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Anisotropic Partial Volume CSF Modeling for EEG Source Localization

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Abstract

Electromagnetic source localization (ESL) provides non-invasive evaluation of brain electrical activity for neurology research and clinical evaluation of neurological disorders such as epilepsy. Accurate ESL results are dependent upon the use of patient-specific models of bioelectric conductivity. While the effects of anisotropic conductivities in the skull and white matter have been previously studied, little attention has been paid to the accurate modeling of the highly conductive cerebrospinal fluid (CSF) region.

This study examines the effect that partial volume errors in CSF segmentations have upon the ESL bioelectric model. These errors arise when segmenting sulcal channels whose widths are similar to the resolution of the magnetic resonance (MR) images used for segmentation, as some voxels containing both CSF and grey matter cannot be definitively assigned a single label. These problems, particularly prevalent in pediatric populations, make voxelwise segmentation of CSF compartments a difficult problem. Given the high conductivity of CSF, errors in modeling this region may result in large errors in the bioelectric model.

We introduce here a new approach for using estimates of partial volume fractions in the construction of patient specific bioelectric models. In regions where partial volume errors are expected, we use a layered gray matter-CSF model to construct equivalent anisotropic conductivity tensors. This allows us to account for the inhomogeneity of the tissue within each voxel. Using this approach, we are able to reduce the error in the resulting bioelectric models, as evaluated against a known high resolution model. Additionally, this model permits us to evaluate the effects of sulci modeling errors and quantify the mean error as a function of the change in sulci width.

Our results suggest that both under and over-estimation of the CSF region leads to significant errors in the bioelectric model. While a model with fixed partial volume fraction is able to reduce this error, we see the largest improvement when using voxel specific partial volume estimates. Our cross-model analyses suggest that an approximately linear relationship exists between sulci error and the error in the resulting bioelectric model. Given the difficulty of accurately segmenting narrow sulcal channels, this suggests that our approach may be capable of improving the accuracy of patient specific bioelectric models by several percent, while introducing only minimal additional computational requirements.

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Keywords

electromagnetic; source; localization

1. Introduction

Using non-invasive voltage measurements from scalp electrodes, EEG source localization (ESL) can estimate the underlying pattern of current activity present within the brain (Salmelin and Baillet (2009)). This capability is used clinically in the identification of seizure foci for surgical planning in epilepsy (Plummer et al. (2010); Michel et al. (2004); Brodbeck et al. (2010)), as well as in neurology research to pinpoint the location of evoked potentials (Bocquillon et al. (2011)). In both cases, precise localization is dependent upon the construction of accurate models of electrical propagation (Wolters et al. (2006); Huiskamp et al. (1999)). The models used frequently by clinical software represent the head as a series of three concentric spheres, and fail to account for the unique geometry of each patient (Hallez et al. (2007); Vallaghé and Clerc (2009)). Advanced magnetic resonance (MR) imaging studies and image processing algorithms provide the structural information necessary to construct patient specific electrical models. Previous studies have shown that incorporating this information about tissue structure and anisotropy can result in significant improvement to the bioelectric model (Wolters et al. (2006); Rullmann et al. (2009); Güllmar et al. (2010)). When these models are used to construct the lead field matrices relating electrode voltage measurements to cortical current activity, improved modeling can lead to subsequent improvements in the accuracy of resulting source localizations.

While the effects of skull and white matter anisotropies have previously been examined (Haueisen et al. (2002); Marin et al. (1998)), one aspect of patient specific modeling which has yet to be addressed is the importance of accurately modeling the cerebrospinal fluid (CSF) region. With a well established conductivity of 1.79 S/m, CSF is significantly more conductive than the brain tissue it surrounds (Hallez et al. (2007)). Furthermore, the skull has a significantly lower conductivity than either the brain or CSF regions. This combination of layers results in a low pass filter effect which significantly reduces the spatial resolution of the EEG signal as it propagates from cortex to scalp. Additionally, CSF extends deep into the sulci, potentially offering a rapid propagation path for currents located deep within the brain. However, accurate automated segmentation of sulci from MRI images is a difficult problem, particularly in a pediatric population. Partial volume effects within narrow sulci can result in the mislabeling of sulcal voxels as cortical tissue. This mismatch between model and physical reality will result in inaccurate modeling of electrical propagation, and subsequently introduce error into the source localization images.

In this study, we investigated the effects of partial volume errors on the modeling of CSF filled sulci regions. When computing voxelwise brain segmentations, partial volume effects can make accurate identification of sulcal CSF extremely difficult. Modern MRI imaging protocols typically have spatial resolution on the order of 1mm, however many sulcal channels can have widths which are equal to or narrower than this. In such cases, it can be difficult or impossible to determine whether a particular voxel should be labeled as grey matter or CSF. In many cases, neither label is suitable, as the voxel in question is in fact a mixture of both types. In such cases, no segmentation algorithm is capable of properly modeling the true structure of the brain using singularly labeled voxels alone.

To help compensate for improperly modeled sulci, we introduce an approach for constructing anisotropic conductivities within voxels fractionally composed of grey matter and CSF. When a voxel in the MR image covers both grey matter and CSF regions, the

effective conductivity within that voxel will best be represented as an anisotropic tensor. At the boundary between the grey matter and CSF, the fine scale structure of the regions will be well described using multiple parallel layers. The key to using this information in the construction of a coarse scale bioelectric model is the identification of potential sulci locations and the associated grey matter surface normals. Together, these allow layered models to be constructed at each voxel, representing the effective anisotropic conductivities resulting from partial volume effects. To achieve this, we employ a voxel based approach for processing segmentation images to extract previously unidentified sulci locations (Hutton et al. (2008)). This algorithm repeatedly solves Laplace's equation to determine tissue thicknesses as a grey matter volume is iteratively constructed layer by layer. After each iteration, thickness greater than expected from the current number of layers will result from the opposite sides of sulci coming into contact with one another. These voxels are labeled as potential sulci locations. Streamlines are also computed as a byproduct of solving Laplace's equation, and these can be used as estimates of the grey matter surface normal at each point. Estimates of the partial volume fractions of gray matter and cerebrospinal fluid are used to construct a layered model with an overall anisotropic conductivity.

To compute the accuracy of our anisotropic sulci model and compare it and other anisotropic approximations against a known ground truth model, we use a finite difference method (FDM) approach which allows for arbitrary anisotropic conductivities within each voxel (Saleheen and Ng (1997)). Using this approach, we construct a bioelectric propagation model at the full resolution of the structural MRI scans (approximation 1mm isotropic voxels). Solution of the FDM problem is then achieved using the preconditioned conjugate gradient (PCG) method. We use the relative difference metric and magnitude error to evaluate the performance of each model, as compared against one another as well as against a high resolution "ground truth" model. These provide us with three dimensional maps of model error, from which we examine the mean and standard deviation of errors within the cortical tissue, where the EEG signals of interest arise. Our results indicated that failing to accurately identify the location of CSF filled sulci can have a substantial effect upon the resulting structure of the lead field matrices. Using anisotropic conductivities in sulci regions results in a significant reduction in the both the magnitude and topography errors see throughout the head. The resulting improvement in the accuracy of the overall lead field model will subsequently be reflected in improvements to source localization accuracy.

2. Methods

2.1. MRI Data Collection

T1 and T2 weighted MRI scans were collected from an 18 year old male epilepsy patient using a Siemens Magnetom 3T scanner. The MRI protocol was based on routine clinical imaging, extended with diffusion imaging (DWI). The imaging protocol included isotropic 1×1×1 mm 3D MPRAGE T1w images obtained with a 32-channel head coil (24cm FOV, 1.0mm thick contiguous slices, sagittal slices covering the entire head, TR/TE=1410ms/2.27ms, matrix 256×256, TI=800 ms, flip angle=9 deg, iPAT = 2), requiring a scan time of approximately 6 min; a high resolution T2-weighted image will be acquired utilizing a T2 TSE sequence (24cm FOV, 1.0mm thick contiguous slices covering the entire brain, TR/TE=3000/80 ms, 256×256 matrix, 1 NEX, iPAT=2) requiring a scan time of approximately 6 min; a 3D FLAIR sequence providing visualization of potential lesions (240mm FOV, 1.0mm thick contiguous slices, TR/TE=6000ms/386ms, matrix 256×256, iPAT=2) requiring about 7 min; diffusion imaging (Reese et al. (2003)) acquired in the axial plane, utilizing 30 images with b=1000 s/mm² and 5 b=0 images (22 cm FOV, slice thickness=2.0mm, TE=88 ms, TR=10s, 128×128 matrix, 1 NEX, iPAT=2, modified as necessary to facilitate completion of the scan if the subject was unable to remain perfectly still).

2.2. Registration and Image Segmentation

A segmentation of the intracranial cavity and a tissue class segmentation (gray matter, white matter, cerebrospinal fluid) were created from the structural MRI (Grau et al. (2004); Weisenfeld and Warfield (2009)). Compensation for residual distortion and patient motion in the DWI was achieved by aligning the DWI to the T1w MPRAGE scan, with appropriate reorientation of the gradient directions (Ruiz-Alzola et al. (2002); Peters et al. (2012)). Tensors were estimated using robust least squares, and were displayed via color-coding (Doeke et al. (1991)).

The scalp compartment for the bioelectric model was generated by applying a manual threshold to the T1 weighted MR image, with any holes filled using a morphological approach. Lacking an anatomically accurate skull segmentation, we generated the skull regions by dilating the inter cranial cavity generated during the tissue class segmentation. This creates a skull region which reasonably approximates the true bone volume, and allows for accurate computations.

2.3. Finite Difference Model

Accurate simulation of electrical propagation within the brain requires numerical solution of Maxwell's equations on an inhomogeneous, anisotropic medium.

$$\nabla \cdot (\sigma \nabla \Phi) = -\nabla \cdot \mathbf{j} \quad \text{in } \Omega \quad (1)$$

here, $\mathbf{j}$ are the cortical current sources, σ is the spatially varying conductivity within the head, and Φ is the voltage potential, and Ω is the physical head region. On the head surface ($\Gamma = \partial\Omega$), Neumann boundary conditions apply:

$$(\sigma \nabla \Phi \cdot \hat{n})|_{\Gamma} = 0 \quad (2)$$

To achieve this, we use a finite difference (FD) approach which allows for the incorporation of arbitrary anisotropic conductivities within each computational node (Saleheen and Ng (1997)). This approach uses a transition layer technique to ensure that the finite difference representation of Poisson's equation is valid at every point within the volume. The resulting computational nodes are located at the corners of each voxel within the computational grid. Every computational node fully enclosed in the volume thus has eighteen neighbors, and a total of 19 nonzero values in the associated row of the finite difference matrix. The resulting large scale linear algebraic system was solved using a preconditioned conjugate gradient approach.

2.4. Assignment of Tissue Conductivities

Each element in the finite difference model corresponds to a voxel in the segmented MR image, and must be assigned a conductivity tensor. For the grey matter, CSF, skull, and soft tissue regions, we assume the conductivity to be isotropic. For these regions, the following conductivities were used (Hallez et al. (2007)): soft tissue = $0.33 S/m$, skull = $0.012 S/m$, CSF = $1.79 S/m$, and gray matter = $0.33 S/m$.

2.4.1. White Matter Anisotropy—Conductivity within white matter tracts has previously been shown to be directly related to the diffusion tensors measured by dtMRI (Tuch et al. (2001)). We use the method developed by Tuch to compute anisotropic conductivity tensors for each white matter element from the corresponding coregistered diffusion tensor image, using the full fractional linear relationship to relate the diffusion and conductivity tensors (Tuch et al. (2001)). An eigen-decomposition of the diffusion tensor is first obtained, and the

eigenvalues of the diffusion tensor are related to the eigenvalues of the conductivity tensor as:

$$\sigma_v = \sigma_e \left[1 + \frac{3(d_v - d_e)(\beta_d + 2)}{d_v(4\beta_d^3 - 5\beta_d - 2) + d_e(8\beta_d^3 - 7\beta_d + 2)} \right] \quad (3)$$

where σ_v is the conductivity tensor eigenvalue to be computed, d_e is the extracellular diffusion coefficient, d_v is the measured diffusion tensor eigenvalue, and β_d is a dimensionless contrast factor defined as $\beta_d = (d_i - d_e)/(d_i + 2d_e)$ with d_i being the intracellular diffusion coefficient. We use values of $d_i = 0.117$, $d_e = 2.04$ and $\sigma_e = 1.52$ as established in (Tuch et al. (2001)). The diffusion tensor image was thus used to compute the conductivity tensor within each voxel identified as white matter by the segmentation procedure.

2.5. Anisotropic Conductivities for Partial Volume Effects

To account for partial volume effects in sulci regions, we use an approach which generates anisotropic conductivities for voxels expected to contain partial volume artifacts. This approach can be summarized in three steps:

1. Use a voxel based approach to extract probable sulci locations.
2. Compute a conductivity tensor based on a layered model and the CSF volume fraction
3. Define a transform to shift the conductivity tensor from the coordinate system in which it was defined to the coordinate system of the overall problem.

2.5.1. Sulci Identification—We use the method from (Hutton et al. (2008)) to extract sulci locations missed during the initial statistical segmentation of the collected MR images. Originally developed as a voxel based approach for computing cortical thicknesses, we use this algorithm to identify the probable locations of sulci missed during the original segmentation procedure due to partial volume effects.

The algorithm functions by iteratively adding single voxel layers of cortex atop the underlying white matter. Following the addition of each layer, every newly added voxel is checked to determine whether its addition closes the two side of a sulcus together. This check is based upon comparing the current cortical thickness at each voxel against the expected cortical thickness, given the current number of cortical layers which have been added. When the thickness at a newly added cortical voxel is found to be higher than expected, this will be due to the two sides of a sulcus coming into contact. The voxels where this occurs are labeled as sulci voxels, and the next iteration begins with the addition of another layer of cortex.

To determine cortical thicknesses, Laplace's equation is solved on the current cortical layer and gradient streamlines are evaluated. We then used a Eulerian PDE approach (Yezzi and Prince (2003)) to compute tissue thicknesses from these streamlines. Note that this differs from the integrated trajectory approach used in (Hutton et al. (2008)).

To ensure accurate identification of sulci with physically appropriate topology, we have added two additional steps to this procedure. First, after growing the current cortical layer, we additionally allow the current sulci regions to grow into voxels that have not been labeled by the algorithm. The assumption here is that if the addition of a new cortical layer does not completely bury the existing sulcal voxels, that those voxels are part of a wide sulcus, and available neighbors are sulci voxels as well. This helps to expand the sulci into relatively large internal regions of CSF, such as within the lateral (Sylvian) fissure.

Second, in addition to checking the thickness of potential cortical voxels, we also check to ensure that the topology of the cortex will not be altered by the addition of any individual voxel. Because the cortex exists as a single layer atop the white matter, the two regions will share the same topology. By checking that the topology of the cortex does not change as additional layers are added, we prevent sulci from being closed off, and ensure that the sulci will be continuous regions.

Figure 3(b) shows the segmentation as originally obtained from the MR images. The final segmentation after model-based sulci extraction is seen in Figure 3(c). Note that there are a significant number of sulci visible in the T1 images of 3(a) that are not seen in the original segmentation. These appear clearly after the model based sulci extraction, however the extent of these sulci appears to be overestimated. This suggests that modeling the detected sulci as purely CSF is inappropriate, and that a mixed model of grey matter and CSF will be required to obtain optimal results.

2.5.2. Partial Volume Anisotropic Conductivities—We now seek a method by which we can assign an anisotropic equivalent conductivity tensor to each voxel identified as sulci by the above extraction procedure. Note that these anisotropic conductivities are used only within identified sulci, and voxels labeled as CSF by the original tissue class segmentation are treated as fully comprised of CSF. To construct our model, we assume first that each identified sulcal voxel is comprised of some fraction of CSF. Because the cortex forms a smooth 3D sheet, the CSF layer within the sulci will likewise form a single continuous layer, parallel to the surface of the cortex. Within a voxel, the presence of CSF can significantly alter overall conductivity, particularly along directions which coincide with the cortical surface.

To construct anisotropic conductivities, we assume that the distribution of grey matter and CSF within each individual voxel can be modeled using a multi-layer approach as shown in Fig 4(a). Here, we see a layer of CSF (light grey), sandwiched between two layers of grey matter. We assume that for some choice of coordinate system, the local geometry fits this model. Note that the number and ordering of layers is unimportant, as long as all layers are similarly oriented. To construct a conductivity tensor in this coordinate space, we need to compute a conductivity along each of the primary axes. Looking at Fig 4(a), we can see that the flow of electricity along the Y and Z-axes will be parallel to the planes of CSF and grey matter. We can thus use parallel circuit theory to compute the overall conductivity along these axes as:

$$\sigma_{yz} = f_{csf} \sigma_{csf} + (1 - f_{csf}) \sigma_{grey} \quad (4)$$

Here, f_{csf} is the fraction of the voxel filled with CSF, $\sigma_{csf} = 1.79 S/m$ is the conductivity of CSF, and $\sigma_{grey} = 0.33 S/m$ is the conductivity of grey matter. To compute the conductivity along the X-axes, we note that the flow of current will be across the CSF and grey matter planes, resulting in a series electric circuit. This allows us to compute the conductivity along the X-axes using the equation:

$$\sigma_x = \frac{\sigma_{csf} \sigma_{grey}}{f_{csf} \sigma_{grey} + (1 - f_{csf}) \sigma_{csf}} \quad (5)$$

With conductivities along each of the primary axes computed, we can construct a conductivity tensor in this coordinate space based on the fraction of CSF within the voxel as:

$$\mathbf{S} = \begin{bmatrix} \sigma_x & 0 & 0 \\ 0 & \sigma_{yz} & 0 \\ 0 & 0 & \sigma_{yz} \end{bmatrix} \quad (6)$$

This approach will result in conductivity tensors which are interpolated between being fully CSF filled (Isotropic with $\sigma = 1.79\text{S/m}$) and fully gray matter (Isotropic with $\sigma = 0.33\text{S/m}$), as shown in Figure 4(c).

The computed equivalent conductivity tensor is, however, only valid within the particular coordinate system where the multilayer model is satisfied. That is, the coordinate system where the X-axis is perpendicular to the layers of the model, and the Y and Z-axes are parallel to it. This is an assumption which will in general not be satisfied at most voxels within a realistic model. The X-axis in this system corresponds to the cortical surface normal. Thus, within an individual patient's bioelectric model, the resulting conductivity tensor must be rotated by an orthogonal bases transform to properly orient it with the cortical surface.

2.5.3. Coordinate Transform—To construct the transform, we use supplemental information generated during the sulci detection process. After Laplace's equation is solved, gradients are computed to obtain the streamlines. These gradients can be interpreted as surface normals, and provide sufficient information to estimate the orientation of the CSF plane within the detected sulci voxels.

For each voxel we compute this estimate using the surface normals at each of its 26 neighbors. A matrix containing all normal vectors is constructed as:

$$\mathbf{M} = \begin{bmatrix} x_1 & x_2 & \dots & x_{26} \\ y_1 & y_2 & \dots & y_{26} \\ z_1 & z_2 & \dots & z_{26} \end{bmatrix} \quad (7)$$

where the triplet (x_i, y_i, z_i) represents the normal vector at the i^{th} neighboring voxel. Note that in many cases, some of these triplets will be composed entirely of zeros, because the corresponding voxel is labeled as sulci or CSF, rather the grey matter in the cortex. Inclusion of these zeros within the matrix $\mathbf{M}$ does not affect the resulting computations.

Taking the compact singular value decomposition of the matrix $\mathbf{M}$ yields:

$$\mathbf{M} = \mathbf{U} \sum \mathbf{V}^T \quad (8)$$

where $\mathbf{U}$ is a 3×3 matrix of vectors defining the principal components of the neighboring normal vectors. The first principal component is used as an estimate of the cortical surface normal within the partial volume voxel under consideration.

The final anisotropic conductivity tensor is constructed by using the principal components to rotate the tensors $\mathbf{S}$ into the appropriate orientation:

$$\mathbf{S}_{\text{final}} = \mathbf{U} \mathbf{S} \mathbf{U}^T. \quad (9)$$

This process was repeated for each voxel that the sulci detection procedure identified as being partially CSF filled. This process is diagrammed in Figure 4(b). Here, the gray discs represent the estimated cortical surface plane at each neighboring cortical voxel, and the red

ellipsoid denotes the anisotropic conductivity tensor after rotation from the coordinate space of Eq(6), where it was generated, into a space appropriate for the cortical geometry. For this example, a partial volume fraction of $f_{csf} = 0.5$ was chosen as it results in a tensor whose orientation in three dimensions is easily seen. Note that only 11 cortical surface patches are shown, as the remaining 15 neighboring voxels are CSF filled, and thus do not contribute to the estimate of the cortical surface orientation.

2.6. Simulation Setup

To act as ground truth for comparison, a high resolution finite difference model was created at twice the resolution of the original MRI scans (0.5mm isotropic voxels). This model was initially generated as a direct $2\times$ upsampling of the segmented MR image. Additional sulci were then manually added to simulate features too small to be identified and segmented at the original MRI resolution. This entailed adding single voxel wide sulci to the segmentation image, using the T2 weighted MR as a guide. Figure 5(a) shows slices from this model after the addition of the 0.5mm sulci. A histogram of the partial volume fractions of voxels within the identified sulcal regions is shown in 5(b). The mean volume fraction was 0.2048, with a standard deviation of 0.2441.

Because the model at $2\times$ resolution has on the order of $134\epsilon 6$ elements and requires in excess of 100GB of memory space to execute computations, additional steps are necessary to obtain a computationally tractable problem. To achieve this, we use a geometric multi grid approach to move the problem from the high resolution 0.5mm grid back to the original 1mm grid of the MRI (Wolters et al. (2002)). Restriction and prolongation operators are defined, which define maps between the fine and coarse grids using averaging (restriction) and interpolation (prolongation), and are subsequently applied to the finite difference matrix at the fine resolution grid as:

$$\mathbf{K}_c = \mathbf{L}_r \mathbf{K}_f \mathbf{L}_p \quad (10)$$

Here, $\mathbf{K}_f$ is the FDM matrix on the fine grid, $\mathbf{L}_p$ is the prolongation matrix mapping from coarse to fine grid, and $\mathbf{L}_r$ is the restriction matrix mapping from fine to coarse grid. The resulting matrix $\mathbf{K}_c$ is a finite difference matrix defined at the original resolution of the MRI (And therefore represents a computationally tractable problem), while still incorporating information from the high resolution model.

A further twelve models were constructed, using our anisotropic conductivity approach. Eleven of these were constructing using a single CSF partial volume fraction at all sulcal voxels in the head. This fraction was set between 0 and 1, in steps of 0.1. The final model used voxel-specific partial volume fractions. For the purpose of this study, we assumed these fractions to be known, and extracted them directly from the high resolution model.

Simulations and analyses used a pattern of 128 electrodes corresponding to the Electrical Geodesics Hydrocel GSN 128 (Electrical Geodesics Inc., Eugene OR). A reference electrode located immediately posterior to C_z (Electrode 80 in the EGI net) was used for all computations. Electrode locations were identified using photogrammetry, and coregistered to the subjects head using a previously described approach (Spiclin et al. (2008)). The lead field matrix relating cortical currents and scalp voltages was then generated using the lead field bases approach (Weinstein et al. (2000); Hallez et al. (2007)). For each of the remaining 127 electrodes, the associated row of the lead field matrix was computed by solving the finite difference problem with a positive current injected at the electrode under consideration and a negative current at the reference electrode. Solution of the large scale linear system yields a map of the voltages induced within the head, the gradient of which

reflects the sensitivity of a voltage measurement between the two electrodes to current activity within the head. Because the EEG signal is primarily cortical in nature, arising from pyramidal neurons oriented perpendicular to the surface of the cortex, we further constrained the lead field matrix to only those voxels within the cortex, and constrained the direction of the dipole using the extracted cortical surface normals.

2.7. Comparison Metrics

Two statistical metrics are used for quantitative comparison of the constructed lead field matrices (Meijs (1989)). The first of these is the relative difference metric (RDM):

$$\text{RDM} = \sqrt{\sum_{i=1}^m \left(\frac{u_a^{[i]}}{\sqrt{\sum_{i=1}^m (u_a^{[i]})^2}} - \frac{u_b^{[i]}}{\sqrt{\sum_{i=1}^m (u_b^{[i]})^2}} \right)^2} \quad (11)$$

Here, u_a and u_b are the two quantities being compared, both being vectors of length m . The normalization of each component term makes the RDM a measure of the topographical error between the two signals being compared with minimum $\text{RDM} = 0$.

While the RDM measures the relative difference in topography between the two data sets, the magnitude error (MAG):

$$\text{MAG} = \frac{\sqrt{\sum_{i=1}^m (u_b^{[i]})^2}}{\sqrt{\sum_{i=1}^m (u_a^{[i]})^2}}, \quad (12)$$

measures the overall difference in expected intensity and has minimum $\text{MAG} = 1$. Because MAG is minimized at $\text{MAG} = 1$, and can take on values both higher and lower than this value, we compute mean values using the formula:

$$\text{mean(MAG)} = \frac{1}{m} \sum_{i=1}^m 10^{(\log_{10}(\text{MAG}_i))}. \quad (13)$$

Mean MAG values will thus always be greater than one, but still represent the mean error in magnitude across the volume.

For our analyses, the RDM and MAG metrics were applied to compare corresponding columns from lead field matrices from two different bioelectric models. The values in a particular column of lead field matrices are the sensitivities of all electrode voltage measurement to the presence of electrical current at a particular point within the head. For each comparison between two models, this resulted in a single RDM and MAG value for each spatial point within the cortical grey matter.

This choice of metrics measures how the topography and magnitude of the modeled electrode voltages will change based on model selection. The ideal goal being to construct an approximate model based solely on the MR data that results in RDM measures as close to 0 and MAG metrics as close to 1 as possible. To quantify the distribution of RDM and MAG volumes across each tissue type, we approximate the distributions as Gaussian, and examine the means and standard deviations.

3. Results

This study was designed to evaluate both the impact of mislabeling cerebrospinal fluid regions in deep sulci due to partial volume effects and the potential for using anisotropic conductivity tensors to correct for the resulting error. To achieve this, we constructed lead field matrices for each of the twelve bioelectric models described above. These matrices were compared against one another to generate MAG and RDM values at each spatial point in the cortex. Two sets of comparisons were made. The first used the models with fixed CSF volume fraction and compared these against one another. This yields a measure of the change in model accuracy as the relative size of sulci is changed. The second set compares the model generated using the known high resolution model with each of the fixed volume fraction models as well as the model using voxel specific volume fractions. This comparison evaluates our models potential to compensate for errors introduced when partial volume effects make labeling of mixed CSF/grey matter voxels difficult.

3.1. Fixed Volume Fraction

We first evaluated the effects of using a fixed volume fraction within each sulci element. By ranging the volume fraction of CSF from 0 to 1, we can examine the changes in the model as we shift from treating the original segmentation as correct to treating the extracted sulci as being fully filled with CSF.

Figure 6 displays plots of the mean magnitude (MAG) and topographic (RDM) error between all pairs of models with fixed volume fractions. Because changing the volume fraction allows interpolation between fully closed (PV=0) and fully open (PV=100) sulci, these plots demonstrate and quantify how errors in sulci modeling can potentially affect the resulting lead field matrices. Fig 6(a) and (c) both show an approximately linear relationship relating CSF fraction to the resulting MAG and RDM errors. Plotting the difference in CSF fraction against RDM and MAG errors yields plot 6(b) and 6(c), to which linear fits can be applied to obtain $MAG = 0.002595 * DIFF + 1.007$ with $R^2 = 0.9774$ and $RDM = 0.00144 * |DIFF| + 0.01321$ with $R^2 = 0.9684$, where DIFF represents the difference in volume fraction between the two models. This suggests that every 10% error in modeling the size of the CSF spaces will yield approximately a 2.5% magnitude error and a 1.5% topographic error in the resulting lead field matrix.

3.2. High Resolution Model

Our second analysis compared the eleven models with fixed partial volume fraction, as well as the model with voxel specific volume fractions, against the “true” high resolution model. While this is a purely synthetic model, it provides an ideal situation to evaluate the capacity of our anisotropic conductivity model to compensate for partial volume errors in sulcal regions. Because the true geometry and CSF volume fractions are known, this allows us to evaluate our algorithm in an ideal case. With patient data, it is impossible to know with absolute certainty where the errors in segmentation lie, and estimates must be made of the partial volume fractions.

Figure 7 charts the mean magnitude error for each of the models, and displays both a 3D full brain rendering and as well as individual slices of the error at individual voxels. Minimum average MAG error of 1.0799 is obtained with a fixed partial volume fraction of 40%. This is actually less than the mean error of 1.0903 with the voxel specific volume fractions, although the individualized model has a lower standard deviation (STD = 0.0731, as opposed to STD = 0.0787 with a fixed 40% fraction), and a mean error which is nearly as low as the 40% model. In both cases, the mean magnitude error is significantly lower than is

seen with the original segmentation ($MAG = 1.1490$). This represents a 46% reduction in error for the 40% fixed fraction model, and a 39% reduction for the individualized model.

While magnitudes are both over and underestimated in all cases, the majority of voxels have their intensity overestimated by this approach ($MAG > 1$), as demonstrated in Figure 8. Minimum and maximum MAG values were approximately the same across all models (Minimum 0.25, maximum 2.6), the number of voxels with outlying MAG values varied widely. With the original segmentation, there were 95 voxels with 100% or greater magnitude error ($MAG > 2$ or $MAG < 0.5$), while the 40% fixed model had on 33 such voxels, and the model with individualized volume fractions had only 10. Tightening the error bound to 50% ($MAG > 1.5$ or $MAG < 0.6667$) resulted in 24413 voxels being identified in the model based on the original segmentation, 2073 voxels in the fixed 40% model, and only 719 voxels in the full partial volume model. So, while the mean values are marginally improved, the number of outlying voxels is significantly reduced by using individualized volume fractions.

The 3D rendering in Figure 7 shows an overall decrease in magnitude error when using voxel specific partial volume fractions (as compared to using the original segmentation which is missing a large number of sulci). The largest magnitude errors are seen directly within the sulcal regions, with errors decreasing as the inner and outer boundaries of the grey matter are reached. Interestingly, those voxels whose magnitude was underestimated lie primarily deep within the brain at the interface between grey and white matter. Overall, the errors are spread relatively evenly throughout the brain, however the maximum errors appear along the inferior surface of the brain far from the electrodes, as well as in the CSF spaces dividing the two hemispheres. This underestimating of the impact of deeply situated sources, while simultaneously overestimating the effect of superficial sources may in part explain the difficulty in accurately localizing activity from deep cortical sources.

A corresponding set of images for the RDM metric are shown in Figure 9. For the RDM, minimal error of 0.0605 is obtained when using voxel specific partial volume fractions. This value is approximately 13% lower than the best fixed volume fraction model, 30%, which has a mean error of 0.0696, and is 24% lower than the 0.0798 mean RDM obtained with the original segmentation. Also of note is that the voxel specific model sees a decrease in standard deviation as compared to the fixed fraction models ($STD = 0.0398$ with individual fractions, while $STD = 0.0433$ and $STD = 0.0542$ for the fixed 30% model and original segmentation, respectively).

Similarly to magnitude, the minimum and maximum RDM seen in each model was approximately the same (Min 0.005, Max 1.75) and improving the model significantly reduced the number of voxels with outlying RDM values, as seen in Fig 10. The original segmentation resulted in a model with 1008 voxels exhibiting an RDM greater than 0.5, while the fixed 40% model had 769, and the full partial volume model had 343. Using a cutoff RDM of 0.25, those numbers increased to give the original segmentation 15079 voxels, the 40% model 15210, and the full partial volume model 4761.

As with the MAG, there is a general decrease in RDM seen across the brain, with the greatest improvements coming within the identified sulcal regions. Again, deep sulci and the inferior surface of the brain show the largest errors. In many of the deeper sulci, RDM errors can consistently be as high as 10% or more.

4. Discussion

We have presented here an analysis of the effects of sulci modeling on the lead fields generated for electromagnetic source localization. A realistic five compartment head model

was generated from segmentation of high resolution structural MRI, and anisotropic white matter tracts were obtained from dtMRI. Coupled with a finite difference model capable of incorporating arbitrary anisotropic conductivities, we computed a range of models to investigate the effects of error in the modeling of sulcal CSF regions. Using the relative difference metric and magnitude errors, we examined the effects of changing sulci width on the resulting lead field matrices, thereby generating three dimensional maps of model error.

Our results suggest that accurate modeling of CSF within narrow sulcal channels is important to the overall accuracy of the bioelectric model. Minor changes in the structure of these regions can lead to significant average error across the cortex, with individual cortical voxels exhibiting higher error levels. A cross analysis of models with differing degrees of anisotropy within sulci enabled us to establish a linear relationship between the average error in the width of the sulcal channels and the resulting topographic and magnitude error seen in the lead field matrix. This comparison is of particular importance because changes in the lead field matrix will likely be reflected in alterations to the source localization images. The importance of accurate CSF modeling further indicates the importance of patient specific modeling in general. While atlas based approaches will offer an improvement over current clinical standard three shell models, the lack of patient specific detail will limit the overall accuracy. Particularly in a patient population being evaluated for epilepsy surgery, the prevalence of genetic malformations and previous resection surgeries will make patient specific modeling even more critical.

To help compensate for the errors induced by sulcal CSF spaces with partial volume artifacts, we introduced an approach which uses anisotropic conductivity tensors within voxels expected to be fractionally composed of both grey matter and CSF. This approach uses extracted cortical surface normals and a parallel layer model to compute equivalent anisotropic conductivity tensors. While even a globally fixed partial volume fraction was capable of offering improvements over the originally segmented image, the greatest reduction in error was seen with a model implementing individual estimates of CSF fraction at each voxel. Obtaining these estimates in a real world situation should be of relatively minimal difficulty when otherwise implementing patient specific bioelectric models. Statistical segmentation approaches will frequently generate probability maps for each tissue type as part of their intermediate computations. The final segmentation is generated as the maximum likelihood from this map, but relative probabilities of CSF and grey matter could be used directly as estimates of the partial volume fractions. The only additional computation required by such a model would be determining the orientation and magnitudes of the anisotropic conductivity tensors associated with each partially volumed voxel.

Magnitude and topography errors were greatest within those voxels affected by partial volume effects. In general, magnitude errors were generally greater than 1, indicating an overestimation of the voxel's contribution to the EEG signal. By itself, magnitude error will not necessarily impact the resulting source localizations. If, for example, all voxels had identical magnitude error, it would be equivalent to applying a scaling factor to the lead field matrix, and would only be of importance if trying to obtain precise quantitative measurements of cortical currents. Inhomogeneity in magnitude, however, will potentially disrupt localizations, as incorrectly weighting the contribution of individual voxels will result in the current source at that voxel being incorrectly estimated. Relationships between voxels will also be affected, which is of particular importance for distributed localization approaches, which frequently use correlation between neighboring voxels to regularize the problem and constrain the solution space.

Unlike magnitude error, topographic error will always have an effect on localization accuracy. Changing the modeled voltage distribution at the scalp means that the signal

modeled given the true activity will not match the collected data. Because of this fundamental mismatch, there will be some level of error introduced into the solution.

To conclude, this study demonstrates that minor changes to the structure of CSF filled sulci have the potential to yield significant changes in the magnitude and topography of the resulting expected EEG signal. Using anisotropic conductivity tensors within regions affected by partial volume artifacts can help to reduce these errors. While it is safe to assume that changes to the lead field matrix will result in subsequent changes to the source localizations obtained, the question remains regarding what lead field errors induce only minimal changes in localization, and which directly degrade accuracy and should be addressed. Further experiments will be necessary to determine these relationships, by computing localizations using a range of forward models and examine the resulting accuracy of the solutions.

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4. Highlights

- We present a method for bioelectric modelling of sulci using anisotropic conductivities.
- We examine the effects of errors in sulcal segmentation on the bioelectric model.
- Partial volume errors in sulci can cause modelling errors of 30% or more.
- Anisotropic conductivities more accurately model partial volume regions.

Figure 1. Structure MRI Images

Left to right are axial, coronal and sagittal slices for a) the collected T1 weighted image and b) the collected T2 weighted image.

Figure 2. Anisotropic Conductivity Tensors

Fiber orientation is denoted by color, with red denoting left-right, green marking anterior-posterior, and blue being superior-inferior.

Figure 3. Brain Segmentation Before/After Model Based Sulci Extraction

A) Axial, coronal and sagittal slices of collected T1 data used for segmentation. B) Original segmentation obtained using automated procedure. C) Segmentation following model based sulci extraction.

Figure 4. Construction of Partial Volume Anisotropic Conductivities

a) Multi-layer model used to construct anisotropic conductivities. Conductivity along the X-axis (Across layers) will be computed using series conductors, while conductivity along the Y and Z-axes (Parallel to the layers) will use parallel conductors. b) Graphical illustration of the relationship between neighboring normal vectors and the final tensor orientation. Disks represent estimates of cortical surface orientation at each neighboring voxel (i.e.- The plane perpendicular to the normal vector), while the red ellipse is the anisotropic conductivity tensor after rotation into the appropriate cortical plane. A partial volume fraction of $f_{CSF}=0.5$ was chosen to enhance visibility of the tensor orientation. c) Conductivity tensors as f_{CSF} is varied from 0 (entirely grey matter) to 1 (entirely CSF).

Figure 5. Segmentation for High Resolution Model

a) Segmentation for “True” model used as ground truth. Narrow sulci have been added using a selective erosion procedure which created sulci. b) Histogram of CSF partial volume fractions in “true” model for voxels identified as potential sulci. Mean fraction 0.2048, standard deviation 0.2441.

Figure 6. Cross Analysis of Models with Fixed Partial Volume Fraction

Plots of RDM and MAG differences between all pairs of models with fixed volume fraction. In both plots, X and Y axes indicate the percentage of volume occupied by CSF. Curves plotted underneath the surface are isocontours. (a) Plot of magnitude error showing approximately linear relationship between change in volume fraction and MAG error. Note that $MAG(a, b) = 1/MAG(b, a)$. (b) Linear fit to MAG data. Plotting difference in volume fraction against resulting MAG, a linear fit $y = 0.002595x + 1.007$ with $R^2 = 0.9774$ is obtained. (c) Plot of topographic error (RDM) showing a similar nearly linear relationship between volume fraction and error. The plot is symmetric along $X = Y$ because $RDM(a, b) = RDM(b, a)$. (d) Plot of absolute value of difference in volume fraction against resulting RDM. A linear fit results in $y = 0.00144x + 0.01321$ with $R^2 = 0.9684$.

Figure 7. Magnitude Error between Models

a) Mean MAG error and standard deviation for all fixed volume fraction models (blue) and for the model with voxel specific volume fractions (red). b) Full brain and slice images of MAG error for model using original segmentation (PV Fraction = 0). Note that minimum MAG = 1, thus voxels in red overestimate signal magnitude, while those in blue underestimate it. c) Full brain and slice images for model with voxel specific partial volume fractions.

Figure 8. Histogram of Magnitude Errors

Histogram of magnitude error (MAG) for: a) Model built from original segmentation b) Anisotropic sulci with fixed volume fraction of 40% c) Anisotropic sulci with partial volume fractions set for each individual voxel.

Figure 9. Topography Error between Models

a) Mean RDM error and standard deviation for all fixed volume fraction models (blue) and for the model with voxel specific volume fractions (red). b) Full brain and slice images of MAG error for model using original segmentation (PV Fraction = 0). c) Full brain and slice images for model with voxel specific partial volume fractions.

Figure 10. Histogram of Topography Errors

Histogram of topography error (RDM) for: a) Model built from original segmentation b) Anisotropic sulci with fixed volume fraction of 30% c) Anisotropic sulci with partial volume fractions set for each individual voxel.