Using Spherical Harmonic Functions for Residual Bootstrap Analysis of HARDI

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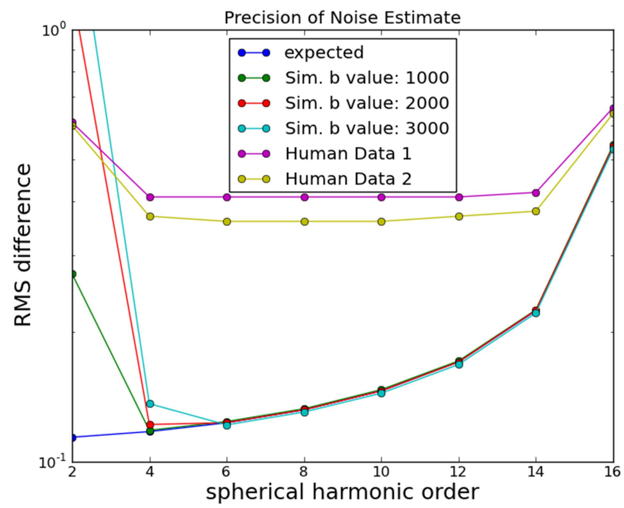
Introduction: In this work we explore using the spherical harmonic (SH) functions as a model for residual bootstrap analysis to compute uncertainty estimates of HARDI data. As an example application, we will estimate the uncertainty of the measured diffusion signals or the noise. We do this for two reasons, first good estimates of the signal uncertainty are useful in themselves because they allow estimation of SNR and assessment of image quality, and second because estimates of signal uncertainty are intrinsic to the bootstrap analysis of any other metrics of interest. A bootstrap procedure that poorly estimates signal uncertainty is suspect when applied to estimate any other metric derived from the signal. While the SH functions have commonly been used to fit diffusion signals in the context of q-ball modeling and constrained spherical deconvolution of HARDI data, they have to date not been explored as a candidate for residual bootstrap. Instead restrictive diffusion models have been proposed such as the tensor[1] and multi-tensor[2]; in comparison the SH functions have several properties that that are desirable in the context of bootstrap analysis. First, because the signal can be represented as a linear function of the SH functions, computing residuals is fast and those residuals can be easily leverage corrected. Second, because the SH representation of the diffusion signal is simply a change in basis, no assumptions are made about the diffusion signal and model failure cannot be a source of error in the bootstrap analysis, if a sufficiently high SH order is used. Previous work in this area suggests that SH orders 6 or 8 should be sufficient to fit HARDI data[3]. In this work we show that in fact uncertainty measures derived from the SH functions are both accurate and precise and give guidance in choosing the SH order for this kind of analysis.

Methods: In this work we used both simulations and human data to assess the accuracy and precision of bootstrap estimates for signal uncertainty or noise. For the purposes of this work we define the noise level to be the variance of the signal measurement and we define signal to noise ratio (SNR) to be the mean signal of images with no diffusion weighting divided by the square root of the noise level. To simulate noise free signals we used a tensor model of diffusion. We used FA and MD values, taken from the literature, of .7 and .5 x 10^{-3}mm/s respectively. We scaled the simulated signal and added rician noise such that the noise level was 1. We repeated this simulation for b values between 1000 to 3000 and SNR from 10 to 50. For this work we also collected human data using a single subject in a Skyra 3T scanner. We collected a HARDI data set with voxel size 2.2mm isotropic, b value of 2000 and 160 gradient directions. We also collected a scan where we repeated 2 gradient directions 32 times each and all other parameters were the same as above. To align and eddy correct the images, FSL's eddy_correct was used with the average of all non-diffusion weighted volumes as the reference. To calculate the bootstrap estimate of the noise, the SH functions of even order were fit to the diffusion signals using the least squares estimate. We then computed residuals and corrected the residuals by their leverage[4]. The variance of the bootstrap samples, which happens to be the same as the variance of the leverage corrected residuals, is the bootstrap estimate of the noise. The repeat estimate of the noise is the variance of repeated signal measurements with the same gradient.



This figure shows the RMS difference between bootstrap estimates of the noise at each SH order and the simulated value. For human data it shows the RMS difference between the bootstrap and the repeat estiamtes.

Results: We computed the bootstrap estimate of the noise and found that on average the noise estimate converged to the expected value of 1 if a sufficiently high spherical harmonic order was used. For the best convergence, maximum SH order of at least 4 or 6 was required depending on the SNR and b value. To measure the precision of these estimates, we calculated the root mean square (RMS) deviation from the expected value over many noise samples (shown in the figure for different b values at SNR of 50). At b value of 3000 and high SNR, the most precise noise estimate occurred at SH order 6 and at the lower b values at SH order 4. We see in the figure that the precision of the noise estimate deteriorate at higher SH order. This is consistent with the reduction in degrees of freedom at higher SH orders. Using our human data, we computed the mean SNR of the diffusion-weighted images by using both the bootstrap and the repeat estimates of the noise. The table shows the average SNR estimate obtained using both methods. We also looked at the consistency between repeat estimates of the noise level and the bootstrap estimates of the noise level by taking RMS difference between the bootstrap estimates and each of the two repeat noise estimates. These results are also shown in the figure, they are scaled to median noise value in the image. Because we do not have true noise values for each voxel in the human data, we only have estimates, the RMS difference cannot be as low as those observed in simulations. However RMS differences show the same trend in human data that they show in simulation. Also voxel-wise bootstrap and repeat noise estimates were highly correlated and the residuals followed the expected non-central chisquared distribution.

	B2	B4	B6	B8	B10	B12	B14	B16	R1	R2
SNR Estimate	40.9	46.9	47.5	47.6	47.7	47.5	47.4	42.3	44.8	47.1

Estimate of mean SNR using bootstrap and repeated measurements to estimate noise. B2 – B16 are bootstrap estimates derived with corresponding SH order. R1 and R2 are estimates derived from two independent sets of repeated measurements.

Conclusion: Because most of the diffusion signal is concentrated at low SH order the residuals from fitting SH functions to HARDI data are dominated by noise. Also because the residuals can be corrected for leverage, accurate bootstrap estimates can be obtained using these residuals if maximum SH order is sufficiently high. However because using higher SH order requires many degrees of freedom, the precision of bootstrap estimates suffers at high SH order. Even though we only compute bootstrap estimates for one metric here, namely noise level, this methodology is fast and is not model specific so it can be applied to estimate uncertainty of any metric derived from single shell HARDI data.

References:

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