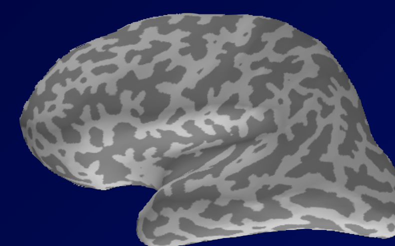
MEG/EEG Source Localization Methods

Matti Hämäläinen



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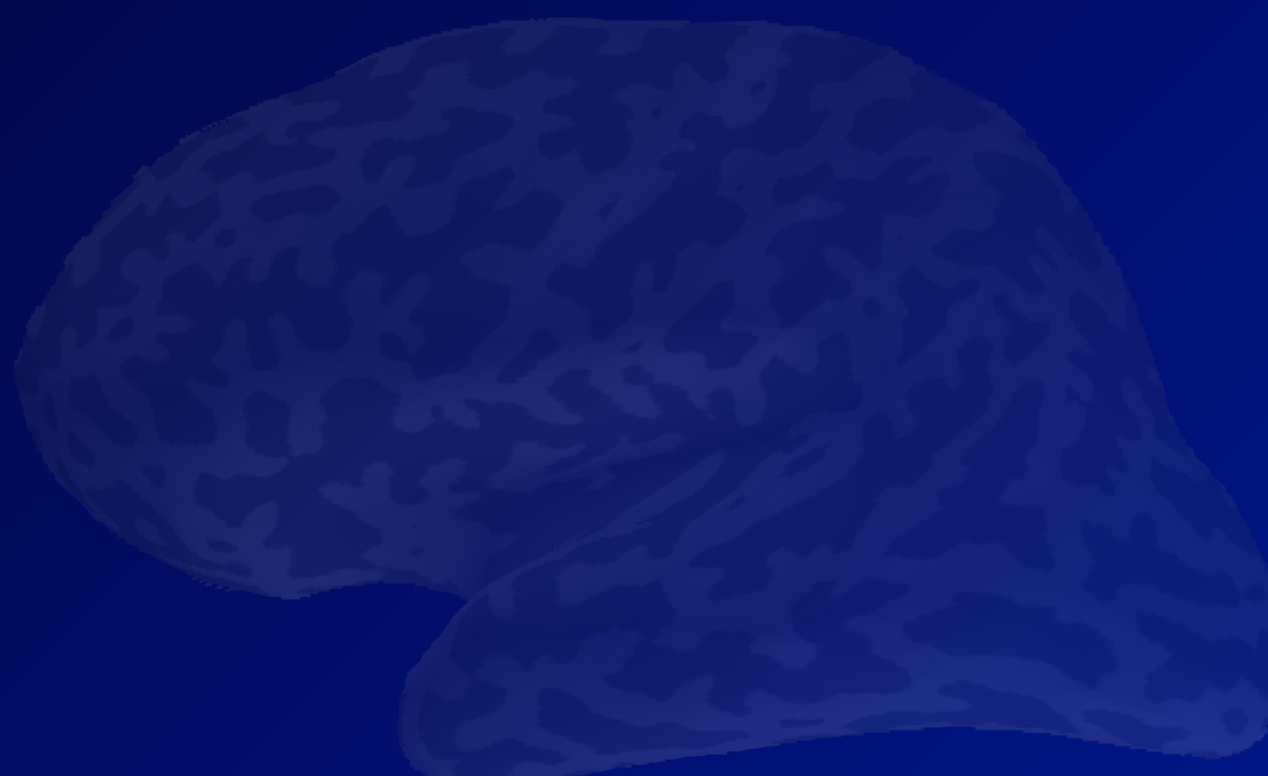
Olli V. Lounasmaa Laboratory
Aalto University, School of Science
Espoo, Finland

Contents

- Introduction to MEG and EEG source estimation
- Current dipole models
- Anatomically and functionally constrained source estimates

MEG and EEG source estimation

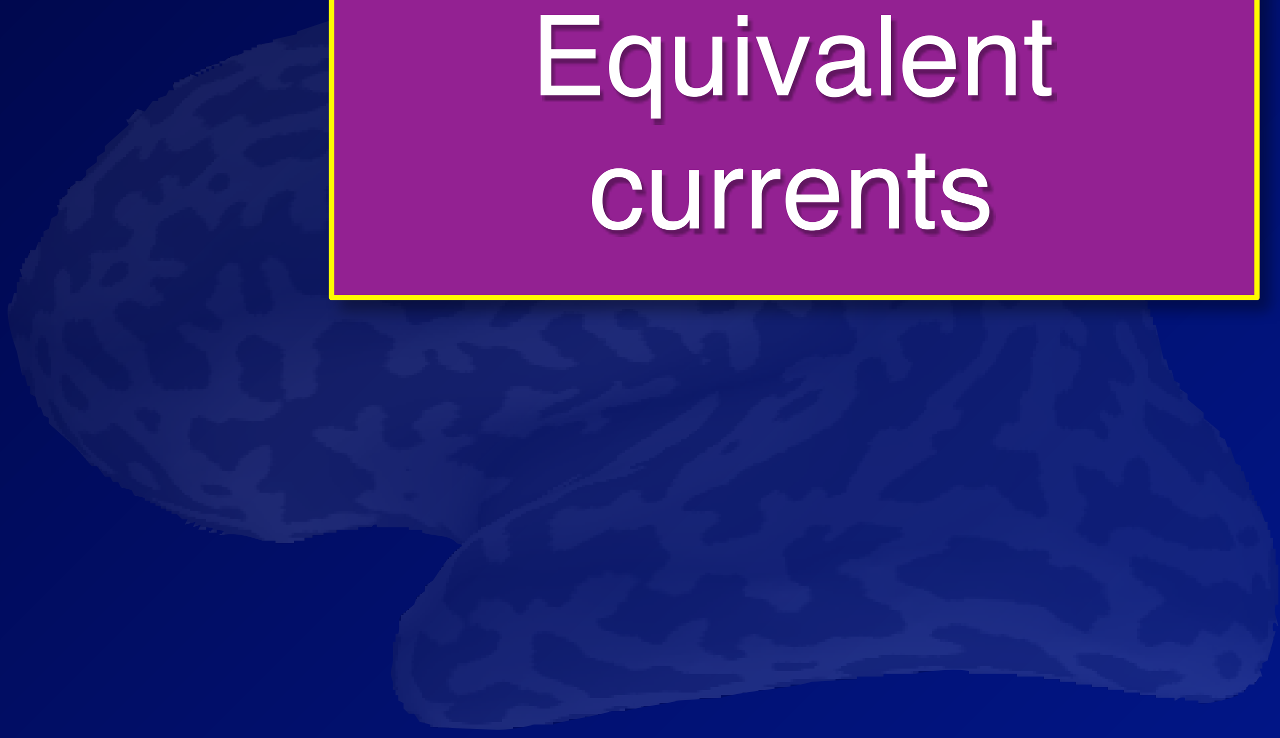


The Inverse Problem

Find the current distribution that generated the measured MEG/EEG

EEG/MEG

Equivalent currents



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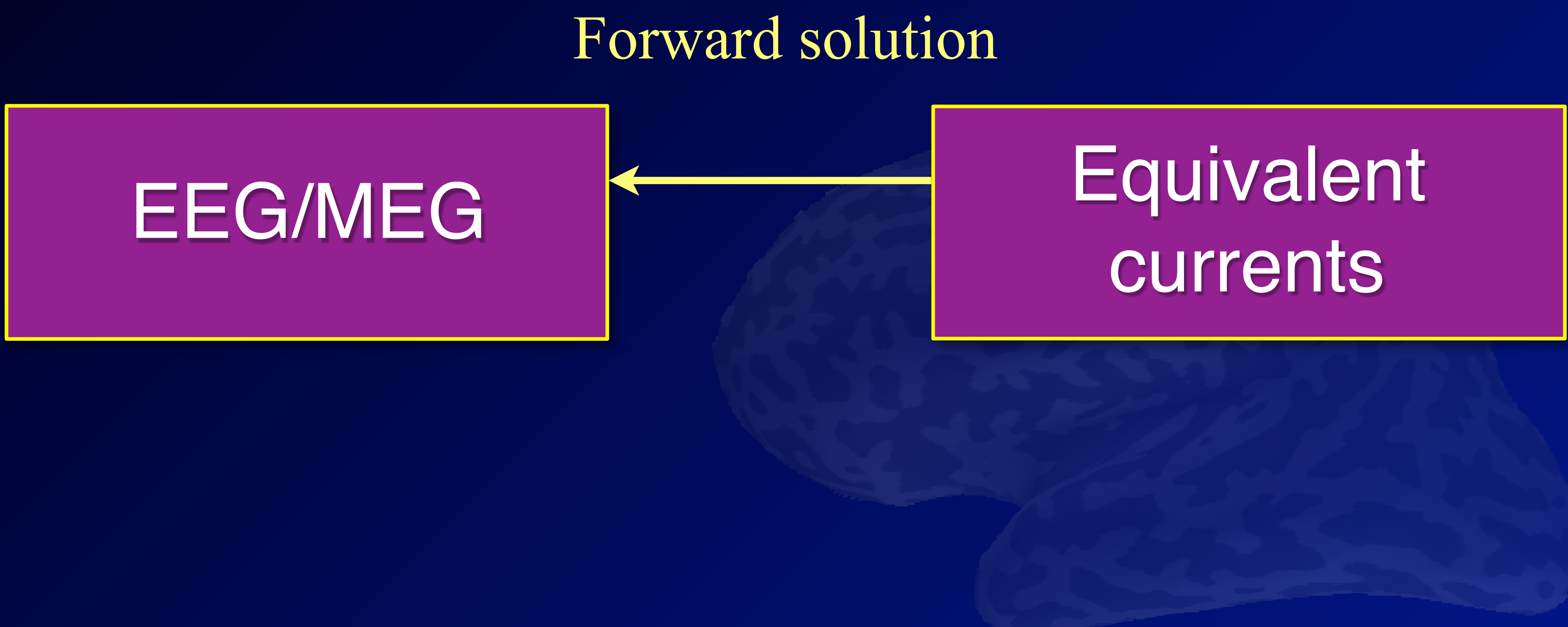


The Inverse Problem

Find the current distribution that generated the measured MEG/EEG

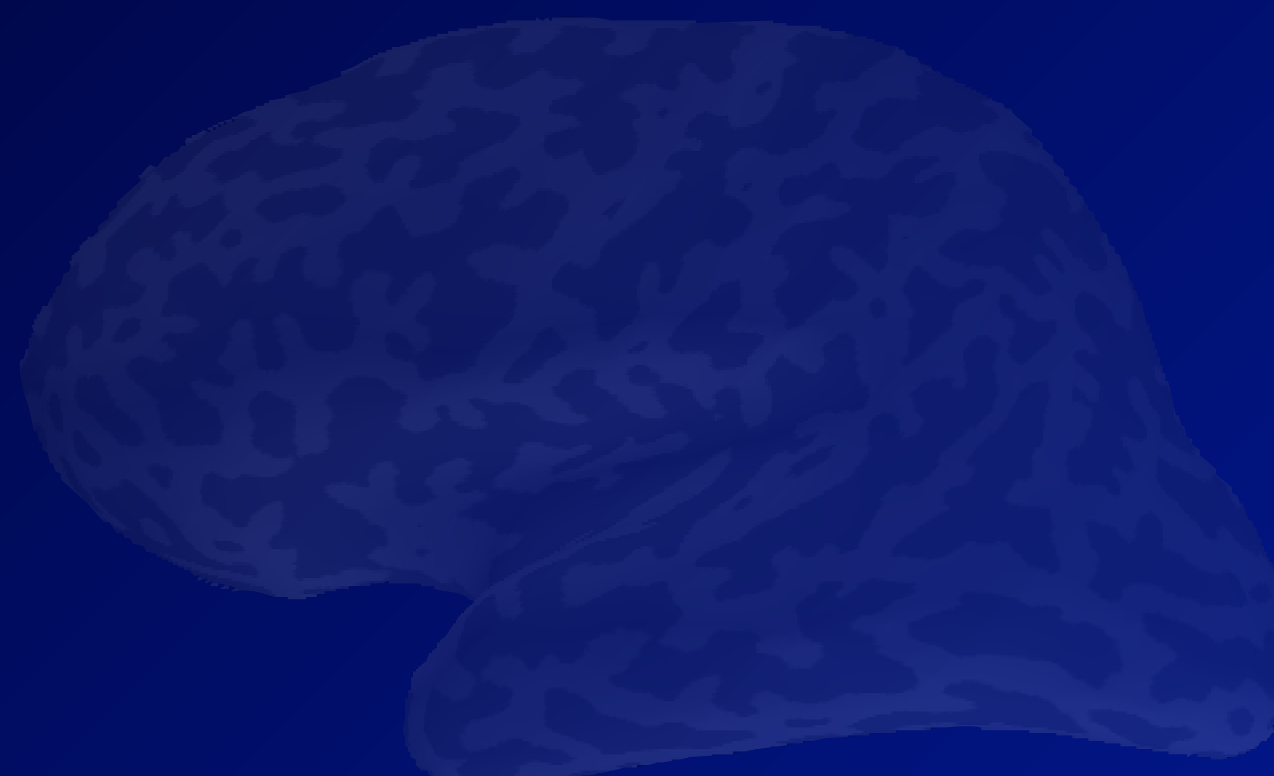
Forward solution

EEG/MEG

Equivalent currents

Inverse estimate

Another Kind of an Inverse Problem



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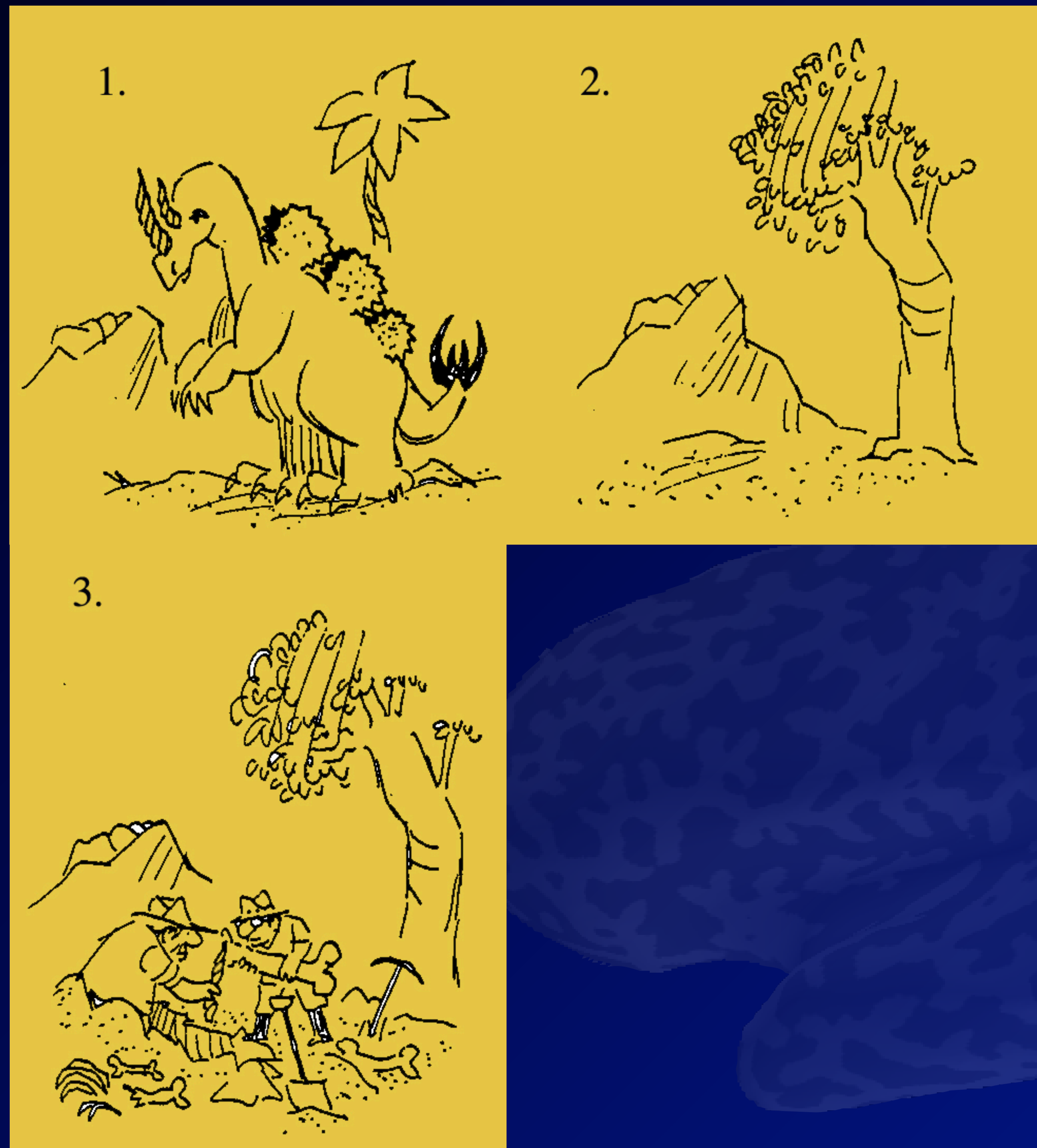

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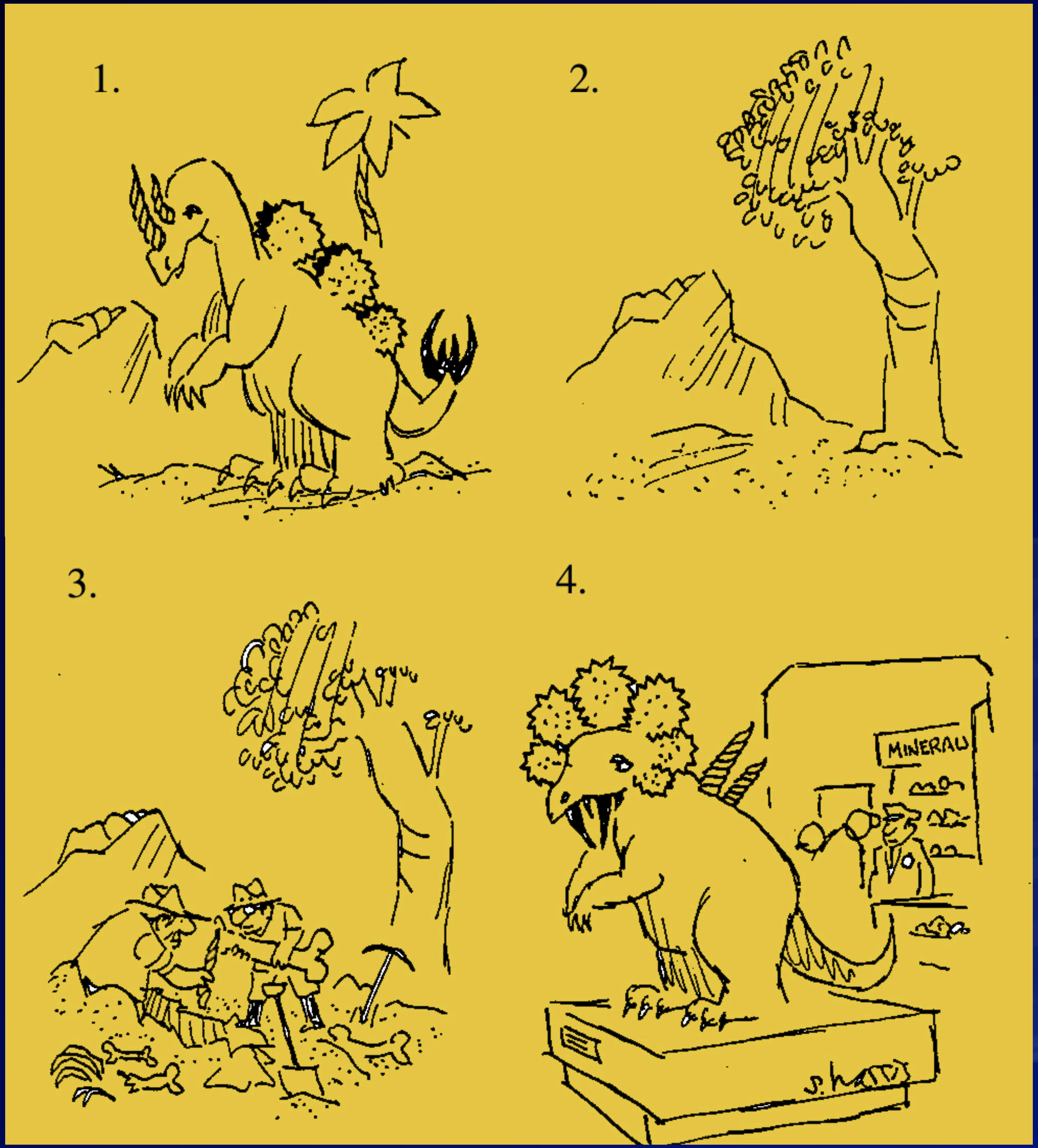
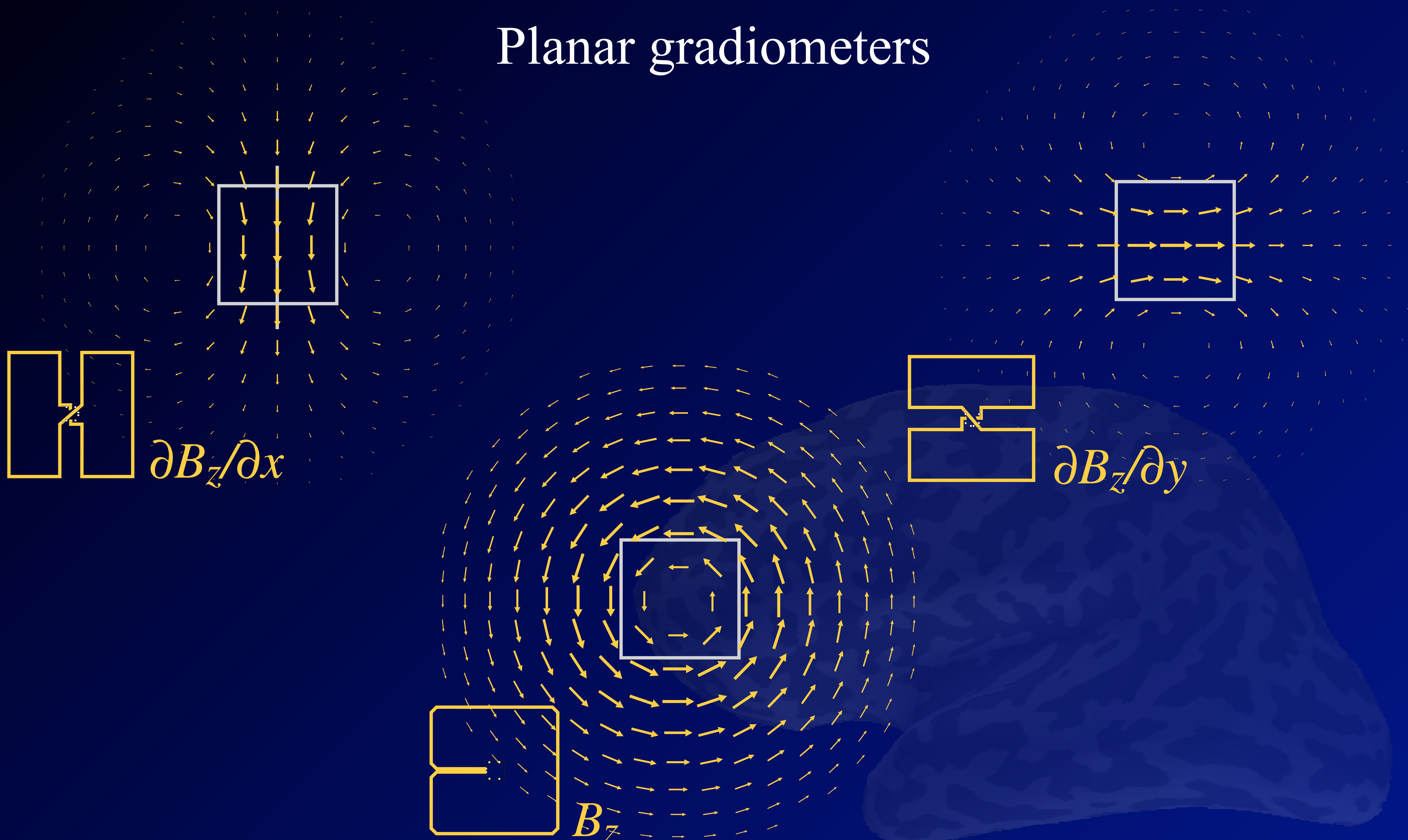


Lead fields

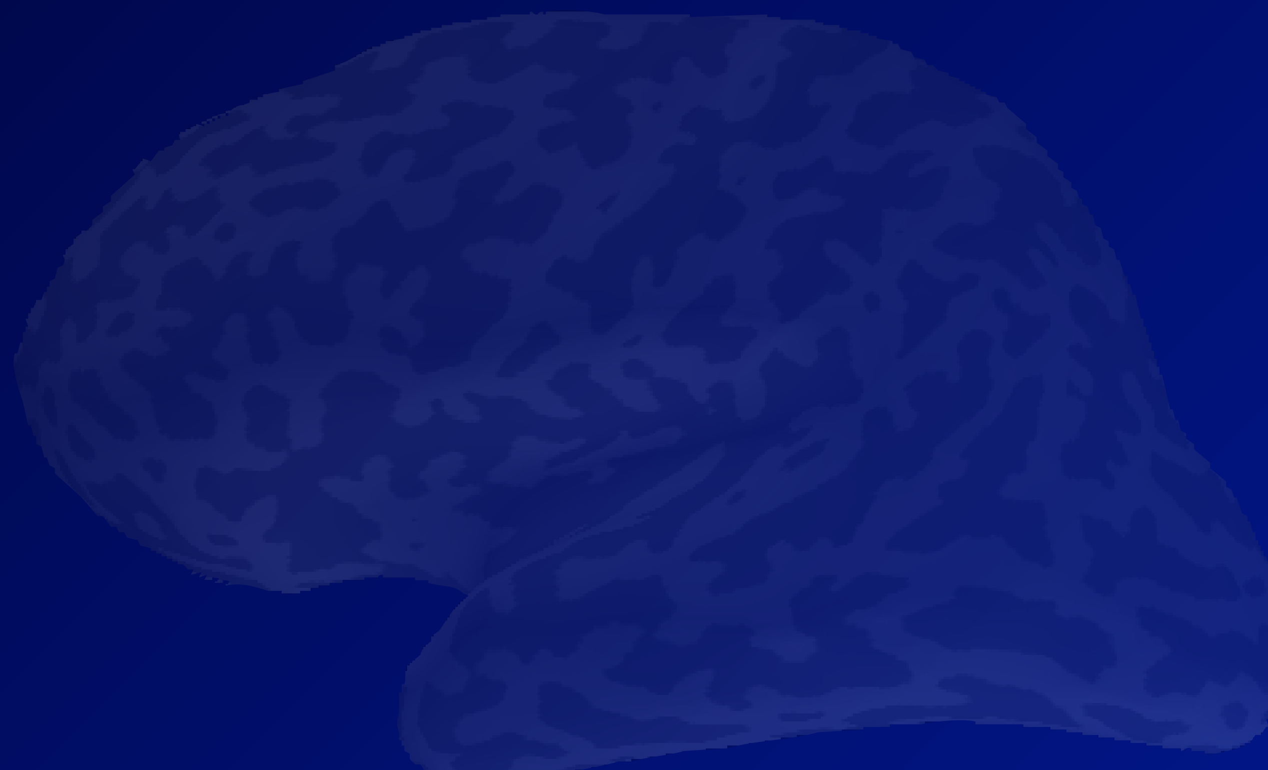
Planar gradiometers



Magnetometer

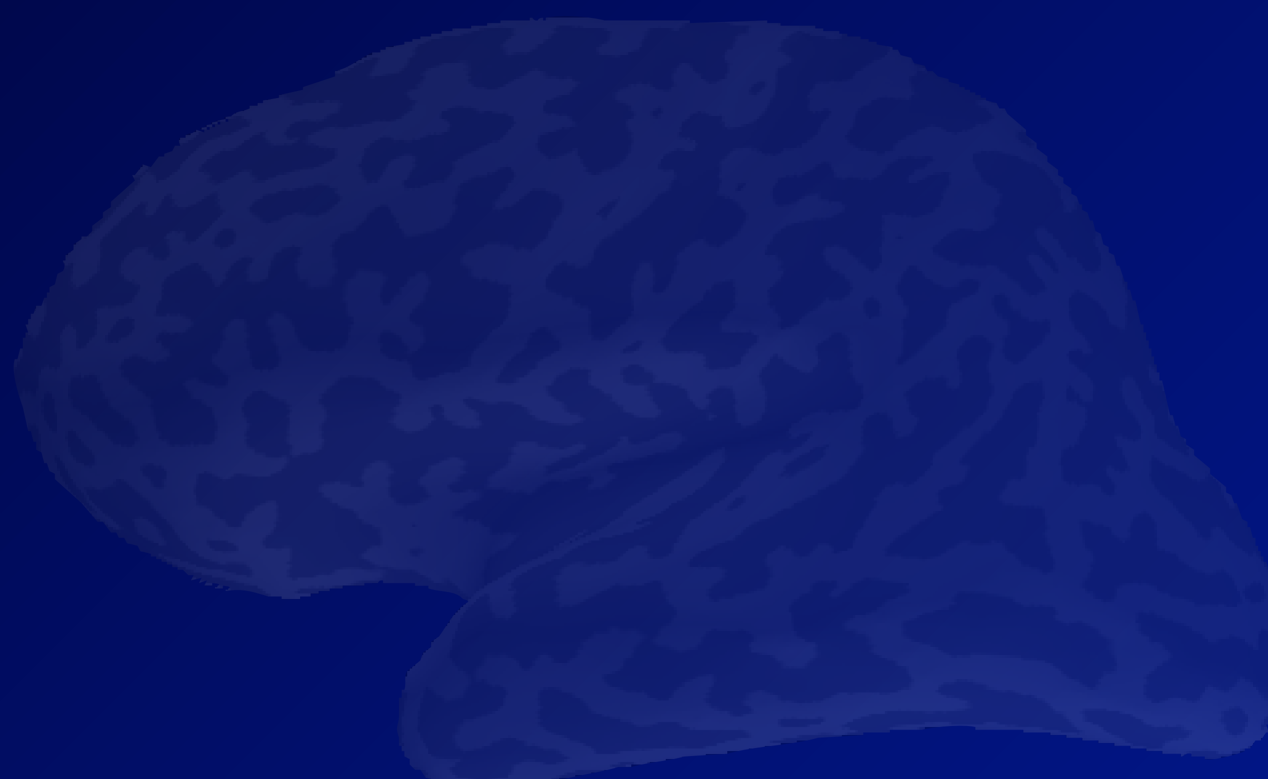
Cohen, 1979

MEG/EEG Inverse Problem



MEG/EEG Inverse Problem

- An ill-posed problem
  - Many different current distributions can explain the data
  - Solution may be sensitive to noise, *i.e.*, unstable



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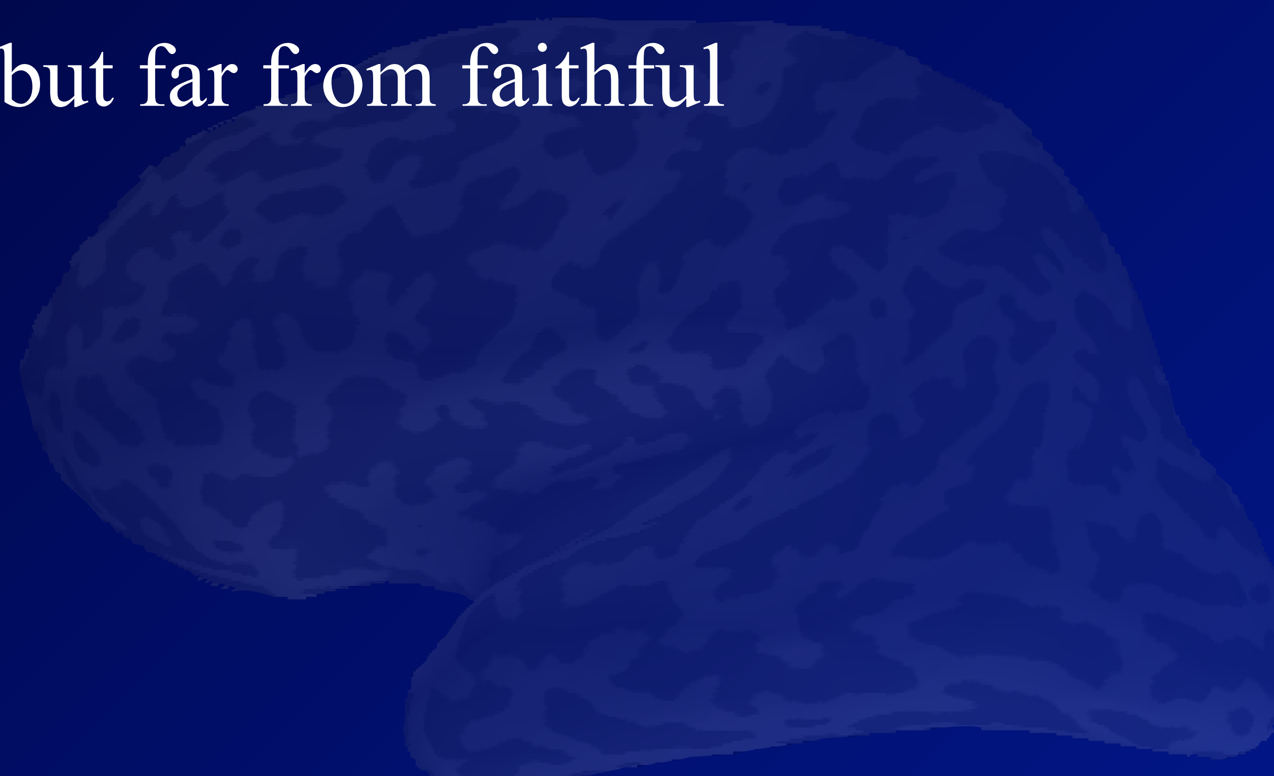
  - A solution can be unique but far from faithful



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- Additional constraints are useful
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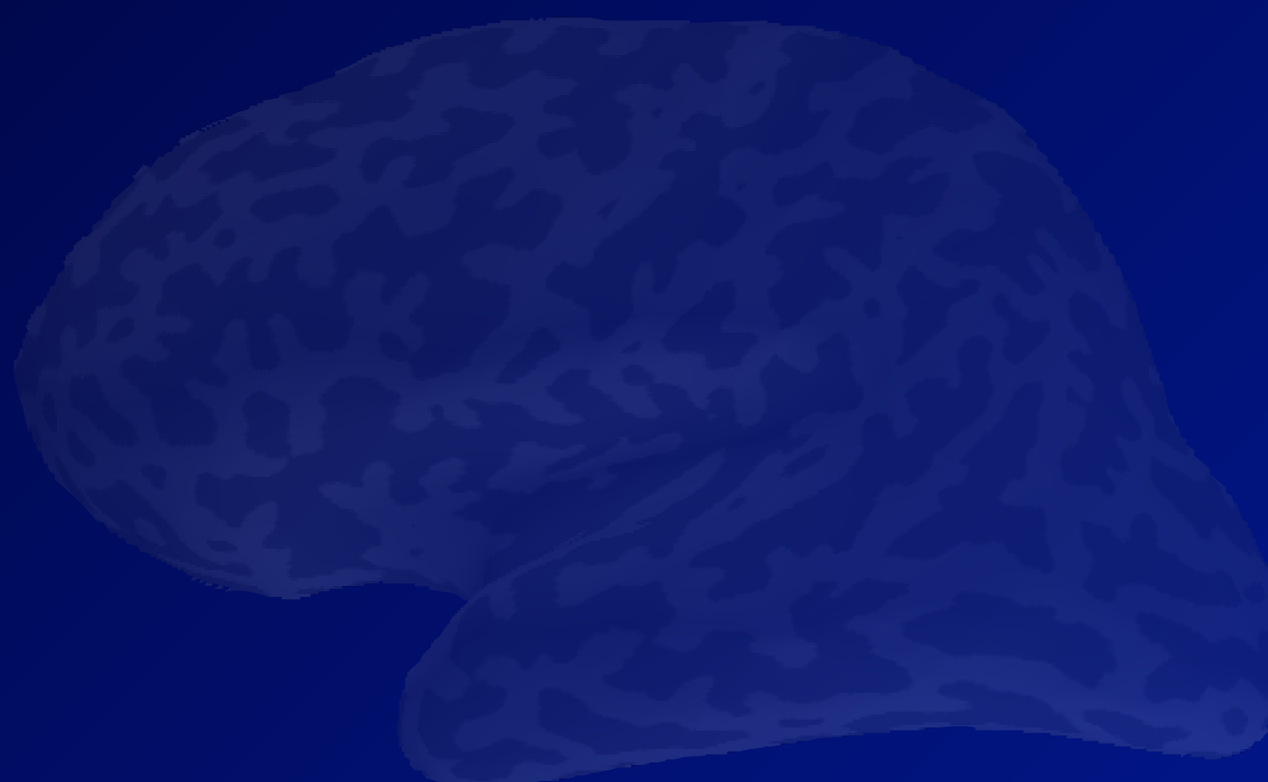
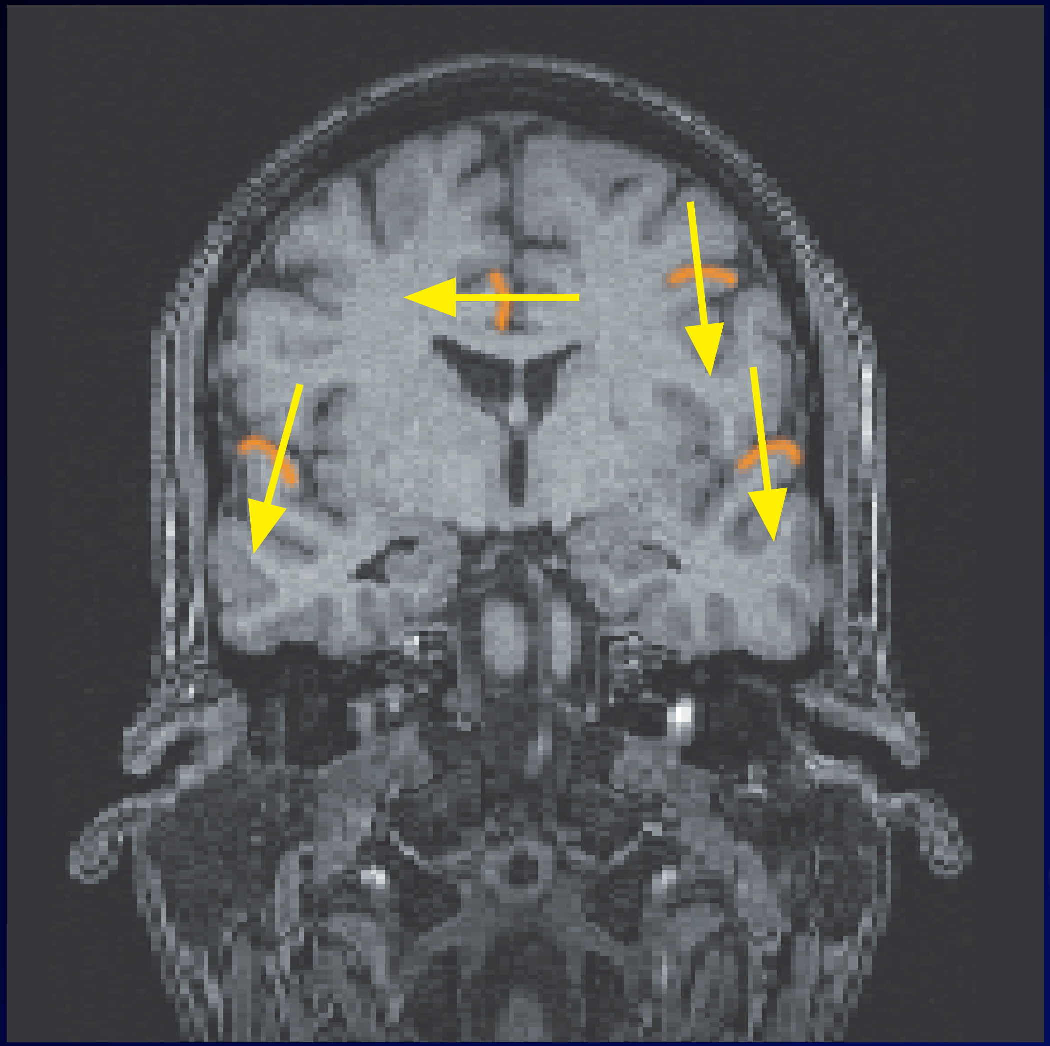
- Computational challenges
  - How to find the optimal solution once the cost function has been specified?

Current dipole models



Example: The time-varying current-dipole model



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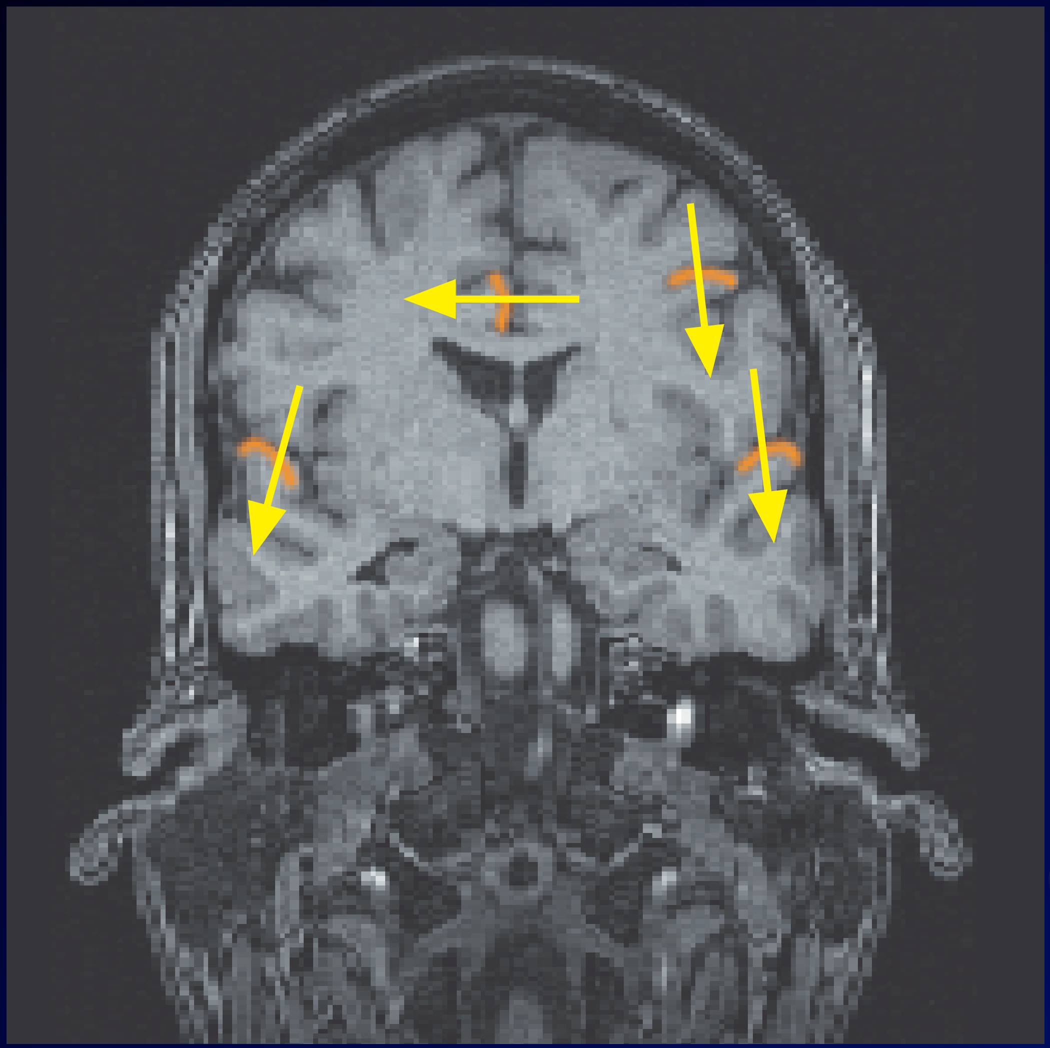

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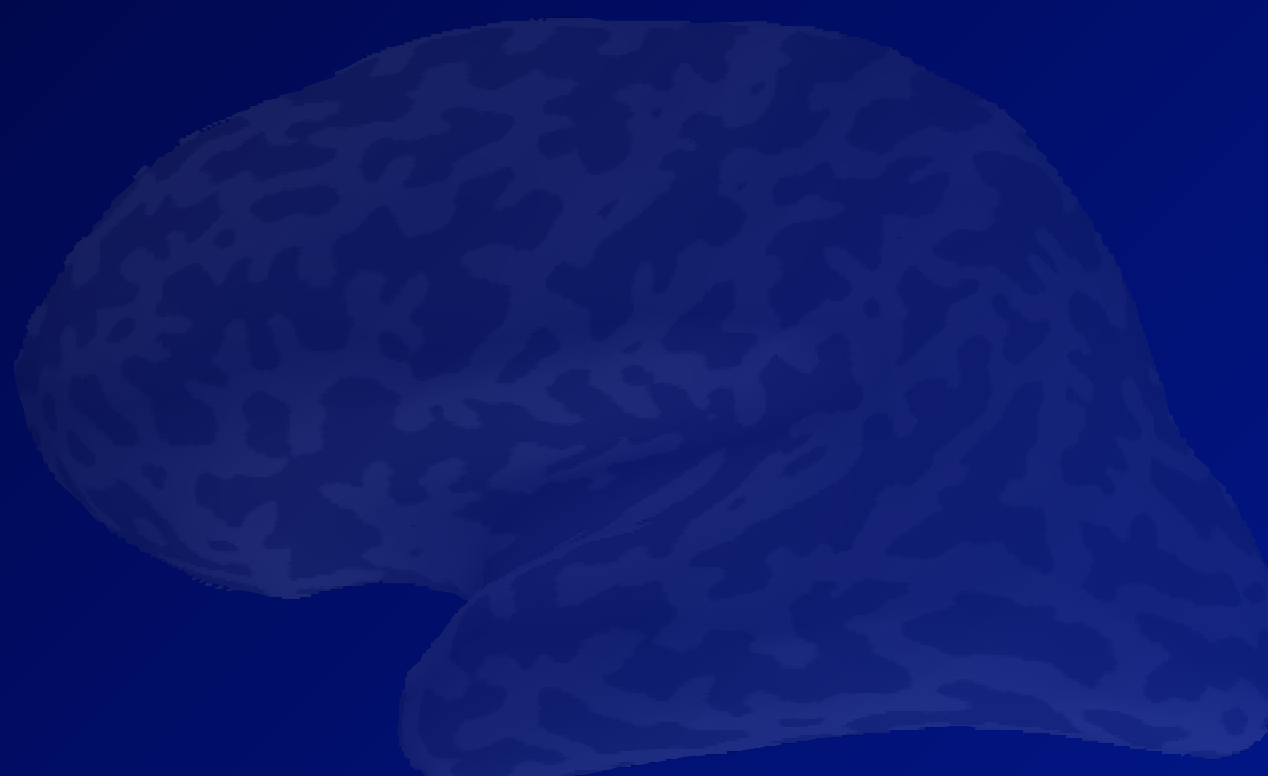
Scherg *et al.*, 1984

Model for the measurement

- Data predicted by the forward model + additive zero-mean Gaussian noise with a known spatial covariance matrix:



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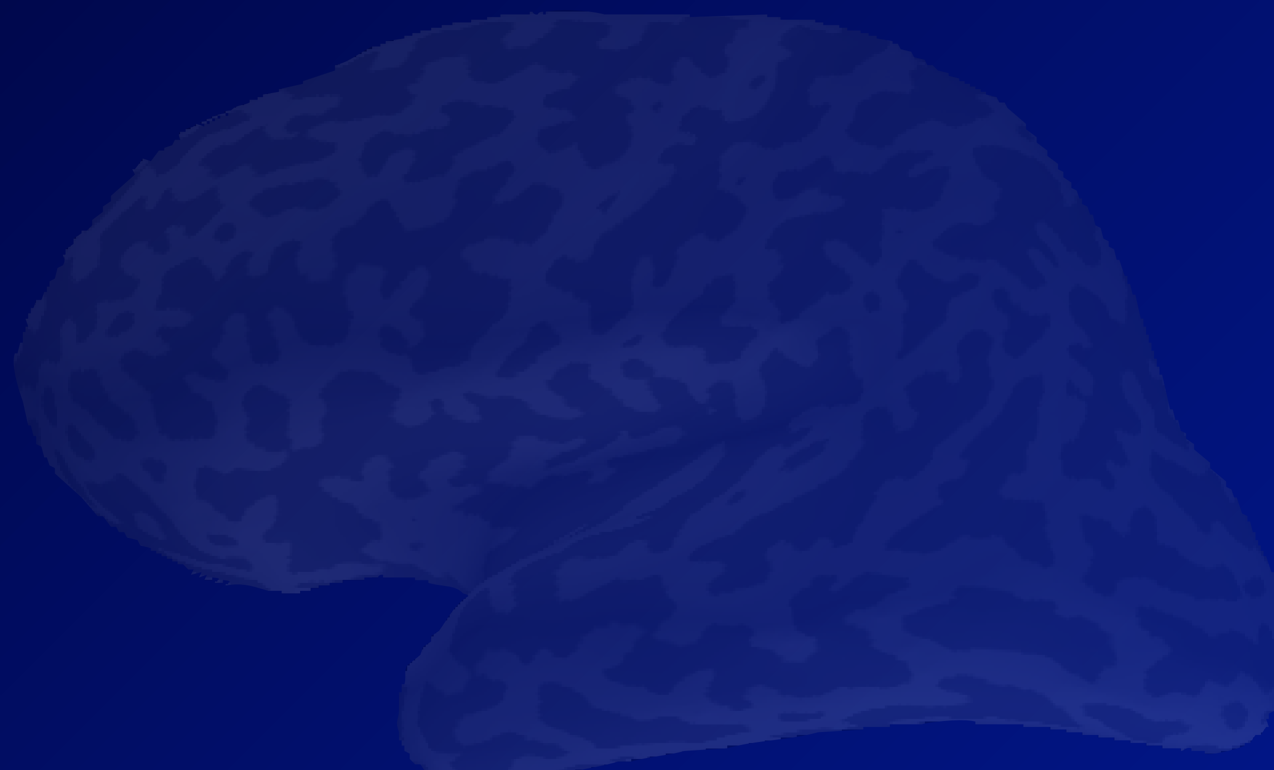

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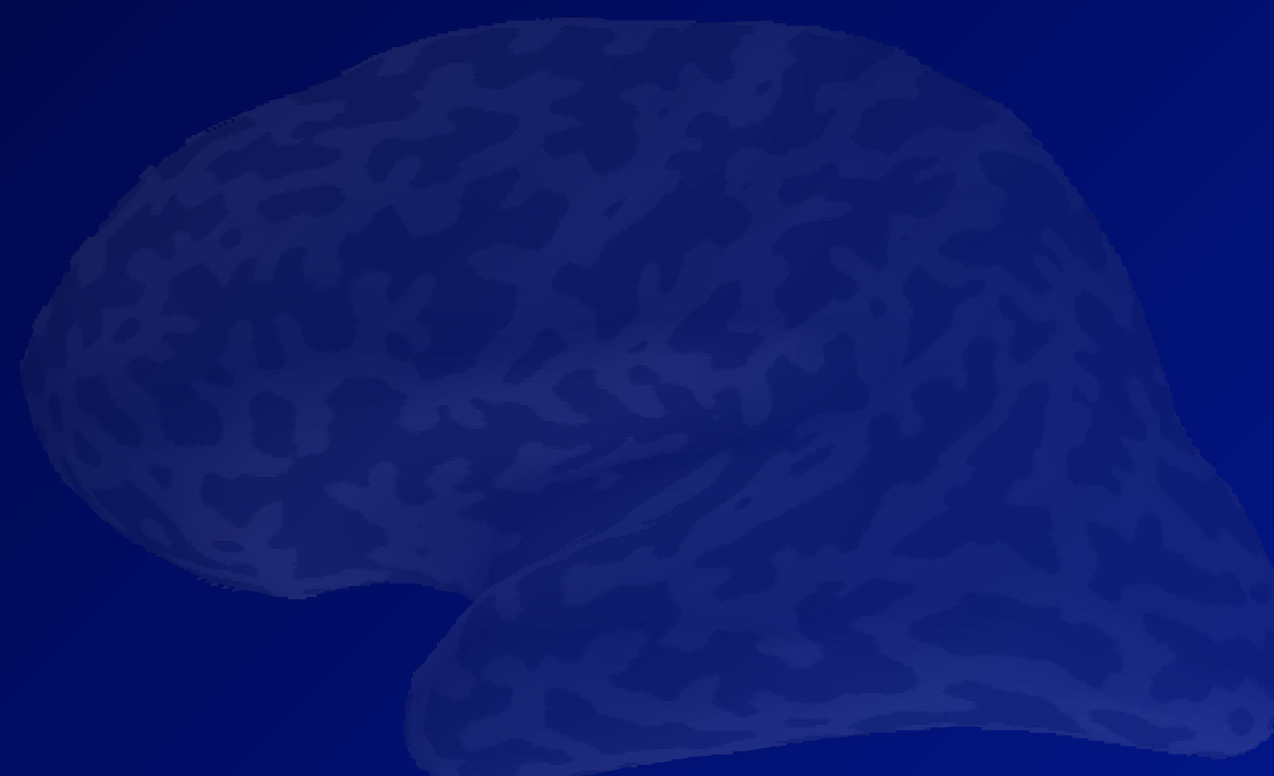
Data produced by unit dipoles at known locations



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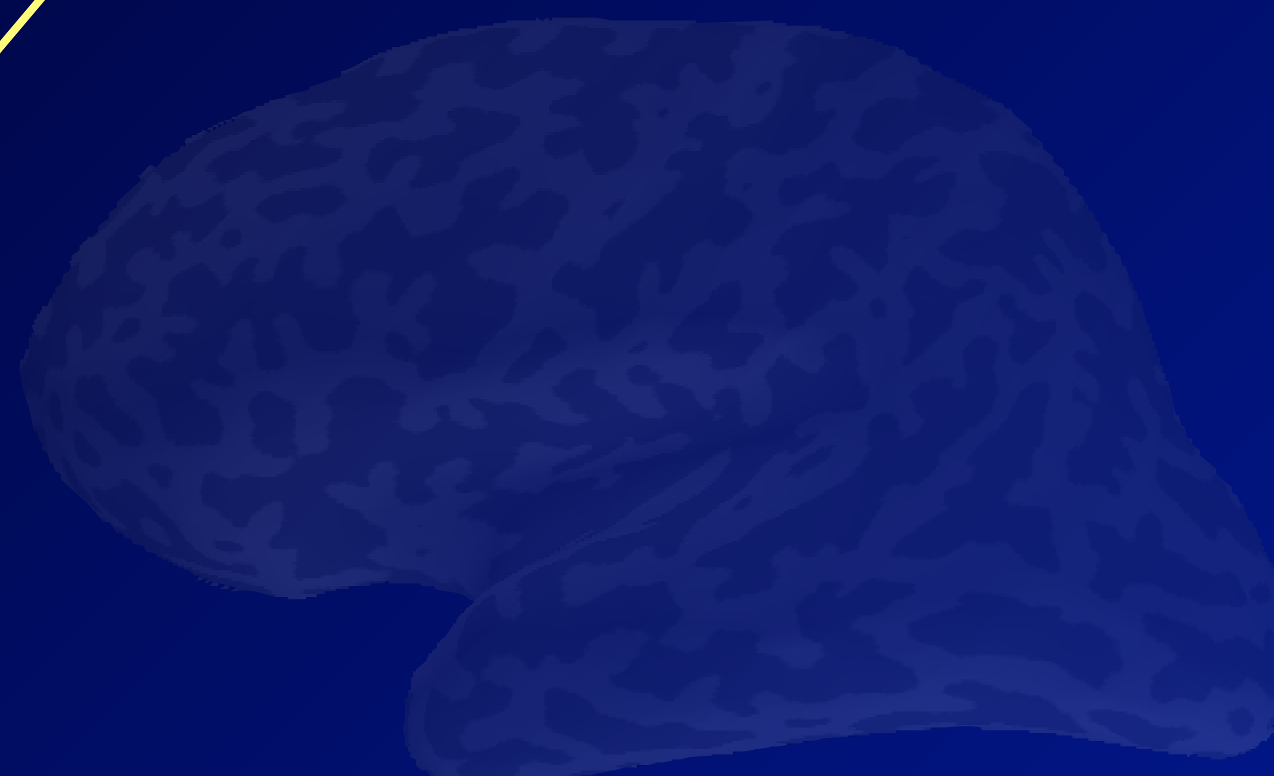

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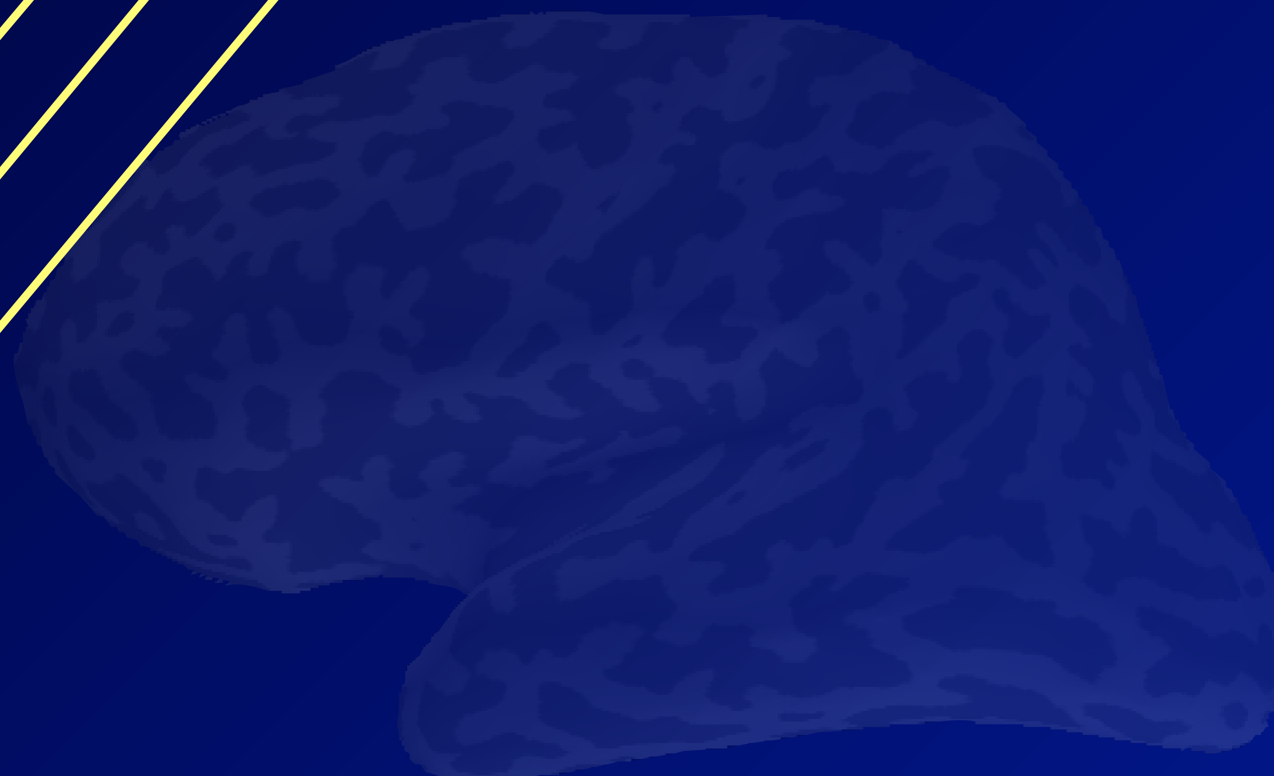
Dipole locations

Dipole orientations

Source waveforms



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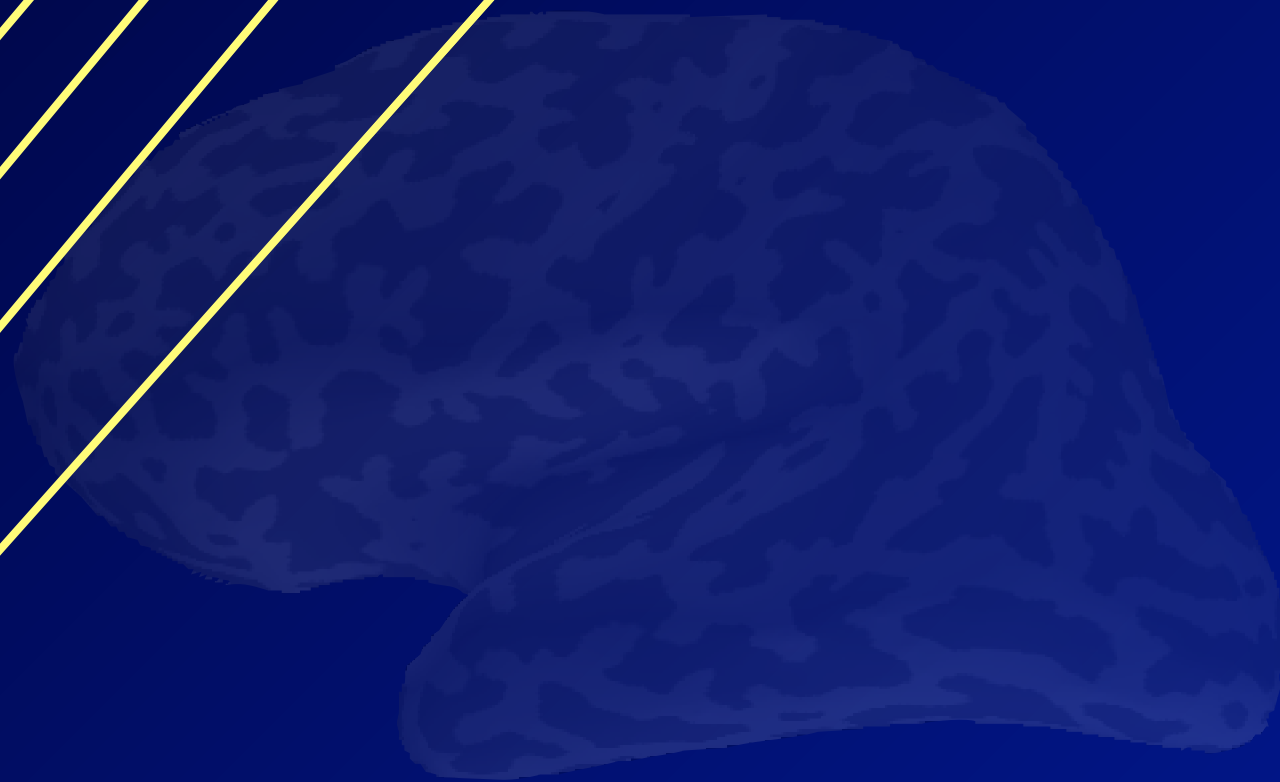
Source waveforms

Noise



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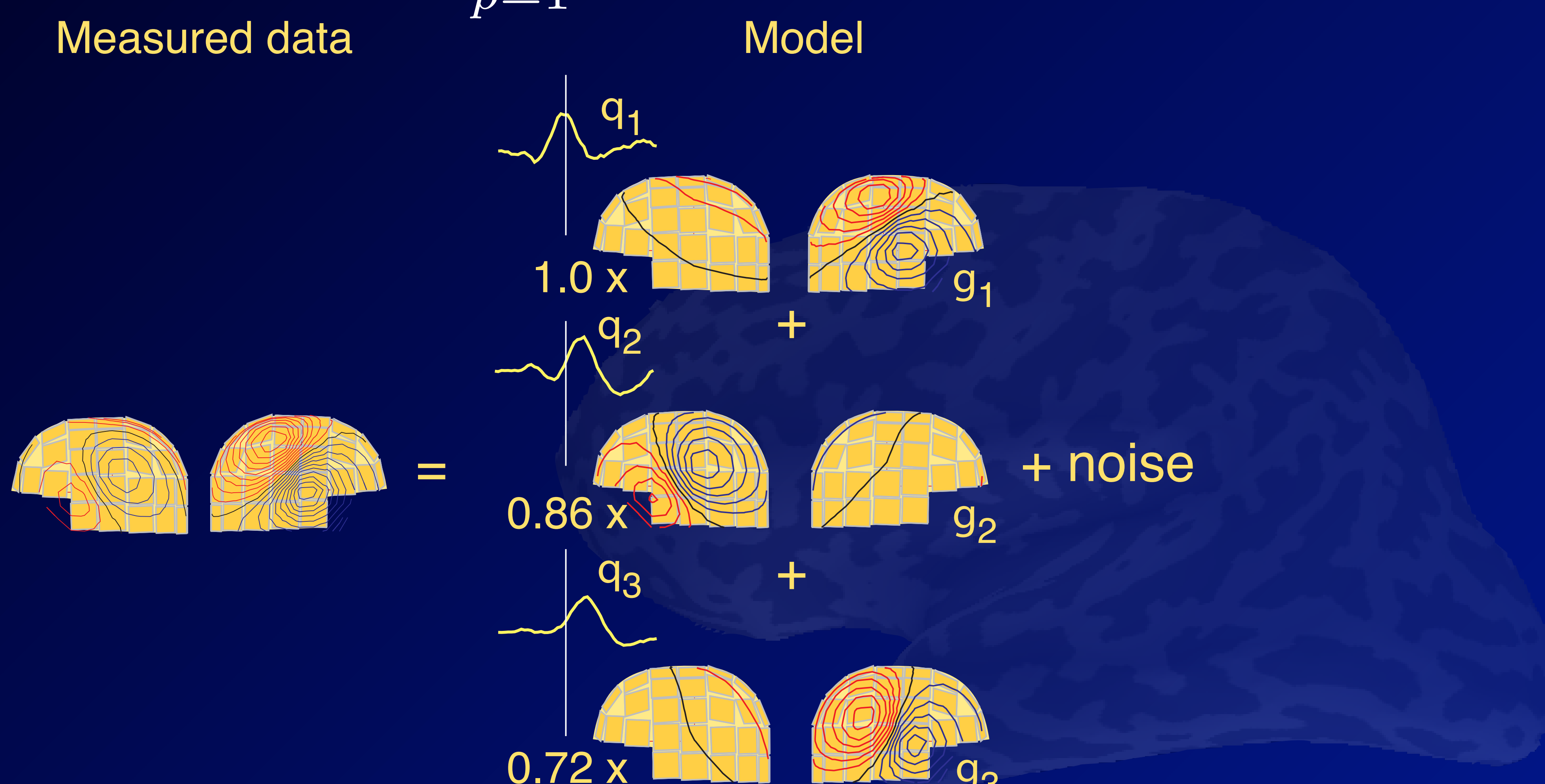
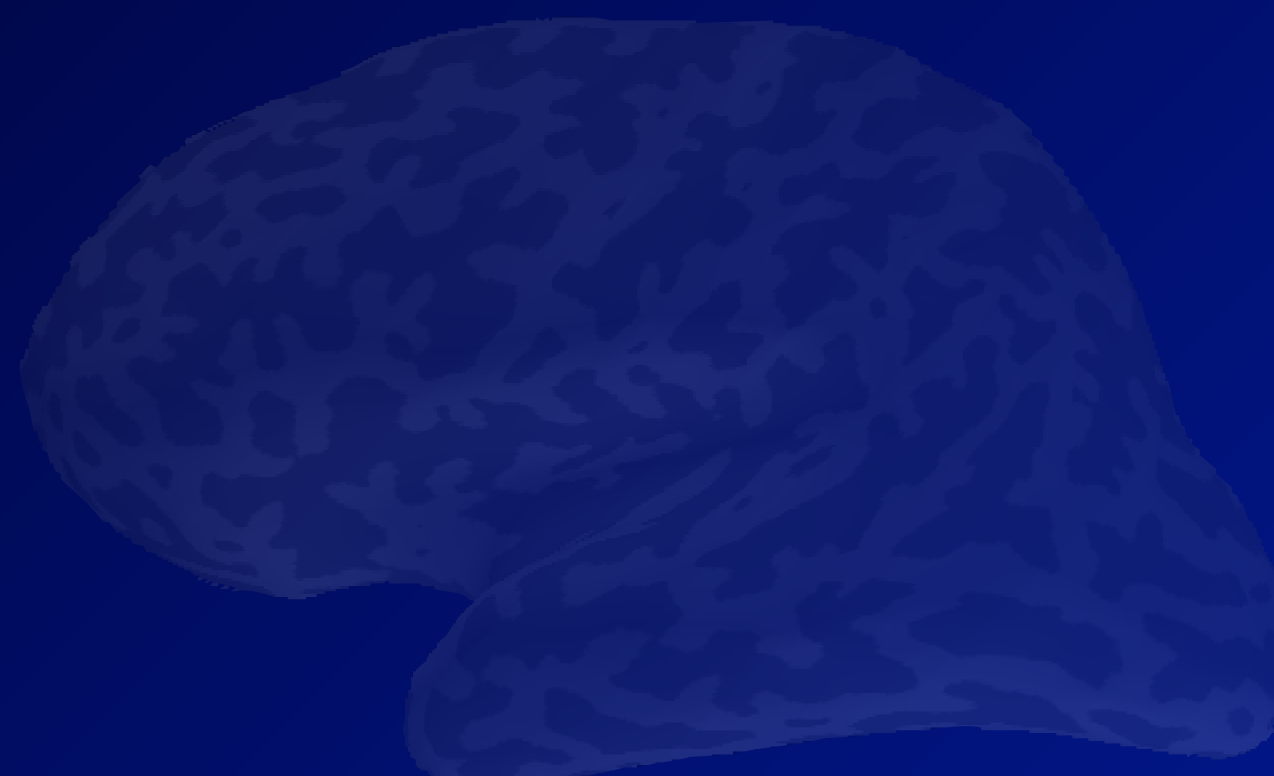


Fitting

$$\{\hat{\mathbf{q}}_p, \hat{\mathbf{r}}_p\} = \mathrm{argmin}_{\{\mathbf{q}_p, \mathbf{r}_p\}} ||\mathbf{B}_{\mathrm{meas}} - \mathbf{B}_{\mathrm{model}}||^2$$



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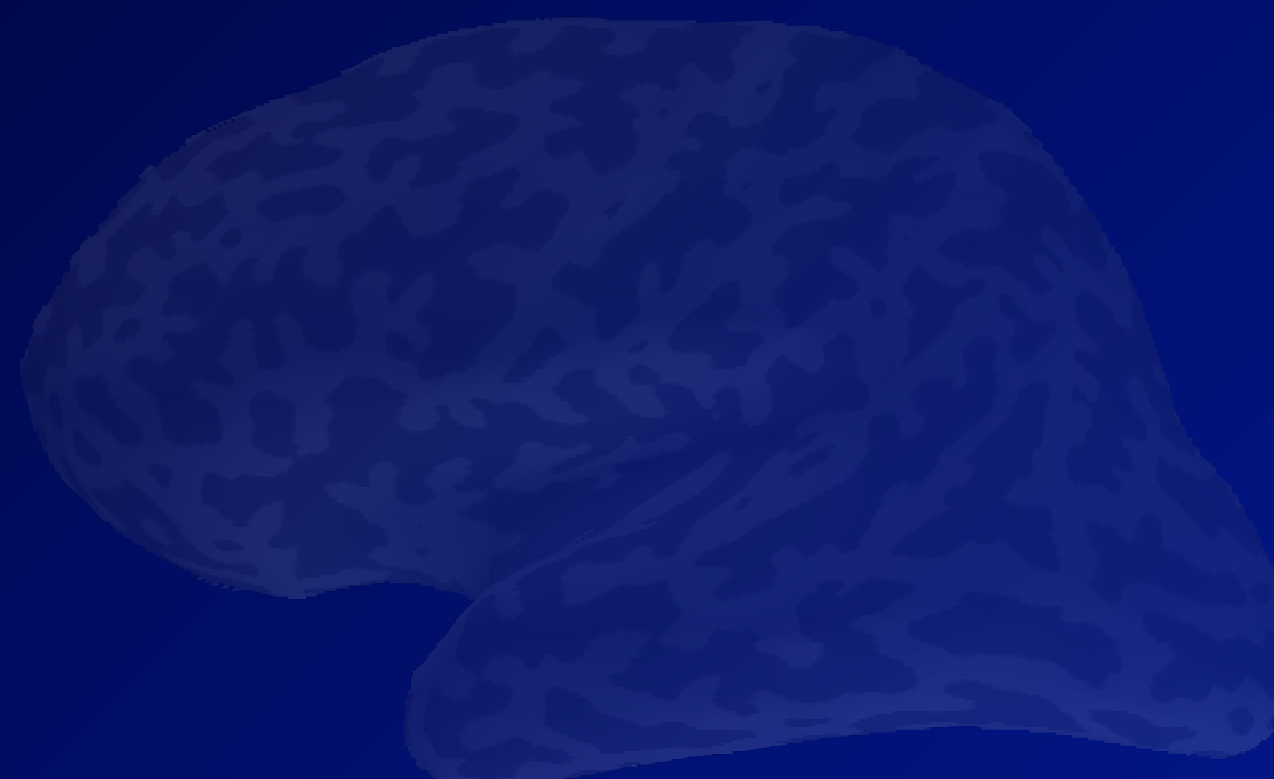

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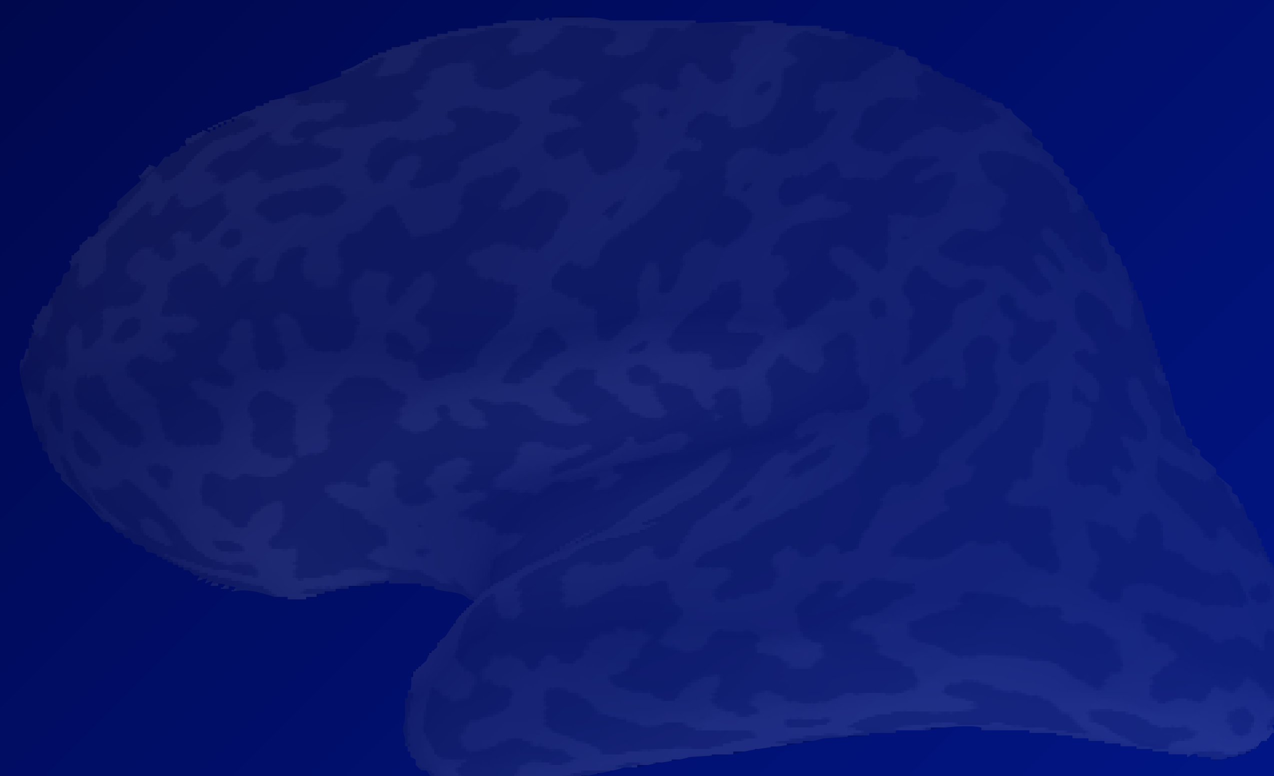

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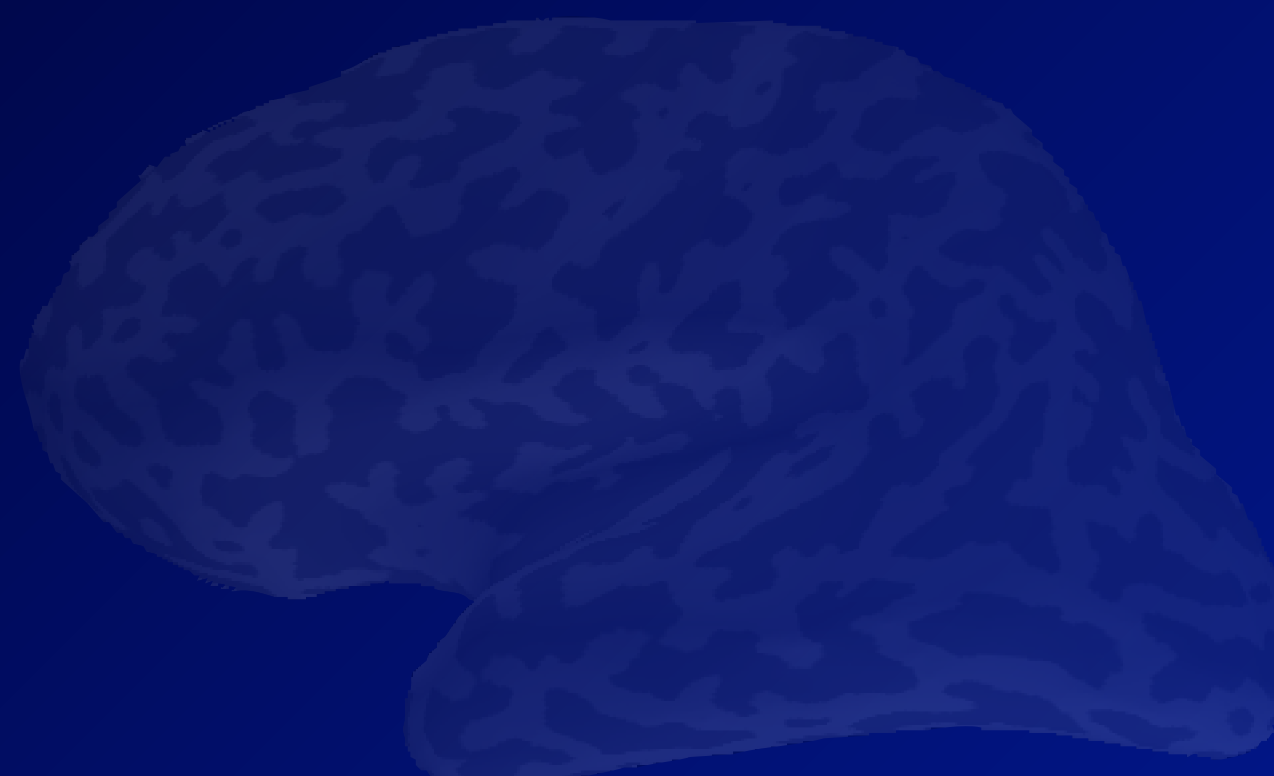

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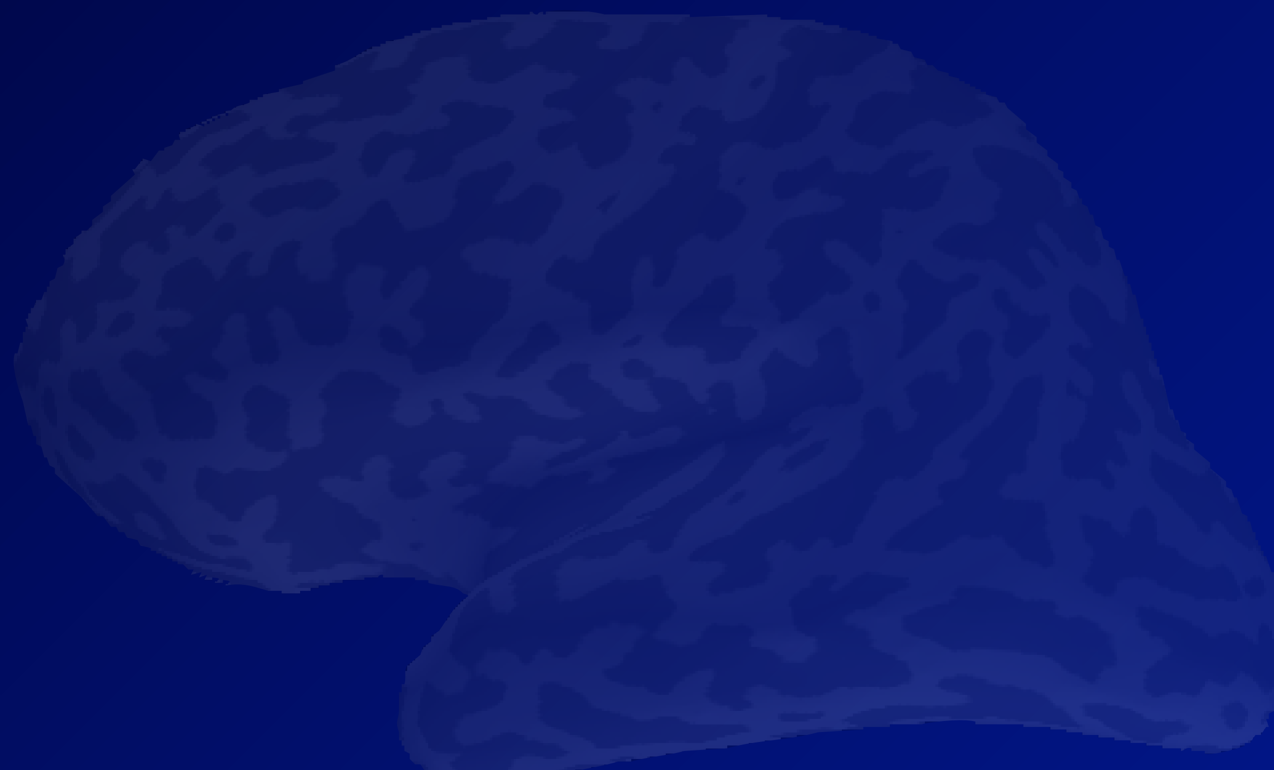

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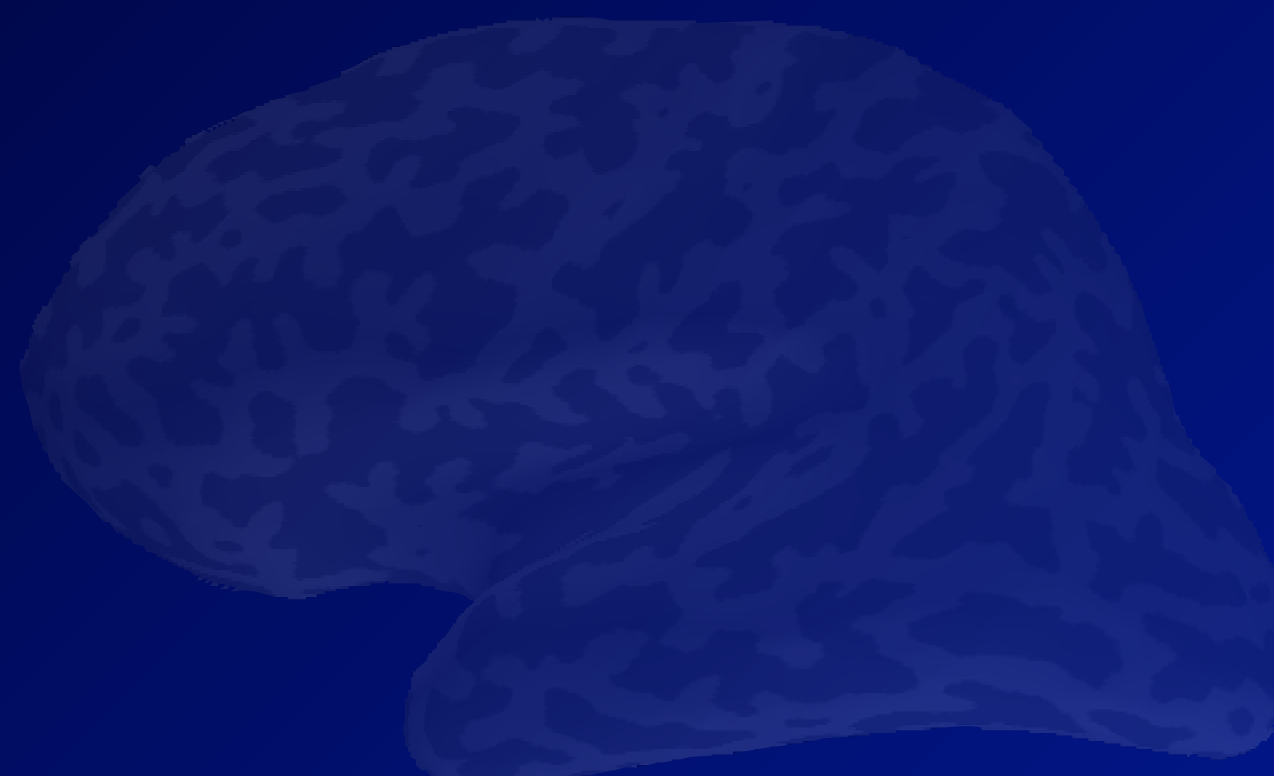

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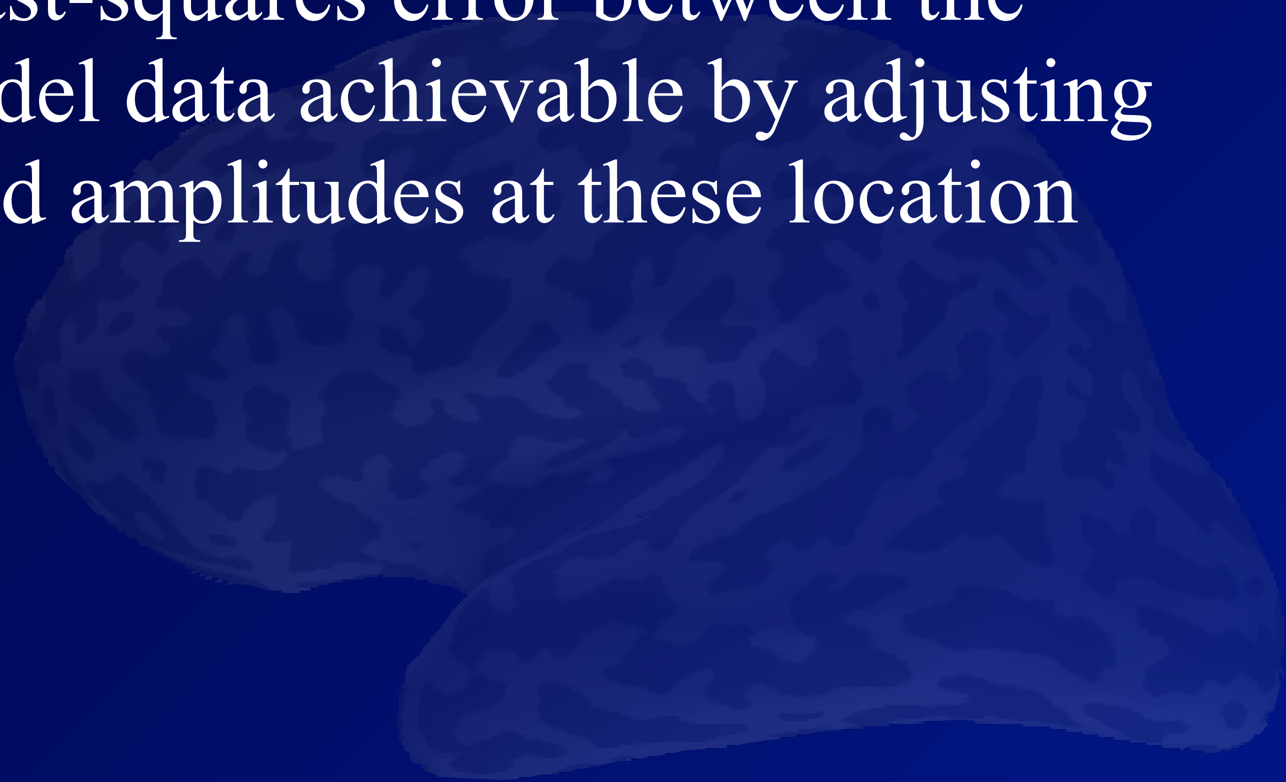

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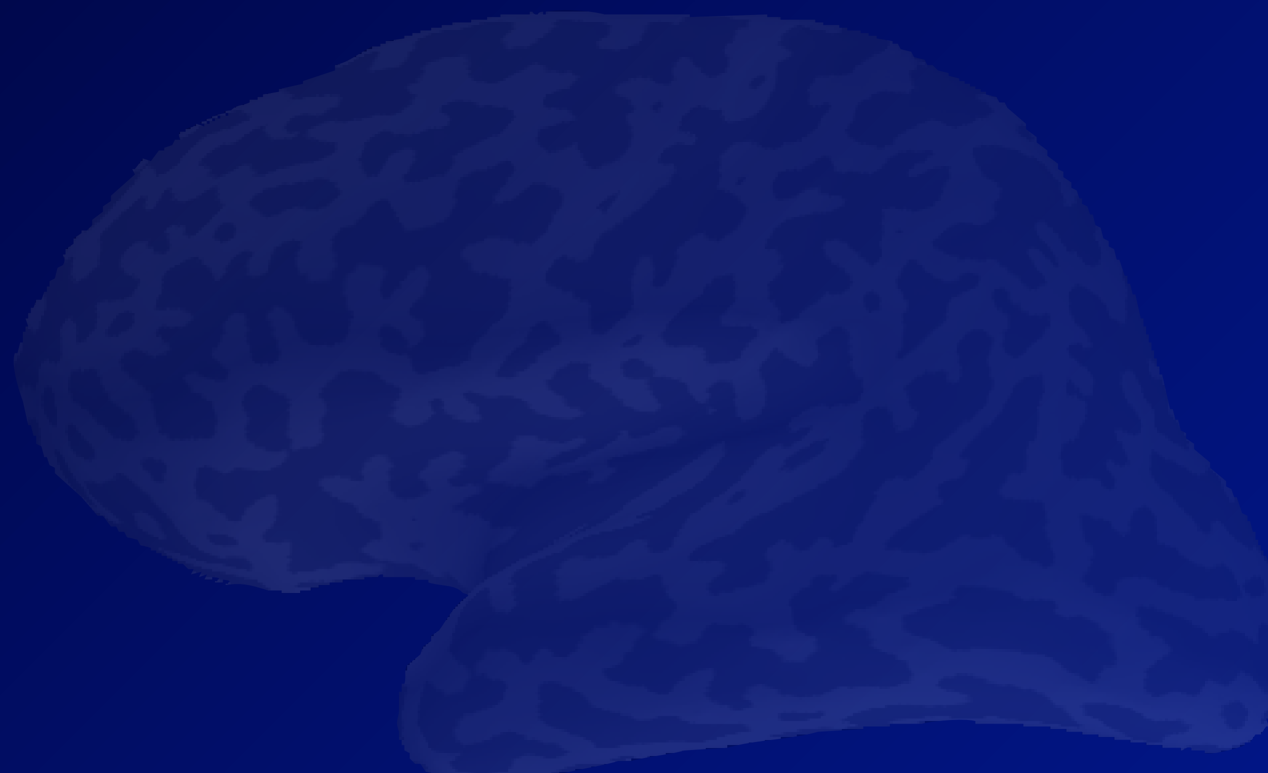
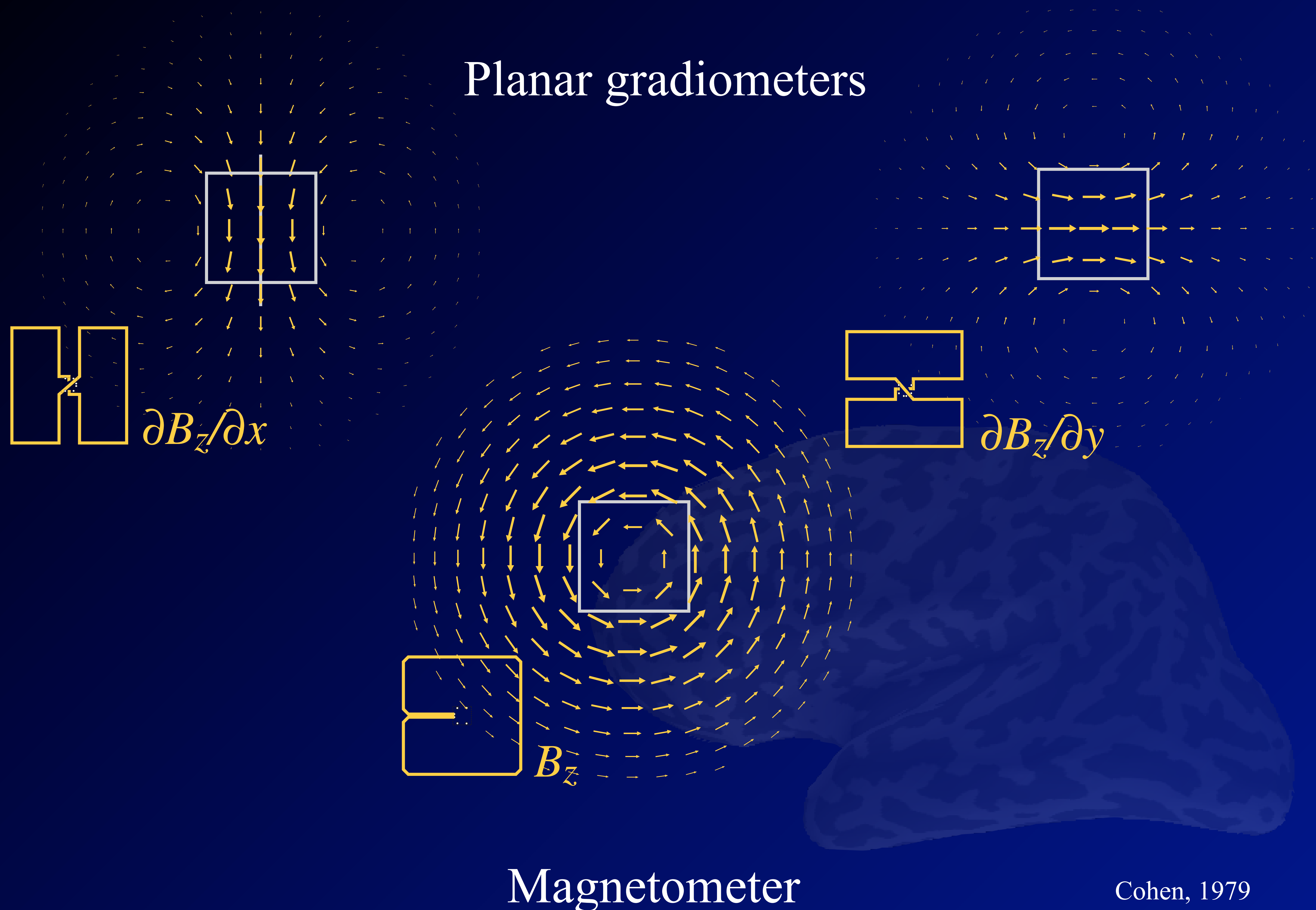
Heuristic strategies

- Try to select time points when only one dipole is active
- Use channel selections
- Construct the model dipole-by-dipole

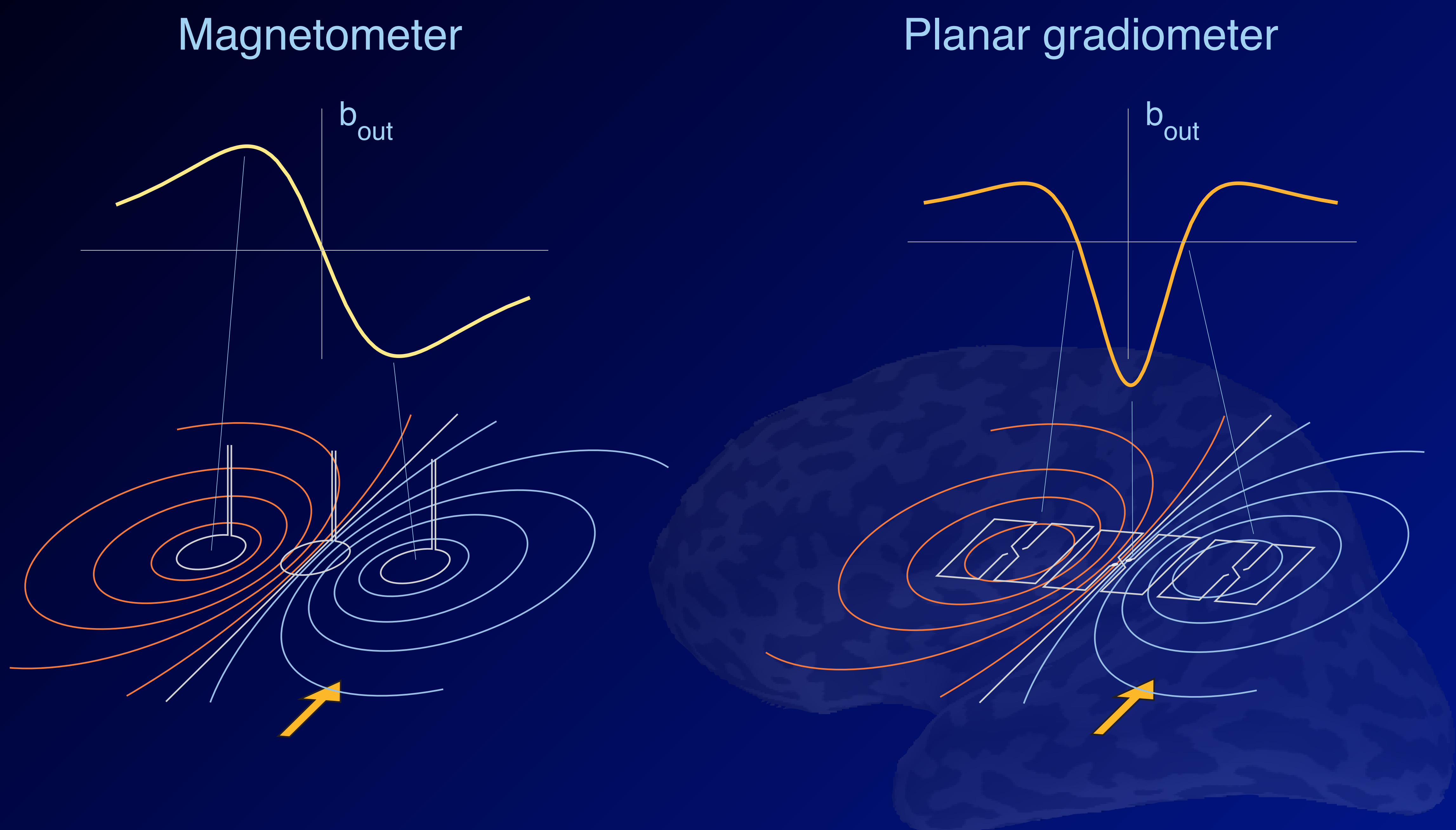


Vectorview sensor triplets (306 = 3 x 102)

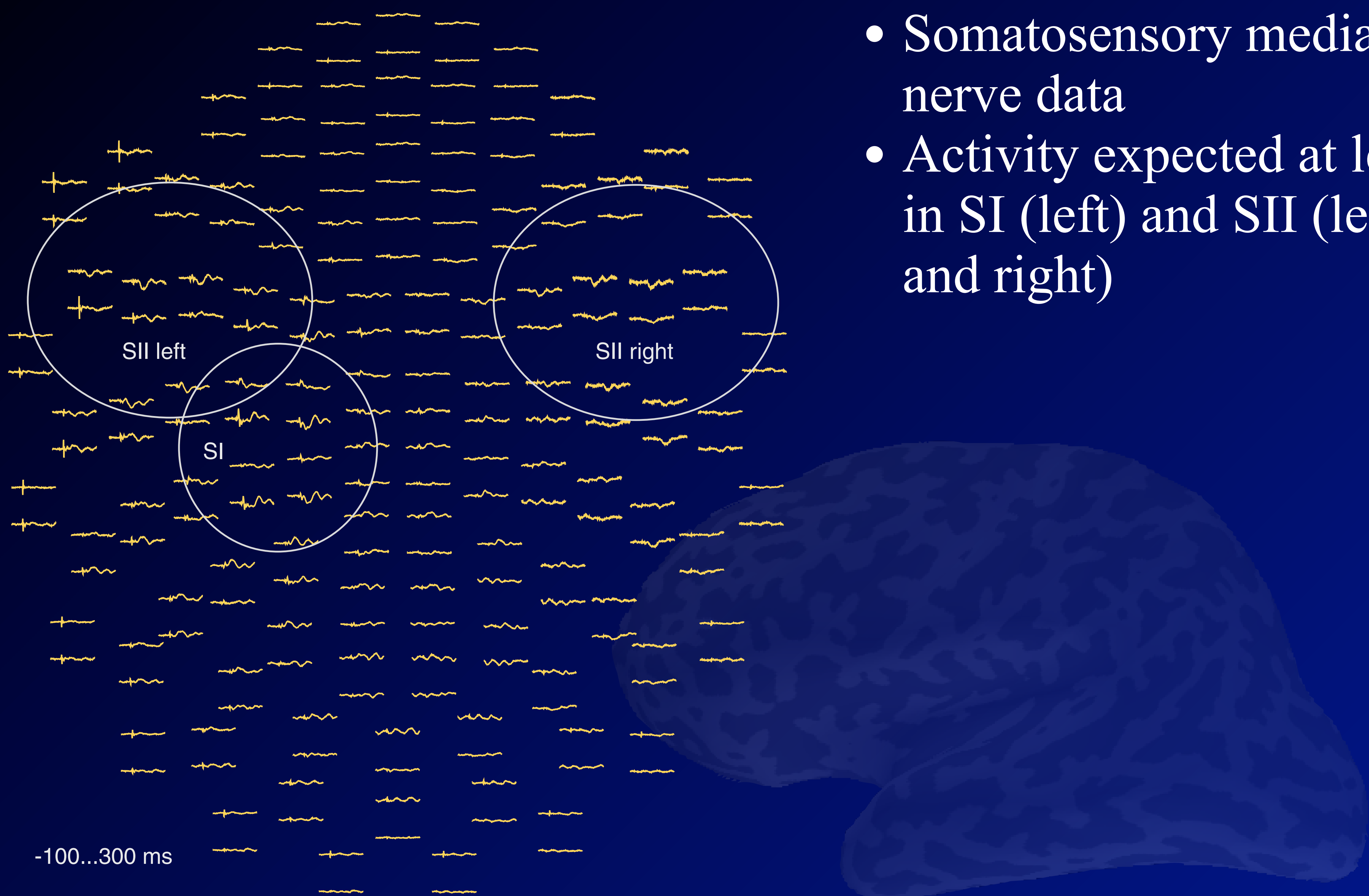


Cohen, 1979

Magnetometers and planar gradiometers



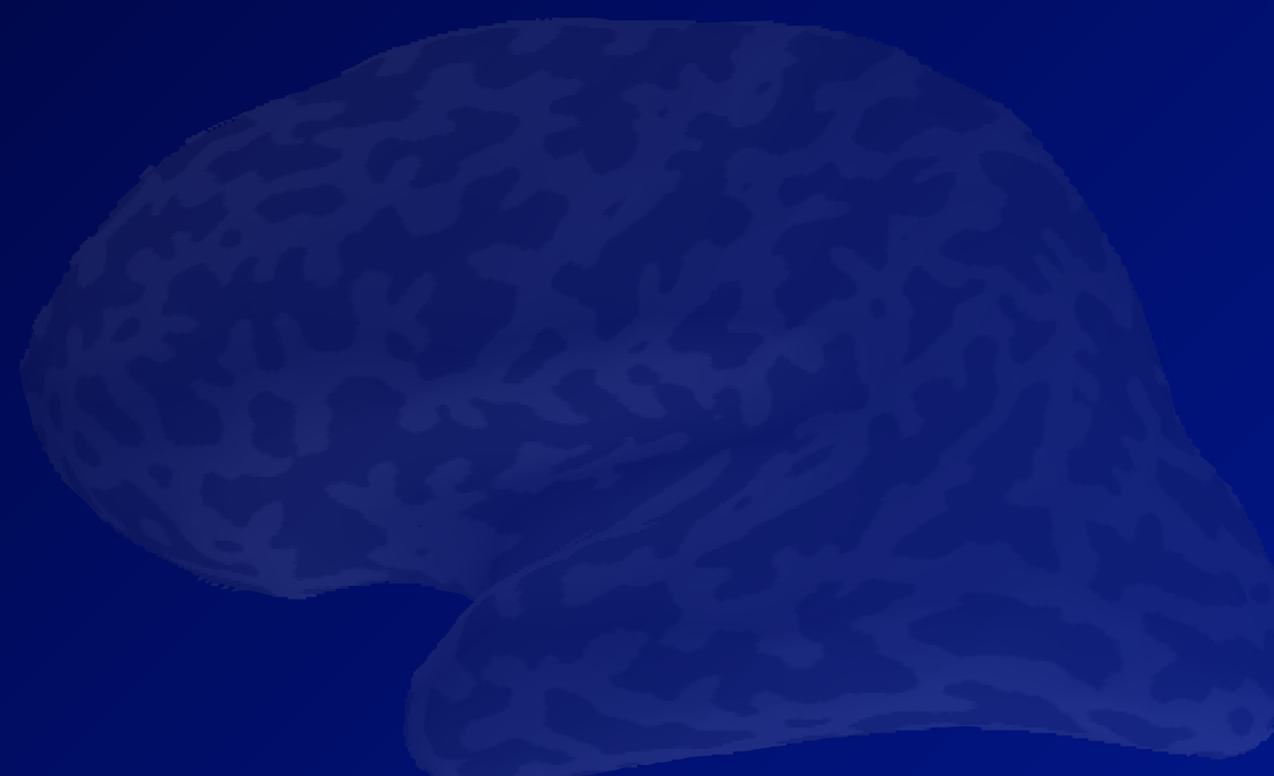
An example of averaged MEG data



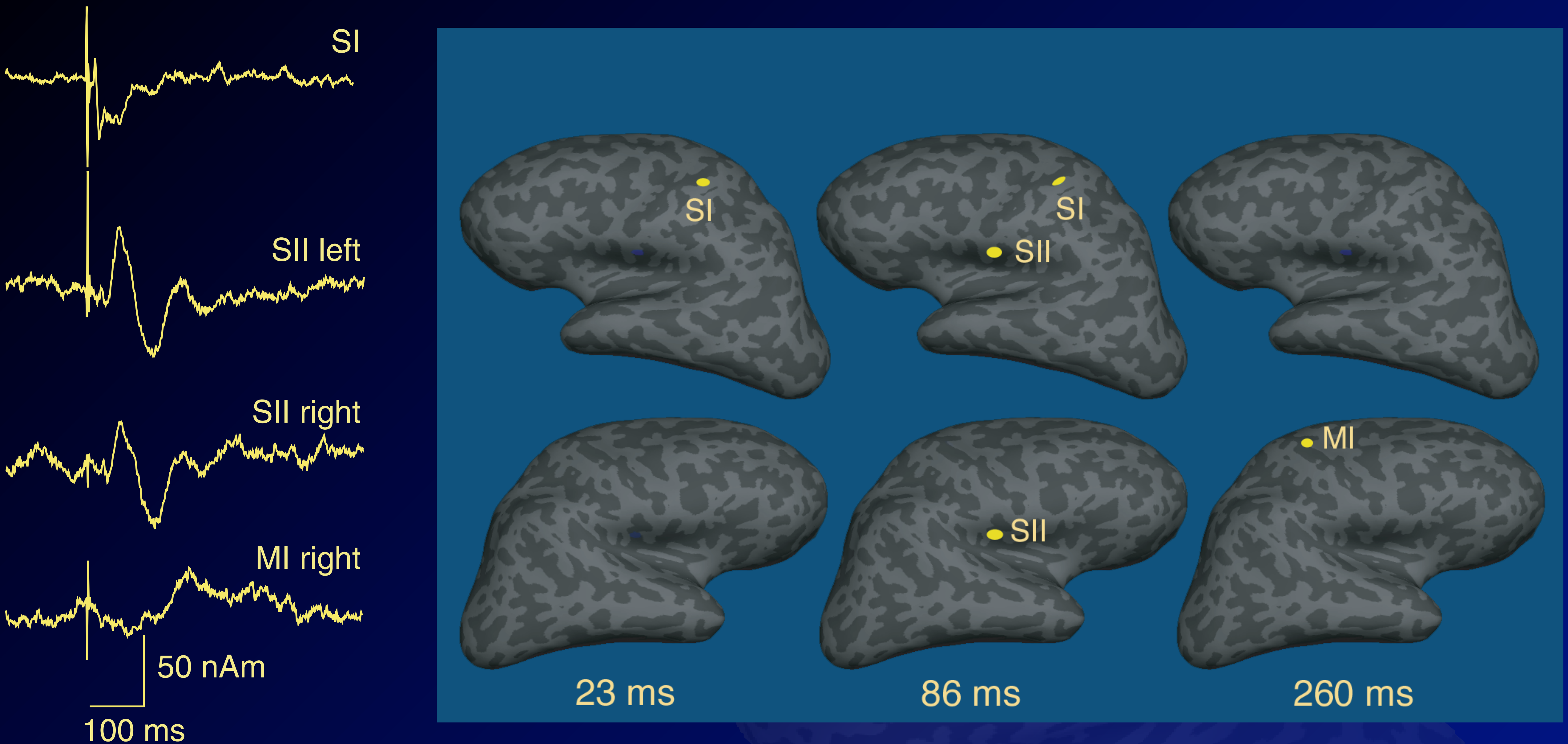
- Somatosensory median nerve data
- Activity expected at least in SI (left) and SII (left and right)

Possible strategy

- Fit SI at an early latency when it is active alone
- Fit the two SII responses using channel selections
- Fine tune SII fitting by keeping SI dipole fixed



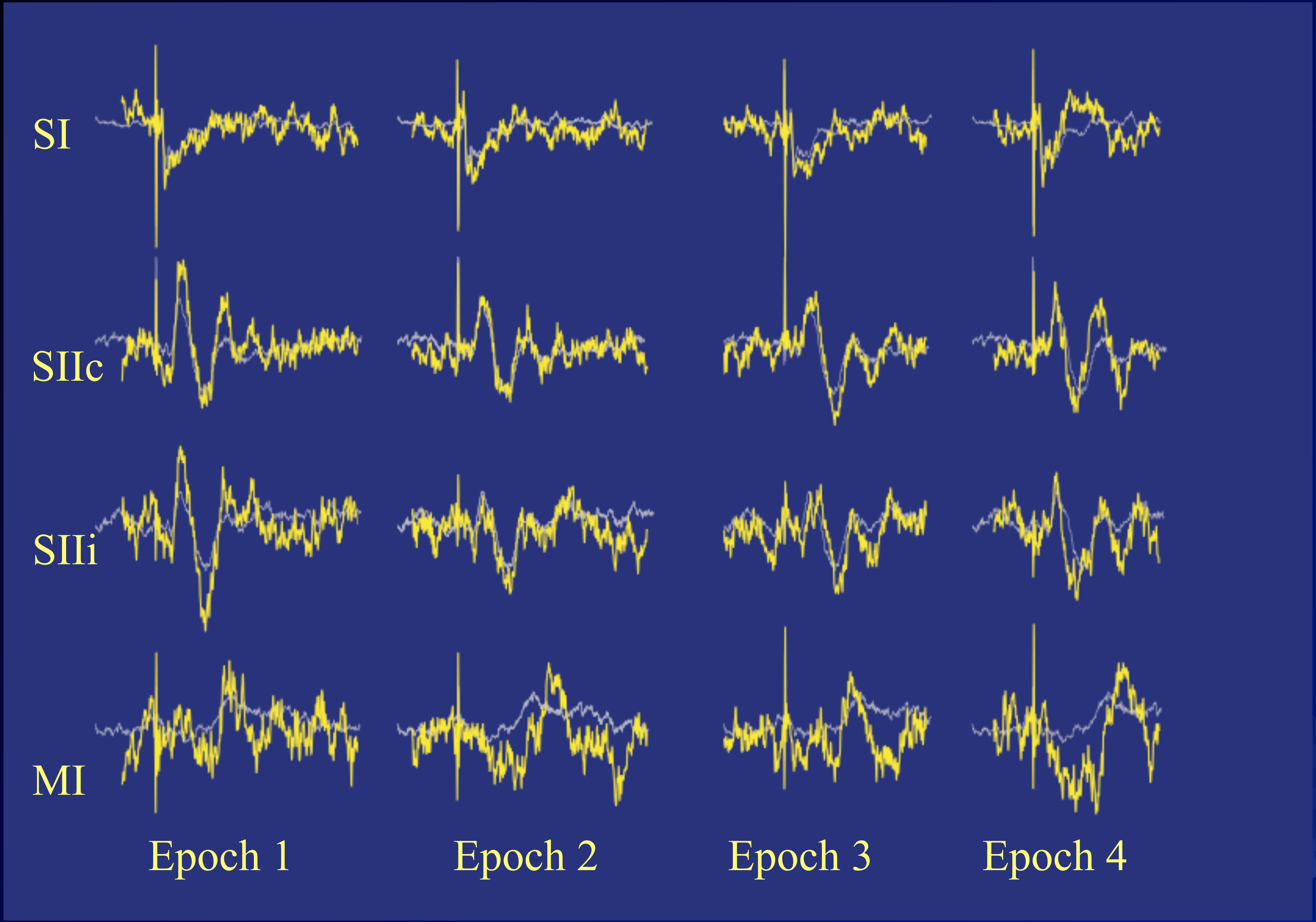
Dipole analysis: SEF with a motor task



Raij *et al.*

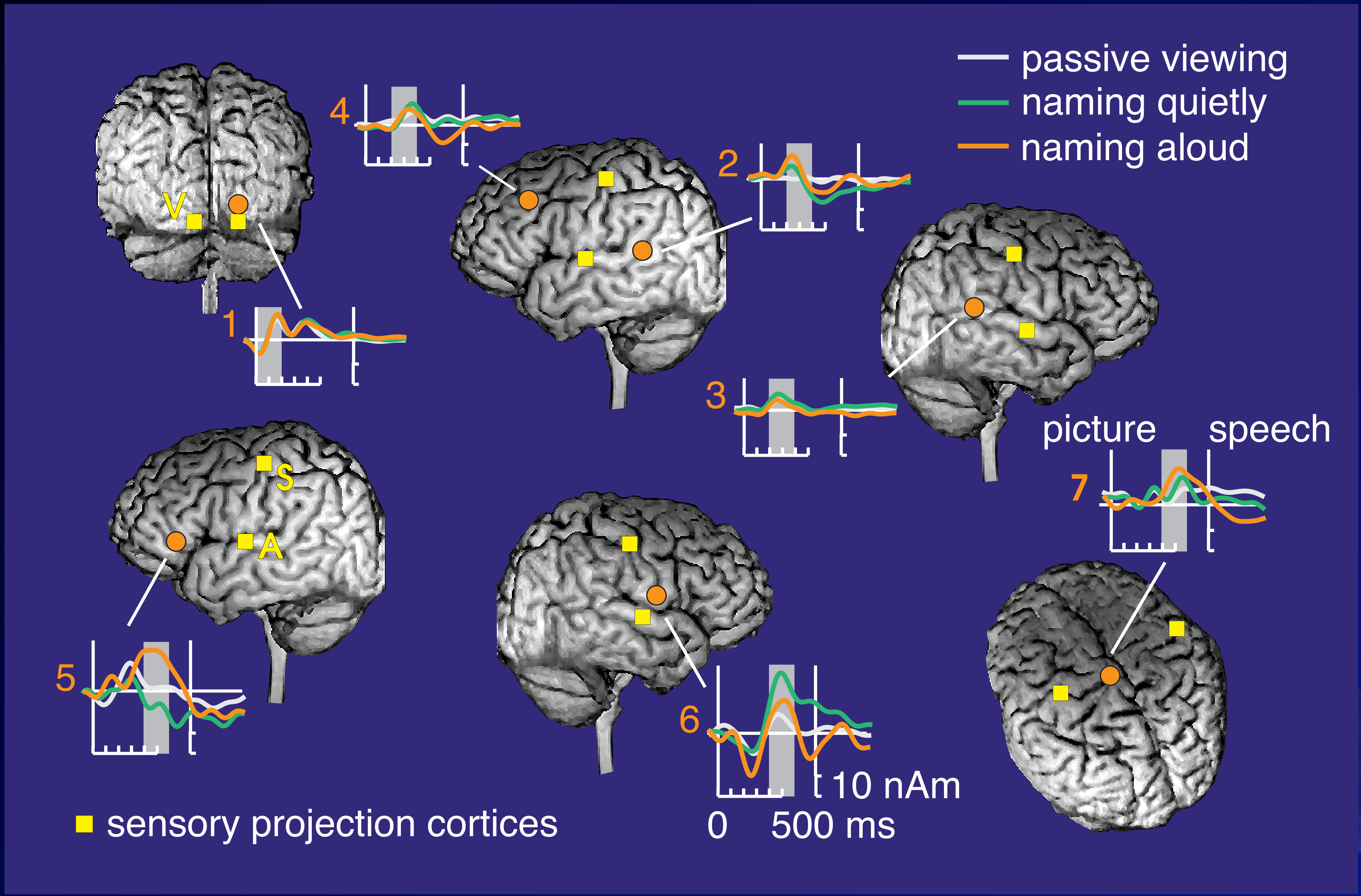
Source waveforms **Source locations**

Single-epoch analysis



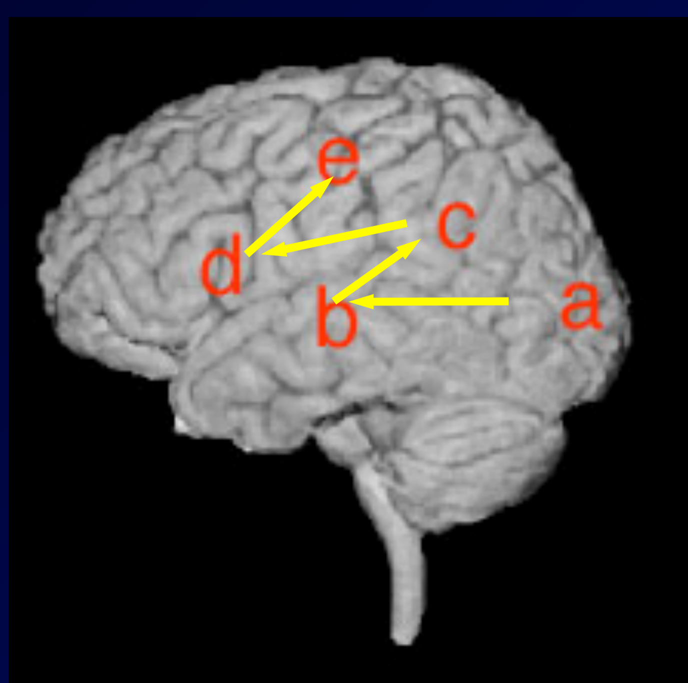
Raij *et al.*

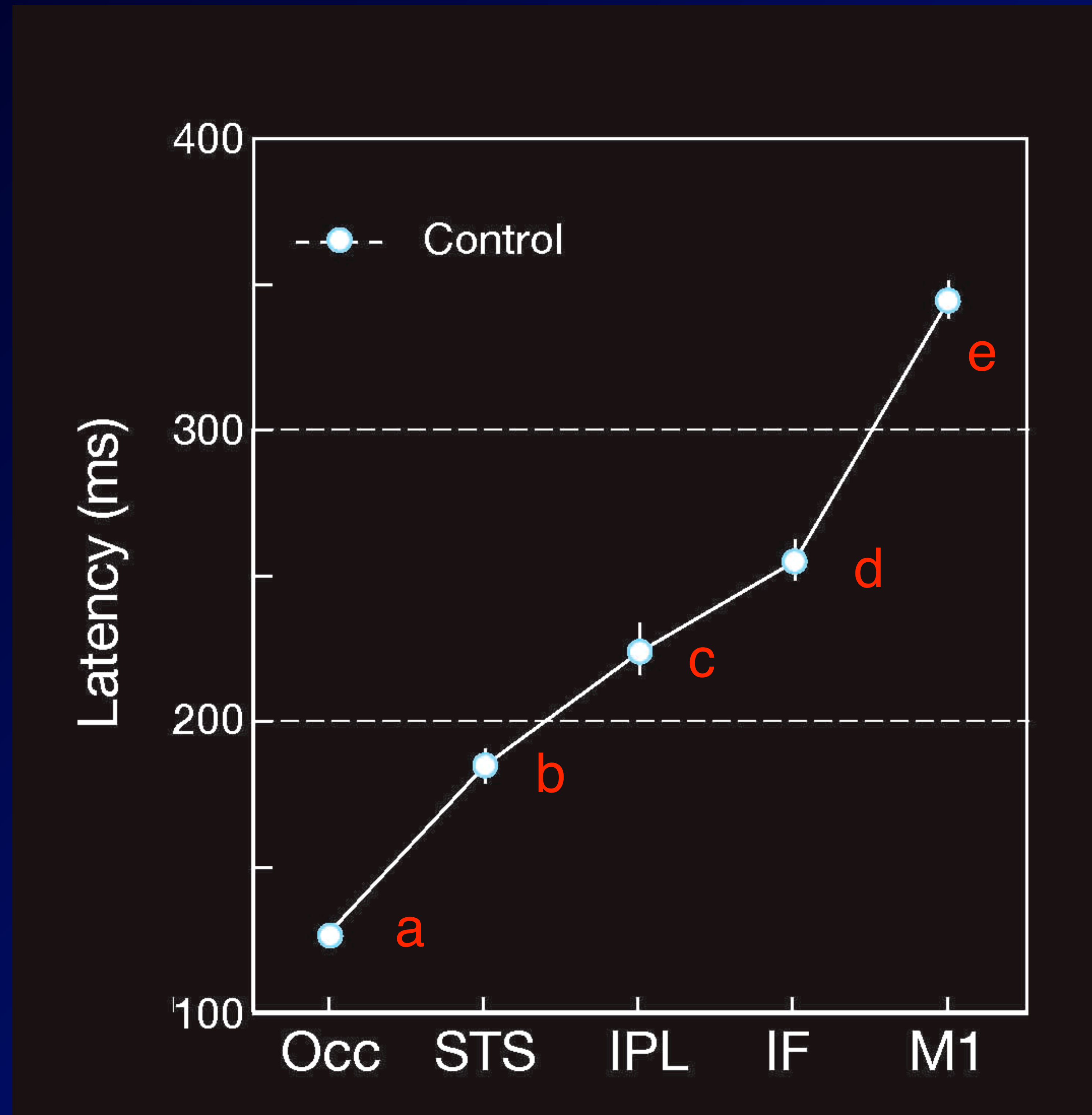
Dynamics of Brain Activation in Picture Naming



Salmelin et al., Nature 1994

Imitation of orofacial gestures





Nishitani & Hari, Neuron 2002; Nishitani et al. Ann Neurol 2004

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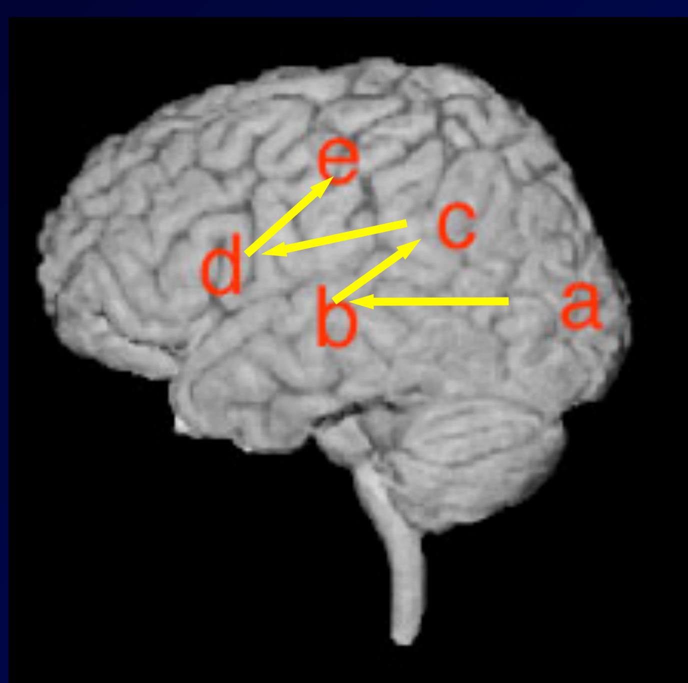

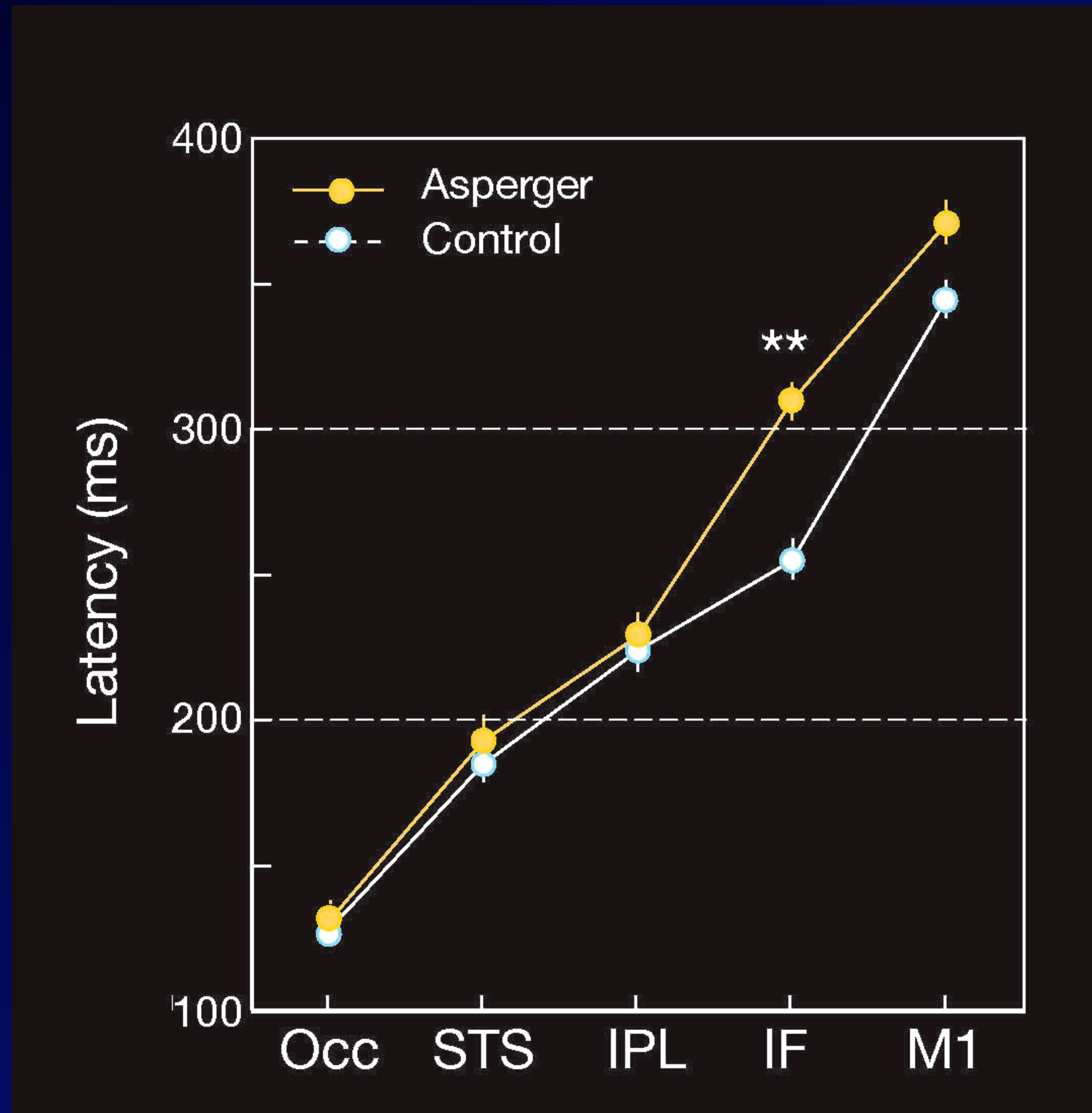

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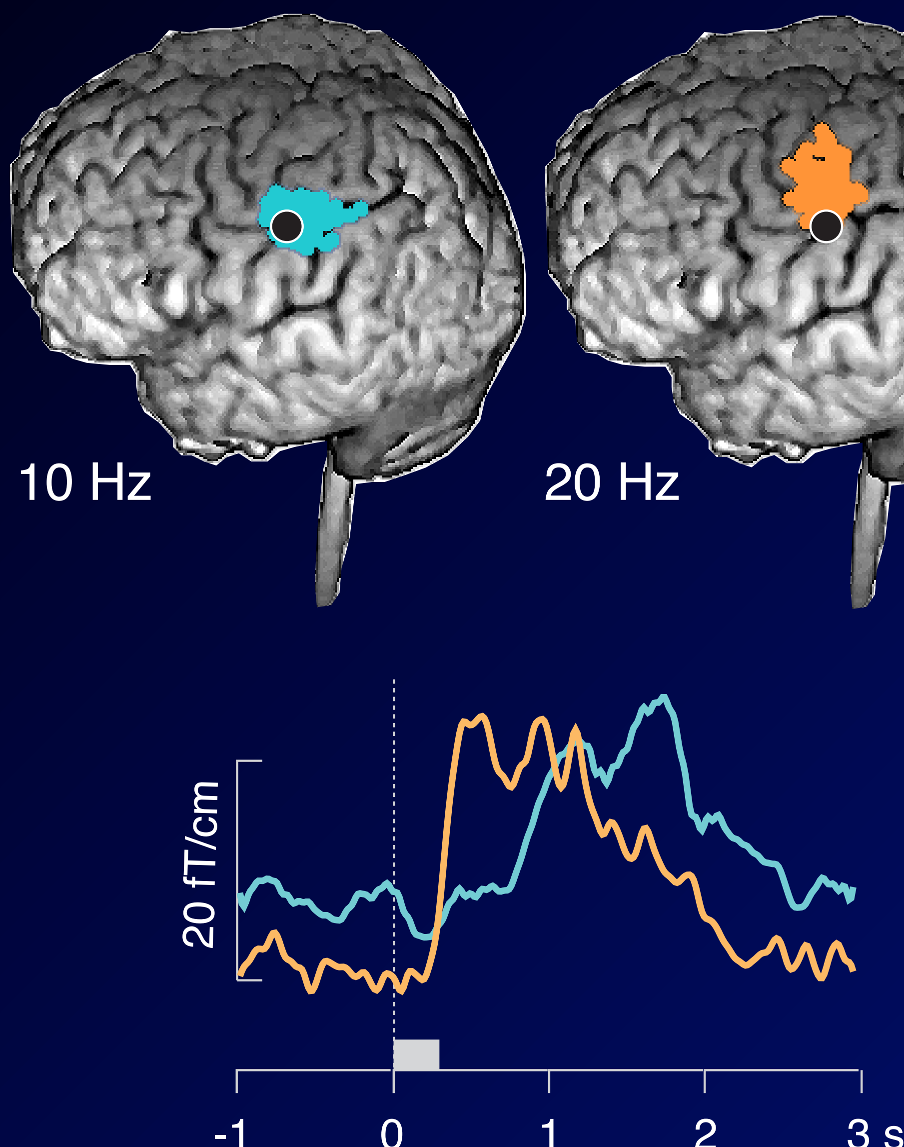
Spatiotemporal analysis of the somatomotor (m) rhythms

Modulation with finger movements



Salmelin et al., NeuroImage, 1995

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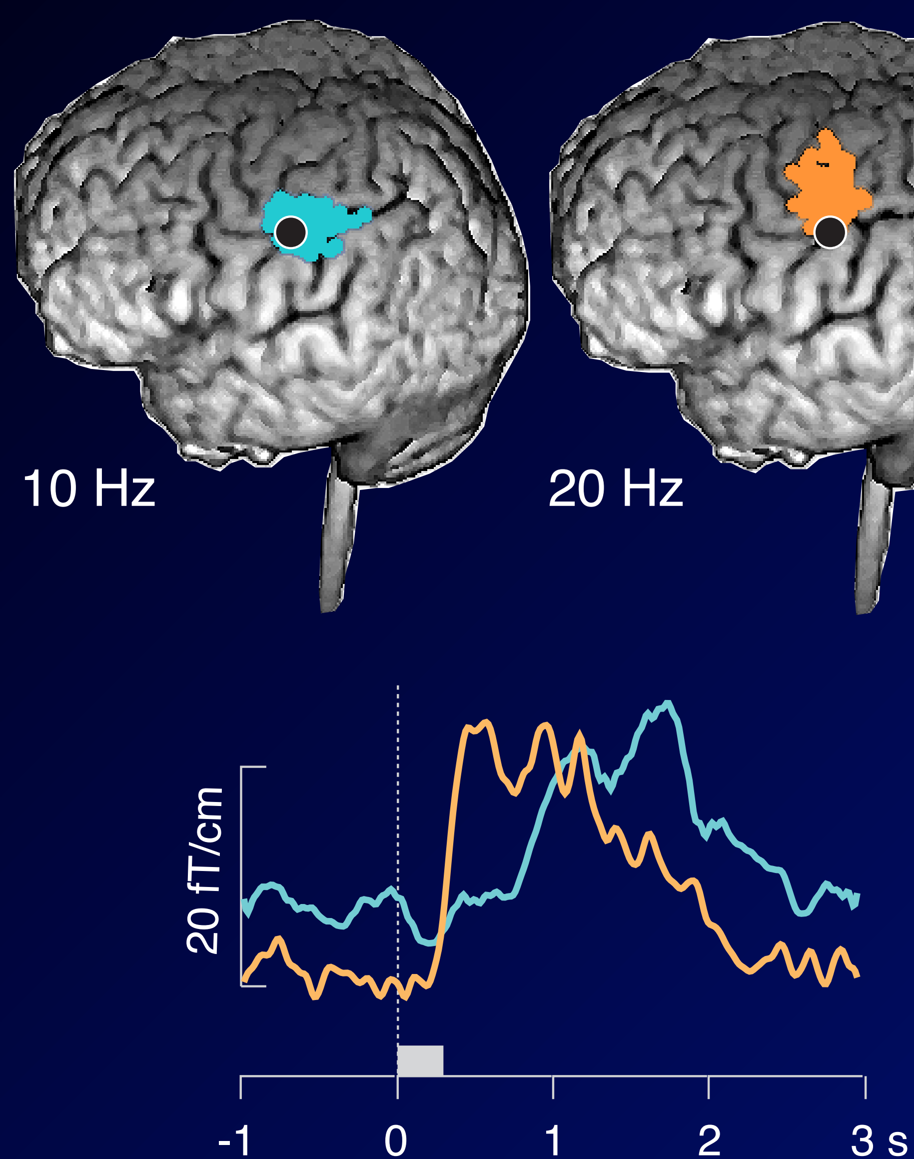
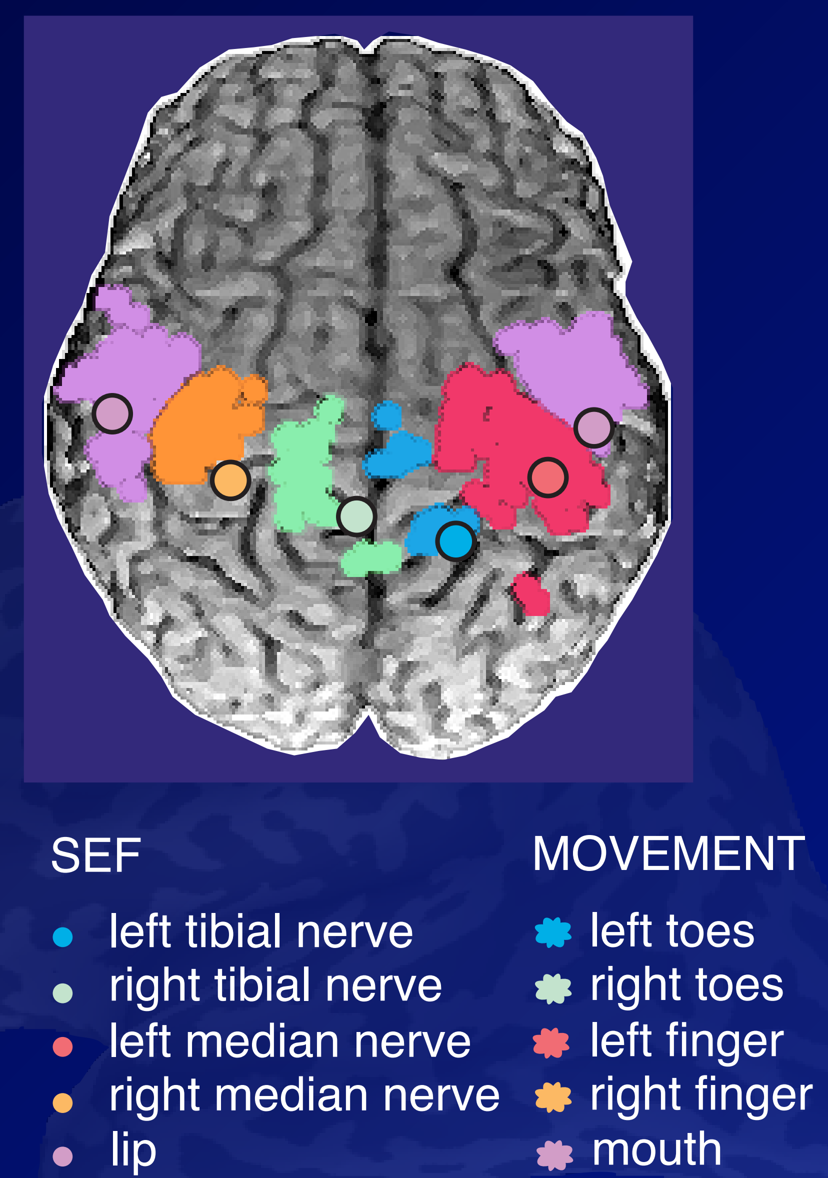


Homunculus of the 20-Hz component

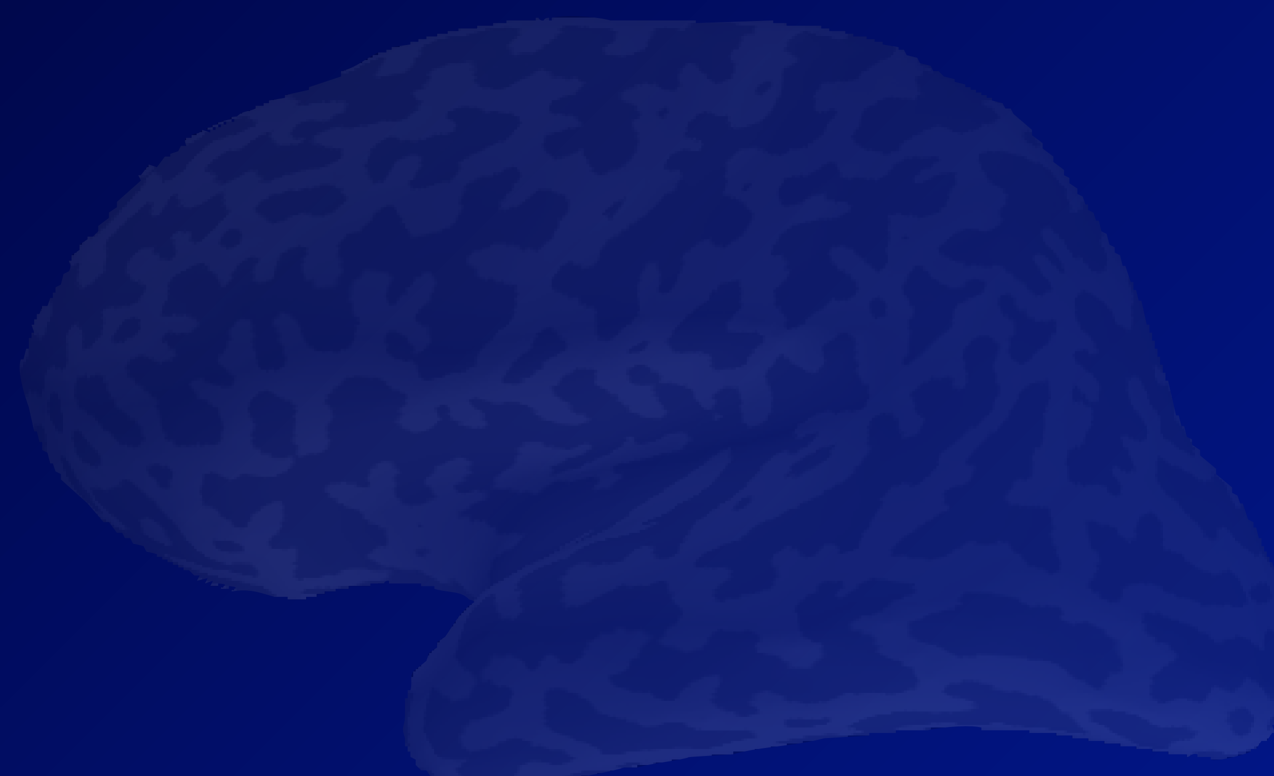


Salmelin et al., NeuroImage, 1995

Dipole models: caveats

- It is difficult to find the optimal dipole locations automatically:
  - Heuristics: Build the model one dipole at a time
  - Genetic algorithms: Find the global minimum
  - Multistart simplex: Perform a lot of fits with different initial guesses
  - MUSIC algorithms: Possible to scan one dipole at a time
- The least-squares solution might not be closest to the truth
- Sources might be too extended to be represented by a dipole

Anatomically and functionally constrained source estimates



Motivation to use distributed source models

- Account for non-focal (extended) sources
- Automatic analysis without heuristic choices often needed in multidipole models
- Incorporate anatomical and functional MRI constraints
- Lower SNR data can be processed
- If the estimate is linear the data any signal processing can be applied in the source space
- Surface or volume based group averaging can be employed

Minimum-Norm Solutions

- Grid of dipoles in a volume or on a surface
- Underdetermined: $n_{\text{sources}} \gg n_{\text{meas}}$
- Find an optimal solution among those fitting the data

$$\hat{\mathrm{q}} = \mathrm{argmin}_{\mathbf{q}} \left(||\mathbf{y} - \mathbf{G}\mathbf{q}||^2_{\mathbf{C}} + ||\mathbf{q}||^p_{\mathbf{R}} \right)$$

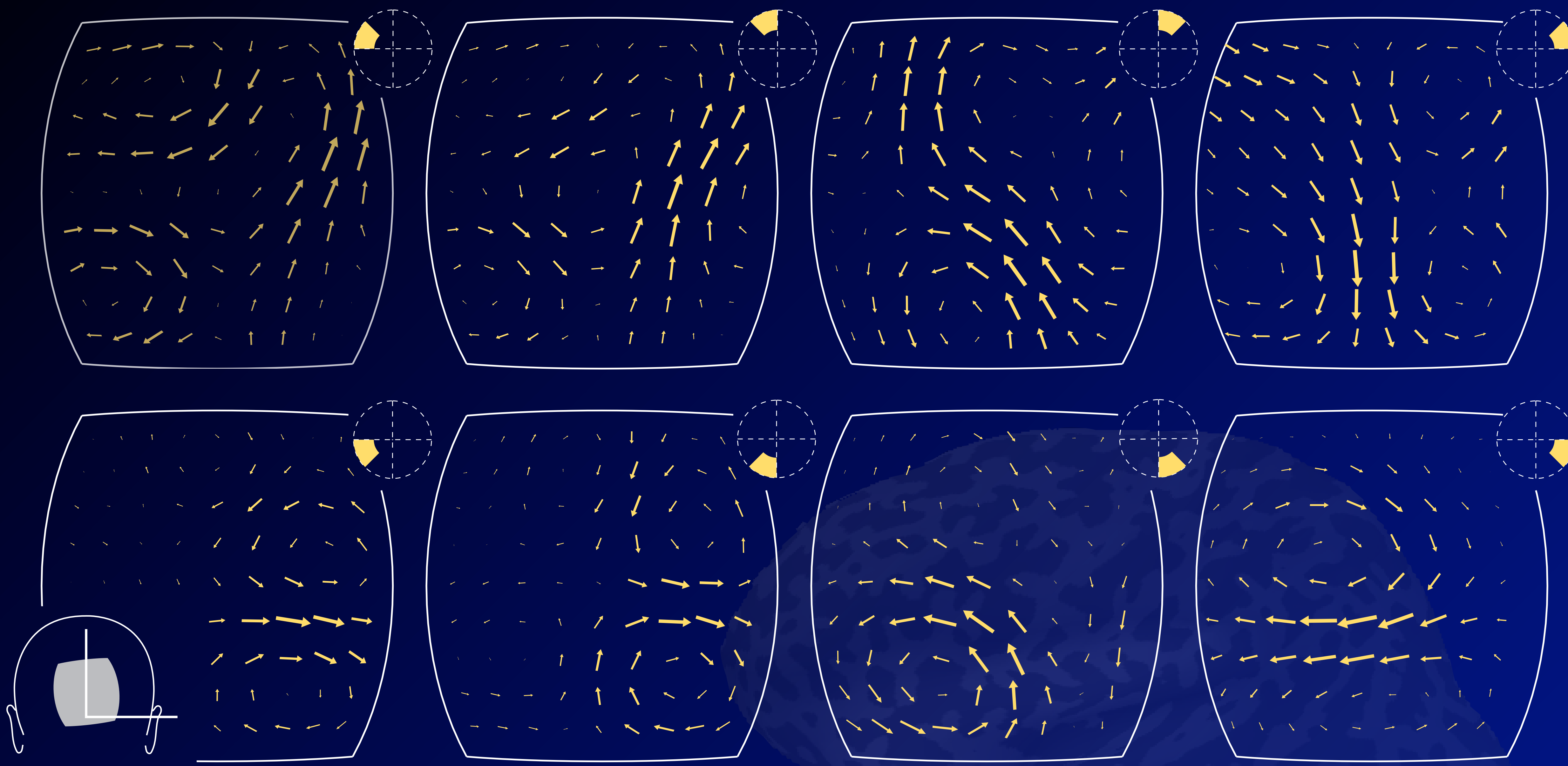
Examples:

– Minimum-norm estimates (MNE): $p = 2$

– LORETA: $p = 2$, R = Laplacian operator

– Minimum-current estimates (MCE): $p = 1$

Retinotopic mapping with MNE



MEG array

Peripheral checkerboard octant stimuli, t = 80 ms

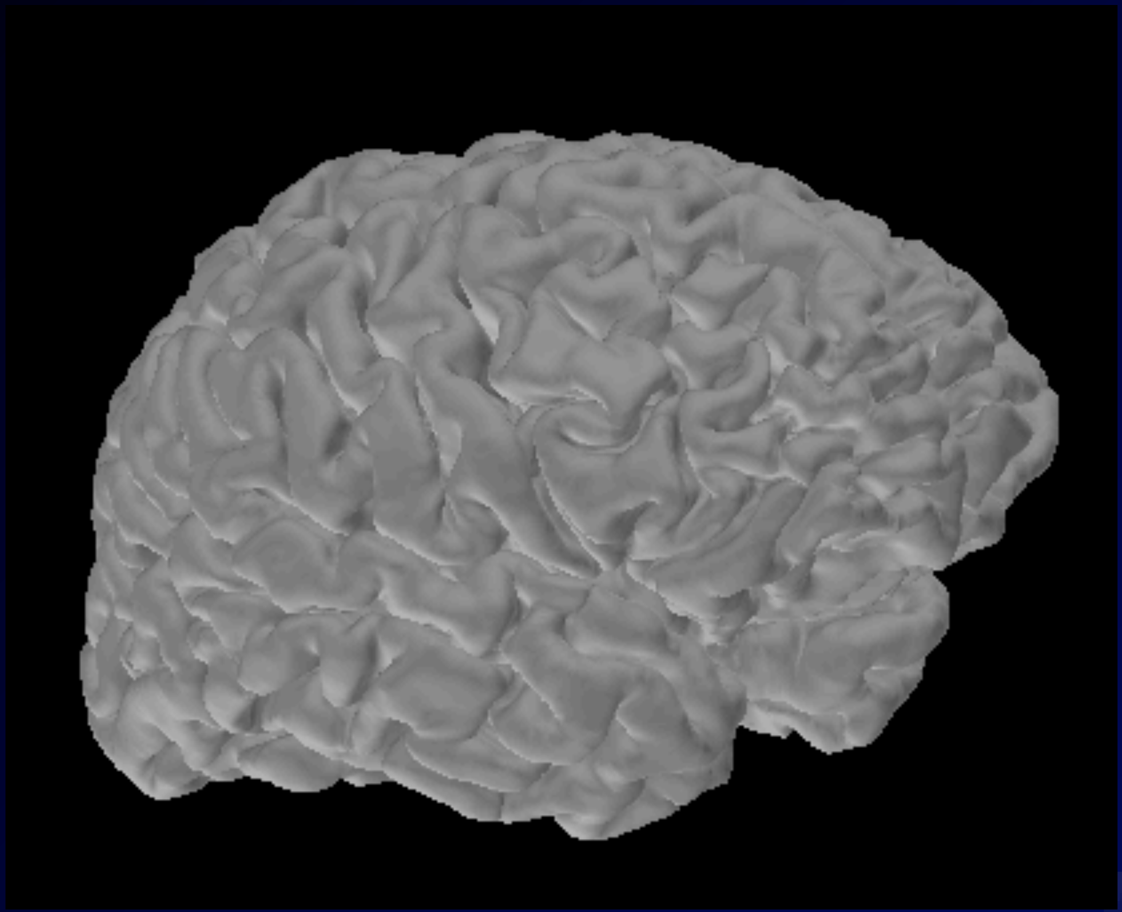
Ahlfors *et al.* 1992

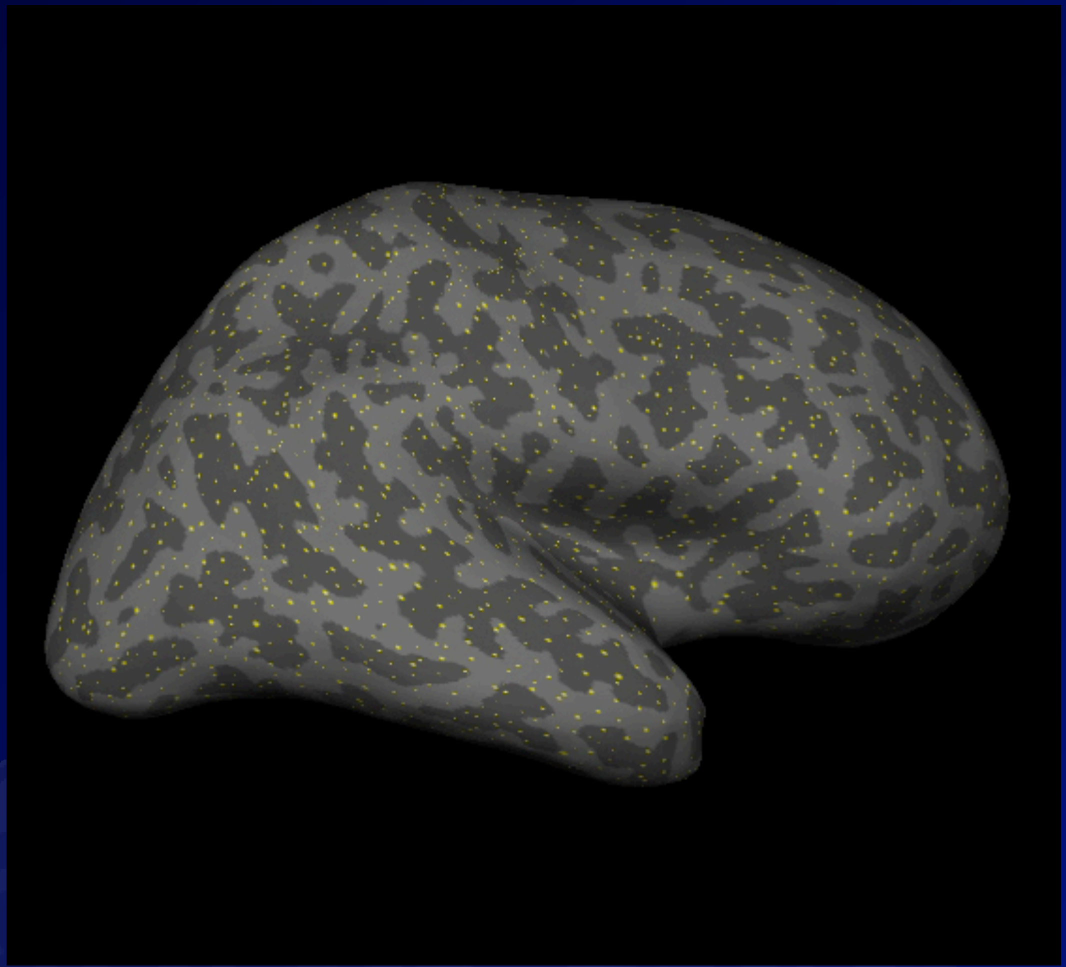
Modern MNE

- Source locations (and orientations) constrained to the cortical mantle
- Forward solution with BEM
- Full noise-covariance matrix estimates computed from raw data
- Display on an inflated cortex to reveal the sulci
- Compute statistics
- Combined MEG and EEG solutions
- fMRI-guided solutions

Dale *et al.* 2000

Cortical Source Location Constraints

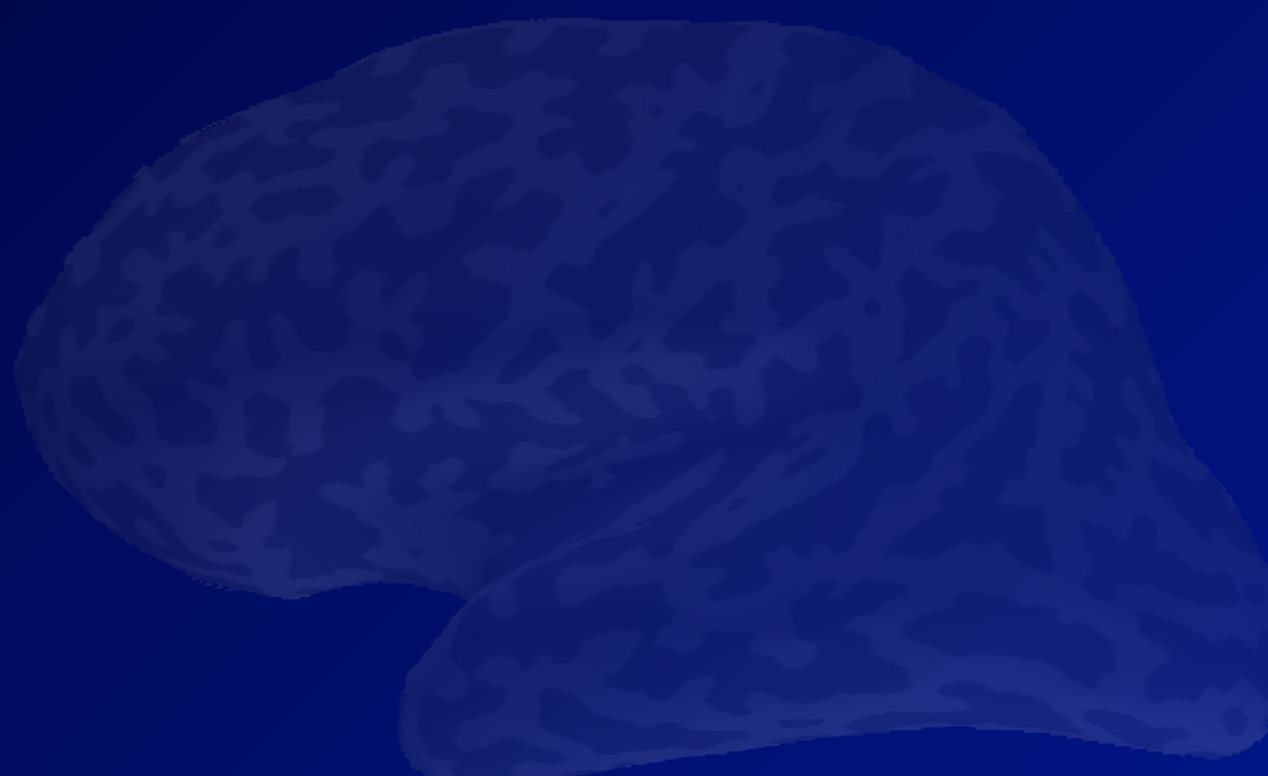




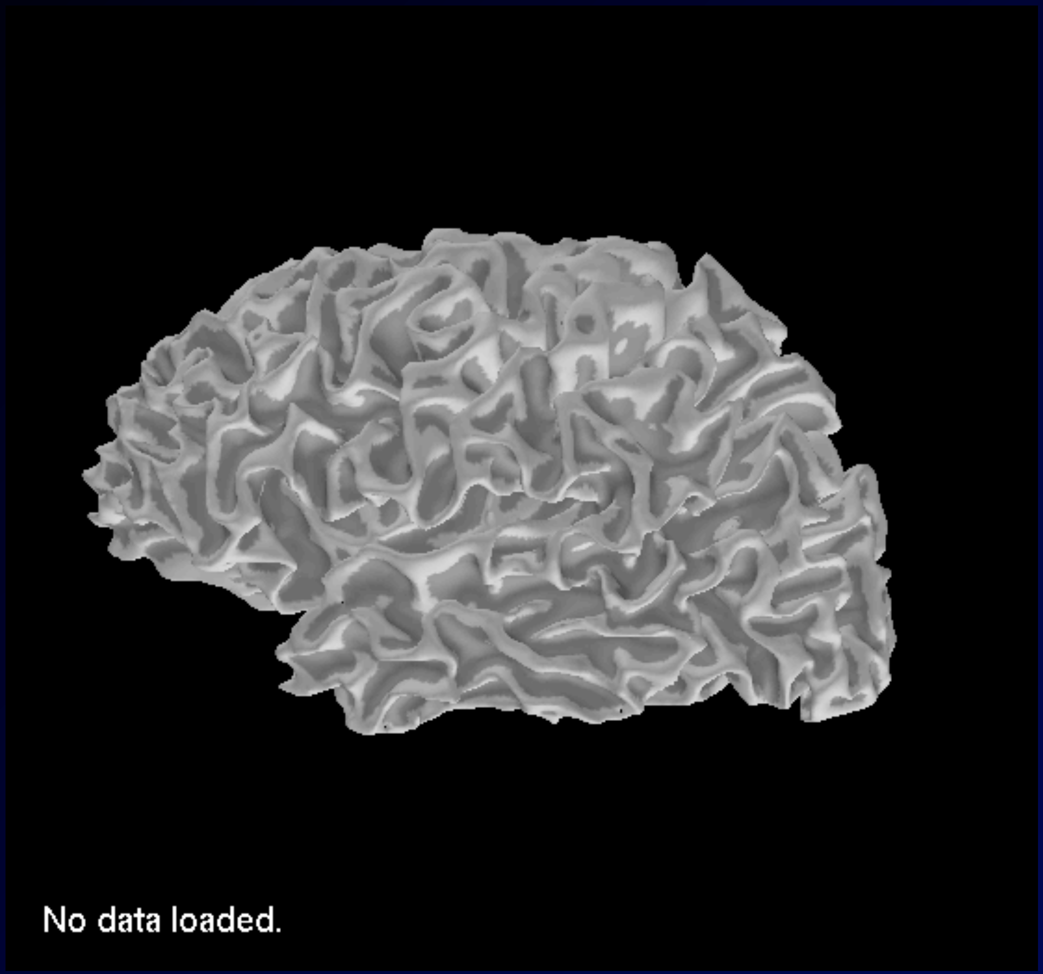
Tessellation of the cortex: Source location and orientation information

For source estimation, the surface is typically decimated, resulting in 6000 - 10000 source locations

Inflated Cortex



Inflated Cortex



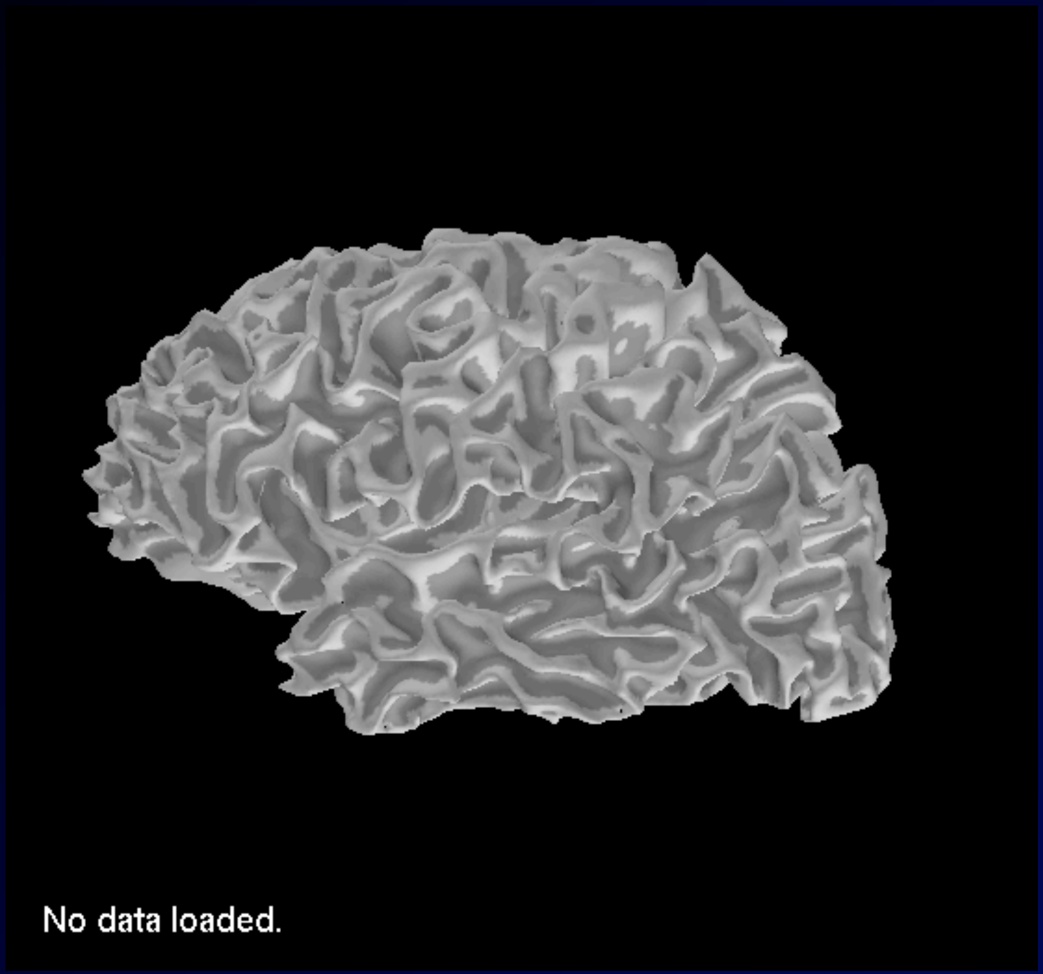
Topologically correct tessellation can be inflated

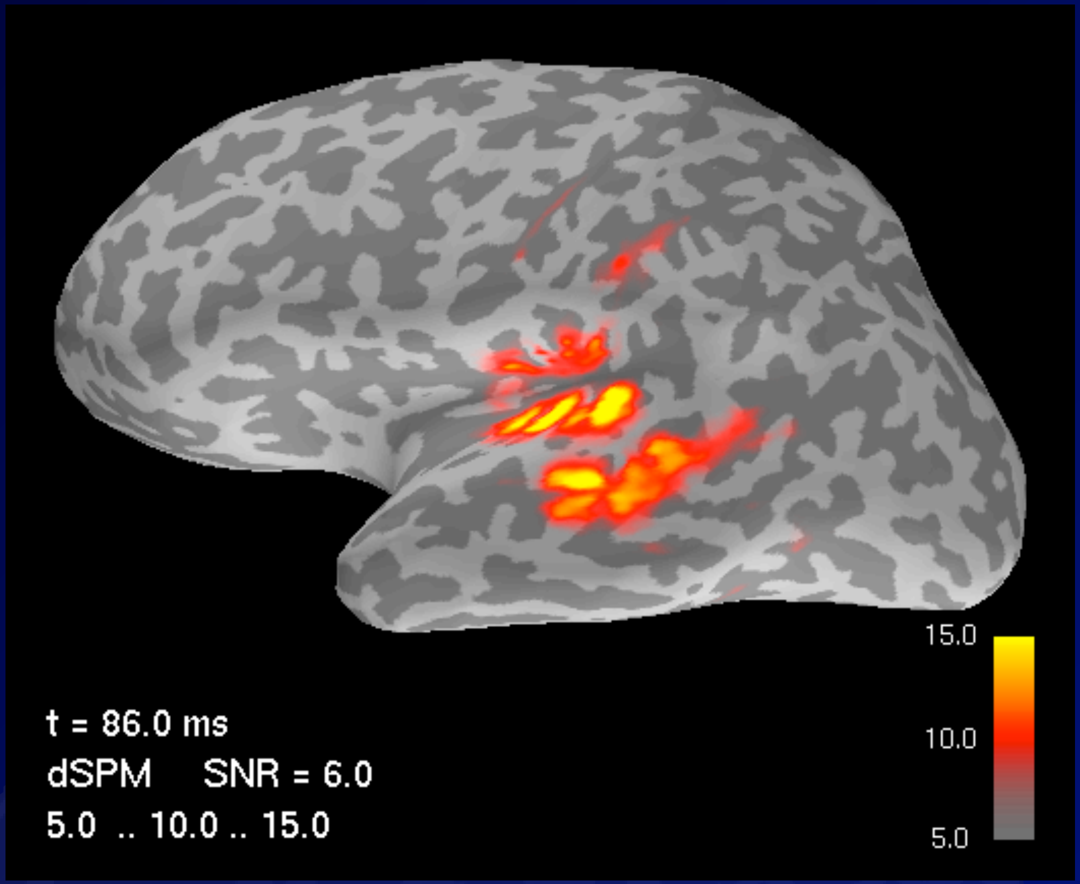
Inflated Cortex

Topologically correct tessellation can be inflated

Dale, Fischl, Sereno *et al.*

Inflated Cortex



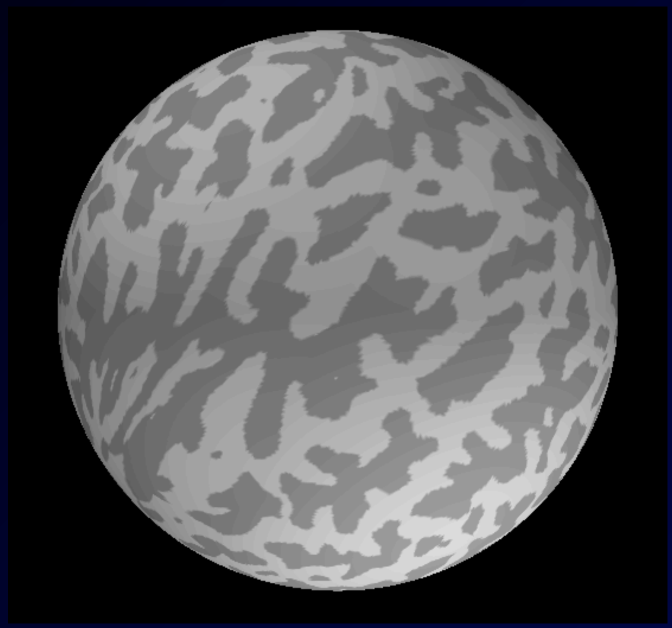


Topologically correct tessellation can be inflated

Dale, Fischl, Sereno *et al.*

Inflation to a Sphere and Registration

Individual



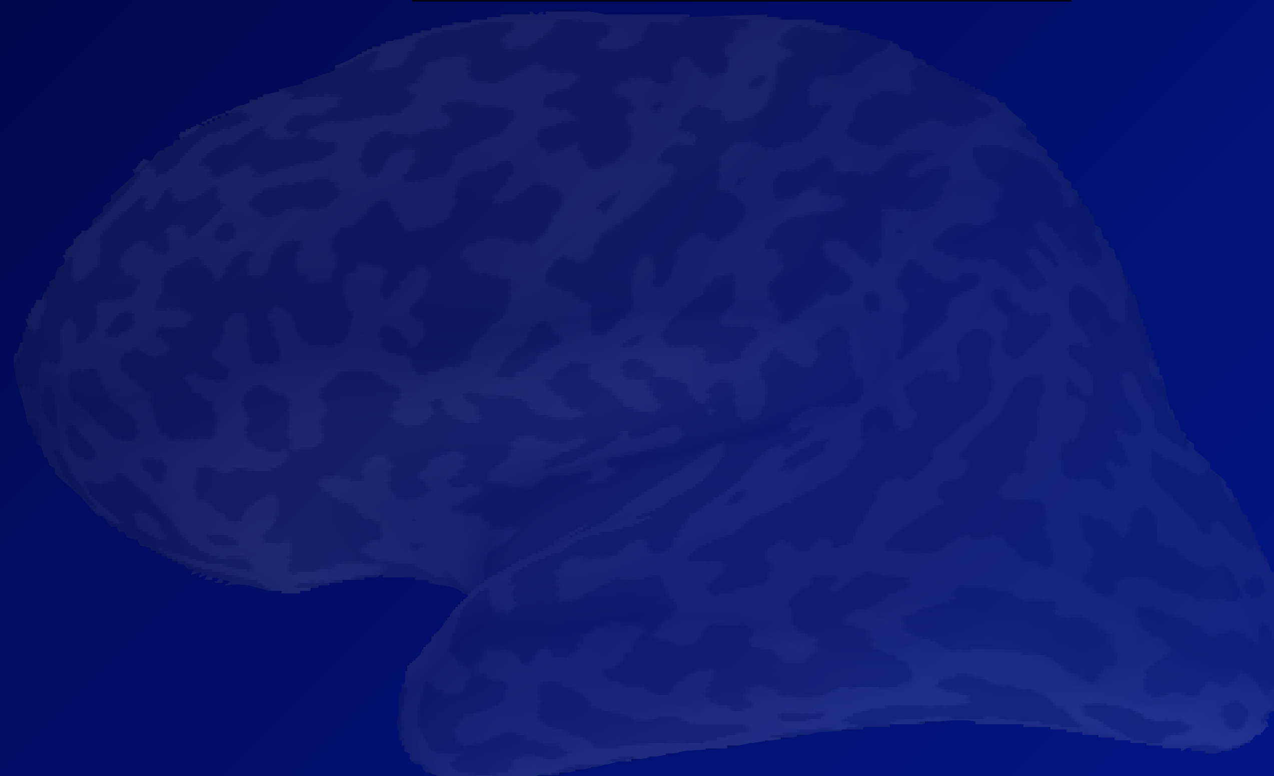
Inflation to a Sphere and Registration

Individual

Align sulcal patterns

to the average brain

Aligned with average brain



Inflation to a Sphere and Registration

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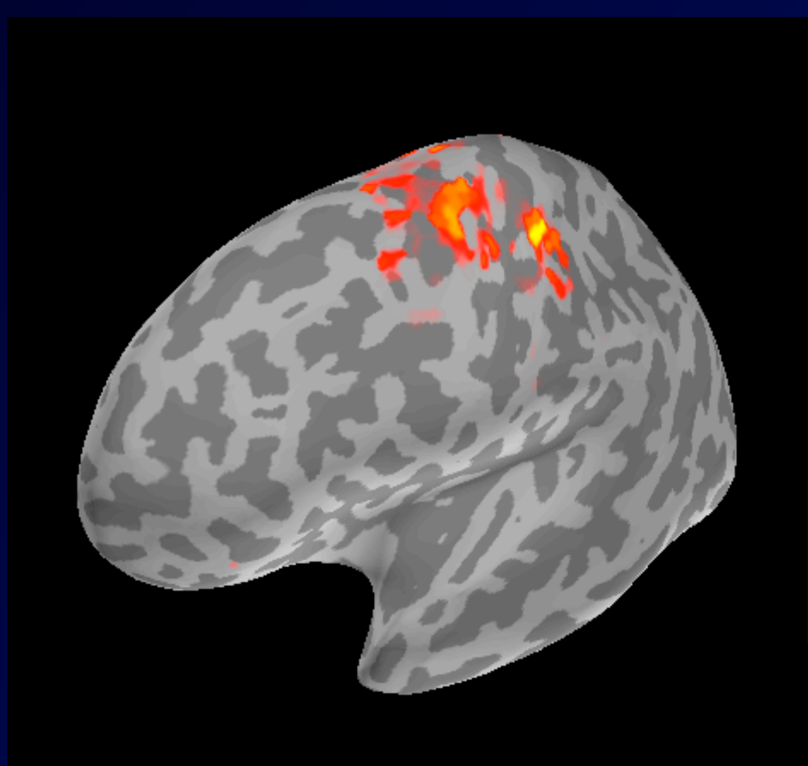
MEG activity estimate



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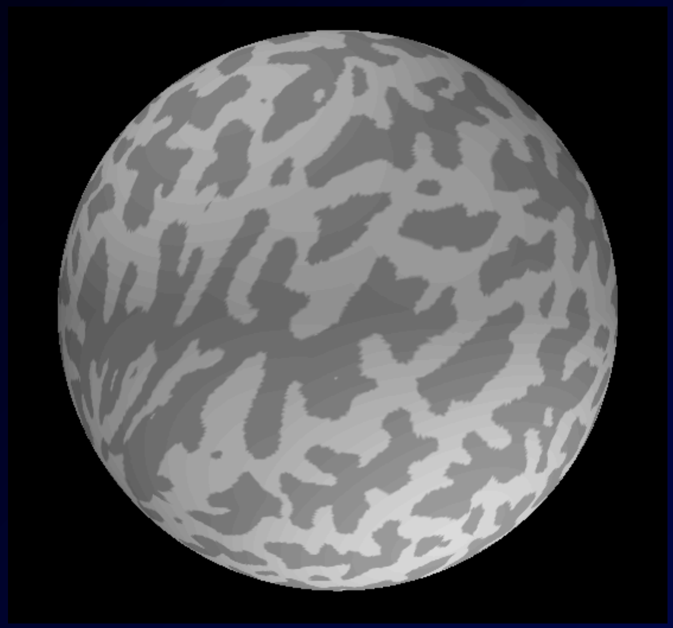

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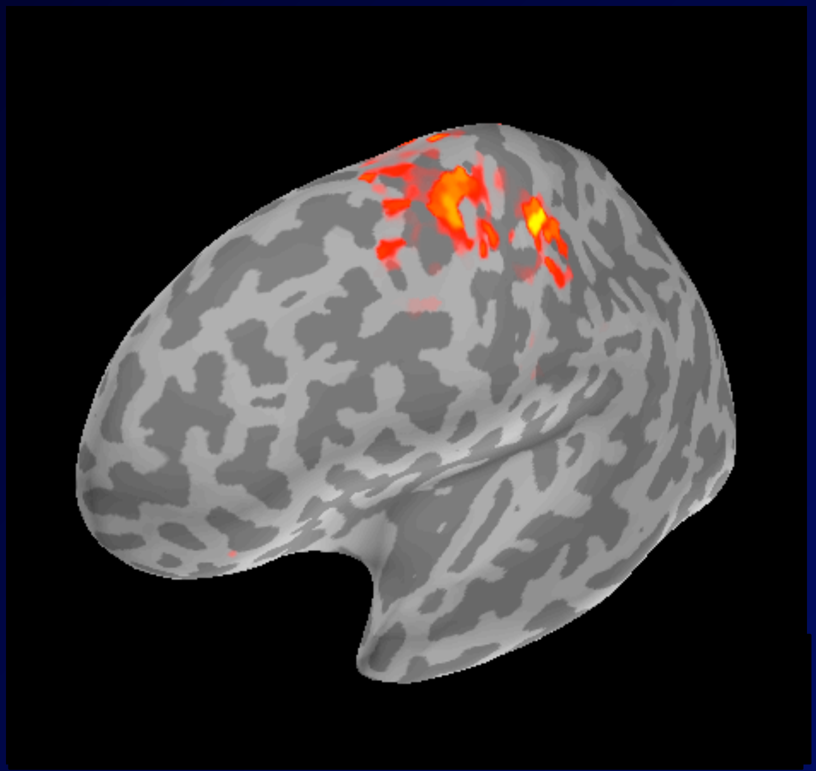
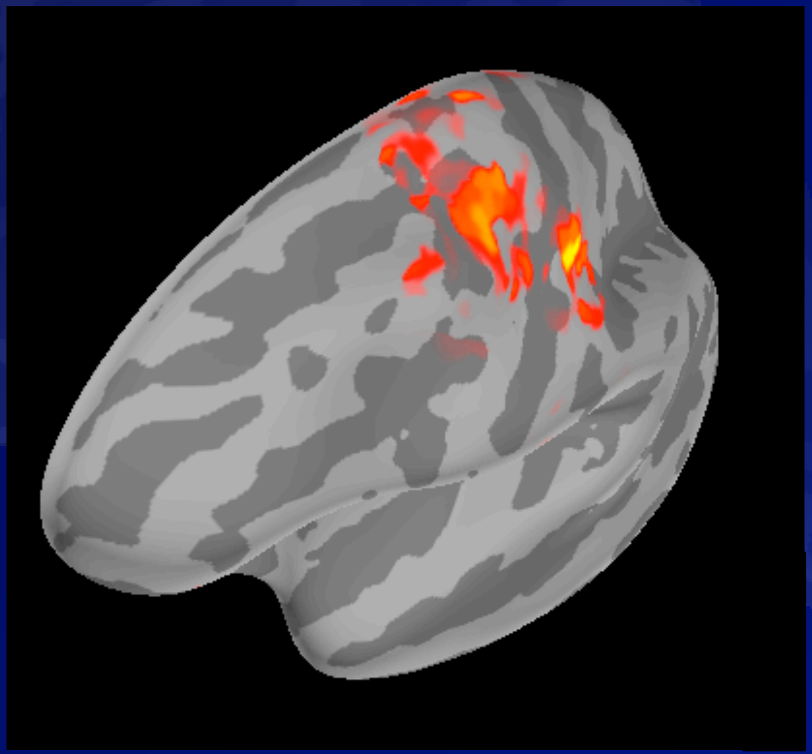
MEG activity estimate



Morph

Mapped to the average brain

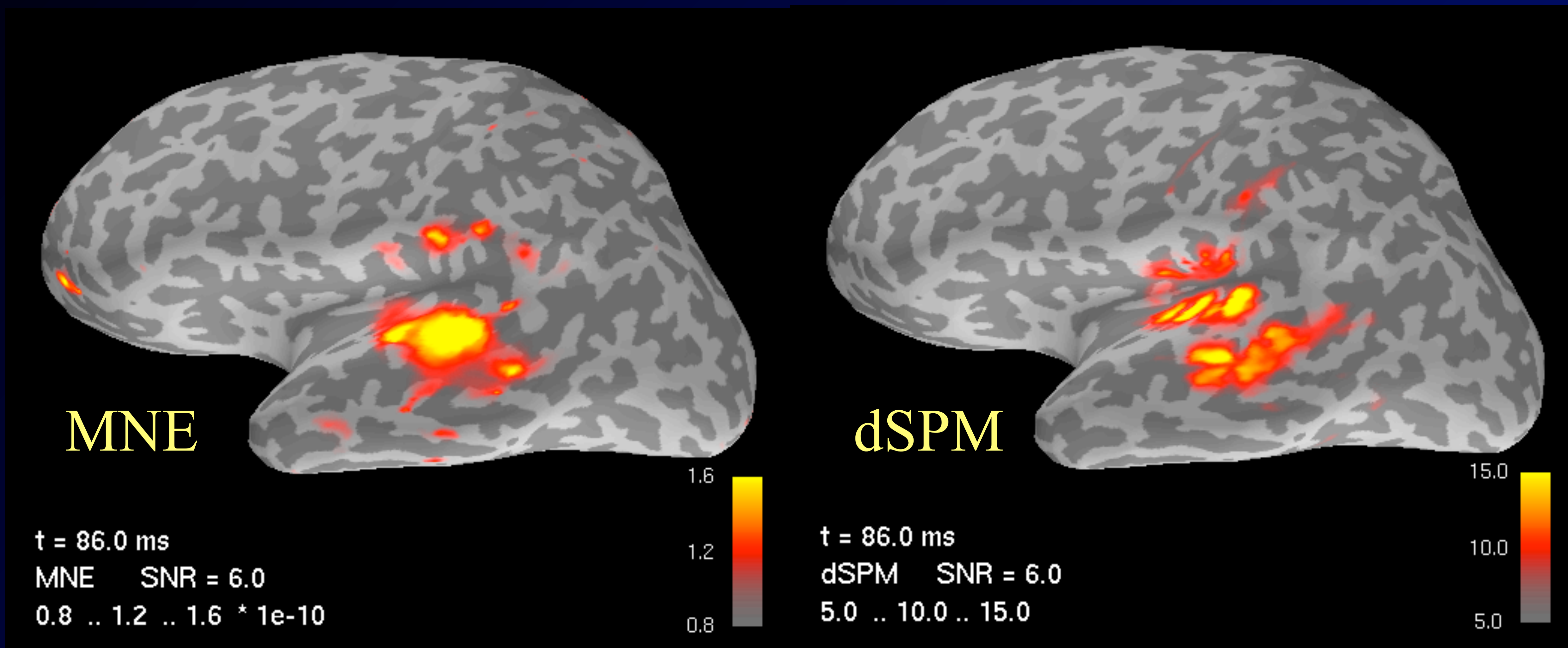


Noise normalization

- Convert the current values into a test statistic
  - dSPM (Dale *et al.*)
  - sLORETA (Pascual-Marqui *et al.*)
- Divide the current with its standard deviation
- Analyze MEG/EEG data like fMRI or PET

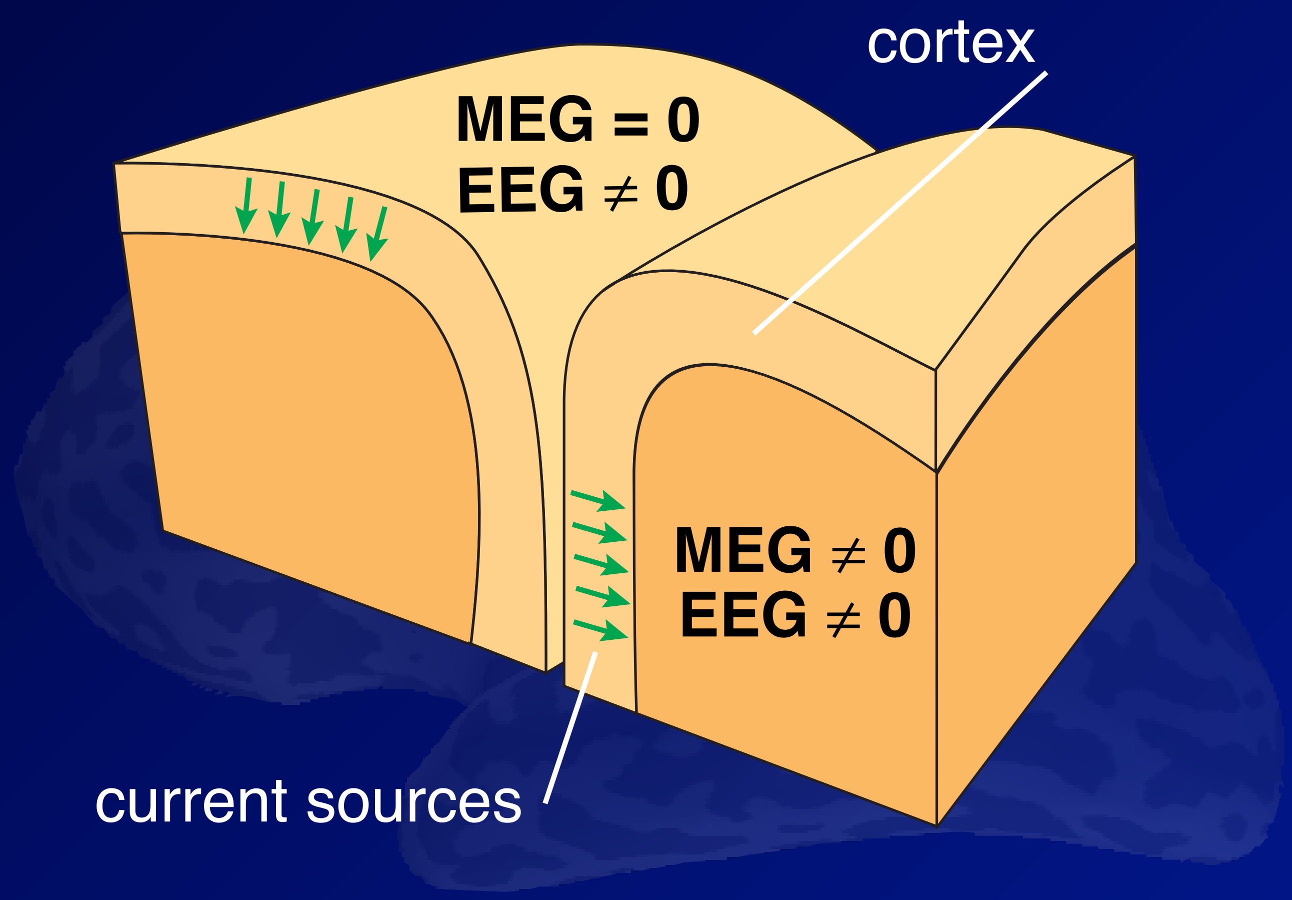
Dale *et al.* 2000

MNE and dSPM



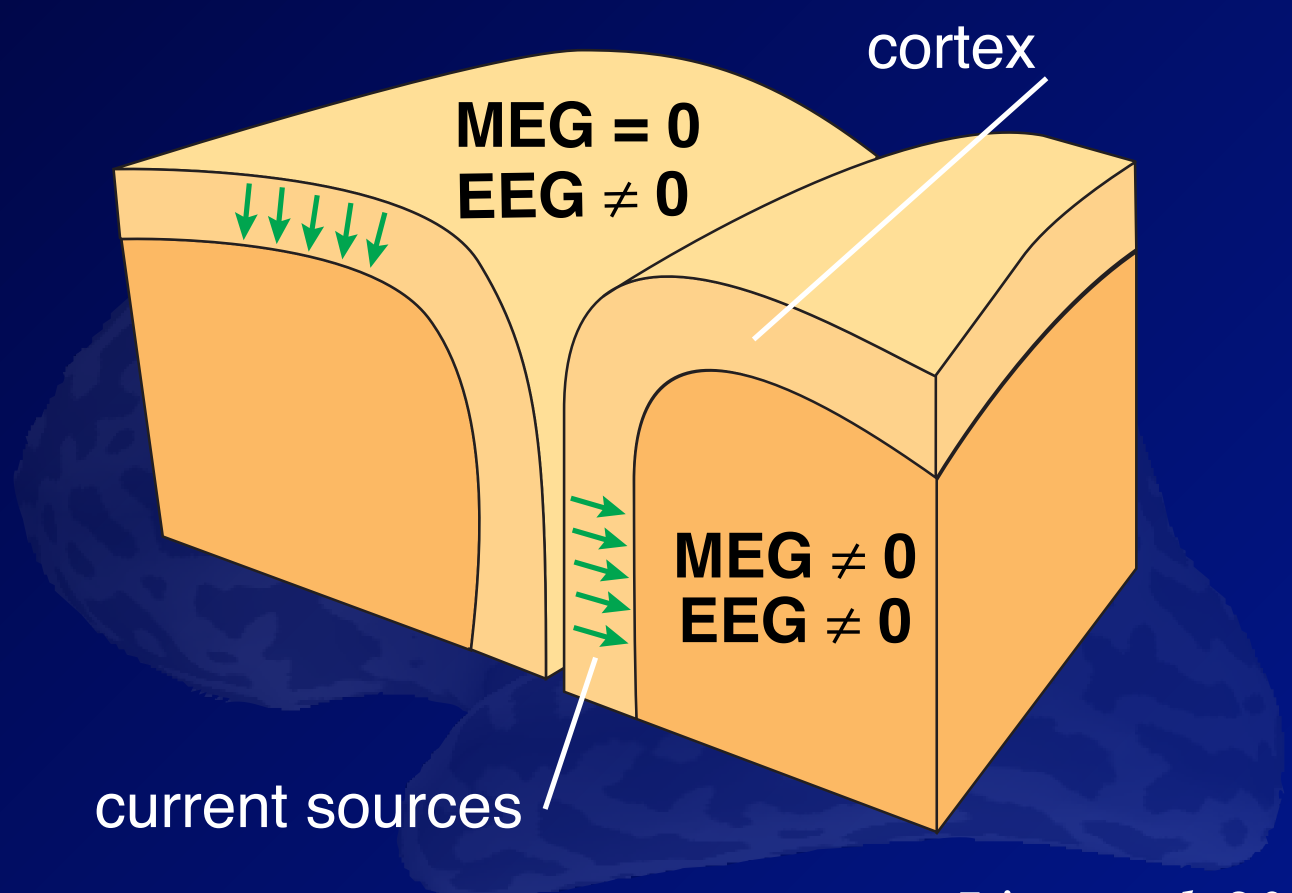
- Auditory MEG data
- Source locations constrained to the cortex
- No orientation constraint
- dSPM and sLORETA produce very similar results with real data

Loose orientation constraint



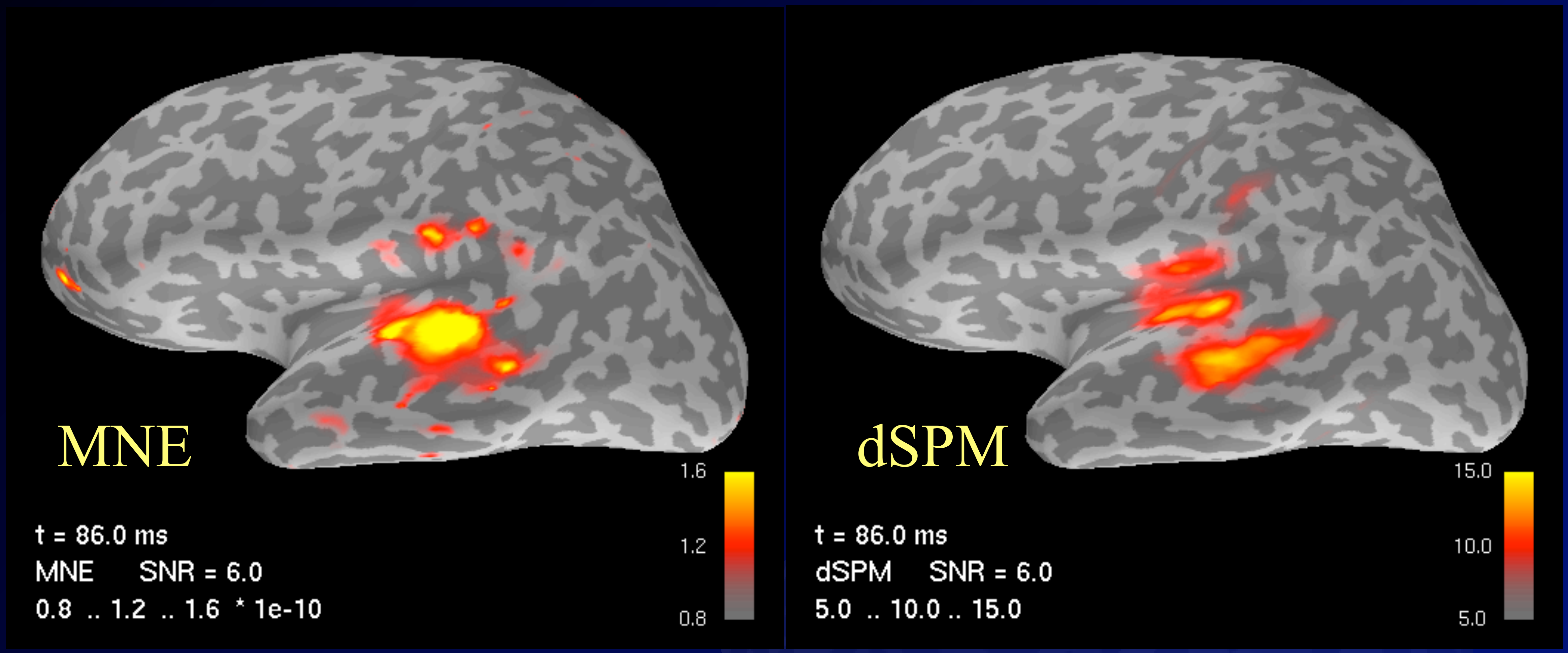
Loose orientation constraint

- Penalize current components tangential to the cortex
- Takes the finite spacing between elementary sources into account



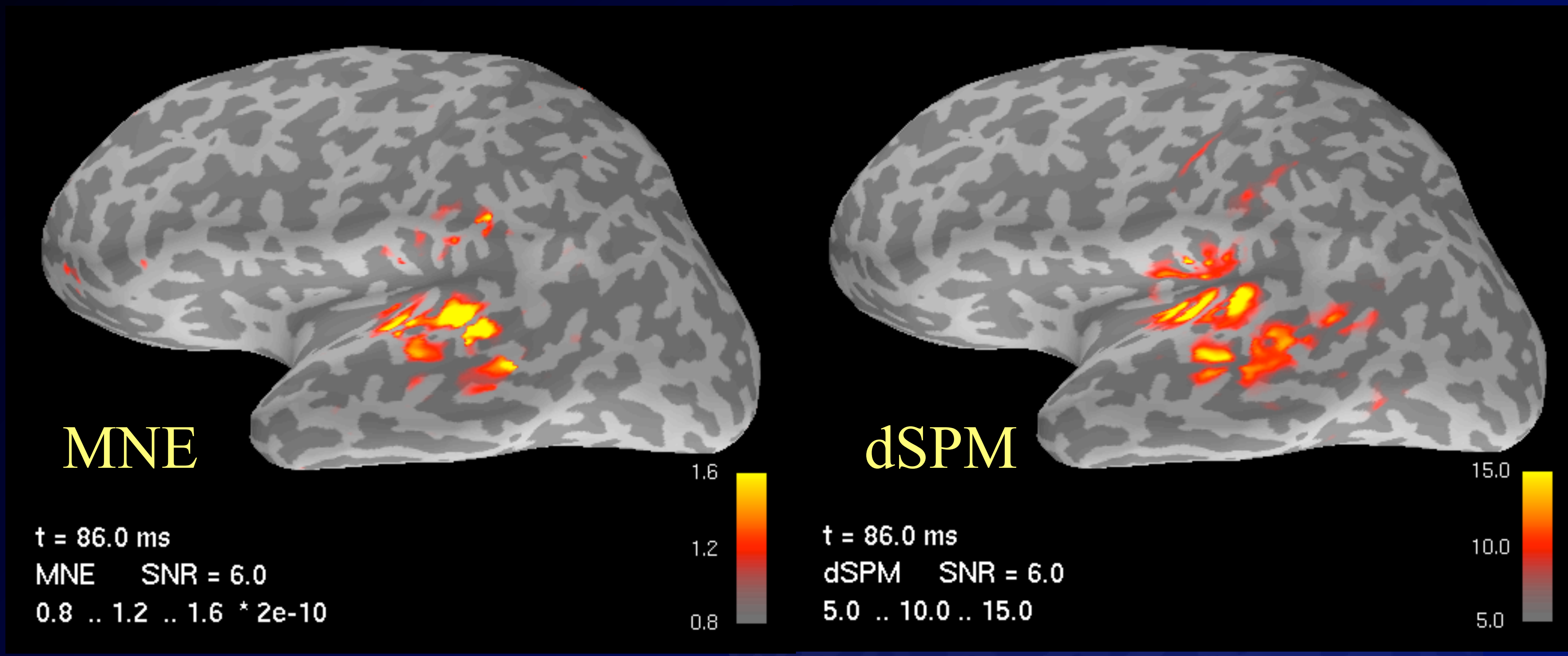
Lin *et al.* 2006

Effect of the orientation constraint



- Auditory responses to short tones
- Depth-weighted MNE and dSPM
- Without and with loose orientation constraint
- The orientation constraint rules out infeasible sources

Effect of the orientation constraint



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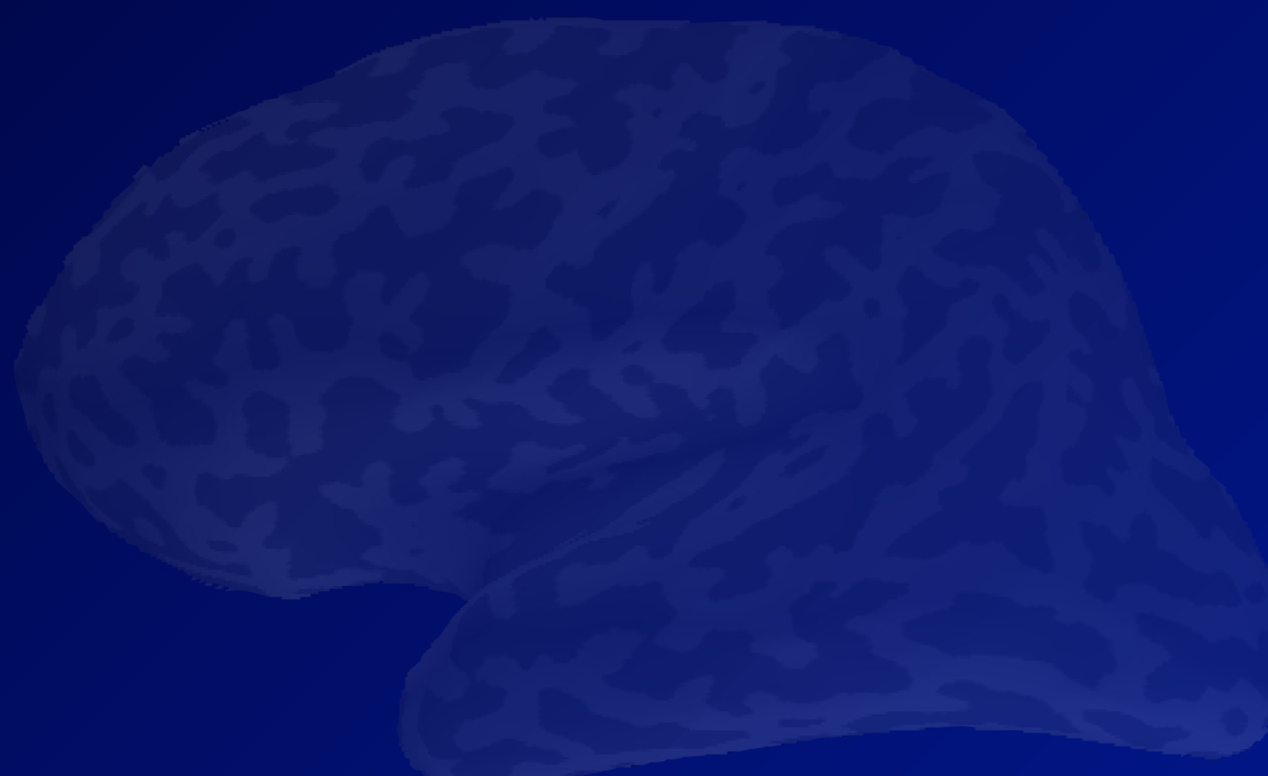
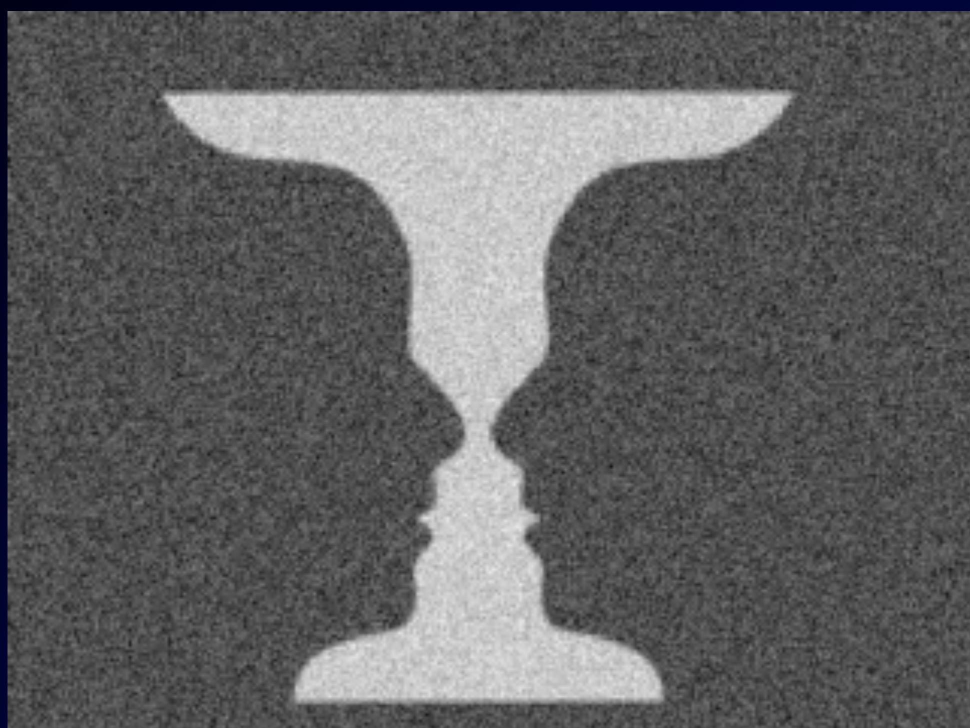
Visual percepts of an ambiguous scene



Parkkonen *et al.*, PNAS, 2008

Visual percepts of an ambiguous scene



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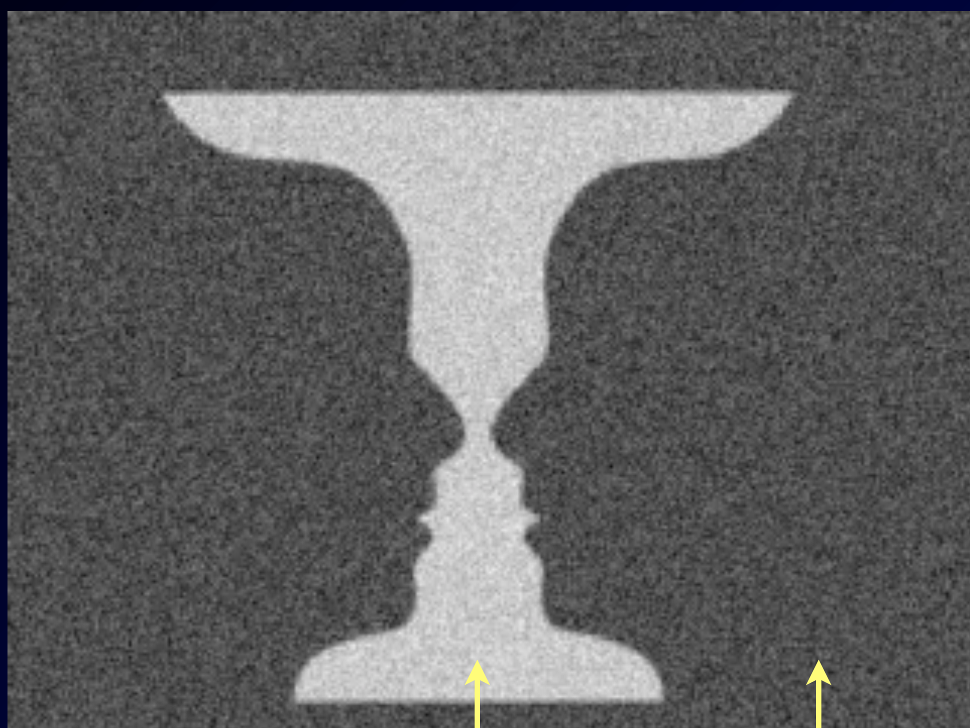
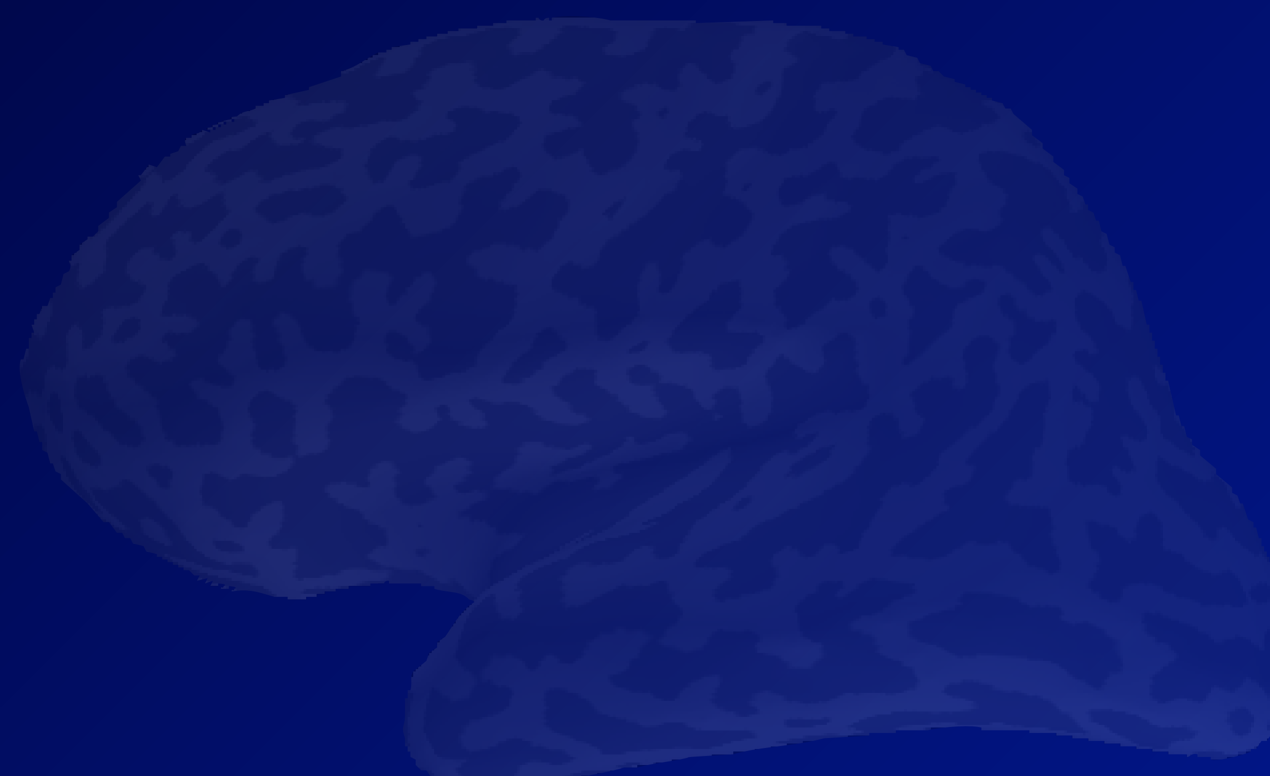


Noise: 12 Hz 15 Hz



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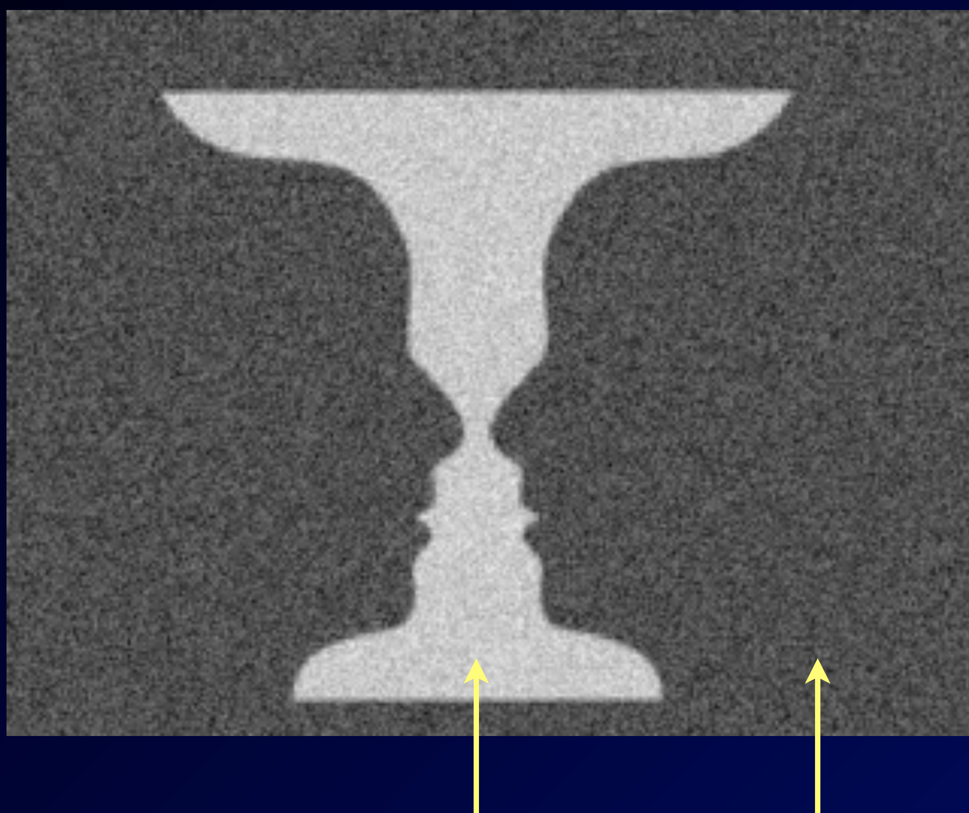

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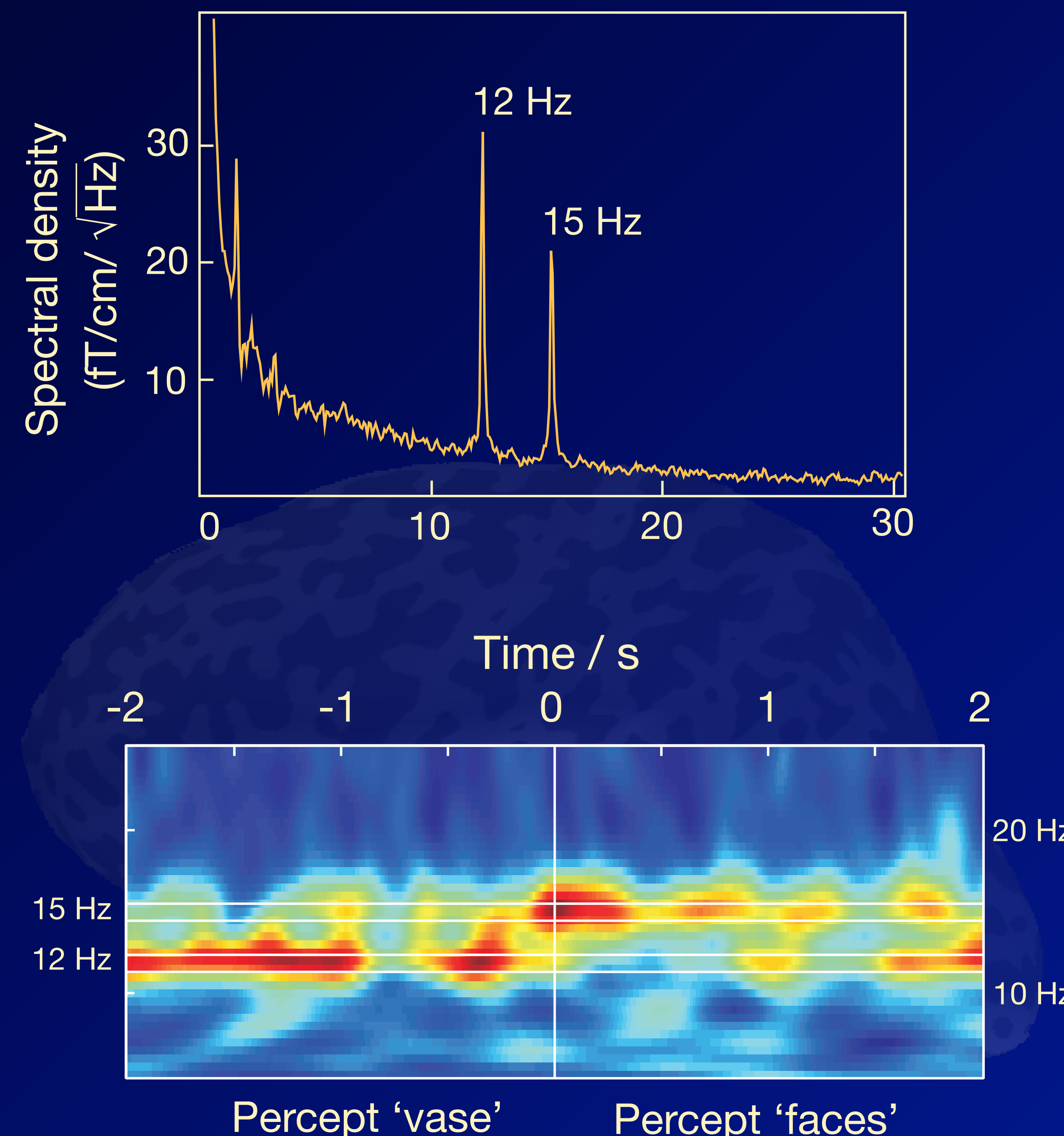
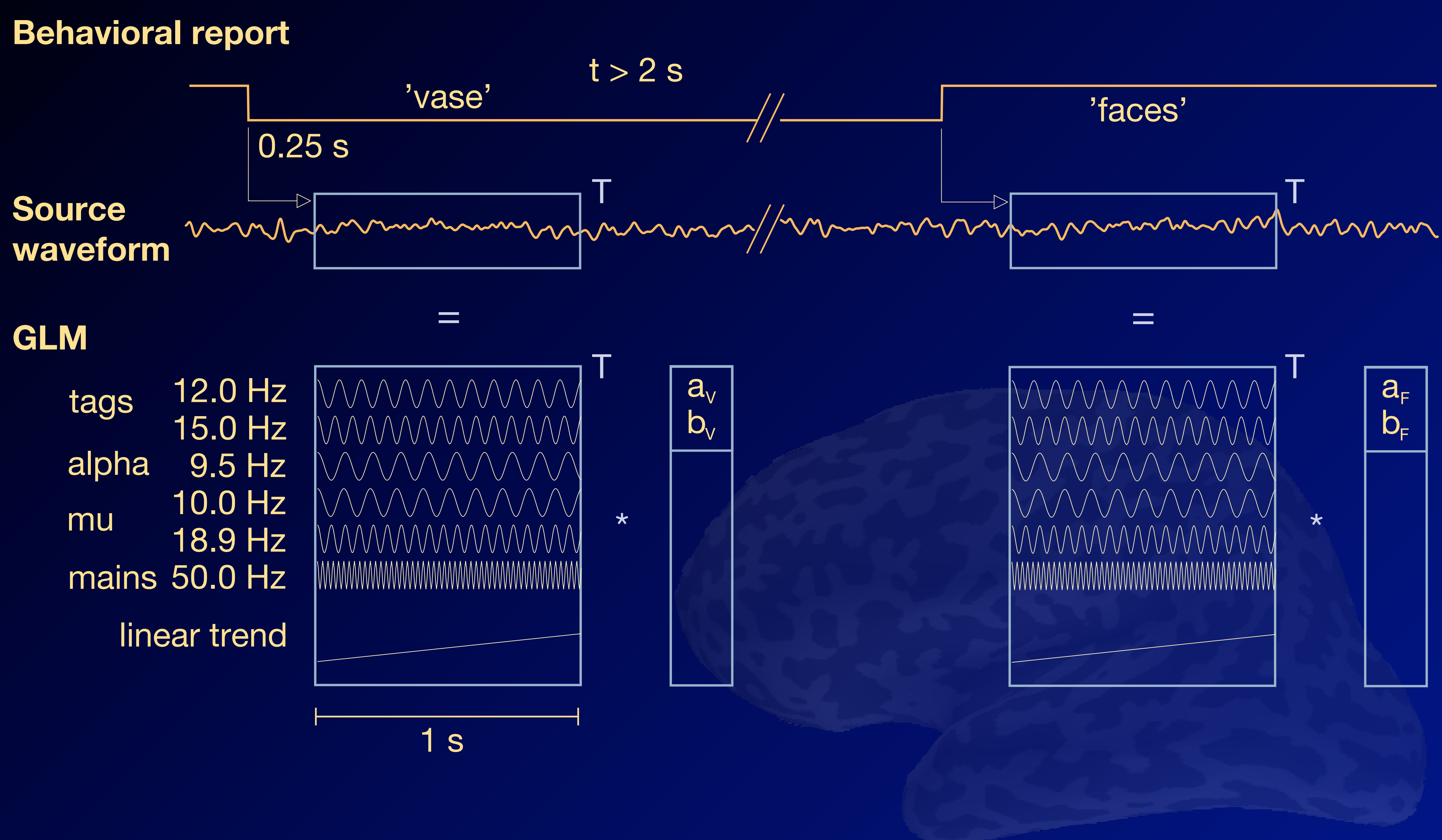
MEG signals at an occipital sensor



Parkkonen *et al.*, PNAS, 2008

Extract tag-related activity: MNE + GLM

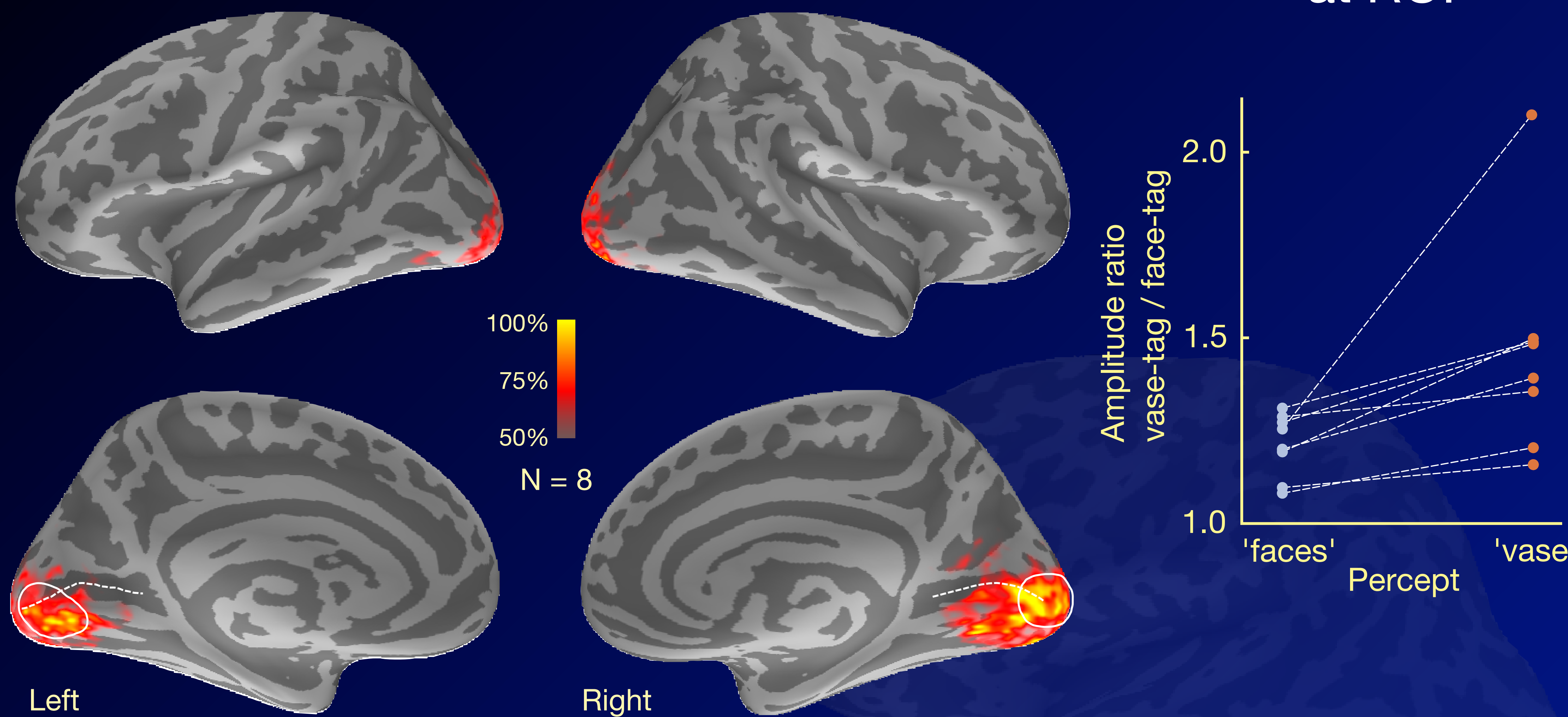


Parkkonen *et al.*, PNAS, 2008

Group analysis

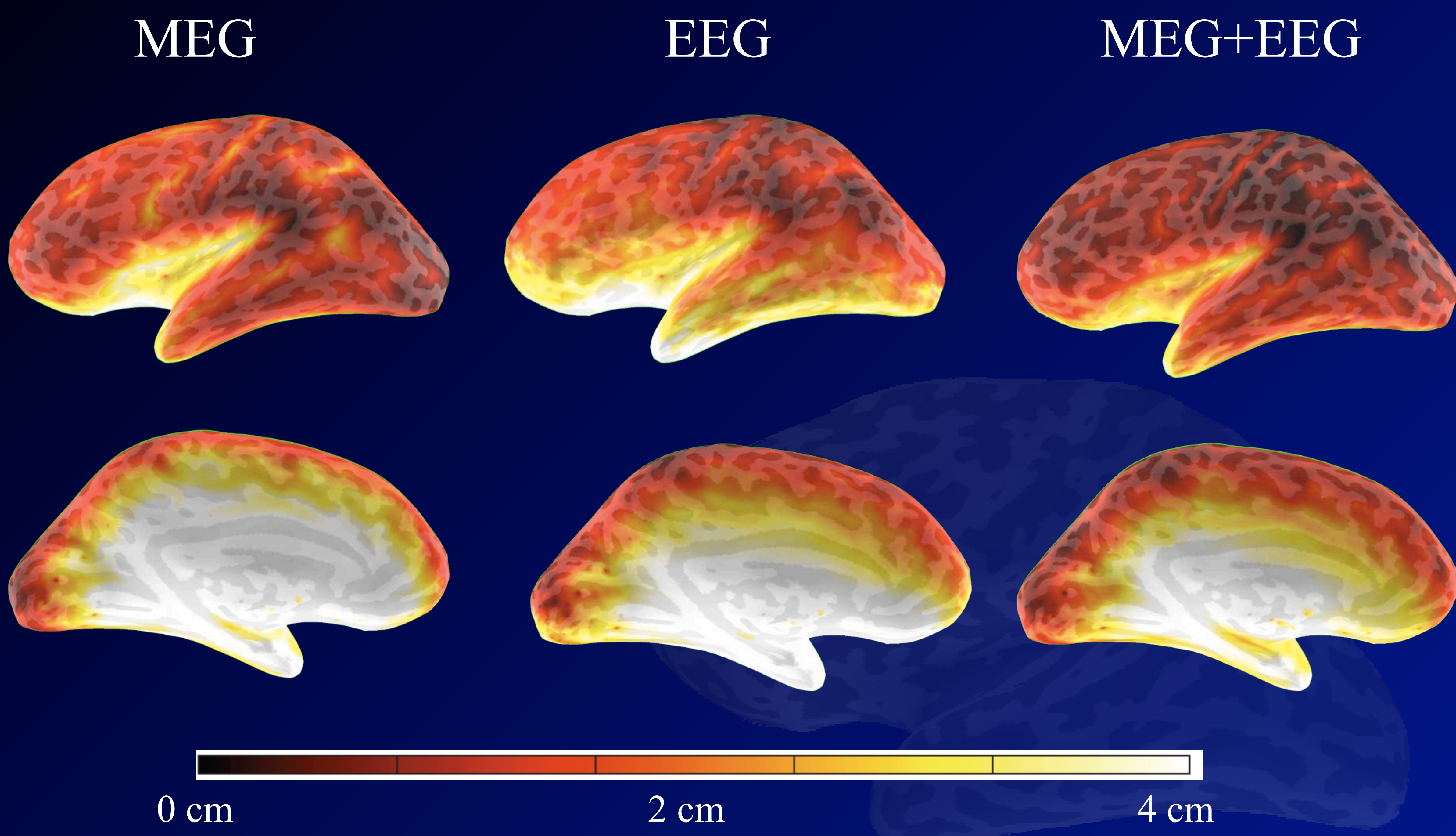
Significant activity in either tag frequency

Amplitude ratio at ROI



Parkkonen *et al.*, PNAS, 2008

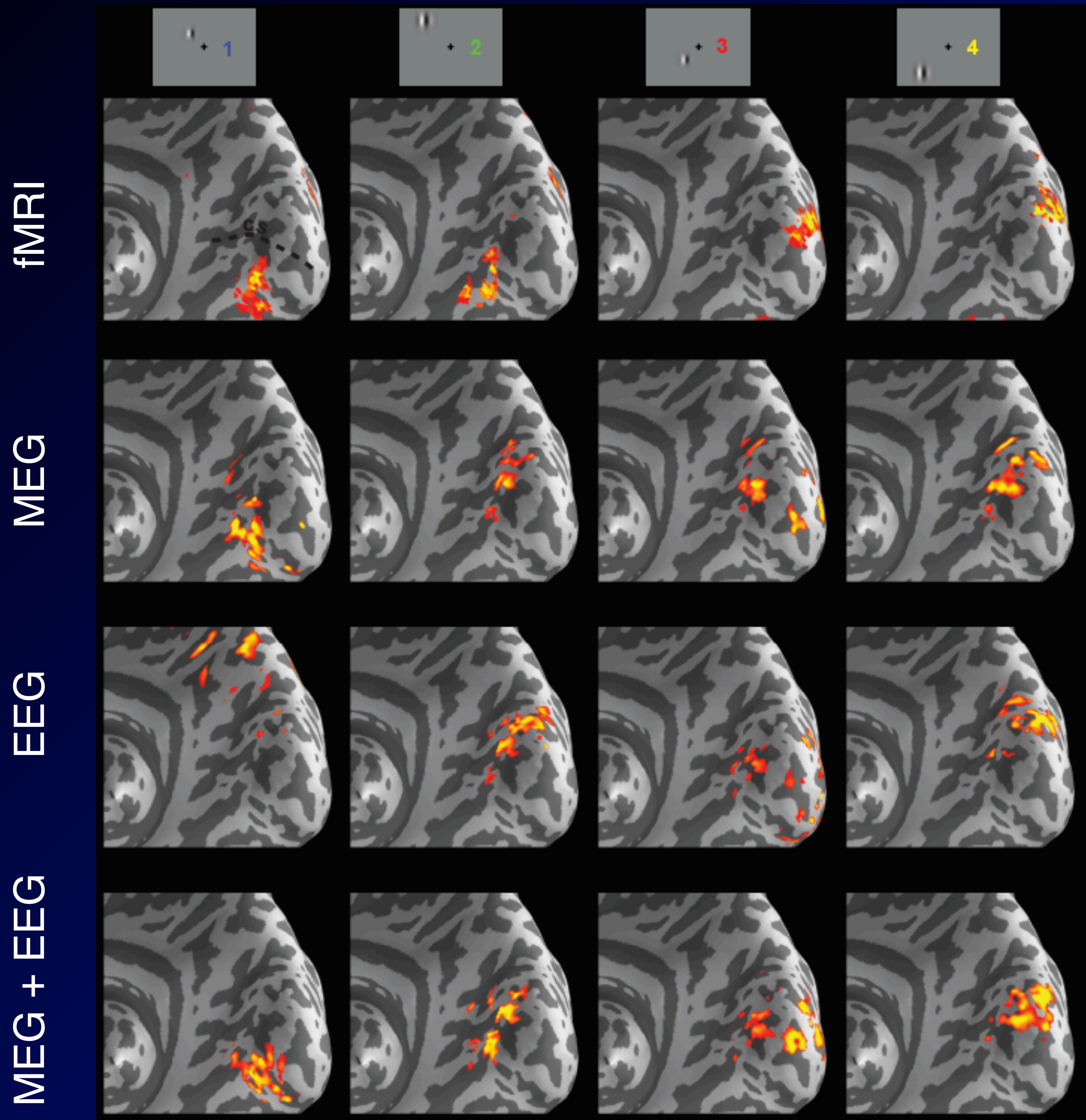
Spatial dispersion of cortically-constrained MEG and EEG source estimates



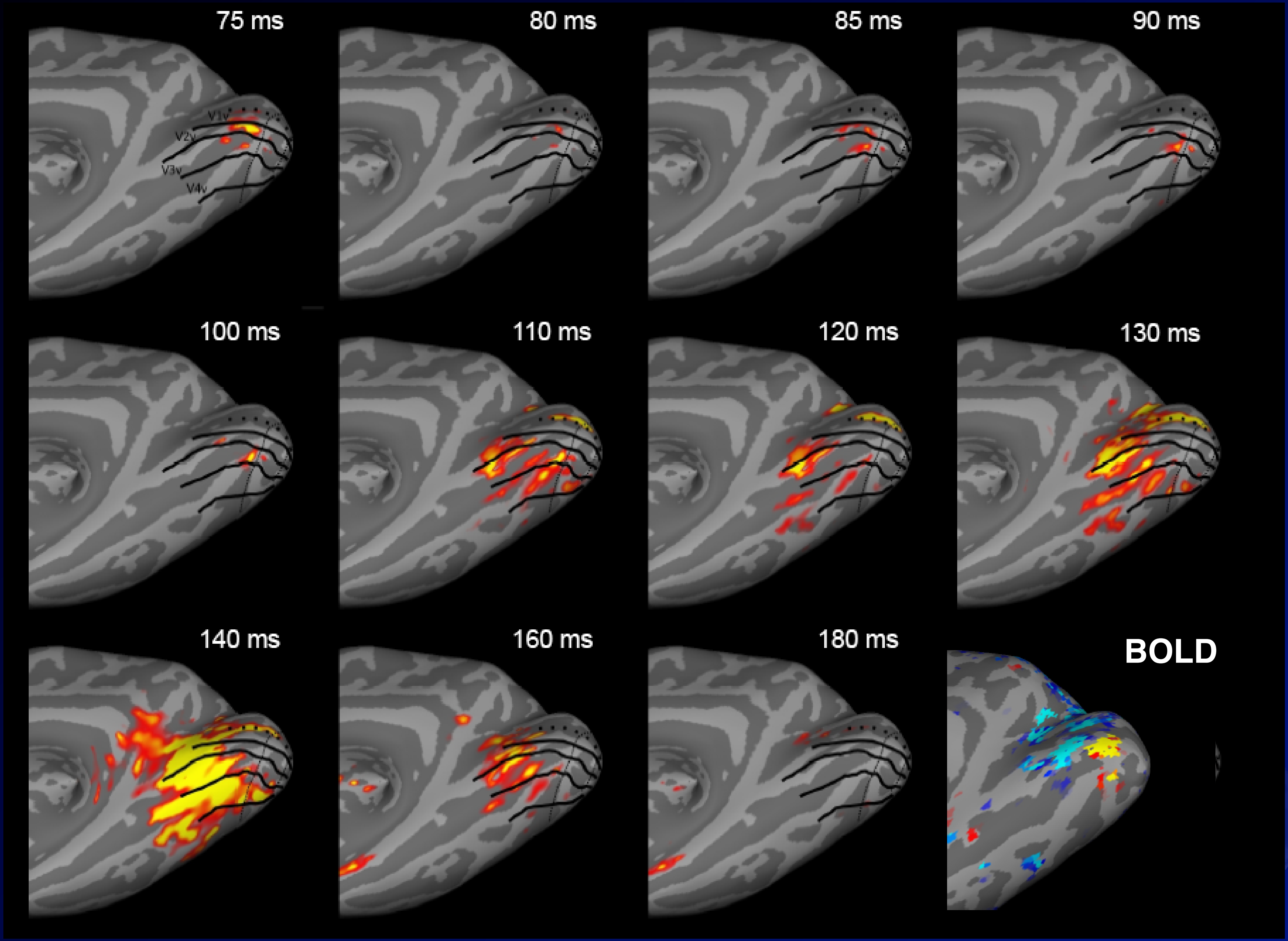
Molins *et al.* 2008

Matti Hämäläinen 8/2013

Comparison of MEG, EEG, and fMRI (dSPM)



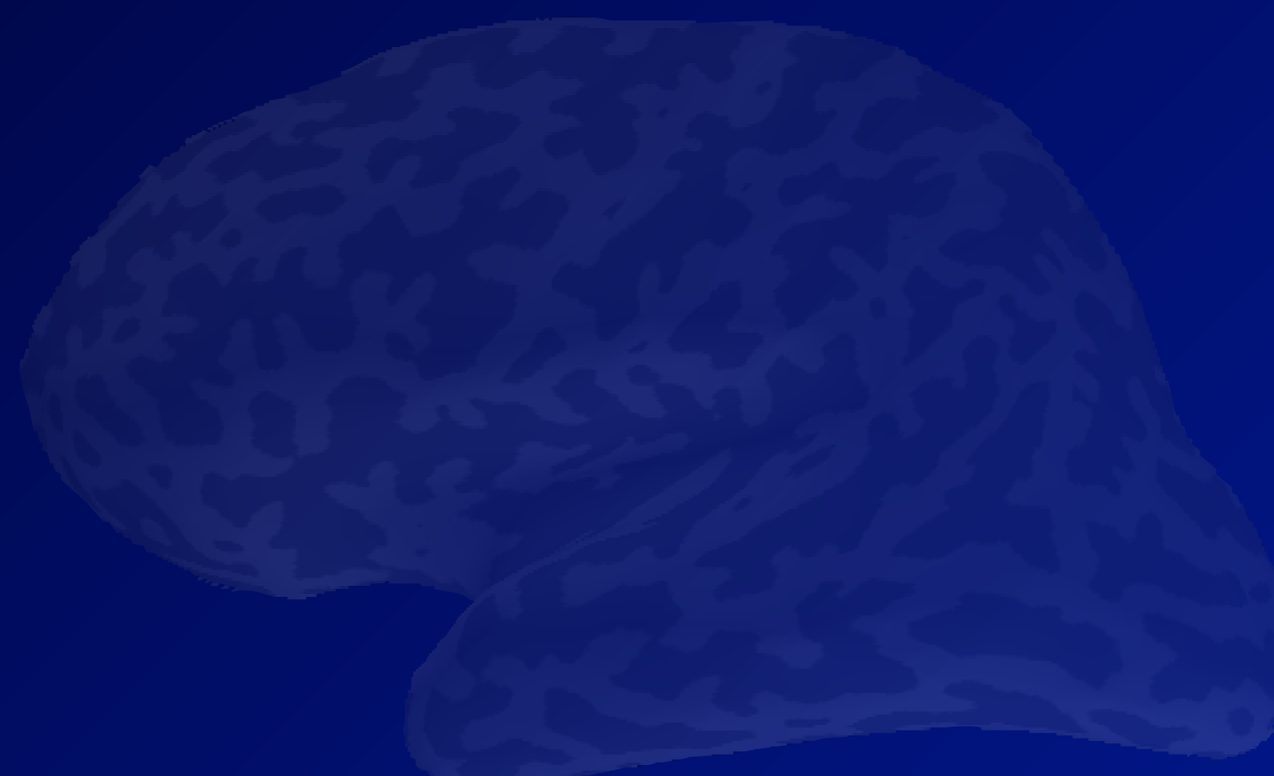
MEG/EEG response dynamics



Sharon *et al.*, SFN, 2005

fMRI-guided estimates

- Prioritize locations of significant fMRI activity (increase source variance)
- fMRI incorporated as a constraint, not an integrated analysis procedure



Dale *et al.* 2000

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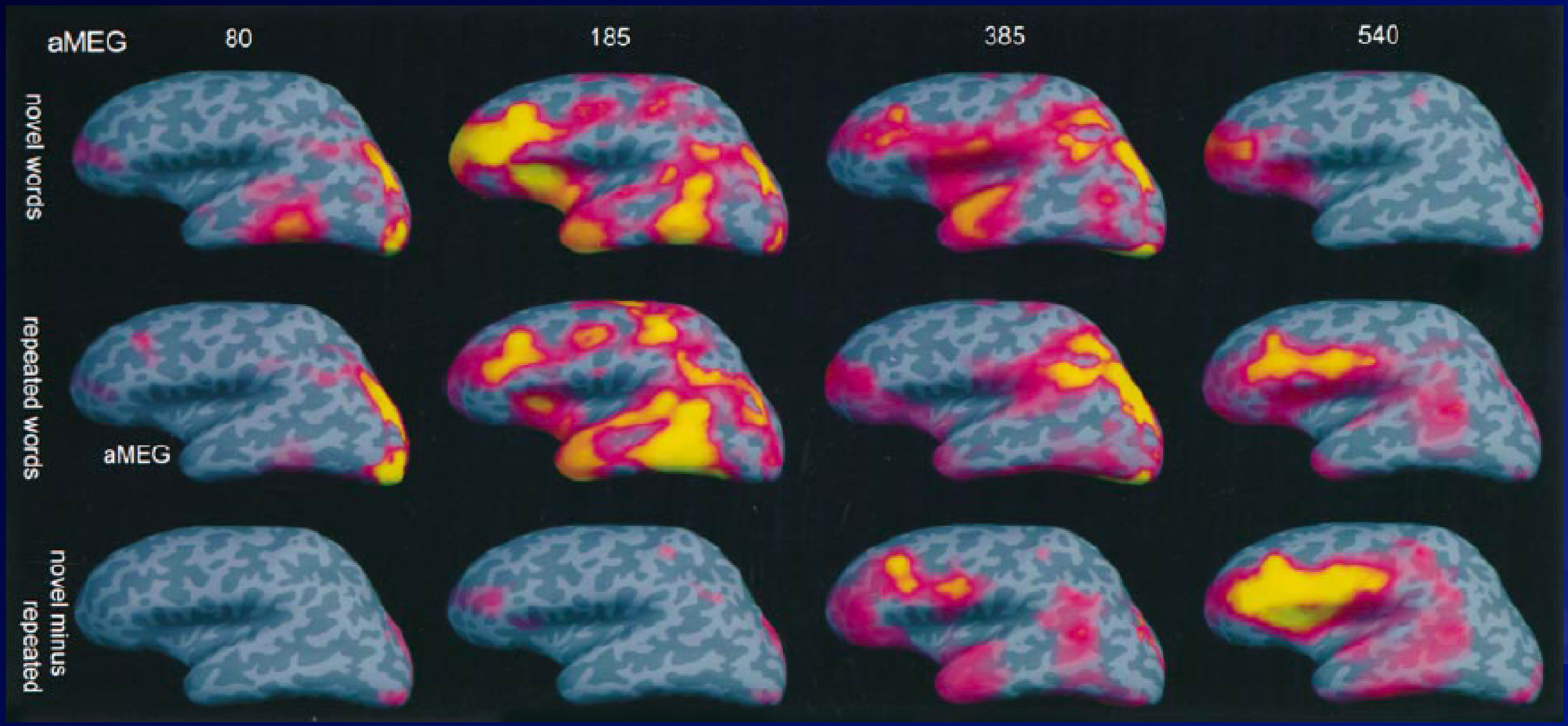

Dale *et al.* 2000

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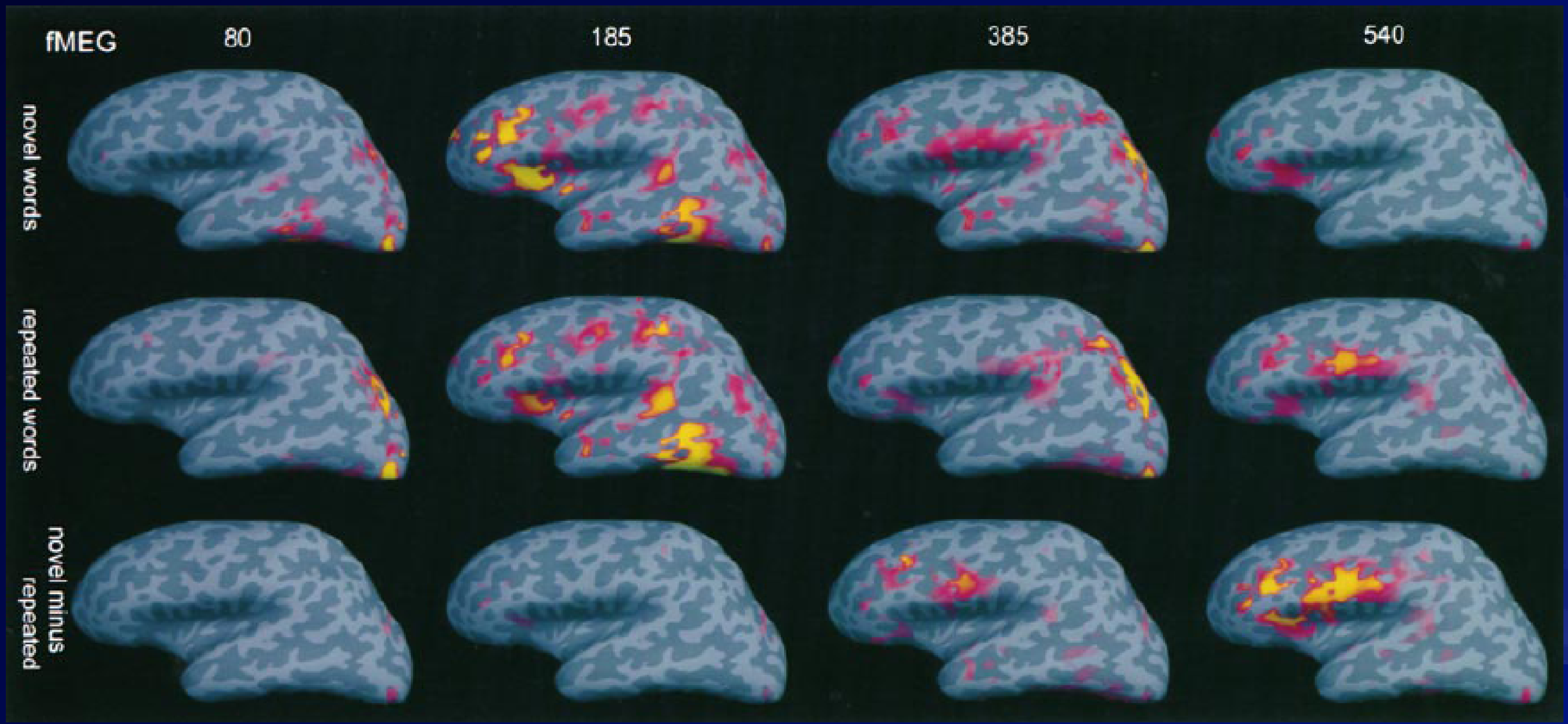
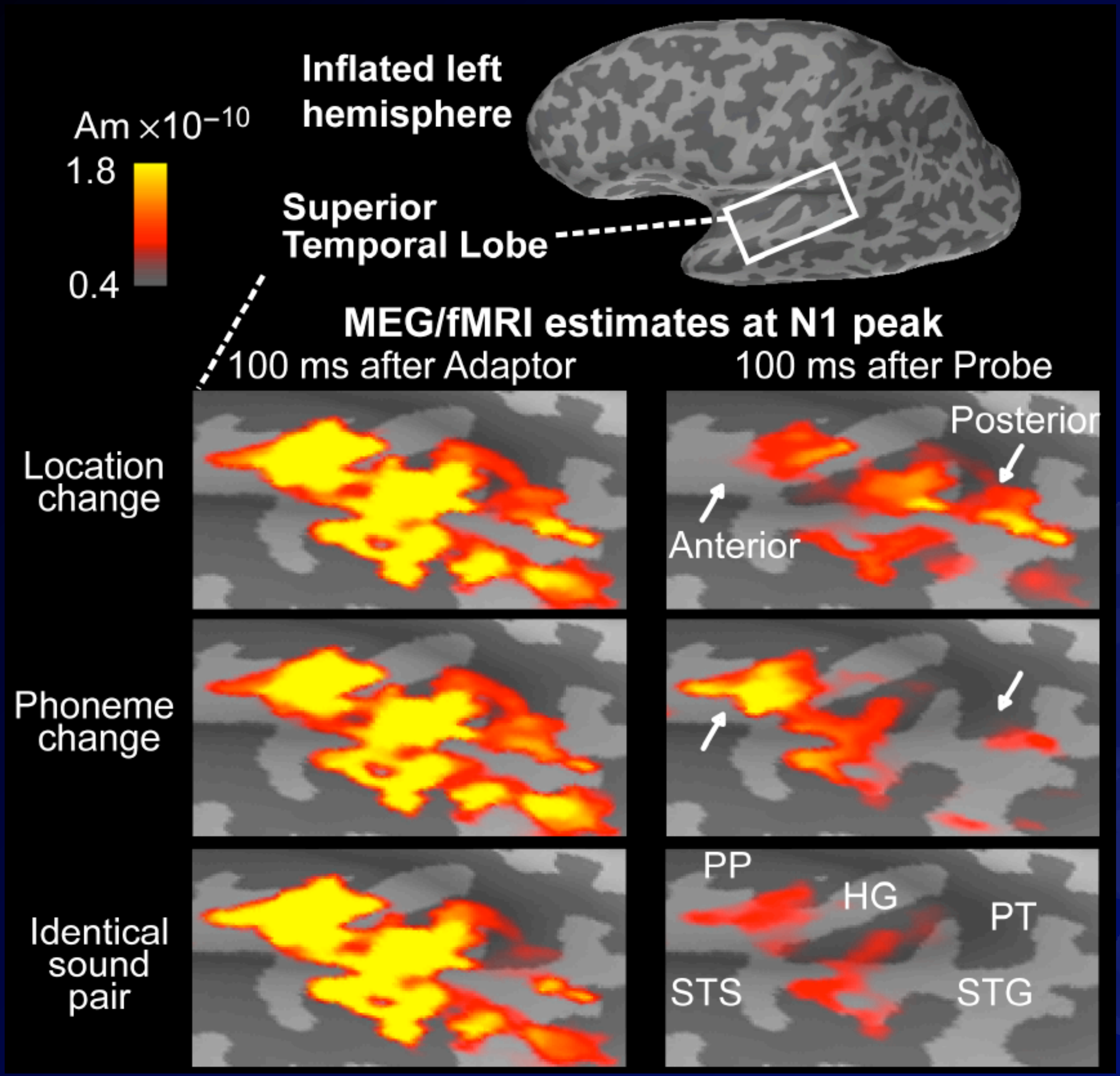


Dale *et al.* 2000

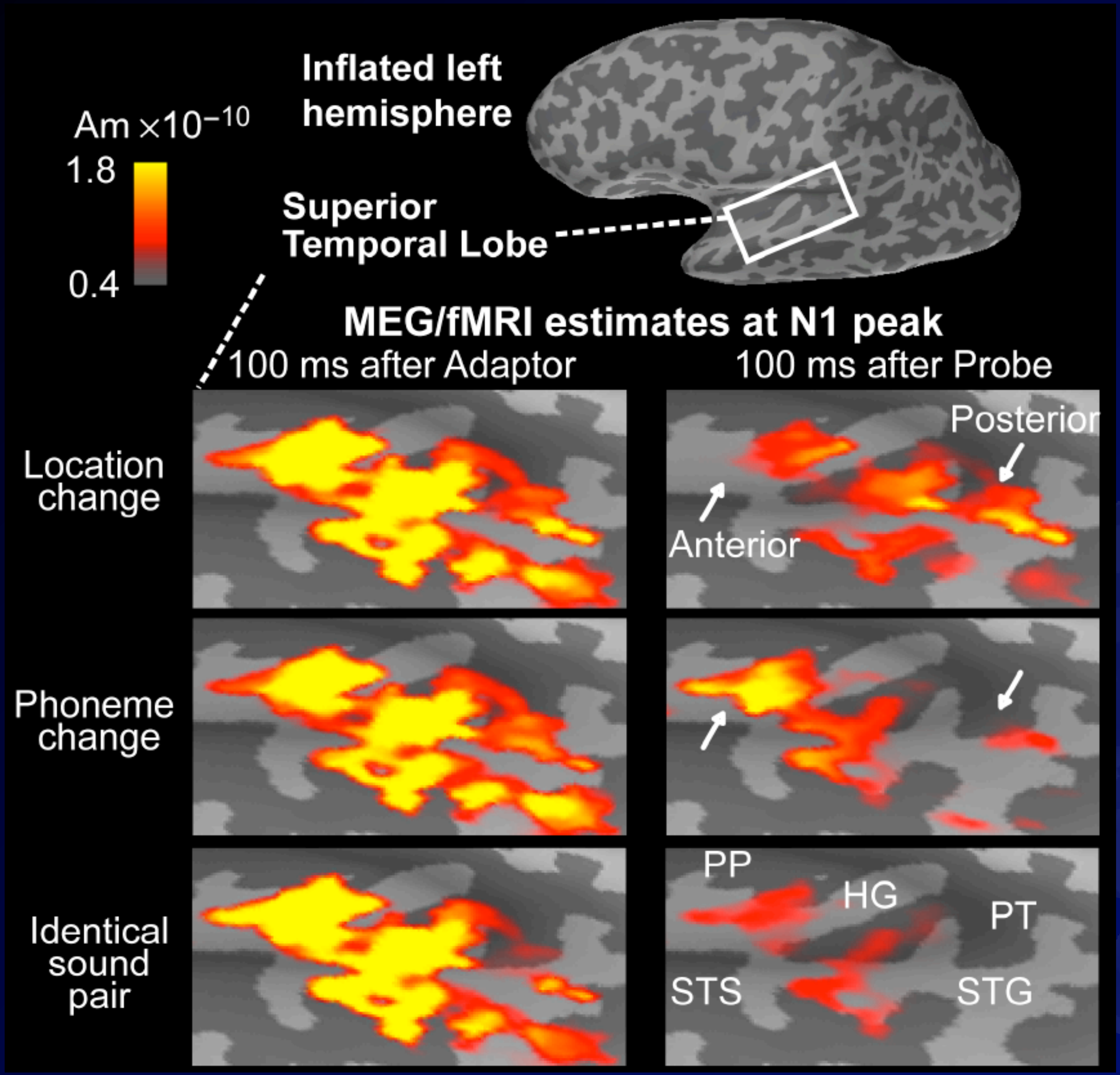
What and Where pathways in the auditory cortex



fMRI weighted MEG estimates to sound pairs which were different in location, phonemic content, or neither

Ahveninen *et al.*, PNAS, 2004

What and Where pathways in the auditory cortex



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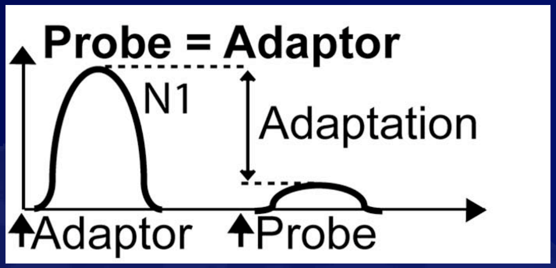

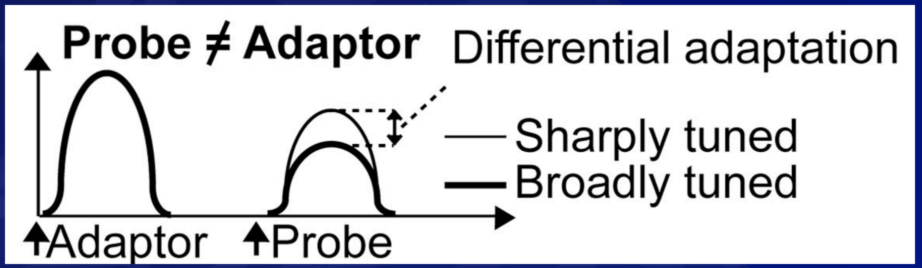

Ahveninen *et al.*, PNAS, 2004

MEG/EEG and fMRI: Similarities and differences

- An ill-posed inverse problem is not involved in fMRI analysis: better spatial resolution
- MEG/EEG have an exquisite temporal resolution
- Both fMRI and MEG/EEG are most likely related to LFPs measured at the microscopic level
- Synchronous activity has an overwhelming contribution to MEG/EEG
- fMRI is an indirect measure of brain activity:
  – Transient changes may remain undetected
  – Sustained weak activity may be more easily detectable
- fMRI does not suffer from cancellation related to different source orientations

Why both MEG and EEG?

- Sources at the periphery of the sensor arrays can be estimated better when both modalities are available
- Different cancellation properties for multiple focal sources and extended source patches
- Missing signal in one modality is valuable information for the interpretation of the other
- Initial combined MEG/EEG experiments can provide valuable guidelines for further single-modality (MEG or EEG) large-cohort or clinical studies

Seppo Ahlfors
Jack Belliveau
Anders Dale (UCSD)
Bruce Fischl
Polina Golland (MIT/CSAIL)
Riitta Hari (HUT)
Fa-Hsuan Lin
Maria Mody
Antonio Molins
Wanmei Ou (MIT/CSAIL)
Lauri Parkkonen (HUT)
Tommi Raij
Bruce Rosen
Riitta Salmelin (HUT)
Dahlia Sharon (Stanford)
Daniel Wehner
Thomas Witzel

www.nmr.mgh.harvard.edu

Thank you!