Dependence of axon diameter index on maximum gradient strength

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Introduction: The active imaging algorithm [1] optimises diffusion MRI protocols for mapping axon diameter without knowledge of fibre orientation and from a sparse set of measurements. The idea potentially provides new and valuable indices of axon diameter from images acquired from live subjects using standard clinical scanners [5]. However, the method in [5] provides only a single summary statistic, or index, of the distribution of axon diameters in white matter and the nature of the index remains unclear. Here we study the dependence of the axon diameter index on the maximum gradient strength G_max available on the scanner. We used an experimental MR scanner with G_max up to 400 mT/m, but optimised protocols for various smaller G_max, acquired data on a fixed tissue sample and compared maps of the axon diameter index.

Method: We used the experiment design framework in [1] to tune multi-shell HARDI protocols for simultaneous sensitivity to a priori axon diameters of 1, 2 and 4 μm. The procedure provides three unique combinations of gradient strength (G), pulse-width (δ) and the pulse separation (Δ). A simple extension to the framework determines the optimal division of 360 measurements into different sized sets of gradient directions for each combination and b=0 measurements. Four optimal protocols for fixed monkey brain tissue on a 4.7T Varian experimental MR scanner were designed with different maximum gradient strength G_max of 60, 140, 200 and 300 mT/m. The three unique b values at each G_max are [1355, 2368, 5415], [2007, 3368, 9422], [2242, 3791, 11329] and [2421, 4609, 111329] s/mm², respectively and acquired in [91, 99, 102], [98, 105, 87], [100, 105, 84] and [102, 105, 82] gradient directions. The remaining images in each optimised protocol have b=0 to make the total 360, NEX=1, 30 sagittal slices covering the midsagittal plane of corpus callosum (CC), TR=2500 ms, isotropic 0.5 mm voxels, and TE was [71.5, 52, 46, 39.1] ms. Data were acquired on a fixed Vervet monkey brain prepared as [6] in a scanning session lasting 168 hrs. While scanning, the temperature around the tissue was 20°C (±1°C). We fit a four-compartment model, derived from the three-compartment white-matter models of [2,4], as in [5], to each of the acquired datasets to obtain a single index of axon diameter in each voxel. For data analysis, the midsagittal plane of the CC was subdivided into 10 regions as in [7]. Accompanying simulation experiments were used to give insight into the sensitivity of each optimised protocol to a wide range of true axon diameters.

Results: Figure 1 shows that, for each G_max, the axon diameter index within regions of the CC follows the low-high-low trend known from histological data [7,8]. However, in comparison to the mean axon diameter weighted by axon volume, which we might expect the index to approximate, the axon diameter index is consistently about twice as high as for histological data. Overestimation is most significant for the lowest G_max of 60 mT/m. The results stabilise at higher G_max (>60 mT/m), although the standard error decreases steadily as G_max increases. Figure 2 shows maps of the axon diameter index at G_max of 140, 200 and 300 mT/m, which illustrates the difference in noise level nicely. The G_max = 300 mT/m map is less noisy and has higher spatial coherence and contrast in the 1.5-5 μm range. Simulations in figure 3 support the findings in figures 1 and 2. Axons diameters less than about 3 μm appear indistinguishable for low G_max (60 mT/m) but smaller diameters become more distinguishable as G_max increases.

Discussion and conclusion: The axon diameter index is sensitive to available G_max, but we observe good consistency for G_max = 140mT/m and above. For the lowest G_max of 60 mT/m, the axon diameter index is skewed towards higher values, because of lack of sensitivity to lower diameters. However, as G_max increases to 140 mT/m and above we gain sensitivity to the full a priori range of axon diameters used in the experiment design optimization. As G_max increases above 140 mT/m, the gain is largely just in SNR which reduces noise without changing the axon diameter indices significantly. However, we expect that larger G_max enables tuning of the protocol for smaller a priori axon diameter values, which increases the sensitivity of the axon diameter index to smaller populations of axons. Further work will consider which populations of a priori axons diameters are important to target for specific applications and determine which G_max is required for optimal sensitivity to each population.

References 1 Alexander MRM08, 2 Stanisz MRM95. 3 Assaf MRM08. 4 Barazany BRAIN09. 5 Alexander ISMRM09, 6 Dyrby ISMRM08. 7 Aboitz B. Res. 92. 8 Lamantia JCN90.

Fig. 1: Maps of mean axon diameter (±standard error) versus G_max shown in sub-region of CC from anterior: G1-3 (genu), M1-3 (mid-body), I (isthmus) and S1-3 (splenium).

Fig. 2: Axon diameter index map in the midsagittal plan of the CC with a G_max of 140 (left), 200 and 300mT/m. Results improves with higher G_max as seen in e.g. the region of splenium (circle).

Fig. 3: Posterior distributions on various true axon diameters from each optimised protocol using the MCMC procedure in [1].

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