Time resolved electrophysiological brain imaging using MEG and EEG

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ICM Institut du Cerveau et de la Moelle épinière

DE LA RECHERCHE À L'INDUSTRIE cea

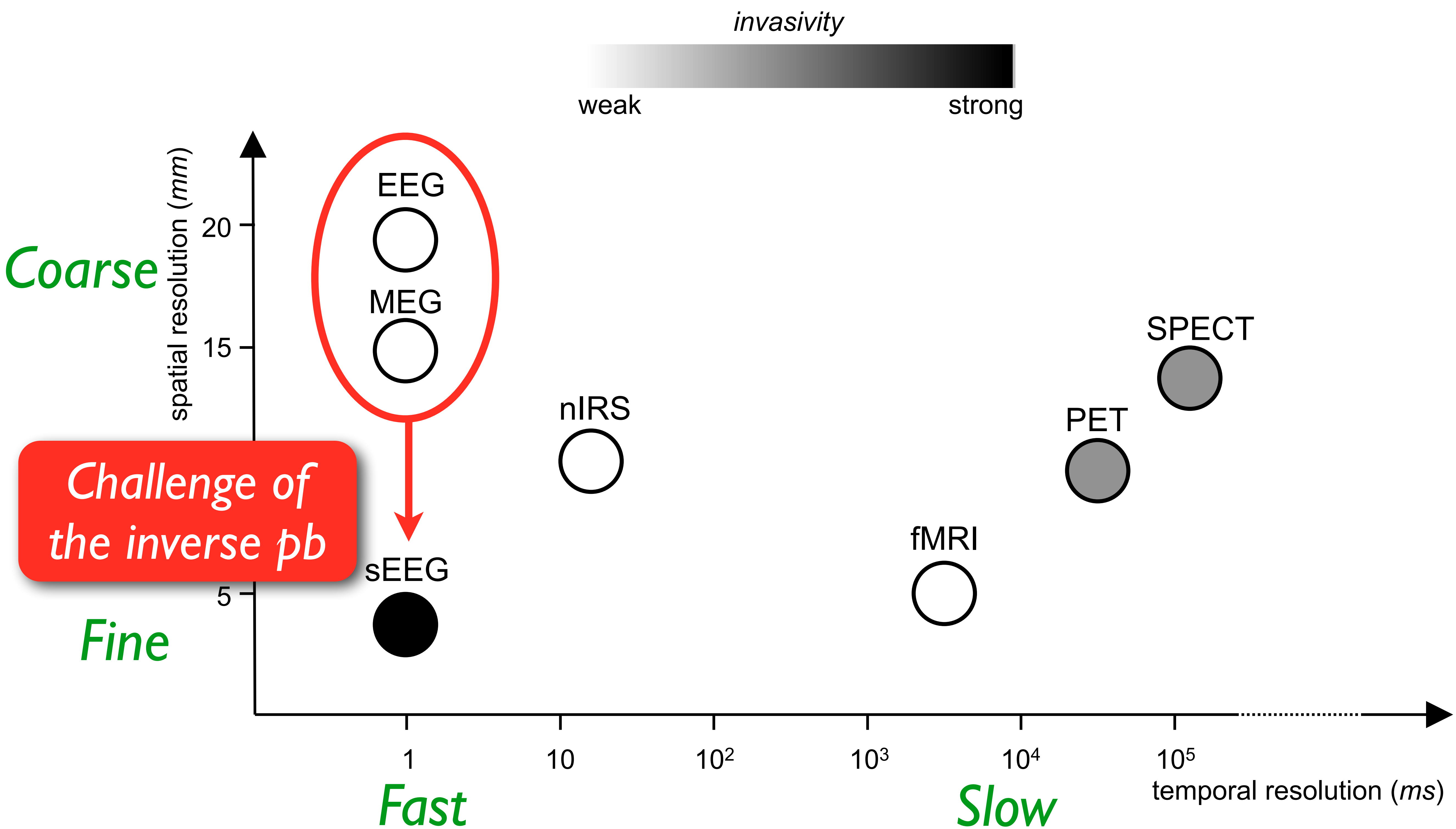
MEG NeuroSpin

MNE MEG + EEG ANALYSIS & VISUALIZATION

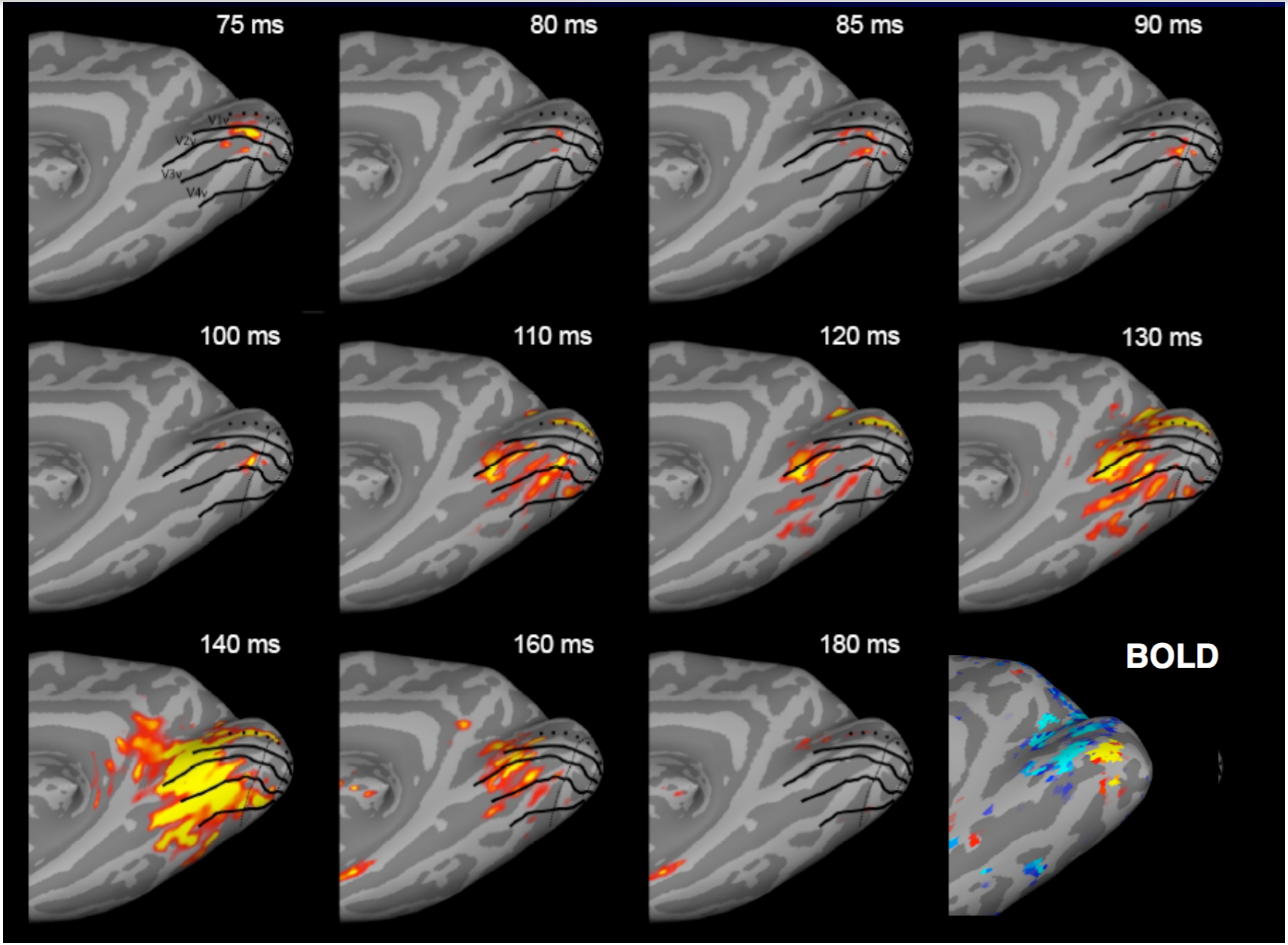
3 claims

- you should care about MEG and EEG
- The choice of your statistical model for source localization reflects hypotheses about brain sources
- The success of your source localization depends on domain knowledge and proper signal processing

fast brain imaging methods

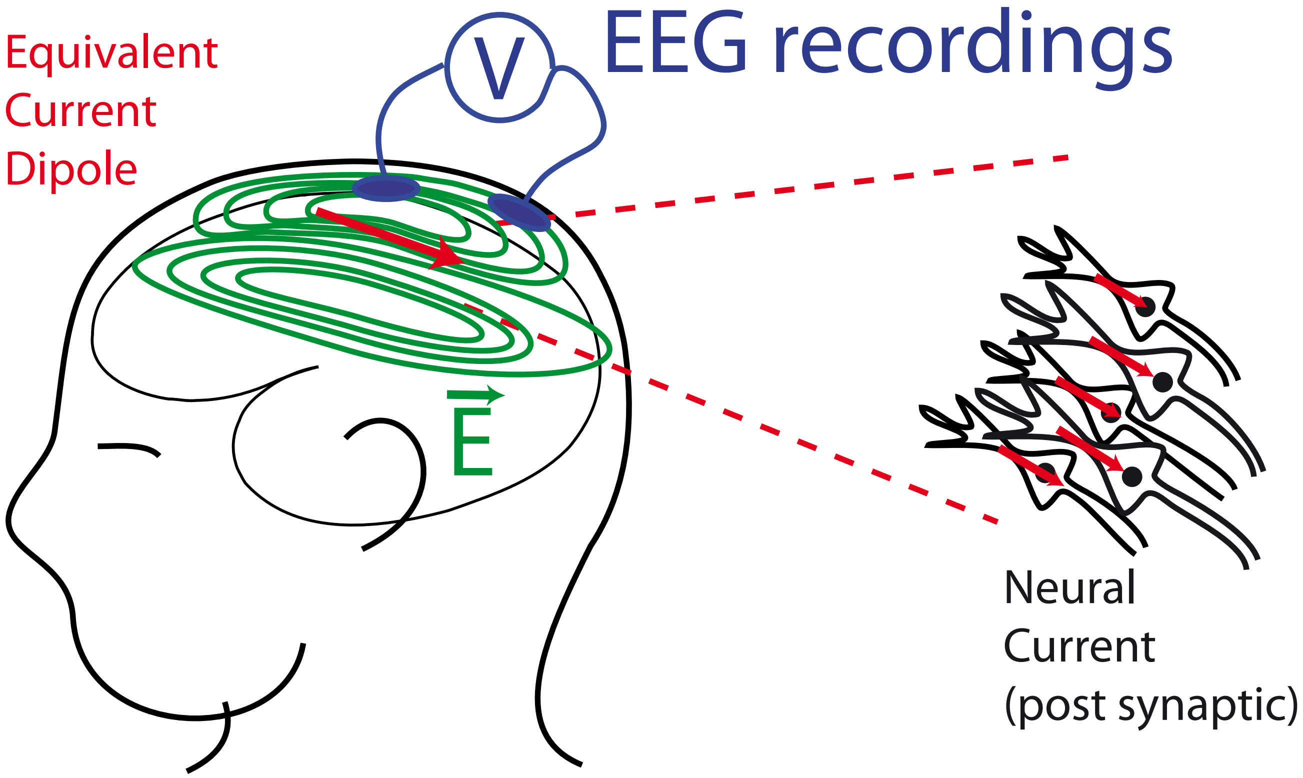


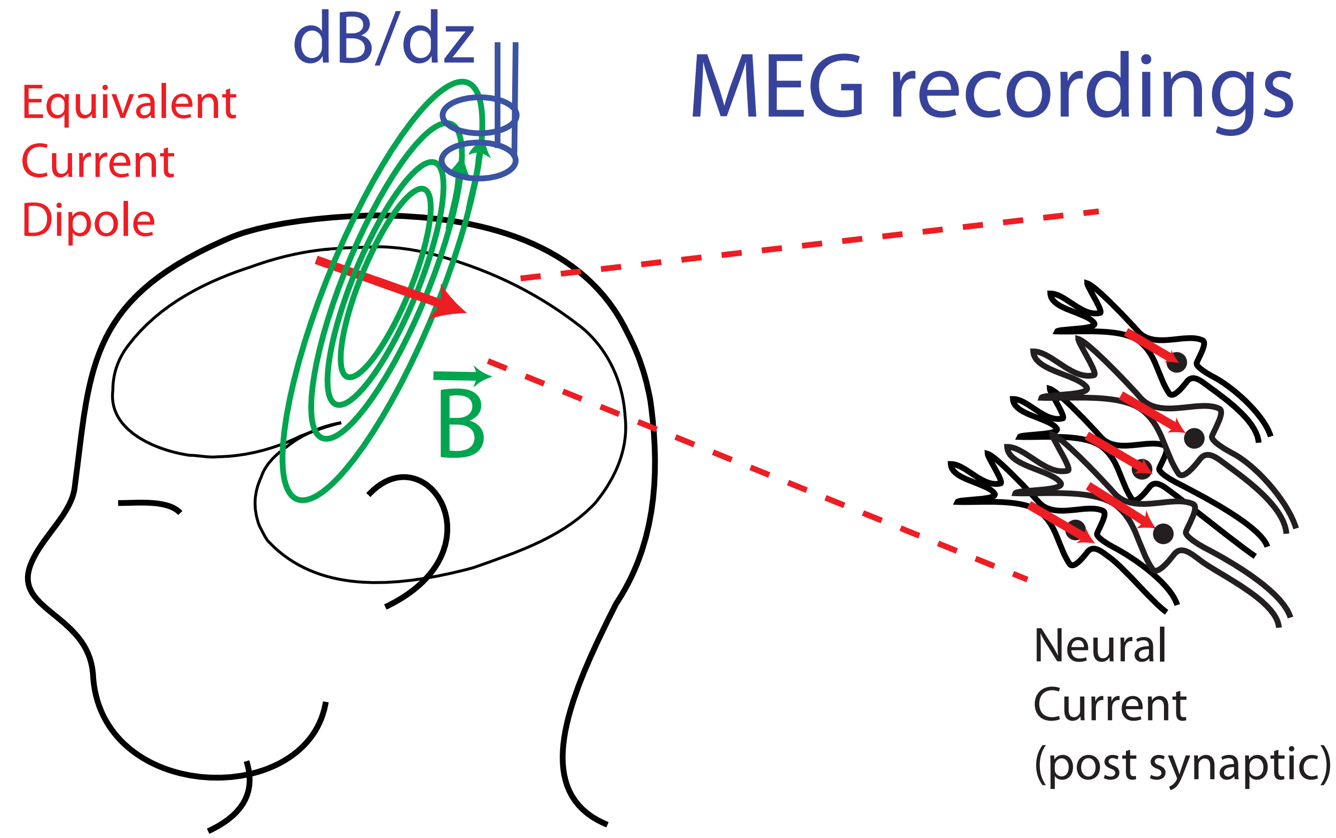
#temporal_resolution



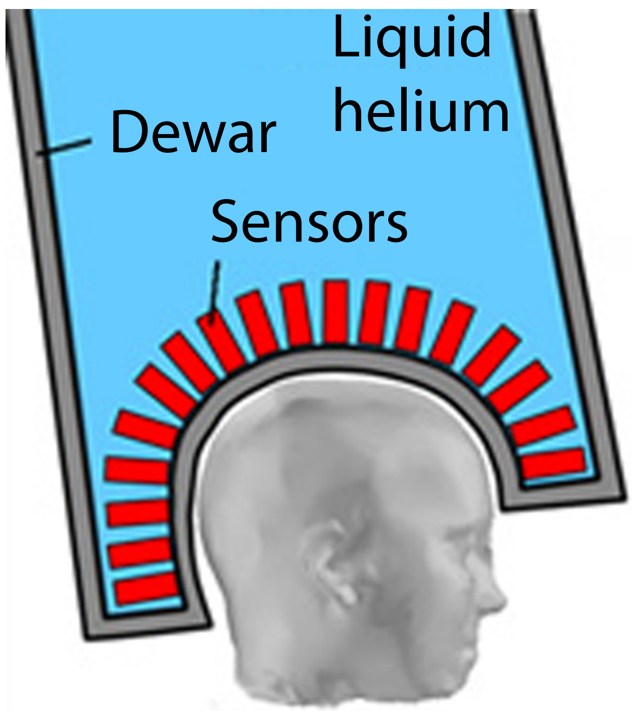
Sharon et al. 2005, SfN

yeah imaging!— sources?





First EEG recordings in 1929 by H. Berger

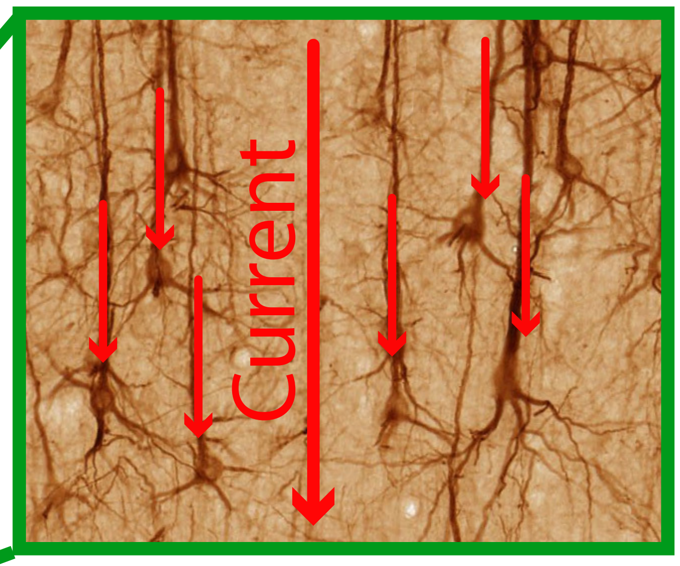


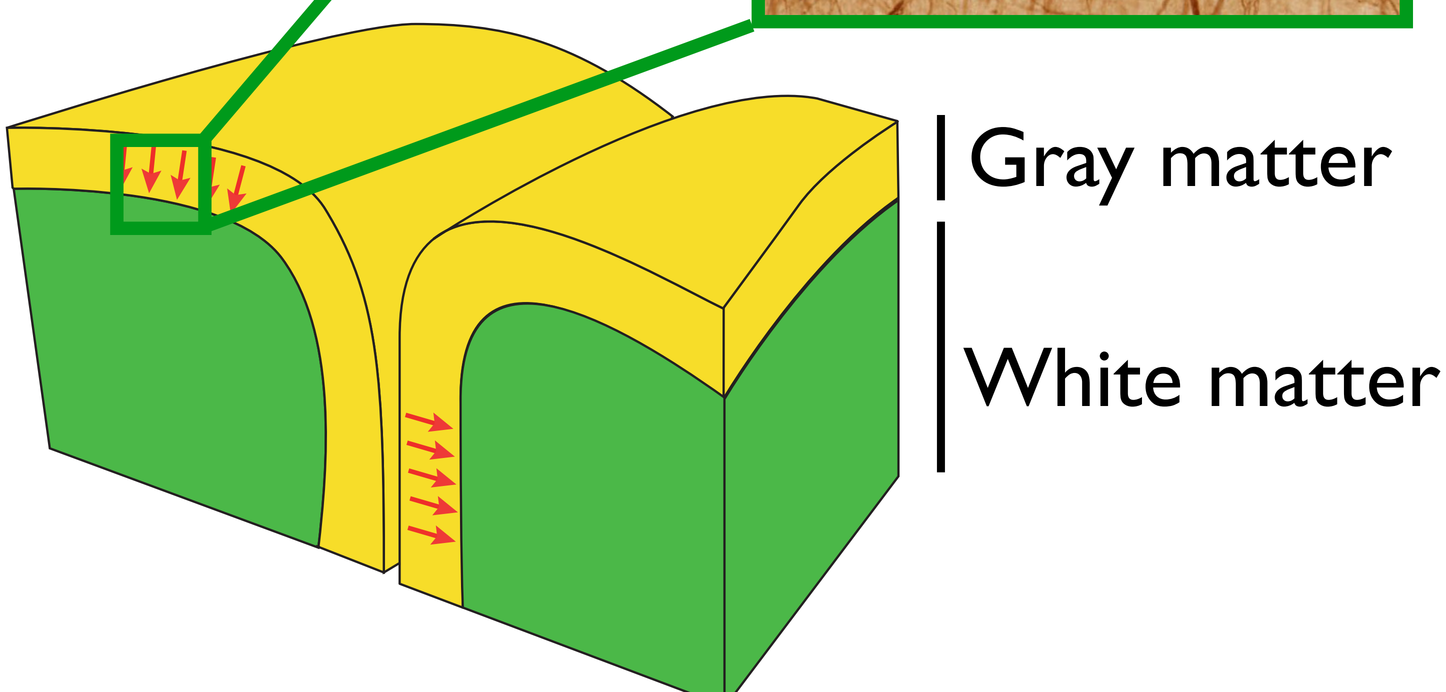
Hôpital La Timone
Marseille, France

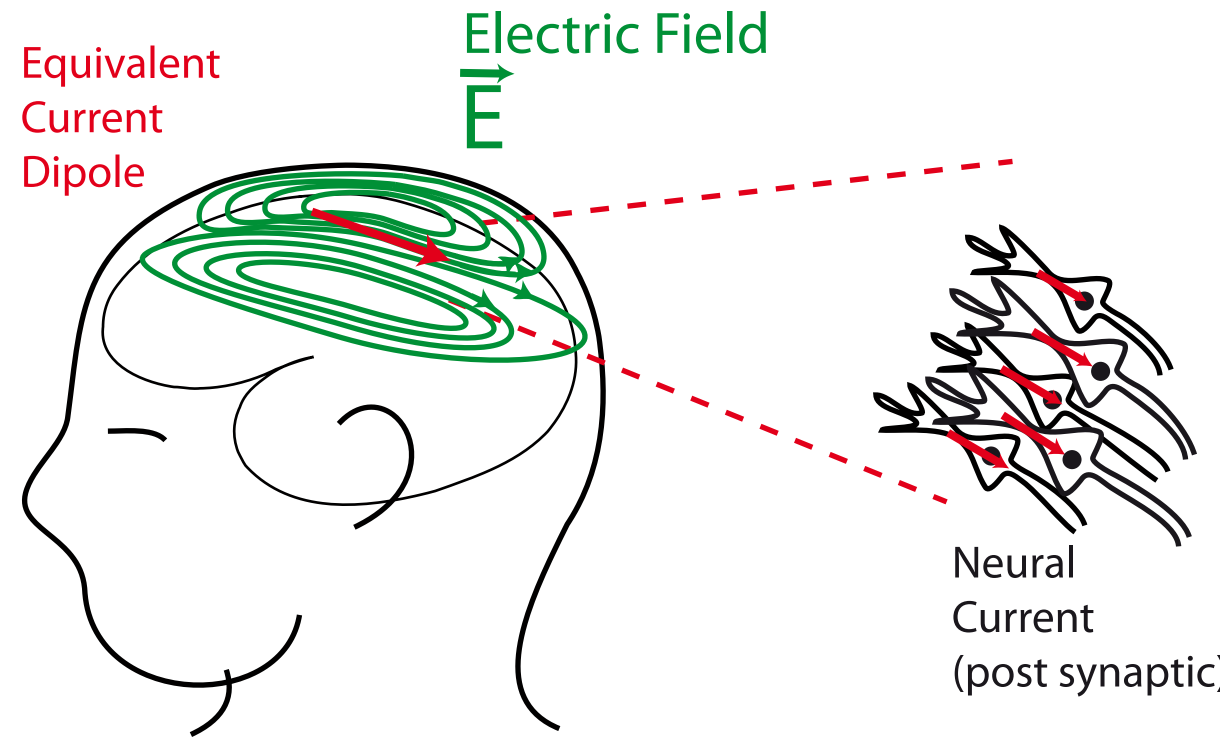
#sources #MEG #EEG

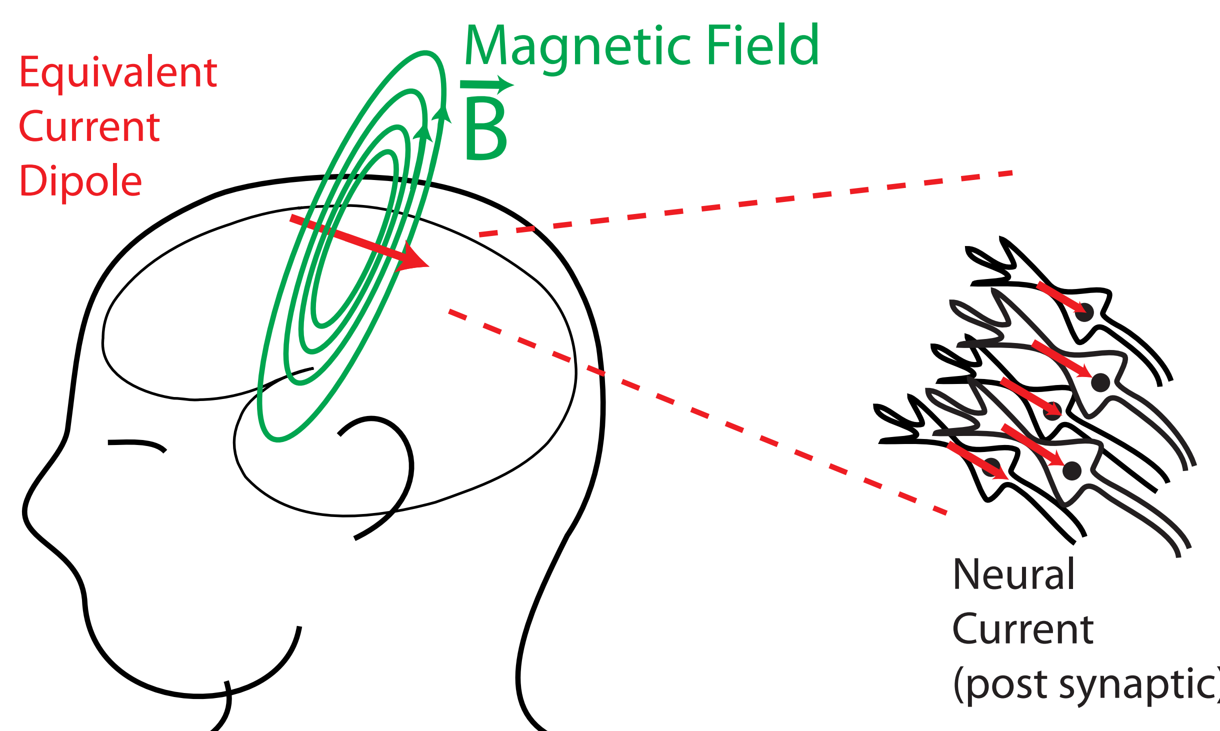
Large cortical pyramidal cells organized in macro-assemblies with their **dendrites normally oriented to the local cortical surface**

$Q = I \times d$
(10 to 100 nAm) with the equivalent current dipole (ECD) model



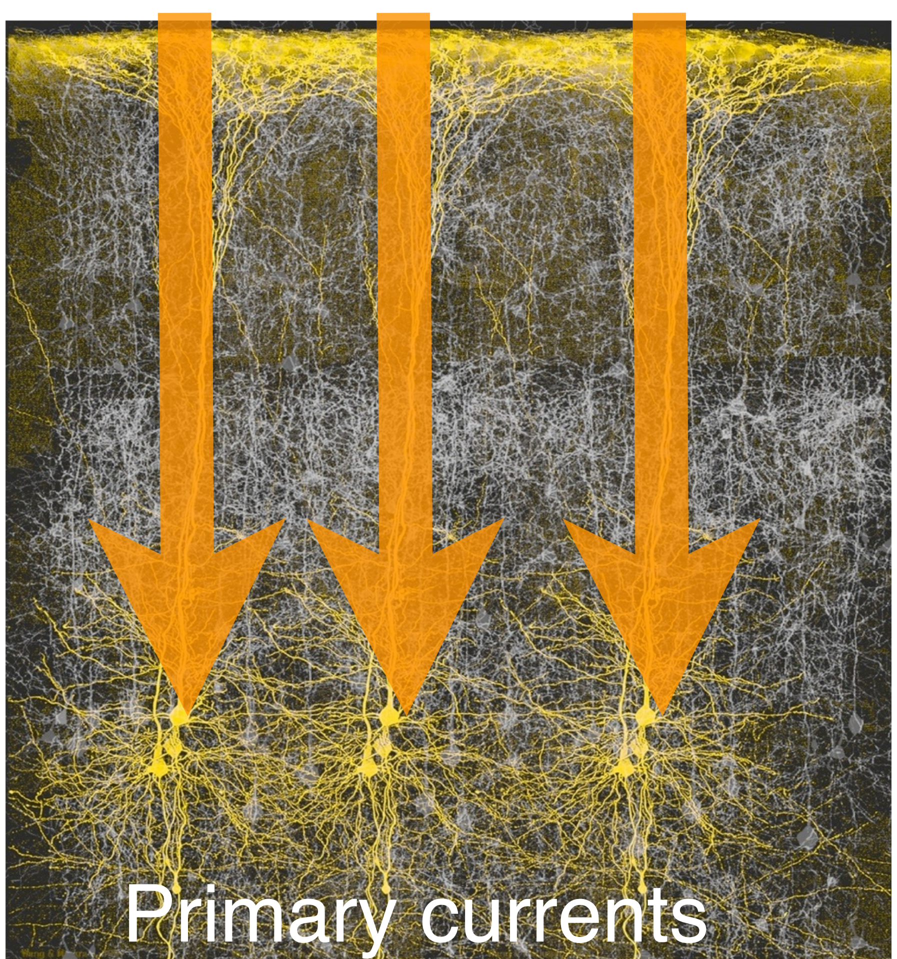






MEG+EEG are complementary

Large cortical pyramidal cells organized in macro-assemblies with their **dendrites normally oriented to the local cortical surface**



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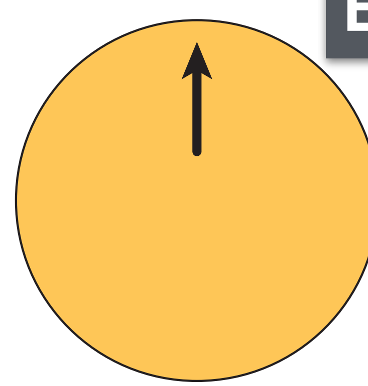
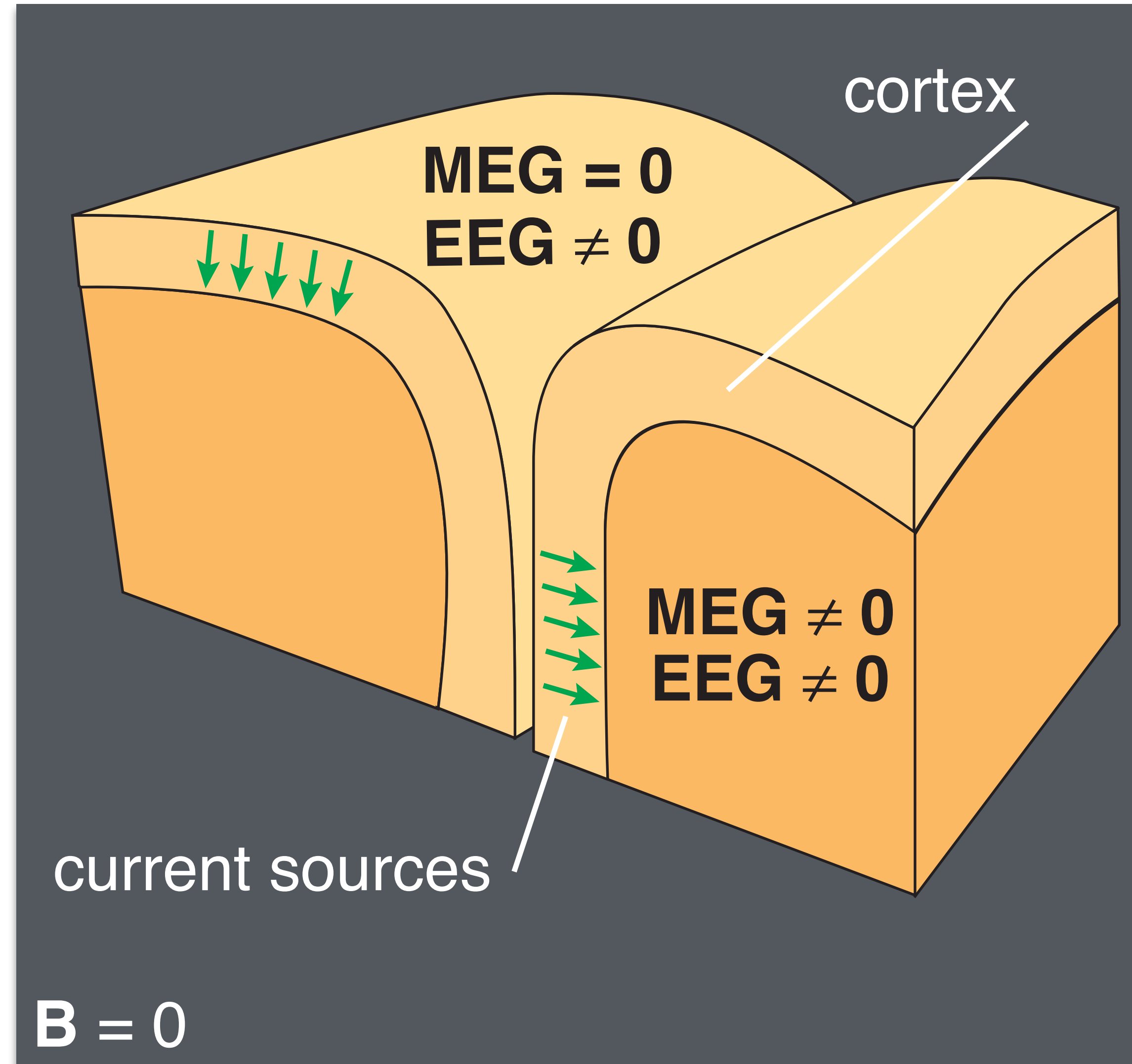
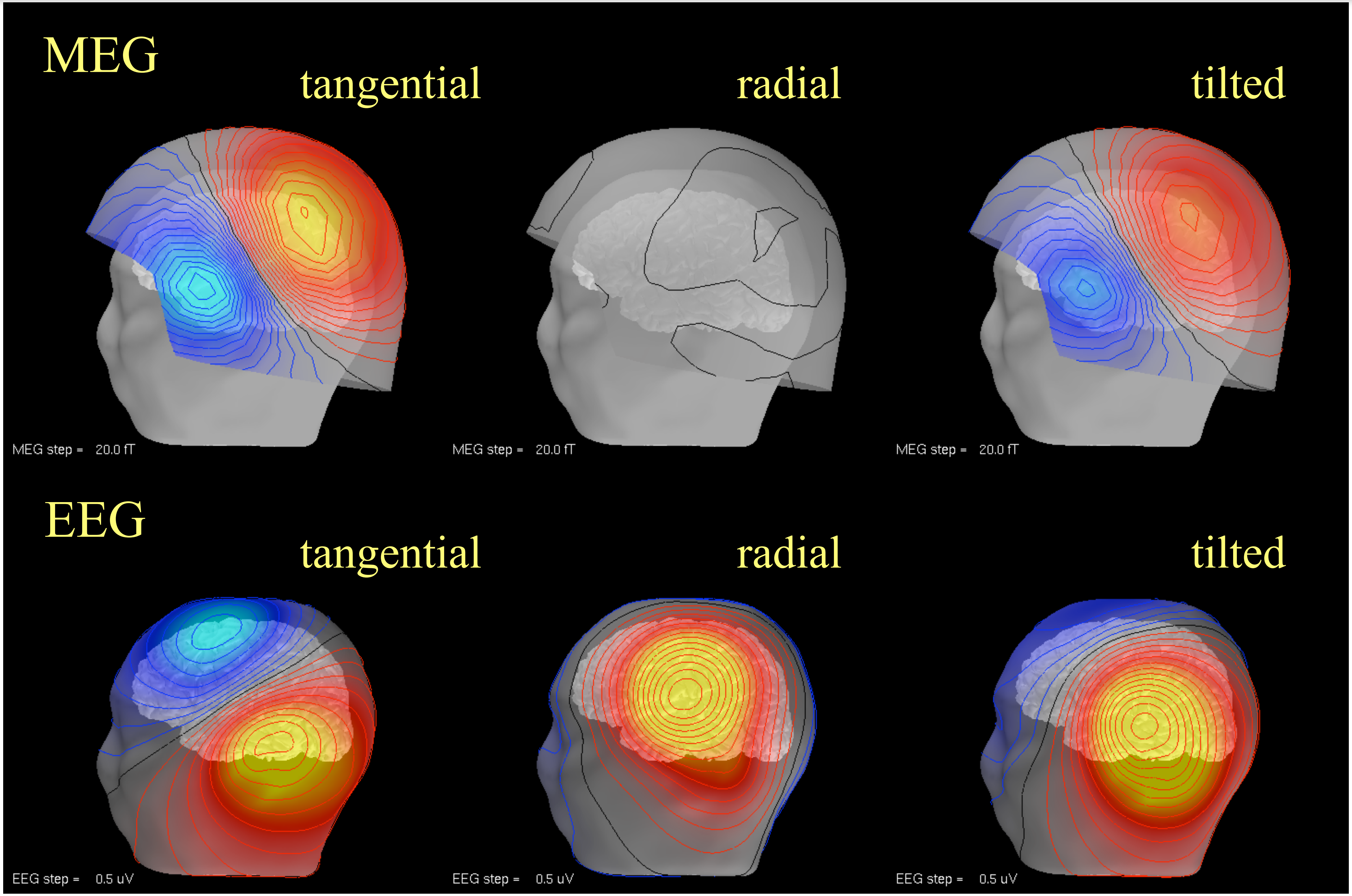


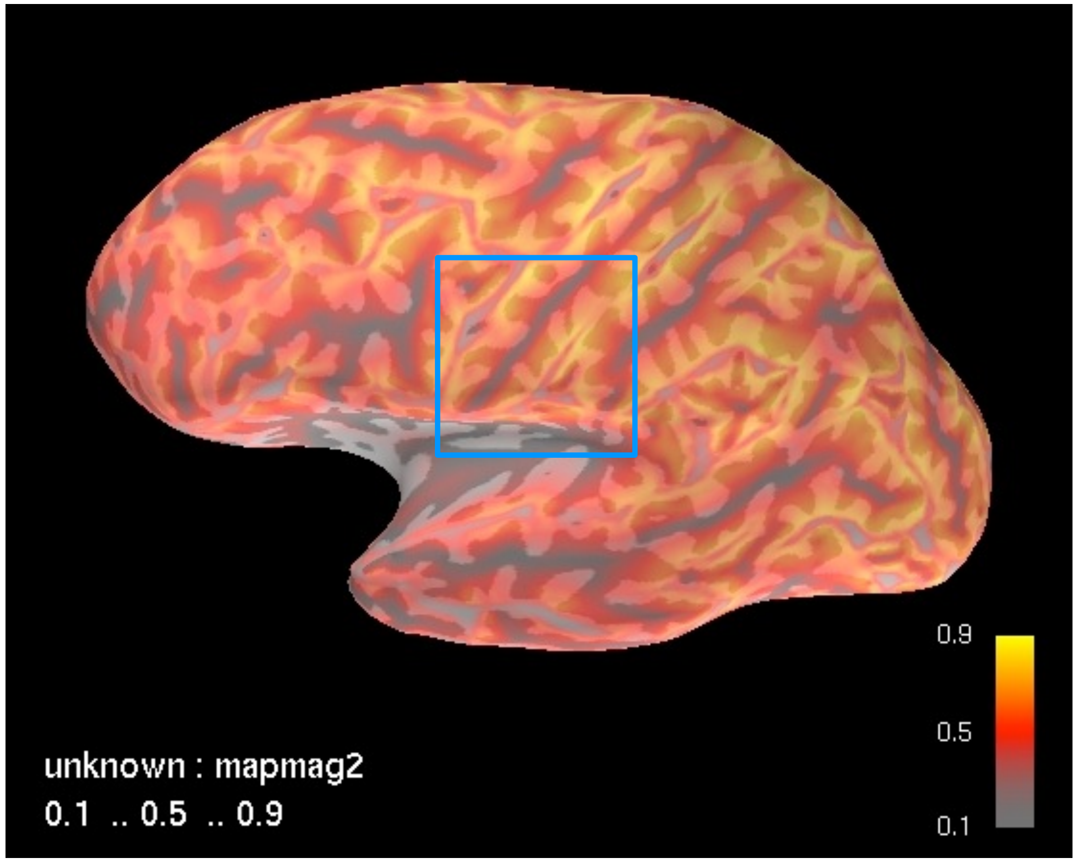


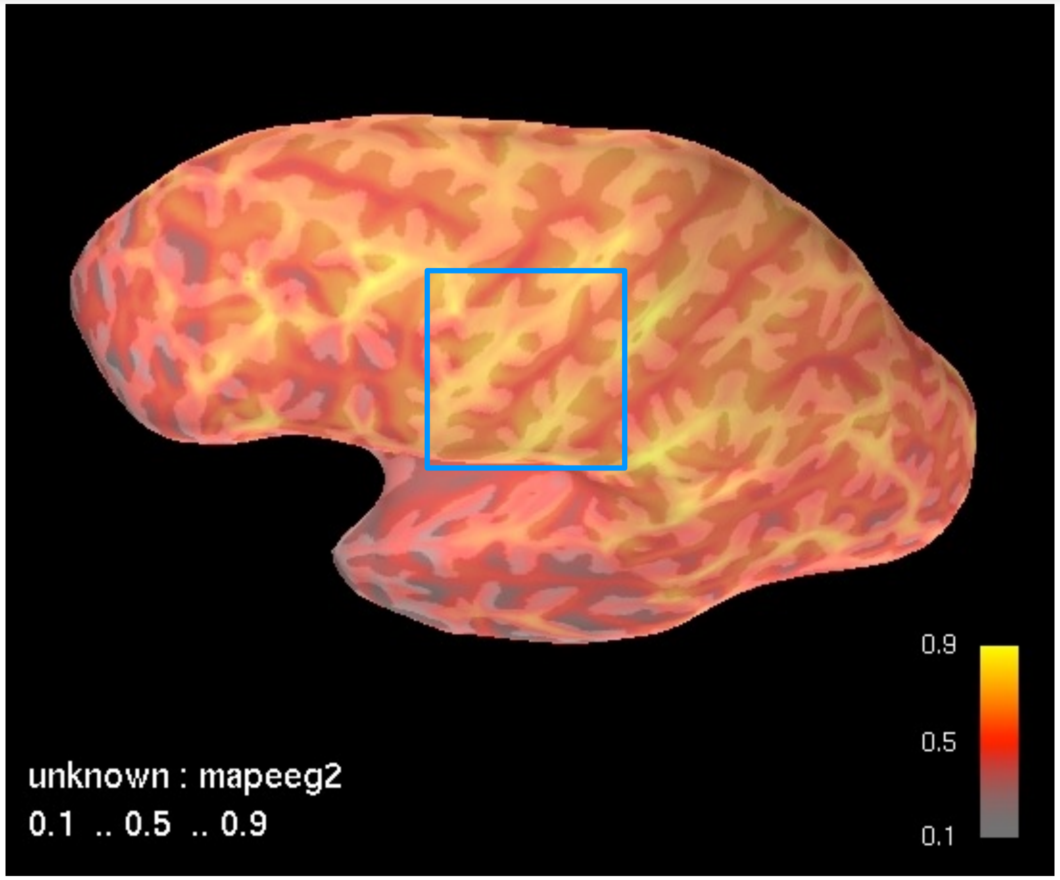
MEG+EEG are complementary



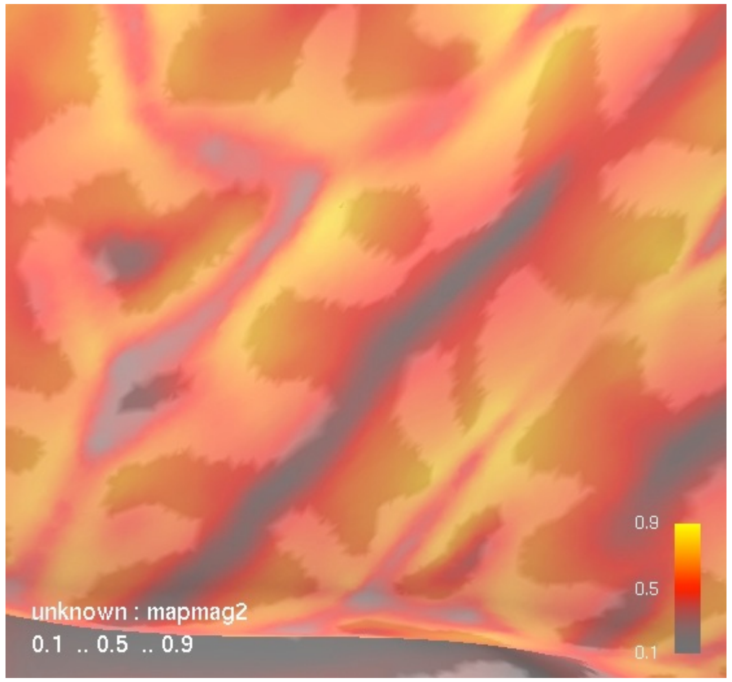
MEG has only one prototypical field pattern

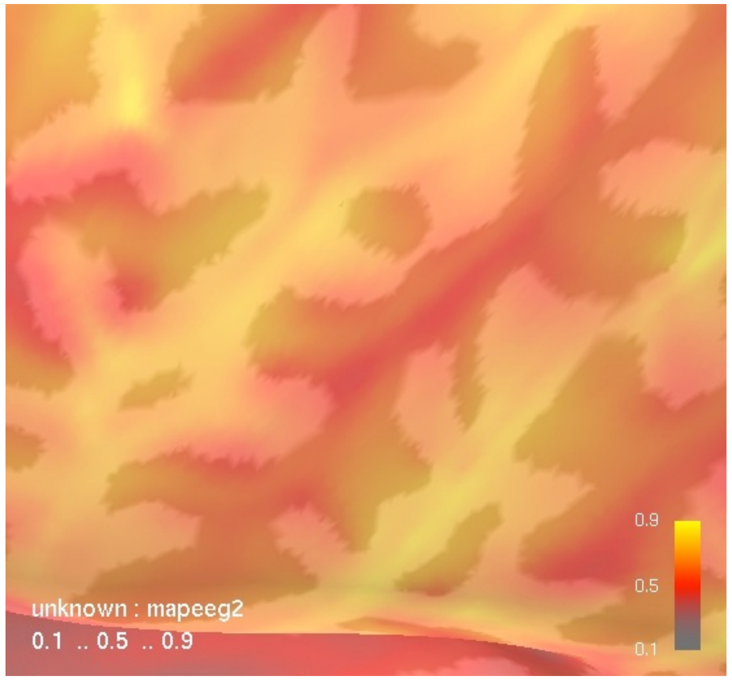
MEG+EEG are complementary





MEG

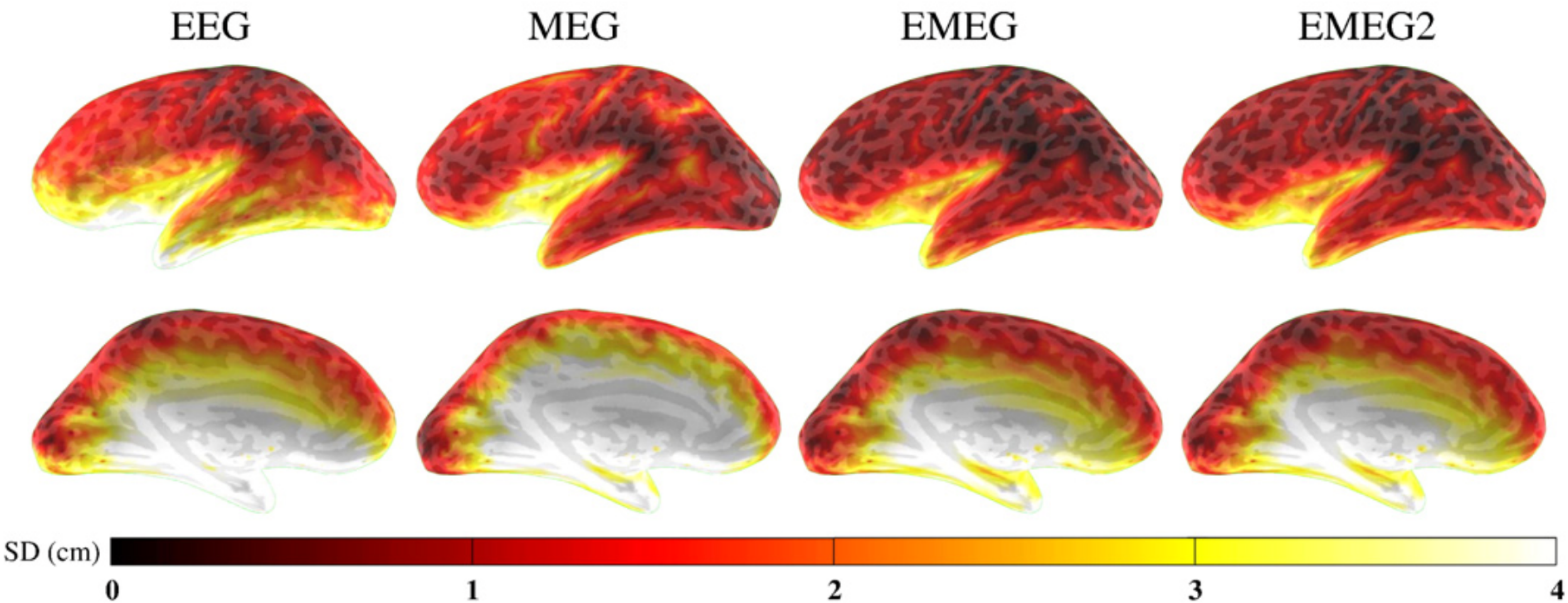




EEG

sensitivity across cortical regions

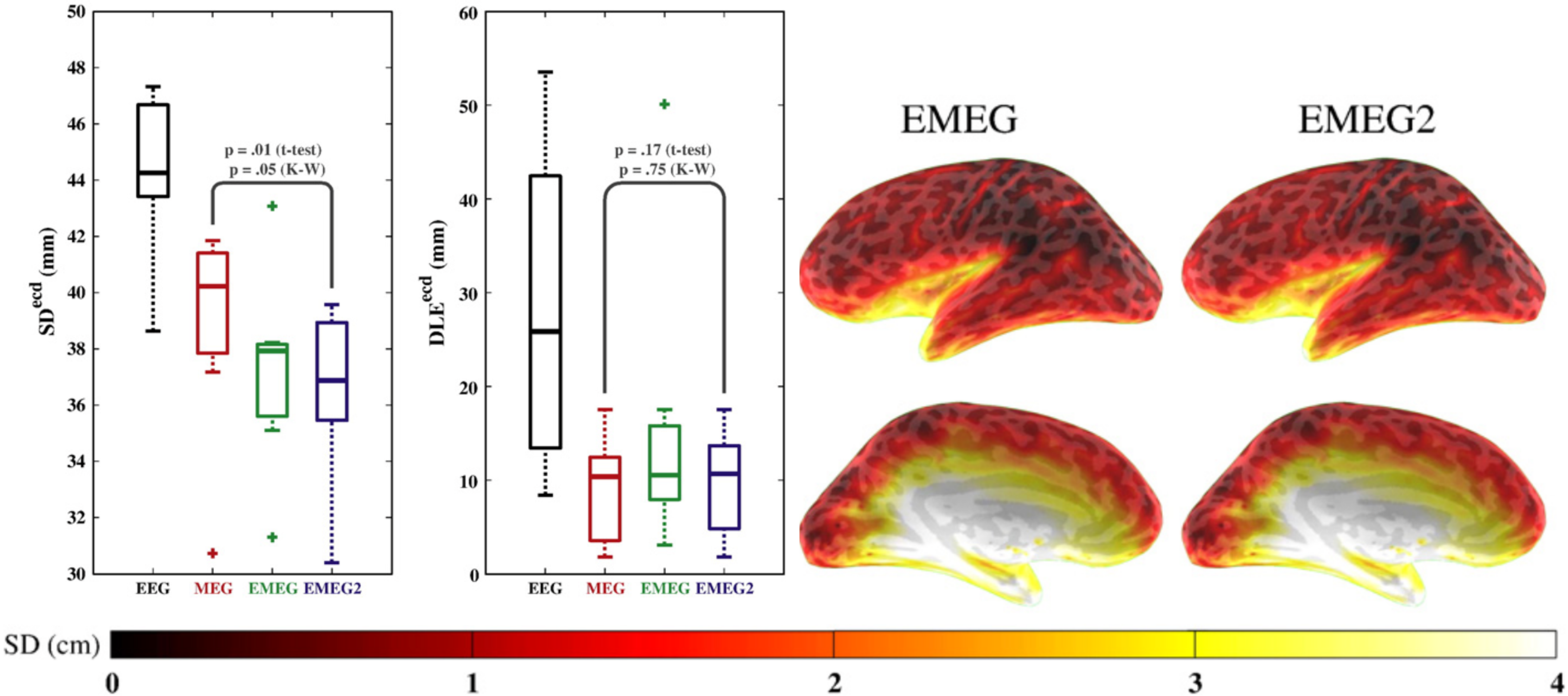
MEG+EEG are complementary



spatial dispersion of combined MEG+EEG

Molins, Stufflebeam, Brown and Hämäläinen, 2008, Neuroimage

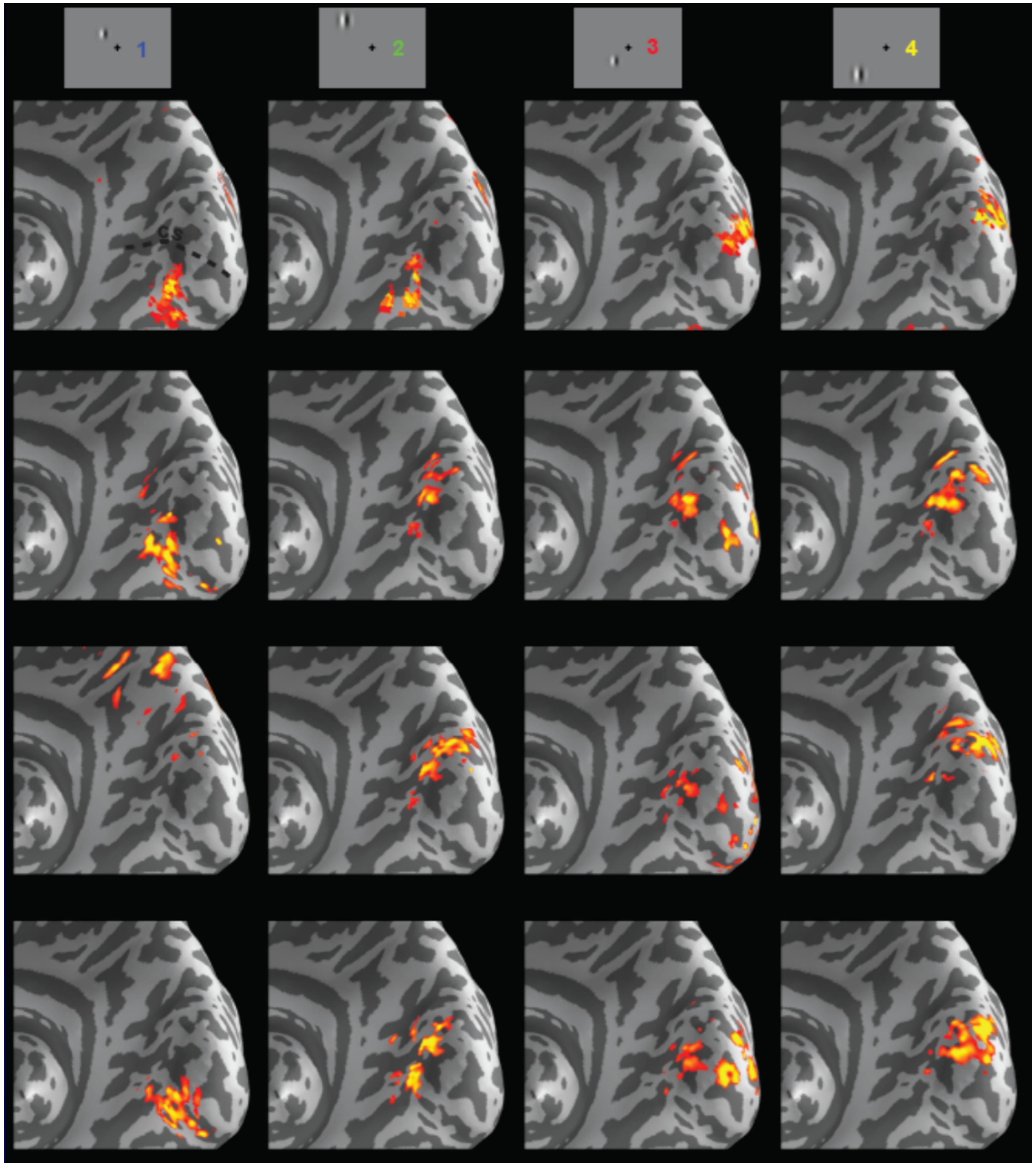
MEG+EEG are complementary



spatial dispersion of combined MEG+EEG

Molins, Stufflebeam, Brown and Hämäläinen, 2008, Neuroimage

MEG+EEG map better on BOLD



fMRI

MEG

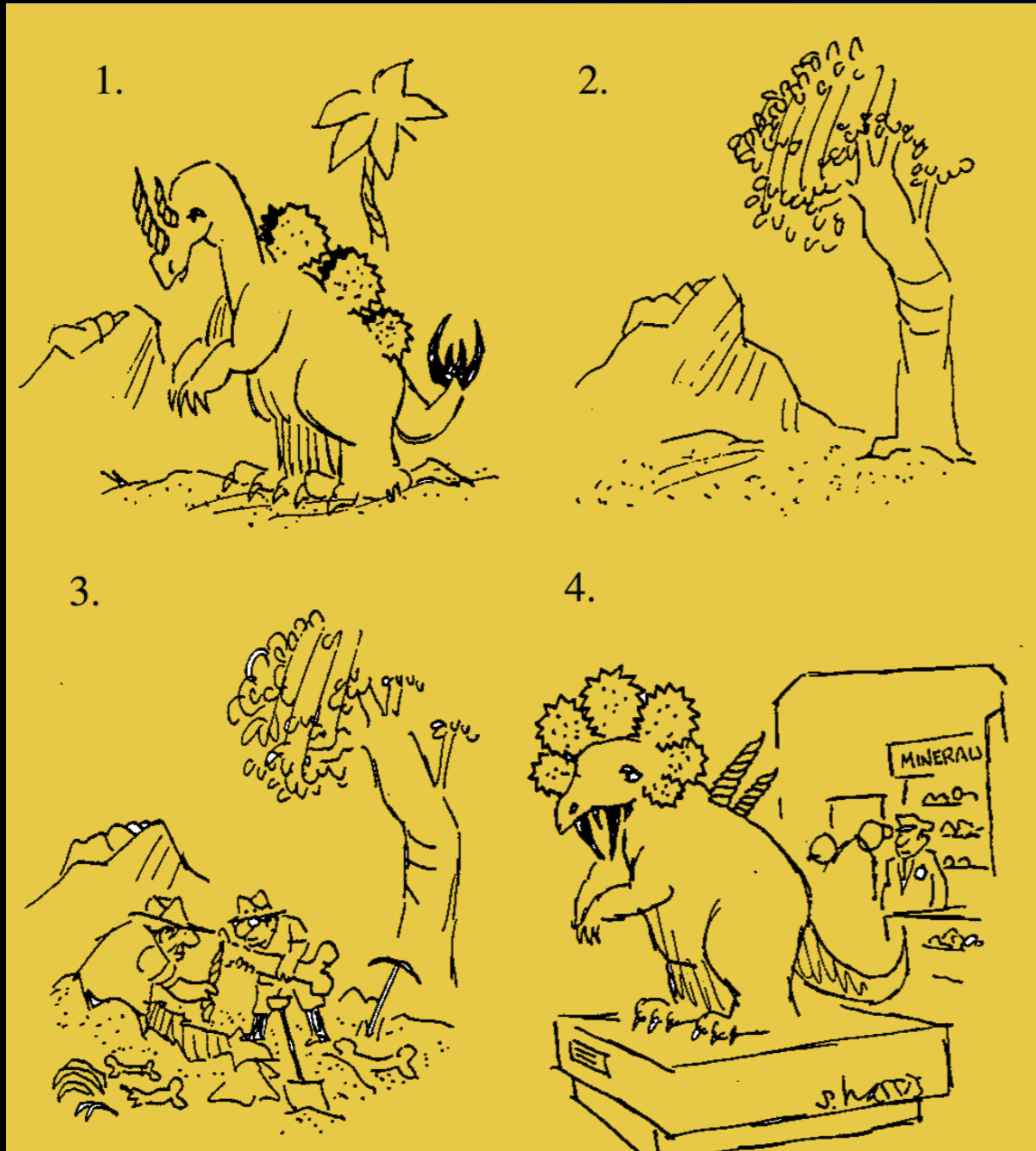
EEG

MEEG

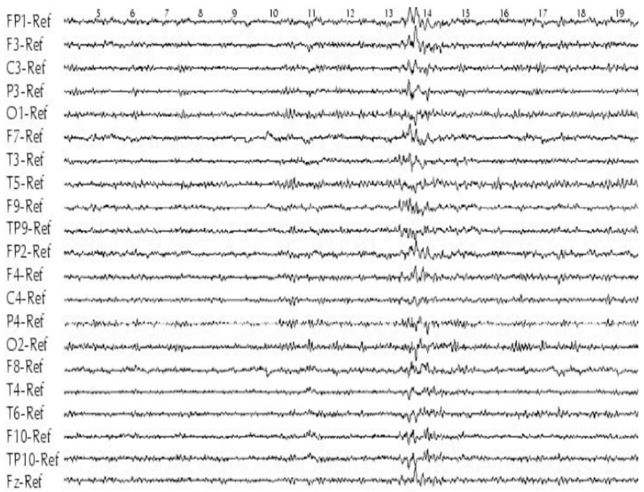
Sharon et al. 2007, NeuroImage

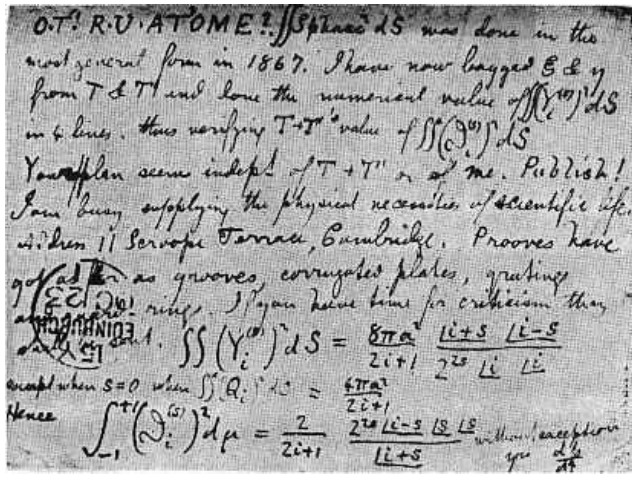
MEG, EEG and statistics

Basic concepts, notations, modeling strategies


1.
2.
3.
4.
s.harris

inverse and forward problems

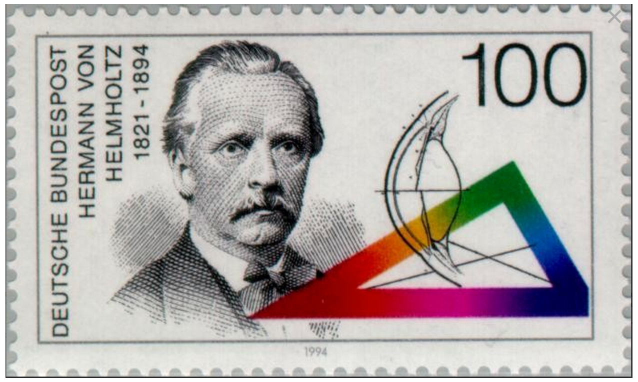




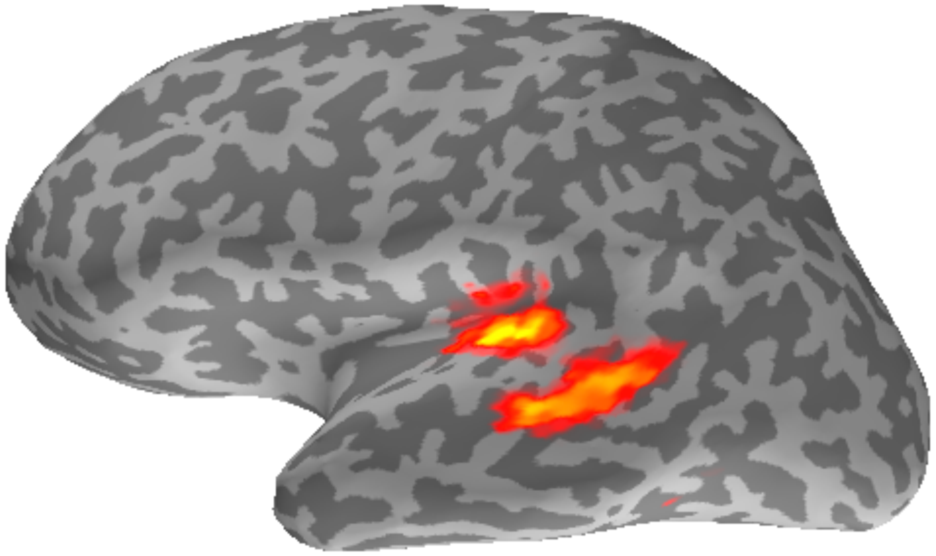
can be solved

MEG/EEG

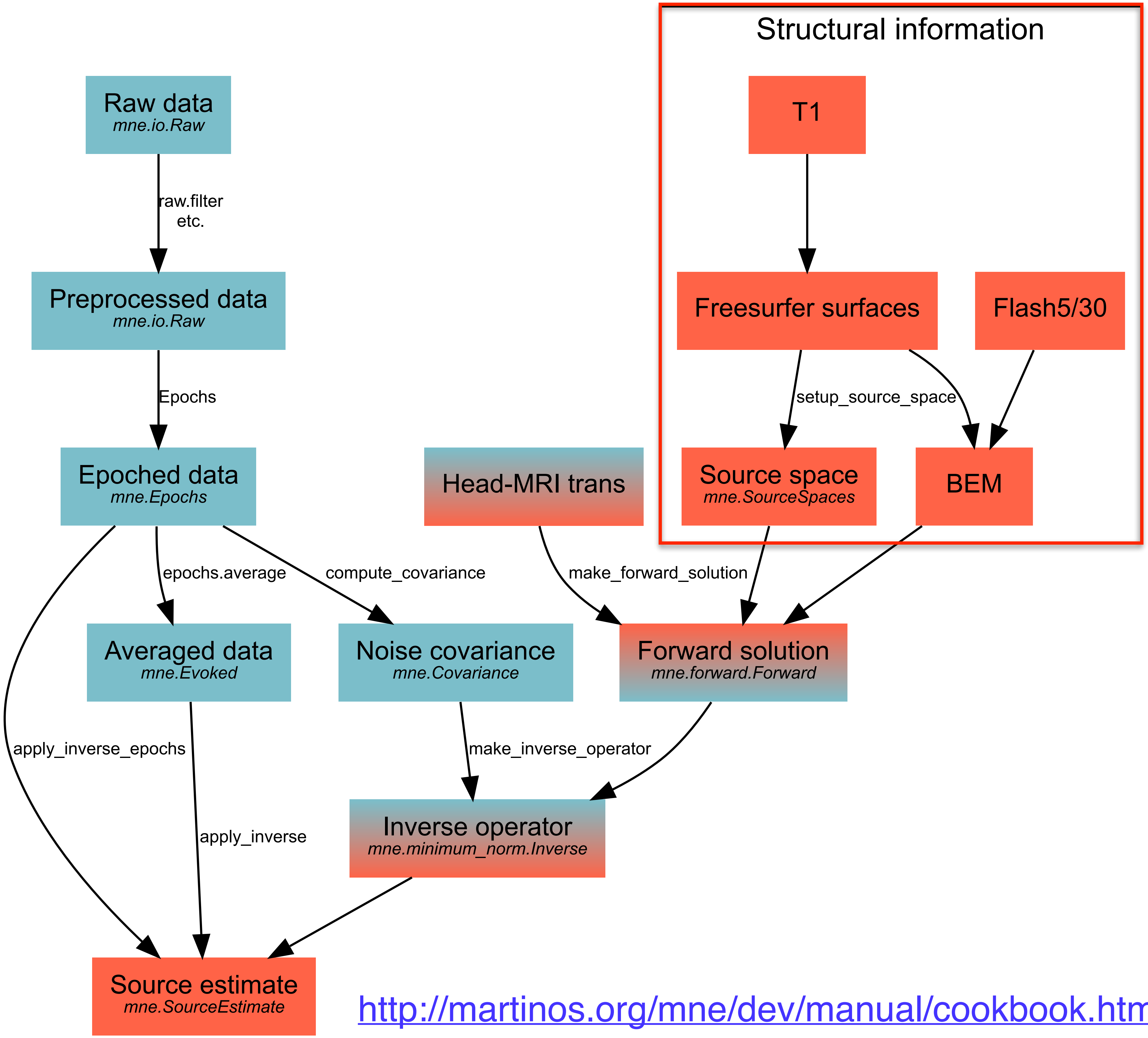
equivalent currents



ill-posed:
can only be
approximated



inverse modeling workflow

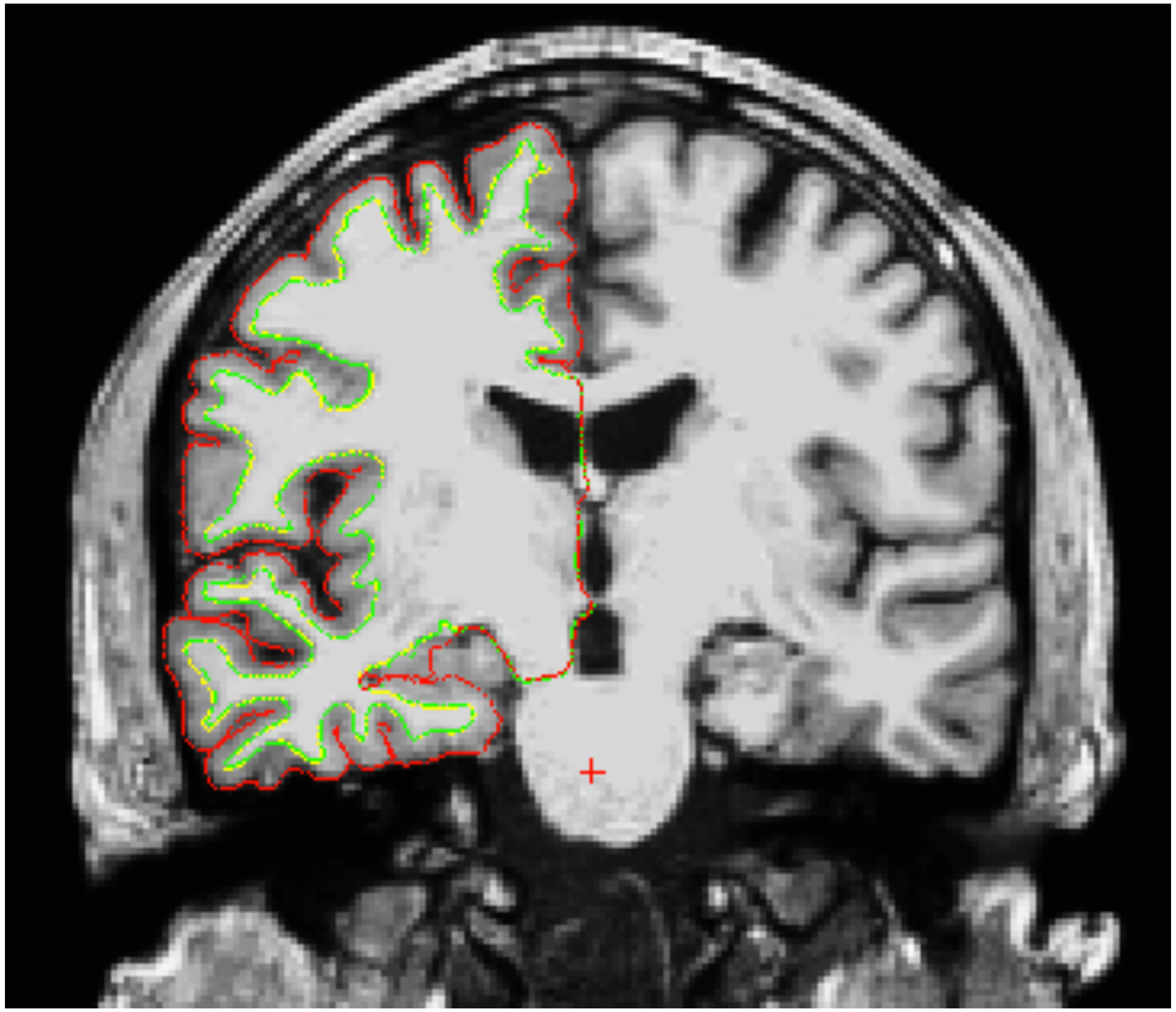


http://martinos.org/mne/dev/manual/cookbook.html

Freesurfer recon-all

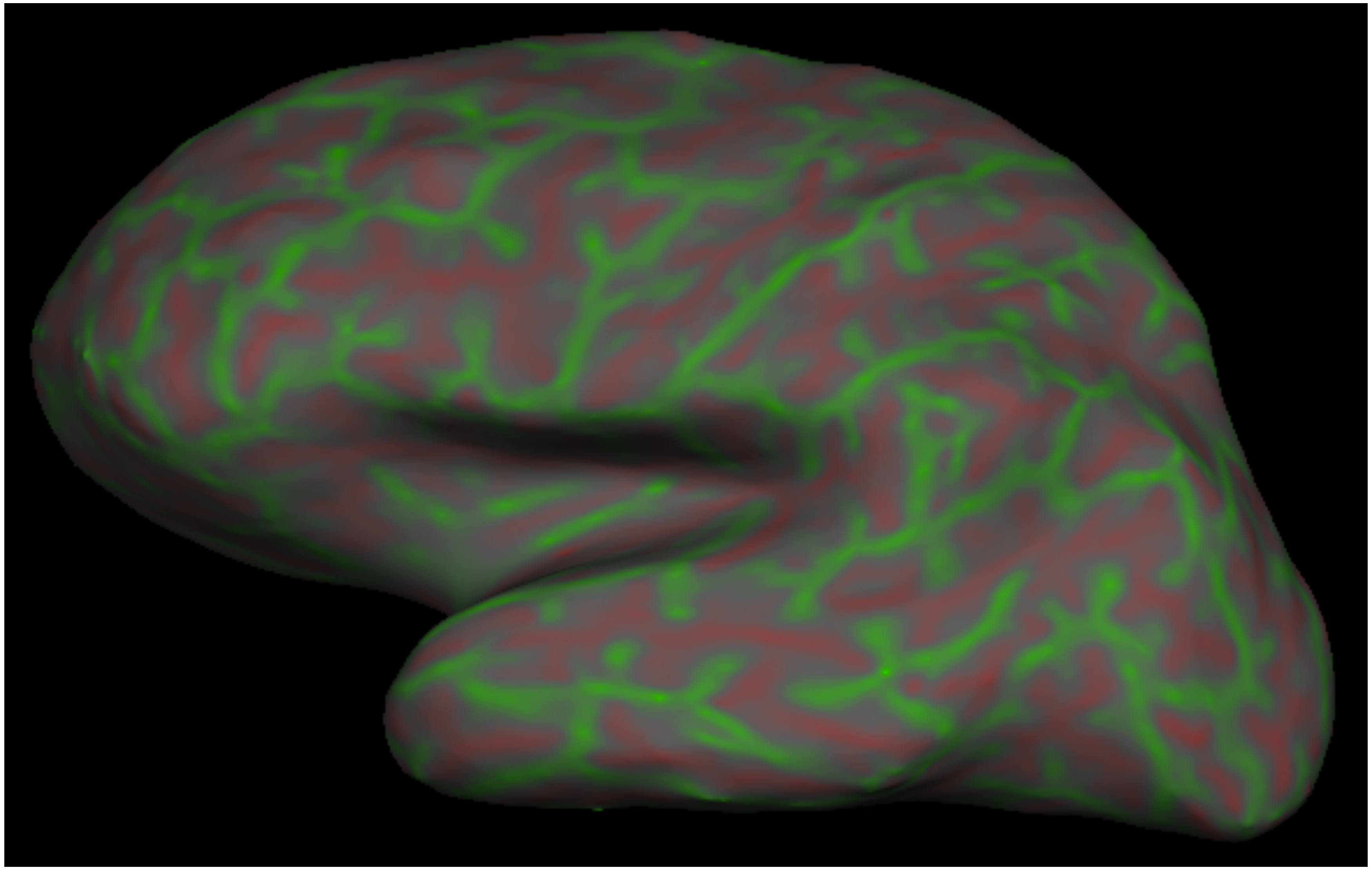
check segmentation with:

$ tkmedit ${SUBJECT} T1.mgz -surface rh.white



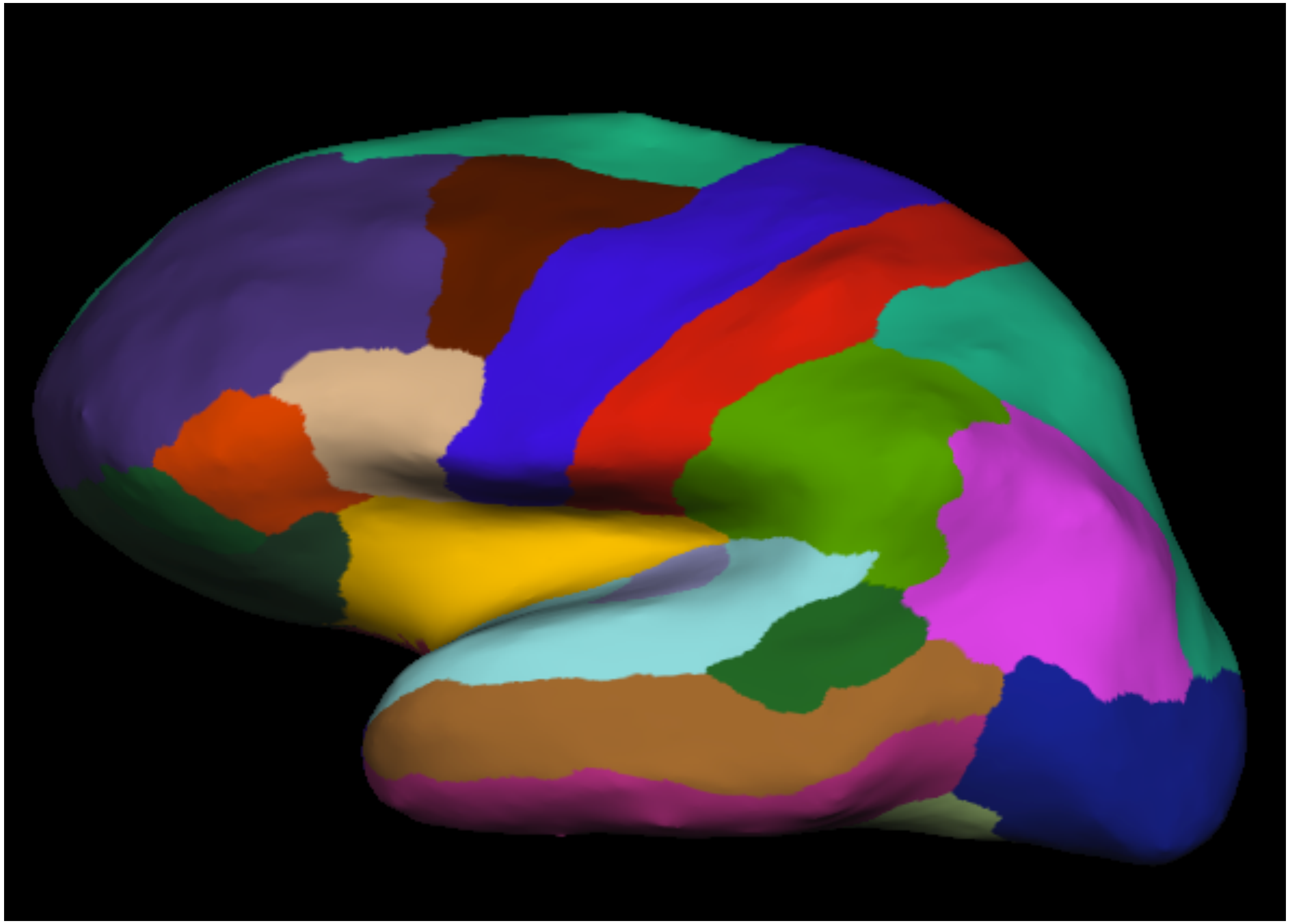
recon all — surfaces

$ tksurfer sample lh inflated -curv

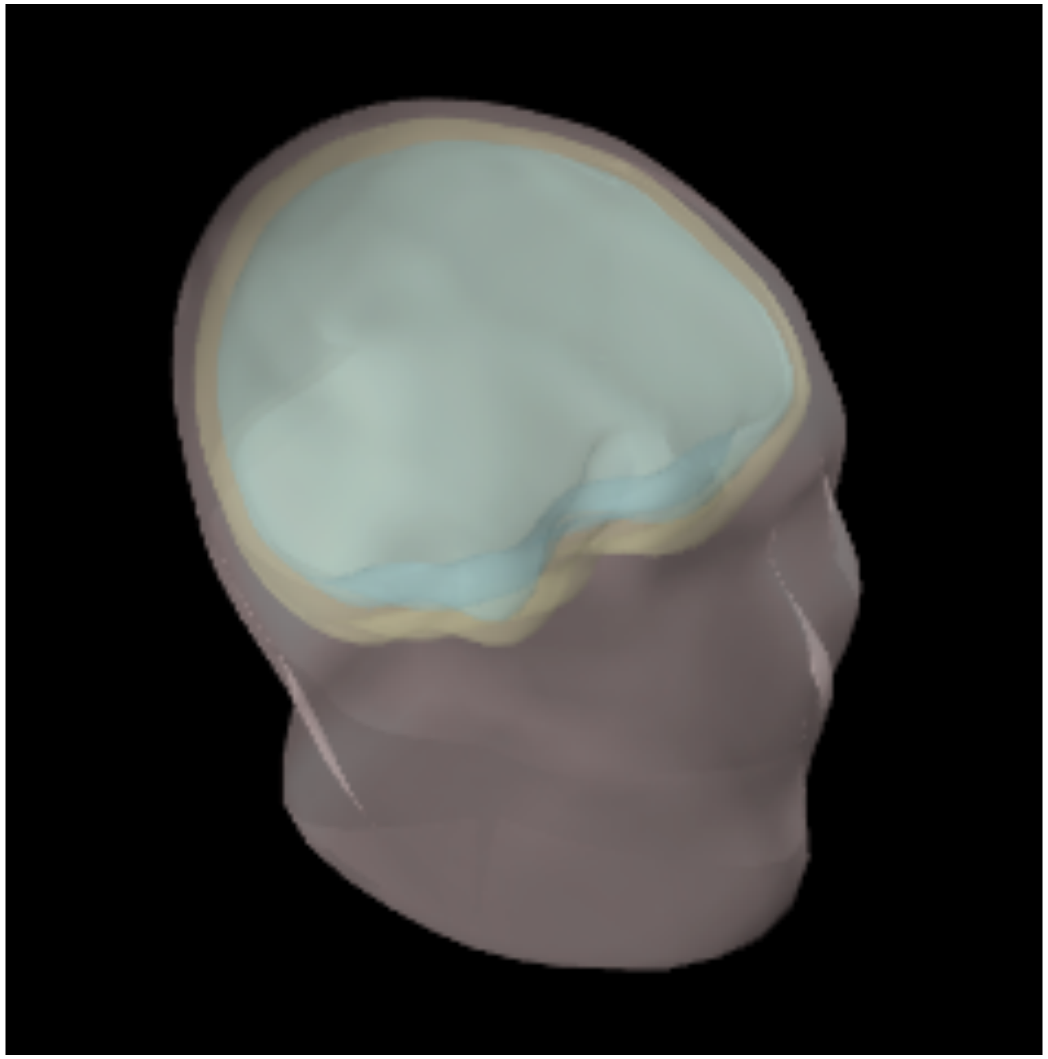


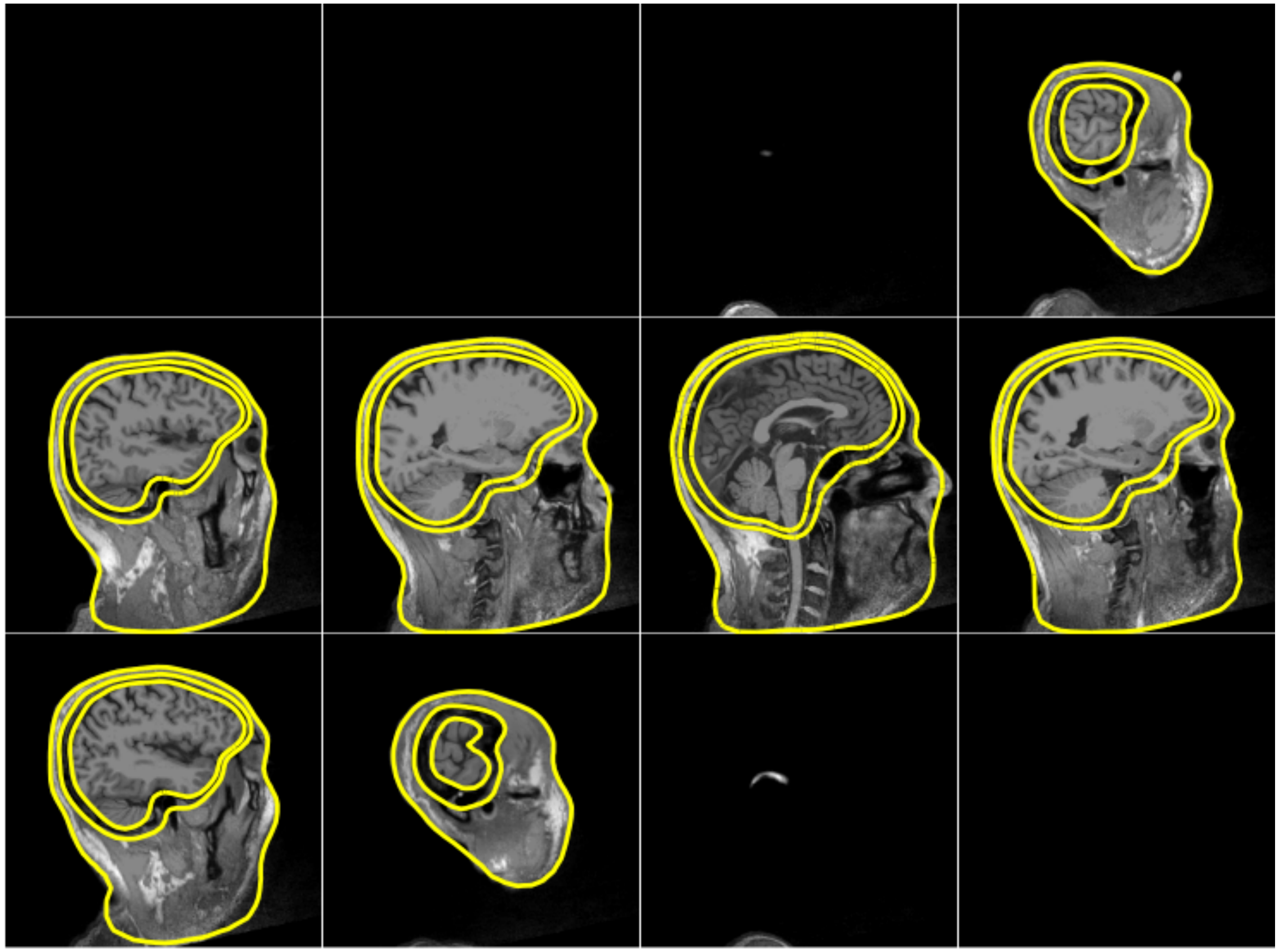
recon all — labels

```
$ tksurfer sample lh inflated -annotation aparc
```



BEM surfaces

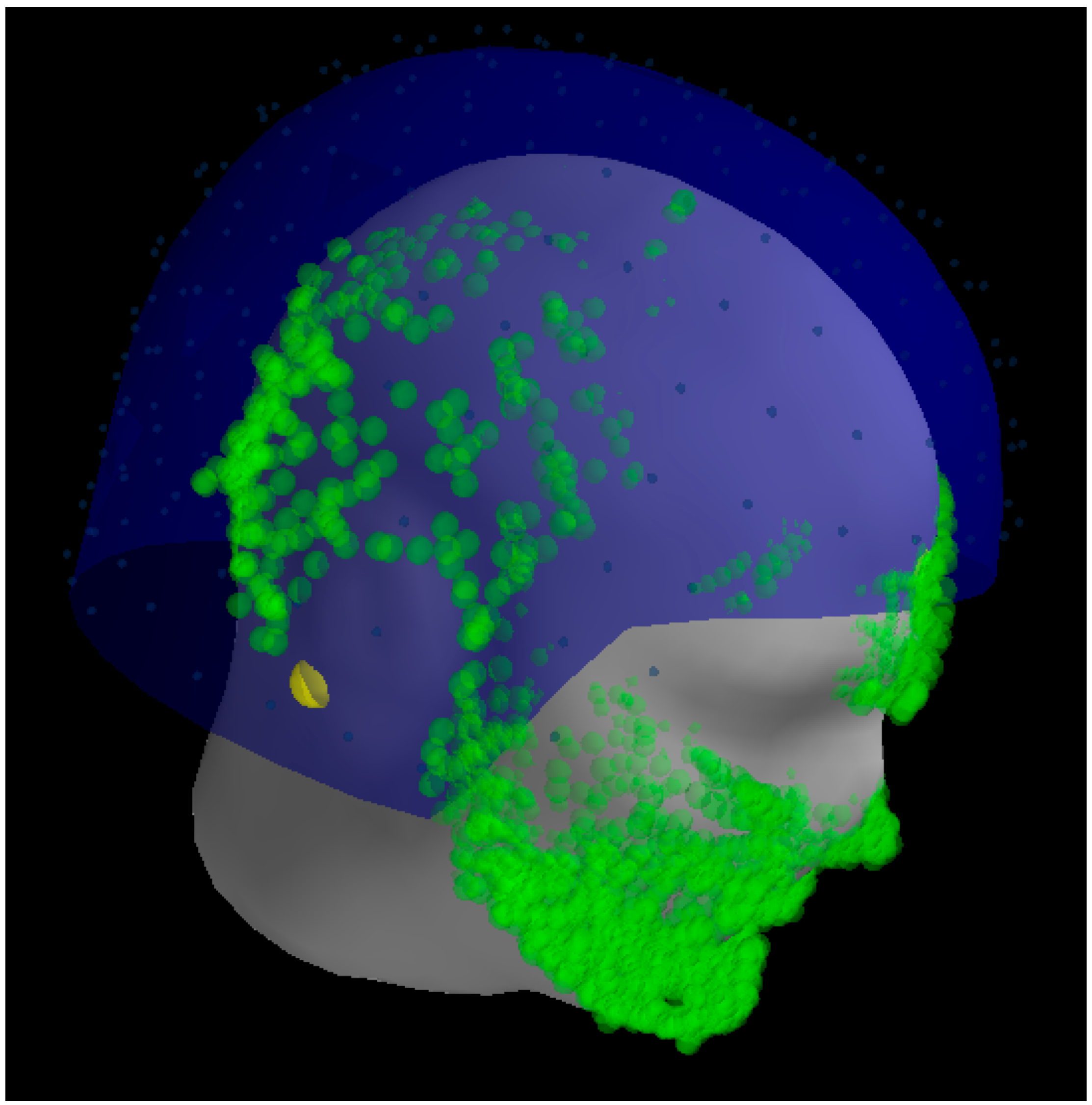




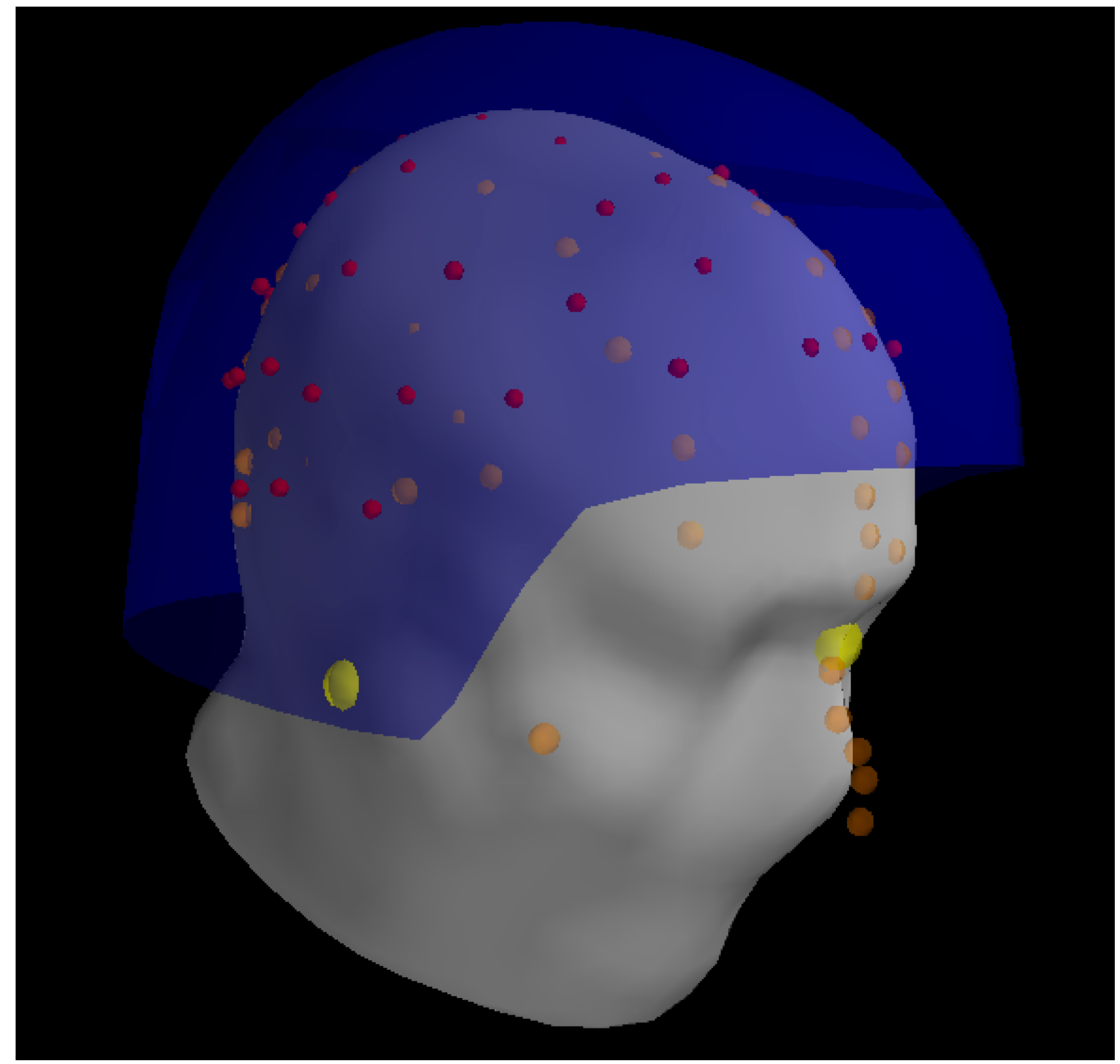
For EEG: 3 layer boundary element model (BEM):

1) brain 2) skull 3) head

MEG (and EEG?) Coregistration

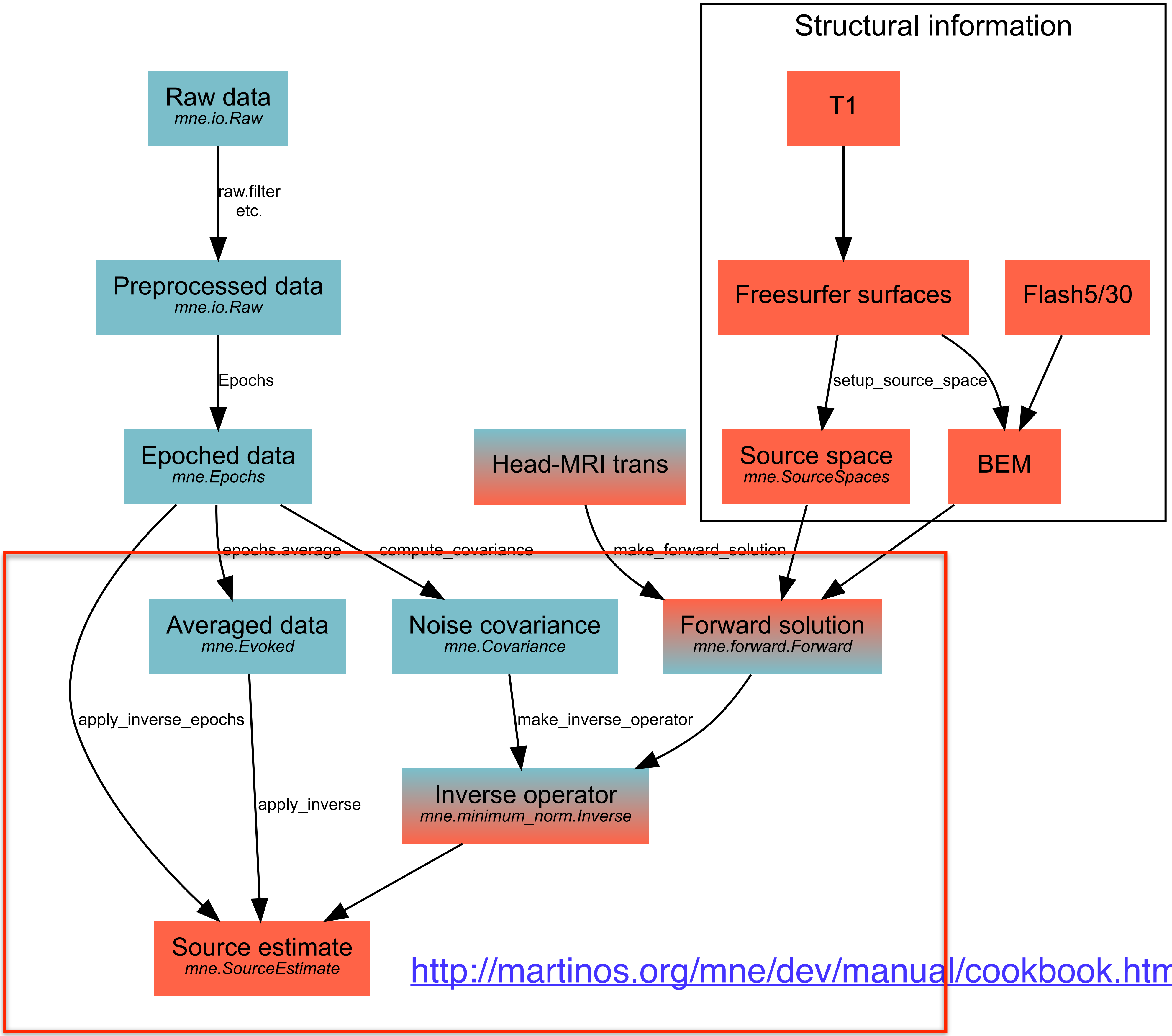


MEG + headshape points



MEG + EEG electrodes + fiducials

inverse modeling workfow



http://martinos.org/mne/dev/manual/cookbook.html

M/EEG Measurements: Notation

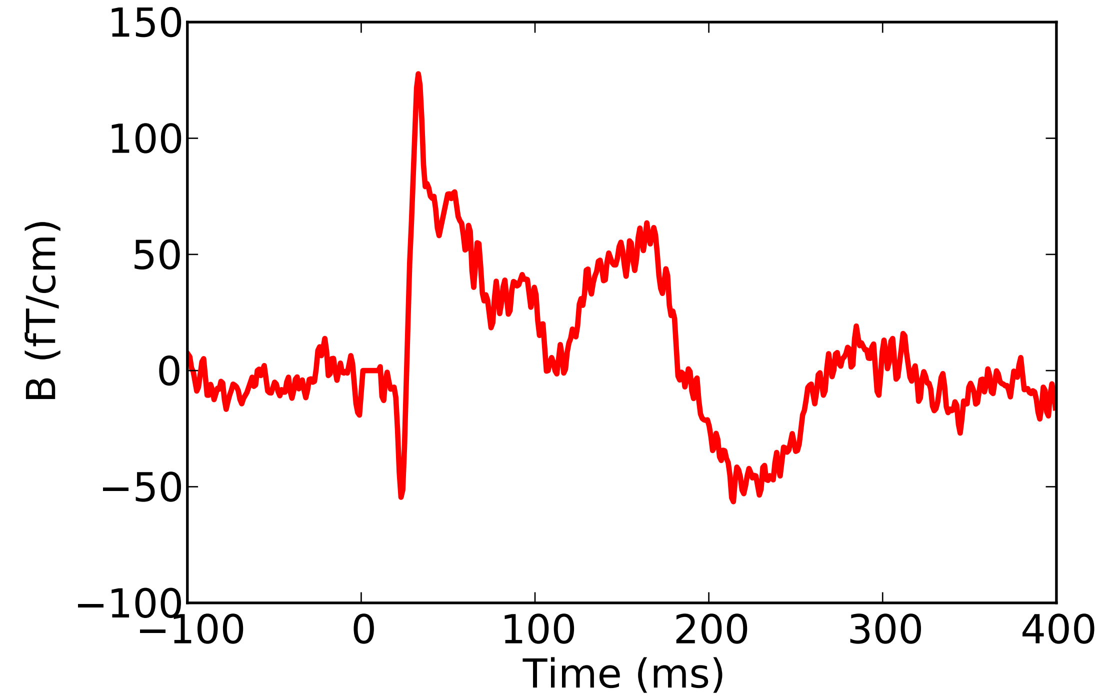
$$\mathbf{M} = \begin{bmatrix} \; \end{bmatrix} \in \mathbb{R}^{d_m \times d_t}$$

MEG and/or EEG

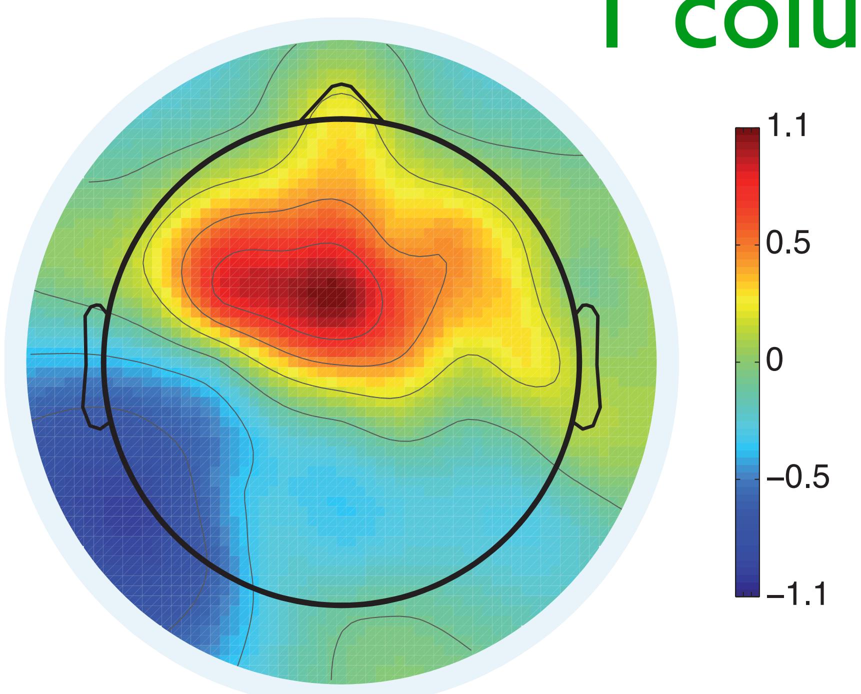
d_m : Nb of sensors

d_t : Nb of time points

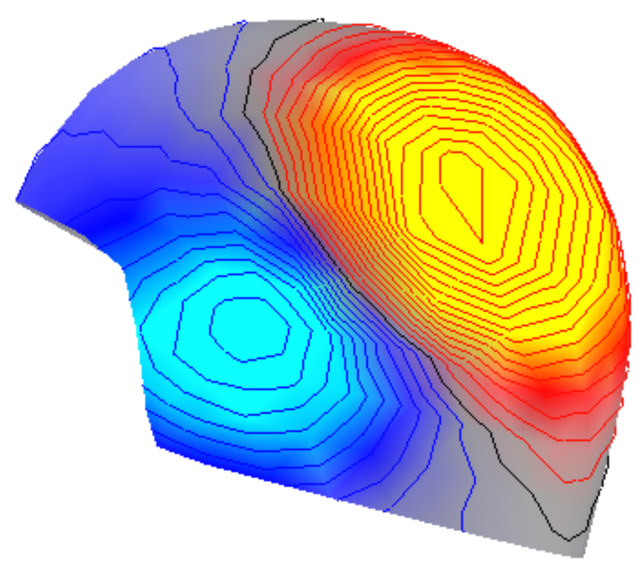
1 column



1 row = 1 time series on 1 sensor



2D topography



3D topography

L2 a.k.a. Minimum Norm Estimates (MNE)

$$\phi(\mathbf{X}) = \|\mathbf{W}\mathbf{X}\|_F^2 = \sum_{i,j} w_i^2 x_{ij}^2 = \|\mathbf{X}\|_{\mathbf{\Sigma},2}^2$$

$$\mathbf{W}^2 = \mathbf{\Sigma}$$ *source covariance*

Leads to a **closed form solution** (matrix multiplication):

$$\hat{X} = RG^t(GRG^t + C)^{-1}Y$$

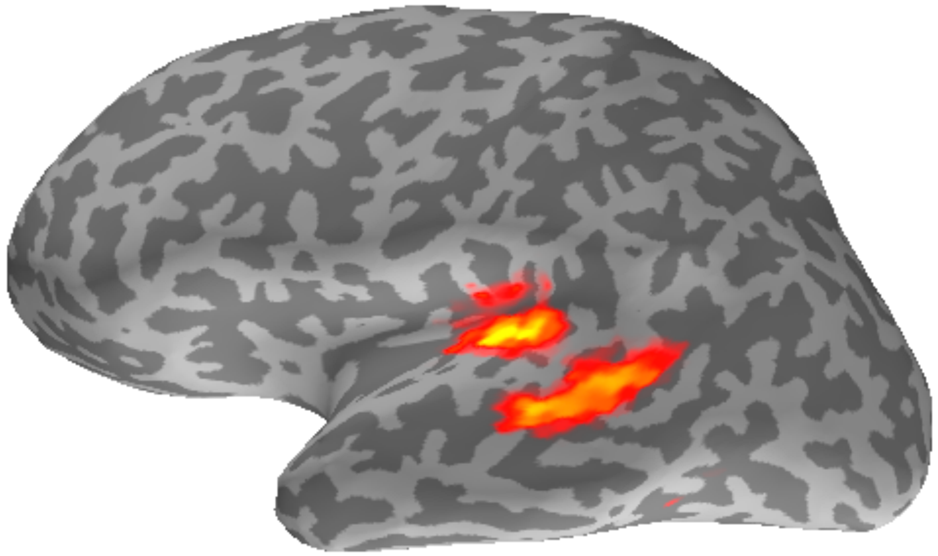
[Tikhonov et al. 77, Wang et al. 92, Hämäläinen et al. 94]

Remarks:

- **Really fast** to compute (SVD of **G**), hence very much used in the field.
- In practice, it's **much more complicated** (whitening data, correcting artifacts, channels with different SNRs, setting λ based on SNR, loose orientation, SNR varies with time...)

THM: A lot of domain knowledge to make it work

y = Xw+E : An ill-posed problem



Standard statistics notations

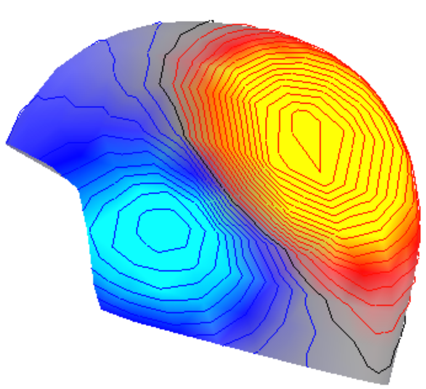
w (or β)

regression coefficients

$d_x \approx 10000$

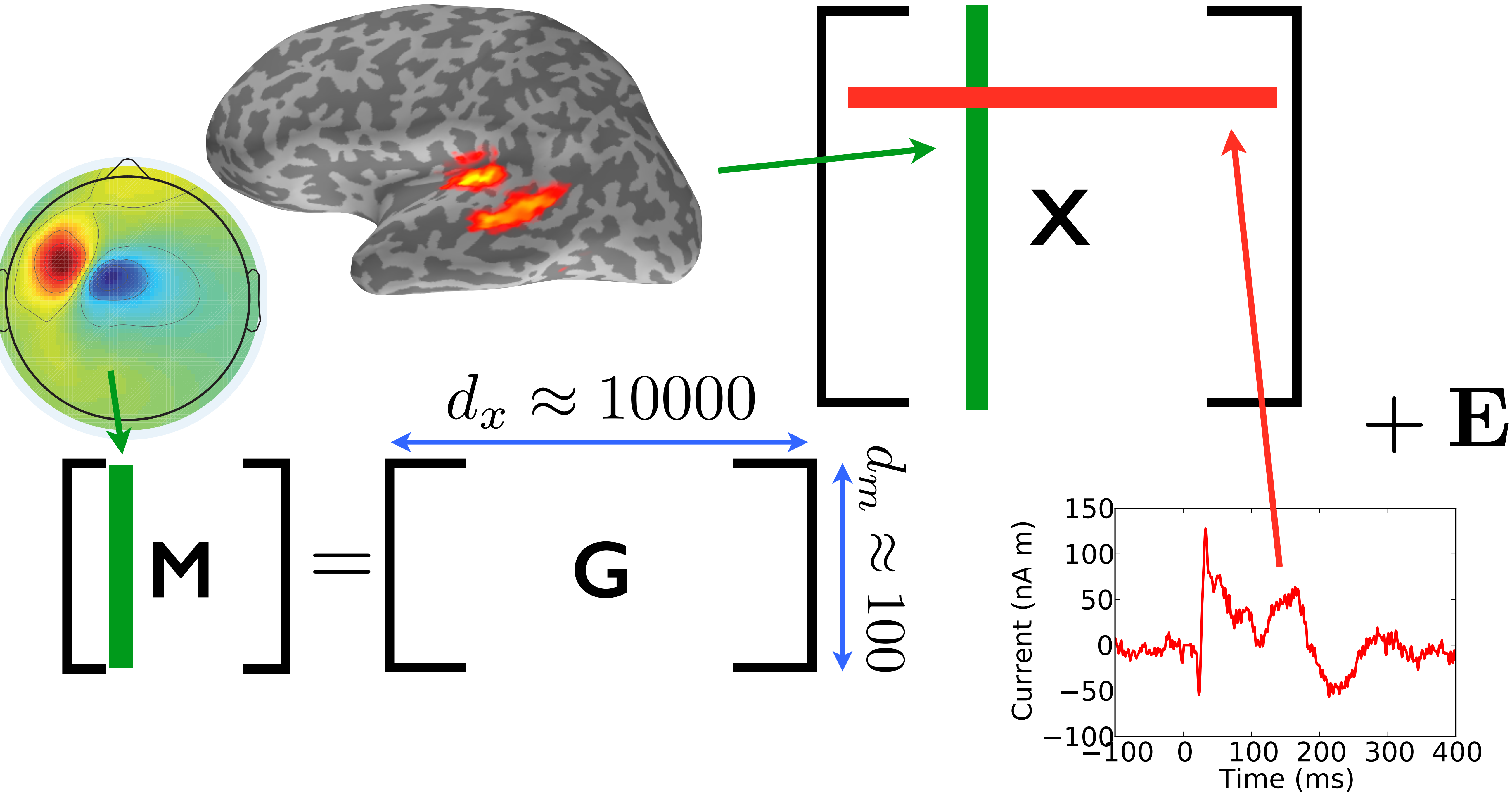
$$\mathbf{y} = \underbrace{\mathbf{X}}_{\text{design matrix}} \mathbf{w} + \mathbf{E}$$

$d_m \approx 100$



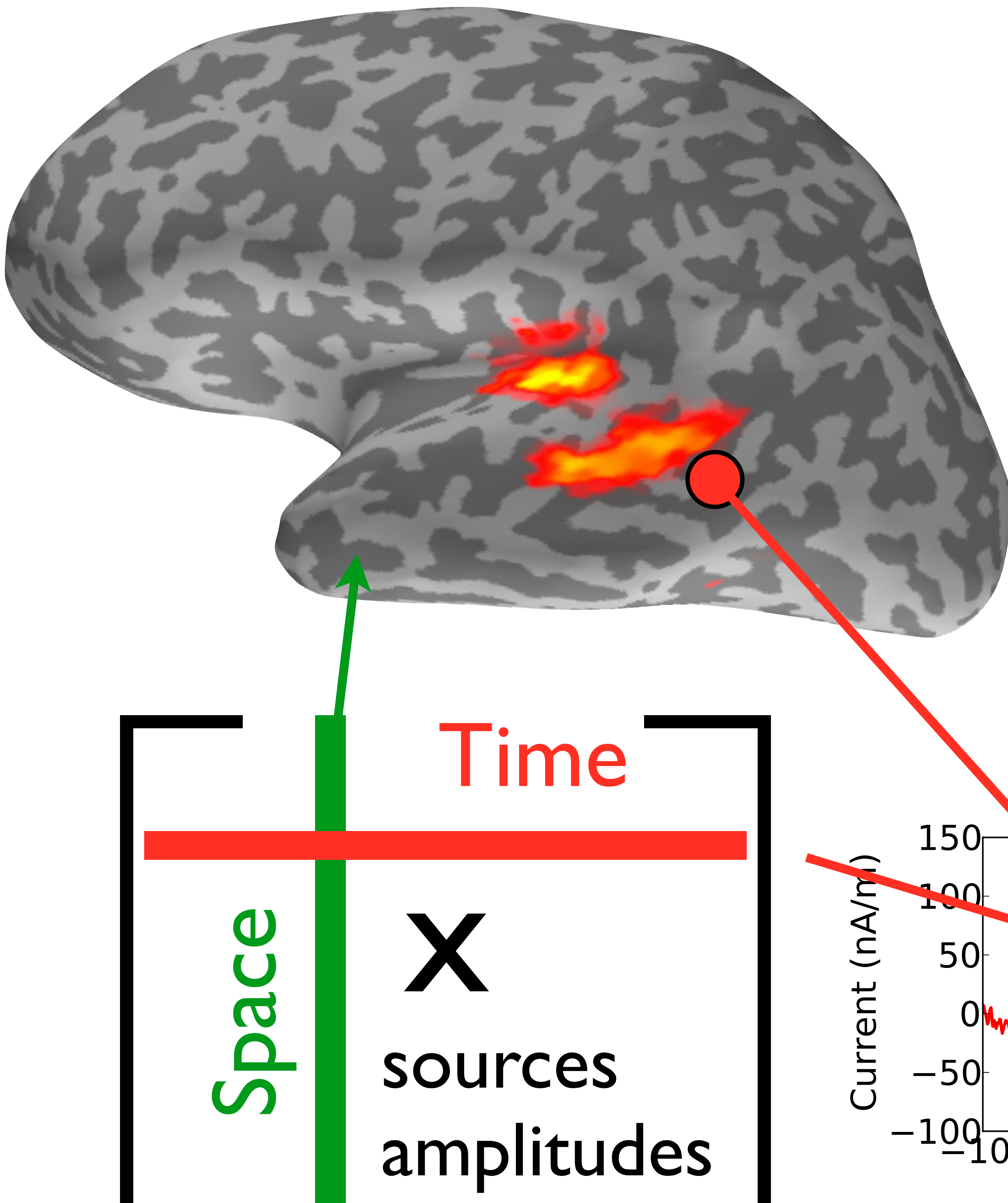
THM: At **each time instant** the M/EEG inverse problem **IS** a **regression** with more variables than observations

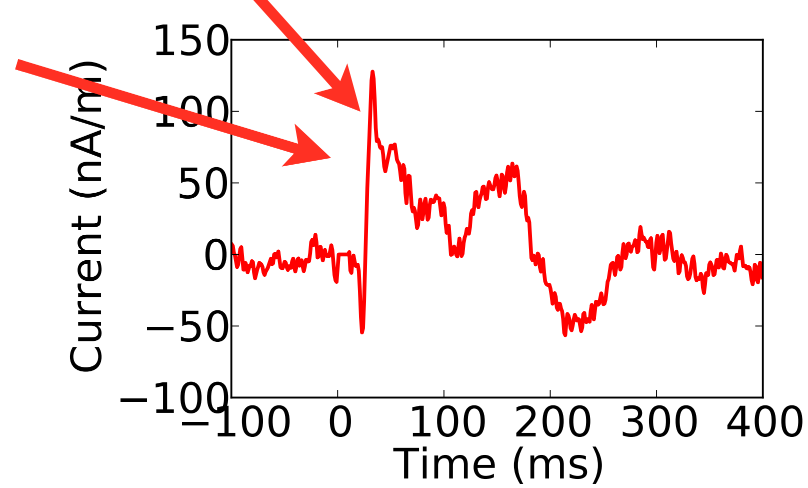
Basic distribtued model: $M = GX+E$



Linear problem with more unknowns than the number of equations: it's ill-posed => Regularize

Distributed model



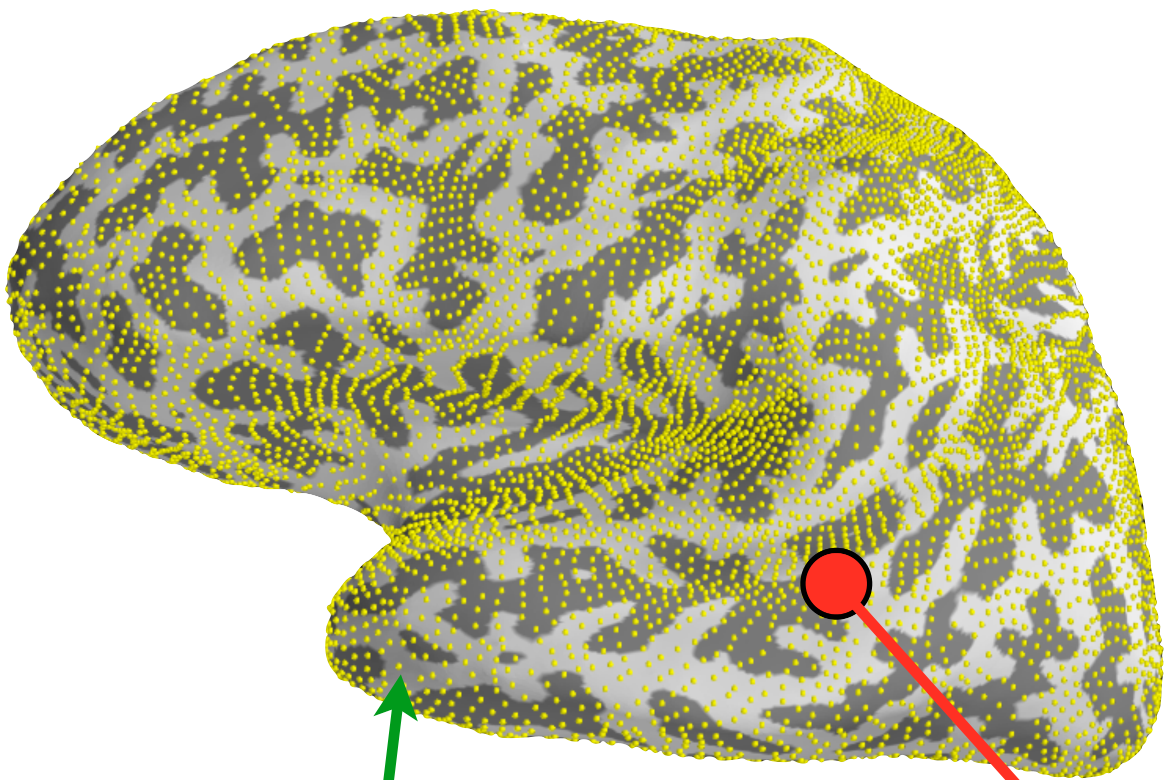


Position 5000 candidate sources over each hemisphere (e.g. every 5mm)

Scalar field defined over time

[Dale and Sereno 93]

Distributed model



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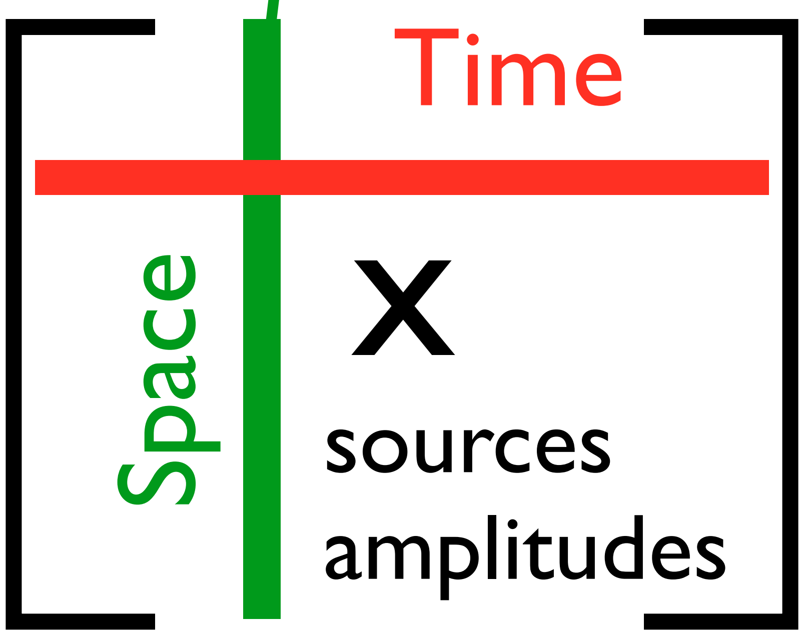

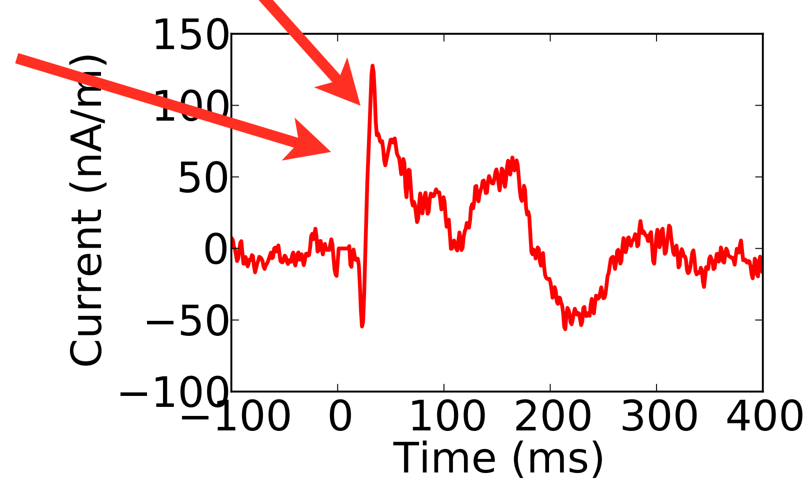

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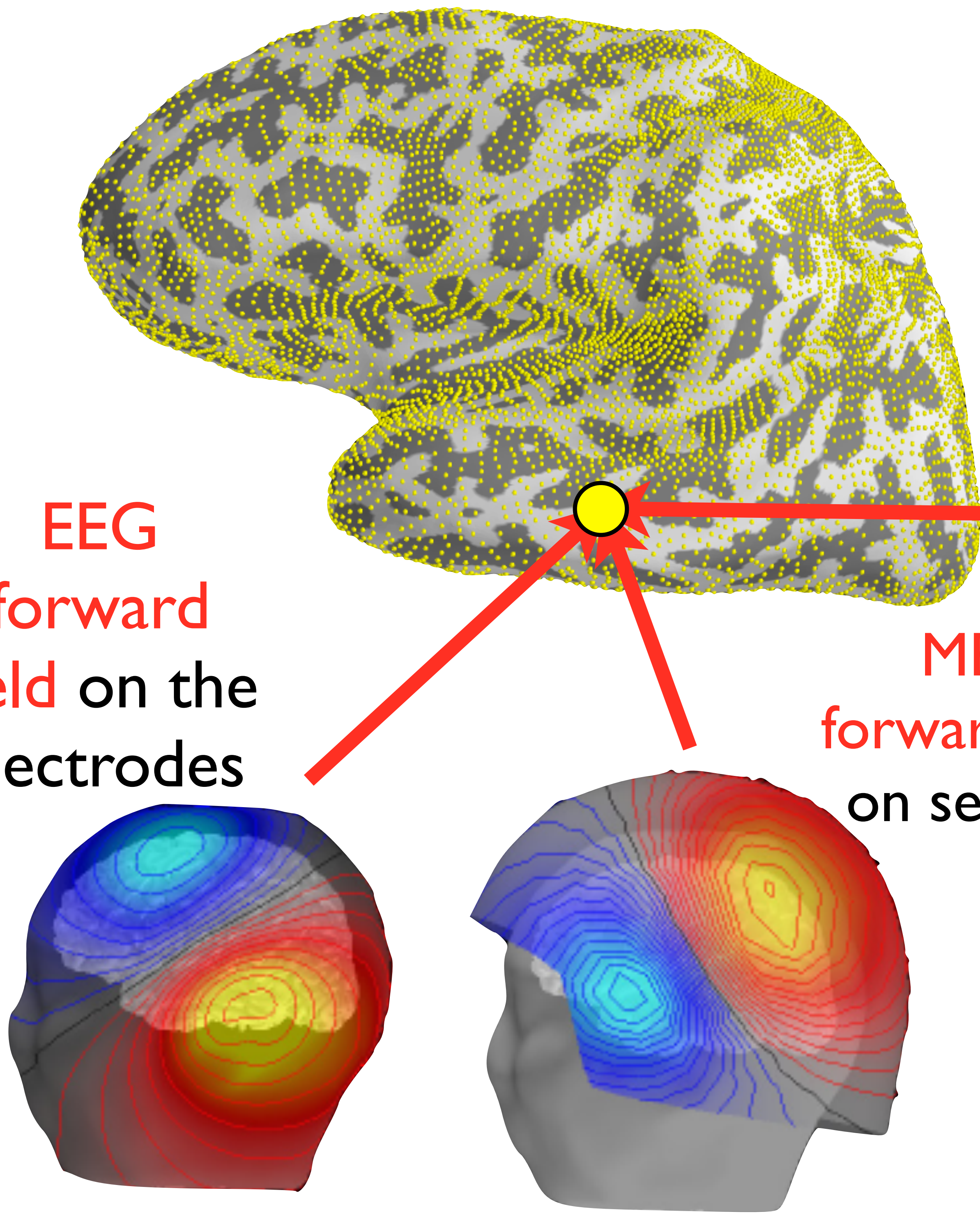
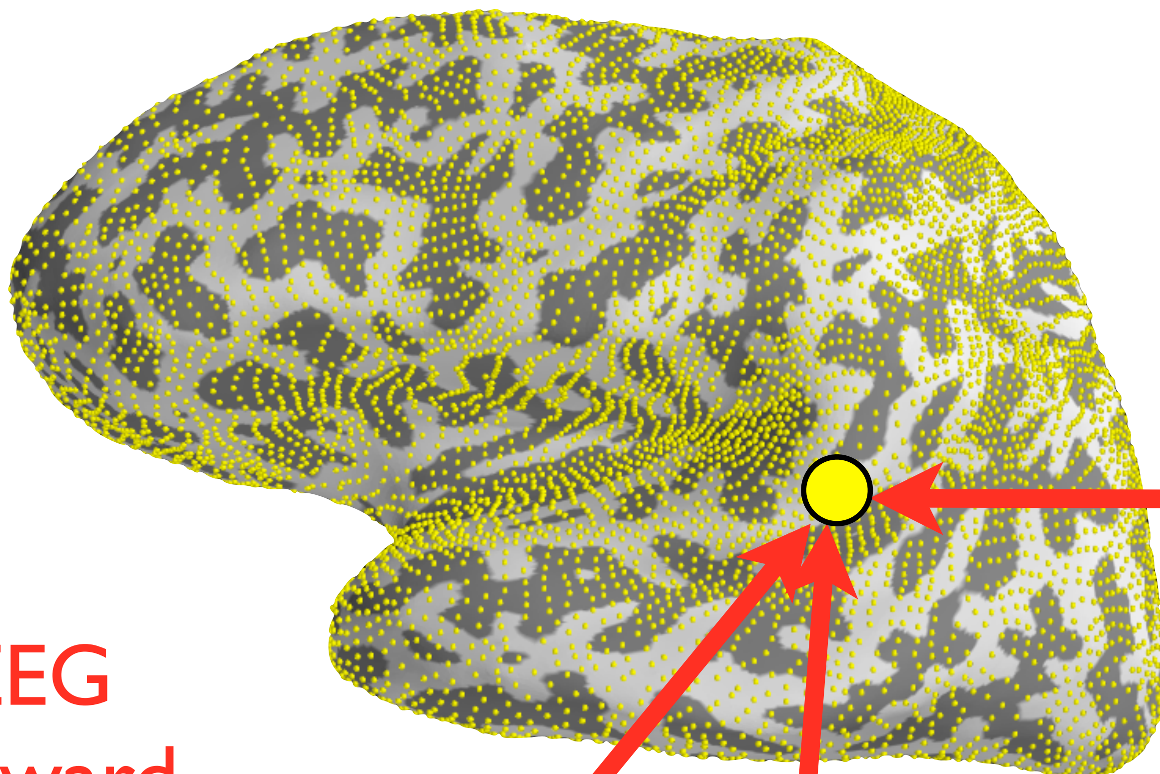


$$G = \begin{bmatrix} G_{EEG} \\ \hdashline G_{MEG} \end{bmatrix}$$

G is the gain matrix obtained by concatenation of the forward fields

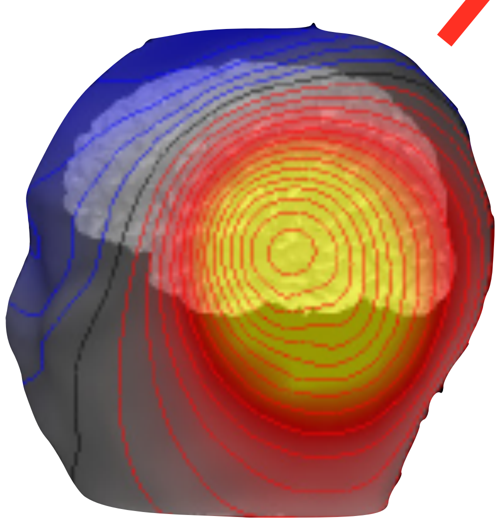
Distributed model



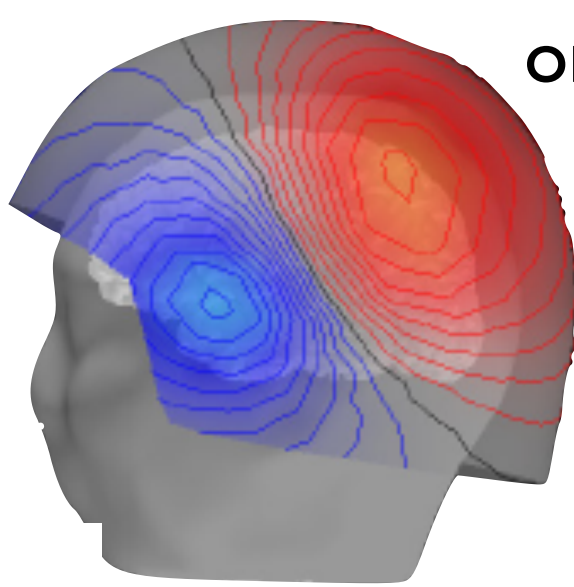
one column = Forward field of one dipole

$$G = \begin{bmatrix} G_{EEG} \\ \hdashline G_{MEG} \end{bmatrix}$$

EEG forward field on the electrodes

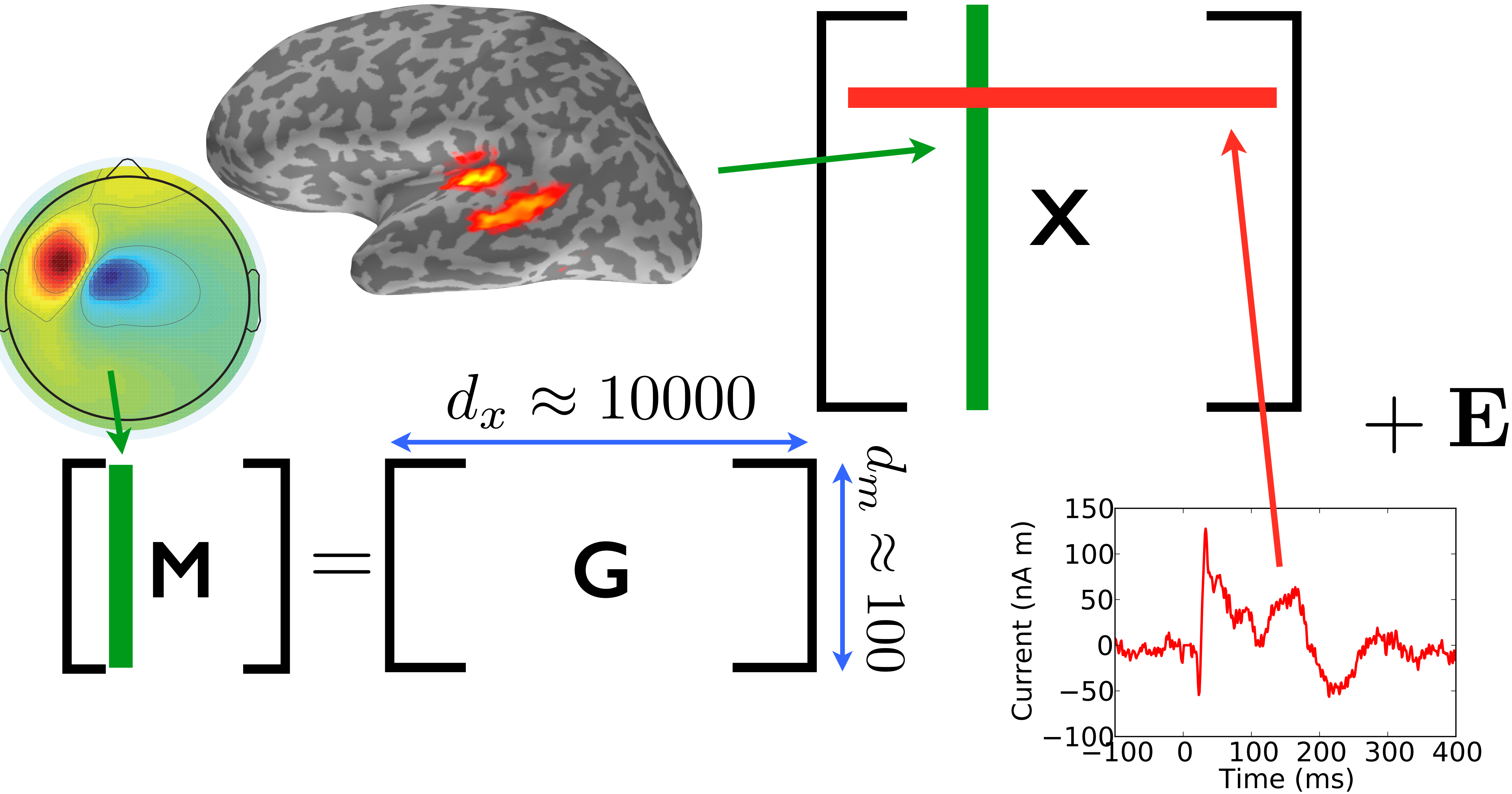


MEG forward field on sensors



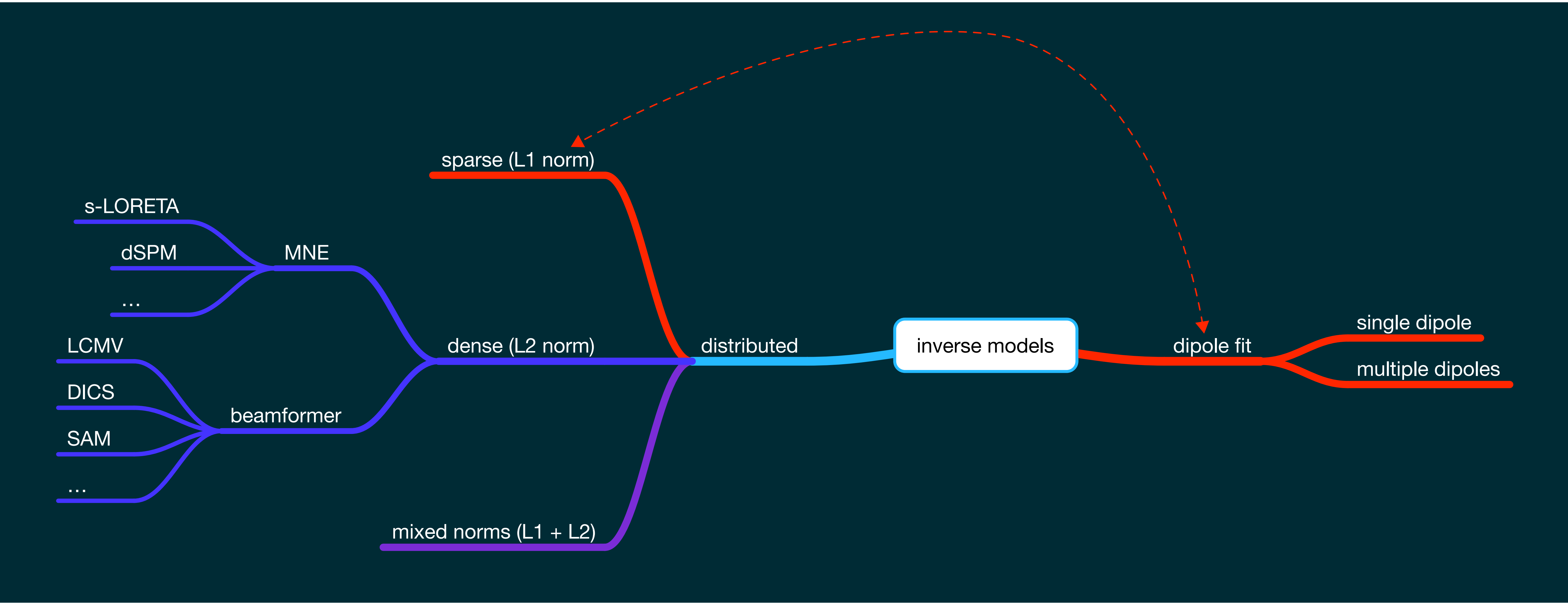
G is the gain matrix obtained by concatenation of the forward fields

M = GX+E : An ill-posed problem



Linear problem with more unknowns than the number of equations: it's ill-posed => Regularize

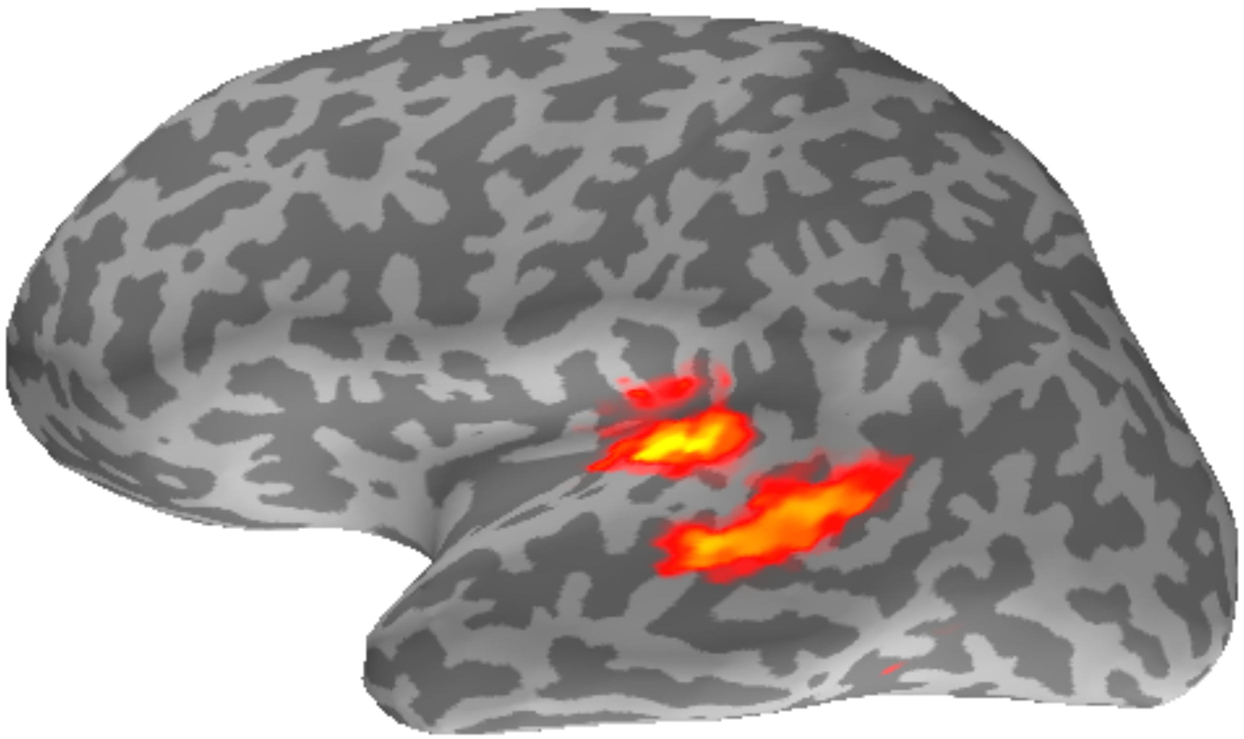
What's my model?



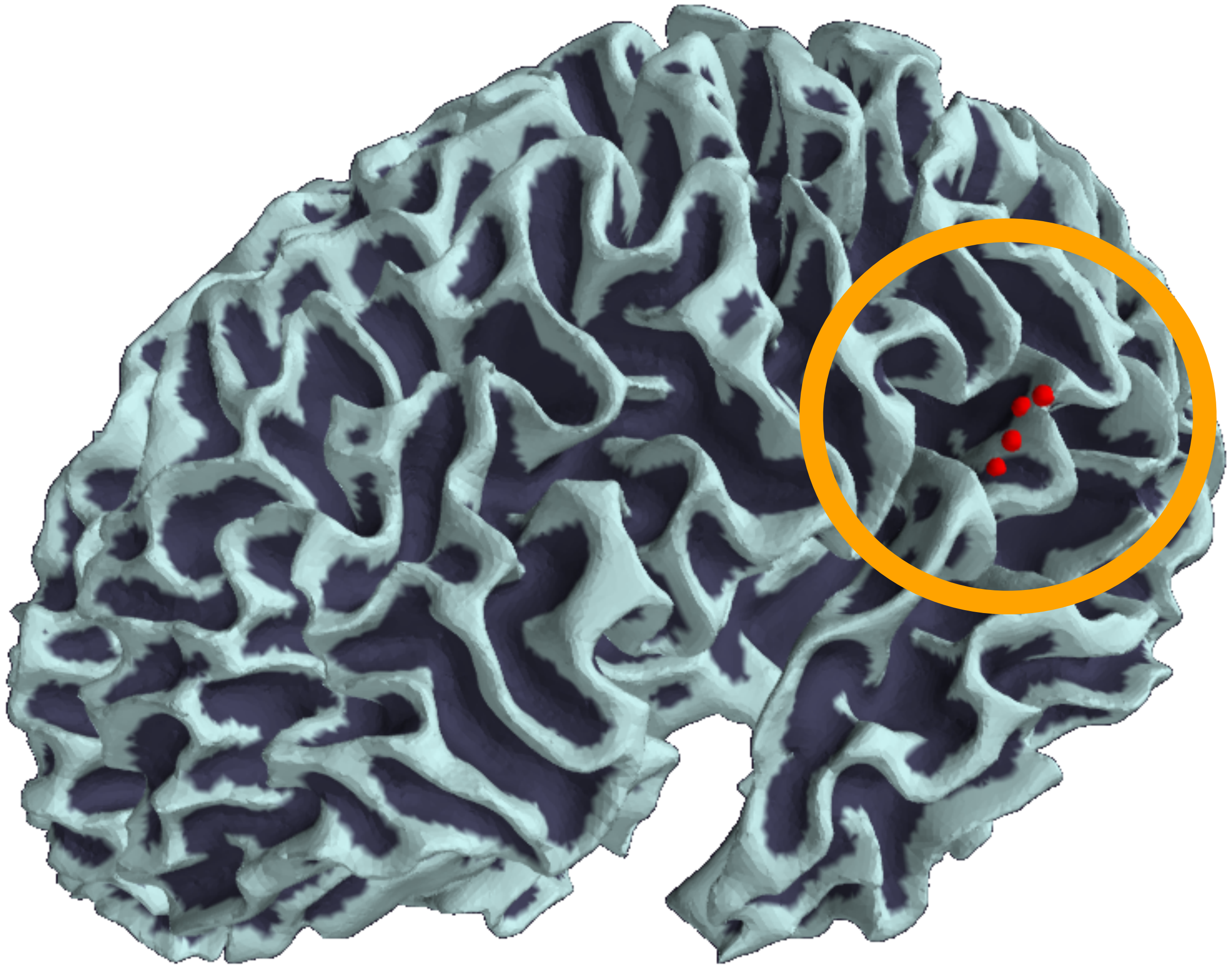
L1 vs L2 norms on combined M/EEG data

Activation in left-auditory cortex

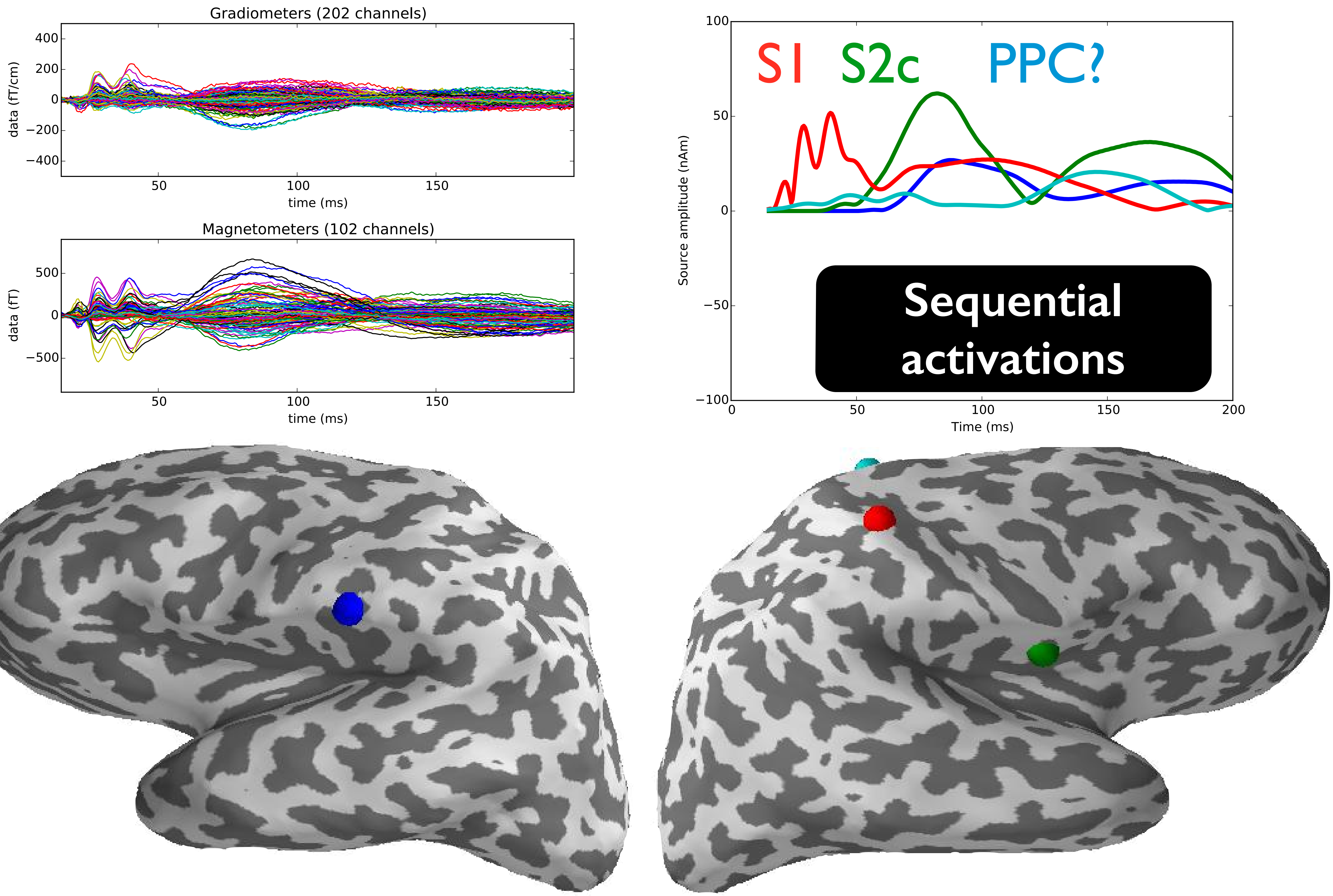
L2 result (thresholded)



L1 result



L1,2 mixed norm on MEG data



Inverse problem framework

Penalized (variational) formulation (with whitened data):

$$\mathbf{X}^* = \arg\min_{\mathbf{X}} \|\mathbf{M} - \mathbf{G}\mathbf{X}\|_F^2 + \lambda\phi(\mathbf{X}), \lambda > 0$$

Data fit Regularization

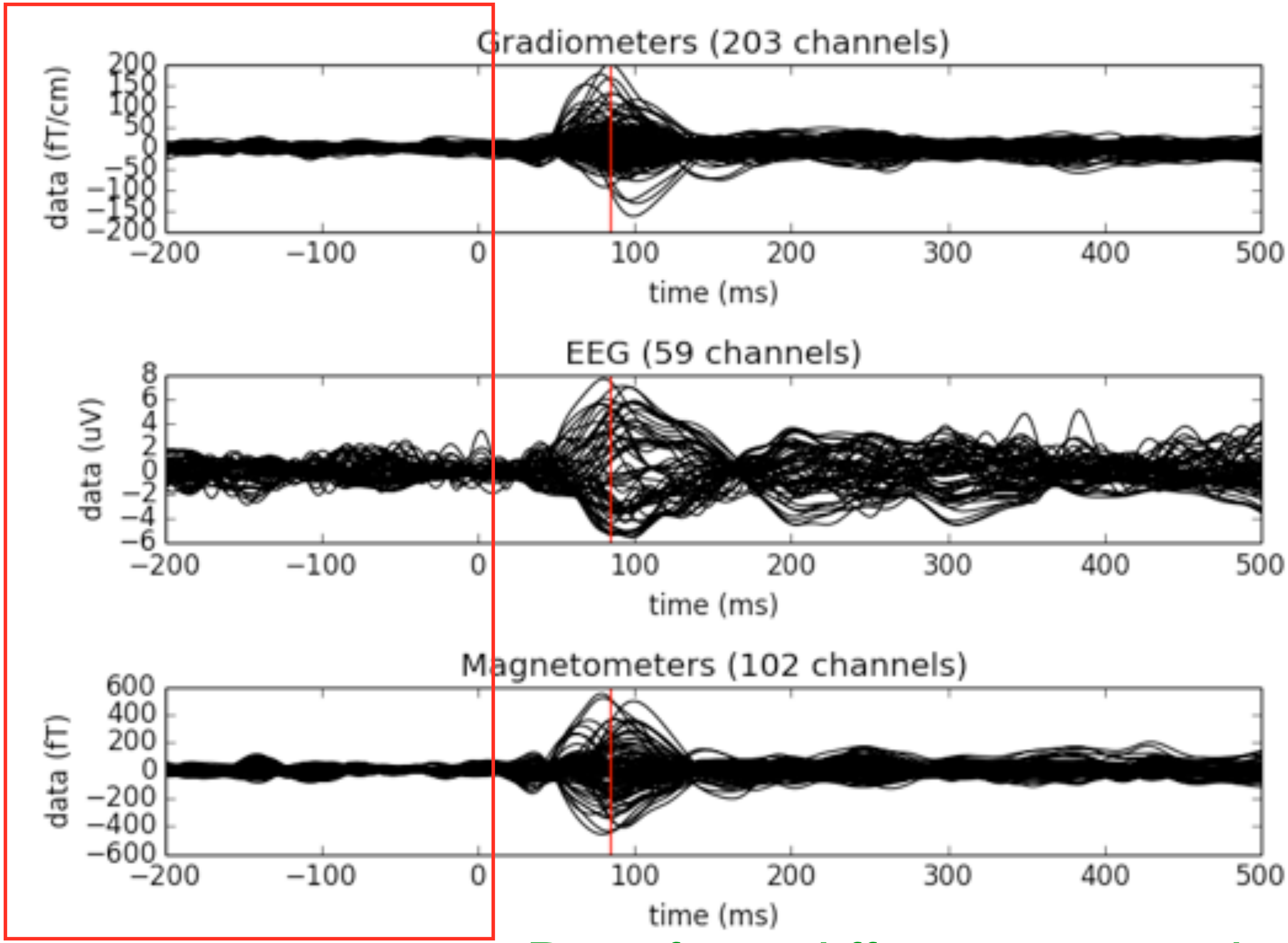
λ : Trade-off between the data fit and the regularization

where $\|\mathbf{A}\|_F^2 = \mathbf{tr}(\mathbf{A}^T\mathbf{A})$

How do you whiten data?

Inverse models require appropriate preprocessing

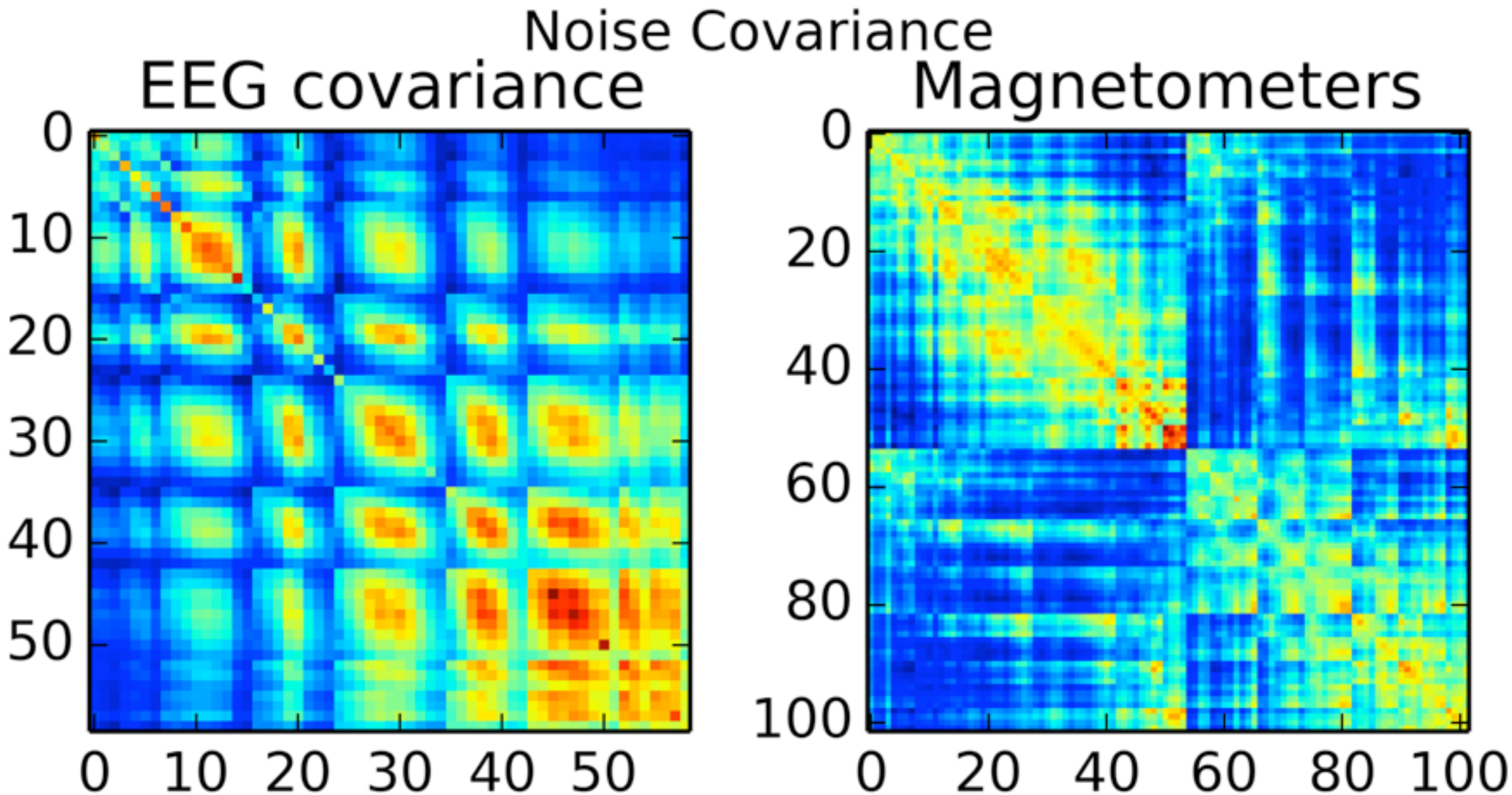
Challenge: M/EEG fusion



Baseline

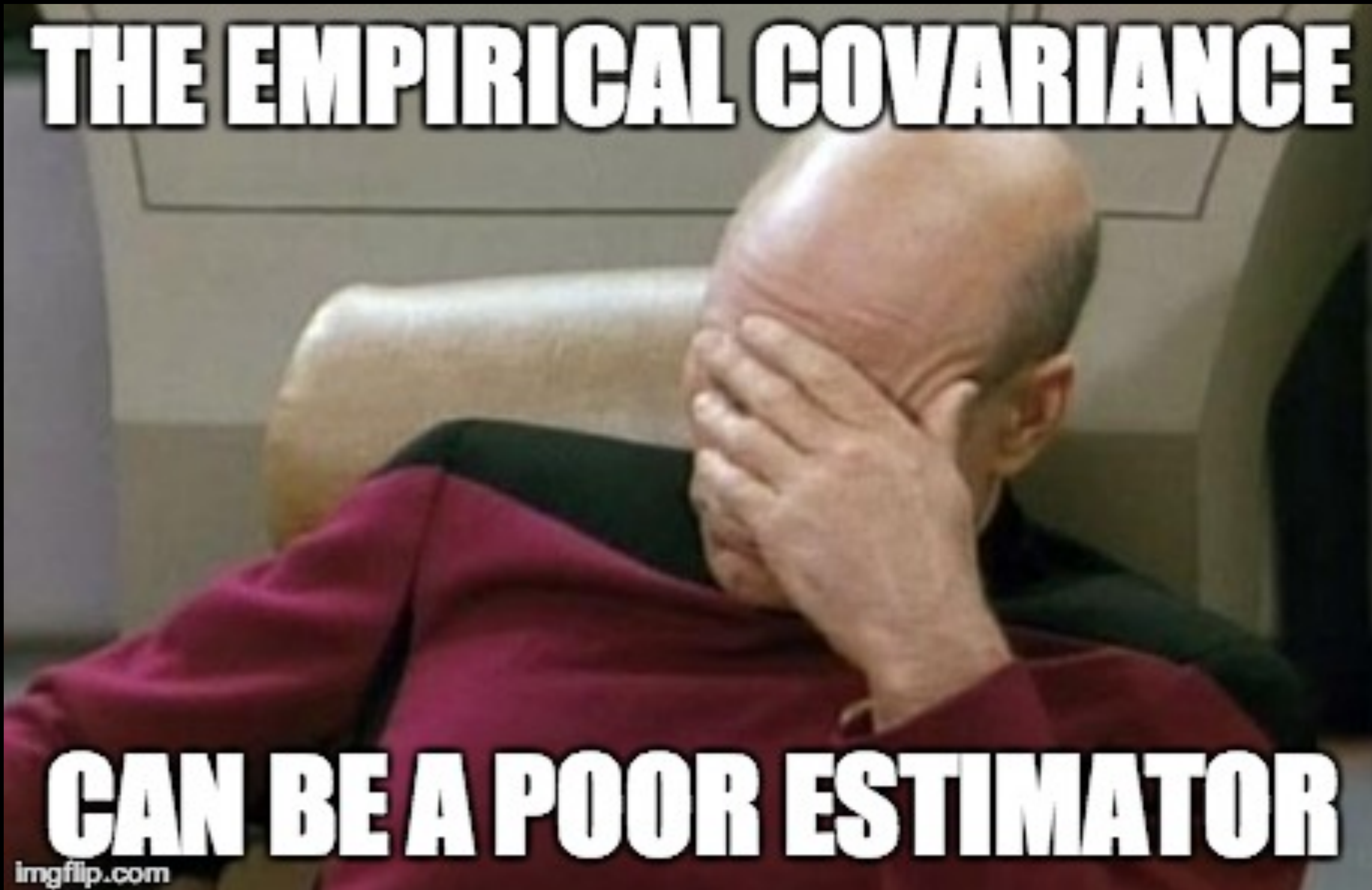
Data from different sensors have to be put on the same scale.

Challenge: M/EEG fusion



$$C = \frac{1}{T} M M^t$$

With whitened data the covariance would be diagonal


THE EMPIRICAL COVARIANCE
CAN BE A POOR ESTIMATOR
imgflip.com

Model selection: Log-likelihood

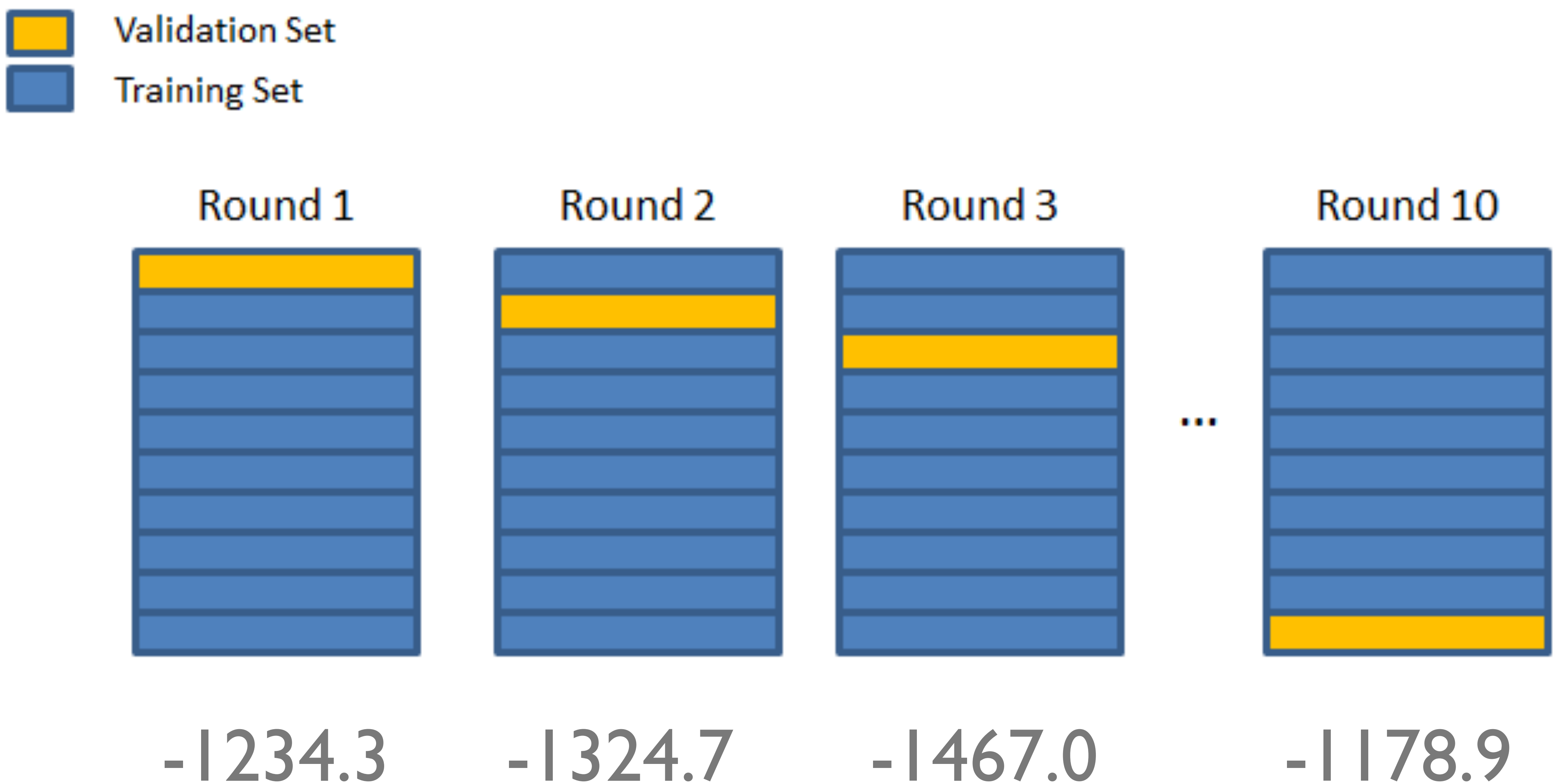
Given my model C how likely are unseen data Y?

$$\mathcal{L}(Y|C) = -\frac{1}{2T}\mathrm{Trace}(YY^tC^{-1}) - \frac{1}{2}\log((2\pi)^N \det(C))$$

Higher log likelihood = better C & better whitening

[Engemann, D. and Gramfort, A., NeuroImage (2015)]

Cross-validation



average log likelihood and select the best model

[Engemann, D. and Gramfort, A., NeuroImage (to appear)]

We compared 5 strategies:

simple, fast

1. Hand-set (REG)

$$C' = C + \alpha I, \quad \alpha > 0$$

2. Ledoit-Wolf (LW)

$$C_{LW} = (1 - \alpha)C + \alpha\mu I \qquad \mu = \mathrm{mean}(\mathrm{diag}(C))$$

3. Cross-validated shrinkage (SC)

$$C_{SC} = (1 - \alpha_{CV})C + \alpha_{CV}\mu I$$

4. Probabilistic PCA (PPCA)

$$C_{PPCA} = HH^t + \sigma^2 I_N$$

5. Factor Analysis (FA)

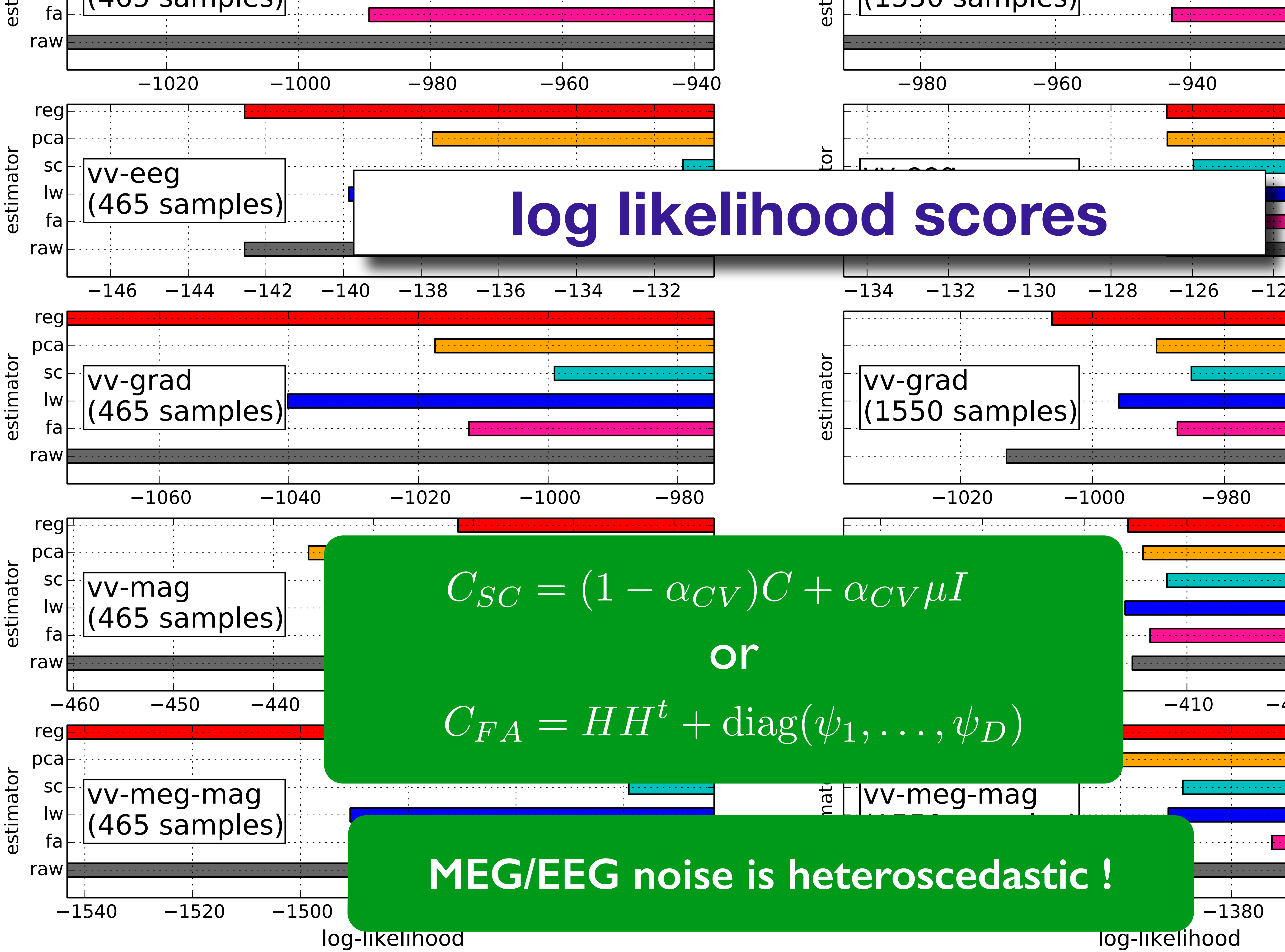
$$C_{FA} = HH^t + \mathrm{diag}(\psi_1, \ldots, \psi_D)$$

complex, slow

[Engemann, D. and Gramfort, A., NeuroImage (2015)]

MEG and EEG data

key	dataset and channel type
bti-mag	4D Magnes 3600 WH magnetometers
ctf-mag	CTF-275 axial gradiometers
vv-eeg	VectorView EEG electrodes
vv-grad	VectorView planar gradiometers
vv-mag	VectorView magnetometers
vv-meg-grad	VectorView planar gradiometers, combined estimation
vv-meg-mag	VectorView magnetometers, combined estimation



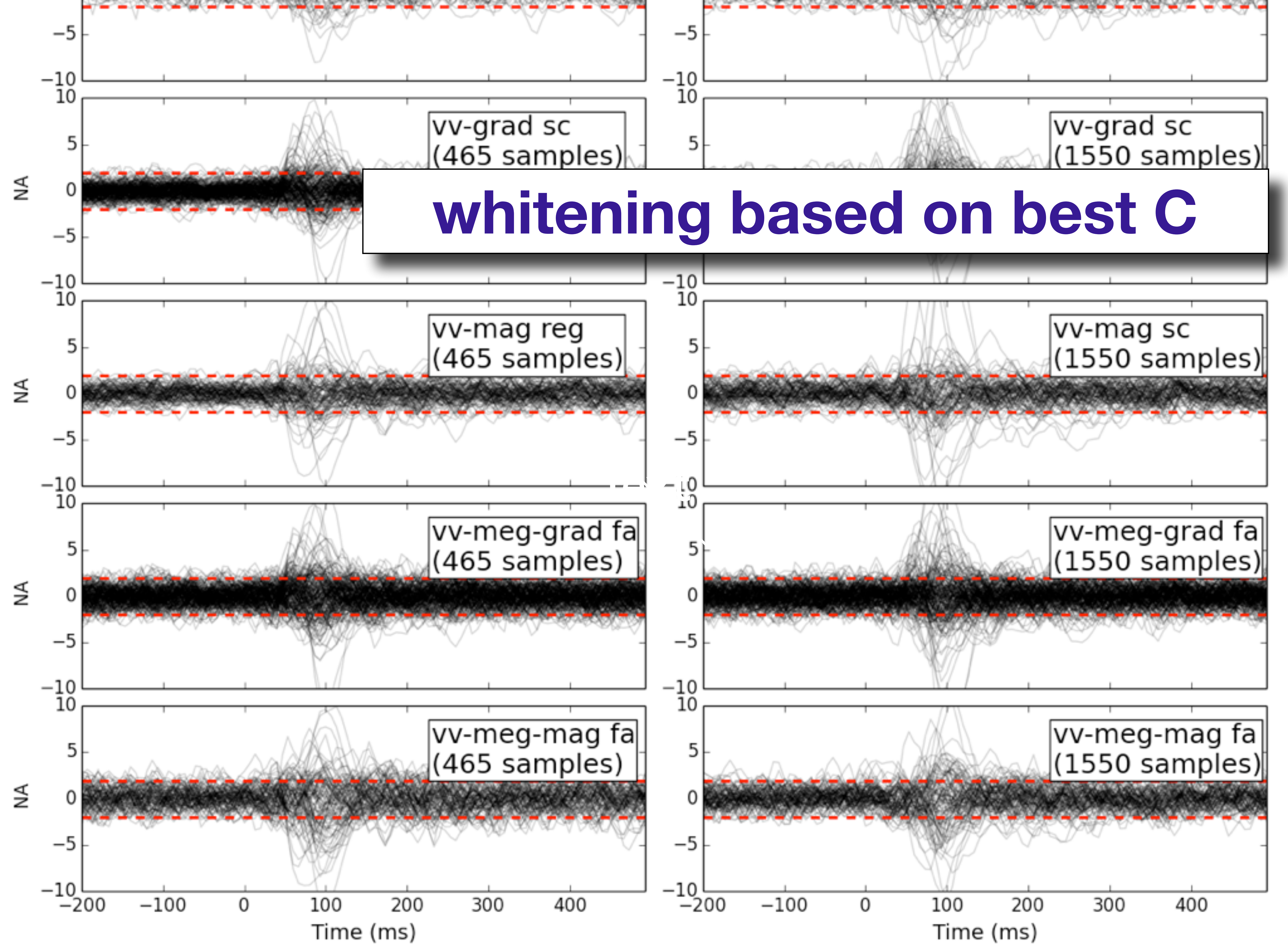
log likelihood scores

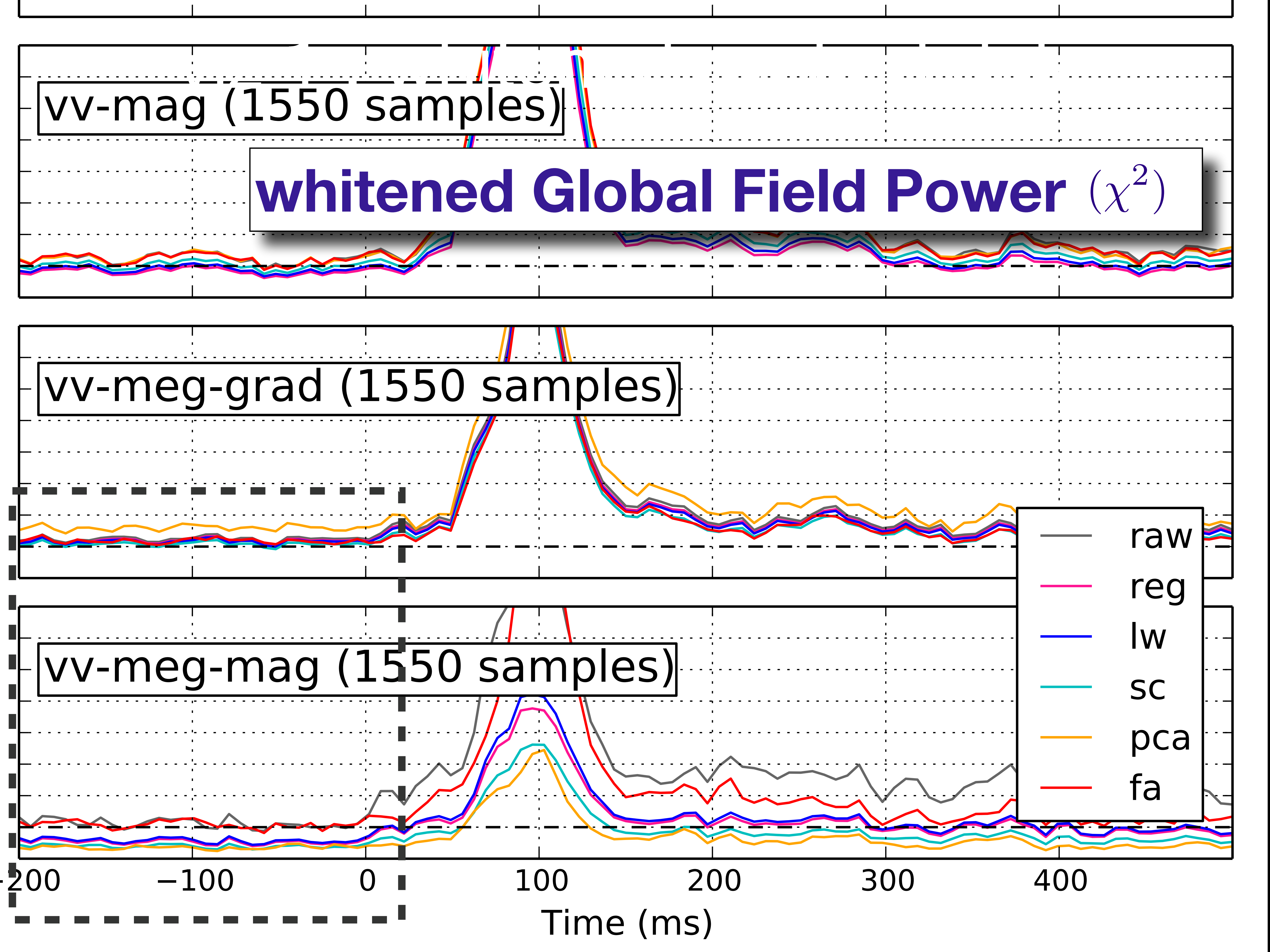
$$C_{SC} = (1 - \alpha_{CV})C + \alpha_{CV}\mu I$$

or

$$C_{FA} = HH^t + \mathrm{diag}(\psi_1, \ldots, \psi_D)$$

MEG/EEG noise is heteroscedastic !


whitening based on best C
vv-grad sc
(465 samples)
vv-grad sc
(1550 samples)
vv-mag reg
(465 samples)
vv-mag sc
(1550 samples)
vv-meg-grad fa
(465 samples)
vv-meg-grad fa
(1550 samples)
vv-meg-mag fa
(465 samples)
vv-meg-mag fa
(1550 samples)
NA
Time (ms)



vv-mag (1550 samples)
whitened Global Field Power (χ^2)
vv-meg-grad (1550 samples)
vv-meg-mag (1550 samples)
raw
reg
lw
sc
pca
fa
−200
−100
0
100
200
300
400
Time (ms)

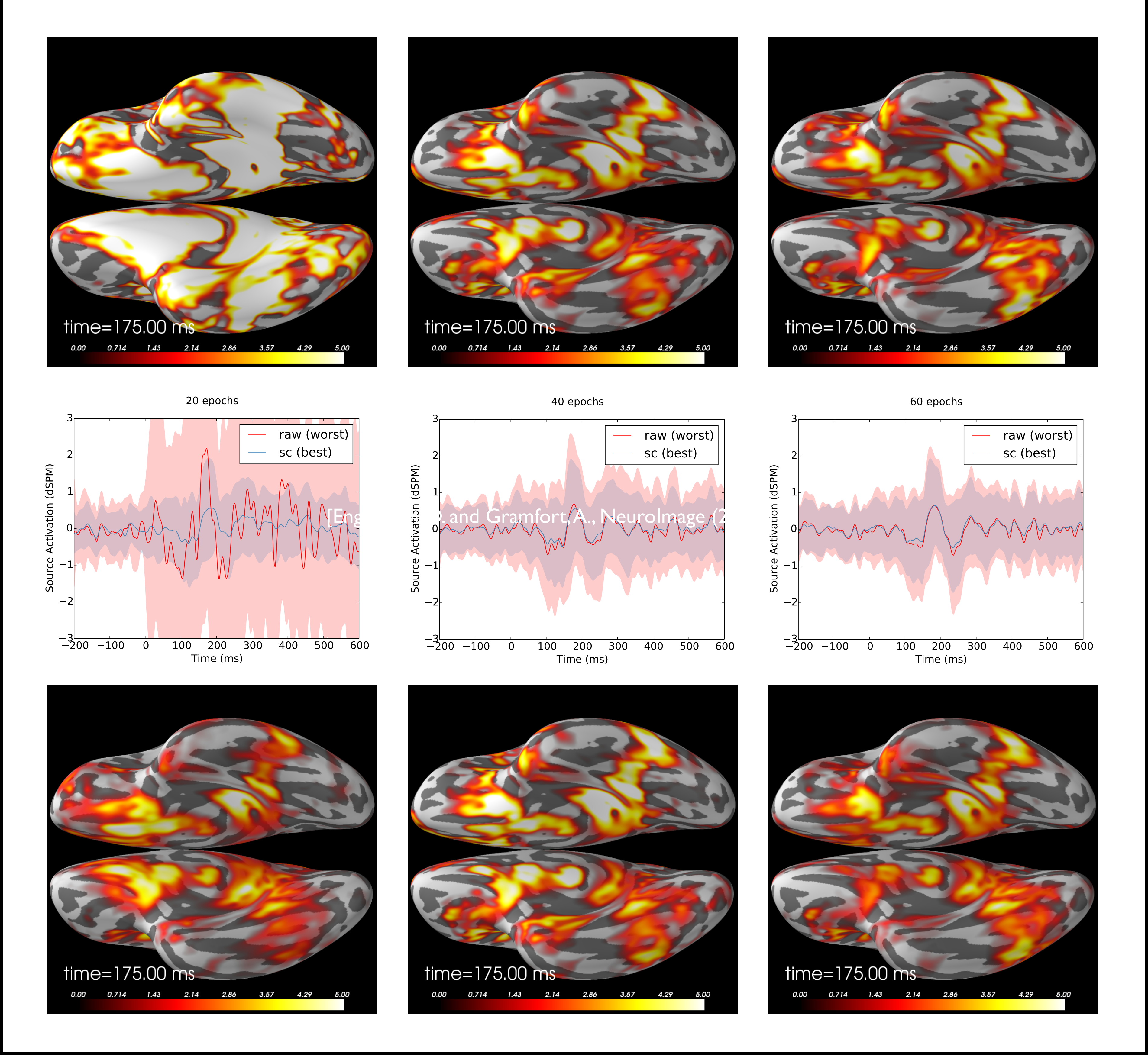

Should we care?

20 epochs 40 epochs 60 epochs

worst

best

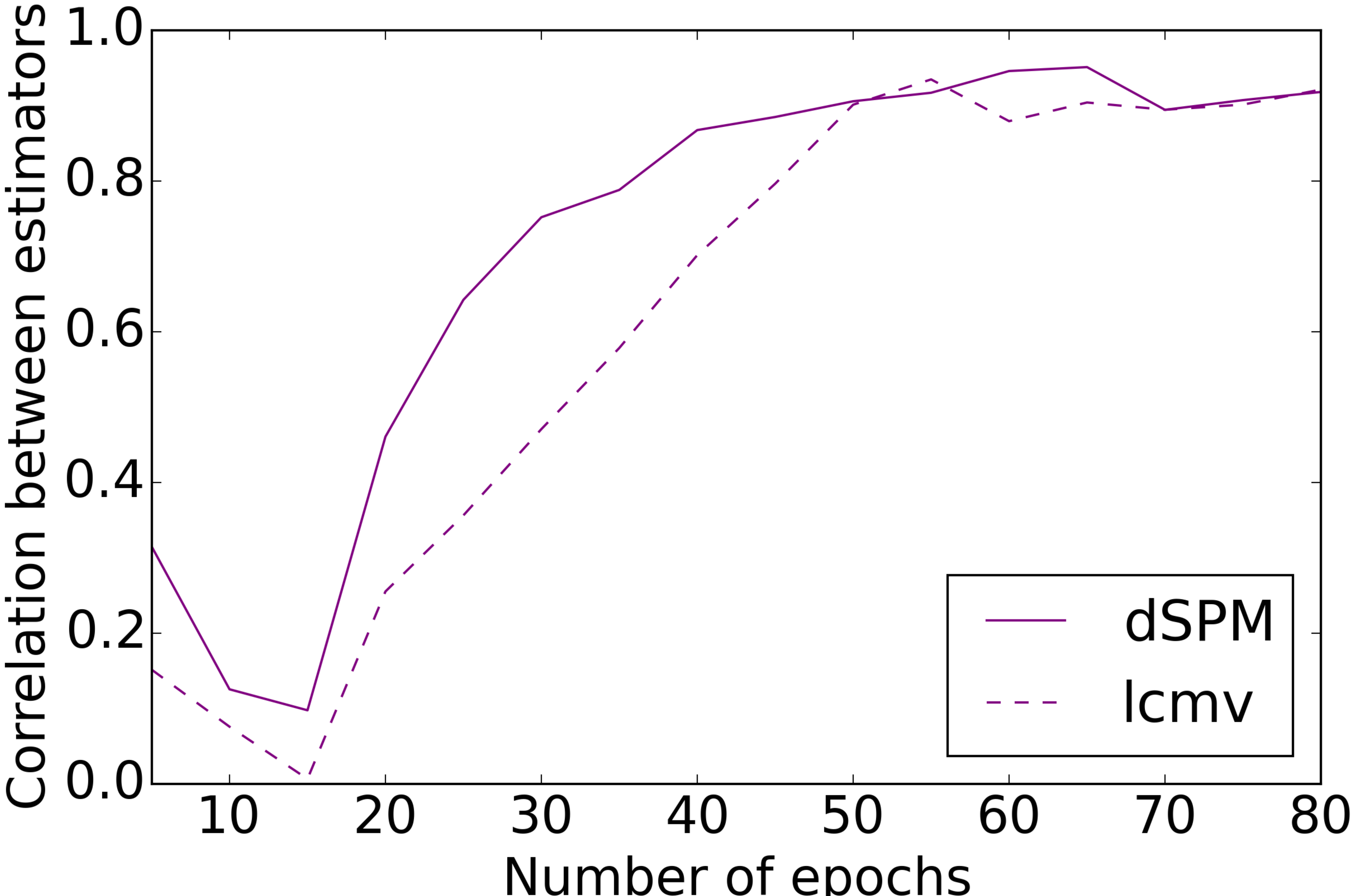
std



faces > scrambled SPM faces dataset

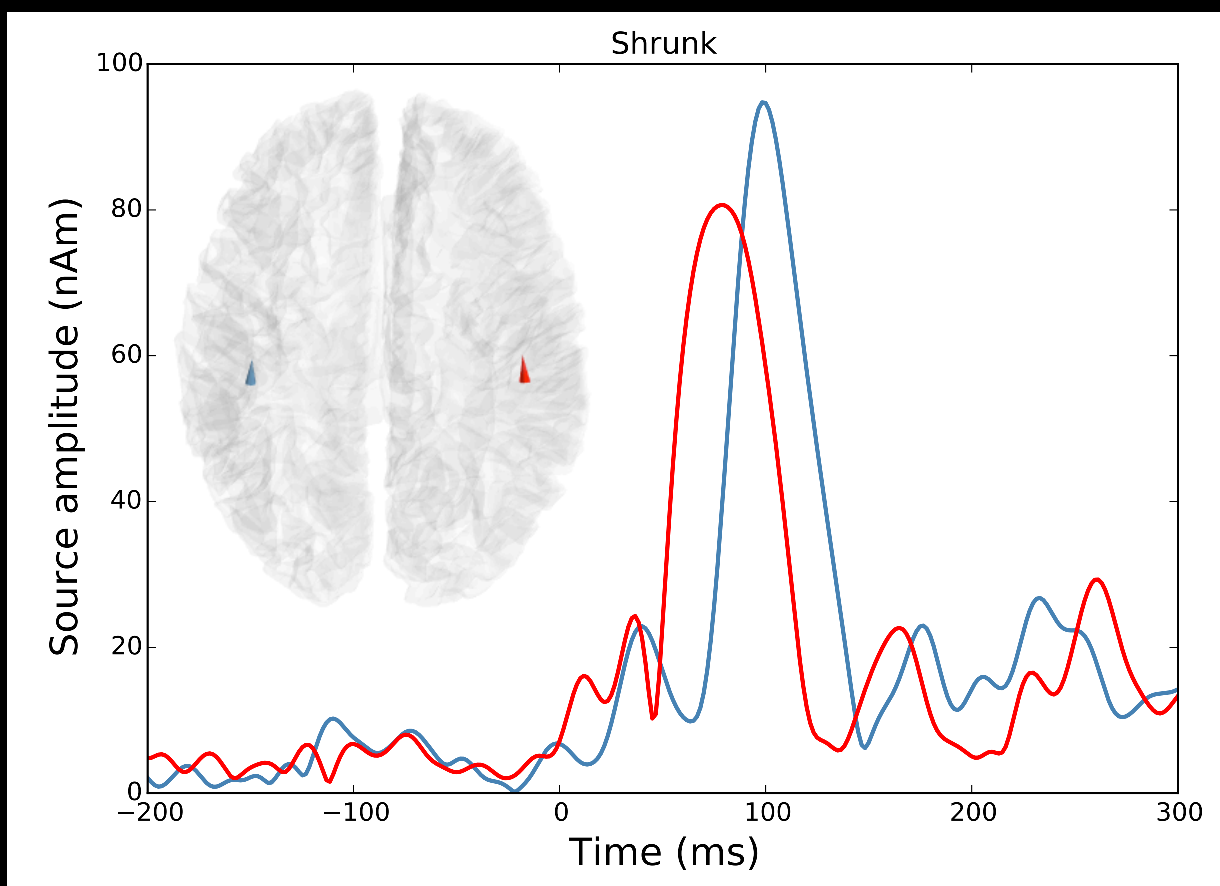
Engemann, D. and Gramfort, A., NeuroImage (2015)

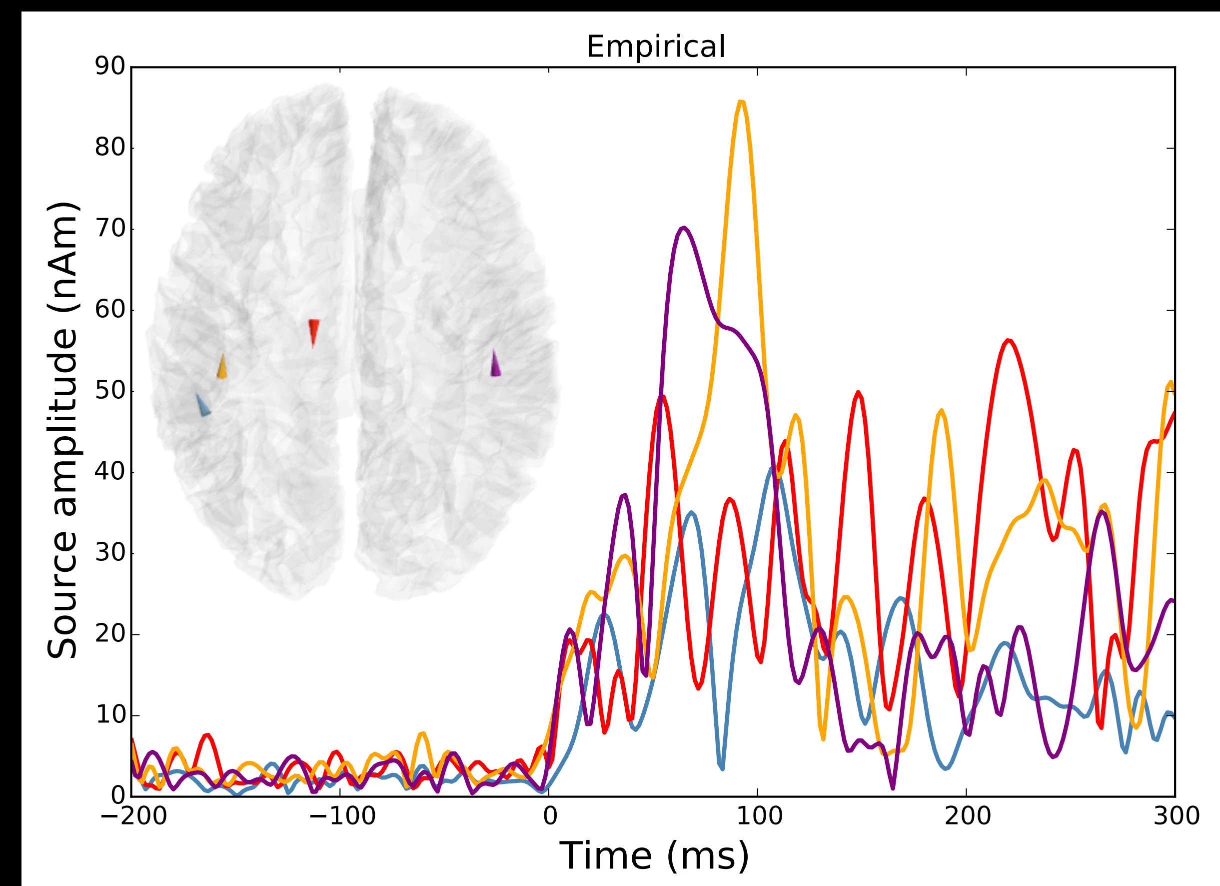
correlation between bad and good source estimates



Engemann D., Strohmeier D., Larson E., and Gramfort A., PRNI proceedings (2015)

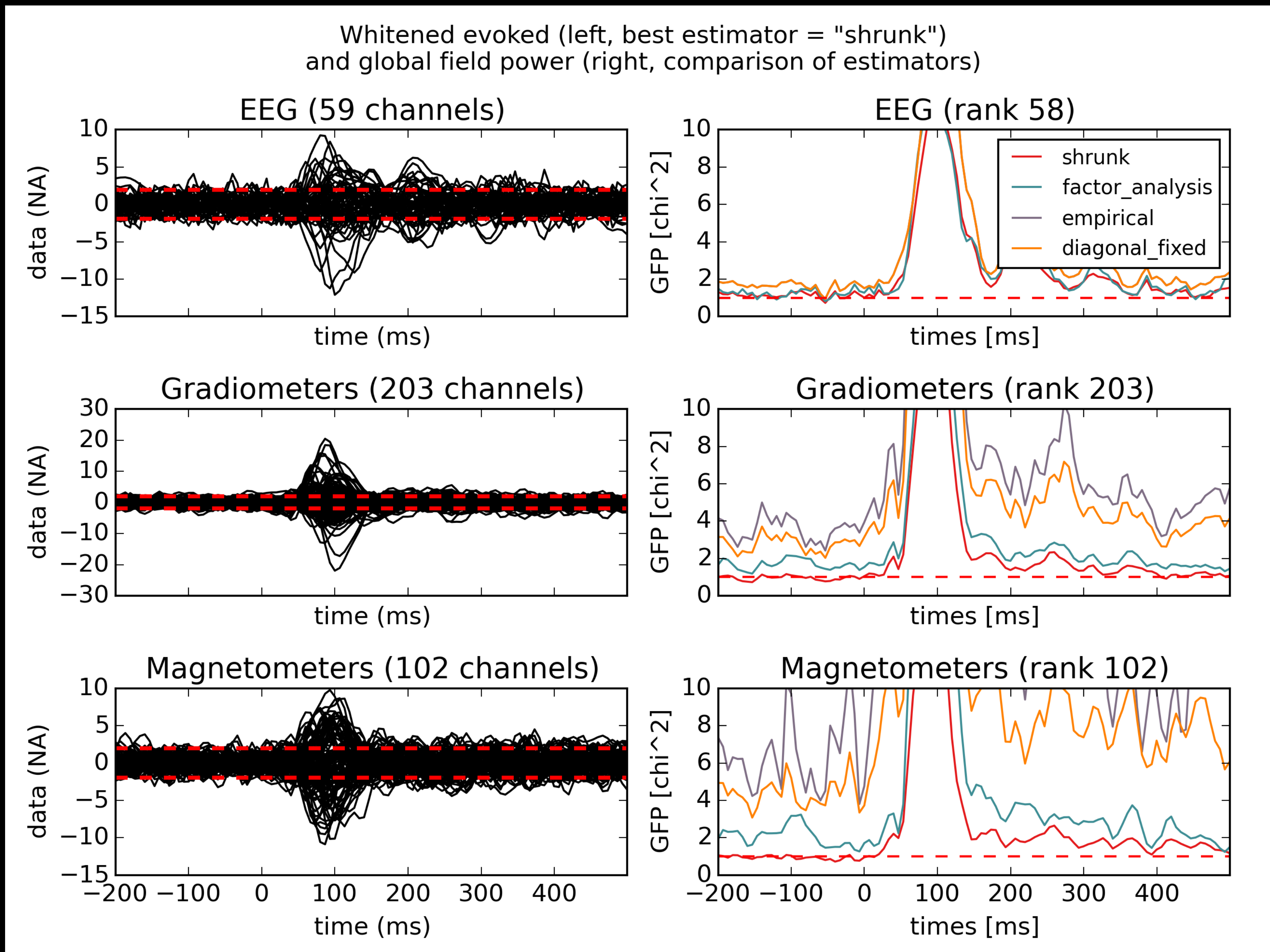
sparse slolvers and covariance





Engemann D., Strohmeier D., Larson E., and Gramfort A., PRNI proceedings (2015)

```
# Authors: Denis A. Engemann <denis.engemann@gmail.com>
#          Alexandre Gramfort <alexandre.gramfort@telecom-paristech.fr>
#
# License: BSD (3-clause)
```




```
t-0-40_raw.fif'
ilt-0-40_raw-eve.fif'

=1, tmin=-.2, tmax=0.5,
 exclude='bads'),
3, eeg=80e-6))

########################
d show whitening
max=0, method='auto',
ors=True)
```

```
evoked = epochs.average()
evoked.plot()  # plot evoked response
evoked.plot_white(noise_covs)  # compare estimators
```

```python
# Authors: Denis A. Engemann <denis.engemann@gmail.com>
#          Alexandre Gramfort <alexandre.gramfort@telecom-paristech.fr>
#
# License: BSD (3-clause)

import mne

data_path = mne.datasets.sample.data_path()
raw_fname = data_path + '/MEG/sample/sample_audvis_filt-0-40_raw.fif'
event_fname = data_path + '/MEG/sample/sample_audvis_filt-0-40_raw-eve.fif'

raw = mne.io.Raw(raw_fname, preload=True)
raw.info['bads'] += ['MEG 2443']
raw.filter(1, 30)

epochs = mne.Epochs(
    raw, events=mne.read_events(event_fname), event_id=1, tmin=-.2, tmax=0.5,
    picks=mne.pick_types(raw.info, meg=True, eeg=True, exclude='bads'),
    baseline=None, reject=dict(mag=4e-12, grad=4000e-13, eeg=80e-6))

###############################################################################
# Compute covariance using automated regularization and show whitening
noise_covs = mne.cov.compute_covariance(epochs[:20], tmax=0, method='auto',
                                        return_estimators=True)

evoked = epochs.average()
evoked.plot()  # plot evoked response
evoked.plot_white(noise_covs)  # compare estimators
```

3 claims

- you should care about MEG and EEG
- The choice of your statistical model for source localization reflects hypotheses about brain sources
- The success of your source localization depends on domain knowledge and proper signal processing