Session Title: Thinking Outside the Black Box—A Self-Help Guide to Neuroimaging Analysis
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Highlights

- Results of diffusion MRI analysis depend on both image quality and analysis algorithms.
- Robust study results rely on quality assurance at multiple points in the analysis pipeline.
- Algorithms that solve many common data problems have been developed, however these may not all be available in the same analysis package.

Title: The tracts less travelled—best practices for diffusion MRI analysis

Target Audience: Investigators using diffusion MRI in human and animal studies

Outcome/Objectives: Attendees will learn about common pitfalls in diffusion MRI analysis and how they can be addressed.

INTRODUCTION: The results of diffusion MRI (DMRI) studies depend critically on details of the data analysis pipeline. These include how image quality problems are addressed before model fitting, the algorithms used to estimate model parameters, and how parameters are compared across individuals and/or time-points. An excellent source of information on potential pitfalls in diffusion MRI data processing is the review by Jones and Cercignani (2010).

PREPROCESSING: Many image quality problems are easiest to address before model fitting, i.e., in the preprocessing stage. These include image distortions (due to field errors produced by magnetic susceptibility effects and eddy currents) and head motion. Two simple approaches to susceptibility-related distortions rely on additional image data. One is based on a direct field error measurement and subsequent de-warping of the image (Reber et al, 1998). A second strategy relies on acquiring echo planar images in pairs with opposite phase encoding direction (Chang and Fitzpatrick, 1992; Morgan et al, 2004). Eddy current-induced distortions can be corrected using affine, slice-by-slice registration to a non-diffusion weighted image (Jezzard and Balaban, 1995; Haselgrove and Moore, 1996). Head motion can be corrected by conventional affine 3D volume registration. Since head rotation changes the diffusion weighting directions in the head's frame of reference, the weighting ("b") matrix must be adjusted to account for this effect (Leemans and Jones, 2009).

MODEL FITTING: For diffusion tensor imaging (DTI), there are three broad categories of algorithms for fitting the model parameters. In each case, the signal is assumed to depend exponentially on the elements of the diffusion tensor. Hence, the log of the signal is linear in the tensor elements. The most time-efficient fitting method is Ordinary Least Squares (OLS), which assumes the same distribution of noise for each measurement of log-transformed signal. In fact this approximation underestimates the variance of lower signal measurements. Weighted Least Squares (WLS) provides more realistic estimates of data variance and is nearly as fast. However, Nonlinear Least Squares (NLLS) has been shown to produce more accurate estimates of tensor elements in the majority of brain voxels (Jones and Cercignani, 2010), although it is more computationally intensive. Hence, NLLS is preferable except when computation time is critical. Bias in tensor estimates, due to image noise (Basser and Pajevic, 2000; Anderson, 2001), can be evaluated in acquired data using the simulation and extrapolation (SIMEX) method (Lauzon et al, 2013).

COMPARISON ACROSS INDIVIDUALS: Comparison of image data across subjects relies on unbiased estimates in each region/position within a subject as well as accurate spatial mapping between individuals. Voxel-based methods, originally developed for functional imaging (Friston et al, 1995), can easily be applied to diffusion imaging, although the strong contrast in fractional anisotropy (FA) maps, for example, makes registration and partial volume averaging errors more likely to produce artifactual results. Hence, it is critical to check the quality of registration to the common space prior to voxel-based analysis. Smoothing filters are typically applied to individual FA maps in order to increase SNR, reduce the effects of registration errors, and improve the statistical distribution of sample noise. However, smoothing also increases partial volume averaging and strongly filters the results of statistical tests (Jones, 2005). Tract-based spatial statistics (TBSS; Smith et al, 2006) is more robust to registration errors. However, the spatial and statistical distributions of FA maps should still be checked prior to statistical modeling in TBSS to guarantee reliable results.

CONCLUSION: There are several important choices to be made in defining an analysis pipeline for diffusion MRI. Results depend on both the problems present in the data and the efficacy of the algorithms in addressing those problems. Robust results depend on anticipating data quality limitations by using algorithms that address the likely problems effectively. As with all automated analysis, careful attention to quality control along the pipeline is necessary to guarantee reproducible results.

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