Using statistical resampling and geometric least squares to improve DTI measures efficiently

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Introduction: While diffusion tensor imaging (DTI) is an increasingly popular and reliable method for studying brain activity and development, several aspects of the analysis require improvement. For example, noisy data are susceptible to yielding negative eigenvalues, which are inconsistent with the basic model assumptions and can lead to bias of results. Confidence intervals which accurately reflect the uncertainty due to noise levels should be produced for final tensor values, D_i, and eigen-quantities as well. Here, improved techniques for gathering and analyzing DTI data are investigated, combining a 'geometric approach' of ellipsoid fitting and statistical resampling to obtain the diffusion tensor and associated values. This method may also be used to greatly decrease the number of gradients required per sequence, thereby reducing the amount of scanner time and potential for introducing motion artifacts.

Methods: In this theoretical study to evaluate the accuracy of processing methods, a realistic trial set of data was created, with ellipsoids spanning a wide range of axial ratios and symmetries. DTI measures were simulated, for cases of N=12, 18 and 32 gradients, with Gaussian-distributed noise of different signal-to-noise ratios (SNRs) added to signal 'measurements' in each case. All codes have been written ANSI C, with the additional use of functions from the publicly available GNU Scientific Library and Gnuplot packages.

DTI measures were converted to coordinates of a quadratic surface, and an existing, very efficient algorithm for ellipsoid fitting was utilized, which performs a least squares analysis under the assumption that coordinate values have been perturbed about the 'true' ellipsoid with a Gaussian noise. For each ellipsoid, fitting was first performed on the entire gradient set, and then also repeatedly performed on a randomly chosen subset of gradient values using the jackknife resampling technique, resulting in a large (~1000-10000) sample distribution. Estimates of diffusion tensor and eigen-quantities from both cases were compared with the actual ellipsoid values, and the distribution standard deviations used for confidence intervals.

Results: Within each sample created by the jackknife resampling, tensor averaging was used to estimate final the D_i, in order to reduce known biases from eigenvalue sorting. Values from the full-gradient fit were similar in all cases to the averages of the jackknife distribution, with typically the latter being more accurate. Only in cases of low SNR~10 were negative eigenvalues present, and typically in only <10% of the distribution; these values were not included in estimating the diffusion ellipsoid. In general, the errors of the obtained eigenvalues and ellipsoid invariants calculated were approximately less than or equal to 1/SNR. Various anisotropy measures, such as fractional and scaled relative anisotropy, were obtained with similar levels of accuracy. Standard measures of ellipsoid orientation yielded greater variation but were often of similar accuracy, with degeneracies taken into account.

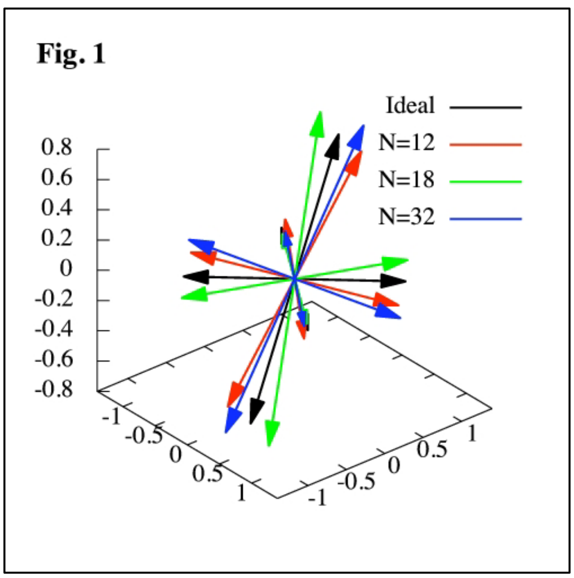

Fig. 1 shows the results of fitting noisy data with SNR=20 for the cases of N=12,18 and 32 gradients (NB: the particular signal noise values are different in each case, but always Gaussian with same standard deviation). For each gradient set, similar accuracy of fitting is obtained, with eigenvalue error <5% and with the standard ellipsoid overlap measure >96% in all cases.

By adjusting the number of gradients fitted per jackknife iteration, the sample standard deviations could be used as confidence intervals for quantities. Such quantities have been shown to be useful in applications of DTI such as tractography.

Conclusion: This method of combining jackknife resampling and ellipsoid fitting has been shown to reasonably reproduce an underlying DT ellipsoid within estimated confidence intervals. These techniques can be used to increase reliability of ellipsoid estimates in noisy data on a per-pixel basis. Whereas other studies using statistical resampling have typically required > 32 gradients for reasonable results, the method presented here can in fact be used to decrease the number of gradients to 12-18, significantly reducing scanner time. Furthermore, this procedure may be useful analyzing partial data sets in which motion has occurred.