HARDI-based methods for fiber orientation estimation

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Purpose

Diffusion tensor imaging (DTI) [1] has become the method of choice for assessing white matter (WM) 'integrity' and 'connectivity'. However, in voxels containing multiple fiber orientations (a condition often referred to as 'crossing fibers'), the model has been shown to be inadequate [2]. Such voxels occur frequently throughout the WM, due to partial volume effects between adjacent tracts. This has important implications for fiber tractography and WM 'integrity' metrics based on DTI [3, 4]. In such regions, the orientation extracted from the diffusion tensor is unreliable, introducing both false positives and false negatives in DTI tractography results. It also complicates the interpretation of DTI derived diffusion indices such as fractional anisotropy (FA), which are often suggested for use as surrogate markers of 'WM integrity'. Several methods have been proposed to extract fiber orientation information from the diffusion-weighted (DW) signal, many of them relying on the high angular resolution diffusion imaging (HARDI) protocol [5]. The purpose of this presentation is to review the most widely-used methods for extracting fiber orientation information from single-shell HARDI data. We begin by introducing the crossing fiber problem of DTI. Next, we explain the concept of HARDI and provide an overview of the different HARDI-based fiber reconstruction approaches together with their pros and cons. As an illustrative example, we will show results on a representative HARDI dataset using several freely available software packages.

Outline of content

The crossing fiber problem: The problem of DTI in crossing fiber regions stems from the fact that it can only model Gaussian diffusion. Being a uni-modal function, the Gaussian function is not equipped to deal with multiple fiber configurations. As a consequence the DTI model provides misleading orientation and integrity information in regions containing crossing fibers. This problem will be made tangible by showing diffusion tensors calculated from simple 'crossing fiber' simulations.

High angular resolution diffusion imaging (HARDI): HARDI measures the DW signal using a larger number of uniformly-distributed DW gradient directions than required for DTI, in order to capture the higher angular frequencies of the DW signal that are not adequately modeled by a single diffusion tensor (DT) [5]. The audience will be familiarized with the concept of HARDI by showing the raw HARDI signal profiles that emanate from simple crossing fiber configurations. We will also introduce the concept of *q*-space [6].

HARDI-based multi-fiber reconstruction methods: Several methods based on HARDI data have been proposed that are able to recover multiple fiber orientations in voxels containing complex fiber configurations. We will provide an overview of the most widely-used methods and introduce their pros and cons. The methods can be broadly categorized in two distinct classes: model-free approaches and model-based approaches.

Model-free approaches: Q-space approaches rely on the Fourier relationship between the spin displacement probability density function (the spin propagator) and the DW signal attenuation in *q*-space [6]. Since they don't require explicit modeling of the spin propagator they are typically considered model-free. While it is possible to recover the full 3D propagator, this requires data to be acquired over multiple *q*-space shells, rendering acquisition time very long [7]. However, by making assumptions about the radial dependence of either the propagator or the DW signal, it is possible to use single-shell HARDI data to recover the angular information of the propagator. Methods in this category include q-ball imaging (QBI) [8], PAS-MRI [9], and diffusion orientation transform [10].
Q-ball imaging (QBI): QBI approximates the diffusion orientation density function (dODF), which is the radial projection of the spin propagator on the unit-sphere, by means of the Funk-Radon transform (FRT) of the single-shell DW signal. Q-ball imaging is computationally light, as the FRT can be formulated as a single matrix multiplication. An important concern with the QBI approach is that the dODF does not correspond directly to the quantity of interest, i.e., the fiber orientations. Although water molecules are most likely to move along the fiber orientation, moves along other orientations are still common. As a consequence, closely aligned fiber orientations will be blurred together and thus be identified as a single fiber orientation. Additionally, this overlapping has been shown to introduce a bias in the estimated fiber orientations [11]. Another concern is that the FRT approximation is only valid for data acquired at high b-values. In practice, QBI is typically performed using moderate b-values to ensure adequate SNR. This will introduce additional blurring in the dODF, which will reduce the angular resolution and may introduce an additional bias in the estimated fiber orientations [12].

Model-based approaches: Model-based approaches rely on an explicit model that provides an estimate of the DW signal arising from a number of fiber populations. An important advantage over QBI is that these methods directly estimate the quantity of interest: the fiber orientations.
Multi-tensor models: The multi-tensor model extends the single-tensor model to handle multiple fiber orientations [5]. The DW signal is assumed to originate from a mixture of *n* distinct compartments, each characterized by its own diffusion tensor (no exchange). An additional isotropic compartment is sometimes included to account for CSF or gray matter contamination [13, 14]. As the increased number of unknowns can cause instabilities in the model fit, the number of unknowns is usually reduced by placing constraints on the composing tensors. One of the most widely used multi-tensor models is called the ball-and-sticks model, in which the DW signal is fitted to a combination of sticks, which represent different fiber populations with infinite anisotropy; and a ball, which represents the isotropic compartment [14]. An important issue of the multi-tensor models is that they require an estimate of the number of fiber populations *n* to include into the model. Typically, this is achieved by model-selection, comparing the goodness of fit for different *n* [15]. Other methods use Bayesian automated relevance determination to drive the volume fractions of excess fiber populations to zero [13, 14].
Spherical deconvolution: Spherical deconvolution methods assume a continuous distribution of fiber orientations instead of a discrete number of fiber populations [16]. This enables the DW signal to be modeled as the convolution of the fiber orientation distribution function (fODF), which gives the fraction of fibers that are aligned along each orientation, with a response function, which is the DW signal measured from a single fiber population. It is then possible to recover the fODF by performing spherical deconvolution. In practice, the deconvolution operation is ill-posed, requiring constraints to be placed on the solution fODF. Most implementations introduce a non-negativity constraint [17, 18], others include a maximum entropy term [19].

Real data example: A representative HARDI dataset will be processed using QBI (as implemented in [20]), the multi-tensor model (as implemented by FSL's bedpostx [14]) and spherical deconvolution (as implemented in MRtrix [17]) in order to make the pros and cons more tangible. We will also briefly discuss the impact of various user-specified parameters and options on the output.

Summary

We have introduced the crossing fiber problem and reviewed the most widely used methods for extracting fiber orientation information from HARDI data. From this short overview, the need for multi-fiber reconstruction algorithms should be clear. It will also provide a broad understanding of the advantages and limitations of the different multi-fiber reconstruction methods available. The audience will also be familiar with the implications of applying DTI in regions containing complex fiber architecture.

References: [1] Basser PJ, Biophys J 66:259-267, 1994; [2] Alexander AL et al., MRM 45(5), 2001; [3] Wheeler-Kingshott CA & Cercignani M, MRM 61:1255-60, 2009; [4] Jones DK, Imaging in Medicine 2:341-55, 2010; [5] Tuch DS et al., MRM 48:577-82, 2002; [6] Callaghan PT et al., J. Physics E 21:820, 1988; [7] Wedeen VJ et al., MRM 54:1377-86, 2005; [8] Tuch DS, MRM 52:1358-72, 2004; [9] Jansons KM & Alexander DC, Inverse Problems 19:1031-46, 2003; [10] Özarslan E et al., NeuroImage 31:1086-103, 2006; [11] Zhan W & Yang Y, J Magn Reson 183:193-202, 2006; [12] Tournier JD et al., NeuroImage 35:1459-72, 2007; [13] Hosey T et al., MRM 54:1480-9, 2005; [14] Behrens TEJ et al., NeuroImage 34:144-55, 2007; [15] Parker GJM & Alexander DC, IPMI 17:684-95, 2003; [16] Tournier JD et al., NeuroImage 23:1176-85, 2004; [17] Tournier JD et al., NeuroImage 35:1459-72, 2007; [18] Dell'acqua F et al., NeuroImage 49:1446-58, 2010; [19] Alexander DC, IPMI 19:76-87, 2005; [20] Descoteaux M et al., MRM 58:497-510, 2007