Evaluating the Impact of White Matter Conductivity Anisotropy on Reconstructing EEG Sources by Linearly Constrained Minimum Variance Beamformer

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Abstract EEG source imaging aims to reconstruct the neural activities of the brain accountable for the recorded scalp potentials. This procedure requires solving two problems, namely, forward and inverse problems. For the forward problem, the head is modeled as a volume conductor and the Poisson’s equation that describes the relation between neural activities and the observed EEG signals is solved. In this study, we enhanced the forward model by considering the white matter anisotropic conductivity tensor estimated from diffusion-weighted images. The second step is to solve the inverse problem in which the activity of the brain sources is estimated from measured data using the forward solution obtained in the previous step. Spatial filtering, also called beamforming, is an inverse method that reconstructs the time course of the source at a particular location by a linear combination of the sensor space data. We evaluated quantitatively the impact of the enhanced anisotropic forward model on linearly constrained minimum variance beamformer for both superficial and deep sources in a simulation environment, in terms of normalized mean squared error. Results showed that the anisotropic head forward model moderately enhanced the reconstruction of the sources, especially deep thalamic and olfactory sources.

Keywords: EEG forward problem, white matter conductivity anisotropy, source reconstruction, spatial filtering, minimum variance beamformer.

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1. Introduction

The aim of brain source imaging is to localize and reconstruct the neuronal activity responsible for the observed EEG/MEG signals. This leads to source localization which has clinical applications such as presurgical planning [1], seizure localization [2] and functional mapping of brain regions [3]. The process of brain source reconstruction entails solving a forward and an inverse problem.

In the forward problem, the head is modeled as a volume conductor. In a very simple case, the whole head is modeled as a sphere. A more accurate model is a three-layer sphere-shaped head model which assumes that the head is composed of three concentric spherical shells representing brain, skull, and scalp layers. Computing this model is efficient because it allows using analytical solution [4].

More exact and realistic geometry can be obtained using high resolution three-dimensional (3D) MRI/CT scans in which different tissues of the head are automatically segmented and their corresponding conductivities are set in the model. Often, the head is segmented into the following tissue types including gray matter, white matter, cerebrospinal fluid (CSF), scalp, and skull. It has been shown that conductivity values of the head tissues influence the magnetic field resulting from a dipolar source, especially for deep dipole sources [5].

In one study [6], the skull was segmented into spongy and compact layers with the former having a much higher conductivity value than the latter. This study showed that skull anisotropy has a smearing effect on the forward potential computation. However, it has been reported that accurate segmentation and modeling
of skull based on CT images has a major effect on reducing localization error than considering anisotropic model [7]. Apart from the skull, it is known that the conductivity of neuron fibers (the white matter of the brain) is approximately ten times larger in the parallel direction compared to the transverse direction [8]. Based on diffusion tensor images (DTIs), the fiber tracts of the brain can be constructed. It is assumed that the conductivity tensors of the tract share the same eigenvectors with the effective diffusion tensors measured by diffusion tensor MRI [9, 10]. Experimental data obtained from visual stimulation suggest that anisotropic models incorporating realistic white matter anisotropic conductivity do not substantially improve the accuracy of EEG dipole localization in the primary visual cortex [11]. Forward modeling based on the white matter anisotropic assumption becomes important in reconstruction and localization of deep sources neighboring the white matter tissues [12].

After obtaining the leadfield matrix the inverse problem can be solved. The EEG inverse problem deals with identifying the source activity from noisy EEG measurements. The solution for the EEG inverse problem is not unique and is highly sensitive to small changes in the noisy measurements. In general, EEG inverse algorithms are classified into two classes, parameter-estimation and imaging methods. One class of imaging algorithms is spatial filters which are also called beamformers in signal processing contexts. A beamformer is a linear operator applied to the measured data to estimate the strength of activity at a particular location in the model. They are categorized in two adaptive and non-adaptive classes depending on whether their weights depend only on the geometry of the measurements or on the covariance matrix of the measured data, too [13]. The most common spatial filter is the linearly constrained minimum variance (LCMV) beamformer which minimizes beamformer output power subject to linear spatial constraints [14]. Although minimum variance beamformers are more sensitive to changes in magnitude, depth, and frequency of the source, they have higher gains and superior spatial resolution compared to the minimum norm beamformers [15]. Despite its simplicity and good performance, LCMV has some problems such as poor ability in reconstructing correlated sources [16]. Therefore, some modifications are applied to enhance its performance in the case of correlated sources [16, 17].

Previous studies such as Wolters et al. [6] investigated the effect of anisotropy of skull and white matter conductivity through visualization of field distributions, isopotential surfaces, and return current flow and through statistical error measures including relative difference measure (RDM) and magnification factor (MAG). RDM quantifies the topography error and MAG indicates errors in magnitude between the isotropic and anisotropic forward solutions. Similarly, Lee et al. [11] evaluated the white matter anisotropy in forward problem scope using RDM and MAG metrics. Moreover, they computed the single-dipole source localization errors in millimeter. The study by Gülmar et al. [10] was somehow similar to these two papers but was performed on electrocorticography (ECoG) signals that are recorded invasively and hence with higher signal-to-noise ratio (SNR). Considering these studies, the direct effect of an anisotropic head forward model on inverse problem algorithms, and especially on beamforming approaches which reconstruct the temporal activity of brain sources, has not been taken into consideration. In single-dipole source localization, such as in Lee’s study [11], the location is estimated just in one time instance, but in beamforming approach, the activity in a time window is considered. On the other hand, since the focus in beamforming is on temporal activity estimation, the error is defined in terms of the L2-norm of the amplitude of the reconstructed source rather than in terms of 3D spatial location in millimeters.

The aim of the current paper is to evaluate to what extent considering the white matter anisotropic conductivity can reduce the reconstruction error of LCMV beamformer. The rest of the paper is organized as follows: In section 2, steps required for constructing the isotropic and anisotropic realistic head forward models are provided. Then, the theory of LCMV will be discussed. In section 3, the simulation procedure and evaluation results are provided. Finally, in section 4 we will go through the discussion.

2. Material and Methods

This section outlines the MRI data acquisition protocols, the steps required for constructing realistic head forward models (HFM), the details of the LCMV beamformer, and the procedure of generating synthetic EEG signals.

2.1 MRI and DTI Data Acquisition

The realistic HFM were generated from structural MRI and DTI data of four healthy subjects (one female) with an average age of 32.25 years. All the subjects gave written consent form before the experiment began. This study was approved by the Ethics Committee on Research at Tehran University of Medical Sciences. MR data acquisition was performed on a 3-T whole-body scanner (TrioTim; Siemens Medical Solutions, Erlangen, Germany) equipped with the standard 64 channel head coil. For extraction of anatomical information of the brain structure, we applied a 3D magnetization prepared rapid acquisition gradient echo sequence (TR/TE 1800/3.4 ms, 1 mm isotropic matrix, 256 × 256 mm² field of view (FOV), 176 slices).
Diffusion MRI consisted of a multi-shot diffusion-weighted echo-planar imaging pulse sequence. For our purpose, the following parameters were set: TR/TE 9600/101 ms, 128 × 128 matrix size, 240 × 240 mm² FOV, 2 mm slice thickness, and 1502 Hz/pixel bandwidth. Sixty-eight slices with no intersectional gap and an isotropic voxel size of 2 × 2 × 2 mm³ were acquired. Diffusion gradient encoding vectors were applied through 64 non-collinear/planer directions with \( b = 1000 \text{ s/mm}^2 \). Additionally, for decreasing the effect of noise on DTI model estimations, two \( b = 0 \text{ s/mm}^2 \) (no diffusion gradient) images were acquired at the start of diffusion encoding gradients. The sequence design was based on balanced diffusion gradients in order to minimize eddy current artifact. The head of the subject was fixed in a headrest to minimize artifacts secondary to an unavoidable motion.

After acquisition of diffusion weighted images (DWIs), the eddy current distortions and subject head motions were corrected using FSL software [18]. Then, rotation parameters were extracted, and accordingly gradient vectors (equivalent to B-matrix in DTI data) were also rotated. The non-local-means algorithm was applied on DWI data to reduce noise effects. Finally, all images were transformed to the Montreal Neurological Institute (MNI) T1-weighted template using FLIRT [19] in two steps. First, non-diffusion weighted image (b0 image) was registered to the same individual’s high-resolution T1-weighted image. Second, the high resolution image was registered to the MNI standard template using the transformation matrix with 12 degrees of freedom. Next, these two steps were combined into one registration matrix which was applied to register the DWI data into the MNI space. DTI model parameters were extracted from raw DWI data using a technique of robust estimation of tensors by outlier rejection [20]. For each voxel, scalar and vector parameters related to DTI model (eigenvalues and eigenvectors) were estimated by eigen-decomposition of estimated diffusion matrix. As will be shown in the following sections, the extracted parameters will be applied as a conductivity tensor to the volume conductor modeling of the brain.

2.2 EEG Forward Problem
In this section, we present the steps of preparing finite element head forward modeling to generate the isotropic and anisotropic HFMs.

2.2.1 Volume Segmentation and Mesh Generation
In models with realistic geometry, different tissues of the head must be segmented. Prior to segmentation, T1-weighted MRI was registered to MNI template in FSL software [18] by a normalized mutual information cost function and trilinear interpolation. The 3D MRI segmentation was done in FieldTrip toolbox [21] into five tissue types; namely, CSF, gray matter, scalp, skull and white matter. Figure 1 shows 3 slices of T1-weighted MRI and the result of the segmentation in coronal, sagittal and axial planes.

A volumetric mesh from the segmented MRI was generated with hexahedral elements and a node shift parameter equal to 0.1 to smooth the abrupt transitions and right angles of the cubic elements [9]. The dimension of the elements was selected as 1 × 1 × 1 mm³. The outer surface of the hexahedra mesh and a cross-section is shown in Fig. 2.

2.2.2 Mesh Electrical Conductivity Assignment
For generating an isotropic HFM, the following constant conductivity values are assigned to each element of the mesh [11]: scalp = 0.35 S/m, skull = 0.0132 S/m, CSF = 1.79 S/m, gray matter = 0.33 S/m, and white matter = 0.14 S/m.

To consider the conductivity anisotropy in the white matter elements of the mesh, it is assumed that the conductivity tensors have the same principal direction (e-
trans i.e. 0.65 vs. 0.065 S/larger than field matrix, box [24]. The solution of forward problem is called lead-FEM via SimBio Software available in FieldTrip tool - Fig. 2.

Prior to solving the above equation numerically, the recording electrode to a unit magnitude dipole situated at 3D location r. This matrix will be used in solving the inverse problem.

2.3 EEG Inverse Problem
2.3.1 Data Model

The forward problem leads to the following linear transformation from high dimensional source space to the low dimensional sensor space:

\[ x(t) = L(r)S(r,t) + n(t) \]  

where L denotes the forward operator, x corresponds to the measured EEG signals, S contains the unknown amplitudes of the brain sources, n is the additive sensor noise usually supposed to be white Gaussian, r is the 3D location vector, and t denotes the time instances. If we denote the number of electrodes by \( d_m \) and the number of sources by \( d_s \), then we will have \( x \in \mathbb{R}^{d_m \times 1} \), \( L \in \mathbb{R}^{d_m \times (d_s \times 3)} \), \( S \in \mathbb{R}^{(d_s \times 3) \times 1} \) and \( n \in \mathbb{R}^{d_m \times 1} \).

2.3.2 LCMV Beamformer

Spatial filtering, often called beamforming in signal processing contexts, is a linear method that estimates neural activity in the desired location \( r \) while suppressing the activity coming from other locations. In this technique, a \( d_m \times 3 \) weight matrix; namely, filter coefficients, is designed by minimizing the source variance. The weights, denoted by \( W(r) \), are multiplied by the measurement data to estimate the source activity as:

\[ \hat{s}(r,t) = W^T(r)x(t) \]  

where \( \hat{s} \in \mathbb{R}^{3 \times dt} \) represents the temporal activity of the source located at \( r \) and \( dt \) denotes the number of time points. According to different possible spatial constraints available, several versions of LCMV beamformer exist. For example, equation (5) describes the cost function of the vector minimum variance beamformer with unit gain constraint. \( R \) is the covariance matrix of the measurements, and \( l(r) \) is the \( d_m \times 3 \) leadfield matrix related to the source located at location \( r \).

\[ W(r) = \arg_{w} \min W^T(r)RW(r), \quad \text{subject to} \quad W^T(r)l(r) = l(3) \]

Using the Lagrange multipliers method, the optimization problem is simply solved and the closed form solution is obtained as:

\[ W(r) = R^{-1}l(r)[l^T(r)R^{-1}l(r)]^{-1} \]

Moving the filter pointing location throughout the brain space, a spatial pattern of neural activity or power as a function of location is acquired. The pattern of neural power can be used for solving the source localization problem, such that the regions with the highest neural power would be interpreted as the source location.

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**Fig. 3** Fusion of white matter fiber orientation map (principal tensor eigenvector) on T1-weighted MRI in coronal (left), sagittal (middle) and axial (right) views. Red, green, and blue indicate mediolateral, antero-posterior, and superioinferior directions, respectively [23].
2.4 Synthetic EEG Data Generation

In general, we can suppose that what is observed as EEG is coming from three origins. The first one is the brain background activity that is always present and relates to the normal functioning of the brain. The second origin is the target source which is the brain response to the stimuli, and our interest is to localize its position or reconstruct its activity in time. The last one is the recording electrodes additive noise, but with recent improvements such as active electrodes [25] it might have less effect on the measured signals.

Therefore, for producing background EEG, 20 random point current sources were located in the mesh gray matter elements. The time course of the dipoles had Gaussian distribution with a zero mean and a variance of 100 nAm. The sampling frequency of EEG was assumed to be 1000 Hz so a total number of 2000 data points were generated for each dipole time course. Then, using these sources, the background EEG was generated based on the forward model equation (3) for two isotropic and anisotropic HFMs.

For simulating the target response of the brain, in four separate scenarios, we located a desired current source in the interested regions of the brain. We selected the anatomical regions in a way to cover both superficial and deep sources as well as radial and tangential orientations [6]. The location and orientation of the target source were defined as follows: a cortical radially oriented source in the left motor cortex, a cortical tangentially oriented source in the left motor cortex, a subcortical radially oriented source in the left thalamus, and a deep radially oriented source in the left olfactory cortex. The superficial radially and tangentially oriented sources can be located in gyri and within the walls of sulci, respectively, but deep sources are mainly considered radial. We assumed radial and tangential orientations approximately in the inferior-superior and posterior-anterior directions, respectively. Figure 4 shows the location and orientation of the four simulated dipoles in head space which will be reconstructed via solving the inverse problem.

Finally, considering the recording electrodes noise level, we took three noiseless/noisy test conditions: a sensor noise-free condition, and two noisy conditions with additive white Gaussian distribution at SNR of 20 and 10 dB. The noise is denoted by \( n(t) \) in equation (3) and is added to the synthetic EEG originating from brain non-target activity and the simulated source under two HFMs. The objective is to reconstruct the time course of the simulated source.

The random activity of the radially oriented target source at motor cortex, a sample of the generated EEG signal as well as the corresponding topoplots of EEG at two time instances are shown in Fig. 5.

For evaluating the quality of the reconstructed time course of the simulated source, we used normalized mean squared error defined as

\[
NMS E = \frac{\| S(\mathbf{r}) - \hat{S}(\mathbf{r}) \|_2}{\| S(\mathbf{r}) \|_2} \quad \text{(7)}
\]

where \( S(\mathbf{r}) \) and \( \hat{S}(\mathbf{r}) \) are the original and reconstructed...
time course of the source at location \( r \) at all the time instances, respectively. \( \| \cdot \|_2 \) denotes L2-norm defined as the square root of the sum of the vector values squared.

We computed the reconstruction error of LCMV beamformer for the four simulated sources under different sensor noise conditions, using isotropic and anisotropic HFMs. To avoid inverse crime, we used a slightly modified leadfield matrix for reconstruction in equation (6) that was different from the leadfield which was used for synthetic EEG generation. This was done by changing the location of the source grids.

To account for the variability of background EEG, for each study subject and for each simulation scenario, we ran the simulations 100 times with different random parameters and noise signals and calculated the normalized mean square error (NMSE) of the LCMV beamformer. Therefore, for each simulation scenario, we have two groups of reconstruction errors belonging to the isotropic and anisotropic HFMs. Every group has 400 data samples (4 subjects multiplied by 100 iterations) which are adequate for conducting a paired-sample \( t \)-test with significance level of 0.05 to examine whether the difference between the two error groups is statistically important.

### 3. Results

The average NMSE and its variance are computed based on the isotropic and anisotropic HFMs across all the iterations and all the study subjects. The results are provided in Tables 1 through 3 for 3 SNR values of infinity (corresponding to no sensor noise condition), 20 and 10 dB, respectively. For easy observation of the impact of using anisotropic HFM on the beamformer’s performance, we computed the normalized difference of the NMSEs between two HFMs using the formulation below (Table 4).

\[
\frac{(NMSE_{\text{iso}} - NMSE_{\text{aniso}})}{NMSE_{\text{iso}}} \times 100
\]  

(8)

Before any conclusion, we have to determine whether the differences shown in Tables 1 to 3, or equivalently the improvements presented in Table 4 are statistically significant. We applied a paired-sample \( t \)-test on the two NMSE groups obtained based on isotropic and anisotropic HFMs. The first obvious point in Table 4 is that for the extreme case of no additive noise (\( \text{SNR} = \infty \)), the negligible differences observed between the two HFMs are not meaningful. However, by decreasing SNR i.e. adding more sensor noise, the differences increase and become statistically significant. For example, in the case of radial cortical source, LCMV has an approximately 3% better performance based on anisotropic HFM. This enhancement increases to 5% for the tangential cortical source. On the other hand, in the case of the subcortical source located in the thalamus and the deep source of the olfactory cortex, LCMV performs 9% and 8% better un-

| Table 1 | The average NMSE of LCMV beamformer across all the subjects for four simulated sources using the isotropic and anisotropic HFMs under no sensor noise. |
|---------|-------------------------------------------------|
| Simulated source | Isotropic HFM | Anisotropic HFM |
| Motor cortex (radial) | 0.0992 ± 0.0003 | 0.0988 ± 0.0002 |
| Motor cortex (tangential) | 0.0988 ± 0.0002 | 0.0988 ± 0.0002 |
| Thalamus (radial) | 0.1000 ± 0.0007 | 0.0988 ± 0.0002 |
| Olfactory cortex (radial) | 0.1022 ± 0.0045 | 0.0988 ± 0.0002 |

| Table 2 | The average NMSE of LCMV beamformer across all the subjects for four simulated sources using the isotropic and anisotropic HFMs under \( \text{SNR} = 20 \text{ dB} \). |
|---------|-------------------------------------------------|
| Simulated source | Isotropic HFM | Anisotropic HFM |
| Motor cortex (radial) | 0.1975 ± 0.0005 | 0.1972 ± 0.0005 |
| Motor cortex (tangential) | 0.1910 ± 0.0005 | 0.1866 ± 0.0003 |
| Thalamus (radial) | 0.3436 ± 0.0044 | 0.3137 ± 0.0099 |
| Olfactory cortex (radial) | 0.3080 ± 0.0049 | 0.2841 ± 0.0033 |

| Table 3 | The average NMSE of LCMV beamformer across all the subjects for four simulated sources using the isotropic and anisotropic HFMs under \( \text{SNR} = 10 \text{ dB} \). |
|---------|-------------------------------------------------|
| Simulated source | Isotropic HFM | Anisotropic HFM |
| Motor cortex (radial) | 0.2671 ± 0.0023 | 0.2600 ± 0.0027 |
| Motor cortex (tangential) | 0.2393 ± 0.0021 | 0.2275 ± 0.0014 |
| Thalamus (radial) | 0.5069 ± 0.0056 | 0.4510 ± 0.0248 |
| Olfactory cortex (radial) | 0.4703 ± 0.0073 | 0.4190 ± 0.0054 |
under anisotropic HFM, respectively; these numbers increase to 11% and 12%, respectively, by decreasing SNR to 10 dB. Therefore, we can say that the anisotropic model results in less reconstruction error for subcortical sources, especially when SNR decreases. Moreover, according to the t-test applied to the reconstruction errors underlying the two HFMs, the difference observed between the performance of the beamformer under SNR = 10 is significant for all the sources. In the case of the thalamus, the findings are consistent with previous studies [5], since it is surrounded with white matter, and considering the conductivity anisotropy leads to more accurate forward and consequently inverse solutions.

4. Discussion

In this paper, we enhanced the realistic head forward model by considering white matter conductivity anisotropy in solving the forward problem. Previous studies evaluated the influence of anisotropic conductivity in terms of statistical difference metrics such as RDM and MAG [6, 11, 26]. Here, we investigated the final impact of this model enhancement in terms of beamformer normalized reconstruction error.

It is noteworthy that improvements in signal acquisition systems such as active electrodes equipped with unity gain amplifier [25] as well as improved artifact removal methods [27] applied to preprocessing EEG signals have led to reduced sensor noise. On the other hand, in studies without HFM or distributed random sources model, the noisy EEG is simulated just by adding white Gaussian noise. However, as shown in this study, using HFM and distributed random sources enabled us to simulate the effect of non-target background activity of the brain in a more realistic manner, and subsequently allowed amplitude reduction of the additive noise. Therefore, high SNR additive noise scenarios are possible, under which LCMV filter achieves higher performance based on anisotropic HFM. However, in order to follow the traditional noise effect on reconstruction performance, we also considered adding a white Gaussian noise with SNRs equal to 20 and 10 dB, which simulates recording noise of electrodes. The level of improvement is different for the four simulated sources under different SNRs.

5. Conclusion

Based on the results summarized in Table 4, we conclude that considering anisotropic conductivity for white matter elements of the HFM moderately reduces the reconstruction error of LCMV beamformer. For future work, in addition to a realistic head model, we have plans to use real EEG signals acquired under electrical stimulation experiment. Electrical stimulations can generate focal sources in the well known regions of the brain, i.e. somatosensory cortex. Therefore, the real influence of white matter anisotropy can be investigated better, since the real location and stimulation protocol is truly known.

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