



MRC Cognition
and Brain
Sciences Unit



UNIVERSITY OF
CAMBRIDGE

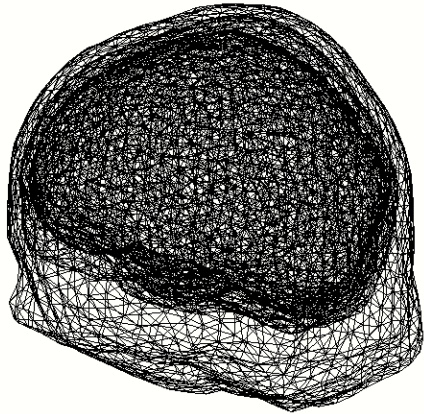
EEG/MEG 2: (Linear) Source Estimation

Olaf Hauk

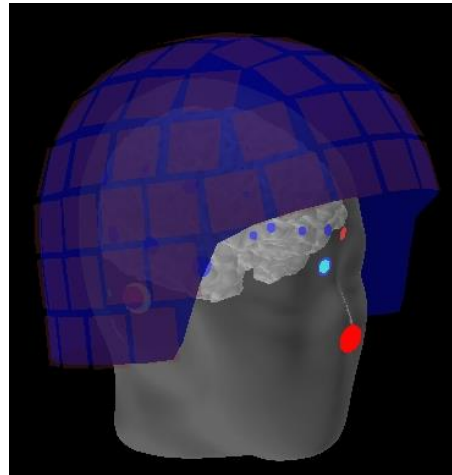
olaf.hauk@mrc-cbu.cam.ac.uk

Ingredients for Source Estimation

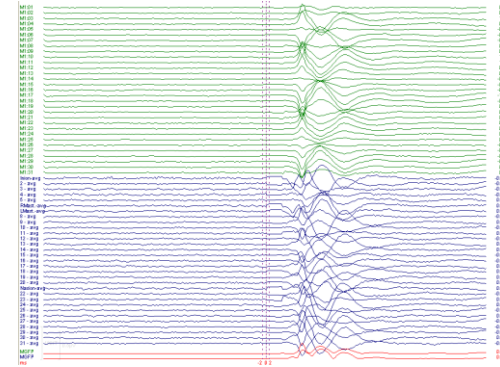
Volume Conductor/
Head Model



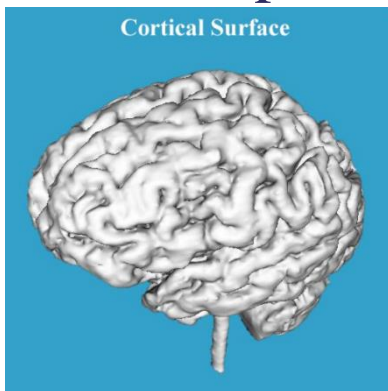
Coordinate
Transformation



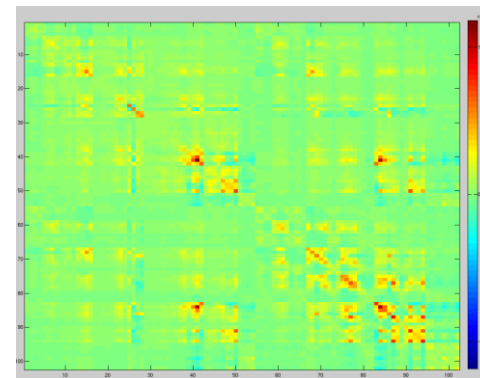
MEG data



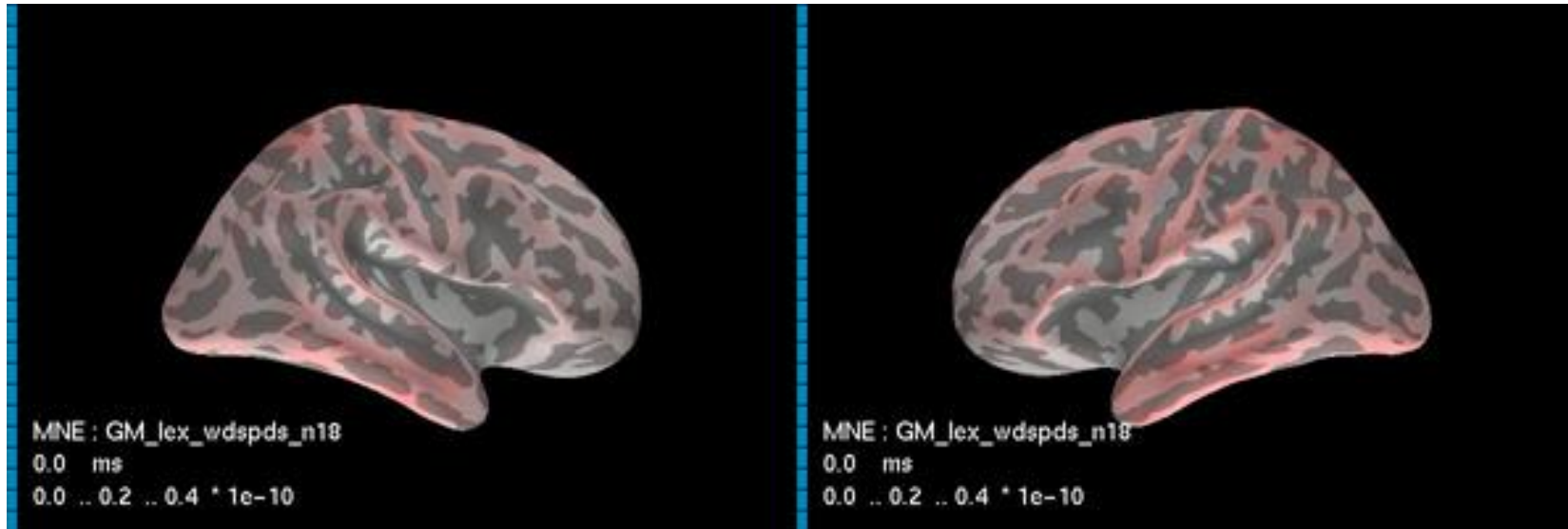
Source Space



Noise/Covariance Matrix



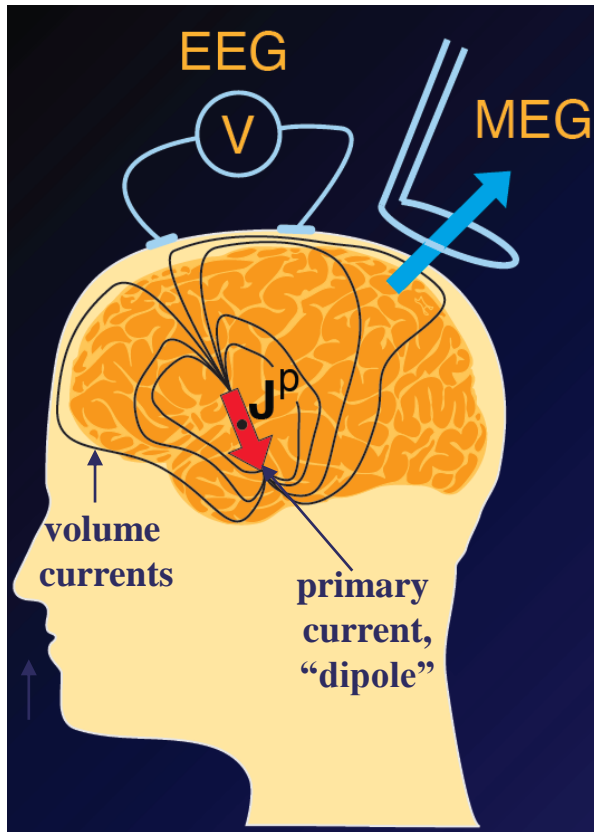
Our Goal: Spatio-Temporal Brain Dynamics “Brain Movies”



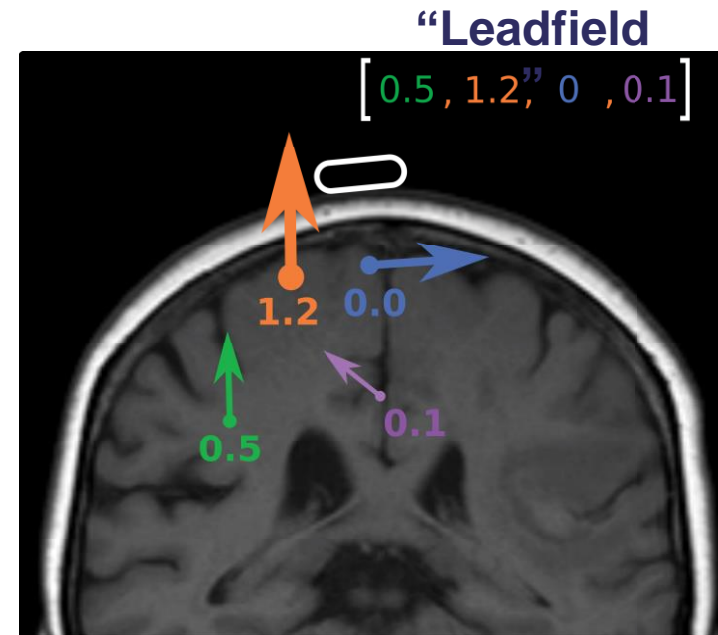
The EEG/MEG Inverse Problem

The EEG/MEG Forward Problem

EEG/MEG measure the primary sources indirectly



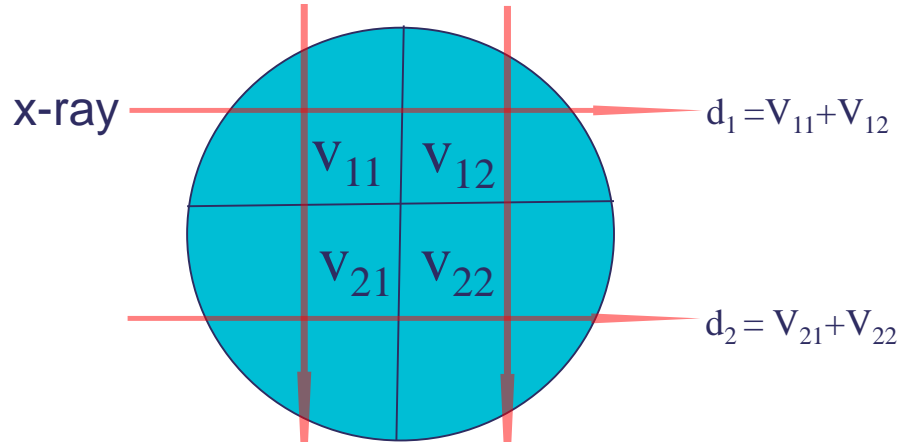
Sensors are differently sensitive to different sources



Hauk, Stenroos, Tieder. In: Supek S, Aine C (eds), "Magnetoencephalography: From Signals to Dynamic Cortical Networks, 2nd Ed."

EEG/MEG “Scanning” is not “Tomography”

Tomography (CT, fMRI...)



$$d_3 = V_{11} + V_{21} \quad d_4 = V_{12} + V_{22}$$

$$d_1 = V_{11} + V_{12}$$

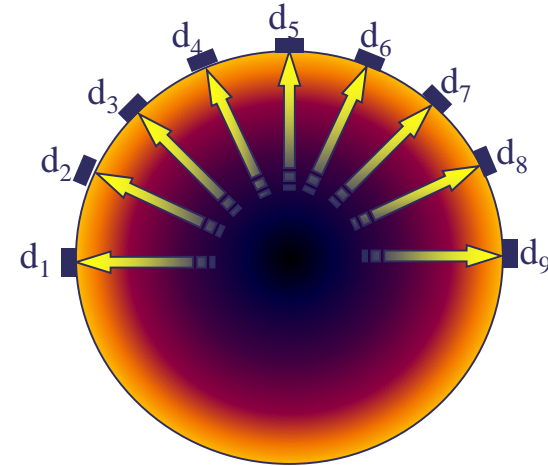
$$d_2 = V_{21} + V_{22}$$

$$d_3 = V_{11} + V_{21}$$

$$d_4 = V_{12} + V_{22}$$

Available information is determined by the equipment/experimenter

EEG/MEG



$$d_1 = V_{11} + V_{12} + V_{13} + V_{14} \dots$$

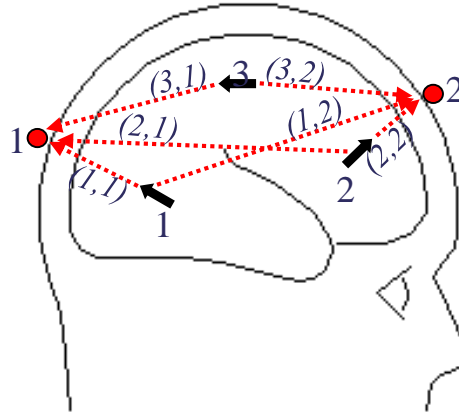
$$d_2 = V_{21} + V_{22} + V_{23} + V_{24} \dots$$

Information is lost during measurement

Cannot be retrieved by mathematics

Inherently limits spatial resolution

The EEG/MEG Forward Problem



| data | “leadfield” | dipoles | ? | dipoles | inverse | data |
|---|---|---|----------------------------------|---|--|--|
| $\begin{matrix} \bullet \\ \bullet \end{matrix} \begin{pmatrix} d_1 \\ d_2 \end{pmatrix}$ | $= \begin{pmatrix} 0.5 & 0 & 0.3 \\ 0 & 1 & -0.3 \end{pmatrix}$ | $\begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix}$ | $\xrightarrow{\text{inversion}}$ | $\begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix}$ | $= \begin{pmatrix} 1.5034 & 0.1241 \\ 0.2483 & 0.9379 \\ 0.8276 & -0.2069 \end{pmatrix}$ | $* \begin{pmatrix} d_1 \\ d_2 \end{pmatrix}$ |

$$j_1 + j_2 = 1$$

under-determined problem, no unique solution

$$\mathbf{d} = \mathbf{L}\mathbf{j}$$

d: data (n_sensors x 1) **L**: “leadfield” (n_sensors x n_dipoles), **j**: dipoles (n_dipoles x 1)
 Usually n_dipoles >> n_sensors.

Why Inverse “Problem”?

Without additional constraints the solution is non-unique, i.e. there are infinitely many solutions

What is the solution to

$$x_1 + x_2 = 1$$

Maybe

$$x_1 = 0 ; x_2 = 1 \quad ?$$

$$x_1 = 1 ; x_2 = 0 \quad ?$$

$$x_1 = 1000 ; x_2 = -999 \quad ?$$

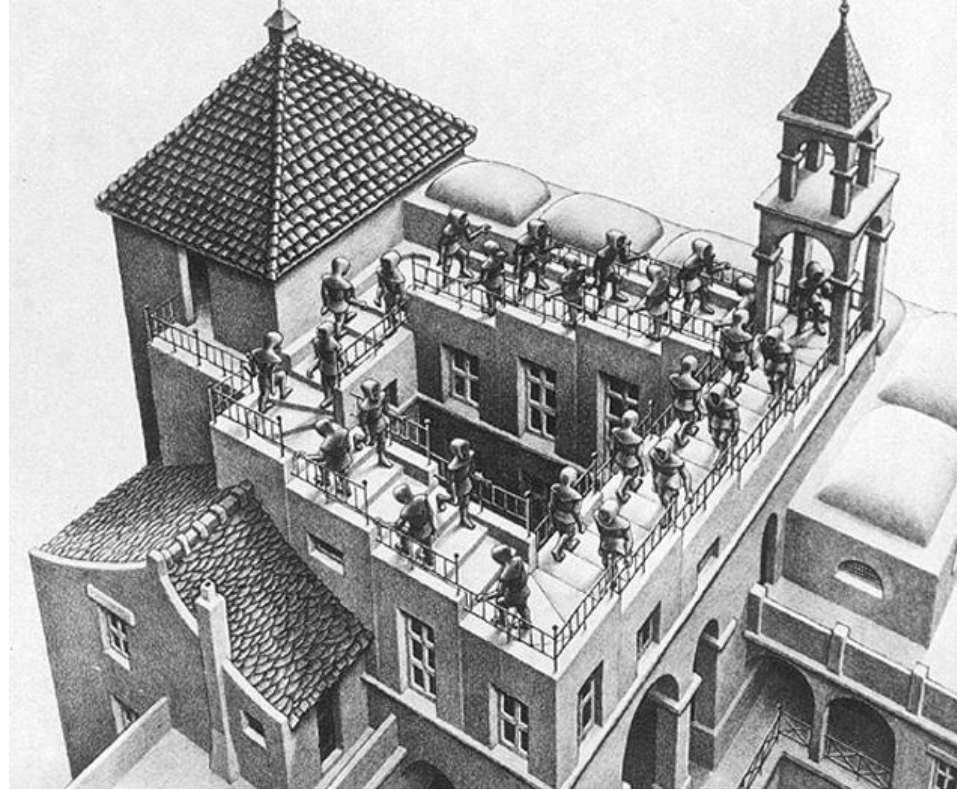
$$x_1 = \pi ; x_2 = (1-\pi) \quad ?$$

The “minimum norm solution” is:

$$x_1 = 0.5 ; x_2 = 0.5$$

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

Why Inverse “Problem”?



M.C. Escher

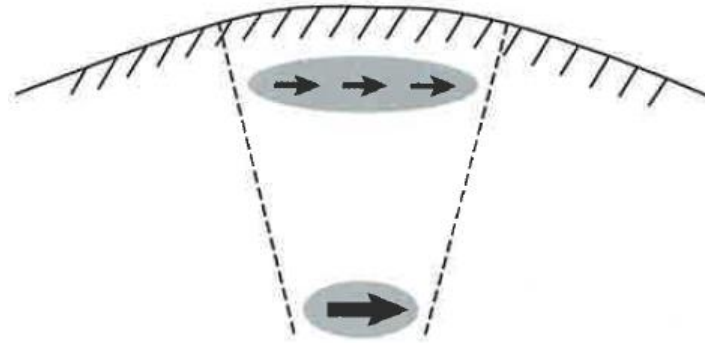
In EEG/MEG “signal space”, we see a faint shadow of activity in “source space”.

If you are not shocked by the EEG/MEG inverse problem...

... then you haven't understood it yet.

(freely adapted from Niels Bohr)

Examples for Non-Uniqueness

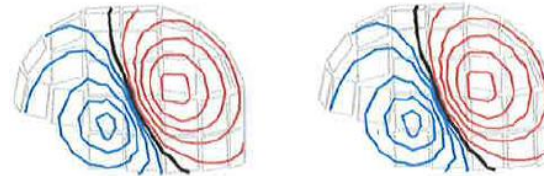


A distributed superficial distribution may be indistinguishable from a focal deep source.

Examples for Non-Uniqueness

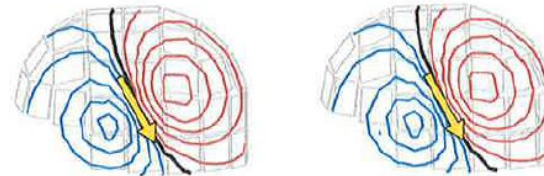


Field Patterns



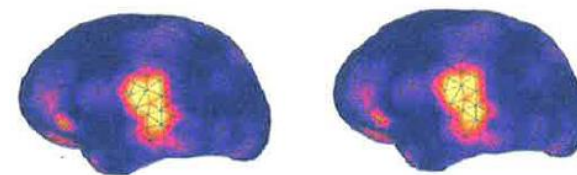
Same Field Patterns

Dipole Model



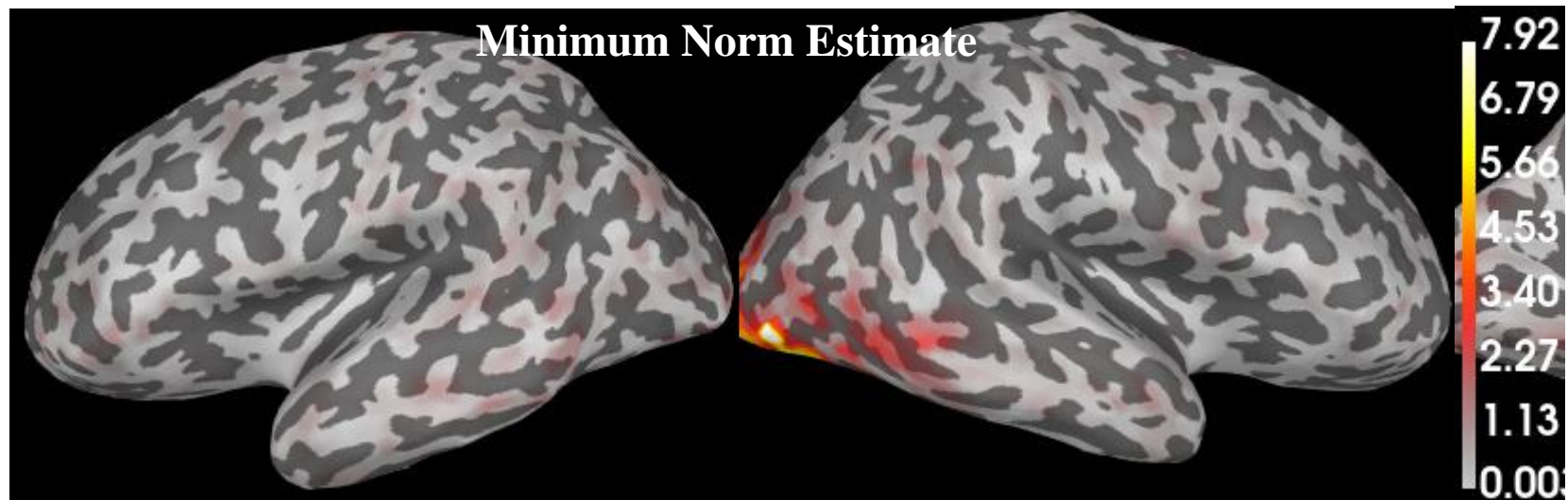
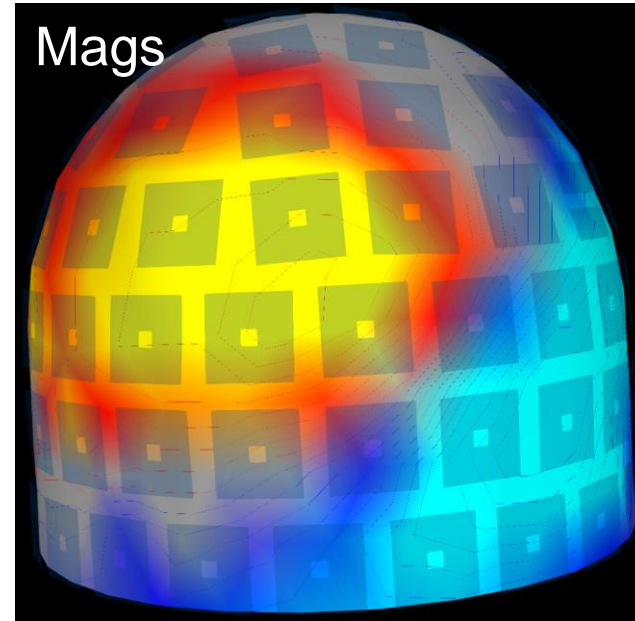
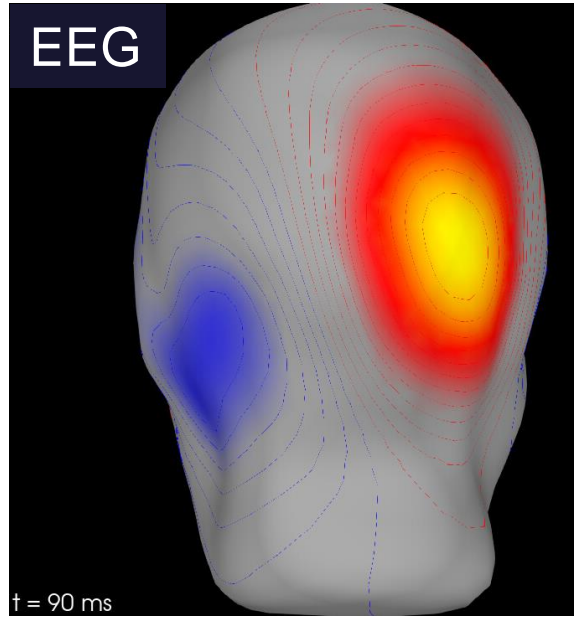
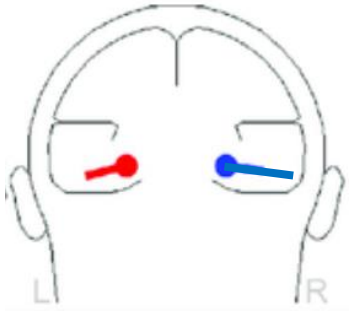
Same Source Estimates

Minimum Norm Estimates



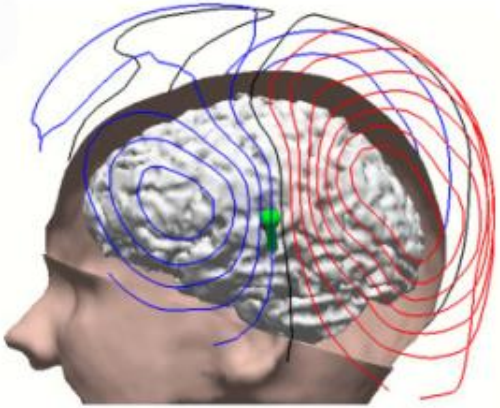
Example: Visually Evoked Activity ~100 ms

Checkerboard to
left visual field

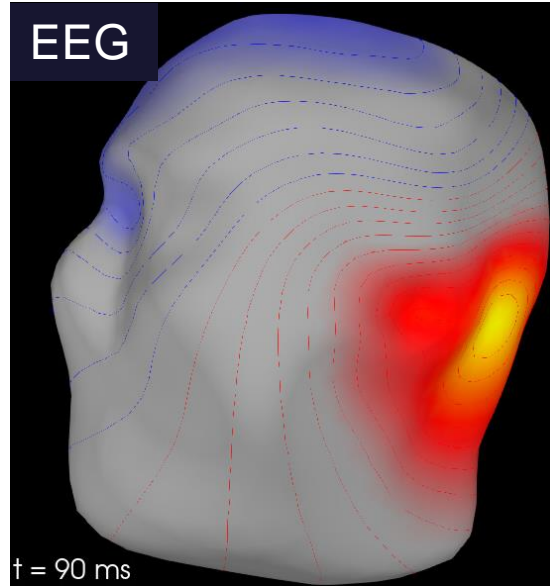


Example: Auditorily Evoked Activity

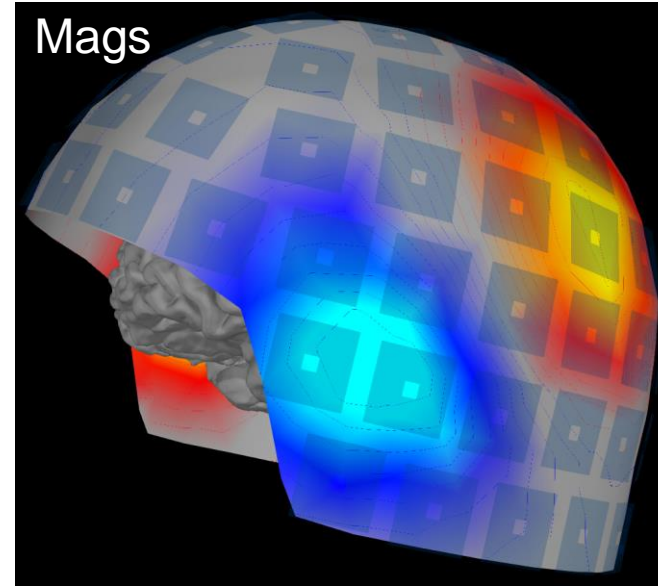
Tone to right ear



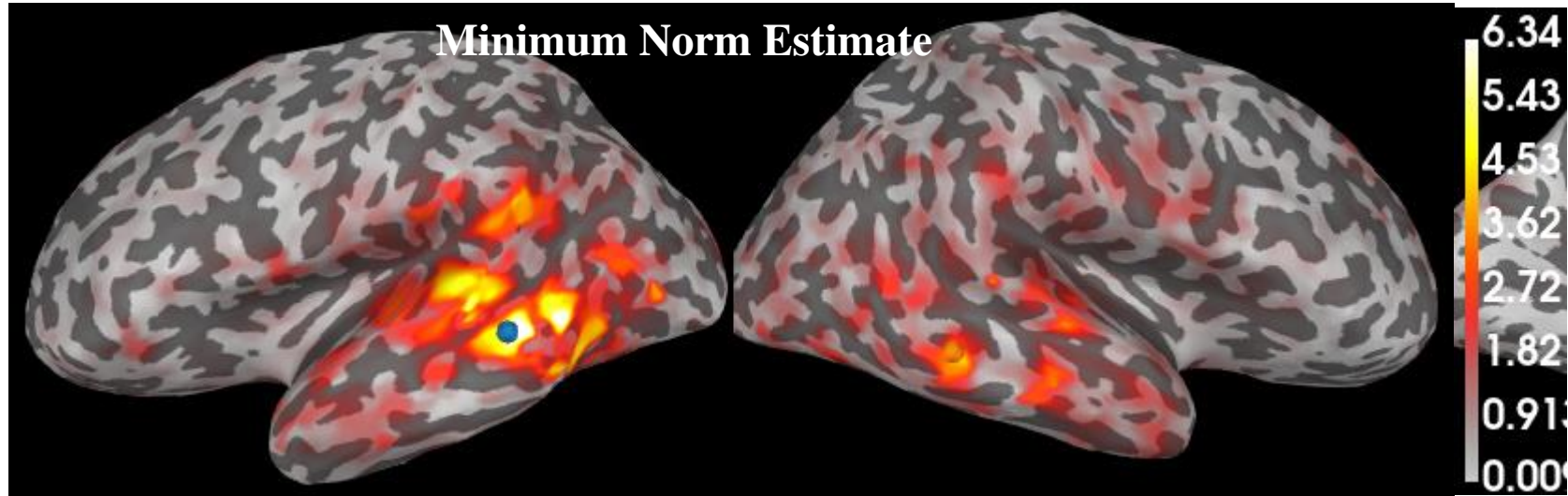
EEG



Mags



Minimum Norm Estimate

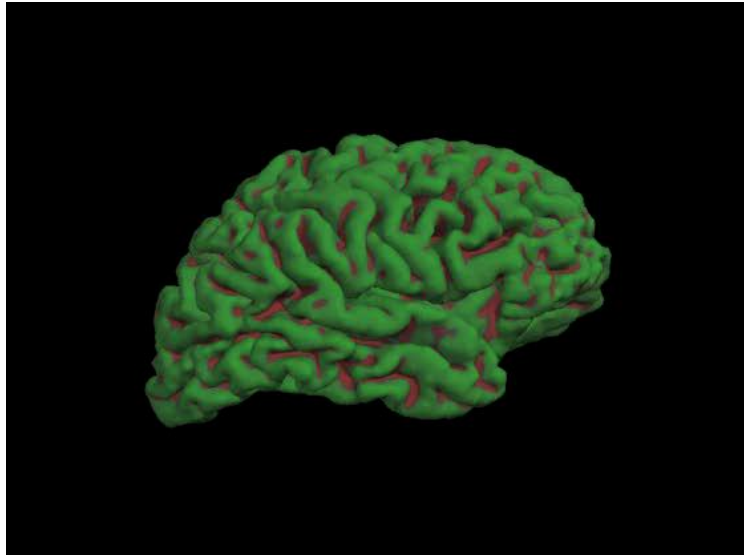


The Forward Problem and Head Modelling

Source Space and Head Model

Source Space

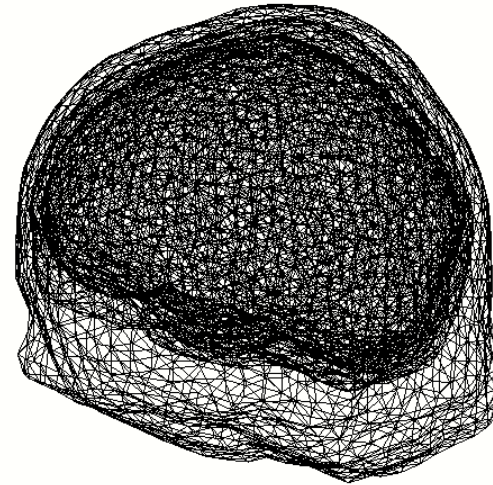
Where active sources may be located,
e.g. grey matter, 3D volume



<http://www.cogsci.ucsd.edu/~sereno/movies.html>

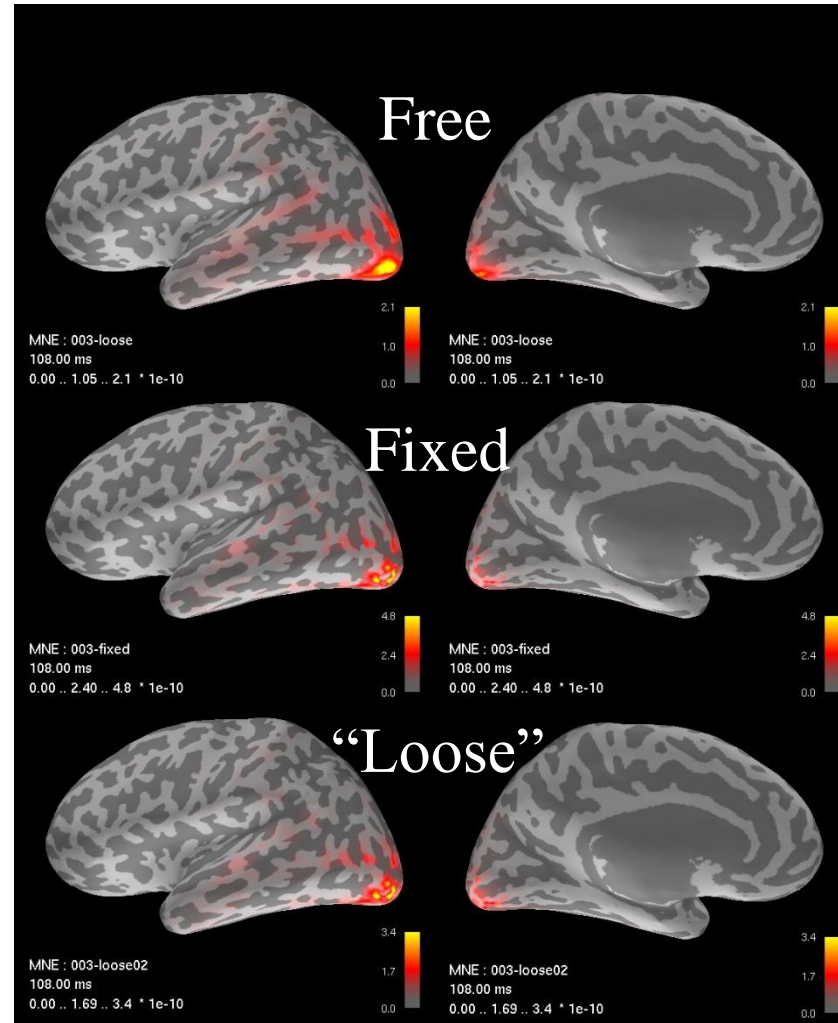
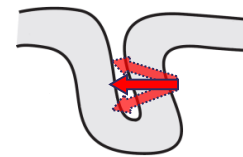
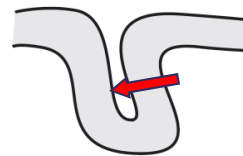
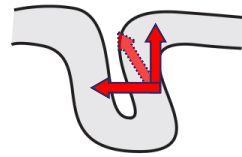
Volume Conductor/Head Model

How we model conductivities/currents/potentials/fields in the head
e.g. sphere or realistic 1- or 3-compartments from MRI

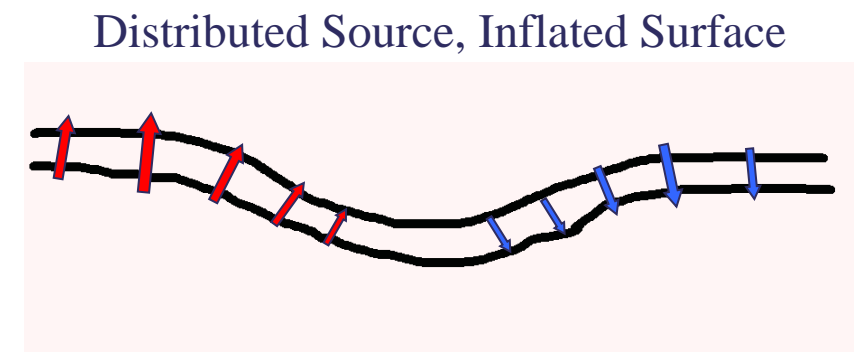
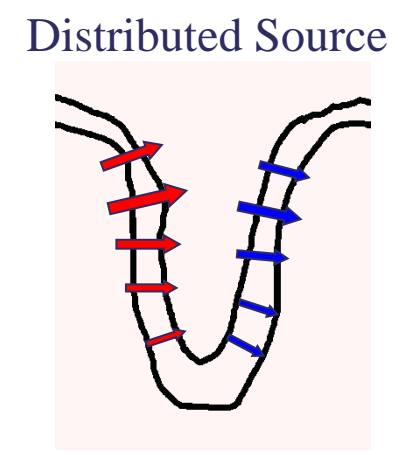
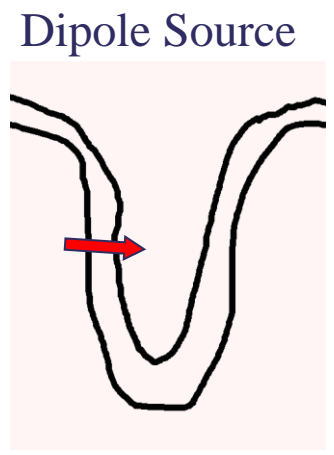


Sometimes “standard head models” are used, when no individual MRIs available.
SPM uses the same “canonical mesh” as source space for every subjects, but adjusts it individually.

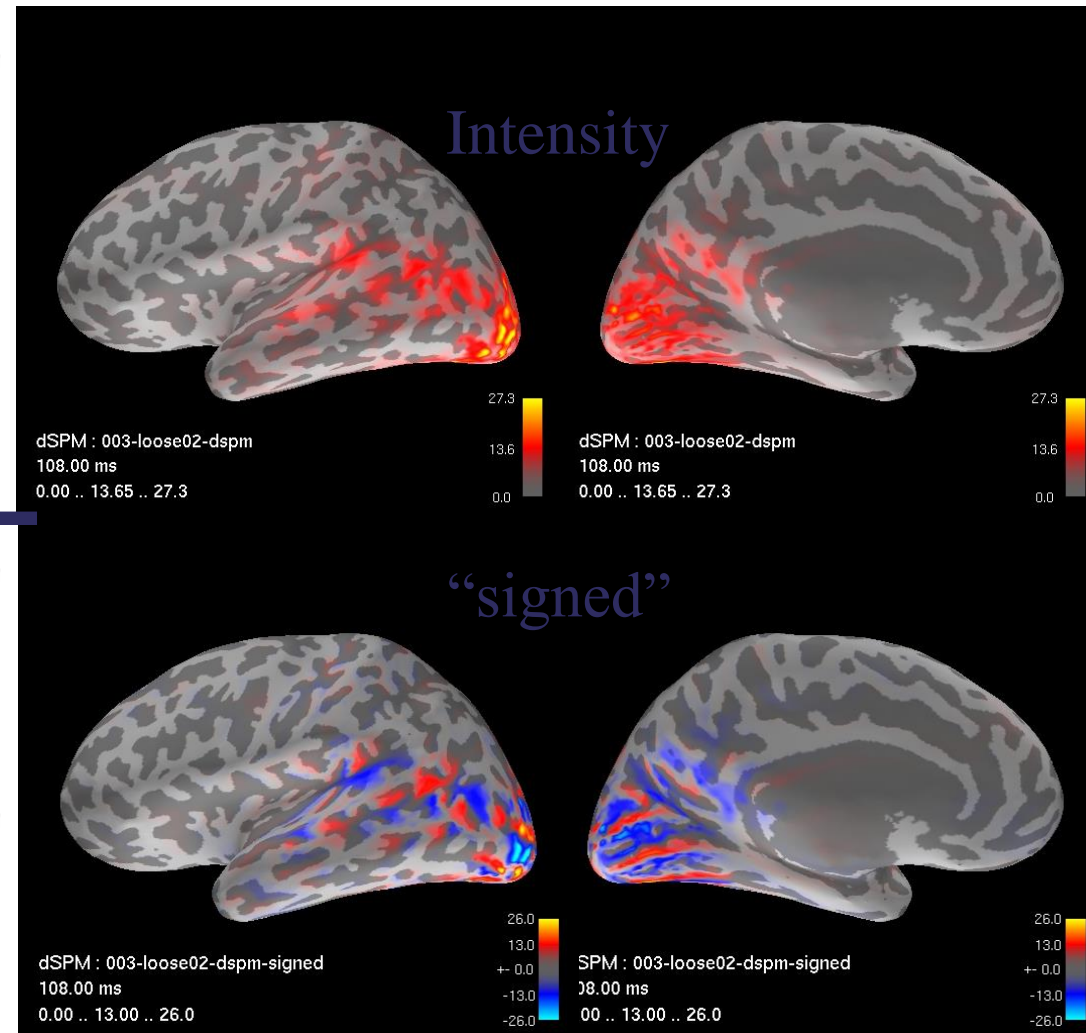
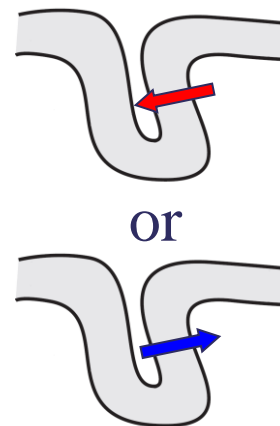
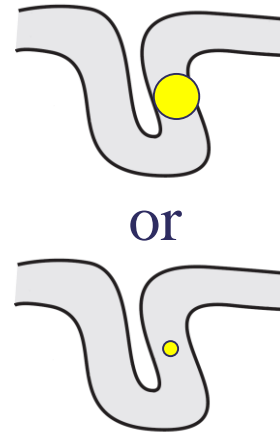
Source Orientation Constraints



Direction of Current Flow



Direction of Current Flow

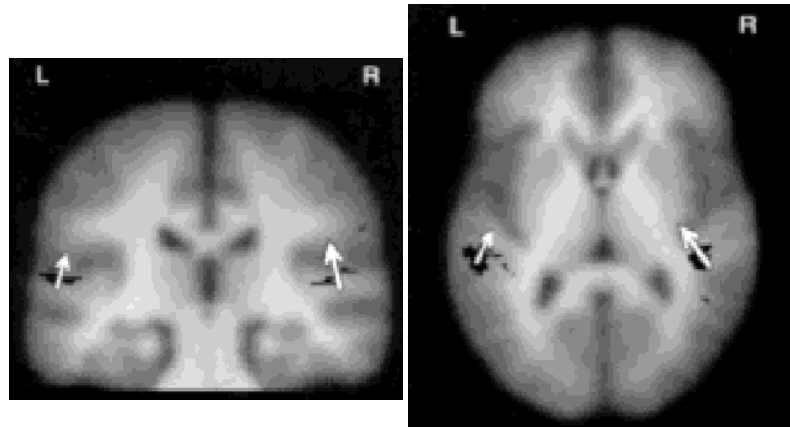


Solutions To The Inverse Problem – Source Estimation

Paths To Uniqueness

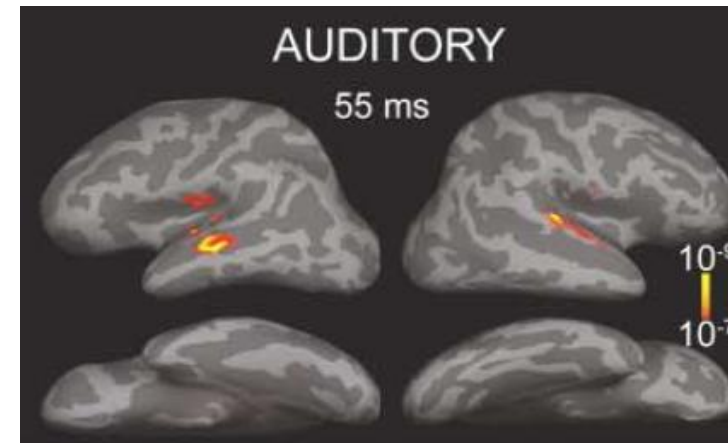
Dipole Fitting/Scanning

1. Assume there are only a few distinct sources
2. Iteratively adjust the location, orientation and strength of a few dipoles...
3. ...until the result best fits the data



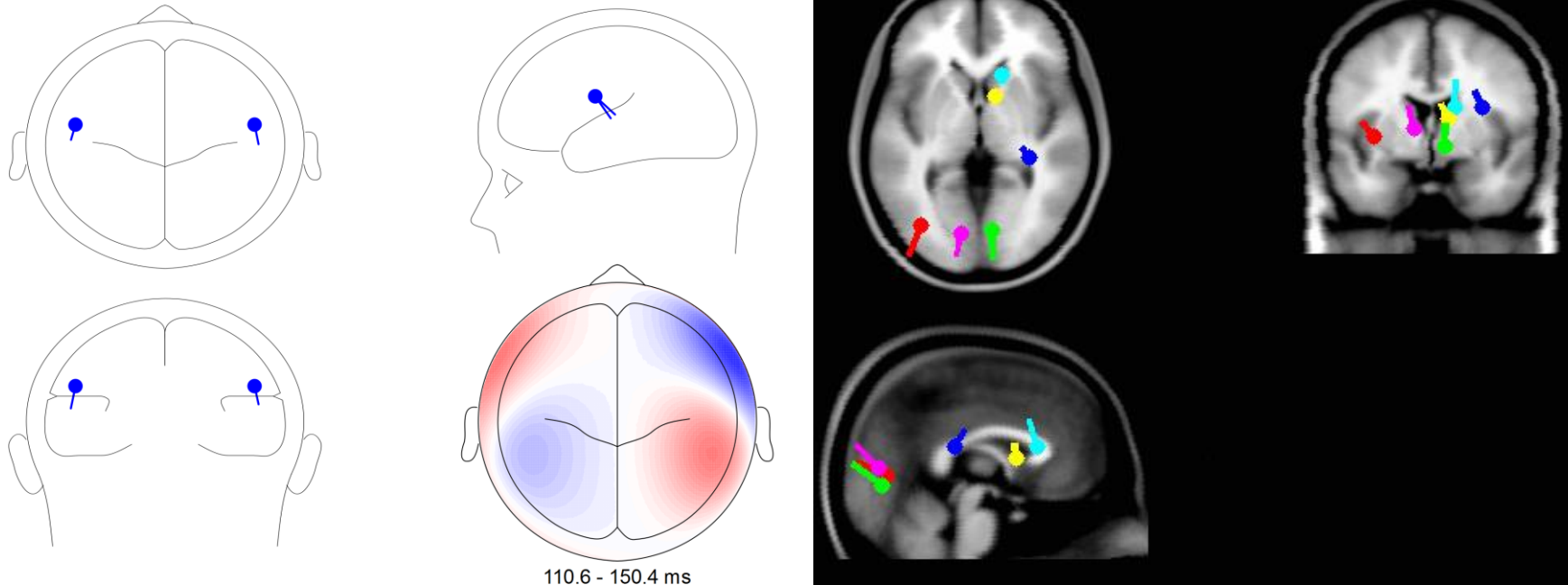
Distributed Sources

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



Hypothesis Testing - Dipole Fitting

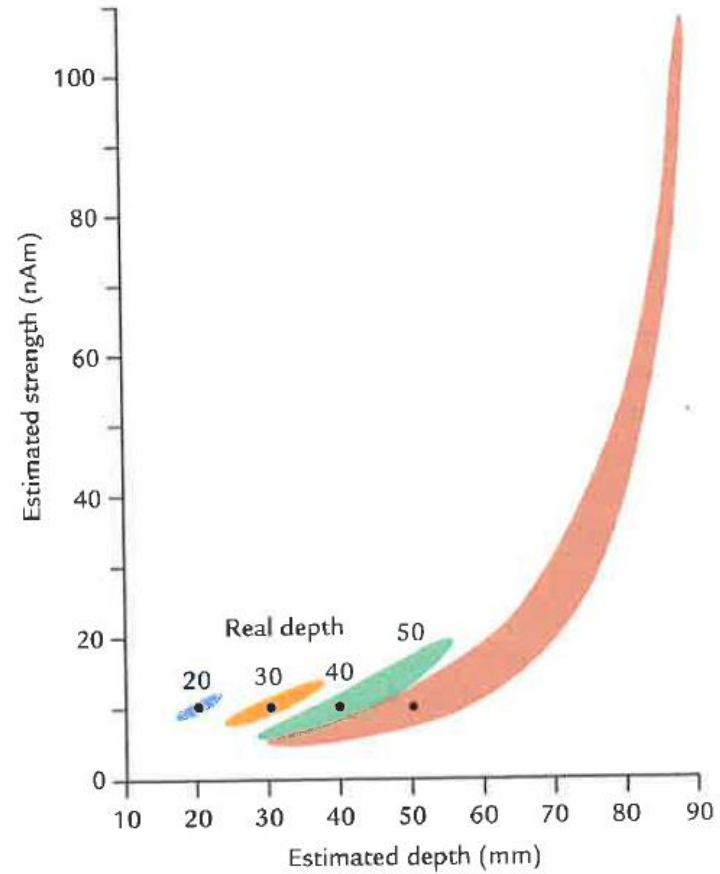
Explicit assumptions about the number of **focal sources (dipoles)** are tested by fitting dipole models to the data. The common criterion for the selection of models is the **goodness-of-fit**.



It can be hard to choose the appropriate number of dipoles – a priori knowledge is required. Solutions for several/many dipoles can get stuck in local minima, and may not be robust to noise.

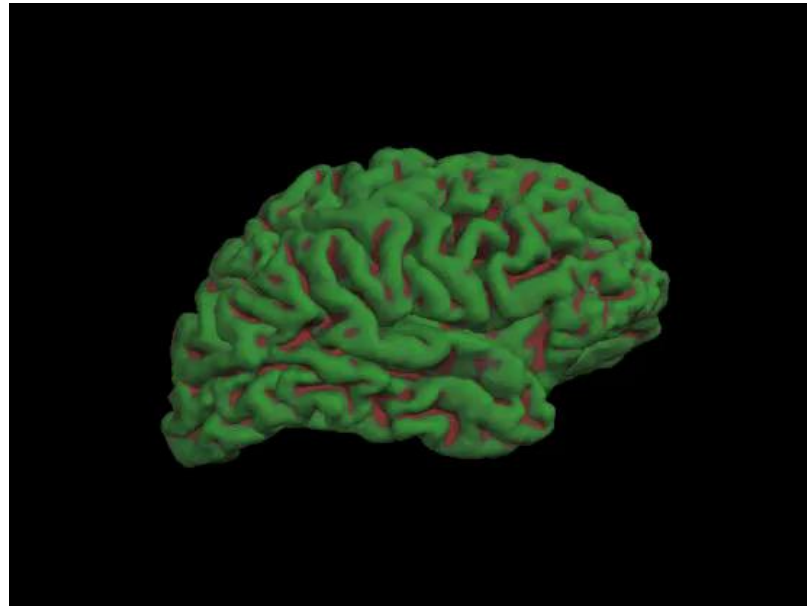
Assumptions Cannot Completely Remove Uncertainty

95% CIs for single dipole source



Dipole Scanning

We may have reasonable assumptions about possible locations for isolated dipole sources, e.g. on the cortical surface.



<http://www.cogsci.ucsd.edu/~sereno/movies.html>

Dipole scan: Fit dipoles vertex-by-vertex and plot the goodness-of-fit as a distribution.

The maxima in this distribution point to possible dipole locations.

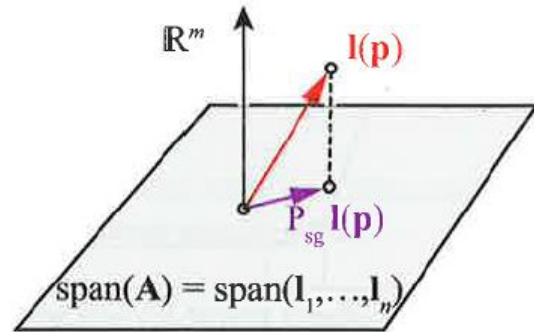
The locations are reliable if there is only one dipole, or if multiple dipole topographies are mutually orthogonal (e.g. far apart).

This is not a “distributed source solution”.

Multi-Dipole Scan: MUSIC

(Multiple Source Signal Classification)

Data and Noise Subspaces



Ilmoniemi & Sarvas, "Brain Signals", MIT 2019

Classical MUSIC

- 1) Obtain a spatio-temporal data matrix F , comprising information from m sensors and n time slices. Decompose F or FF^T and select the rank of the signal subspace to obtain $\hat{\Phi}_s$. Overspecifying the true rank by a couple of dimensions usually has little effect on performance. Underspecifying the rank can dramatically reduce the performance.
- 2) Create a relatively dense grid of dipolar source locations. At each grid point, form the gain matrix G for the dipole. At each grid point, calculate the subspace correlations $\text{subcorr}\{G, \hat{\Phi}_s\}$.
- 3) As a graphical aid, plot the inverse of $\sqrt{1 - c_1^2}$, where c_1 is the maximum subspace correlation. Correlations close to unity will exhibit sharp peaks. Locate r or fewer peaks in the grid. At each peak, refine the search grid to improve the location accuracy, and check the second subspace correlation. A large second subspace correlation is an indication of a "rotating dipole."

Mosher & Leahy, IEEE-TBME 1998

Recursively Applied (RAP) MUSIC

- 1) Estimate number of dipoles, e.g. using PCA/SVD.
- 2) Run MUSIC for one dipole.
- 3) Run MUSIC for 2nd dipole, partialling out dipole 1.
- 4) Repeat for estimated number of dipoles.

See e.g. for overview and recent updates of MUSIC algorithms:

Ilmoniemi & Sarvas, "Brain Signals", MIT 2019; Mäkelä et al., NI 2018 ("TRAP MUSIC", <https://pubmed.ncbi.nlm.nih.gov/29128542/>)

One problem with MUSIC algorithms: They don't give you source time courses.

“Spatial Filters”: Beamformers

Assumptions:

- All sources captured in data covariance matrix \mathbf{C} (signal and noise)
- We are interested in one source i in many sources

Aim:

Design a spatial filter \mathbf{w}_i which projects maximally on the source of interest and minimally on noise sources.

Project on source of interest: $\mathbf{w}_i^T \mathbf{f}_i$

Suppress noise: $\min(\mathbf{w}_i^T \mathbf{C} \mathbf{w}_i)$

$$\mathbf{w}_i = \frac{\mathbf{f}_i^T \mathbf{C}^{-1}}{\mathbf{f}_i^T \mathbf{C}^{-1} \mathbf{f}_i}$$

Linearly-Constrained
Minimum-Variance
(LCMV) Beamformer

Van Veen et al., 1997, <https://pubmed.ncbi.nlm.nih.gov/9282479/>

Create and apply these spatial filters vertex-by-vertex (dipole-by-dipole) and plot the distribution (possibly normalised by noise variance).

Spatial filters can also produce time courses for every source.

But note: The “spatial filter” interpretation applies to all linear methods, including MNE-type methods.

Beamformers are adaptive - i.e. not strictly linear

The “linearly-constrained maximum-variance” (LCMV) beamformer

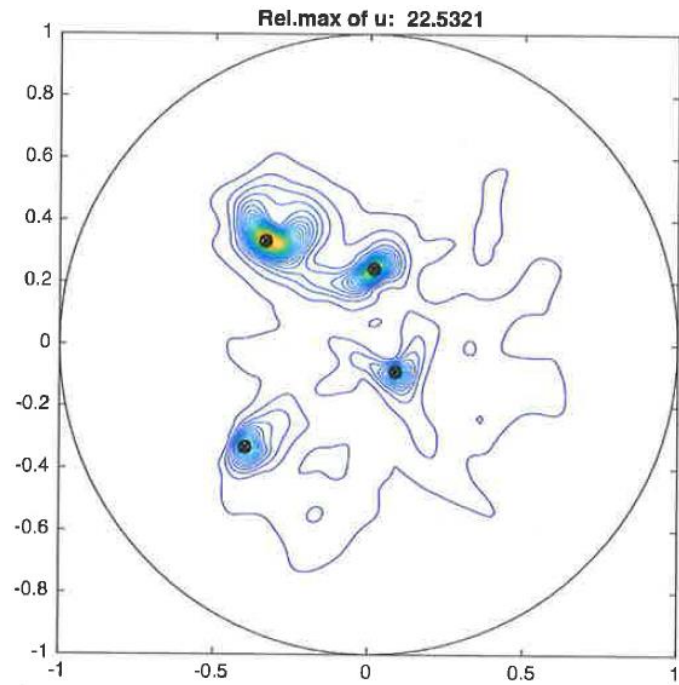
$$\mathbf{SF}_{LCMV}(i) = \frac{\tilde{\mathbf{L}}_{.i}^T \mathbf{C}_d^{-1}}{\tilde{\mathbf{L}}_{.i}^T \mathbf{C}_d^{-1} \tilde{\mathbf{L}}_{.i}}$$

depends on the **data** covariance matrix (“adaptive”).

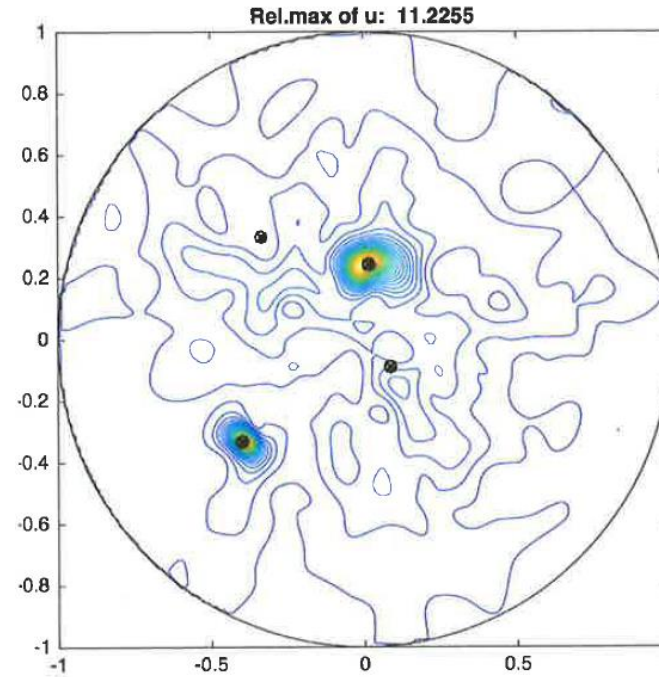
Beamformers result in linear transformations of the data (“spatial filters”), but those transformations strongly depend on the data of interest.

=> Beamformers are data-dependent and not linear with respect to the sources of interest.

Beamforming Is Problematic For Highly Synchronous Sources



4 non-synchronous sources

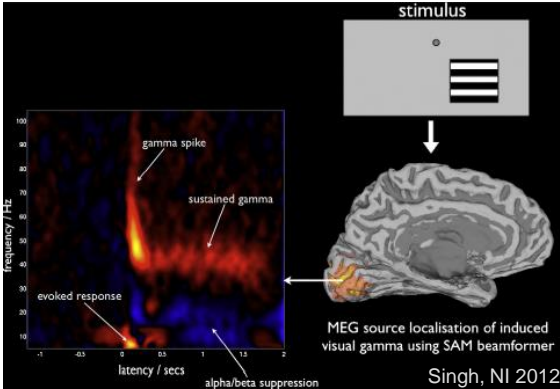


2 non-synchronous,
2 synchronous sources

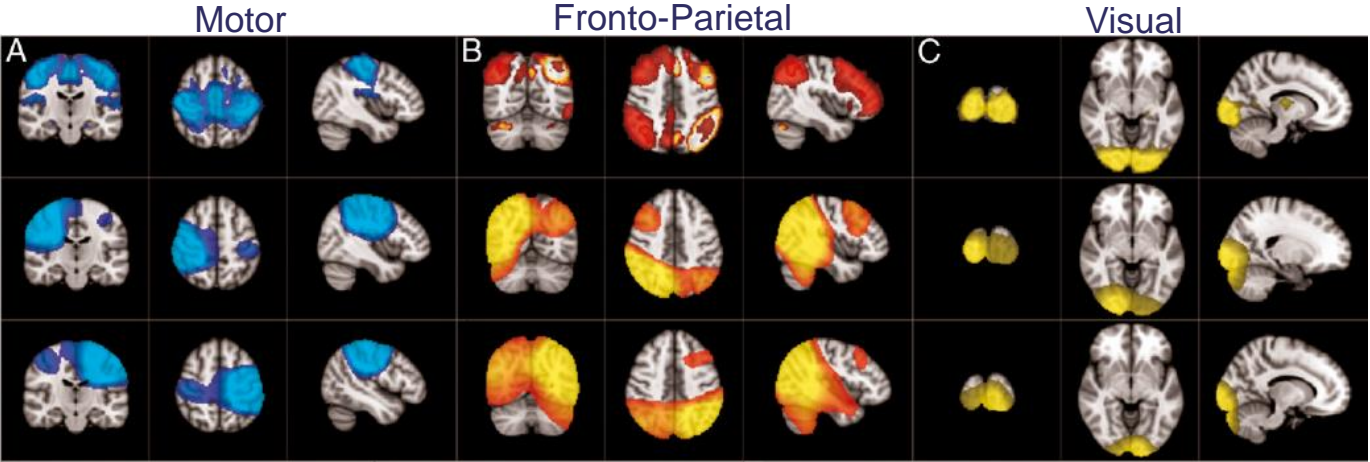
Beamformers are designed for – and work best for – small numbers of focal sources with uncorrelated time courses.

Beamformers Are Popular for Rhythmic Brain Activity and Resting State Activity

Visual Gamma Band Response



Resting State Networks



Brookes et al. PNAS 2011

Beamformers Are Popular for Rhythmic Brain Activity and Resting State Activity...

...but the choice of source estimation method should be based on knowledge (or its absence) about the source distribution.

Is there anything in rhythmic/oscillatory or resting state activity that favours some source distributions more than others (e.g. number of sources, focality/sparsity, location)?

For example, visual gamma band sources may be focal, but resting state networks may be distributed.

Minimum Norm Estimation Of Distributed Sources

$$\mathbf{L}\mathbf{s} = \mathbf{d} \Rightarrow \|\mathbf{L}\mathbf{s} - \mathbf{d}\|^2 = 0$$

(ignore noise for now)
subject to constraint

$$\|\mathbf{s}\|_2 = \min$$

yields the Minimum-Norm Least-Squares solution (“L2”)

$$\hat{\mathbf{s}} = \mathbf{G}_{MN}\mathbf{d}$$

with

$$\mathbf{G}_{MN} = \mathbf{L}^T (\mathbf{L}\mathbf{L}^T)^{-1}$$

But this is the result of mathematical desperation, and not based on physiology or what we want to know (e.g. localisation of multiple sources).

There Are Many Norms, e.g. L1 vs L2 – Sparseness vs Smoothness

Minimising the L2 norm, $\|s\|_2 = |s_1|^2 + |s_2|^2 + \dots + |s_N|^2$ penalizes large values in s
 \Rightarrow “smooth”

Minimising the L1 norm, $\|s\|_1 = |s_1| + |s_1| + \dots + |s_N|$ prefers large values in s
 \Rightarrow “sparse”

For example:

$$x_1 + 2x_2 = 1$$

L2 solution: (0.2, 0.4)

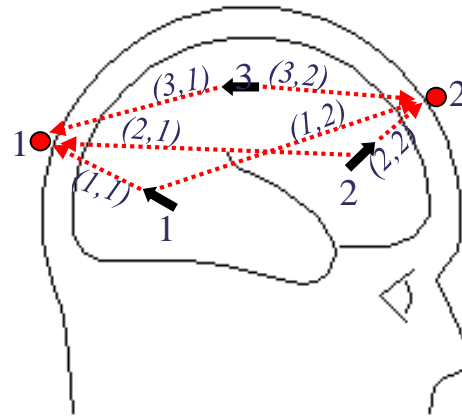
L2-norm $0.2^2 + 0.4^2 \sim 0.45$, L1-norm $0.2 + 0.4 = 0.6$

L1 solution: (0, 0.5)

L2-norm 0.5, L1-norm 0.5

Noise and Regularisation in EEG/MEG Source Estimation

The EEG/MEG Inverse Problem



| data | “leadfield” | dipoles | ? | dipoles | inverse | data |
|---|---|---|----------------------------------|---|--|--|
| $\begin{matrix} \bullet \\ \bullet \end{matrix} \begin{pmatrix} d_1 \\ d_2 \end{pmatrix}$ | $= \begin{pmatrix} 0.5 & 0 & 0.3 \\ 0 & 1 & -0.3 \end{pmatrix}$ | $\begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix}$ | $\xrightarrow{\text{inversion}}$ | $\begin{pmatrix} j_1 \\ j_2 \\ j_3 \end{pmatrix}$ | $= \begin{pmatrix} 1.5034 & 0.1241 \\ 0.2483 & 0.9379 \\ 0.8276 & -0.2069 \end{pmatrix}$ | $* \begin{pmatrix} d_1 \\ d_2 \end{pmatrix}$ |

$$\mathbf{d} = \mathbf{L}\mathbf{j}$$

\mathbf{d} : data ($n_{\text{sensors}} \times 1$) \mathbf{L} : “leadfield” ($n_{\text{sensors}} \times n_{\text{dipoles}}$), \mathbf{j} : dipoles ($n_{\text{dipoles}} \times 1$)
 Usually $n_{\text{dipoles}} \gg n_{\text{sensors}}$.

(In)Stability – Sensitivity to Noise

No linear dependence between rows/columns:

$$\begin{pmatrix} 2 & 0 \\ 0 & 2 \end{pmatrix} \xrightarrow{\text{Inversion}} \begin{pmatrix} 1/2 & 0 \\ 0 & 1/2 \end{pmatrix}$$

Some linear dependence:

$$\begin{pmatrix} 2 & 1 \\ 1 & 2 \end{pmatrix} \xrightarrow{\text{Inversion}} \begin{pmatrix} 2/3 & -1/3 \\ -1/3 & 2/3 \end{pmatrix}$$

High linear dependence:

$$\begin{pmatrix} 2 & 1.999 \\ 1.999 & 2 \end{pmatrix} \xrightarrow{\text{Inversion}} \begin{pmatrix} 500.13 & -499.87 \\ -499.87 & 500.13 \end{pmatrix}$$

Noise and Regularization

Explaining the data 100% may not be desirable – some of the measured activity is not produced by sources in the model.

Explaining noise may require larger amplitudes in source space than the signal of interest:

Overfitting may seriously distort the solution (“variance amplification” in statistics/regression).

Leaving Variance Unexplained

$$\mathbf{L}\mathbf{s} = \mathbf{d} + \boldsymbol{\varepsilon} \Rightarrow \|\mathbf{L}\mathbf{s} - \mathbf{d}\|^2 \leq e, \text{ s.t. } \|\mathbf{s}\|_2 = \min$$

This is equivalent to minimising the cost function

$$\|\mathbf{L}\mathbf{s} - \mathbf{d}\|^2 + \lambda\|\mathbf{s}\|^2, \lambda > 0$$

We can give sensors different weightings,
e.g. based on their noise covariance matrix \mathbf{C} :

$$\|\mathbf{C}^{-1}(\mathbf{L}\mathbf{s} - \mathbf{d})\|^2 = \|\mathbf{L}\mathbf{s} - \mathbf{d}\|_{\mathbf{C}}^2 = e$$

$$\|\mathbf{L}\mathbf{s} - \mathbf{d}\|_{\mathbf{C}}^2 + \lambda\|\mathbf{s}\|^2, \lambda > 0$$

$$\mathbf{G}_{MN} = \mathbf{L}^T (\mathbf{L}\mathbf{L}^T + \lambda\mathbf{C}^{-1})^{-1}$$

λ (Lambda) is the regularisation parameter that determines how much variance we want to leave unexplained.

“Whitening” and Choice of Regularisation Parameter

Whitened data have a noise covariance that is the identity matrix – i.e. noise is “white” (uncorrelated) noise.

$$\mathbf{G}_{MN} = \mathbf{L}^T (\mathbf{L}\mathbf{L}^T + \lambda \mathbf{C}^{-1})^{-1}$$

can also be written as

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

where $\widetilde{\mathbf{L}}$ is the “whitened” leadfield $\mathbf{C}^{-1/2}\mathbf{L}$, and scaled such that $\text{trace}(\widetilde{\mathbf{L}}\widetilde{\mathbf{L}}^T) = \text{trace}(\mathbf{I})$.

$\widetilde{\mathbf{L}}$ and λ can now be interpreted in terms of signal-to-noise ratios.

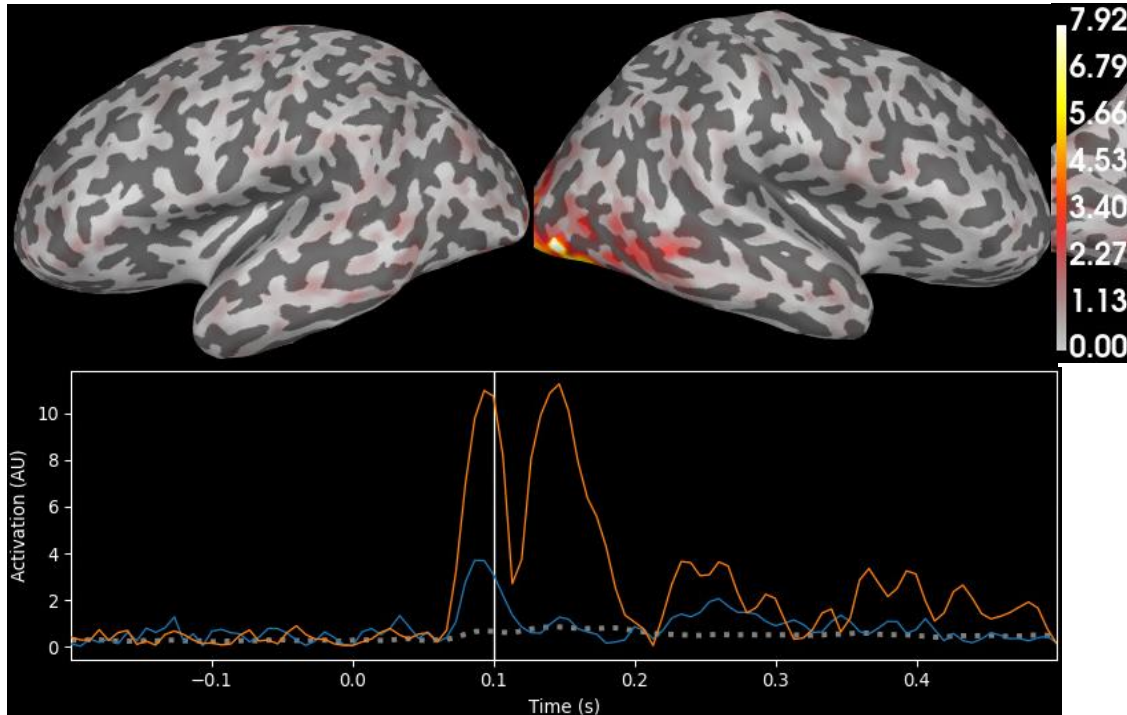
A reasonable choice for λ is then the approximate SNR of the data (e.g. in MNE software) –

usually heuristically chosen to be 3 (evoked) or 1 (raw/continuous).

The Effect of Regularisation

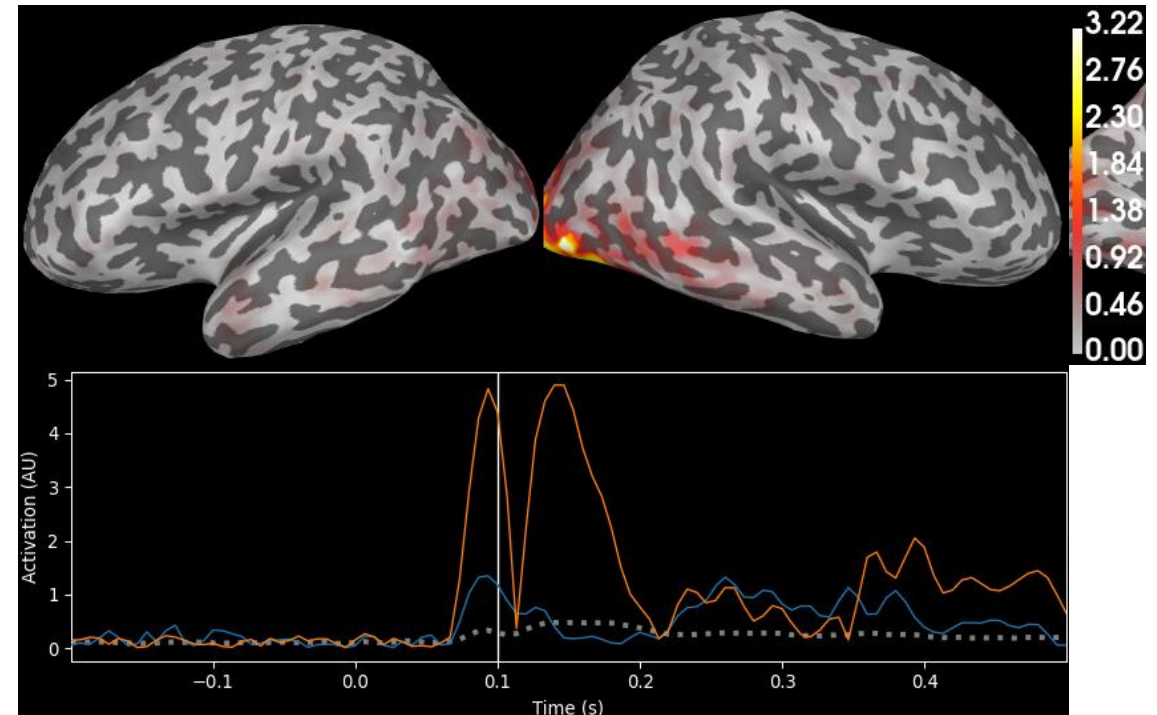
Suppressing Noise by “Smoothing”

“Evoked”
SNR=3



var=64.8%

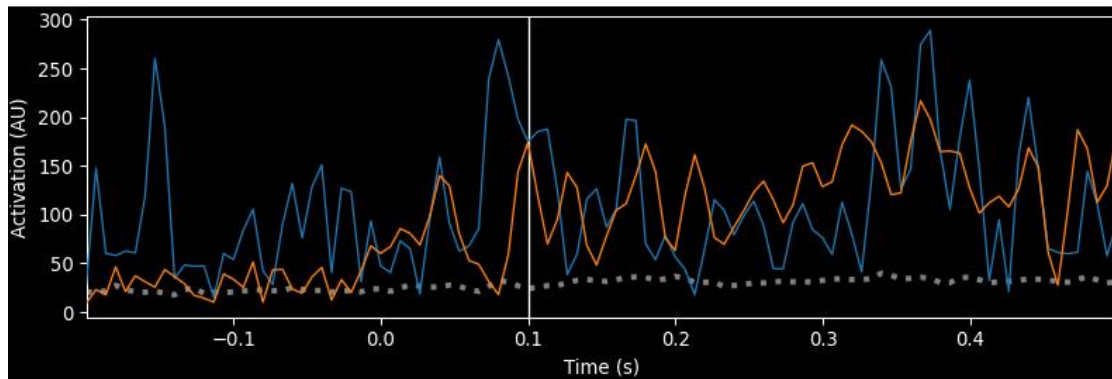
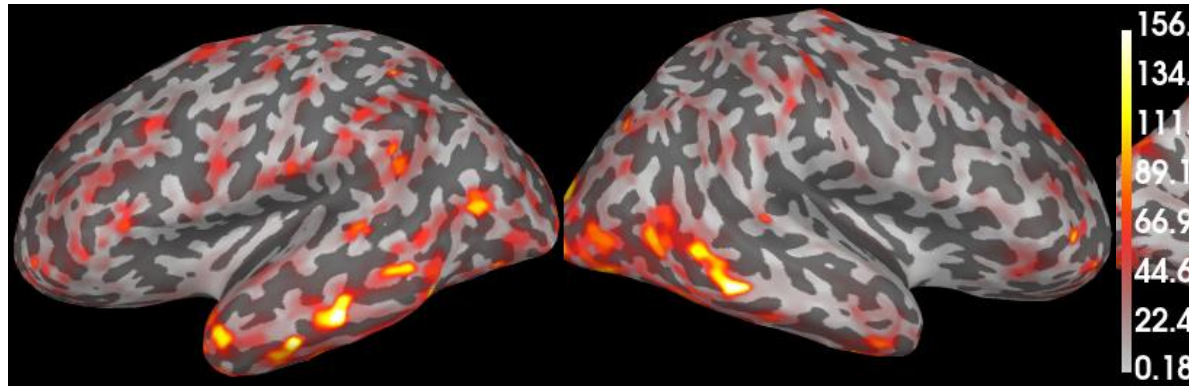
“Single trial”
SNR=1



var=51.5%

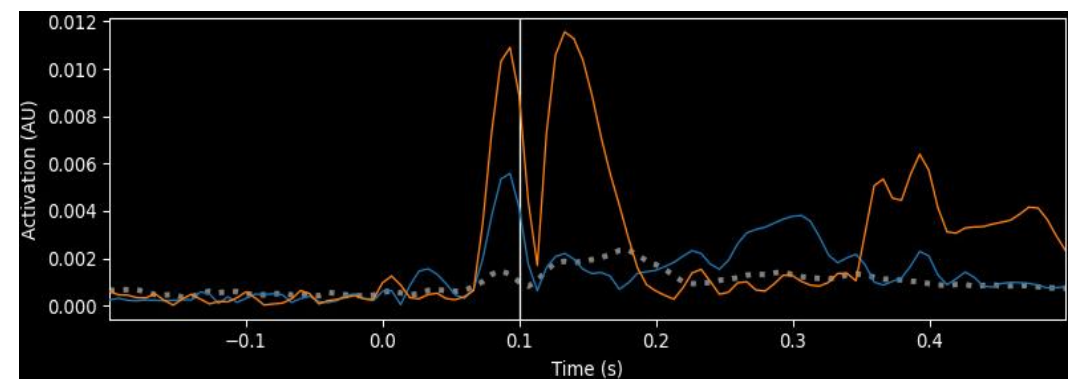
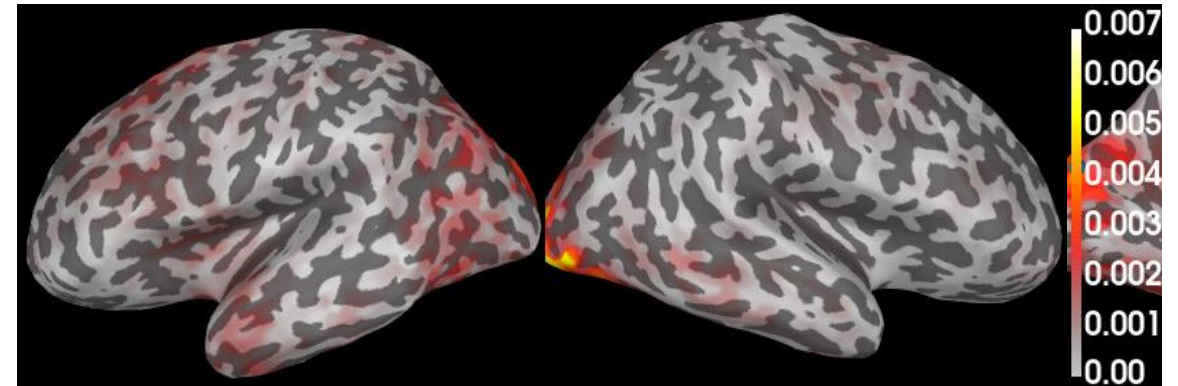
The Effect of Regularisation ~ Over- and Under-Fitting

Over-fitting
“Under-smoothing”
SNR=300



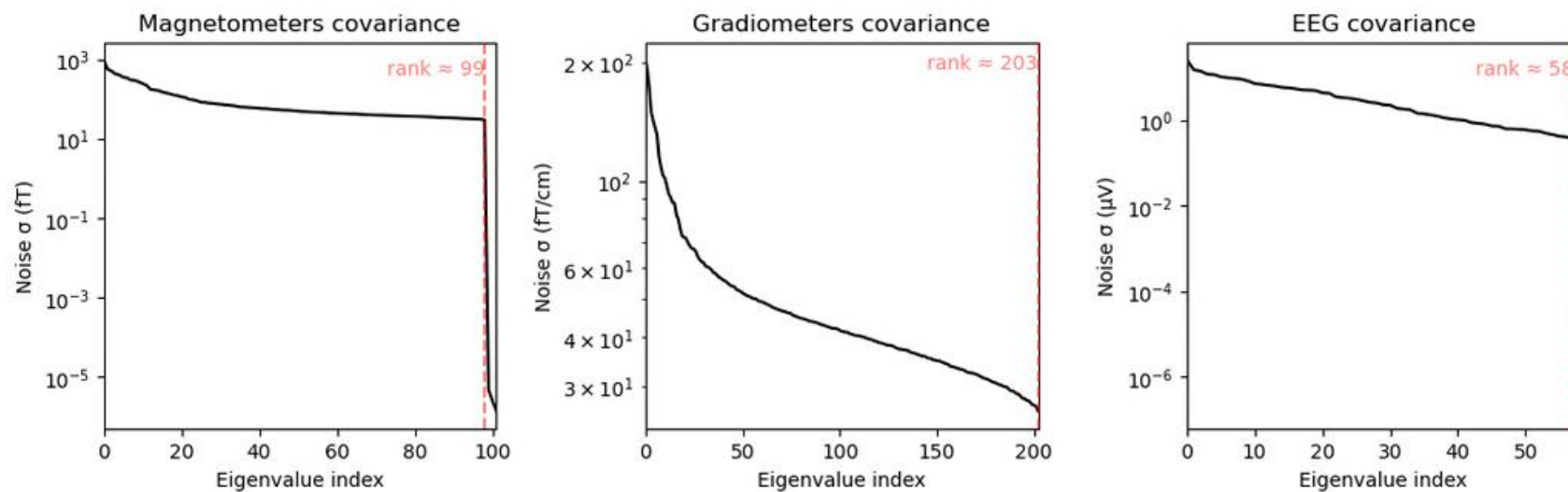
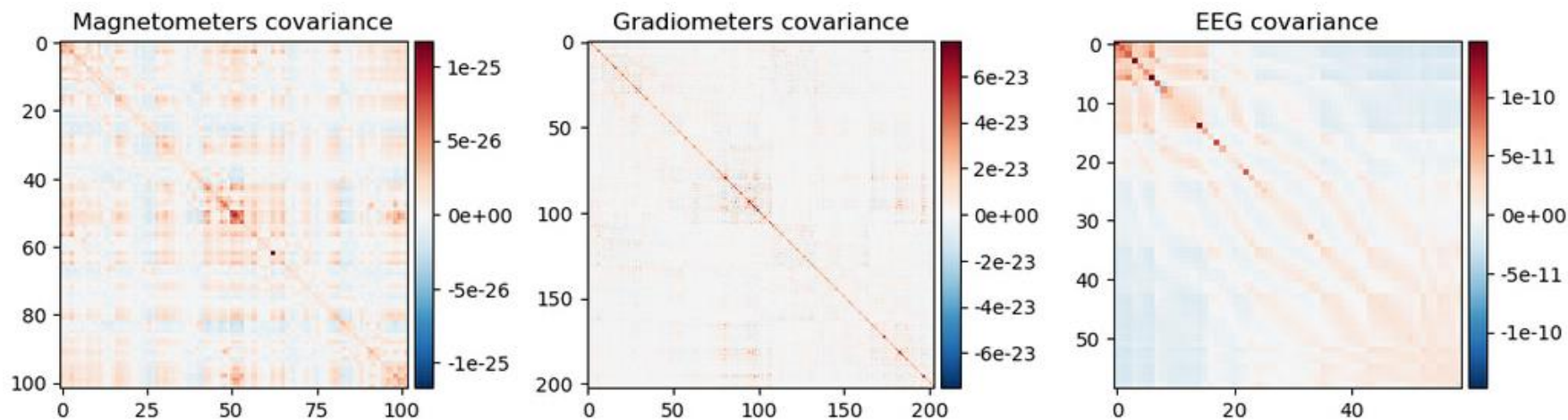
var=95.2%

Under-fitting
Over-smoothing
SNR=0.03



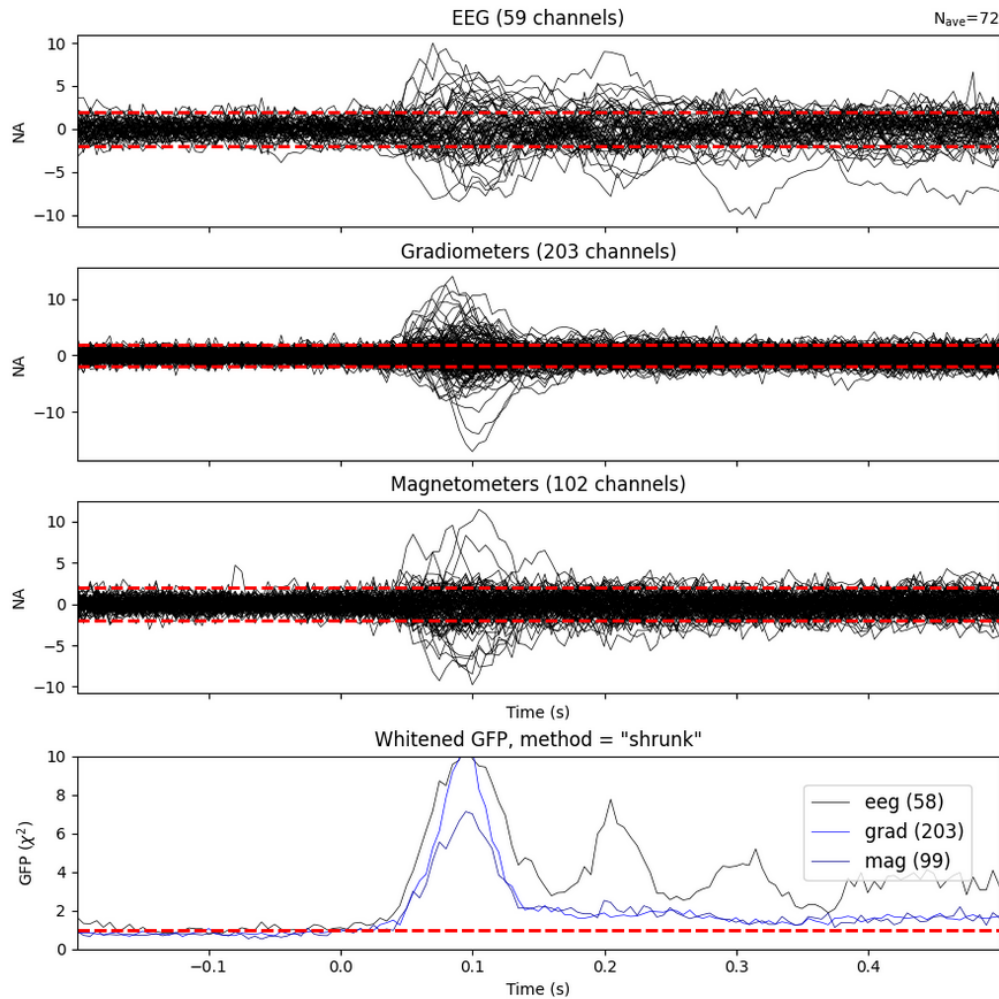
var=0.4%

Noise Covariance Matrices

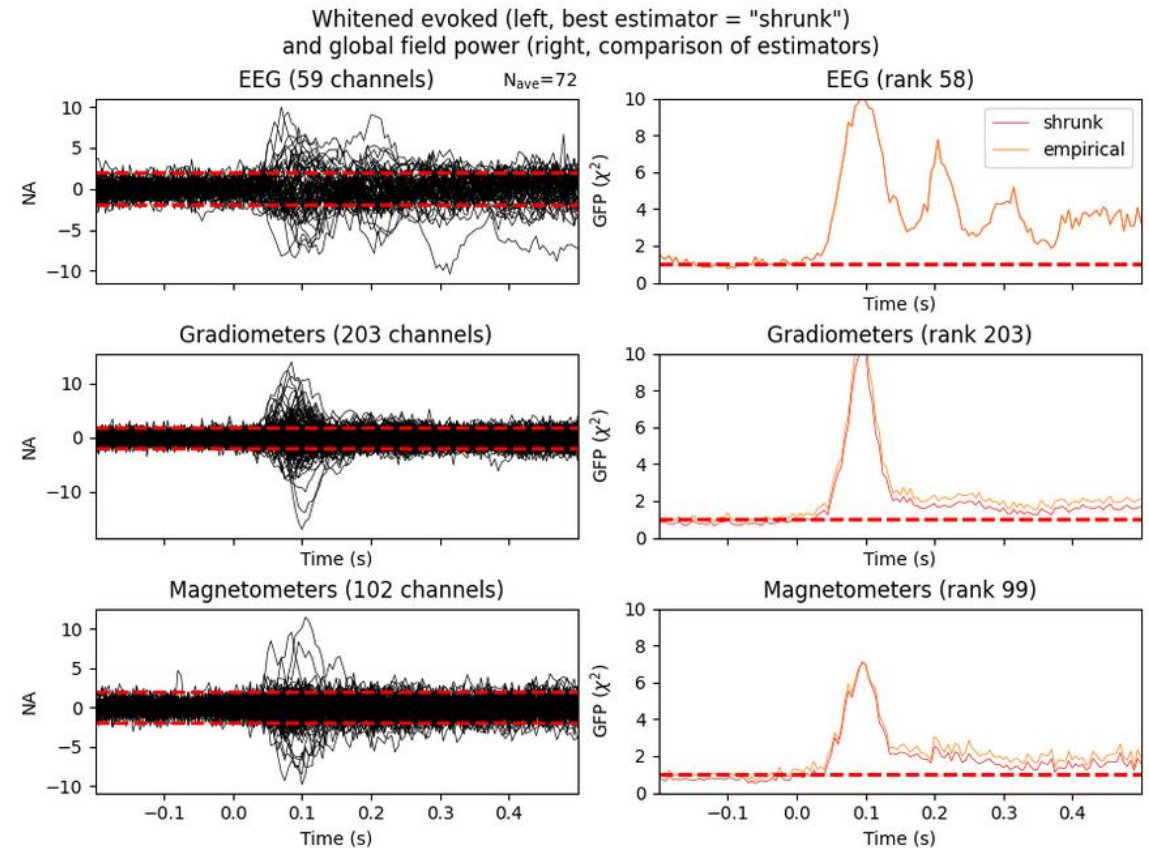


Covariance Estimation and “Whitening”

Whitened data should have a average SNR~1 in the baseline:



Whitening performance as criterion to choose the best covariance matrix:



https://mne.tools/stable/auto_tutorials/forward/90_compute_covariance.html

Engemann & Gramfort, NI 2015, <https://pubmed.ncbi.nlm.nih.gov/25541187/>

Noise and Regularization

1. Noise estimation:
 - a) For distributed source methods, baseline activity is not “noise”.
 - b) “Empty room recordings” not available for EEG, and may under-estimate noise.
2. Estimation of noise covariance matrix is important, and will usually need regularisation itself. Visualise the matrix, and check whitening performance on your data. (Also relevant for beamformers).
3. Choice of regularisation parameter involves some heuristics, and depends on SNR. Check plausibility of source estimation results on “simple” data (e.g. early evoked responses).



MRC Cognition
and Brain
Sciences Unit



UNIVERSITY OF
CAMBRIDGE

Thank you

MRC Cognition and Brain Sciences Unit

 @MRCCBU

mrc-cbu.cam.ac.uk