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Analyze This! Practicalities of fMRI and Diffusion Data Analysis

Diffusion Analysis Using TrackVis

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Syllabus

The goal of this interactive presentation is to review the Diffusion Toolkit data processing pipeline and the TrackVis data analysis platform. The following outline provides an overview of the key features associated with Diffusion Toolkit and TrackVis, as well as the literature supporting these features. Studies that have utilized these diffusion processing and analysis tools are also provided for reference.

Overview:

1) Software Developers: Ruopeng Wang and Van J. Wedeen, Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
2) Website: www.trackvis.org
3) Platforms: Windows, Mac OS X, Linux
4) Diffusion data types: DTI, DSI, HARDI/Q-ball
5) Diffusion file types: DICOM, Nifti, Analyze
6) Interface: Graphic User Interface (GUI) and/or command-line
7) Software:
    a. Diffusion Toolkit: diffusion data reconstruction and fiber tracking
    b. TrackVis: deterministic tractography analysis

Diffusion Toolkit (DTK):

1) GUI:
    a. Left panel provides main workspace for selecting imaging model (DTI, HARDI/Q-Ball, or DSI), identifying diffusion data files for processing, selecting gradient table, creating file names, and setting thresholds (i.e. mask and angle)
    b. Right panel provides workspace for selecting input/output file types, propagation algorithm (see below), and option of selecting second mask image (e.g. brain mask, FA mask, etc)
2) Propagation Algorithms:

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a. Fiber Assignment by Continuous Tracking (FACT)[1] → most commonly used
b. 2nd-order Runge Kutta[2]
c. See the following studies for comparison of these two methods: [3,4]

3) Gradient Table:
   a. DTK is equipped with several standard Siemens and GE gradient tables
   b. However, *it is critical to ensure that the gradient table associated with your diffusion sequence is used to process your data* → new gradient tables can be added by clicking the "Edit" button next to the dropdown menu, and then clicking the "+" button. DTK will automatically insert commas between the gradient vectors if you copy/paste a three-column list of vectors from Excel or from a text file.
   c. If your gradient table includes notation for the b0 (i.e. b=0 sec/mm^2) volumes as "0, 0, 0", then DTK will automatically recognize the number of b0's and will display this number in the field "Number of b0 volumes." However, DTK also allows you to enter a gradient table that does not have the b0 volumes listed, in which case you must manually enter this number in the field "Number of b0 volumes".
4) Number of Diffusion Directions:
   a. The field "Number of directions" will automatically recognize the number of diffusion-encoding directions in your gradient table if you are utilizing the DTI or HARDI/Q-ball model.
   b. If you are using the DSI model, you must select 124, 257, or 514 directions. A DSI matrix file will then be automatically be entered into the field "Recon matrix file".
5) Image Orientation:
   a. The select box "Auto" should typically be checked for "Image orientation".
   b. It is critically important to remember to check the box "Apply gradient orientation correction (Siemens DTI only)" if you are acquiring diffusion data on a Siemens MRI scanner.
6) Mask Threshold:
   a. If the "Auto" option is checked, tracking will be performed using the diffusion signal as an automatic threshold.
   b. Other commonly used thresholds include a binarized brain mask (e.g. generated by the Brain Extraction Tool in FSL[5]) and an FA mask.
   c. When an FA mask is used, a commonly used threshold is FA ≥ 0.2, although lower FA thresholds may increase the sensitivity for detecting fiber tracts that pass through grey matter nuclei and/or in regions of the brain with a high density of crossing fibers (e.g. the brainstem tegmentum)[6]
7) Angle Threshold:
   a. Thresholds of 40-45˚ are commonly used in analyses of white matter tracts in the cerebral hemispheres, but more liberal thresholds of up to 60˚ may be appropriate for analyses of white matter tracts that take sharper turns, such as those traveling from the brainstem to the diencephalon.[6]
8) Orientation Patch:

a. Some gradient tables do not produce neuroanatomically accurate tracts (see tract validation test below) despite accurate entry of the gradient table. This error may be attributable to vendor-specific MRI scanner software platforms that introduce unanticipated changes in the way that the gradient table is recognized by DTK. In this case, it can be difficult to determine the orientation of the error, and thus one may need to apply orientation patches by either inverting (Invert X, Invert Y, or Invert Z), or swapping (SWAP X/Y, SWAP Y/Z, or SWAP Z/X) the vectors in the gradient table.

9) Spline Filter:
   a. This button should generally be selected to smooth the original track file with a B-spline filter. The tracts appear more aesthetically appealing without losing any of the original vector data.
10) Transform Track:
   a. This feature can be selected under the "Tools" Menu and enables transformation of DTK-generated fiber tracks into a new target space (e.g. MNI space).
   b. Of note, coregistration matrices must be linear and must use FSL or FreeSurfer tools.

TrackVis:

1) Regions of Interest (ROIs):
   a. Sphere, hand-drawn, or uploaded as a nifty/analyze file (e.g. from an atlas)
2) Creating Fiber Tracts:
   a. Single ROI approach: manually trace or automatically segment a white matter ROI, such as the corpus callosum, and then use this ROI as a "seed" for the generation of fiber tracts passing through it.
   b. Multi-ROI approach: to virtually dissect two different bundles of fiber tracts that pass through the same region of white matter, a two-ROI approach may be used, as described by Catani and de Schotten.[7] For example, the uncinate fasciculus fiber tracts cannot be isolated by tracing a single ROI in the external capsule because the inferior frontooccipital fasciculus also courses through this region. Thus, to virtually dissect the uncinate fasciculus from the inferior frontooccipital fasciculus, one can trace ROIs in the anterior temporal lobe and the external/extreme capsules and then perform a tractography algorithm in which only the fiber tracts that pass through both ROIs are displayed.
   c. Inclusion/exclusion of ROIs: the "AND", "OR", and "NOT" functions can be used to refine the tractography results according to pre-specified neuroanatomic criteria.
   d. Tract validation check: before undertaking an analysis, ALWAYS check a few well known fiber tracts to ensure that they appear neuroanatomically accurate → consider checking transcallosal fiber tracts using a single corpus callosum ROI and corticospinal tracts using a dual ROI approach

involving the cerebral peduncle and posterior limb of the internal capsule. Neuroanatomic accuracy can be checked against several atlases, such as the Catani and de Schotten Atlas.[7]

3) Quantitative Measurements:
    a. ROI stats: FA, ADC and other diffusion metrics can be extracted for each ROI by clicking on the "View" button next to "More Stats" in the Track Property menu.
    b. Tract stats: mean FA, mean ADC, tract number, and other diffusion metrics can be extracted for each bundle of fiber tracts.
    c. Number of tract disconnections: one can measure the number of tracts that terminate within a specific ROI by selecting the "Either End" criterion for the ROI in the Track Property menu. This approach provides the basis for the DISCONNECT segmentation technique (Delineation of Intact and Severed Components Of Neural NEtwork ConnecTions) that has been used to quantify the burden and spatial distribution of white matter injury in patients with traumatic axonal injury.[8]
4) Data Visualization:
    a. One of TrackVis' strengths is its well-designed and user-friendly data visualization platform, which allows for 3-dimensional visualization of tracts, robust zoom functionality, and easy manipulation of ROI and fiber tract transparency. With regard to the zoom functionality, the viewer can zoom inside of small lesions and view tract disruptions within these lesions.[8]
    b. A variety of scalars (e.g. FA, ADC) can be used to indicate changes in scalar values along fiber tracts (each segment of a tract is automatically labeled with a scalar color).
5) Human and Animal Studies using TrackVis:
    a. White matter tracts within the cerebral hemispheres: [9-14]
    b. White matter tracts within the cerebellar hemispheres: [15,16]
    c. White matter tracts within the brainstem: [6,8,10,17]
    d. White matter tracts in the developing brain: [11-13,18]
6) Limitations:
    a. Regardless of which ROI methodology or tractography algorithm is being used, it is important to emphasize that tractography is an inferential technique in which white matter tracts are reconstructed on the basis of water diffusion measurements. The number of axons that corresponds to a single fiber tract remains unknown. Furthermore, the number of fiber tracts that is calculated in any tractography analysis is significantly affected by data acquisition parameters. Although studies have begun to validate tractography with gold-standard histopathology results in the human brain and spinal cord,[8,19] tractography results should always be interpreted with caution given the inherent limitations of the technique.[20]

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