

An Introduction to Diffusion Tensor Image Analysis

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KEYWORDS

- Diffusion Tensor MRI • DTI • Brain imaging
- Tractography • Review

Diffusion tensor magnetic resonance imaging (DTI) is a relatively new technology that is popular for imaging the white matter of the brain. This article provides a basic and broad overview of DTI to enable the reader to develop an intuitive understanding of these types of data, and an awareness of their strengths and weaknesses. The authors have tried to include equations for completeness, but these are not necessary for understanding the content. Wherever possible, more in-depth technical articles or books are suggested for further reading. The authors especially recommend the new diffusion MRI textbook,¹ the introductory paper on fiber tracts and tumors,² the white matter atlas book,³ and the review of potential pitfalls in DTI analysis.⁴ The remainder of this article addresses basic questions about DTI (the what, why, and how of DTI), followed by a discussion of issues in interpretation of DTI, and finally an overview of more advanced diffusion imaging methods and future directions.

WHY DTI? A BRIEF HISTORY OF DTI AND ITS IMPACT ON CLINICAL RESEARCH

The diffusion tensor was originally proposed for use in MRI by Peter Basser in 1994.^{5,6} Before DTI, diffusion MRI^{7,8} had developed from research in diffusion nuclear magnetic resonance.⁹ Before

the diffusion tensor model was introduced, the orientation of the axons in a tissue sample had to be known to measure anisotropic diffusion, and therefore only fixed samples could be scanned, such as the axon of the giant squid.¹⁰ The introduction of the diffusion tensor model allowed, for the first time, a rotationally invariant description of the shape of water diffusion. The invariance to rotation was crucial because it enabled application of the DTI method to the complex anatomy of the fiber tracts in the human brain.¹¹ However, the diffusion tensor is not able to fully describe crossing of the fiber tracts.^{12,13}

The popularity of DTI has been enormous. It has been applied to a tremendous variety of neuroscientific studies,^{14–16} including schizophrenia,¹⁷ traumatic brain injury,¹⁸ multiple sclerosis,^{19,20} autism,²¹ and aging.²² Anatomic investigations have been undertaken regarding the structure of the language network,^{23,24} the asymmetry of the white matter in twins and siblings,²⁵ and the location, asymmetry, and variability of the fiber tracts.²⁶ Recent investigations have attempted to model the human “connectome” by analyzing structural versus functional brain connectivity as measured with DTI and functional MRI.^{27,28} DTI has also been applied for neurosurgical planning and navigation.^{29–32} A large prospective study showed that addition of preoperative DTI to

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neuronavigation increased tumor resection and survival and decreased neurologic morbidity.³³

WHAT IS DTI?

DTI is a sensitive probe of cellular structure that measures the diffusion of water molecules. The measured quantity is the diffusivity or diffusion coefficient, a proportionality constant that relates diffusive flux to a concentration gradient⁸ and has units of $\frac{mm^2}{s}$. Unlike the diffusion in a glass of pure water, which would be the same in all directions (isotropic), the diffusion measured in tissue varies with direction (is anisotropic). The measured macroscopic diffusion anisotropy is the result of microscopic tissue heterogeneity.⁶ In the white matter of the brain, diffusion anisotropy is primarily caused by cellular membranes, with some contribution from myelination and the packing of the axons.^{11,34,35} Anisotropic diffusion can indicate the underlying tissue orientation (Fig. 1).

The diffusion tensor describes the diffusion of water molecules using a Gaussian model. Technically, it is proportional to the covariance matrix of a three-dimensional Gaussian distribution that models the displacements of the molecules. The tensor is a 3×3 symmetric, positive-definite matrix, and these matrix properties mean that it has three orthogonal (mutually perpendicular) eigenvectors and three positive eigenvalues. The major eigenvector of the diffusion tensor points in the principal diffusion direction (the direction of the fastest diffusion). In anisotropic fibrous tissues, the major eigenvector also defines the fiber tract axis of the tissue,⁶ and thus the three orthogonal eigenvectors can be considered a local fiber coordinate system. (This interpretation is only strictly true in regions where fiber tracts do not cross, fan, or branch.) The three positive eigenvalues of the tensor ($\lambda_1, \lambda_2, \lambda_3$) give the diffusivity in the direction of each eigenvector. Together, the eigenvectors and eigenvalues define an ellipsoid that

represents an isosurface of (Gaussian) diffusion probability: the axes of the ellipsoid are aligned with the eigenvectors and their lengths are $\sqrt{2\tau\lambda_i}$.⁶ Fig. 2 shows three diffusion tensors chosen from different regions of the human brain to illustrate possible shapes of the ellipsoid.

HOW IS DTI MEASURED?

To measure diffusion using MRI, magnetic field gradients are used to create an image that is sensitized to diffusion in a particular direction. Through repeating this process of diffusion weighting in multiple directions, a three-dimensional diffusion model (the tensor) can be estimated. In simplified terms, diffusion imaging introduces extra gradient pulses whose effect “cancels out” for stationary water molecules, and causes a random phase shift for molecules that diffuse. Because of their random phase, signal from diffusing molecules is lost. This loss of signal creates darker voxels (volumetric pixels), meaning that white matter fiber tracts parallel to the gradient direction will appear dark in the diffusion-weighted image for that direction (Fig. 3).

Next, the decreased signal (S_k) is compared with the original signal (S_0) to calculate the diffusion tensor (D) by solving the Stejskal-Tanner Equation (1).³⁶ This equation describes how the signal intensity at each voxel decreases in the presence of Gaussian diffusion:

$$S_k = S_0 e^{-b \hat{g}_k^T D \hat{g}_k} \tag{1}$$

In this equation, S_0 is the original image intensity at the voxel (measured with no diffusion-sensitizing gradient) and S_k is the intensity measured after the application of the k th diffusion-sensitizing gradient in the (unit) direction $\hat{g}_k$. The product $\hat{g}_k^T D \hat{g}_k$ represents the diffusion coefficient (diffusivity) in direction $\hat{g}_k$. Because the entire set of diffusion-weighted images is used (giving many

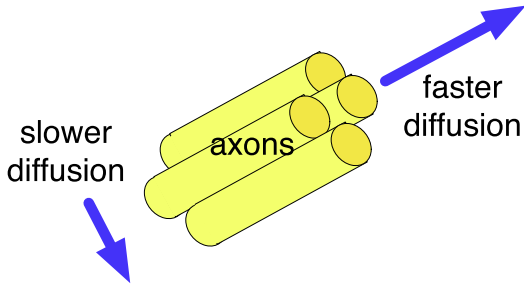


Fig. 1. Illustration of anisotropic diffusion, in the ideal case of a coherently oriented tissue. This example compares the diffusion measured parallel and perpendicular to the axons in a white matter fiber tract.

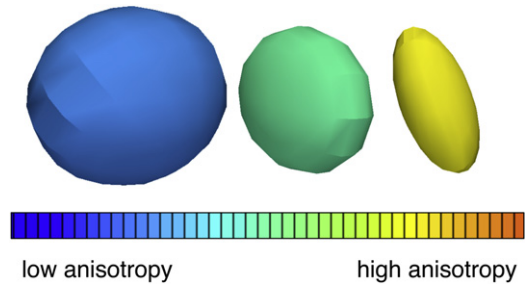


Fig. 2. Three example diffusion tensors, selected from a diffusion tensor magnetic resonance imaging scan of the human brain to illustrate differences in tensor anisotropy and orientation.

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