TRACULA:
Principles and usage

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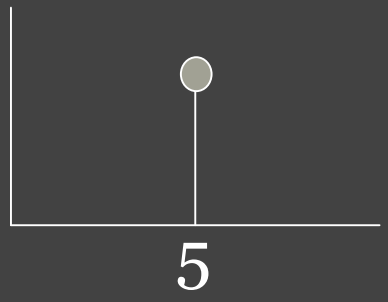
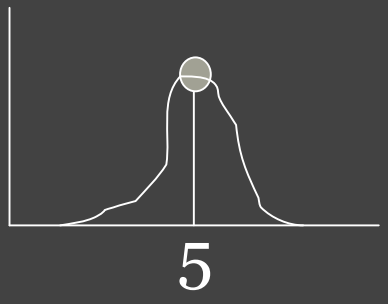
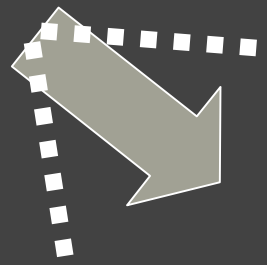
Deterministic vs. probabilistic

- Deterministic methods give you an estimate of model parameters

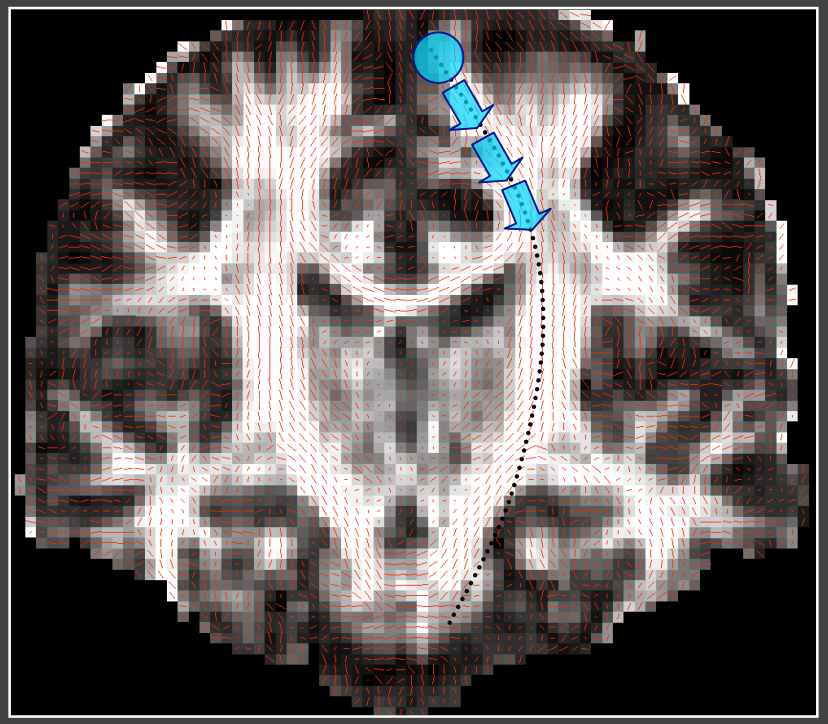


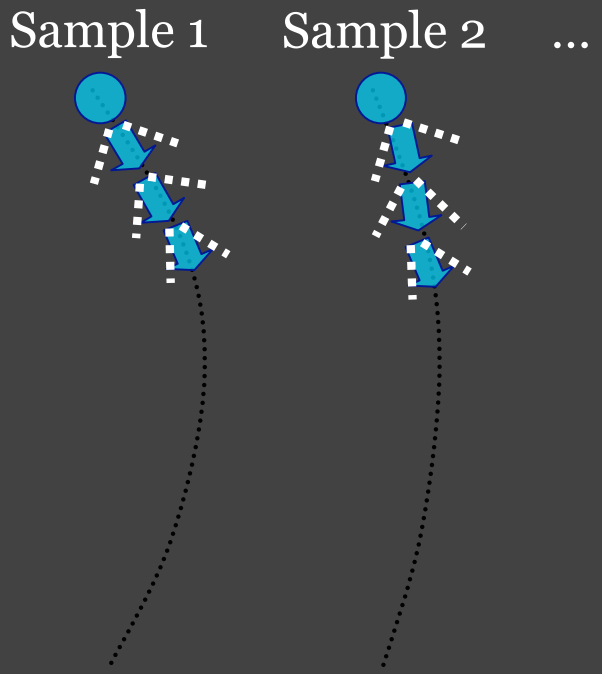
- Probabilistic methods give you the uncertainty (probability distribution) of the estimate





Deterministic vs. probabilistic

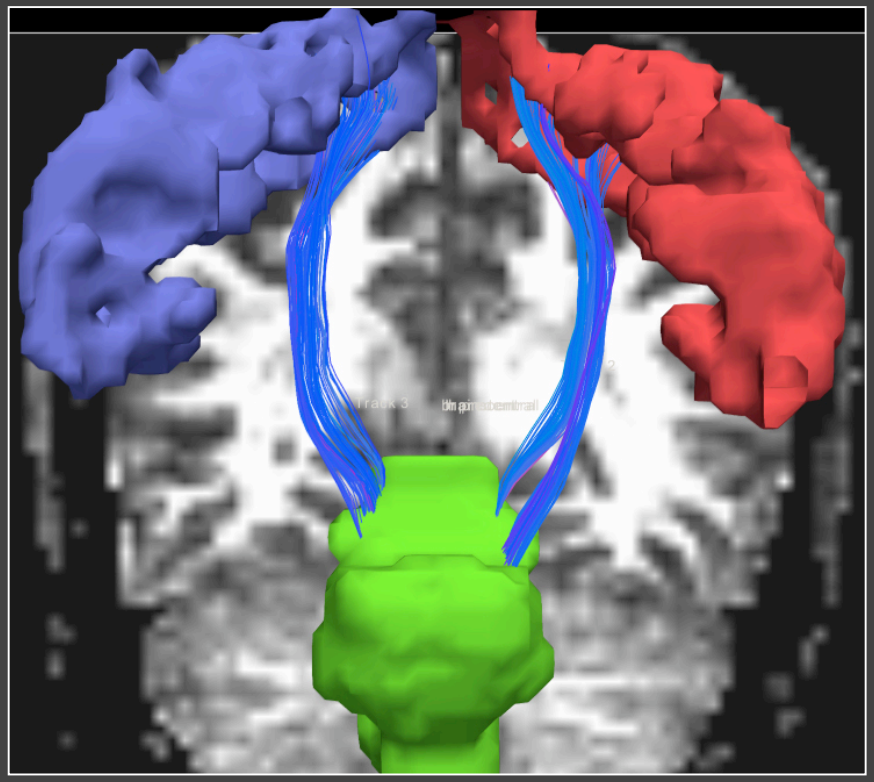


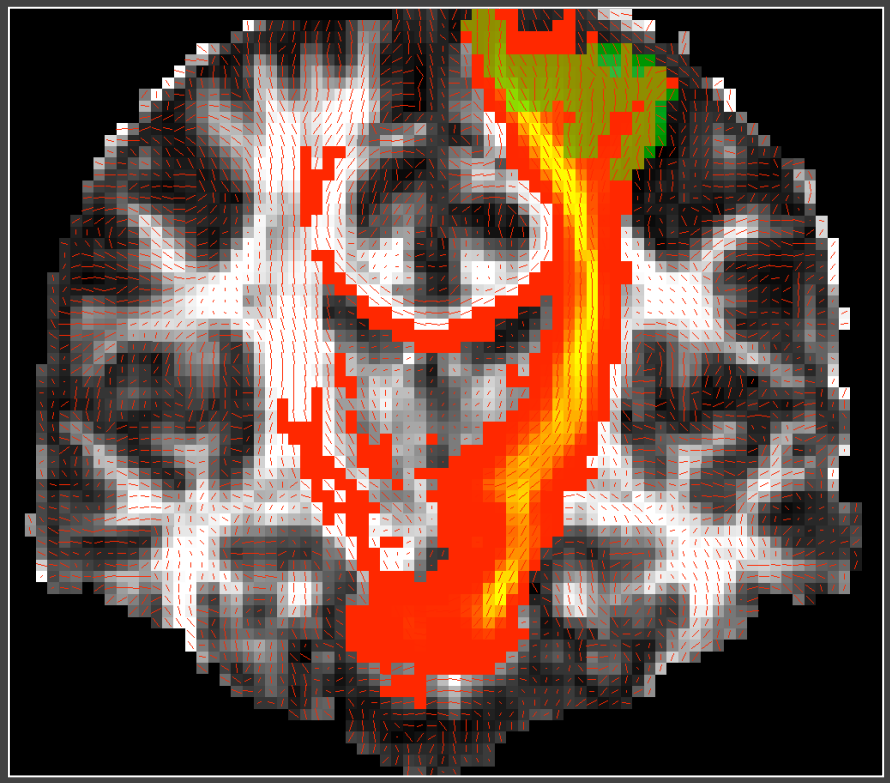


Deterministic tractography:
One streamline per seed voxel

Probabilistic tractography:
Multiple streamline samples per seed voxel (drawn from probability distribution)

Deterministic vs. probabilistic





Deterministic tractography:

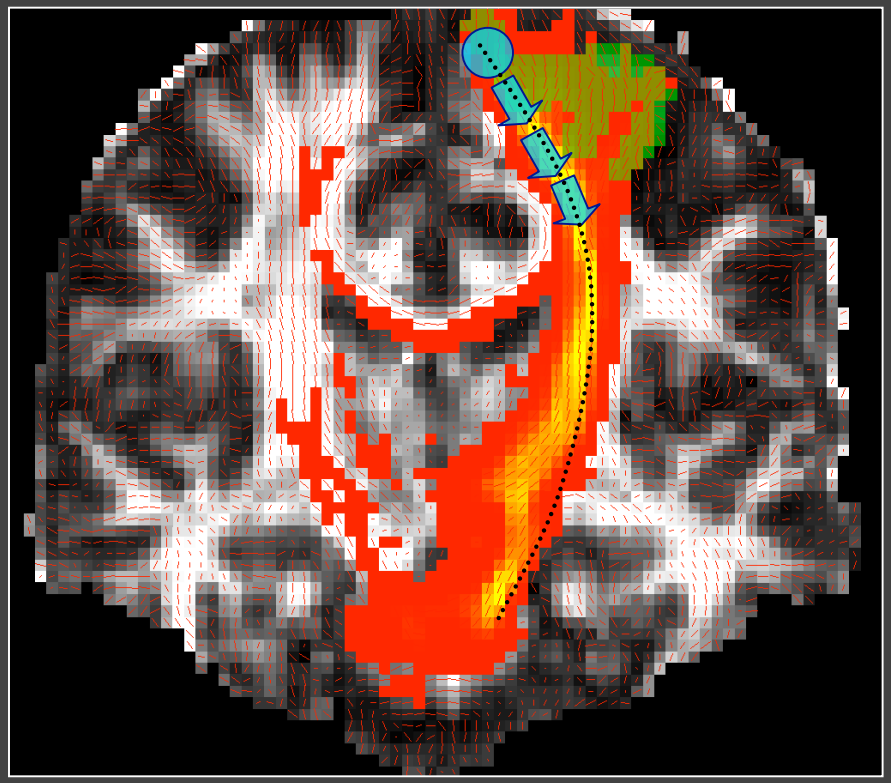
One streamline per seed voxel

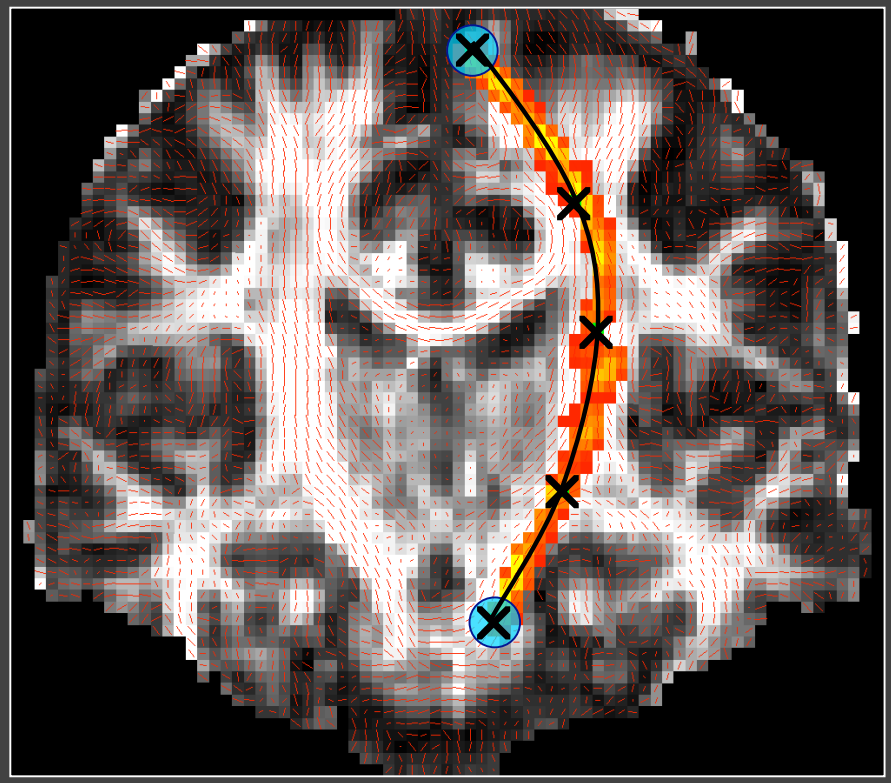
Probabilistic tractography:

A probability distribution

(sum of all streamline samples from all seed voxels)

Local vs. global





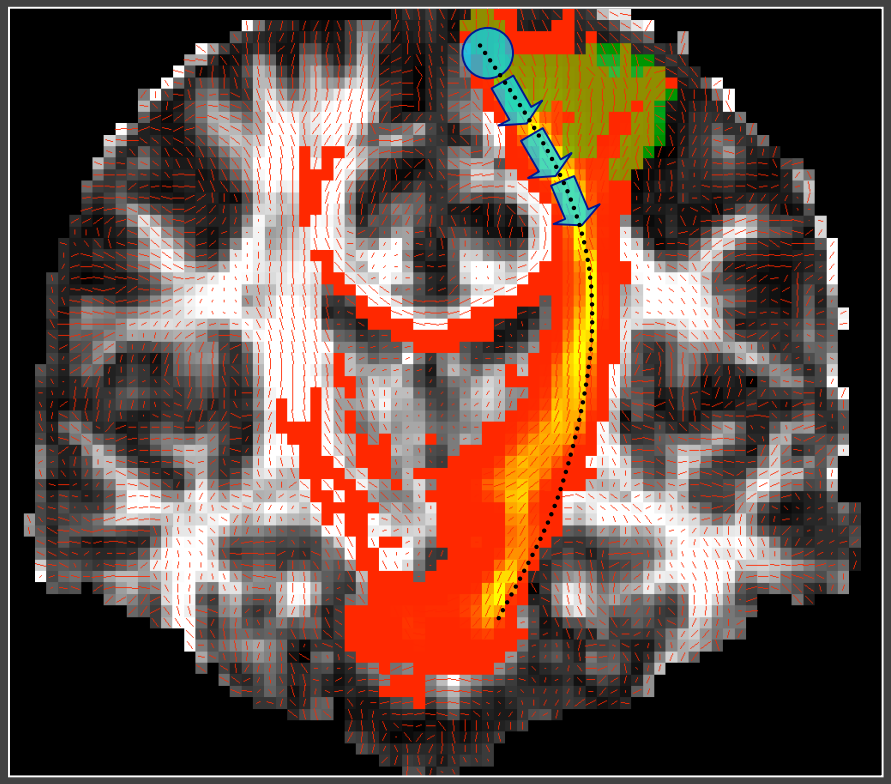
Local tractography:

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

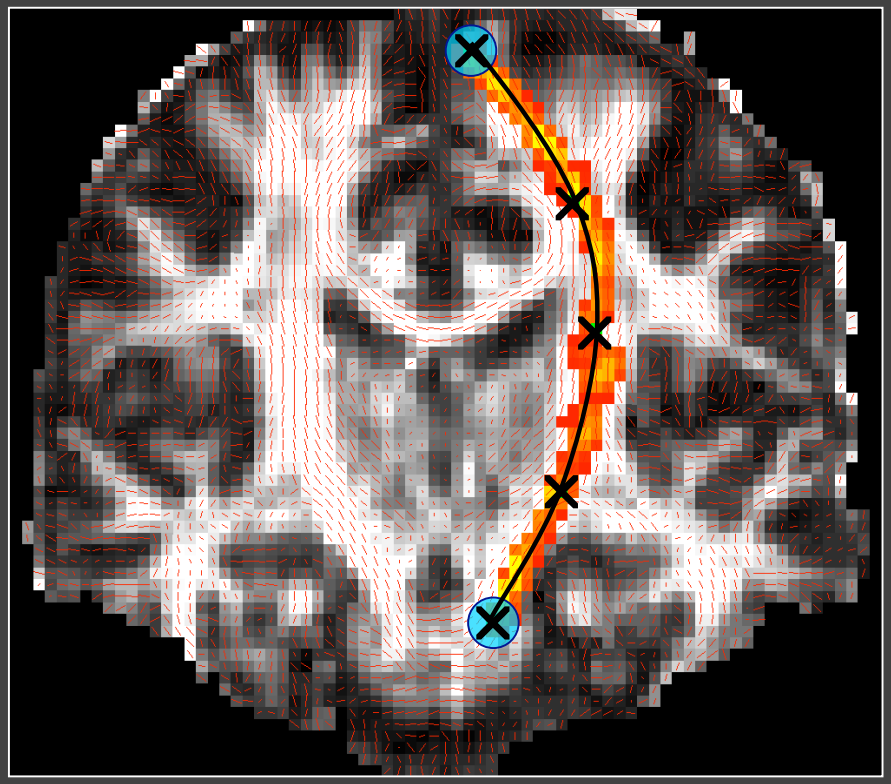


- Best suited for exploratory study of connections

- 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.*, pathaway 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

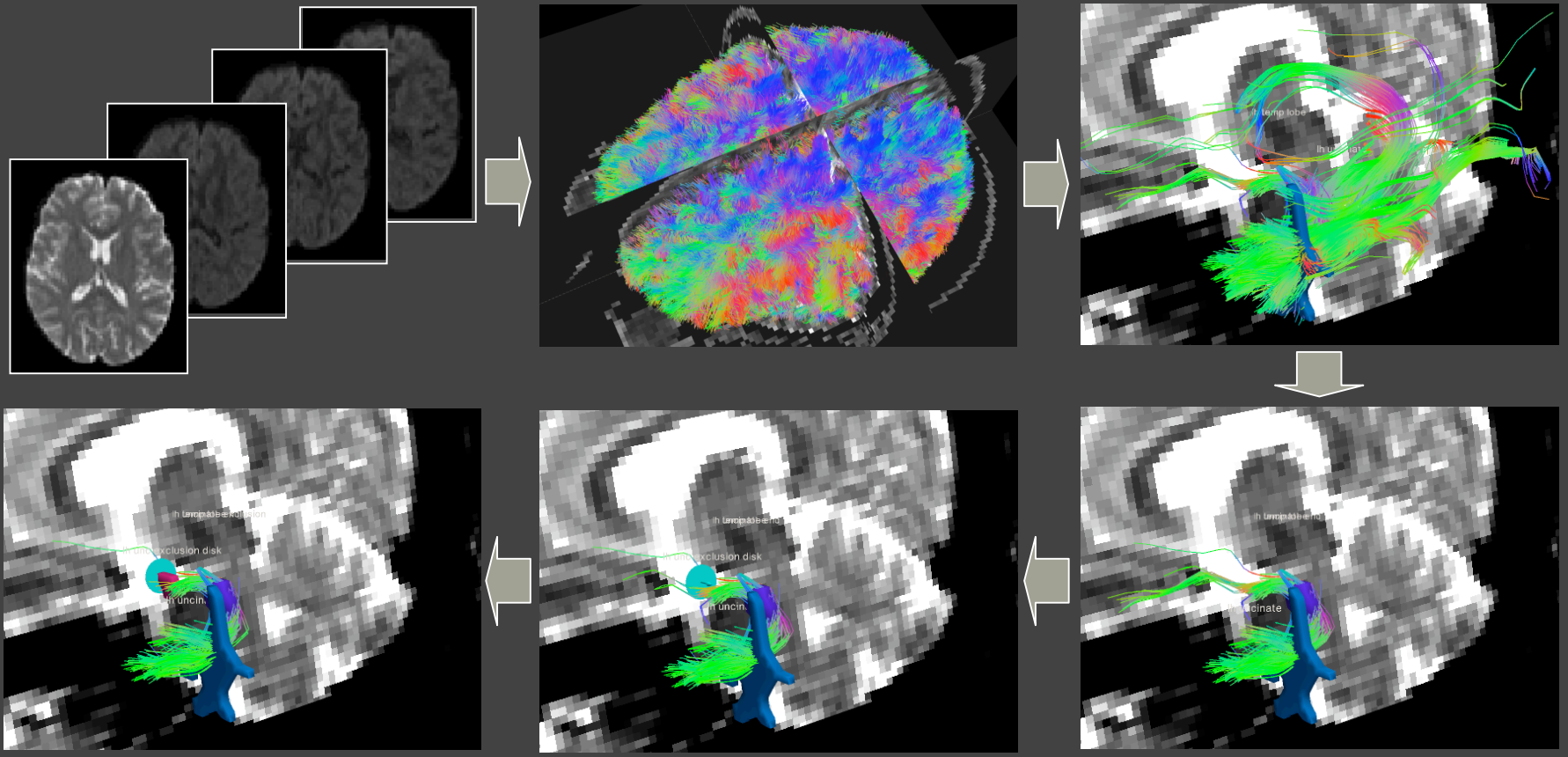
TRACULA

- 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

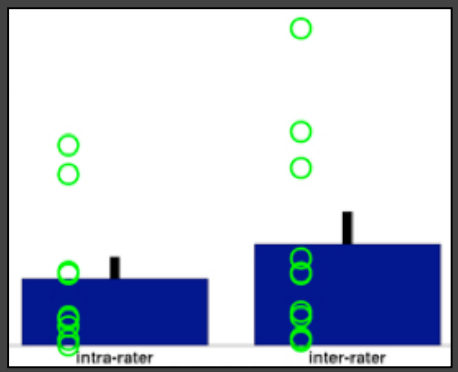
- Get whole-brain tract solutions, edit manually
- Use knowledge of anatomy to isolate specific pathways



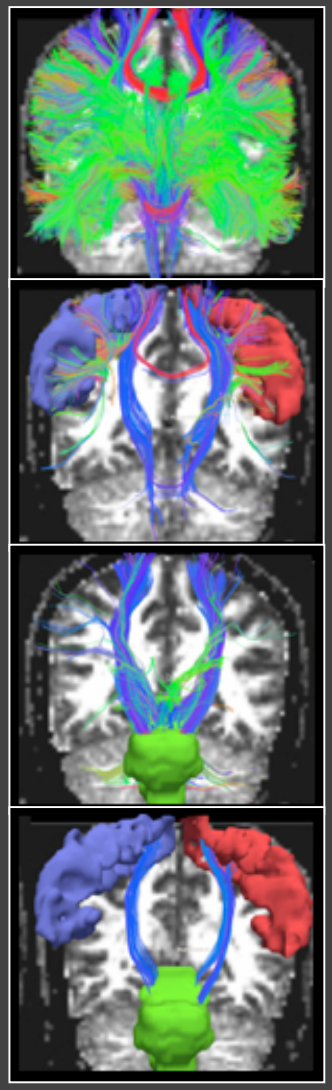
White-matter pathway atlas

- 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

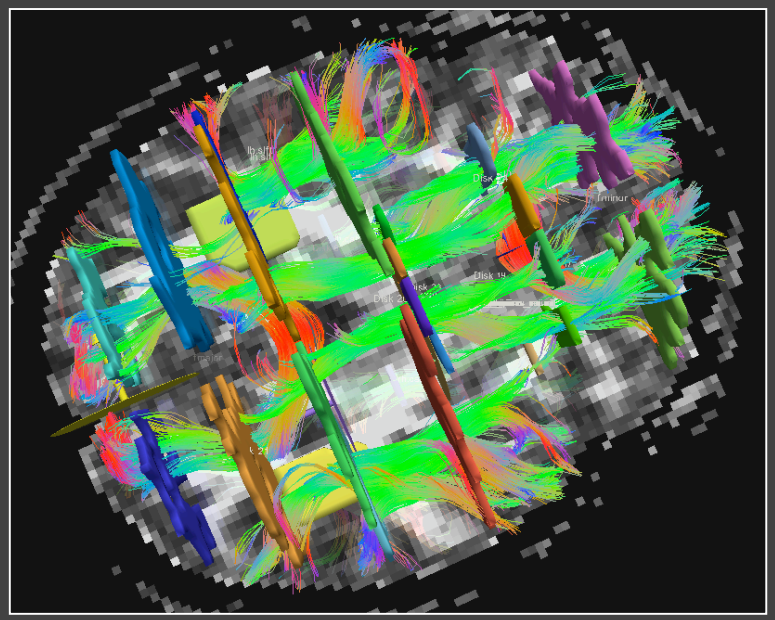


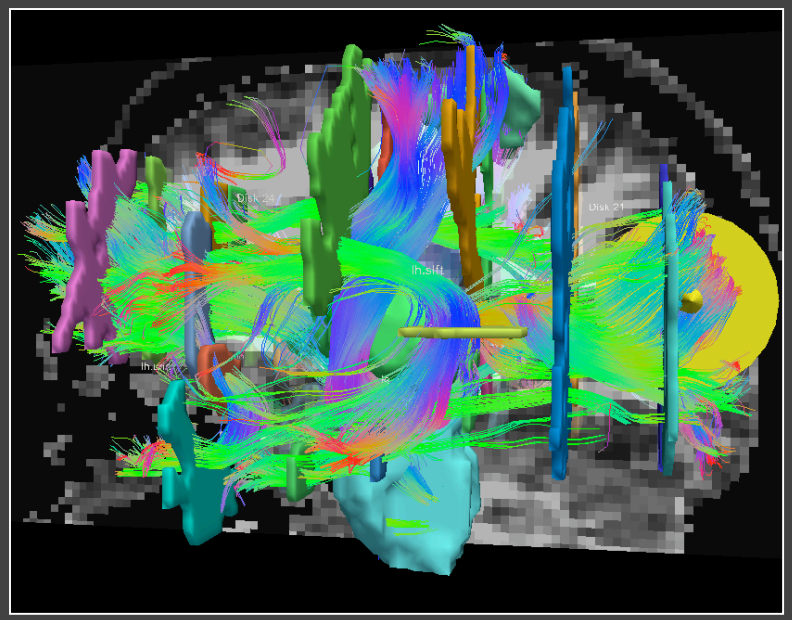
Intra/inter-rater errors:
1mm/2mm on average



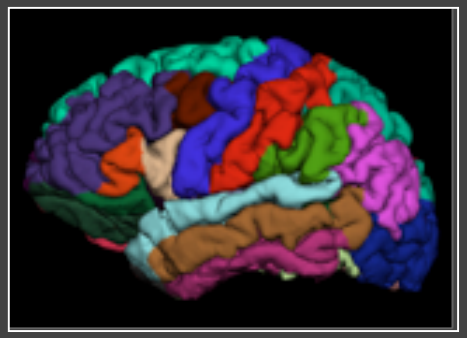
White-matter pathway atlas

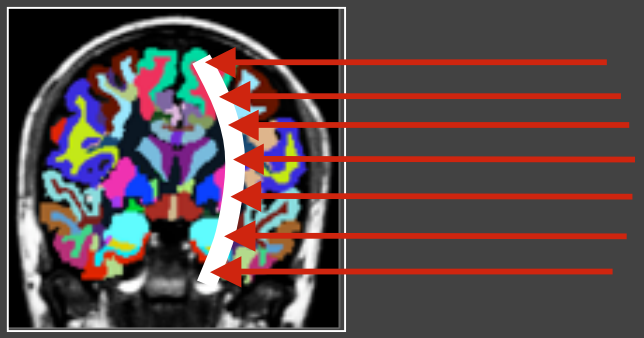
- Manual labeling of paths in training subjects performed in Trackvis





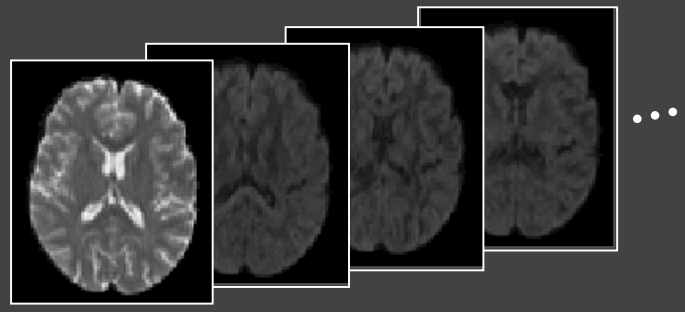
- Anatomical segmentation maps of training subjects from FreeSurfer



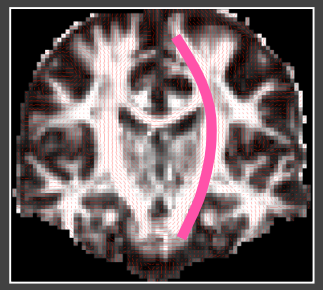


Probabilistic model

Have image data $\boldsymbol{Y}$



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 $\boldsymbol{Y}$

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

  - $p(\boldsymbol{Y} \mid \mathcal{F})$: Uncertainty due to imaging noise

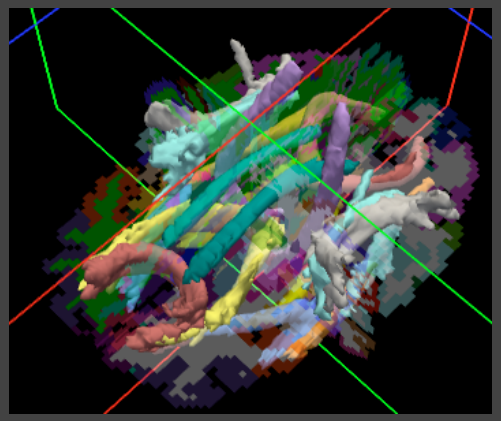
    Fit of pathway orientation to ball-and-stick model parameters [Jbabdi *et al.*, '07]
  - $p(\mathcal{F})$: Uncertainty due to anatomical variability

    Fit of pathway to prior anatomical knowledge from training set [Yendiki *et al.*, '11]

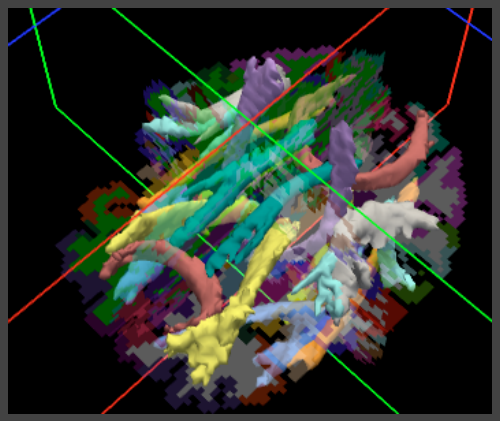
Schizophrenia study

Data courtesy of Dr. Randy Gollub and MIND Institute

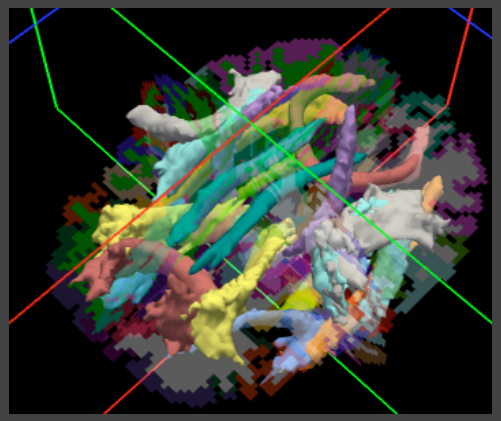
- Reconstruct pathways in 34 SZ patients and 23 healthy controls



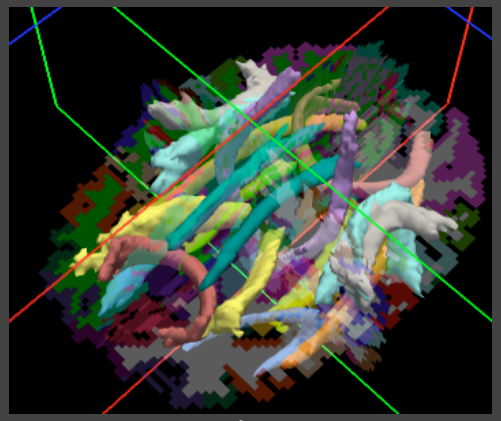
Control 1



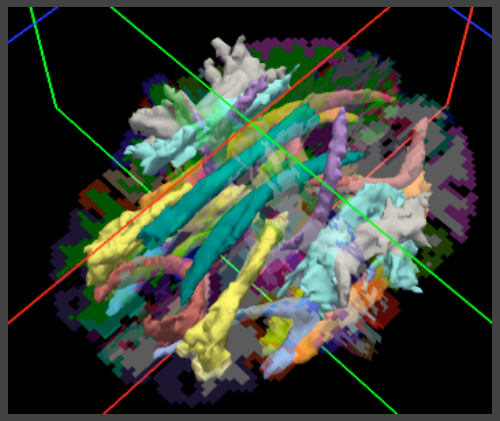
Control 2



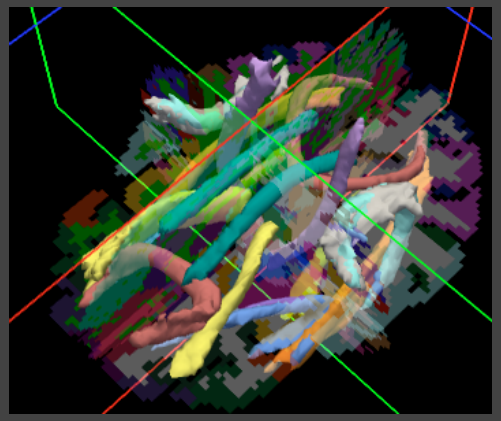
Control 3



Patient 1



Patient 2

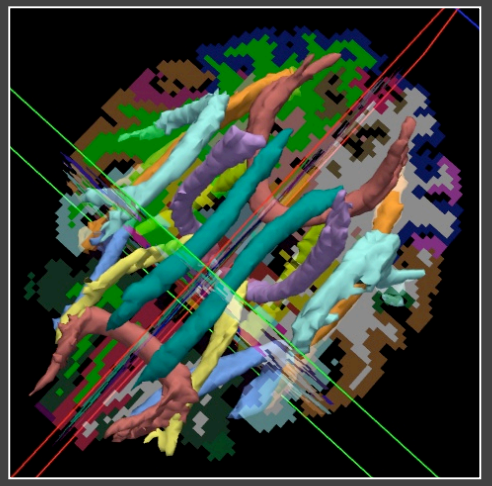


Patient 3

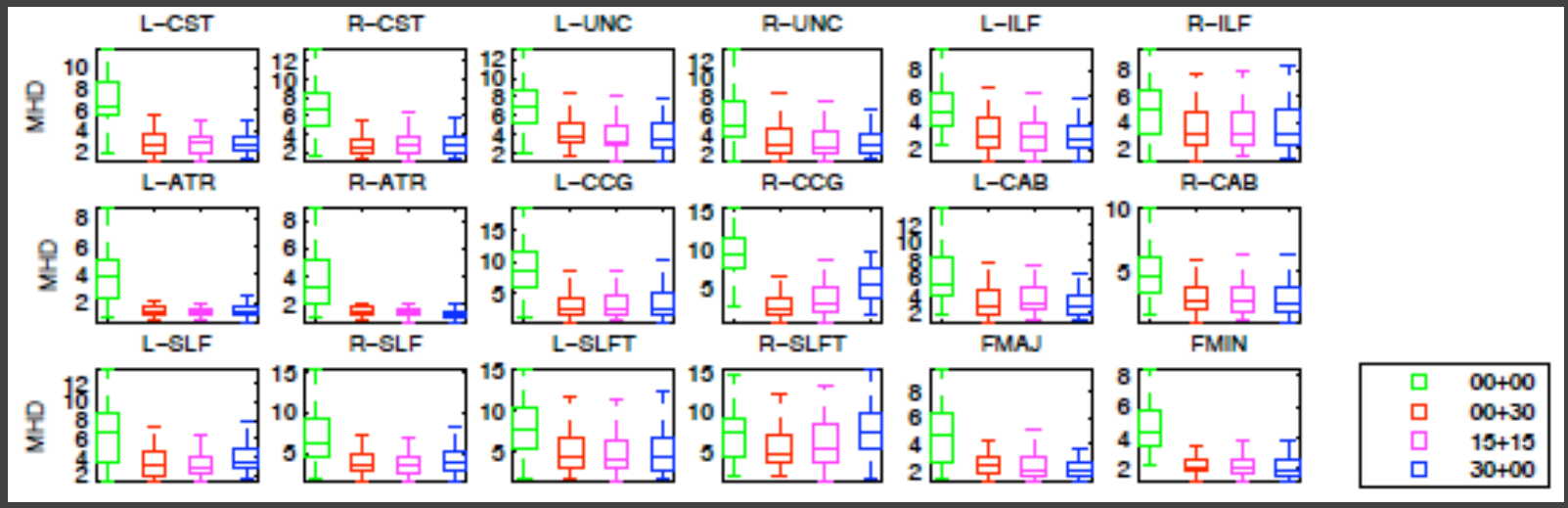
Schizophrenia study

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:

```
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 -prep -c dmrirc
```

- Includes the following steps:
  - Image corrections: `-corr`
  - NEW: Quality assessment : `-qa`
  - Intra-subject registration (DWI to T1) : `-intra`
  - Inter-subject registration (T1 to template) : `-inter`
  - Anatomical masks and labels : `-mask`
  - Tensor fit : `-tensor`
  - Anatomical priors : `-prior`
- Can do some of the steps only (assuming previous steps have been done):
  - `trac-all -corr -qa -c dmrirc`
- Or exclude some of the steps (assuming they have been done previously):
  - `trac-all -prep -nocorr -noqa -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

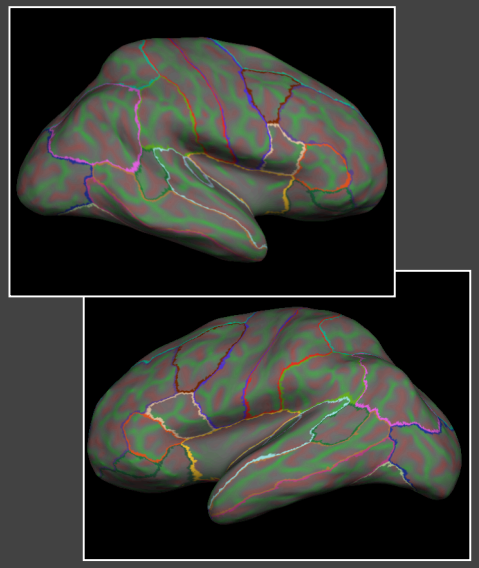
```
trac-all -intra -c dmrirc
```

- Register the individual DWI to the individual T1
- Option 1: `set doregflt = 1`
  - Affine registration with `flirt`
- Option 2: `set doregbbr = 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
```

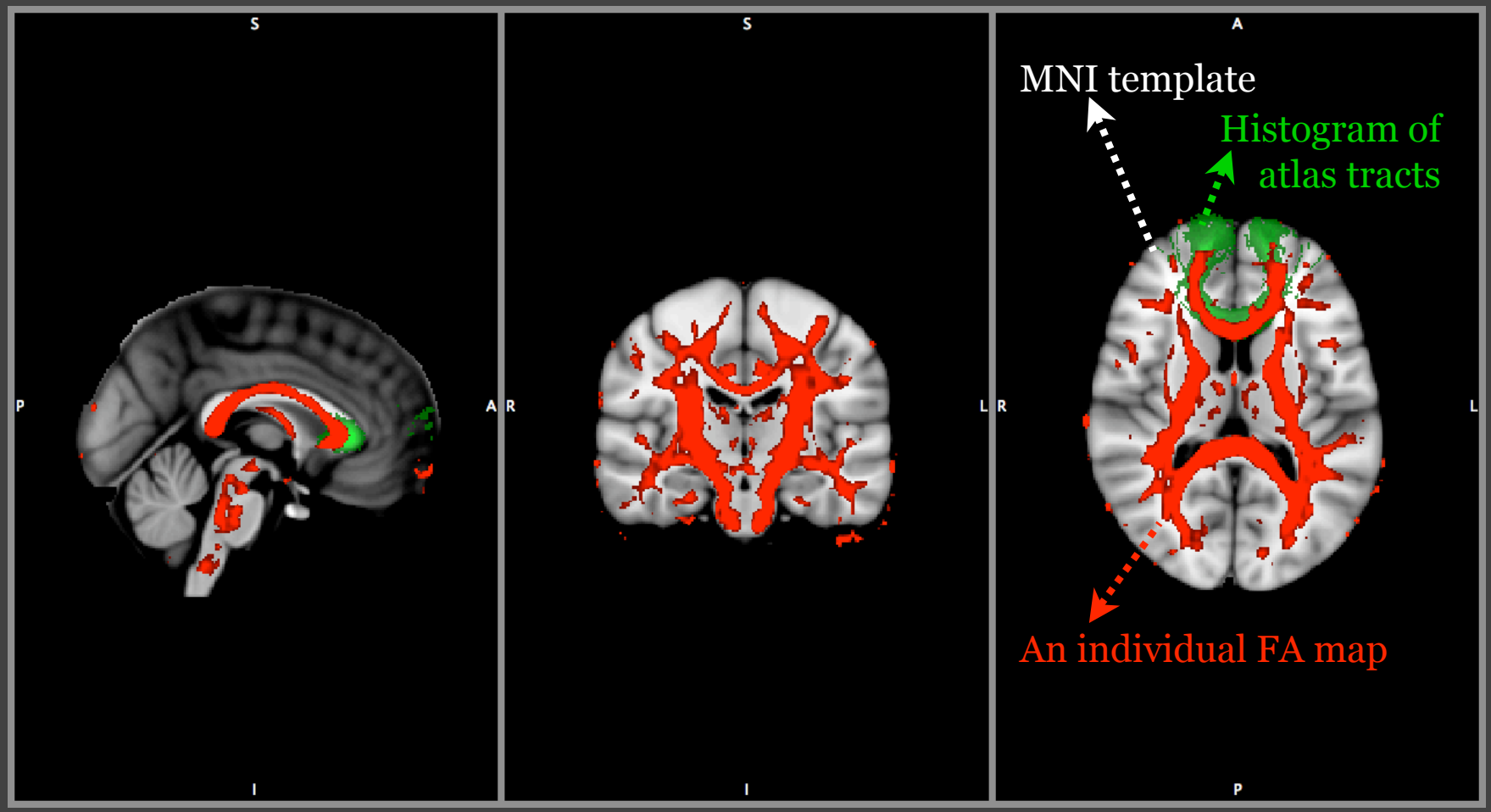
- Register the individual T1 to a common template space
- Option 1: `set doregmni = 1`
  - Affine registration with `flirt`
  - By default registers to MNI template (avg 152)
  - Target template image can be specified with:
    `set mnitemp = …`
- Option 2: `set doregcvs = 1`
  - Non-linear registration 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`

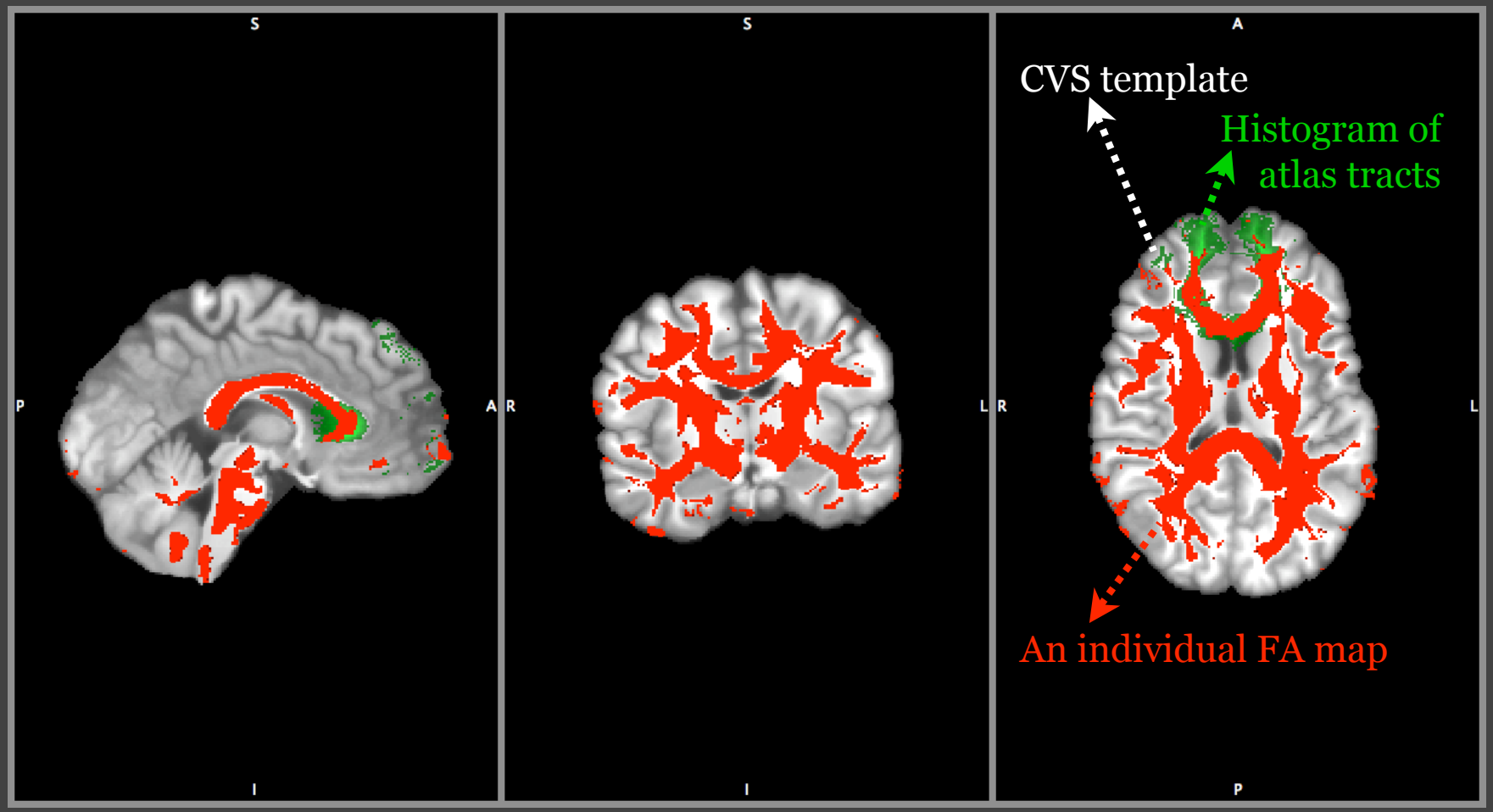
Inter-subject registration: MNI

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
```

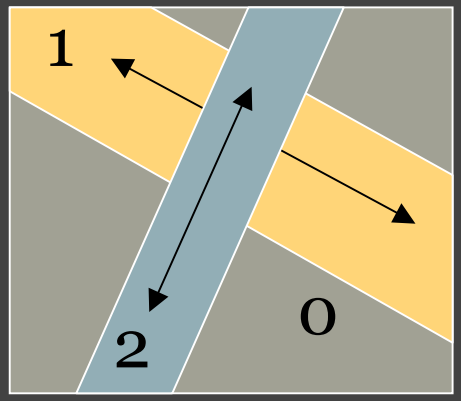
- Computes anatomical priors from tract atlas
- By default, the 33 subjects provided with TRACULA are used, but this can be changed:
  ```
  set trainfile = $FREESURFER_HOME/trctrain/trainlist.txt
  ```
- To process only a subset of the 18 pathways:
  ```
  set pathlist = (lh.cst_AS rh.cst_AS)
  ```
- 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
```