

# **EEG/MEG 2:** Head Modelling and Source Estimation Olaf Hauk

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### Ingredients for Source Estimation





Coordinate Transformation



#### MEG data



#### Noise/Covariance Matrix







### Our Goal: Spatio-Temporal Brain Dynamics "Brain Movies"





### Forward And Inverse Problem

(and some solutions)

### The EEG/MEG Forward Problem



# EEG/MEG measure the primary sources indirectly



# Sensors are differently sensitive to different sources



Hauk, Strenroos, Treder. In: Supek S, Aine C (edts), "Magnetoencephalography: From Signals to Dynamic Cortical Networks, 2nd Ed."



### EEG/MEG "Scanning" is not "Tomography"





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



### Why Inverse "Problem"?



In "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)

### Non-Uniquely Solvable Problem

What is the solution to

 $\begin{aligned} x_1 + x_2 &= 1 \\ \text{Maybe} \end{aligned}$ 

 $x_1 = 0; x_2 = 1$  ?

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

- x<sub>1</sub> = 1000 ; x<sub>2</sub> = -999 ?
- $x_1 = \pi$ ;  $x_2 = (1-\pi)$  ?

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.



## The Goal:

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Once We Have Stated the Forward Problem, We Are Ready Address the Inverse Problem



MNE produces solution with minimal power or "norm":

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



#### **Examples for Non-Uniqueness**



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

Jensen & Hesse, chap. 7 in "MEG", OUP 2010, Hansen/Kringelbach/Salmelin (edts.) See also Krishnaswamy et al. PNAS 2017 for approaches for deep sources, <u>https://www.pnas.org/content/114/48/E10465</u>

### **Examples for Non-Uniqueness**





### Example: Visually Evoked Activity ~100 ms





Magnetometers



Gradiometers



EEG



Minimum Norm Estimate

#### Example: Auditorily Evoked Activity











Minimum Norm Estimate

### The Forward Problem and Head Modelling



#### Source Space and Head Model



#### Source Space

Which sources are modelled 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, 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.



#### Normalising (Morphing) Cortical Surfaces



Gramfort et al., NI 2014

#### Source Spaces: Cortical Surface Segmentation





#### Spatial Sampling of Cortical Surfaces



10.034 vertices, 20.026 triangles of 10 mm<sup>2</sup> surface area



79.124 vertices, 158.456 triangles of 1.3 mm<sup>2</sup> surface area





Baillet, chap. 5 in "MEG", OUP 2010, Hansen/Kringelbach/Salmelin (edts.)

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#### **Volumetric Source Spaces**



Pascqual-Marqui, PTRS-A 2011





## Coregistration of EEG/MEG and MRI Spaces

#### Coordinate Transformation







### Accurate Coregistration Is Important

Coregistration errors affect the forward model, and therefore everything that follows. For example, connectivity analysis:



Functional Connectivity Metrics

Chella et al., NI 2019



#### Head Modelling – Tissue Compartments



## Head Models With Different Levels of Detail



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### More Complex Head Models

The use of 3-layer (brain, skull, scalp) BEM models based on individual MRI images is recommended for accurate EEG/MEG source reconstruction.

For MEG-only, single shell BEMs and local/corrected sphere models can provide reasonable approximations.

These approaches are available in all major EEG/MEG software packages.

But heads are more complex:

White Matter Gray Matter CSF Skull Compacta Skull Spongiosa Skin





Vorwerk et al., NI 2014

It is not obvious how to translate this into more accurate estimate for conductivity distributions.





### Conductivities Of Tissues Can Only Be Approximated

**Table 2** Isotropic conductivity values of single tissue types used in human head volume conductor modeling

Tissue	Conductivity in S/m	Reference
Brain gray matter	0.45	Logothetis et al. 2007
Brain white matter	0.1	Akhtari et al. 2010
Spinal cord and cerebellum	0.16	Haueisen et al. 1995
Cerebrospinal fluid	1.79	Baumann et al. 1997
Hard bone (compact bone)	0.004	Tang et al. 2008
Soft bone (spongiform		
bone)	0.02	Akhtari et al. 2002
Blood	0.6	Gabriel et al. 2009
Muscle	0.1	Gabriel et al. 1996, 2009
Fat	0.08	Gabriel et al. 2009
Eye	1.6	Pauly and Schwan 1964; Lindenblatt and Silny 2001
Scalp	0.43	Geddes and Baker 1967
Soft tissue	0.17	Haueisen et al. 1995
Internal air	0.0001	Haueisen et al. 1995



### Boundary Element Models Are Relatively Robust Against Conductivity Errors

Stenroos & Hauk, NI 2013 https://pubmed.ncbi.nlm.nih.gov/23639259/

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### Infant Skulls – Fontanelles and Sutures



#### Relative error between models with and without fontanelles/sutures



Lew et al., NI 2013

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### Conclusion – Head Modelling



3-compartment BEM models are currently state-ofthe-art for EEG/MEG source estimation.

Single-shell approximations are still common for MEG.

More detailed head models may increase accuracy, but require more accurate data and information, such as accurate MRI segmentations and conductivity values. (see e.g. Vorwerk et al., BioMeg Eng Online 2018) for Fieldtrip FEM pipeline)

There is no right or wrong, there are only different approximations – know your limits.



### The Forward Problem Is Linear – Superposition Principle

Superposition In Sensor Space



source 1



### Sensitivity of EEG and MEG





## MEG Is Less Sensitive To Spatially Extended Sources Than EEG



#### Extended Sources: 10 mm radius



#### Extended Sources: 16 mm radius



Goldenholz et al., HBM 2009 https://pubmed.ncbi.nlm.nih.gov/18465745/

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### Solutions To The Inverse Problem – Source Estimation

## 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




## **Dipole Scanning**





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" (more on that later).



## Multi-Dipole Scan: MUSIC

(Multiple Source Signal Classification)

#### Data and Noise Subspaces



#### **Classical MUSIC**

- Obtain a spatio-temporal data matrix *F*, comprising information from *m* sensors and *n* time slices. Decompose *F* or *FF<sup>T</sup>* and select the rank of the signal subspace to obtain \$\hfi\u03c6<sub>s</sub>\$. Overspecifying the true rank by a couple of dimensions usually has little effect on performance. Underspecifying the rank can dramatically reduce the performance.
- 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 subcorr{G, Φ<sub>s</sub>}.
- 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."

#### Recursively Applied (RAP) MUSIC

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

Mosher & Leahy, IEEE-TBME 1998

See e.g. for overview and recent updates of MUSIC algorithms: Ilmoniemi & Sarvas, "Brain Signals", MIT 2019; Mäkelä et al., NI 2018 ("TRAP MUSIC", <u>https://pubmed.ncbi.nlm.nih.gov/29128542/</u>)

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

#### "Spatial Filters": Beamformers

#### Assumptions:

- All sources captured in data covariance matrix 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: 
$$\mathbf{w}_i^T \mathbf{f}_i$$

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

 $\mathbf{w}_i = \frac{\mathbf{f}_i^T \mathbf{C}^{-1}}{\mathbf{f}_i^T \mathbf{C}^{-1} \mathbf{f}_i} \qquad \text{Linearly-Constrained} \\ \text{Minimum-Variance}$ (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.

> e.g. Hauk&Stenroos, HBM 2013, https://pubmed.ncbi.nlm.nih.gov/23616402/ Hauk et al., bioRxiv 2019, https://www.biorxiv.org/content/10.1101/672956v1



#### Beamformers



The "linearly-constrained maximum-variance" (LCMV) beamformer

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

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 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 Popular for Rhythmic Brain Activity and Resting State Activity



Brookes et al. PNAS 2011

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Resting State Networks 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



## Minimum Norm Estimation Of Distributed Sources



$$\begin{split} Ls &= d \implies \|Ls - d\|^2 = \mathbf{0} \\ & \text{(ignore noise for now)} \\ & \text{subject to constraint} \end{split}$$

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

#### yields the Minimum-Norm Least-Squares solution ("L2")

 $\hat{s} = G_{MN} \mathbf{d}$ 

with

 $\boldsymbol{G}_{\boldsymbol{M}\boldsymbol{N}} = \mathbf{L}^T (\mathbf{L}\mathbf{L}^T)^{-1}$ 

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



## There Are Many Norms, e.g. L1 vs L2 -Sparseness

Minimising the L2 norm,  $\|\mathbf{s}\|_2 = |s_1|^2 + |s_2|^2 + ... + |s_N|^2$  penalizes large values in  $\mathbf{s} =$  "smooth"

Minimising the L1 norm,  $\|\mathbf{s}\|_1 = |s_1| + |s_1| + ... + |s_N|$  prefers large values in  $\mathbf{s}$  $\Rightarrow$  "sparse"

For example:

 $x_1 + 2x_2 = 1$ 

L2 solution: (0.2, 0.4) L2-norm 0.2<sup>2</sup>+0.4<sup>2</sup>~0.45, L1-norm 0.2+0.4=0.6

> L1 solution: (0, 0.5) L2-norm 0.5, L1-norm 0.5



Bayes' rule:

 $p(\mathbf{s}|\mathbf{d}) \sim p(\mathbf{d}|\mathbf{s}) * p(\mathbf{s})$ posterior ~ likelihood \* prior

Assume normal distribution for noise:

$$p(\mathbf{d}|\mathbf{s}) = \left(\frac{\beta}{2\pi}\right)^{M/2} exp\left(-\frac{\beta}{2}\|\mathbf{L}\mathbf{s} - \mathbf{d}\|^2\right)$$

Thus, minimise

$$-2log(p(\mathbf{s}|\mathbf{d})) = -2log(p(\mathbf{d}|\mathbf{s})) - 2log(p(\mathbf{s})) = \beta \|\mathbf{L}\mathbf{s} - \mathbf{d}\|^2 - 2log(p(\mathbf{s}))$$

e.g. Henson et al., 2011, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3160752/

"Most likely" is still not what we want to know – Does the method do what we want it to do?



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## Let's Start Again: The "Blurry Image" Analogy





## The Superposition Principle A "Constraint-Free" Interpretation of Linear Methods





#### Astronomy



https://en.wikipedia.org/wiki/Point\_spread\_function



0.8 -0.6 -0.4 -

-10

0.8

0.2

-10

0.7 0.6 0.5 0.4

0.2

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If you know the behaviour for point sources, you can predict the behaviour for complex sources



#### Linear Methods – Superposition Principle

Superposition In Source Space



#### **Example Point-Spread Functions**



Hauk, Strenroos, Treder. In: Supek S, Aine C (edts), "Magnetoencephalography: From Signals to Dynamic Cortical Networks, 2nd Ed."



## Spatial Resolution of Source Estimation Is Complex

Spatial resolution depends on:

modelling assumptions number of sensors (EEG/MEG or both) source location source orientation signal-to-noise ratio head modeling

=> difficult to make general statement

#### Spatial Resolution – A Naïve Estimate

With *n* sensors:

- -> *n* independent measurements
- -> *n* independent parameters estimable
- -> at best separate activity from *n* brain regions

Sensors are not independent, data are noisy: ~ 50 degrees of freedom

Volume of source space: Sphere 8cm minus sphere 4 cm: volume ~1877 cm<sup>3</sup>





#### **Resolution Matrix**





Relationship between estimated and true source distribution.

## MNE Has An Optimal Resolution Matrix



 $\hat{\mathbf{s}} = \mathbf{R}\mathbf{s}$ 

The closer **R** is to the identity matrix, the closer our estimate is to the true source.

Therefore, let us minimise the difference between **R** and the identity matrix in the least-squares sense:

$$\|\boldsymbol{R} - \boldsymbol{I}\|_2 = \min$$

This leads to the **Minimum Norm Estimator (MNE)**:

 $\boldsymbol{G}_{\boldsymbol{M}\boldsymbol{N}} = \mathbf{L}^T (\mathbf{L}\mathbf{L}^T)^{-1}$ 

Its resolution matrix  $\mathbf{R}_{\mathbf{MN}} = \mathbf{L}^T (\mathbf{L} \mathbf{L}^T)^{-1} \mathbf{L}$  is symmetric.

#### **Spatial Resolution:** Point-Spread and Cross-Talk/Leakage



# Cross-Talk Function (CTF)



How other sources may affect the estimate for this source

Point-Spread Function (PSF)



How this source affects estimates for other sources

Hauk, Strenroos, Treder. In: Supek S, Aine C (edts), "Magnetoencephalography: From Signals to Dynamic Cortical Networks, 2nd Ed."



# PSFs and CTFs for Some ROIs

For MNE, PSFs and CTFs turn out to be the same



Good





# PSFs and CTFs for Some ROIs

For MNE, PSFs and CTFs turn out to be the same



#### Less good



# Localisation Bias Has Consequences for ROI analysis







Desikan-Killiany Atlas parcellation





## Quantifying Resolution From PSFs and CTFs



It's not just peak localisation that counts, but also spatial extent of the distribution.

## **Resolution Metrics For PSFs/CTFs**



- MEG+EEG: Elekta Vectorview (360+70 channels), Wakeman & Henson open data set
- Whitened leadfields and data to combine sensor types
- Methods Comparison:
  - L2-MNE
  - depth-weighted L2-MNE
  - dSPM
  - sloreta
  - 2 LCMV beamformers (pre- and post-stimulus covariance matrices)
- Resolution Metrics:
  - Peak Localisation Error
  - Spatial Dispersion (extent)

#### Sensitivity Maps RMS of Leadfield Columns



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Hauk/Stenroos/Treder, bioRxiv 2019 | see also Molins et al., NI 2008



#### **Peak Localisation Error**



Hauk/Stenroos/Treder, bioRxiv 2019, <u>https://www.biorxiv.org/content/10.1101/672956v1</u>, see also Hauk/Wakeman/Henson, NI 2011

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Hauk/Stenroos/Treder, bioRxiv 2019, <u>https://www.biorxiv.org/content/10.1101/672956v1</u>, see also Hauk/Wakeman/Henson, NI 2011



# Anatomical Parcellations May Not Be Optimal For EEG/MEG



Farahibozorg, Henson, Hauk, NI 2018



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#### Adaptive Parcellations For EEG/MEG



Farahibozorg, Henson, Hauk, NI 2018

Noise and Regularisation



#### (In)Stability – Sensitivity to Noise





Similar topographies are difficult to distinguish, especially in the presence of noise.

Thanks to Matti Stenroos.





#### Noise and Regularization Over- And Under-Fitting

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).

"Regularisation" results in a spatially smoother solution that is less affected by noise. The degree of smoothing depends on the "regularisation parameter" (also called "lambda").

Underfitting (over-smoothing) may waste spatial resolution.

#### Regularisation Can Take Into Account Noise covariance



Some channels are noisier than others  $\Rightarrow$  They should get different weights in your analysis

#### Sensors are not independent

=> Sensors that carry the same information should be downweighted relative to more independent sensors

(Full) Noise Covariance Matrix



(Diagonal) Noise Covariance Matrix (contains only variance for sensors)



#### Leaving Variance Unexplained

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$$Ls = d + \epsilon \Rightarrow ||Ls - d||^2 \le e, s.t. ||s||_2 = min$$

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 C:

$$\|\mathbf{C}^{-1}(\mathbf{L}\mathbf{s} - \mathbf{d})\|^{2} = \|\mathbf{L}\mathbf{s} - \mathbf{d}\|^{2}_{C} = \mathbf{e}$$
$$\|\mathbf{L}\mathbf{s} - \mathbf{d}\|^{2}_{C} + \lambda \|\mathbf{s}\|^{2}, \lambda > 0$$

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

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


## Whitening and Choice of Regularisation Parameter

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

can also be written as  $\boldsymbol{G}_{\widetilde{\boldsymbol{M}}N} = \tilde{\mathbf{L}}^T (\tilde{\mathbf{L}}\tilde{\mathbf{L}}^T + \lambda \mathbf{I})^{-1}$ 

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

 $\tilde{L}$  and  $\lambda$  can now be interpreted in terms of signal-to-noise ratios.

A reasonable choice for  $\lambda$  is then the approximate SNR of the data.

## Trade-off norm-variance, smoothness

Source at fixed excentricity 71% (60mm)

t 0.1 Regularisation parameter T relative to optimal value 0.2 1 t 0.5 t 1 t 2 5 10 MNLS MNLS MNLS MNLS rel. tangential dip. radial dipoles tangential dip. radial dipoles dev. SNR = 68 SNR = 77 SNR = 7SNR = 8



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## Regularisation: Bayesian L2

Minimise cost function  $F(\mathbf{s}) = \beta \|\mathbf{L}\mathbf{s} - \mathbf{d}\|_{C}^{2} - 2\log(p(\mathbf{s}))$ If we assume  $p(\mathbf{s})$  is Gaussian  $p(\mathbf{s}) = \left(\frac{\alpha}{2\pi}\right)^{N/2} exp\left(-\frac{\alpha}{2} \|\mathbf{s}\|^2\right)$ This leads to the cost function  $\Rightarrow F(\mathbf{s}) = \beta \|\mathbf{L}\mathbf{s} - \mathbf{d}\|_{\mathcal{C}}^2 + \alpha \|\mathbf{s}\|^2 \sim \|\mathbf{L}\mathbf{s} - \mathbf{d}\|_{\mathcal{C}}^2 + \frac{\alpha}{\beta} \|\mathbf{s}\|^2$ 

=> Equivalent to cost function for the L2 minimum-norm solution.

e.g. Henson et al., 2011, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3160752/