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# How accurately can the diffusion profiles indicate multiple fiber orientations? A study on general fiber crossings in diffusion MRI

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**Abstract**

The q-space imaging techniques and high angular resolution diffusion (HARD) imaging have shown promise to identify intravoxel multiple fibers. The measured orientation distribution function (ODF) and apparent diffusion coefficient (ADC) profiles can be used to identify the orientations of the actual intravoxel fibers. The present study aims to examine the accuracy of these profile-based orientation methods by comparing the angular deviations between the estimated local maxima of the profiles and the real fiber orientation for a fiber crossing simulated with various intersection angles under different *b* values in diffusion-weighted MRI experiments. Both noisy and noise-free environments were investigated. The diffusion spectrum imaging (DSI), q-ball imaging (QBI), and HARD techniques were used to generate ODF and ADC profiles. To provide a better comparison between ODF and ADC techniques, the phase-corrected angular deviations were also presented for the ADC method based on a circular spectrum mapping method. The results indicate that systematic angular deviations exist between the actual fiber orientations and the corresponding local maxima of either the ADC or ODF profiles. All methods are apt to underestimation of acute intersection and overestimation of obtuse intersection angle. For a typical slow-exchange fiber crossing, the ODF methods have a non-deviation zone around the 90° intersection. Before the phase-correction, the deviation of ADC profiles approaches a peak at the 90° intersection, while after the correction the ADC deviations are significantly reduced. When the *b* factor is larger than 1000 s/mm$^2$, the ODF methods have smaller angular deviations than the ADC methods for the intersections close to 90°. QBI method demonstrates a slight yet consistent advantage over the DSI method under the same conditions. In the noisy environment, the mean value of the deviation angles shows a high consistency with the corresponding deviation in the nose-free condition.
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## 1. Introduction

Diffusion tensor imaging (DTI) has been established as a powerful tool for non-invasive investigation of white matter structures and connectivities in vivo [1–3]. Fiber tracking techniques have also been developed to delineate neural pathways based on the assumption that the major eigenvector of the diffusion tensor should be oriented parallel with local white matter fibers [4–6]. However, the validity of the DTI-based tractography is confounded by the fact that the primary eigenvector of the diffusion tensor may be seriously biased from the actual fiber direction if multiple fiber compartments share a single voxel [7,8]. This inability of DTI is technically due to the fact that the tensor model is a 2nd order approximation of a possible complex diffusion pattern [9], and consequently can provide only one global maximal direction corresponding to the primary eigenvector. In recent years, more elaborate acquisition and analysis strategies, including q-space imaging and high angular resolution diffusion (HARD) imaging techniques have been developed to tackle this challenge [10–24].

Q-space imaging techniques identify multiple fibers components by calculating the probability distribution function (PDF) of the diffusion process in each voxel, based on the Fourier transform (FT) relationship between

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the PDF of diffusion displacement and the diffusion-weighted signal attenuation in q-space [10–12]. Even under the practical setting of finite pulse width, there is growing evidence that the estimated PDF is still a reasonable description of local diffusion and microstructural organization in brain tissues [13]. Diffusion spectrum imaging (DSI) has been proposed to estimate the diffusion PDF from a large number of data acquisitions in 3D q-space [14]. A study to assess the accuracy of DSI was performed on phantoms and animal models in practical MRI settings [15]. In DSI, the multiple fiber orientations are usually represented by the PDF angular structure, i.e. the orientation distribution function (ODF) that can be obtained by a radial integral of the PDF [15]. A modified technique, named q-ball imaging (QBI), has been proposed to acquire data only on a spherical surface in the q-space and to estimate the ODF directly from these data [16,17]. For both DSI and QBI methods, it is generally assumed that the multiple local maxima of the ODF profile should represent the actual orientations of multiple intravoxel fibers [15–17].

High angular resolution diffusion (HARD) techniques have also been developed to characterize the apparent diffusion coefficient (ADC) profiles for the intravoxel fibers [18–24]. Alexander et al. [20] and Frank [21] proposed the idea of using spherical harmonic decomposition (SHD) to characterize the 3-D apparent diffusion coefficient (ADC) profile measured by HARD imaging. In general, the lower order (0th or 2nd) spherical harmonics represent the isotropic diffusion or single fiber diffusion patterns, while the higher orders (4th or higher) represent non-Gaussian patterns associated with intravoxel multiple fiber components. Zhan et al. proposed a "diffusion circular spectrum mapping" (DCSM) method that examines only the ADC distribution along the circle spanned by the major and medium eigenvectors, and applies a 1-D FT onto this circular ADC distribution [22,23]. Unlike the q-space techniques, the local maxima of ADC profiles generally cannot be used to directly represent the orientations for the intravoxel crossing fibers. However, the orientations of the fiber crossings may be identified by incorporating both amplitude and phase information of the decomposed harmonics of the ADC profile, as demonstrated in [23].

The ability to identify fiber-crossings in both q-space and HARD imaging techniques stem from a common characteristic of ODF and ADC profiles, i.e. both methods allow multiple local maxima to appear on the estimated profiles. The angular accuracy of the local maxima in the profiles with respect to the actual fiber orientations would be crucial for the fiber tracking techniques because of the accumulative manner of the angular deviations along the tracking trajectory [15–17,19]. In previous studies, a mismatch between the orientation of a fiber crossing and the local maxima of its ADC profile has been pointed out [20,23,24], and the change of ODF profile sharpness has been reported [16,17]. Recently, Ozarslan et al. proposed a method applying the SHD technique to the ODF profiles and examined the orientation deviations for a few multiple fiber cases [25]. However, a systematic investigation onto the angular deviations between the local maxima of the ODF/ADC profiles and the orientations of the real intravoxel fibers have not yet been performed. The explicit relationship between the angular deviation and various conditions of the fiber crossing, e.g. the intersection angle, $b$ factor, and noise level, remains unclear. Moreover, no effort has been reported in comparing the accuracy of identifying multiple-fiber orientations among various q-space and HARD imaging techniques. Resolving these issues is necessary to allow these beyond-tensor diffusion MRI techniques to serve as reliable tools in delineating white matter structures and neuronal pathways.

In this paper, a simulation study is presented to address the questions described above. A "general fiber crossing" with various intersection angles (0°–180°) is used to simulate the diffusion-weighting MRI experiments with different $b$ values (1000–10,000 s$^2$/mm). The effects of imaging noise are also investigated by simulating both noise-free and noisy environments with different noise levels. The HARD, DSI and QBI techniques are implemented to estimate the ADC and ODF profiles of the general fiber crossing with various parameters. The angular deviations of the local maxima of the diffusion profiles are measured by the angle between the directions of the estimated local maxima and the known corresponding fiber orientations. To ensure a better comparison between ADC and ODF methods, the DCSM phase technique in [23] is also implemented to provide the corrected deviation angles for the ADC profiles.

## 2. Method

### 2.1. ADC modeling

The effective ADC profile $D(\theta,\phi)$ $(0 \leqslant \theta \leqslant \pi, 0 < \theta \leqslant 2\pi)$ of an ideal cylindrical symmetric single fiber can be written [26] as

$$D(\theta,\phi) = \frac{\mathbf{V}^{\mathrm{T}}}{\|\mathbf{V}\|} \cdot \mathbf{A}^{\mathrm{T}} \cdot \begin{bmatrix} \lambda_1 & & \\ & \beta\lambda_1 & \\ & & \beta\lambda_1 \end{bmatrix} \cdot \mathbf{A} \cdot \frac{\mathbf{V}}{\|\mathbf{V}\|} \tag{1}$$

where $\mathbf{V}$ denotes the vector of diffusion encoding direction and $\lambda_1$ is the maximal ADC measured in the direction parallel to the fiber. The ratio $0 < \beta < 1$ reflects the degree of linear anisotropy. $\mathbf{A}$ is the rotation matrix determined by the fiber orientation whose spherical coordinates $(\theta,\phi)$ $(0 \leqslant \theta \leqslant \pi$, $0 < \theta \leqslant 2\pi)$ represent the polar and azimuthal angle, respectively, such that

$$\mathbf{A} = \begin{bmatrix} \sin\phi & -\cos\phi & 0 \\ \cos\phi\cos\theta & \sin\phi\cos\theta & -\sin\theta \\ \cos\phi\sin\theta & \sin\phi\sin\theta & \cos\theta \end{bmatrix} \tag{2}$$