Hierarchical Bayesian Models for EEG Inversion: Depth Localization and Source Separation for Focal Sources in Realistic FE Head Models

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Abstract

The recovery of brain networks involving deep-lying sources by means of EEG/MEG recordings is still a challenging task for any inverse method. Hierarchical Bayesian modeling (HBM) emerged as a unifying framework for current density reconstruction (CDR) approaches comprising most established methods as well as offering promising new methods. Our work examines the performance of HBM for source configurations consisting of few, focal sources when used with realistic, high resolution Finite Element (FE) head models. The main foci of interest are the right depth localization, a well known systematic error of many CDR methods, and the separation of single sources in multiple-source scenarios. Both aspects are very important in clinical applications, e.g., in presurgical epilepsy diagnosis. The results of our simulation studies show, that HBM is a promising framework for these tasks, which is able to improve upon established CDR methods in many aspects. For challenging multiple-source scenarios where the established methods show crucial errors, promising results are attained. In addition, we introduce Wasserstein distances as performance measures for the validation of inverse methods in complex source scenarios.

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The recovery of brain networks involving deep-lying sources by means of EEG/MEG recordings is still a challenging task for any inverse method. Hierarchical Bayesian modeling (HBM) emerged as a unifying framework for current density reconstruction (CDR) approaches comprising most established methods as well as offering promising new methods. Our work examines the performance of HBM for source configurations consisting of few, focal sources when used with realistic, high resolution Finite Element (FE) head models. The main foci of interest are the right depth localization, a well known systematic error of many CDR methods, and the separation of single sources in multiple-source scenarios. Both aspects are very important in clinical applications, e.g., in presurgical epilepsy diagnosis. The results of our simulation studies show, that HBM is a promising framework for these tasks, which is able to improve upon established CDR methods in many aspects. For challenging multiple-source scenarios where the established methods show crucial errors, promising results are attained. In addition, we introduce Wasserstein distances as performance measures for the validation of inverse methods in complex source scenarios.

1 Introduction

This article comprises particular results from a diploma thesis [1]. The focus of the presentation is on the practical application, properties and results of the methods, aiming to get the reader interested in this new branch of inference strategies. A comprehensive description of the inverse problem of EEG/MEG, the concepts of Bayesian modeling and algorithmic and implementation aspects can be found in [1]. Mathematical formulas are intentionally avoided to the maximum extent possible.

1.1 Current Density Reconstructions and Hierarchical Bayesian Modeling

We consider the instantaneous inverse problem of EEG/MEG in the formulation of *current density reconstructions* (*CDR*), i.e., we want to find a solution to the matrix equation

$$b = L \cdot s, \tag{1}$$

where b is the m-dim. vector of the measured potentials, s is the n-dim. vector describing the discretized source activity as the amplitudes of n elementary sources with fixed locations and orientations and L is the *lead-field* or *gain* matrix of size m x n, which contains our (forward) model for the relation between source activity and measured data. Since $n \gg m$, infinitely many solutions to (1) exist. Additionally, L is ill-conditioned due to the characteristics of the forward problem, which is crucial since the data is corrupted by noise. More details on these issues can be found in [1]. One approach to overcome the above difficulties is to account for the high uncertainty and under-determinateness of the problem explicitly by formulating the inverse problem as a *statistical estimation problem*. The aim is to make statistical inferences about the real source configuration based on the information given by the measurements and the *a-priori* knowledge about the underlying brain activity. This concept is called *Bayesian modeling*. Formally, the information about the measurement b is encoded in a probability density called *likelihood* and our a-priori knowledge about the source activity s in a density called *prior*. The solution of the inverse problem within this framework is the probability density of s, conditioned on b, which can be computed using Bayes rule of conditional probability. This density reflects all available information about s by merging the information we have *before* the measurement (the prior) and *after* the measurement (the likelihood) and is thus called *posterior* density. There are two popular inference strategies to obtain a concrete estimate for s from the posterior: The *maximum a-posteriori* (*MAP*) estimate is the value of s which maximizes the posterior. Practically, its computation needs high dimensional *optimization* techniques. The *conditional mean* (*CM*) estimate is the expected value of the posterior. Practically, its computation needs high dimensional *integration* techniques. *Hierarchical Bayesian modeling* (*HBM*) denotes a specific construction principle in Bayesian modeling that recently attracted attention in EEG/MEG (see, e.g., [2-6]). We refer to [1] and [5] for a comprehensive introduction of the concepts behind this approach. In summary, the stochastic model is extended by an additional level of inference, represented by a new class of parameters called *hyperparameters*, which determine the general behavior of the model. Our a-priori knowledge about their value is, again, encoded in a probability density called *hyperprior*. HBM is a promising framework for sophisticated reconstruction tasks like *multimodal integration, spatio-temporal extension* or the modeling of *neural inhibition* or *excitation* (see [1,2,5]). The specific HBM we use was introduced in [2] and further examined in, e.g., [3,5,6]. It reflects the a-priori knowledge, that the source activity consists of few, focal sources , but does not constrain their number beforehand, like *dipole-fitting* approaches do.

1.2 Depth Bias and Masking

Many inverse methods fail to reconstruct deep-lying sources in the right depth, reconstructing them too close to the skull. This effect is called *depth bias*, and is a well known systematic error which limits the value of many inverse methods for clinical applications like presurgical epilepsy diagnosis. *Masking* describes the effect that deep-lying sources are not visible in the estimated activity, if near-surface ones are simultaneously active. Again, the oversight of these sources can lead to crucial errors in clinical applications, e.g., in the diagnosis of patients suffering from multi focal epileptiform discharges. Details and references for these topics can be found in 4.1. in [1].

2 Methods

2.1 Head Model and Source Space

The head model for our studies is a *Finite Element* (*FE*) model consisting of the compartments skin, skull compacta, skull spongiosa, eyes and a homogeneous inner brain compartment (see **Figure 1**). Details and references on head modeling and model generation are given in [1]. We did not distinguish between the inner brain compartments (csf, white and gray matter) to have a innermost compartment without holes and enclosures where we can place the test sources. This facilitates the interpretation of the results of our studies.

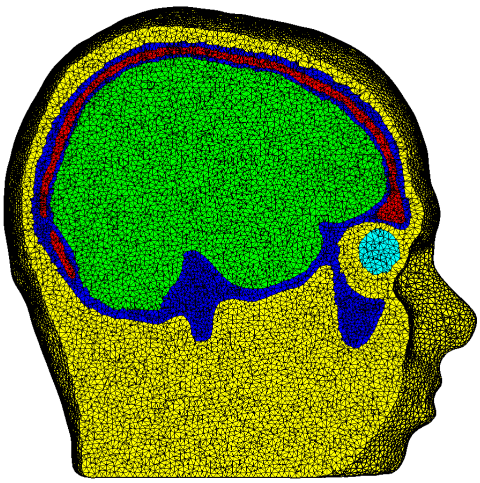

Figure 1 Realistic, high resolution FE head model (3.176.162 tetrahedron elements) with homogeneous inner brain compartment.

A source space of 1.000 nodes based on a regular grid is used (grid size: 10.99 mm). At each location 3 orthogonal dipoles are placed. An artificial sensor configuration is chosen that consists of 134 EEG electrodes that are distributed uniformly over the head surface. The reason for this is to distinguish the effect of *insufficient sensor coverage* from the effect of depth bias (see [1]).

2.2 Inverse Methods

To keep the presentation simple, not all inverse methods that rely on the HBM and were considered in [1] are considered in this article. In addition, simpler names are chosen to distinguish them. We will consider different methods for MAP estimation: MAP1 was introduced in [6], MAP2 and MAP3 were proposed in [1]. For CM estimation, we will rely on a scheme proposed in [3] and [6]. The choice of the parameters of the HBM and the estimation methods is a non trivial issue, which is treated in detail in [1]. Opposed to the new HBM-based methods, the well established *minimum norm estimate* (*MNE*), *sLORETA*, and two *weighted minimum norm estimates* (*WMNE*) are considered (L2-type and regularized L-inf-type weighting, denoted WMNE1 and WMNE2). The WMNE were proposed with the explicit intention to compensate for depth bias. All details and references for theses methods can be found in [1].

2.3 Validation Measures

We will use the following measures to evaluate our results: The *depth* of a location in the head model is defined as the minimal distance to one of the sensors. For single sources, the well known *dipole localization error* (*DLE*) is the distance from the real location of the source to the source space node with the largest estimated current amplitude. The *spatial dispersion* (*SD*) is a measure of the spatial extent of the source (see [1] for details). The DLE can only be used for single sources (the extension to multiple sources is not trivial) and is only sensitive to localization and in contrast, the SD does not account for localization at all. To overcome these limitations, we introduced and examined a novel validation measure in [1] that is sensitive to both localization and spatial extent mismatches, works in arbitrary complex source scenarios and with arbitrary estimation formates (sLORETA, e.g. yields standardized activity estimates rather than real current amplitudes): The *earth mover's distance* (*EMD*) is a distance measure between probability densities. It measures the minimal amount of work to transfer the mass of one density into the other. Illustratively, one can think of one density as a pile of sand, and of the other as a bunch of holes. Then the EMD is the minimal amount of work one needs to fill up the holes with the sand. The EMD has many advantages over the other validation measures and is sensitive to many desired features. More details and a closer examination are given in [1].

2.4 Simulation Studies

In the first study, only single dipole sources are considered: 1.000 dipoles with random locations and orienta-

tions are placed in the inner compartment. Note that they are not explicitly placed on the source space nodes (which would be an *inverse crime* [1,6] and would lead to overoptimistic results). White noise at noise levels (nl) of 5% and 10% is added to the data.
In the second study the dipoles used in the first study are combined to form 500 source configurations each consisting of a deep-lying and a near-surface dipole: The dipoles are evenly divided into three parts by their depth. Then one dipole from the part with the largest, and one from the part with the smallest depth are randomly picked. White noise at a noise level of 5% is added to the data.

3 Results

3.1 First Study: Depth Bias

The mean distance from the test sources to the next source space node was 5.27 mm. This is a lower bound for both DLE and EMD. **Table 1** shows the mean results of all methods. The depth bias is examined by the use of scatter plots (**Figures 2-4**): On the horizontal and vertical axis, the depth of the real source and of the source space node with the largest source estimate amplitude are plotted, respectively. A mark in the area underneath the $y = x$ line indicates that the dipole was reconstructed too close to the surface. If a method shows a clear tendency to favor this area, it suffers from depth bias (see, e.g., the MNE in Figure 3). A method performs well if its marks are tightly distributed around the $y = x$ line. For an easier visualization, only the first 250 sources are shown, and the methods were grouped such that their marks overlap the least. Since we found that the addition of noise has no systematic impact on the phenomenon of depth bias we omitted the plots for the 10% noise level case.
The results suggest, that the HBM-based methods CM, MAP2 and MAP3 improve upon the established ones for this specific source scenario, with MAP3 showing the best performance in every aspect examined (since the real source is a single dipole, a low SD is desirable) . Furthermore, they do not seem the suffer from systematic depth mis-localization.

Table 1 Mean validation measures for the first study.

	EMD (mm)		**DLE** (mm)		**SD**	
	5% nl	10% nl	5% nl	10% nl	5% nl	10% nl
CM	7.31	10.28	6.27	7.59	1.2e-03	2.7e-3
MAP1	28.12	53.70	27.00	37.33	1.1e-02	2.9e-1
MAP2	6.08	7.30	5.86	7.31	2.3e-04	9.4e-6
MAP3	5.95	6.74	5.81	6.74	1.4e-05	8.6e-7
MNE	53.23	55.93	29.47	30.68	2.4e-01	2.9e-1
WMNE1	52.19	54.92	30.35	34.05	2.5e-01	3.1e-1
WMNE2	49.58	52.43	29.38	25.07	2.2e-01	2.9e-1
sLORETA	40.56	44.94	6.14	7.36	1.9e-01	2.4e-1

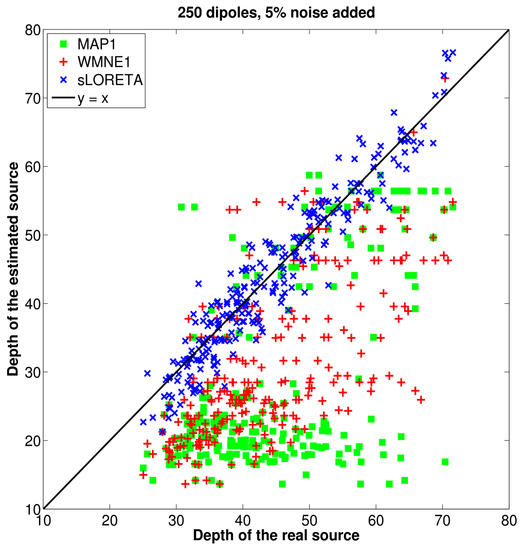

Figure 2 MAP1, WMNE1 and sLORETA.

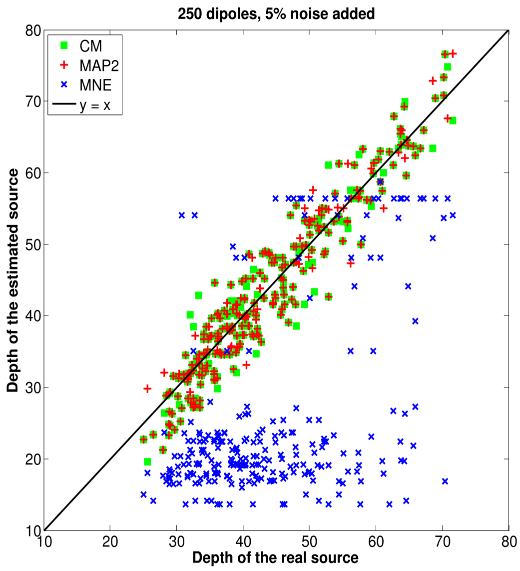

Figure 3 CM, MAP2 and MNE.

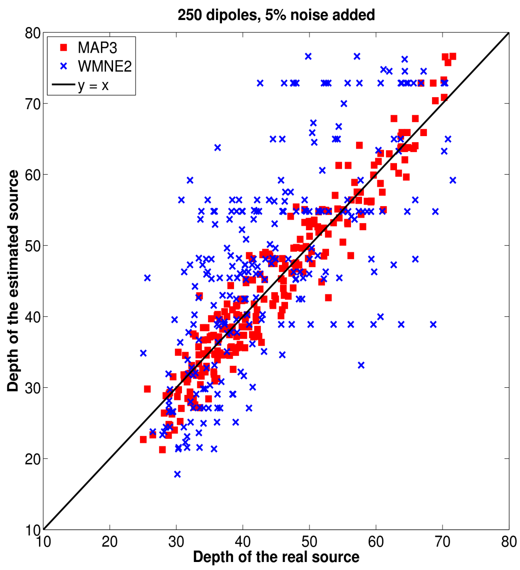

Figure 4 MAP3 and WMNE2.

3.2 Second Study: Masking

We show an initial example, where the effect of masking is very pronounced. In **Figures 5-7** the two green cones represent two sources of which the bottom left one is very close to the sensors whereas the top right one is very distant (see Figure A.21 in [1] for more detailed images). Figure 5 shows the (vector) MNE result with red-yellow cones, Figure 6 shows the (scalar) sLORETA result as red-yellow spheres. Even a careful successive thresholding of the estimated source amplitudes does not reveal any evidence for the presence of the deep-lying source. The MAP3 method proposed in [1] is able to detect both sources (see Figure 7, remember that the test sources are placed in between the source space grid nodes). **Table 2** shows the mean results of all methods. Remember that the DLE is no longer available in this source scenario.

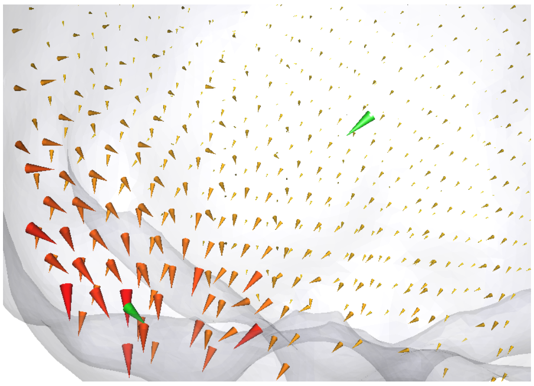

Figure 5 MNE result for the initial example.

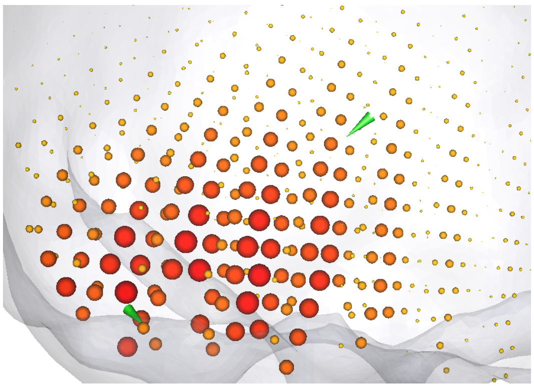

Figure 6 sLORETA result for the initial example.

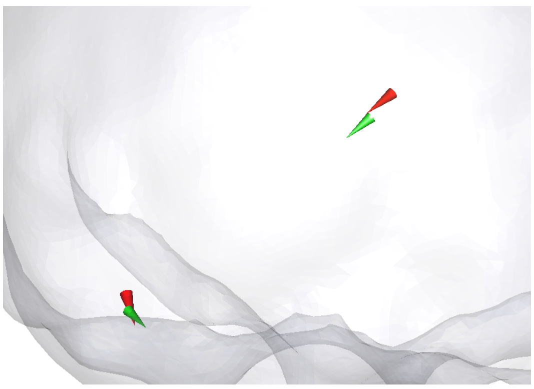

Figure 7 MAP3 result for the initial example.

Table 2 Mean validation measures for the second study.

	CM	MAP1	MAP2	MAP3	MNE	WMNE1	WMNE2	sLORETA
EMD	15.01	43.25	12.42	13.52	44.55	43.79	41.84	36.40
SD	3.1e-3	1.4e-3	8.3e-4	7.6e-4	2.2e-1	2.5e-1	2.4e-1	1.9e-1

The initial example showed that the examined source scenario is a very challenging one. However, CM, MAP2 and MAP3 show promising results even in this case.

3.3 EMD as a Validation Measure

From Table 1 the behavior of the EMD can compared to the DLE and the SD, which are only sensitive to localization or the spatial extent, respectively. Only methods that perform well in both aspects attain a low EDM: sLORETA is well known for giving well-localized but blurred estimates of single focal sources. This is reflected in a high EMD, when compared to methods attaining similar DLEs while also reflecting the source extend (i.e., also attaining a low SD). A further main advantage of the EMD is that it is applicable in more complex source scenarios, where no other validation tools are applicable anymore.

4 Conclusion

Hierarchical Bayesian modeling is a promising framework for EEG source localization, which is able to improve upon established CDR methods for the source scenarios examined in many aspects. Wasserstein metrics, in particular the EMD, are promising validation tools for future research on more complex source scenarios.

5 References

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