Westfälische
Wilhelms-Universität
Münster

Hierarchical Bayesian Approaches to the Inverse Problem of EEG/MEG Current Density Reconstruction

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Overview

Diploma thesis in applied mathematics.

Cooperation between:

FACHBEREICH 10
MATHEMATIK UND
INFORMATIK

Workgroup Imaging
Prof. Dr. Martin Burger
Institute for Computational
and Applied Mathematics

IBB
Institute for
Biomagnetism and
Biosignalanalysis

Workgroup Methods in
Bioelectromagnetism
PD. Dr. Carsten Wolters
Institute for Biomagnetism
and Biosignalanalysis

Classification/Outline

"Hierarchical Bayesian Approaches to the Inverse Problem of EEG/MEG Current Density Reconstruction"

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- EEG/MEG current density reconstruction: The application, a biomedical imaging modality used in brain research/clinical diagnosis.

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- EEG/MEG current density reconstruction: The application, a biomedical imaging modality used in brain research/clinical diagnosis.
- Inverse problems: The mathematical field of research, rooted in applied functional analysis and statistical inference.

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"Hierarchical Bayesian Approaches to the Inverse Problem of EEG/MEG Current Density Reconstruction"

- EEG/MEG current density reconstruction: The application, a biomedical imaging modality used in brain research/clinical diagnosis.
- Inverse problems: The mathematical field of research, rooted in applied functional analysis and statistical inference.
- Hierarchical Bayesian approaches: Statistical inference framework suited for the inverse problem of EEG/MEG.

Classification/Outline

Also important (and most work) but not covered by this talk:

- Mathematical modeling of bioelectromagnetism.
- Finite element modeling for EEG/MEG.
- Algorithms and implementation.

Focus on introduction to *topics* and *concepts*, not on *formulas*...

Electroencephalography (EEG) and Magnetoencephalography (MEG)

Aim: Reconstruction of brain activity by non-invasive measurement of induced electromagnetic fields outside of the skull.

Source reconstruction in EEG/MEG: An inverse problem

Reconstruction of brain activity by non-invasive measurement of induced electromagnetic fields outside of the skull.

$\Longrightarrow$ Typical inverse problem

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What's an inverse problem in general?

Setting:

- Interesting quantity; Not directly observable.
- Interesting quantity is cause for derived quantity which is observable.
- Relation given by PDEs:
  - Interesting quantity: Source term or parameter.
  - Derived quantity: Function of the solution.
- Direct problem: Calculate the observable result of a given cause.
- Inverse problem: Reconstruct the cause that led to an observed result.
  (More general: Infer information about interesting quantity based on observation and computational model)

Characteristic features of inverse problems

Hadamard's definition of *well-posed* problems:

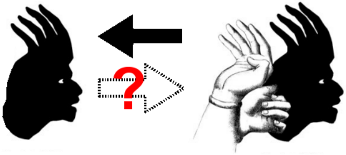
1. A solution exists.
2. The solution is unique.
3. The solution depends continuously on the data.

If one of the conditions does not hold, the problem is called ill-posed.

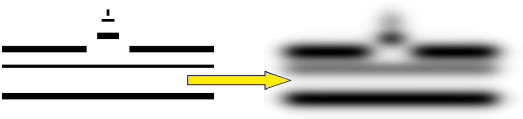
Inverse problems are typically ill-posed.

Jacques Salomon Hadamard
(1865-1963)

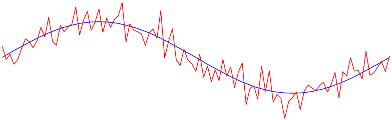
What about the inverse problem of EEG/MEG?



- (Presumably) under-determined



- Severely ill-conditioned



- Low SNRs

Summary: The problem is severely ill-posed:

Measurements alone are insufficient and unsuitable to determine solution.

$\Longrightarrow$ Incorporation of a-priori information about the solution in an explicit or implicit way:

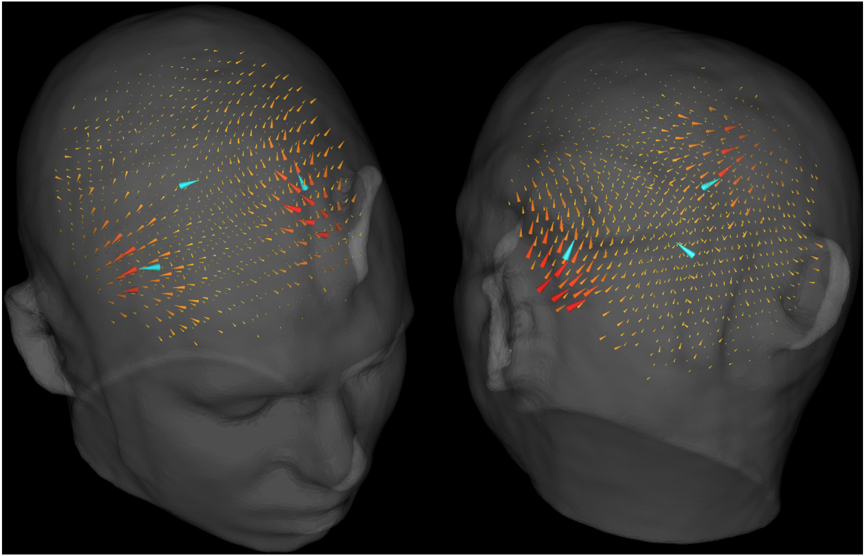
- Knowledge about general/specific brain activity?
- Mathematical formulation?
- Computational implementation?

$\Longrightarrow$ Variety of inverse methods for EEG/MEG

Our focus: Hierarchical Bayesian inference for current density reconstruction (CDR)

Current Density Reconstruction

Discretization of an underlying continuous current distribution by large number of current dipoles with fixed location and orientation.



Current Density Reconstruction

Lead-field matrix concept:

- $\mathrm{L} \in \mathbb{R}^{m \times n}$; columns represent measurements at m sensors caused by the n single current dipoles.
- Linear combination of the dipoles is represented by source vector $s \in \mathbb{R}^n$.
- Measurements $b \in \mathbb{R}^m$ caused by s can then be calculated via:

$$b = \mathrm{L}\, s$$

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Infer s from b? Apparently ill-posed problem:

- $n \gg m. \implies b = \mathrm{L}\, s$ is under-determined.
- L inherits the bad condition of the continuous problem.
- Noise $\mathcal{E} \sim \mathcal{N}(0, \sigma^2 \mathrm{Id})$ is added to signal.

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High uncertainty and under-determinateness of a problem?

$\implies$ Account for them explicitly by formulating the problem in a statistical framework

Strategy of Bayesian Inference

1. Make stochastic model for the relation between parameters, data and noise.

- $B = \mathrm{L}\, s + \mathcal{E}$ b is now random vaiable B
- Compute probability density of B given s: $p_{like}(b|s)$ (likelihood)

Strategy of Bayesian Inference

1. Make stochastic model for the relation between parameters, data and noise: $p_{like}(b|s)$.

2. Supplement information given by the data by a-priori information about the parameters of interest. $\longrightarrow$ Bayesian modeling:

- s is considered to be a random variable itself ($s \to S$).
- Its distribution $p_{prior}(s)$ reflects a-priori assumptions/knowledge.
- Task of the prior: Render the estimation problem well-posed.

Strategy of Bayesian Inference

1. Make stochastic model for the relation between parameters, data and noise: $p_{like}(b|s)$.

2. Supplement information given by the data by a-priori information about the parameters of interest: $p_{prior}(s)$

3. Merge information before the measurement (prior) with the information gained after performing the measurement (likelihood) by Bayes rule:

$$p_{post}(s|b) = \frac{p_{like}(b|s)p_{prior}(s)}{p(b)}$$

- Conditional distribution of S given B is called posterior distribution.
- Represents all information on S given the realization of $B = b$.
- Complete solution to the inverse problem in Bayesian Inference

Strategy of Bayesian Inference

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4. Exploit a-posteriori information by infering point estimates:
   1. *Maximum a-posteriori-estimate (MAP)*: $\hat{s}_{\mathrm{MAP}} := \operatorname{argmax}_{s \in \mathbb{R}^n} \; p_{post}(s|b)$.
      Practically: High-dimensional optimization problem.
   2. *Conditional mean-estimate (CM)*: $\hat{s}_{\mathrm{CM}} := \mathbb{E}\left[s|b\right] = \int_{\mathbb{R}^n} s \; p_{post}(s|b) ds$.
      Practically: High-dimensional integration problem.

Empirical Bayesian Inference

Problem: Brain activity is too complex (or our knowledge is too limited) to be captured in a fixed but sufficiently informative prior.

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Sounds like...

...but can be formulated into a consistent, statistical reasoning by adding a new dimension of inference: Hyperparameters and hyperpriors.

Top-down construction scheme $\rightarrow$ Hierarchical Bayesian modeling (HBM).

Hierarchical Bayesian Modeling (HBM)

Overview:

- Current trend in all areas of Bayesian inference.
- Flexible framework for the construction and automatic, data-driven reduction of complex models.
- Different levels for the embedding of qualitative or quantitative a-priori information.
- Comprises many former methods and offers new ways of inference.

Example: Hierarchical Bayesian Modeling of Focal Activity

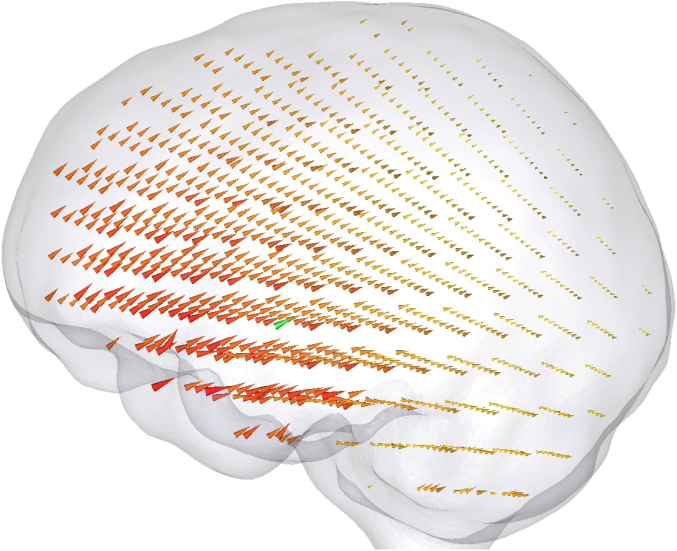
Wanted: A prior promoting focal source activity.

First try:

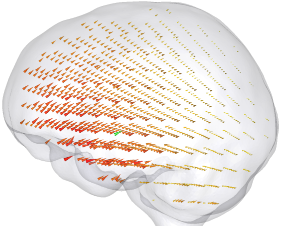
- Take Gaussian prior with zero mean and covariance $\Sigma_s = \gamma \cdot \mathrm{Id}, \quad \gamma > 0$ (*Minimum norm estimation*).
- Compute MAP or CM estimate (equal)!

Example: Hierarchical Bayesian Modeling of Focal Activity

First try: NOT a focal reconstruction.



Example: Hierarchical Bayesian Modeling of Focal Activity



What went wrong?

- Gaussian variables = characteristic scale given by variance. (not *scale invariant*)
- All sources have variance $\gamma \Longrightarrow$ Similar amplitudes are likely.
- $\Longrightarrow$ Focal activity is very unlikely.

Example: Hierarchical Bayesian Modeling of Focal Activity

Idea:

- Let sources at single locations i have different variances γ_i.
- Let the data determine $\gamma_i \Longrightarrow$ New level of inference!
    - $\boldsymbol{\gamma} = (\gamma_i)_i$ are called hyperparameters.
    - Bayesian inference: $\boldsymbol{\gamma}$ are random variables as well.
    - Their prior distribution $p_{hyper}(\boldsymbol{\gamma})$ is called hyperprior.

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- Encode focality assumption into hyperprior:
  - Focality: Nearby sources should a-priori not be mutually dependent.
  - Focality: Most sources silent, few with large amplitude;
  - No location preference for activity should be given a priori.

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  - γ_i should be stochastically independent.
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  - γ_i should be stochastically independent.
  - Sparsity inducing hyperprior, e.g., inverse gamma distribution.
  - No location preference for activity should be given a priori.

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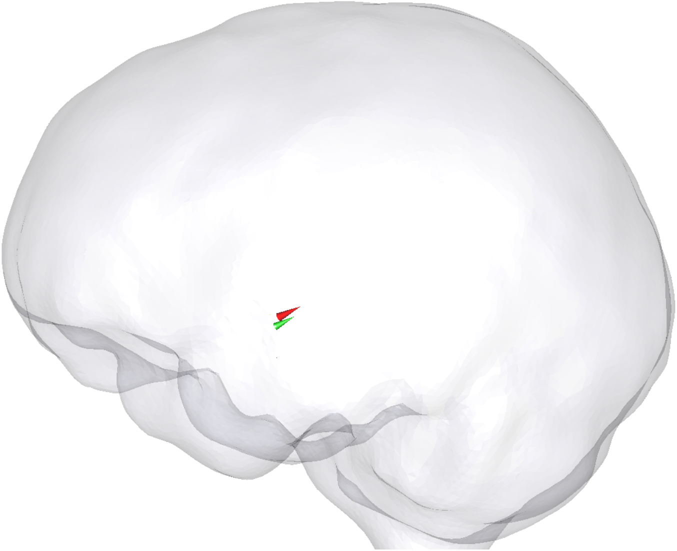
- Encode focality assumption into hyperprior:
  - γ_i should be stochastically independent.
  - Sparsity inducing hyperprior, e.g., inverse gamma distribution.
  - γ_i should be equally distributed.

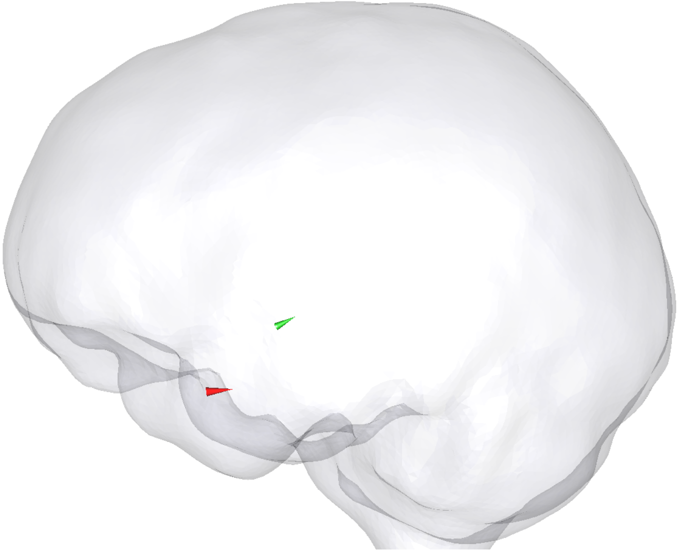
Example: Hierarchical Bayesian Modeling of Focal Activity

Full-CM estimate computed via blocked Gibbs MCMC integration, see Calvetti et al., 2009.



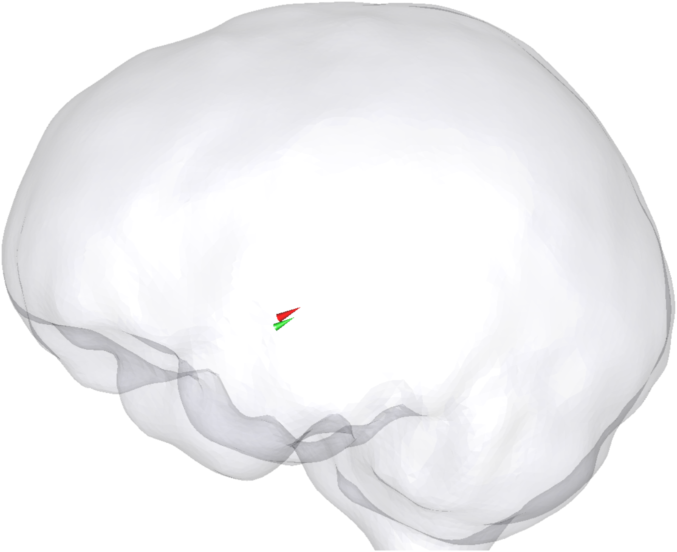
Example: Hierarchical Bayesian Modeling of Focal Activity

Full-MAP estimate computed as in Calvetti et al., 2009.



Example: Hierarchical Bayesian Modeling of Focal Activity

Full-MAP estimate proposed by us (higher posterior probability than former one).



Studies: Motivation

Tasks for EEG/MEG in presurgical epilepsy diagnosis

- *Focal epilepsy* is believed to originate from networks of focal sources.
- Active in inter-ictal spikes.
- Task 1: Determine number of focal sources (*multi focal epilepsy*?).
- Task 2: Determine location and extend of sources.

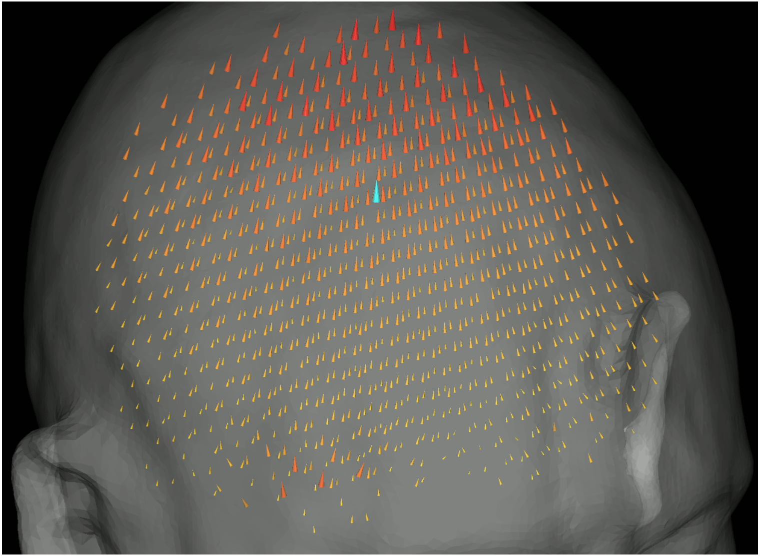
Problems of established inverse methods:

- Depth-Bias: Reconstruction of deeper sources too close to the surface.
- Masking: Near-surface sources “mask“ deep-lying ones.

Can hierarchical Bayesian inference do better?
$\rightarrow$ Systematic examination via simulation studies.

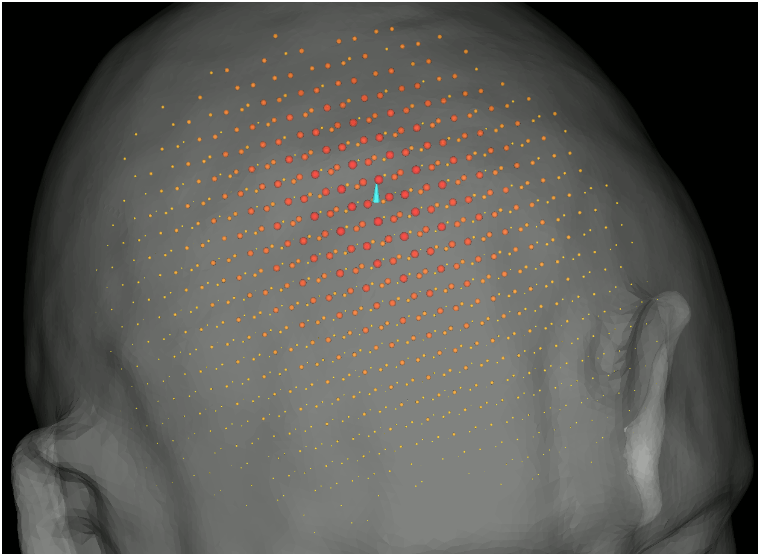
Depth Bias Study: Illustration

One source moving into the depth: Minimum norm estimate (MNE).



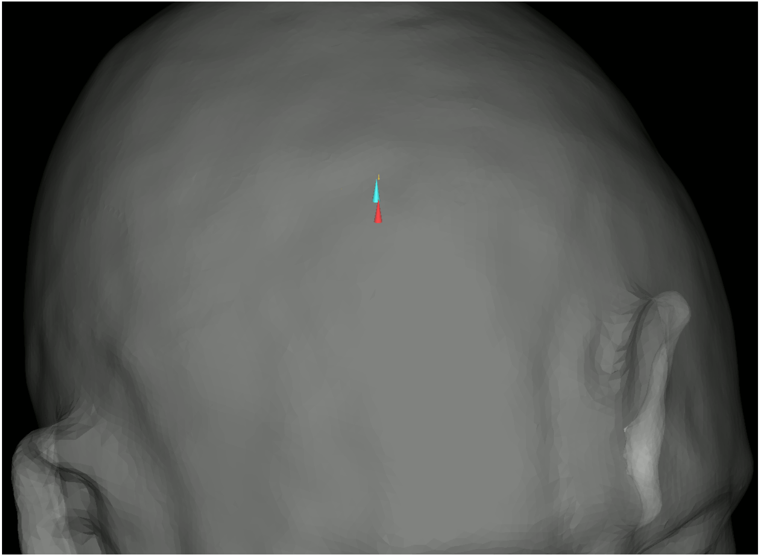
Depth Bias Study: Illustration

One source moving into the depth: sLORETA.



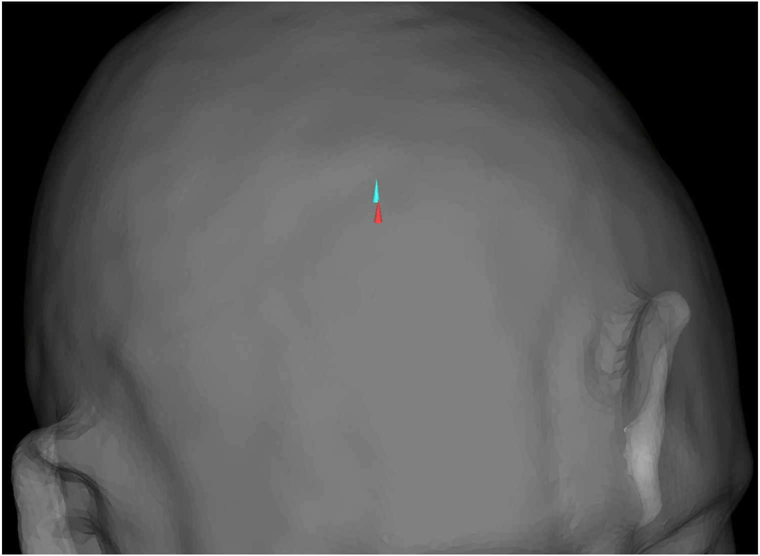
Depth Bias Study: Illustration

One source moving into the depth: CM for specific HBM.



Depth Bias Study: Illustration

One source moving into the depth: MAP for specific HBM.



Depth Bias Study: Results

Study:

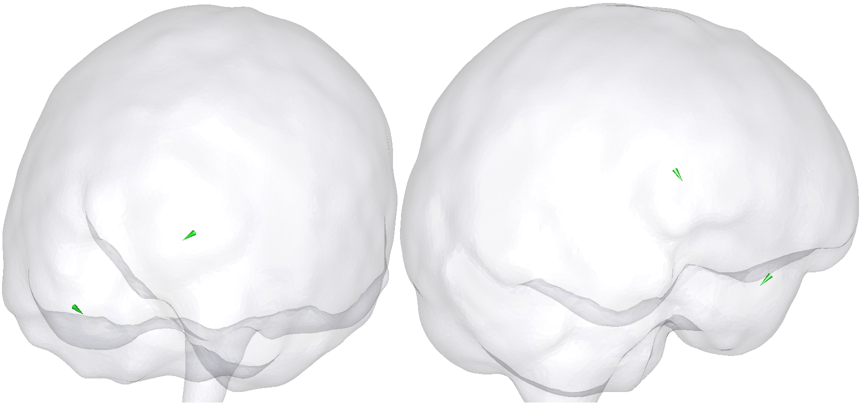
- Systematic study over 1000 dipoles; random location and orientation.
- Noise level 5%.
- Reconstructions were compared using different performance measures.
- Specific examination of depth bias.

Results of CM and MAP estimates for single sources:

- Good performance in all validation measures.
- Seem to have no depth bias.
- Good approximations to the real current density with respect to orientation, amplitude and spatial extend.
- MAP estimate yields best results in every examined aspect.

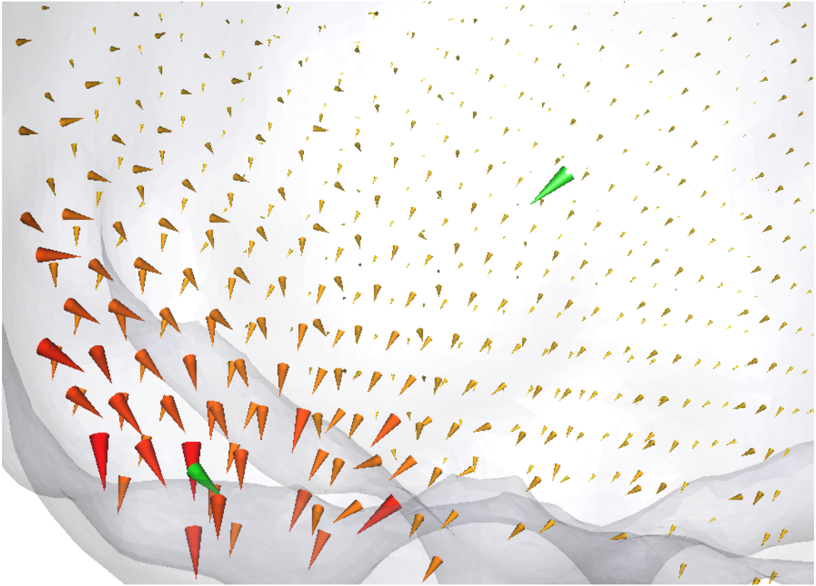
Masking Study: Illustration

Reference sources.



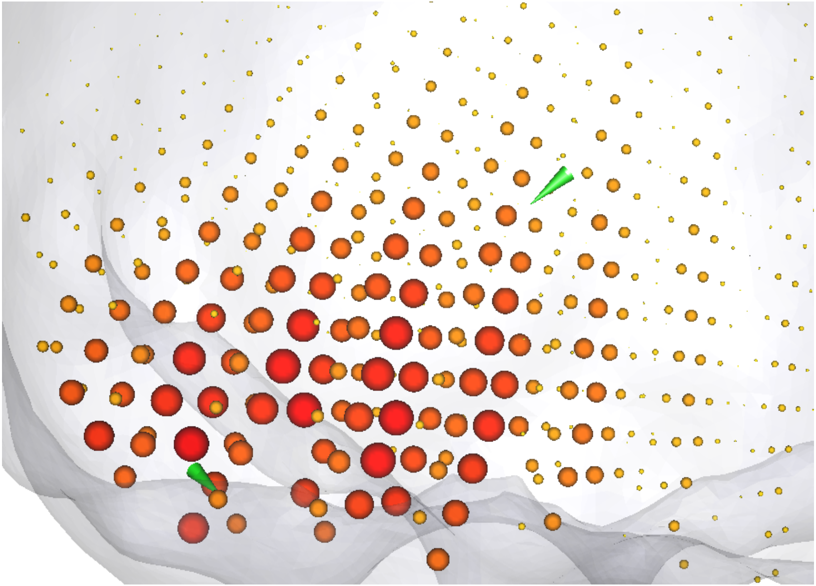
Masking Study: Illustration

MNE result and reference sources



Masking Study: Illustration

sLORETA result and reference sources

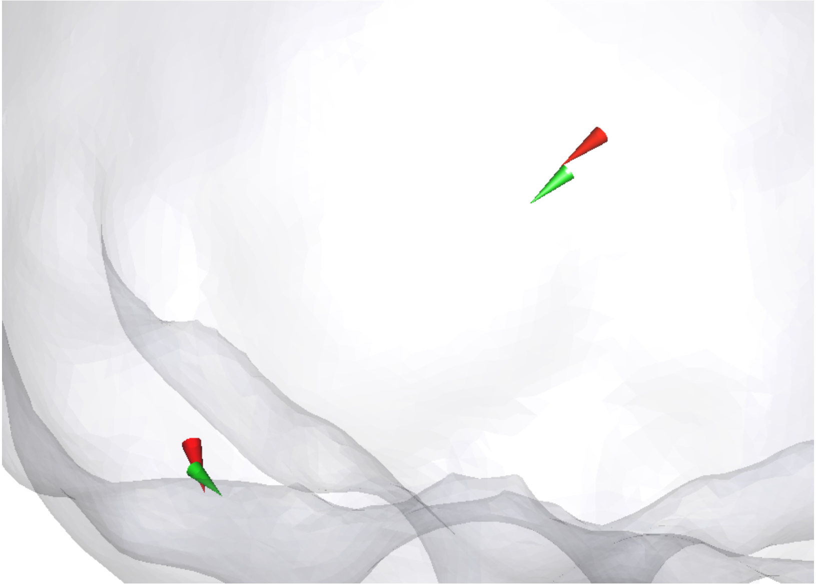


Masking Study: Illustration

CM result and reference sources

Masking Study: Illustration

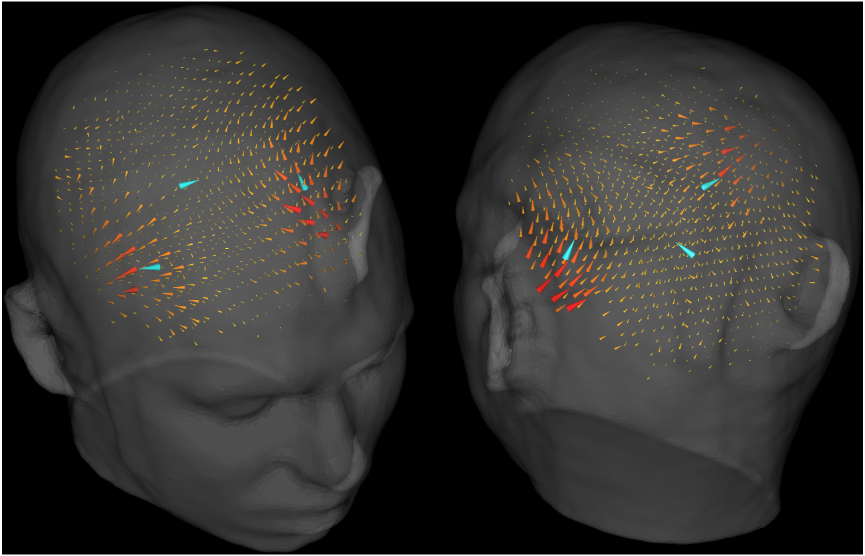
MAP result and reference sources



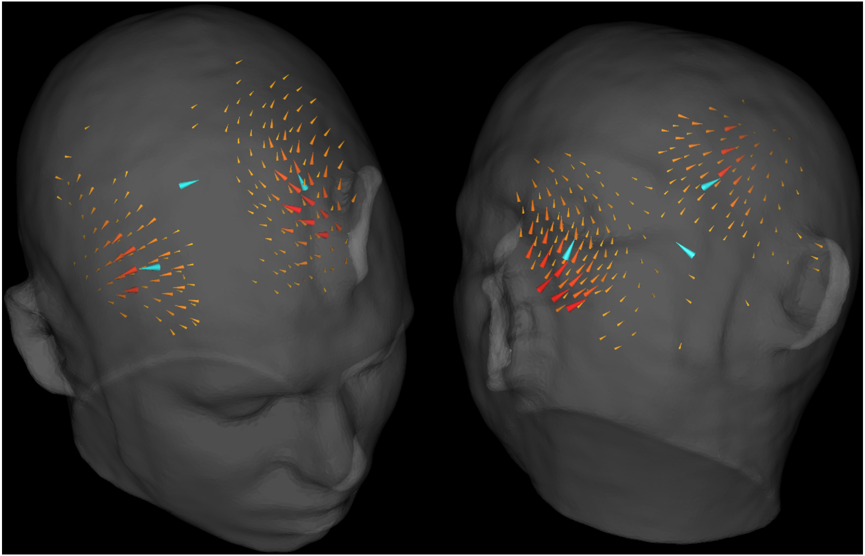
Masking Study: Results

- Systematic study of 1000 source configurations consisting of one near-surface and one deep-lying dipole.
- Noise at a noise level of 5%.
- Reconstructions were compared using a new performance measure based on *optimal transport* (a *Wasserstein metric*).
- HBM based MAP and CM estimation yield best results.

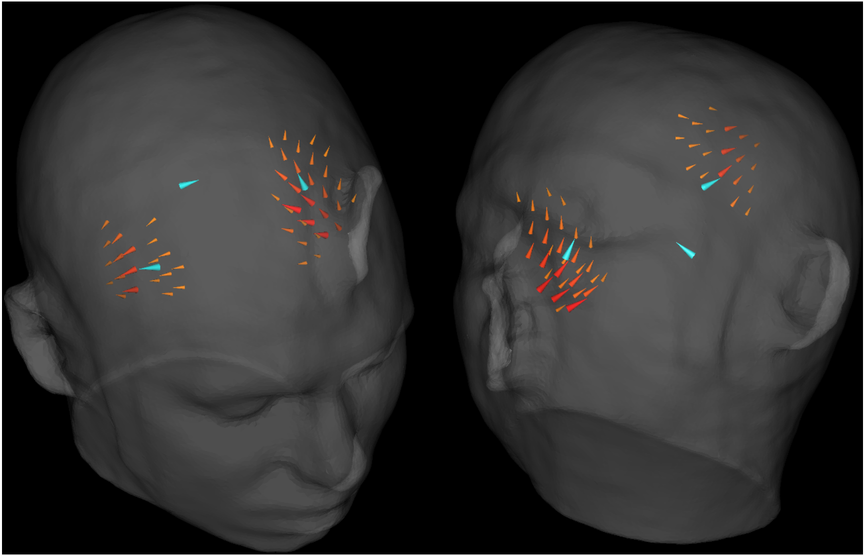
Three Dipoles: MNE



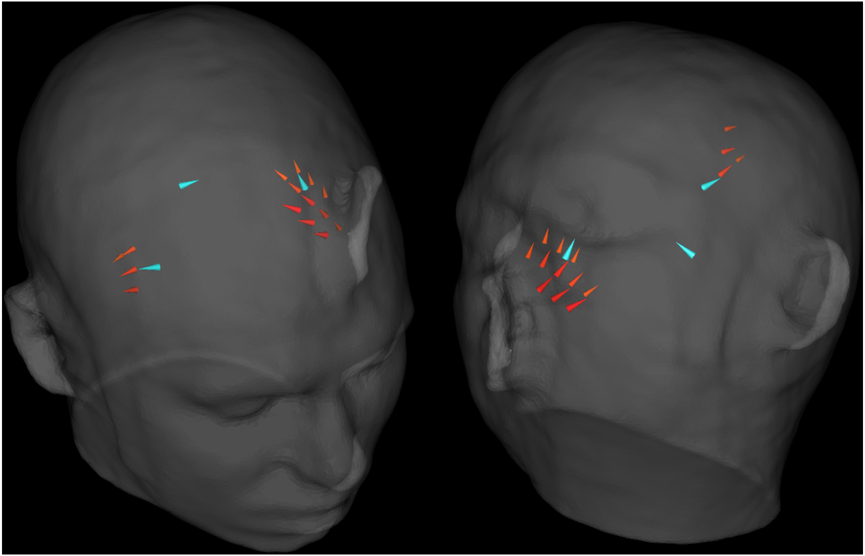
Three Dipoles: MNE, threshold = 30%



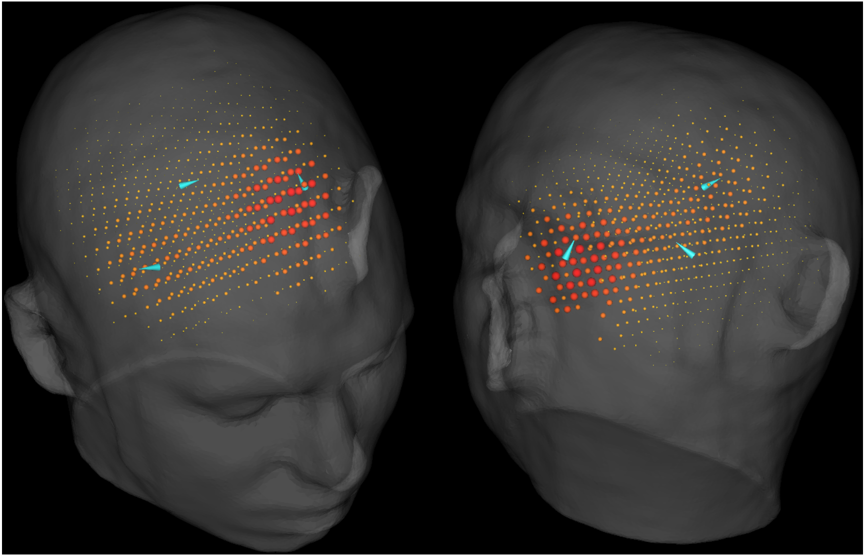
Three Dipoles: MNE, threshold = 50%



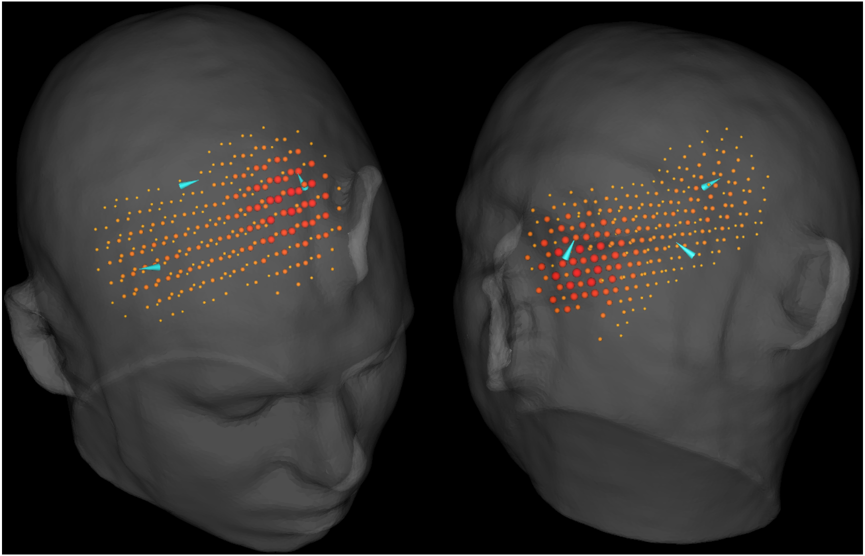
Three Dipoles: MNE, threshold = 70%



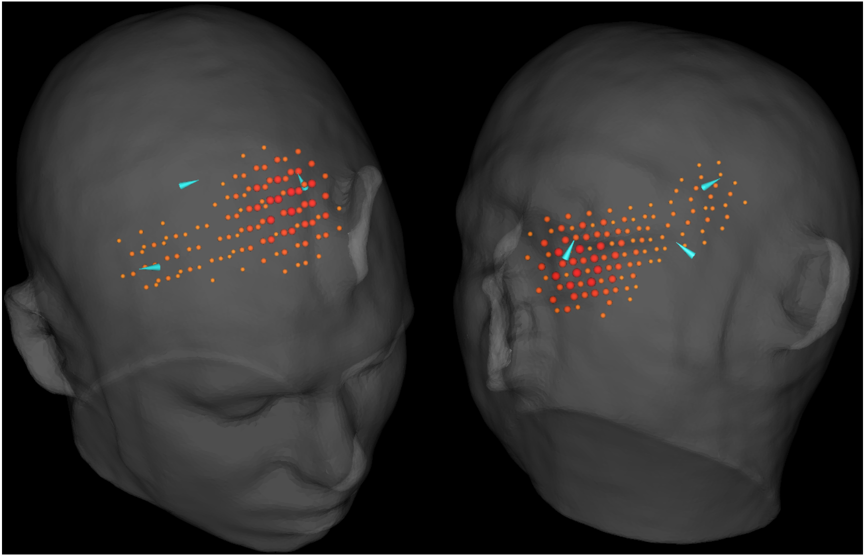
Three Dipoles: sLORETA



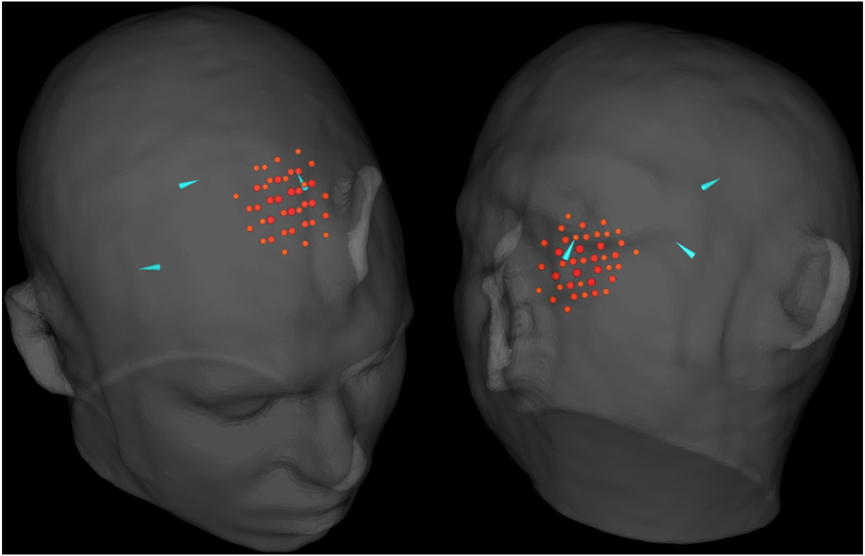
Three Dipoles: sLORETA, threshold = 30%



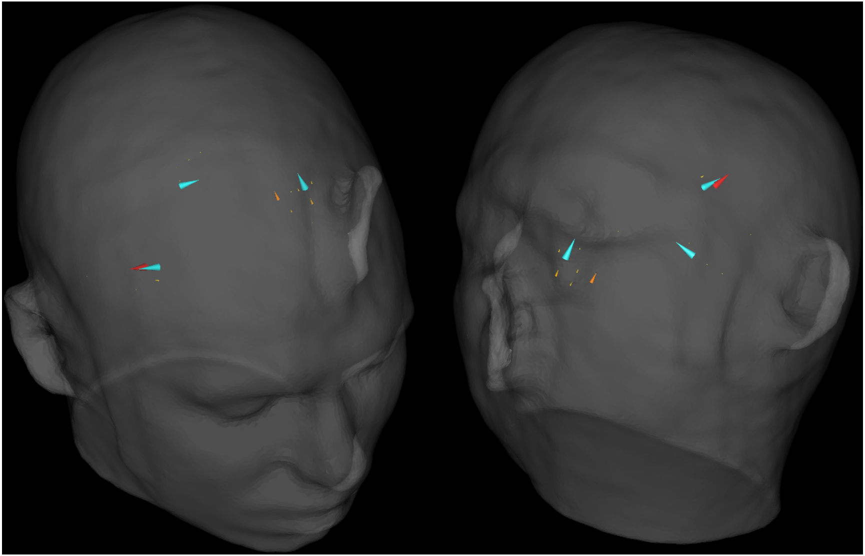
Three Dipoles: sLORETA, threshold = 50%



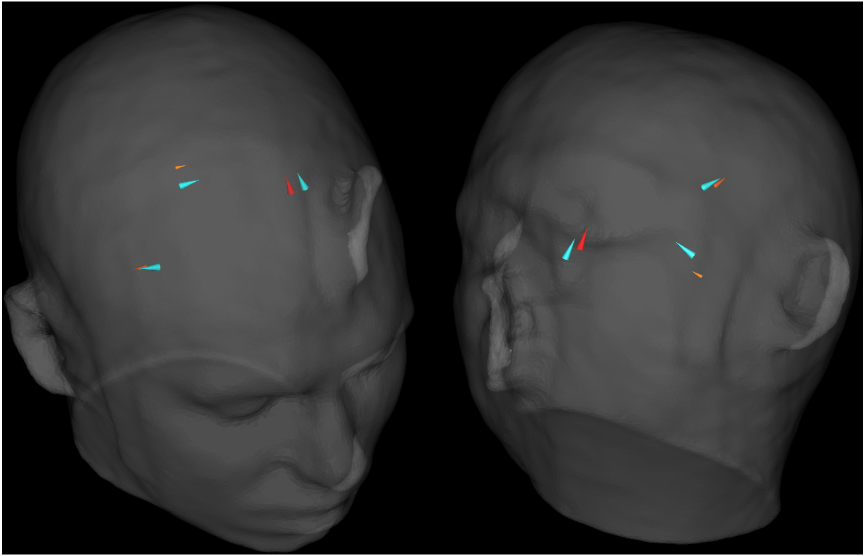
Three Dipoles: sLORETA, threshold = 70%



Three Dipoles: CM



Three Dipoles: MAP



Take Home Messages & Conclusions

General:

- Inverse problems deal with infering information from indirect measurements.
- Inverse problems are ill-posed.
- Bayesian inference is a suitable framework to deal with the ill-posedness.
- Empirical Bayesian inference helps in the absence of proper a-priori information.

Specific results for EEG/MEG

- Hierarchical Bayesian modeling is a promising framework for EEG/MEG.
- Promising results for deep sources (no depth bias).
- Promising results for challenging multiple source scenarios (no masking).

Main References

David Wipf and Srikantan Nagarajan.
A unified Bayesian framework for MEG/EEG source imaging.
Neuroimage, 44(3):947-66, February 2009

Daniela Calvetti, Harri Hakula, Sampsa Pursiainen, and Erkki Somersalo.
Conditionally Gaussian hypermodels for cerebral source localization.
SIAM J. Imaging Sci., 2(3):879-909, 2009

Jari Kaipio and Erkki Somersalo.
Statistical and Computational Inverse Problems,
Volume 160 of Applied Mathematical Sciences. Springer New York, 2005.

Thank you

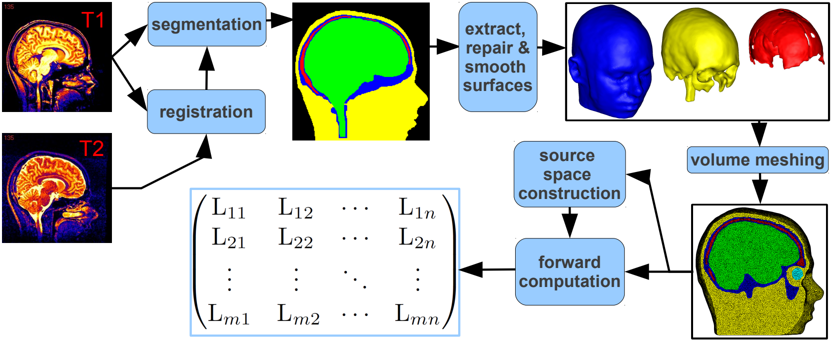
for

your attention!

Software

- Model generation: FSL, CURRY, Tetgen.
- Forward simulation: SimBio.
- Inverse computation: Matlab.
- Volume Visualization: SCIRun.

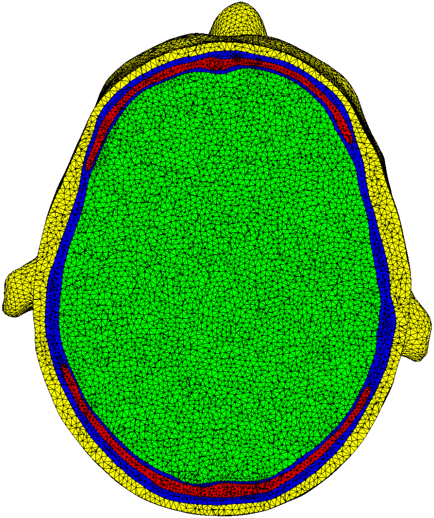
Studies: Head Model Generation Pipeline

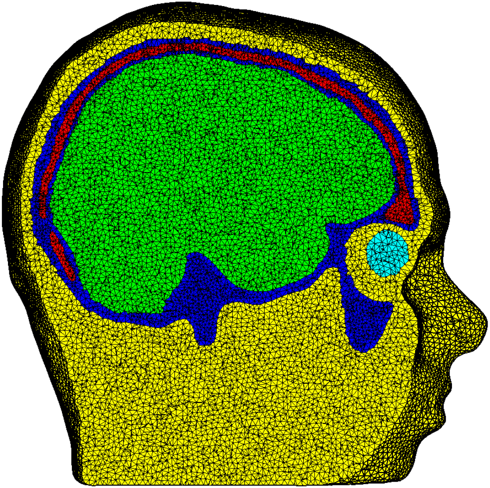


$$\begin{pmatrix} L_{11} & L_{12} & \cdots & L_{1n} \\ L_{21} & L_{22} & \cdots & L_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ L_{m1} & L_{m2} & \cdots & L_{mn} \end{pmatrix}$$

Studies: Tetrahedron Head Model

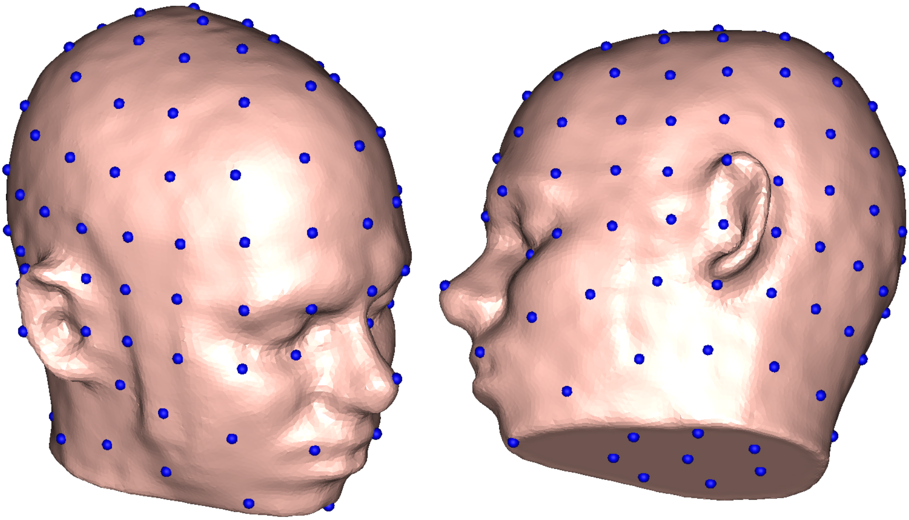
- Compartments: Skin, eyes, skull compacta and skull spongiosa, inner brain.
- 512 394 FEM nodes and 3 176 162 tetrahedra





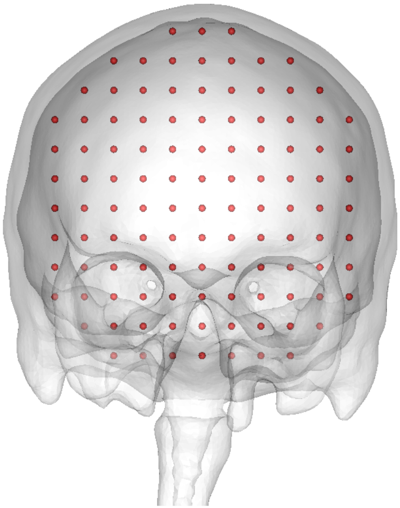
Studies: Sensor Configuration

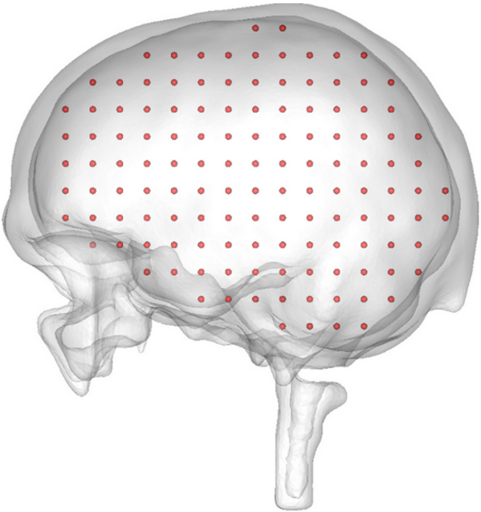
Artificial full-coverage EEG sensor cap (134 sensors).
Reason: Exclude effect of insufficient sensor coverage.



Studies: Source Space Nodes

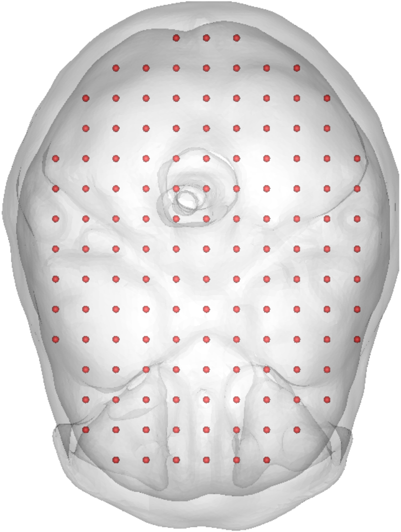
1000 source space nodes based on a regular grid.

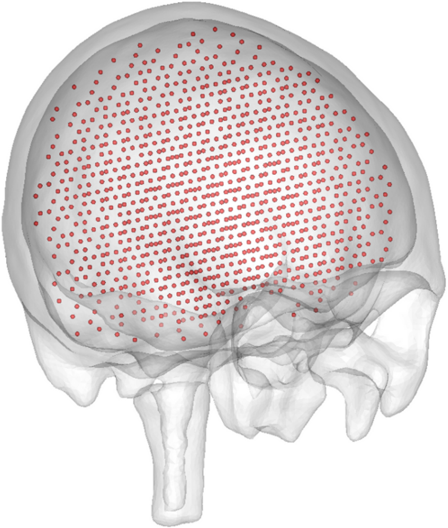




Studies: Source Space Nodes

1000 source space nodes based on a regular grid.



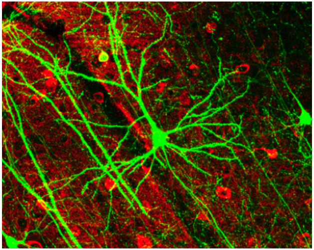


Neural Generators

Signals derive from the net effect of ionic currents flowing in the dendrites of neurons during correlated synaptic transmission.

EEG: Extracellular volume currents produced by postsynaptic potentials.
$\rightarrow$ strongly dependent on tissue's conductivity.

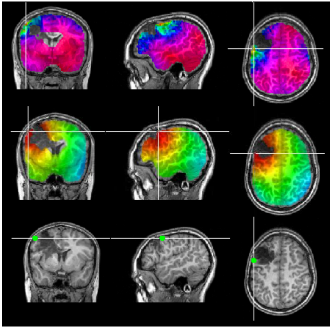
MEG: Intracellular currents associated with these postsynaptic potentials.
$\rightarrow$ less dependent on tissue's conductivity.

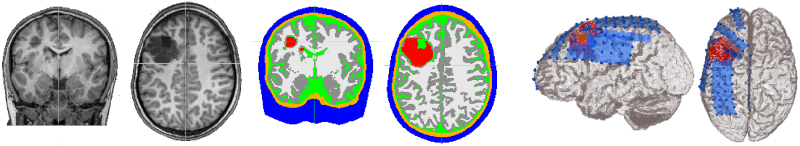


source: Wikimedia Commons

Applications of EEG/MEG

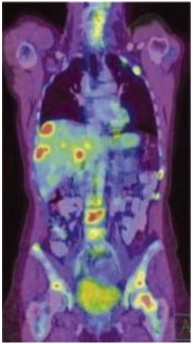
- Main clinical application: Epilepsy, esp. presurgical diagnosis.
- Main scientific applications:
  - Examination tool in cognitive neuroscience.
  - Validation of therapeutic approaches in clinical neuroscience.

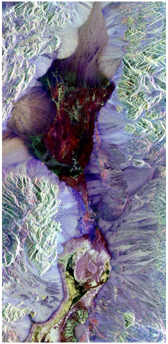


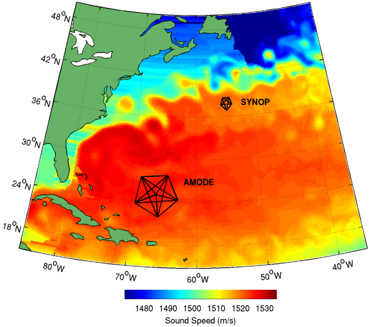


Applications of inverse problems

- Biomedial imaging
- Computer vision, machine learning
- Geophysics, oceanography
- Remote sensing
- Nondestructive testing
- Astronomy







Normal Statistical Inference

Principles of normal statistical inference:

- Make stochastic model for the relation between parameters, data and noise:

$$B = \mathrm{L}\, s + \mathcal{E} \qquad b \text{ is now random vaiable } B$$

- Infer parameters of interest by a statistical inference strategy, e.g., maximum likelihood estimation:
  - Compute probability density of B given $S = s$: $p_{like}(b|s)$ (likelihood).
  - Maximize $p_{like}(b|s)$ w.r.t. s: $\hat{s}_{\mathrm{ML}} := \operatorname{argmax}_{s \in \mathbb{R}^n} \; p_{like}(b|s)$.
  - Leads to $b = \mathrm{L}\, s$ again...

For typical inverse problems:
Doomed to fail, since ill-posed, only accounts for measurement uncertainty.

Example: Gaussian Scale Mixtures for Focal Activity

In formulas:

$$p_{prior}(s|\gamma) \sim \mathcal{N}(0, \Sigma_s(\gamma)), \quad \text{where} \quad \Sigma_s(\gamma) = \operatorname{diag}(\gamma_i \cdot \mathrm{Id}_3, i = 1, \ldots, k)$$

$$p_{hyper}(\gamma) = \prod_{i=1}^{k} p^i_{hyper}(\gamma_i) = \prod_{i=1}^{k} p_{hyper}(\gamma_i) = \prod_{i=1}^{k} \frac{\beta^\alpha}{\Gamma(\alpha)} \gamma_i^{-\alpha-1} \exp\left(-\frac{\beta}{\gamma_i}\right)$$

$\alpha > 0$ and $\beta > 0$ determine *shape* and *scale*, $\Gamma(x)$ denotes the Gamma function.

Joint prior: $\quad p_{pr}(s, \gamma) = p_{prior}(s|\gamma)\, p_{hyper}(\gamma)$

Implicit prior: $\quad p_{pr}(s) = \int p_{prior}(s|\gamma)\, p_{hyper}(\gamma) d\gamma$

$$= \int \mathcal{N}(0, \Sigma_s(\gamma))\, p_{hyper}(\gamma) d\gamma \quad \rightsquigarrow \text{“Gaussian scale mixture”}$$

Example: Gaussian Scale Mixtures for Focal Activity

Posterior, general:

$$p_{post}(s, \gamma | b) \propto p_{like}(b|s)\; p_{prior}(s|\gamma)\; p_{hyper}(\gamma)$$

$$\text{Comparison:} \quad p_{post}(s|b) \propto p_{like}(b|s)\; p_{prior}(s)$$

Posterior, concrete:

$$p_{post}(s, \gamma | b) \propto$$
$$\exp\left(-\frac{1}{2\sigma^2}\|b - L\,s\|_2^2 - \sum_{i=1}^{k}\left(\frac{\frac{1}{2}\|s_{i*}\|^2 + \beta}{\gamma_i} + (\alpha + \tfrac{5}{2})\ln\gamma_i\right)\right)$$

Analytical advantages...

- Energy is quadratic with respect to s
- Factorizes over γ_i's.

and disadvantages...

- Energy is non-convex w.r.t. (s, γ) (posterior is multimodal)

Full-, Semi-, and Approximate Inversion

Two types of parameters $\longrightarrow$ more possible ways of inference.

Full-MAP: Maximize $p_{post}(s, \gamma | b)$ w.r.t. s and γ.

Full-CM: Integrate $p_{post}(s, \gamma | b)$ w.r.t. s and γ.

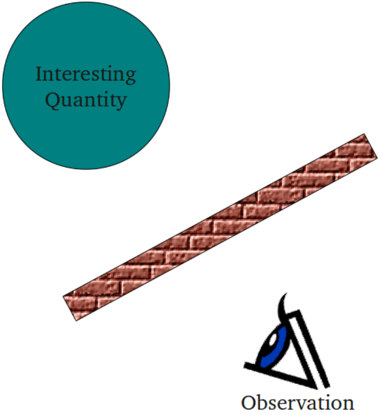
γ-MAP: Integrate $p_{post}(s, \gamma | b)$ w.r.t. s, and maximize over γ, first. Then use $p_{post}(s, \hat{\gamma}(b) | b)$ to infer s. (*Hyperparameter MAP/Empirical Bayes*)

S-MAP: Integrate $p_{post}(s, \gamma | b)$ w.r.t. γ, and maximize over s.

VB: Assume approximative factorization $p_{post}(s, \gamma | b) \approx \hat{p}_{post}(s|b)\, \hat{p}_{post}(\gamma | b)$; Approximate both with distributions that are analytically tractable.

Focus of our work: Fully Bayesian inference.

What's an inverse problem in general?



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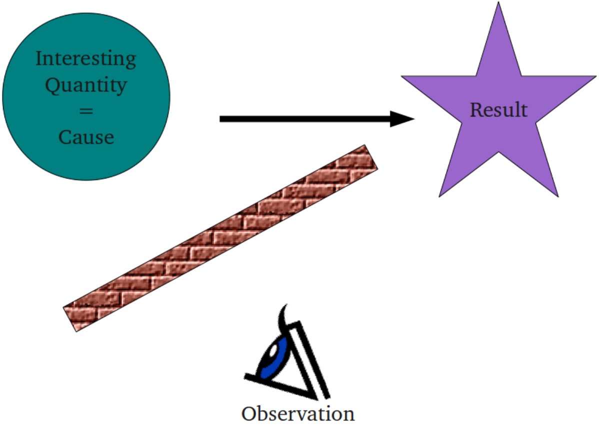

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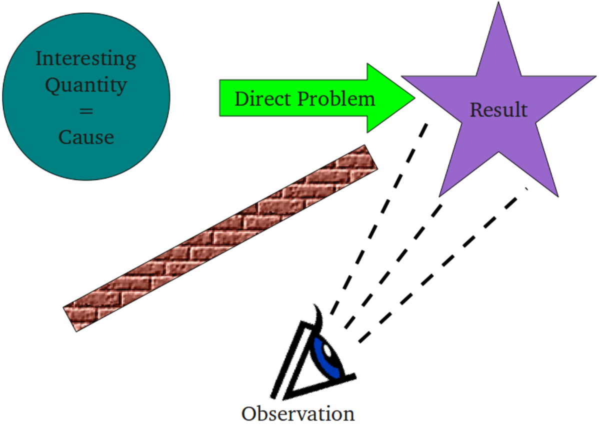
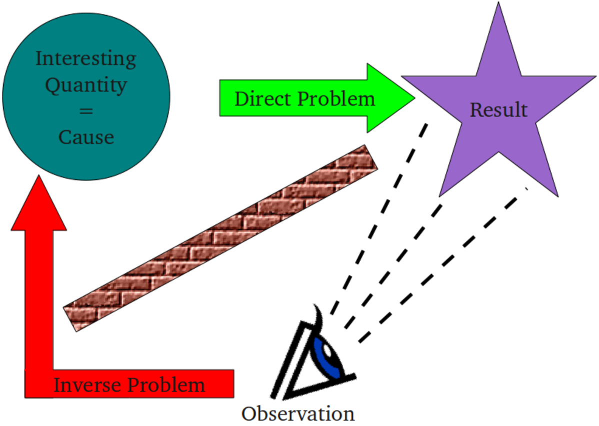


Direct problem: Calculate the observable result of a given cause.

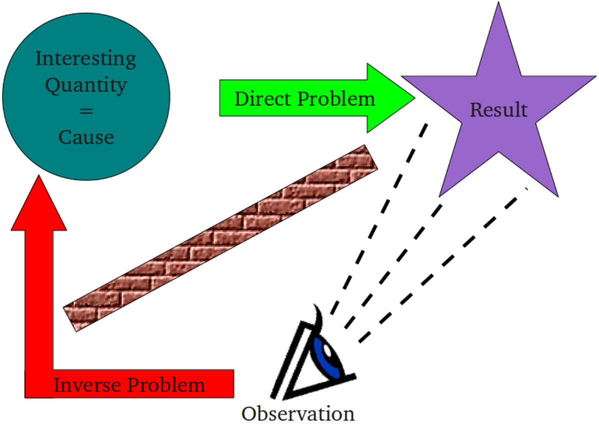
What's an inverse problem in general?



Direct problem: Calculate the observable result of a given cause.

Inverse problem: Reconstruct the cause that led to an observed result.
(More general: Infer information about interesting quantity based on observation and computational model)

What's an inverse problem in general?



Direct problem: Calculate the observable result of a given cause.

Inverse problem: Reconstruct the cause that led to an observed result.
(More general: Infer information about interesting quantity based on observation and computational model)

Solving the inverse problem necessitates modeling and solving the direct problem
($\rightarrow$ *rest of the IBB work group*)