

# Diffusion Simulation Tractography for High Angular Resolution Diffusion Imaging

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**Introduction** While the standard diffusion tensor imaging (DTI) approach has proven to be a valuable tool in detecting local tissue structure and reconstructing neural fiber networks in brain, it cannot accurately reveal the white matter structure in the presence of multiple fiber orientations within a single voxel. In particular, for crossed fibers, the second-order diffusion tensor model fails to describe such a mixture of fiber orientations and the principal axis of the tensor in general will not lie along any of those directions. Recently, high angular resolution diffusion imaging (HARDI) methods [1,2] have been proposed to capture and estimate the multiple fiber populations in complex tissues, where the diffusion imaging is used with diffusion-weighting applied along many gradient directions with high sensitivity (large b-values). Here, based on the HARDI technique, we present a novel tractography approach to map white matter connections in regions with entangled fiber tracts.

**Methods** The proposed fiber tract mapping method extends the DTI-based diffusion simulation tractography (DST) [3] to accommodate the HARDI technique. The HARDI-based DST requires a more sophisticated diffusion simulation over brain tissues, which is governed by the generalized diffusion equation [4],

$\rho_t = \nabla_k (D_{kl}^{(2)} \nabla_l \rho + D_{klm}^{(3)} \nabla_{lm} \rho + D_{klmn}^{(4)} \nabla_{lmn} \rho + D_{klmno}^{(5)} \nabla_{lmno} \rho + D_{klmnop}^{(6)} \nabla_{lmnop} \rho + \dots)$ . Here we use the notation:  $\nabla_{i_1 i_2 \dots i_n} = \partial^n / \partial x_{i_1} \partial x_{i_2} \dots \partial x_{i_n}$ . The coefficient  $D_{i_1 i_2 \dots i_n}^{(n)}$  is an  $n$ -th order tensor, where the superscript  $n$  in parentheses indicates the order of the tensor and the subscript indicates the coordinate.  $x_i$  is the  $i$ -th spatial coordinate ( $i = 1, 2, 3$ ),  $\rho$  the concentration, and  $t$  the independent time variable. However, the odd rank tensor has to be ignored since negative diffusion coefficients are non-physical, which is implied by the generalized Stejskal-Tanner formula [5]. In order to derive the components of higher rank diffusion tensors, we first calculate the spherical harmonic decomposition coefficients,  $a_{lm}$ , using the spherical harmonic transform of the HARDI measurements [6]. Then we substitute the apparent diffusion

coefficient,  $D_{ADC}(g) = \sum_{l=0}^3 \sum_{m=-l}^l \sum_{i_1=1}^3 \dots \sum_{i_n=1}^3 D_{i_1 i_2 \dots i_n}^{(n)} g_{i_1} g_{i_2} \dots g_{i_n}$ , along the gradient direction into the spherical harmonic transform formula

$a_{lm} = \int_0^{2\pi} \int_0^\pi D_{ADC}(\theta, \varphi) Y_l^m(\theta, \varphi) \sin(\theta) d\theta d\varphi$ , where  $(\theta, \varphi)$  is the spherical coordinates,  $g = (g_1 g_2 g_3)^T = (\sin \theta \cos \varphi \quad \sin \theta \sin \varphi \quad \cos \theta)^T$ ,  $Y_l^m$  is the spherical harmonics and the superscript \* denotes complex conjugation. In the current implementation, we only consider the generalized diffusion tensor up to rank 4 although the method is general and can be extended to higher orders.

The HARDI-based DST algorithm starts from each seeded voxel and conducts the diffusion simulation over its associated computational kernel. A diffusion front is then constructed, from which additional seeded voxels will be picked in terms of the diffusion distance map and the vector transition angle. For the next round, each of the newly selected voxels will be used to generate a front by simulating a diffusion process in its own kernel. The same procedure will be repeatedly performed until no more voxels can be selected. Fiber tract can thus be reconstructed through back propagation by following continuously the predecessor voxels, which will lead to a tree structure-like pathway that ends at the starting seeded voxel. Since diffusion tensor with higher rank is involved, the generalized fractional anisotropy (GFA) measure is used to prevent tracking from entering areas with low anisotropy, which is based on the variance of the normalized diffusion coefficients and a scaled entropy index that treats the function as a probability distribution function [7].

**Data Acquisition** The HARDI data were acquired on a GE 3T Excite HDx scanner using EPI with a dual spin echo for eddy current compensation. The imaging parameters were FOV=240mm, TR=10900ms, TE=93100ms, acquisition matrix = 128 × 128. 61 diffusion encoding directions with b-value of 2500s/mm<sup>2</sup> and one reference image were acquired. The reconstruction matrix was 256 × 256, resulting in an in-plane resolution of 0.938 × 0.938 mm<sup>2</sup>. 32 axial slices were acquired with slice thickness of 3mm. The dataset was resampled to have an isotropic voxel size of 0.938mm.

**Results** In order to examine the capability of the HARDI-based DST method on handling regions with crossing fibers, we chose the corticospinal tract to reconstruct. The tracking started from a single seeded voxel in the internal capsule, as shown the yellow dot in Fig. 1. Before the corticospinal tract reaches up the motor cortex, it goes through the region of centrum semiovale (the white inset in Fig. 1) where each single voxel contains a mixture of fibers from the corpus callosum, corticospinal tract, and the superior longitudinal fasciculus. This is a region of complex fiber architecture known to cause problems with the second-order DTI tracking algorithms, as demonstrated by the DTI-based DST method in Fig. 2. In comparison, the results from our HARDI-based DST method are shown in Fig. 3 and clearly show the ability to track through the complex region. Both reconstructions are overlaid on the fractional anisotropy map for anatomical references, where fibers are color-encoded with FA and GFA values, respectively.

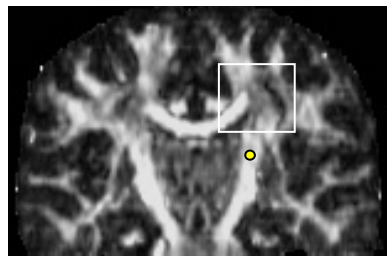


Fig. 1

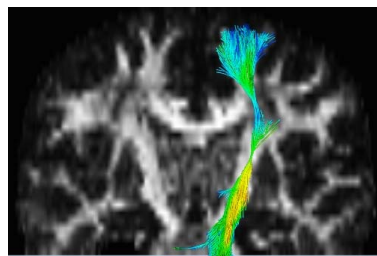


Fig. 2

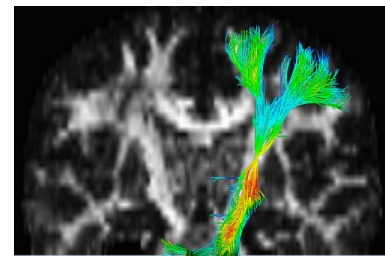


Fig. 3

**Conclusion** Regions of complex fiber architecture are common in the brain and pose a significant problem for standard DTI based tracking methods, therefore limit the utility of HARDI acquisition technique. Here we have proposed an extension of our previously demonstrated DST method to HARDI data that has potentials to overcome these limitations and thus provide more information about connectivity in the brain.

**References** [1] Tuch et al., Magn Reson Med, 2002, 48:577-582. [2] Frank, Magn Reson Med, 2002, 47:1083-1099. [3] Kang et al., IEEE Trans Med Imag, 2005, 24(9): 1127-1137. [4] Liu et al., Magn Reson Med, 2004, 51: 924-937. [5] Ozarslan et al., Magn Reson Med, 2003, 50:955-965. [6] Anderson, Magn Reson Med, 2005, 54: 1194-1206. [7] Ozarslan et al., Magn Reson Med, 2005, 53:866-876.

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