Explicit Formula for Diffusion Orientation Distribution Function using a Kurtosis Approximation

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Target audience: This work presents an analytical representation for the diffusion orientation distribution function (dODF) based on the diffusion tensor (DT) and diffusional kurtosis tensor (DKT). It is relevant for those interested in applying diffusion magnetic resonance imaging to the estimation of white matter fiber bundle orientation, particularly with regard to approaches that incorporate non-Gaussian effects. This explicit dODF formula may potentially be combined with white matter fiber tractography (FT) algorithms to improve accuracy and increase sensitivity to fiber crossings.

Purpose: The most commonly applied FT methods are based on diffusion tensor imaging (DTI) and have important advantages including relatively short image acquisition times and simple prescriptions for estimating fiber bundle orientations from the DT.[1] However, DTI utilizes a Gaussian approximation for the diffusion probability density function (dPDF) that limits its accuracy for predicting fiber bundle orientations and its sensitivity to intra-voxel fiber crossings. Here we describe a new explicit formula for the dODF that includes non-Gaussian diffusion effects through the DKT and investigate, with numerical simulations, the extent it can improve the quantification of fiber bundle orientation. This may be of practical utility as the DKT can be measured with diffusional kurtosis imaging (DKI).[2]

Methods: The dODF may be defined by $\psi_\alpha(\mathbf{n}) \equiv Z_\alpha^{-1}\int_0^\infty s^\alpha ds\, P(s\mathbf{n},t)$, where $\psi_\alpha(\mathbf{n})$ is the dODF in a direction given by a unit vector $\mathbf{n}$, $P(\mathbf{s},t)$ is the dPDF for a water molecule displacement $\mathbf{s}$ over a diffusion time t, and Z_α is a normalization constant. The power α affects the radial weighting of the ODF, with larger α corresponding to a greater sensitivity for long diffusion displacements. The maxima of the dODF are interpreted as indicating fiber bundle directions. The Gaussian approximation for the dODF, corresponding to DTI, is $\psi_{\alpha,G}(\mathbf{n}) = (\mathbf{n}^T\!\cdot\mathbf{U}\cdot\mathbf{n})^{-(\alpha+1)/2}$, where $\mathbf{U} \equiv \overline{D}\mathbf{D}^{-1}$, $\mathbf{D}$ is the DT and $\overline{D}$ is the mean diffusivity, and with the normalization constant Z_α being chosen so as to make the dODF dimensionless. For this Gaussian dODF, the maxima coincide with the direction of the principal DT eigenvector and are independent of α. An improved approximation that gives the leading non-Gaussian corrections is

$$\psi_{\alpha,K}(\mathbf{n}) \equiv \psi_{\alpha,G}(\mathbf{n})\cdot\left\{1+\frac{1}{24}\sum_{i,j,k,l}\left[3U_{ij}W_{ijkl}U_{kl}-6(\alpha+1)U_{ij}W_{ijkl}V_{kl}+(\alpha+1)(\alpha+3)V_{ij}W_{ijkl}V_{kl}\right]\right\}, \qquad \text{where } V_{ij}\equiv\frac{(\mathbf{U}\cdot\mathbf{n})_i(\mathbf{U}\cdot\mathbf{n})_j}{(\mathbf{n}^T\cdot\mathbf{U}\cdot\mathbf{n})}. \qquad (1)$$

Here W_{ijkl} represents the components of the DKT and the sums on the indices (i, j, k, l) are carried out from 1 to 3. It is also of interest to consider the non-Gaussian part of the dODF defined by $\Delta_{\alpha,K} \equiv \psi_{\alpha,K} - \psi_{\alpha,G}$. To investigate the relative accuracies for $\psi_{\alpha,G}$, $\psi_{\alpha,K}$ and $\Delta_{\alpha,K}$, multiple Gaussian compartment models were constructed to simulate voxels with intersecting fiber bundles. One type of model consisted of a dominant fiber bundle having a volume fraction of 0.8 together with an admixture of a subdominant bundle having a volume fraction of 0.2. A second type consisted of two bundles having equal volume fractions of 0.5. For the first model type, we calculated the error in the predicted angle for the dominant fiber bundle. For the second model type, we compared predicted fiber crossing angles to the exact values only for $\psi_{\alpha,K}$ and $\Delta_{\alpha,K}$, as $\psi_{\alpha,G}$ does not directly resolve intra-voxel fiber crossings. Each individual bundle was composed of two Gaussian compartments corresponding to intra-axonal and extra-axonal water. The intrinsic intra-axonal diffusivity was set to 1.0 μm^2/ms, the intrinsic extra-axonal diffusivity was set to 2.3 μm^2/ms, and the tortuosity for extra-axonal water diffusing perpendicular to the axons was set to 2.56.

Results: Figure 1 shows angular errors for the first model type. For the full DKT approximation of Eq. (1), the maximum error over the full range of intersection angles is least for α = 4 (3.3°), while for the non-Gaussian part the maximum error is least for α = 3 (2.8°). Black reference curves are included to show the angular error for the Gaussian approximation, which has a maximum error of 7.2°. Thus for this example, use of Eq. (1) may reduce the maximum error by over 60%. Figure 2 shows, for models of the second type, that the accuracy of the crossing angles predicted by Eq. (1) tends to improve with increasing α, up to α of about 3 or 4, and that the non-Gaussian part is more accurate than the full DKT approximation. For crossing angles less than about 30°, neither approximation was able to detect the fiber crossing.

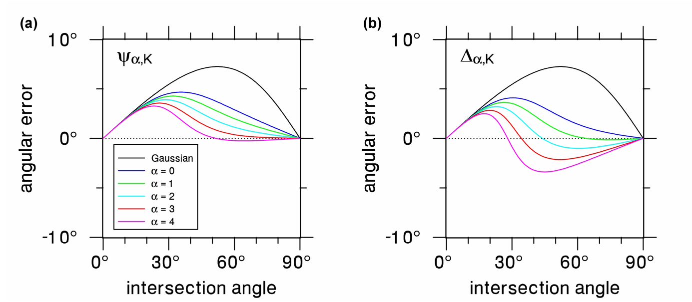

Figure 1. Angular error in predicted direction of a dominant fiber bundle as a function of the intersection angle with an admixture of a subdominant bundle. The black curves in (a) and (b) are for the Gaussian approximation. (a) also shows the full DKT approximation of Eq. (1) for various α values, and (b) shows the corresponding non-Gaussian parts.

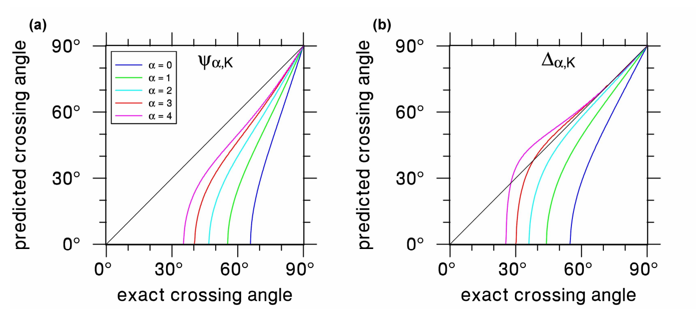

Figure 2. Predicted vs. exact crossing angles for two fiber bundles with equal volume fractions. (a) shows the DKT approximation of Eq. (1) for various α values, and (b) shows the corresponding non-Gaussian parts. The black diagonal lines of unit slope are included as references.

Discussion: The DKT approximation for the dODF given by Eq. (1) provides a convenient method of using non-Gaussian diffusion effects to improve upon the Gaussian approximation obtainable with DTI. The DKT is measurable with DKI, and the explicit analytical representation of Eq. (1) can facilitate its incorporation into FT algorithms. Our numerical results suggest that Eq. (1) can both improve the accuracy of the predicted fiber bundle direction and quantify fiber crossings that are undetectable with the Gaussian approximation. Equation (1) simplifies and generalizes a previously proposed kurtosis-based dODF approximation, which was restricted to α = 0 and required a numerical integration.[3] Our results also indicate that the accuracy of the DKT approximation depends significantly on α and that the non-Gaussian portion may be more accurate than the full dODF. Although a number of alternative non-Gaussian dODF approximations have been proposed (e.g., Q-ball imaging), the application of Eq. (1) to FT may be useful when a DKI dataset is available.

Conclusion: We have presented an explicit analytical formula for incorporating non-Gaussian effects into the calculation of the dODF. Compared to a Gaussian approximation, this formula improves accuracy and allows for the detection of crossing fibers. The formula depends only on the DT and DKT and can thus be evaluated with a standard DKI dataset.

References: **1.** Lazar M. Mapping brain anatomical connectivity using white matter tractography. NMR Biomed. 2010;23(7):821-835. **2.** Jensen JH, Helpern JA. MRI quantification of non-Gaussian water diffusion by kurtosis analysis. NMR Biomed. 2010;23(7):698-710. **3.** Lazar M, Jensen JH, Xuan L, Helpern JA. Estimation of the orientation distribution function from diffusional kurtosis imaging. Magn Reson Med. 2008;60(4):774-881. **Grant sponsors**: NIH (1R01AG027852, 1R01EB007656); NSF/EPSCoR (EPS-0919440).