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RESEARCH ARTICLE

Extreme Diffusion Values for non-Gaussian Diffusions

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A new Magnetic Resonance Imaging (MRI) model, called Diffusion Kurtosis Imaging (DKI), was recently proposed, to characterize the non-Gaussian diffusion behavior in tissues. DKI involves a fourth order three dimensional tensor and a second order three dimensional tensor. Similar to those in the Diffusion Tensor Imaging (DTI) model, the extreme diffusion values and extreme directions associated to this tensor pair play important roles in DKI. In this paper, we study the properties of the extreme values and directions associated to such tensor pairs. We also present a numerical method and its preliminary computational results.

1. Introduction

Magnetic resonance imaging in tissues has been used to infer anatomical structure and to aid in the diagnosis of many pathologies [11, 13]. Nowadays, the most successful and popular magnetic resonance (MR) technique is the diffusion tensor imaging, which uses a second order tensor D to quantify a diffusion anisotropy [3, 8]. When the diffusion process is Gaussian, the MR signal attenuates exponentially as a function of b-value, i.e.,

$$\ln(S(b)) = \ln(S(0)) - bD_{app}, \tag{1}$$

where

$$D_{app} = Dx^2 = \sum_{i,j=1}^{3} D_{ij}x_i x_j, \tag{2}$$

is the apparent diffusion coefficient (ADC) along the gradient direction $x = (x_1, x_2, x_3)$ with components x_i, $i = 1, 2, 3$ and $\sum_{i=1}^{3} x_i^2 = 1$,

$$b = (\gamma \delta g)^2 \left(\Delta - \frac{\delta}{3} \right)$$

and g is the gradient strength, γ is the proton gyromagnetic ratio, δ is a pulse duration, Δ is a time interval between the centers of the diffusion sensitizing gradient pulse, and D is a symmetric second order tensor with elements D_{ij}, $i, j = 1, 2, 3$.

The success of DTI is based on the assumption that water molecules obey Gaussian diffusion in biological tissues. In reality, we often meet diffusions that are non-Gaussian in the confining environment of biological tissues, causing that the DTI model breaks down [1, 3]. For example, when DTI is used in regions where the fibers cross or merge, difficulty is often encountered since with current MR resolution, voxel averaging of different fiber tracts is frequent and unavoidable.

To overcome this problem, new MR imaging models [2, 9, 14] have been proposed, which use higher order tensors, rather than just a second order tensor used in DTI, to characterize the process of diffusion. One of such new MR imaging models is diffusion kurtosis imaging [6, 10]. In that model, a fourth order three dimensional fully symmetric tensor, called the diffusion kurtosis (DK) tensor, is proposed to describe the non-Gaussian behavior of water molecules in tissues. That is, it is assumed that the MR signal attenuates as a function of b-value in the following way,

$$\ln(S(b)) = \ln(S(0)) - bD_{app} + \frac{1}{6}b^2 D_{app}^2 K_{app}, \qquad (3)$$

where K_{app} is the apparent kurtosis coefficient (AKC) along x,

$$K_{app} = \frac{M_D^2}{D_{app}^2} W x^4, \qquad (4)$$

$$W x^4 \equiv \sum_{i,j,k,l=1}^{3} W_{ijkl} x_i x_j x_k x_l,$$

and

$$M_D = \frac{D_{11} + D_{22} + D_{33}}{3}$$

is the mean diffusivity.

For the DTI model, Pierpaoli and Basser [15] pointed out "The most intuitive and simplest rotationally invariant indices are ratios of the principal diffusivities, such as the dimensionless anisotropy ratio λ_1/λ_3 that measures the relative magnitudes of the diffusivities along the fiber-tract direction and one transverse direction." In DKI, the D-eigenvalues of W and the D-eigenvector associated with these eigenvalues also play important roles. They describe the extreme AKC values and the extreme deviations of the diffusion from Gaussian diffusion, and are invariant under rotations of the co-ordinate systems [19, 21]. However, some important properties in the DKI model need to be studied further. For example, which direction is the fastest/slowest diffusion direction in the DKI model? How can we measure the

anisotropy of the tissue? To answer these questions, we have to find the extreme points associated to the diffusion tensor D and the diffusion kurtosis tensor W together. In this paper, we study these problems and propose a numerical method to find such extreme points. We also present some numerical examples to illustrate the method.

2. Notation and Preliminary Results

We use the notation in [4, 12, 16–19] for the tensors and vectors. We use $x = (x_1, x_2, x_3)^T$ to denote the direction vector, which is denoted as $n = (n_1, n_2, n_3)^T$ in [6, 10]. According the result of [6], the ADC and AKC for a single direction should satisfy the relationship (3), i.e.,

$$\ln[S(b)] = \ln[S(0)] - bD_{\text{app}} + \frac{1}{6}b^2 D_{\text{app}}^2 K_{\text{app}}. \tag{5}$$

D is a second order tensor and W is a fourth order tensor, whose elements are obtained by filling experimental data into equation (5) and solving the resulting system of linear equations by singular value decomposition or least squares methods. Let the eigenvalues of D be $\alpha_1 \geq \alpha_2 \geq \alpha_3$. Then the mean diffusivity [3] can be calculated by

$$M_D = \frac{\alpha_1 + \alpha_2 + \alpha_3}{3}.$$

In the DTI model, one assumes that the diffusion obeys a Gaussian distribution and there is no quadratic term in (5), i.e., the ADC for a single direction should satisfy the relationship (1)

$$\ln[S(b)] = \ln[S(0)] - bD_{\text{app}}. \tag{6}$$

In this case, the directions of the fastest and the slowest diffusion are eigenvectors associated to the largest and the smallest eigenvalues of the second order tensor D, which can be obtained via solving the optimization problems

$$\begin{array}{ll} \max & Dx^2 \\ \text{s.t.} & x^T x = 1, \end{array} \tag{7}$$

and

$$\begin{array}{ll} \min & Dx^2 \\ \text{s.t.} & x^T x = 1, \end{array} \tag{8}$$

respectively. For the DKI model, the study in [19] was focused on the properties of W which can be used to measure the deviation of the diffusion from a Gaussian one. For example, the AKC value is used to measure the average deviation; the largest and smallest D-eigenvalues of the fourth order tensor W, defined as

$$\begin{array}{ll} \max & Wx^4 \\ \text{s.t.} & Dx^2 = 1, \end{array} \tag{9}$$

and

$$\begin{aligned} \min \quad & Wx^4 \\ \text{s.t.} \quad & Dx^2 = 1, \end{aligned} \tag{10}$$

can be used to measure the largest and the smallest deviation from Gaussian diffusion and the associated eigenvectors are the fastest and the slowest deviation directions.

In a similar way as in the DTI model, we are now going to find the fastest and the slowest diffusion values and the associated diffusion directions of water molecules in the tissue, under a non-Gaussian diffusion that has relationship (5). That is, we need to solve the following optimization problems

$$\begin{aligned} \max \quad & Dx^2 - \tfrac{1}{6}bM_D^2 Wx^4 \\ \text{s.t.} \quad & x^T x = 1, \end{aligned} \tag{11}$$

and

$$\begin{aligned} \min \quad & Dx^2 - \tfrac{1}{6}bM_D^2 Wx^4 \\ \text{s.t.} \quad & x^T x = 1. \end{aligned} \tag{12}$$

The solutions of (11) and (12) depend on the second order tensor D and the fourth order tensor W. Thus, our tasks are to find some useful properties of solutions of (11) and (12), the extreme values and the associated extreme directions of a tensor pair (D, W), and to design numerical methods for finding such values and directions.

It is known that Dx is a vector in $\Re^3$ with its ith component as

$$(Dx)_i = \sum_{j=1}^{3} D_{ij}x_j,$$

for $i = 1, 2, 3$. As in [16–19], we denote Wx^3 as a vector in $\Re^3$ with its ith component as

$$(Wx^3)_i = \sum_{j,k,l=1}^{3} W_{ijkl}x_j x_k x_l,$$

for $i = 1, 2, 3$. Without loss of generality, we assume that D is positive definite. Then $\alpha_1 \geq \alpha_2 \geq \alpha_3 > 0$. In practice, this assumption is natural, as the ADC value should be positive in general.

3.   Properties of the Extreme Values

The critical points of problems (11) and (12) satisfy the following equation for some $\lambda \in \Re$:

$$\begin{cases} Dx - \tfrac{1}{3}bM_D^2 Wx^3 = \lambda x, \\ x^T x = 1. \end{cases} \tag{13}$$

Let $\bar{W} = \frac{1}{3}bM_D^2W$. Then (13) can be rewritten as

$$\begin{cases} Dx - \bar{W}x^3 = \lambda x, \\ x^T x = 1. \end{cases} \qquad (14)$$

A real number λ satisfying (13) with a real vector x is called an extreme diffusion value of the non-Gaussian diffusion, and the real vector x associated to λ is called an extreme diffusion direction.

The following theorem shows the existence of the extreme diffusion values.

THEOREM 3.1 *The extreme diffusion values always exist. If x is a solution of (14) associated with an extreme diffusion value λ, then*

$$\lambda = Dx^2 - \bar{W}x^4. \qquad (15)$$

The largest diffusion value is equal to $\lambda_{\max}$, and the smallest diffusion value is equal to $\lambda_{\min}$.

Proof. The feasible regions of (11) and (12) are compact and their objective functions are continuous. Hence, each of these two optimization problems has at least one solution, which must satisfy (14) with corresponding Lagrangian multipliers. Hence, the largest diffusion value and the smallest diffusion value always exist and (15) follows from the fact (14) directly. This completes the proof. □

The following theorem shows an important property of the extreme diffusion values.

THEOREM 3.2 *The extreme diffusion values of a non-Gaussian diffusion are invariant under rotations of coordinate systems.*

Proof. With a rotation, x, D and $\bar{W}$ are converted to $y = Px$, $\hat{D} = DP^2$, and $\hat{W} = \bar{W}P^4$, respectively. Here, $P = (p_{ij})$ is the rotation matrix and the elements of $\hat{D}$ and $\hat{W}$ are defined by

$$\hat{D}_{ij} = \sum_{i',j'=1}^{3} D_{i'j'} p_{i'i} p_{j'j},$$

and

$$\hat{W}_{ijkl} = \sum_{i',j',k',l'=1}^{3} \bar{W}_{i'j'k'l'} p_{i'i} p_{j'j} p_{k'k} p_{l'l},$$

see [16] for the definition of orthogonal similarity. If λ is an extreme diffusion value with an extreme direction x, then we have

$$\begin{cases} \hat{D}y - \hat{W}y^3 = \lambda y, \\ y^T y = 1, \end{cases}$$

indicating that λ is still an extreme diffusion value in the new coordinate system. Thus, extreme diffusion values of non-Gaussian diffusion are invariant under rotations of coordinate systems. □

4. A Method for Finding the Extreme Points

To find the extreme diffusion values in DKI, we need to solve optimization problems (11) and (12), which are optimization problems with polynomial objective functions and constraints. The first-order optimal conditions for (11) and (12) are system of polynomial equations (13). For solving this system of polynomial equations, we can use Groebner bases and resultants in elimination theory, see [5, 20]. However, using such methods directly to (13) may be time consuming. Moreover, the final one variable equation derived from (13) may have higher degree, which makes it sensitive to the coefficients.

In the following, we propose a direct method to solve (13), which fully uses the structure of the problem. The first step is to eliminate λ from the system and then uses the last equation to eliminate x_3 from the system. Finally, it solves a system of polynomial equations with two variables, adopting the method of resultants.

Note that Theorem 3.2 indicates that we may rotate the co-ordinate system such that the three orthogonal eigenvectors of D are used as the co-ordinate base vectors. In that co-ordinate system, the representative matrix of D is a diagonal matrix. Therefore, we may assume that

$$D = \begin{pmatrix} \alpha_1 & 0 & 0 \\ 0 & \alpha_2 & 0 \\ 0 & 0 & \alpha_3 \end{pmatrix},$$

which implies that $\hat{W} = \bar{W}$. Consequently, (14) can be written as

$$\begin{aligned}
&\hat{W}_{1111}x_1^3 + 3\hat{W}_{1112}x_1^2x_2 + 3\hat{W}_{1113}x_1^2x_3 + 3\hat{W}_{1122}x_1x_2^2 + 6\hat{W}_{1123}x_1x_2x_3 \\
&+3\hat{W}_{1133}x_1x_3^2 + \hat{W}_{1222}x_2^3 + 3\hat{W}_{1223}x_2^2x_3 + 3\hat{W}_{1233}x_2x_3^2 + \hat{W}_{1333}x_3^3 = (\alpha_1 - \lambda)x_1, \\
&\hat{W}_{2111}x_1^3 + 3\hat{W}_{1122}x_1^2x_2 + 3\hat{W}_{1123}x_1^2x_3 + 3\hat{W}_{1222}x_1x_2^2 + 6\hat{W}_{1223}x_1x_2x_3 \\
&+3\hat{W}_{1233}x_1x_3^2 + \hat{W}_{2222}x_2^3 + 3\hat{W}_{2223}x_2^2x_3 + 3\hat{W}_{2233}x_2x_3^2 + \hat{W}_{2333}x_3^3 = (\alpha_2 - \lambda)x_2, \\
&\hat{W}_{1113}x_1^3 + 3\hat{W}_{1123}x_1^2x_2 + 3\hat{W}_{1133}x_1^2x_3 + 3\hat{W}_{1223}x_1x_2^2 + 6\hat{W}_{1233}x_1x_2x_3 \\
&+3\hat{W}_{1333}x_1x_3^2 + \hat{W}_{2223}x_2^3 + 3\hat{W}_{2233}x_2^2x_3 + 3\hat{W}_{2333}x_2x_3^2 + \hat{W}_{3333}x_3^3 = (\alpha_3 - \lambda)x_3, \\
&x_1^2 + x_2^2 + x_3^2 = 1.
\end{aligned}$$

$$(16)$$

Note that the coefficients in the above equations come from the fact that the tensor $\hat{W}$ is symmetric, i.e., its entries $\hat{W}_{ijkl}$ are invariant under any permutation of their indices i, j, k and l.

To find the extreme diffusion values and the associated extreme diffusion directions, we have to solve the above system of polynomial equations on x_1, x_2, x_3 and λ. For this system of equations, we have the following result.

THEOREM 4.1 *We have the following results on the extreme diffusion values and their associated extreme diffusion directions.*

(a). *If $\hat{W}_{1112} = \hat{W}_{1113} = 0$, then $\lambda = \alpha_1 - \hat{W}_{1111}$ is an extreme diffusion values of the non-Gaussian diffusion with the extreme diffusion direction $x = (1, 0, 0)^\top$.*

(b). *For any real roots t of the following equations:*

$$\begin{cases} \hat{W}_{1112}t^4 - (\hat{W}_{1111} - 3\hat{W}_{1122} - \alpha_1 + \alpha_2)t^3 - 3(\hat{W}_{1112} - \hat{W}_{1222})t^2 \\ -(3\hat{W}_{1122} - \hat{W}_{2222} - \alpha_1 + \alpha_2)t - \hat{W}_{1222} = 0, \\ \hat{W}_{1113}t^3 + 3\hat{W}_{1123}t^2 + 3\hat{W}_{1223}t + \hat{W}_{2223} = 0, \end{cases} \qquad (17)$$

$$\lambda = Dx^2 - \hat{W}x^4$$

is an extreme diffusion values with the corresponding extreme diffusion direction

$$x = \pm\frac{1}{\sqrt{1+t^2}}(t,1,0)^\top. \tag{18}$$

(c). $\lambda = Dx^2 - \hat{W}x^4$ *and*

$$x = \pm\frac{1}{\sqrt{u^2+v^2+1}}(u,v,1)^\top \tag{19}$$

constitute an extreme diffusion values and extreme diffusion direction pair, where u and v are real solutions of the following system of polynomial equations

$$\begin{cases} \hat{W}_{1113}u^4 + 3\hat{W}_{1123}u^3v - (\hat{W}_{1111} - 3\hat{W}_{1133} - \alpha_1 + \alpha_3)u^3 + 3\hat{W}_{1223}u^2v^2 \\ -(3\hat{W}_{1112} - 6\hat{W}_{1233})u^2v - 3(\hat{W}_{1113} - \hat{W}_{1333})u^2 \\ +(3\hat{W}_{2233} - 3\hat{W}_{1122} - \alpha_3 + \alpha_1)uv^2 \\ +\hat{W}_{2223}uv^3 - (6\hat{W}_{1123} - 3\hat{W}_{2333})uv - (3\hat{W}_{1133} - \hat{W}_{3333} - \alpha_1 + \alpha_3)u \\ -\hat{W}_{1222}v^3 - 3\hat{W}_{1223}v^2 - 3\hat{W}_{1233}v - \hat{W}_{1333} = 0, \\ \hat{W}_{1113}u^3v - \hat{W}_{1112}u^3 + 3\hat{W}_{1123}u^2v^2 - (3\hat{W}_{1122} - 3\hat{W}_{1133} - \alpha_2 + \alpha_3)u^2v \\ -3\hat{W}_{1123}u^2 + 3\hat{W}_{1123}uv^3 - (3\hat{W}_{1222} - 6\hat{W}_{1233})uv^2 \\ -(6\hat{W}_{1223} - 3\hat{W}_{1333})uv - 3\hat{W}_{1233}u - 3(\hat{W}_{2223} - \hat{W}_{2333})v^2 \\ +\hat{W}_{2223}v^4 - (\hat{W}_{2222} - 3\hat{W}_{2233} - \alpha_2 + \alpha_3)v^3 \\ -(3W_{2233} - \alpha_2 - \hat{W}_{3333} + \alpha_3)v - \hat{W}_{2333} = 0. \end{cases} \tag{20}$$

All the extreme diffusion values and the associated directions are given by (a), (b) and (c) if $\hat{W}_{1112} = \hat{W}_{1113} = 0$, *and by (b) and (c) otherwise.*

Proof. It is direct to check that (a) holds.
Setting $x_3 = 0$, $x_2 \neq 0$ and using the third equation in (16), we have

$$\begin{cases} (\hat{W}_{1111} + \alpha_1)x_1^3 + 3\hat{W}_{1112}x_1^2x_2 + (3\bar{W}1122 + \alpha_1)x_1x_2^2 + \hat{W}_{1222}x_2^3 = \lambda x_1, \\ \hat{W}_{2111}x_1^3 + (3\hat{W}_{1122} + \alpha_2)x_1^2x_2 + 3\bar{W}_{1222}x_1x_2^2 + (\hat{W}_{2222} + \alpha_2)x_2^3 = \lambda x_2, \\ \hat{W}_{1113}x_1^3 + 3\hat{W}_{1123}x_1^2x_2 + 3\hat{W}1223x_1x_2^2 + \hat{W}_{2223}x_2^3 = 0, \\ x_1^2 + x_2^2 = 1. \end{cases}$$

Let $t = x_1/x_2$. Then from the first three equations, we have (17) and from the last equation we have (18). This proves (b).

If $x_3 \neq 0$, then from the fourth equation in (16), we have

$$
\begin{cases}
(\hat{W}_{1111} + \alpha_1)x_1^3 + 3\hat{W}_{1112}x_1^2 x_2 + 3\hat{W}_{1113}x_1^2 x_3 + (3\hat{W}1122 + \alpha_1)x_1 x_2^2 \\
\quad +6\hat{W}_{1123}x_1 x_2 x_3 + (3\hat{W}_{1133} + \alpha_1)x_1 x_3^2 + \hat{W}_{1222}x_2^3 \\
\quad +3\hat{W}_{1223}x_2^2 x_3 + 3\hat{W}_{1233}x_2 x_3^2 + \hat{W}_{1333}x_3^3 = \lambda x_1, \\
\hat{W}_{2111}x_1^3 + (3\hat{W}_{1122} + \alpha_2)x_1^2 x_2 + 3\bar{W}_{1123}x_1^2 x_3 + 3\hat{W}_{1222}x_1 x_2^2 + 6\hat{W}_{1223}x_1 x_2 x_3 \\
\quad +3\hat{W}_{1233}x_1 x_3^2 + (\hat{W}_{2222} + \alpha_2)x_2^3 + 3\hat{W}_{2223}x_2^2 x_3 \\
\quad +(3\hat{W}_{2233} + \alpha_2)x_2 x_3^2 + \hat{W}_{2333}x_3^3 = \lambda x_2, \\
\hat{W}_{1113}x_1^3 + 3\hat{W}_{1123}x_1^2 x_2 + (3\bar{W}_{1133} + \alpha_3)x_1^2 x_3 + 3\hat{W}1223 x_1 x_2^2 + 6\hat{W}_{1233}x_1 x_2 x_3 \\
\quad +3\hat{W}_{1333}x_1 x_3^2 + \hat{W}_{2223}x_2^3 + (3\hat{W}_{2233} + \alpha_3)x_2^2 x_3 \\
\quad +3\hat{W}_{2333}x_2 x_3^2 + (\hat{W}_{3333} + \alpha_3)x_3^3 = \lambda x_3, \\
x_1^2 + x_2^2 + x_3^2 = 1.
\end{cases}
$$

$$(21)$$

Let $u = x_1/x_3$ and $v = x_2/x_3$. Then (c) follows immediately from the above system of equations. $\qquad\square$

To find all the extreme diffusion values and the corresponded diffusion directions for non-Gaussian diffusion, from Theorem 4.1, we need to solve systems of equations (17) and (20). (17) is a system of polynomial equations of one variable t, which can be solved efficiently. (20) is a system of polynomial equations of two variables u and v. For solving such equations, we first regard it as a system of polynomial equations of variable u and rewrite it as

$$
\begin{cases}
\gamma_0 u^4 + \gamma_1 u^3 + \gamma_2 u^2 + \gamma_3 u + \gamma_4 = 0, \\
\tau_0 u^3 + \tau_1 u^2 + \tau_2 u + \tau_3 = 0,
\end{cases}
$$

where $\gamma_0, \cdots, \gamma_4$, $\tau_0, \cdots, \tau_3$ are polynomials of v, which can be calculated by (20). The above system of polynomial equations in u possesses solutions if and only if its resultant vanishes [5]. The resultant of this system of polynomial equations is the determinant of the following 7×7 matrix

$$
V := \begin{pmatrix}
\gamma_0 & \gamma_1 & \gamma_2 & \gamma_3 & \gamma_4 & 0 & 0 \\
0 & \gamma_0 & \gamma_1 & \gamma_2 & \gamma_3 & \gamma_4 & 0 \\
0 & 0 & \gamma_0 & \gamma_1 & \gamma_2 & \gamma_3 & \gamma_4 \\
\tau_0 & \tau_1 & \tau_2 & \tau_3 & 0 & 0 & 0 \\
0 & \tau_0 & \tau_1 & \tau_2 & \tau_3 & 0 & 0 \\
0 & 0 & \tau_0 & \tau_1 & \tau_2 & \tau_3 & 0 \\
0 & 0 & 0 & \tau_0 & \tau_1 & \tau_2 & \tau_3
\end{pmatrix},
$$

which is a polynomial equation in variable v. After finding all real roots of this polynomial, we can substitute them to (20) to find all the real solutions of u. Correspondingly, all the extreme diffusion values and the associated diffusion directions can be found.

5.   Algorithm Description

We now give our algorithm for solving (13).

Algorithm. A Direct Algorithm for (13)

Input: The second-order diffusion tensor D, the fourth-order kurtosis tensor W and the b value.

Output: The extreme diffusion values and the associated diffusion directions.

S1. Find the decomposition of $D = P\Lambda P^T$, where Λ is a diagonal matrix whose diagonal elements are eigenvalues of D, $\alpha_1 \geq \alpha_2 \geq \alpha_3 > 0$, and P is a orthogonal matrix whose columns are eigenvectors of D.

S2. Let $\bar{W} = \frac{1}{3} b M_D^2 W$, where

$$M_D = \frac{\alpha_1 + \alpha_2 + \alpha_3}{3}$$

and $\hat{W} = \bar{W} P^4$, i.e.,

$$\hat{W}_{ijkl} = \sum_{i',j',k',l'=1}^{3} \bar{W}_{i'j'k'l'} p_{i'i} p_{j'j} p_{k'k} p_{l'l}.$$

S3. Let

$$g(v) := \det V,$$

where V is the 7×7 matrix defined by (4) and find the zeros of $g(v)$.

S4. For every real zeros v_i found at the above step, substitute it into (17) to find the solution u_j.

S5. From each pair of v_i and u_j found at the above two steps, form the extreme diffusion directions and the extreme diffusion values. $\qquad\square$

6. Numerical Examples

In this section, we report some computational results on the extreme diffusion values and the associated diffusion directions of a second order and a fourth order tensor pair that derived from data of MRI experiments on rat spinal cord specimen fixed in formalin. The MRI experiments were conducted on a 7 Tesla MRI scanner at Laboratory of Biomedical Imaging and Signal Processing at The University of Hong Kong.

In MRI experiments, the AKC and ADC values for a given gradient $x \in R^3$ can be determined by acquiring data at three or more b values [6] including b=0. In our experiments, we take six b values 0, 800, 1600, 2400, 3200 and 4000, in unit of s/mm^2. In each example, we take 30 gradient directions and get the corresponding AKC and ADC values as the averages of the 9 pixels. From these ADC and AKC values, we obtain the elements of the diffusion tensor D and the diffusion kurtosis tensor W by using the least squares method, discussed in [6] and [10].

Example 1. Our first example is taken from the white matter. The diffusion tensor D is

$$D = \begin{pmatrix} 0.1755 & 0.0035 & 0.0132 \\ 0.0035 & 0.1390 & 0.0017 \\ 0.0132 & 0.0017 & 0.4006 \end{pmatrix} * 10^{-3}$$

in unit of mm^2/s. The eigen-decomposition of the diffusion tensor D is $\hat{D} = DP^2$, where $\hat{D}$ is a diagonal matrix whose diagonal elements are $(\alpha_1, \alpha_2, \alpha_3) = (0.4013, 0.1751, 0.1387) * 10^{-3}$ and

$$P = \begin{pmatrix} 0.0584 & 0.9939 & 0.0938 \\ 0.0073 & 0.0935 & -0.9956 \\ 0.9983 & -0.0589 & 0.0018 \end{pmatrix}.$$

The fifteen independent elements of the diffusion kurtosis tensor W are $W_{1111} = 0.4982$, $W_{2222} = 0$, $W_{3333} = 2.6311$, $W_{1112} = -0.0582$, $W_{1113} = -1.1719$, $W_{1222} = 0.4880$, $W_{2223} = -0.6162$, $W_{1333} = 0.7639$, $W_{2333} = 0.7631$, $W_{1122} = 0.2236$, $W_{1133} = 0.4597$, $W_{2233} = 0.1519$, $W_{1123} = -0.0171$, $W_{1223} = 0.1852$ and $W_{1233} = -0.4087$, respectively. It is easy to find that

$$M_D^2 = \left(\frac{D_{11} + D_{22} + D_{33}}{3} \right)^2 = 5.6813 \times 10^{-8}.$$

To find the largest and the smallest diffusion values, we need first obtain the largest and the smallest D-eigenvalues. For given b value, we can use the method proposed in Section 4 to compute all the extreme diffusion values and the associated diffusion directions. Table 1 lists the results for $b = 2400$ (s/mm^2).

Table 1. Extreme diffusion values and directions of (D, W).

	x_1	x_2	x_3	$\lambda \times 10^3$
1	-0.5400	-0.8413	0.0258	0.2483
2	0.1487	-0.9656	0.2135	0.1499
3	-0.2051	0.9251	0.3195	0.1438
4	-0.6674	0.6483	0.3665	0.2212
5	0.7043	-0.5416	0.4589	0.2795
6	-0.9957	-0.0675	0.0632	0.3288
7	0.0319	0.5815	0.8129	0.1531
8	0.0466	-0.4651	0.8840	0.1278
9	-0.5908	-0.3367	0.7332	0.2206
10	0.6435	0.2619	0.7192	0.2170
11	-0.5459	0.1195	0.8293	0.2183

From the above table we can see that the largest and the smallest diffusion values for this example are 0.3288×10^{-3} and 0.1278×10^{-3} (mm^2/ms), attained at

$$(-0.9957, -0.0675, 0.0632)^\top \quad \text{and} \quad (0.0466, -0.4651, 0.8840)^\top,$$

respectively.

To show the dependence of the extreme diffusion values on the b values, we plot the largest and the smallest diffusion values as functions of the b values. Figure 1 shows the result, where the y-axis is scaled to 10^3.

To give some insight to the difference between the DTI and DKI, we also plot the largest diffusion values in these two models, as functions of b values, and the result is Figure 2.

Figure 2 clearly shows that when b is too small, the linear model (6) can model the diffusion behavior quite well; while as b value becomes larger, the difference between the two models (5) and (6) is more obvious.
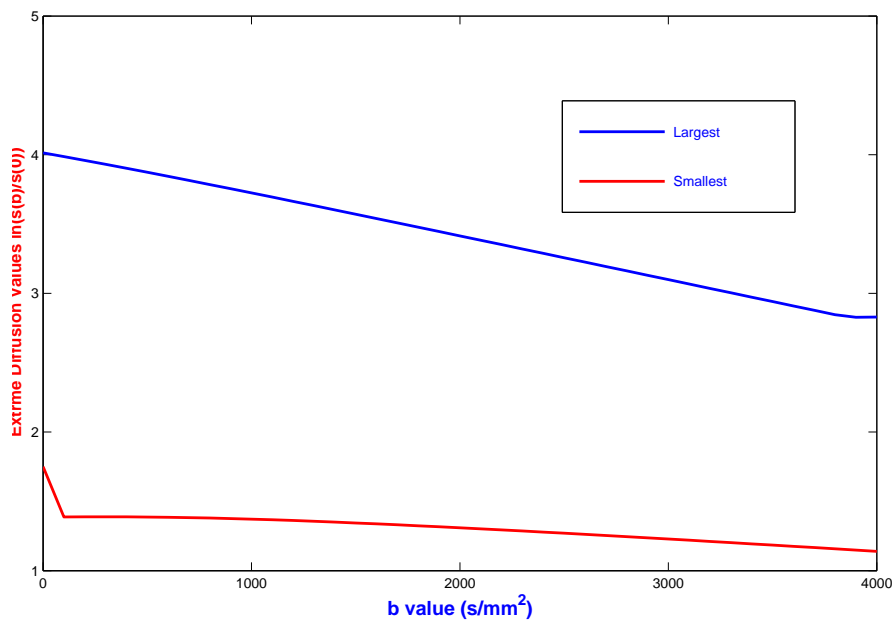
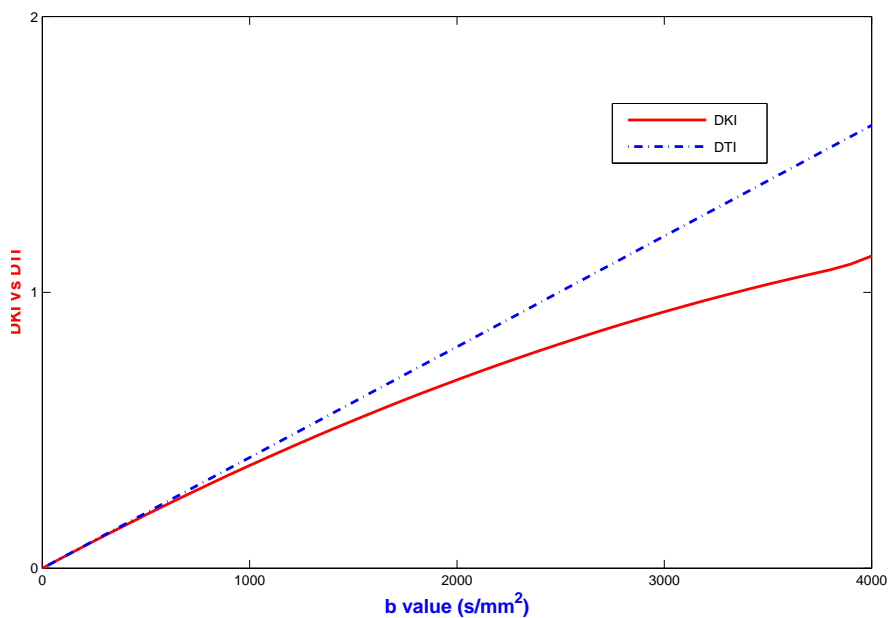Figure 1. Largest and Smallest Diffusion Values as functions of b values.

Figure 2. Largest bD_{app} VS $bD_{app} - \frac{1}{6}b^2 D_{app}^2 K_{app}$ as functions of b.

Example 2. Our second example is taken from the gray matter. The diffusion tensor D is

$$D = \begin{pmatrix} 1.2455 & -0.0169 & -0.0012 \\ -0.0169 & 1.6921 & 0.0077 \\ -0.0012 & 0.0077 & 1.1937 \end{pmatrix} * 10^{-3}$$

in unit of mm^2/s. The eigen-decomposition of the diffusion tensor D is $\hat{D} = DP^2$, where $\hat{D}$ is a diagonal matrix whose diagonal elements are $(\alpha_1, \alpha_2, \alpha_3) = (1.6928, 1.2448, 1.1936) * 10^{-3}$ and

$$P = \begin{pmatrix} 0.0379 & -0.9991 & 0.0174 \\ -0.9992 & -0.0381 & -0.0148 \\ -0.0154 & 0.0168 & 0.9997 \end{pmatrix}.$$

The fifteen independent elements of the diffusion kurtosis tensor W are $W_{1111} = 0.1171 \times 10^{-5}$, $W_{2222} = 0.2665 \times 10^{-5}$, $W_{3333} = 0.1425 \times 10^{-5}$, $W_{1112} = -0.0009 \times 10^{-5}$, $W_{1113} = 0.0031 \times 10^{-5}$, $W_{1222} = 0.0026 \times 10^{-5}$, $W_{2223} = 0.0046 \times 10^{-5}$, $W_{1333} = 0.0044 \times 10^{-5}$, $W_{2333} = -0.0008 \times 10^{-5}$, $W_{1122} = 0.0456 \times 10^{-5}$, $W_{1133} = 0.0348 \times 10^{-5}$, $W_{2233} = 0.0681 \times 10^{-5}$, $W_{1123} = 0.0016 \times 10^{-5}$, $W_{1223} = -0.0015 \times 10^{-5}$ and $W_{1233} = 0.0013 \times 10^{-5}$, respectively. We can find that

$$M_D^2 = \left(\frac{D_{11} + D_{22} + D_{33}}{3} \right)^2 = 1.8964 \times 10^{-6}.$$

For $b = 2400$ (s/mm^2), we can use the method proposed in Section 4 to compute all the extreme diffusion values and the associated diffusion directions. Table 2 lists the results.

Table 2. Extreme diffusion values and directions of (D, W).

	x_1	x_2	x_3	$\lambda \times 10^3$
1	-0.4485	0.8938	0	1.3349
2	0.6697	-0.7426	0.0001	1.4457
3	0.6697	0.7426	0.0001	1.4457
4	-0.0000	1.0000	0.0001	1.2448
5	-1.0000	-0.0000	0.0000	1.6926
6	0.7070	0.0002	0.7072	1.4430
7	-0.7070	-0.0001	0.7072	1.4430
8	0.0000	-0.0001	1.0000	1.1934

From the above table we can see that the largest and the smallest diffusion values for this example is 1.6926×10^{-3} and 1.1934×10^{-3} (mm^2/ms), attained at

$$(-1.0000, -0.0000, 0.0000)^\top \quad \text{and} \quad (0.0000, -0.0001, 1.0000)^\top,$$

respectively.

To show the dependence of the extreme diffusion values on the b values, we list the largest and the smallest diffusion values for different b values in the following table (scaled to 10^3).

Table 3. Extreme diffusion values of (D, W).

b	800	1600	2400	3200	4000
Largest	1.4425	1.4419	1.4412	1.4406	1.4399
Smallest	1.1932	1.1928	1.1925	1.1921	1.1917

Table 3 shows that both the largest and the smallest diffusion values are decreasing function of the b value; however, the speed to decrease is not as clear as the first example. The reason is that in the second example, the elements of the diffusion

kurtosis tensor W is too small, comparing to those of the diffusion tensor D. In other words, the diffusion in the second example is more likely to be a Gaussian diffusion.

To give some insight to the difference between the DTI and DKI, we also plot the largest diffusion values in these two models, as functions of b values, and the result is Figure 3.
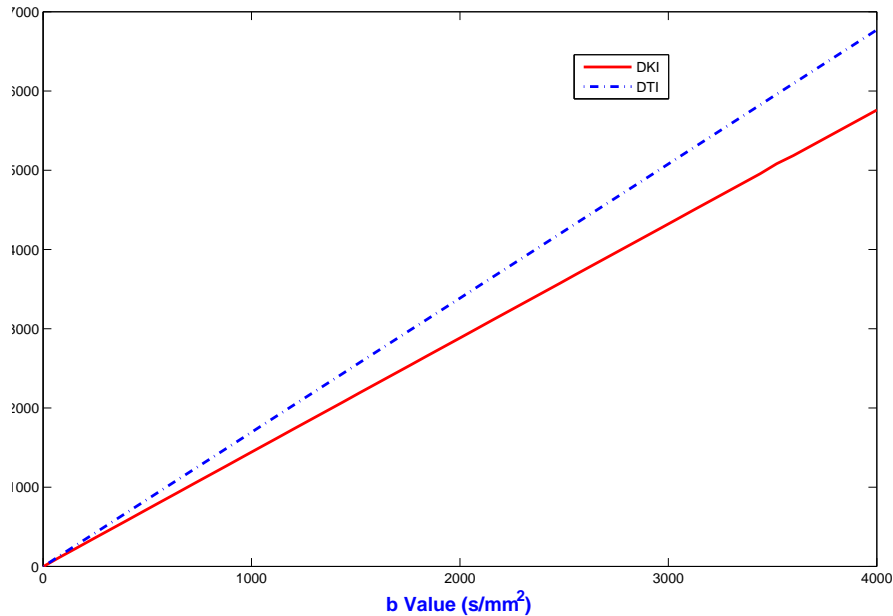

Figure 3. Largest bD_{app} VS $bD_{app} - \frac{1}{6}b^2 D_{app}^2 K_{app}$ as functions of b.

7. Final Remarks

In this paper, we proposed the extreme diffusion values and the associated diffusion directions, which are the extreme values and the extreme points associated to the diffusion tensor and the diffusion kurtosis tensor. We analyzed some properties of the extreme diffusion values and proposed a numerical method for finding such values and the associated directions. These values and directions are potentially useful for understanding tissue microstructure.

It is believed that noise will be of greater effects on the solution because higher diffusion gradients are used in DKI and the least squares method is used for estimating the fourth order tensor, W. The effects of Rician noise will be likely similar to those in the case of diffusion tensor imaging, as studied in [7]. A study on such a noise effect will be a future further work.

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