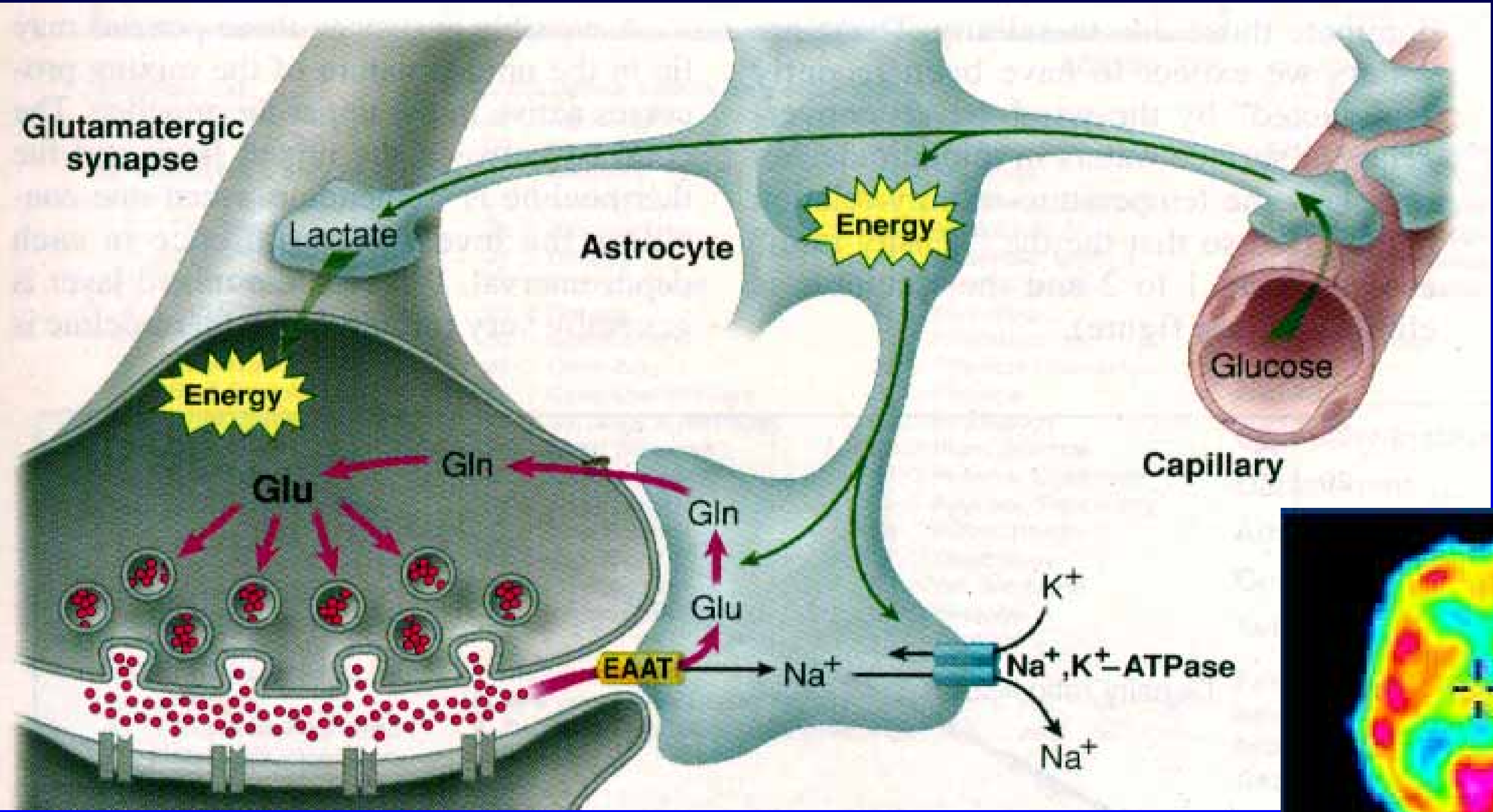
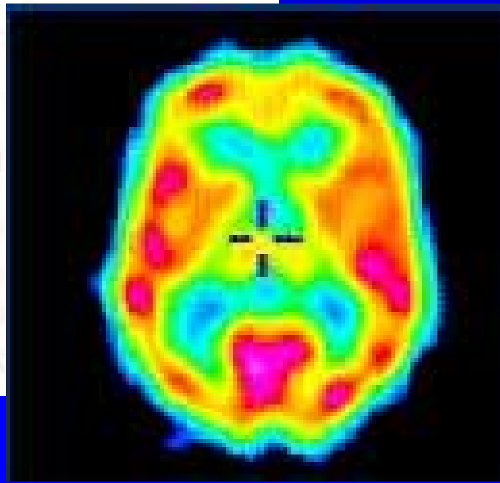
Food for thought



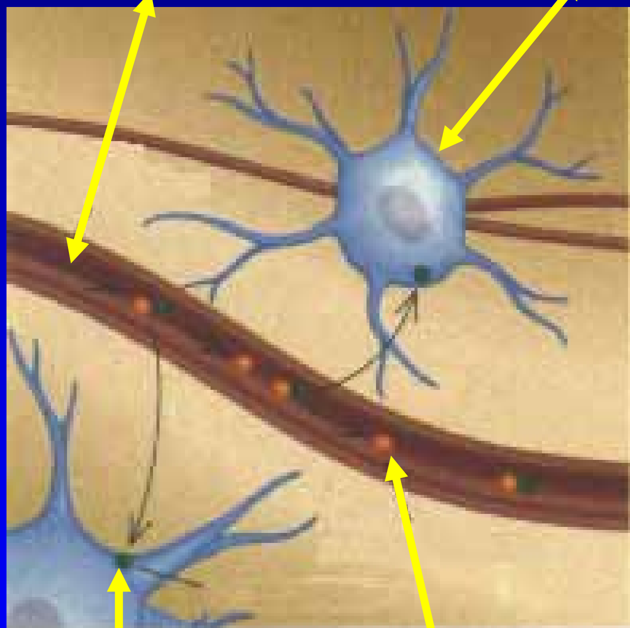


Magistretti et al., Science, 1999

Hemodynamic response

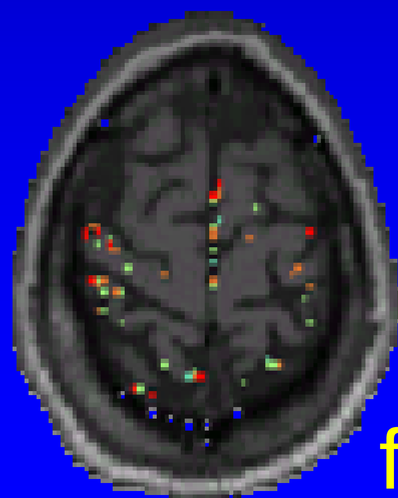
Blood flow

↑Neuroelectrical activity



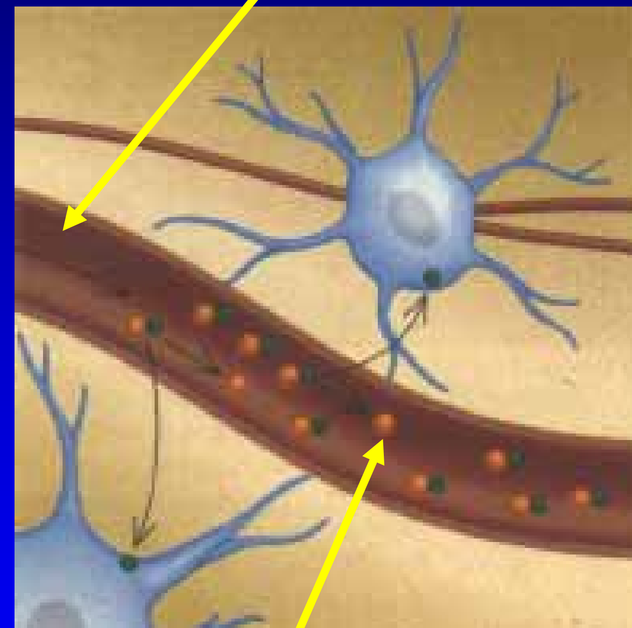
Oxygen

Hemoglobin



fMRI signal

↑Blood flow



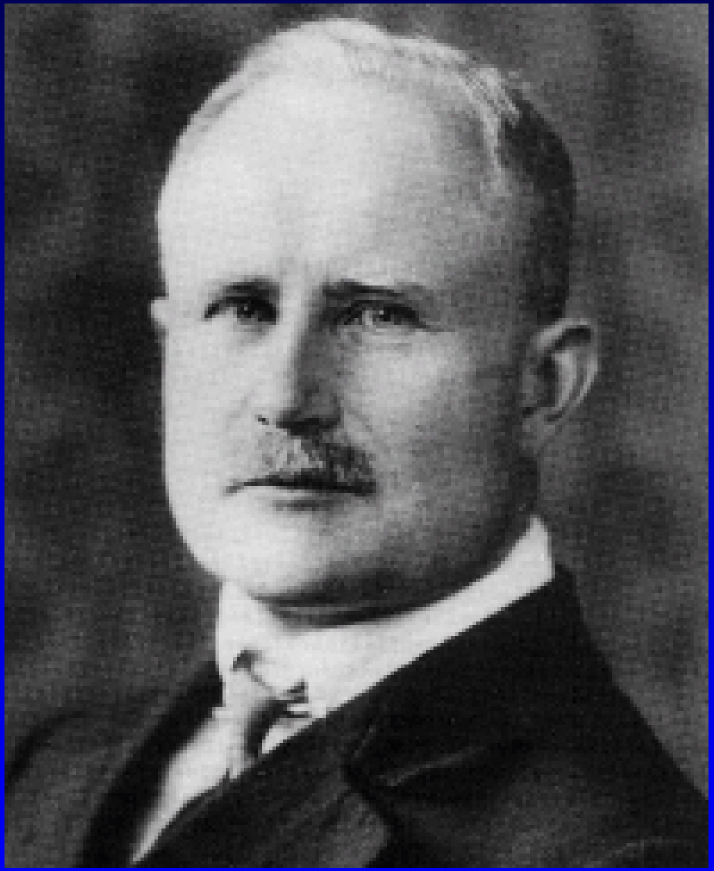
↓Deoxyhemoglobin

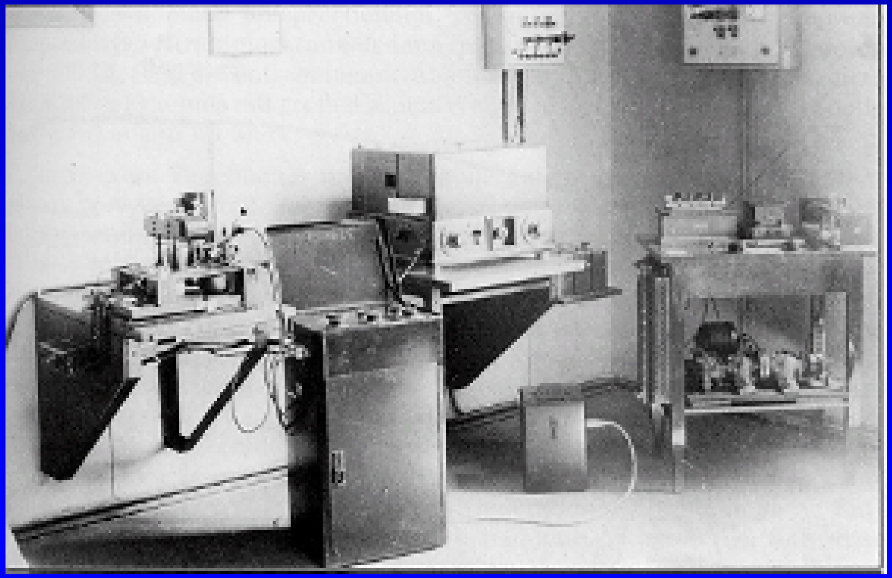
Questions about the integration of EEG/MEG with the fMRI

- What are the techniques to usefully relate EEG/MEG and fMRI?
- What is the evidence for true synergy?
- What behavioral and analysis methods are successful?
- What do we expect in the near future?

Human brain produces measurable signals on the scalp

- ☞ Hans Berger in 1929 produced the first report on the measurement of electrical activity in man over the scalp surface
- ☞ He hoped that EEG could represent a sort of “window on the mind”

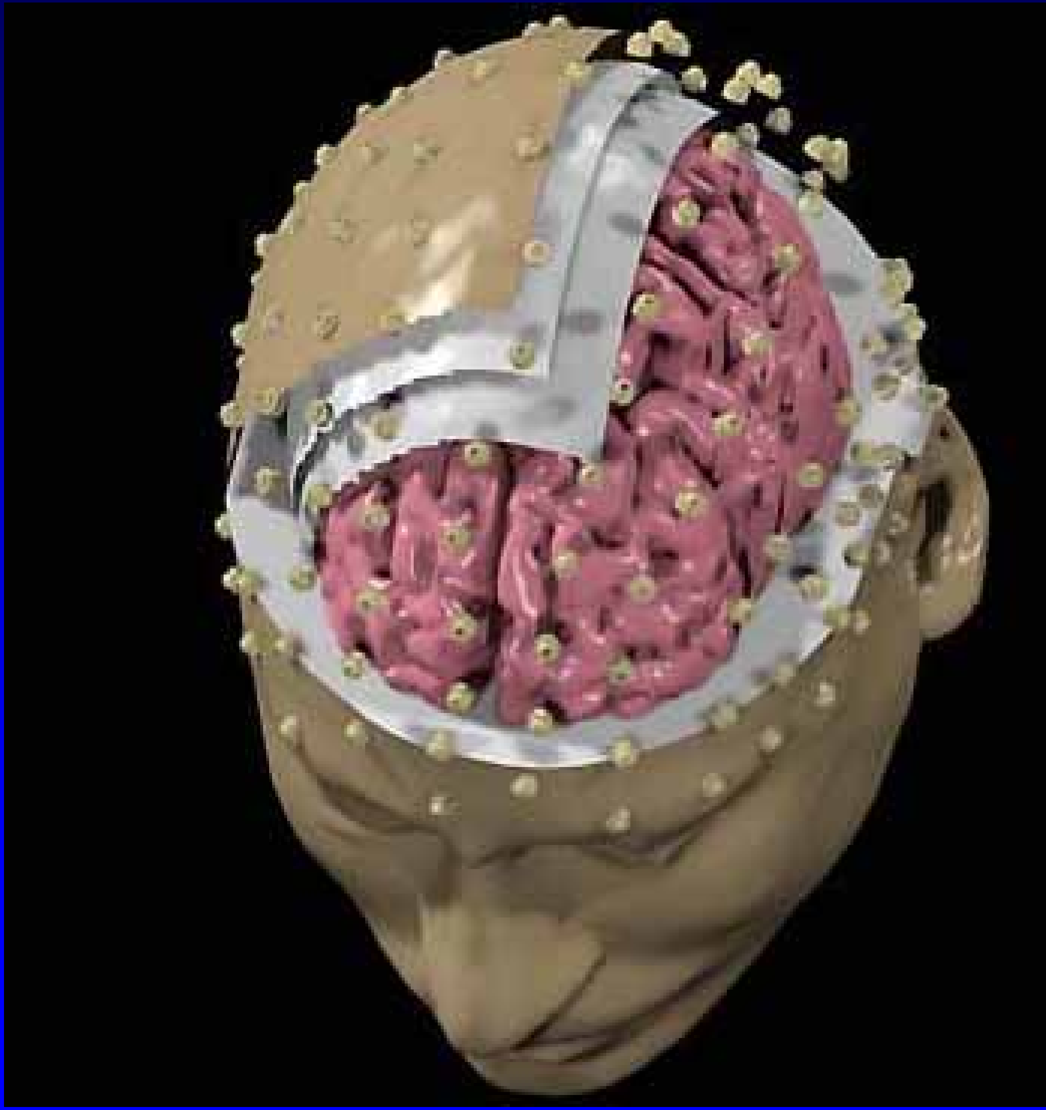




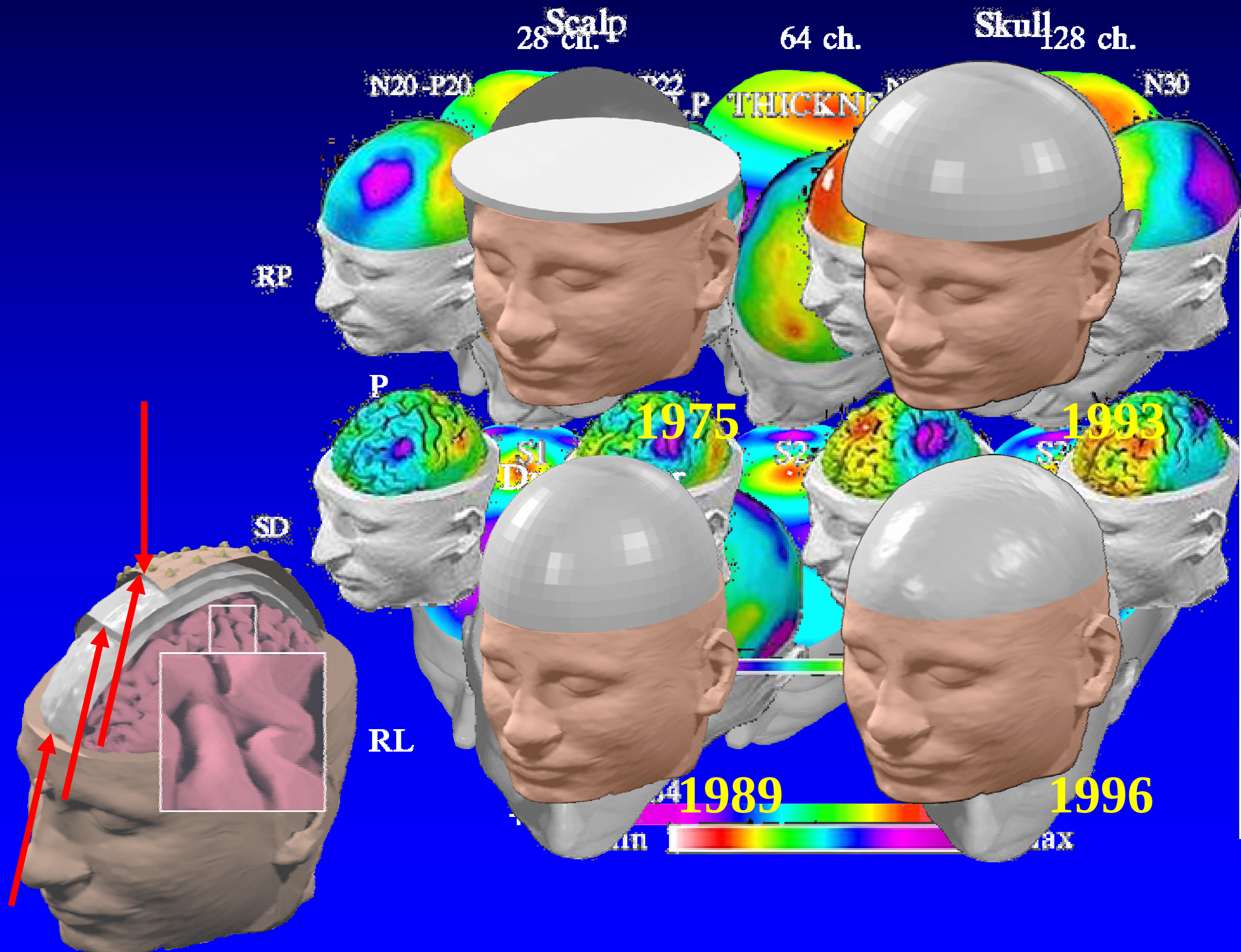
Berger’s equipment

High Resolution Electroencephalography (HREEG)

- Brain activity elicited a time varying potential distribution over the cortical surface
- Such potential distribution are still measurable at the scalp level
- Due to low scalp conductivity the EEG Signal to noise ratio is very low
- HREEG => Sampling the potential distribution with an high number of electrodes, MRI images for realistic head modeling and spatial deblurring algorithms



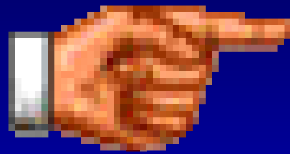
Steps to improve the spatial details of recorded EEG Data

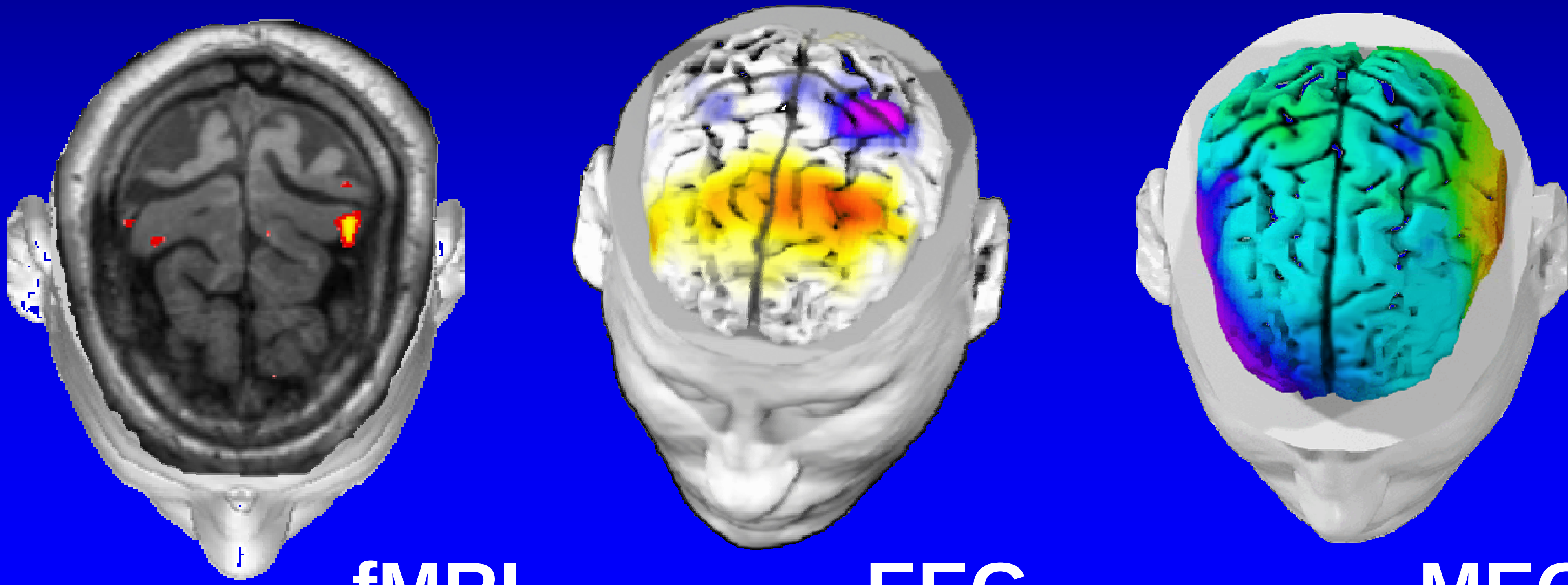


Insert the geometry of skull and dura mater in inverse calculation

The neuroimaging puzzle

- Different neuroimaging techniques, same experimental paradigm
- (unilateral right middle finger movement)



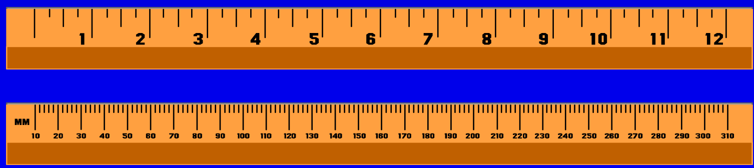


fMRI EEG MEG

The linear inverse problem

$$\xi = \underset{x}{\operatorname{argmin}} \left(\|Ax - b\|_M^2 + \lambda^2 \|x\|_N^2 \right)$$

The difference between modeled and measured potentials/fields is minimized, together with the energy of the sources

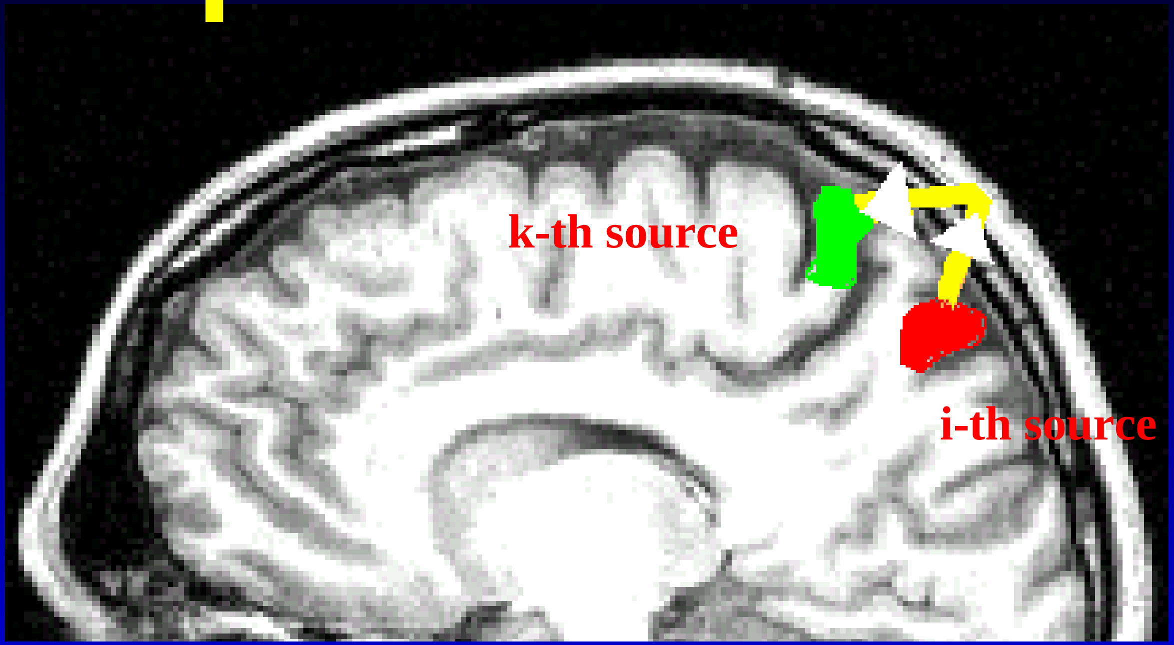


A is the lead field matrix
x is a vector in the source space
b is the measured data vector
λ is a regularization parameter
M is the metric for the data space
N is the metric for the source space
ξ is the solution vector

☞Solutions ξ are obtained by using x = G b where

$$G = N^{-1} A' \left(A N^{-1} A' + \lambda M^{-1} \right)^{-1}$$

Dipolar Localization Error (DLE)



$$x_{Est} = Gb = GAx_{True}$$

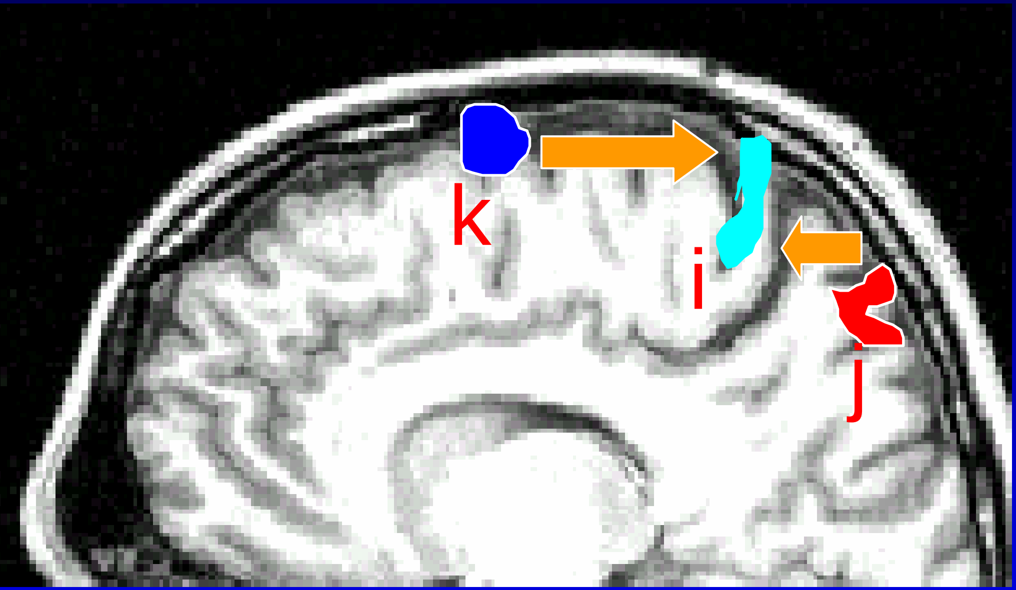
$$x_{Est} = Rx_{True}$$

$$\boldsymbol{x}_{Est} = \boldsymbol{R}\delta_i = \boldsymbol{R}_{\cdot i}$$ i-th column of the resolution matrix R

$$\hat{\boldsymbol{i}} = \arg\max_{k} \left\| \boldsymbol{R}_{ki} \right\|$$ index of the maximum of the i-th column of the resolution matrix R

$$\boldsymbol{DLE}_{i} = \left\| \vec{\boldsymbol{r}}_i - \vec{\boldsymbol{r}}_{\hat{i}} \right\|$$ distance between the two sources

Resolution Kernels

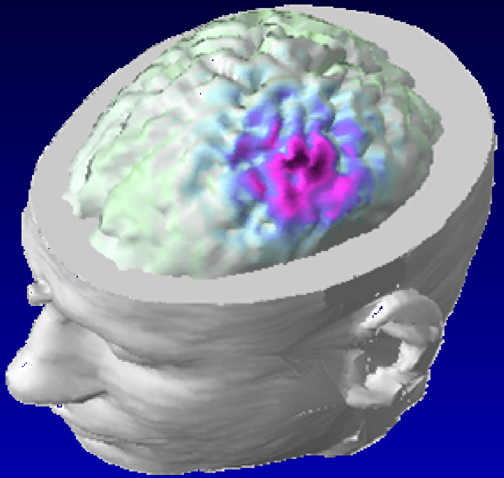


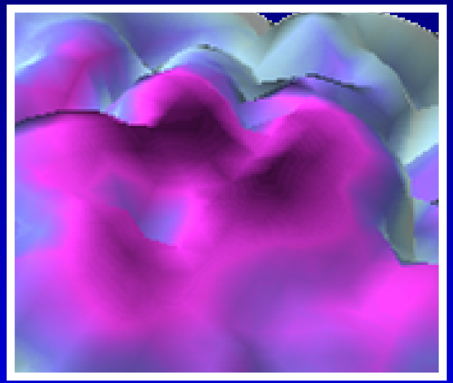
$$x_{Est_i} = \sum_{k=1}^{N} R_{ik} \, x_{True_k}$$

- The R_{ik}s define how the different sources other than the i-th contributed to the estimation to the i-th itself
- The R_{ik}s belongs to the i-th row of the resolution matrix and are called Resolution Kernels

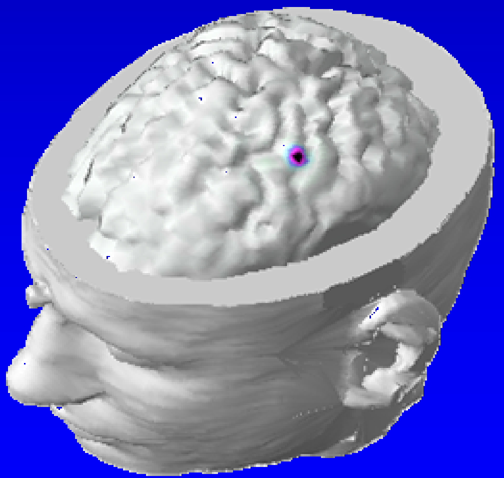
The Resolution Kernel

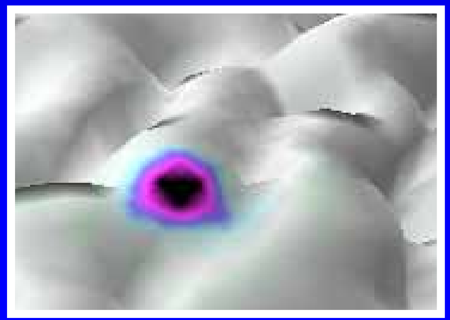
- **Bad Resolution Kernel**
  - large peak around the maximum
  - one or more peaks located far from the source position





- **Good Resolution Kernel**
  - narrow peak around the maximum
  - one peak located at the source position





From current strength to probability maps

- ☞ How obtain a measure of the uncertainty of current estimations due to the EEG/MEG noise (n) ?

- ☞ Under the null hypothesis of no activation the Z is distributed as a Gaussian distribution

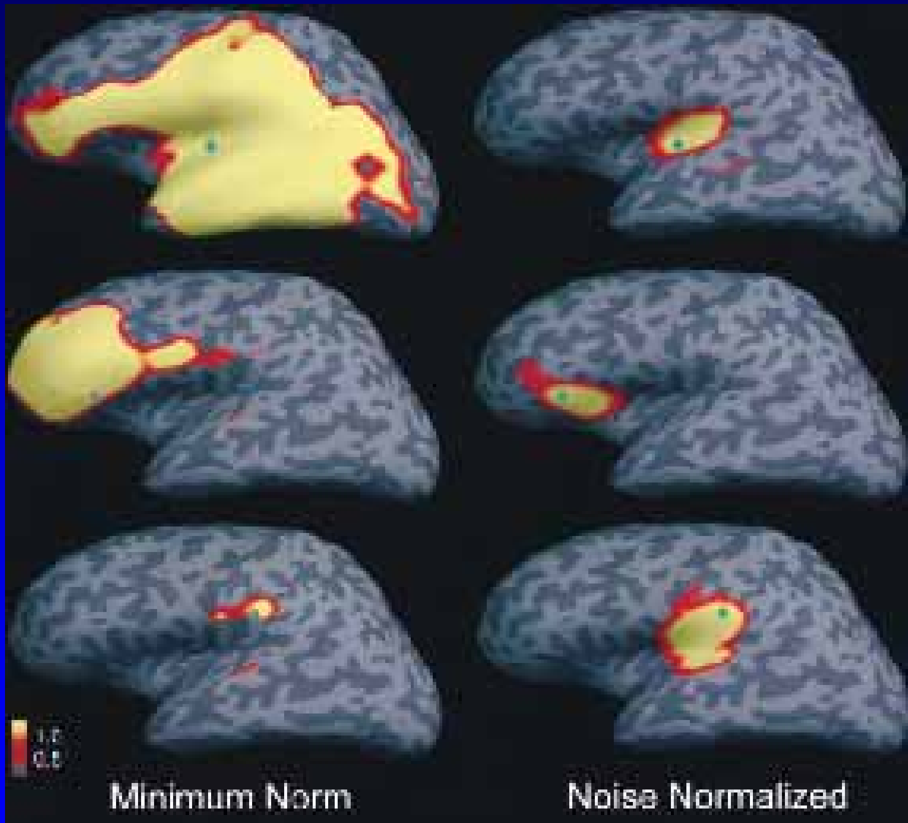
$$\sigma^2_{Noise} = Gnn'G' = GCG'$$

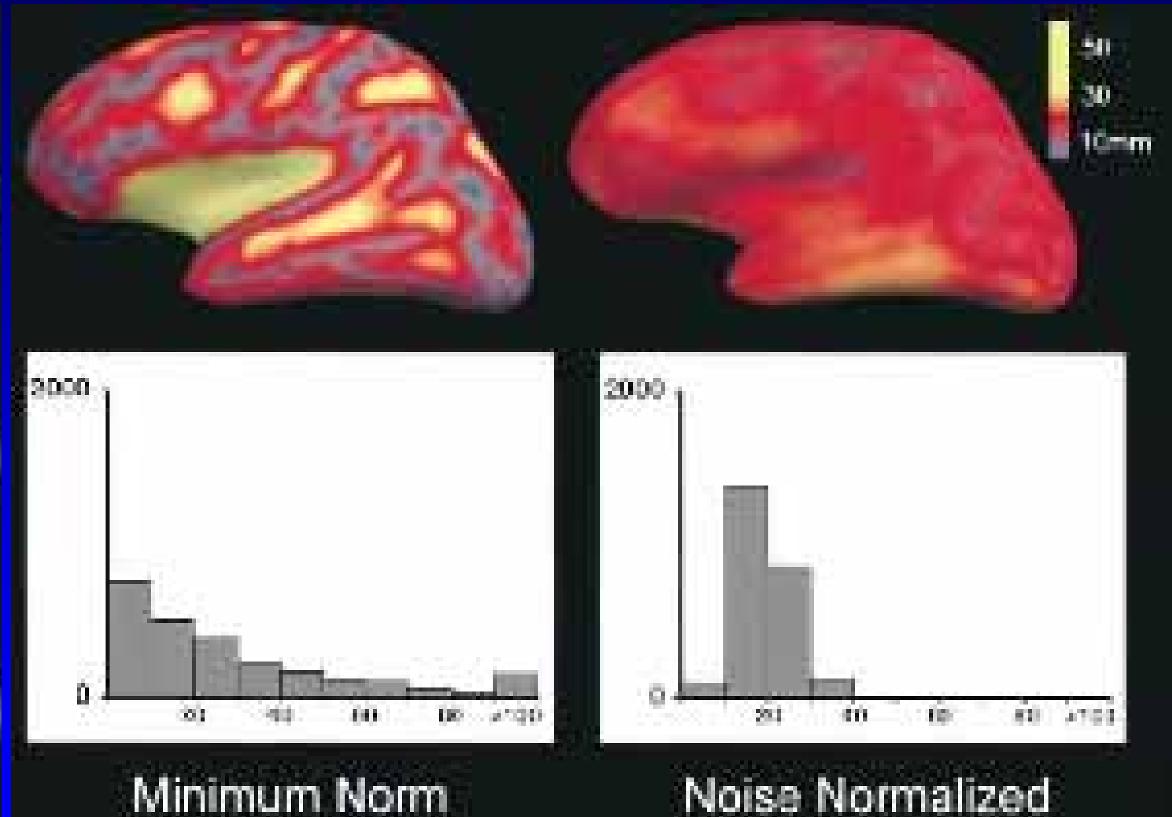
$$Z_i(t) = \frac{G \cdot b(t)}{\sqrt{GCG'}}$$

- ☞ In the case of three component for each dipole the q as a sum of squares is distributed as a Fisher distribution ($F_{3,n}$)

$$q_i(t) = \frac{\left[\sum_{k=1}^{3} G_k \cdot b(t)\right]^2}{\sum_{k=1}^{3} G_k \cdot C \cdot G_k'}$$

From current strengths to probability maps



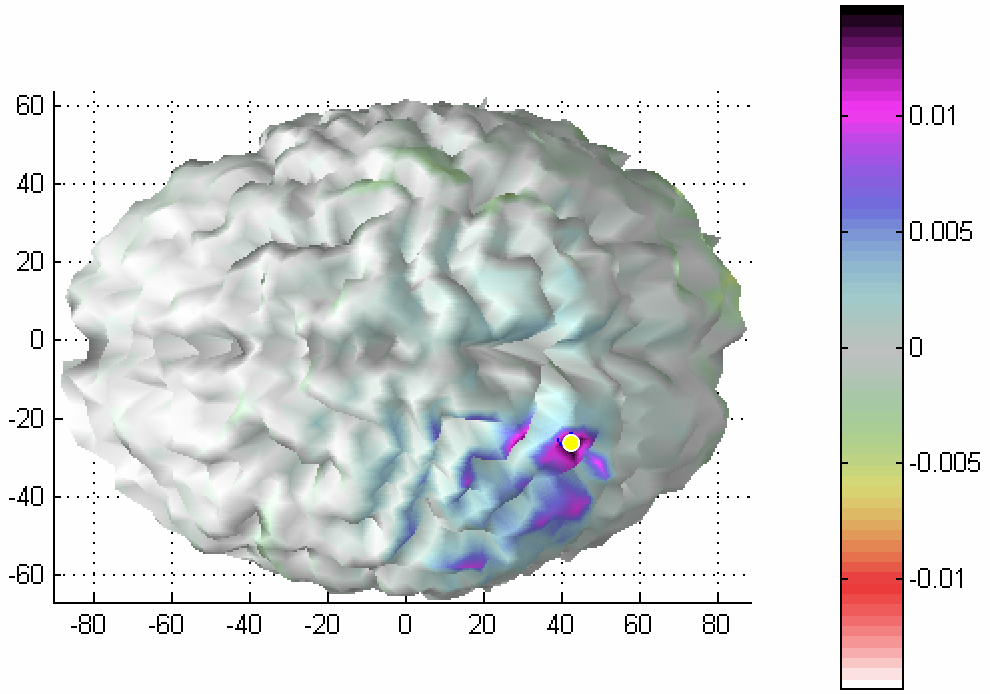


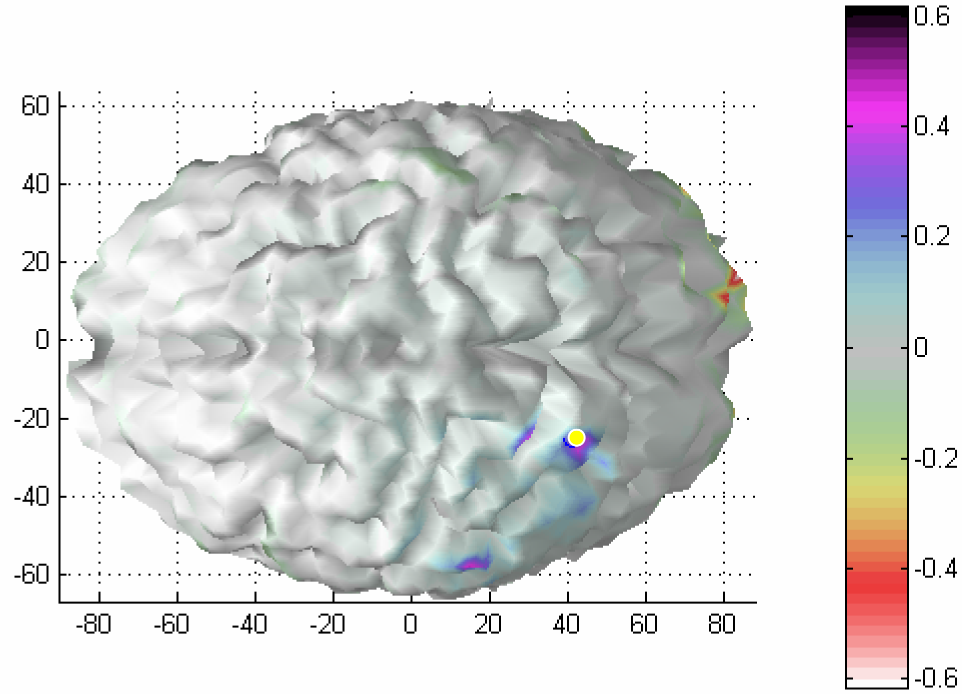
Point spread functions (DLE)

Distribution of the PSF (DLE)

Dale et al., 2000

From current strengths to probability maps





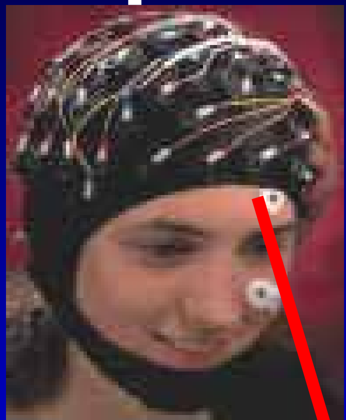
Actual dipole position

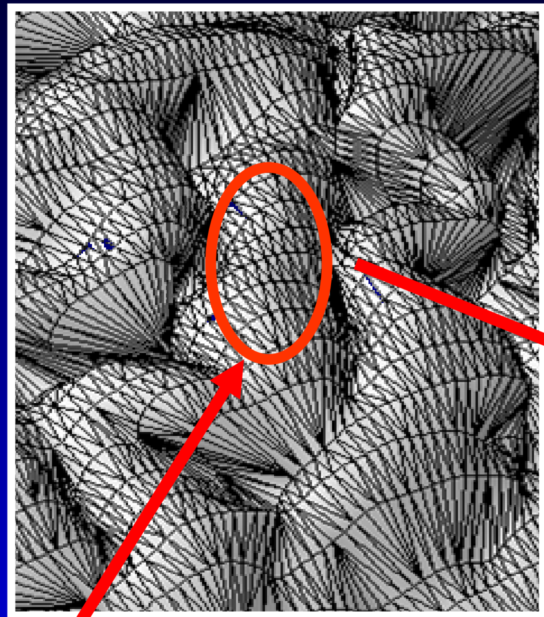
Weighted minimum norm Resolution kernel

Noise normalized Resolution kernel

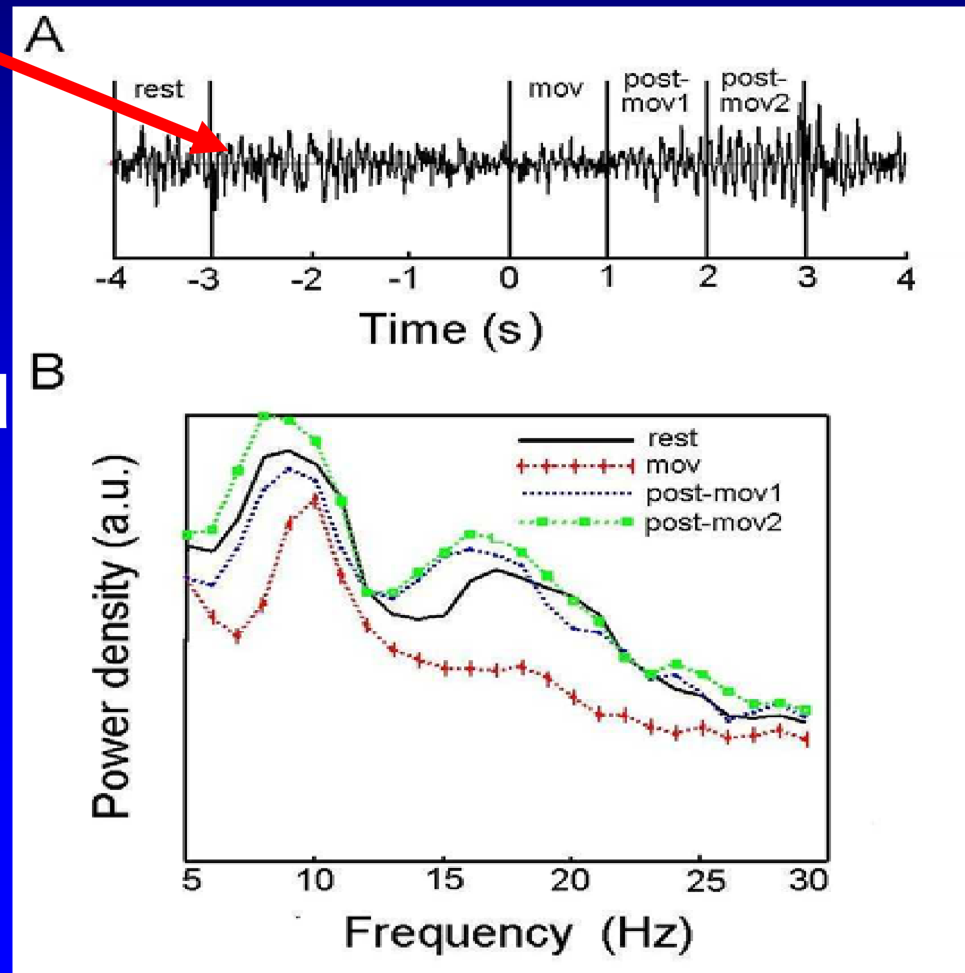
From scalp to cortical EEG in RoIs

Scalp EEG

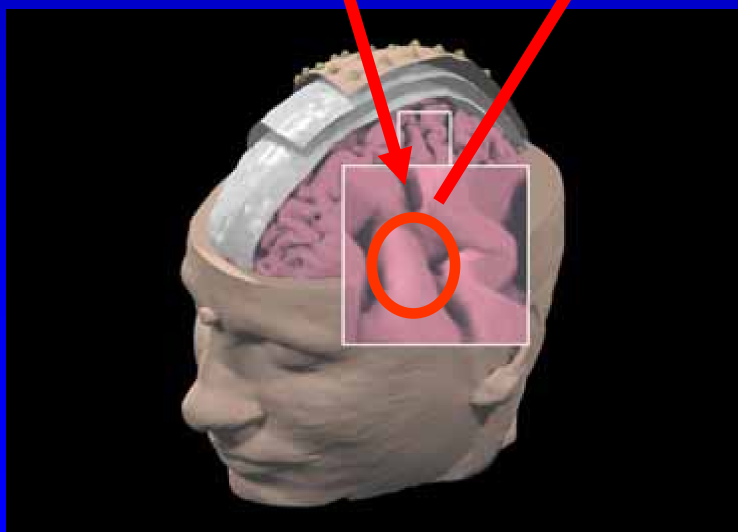




Linear inverse estimates within a RoI are collapsed (mean)

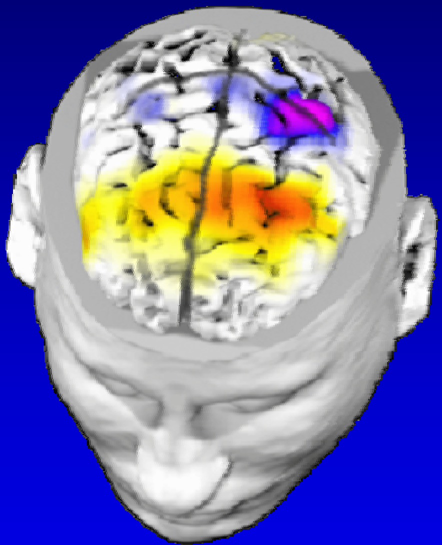


M1 Hand area RoI

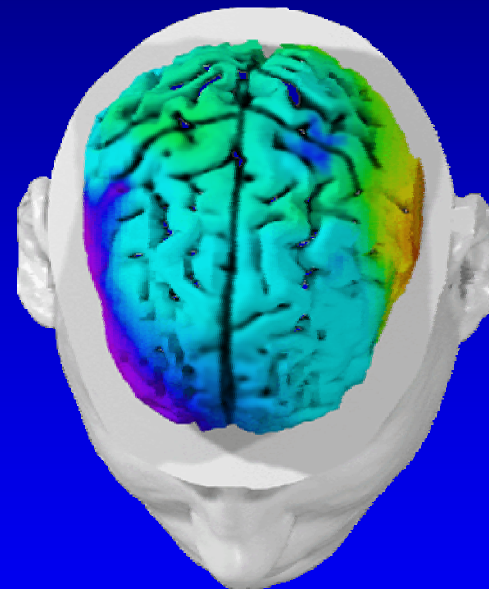


"Virtual" electrode

Integration of EEG and MEG data



EEG



MEG

Integration of EEG and MEG data

Why:

Different sensitivities to the neural sources

Increased amount of information

Question: How we can fuse femtoTesla and microVolt?

Answer: normalizing the measures with noise standard deviation

How:

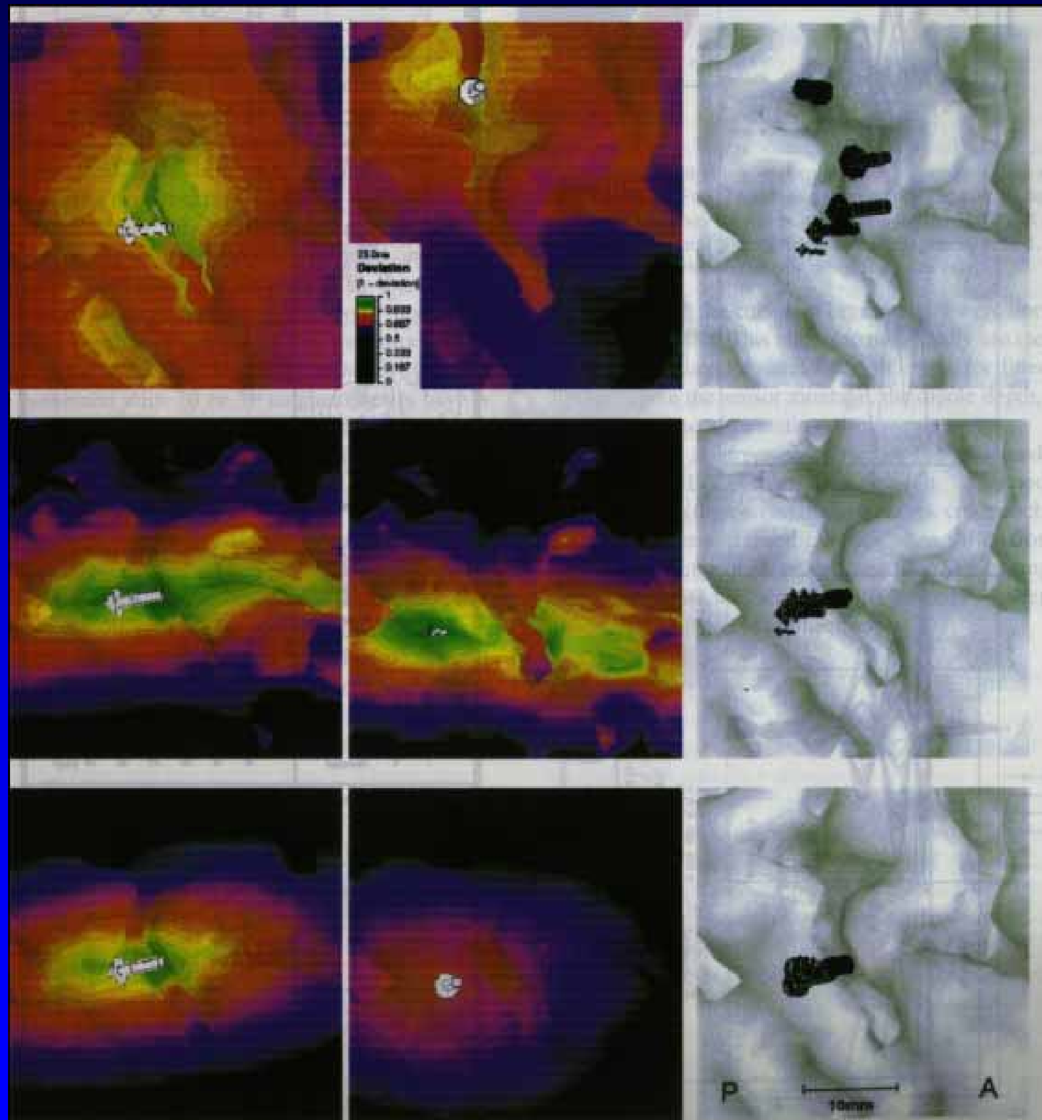
Mahalanobis metric for data space

Column normalization for the source space

$$\xi = \underset{x}{\operatorname{argmin}} \left(\left\| Ax - b \right\|_M^2 + \lambda^2 \left\| x \right\|_N^2 \right)$$

Integration of EEG and MEG data

20 ms 23 ms 18..24 ms



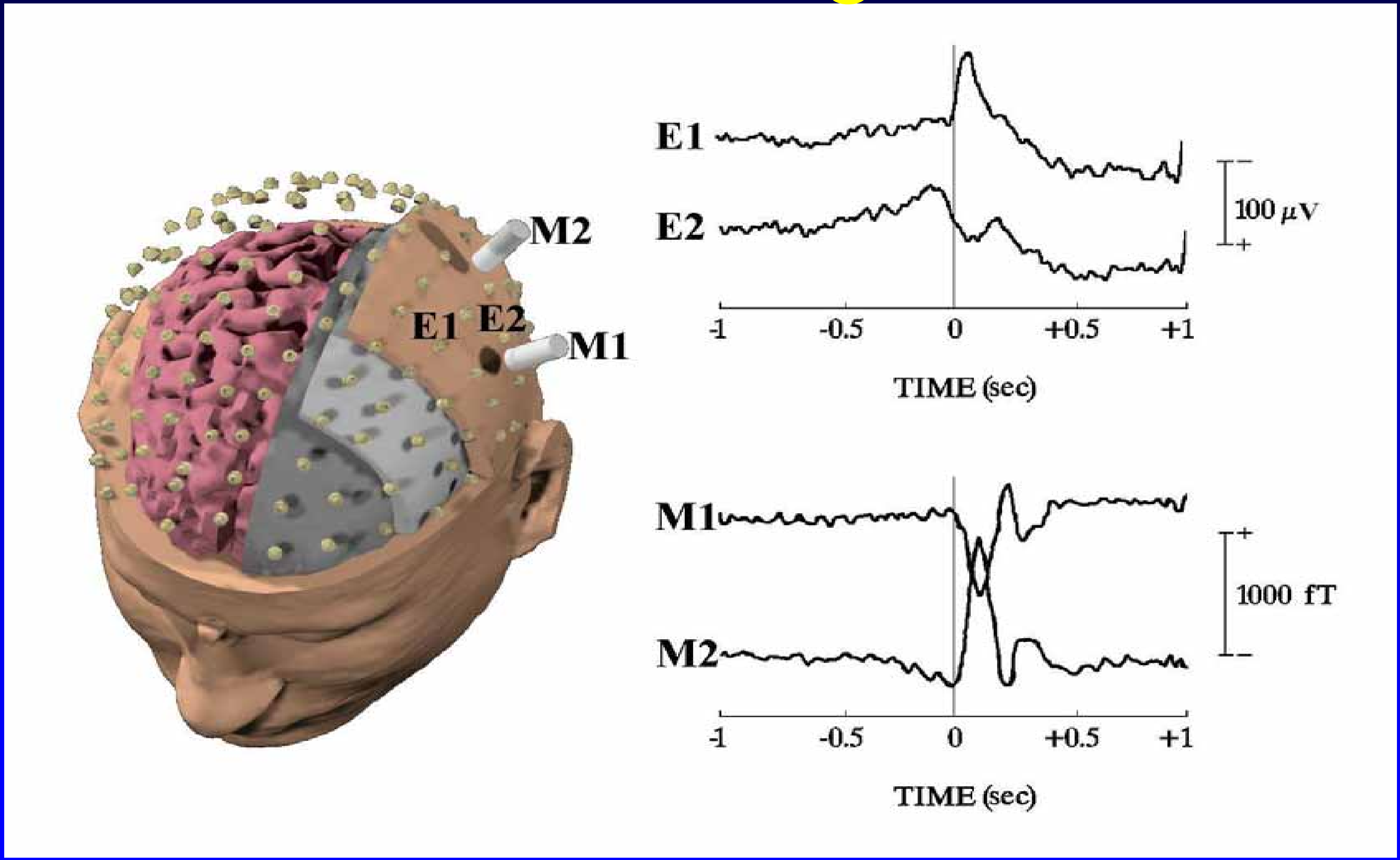
EEG — SEPs

MEG — SEFs

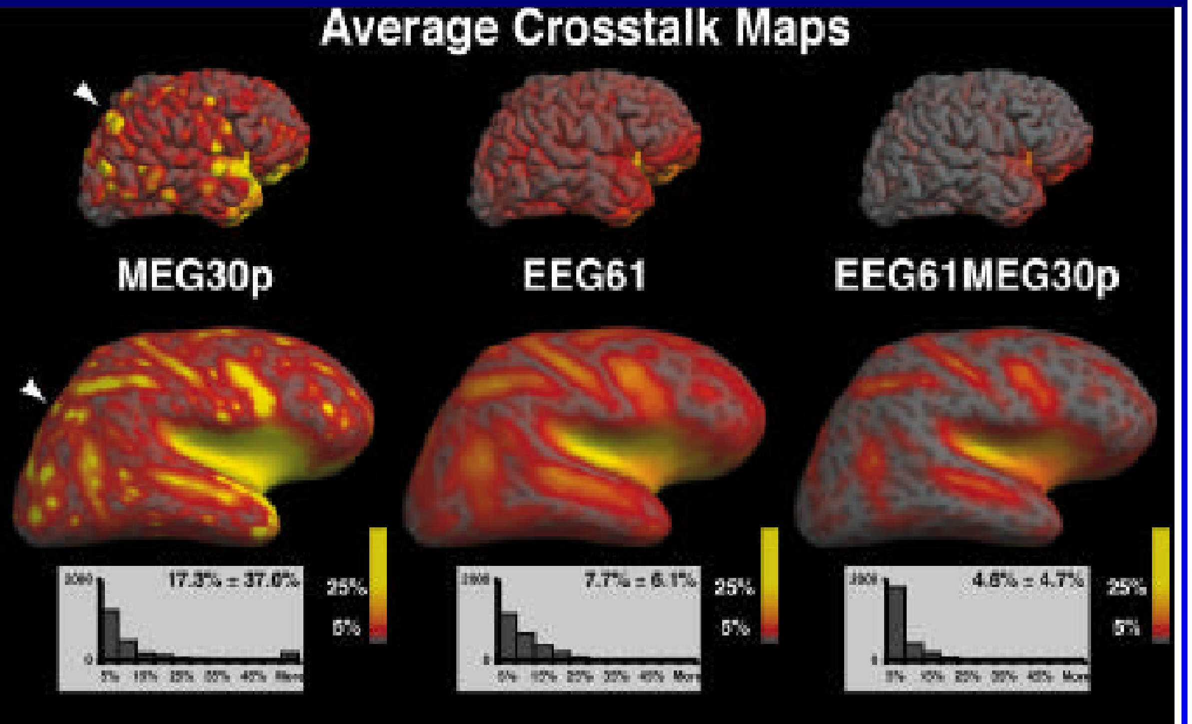
EEG + MEG

Fuchs et al., EEG J., 1998

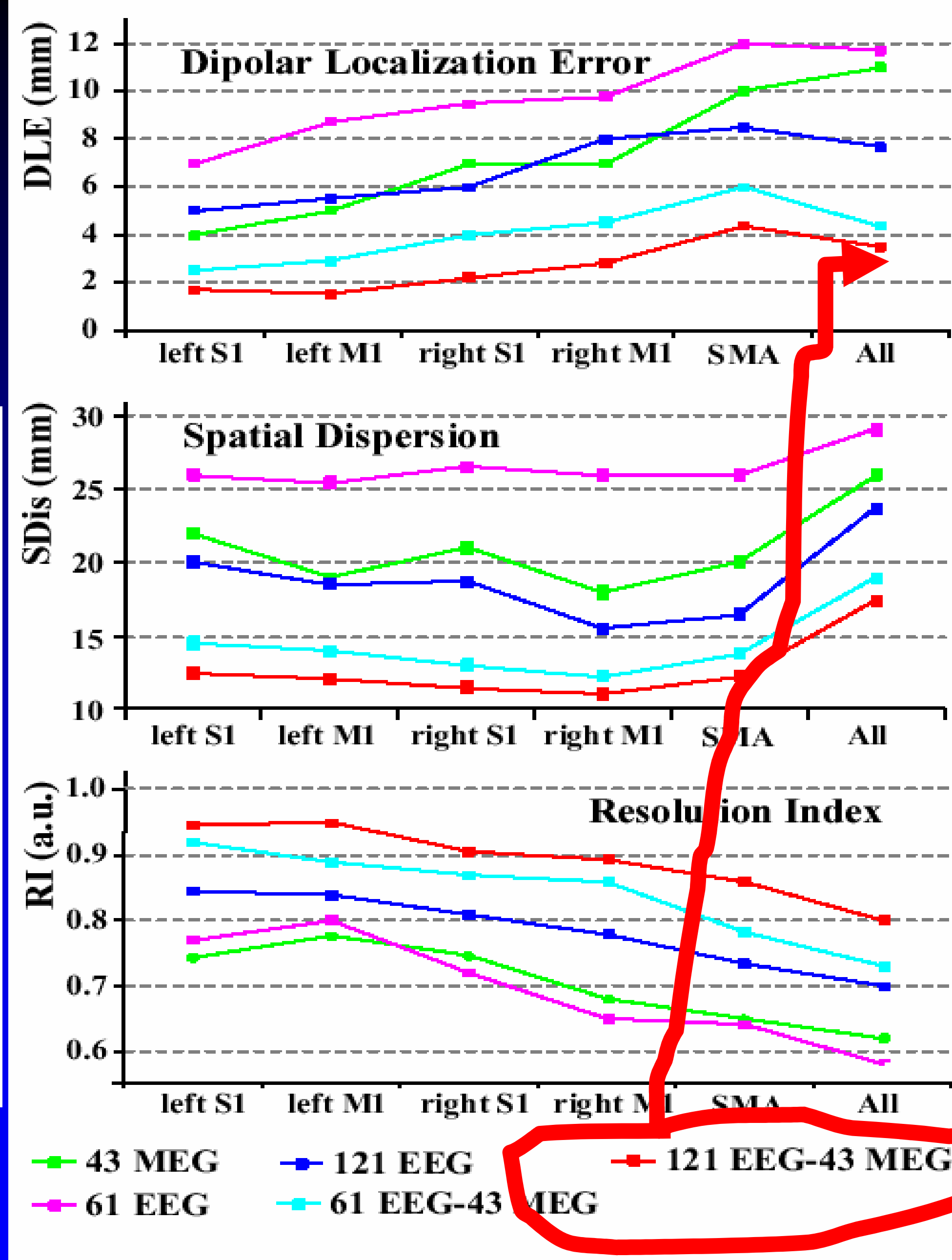
The EEG and MEG movement-related recordings



EEG, MEG and EEG/MEG indexes

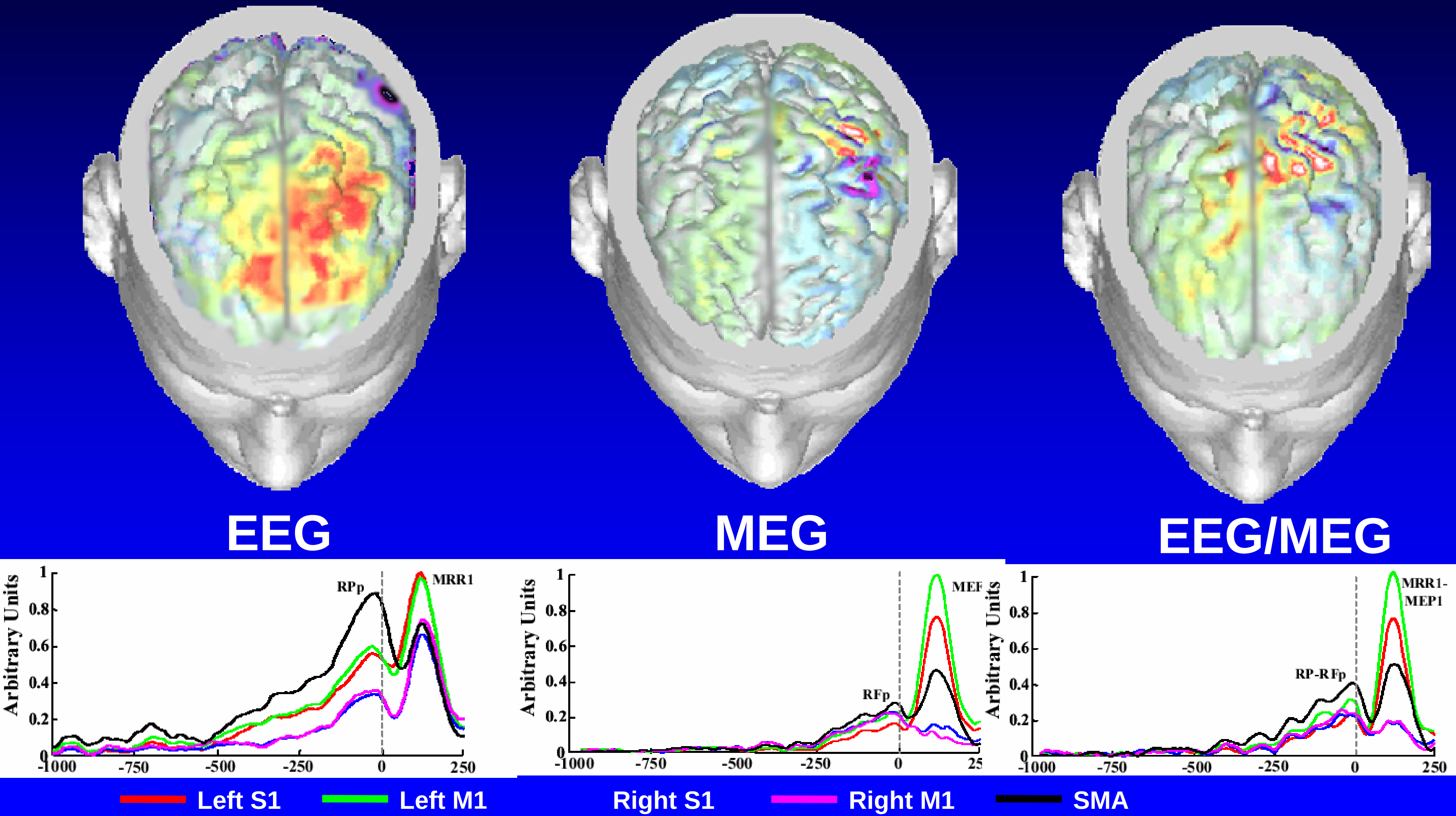


Liu et al., 2000

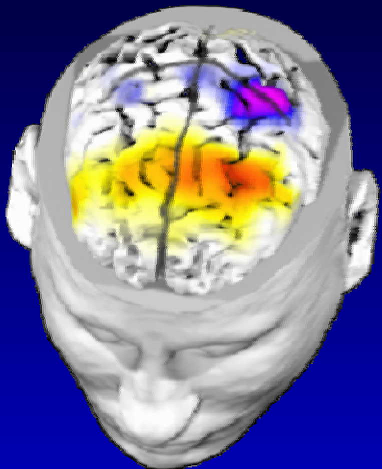


Babiloni et al., 2000

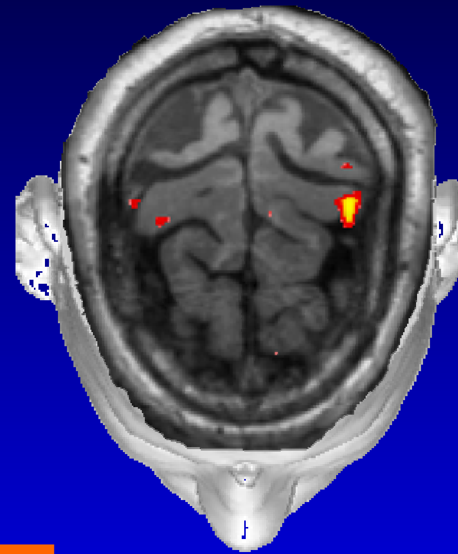
EEG/MEG integration

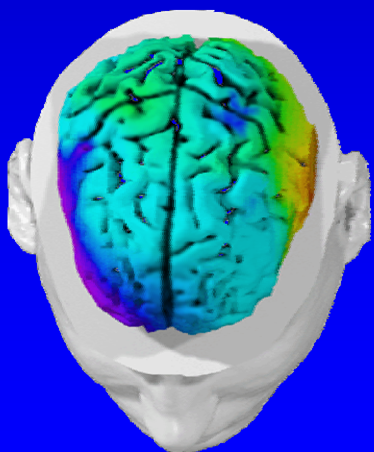


Integration of EEG or MEG data with fMRI

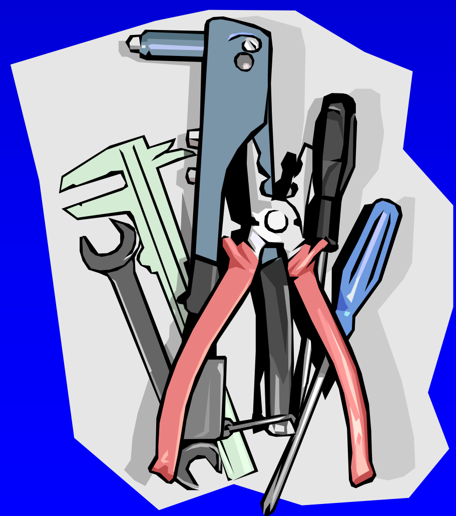


EEG





MEG



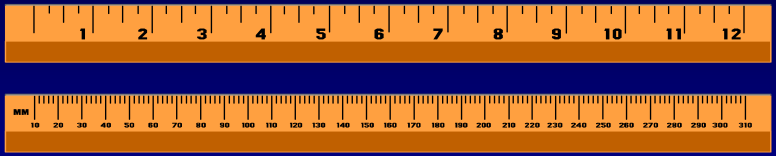
fMRI

Combining EEG and/or MEG with fMRI

Why:

Different spatial resolution

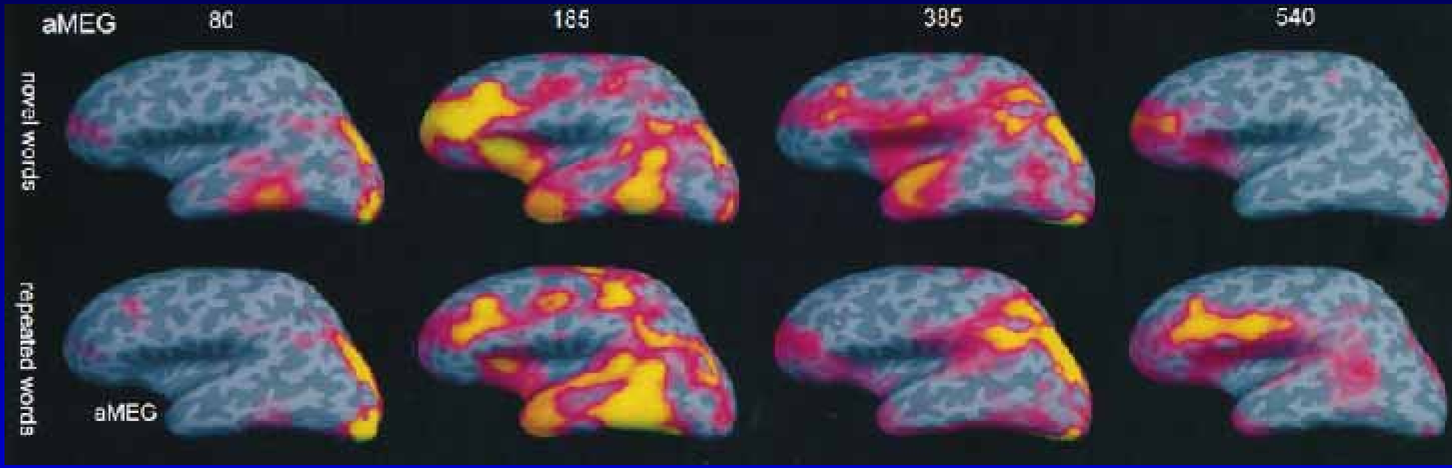
Different time resolution



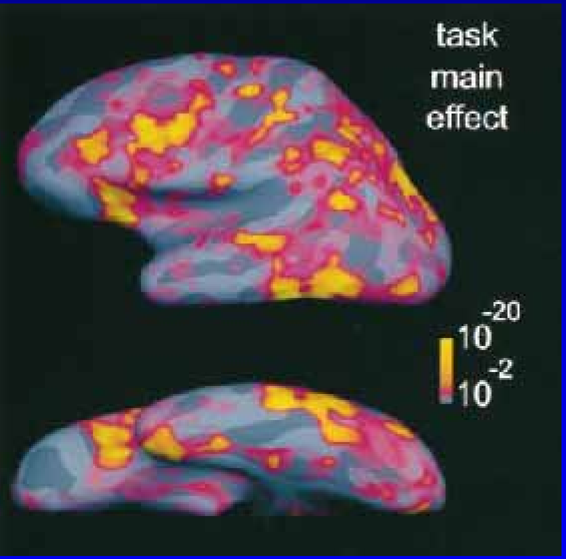
- How:
  - Mahalanobis metric for the data space (M)
  - Metric on the source space (N) that takes into account:
    - visibility from the sensors (column normalization); ($\| A_{.i} \|^2$)
    - source activity as expressed by fMRI signal α; $g(\alpha)$

Integration of MEG and fMRI

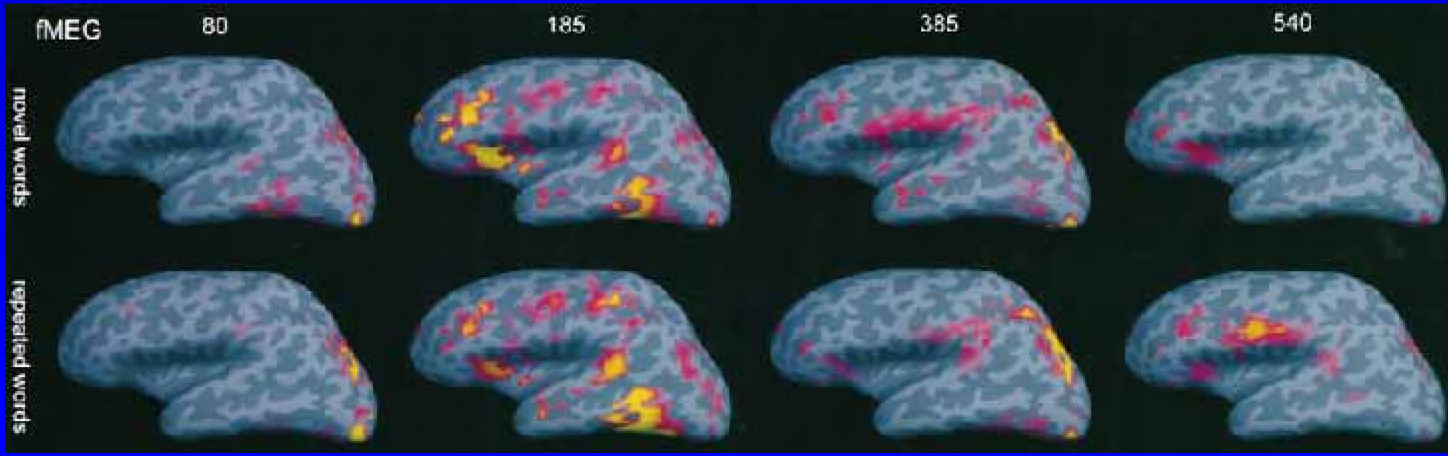
MEG solutions



fMRI solutions



fMRI-constrained MEG solutions



Dale et al., Neuron, Vol. 26, 55–67, April, 2000,

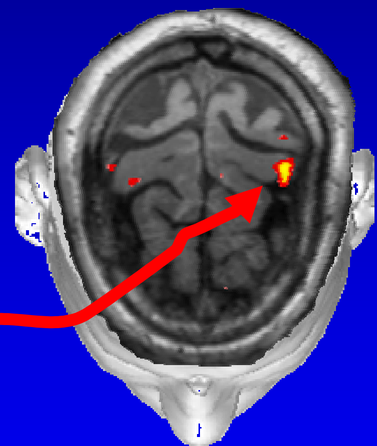
Combining EEG or MEG with fMRI

☞Solutions ξ are obtained by using x = G b where

$$G = N^{-1} A' \left(A N^{-1} A' + \lambda M^{-1} \right)^{-1}$$

☞Proposed metric for integration of EEG, MEG and fMRI data

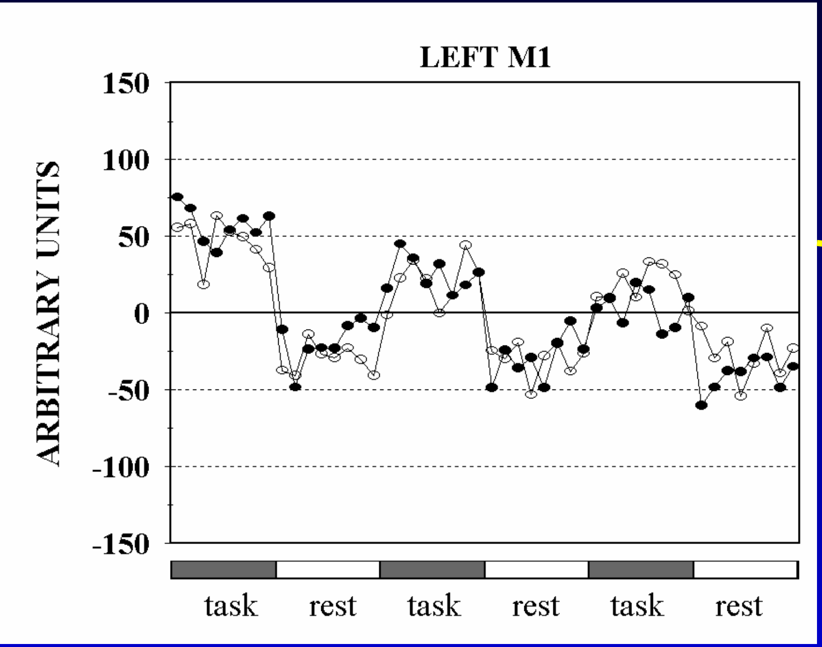
$$N_{ii} = \frac{\left\| A_{.i} \right\|_2^2}{1 + K\alpha} = \frac{\left\| A_{.i} \right\|_2^2}{g(\alpha)}$$

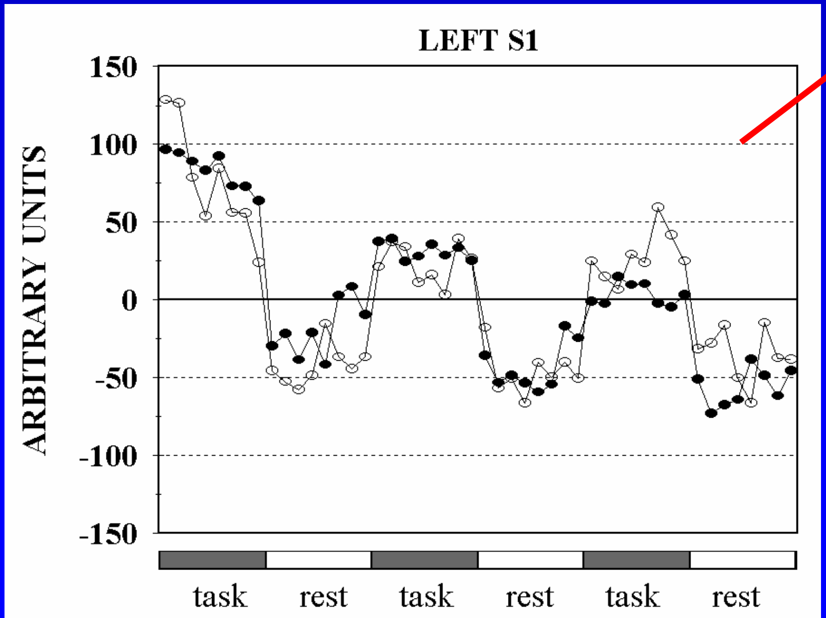


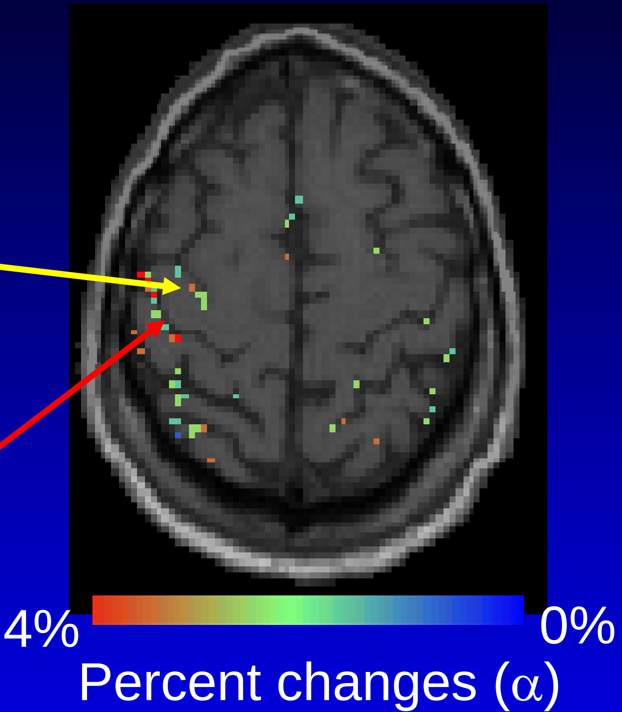
Solution of the electromagnetic inverse problem with fMRI constraints when $K\alpha >> 1$

Solution of electromagnetic inverse problem without fMRI constraints when $K\alpha << 1$

Block-design fMRI signals





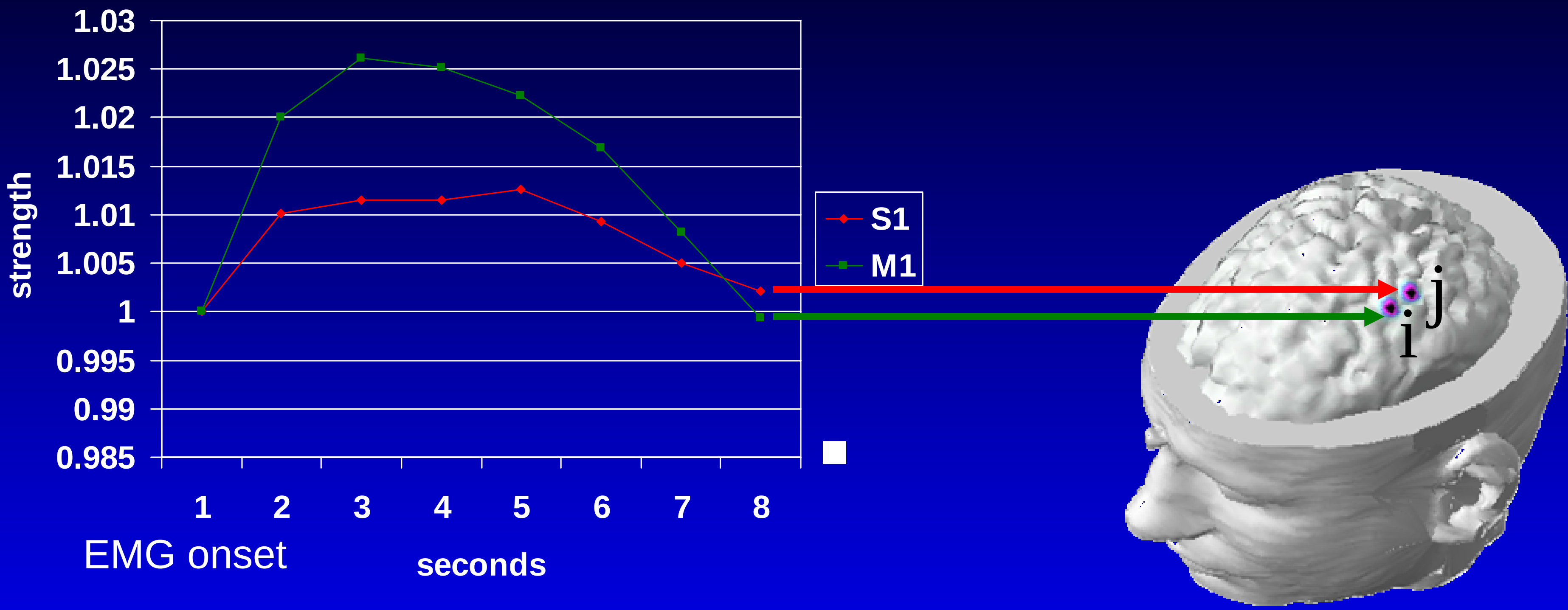


Information on hemodynamic behaviour of cortical sources are provided on a temporal scale of minutes

Diagonal metric N

$$N_{ii}^{-1} = \left\| A_{\cdot i} \right\|_2^{-2} g\left(\alpha_i\right)^2$$

Event-related fMRI signals

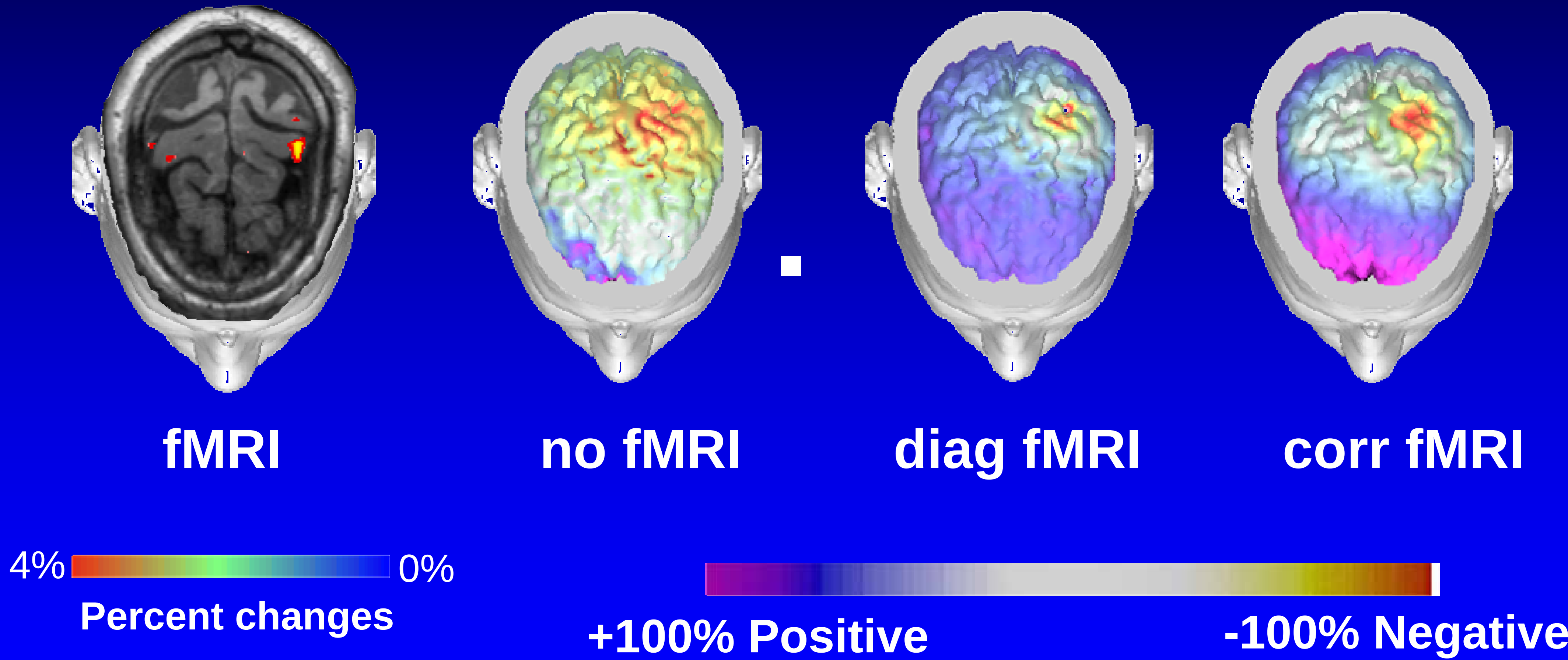


☞Hemodynamical behavior estimated by the correlation between the event-related fMRI signals from the cortical areas i and j on a seconds scale

☞Full source metric N

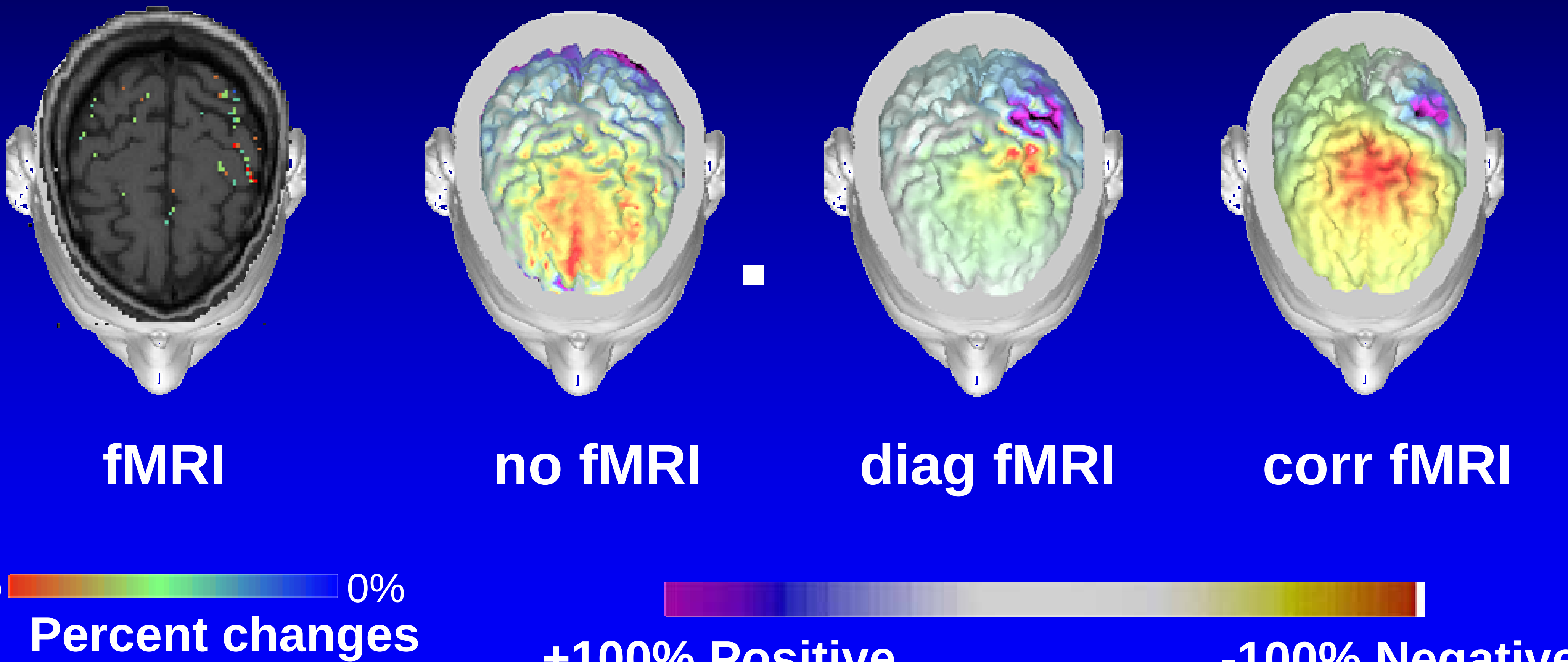
$$N_{ij}^{-1} = \left\|A_{\cdot i}\right\|_2^{-1} \cdot \left\|A_{\cdot j}\right\|_2^{-1} \cdot g\left(\alpha_i\right) \cdot g\left(\alpha_j\right) \cdot Corr\,(i, j)$$

Temporal domain: movement onset (0 msec)



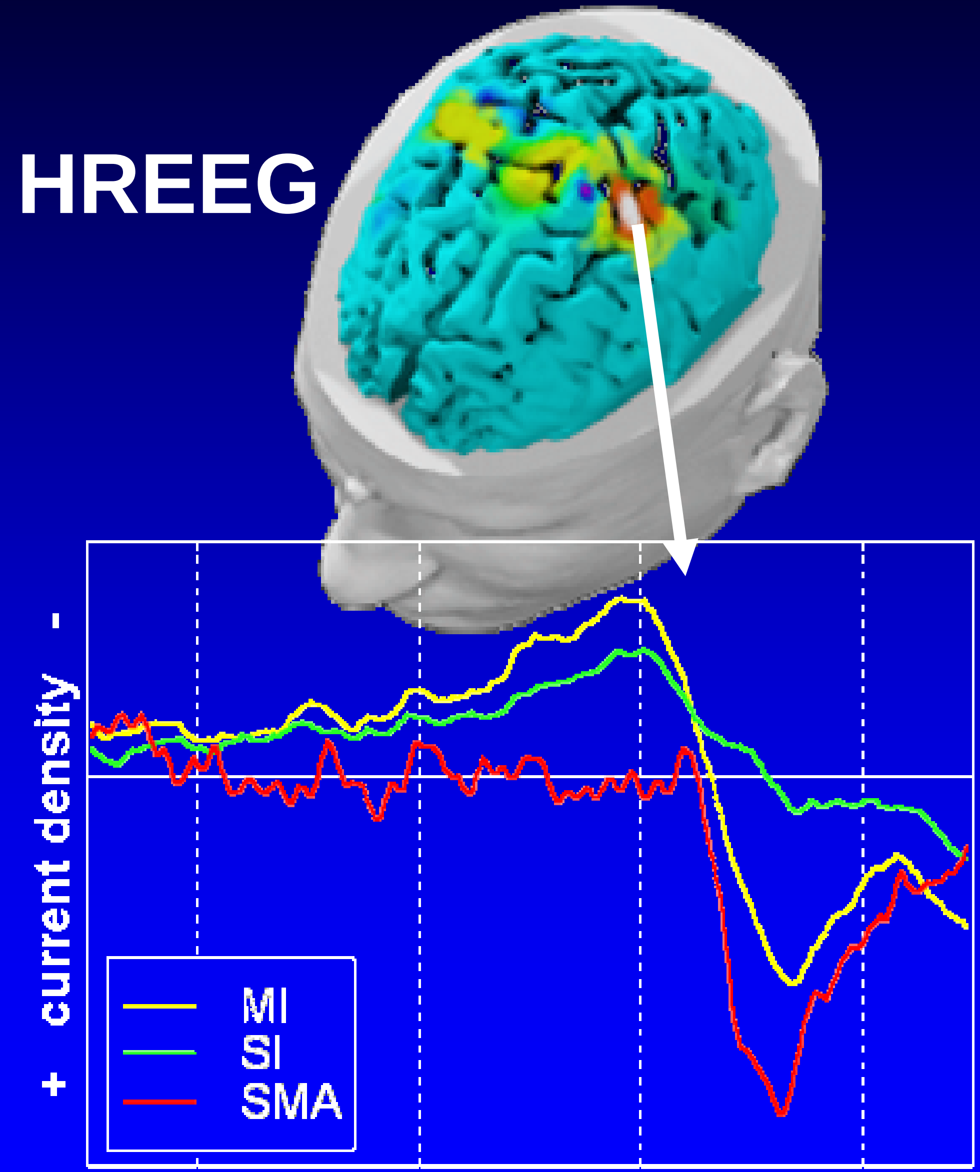
Unilateral right middle finger movement

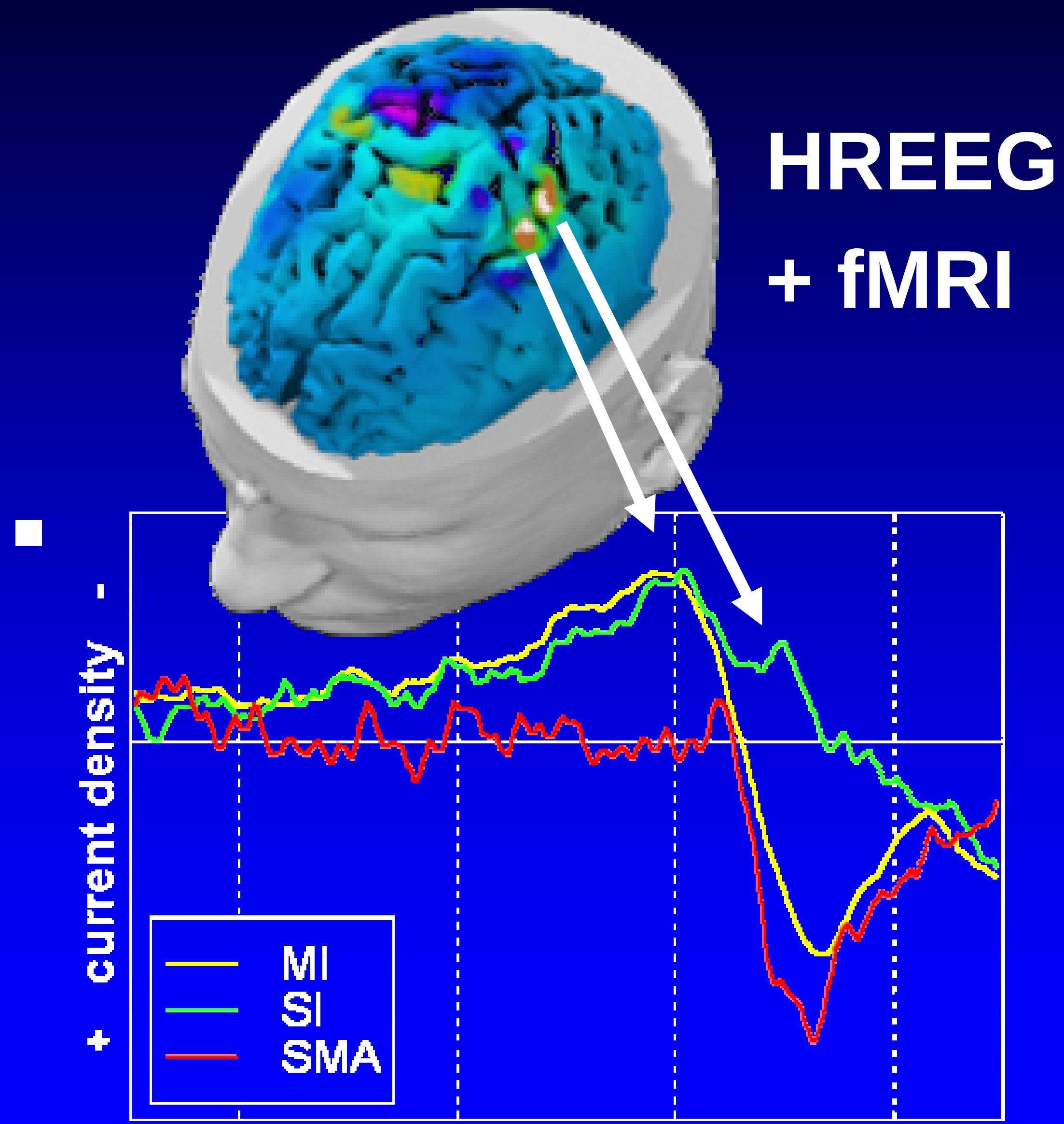
Temporal domain: reafference peak (+110 msec)



Unilateral right middle finger movement

Movement-related cortical dynamics





From current strength to probability maps

- How obtain a measure of the uncertainty of current estimations due to the EEG/MEG noise (n) ?

- Under the null hypothesis of no activation the Z is distributed as a Gaussian distribution

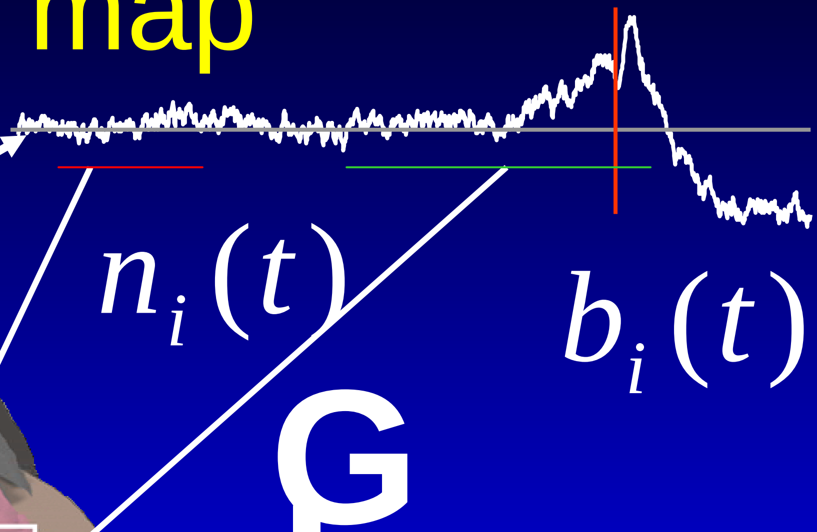
$$\sigma^2_{Noise} = Gnn'G' = GCG'$$

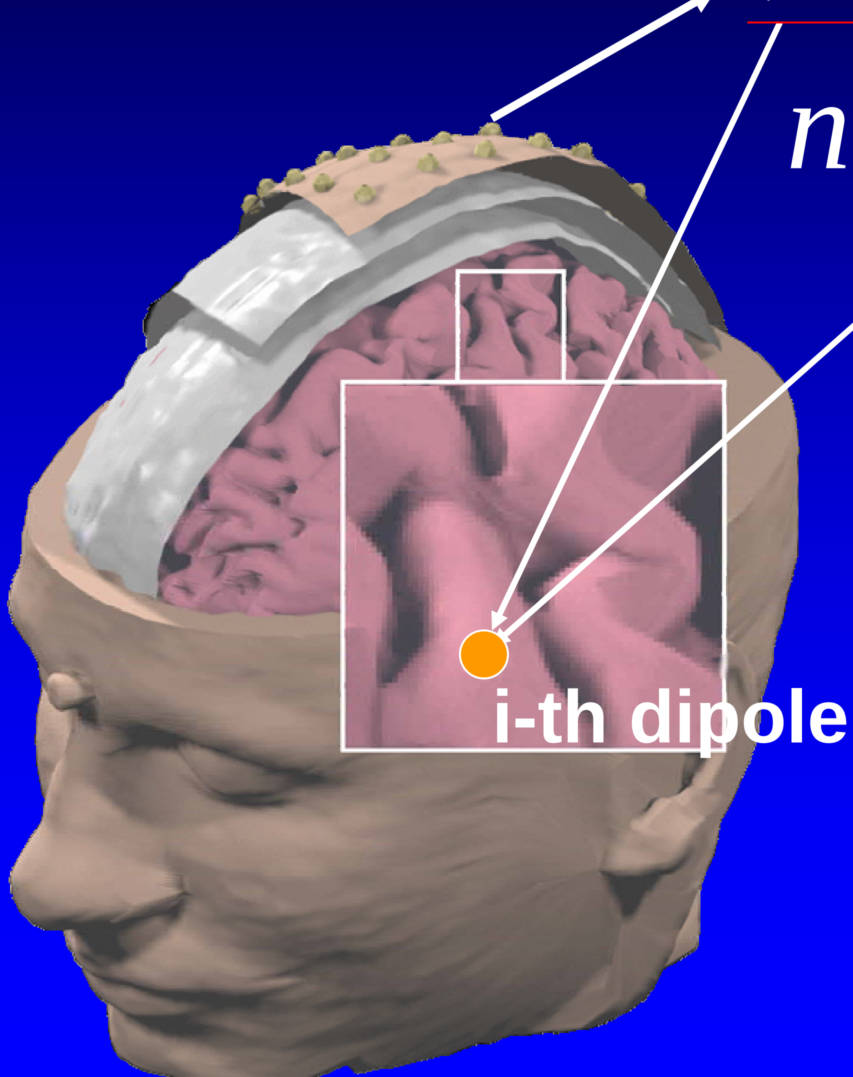
$$Z_i(t) = \frac{G \cdot b(t)}{\sqrt{GCG'}}$$

- In the case of three component for each dipole the q as a sum of squares is distributed as a Fisher distribution ($F_{3,n}$)

$$q_i(t) = \frac{\left[\sum_{k=1}^{3} G_k \cdot b(t)\right]^2}{\sum_{k=1}^{3} G_k \cdot C \cdot G_k'}$$

Temporal domain: from current strength to probabilistic map



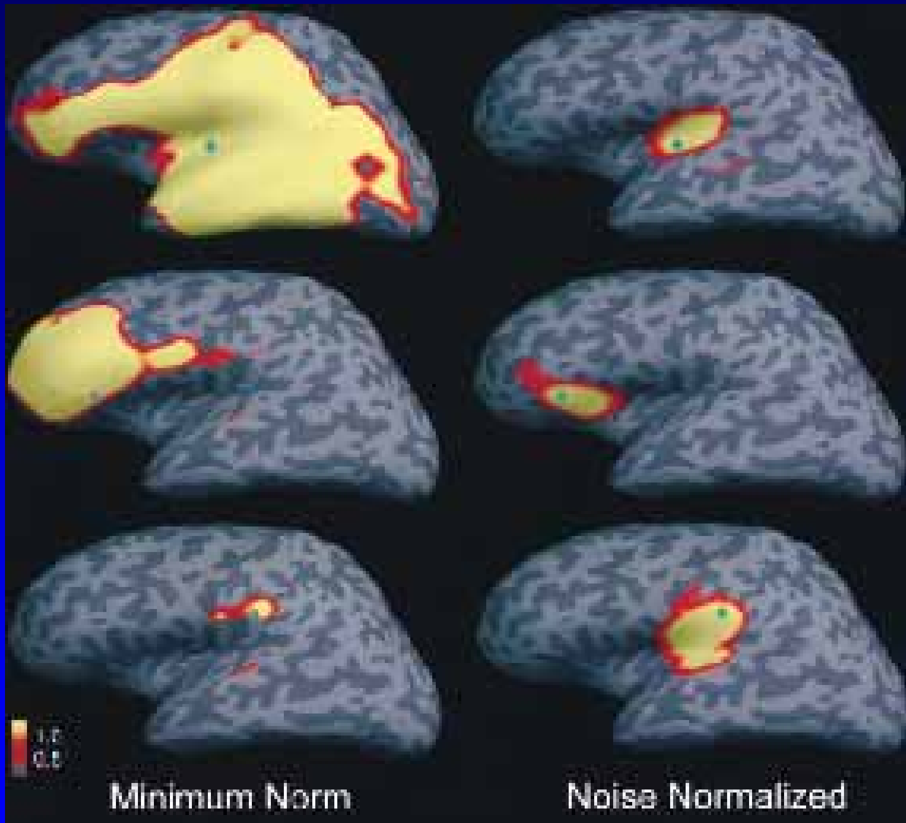


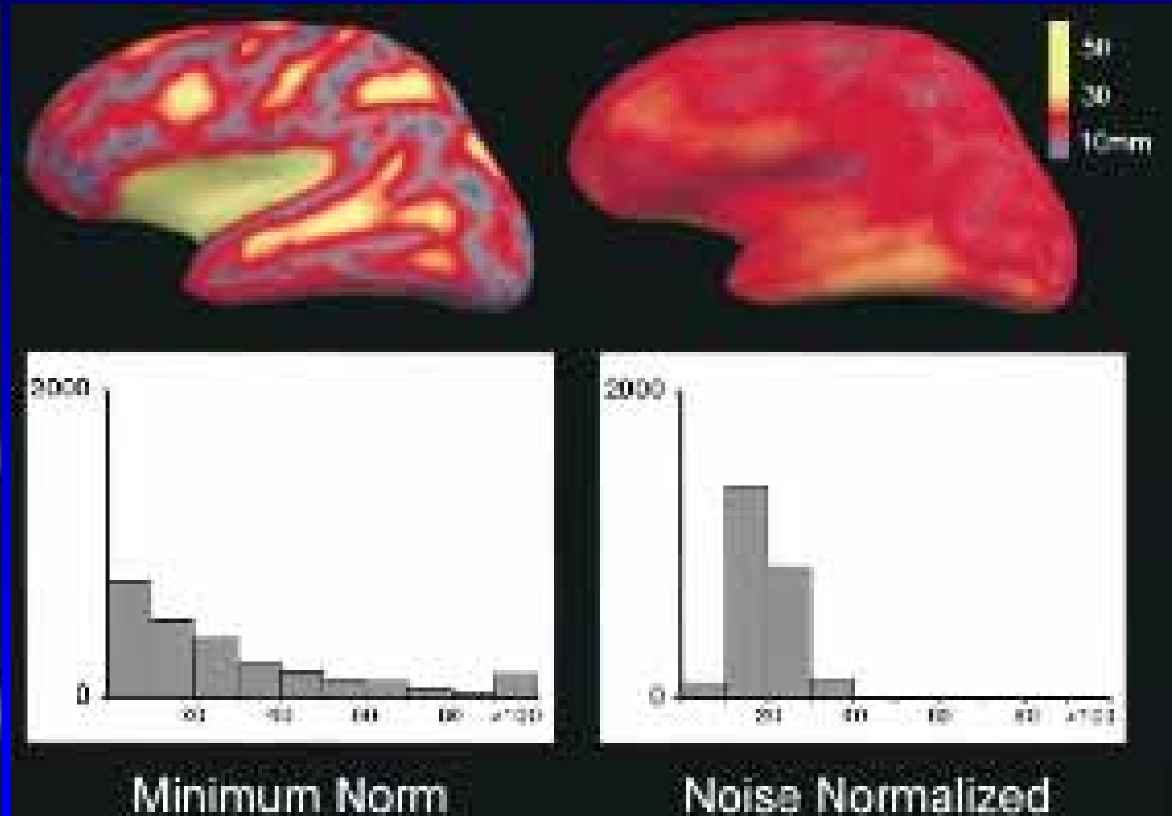
$$\sigma^2{}_{Noise\,i} = [\; Gnn'G' \;]_i = [\; GCG' \;]_i$$

$$Z_i(t) = \frac{[\; G \cdot b(t) \;]_i}{[\; \sqrt{GCG'} \;]_i}$$

Dale et al, Neuron,2000
Liu, 2000, PhD thesis

From current strengths to probability maps



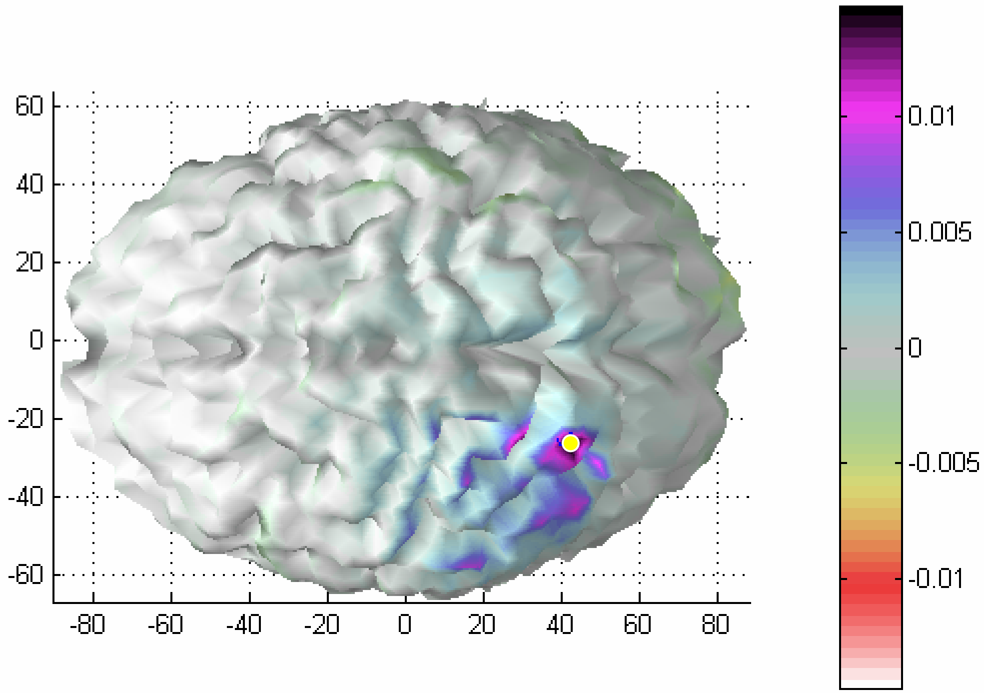


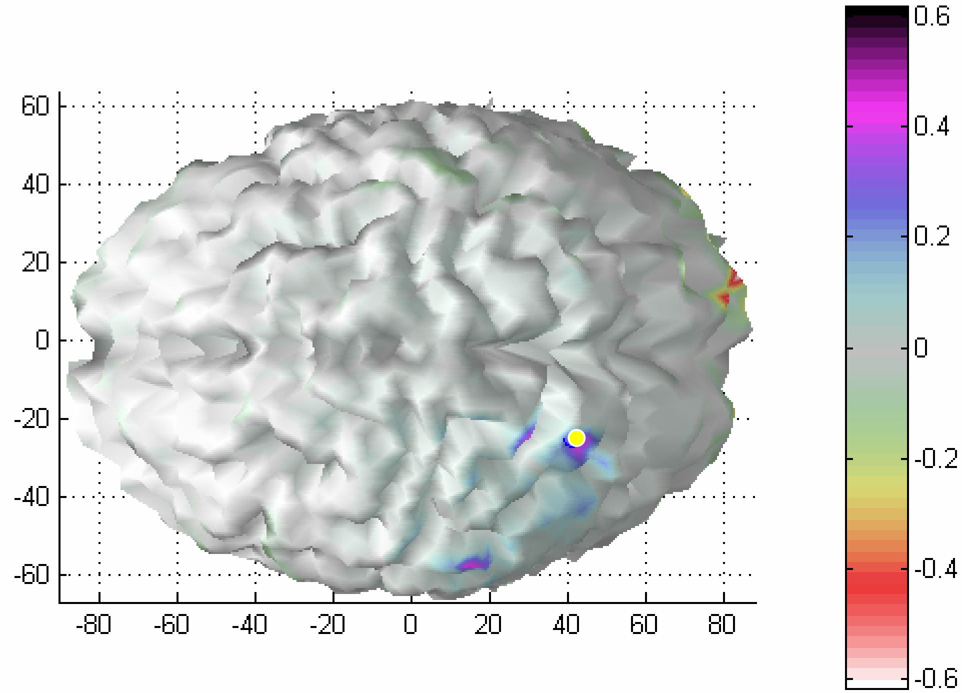
Point spread functions (DLE)

Distribution of the PSF (DLE)

Dale et al., 2000

From current strengths to probability maps



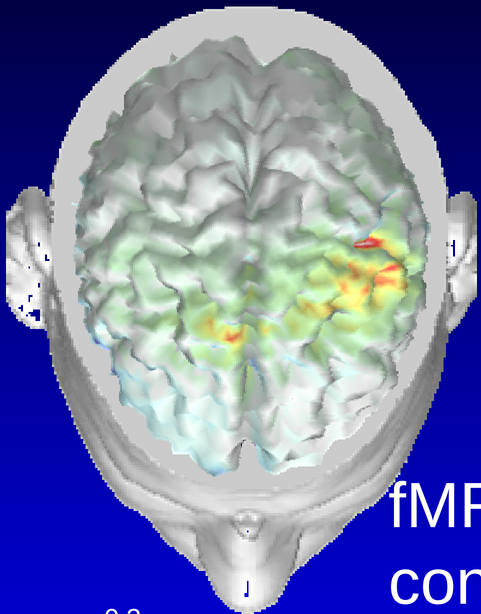


Actual dipole position

Weighted minimum norm
Resolution kernel

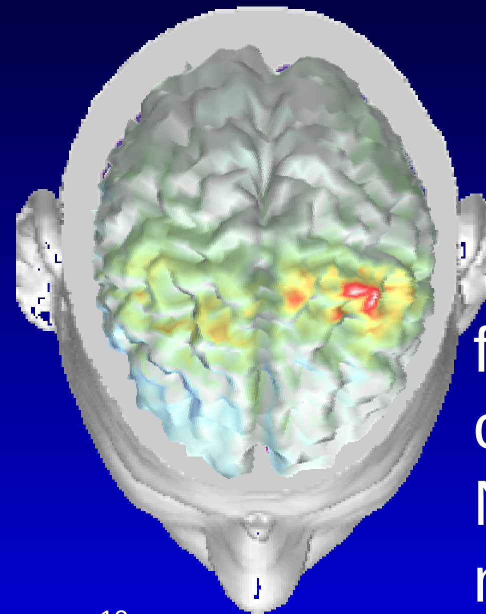
Noise normalized
Resolution kernel

Movement-related cortical dynamics



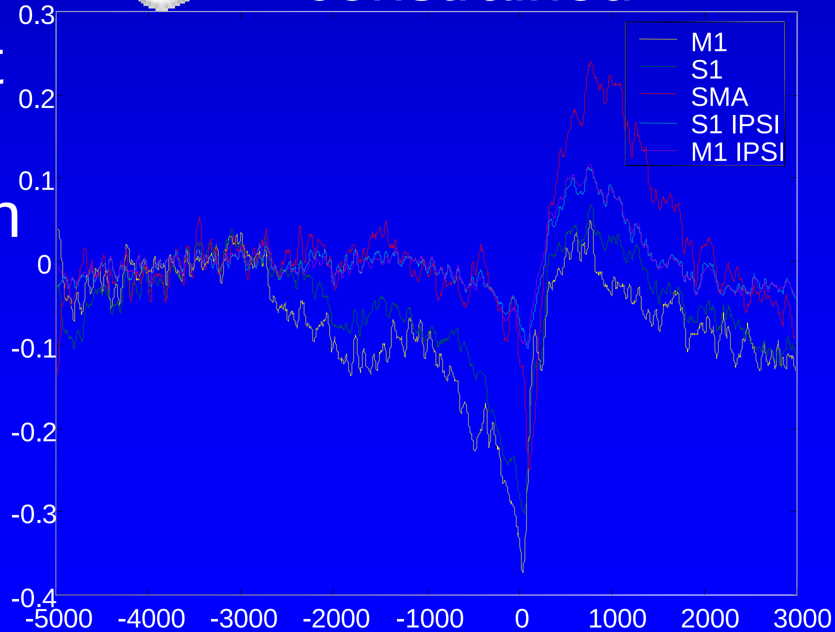
fMRI-
constrained

t= +50 ms

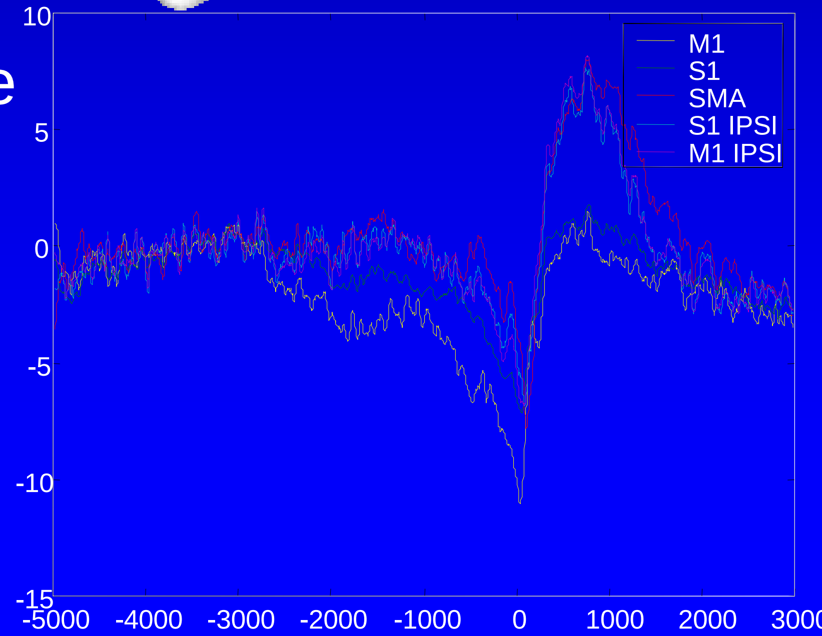


fMRI-
constrained
Noise-
normalized

Current
density
strength

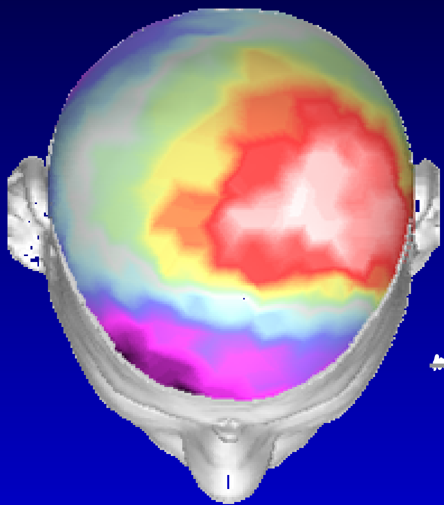


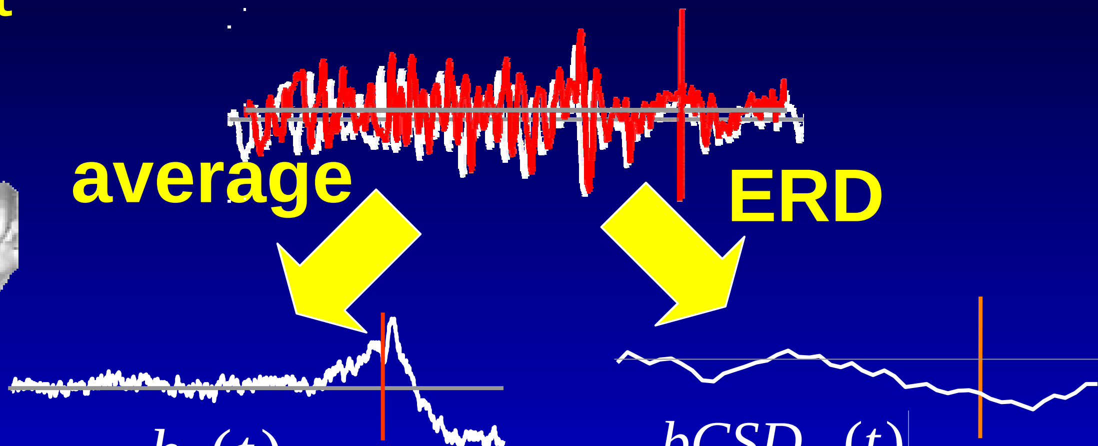
Z score



Frequency-based linear inverse source estimation

EMG onset

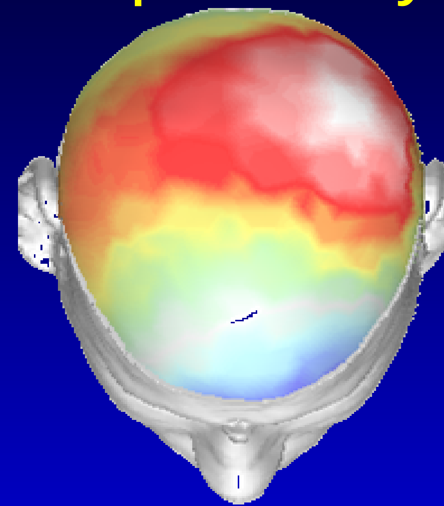




$\underline{b}_i(t)$

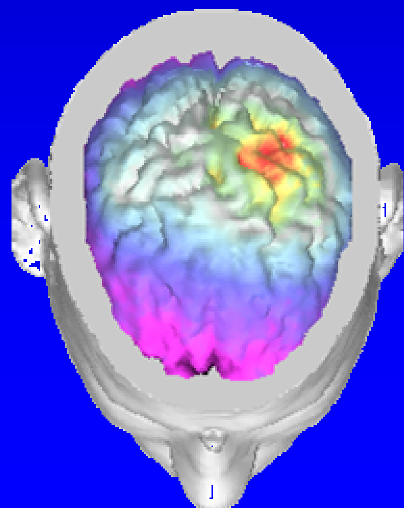
$bCSD_{ii}(t)\big|_f$

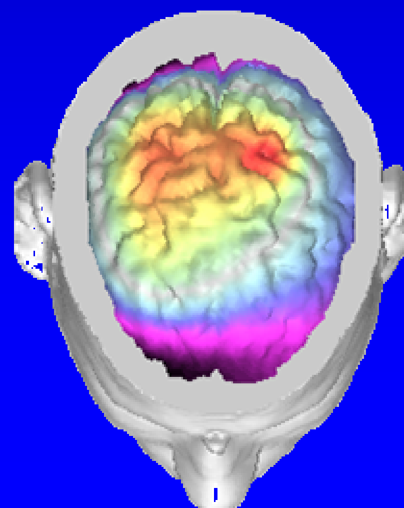
Alpha desync.



$$bCSD_{ij}(f;T) \equiv B_i(f;T) \cdot B_j(f;T)^*$$

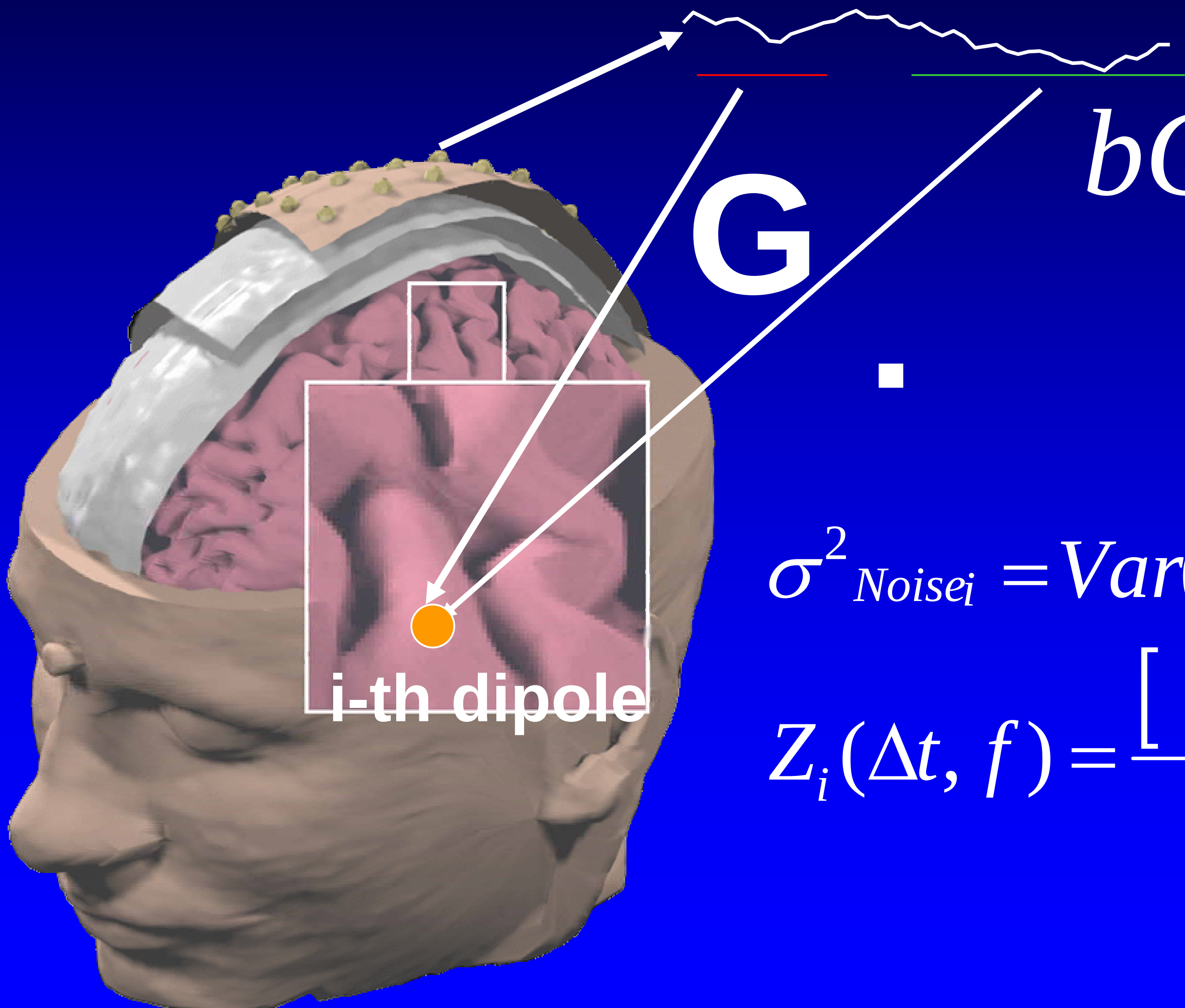
$$\underline{x}(t) = \underline{\underline{G}} \cdot \underline{b}(t)$$





$$\underline{\underline{xCSD}}(f) = \underline{\underline{G}} \cdot \underline{\underline{bCSD}}(f) \cdot \underline{\underline{G'}}$$

Frequency domain: from current strength to probabilistic map



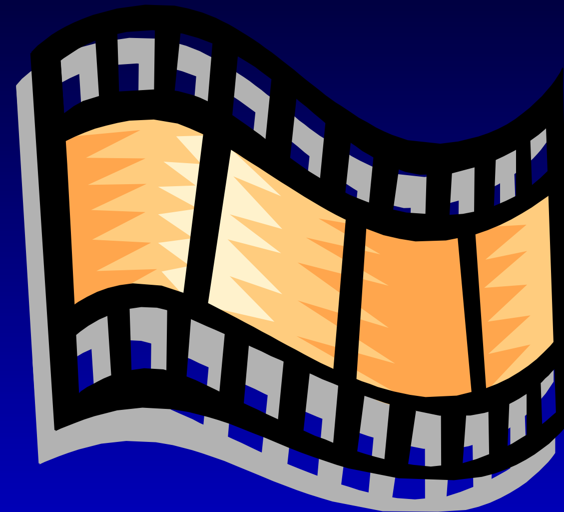
$$bCSD_{ii}(\Delta t)\Big|_{f}$$

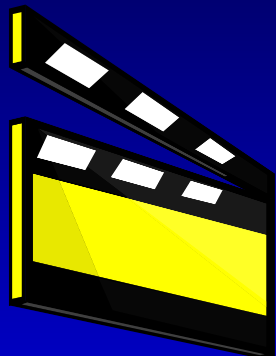
$$\cdot$$

$$\sigma^2_{Noise\,i} = Var(bCSD_{ii}(\mathrm{T}, f))$$

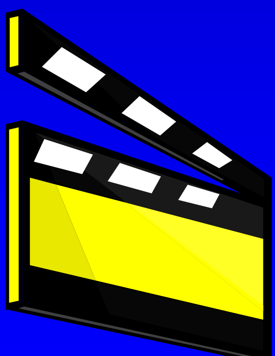
$$Z_i(\Delta t, f) = \frac{\left[\, G \cdot bCSD_{ii}(\Delta t, f) G' \right]_i}{\sigma_{Noise\,i}}$$

HREEG-Movies

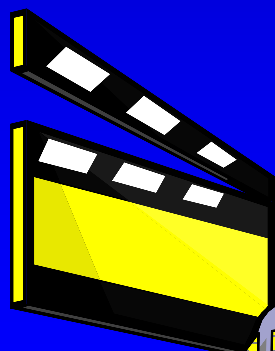




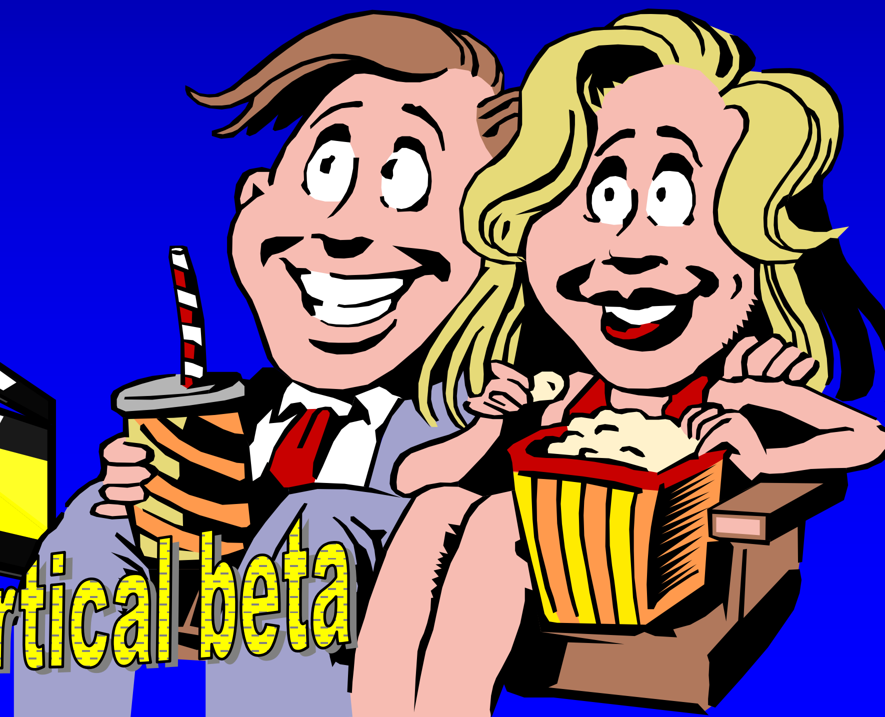
scalp ERD beta



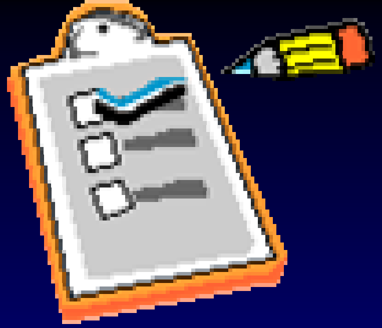
cortical ERD beta



Z-score cortical beta



Conclusions



- ☞High resolution EEG improved spatial details of the raw EEG potential distributions with respect to the standard EEG techniques
- ☞Multimodal integration of high resolution EEG data with those provided by MEG and fMRI techniques is possible in the framework of linear inverse problem
- ☞Information about sources correlation estimated from event-related fMRI can be inserted in the solution of the linear inverse problem by using a full source metric N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