

DIFFUSION KURTOSIS IMAGING: ROBUST ESTIMATION FROM DW-MRI USING HOMOGENEOUS POLYNOMIALS

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ABSTRACT

Several tensor-based models have been presented in literature for parameterizing the water diffusion in Diffusion-Weighted MRI datasets, namely Diffusion Tensor Imaging (DTI), Generalized Tensor Imaging (GTI), and Diffusion Kurtosis Imaging (DKI). In this paper we use homogeneous trivariate polynomials to show that GTI is a special case of DKI for single angular shell acquisitions, and then we employ the theory for imposing positive semi-definite (PSD) constraints to GTIs in order to perform robust estimation of the DKI parameters. We propose a novel framework for DKI estimation that simultaneously imposes constraints to the diffusivity function, diffusion tensor and diffusion kurtosis. These three constraints are parameterized explicitly as a set of linear systems that can be efficiently solved using the non-negative least squares technique. The robustness of our framework is demonstrated using synthetic and real data from a human brain.

Index Terms— Diffusion Kurtosis Imaging, Generalized Diffusion Tensors, Homogeneous Polynomials

1. INTRODUCTION

In Diffusion Tensor Imaging (DTI) [1], rank-2 tensors have been used to model the water diffusion in a given Diffusion-Weighted (DW) MRI dataset using the Stejskal-Tanner signal attenuation model:

$$S = S_0 e^{-bd(\mathbf{g})} \quad (1)$$

where $d(\mathbf{g})$ is the diffusivity function, S is the observed signal associated with the diffusion sensitizing magnetic gradient orientation \mathbf{g} and the diffusion weighting b , and S_0 is the observed non diffusion-weighted signal ($b = 0s/mm^2$).

In Generalized Tensor Imaging, tensors of higher rank (e.g. 4) have replaced the rank-2 tensor in $d(\mathbf{g})$. The main

advantage of GTI model is the ability to approximate multi-lobed diffusivity profiles [2]. A combination of rank-2 and rank-4 tensors have been employed in Diffusion Kurtosis Imaging to model the apparent kurtosis of the non-Gaussian water diffusion [3]. It has been shown that various invariant characteristics and inherent quantities of kurtosis can be computed from the parameters of the rank-2 and rank-4 tensors in DKI [4] that can be used as indicators of diffusion pattern anomalies due to various pathogenic conditions in neural tissue [5, 6, 7].

The robust estimation of the parameters in the DKI model is essential especially in the case of computing kurtosis-based biological markers for clinical purposes. We should emphasize here that GTI and DKI models are more prone to noise in the data compared to DTI due to the large number of unknown higher order coefficients that need to be estimated.

In this paper we present a novel method for robust DKI estimation from a given DW-MRI dataset. In the proposed framework we express tensors in their equivalent trivariate homogeneous polynomial form. Using homogeneous polynomials we establish a mathematical relationship between the parameters in GTI and DKI models, and we employ it in order to impose explicitly positivity constraints to various quantities in the diffusion kurtosis model. More specifically our method guarantees that the estimated parameters correspond to a positive diffusivity function, positive rank-2 diffusion tensor, and constrained apparent kurtosis. Furthermore, we show how to implement explicitly all three constraints as a set of linear systems with non-negative least squares solutions. Finally, we performed quantitative comparison of each constraint under various levels of Rician noise in the data. The results conclusively demonstrate the robustness of the proposed framework and motivate the need for constrained estimation of the DKI parameters.

The contributions in this paper are threefold: 1) we present a novel method for robust DKI estimation, 2) we use homogeneous polynomials to show that GTI is a special case of DKI, and therefore should not be treated as different techniques [7], and 3) we show how to explicitly parameterize the problem in the convenient form of linear systems.

The source code of the methods presented in this paper is available in fanDTasia Matlab DW-MRI toolbox through Matlab Central File Exchange (www.mathworks.com/matlabcentral/fileexchange/). This research was funded in part by US Army W81XWH-08-1-0725, PT075827, and NIH EB007082.

2. HOMOGENEOUS POLYNOMIALS

Any homogeneous polynomial in 3 variables (x_1, x_2, x_3) of degree n can be written in the following form

$$h(\mathbf{x}) = \sum_{i+j+k=n} x_1^i x_2^j x_3^k T_{i,j,k} \quad (2)$$

where x_i is the i^{th} component of the variable vector $\mathbf{x} = [x_1 \ x_2 \ x_3]^T$, and $T_{i,j,k}$ are the polynomial coefficients. The number of unique polynomial coefficients in Eq. 2 equals to $\frac{(2+n)!}{2(n)!}$, where n is the degree of the polynomial. In the cases of $n = 2, 4, 6$ the number of unique coefficients is 6, 15, 28 respectively. If we stuck all polynomial coefficients into one vector \mathbf{t} , Eq. 2 can be further simplified as $h(\mathbf{x}) = v_n(\mathbf{x})^T \mathbf{t}$, where $v_n(\mathbf{x})$ is a vector that contains all n -degree monomials of the variables in \mathbf{x} . For example in the case of $n = 2$, \mathbf{t} is a 6 dimensional coefficient vector, and $v_2(\mathbf{x})$ is the corresponding 6D vector of monomials $(x_3^2, x_2x_3, x_2^2, x_1x_3, x_1x_2, x_1^2)^T$, and $v_4(\mathbf{x})$ is the corresponding 15D vector of monomials $(x_3^4, x_2x_3^3, x_2^2x_3^2, x_2^3x_3, x_2^4, x_1x_3^3, x_1x_2x_3^2, x_1x_2^2x_3, x_1x_3^2, x_1^2x_2x_3, x_1^2x_2^2, x_1^3x_2, x_1^4)^T$.

The space of n^{th} degree homogeneous polynomials in 3 variables will be denoted by \mathcal{H}_3^n . If we restrict the input variables to be $\mathbf{x} \in S_2$ (i.e. unit vectors), then for any $h(\mathbf{x}) \in \mathcal{H}_3^n$, there exists another polynomial $h'(\mathbf{x}) \in \mathcal{H}_3^{n+2}$ such that $h(\mathbf{x}) = h'(\mathbf{x}) \forall \mathbf{x} \in S_2$. According to this property any spherical function parametrized as a homogeneous polynomial of degree 2 can be written as an equivalent homogeneous polynomial of degree 4, because the former belongs to a subspace of the latter. For instance $h(\mathbf{x}) = h(\mathbf{x})(x_1^2 + x_2^2 + x_3^2) = h'(\mathbf{x})$, where $h \in \mathcal{H}_3^2$, $h' \in \mathcal{H}_3^4$, and $\mathbf{x} \in S_2$.

In the next sections we will use homogeneous polynomials to parameterize the diffusion and the kurtosis in DW-MRI.

3. DIFFUSION KURTOSIS

The acquired Diffusion-Weighted MR signal can be modeled by incorporating the kurtosis component of the diffusion [3] in the Stejskal-Tanner equation (Eq. 1) as follows:

$$S(b, \mathbf{g}) = S_0 e^{-bd(\mathbf{g}) + \frac{b^2 \bar{d}^2}{6} w(\mathbf{g})} \quad (3)$$

where \mathbf{g} is the sensitizing gradient direction (unit vector), b is the applied diffusion weighting, $d(\mathbf{g}) \in \mathcal{H}_3^2$ is the diffusion tensor in a polynomial form, $w(\mathbf{g}) \in \mathcal{H}_3^4$ is the kurtosis tensor in a polynomial form, and $\bar{d} = \int_{S_2} d(\mathbf{g}) d\mathbf{g} / 4\pi$ is the mean diffusivity. We should note here that Eq. 3 is identical to the standard diffusion kurtosis (DKI) model introduced by J.H. Jensen et al. in [3], since there is equivalence between the commonly used tensor forms and the homogeneous polynomials employed here.

For a fixed b value the model in Eq. 3 can be simplified by using the property in Sec. 2 as follows:

$$S(b, \mathbf{g}) = S_0 e^{-bt(\mathbf{g})} \quad (4)$$

where $t(\mathbf{g}) \in \mathcal{H}_3^4$ such that $t(\mathbf{g}) = d(\mathbf{g}) - \frac{\bar{d}^2 b}{6} w(\mathbf{g}) \forall \mathbf{g} \in S_2$. The model in Eq. 4 is known as the generalized tensor imaging (GTI) model [2]. One of the advantages of the degree-4 homogeneous polynomial parameterization of the diffusivity in Eq. 4 is that it has been well studied and there have been proposed several techniques for imposing positivity constraint to the polynomial estimated from DW-MRI data [8, 9].

In the case of single shell acquisitions Eq. 3 and Eq. 4 are identical (for the single given b), since the degree-2 polynomial $d(\mathbf{g})$ in Eq. 3 can be written as a ternary quartic (degree-4 homogeneous polynomial) due to the property discussed in Sec. 2. Based on the above, it can be easily shown that the parametrization in the DKI model (Eq. 3) is redundant for single shell acquisitions and the GTI model (Eq. 4) should be used instead. Hence, the unknown parameters in the DKI model can be estimated from DW-MRI with at least 2 shells.

In the next section we present a novel method for robust DKI estimation using constrained homogeneous polynomials.

4. ROBUST ESTIMATION OF KURTOSIS

In order to estimate accurately the parameters of the diffusion kurtosis model (Eq. 3) from a DW-MR dataset, we need to impose certain constraints to the estimated coefficients. In our discussion we will assume that the given dataset consists of the DW-MRI signal attenuation $S(b_i, \mathbf{g}_{i,j})/S_0$ acquired using N shells that correspond to diffusion weightings b_1, \dots, b_N and different sets of sensitizing gradients $\mathbf{g}_{i,1}, \dots, \mathbf{g}_{i,N'_i}$ for each shell ($i \in \{1, \dots, N\}$).

4.1. Positive diffusivity function

In the presence of oriented diffusion the acquired DW-MRI signal response is monotonically decreasing with b . This leads to positive diffusivity functions in the exponent of the Stejskal-Tanner model, i.e. $t(\mathbf{g}) > 0$ in Eq. 4. Therefore, the need for positivity constraints is essential since negative diffusivity values are unnatural and it has been shown that positive-definite diffusion models are robust and reduce significantly the fitting errors [9].

We will impose this constraint using degree-4 homogeneous polynomials $t(\mathbf{g}) = v_4(\mathbf{g})^T \mathbf{t}$ in Eq. 4 and employing the unified framework presented in [9] which imposes positivity to any even degree polynomial. The method will be applied separately to the signal from each shell and will produce N positive polynomials $t_1(\mathbf{g}), \dots, t_N(\mathbf{g})$ associated with b_1, \dots, b_N . The coefficients of the i^{th} polynomial can be computed as $\mathbf{t}_i = \mathbf{C}_4 \mathbf{x}_i$, where \mathbf{C}_4 is a fixed $15 \times M$ basis with the coefficients of M degree-4 tensors that span the boundary of the PSD space [9], and \mathbf{x}_i is a M -dimensional vector with non-negative entries, which is computed as the non-negative least squares solution [10] to the following linear system:

$$\begin{pmatrix} v_4(\mathbf{g}_{i,1})^T \\ \vdots \\ v_4(\mathbf{g}_{i,N'_i})^T \end{pmatrix} \mathbf{C}_4 \mathbf{x}_i = \begin{pmatrix} -\log(S(b_i, \mathbf{g}_{i,1})/S_0) \\ \vdots \\ -\log(S(b_i, \mathbf{g}_{i,N'_i})/S_0) \end{pmatrix}. \quad (5)$$

After computing the polynomial coefficient vectors \mathbf{t}_i , we can estimate the coefficients vectors \mathbf{d} and \mathbf{w} of the polynomials $d(\mathbf{g})$ and $w(\mathbf{g})$ in Eq. 3 by solving the $15N \times 21$ linear system:

$$\begin{pmatrix} b_1 \mathbf{A} & -b_1^2/6\mathbf{I}_{15} \\ \dots & \dots \\ b_N \mathbf{A} & -b_N^2/6\mathbf{I}_{15} \end{pmatrix} \begin{pmatrix} \mathbf{d} \\ \mathbf{w} \end{pmatrix} = \begin{pmatrix} \mathbf{t}_1 \\ \dots \\ \mathbf{t}_N \end{pmatrix} \quad (6)$$

where \mathbf{A} is a fixed 15×6 matrix that converts the coefficients of a degree-2 polynomial to the coefficients of the equivalent degree-4 polynomial (equivalence in S_2 domain as discussed in Sec. 2), and \mathbf{I}_{15} is the 15-dimensional identity matrix.

The system can be solved by computing the pseudo-inverse matrix. Then the diffusion and kurtosis components are given by $d(\mathbf{g}) = v_2(\mathbf{g})^T \mathbf{d}$ and $w(\mathbf{g}) = v_4(\mathbf{g})^T \mathbf{w}/d^2$. Note that the estimated DKI parameters satisfy the positivity constraint of the diffusivity function.

4.2. Positive apparent diffusion

In addition to the constrained optimization in Sec. 4.1 we can also enforce the estimated diffusion tensor or its corresponding polynomial $d(\mathbf{g})$ to be positive as well. This can be achieved by modifying the system in Eq. 6 as follows:

$$\begin{pmatrix} b_1 \mathbf{A} \mathbf{C}_2 & -b_1^2/6\mathbf{I}_{15} \\ \dots & \dots \\ b_N \mathbf{A} \mathbf{C}_2 & -b_N^2/6\mathbf{I}_{15} \end{pmatrix} \begin{pmatrix} \mathbf{x} \\ \mathbf{w} \end{pmatrix} = \begin{pmatrix} \mathbf{t}_1 \\ \dots \\ \mathbf{t}_N \end{pmatrix} \quad (7)$$

where \mathbf{C}_2 is a fixed predefined matrix of size $6 \times M$ that contains M bases of degree-2 [9], and \mathbf{x} is an unknown M -dimensional vector with non-negative entries. The solution can be computed by initializing \mathbf{x} and \mathbf{w} to be zero vectors and then by iteratively solving for \mathbf{x} and \mathbf{w} using non-negative least squares [10] and pseudo-inverse respectively as follows:

$$\begin{pmatrix} b_1 \mathbf{A} \mathbf{C}_2 \\ b_N \mathbf{A} \mathbf{C}_2 \end{pmatrix} \mathbf{x} = \begin{pmatrix} \mathbf{t}_1 + b_1^2 \mathbf{w}/6 \\ \dots \\ \mathbf{t}_N + b_N^2 \mathbf{w}/6 \end{pmatrix} \quad (8)$$

$$\begin{pmatrix} -b_1^2/6\mathbf{I}_{15} \dots \\ -b_N^2/6\mathbf{I}_{15} \end{pmatrix} \mathbf{w} = \begin{pmatrix} \mathbf{t}_1 - b_1 \mathbf{A} \mathbf{C}_2 \mathbf{x} \\ \dots \\ \mathbf{t}_N - b_N \mathbf{A} \mathbf{C}_2 \mathbf{x} \end{pmatrix}.$$

After that, the positive-definite diffusion tensor coefficients are given by $\mathbf{d} = \mathbf{C}_2 \mathbf{x}$. This process guarantees that both diffusion tensor and diffusivity function are positive.

4.3. Constrained apparent kurtosis

Finally, we can also restrict the apparent kurtosis to be larger than $-3/7$, which is the kurtosis limit for regions that consist of water confined to spherical pores [3]. This can be done by simply modifying the first system in Eq. 8 as follows:

$$\begin{pmatrix} b_1 \mathbf{A} \mathbf{C}_2 \\ \dots \\ b_N \mathbf{A} \mathbf{C}_2 \end{pmatrix} \mathbf{x}' = \begin{pmatrix} \mathbf{t}_1 + b_1^2 \mathbf{w}/6 - b_1 \alpha \mathbf{s} \\ \dots \\ \mathbf{t}_N + b_N^2 \mathbf{w}/6 - b_N \alpha \mathbf{s} \end{pmatrix} \quad (9)$$

where $\alpha = \sqrt{\max\{0, \max_{\mathbf{g} \in S_2} -7/3 v_4(\mathbf{g})^T \mathbf{w}\}}$, \mathbf{s} is the 15-dimensional coefficient vector of the degree-4 polynomial representing the unit isotropy, and \mathbf{x}' is a M -dimensional non-negative vector which is related to \mathbf{x} by: $\mathbf{x} = \mathbf{x}' + 3\alpha/M \begin{pmatrix} 1 \\ \dots \\ 1 \end{pmatrix}$. The obtained solution satisfies all three constraints covered in Sections 4.1, 4.2 and 4.3.

Table 1. Definitions of various matrices used in our method

Matrix	Size	Contents
$v_2(\mathbf{g})$	6×1	$(g_3^2 \ g_2 g_3 \ g_2^2 \ g_1 g_3 \ g_1 g_2 \ g_1^2)^T$
$v_4(\mathbf{g})$	15×1	$(g_3^4 \ g_2 g_3^3 \ g_2^2 g_3^2 \ \dots \ g_1^3 g_2 \ g_1^4)^T$ (see Sec. 2)
\mathbf{A}	15×6	$\begin{pmatrix} 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 1 \end{pmatrix}^T$
\mathbf{s}	15×1	$(1 \ 0 \ 2 \ 0 \ 1 \ 0 \ 0 \ 0 \ 0 \ 2 \ 0 \ 2 \ 0 \ 0 \ 0 \ 1)^T$
\mathbf{C}_2	$6 \times M$	fixed set of positive-definite basis [9]
\mathbf{C}_4	$15 \times M$	fixed set of positive-definite basis [9]

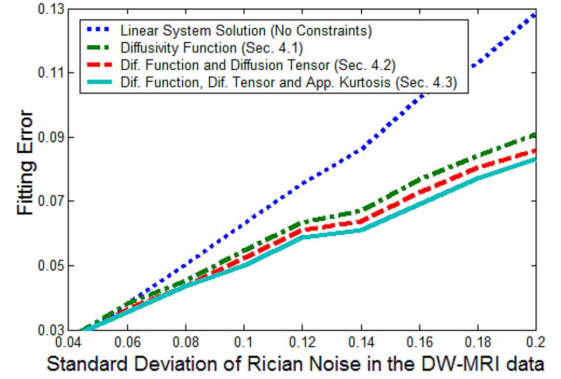


Fig. 1. Comparison of various methods for DKI estimation from a synthetic DW-MRI dataset with various noise levels.

5. EXPERIMENTAL RESULTS

In this section we demonstrate the proposed method using synthetic and real DW-MRI data from a human brain.

Diffusion weighted images from the brain of a healthy volunteer were acquired on a 3T Siemens Tim Trio scanner at the University of Maryland MR Research Center. The protocol used a diffusion weighted single-shot echo planar imaging sequence with 64 directions. 2 b-values were collected ($b = 500$ and 1500 s/mm^2) for each direction together with S_0 .

In order to test the robustness of the proposed DKI estimation method we selected a region of 100 voxels with high signal to noise ratio and then we constructed a synthetic noisy dataset by adding to the corresponding DW-MRI signal attenuation (S/S_0) different levels of Rician noise with standard deviation in the range 0.04-0.2. Then we fit the DKI model (Eq. 3) to the synthetic dataset using 4 different methods: a) linear fitting without constraints, b) imposing positivity to the diffusivity function (Sec. 4.1), c) imposing positivity to both diffusivity function and diffusion tensor (Sec. 4.2), d) imposing positivity similarly to c and also constraining the apparent kurtosis (Sec. 4.3). We compared the obtained estimates with the original dataset without noise (considered here as ground truth) using the following error metric $\sum_{b, \mathbf{g}} (S_{fitted} - S_{truth})^2$. Figure 1 shows a comparison

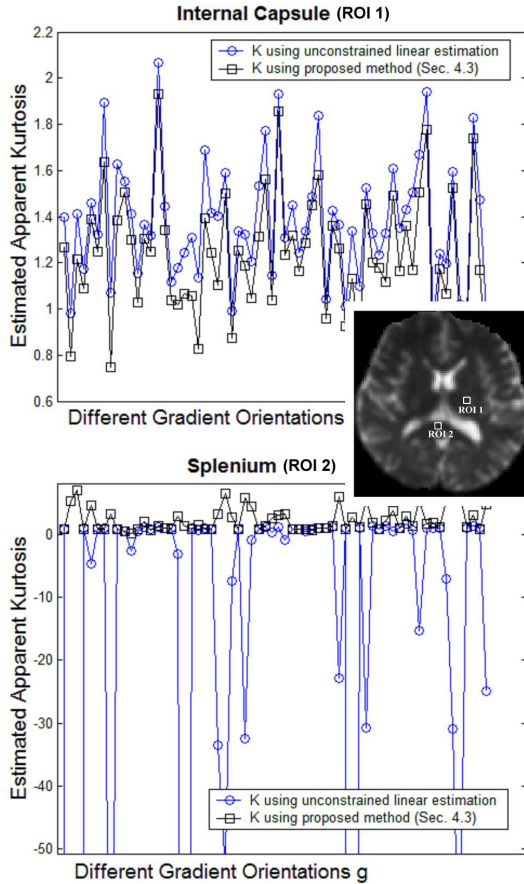


Fig. 2. Comparison of the apparent kurtosis estimated in two ROIs (Splenum and Internal Capsule, shown in the S_0 image) by a) an unconstrained linear solver, and b) the proposed method (Sec. 4.3) which yielded more natural (biologically-feasible) values, with $K > -3/7$.

of the observed fitting errors. Our methods produced a significantly smaller error than the unconstrained method which demonstrates the robustness of the proposed algorithms and also indicates the need for constrained optimization when estimating the DKI parameters. Among all methods, the one discussed in Sec. 4.3 yielded the smallest errors as expected.

Furthermore, we applied the aforementioned methods to a real human brain dataset. After estimating the DKI parameters, we computed the apparent kurtosis, given by

$$K(\mathbf{g}) = v_4(\mathbf{g})^T \mathbf{w} / (v_2(\mathbf{g})^T \mathbf{d})^2. \quad (10)$$

Figure 2 shows a comparison of the estimated apparent kurtosis in two regions of interest (ROIs): 1) Internal Capsule (FA $\sim 0.6 - 0.7$), and 2) Splenum (FA $\sim 0.8 - 0.9$). Although in the first case the kurtosis estimated by both methods has similar values, in the case of splenum the unconstrained method yielded unnaturally small values (< -2000) in contrast to the results obtained by our method. This is because the highly compact axons in the region of splenum made the

unconstrained method to estimate unnatural negative diffusivity values due to the high anisotropy in the ROI. On the other hand, the proposed method produced more natural kurtosis values which demonstrated the efficiency of our technique.

6. CONCLUSIONS

In this paper we presented a novel method for robust estimation of the diffusion kurtosis parameters. The proposed method guarantees the positive-definite property to the estimated diffusivity function as well as diffusion tensor and also constrains the estimated apparent kurtosis. Another advantage of the proposed method is its rigorous formulation as a set of linear systems that can be solved efficiently by using non-negative least squares or pseudo-inverse calculation. Finally, the robustness and efficiency of our method was demonstrated using synthetic as well as real DW-MRI datasets.

7. REFERENCES

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