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Hierarchical Fully-Bayesian Inference for EEG and MEG

"Matti Hämäläinen is visiting us - Workshop"



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Diplomarbeit in Mathematik

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

eingereicht von
Felix Lucka

Münster, 10. März, 2011



FACHBEREICH 10
MATHEMATIK UND
INFORMATIK



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NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Hierarchical Bayesian inference for the EEG inverse problem using realistic FE head models: Depth localization and source separation for focal primary currents

Felix Lucka^{a,b,*}, Sampa Porsiaainen^c, Martin Burger^a, Carsten H. Wolters^b

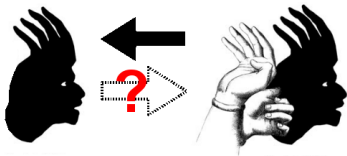
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^c Department of Mathematics, Tampere University of Technology, Finland



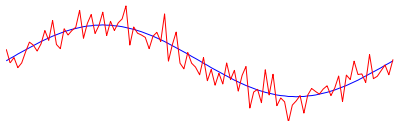
Reconstruction of brain activity by non-invasive measurement of induced electromagnetic fields?



▶ (Presumably) **under-determined**



▶ Severely **ill-conditioned**



▶ Low **SNRs**

Summary: The inverse problem is **severely ill-posed**.

Measurements **alone** are insufficient and unsuitable to determine solution.

⇒ Incorporation of **a-priori information** about the solution in an explicit or implicit way:

- ▶ Knowledge about general/specific brain activity?
- ▶ Integration of multimodal information (fMRI, DW-MRI, PET, NIRS)?
- ▶ Mathematical formulation?
- ▶ Computational implementation?

⇒ Variety of inverse methods for EEG/MEG

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

Current Density Reconstruction

Lead-field matrix concept:

- ▶ $L \in \mathbb{R}^{m \times n}$; 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:

$$b = L s$$

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Infer s from b ? Apparently ill-posed problem:

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

Common approaches:

- ▶ **Variational regularization**
- ▶ **(Hierarchical) Bayesian inference**
- ▶ **Spatial scanning methods/beamforming**

Strategy of Bayesian Inference

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

▶ $B = Ls + \mathcal{E}$ b is now random variable 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. → **Bayesian modeling**:
 - ▶ s is considered to be a random variable itself ($s \rightarrow S$).
 - ▶ 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

1. Make stochastic model for the relation between parameters, data and noise:
 $p_{\text{like}}(b|s)$.
2. Supplement information given by the data by a-priori information about the parameters of interest: $p_{\text{prior}}(s)$
3. Merge information before the measurement (prior) with the information gained after performing the measurement (likelihood) by Bayes rule: $p_{\text{post}}(s|b)$
4. Exploit a-posteriori information by **inferring point estimates**:
 1. *Maximum a-posteriori-estimate (MAP)*: $\hat{s}_{\text{MAP}} := \operatorname{argmax}_{s \in \mathbb{R}^n} p_{\text{post}}(s|b)$.
Practically: High-dimensional **optimization** problem.
 2. *Conditional mean-estimate (CM)*: $\hat{s}_{\text{CM}} := \mathbb{E}[s|b] = \int_{\mathbb{R}^n} s p_{\text{post}}(s|b) ds$.
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.



Empirical Bayesian Inference

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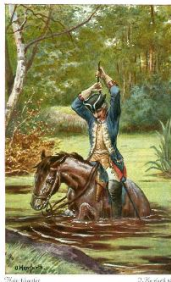
Solution: Let the same data determine the prior used for the inference based on this data!

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

→ **Parametric Empirical Bayesian inference**

Top-down construction scheme → **Hierarchical Bayesian modeling (HBM)**.

Hierarchical Bayesian Modeling (HBM) for CDR: Overview

- ▶ Current trend in all areas of Bayesian inference.
- ▶ Further development **weighted minimum norm** schemes.
- ▶ Flexible framework for the construction of complex models with different levels for the embedding of different **qualitative and quantitative a-priori information**: *Spatial, temporal, multimodal, functional, anatomical, neuro-physiological...*
- ▶ Adds an adaptive, data-driven model reduction element into the estimation.
- ▶ Embeds several heuristic approaches into sound mathematical framework.
- ▶ Comprises many former EEG/MEG methods like MNE, WMNE, LORETA, sLORETA, FOCUSS, MCE,...
- ▶ Offers various new ways of inference: Full-MAP, Full-CM, γ -MAP, S-MAP, VB



David Wipf and Srikantan Nagarajan.

A unified Bayesian framework for MEG/EEG source imaging.

[Neuroimage, 44\(3\):947-66, February 2009](#)

Example: Hierarchical Bayesian Modeling of Focal Activity

Wanted: A prior promoting focal source activity.

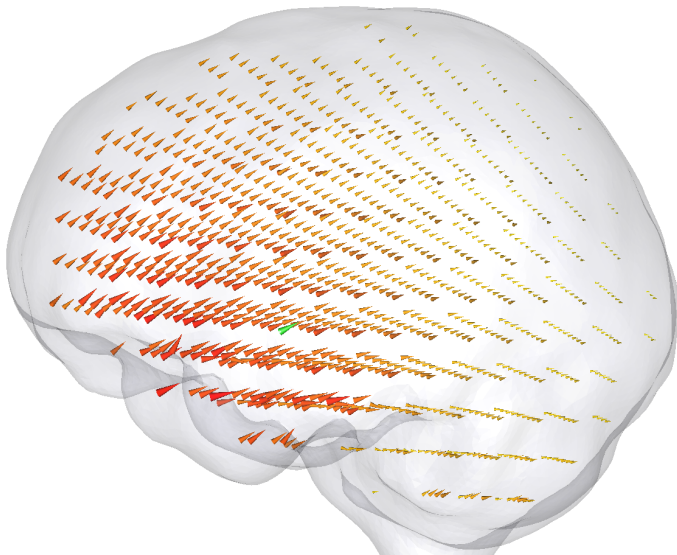
First try:

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

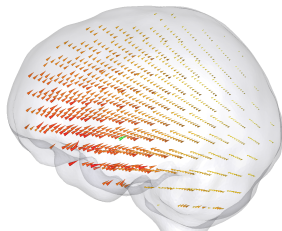
$$\begin{aligned}\hat{s}_{\text{MAP}} &:= \operatorname{argmax}_{s \in \mathbb{R}^n} \left\{ \exp \left(-\frac{1}{2\sigma^2} \|b - Ls\|_2^2 - \frac{1}{2\gamma} \|s\|_2^2 \right) \right\} \\ &= \operatorname{argmin}_{s \in \mathbb{R}^n} \left\{ \|b - Ls\|_2^2 + \frac{\sigma^2}{\gamma} \|s\|_2^2 \right\}\end{aligned}$$

Example: Hierarchical Bayesian Modeling of Focal Activity

First try: NOT a focal reconstruction.



Example: Hierarchical Bayesian Model for Focal Activity



What went wrong?

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

Example: Hierarchical Bayesian Model for Focal Activity

Idea:

- ▶ Let sources at single locations i , $i = 1, \dots, k$ have different variances γ_i .
- ▶ Let the data determine $\gamma_i \implies$ **New level of inference!**
 - ▶ $\gamma = (\gamma_i)_{i=1, \dots, k}$ are called **hyperparameters**.
 - ▶ Bayesian inference: γ are random variables as well.
 - ▶ Their prior distribution $p_{\text{hyper}}(\gamma)$ 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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- ▶ 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 Model for Focal Activity

In formulas:

$$p_{\text{prior}}(s|\gamma) \sim \mathcal{N}(0, \Sigma_s(\gamma)), \quad \text{where } \Sigma_s(\gamma) = \text{diag}(\gamma_i \cdot Id_3, i = 1, \dots, k)$$

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

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

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

Implicit prior:
$$p_{\text{pr}}(s) = \int p_{\text{prior}}(s|\gamma) p_{\text{hyper}}(\gamma) d\gamma$$
$$= \int \mathcal{N}(0, \Sigma_s(\gamma)) p_{\text{hyper}}(\gamma) d\gamma \rightsquigarrow \text{“Gaussian scale mixture”}$$

(actually a Student's t-distribution with $2(\alpha + 1)$ degrees of freedom)

Example: Hierarchical Bayesian Model for Focal Activity

Posterior, general:

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

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

Posterior, concrete:

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

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**)

Excursus: Full-, Semi-, and Approximate Inversion

Two types of parameters \rightarrow 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 .

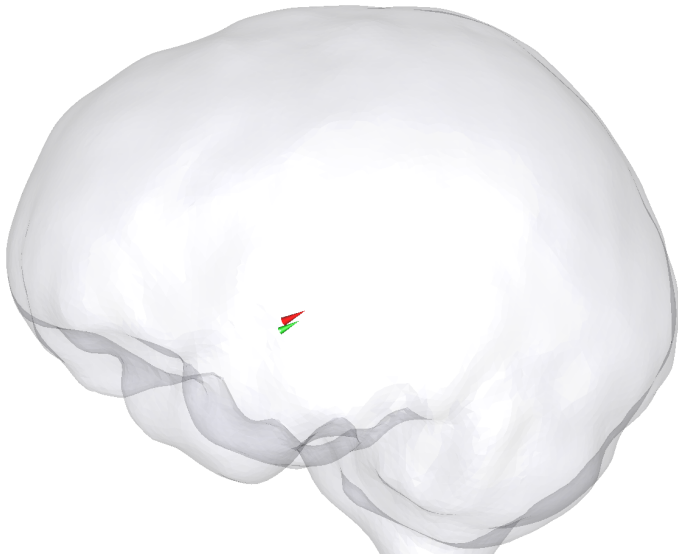
VB: Assume approximative factorization

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

Focus of our work: **Fully Bayesian inference.**

Example: Hierarchical Bayesian Modeling of Focal Activity

Full-MAP estimate



Starting Point for our Studies

- ▶ A specific HBM aims to recover source configurations consisting of **few, focal sources** (introduced in Sato et al., 2004; further examined in Nummenmaa et al., 2007; Wipf and Nagarajan, 2009; Calvetti et al., 2009)
- ▶ Calvetti et al., 2009 found promising first results for certain inference strategies for **deep-lying sources** and the **separation of multiple (focal) sources**.

Limitations of Calvetti et al., 2009 :

- ▶ Specific results were not convincing; reason unclear.
- ▶ No systematic examination; only two source scenarios.
- ▶ Head models insufficient.

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Why are we interested in that?

(rhetorical question to switch to another talk in an elegant way...)

Tasks and Problems for EEG/MEG in Presurgical Epilepsy Diagnosis

EEG/MEG in epileptic focus localization:

- ▶ *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.

Unknown number and spatial extend of sources?

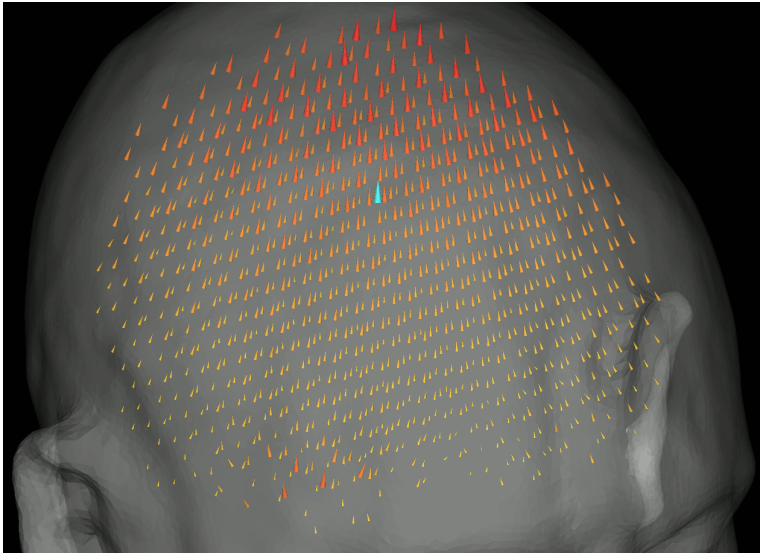
→ **Current density reconstruction (CDR).**

Problems of established CDR methods:

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

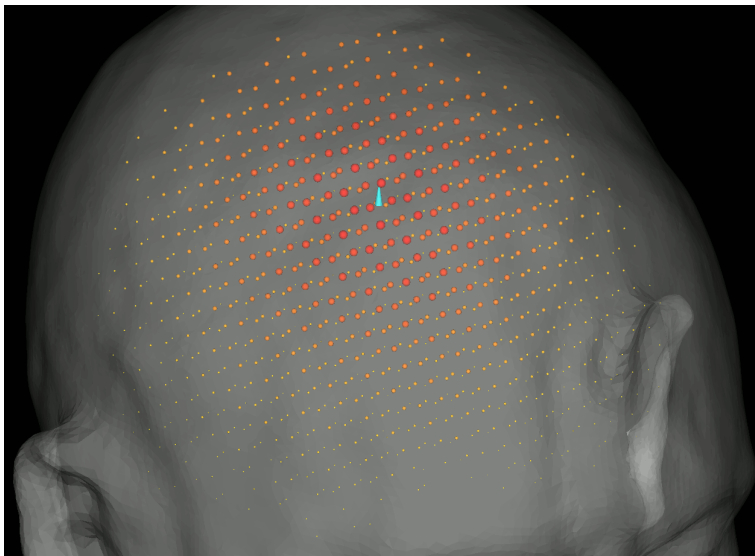
Depth Bias: Illustration

One deep-lying reference source (blue cone) and minimum norm estimate (MNE, Hämäläinen and Ilmoniemi, 1994).



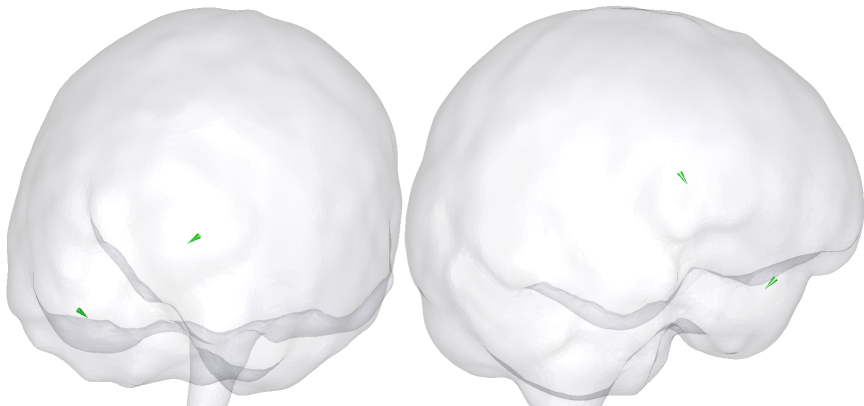
Depth Bias: Illustration

One deep-lying reference source (blue cone) and sLORETA result (Pascual-Marqui, 2002).



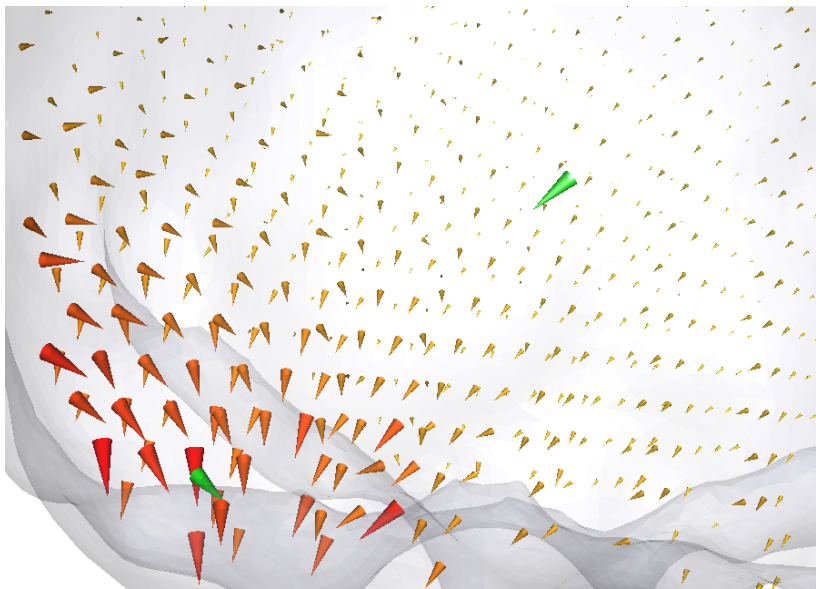
Masking: Illustration

Reference sources.



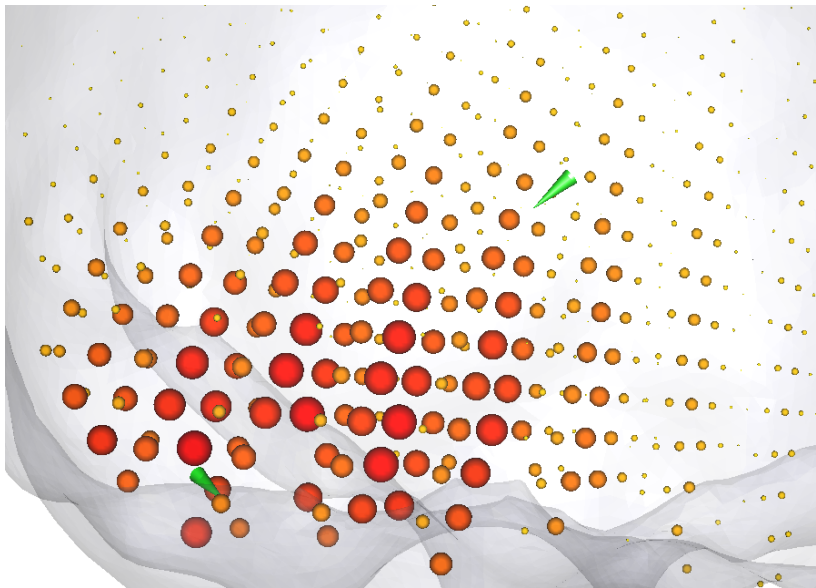
Masking: Illustration

MNE result and reference sources (green cones).



Masking: Illustration

sLORETA result and reference sources (green cones).



Diploma Thesis and Neuroimage Paper (EEG only!)

Key question

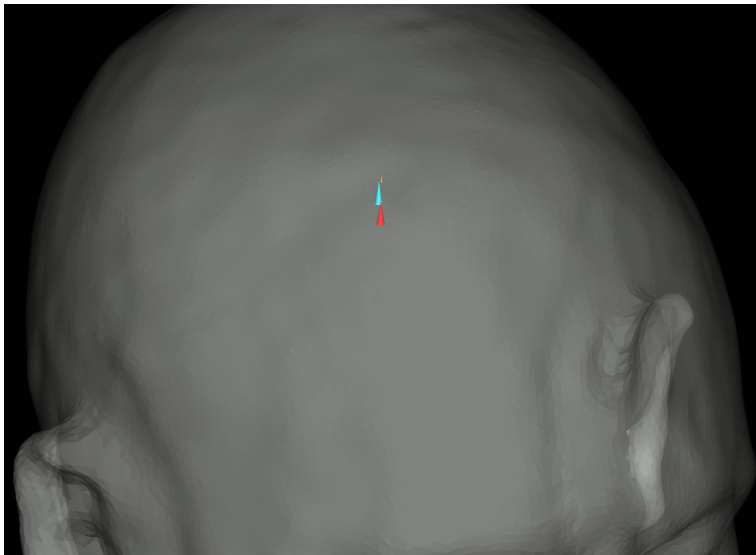
Can Full-MAP and Full-CM for HBM overcome the limitations (depth-bias, masking) of established CDR methods?

Work program:

- ▶ Implementation of Full-MAP and Full-CM inference for HBM with **realistic, high resolution Finite Element (FE) head models**.
- ▶ Propose **own algorithms** for Full-MAP estimation.
- ▶ Introduction of suitable **performance measures for validation** of simulation studies.
- ▶ **Systematic examination** of performance concerning depth-bias and masking in **simulation studies**.

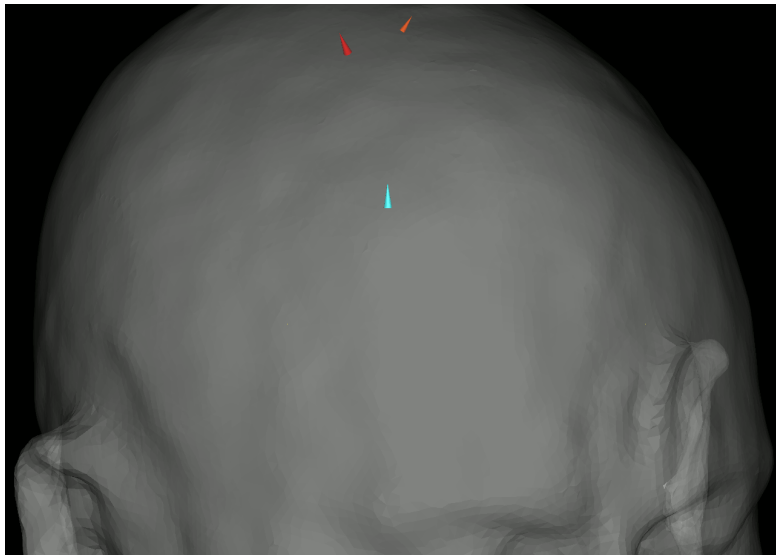
Results Depth Bias: Illustration

One deep-lying reference source (blue cone) and Full-CM result.



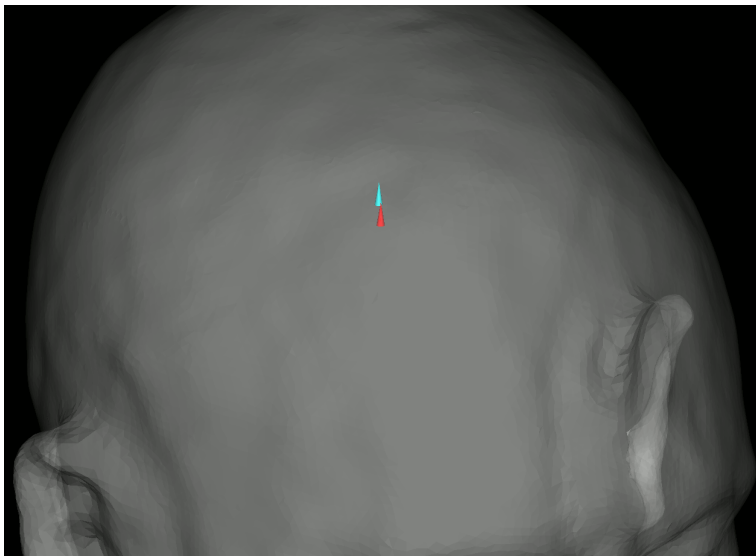
Results Depth Bias: Illustration

One deep-lying reference source (blue cone) and Full-MAP result proposed by Calvetti et al., 2009.



Results Depth Bias: Illustration

One deep-lying reference source (blue cone) and Full-MAP result proposed by us.



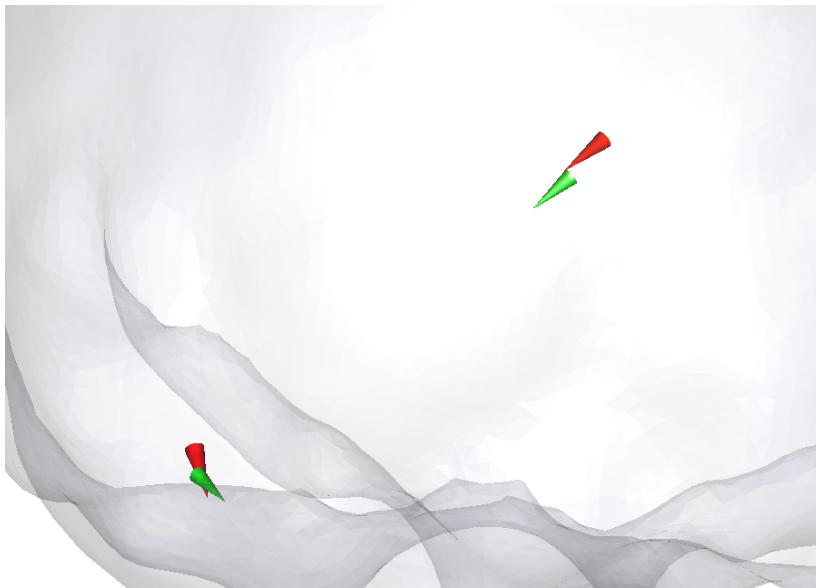
Results Masking: Illustration

Full-CM result and reference sources (green cones).



Results Masking: Illustration

Full-MAP result (by our algorithm) and reference sources (green cones).



Systematic Studies: Summary

Study 1 (depth-bias):

- ▶ Reconstruction of single 1000 dipoles; random location and orientation.
- ▶ Reconstructions were compared using different performance measures.
- ▶ Specific examination of depth bias.

Study 2 (masking):


- ▶ Reconstruction of 1000 source configurations consisting of one near-surface and one deep-lying dipole.
- ▶ Reconstructions were compared using a performance measure based on *optimal transport* (called *earth mover's distance*, a *Wasserstein metric*).

Systematic Studies: Summary

Results for Full-MAP and Full-CM estimation:

- ▶ Good performance in all validation measures.
- ▶ No depth bias.
- ▶ Good results w.r.t. orientation, amplitude and spatial extend.
- ▶ Full-MAP estimate (by our algorithm): Best results in every aspect examined.

Full results:

-  Felix Lucka., Sampsa Pursiainen, Martin Burger, Carsten H. Wolters. 2012. Hierarchical Bayesian Inference for the EEG Inverse Problem using Realistic FE Head Models: Depth Localization and Source Separation for Focal Primary Currents. [Neuroimage 61\(4\), 1364-1382.](#)



Conclusions, Diploma Thesis and Neuroimage paper

Key question

Can Full-MAP and Full-CM for HBM overcome the limitations (depth-bias, masking) of established CDR methods?

Conclusions, Diploma Thesis and Neuroimage paper

Key question

Can Full-MAP and Full-CM for HBM overcome the limitations (depth-bias, masking) of established CDR methods?

Results

- ▶ Hierarchical Bayesian modeling used with realistic head modeling is a promising framework for EEG CDR.
- ▶ Promising results for deep sources (no depth bias).
- ▶ Promising results for challenging multiple source scenarios (no masking).

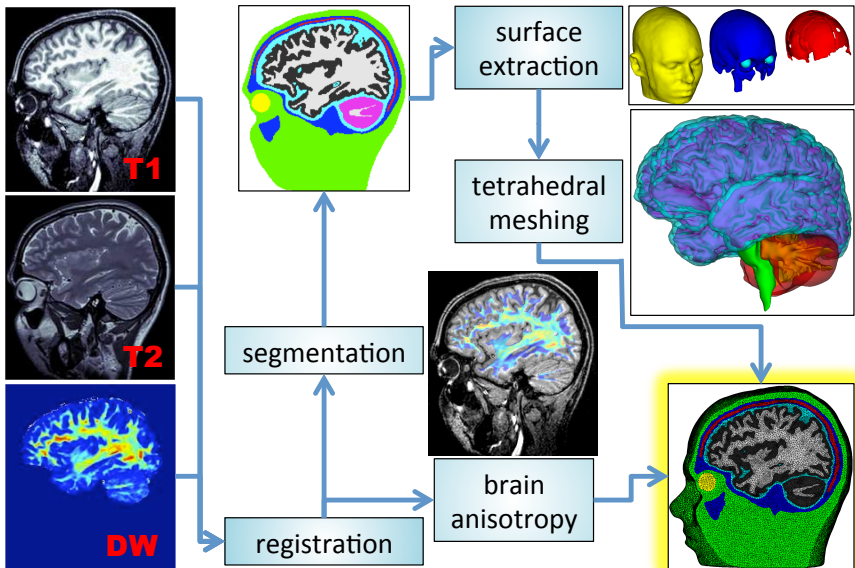
★ A promising tool for the analysis of neurophysiological data. ★



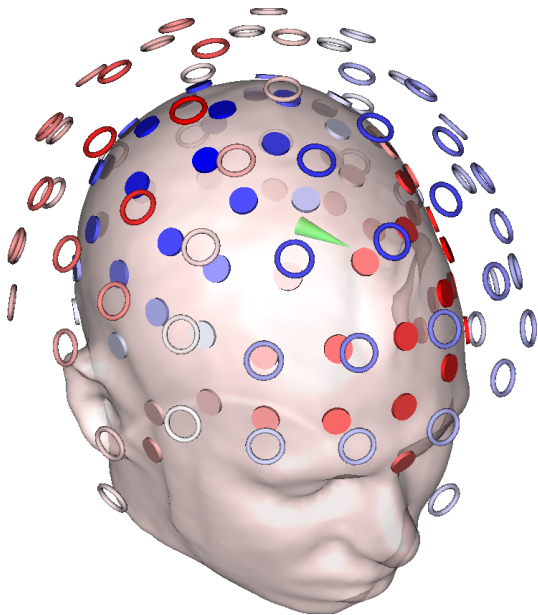
We addressed two questions that were posed in the outlook of the paper:

- ▶ **EEG vs. MEG and EEG/MEG combination (EMEG):**
 - ▶ Do our findings also apply for MEG?
 - ▶ Previously (e.g., Molins et al., 2008), the differences between EEG and MEG have mainly been examined by established inverse methods. How are things for fully-Bayesian inference for HBM?
- ▶ **Realistic Head Model:** Formerly, we used a simplified head model with a homogenous inner brain (to facilitate the interpretation of the results). Especially for EEG/MEG combination, the use of a realistic, individual and anisotropic head model is mandatory.

Model Setup: Modeling Pipeline



Model Setup: Sensor Configuration



Simulation Studies

Inverse Methods:

- ▶ Three fully-Bayesian HBM methods:
 - ▶ Full-MAP estimates
 - ▶ Full-CM estimates
 - ▶ Full-NM (Near-Mean) estimates
- ▶ Minimum norm estimates (MNE) with different weightings (WMNE).
- ▶ sLORETA

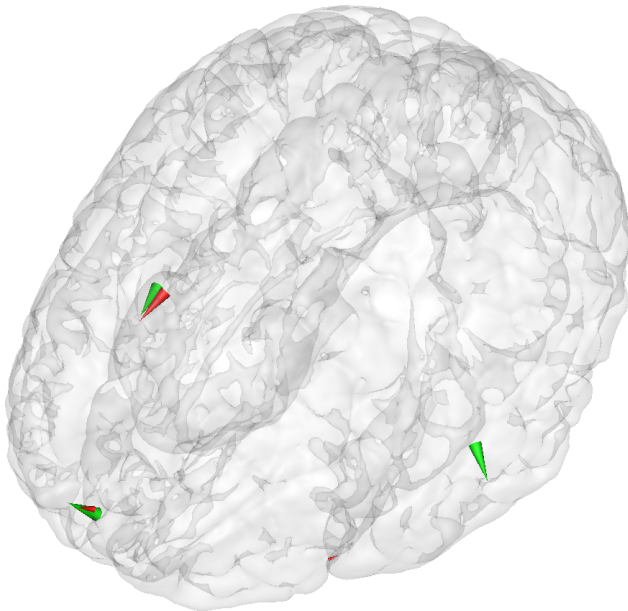
Simulation studies (similar to Neuroimage paper):

1. Single dipole recovery \rightarrow localization, focality, depth-bias.
2. Two dipole recovery \rightarrow source separation.

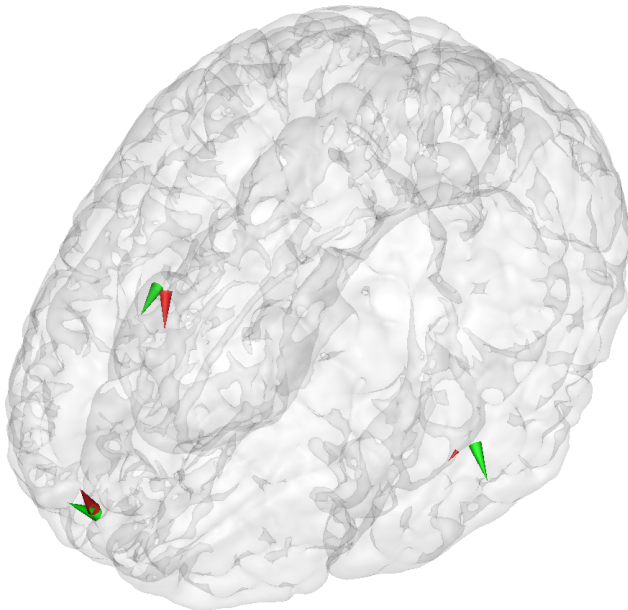
Source configurations were reconstructed using

- (a) EEG alone (b) MEG alone (c) EMEG data

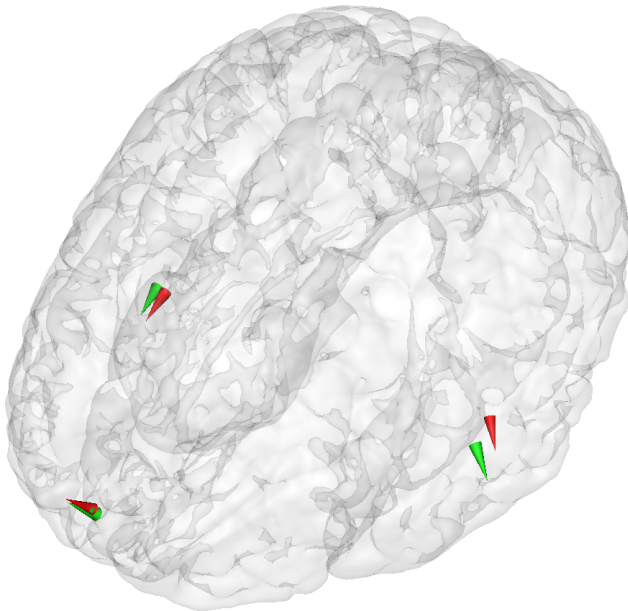
Exemplary Three Dipole Scenarios 1: HBM-NM Estimate, EEG alone



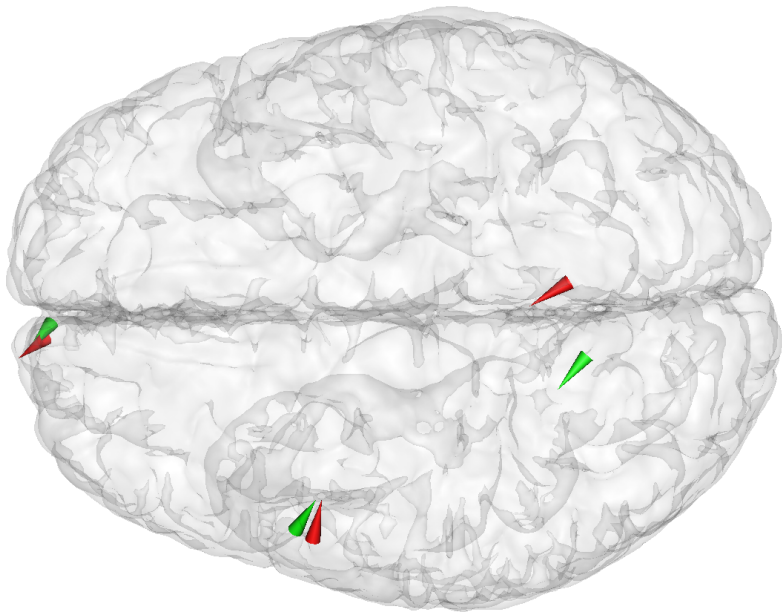
Exemplary Three Dipole Scenarios 1: HBM-NM Estimate, MEG alone



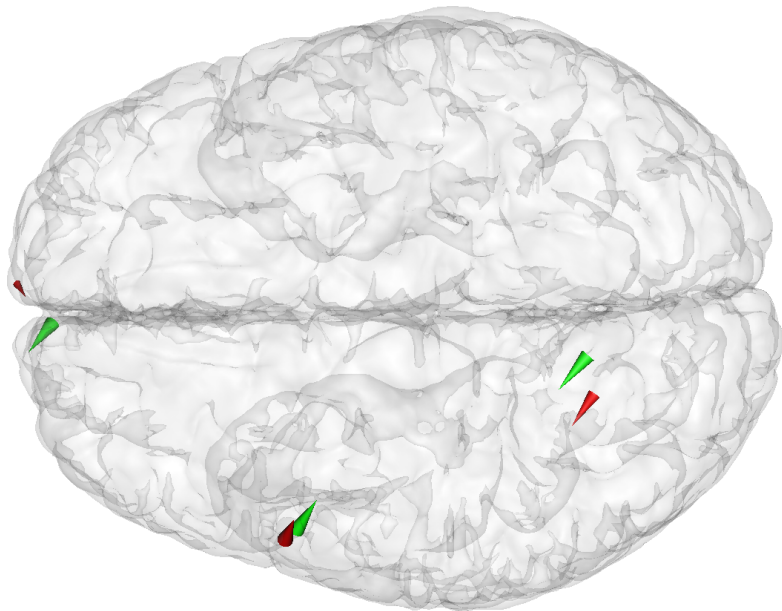
Exemplary Three Dipole Scenarios 1: HBM-NM Estimate, EMEG



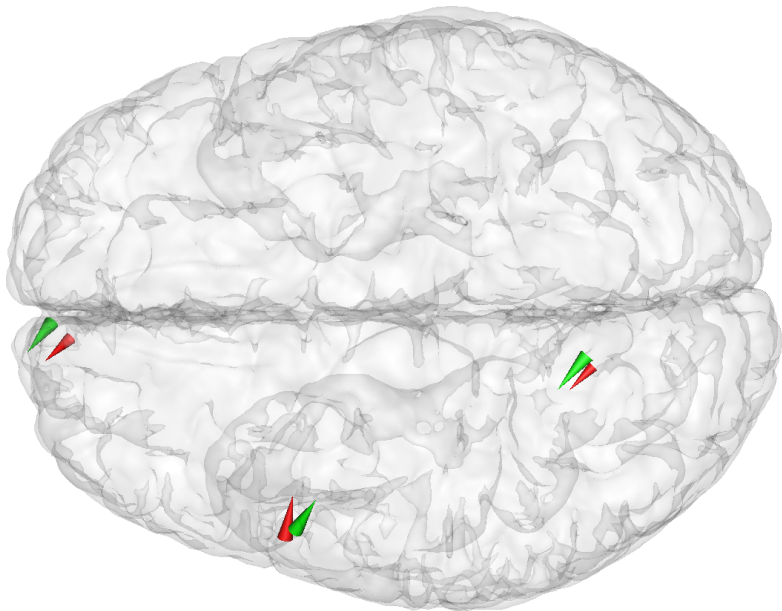
Exemplary Three Dipole Scenarios 2: HBM-NM Estimate, EEG alone



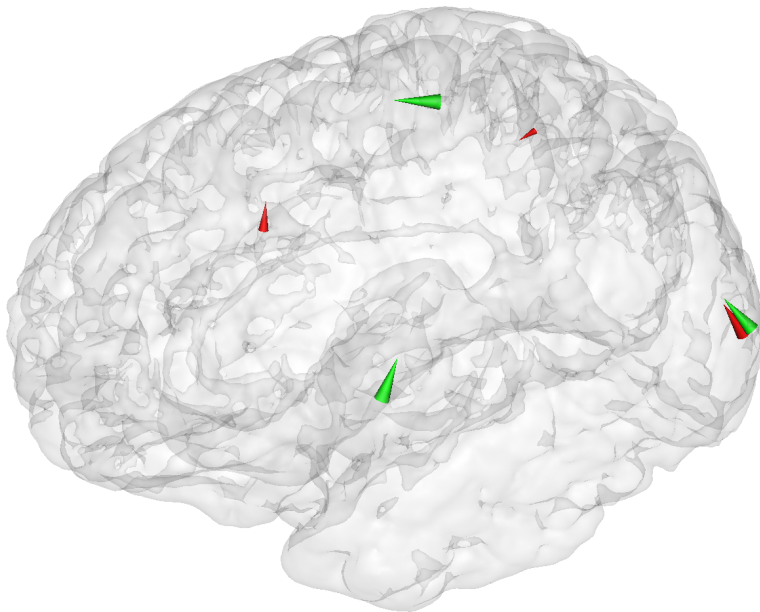
Exemplary Three Dipole Scenarios 2: HBM-NM Estimate, MEG alone



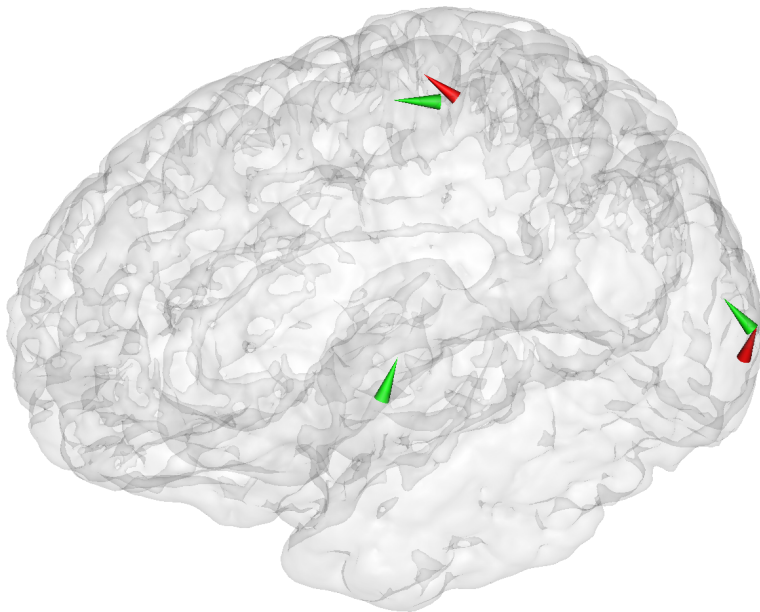
Exemplary Three Dipole Scenarios 2: HBM-NM Estimate, EMEG



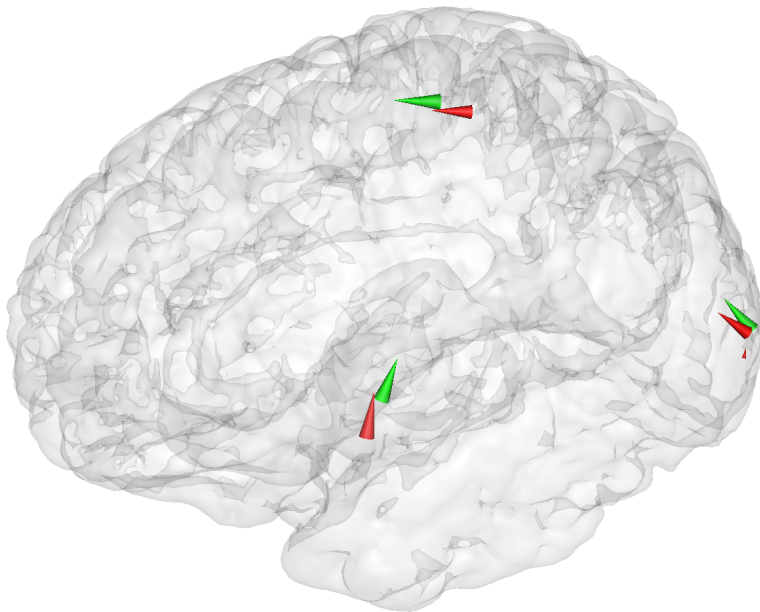
Exemplary Three Dipole Scenarios 3: HBM-NM Estimate, EEG alone



Exemplary Three Dipole Scenarios 3: HBM-NM Estimate, MEG alone



Exemplary Three Dipole Scenarios 3: HBM-NM Estimate, EMEG



Biomag Results and Conclusions, EEG vs. MEG

Results:

- ▶ HBM methods and sLORETA do not show a depth bias in any modality.
- ▶ Weighting of MNE to avoid depth bias in all modalities is difficult and comes at the cost of other draw-backs.
- ▶ The average localization performance (mean DLE) of HBM methods is equal for EEG and MEG. For WMNE variants and sLORETA, it is better for MEG.
- ▶ The mean EMD (localization + spatial extend) is better for EEG than MEG for all methods, although the differences are differently pronounced.

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Conclusions:

- ▶ Statements about localization properties of single modalities cannot be made without a reference to the inverse method used. This is a feature of the ill-posed nature of the EEG/MEG inverse problem.
- ▶ For all MNE variants and sLORETA, MEG offers a better localization (DLE) of single dipoles while having a higher EMD \implies better localization comes at the costs of a larger blurring.

Biomag Results and Conclusions, EEG/MEG Combination

Results:

- ▶ The combination improves the average performance of all methods (measured in EMD and DLE).
- ▶ The improvement of the EMD of HBM methods for multiple source scenarios is larger than for established methods.
- ▶ The combination reduces variance and outliers in the error statistics.
- ▶ The depth localization does not always profit from combination, especially if a single modality is very weak in that aspect.

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Conclusions:

- ▶ EEG/MEG combination stabilizes and improves source reconstruction to a considerable amount.
- ▶ Fully-Bayesian HBM methods profit from EEG/MEG combination especially for source separation in multiple source scenarios. This further underlines the potential of these methods for complex sources scenarios in real applications.

Outlook & Future Work

- ▶ **Current focus:** Processing of real data:
 - ▶ combined AEP/AEF and SEF/SEP data;
 - ▶ interictal epileptic activity;
- ▶ Practical aspects of EEG/MEG combination: Noise rescaling, volume conductor calibration and sensor weighting.
- ▶ Temporal extension of our HBM methods.
- ▶ Generalization of the specific HBM
 - ▶ to also recover more extended source scenarios;
 - ▶ to model inhibition, excitation and synchrony between brain areas;
 - ▶ to incorporate multimodal information from, e.g., DW-MRI, PET, SPECT, fMRI, NIRS;
- ▶ Comparison of HBM methods and EEG and MEG for extended source configurations.
- ▶ Comparison to other HBM-based methods like variational Bayesian approaches.

Thank you
for your
attention!



Software used by our group:

- ▶ Registration: FSL, FAIR;
- ▶ Segmentation: FSL, CURRY;
- ▶ FEM Meshing: Tetgen, vgrid, iso2mesh;
- ▶ FEM Computation: **SimBio**;
- ▶ Data Preprocessing: CURRY, BESA;
- ▶ Inverse computation: Matlab;
- ▶ Volume Visualization: SCIRun;
- ▶ Everything else & software integration: Matlab;