Exploring analytic models of the diffusion MR signal in fixed rat brain tissue

E. Panagiotaki[1], H. M. Fonteijn[1], S. Nedjati-Gilani[1], M. G. Hall[1], and D. C. Alexander[1]

[1]Centre for Medical Image Computing, Computer Science, University College London, London, United Kingdom

Introduction This work compares three models of diffusion in fixed white matter (WM). The models are the diffusion tensor (DT) [1] which assumes Gaussian diffusion and does not account for restriction, Behrens' model (ball and stick) [2] which is the simplest possible model including restriction and Alexander's [3] simplified version of CHARMED [4] (cylinder model), which incorporates non-zero pore size and anisotropic extracellular diffusion. Our work is similar to that of Stanisz et al [5] who uses a three compartment model to study the spinal cord using diffusion NMR spectroscopy. However, our study is with diffusion MRI on brain tissue. We create a protocol to allow examination of parallel and perpendicular signals in brain white matter, acquire diffusion-weighted data with a wide range of imaging parameters and compare the three models.

Methods The experiment acquires diffusion-weighted MR images of a fixed male rat brain using a small bore 9.4T scanner (Varian) with maximum gradient strength 400mT/m. We use a five direction-encoding scheme: we choose a left-right central direction that Corpus Callosum (CC) fibres are parallel to in places, and four evenly spaced directions perpendicular to the central direction which provide perpendicular signals in voxels with left-right fibres. Figure 1 illustrates the scheme in the brain. We use the pulse-gradient spin-echo (PGSE) sequence for 67 diffusion weightings: five diffusion times Δ = 10, 20, 30, 40, 50ms, gradient durations δ = 3ms for all Δ and δ = 30ms for Δ = 40, 50ms and gradient strength G varied from 40 to 400mT/m in ten steps of 40mT/m (three low G measurements failed). The *b* values range from 2×10^7s/m² to 4.1×10^{11}s/m². We use different echo times (TE) and repetition times (TR) for each combination (the shortest TE and TR allowed) and correct for T2 dependence by acquiring separate *b*=0 images for each parameter combination. We also perform a separate diffusion tensor imaging (DTI) acquisition using a 42-direction scheme with *b* value 4.5768×10^9s/m² and six *b*=0 measurements. The in-plane field of view is 3.5cm. The matrix size is 256x256 and the slice thickness is 0.5mm. In total we acquire 450 images in approximately 48 hours.

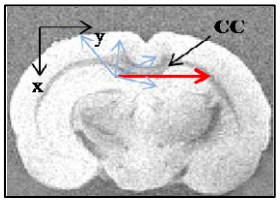

Figure 1. The red arrow indicates the central gradient direction used for the encoding scheme and the blue arrows indicate the four directions perpendicular to the central.

Experiments To study parallel and perpendicular signal attenuation we choose a region of interest (ROI) that has principal fibre direction in alignment with the central direction. We manually segment the CC on a fractional anisotropy (FA) map from the DTI acquisition and threshold for voxels in which the principal direction of the DT is parallel to the central gradient direction, allowing a maximum offset of 5°. We average the data contained within all 14 voxels of the ROI, fit the three models to the data and synthesise diffusion-weighted data from the fitted models. The fitting procedures for the DT and the ball and stick model are in Camino [6] and the cylinder model fitting uses custom Matlab code. The best fit microstructure parameters from the cylinder model after 500 perturbations on the starting parameters are: volume fraction 0.36, intrinsic diffusivity 3.5×10^{-10}m²/s, perpendicular extracellular diffusivity 2.5×10^{-10}m²/s, axon radius 1.2×10^{-6}m. We construct synthetic diffusion-weighted data for each model and add Rician noise over 500 iterations, then take the mean to incorporate Rician noise bias.

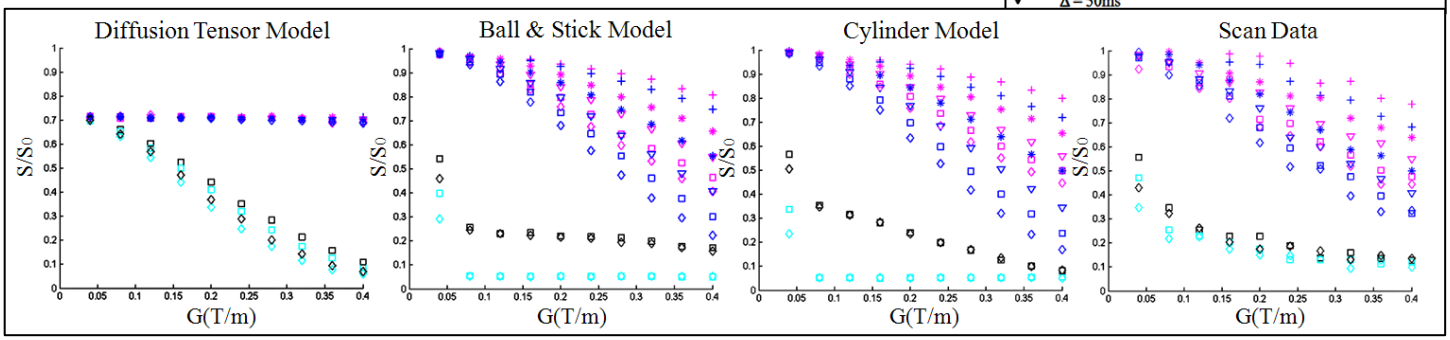

Figure 2. Results of data synthesised from the analytic models and the scan data from the PGSE experiment. The normalised signal S/S0 is plotted at all values of Δ, δ as a function of the gradient strength G for the parallel and the perpendicular directions.

Results We compare data synthesised from the three models by plotting the normalised signal S/S_0 at all values of Δ and δ as a function of the gradient strength G for the parallel and perpendicular directions (Figure 2). In all models we see strong dependence on sample orientation, indicating the anisotropy of the CC. Less diffusion attenuation is observed for lower Δ. These results are in agreement with previous studies of diffusion in white matter [5]. The biggest departures are for large δ in the parallel direction. We hypothesise that these departures come from more than just noise. To confirm the hypothesis Figure 3 compares the normalised signal S/S_0 for the scan data and the cylinder model with δ = 30ms and Δ = 50ms for the parallel direction indicating the range of Rician noise over 500 realisations.

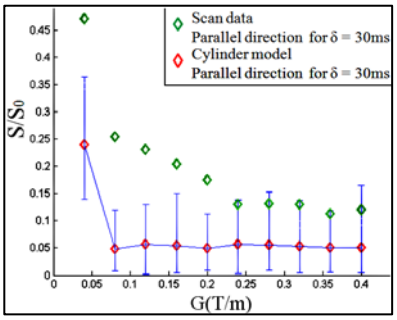

Figure 3 Plot of the normalised signal at δ=30ms against the gradient strength of the scan data and the cylinder model for the parallel direction. The error bars indicate the minimum and maximum Rician noise over 500 iterations.

Discussion and Conclusions The synthesised data from the DT model shows a significant departure from the scan data and confirms expectancies that the model is poor for high *b* value data. The ball and stick model does surprisingly well and approximates the scan data over the whole range of the gradient strength but does not capture the signal for δ = 30ms where departures are clear. There is no clear qualitative improvement of the cylinder model over the ball and stick model. However the mean squared error (MSE) is lower for the cylinder model in both directions: for the ball and stick model MSE is 0.166 parallel and 0.142 perpendicular, while for the cylinder model it is 0.005 and 0.001, which reveals that in fact the cylinder model provides a much better fit. All models assume free diffusion in the parallel direction. The key departure for all models is in the parallel direction at δ=30ms. Figure 3 shows that the most likely reason for this departure comes from restriction in the parallel direction possibly from glial cells or non-parallel fibres. Stanisz et al [5] make a similar observation in the spinal cord and model the effect by introducing spherical glial cells which restrict diffusion in all directions. Our results show that the cylinder model is good for describing the perpendicular direction. For the parallel direction an additional restriction is needed, either using Stanisz's glial cells or a non-trivial model of the fibre orientation distribution.

References and Acknowledgements[1] Basser et al, Biophys J 66:259-267, (1994), [2] Behrens et al, MRM 50:1077-1088, (2003), [3] Alexander et al, MRM 60: 439-448, (2008), [4] Assaf et al, NeuroIm 27: 48-55, (2005), [5] Stanisz et al, MRM 37:103-111, (1997), [6] Cook et al, ISMRM, 14:2759, (2006)

This work is funded by the EPSRC grant EP/E056938/1