More about DTI-tracking:
Practicalities and programs

AFNI Bootcamp (SSCC, NIMH, NIH)
Outline

+ Practicalities around tracking with AFNI/FATCAT
+ 3dTrackID’s “modes” (a.k.a. styles or types) of tracking
  - and calculating tensor parameter uncertainty
+ Setting up networks of target ROIs with 3dROIMaker
  - examples from anatomical parc/seg and FMRI
+ Checking gradients
+ Additional tracking features
Network tracking paradigm: recall

Useful generalization of AND-logic: “Network tracking” through several target ROIs simultaneously. Find tracts in WB that go through any pair in a set of targets, where the targets make sense to think about together.

Note that the connections can be “sparse”: not every target is connected to every other target. (Physiologically, we would not expect otherwise...)

Note that the connections can be “sparse”: not every target is connected to every other target. (Physiologically, we would not expect otherwise...)
Network tracking paradigm: recall

- FMRI (e.g., thresholded seed-based or ICA maps)
- Anatomical parc/seg (e.g., FreeSurfer)
- Spheres/simple ROIs (can map across group)
Network tracking paradigm: points

Main criteria for making target ROI networks
+ define meaningful regions (-> sensical to be together for hypothesis)
+ make sure targets border on FA-WM
+ for group analysis, create equivalent/consistent regions across group
Network tracking paradigm: points

Main criteria for making target ROI networks
+ define meaningful regions (-> sensical to be together for hypothesis)
+ make sure targets border on FA-WM
+ for group analysis, create equivalent/consistent regions across group

... Then
+ targets can be defined in subject’s own DTI space
+ main quantity: matrix of structural properties for each network
Main criteria for making target ROI networks
+ define meaningful regions (-> sensical to be together for hypothesis)
+ make sure targets border on FA-WM
+ for group analysis, create equivalent/consistent regions across group

... Then
+ targets can be defined in subject’s own DTI space
+ main quantity: matrix of structural properties for each network

Different than “voxelwise comparisons”
+ Here, don’t need to warp to standard space/WM skeleton
  -> avoid (some) alignment issues/demands
+ Here: calc “network-wide” properties, then zoom in (big -> small)
  voxelwise comps: calc voxel diffs and build “clusters” (small -> big)
+ Here, WM structure matters; voxelwise comps ignore this.
Combining FMRI and DTI
(much applies to any target network)
Tools for combining FC and SC:

Combining functional and tractographic connectivity will require:
+ determining networks from FMRI, parcellation or other data;
+ finding correlations and local properties of functional networks;
+ turning GM ROIs into targets for tractography;
+ doing reasonable tractography to find WM ROIs;
+ estimating stats on WM ROIs...
Tools for combining FC and SC:

Combining functional and tractographic connectivity will require:
+ determining networks from FMRI, parcellation or other data;
+ finding correlations and local properties of functional networks;
+ turning GM ROIs into targets for tractography;
+ doing reasonable tractography to find WM ROIs;
+ estimating stats on WM ROIs...

**FATCAT:** Functional And Tractographic Connectivity Analysis Toolbox *(Taylor & Saad, 2013, BC; Taylor et al. 2015, BC)*

Demos in AFNI: @Install_FATCAT_DEMO, @Install_FATMVM_DEMO
Schematic for combining FMRI and DTI-tractography via FATCAT

**FATCAT goals:**
+ Do useful tasks
+ Integrate with existing pipelines/software
+ Derive/use information from the data itself
+ Be “simple” to implement
+ Be network-oriented, when possible
+ Be efficient
+ Be flexible and able to grow

*(Taylor, Chen, Cox & Saad, 2016)*
Main focus today on DTI-tractography, including making ROIs from FMRI

Schematic for combining FMRI and DTI-tractography via FATCAT

FATCAT goals:
+ Do useful tasks
+ Integrate with existing pipelines/software
+ Derive/use information from the data itself
+ Be “simple” to implement
+ Be network-oriented, when possible
+ Be efficient
+ Be flexible and able to grow

(Taylor, Chen, Cox & Saad, 2016)
Motivating example

*Network view of both functional and structural data*
FMRI: GM Networks

(Biswal et al., 2010 PNAS)
Functional connectivity networks of distinct GM regions, from BOLD time series during task or rest/no task.

+ Quantify GM properties: ALFF, fALFF, RSFA, $\sigma$, ReHo, GMV, etc.

+ Quantify network props: seedbased correlation, ICA, graph theoretical measures, etc.
Sidenote:

*Mention of a few of the FMRI tools*
For {RS- | TB-}FMRI: correlation matrices

+ 3dNetCorr: calculated post-processing, input time series data + network maps
  - can be multi-brick maps, 1 network per brick
  - calculate average time series per ROI, correlation among network ROIs
  - outputs correlation matrix/matrices, (can also do Fisher-Z transform output)

++ Can also calculate ReHo, ALFF, fALFF, etc.
in FATCAT/AFNI.
Applying tractography
FMRI provides:
maps of (GM) regions working together

GM ROIs network:

- Somatomotor
- Dorsal attention
- Control
- Default mode

Raichle (2010, TiCS)
FMRI provides: maps of (GM) regions working together

GM ROIs network:
- Somatomotor
- Dorsal attention
- Control
- Default mode

Associated WM ROIs

Raichle (2010, TiCS)
FMRI provides: maps of (GM) regions working together

GM ROIs network:
- Somatomotor
- Dorsal attention
- Control
- Default mode

Associated WM ROIs

Our goal for tractography ->
estimate likely/probable locations of WM associated with GM, and relate ROI quantities with functional/GM properties
Describing and comparing “modes” of tracking in 3dTrackID, with example network of targets:

SUMA view of targets from FMRI (axial view, S->I)
Tracking modes: **DET**

**Deterministic tracking**
+ For each FA-WM voxel (e.g., FA>0.2), place seedpoint(s), track from each until stop criterion reached, and keep tracts through ROIs (AND- or OR-logic).
+ Can delete “bad” bundles with too few tracts.

+ Output:
  tract bundles,
  volumetric map of WMCs,
  **and matrix of structural properties.**

--> **DET** is OK for quick testing, QC, general data checking, but does not take into account uncertainty; don’t know how reliable or noise-dependent results are. Mostly just used for quick, WB QC.
Tracking modes: **MINIP**

Mini-probabilistic tracking
+ For each FA-WM voxel (e.g., FA>0.2), place seedpoint(s), track from each until stop criterion reached, and keep tracts through ROIs (AND- or OR-logic);
+ **Then**, perturb every tensor randomly, according to its estimated uncertainty (-> desc. below), and then do WB tracking. Repeat a few (~5-7) times.
+ Can delete “bad” bundles with too few tracts.

+ Output:
  - tract bundles,
  - volumetric map of WMCs,
  - *and* matrix of structural properties.

--> **MINIP** improves on DET: accounts for noise; easier to detect spurious bundles; better vis. than DET. But no voxelwise thresholding...
Tracking modes: **PROB**

*(full) probabilistic tracking*

+ For each FA-WM voxel (e.g., FA > 0.2), place seedpoint(s), track from each until stop criterion reached, and keep tracts through ROIs (AND- or OR-logic);

+ **Then**, perturb every tensor randomly, according to its estimated uncertainty (-> desc. below), and then do WB tracking. Repeat many (~thousands) times.

+ Threshold tract count **per voxel** to make WMC.

+ Output:
  - volumetric map of WMCs,
  - *and* matrix of structural properties.

--> **PROB** is most robust tracking: noise most strongly accounted for, and each WMC is built with **per voxel** criterion of tract counts. Produces best “likelihood” map of WMC.
Bundles/WMCs comparisons per mode

DET  MINIP  PROB

No bundles output
They are only used to build up prob. map
Bundles/WMCs comparisons per mode

Importantly, each mode **automatically** makes a file containing matrices of structural properties

-> these will be used for quantitative analysis & statistical modeling.
3dTrackID: choosing a “mode”

**DET**
- Initial, quick QC of full DWI data (e.g., WB tracking)
- Check gradient flip (-> @GradFlipTest)

**MINIP**
- Quick network check
- Visualize tract bundles, esp. for example figure
- Requires uncert. calc. (3dDWUncert)

**PROB**
- **The choice for quantitative work**
- Can also visualize WMCs as RGB or per-bundle coloring
- Requires uncert. calc. (3dDWUncert)
- Is slower.... but not too bad.
3dTrackID: control tracts at surface boundaries

A. Default: between and within target

B. uncut_at_rois: no trimming

C. -targ_surf_stop: between targets and includes surface

D. -targ_surf_twixt: between targets only

@GradFlipTest: track WB to check grad format

+ Software and scanners have different definitions of +/- when interpreting scan directions. So, use WB tracking via @GradFlipTest to check and 1dDW_Grad_o_Mat++ to adjust/fix.

unflipped
flipped “x”
flipped “y”
flipped “z”


(Taylor et al. 2015, BC)
Making network of targets for tracking
Ex. 1: from FreeSurfer parc/seg
Ex. 2: from FMRI maps
3dROI-maker: (controlled) ROI inflation

+ Target ROIs may be slightly “cut off” from the FA-WM masks, due to thresholding (e.g., FMRI) or alignment/resampling (e.g., FS/template or FMRI).

Can use **3dROI-maker** to inflate targets a little to fill in gaps while not overrunning WM or other targets.

Ex. 1: **olay**: FS targets pre-inflation; **ulay**: FA>0.2 mask

https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/MakingROIs.html
3dROIMaker: (controlled) ROI inflation

+ Target ROIs may be slightly “cut off” from the FA-WM masks, due to thresholding (e.g., FMRI) or alignment/resampling (e.g., FS/template or FMRI).
Can use 3dROIMaker to inflate targets a little to fill in gaps while not overrunning WM or other targets.

Ex. 1:  olay: FS targets pre-inflation;  ulay: FA>0.2 mask

https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/MakingROIs.html
1) Start with some FC map (seed-based correlation, ICA, etc.)
   Here:  
   \( \text{olay} = \text{ICA map (Z-score values)} \)
   \( \text{ulay} = \text{FA map} \)
Ex. 2: FMRI-derived targets

2) Threshold FC map voxelwise and for size of clusters -> isolated ROIs

Here:

- olay = map of regions after thresholding
- ulay = mask of FA>0.2 (→ FA-WM)
Ex. 2: FMRI-derived targets

3) Inflate isolated targets a small amount, constrain with FA-WM

Here: olay = inflated ROIs -> targets for tracking
      ulay = mask of FA>0.2 (-> FA-WM)
3dROI: additional features

+ Can remove overlap of regions with WM or CSF

+ Inflation options: inflation can stop just before or just after overlapping with FA-WM

+ Select subsets of ROIs with $N$ highest values

+ Apply a “refset” to have consistent numbering+labelling of ROIs
How do we estimate tensor parameter noise/uncertainty for MINIP and PROB tracking?
Recall: noise in DW signals

MRI signals have additive noise

\[ S_i = S_0 e^{-b g_i^T D g_i} + \varepsilon, \]

where \( \varepsilon \) is (Rician) noise, with the effect of leading to errors in surface fit, equivalent to \textit{rotations} and \textit{rescalings} of ellipsoids:

'Eun-noisy' vs perturbed/noisy fit

EPI distortions, subject motion, et al. also warp ellipsoids.
DTI Uncertainty

- We use jackknife resampling (e.g., Efron 1982)
  - Other studies have used bootstrapping (e.g., Jones 2003), or theoretical estimates (Jeong & Anderson 2008)
  - Jackknifing is efficient (just need one data set unlike bootstrap), simpler than theory, since, e.g., SNR is likely not constant across voxels
Jackknifing

- Basically, take $M$ acquisitions

  e.g., $M=12$
Jackknifing

- Basically, take $M$ acquisitions
- Randomly select $M_j < M$ to use to calculate quantity of interest
  - standard nonlinear fits

\[ \begin{bmatrix} D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23} \end{bmatrix} = \ldots \]

\[ e.g., M=12 \]
\[ M_j=9 \]
Jackknifing

- Basically, take $M$ acquisitions
- Randomly select $M_J < M$ to use
to calculate quantity of interest
  - standard nonlinear fits
- Repeatedly subsample large number ($\sim 10^3-10^4$ times)

\[
\begin{bmatrix}
D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23}
\end{bmatrix} = \ldots
\]

\[
\begin{bmatrix}
D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23}
\end{bmatrix} = \ldots
\]

\[
\begin{bmatrix}
D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23}
\end{bmatrix} = \ldots
\]

\[
\ldots
\]
Jackknifing

- Basically, take $M$ acquisitions
- Randomly select $M_j < M$ to use to calculate quantity of interest
  - standard nonlinear fits
- Repeatedly subsample large number ($\sim10^3$-$10^4$ times)
- Analyze distribution of values for estimator (mean) and confidence interval
  - sort/percentiles
    - (not so efficient)
  - if Gaussian, e.g. $\mu \pm 2\sigma$
    - simple

\[ \begin{bmatrix} D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23} \end{bmatrix} = \ldots \]
\[ \begin{bmatrix} D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23} \end{bmatrix} = \ldots \]
\[ \begin{bmatrix} D_{11} & D_{22} & D_{33} & D_{12} & D_{13} & D_{23} \end{bmatrix} = \ldots \]

\[ \ldots \]
Uncertainty estimation

+ 3dDWUncert estimates

1) bias and $\sigma$ of the first eigenvector $e_1$ (main direction of diffusion), for two degrees of freedom: how much it could tip toward either $e_2$ or $e_3$:

2) and the bias and $\sigma$ of (scalar) FA.

(Taylor & Saad. 2013, BC)
Uncertainty example

+ Can see difference in $e_1$ uncertainty along $e_2$ and $e_3$ (in rads).

+ Tissue-dependent differences in FA uncertainty.

(Taylor & Saad. 2013, BC)
FATCAT addenda: 
1) HARDI tracking
Higher order models

DTI tractography:
+ susceptible to false negatives, difficulty with long range tracts (noise/error accumulation)
+ Major diffusion can be average of multiple paths
+ Voxels can have low FA from several WM paths, false ending
+ Can't resolve complex underlying architecture
  - Jeurissen et al. (2012, HBM): 60-90% of WM voxels estimated to have multiple fibers

(Jeurissen et al., 2012)
HARDI

+ High Angular Resolution Diffusion Imaging:
  - DSI, ODF, Qball, FOD...
  - model multiple fiber bundle directions per voxel
  - generally need more scan time and acquisitions and computational power, much higher b-values
  - still can't resolve intravoxel tract behavior (which of multiple paths?)
  - higher DW → lower signal, so susceptible to noise

(Jeurissen et al., 2012)
HARDI

+ High Angular Resolution Diffusion Imaging:
  - DSI, ODF, Qball, FOD...
  - model multiple fiber bundle directions per voxel
  - generally need more scan time and acquisitions and computational power, much higher b-values
  - still can't resolve intravoxel tract behavior (which of multiple paths?)
  - higher DW → lower signal, so susceptible to noise

FATCAT can now track through HARDI data

→ HARDI reconstruction done outside AFNI (e.g., DSI-Studio, Diffusion Toolkit, ...), and outputs tracked in FATCAT.

(Jeurissen et al., 2012)
Example: 3dTrackID on HARDI data

Ex: Human Connectome Project subject, 288 grads, HARDI reconstructed with GQI in DSI-Studio.
FATCAT addenda:
2) 'Connectome'-type tracking
“Connectome”: parcellation of GM

Example (script available in FATCAT_DEMO):
+ FreeSurfer parcellation into >112 ROIs.
+ Selected 80 cortical GM ROIs.
+ Used 3dROIMaker to inflate by 1 voxel, up to FA>0.2.
  (+ NEW: keep labeltable labels and use them in output.)
+ '3dTrackID' among the regions
Example (script available in FATCAT_DEMO):
+ FreeSurfer parcellation into >112 ROIs.
+ Selected 80 cortical GM ROIs.
+ Used 3dROIMaker to inflate by 1 voxel, up to FA>0.2.
 (+ NEW: keep labeltable labels and use them in output.)
+ '3dTrackID' among the regions

and a few seconds later...
“Connectome”: tracking
SUMMARY

+ We motivated using subject data to make networks of targets
  - e.g., FMRI or anatomical parcellation
+ Tracking estimates most likely locations of WMCs
  - Use **PROB** mode in 3dTrackID for best estimation
  - 3dDWUncert to estimate DT parameter uncertainty
+ Quantitative output: matrices of properties in tracked WMCs
+ 3dROIMaker is useful for making target ROIs
+ Checking/fixing grads: @GradFlipTest + 1dDW_Grad_o_Mat
+ 3dTrackID also has HARDI-compatible functionality