Measuring Error of Diffusion MRI-based Brain Connectivity Matrices with Residual Bootstrap
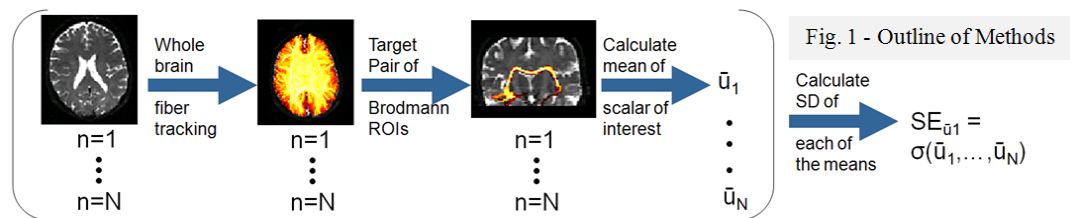
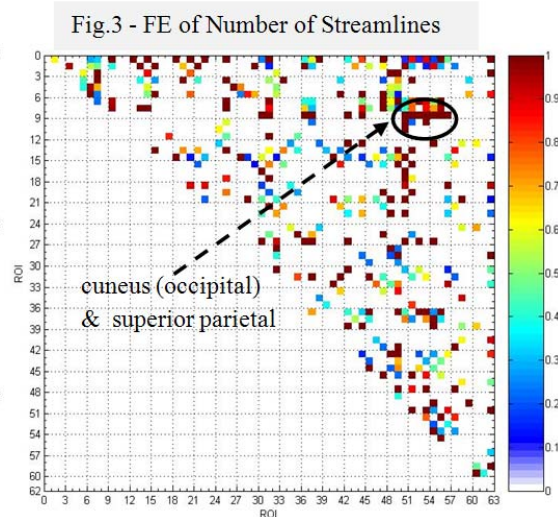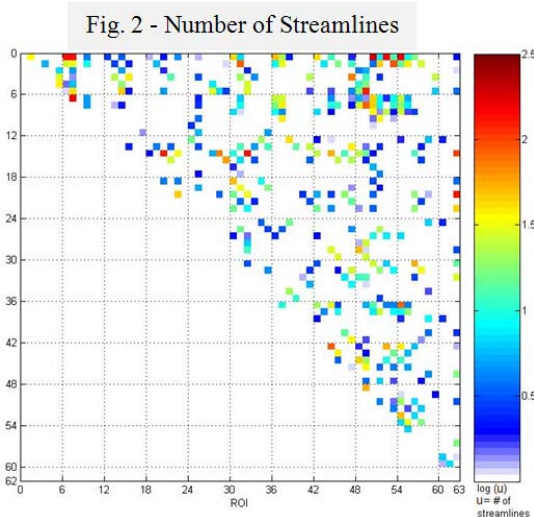**C. T. Nguyen[1,2], R. G. Henry[2,3], and S. Chung[2,3]**

[1]Bioengineering, University of California Berkeley, Berkeley, CA, United States, [2]Center for Molecular and Functional Imaging, Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, United States, [3]Graduate Group in Bioengineering, University of California San Francisco and Berkeley, San Francisco, CA, United States

Introduction: Brain connectivity matrices are highly resourceful representations of network connectivity relating specialized regions of the brain to function. Constructing connectivity matrices were normally created observing post-mortem tracer injected mammalian specimens [8] in which connection patterns were characterized as exhibiting "small-world" attributes [11]. Recently, noninvasive techniques using diffusion MRI were used to construct in-vivo connectivity matrices and networks [1,4-7,9]. However with the existence of numerous fiber tracking techniques, using diffusion MRI to construct connectivity networks leads to ambiguity in interpreting results because critical evaluation of connectivity is dependent on the implemented fiber tracking algorithm. We propose a method to measure error in obtaining connectivity matrices allowing for greater confidence in interpreting results.

Methods: Error is measured with the use of a residual bootstrap approach; an empirical non-parametric statistical technique based on data resampling that has previously been used to quantify uncertainties in diffusion MRI parameters [2,3,5]. The residual bootstrap approach is able to yield unbiased standard errors of constructed connectivity matrices regardless of implemented fiber tracking technique. We constructed a simple connectivity matrix that examines the number of streamlines between pairs of 63 Brodmann ROIs of a normal control subject; although any parameter can be examined such as FA or ADC. For further simplicity, we chose to use the FACT algorithm but as previously stated any fiber tracking algorithm can be used. Residual bootstrap resampling (N = 1000 gold standard; N = 200 asymptotic limit) was performed to yield standard errors of the number of tracks between the pairs of ROIs (Fig. 1).

Fig. 1 - Outline of Methods

$$SE_{\bar{u}_1} = \sigma(\bar{u}_1, \ldots, \bar{u}_N)$$

Results: Below, we present the connectivity matrix of number of streamlines and a useful fractional error (FE) matrix in which we normalize the standard error with the number of streamlines (Fig. 2,3). The fractional error matrix reveals that for the majority of pair of ROIs there exists large error demonstrating the variability that exists in implementing a non robust fiber tracking algorithm. Observing a particular pair of ROIs, the cuneus (occipital lobe) and superior parietal, the FE matrix shows high variability in the number of streamlines demonstrating the inconsistency of the FACT algorithm in tracking those regions. This is consistent with previous literature in which crossing fibers are most likely to exist between those two regions in which a deterministic fiber tracking algorithm may fail to resolve [10].

Fig. 2 - Number of Streamlines

Fig.3 - FE of Number of Streamlines

cuneus (occipital) & superior parietal

Discussion/Conclusion: Connectivity matrices provide a wealth of information and are useful in characterizing the connections between different regions of the brain. However our results illustrate the error that may exist in constructing connectivity matrices and the need to quantify variability that may result in choosing a particular fiber tracking algorithm. As a result of quantifying this variability, connectivity matrices constructed with different fiber tracking algorithms can be compared and interpreted.

[1]Behrens, T.E., et al, 2003. Nat. Neurosci. 6, 750–757. [2]Chung, S., et al. 2008. NeuroImage 39, 1693-1705. [3]Chung, S., et al., 2006a. NeuroImage 33, 531–541. [4]Conturo, T.E., et al.., 1999. Proc. Natl. Acad. Sci. U. S. A. 96, 10422–10427. [5]Jones, D.K. and Pierpaoli, C. 2005. MRM. 53, 1143-49 [6]Koch, M.A., et al., 2002. NeuroImage 16, 241–250. [7]Hagmann, P., et al.2006. Proc. ISMRM 436. [8]Felleman DJ, 1997. Comp Neurology. 379, 353-360. [9]Iturria-Medina, Y., et al. 2007. NeuroImage 36, 645–660. [10] Wiegell et al. 217 (3): 897. (2000) [11] Hilgetag and Kaiser, 2004. Neuroinformatics. 2, 353-360.