What are we measuring with M/EEG?

(And what are we measuring with?)

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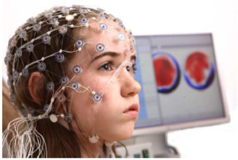
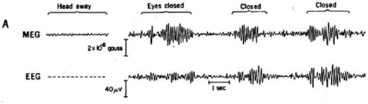
Outline

MEG and EEG are different views of the same neural sources

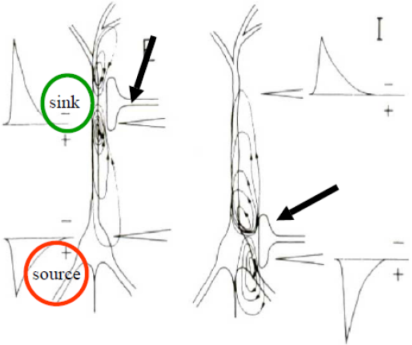
- Both record synchronized neural activity at a very high temporal resolution
- EEG ⇒ differences in electric potential at the skalp
- MEG ⇒ magnetix flux density outside the head





Origin of M/EEG signal

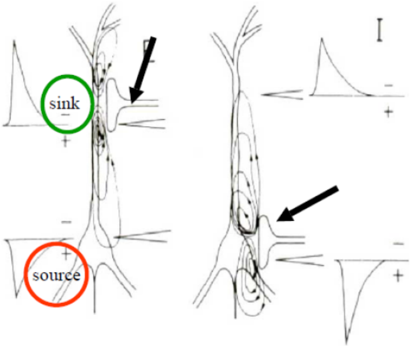
- Synaptic input leads to ionic currents across the postsynaptic membrane
    - EPSP (often at apical dendrites): influx of positive Na^+ ions
    - IPSP (often at the soma): influx of negative Cl^- ions



Lopes da Silva, Mag. Res. Imag., 2004

Origin of M/EEG signal

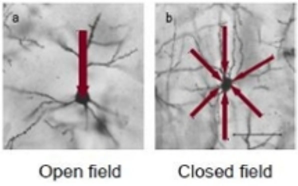
- Intracellular currents flow from the apical dendrite to the soma
- Extracellular volume currents complete the loop of ionic flow so that there is no build-up of charge

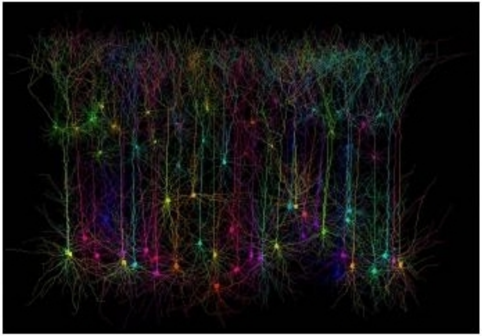


Lopes da Silva, Mag. Res. Imag., 2004

From a single neuron to a neural assembly

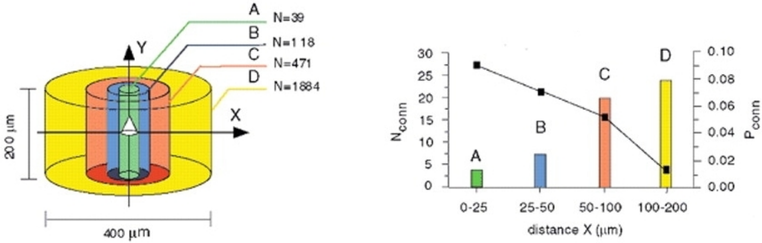
- A large number of simultaneously active neurons are needed to generate a measurable M/EEG signal





Churchill, BMC Neuroscience 2004/Häusser and Cuntz (Wellcome Images)

High local lateral connectivity means that near by cells share similar excitation patterns

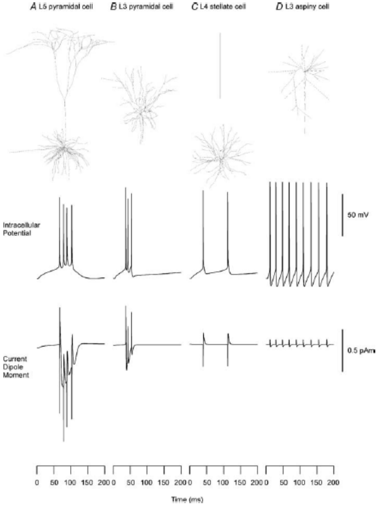


Holmgren et al. 2003

The current dipoles across a small cortical area are often summarised to an Equivalent Current Dipole (ECD).

Realistic modelling of current sources

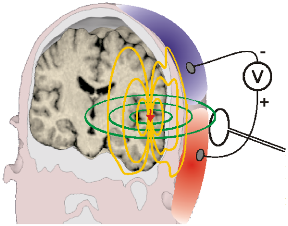
- Neuronal models of detailed morphology were excited by virtually injecting current
- ECD moment was estimated by summing elementary dipoles across neural segments
- 50 000 cells sufficient to generate a dipolar source of 10nAm
- Sodic spikes with large current densities $\Rightarrow$ about 10 000 synchronous neurons could yield an MEG measurable signal

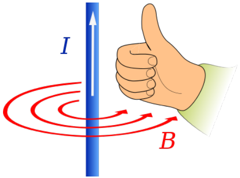


S. Murakami et al., J. Physiol, 2006

Primary intracellular currents give rise to volume currents and a magnetic field

- Volume currents yield potential differences on the scalp that can be measured by EEG (Ohm's law: $J = \sigma E$)
- MEG measures magnetic fields induced mainly by primary currents based on excitatory activity (Okada et al. 1997)





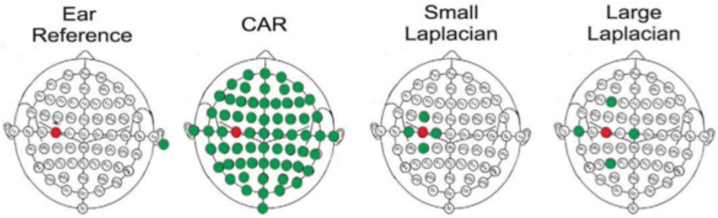
Baillet: MEG consortium

Mini Summary I

- M/EEG signal originates from postsynapic potentials, typically at the apical dendrites of pyramidal cells
- The primary intracellular currents give rise to both volume currents and a magnetic field
- About 50 000 simultaneously pyramidal cells give rise to a measurable M/EEG signal

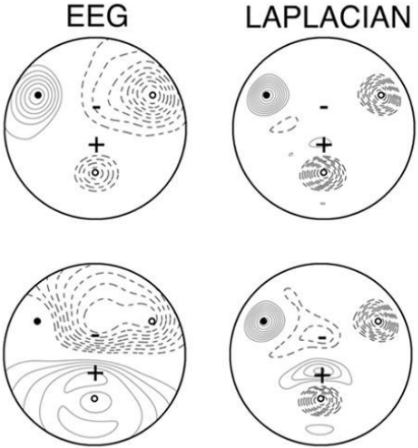
Measuring potential differences with EEG

- The representation of the EEG channels is referred to as a montage
  - Bipolar ⇒ represents difference between adjacent electrodes
  - Unipolar/Referential ⇒ potential difference between electrode and designated reference
- The potential differences are then amplified and filtered



McFarland et al., 1997

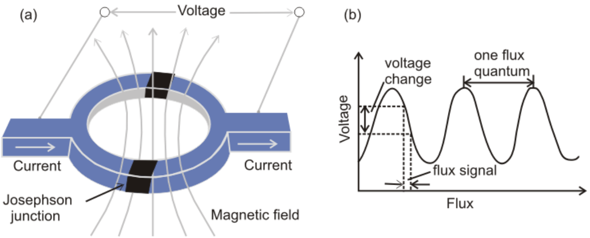
Laplacian montages are most sensitive to superficial sources in EEG



Srinivasan et al., Prog Brain Res, 2007

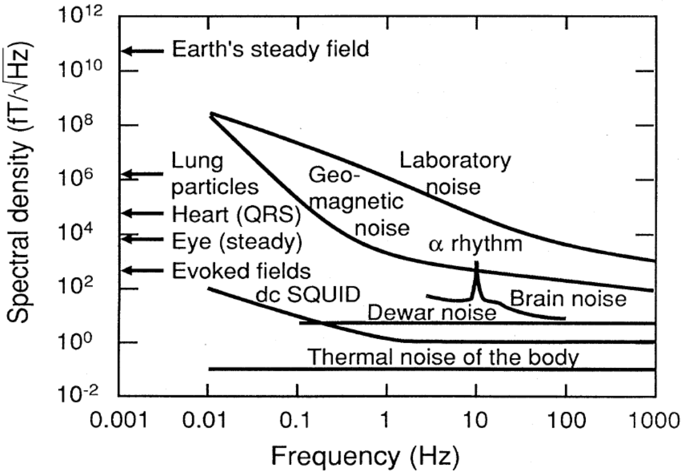
Measuring tiny magnetic fields: the SQUID

- SQUIDs are ultrasensitive detectors of magnetic flux made of a superconducting ring interrupted by one or two Josephson junctions
- SQUIDs can measure field changes of the order of 10^{-15} (femto) Tesla (compare to the earth's field of 10^{-4}Tesla)
- Cooling achieved by liquid Helium
- Output signal is a magnetic flux dependent voltage



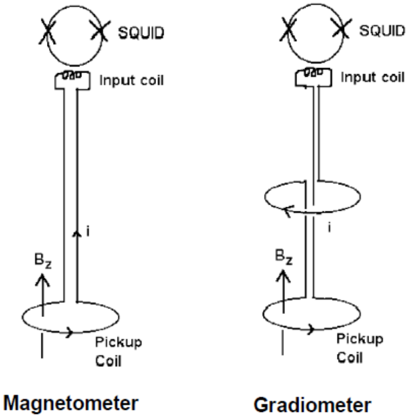
Adapted from J Clarke, Scientific American 1994

The high sensitivity means we also record a lot of noise



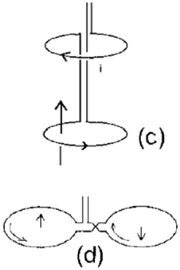
Hämälainen 1993

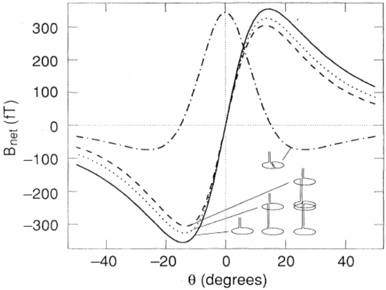
Flux converters can enhance the sensitivity of the SQUIDs to magnetic fields



Axial and planar gradiometers have different depth profiles

- Axial gradiometers are aligned orthogonally to the scalp and record gradient of magnetic field along the radial direction
- Planar gradiometers consist of two detector coils on the same plane
- The gradiometer configuration is important for the interpretation of the data

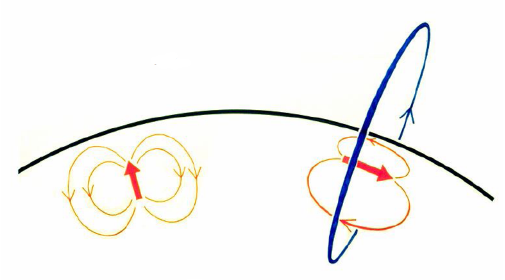




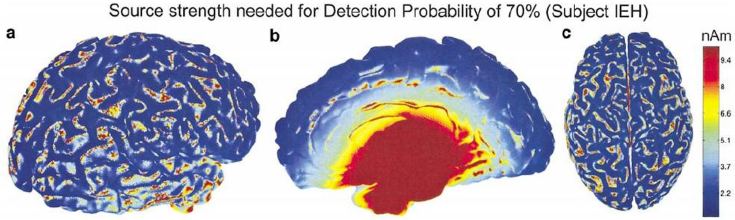
Vrba 2001, Hämälainen 1993

Given a spherical conductor, radial source do not give rise to an external magnetic field

- Biot-Savart‘s law can be used to describe the magnetic field generated by an electric current
- In the special case of a spherically symmetric volume conductor MEG is only sensitive to the tangential component of the primary current
- The tangential component can be computed without knowing the conductivity profile



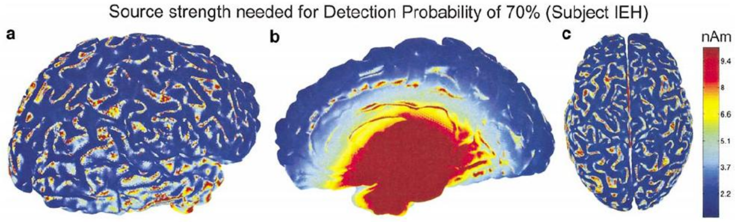
Gyral sources remain partly visible



Hillebrand and Barnes 2002

- Pyramidal cells are aligned perpendicularly to the cortex surface ⇒ gryral sources are most radial
- But they are very close to the sensors and are surrounded by non-radial cortex to which MEG is highly sensitive

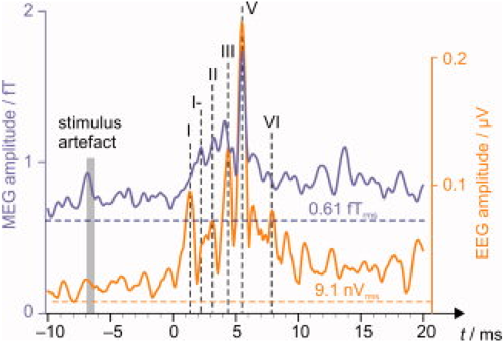
Depth is a limiting factor in MEG measurements



Hillebrand and Barnes 2002

- Magnetic field strength decreases steeply with distance ($\frac{1}{r^2}$)
- Deeper sources are more radial

But we can see deep sources, can't we?

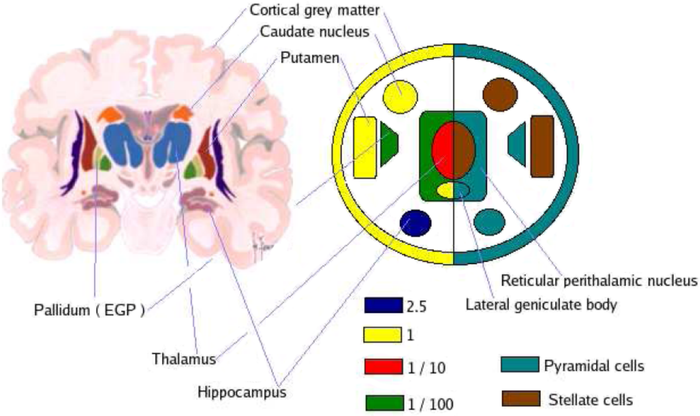


Parkkonen et al. 2009

But we can see deep sources, can't we?

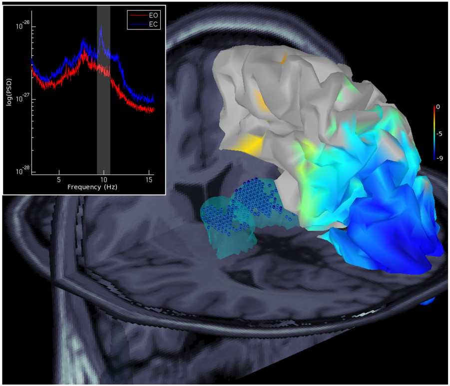
- Increase the signal-to-noise ratio and incorporate previous knowledge!
- Increasing number of papers published in recent years, e.g.:
    - Thalamus (Tesche, Brain Res 1994, Roux, J Neurosc 2013)
    - Cerebellum and Thalamus (Timmermann, Brain 2002)
    - Hippocampus (Riggs, Neuroimage 2008)
    - ...

What are the deep brain neural generators of M/EEG signals?



Attal et al., 2007

Using realistic models fascilitates the detection of thalamic alpha band activity

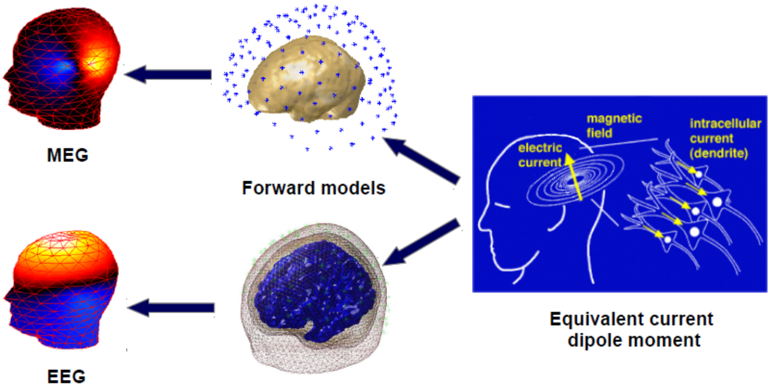


Attal et al., 2013

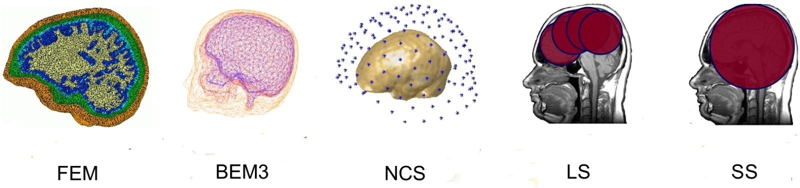
Mini Summary II

- MEG is less sensitive, but not blind to radial sources
- Sensitivity decreases steeply with depth, but accumulating evidence that we can measure the activity of deep sources
- Ability to detect deep sources depends on several factors, e.g. the signal to noise ratio, the cytoarchitecture of the deep structures, the forward model applied ...

Forward models predict the M/EEG surface signals to current dipoles in the brain

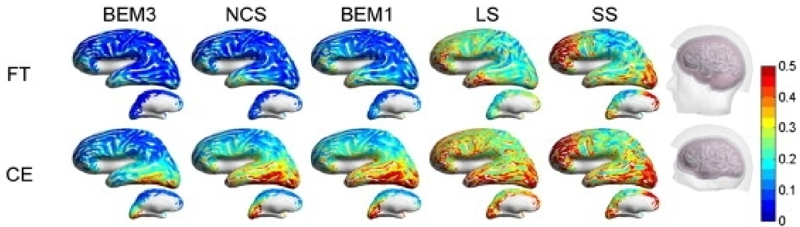


Headmodels show different degrees of complexity



- The simpler models are not sufficient to predict the electric potential differences at the scalp
- Complex models are (1) computationally more expensive and (2) require more prior knowledge about the anatomy and conductivity values

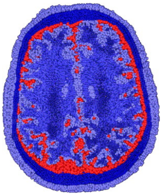
MEG also may benefit from using more complex headmodels

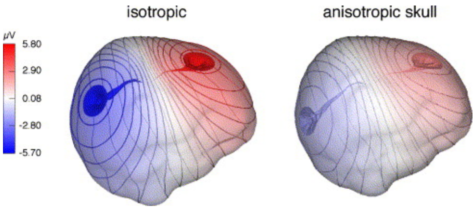


Stenroos, Neuroimage 2014

EEG is strongly affected by skull anisotropy

- Finite element head models with skull or white matter anisotropy were investigated for EEG and MEG simulations
- WM anisotropy had a significant effect on both methods
- While MEG was hardly affected by skull anisotropy, potential differences on the scalp as measured by EEG are severely smeared





Wolters et al. 2006

Summary

- Electromagnetic signals predominantely based on aggregate post-synaptic currents of tens of thousands of pyramidal cells
- MEG is most sensitive to tangential sources, while EEG 'sees' both components
- EEG has a higher sensitivity to deep sources, but is limited by head model accuracy
- Forward models describe how primary currents in the brain give rise to electric potentials or magnetic fields at the head surface