The Inverse Problem of EEG/MEG

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Introduction
What is the inverse problem of EEG/MEG?

Adapted from Becker, Albera, Comon, et al.
What is the inverse problem of EEG/MEG?

Magneto-encephalography (MEG): 
"neuromagnetic inverse problem is to estimate the cerebral current sources underlying a measured distribution of the magnetic field" [2]

Electro-encephalography (EEG): 
"measurements of the voltage potential [...] to estimate the current sources inside the brain " [3]
Helmholtz’s fundamental finding

"[...] The fact that a current within a conductor cannot be completely identified from measurements of the magnetic field it generates in the exterior of the conductor was known to Helmholtz since 1853" [6]
The Forward Problem
Maxwell’s equations

1. \[ \nabla \vec{E} = \frac{\rho}{\varepsilon_0} \]  
2. \[ \nabla \times \vec{E} = -\mu \frac{\partial \vec{B}}{\partial t} \]  
3. \[ \nabla \vec{B} = 0 \]  
4. \[ \nabla \times \vec{B} = \mu \left( \vec{J} + \varepsilon \frac{\partial \vec{E}}{\partial t} \right) \]
Simplifying assumptions and the quasistatic approximation (I)

- Appropriate volume conductor model provided (from sphere → realistic model)
- Quasistatic regime, i.e. neglect the contribution of $\frac{\partial \vec{B}}{\partial t}$ and $\frac{\partial \vec{E}}{\partial t}$ [7]
- Magnetic permeability $\mu_0$ everywhere [7]
- Total current density $\vec{J}$: sum of $\vec{J}^p$ (primary current) and (volume return current) $\vec{J}^v$ [2]
  - $\vec{J}^p$: originates from the bioelectric source / result of neuronal activity
  - $\vec{J}^v$: passive (Ohmic) current $\vec{J}^v = \sigma \vec{E}$
Simplifying assumptions and the quasistatic approximation (II)

Adapted from Haari and Puce
Quasistatic approximation in detail

Is the contribution of the temporal derivatives $\frac{\partial \vec{B}}{\partial t}$ and $\frac{\partial \vec{E}}{\partial t}$ negligible? [2]

Assume: $\vec{E} = \vec{E}_0 \cdot e^{i2\pi ft}$, where $f \sim 100 \text{ Hz}$

▶ Is it legitimate to neglect $\frac{\partial \vec{E}}{\partial t}$?

▶ 4. Maxwell equ. + $\vec{J} = \sigma \vec{E} + (\epsilon - \epsilon_0) \frac{\partial \vec{E}}{\partial t}$

▶ $|\epsilon \frac{\partial \vec{E}}{\partial t}| << |\sigma \vec{E}|$

▶ $\epsilon 2\pi f << \sigma \rightarrow 2\pi f \frac{\epsilon}{\sigma} \sim 10^{-3} << 1$

▶ Is it legitimate to neglect $\frac{\partial \vec{B}}{\partial t}$?

▶ 2. + 4. Maxwell equ. $\rightarrow \nabla \times \nabla \times \vec{E} = -\mu \frac{\partial}{\partial t} \nabla \times \vec{B} = -i2\pi f \mu_0 (\sigma + i2\pi f \epsilon) \vec{E}$

▶ Characteristic length: $\lambda_{\text{Charact}} \sim 65 \text{ m}$
Field equations for the biomagnetic/-electric problem

\[ \vec{E} = \nabla V \] (5)

\[ \nabla \times \vec{B} = -\mu_0 \vec{J} \] (6)

\[ \vec{J} = \vec{J}^v + \vec{J}^p = \vec{J}^p + \sigma \vec{E} \] (7)

\[ \nabla \vec{B} = 0 \] (8)
Solution of the forward problem

Scalar potential $V$ [2]

$$\triangle V = \frac{1}{\sigma} \vec{J}^p \quad \quad \vec{V}(\vec{r}) \rightarrow 0, \ | \vec{r} | \rightarrow 0 \quad (9)$$

with appropriate boundary conditions.

Integral formula for $B$ [2]

$$\vec{B}(\vec{r}) = \frac{\mu_0}{4\pi} \int_G \frac{\vec{J}(\vec{r}') \times \vec{R}}{R^3} d\nu' \quad \quad \vec{B}(\vec{r}) \rightarrow 0, \ | \vec{r} | \rightarrow 0 \quad (10)$$

$$\vec{J} = \vec{J}^v + \vec{J}^p$$
The Inverse Problem - General Aspects
Helmholtz’s fundamental finding

"[...] The fact that a current within a conductor cannot be completely identified from measurements of the magnetic field it generates in the exterior of the conductor was known to Helmholtz since 1853" [6]

"... because electromagnetic field measurements could equivalently arise due to different source configurations ... the electromagnetic inverse problem is thus ill posed" [9]
Hadamard’s definition of a well-posed problem

Let \( F : X \rightarrow Y \) be the forward problem, where the inverse problem is to find \( F^{-1} \).

As proposed by Hadamard the inverse problem is well-posed if the solution to it

- ... exists
- ... is unique
- ... is stable.

A problem is ill-posed if one of the conditions above is violated.
Non-uniqueness

Adapted from Hämäläinen

<table>
<thead>
<tr>
<th></th>
<th>Radial dipol in spherically sym. conductor</th>
<th>Magnetically silent</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Closed loop current</td>
<td>Electrically silent</td>
</tr>
<tr>
<td>B</td>
<td>$</td>
<td>\vec{J}_p</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Toy model: La Place equation (I)[11]
The Inverse Problem - General Aspects
Ill-Posedness of the Inverse Problem

Toy model: La Place equation (II) [11]

Given a function \( g \) and the forward problem described by La Place equation:

\[ \nabla^2 \psi(x, y) = 0 \text{ in } \Omega \]

\[ \nabla \psi \cdot \vec{n} \text{ on } B, C, D \]

\[ \psi(x, 1) = g \text{ on } A \]

\[ \rightarrow \text{ Calculate values of } \psi \text{ on } C \]

Inverse problem - measure \( f(x) \) on \( C \):

\[ \rightarrow \text{ Calculate values of } g \text{ on } A \]
Toy model: La Place equation (III) [11]

**Ansatz:**

\[ \psi_k(x, y) = \cos(k\pi x) \cdot \sin(k\pi x) \]  \hspace{1cm} (11)

**Boundary conditions + linearity yield:**

\[ \psi(x, y) = A_0 + \sum_{k=0}^{\infty} A_k \cdot \cos(k\pi x) \cdot \cosh(k\pi y) \]  \hspace{1cm} (12)

Assume that \( g \) can be expanded in cosine series:

\[ g(x) = \sum_{k=0}^{\infty} A_k(g) \cdot \cos(k\pi x) \]  \hspace{1cm} (13)
Toy model: La Place equation (IV) [11]

The solution of the forward problem is:

\[ \psi(x, y) = \sum_{k=0}^{\infty} \frac{A_k(g)}{cosh(k\pi)} \cdot cos(k\pi x) \] (14)

The forward problem is well-behaved:

- higher frequencies are exponentially damped (\( \sim \frac{1}{e^x} \))
- smaller spatial variations do contribute less
Toy model: La Place equation (V) [11]

Recall the solution of the forward problem:

\[
\psi(x, y) = \sum_{k=0}^{\infty} \frac{A_k(g)}{cosh(k\pi)} \cdot cos(k\pi x) = \sum_{k=0}^{\infty} A_k(\psi) \cdot cos(k\pi x) \tag{15}
\]

Solution of the inverse problem:

\[
g(x) = \sum_{k=0}^{\infty} A_k(\psi) \cdot cosh(k\pi) \cdot cos(k\pi x) \tag{16}
\]

The inverse problem is ill-posed:

- higher frequencies propagate exponentially (\(\sim e^x\))
- smaller spatial variations do contribute more
General conclusions

We have seen how inverse problems can violate two of Hadamard’s conditions, namely

- Uniqueness
- Stability

In fact, this is the case for the inverse problem of EEG/MEG, which is severely ill-posed [2]
The Inverse Problem - Solution Approaches
Distributed models and dipolar models

Solution approaches can be divided into 2 general classes according to the underlying physical model [12]:

**Distributed models:**
- "large number of focal elementary sources with fixed locations/orientations" [13]
- "assume a continuous current distribution" [12]
- "solve a linear inverse problem" (lead field concept) [12]

→ **Regularization**

**Dipolar models:**
- small number of dipoles (∼ 10)
- highly non linear dependence [12]

→ **Probabilistic**
Probabilistic approach - motivation

Main idea:

▶ One straightforward solution approach is to "cast the inverse problem as a problem of statistical inference" [12]

▶ "unknown and the measurements are modelled as a random variable" [2]

▶ "solution of the inverse problem is a probability density function of the unknown" [12]
Probabilistic approach (I) [2]

(Unknown) current distribution: \( \vec{x} \)

(Unknown) magnetic field: \( \vec{b} \)

Probability densities (Bayesian - a priori / a posteriori):

\[
\psi_x(\vec{x}) \quad (17)
\]

\[
\rho_x(\vec{x}) \quad (18)
\]

Noise is characterized by:

\[
v(\vec{b}_{obs}|\vec{b}) \quad (19)
\]

Forward model (probability to observe \( \vec{b} \) given \( \vec{x} \)):

\[
\theta(\vec{b}|\vec{x}) \quad (20)
\]

\[
\psi_x(\vec{x}) = C_0 \rho_x(\vec{x}) \int v(\vec{b}_{obs}|\vec{b}) \theta(\vec{b}|\vec{x}) d\vec{b} \quad (21)
\]
Probabilistic approach (II) [2]

\[
\psi_x(\vec{x}) = C_0 \rho_x(\vec{x}) \int v(\vec{b}_{obs} | \vec{b}) \theta(\vec{b} | \vec{x}) d\vec{b}
\]  

(22)

Assume that errors do not depend on the input, i.e.:

\[
\vec{b}_{obs} = \vec{b} + \eta_b
\]  

(23)

\[
v(\vec{b}_{obs} | \vec{b}) = f_b(\eta_b)
\]  

(24)

\[
\psi_x(\vec{x}) = C_0 \rho_x(\vec{x}) \int f_b(\vec{b}_{obs} - \vec{b}) \theta(\vec{b} | \vec{x}) d\vec{b}
\]  

(25)

Assume a current dipole (in a sphere) being the source (model function \(g\)):

\[
\psi_x(\vec{x}) = C_0 \rho_x(\vec{x}) f_b(\vec{b}_{obs} - \vec{g}(\vec{x}))
\]  

(26)
Probabilistic approach with Gaussian errors [2]

Assume $\eta_b$ to be normally distributed (cov. matrix $\Sigma_{\eta_b}$, mean $E_{\eta_b} = 0$)

The maximum-likelihood estimate (MLE) in the case of Gaussian errors corresponds to the OLS estimate (BLUE):

$$S(\vec{x}) = [\vec{b}_{obs} - \vec{g}(\vec{x})]^T \Sigma^{-1} [\vec{b}_{obs} - \vec{g}(\vec{x})]$$ (27)

"If the neural source is modelled by a current dipole, the MLE is commonly called the equivalent current dipole (ECD)" [2]

However, one can make other assumptions on noise, source model, ...

For example, instead of using one dipole one can assume a source model of multiple dipoles

$\rightarrow$ would have to deal with so called marginal distributions
The lead field (I)

"Discretization of an underlying continuous current [...] by large number of current dipoles with fixed location and orientation" [13]

To do so, define the so called lead field:

\[ \vec{B} \text{ and } \vec{E} \text{ depend linearly on the current } \vec{J}^p \]

Define a linear map - one for the magnetic field and one for the scalar potential respectively:

\[ \Lambda_i(\vec{r}) \]  \hspace{1cm} (28)

\[ \Lambda_i^E(\vec{r}) \]  \hspace{1cm} (29)

On what depends \( \Lambda_i(\vec{r}) \) in general? → \( \Lambda_i(\vec{r}) \) encapsulates forward model
The lead field (II)

Thus, given the lead field, the forward problem can be formulated as:

- **Measurements (made at m sensors):** \( \vec{b} \in \mathbb{R}^m \)

- **Source currents, i.e. N single current dipoles:** \( \vec{s} \in \mathbb{R}^n \)

- **Lead field (forward model):** \( \Lambda \in \mathbb{R}^{m \times n} \)

\[ \vec{b} = \Lambda \cdot \vec{s} \]  
(30)
The lead field - solution approach

\[ \vec{b} = \Lambda \cdot \vec{s} \]

\[ \vec{s} = \Lambda^{-1} \cdot \vec{b} \]

\[\rightarrow\] Straightforward approach: invert the matrix \( \Lambda \)

In general, the columns of \( \Lambda \) can be "nearly" linearly dependent / ill-conditioned problem (numerically instable) [2]

We will look at two different methods

\[\rightarrow\] Minimum-norm estimate

\[\rightarrow\] Regularization approaches
The lead field concept: minimum norm estimate (I)

Recall the lead field concept, where the (solution) current was given by:

\[ \vec{s} = \Lambda^{-1} \cdot \vec{b} \]

By construction currents solving the inverse problem will necessarily be \( \in F = \text{span}(L_1, \ldots, L_n) \)

\[ \rightarrow \vec{J}^* = \sum_{j=1}^{n} w_j \cdot L_j \]

Minimum norm estimate: Search for "current distribution with the smallest overall amplitude capable of explaining the measured signals in the sense of the norm defined by ..." [2]
The lead field concept: minimum norm estimate (II)

Minimum norm estimate [14]:

\[ \vec{J}^* = \arg \min_{\vec{s}} \left( \vec{s}^T \vec{M}_s^{-1} \vec{s} \right) + \lambda |\vec{b} - \Lambda \cdot \vec{s}|^2 \]

\( \lambda \): weighting factor

"[...] inverse problem is inherently ill-posed, the search for an appropriate imaging method is concerned with finding a way to choose within a set of images that produce essentially the same fit to the data" [14]
Minimum norm estimate: interpretation

Minimum norm estimate [14]:

\[ \vec{J}^* = \arg\min_{\vec{s}} (\vec{s}^T \vec{M}^{-1} \vec{s}) + \lambda |\vec{b} - \Lambda \cdot \vec{s}|^2 \]

\(\lambda\): weighting factor

The solution given by the MNE estimate is non-unique in the sense that any arbitrary vector \(\vec{J}_\perp\) can be added to it [2]

\(\vec{J}_\perp \in F^\perp\) (orthogonal complement)

Recall: non-uniqueness of the inverse problem ...
Minimum norm estimate and regularization

Minimum norm estimate [14]:

$$\vec{J}^* = \arg \min_{\vec{s}} (\vec{s}^T M_\vec{s}^{-1} \vec{s}) + \lambda |\vec{b} - \Lambda \cdot \vec{s}|^2$$

$\lambda$: weighting factor

$\rightarrow M_\vec{s} = WW^T$

$M_\vec{s}$ symmetric positive-definite

$\rightarrow$ the solution is: $\vec{J}^* = W(\Lambda W)^\dagger \vec{b}$

$W(\Lambda W)^\dagger$ being the pseudo-inverse

"Ill conditioning and high sensitivity to noise" [14]
Tikhonov regularization

Idea:
Replace the original (ill-conditioned problem) with a problem changed slightly such that it becomes numerically stable + still a good approximation

\[ J^* = \arg\min_s |\vec{b} - \Lambda \cdot \vec{s}|^2 + \lambda \cdot \vec{s}^T M_s^{-1} \vec{s} \]

where \( \vec{s}^T M_s^{-1} \vec{s} \) is the "penalty function" and \( \lambda \) a weighting factor.

- for \( M = 1 \): minimum norm estimate
- variety of regularization techniques
Regularization: example

Adapted from Parkonen

Same underlying data ...
Conclusions
Conclusions (I)

- 2 general characteristics of the inverse problem of EEG/MEG:
  - Non-uniqueness
  - Numerical instability / ill-conditioned
- 2 classes of approaches:
  - Distributed models
  - Dipolar models
Conclusions (II)

- Dipolar models?
  - Probabilistic approach: encapsulate unknowns via statistical uncertainty
  - Complex models (highly non-linear)
  - Only few dipoles

- Distributed models?
  - Lead field concept: simplified model (linear model)
  - Large number of dipoles with fixed location/orientation
  - Tune the model numerically (-> various regularization approaches)
Appendix


References II


