Pitfalls in the Reconstruction of Fibre ODFs Using Spherical Deconvolution of Diffusion MRI Data

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Introduction We report a previously overlooked – but important pitfall in spherical deconvolution approaches for reconstructing fibre orientation distribution functions (fODF's) that arises specifically from the use of a spherical harmonic (SH) basis. Moreover, we show that this pitfall can be avoided by using alternative (non-SH) SD approaches. Spherical deconvolution based HARDI techniques assume that fODFs can be recovered through deconvolution of an idealised response function pertaining to a 'single fibre population' from the observed diffusion weighted (DW) signal. Since this response function cannot be known *a priori*, estimates are often derived from areas of high anisotropy (FA > 0.8). While such estimates may be appropriate for study of healthy adult white matter, development[1], disease, or study of a different tissue type (e.g. muscle) can result in significant changes in diffusion characteristics, creating a marked difference between the assumed (calibration, *C*) and actual (target, *T*) fibre response profiles (i.e., 'mis-calibration'). We explore the effects of mis-calibration on two published SD techniques – constrained spherical harmonic deconvolution (CSHD[2]) and damped Richardson-Lucy (dRL[3,4]). To elucidate the issue, we present results from single fibre populations (all fibres aligned along the same axis).

Methods DW data were simulated for a 60 direction b=2000s/mm^2 scheme sampling a single fibre population with Trace = 2.1x10^{-3} mm^2/s, varying FA (0.1<FA<0.9) and SNRs of 10, 30, 50 and ∞ with 500 repetitions per noisy FA/SNR pairing. For all possible calibration/target/SNR tuples (*C*=0.1-0.9, *T*=0.1-0.9, SNR=10, 30, 50, ∞) both CSHD and dRL were applied and all fODF peaks recovered. From these data we extract: 1. 95% cone of uncertainty in peak fibre orientation for each tuple; 2. Quantity and magnitudes of spurious fODF peaks; 3. Angular distribution of spurious peaks with respect to true fibre orientation: 4; Likely tractography failure rates with failure defined by (a) an incoming fibre trajectory subtending a spurious peak at an angle below a defined tractography threshold (35°); (b) false negative or (c) false positive results where bias in fibre orientation causes erroneous fibre reconstruction. To derive a frequency of failure we consider 100 uniformly distributed vectors as incoming fibre trajectories and sum the total number of failures (defined above), taking the average over 500 repetitions per (*C/T/SNR*) tuple.

Results Both CSHD and dRL generate erroneous fODF peaks when the calibration anisotropy exceeds that of the target; however, the techniques differ in their propensity for errors and SNR dependence. CSHD displays a strong linear relationship between the onset of spurious peaks/increased uncertainty and the degree of mis-calibration (T<0.66*C*, *T*<0.5*C*, Fig. 1a) independent of *SNR*. The number of spurious peaks produced per *C/T* pair increases with SNR and thus causes an apparently counter-intuitive increase in tractography failure rate. DRL performs similarly to CSHD at low SNR but as SNR increases, DRL has substantially better immunity to mis-calibration (Fig. 1b) Similarly, while dRL's spurious peaks are disorganised in distribution, CSHD demonstrates clusters of spurious peaks at angles of 54, 90 and 126 degrees (i.e. the 'magic angles') irrespective of the SNR.

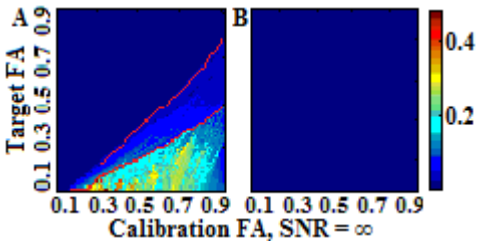

Fig. 1. Spurious peak magnitudes. Red lines indicate boundaries between peak regions. Note there are no spurious peaks in the dRL result.

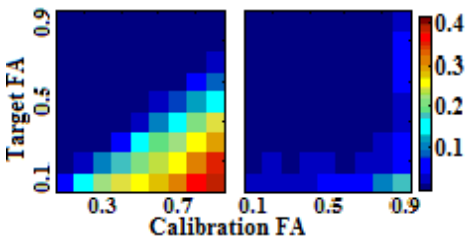

Fig. 2. Tractography failure rates at a 35° threshold, CSHD left, dRL right. SNR = 30.

Discussion/Conclusion Despite substantial focus on the ability of new SD methods to resolve crossing fibres, accurate resolution of single fibre fODF's is rarely tested – yet is surprisingly non trivial. This is particularly true of CSHD which displays a consistent vulnerability to mis-calibration that is independent of noise-induced error. The CSHD spurious peaks are seen to coincide exactly with the zero-crossings/minima of the 2nd order Legendre polynomial (i.e. the harmonic with the highest 'single fibre' descriptive power). These peaks arise due to descriptive deficiencies in the harmonic representation scheme which, as target anisotropy decreases (spurious peaks only occur as calibration exceeds target FA), resulting in increasing residuals that are interpreted as additional fibres. Since dRL does not employ such a harmonic basis for parametrization, it does not exhibit the same sensitivity to mis-calibration and so, with the exception of very low SNR's, can largely be considered calibration-agnostic (Fig. 2). Thus, in cases where a 'one-size fits all' single-fibre response function is inappropriate, dRL outperforms methods based on a spherical harmonic basis.

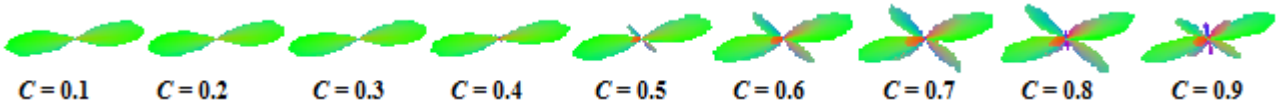

Fig. 3. Emergence of spurious CSHD peaks as increasing degrees of mis-calibration are introduced (0.1-0.9). T=0.3 with SNR of 30. Notice that as T falls below 0.66C (C=0.4 transitioning to C = 0.5) the first noticeable spurious peaks form and then as T reaches 0.5C (C=0.6) these peaks increase markedly in magnitude.

References: 1. Suzuki *et al.* NMR in Biomed. 2006 16(5):257-260. 2. Tournier *et al.* NeuroImage. 2004 23:1176-1185. 3. Dell'Acqua *et al.* NeuroImage 2010 49:1446-1458. 4. Dell'Acqua *et al.* NeuroImage 2007 54:462–472.