Data-driven optimisation of multi-shell HARDI

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PURPOSE: A number of recently proposed methods in diffusion MRI analysis require the acquisition of multi-shell high angular resolution diffusion imaging (mHARDI) data, whereby the diffusion signal is measured along uniformly distributed directions over a number of 'shells' with different b-values. Ideally, these acquisitions would be optimised to provide the most eloquent data possible, irrespective of the particular analysis framework. This is particularly important for non-standard applications such as neonatal imaging (the cohort of interest here), where the tissue undergoes rapid changes, and little is known about how this would affect the diffusion weighted (DW) signal. Recently, an approach has been proposed to optimise single-shell acquisition parameters based on the information content of the DW signal[1]. In this study, we use a similar approach to optimise the number of shells and the corresponding number of DW directions for each shell.

METHODS: We assume tissue consists of a number of non-exchanging components, each characterized by its own diffusion 'signature' – the component's DW signal as a function of *b*-value – and orientation dependence (a generalization of the framework used in e.g. CHARMED[2], NODDI[3], MT-CSD[4]). Our aim is to identify mHARDI parameters that maximize the contrast-to-noise ratio (CNR) of these signatures. We focus on the mean DW signal as a function of *b*-value to remove any dependence on the orientation of the tissue, and optimize the acquisition for maximum sensitivity to their densities.

Data acquisition & processing: mHARDI data were collected from 5 neonates scanned at term-equivalent age over *b*-values: 0, 500, 1000, 2000, 3000 & 4000 s/mm^2 (50 DW directions per b≠0 shell), on a Philip 3T Achieva system, with 2×2×3 mm^3 voxels. The parents gave written consent prior to scanning. The data were corrected for motion and eddy-currents using FSL5's EDDY[5] routine. The mean DW signal per shell was estimated as the l=0 term of a Rician-bias corrected spherical harmonic fit (i.e. its DC term).

Data analysis: Given a mHARDI dataset, tissue signatures can be derived by forming the $n_{vox}\times n_b$ matrix of the mean DW signal per shell per voxel, and using matrix factorization methods to decompose it into n_b characteristic signatures (*b*-value dependences) with corresponding weights per voxel (spatial dependences). In this study we use singular value decomposition to estimate these signatures and their corresponding average effect sizes (i.e. their RMS weights over all voxels). We define overall CNR as $\kappa = (\sum_i \sigma_i/\varepsilon_i)^{-1}$, where ε_i and σ_i refer respectively to the effect size and its variance for each signature of interest – note that this measure is dominated by the term with lowest CNR. If the weights vector is given by $w = Ms$, where M is the inverse of the (square) signature matrix and s is the vector of measurements, propagation of uncertainty states that the variance-covariance matrix of w is $Q = M\Sigma M^T$. If the bth shell consists of n_b measurements, the variance of the corresponding mean DW signal will be proportional to σ^2/n_b (σ^2 is the variance of the noise), yielding $Q = \sigma^2 M\ \mathrm{diag}(1/n_b)\ M^T$, and the variance of the ith weight is $\sigma_i^2 = Q_{i,i} = \sigma^2 \sum_b m_{ib}^2/n_b$. Substituting into the equation for κ and using the method of Lagrange multipliers to optimise subject to constant $\sum_b n_b$, the optimal number of DW directions for the bth shell can be shown to be ${n_b}^2 \propto \sum_i (m_{ib}/\varepsilon_i)^2$.

The above analysis provides the relative number of directions for optimal overall CNR per unit time given a fixed set of *b*-values. The *b*-values themselves can be optimised provided the DW signal can be estimated at those *b*-values. While it would in theory be possible to measure the DW signal over a dense set of *b*-values, this is impractical, particularly in a neonatal cohort as is the case here. In this study, we use an appropriate interpolation method (Matlab's PCHIP cubic spline interpolation, which guarantees monotonicity) to estimate the signal at any set of *b*-values from the data actually measured. The optimal *b*-values are then estimated using multidimensional minimization to identify the set of n_b *b*-values that provides the best value of κ (overall CNR) for the signatures identified at those *b*-values, with the relative number of DW directions per shell set as above.

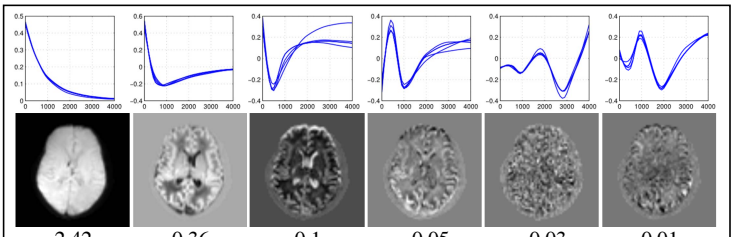

Figure 1: tissue signatures for all 5 subjects as a function of *b*-value (top row), corresponding spatial weights per voxel for a representative subject (middle row) and average effect sizes (bottom row). The first 4 components seem to contain relevant information, while the remaining two are more likely related to imaging and physiological noise.

RESULTS: Figure 1 shows the signatures estimated using SVD for all subjects, and the spatial distribution of corresponding weights for a representative subject. The effect size of the signatures decreases sharply, with that of the 4th signature being only ~1% of the first. In all subjects, the first 4 weights maps all display clear anatomical content, while the remainder tended to be dominated by noise (see figure 1). We therefore used the approach outlined above to identify the best 4-shell sequence. The corresponding optimal *b*-values, number of DW directions per shell, and CNR per tissue signature are shown in table 1 and figure 2.

***b* (s/mm^2)**	0	402	988	2643
%N_{DW}	6%	21%	30%	43%
CNR	145.1	20.4	5.0	3.5

Table 1: the optimal *b*-values for neonatal data (top row) and their corresponding relative number of DW directions (middle row) assuming 4 signatures of interest. Bottom row: CNR of each signature assuming a total of 100 DW volumes with $SNR_{b=0} = 30$.

DISCUSSION: This analysis allows the DW signal's *b*-value dependence to be expressed using a set of linear basis functions, derived using a fully data-driven approach. This allows the data to be expressed using a reduced representation (by focusing on terms with anatomically linked spatial patterns), and to optimise the acquisition for maximum sensitivity to their detection. As such, it provides a framework for the optimization of mHARDI based on the information content of the DW signal, with no reliance on any specific reconstruction algorithm.

A potential limitation of this analysis is that is does not currently account for the orientation dependence of the various signatures, and their inclusion in the model may affect the results to some extent. However, we anticipate this would not alter the results substantially, since accurate estimation of each signature's angular features will rely on eliminating contamination from the other components, which is best achieved using the parameters provided by the present analysis. Note also that the higher shells already contain larger numbers of DW directions, and should therefore provide good angular information content. This will be investigated further in future work.

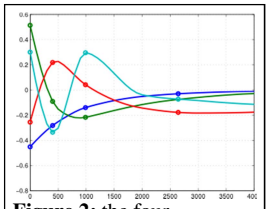

Figure 2: the four signatures of interest with the optimal *b*-values shown as filled circles.

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