The Effects of Intra-voxel Fiber Architecture on the Diffusion Tensor Parameters

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INTRODUCTION: Diffusion Tensor Imaging (DTI) has established itself as a powerful tool in the characterization of anisotropic diffusion of water molecules within white matter (WM). With voxel sizes on the order of millimeters in a typical DTI experiment, the measured signal contains contributions from many individual axonal fibers. DTI methods of data analysis typically assume coherent fiber architecture: tracts containing many nerve fibers running in parallel which exhibit axially symmetric diffusion. This situation is easily expressed in terms of a symmetric diffusion tensor with eigenvalues $\lambda_1 >> \lambda_2 = \lambda_3$. In reality, the two minor eigenvalues of the diffusion tensor are rarely equal which can be attributed to a combination of signal noise and varying degrees of directional coherence of the nerve fibers within each voxel. This study uses numerical simulations to model the effects that various axonal fiber trajectories have on the measurable diffusion tensor.

METHODS: Four intra-voxel fiber trajectories shown in Figure 1a-d were simulated. A reference diffusion tensor $\mathbf{D_0}$ was chosen having eigenvalues $\lambda_1 = 2.5\times10^{-3}$ mm^2/s and $\lambda_2 = \lambda_3 = 0.5\times10^{-3}$ mm^2/s. These values approximate axially symmetric, highly anisotropic diffusion of the magnitude typically found in the human white matter. For each of the trajectories, the angle between the tangent to the line in the xy plane and the x axis was calculated at 100 points spaced evenly across the simulated voxel. These angles were used to rotate 100 instances of $\mathbf{D_0}$ about its z axis. Apparent diffusion coefficients (ADCs) for each of these 100 tensors were calculated along six standard gradient directions[1]. The means of the six ADCs were fit using a least-squares regression to estimate the average diffusion tensor for the voxel. Monte Carlo simulations were performed to analyze the effects of noise on the resulting diffusion tensors. ADCs at each gradient orientation were calculated at b=1000 s/mm^2. Complex noise modeled by two independent zero-mean Gaussian variables, $\eta \sim N(0,\sigma)+iN(0,\sigma)$, was then added and the ADCs were recalculated based on the magnitude of the real and imaginary signal components. The simulations were conducted for SNRs ranging from 20 to 1000. All calculations were performed using MATLAB (Mathworks, Natick, MA).

RESULTS: Figure 1e-f shows the diffusion tensor profiles resulting from each of the simulated fiber trajectories. As expected, the diffusion tensor for the straight line trajectory was equal to $\mathbf{D_0}$. For the remaining trajectories λ_1 decreased, λ_2 increased and λ_3 remained unchanged. Figure 1j-l shows that at low SNR, λ_1 and λ_2 were overestimated while λ_3 was underestimated. Below an SNR of 150, differences in λ_2 and λ_3 were predominantly caused by noise, whereas at high SNR the differences between the minor eigenvalues were a result of non-uniform fiber architectures. For all trajectories, Fractional Anisotropy (FA) decreased with increasing SNR. In the absence of noise, the FA for trajectories a,b,c and d were 0.77, 0.65, 0.72 and 0.69 respectively.

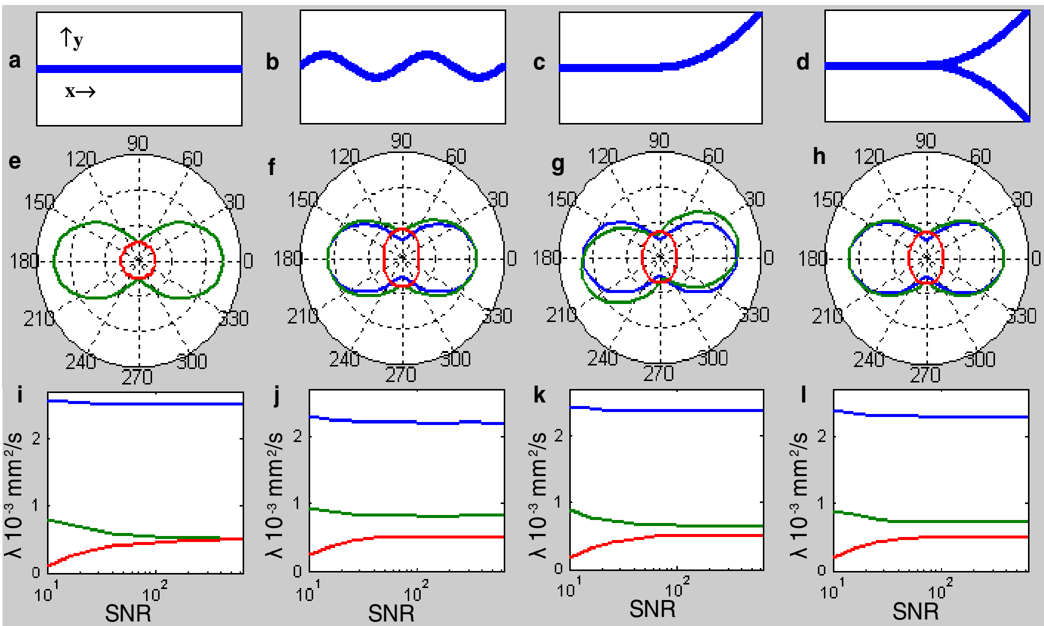

Figure 1. Simulated fiber trajectories. Functions were calculated at 100 evenly spaced points between $-0.5<x<0.5$ in the z=0 plane. **a:** Straight line: $f_a(x)=0$. **b:** Sinusoid: $f_b(x)=0.05\sin(4\pi x)$. **c:** Curve: $f_c(x)=0$ for $x<0$ and $f_c(x)=x^2$ for $x\geq0$. **d:** Two diverging fibers: $f_{d1}(x)=f_c(x)$ and $f_{d2}(x)=-f_c(x)$ **e-h:** Mean ADC measurements for each voxel plotted in polar coordinates for the xy (blue), xz (green), and yz (red) planes. **i-l:** Mean eigenvalues calculated with varying levels of noise present: λ_1(blue), λ_2(green) and λ_3(red).

DISCUSSION: As expected, small SNR is a major contributor to measured differences in λ_2 and λ_3. However, for DTI data with sufficiently high SNR, differences between λ_2 and λ_3 indicate non-uniform fiber architecture within the voxel. In this case, the assumption of axially symmetric diffusion is no longer valid and results in under/overestimation of the minor eigenvalues. Repeating the simulations with an increased number of gradient orientations produced similar results, although eigenvalues converged at lower SNR. This was to be expected since increasing the number of gradient orientations indirectly averages out the effects of noise. Variants of the simulations were also performed in three dimensions. In the case of four diverging fibers (analogous to Figure 1d with a pair of fibers in the xy plane and a second set in the xz plane), λ_2 and λ_3 converged for sufficiently high SNR. Though axially symmetric, FA was reduced relative to $\mathbf{D_0}$.

CONCLUSIONS: Various simulated fiber trajectories were shown to have similar effects on the measured diffusion tensor. A reduced FA and increased axial asymmetry in each case demonstrates the inability of the diffusion tensor methodology to resolve differences in intra-voxel fiber structures. Any hope of differentiating between fiber architectures on a sub-voxel level will require both an increase in measured gradient orientations and a framework beyond the diffusion tensor. Relatively high levels of SNR are required before non-uniform fiber architectures contribute significantly to differences in λ_2 and λ_3 above signal noise.

REFERENCES:

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