Quantitative Analysis of Structural Connectivity Using Fiber Tracking and Non-Parametric Statistics

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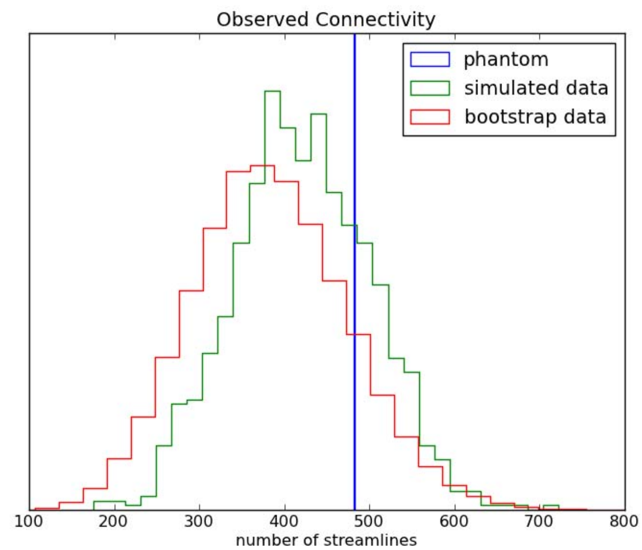
Introduction: Diffusion MRI and fiber tracking of the brain allow us to interrogate the structural connectivity and segment bundles of white matter. Despite widespread use, it can be very difficult to interpret and compare fiber tracking results because we don't know to what extent these results are influenced by our fiber tracking methodology and noise in our data sets. In this study we look at the possibility of using non-parametric bootstrap statistics to define a confidence density for fiber tracking metrics and use the streamlines as an example of such an approach.

Methods: A fiber tract phantom was created by fiber tracking the corticospinal tract of a healthy individual in order to simulate data acquisitions at different signal to noise (SNR) ratios. The phantom construction included fitting an Orientation Probability Density Function (OPDF) (Tristen-Vega et al. 2009) in each voxel and tracking their peaks from the cerebral peduncle to the precentral gyrus. The region of this tract was then dilated and the OPDFs from the dilated region taken as the phantom. Using OPDFs in each voxel instead of tensors maintains more realistic structures within the tract, as for example crossing voxels. The phantom was then split into smaller components by creating two regions on the inferior (cerebral peduncle) end of our tract and four regions in the superior (cortical) end of the tract. The goal of the study was then to measure confidence in connectivity metrics relating the ends of the tract. The eight components were allowed to overlap so that the same streamlines may belong to more than one component; two of the components showed no connectivity in the noise free case. 980 simulated acquisitions were generated by adding Rician noise, with SNR 10, to our phantom. Each of our simulated acquisitions were tracked and the number of streamlines connecting the respective regions counted. This gives us the distribution of observations we might expect if our phantom represented the underling structure of the tract. We then bootstrap each of the simulated data sets 1000 times using the residual bootstrap (Berman et al. 2008) and fiber tracked each bootstrap data set, which gave the bootstrap distribution of observations for each of the simulated data sets.. Using the bootstrap distribution we assigned a confidence interval to each observation of the simulated data sets.



Results: The figure to the right shows the distribution of observations, for one segment of our tract, that we can expect from a noise sample. We can see that this distribution is not centered at the noise free value meaning we have a biased estimator. The bootstrap procedure simulates adding noise to a noise free sample but because it uses a biased estimate as it's starting point, it is further biased. Roughly speaking the bootstrap is biased relative to the simulated observations in the same way that the simulated observations are biased relative to the noise-free value. Table 1 shows the lower and upper coverage properties of the uncorrected (uc) and bias corrected (bc) 90% confidence bootstrap intervals. The coverage is defined as the frequency with which the simulated observations lie below the lower confidence limit or above the upper confidence limit for the lower and upper coverage respectively. If our 90% confidence interval was symmetric and accurate we would expect both the lower and upper confidence to be 5%. Because our estimate is biased, the uncorrected coverage is very unsymmetrical, the bias corrections helps to produce a more symmetric coverage.

	a	b	c	d	e	f	g	h	Total
Noise free streamlines	238	22	107	149	0	12	24	0	487
Coverage, uc, lower	0%	0%	0%	0%	0%	0%	0%	0%	0%
Coverage, uc, upper	15%	1%	24%	0%	0%	8%	18%	0%	25%
coverage, bc, lower	19%	13%	7%	13%	1%	9%	7%	14%	11%
coverage, bc, upper	15%	17%	30%	18%	0%	30%	30%	0%	21%

Table 1: The number of streamlines assigned to each tract segment without noise and the lower and upper coverage for the uncorrected and bias corrected 90% confidence bootstrap intervals for each of the eight tract segments.

Discussion: Streamlines carry the information about the probability of connecting regions with fiber tracking algorithms. Bayesian methods with a multi-tensor model have been used to convert this information to a posterior probability (Jabadi et al. 2007); however such approaches are known to have inaccurate coverage for nonlinear processes and has been described as a linear approximation to a confidence density. Here we present the bootstrap method of estimating the confidence density that does not depend on an explicit model of the diffusion, is computationally relatively efficient, and provides a built-in framework for estimating the needed corrections due to nonlinear effects. This procedure can be applied to any parameter. Further improvements to the derived confidence limits include corrections for skewness (acceleration factor in the Bca correction).

References:

J. Berman et. al., Probabilistic streamline q-ball tractography using the residual bootstrap, *NeuroImage,* 39 1 (2008)

B. Efron, R. J. Tibshirani, *An Introduction to the Bootstrap*, Champman & Hall/CRC 1993

S Jbabdi et al., A Bayesian framework for global tractography. *Neuroimage.* (2007)

A. Tristán-Vega et al., 2009, Estimation of fiber orientation probability density functions in high angular resolution diffusion imaging. *NeuroImage*, 47 2 (2009)