Influence of anisotropic white matter modeling on EEG source localization

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***Abstract*— We study the influence of the anisotropic white matter within the ElectroEncephaloGraphy source localization problem. To this end, we consider three cases of the anisotropic white matter modeled in two concrete cases: by fixed or variable ratio. We extract information about highly anisotropic areas of the white matter from real Diffusion Weighted Imaging data. To validate the compared anisotropic models, we introduce the localization dipole and orientation errors. Obtained results show that the white matter model with a fixed anisotropic ratio leads to values of dipole localization error close to $1\,cm$ and may be enough in those cases avoiding localized analysis of neural brain activity. In contrast, modeling based on the anisotropic variable rate assumption becomes important in tasks regarding analysis and localization of deep sources neighboring the white matter tissue.**

I. Introduction

There are several techniques for monitoring and extracting from the human brain more elaborate information that should provide better results in clinical applications like medical treatment, surgery planning, or even more generalized brain research tasks. Among those non-invasive techniques, the combination of magnetic resonance imaging (MRI) with ElectroEncephaloGraphy (EEG) functional analysis has shown to raise performance of their single modality case. Moreover, extracted multi-modal information is useful in diagnosis and preoperative stages of brain surgery, being usually the only suitable analysis tool due to the high risk of alternative surgical interventions.

Mostly, clinical brain surgeries embrace localization of neural activity sources to be carried out with high accuracy. Owing to this reason, active current dipoles inside the brain are localized via EEG using a conductivity model of the human head volume (termed the source localization problem). Moreover, estimation of potentials in the scalp, dipole sources, and conductivity volume involve the solution of two different problems: *i*) The forward problem, calculating the potential of the electrodes on the scalp for a given source configuration. *ii*) The inverse problem, estimating the source parameters from the potential of the electrodes [4]. Nonetheless, to improve accuracy of estimated source parameters in the inverse problem, a structural head model is required that must include adequate conductivity modeling of the different head tissues (scalp, skull, gray matter, white matter, among others).

The simplest structural approach models spherical layers only with isotropic behavior of the tissue conductivity, but it provides low accuracy that induces values of localization error up to $15\,mm$, as discussed in [5]. To cope with this issue, the white matter model can involve conductivity inhomogeneity though this approach poses a challenge because of the presence of the anisotropic variability. Thus, there are two main models of anisotropic white matter conductivity: the simpler one that assumes a constant anisotropic ratio, and the one assuming variable anisotropic ratios that are estimated from the input head image data.

In this work, we compare three modeling cases of the anisotropic white matter combining fixed and variable ratios. Information about highly anisotropic areas of the white matter is extracted from real DWI-MRI recordings (Diffusion Weighted Imaging - Magnetic Imaging Resonance). To validate the compared anisotropic models, we introduce the error of dipole localization and orientation. Obtained results show that the anisotropic white matter has a significant effect in the EEG source analysis, and must be included in studies where the accuracy is an important factor. Besides, the test shows that deep source analysis benefits of the inclusion of variable anisotropic white matter ratio.

II. Methods

A. MRI Brain Tissue Segmentation

Since the representation of electromagnetic conductivity requires the geometric anatomical head model, we employ the hierarchical local binary fitting (LBF) graph-cut approach, proposed in [1], to segment from patient MRI data the main head structures, namely, scalp, skull, cerebro-spinal fluid (CSF), white and gray matter. In the LBF, structures are pair-wise segmented from the most outer to the most inner, in accordance to the intrinsic anatomical constraints of the head structures. This algorithm minimizes the energy inside a given MRI region Ω regarding the provided partitions $\Gamma{=}\{\Omega_0, \Omega_1\}$, as stated in the following optimization problem:

$$\Gamma^* = \arg\min \int_{\Omega} \mathcal{E}(\Gamma, \boldsymbol{\rho}) d\boldsymbol{r} \tag{1}$$

$$\text{s.t.: } \Omega_0 \cup \Omega_1 = \Omega, \text{and } \Omega_0 \cap \Omega_1 = \emptyset$$

$$\text{being } \mathcal{E}(\Gamma, \boldsymbol{\rho}) = \sum_{i=0}^{1} \int_{\Omega_i} \kappa(\boldsymbol{\rho} - \boldsymbol{\rho}') ||f(\boldsymbol{\rho}) - f(\boldsymbol{\rho}')||^2 d\boldsymbol{\rho}'$$

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where $\kappa(\boldsymbol{\rho}-\boldsymbol{\rho}')$ is a spatial similarity measure between voxels $\boldsymbol{\rho},\boldsymbol{\rho}'\in\Omega$ and $f(\boldsymbol{\rho})$ corresponds to the MR intensity at $\boldsymbol{\rho}$-th voxel. Fig. 1 shows examples of the axial, coronal, and sagittal views for the segmented data set.

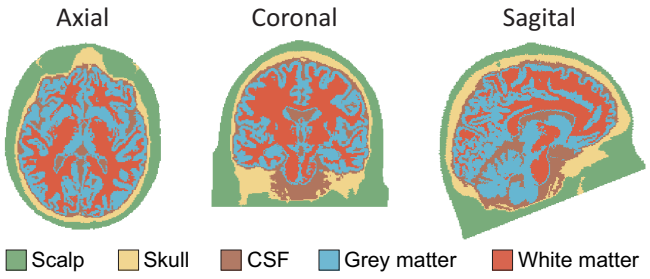

Fig. 1. Computed anatomical head model by using the hierarchical LBF graph-cut approach.

B. DWI tensor

Although MRI-*T1* data are commonly employed to build structural head models, there is no provided information about anisotropic conductivity in each voxel. However, anisotropic conductivity shares common eigenvectors with DWI diffusion tensors [9]. Therefore, symmetrical diffusion tensors, $\boldsymbol{D}\in\mathbb{R}^{3\times3}$, have eigenvalues that express voxel molecular mobility along the local directions, (x,y,z), where the ratio in each voxel between the largest eigenvalue to the average of the two other eigenvalues of the diffusion tensor is not a fixed, but a variable value. More precisely, provided the eigenvalue set $\boldsymbol{\lambda}=\{\lambda_i\}$ which is computed from $\boldsymbol{D}$ for each voxel, we consider the following two measures that describe the degree of the anisotropy in the white matter:

– *Fractional Anisotropy, (FA),*

$$\nu_{FA}=\frac{\sqrt{3}}{\sqrt{2}}\frac{\sqrt{(\boldsymbol{E}\{\lambda_i\}-\lambda)^2}}{\sqrt{(\boldsymbol{E}\{\lambda_i\})^2}} \tag{2}$$

where $\lambda=\boldsymbol{E}\{\lambda_i : i=1,2,3\}$ and it holds that $\lambda_i \geq \lambda_{i+1}$. Notation $\boldsymbol{E}\{\cdot\}$ stands for the average operator. Values of ν_{FA} range from 0 to 1, where a fully anisotropic tissue has a factor $\nu_{FA}=1$, while an isotropic one gets ν_{FA} tending to zero.

– *Anisotropy Ratio (AR),*

$$\nu_{AR}=\frac{\lambda_1}{\boldsymbol{E}\{\lambda_i : i=1,2\}} \tag{3}$$

where $\nu_{AR}\in\mathbb{R}^+$. So, the larger the value - the more anisotropic the white matter.

It is worth noting that DWI data is commonly affected by the measurement noise. Thus, prior to compute the eigenvalue set, we denoise DWI data by carrying out the partial-differential-equation-smoothing filtering suggested in [2].

C. Forward Problem Framework

In the EEG source location, the forward problem estimates the electrode potential field, $\boldsymbol{V}$, placed at a specific point, (x,y,z), on the scalp that is generated due to current sources in the brain. Sources are modeled as current dipoles placed at position $\boldsymbol{r}\in\mathbb{R}^3$ with orientation $\boldsymbol{d}\in\mathbb{R}^3$. The scalar-valued potential $V(x,y,z)\subset\boldsymbol{V}$ on the surface of a conductive volume x,y,z is defined by the Poisson equation as follows:

$$\nabla\left(\Sigma(x,y,z)\nabla V(x,y,z)\right)=I\delta(\boldsymbol{r}-\boldsymbol{r}_1)-I\delta(\boldsymbol{r}-\boldsymbol{r}_2) \tag{4}$$

where $I\in\mathbb{R}$ represents the current dipole magnitude, $\boldsymbol{\Sigma}\in\mathbb{R}^{3\times3}$ is the conductivity tensor, and $\boldsymbol{r}_1$ and $\boldsymbol{r}_2$ are the two concrete coordinates determining the dipole direction. Notation $\delta(\cdot)$ stands for the delta function.

In case of the isotropic volumes, the conductivity $\Sigma(x,y,z)$ is scalar-valued, while in the anisotropic case, it becomes a tensor in the following form:

$$\boldsymbol{\Sigma}_h^{(j)}=\boldsymbol{T}^{(j)\top}\boldsymbol{\Sigma}_s^{(j)}\boldsymbol{T}^{(j)} \tag{5}$$

where $\boldsymbol{\Sigma}_h^j$ is the conductivity head matrix defined in the uniform Cartesian coordinate system at the element j; $\boldsymbol{T}\in\mathbb{R}^{3\times3}$ is the orthogonal matrix of unit length eigenvectors that is a rotation transfer matrix from the local to the global coordinate system; $\boldsymbol{\Sigma}_s^{(j)}=\mathrm{diag}(\sigma_{rad}^{(j)},\sigma_{\tan}^{(j)},\sigma_{\tan}^{(j)})$ is a diagonal matrix holding the local conductivity values in the tangential, $\sigma_{\tan}^{(j)}$, and radial directions, $\sigma_{rad}^{(j)}$, respectively. Additionally, for modeling anisotropic white matter conductivity, we use the volume constrain [9].

D. Forward Solution

For the numerical case, Eq. (4) is solved using the anisotropic finite difference method for the concrete 18-neighborhood representation as proposed in [5]:

$$\sum_{i=1}^{18}a_i\boldsymbol{\phi}_i-\left(\sum_{i=1}^{18}a_i\right)\boldsymbol{\phi}_0=I\delta(\boldsymbol{r}-\boldsymbol{r}_1)-I\delta(\boldsymbol{r}-\boldsymbol{r}_2) \tag{6}$$

where the coefficient set $\{a_i\in\mathbb{R}\}$ holds the conductivity values and ensures the Dirichlet and Neumann boundary conditions [7], $\boldsymbol{\phi}_i\in\mathbb{R}^{1\times N_Z}$ is each discrete potential, being N_Z the non zero voxels where head tissues are present, $\boldsymbol{\phi}_0$ is the potential at the neighborhood origin.

Generally speaking, Eq. (6) results in a linear system $\boldsymbol{A\Phi}=\boldsymbol{I}$ with unknown terms, $\boldsymbol{\Phi}$, that is solved using the *successive over relaxation* approach. However, the system implementation requires a high computational burden. To overcome this drawback, precalculated reciprocity potentials are employed to speed up the computation of the inverse solution.

E. EEG dipole source estimation

Within the inverse problem framework, we estimate the pairwise dipole parameters $(\hat{\boldsymbol{r}},\hat{\boldsymbol{d}})$ by calculating the best electrode potentials, $\boldsymbol{v}_m$, that we minimize as follows [5]:

$$(\hat{\boldsymbol{r}},\hat{\boldsymbol{d}})=\min_{\boldsymbol{r},\boldsymbol{d}}\left\{\frac{\|\boldsymbol{v}_e-\boldsymbol{v}_m(\boldsymbol{r},\boldsymbol{d})\|_2^2}{\|\boldsymbol{v}_e\|_2^2}+c(\boldsymbol{r})\right\} \tag{7}$$

where the values $\boldsymbol{v}_e\in\mathbb{R}^{N_d\times1}$ are the vector of electrode potentials of the analytical reference model; $\boldsymbol{v}_m\in\mathbb{R}^{N_d\times1}$ are the electrode potential vector estimated by the numerical test models, being N_d the number of considered dipoles; and the

term $c(\boldsymbol{r})\in\mathbb{R}^{+}$ is a penalization parameter that is set to zero for dipole positions inside the gray matter, otherwise they are very large. Notation $\|\cdot\|_2$ stands for the Euclidean norm.

The minimizing procedure in Eq. (7) includes both the *reference* and *test* models to estimate the dipole error. Therefore, we initially compute the electrode potentials $\boldsymbol{v}_e$, and then the dipole parameters, $(\hat{\boldsymbol{r}}, \hat{\boldsymbol{d}})$. Namely, we introduce the following two error measures:

– the dipole localization error (DLE),

$$\varepsilon_L = \|\hat{\boldsymbol{r}} - \boldsymbol{r}\|_2$$

– the dipole orientation error (DOE),

$$\varepsilon_O = \arccos\left(\frac{\hat{\boldsymbol{d}}^{\top}\boldsymbol{d}}{\|\boldsymbol{d}\|_2\,\|\hat{\boldsymbol{d}}\|_2}\right)$$

III. Experimental Setup

A. DWI and Structural MRI Database

Structural MRI and DWI data were taken from IDA-LONI database publicly available[1]. The MR was a $T1$ sequence of a healthy 24-years male subject. The data were acquired on a SIEMENS Trio Tim $3T$ MRI Scanner with a $1\times1\times1\,mm$ resolution. A DWI sequence with 72 slices was acquired with an echo spin sequence having the following parameters: 64 directions, repetition time was $890.0\,ms$, echo time was 88.0 *ms*, thickness of $2.0\,mm$, and voxel size - $1.98\times1.98\times1.98\,mm$. To correct subject orientation and geometrical distortions, the $T1$ and *DWI-MRI* data were aligned with a voxel similarity-based affine registration procedure. The registered *DWI* data were re-sampled to $1\times1\times1\,mm$ using the *FSL* toolbox. Therefore, four realistic head models reconstructed from MRI-DWI data with different white matter conductivities were considered. Each head model was segmented with the LBF method, explained in § II-A, setting a Gaussian kernel, $\kappa(\cdot)$, with scale σ=3 and, at least, five different tissues were considered (see Fig. 1). We used the AFDRM numerical algorithm to get the forward calculations in a normalized model with 1×1×1,*mm* voxel partition, and the registered *DWI* data were used to approximate the anisotropic conductivity tensors in the white matter.

B. Simulation of Whiter Matter Conductivity

We consider three different simulations to analyze the influence of the anisotropic white matter on the EEG source localization problem. All models used the following isotropic conductivity values for the tissue areas different to the white matter: scalp=$0.33\,S/m$, skull=0.02 *S/m*, CSF=$1.78\,S/m$, grey matter=$0.33\,S/m$. Additionally, we use an isotropic conductivity model for the EEG source estimation fixing the white matter conductivity value as $0.02\,S/m$.

1) Simulation A: In this case, we estimate values of both dipole localization and orientation errors that appear when omitting anisotropic conductivity in the tissue. To this end, we set the anisotropic white matter conductivity using a fixed $1:0.11$ (radial:tangential) ratio with a volume constrain, considering the isotropic conductivity value as $0.14\,S/m$ as assumed in [9]. This simulation aims to measure the influence of neglecting the anisotropic white matter on the EEG source estimation.

2) Simulation B: We assess the accuracy of EEG source localization because of the introduced anisotropic measure FA in the white matter. In this case, we set the anisotropic white matter conductivity using the *FA* variable ratio with a volume constrain that assumes an isotropic conductivity value of $0.14\,S/m$. Thus, we aim at analyzing the influence of the *FA* anisotropic ratio obtained from the *DWI* data eigenvalues.

3) Simulation C: This case is similar to the simulation B, but instead of the *FA* we make use of the AR measure given in [6]. The isotropic conductivity is also fixed as $0.14\,S/m$.

For the above described simulations, we test all considered models using the *10-20* EEG standard system with 23 electrodes and 22 leadpairs in a reciprocity approach with 3331498 non zero potentials. For a single leadpair calculation, the algorithm takes about $50\,min$ using an `Intel Xeon processor` with 64Gb RAM. For the dipole estimation, we fix a set of 6359 dipole sources contained only in the gray matter with a $5\,mm$ separation between neighboring sources. Testing is carried out in three different dipole orientations (x, y, and z), resulting in 19077 calculations.

IV. Results and Discussion

The influence of anisotropic white matter on the accuracy of the EEG source localization is considered as follows: In case of the simulation *A*, either estimated error measures accuracy when neglecting the anisotropic nature of white matter in the conductivity model, while in the simulations *B* and *C* both errors reflect measures the source localization performance when neglecting the variable ratio of the anisotropic white matter.

As shown in Table I, DLE and DOE achieve the lowest values for the simulation *A*. These expected results can be explained since the model does not assume highly anisotropic areas of the white matter, that is, the model has the same anisotropic ratio throughout the tissue. In turn, simulation *B* provides larger DLE and DOE values due to the inclusion of information extracted from DWI data, making known the highly anisotropic areas in the white matter. Therefore, the model more accurately computes influence of anisotropic white matter. Lastly, the simulation *C* performs a bit lower error values since the used variable anisotropic ratio (that is, AR) is smoother that the one used in the case *B* (i.e., FA).

TABLE I
Performed error values of Dipole Localization and Orientation

case	ε_L [*mm*]	ε_O [*deg*]
A	2.33 ± 1.32, max $=9.400$	11.06 ± 7.48, max $=55.74$
B	2.64 ± 1.53, max $=12.23$	12.73 ± 9.47, max $=63.44$
C	2.58 ± 1.48, max $=11.47$	11.92 ± 7.98, max $=59.44$

It is worth noting that achieved DLE and DOE values are highly correlated in all three simulations; this fact is

[1]https://ida.loni.usc.edu/login.jsp

due to their pairwise source-based calculation. Nonetheless, the mean DLE values highly differ from their corresponding maximum value. The same situation remains for the DOE error, but in a lower degree. Significant separation between estimated mean and maximum values accounts for the presence of several white matter areas having very dissimilar anisotropic values, specially, in the deeper areas of the brain. Obtained results show significant influence of the anisotropic variable ratios of deep brain sources reaching values of $12\,mm$ and $60\,deg$ for DLE and DOE, respectively.

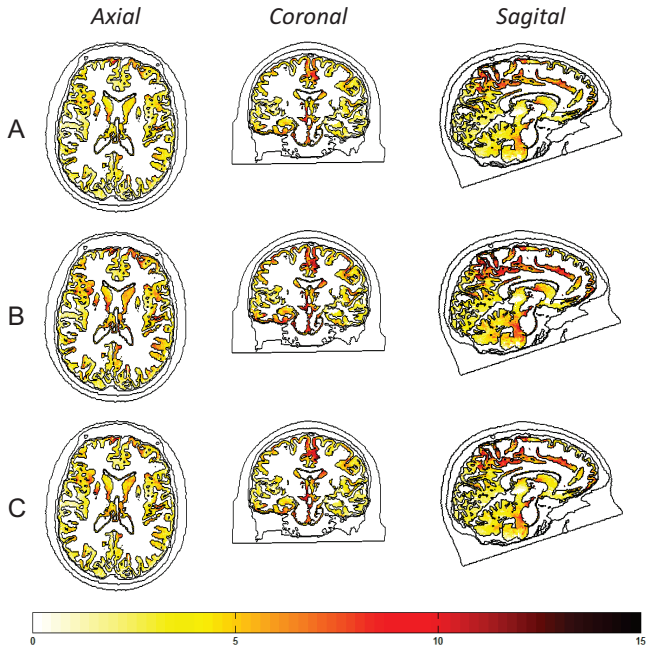

Fig. 2. Estimated DLE values for all considered simulations.

To get a better interpretation about the influence of the considered anisotropic model, Fig. 2 shows performed DLE values, where each row represents each one of the described above simulations, while the columns display three different plane views (Axial, Coronal, and Sagittal). As seen in the coronal and sagittal views, the largest DLE values are in brain deeper zones (namely, in the corpus callosum). Particularly, the more surrounded by white matter tissue the sources are - the higher the DLE value, as seen in interhemispheric space of the coronal view as well as in the corpus callosum of sagittal view.

From estimating the spatial distribution of DLE, one may infer that anisotropic modeling that assumes variable rates might be not necessary in general cases of study where concrete brain regions do not matter. In contrast, analysis and localization of deep sources neighboring white matter tissue should be more accurately modeled, particularly, using the proposed anisotropic variable rate assumption. This may be the case of the Parkinson disease [8].

V. Conclusions and Future Work

We study the influence of the anisotropic white matter within the EEG source localization problem. To this end, we consider three cases of the anisotropic white matter modeled by either fixed or variable ratio. Information about highly anisotropic areas of the white matter is extracted from real DWI data. To validate the compared anisotropic models, we introduce the dipole and orientation errors.

Obtained results show that the white matter model with a fixed anisotropic ratio leads to DLE values close to $1\,cm$ and may be enough in those cases avoiding localized analysis of neural brain activity. In contrast, modeling based on the anisotropic variable rate assumption becomes important in tasks regarding analysis and localization of deep sources neighboring the white matter tissue.

As a future research, we plan to analyze the EEG source localization errors using state of the art inverse solution such as *multiple sparse priors* approach [3] employing the white matter conductivity models of this work.

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