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A review of diffusion tensor magnetic resonance imaging computational methods and software tools

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ABSTRACT

In this work we provide an up-to-date short review of computational magnetic resonance imaging (MRI) and software tools that are widely used to process and analyze diffusion-weighted MRI data. A review of different methods used to acquire, model and analyze diffusion-weighted imaging data (DWI) is first provided with focus on diffusion tensor imaging (DTI). The major preprocessing, processing and post-processing procedures applied to DTI data are discussed. A list of freely available software packages to analyze diffusion MRI data is also provided.

1. Introduction

Whereas conventional magnetic resonance imaging (cMRI) provides methods to map the anatomy or tissue volume, diffusion-weighted imaging (DWI) of random translational water molecules offers quantitative anisotropy and orientation information that has been utilized to map the integrity or architecture of the soft tissue in the central nervous system [1–6]. Contributors to diffusion tensor anisotropy include cellular membranes, axons, myelin sheaths, and other factors [7]. Water molecular diffusion in cerebral white matter is less restricted along the axon than it is when perpendicular to the compact bundles and hence it is termed anisotropic (see Fig. 1). Gray matter is less anisotropic, while diffusion in barrier free tissue (e.g. edema and cerebrospinal fluid) is isotropic [8–10].

2. Mathematical background

In general, DWI data are acquired on a prescribed volume (e.g. brain) by repeating the acquisition while altering the magnitude or orientation of the diffusion-sensitizing gradients. Hence, the DWI data acquired are generally multidimensional and can always be pooled as 4D data (e.g. in space x, y, z and diffusion encoding). Diffusion-weighted data are occasionally repeated in time and are magnitude-averaged to enhance the signal-to-noise ratio (SNR). This data averaging can be done by the scanner software. Depending on the acquisition protocol, the DWI data may undergo model-based single or multiple diffusion tensor imaging (DTI) or model-free analysis to obtain scalar and vector metrics that can be used to map the tissue connectivity [11–13]. Currently, there are three diffusion MRI books [11–13] and several reviews on diffusion MRI [3–6,14–19]. The sections below provide a short overview of the basics of diffusion MRI applied to whole brain human brain mapping in health and disease.

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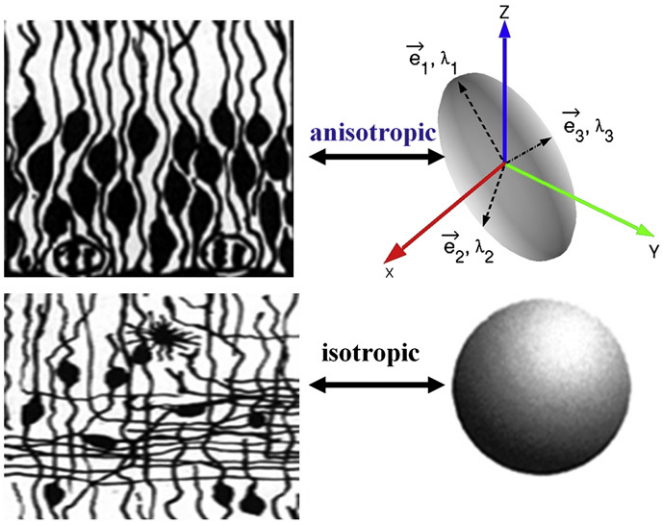

Fig. 1. Illustration of diffusion anisotropy using the ellipsoid representation of the single tensor model.

2.1. Model-based diffusion tensor imaging

Mathematically, the kth signal S_k obtained from a volume element upon applying a diffusion-weighting or b-factor b_k along the unit vector g_k can be modeled using the Gaussian mixture model (GMM) [5] as the superposition of different slowly exchanging positive-definite and symmetric tensors $\mathbf{D_n}$, each with a population fraction f_n:

$$S_k = S_0 \sum_{n=1}^{N} f_n \exp(-b_k \hat{g}_k \mathbf{D_n} \hat{g}_k) + \eta_k \tag{1}$$

where $\mathbf{D_n}$ refers to a second rank and positive-definite tensor with three unique diagonal and three unique off-diagonal elements, which can be represented by a 3×3 symmetric matrix [1–3,11–13]:

$$D = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix} \tag{2}$$

In Eq. (1), S_0 refers to the reference signal obtained without diffusion-sensitization (e.g. $b=0$). The sum of all population fractions is unity:

$$\sum_{n=1}^{N} f_n = 1 \tag{3}$$

In Eq. (1), the apparent diffusion coefficient (ADC) can be defined as

$$ADC_k(\hat{g}_k, b_k) = -\frac{1}{b_k} \log\left(\frac{S_k}{S_0}\right) \tag{4}$$

The system of equations described in Eq. (1) can be expressed as a matrix equation after defining $y_k = S_k/S_0$:

$$y_{K\times 1} = A_{K\times N} f_{N\times 1} + \hat{\eta}_k \tag{5}$$

This system of equations obtained from all measurements can be solved using constrained or regularized non-linear least-squares fit methods for the unknown diffusivities for the fractions [20–27]; this analysis is the basis for single or multiple diffusion tensor imaging (DTI). For a system with a single unknown tensor ($N=1$), Eq. (1) can be simplified by taking the logarithm to obtain a linear system of equations:

$$ADC_k = \hat{g}_k D \hat{g}_k = D_{xx} g_x^2 + D_{yy} g_y^2 + D_{zz} g_z^2 + 2D_{xy} g_x g_y + 2D_{xz} g_x g_z + 2D_{yz} g_y g_z \tag{6a}$$

This equation can also be written as

$$ADC_k = \sum_{i=1}^{i=3} \sum_{j=1}^{j=3} g_k(i) g_k(j) D_{ij} \tag{6b}$$

A generalization of this equation assumes the presence of high order tensors (HOT) and forms the basis of generalized DTI [28–30]. To solve this linear system of equations for the 6 diffusion tensor elements, a minimum of six independent diffusion-weighted measurements are needed in addition to the reference map (S_0). In general, more than seven measurements are acquired with different diffusion b-factors and non-collinear orientations. Examples of non-collinear or uniformly distributed diffusion encoding sets are provided in Fig. 2.

The over-determined system described by Eq. (6) can be solved by least-squares and singular value decomposition (SVD) methods [28–30].

In the case where a single-b-factor is selected based on some known range of ADC, the orientations of the encoding vectors have to be uniformly distributed in three-dimensional space [31–43]. The optimization of diffusion encoding schemes for white matter fibers with selected orientations, such as skeletal muscle or spinal cord, has been discussed by Peng and Arfanakis [44]. In the case where non-zero b-factors are acquired along with at least 15 encoding measurements for each b-factor, diffusion kurtosis imaging (DKI) methods may be used [45,46]. Additional data-driven methods such as principal component analysis (PCA) or independent component analysis (ICA) may use the moments of the measured data [47–50].

In the general case where N diffusion tensors with rank two are sought, $6N$ variables need to be determined in addition to $N-1$ unknown population fractions subject to Eq. (3) or a total of $6N+(N-1)$ unknowns.

Analysis of diffusion-weighted data acquired at finite SNR, angular and spatial resolutions according to the multi-tensor model may lead generally to unstable results as the exact number (N), population fractions (f), diffusion tensor orientation, and magnitude are unknown. The two-tensor case has received some attention as it appeals to the determination of the extent of fast and slow diffusion compartments in a voxel [51–53] or the interesting case of enclosed or intravoxel crossing fibers [54–57]. The fast and slow diffusion tensor decoupling requires diffusion measurements with different b-factors (e.g. $b=1000$ and 4000 s mm^{-2}), while the case of multiple crossing fibers was modeled with uniformly distributed orientations at clinically attainable b-factors (e.g. $b\sim 1000$ s mm^{-2}). In general, the two-tensor modeling problem can be solved if sufficient data are acquired at acceptable SNR using non-linear fitting approaches or can be regularized to reduce the number of unknowns by assuming a cylindrical symmetry of the unknown fibers [20–27].

2.2. Model-free approaches

Data-driven or model-free approaches may require longer acquisition times and the diffusion-weighted data have to be acquired according to prescribed paradigms [13]. Data-driven approaches with high angular resolution diffusion (HARDI) measurements with two b-factors may use spherical harmonic decomposition (SHD) [58–63] that is based on the expansion of the measured apparent diffusion coefficient data in terms of a complete orthonormal set (e.g. spherical Legendre polynomials Y_l^m). Mathematically, this can be expressed as

$$ADC(\theta,\varphi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{m=l} a_{lm} Y_l^m(\theta,\varphi) \tag{7}$$

It has been shown that single fibers correspond to $l=0$, 2 and two fibers may be represented by $l=0$, 2, 4, while acquisition