High angular resolution diffusion-weighted imaging (HARDI): beyond the diffusion tensor model

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The diffusion tensor model and the crossing fibre problem

Since its introduction in 1994 [1], diffusion tensor imaging (DTI) has rapidly become established as the method of choice for assessing white matter 'integrity' and connectivity. However, there is now a growing recognition that the assumptions underlying the diffusion tensor model are rarely met in practice [e.g. 2,3]. In particular, it is now clear that each voxel cannot be assumed to contain a single, coherently oriented bundle of white matter axons. Voxels containing multiple fibre orientations can readily be observed using relatively routine data acquisition protocols (see Figure 1), and it has recently been shown that crossing fibres can be detected in over 90% of white matter voxels [4]. This has serious implications for DTI: it calls into question the validity of using fractional anisotropy [5] or radial and axial diffusivities to assess white matter 'integrity' [2,3], and of using DTI-derived white matter orientations estimates for tractography, particularly for smaller white matter tracts [e.g. 6].

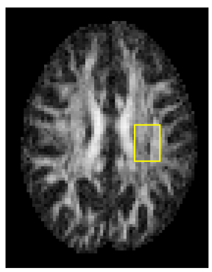
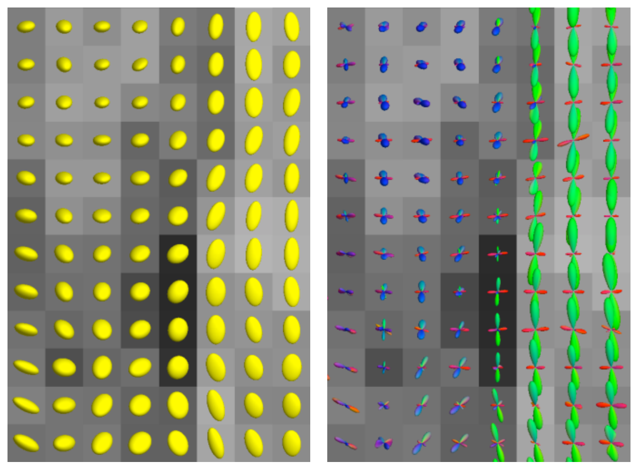

Figure 1: an example of crossing fibres in the human brain. The ROI is located in the periventricular white matter, as shown in the axial FA map. Left: results obtained using the diffusion tensor model. Right: results obtained using spherical deconvolution [7]. As can be appreciated, the diffusion tensor model is unable to detect or characterise the multiple fibre orientations present. Data acquired on a 1.5T Siemens Avanto, 2.1×2.1×3 mm^3 voxels, 37 contiguous slices, 60 DW directions, b = 3,000 s/mm^2.

High angular resolution diffusion-weighted imaging (HARDI)

A number of methods have been proposed to extract more information from the diffusion-weighted (DW) signal, many of them based on the HARDI acquisition protocol [8]. In essence, this consists of measuring the DW signal using a much larger number of uniformly distributed DW gradient directions than required for DTI, so as to capture the higher angular frequency features of the DW signal that are not adequately modelled by a single diffusion tensor. There are two distinct approaches by which these algorithms extract information from HARDI data:

***q*-space and the spin propagator:** according to the *q*-space formalism, there is a Fourier relationship between the spin propagator (the spin displacement probability density function) and the distribution of the DW signal over *q*-space (the space of DW gradient amplitude vectors). While it is possible to characterise the DW signal over 3D *q*-space (as in diffusion spectrum imaging (DSI) [9]), this leads to long scan times. However, by making assumptions about the radial dependence of either the DW signal, or of the spin propagator, it is possible to use HARDI data (acquired on a spherical shell in *q*-space), to recover the spin propagator (or at least its angular dependence). Such methods include Q-ball imaging [10], persistent angular structure MRI [11], and the diffusion orientation transform [12].

Mixture models and the fibre orientation distribution: in a crossing fibre region, the DW signal measured is the sum of the DW signals emanating from each distinct fibre bundle. Thus, if a suitable model exists for a single fibre population, it can be used to model the DW signal for multiple fibre populations. The problem then becomes one of solving the inverse problem to recover the fibre orientations and corresponding volume fractions that best explain the measured DW data. A number of multi-tensor fitting algorithms have been proposed based on this premise [e.g. 6,8,13]. Furthermore, if the number of distinct fibre orientations included in the model is allowed to tend to infinity, this naturally extends to the concept of spherical deconvolution [e.g. 7,14-17] to recover the fibre orientation distribution (FOD).

Towards a replacement for fractional anisotropy: apparent fibre density

Although many of these algorithms were developed to extract fibre orientations, there is an increasing need for methods to assess white matter 'integrity' (i.e. to find alternatives for FA). While attempts are being made to characterise the distribution of axonal radii [18,19], another candidate may be the volume fractions as identified by mixture model approaches [e.g. 20,21]. While still in their infancy, methods have recently been proposed to perform non-linear registration of FOD images, including appropriate re-orientation and modulation, thus enabling group comparisons or correlations of 'apparent fibre density' between patients and controls [22]. These approaches can potentially provide more reliable and more readily interpretable results than the commonly used DTI-derived anisotropy measures.

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