EEG/MEG 2:

Spatial Resolution and Nonlinear Methods

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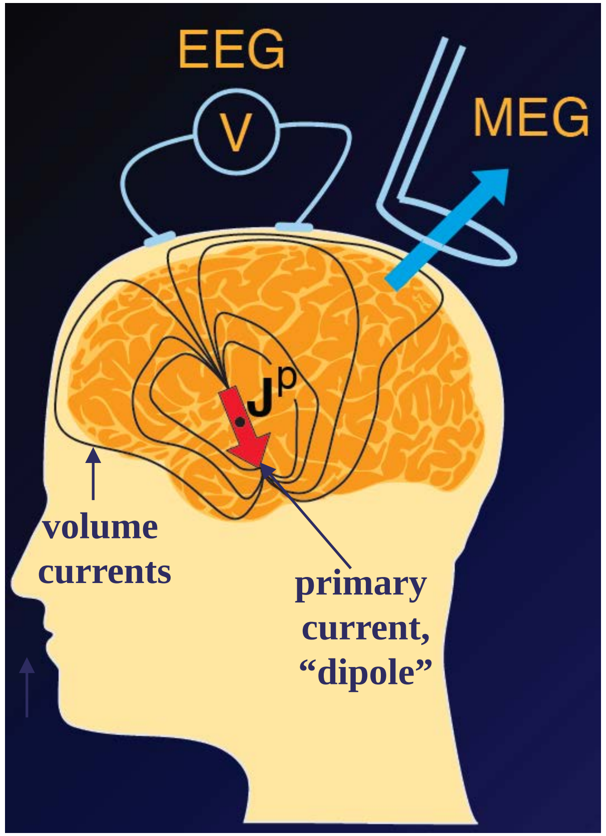
COGNESTIC 2022

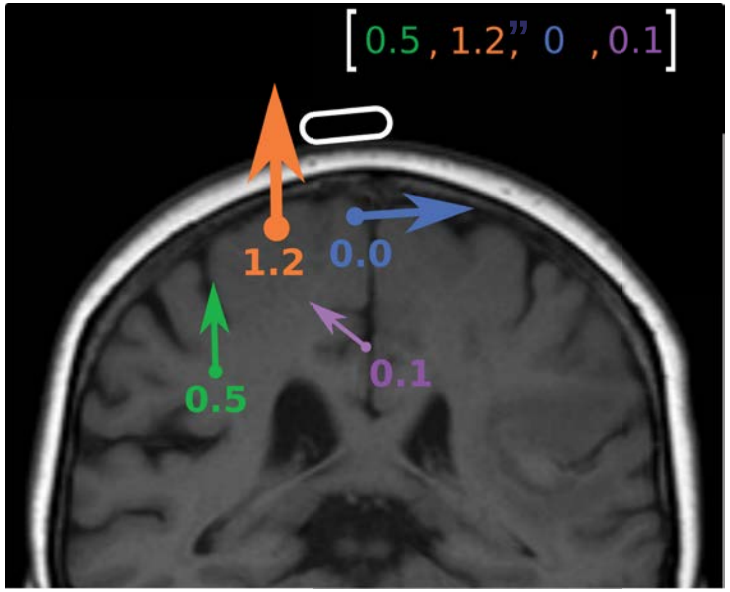
The EEG/MEG Forward Problem

EEG/MEG measure the primary sources indirectly



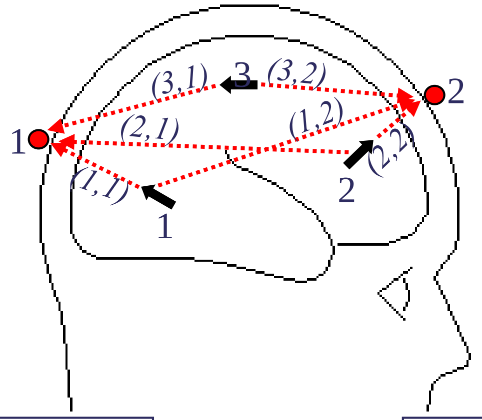
Sensors are differently sensitive to different sources

"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

data "leadfield" dipoles

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

?

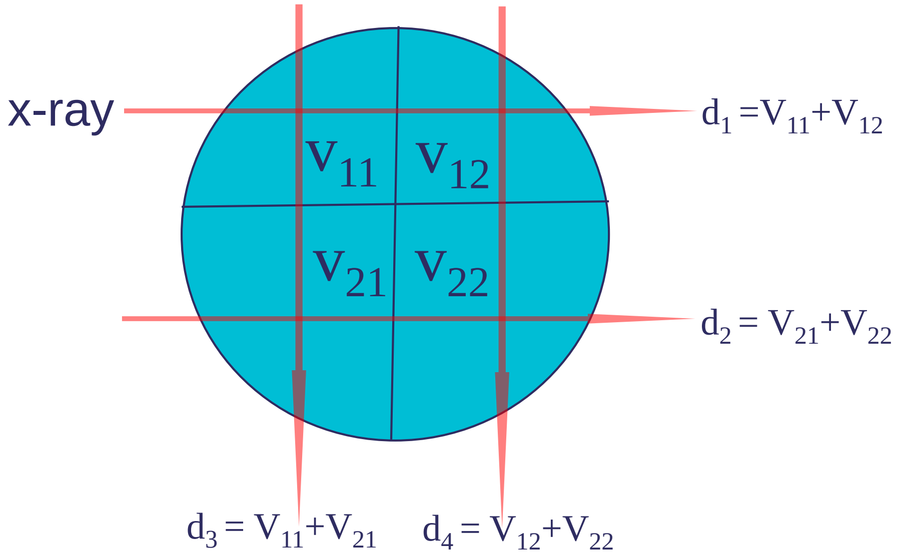
inversion

dipoles inverse data

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

EEG/MEG “Scanning” is not “Tomography”

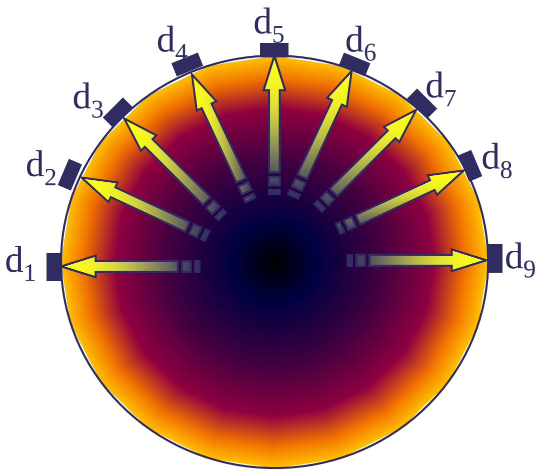
Tomography (CT, fMRI…)



$$d_1 = V_{11}+V_{12}$$
$$d_2 = V_{21}+V_{22}$$
$$d_3 = V_{11}+V_{21}$$
$$d_4 = V_{12}+V_{22}$$

Available information is determined by the equipment/experimenter

EEG/MEG



$$d_1 = V_{11}+V_{12}+V_{13}+V_{14} \ldots$$
$$d_2 = V_{21}+V_{22}+V_{23}+V_{24} \ldots$$

Information is lost during measurement

Cannot be retrieved by mathematics

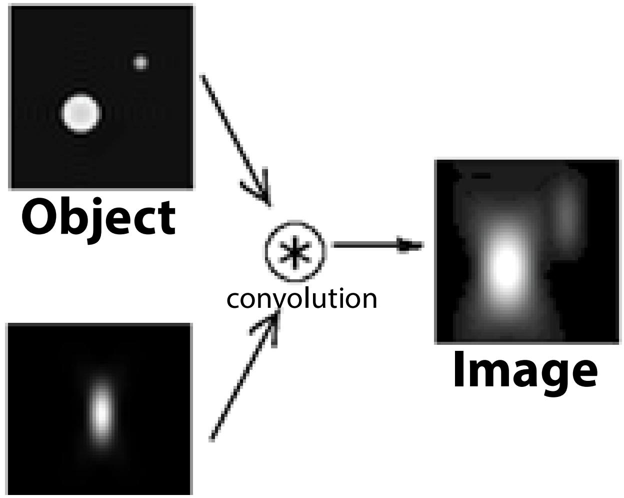
Inherently limits spatial resolution

Let’s Start Again:
The “Blurry Image” Analogy

Just because the brain is complicated doesn’t mean source estimation has to be complicated

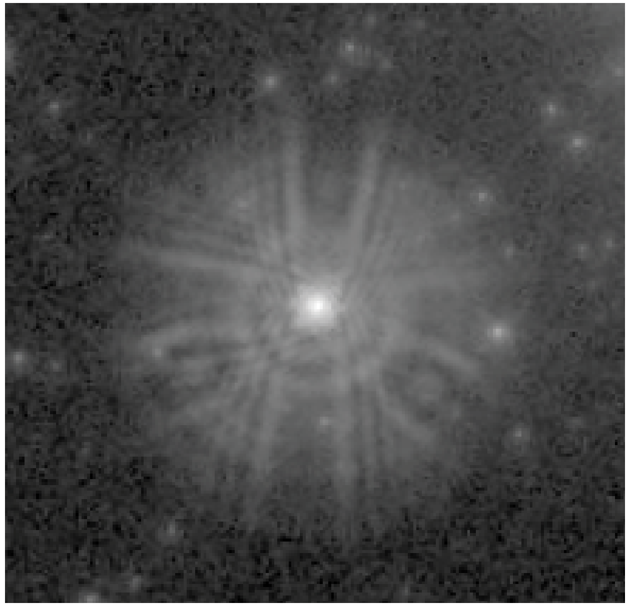
The Superposition Principle
A “Constraint-Free” Interpretation of Linear Methods

Microscopy



Point-Spread Function
PSF

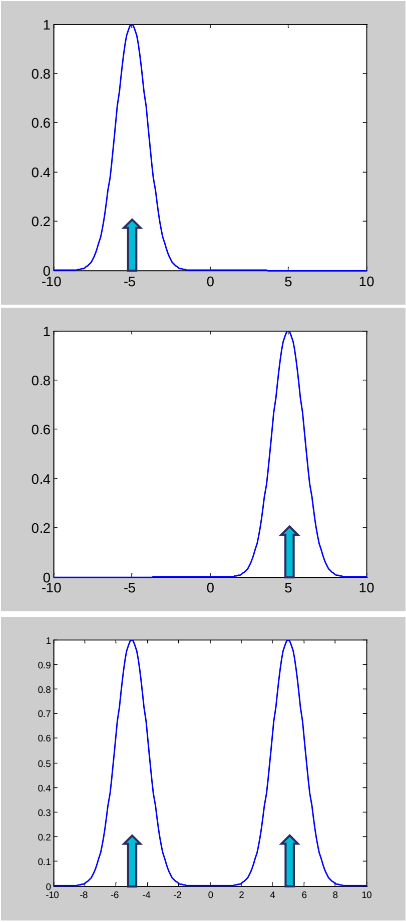
Astronomy

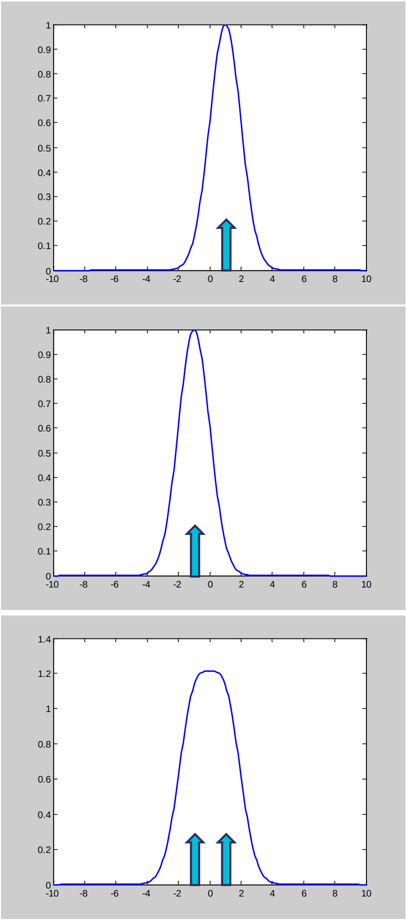


https://en.wikipedia.org/wiki/Point_spread_function

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

Superposition Principle

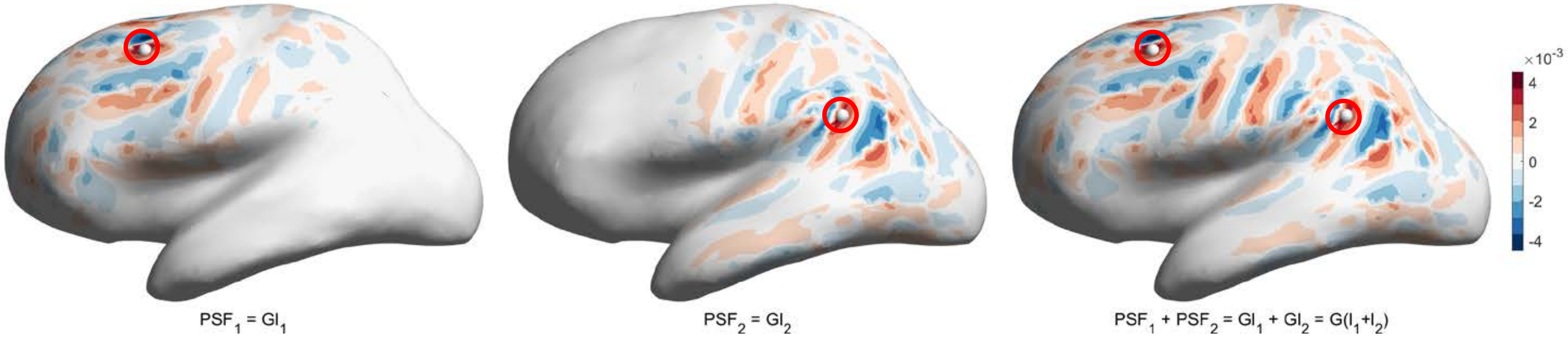




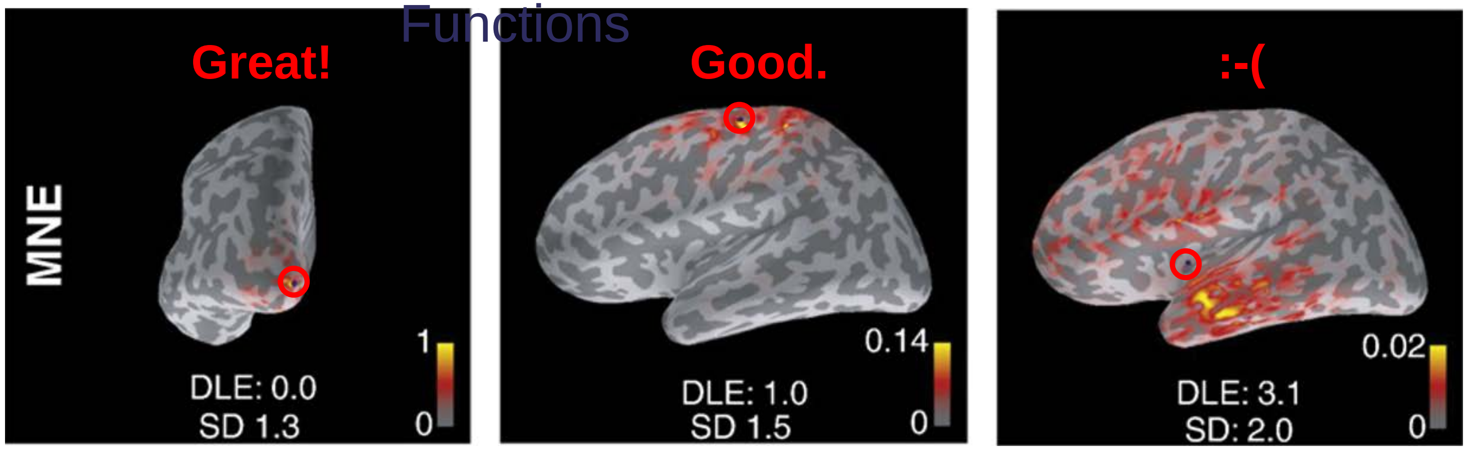
If you know the behaviour for point sources,
you can predict the behaviour for complex sources

Linear Methods – Superposition Principle

Superposition In Source Space



Example Point-Spread Functions



Hauk, Strenroos, Treder. In: Supek S, Aine C (edts), "Magnetoencephalography:

Spatial Resolution of Source Estimation Is Complex

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

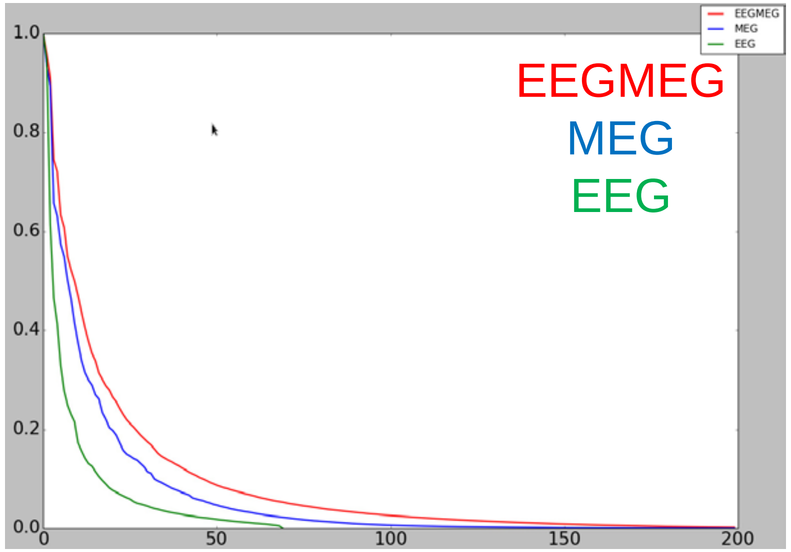
With ***n* sensors**:
-> *n* independent measurements
-> *n* independent parameters estimable
-> at best separate activity from *n* brain regions

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

Volume of source space:
Sphere 8cm minus sphere 4 cm: volume ~1877 cm^3

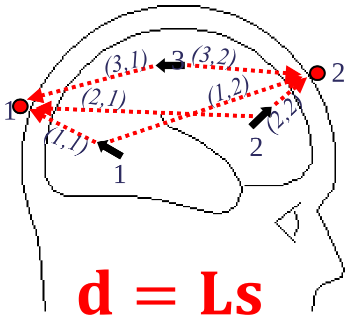
"Resel": 38 cm^3 -> $\underline{3.4}^3$ cm^3

SVD of Leadfields



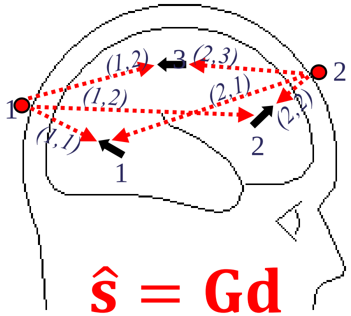
Resolution Matrix

Forward Problem



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

Linear Inverse Problem



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

$$\hat{\mathbf{s}} = \mathbf{G}\mathbf{L}\mathbf{s} \stackrel{\text{def}}{=} \mathbf{R}\mathbf{s}$$

Relationship between estimated and true source distribution.

e.g. Hauk/Stenroos/Treder, bioRxiv 2019
https://www.biorxiv.org/content/10.1101/672956v1

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:

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

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

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

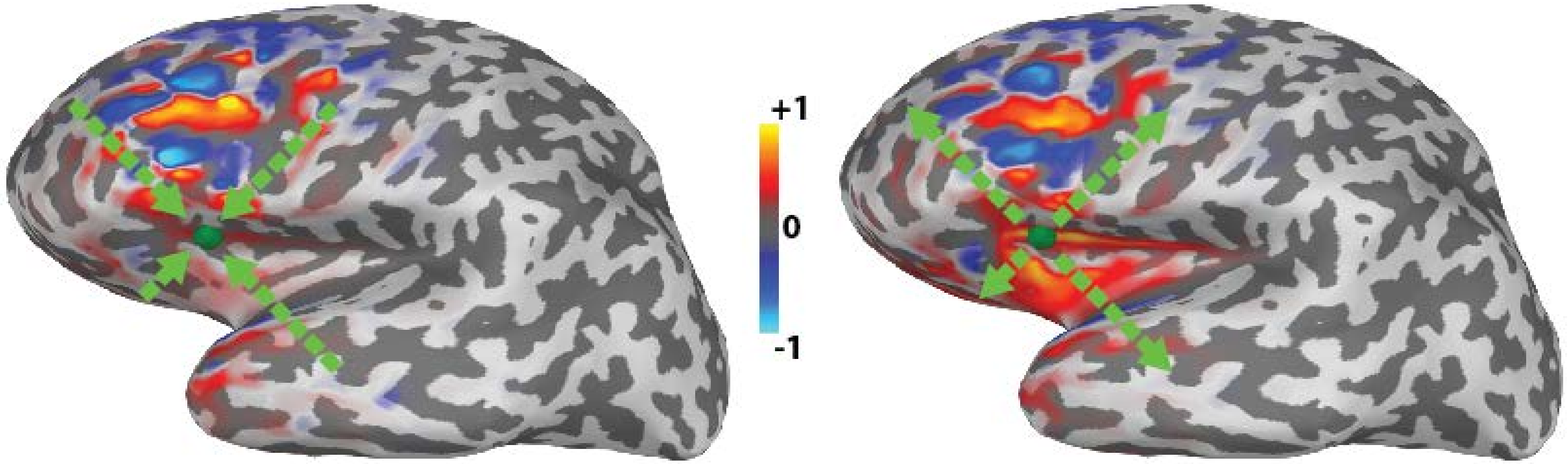
Its resolution matrix $\boldsymbol{R}_{\boldsymbol{MN}} = \mathbf{L}^T(\mathbf{L}\mathbf{L}^T)^{-1}\mathbf{L}$ is symmetric.

e.g. Hauk/Stenroos/Treder, bioRxiv 2019
https://www.biorxiv.org/content/10.1101/672956v1

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

Cross-Talk Function
(CTF)

Point-Spread Function
(PSF)



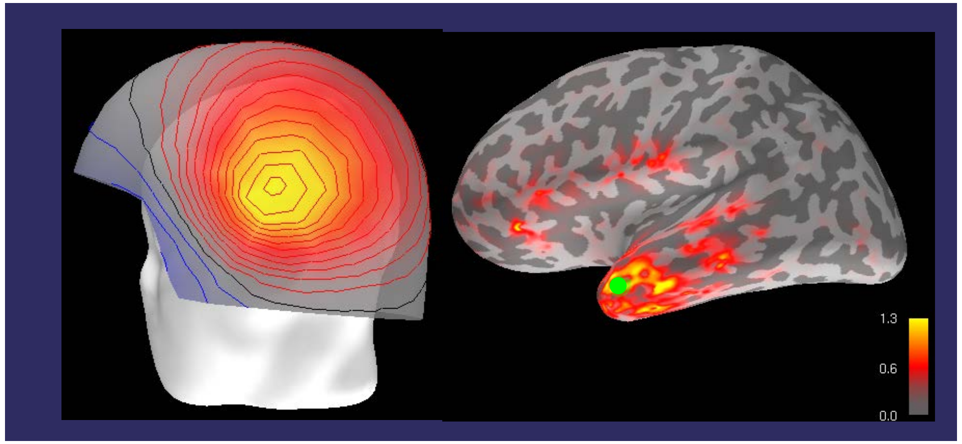
How other sources may affect the estimate for this source

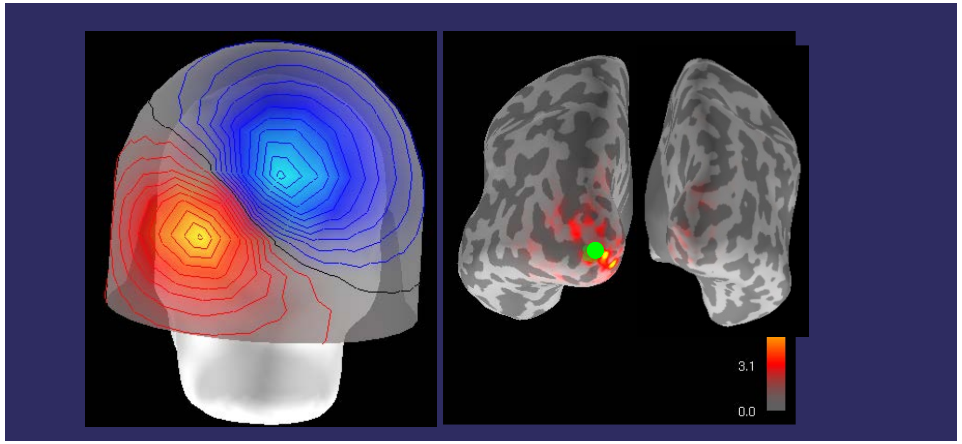
How this source affects estimates for other sources

e.g. Hauk, Stenroos, Treder, Neuroimage 2022
https://www.sciencedirect.com/science/article/pii/S1053811922002993

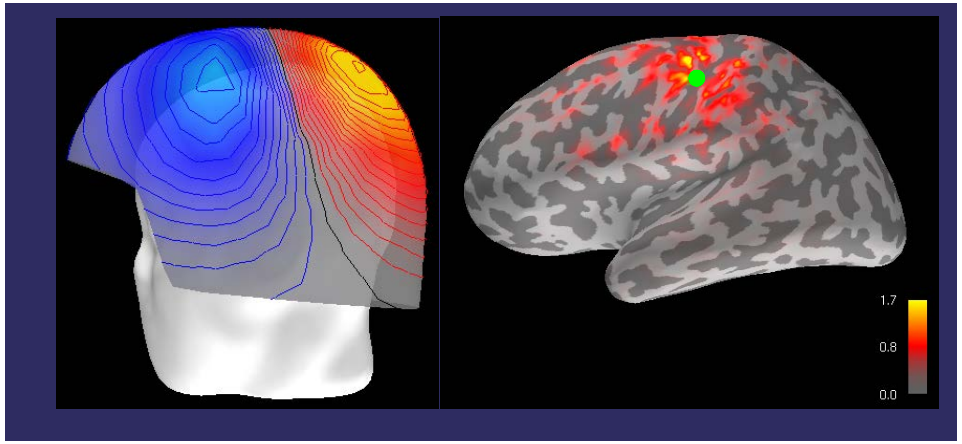
PSFs and CTFs for Some ROIs

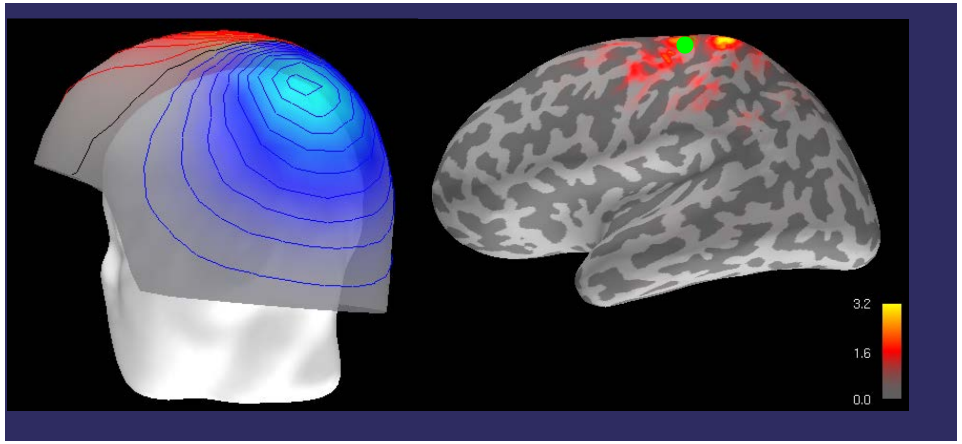
For MNE, PSFs and CTFs turn out to be the same





Good





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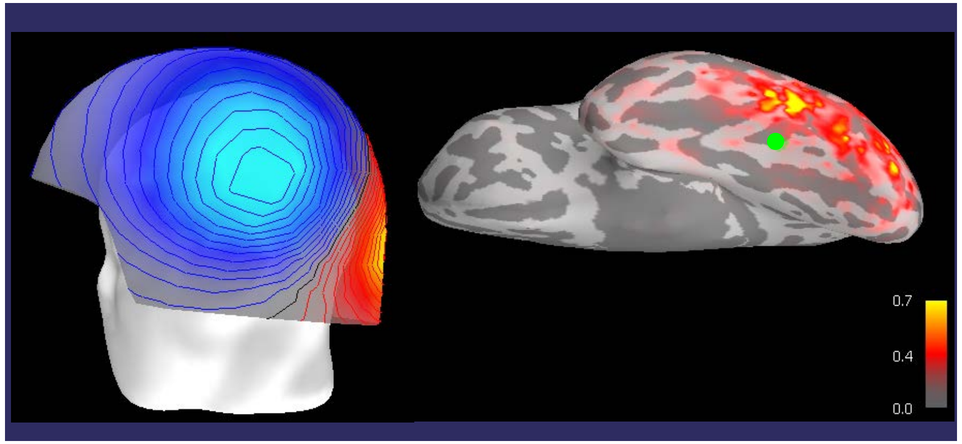
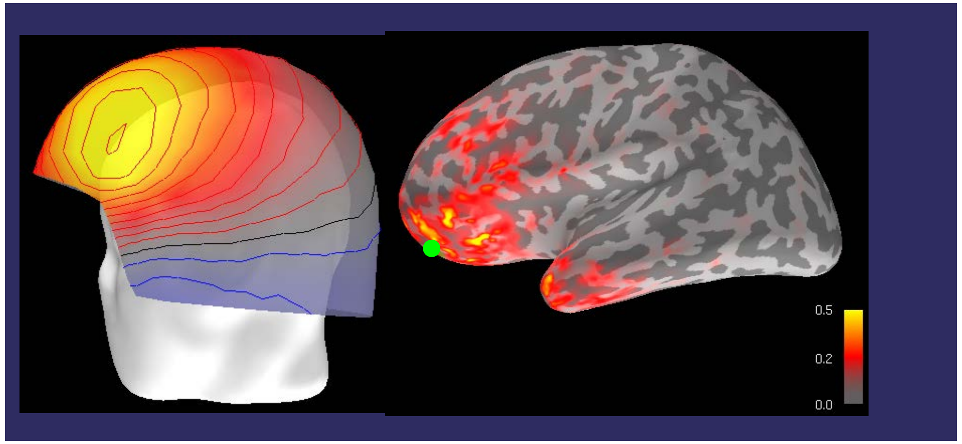
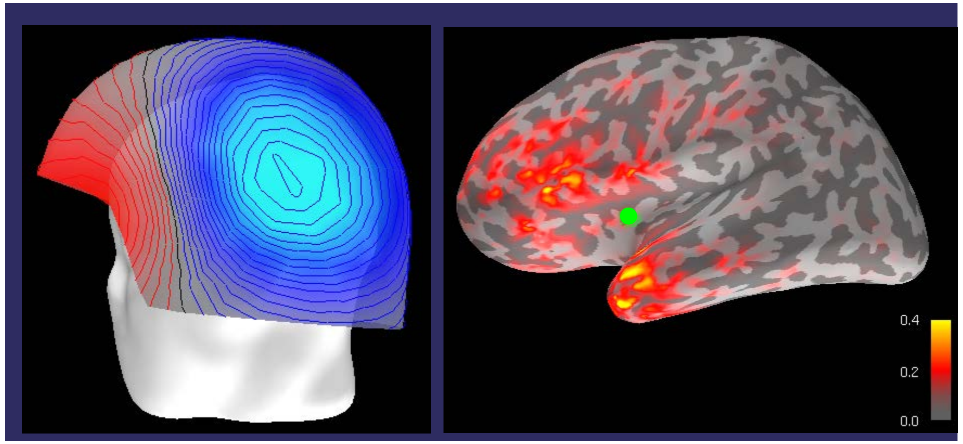


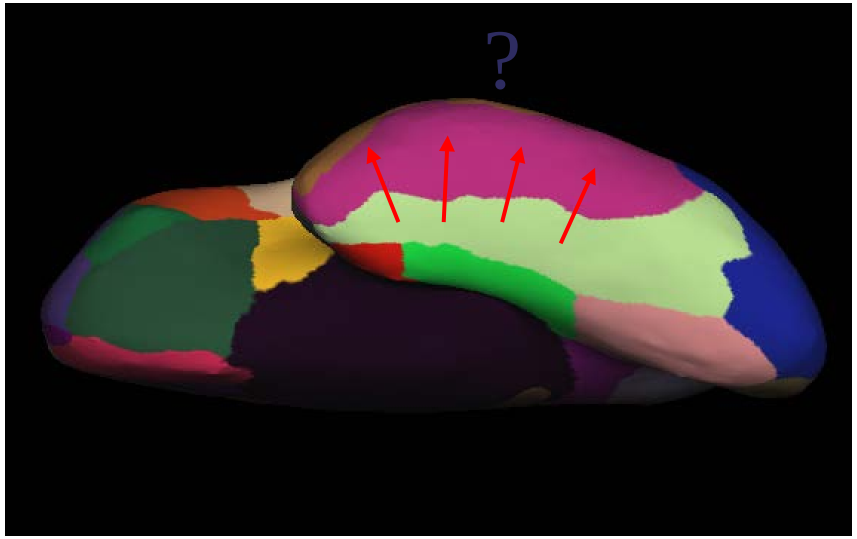


Less good

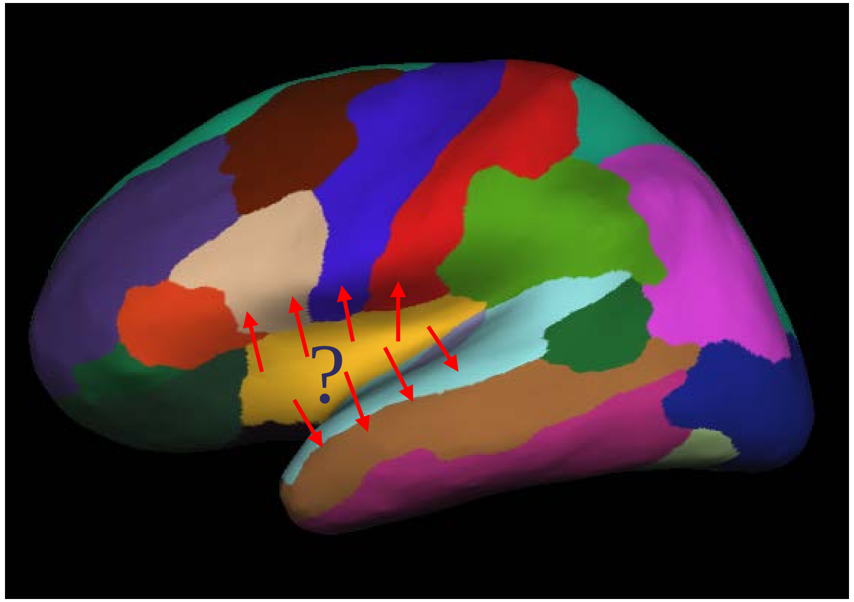


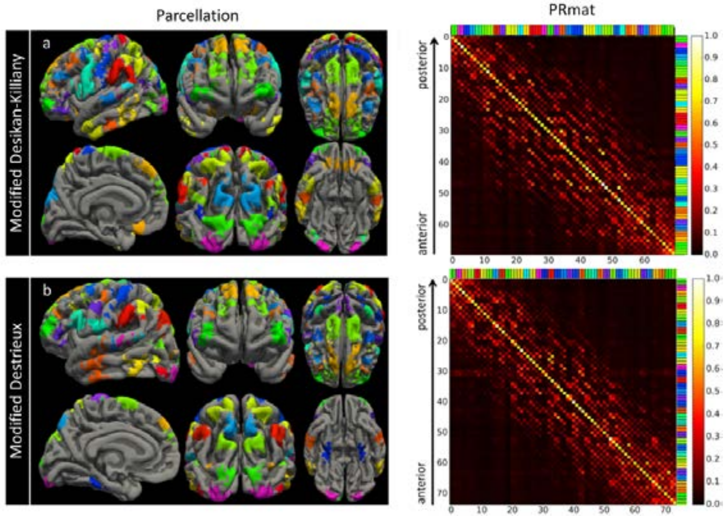
Localisation Bias Has Consequences for ROI analysis

PSFs/CTFs Can Tell You How It Looks Like



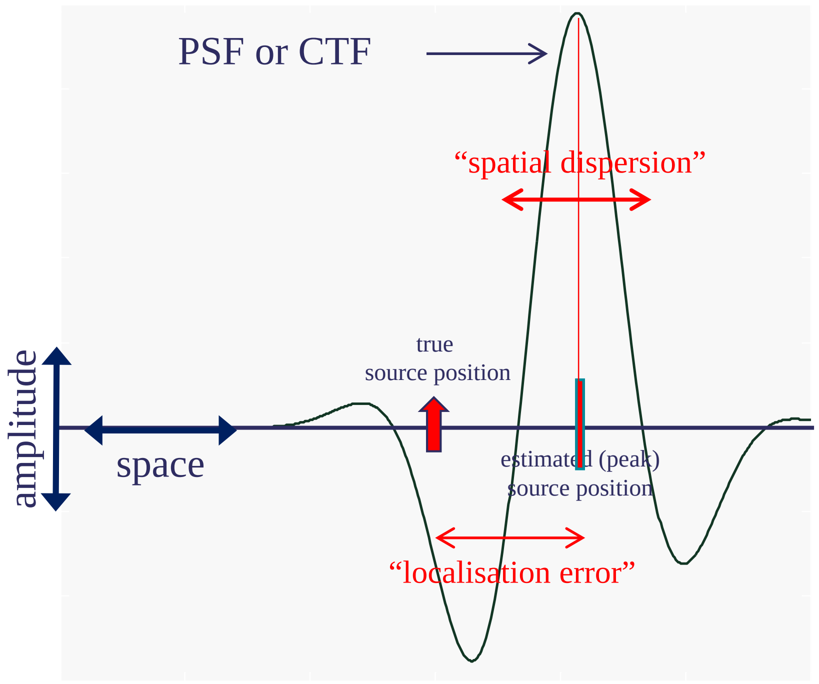
Desikan-Killiany Atlas parcellation

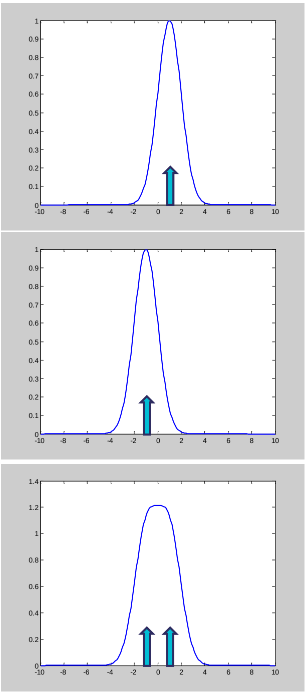




Adaptive cortical parcellation based on resolution matrix are possible: Farahibozorg/Henson/Hauk NI 2018 https://pubmed.ncbi.nlm.nih.gov/28893608/

Quantifying Resolution From PSFs and CTFs

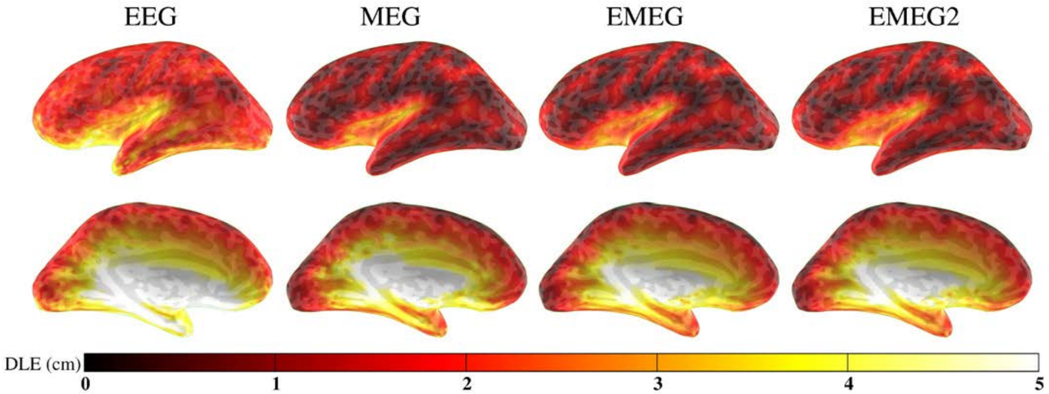




It's not just peak localisation that counts, but also spatial extent of the distribution.

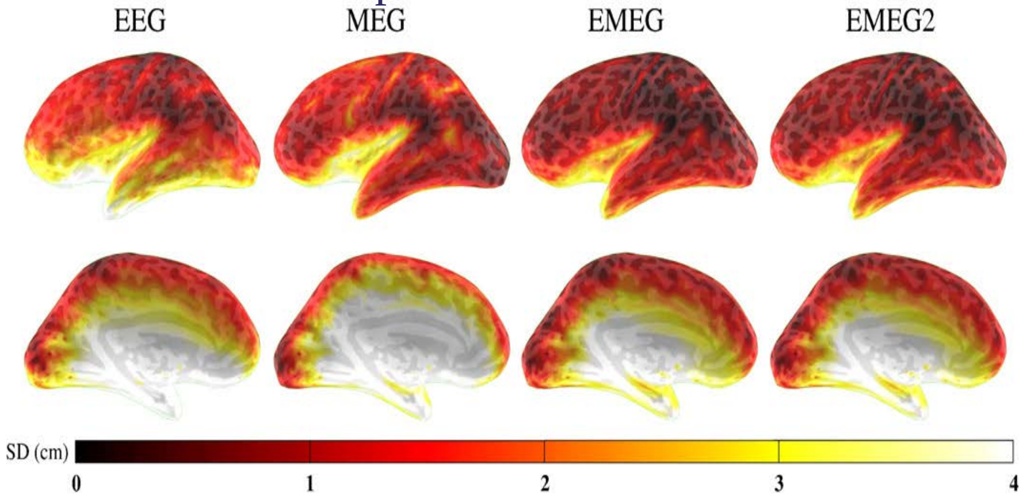
Whole-Brain Maps of Resolution Metrics

Peak Localization Error



Molins et al., Neuroimage 2008

Spatial Deviation



Combining EEG and MEG improves spatial resolution.

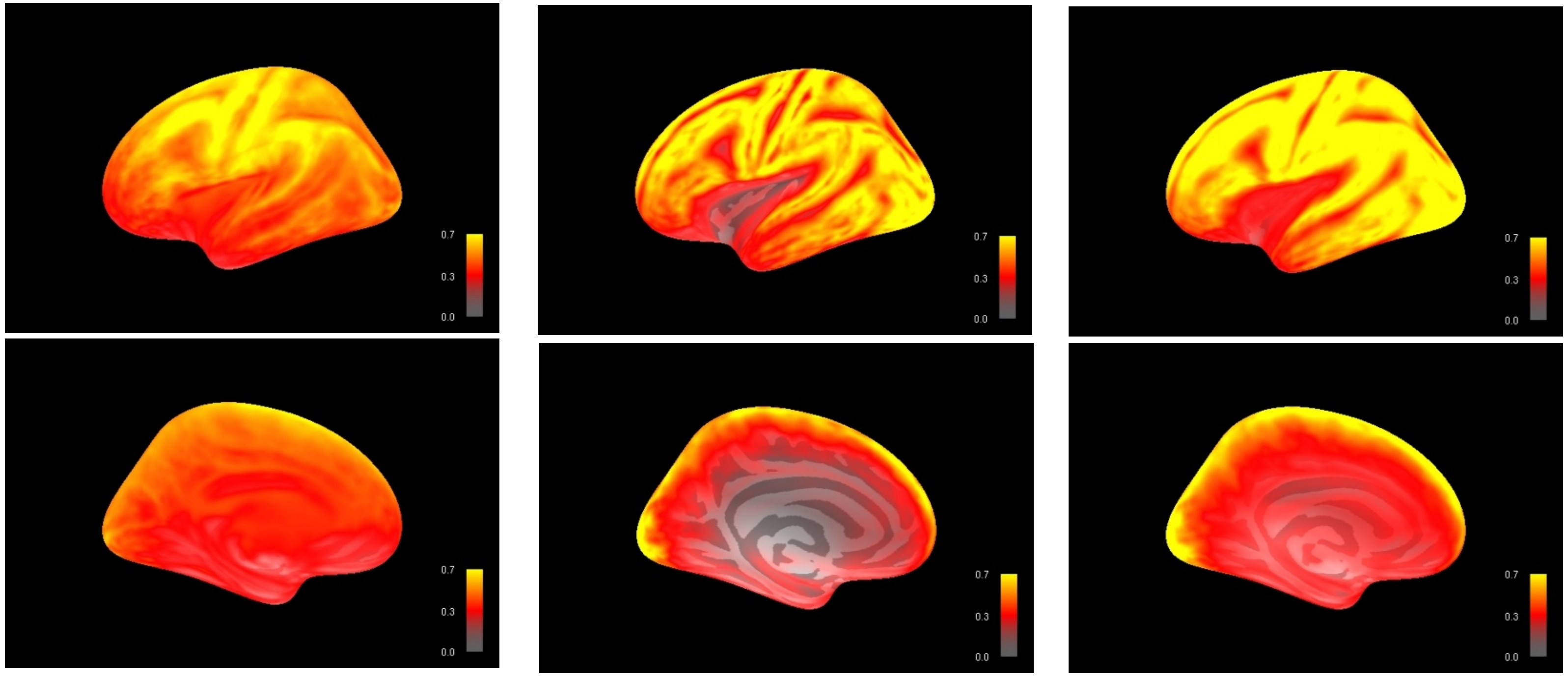
Sensitivity Maps

RMS of Leadfield Columns

EEG
70 electrodes

MEG
102 mags + 204 grads

EEG+MEG
102 mags + 204 grads



Combining EEG and MEG improves sensitivity.

Also: Goldenholz et al, HBM 2009

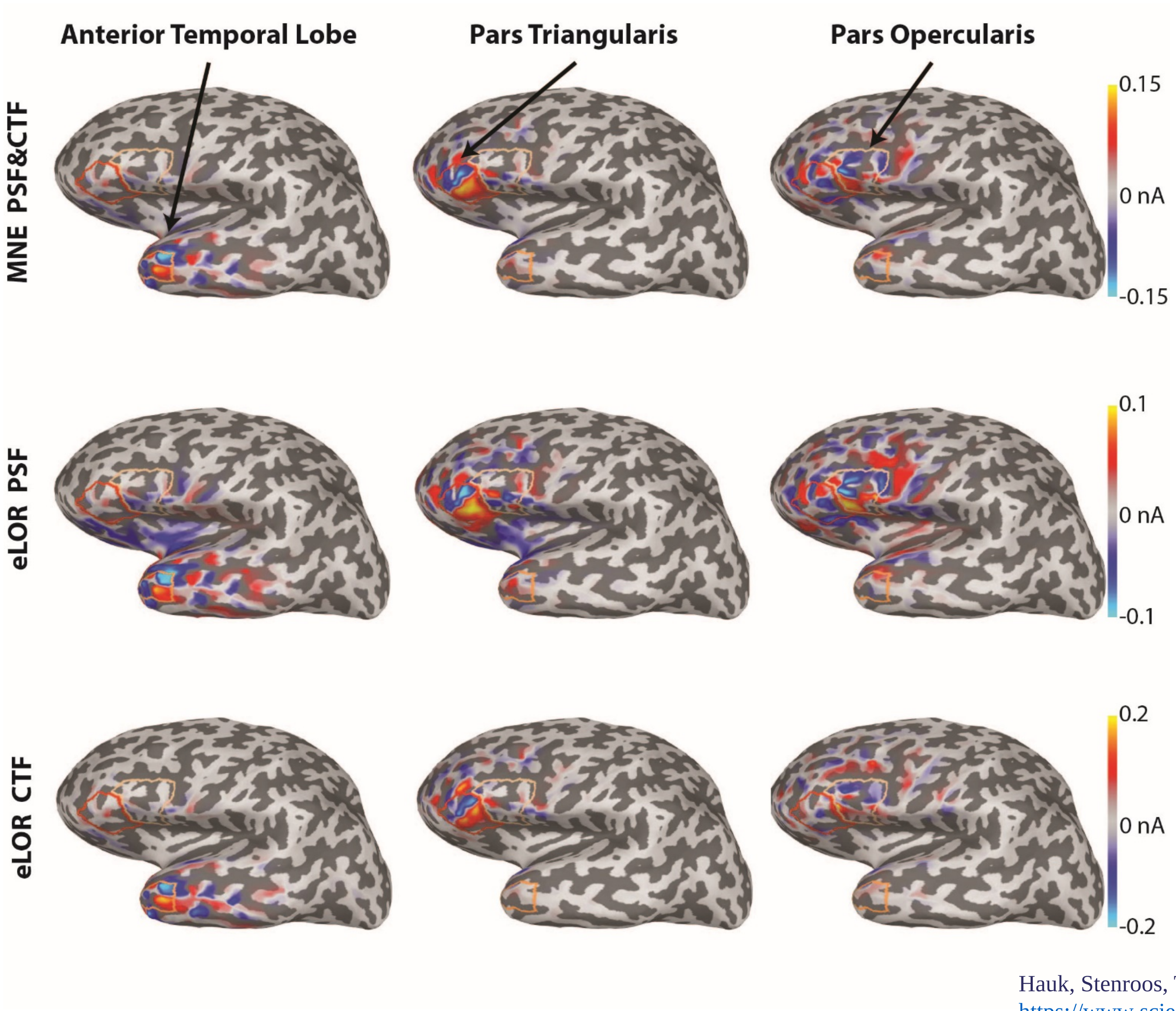
Methods Comparison

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

Hauk, Stenroos, Treder, Neuroimage 2022
https://www.sciencedirect.com/science/article/pii/S1053811922002993

Example PSFs and CTFs for MNE and eLORETA

Note: For MNE PSFs and CTFs are the same



Hauk, Stenroos, Treder, Neuroimage 2022
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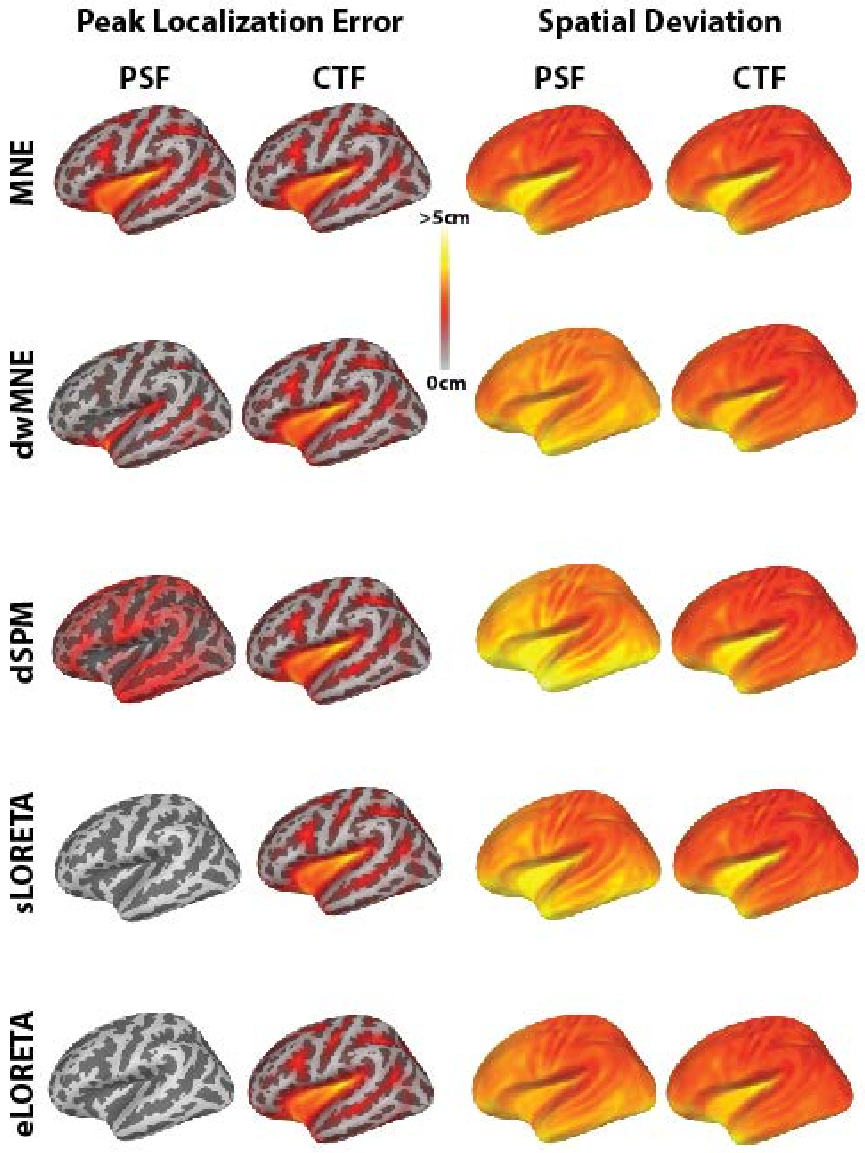
Comparing Estimators – MNE-type



Hauk, Stenroos, Treder, Neuroimage 2022
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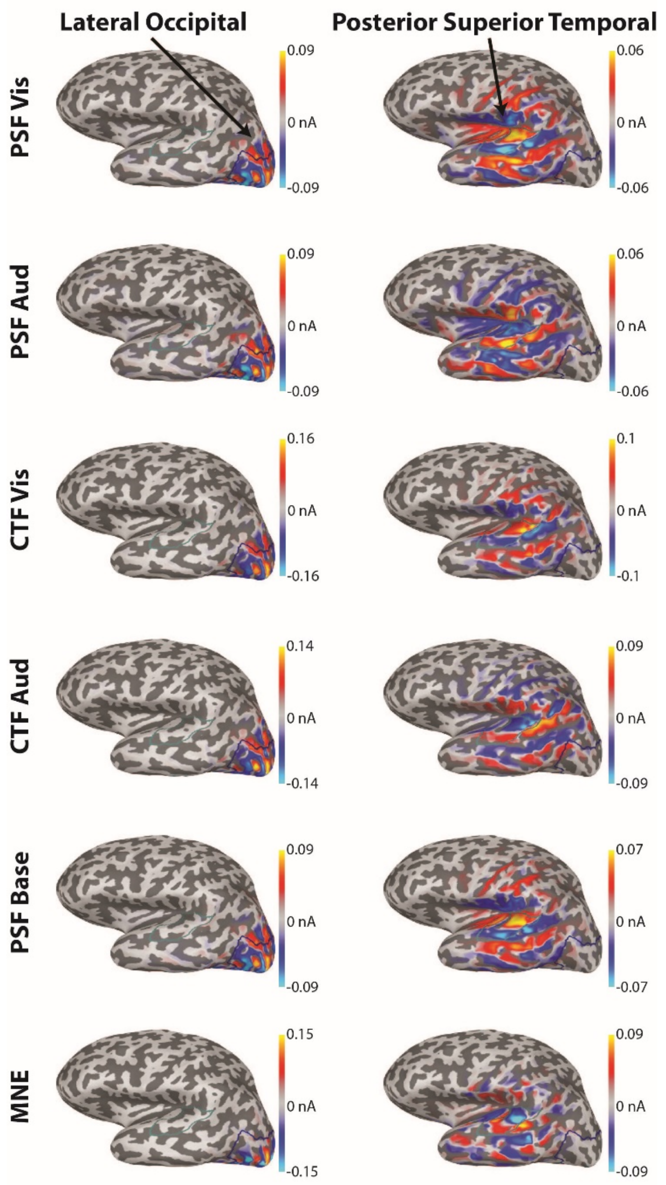
Example PSFs and CTFs for Beamformers



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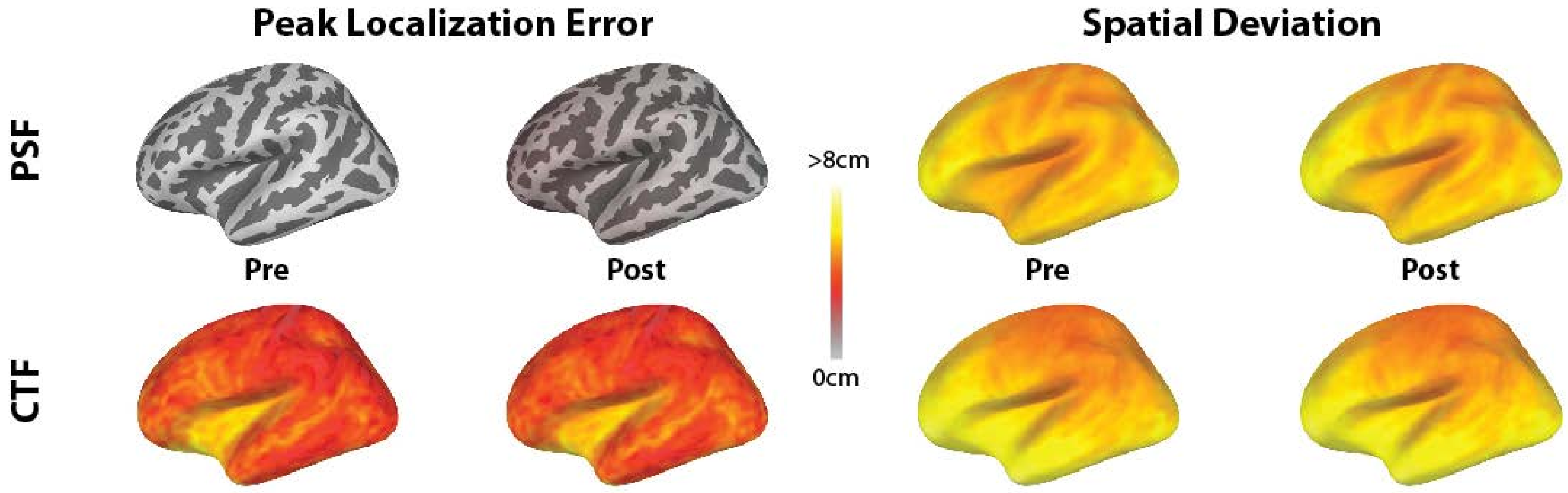
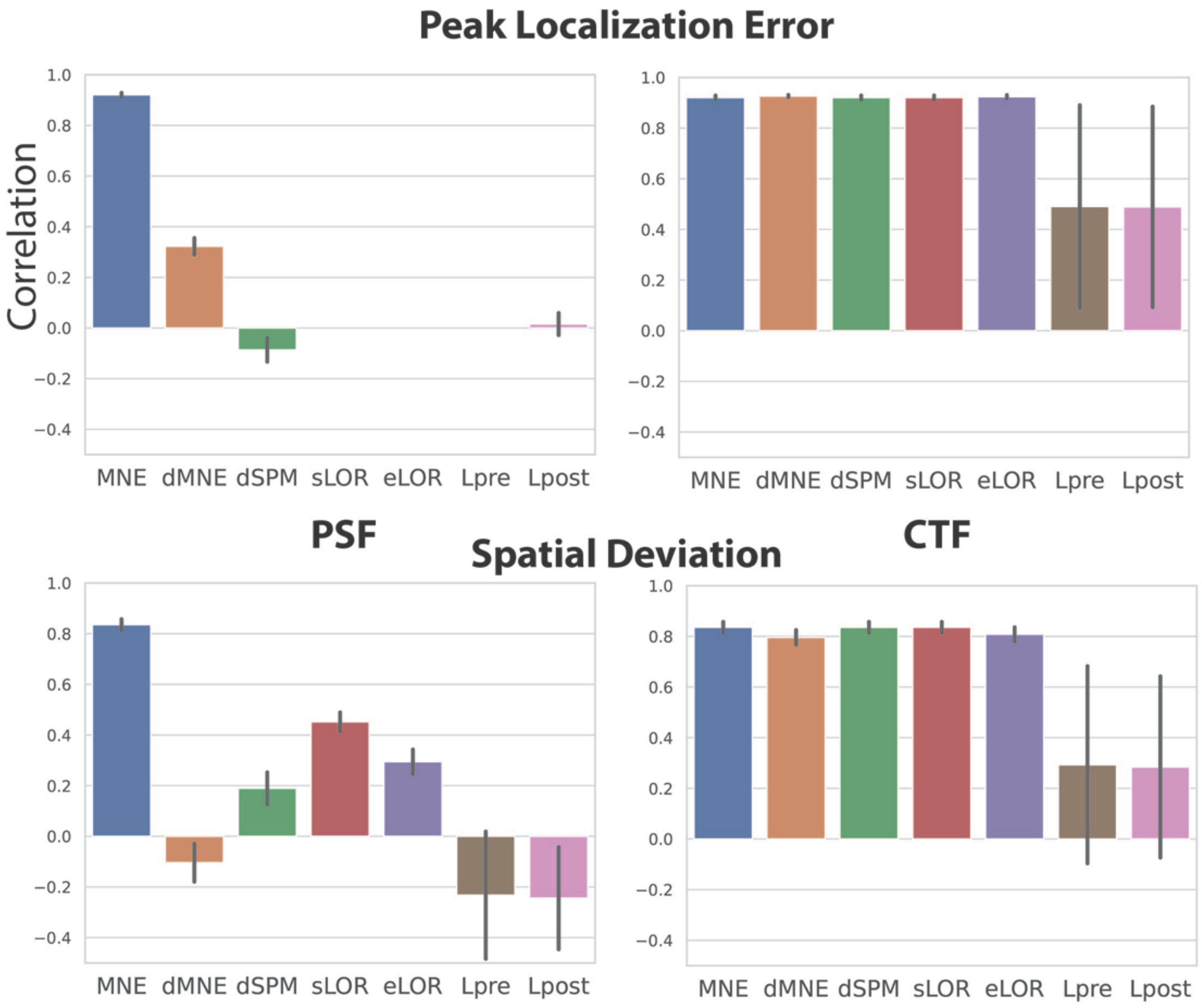
Comparing Estimators – Beamformers



Hauk, Stenroos, Treder, Neuroimage 2022
https://www.sciencedirect.com/science/article/pii/S1053811922002993

Comparing Estimators – Correlations With Depth



Hauk, Stenroos, Treder, Neuroimage 2022
https://www.sciencedirect.com/science/article/pii/S1053811922002993

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.

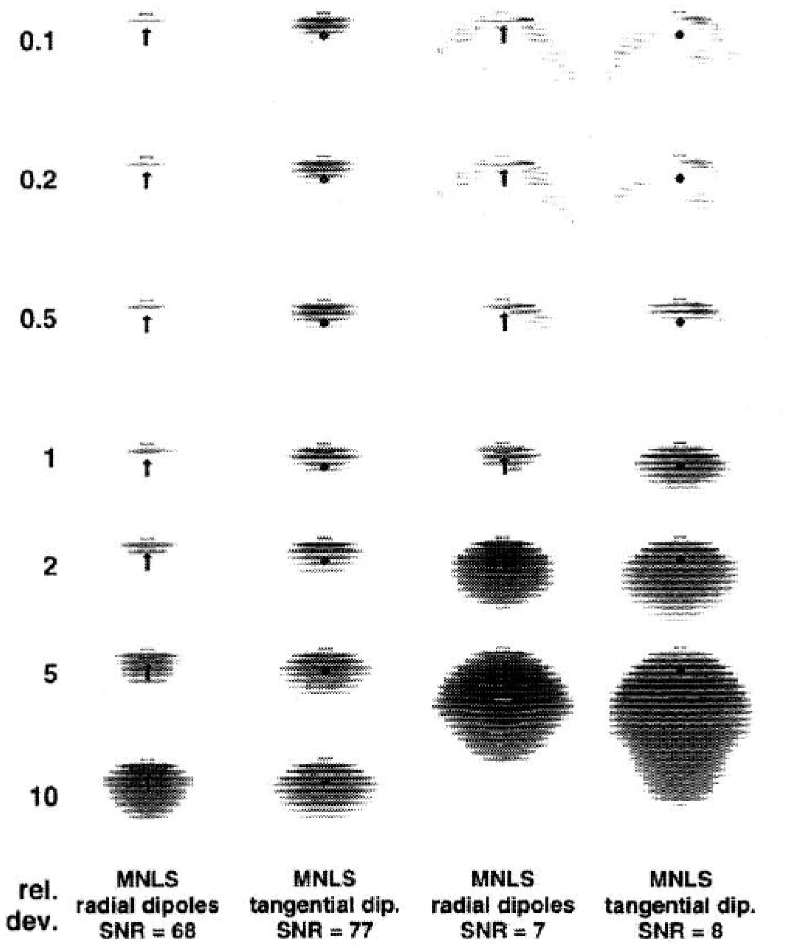
⇒ The tools (PSFs/CTFs, resolution metrics) can be applied to individual datasets – try it yourself!

Noise and Regularisation

Trade-off norm-variance, smoothness

Source at fixed excentricity 71% (60mm)

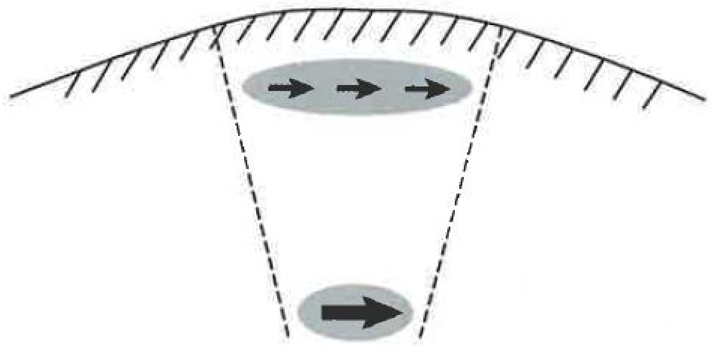
Regularisation parameter
relative to optimal value



Fuchs et al., J Clin Neurophys 1999

Adding priors (and biases)

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,
https://www.pnas.org/content/114/48/E10465

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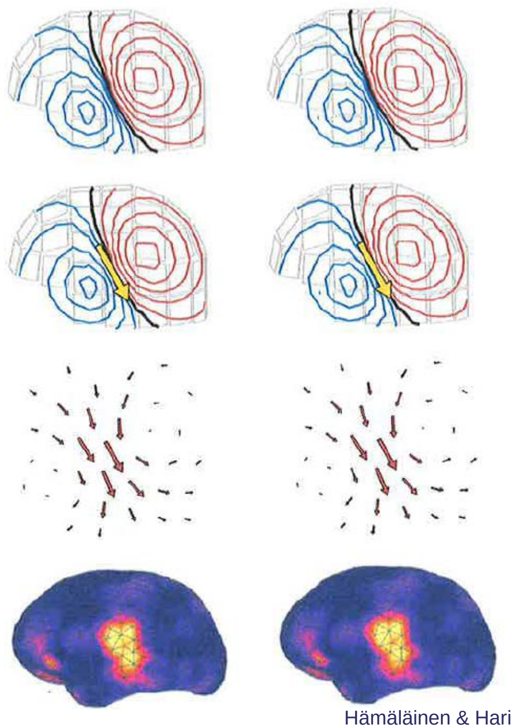


Field Patterns

Same Field Patterns

Dipole Model

Same Source Estimates

Minimum Norm Estimates

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

The Inverse "Problem"

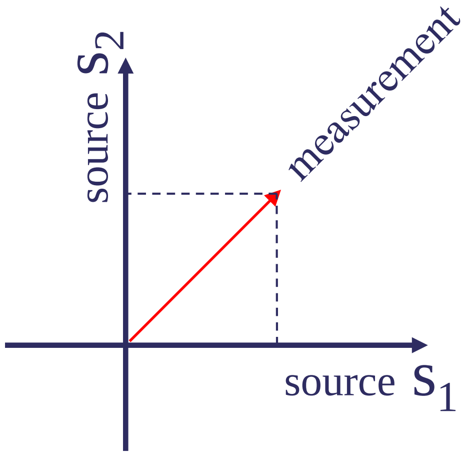
How can we make the problem "more unique"?

How can we reduce the number of unknowns?

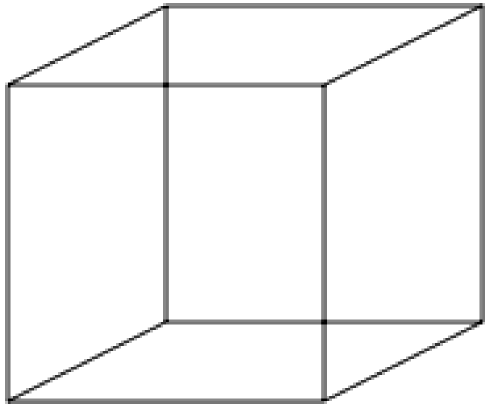
Do we know anything about our sources,
except that they produce our EEG/MEG data?

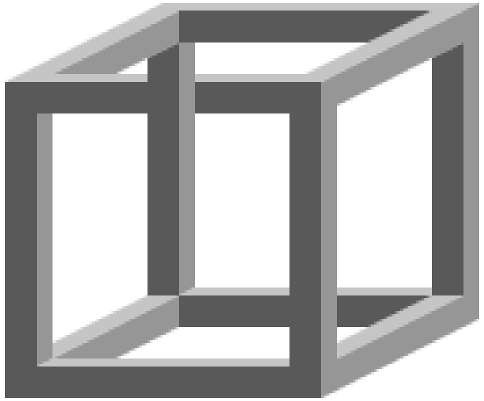
How Can “Priors” Help With These Problems?

We are losing information in the measurement



The information in the measurement is not enough to reconstruct its source.





?

http://www.pxleyes.com/photoshop-picture/502fba7537141/The-Classic-Optical-Room.html

How Can We Combine Measurement Modalities?

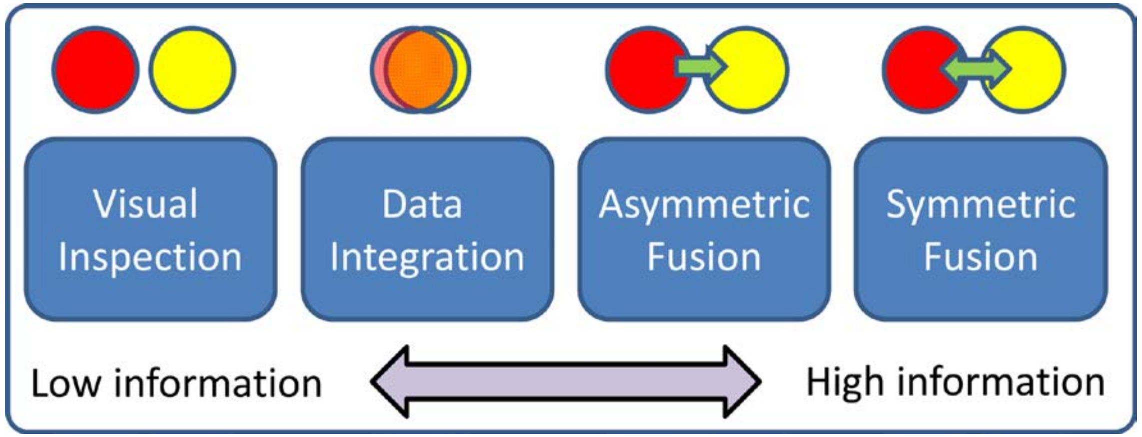
“Converging Evidence”:
Compare results from different modalities, determine commonalities and differences.

“(Asymmetric) Fusion”:
Use one modality as a constraint for another.
(e.g. EEG->fMRI, fMRI->EEG/MEG)

“Neural Modelling” (“Symmetric Fusion”):
Use of a common neural model that accounts for signals in all modalities.
(e.g. EEG<->MEG)

e.g. Horwitz&Poeppel, HBM 2002; Henson et al., HBM 2010

Each of these options poses different challenges with respect to modelling assumptions and complexity.



Calhoun & Sui, Biol Psych Cogn Nsc 2017

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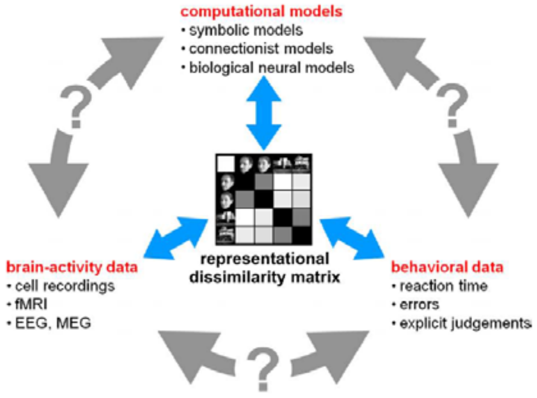
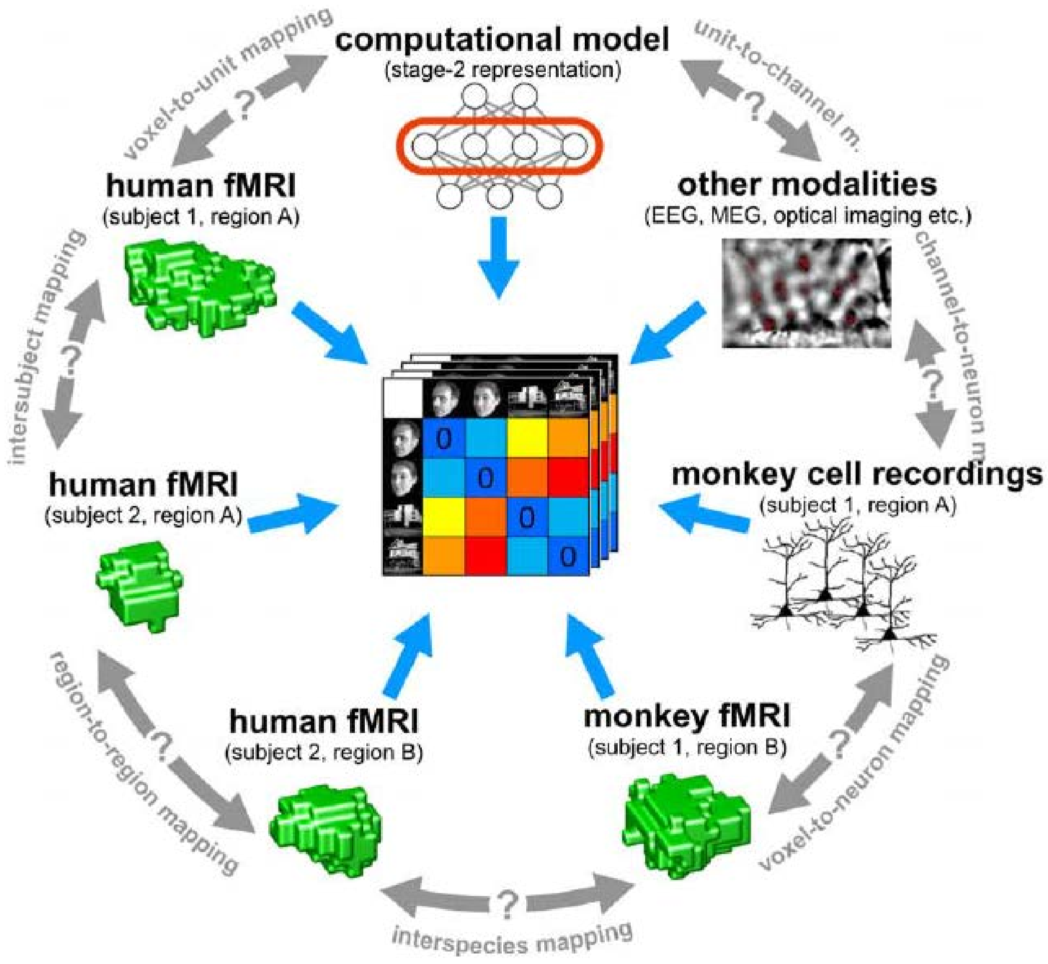
Comparing Representational Dissimilarity Across Neuroimaging Methods





Kriegeskorte et al., Front Syst Nsc 2008

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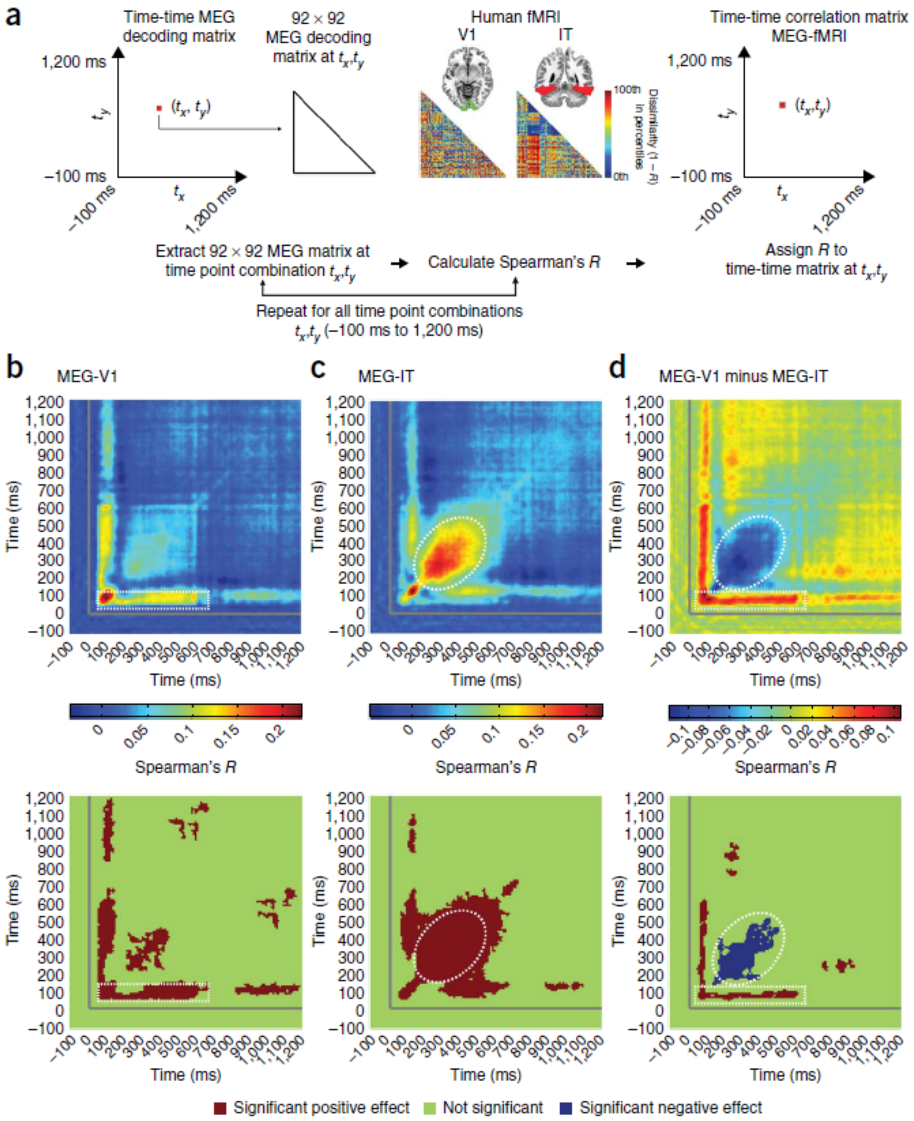

Cichy et al., Nat Nsc 2014

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Problems Integrating EEG/MEG And fMRI

1. Metabolic activity can occur without EEG/MEG activity.
2. EEG/MEG activity can occur without BOLD activity.
3. EEG/MEG and metabolic activity may have common sources, but are not fully spatially overlapping.
4. EEG/MEG and metabolic activity have different time courses.

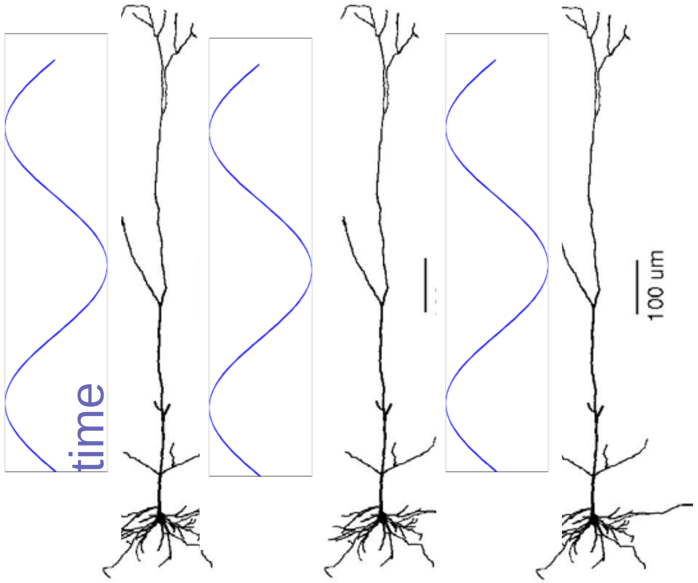
Note: Usually EEG/MEG and fMRI are acquired in different sessions, causing:

a) inter- and intra-subject variability (same or different subjects in different sessions)
b) differences in scanning position (supine, seated)
c) differences in scanning environment (e.g. scanner noise)

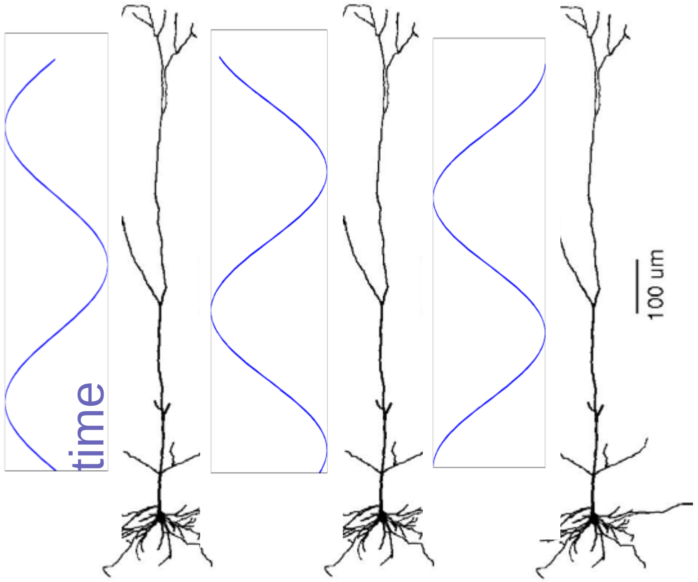
e.g. Poline et al., in “MEG – An Introduction to Methods”

Problems Integrating EEG/MEG And fMRI

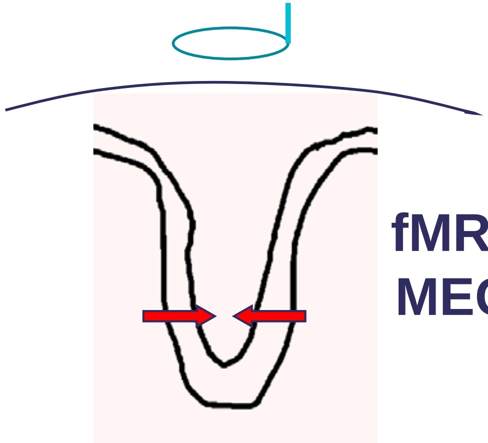
Synchronous: fMRI↑ MEG↑



Asynchronous: fMRI↑ MEG↓

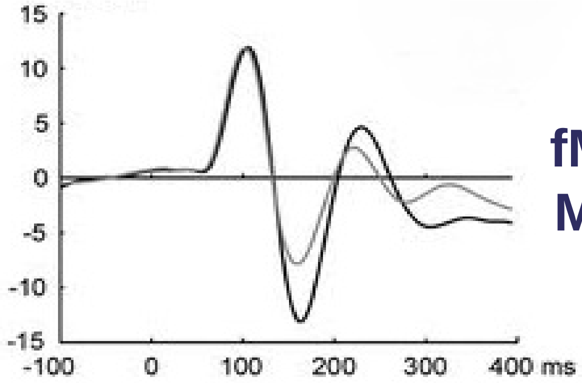


Source Configuration



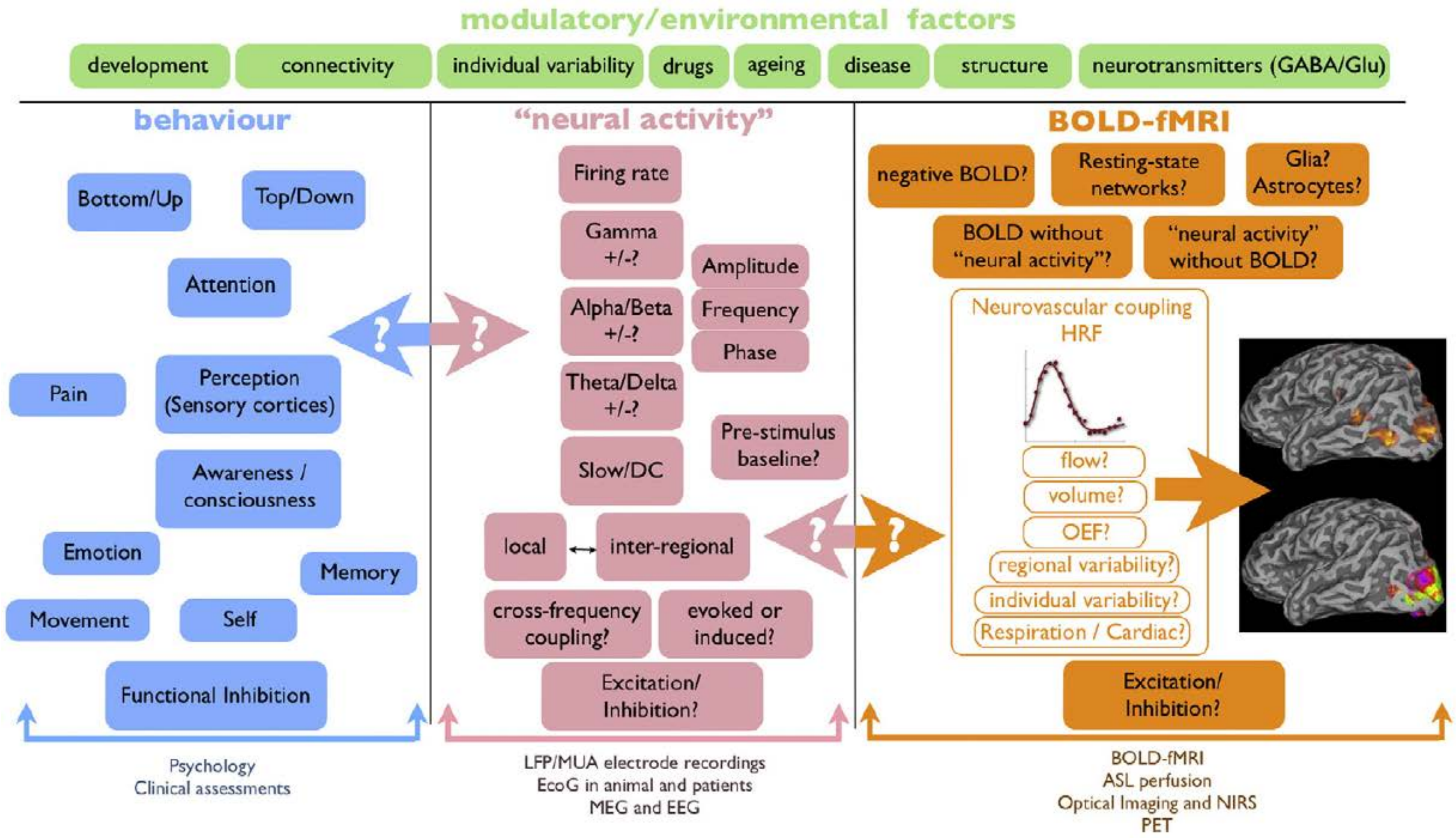
fMRI ↑
MEG ↓

Time Scale



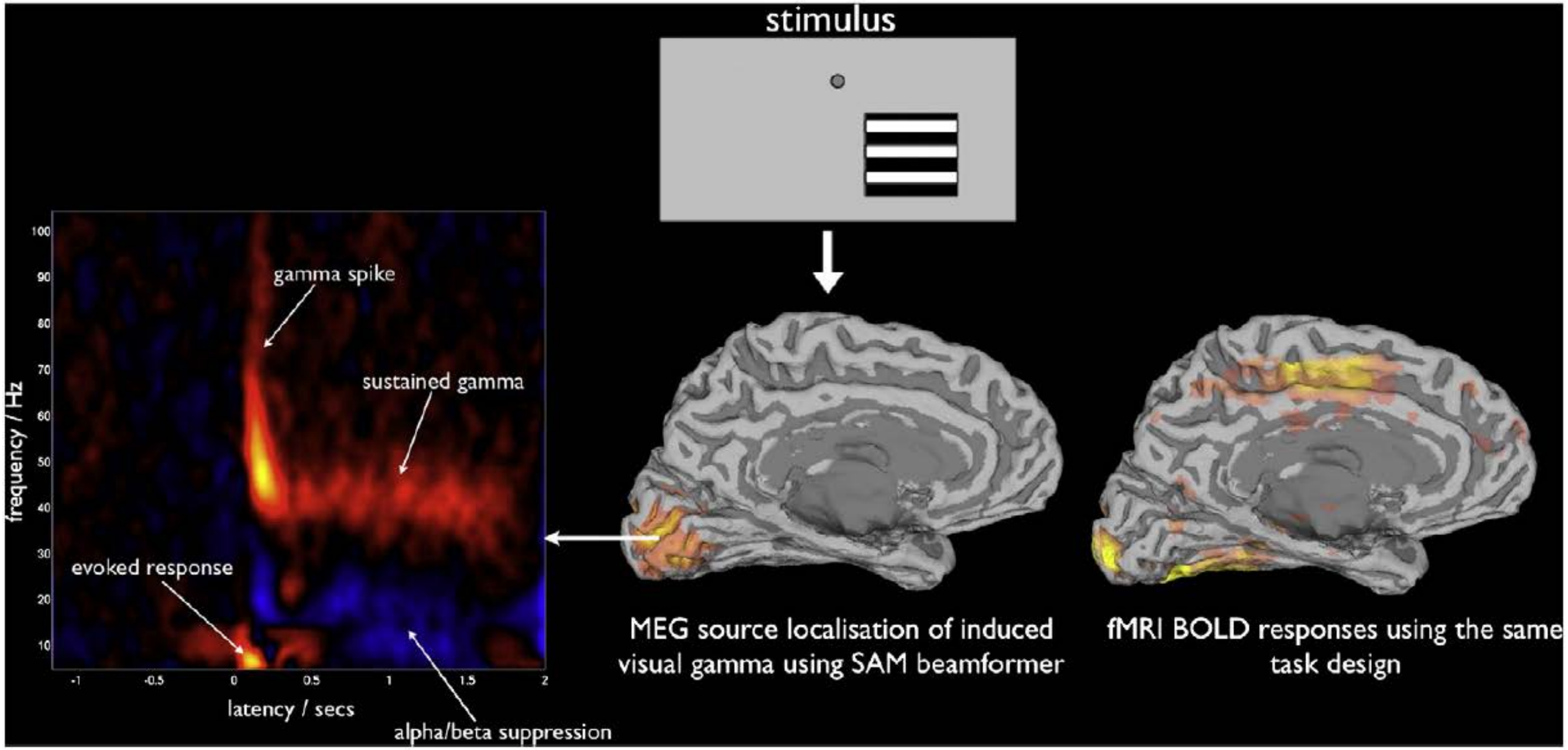
fMRI ↓
MEG ↑

Which “Neural Activity” Do You Mean?



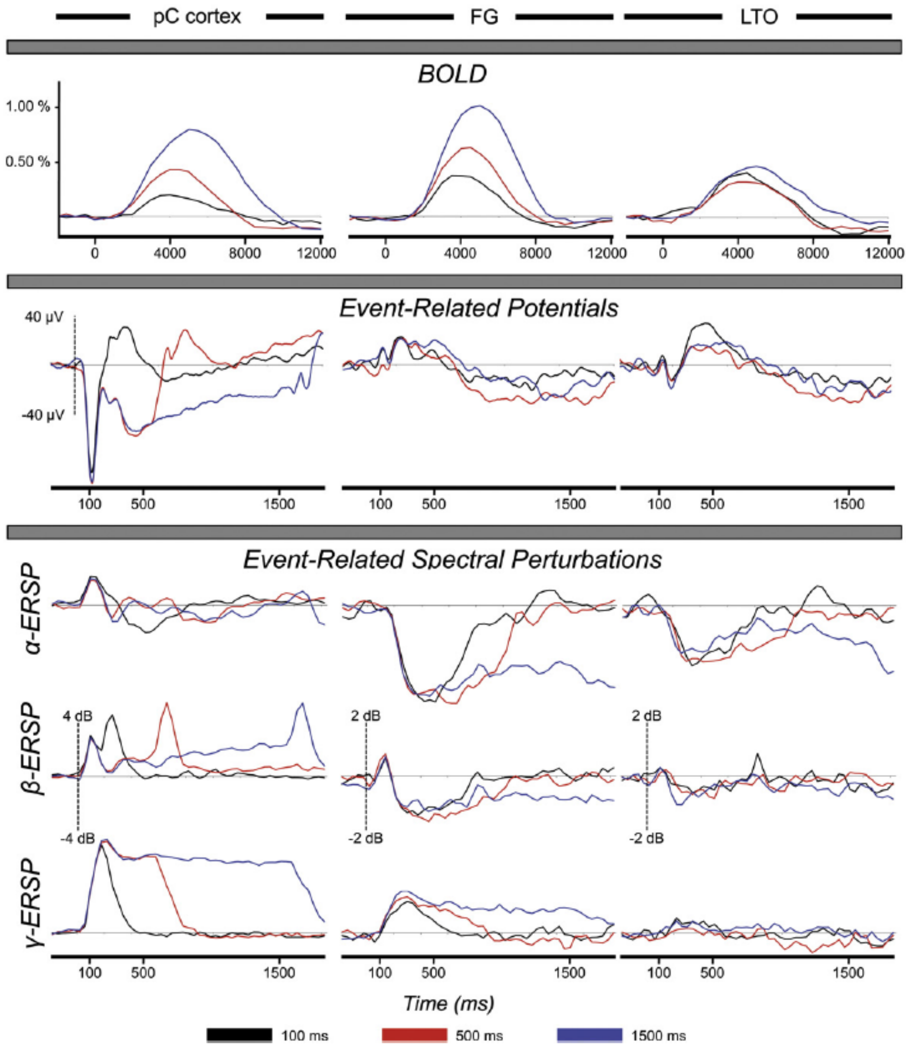
Singh, NI 2012

Which "Neural Activity" Do You Mean?



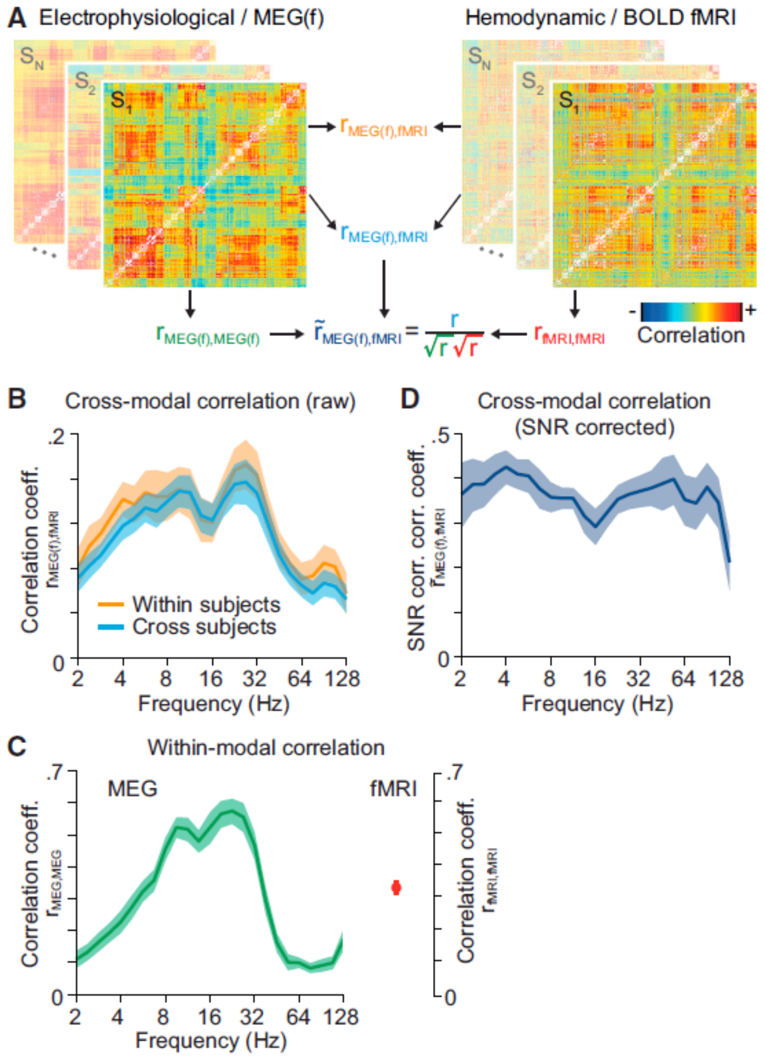
Singh, NI 2012

BOLD Correlated With High-Frequency Spectral Perturbations



Engell et al., NI 2012

BOLD fMRI Correlation Reflects Frequency-Specific Neuronal Correlation



Hipp&Siegel, Curr Biol 2015

Problems Integrating EEG/MEG And fMRI

Liu et al., PNAS 1998:

1) “**Fundamental mis-specifications** can arise because EEG and MEG and fMRI measure physically different aspects of brain function.”
2) “**Experimental mis-specifications** refer to measurement or estimation errors that can be corrected, at least in theory”.

“Weighting” and “Priors”

$$P(\mathbf{j}(\mathbf{r},t)|\mathbf{x}(t)\ \&\ f(\mathbf{r},t)) = \frac{P(\mathbf{x}(t)|\mathbf{j}(\mathbf{r},t))\,P(f(\mathbf{r},t)|\mathbf{j}(\mathbf{r},t))\,P(\mathbf{j}(\mathbf{r},t))}{P(\mathbf{x}(t)\ \&\ f(\mathbf{r},t))}$$

If source strengths and priors can be modelled as multivariate Gaussian distributions, then the maximum a posteriori probability (MAP) estimate is the minimum norm estimate:

$$\hat{\mathbf{s}}(t) = \mathbf{W}\mathbf{x}(t),\ \text{where}\ \mathbf{W} = \mathbf{R}\mathbf{A}^T(\mathbf{A}\mathbf{R}\mathbf{A}^T + \mathbf{C})^{-1}$$

A: Leadfield
R/C: Source/noise covariance

$0<\mathbf{R}_{ii}<1$
depending on fMRI

Dale et al., Neuron 2000, also Liu et al., PNAS 1998

Relative Weighting of fMRI

Ideally, this requires knowledge about “fMRI visible” and “fMRI invisible” sources –
if we knew those, we wouldn’t need source estimation anymore.

“The optimal fMRI weighting, which depends on the confidence in the hypothesis that neuronal and hemodynamic activity are tightly coupled, currently cannot be determined *a priori*.”
Liu et al., PNAS 1998

Relative Weighting of fMRI

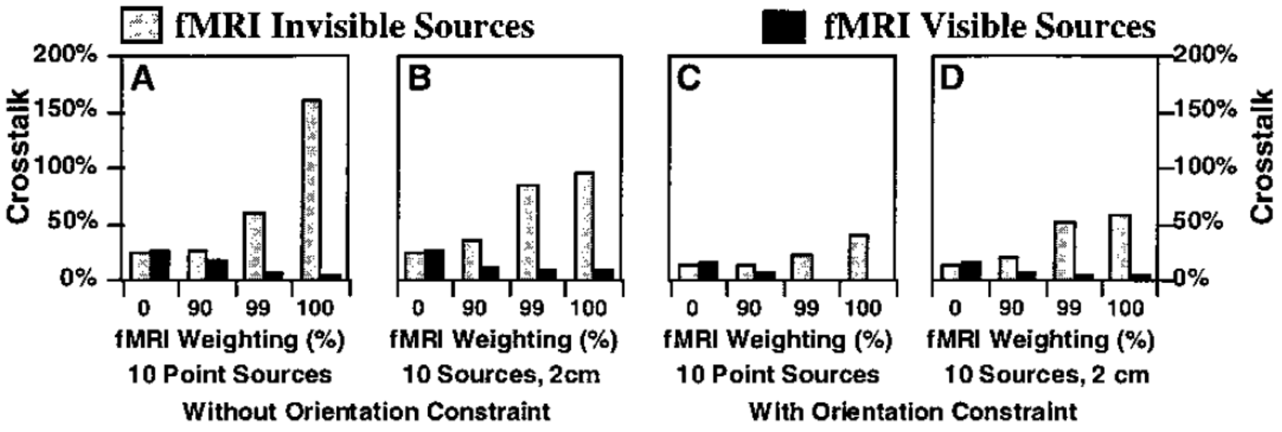


FIG. 3. Crosstalk versus relative fMRI weighting. Crosstalk is shown for 10 sources (point and 2 cm in diameter), with and without orientation constraint. The relative fMRI weighting was either 0%, 90%, 99%, or 100%. The optimal fMRI weighting requires a compromise between resolving fMRI visible sources (i.e., higher fMRI weighting) and minimizing distortion from fMRI invisible sources (i.e., lower fMRI weighting). The results indicate that a 90% fMRI weighting greatly reduces the crosstalk from fMRI visible sources, while only slightly increasing the crosstalk from fMRI invisible sources.

Liu et al., PNAS 1998

Relative Weighting of fMRI

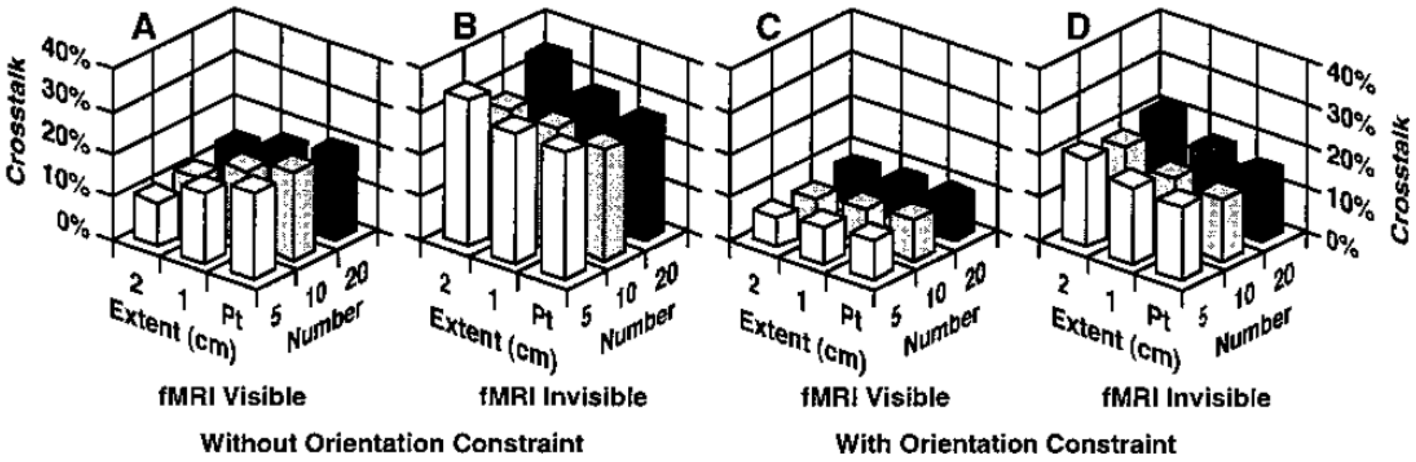


FIG. 4. Crosstalk versus extent and number of sources. Crosstalk is shown for a variety of extents and numbers of sources. The extent of sources was either point, 1 cm or 2 cm in diameter, and the number of sources was 5, 10, or 20 (indicated by different gray scale). A partial fMRI weighting of 90% was used in these simulations. The results indicate that the crosstalk is relatively independent of source extent and number. This demonstrates that the proposed linear estimation method is appropriate for modeling multiple, extended areas of activation, as typically encountered in functional neuroimaging studies.

Liu et al., PNAS 1998

fMRI And EEG/MEG Integration: Examples

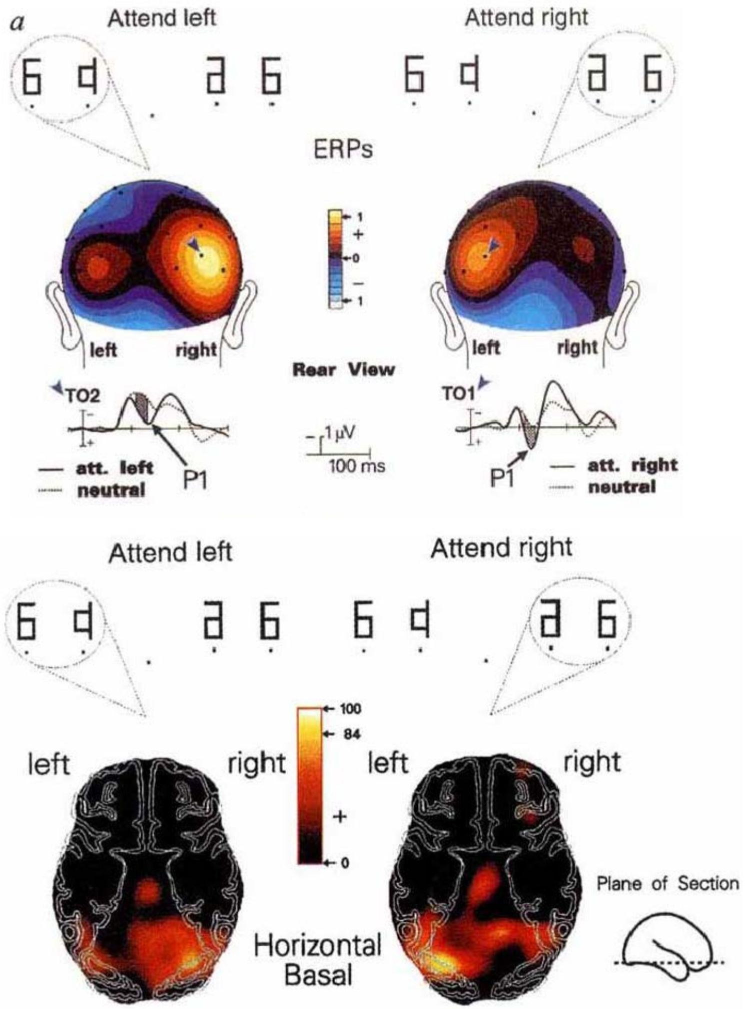
Dale et al., Neuron 2000

Multimodal Integration: Examples

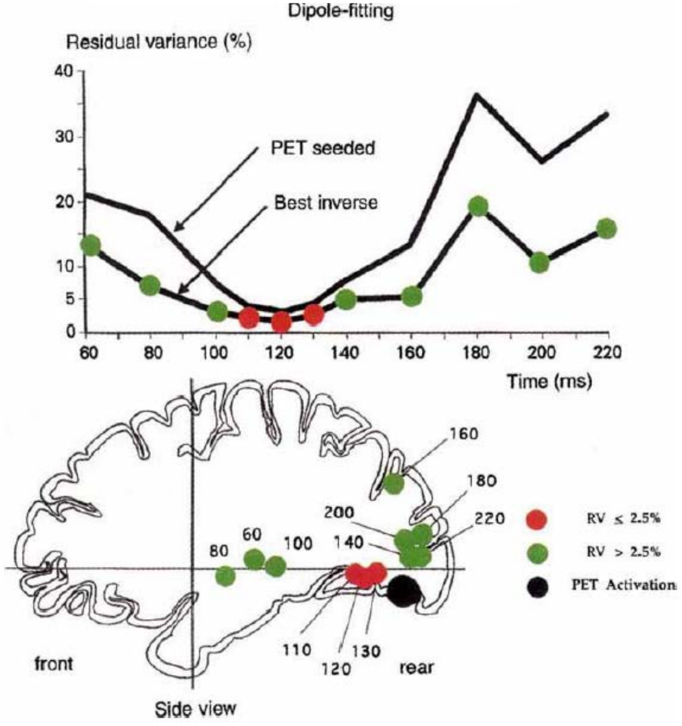
Hypothesis-Guided Dipole Modelling

ERPs

PET



PET-constrained
Dipole Modelling



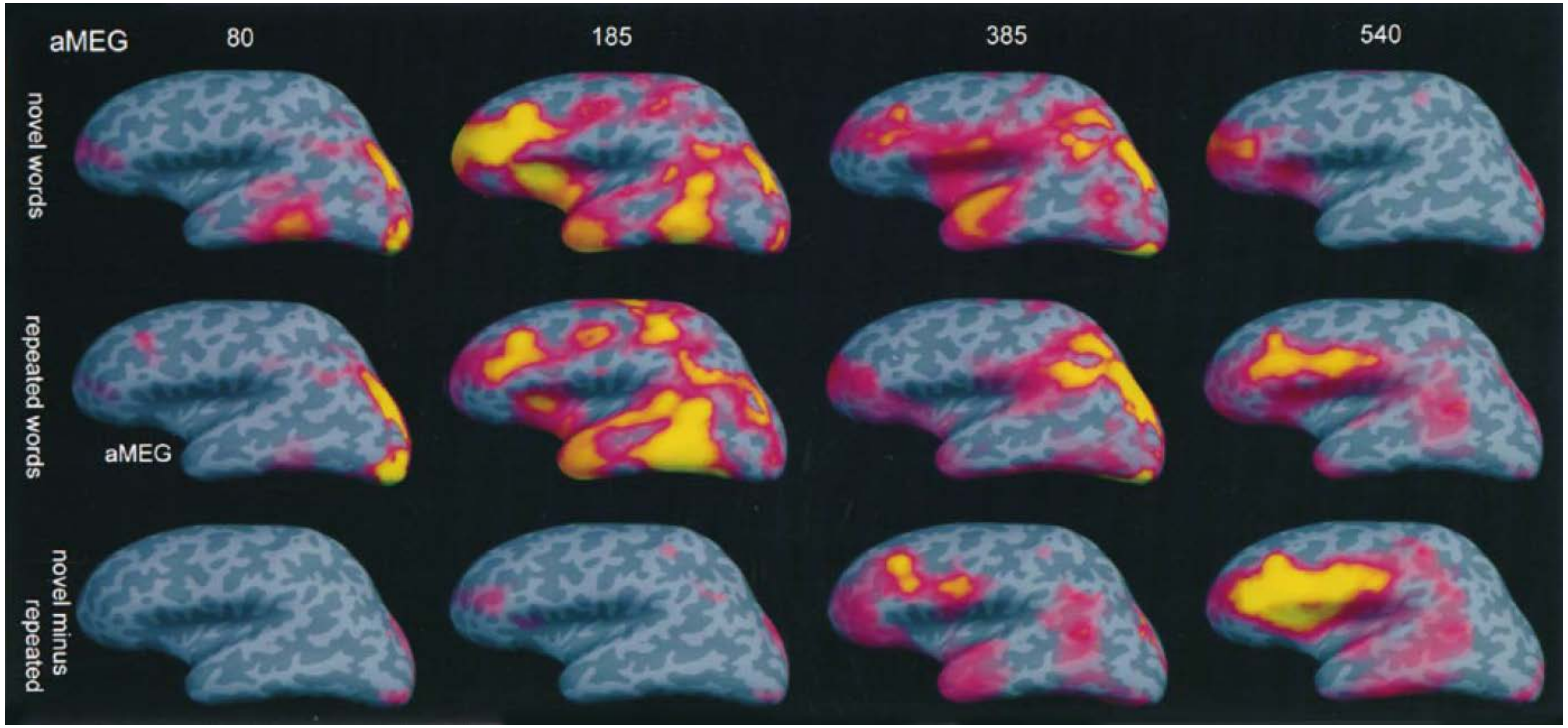
Heinze et al., Nature 1994

Multimodal Integration: Examples

Minimum-Norm Estimation

Word-evoked activity – MEG Only

Single subject, dSPM maps, p<0.001

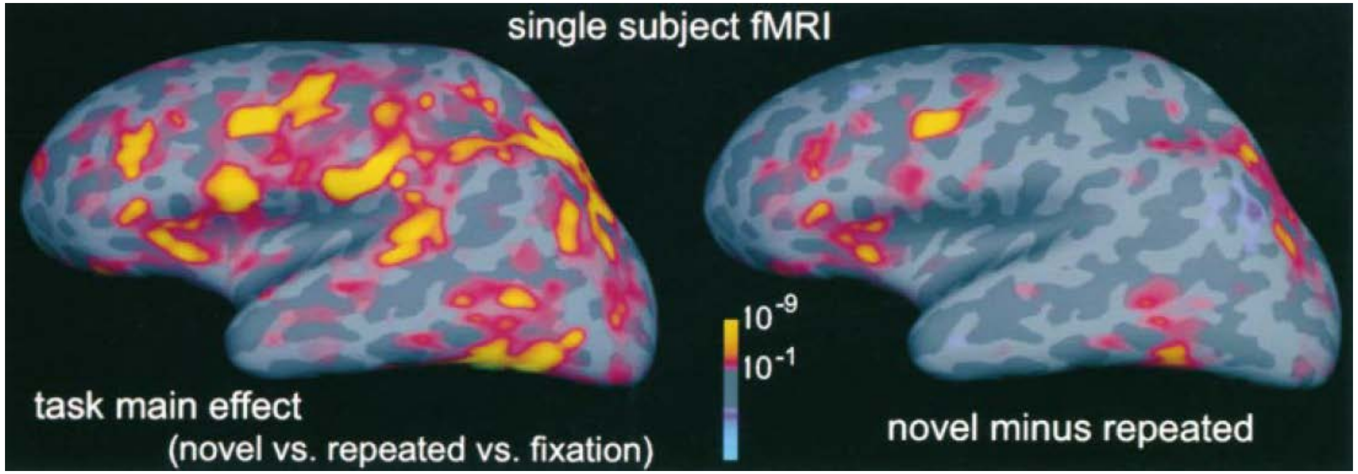


Dale et al., Neuron 2000

Multimodal Integration: Examples

Minimum-Norm Estimation

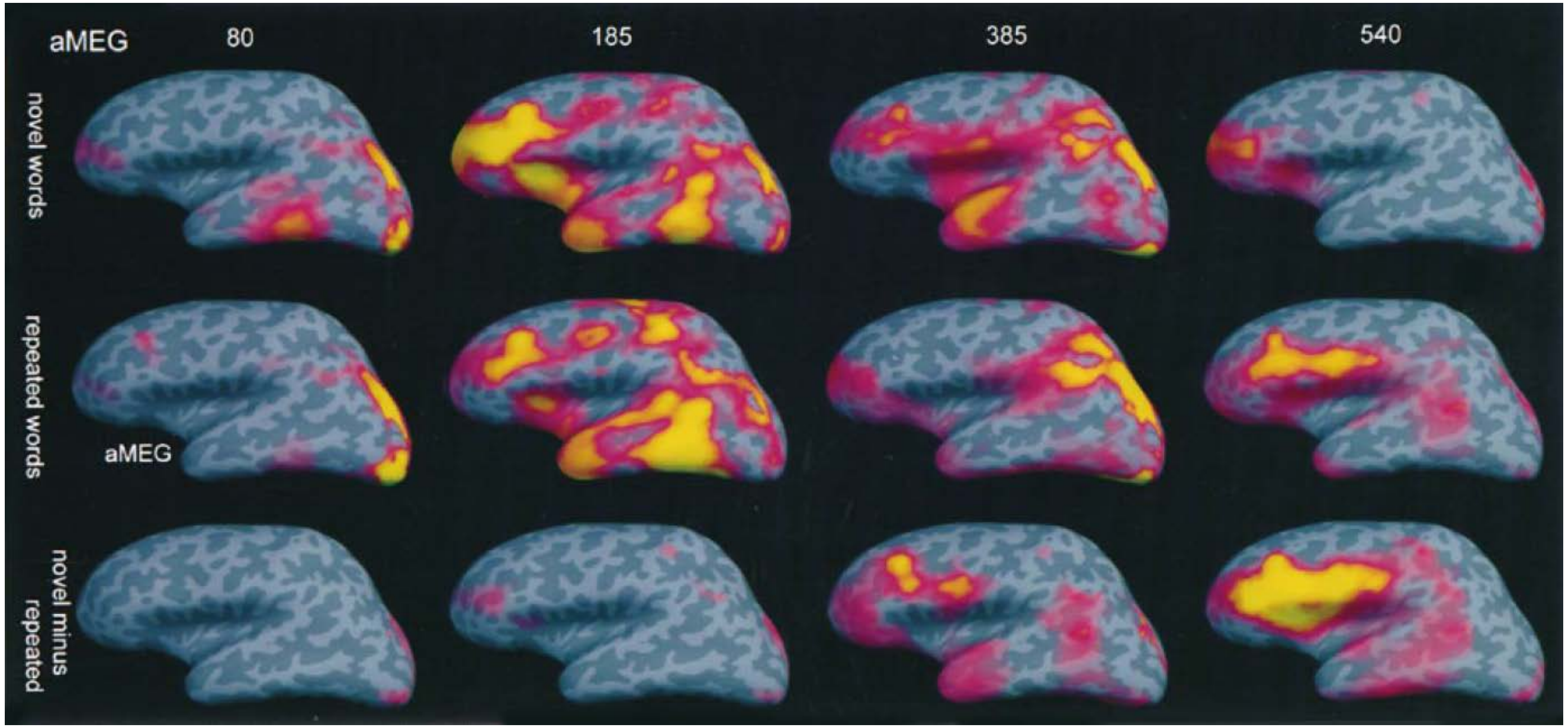
Word-evoked activity – fMRI



Dale et al., Neuron 2000

Multimodal Integration: Examples
Minimum-Norm Estimation

Word-evoked activity – MEG only
Single subject, dSPM maps, p<0.001

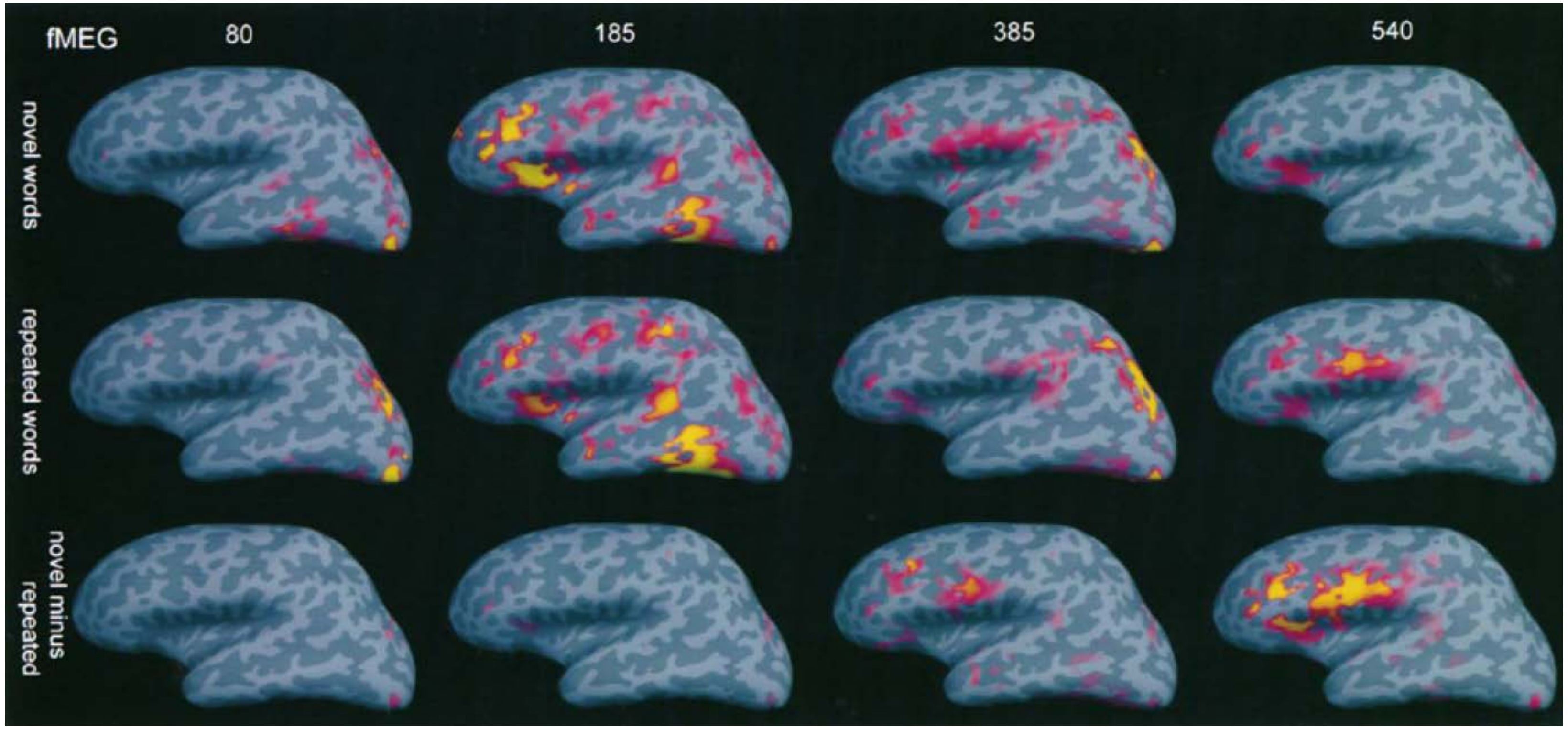


Dale et al., Neuron 2000

Multimodal Integration: Examples
Minimum-Norm Estimation

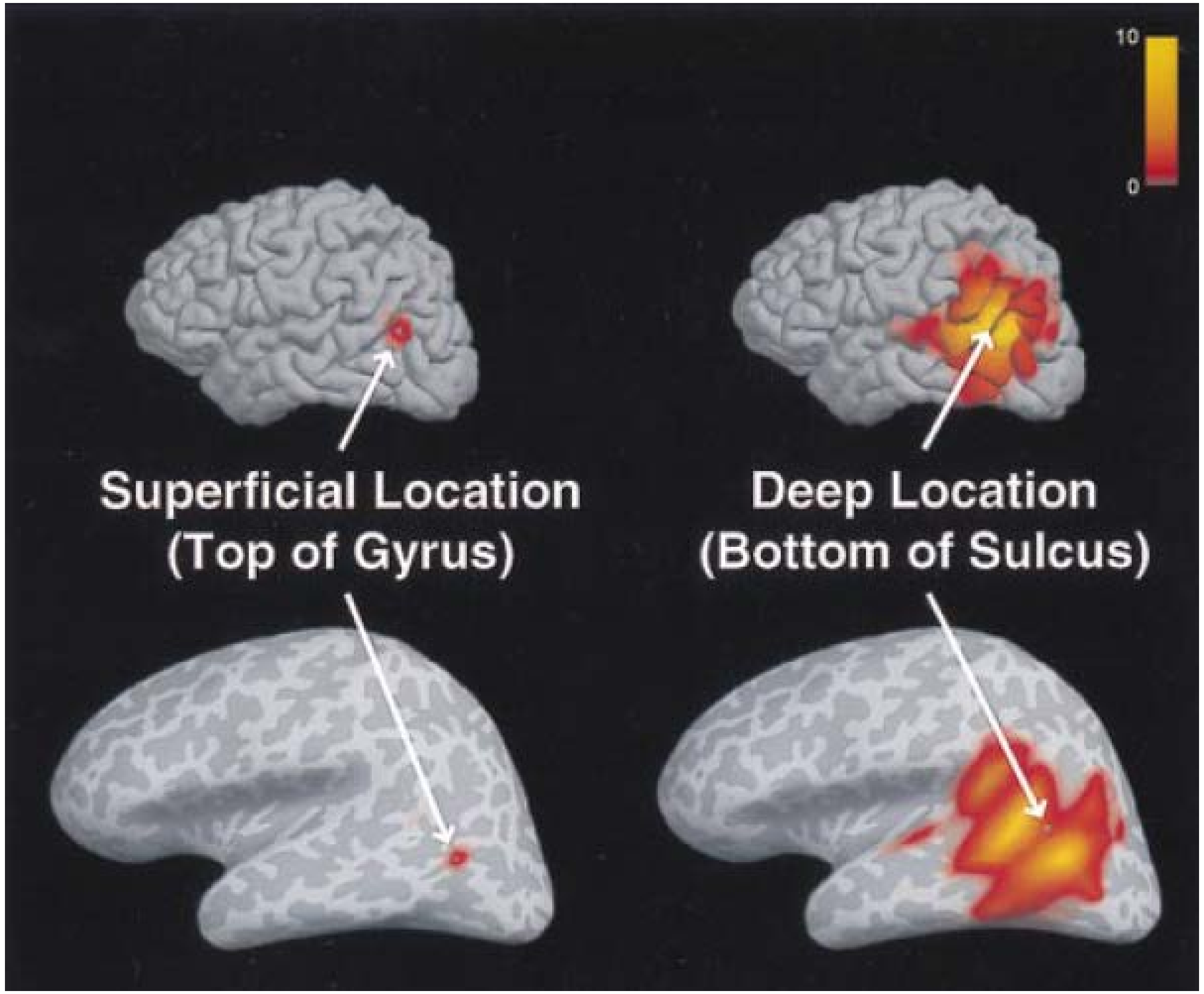
Word-evoked activity – MEG+fMRI

Single subject, dSPM maps, p<0.001



Dale et al., Neuron 2000

(How) Can We Estimate Deep Sources?



Liu et al., PNAS 1998

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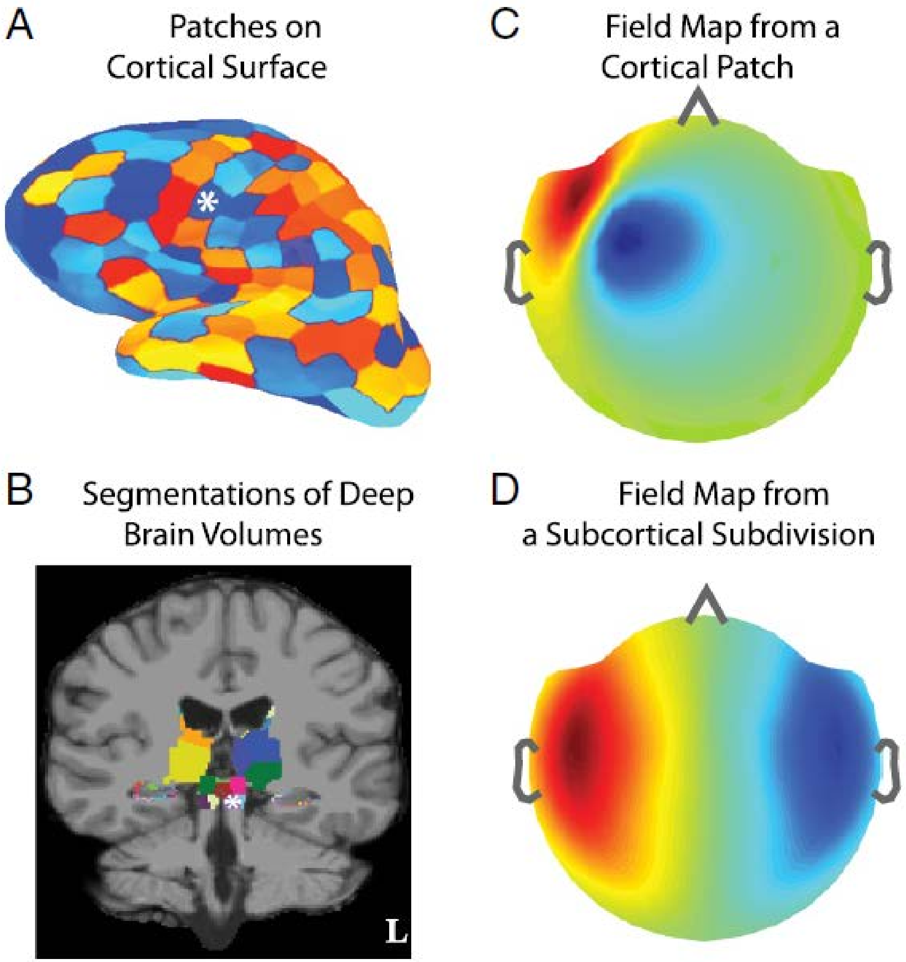

Krishnaswami et al., PNAS 2017
https://www.pnas.org/doi/10.1073/pnas.1705414114

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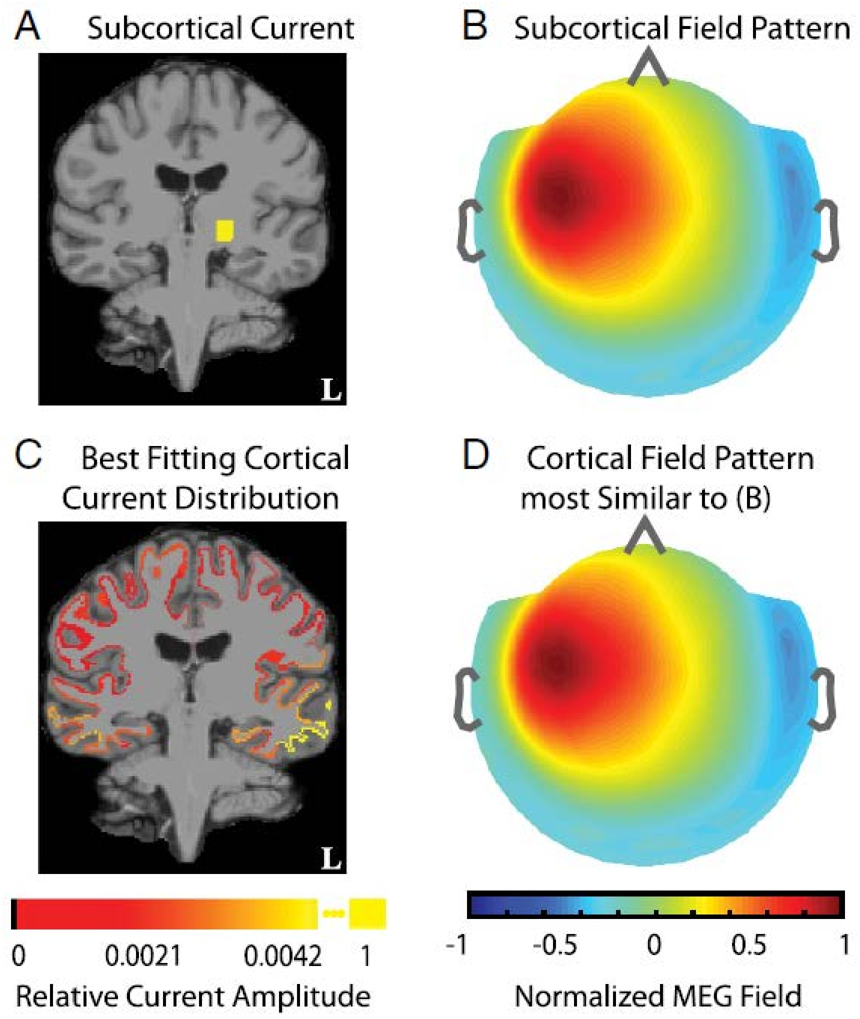

Krishnaswami et al., PNAS 2017
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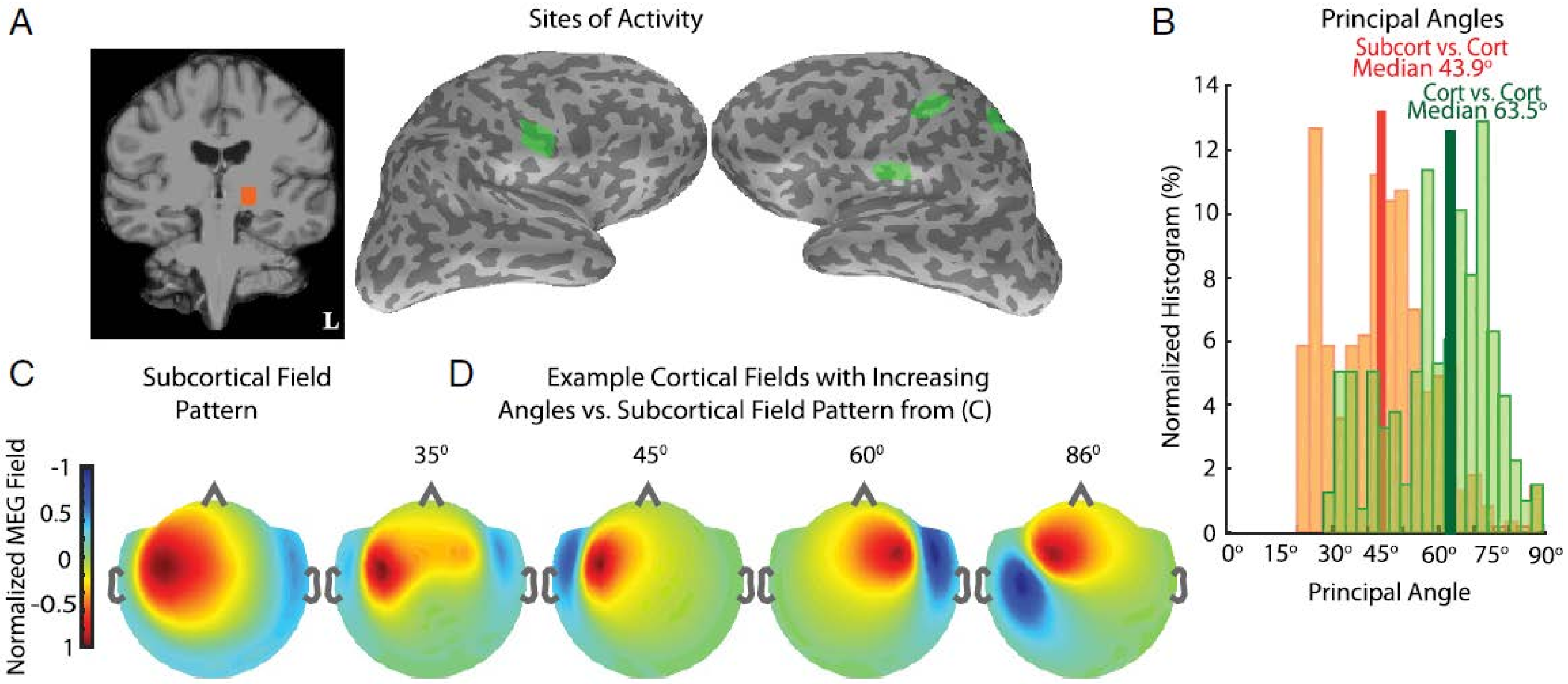

Krishnaswami et al., PNAS 2017
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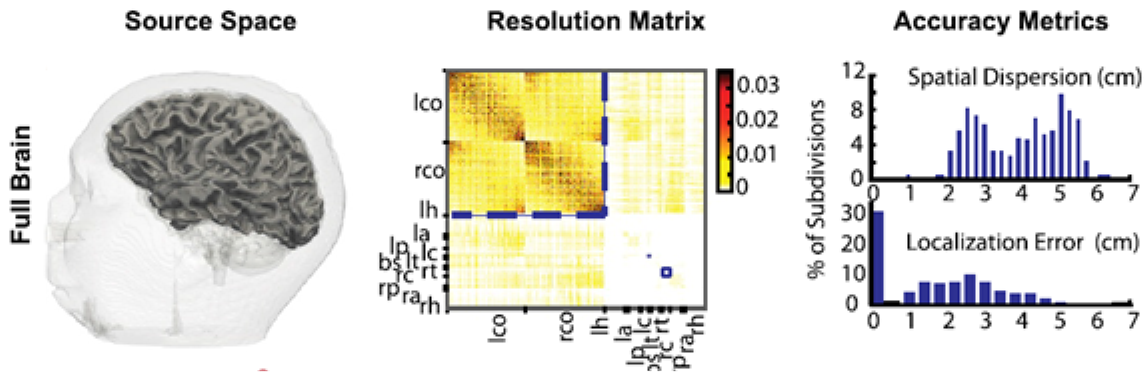
(How) How Can We Estimate Deep Sources?
The Importance Of Sparsity



Krishnaswami et al., PNAS 2017
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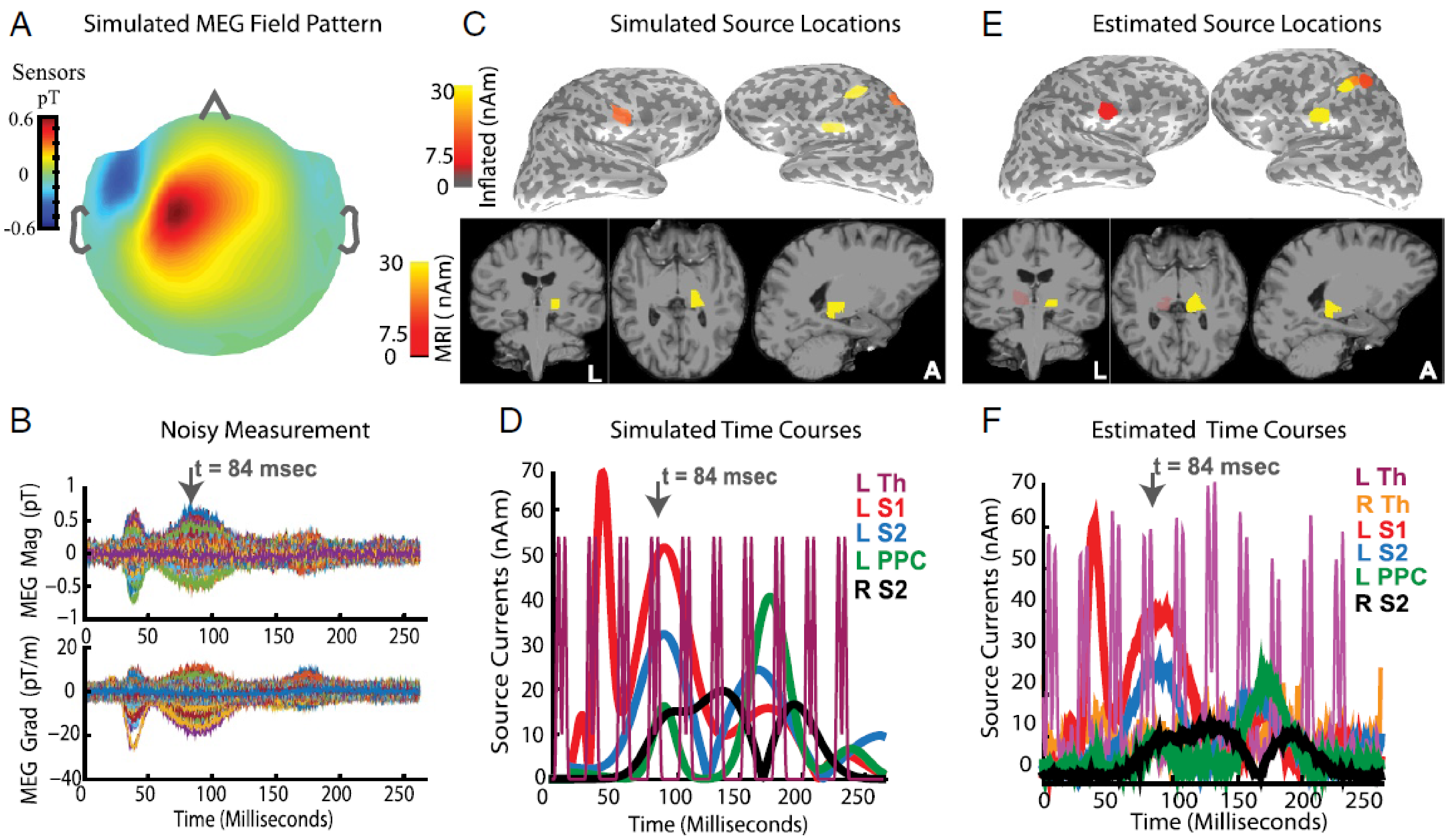
(How) How Can We Estimate Deep Sources?

The Importance Of Sparsity



Krishnaswami et al., PNAS 2017
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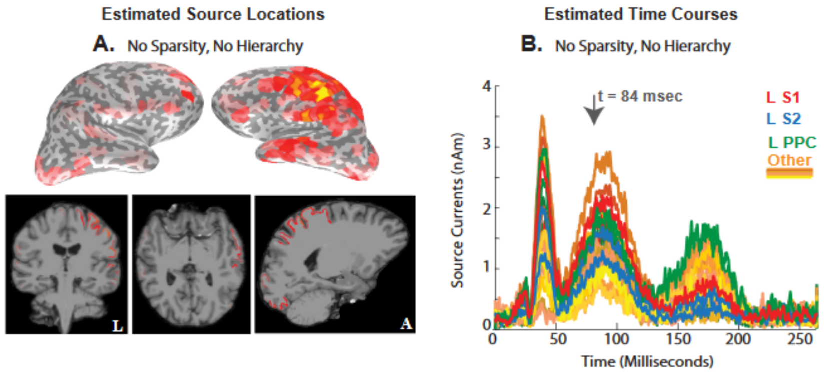
(How) How Can We Estimate Deep Sources?

Sparsity And Hierarchy Are Key



Krishnaswami et al., PNAS 2017
https://www.pnas.org/doi/10.1073/pnas.1705414114

Conclusions

- Priors lead to a bias of your solution towards what you already know.
- The link between the physiology of EEG/MEG and fMRI is not well understood.

  The usefulness of priors depends on the individual case.
- Priors can be implemented as weightings or source covariance matrices in the (Bayesian) minimum-norm framework.
- Prior information on the location and sparsity of sources is particularly useful (required) for deep sources.

Thank you