IMPROVED PRECISION IN THE CHARMED MODEL OF WHITE MATTER THROUGH SAMPLING SCHEME OPTIMIZATION AND MODEL PARSIMONY TESTING

S. De Santis[1,2], Y. Assaf[3], C. J. Evans[1], and D. K. Jones[1]
[1]CUBRIC, School of psychology, CARDIFF University, United Kingdom, [2]Physics department, Sapienza University, Rome, Italy, [3]Tel Aviv University, Israel

Introduction
The composite hindered and restricted model of diffusion (CHARMED) was proposed a few years ago to characterise anisotropic water diffusion in brain white matter [1]. It contains a hindered extra-axonal compartment, whose properties are characterised by an effective diffusion tensor, and one (or more) intra-axonal compartments, whose properties are characterised by a restricted model of diffusion within cylinders. A CHARMED protocol consists of diffusion weighted (DW) images acquired over a wide range of b-values (up to 10000s/mm^2) across different gradient directions. The model is able to provide various micro-structural parameters, such as the nerve fibre orientation(s), the T_2-weighted extra- and intra-axonal volume fractions, and the principal diffusivities, which can potentially be more specific in characterising white matter structure as compared to conventional diffusion tensor imaging. Nevertheless, this is at the cost of an increased acquisition time which is challenging for clinical applications, and an elaborate post-processing step, which involves the estimation of several parameters whose confidence intervals can be large. In this work, we developed a comprehensive optimisation of both the experimental acquisition scheme and data processing. An optimized gradient sampling scheme is proposed based on the electrostatic repulsion algorithm [2], combined with optimised ordering [3] and extended to different b-value shells. In addition, parsimonious model selection criteria [4], based on Bayesian information, are used to choose among different number of restricted compartments (RC's). Marked improvements in data quality are demonstrated using a bootstrap approach.

Methods
A CHARMED protocol [1] was applied on one healthy young subject at 3T. DW data (TR/TE=12000/122ms,Δ/δ=50/43ms) were obtained at b-values of 937, 1875, 2812, 3750, 4687.5, 5625, 6562.5 and 7500s/mm^2 across 192 directions. A b=0 s/mm^2 image was interleaved every 20 scans. The gradient scheme was divided into 16 subsets of 31 measurements, each sampling all the b-value shells. The electrostatic energy-minimisation between each orientation is weighted according to its temporal order during acquisition within each b-value shell: in this way, should the acquisition be corrupted or terminated before completion because of subject non-compliance, the highest possible data quality obtainable for that number of measurements is reached. DW data were corrected for eddy current/motion and analysed with the CHARMED model proposed in [1], but the number of RC's was chosen between 0, 1, 2 and 3 on the basis of a Bayesian Information Criterion (BIC). 500 datasets were generated with the wild bootstrap method to estimate the confidence intervals on the obtained parameters. To simulate the output of an acquisition terminated prematurely due to subject non-compliance, the same analysis was run on 15 truncated datasets obtained by removing blocks of 10 (or 11 when needed) measurements at a time. As such, after every 3 truncation steps, a whole subset of 31 measurements is eliminated.

Results and Discussion
In Fig.1a left, the number of RC's, as chosen on the basis of BIC, are reported voxel-wise in different colours (superimposed on a b=0 s/mm^2 image). The pattern is entirely consistent with known anatomical features (0 in the CSF, 1 in the Corpus Callosum, 2 or 3 in WM areas characterised by different fibre orientations). Fig.1a also shows the signal intensity for different measurements (ordered from the lower to the higher b-value) for four different voxels, characterized by 0, 1, 2 and 3 RC's respectively. Introducing a BIC means that a higher number of RC's, and thus a higher number of fitting parameters, is invoked only when the fit quality is sufficiently improved. This implies that, for example, one can obtain a better confidence in the estimated fibre orientation, as shown in Fig.1b when fitting parsimoniously to the data. Lower standard deviations are also obtained on estimated scalar parameters (data not shown).
Fig.1c shows the number of transitions from a higher to a lower number of RC's (identified by the BIC) as a result of series truncation. The number of transitions was calculated for each truncated dataset with respect to the complete dataset and normalised to the total number of transitions, for the 4 possible cases Δn=0 (number of RC's does not change), Δn=1 (RC's changing from 3 to 2, or from 2 to 1, or else from 1 to 0), Δn=2 (RC changing from 3 to 1 or from 2 to 0) and Δn=3 (RC changing from 3 to 0). Clearly, as the total number of measurements is reduced, the number of distinguishable compartments also reduces. However, this reduction is markedly less dramatic for data collected with the optimised gradient scheme as compared to that obtained on the same dataset, but whose order is randomly shuffled prior to truncation.

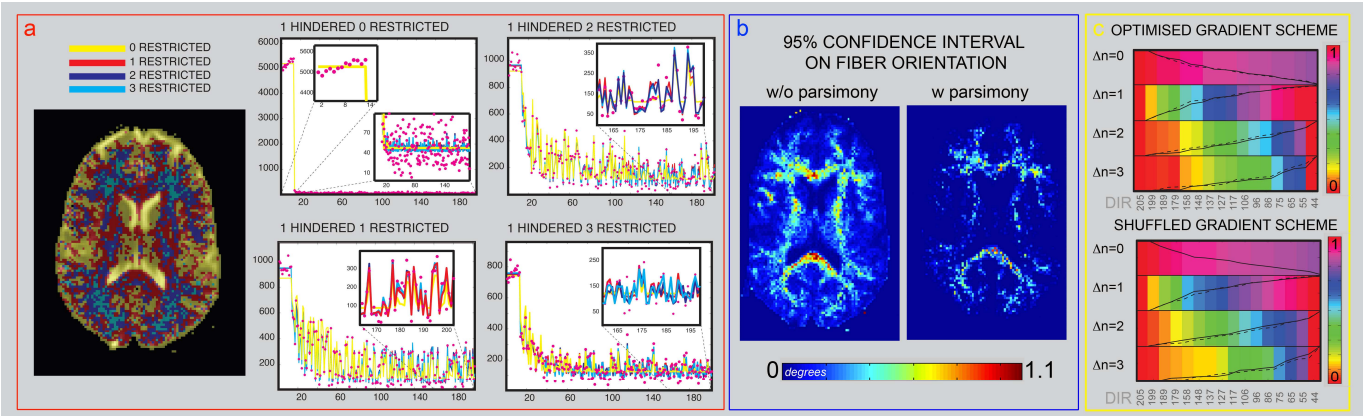

Fig1a. Left: number of RC as identified by BIC superimposed on a b=0 s/mm^2 image. Right: signal intensity (dots) for 4 voxels characterized by 0,1,2 and 3 RC's respectively and Levenberg-Marquardt fit with 0 (yellow), 1 (red), 2 (blue) and 3 (cyan) RC's. **Fig1b.** Map of the confidence in fibre orientation (weighted by the RC fraction) obtained with and without applying model parsimony. The confidence intervals are computed by the percentile method [5]. **Fig1c**. Number of transitions from a higher to a lower number of RC's for the optimised gradient scheme (upper panel) and for a dataset generated shuffling the gradient orientation sequence (lower panel). In each transition map, the same trend is superimposed as a continuous line and compared to that of the other scheme.

Conclusion
We have developed a comprehensive optimised CHARMED pipeline, comprising an optimised data acquisition scheme and an analysis approach that incorporates a model parsimony. This approach clearly improves the data quality and results in better confidence in the estimated parameters.
References: [1] Assaf Y and Basser P NeuroImage 2005;27:48 [2] Jones DK et al. Magn Res Med 1999;42:515 [3] Dubois et al. Magn Reson Mater Phy 2006;19:134; Cook PA et al. J Magn Res Im 2007;25:1051 [4] Freidlin et al. IEEE Trans Med Im 2007;26:1576 [5] Jones DK Magn Res Med 2003;49:7