Deep sources localization in MEG/EEG

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http://www.cenir.org
MEG source physiology

MEG signals <- macrocolumns in cortical sheet

Suffisant numbers of pyramidal neurones

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
Mathematical model of the data (linear!):

\[ M = G \cdot S + n \]

- \( M \) => 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.

\( \text{Nb Sensors} \) => Nb Sensors

\[ \text{Maxwell Equations} \]
In depth investigation ...

Hillebrand & Barnes NeuroImage 2001

Hauk & all NeuroImage 2011

Sensitivity at the cortical level

Gradiometers

Magnetometers

Source location

Sensor type

Sensor location
In depth investigation …

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

Table 1. Global characteristics of the DBA model.

<table>
<thead>
<tr>
<th>Structures (Left)</th>
<th>Cortex</th>
<th>Hippocampus</th>
<th>Amygdala</th>
<th>Thalamus</th>
<th>LGN</th>
<th>EGP</th>
<th>Putamen</th>
<th>RPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface</td>
<td>Volume (cm^2</td>
<td>cm^3)</td>
<td>750</td>
<td>15</td>
<td>1</td>
<td>8</td>
<td>0.2</td>
<td>1.5</td>
</tr>
<tr>
<td>Number of vertices</td>
<td>4619</td>
<td>900</td>
<td>273</td>
<td>1043</td>
<td>229</td>
<td>453</td>
<td>1029</td>
<td>529</td>
</tr>
<tr>
<td>Cell type</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>C</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>DMD (Γ</td>
<td>Γ)</td>
<td>0.25</td>
<td>0.4</td>
<td>1</td>
<td>0.025</td>
<td>0.25</td>
<td>0.0025</td>
<td>0.25</td>
</tr>
<tr>
<td>Neural current for patch sizes 1 to 5 (Γ)</td>
<td>25 to 125</td>
<td>40 to 200</td>
<td>100 to 500</td>
<td>2.5 to 12.5</td>
<td>25 to 125</td>
<td>0.25 to 1.25</td>
<td>25 to 125</td>
<td>0.25 to 1.25</td>
</tr>
</tbody>
</table>
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
\[ M = G.s + n \]

\[ W = R G^T (G R G^T + C)^{-1} \]

Estimation of sources activity:

\[ \hat{S} = W \cdot M \]
Inverse Operator

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

\[ \hat{S} = W \cdot M \]
Theoretical bias?

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)

\[
\hat{S} = W.M \\
\hat{S} = W.G.S \\
\hat{S} = R.S
\]

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

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

Monte Carlo Simulations:
  - Cortical & DBA activations:
    - 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

In practice

Dumas et al - PlosOne - 2013

Let’s go deeper…

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 other sources (biological and artefacts!)

\[ \hat{s}_0(t) = w_0^T x(t) \]

Same results for $s$.
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

a

Encoding task

1   2   3   4   5   6   1   2   3   ... 36

b

Position 1   ...   Position 6   ...   Position 1 (next event)

b

Model simulation results

0.05   0.10   0.15   0.20   0.25   0.30   0.35

0   1   2   3   4   5   6   1   2   3   4   5   6

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!

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