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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 behaviour 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.

Keywords: diffusion kurtosis tensors; extreme diffusion values; extreme diffusion directions; anisotropy

1. Introduction

Magnetic resonance imaging (MRI) in tissues has been used to infer anatomical structure and to aid in the diagnosis of many pathologies [11,14]. Nowadays, the most successful and popular MR technique is the diffusion tensor imaging (DTI), 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

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

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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 centres 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 the DTI model to break down [1,3]. For example, when DTI is used in regions where the fibres cross or merge, difficulty is often encountered since with current MR resolution, voxel averaging of different fibre tracts is frequent and unavoidable.

To overcome this problem, new MRI models [2,9,13] have been proposed, which use higherorder tensors, rather than just a second-order tensor used in DTI, to characterize the process of diffusion. One of such new MRI models is diffusion kurtosis imaging (DKI) [6,10]. In that model, a fourth-order three-dimensional fully symmetric tensor, called the DK tensor, is proposed to describe the non-Gaussian behaviour 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:

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

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

$$K_{\rm app} = \frac{M_D^2}{D_{\rm app}^2} W x^4, \tag{4}$$
$$W x^4 \equiv \sum_{i,j,k,l=1}^3 W_{ijkl} x_i x_j x_k x_l$$

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 fibre-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 coordinate 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 DK 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 to the result of [6], the ADC and AKC for a single direction should satisfy the relationship (3), i.e.

$$\ln[S(b)] = \ln[S(0)] - bD_{app} + \frac{1}{6}b^2 D_{app}^2 K_{app}.$$
(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 $\alpha_1 \ge \alpha_2 \ge \alpha_3$. 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 Equation (5), i.e. the ADC for a single direction should satisfy the relationship (1)

$$\ln[S(b)] = \ln[S(0)] - bD_{app}.$$
 (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 by solving the optimization problems

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

and

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

$$\begin{array}{ll}
\min & Wx^4 \\
\text{s.t.} & Dx^2 = 1,
\end{array}$$
(10)

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

In a similar way as in the DTI model, we would now 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

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max $Dx^2 - \frac{1}{6}bM_D^2Wx^4$

s.t. $x^{T}x = 1$.

(11)

(12)

problems:

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and

s.t. $x^{T}x = 1$. The solutions of Equations (11) and (12) depend on the second-order tensor *D* and the fourthorder tensor *W*. Thus, our tasks are to find some useful properties of solutions of Equations (11) and (12), the extreme values and the associated extreme directions of a tensor pair (*D*, *W*), and

min $Dx^2 - \frac{1}{6}bM_D^2Wx^4$

to design numerical methods for finding such values and directions.

It is known that Dx is a vector in \Re^3 with its *i*th 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 *i*th 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, $\alpha_1 \ge \alpha_2 \ge \alpha_3 > 0$. 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 $\lambda \in \Re$:

$$Dx - \frac{1}{3}bM_D^2Wx^3 = \lambda x, \quad x^{\mathrm{T}}x = 1.$$
 (13)

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

$$Dx - \bar{W}x^3 = \lambda x, \quad x^{\mathrm{T}}x = 1.$$
(14)

A real number λ satisfying Equation (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 Equation (14) associated with an extreme diffusion value λ , then

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

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

Proof The feasible regions of Equations (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 Equation (14) with the corresponding Lagrangian multipliers. Hence, the largest and smallest diffusion values always exist and Equation (15) follows from Equation (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 \overline{W} are converted to y = Px, $\hat{D} = DP^2$, and $\hat{W} = \overline{W}P^4$, 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

$$\hat{D}y - \hat{W}y^3 = \lambda y, \quad y^{\mathrm{T}}y = 1,$$

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 the 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 problems with polynomial objective functions and constraints. The first-order optimal conditions for Equations (11) and (12) are the 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 in Equation (13) may be time-consuming. Moreover, the final variable equation derived from Equation (13) may have a higher degree, which makes it sensitive to the coefficients.

In the following, we propose a direct method to solve Equation (13), which fully uses the structure of the problem. The first step is to eliminate λ from the system and then use 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 coordinate system such that the three orthogonal eigenvectors of D are used as the coordinate base vectors. In that coordinate 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, Equation (14) can be written as

$$\hat{W}_{1111}x_1^3 + 3\hat{W}_{1112}x_1^2x_2 + 3\hat{W}_{1113}x_1^2x_3 + 3\hat{W}_{1122}x_1x_2^2 + 6\hat{W}_{1123}x_1x_2x_3 + 3\hat{W}_{1133}x_1x_3^2 + \hat{W}_{1222}x_2^3 + 3\hat{W}_{1223}x_2^2x_3 + 3\hat{W}_{1233}x_2x_3^2 + \hat{W}_{1333}x_3^3 = (\alpha_1 - \lambda)x_1, \hat{W}_{2111}x_1^3 + 3\hat{W}_{1122}x_1^2x_2 + 3\hat{W}_{1123}x_1^2x_3 + 3\hat{W}_{1222}x_1x_2^2 + 6\hat{W}_{1223}x_1x_2x_3 + 3\hat{W}_{1233}x_1x_3^2 + \hat{W}_{2222}x_2^3 + 3\hat{W}_{2223}x_2^2x_3 + 3\hat{W}_{2233}x_2x_3^2 + \hat{W}_{2333}x_3^3 = (\alpha_2 - \lambda)x_2, \hat{W}_{1113}x_1^3 + 3\hat{W}_{1123}x_1^2x_2 + 3\hat{W}_{1133}x_1^2x_3 + 3\hat{W}_{1223}x_1x_2^2 + 6\hat{W}_{1233}x_1x_2x_3 + 3\hat{W}_{1333}x_1x_3^2 + \hat{W}_{2223}x_2^3 + 3\hat{W}_{2233}x_2^2x_3 + 3\hat{W}_{2333}x_2x_3^2 + \hat{W}_{3333}x_3^3 = (\alpha_3 - \lambda)x_3, x_1^2 + x_2^2 + x_3^2 = 1.$$
 (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 value of the non-Gaussian diffusion with the extreme diffusion direction $x = (1, 0, 0)^{\text{T}}$.
- (b) For any real root t of the equations

$$\hat{W}_{1112}t^{4} - (\hat{W}_{1111} - 3\hat{W}_{1122} - \alpha_{1} + \alpha_{2})t^{3} - 3(\hat{W}_{1112} - \hat{W}_{1222})t^{2} - (3\hat{W}_{1122} - \hat{W}_{2222} - \alpha_{1} + \alpha_{2})t - \hat{W}_{1222} = 0, \hat{W}_{1113}t^{3} + 3\hat{W}_{1123}t^{2} + 3\hat{W}_{1223}t + \hat{W}_{2223} = 0, \lambda = Dx^{2} - \hat{W}x^{4}$$
(17)

is an extreme diffusion value with the corresponding extreme diffusion direction

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

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

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

constitutes an extreme diffusion value and extreme diffusion direction pair, where u and v are real solutions of the following system of polynomial equations:

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

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

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

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

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

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

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

To find all the extreme diffusion values and the corresponding diffusion directions for non-Gaussian diffusion, from Theorem 4.1, we need to solve the systems of Equations (17) and (20). Equation (17) is a system of polynomial equations of one variable t, which can be solved efficiently.

Equation (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

$$\gamma_0 u^4 + \gamma_1 u^3 + \gamma_2 u^2 + \gamma_3 u + \gamma_4 = 0,$$

$$\tau_0 u^3 + \tau_1 u^2 + \tau_2 u + \tau_3 = 0,$$

where $\gamma_0, \ldots, \gamma_4, \tau_0, \ldots, \tau_3$ are polynomials of v, which can be calculated by Equation (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 7 × 7 matrix

	γ0	γ_1	γ_2	γ_3	γ_4	0	0 /	
	0	γ_0	γ_1	γ_2	γ3	γ_4	0	
	0	0	γ_0	γ_1	γ_2	γ_3	γ_4	
V :=	$ au_0$	$ au_1$	$ au_2$	$ au_3$	0	0	0	,
	0	$ au_0$	$ au_1$	$ au_2$	$ au_3$	0	0	
	0	0	$ au_0$	$ au_1$	$ au_2$	$ au_3$	0	
	0	0	0	$ au_0$	$ au_1$	$ au_2$	τ_3	

which is a polynomial equation in variable v. After finding all real roots of this polynomial, we can substitute them to Equation (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 Equation (13).

ALGORITHM A direct algorithm for Equation (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, $\alpha_1 \ge \alpha_2 \ge \alpha_3 > 0$, and P is an orthogonal matrix whose columns are eigenvectors of D.
- **S2.** Let $\overline{W} = 1/3bM_D^2W$, 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 \times 7 matrix defined by Equation (4), and find the zeros of g(v).

- **S4.** Substitute every real zero v_i found in the previous step, into Equation (17) to find the solution u_j .
- **S5.** From each pair of v_i and u_j found in the previous two steps, form the extreme diffusion directions and the extreme diffusion values.

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 was derived from the data of MRI experiments on rat spinal cord specimen fixed in formalin. The MRI experiments were conducted on a 7 Tesla MRI scanner at the Laboratory of Biomedical Imaging and Signal Processing at the University of Hong Kong.

In the 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 units of s/mm². In each example, we take 30 gradient directions and obtain 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 DK tensor *W* by using the least squares method, discussed in [6] and [10].

Example 6.1 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 units of mm²/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 15 independent elements of the DK 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 to first obtain the largest and the smallest *D*-eigenvalues. For a 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/mm²).

From Table 1, we can see that the largest and the smallest diffusion values for this example are 0.3288×10^{-3} and 0.1278×10^{-3} (mm²/ms), attained at

$$(-0.9957, -0.0675, 0.0632)^{T}$$
 and $(0.0466, -0.4651, 0.8840)^{T}$,

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 shown in Figure 2.

	<i>x</i> ₁	<i>x</i> ₂	<i>x</i> ₃	$\lambda imes 10^3$
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

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

Figure 2 clearly shows that when b is too small, the linear model (6) can model the diffusion behaviour quite well; while as the b value becomes larger, the difference between the two models (5) and (6) is more obvious.

Example 6.2 Our second example is taken from the grey matter. The diffusion tensor D is

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



Figure 1. Largest and smallest diffusion values as functions of b values.



Figure 2. Largest bD_{app} versus $bD_{app} - 1/6b^2 D_{app}^2 K_{app}$ as functions of b.

in units of mm²/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 15 independent elements of the DK tensor W are $W_{1111} = 0.1171 \times 10^{-5}$, $W_{2222} = 0.2665 \times 10^{-5}$, $W_{3333} = 0.1425 \times 10^{-5}$, $W_{1112} = -0.0009 \times 10^{-5}$, $W_{1113} = 0.0031 \times 10^{-5}$, $W_{1222} = 0.0026 \times 10^{-5}$, $W_{2223} = 0.0046 \times 10^{-5}$, $W_{1333} = 0.0044 \times 10^{-5}$, $W_{2333} = -0.0008 \times 10^{-5}$, $W_{1122} = 0.0456 \times 10^{-5}$, $W_{1133} = 0.0348 \times 10^{-5}$, $W_{2233} = 0.0081 \times 10^{-5}$, $W_{1123} = 0.0016 \times 10^{-5}$, $W_{1223} = -0.0015 \times 10^{-5}$, 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 $b = 2400 \text{ (s/mm}^2)$, 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.

From Table 2, we can see that the largest and the smallest diffusion values for this example are 1.6926×10^{-3} and 1.1934×10^{-3} (mm²/ms), attained at

$$(-1.0000, -0.0000, 0.0000)^{\mathrm{T}}$$
 and $(0.0000, -0.0001, 1.0000)^{\mathrm{T}}$,

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 Table 3 (scaled to 10^3).

	<i>x</i> ₁	<i>x</i> ₂	<i>x</i> ₃	$\lambda imes 10^3$
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

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

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 functions 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 DK tensor W are too small, compared with those of the diffusion tensor D. In other words, the diffusion in the second example is more likely to be Gaussian.

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 shown in Figure 3.



Figure 3. Largest bD_{app} versus $bD_{app} - 1/6b^2 D_{app}^2 K_{app}$ 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 DK tensor. We analysed 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 the tissue microstructure.

It is believed that noise will be of greater effect 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 DTI, as studied in [7]. A study on such a noise effect will be a future work.

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