

Improved detection of non-Gaussian diffusion with nonlinear fitting at high b-values

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INTRODUCTION: Diffusion Tensor Imaging (DTI) is a technique for studying the bulk diffusion properties of water molecules in tissue. Diffusion information can be used to infer the organizational structure of white matter pathways in the brain. It is well known that the tensor model is limited to describing a single population of fibers running in parallel. While this is generally sufficient for the majority of voxels in white matter, more complex architectures including crossing, bending, and diverging fibers, are known to exist. Applying the tensor model in these situations can lead to misinterpretations of DTI results.

The inadequacy of the diffusion tensor model has motivated the development of higher-order modeling techniques including q-space, q-ball, and PAS-MRI [1]. These advanced reconstruction schemes require the acquisition of more data, usually in the form of additional sampling directions. Although increased data allows the fitting of more complex models, the question remains as to whether or not these higher-ordered models are always necessary. In voxels for which the underlying architecture is adequately described by a tensor, the use of higher-order models can actually introduce additional error due to over-fitting.

Alexander et al. proposed a model-selection algorithm for classifying voxels into categories of isotropic Gaussian, non-isotropic Gaussian (equivalent to the diffusion tensor) and non-Gaussian diffusion [2]. This technique involves the fitting of a hierarchical set of models based on the spherical harmonic (SH) series, and selecting the most appropriate model using an f-test. It performs reasonably well for fibers crossing at 90 degrees and in equal volume fractions, but suffers as the separation angle is reduced and/or the volume fractions become more imbalanced. Because non-Gaussian diffusion is more apparent at high b-values [3], it may be possible to improve classifier performance by imaging at b-values greater than 1000 s/mm². However, the linear-least squares algorithm commonly used to fit SH models performs poorly if the b-value is increased too much. In addition, high b-values combined with high diffusivity can result in signal measurements close to the noise floor. In this situation, magnitude bias can result in a “squashed peanut” artifact [4], which itself resembles non-Gaussian diffusion.

In this study we develop a nonlinear fitting routine which compensates for the magnitude bias in regions of low SNR. This method is suitable for fitting SH models at high b-values. This should result in an improved ability to detect voxels for which the diffusion tensor model is insufficient.

THEORY: It is possible to fit the SH models nonlinearly using a procedure similar to Ref. 2, but it requires the use of a constrained algorithm to ensure that the fitted signal has no imaginary component. Alternatively, we can fit the even-ordered set of Generalized Diffusion Tensor (GDT) models without the need for constraints. These two families of models, GDT and SH, are theoretically equivalent, and we can easily convert between the two [5]. The lack of constraints makes fitting GDTs conceptually easier and reduces computational demands. We follow the notation of Ref. 6, replacing the log-transformed signal column vector \mathbf{Y}_r , with the pre-transformed magnitude signal, $\mathbf{Y}_r = [S_1/S_0 \ S_2/S_0 \ \dots \ S_m/S_0]^T$. The magnitude of the diffusion equation can be written in matrix form as $\mathbf{Y}_r = \exp(\mathbf{B}_r \mathbf{X}_r)$. We can then use a nonlinear fitting algorithm to minimize the following equation:

$$\sum_{k=1}^m \left(S_k - \sqrt{S_0^2 \exp(-b_{i_1 i_2}^{(2)} D_{i_1 i_2}^{(2)} + b_{i_1 i_2 i_3 i_4}^{(4)} b_{i_1 i_2 i_3 i_4}^{(4)})^2 + \sigma^2} \right)^2 \quad (1)$$

Note the noise-estimation parameter, σ , which is measured from a background region of the images [7]. When $\sigma=0$, equation 1 reduces to a standard nonlinear fit. The σ parameter compensates for the magnitude bias in regions of low SNR. This is similar to a scheme originally proposed by Jones et al. [4] and modified by Fobel et al. [7].

METHODS: DTI data was obtained from a healthy volunteer using a 3T GE system. Imaging parameters were as follows: 55 gradient orientations, 10 b₀ images, 2.6 mm isotropic voxels, and 42 slices. 3 data sets were collected sequentially, with b-values of 1000, 2000 and 3000 s/mm². TE was minimized for each b-value resulting in values of 85, 97 and 105 ms respectively. A brain mask was created by thresholding the b=1000 s/mm² data as in Ref 2. The mean SNR across the entire brain mask for the b₀ images was 29, 25, and 24; the reductions resulting from T₂ relaxation effects. We fit GDT models of orders 0, 2, and 4 using both linear-least squares and the newly introduced magnitude-corrected nonlinear fit. F-test classification thresholds were set so that 99% of diffusion tensors with FA<0.9 were correctly classified by Monte Carlo simulations. Simulations were performed using MATLAB (Mathworks, Natick, MA) and the dwi-toolbox [8] for a two tensor model with various volume fractions and separation angles. The SNR, b-value and gradient orientations were matched to the clinical experiment. Simulations were repeated 10 000 times for each separation angle/volume fraction pair.

RESULTS&DISCUSSION: Figures a-c clearly demonstrate a significant increase in the number of voxels classified as non-Gaussian at b-values greater than 1000 s/mm² using the magnitude-corrected fit. Across the entire brain, the proportion of 4th order voxels was 1.9%, 3.9%, and 3.2%, for b=1000, 2000 and 3000 s/mm² respectively. The magnitude-corrected fit outperformed the linear fit in all cases. The simulation results in Figures d and e show a remarkable improvement in the ability to detect non-Gaussian voxels, especially for reduced separation angles and imbalanced volume fractions. At b=3000 s/mm², the advantages of the higher b-value seem to be partially reduced by a loss in SNR caused by the longer TE. TE is limited primarily by the maximal gradient strength, so improved imaging hardware may alleviate this effect somewhat. Simulations show that averaging multiple NEX improves classifier performance even further, but time constraints may force a tradeoff between the number of directions and the number of NEX. This will be an area of future study. Additionally, although this data implies that the “optimal” b-value, under this set of experimental conditions, is somewhere in the range of 1000-3000 s/mm², the precise value is unknown.

CONCLUSIONS: Magnitude-corrected nonlinear fitting allows for improved estimation of the SH and GDT models at high b-values. This technique significantly improves the ability to detect regions of complex fiber architecture for which the diffusion tensor is insufficient. This information is critical for correctly interpreting DTI results, and in providing justification for the use of higher-order models on a voxel-by-voxel basis. This fitting technique should also be useful in other areas of the diffusion community that utilize the SH and/or GDT basis functions, e.g. spherical deconvolution and q-ball imaging.

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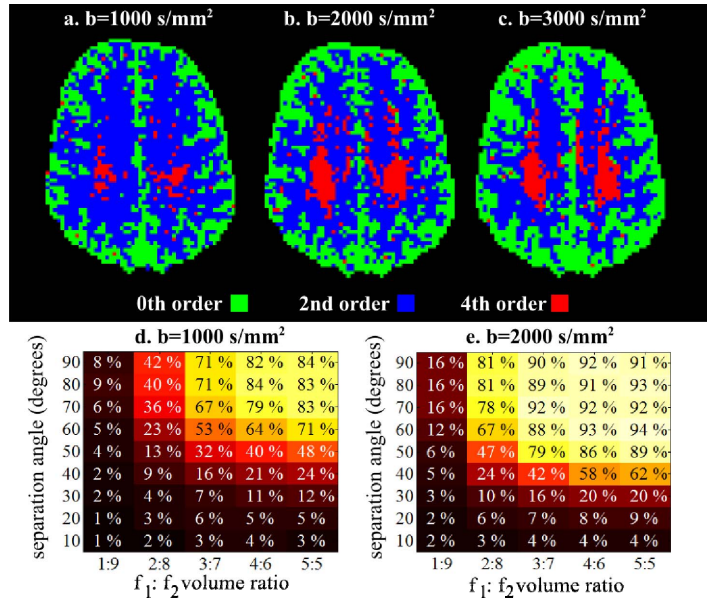


Figure a-c. Classification maps calculated using the magnitude-corrected nonlinear fit for different b-values. **d-e.** Percentage of simulated crossing fibers classified as 4th order for b=1000 and 2000 s/mm².