TRACULA: Principles and usage

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Deterministic vs. probabilistic

- **Deterministic methods** give you an estimate of model parameters

- **Probabilistic methods** give you the uncertainty (probability distribution) of the estimate
Deterministic vs. probabilistic

**Deterministic tractography:**
One streamline per seed voxel

**Probabilistic tractography:**
Multiple streamline samples per seed voxel (drawn from probability distribution)
Deterministic vs. probabilistic

**Deterministic tractography:**
One streamline per seed voxel

**Probabilistic tractography:**
A probability distribution
(sum of all streamline samples from all seed voxels)
Local vs. global

Local tractography:
Fits pathway step-by-step, using local diffusion orientation at each step

Global tractography:
Fits the entire pathway, using diffusion orientation at all voxels along pathway length
Local tractography

- Best suited for exploratory study of connections
- All connections from a seed region, not constrained to a specific target region
- How do we isolate a specific white-matter pathway?
  - Thresholding?
  - Intermediate masks?
- Non-dominant connections are hard to reconstruct

- Results are not symmetric between “seed” and “target” regions
- Sensitive to areas of high local uncertainty in orientation (e.g., pathway crossings), errors propagate from those areas
Global tractography

- Best suited for reconstruction of known white-matter pathways
- Constrained to connection of two specific end regions
- Not sensitive to areas of high local uncertainty in orientation, integrates over entire pathway
- Symmetric between “seed” and “target” regions

- Need to search through a large solution space of all possible connections between two regions:
  - Computationally expensive
  - Sensitive to initialization
TRACULA

- Reconstruct 18 major white-matter pathways with no manual intervention
- Global probabilistic tractography with prior information on tract anatomy from training subjects
- Learn from training subjects which anatomical regions each pathway typically goes through/next to
- Constrain pathway in new subject based on this prior anatomical knowledge
- Ad-hoc anatomical constraints are often used by other methods: constraints on path bending angle or length, WM masks, ...
Tractography takes time

- Get whole-brain tract solutions, edit manually
- Use knowledge of anatomy to isolate specific pathways
White-matter pathway atlas

- Labeling based on an established protocol [Wakana ‘07]
- Corticospinal tract
- Inferior longitudinal fasciculus
- Uncinate fasciculus
- Corpus callosum
  - Forceps major
  - Forceps minor
- Anterior thalamic radiation
- Cingulum
  - Cingulate (supracallosal)
  - Angular (infracallosal)
- Superior longitudinal fasciculus
  - Parietal
  - Temporal

Intra/inter-rater errors: 1mm/2mm on average
White-matter pathway atlas

- **Manual labeling** of paths in training subjects performed in Trackvis

- **Anatomical segmentation maps** of training subjects from FreeSurfer
Probabilistic model

Have image data $Y$  
Want most probable path $\mathcal{F}$

- Determine the most probable path based on:
  - What the images tell us about the path (likelihood)
  - What we already know about the path (prior)
- Estimate posterior probability of path $\mathcal{F}$ given images $Y$

$$p(\mathcal{F} \mid Y) \propto p(Y \mid \mathcal{F}) \cdot p(\mathcal{F})$$

  - $p(Y \mid \mathcal{F})$: Uncertainty due to imaging noise
    Fit of pathway orientation to ball-and-stick model parameters [Jbabdi et al., ‘07]
  - $p(\mathcal{F})$: Uncertainty due to anatomical variability
    Fit of pathway to prior anatomical knowledge from training set [Yendiki et al., ‘11]
Schizophrenia study
Data courtesy of Dr. Randy Gollub and MIND Institute

- Reconstruct pathways in 34 SZ patients and 23 healthy controls
Schizophrenia study

Data courtesy of Dr. Randy Gollub and MIND Institute

• Reconstruct pathways with:
  – No training subjects
  – 30 healthy training subjects
  – 15 healthy / 15 SZ training subjects
  – 30 SZ training subjects

• Evaluate distance b/w automatically reconstructed and manually labeled pathways
Usage

- All processing options are defined in a configuration file, `dmrirc`

- **Step 1**: Pre-processing (distortion compensation, registration, etc.)
  `trac-all -prep -c dmrirc`

- **Step 2**: Fitting of ball-and-stick model (FSL’s bedpostx)
  `trac-all -bedp -c dmrirc`

- **Step 3**: Reconstruct pathways
  `trac-all -path -c dmrirc`
Configuration file

• Example configuration file:
  
  $FREESURFER_HOME/bin/dmrirc.example

• The simplest configuration file possible, using all default options and only defining inputs:

```python
setenv SUBJECTS_DIR /path/to/fs/output/directory
set subjlist = (subjA subjB ...)
set dcmlist = (/path/to/A/1.dcm /path/to/B/011-1.dcm ...)
set bvecfile = /path/to/bvecs.txt
set bvalfile = /path/to/bvals.txt
```

• Same gradient vectors and b-values assumed for all scans

• Can specify trac-all output directory different from recon-all
  
  $SUBJECTS_DIR:
  
  set dtroot = /path/to/tracula/output/directory
Pre-processing

trac-all \texttt{-prep} \texttt{-c} dmrirc

- Includes the following steps:
  - Image corrections: \texttt{-corr}
  - NEW: Quality assessment: \texttt{-qa}
  - Intra-subject registration (DWI to T1): \texttt{-intra}
  - Inter-subject registration (T1 to template): \texttt{-inter}
  - Anatomical masks and labels: \texttt{-mask}
  - Tensor fit: \texttt{-tensor}
  - Anatomical priors: \texttt{-prior}

- Can do some of the steps only (assuming previous steps have been done):
  - trac-all \texttt{-corr} \texttt{-qa} \texttt{-c} dmrirc

- Or exclude some of the steps (assuming they have been done previously):
  - trac-all \texttt{-prep} \texttt{-nocorr} \texttt{-noqa} \texttt{-c} dmrirc
Image corrections

trac-all -corr -c dmrirc

- Uses standard FSL tools to mitigate eddy-current and susceptibility distortions

- To perform eddy-current correction (registration-based) and apply the same rotations to the gradient vectors as to the images:
  
  set doeddy = 1
  set dorotbvecs = 1

- To perform susceptibility distortion correction (field map-based):
  
  set dob0 = 1
  set b0mlist = (/path/to/A/b0m-1.dcm ...)
  set b0plist = (/path/to/A/b0p-1.dcm ...)
  set echospacing = 0.7
New: Quality assessment

trac-all -qa -c dmrirc

- Compute 4 measures of head motion from the diffusion images:
  - Translational motion
  - Rotational motion
  - Frequency of intensity drop-outs
  - Severity of intensity drop-outs

- Can be used to match groups for head motion or as regressor in statistical analyses of anisotropy and diffusivity
Intra-subject registration

trac-all -intra -c dmrirc

- Register the individual DWI to the individual T1

- **Option 1:** set doregflt = 1
  - Affine registration with flirt

- **Option 2:** set doregbbbr = 1
  - Affine registration with bbregister
  - Boundary-based registration using intensity gradient across surface
  - This is the default option
Inter-subject registration

`trac-all -inter -c dmrirc`

- Register the individual T1 to a common template space

  - **Option 1:** `set doregmni = 1`
    - Affine registration with `flirt`
    - By default registers to MNI template (avg 152)
    - Target template image can be specified with:
      `set mnitemp = ...`

  - **Option 2:** `set doregcvs = 1`
    - Non-linear registration with `mri_cvs_register`
    - By default registers to the CVS template (avg 35)
    - Target template subject can be specified with
      `set cvstemp = ...`
      `set cvstempdir = ...`

$FREESURFER_HOME/bin/subjects/cvs_avg35
Inter-subject registration: MNI

Affine registration of individuals to the MNI template
Inter-subject registration: CVS

Non-linear registration of individuals to the CVS template
Anatomical masks and labels

trac-all -mask -c dmrirc

- Maps aparc+aseg, cortex, and white-matter masks
- By default, use a dilated version of the anatomical aparc+aseg as the brain mask for all subsequent processing
  set domaskanat = 1
- Otherwise, it’s possible to use a brain mask obtained from the low-b with FSL BET, and set the BET threshold
  set thrbet = 0.3
Tensor fit

trac-all -tensor -c dmrirc

- Tensors are NOT used for tractography in TRACULA!
- Tensors are only used to compute maps of FA, MD, RD, AD
- This step also transforms FA, MD, RD, AD volumes to the common template space (MNI or CVS) - not used by TRACULA but could be used in a voxel-based analysis
Anatomical priors

trac-all  -prior  -c dmrirc

• Computes anatomical priors from tract atlas

• By default, the 33 subjects provided with TRACULA are used, but this can be changed:
  set trainfile = $FREESURFER_HOME/trctrain/trainlist.txt

• To process only a subset of the 18 pathways:
  set pathlist = (lh.cst_AS rh.cst_AS)

• For each pathway specify how many control points:
  set ncpts = (6 6)
Ball-and-stick model fit

trac-all -bedp -c dmrirc

• This step simply runs FSL bedpostX to fit the ball-and-stick model of diffusion to every voxel in the brain mask

• This can take a while, but it’s possible to run every slice in parallel

• To specify the maximum number of anisotropic compartments per voxel (default: 2)
  set nstick = 3
Pathway reconstruction

```
trac-all -path -c dmrirc
```

- Reconstruct the 18 pathways (or a subset) using a random sampling algorithm

- Pick an initial guess for the path from the training subjects in the atlas (the only step that requires decent alignment between individual and atlas!)

- At every iteration, perturb control points of path and compute its fit to diffusion data and to anatomical priors from atlas

- To specify number of paths to sample (default: 7500)
  ```
  set nsample = 10000
  ```