# Constrained maximum likelihood estimator for more accurate diffusion kurtosis tensor estimates

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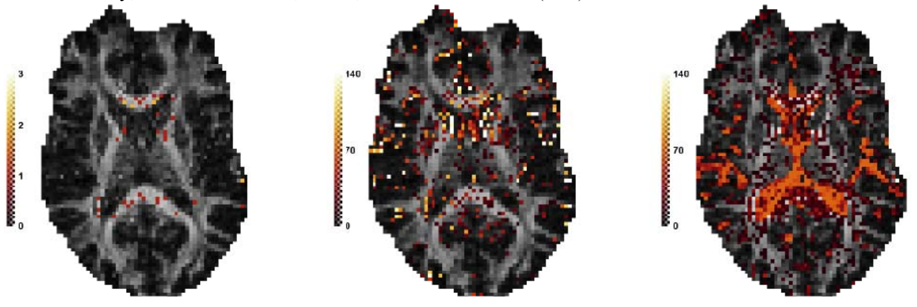
**Introduction/Purpose:** Diffusion kurtosis imaging (DKI), a higher order diffusion model, was introduced as an extension of the diffusion tensor imaging (DTI)[1,2]. In DKI, the Gaussian and non-Gaussian diffusion are quantified by the apparent diffusion coefficient (Dapp) and the apparent excess kurtosis (Kapp), respectively, on a direction-dependent basis. From the diffusion weighted data 4th order 3D, fully symmetric tensor - the diffusion kurtosis tensor (DKT) - can be estimated in addition to the diffusion tensor (DT). From both diffusional tensors, one can derive several scalar measures such as fractional anisotropy (FA), radial-, axial-, and mean diffusivity, as well as radial-, axial-, and mean kurtosis (MK). As diffusion of water molecules is a physical property of the tissue being measured, the tensors estimates and the derived parameters must be physically and biologically meaningful. Therefore, the following constraints should be satisfied when estimating either of the tensors:

$$\begin{cases} \#1 \text{ positive definite DT}, \\ \#2\ K_{app}(\mathbf{n}) > 0, \\ \#3\ K_{app}(\mathbf{n}) < \frac{3}{b\mathrm{D}_{\mathrm{app}}(\mathbf{n})} \end{cases}$$

with **n** each arbitrary direction. The lower bound on $K_{app}(\mathbf{n})$ as defined in #2 is in agreement with the compartment tissue model of diffusion, which predicts positive kurtosis. The upper bound on $K_{app}(\mathbf{n})$ (#3) should not be exceeded to guarantee the DKI model function to decrease with the b-value in the range of acquired b-values. Unfortunately, tensors estimated with least squares estimators tend to systematically deviate from their true underlying values. In many cases, up to 70% of all human brain voxels, they even converge to physically irrelevant tensor values (see Fig. 1) due to noise and imaging artifacts. In this work, we present a framework to obtain accurate and robust estimates of the tensors using the DKI model, while enforcing the constraints. Both tensors are estimated by maximizing the joint likelihood function of all Rician distributed observations given the DKI model. A Rician noise model was required to avoid significant overestimation of the kurtosis values[2].




(a) constraint #1 (b) constraint #2 (c) constraint #3

**Fig. 1 Spatial distribution of constraint violations of diffusional tensors estimated with an unconstrained ML estimator. The number of constraint violations are shown as color encoded maps, overlaying an FA map. In (a), the color intensity relates to the number negative DT-eigenvalues with a maximum of 3. In (b,c), the color intensity relates to the number of gradient directions for which, respectively, constraint #2 or #3 was not satisfied. The intensity is within the range [0 140] as the constraints were evaluated in all 140 gradient directions used to acquire the DW data.**

**Methods**: Diffusion weighted (DW) data, 2.2 mm nominal isotropic resolution, of a healthy male volunteer were acquired on a 3T Scanner with a single-channel head coil. Diffusion weighting was applied according to an optimized DW gradient encoding scheme[3] that consists out of 25, 40 and 75 DW gradients, isotropically distributed over 3 shells with $b$ = 500, 1000, 2800 s/mm$^2$, respectively. In addition, 10 non-DW images ($b_0$) were acquired. As the magnitude DW data are Rice distributed, the actual probability distribution function of the magnitude of the observed DW signal is given by:

$$p(y_n|S_{dki}(b_n,\boldsymbol{g}_n;\theta),\sigma) = \frac{y_n}{\sigma^2} e^{\left(-\frac{y_n^2+(S_{dki}(b_n,\boldsymbol{g}_n;\theta))^2}{2\sigma^2}\right)} I_0\left(\frac{y_n S_{dki}(b_n,\boldsymbol{g}_n;\theta)}{\sigma^2}\right).$$

Note that $y_n$ is the $n^{th}$out of $N$ observation after applying diffusion weighting with strength $b_n$ and gradient direction $\boldsymbol{g}_n$.The underlying magnitude signal, $S_{dki}(b_n,\boldsymbol{g}_n;\theta),\sigma)$, is calculated by the DKI model[1]. The noise level σ was estimated from the histogram mode of the image background. Furthermore, $I_0$ is the order zero modified Bessel function of the first kind. The parameter vector **θ**, which consist of $b_0$, 6 independent DT and 15 independent DKT elements, was estimated from the independent DWIs with ML estimator in each voxel by substituting the observed values for the stochastic variables and maximizing over the parameters:

$$\widehat{\boldsymbol{\theta}}_{ML} = \arg\max_{\boldsymbol{\theta}} \sum_{i=1}^{N} \ln p(y_n|S_{dki}(b_n,\boldsymbol{g}_n;\theta),\sigma).$$

This equation was solved by a numeric optimization using the Nelder-Mead simplex algorithm. Constraint #1 is imposed by representing the DT by its Cholesky decomposition, while #2 an #3 were imposed as a set of linear and non-linear constraints.

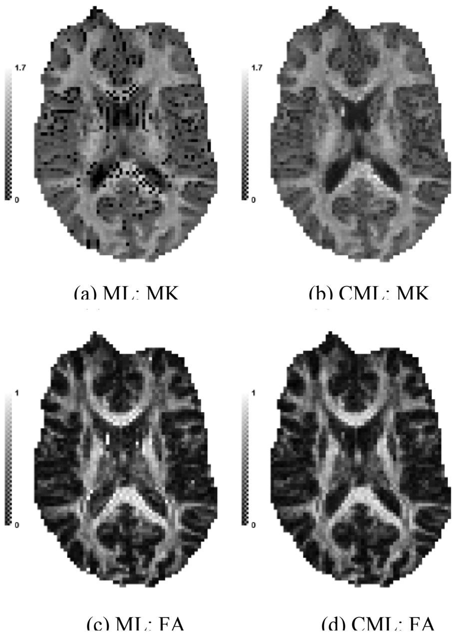



**Fig. 2 The MK (a, b) and FA (c, d) maps of the same axial slice, computed with unconstrained (a,c) as well as the constrained (b,d) ML estimators. The MK maps were scaled between 0 and 1.7, the FA maps between 0 and 1.**

**Results and Discussion:** In Fig. 2, MK and FA maps of the same axial slice, computed with unconstrained as well as the constrained ML estimators, are shown. Using the unconstrained estimator, constraint violations of #1 and #2 are noticeable by the black voxels in the MK map (Fig. 2a) and the hyper intense FA values (Fig. 2c), respectively. . Fig 2b and Fig 2d show that including the constraints substantially reduces these artifacts. A more elaborate overview of the constraint violations is given in Fig. 1. By comparing our method to more commonly used (constrained) weighted least squared estimators[4], it was shown that not accounting for the proper noise statistics in MR images yields significantly increased kurtosis values (results not shown).

**Conclusion:** We showed that unconstrained estimators fail to provide physically and biologically meaningful estimates of either of the diffusional tensors in approximately 70% of all WM voxels. Therefore, we proposed to simultaneously estimate all unknown model parameters with a constrained ML estimator, which includes the Rician noise model.

**References:** [1] Jensen JH et.al. (2005) MRM 53(6):1432-1440, [2] Veraart et al. (2010) MRM in press [3] Poot et al. (2010) IEEE TMI 29(3): 819-829, [4] Tabesh et al. (2010)MRM in press