Food for thought

Magistretti et al., Science, 1999
Hemodynamic response

Blood flow

↑ Neuroelectrical activity

Blood flow

↓ Deoxyhemoglobin

fMRI signal
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”.
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

1. Insert the scalp thickness in the SL computation.
2. 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)
The linear inverse problem

\[ \xi = \arg \min_x \left( \|Ax - b\|_M^2 + \lambda^2 \|x\|_N^2 \right) \]

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
- \( \lambda \) is a regularization parameter
- \( M \) is the metric for the data space
- \( N \) is the metric for the source space
- \( \xi \) is the solution vector

Solutions \( \xi \) 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)

\[ x_{Est} = Gb = GAx_{True} \]

\[ x_{Est} = Rx_{True} \]

\[ x_{Est} = R\delta_i = R_i \]

\[ \hat{i} = \text{arg max}_k \| R_{ki} \| \]

\[ DLE_i = \| \vec{r}_i - \vec{r}_{\hat{i}} \| \]

i-th source

k-th source

i-th column of the resolution matrix R

index of the maximum of the i-th column of the resolution matrix R

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.

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

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

$$Z_i(t) = \frac{G \cdot b(t)}{\sqrt{GCG}}$$

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

- Weighted minimum norm Resolution kernel
- Noise normalized Resolution kernel

○ Actual dipole position
From scalp to cortical EEG in RoIs

Scalp EEG

Linear inverse estimates within a RoI are collapsed (mean)

M1 Hand area RoI

“Virtual” electrode

A

rest

mov

post-mov1

post-mov2

Time (s)

-4

-3

-2

-1

0

1

2

3

4

B

Power density (a.u.)

rest

mov

post-mov1

post-mov2

Frequency (Hz)

5

10

15

20

25

30
Integration of EEG and MEG data
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

\[ \xi = \arg\min_x \left( \| Ax - b \|_M^2 + \lambda^2 \| x \|_N^2 \right) \]
Integration of EEG and MEG data

- EEG
- MEG
- EEG + MEG

20 ms
23 ms
18..24 ms

SEPs
SEFs

Fuchs et al.,
EEG J., 1998
The EEG and MEG movement-related recordings

![Diagram showing EEG and MEG recordings with labeled electrodes and time plots.](image-url)
EEG, MEG and EEG/MEG indexes

Liu et al., 2000

Babiloni et al., 2000
EEG/MEG integration

EEG

MEG

EEG/MEG

Left S1  Left M1  Right S1  Right M1  SMA

Arbitrary Units

Arbitrary Units
Integration of EEG or MEG data with 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 \( \alpha \); \( g(\alpha) \)
Integration of MEG and fMRI

fMRI solutions

MEG solutions

fMRI-constrained MEG solutions

Dale et al., Neuron, Vol. 26, 55–67, April, 2000,
Combining EEG or MEG with fMRI

Solutions $\xi$ are obtained by using $x = Gb$ where

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

Proposed metric for integration of EEG, MEG and fMRI data

$$N_{ii} = \frac{\|A_i\|^2_2}{1 + K\alpha} = \frac{\|A_i\|^2_2}{g(\alpha)}$$

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

Solution of electromagnetic inverse problem without fMRI constraints when $K\alpha << 1$
Information on hemodynamic behaviour of cortical sources are provided on a temporal scale of minutes. Diagonal metric N

\[ N_{ii}^{-1} = \|A \cdot i\|_2^{-2} g(\alpha_i)^2 \]
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 \( N_{ij}^{-1} \) is given by:

\[
N_{ij}^{-1} = \left\| A_i \right\|_2^{-1} \cdot \left\| A_j \right\|_2^{-1} \cdot g(\alpha_i) \cdot g(\alpha_j) \cdot Corr(i, j)
\]
Temporal domain: movement onset (0 msec)

Unilateral right middle finger movement

Percent changes
-100% Negative 0% +100% Positive
Temporal domain: reafference peak (+110 msec)

Unilateral right middle finger movement
Movement-related cortical dynamics

HREEG + fMRI
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

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

\[
\sigma^2_{\text{Noise}} = Gnn'G' = GCG'
\]

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

\[
q_i(t) = \left( \sum_{k=1}^{3} G_k \cdot b(t) \right)^2 \sum_{k=1}^{3} G_k \cdot C \cdot G_k'
\]
Temporal domain: from current strength to probabilistic map

\[ \sigma^2_{\text{Noise}_i} = \left[ Gnn'G' \right]_i = \left[ GCG' \right]_i \]

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

Dale et al, Neuron, 2000
Liu, 2000, PhD thesis
From current strengths to probability maps

Point spread functions (DLE)  Distribution of the PSF (DLE)

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From current strengths to probability maps

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Actual dipole position
Movement-related cortical dynamics

Current density strength

+100% Z=10

-100% Z=-10

fMRI-constrained Noise-normalized

Z score

t= +50 ms
Frequency-based linear inverse source estimation

EMG onset

average

ERD

Alpha desync.

\( b_{\vec{i}}(t) \)

\( b_{\text{CSD}}(f; T) \equiv B_i(f; T) \cdot B_j(f; T)^* \)

\[
\bar{x}(t) = G \cdot \underline{b}(t)
\]

\[
\underline{x}_{\text{CSD}}(f) = G \cdot b_{\text{CSD}}(f) \cdot G'
\]
Frequency domain: from current strength to probabilistic map

\[ \sigma^2_{Noise_i} = Var(bCSD_{ii}(T, f')) \]

\[ Z_i(\Delta t, f) = \left[ \frac{G \cdot bCSD_{ii}(\Delta t, f)G'}{\sigma_{Noise_i}} \right]_i \]
HREEEG-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 $N$. 