“Will it ever happen that mathematicians will know enough about the physiology of the brain, and neurophysiologists enough of mathematical discovery, for efficient cooperation to be possible”

Jacques Hadamard (mathematician, 1865-1963)
M/EEG source analysis

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Ill-posed inverse problem
Why a Bayesian approach?

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From sources to sensors
Sensors

Bayesian inference
ECD model
Imaging models
Setting priors
Empirical Bayes
Comparing models
Group inference
EEG/MEG fusion

Example
MMN study
Group multimodal inference

Well-posed inverse problem:
- a solution exists ✓
- the solution is unique ✗
- the solution is stable ✗

Jacques Hadamard (mathematician, 1865-1963)
Introduction

Ill-posed inverse problem
Why a Bayesian approach?

Bayesian inference enables:
- to incorporate priors on the solution
- to account for uncertainty through probabilitic distributions
- to yield a unique and optimal solution given a likelihood model and priors over model parameters

M/EEG source analysis

Introduction

EEG
MEG
reconstruction / inversion

likehood / predictive / forward

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A particular generative model is fully defined by:

- A data likelihood density function $p(Y|\theta)$
- A prior distribution over source parameters $\theta$
Sources

 observable from scalp:
the synchronous and additive activities of numerous neighbouring neurons

$\theta$:
- Dipole location $(x, y, z)$
- Dipole orientation $(Ox, Oy, Oz)$
- Dipole strength

M/EEG source analysis

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**Equivalent Current Dipole (ECD)**
- Only a few activated sources
- Each source corresponds to a fairly large brain area
- Each source activity is modelled by one current dipole

Only a few parameters $\theta$ to be estimated
(location, orientation and strength)

**Distributed or imaging approach**
- The whole brain/cortex may be active
- The source space is discretized using a grid over the whole brain (voxels) or a cortical mesh (nodes)
- Each voxel or node is the location of a dipolar source
- Each dipole models the activity of a small brain region

Many parameters $\theta$ to be estimated
(strength only)
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From sources to sensors

- Predicting the sensor data $Y$ from known source parameters $\theta$:
  - requires solving the Maxwell’s equations in a quasi-static regime
  - amounts to solving a well-posed forward problem
  - involves approximations
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EEG is sensitive to both radial and tangential sources

EEG is sensitive to conductivities

MEG is barely sensitive to radial sources

MEG is barely sensitive to conductivities
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**Simple Head Model**

*Concentric spheres*

**Pros:**
- Fast analytic solution

**Cons:**
- Heads are not spherical

**Realistic Head Model**

*Scalp (skin-air boundary)*
*Outer Skull (bone-skin boundary)*
*Inner Skull (CSF-bone boundary)*

**Realistic geometry**

**Cons:**
- Slow approximate numerical solutions
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- Automated extraction of individual meshes

Mattout et al., Comp. Int & Neuro, 2007

From sources to sensors

Template meshes in MNI space

Canonical (individual) mesh
M/EEG source analysis

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- Data features $\mathbf{Y}$ to be fitted/explained
  - Evoked response
  - Induced response
  - Steady-state response

- Accounting for noise $\mathbf{\varepsilon}$ in the data
  \[
  \mathbf{Y} = \mathbf{g}(\mathbf{\theta}) + \mathbf{\varepsilon}
  \]

  Gaussian noise
  \[
  p(\mathbf{\varepsilon}) = \mathcal{N}(\mathbf{0}, \mathbf{C}_\mathbf{\varepsilon})
  \]

  Data likelihood
  \[
  p(\mathbf{Y}|\mathbf{\theta}) = \mathcal{N}(\mathbf{g}(\mathbf{\theta}), \mathbf{C}_\mathbf{\varepsilon})
  \]
Bayesian inference

\[
P(\theta | Y, M) = \frac{P(Y | \theta, M) P(\theta | M)}{P(Y | M)}
\]

Generative model \( M \)

\[
p(Y | \theta, M) \quad p(\theta | M)
\]

Evidence

Posterior

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• A Bayesian model for Equivalent Current Dipole (ECD) solutions
  - Enables to put priors on source parameters
  - Enables formal model comparison (e.g. on number of sources or initial conditions)
• **A Bayesian model for Equivalent Current Dipole (ECD) solutions**
  - Enables to put priors on source parameters
  - Enables formal model comparison (e.g. on number of sources or initial conditions)
A Bayesian model for Distributed / Imaging solutions
- Many dipoles with fixed location and orientation
- Dipole strength \( \Rightarrow \) linear model

\[ Y = K \cdot \theta + \varepsilon \]

\[ p(Y|\theta) = N(K \cdot \theta, C_\varepsilon) \]
A Bayesian model for Distributed / Imaging solutions
- Many dipoles with fixed location and orientation
- Dipole strength $\theta$ -> linear model

\[ p(\theta) = N(0, C_\theta) \]

The proba. of a large intensity is small

Setting priors
**M/EEG source analysis**

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**Setting priors**

- **Alternative priors correspond to alternative prior covariance matrices**
  \[ p(\theta) = N(0, C_\theta) \]
  Ndip x Ndip

- **Typical priors**

  - i.i.d or Minimum norm
  - Single dipole
  - Smoothness (like LORETA)
• Alternative priors correspond to alternative prior covariance matrices

\[ p(\theta) = N(0, C_\theta) \]

\( Ndip \times Ndip \)

• More advanced priors

- *fMRI based* (Henson et al., Hum. Brain Map., 2010)
- *Data or Lead-field based* e.g. (Beamformer or MSP) (Mattout et al., NeuroImage, 2005)
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• Multivariate Sparse Priors (MSP)

\[ C_\theta = \lambda_1 \cdot Q_1 + \lambda_2 \cdot Q_2 + \lambda_3 \cdot Q_3 + \cdots + \lambda_n \cdot Q_n \]

Model (Hyper)parameters

Empirical Bayes

Inference (iterative) process

Accuracy
Free Energy
Complexity

Philips et al., NeuroImage, 2005
Mattout et al., NeuroImage, 2006
Friston et al., NeuroImage, 2008
Lopez et al., NeuroImage, 2014
Comparing priors using log-evidence (free energy) \( F \approx p(Y|M) \)

- \( Y \) : observed data
- \( \tilde{\Theta} \) : estimated source intensities
- \( \tilde{Y} \) : predicted data

Explained variance

Free-energy

11% 96% 97% 98%
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Comparing models

• Any assumption (part of model M) can be formally tested on real data using Bayesian model comparison

- Spherical head model
- Realistic surfacic model (BEM)

- No evidence in favor of individual vs. Inverse-norm mesh
- Evidence in favor of BEM head model
- Evidence in favor of high + fixed vs. low + free

Mattout et al., NeuroImage, 2007
Henson et al., NeuroImage, 2007
Henson et al., NeuroImage, 2009

Biophysics

Anatomy

Sources
Mesh resolution (High / Low)
Dipole orientation (fixed / free)
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• MSP based source reconstruction for a single subject

\[ \eta, \Omega \]

\[ Q_1, Q_2, \ldots, \]

\[ C_\theta \]

\[ \lambda_i \]

\[ \theta \]

\[ K \]

\[ Y \]

\[ \varepsilon \]

\[ Q_1^\varepsilon, Q_2^\varepsilon, \ldots, \]

\[ C_\varepsilon \]

Friston et al., NeuroImage, 2008
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- **MSP based source reconstruction for multiple subjects**

A two-step procedure:
- Estimating the group prior variance
- Estimating the individual source intensities

Litvak and Friston, NeuroImage, 2008
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• MSP based source reconstruction for **multimodal data**

Henson et al., NeuroImage, 2011
Gareth Barnes
Anne Caclin
Jean Daunizeau
Guillaume Flandin
Karl Friston
Rik Henson
Stefan Kiebel
Françoise Lecaignard
Vladimir Litvak
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