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Geometrically constrained two-tensor model for crossing tracts in DWI

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Abstract

MR diffusion tensor imaging (DTI) of the brain and spine provides a unique tool for both visualizing directionality and assessing intactness of white matter fiber tracts in vivo. At the spatial resolution of clinical MRI, much of primate white matter is composed of interdigitating fibers. Analyses based on an assumed single diffusion tensor per voxel yield important information about the average diffusion in the voxel but fail to reveal structure in the presence of crossing tracts. Until today, all clinical scans assume only one tensor, causing potential serious errors in tractography. Since high angular resolution imaging remains, so far, untenable for routine clinical use, a method is proposed whereby the single-tensor field is augmented with additional information gleaned from standard clinical DTI. The method effectively resolves two distinct tract directions within voxels, in which only two tracts are assumed to exist. The underlying constrained two-tensor model is fitted in two stages, utilizing the information present in the single-tensor fit. As a result, the necessary MRI time can be drastically reduced when compared with other approaches, enabling widespread clinical use. Upon evaluation in simulations and application to in vivo human brain DTI data, the method appears to be robust and practical and, if correctly applied, could elucidate tract directions at critical points of uncertainty.

Keywords: White matter; Diffusion tensor; Tractography; Crossing tracts; Anisotropy

1. Introduction

Two of the major uses of diffusion tensor imaging (DTI) in the central nervous system are in tract tracing and quantitative white matter analysis. In white matter tractography, the shape of the anisotropic diffusion tensor is used to delineate fiber tract direction and trace brain connections from voxel to voxel [1–3]. For quantitative analyses of possible white matter anomalies, parameters derived from the diffusion tensor can be associated with tissue microstructure [4,5] and compared between health and disease. The runaway success of DTI (with a single tensor) is in general attributable to the elegance, simplicity and utility of the theory. A variety of diseases, about which white matter injury is known or hypothesized, have been investigated using DTI — including multiple sclerosis, amyotrophic lateral sclerosis, epilepsy, Alzheimer's disease, brain tumors, cerebral ischemia and schizophrenia (for recent reviews, see Refs. [6,7]).

From the fitted tensor in each voxel, one usually extracts the principal direction of diffusion, the apparent diffusion constants in three perpendicular directions and the diffusion anisotropy. The diffusion tensor in each voxel can be visualized as an ellipsoid — the three axes of the ellipsoid correspond directly to the three eigenvalues and eigenvectors of the diffusion tensor [8]. The diffusion parallel to the axis of the tracts is usually considered to be approximately free and, thus, adequately described by a single diffusivity. The diffusion perpendicular to the tracts is much lower — thus creating diffusion anisotropy. The lower diffusivity can be hypothesized as due to barriers that either hinder or restrict the diffusion. Diffusion anisotropy is an important parameter in investigations using DTI to assess anatomical connectivity. The anisotropy is assumed to reflect the

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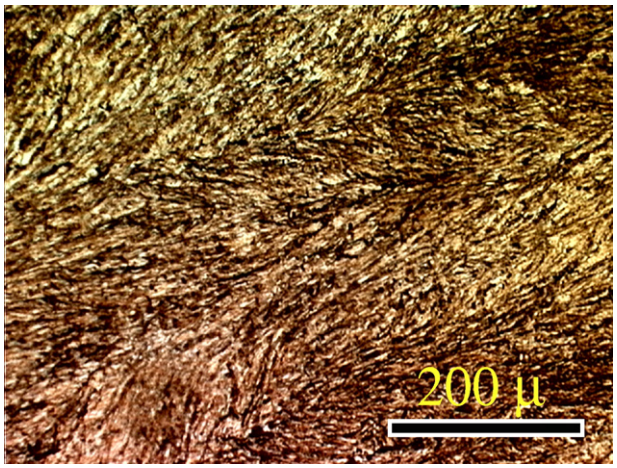

Fig. 1. Region of prefrontal white matter in macaque brain slice (silver stain; histology was courtesy of V. Berezovskii, Department of Neurobiology, Harvard Medical School).

organization and density of tracts within a voxel. Popular measures of anisotropy include the fractional anisotropy [9], the angular variance of the apparent diffusion constant [10] and geometric measures of anisotropy [11]. The last group is composed of three geometrically intuitive indices derived from the diffusion tensor — linear, planar and spherical — where each index describes the similarity of the diffusion ellipsoid to a line, plane or sphere, respectively. Recognition that a nonlinear tensor shape in white matter probably implies more than one distinct fiber bundle in a voxel is implicit in the latter report.

Upon inspection of histology, much of the white matter in primates is composed of multiple interdigitating fibers. Fig. 1 shows an area of the macaque prefrontal white matter in a silver-stained slice. DTI fits the average diffusion in the voxel, but on the spatial scale of MRI, many voxels will contain more than one main fiber direction. Fitting diffusion data from heterogeneous white matter voxels to a single tensor can lead to errors in both the assessment of white matter tract disruption and the computed tract direction.

High angular resolution diffusion-weighted imaging (DWI) has been proposed as a way of increasing the directional information in order to try to resolve crossing tracts [12]. This approach requires the acquisition of a large number of diffusion-weighted images using gradients in many directions (usually >100). A number of methods have been proposed for analyzing data acquired at high angular resolution. Both Tuch et al. [13] and Alexander et al. [14] have proposed fitting two tensors to diffusion data, acquired with 126 and 162 gradient directions, respectively. The former study constrained the two tensors by specifying the values of both sets of eigenvalues to be [1.5, 0.4, 0.4] $\mu m^2/ms$. The latter study attempted to fit the data to a general two-tensor model but reported that the data did not provide sufficient information for resolving two components.

Diffusion-weighted data can also be analyzed without an underlying model, as in q-ball imaging [15]. Using 252 diffusion directions, considerable neural architecture was revealed using this method. A related model-free analysis method can be applied when a complete 3D Cartesian space of diffusion-weighted gradients is applied, that is, multiple gradient directions and multiple gradient strengths. In this case, there exists a possibility to perform a version of q-space analysis [16–18]. (The most commonly used measure of diffusion weighting is termed b and is approximately given by $b \approx q^2\Delta$, where Δ is the time between gradient pulses and $q \approx \delta g$, where δ is the duration of each gradient pulse and g is the gradient strength. The exact relationship between b and q depends on the details of the pulse sequence.) q-Space imaging uses the Fourier relation between the spatial displacement of the spins and the MR signal (measured with respect to q) in order to estimate that displacement.

A model of white matter diffusion, combining elements of hindered and restricted diffusion, has recently been proposed by Assaf et al. [19] to explain the apparent non-Gaussian diffusion observed at high b values. Here, as in q-space imaging, diffusion-weighted data are collected with multiple gradient directions and multiple gradient strengths. This model was shown to allow discrimination of crossing tracts in a phantom from 496 measurements with b values up to 44,000 s/mm^2.

To summarize the above-described methods for discriminating crossing tracts, it is apparent that crossing tracts can be resolved to some degree when enough gradient directions are applied. However, the duration of the scans is long, as compared with the time available for practical clinical applications; thus, there is a clear need to resolve crossing tract information in clinically acceptable DWI scan times. Model-free methods will always require high angular resolution data acquisition; hence, our approach here has been to simplify the two-tensor model in a geometrically intuitive way. The adherence to the tensor description is utilitarian and rests on the empirically observed Gaussian character of the diffusion at low diffusion weightings ($b \leq 1000$ s/mm^2).

We demonstrate that whole-brain DWI data acquired in 6 min are sufficient for effectively resolving two tract directions when no more than two tracts are assumed to populate the voxel. Calculation of the tract directions is achieved by taking into account the geometry associated with two separable fiber bundles within each of the analyzed voxels and by utilizing the information gleaned from single-tensor analysis. The underlying model assumes that two cylindrically symmetric tensors can adequately describe the diffusion in two tracts, with a few additional, physically reasonable constraints. No assumptions are made about compartments, restriction or general diffusive behavior as a function of b or q. The model only requires the geometric assumption of cylindrical symmetry and uses apparent diffusion coefficients. While the single-tensor model will always fail in voxels with complicated tissue architecture, the two-tract model will generally improve the analysis of