What are we measuring with M/EEG?

(And what are we measuring with?)

Saskia Helbling

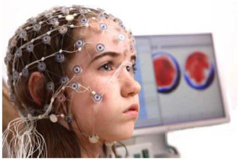
MRC Cognition and Brain Sciences Unit Cambridge

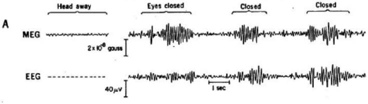
SPM course, May 16, 2016

Outline

MEG and EEG are different views of the same neural sources

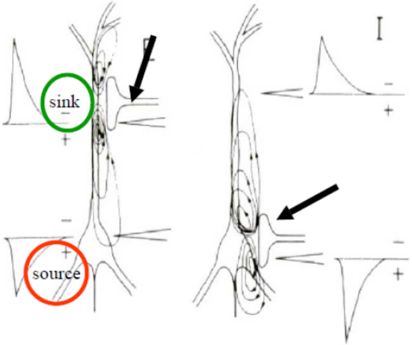
- Both measure direct electrophysiological signals at a very high temporal resolution
- EEG ⇒ differences in electric potential at the skalp
- MEG ⇒ changes in magnetix flux density outside the head





Origin of M/EEG signal

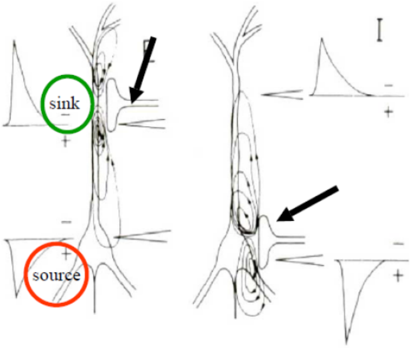
- Synaptic input leads to ionic currents across the postsynaptic membrane
  - EPSP at apical dendrites: influx of positive Na^+ ions
  - IPSP at the soma: influx of negative Cl^- ions



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

Origin of M/EEG signal

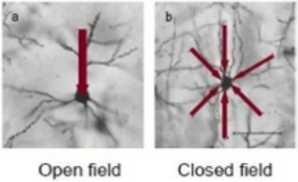
- Intracellular currents flow from the apical dendrite to the soma
- Extracellular volume currents complete the loop of ionic flow so that there is no build-up of charge

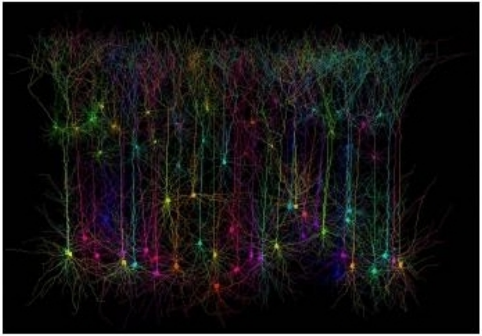


Lopes da Silva, Mag. Res. Imag., 2004

From a single neuron to a neural assembly

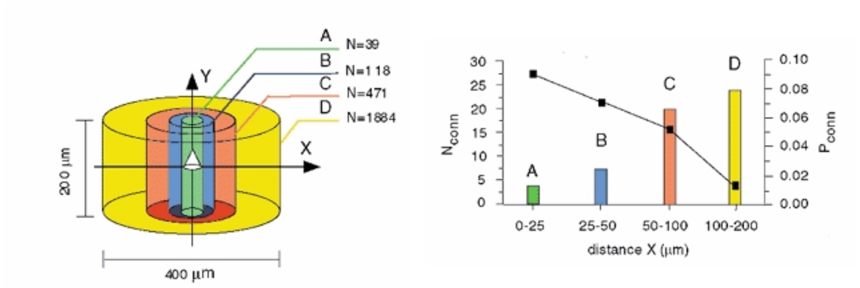
- A large number of simultaneously active neurons are needed to generate a measurable M/EEG signal





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

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

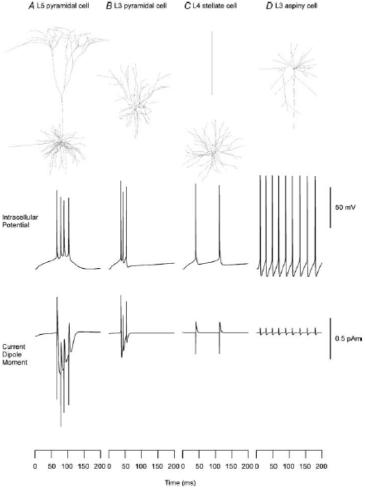


Holmgren et al., 2003

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

Realistic modelling of current sources

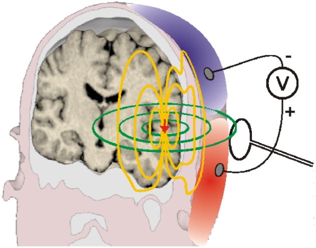
- Neuronal models of detailed morphology were excited by virtually injecting current
- ECD moment was estimated by summing elementary dipoles across neural segments
- 50 000 cells sufficient to generate a dipolar source of 10nAm
- Spikes produce large current densities ⇒ about 10 000 synchronous neurons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

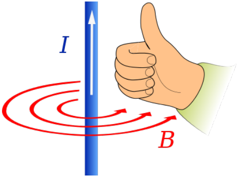


S. Murakami et al., J. Physiol, 2006

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)





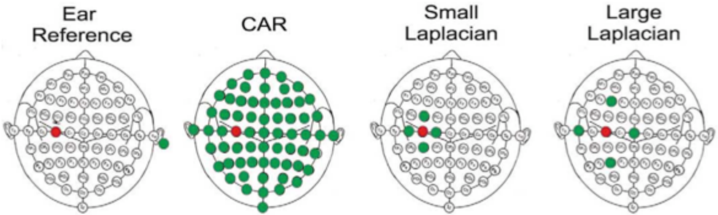
Baillet: MEG consortium

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 active pyramidal cells give rise to a measurable M/EEG signal

Measuring potential differences with EEG

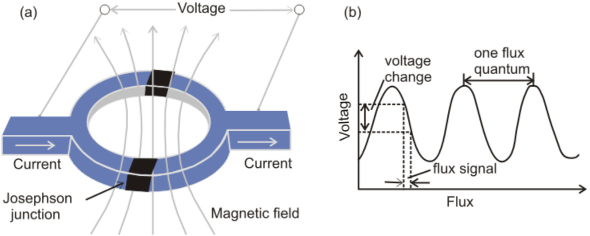
- The representation of the EEG channels is referred to as a montage
  - Unipolar/Referential ⇒ potential difference between electrode and designated reference
  - Bipolar ⇒ represents difference between adjacent electrodes
- Potential differences are then amplified and filtered
- The ground is important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



McFarland et al., 1997

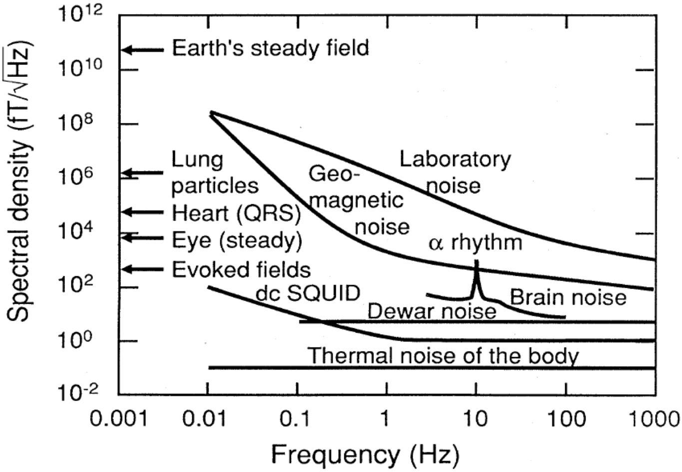
Measuring tiny magnetic fields: the SQUID

- SQUIDs are ultrasensitive detectors of magnetic flux made of a superconducting ring interrupted by one or two Josephson junctions
- Output signal is a magnetic flux dependent voltage
- 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



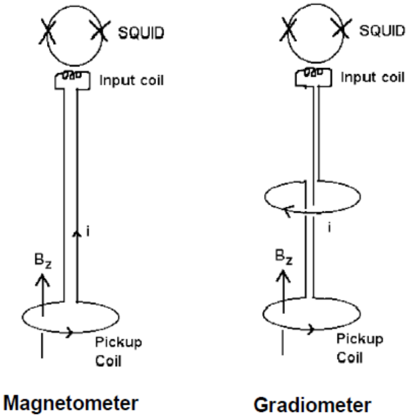
Adapted from J Clarke, Scientific American 1994

The high sensitivity means we also record a lot of noise



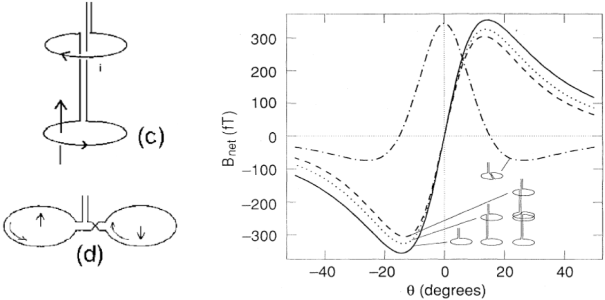
Hämälainen, 1993

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



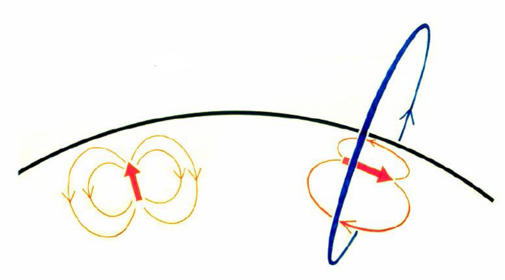
Axial and planar gradiometers have different sensitivity profiles

- 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
- Knowledge about the gradiometer configuration is important for the interpretation of the data

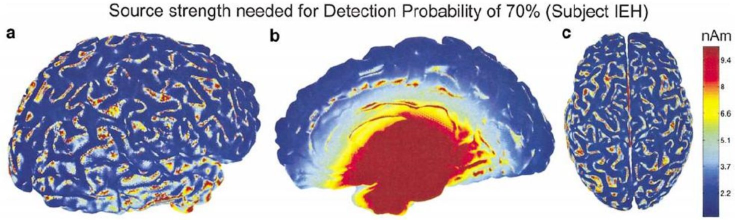


Given a spherical conductor, radial source do not give rise to an external magnetic field

- 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 (Sarvas, 1987)



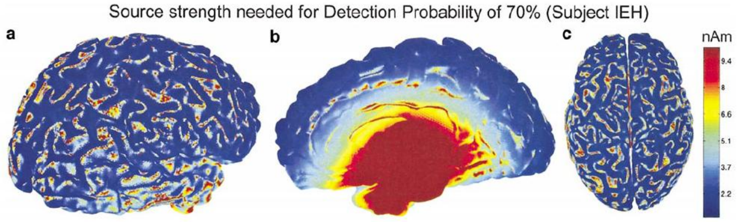
Gyral sources remain partly visible



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

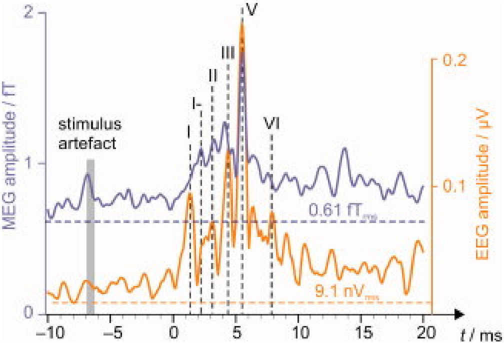
Depth is a limiting factor in MEG measurements



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?

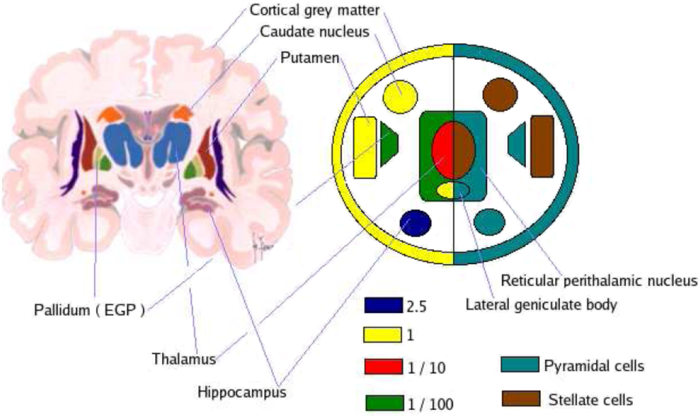


Parkkonen et al., 2009

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

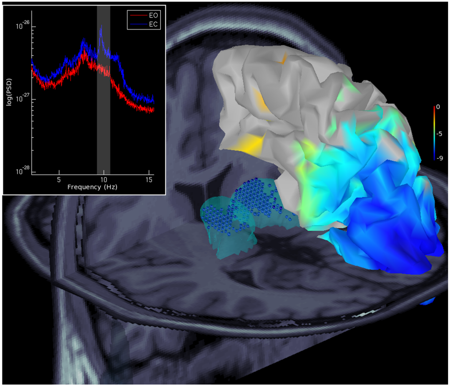
- Increase the signal-to-noise ratio and incorporate previous knowledge!
- Increasing number of papers published in recent years, e.g.:
    - Thalamus (Tesche et al., 1994, Roux et al., 2013)
    - Cerebellum and Thalamus (Timmermann et al., 2002)
    - Hippocampus (Riggs et al., 2008)

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



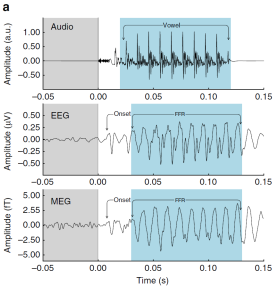
Attal et al., 2007

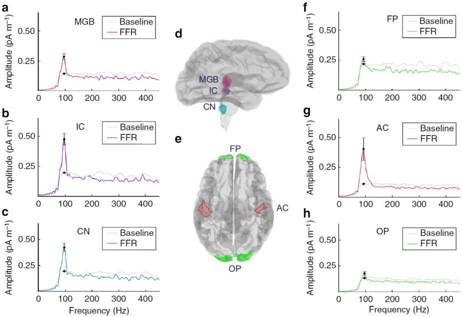
Using realistic models facilitates the detection of thalamic alpha band activity...



Attal et al., 2013

…and subcortical sources of the auditory frequency following response



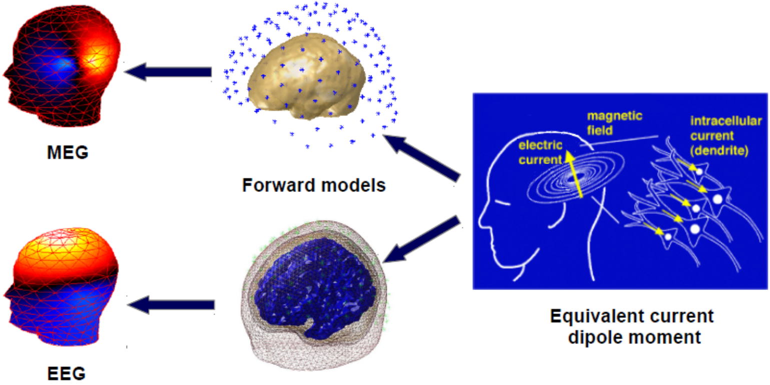


Coffey et al., 2016

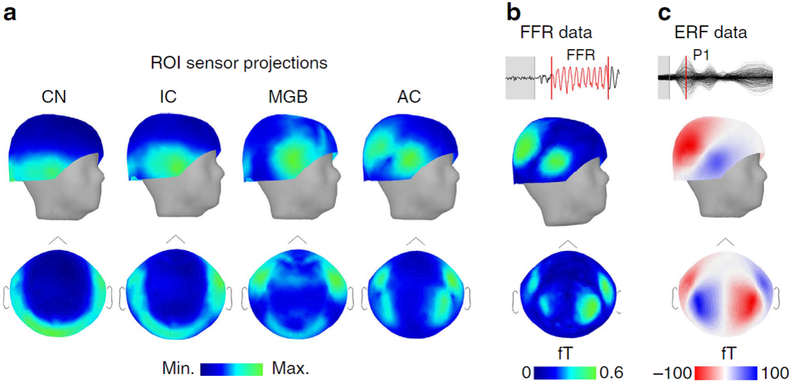
Mini Summary II

- 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

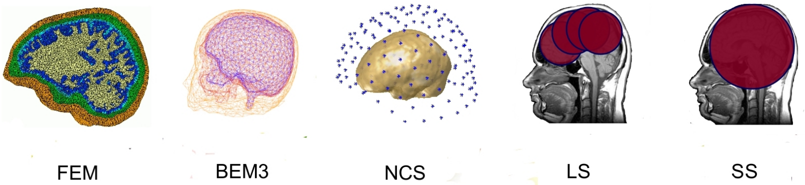


Forward models predict the M/EEG surface signals to current dipoles in the brain



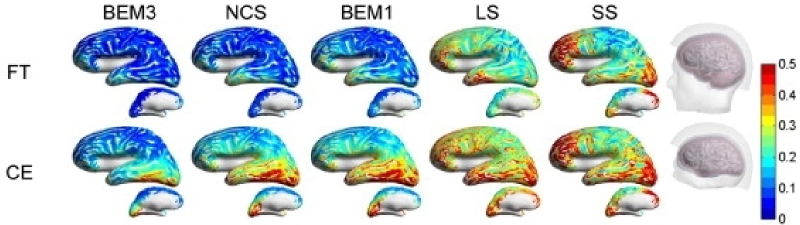
Coffey et al., 2016

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

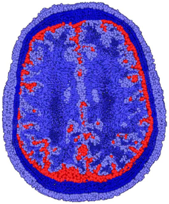
MEG also may benefit from using more complex headmodels

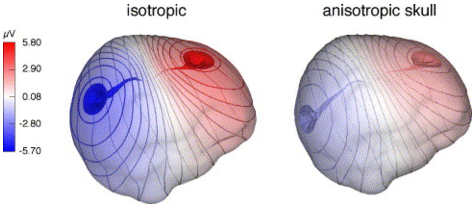


Stenroos et al., 2014

EEG is strongly affected by skull anisotropy

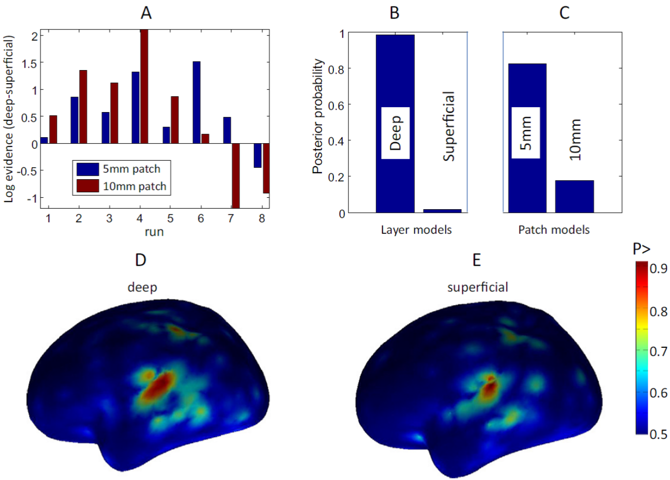
- Finite element head models with skull or white matter anisotropy were investigated for EEG and MEG simulations
- WM anisotropy had a significant effect on both methods
- While MEG was hardly affected by skull anisotropy, potential differences on the scalp as measured by EEG are severely smeared





Wolters et al. 2006

Using laminar forward models to distinguish between deep and superficial cortical sources



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

Acknowledgments

Many thanks to

- Stefan Kiebel
- Gareth Barnes
- Lucia Troebinger
- and all the other former presenters at the M/EEG SPM course