Basics of measurement and modeling of MEG

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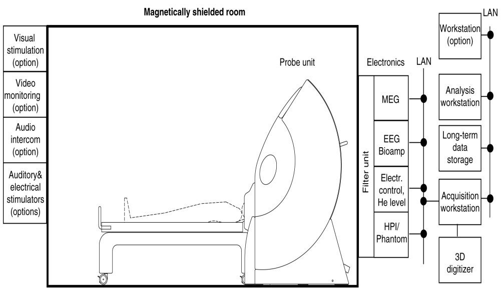
- Basics of MEG
  - technology
  - origins of the signal
  - measurement and noise
- Data analysis
  - source reconstruction
  - neuronal oscillations
  - connectivity

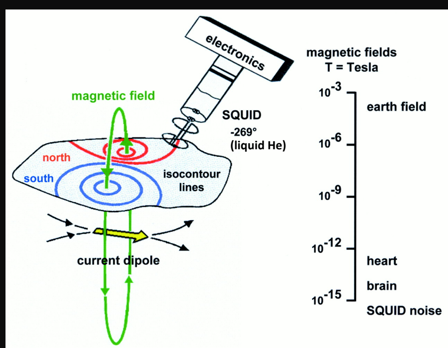
MEG components

- Magnetometer device
  - sensors
  - electronics
  - software
- Magnetically shielded room
- Electric signal amplifiers
- Stimulus devices
- Response devices
- Monitoring etc. devices

System block diagram

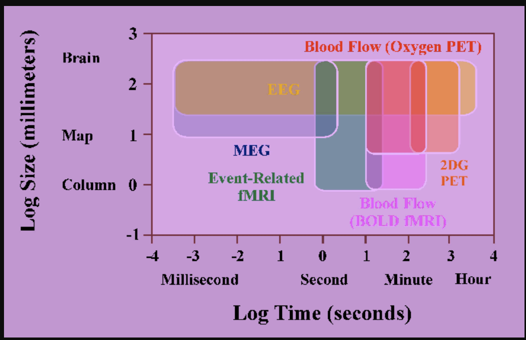


MEG principle



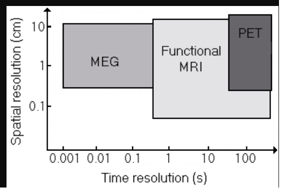
SQUID = Superconducting Quantum Interference Device

Neuroimaging methods



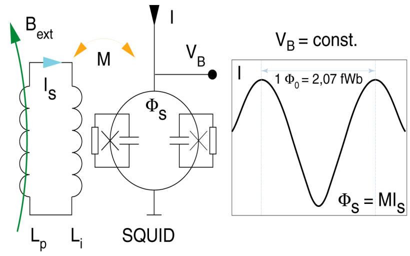
Spatiotemporal MEG?

- measures magnetic fields directly generated by neuronal activity at a high sampling rate
  => Excellent temporal resolution
- Field measurements possible only > 30 mm away from sources
  => moderate spatial resolution



SQUID readout principle

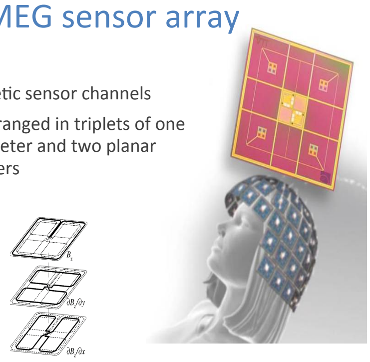
- **S**uperconducting **QU**antum **I**ntereference **D**evice
- SQUIDs needed to detect this small magnetic fields



B_{ext}: the measured magnetic field

MEG sensor array

- 306 magnetic sensor channels
- Sensors arranged in triplets of one magnetometer and two planar gradiometers

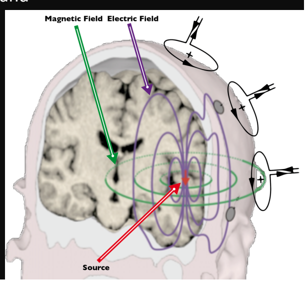


Courtesy of Elekta 10

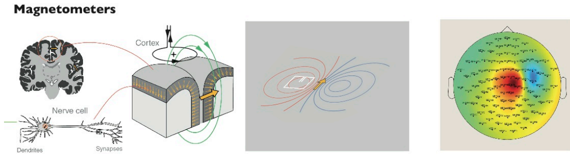
MEG sensor arrangement

306 channels in triple sensors:
- 102 magnetometers
- 204 planar gradiometers

Measure the normal component and its tangential derivatives

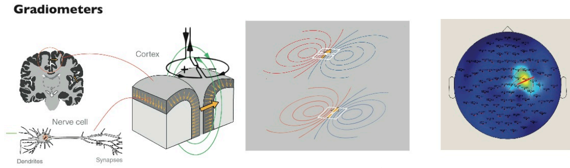


Magnetometers



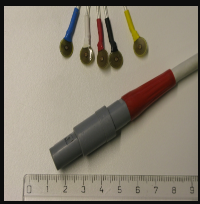
Pick-up coil geometry defines the sensitivity profile of a sensor

Gradiometers



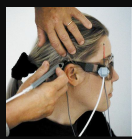
Measurement set-up | Pick-up coils sample the field | Measured topography

Head Position Indicator coils



During MEG measurement, current inserted to coils
=> they can be localized due to the magnetic field

3D digitizer



Establishes the relationship between the head anatomy and the HPI coils in 3-d space

Trigger interface system

- Synchronization of external events to brain events
- Merged to MEG data stream
- 16 ch I/O

Noise in MEG signals

- Non-neuronal magnetic signals from the body
  - Heart
  - Retina
  - Muscles (ocular, scalp, neck, jaws, breathing)
  - Magnetized objects
- External noise sources
  - Traffic, electric lines, motors and devices, Earth, …

Rejection of noise in MEG signals

Magnetically shielded room:

- layered mu-metal and aluminium
- High permeability
  => ”catches” and aligns magnetic field lines
- Works as Faraday’s cage for EEG as well
- Shielding factors of ~10^6
- from DC to radio frequencies

Rejection of noise in MEG signals

Signal processing techniques

- spatial and frequency filtering methods
- Maxwell filtering (”SSS” by Elekta)
- Signal decomposition methods (PCA, ICA)

Reference sensors / compensation coils

- Internal active shielding, IAS

Rejection of noise in MEG signals

It is best to minimize noise in the first place:

- check the environment
- empty-room test measurement
- test measurement with the subject
- monitor signals during data acquisition

Concurrent EEG

- Simultaneous EEG possible
- Non-magnetic electrodes & leads required
- No additional interference from MEG
  - movement artifacts
  - size constraints
  - preparation time
- Also EOG, EKG, EMG, …

Other device options at MEG

- Stimulation devices
  - Visual, auditory, somatosensory
- Response devices
  - Finger pads, accelerometers,
- Monitoring devices
  - cameras, microphones, eye-tracking

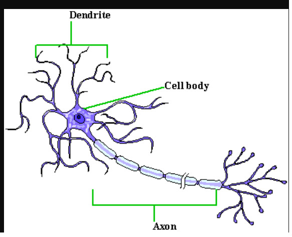
Do we see a neuronal signal with MEG?

- Neurophysiology & physics

Neurophysiology

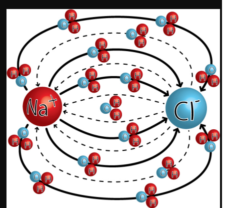
- Neurons
  - Axon, soma and dendrites
- Synapses

- Electric phenomena
  - Action potentials
  - Post-synaptic potentials



Neurophysiology

- *Ions* are the basis of electric phenomena in biology
  - K^+, Na^+, Cl^-, Ca^{2+}

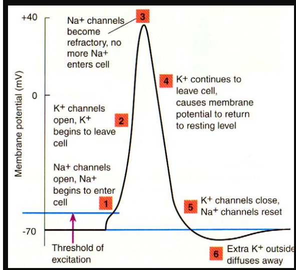


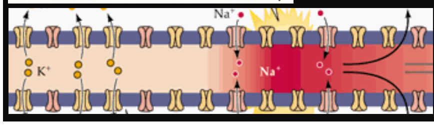
- Electrically charged =>
  - Generate an electric field
  - movement = electric current
    ⇒ Magnetic field

- Physics of magnetic and electric fields known for 150 years
  - Maxwell's equations

$$\nabla \cdot \mathbf{E} = \frac{\rho}{\varepsilon_0}$$
$$\nabla \cdot \mathbf{B} = 0$$
$$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t}$$
$$\nabla \times \mathbf{B} = \mu_0 \mathbf{J} + \mu_0 \varepsilon_0 \frac{\partial \mathbf{E}}{\partial t}$$

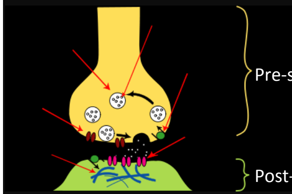
Action potential (AP)





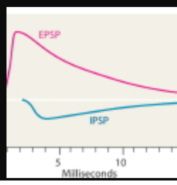
Very short duration (~ 1 ms)
High upper limit for frequency
Signals "outward" traffic
Quadrupolar field – decays fast over distance

Postsynaptic potential (PSP)



Pre-synaptic cell

Post-synaptic cell



- Longer duration than for AP
- Signals "inward" traffic to a region
- Dipolar field – decays slower over distance

What is needed for a signal?

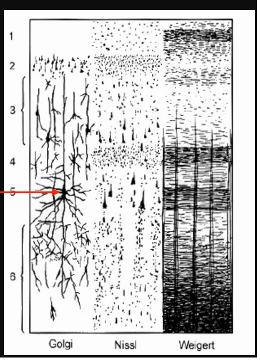
What is needed for a signal?

- several cells:
  - Fields linearly additive
    - same location and direction => cumulation
  - Activation at the same time (*synchronous*)
  - Field geometry that decays slowly with distance
    - Dipolar rather than higher order fields
  - Large currents

Cortical gray matter

Layer 5 large pyramidal cells are considered important for generation of the MEG signal

Roughly speaking, order of 10000s of cells needed for a signal



MEG or EEG sees better?

EEG measures the electric potential difference between two electrodes. The potential difference is due to extracellular *volume currents* flowing in a resistive medium (scalp). Volume currents are induced by intracellular *primary currents*.

MEG measures the magnetic field generated by *primary currents* outside the head. Secondary *volume currents* usually contribute to the field.

- In EEG we have the *reference* problem; MEG is reference-free
- EEG signal depends on the conductivity geometry highly, MEG signal somewhat

MEG or EEG sees better?

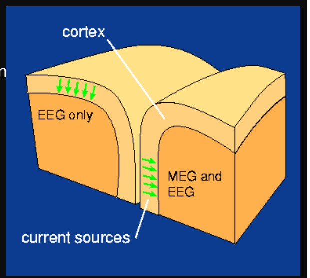
- MEG is less affected by tissue conductivity
  - Easier and more accurate source modeling
  - Model inaccuracies affect MEG less
  - ”Invisible” sources in MEG
  - Signal attenuates strongly over distance
  - Signal changes with head location
- EEG often sees stronger / additional signals
  - More sensitive to deep sources
- Why not use both?

Sources of the signal

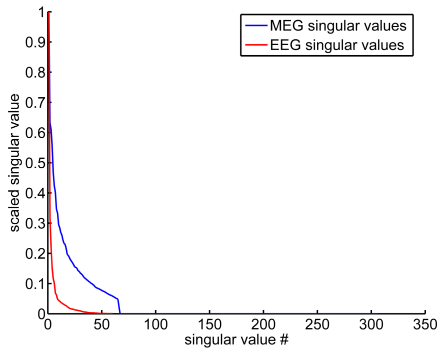
Theory and modeling show that

- MEG signal originates mainly in the walls of the cortical sulci
- EEG signal can be generated anywhere

- signals from deep structures are substantially weaker



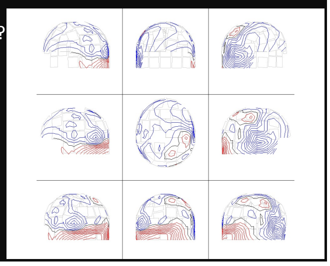
Degrees of freedom in MEG and EEG data
estimated by singular value matrix decomposition



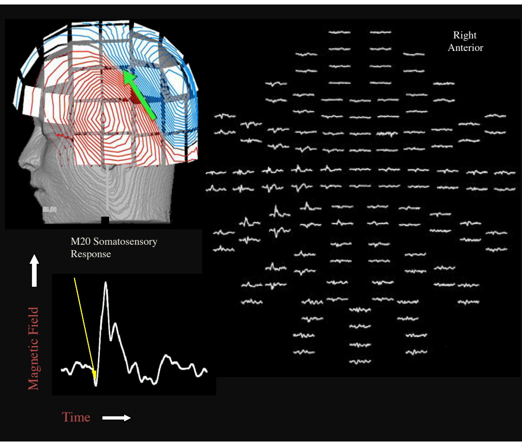
Interpreting the MEG signal

MEG measurement provides information on the magnetic field around the head for each millisecond of the measurement

- A lot of information!
- ... but what is it good for?



Elekta Neuromag software

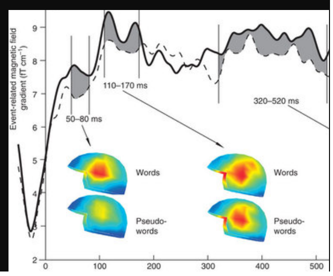


Interpreting the MEG signal

Conventional approaches for an event-related experiment:

- Average evoked responses (on single channels)
- Averaged field distribution (on single latencies)

Reveals local modulation by stimulus parameter, task, etc.



Source modeling of MEG data

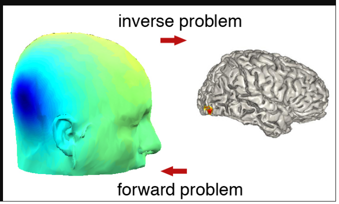
- Channel-level analysis reveals effect timing
- Anatomically specific findings require transforming the channel-space data to source-space data
- Requires knowledge of the system and understanding of electromagnetic field theory

Source reconstruction, *a.k.a.* inverse modeling

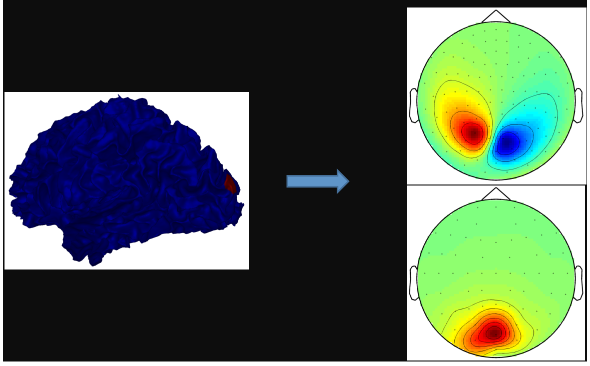
- Relates the channel information to activity in actual brain regions
- A bunch of different approaches / practices used; even more proposed for use
  - None of these is the correct one!
    - No unique solution exists
- Highly affects the relevance of further analyses!
  - can be dangerous if done wrong

Forward or inverse problem?

- forward: what kind of field is generated by a given source?
- inverse: what kind of source configuration may generate the measured magnetic field?

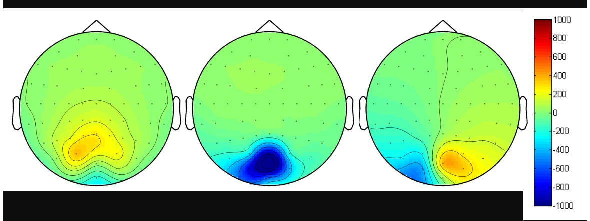


Topographies of a current dipole



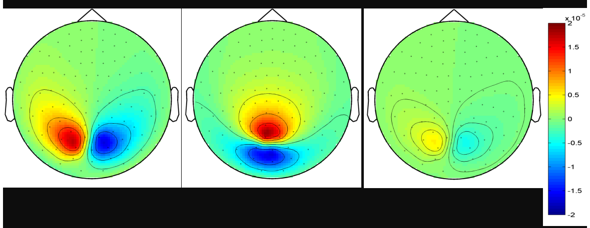
Topographies of a current dipole in three orientations

EEG

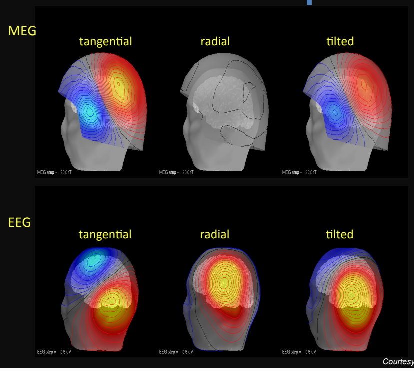


Topographies of a current dipole in three orientations

MEG



MEG and EEG dipole fields



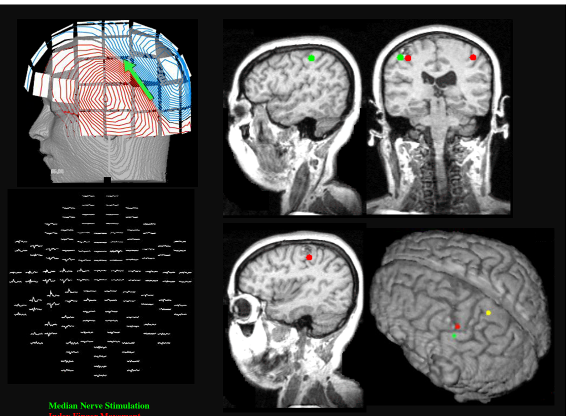
Courtesy of Prof. Matti Hämäläinen

Methods for inverse modeling

- dipole models
  - specify 1-4 dipoles; fixed, moving, rotating, ...
- distributed current solutions
  - Minimum norm estimates (MNE)
  - LORETA (low resolution tomography)
- beamformers
  - adaptive estimates for source strength per voxel
  - not real/complete inverse solutions; properties unknown
- signal decomposition methods
  - explain the data with interpretable components
  - do not go to source space at all

Point-like source models

- Equivalent current dipole (ECD)
  - infinitesimally short current "line"
  - orientation and strength
  - models the activity of a small patch of the cortex
  - fitted to the measured data in the least-squares sense
  - a single dipole or multiple dipoles
  - **the most common MEG/EEG source model**



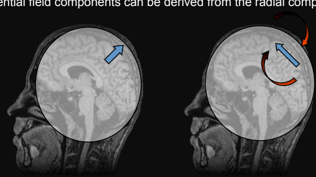
Source modeling in a sphere

For MEG sphere model, we need:
- Origin of the sphere
- Sensor information
- Theory, e.g. the field of a current dipole

Radial and tangential dipole

in a spherical head model

Outside of the sphere:
- Radial dipoles generate zero magnetic field (but EEG sees them!)
- MEG arises from tangential dipoles
- Radial component of the magnetic field does not depend on conductivity profile
  - but the electric field does!
- Tangential field components can be derived from the radial comp.



A radial dipole　　A tangential dipole

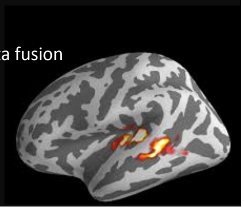
courtesy of Elekta

Source modeling in evoked response studies

Traditionally, (single) dipole modeling has prevailed

Distributed source models estimate source current strength all over the cortex

- Helps interpret the findings
- May work as a sanity check
- A straightforward way to MEG/EEG data fusion



Source modeling in realistic anatomy

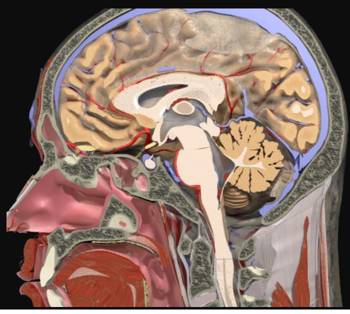
We first need
- The anatomy
- Potential signal sources
- Electric model of tissue properties
- Measurement geometry & forward model
- Inverse modeling theory (*a priori* assumptions)

This will take a while...

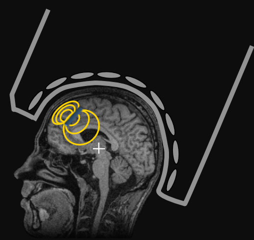
Cranial anatomy

Skin
Skull
Cerebrospinal fluid
Gray matter
White matter

- These have varying electric properties!

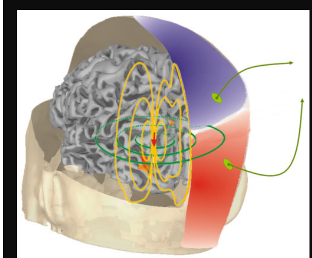


Macroscopic currents in the brain

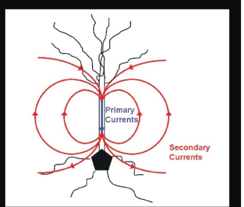


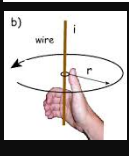
- ***Primary current:*** small source of impressed electric current
- ***Secondary** or **volume currents:*** complete the circuit driven by the primary (passive / ohmic)
- Electric properties of the tissue limit the currents

Fields from the currents



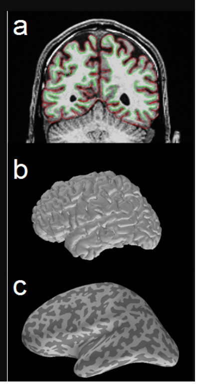
Magnetic field
Electric field





Anatomical information

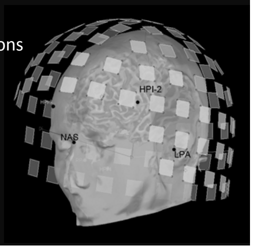
- From magnetic resonance images (MRIs)
- White & gray matter, skull, and scalp need to be segmented
- Current sources are localized to the cortex (source model)
- Conductivity model (3-layer)



Forward model

Based on head model, device geometry, and the relationship between these two

- Segmented MRI
- Realistic tissue conductivities
- Cortically constrained source locations
- Field computations using boundary element method (BEM)
- Sensor information
- Head position information (HPI)



PARENTAL
ADVISORY
EXPLICIT CONTENT

MATHEMATICAL

Linear forward and inverse problem

M/EEG problems are linear => matrices

$$Gx = y$$

G is the forward model
x are the source activations
y is the measurement result (when forgetting noise)

We are looking for

$$x = G^{-1}Gx = G^{-1}y$$

G^{-1} or inverse of *G* is a matrix for which $G^{-1}G=1$

Unluckily, such a matrix does not exist in this case.

Forward and inverse problem

Typically in MEG: 306 channels
Typical source model: ~6000 sources

- More unknowns than data points
  => infinite number of "correct" solutions

Which one should we choose?

The minimum norm estimate

We impose *a priori* information to select only one of the infinite correct solutions

MNE supposes that:

- Source amplitudes are normally distributed with known co-variance
- The measurement includes normally distributed noise with a known co-variance
- (Sources are located in the cortical gray matter)

A priori information could be something else
⇒ different (perhaps equally correct) solution

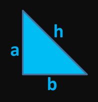
Problems: difficult to validate
sensitive to noise

Minimum norm estimate

MNE is the solution with the smallest total source energy; in mathematical terms, the minimum L^2-norm:

$$|x|=\mathrm{sqrt}(x_1^2 + x_2^2 + \ldots + x_n^2)$$

cf. Pythagoras: $h = \mathrm{sqrt}(a^2 + b^2)$



Such solutions are generally found using the pseudoinverse of G, G^+ :

$$x = G^+y = G^T(GG^T)^{-1}y$$

We more often use a regularized solution:

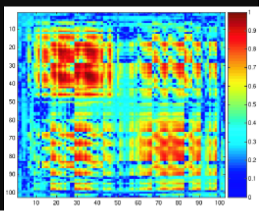
$$\textbf{MNE: } x = RG^T(GRG^T + \lambda^2 C)^{-1}y$$

R source covariance (often diagonal => sources *a priori* independent)
G gain matrix (forward solution)
C noise covariance

Noise covariance matrix – statistics of non-interesting signals

- Is needed for the inverse model
- Is used to give the noisiest signals the lowest significance

Noise covariance matrix for 102 magnetometers from an empty-room MEG measurement



Unmodeled noise in MEG

= sensor noise components not included in noise covariance

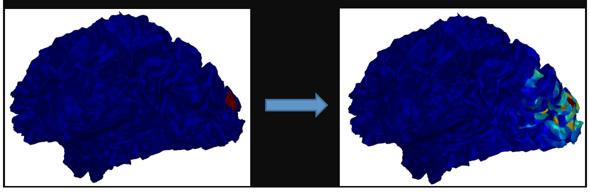
- Bioelectric sources of the subject: EKG, EOG. EMG
- Clothing, dental work, jewelry, surgery, ...
- Head movements
- Radio frequency interference
- Stimulator devices
- Transient external noise

MNE models these as currents in the cortex!

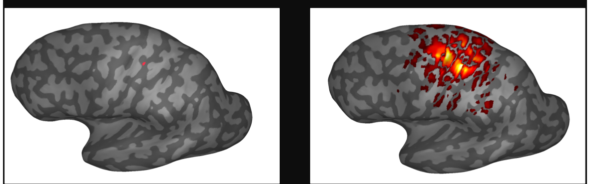
- So clean up your data first

An example MNE solution in an idealized case

✓ Single localized source
✓ High sensitivity for the source
✓ No noise (ambient, brain, sensor)
✓ Known head anatomy, location, conductivity
✓ MEG+EEG



MNE point-spread

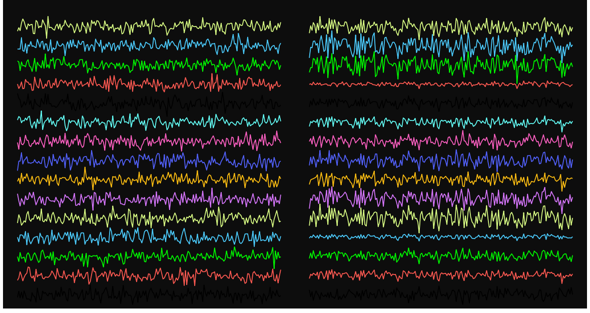


Original simulated point-like source

MNE solution after a simulated measurement

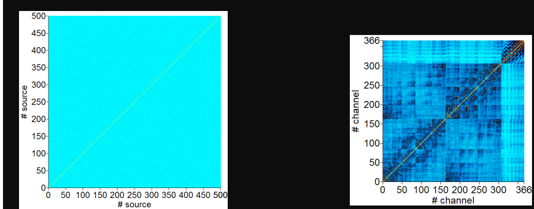
Simulated MNE sources

Simulated random activity in all 7000 sources (*left*)
MNE of source activity, after a virtual MEEG measurement (*right*)



Signal space correlations

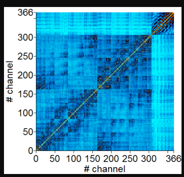
Several sensors are sensitive to a given current source
=> channel signals are always mutually correlated

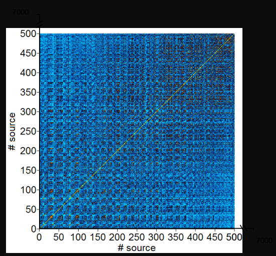


Simulated independent sources → forward modeling → MEG and EEG channel correlations

MNE with simulated noise

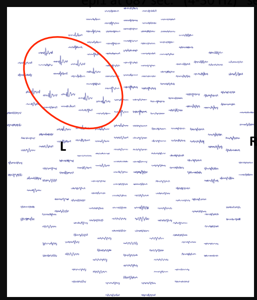
Strong correlations emerge in source reconstructions, even when the sources are originally independent!

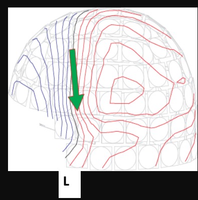




MEG and frontal lobe epilepsy

epi1 at 687 sec. (4-30 Hz) sensor space

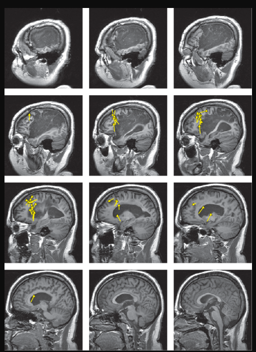


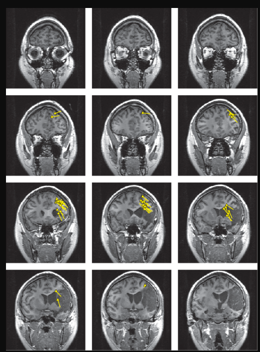


- Detects and localizes non-redundant epileptic
- Helps surgery planning
- Improves treatment results

[Dr. M.Funke, University of Utah]

MEG and frontal lobe epilepsy





[Dr. M.Funke, University of Utah]

MEEG data preprocessing

Data include several artifacts that might cause unpredictable errors in source localization and affect response size and shape, destroying it all

Getting rid of non-neuronal MEEG signal components using ICA:
- low-frequency components (blinks, movements, heart)
- high-frequency components (saccades, muscles)

- several rejection criteria for ICs:
  - scalp topography
  - frequency content
  - time courses wrt. experiment
  - correlation with EOG/EKG
  - higher-order statistical properties