Estimation of fiber Orientation Probability Density Functions in High Angular Resolution Diffusion Imaging

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A B S T R A C T

An estimator of the Orientation Probability Density Function (OPDF) of fiber tracts in the white matter of the brain from High Angular Resolution Diffusion data is presented. Unlike Q-Balls, which use the Funk–Radon transform to estimate the radial projection of the 3D Probability Density Function, the Jacobian of the spherical coordinates is included in the Funk–Radon approximation to the radial integral. Thus, true angular marginalizations are computed, which allows a strict probabilistic interpretation. Extensive experiments with both synthetic and real data show the better capability of our method to characterize complex microarchitectures compared to other related approaches (Q-Balls and Diffusion Orientation Transform), especially for low values of the diffusion weighting parameter.

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Introduction

Diffusion MRI is a recent MR modality that has made possible to characterize the white matter architecture in the brain in vivo (Basser et al., 1996). A popular model of the diffusion profile is based on the Gaussian assumption, which allows the diffusion to be modeled with a single covariance matrix, namely the diffusion tensor. With the advent of parallel imaging and better scanners, it is today feasible to acquire a larger number of diffusion weighted images in clinical time, the so-called High Angular Resolution Diffusion Imaging (HARDI). An advantage of HARDI is that it can better model more complex fiber architectures others than one single fiber bundle at each image voxel, such as crossing, bending, or kissing fibers.

A number of HARDI techniques have recently appeared, and among them Q-Ball imaging, which is based on the Funk–Radon Transform (FRT, (Tuch, 2004)), has gained popularity mainly because it can be robustly computed with closed-form expressions (Descoteaux et al., 2007) and does not require any assumptions about the behavior of the diffusion signal outside of the sampled sphere (Campbell et al., 2005; Perrin et al., 2008; Poupon et al., 2008).

Q-Balls use the FRT to approximate the Orientation Distribution Function (ODF) as the radial projection (integral) of the 3D Probability Density Function (PDF). An alternative approach to represent the orientation distribution is to marginalize the radial part of the PDF. Although these two approaches at first seem equivalent, a major difference for the latter is that the Jacobian of the spherical coordinates is included in the radial integral defining the marginalization, computing an angular function which is a true marginal PDF with a valid probabilistic interpretation. An estimator of such a function (the Orientation Probability Density Function, OPDF) is presented here. Like Q-Balls, our estimator is based on the FRT, so only very weak assumptions have to be made about the behavior of the diffusion signal outside the sampled sphere. As an additional contribution, we propose a matrix implementation that allows to compute it in a very fast and robust way. Our preliminary results indicate that this probabilistic approach better resolves fiber crossings compared to other related approaches (Q-Balls and Diffusion Orientation Transform), especially for low values of the diffusion weighting parameter. Results on brain HARDI data also show promising results indicating the ability to visualize regions of crossing fibers.

Background

The generalized gradient diffusion equation

An assumption inherent to diffusion imaging is that the probability of the displacement of a water molecule in a given angular direction is related to the presence of a fiber bundle in this same direction. Under
the assumption of narrow pulses, i.e., the duration of the sensitizing gradients $\delta$ is much smaller than the time between pulses $\Delta$; the PDF of the displacement of a water molecule to a position $R \in \mathbb{R}^3$ is given by the Fourier transform of the attenuation signal $E(\mathbf{q})$ (Callahan, 1991):

$$P(R) = \mathcal{F}(E(\mathbf{q}))(\mathbf{R}) = \int_{\mathbb{R}^3} E(\mathbf{q}) \exp(-2niq \cdot \mathbf{R}) \, dq$$

(1)

where $\mathbf{q} = \gamma \delta / 2NG = \mathbf{g}G / \parallel \mathbf{G} \parallel$ with $\gamma$ the gyromagnetic ratio, and $\mathbf{g} = G / \parallel \mathbf{G} \parallel$ is the unitary direction of the magnetic field gradient. In Diffusion Spectral Imaging (DSI), the whole $q$-space or at least a representative subspace of $\mathbb{R}^3$ is sampled, so the Fourier transform may be numerically computed to calculate $P(R)$ and infer the underlying fiber population (Tuch et al., 2003; Wedeen et al., 2005). This technique requires the sampling of all directions $\mathbf{g}$ and all magnitudes $q$, which clearly reduces its clinical usefulness.

**Sphere sampling of the diffusion signal**

To avoid the need to sample the whole $q$-space, the main assumption of Diffusion Tensor Imaging (DTI) is that the PDF of the displacement may be accurately described by a Gaussian process, so Eq. (1) reduces to the well-known Stejskal–Tanner equation (Stejskal and Tanner, 1965):

$$P(R) = \frac{1}{\sqrt{(4\pi)^3 |D|}} \exp\left(-\frac{R^T D^{-1} R}{4\tau}\right) \exp\left(-\mathbf{b}^T \mathbf{D} \mathbf{g}\right)$$

(2)

where $\tau = \Delta - \delta / 3$ is the effective diffusion time and $\mathbf{b} = 4\pi\eta q^2$ is the diffusion weighting parameter. The symmetric, positive-definite covariance matrix $D$ is the Diffusion Tensor (DT). The only unknowns are the six free components (due to the symmetry of the DT), so it is enough to know the value of $P(R)$ for six independent gradient directions $\mathbf{g}$ and one single $q$, since $D$ does not depend on $q$. More gradient directions may be acquired to palliate the effect of noise, and one single $q$ may be numerically computed to calculate $P(R)$ and infer the underlying fiber population (Tuch et al., 2003; Wedeen et al., 2005). This technique requires the sampling of all directions $\mathbf{g}$ and all magnitudes $q$, which clearly reduces its clinical usefulness.

**Inference of orientation information**

Although $E(\mathbf{q})$ is in general not completely characterized in HARDI, it is not necessary to either to completely characterize $P(R)$ (the probability density of each displacement), but only its underlying orientation information (displacements in the same directions are associated to the same fiber bundle); for each orientation $\mathbf{r}$ given by $(\theta, \phi)$, the expression for the marginal probability is:

$$p(\mathbf{r}) = p(\theta, \phi) = \int_0^\infty P(\mathbf{R}) R^2 \sin \theta dR$$

(5)

with $R = \|\mathbf{R}\|$. The term $R^2 \sin \theta$ is the Jacobian of the transformation to spherical coordinates and it is therefore required to compute actual probabilities so that the integral of $P(\mathbf{R})$ equals 1:

$$\int_0^\infty \int_0^3 P(\mathbf{R}) dR d\mathbf{r} = \int_0^\pi \int_0^{2\pi} \int_0^\infty P(\mathbf{R}) R^2 \sin \theta dR d\phi d\theta = \int_0^\pi \int_0^{2\pi} \int_0^\infty P(\mathbf{R}) R^2 dR d\phi d\theta = \int_0^\pi \int_0^{2\pi} \Phi(\theta, \phi) \sin(\theta) d\phi d\theta = 1$$

(6)

where $\Phi(\theta, \phi) \equiv \Phi(\mathbf{r})$ is the OPDF defined as:

$$\Phi(\theta, \phi) = \Phi(\mathbf{r}) = \int_0^\infty P(\mathbf{R}) R^2 dR$$

(7)

In the last integral of Eq. (6) the term $\sin(\theta)$ is once again due to the spherical coordinates system, i.e., it is required to compute the integral over the surface of the sphere. The orientation information for each direction $\mathbf{r}$ is characterized by the OPDF, which is a true probability density since its integral over all possible directions is 1. This definition has been already proposed before in Wedeen et al., 2005) as a “weighted radial summation”, although this approach, based on DSI, highly differs from the work here presented. Nevertheless, it turns out that it is usually easier to compute the ODF (Tuch et al., 2003) as the radial projection of $P(\mathbf{R})$:

$$\Psi(\theta, \phi) = \Psi(\mathbf{r}) = \int_0^\infty P(\mathbf{R}) R dR$$

(8)
The Jacobian of the spherical coordinates is dropped from the definition of $\Psi(r)$, so this function does not represent a true Probability Density Function, as has been noted before (Tuch, 2004; Tuch et al., 2003). In practice, this has the effect of blurring the orientation function at each direction is represented as the value of the orientation function at each direction is represented as the distance of the surface to the origin. As may be seen, both $\Phi(r)$ and $T(r)$ have sharper profiles than $\Psi(r)$. The blurring in the orientation information provided by the ODF ($\Psi(r)$) is a source of uncertainty in the estimation of fiber directions: two fiber bundles crossing in close directions would be more difficult to distinguish with the ODF than with the OPDF, since the two local maxima of the ODF could hinder each other. This statement will be thoroughly validated in the Results and discussion section.

The Funk–Radon Transform

The advantage of using the ODF relies on the fact that it may be accurately approximated by the Funk–Radon transform $G$ of the attenuation signal, defined for a given unitary direction $r$ as (Tuch, 2004; Tuch et al., 2003):

$$G(E(q)) = \int_{q=q_0}^{q_{\infty}} \int_{0}^{2\pi} \int_{0}^{\pi} P(R) J_0(2Rq_0) \rho \varphi d\rho d\varphi dR$$

$$= 2Z \int_{q=q_0}^{q_{\infty}} P(R) dR = 2Z \Psi(r)$$

(9)

where $\rho$ and $\varphi$ are the coordinates of a cylindrical system with the $z$ axis aligned with $r$: the integral of $E(q)$ along the equator perpendicular to $r$ (with radius $q_0$) is proportional to the integral of $P(R)$ inside a tube along $r$ given by the lobes of the Bessel function $J_0$: the larger the intensity of the sensitizing gradients $b_0 = 4\pi\gamma g_0^2$, the narrower the Bessel kernel and the better the approximation, see Fig. 2. $Z$ is a normalization constant. In this case only the values of $E$ along the equators of the sphere $S$ are required, so no assumption has to be made about the behavior of $E$ outside $S$. This is the principle of Q-Ball imaging as introduced in Tuch, (2004); Tuch et al. (2003). This technique was designed to estimate the ODF but not the OPDF, so the aim here is to use the FRT to build an estimator of the OPDF. The blurring due to the Bessel kernel will be discussed in the Methods section.

Spherical Harmonics Expansion

Since both the attenuation signal $E$ and the OPDF $\Phi$ are functions defined on a sphere, it is very convenient to represent them in the basis of Spherical Harmonics (SH), see for example Frank (2002). SH are defined as the eigenfunctions of the Laplace–Beltrami operator:

$$\Delta_l Y(\theta, \phi) = \frac{1}{\sin \theta} \frac{\partial}{\partial \theta} \left( \sin \theta \frac{\partial Y(\theta, \phi)}{\partial \theta} \right) + \frac{1}{\sin^2 \theta} \frac{\partial^2 Y(\theta, \phi)}{\partial \phi^2} = \lambda Y(\theta, \phi)$$

(10)

and may be put in the form:

$$Y_l^m(\theta, \phi) = \sqrt{\frac{2l + 1}{4\pi} \frac{(l-m)!}{(l+m)!}} P_l^m(\cos \theta) e^{im\phi}$$

(11)

$$v_l^m = -l(l+1), \quad m = -l, -l+1, \ldots, l$$

where $P_l^m$ are the associated Legendre polynomials; since the functions we are representing have all radial symmetry, it is enough to consider even orders, $l = 0, 2, 4, \ldots$, see Descoteaux et al. (2006) and Appendix B for more details. It has been proven by Descoteaux et al. (2007) that SH are eigenfunctions as well for the FRT. As a final remark, it has been proven that the SH decomposition of the ADC is equivalent to its representation with higher order tensors (Descoteaux et al., 2006).
Methods

Estimation of the OPDF from the attenuation signal

Our goal is to estimate the OPDF (\(\Phi(r)\)) as defined in Eq. (7). From Eq. (9), we know that the integral of a function along the direction \(r\) may be approximated by the integral on an equator perpendicular to \(r\) (i.e., the FRT evaluated at \(r\)) of its inverse Fourier transform. It is clear from Eq. (7) that the function to integrate is \(R^2P(R)\), so:

\[
\Phi(r) = \int_0^\infty R^2P(R) dR = \frac{1}{2} \int_0^\infty R^2P(R) dR = \frac{1}{2} Z R \tilde{E} q \left( E q \right) (r)
\]

(12)

where we have used the approximation given by Eq. (9) to integrate \(R^2 P(R)\). The unknown function \(\tilde{E} q \left( E q \right)\) is easy to determine, since it has to be the inverse Fourier transform of \(R^2 P(R)\); from basic Fourier analysis theory:

\[
\tilde{E} q \left( E q \right) = \frac{1}{2 \pi} \int_{-\pi}^{\pi} E q \left( E q \right) = C \cdot \tilde{G} (E q) (r)
\]

(13)

where now \(q = \left[ q_1, q_2, q_3 \right]^T\); the right hand side of Eq. (13) is clearly the Laplacian of \(E q\). Using this result in Eq. (12), our estimator may be written:

\[
\Phi(r) \approx \frac{1}{2} Z \tilde{G} \left( \frac{1}{4\pi} E q \right) (r) = C \cdot \tilde{G} (E q) (r)
\]

(14)

for a negative constant \(C\). Once again, due to the spherical symmetry of the problem, it makes sense to use the spherical coordinates representation of the Laplacian operator:

\[
\Delta E = \frac{\partial}{\partial q_1} \frac{\partial}{\partial q_1} E q + \frac{\partial}{\partial q_2} \frac{\partial}{\partial q_2} E q + \frac{\partial}{\partial q_3} \frac{\partial}{\partial q_3} E q
\]

(15)

The problem reduces to estimate the Laplacian of the attenuation signal \(E q\) in the sampled sphere at \(b_0\) to compute its FRT, which in turn may be decomposed in a radial part and a part which is proportional to the Laplace–Beltrami operator. Expressions for the tensor model may be found in Appendix A.

Estimation of \(\Delta_0\)

As said before, SH are eigenfunctions of the Laplace–Beltrami operator, so once the attenuation signal has been expressed in the basis of SH the second term in Eq. (15) is trivial to compute:

\[
E(q_0, g) = \sum_{l=0}^{L} \sum_{m=-l}^{l} C_{lm}^n \psi_l^m (g) \frac{1}{q^2} \Delta_0 E(q_0, g)
\]

(16)

\[
= \frac{1}{q^2} \sum_{l=0}^{L} \sum_{m=-l}^{l} \lambda_l (1 + 1) C_{lm}^n \psi_l^m (g)
\]

where \(C_{lm}^n\) are the coefficients of the SH expansion, computed as in Descoteaux et al. (2007), and in practice the sum is truncated to a few terms \(l \leq L\).

Estimation of \(\Delta q\)

The radial term in Eq. (15) is more difficult to compute since we have information only in the sphere of radius \(q_0\). Going back to Eq. (4), the assumption of a nearly constant ADC, underlying in higher order tensors or DOT, may be used to analytically compute the first derivative of \(E\):

\[
\frac{\partial E(q, g)}{\partial q} = \frac{1}{\partial q} \exp \left( -4\pi \tau q^2 D(q, g) \right)
\]

(17)

with the assumption of a constant ADC, \(\partial q \partial q = 0\) since it is assumed that \(D(q, g) = D(q, g) = D(q, g)\) for all \(q\); on the contrary, we only need to assume that \(\partial q \partial q \ll 2q / q_0\) so that we may neglect the derivative \(\partial q \partial q \) and therefore estimate \(\partial E / \partial q\) from one single \(q\). Qualitatively speaking, this is equivalent to assume that the attenuation signal for a given spatial direction \(g\) changes much faster than the shape of the ADC at this particular direction does. This assumption is checked in the final part of the numerical validation. Finally, we may estimate \(\Delta q\) as:

\[
\Delta q E(q_0, g) = -8\pi \tau q^2 D(q_0, g) \left( 3 - 8\pi \tau q^2 D(q_0, g) \right) E(q_0, g)
\]

(18)

Issues in the computation of the FRT

The blurring due to the Bessel kernel in the FRT (see the Funk–Radon Transform section) has an additional side effect in our case due to \(b_0\) is not positive (see Fig. 2, right). Consider the expression of the Laplacian for the tensor model given in Appendix A by Eq. (A.3) (for more complex models, the linearity of the problem may be used to infer identical conclusions); due to the positive-definite character of \(D\), it may be possible to find that, for the directions of maximum diffusion (largest \(\left| D(q) \right|\)):

\[
-8\pi \tau \left( -8\pi \tau \| D q \|^2 + \text{trace}(D) \right) E(q) > 0
\]

(19)

and so certain directions of \(q\), once the factor \(-1 / (4\pi 2)\) is applied, contribute to the FRT integral with negative values. This means that the integrals corresponding to certain directions \(r\) of the OPDF orthogonal to the directions \(q\) of maximum diffusion may be negative. Therefore, the modulus of the OPDF estimation has to be computed in all cases.

The Orientation Probability Density Transform

An overview of the whole estimation scheme may be seen in Fig. 3. The radial part of the Laplacian is expanded in the SH basis so that we may use the linearity of this expansion to compute the SH coefficients of the whole estimator. The synthesis formula of the SH, see Appendix B, may be used to compute the estimated probability density for any arbitrary direction \(r\), not necessarily corresponding to one of the original sampled directions. As an analogy

![Fig. 3. Summary of the proposed OPDF estimator, the so-called OPDT.](image-url)
with the DOT, we define the Orientation Probability Density Transform (OPDT) as the estimator described in Fig. 3.

OPDT is based on the Q-Balls implementation by Descoteaux et al. (2007), so it is fast and robust, and may be represented as a set of matrix computations as described in Appendix B. On the other hand, OPDT may be seen as a kind of contrast-enhanced Q-Ball. OPDT is computed as the FRT of the diffusion signal corrected with the attenuation signal. The curves stop when the estimators are not able to detect the fiber crossings. The curves stop when the estimators are not able to detect the fiber crossings.

Table 1

<table>
<thead>
<tr>
<th>$l_j$</th>
<th>$f^{-1}$ for different ratios of $e_2/e_1$ (Descoteaux et al., 2009 Eq. (13)); in the last row, $f^{-1}$ are computed based on the Laplace–Beltrami operator.</th>
<th>$l_j=2$</th>
<th>$l_j=4$</th>
<th>$l_j=6$</th>
<th>$l_j=8$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$e_2/e_1=0.5$</td>
<td>$0.159$</td>
<td>$3.53$</td>
<td>$36.16$</td>
<td>$301.96$</td>
<td>$2292.1$</td>
</tr>
<tr>
<td>$e_2/e_1=0.2$</td>
<td>$0.159$</td>
<td>$1.61$</td>
<td>$7.44$</td>
<td>$27.95$</td>
<td>$95.41$</td>
</tr>
<tr>
<td>$e_2/e_1=0.1$</td>
<td>$0.159$</td>
<td>$1.20$</td>
<td>$4.07$</td>
<td>$11.24$</td>
<td>$28.23$</td>
</tr>
</tbody>
</table>

The $l_j$ denotes the order of the SH (see Appendix B for details on notation).

The shaded region in Fig. 3 represents the mean error in the angle of the detected fibers as a function of the original angle between fibers. The curves stop when the estimators are not able to detect the fiber crossings (there are not two maxima in the orientation function).
For DOT we use \( R_0 = 12 \, \mu m \). Although a higher value (\( R_0 = 25 \, \mu m \)) may yield more accurate estimates for noise-free scenarios (Özarslan et al., 2006); (Prčkovska et al., 2008), in the presence of noise its performance is highly degraded. According to our experience, \( R_0 = 12 \, \mu m \) is the best trade-off between accuracy and robustness to noise in a real situation, so we keep this value in all our experiments to achieve a fair comparison.

For the noisy scenarios, we corrupt the simulated signal \( E(q) \) with Rician noise (Drumheller, 1993). Although the attenuation signal is computed as the quotient between the DWI signals and the baseline image, i.e., as the quotient between two Rician-distributed signals (Gudbjartsson and Patz, 1995), DWI are always much more noisy than the baseline; moreover, several baseline images are often available in HARDI data sets, so we consider the baseline is almost noise-free and therefore \( E(q) \) is closely enough to Rician distributed.

### Capability of resolving two crossing fibers

The capability of correctly resolving two crossing fibers and the accuracy in the determination of their directions is a standard benchmark for the assessment of micro-architecture resolution capabilities (Descoteaux et al., 2007; Özarslan et al., 2006; Prčkovska et al., 2008; Tournier et al., 2007, 2008; Tuch, 2004). For the noisy scenarios, we corrupt the simulated signal \( E(q) \) with Rician noise (Drumheller, 1993).

From this section we may conclude that OPDT is preferable: first to resolve fibers crossing in low angles, and second for low values of \( b_0 \); the third conclusion is that the OPDF is able to yield more accurate results and a higher angular contrast in most of cases.

### Behavior in the presence of noise

Although conventional MRI shows very good Signal to Noise Ratio (SNR), this is not the case in DTI/HARDI data sets; moreover,
higher values of $b_0$ yield stronger attenuation which for the same noise power $\sigma_n^2$ produces poor SNR. In this section we study the effect of varying the Peak Signal to Noise Ratio (PSNR, defined here as the maximum value of the baseline divided by $\sigma_n$ of the Rician-distributed signal $E(q)$) in the accuracy of the estimators. Analogous results to that of Fig. 4 may be found in Fig. 6 for S-1 (PSNR = 13.3), S-2 (PSNR = 13.3), S-4 (PSNR = 5) and S-5 (PSNR = 5).

Fig. 6. Mean error in the angle of the detected fibers as a function of the original angle between fibers in the presence of noise. Results are the average of 100 Montecarlo trials. In this case we consider a failure when the estimator is not able to detect the two fibers in the 50% of the trials.

Fig. 7. Estimates of the fiber population for S-4 with Q-Balls (top), DOT (middle) and OPDT (bottom), for crossing angles, from left to right: 90°, 75°, 65° and 60°. Rician noise with PSNR = 5 has been added to $E(q)$. 

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Obviously, noise worsens the accuracy of all the estimators. A number of techniques to palliate this effect have been successfully used in the literature (Clarke et al., 2008; Tristán-Vega and Aja-Fernández, 2008). In this case using more gradient directions improves both the minimum angle detectable and the accuracy. Note that increasing $b_0$ improves the result even when the SNR dramatically decreases.

The advantage of using OPDT is evident for lower $b_0$; for higher $b_0$, both OPDT and DOT show the same capability to resolve fiber crossings, but OPDT is slightly more accurate. Contrary to the behavior shown in Fig. 4, Q-Ball is now more accurate for higher $b$-values, especially for $N=200$. Qualitatively speaking, Q-Ball works by averaging the attenuation signal in a whole equator perpendicular to the direction of interest; therefore this estimator is indeed more robust to noise than OPDT, which is based on derivatives computed on the attenuation signal, accentuating the effect of noise. Besides, it has been previously described that there is a side effect in OPDT for noisy environments: the

![Fig. 8. Estimates of the fiber population with three crossing fibers for S-2 with PSNR = 13.3 (top) and S-5 with PSNR = 5 (bottom).](image)

![Fig. 9. Pseudo-color representation of $(2D/q)/(\partial D/\partial q)$ (error in the estimation of $\Delta q$, left) and $\Delta q/\Delta q$ (relative importance of $\Delta q$, right) for 2 (top) and 3 (bottom) crossing fibers. We represent half the $(\theta, \phi)$ space since the attenuation signal is symmetric. Fiber directions are represented as black spots, and values greater than 10 have been clipped to this value in all cases.](image)
OPDF estimated may yield negative values which have to be corrected by taking the modulus. This is a clear limitation of OPDT.

Nevertheless, the signal average inherent to Q-Balls produce an angular blurring of the orientation information, which justifies the fact that OPDT is able to recover lower crossing angles even in noisy scenarios. For low $b$-values, this blurring is more important than the effect of noise, and both OPDT and DOT perform better than Q-Ball for all crossing angles.

First, note that a $b_0$ value of 1200 s/mm² is more realistic in practical applications than 3000 s/mm², so the advantage of OPDT remains clear; second, for $b_0=3000$ s/mm² OPDT has an accuracy close to that of Q-Balls with the same capability as DOT to resolve crossings. An analogous representation to that of Fig. 5 is shown in Fig. 7 for scenario S-4 with PSNR=5. Consistently with the results in Fig. 6, Q-Balls give closer estimates to the true fibers, but its representation of the fiber populations is less intuitive and more blurred, failing to find the two populations before DOT or OPDT do, so the third important point is the better representation capability of OPDT and DOT.

Resolution of more complex architectures

For illustrative purposes we show in Fig. 8a situation with three crossing fibers; directions are: $(\theta_1, \phi_1) = (\pi/2, 0)$, $(\theta_2, \phi_2) = (\pi/2, \pi/2)$ and $(\theta_3, \phi_3) = (\pi 3/20, \pi/2)$; eigenvalues of $D_1$ are: $[2, 0.2, 0.3] \cdot 10^{-3}$, $[1.8, 0.4, 0.3] \cdot 10^{-4}$ and $[2, 0.1, 0.1] \cdot 10^{-3}$ mm²/s. We test scenarios S-2 with PSNR=13.3 and S-5 with PSNR=5.

Q-Balls completely blurs the orientation information and are not able to distinguish the three fibers. DOT fails to recover the three fibers for S-2, but for S-5 it is able to detect all of them with a mean error of 18°. OPDT is able to yield acceptable results in both situations, with respective mean errors of 10° and 16°.

Fig. 10. Relative error (averaged for $N=100$ gradient directions) in the estimation of the Laplacian as a function of the angle between 2 crossing fibers.

Fig. 11. Axial slice in the upper brain (the FA map of the whole slice is represented for illustrative purposes). Several important tracts may be identified: the superior longitudinal fasciculus (slf), the superior corona radiata (scr), the cingulus (cg) and the corpus callosum (cc). Glyph surfaces are colored here with the common convention of color per orientation.
We may conclude that OPDT is more accurate and robust as well for complex micro-architectures. As mentioned before, its advantage is clear for lower $b_0$ values.

Accuracy in the approximation of the Laplacian

We show in Fig. 9 a pseudo-color representation of $\frac{(2D/q)/(\partial D/\partial q)}{\Delta b/\Delta q}$ (see Eq. (17)) and $\Delta b/\Delta q$ (see Eq. (15)), computed as described in Appendix A for 2 and 3 crossing fibers. We show averaged values of these quotients for all $b_0$ between 1000 and 3000 s/mm². In most of the $(\theta, \phi)$ space $\frac{(2D/q)/(\partial D/\partial q)}{\Delta b/\Delta q}$ is greater than 10, and besides $\Delta b$ represents more than the 90% of the total value of $\Delta$, so the error is negligible. The greatest errors (small $\frac{(2D/q)/(\partial D/\partial q)}{\Delta b/\Delta q}$) are committed in the directions of the fiber bundles. However, with 2 fibers these directions correspond to zones where $\Delta b$ is clearly greater, so the overall error is small. With 3 fibers there are directions where $\frac{(2D/q)/(\partial D/\partial q)}{\Delta b/\Delta q}$ is small and $\Delta b/\Delta q$ is less than 10, but minima of $\frac{(2D/q)/(\partial D/\partial q)}{\Delta b/\Delta q}$ never overlap with minima of $\Delta b/\Delta q$. Therefore, we may conclude first that more complicated micro-architectures yield greater errors, and second that the relative error due to $\Delta b$ remains moderated compared to the total value of $\Delta = \frac{q_0}{C_0/C_1}$.

To support these conclusions, we show in Fig. 10 the relative error in the estimation of the Laplacian as a function of the angle between 2 crossing fibers. The error decreases in all cases as the fibers get closer, since the structure of $E(q)$ is simpler. Compared to Fig. 4, note that with OPDT the angular error anomaly decreases for fibers in angles below 50° or 60°, which may be explained by the fact that from 50° and below the relative error in $\Delta b$ dramatically decreases. When the fibers get too close, however, the estimator is

Fig. 12. Detail of the regions highlighted in Fig. 11. OPDT is able to detect fiber crossings even for $b_0 = 700$ s/mm²; note that region 2 is especially difficult due to the small angles of crossing.

Fig. 13. Axial slice of the midbrain, where the middle cerebellar peduncle (mcp), the pontine crossing tract (pct), the corticopontine tract (cpt), the corticospinal tract (cst), the medial lemniscus (ml) and the inferior cerebellar peduncle (icp) may be identified.
not able to resolve them and the error increases not depending on the error in $\Delta_q$.

Note that the error in $\Delta_q$ is obviously more important with lower $b_0$; our assumption implies that the exponential decay of $E(q)$ is much faster than the change in the shape of the ADC, and decreasing $b_0$ slows the decay of $E(q)$. Nevertheless we have previously shown that OPDT is more advantageous for lower $b_0$, so we may conclude that the error in the estimation of $\Delta_q$ is negligible; moreover, note that in the noisy case (see Fig. 6) the aforementioned artifact near $50°$–$60°$ is not present, so we may infer that the effect of noise is more important than the error in the approximation of $\Delta_q$ itself.

In vivo experiments

To test the behavior of the proposed estimator on real data, we use a HARDI volume of a volunteer, scanned in a 1.5 T GE Echospeed system (scanning sequence: Max. gradient amplitudes: 40 mT/M. Rectangular FOV 220 × 165 mm. 128 × 96 scan matrix (256 × 192 image matrix). 4 mm slice thickness, 1 mm inter(slice) distance. Receiver bandwidth 6 kHz. TE 70 ms; TR 80 ms (effective TR 2500 ms). Scan time 60 s/slice). It comprises 8 non-weighted baseline images and 51 independent gradient directions with diffusion weighting parameter $b_0=700$ s/mm$^2$. We deliberately choose such a small $b$ value to demonstrate the representation capabilities of OPDT even for very extreme conditions. The data set has been denoised with the filter proposed in Tristán-Vega and Aja-Fernández (2008).

In Fig. 11 a representative slice is shown; as can be seen, OPDT is able to yield anatomically correct results (Mori et al., 2005): the longitudinal fasciculus (green, left hand) goes longitudinally from top to bottom, as well as the cingulus (green, right hand), while the corpus callosum (red, right hand) crosses the cingulum from left to right and the corona radiata (blue, center) is perpendicular to the plane of the slice. More interestingly, OPDT is able to resolve the fiber crossings inside the highlighted zones (the horizontal red parts of the longitudinal fasciculus cross transversely with its longitudinal part in 1 and 2, and the corpus callosum crosses the cingulus in 3). These regions are shown in detail in Fig. 12.

To finish, we show in Fig. 13 an axial slice of the midbrain, where the fiber configuration is especially complicated. The main orientations given by OPDT are still anatomically correct (Mori et al., 2005), and yet the especially complicated crossings between the middle cerebellar peduncle and the pontine crossing tract in the highlighted zone are correctly detected. A detailed view of this zone is shown in Fig. 14.

Conclusion

We have introduced a simple, robust, yet very accurate estimator, the OPDT, for the probability density of fiber populations in a given direction. Its complexity is comparable to that of Q-Balls or DOT, but it can better resolve fiber crossings and represent fiber populations in many situations. Besides, it has a correct probabilistic interpretation: Q-Balls only estimate radial projections of true probability densities (the ODF), and DOT estimates only the value of the probability density at a given radius $R_0$. On the contrary, OPDT is an estimator of true marginal probability densities (OPDF), which turns out to be an important property in the representation of fiber populations. Compared to other related methods, the main assumption of our approach, i.e., the slow variation of the ADC, is rather conservative and has been proven not to be a limitation (yet its effect is hindered by the effect of noise), which gives OPDT the advantage of Q-Balls of not needing to assume any kind of underlying model, therefore showing general validity whenever Eq. (1) holds.

The proposed estimator is more advantageous for low $b_0$ values, so its computation is not very restrictive on the machinery used to acquire the diffusion images. In fact, the main utility of OPDT is in scenarios of low $b_0$.

On the contrary, for higher values of $b_0$ the accuracy in the estimation is not so clearly improved by OPDT compared to Q-Balls or DOT. In this sense, OPDT has two main drawbacks:

- The computation of the FRT produces negative values of the orientation information which have to be corrected by taking the modulus. This is an issue especially for very noisy scenarios, for example in images acquired with a high $b_0$ where the SNR is highly degraded. In these cases Q-Balls may be preferable, since their accuracy is similar to that of OPDT for high $b_0$ and they are more robust to noise due to the FRT averaging.
- Although only in a local sense, we still need to make an assumption on the behavior of the ADC outside the sampled sphere. This assumption is very weak but compared to Q-Balls, for which absolutely no assumption is required, it is still a drawback.

As a final remark, the value of $R_0$ for DOT used in our experiments is not optimal for noise-free scenarios, where taking $R_0=25\mu m$ may highly improve the accuracy of the estimation for high $b_0$. This improvement may even outperform OPDT in some situations. The problem is that using a high $b_0$ (which is necessary for DOT to work properly) results in an exponential worsening of the SNR. As a consequence, these two conditions (high $b_0$ and high SNR) are not compatible in general, unless an adequate denoising scheme (whose necessity in HARDI has been widely reported previously; Clarke et al., 2008; Descoteaux et al., 2008) is implemented.

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A. Expressions of the Laplacian for the tensor model

A.1. Laplacian in Cartesian coordinates

With the notation in Eq. (13), the Stejskal–Tanner equation may be written in the form:

\[ E(q) = \exp(-4\pi q^2 \Delta q) \]

(A.1)

and so, due to the symmetry of the diffusion tensor:

\[ \frac{\partial}{\partial q_i} E(q) = -4\pi q \left( 1, 0, 0 \right) D q + q ^2 \left( 1, 0, 0 \right) ^T E(q) \]

\[ \frac{\partial ^2}{\partial q_i ^2} E(q) = -8\pi \left( -8\pi \left( 1, 0, 0 \right) D q \right) ^2 + \left( 1, 0, 0 \right) \left( 1, 0, 0 \right) ^T E(q) \]

(A.2)

Computing the corresponding terms for \( q_2 \) and \( q_3 \), the expression for the Laplacian is:

\[ \Delta E = -8\pi \left( -8\pi \left( 1, 0, 0 \right) D q \right) ^2 + \text{trace}(D) D q \]

(A.3)

A.2. Radial projection of the Laplacian

From Eq. (2) and taking into account that \( b = 4\pi q^2 \), \( \Delta \), may be written as:

\[ q^2 \frac{\partial}{\partial q} E(q) = q^2 \left( -8\pi q g^T D g \right) E(q) \]

\[ \Delta E(q) = \left( q^2 \left( -8\pi q g^T D g \right) - 24\pi q^2 g^T D g \right) E(q) \]

\[ + 8q^2 \pi q g^T D g \left( 8\pi q^2 D q - 3 \right) E(q) \]

(A.4)

Note that this last equation is formally identical to the expression in Eq. (18). Moreover, for the tensor model \( q^2 D(q, g) = q^2 g^T D g \Delta \), \( D(q, g) = g^T D g \), and Eq. (18) is the exact expression of \( \Delta \).

B. Matrix computation of the OPDT

The analysis and synthesis equations of the SH expansion, as well as the expression of the FRT, may be written as matrix operations (Descoteaux et al., 2007). In this Appendix we extend this work to the OPDT; we derive the matrix computation of the Laplacian and then exploit the properties of the resulting matrices to give a closed-form representation.

B.1. Notation

Like in Descoteaux et al. (2007), we change the indexation of the SH basis to represent them with one single index \( j \). For each even order \( l \), it is easy to note that we have \( H_l = 2l + 1 \) basis functions \( Y_l^m \), so the following indexation may be used:

\[ \left\{ Y_{j} \left| j = \frac{l}{2} (l - 1), \ldots, \frac{l}{2} (l + 3) \right. \right\} = \left\{ Y_{l}^{m} \right\} \text{, } l \text{ even } \]

(B.1)

Besides, we use the notation:

\[ j_{l} : l = \frac{l}{2} (l - 1), \ldots, \frac{l}{2} (l + 3), l \text{ even } \]

(B.2)

for the order of the \( j \)-th SH. It is easy to note that the total number of SH basis functions for an expansion up to order \( L = 2l \) is

\[ H = \sum_{m=-l}^{l} q^m H_{2l} = (L/2 + 1)(L + 1) \].

The set of \( N \) sampling directions of \( E(q) \) is denoted as \( \Theta = \left\{ (\theta_1, \phi_1), (\theta_2, \phi_2), \ldots, (\theta_N, \phi_N) \right\} = \left\{ (g_1, g_2), \ldots, g_N \right\} \); the set of \( N' \) sampling directions for which the ODF or the OPDF is computed is \( \Theta' = \left\{ (\theta_1', \phi_1'), (\theta_2', \phi_2'), \ldots, (\theta_{N'}, \phi_{N'}) \right\} = \left\{ (r_1, r_2, \ldots, r_N) \right\} \).

Therefore, we may define the \( N \times 1 \) vectors \( E \) (attenuation signals) and \( D \) (log-signal); the \( R \times 1 \) vectors \( C \) (SH coefficients of \( E \) or \( \Delta E \)) and \( C' \) (the SH coefficients of the ODF or the OPDF); the \( N' \times 1 \) vector \( P \) (the ODF or OPDF at each direction in \( \Theta' \)) as:

\[ \begin{align*}
E_i &= E(g_0 g_i); \\
D_i &= \log E(g_0 g_i); \\
C_j &= C_j^i; \\
C'_j &= C_j^i \times \left( H \times 1 \right) \\
P_i &= \Psi(r_i) or \phi_i; \\
\end{align*} \]

\[ (N' \times 1) \]

We define the matrix of eigenvalues of the SH basis \( L \) and the FRT matrix \( F \) as \( H \times H \) diagonal matrices of the form (Descoteaux et al., 2007):

\[ \begin{align*}
(L)_{ij} &= -l_i^2 (l_j + 1); \\
(F)_{ij} &= \begin{cases} 1, & j = 0 \\
2\pi (l_i^2 + 1 \cdot 3 \cdot 5 \cdot \ldots \cdot (l_i - 1)) / 2 \cdot 4 \cdot 6 \cdot \ldots \cdot l_i, & j > 0 \end{cases} \\
\end{align*} \]

(B.4)

Finally, we define the matrix \( B \) (resp. \( B' \)) as the \( N \times H \) (resp. \( N' \times H \)) matrix of the evaluations of the \( H \) SH basis functions in the set \( \Theta \) (resp. \( \Theta' \)):

\[ \begin{align*}
B_{ij} &= Y_{ij}(\theta_i, \phi_i); \\
B'_{ij} &= Y_{ij}(\theta_i', \phi_i); \\
\end{align*} \]

(B.5)

B.2. Q-Balls computation

The SH analysis equation is posed by (Descoteaux et al., 2007) as a regularized Least Squares (LS) problem, so:

\[ C = \left( B' \Lambda + \lambda L^2 \right)^{-1} B' E \]

(B.6)

where \( \lambda \) is the regularization parameter; the product with \( L^2 \) is used to penalize higher values of the Laplacian, i.e. higher energies of the second derivatives. Since \( SH \) are eigenfunctions for the FRT, the following expression holds:

\[ C' = F C = F \left( B' \Lambda + \lambda L^2 \right)^{-1} B' E \]

(B.7)

It only remains to evaluate the SH expansion at the directions in \( \Theta' \) to obtain:

\[ P = B' C' = B' F \left( B' \Lambda + \lambda L^2 \right)^{-1} B' E \]

(B.8)

Note that the whole Eq. (B.8) may be precomputed for all voxels except for the product with \( E \), so the estimation of \( \Psi(r) \) requires only a product of an \( N' \times N \) matrix by an \( N \times 1 \) vector.

B.3. OPDT computation

From the scheme in Fig. 3 and the LS representation in Eq. (B.6), together with the definition of \( D \) in Eq. (B.4) it follows:

\[ C = \left( B' \Lambda + \lambda L^2 \right)^{-1} B' \left( \frac{2}{q_0^2} D \cdot (3 + 2D) \cdot E \right) \]

\[ + \frac{1}{q_0^2} L (B' \Lambda + \lambda L^2)^{-1} B' E \]

(B.9)
where the dot products must be understood as element-wise operations. The first term in Eq. (B.9) is the SH decomposition of the approximation of $\Delta_\alpha$ as in Eq. (18). In the second term, we first compute the SH expansion of $\mathbf{E}$ and then use the property of the SH of being eigenfunctions of the Laplace–Beltrami operator to compute $\Delta_\alpha$. Taking into account that both $\mathbf{L}$ and the $\mathbf{S}$ matrix $(\mathbf{B}^T\mathbf{B} + \lambda \mathbf{L}^2)^{-1}$ are symmetric matrices and therefore they commute, we may write:

$$
C = \frac{1}{q_0} \left( \mathbf{B}^T \mathbf{B} + \lambda \mathbf{L}^2 \right)^{-1} \left( 2\mathbf{B}^T [\mathbf{D} \cdot (3 + 2\mathbf{D}) \cdot \mathbf{E}] + \mathbf{L} \mathbf{B}^T \mathbf{E} \right) \quad \text{(B.10)}
$$

And finally the estimator of $\Phi(\mathbf{r})$ is written:

$$
P = \frac{1}{4\pi^2 q_0} \mathbf{B}^F \left( \mathbf{B}^T \mathbf{B} + \lambda \mathbf{L}^2 \right)^{-1} \left( 2\mathbf{B}^T [\mathbf{D} \cdot (3 + 2\mathbf{D}) \cdot \mathbf{E}] + \mathbf{L} \mathbf{B}^T \mathbf{E} \right) \quad \text{(B.11)}
$$

Note that we do not have to know the exact value of $q_0$ if we normalize $\Phi(\mathbf{r})$, as opposed to the case of the DOT, see Özarslan et al. (2006, Appendix A, Eq. (28)). The $N \times H$ matrix $\mathbf{B}^F \left( \mathbf{B}^T \mathbf{B} + \lambda \mathbf{L}^2 \right)^{-1}$ and the $N \times H$ matrix $\mathbf{L} \mathbf{B}^T$ may be precomputed, so for each voxel we have to compute $N$ logarithms, $2N$ products (the radial part of the Laplacian), two products of an $N \times H$ matrix by an $N \times 1$ vector, and a product of an $N^2 \times 1$ matrix by an $N \times 1$ vector.

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