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Review of orientation distribution function (ODF) calculation methods

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Review of Orientation Distribution Function (ODF) Calculation Methods

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Abstract

This review summarizes and discusses the various methods for calculating an orientation distribution function (ODF) in high angular resolution diffusion imaging (HARDI). It compresses a variety of articles on the subject into a single, consistent, coherent document. In doing so, we hope to clarify the relations between the various ODF calculation methods and provide as single reference document for those wishing to review or use these methods. We also discuss the assumptions made and specific problems associated with ODF calculations.

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Chapter 1

Introduction

1.1 Motivation

The goal of this paper is to summarize the knowledge that is available regarding various methods for calculating an orientation distribution function (ODF) in high angular resolution diffusion imaging (HARDI) and to analyze these methods for potential downfalls and specific assumptions. By doing so, we hope to make information about ODF calculation methods available in a single, clear, consistent document so as to avoid confusion regarding what specific assumptions must be made for certain methods and what the strong and weak points of each method are.

We will start with a brief explanation of general HARDI theory and an overview of the two primary ODF calculation methods for HARDI. We also discuss the structure of this report.

1.2 HARDI theory

High angular resolution diffusion imaging (HARDI) functions on the physical principle of the Brownian motion of water molecules within a restricted compartment. With Brownian motion we refer to the random movement of molecules due to thermal energy and collisions with other molecules in the fluid medium. HARDI makes use of the anisotropy of diffusion in a restricted compartment to calculate the lay of fibres within tissues.

Though the exact combination of structures that leads to diffusion anisotropy in neural tissue has yet to be uncovered, the fact remains that this anisotropy has been observed [3]. The basic premise is that water diffuses more easily along the axis of a fibre than perpendicular to it. This means that detection of the peaks of a diffusion pattern will help to determine the lay of the fibres in the image.

The original work on diffusion imaging was published by Stejskal and Tanner in 1965 [9]. Since then, a variety of methods has been developed to convert the diffusion measurements that were described in this paper into images that are easy to interpret for physicians. We focus here on the calculation of an orientation distribution function (ODF).

1.3 ODF calculation methods in HARDI

In order to be able to use tractography algorithms on HARDI data, it is first necessary to compute the direction(s) of strongest diffusion in each voxel. One manner of doing this is to calculate the orientation distribution function (ODF) per voxel. This function can be seen as a sphere deformed to be proportional to the diffusion probability density function in each radial line.

An ODF calculation is generally performed for either one of the variations of Q-ball imaging (QBI) or in the diffusion orientation transform-ODF (DOT-ODF) method. The advantage of Q-ball imaging is that it does not require a diffusion model for its calculations (though it does assume the diffusion to be symmetrical) [2]. Also, DOT-ODF assumes that diffusion takes place according to a Gaussian model, which may not be accurate, depending on the gradient characteristics of the scan. [2]

Q-ball imaging transforms the real domain to q-space (this is akin to what the conversion to k-space is for T1- or T2-weighted magnetic resonance (MR) imaging) and performs the necessary calculations in this new domain. It is important for this method to use the correct definition of a probability density function in the calculations, as failure to do so results in artificial weighting of- and broadening of the peaks of the ODF.

DOT-ODF assumes a Gaussian model of diffusion (which equates to exponential diffusion signal decay). This may be problematic due to the current attainable resolution for HARDI voxels: roughly $10mm^3$ [2].

In this review we discuss the Q-ball imaging and DOT-ODF methods in terms of the basic principles and the strengths and weaknesses of each.

1.4 Setup of report

In the following chapter, we discuss the various aspects of Q-ball imaging, starting with one of the most important works on this subject by Tuch. Using this as foundation, we discuss the problems that arise when following

Tuch's paper, especially as discussed by Barnett. We then present several alternatives to the "standard" Q-ball imaging method and conclude by summarizing the strenghts and weaknesses of the approach.

In the third chapter, we consider the DOT-ODF method, starting with an overview of the theory. We then discuss in detail the strengths and weaknesses of this method using the assumptions it requires as starting point.

We conclude with an overview of the two methods' strenghts and weaknesses and conclude that at this moment Q-ball imaging using a correct definition of a probability density function is the most broadly applicable method due to its lack of underlying signal model assumptions.

For an overview of the symbols and most important formulae used in the report, we refer the reader to the appendices.

Chapter 2

Q-ball ODF

This chapter presents a discussion regarding the Q-ball imaging method for calculating a orientation distribution function. The required theory is presented first, followed by a discussion regarding the weaknesses of the method and potential alternatives. Concluding remarks regarding the strengths and weaknesses of the method are made in the last section.

2.1 Tuch's Q-ball ODF calculation

The first work specifically regarding Q-ball imaging was an article published in 2004 by David Tuch. We will first present the theory as described in this article, as it provides a good foundation from which to launch further discussions on Q-ball imaging.

2.1.1 The conditional diffusion PDF and the MR signal

We will represent the conditional probability that a spin originally at $\boldsymbol{r_0}$ has migrated in the direction and distance indicated by $\boldsymbol{R}$ in time τ with $\mathsf{P}(\boldsymbol{R}+\boldsymbol{r_0},\tau,\boldsymbol{r_0})$.

In magnetic resonance imaging (MRI), the observed signal is a result of the average spins in the voxel. This average is given by [7]:

$$P(\boldsymbol{R},\tau) = \int \rho(\boldsymbol{r_0})\mathsf{P}(\boldsymbol{R}+\boldsymbol{r_0},\tau,\boldsymbol{r_0})d\boldsymbol{r_0} \tag{2.1}$$

Here, $\rho(\boldsymbol{r_0})$ is the initial spin density of the voxel. Note that Tuch chooses to refer to $P(\boldsymbol{R},\tau)$ as the diffusion probability density function and to $\mathsf{P}(\boldsymbol{R}+\boldsymbol{r_0},\tau,\boldsymbol{r_0})$ as the *conditional* diffusion probability density function [7].

The relation between $P(\boldsymbol{R},\tau)$ and the normalized MR signal is given by the Fourier transform [7]:

$$P(\boldsymbol{R}, \tau) = \mathcal{F}[E(\boldsymbol{q})] \tag{2.2}$$

In this case, E represents the normalized MR signal ($E(\boldsymbol{q}) = S(\boldsymbol{q})/S_0$ - where S is the true MR signal and S_0 is the static field MR signal) and $\mathcal{F}$ represents a Fourier transform with respect to $\boldsymbol{q}$, the diffusion wave vector given by [7]:

$$\boldsymbol{q} = \frac{\gamma\delta\boldsymbol{g}}{2\pi} \tag{2.3}$$

Where γ is the gyromagnetic ratio, δ is the gradient pulse duration, and $\boldsymbol{g}$ is the diffusion gradient vector. Note that $\boldsymbol{q}$ is reciprocal to $\boldsymbol{r} - \boldsymbol{r_0}$ [7].

In vivo, the reconstruction of the desired conditional PDF via the complex Fourier transform becomes impossible due to the corruption of the phase of the signal by biological motion [7]. Instead, one can choose to reconstruct the signal using the modulus Fourier transform, which Tuch proves to be equivalent to the complex transform under the given conditions in his thesis [13]. We thus get:

$$P(\boldsymbol{R}, \tau) = \mathcal{F}[|E(\boldsymbol{q})|] \tag{2.4}$$

Important to note is that this equation only holds if there is no appreciable diffusion during the diffusion encoding period. According to Tuch, “This condition requires that the diffusion mixing length associated with the diffusion encoding time is smaller than a characteristic diffusion restriction size of the material.” [7] The requirement for short diffusion pulses is also called the “narrow pulse condition”. We discuss the problems associated with this condition later in the chapter.

The narrow gradient pulse approximation is given by [4]:

$$S(\boldsymbol{g}) = \int \rho(\boldsymbol{r_0}) \int P(\boldsymbol{r} - \boldsymbol{r_0}, \tau) \exp{(i\gamma\delta\boldsymbol{g} \cdot (\boldsymbol{r}))} d(\boldsymbol{r}) d\boldsymbol{r_0} \tag{2.5}$$

Stejskal and Tanner found that if both diffusion with tensor $\boldsymbol{D}$ and directed flow with velocity $\boldsymbol{v}$ occur, then [9]:

$$S(\boldsymbol{g}) = S(0) \exp{(-\gamma^2\delta^2\boldsymbol{g} \cdot \boldsymbol{D} \cdot \boldsymbol{g}\Delta - i\gamma\delta\boldsymbol{g} \cdot \boldsymbol{v}\Delta)} \tag{2.6}$$

If the pulse is finite, then the Δ in the first term of the exponent is replaced by effective time $\Delta - \frac{1}{3}\delta$. The second term remains unaltered in this case [4] [9].

In Tuch’s case, the finiteness of the pulse implies that the resulting $P(\boldsymbol{R}, \tau)$ is a center of mass propagator [7].

This all being said, what we are truly interested in is the tissue orientation, which is derived from $P(\boldsymbol{R},\tau)$ via the orientation distribution function (ODF).

2.1.2 Derivation of the ODF formula

To calculate diffusion orientations from $P(\boldsymbol{R},\tau)$, Tuch introduces his formula for the orientation distribution function, which we will subsequently refer to as the tODF (Tuch's ODF). Note that the equation below describes the radial projection of $P(\boldsymbol{R},\tau)$ [7].

$$tODF(\boldsymbol{u}) = \frac{1}{Z}\int_0^\infty P(r\boldsymbol{u},\tau)dr \tag{2.7}$$

In this formula, Z is a dimensionless normalization constant which ensures that the tODF is normalized to unit mass. Note however, that to define the ODF over a proper sphere (it is now a distribution over radial projections), integration over solid angle elements would be required [7].

Unfortunately, direct reconstruction of the ODF from $P(\boldsymbol{R},\tau)$ has the following disadvantages [7]:

- The mapping between a Cartesian grid and spherical coordinates performed for the radial projection introduces Cartesian artifacts in the ODF.
- Radial projection is highly inefficient, since a large portion of the available data is discarded.
- Strong pulsed field gradients are required to satisfy the Nyquist condition for diffusion in cerebral white matter.

Sampling the ODF directly on a spherical shell in reciprocal space is significantly more efficient, and so Tuch proceeds to derive a relation for the tODF that no longer depends on $P(\boldsymbol{R},\tau)$. To do so, he requires the use of the Funk-Radon transform, otherwise known as the Funk transform.

2.1.3 The Funk-Radon transform (FRT)

Please note that Tuch actually extends the *Funk-Radon Transform (FRT)*, also known under the name Funk transform, to represent the FRT at a given radius. Compare the following:

The original Funk-Radon transform:

$$\mathcal{M}[f](\boldsymbol{n}) = \int_{S_u} f(\boldsymbol{x})\delta(\boldsymbol{x}\cdot\boldsymbol{n})d\boldsymbol{x} \tag{2.8}$$

This is an even function ($\mathcal{M}[f](\boldsymbol{n}) = \mathcal{M}[f](-\boldsymbol{n})$) in which the $d\boldsymbol{x}$ is the normalized Haar measure on the unit sphere S_u and the δ is a Dirac delta [14]. Also note that the Funk transform annihilates all odd functions (i.e. it transforms continuous even functions to continuous even functions [7].

Tuch's modified Funk-Radon transform [7]:

$$\mathcal{M}[f](\boldsymbol{n}, R) = \int_{S_u} f(\boldsymbol{x})\delta(\boldsymbol{x} \cdot \boldsymbol{n})\delta(|\boldsymbol{x}| - R)d\boldsymbol{x} \tag{2.9}$$

Note that the additional Dirac delta ($\delta(|\boldsymbol{x}| - R)$) ensures that the transform integrates to zero on all but the desired radius. It does not change the fact that the FRT is even. In calculations for Q-ball imaging, R will be taken as Q, the radius of the sampling sphere in Q-space [7].

Now Tuch claims that via the FRT, one can derive the tODF as being equivalent to the following [7]:

$$tODF(\boldsymbol{u}) \approx \frac{1}{Z}\int_{S_u} E(\boldsymbol{q})\delta(\boldsymbol{q} \cdot \boldsymbol{u})\delta(|\boldsymbol{q}| - Q)d\boldsymbol{q} = \frac{1}{Z}\mathcal{M}[E(\boldsymbol{q})] \tag{2.10}$$

We will describe step-by-step how he comes to this conclusion [7].

1. We begin by noting that in cylindrical coordinates, the real-space vector is written $\boldsymbol{r} - \boldsymbol{r_0} = \hat{\boldsymbol{r}} = (r, \theta, z)$ and the Fourier space vector is written $\boldsymbol{q} = (q, \vartheta, \zeta)$.
2. Without loss of generality, take the z-axis to be the direction of interest ($\boldsymbol{u}$).
3. Now we can write the radial projection as $p(r, \theta) = \int_{-\infty}^{\infty} P(r, \theta, z, \tau)dz$
4. The FRT (Tuch's version) of the signal is given by:

$$\mathcal{M}[E] = \int_{S_u} E(Q, \vartheta, 0)d\vartheta = \int_{S_u} E(q, \vartheta, \zeta)\delta(Q - q)\delta(\zeta)qdqd\vartheta d\zeta \tag{2.11}$$

5. Substitution of the Fourier relation between the signal and $P(\boldsymbol{R}, \tau)$ leads to:

$$\mathcal{M}[E] = \int_{S_u} P(r, \theta, z)\exp 2\pi i(z\zeta + qr\cos(\theta - \vartheta))\delta(Q - q)\delta(\zeta)qrdqd\vartheta d\zeta drd\theta dz \tag{2.12}$$

6. Integrate over z and ζ to obtain:

$$\mathcal{M}[E] = \int_{S_u} p(r,\theta) \exp 2\pi iqr \cos(\theta - \vartheta)\delta(Q-q)\delta(\zeta) qrdqd\vartheta drd\theta \tag{2.13}$$

7. Expand the exponential into cylindrical waves using the cylindrical wave expansion (Bessel function identity or Jacobi-Anger expansion):

$$\exp ix\cos\alpha = \sum_{n=-\infty}^{\infty} i^n J_n(x) \exp in\alpha \tag{2.14}$$

   to get:

$$\exp 2\pi iqr \cos(\theta - \vartheta) = \sum_{n=-\infty}^{\infty} i^n J_n(2\pi qr) \exp in \cos(\theta - \vartheta) \tag{2.15}$$

8. Integrate over q and ϑ to obtain:

$$\mathcal{M}[E] = Q \int_{S_u} \sum_{n=-\infty}^{\infty} \frac{i}{n} \exp -(3/2)\pi ni + in\theta(1 - \exp 2\pi ni) p(r,\theta) J_n(2\pi Qr) rdrd\theta \tag{2.16}$$

9. Note that $\frac{(1-\exp 2\pi ni)}{n} = 0$ for all nonzero n, so only the $n = 0$ term contributes. We find:

$$\lim_{x \to 0} \frac{(1-\exp 2\pi ni)}{n} = -2\pi i \tag{2.17}$$

10. This gives us a final result of:

$$\mathcal{M}[E] = 2\pi Q \int_{S_u} p(r,\theta) J_0(2\pi Qr) rdrd\theta \tag{2.18}$$

2.2 Problems with Tuch's Q-ball method

This section presents the discussions on the problems with Tuch's Q-ball imaging method presented by Barnett and Aganj and colleagues in their respective articles.

2.2.1 Discussion of the Tuch Q-ball ODF by Barnett

Barnett, in his 2009 article, discusses the flaws he sees in Tuch's Q-ball ODF calculations. We summarize his ideas here.

The first remark regarding problems with the Tuch Q-ball ODF made by Barnett concerns Tuch's ODF definition. Recall from our discussion on Tuch's method that he defines his ODF as [7]:

$$tODF(\boldsymbol{u}) = \frac{1}{Z}\int_0^\infty P(r\boldsymbol{u}, \tau)dr \tag{2.19}$$

Barnett notes that a more natural way to define the ODF is [1]:

$$bODF(\Theta, \Phi) = \int_0^\infty r^2 P(r, \Theta, \Phi)dr \tag{2.20}$$

The problem with Tuch's method is that the defined ODF lacks the r^2 factor required for the conversion to spherical coordinates from Cartesian coordinates. This means that the resulting ODF is not a probability density function and must be renormalized to be interpreted as such. Additionally, in Tuch's ODF small displacements are weighted more heavily than large ones, causing a significant broadening of the ODF's peaks with respect to Barnett's ODF. [1]
As benefits of his ODF, Barnett names the fact that it is a probability density function and that all volume elements are weighted equally in displacement space. To see that it is indeed a probability density function, note that: [1]

$$\int_0^{2\pi}\int_0^{\pi} sin(\Theta) bODF(\Theta, \Phi)d\Theta d\Phi = 1 \tag{2.21}$$

The second major problem that Barnett sees in Tuch's method is what he and Tuch refer to as the "Q-ball approximation". This is the equation that states that $tODF \approx qODF$, where $qODF$ is the true ODF, equal to the $bODF$. However, this would mean that the following relationship would have to hold [1]:

$$\int_0^\infty \rho' J_0(2\pi q\rho')P(\rho', \varphi', z')d\rho' \approx \frac{1}{2\pi}P(\rho' = 0, z') \tag{2.22}$$

In order for the above approximation to hold, the kernel $\rho' J_0(2\pi q\rho')$ must integrate to 1 and be concentrated near zero. In fact, it is neither. It integrates to 0 and, in addition to being equal to 0 in 0, oscillates within an envelope proportional to $\sqrt{\rho'}$ [1]. Therefore, the kernel is not, as is Tuch's claim, a good approximation to a delta pulse. That being said, Barnett does note that the $tODF$ still contains useful information about the directional dependence of $P(r, \Theta, \Phi)$

Note that the exact degree of difference between the $tODF$ and the $bODF$ depends on the shape of the diffusion PDF. Sharper peaks in the diffusion PDF will lead to a greater degree of difference due to the broadening that occurs in the $tODF$.

2.2.2 Discussion of the Tuch Q-ball ODF by Aganj et al.

Aganj and colleagues note in their 2009 article that the tODF differs from the true ODF in that it does not take into account the correct integration method along a constant solid angle. Like Barnett, they point out that a factor r^2 is missing from the calculations, performed in spherical coordinates. This, according to them, results in a function that is not normalized, nor as sharp as it would be if the correct factor was used in the calculations, which in turn leads to a need for computationally expensive post-processing [10].

2.3 Other Q-ball calculation methods

2.3.1 Conversion formula given by Barnett

It is noted in the Barnett article that Tuch's ODF, while mathematically incorrect, does contain useful information regarding the orientation distribution of the diffusion in a voxel. In fact, Barnett goes on to find a relation between the *tODF* and the *qODF*. For details, the reader is referred to the Barnett article, wherein Barnett inverts the Hankel transform in one of the appendices to obtain the following equation [1]:

$$\begin{aligned} tODF(\Theta,\Phi) &= \frac{1}{2Z_0}\int_0^\infty \mathcal{M}(q;\Theta,\Phi)[E]dq \\ &= \frac{1}{2Z_0}\int_0^\infty Z(q)bODF(q;\Theta,\Phi)dq \end{aligned} \tag{2.23}$$

In these equations, Z_0 and $Z(q)$ are given by the equations below. Using this formula, the tODF can be converted into the proper bODF (also known as qODF) [1].

$$Z_0 = \int_0^{2\pi}\int_0^{\pi}\sin(\Theta)\int_0^\infty \mathsf{P}(r,\Theta,\Phi)drd\Theta d\Phi \tag{2.24}$$

$$Z(q) = \int_0^{2\pi}\int_0^{\pi}\sin(\Theta)\mathcal{R}(q;\Theta,\Phi)d\Theta d\Phi \tag{2.25}$$

where

$$\mathcal{R}(q;\Theta,\Phi) = q\int_0^{2\pi} E(q'_\rho = q, q'_\Phi, q'_x = 0)dq'_\Phi \tag{2.26}$$

2.3.2 Analytical Q-ball imaging

The analytical Q-ball method developed by Descoteaux and colleagues presents a faster solution to the Q-ball method developed by Tuch, which they claim to be up to 15 times faster than the numerical method which Tuch used. Note, however, that they assume that Tuch's ODF approximation formula, given below, is correct.

$$tODF \approx qODF(= bODF) \tag{2.27}$$

In analytical Q-ball imaging, spherical harmonics form the basis of calculations. The signal acquired from the scanner is modelled using a high-order spherical harmonics series through a regularization method referred to a "Laplace-Beltrami regularization" [8].

The explanation od Descoteaux and colleagues begins with a referral to the Tuch paper for proof of the relation between the Q-ball ODF and the Funk-Radon transform. We take note that Descoteaux uses Tuch's extended version of this transform for a sphere of radius 1, as he defines this transform as [8]:

$$\mathcal{M}_D[E](\boldsymbol{u}) = \int_{|\boldsymbol{q}|=1} \delta(\boldsymbol{u}^T\boldsymbol{q})E(\boldsymbol{q})d\boldsymbol{q} \tag{2.28}$$

Consider a spherical harmonic Y_l^m. Here, l represents the order and m the phase factor. It is defined by the formula [8]:

$$Y_l^m(\theta,\phi) = \sqrt{\frac{2l+1}{4\pi}\frac{(l-m)!}{(l+m)!}}P_l^m(\cos\theta)e^{im\phi} \tag{2.29}$$

Here, the angles θ and ϕ are defined according to convention (i.e. $0 \leq \theta \leq \pi$ and $0 \leq \phi \leq 2\pi$) and P_l^m is the Legendre polynomial [8].

Next, a new basis ($\mathbf{Y}$) is introduced using a newly-defined index j, which is defined for $k = 0, 2, 4, ..., l$ and $m = -k, ..., 0, ..., k$ as follows [8]:

$$j := j(k,m) = \frac{k^2+k+2}{2} + m \tag{2.30}$$

Take note here that with this definition, only the spherical harmonics of even order will be used, and thus the complex part of the MR signal is discarded. The new basis is then defined as [8]:

$$Y_j = \begin{cases} \sqrt{2} \cdot Re(Y_k^m) \text{ if } -k \leq m < 0 \\ Y_k^0 \text{ if } m = 0 \\ \sqrt{2} \cdot Im(Y_k^m) \text{ if } 0 < m \leq k \end{cases} \tag{2.31}$$

The basis defined by these elements is real, orthonormal, and symmetric.

Descoteaux and colleagues then approximate the MR signal as follows [8]:

$$E(\theta_i, \phi_i) = \sum_{j=1}^{\frac{1}{2}(l+1)(l+2)} c_j Y_j(\theta_i, \phi_i) \tag{2.32}$$

This redefines the question of finding a representation for the MR signal to one of finding the coefficients corresponding to the newly-defined spherical harmonics basis. However, implicit in this representation lies again the assumption that the ODF is symmetric, which, given the current scan resolution, may be problematic.

2.3.3 Exact Q-ball imaging (E-QBI)

The exact Q-ball imaging method developed by Canales-Rodriguez and colleagues differs from Tuch's method primarily in its paractical calculation and little in theory. It therefore suffers from the same problems caused by the failure to use the correct definition of the probability density function.

To consider the method of E-QBI, we refer back to the discussion on Tuch's Q-ball method and recall that the modulus Fourier transform and the normal Fourier transform, under the conditions under which the diffusion signal is obtained, are equivalent. This means that if $E[\boldsymbol{q}]$ is the signal and $\mathcal{F}$ is the Fourier transform,

$$P(\boldsymbol{R}, \tau) = \mathcal{F}[|E(\boldsymbol{q})|] \tag{2.33}$$

Written out, this is:

$$P(\boldsymbol{R}, \tau) = \int |E[\boldsymbol{q}]| \exp(-2\pi i \boldsymbol{r} \cdot \boldsymbol{q}) d\boldsymbol{q} \tag{2.34}$$

Canales-Rodriguez and colleagues then introduce an auxiliary parameter λ and rewrite $\boldsymbol{r} - \boldsymbol{r_0} = \rho \hat{\boldsymbol{r}}$, where ρ is the length of $\boldsymbol{r} - \boldsymbol{r_0}$ and $\hat{\boldsymbol{r}}$ is its direction. They then rewrite the above equation into [6]:

$$P(\rho, \hat{\boldsymbol{r}}, \tau) = \int |E[\boldsymbol{q}]| \int \exp(-2\pi i \rho \lambda) \delta(\hat{\boldsymbol{r}} \cdot \boldsymbol{q} - \lambda) d\lambda d\boldsymbol{q} \tag{2.35}$$

Note here that $\delta(\cdot)$ is the Dirac delta function.

Next, they define the three-dimensional Radon transform of the modulus diffusion signal evaluated at λ and $\hat{\boldsymbol{r}}$ as [6]:

$$|\hat{E}[\lambda, \hat{\boldsymbol{r}}]| = \int |E[\boldsymbol{q}]|\delta(\hat{\boldsymbol{r}} \cdot \boldsymbol{q} - \lambda)d\boldsymbol{q} \tag{2.36}$$

Note that this is equivalent to the Funk-Radon transform referred to by Tuch.

This means that the conditional diffusion PDF can be rewritten as [6]:

$$P(\rho, \hat{\boldsymbol{r}}, \tau) = \int |\hat{E}[\lambda, \hat{\boldsymbol{r}}]| \exp\left[-2\pi i \rho \lambda\right] d\lambda \tag{2.37}$$

Interestingly, like Tuch, the authors of the article in question assume that the Q-ball ODF (for this method, we call it the *eqODF*) should be calculated according to [6]:

$$eqODF(\hat{\boldsymbol{r}}) = \frac{1}{Z} \int P(\rho, \hat{\boldsymbol{r}}) d\rho \tag{2.38}$$

After some manipulation, they conclude this to be equal to [6]

$$eqODF(\hat{\boldsymbol{r}}) = \frac{1}{Z} \int_{\rho \perp \hat{\boldsymbol{q}}} S(\hat{\boldsymbol{q}}) d\hat{\boldsymbol{q}} \tag{2.39}$$

where

$$S(\hat{\boldsymbol{q}}) = \int_0^\infty \hat{E}(q, \hat{\boldsymbol{q}}) q dq \tag{2.40}$$

There follows a discussion on the practical aspects of the calculation method, which we discuss below. We take note of the normalization problem in this approach akin to the problem in Tuch's approach. This arises due to the choice to neglect the ρ^2 term that should be included in integral 2.38 in order to calculate a true probability density function. Making this choice leads to broadening of the ODF's peaks. For this reason, exact Q-ball imaging may not be a good alternative to Tuch's approach.

Regarding the practical implementation details, Canales-Rodriguez and colleagues offer the reader the choice of expanding the equations for the MR signal and the *eqODF* in terms of spherical harmonics or choosing a model and using this to calculate the *eqODF*. In the case that the reader chooses to use spherical harmonics, the following formulae apply [6]:

$$eqODF(\hat{\boldsymbol{r}}) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} o_{lm} Y_{lm}(\hat{\boldsymbol{r}}) \tag{2.41}$$

and

$$S(\hat{\boldsymbol{q}}) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} s_{lm} Y_{lm}(\hat{\boldsymbol{q}}) \tag{2.42}$$

Here, o_{ab} and s_{ab} are spherical harmonic coefficients and $Y_{ab}(\cdot)$ is the spherical harmonic term. This leads to the equation [6]:

$$eqODF(\hat{\boldsymbol{r}}) = \frac{1}{2\sqrt{\pi} s_{00}} \sum_{l=0}^{\infty} \sum_{m=-l}^{l} s_{lm} P_l(0) Y_{lm}(\hat{\boldsymbol{r}}) \tag{2.43}$$

where P_l is the Legendre polynomial of order l [6].

If the reader wishes to consider model-based reconstructions, he or she can use the assumptions about the system to derive the desired formulae. Canales-Rodriguez and colleagues give an example in which they assume that the normalized diffusion signal E attenuates mono-exponentially as follows [6]:

$$E(q, \hat{\boldsymbol{q}}) = \exp[-4\pi^2 t q^2 ADC(\hat{\boldsymbol{q}})] \tag{2.44}$$

where $ADC(\cdot)$ is the apparent diffusion coefficient and t the effective diffusion time [6].

Note that the diffusion propagator that will be derived is similar to the diffusion orientation transform (DOT) ODF discussed in the next chapter. The main difference is the fact that E-QBI reconstructs a projection of the propagator and DOT reconstructs a single contour.

The radial projection of the MR signal is then given by [6]:

$$S(\hat{\boldsymbol{q}}) = \int_0^{\infty} \exp[-4\pi^2 t q^2 ADC(\hat{\boldsymbol{q}})] q dq \tag{2.45}$$

Using the standard integral below with $a = 4\pi^2 t ADC(\hat{\boldsymbol{q}})$ and $m = 1$ [6]

$$\int_0^{\infty} \exp[-aq^2] q^m dq = \frac{1}{2}\Gamma(\frac{m+1}{2}) a^(- \frac{(m+1)}{2}) \tag{2.46}$$

we obtain [6]:

$$S(\hat{\boldsymbol{q}}) \propto \frac{1}{ADC(\hat{\boldsymbol{q}})} \tag{2.47}$$

This makes it possible to use equation 2.43 and the harmonic coefficients from the series [6]

$$\frac{1}{ADC(\hat{\boldsymbol{q}})} = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} s_{lm} Y_{lm}(\hat{\boldsymbol{q}}) \tag{2.48}$$

to calculate the *eqODF*.

2.3.4 Constant solid angle Q-ball imaging (CSA-QBI)

Noting, as Barnett did in his article, the failure of Tuch to use the correct definition of the probability density function, Aganj and colleagues set out to rework the Q-ball imaging method using a constant solid angle element as the basis for integration.

Without loss of generality, Aganj et. al assume the $\boldsymbol{r_0}$ in $P(\boldsymbol{R}, \tau)$ is the origin of the system. This gives us $P(\boldsymbol{r}, \tau)$ as the conditional diffusion PDF. Also, it means that $P(\boldsymbol{r}, \tau)dxdydz$ represents the probability that a spin originally at the origin will have migrated to the volume $dxdydz$ located at $\boldsymbol{r}$ in time τ. We transform the system into spherical coordinates, parameterized by (r, θ, ϕ), where $\boldsymbol{r} = r\boldsymbol{u} = (r\sin(\theta)\cos(\phi), r\sin(\theta)\sin(\phi), r\cos(\theta))$. Then $dxdydz$ becomes $r^2\sin(\theta)drd\theta d\phi$. [10] Thus, the true ODF, according to Aganj and colleagues (aODF) is given by the following formula [10]:

$$aODF(\boldsymbol{u}) = \int_0^{\infty} P(r\sin(\theta)\cos(\phi), r\sin(\theta)\sin(\phi), r\cos(\theta))r^2\sin(\theta)drd\theta d\phi \tag{2.49}$$

and is equivalent to the *bODF*. We can rewrite this as:

$$aODF(\boldsymbol{u}) = \int_0^{\infty} P(r\boldsymbol{u})r^2 d\boldsymbol{u} \tag{2.50}$$

Note here the difference with Tuch's ODF definition. The above integral is inherently normalized and dimensionless. It represents the integral of probability in a small cone with constant solid angle. This means that the artificial broadening of the ODF's peaks that occurs in Tuch's definition of the Q-ball ODF does not occur here.

Aganj and colleagues start their discussion on the practical calculation of the *aODF* with the following two remarks [10]:

1. The Fourier transform of $P(\boldsymbol{r})|\boldsymbol{r}^2|$ is equal to $-\nabla^2 E(\boldsymbol{q})$, with ∇^2 the Laplacian operator.

2. For a symmetric function f that maps the $\mathbb{R}^3$ to the real line and has the Fourier transform function $\hat{f}(\boldsymbol{q})$ and an arbitrary unit vector $\boldsymbol{u}$, the following equation holds:

$$\int_0^\infty f(r\boldsymbol{u})dr = \frac{1}{8\pi^2}\int\int_{\perp\boldsymbol{u}} \hat{f}(\boldsymbol{q})d^2\boldsymbol{q} \tag{2.51}$$

Here, $\perp \boldsymbol{u}$ is the plane perpendicular to the vector $\boldsymbol{u}$ [10].

This leads to the following expression for the *aODF* [10]:

$$aODF(\boldsymbol{u}) = -\frac{1}{8\pi^2}\int\int_{\perp\boldsymbol{u}} \nabla^2 E(\boldsymbol{q})d^2\boldsymbol{q} \tag{2.52}$$

Without loss of generality, the coordinates are chosen such that $\perp \boldsymbol{u}$ is the $q_x - q_y$ plane (or $\boldsymbol{z} = \boldsymbol{u}$). This means that $d^2\boldsymbol{q} = qdqd\phi$. The Laplacian is rewritten in terms of spherical coordinates and the surface integral calculated by fixing $\theta = \frac{\pi}{2}$. This gives [10]:

$$aODF(\boldsymbol{z}) = -\frac{1}{8\pi^2}\int_0^{2\pi}\int_0^\infty \frac{1}{q}\frac{\partial^2}{\partial q^2}(qE) + \frac{1}{q^2}\nabla_b^2 E q dq d\phi \tag{2.53}$$

When the first term is worked out, it is found to equal -2π. The assumptions made to come to this conclusion are that the diffusion signal and its radial derivative go to zero sufficiently fast as $q \to \infty$ and that the derivative is bounded at the origin [10]. Keeping $\theta = \frac{\pi}{2}$, this gives [10]:

$$aODF(\boldsymbol{z}) = \frac{1}{4\pi} - \frac{1}{8\pi^2}\int_0^{2\pi}\int_0^\infty \frac{1}{q}\nabla_b^2 E(\boldsymbol{q}) dq d\phi \tag{2.54}$$

To compute the remaining integral, values of $E(\boldsymbol{q})$ are required for the entire q-space [10]. This requires either a great deal of measurements or the application of a model.

2.4 Strengths and weaknesses of Q-ball methods

We summarize here the strengths and weaknesses of the Q-ball imaging method in its general form.

2.4.1 Strengths of Q-ball Imaging

To summarize, the strengths of Q-ball imaging are:

- It is model-independent, i.e. based only on the acquired signal, without assumptions as to the underlying diffusion patterns.
- It is robust and fast in comparison to other methods.

2.4.2 Weaknesses of Q-ball Imaging

We conclude that Q-ball imaging is weak in the following areas:

- The ODF is assumed to be perfectly symmetrical. This may not be the case, especially at the current level of resolution.
- The narrow pulse condition is assumed to be satisfied, which is currently not the case.
- It is assumed that the medium consists of a set of long, thin pipes

Chapter 3

DOT-ODF

In this chapter we discuss the DOT method for calculating an orientation distribution function. We begin with an overview of DOT theory and then proceed to discuss the various assumptions the method makes and the potential consequences thereof.

3.1 DOT-ODF theory

Here we consider the theory that governs the use of the DOT-ODF method. We use notation consistent with that used in the previous chapter for Q-ball imaging.

We recall from the previous chapter that the relationship between the modulus MRI signal ($|E|$) and the diffusion propagator (P), assuming symmetry of diffusion and the fact that the narrow pulse condition (see our discussion in the previous chapter) is met, is given by [12] [5]:

$$P(\rho, \hat{\boldsymbol{r}}) = \oint_{\Omega} \int_{0}^{\infty} |E(q, \hat{\boldsymbol{q}})| \exp\left(-2\pi i \rho q \hat{\boldsymbol{r}} \hat{\boldsymbol{q}}\right) q^2 dq d\hat{\boldsymbol{q}} \tag{3.1}$$

Here, $\boldsymbol{q} = q\hat{\boldsymbol{q}}$ and $\boldsymbol{r} = \rho\hat{\boldsymbol{r}}$ are the q-space and real-space vectors respectively, separated into their lengths and unit vectors. Also note that $q = \dfrac{\gamma G \tau}{2\pi}$, where G and τ are respectively the intensity and duration of the magnetic field gradient and γ is the gyromagnetic ratio of protons (the diffusing species) [5].

Ω represents the set of all possible directions of the $\hat{\boldsymbol{q}}$ unit vector, equivalent to the unit sphere in q-space. The integral over the surface of this unit sphere is given by [5]:

$$\oint_{\Omega} d\hat{\boldsymbol{q}} = \int_{0}^{2\pi} \int_{0}^{\pi} \sin\left(\theta\right) d\theta d\phi \tag{3.2}$$

In the diffusion orientation transform (DOT) calculations, one assumes that the signal E attenuates mono-exponentially, leading to the equation [5]:

$$|E(q,\hat{\boldsymbol{q}})| = \exp\left(-4\pi^2 t q^2 D[\hat{\boldsymbol{q}}]\right) \tag{3.3}$$

Here, t is the effective experimental diffusion time and $D[*]$ represents the apparent diffusion coefficient or diffusivity profile [5]. The diffusivity profile can be represented using a spherical-harmonic expansion, according to the diagram below [12]:

$$D[\boldsymbol{u}] \underset{\overleftarrow{LS}}{\overset{\overrightarrow{SHT}}{\longrightarrow}} a_{lm} \tag{3.4}$$

SHT stands for "spherical harmonic transform", while LS stands for "Laplace series expansion". The a_{lm} are the spherical harmonic coëfficients.

In addition, the DOT makes use of the plane wave expansion in terms of spherical wave functions, given by [5]:

$$\exp\left(-2\pi i \rho q \hat{\boldsymbol{r}}\hat{\boldsymbol{q}}\right) = \lim_{N\to\infty} 4\pi \sum_{l=0}^{N} \sum_{m=-l}^{l} (-i)^l J_l(2\pi q\rho) Y_{lm}(\hat{\boldsymbol{r}}) \overline{Y_{lm}}(\hat{\boldsymbol{q}}) \tag{3.5}$$

In this equation, $J_l(*)$ is the spherical Bessel function of the first kind with the given input. $Y_{lm}(*)$ and $\overline{Y_{lm}}(*)$ are the spherical harmonic of order l and its complex conjugate respectively [5].

Using the mono-exponential attenuation equation and the plane wave expansion, we can rewrite the diffusion propagator as [5]:

$$P(\rho,\hat{\boldsymbol{r}}) = \lim_{N\to\infty} \sum_{l=0}^{N} \sum_{m=-l}^{l} (-1)^{l/2} Y_{lm}(\hat{\boldsymbol{r}}) \oint_{\Omega} Y_{lm}^{*}(\hat{\boldsymbol{q}}) I_l(\rho,\hat{\boldsymbol{q}}) d\hat{\boldsymbol{q}} \tag{3.6}$$

Here, we can expand $I_l(\rho,\hat{\boldsymbol{q}})$ using spherical harmonics (for details see [5]):

$$I_l(\rho,\hat{\boldsymbol{q}}) = \lim_{N\to\infty} \sum_{l'=0}^{N} \sum_{m'=-l'}^{l'} a^{l}_{l'm'} Y_{l'm'}(\hat{\boldsymbol{q}}) \tag{3.7}$$

Next, we use the remark from Canales-Rodriguez and colleagues' 2010 paper, which says that an ODF can be written in a general form as follows:

$$ODF_n(\hat{\boldsymbol{r}}) = \frac{1}{Z_n} \int_0^{\infty} \rho^n P(\hat{\boldsymbol{r}},\rho) d\rho \tag{3.8}$$

ODF_0 resembles Tuch and Descoteaux' definitions of the ODF, whereas ODF_2 comes closer to the definitions of Barnett and Aganj and colleagues.

Again using spherical harmonics, Canales-Rodriguez and colleagues obtain [5]:

$$ODF_0(\hat{\boldsymbol{r}}) \propto \sum_{l=0}^{\infty} \sum_{m=-l}^{l} P_l(0) d_{lm} Y_{lm}(\hat{\boldsymbol{r}}) \tag{3.9}$$

and:

$$ODF_2(\hat{\boldsymbol{r}}) = \frac{4}{\pi} \sum_{l=0}^{\infty} \sum_{m=-l}^{l} (-1)^{l/2} f_{lm} \chi_l Y_{lm}(\hat{\boldsymbol{r}}) \tag{3.10}$$

with

$$\chi_l = \begin{cases} g_l & \text{if } \forall l \neq 0 \\ \dfrac{2\pi^{l/2}|h_0|}{f_{00}} & \text{if } l = 0 \end{cases} \tag{3.11}$$

and g_l and h_l are coefficients obtained by solving [5]:

$$\Phi_{l,n}(\hat{\boldsymbol{q}}) = \frac{\Gamma(\frac{l+3}{2})}{2^{l+3}\pi^{3/2}\Gamma(l+\frac{3}{2})[D(\hat{\boldsymbol{q}})t]^{\frac{l+3}{2}}} \int_0^{\infty} \rho^{l+n} {}_1F^1\left(\frac{l+3}{2}; l+\frac{3}{2}; -\frac{\rho^2}{4D(\hat{\boldsymbol{q}})t}\right) d\rho \tag{3.12}$$

Note that the above equation, for $n = 2$, has the general solution [5]:

$$\Phi_{l,2}(\hat{\boldsymbol{q}}) = \frac{4}{\pi}\{g_l\left[\kappa + \log\left(\frac{1}{D(\hat{\boldsymbol{q}})t}\right)\right] - h_l\} \tag{3.13}$$

3.2 Strengths and weaknesses of DOT-ODF

3.2.1 The mono-exponential signal attenuation model

Canales-Rodriguez and colleagues used a far-field analysis (used commonly in electromagnetism physics) to study the effects of the mono-exponential signal attenuation assumption on image quality. They defined the far-field limit as being $\rho q >> \dfrac{(N+1)}{2\pi}$. The far-field pattern of the diffusion propagator (P_{FF}) predicted by the DOT method can then be written as [5]:

$$P_{FF} = \frac{1}{[4\pi D(\hat{\boldsymbol{r}})t]^{3/2}} \exp\left[-\frac{\rho^2}{4D(\hat{\boldsymbol{r}})t}\right] \tag{3.14}$$

In the far-field limit, Canales-Rodriguez and colleagues conclude, the mono-exponential signal attenuation assumption leads to a calculated diffusion propagator that does not accurately reflect the underlying microgeometry of the tissue. The maxima of this diffusivity profile in general do not coincide with the main axes of the medium. Their results imply that there is a limit to the displacements that DOT can accurately quantify. There seems to be a critical radius in real space beyond which the diffusion propagator becomes biased, likely in the medium- to large displacements limit (Canales-Rodriguez and colleagues do not specify what they consider a "large" displacement) [5].

3.2.2 Consequences of multi-exponential models

The extension of the DOT model to the multi-exponential signal attenuation case is called "trivial" by Ozarslan and Canales-Rodriguez [12] [5]. However, while this leads to increased accuracy of the model, the parameter estimation for higher-order models requires highly time-intensive sampling schemes. This may make such a multi-exponential model undesirable for use in a clinical setting [5].

3.2.3 Gaussian diffusivity

Note that with the use of exponential models, the assumption of Gaussian diffusivity is implied. However, considering that a typical HARDI voxel has a volume in the order of $10mm^3$ and thus contains thousands of cells, this is not a trivial assumption. In fact, only at low b or q values does a Gaussian model adequately describe the motion of water molecules in brain tissue [2]. However, high b or q values are often desirable in diffusion imaging techniques due to the time required for molecules to diffuse [11]. This leads to a conflict and implies that models that permit non-Gaussian diffusivity would be the wiser choice.

3.2.4 Finite sampling of q-space

The use of a Fourier transform defined on the whole of q-space when really the support in q-space is finite leads to a blurred form of the diffusion propagator being calculated, which has decreased contrast and angular resolution. Canales-Rodriguez et. al. prove this by remarking that a model-free diffusion propagator (which we will refer to as P_F, in accordance with their notation) would have the form [5]:

$$P_F(\rho, \hat{\boldsymbol{r}}) = \oint_{\Omega} \int_0^{\infty} |E(q, \hat{\boldsymbol{q}})| \Pi(\frac{q}{q_{max}}) \exp\left(-2\pi i \rho \hat{\boldsymbol{r}} \hat{\boldsymbol{q}}\right) q^2 dq d\hat{\boldsymbol{q}} \qquad (3.15)$$

Here, $\Pi(*)$ is a filter in q-space defined as follows:

$$\Pi(\frac{q}{q_{max}}) = \begin{cases} 1, \forall q \leq q_{max} \\ 0, \forall q > q_{max} \end{cases} \tag{3.16}$$

Note that q_{max} is the maximum experimental value of q.

Note then that with Bracewell's convolution theorem, the filtered diffusion propagator can be rewritten in terms of the true diffusion propagator (P) as follows [5]:

$$P_F = P \otimes \mathbb{F}\{\Pi\} \tag{3.17}$$

In this equation, $\otimes$ is a convolution operator and $\mathbb{F}(*)$ is the three-dimensional continuous Fourier transform of the filter. This Fourier transform evaluates to [5]:

$$\mathbb{F}\{\Pi\} = 4\pi \frac{\sin(2\pi q_{max} R) - 2\pi q_{max} R \cos(2\pi q_{max} R)}{(2\pi R)^3} \tag{3.18}$$

In the words of Canales-Rodriguez and colleagues,

> [...] the estimated intensity for the diffusion propagator at a particular point $\boldsymbol{r}$ arises from the contributions of all points of the space, their real intensities weighted by ... $\mathbb{F}\{\Pi\}$ depending on the distance R to the considered point.

This means that the model-free propagator will suffer from decreased angular resolution and decreased contrast. In order to counteract the effects of the convolution with the filter's Fourier transform, a deconvolution algorithm would have to be designed and implemented. This has not been done to date to the knowledge of the author.

3.2.5 Truncation of the spherical harmonic series

Recall from equation 3.15 that we took the limit of N to infinity. For practical calculations, however, N must be limited to a finite number. This finite N is then used in the calculation of the plane wave expansion and the diffusion propagator. Within a sphere of radius $\rho = \frac{N}{2\pi q}$ the truncated series still gives a rigorous representation of the plane wave, but the wave field decays rapidly outside of this sphere [5]. The truncated plane wave therefore acts as a low-pass filter in q-space [5]. One may continue to use the convolution equation given in the previous section, but this time with a different maximum value for the filter ($q_{max} = \frac{N}{2\pi\rho}$). This means that [5]:

$$\mathbb{F}\{\Pi\} = \frac{1}{2\pi^2 R^3} \left[\sin\left(\frac{NR}{\rho}\right) - \frac{NR}{\rho} \cos\left(\frac{NR}{\rho}\right) \right] \tag{3.19}$$

Only in the limit $N \to \infty$ does the calculated diffusion propagator resemble the true diffusion propagator. The truncation reduces the angular resolution of the calculated diffusion propagator.

Chapter 4

Conclusions

4.1 Strengths and weaknesses of Q-ball imaging and DOT-ODF

In this section we summarize the strengths and weaknesses of the Q-ball imaging- and DOT methods for calculating an ODF. In doing so, we hope to help the reader decide wisely between the two options.

The strenghts of Q-ball imaging are its speed and robustness in comparison to other methods and (primarily) its lack of an underlying signal model aside from the assumption of symmetry in the diffusion pattern. Weaknesses include the assumption regarding the medium (it consists of a set of long, thin pipes - the true structure is far more complex), the assumption that the narrow pulse condition is satisfied (this is currently simply not the case), and the previously mentioned assumption of a symmetric diffusion pattern (at the current resolution this is not a trivial assumption).

In the case of the DOT-ODF method, strengths include its supposed accuracy and speed, though these relative to the Q-ball method are not discussed. [12] Weaknesses of the method include the underlying assumption of exponential signal decay (which implies a Gaussian diffusion pattern), a sampling time-intensive expansion to multi-exponential models, finite sampling of q-space (leading to a blurred diffusion PDF), and in the calculations, the practical necessity of truncating the model's spherical harmonic series (which also leads to blurring and broadening of the ODF peaks).

4.2 Remarks

Based on the strengths/weaknesses analysis of the Q-ball imaging- and DOT ODF calculation methods, the author suggests that Q-ball imaging, in its expanded form where the correct definition of a probability density function is used, is the most widely applicable of the two. However, it may be possible, if HARDI resolution increases and more is known about the underlying diffusion characteristics of the medium, to use the DOT method for certain parts of the anatomy and Q-ball imaging for the rest.

4.3 Suggestions for further research

Considering that one of the primary problems in both the Q-ball imaging and DOT methods is the assumption of a perfectly symmetric diffusion pattern, it may be interesting to perform further research regarding methods that allow for non-symmetric diffusion patterns. Given the current level of resolution, this will likely lead to large improvements in the accuracy of the reconstruction of fibres.

Appendix A

Formula list

A.1 General relations

1. Average of spins in a given voxel *or* diffusion probability density function (according to D. Tuch):

$$P(\boldsymbol{R}, \tau) = \int \rho(\boldsymbol{r_0}) \mathsf{P}(\boldsymbol{R} + \boldsymbol{r_0}, \tau, \boldsymbol{r_0}) d\boldsymbol{r_0} \tag{A.1}$$

2. Relation between average of spins in a given voxel and the magnetic resonance signal:

$$P(\boldsymbol{R}, \tau) = \mathcal{F}[E(\boldsymbol{q})] \tag{A.2}$$

3. Diffusion wave vector:

$$\boldsymbol{q} = \frac{\gamma \delta \boldsymbol{g}}{2\pi} \tag{A.3}$$

A.2 Q-ball relations

1. Tuch's Q-ball ODF (tODF):

$$tODF(\boldsymbol{u}) = \frac{1}{Z} \int_0^{\infty} P(r\boldsymbol{u}, \tau) dr \tag{A.4}$$

2. Funk-Radon transform:

$$\mathcal{M}[f](\boldsymbol{n}) = \int_{S_u} f(\boldsymbol{x}) \delta(\boldsymbol{x} \cdot \boldsymbol{n}) d\boldsymbol{x} \tag{A.5}$$

3. Tuch's modified Funk-Radon transform:

$$\mathcal{M}[f](\boldsymbol{n}, R) = \int_{S_u} f(\boldsymbol{x}) \delta(\boldsymbol{x} \cdot \boldsymbol{n}) \delta(|\boldsymbol{x}| - R) d\boldsymbol{x} \tag{A.6}$$

4. Barnett's Q-ball ODF:

$$bODF(\Theta, \Phi) = \int_0^{\infty} r^2 P(r, \Theta, \Phi) dr \tag{A.7}$$

A.3 DOT-ODF relations

1. Mono-exponential signal attenuation:

$$|E(q, \hat{\boldsymbol{q}})| = \exp\left(-4\pi^2 t q^2 D[\hat{\boldsymbol{q}}]\right) \tag{A.8}$$

2. DOT-ODF, general form:

$$ODF_n(\hat{\boldsymbol{r}}) = \frac{1}{Z_n}\int_0^\infty \rho^n P(\hat{\boldsymbol{r}}, \rho) d\rho \tag{A.9}$$

3. DOT-ODF, $n = 0$:

$$ODF_0(\hat{\boldsymbol{r}}) \propto \sum_{l=0}^{\infty}\sum_{m=-l}^{l} P_l(0) d_{lm} Y_{lm}(\hat{\boldsymbol{r}}) \tag{A.10}$$

4. DOT-ODF, $n = 2$:

$$ODF_2(\hat{\boldsymbol{r}}) = \frac{4}{\pi}\sum_{l=0}^{\infty}\sum_{m=-l}^{l} (-1)^{l/2} f_{lm} \chi_l Y_{lm}(\hat{\boldsymbol{r}}) \tag{A.11}$$

Appendix B

Symbol list

1. $P(\boldsymbol{R}, \tau)$: Average of spins in a given voxel *or* diffusion probability density function (according to D. Tuch)
2. $\rho(\boldsymbol{r_0})$: Initial spin density of voxel
3. $\mathcal{F}$: Fourier transform
4. $S(\cdot)$: Magnetic resonance signal, full, diffusion-weighted image
5. S_0: Magnetic resonance signal, static field image
6. $E(\cdot) = \dfrac{S(\cdot)}{S_0}$: Normalized magnetic resonance signal
7. $\boldsymbol{q}$: Diffusion wave vector
8. γ: Gyromagnetic ratio
9. δ: Gradient pulse duration
10. $\boldsymbol{g}$: Diffusion gradient vector
11. Z: Dimensionless normalization constant used to ensure that Tuch's Q-ball ODF has unit mass
12. $\mathcal{M}$: Funk-Radon transform

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