Introduction to Source Estimation: Distributed Anatomically Constrained Source Models

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Introduction
• The primary current is related to the postsynaptic activity

• The primary current generates a potential distribution (EEG) and the associated volume currents

• The primary and volume currents together also create a magnetic field (MEG)

• However, the net effect of volume currents is rather straightforward to take into account in MEG whereas the it is difficult to compute the EEG potential distribution accurately
Focal, extended, and distributed sources

- **Focal source**: indistinguishable from a current dipole
- **Extended source**: large patch of cortex
- **Distributed source**: several focal or extended sources at different locations
Example: The time-varying current-dipole model

- The neural currents on a few-cm$^2$ patch of cortex are approximated with a current dipole
- Dipole locations are fixed over time
- Dipole amplitudes are allowed to vary

Scherg et al., 1984 (?)
Dipole models: caveats

• It is difficult to find the optimal dipole locations automatically

• The least-squares solution might not be closest to the truth

• Sources might be too extended to be represented by a dipole
Motivation to use distributed source models

• Account for non-focal sources
• Automatic analysis without heuristic choices often needed in multidipole models
• Incorporate anatomical and functional MRI constraints
• Lower SNR data can be processed
• Transformation of data to brain space without strong assumptions about the sources
Distributed source models

• Grid of dipoles in a volume or on a surface
• Find an optimal solution among those fitting the data

\[ y = Gq + \epsilon \]

\[ E\{\epsilon\epsilon^T\} = C \]

\[ \hat{q} = \arg\min_q \left( ||y - Gq||^2_C + f(q) \right) \]

• The second source penalty term expresses the \textit{a priori} assumptions
Minimum-Norm Solutions

The source penalty term is selected as a weighted norm of the current distribution:

\[ \hat{q} = \arg\min_q \left( \|y - Gq\|_C^2 + \|q\|_R^p \right) \]

Examples:
- Minimum-norm estimates (MNE): \( p = 2 \)
- LORETA: \( p = 2 \), \( R = \) Laplacian operator
- Minimum-current estimates (MCE): \( p = 1 \)
First $L_2$ Minimum-Norm Estimates

Median-nerve SEF
45 single-channel measurements = 9000 stimuli

Hämäläinen and Ilmoniemi 1984
Modern MNE

- Source locations (and orientations) constrained to the cortical mantle
- Forward solution with BEM
- Full noise-covariance matrix estimates computed from raw data
- Display on an inflated cortex to reveal the sulci
- Compute statistics
- Combined MEG and EEG solutions
- fMRI-guided solutions

Dale et al. 2000
How is the MNE computed?

$L_2$-norm minimum-norm estimate (MNE)

$$\hat{q} = RG^T(GRG^T + \lambda^2 C)^{-1}y$$

G: forward solution
C: noise-covariance matrix
R: source covariance matrix
Linear estimate: easy to compute
Summary of the L$_2$-norm solution (MNE)

- Select the source space
- Require that the solution reproduces the measured data
- Select the current distribution which has the minimum overall power
- Easy to compute
- Hard to justify by physiology
- A convenient way to represent the data in terms of sources
Cortical Surface Geometry
Cortical Source Location Constraints

Tessellation of the cortex: Source location and orientation information

For source estimation, the surface is typically decimated, resulting in 6000 - 10000 source locations
Inflated Cortex

Topologically correct tessellation can be inflated

Dale, Fischl, Sereno *et al.*
Inflation to a Sphere and Registration

Individual

Aligned with average brain

Align sulcal patterns to the average brain

MEG activity estimate

Mapped to the average brain

Morph
Meshes for BEM Forward Solution
Boundary-Element Forward Solution

- The head is assumed to consist of compartments with homogeneous, isotropic electrical conductivity
- MEG: One compartment (brain)
- EEG: Three compartments (scalp, skull, brain)
Forward models for MEG and EEG

**Homogeneous model:**
- Skull taken as an insulator,
- Result independent of conductivity

**Multilayer model:**
- Skull and scalp taken into account,
- Conductivities needed

**Experimental validation:** Okada et al., 1999

Theoretical analysis: Hämäläinen and Sarvas, 1989

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MRI-based Conductor Geometry for Forward Models

- **Scalp:** straightforward
- **Inner skull:** doable
- **Outer skull:** painful
M RI-based Conductor Geometry for Forward Models

Scalp: straightforward

Inner skull: doable

Outer skull: painful

Facilitate segmentation with suitable MRI data:
Acquire multi-echo flash data to reconstruct images with appropriate contrasts for segmentation
Coregistration
Early MEG/MRI alignment

A coordinate system based on fiducial landmarks

Make landmarks visible in MRI and identify them from the images

Williamson *et al.* 1991
Are fiducial markers needed?

- Smooth head surface for forward modeling
- Accurate head surface for picking the fiducials

Both reconstructions can be automatically generated from the MRIs
Contemporary MEG/MRI Alignment

- Use the traditional method for approximate alignment
- Iterative closest-point algorithm for iterative refinement
The Inverse Operator
How is the MNE computed?

L₂-norm minimum-norm estimate (MNE)

\[ \hat{q} = R G^T (G R G^T + \lambda^2 C)^{-1} y \]

G: forward solution
C: noise-covariance matrix
R: source covariance matrix

Linear estimate: easy to compute
Noise normalization

- Convert the current values into a test statistic
  - dSPM (Dale et al.)
  - sLORETA (Pascual-Marqui et al.)
- Divide the current with its standard deviation
- Analyze MEG/EEG data like fMRI or PET
- Reduces location bias
- Point-spread more uniform
- Auditory MEG data
- Source locations constrained to the cortex
- No orientation constraint
- dSPM and sLORETA produce very similar results with real data
Primary currents on the cortex

Primary currents

MEG = 0
EEG ≠ 0

MEG ≠ 0
EEG ≠ 0

current sources

cortex
Loose orientation constraint

- Compute the forward solution in a surface-based coordinate frame
- Adjust R so that the variance of the current components tangential to the cortex is smaller than that of the normal component

Lin et al. 2006
Effect of the orientation constraint

- Auditory responses to short tones
- Depth-weighted MNE and SPM
- Without and with loose orientation constraint
- The orientation constraint rules out infeasible sources
Effect of the orientation constraint

- Auditory responses to short tones
- Depth-weighted MNE and SPM
- Without and with loose orientation constraint
- The orientation constraint rules out infeasible sources
Depth weighting

- The source variance is made larger with depth
- Counteracts the superficial bias
Effect of additional constraints

MNE

Unweighted
Depth-weighted
Depth-weighted and LOC

dSPM
MNE, dSPM, or sLORETA?

• In principle, the question does not make very much sense
• Noise-normalized estimates and MNE serve different purposes
• sLORETA and dSPM: help to decide where the activity is significantly different from baseline noise
• MNE should be consulted for the actual current values
• Use dSPM or sLORETA and MNE
Combination of MEG and EEG (dSPM)

MEG only

t = 84.4 ms

dSPM  SNR = 3.0
6.0..12.0..20.0

MEG and EEG

t = 84.4 ms

dSPM  SNR = 4.1
6.8..13.6..22.7
Comparison of MEG, EEG, and fMRI

Sharon et al. 2007
Comparison of localization errors

Sharon et al. 2007

Mean peak-to-peak distance to fMRI / mm

- **dSPM**
  - MEG: 0.7
  - EEG: 8.3
  - MEG + EEG: 10.8

- **ECD**
  - MEG: 0.8
  - EEG: 14.5
  - MEG + EEG: 23.1

- **depth-weighted MNE**
  - MEG: 19
  - EEG: 4.6
  - MEG + EEG: 28.9

**Note:**
- * indicates significance at p < 0.05.
fMRI-guided estimates

- Increase the source variance at locations of significant fMRI activity
- MNE is strongly affected
- dSPM is only weakly affected
fMRI-guided MNE and dSPM

S1 active

A1 active

MNE

dSPM

$R_{\text{off}}/R_{\text{on}} = 1$
fMRI-guided MNE and dSPM

S1 active

A1 active

\( R_{\text{off}} / R_{\text{on}} = 0.1 \)
fMRI-guided MNE and dSPM

S1 active

A1 active

\[ \frac{R_{off}}{R_{on}} = 0.02 \]
fMRI-weighted MEG

dSPM statistic with fMRI as an a priori weight

Dale et al. 2000
fMRI-weighted MEG

dSPM statistic with fMRI as an a priori weight

Dale et al. 2000
fMRI-weighted MEG

dSPM statistic with fMRI as an a priori weight

Dale et al. 2000
Concluding remarks
Both MNE and ECD can point the approximate location of the source.

The extent of the source is difficult to determine.

Hämäläinen and Hari 2002
Analysis of MEG data

- Sensor data: Minimal assumptions, always available.
- MNE/dSPM: General assumptions, easy to compute.
- Dipole models: Specific assumptions, challenging estimation.

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