The EEG Forward / Inverse Problem

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EEG Sources

Baillet et al, 2001
The forward and inverse problems

Forward Problem

$X = LS$

Inverse Problem

$S = L^{-1}X$

= 1000s of FP solution

EEG/MEG
Source localization is ill-posed

\[ X = LS + n \]

X: scalp recorded potentials
S: current density vector
L: transfer matrix ‘the head volume conductor model’

The inverse problem refers to finding S given known X.

\[ O(S) = \min \| X - LS \|^2 \]

Infinite solutions!

Apply electrophysiological neuroanatomical constraints

1. The electrical forward head model used
2. The inverse solution approach
The head volume conduction model

Simple Head Models
- Single layer sphere, spheroid
- 3-4 layer sphere

Realistic Head Models
- Boundary Element (BEM)
- Finite Element (FEM)
- Finite Difference (FDM)

ANALYTICAL SOLVER
Simple, fast, but not accurate

NUMERICAL SOLVER
Represents head shape better, but computationally complex
Neuroelectromagnetic Forward Head Modeling Toolbox

http://sccn.ucsd.edu/nft
Numerical Head Models

NFT BEM mesh

Generated using Tetgen from NFT BEM mesh
Formulation of the Forward Problem

\[ \nabla \cdot (\sigma \nabla \Phi) = -\nabla \cdot J^P \quad \text{inside } V \]

\[ \sigma \frac{\partial \Phi}{\partial n} = 0 \quad \text{on } S \]

\( \sigma(x,y,z) \): conductivity distribution

\( \vec{p} \): current source

Reference: Gulrajani, R., Bioelectricity and biomagnetism
BEM Formulation

Integral equation for Potential Field:

\[
\phi(\vec{r}) = 2g(\vec{r}) + \frac{1}{2\pi} \sum_{k=1}^{n} \left( \frac{\sigma_k^- - \sigma_k^+}{\sigma_i^- + \sigma_i^+} \right) \int_{S_k} \phi(\vec{r}') \frac{\vec{R}}{R^3} \cdot d\vec{S}_k(\vec{r}')
\]
Boundary Element Method (BEM)
Model Formulation

Integrating the previous integral equation over all elements a set of equations are obtained.

In matrix notation for the potential field we obtain

\[ \Phi_{M \times 1} = C_{M \times M} \Phi + g_{M \times 1} \]
\[ \Phi = [I - C]^{-1} g \]
\[ \Phi = A^{-1} g \]

\( M \): number of nodes

The expression for the magnetic field:

\[ B_{n \times 1} = B_0 + H_{n \times M} \Phi \]

\( n \): number of magnetic sensors
The transfer matrix

Electrode potentials

\[ \Phi_e = D A^{-1} g \]

\[ \Phi_e \quad \text{mx1 vector of electrode potentials} \]

D is an \( m \times M \) sparse matrix to select \( m \) rows of \( A^{-1} \)

Let the transfer matrix \( E \) be defined as:

\[ E = D A^{-1} \]

Taking the transpose of both sides, and multiplying by \( A^T \)

\[ A^T e_i = d_i \]
The NFT BEM implementation

- Quadratic elements
  - Isoparametric
  - Better interpolation
- Recursive integration
- IPA
- Intersecting surfaces
The FEM transfer matrix

- FEM computes volume potentials
  - Solving the matrix for every source is slow
  - We only need potentials at electrode locations

- Use the reciprocal formulation:
  - Inject current at electrodes, solve volume potentials
Inverse Problem Approaches

**Equivalent dipole Methods**
- Overdetermined
- Searches for parameters of a number of dipoles
- Nonlinear optimization techniques
- May converge to local minima
- Non-linear least squares, beamforming, MUSIC, simulated annealing, genetic algorithms, etc.

**Linear distributed Methods**
- Underdetermined
- Searches for activation in given locations.
- Linear optimization techniques
- Needs additional constraints
- Bayesian methods, MNE, LORETA, LAURA, etc.
Independent EEG Components are Dipolar


http://www.plosone.org/article/info:doi/10.1371/journal.pone.0030135
The equivalent current dipole (ECD)

\[ O(S) = \min \| X - LS \|^2 \]

6 parameters are estimated for each dipole: Location, orientation and strength
Linear distributed source models

\[ X = LS \]

L is the lead field matrix:
Potential vectors of all possible solutions

Anatomical constraint:
Sources are in the cortex & perpendicular to the cortex
Multi-scale patch-basis source localization using Sparse Bayesian Learning (SBL)

\[ D_{ij} = \text{geodesic\_distance}(i,j) \]
\[ D_{ij} = \text{Inf} \quad \text{if} \quad D_{ij} > \text{scale} \]
\[ W_{ij}^{(k)} = \text{gauss}(D_{ij},\sigma_k) = \frac{1}{\sqrt{2\pi\sigma_k^2}} \exp\left(-\frac{D_{ij}^2}{2\sigma_k^2}\right) \]
\[ \sigma_k = \text{scale}/3 \]

Three truncated Gaussian patches of different scales (radii)

<table>
<thead>
<tr>
<th>radius</th>
<th>10 mm</th>
<th>6 mm</th>
<th>3 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sigma_k )</td>
<td>3.33 mm</td>
<td>2 mm</td>
<td>1 mm</td>
</tr>
</tbody>
</table>

\( X = LS \)
\( L := [m \times v] \quad \text{Lead field matrix} \)
\( \tilde{L} = [LW^{(1)} \cdots LW^{(3)}]_{m \times 3v} \)

\( X = A\hat{S} \)
\( \hat{S}_q := [1 \times T] \quad \text{q}^{\text{th}} \text{ IC activation} \)

\( A_q = \tilde{L}\tilde{M}_q + \hat{U}_q \)
\( \tilde{L}^{-1} = \text{SBL}(A_q, \tilde{L}) \)
\( \tilde{M}_q = \left[ \tilde{L}^{-1} A_q \right]_{3v \times 1} \)
\( M_q = \text{reshape}(\tilde{M}_q, v \times 3) \)
\( M_q = \sum_{i=1}^{3} \tilde{M}_q(:,i) \)
\( P_q = M_q \hat{S}_q \quad \text{[v x T] cortical surface potentials for q}^{\text{th}} \text{ IC} \)

SBL simulation study using an MNI head model (SNR=50)

Three examples:

<table>
<thead>
<tr>
<th>Type</th>
<th>Scale (mm)</th>
<th>Max. dis. (mm)</th>
<th>Energy dif.</th>
<th>DF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gyral</td>
<td>10</td>
<td>0</td>
<td>1.5</td>
<td>103.8</td>
</tr>
<tr>
<td>Sulcul</td>
<td>10</td>
<td>1.01</td>
<td>29.8</td>
<td>101.4</td>
</tr>
<tr>
<td>Sulcul</td>
<td>5</td>
<td>2.12</td>
<td>4.1</td>
<td>37.6</td>
</tr>
<tr>
<td>Dual</td>
<td>10</td>
<td>11.6</td>
<td>29.3</td>
<td>89.2</td>
</tr>
<tr>
<td>Gyral</td>
<td>5</td>
<td>1.01</td>
<td>4.7</td>
<td>41.3</td>
</tr>
<tr>
<td>Sulcul</td>
<td>12</td>
<td>1.8</td>
<td>10.6</td>
<td>125.5</td>
</tr>
</tbody>
</table>

Term | Definition
--- | ---
max displacement | geodesic distance between original and reconstructed patch centers
energy difference | |original energy - reconstructed energy|
degree of focalization (DF) | reconstructed energy / original energy

Comparison of methods

source

SCS
Cheng Cao, 2012
	e/o A. Ojeda

Patch-based SBL

sLORETA
c/o A. Ojeda
Epilepsy data: forward modeling

NFT volume conduction model from MRI

Cortical source space model from MRI (Freesurfer)

BEM model:
Plastic sheet
Skull with craniotomy
Scalp

80,000 source vertices

Z. Akalin Acar - Head Modeling and Cortical Source Localization in Epilepsy
Cortical activity of seizure components

Activations of 13 seizure components

Summed cortical activity of seizure components

\[ \text{Movie}(t) = \sum_{i=1}^{13} S_i \times \text{Act}_i(t) \]
Effects of Forward Model Errors on EEG Source Localization

1. Head modeling errors
2. Skull conductivity mis-estimation errors
3. Co-registration errors
4. Low electrode numbers and coverage

Akalin Acar and Makeig, 2013, *Brain Topography*
Head Model Comparison

- **Reference Head Model**
  - From whole head T1 weighted MR of subject
  - 4-layer realistic BEM model

- **MNI Head model**
  - From the MNI head
  - 3-layer and 4-layer template BEM model

- **Warped MNI Head Model**
  - Warp MNI template to EEG sensors

- **Spherical Head model**
  - 3-layer concentric spheres
  - Fitted to EEG sensor locations
Neuroelectromagnetic Forward Head Modeling Toolbox

http://sccn.ucsd.edu/nft
The Reference Head Model

- 18541 nodes
- 37090 elements
  - 6928 Scalp
  - 6914 Skull
  - 11764 CSF
  - 11484 Brain
The MNI Head Model

- **4-layer**
  - 16856 nodes
  - 33696 elements

- **3-layer**
  - 12730 nodes
  - 25448 elements

Brain | CSF | Skull | Scalp
The Warped MNI Head Model

Registered MNI template

Warped MNI mesh
Electrode-warped head models

S1  S2  S3  S4

After electrode position model warping
Tissue conductivity boundaries

Scalp, skull, CSF and brain tissue boundaries for a four-layer MR-based realistic, four-layer warped MNI, and four-layer MNI head models plotted on a sagittal slice of subject S1.
The Spherical Head Model

3-Layer model
Outer layer is fitted to electrode positions
Head Modeling Errors

- Solve FP with reference model
  - 3D grid inside the brain.
  - 3 Orthogonal dipoles at each point
  - ~7000 dipoles total
  - 4 subjects

- Localize using other head models
  - Single dipole search.

- Plot location and orientation errors
Localization errors may go up to 3 cm when spherical head models are used for source localization. The errors are largest in the inferior regions where the spherical models diverged most from the 4-layer realistic model.
3-Layer MNI Model
Dipole Location Errors

3-Layer MNI

3-Layer Warped MNI
4-Layer MNI Model
Dipole Location Errors

4-Layer MNI

4-Layer Warped MNI
Observations

- **Spherical Model**
  - Location errors up to 2.5 cm. Cortical areas up to 1.5 cm.
  - 4-layer and 3-layer models gave very similar localization results.
  - Including cheek and neck electrodes increased localization error.

- **3-Layer MNI**
  - Large errors where models do not agree.
  - Higher around chin and the neck regions.

- **4-Layer MNI**
  - Similar to 3-Layer MNI.
  - Smaller in magnitude.
Effect of cheek electrodes on SPH
Localization error distributions
Residual variance histograms
Electrode co-registration errors

- Solve FP with reference model
- Shift all electrodes and re-register
  - 5° backwards
  - 5° left
- Localize using shifted electrodes
- Plot location and orientation errors
Location errors with 5° electrode shift
Observations

- Errors increase close to the surface near electrode locations.

- Changing or incorrectly registering electrodes may cause 5-10 mm localization error.
Head tissue conductivity values

- **Scalp**: 0.33 S/m
- **Skull**: 0.0032 S/m (0.08-0.0073 S/m)
- **CSF**: 1.79 S/m
- **Brain**: 0.33 S/m
Skull conductivity measurement

Measurement of skull conductivity

In vivo

Hoekama et al, 2003

In vitro

MREIT
Magnetic stimulation
Current injection

He et al, 2005
## Skull conductivity uncertainty

### Brain to skull ratio

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Ratio</th>
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<tbody>
<tr>
<td>Rush and Driscoll</td>
<td>1968</td>
<td>80</td>
</tr>
<tr>
<td>Cohen and Cuffin</td>
<td>1983</td>
<td>80</td>
</tr>
<tr>
<td>Oostendorp et al</td>
<td>2000</td>
<td>15</td>
</tr>
<tr>
<td>Lai et al</td>
<td>2005</td>
<td>25</td>
</tr>
</tbody>
</table>

### Measurement

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Age</th>
<th>σ (mS/m)</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agar-agar phantom</td>
<td>–</td>
<td>43.6</td>
<td>7.5</td>
</tr>
<tr>
<td>Patient 1</td>
<td>11</td>
<td>80.1</td>
<td>4</td>
</tr>
<tr>
<td>Patient 2</td>
<td>25</td>
<td>71.2</td>
<td>4.6</td>
</tr>
<tr>
<td>Patient 3</td>
<td>36</td>
<td>53.7</td>
<td>6.2</td>
</tr>
<tr>
<td>Patient 4</td>
<td>46</td>
<td>34.4</td>
<td>9.7</td>
</tr>
<tr>
<td>Patient 5</td>
<td>50</td>
<td>32.0</td>
<td>10.3</td>
</tr>
<tr>
<td>Post mortem skull</td>
<td>68</td>
<td>21.4</td>
<td>15.7</td>
</tr>
</tbody>
</table>
Testing effects of skull conductivity mis-estimation

- Solve FP with reference model
  - Brain-to-Skull ratio: 25

- Generate test models
  - Same geometry
  - Brain-to-Skull ratio: 80 and 15

- Localize using test model

- Plot location and orientation errors
Skull conductivity mis-estimation
Effects of white matter layer

White matter conductivity: 0.14 S/m

White matter surface obtained using Freesurfer

Reduced WM surface with 10,240 faces for BEM model
Effects of white matter

A

↑ RLS-5
↓ RLS-4

B

↑ RLS-5
↓ wMNI-4

0mm

15

10

5
Effects of the number of electrodes and their scalp coverage
Induced localization errors
Localization error

Magnitude-sorted localization error distributions for source localizations performed using the sensor distributions.
Summary

- If we have an MRI head image of the subject:
  - Subject specific head model
  - Distributed source localization
- If we don’t have an MRI
  - Warped 4-layer MNI model
  - Dipole source localization
- **Skull conductivity estimation is as important as the head model used.**
- Number of electrodes should be 64 or higher.
- WM modeling does not have much effect on source localization for cortical sources.
Localization of cortical patch sources

- **Source space**: patches tangent to the cortex.
- **80,000 dipole elements** using tessellated FreeSurfer gray matter surface.
- For each dipole element: three gaussian-tapered cortical patches of sizes with geodesic radii of 10 mm, 6 mm, and 3 mm.
The forward problem is solved for a subset of 8,000 points for every patch size. Potential maps from these multi-scale patch sources are generated and localized using a single equivalent dipole.
Localization errors (in cm)

Inflated cortex

RLS

4-wMNI

SPH

FP: Source = patch, IP dipole source localization
Histograms of percent residual variance

Histograms of percent residual scalp map variance for source estimates based on three head models and three patch sizes.
Histograms of percent orientation errors for source estimates for three patch sizes for Realistic (left), warped MNI (middle) and spherical (right) head models.
When the patch size is small the source can be better modeled as a point source. As the patch size gets larger, the dipole is localized farther away, below the patch, so the errors increase. However, with the realistic mesh, the maximum error is only 2 mm for 10 mm patch.

As the patch size gets larger (10, 15, 20, 25 mm) the errors increase slightly. Median errors become 1 → 2.1 mm.

The errors for the equivalent dipoles fitted using the realistic model is below 2 mm, which suggests that a dipole source model is suitable for most purposes. These source modeling errors are much lower than the errors introduced by the head model.
Cortical anisotropy

- Directional conductivity for WM.
- WM anisotropy can be obtained from diffusion tensor imaging (DTI).
- Anisotropy ratio = 9:1
Effects of WM anisotropy

Gullmar, 2010
The 3-layer skull

Skull anisotropy -> Skull inhomogeneity (3-layer skull)
(Sadleir 2007, Dannhauer 2011)
More elaborate head models: A 10-tissue segmentation!

Ramon 2006, Fiederer 2012
Our child head modeling project

4-layer FEM head model

4-layer BEM head model

1-year old head model

Data from April Benasich lab, Rutgers
Age-specific template head models

Sanchez 2011
Thank you...

Swartz Center for Computational Neuroscience