Forward and Inverse Problem of EEG

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Generators of EEG

Baillet et al, 2001
Forward and inverse problem

Forward Problem

\[ X = LS \]

Inverse Problem

\[ S = L^{-1}X \]

= 1000s of FP solution
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 head model used,
2. The inverse solution itself
Head volume conductor 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
Numerical Head Models

BEM

NFT BEM mesh

FEM

Generated using Tetgen from NFT BEM mesh
Formulation of the FP

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

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

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

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

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

Integral equation for Potential Field:

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

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

In matrix notation for the potential field we obtain

$$\Phi_{M\times1} = C_{M\times M} \Phi + g_{M\times1} \quad \Phi = [I - C]^{-1} g \quad \Phi = A^{-1} g$$

$M$: number of nodes

The expression for the magnetic field:

$$B_{n\times1} = B_0 + H_{n\times M} \Phi$$

$n$: number of magnetic sensors
Transfer matrix

Electrode potentials

\[ \Phi_e = DA^{-1}g \]

\( \Phi_e \)  mx1 vector of electrode potentials

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

Let the transfer matrix E be defined as:

\[ E = DA^{-1} \]

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

\[ A^T e_i = d_i \]
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

**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.
Equivalent current dipole (ECD)

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

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

\[ X = LS \]

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

Anatomical constraint: Sources are on the cortex perpendicular to the cortex
Multi-scale patch-basis source localization with Sparse Bayesian Learning

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

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>

\[ X = LS \]
\[ L : = [m \times v] \quad \text{Lead field matrix} \]
\[ \tilde{L} = [LW^{(1)} \cdots LW^{(3)}]_{m \times 3v} \]
\[ X = A\hat{S} \]
\[ \hat{S}_q := [1 \times T] \quad q^{th} \text{IC activation} \]

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

SBL Simulation Study with MNI model (SNR=50)

<table>
<thead>
<tr>
<th>Three examples:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>original</td>
<td>reconstructed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Source (x 15)</th>
<th>Max. dis. (mm)</th>
<th>Energy dif.</th>
<th>DF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Scale (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gyral</td>
<td>10</td>
<td>0</td>
<td>1.5</td>
</tr>
<tr>
<td>Sulcul</td>
<td>10</td>
<td>1.01</td>
<td>29.8</td>
</tr>
<tr>
<td>Sulcul</td>
<td>5</td>
<td>2.12</td>
<td>4.1</td>
</tr>
<tr>
<td>Dual</td>
<td>10</td>
<td>11.6</td>
<td>29.3</td>
</tr>
<tr>
<td>Gyral</td>
<td>5</td>
<td>1.01</td>
<td>4.7</td>
</tr>
<tr>
<td>Sulcul</td>
<td>12</td>
<td>1.8</td>
<td>10.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>max displacement</td>
<td>geodesic distance between original and reconstructed patch centers</td>
</tr>
<tr>
<td>energy difference</td>
<td></td>
</tr>
<tr>
<td>degree of focalization (DF)</td>
<td>reconstructed energy / original energy</td>
</tr>
</tbody>
</table>
Neuroelectromagnetic Forward Head Modeling Toolbox

http://sccn.ucsd.edu/nft
NFT - Segmentation

Image Segmentation

1. Anisotropic Filtering
   - Number of iterations: 5
   - Image diffusion: 3

2. Scalp Segmentation

3. Brain Segmentation
   - Cerebellar low point: x=135, y=135, z=110
   - White matter seed point: x=0.4, y=0.4

4. Outer Skull Segmentation
   - Center of one eye: z=110

5. Inner Skull Segmentation

Display Image
- MR image
- Filtered image
- Scalp mask
- Brain mask
- Outer skull mask
- Inner skull mask

Save Results
- Output Folder: (data/projects/zevne/c/comm_on/home/zevne/toli/dename)
- Run anisotropic filtering

NFT: MR segmentation

(x,y,z) = (128, 128, 128)
NFT – Mesh generation

From a magnetic Resonance Image
- Image Segmentation
- Mesh Generation

Source Space Generation
- Electrode Co-Registration

Mesh generation parameters:
- Load Segmentation: /data/projects/zeynep/common/home_zeynep/jo/deneeme/dene_rea/SubjA_segments
- Output Folder: /data/projects/zeynep/common/home_zeynep/jo/deneeme/dene_rea
- Mesh name: SubjectA
- # of layers: 4
- Linear
- Quadratic
- Number of nodes per layer: 7000
- Local mesh refinement
- Edge length: 2.1
- Distance between meshes: 0.1

Start Mesh Generation
- Generate linear FEM mesh
- Generate quadratic FEM mesh

Status
NFT – source space generation

Generates a simple source space:
Regular Grid inside the brain
With a given spacing and distance to the mesh
NFT – electrode co-registration

From a magnetic Resonance Image

Image Segmentation

Mesh Generation

Source Space Generation

Electrode Co-Registration

Load sensor locations /data/projects/zeynep/common/home_zeynep/jo/deneme/jop3.raw.el

Mesh folder /data/projects/zeynep/common/home_zeynep/jo/deneme/dene_real

Initial co-registration

Translation 0.2 0.5
Rotation 0 0.25 -1.5708

Complete co-registration

Translation
Rotation

Save initial reg.

Save complete reg.

Computing translation and rotation parameters...
NFT – Template warping

NFT: Template head model warping

Load sensor data

Output Folder

# of layers (3 or 4)

MNI head model

Warped MNI head model

Mesh Warped
NFT – Forward problem solver

- MATLAB interface to numerical solvers
- Boundary Element Method or Finite Element Method
  - EEG Only (for now)
  - Interfaces to the Matrix generator executable written in C++
- Other computation done in MATLAB
- Generated matrices are stored on disk for future use.
NFT - Forward Problem Solver (BEM)
NFT – Forward Problem Solver (FEM)
NFT – Dipole fitting

- Requires EEGLAB integration to access Component indices.
- Uses FieldTrip in EEGLAB for dipole fitting.

http://www.sccn.ucsd.edu/nft
Effects of Forward Model Errors on EEG Source Localization

MODELING ERRORS
Head Model Generation

- 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
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
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 4 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 Location Errors

3-Layer MNI

3-Layer Warped MNI
4-Layer MNI Location Errors

4-Layer MNI

4-Layer Warped MNI
Observations

- **Spherical Model**
  - Location errors up to 3.5 cm. Cortical areas up to 1.5 cm.

- **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.
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 conductivities

- **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

### Brain to skull ratio

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Ratio</th>
</tr>
</thead>
<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>
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</table>

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Age</th>
<th>$\sigma$ (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>
Effect of Skull Conductivity

- 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
Effect of white matter

White matter conductivity: 0.14 S/m

White matter surface obtained using Freesurfer

Simplified WM BEM model
Effect of white matter
Number of electrodes and coverage
Location errors
Summary

- If we have MRI of the subject:
  - Subject specific head model
  - Distributed source localization
- If we don’t have MRIs
  - Warped 4-layer MNI model
  - Dipole source localization
- Skull conductivity estimation is as important as the head model used.
- WM modeling does not have much effect on source localization.
Epilepsy Head Modeling

CASE STUDY
Epilepsy is a neurological disorder characterized by seizures. It affects approximately 50 million people worldwide, with 30% not being controlled with medical therapy. About 4.5% of patients are potential candidates for surgical treatment.
Electrocorticography

ECoG recording

ECoG grid and strips

Macro and micro Electrodes (Mayo Clinic)

Depth electrodes
iEEG data
Solution of the forward problem using realistic head models (BEM, open skull)

MRI/CT head image

Segmentation

Mesh Generation

Data co-registration

AMICA decomposition

Sparse Bayesian Learning

Component Sources

Cluster Sources

PMI Clusters

Source space

Multiscale EEG data
Forward modeling

Z. Akalin Acar - Head Modeling and Cortical Source Localization in Epilepsy

BEM model:
- Plastic sheet
- Skull with craniotomy hole
- Scalp

Cortex (Freesurfer)

80 000 source vertices
Analyzing Epilepsy Recordings

- Pre-Surgical Evaluation
- Rest Data
- 78 ECoG (subdural EEG) electrodes
- 29 scalp electrodes
- Surgical Outcome: Positive (seizure free)
- Provided by Dr. Greg Worrell, Mayo Clinic

16 min of data, 2 seizures
ICA decomposition

Extended Infomax ICA Decomposition
16 seizure components (ICs) selected
Independent Components

Potentials on scalp

Potentials on plastic sheet

On the brain surface

IC 1

IC 2
Source Localization Results

- Dipole source localization
- Distributed source localization - SBL

IC 1
- Radial source
- Gyral source

IC 2
- Tangential source
- Sulcal source
Cortical activity of seizure components

Activations of 13 seizure components

Movie(t) = \sum_{i=1}^{13} S_i \times Act_i(t)
Thank you...

Swartz Center for Computational Neuroscience
Algebraic formulation of the FP

Scalp potentials for $N$ electrodes and $p$ dipoles:

$$ V(r) = \sum_{i}^{p} g(r, r_{dip}, d_i) = \sum_{i}^{p} g(r, r_{dip}, e_{d_i}) d_i $$

$$ V = \begin{bmatrix} V(r_1) \\ \vdots \\ V(r_N) \end{bmatrix} = \begin{bmatrix} g(r_1, r_{dip}, e_{d_1}) & \cdots & g(r_1, r_{dip}, e_{dp}) \\ \vdots & \ddots & \vdots \\ g(r_N, r_{dip}, e_{d_1}) & \cdots & g(r_N, r_{dip}, e_{dp}) \end{bmatrix} \begin{bmatrix} d_1 \\ \vdots \\ d_p \end{bmatrix} = G(\{r_j, r_{dip_i}, e_{d_i}\}) \begin{bmatrix} d_1 \\ \vdots \\ d_p \end{bmatrix} $$

For $N$ electrodes and $p$ dipoles and $T$ discrete time samples:

$$ V = \begin{bmatrix} V(r_1, 1) & \cdots & V(r_1, T) \\ \vdots & \ddots & \vdots \\ V(r_N, 1) & \cdots & V(r_N, T) \end{bmatrix} = G(\{r_j, r_{dip_i}, e_{d_i}\}) \begin{bmatrix} d_{1,1} & \cdots & d_{1,T} \\ \vdots & \ddots & \vdots \\ d_{p,1} & \cdots & d_{p,T} \end{bmatrix} $$

$$ V = GD + n $$
To Solve the Forward Problem

WE NEED

- Head Model
  - Conductivity values
  - Geometry
- Source distribution
  - Magnitude
  - Location
  - Direction
- Field Locations
- Solver
Anisotropy

- Directional conductivity for skull and WM.
- WM anisotropy can be obtained from diffusion tensor imaging (DTI).
- WM anisotropy ratio = 9:1
- Skull ratio = 10:1
Anisotropy

Return currents for a left thalamic source on a coronal cut
Wolters et al, 2006
Potential fields on the scalp

Shallow tangential source

Deep tangential source

right

front
top view of head

left

front
Potential fields on the scalp

Shallow radial source

Deep radial source

right

front

top view of head

left

front