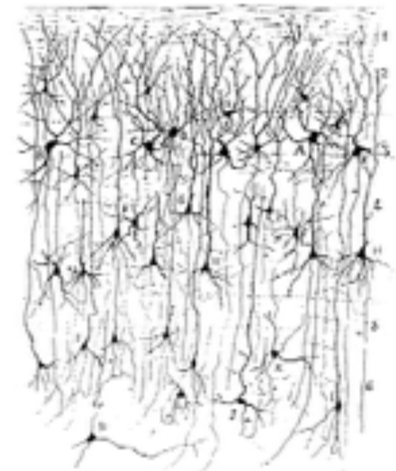
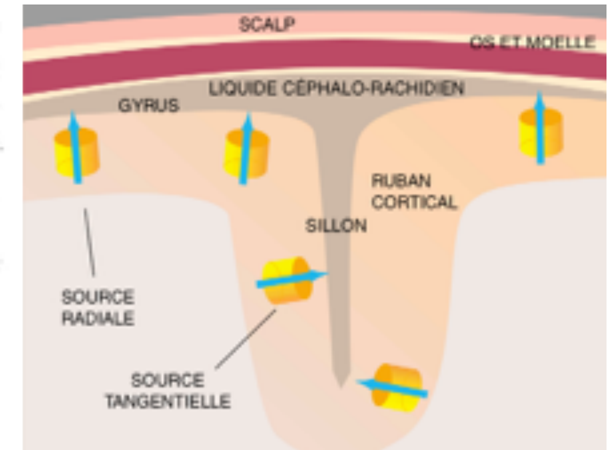
Deep sources localization in MEG/EEG

Denis Schwartz

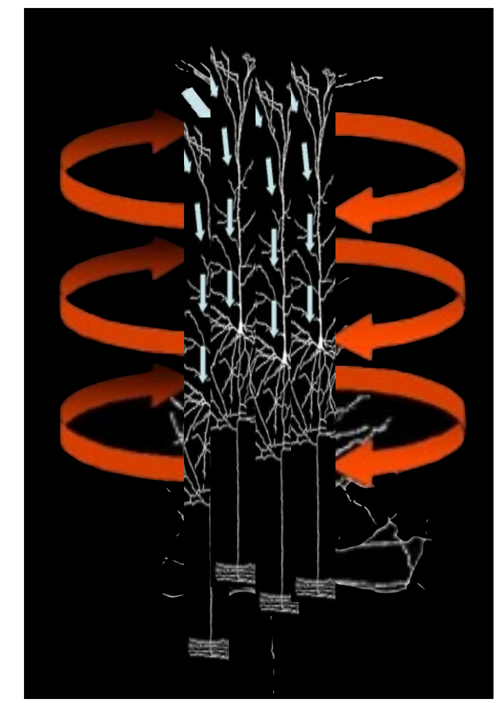
http://www.cenir.org

MEG source physiology

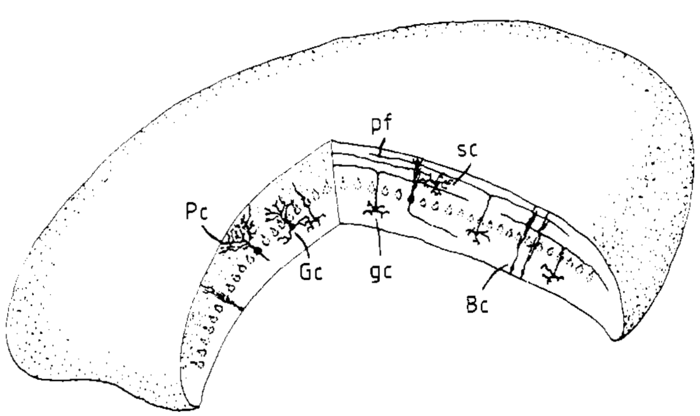


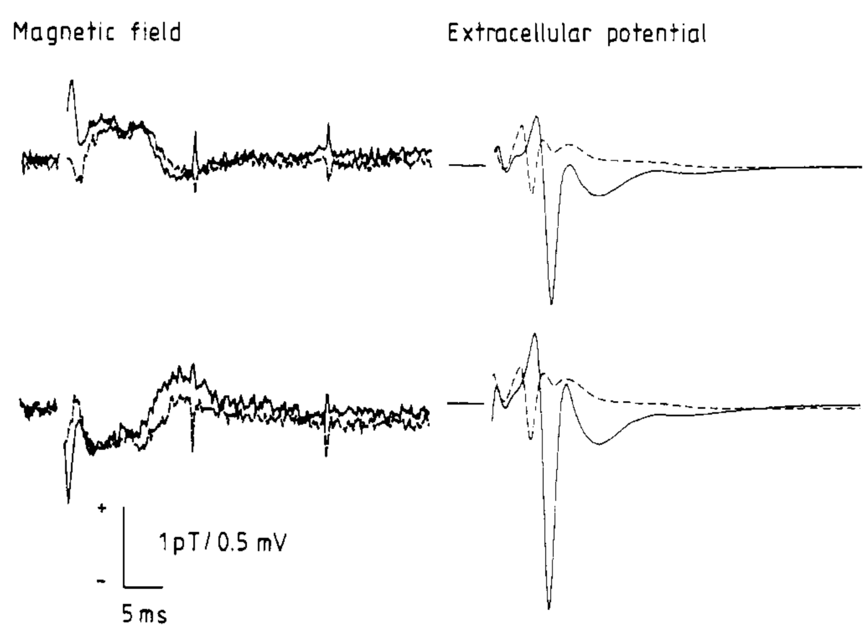


MEG signals <- macrocolumns in cortical sheet



Suffisant numbers of pyramidal neurones



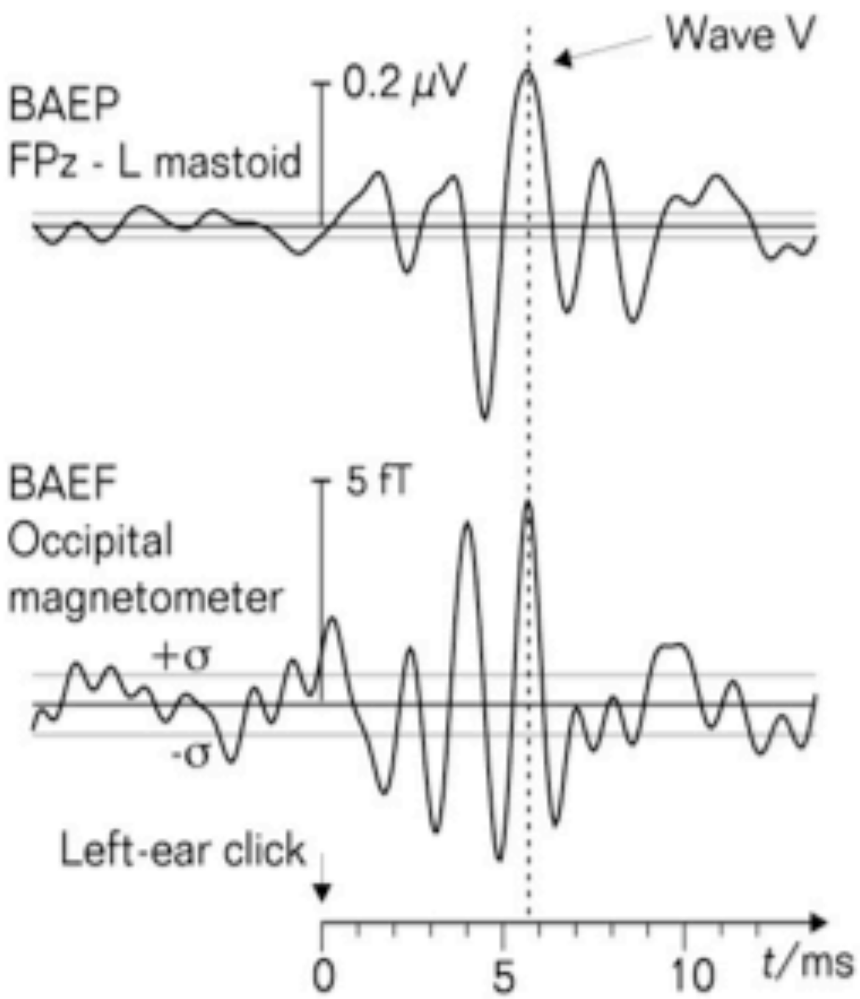


Okada, Lauritzen & Nicholson Phys. Med. Biol., 1987

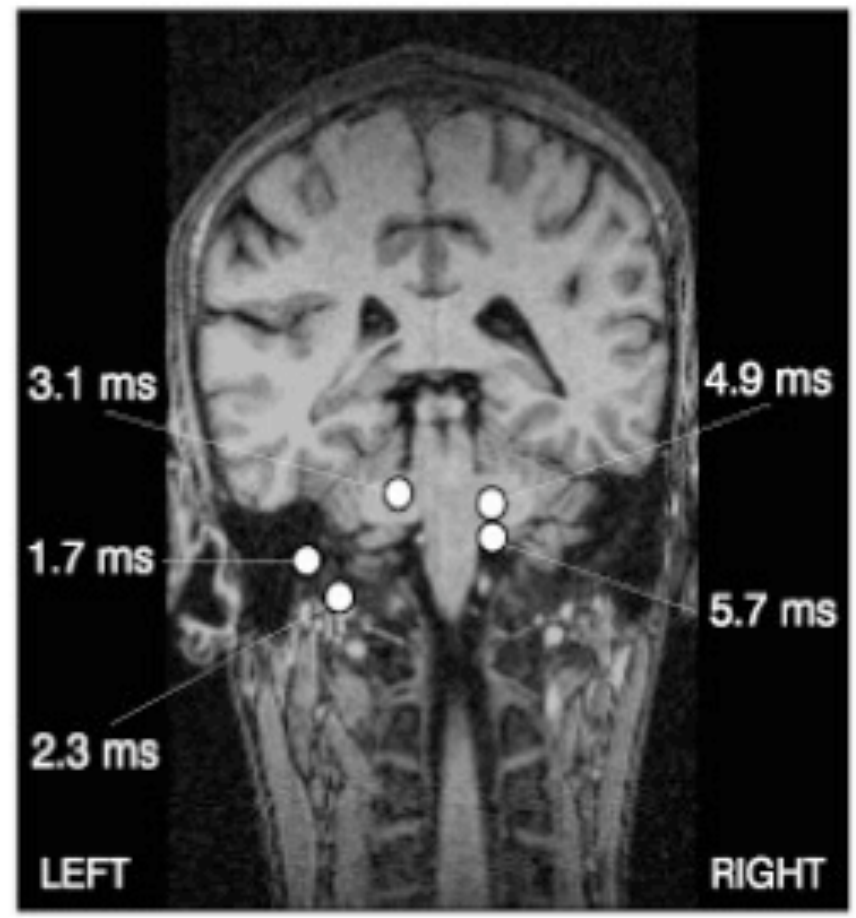
Can MEG see deep?

STIMULUS:
0.6-ms auditory clicks to left ear
111 ms ISI, 15000 epochs averaged

RESPONSES:
Shown with pass-band 160 – 900 Hz



ANALYSIS:
- individual BEM models
- equivalent current dipoles



NOTE: All sources visualized on a single MRI slice.

Parkkonen et al. 2002

Can MEG see deep?

Let’s go back to theory

Model

Mathematical model of the data (linear!):

Nc x Nt

MEG / EEG measures

Ns x Nt

$$M = G.S + n$$

Noise

Cortical activity

Forward operator

Ns x Nt

Nc x Ns

Nc => Number of sensors

Nt => Number of time points

Ns => Number of sources

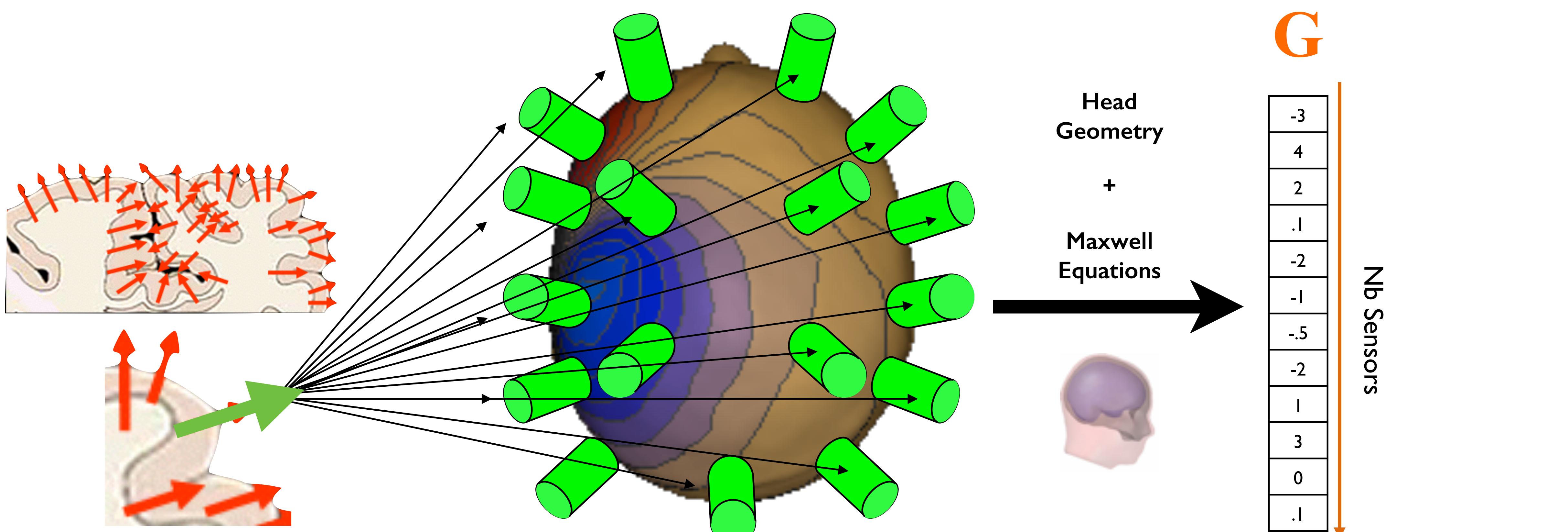
M => **known** MEG or EEG signals

G => **known** forward operator

S => cortical currents

N => zero-mean additive noise

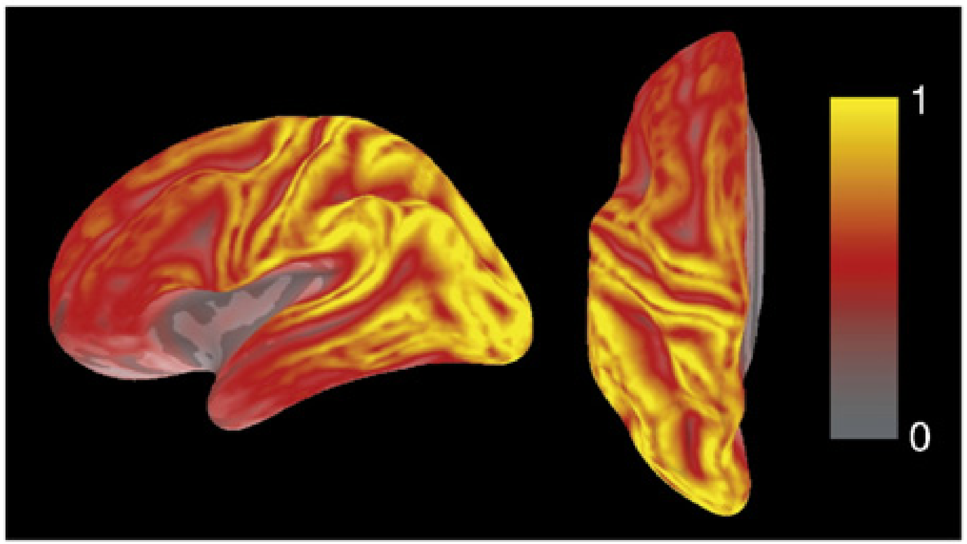
G explains the magnetic field created by a set of sources with known location & direction on each sensor



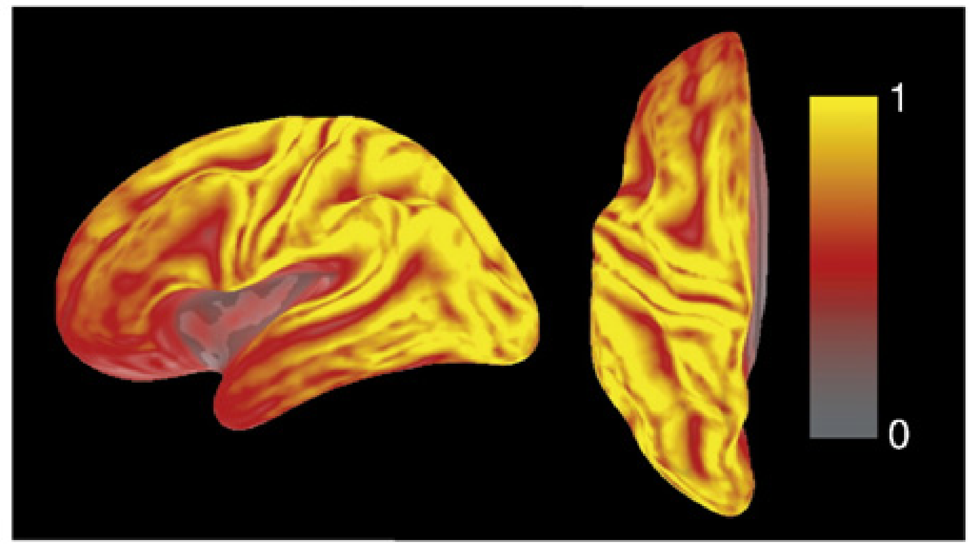
In depth investigation …

Hillebrand & Barnes NeuroImage 2001

Haut & all NeuroImage 2011

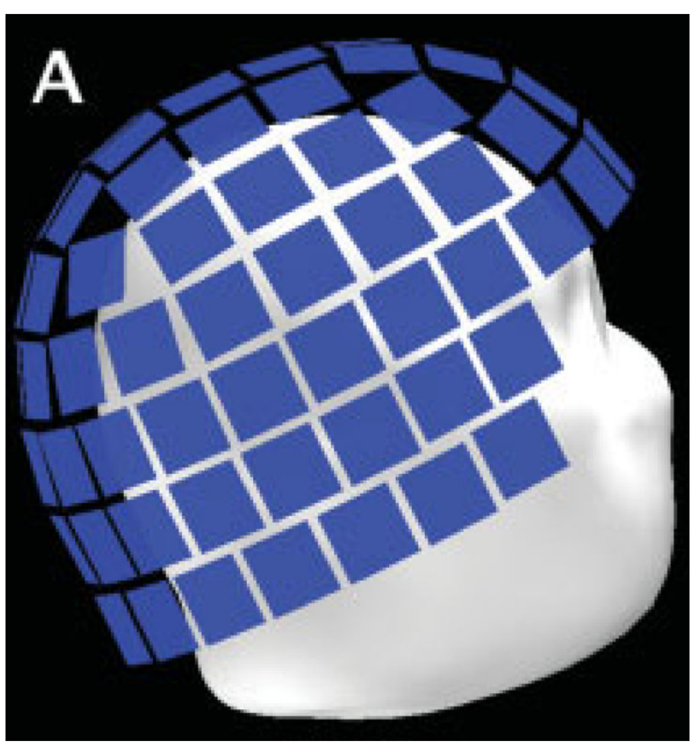


Gradiometers



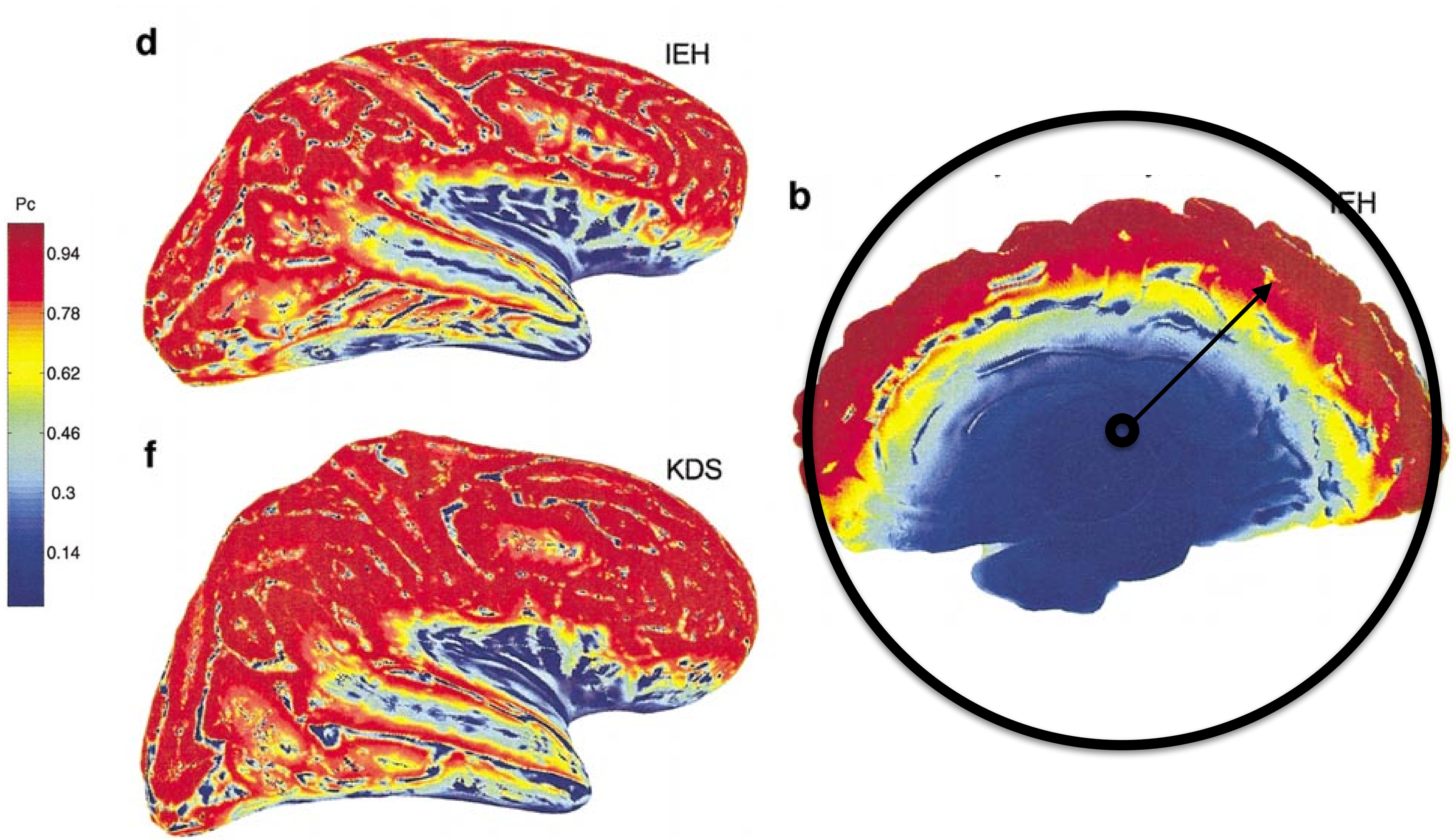
Magnetometers

Sensitivity at the cortical level

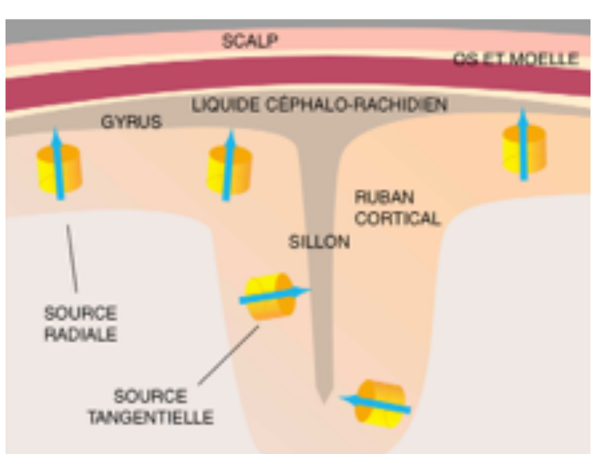


- Source location
- Sensor type
- Sensor location

In depth investigation …



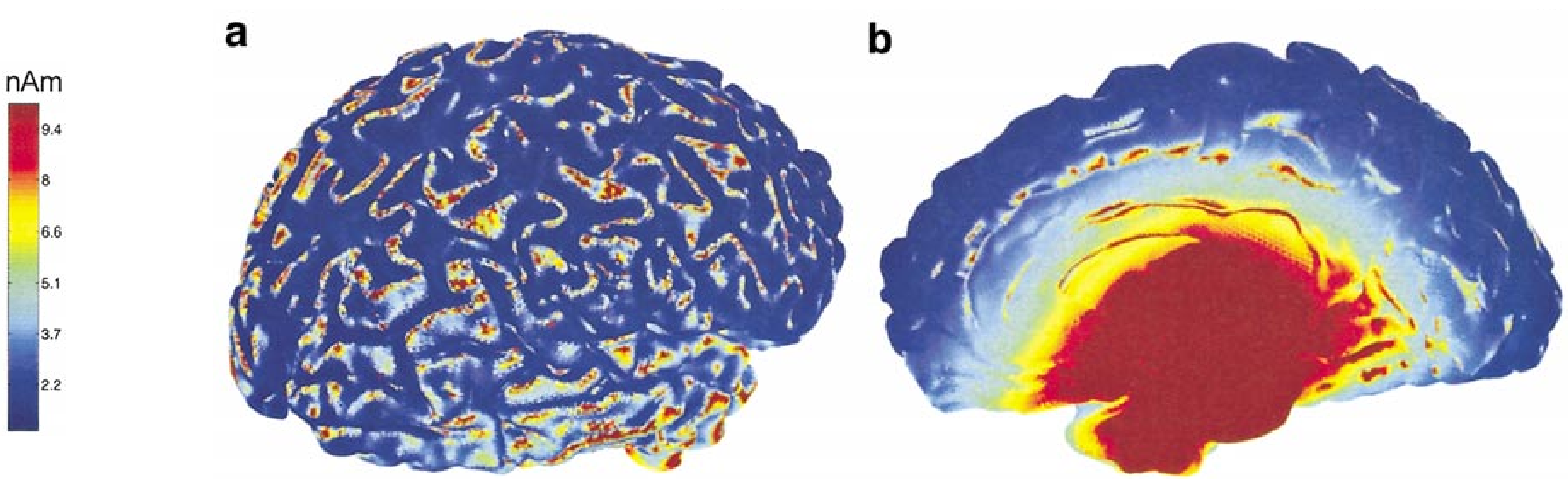
Probability of detection



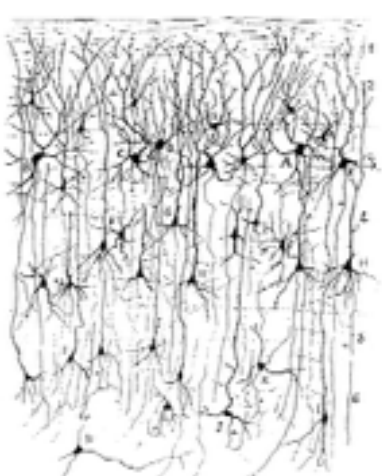
- Sources parameters: location, orientation

  -> Depth

In depth investigation …



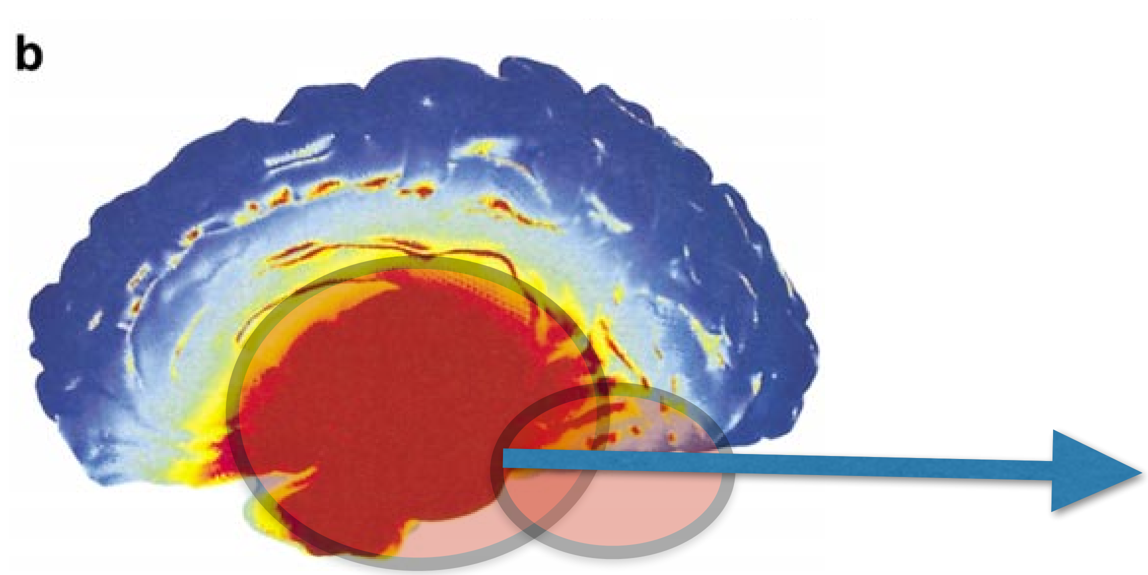
Source strength for 70% of detection



- Sources parameters: strength, density, spatial organisation

In depth investigation …

- ☑ Sensor type
- ☑ Sensor location
- ☑ Sources parameters
- ☐ Source space model:
  - Missing parts: Deep nuclei, hippocampus, amygdala, cerebellum
- ☐ Sources parameters
  - Is a unified model adapted?
  - location, strength (density of cells), but also geometry (orientation)



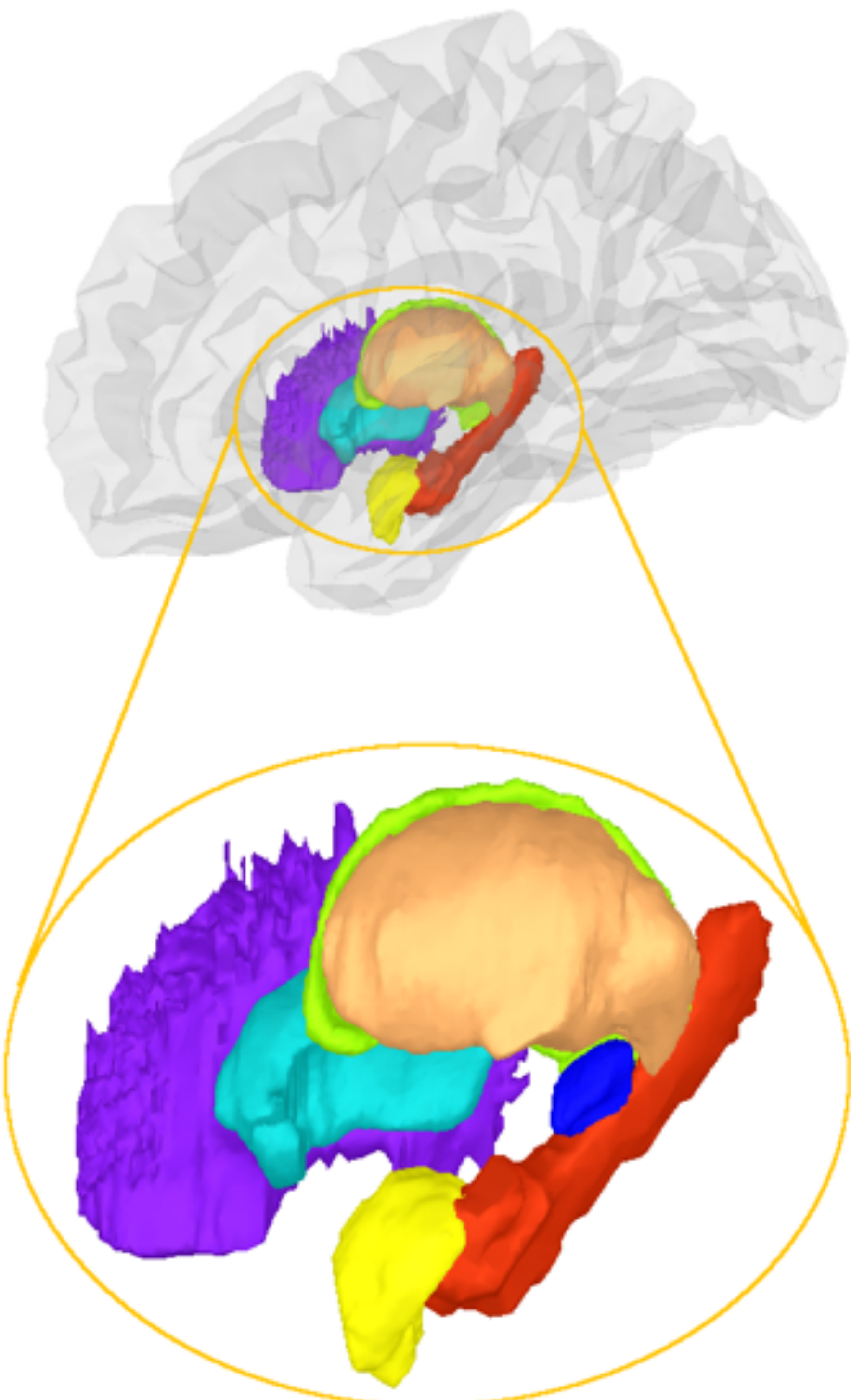
Can we go further… deeper?

➡ Survey of the potential biases and of the spatial resolution in deeper part of the brain

- ➡ **Evaluate detectability structure by structure**
- ➡ **Evaluate localisation errors**

Attal & Schwartz PlosOne 2013

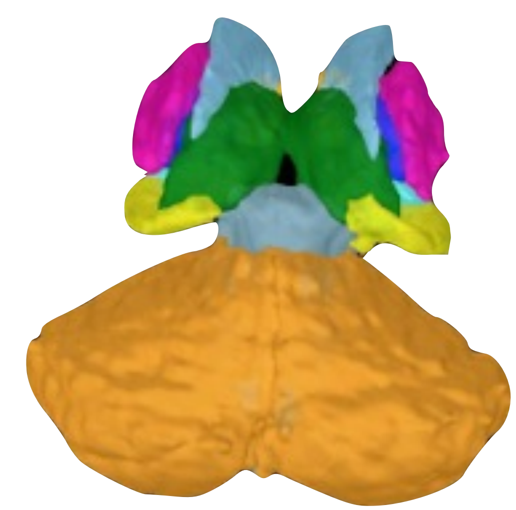
Anatomical model



- ➡ Cortex segmentation

- ➡ Basal ganglia
- ➡ Hippocampus & Amygdala
- ➡ Cerebellum

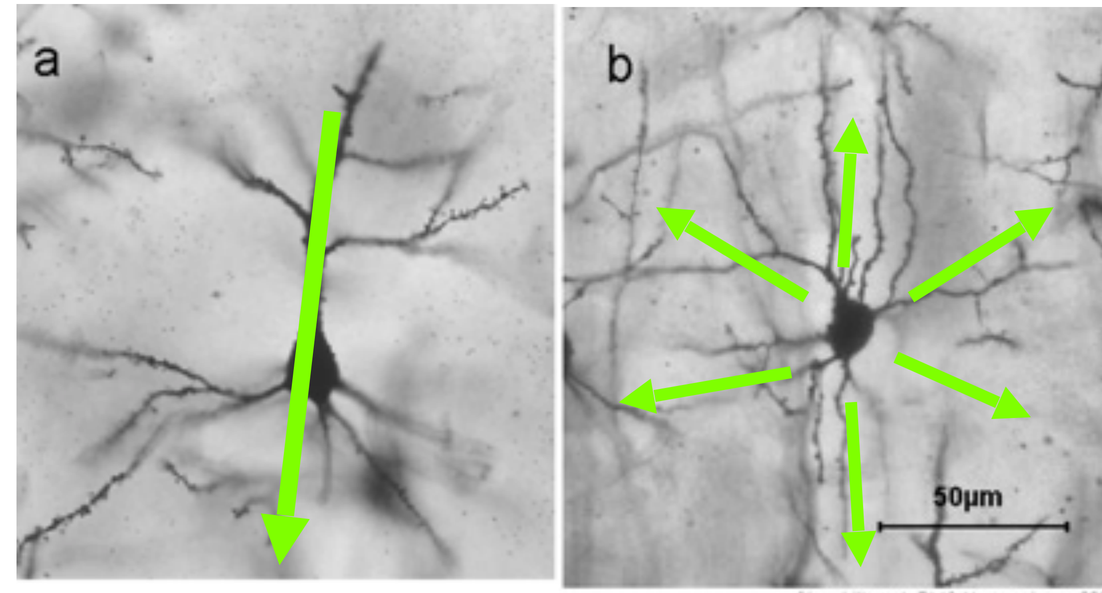
FreeSurfer or others



Electrophysiological model

➡ Detailed specific **electrophysiological** priors for each structure:

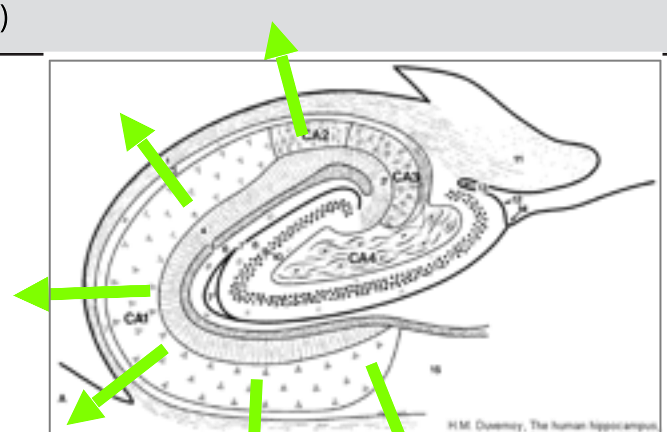
- **Source orientations**
- **Neural current**
- **Surface or Volumetric mesh**

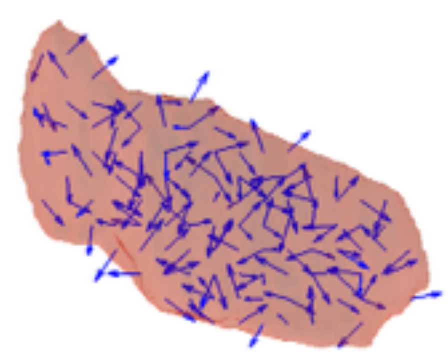


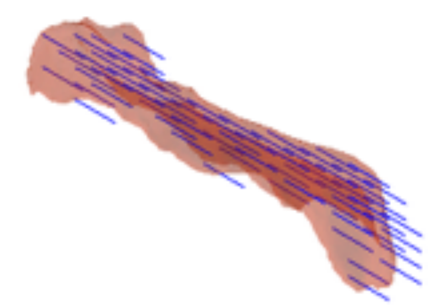
Churchill et al. BMC Neuroscience 2004

Table 1. Global characteristics of the DBA model.

	Surface mesh		Volumetric mesh					
Structures (Left)	**Cortex**	**Hippocampus**	**Amygdala**	**Thalamus**	**LGN**	**EGP**	**Putamen**	**RPN**
Surface | Volume (cm^2 | cm^3)	750	15	1	8	0.2	1.5	9	2
Number of vertices	4619	900	273	1043	229	453	1029	529
Cell type	O	O	O	C	O	O	C	O
DMD (Γ|Γ)	0.25	0.4	1	0.025	0.25	0.0025	0.25	0.0025
Neural current for patch sizes 1 to 5 (Γ)	25 to 125	40 to 200	100 to 500	2.5 to 12.5	25 to 125	0.25 to 1.25	25 to 125	0.25 to 1.25

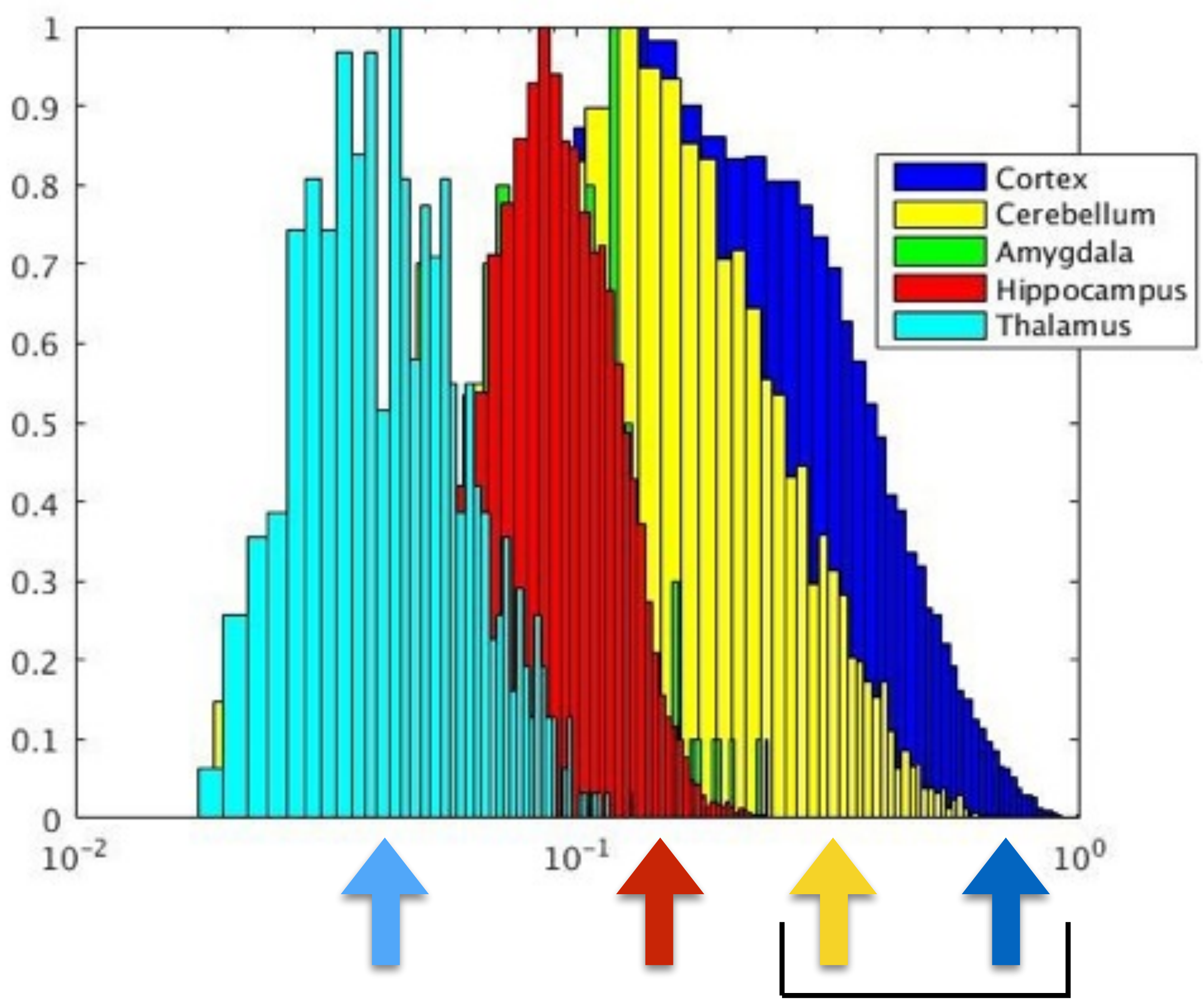


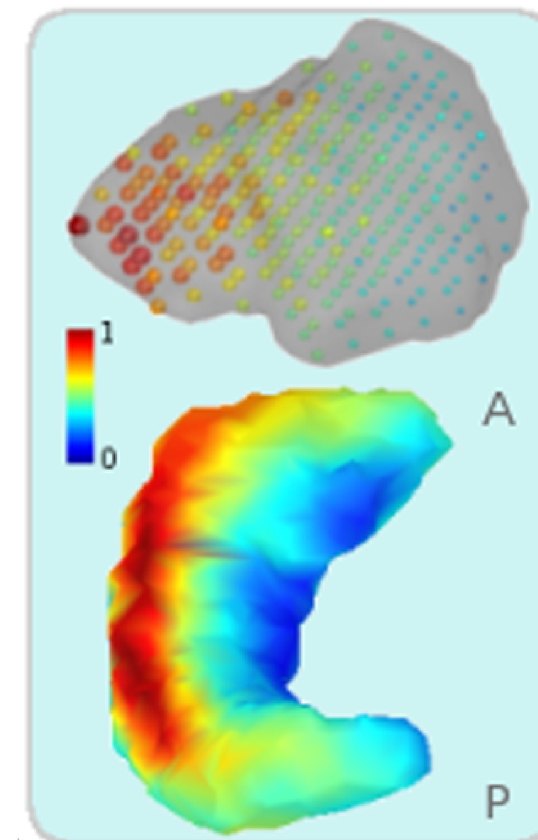


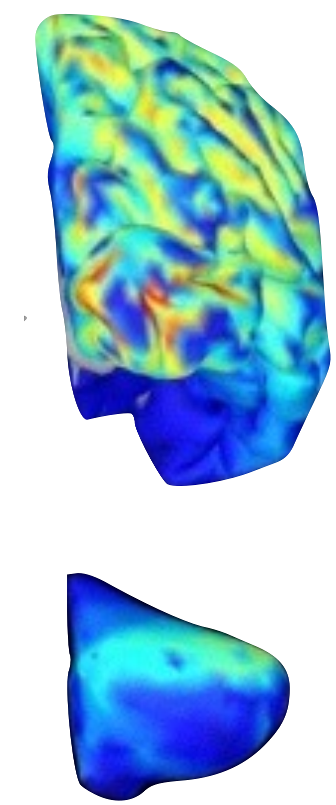


Can we detect something?

➡ Contribution of each structure to the signal at the sensor level (column of G)







➡ Cortex and cerebellum contributions equivalent

➡ Thalamus detection questionable

Inverse Operator (Imaging Kernel)

$M = G.s + n$

$$W = \underbrace{R}_{\text{Sources Covariance}} G^T.(GRG^T + \underbrace{C}_{\text{Noise Covariance}})^{-1}$$

Estimation of sources activity

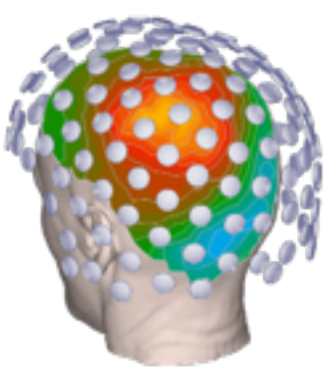
$$\hat{S} = W.M$$

Inverse Operator

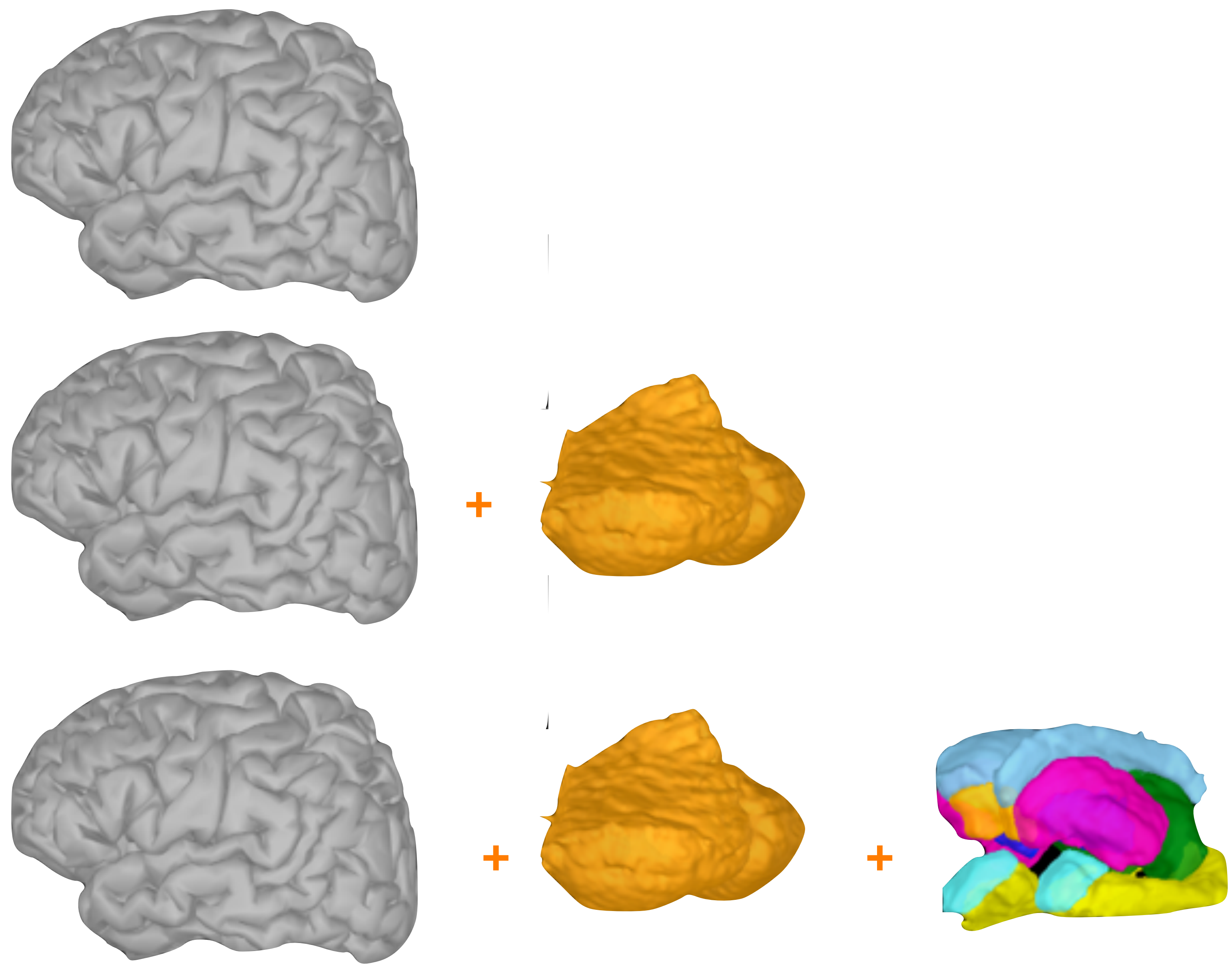
Inversion : Minimum norm -> Distribute the sensors energy on the source space as a whole

Sensor space

Source space



$$\hat{S} = W.M$$

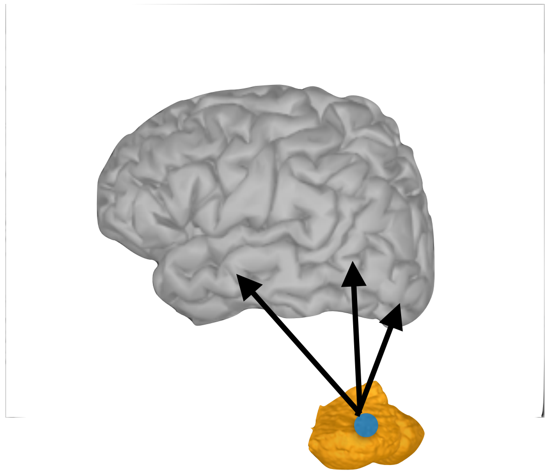


Theoretical biais?

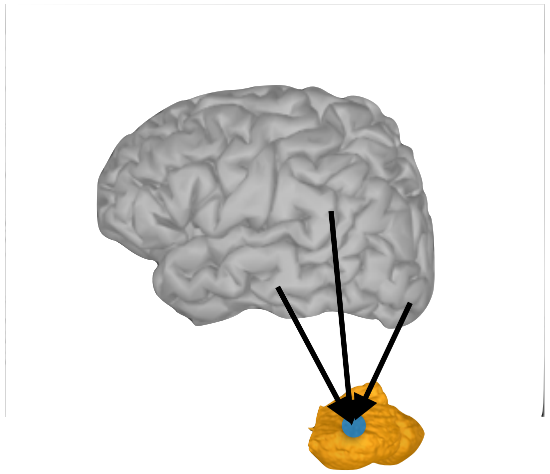
$$\hat{S} = W.M$$
$$\hat{S} = W.G.S$$
$$\hat{S} = R.S$$

Point Spread Function and Cross talk function: the resolution matrix R

POINT SPREAD FUNCTION - PSF: How is a point source distorted by the inverse estimator? (Columns of R)



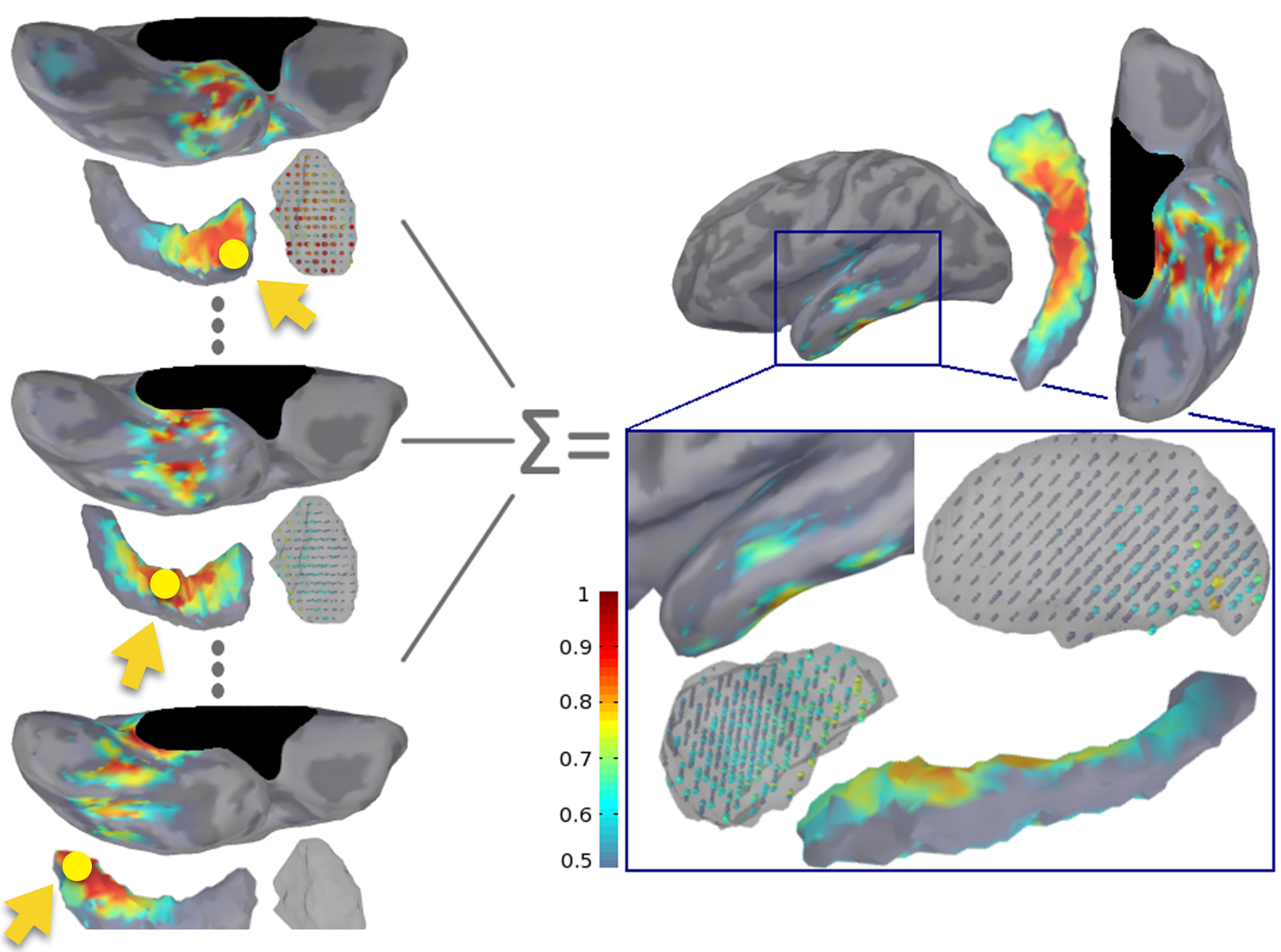
CROSS TALK FUNCTION - CTF: How does a point source in one location affect the amplitude estimation for a source in another location? (Rows of R)

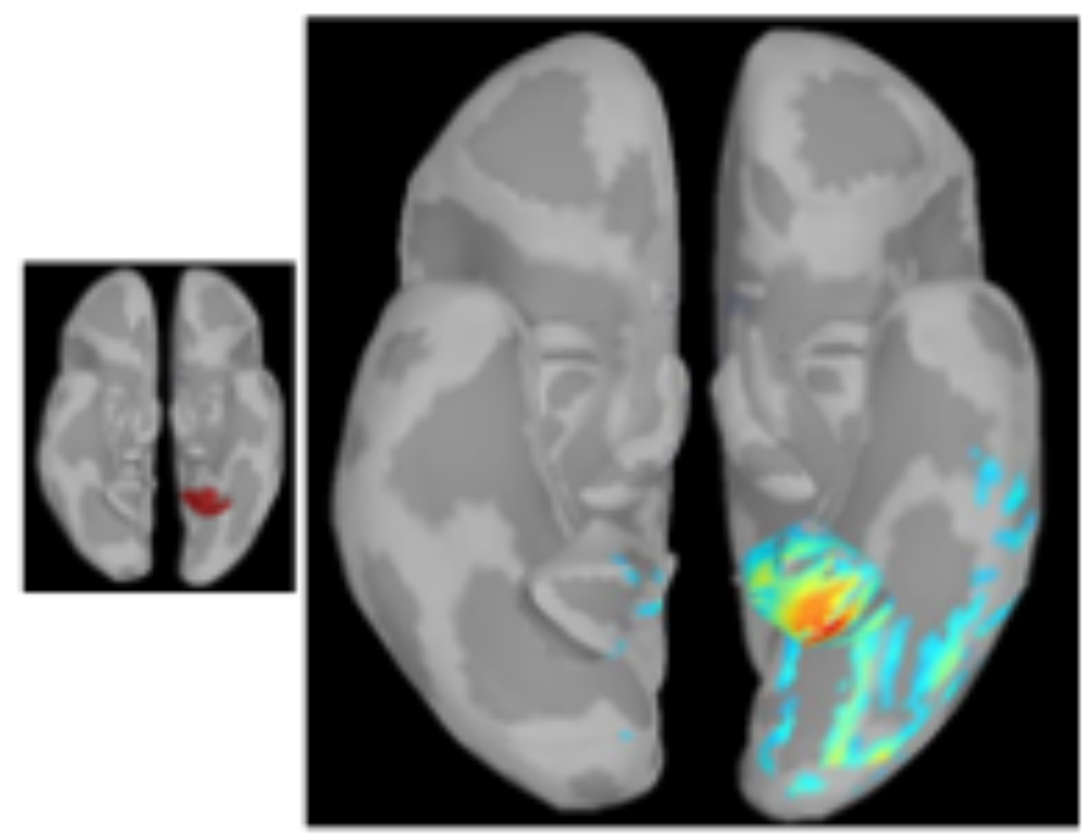


Backus and Gilbert, 1968; Menke, 1989, Grave de Peralta Menendez et al., 1997; Liu et al., 2002; Molins et al., 2008)

Theoretical biais?

Point Spread Function: How the activity of a given area is spreading through localisation

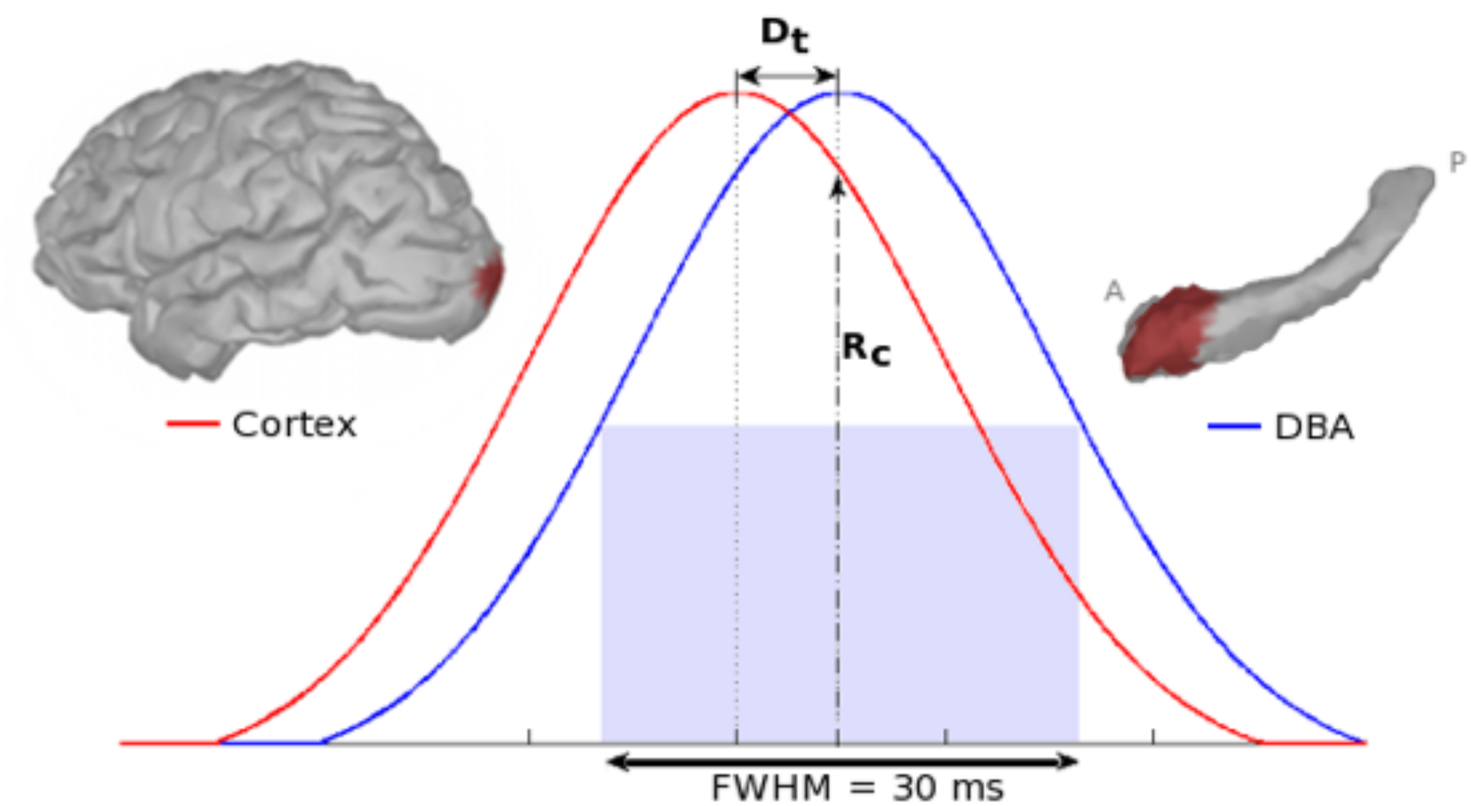




Localization errors

Monte Carlo Simulations:

- <u>Cortical & DBA activations:</u>
  - Simulated neural currents for several size of patches



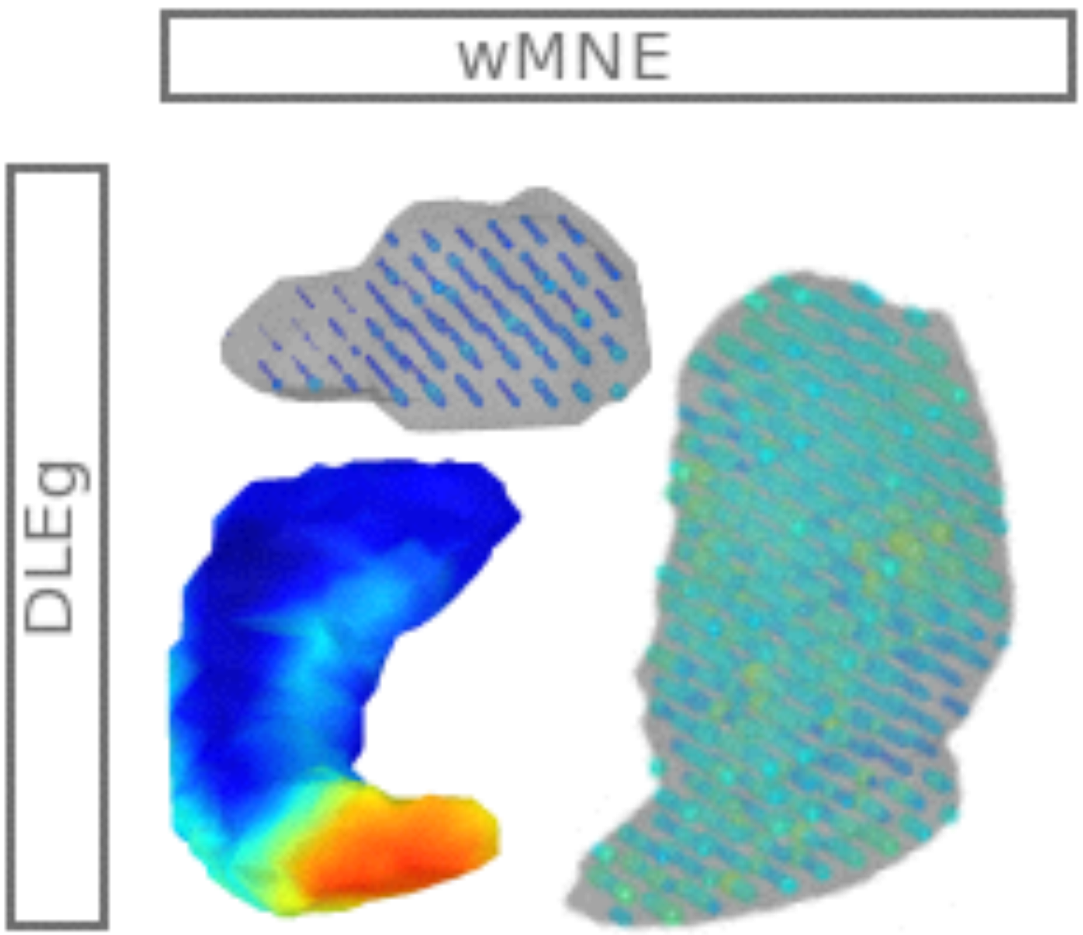
Localization errors

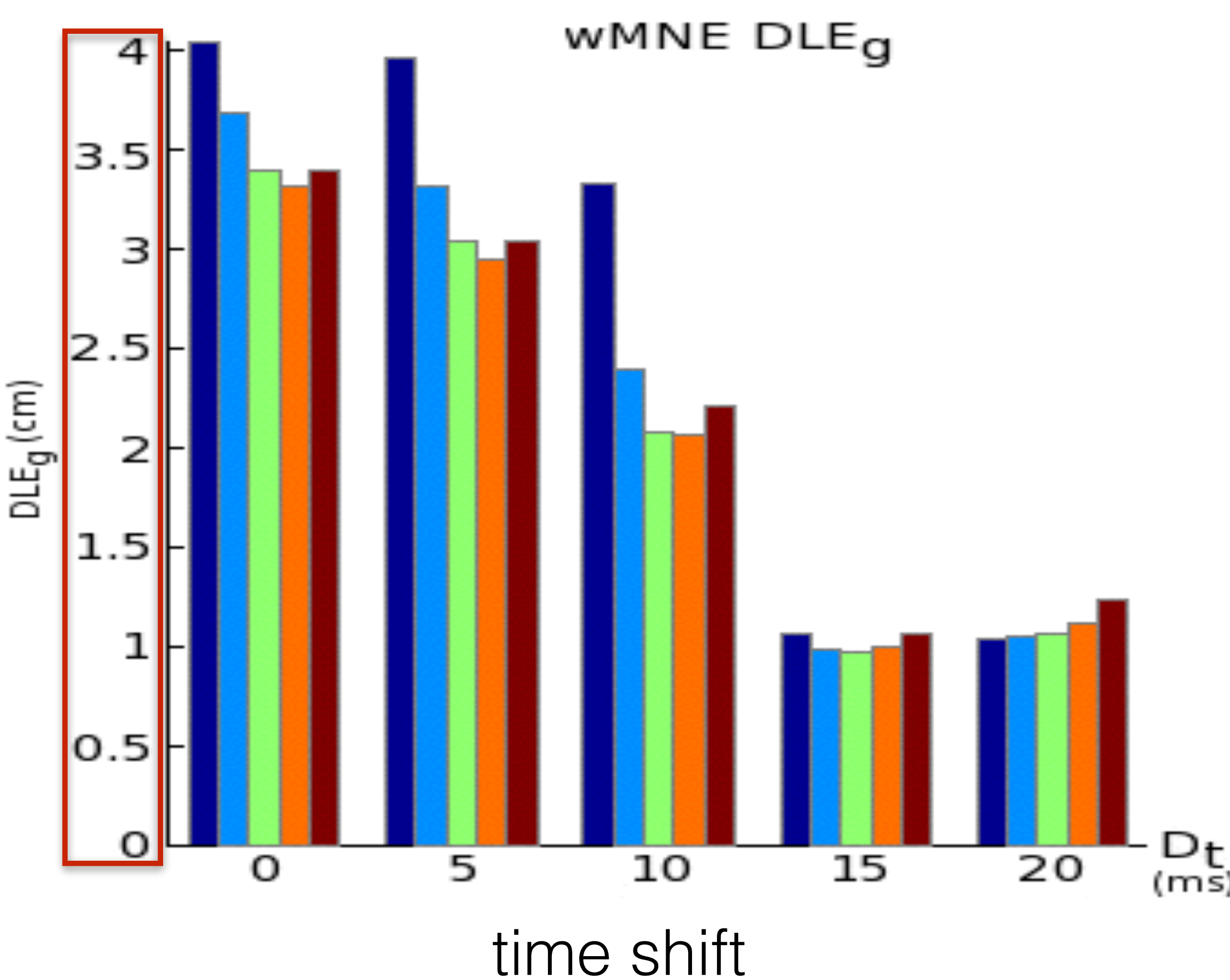
One source in hippocampus & one source in occipital cortex

At best 1 to 2 cm in the hippocampus:

- size of the source
- temporal overlap between sources

Temporal overlap < 25% between cortical and deep sources



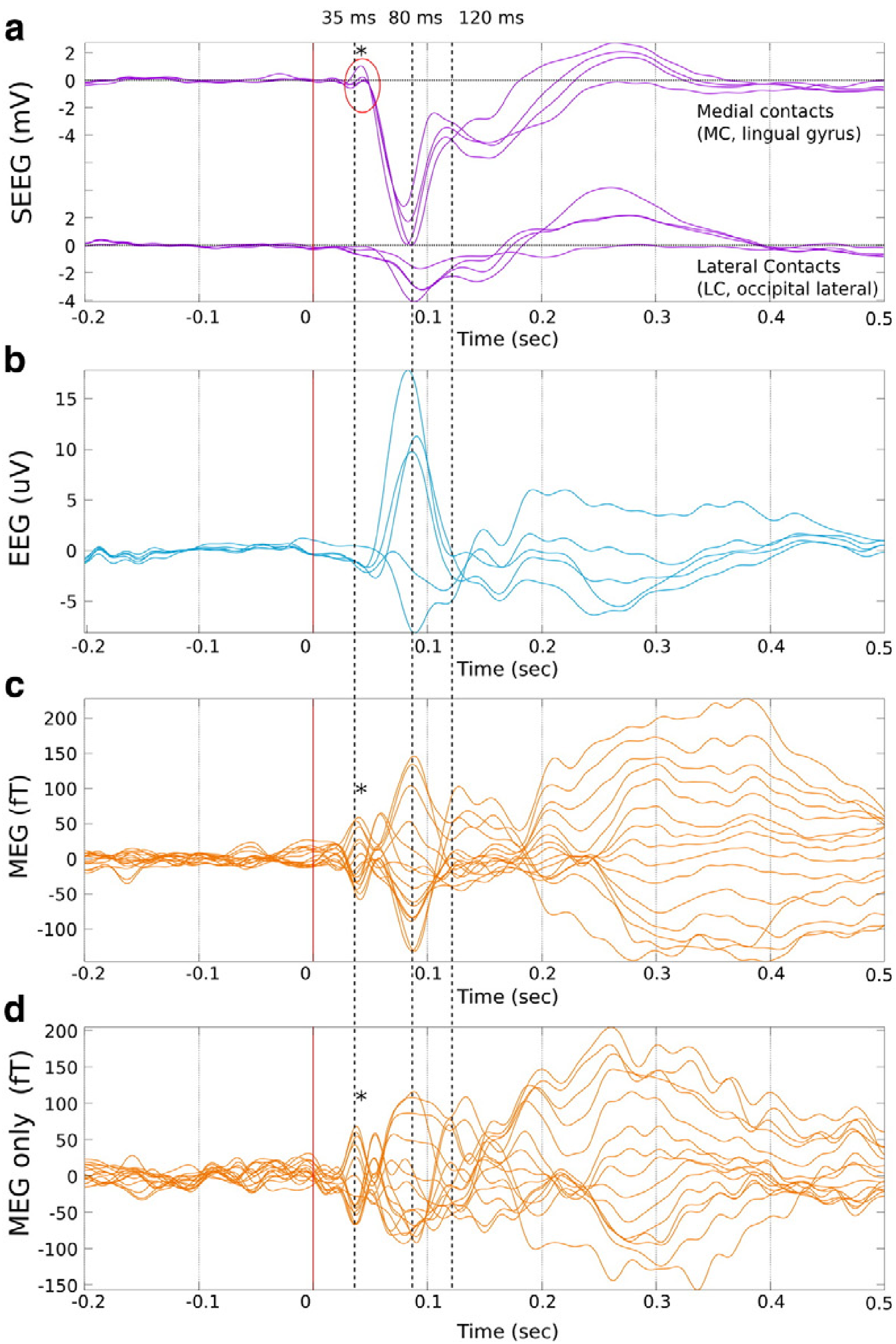


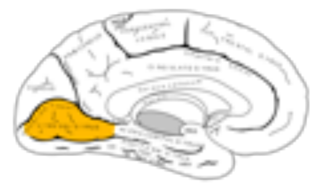
- From a purely theoretical point of view:
  - We should be able to record something (H & A + Cereb)
  - Signal strength depend on a lot of parameters
  - Sources, sensors, registration, models and localisation algorithms
  - Spatial resolution will be limited

Can MEG see deep?

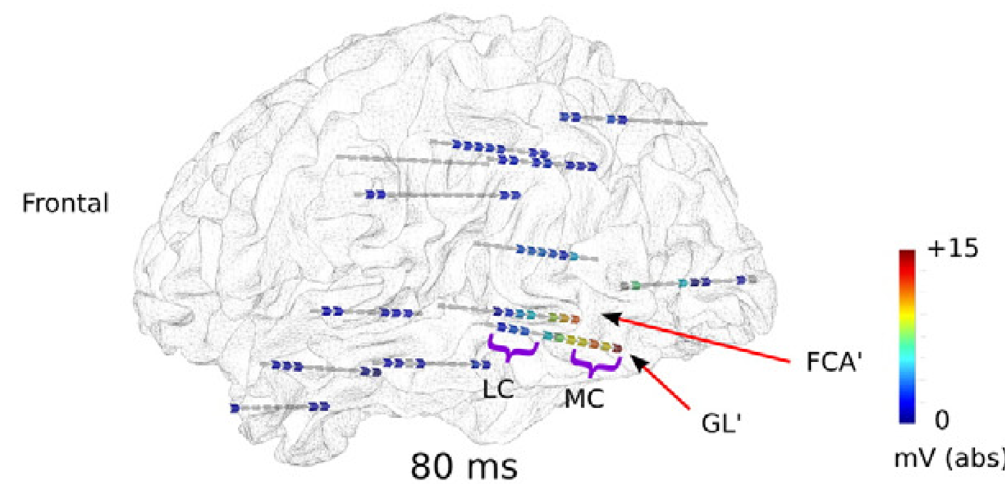
Experimental data

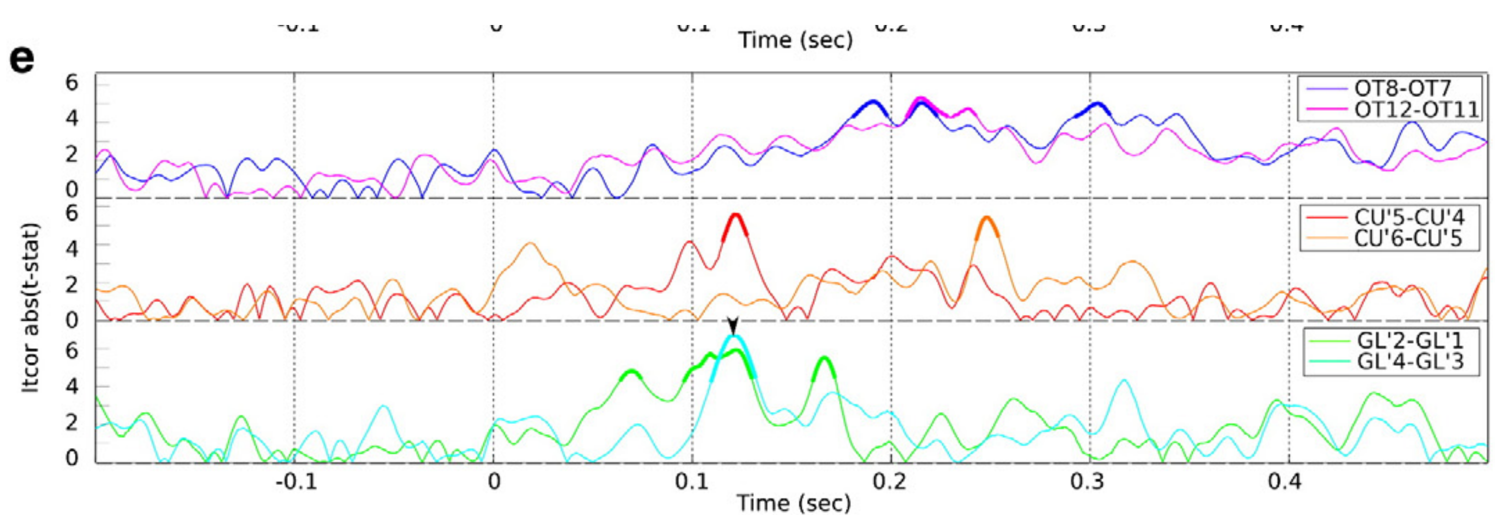
How to validate / evaluate



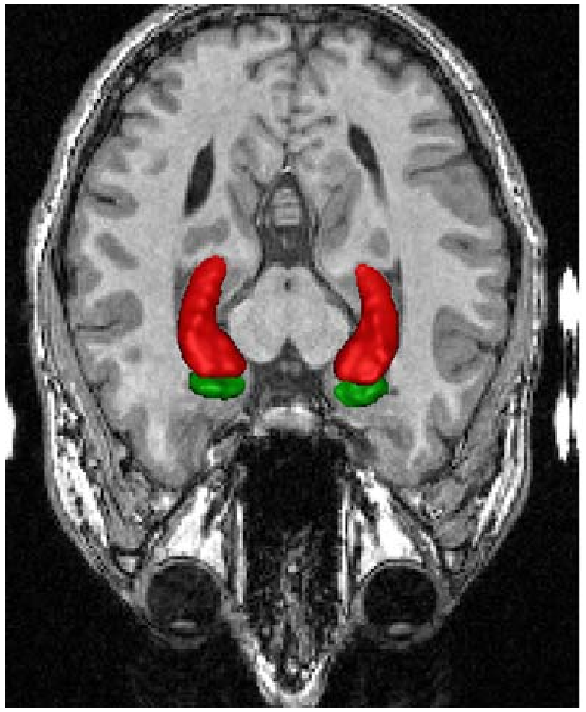


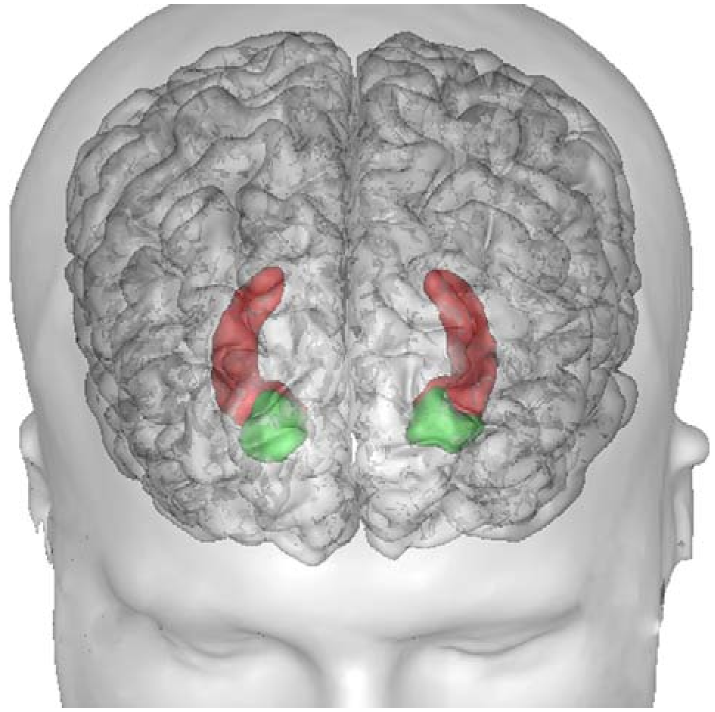
Dubarry AS, Badier JM, Trébuchon-Da Fonseca A, et al. Simultaneous recording of MEG, EEG and intracerebral EEG during visual stimulation: From feasibility to single-trial analysis. Neuroimage. 2014;99:548-558. doi:10.1016/j.neuroimage.2014.05.055.



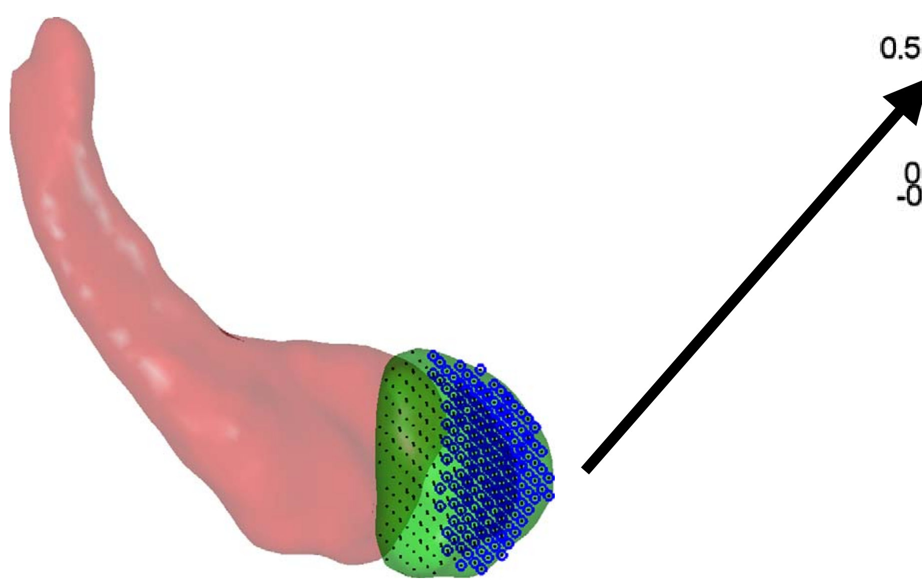


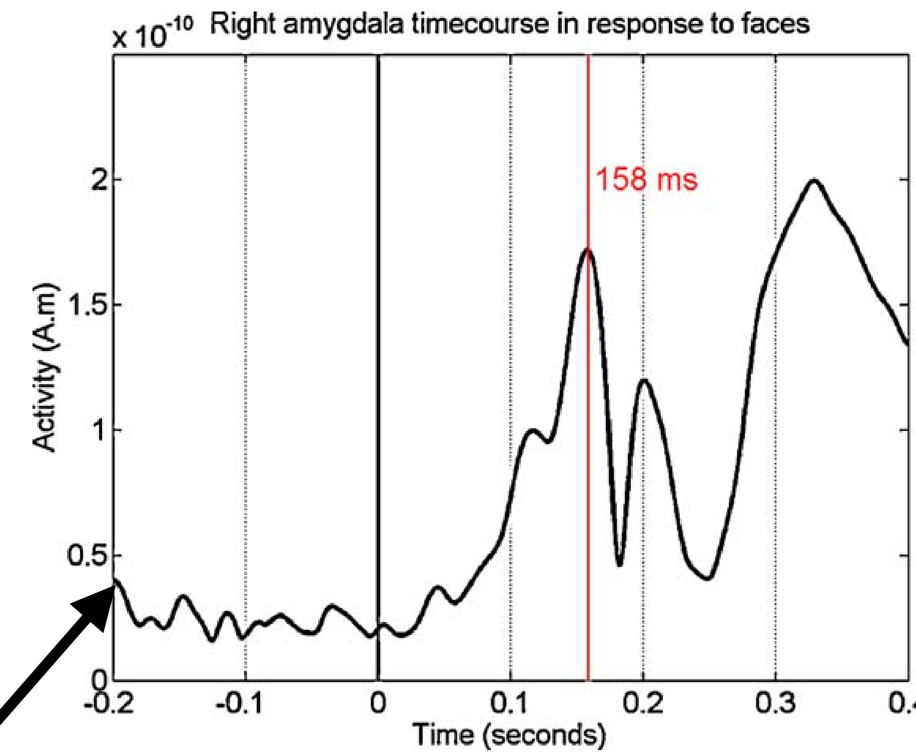
In practice





Dumas et al - PlosOne - 2013

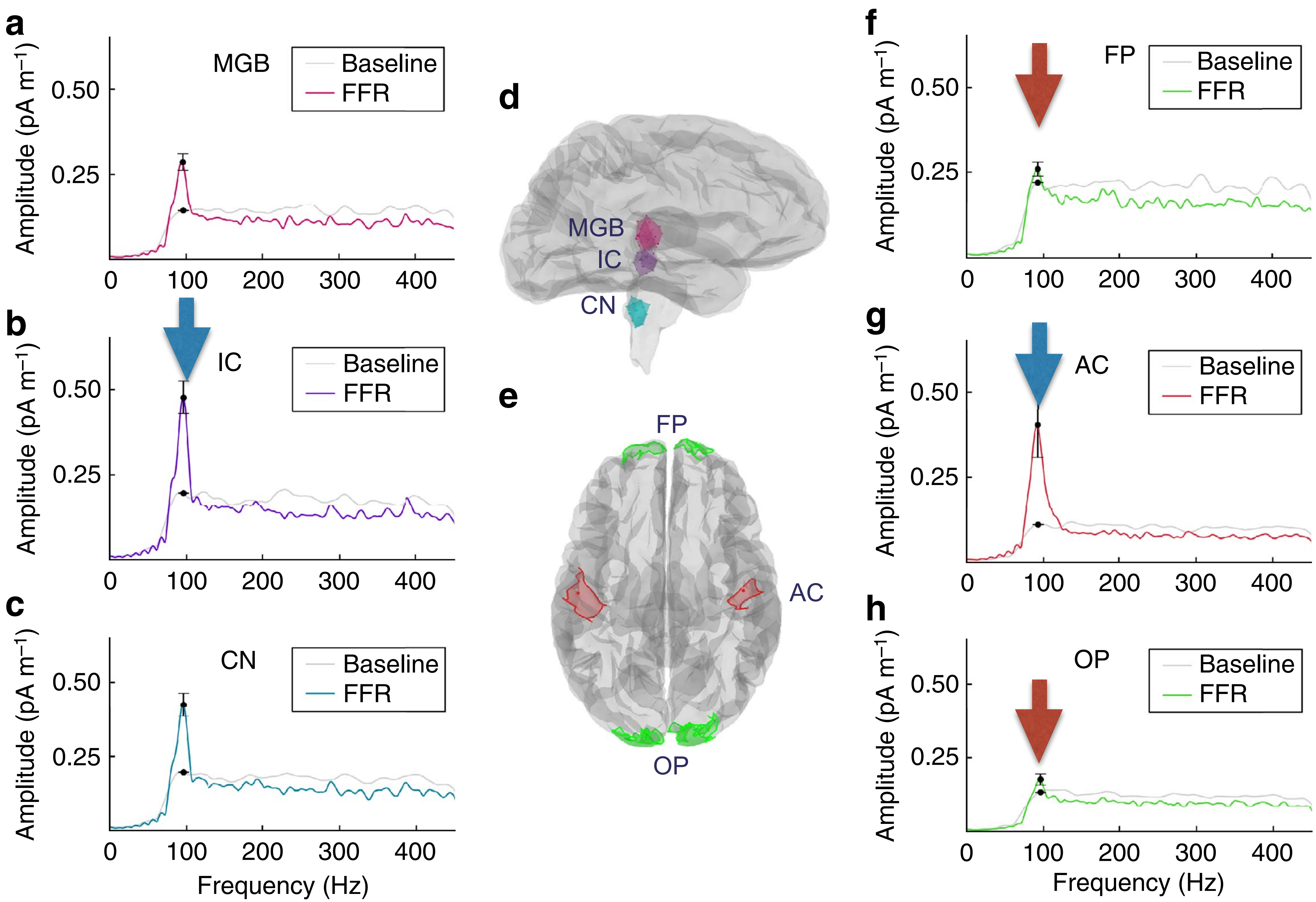




Dumas T, Dubal S, Attal Y, Chupin M, Jouvent R, et al. (2013) MEG Evidence for Dynamic Amygdala Modulations by Gaze and Facial Emotions. PLoS ONE 8(9): e74145. doi:10.1371/journal.pone.0074145

Let’s go deeper…

Coffey, E. B. J. et al. Cortical contributions to the auditory frequency-following response revealed by MEG. Nat. Commun. 7:11070 - (2016)



Beyond MNE approaches

Using beamformer approaches (LCMV, SAM, D.I.C.S …)

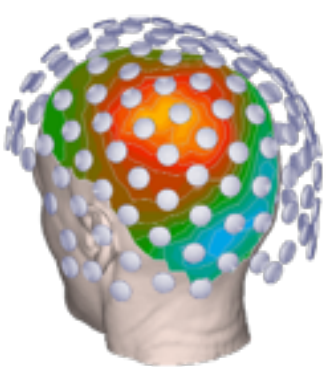
Complete source space model not needed

Just need a scanning grid

Inverse Operator

Inversion : beamformer -> Compute **the source energy at a given location by minimising the contribution from all others sources (biological and artefacts !)**

Sensor space | Source



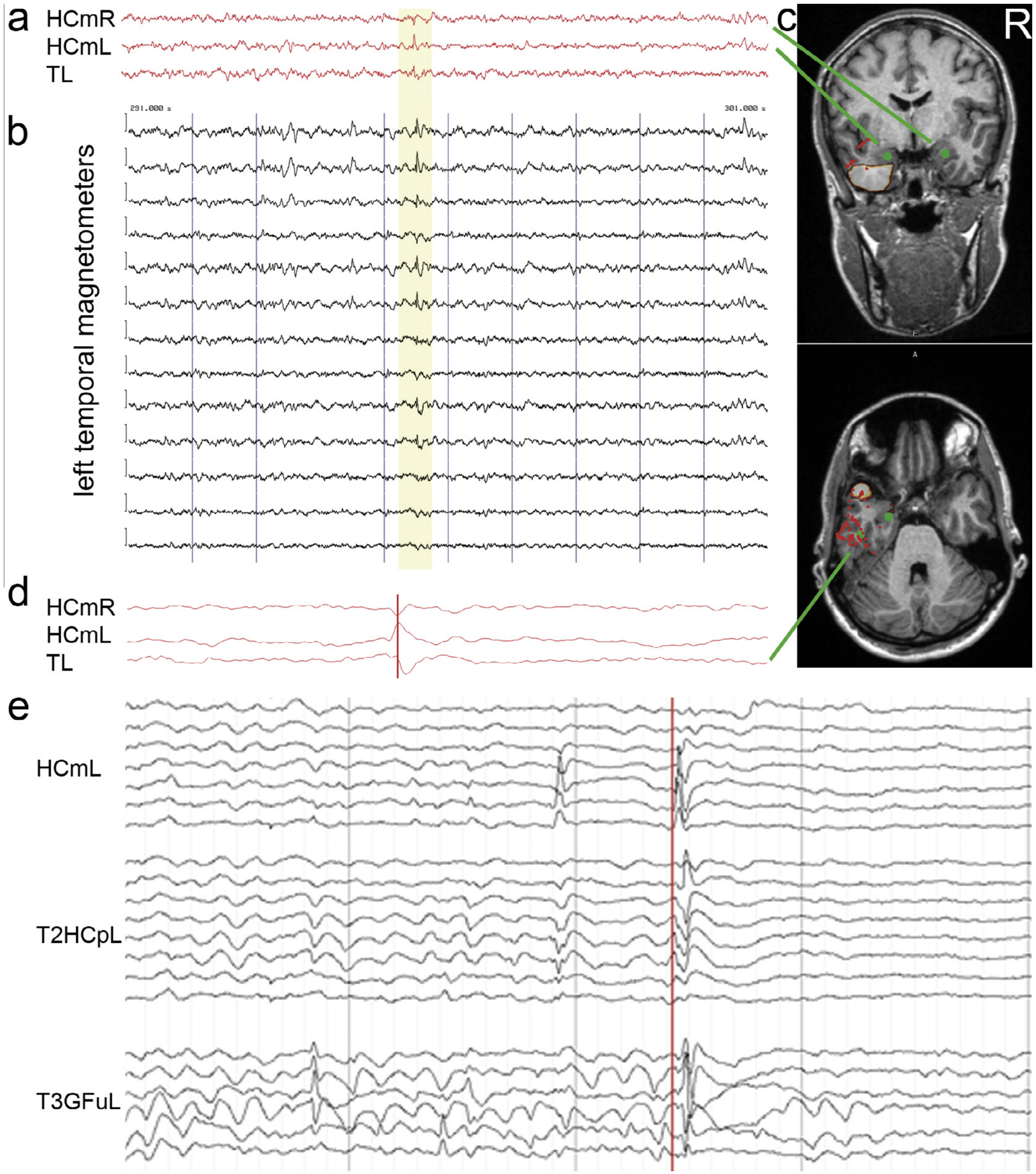
$$\hat{s}_\theta(t) = \mathbf{w}_\theta^T \mathbf{x}(t)$$

Does MEG see deep -> YES

Leaking is still present

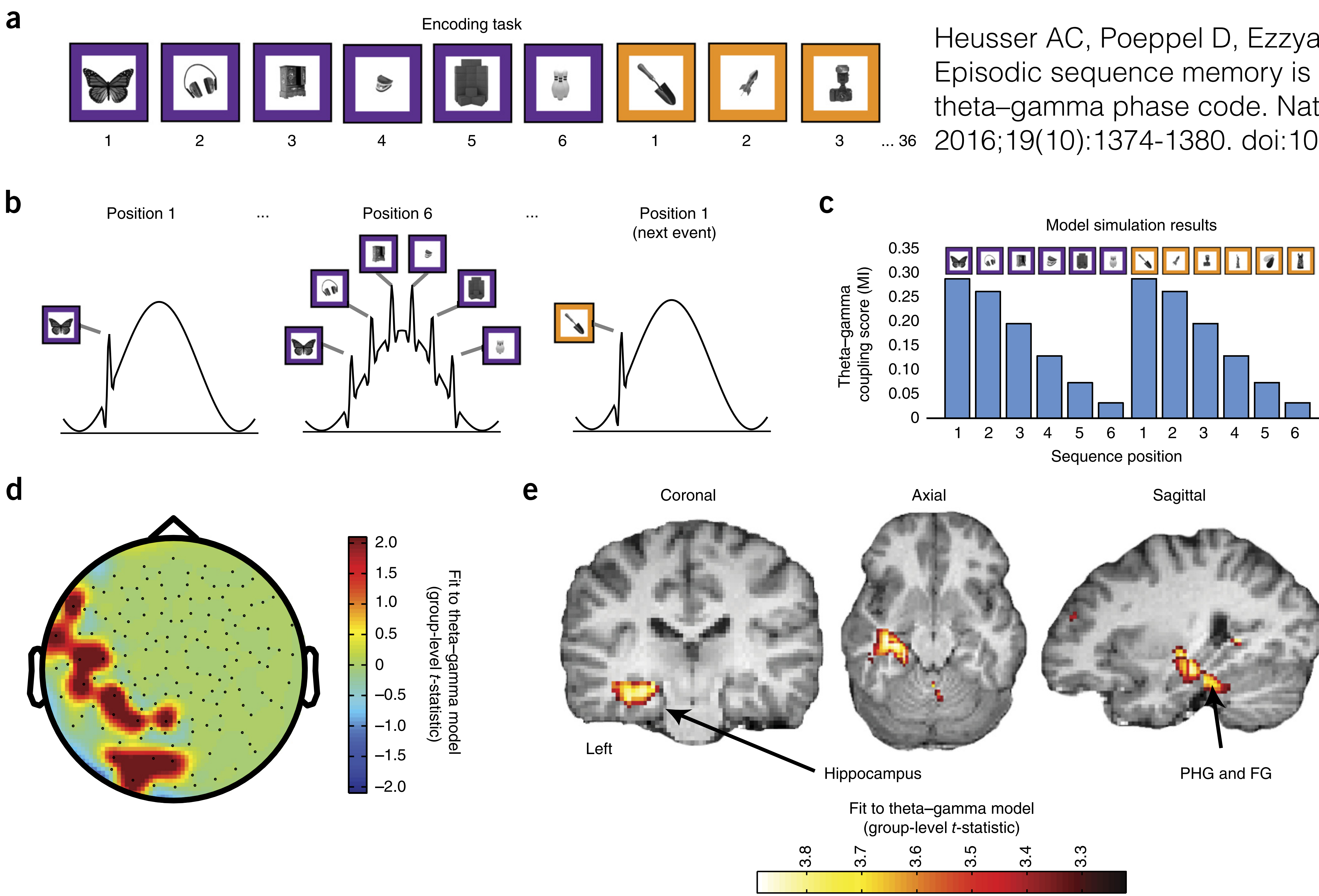
Need enough data to achieve stable results

Hippocampus again



A. Hillebrand, & Coll, Detecting epileptiform activity from deeper brain regions in spatially filtered MEG data, Clinical Neurophysiology, Volume 127, Issue 8, 2016,

Hippocampus



Heusser AC, Poeppel D, Ezzyat Y, Davachi L. Episodic sequence memory is supported by a theta–gamma phase code. Nat Neurosci. 2016;19(10):1374-1380. doi:10.1038/nn.4374.

Conclusion

➡ Yes it can be done but physic laws prevail!

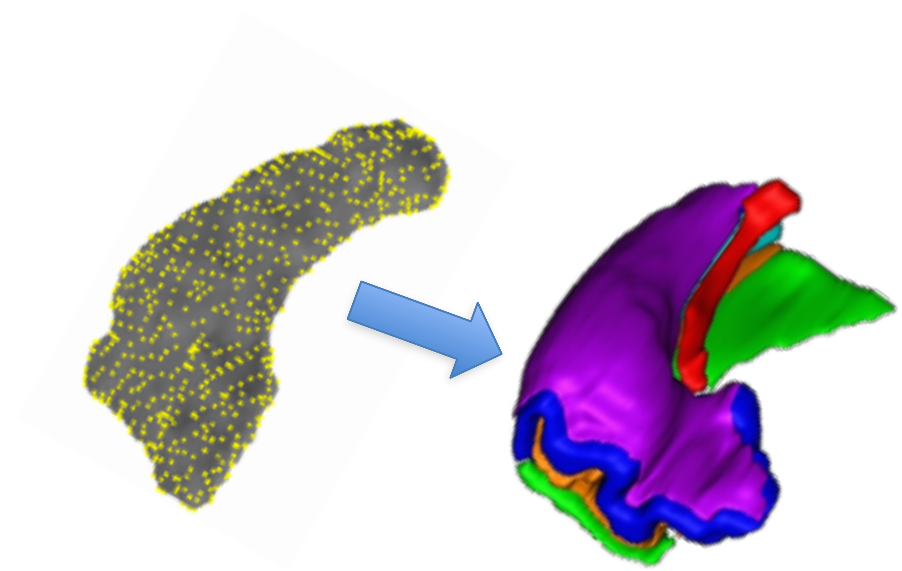
➡ Hippocampus, Amygdala, Cerebellum

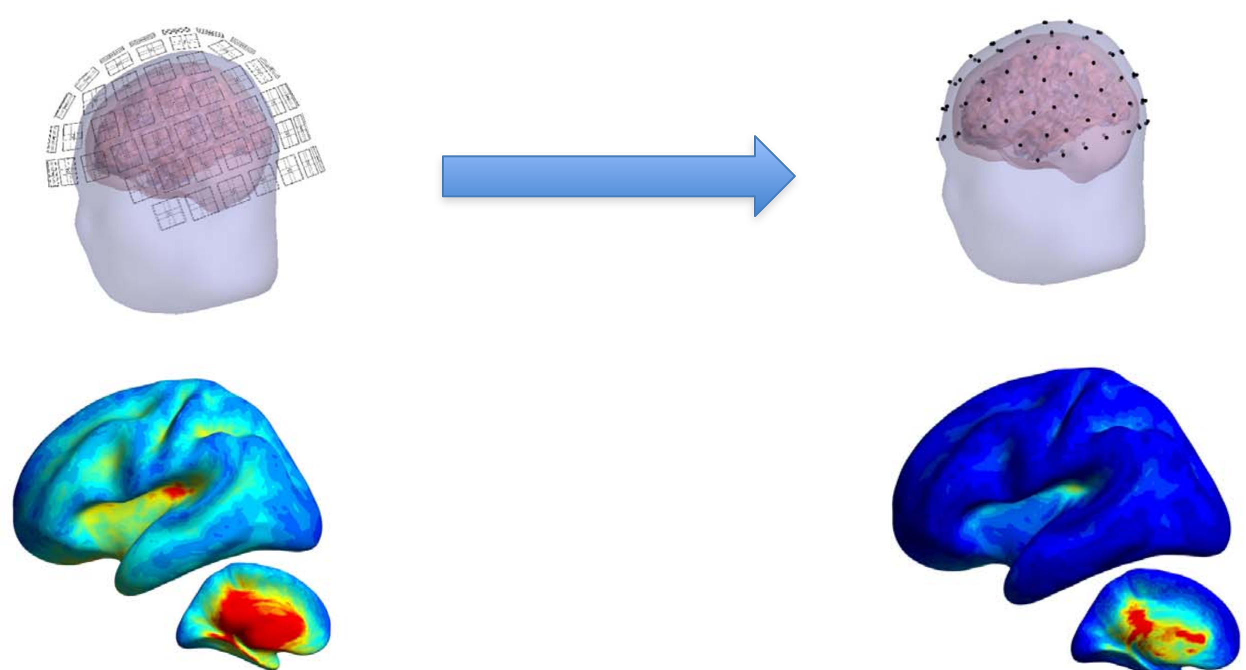
➡ Need careful planning when designing the experiment

- ➡ SNR, contrast, measures, methods

➡ Improvements possible

- ➡ Better models (anatomy, physiology)
- ➡ Sensors closer to the brain





Livanainen & all NeuroImage 2017

Tack !

MEG/EEG Team

Yohan Attal
Angie Fasoula
Pauline Laviron

Aliénor Richard

Nathalie George

Jean-Michel Badier — Aix-Marseille Université - Laboratoire MEG - TIMONE – Marseille

Claude Delpuech — CERMEP. Département MEG. Bron

Etienne Labyt — Clinatec, CEA, MINATEC campus, Grenoble

Papers

Attal Y, Schwartz D. Assessment of subcortical source localization using deep brain activity imaging model with minimum norm operators: a MEG study. PLoS One. 2013;8(3):e59856. doi:10.1371/journal.pone.0059856.
Coffey EBJ, Herholz SC, Chepesiuk AMP, Baillet S, Zatorre RJ. Cortical contributions to the auditory frequency-following response revealed by MEG. Nat Commun. 2016;7:11070. doi:10.1038/ncomms11070.
Dubarry AS, Badier JM, Trébuchon-Da Fonseca A, et al. Simultaneous recording of MEG, EEG and intracerebral EEG during visual stimulation: From feasibility to single-trial analysis. Neuroimage. 2014;99:548-558. doi:10.1016/j.neuroimage.2014.05.055.
Dumas T, Dubal S, Attal Y, et al. MEG evidence for dynamic amygdala modulations by gaze and facial emotions. PLoS One. 2013;8(9):e74145. doi:10.1371/journal.pone.0074145.
Gavaret M, Dubarry A-S, Carron R, Bartolomei F, Trébuchon A, Bénar C-G. Simultaneous SEEG-MEG-EEG Recordings Overcome the SEEG Limited Spatial Sampling. Vol 128.; 2016. doi:10.1016/j.eplepsyres.2016.10.013.
Hauk O, Wakeman DG, Henson R. Comparison of noise-normalized minimum norm estimates for MEG analysis using multiple resolution metrics. Neuroimage. 2011;54(3):1966-1974. doi:10.1016/j.neuroimage.2010.09.053.
Heusser AC, Poeppel D, Ezzyat Y, Davachi L. Episodic sequence memory is supported by a theta–gamma phase code. Nat Neurosci. 2016;19(10):1374-1380. doi:10.1038/nn.4374.
Hillebrand A, Barnes GR. A Quantitative Assessment of the Sensitivity of Whole-Head MEG to Activity in the Adult Human Cortex. Neuroimage. 2002;16(3):638-650. doi:10.1006/nimg.2002.1102.
Iivanainen J, Stenroos M, Parkkonen L. Measuring MEG closer to the brain: Performance of on-scalp sensor arrays. Neuroimage. 2017;147(December):542-553. doi:10.1016/j.neuroimage.2016.12.048.
Lin FH, Witzel T, Ahlfors SP, Stufflebeam SM, Belliveau JW, Hämäläinen MS. Assessing and improving the spatial accuracy in MEG source localization by depth-weighted minimum-norm estimates. Neuroimage. 2006;31(1):160-171. doi:10.1016/j.neuroimage.2005.11.054.
Meyer SS, Rossiter H, Brookes MJ, Woolrich MW, Bestmann S, Barnes GR. Using generative models to make probabilistic statements about hippocampal engagement in MEG. Neuroimage. 2017;149(January):468-482. doi:10.1016/j.neuroimage.2017.01.029.
Okada Y, Lauritzenss M, Nicholson C. MEG source models and physiology. Phys Med Biol. 1987;32(1):43-51.
Parkkonen L, Fujiki N, Mäkelä JP. Sources of auditory brainstem responses revisited: Contribution by magnetoencephalography. Hum Brain Mapp. 2009;30(6):1772-1782. doi:10.1002/hbm.20788.