

# Magnetoencephalography: An introduction to methods and its application to natural speech stimuli

Oberseminar Medizinische Physik

Till Habersetzer, 17.11.2020



# Table of contents

- Neurons as current generators
- MEG sensors
- Head movements (and different coordinate systems during subject preparation
  - Co-registration with anatomical MRI)
- Source modelling
  - Forward and inverse modelling
- Natural speech stimuli in M/EEG analysis
  - Encoding/ decoding models
  - Reconstruction of speech envelope and neurophysiological measurement of speech intelligibility

# MEG-lab

Measurement of **electromagnetic** activity of the brain:

- **Magnetoencephalography (MEG)**
- **Electroencephalography (EEG)**

Magnetically shielded room with MEG



Room for preparation of  
subject + operation of MEG

[1]

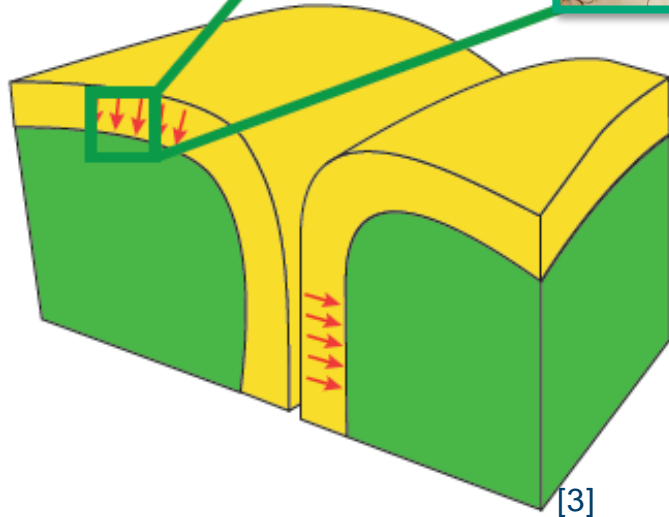
# Neurons as current generators

Large cortical pyramidal cells organized in macro-assemblies with their **dendrites normally oriented to the local cortical surface**

$Q = I \times d$   
(10 to 100 nAm) with the  
equivalent current  
dipole (ECD) model



[2]



[3]

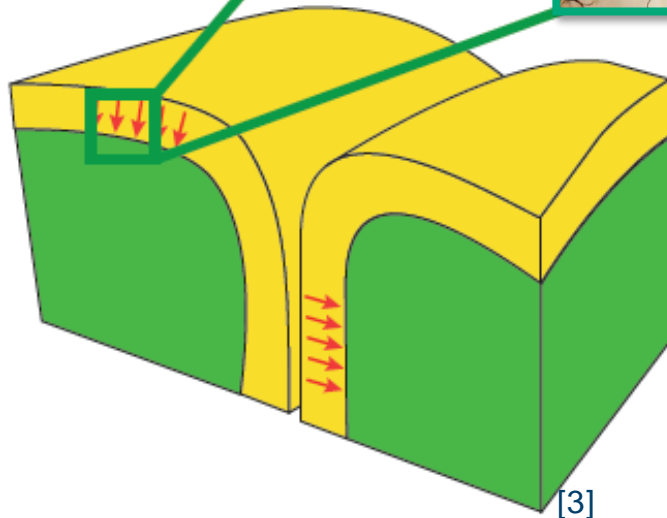
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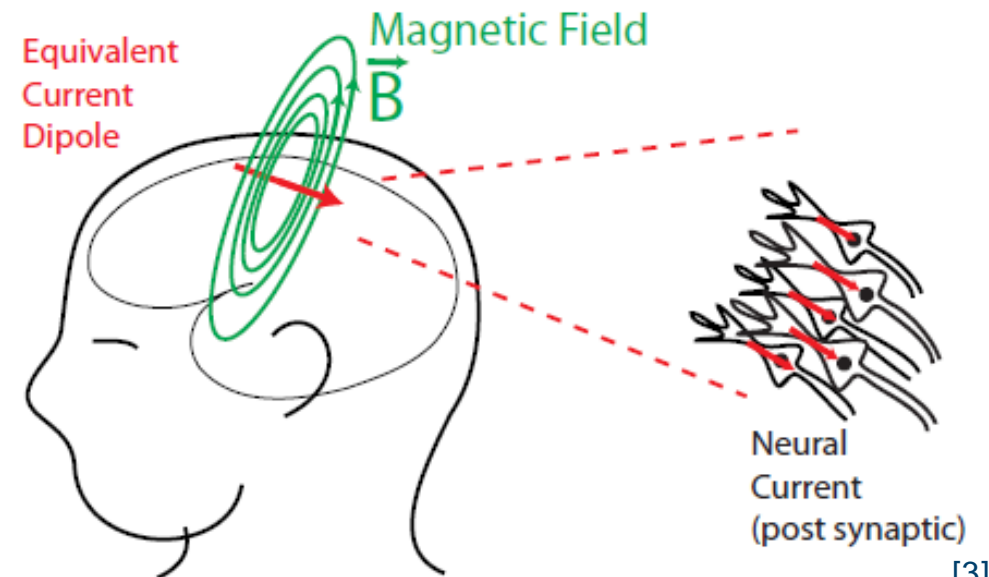
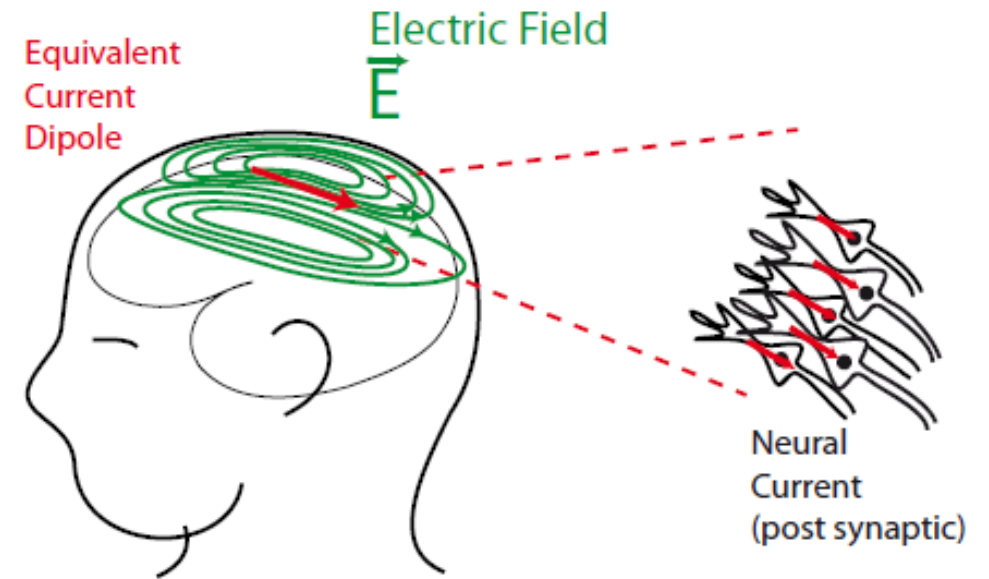
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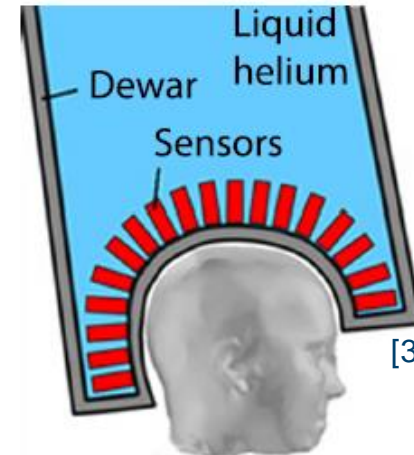
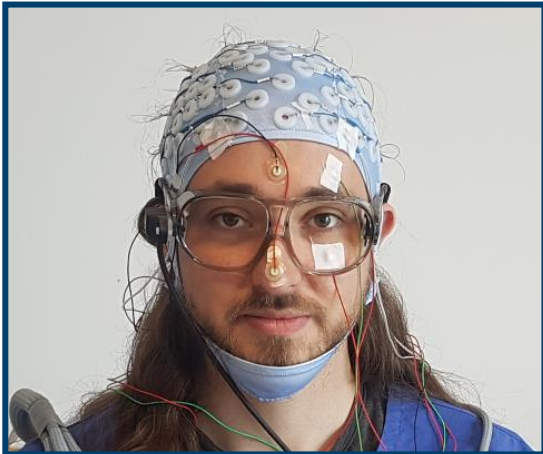
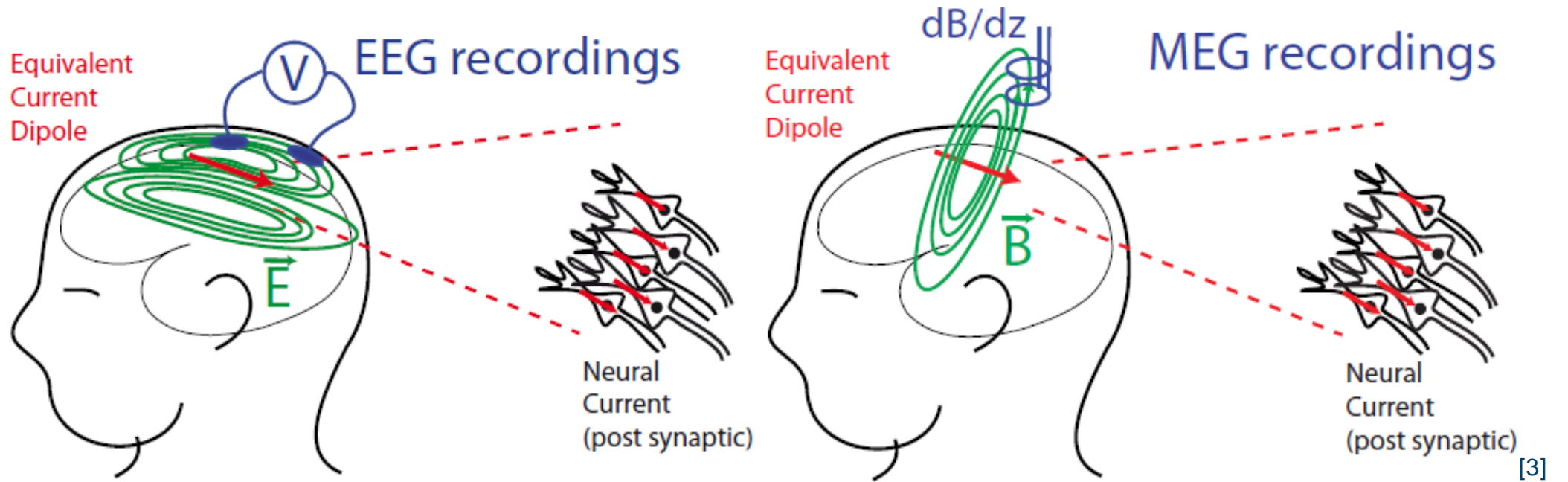
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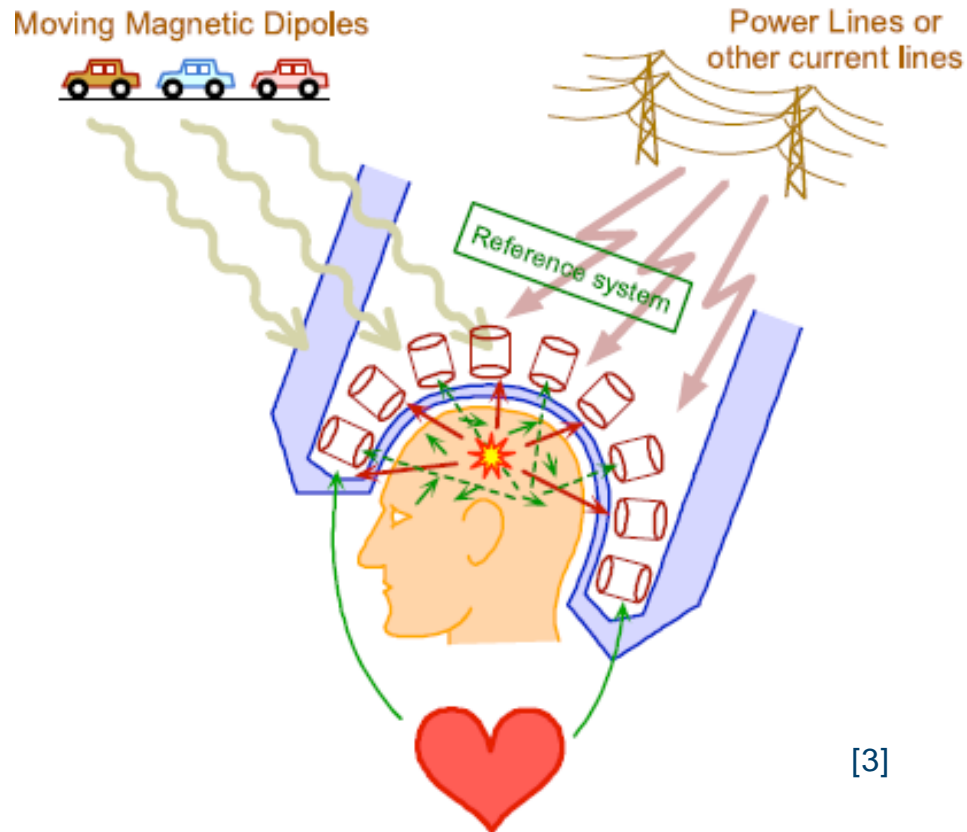


# EEG & MEG systems



[1]

# Sources of magnetic fields



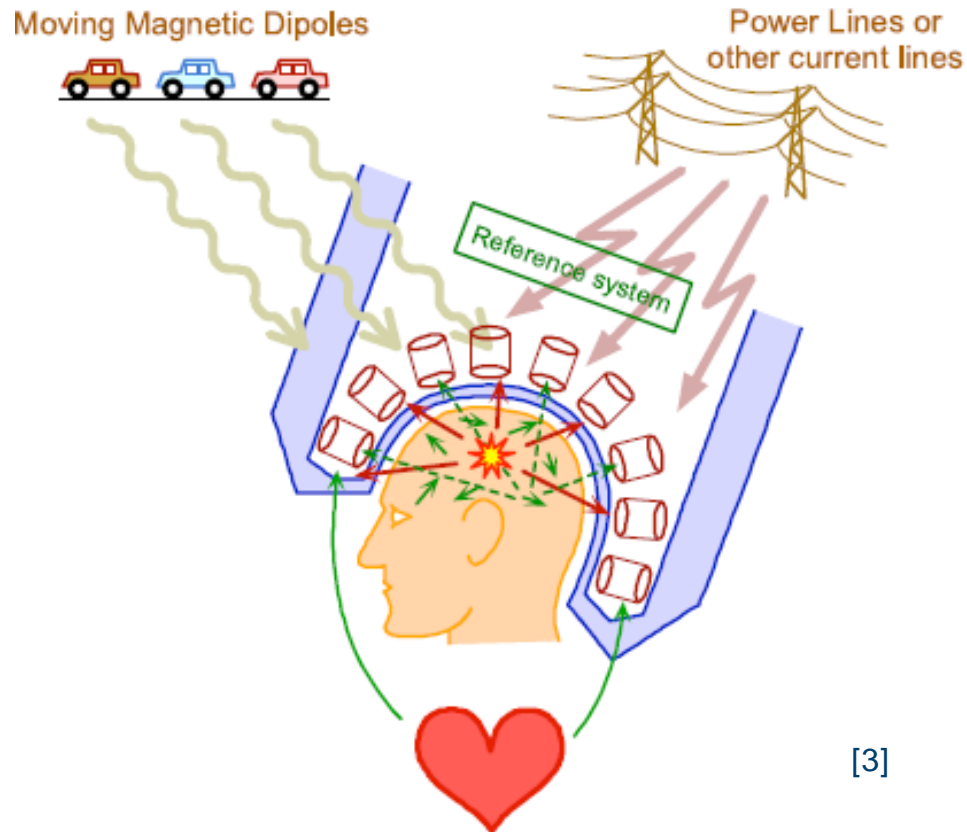
[3]

Look at the units!

10,000,000,000,000,000	
1,000,000,000,000,000	MRI
100,000,000,000,000	
10,000,000,000,000	
1,000,000,000,000	
100,000,000,000	
10,000,000,000	Earth's static field
1,000,000,000	
100,000,000	Urban Noise
10,000,000	
1,000,000	
100,000	Heart
10,000	Skeletal Muscle
1,000	Epileptic Spike
100	Evoked Responses
1	Limit of SQUID resolution

Magnetic field strength density measured in femtotesla (fT) (Proudfoot et al. 2014)

# Sources of magnetic fields



Look at the units!

10,000,000,000,000,000	
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1,000,000	
100,000	Heart
10,000	Skeletal Muscle
1,000	Epileptic Spike
100	Evoked Responses
1	Limit of SQUID resolution

Extremely complicated and expensive method to measure the train schedule!

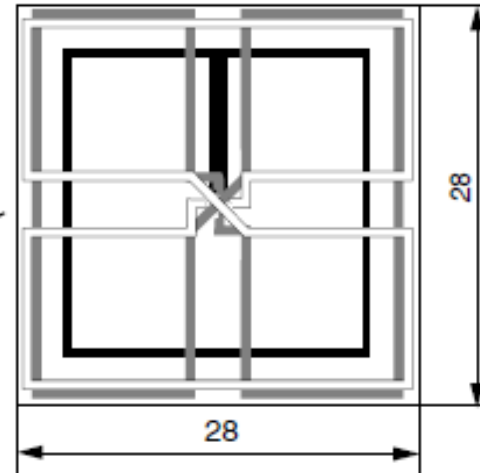
Magnetic field strength density measured in femtotesla (fT) (Proudfoot et al. 2014)



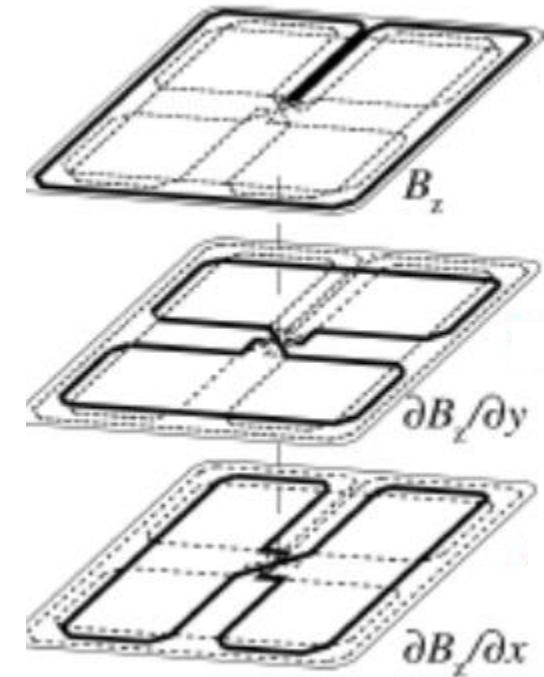
# MEG sensors



[3]



[4]



[3]

## Elekta Neuromag TRIUX MEG system

- 102 triple sensor detector units
  - ▶  $\Sigma$  306 sensors

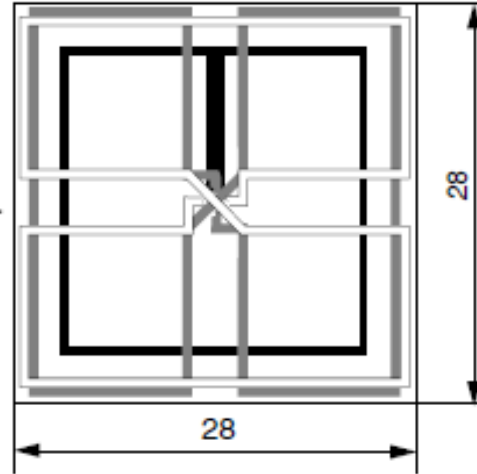
## Per triple detector sensor unit

- 1x magnetometer, 2x planar gradiometers

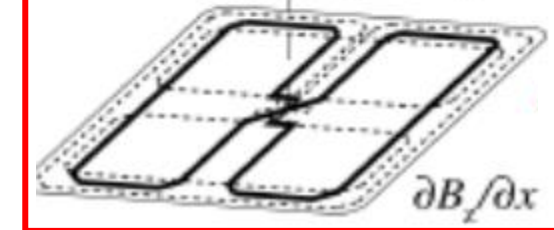
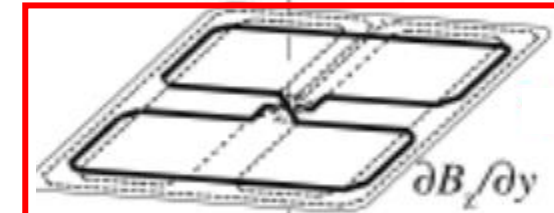
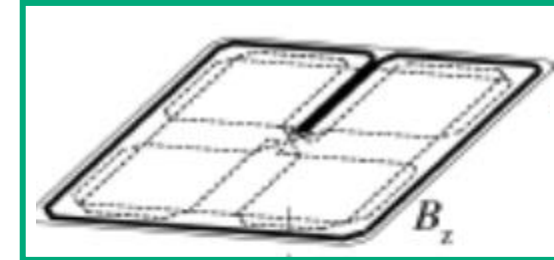
# MEG sensors



[3]



[4]



[3]

## Elekta Neuromag TRIUX MEG system

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### Per triple detector sensor unit

- 1x magnetometer, 2x planar gradiometers

## Magnetometer

- general magnetic fields
- very sensitive overall, noisy

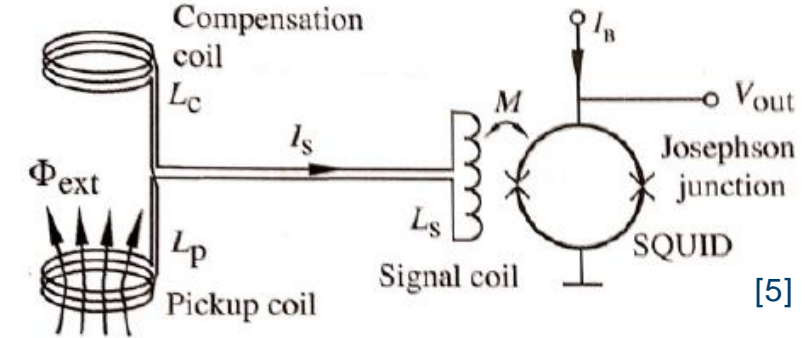
## Planar gradiometer

- focal magnetic fields
- most sensitive to fields directly underneath

# MEG sensors

## MEG uses sophisticated sensing technology

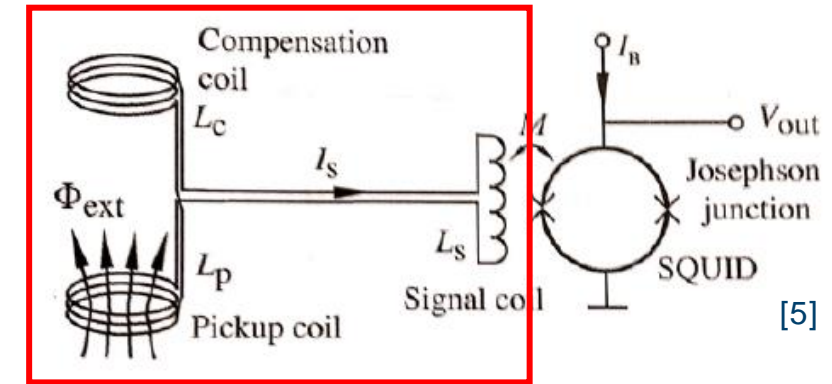
- SQUID (Superconducting Quantum Interference Device) sensor
- fully understanding of SQUIDs requires
  - quantum mechanical treatment
  - superconductivity



# MEG sensors

## MEG uses sophisticated sensing technology

- SQUID (Superconducting Quantum Interference Device) sensor
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  - superconductivity

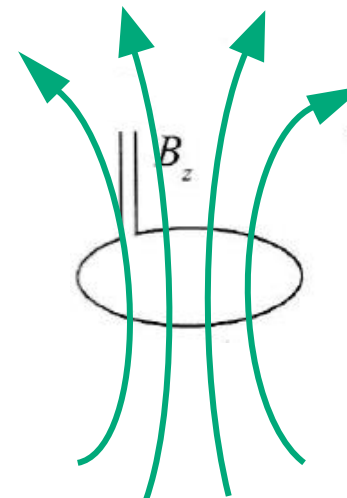


Different types of **flux transformers** are available which couple the signal to the SQUID

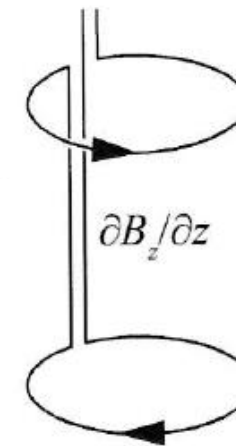
## Basic principle

Magnetic flux across coil surface induces an electrical current in the coil wiring material, whose amplitude is instantaneously proportional to the magnetic field.

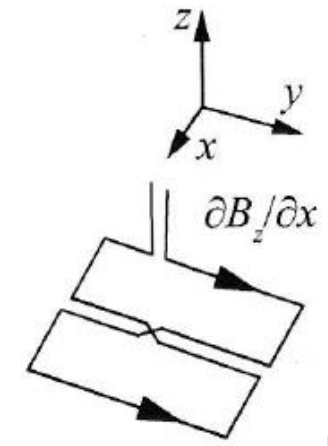
Magnetometer



Axial gradiometer



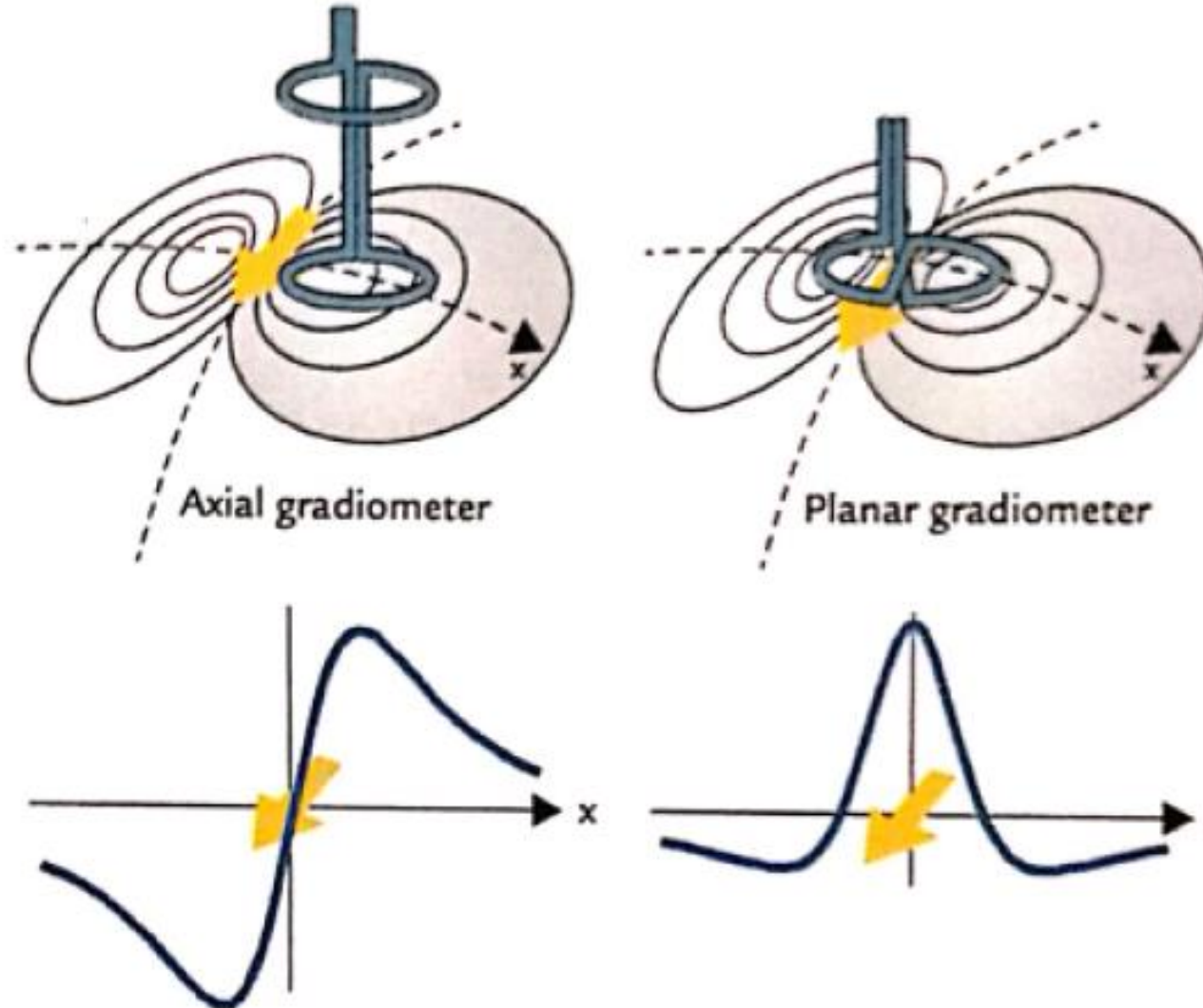
Planar gradiometer



[5]

# MEG sensors – sensitivity profile

## Influence of flux transformers on the measured **field distribution** and **signal strength**



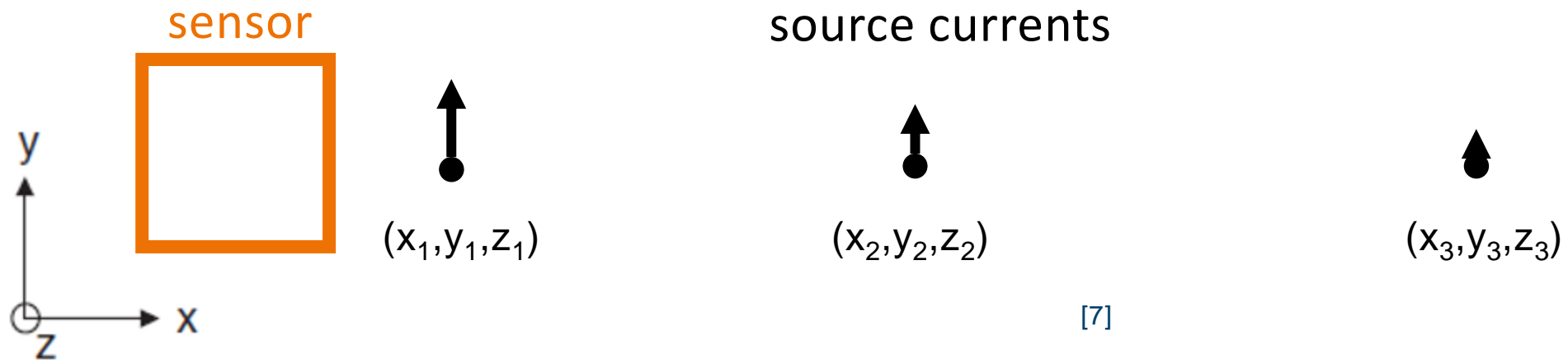
- Gradiometers in general insensitiv to homogeneous fields
- **Axial gradiometer/ magnetometer** peaks for signals around the rim of the sensor
- **Planar gradiometer** gives maximum signals for sources right beneath them

[7]



# MEG sensors – sensitivity profile

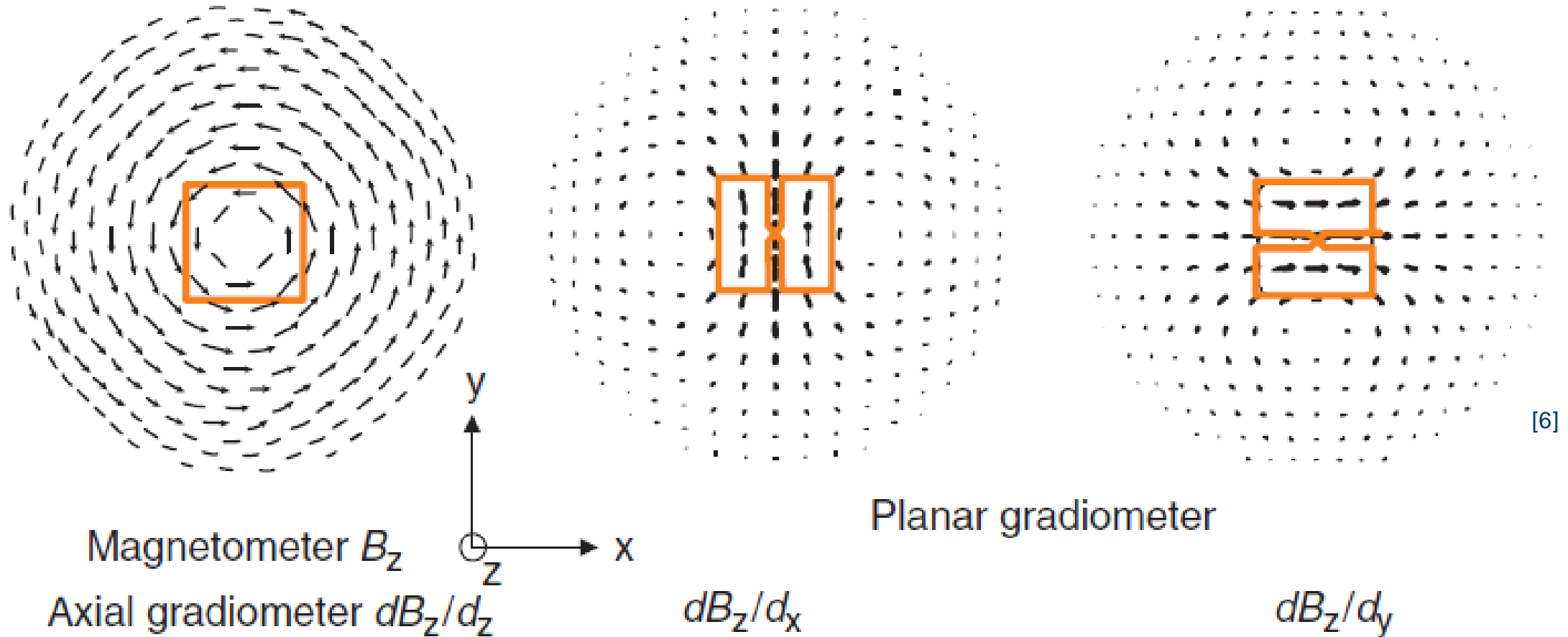
- Formally, these spatial sensitivity patterns of the sensors can be described with the concept of a *lead field*
- Fictitious **vector field** for a given sensor whose value at a spatial location gives the **direction of the current that yields the maximal output** at that location, and the **gain** with which the source current affects the output of the sensor.
- Thus, each sensor type, or pick-up coil geometry, has a specific lead field



[7]

# MEG sensors – sensitivity profile

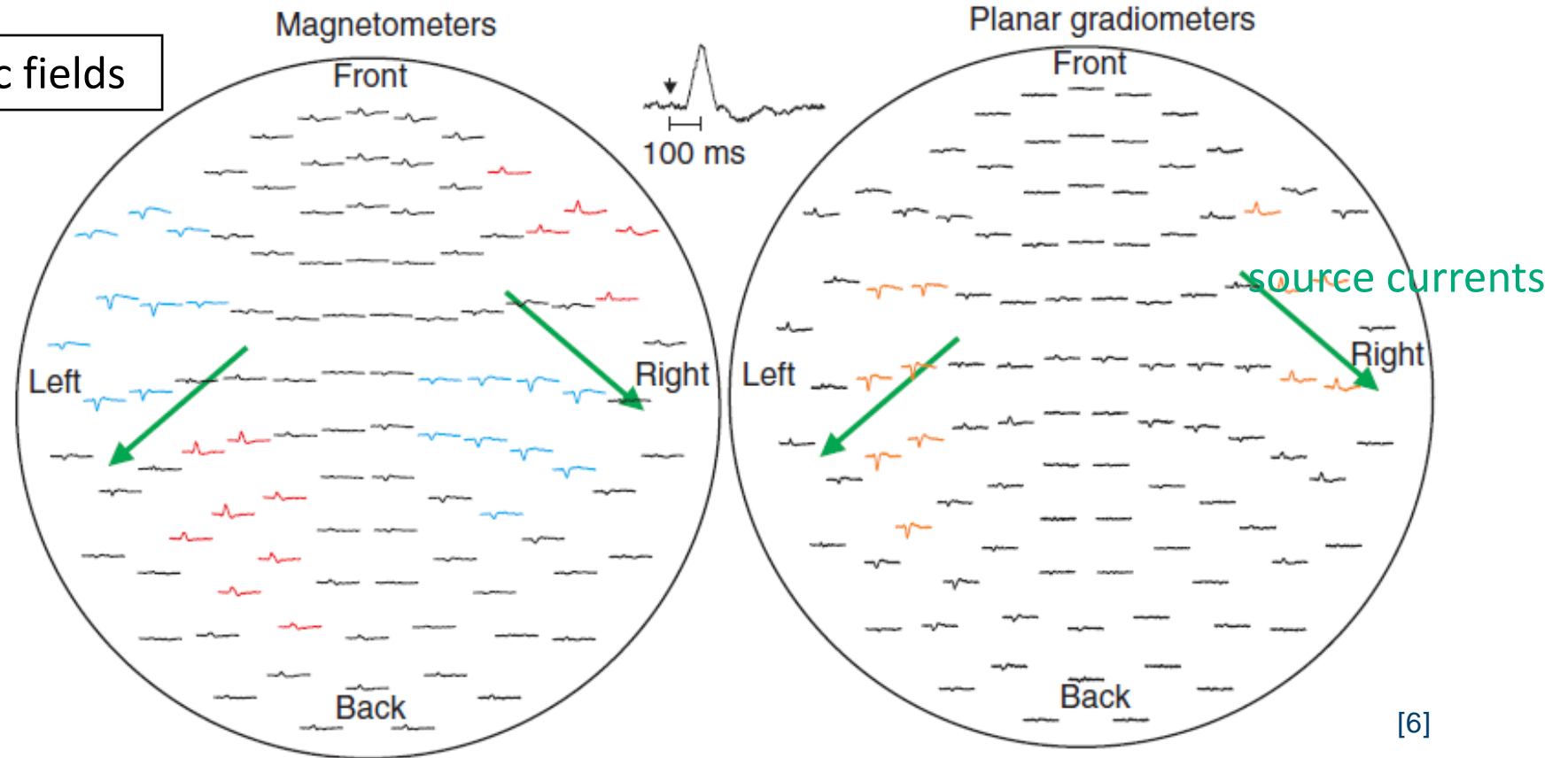
Lead fields of a **magnetometer/axial gradiometer**, and two orthogonal **planar gradiometers** with the field components they measure



# MEG sensors

- Leadfields have practical relevance also when **interpreting MEG data visually**
- **Knowing the sensitivity pattern of the sensors is essential for the correct interpretation of the data**

Auditory evoked magnetic fields



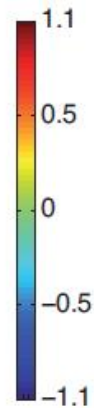
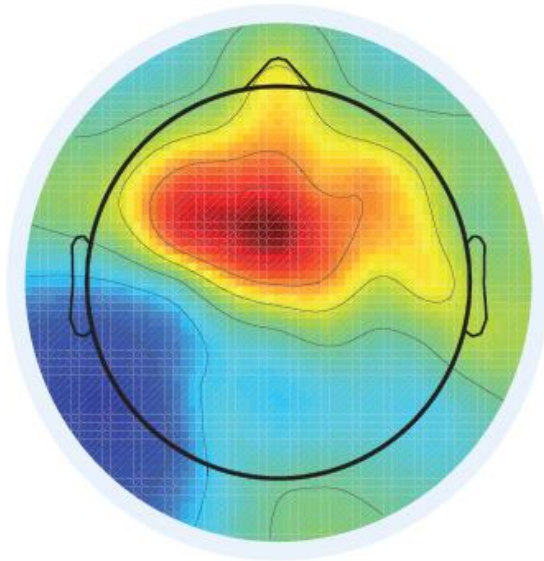
**Magnetometer** signals exhibit two maxima with opposite signs, somewhat off the active brain region

**Planar gradiometer** signals show a single peak on top of the source

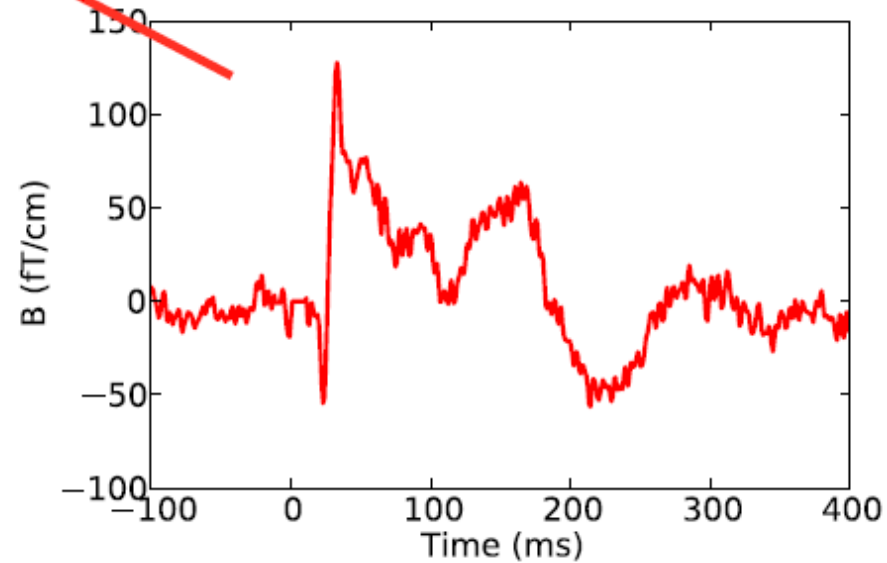
# M/EEG Measurements: Notation

$$\mathbf{M} = \begin{bmatrix} \text{MEG and/or EEG} \end{bmatrix} \in \mathbb{R}^{d_m \times d_t}$$

$d_m$  : Number of sensors  
 $d_t$  : Number of time points



[3]



[3]

**1 column = 1 topography**

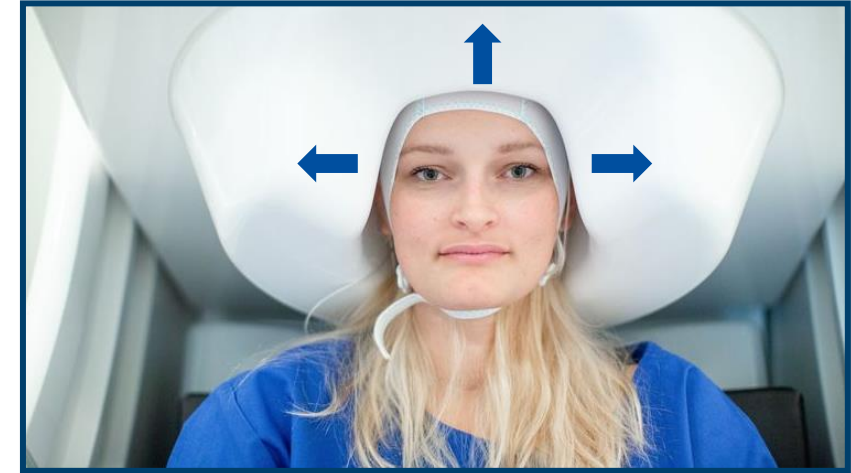
**1 row = 1 time series on 1 sensor**

# Head movements

## Blessing and curse of MEG

- Dewar with spatially fixed sensors position
- Need to know where patient is in sensor array

Movement of the head changes position of the brain relative to the sensors in the helmet and therefore the measured signal strength



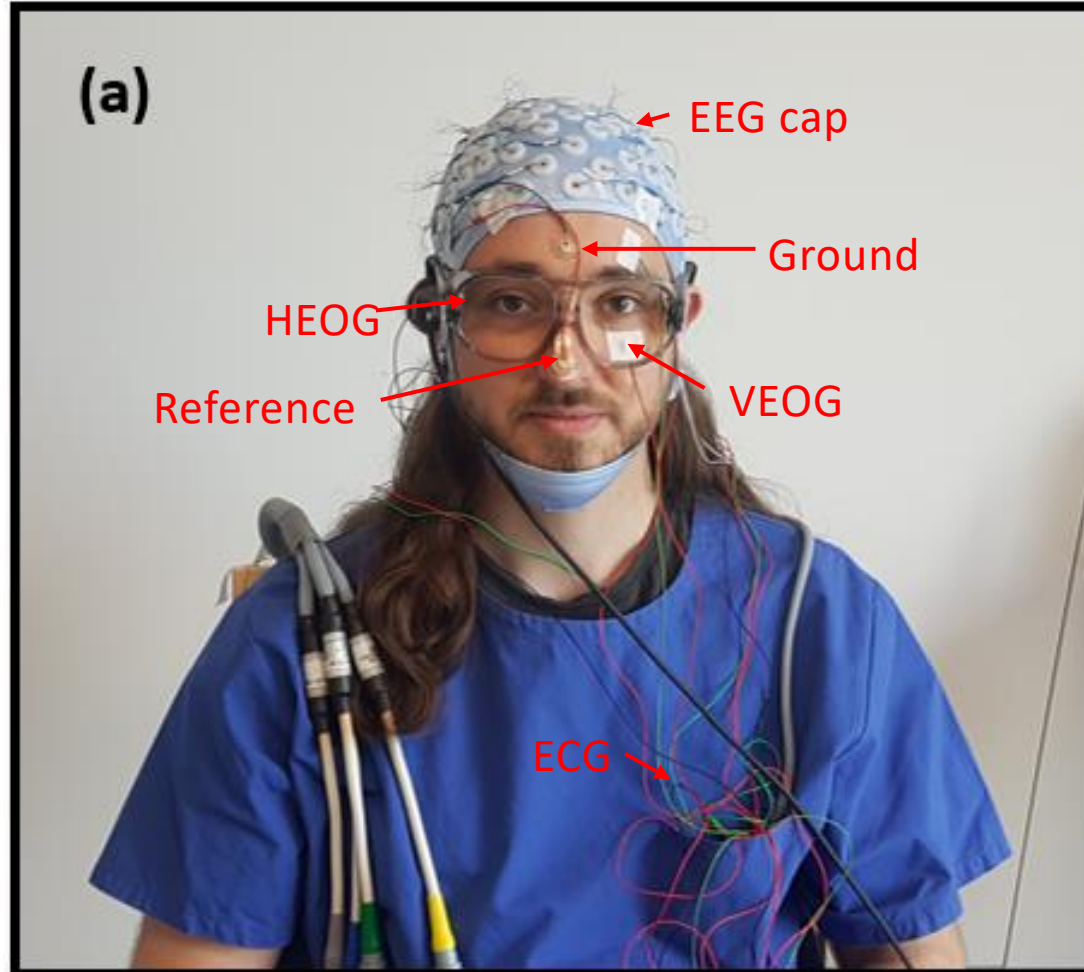
[1]

- Changes in head position during MEG sessions may cause significant **errors in source localization**
  - Mixture of different head positions over time **adds variance** to the data that is not accounted for by the experimental manipulation
  - Thus head movements may **deteriorate statistical sensitivity** when analyzing MEG on both sensor and source levels
- It is therefore recommended **to track the head movements** and incorporate them in the offline MEG analysis

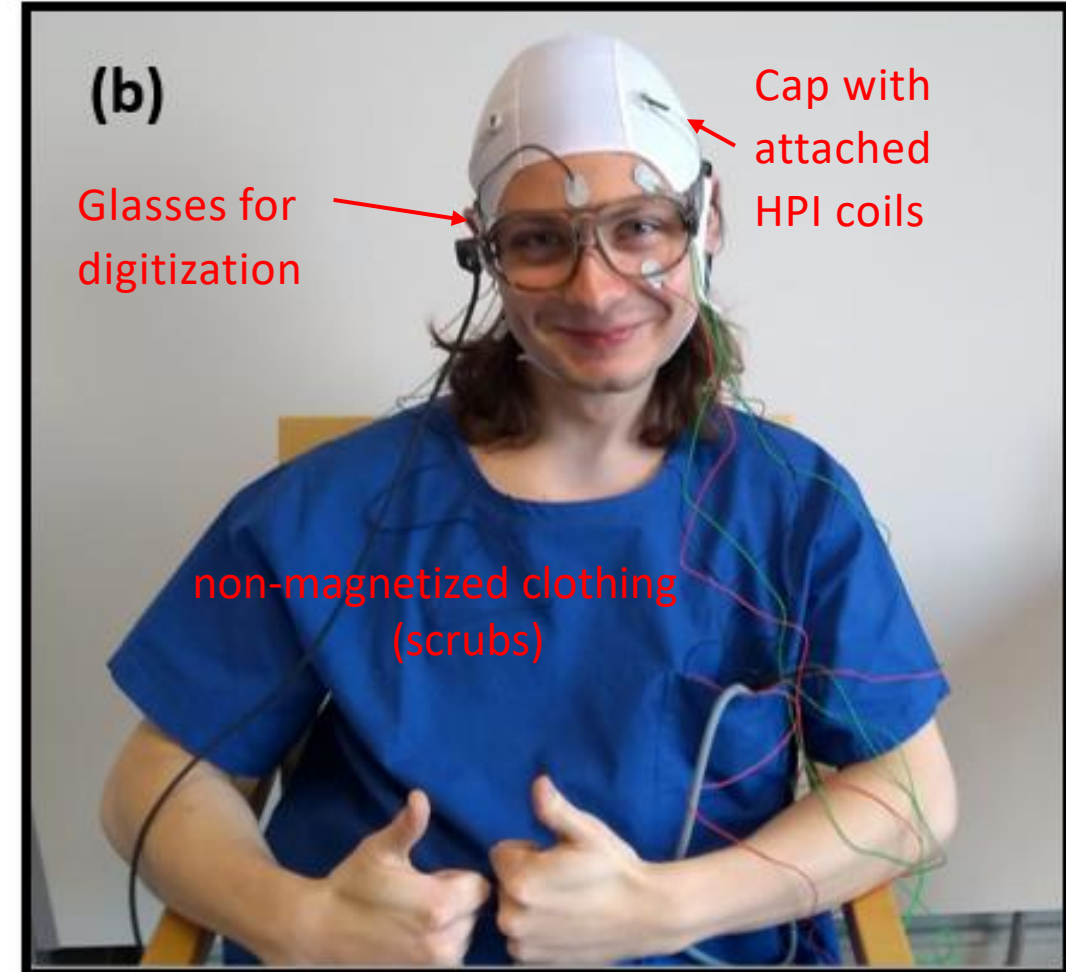


# Subject preparation

## Simultaneous MEG and EEG measurement

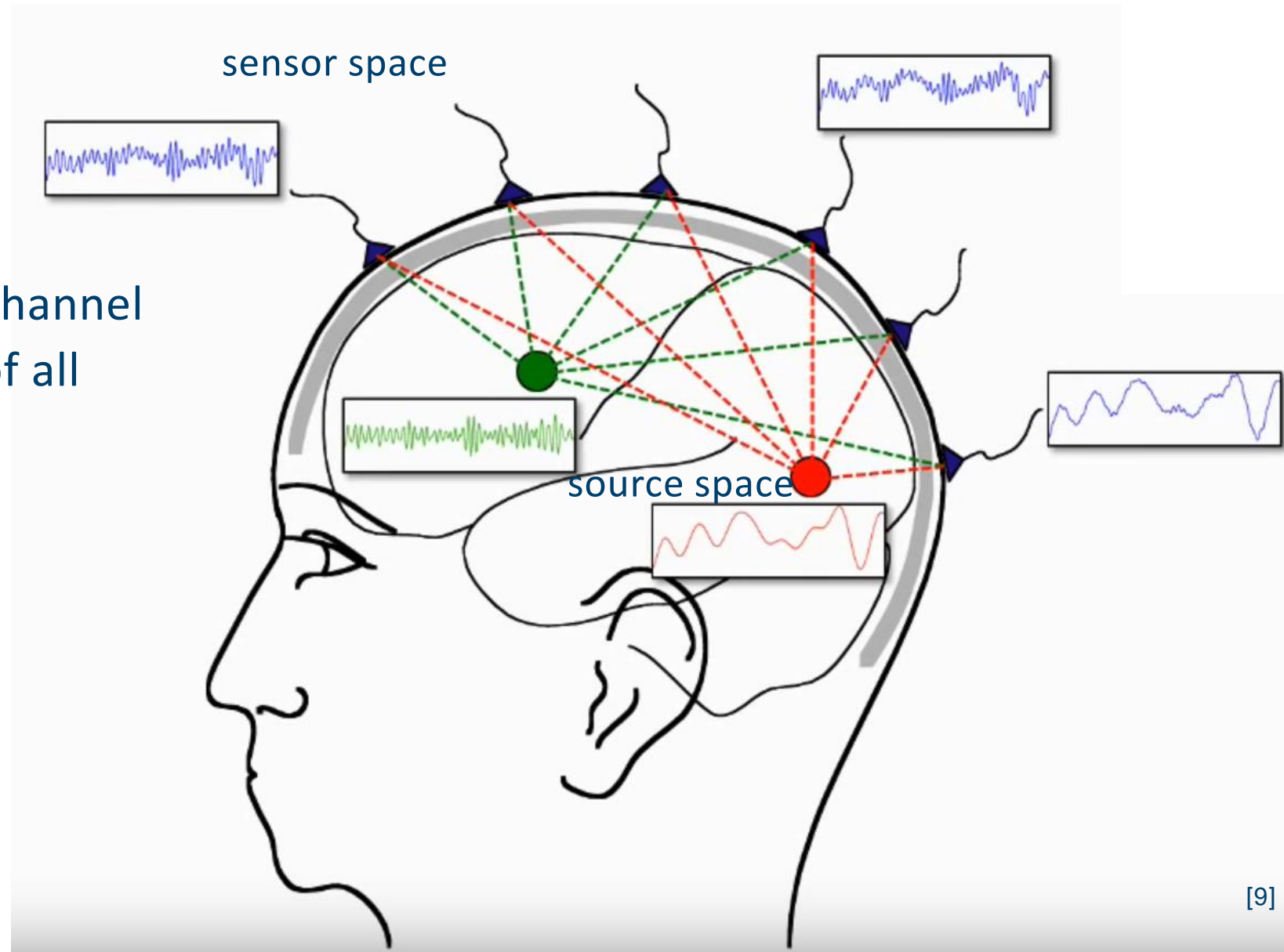


## MEG measurement



# Some words about source reconstruction

- Activity on each channel is superposition of all source activities



# Why source reconstruction?

## Motivation 1

### Strong points of MEG and EEG

- Temporal resolution ( $\sim 1\text{ms}$ )
- Characterize individual components of ERP
- Oscillatory activity
- Disentangle dynamics of cortical networks

### Weak points of EEG and MEG

- Measurement on outside of brain
- Overlap of components
- Low spatial resolution (compared to fMRI)

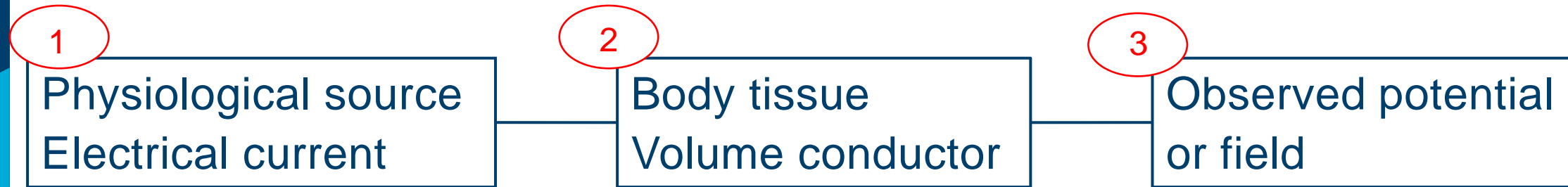
# Why source reconstruction?

## Motivation 2

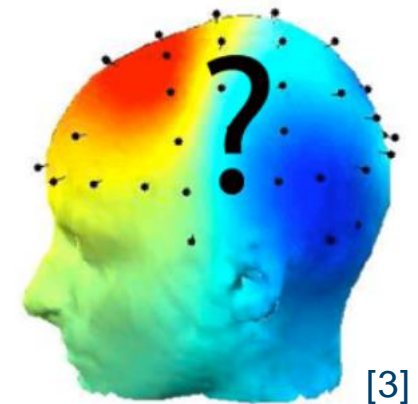
- If you find an ERP/ERF component, you want to characterize it in physiological terms
- Measured sensor signals are superpositions of all source signals and therefore fairly complex and often not easy to interpret
  - Disentangle overlapping source time series
- shape and signal strength of the measured sensor signals vary strongly due to
  - the position of the head relative to the sensors and
  - the different sensor types (magnetometer, gradiometer etc.)
    - Sensor signals of different MEG systems are difficult to compare

# Source modelling: overview

*forward model*



*inverse model*

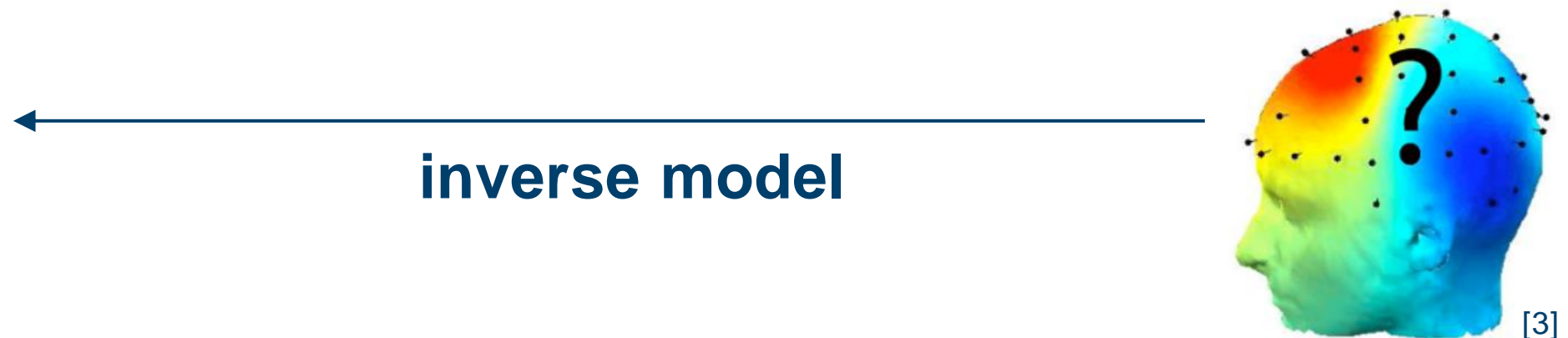
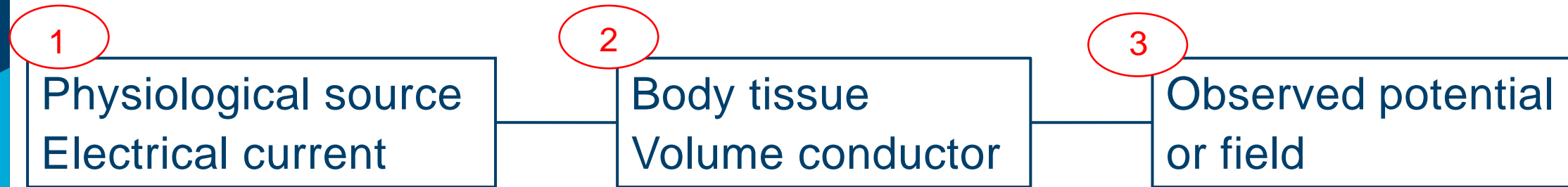


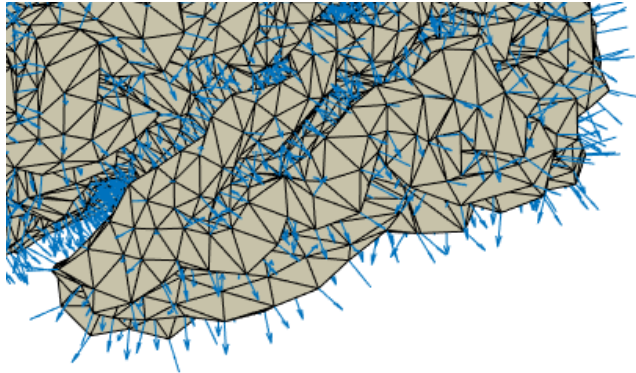
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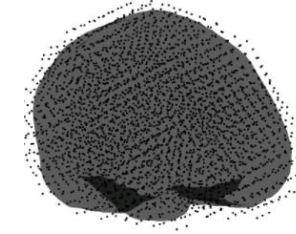
# Source modelling: overview

**Solving** *forward model* **gives lead fields**

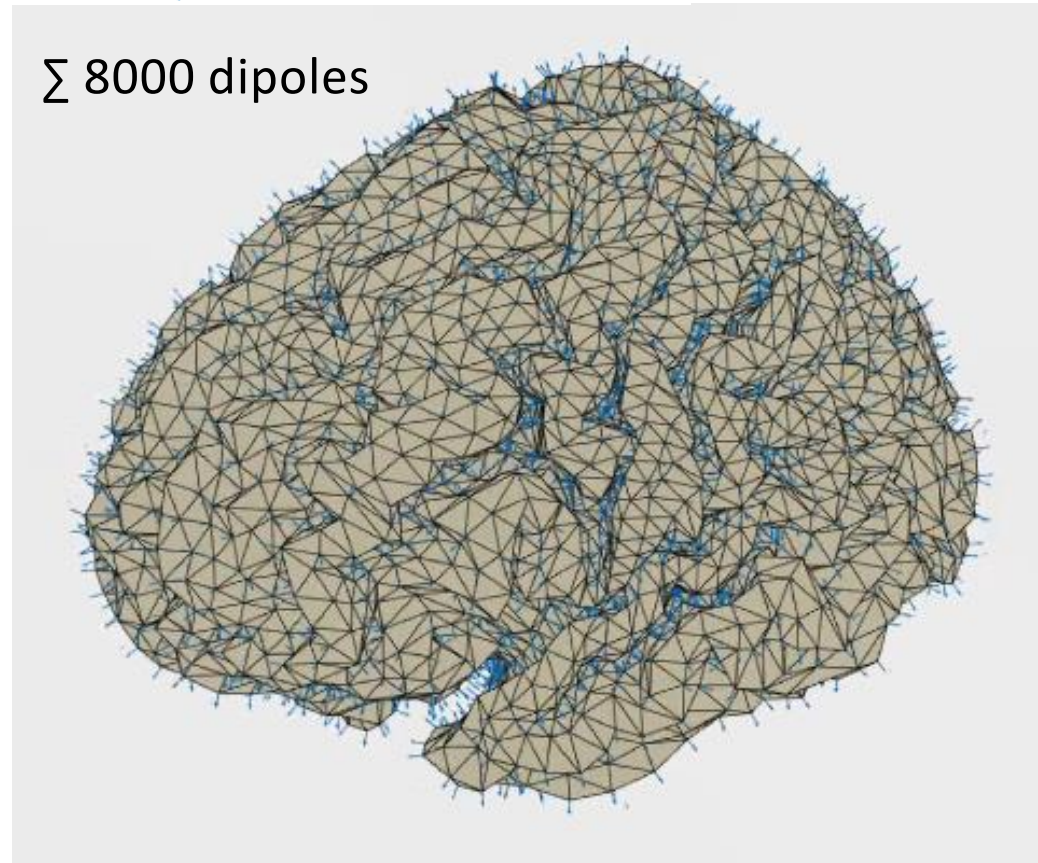




**Surface-based source model based on a surface description of the cortical sheet**  
(volumetric source models are also possible)

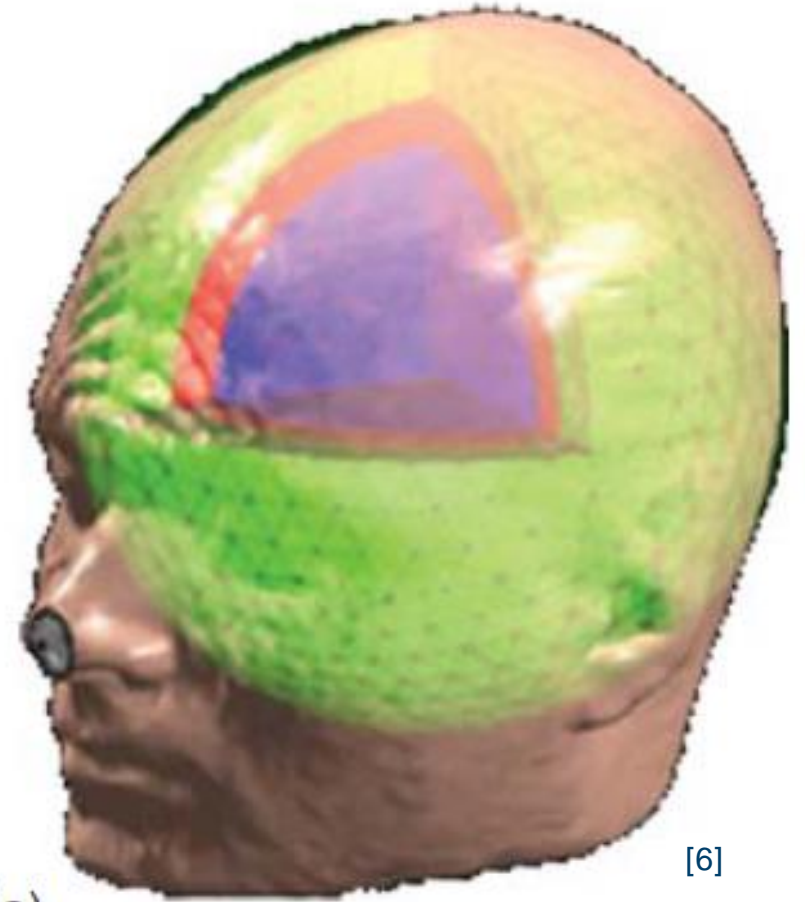


$\Sigma$  8000 dipoles



- Triangulated cortical mesh, ideally consisting of a number of triangles that form a topological sphere for each of the cerebral hemispheres
- Meshes have typically > 100000 vertices per hemisphere, but can be downsampled (~4000 vertices per hemisphere)
- Each vertex describes the location of a current dipole which dipole moment is to be estimated (blue vectors in figure)

- Describes electrical properties of tissue
  - Describes geometrical model of the head
  - Describes how the currents flow, not where they originate from
- 
- Simplest volume conduction model is a **spherical volume conduction model**
  - Spherical approximation of the geometry of the head tissue (e.g. brain, skull, scalp)
    - works reasonably well
  - Has an analytical solution!

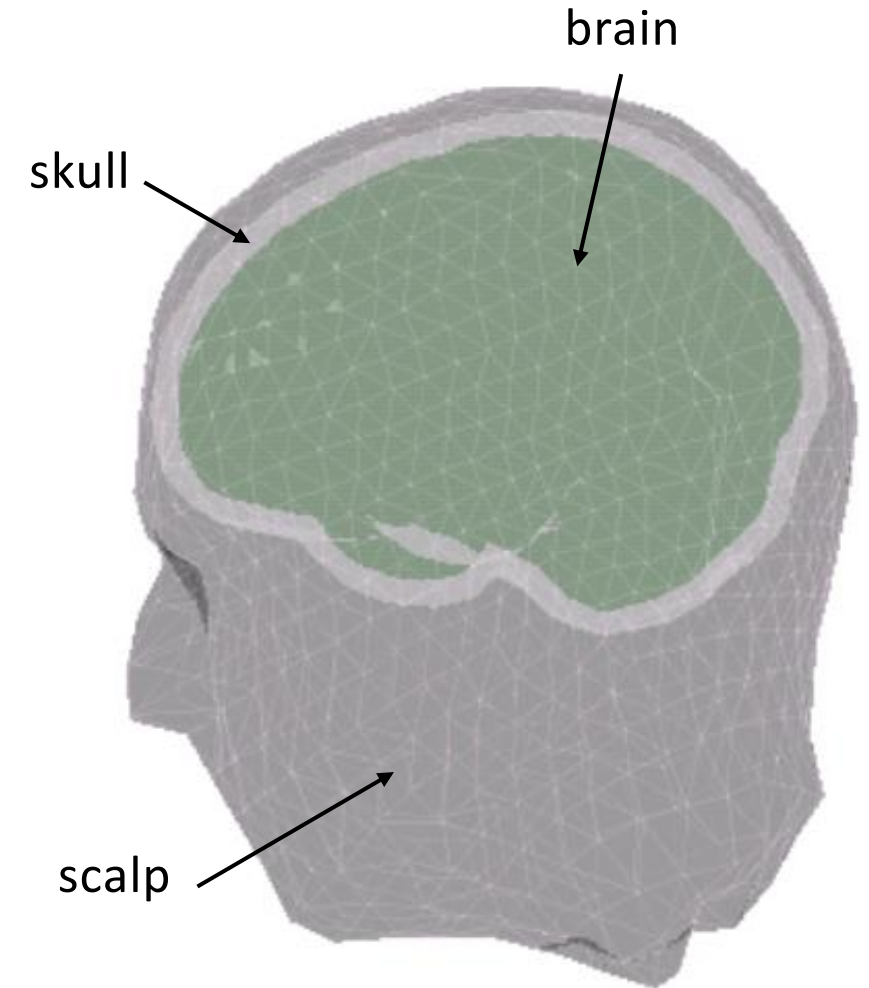


[6]

- Computational methods for volume conduction problem that allow for realistic geometries
  - Boundary Element Method (BEM)
  - Finite Element Method (FEM)
  - Finite Difference Method (FDM)

## BEM: Geometrical description

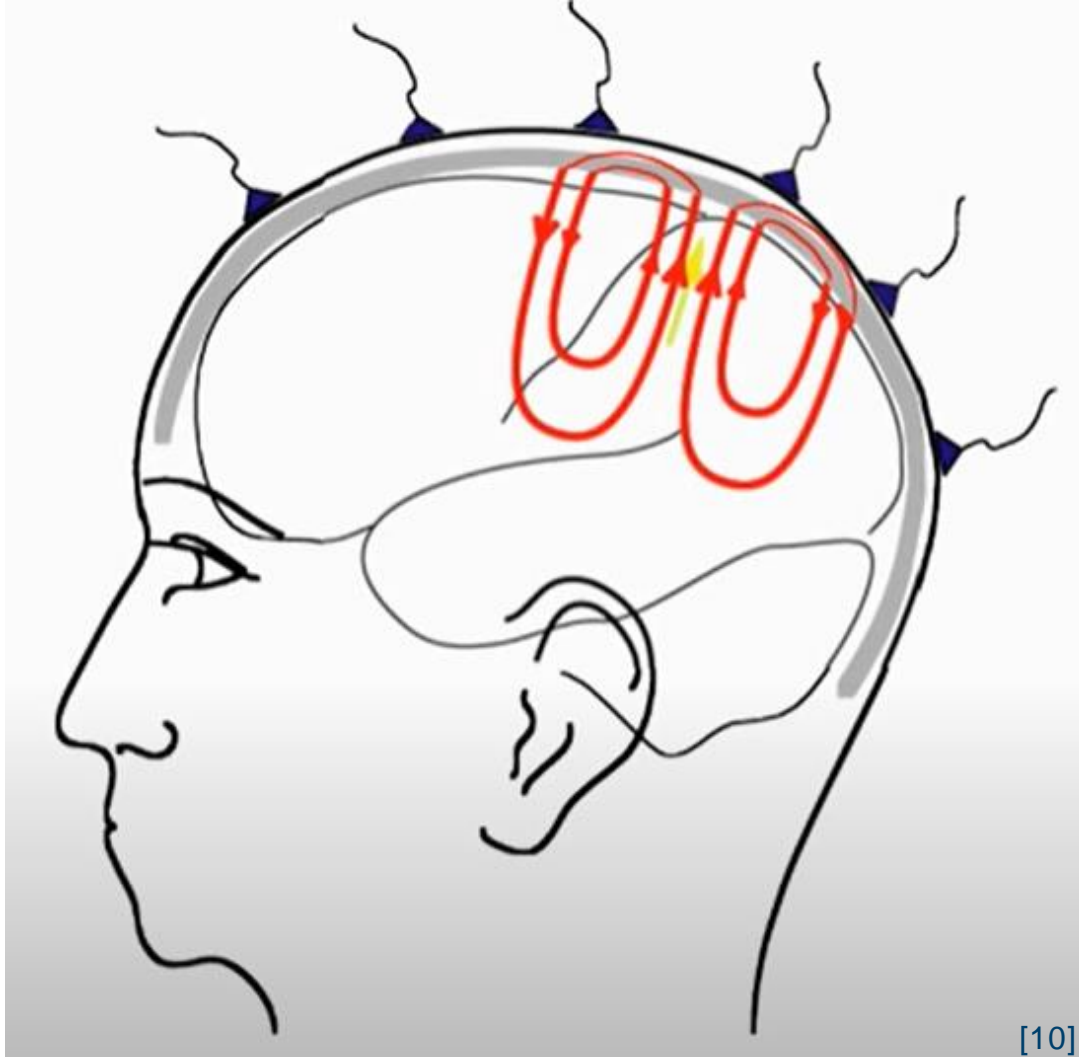
- Triangulated surfaces describe boundaries between different tissues/compartments (e.g. brain, skull, scalp, (CSF))
- Conductivity of tissues is supposed to be homogeneous and isotropic within each layer
- Derived by segmenting structural MRIs for different tissue types and then triangulating the resulting surfaces



BEM volume conduction model



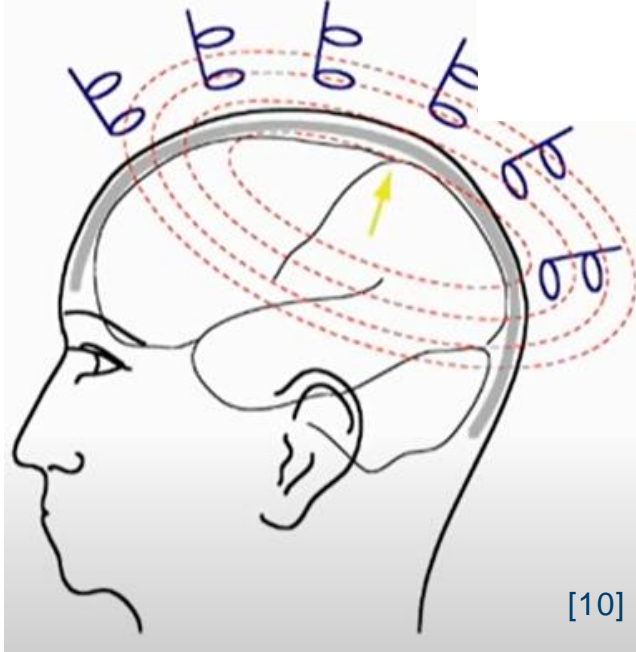
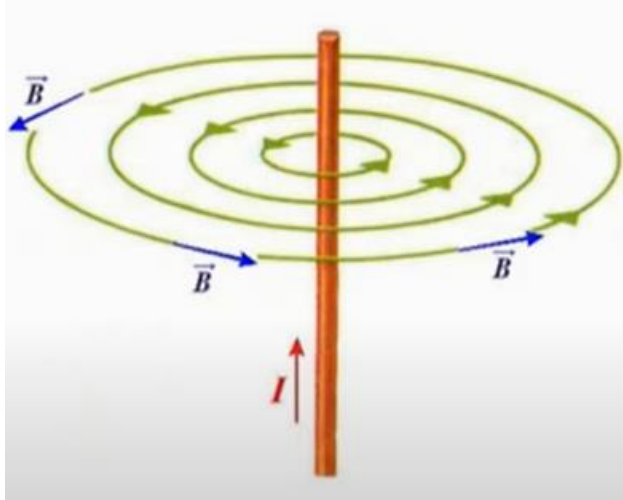
## EEG volume conduction



- Potential difference between electrodes corresponds to current flowing through skin
- Only tiny fraction of current passes through the skull
- Therefore the model should describe the skull and skin **as accurately as possible**
- EEG measures only the volume currents not the primary currents

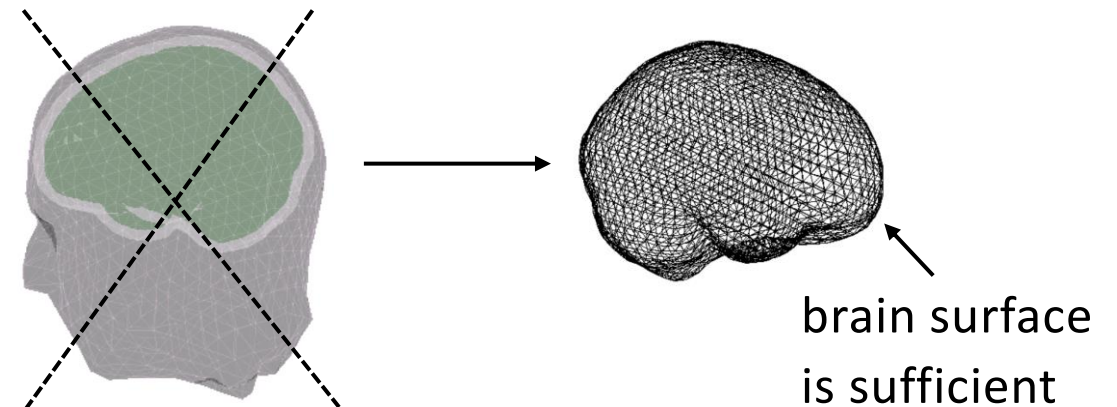


## Electrical current → magnetic field



## MEG volume conduction

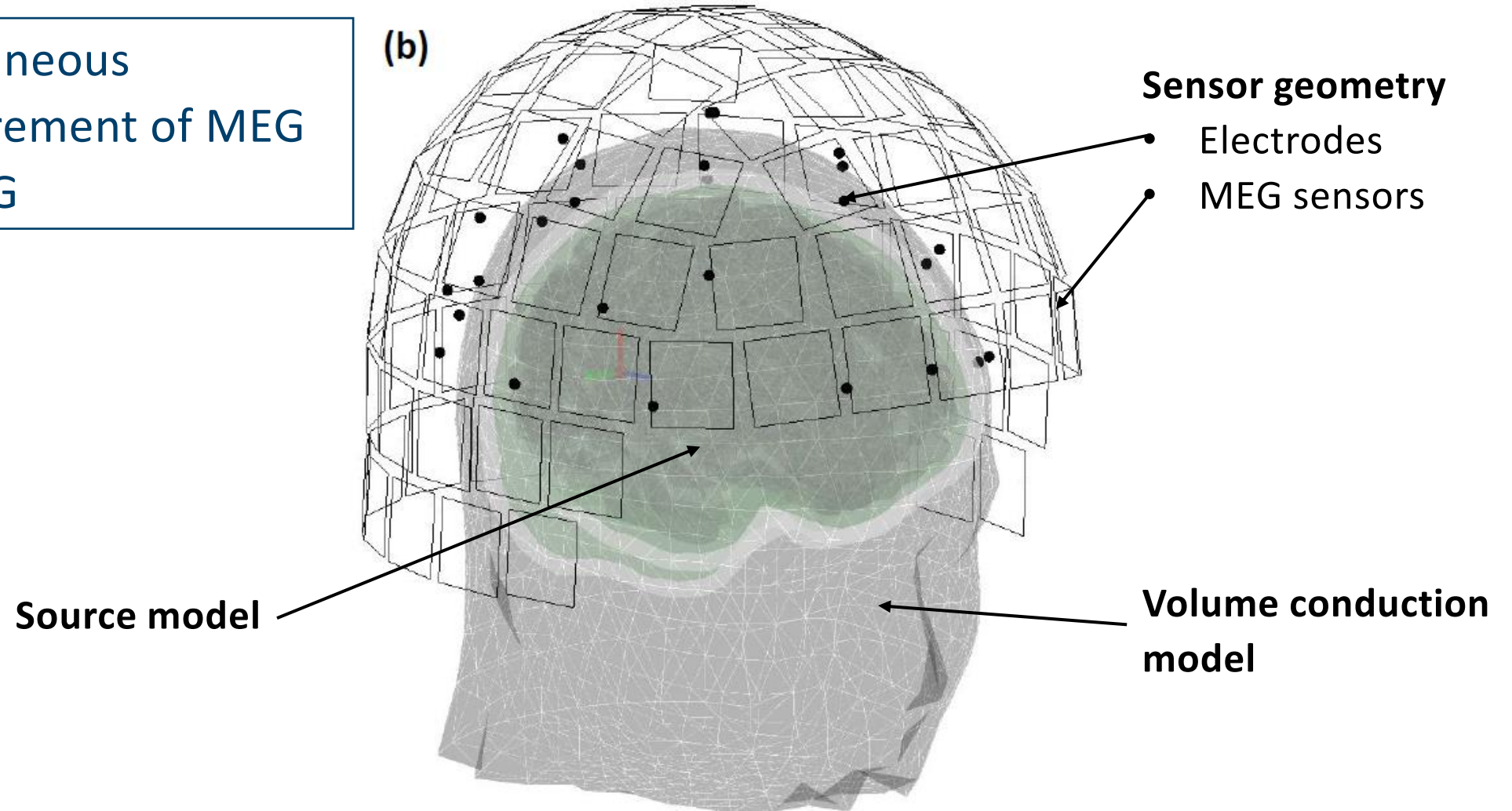
- MEG measures the magnetic field due to the **primary neuronal current**, but also due to the **volume currents**
  - Only tiny fraction of current passes through the poorly conductive skull
- Therefore skull and skin **are usually neglected** in MEG model



## 3 knowledge of sensor geometry

- need know the position of each sensor (magnetometer, electrode etc.) relative to source model and volume conduction model

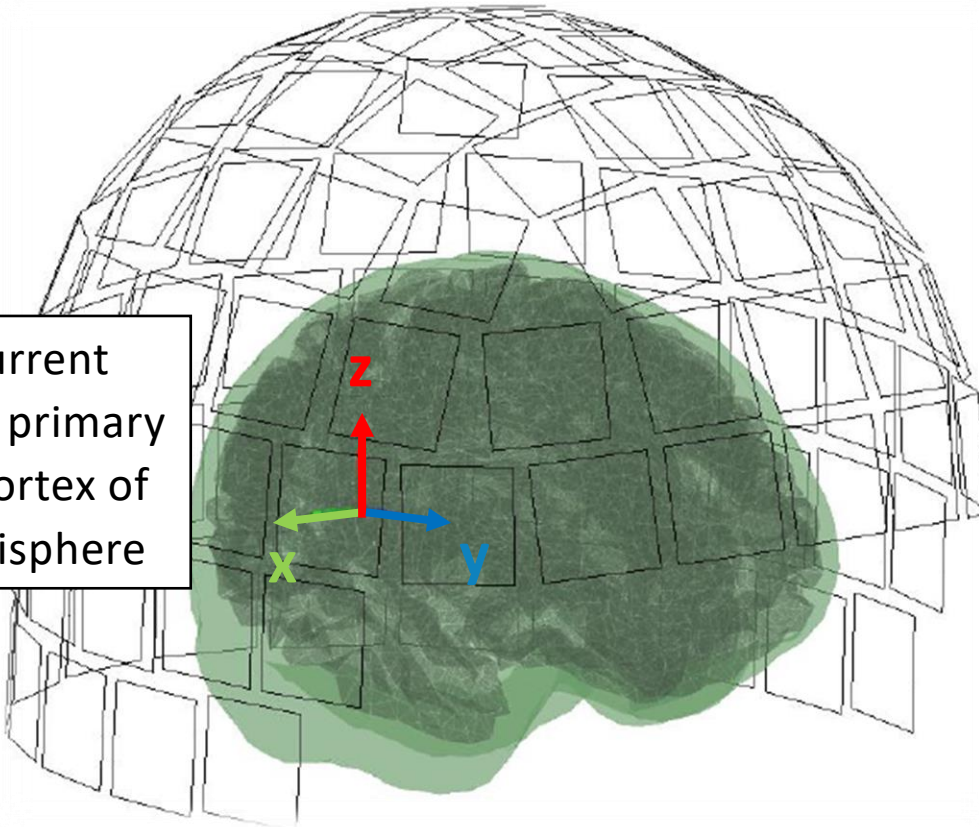
Simultaneous  
measurement of MEG  
and EEG



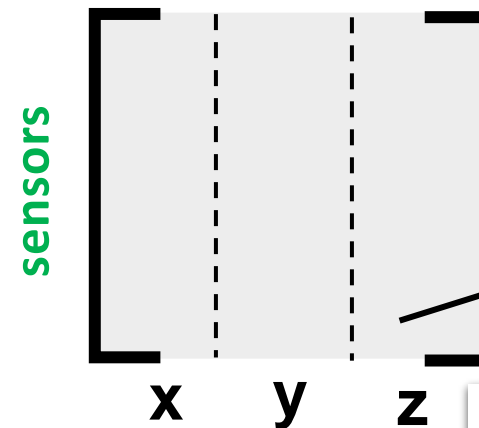
# Solution of forward model: Lead fields

- **lead fields** represent by definition the **field distribution** across all channels due to a **unitary current dipole** placed with a given **position** and **orientation**.  
(dipole moment  $\mathbf{Q}$  is unit vector  $|\mathbf{Q}| = 1$ )

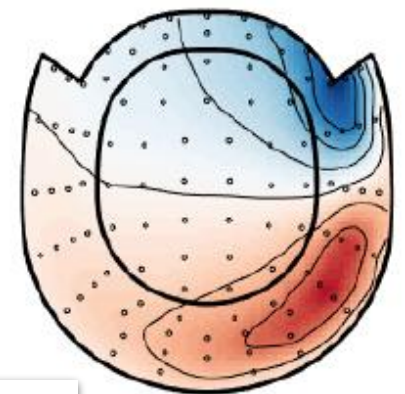
Unitary current dipoles in primary auditory cortex of right hemisphere



Lead field matrix for each dipole position



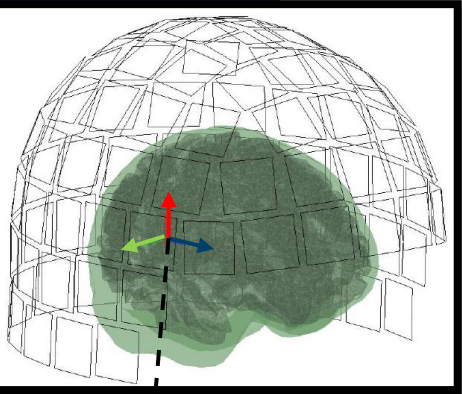
Lead field for **magnetometers** due to unitary dipole in **z-direction**



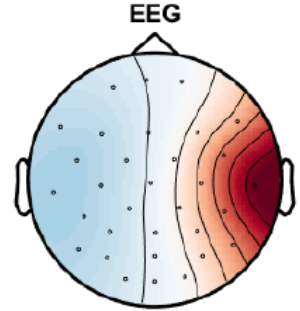
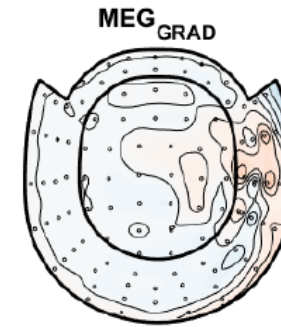
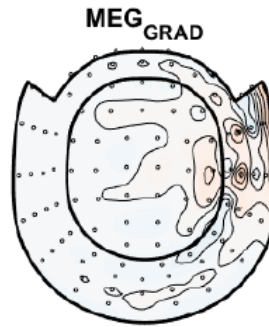
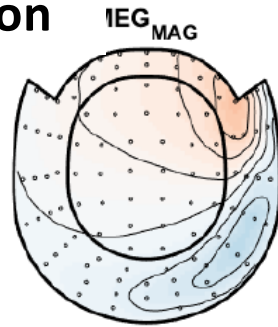


# Lead fields

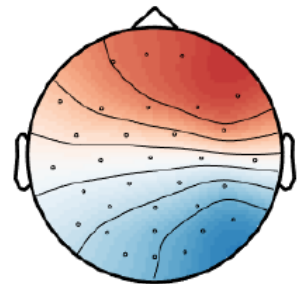
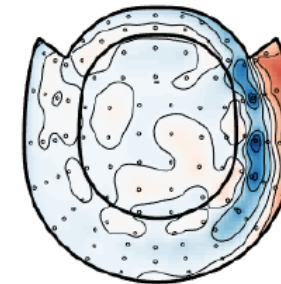
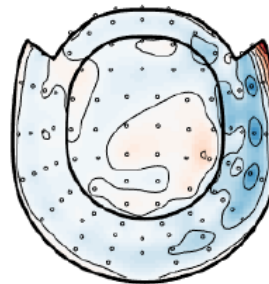
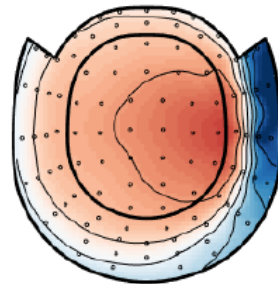
## Dipole orientation



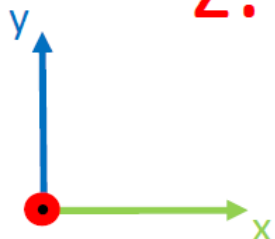
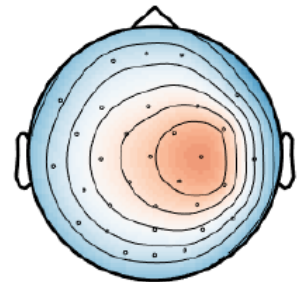
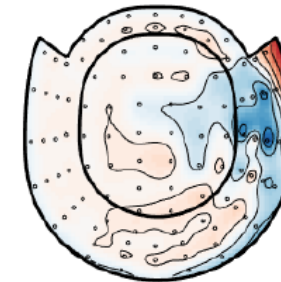
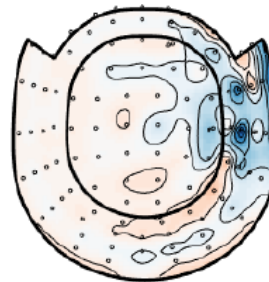
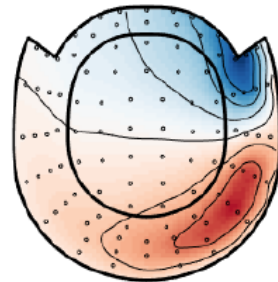
x:



y:



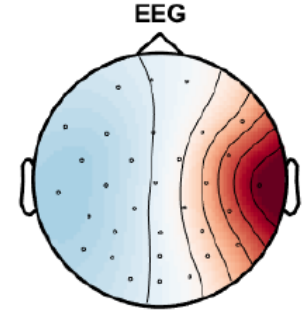
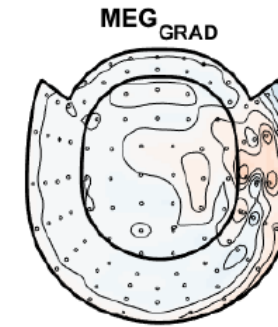
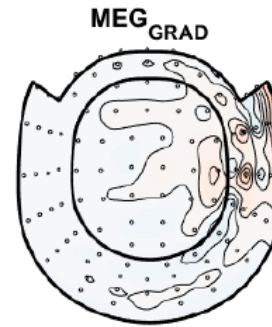
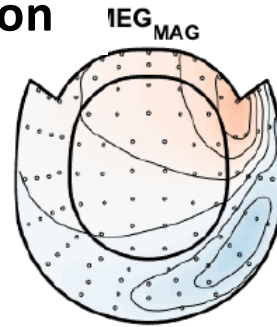
z:



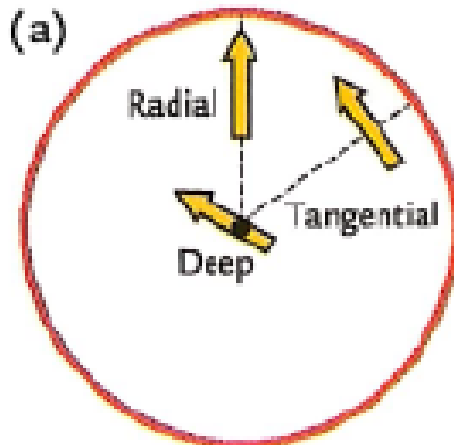
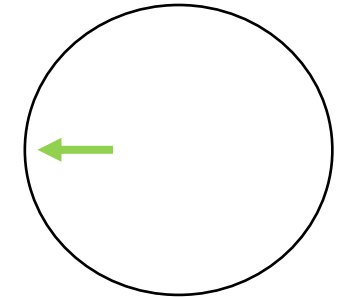
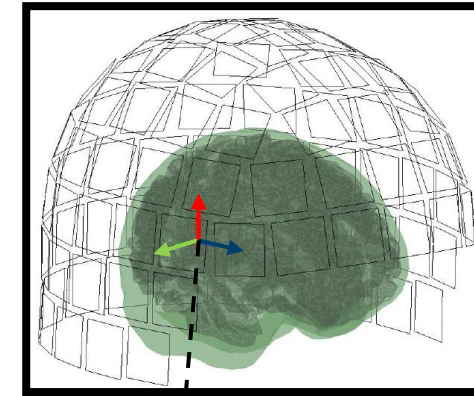
# Lead fields

## Dipole orientation

X:



Green unitary dipole is radially oriented in the head → leads to weak signals in MEG sensors

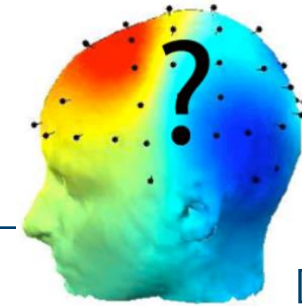


### In general:

- MEG is sensitive to tangential sources but insensitive to radial sources
- EEG is sensitive to both radial and tangential oriented sources
- Theoretically: A radially oriented current dipole produces no magnetic field outside a spherically symmetric volume conductor and is thus invisible for MEG (Baule and McFee 1965; Grynszpan and Geselowitz 1973)

# Solving the inverse problem

Find the current generators that produced the M/EEG measurements



[3]

## Inverse methods

- **Single and multiple dipole models**

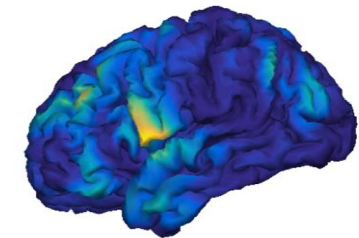
Minimize error between model and measured potential/field



[6]

## Distributed source models

- Perfect fit of model to the measured potential/field  
Additional constraint on source smoothness, power or amplitude



- **Spatial filtering**

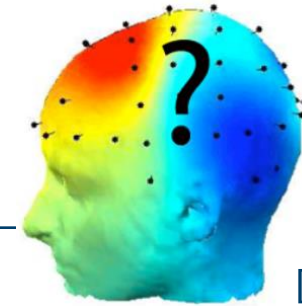
Scan the whole brain with a single dipole and compute the filter output at every location

- Beamforming (e.g. LCMV, SAM, DICS)
- Multiple Signal Classification (MUSIC)



# Solving the inverse problem

Find the current generators that produced the M/EEG measurements



[3]

## Inverse methods

- **Single and multiple dipole models**

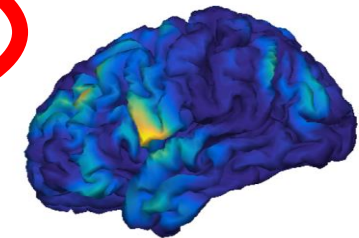
Minimize error between model and measured potential/field



[6]

- **Distributed source models**

- Perfect fit of model to the measured potential/field  
Additional constraint on source smoothness, power or amplitude



- **Spatial filtering**

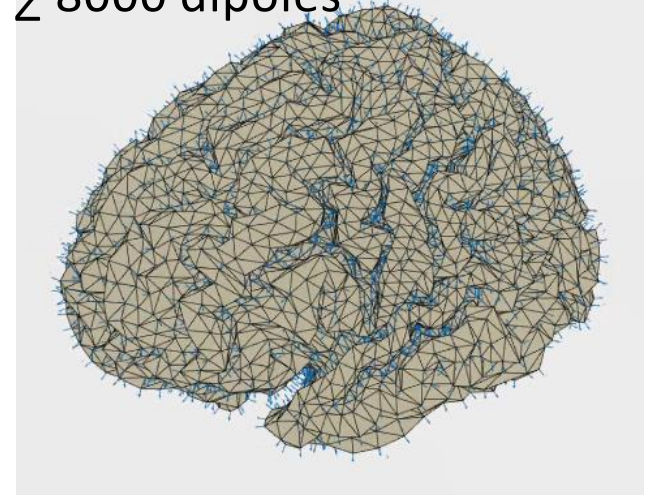
Scan the whole brain with a single dipole and compute the filter output at every location

- Beamforming (e.g. LCMV, SAM, DICS)
- Multiple Signal Classification (MUSIC)

# Distributed source models

- **Position of the source is not estimated as such**
  - Predefined source model with known dipole positions (3D volume or cortical sheet)
- **Dipole moment at each position is estimated**
  - In principle easy to solve, however...
  - More “unknowns” (parameters) than “knowns” (measurements)
    - e.g. 8000 dipoles vs. 306 MEG channels
  - Infinite number of solutions can explain the data perfectly
    - Silent sources (radially oriented dipoles) can be added to each solution for MEG
  - Additional constraints are required to find a unique solution
  - Linear estimation problem

$\Sigma$  8000 dipoles



# Distributed source models

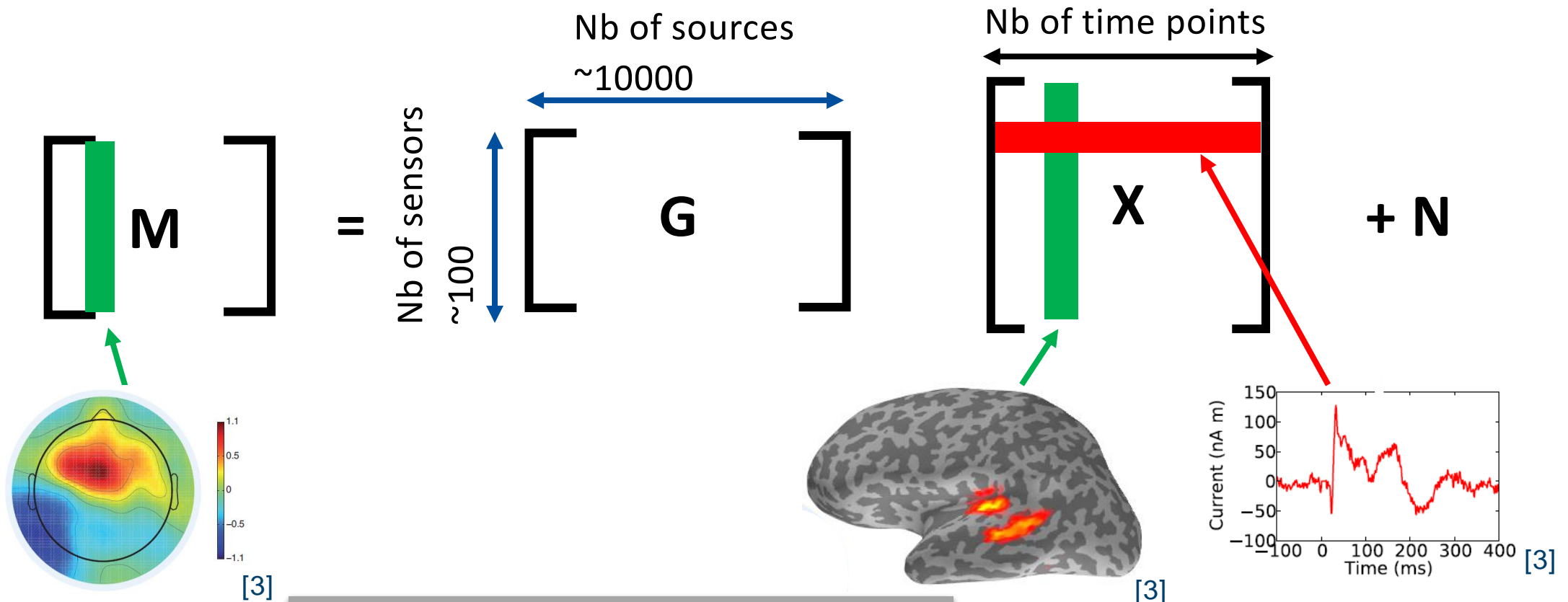
Inverse problem:  $M = GX + N$  (Linear equation)

Measurements  $M$

Forward matrix  $G$   
contains lead fields

Source signals  $X$

Noise  $N$



**Objective: Estimate  $X$  given  $M$  and  $G$**

# Distributed source models

Inverse problem:  $\mathbf{M} = \mathbf{GX} + \mathbf{N}$  (Linear equation)

$$\mathbf{X}^* = \arg \min_{\mathbf{X}} \underbrace{\|\mathbf{M} - \mathbf{GX}\|_F^2}_{\text{Data fit}} + \underbrace{\lambda \phi(\mathbf{X})}_{\text{Regularization}}, \lambda > 0$$

$\lambda$  : Trade-off between the **data fit** and the **prior**

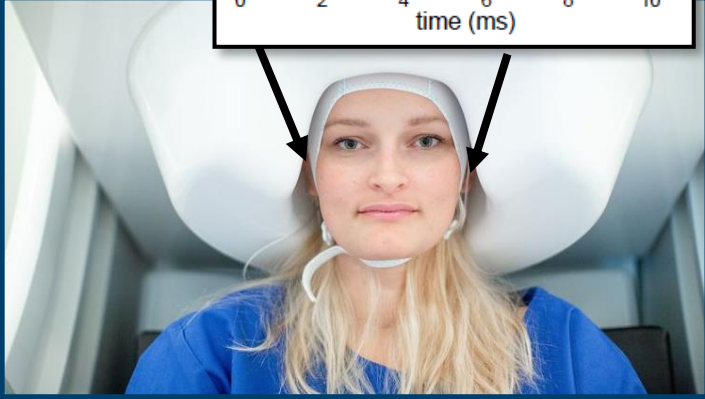
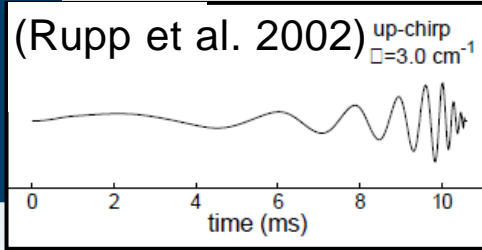
where  $\|\mathbf{A}\|_F^2 = \sum_{ij} a_{ij}^2$

$\phi(\mathbf{X})$ : Penalty term that imposes **additional constraints** on the sources  
(Smoothness, strength of source distribution or other prior beliefs)

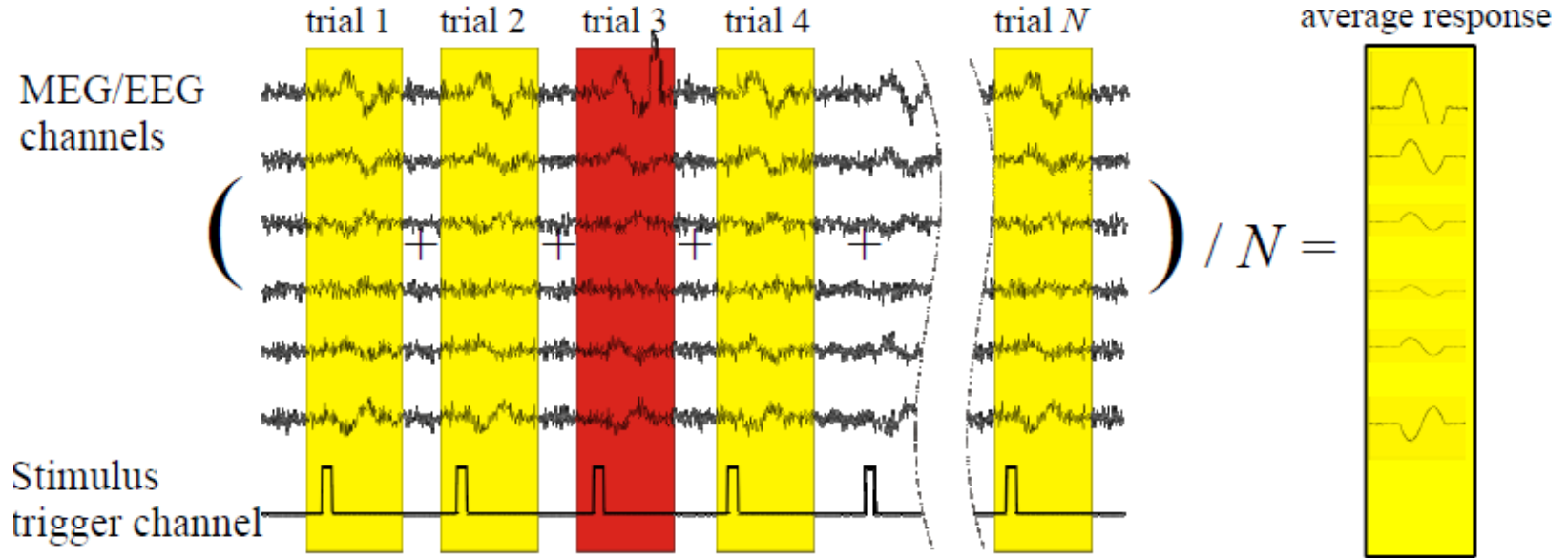
e.g.  $\phi(\mathbf{X}) : \|\mathbf{XRX}^T\|_F^2$  weighted norm of estimated sources

Searching for sources with minimal norm leads to **Minimum Norm Estimates (MNE)**

# MNE for auditory evoked fields

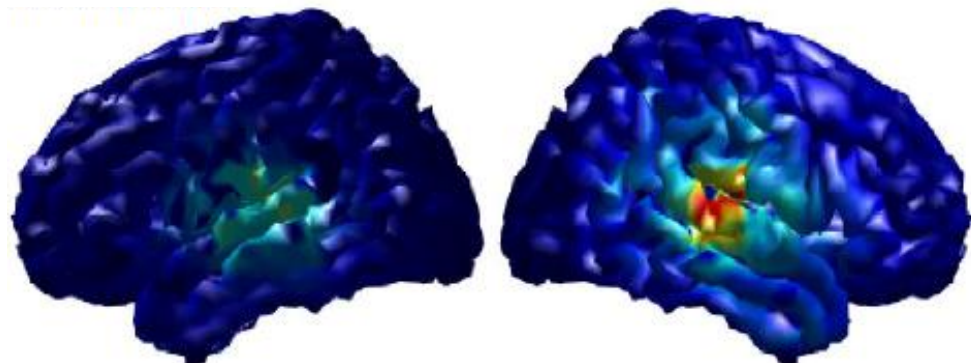


[1]

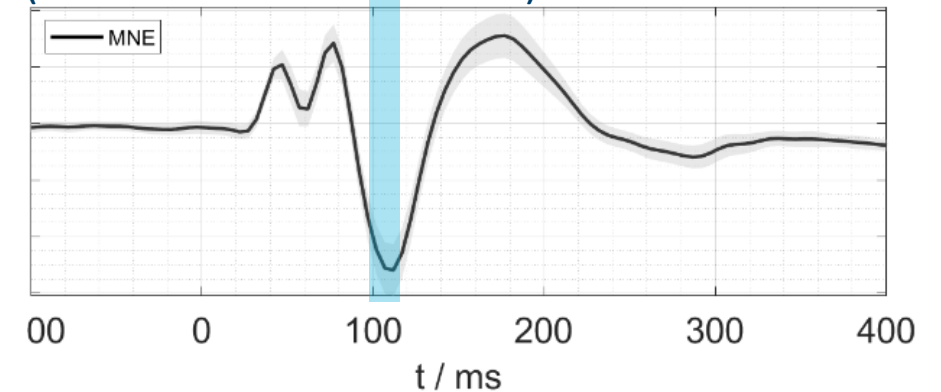


[11]

Inverse modelling with MNE



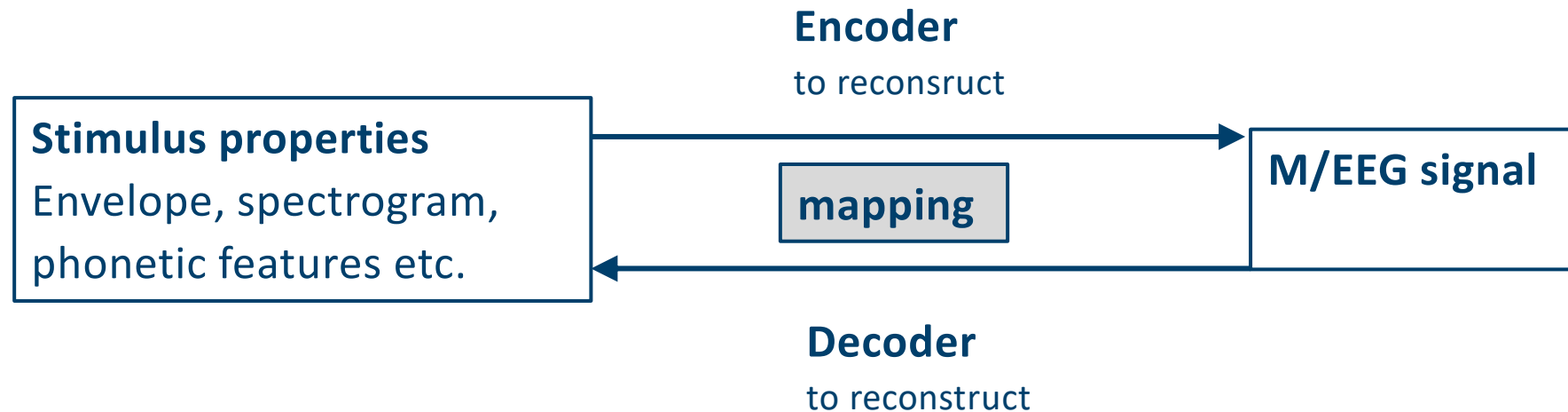
Response in right primary auditory cortex  
(characteristic waveform)



# Using natural speech stimuli

**Use modelling approach to work with natural/ continuous speech stimuli (e.g. words, sentences etc.)**

**Idea:** Use mapping between M/EEG signal and stimulus to investigate which stimulus properties are best represented in cortical signals

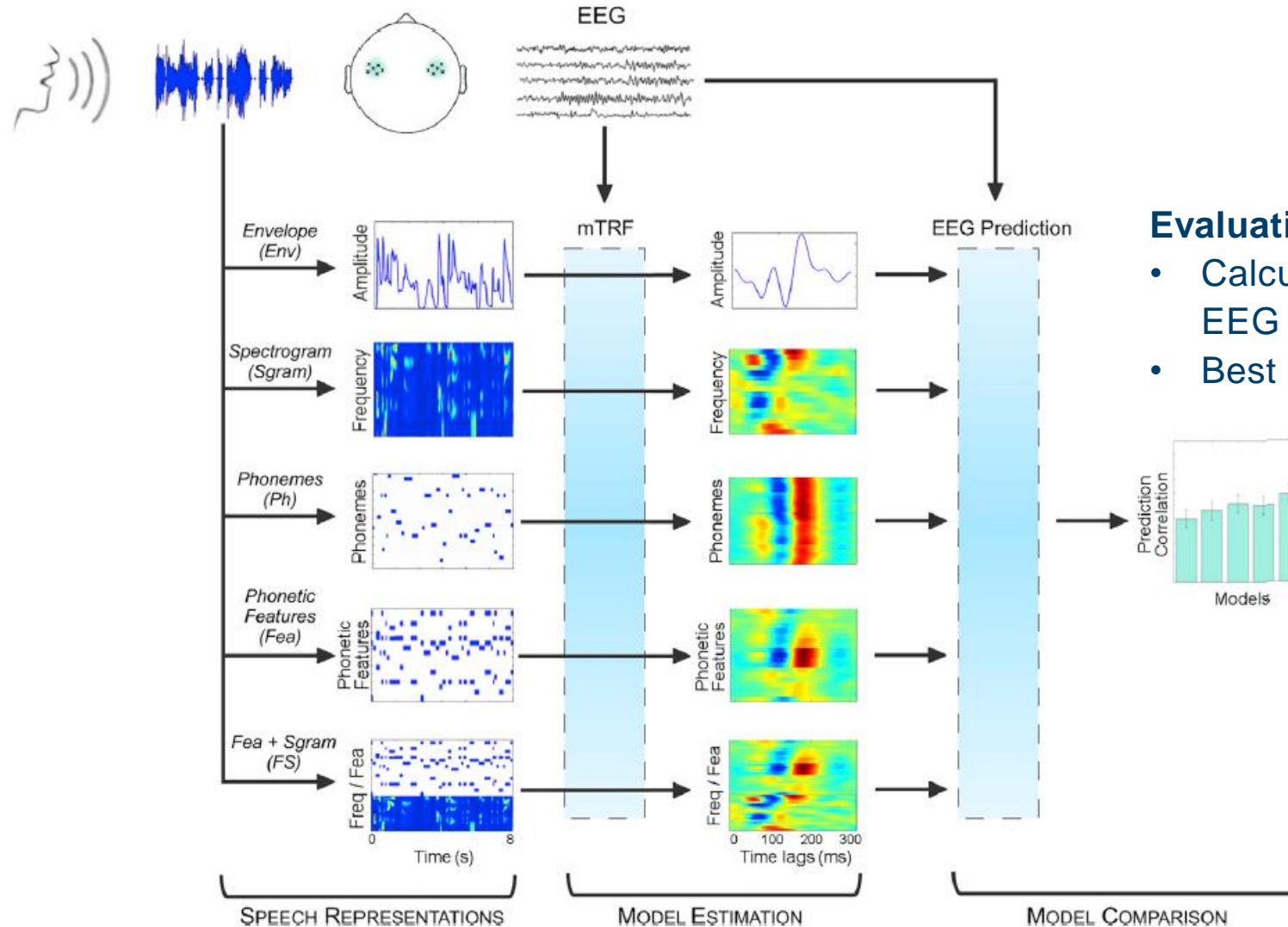


Functions for **mapping** can be linear or non-linear (e.g. neural networks)



# Using natural speech stimuli

- Subjects listened to audiobook and EEG was simultaneously recorded
- Used encoder to predict EEG signal given different speech representations



## Evaluation of reconstruction accuracy

- Calculate correlation between predicted EEG and original EEG signal
- Best model delivers highest correlation

(Di Liberto et al. 2015)

# Reconstruction of speech envelope given M/EEG signals

$$\hat{s}(t) = \sum_{n=1}^N \sum_{\tau} \mathbf{g}(\tau, n) \mathbf{y}(t + \tau, n)$$

reconstruction  $\hat{s}(t)$   
 sum over MEG channels  $N$   
 sum over latencies  $\tau$   
 decoder  $\mathbf{g}(\tau, n)$   
 M/EEG signal  $\mathbf{y}(t + \tau, n)$

Reconstructed envelope  $\hat{s}(t)$

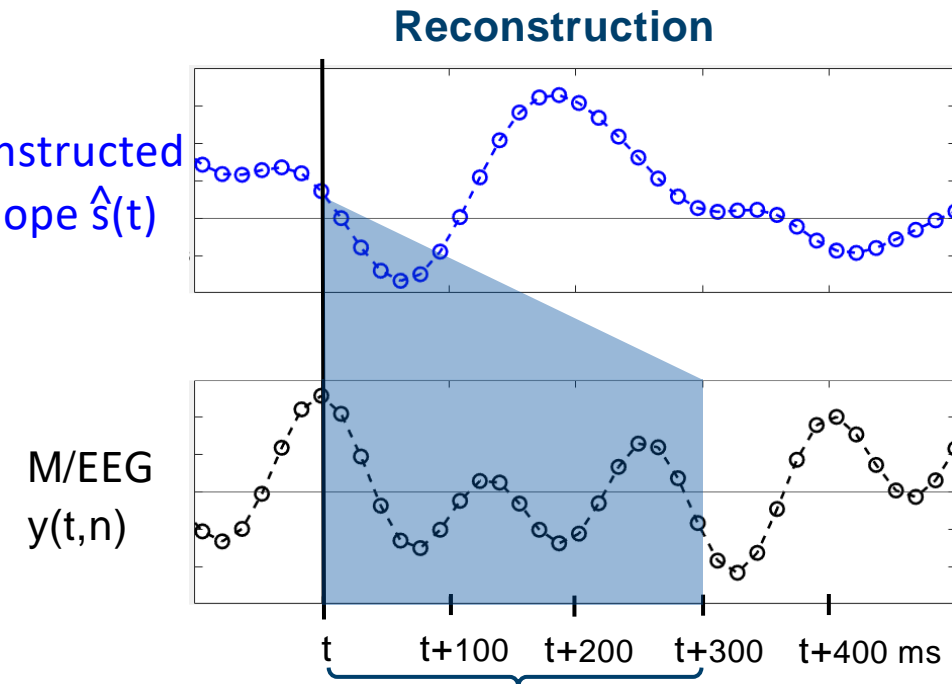
The matrix  $\mathbf{g}$  (decoder) can be determined by minimizing a least-squares objective function

$$\mathbf{g} = \arg \min E (|\hat{s}(t) - s(t)|^2)$$

Solving this analytically results in calculation of the normalized reverse correlation

$$\mathbf{g} = (\mathbf{Y}^T \mathbf{Y} + \lambda \mathbf{M})^{-1} \mathbf{Y}^T \mathbf{s}$$

M/EEG measurements  $\mathbf{Y}$   
 regularization  $\lambda \mathbf{M}$   
 speech envelope  $\mathbf{s}$



Temporal integration window  
e.g.  $[\tau=0 \text{ ms}, \tau=300 \text{ ms}]$   
or  
use single latencies only

(O'Sullivan et al. 2015, Crosse et al. 2016)

# Speech Intelligibility Predicted from Neural Entrainment of the Speech Envelope

- Done by Vanthornhout et al. (2018) with EEG
- was part of my master thesis with MEG under the supervision of Prof. Dr. Bernd Meyer (Communication Acoustics)

## Use neural entrainment of speech envelope to measure speech intelligibility

Speech envelope evokes a marked “envelope-following” neural response (in the auditory cortex) and thereby temporally aligns ongoing (auditory) cortical activity in the delta/theta (1–8 Hz) range to it

### Why is it useful?

- It can provide **valuable information additional to behaviorally measured speech intelligibility** in a population **where cognitive factors play a role**, such as in **aging** individuals, or during **auditory rehabilitation** after fitting an auditory prosthesis
- It enables **completely automatic measurement** which is invaluable **for testing individuals who cannot provide feedback**, for **automatic fitting** of auditory prostheses, and for closed-loop auditory prostheses that continuously adapt their function to the individual listener in a specific and changing listening environment

# Speech Intelligibility Predicted from Neural Entrainment of the Speech Envelope

## One experimental block of performed MEG study with 24 subjects

Subjects listened to OLSA-sentences



[1]

### Oldenburg Sentence Test (OLSA) in MEG

1-2 training lists	SRT measure- ment (1 list)	break	6 lists <ul style="list-style-type: none"> <li>• 20 sentences each</li> <li>• Different SNRs</li> <li>• <math>\Sigma</math> 120 sentences</li> </ul>
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known

### Determine SNR for given intelligibility

List number	1	2	3	4	5	6
Speech intelligibility / %	20	40	50	60	80	95

$$p(x) = \frac{1}{1 + e^{-4m(x-L_{50})}}$$

SNR

Use psychometric function  
(Wagener et al. 1999)

# Speech Intelligibility Predicted from Neural Entrainment of the Speech Envelope

- 20 sentences per speech intelligibility:
- $\Sigma$  120 sentences

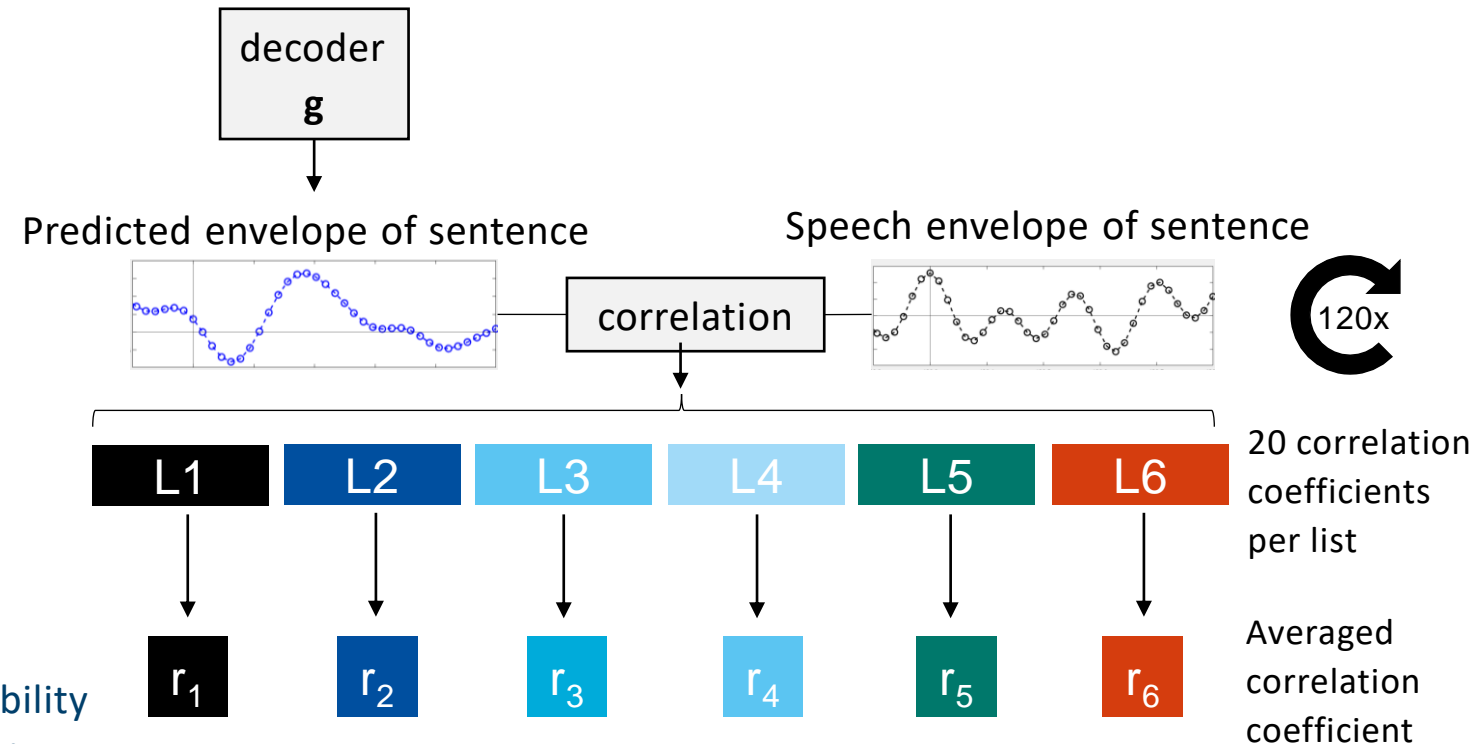
List number	1	2	3	4	5	6
Speech intelligibility / %	20	40	50	60	80	95

1. Train decoder on audio book

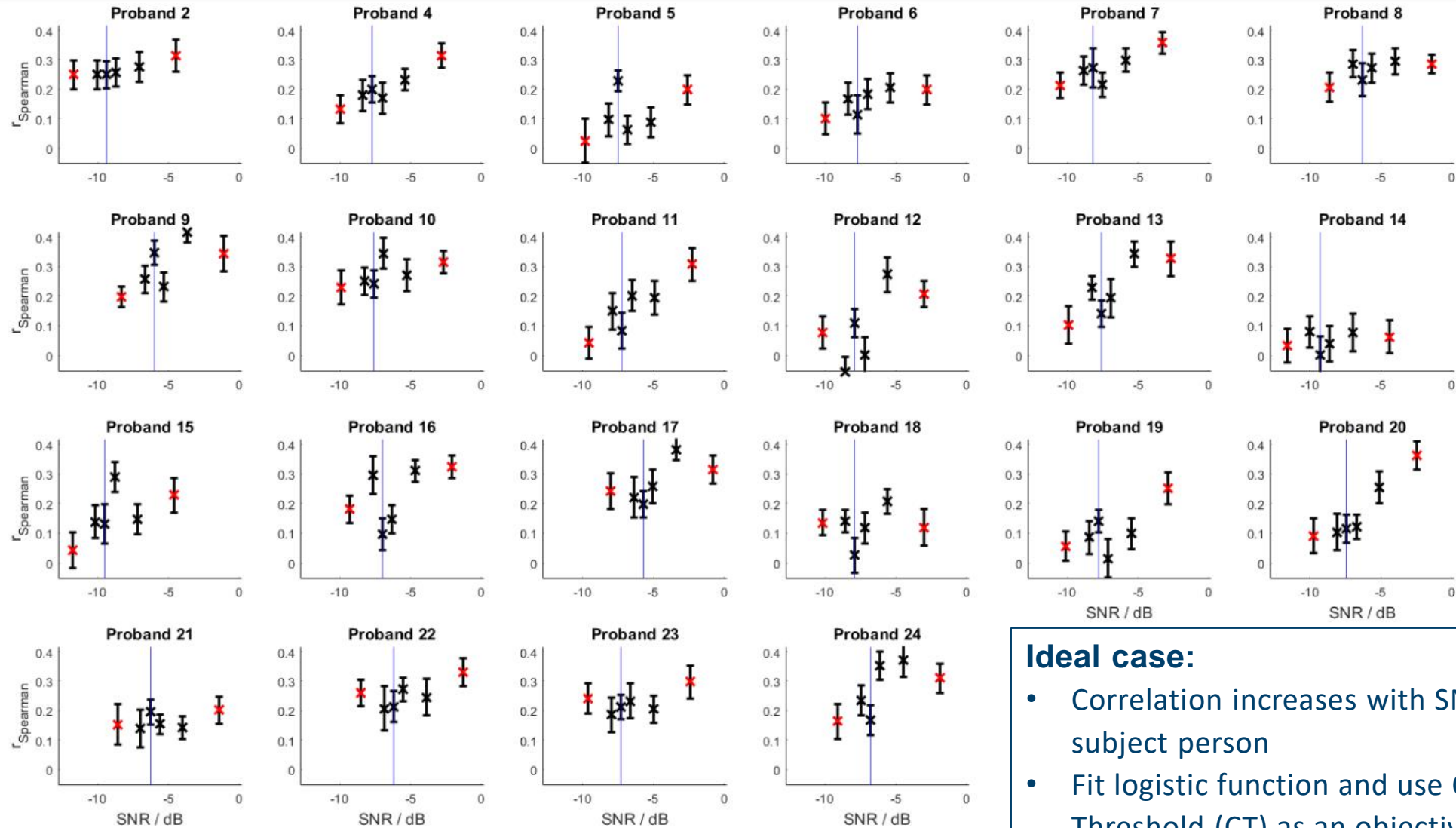
2. Predict envelope of each OLSA-sentence with MEG signal

3. Calculate correlation coefficients between prediction and envelope of sentence

4. Calculate average of all 20 correlation coefficients per SNR or speech intelligibility  
► 6 correlation coefficients per subject



# Speech Intelligibility Predicted from Neural Entrainment of the Speech Envelope

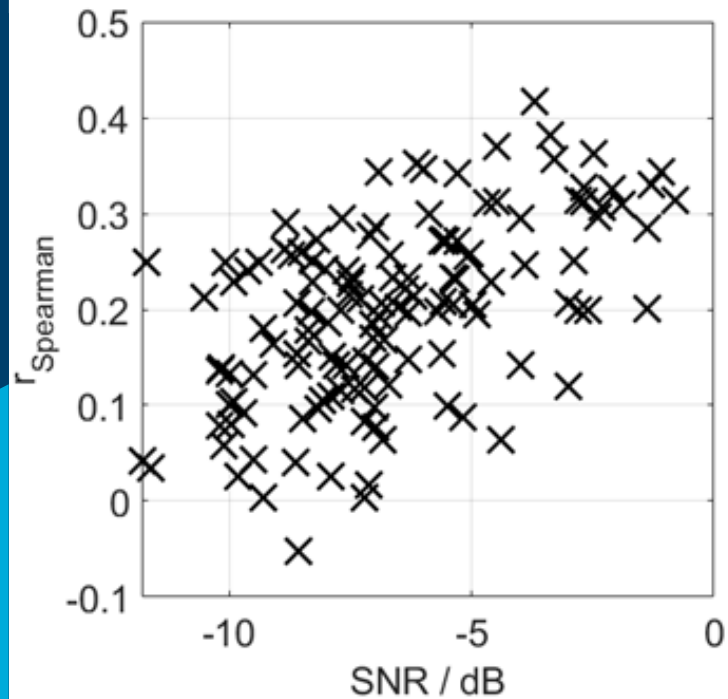


## Ideal case:

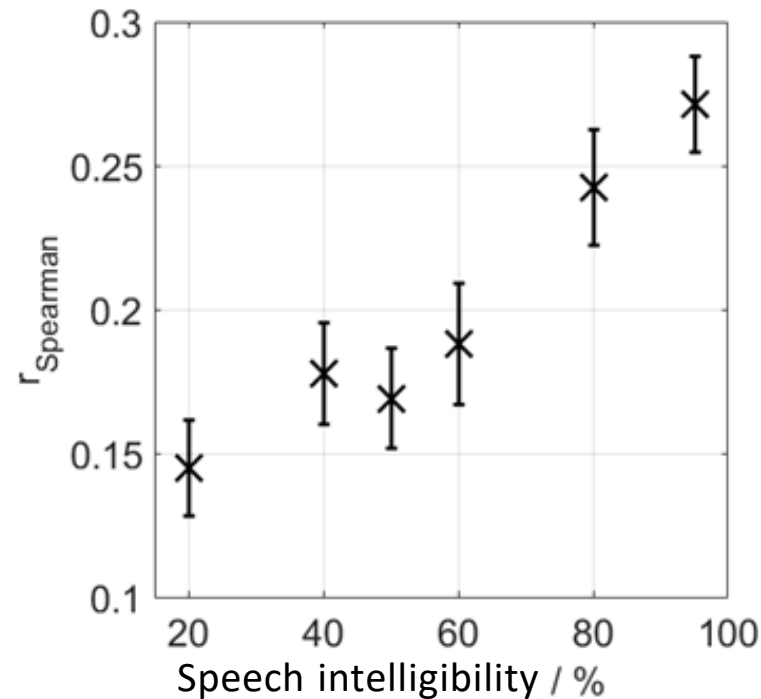
- Correlation increases with SNR for each subject person
- Fit logistic function and use Correlation Threshold (CT) as an objective measure to the SRT (Vanthornhout et al., 2018)



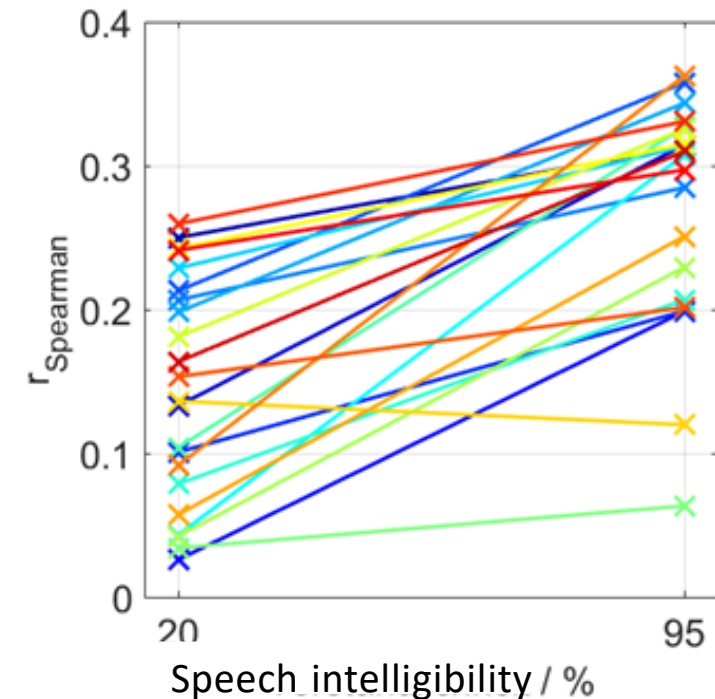
# Speech Intelligibility Predicted from Neural Entrainment of the Speech Envelope



$$r_{\text{Pearson}} = 0.54 \text{ (} p < 0.001 \text{)}$$



$$r_{\text{Pearson}} = 0.97 \text{ (} p < 0.002 \text{)}$$

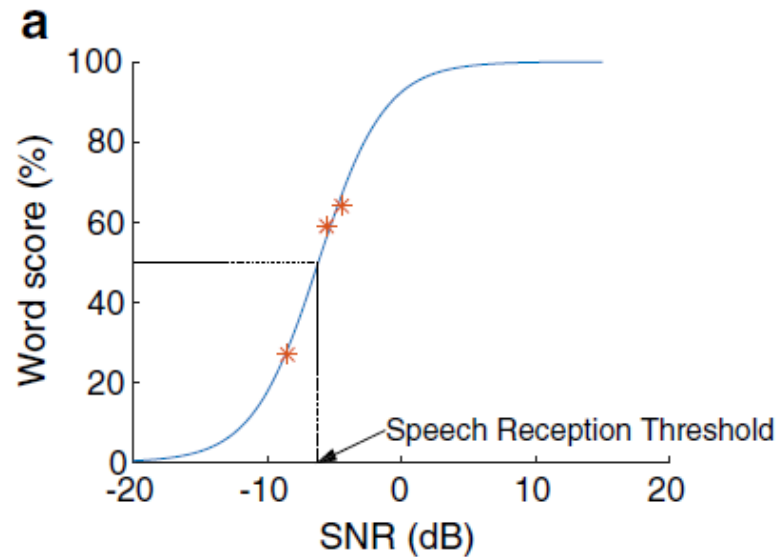


Paired sample t-Test  
( $p < 0.001$ )

- Correlation coefficient increases significantly with speech intelligibility of OLSA-sentence
- results give evidence towards an objective and automatic way of assessing neural processing of presented speech

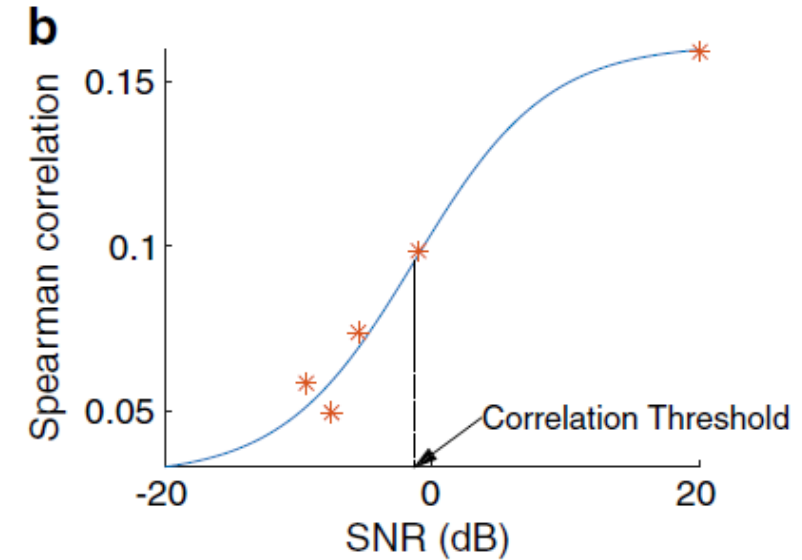
## Results from Vanthornhout et al. (2018)

### Behavioral measurement of speech intelligibility



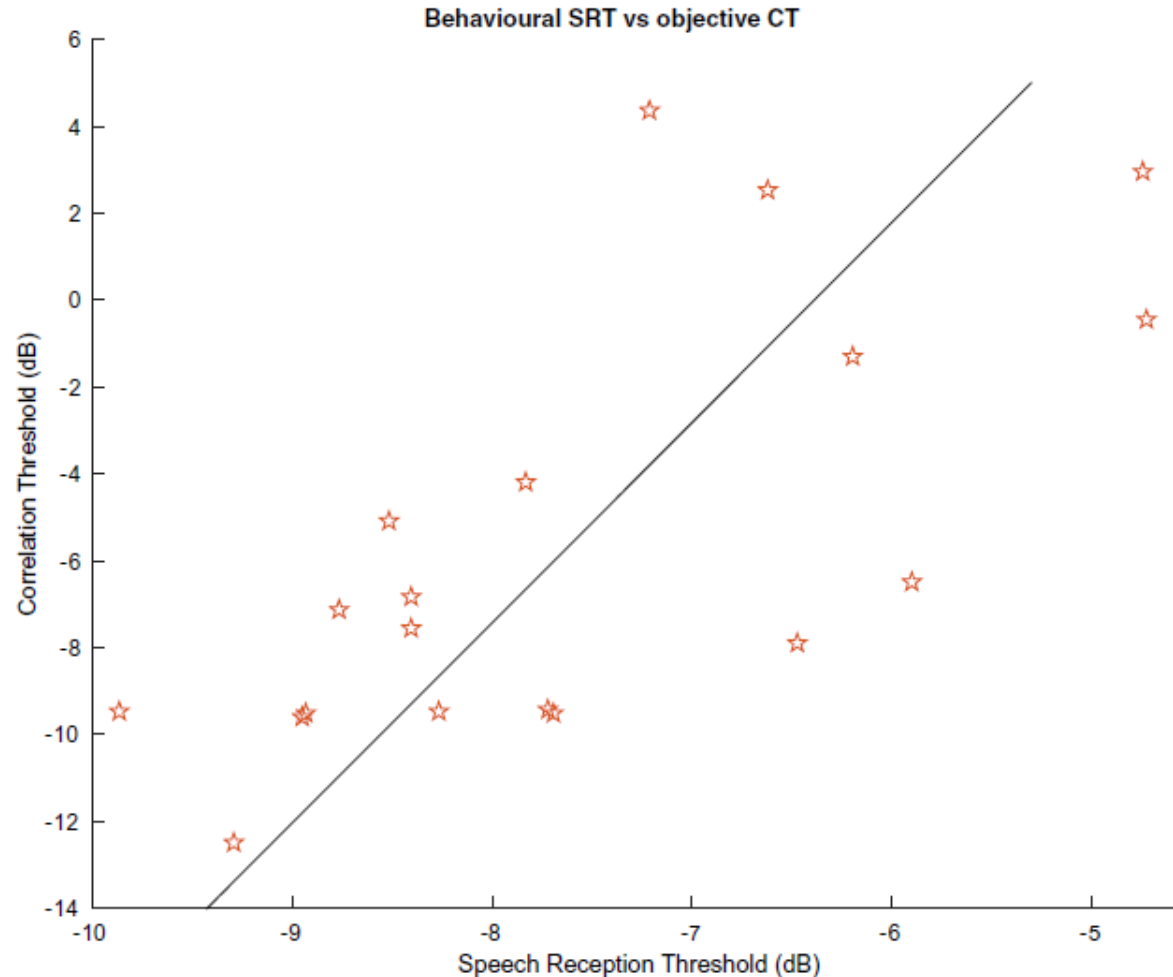
**Fig. 4.** Behavioral and objective results for one subject. **a** The percentage of words correctly understood increases with increasing SNR. The blue line is a sigmoid function fitted on these data, from which we can estimate the speech reception threshold (SRT). **b** The Spearman correlation

### Electrophysiological measurement of speech intelligibility



between actual speech envelope and speech envelope extracted from the EEG response increases with increasing SNR. The blue line is a sigmoid function fitted on these data, from which we can estimate our objective measure, the correlation threshold (CT)

## Results from Vanthornhout et al. (2018)



- Significant correlation between the objectively measured CT and behaviorally measured SRT
- Demonstrates an electrophysiological measure of neural processing of running speech

**Fig. 6.** Electrophysiological versus behavioral measure (Pearson's  $r=0.69$ ,  $p=0.001$ ). The electrophysiological measure (correlation threshold, CT) is the midpoint of each psychometric function. The behavioral measure (speech reception threshold, SRT) is the stimulus SNR at which the subject can understand 50 % of the words

Thank you!

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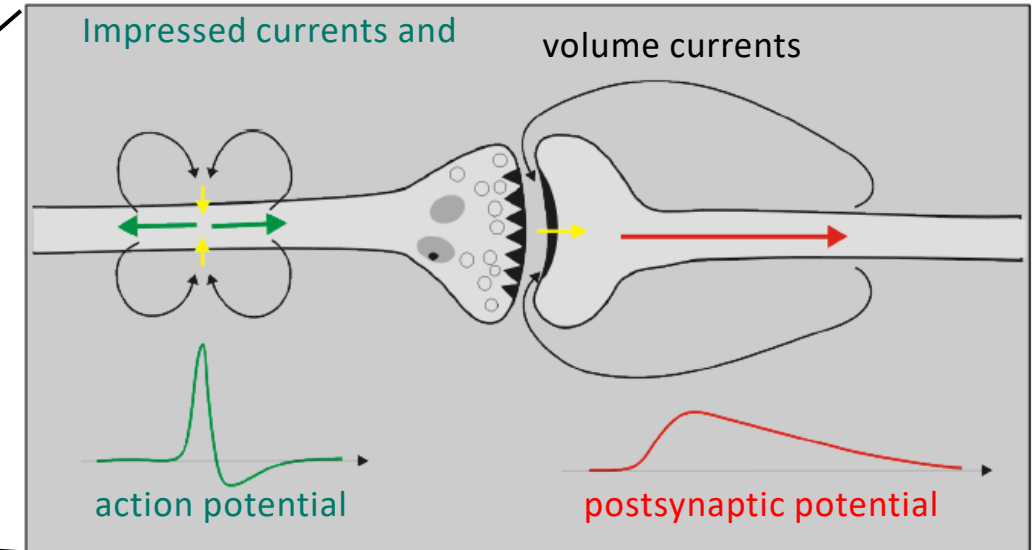
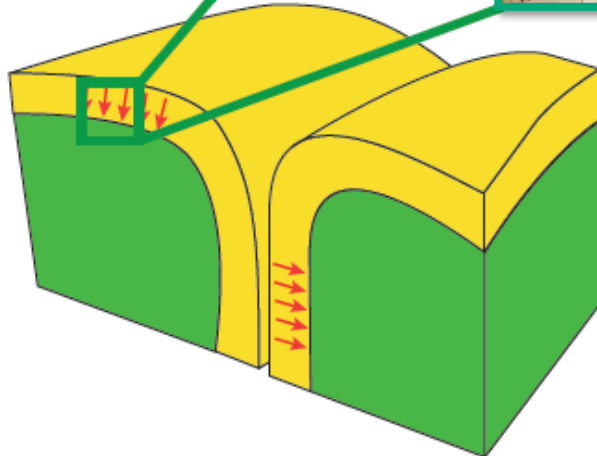
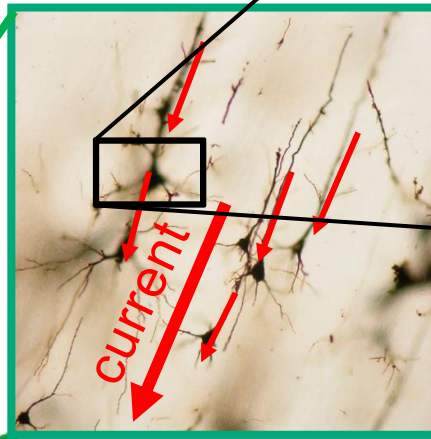
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# Neurons as current generators

Large cortical pyramidal cells organized in macro-assemblies with their **dendrites normally oriented to the local cortical surface**

$Q = I \times d$   
(10 to 100 nAm) with the  
equivalent current  
dipole (ECD) model



## Impressed currents $J_i(r)$

- due to electrochemical gradients and open ion channels across the cell membrane

## Primary currents $J_p(r)$

- due to impressed currents
- currents inside the dendrites and in their vicinity

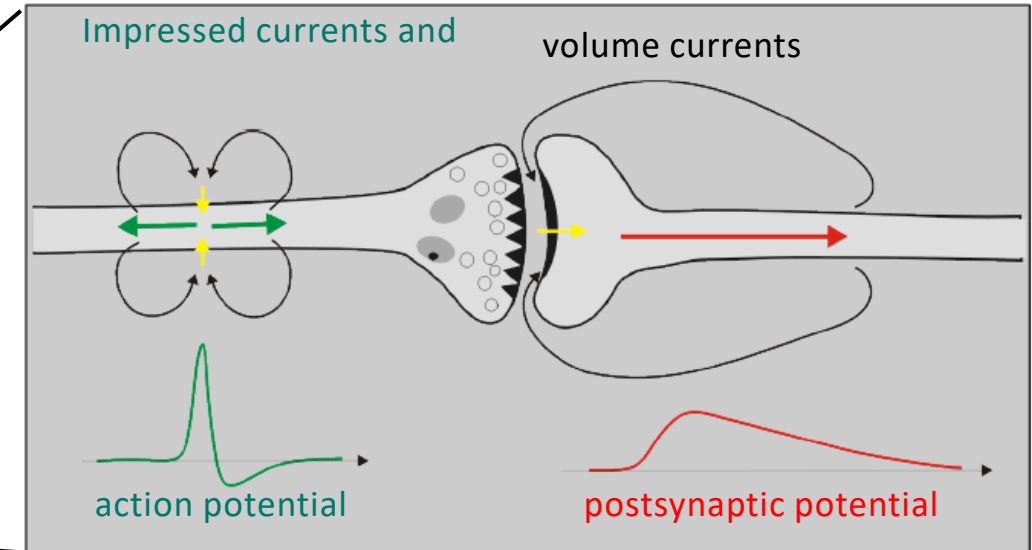
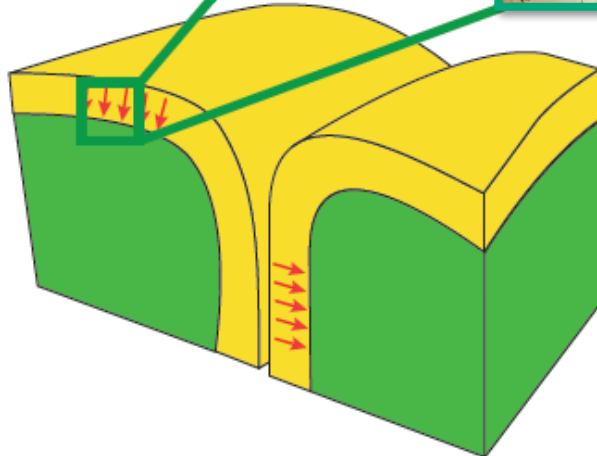
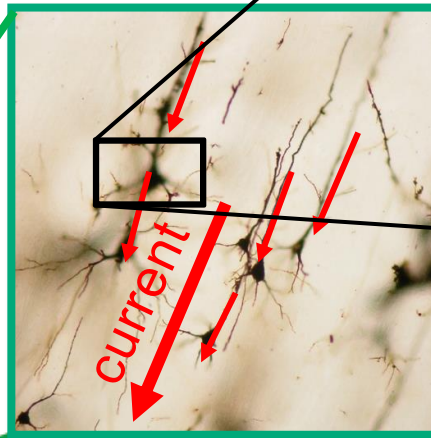
## Volume currents $J_v(r)$

- due to  $J_i$  and  $J_p$
- passive, ohmic current flow

# Neurons as current generators

Large cortical pyramidal cells organized in macro-assemblies with their **dendrites normally oriented to the local cortical surface**

$Q = I \times d$   
(10 to 100 nAm) with the  
equivalent current  
dipole (ECD) model

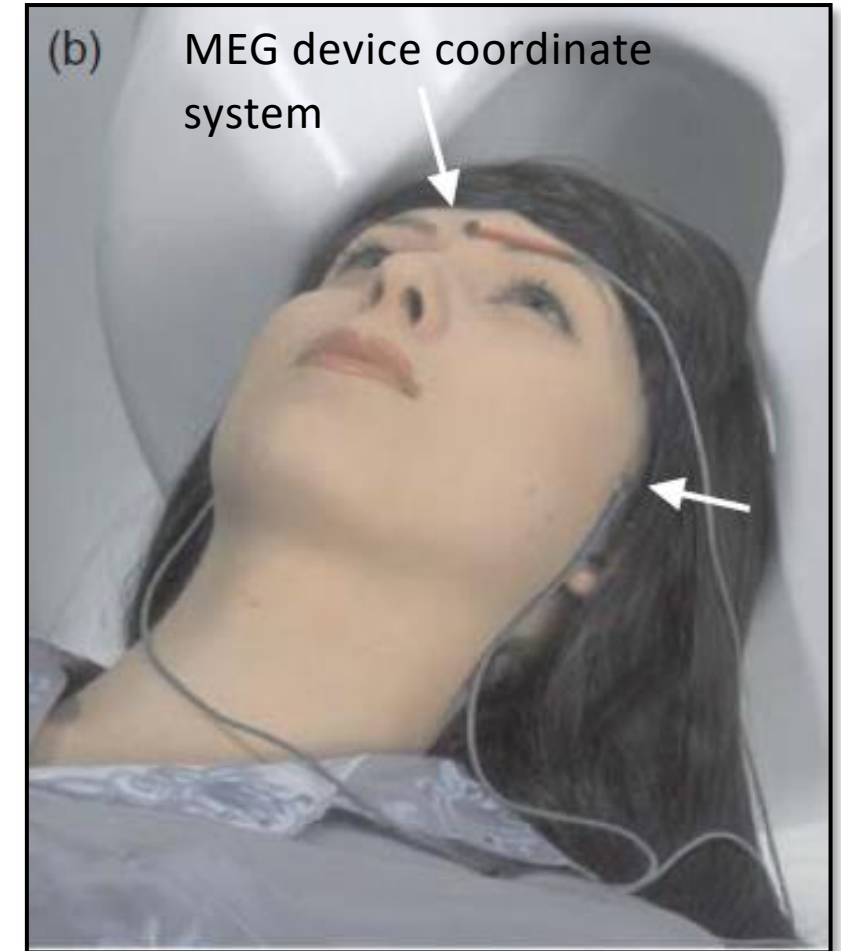


Generally, **all currents** generate a magnetic field!

- **Impressed** currents  $J_i(\mathbf{r})$  can be omitted:  
short distance through the cell membrane  
► negligible contribution to the total field

# Head position measurement

- Head position indicator (HPI) coils are attached on the scalp and digitized with fiducials (anatomical landmarks)
- Activated during MEG measurement to track head position
- Energized HPI coils are magnetic dipoles that emit precise sinusoidal frequency that can be located in the helmet
- Localizing subject's head in the MEG device coordinate system, i.e., with respect to the sensor array

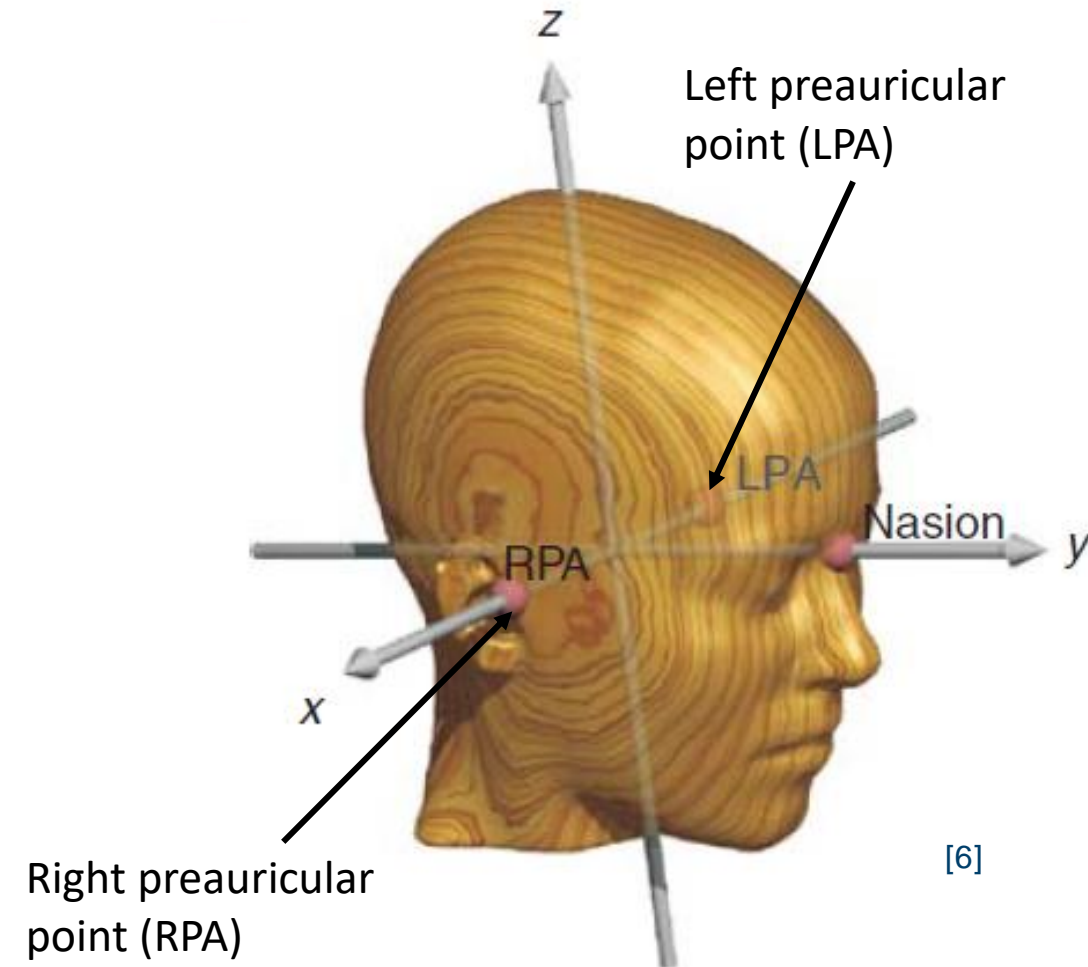


[6]

# Co-registration with anatomical MRI

Locations of HPI coils are unknown relative to the head

- MEG source locations are usually superimposed on anatomical MR images: MEG/MRI co-registration required
- **Head coordinate system** is the link between the MEG and MRI device coordinate systems
- 3 common anatomical landmarks (fiducials) are used to define the head coordinate system



Definition of head coordinate system  
(vendor specific)



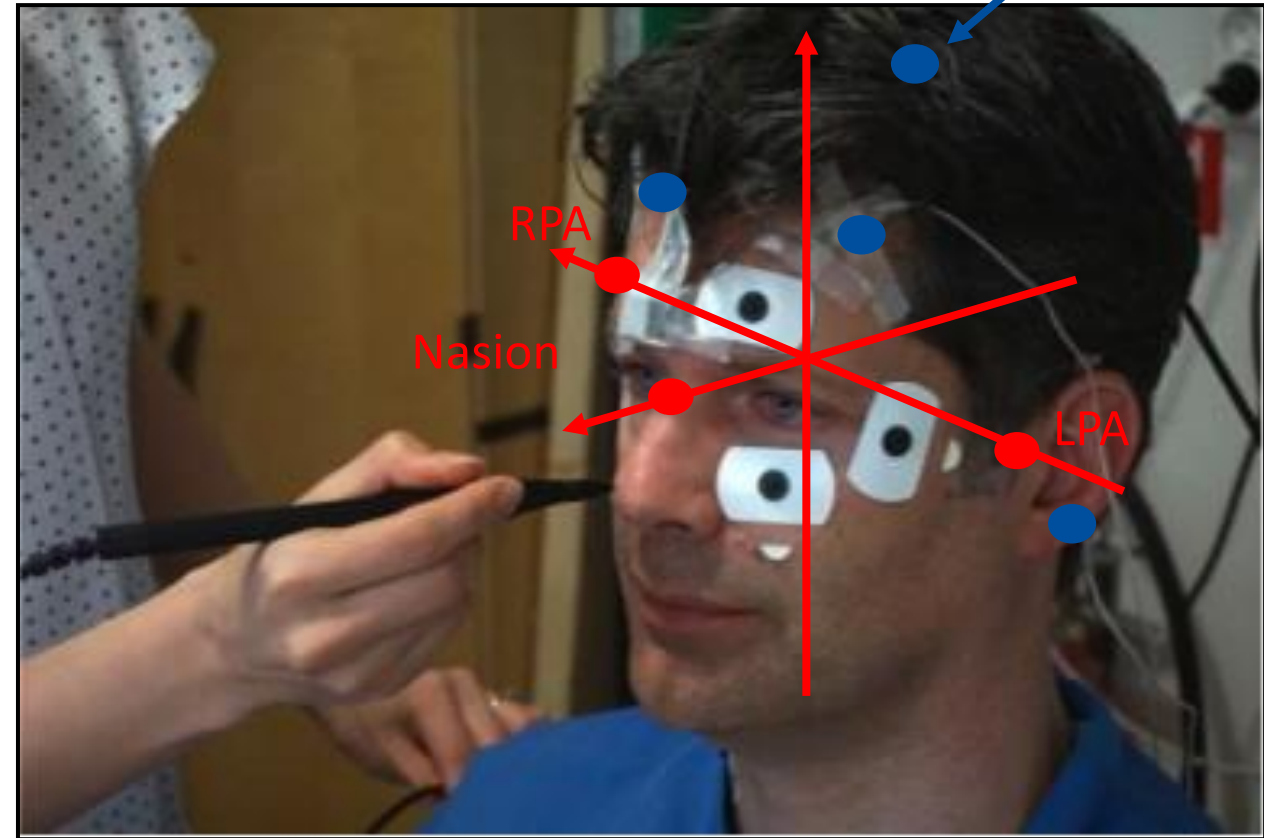
# Co-registration with anatomical MRI

## Digitization

- Initialization of head coordinate system by marking anatomical landmarks Nasion, RPA and LPA with a 3D digitizer
- 3D digitizer is also used for localizing the HPI coils in the head coordinate system
- Thus anatomical landmarks (known in MRI coordinate system) and HPI coils (known in MEG coordinate system) are defined in head coordinate system

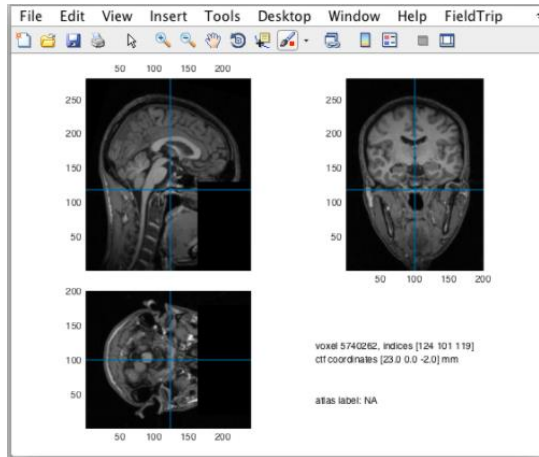
head coordinate system with  
anatomical landmarks

HPI coils



[8]

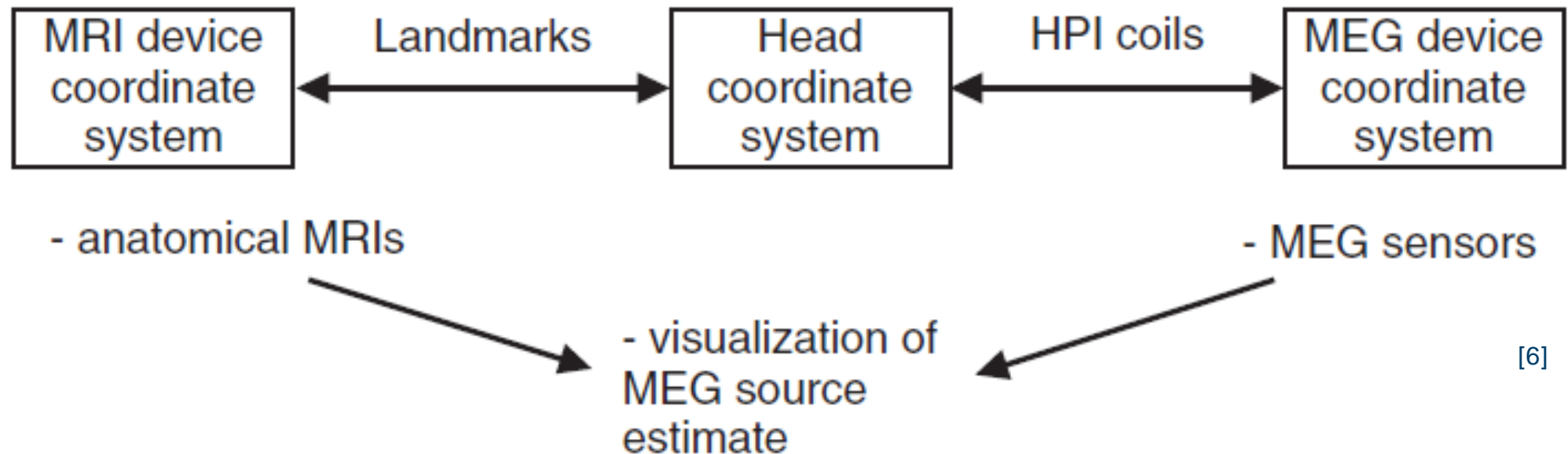
# Co-registration with anatomical MRI



[8]



[6]



[6]