



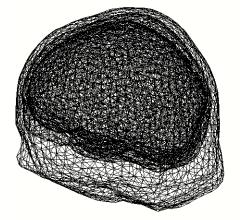
EEG/MEG 2:Head Modelling and Source Estimation Olaf Hauk

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

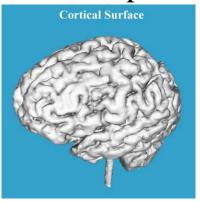
Ingredients for Source Estimation



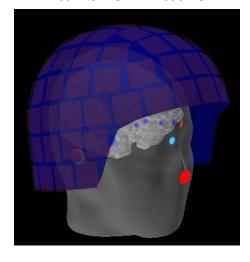
Volume Conductor/ Head Model



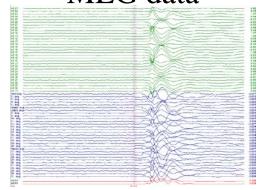
Source Space



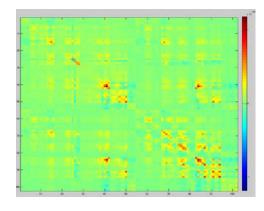
Coordinate Transformation



MEG data

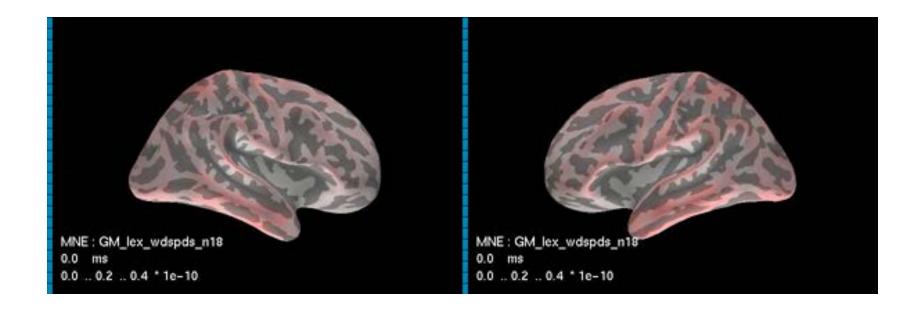


Noise/Covariance Matrix



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





Forward And Inverse Problem

(and some solutions)

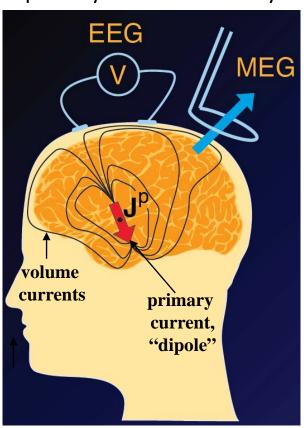




The EEG/MEG Forward Problem

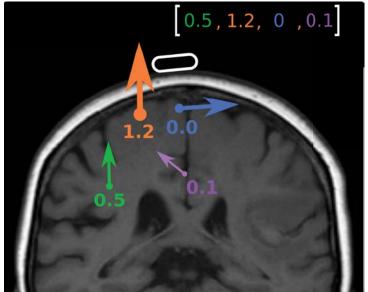


EEG/MEG measure the primary sources indirectly



Sensors are differentially sensitive to different sources

"Leadfield"

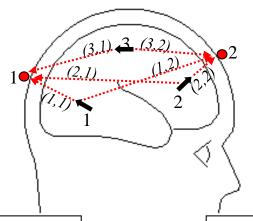


Hauk, Strenroos, Treder. In: Supek S, Aine C (edts), "Magnetoencephalography: From Signals to Dynamic Cortical Networks, 2nd Ed."

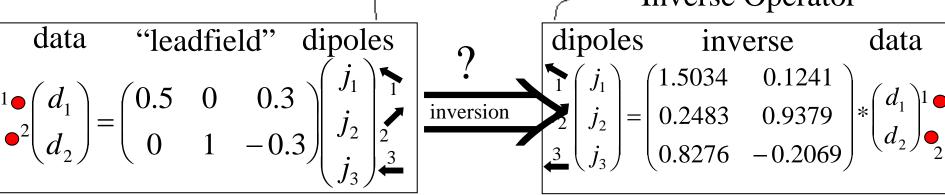
We Have To First State The Forward Problem In Order To Solve The Inverse Problem







Inverse Operator



Non-Unique Inverse Problem



What is the solution to
$$x_1 + x_2 = 1$$

$$x_1 = 0 ; x_2 = 1$$

$$x_1 = 1 ; x_2 = 0$$

$$x_1 = 1000$$
; $x_2 = -999$

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

The "minimum norm solution" is:

$$x_1 = 0.5$$
; $x_2 = 0.5$

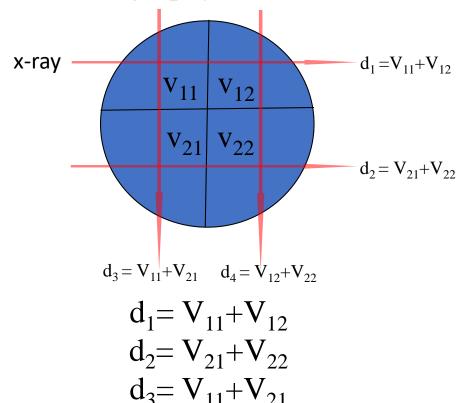
with $(0.5^2 + 0.5^2)=0.5$ the minimum norm among all possible solutions.

EEG/MEG "Scanning" is not "Tomography"





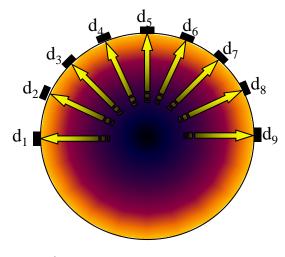
Tomography (CT, fMRI...)



Available information is determined by the equipment/experimenter

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

EEG/MEG



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

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

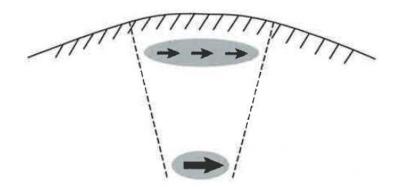
Information is lost during measurement

Cannot be retrieved by mathematics

Inherently limits spatial resolution

Examples for Non-Uniqueness



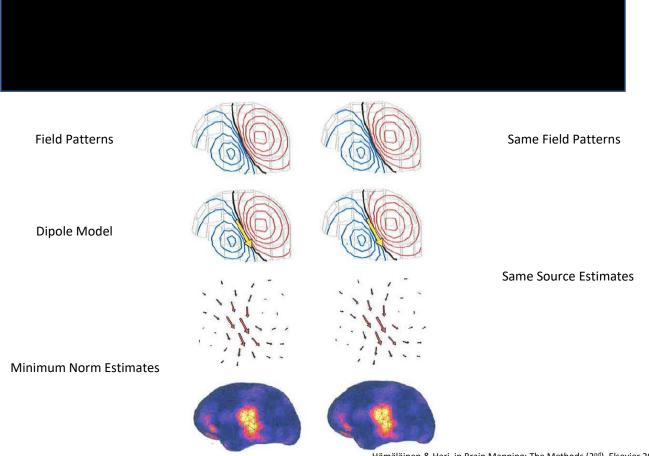


A distributed superficial distribution may be indistinguishable from a focal deep source.

Examples Of Non-Uniqueness



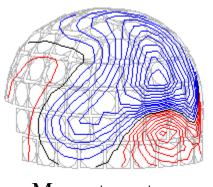




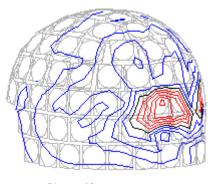
Hämäläinen & Hari, in Brain Mapping: The Methods (2nd), Elsevier 2002

Example: Visually Evoked Activity ~100 ms

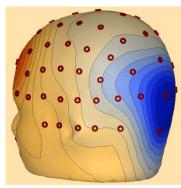




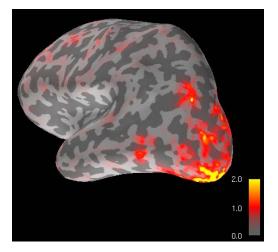




Gradiometers



EEG

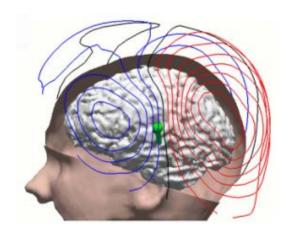


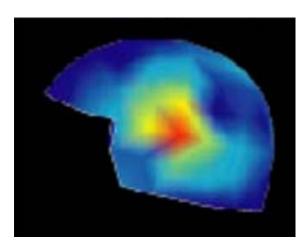
Minimum Norm Estimate

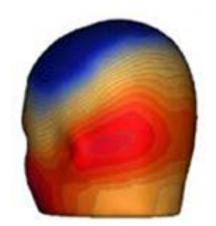
Example: Auditorily Evoked Activity

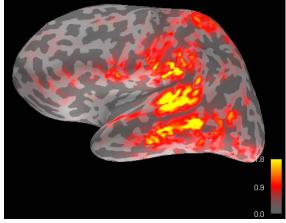












Minimum Norm Estimate

The Forward Problem and Head Modelling



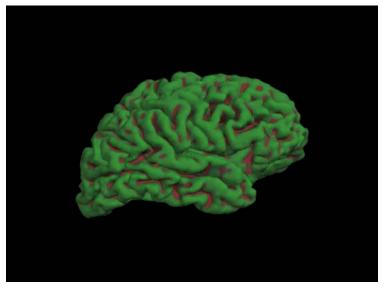


Source Space and Head Model



Source Space

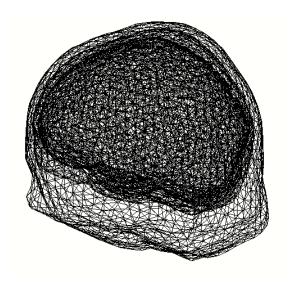
Where active sources may be located, e.g. grey matter, 3D volume



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.

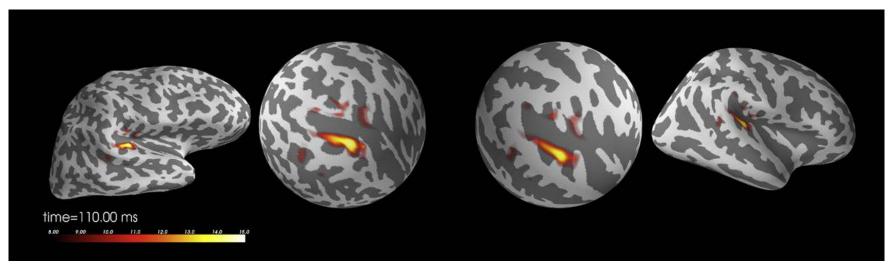
SPM uses the same "canonical mesh" as source space for every subjects, but adjusts it individually.

Normalising (Morphing) Cortical Surfaces





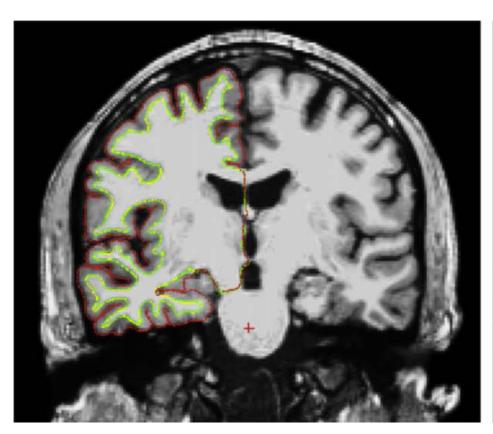
From individual to standard brain

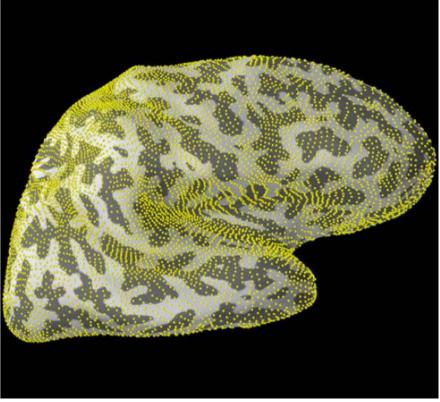


Gramfort et al., NI 2014

Source Spaces: Cortical Surface Segmentation



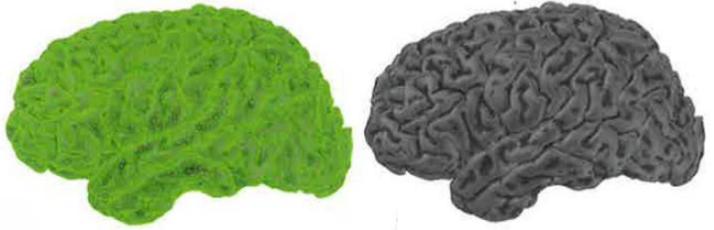




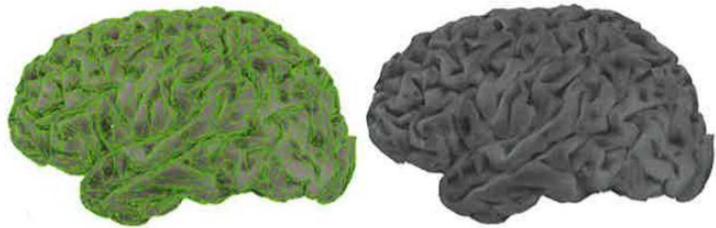
Gramfort et al., NI 2014

Spatial Sampling of Cortical Surfaces

79.124 vertices, 158.456 triangles of 1.3 mm² surface area



10.034 vertices, 20.026 triangles of 10 mm² surface area Sufficient for most EEG/MEG applications





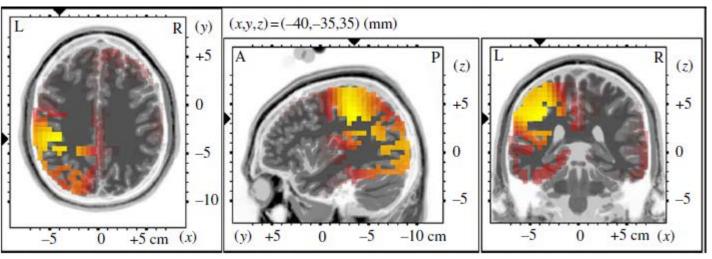


Volumetric Source Spaces Are Possible

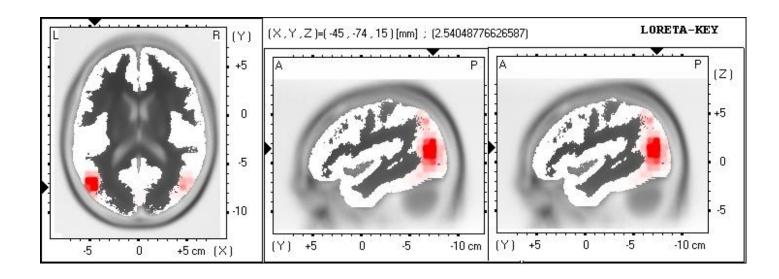
Not always useful considering the inverse problem is already highly underdetermined, but may be the only option for patients with brain damage







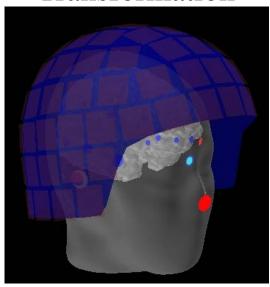
Pascqual-Marqui, PTRS-A 2011



Coregistration of EEG/MEG and MRI Spaces

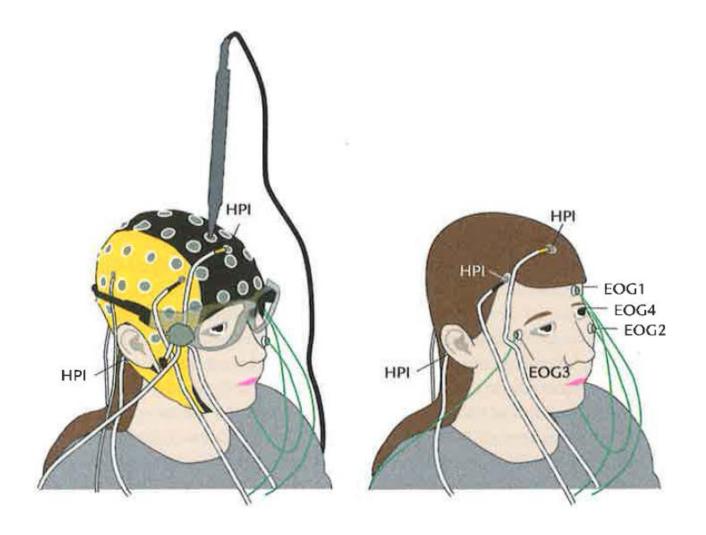


Coordinate Transformation



Coregistration of EEG/MEG and MRI Spaces





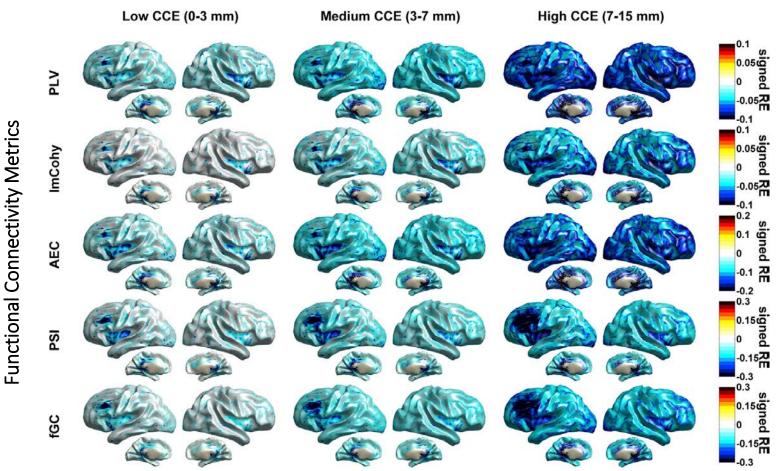
Accurate Coregistration Is Important

Cognition and Brain Sciences Unit

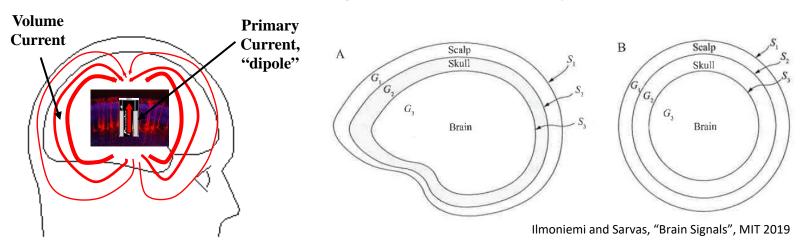
MRC

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

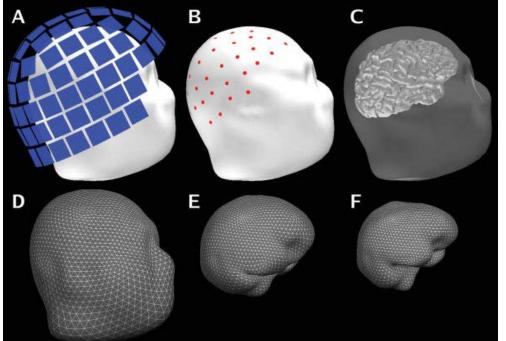
3 levels of coregistration error



Head Modelling – Tissue Compartments



Ingredients for a head model



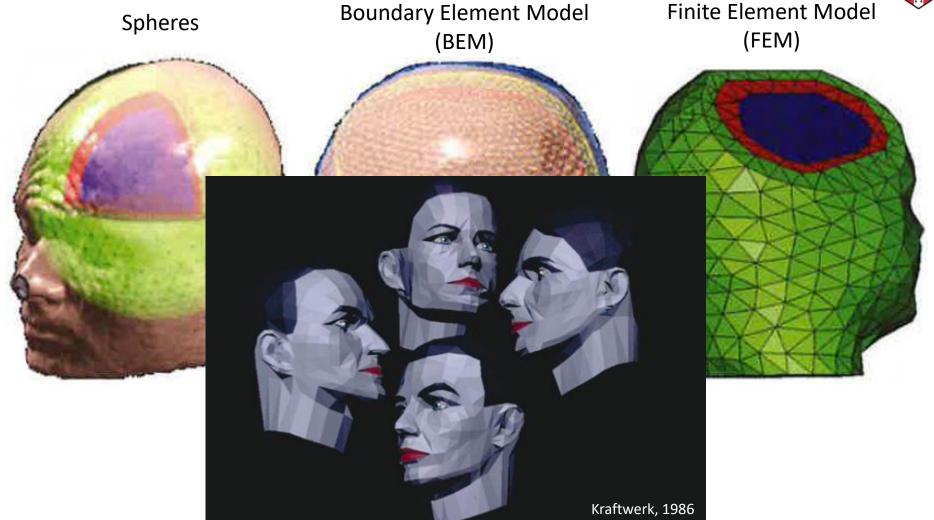




Head Models With Different Levels of Detail







More Complex Head Models

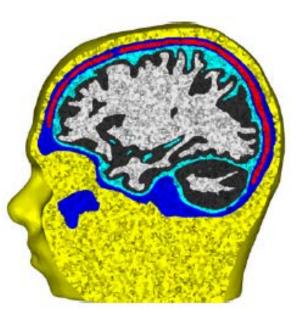
Cognition and Brain Sciences Unit

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

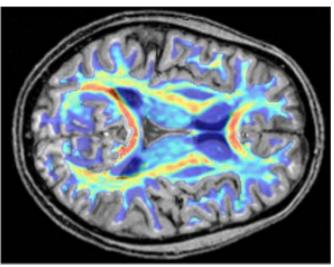
For MEG-only, single shell BEMs and local/corrected sphere models can provide reasonable approximations.

But heads are more complex:

White Matter
Gray Matter
CSF
Skull Compacta
Skull Spongiosa
Skin



Fractional Anisotropy



Vorwerk et al., NI 2014, https://pubmed.ncbi.nlm.nih.gov/24971512/

It is not obvious how to translate this into more accurate estimate for conductivity distributions. FEM Software e.g. https://www.mrt.uni-jena.de/simbio/index.php.

Conductivities Of Tissues Can Only Be Approximated

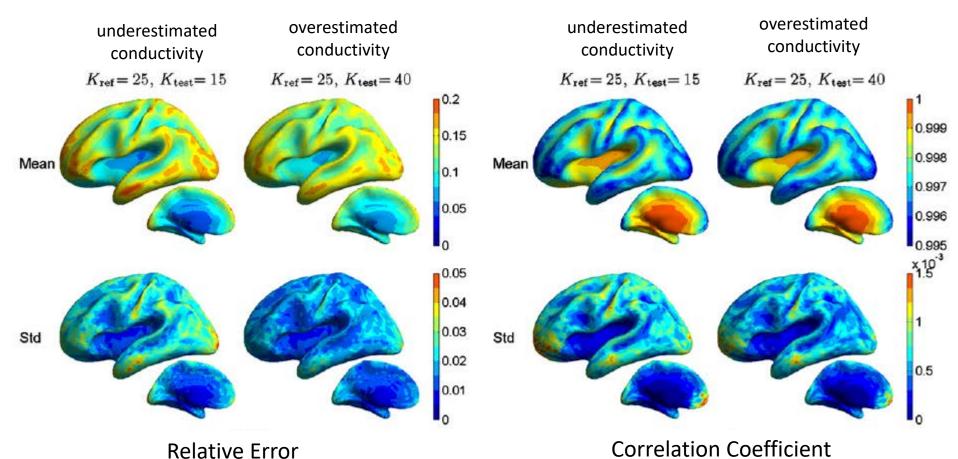


Table 2 Isotropic conductivity values of single tissue types used in human head volume conductor modeling

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

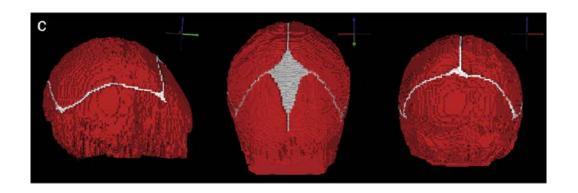
Boundary Element Models Are Relatively Robust Against Conductivity Errors



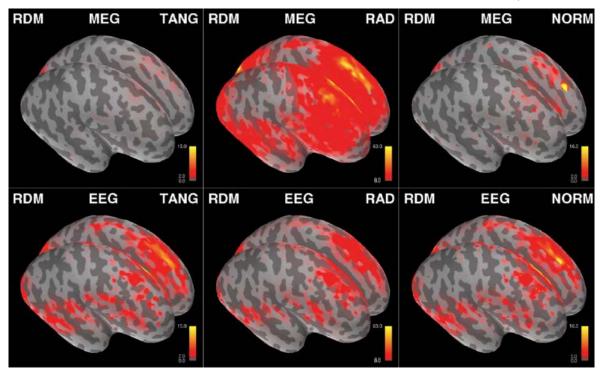


Infant Skulls – Fontanelles and Sutures





Relative error between models with and without fontanelles/sutures



Conclusion – Head Modelling

Cognition and Brain Sciences Unit

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

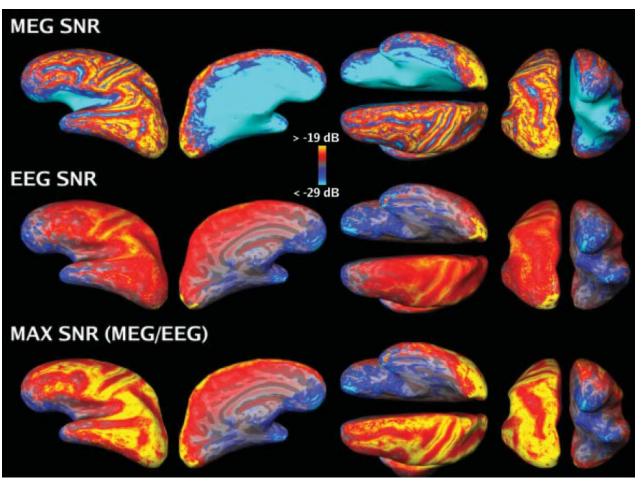
Single-shell approximations are still common for MEG.

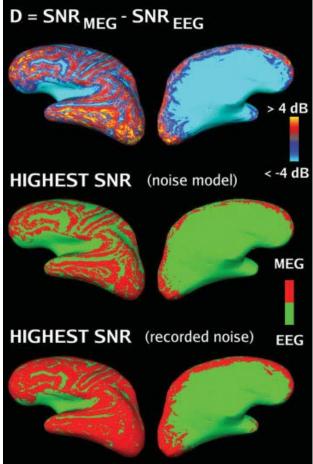
More detailed head models may increase accuracy, but require more accurate data and information, such as accurate MRI segmentations and conductivity values. (See e.g. Vorwerk et al., BioMeg Eng Online 2018) for Fieldtrip FEM pipeline)

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

Sensitivity of EEG and MEG



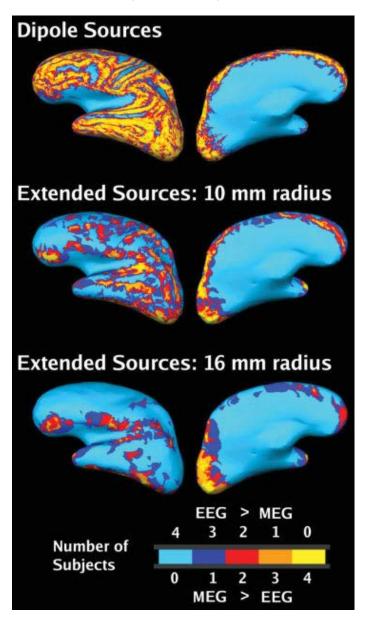




Cogn and Scient



MEG Is Less Sensitive To Spatially Extended Sources Than EEG



Solutions To The Inverse Problem – Source Estimation

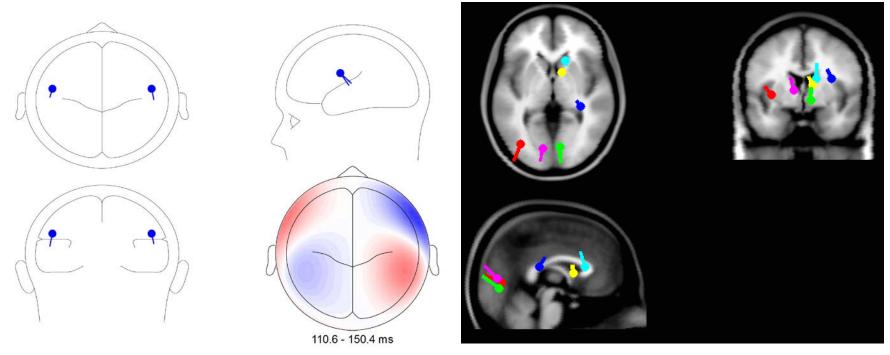


Hypothesis Testing - Dipole Fitting

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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.

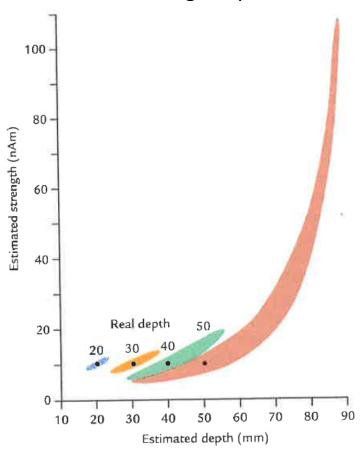
Solutions for several/many dipoles can get stuck in local minima, and may not be robust to noise.

Assumptions Cannot Completely Remove Uncertainty





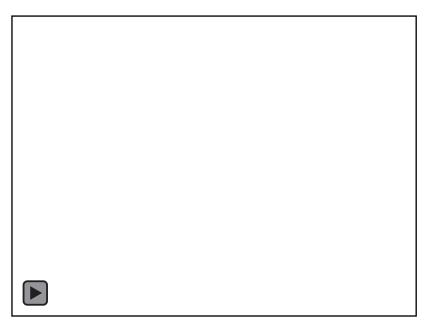




Dipole Scanning



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" (more on that later).

"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:

 $\mathbf{w}_i^T \mathbf{f}_i$

 $\mathbf{w}_{i} = \frac{\mathbf{f}_{i}^{T} \mathbf{C}^{-1}}{\mathbf{f}_{i}^{T} \mathbf{C}^{-1} \mathbf{f}_{i}}$ Linearly-Constrained Minimum-Variance (LCMV) Beamformer

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

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.

Beamformers



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").

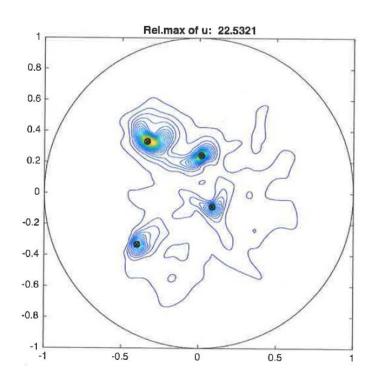
Beamformers result in linear transformations of the data ("spatial filters"), but those transformations strongly depend on the data of interest.

=> Beamformer performance doesn't necessarily generalise across studies, or even different analyses of the same data.

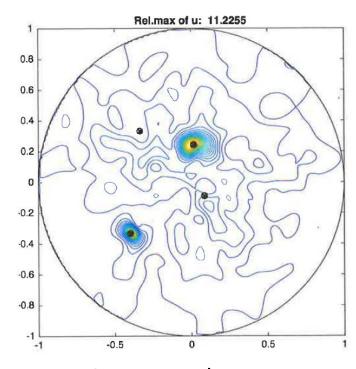
Beamforming Is Problematic For Highly Synchronous Sources







4 non-synchronous sources

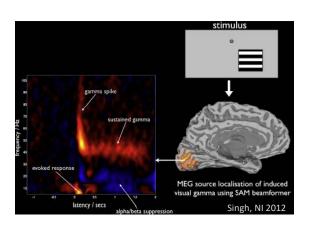


2 non-synchronous,2 synchronous sources

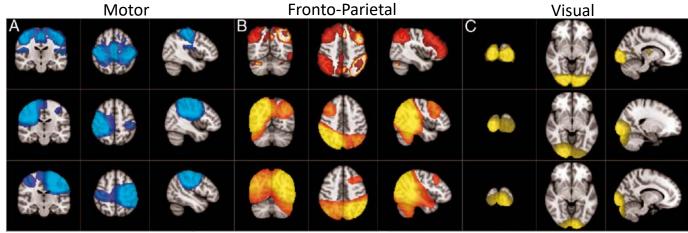
Beamformers Are Popular for Rhythmic Brain Activity and Resting State Activity







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





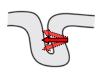
Source Orientation Constraints

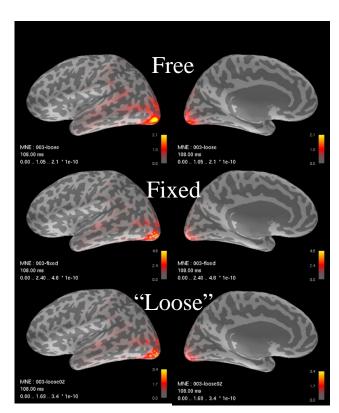










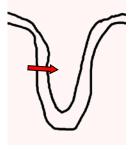


Direction of Current Flow

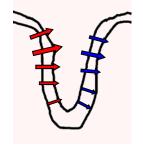




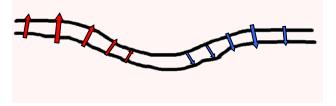




Distributed Source



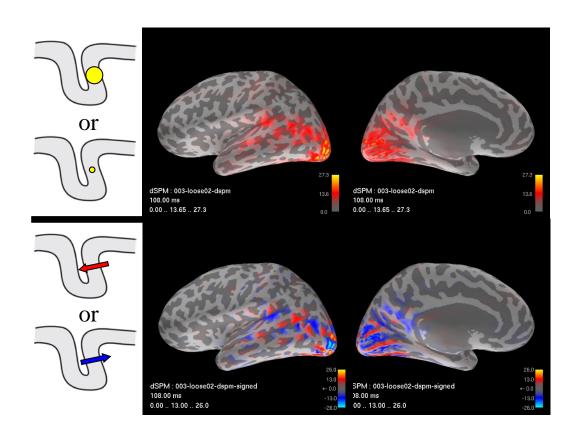
Distributed Source, Inflated Surface



Direction of Current Flow







Minimum Norm Estimation Of Distributed Sources



$$Ls = d \Rightarrow ||Ls - d||^2 = 0$$
(ignore noise for now)
subject to constraint

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

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

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

with

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

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

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



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

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

For example:

$$x_1 + 2x_2 = 1$$

L2 solution: (0.2, 0.4) L2-norm 0.2²+0.4²~0.45, L1-norm 0.2+0.4=0.6

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

There Are Different Optimisation Criteria: Bayesian Approach





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

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

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?

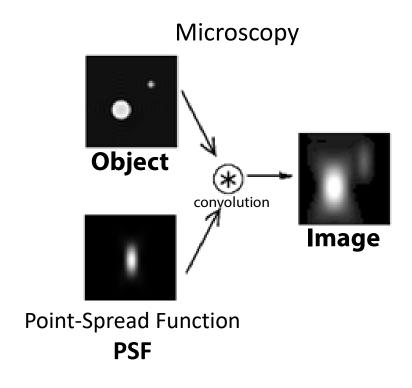
Let's Start Again: The "Blurry Image" Analogy

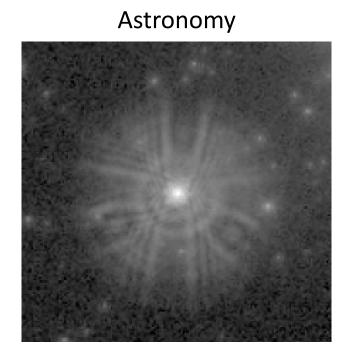




The Superposition Principle

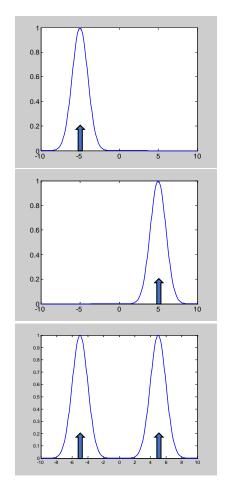


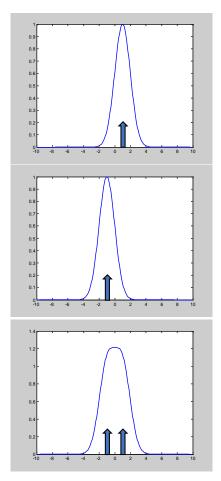




Linear Methods Can Easily Tell Us If They Do What We Want Superposition Principle







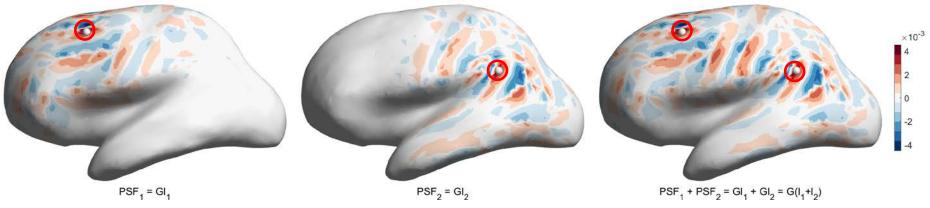
If you know the behaviour for point sources, you can predict the behaviour for complex sources

Linear Methods – Superposition Principle

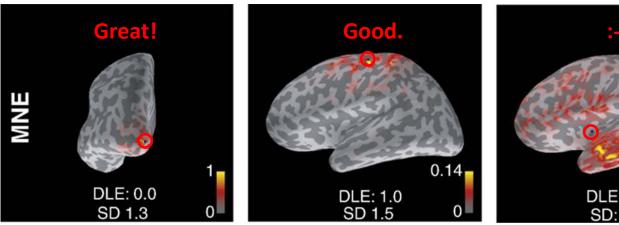


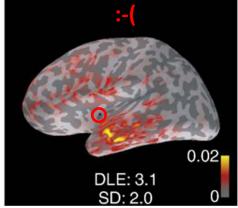


Superposition In Source Space



Example Point-Spread Functions





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





Spatial resolution depends on:

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

=> difficult to make general statement

Spatial Resolution – A Naïve Estimate



With *n* sensors:

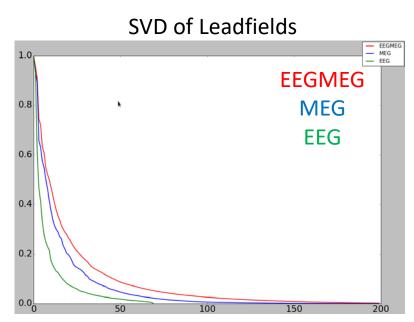
- -> *n* independent measurements
- -> *n* independent parameters estimable
- \rightarrow at best separate activity from n brain regions

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

Volume of source space:

Sphere 8cm minus sphere 4 cm: volume ~1877 cm³

"Resel": $38 \text{ cm}^3 -> 3.4^3 \text{ cm}^3$



Resolution Matrix





$$\hat{\mathbf{s}} = \mathbf{GLs} \stackrel{\text{def}}{=} \mathbf{Rs}$$

Relationship between estimated and true source distribution.

Creating 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:

$$||R - I||_2 = min$$

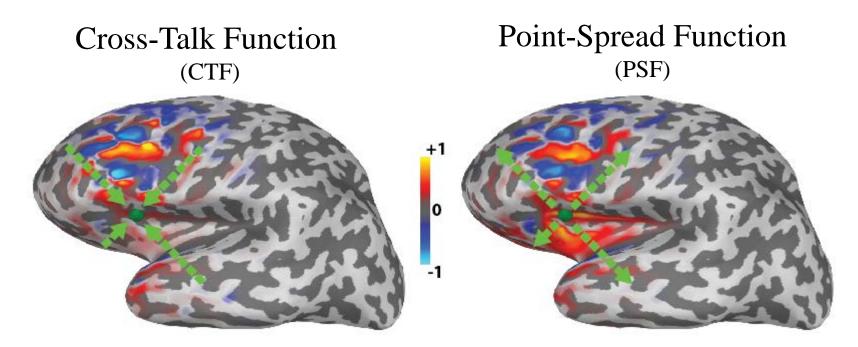
This leads to the **Minimum Norm Estimator (MNE)**:

$$\boldsymbol{G_{MN}} = \mathbf{L}^T (\mathbf{L} \mathbf{L}^T)^{-1}$$

Spatial Resolution / Leakage:

Point-Spread and Cross-Talk





How other sources may affect the estimate for this source "Leakage from"

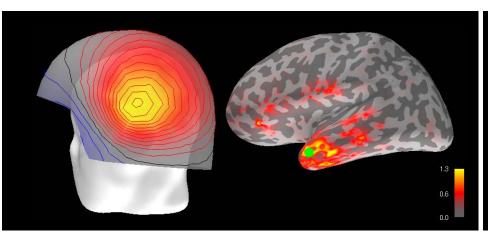
How this source affects estimates for other sources "Leakage to"

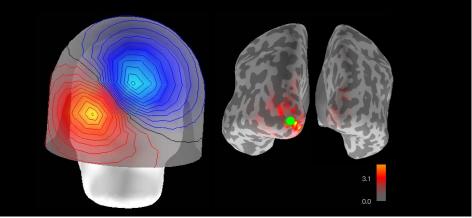
For the L2-MNE estimator, PSFs and CTFs are the same, but beware: this is not the case for other estimators.

PSFs and CTFs for Some ROIs

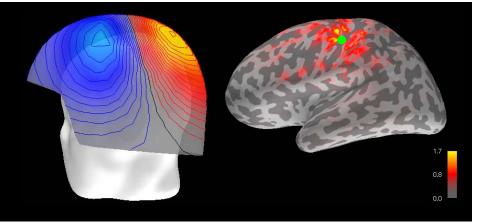
For MNE, PSFs and CTFs turn out to be the same

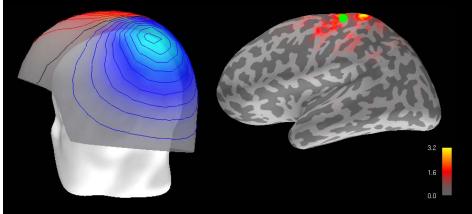






Good

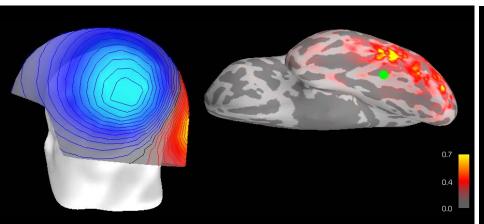


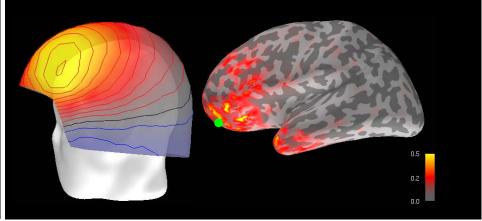


PSFs and CTFs for Some ROIs

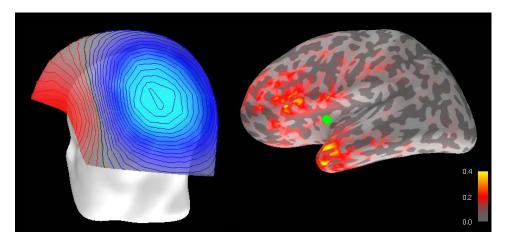
For MNE, PSFs and CTFs turn out to be the same







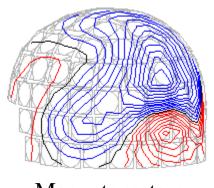
Less good

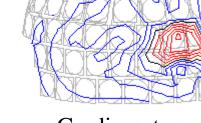


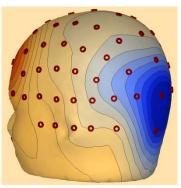
Real example: Visually Evoked Activity ~100 ms







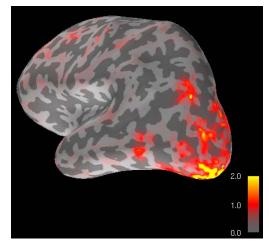




Magnetometers

Gradiometers

EEG

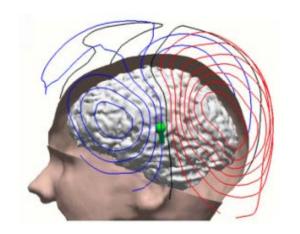


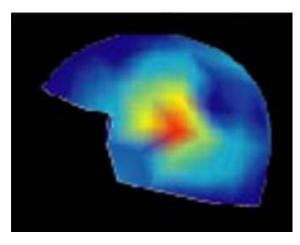
Minimum Norm Estimate

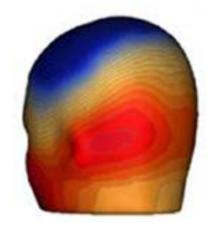
Real example: Auditorily Evoked Activity

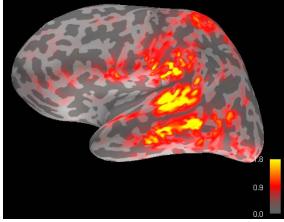








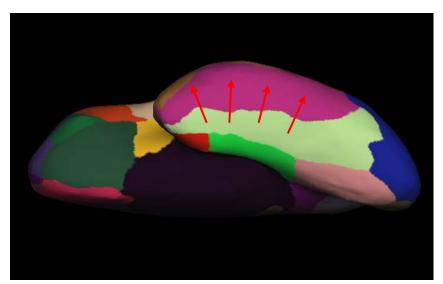




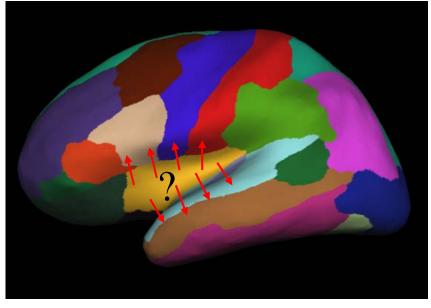
Minimum Norm Estimate

Localisation Bias Has Consequences for ROI analysis

PSFs/CTFs Can Tell You How It Looks Like

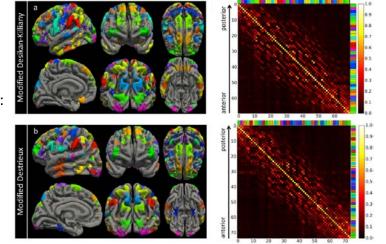


Desikan-Killiany Atlas parcellation



MRC

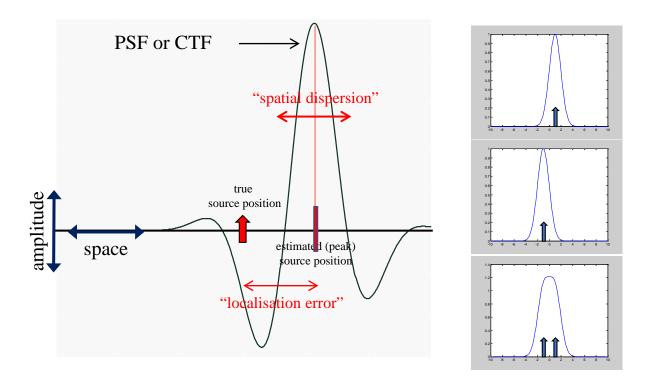
Adaptive cortical parcellation based on resolution matrix are possible: Farahibozorg/Henson/Hauk NI 2018 https://pubmed.ncbi.nlm.nih.gov/28893608/



PRmat

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

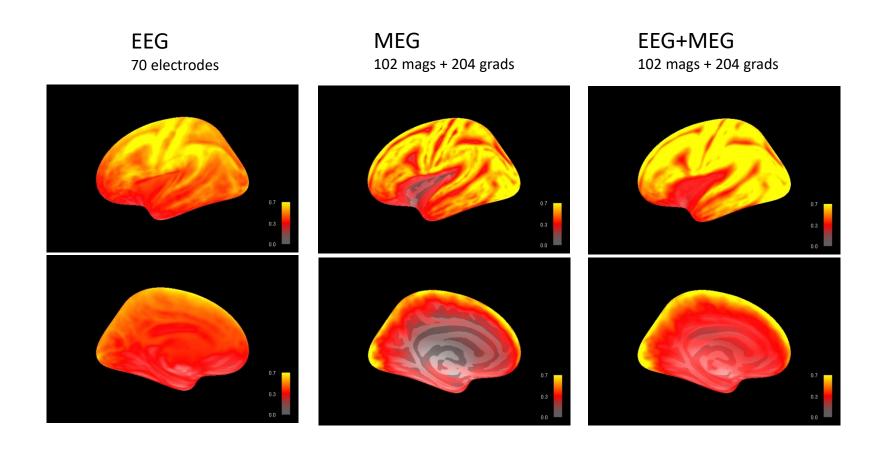


- **MEG+EEG**: Elekta Vectorview (360+70 channels), Wakeman & Henson open data set
- Whitened leadfields and data to combine sensor types
- Methods Comparison:
 - L2-MNE
 - depth-weighted L2-MNE
 - dSPM
 - sLORETA
 - 2 LCMV beamformers (pre- and post-stimulus covariance matrices)
- Resolution Metrics: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

Sensitivity Maps

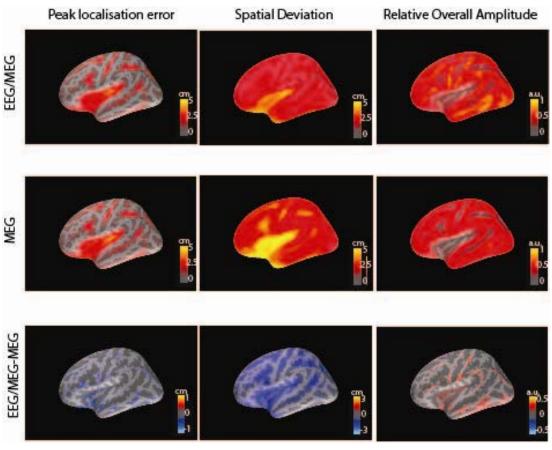
RMS of Leadfield Columns





Combining EEG And MEG Improves Spatial Resolution





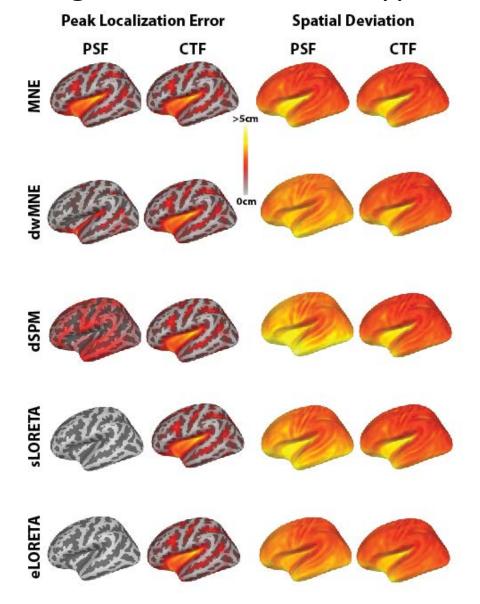
Hauk/Stenroos/Treder, bioRxiv 2019 | see also Molins et al., NI 2008

Comparing Estimators – MNE-type methods



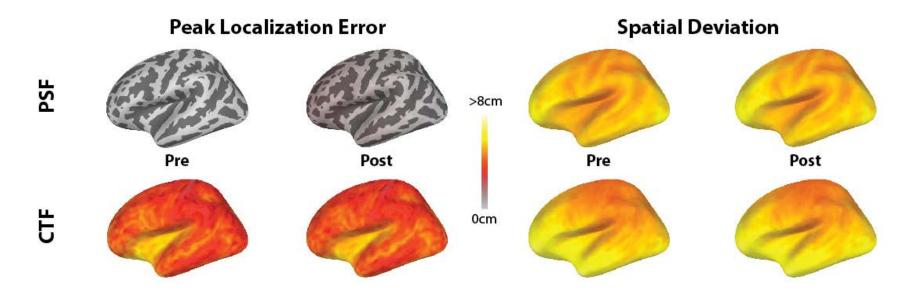
Comparing Estimators – MNE-type methods





Comparing Estimators – Beamformers





Interim Conclusion From Methods Comparison



- Methods vary with respect to localisation error and spatial deviation.
- Improvements in localization error are accompanied by increases in spatial deviation.
- Localisation error for PSFs can be minimised (even to zero), but not for CTFs.
- Spatial deviation for PSFs and CTFs cannot be minimised beyond a certain limit.
- Localisation error for beamformers is low (even zero), but spatial deviation higher than for MNE-type methods.
- Performance of beamformers similar for different covariance matrices.
- ⇒There is no obvious "best method".
- ⇒In this analysis, MNE and eLORETA seem to offer the best compromise between localisation and spatial deviation.
- ⇒The tools (PSFs/CTFs, resolution metrics) can be applied to individual datasets try it yourself!

Noise and Regularisation

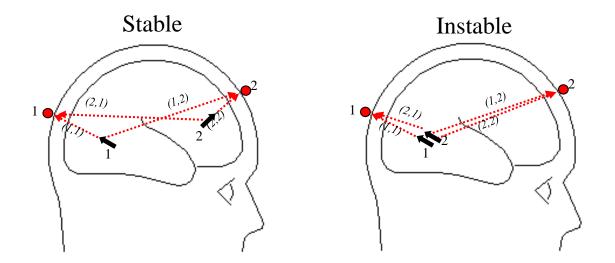


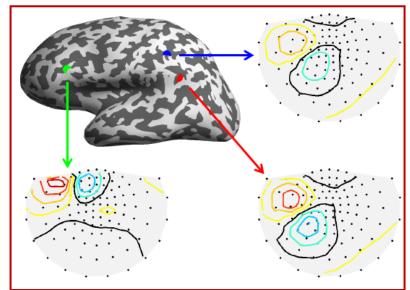


(In)Stability – Sensitivity to Noise



MRC





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.

Leaving Variance Unexplained



$$\mathbf{L}\mathbf{s} = \mathbf{d} + \mathbf{\varepsilon} \Rightarrow \|\mathbf{L}\mathbf{s} - \mathbf{d}\|^2 \le \mathbf{e}$$
, 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 **C**:

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

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

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

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

Whitening and Choice of Regularisation Parameter



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

can also be written as

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

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 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.







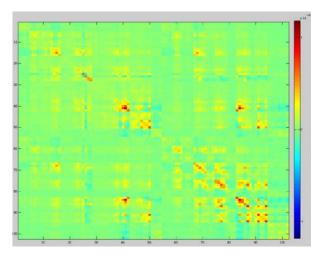
Some channels are noisier than others

⇒They should get different weights in your analysis

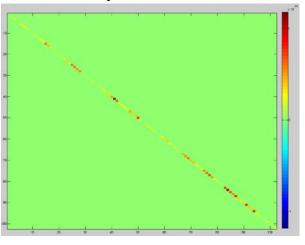
Sensors are not independent

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

(Full) Noise Covariance Matrix



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

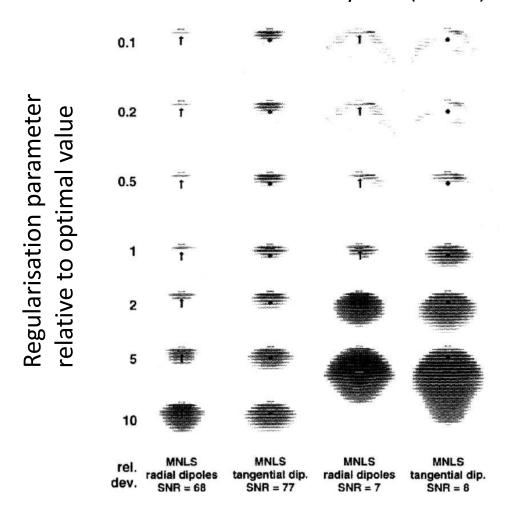


Trade-off norm-variance, smoothness





Source at fixed excentricity 71% (60mm)





Thank you – see you tomorrow.

Please don't forget to provide feedback:

