A New Method to Derive White Matter Conductivity From Diffusion Tensor MRI

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Abstract—We propose a new algorithm to derive the anisotropic conductivity of the cerebral white matter (WM) from the diffusion tensor MRI (DT-MRI) data. The transportation processes for both water molecules and electrical charges are described through a common multicompartment model that consists of axons, glia, or the cerebrospinal fluid (CSF). The volume fraction (VF) of each compartment varies from voxel to voxel and is estimated from the measured diffusion tensor. The conductivity tensor at each voxel is then computed from the estimated VF values and the decomposed eigenvectors of the diffusion tensor. The proposed VF algorithm was applied to the DT-MRI data acquired from two healthy human subjects. The extracted anisotropic conductivity distribution was compared with those obtained by using two existing algorithms, which were based upon a linear conductivity-to-diffusivity relationship and a volume constraint, respectively. The present results suggest that the VF algorithm is capable of incorporating the partial volume effects of the CSF and the intravoxel fiber crossing structure, both of which are not addressed altogether by existing algorithms. Therefore, it holds potential to provide a more accurate estimate of the WM anisotropic conductivity, and may have important applications to neuroscience research or clinical applications in neurology and neurophysiology.

Index Terms—Anisotropy, diffusion tensor MRI (DT-MRI), electrical conductivity, intravoxel fiber crossing, partial volume effects, white matter (WM).

I. INTRODUCTION

In the electroencephalography (EEG) or magnetoencephalography (MEG) based source localization or imaging, the cerebral electrical conductivity is often assumed to be isotropic and piece-wise homogeneous. However, this assumption is not entirely accurate since the conductivity is highly anisotropic within the white matter (WM), wherein the axon fibers connecting neurons are often bundled and directional. Axon bundles form a complicated network of neuronal wiring, and the bundle directions vary dramatically across the WM volume.

Diffusion tensor MRI (DT-MRI) has been shown to provide a new means of mapping the brain conductivity. A hypothesis is often assumed that the electrical conductivity tensor shares the same eigenvectors as the diffusion tensor measurable with DT-MRI [1]. This hypothesis has been further confirmed with a theoretical model [2] that relates the electrical conductivity with the water self-diffusion process using the statistical correlation of the microstructure in a two-phase (i.e., the intracellular and extracellular spaces) anisotropic media [3].

Based on the self-consistent differential effective medium approach (EMA), Tuch et al. deduced a fractional linear relationship between the eigenvalues of the conductivity tensor and those of the diffusion tensor [2], [4]. Replacing the single compartment diffusion model with a multicompartment model, Sekino et al. proposed another algebraic relationship from the Maxwell equations [5], [6]. Although a linear conductivity-to-diffusivity relationship may serve as a sound approximation, direct measurements of the WM conductivity suggest an observable deviation from such an approximation [7], [8]. A linear conductivity-to-diffusivity relationship also fails to consider the partial volume effect in DT-MRI due to the possible presence of the cerebrospinal fluid (CSF), whose conductivity is isotropic and much larger than that of the WM. An alternative method is based on a so-called volume constraint (VC), which constrains the geometric mean of the eigenvalues of the conductivity tensor, so as to avoid some unreasonable conductivity estimation. However, its accuracy may be affected by neglecting the intravoxel fiber crossing [11], [12].

In this study, we propose a new algorithm to extract the conductivity tensor from the diffusion tensor measured by DT-MRI. Both the anisotropic conductivity and diffusivity are accounted for by the same intravoxel microscopic structure. For the first approximation in the macroscopic scale, we model the intravoxel microscopic structure by a discrete multicompartment model. The model coefficients, referred to as the volume fractions (VFs) of multiple compartments, are first computed from the diffusion tensor and then used to estimate the conductivity tensor. We applied this algorithm to the DT-MRI data acquired from two healthy subjects and extracted the anisotropic conductivity distribution. The results were compared with those obtained by using two existing algorithms based upon a linear conductivity-to-diffusivity relationship (Lin) [24] and a VC [10], respectively.

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II. METHODS

A. Self-Diffusion Model

The effective diffusion tensor \( D_{\text{eff}} \) within a voxel is symmetric and positive definite. The eigenvalue decomposition of \( D_{\text{eff}} \) can be written as

\[
D_{\text{eff}} = S_D \cdot \begin{bmatrix}
D_{1\text{eff}} & 0 & 0 \\
0 & D_{2\text{eff}} & 0 \\
0 & 0 & D_{3\text{eff}}
\end{bmatrix} \cdot S_D^T
\]

where \( S_D = [\nu_{D1} \ \nu_{D2} \ \nu_{D3}] \) are the eigenvectors and \( D_i\text{eff} \) are three corresponding eigenvalues \( (D_{1\text{eff}} \geq D_{2\text{eff}} \geq D_{3\text{eff}}) \). The echo attenuation \( E(b) \) for each voxel is given by

\[
E(b) = \exp \left(-b : D_{\text{eff}}\right).
\]

where \( b \) depends on the gradient pulses (timing, amplitude, and shape) in the DT-MRI sequence, and \( \cdot \) stands for the generalized dot product [1], [13], [14].

The cerebral WM is composed of axons and glia bathing in the interstitial fluid (ISF) [15]. The macroscopic diffusion tensor for any WM voxel (typically in a millimeter scale) depends on the combination of individual diffusion processes associated with all the structures within the voxel, including glial cells, ISF, and axons. Since the geometry of glial cells is spherical by approximation [18], the intrinsic diffusion with glial cell barriers can be assumed as isotropic, meaning that it can be described by a diffusion tensor with three equal eigenvalues denoted by \( D_g \).

In contrast, the diffusion process restricted by axon bundles is considered to be rotationally symmetric [19]. Hence, it can be described by a diffusion tensor with the largest eigenvalue \( D_l \), for one direction and two equal eigenvalues \( D_T \) for the other two orthogonal directions [10].

The anisotropic diffusion in a WM voxel arises primarily from the local axon fibers, which may align in a uniform direction or likely in multiple directions due to the intravoxel fiber divergence, convergence, or crossing. Instead of attempting to untangle the complicated fiber configuration in the microscopic scale, we propose to model the intravoxel fiber distribution using three discrete axon compartements aligning along the three orthogonal directions defined by the eigenvectors of the local diffusion tensor. Moreover, by considering the distribution of glial cells as another discrete compartment, the diffusion process within any WM voxel can be modeled as a mixture of diffusion processes within all four compartments (three for axons and one for glial cells). The concept is illustrated in Fig. 1.

Assuming that the exchange across compartments is relatively slow during the diffusion measurement time, the echo attenuations along the three local coordinates can be described as (3) [9], [18], [20]–[23]. (3), as shown at the bottom of page.

\[
f_1 \cdot e^{-bD_T} + f_2 \cdot e^{-bD_T} + f_3 \cdot e^{-bD_T} + (1 - f_1 - f_2 - f_3) \cdot e^{-bD_g} = e^{-bD_{\text{eff}}},
\]

\[
f_1 \cdot e^{-bD_T} + f_2 \cdot e^{-bD_T} + f_3 \cdot e^{-bD_T} + (1 - f_1 - f_2 - f_3) \cdot e^{-bD_g} = e^{-bD_{\text{eff}}},
\]

\[
f_1 \cdot e^{-bD_T} + f_2 \cdot e^{-bD_T} + f_3 \cdot e^{-bD_T} + (1 - f_1 - f_2 - f_3) \cdot e^{-bD_g} = e^{-bD_{\text{eff}}},
\]

\[
f_i \in [0, 1] \quad (i = 1, 2, 3) \quad \sum_{i=1}^{3} f_i \leq 1
\]
σ is linearly related to axon compartment, respectively. The same multicompartment model was used for the electrical conductivity than for the water diffusion. Therefore, intercompartment exchange is effectively much faster for the charges primarily takes place in the extracellular space [4], the electrical conductivity than for the water diffusion. Therefore, we compute the eigenvalues of the effective conductivity as the reference bundles do not fit the WM contaminated by CSF partially experimental noise.

**B. Conductivity Model**

Due to the similarity between the transportation processes of electrical charge carriers and water molecules, the conductivity tensors share the eigenvectors with the measured diffusion tensors [1]. Similar to (1), we can write the effective conductivity tensor as

\[
\sigma_{\text{eff}} = \mathbf{S}_\sigma \cdot \begin{bmatrix}
\sigma_{1\text{eff}}^T & 0 & 0 \\
0 & \sigma_{2\text{eff}}^T & 0 \\
0 & 0 & \sigma_{3\text{eff}}^T
\end{bmatrix} \cdot \mathbf{S}^T_\sigma
\]

where \( \mathbf{S}_\sigma = \mathbf{S}_\delta \).

The same multicompartment model was used for the electrical conductivity. Since the transportation process of electrical charges primarily takes place in the extracellular space [4], the intercompartment exchange is effectively much faster for the electrical conductivity than for the water diffusion. Therefore, we compute the eigenvalues of the effective conductivity as the weighted sums of the conductivity values associated with all compartments, as expressed in

\[
\begin{align*}
\sigma_{1\text{eff}}^T &= f_1 \cdot \sigma_L + f_2 \cdot \sigma_T + f_3 \cdot \sigma_T + f_4 \cdot \sigma_L + f_4 \cdot \sigma_T \\
\sigma_{2\text{eff}}^T &= f_1 \cdot \sigma_T + f_2 \cdot \sigma_L + f_3 \cdot \sigma_T + f_4 \cdot \sigma_L + f_4 \cdot \sigma_T \\
\sigma_{3\text{eff}}^T &= f_1 \cdot \sigma_T + f_2 \cdot \sigma_T + f_3 \cdot \sigma_L + f_4 \cdot \sigma_L + f_4 \cdot \sigma_T.
\end{align*}
\]

The weighting coefficients are the VFs of all compartments determined in the diffusion model by solving (3). \( \sigma_L \) and \( \sigma_T \) are defined as the longitude and transverse conductivities in any axon compartment, respectively. \( \sigma_T \) is set to be a constant. \( \sigma_T \) is linearly related to \( D_T \) while it is confined to be between \( \sigma_{T\text{min}}^T \) and \( \sigma_{T\text{max}}^T \), as expressed in

\[
\sigma_T = D_T \cdot \frac{\sigma_{T\text{max}}^T - \sigma_{T\text{min}}^T}{D_{T\text{max}}^T - D_{T\text{min}}^T} + D_{T\text{max}}^T \cdot \frac{\sigma_{T\text{min}}^T - \sigma_{T\text{min}}^T}{D_{T\text{max}}^T - D_{T\text{min}}^T}.
\]

**C. Data Acquisition**

The MRI data for two subjects (twice for the second subject to verify the consistence of the algorithm) were obtained using a 3 tesla Trio scanner (Siemens, Erlangen, Germany). A three-plane localizer sequence was acquired to position subsequent scans. Scans with T1 and proton density (PD) contrasts were collected for tissue registration. T1 images were acquired coronally, using a 3-D MPRAGE sequence [repetition time (TR) = 2530 ms, echo time (TE) = 3.65 ms, inversion time (TI) = 1100 ms, 224 slices, 1 mm \times 1 mm \times 1 mm voxel, flip angle = 7°, field of view (FOV) = 256 mm \times 176 mm]. PD weighted images were acquired axially using a hyper-echo turbo spin echo (TSE) sequence (TR = 8550 ms, TE = 14 ms, 80 slices, 1 mm \times 1 mm \times 2 mm voxel, flip angle = 120°, FOV = 256 mm). DT-MRI data were acquired axially, aligned with the TSE images, using a dual spin echo, single shot, pulsed gradient, echo planar imaging sequence (TR = 10500 ms, TE = 98 ms, 64 contiguous slices, 2 mm \times 2 mm \times 2 mm voxel, FOV = 256 mm \times 256 mm, 2 averages, b-value = 1000 s/mm^2). Thirteen unique volumes were collected to compute the tensor: a, b = 0 s/mm^2 image and 12 images with diffusion gradients applied in 12 noncollinear directions: (\( G_x, G_y, G_z \) = [1.0, 0.0, 0.5], [0.0, 0.5, 1.0], [0.5, 1.0, 0.0], [0.1, 0.0, 0.5], [-0.5, 0.0, 1.0], [0.0, 1.0, -0.5], [0.0, 1.0, 0.0], [0.1, -0.5, 0.0], [0.0, -0.5, 0.0], [-0.5, 0.0, 1.0]). A dual echo flash field map sequence with voxel parameters common to the DT-MRI was acquired and used to correct the DT-MRI data for geometric distortion caused by magnetic field inhomogeneity (TR = 700 ms, TE = 4.62 ms/7.08 ms, flip angle = 90°, and magnitude and phase difference contrasts).

**D. Image Processing**

The image data were processed using software (BET, FLIRT, FUGUE, and FDT) from the FMRIB Software Library (http://www.fmrib.ox.ac.uk/). FDT was used to correct the diffusion-weighted images for misalignment and distortion caused by the effects of eddy currents. The geometric distortion caused by the magnetic field inhomogeneity was determined from the field map image, and FUGUE was then used to correct each of the 13 eddy-current-corrected diffusion images for this distortion. FDT was then used to compute the diffusion tensor from the 13 eddy-current- and distortion-corrected diffusion images.

The brain was extracted from the T1 and PD acquisitions using BET, then aligned to the dewarped, b = 0 s/mm^2 image using FLIRT, allowing for translations and rotations but no scaling or shear (6 DoF fit).

**III. RESULTS**

We evaluated the proposed VF model by confirming the categorized voxels with the existing knowledge about the WM histology. The WM voxels were categorized into six types (defined in Table I). The number and percentage of voxels in each type are summarized in Table II. In Fig. 2, the voxels are also color coded as red, orange, yellow, blue, white, and green representing the types I–VI, respectively. P1, P2a, and P2b refer to the experimental data on the first subject and twice for the second subject, respectively. For both subjects, types II and III, altogether representing voxels with multidirectional fibers, account for over 85% of the WM voxels, in accordance with the fact that the intravoxel orientational heterogeneity is considerable under the typical voxel size of DT-MRI [15]–[17], [23]. The WM voxels with the partial CSF volume were found on the
TABLE II
STATISTICS OF THE WM VOXELS WITHIN EACH TYPE, INCLUDING THE NUMBER AND THE PERCENTAGE (IN THE PARENTHESES) OF THE VOXELS

<table>
<thead>
<tr>
<th>Group</th>
<th>WM</th>
<th>TYPE I</th>
<th>TYPE II</th>
<th>TYPE III</th>
<th>TYPE IV</th>
<th>TYPE V</th>
<th>TYPE VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>58866</td>
<td>257 (0.44%)</td>
<td>23755 (40.39%)</td>
<td>33346 (56.69%)</td>
<td>1581 (2.69%)</td>
<td>1434 (2.44%)</td>
<td>74 (0.13%)</td>
</tr>
<tr>
<td>P2a</td>
<td>79601</td>
<td>154 (0.19%)</td>
<td>20301 (25.50%)</td>
<td>49023 (62.72%)</td>
<td>3596 (4.52%)</td>
<td>9131 (11.47%)</td>
<td>92 (0.12%)</td>
</tr>
<tr>
<td>P2b</td>
<td>73501</td>
<td>121 (0.16%)</td>
<td>19751 (26.87%)</td>
<td>44833 (61.00%)</td>
<td>3473 (4.73%)</td>
<td>806 (11.84%)</td>
<td>90 (0.12%)</td>
</tr>
</tbody>
</table>

P1, P2a, and P2b refer to the experimental data on the first subject and twice for the second subject, respectively.

Fig. 2. Distribution of the six types of voxels within WM for three groups of DT-MRI data. The slice is about 66 mm below the vertex. P1, P2a, and P2b refer to the experimental data on the first subject and twice for the second subject respectively.

rim of the ventricles filled with the CSF. And the conductivity at the interior of the brain has a higher level of anisotropy than at the exterior, e.g., the splenium of corpus callosum (CCS) and internal capsule (IC) parts show less fiber crossing than other parts.

Fig. 3 shows the distribution of each eigenvalue of the effective conductivity tensors $\sigma_{\text{eff}}$ estimated by using all three algorithms (i.e., VC, Lin, and VF). The VC algorithm resulted in the homogeneous distribution for each eigenvalue. This is obviously undesirable as it ignores the intravoxel orientational heterogeneity. Both the VF and Lin algorithms revealed similarly inhomogeneous distributions for all three eigenvalues. However, relative to the Lin’s results, we found in the VF’s results more voxels on the rim of the ventricles with a close-to-isotropic conductivity. This difference suggests the superiority of the VF algorithm over the Lin algorithm, in light of the fact that the partial volume effect of the CSF exists in those voxels around the ventricles and effectively accounts for a more isotropic conductivity. In addition, in the Lin’s results, the voxels at the rim of the ventricles also had very high values of $\sigma_{\text{eff}}^1$ (over 2 S/m), which is not reasonable since the CSF has the highest conductivity (1.79 S/m) among all the tissues in the brain. For all these voxels, the effective conductivity tensors extracted by using the VF algorithms all had eigenvalues no larger than the conductivity of CSF (1.79 S/m) (see Fig. 4).

IV. DISCUSSION

Previous literature suggested that the WM conductivity is 0.0585 S/m on average [25], and that its component perpendicular to the fiber direction is 0.125 S/m but nine times larger along the fiber direction [8]. These direct measurements also suggest that the conductivity of the cerebral WM varies among the locations within the WM and it also depends on each
individual as well as the pathological or metabolizing condition of the brain. Therefore, mapping the WM conductivity from the noninvasive DT-MRI data is highly desirable.

Some existing algebraic relationships have been formulated based upon the micromechanism of relevant transport processes [2], [4], [5]. These algorithms often rely heavily on some microcosmic parameters that are difficult to obtain in practice, such as the in vivo intra-/extracellular conductivities. Some of these algorithms may also have to simplify the complicated relations as in a linear way. Although recently proposed volume constraints may help retain the histological structure to some degree [10], it often fails to consider the existence of fiber crossing and its variability across the WM volume.

In this study, we proposed a new algorithm to extract the electrical conductivity tensor from the diffusion tensor measured through DT-MRI. By modeling the voxel-wise regional histological structure as a multicompartiment model, the proposed algorithm promises to be able to handle the intravoxel fiber crossing and the partial volume effects of the CSF. Our preliminary results based on the data acquired from two human subjects are in general agreement with our understanding about the WM histology and conductivity. The results also suggest that the proposed VF algorithm outperforms the existing Lin and VC algorithms, in face of the partial volume effect of the CSF and intravoxel orientation heterogeneity.

The diameter of an axon bundle is less than 10 μm on average while the typical voxel size of DT-MRI is about 1–5 mm. According to the postmortem anatomic atlas [16] and some reported fiber tracking studies [11], [12], [17], [26], the axon fibers converge and diverge all along their specific tracts without any definite boundary. For example, the inferior longitudinal and fronto-occipital fasciculi share most of their projections at the occipital lobe and begin to diverge at the posterior temporal lobe as the former stretches to the temporal lobe while the latter stretches to the frontal lobe. Also, the widely scattering cortical U fibers, which are hard to tract for its irregular passages, greatly increase the possibility of the fiber-crossing. Therefore, finding out that about 85% of voxels have various crossing fiber structures appears to be reasonable, although it is certainly desirable to further validate or confirm this finding.

As shown in Fig. 3, the proposed VF algorithm provides more reasonable WM conductivity estimates than the VC algorithm since the latter ignores the intravoxel orientational discrepancies among different voxels by assuming a homogeneous distribution for each eigenvalue of the conductivity tensor. The conductivity distributions estimated by the VF algorithm and the Lin algorithm appear to be mostly similar. However, the Lin algorithm produces more errors for the voxels on the border of the WM and the CSF, as seen in Fig. 4.

In summary, we have proposed a new algorithm for estimating anisotropic electrical conductivity based on the DT-MRI data. The pilot experimental study in two healthy human subjects suggests that the proposed VF algorithm provides a good estimate of the WM anisotropic conductivity and merits further investigation.

REFERENCES

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