Estimation de paramètres électrophysiologiques pour l’imagerie cérébrale

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Introduction

Brain activity can be localized:

- invasively: brain stimulation, depth electrodes
- non-invasively: neuroimaging

- schematic organization
- variability of cortical foldings
- subject-dependent localization of activity
Non-invasive recordings: electric potential

1924: Hans Berger measures electrical potential variations on the scalp.

- birth of Electro-Encephalography (EEG)
- several types of oscillations detected (alpha 10 Hz, beta 15 Hz)
- origin of the signal unclear at the time
- scalp topographies resemble dipolar field patterns
Noninvasive recordings: from electric to magnetic field

A dipole generates both an electric and a magnetic field

- 1963: Magnetocardiography,
- 1972: Magneto-Encephalography (MEG)
  D. Cohen, MIT, measures alpha waves, 40 years after EEG
  Superconductive QUantum Interference Device
  Magnetic shielding

Advantage of MEG over EEG: spatially more focal

[Badier, Bartolomei et al, Brain Topography 2015]
Origin of brain activity measured in EEG and MEG

Pyramidal neurons post-synaptic currents

Current perpendicular to cortical surface

Neurons in a macrocolumn co-activate

[Baillet et al., IEEE Signal Processing Mag, 2001]
Influence of orientation (spherical geometry)

[courtesy of S.Baillet]
Influence of depth (realistic geometry)

Superficial
External cortex

Deep
Internal cortex

MEG

EEG

1
1
1/100
1/3

[courtesy of S.Baillet]
Outline

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2 Forward problem: from Sources to Sensors
   - Solving the Forward problem
   - A nested geometry problem
   - Boundary Element Method

3 Inverse Source Reconstruction
   - Source Models
   - Uniqueness Results
   - Current Source Density Mapping

4 Conductivity estimation
   - A transmission problem
   - Semirealistic geometry
   - Spherical geometry

with Toufic Abboud and Théo Papadopoulo
A nested geometry problem

Nested domains $\Omega_1 \ldots \Omega_N$, constant conductivity $\sigma_1 \ldots \sigma_N$

Outside domain: air $\Omega_{N+1}$ with vanishing conductivity $\sigma_{N+1} = 0$.

Sources limited to domain $\Omega_1$: $\mathbf{J}^p = \{(p_k, q_k)\}_{k=1 \ldots K}$ $K$ dipoles

Quasistatic regime: electric potential $V$ satisfies Poisson equation:

$$\text{div } \sigma \nabla V = \sum_{k=1}^{K} q_k \cdot \nabla \delta p_k = T(\mathbf{J}^p),$$

Laplace fundamental solution: $-\Delta E = \delta_0$ dans $\mathbb{R}^3$ 

$$E(r) = \left(\frac{4\pi}{|r|}\right)^{-1}$$

In infinite homogeneous region $-\Delta \beta_j^p = T(\mathbf{J}^p)$

$$\beta_j^p(r) = \sum_{k=1}^{K} q_k \cdot \nabla E(r - p_k)$$

$$u = V - \sigma_1^{-1} \beta_j^p \text{ harmonic in } \mathbb{R}^3 \setminus \bigcup \{p_k\}.$$
Solving the forward problem

- **simplest model: overlapping spheres**
  - ✓ no meshing required
  - ✓ analytical methods
  - ✗ crude approximation of head conduction, especially for EEG
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  - ✓ only surfaces need to be meshed
  - ✓ Boundary Element Method (BEM)
  - × only isotropic conductivities
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- **most sophisticated model: volume-based conductivity**
  - ✓ detailed conductivity model,
    (anisotropic: tensor at each voxel)
  - ✓ Finite Element Method (FEM),
  - ✗ huge meshes, difficult to handle
Transmission principle through integral operators

\[ V \text{ harmonic in each } \Omega_i, \ i \geq 2 \]

\[ V(x) = \int_{\Omega_i} \left[ E(x - y) \Delta V(y) - V(y) \Delta E(x - y) \right] dy \]

\[ = v^\text{ext}_{i-1}(x) - v^\text{int}_i(x) \]

\[ v^\text{ext}_{i-1}(x) = \int_{S_{i-1}} \left( E(x - y) \frac{\partial V^+}{\partial n_y}(y) - V^+(y) \frac{\partial E}{\partial n_y}(y - x) \right) ds(y) \]

harmonic outside of \( S_{i-1} \)

\[ v^\text{int}_i(x) = \int_{S_i} \left( E(x - y) \frac{\partial V^-}{\partial n_y}(y) - V^-(y) \frac{\partial E}{\partial n_y}(y - x) \right) ds(y) \]

harmonic inside of \( S_i \).

Jumps across \( S_i \):

\[ \varphi_i = v^\text{int}_i - v^\text{ext}_i \]

\[ q_i = \frac{\partial v^\text{int}_i}{\partial n} - \frac{\partial v^\text{ext}_i}{\partial n} \]
Calderon operators

\[ S q(y) = \int_S E(x - y) q(x) \, ds(x) \quad D^* q \text{ adjoint} \]
\[ D \varphi(y) = \int_S \frac{\partial E}{\partial n_x}(x - y) \varphi(x) \, ds(x) \quad N \varphi \text{ hypersingular} \]

Calderon operator: \( H = \begin{pmatrix} -D & S \\ N & D^* \end{pmatrix} \)

Associated projectors: \( C^{\text{ext}} = \frac{l}{2} - H \) and \( C^{\text{int}} = \frac{l}{2} + H \)

\[
\begin{bmatrix} V \\ \partial_n V \end{bmatrix}^{\text{int}}_{S_i} = C^{\text{int}}_i \begin{bmatrix} \varphi_i \\ q_i \end{bmatrix} + H_{i, i-1} \begin{bmatrix} \varphi_{i-1} \\ q_{i-1} \end{bmatrix}
\]
\[
\begin{bmatrix} V \\ \partial_n V \end{bmatrix}^{\text{ext}}_{S_i} = C^{\text{ext}}_i \begin{bmatrix} \varphi_i \\ q_i \end{bmatrix} + H_{i, i+1} \begin{bmatrix} \varphi_{i+1} \\ q_{i+1} \end{bmatrix}
\]

Continuity of \( V \) and \( \sigma \partial_n V \) across surfaces:
- transmission equations
- boundary element approximation
Boundary Elements

Electric potential generated by sources $\mathbf{J}^p$ approximated through linear system:

$$A \mathbf{V} = B(\mathbf{J}^p)$$

Note: potential only defined up to a constant, to be fixed for system inversion

Main steps involved for Boundary Element Method (BEM)

1. Geometry: segment Magnetic Resonance Image to recover surfaces $S_i$ and source space
2. Discretize surfaces $S_i$ (conforming trianglations)
3. Assemble matrices $A$ et $B(\mathbf{J}^p)$ (mixed $P_1/P_0$ elements)
4. Solve $A \mathbf{V} = B(\mathbf{J}^p)$

Magnetic field: apply a matrix representing Biot-Savart to $\mathbf{V}$. 
Symmetric BEM system

\[
\begin{bmatrix}
(\sigma_1+\sigma_2)N_{11} & -2D_{11}^* & -\sigma_2N_{12} & D_{12}^* & -\sigma_1^{-1}S_{11} & -\sigma_2^{-1}S_{12} & D_{23}^* & -\sigma_3N_{23} & D_{23}^* & -\sigma_3^{-1}S_{23} & \cdots & D_{nS}^* & -\sigma_3^{-1}S_{nS} \\
-2D_{11} & (\sigma_1^{-1}+\sigma_2^{-1})S_{11} & D_{12} & -\sigma_2^{-1}S_{12} & D_{22}^* & -\sigma_3^{-1}S_{22} & D_{32}^* & -\sigma_3^{-1}S_{32} & D_{23} & -\sigma_3^{-1}S_{23} & \cdots & D_{nS} & -\sigma_3^{-1}S_{nS} \\
-\sigma_2N_{21} & D_{21}^* & (\sigma_2+\sigma_3)N_{22} & -2D_{22} & (\sigma_2^{-1}+\sigma_3^{-1})S_{22} & D_{32} & (\sigma_1+\sigma_2)N_{33} & -2D_{33} & (\sigma_3^{-1}+\sigma_4^{-1})S_{33} & \cdots & \cdots & \cdots & \cdots \\
D_{21} & -\sigma_2^{-1}S_{21} & -2D_{22} & (\sigma_2^{-1}+\sigma_3^{-1})S_{22} & D_{32} & -\sigma_3^{-1}S_{32} & -2D_{33} & (\sigma_3^{-1}+\sigma_4^{-1})S_{33} & \cdots & \cdots & \cdots & \cdots \\
D_{32} & -\sigma_3^{-1}S_{32} & -\sigma_3N_{32} & D_{32} & -\sigma_3^{-1}S_{32} & -2D_{33} & (\sigma_3^{-1}+\sigma_4^{-1})S_{33} & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\
D_{32} & -\sigma_3^{-1}S_{32} & -\sigma_3N_{32} & D_{32} & -\sigma_3^{-1}S_{32} & -2D_{33} & (\sigma_3^{-1}+\sigma_4^{-1})S_{33} & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
D_{nS} & -\sigma_3^{-1}S_{nS} & -\sigma_3^{-1}S_{nS} & D_{nS} & -\sigma_3^{-1}S_{nS} & -2D_{nS} & (\sigma_3^{-1}+\sigma_4^{-1})S_{nS} & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\
\end{bmatrix} \cdot \begin{bmatrix}
v_1 \\
p_1 \\
v_2 \\
p_2 \\
v_3 \\
p_3 \\
p_{nS}
\end{bmatrix} = \begin{bmatrix}
\sigma_1^{-1}N_{sources} \\
D_{1sources} \\
0 \\
0 \\
0 \\
0 \\
0 \\
\end{bmatrix}
\]
Symmetric BEM software: OpenMEEG

[Gramfort, Papadopoulo, Olivi, Clerc, 2010]

- EEG and MEG
- Electrical Impedance Tomography
- Cortical Mapping
- ElectroCorticography
- Functional Electrical Stimulation
- Intracortical electrodes
- Cochlear Implants
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Inverse Problems

Use measurements and prior knowledge to recover hidden information:

- Source reconstruction
- Conductivity estimation
- Cortical Mapping

Data (MEG, EEG) → Inverse problem → Sources

Conductivity

Sources

Inverse problem

Data (MEG, EEG)

Unobserved potential or current

Maureen Clerc (Inria, France)
## Source reconstruction

<table>
<thead>
<tr>
<th>Two types of source models considered:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>isolated</strong></td>
<td><strong>distributed</strong></td>
</tr>
<tr>
<td><img src="image1.png" alt="Isolated model" /></td>
<td><img src="image2.png" alt="Distributed model" /></td>
</tr>
<tr>
<td>unknowns $\ll$ measurements</td>
<td>unknowns $\gg$ measurements</td>
</tr>
<tr>
<td>sensitivity to model order</td>
<td>indeterminacy</td>
</tr>
<tr>
<td></td>
<td>regularization necessary</td>
</tr>
</tbody>
</table>

Uniqueness of reconstruction: proven for each model.

Ill-posedness, due to instability.
Inverse source reconstruction

Uniqueness problem

Is it possible to determine $J^p$ by measuring $(V, \partial_n V)$ on the scalp? or the magnetic field $B$ on magnetometers?
Inverse source reconstruction

Uniqueness problem

Is it possible to determine $J^p$ by measuring $(V, \partial_n V)$ on the scalp?

or the magnetic field $B$ on magnetometers?

“Silent sources” (Helmholtz, 1853):

- spherically symmetric conductor + radial dipole,  
  \[ B = 0 \quad \text{but} \quad V \neq 0 \]

- current loop $\nabla \cdot J^p = 0$,
  \[ V = 0 \quad \text{but} \quad B \neq 0 \]

- $J^p$ distributed $\perp$ to $S$, with constant magnitude,
  \[ V = 0, \quad B = 0 \]
Uniqueness results for EEG

if \( V \) perfectly measured on the scalp:

- Nested volume model, with homog. conductivities \( \sigma_i \)
- On \( S_N \): \( \sigma \partial_n V = 0 \).
- By linearity: uniqueness proved by proving that if \( V = 0 \) on scalp, then \( J^P = 0 \).

In each volume with no sources, \( \nabla \cdot \sigma_i \nabla V = \sigma_i \Delta V = 0 \).

Continuity across \( S_i \): \( \sigma_i(\partial_n V)^- = \sigma_{i+1}(\partial_n V)^+ \).

Holmgren theorem: unique continuation of harmonic potential whose Cauchy data (Neumann and Dirichlet b.c.) are known on a dense portion of boundary.

Iteratively apply Holmgren:
\( V = 0 \) in each volume, up to innermost surface containing sources.
Uniqueness results

- Distributed source model
  \[ J^p(r) = q(r) \, n(r) \, \delta_S(r) \text{ with } n(r) \perp S \text{ at position } r \]
  - Assumption \( S \subset \Omega_1 \) with constant conductivity
  - Result \( q(r) \) can be determined up to a constant.

  (classical elliptical operator theory)

- Isolated dipole model
  moments and positions of the sources uniquely determined
  [El Badia - Ha Duong 2000]

In spite of uniqueness, the inverse problem remains ill-posed (instability).
Current Source Density mapping

Cortical Source reconstruction: sometimes cumbersome
  - cortical surface highly convoluted, difficult to segment
  - high number of vertices

Alternative approach: mapping current sources on a simpler surface

Recall that electric potential satisfies

$$\text{div } \sigma \nabla V = \nabla \cdot J^p$$

so outside of $\text{supp}(J^p)$, $\text{div } \sigma \nabla V = 0$.

Cortical Mapping principle

Reconstruct normal current on inner skull surface, given that
  - $V$ is known on sensors,
  - $\text{div } \sigma \nabla V = 0$ outside the brain.
(rappel): éléments finis de surface symétriques

\[
\begin{bmatrix}
    (\sigma_1 + \sigma_2)N_{11} & -2D_{11}^* & -\sigma_2N_{12} & D_{12}^* & \cdots \\
    -2D_{11} & (\sigma_1^{-1} + \sigma_2^{-1})S_{11} & \sigma_2^{-1}S_{12} & -\sigma_3N_{23} & \cdots \\
    -\sigma_2N_{21} & D_{21} & D_{22} & -2D_{22} & \cdots \\
    D_{21} & (\sigma_2 + \sigma_1)N_{22} & (\sigma_2^{-1} + \sigma_3^{-1})S_{22} & -\sigma_3N_{32} & \cdots \\
    -\sigma_3N_{32} & D_{32} & D_{33} & -2D_{33} & \cdots \\
    D_{32} & (\sigma_3 + \sigma_4)N_{33} & (\sigma_3^{-1} + \sigma_4^{-1})S_{32} & -\sigma_4N_{43} & \cdots \\
    & & & \vdots & \ddots \\
\end{bmatrix}
\begin{bmatrix}
    \mathbf{v}_1 \\
    \mathbf{v}_2 \\
    \mathbf{v}_3 \\
    \vdots \\
\end{bmatrix}
= 
\begin{bmatrix}
    \sigma_1^{-1}N_{1\text{sources}} \\
    D_{1\text{sources}} \\
    0 \\
    0 \\
    0 \\
    \vdots \\
\end{bmatrix}
\]
Current Source Density mapping

true (simulated)  reconstructed  reconstructed (with noise)

[Maureen Clerc (Inria, France)]

[Clerc Kybic Physics Med Biol 2007]
Current Source Density mapping

[He Neuroimage 2002]
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with Juliette Leblond
and Jean-Paul Marmorat
Conductivity estimation

Conductivity $\sigma$

Relation between sources $J^p$ and potential $V$

$$\nabla \cdot \sigma \nabla V = \nabla \cdot J^p$$

EEG sensitive to ratio $\sigma_{\text{scalp}}/\sigma_{\text{skull}}$

[Rush & Driscoll [1968] 80
Cohen & Cuffin [1983] 80
Oostendorp & al. [2000] 15
Gonçalves, de Munck et al. [2003] $20 - 50$

Challenge: calibrating $\sigma$, non-invasively, in vivo:
- injecting known current on the scalp;
- multimodal measurements (MEG, EEG).

[Vallaghé, Clerc IEEE TBME 2009]
Influence of conductivity on localization

\[ \frac{\sigma_{\text{scalp}}}{\sigma_{\text{skull}}} = 80 \]

\[ \frac{\sigma_{\text{scalp}}}{\sigma_{\text{skull}}} = 40 \]

\[ \frac{\sigma_{\text{scalp}}}{\sigma_{\text{skull}}} = 20 \]

Averaged interictal spike.
Inverse reconstruction using MUSIC.

[courtesy of J-M Badier, La Timone]
Uniqueness of conductivity reconstruction

Problem statement: 3-layer problem

Known $\sigma_1$ and $\sigma_3$:
Is conductivity value $\sigma_2$ uniquely determined from a set of known sources $J^p$ and measurements $V$ (on $S_3$)?

Denote $\Sigma = \begin{bmatrix} I & 0 \\ 0 & \sigma I \end{bmatrix}$
Uniqueness via transmission problem

Notations

\[ X = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} \text{ where } x_i = \begin{bmatrix} \varphi_i \\ q_i \end{bmatrix} \text{ and } U = \begin{bmatrix} \beta_S \\ \partial_n \beta_S \end{bmatrix}_{S_1} \]

Transmission relations lead to:

\[ AX = BU \]

with 

\[ A = \begin{bmatrix} -(\Sigma_1 C_1^{int} + \Sigma_2 C_1^{ext}) & \Sigma_2 H_{12} & 0 \\ -\Sigma_2 H_{21} & -(\Sigma_2 C_2^{int} + \Sigma_3 C_2^{ext}) & \Sigma_3 H_{23} \\ 0 & -\Sigma_3 H_{32} & -(\Sigma_3 C_3^{int} + \Sigma_3 C_3^{ext}) \end{bmatrix} \]

and 

\[ B = \begin{bmatrix} \Sigma_1 & 0 & 0 \end{bmatrix}^T \]

Measurements on \( S_3 \): 

\[ V = CX \]

with 

\[ C = \begin{bmatrix} 0 & 0 & 0 & 0 & -I/2 - D_{33} S_{33} \end{bmatrix} \]
Discriminating source

Transmission from internal sources $U$ to external data $V$:

$$ V = CA^{-1} BU $$

Definitions,

- $\sigma_2$ and $\sigma_2'$ are **$U$-distinguishable** (for a given $U$) if $\sigma_2 \neq \sigma_2 \Rightarrow V \neq V'$.
- $U$ is a **discriminating source** if any two distinct conductivities $\sigma_2$ and $\sigma_2'$ are $U$-distinguishable.

$$ V - V' = (\sigma_2 - \sigma_2') CA_{\sigma_2}^{-1} RA_{\sigma_2'}^{-1} BU $$

$$ = (\sigma_2 - \sigma_2') \Phi(\sigma_2, \sigma_2') U . $$

$U$ is a discriminating source if and only if for all $\sigma_2 \neq \sigma_2'$, $U \notin \text{Ker}\Phi(\sigma_2, \sigma_2')$. 

Semirealistic geometry

$U$-distinguishability property equivalent to: \( \Phi(\sigma_2, \sigma'_2) U \neq 0 \) for given \((\sigma_2, \sigma'_2)\).

\[ \Phi(\sigma_2, \sigma'_2) = CA_{\sigma_2}^{-1} RA_{\sigma_2'}^{-1} B \] can be approximated by Boundary Elements.

Re-implementing Symmetric BEM using dual (barycentric) finite element complex

[Buffa, Christiansen, 2007] [Andriulli et al, 2008]
Spherical geometry

Spherical harmonic bases, order $k$ (harmonic frequency):

$$u_{S_i}(r, \theta, \varphi) = \sum_{k=0}^{\infty} \sum_{m=-k}^{k} \left[ \alpha_{ikm} r^k + \beta_{ikm} r^{-(k+1)} \right] Y_{km}(\theta, \varphi) \in \Omega_i$$

$\alpha_{ikm}$ vs $\beta_{ikm}$ are the spherical harmonic coeffs of harmonic vs anti-harmonic parts of $u_i$ (harmonic inside vs outside $S_i$).

Diagonalization by spherical harmonics lead to:

$$B_2(k)\sigma_2 \beta_{1k} = (A_3(k)\sigma_2^2 + A_2(k)\sigma_2 + A_1(k))$$

so that

$$\Phi(\sigma_2, \sigma'_2) = \frac{B_2(k) (A_3(k)\sigma_2\sigma'_2 - A_1(k))}{(A_3(k)\sigma_2^2 + A_2(k)\sigma_2 + A_1(k))(A_3(k)\sigma'_2^2 + A_2(k)\sigma'_2 + A_1(k))}$$

and uniqueness follows from $\frac{A_1(k)}{A_3(k)} = \sigma_2 \sigma'_2$. Stability results also obtained [Clerc, Leblond, Marmorat, Papageorgakis, 2016]
Conclusions and perspectives

Inverse conductivity problem harder than expected
crucial for EEG because of low skull conductivity
important role of Calderon operators
to be implemented in BEM
antiharmonic projection of infinite potential for inverse source reconstruction
geometry simplification?