

# IMPROVED DETECTION OF NON-GAUSSIAN DIFFUSION WITH NONLINEAR FITTING



R. Fobel and G. J. Stanisiz  
 Medical Biophysics, University of Toronto, ON, Canada  
 & Sunnybrook HSC, Toronto, ON, Canada



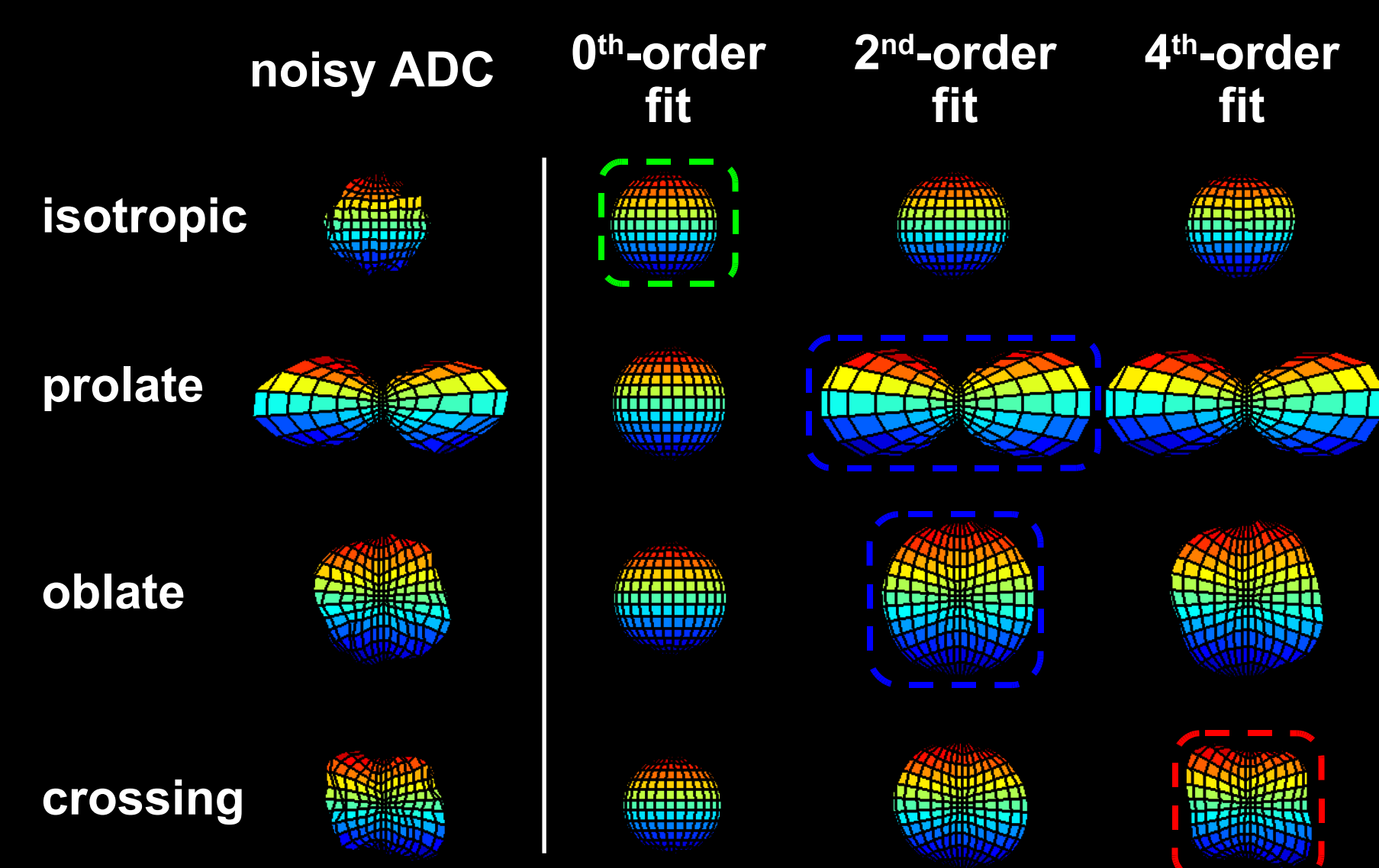
## Introduction

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 (Fig. 1). It performs reasonably well for fibres 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/mm<sup>2</sup>. 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.

Figure 1. Schematic of classification algorithm.



## Theory

It is possible to fit 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. The GDT and SH models are theoretically equivalent and we can easily convert between the two [5]. We follow the notation of Ref. 6, replacing the log-transformed signal column vector  $Y_r$  with the pre-transformed magnitude signal,  $Y_r = [S_r/S_0, S_r/S_0, \dots, S_m/S_0]^T$ . The magnitude of the diffusion equation can be written in matrix form as  $Y_r = \exp(B_r X_r)$ . We can then use a nonlinear fitting algorithm to minimize:

$$\sum_{k=1}^m \left( S_k - \sqrt{S_0^2 \exp^2 \left( -b \frac{D^{(n)}}{l_{12}^2 l_{32}^2 \dots l_{1n}^2} \right) + \sigma^2} \right)^2 \quad (1)$$

Note the noise-estimation parameter,  $\sigma$ , which is measured from a background region of the images [7]. When  $\sigma=0$ , eq. 1 reduces to a standard nonlinear fit. The  $\sigma$  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 2 healthy volunteers using a 3T GE system with an 8-channel head coil. Imaging parameters were as follows: 55 gradient orientations, 10 b<sub>0</sub> images, 2.6 mm isotropic voxels, and 42 slices. 3 data sets were collected sequentially from each subject, with b-values of 1000, 2000 and 3000 s/mm<sup>2</sup>. TE was minimized at each b-value, resulting in values of 85, 97 and 105 ms respectively. A brain mask was created by thresholding the b=1000 s/mm<sup>2</sup> data as in Ref 2. The mean SNR across the entire brain mask for the b<sub>0</sub> images was 71, 59, and 55; the reductions resulting from T<sub>2</sub> 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 and Discussion

The simulation results in Fig. 2 show an improvement in the ability to detect fibre crossings using magnitude-corrected fitting at high b-values. This is especially true for reduced separation angles and imbalanced volume fractions. The performance of the algorithm drops off dramatically at b=3000 s/mm<sup>2</sup> using the linear least-squares fit.

In experiments, the proportion of voxels classified as 4<sup>th</sup>-order across the entire brain was 4.4%, 10.8%, and 11.3%, for b=1000, 2000 and 3000 s/mm<sup>2</sup> respectively. The 3 clusters of 4<sup>th</sup>-order voxels (labeled in Fig. 3) were consistent across both subjects. In general, these became larger as the b-value was increased.

Fig. 4 shows Apparent Diffusion Coefficient profiles for a single voxel sampled from one of these regions of suspected crossings. This example illustrates how the shape becomes increasingly complex as b is increased.

At b=3000 s/mm<sup>2</sup>, 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 classifier performance is highly dependent on SNR and the number of gradient directions (data not shown). Although it can be summarized from these results that the b-value should be greater than 1000 s/mm<sup>2</sup>, a specific "optimal" b-value cannot be determined from this data and is likely to depend on many experimental factors. The simulations are available online [8] and can be modified to suit different experimental scenarios.

Figure 3. Fibre direction and voxel classification maps (using the magnitude-corrected fit).

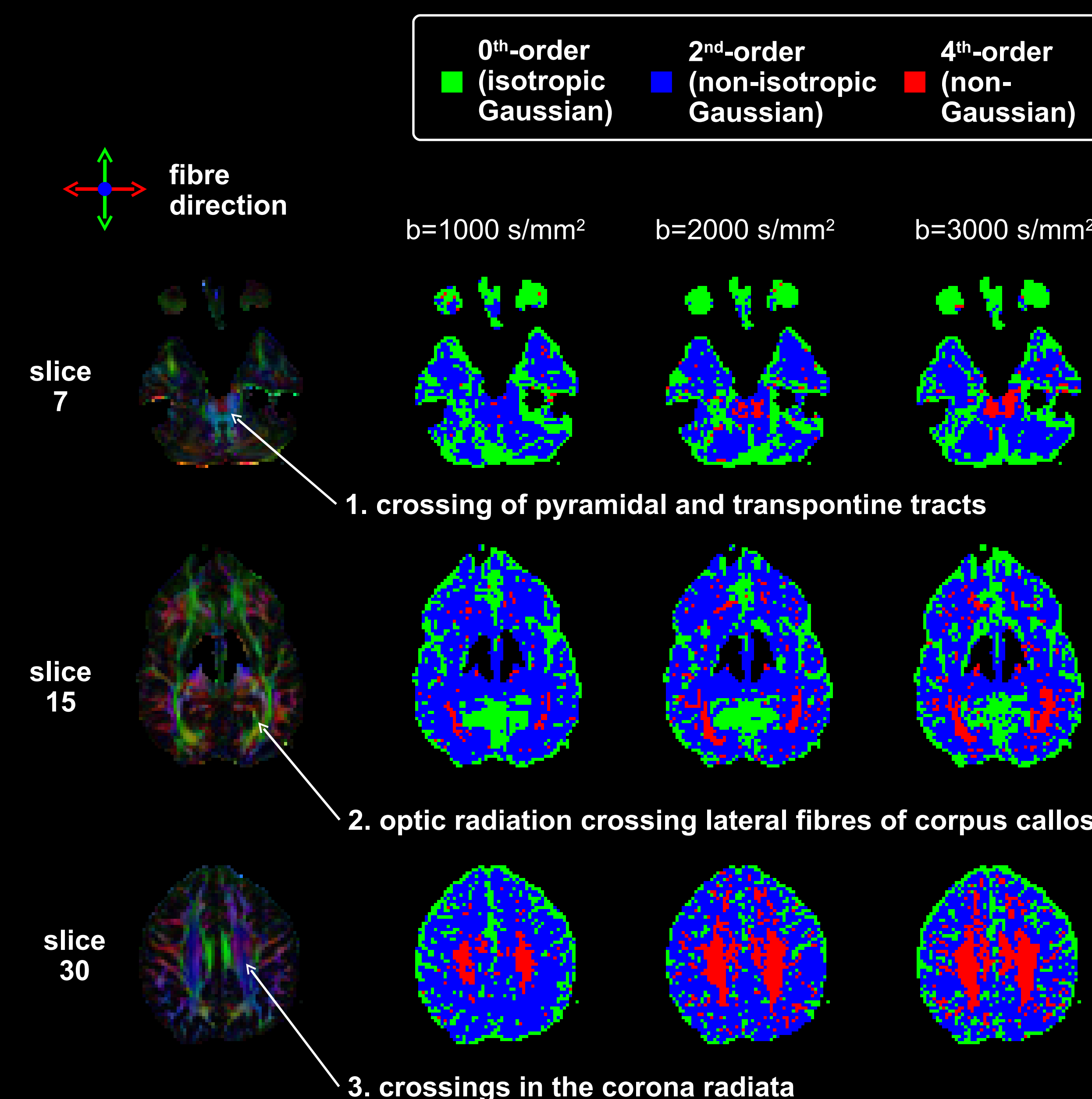


Figure 2. Percentage of crossing fibres classified as 4<sup>th</sup>-order in simulations.

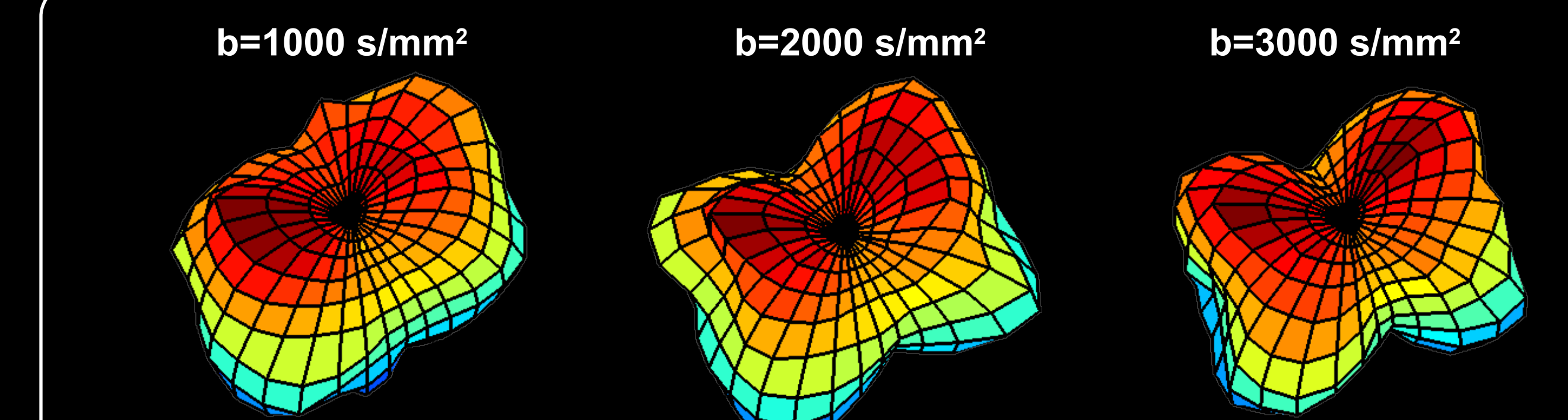
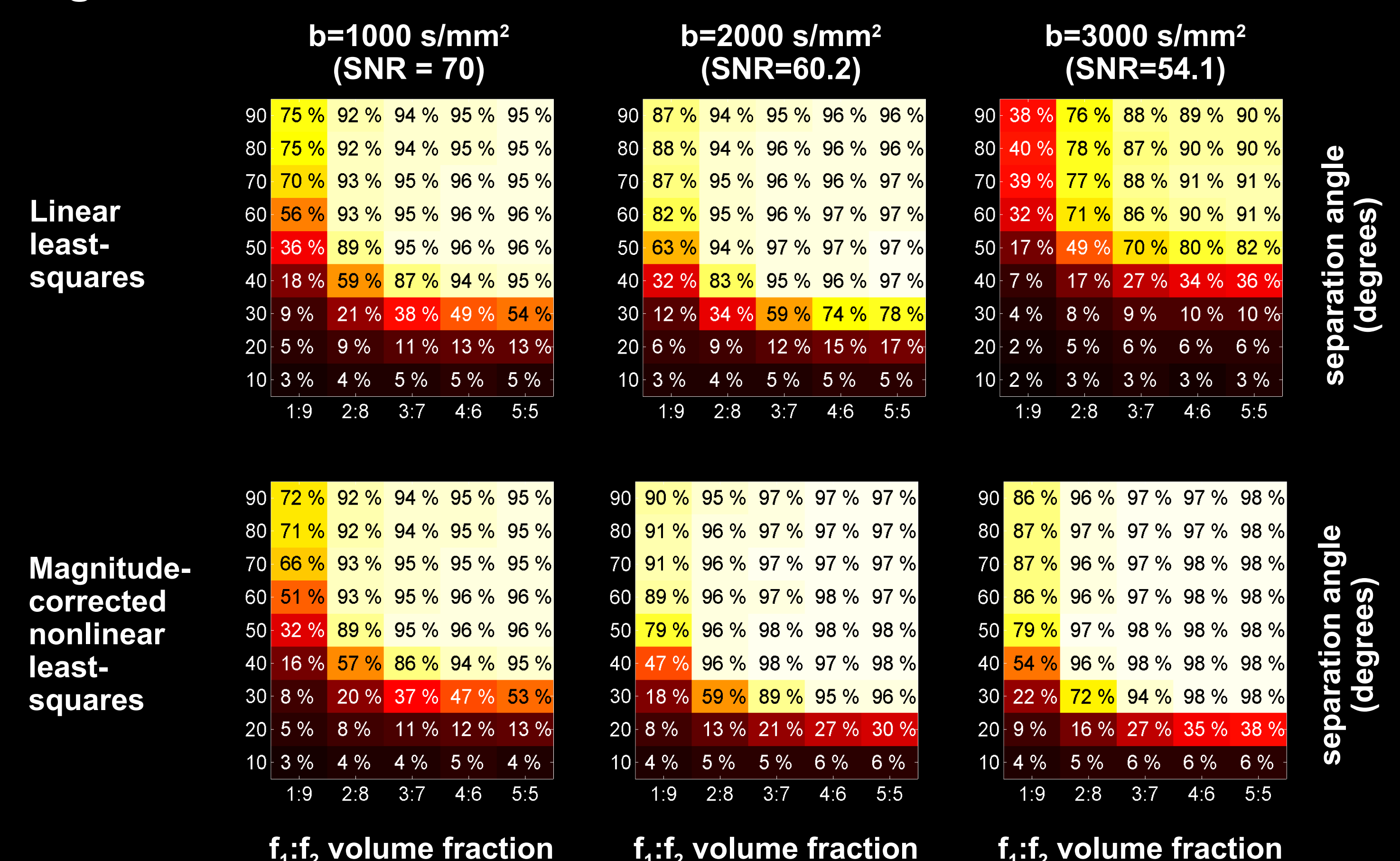


Figure 4. Apparent Diffusion Coefficient profiles for a voxel from cluster 2 in Fig. 3. Note how the shape becomes more complex as the b-value is increased.

## Conclusion

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 fibre 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.

This research was supported by CIHR grant 724180908.

Contact: ryan.fobel@utoronto.ca

References: 1. Alexander. *Ann. NYAS*. 1064:113(2005) 2. Alexander. *MRM*. 48:331(2002) 3. Frank *MRM*. 45:935(2001) 4. Jones. *MRM*. 52:979(2004) 5. Descoteaux. *MRM*. 56:395(2006) 6. Liu. *MRM*. 51:924(2004) 7. Fobel. *Proc. 16<sup>th</sup> ISMRM*. 1593(2007) 8. <http://dwi-toolbox.sourceforge.net>