MEG/EEG Source Estimation Approaches: A Spectrum of Purpose-Built Optimal Tools

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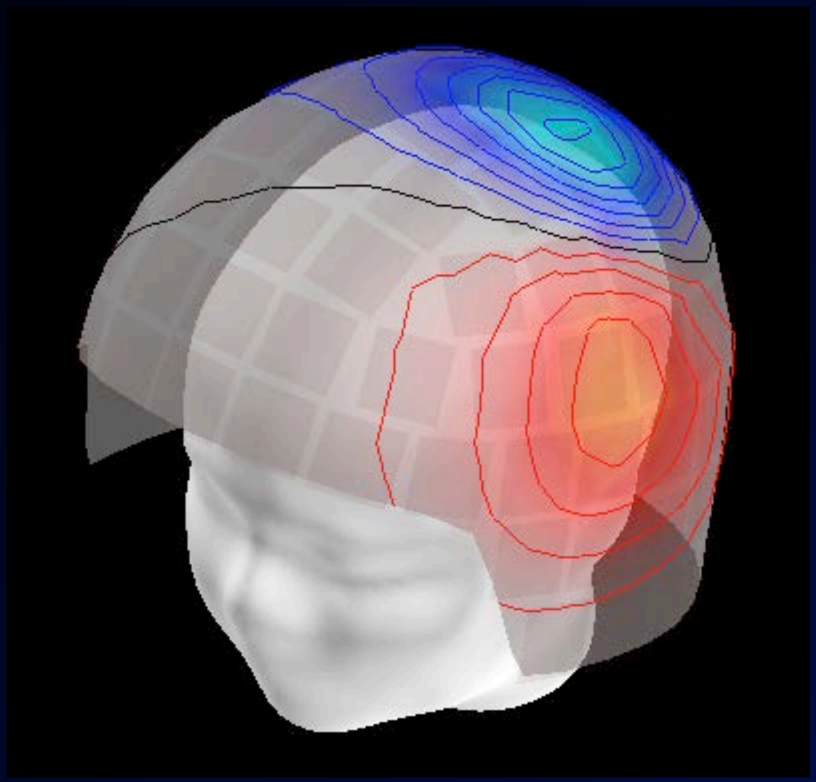
MGH 1811

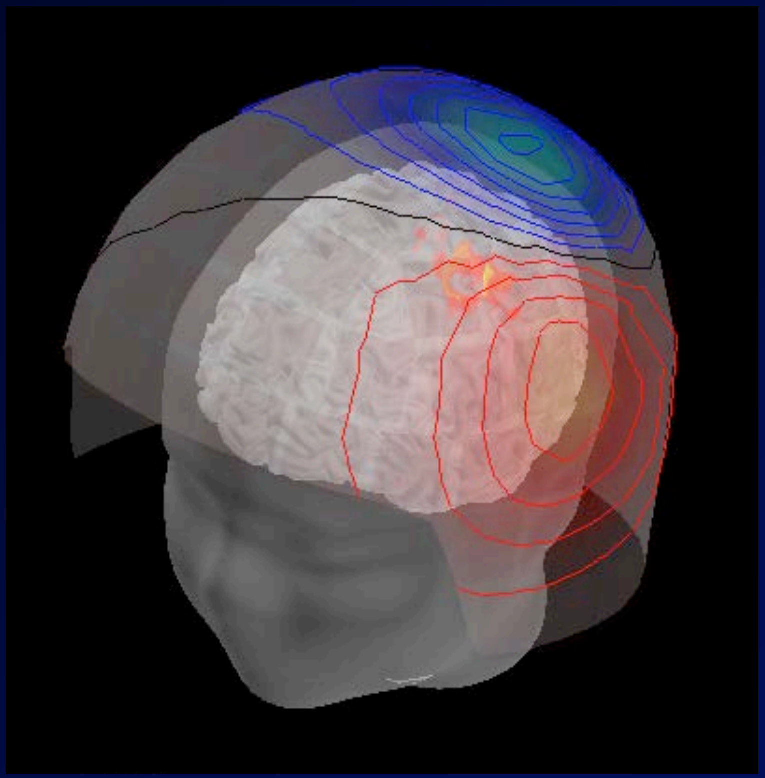
VE RI TAS

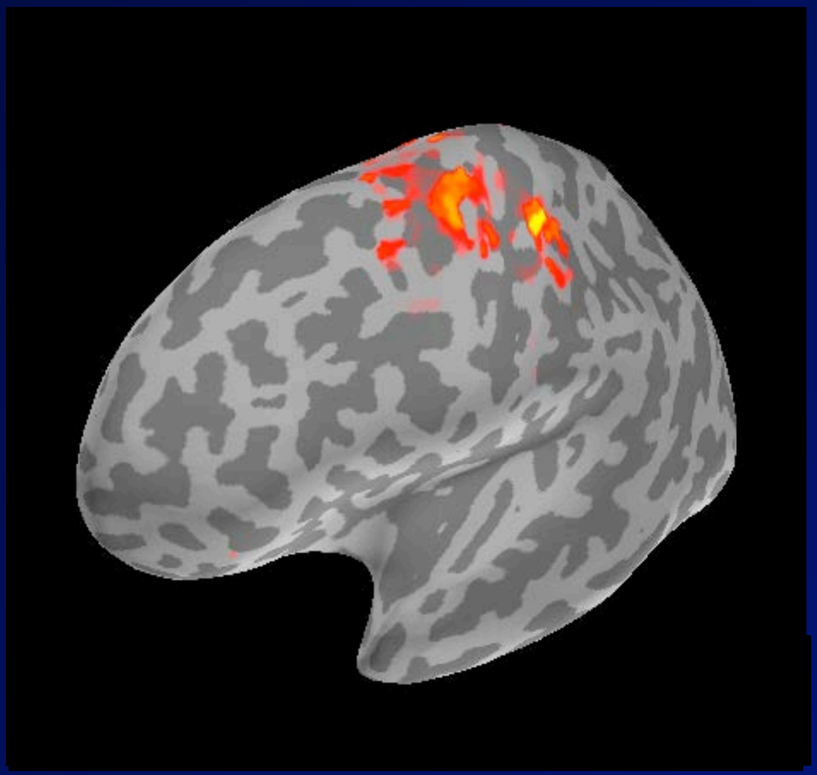
MEG Workshop
McGovern Institute for Brain Research at MIT
May 5, 2019

Source (brain) space instead of sensor space



Sensor space map





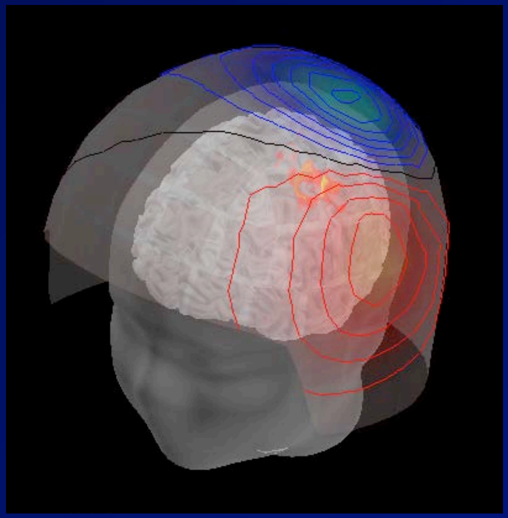
Source estimates

- What kind of information do we use?
- How is this done?
- Examples of discoveries

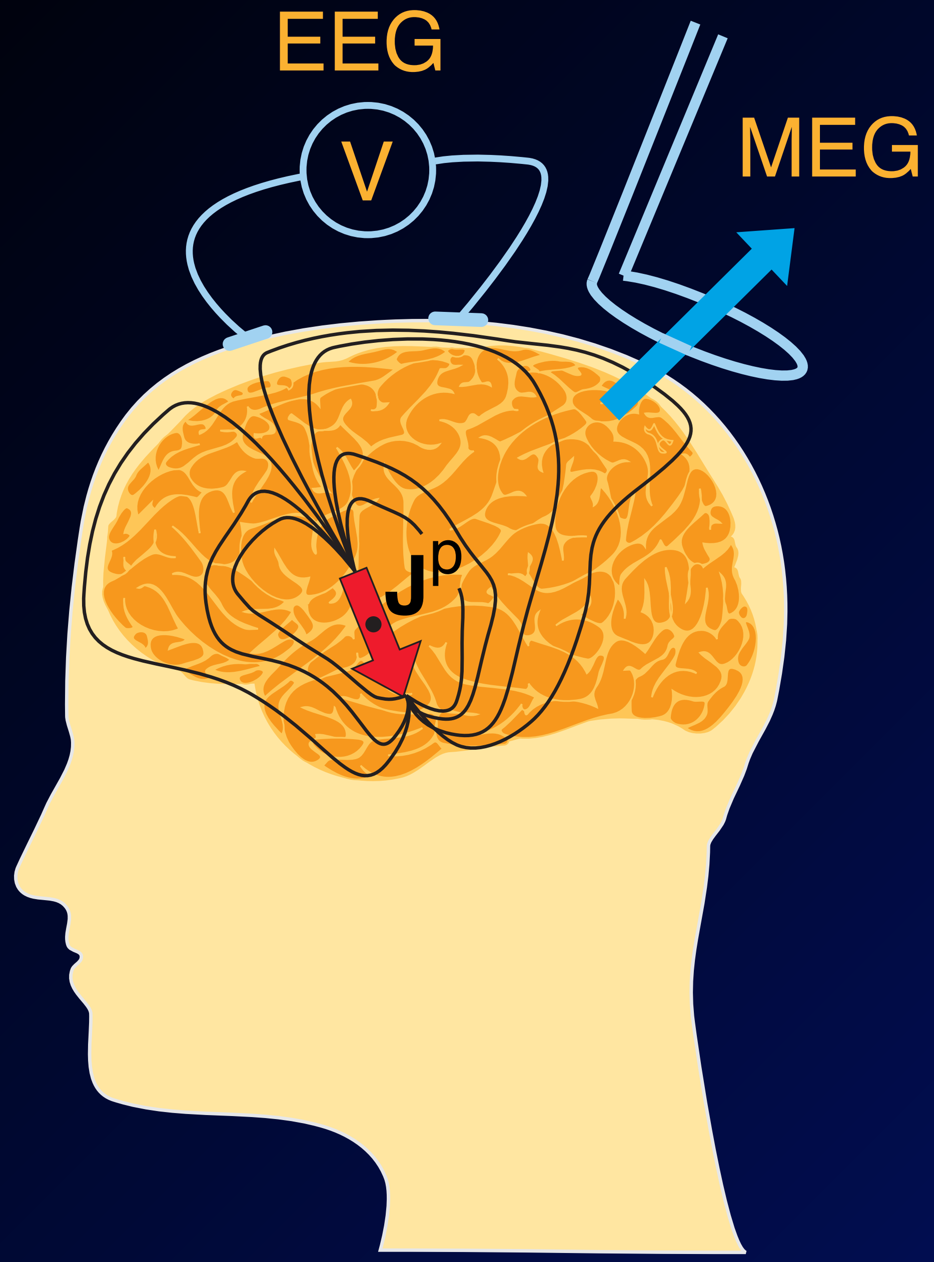
Contents

- MEG and EEG: sources and fields
- Discoveries with dipole models
- Distributed source estimates
- Conclusions

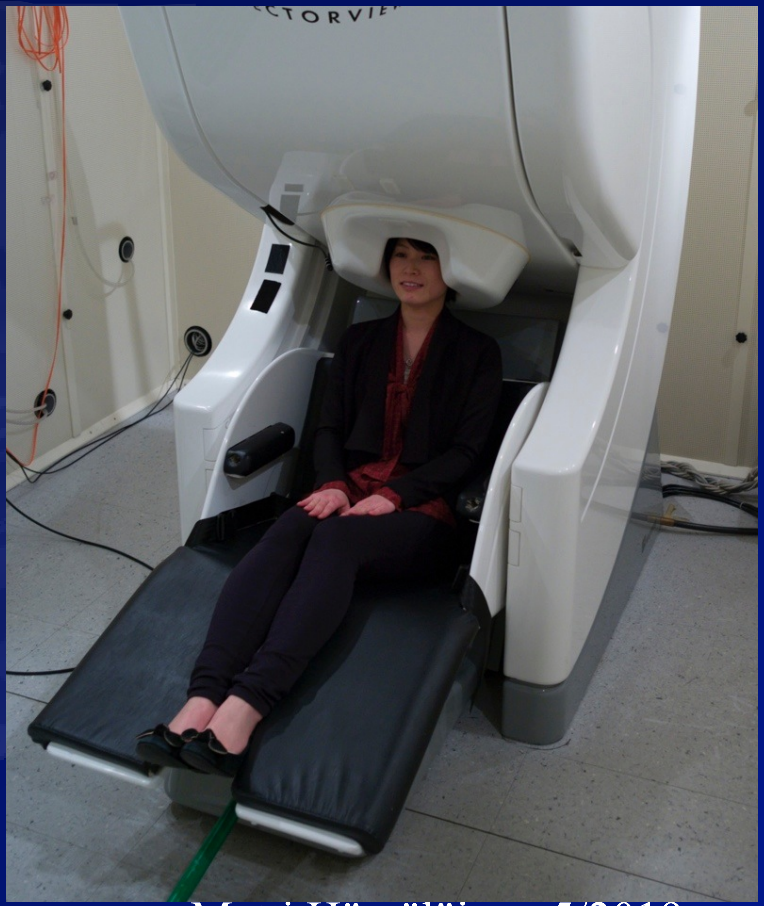
MEG and EEG: Sources and Fields



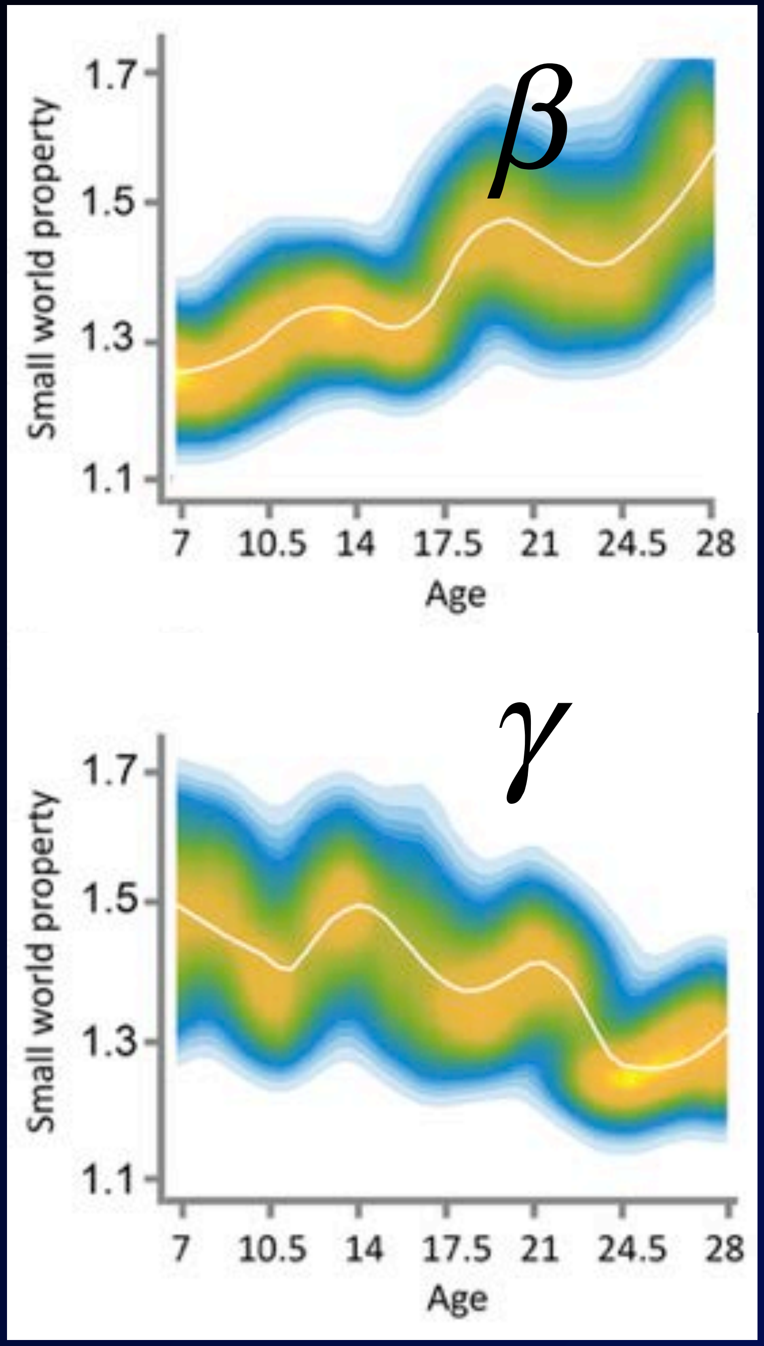
MEG and EEG

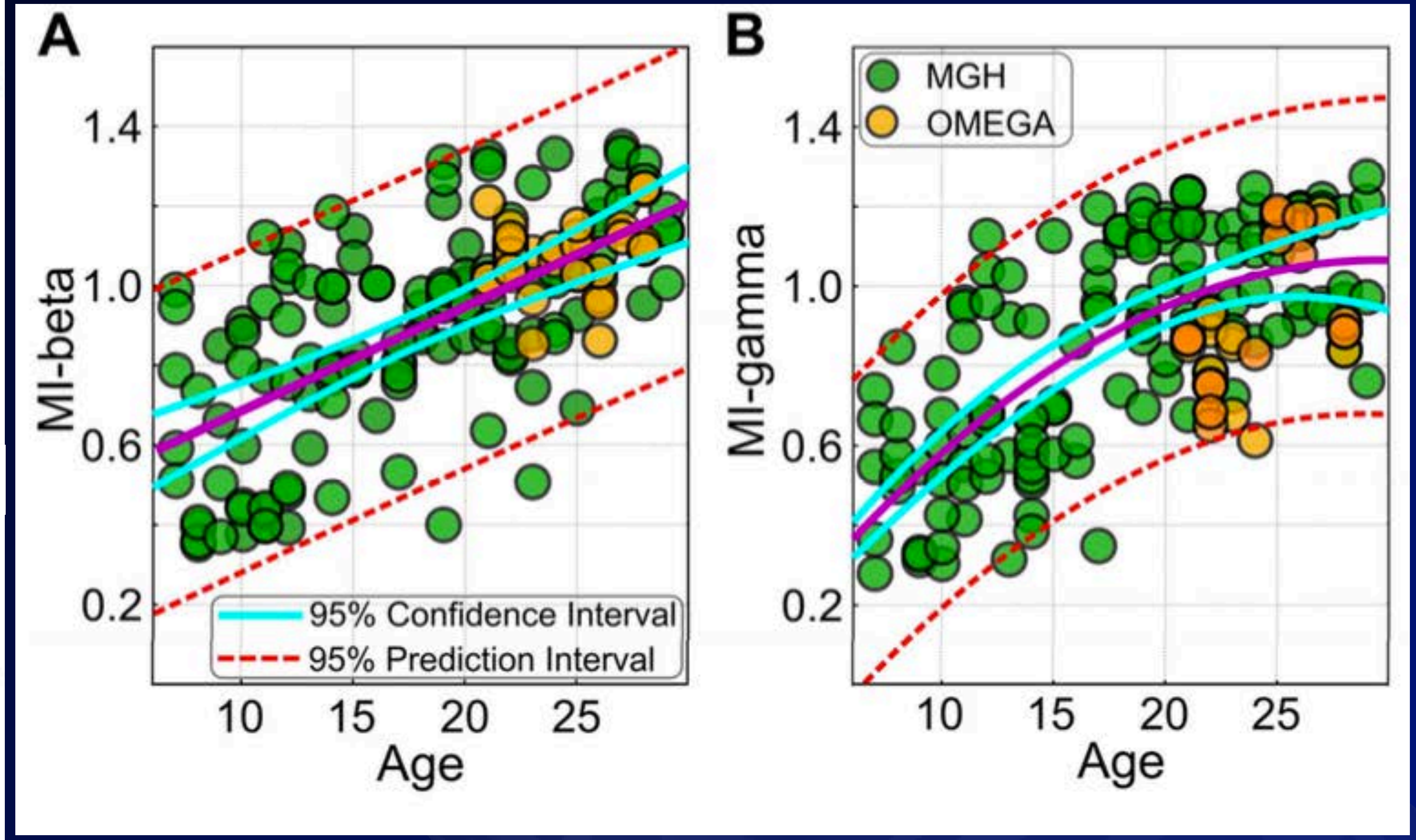


- Measure the electric potential (EEG) magnetic field (MEG) generated by neural currents
- Reasonable spatial resolution
- Real-time measures of brain activity
- Frequency-specific measures of association (connectivity)



Cortical Beta and Gamma Rhythm Resting-State Networks Follow Distinct Maturation Trajectories

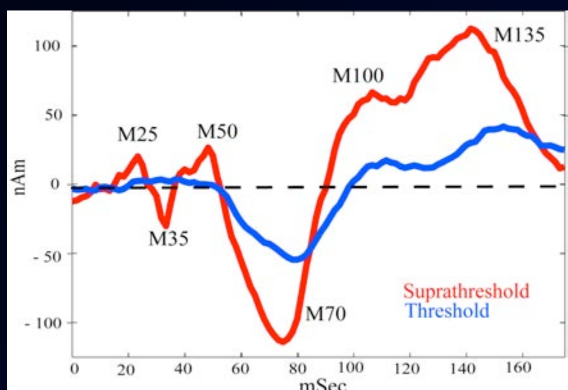


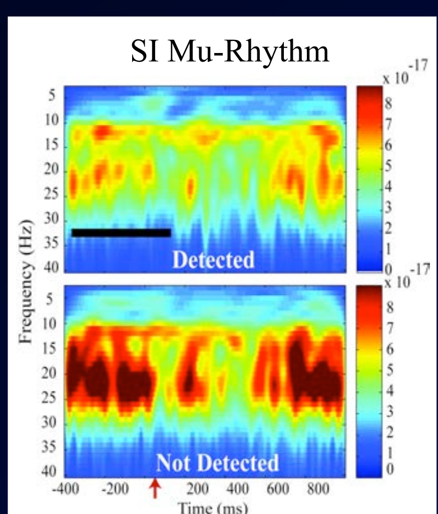


Khan et al., Neuroimage, 2018

Bridging Microscopic and Macroscopic Neurophysiology

MEG Source Estimates

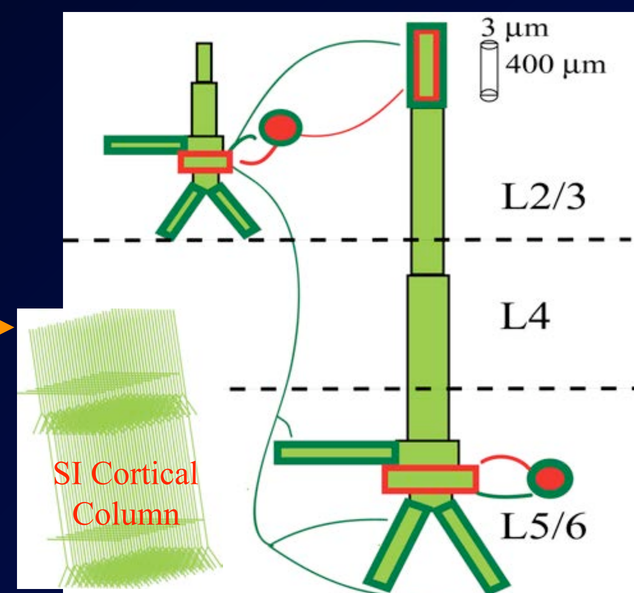




Example subject. Avg n=100 trials

Steven Stufflebeam
Matti Hämäläinen

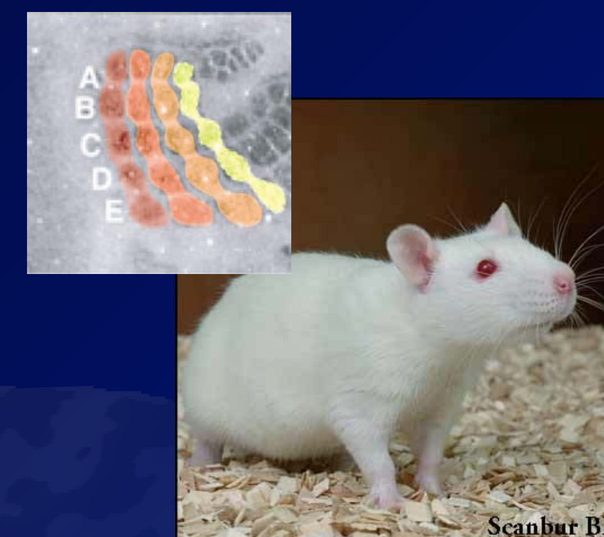
Computational Neural Modeling



Predicted cellular level neural dynamics

Stephanie Jones

Animal Electrophysiology



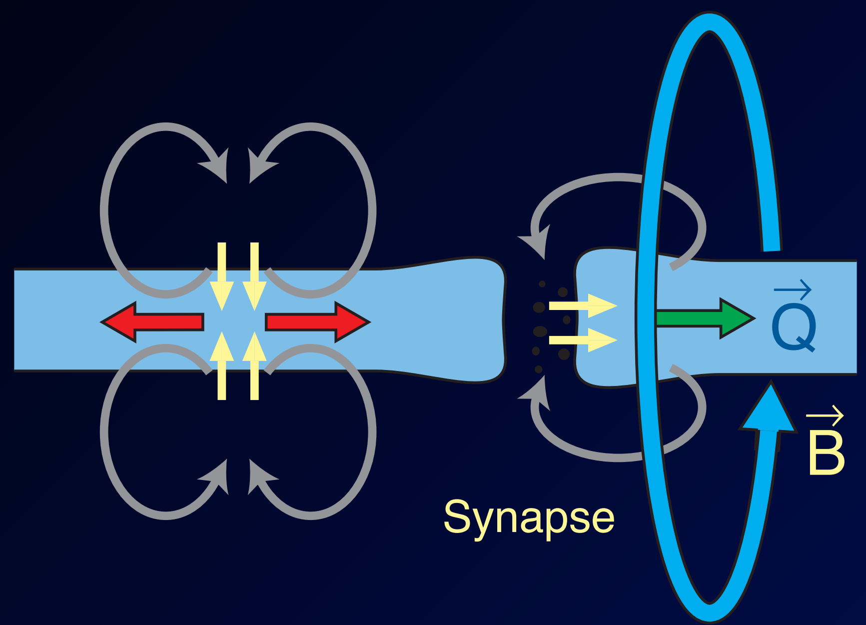
Cellular level details of neural dynamics

Chris Moore

Neural mechanisms of transient neocortical beta rhythms: Converging evidence from humans, computational modeling, monkeys, and mice, Sherman et al., PNAS, 2016

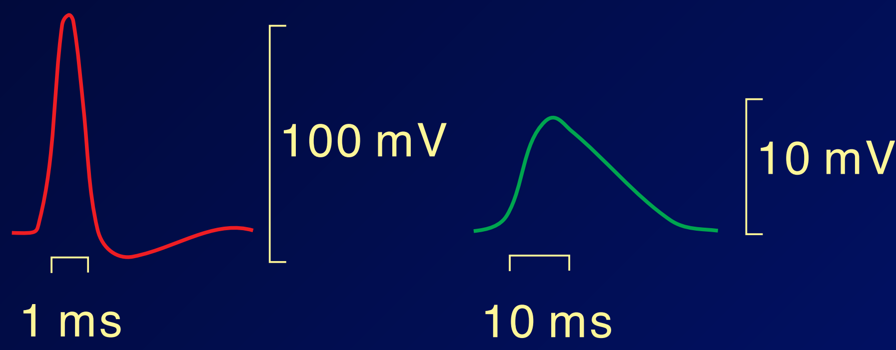
Neural sources of MEG and EEG

Current configurations



Action currents Postsynaptic currents

Time behavior



Action potential Postsynaptic potential

Postsynaptic currents dominate:

- Unidirectional (dipolar) currents
- Longer time course

Signal amplitudes:

- EEG: 0.1 – 100 µV
- MEG: 1 fT – 3 pT

Single PSP:

- 0.02 pAm ≙ 500 000 synapses / 10 nAm (Hämäläinen et al., 1993)
- 0.3 – 0.9 pAm ≙ 11 000 – 33 000 synapses / 10 nAm (Murakami and Okada 2006)

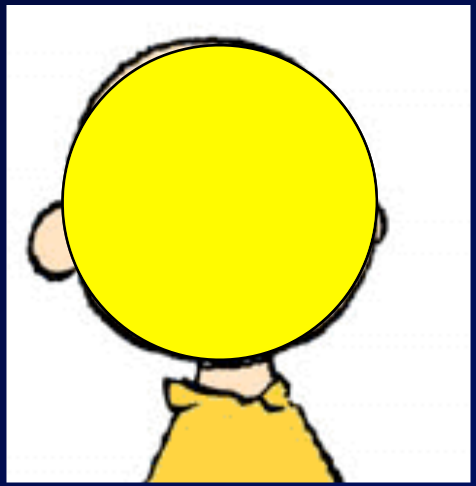
Okada constant: **~ 1 nAm / mm²** (Murakami and Okada, 2015)

Forward models for MEG and EEG

Sphere model

$\sigma = \sigma(r)$

MEG = EEG

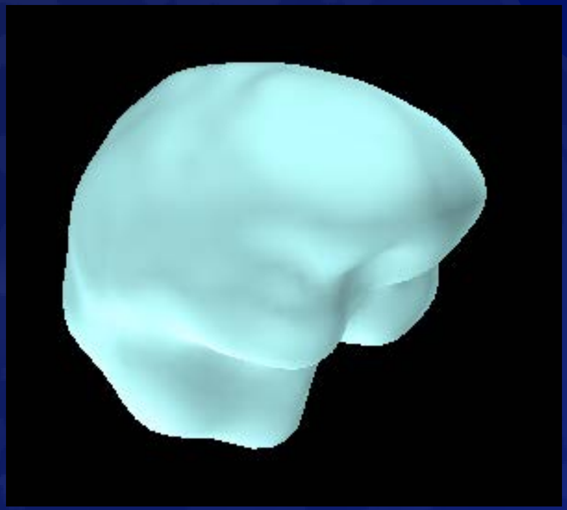


MEG ≠ EEG

Boundary-element models (BEMs)

Skull and scalp taken into account

MEG ≈ EEG

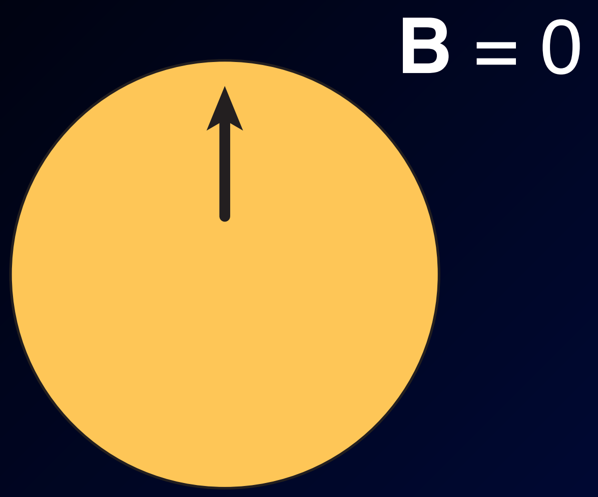


MEG ≠ EEG

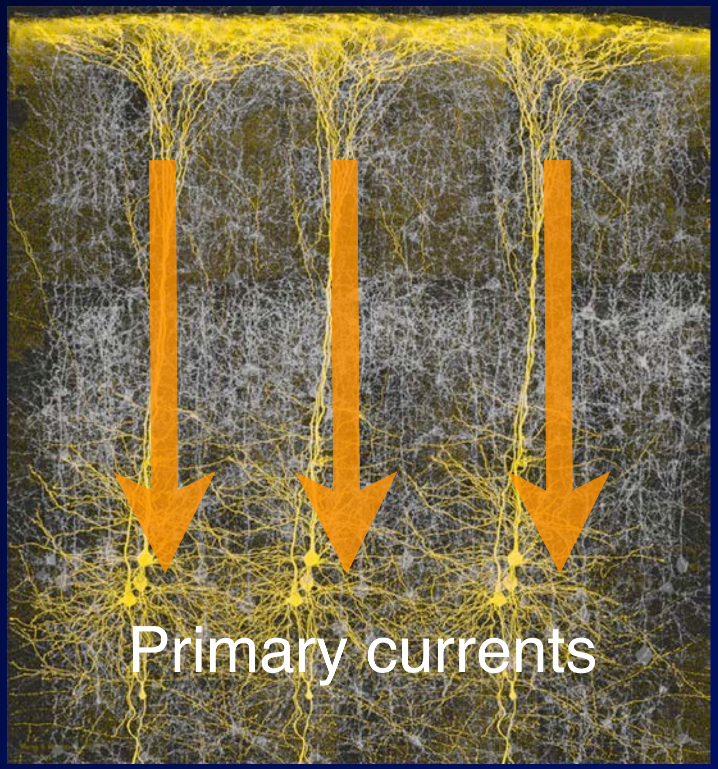
Homogeneous model: skull taken as an insulator

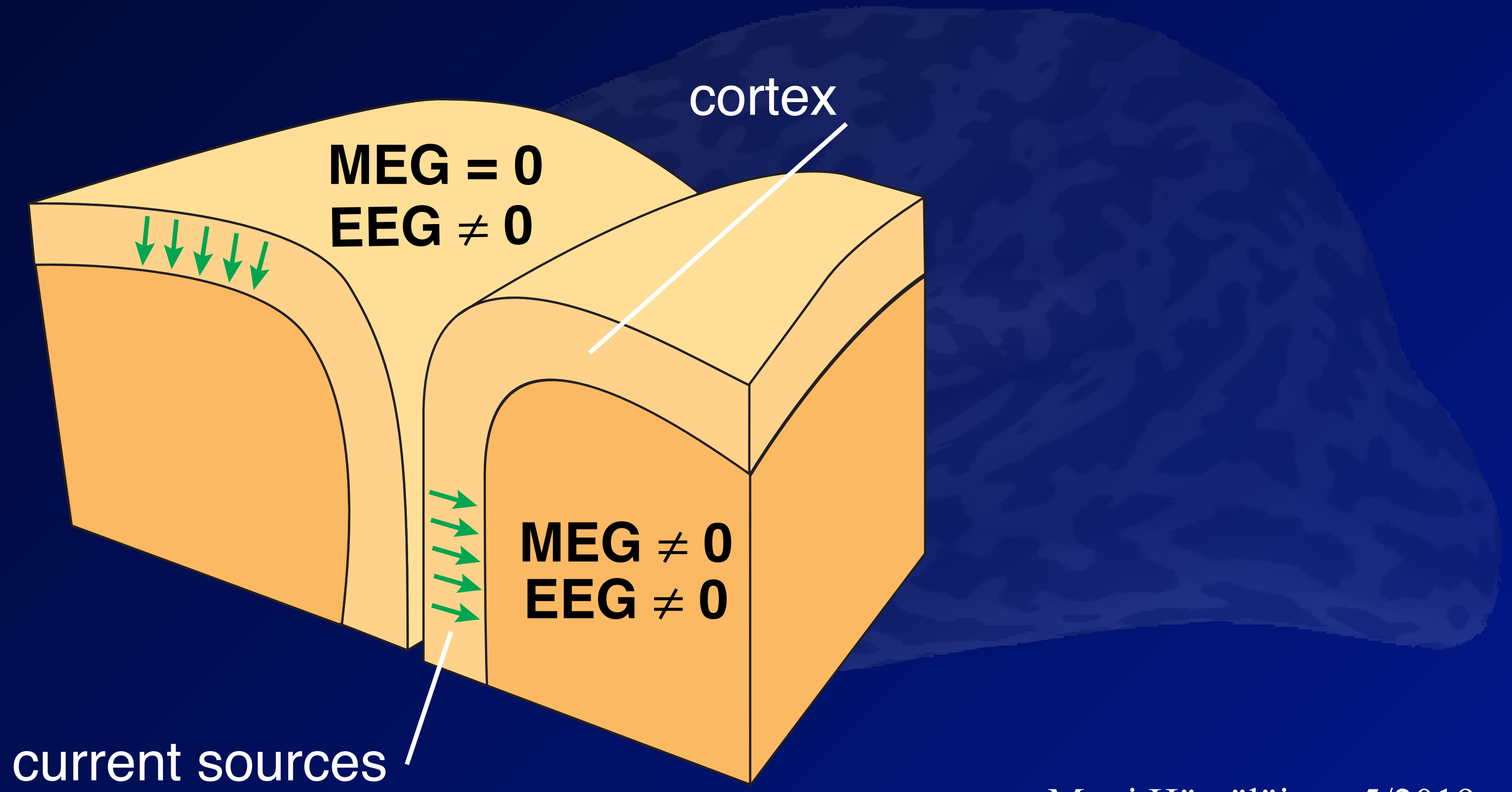
Theoretical analysis: Hämäläinen and Sarvas, 1989
Experimental validation: Okada *et al.*, 1999

Primary currents in the cortex



No magnetic field from radial currents in the sphere model



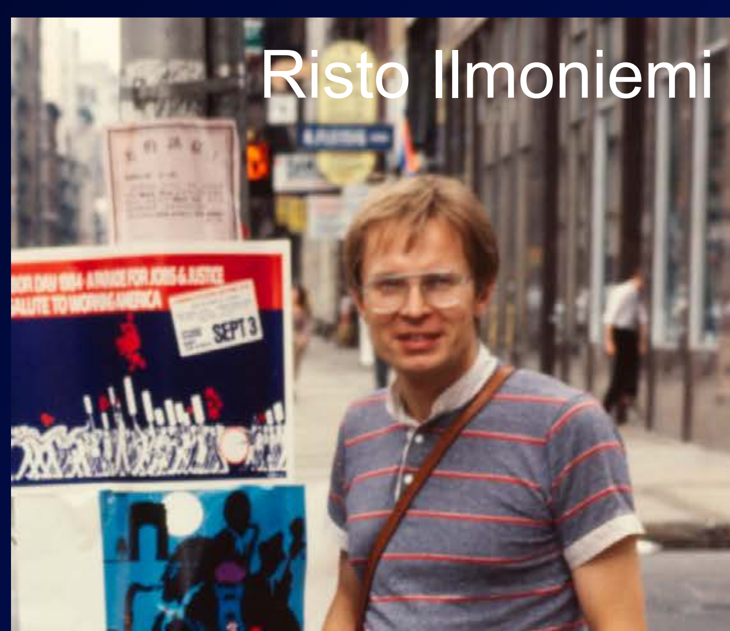


Prediction from the first MNE paper

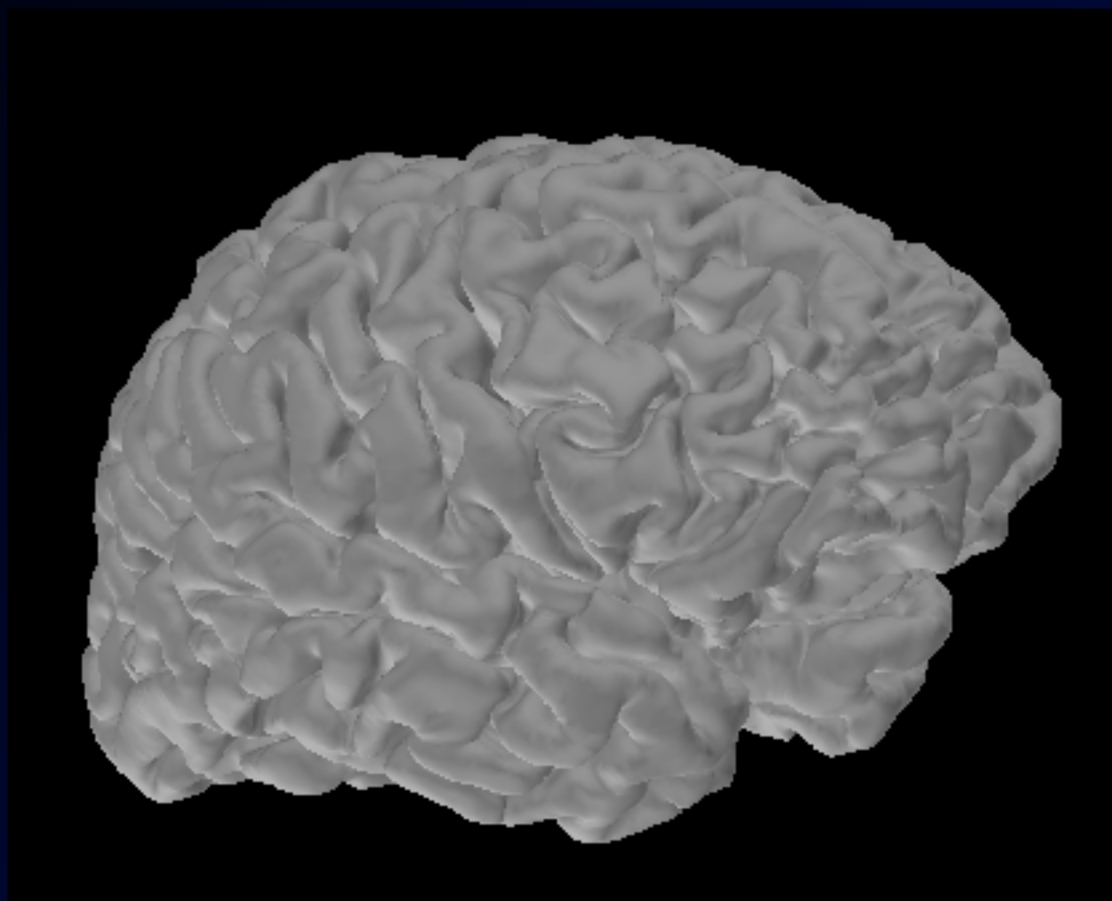
It would be desirable to improve the minimum norm estimates by finding ways to inject some a priori knowledge or assumptions of the experimenter. For example, one could confine the integration area to be the cortex, or one could require that the event in the brain be local.

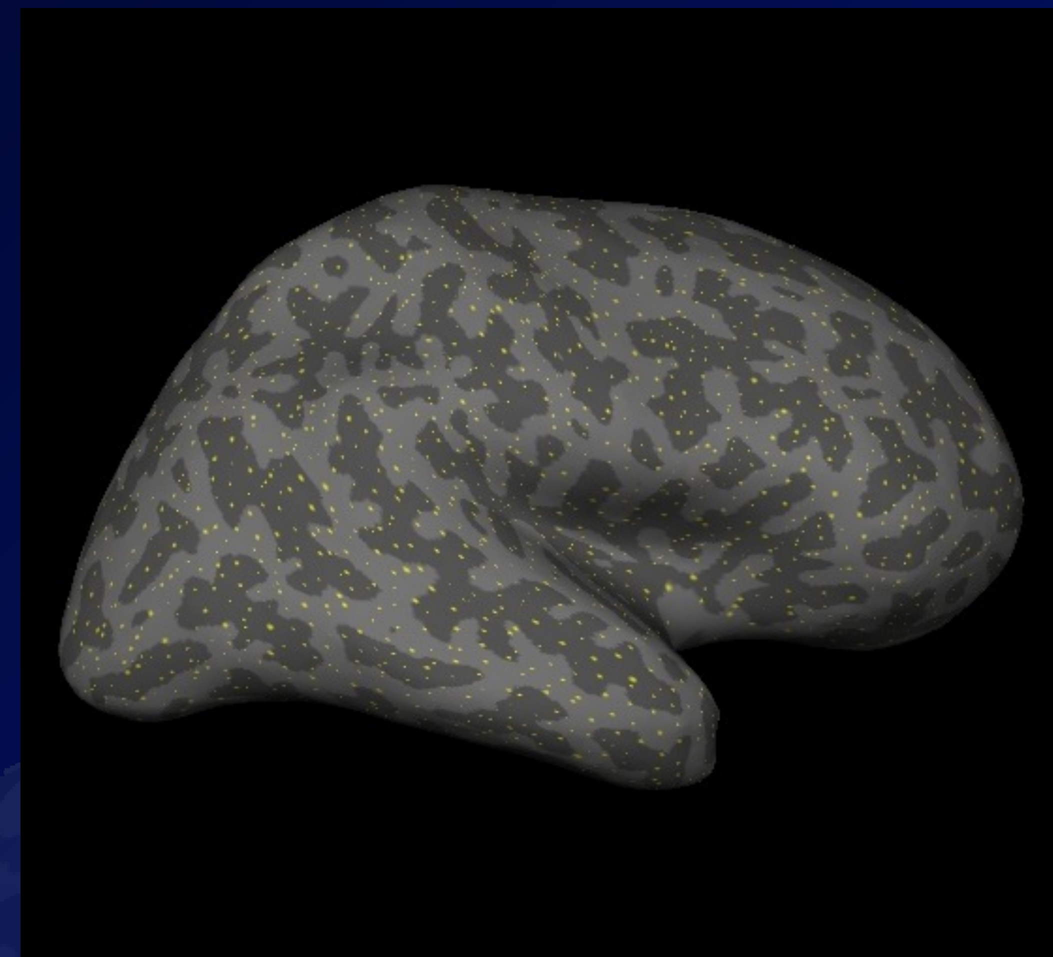
Hämäläinen and Ilmoniemi, 1984

B



Cortical Source Location Constraints

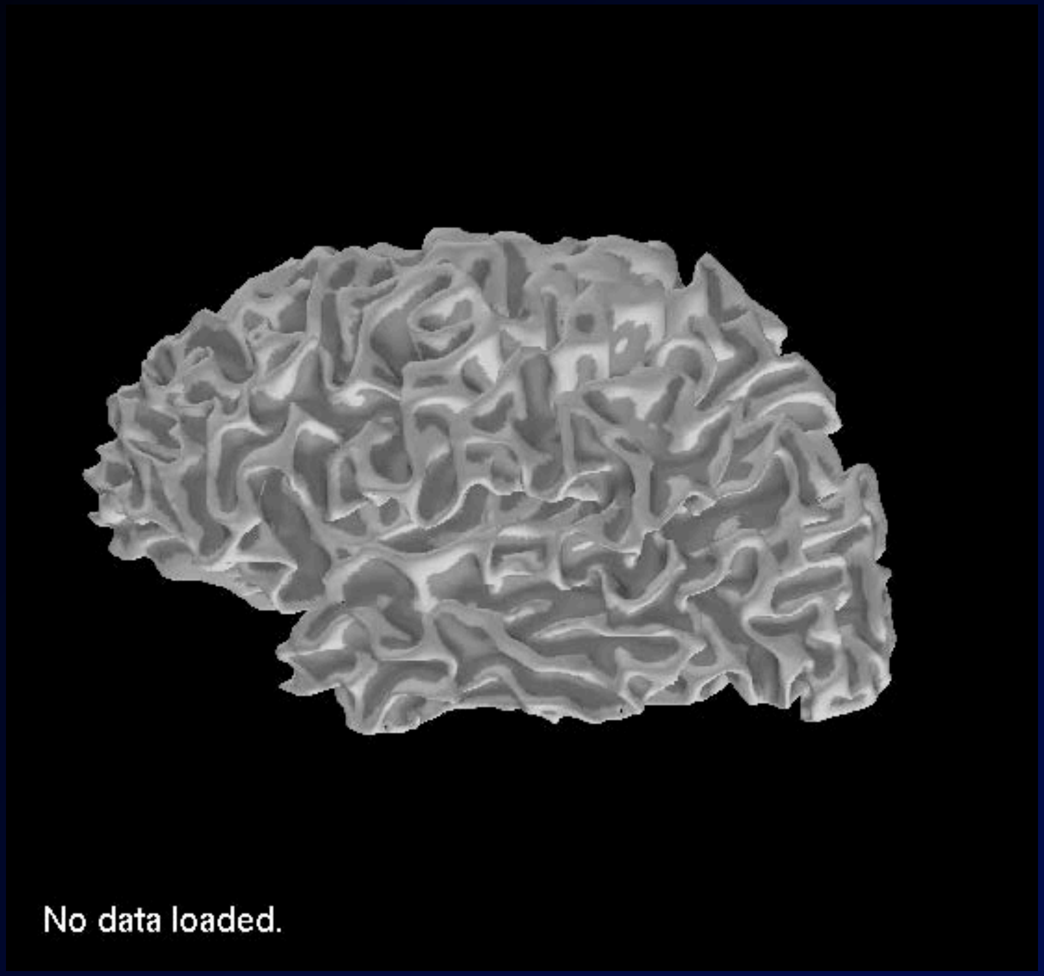


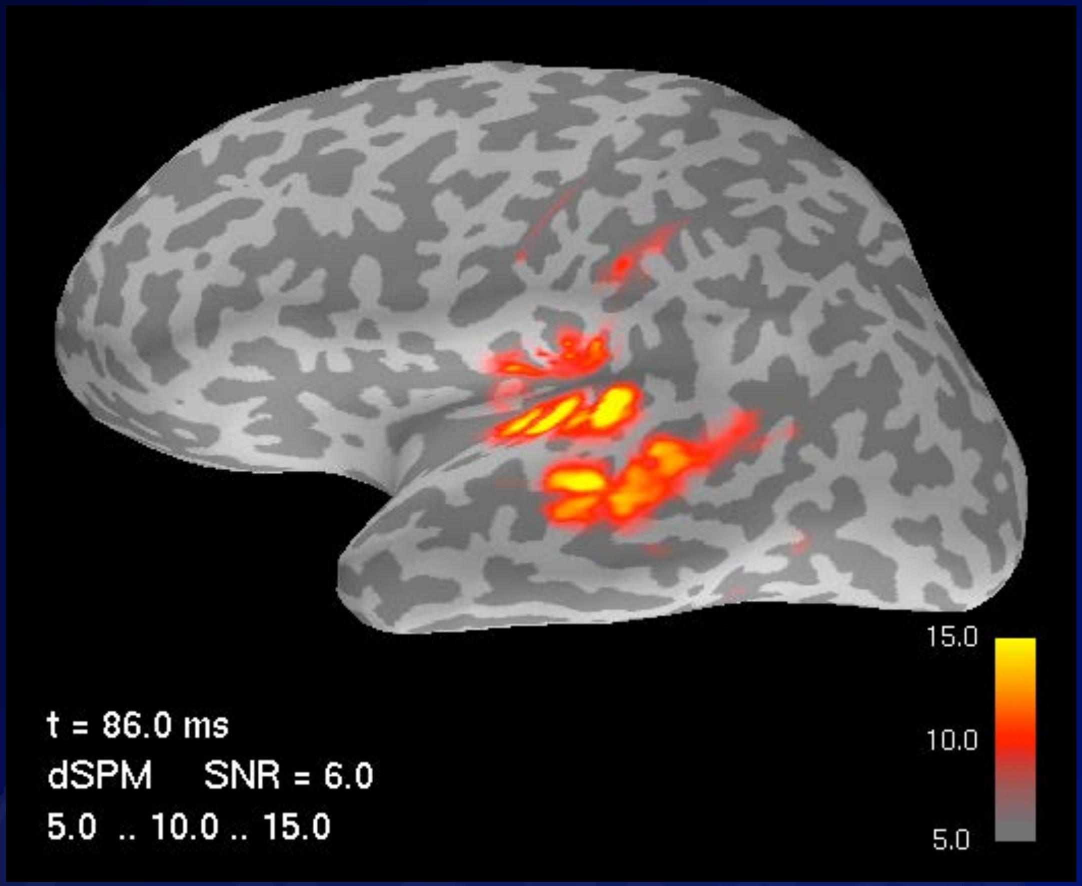


Tessellation of the cortex: Source location and orientation information

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

Inflated Cortex

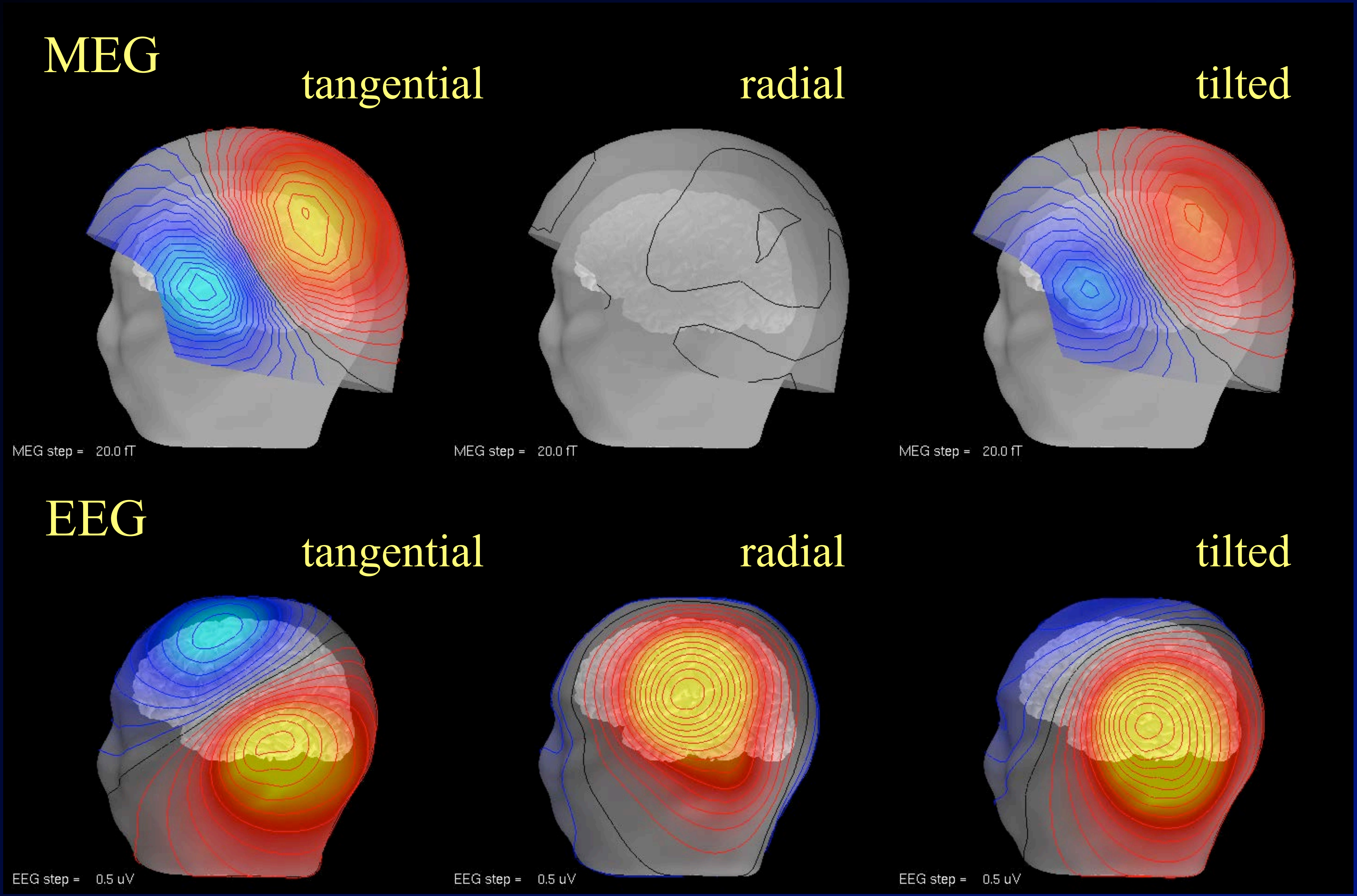




Topologically correct tessellation can be inflated

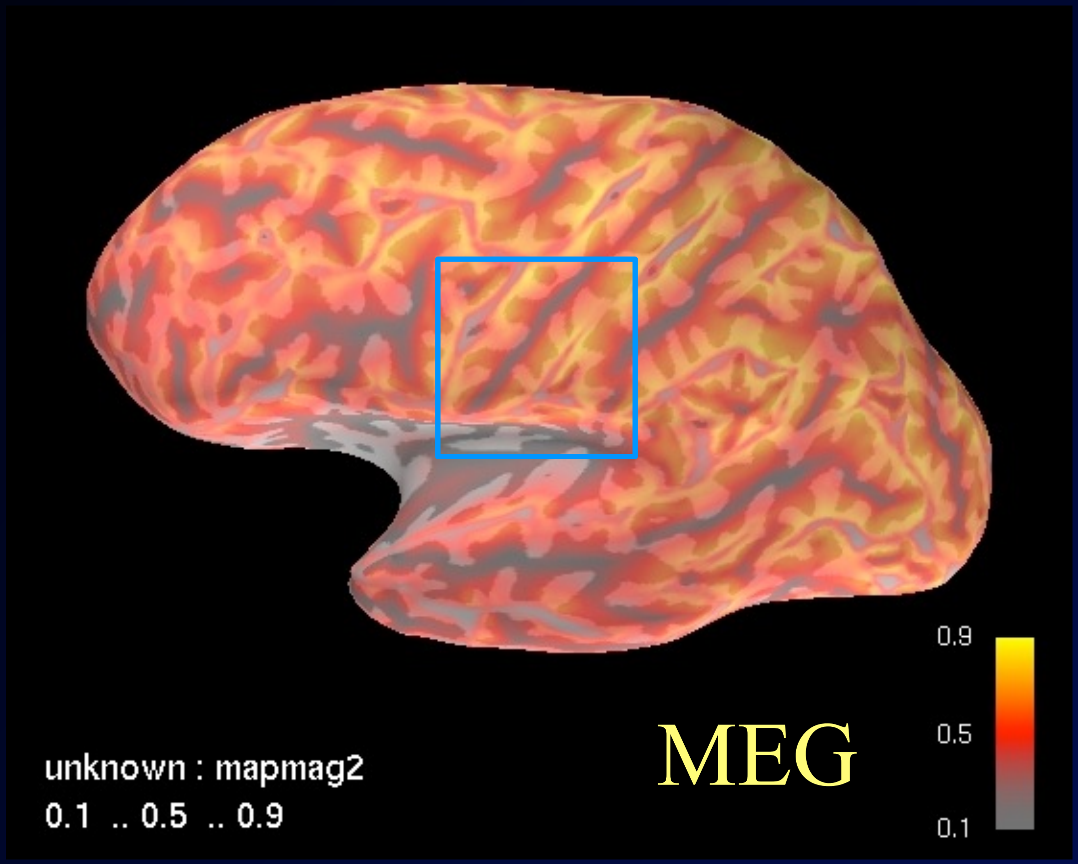
Dale, Fischl, Sereno *et al.*

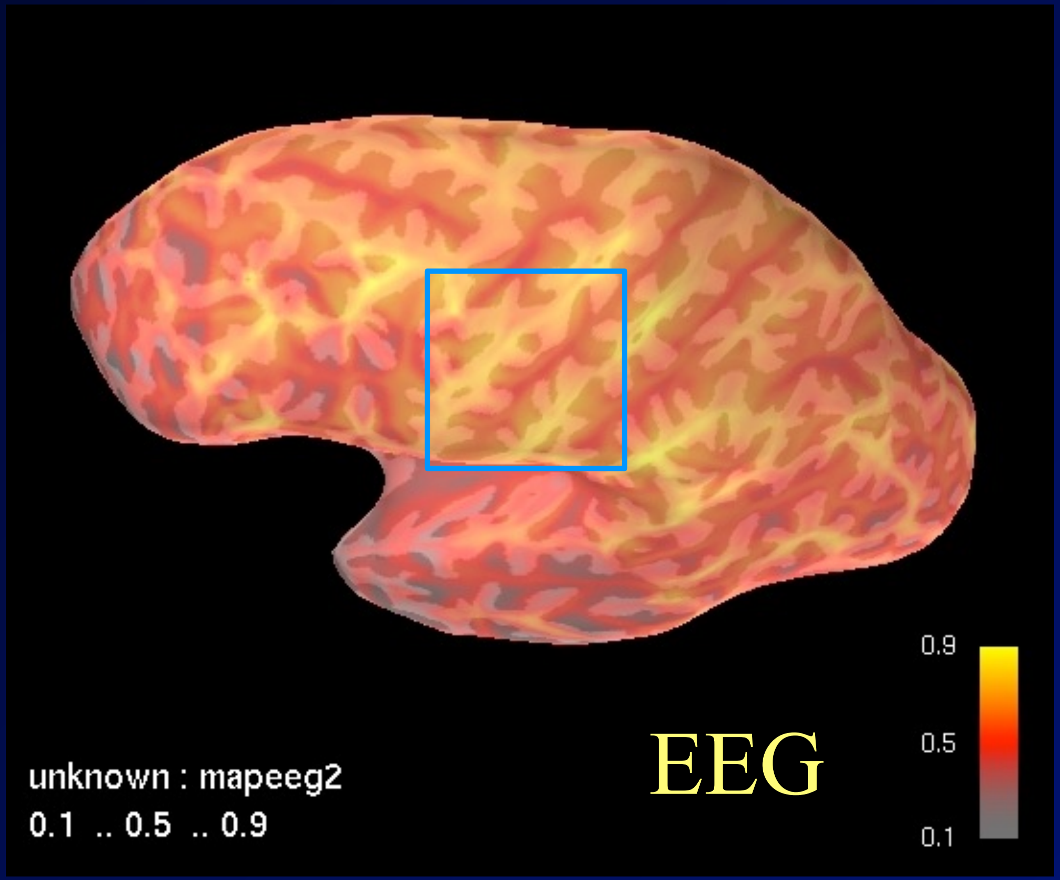
Tangential, radial, and tilted sources

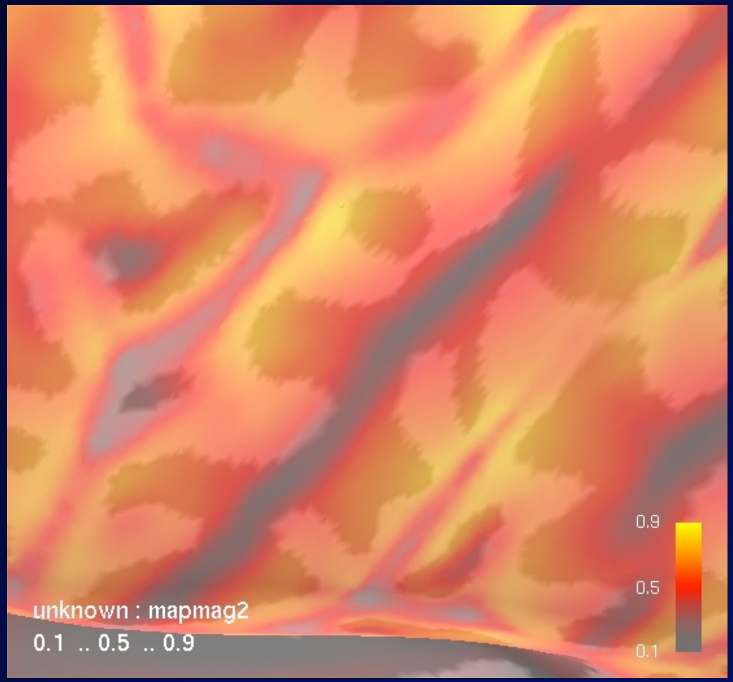


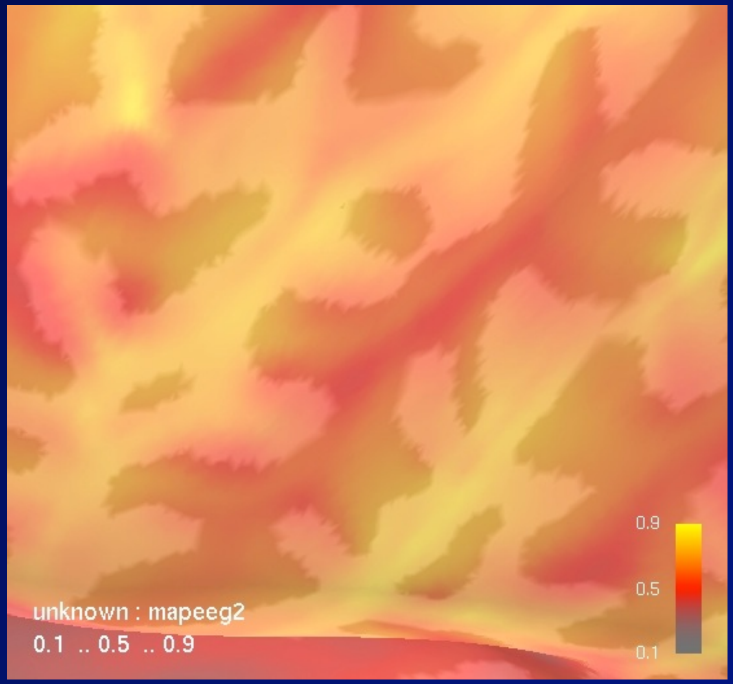
MEG has only one prototypical field pattern

MEG and EEG sensitivity to cortical sources

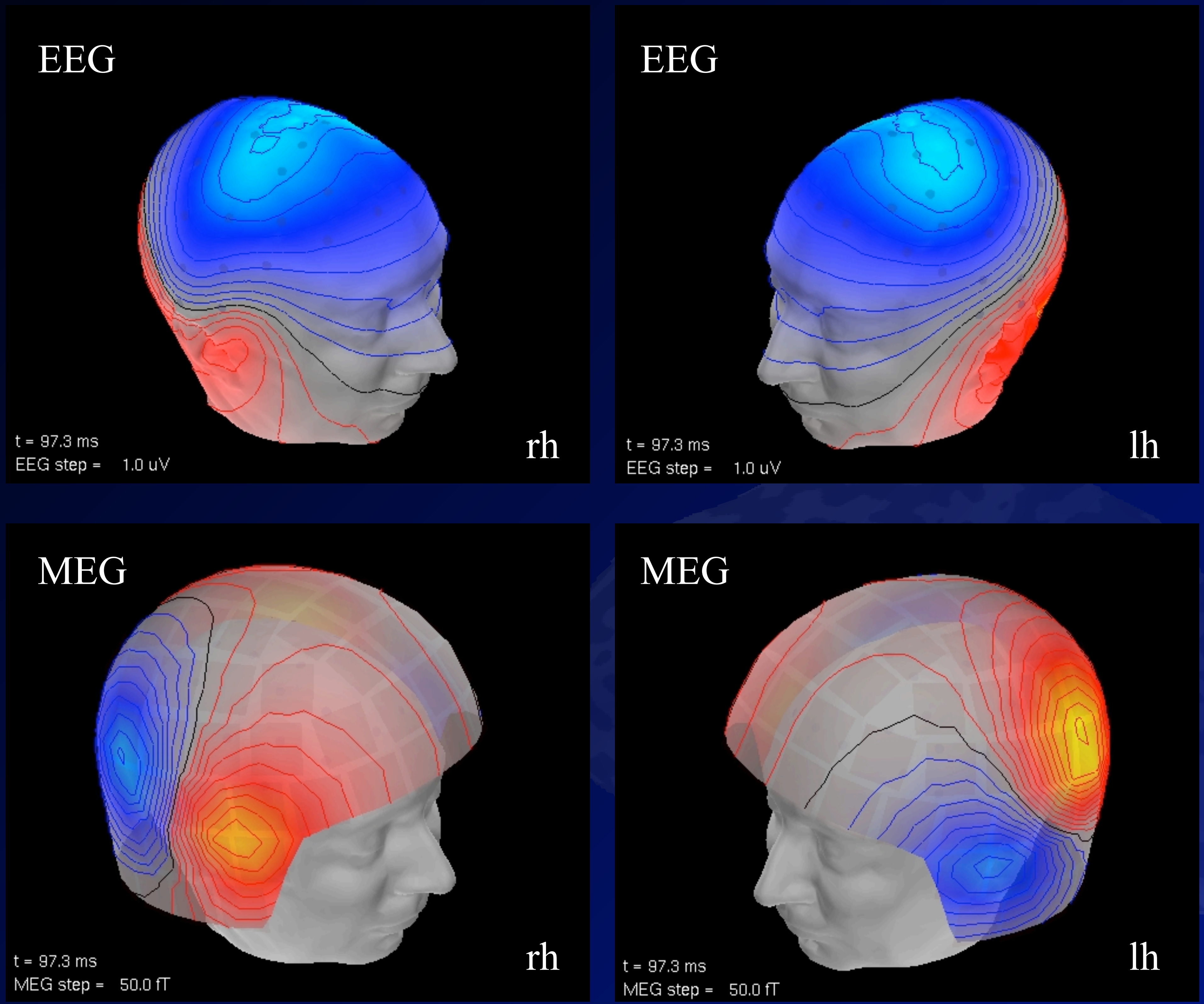






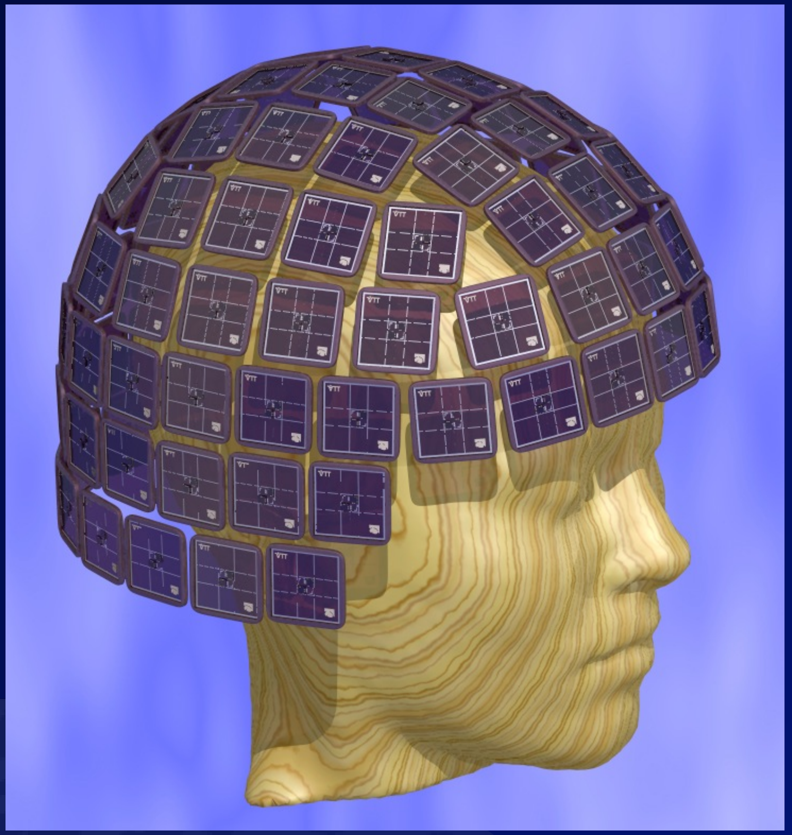


Orthogonal patterns: MEG (or EEG) may benefit



Auditory N100 in EEG and MEG

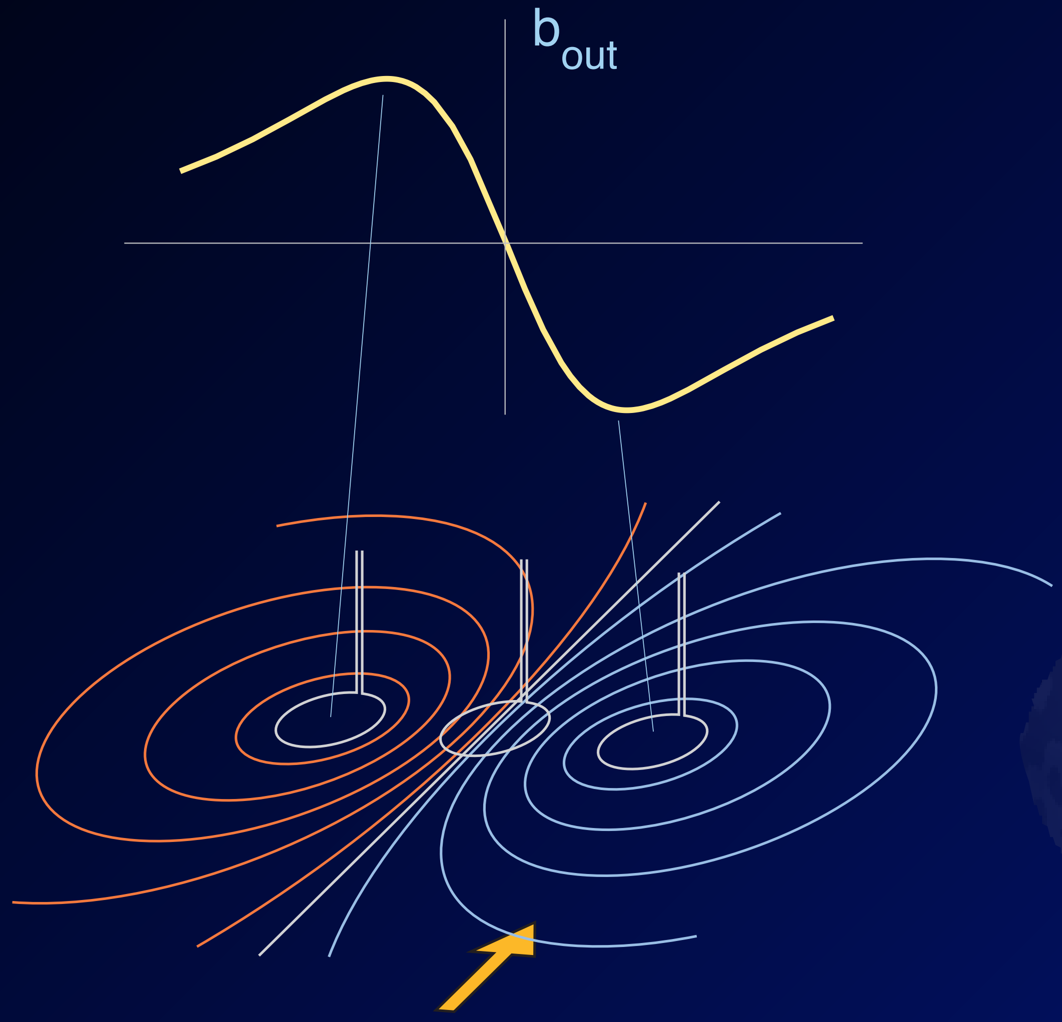
An MEG System



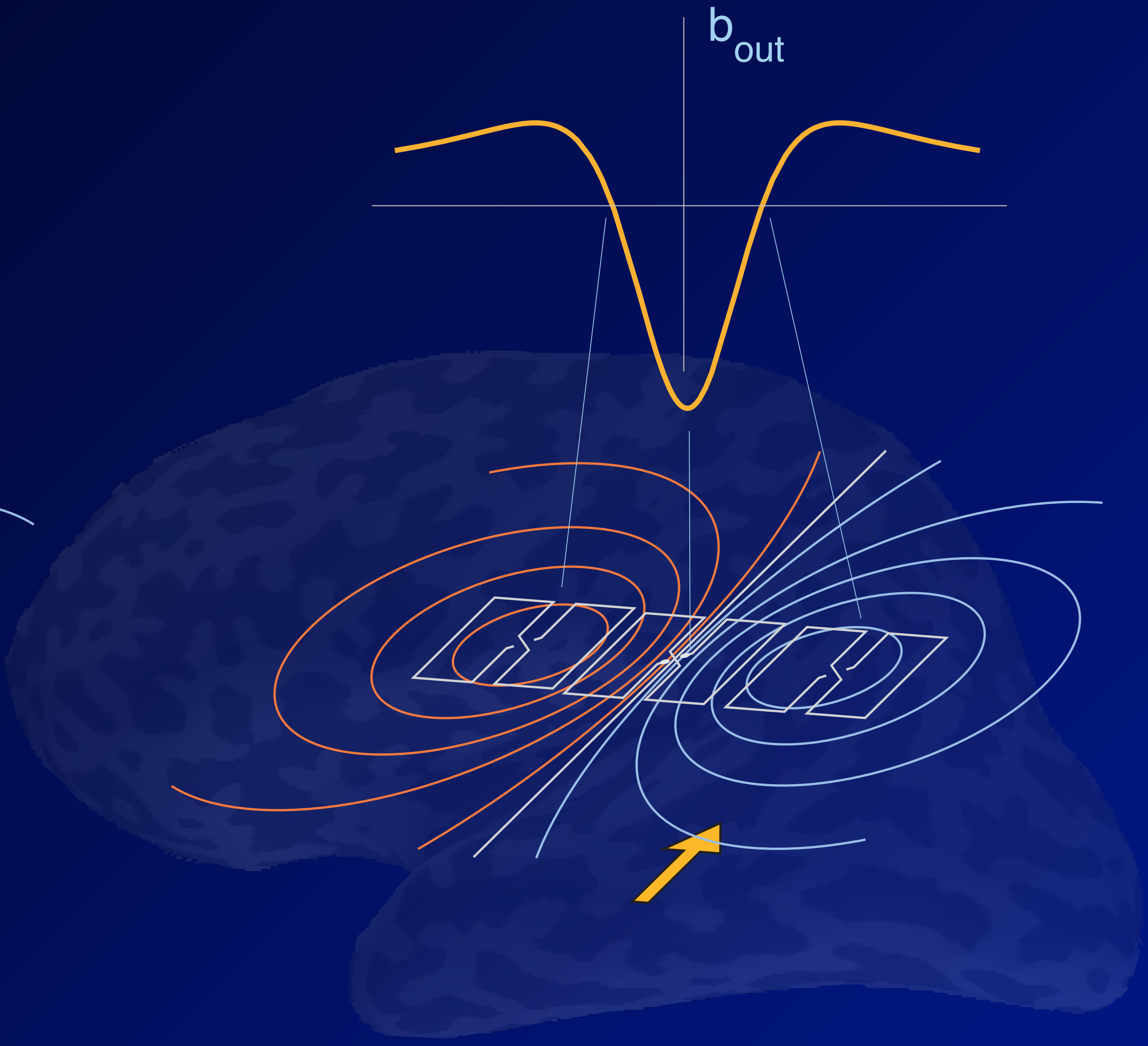
306-channel
SQUID sensor array

Magnetometers and planar gradiometers

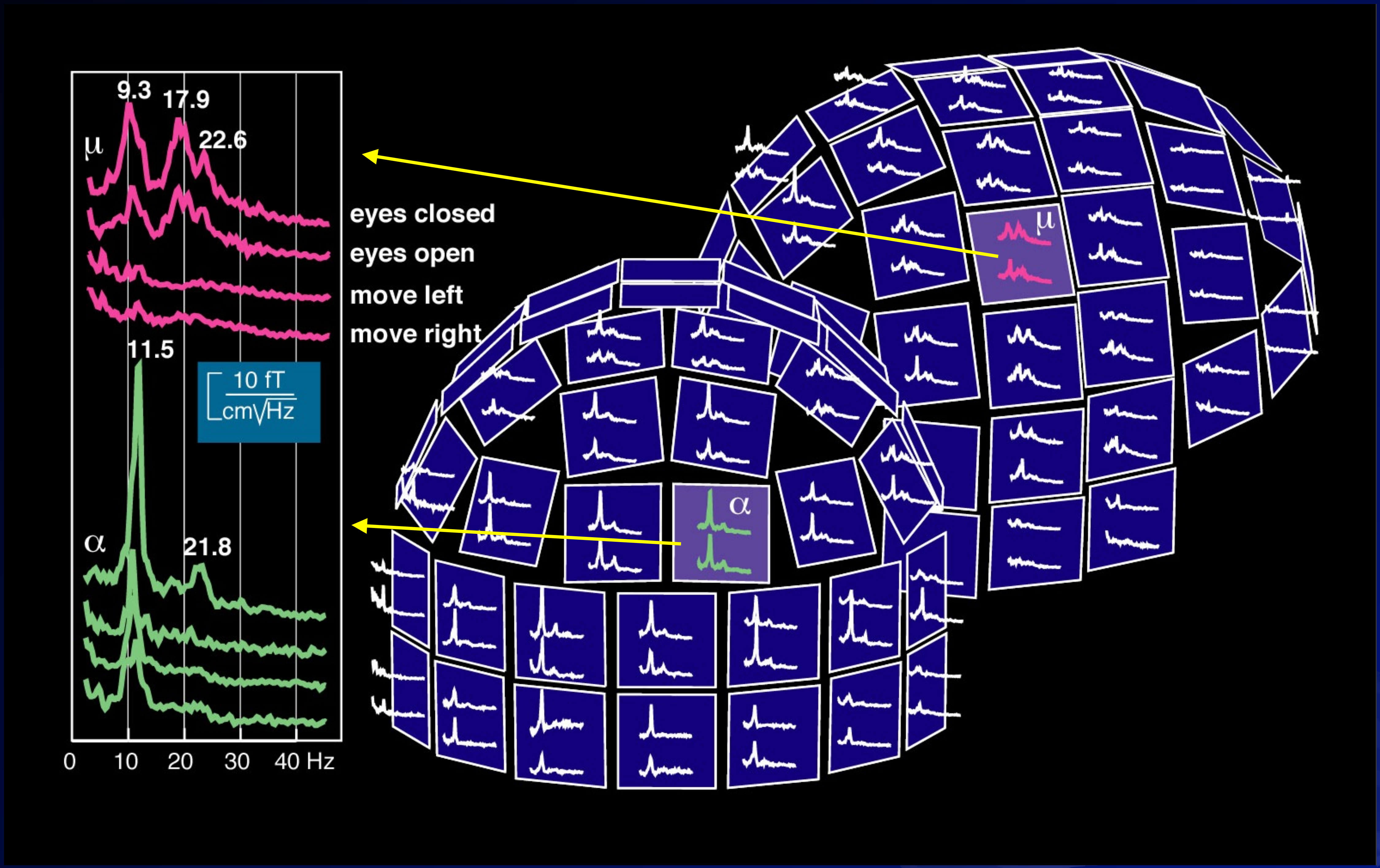
Magnetometer



Planar gradiometer



Modulation of the Alpha and Mu Rhythms



Hari and Salmelin, TINS, 1997

MEG source estimation

The Inverse Problem

- Find the current distribution that generated the measured MEG/EEG

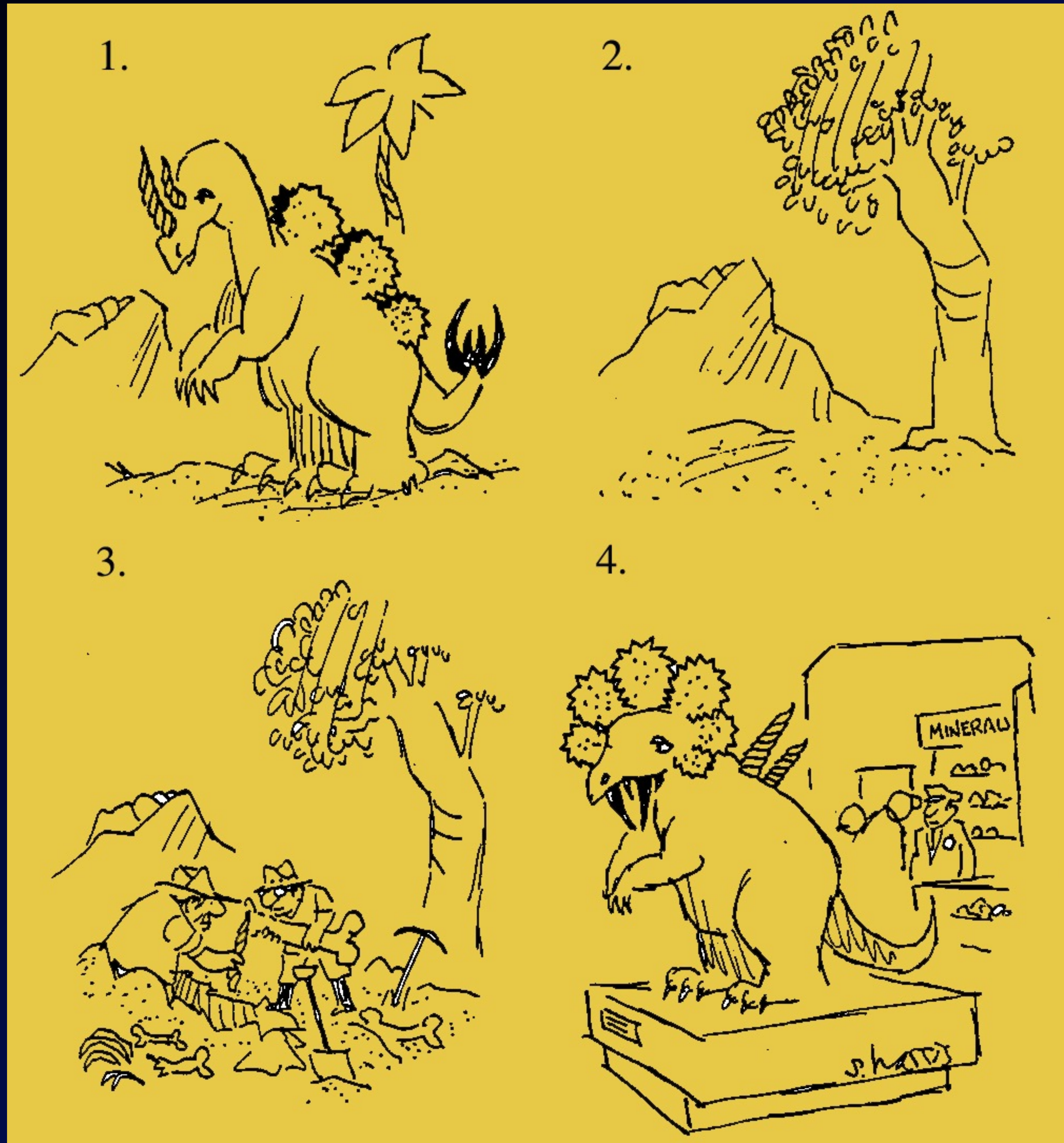
Forward solution

$$\mathbf{y} = \mathbf{G}\mathbf{x} + \mathbf{n}$$

Inverse estimate

$$\{\mathbf{y}, \tilde{\mathbf{n}}; \mathbf{G}\} \rightarrow \tilde{\mathbf{x}}$$

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


1.
2.
3.
4.
MINERAU

Silent sources

No MEG | No EEG | Neither MEG nor EEG

Many Ways to Make the Problem Unique

- Parametric models
  - Assume a limited number of dipoles
  - Overdetermined: more measurements than source parameters
  - Solution obtained by a least squares fit
- Current distribution models
  - Many sources in a volume or on a surface
  - Need an additional constraint: minimize a norm of the current distribution while matchingn the data
  - MNE: overall power minimized
  - Sparse estimates: L1 or mixed-norm approaches

Terminology

- Source model: the elementary source = current dipole
- Inverse model: the definition of the optimality criteria
- Focal source: activated area of small extent

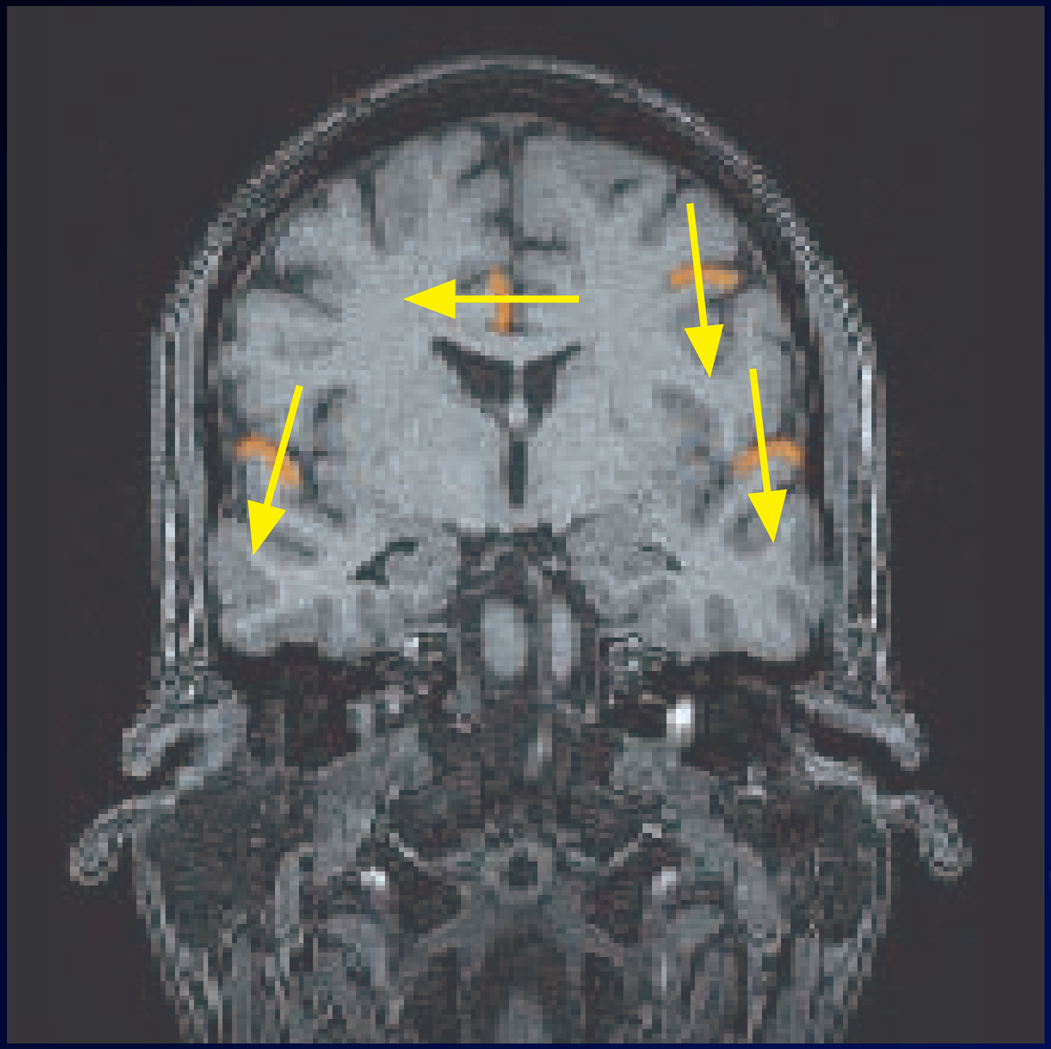
- Extended source: activated area of larger extent

- Distributed sources: many focal or extended sources in different areas of the brain
- Forward model: method for computation of the MEG signals for a given source

$$\sigma = \sigma(r)$$

Discoveries with dipole models

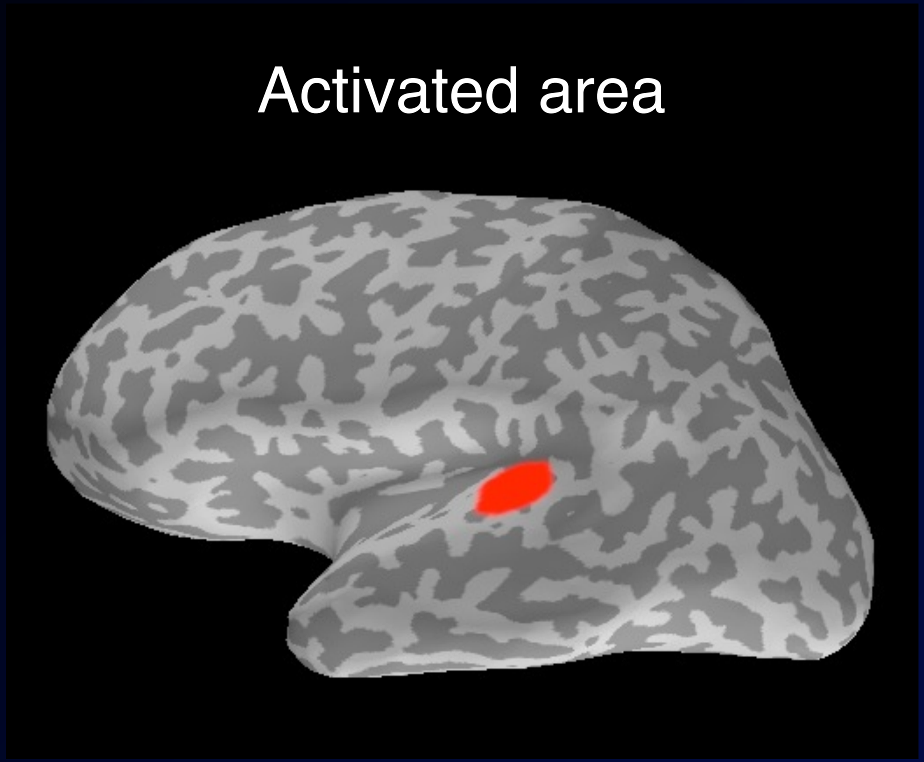
Example: The time-varying current-dipole model

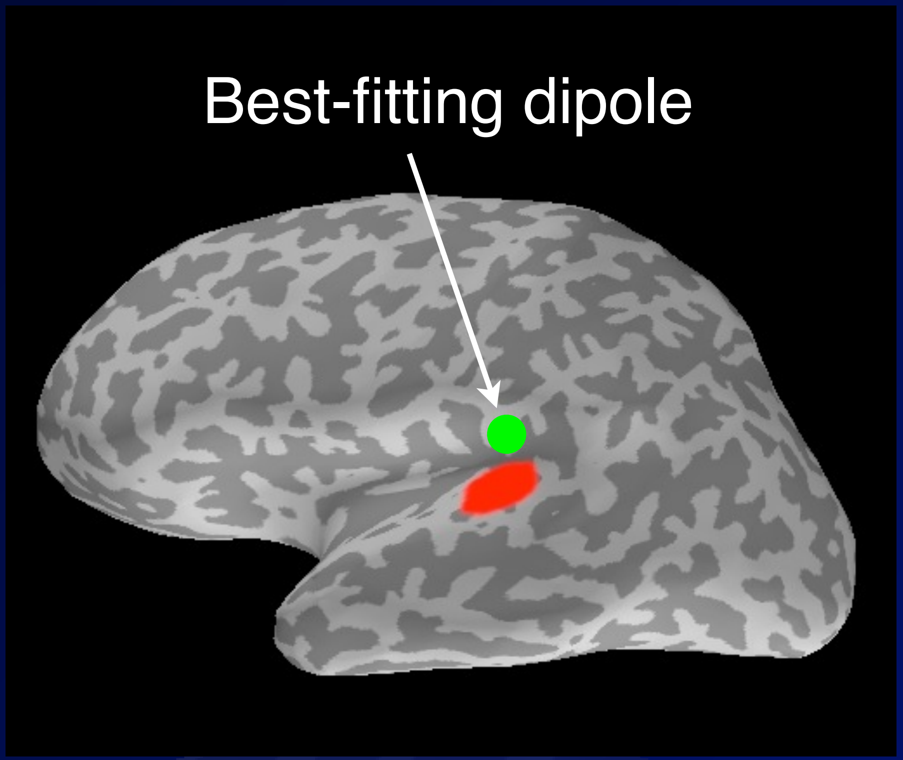


- The neural currents on a few-cm^2 patch of cortex are approximated with a current dipole
- Dipole locations are fixed over time
- Dipole amplitudes are allowed to vary

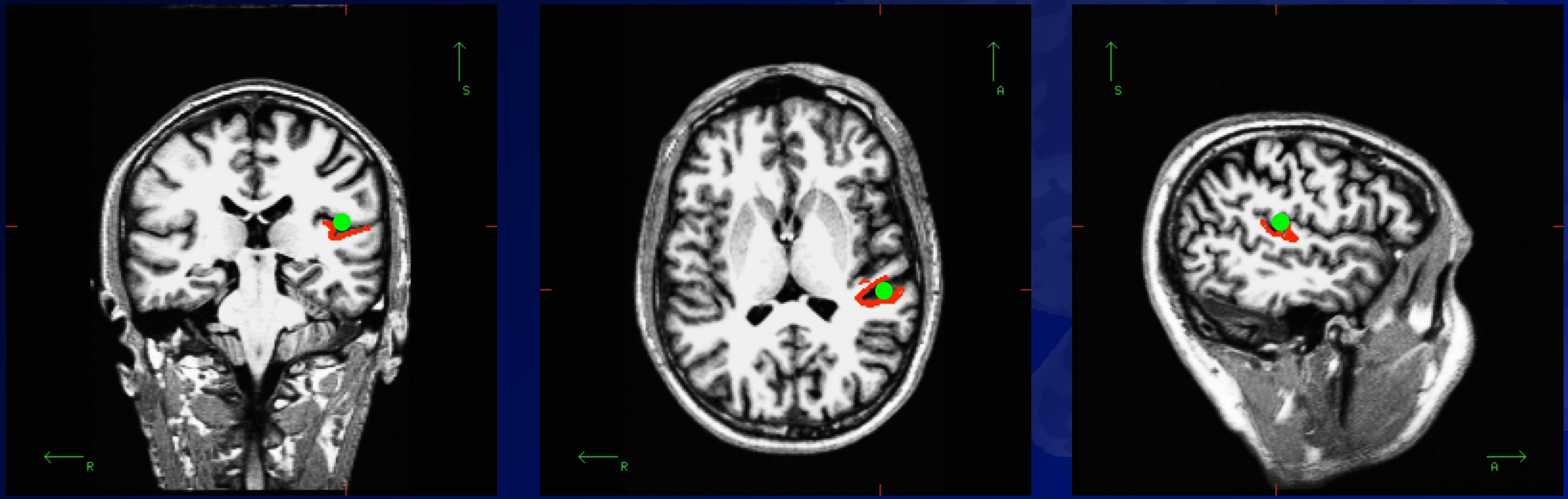
Scherg *et al.*, 1984

Are dipoles good for extended sources?





gof = 99.9%



Fitting

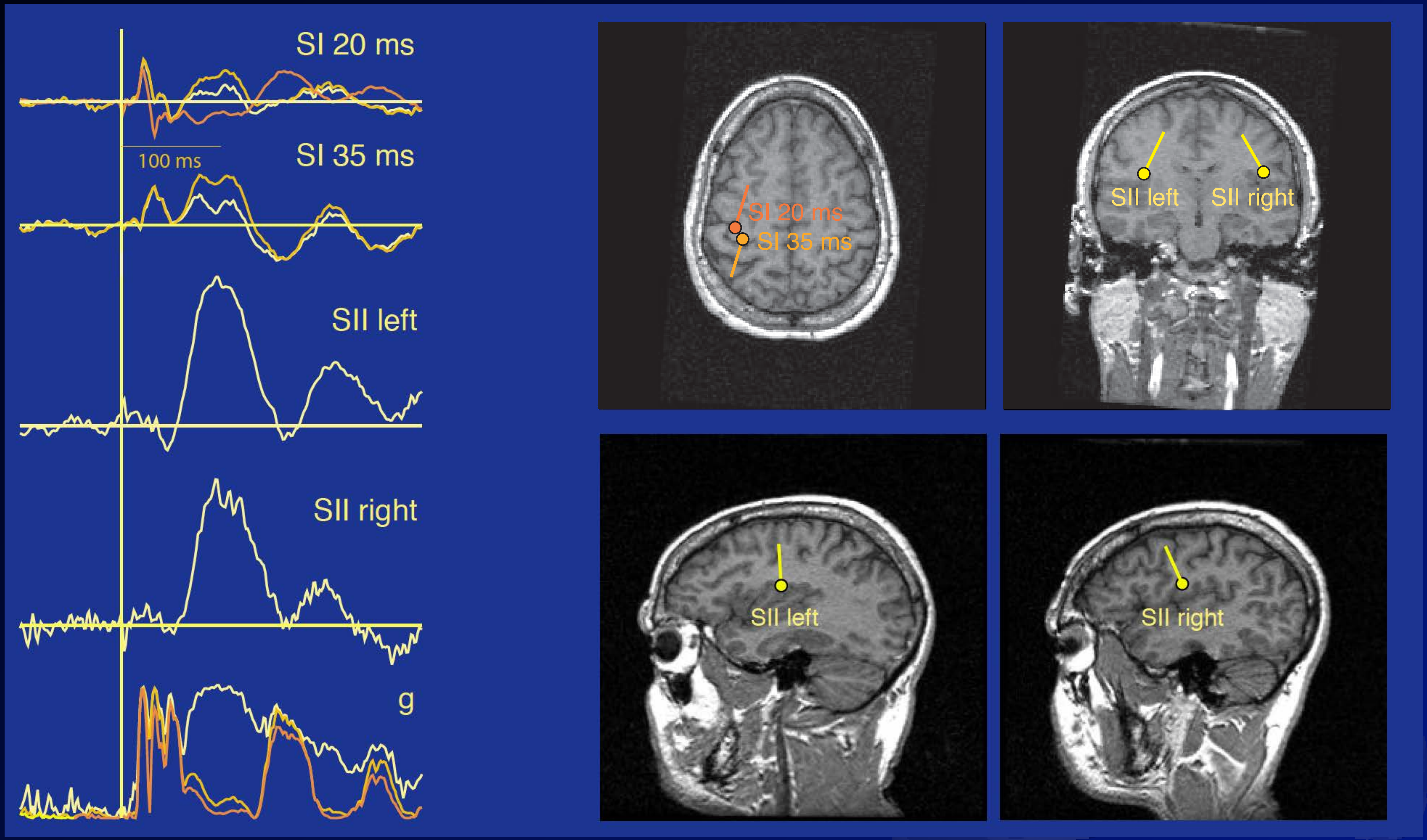
$$\{\hat{\mathbf{q}}_p, \hat{\mathbf{r}}_p\} = \mathrm{argmin}_{\{\mathbf{q}_p, \mathbf{r}_p\}} ||\mathbf{B}_{\mathrm{meas}} - \mathbf{B}_{\mathrm{model}}||^2$$

1. Select the number of dipoles
2. Select initial guesses for dipole locations
3. Calculate the smallest least-squares error between the measurement and the model data achievable by adjusting the dipole orientations and amplitudes at these location
4. If error is the same as in previous iteration step, STOP
5. Find better candidates for the dipole locations
6. Go back to step 3.

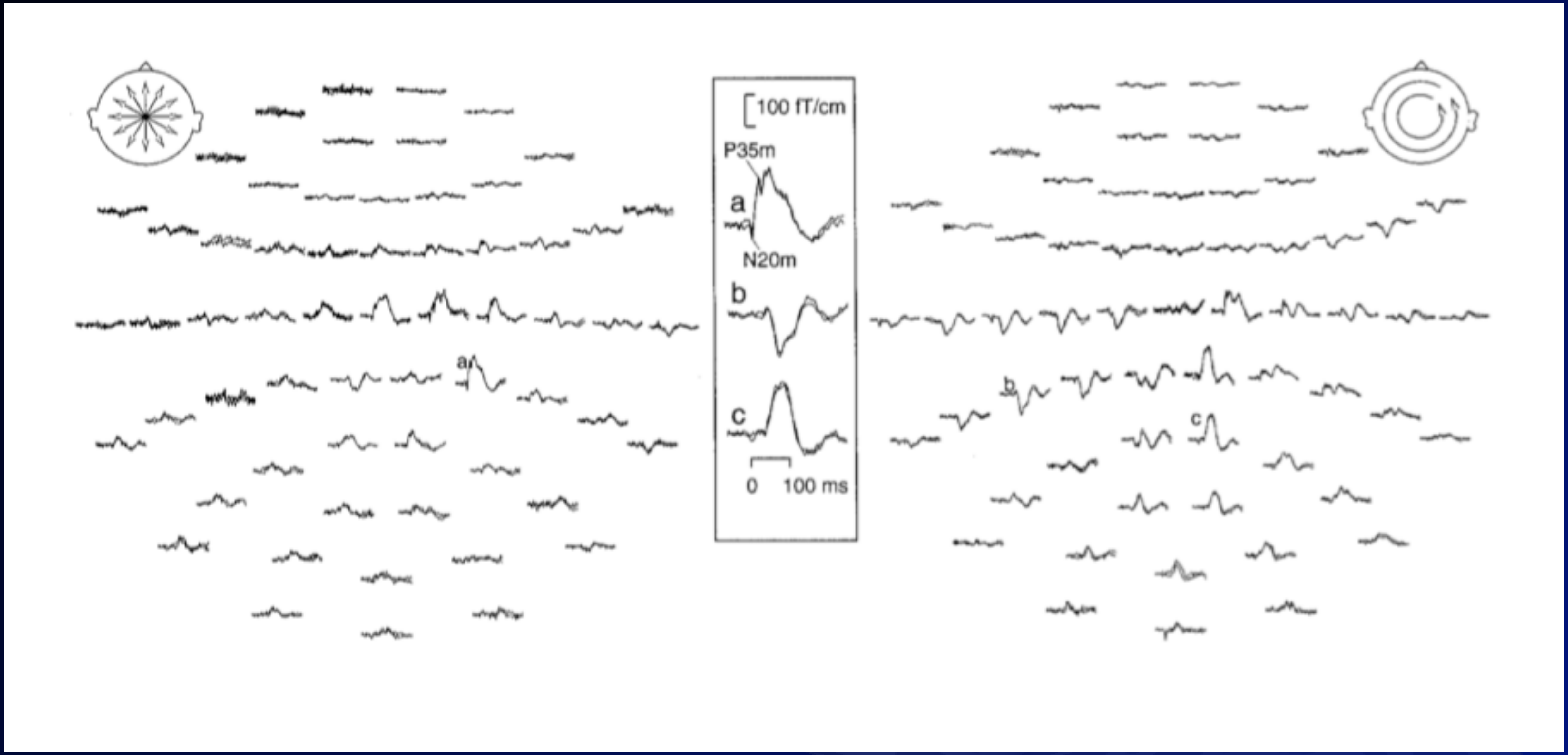
Partly Heuristic strategies

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

Multidipole Model for SEF

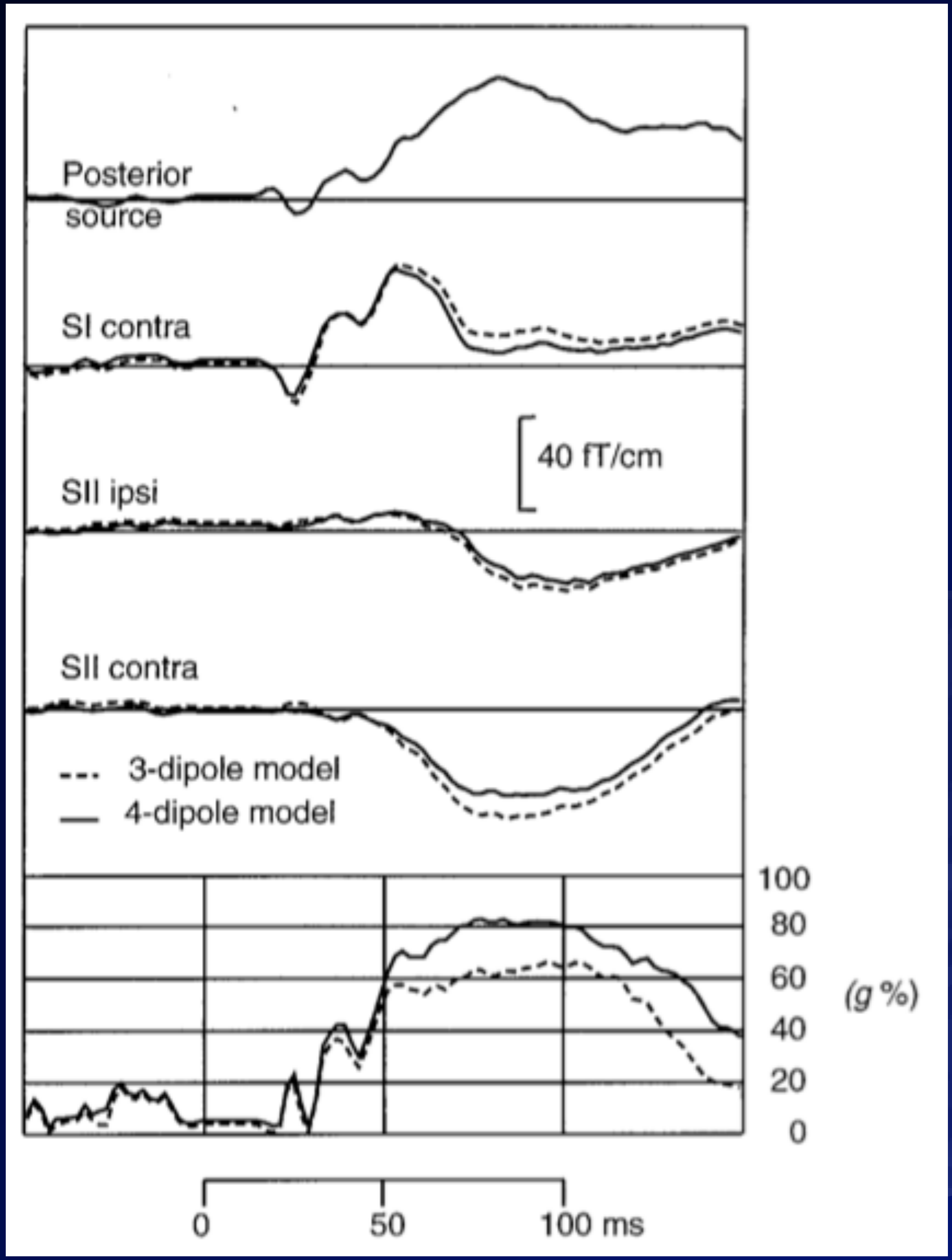


Finding SEF Responses at PPC



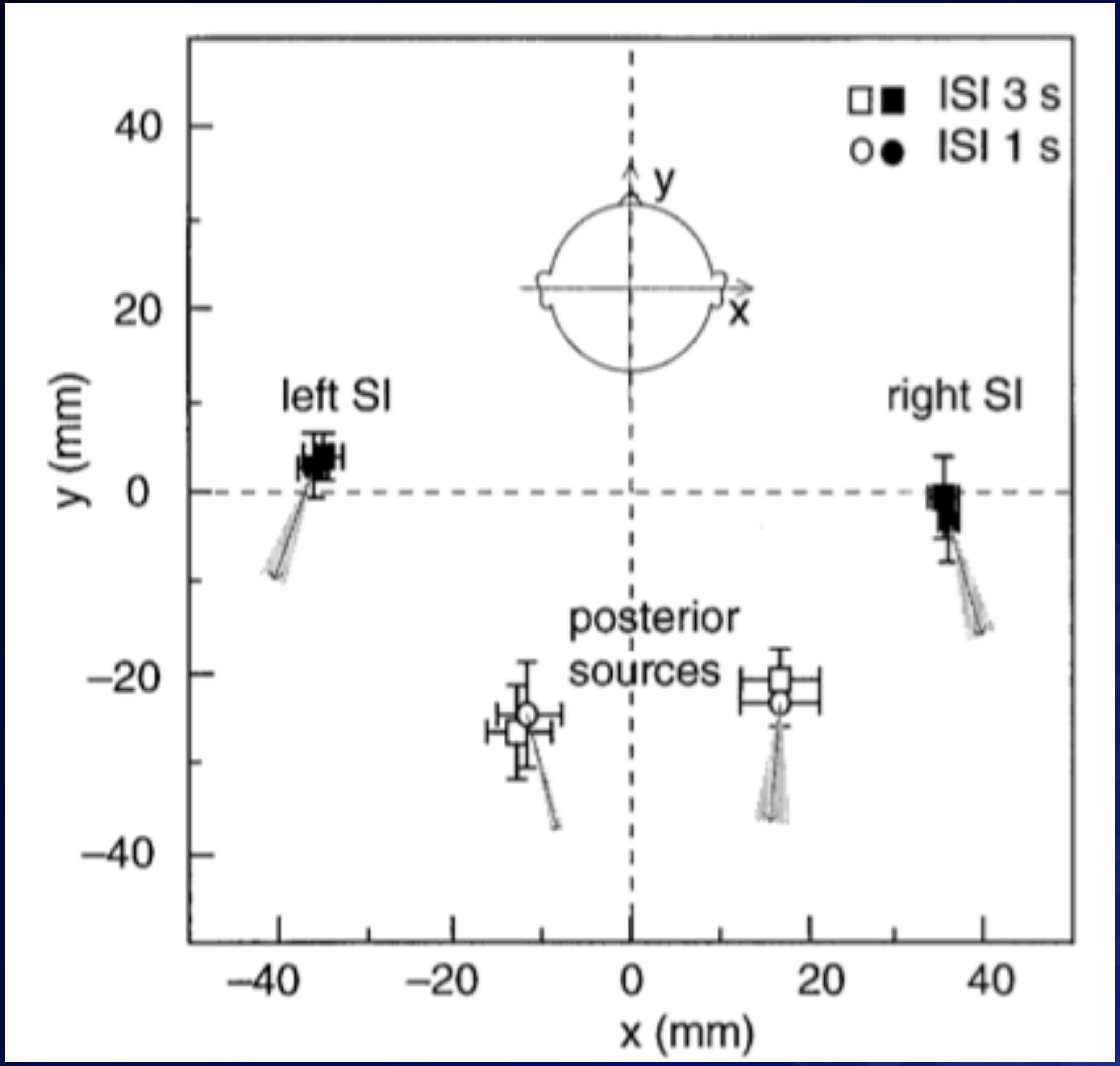
Forss et al., Exp. Brain Res., 1994

The PPC Source Does not Interact with the others



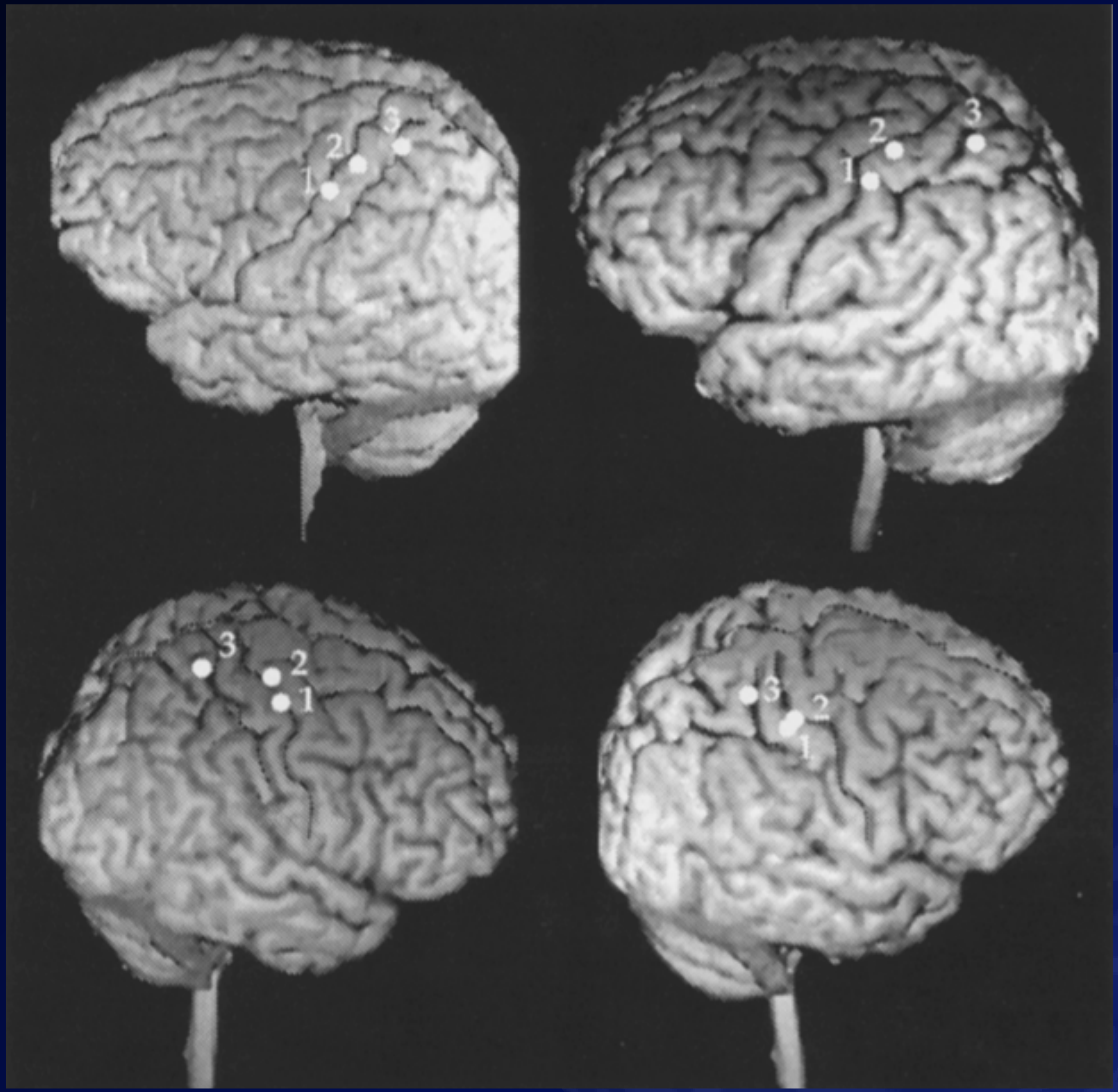
Forss et al., Exp. Brain Res., 1994

The Source Locations are Consistent



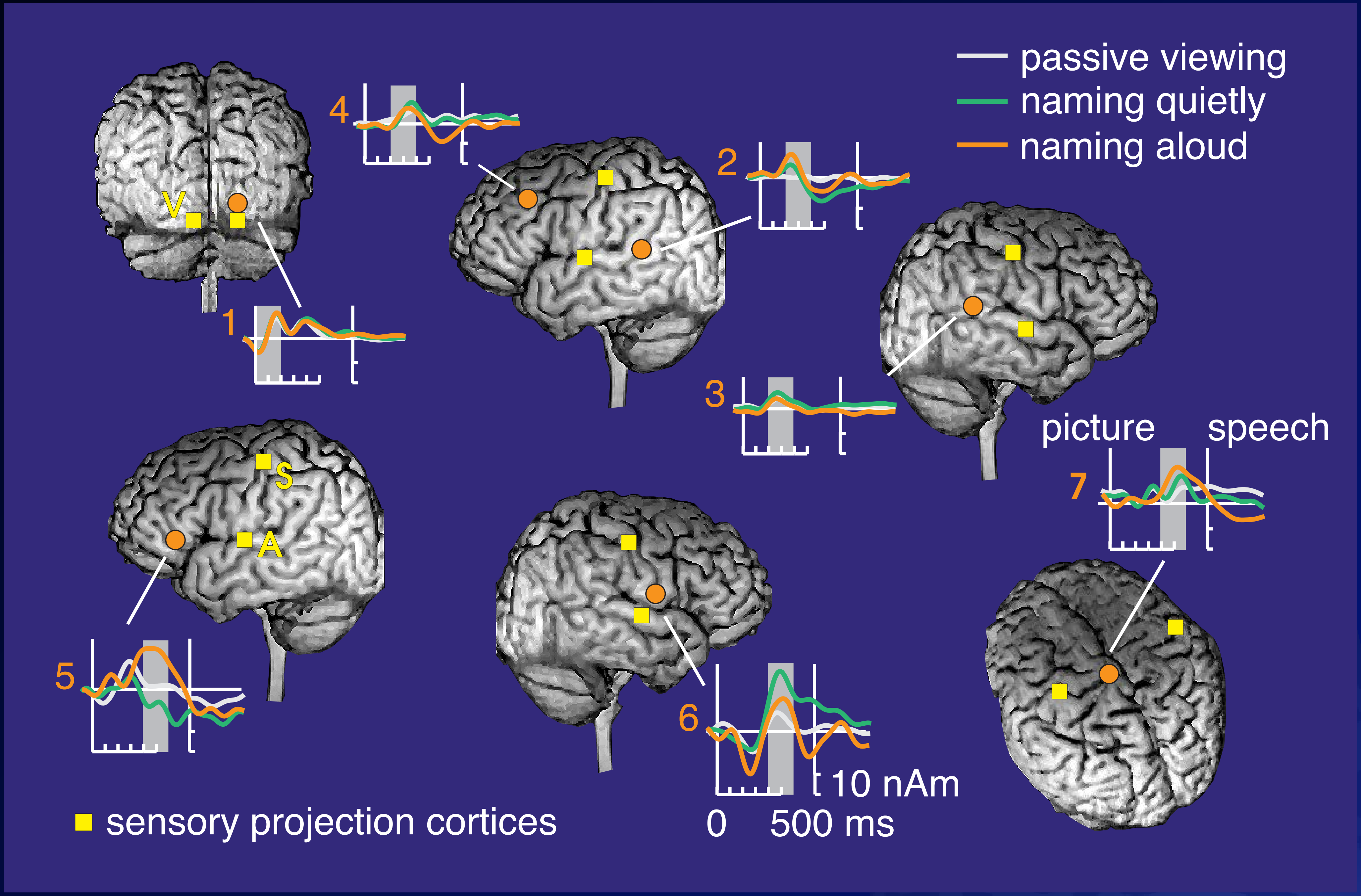
Forss et al., Exp. Brain Res., 1994

The Location at the Postcentral Sulcus Makes Sense



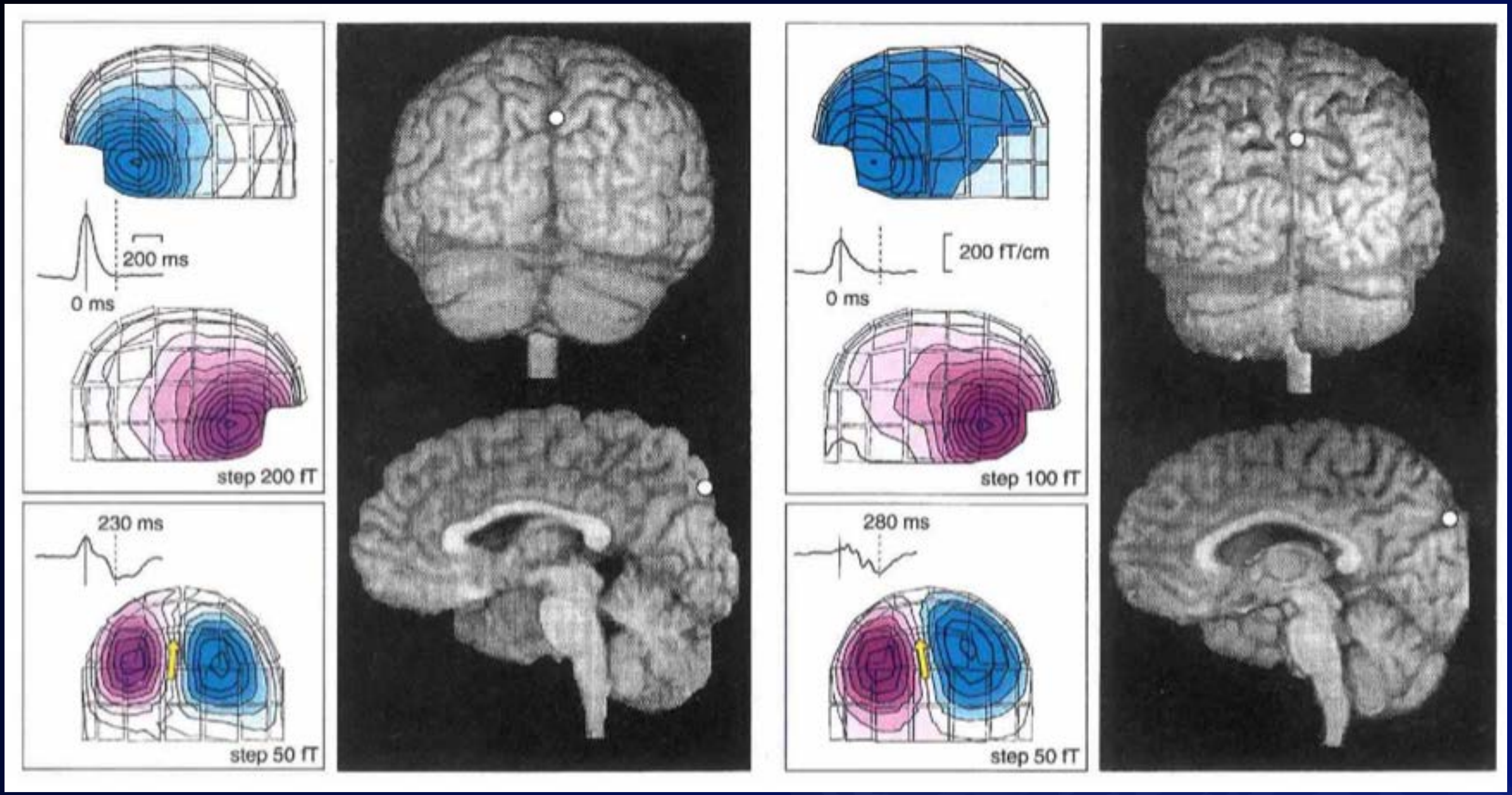
Forss et al., Exp. Brain Res., 1994

Dynamics of Cortical Activity in a Picture Naming Task



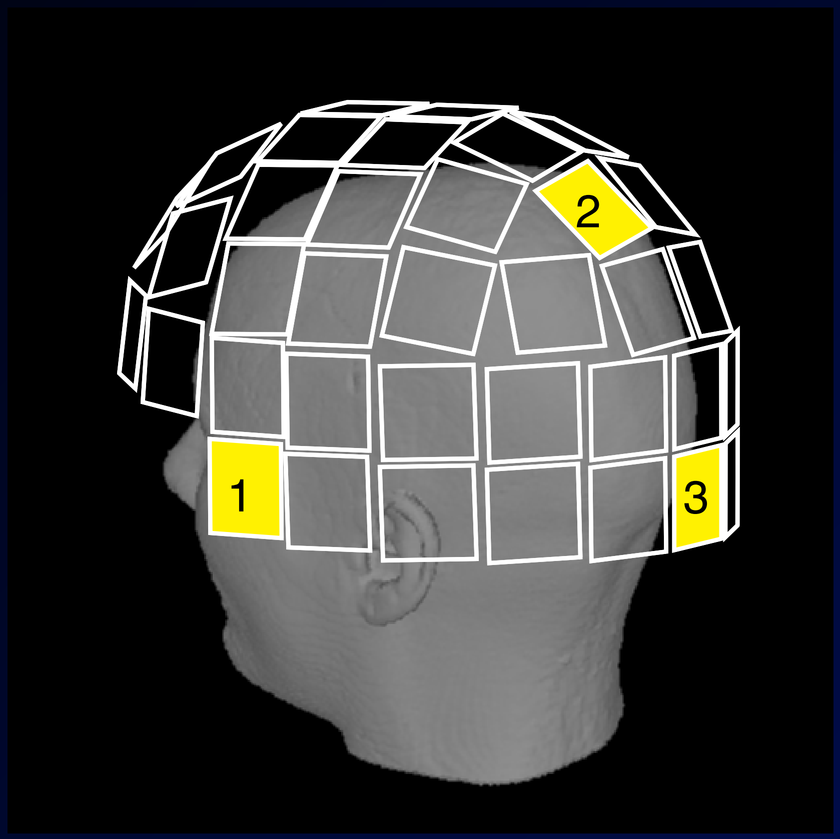
Salmelin et al., Nature, 1994

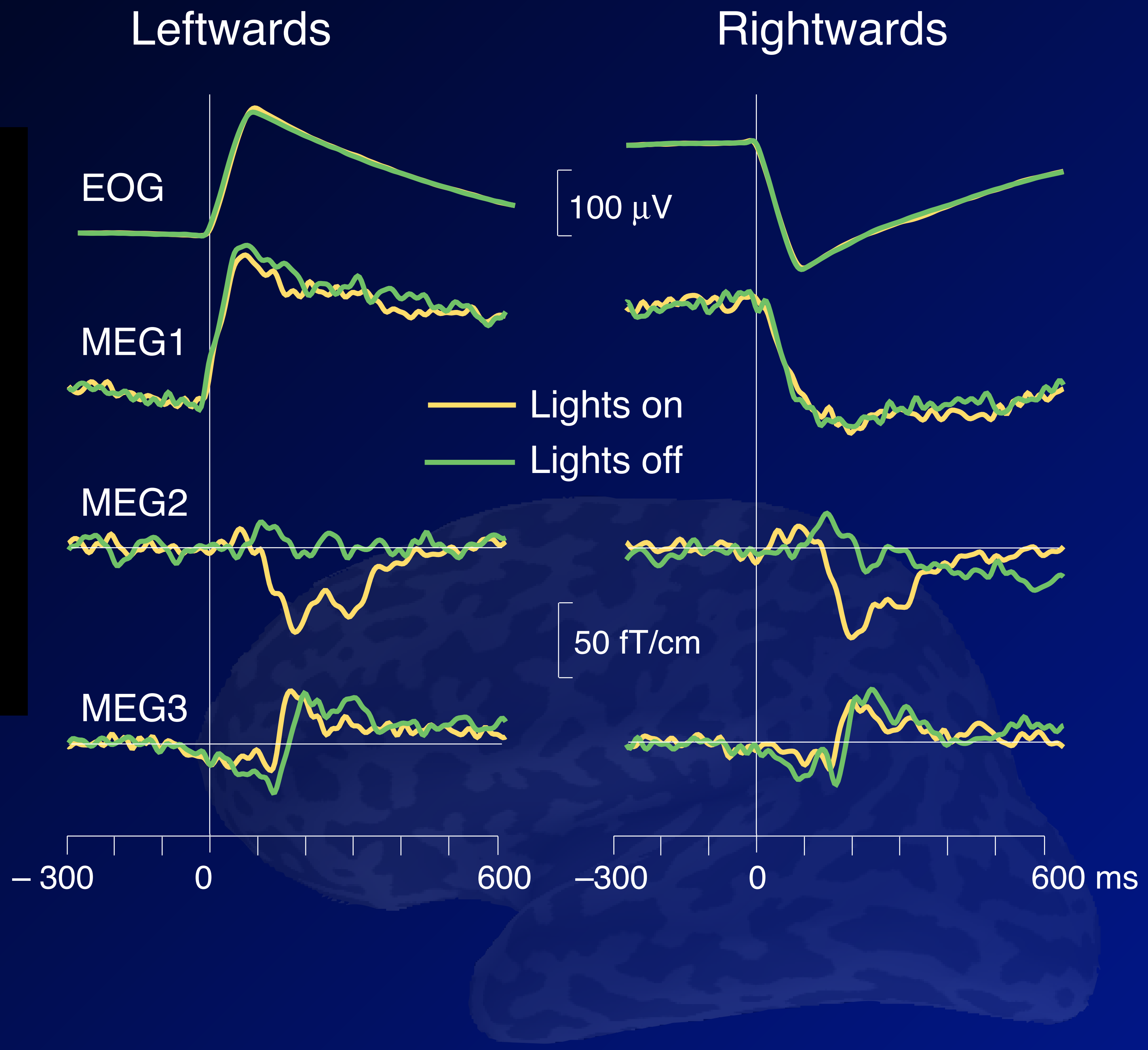
Visual Stability During Eye Blinks



Hari et al., Nature, 1994

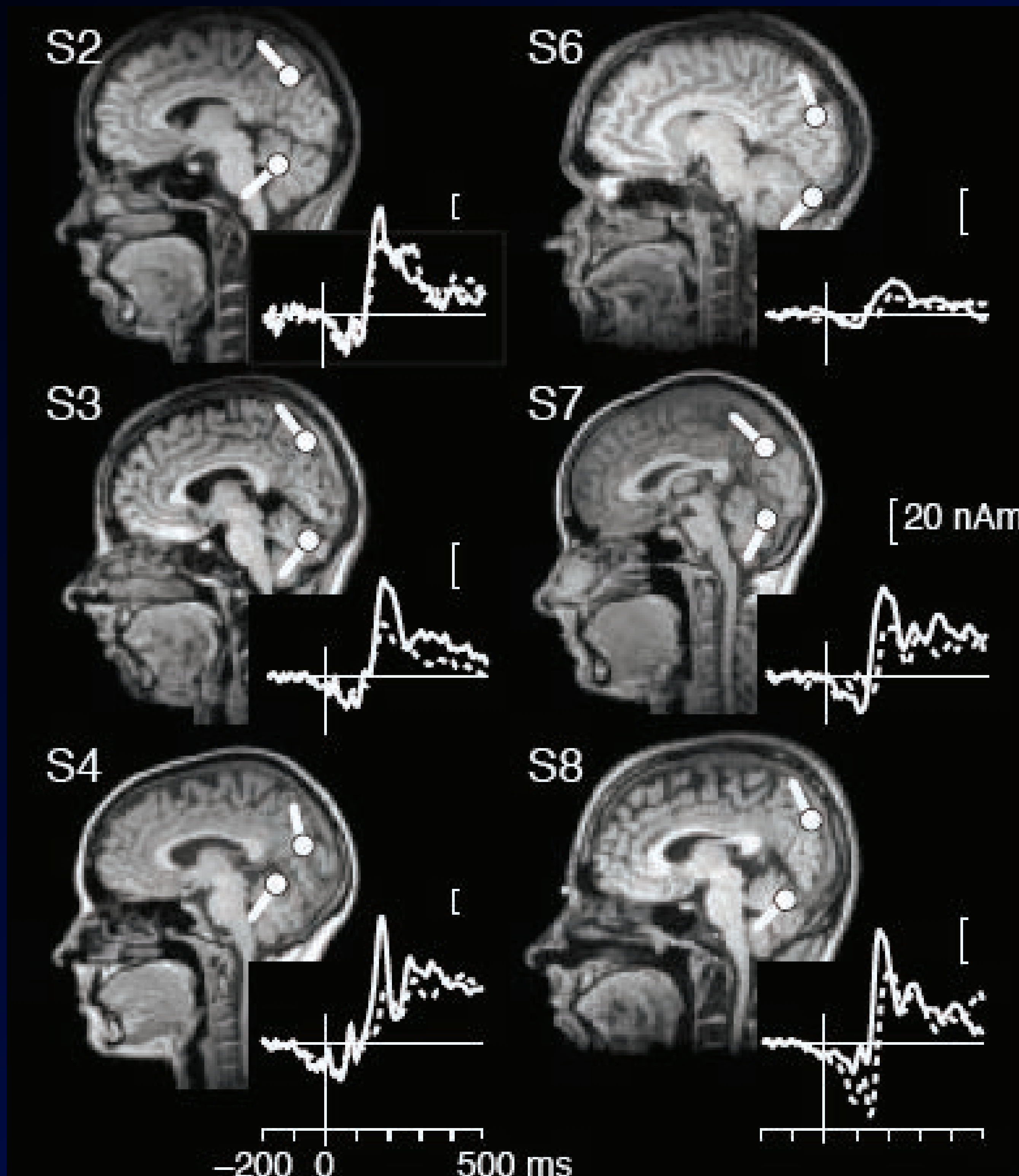
Cerebellar activity associated with saccades





Jousmäki et al., 1996

Source locations and time courses

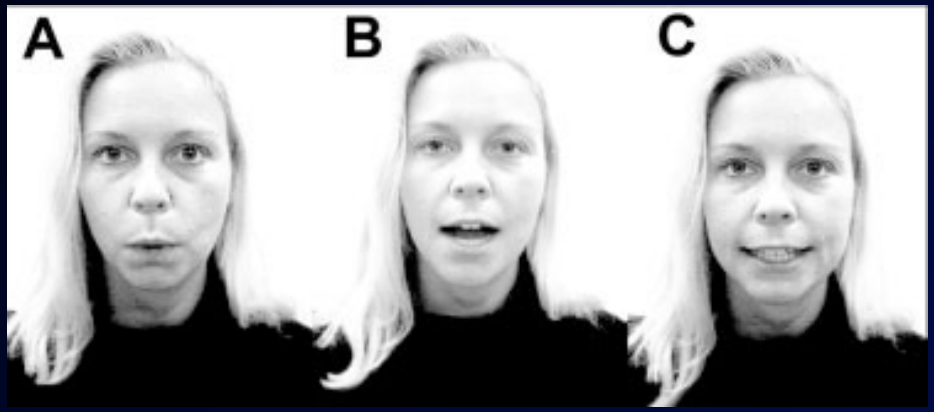


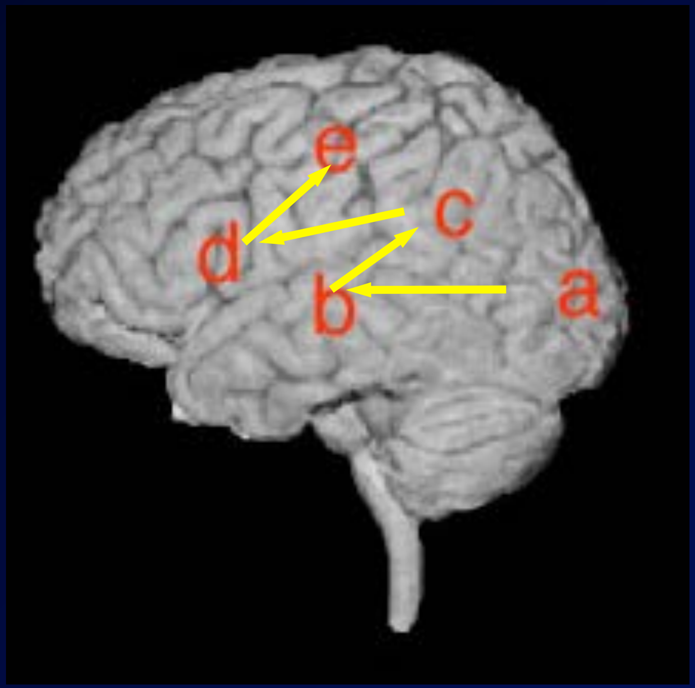
Lights on

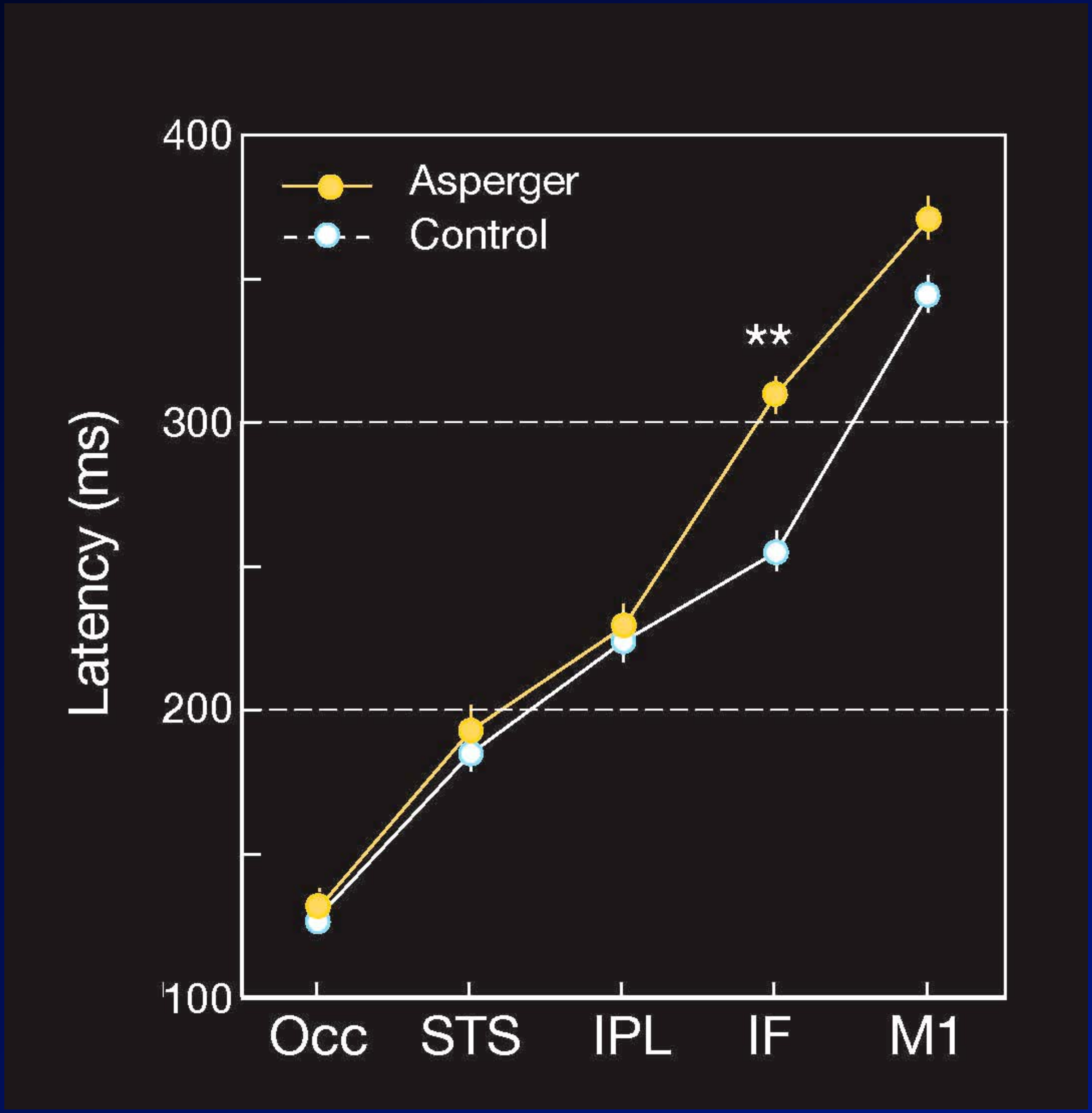
Lights off

Jousmäki et al., 1996

Imitation of orofacial gestures



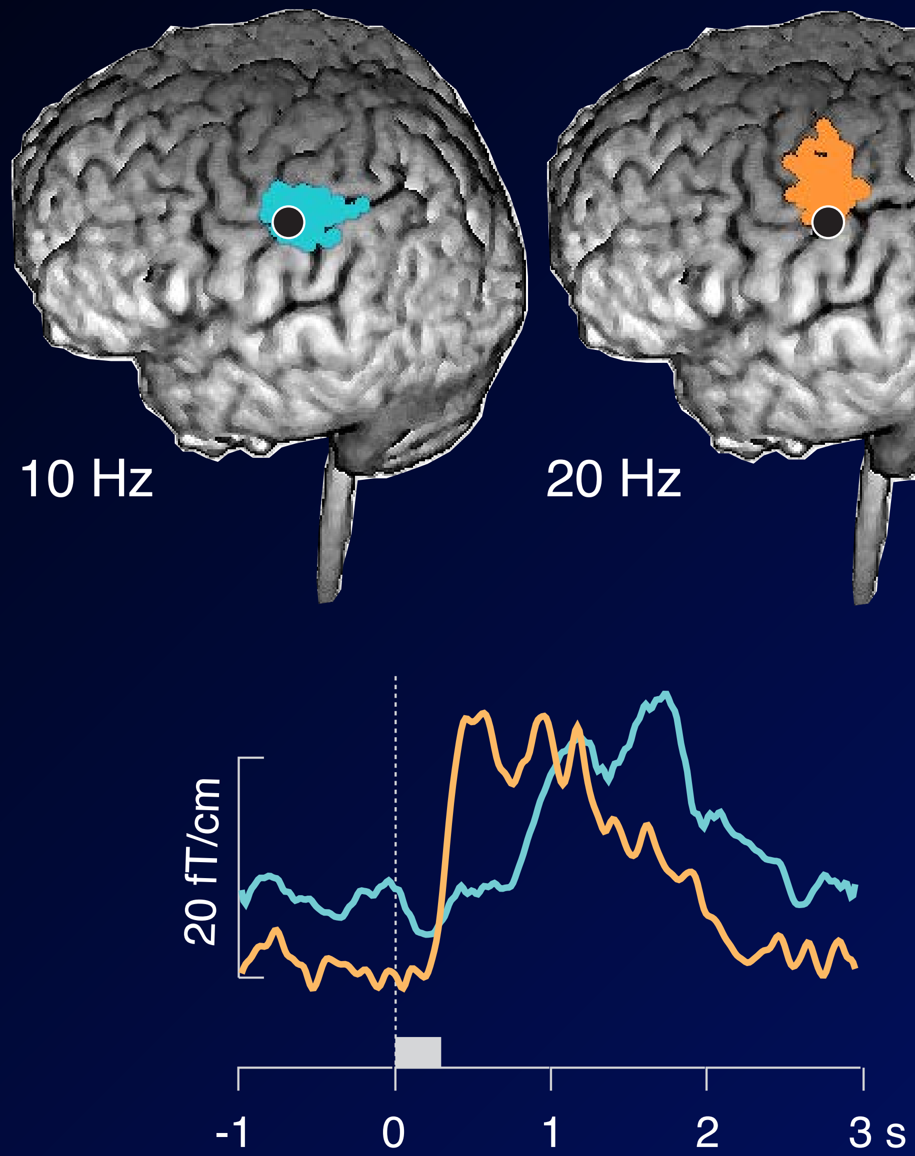




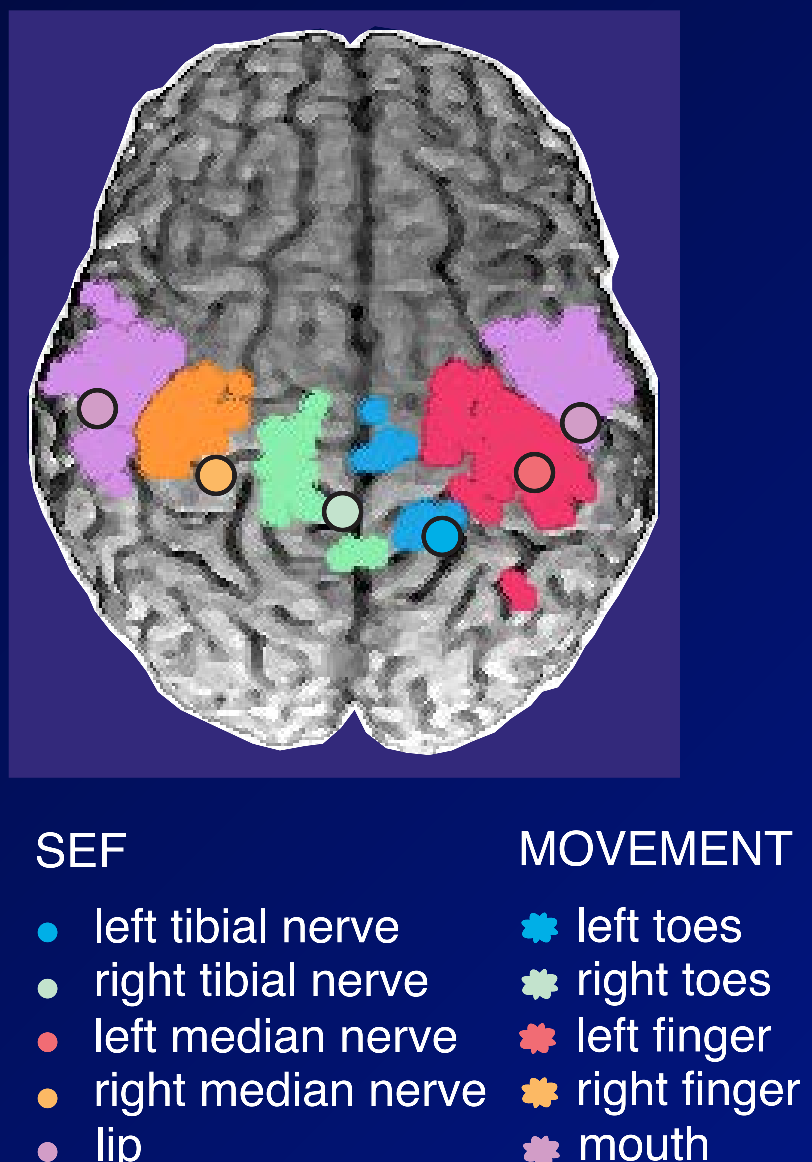
Nishitani & Hari, Neuron 2002; Nishitani et al. Ann Neurol 2004

Spatiotemporal analysis of the somatomotor (μ) rhythms

- Modulation with finger movements



Homunculus of the 20-Hz component



Salmelin *et al.*, NeuroImage, 1995

Dipole models: Summary

- Can be used in a wide variety of situations
- The multi-dipole model can be considered to be an interactive hypothesis testing tool:
  - Build the model
  - Check model significance: should the model be rejected?
  - Check parameter significance (model identifiability): confidence intervals
  - For the significance testing to succeed, noise estimates must be reasonably accurate
- Usually cortical constraints are not applied: dipoles positions can compensate for an inaccurate forward model and as a result the time courses are more accurate
- Dipoles are equivalent sources: the information about source extent is only indirect

“Statistics are really not necessary. I only conduct experiments in which the result is clear.”

Ragnar Granit

Anatomically and functionally constrained source estimates

Minimum-Norm Solutions

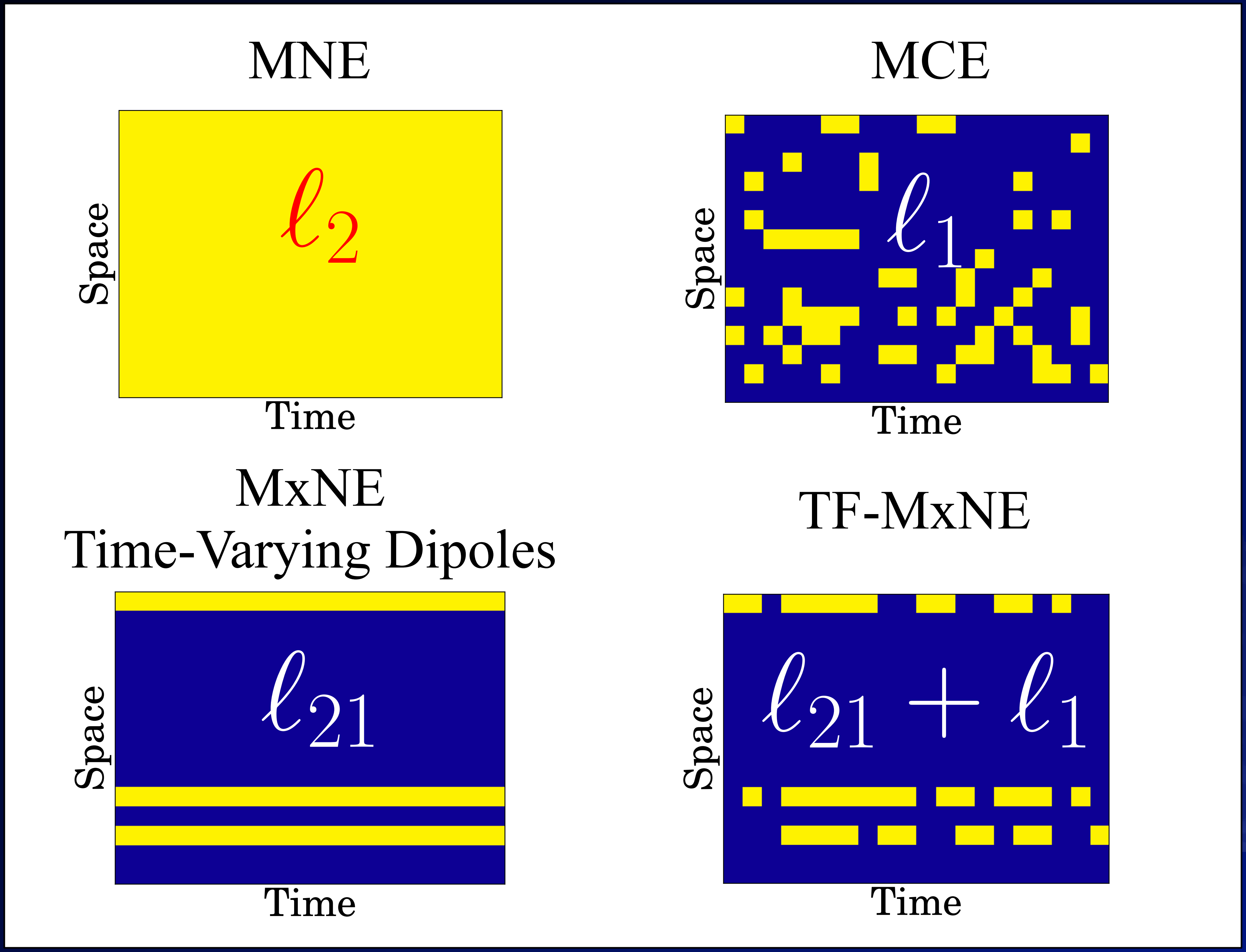
- Grid of dipoles in a volume or on a surface
- Underdetermined: $n_{sources} \gg n_{meas}$
- Find an optimal solution among those fitting the data

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

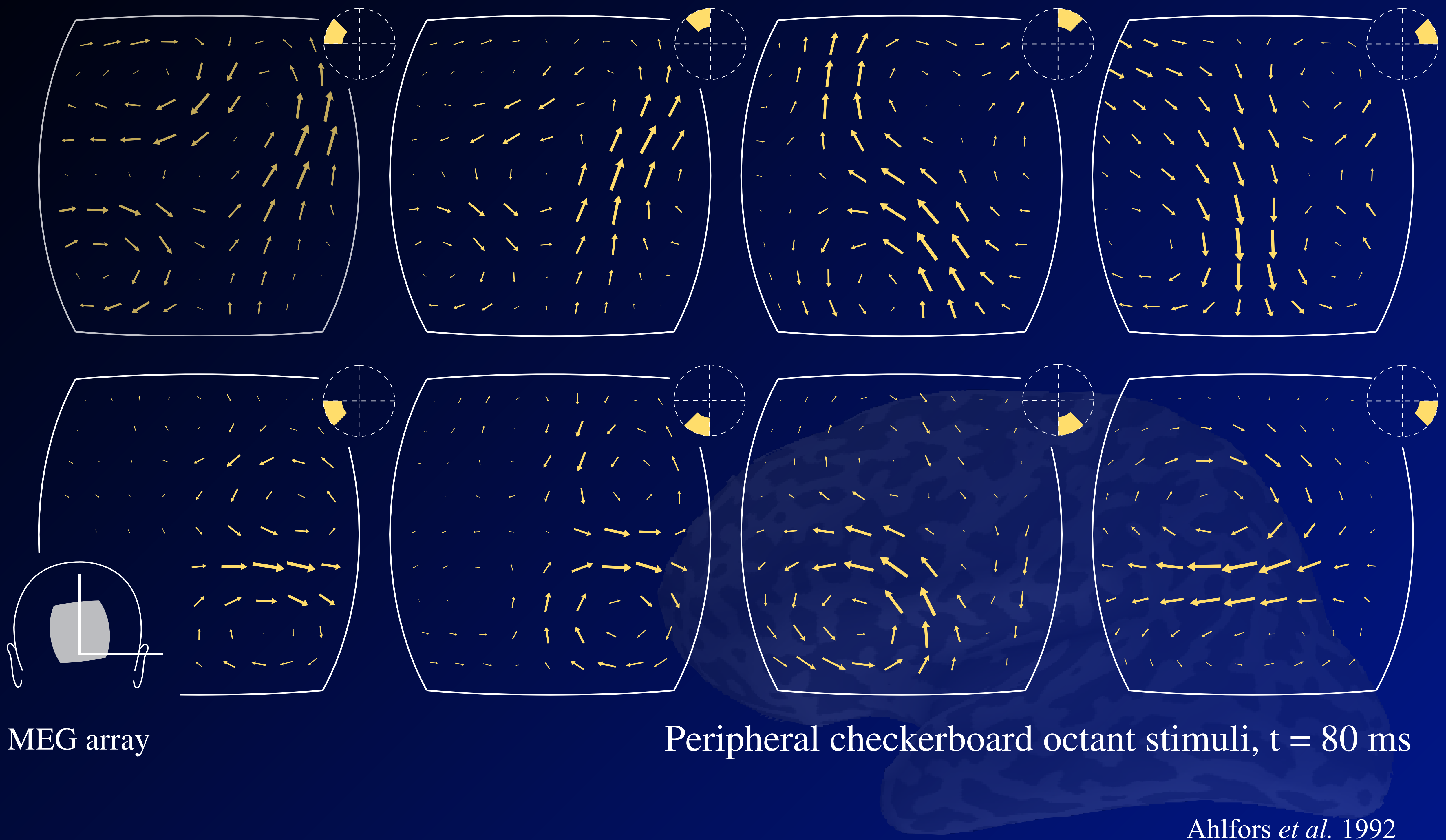
Source modeling priors

- Discrete dipole model: only a few active areas of small extent
- Minimum-norm estimate (MNE): distributed source image, minimum power
- Minimum-current estimate (MCE): sparse estimate, minimum sum of amplitudes
- Mixed-norm estimates (MxNE): sparse in space, smooth in time

Spatio-Temporal Structure of Source Estimates



Early retinotopic mapping with MNE



MEG array

Peripheral checkerboard octant stimuli, t = 80 ms

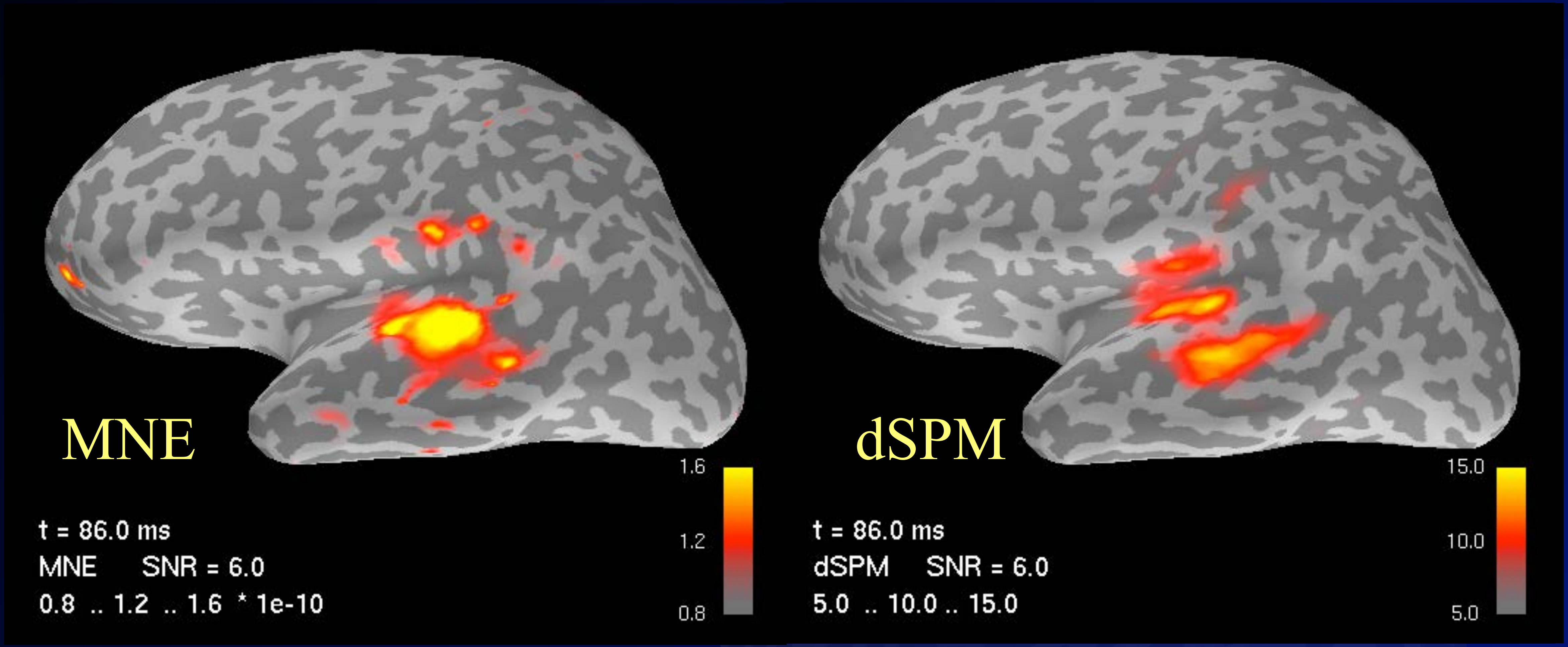
Ahlfors *et al.* 1992

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

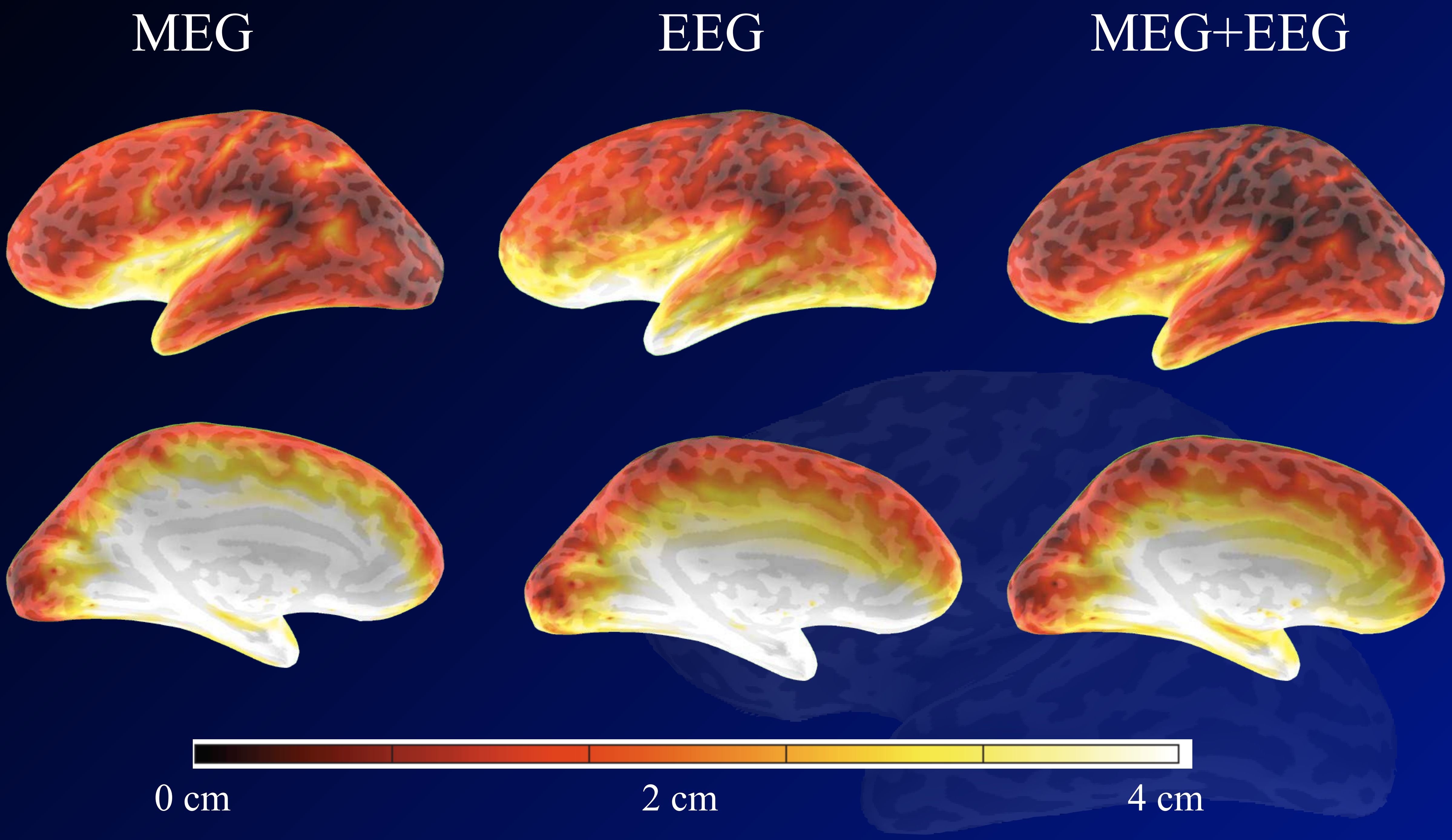
Dale *et al.* 2000

Effect of the orientation constraint



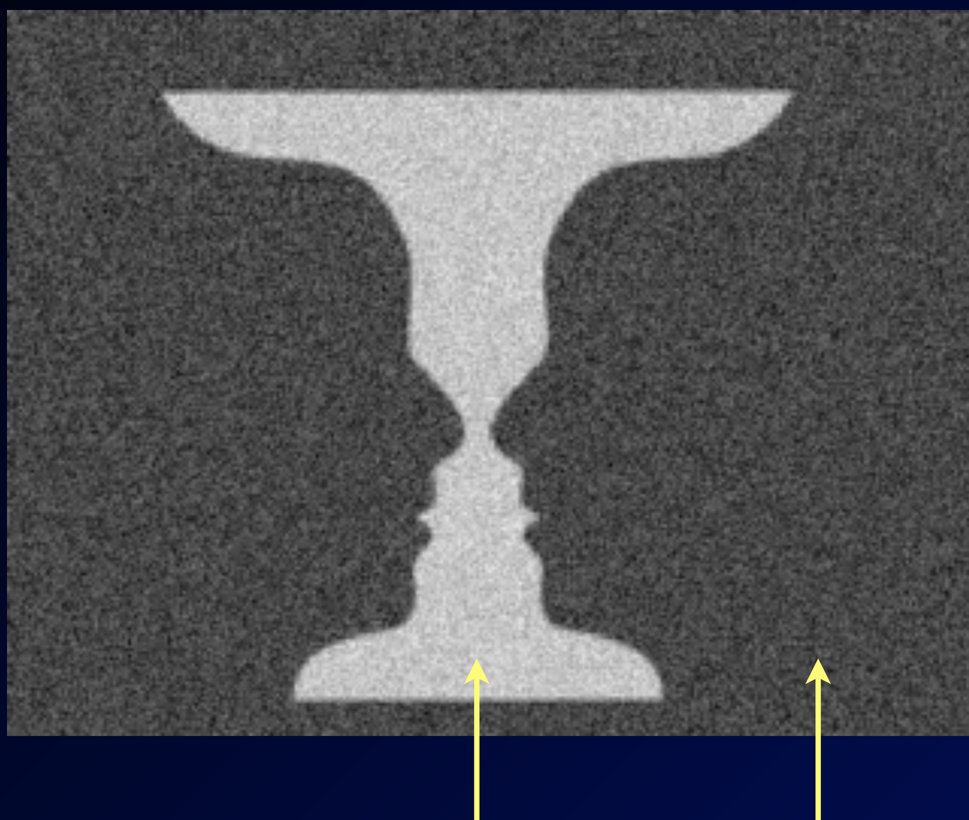
- Auditory responses to short tones
- Depth-weighted MNE and dSPM
- The orientation constraint rules out infeasible sources

Spatial dispersion of cortically-constrained MNE



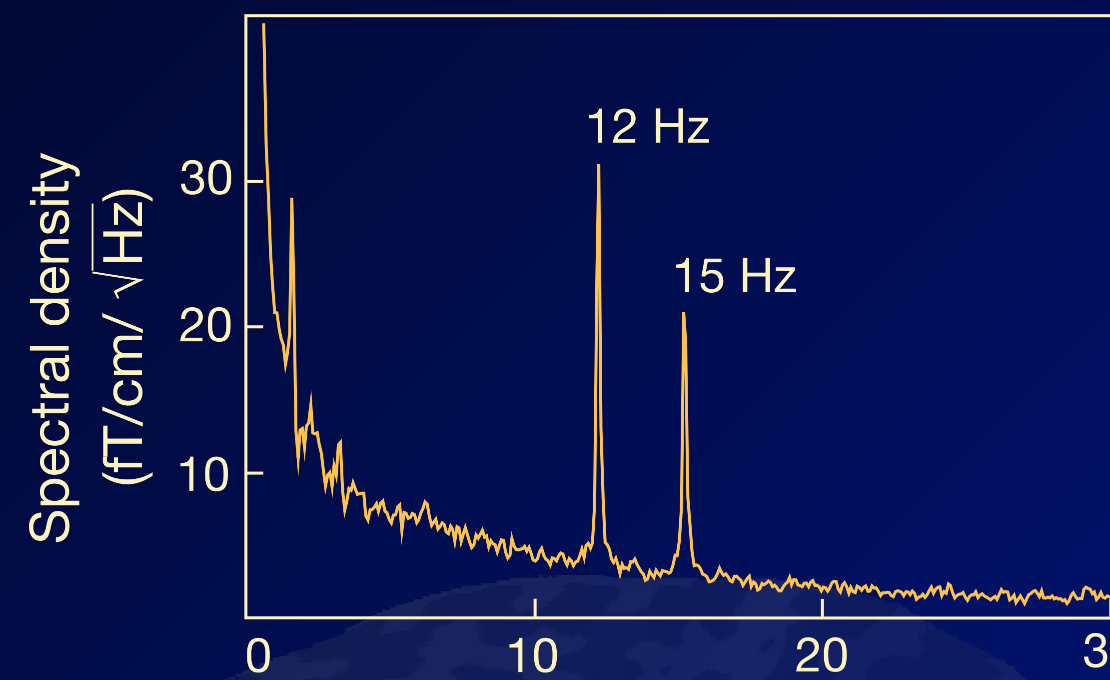
Molins *et al.* 2008

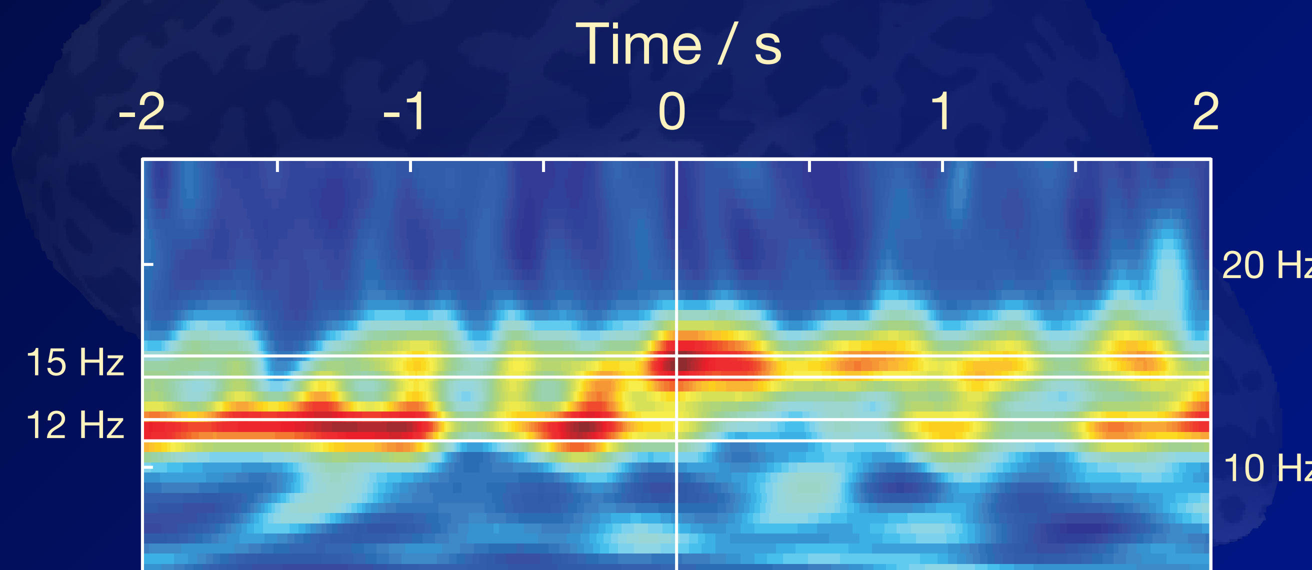
Visual percepts of an ambiguous scene



Noise: 12 Hz 15 Hz

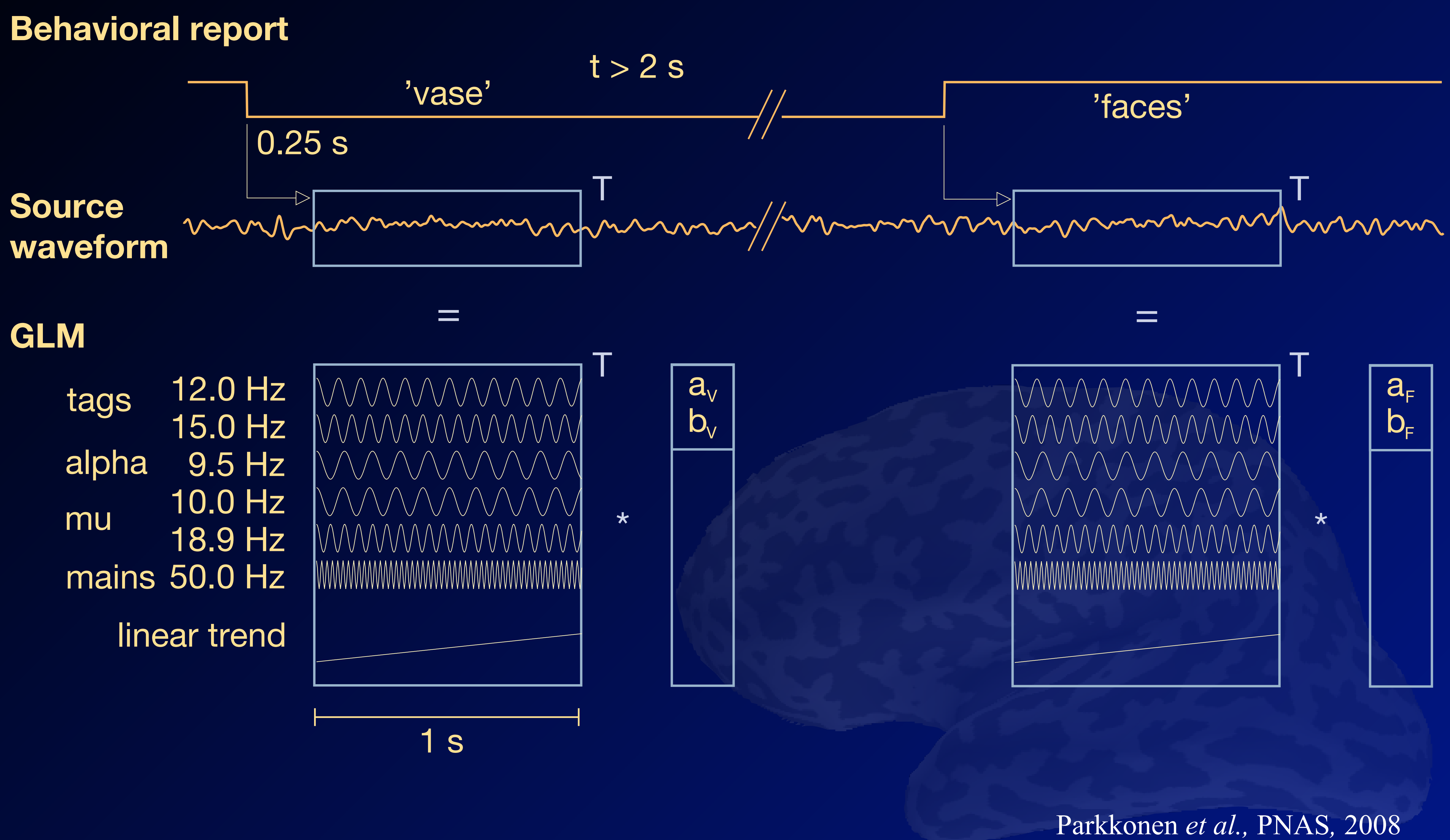
MEG signals at an occipital sensor





Parkkonen *et al.*, PNAS, 2008

Extract tag-related activity: MNE + GLM

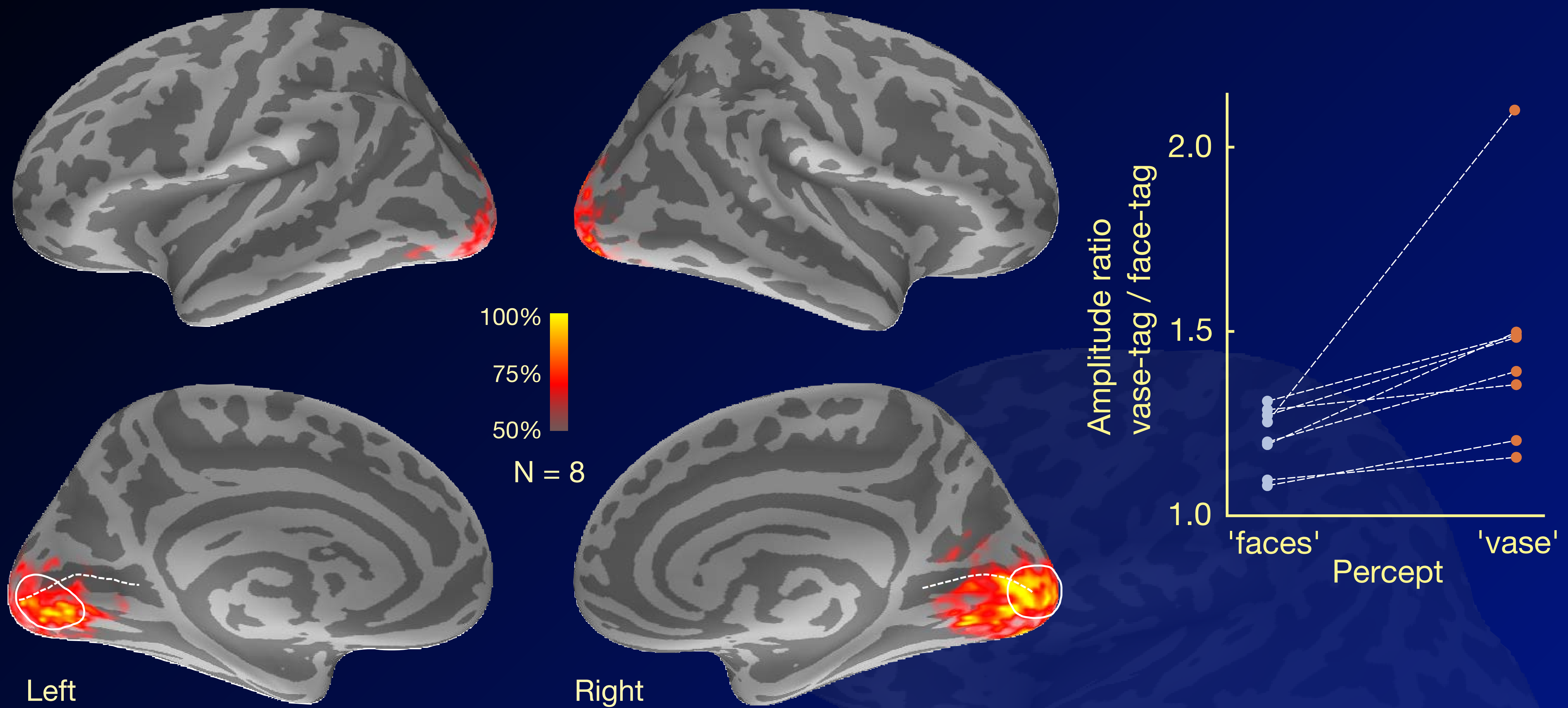


Parkkonen *et al.*, PNAS, 2008

Group analysis

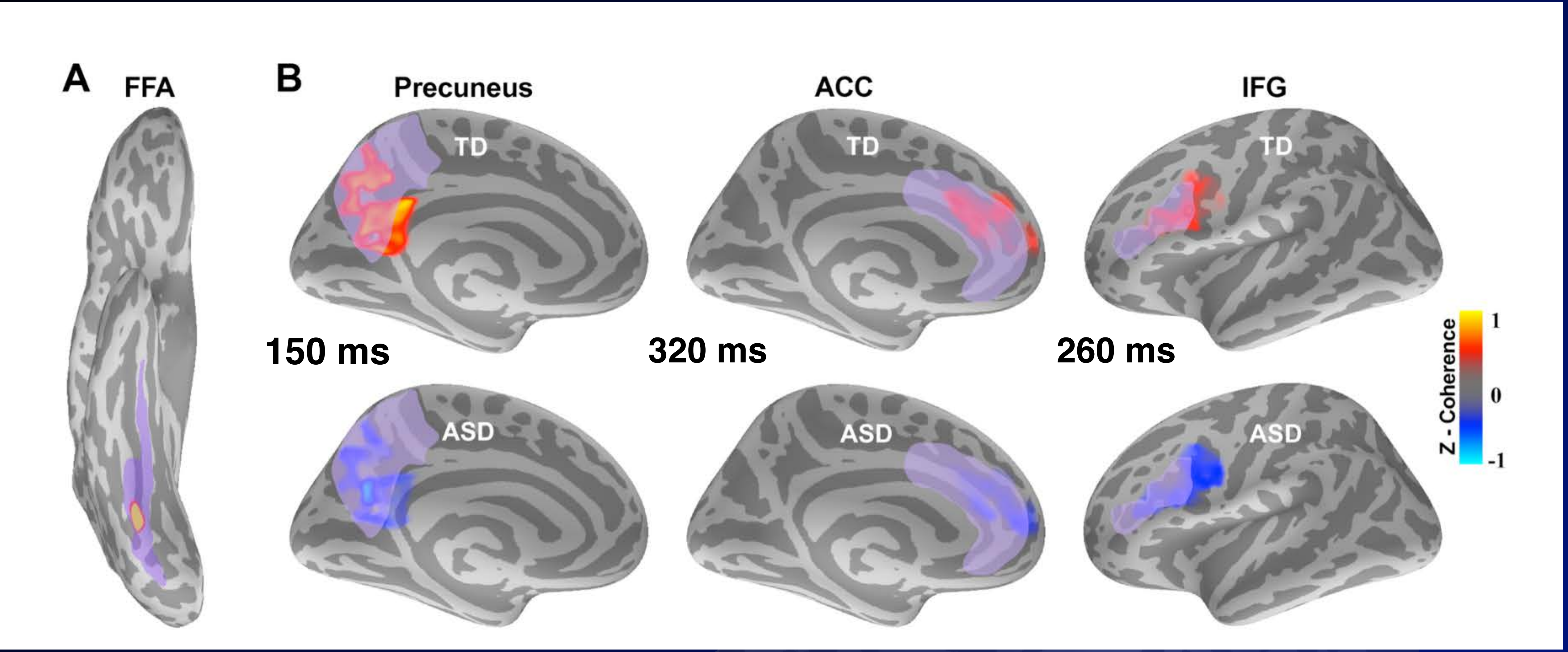
Significant activity in either tag frequency

Amplitude ratio at ROI



Parkkonen *et al.*, PNAS, 2008

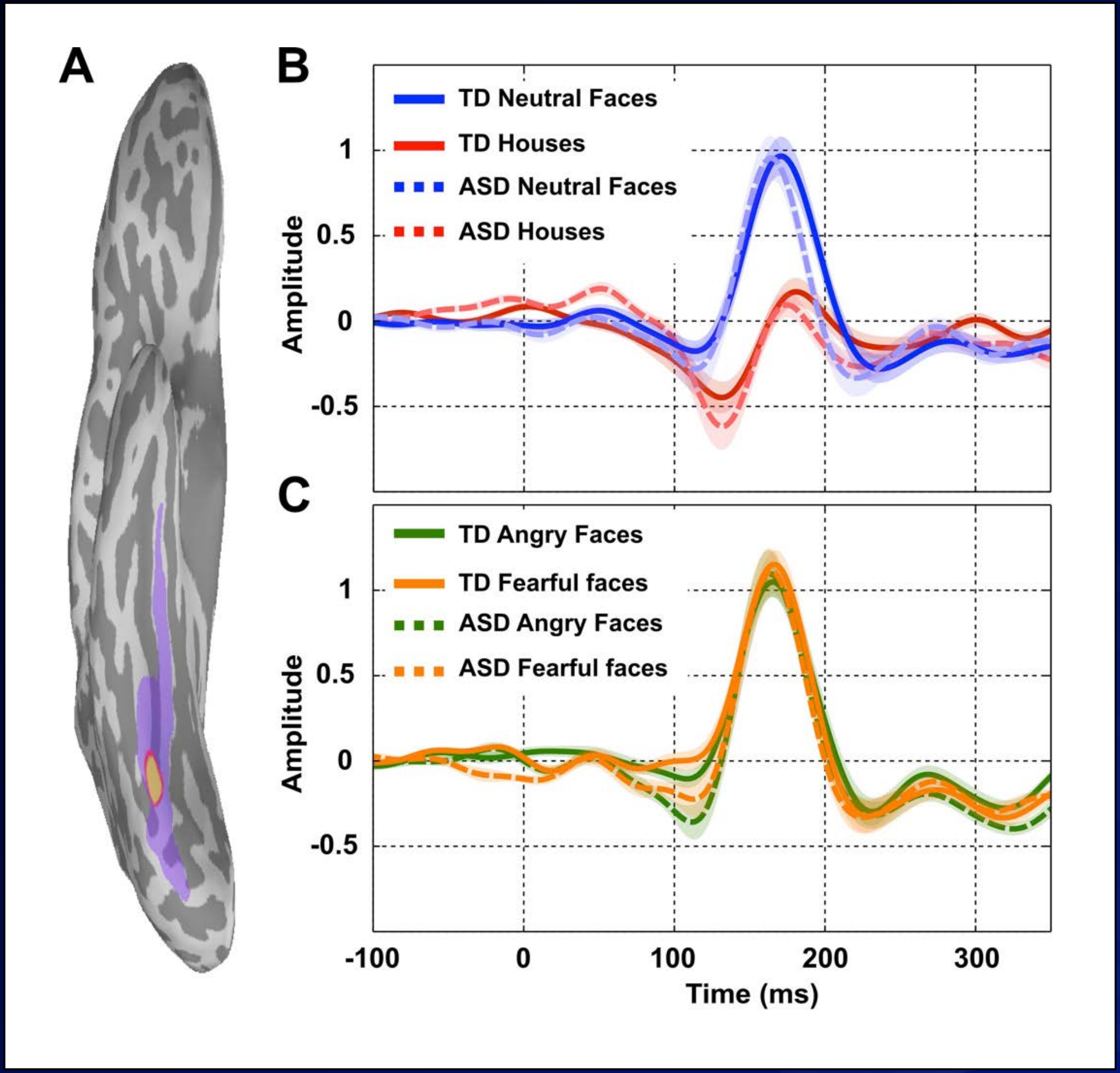
Long-Range Connectivity Differences Between ASD and TD Subjects (MEG)



- FFA seed, normalized (Z) coherence
- Alpha band (8 - 12 Hz)
- Emotional faces > houses
- Houses > emotional faces

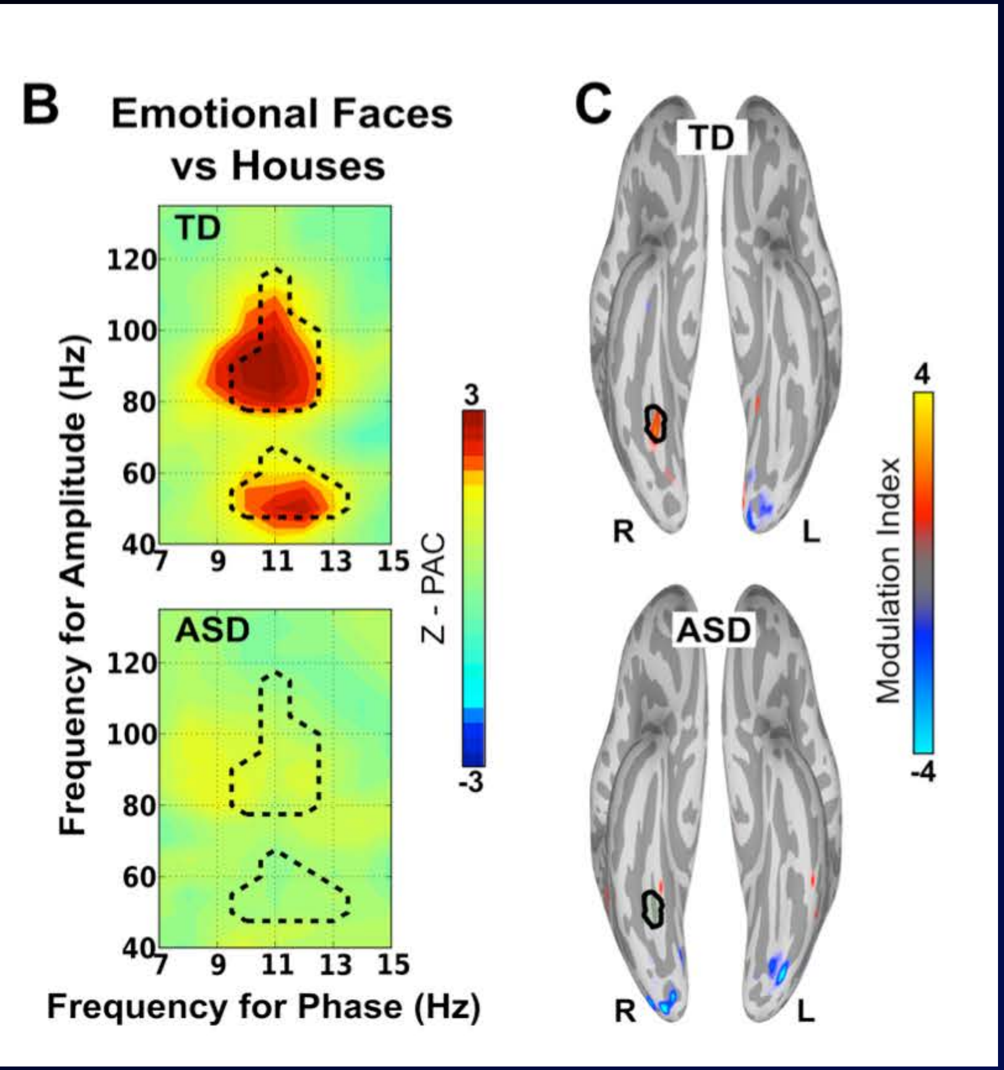
Khan et al., PNAS, 2013

Functional definition of FFA



Khan et al., PNAS, 2013

Local Connectivity Different in FFA only



Tal Kenet and Sheraz Khan, 2018

- Alpha band (8 - 12 Hz) phase and gamma band amplitude coupled
- Phase-Amplitude Coupling differences between emotional faces and houses only in controls

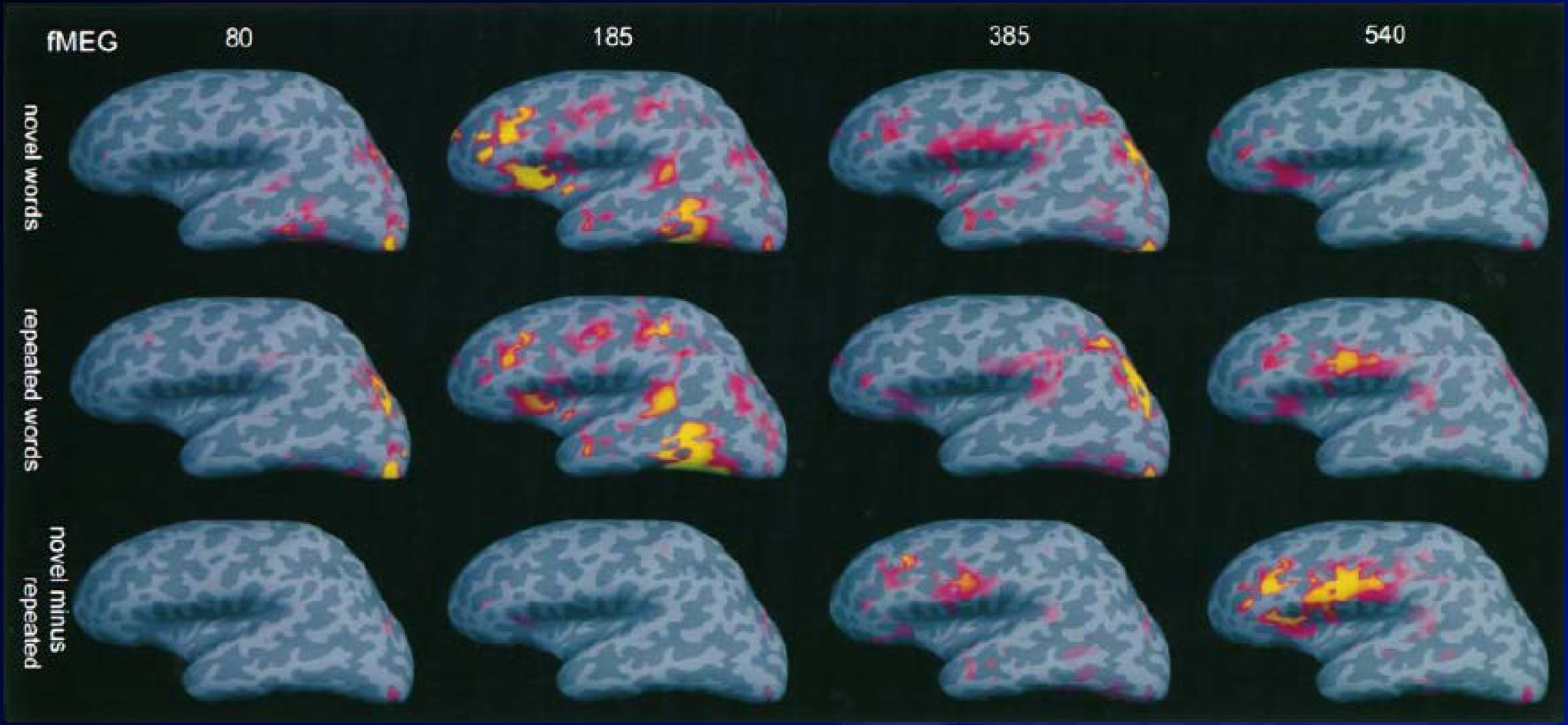
Khan et al., PNAS, 2013

fMRI-guided estimates

- Increase the source variance at locations of significant fMRI activity
- Straightforward to implement
- No specific assumptions made about the hemodynamic coupling, i.e., fMRI/MEG/EEG relationship

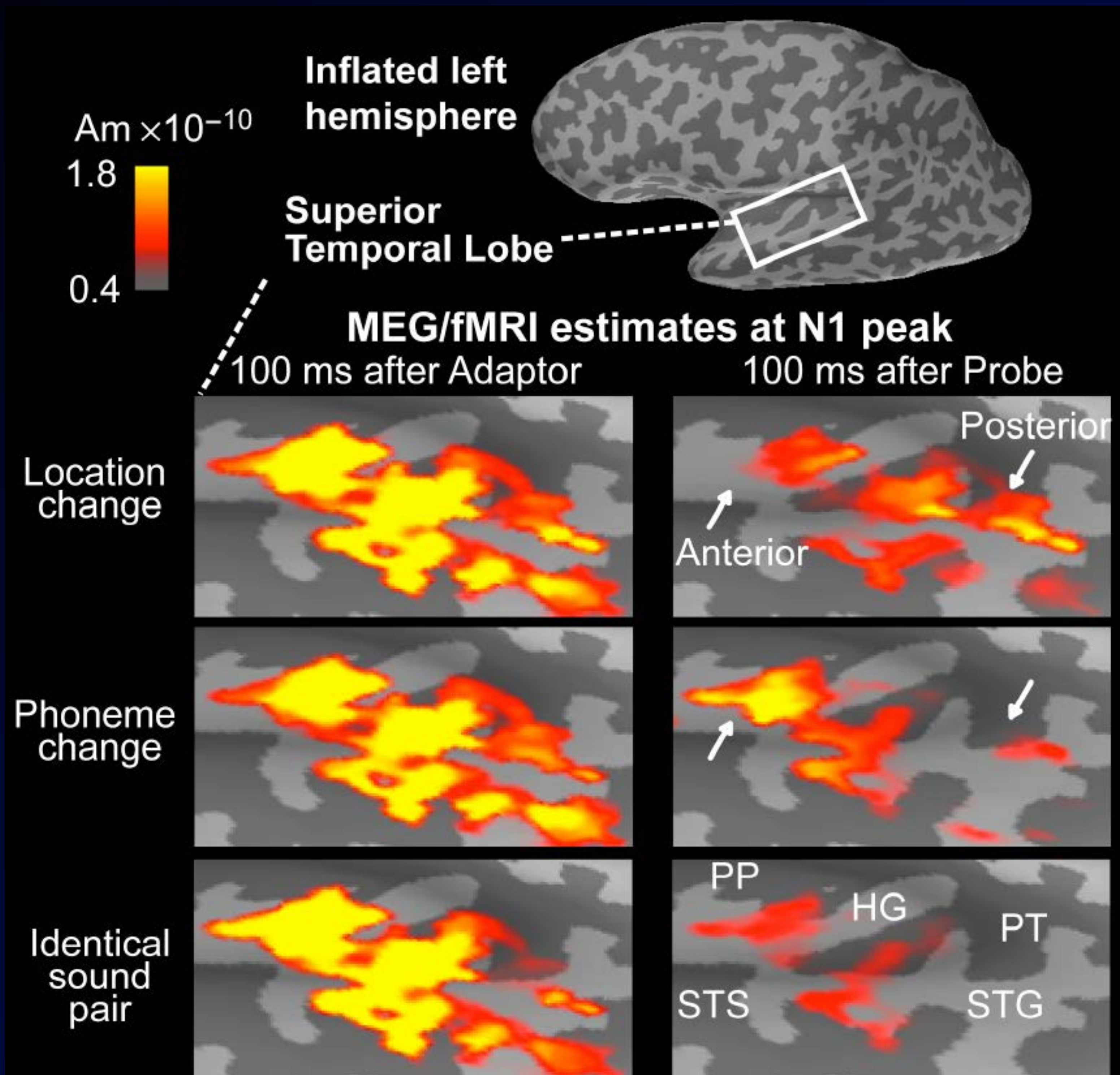
fMRI-guided MEG

dSPM statistic with fMRI as an a priori weight

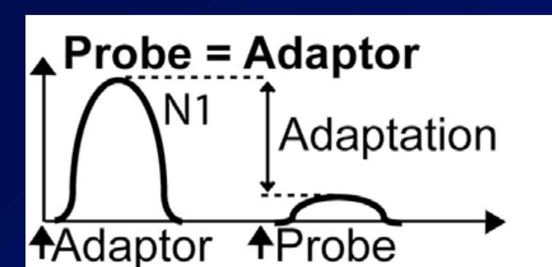


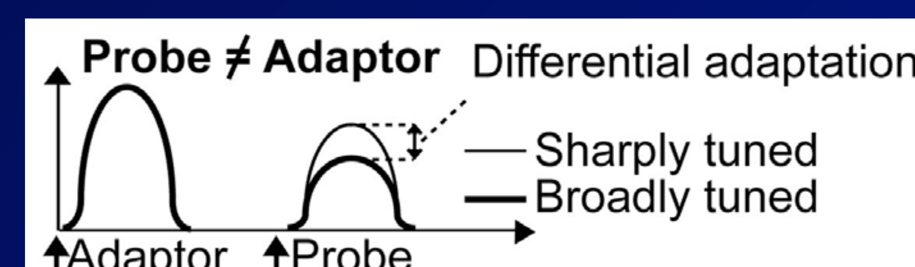
Dale *et al.* 2000

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

An EEG/MEG/fMRI puzzle: Error processing in the cingulate cortex

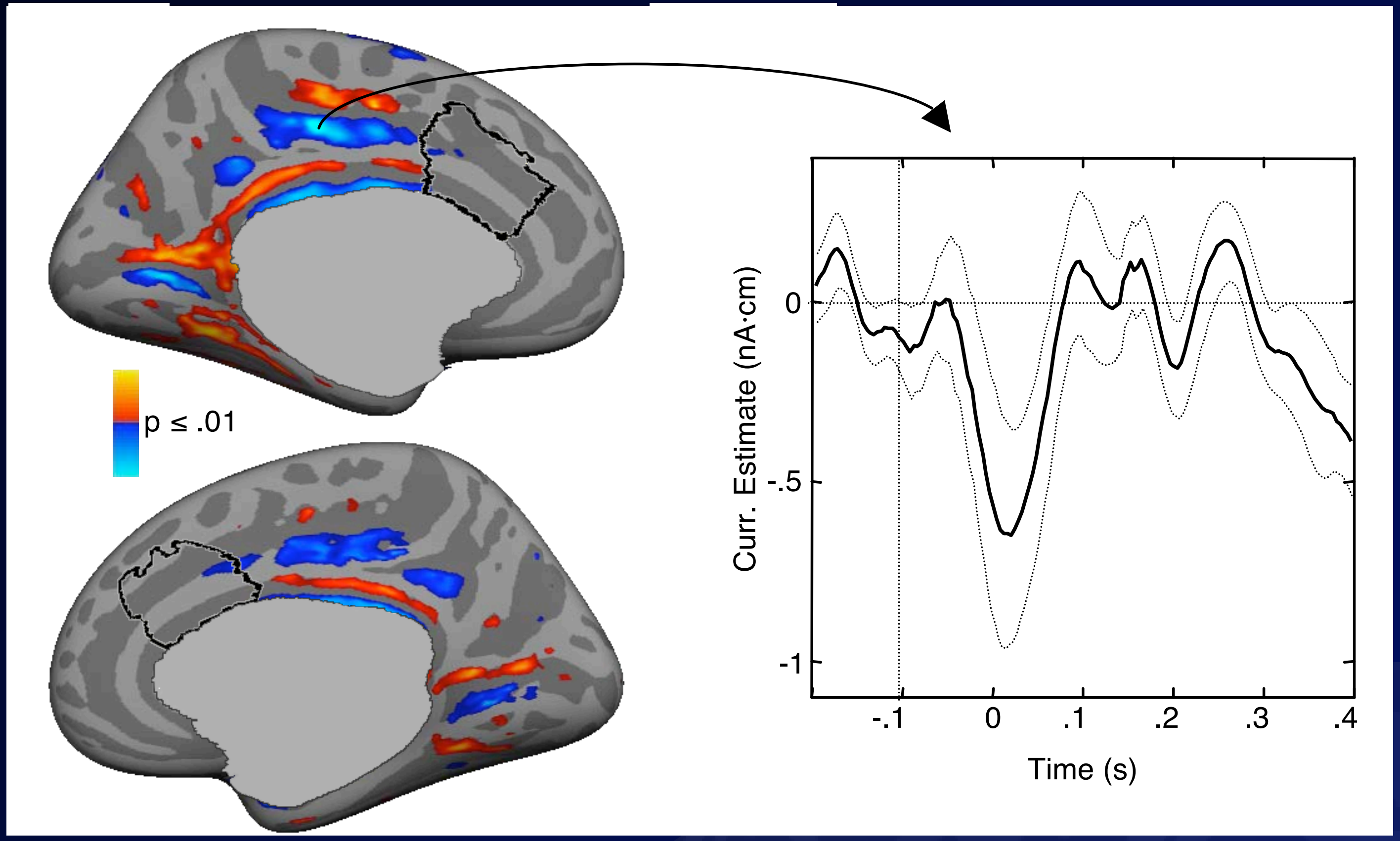
- Previous findings
  - Error-related fMRI activations in dACC
  - Error-related negativity (ERN) which can be attributed to sources in the cingulate cortex
- Our findings in an antisaccade paradigm
  - Clear error-related fMRI activation in dACC
  - Clear EEG ERN, almost no MEG equivalen
  - MEG/EEG source localization: PCC

Dara Manoach, 2018

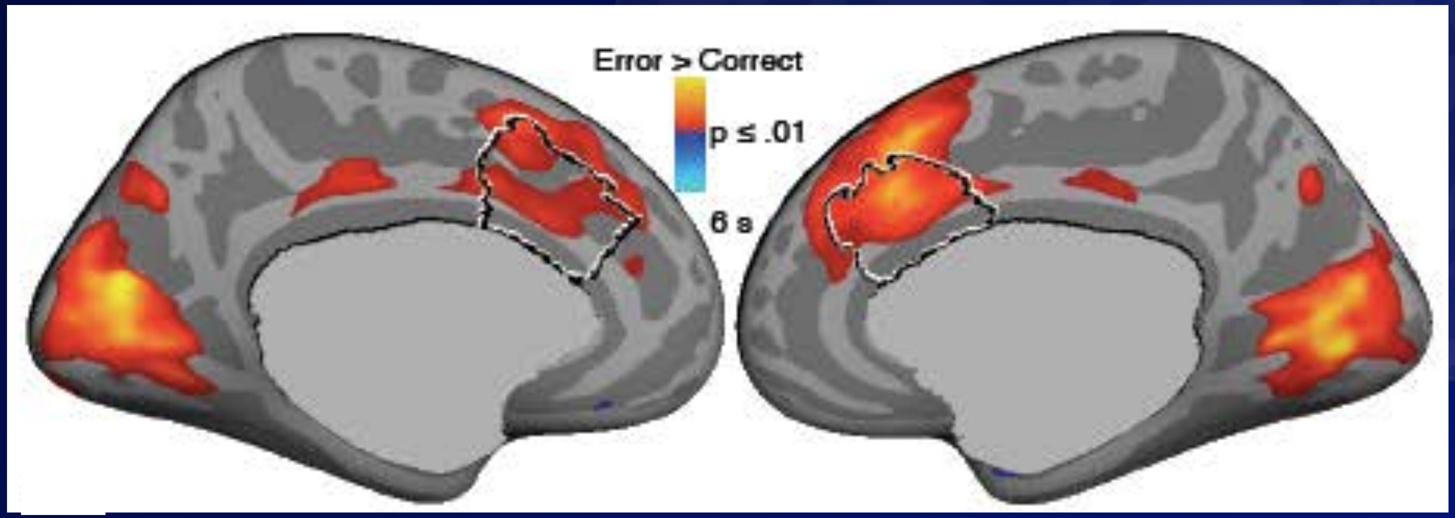
Agam *et al.*, PNAS, 2011

MEG/EEG and fMRI data

MEG/EEG: Error - correct



fMRI: Error vs. Correct



Causal Evidence of Performance Monitoring by Neurons in Posterior Cingulate Cortex during Learning

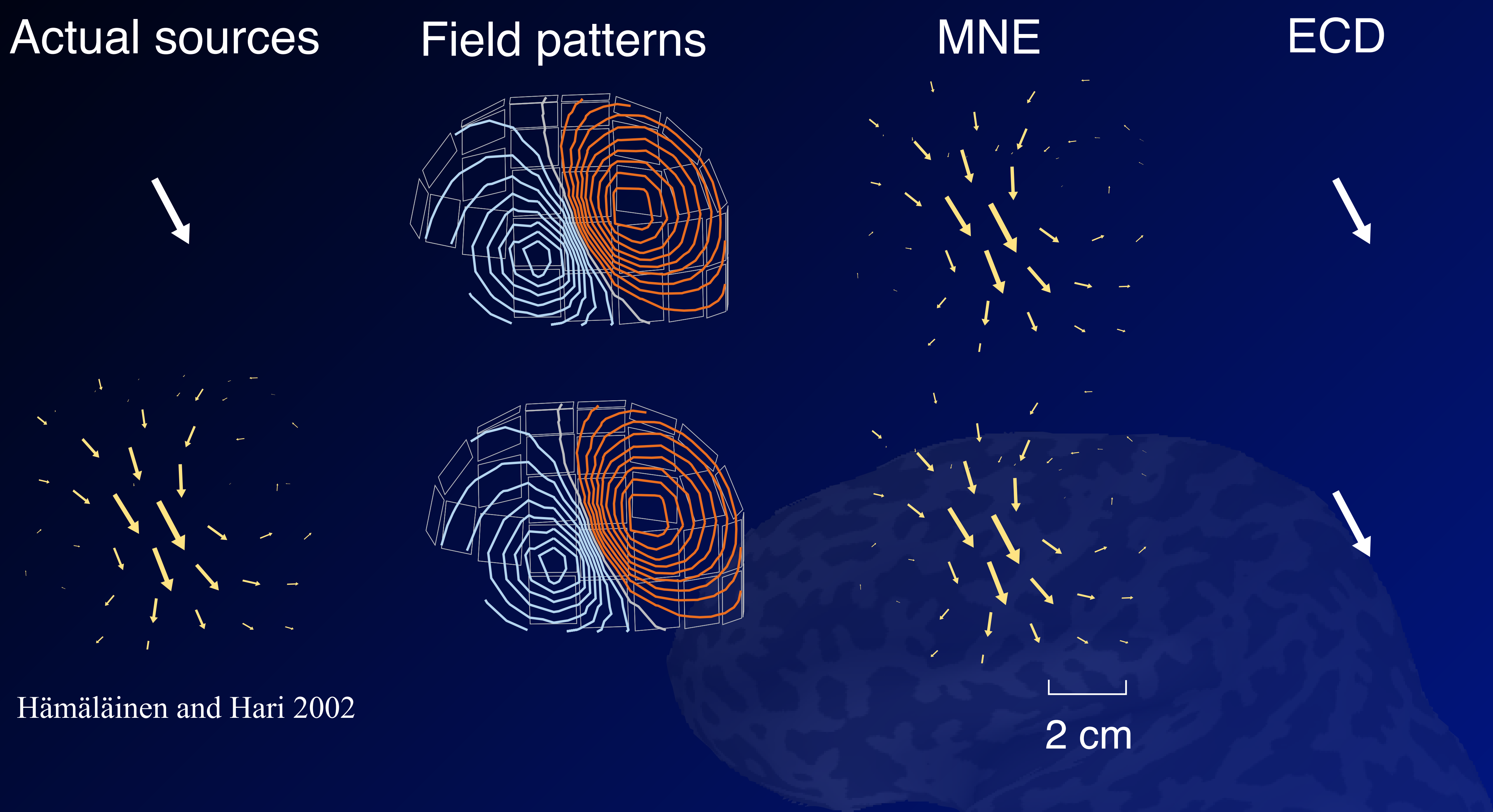
Our findings bear on a recent debate concerning the source of the error-related negativity (ERN), the distinctive change in brain activity following error commission observed with electroencephalography (Gehring et al., 1993). Most studies localize the source of the ERN to the ACC (Holroyd and Coles, 2002). A recent study, however, localized the source of the ERN to CGp (Agam et al., 2011). Here, we confirm that CGp does increase its firing rate following error commission.

Heilbronner and Blatt, Cell, 2013

MNE and friends: Summary

- Distributed solutions using cortical constraints
- Source extents are typically overestimated (in MNE)
- Sparse estimates resemble dipole solutions
- Non-parametric statistics are normally used in group analyses (MNE)
- Pooling sparse estimates is still a challenge
- Comparison with fMRI is often more useful than fusion with it

Inverse problem ambiguity



Hämäläinen and Hari 2002

- Both MNE and ECD can point the approximate location of the source
- The extent of the source is difficult to determine

Open-Source Academic Software

NeuroImage 86 (2014) 446–460

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

ELSEVIER

MNE software for processing MEG and EEG data

Alexandre Gramfort [a,b,c,d,e,*], Martin Luessi [b,c], Eric Larson [f], Denis A. Engemann [g,h], Daniel Strohmeier [i], Christian Brodbeck [j], Lauri Parkkonen [k,l], Matti S. Hämäläinen [b,c]

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Research Article

Brainstorm: A User-Friendly Application for MEG/EEG Analysis

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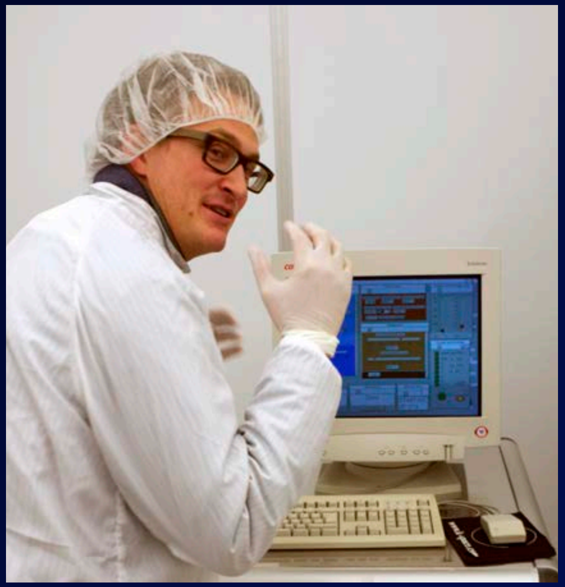
Academic Editor: Robert Oostenveld

Brainstorm is a collaborative open-source application dedicated to magnetoencephalography (MEG) and electroencephalography (EEG) data visualization and processing, with an emphasis on cortical source estimation techniques and their integration with anatomical magnetic resonance imaging (MRI) data. The primary objective of the software is to connect MEG/EEG neuroscience investigators with both the best-established and cutting-edge methods through a simple and intuitive graphical user interface (GUI).



Alex Gramfort, 2015

frontiers in NEUROSCIENCE

METHODS ARTICLE
published: 26 December 2013
doi: 10.3389/fnins.2013.00267

MEG and EEG data analysis with MNE-Python

Alexandre Gramfort[1,2,3]*, Martin Luessi[2], Eric Larson[4], Denis A. Engemann[5,6], Daniel Strohmeier[7], Christian Brodbeck[8], Roman Goj[9], Mainak Jas[10,11], Teon Brooks[8], Lauri Parkkonen[10,11] and Matti Hämäläinen[2,11]

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Academic | ˌækəˈdɛmɪk | *Adjective:* not of practical relevance

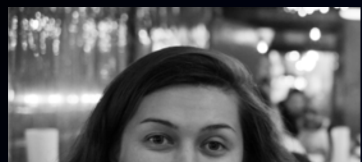
General comments

- Different source estimation methods give converging evidence when interpreted correctly
- Exploration and hypothesis-driven approaches should be used in conjunction
- The scientific questions, experimental design, data analysis approaches, and interpretation interact
- Initial lack of formal hypotheses does not imply your data analysis methods are not principled

Conventional wisdom may be wrong

Do not use a hammer to drive in screws

Science is Done by People





People with different backgrounds work together daily:

“Both information and gossip travel at the speed of light but information travels only 10 meters”

Thank you!

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- NIH R01EB022889
- NIH R01MH106174
- NSF 0958669
- NSF 0959294