EEG/MEG 2:
Source Estimation

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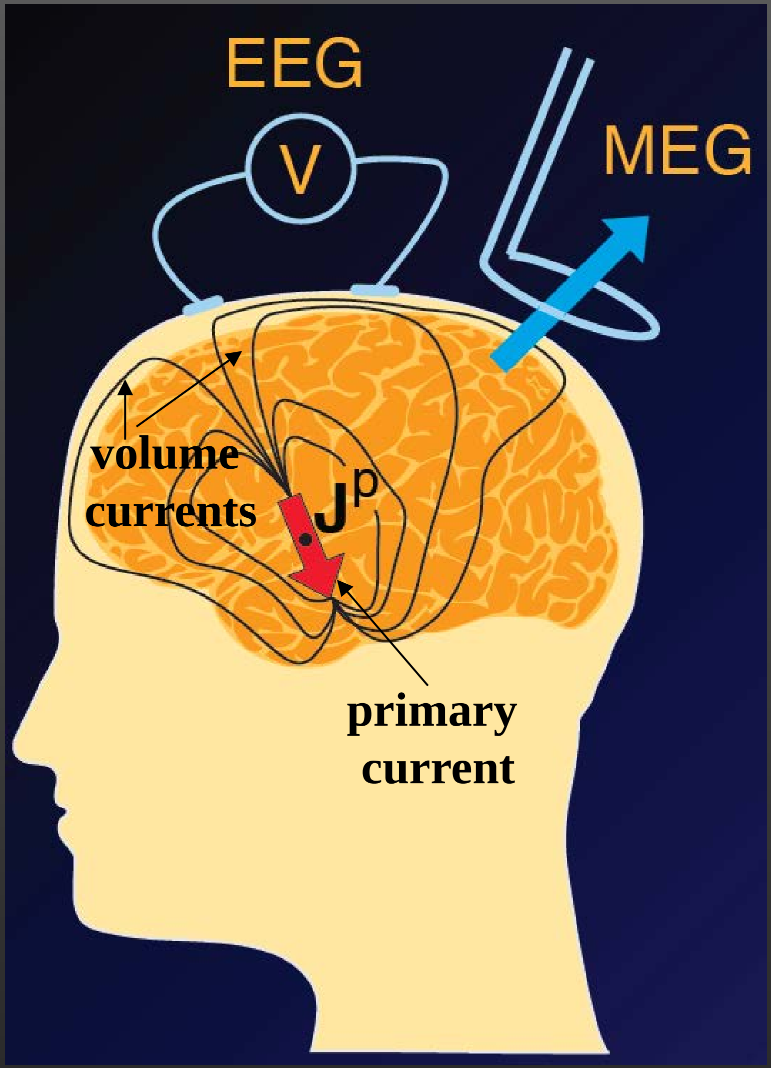
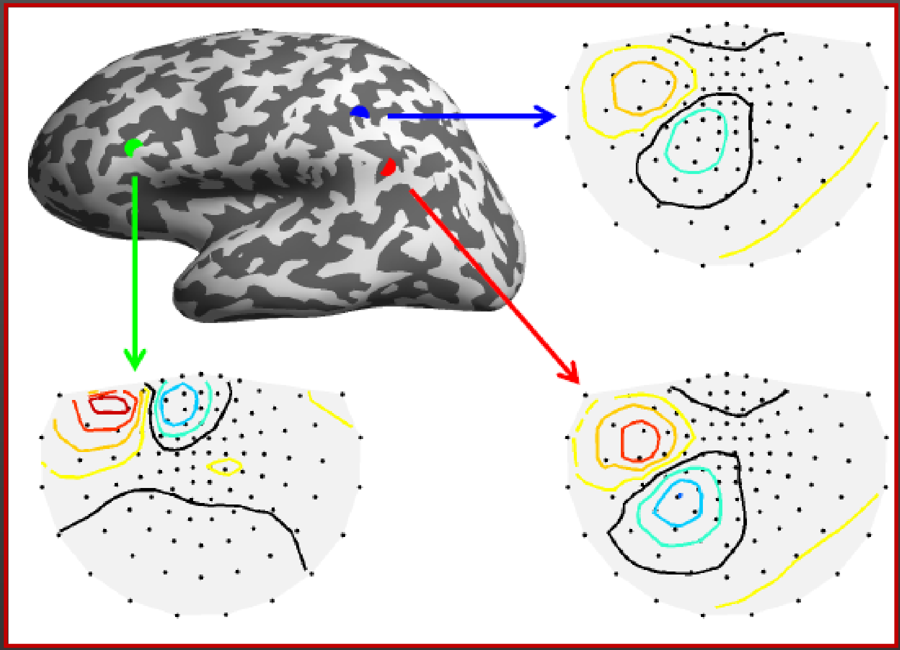
The Inverse Problem



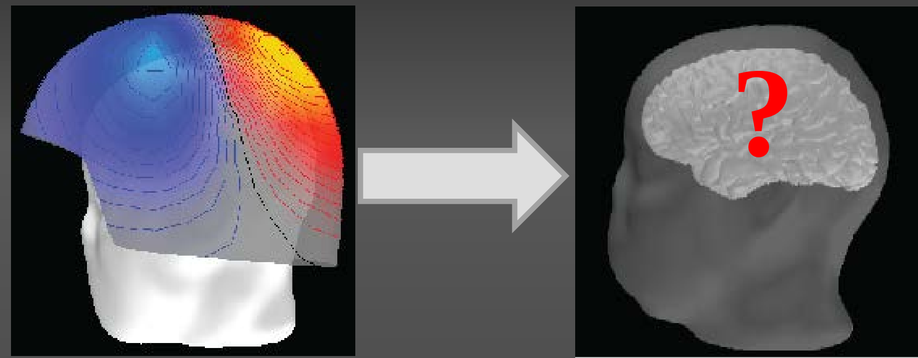
http://www.nmr.mgh.harvard.edu/meg/pdfs/talks/

Different sources may produce similar signal topographies
=> Inherently limits spatial resolution

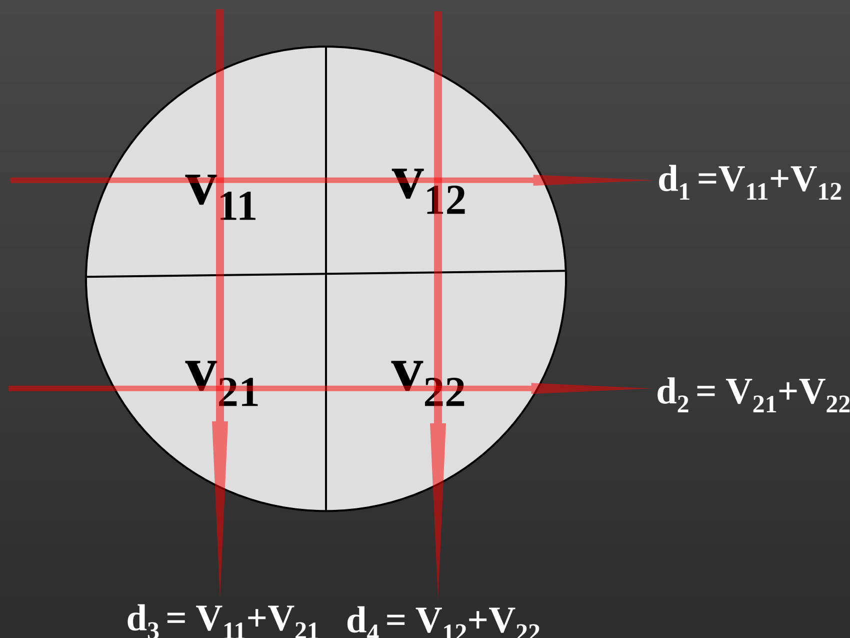


Thanks to Matti Stenroos

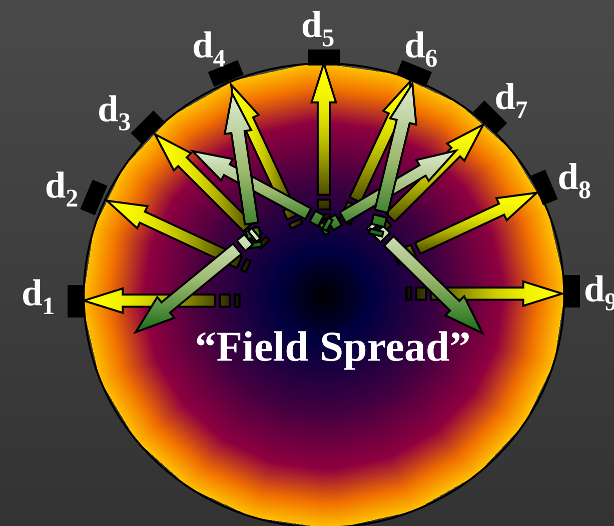
The Inverse Problem



Tomography
(CT, fMRI…)



EEG/MEG



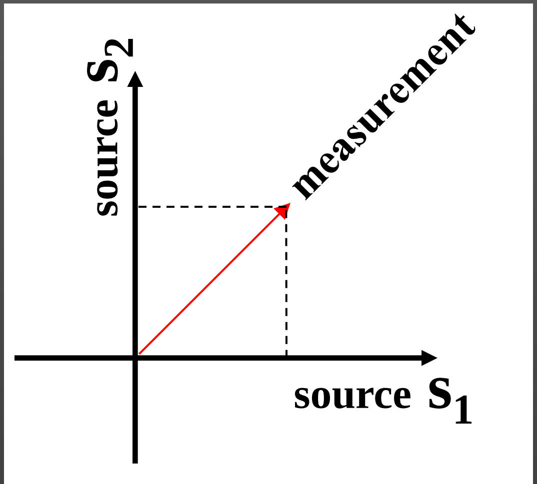
Information is lost during measurement

Cannot be retrieved by mathematics

Inherently limits spatial resolution

The Inverse Problem

Reconstructing information from an incomplete projection:



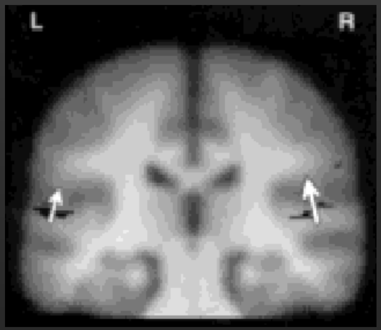
This is like reconstructing a 3D object based on its 2D shadow.

One Strategy: Dipole Modelling

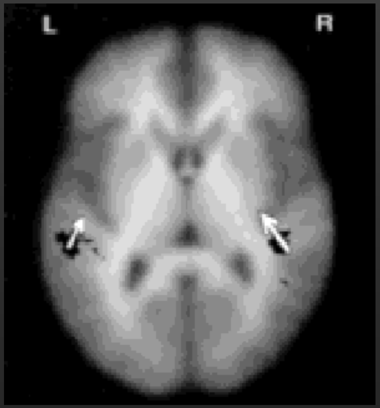
1. **Assume there are only a few spatially distinct sources**

2. **Iteratively adjust the location, orientation and strength of a few dipoles…**

3. **…until the result best fits the data**



Hypothesis testing -
Works well with "simple"data, such as early evoked responses

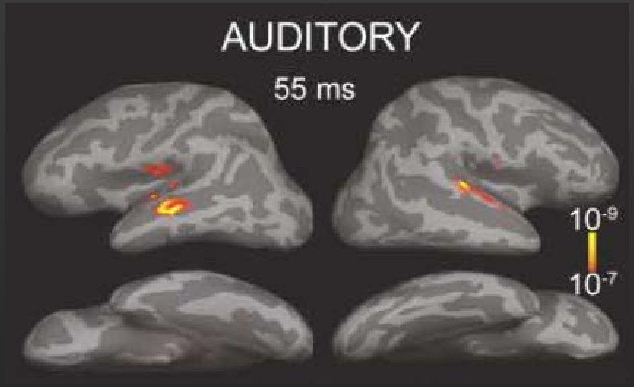


Another Strategy: Distributed Sources

1. Assume sources are everywhere (e.g. distributed across the whole cortex)

2. Find the distribution of source strengths that explains the data…

3. …AND fulfils other constraints

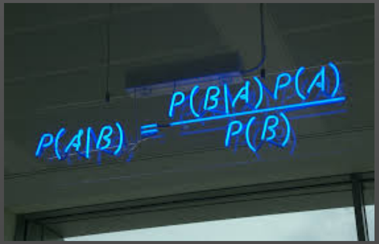


No constraints on locations and number of sources,
but limited spatial resolution
("leakage", "field spread")

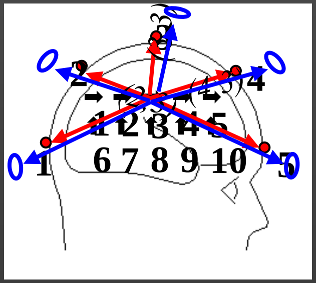
Framing the Inverse Problem

Before you can solve a problem, you have to state it, e.g.

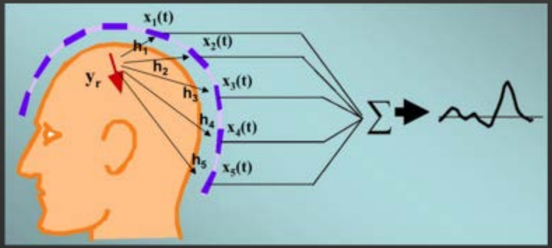
Bayesian Model Estimation



Calculus and Linear Algebra



Spatial Filters, Virtual Sensors



Framing the Inverse Problem

What do I want?

Peaks in my solution should be close to real activity

What have I got?

Usually only the data and a lot of enthusiasm

How can I get as close as possible to what I want with what I've got with as little effort as possible?

You didn't really expect an answer, did you?

It's Not the Maths, It's the Assumptions!

"No frills" solution (Minimum Norm)

$$(\hat{\mathbf{s}}-\hat{\mathbf{s}}_0)^T \mathbf{C}_s (\hat{\mathbf{s}}-\hat{\mathbf{s}}_0) = \min$$
$$(\mathbf{L}\hat{\mathbf{s}}-\mathbf{d})^T \mathbf{C}_d (\mathbf{L}\hat{\mathbf{s}}-\mathbf{d}) = \varepsilon > 0$$

$$\hat{\mathbf{s}} = \hat{\mathbf{s}}_0 + \mathbf{C}_s^{-1}\mathbf{L}^T\left(\mathbf{L}\mathbf{C}_s^{-1}\mathbf{L}^T + \lambda\,\mathbf{C}_d^{-1}\right)^{-1}(\mathbf{d}-\mathbf{L}\hat{\mathbf{s}}_0)$$

"Most likely" solution (Maximum Likelihood)

$$\mathbf{P}(\mathbf{s}) \sim \exp\{-(\hat{\mathbf{s}}-[\mathbf{s}])^T \mathbf{C}_s (\hat{\mathbf{s}}-[\mathbf{s}])\}$$
$$\mathbf{P}(\mathbf{d},\hat{\mathbf{s}}) \sim \exp\{-(\mathbf{d}-\mathbf{L}\hat{\mathbf{s}})^T \mathbf{C}'_d (\mathbf{d}-\mathbf{L}\hat{\mathbf{s}})\}$$

$$\hat{\mathbf{s}} = [\mathbf{s}] + \mathbf{C}_s^{-1}\mathbf{L}^T(\mathbf{L}\mathbf{C}_s^{-1}\mathbf{L}^T + \lambda\mathbf{C}_d^{-1})^{-}(\mathbf{d}-\mathbf{L}[\mathbf{s}])$$

"Best spatial filter" (Beamformer)

$$Min\,(\mathbf{W}(\mathbf{r}_i - \mathbf{t}_i))^2$$
$$Min([\mathbf{G}_{i.}\mathbf{n}]^2) \Rightarrow Min(\mathbf{G}_{i.}\mathbf{C}_n\mathbf{G}_{i.}^T)$$

$$\mathbf{G}_{i.} = (\mathbf{S} + \lambda\mathbf{C}_n)^{-1}\mathbf{u}$$
$$\mathbf{S} = \mathbf{L}\mathbf{L}^T \quad \mathbf{u} = \mathbf{L}_{.i}$$

$$\mathbf{G}_{i.} = (\mathbf{L}\mathbf{L}^T + \lambda\mathbf{I})^{-1}\mathbf{L}_{.i}$$

"Minimum Least-Squares Solution"

$$\hat{\mathbf{s}} = \mathbf{L}^T\left(\mathbf{L}\mathbf{L}^T + \lambda\,\mathbf{I}\right)^{-1}\mathbf{d}$$

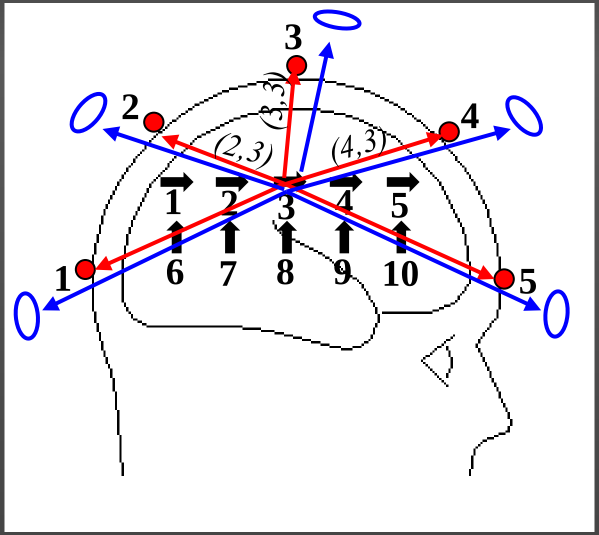
$$\hat{\mathbf{s}} = \mathbf{L}^T\left(\mathbf{L}\mathbf{L}^T + \lambda\,\mathbf{I}\right)^{-1}\mathbf{d}$$

$$\hat{\mathbf{s}} = \mathbf{L}^T\left(\mathbf{L}\mathbf{L}^T + \lambda\,\mathbf{I}\right)^{-1}\mathbf{d}$$

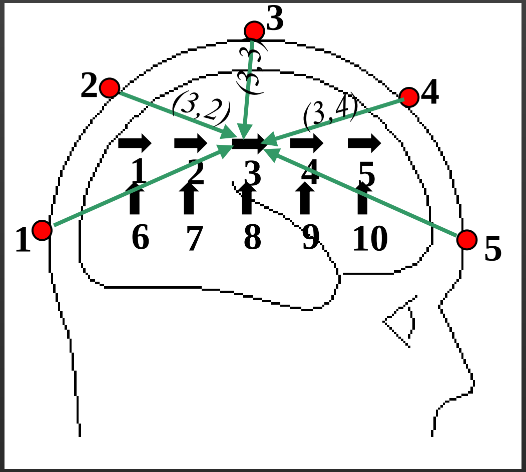
All approaches converge to the same solution if they make optimal use of the same information

e.g. Hauk, Neuroimage 2004

"Forward" and "Inverse" Problems



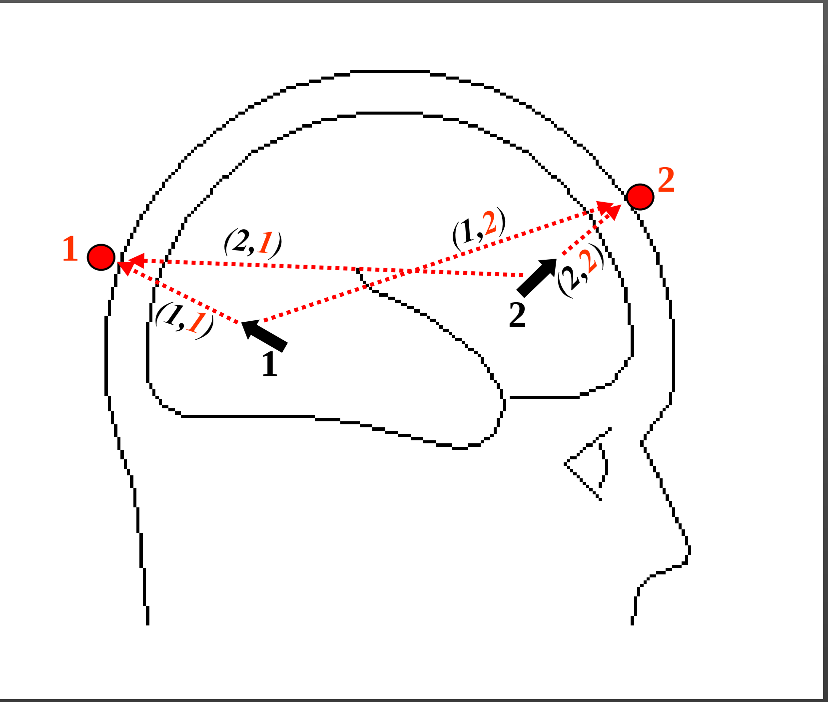
Forward Problem



Inverse Problem

Basic Concepts of Inverse Problems

A uniquely solvable problem



data — "leadfield" — dipoles

$$\begin{pmatrix} d_1 \\ d_2 \end{pmatrix} = \begin{pmatrix} 0.5 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} j_1 \\ j_2 \end{pmatrix}$$

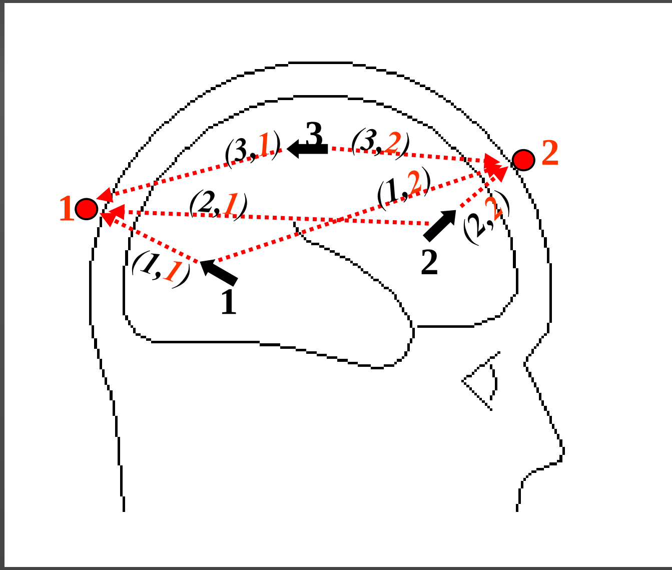
inversion

dipoles — inverse — data

$$\begin{pmatrix} \hat{j}_1 \\ \hat{j}_2 \end{pmatrix} = \begin{pmatrix} 2 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} d_1 \\ d_2 \end{pmatrix}$$

Basic Concepts of Inverse Problems

An ambiguous problem



“Minimum Norm Solution”

data “leadfield” dipoles

$$\begin{pmatrix} d_1 \\ d_2 \end{pmatrix} = \begin{pmatrix} 0.5 & 0 & 0.3 \\ 0 & 1 & -0.3 \end{pmatrix} \begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix}$$

?

inversion

dipoles inverse data

$$\begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix} = \begin{pmatrix} 1.5034 & 0.1241 \\ 0.2483 & 0.9379 \\ 0.8276 & -0.2069 \end{pmatrix} * \begin{pmatrix} d_1 \\ d_2 \end{pmatrix}$$

Produces solution with minimal power or “norm”:

$$\left(j_1^2 + j_2^2 + j_3^2 \right)$$

Basic Concepts of Inverse Problems

What is the solution to

$$\mathbf{x_1 + x_2 = 1}$$

Maybe

$x_1 = 0 ; x_2 = 1$?

$x_1 = 1 ; x_2 = 0$?

$x_1 = 1000 ; x_2 = -999$?

$x_1 = \pi ; x_2 = (1-\pi)$?

The minimum norm solution is:

$$\mathbf{x_1 = 0.5 ; x_2 = 0.5}$$

with $(0.5^2 + 0.5^2)=0.5$ the minimum norm among all possible solutions

Basic Concepts of Inverse Problems

Non-Unique

data "leadfield" dipoles

$$\begin{pmatrix}1\\1\end{pmatrix} = \begin{pmatrix}0.5 & 0 & 0.3\\ 0 & 1 & -0.3\end{pmatrix} * \begin{pmatrix}j_1\\ j_2\\ j_3\end{pmatrix}$$

?

inversion

"Mininum norm solution:"

dipoles inverse data

$$\begin{pmatrix}1.62\\1.18\\0.62\end{pmatrix} = \begin{pmatrix}1.5034 & 0.1241\\ 0.2483 & 0.9379\\ 0.8276 & -0.2069\end{pmatrix} * \begin{pmatrix}1\\1\end{pmatrix}$$

or $\begin{pmatrix}2\\1\\0\end{pmatrix}$ or $\begin{pmatrix}1.81\\1.09\\0.31\end{pmatrix}$ **Infinite possibilities**

So, what CAN the data actually tell you about the sources???

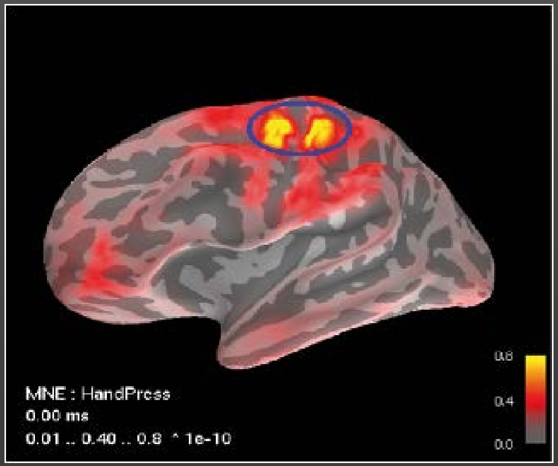
Anything goes?

Spatial Resolution?

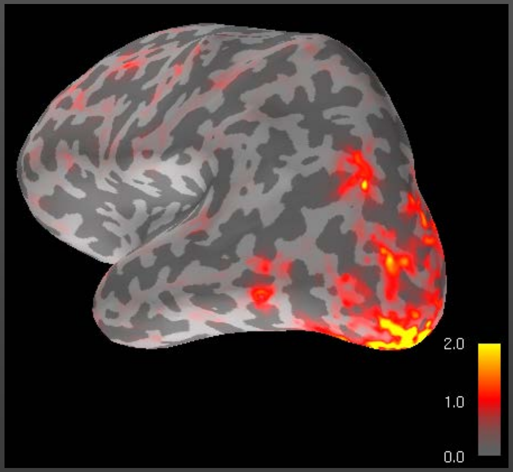
Examples of Minimum Norm Estimates

This is what you may get in real life:

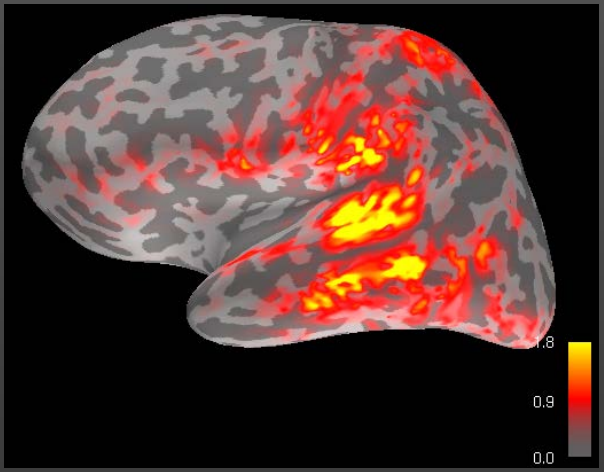
Finger Movement



Visual



Auditory



Linear Systems Analysis

Many methods, such as some minimum estimators and spatial filters, result in linear transformations of your data:
Sources = Operator * Data

Definition of "linear": $f(\alpha x+\beta y) = \alpha f(x) + \beta f(y)$

i.e. linear systems obey the **superposition principle**:

If a source distribution is made up of many point sources, the result of the operator is the sum of the results for the point sources

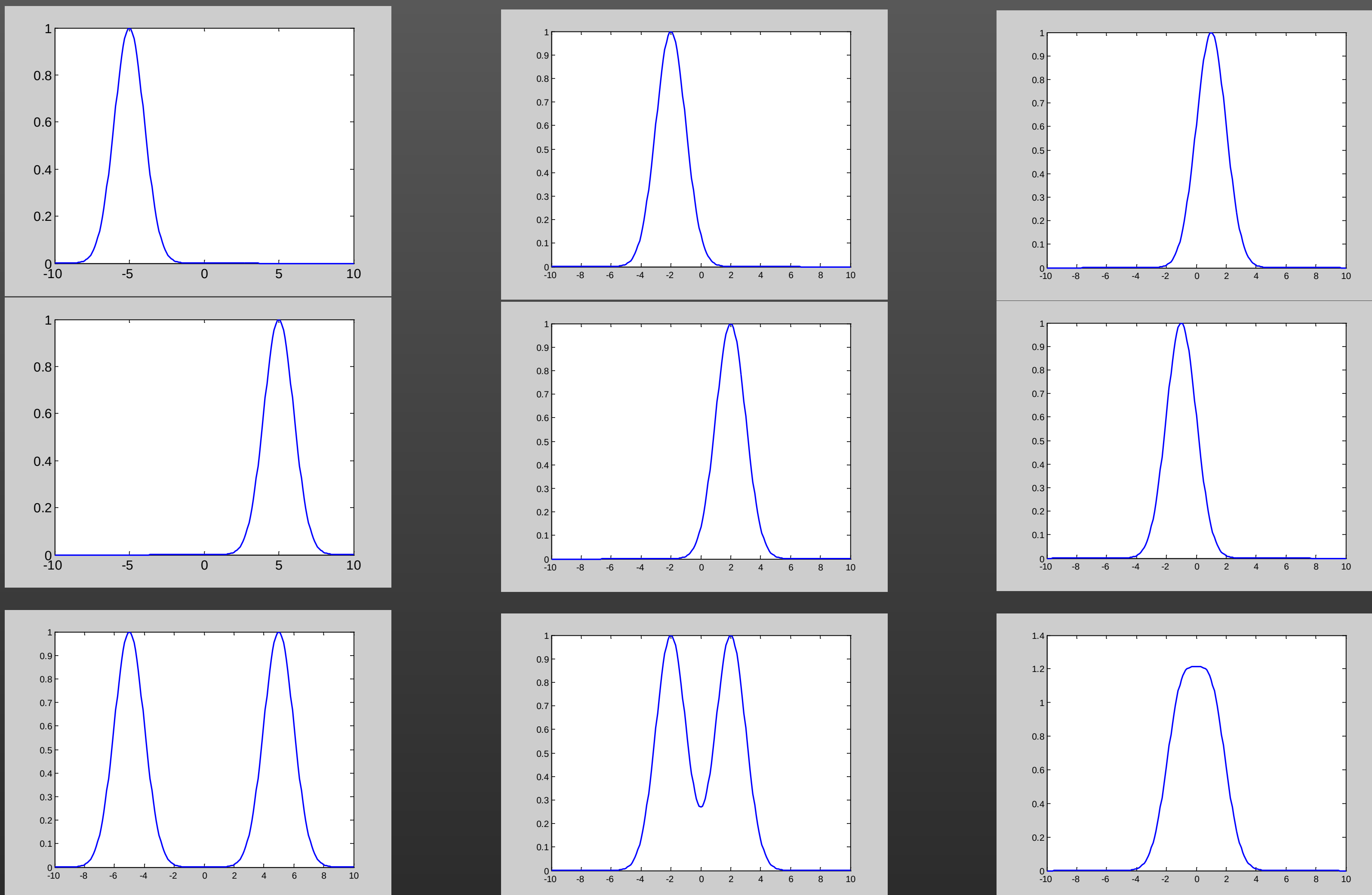
If you know the results of all point sources,
then in principle you have characterised the whole linear system

The result of a point source is often called "Point-Spread Function" (PSF)

For EEG/MEG, a point source is usually called a "dipole"

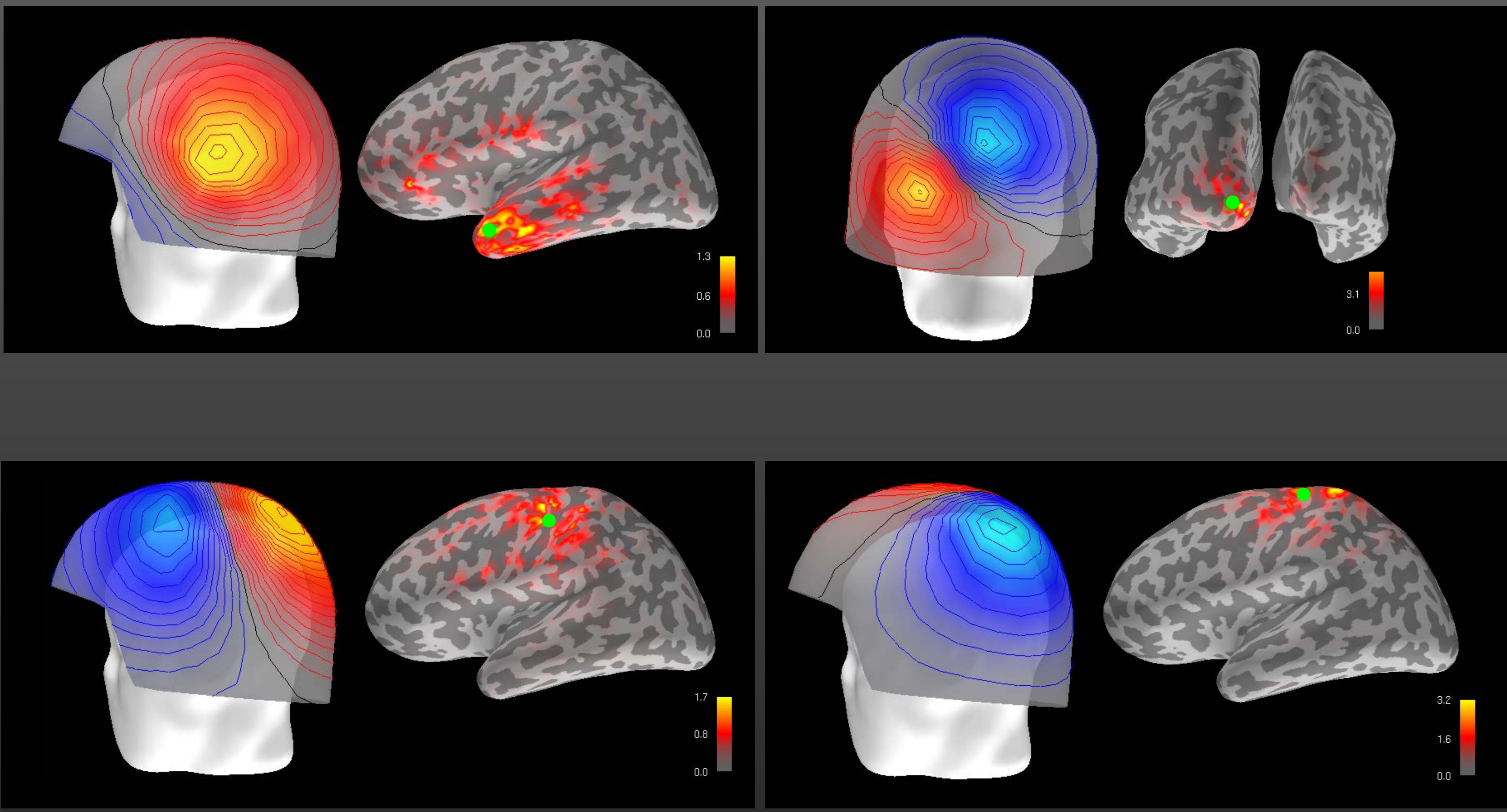
Linear Systems Analysis

Point-spread functions and superposition principle



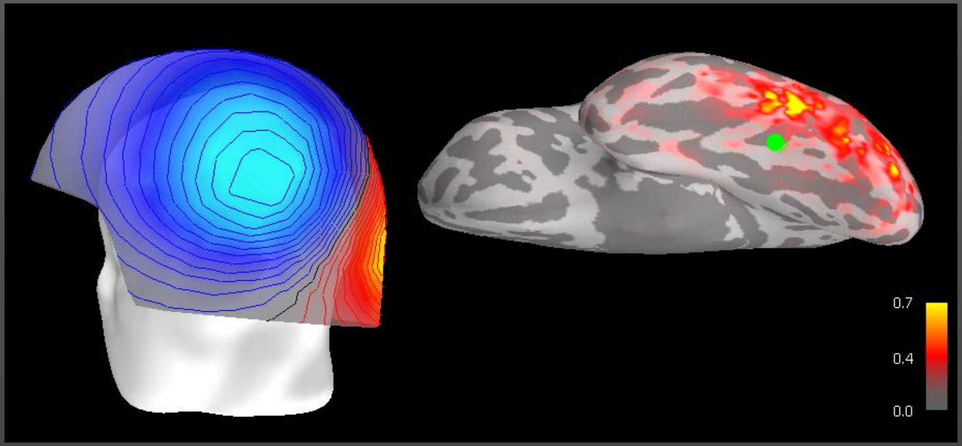
Localisation for "Good" ROIs

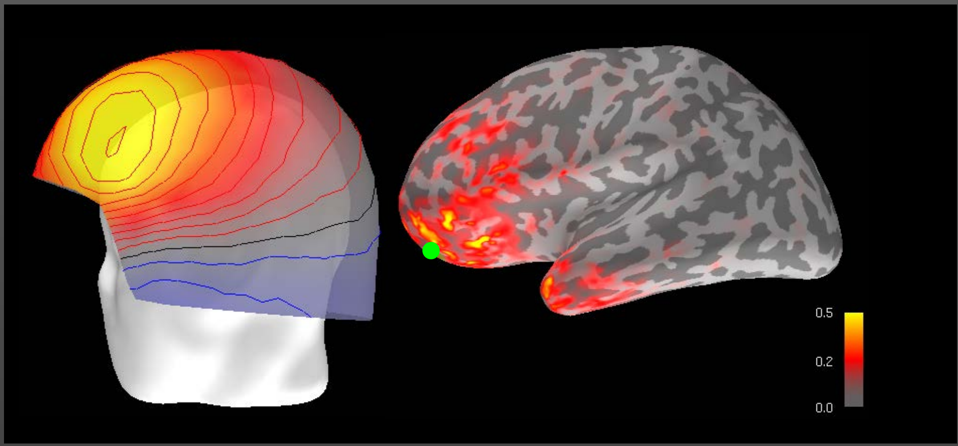
Some point-spread functions

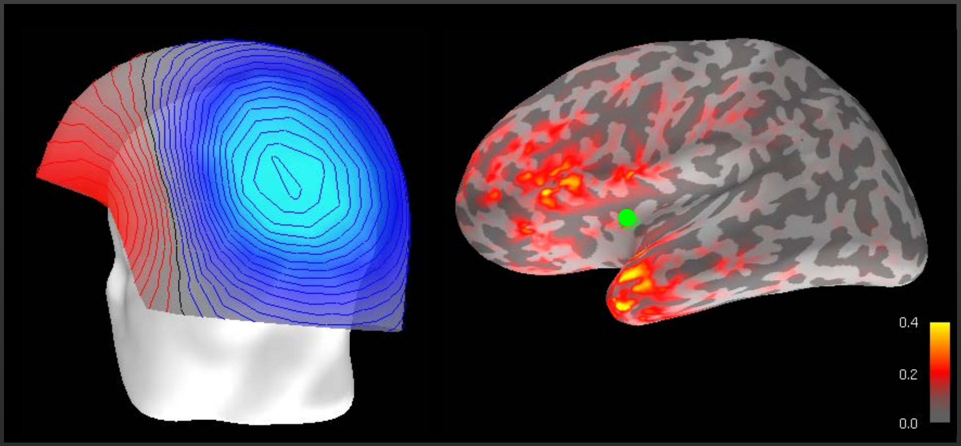


Localisation for "Bad" ROIs

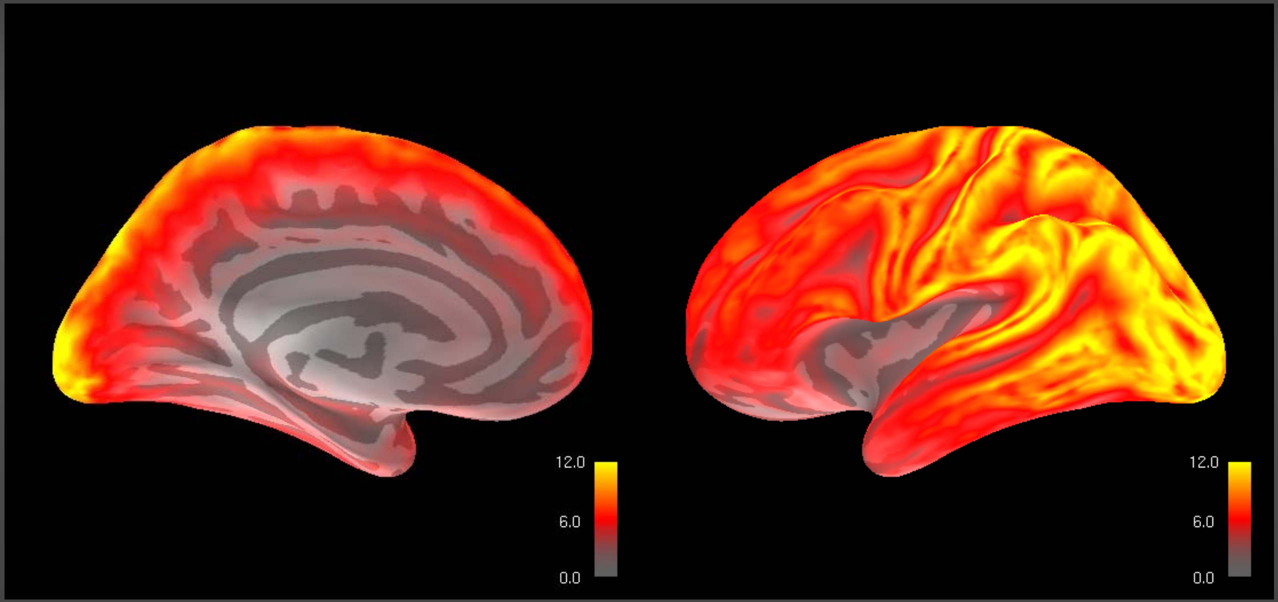
Some point-spread functions

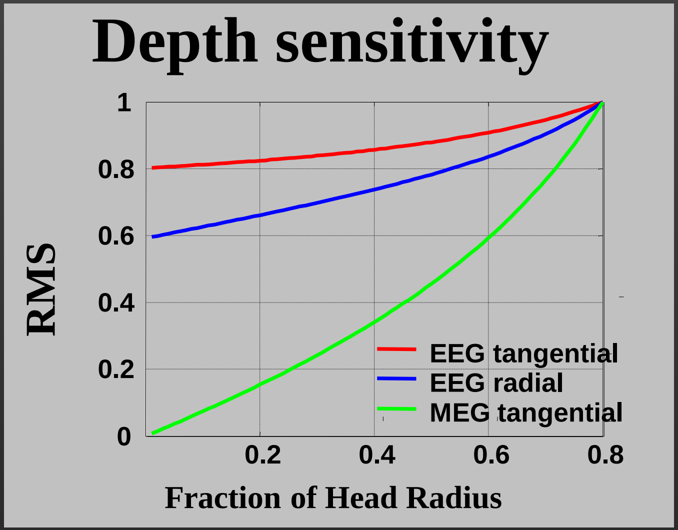




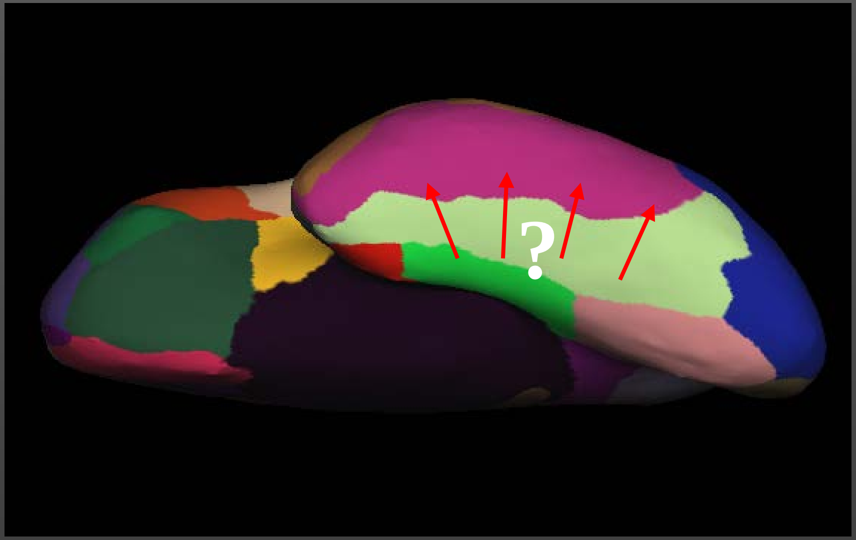


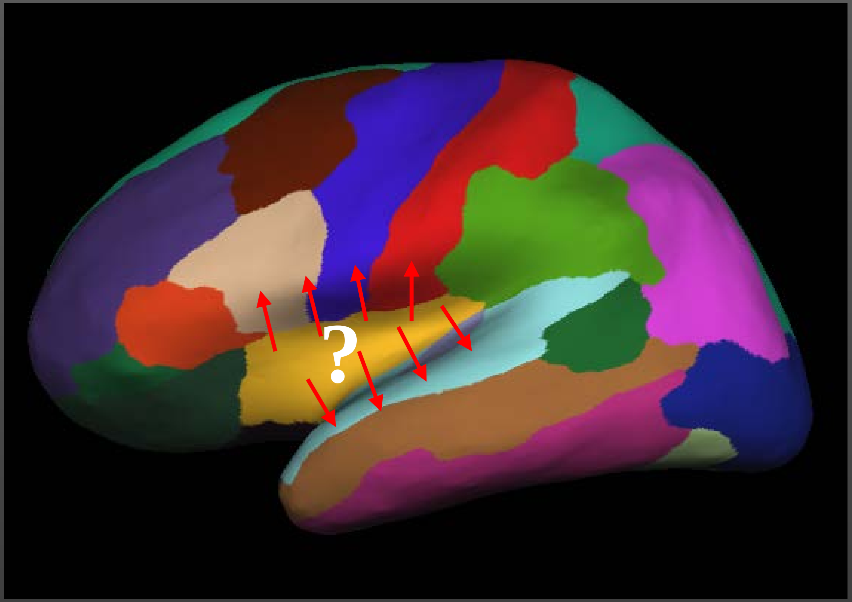
Sensitivity Maps for MEG





Systematic Localisation Bias Can Affect ROI Analyses





Desikan-Killiany Atlas parcellation

Depth information not reliable with either EEG or MEG,

Unless you put in extra information (as in dipole models etc.)

A Rough Estimate of Spatial Resolution

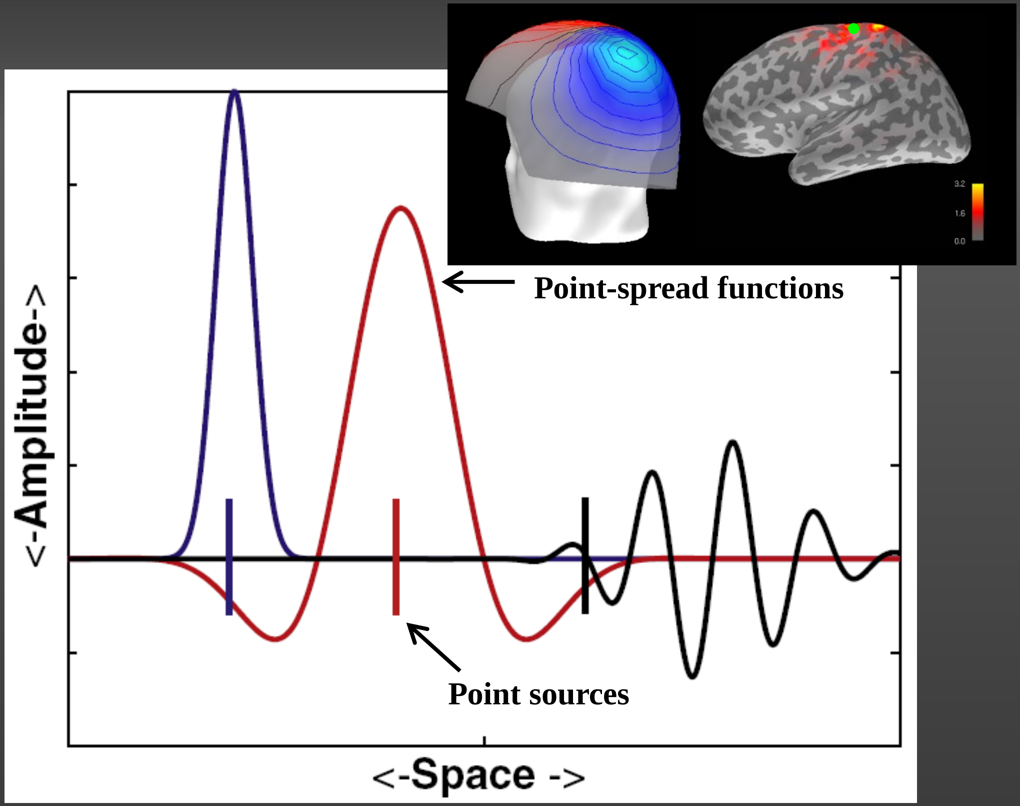
How many independent sources can we separate from each other?

With ***n*** sensors:
-> ***n*** independent measurements
-> ***n*** independent parameters estimable
-> at best separate activity from ***n*** brain regions
Sensors are not independent -> ~ 50 degrees of freedom

Volume of source space:
Sphere 8cm minus sphere 4 cm: volume ~5600 cm^3

"Resel": 113 cm^3 -> **4.8**^3 cm^3

What is "Resolution"?



Your resolution depends on:

modelling assumptions

number of sensors (EEG/MEG or both)

source location

source orientation

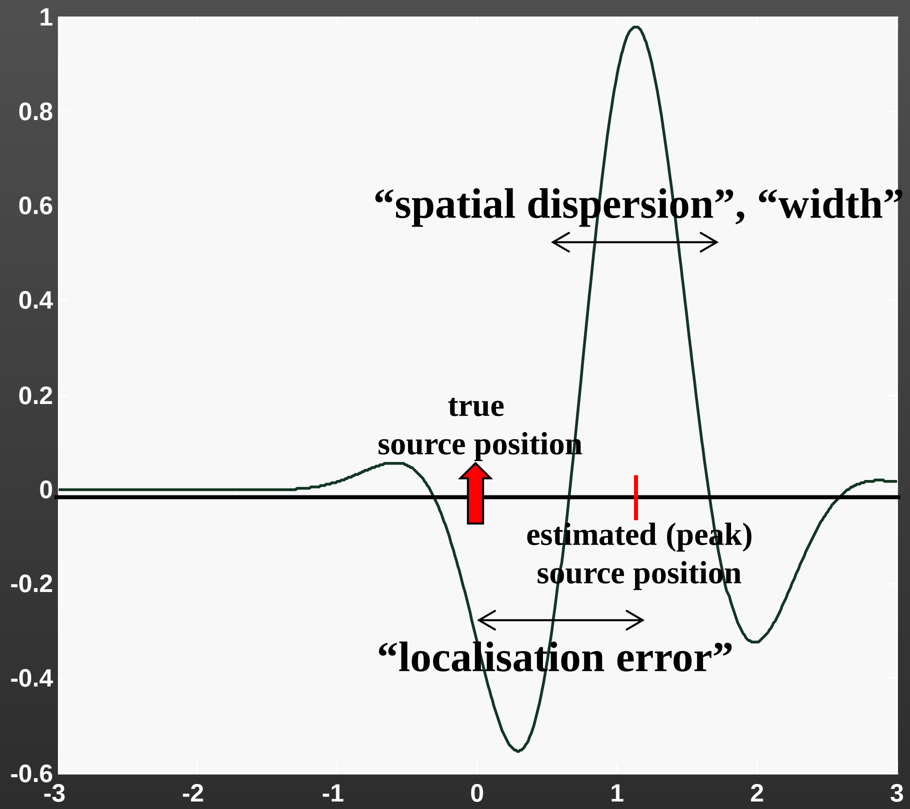
signal-to-noise ratio

head modelling

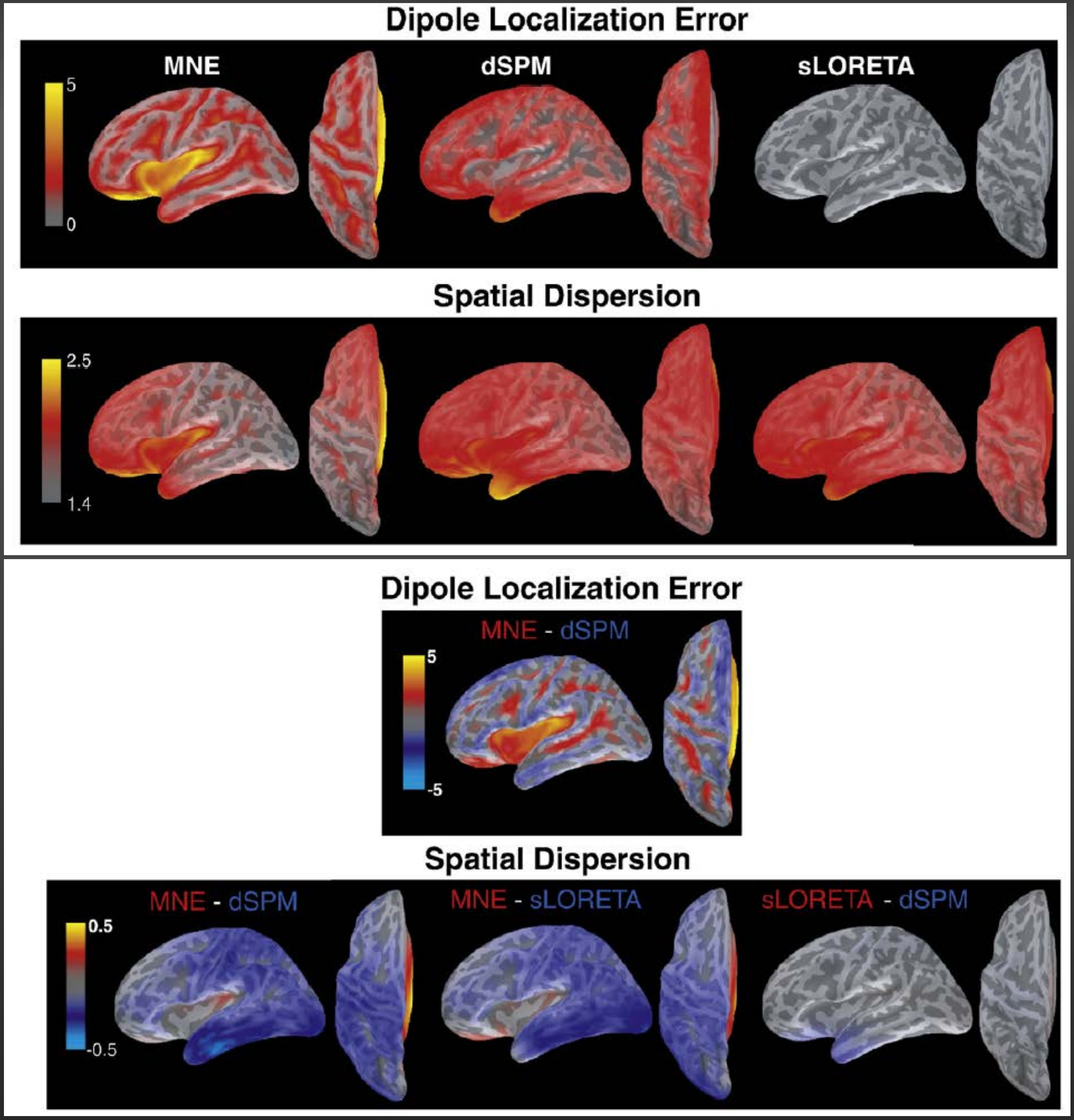
Quantifying "Resolution"

What do we want?

1) **We want to localise peaks**
2) **We want to separate peaks from different sources**



Methods Comparison



Hauk/Wakeman/Henson, Neuroimage 2011

Methods Comparison

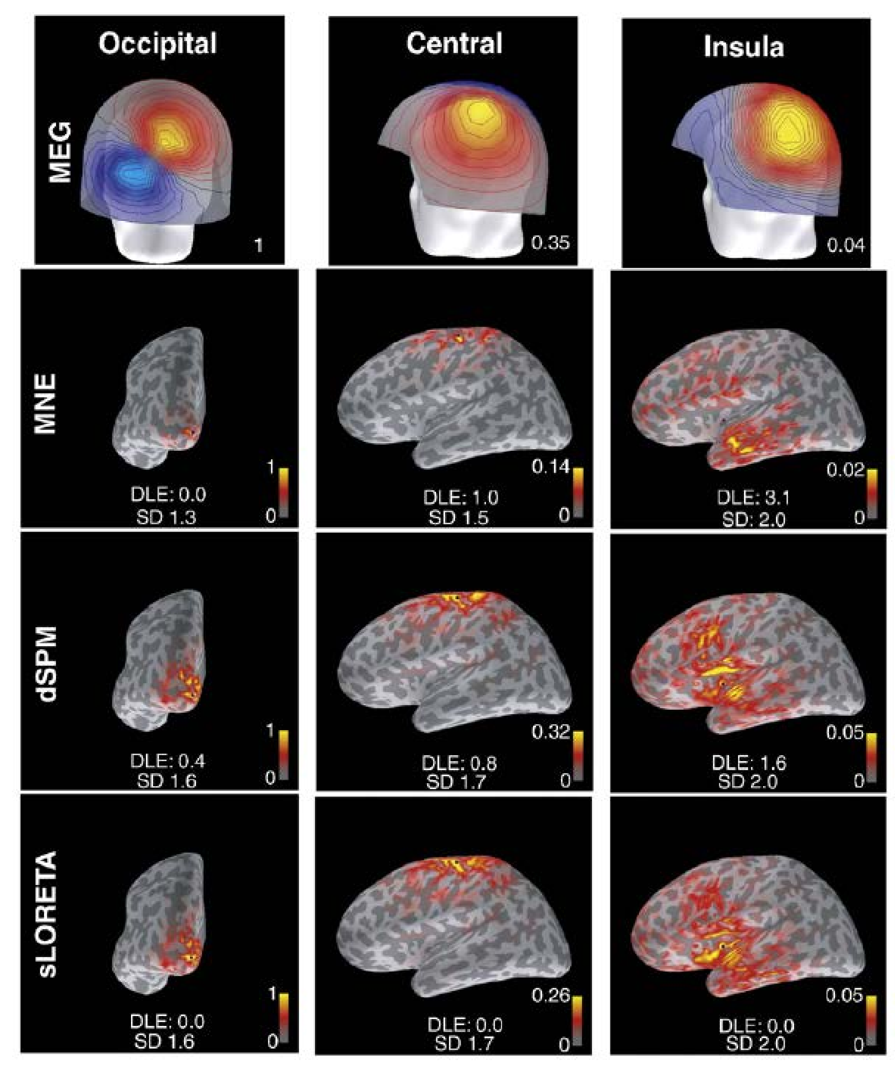
And again: What does "best" mean for you?

Point-spread functions for different methods

MNE

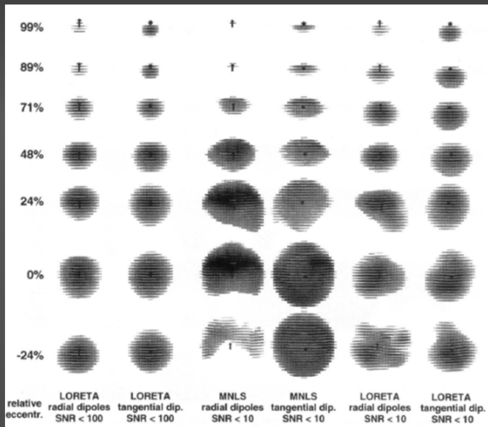
dSPM

sLORETA

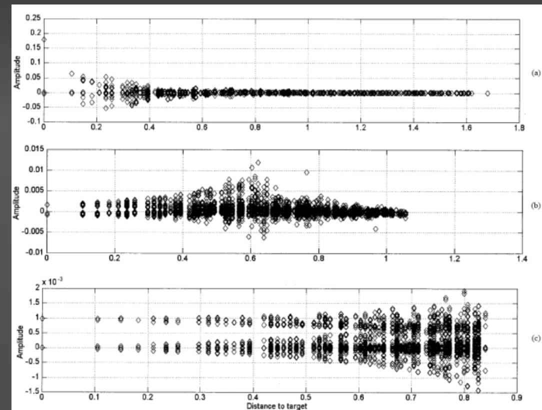


Hauk/Wakeman/Henson, Neuroimage 2011

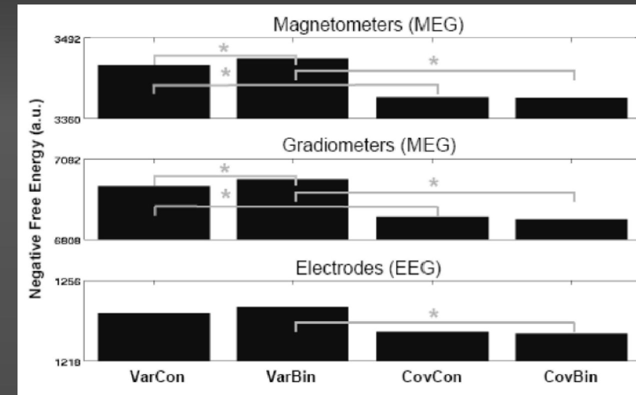
Methods Comparisons



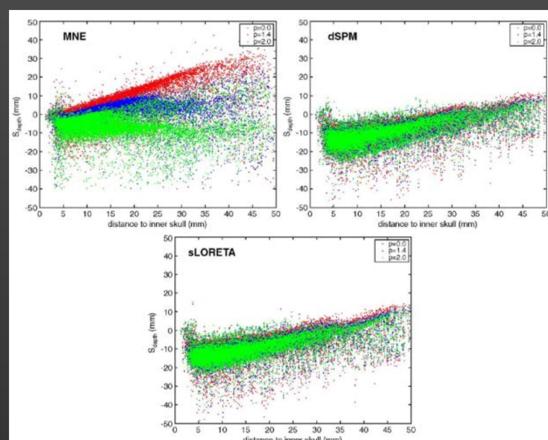
Fuchs et al., J Clin Neurophysiol '99



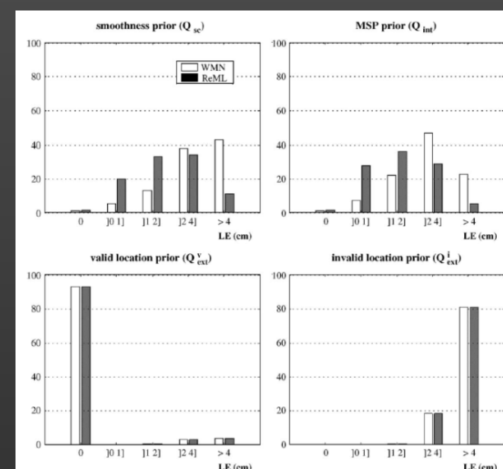
Grave de Peralta & Gonzalez-Andino, IEEE '98



Henson et al., HBM '10



Lin et al., Neuroimage '06

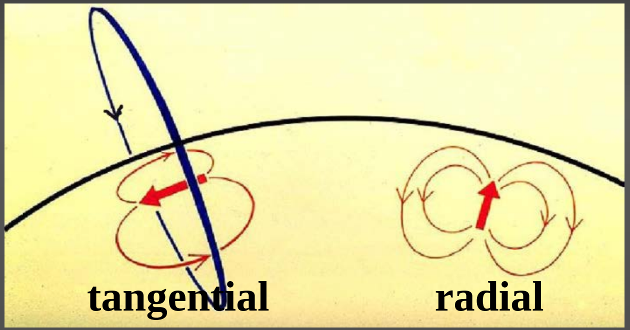


Mattout et al., Neuroimage '06

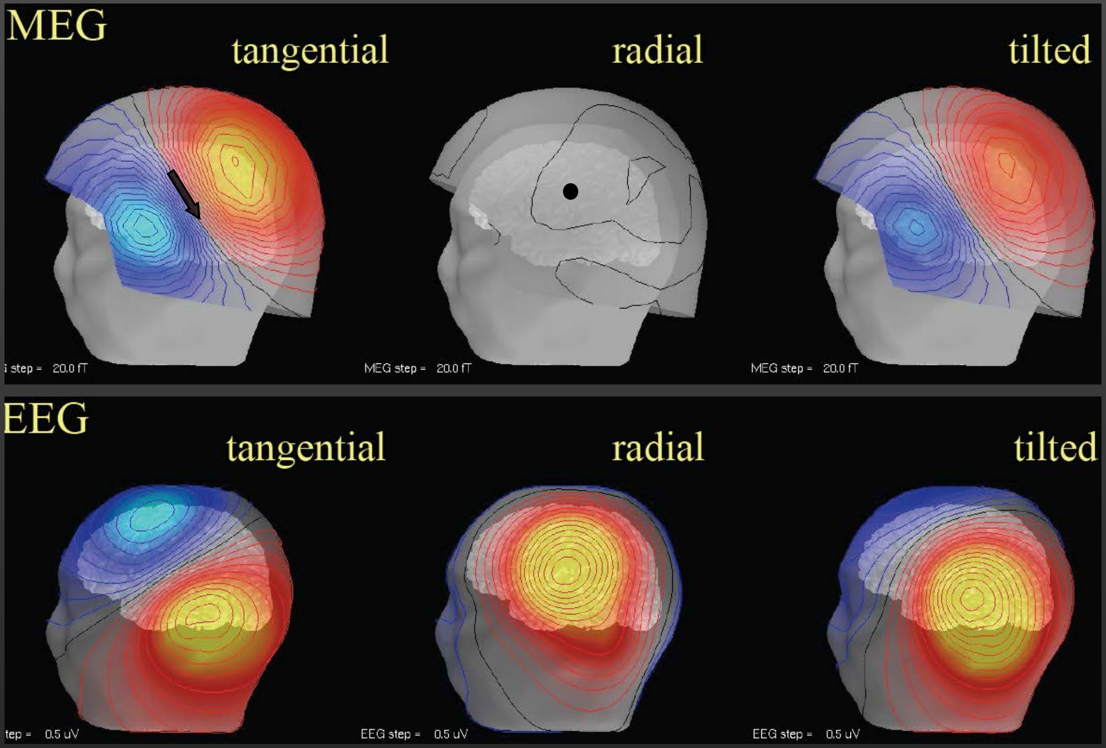
There are lots of approaches –
You have to decide what you need to know.

Do I Need Both EEG and MEG?

Radial dipoles don't produce ANY measureable magnetic fields outside a sphere
(contributions of volume currents cancel each other out)



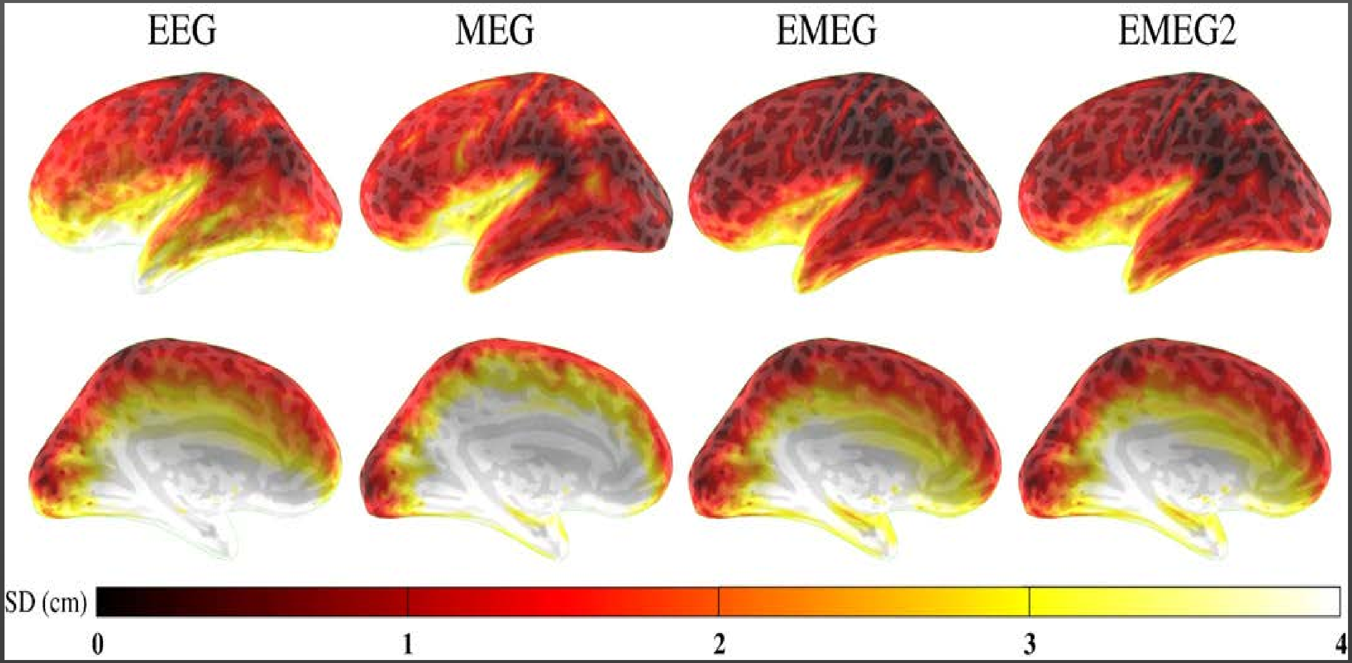
EEG and MEG contain complementary information



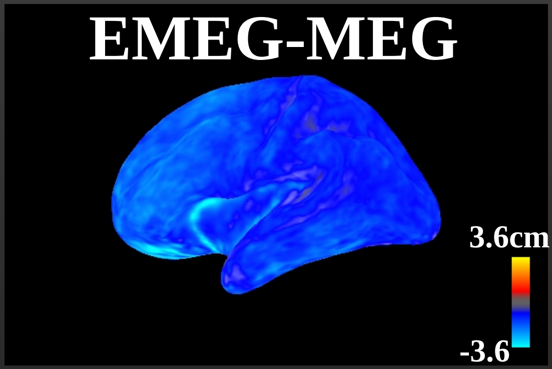
http://www.nmr.mgh.harvard.edu/meg/pdfs/talks

Combining EEG and MEG Improves Resolution

Spatial Extent

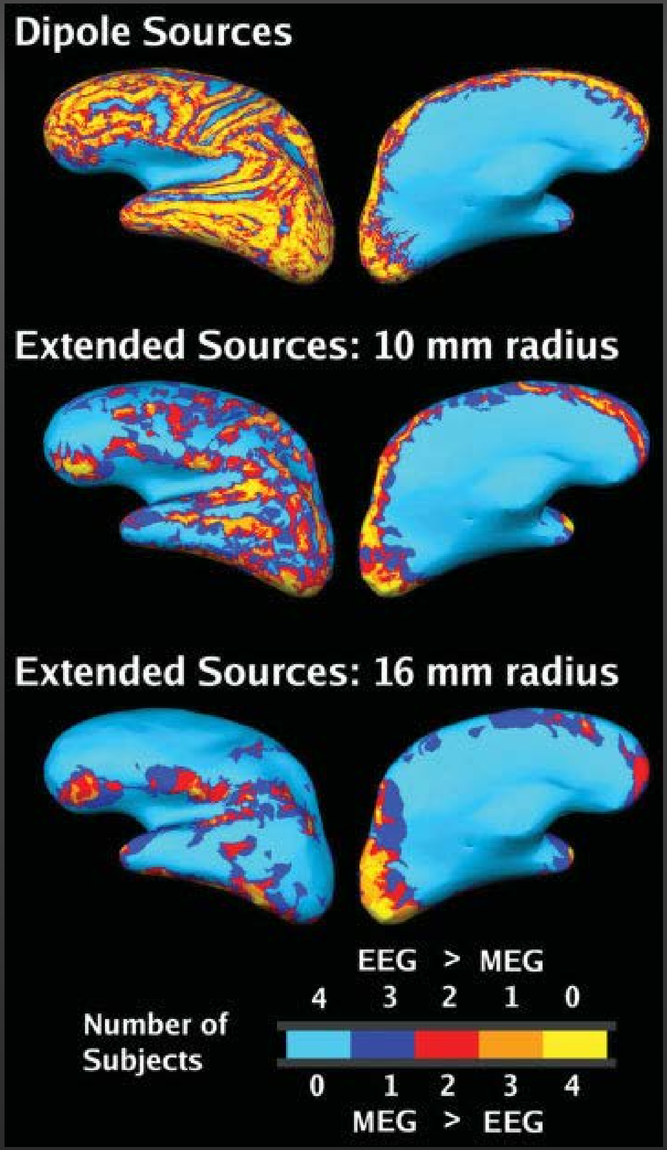


Molins et al., Neuroimage 2008

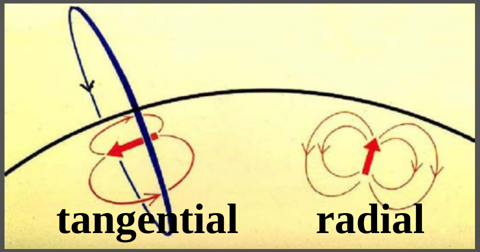


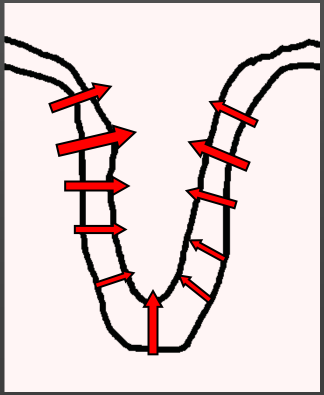
Stenroos&Hauk, in prep

Combining EEG and MEG Increases Sensitivity



Goldenholz et al., HBM '09

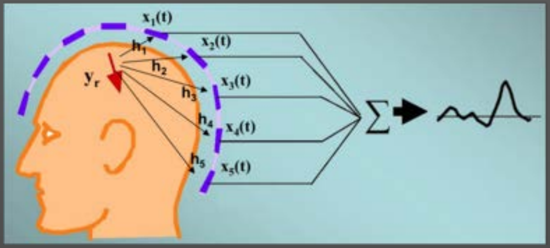


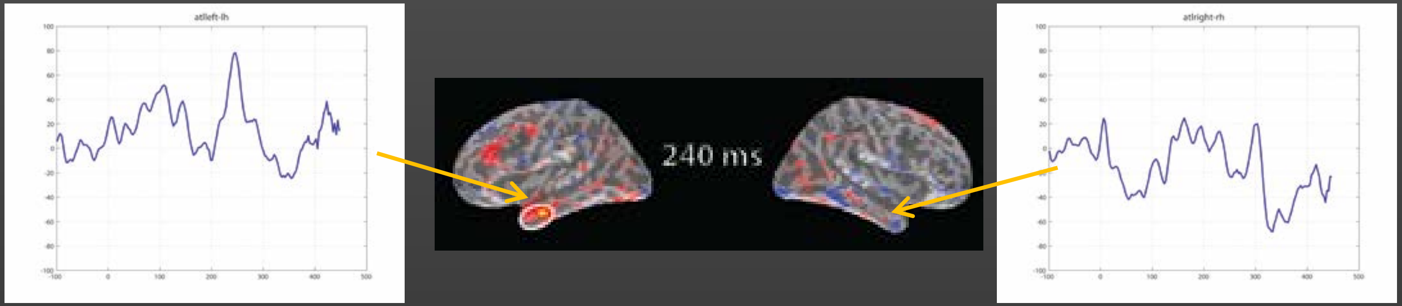


MEG is less sensitive to deeper and extended sources than EEG, but more sensitive to superficial focal sources

Spatial Filters of EEG/MEG Data

“Virtual Sensor”

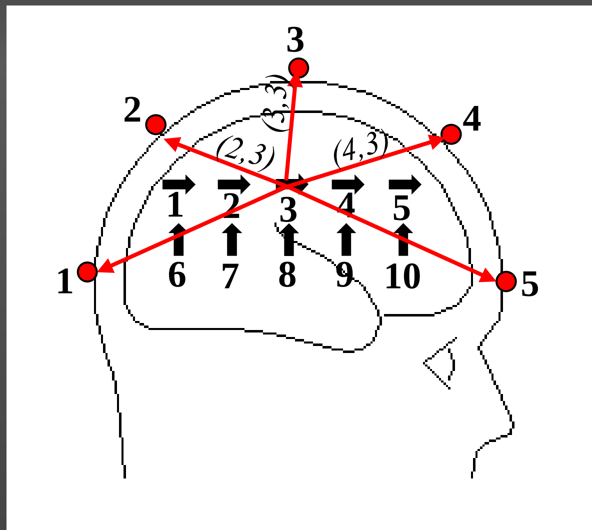




“Spatial Filtering” is another way to look at linear methods

http://www.bci2000.org/wiki/index.php/Programming_Tutorial:Implementing_another_Matlab-based_Filter

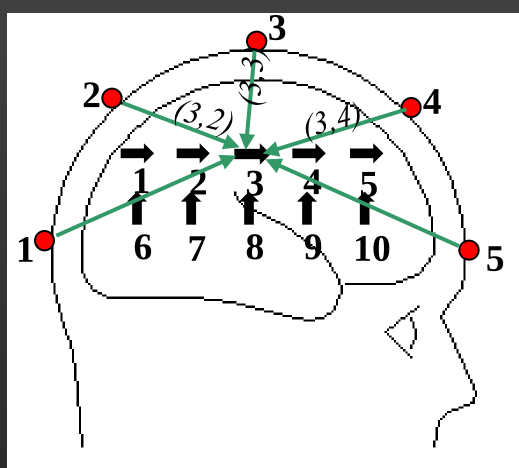
Spatial Filters of EEG/MEG Data



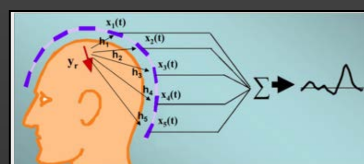
Forward Problem

$$\begin{pmatrix} d_1 \\ d_2 \\ d_3 \\ d_4 \\ d_5 \end{pmatrix} = \mathbf{d} = \sum_{i=1}^{N_s=10} s_i \begin{pmatrix} L_{1i} \\ L_{2i} \\ L_{3i} \\ L_{4i} \\ L_{5i} \end{pmatrix} = \sum_{i=1}^{N_s=10} s_i \mathbf{L}_{\cdot i} = \mathbf{Ls}$$

"Forward Solutions"



Inverse Problem

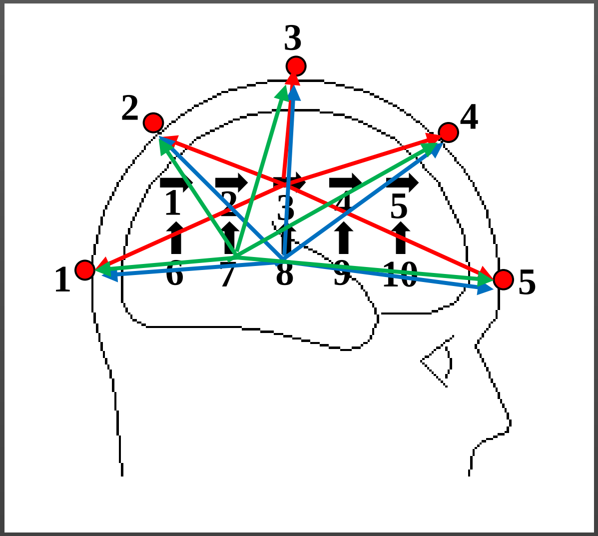


$$s_3 = \sum_{i=1}^{N_c=5} w_i d_i = \begin{pmatrix} w_i & w_i & w_i & w_i & w_i \end{pmatrix} \begin{pmatrix} d_1 \\ d_2 \\ d_3 \\ d_4 \\ d_5 \end{pmatrix} = \mathbf{w}^T \mathbf{d}$$

"Spatial Filter"

"Cross-Talk" or "Leakage"

The data are a "mix" of different sources:



$$\begin{pmatrix} d_1 \\ d_2 \\ d_3 \\ d_4 \\ d_5 \end{pmatrix} = \mathbf{d} = \sum_{i=1}^{N_s=10} s_i \begin{pmatrix} L_{1i} \\ L_{2i} \\ L_{3i} \\ L_{4i} \\ L_{5i} \end{pmatrix} = \sum_{i=1}^{N_s=10} s_i \mathbf{L}_{.i} = \mathbf{L}\mathbf{s}$$

"Leadfield" matrix

The spatial filter output is also a "mix" of different sources:

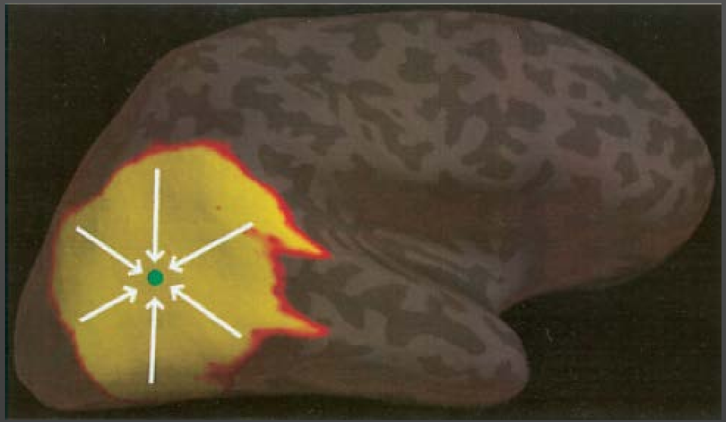
$$\mathbf{w}^T\mathbf{d} = \mathbf{w}^T \sum_{i=1}^{N_s=10} s_i \begin{pmatrix} L_{1i} \\ L_{2i} \\ L_{3i} \\ L_{4i} \\ L_{5i} \end{pmatrix} = \sum_{i=1}^{N_s=10} s_i \left(\mathbf{w}^T \mathbf{L}_{.i}\right) = \mathbf{s}^T\mathbf{CTF}$$

"Cross-Talk Function"

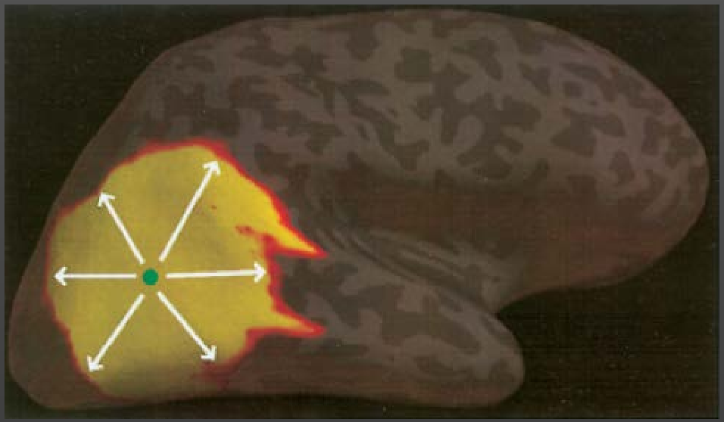
Cross-talk depends on the correlation between the spatial filter and the forward solutions

"Cross-Talk" or "Leakage"

Cross-Talk/Leakage



Point-Spread



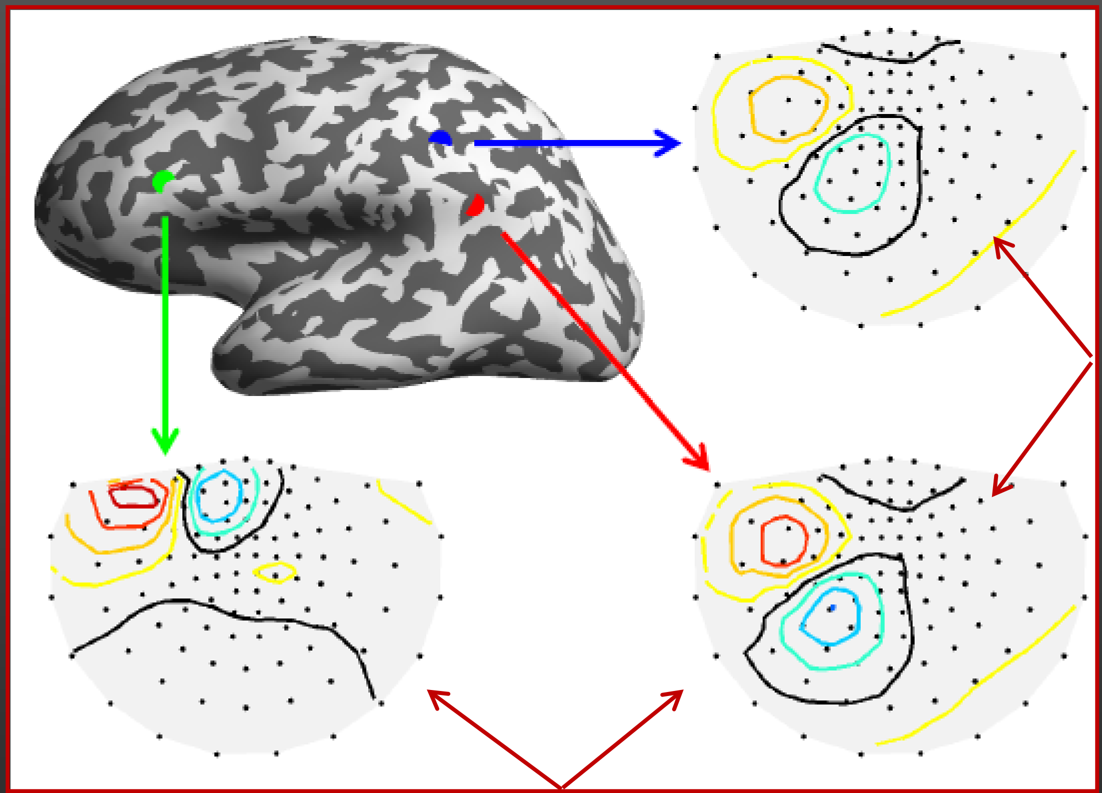
Liu et al., HBM 2002

"How other sources may affect the spatial filter for this source"

"How this source affects other spatial filters"

Cross-Talk Depends on Correlations of Topographies

The higher the correlation between topographies, the more likely there is cross-talk between the sources

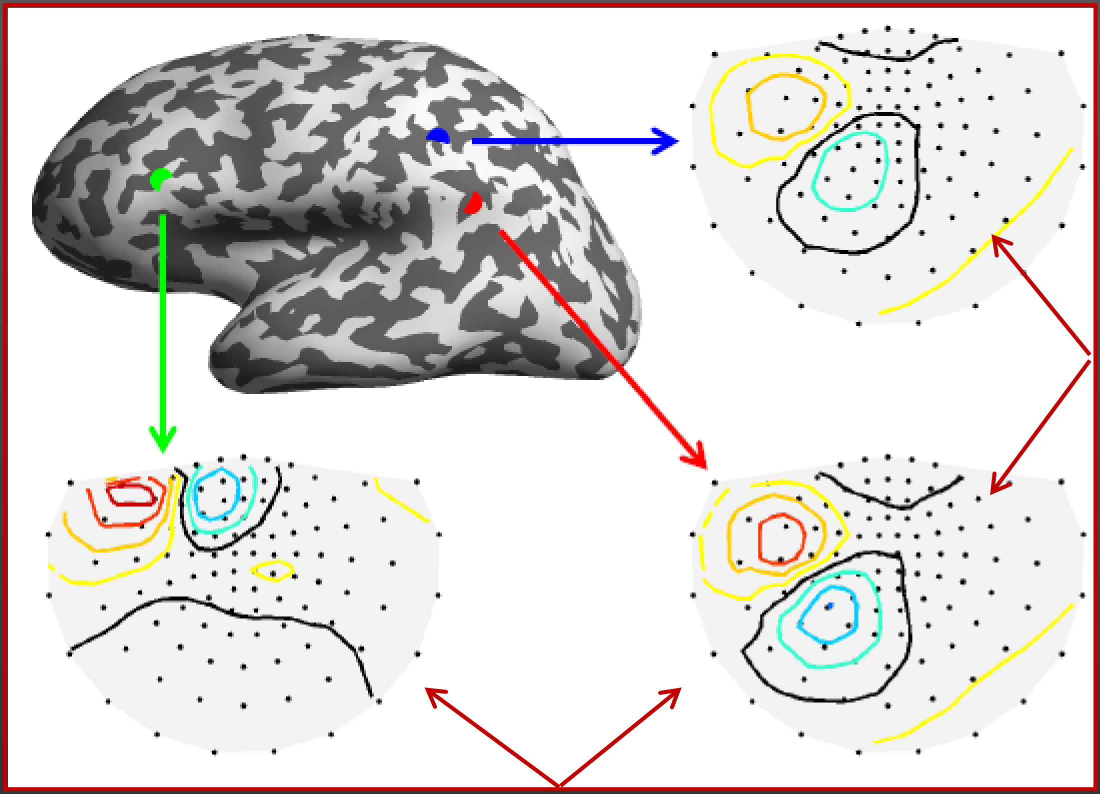


high expected cross-talk

low expected cross-talk

Thanks to Matti Stenroos

Dealing With Noise : "Regularisation"



Difference sensitive to noise

Difference robust to noise

Thanks to Matti Stenroos

Dealing With Noise : "Regularisation"

Some channels are noisier than others

⇒They should get different weights in your analysis

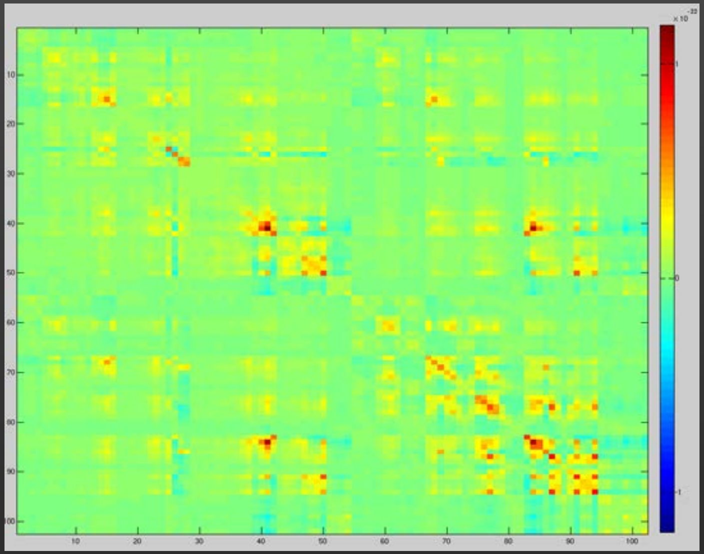
Sensors are not independent

=> Sensors that carry the same information should be down-weighted relative to more independent sensors

In order not to over-explain details in the data that are due to noise, one requires a degree of "smoothness" in the result ("spatial low-pass filter")

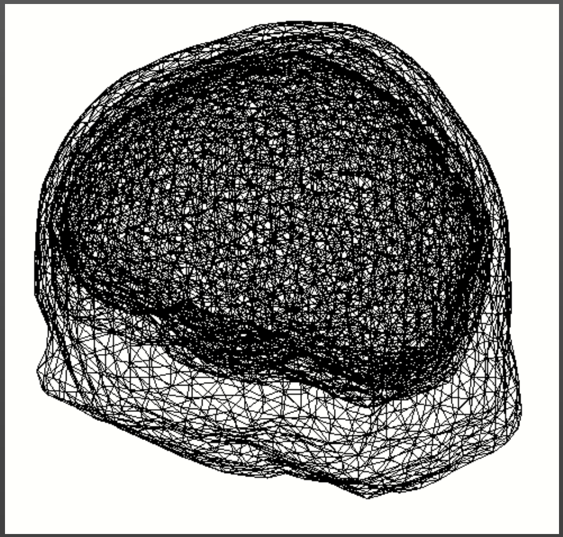
There are different ways to find the optimal "regularisation parameter" (sometimes called "lambda"), but it generally depends on the SNR of your data

A noise covariance matrix

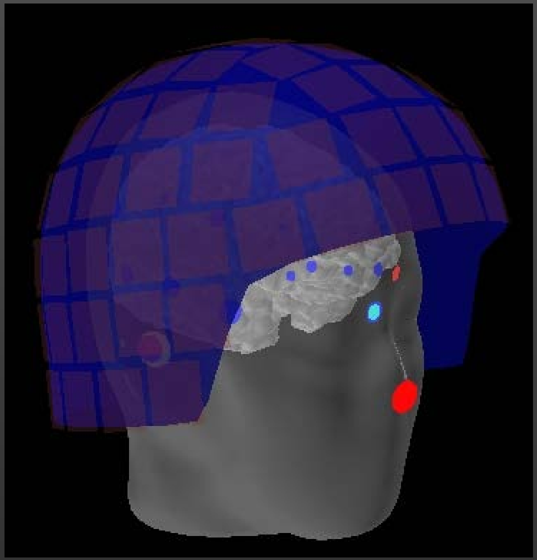


Ingredients for Source Estimation

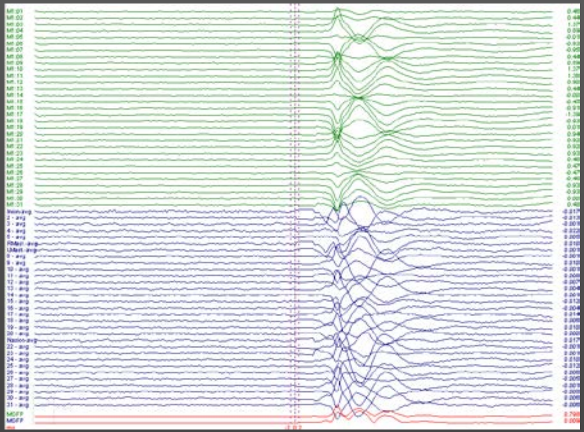
Volume Conductor/
Head Model



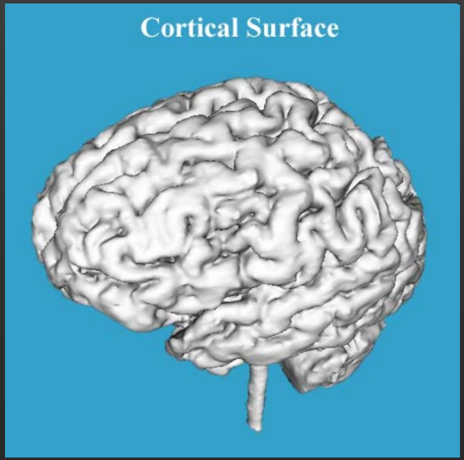
Coordinate
Transformation



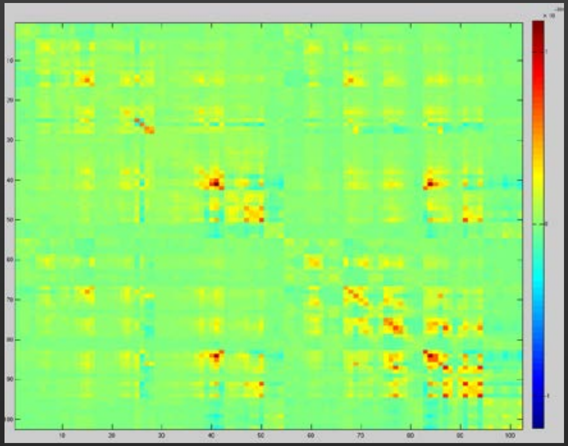
MEG data



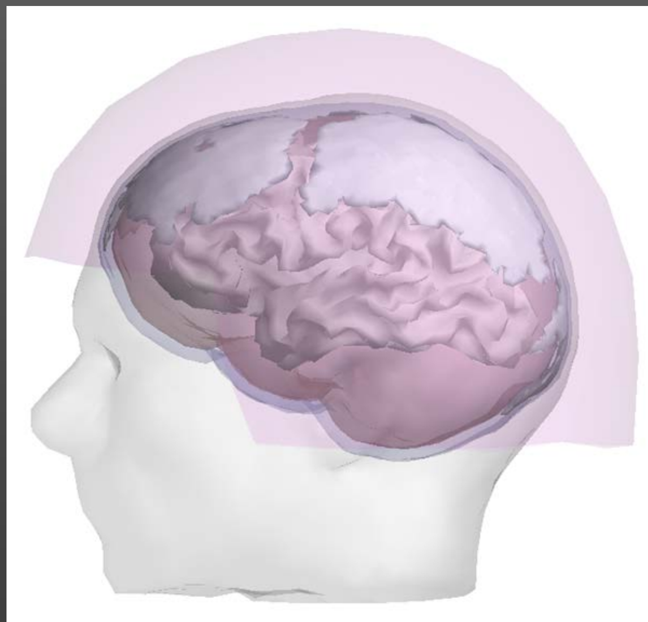
Source Space

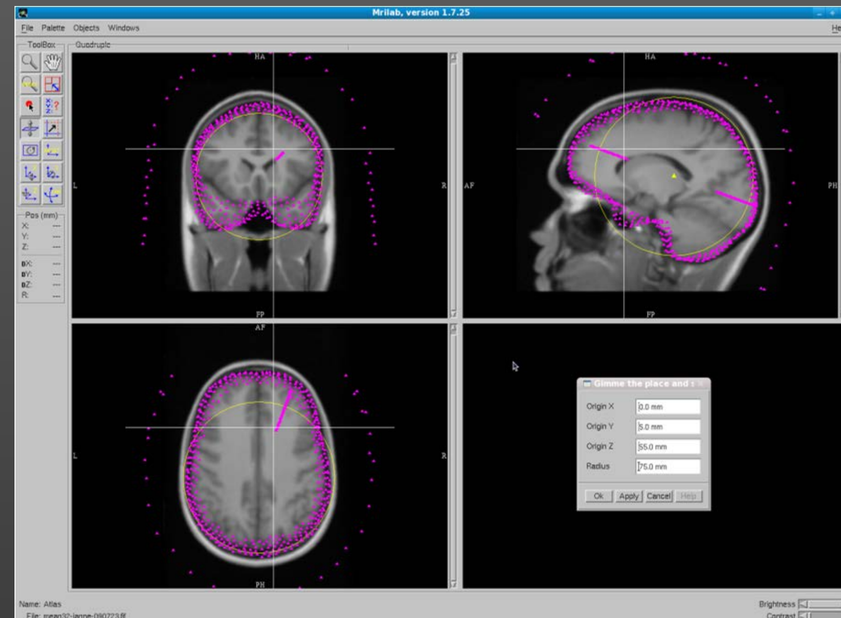


Noise/Covariance Matrix



Head Model for the Forward Solution





State-of-the-art: "3-shell" model comprising inner skull, outer skull, and scalp

(boundary element model, BEM: assumes homogenous conductivities)

Common: spherical approximation

Possible: Voxel-by-Voxel changes in conductivity

(Finite Element Models, FEM)

Software for EEG/MEG Analysis

The paradox of choice…:

Commercial packages (stand-alone)

- CURRY
- ASA
- BESA
- EMSE

Freeware packages (Matlab)

- **SPM 5/8/12** **Workshop March 12th**
- **Fieldtrip**
- NUTMEG
- EEGlab (not MEGlab…)

Freeware packages (Python, C, Matlab)

- **MNE-Python** **Workshop May 15/16**