What are we measuring with M/EEG?

(And what are we measuring with?)

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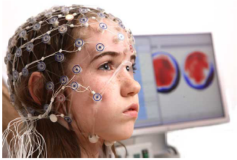
Contents

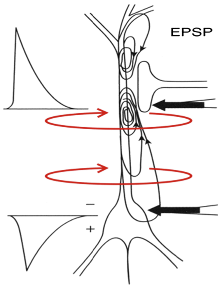
MEG and EEG are measuring the same underlying neural current sources

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



Origin of M/EEG signal

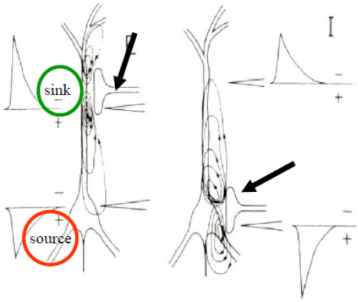
- Synaptic input leads to ionic currents across the postsynaptic membrane
- EPSP: influx of positive Na^{+} ions at apical dendrites leads to depolarisation of the postsynaptic cell
- Extracellular volume currents complete the loop of ionic flow so that there is no build-up of charge



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

The current flow direction depends on the type and location of synaptic input

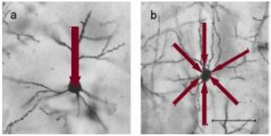
- IPSP : influx of negative Cl^- ions IPSP at the soma
- Again, intracellular currents flow from the pia towards deeper layers of the cortex



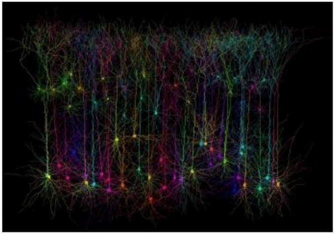
From Lopes da Silva, Mag. Res. Imag., 2004

From a single neuron to a neural assembly

- The geometry of the neuron must give rise to a net dipole current to contribute to the M/EEG signal
- A large number of neurons have to be active simultaneously to generate a measurable M/EEG signal
- Current sources measured by M/EEG mainly originate from the apical dendrites of the perpendicularly aligned pyramidal cells in layer II/III and V

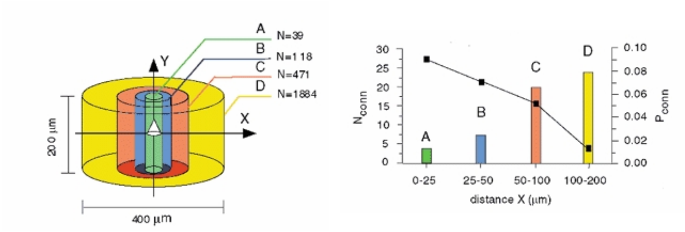


Open field   Closed field



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

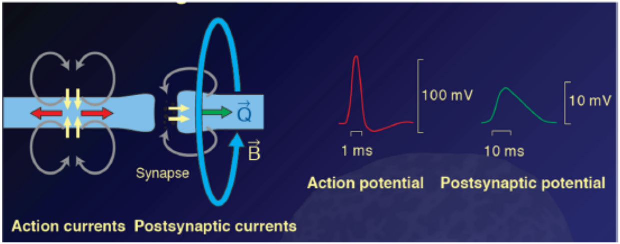
High local lateral connectivity means that near by cells share similar excitation patterns



Holmgren et al., 2003

- The current densities across a small cortical area are often summarised to an Equivalent Current Dipole (ECD)
- This ECD is considered a single point source with a dipole moment Q in $A \cdot m$

M/EEG is sensitive towards postsynaptic potentials, not action potentials

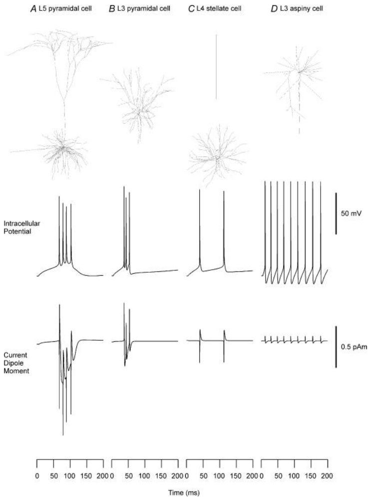


From Hämälainen

- Electric quadropoles decline steeply with distance ($\frac{1}{r^3}$)
- Due to their short duration AP would need to be highly synchronized to lead to a measurable signal (but see for example Curio et al., 2008)
- The cancellation of de- and repolarising currents will be incomplete under some circumstances

Realistic modelling of current sources

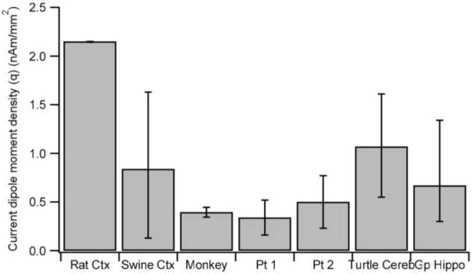
- Neuronal models of detailed morphology were excited by virtually injecting current
- ECD moment was estimated by summing elementary dipoles across neural segments
- 50 000 cells sufficient to generate a dipolar source of 10nAm
- Spikes produce large current densities ⇒ about 10 000 firing neurons could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



Murakami et al., 2006

Current densities and spatial source extent

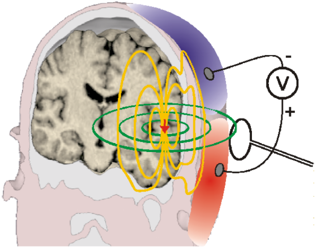
- Pyramidal cells in layer V are larger than in layer II/III and are thought to generate larger current dipole moments (Murakami et al., 2006, Jones et al., 2007)
- The maximal current dipole moment density across brain structures and species was determined to be in the range of 1-2 nAm/mm^2
- Using multivariate decoding Cichy et al., 2015 were able to distinguish between MEG signals from different orientation columns

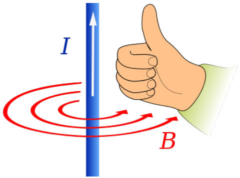


Murakami and Okada, 2015

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

- MEG measures the changes in the magnetic field generated by an electric current (Sarvas 1987, Hämäläinen 1993)
- These magnetic fields are mainly induced by primary currents based on excitatory activity (Okada et al. 1997)
- Volume currents yield potential differences on the scalp that can be measured by EEG

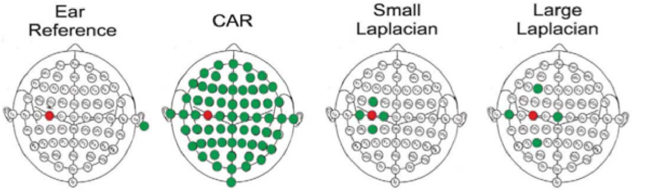




Baillet: MEG consortium

Measuring potential differences with EEG

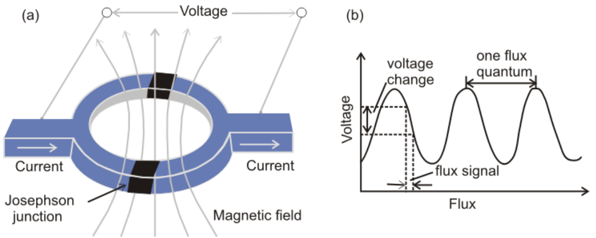
- EEG records potential differences at the scalp using a set of active electrodes and a reference
- The ground electrode is important to eliminate noise from the amplifier circuit
- The representation of the EEG channels is referred to as a montage
  - Unipolar/Referential ⇒ potential difference between electrode and designated reference
  - Bipolar ⇒ represents difference between adjacent electrodes (e.g. ECG, EOG)
- Potential differences are then amplified and filtered



McFarland et al., 1997

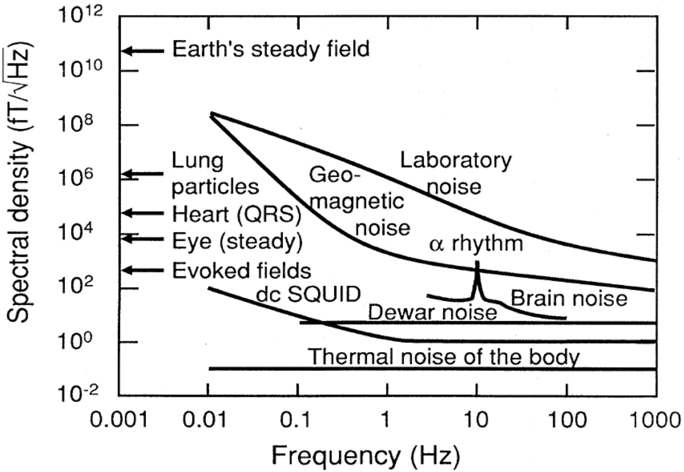
Superconducting quantum interference devises (SQUIDs)

- SQUIDs are ultrasensitive detectors of magnetic flux density (B) 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
- But: recent advances in using optically-pumped magnetometers for MEG (Boto et al., 2016; Boto, Meyer et al., 2017; Iivanainen et al., 2016)



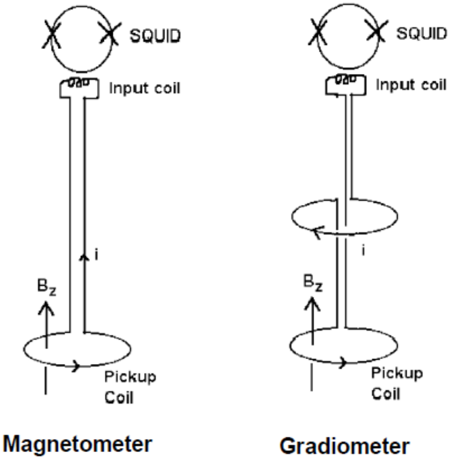
Adapted from J Clarke, Scientific American 1994

The high sensitivity means we also record a lot of noise

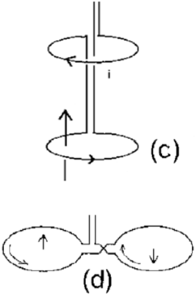


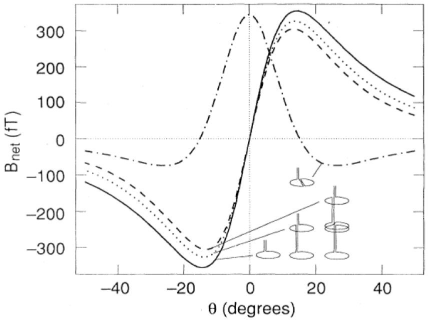
Hämäläinen et al., Rev. Mod. Phys. 1993

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

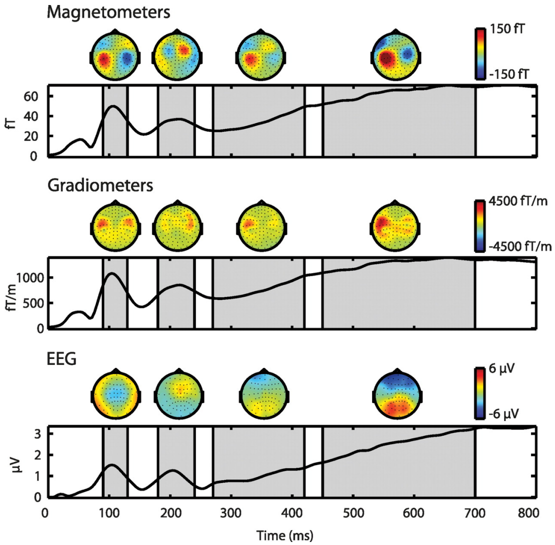


Axial and planar gradiometers have different sensitivity profiles





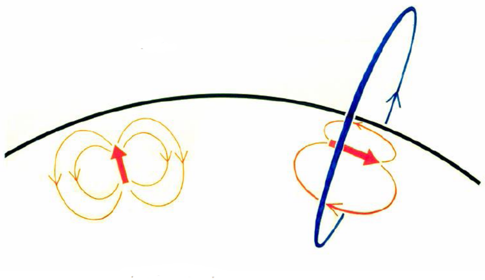
Sensitivity profiles are important when interpreting sensor patterns



From Sohoglu et al., 2012

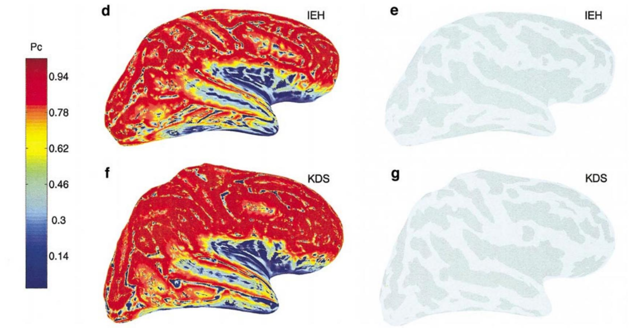
Given a spherical conductor radial source do not give rise to an external magnetic field

- The magnetic field generated by an electric current can be described by Biot-Savart's law
- For 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)



From D. Cohen

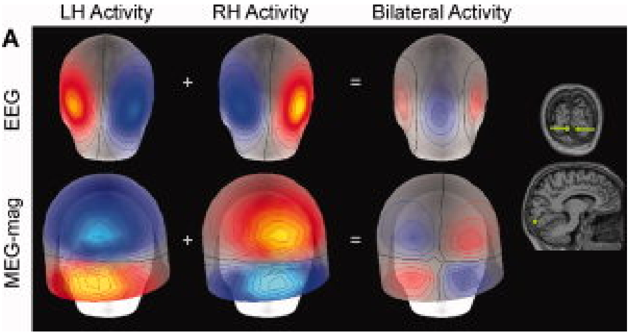
Gyral sources remain partly visible



Hillebrand and Barnes 2002

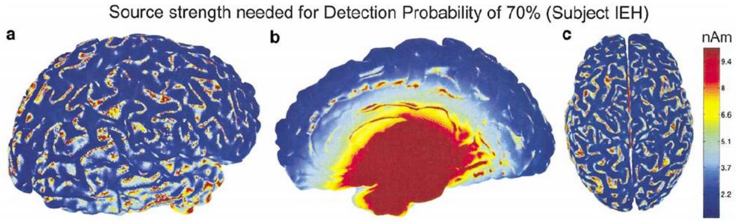
- Pyramidal cells are aligned perpendicularly to the cortex surface $\Rightarrow$ gryral sources are most radial
- But they are very close to the sensors and are surrounded by non-radial cortex to which MEG is highly sensitive

Extended and neighbouring sources can lead to source cancellations



Ahlfors et al., Brain Topog. (2010)

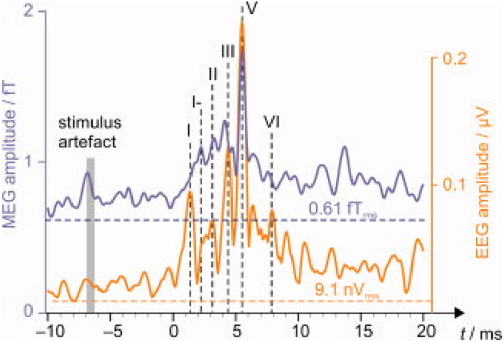
Depth is a limiting factor in MEG measurements



Hillebrand and Barnes, 2002

- Field strength decreases steeply with distance ($\frac{1}{r^2}$)
- As deeper sources are more radial, MEG is particularly insensitive

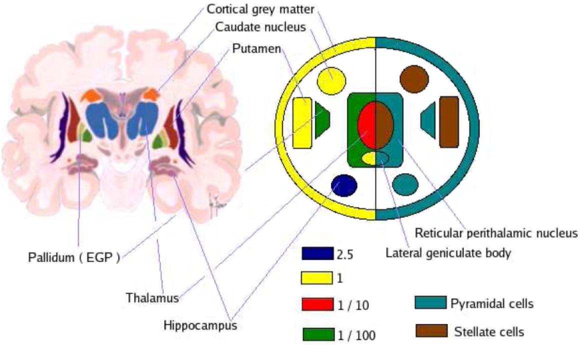
But we can see deep sources, can't we?



Parkkonen et al., 2009

- Increase the signal-to-noise ratio and incorporate previous knowledge (e.g. about timing and frequency range)
- Further examples: Thalamus (Tesche et al., 1994, Roux et al., 2013), Cerebellum and Thalamus (Timmermann et al., 2002), Hippocampus (Riggs et al., 2008) and Amygdala (Balderston et al., 2014)

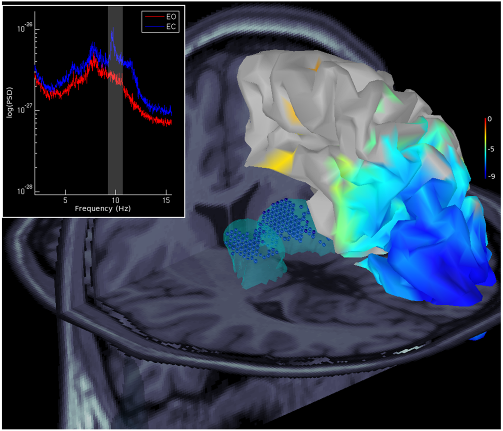
What are the deep brain neural generators of M/EEG signals?



Attal et al., 2007

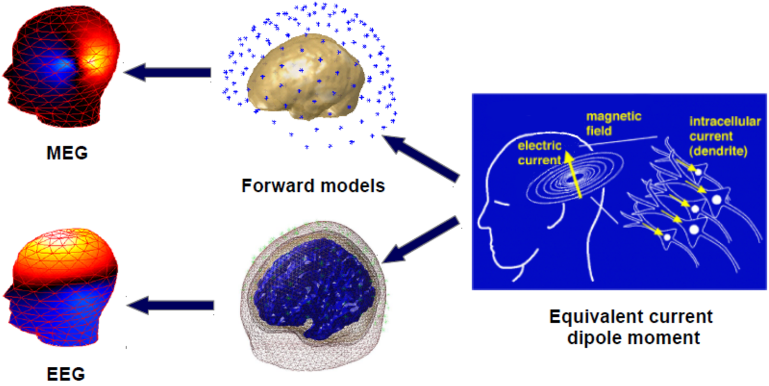
- Some of the first in vitro MEG measurements were performed on cerebellar (Okada and Nicholson, 1988) and hippocampal tissue (Okada et al., 1997)

Using realistic models facilitates the detection of thalamic alpha band activity



Attal and Schwartz, 2013

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



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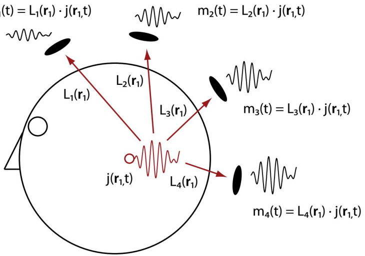


From Wibral et al., 2010

- The leadfields of the forward model describe the sensor patterns evoked by a unit strength source of a given location and orientation
- The leadfield matrix L depends on:
    - the type, location and orientation of sensors
    - the source space we are looking at (e.g. cortical surface or volumetric image)
    - the geometry of the head
    - the conductivity of head tissues

Subcortical and cortical sources of the auditory frequency following response

What are we measuring with M/EEG?

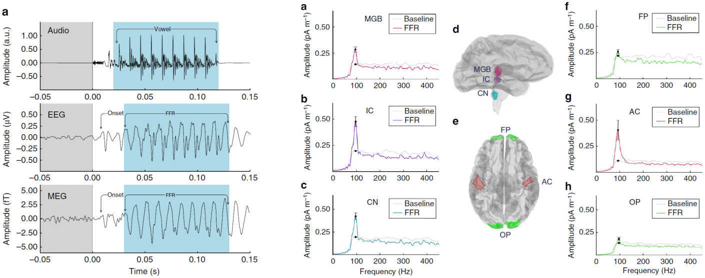
Saskia Helbling

Biophysical origin of M/EEG signals

Instrumentation

Sensitivity to deep and radial sources

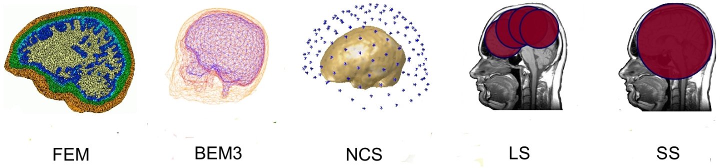
Forward models



Coffey et al., 2016

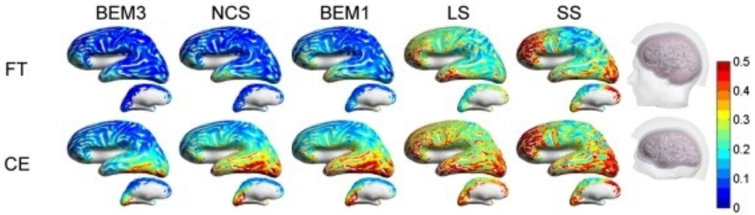
- See Troebinger et al., 2014 for a forward model that incorporate deep and superficial cortical layers and Meyer et al., 2017 for a model describing hippocampal activity

Headmodels can have different degrees of complexity



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

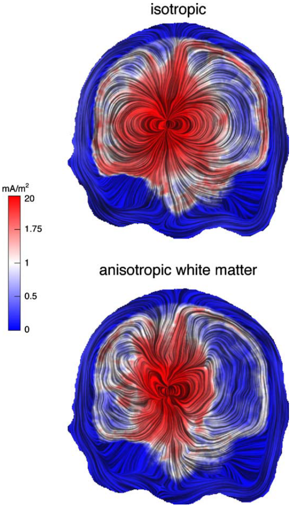
MEG also may benefit from using more complex headmodels



From Stenroos et al., 2014

- Earlier studies used only coarse surface meshes and employed a lower skull conductivity which might have biased the results for MEG to single shell models
- Simpler models are affected by segmentation errors as well

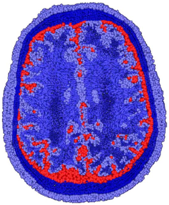
EEG and MEG are affected by white matter anisotropy

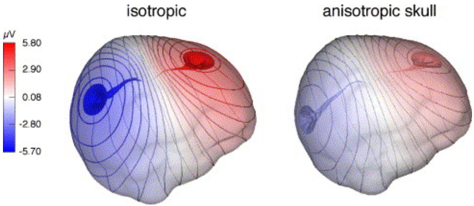


Wolters et al. 2006

EEG is strongly affected by skull anisotropy

- While MEG was hardly affected by skull anisotropy, potential differences on the scalp as measured by EEG are severely smeared
- More recent studies model different skull structures explicitly using isotropic conductivities (Dannhauer et al., HBM, 2011)





Wolters et al. 2006

Summary

- Electromagnetic signals predominantely based on aggregate postsynaptic currents of tens of thousands of pyramidal cells $\Rightarrow$ but other cells types as well as action potentials will also contribute to the signal

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Summary

- Electromagnetic signals predominantely based on aggregate postsynaptic currents of tens of thousands of pyramidal cells $\Rightarrow$ but other cells types as well as action potentials will also contribute to the signal
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- EEG has a higher sensitivity to deep sources, but will be more strongly affected by the conductivity changes between brain, skull and skalp

Summary

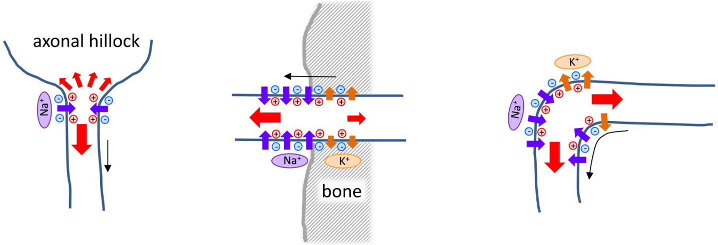
- Electromagnetic signals predominantely based on aggregate postsynaptic currents of tens of thousands of pyramidal cells $\Rightarrow$ but other cells types as well as action potentials will also contribute to the signal
- MEG is more sensitive to tangential than to radial sources, while EEG 'sees' both components
- EEG has a higher sensitivity to deep sources, but will be more strongly affected by the conductivity changes between brain, skull and skalp
- Forward models describe how primary currents in the brain give rise to electric potentials or magnetic fields measured outside the head

Further reading

- An Introduction to the Event-Related Potential Technique by Steven J. Luck
- MEG: An Introduction to Methods, Edited: Hansen, Kringelbach, and Salmelin
- Magnetic Source Imaging of the Human Brain, Edited by Lu and Kaufman
- Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain, Hämäläinen et al., Rev. Mod. Phys. (1993)
- Basic mathematical and electromagnetic concepts of the biomagnetic inverse problem, Sarvas, Phys. Med. Biol. (1987)

Thank you for your attention!

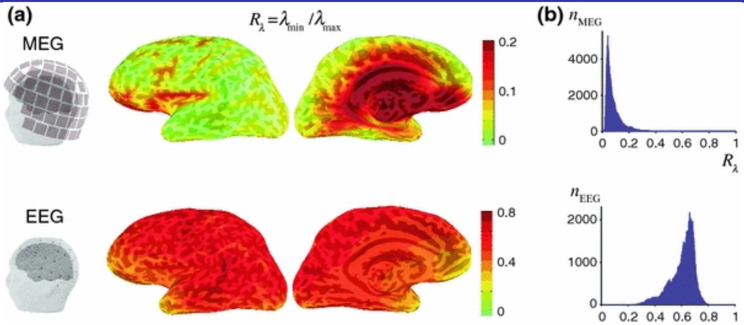
M/EEG is sensitive towards postsynaptic potentials, not action potentials



Courtesey of Thomas Knösche

- Magnetic quadropoles decline steeply with distance ($\frac{1}{r^3}$)
- Due to their short duration AP would need to be highly synchronized to lead to a measurable signal (but see for example Curio et al., 2008)
- The cancellation of de- and repolarising currents will be incomplete under some circumstances

Since the head is not a perfect sphere we are able to detect radial sources to some degree



From Ahlford et al., 2010