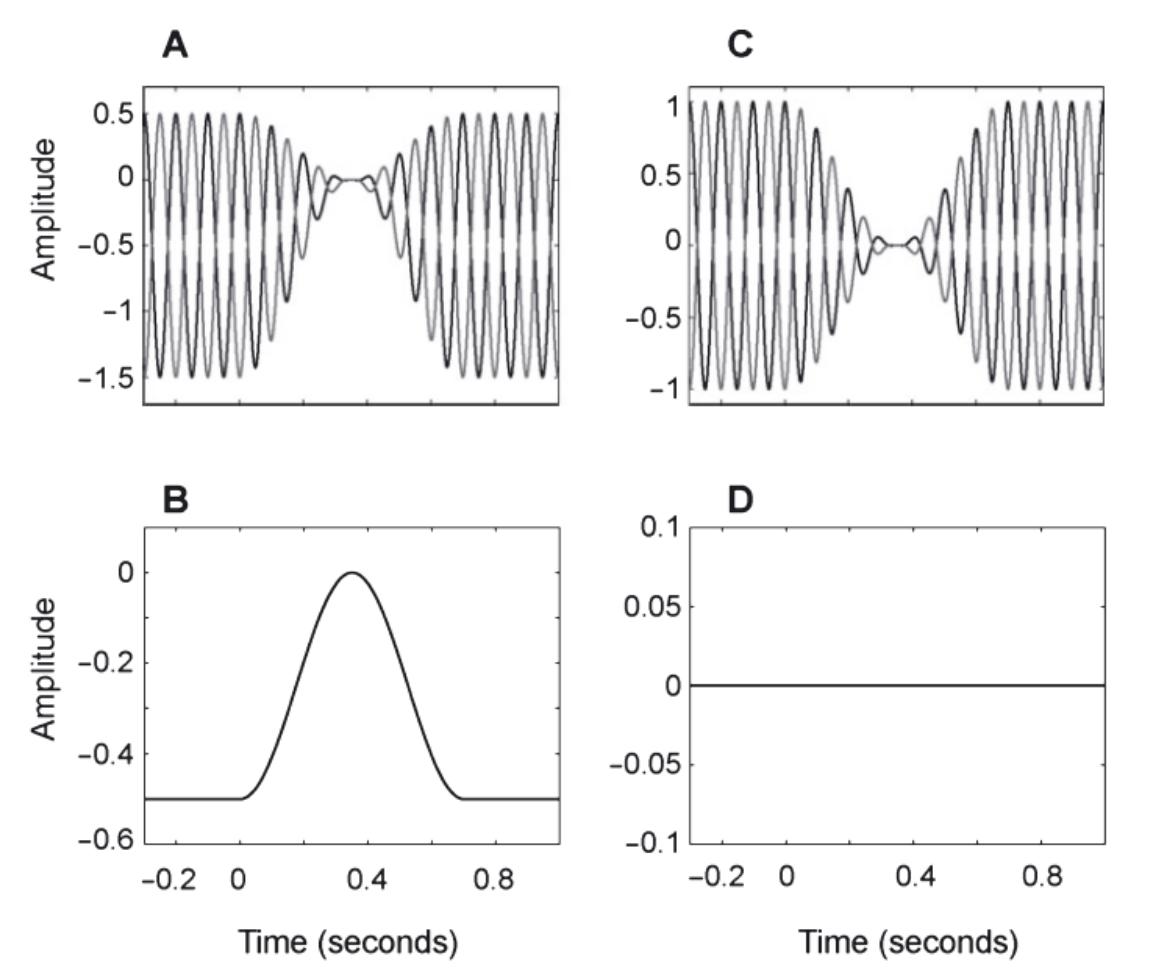
➤ Intracranial recording in epileptic patients



Medial temporal lobe P300
→ Phase reset and power increase

Anterior Medial temporal lobe N400
→Phase reset first then power increase

BS model



When averaging, α oscillations which are assumed at random phase regarding stimulus onset, average to 0 (like SPN model) but here we assume that the stimulus induce a modulation of α amplitude and after averaging the offset remains