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Fiber ball imaging

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ABSTRACT

By modeling axons as thin cylinders, it is shown that the inverse Funk transform of the diffusion MRI (dMRI) signal intensity obtained on a spherical shell in q-space gives an estimate for a fiber orientation density function (fODF), where the accuracy improves with increasing b-value provided the signal-to-noise ratio is sufficient. The method is similar to q-ball imaging, except that the Funk transform of q-ball imaging is replaced by its inverse. We call this new approach fiber ball imaging. The fiber ball method is demonstrated for healthy human brain, and fODF estimates are compared to diffusion orientation distribution function (dODF) approximations obtained with q-ball imaging. The fODFs are seen to have sharper features than the dODFs, reflecting an enhancement of the higher degree angular frequencies. The inverse Funk transform of the dMRI signal intensity data provides a simple and direct method of estimating a fODF. In addition, fiber ball imaging leads to an estimate for the ratio of the fraction of MRI visible water confined to the intra-axonal space divided by the square root of the intra-axonal diffusivity. This technique may be useful for white matter fiber tractography, as well as other types of microstructural modeling of brain tissue.

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Introduction

For strong diffusion weightings (i.e., high b-values), the angular dependence of the diffusion MRI (dMRI) signal intensity in white matter is sensitive to the complex geometries associated with intersecting axonal fiber bundles (Tuch et al., 2002). High-angular-resolution diffusion imaging (HARDI) methods exploit this property to estimate either a diffusion orientation distribution function (dODF) or a fiber orientation density (or distribution) function (fODF) that can be used, for example, as the basis for white matter fiber tractography (Lazar, 2010; Tournier et al., 2011). Q-ball imaging is a particularly elegant HARDI method in which a dODF is derived by taking a Funk transform of the dMRI signal intensity on a spherical shell in q-space (Descoteaux et al., 2007; Hess et al., 2006; Tuch, 2004; Tuch et al., 2003). The Funk transform (Bailey et al., 2003) is a straightforward linear operation that avoids the need for detailed modeling of the microstructure or for nonlinear numerical fitting procedures.

In this paper, we show that the inverse Funk transform of the dMRI signal provides an estimate of a fODF. The difference between a dODF and a fODF is that a dODF reflects the angular dependence of the water diffusion dynamics, while a fODF is meant to describe the angular dependence of the axonal fiber bundles. Typically, fODFs are based on a detailed tissue model for white matter microstructure, with the modeling parameters being determined by fitting to dMRI data (Anderson, 2005; Tournier et al., 2004, 2007). Such approaches have been highly successful (Wilkins et al., 2015), although the necessary calculations can be challenging (Parker et al., 2013). The fiber ball method described here may offer advantages in terms of simplicity and in being based on relatively mild assumptions.

The physical picture underlying fiber ball imaging is that the MRI visible water in white matter can be divided into two non-exchanging pools, one corresponding to water inside the axons and one to water outside the axons. This idealization has been widely used with dMRI for tissue modeling (Assaf et al., 2004; Fieremans et al., 2011; Jespersen et al., 2007; Panagiotaki et al., 2009, 2012; Zhang et al., 2012) and is supported by q-space imaging experiments (Assaf and Cohen, 2000). The extra-axonal water is assumed to be relatively mobile so that the dMRI signal from this pool decreases exponentially with increasing b-value. However, the signal from the intra-axonal water pool has a slower drop-off due to its diffusion being strongly restricted by the axon cell membranes. For this reason, the intra-axonal water becomes the dominant source of signal for large b-values, which enables properties of the intra-axonal space to be more easily calculated.

The primary purpose of this article is to describe the theory for fiber ball imaging and to contrast it with the closely related q-ball imaging method. In particular, we derive the inverse Funk transform

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relationship between the fODF and the dMRI signal intensity in the large b-value limit. We also consider a correction method that may improve the accuracy of the fODF for finite b-values. Finally, we present preliminary results for human brain obtained at 3 T with a b-value of 4000 s/mm^2.

Theory

Assumptions

Fiber ball imaging is based on several general assumptions about water diffusion and white matter microstructure. These are very similar to ones that have been used in prior studies and are commonly considered to be plausible idealizations, although definitive validation has so far not been fully achieved. Our key assumptions are:

1. The water that contributes substantially to the dMRI signal can be divided into two pools, corresponding to intra-axonal and extra-axonal water. This excludes the water within myelin, which makes a relatively small contribution to the signal because of its short T2 relaxation time (Stanisz et al., 1999).
2. The exchange time between the two water pools is large in comparison to the diffusion time of the dMRI sequence so that water exchange can be neglected. Water exchange times in white matter have been measured to be about 1 s (Nilsson et al., 2013) which is indeed long compared to the typical dMRI diffusion times. This assumption substantially simplifies the diffusion dynamics (Fieremans et al., 2010).
3. The diffusivities of the extra-axonal water compartments exceed some minimum value, $D_{e,\min}$, for all diffusion directions. This is what we mean by the extra-axonal water being relatively mobile.
4. The axons can be regarded as thin, straight cylinders. This requires that the q-vector be sufficiently small so that the dMRI signal is not sensitive to the internal geometry of the axons. More specifically, we must have $qa \ll 1$, where q is the magnitude of the q-vector and a is a typical axon radius. In terms of the b-value, this condition can be written as $ba^2 \ll \Delta$, where b is the b-value and Δ is the diffusion time. For a diffusion time of 50 ms and an axon radius of 2 μm (Aboitiz et al., 1992), this gives the condition $b \ll 12,500$ s/mm^2. In addition, the radius of curvature of the axons should be less than the typical diffusion length along the axis of the cylinders so that the straight cylinder approximation is justified. If the radius of curvature is r_c and the intrinsic intra-axonal diffusivity is D_a, this means that $\sqrt{2D_a\Delta} \ll r_c$; for $\Delta = 50$ ms and $D_a = 1.0$ μm^2/ms (Fieremans et al., 2011), one then has $10\ \mu\text{m} \ll r_c$.
5. The b-value is sufficiently large so that $bD_{e,\min} \gg 1$. When this is true, the contribution of the extra-axonal water to the dMRI signal can be neglected due to its exponential decrease with increasing b-value. The prior study of Fieremans and coworkers (Fieremans et al., 2011) found that the extra-axonal diffusivity was typically greater than 0.5 μm^2/ms, which suggests that we need $b \gg 2000$ s/mm^2.
6. All the axons within any given voxel have the same intrinsic intra-axonal diffusivity, D_a, although this may vary between voxels, and $bD_a \gg 1$. This assumption also sets a lower limit on the required b-value, which will depend on D_a. For $D_a = 1.0$ μm^2/ms, we must then have $b \gg 1000$ s/mm^2.

Inverse Funk transform expression for fODF

With the above assumptions, the dMRI signal intensity in white matter takes the form

$$S(\mathbf{n}) = S_0 \int d^3u f(\mathbf{u}) \exp\left[-bD_a(\mathbf{n}\cdot\mathbf{u})^2\right]\delta(|\mathbf{u}|-1), \tag{1}$$

where S_0 is the signal without diffusion weighting, $\mathbf{n}$ is the diffusion-encoding direction (with $|\mathbf{n}| = 1$), δ is the Dirac delta function, and f is the fODF. The fODF is assumed to be independent of the magnitude of $\mathbf{u}$ and is normalized so that

$$f_a = \int d^3u f(\mathbf{u})\,\delta(|\mathbf{u}|-1), \tag{2}$$

where f_a is the fraction of dMRI visible water for the axonal compartment. Without loss of generality, we can also assume, the reflection symmetry property

$$f(\mathbf{u}) = f(-\mathbf{u}). \tag{3}$$

This follows from the fact that our postulated cylindrical geometry for the axons is invariant with respect to a point reflection through the origin.

The Dirac delta function has the representation

$$\delta(x) = \lim_{\varepsilon\to 0} \frac{1}{\sqrt{2\pi\varepsilon}} \exp\left(\frac{-x^2}{2\varepsilon}\right). \tag{4}$$

This allows us to write

$$S(\mathbf{n}) \approx S_0 \sqrt{\frac{\pi}{bD_a}} \int d^3u f(\mathbf{u})\,\delta(\mathbf{n}\cdot\mathbf{u})\ \ \delta(|\mathbf{u}|-1), \tag{5}$$

in the limit that $bD_a \gg 1$ which holds according to Assumption 6. The integral in Eq. (5) is precisely the Funk transform of the fODF (Tuch, 2004). Thus we have

$$S(\mathbf{n}) \approx S_0 \sqrt{\frac{\pi}{bD_a}} T_F(f,\mathbf{n}), \tag{6}$$

with T_f indicating the Funk transform. Note that the signal decreases as $1/\sqrt{b}$, which is much slower than the exponential decrease assumed for the extra-axonal water pool.

The signal calculated from Eq. (6) is automatically invariant under the reflection symmetry $S(\mathbf{n}) = S(-\mathbf{n})$, which is indeed a generic property of the dMRI signal for an ideal experiment (e.g., if background gradients are negligible). Since the Funk transform is invertible for functions with reflection symmetry (Bailey et al., 2003), the fODF can be estimated by using the formula

$$f(\mathbf{n}) \approx \sqrt{\frac{bD_a}{\pi}} T_F^{-1}(S/S_0,\mathbf{n}), \tag{7}$$

where T_F^{-1} signifies the inverse Funk transform.

The Funk transform and its inverse are most conveniently calculated by using spherical harmonic representations for S and f. This is because the spherical harmonics, Y_l^m, are the eigenfunctions of the Funk transform (Descoteaux et al., 2007; Hess et al., 2006). Specifically,

$$T_F(Y_l^m,\mathbf{n}) = 2\pi P_l(0) Y_l^m(\theta,\phi), \tag{8}$$

where (θ,ϕ) are the spherical angles for $\mathbf{n}$ and P_l is the Legendre polynomial. This result allows Eq. (7) to be recast as

$$f(\mathbf{n}) \approx \frac{1}{2\pi}\sqrt{\frac{bD_a}{\pi}} \sum_{l=0}^{\infty} \frac{1}{P_{2l}(0)} \sum_{m=-2l}^{2l} a_{2l}^m Y_{2l}^m(\theta,\phi). \tag{9}$$

Here the parameters a_l^m are the spherical harmonic expansion coefficients for S/S_0 so that

$$S(\mathbf{n}) = S_0 \sum_{l=0}^{\infty} \sum_{m=-l}^{l} a_l^m Y_l^m(\theta,\phi). \tag{10}$$

Because of reflection symmetry for S, the coefficients a_l^m vanish whenever the degree l is an odd integer, and the sum in Eq. (9) is therefore only taken over even degrees of Y_l^m. The result of Eq. (9) is the key expression

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