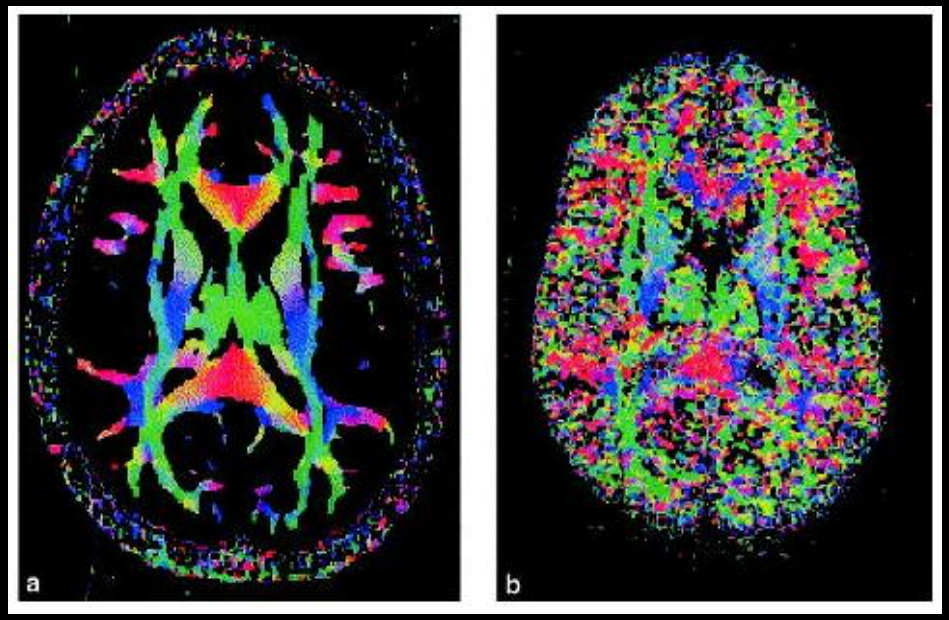
Lecture 5

DIFFUSION TENSOR IMAGING

Diffusion Tensor Imaging (DTI)

- Single Tensor estimation



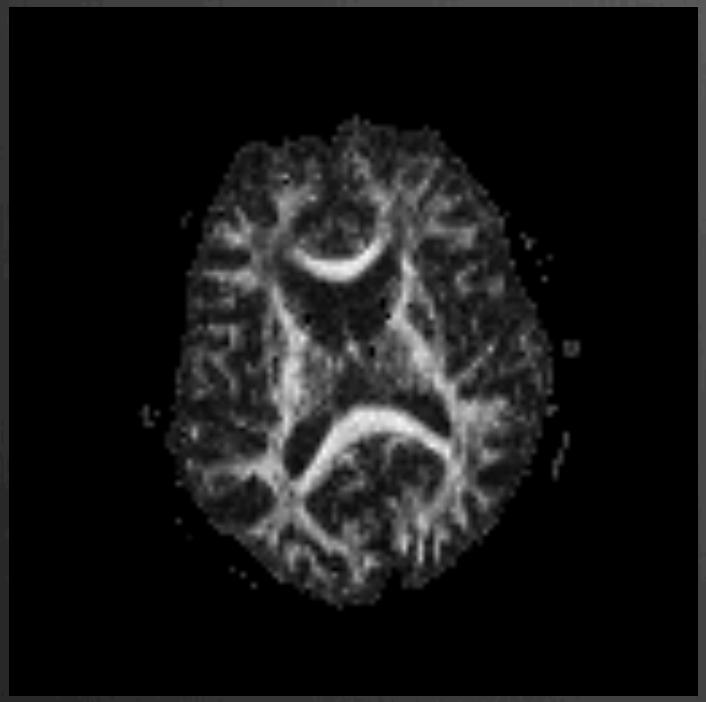
- Estimation of direction is severely affected in the presence of noise*

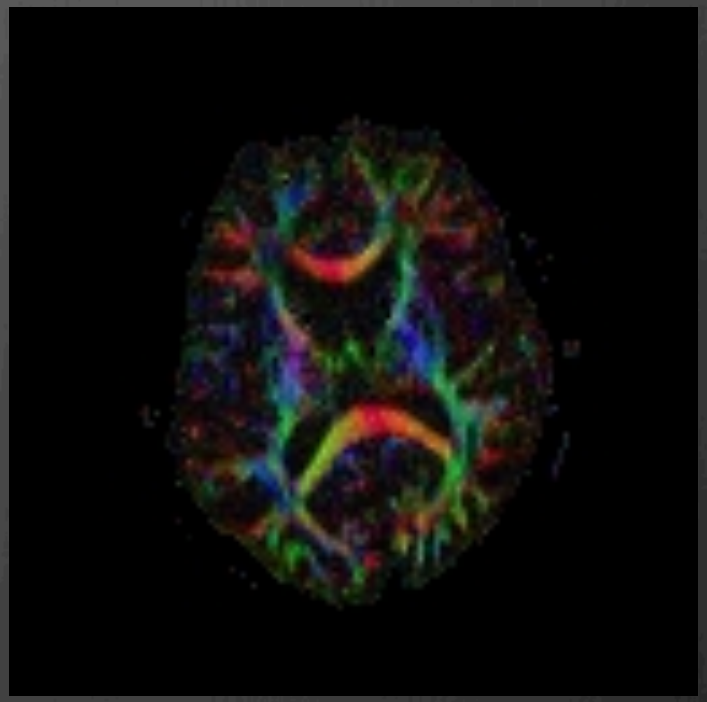
X. Ma, Y. Kadah, S. LaConte, and X. Hu, Magnetic Resonance in Medicine, 2004.

Source of noise in diffusion MRI

- Statistical Noise
  - Magnetic Filed unhomogeneity
  - Eddy currents
  - Thermal Noise
  - background signals caused by precessing tissue magnetization.
- Systematic Noise
  - from a number of patient motion, such as respiration, vascular, and CSF pulsations;
  - receiver-coil or gradient-coil motion; aliasing; and data truncation (Gibbs) artifacts

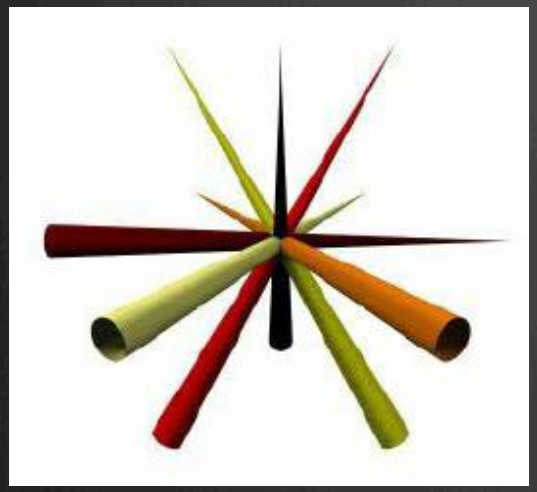
DTI :Anisotropy Maps



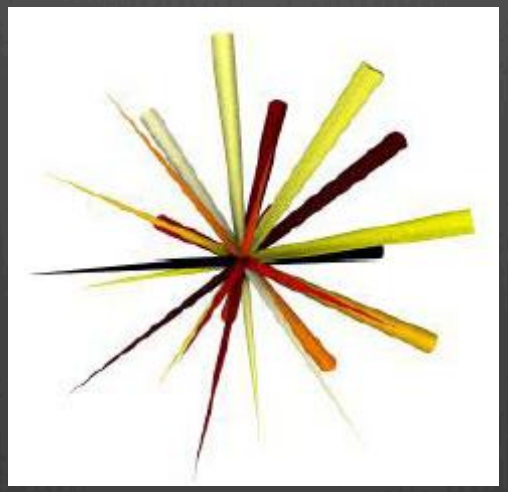


- Grayscale fractional anisotropy map: Lighter shade indicates greater anisotropy
- Color coded directional anisotropy map
  Colors indicates diffusivity along the main coordinate axis (x,y,z)
  (Green = anterior-posterior; red = right-left; blue= craniocaudal)

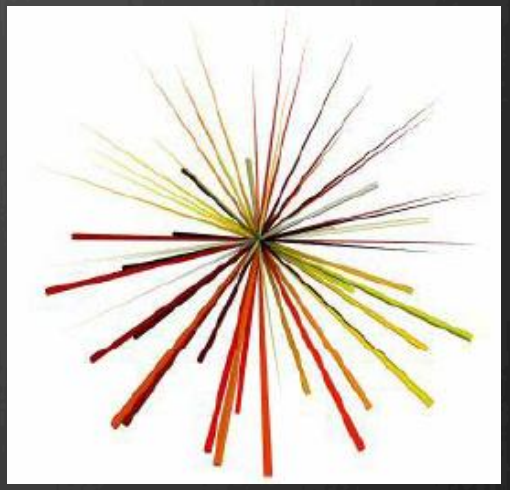
Different Gradient Directions



6 Directions

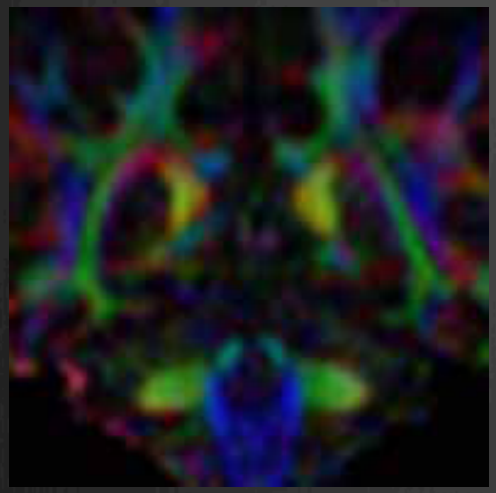


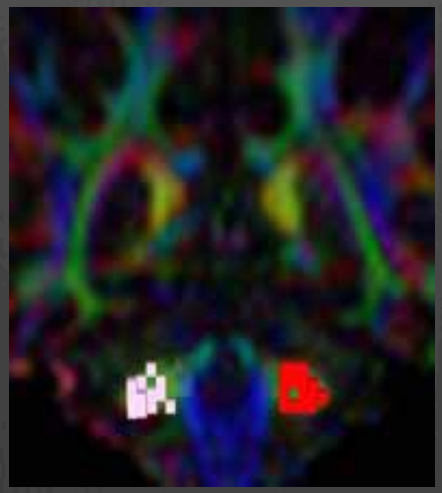
12 Directions

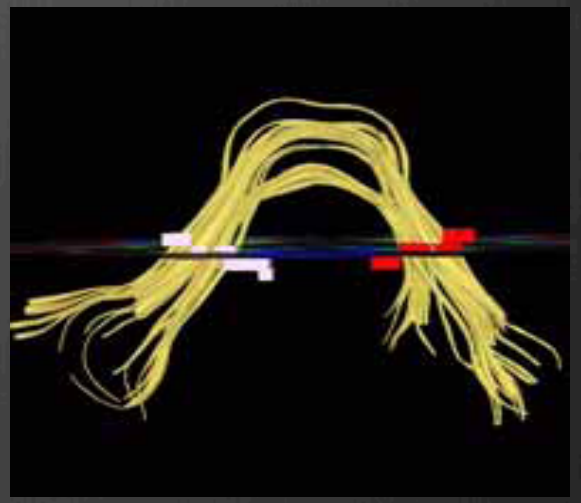


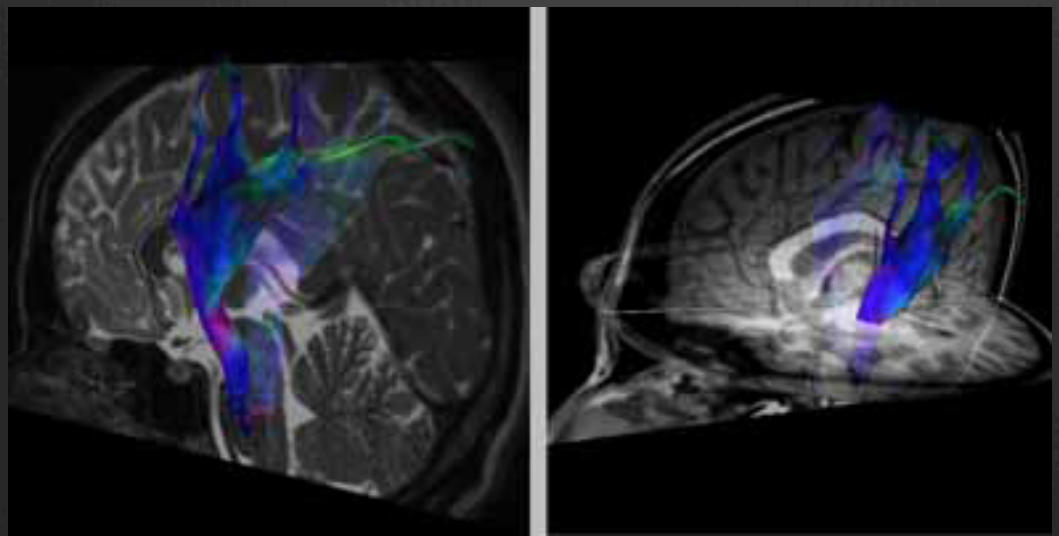
30 Directions

Fiber track (Additional)









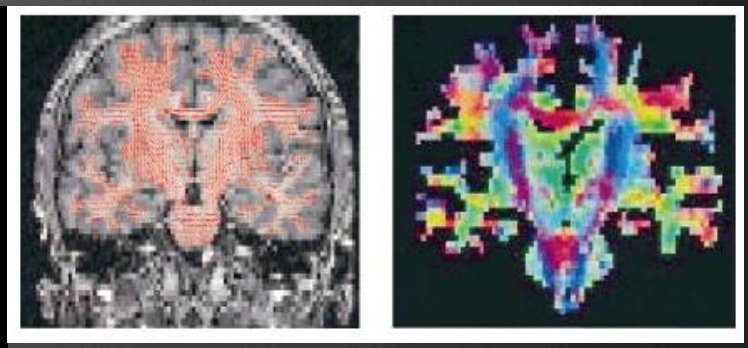
DTI Sequence

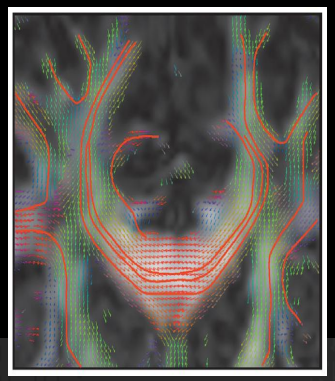
- Repeat the DWI sequence with gradients applied in a number of different directions
- From the contribution of all the different directions we can calculate the direction of diffusion as well as the relative rate (ADC)
- Areas with restricted diffusion will have a directional bias which is used to determine the direction of diffusion

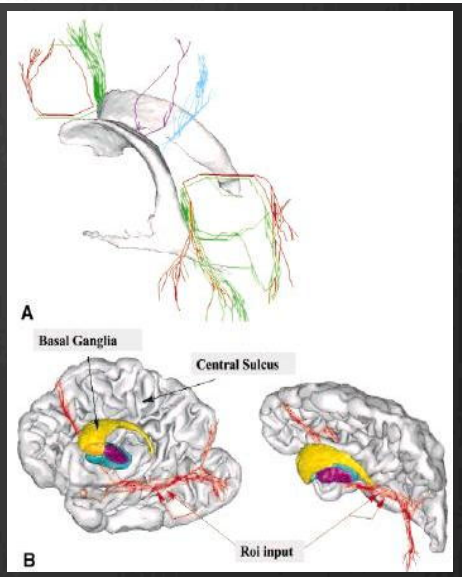
DTI-Based Connectivity Mapping

DTI-Based Connectivity Mapping

- Nerve fibers represent cylindrical-shaped physical spaces with membrane acting like a barrier
  - DT shows diffusion preference along axon
- Measuring the diffusing anisotropy, we can estimate the dominant direction of the nerve bundle passing through each voxel



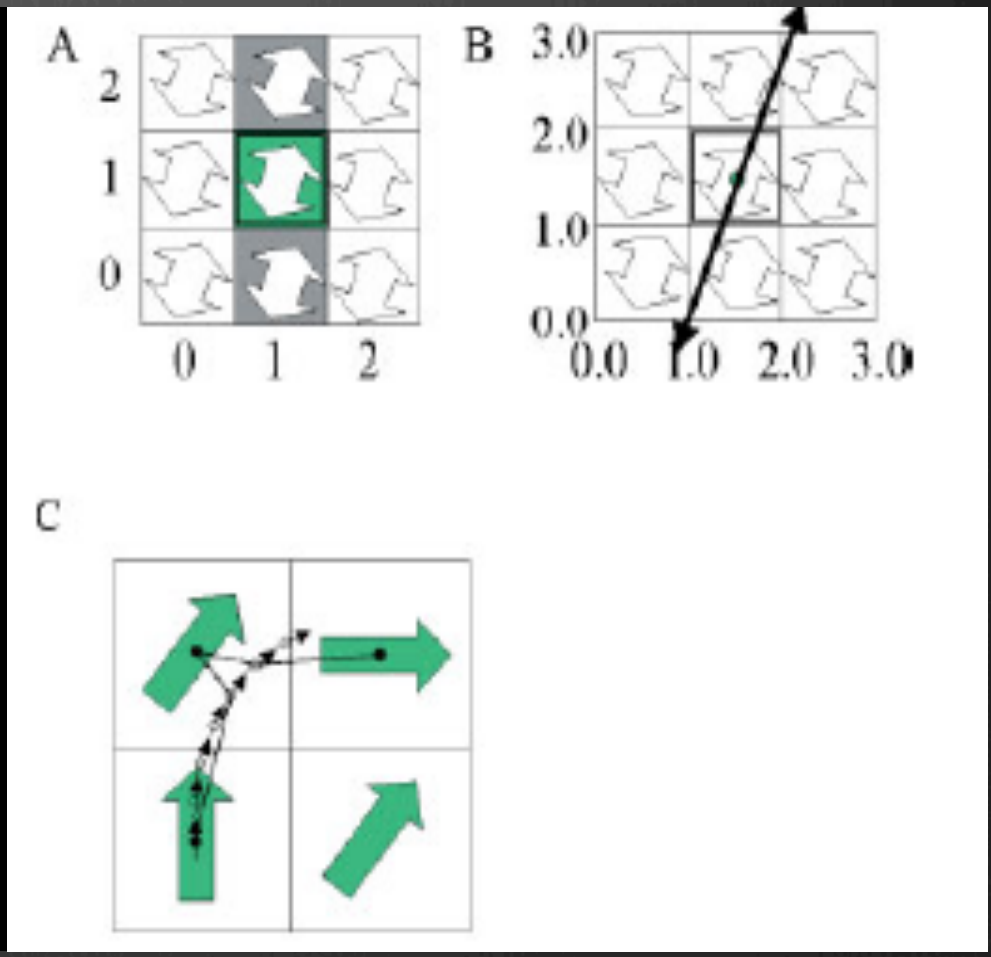




X. Ma, Y. Kadah, S. LaConte, and X. Hu, Magnetic Resonance in Medicine, 2004.

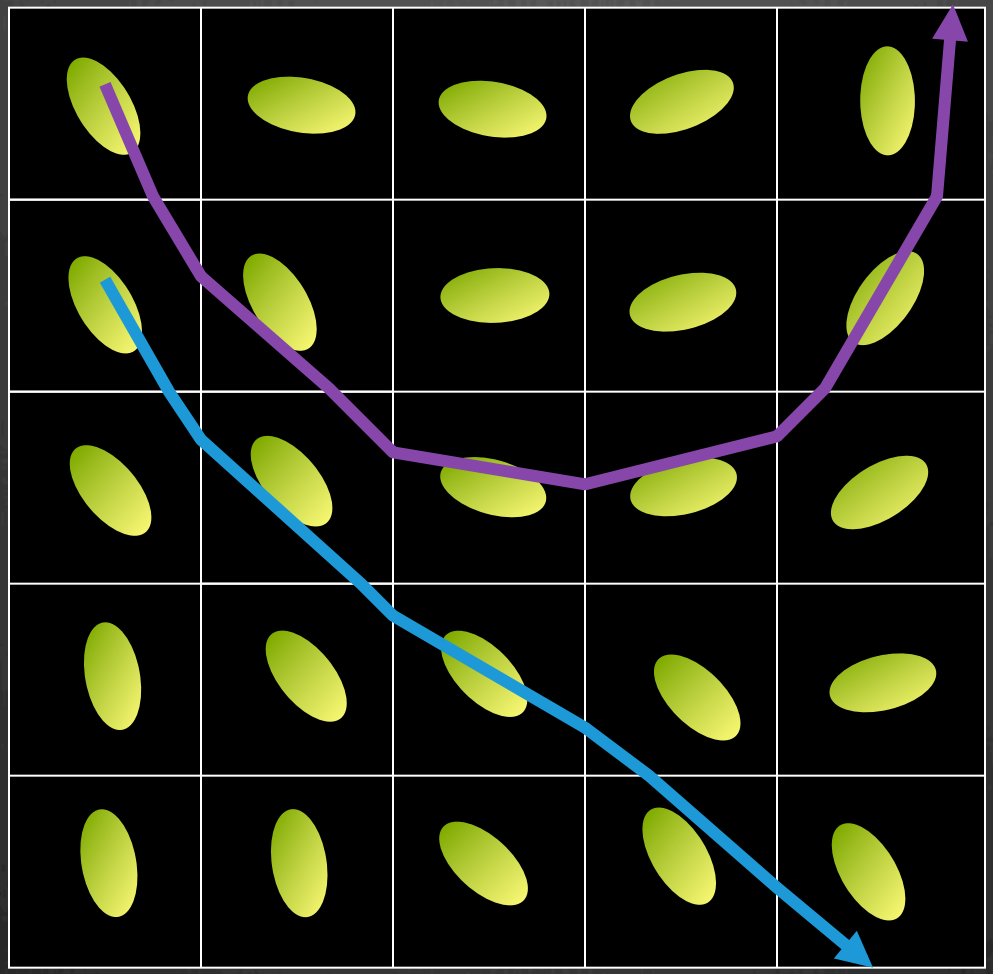
DTI-Based Connectivity Mapping*

- Line Propagation Algorithms.
- Global energy Minimization
  - Fast Marching Technique
  - Simulated annealing approach



S.. Mori et. al, NMR IN BIOMEDICINE, 2002.

Fiber Track Reconstruction



HBWL

Limitations*

- Inaccuracy of Single Tensor Estimation due to
  - Intravoxel Orientational Heterogeneity (IVOH).
  - Contribution from multiple tensors.
- Limited signal to noise Ratio.
- There may not be a single predominant direction of water diffusion.
- Afferent and efferent pathways of axonal fiber tracts cannot be judged.

*S.. Mori et. al, NMR IN BIOMEDICINE, 2002.

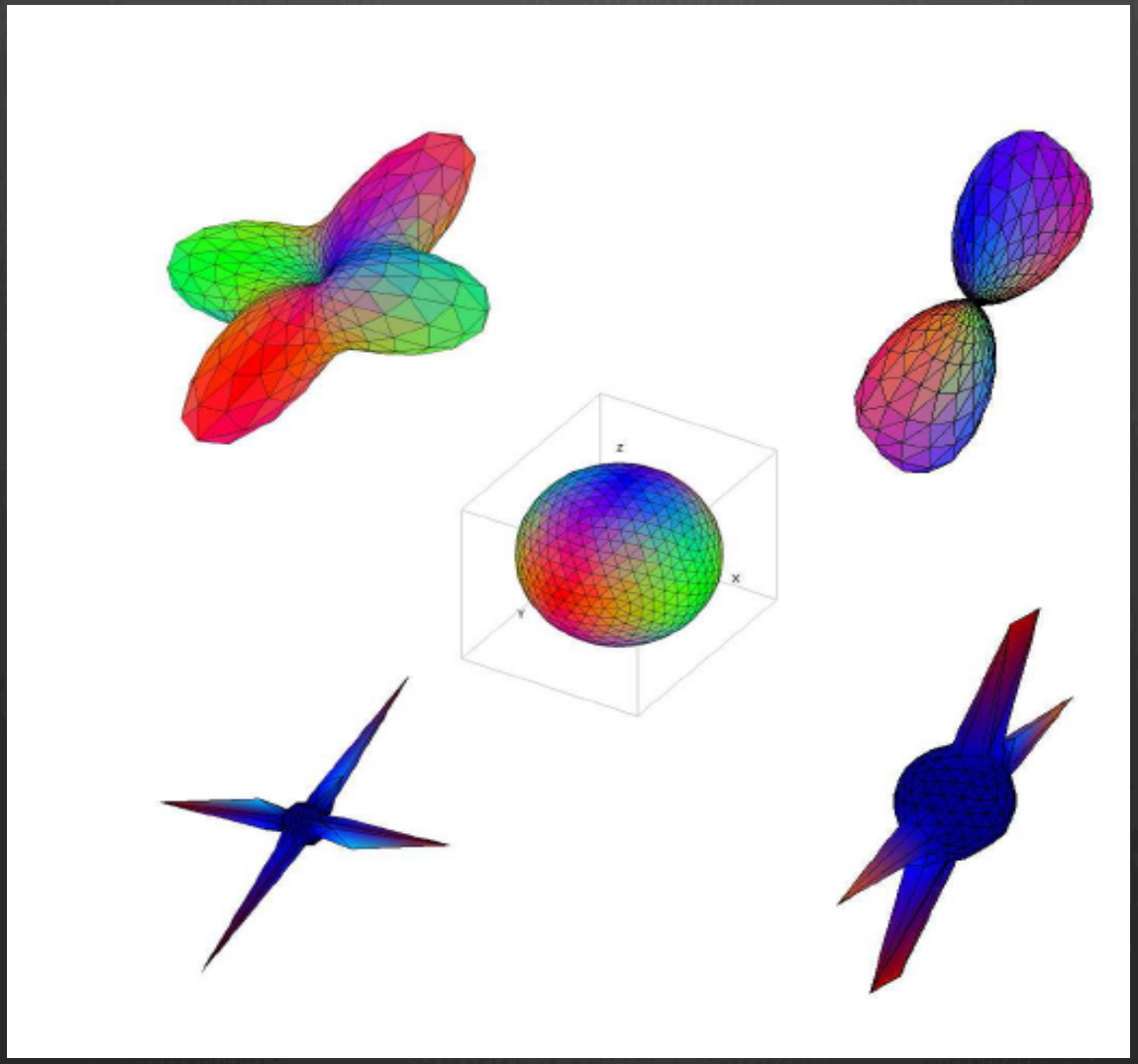
Problem Statement

- Partial voluming is common in practice
- Attenuation due to multi-component diffusion when applying a gradient defined by the diffusion direction is given by,

$$E(\vec{x}) = \sum_{i \in I} \alpha_i \cdot \exp\left(-b \cdot \vec{x}^T \cdot D_i \cdot \vec{x}\right)$$

- It is required to estimate the component tensor and their partial volume ratios
  - 13 unknown for a 2-component model without loss of generality.
  - Nonlinear equations unlike 1-component case

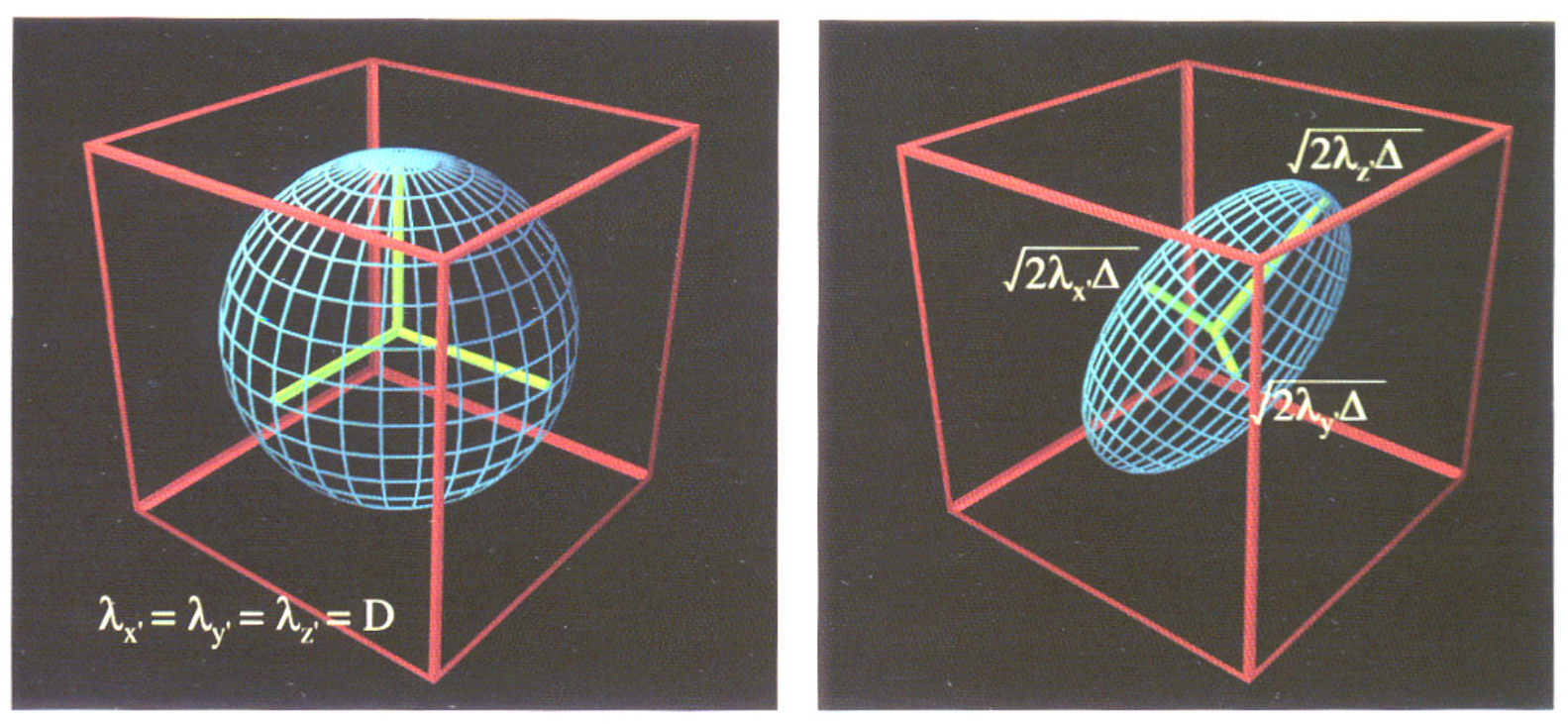
Orientation Distribution function



Research in DTI

- To develop Image denoising Algorithms diffusion Tensor MRI.
- To develop a technique that would allow multiple diffusion components to be computed within a given voxel.
- To predict the behavior of this technique under different conditions of SNR.
- Improve diffusion orientation distribution function.
- Probabilistic fiber tracking that satisfies the anatomical conditions

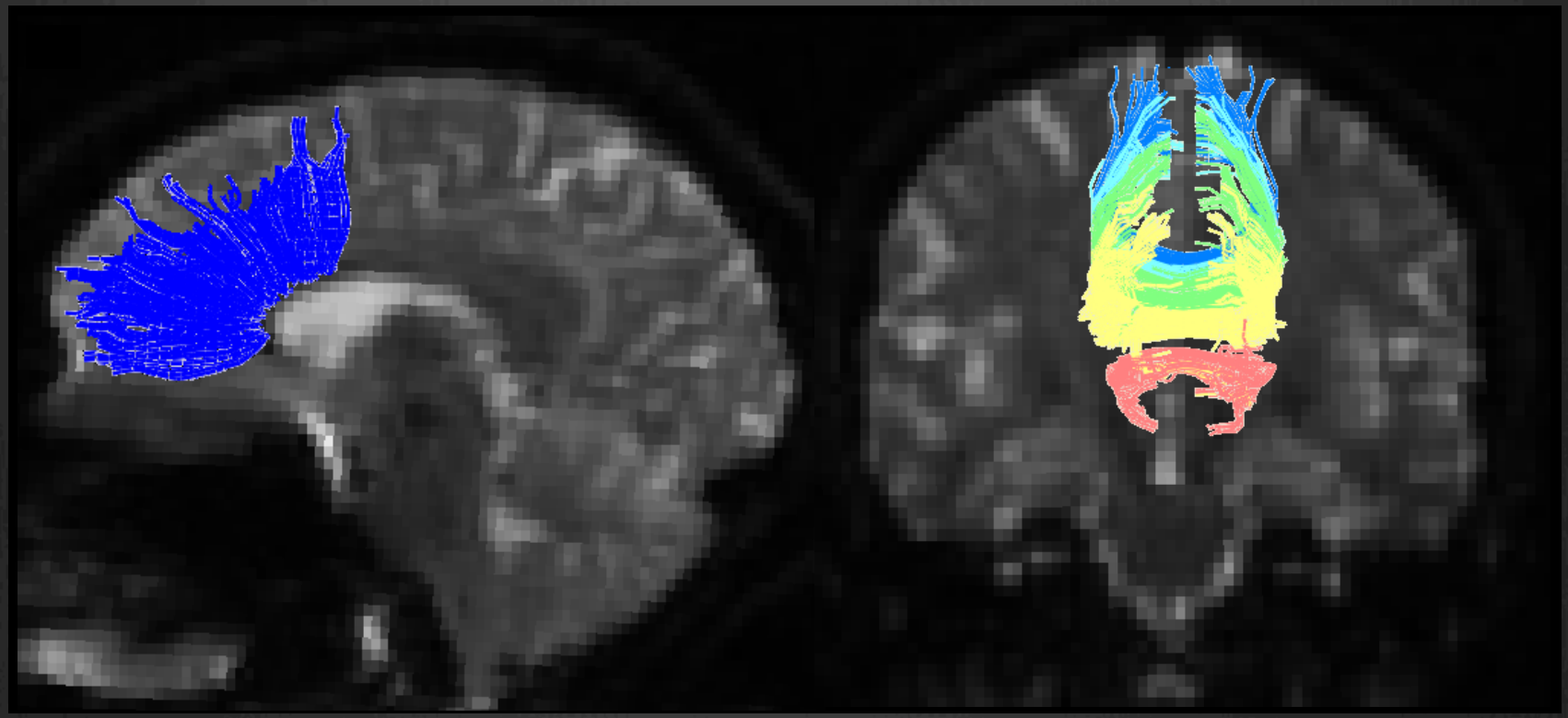
Tensor Model of Isotropy



Isotropic **Anisotropic**

DTI images

Structural Connectivity: Corpus Callosum Tracts



Talaraic Atlas

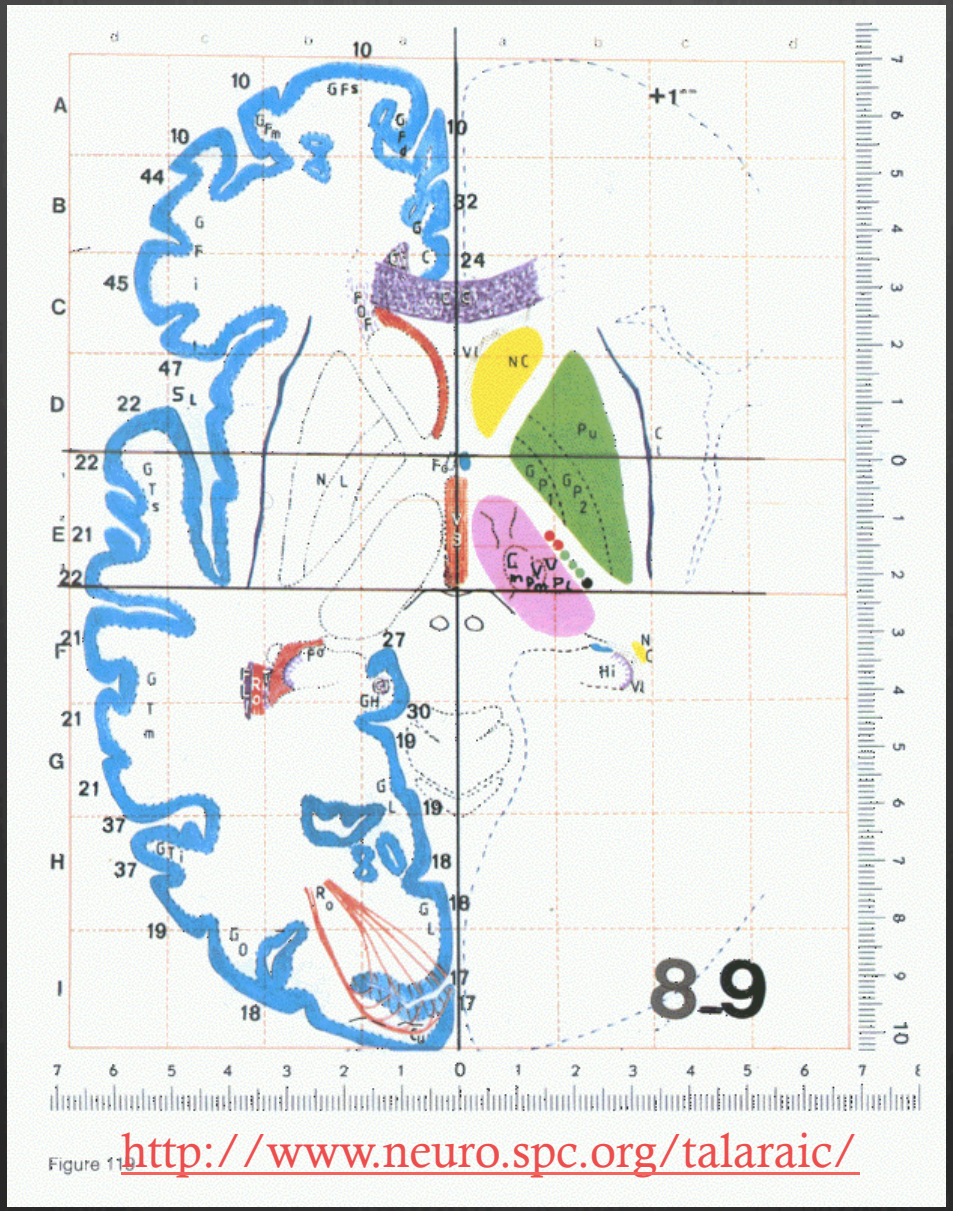
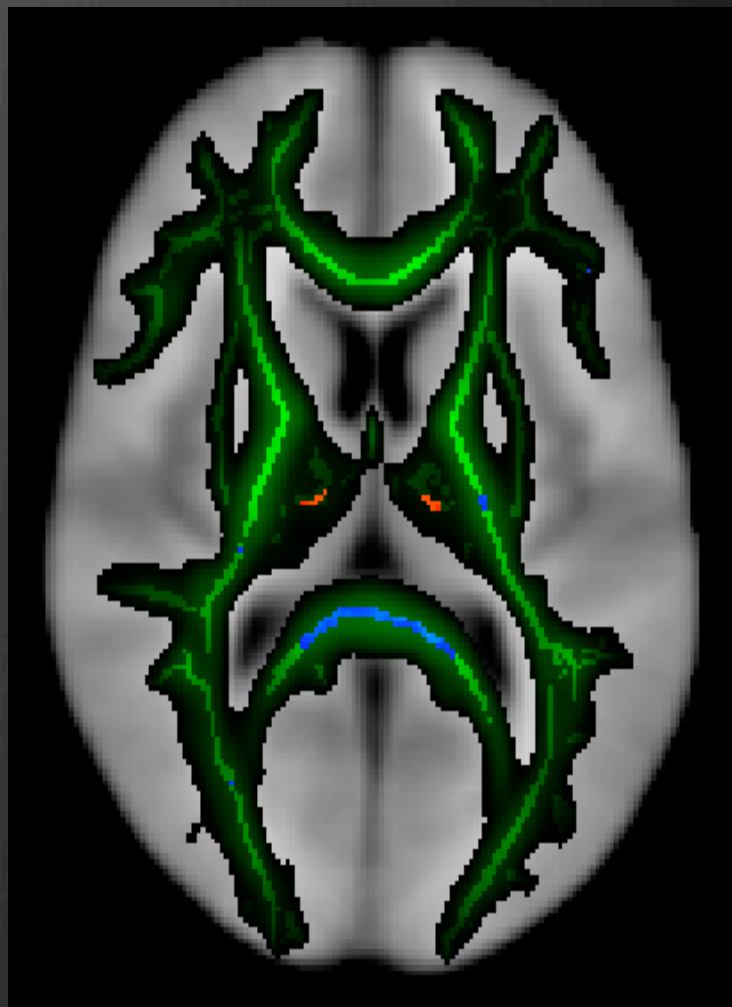


Figure 11

http://www.neuro.spc.org/talaraic/

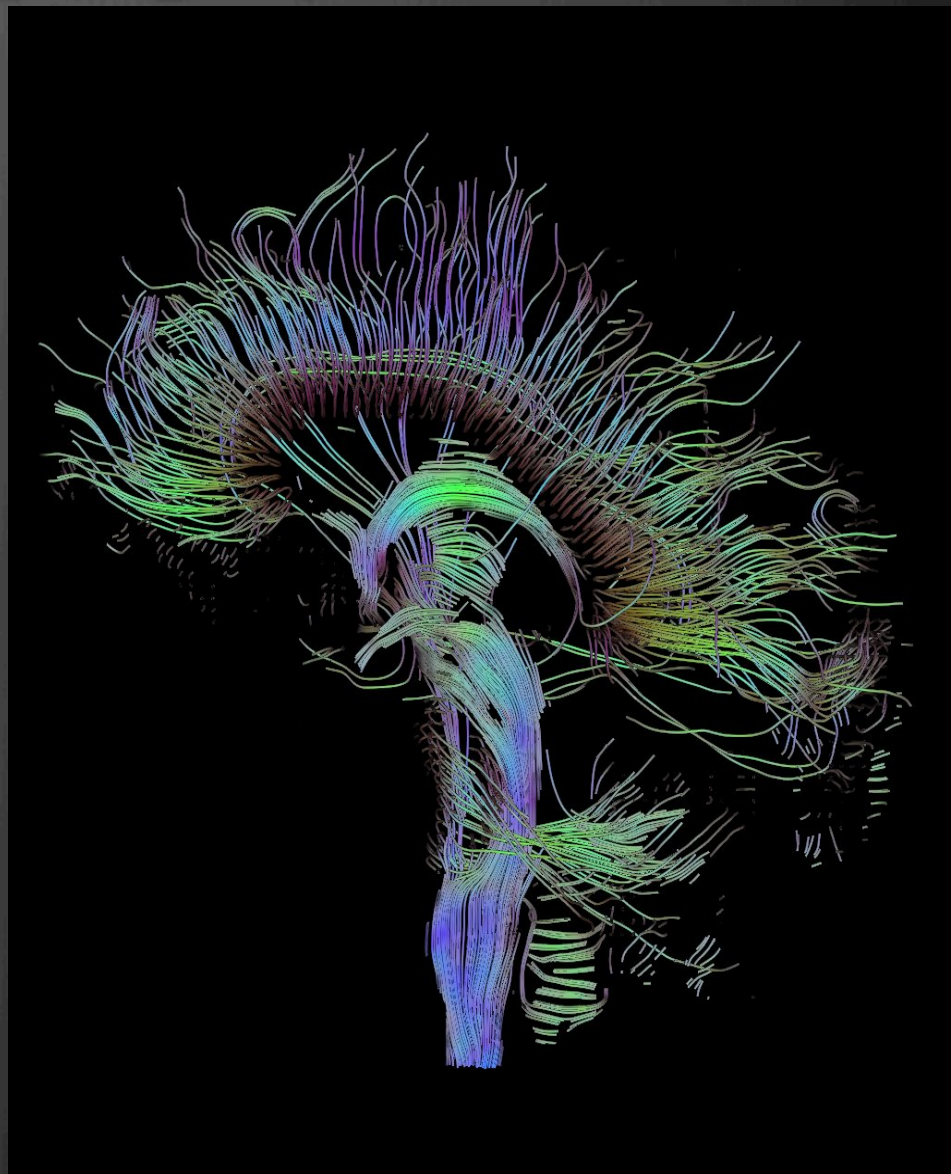
TBSS - Tract-Based Spatial Statistics

- TBSS is a FSL approach to conduct between group comparisons of DTI data.
- projects data onto group-mean tract skeleton, allowing voxelwise analysis
- addresses alignment problems unsolved by nonlinear registration
- Overview
  www.fmrib.ox.ac.uk/fsl/tbss/index.html
- Tutorial www.fmrib.ox.ac.uk/fslcourse/lectures/practicals/fdt/index.htm

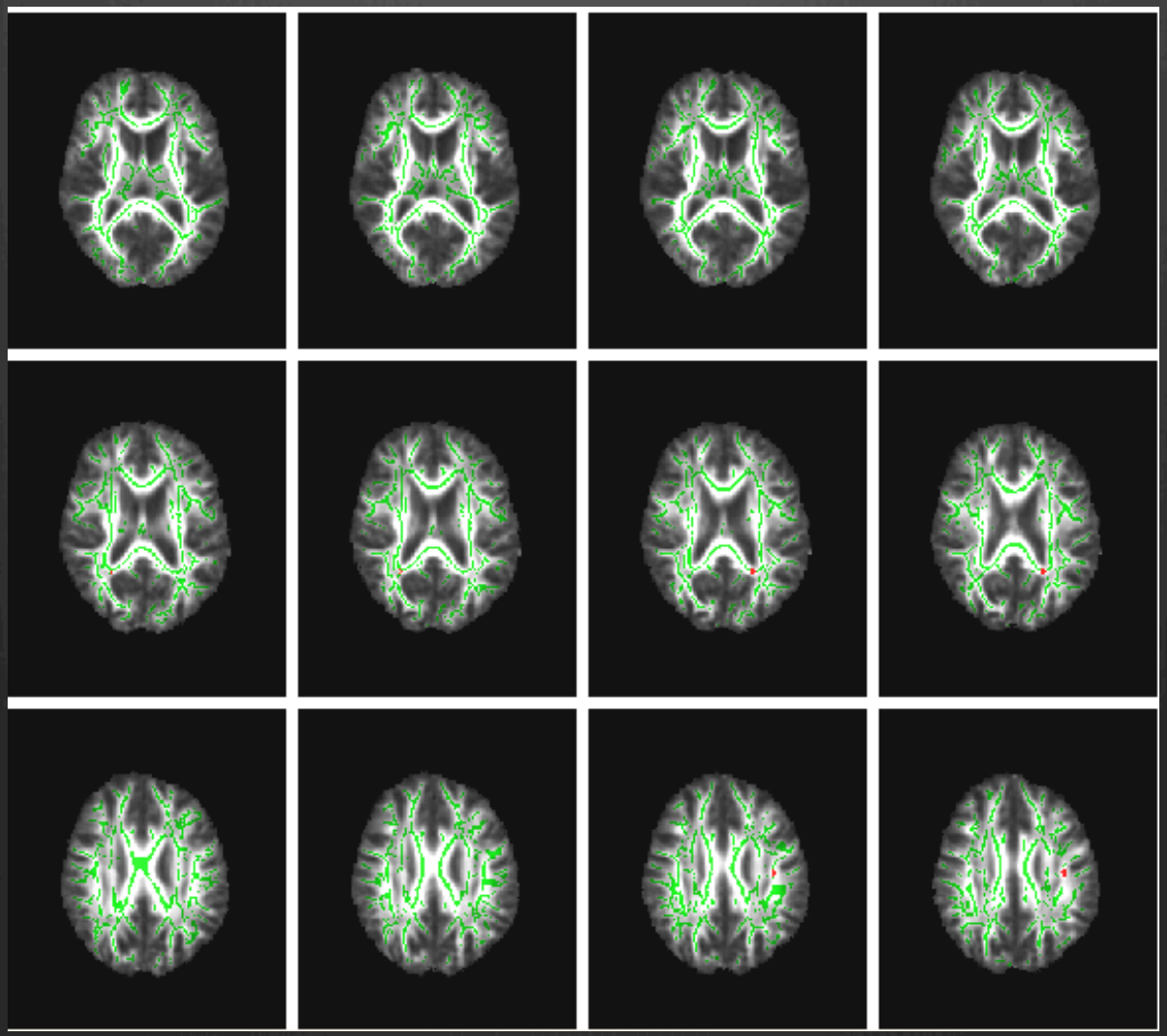


Tractography

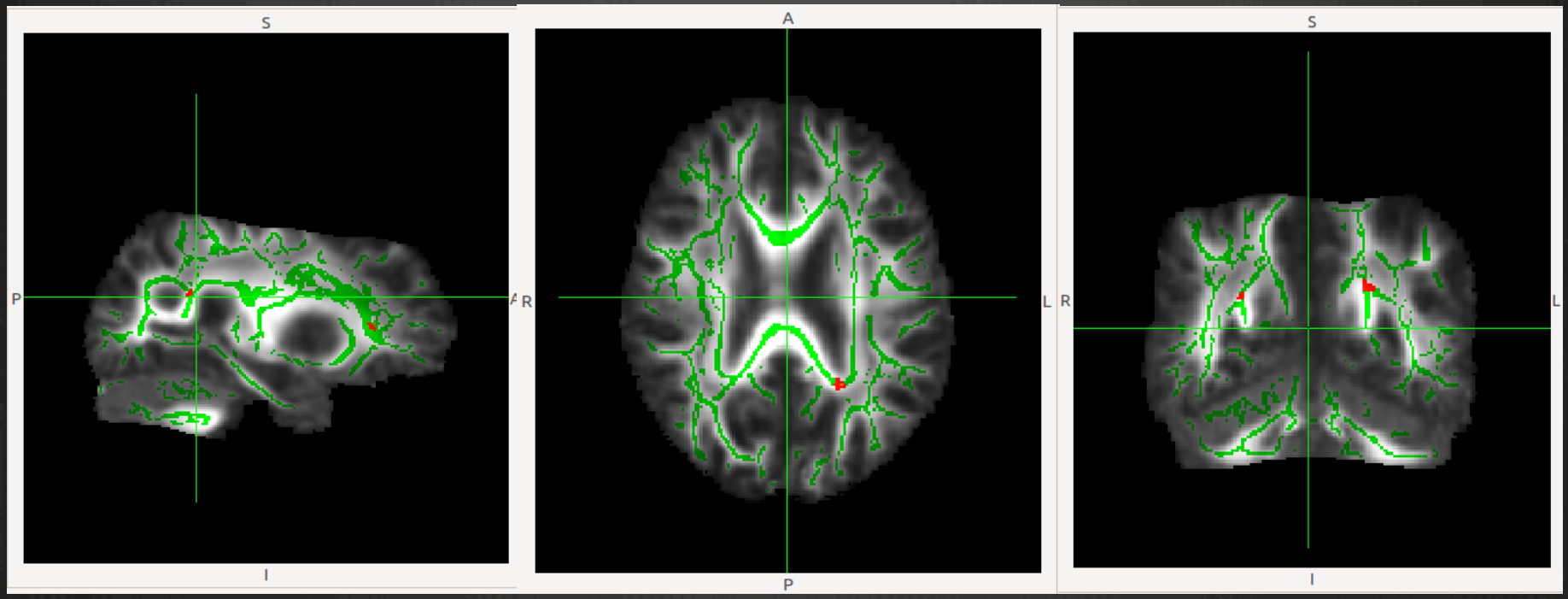
- Programs like medInria allow us to measure integrity of connections between different regions.



TBSS



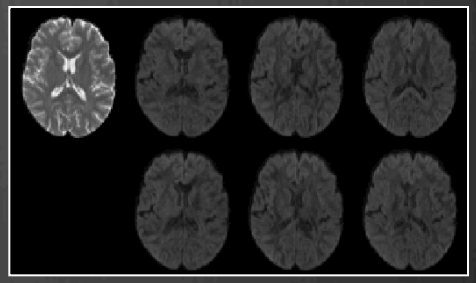
TBSS

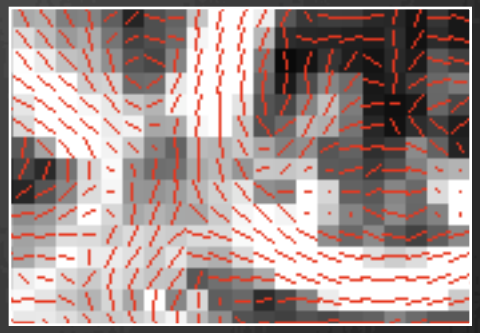


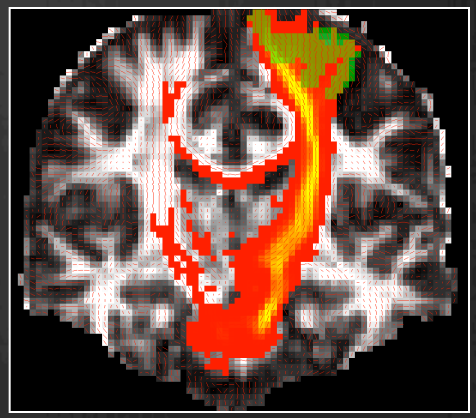
Deterministic vs. probabilistic tractography

Data analysis steps

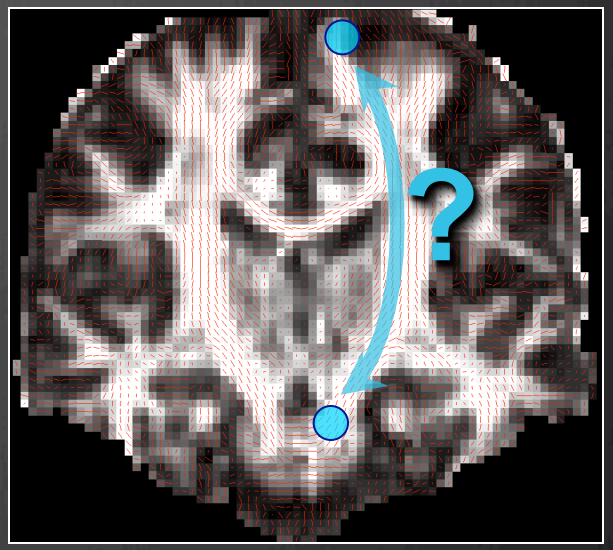
- Pre-process images to reduce distortions
  - Either register distorted DW images to an undistorted (non-DW) image
  - Or use information on distortions from separate scans (field map, residual gradients)
- Fit a diffusion model at every voxel
  - DTI, DSI, Q-ball, …
- Do tractography to reconstruct pathways and/or
- Compute measures of anisotropy/diffusivity and compare them between populations
  - Voxel-based, ROI-based, or tract-based statistical analysis







Tractography studies

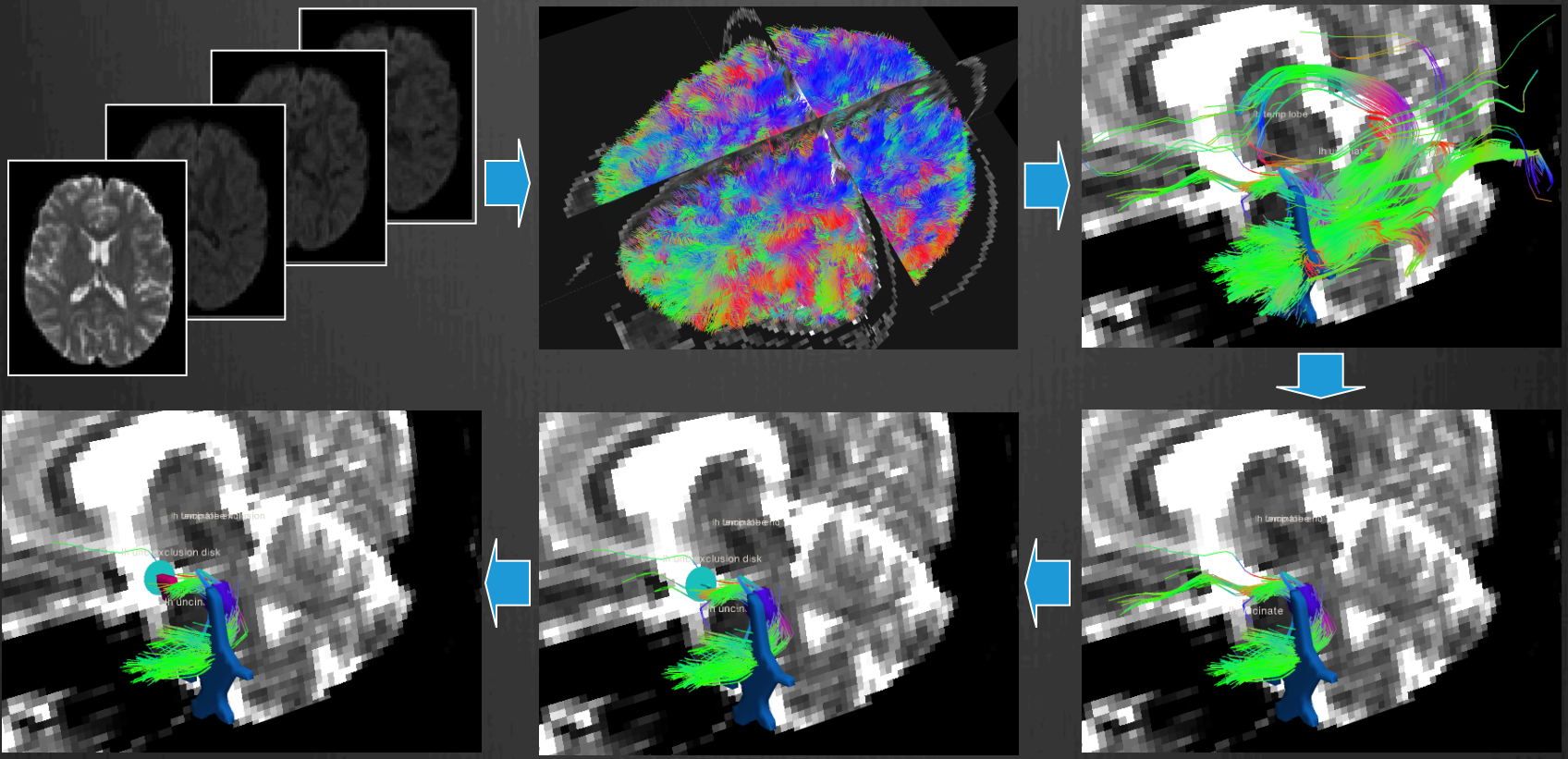


- Exploratory tractography:
  - Example: *Show me all regions that the motor cortex is connected to.*
  - Seed region can be anatomically defined (motor cortex) or functionally defined (region activated in an fMRI finger-tapping task)

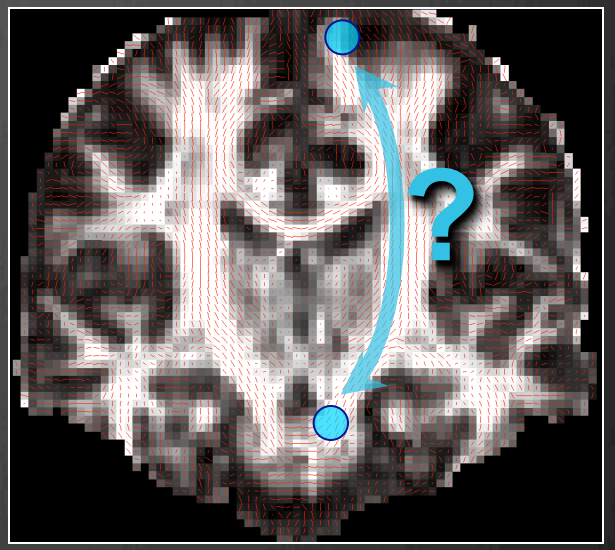
- Tractography of known pathways:
  - Example: *Show me the corticospinal tract.*
  - Use prior anatomical knowledge of the pathway's terminations and trajectory (connects motor cortex and brainstem through capsule)

Tractography takes time

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



Tractography methods



- Use local diffusion orientation at each voxel to determine pathway between distant brain regions

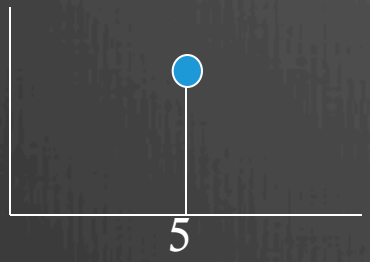
- Local orientation comes from diffusion model fit (tensor, ball-and-stick, etc.)

- Deterministic vs. probabilistic tractography:
  - Deterministic assumes a single orientation at each voxel
  - Probabilistic assumes a distribution of orientations

- Local vs. global tractography:
  - Local fits the pathway to the data one step at a time
  - Global fits the entire pathway at once

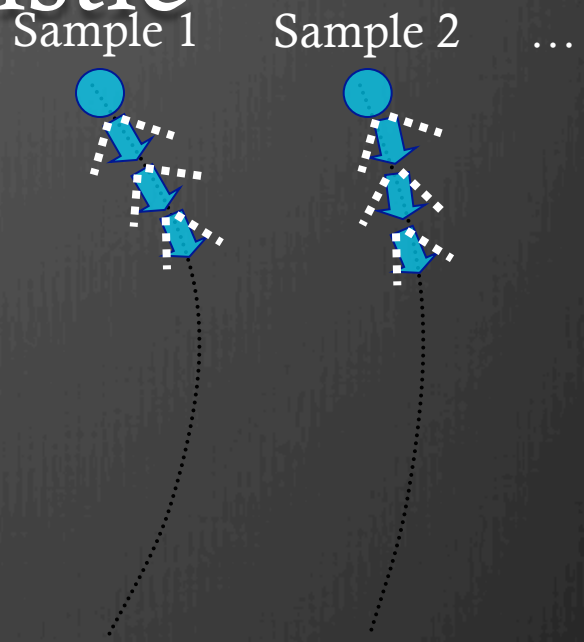
Deterministic vs. probabilistic

- Deterministic methods give you an estimate of model parameters



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

Deterministic vs. probabilistic



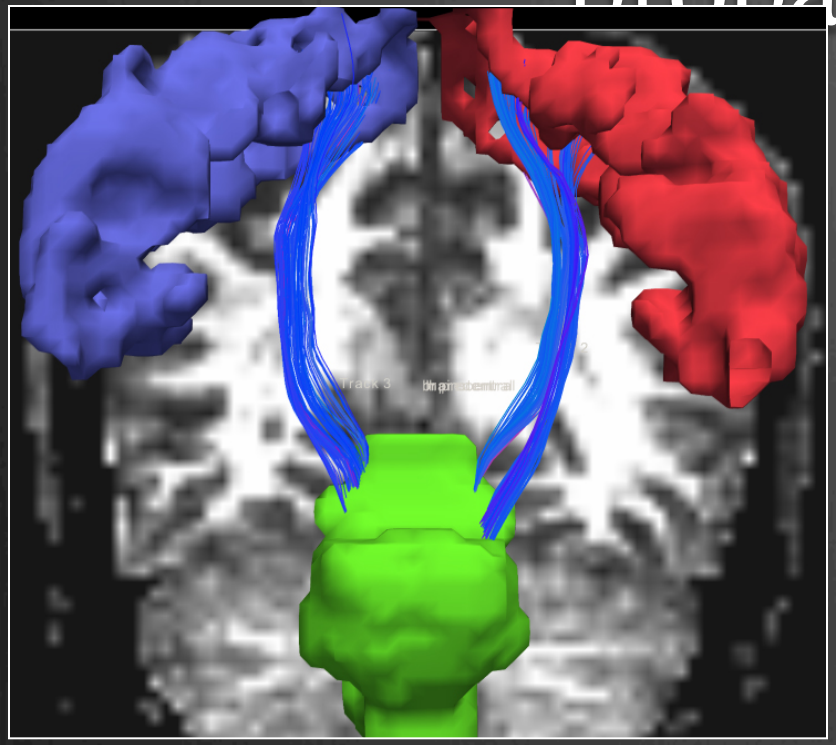
Deterministic tractography:

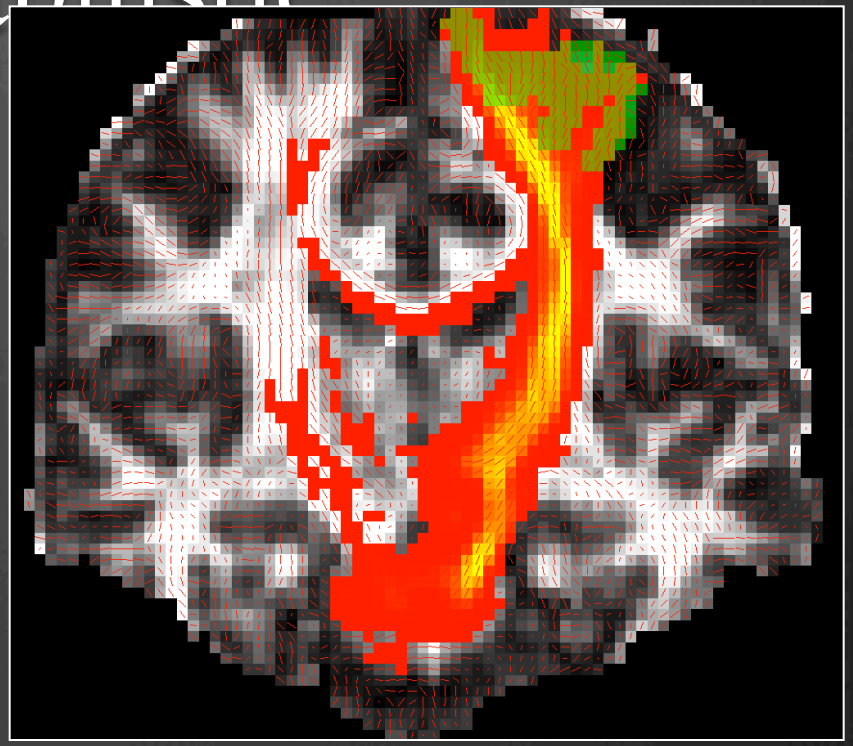
One streamline per seed voxel

Probabilistic tractography:

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

Deterministic vs. probabilistic





Deterministic tractography:

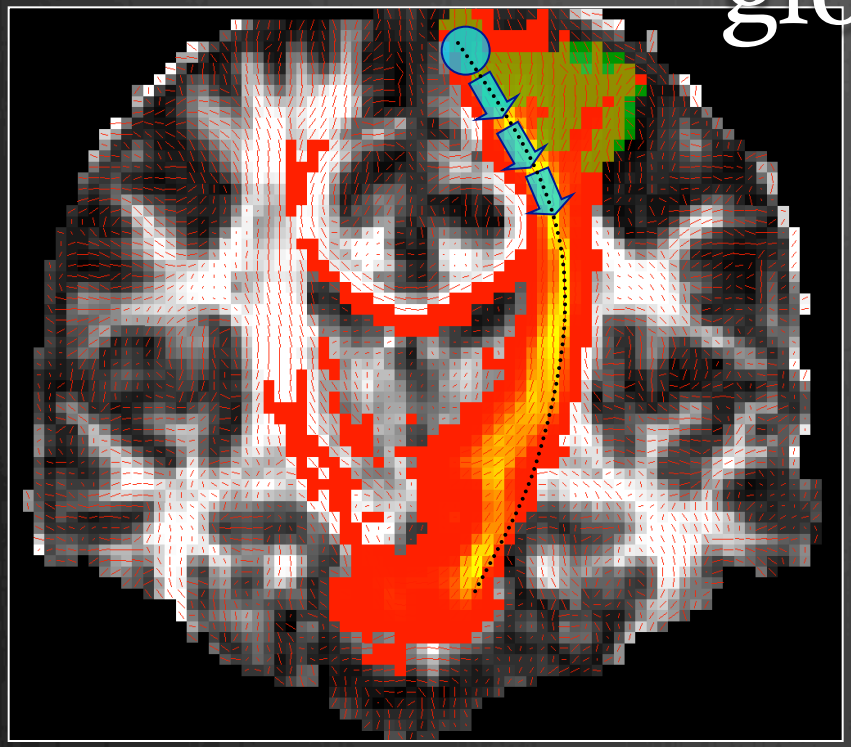
One streamline per seed voxel

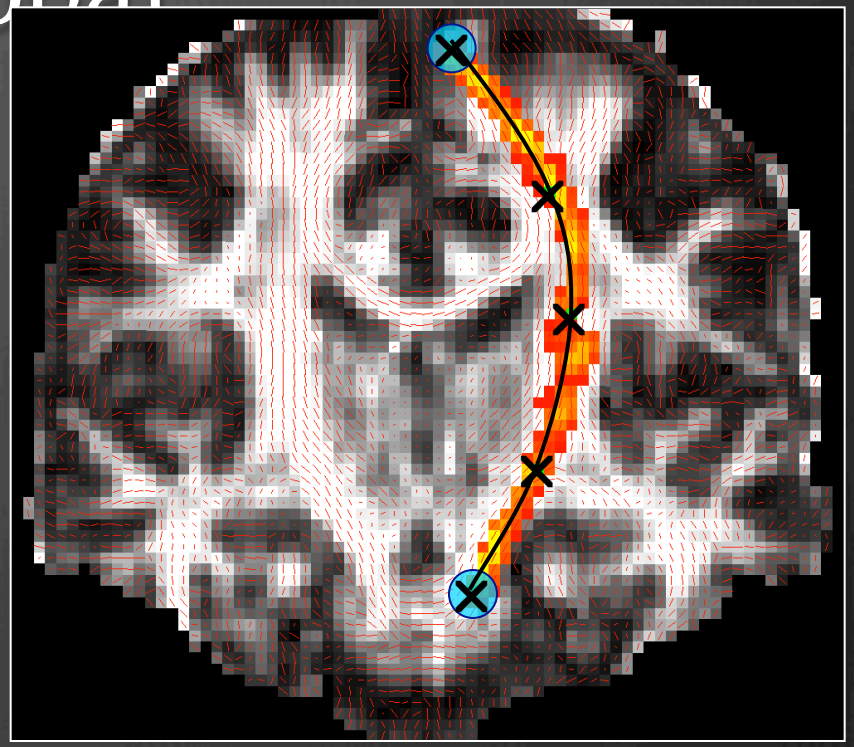
Probabilistic tractography:

A probability distribution

(sum of all streamline samples from all seed voxels)

Local vs. global





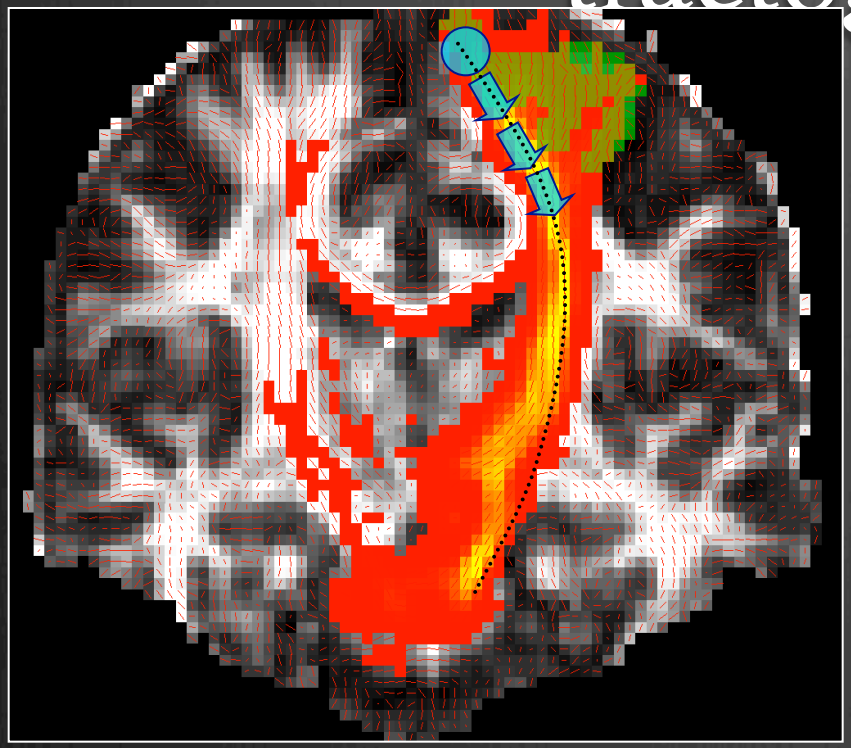
Local tractography:

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

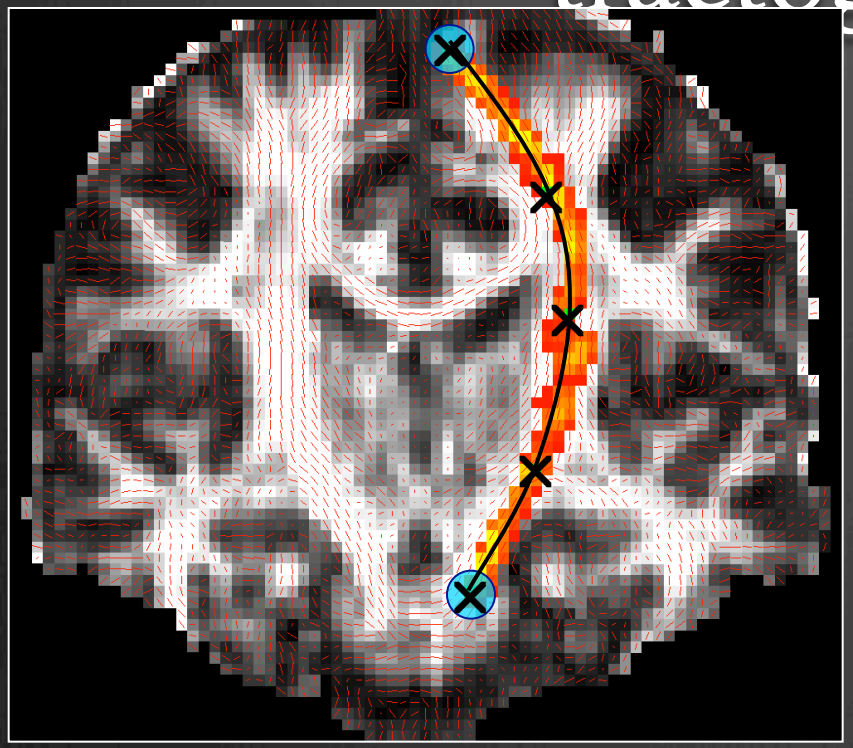


- Best suited for exploratory study of connections

- 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

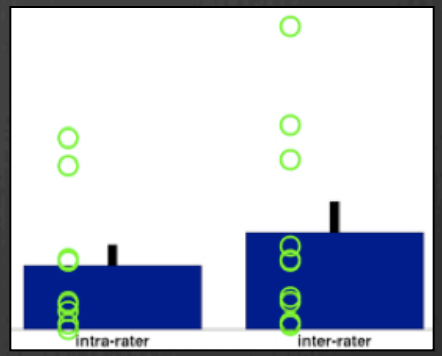
TRACU LA

- TRActs Constrained by UnderLying Anatomy
- 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
- Reconstruct 18 major white-matter pathways
  - No manual intervention in new subjects
  - Robustness with respect to pathway initialization
  - Anatomically plausible solutions
- Ad-hoc anatomical constraints are often used by other methods: constraints on path bending angle or length, WM masks, …

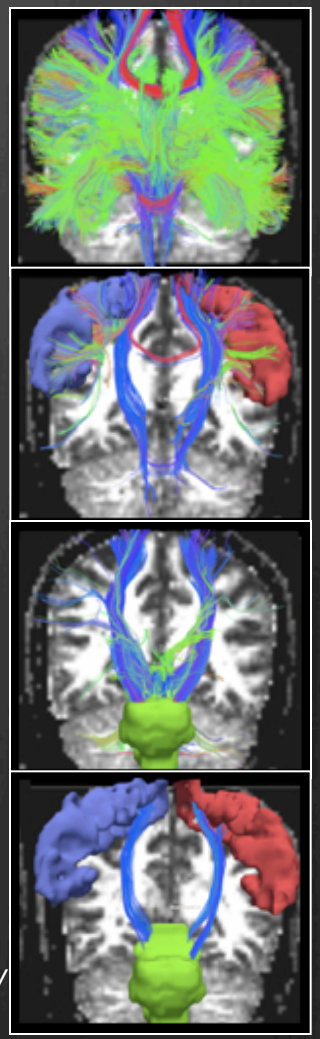
White-matter pathway atlas

- 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

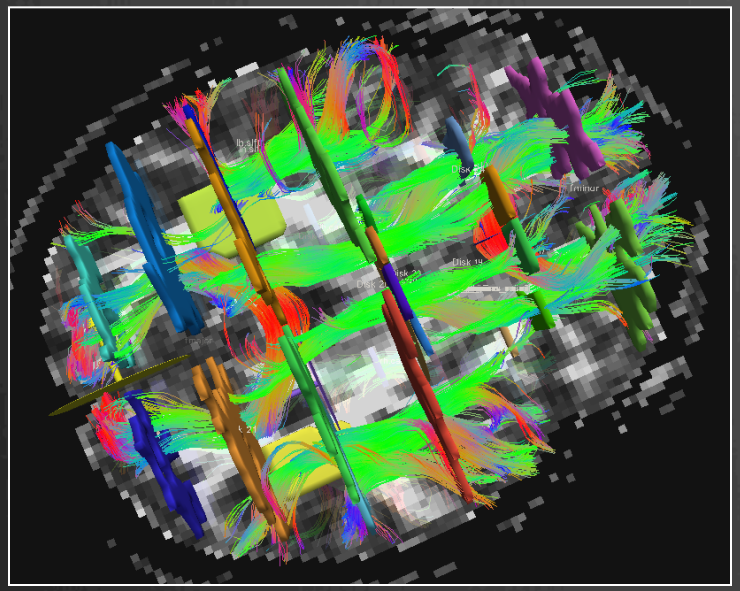


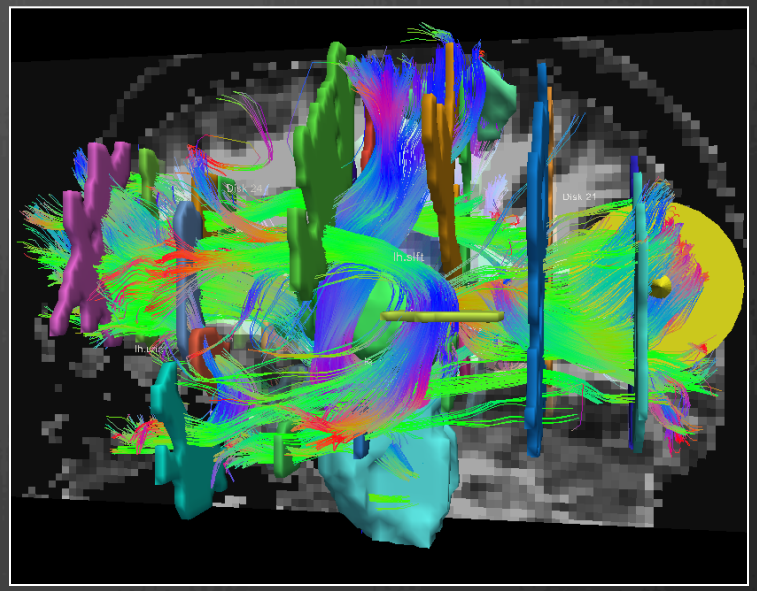
Intra/inter-rater errors: 1mm/ 2mm on average



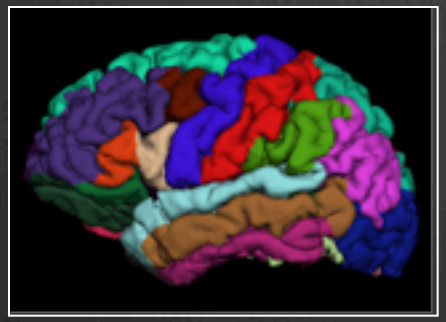
White-matter pathway atlas

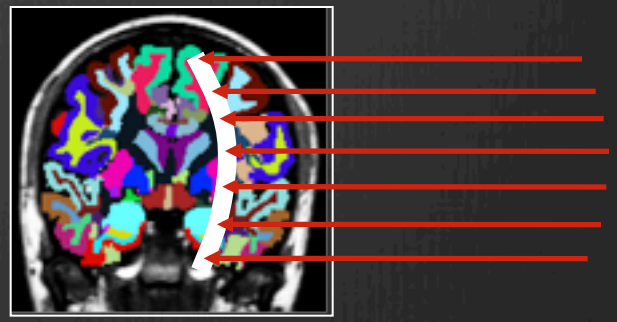
- Manual labeling of paths in training subjects performed in Trackvis





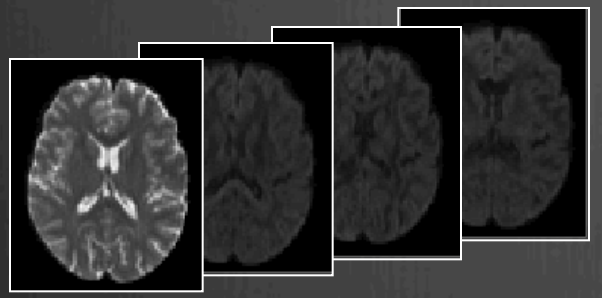
- Anatomical segmentation maps of training subjects from FreeSurfer



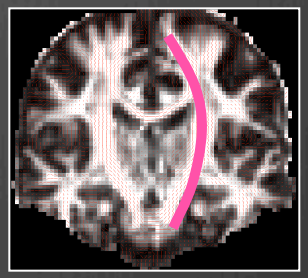


Automated pathway reconstruction

Have image data Y Want most probable path F



…



- Determine the most probable path based on:
  - What the images tell us about the path
  - What we already know about the path
- Estimate posterior probability of path F given images Y

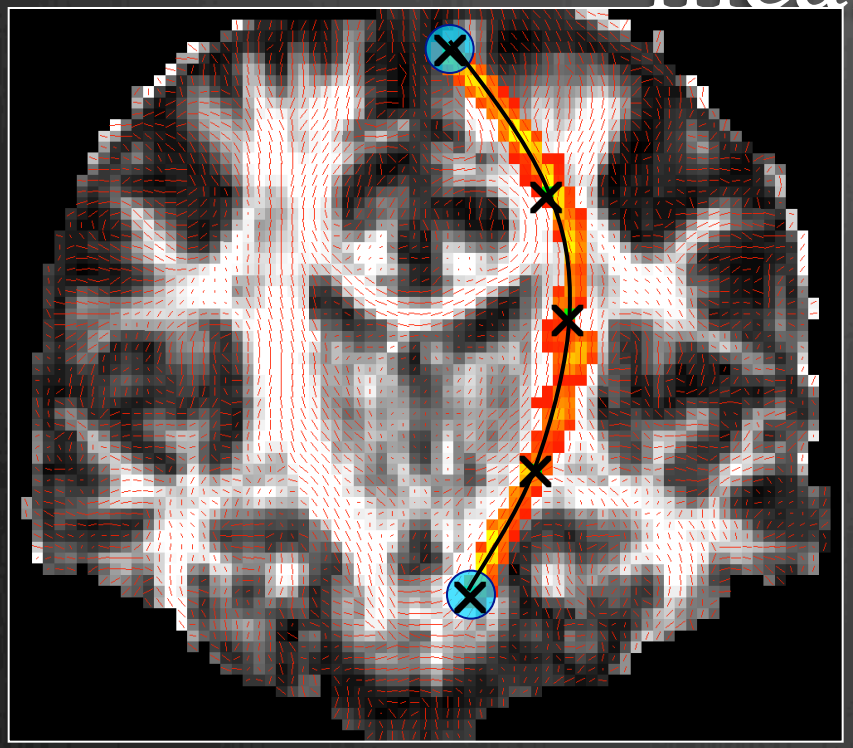
$$p(F \mid Y) \;\propto\; p(Y \mid F)\; p(F)$$

  - $p(Y \mid F)$: Uncertainty due to imaging noise

    Fit of pathway orientation to ball-and-stick model parameters
  - $p(F)$: Uncertainty due to anatomical variability

    Fit of pathway to prior anatomical knowledge from training set

Tract-based measures



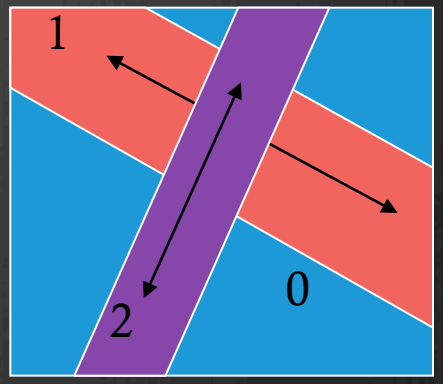
- Reconstruction outputs:
  - Posterior probability distribution of pathway given data (3D)
  - Maximum *a posteriori* pathway (1D)
- Tract-based diffusion measures (FA, MD, RD, AD, etc):
  - Average over pathway distribution
  - Weighted average over pathway distribution
  - Average over MAP pathway
  - As a function of arc length along MAP pathway

Ball-and-stick model fit

Behrens *et al.*, MRM '03
Jbabdi *et al.*, NeuroImage '07

- Multiple diffusion compartments in each voxel:
  - Anisotropic compartments that model fibers (1, 2, …)
  - One isotropic compartment that models everything left over (0)

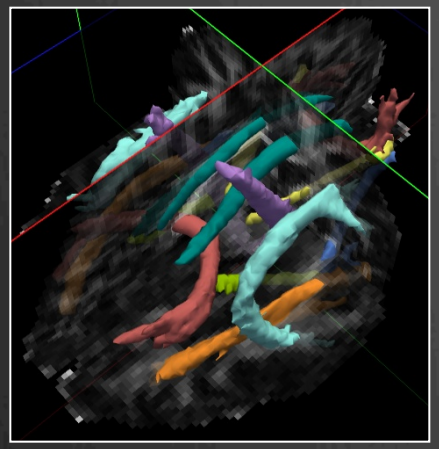
- FSL/bedpostX infers from the data:
  - Orientation angles of anisotropic compartments
  - Volumes of all compartments
  - Overall diffusivity in the voxel

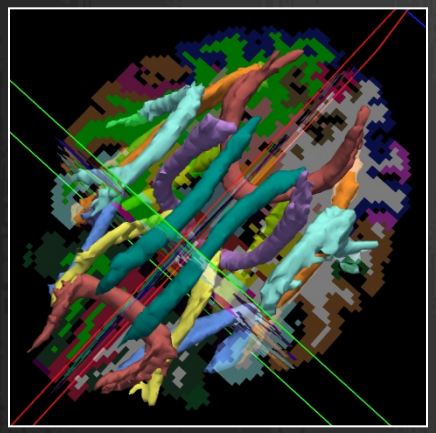


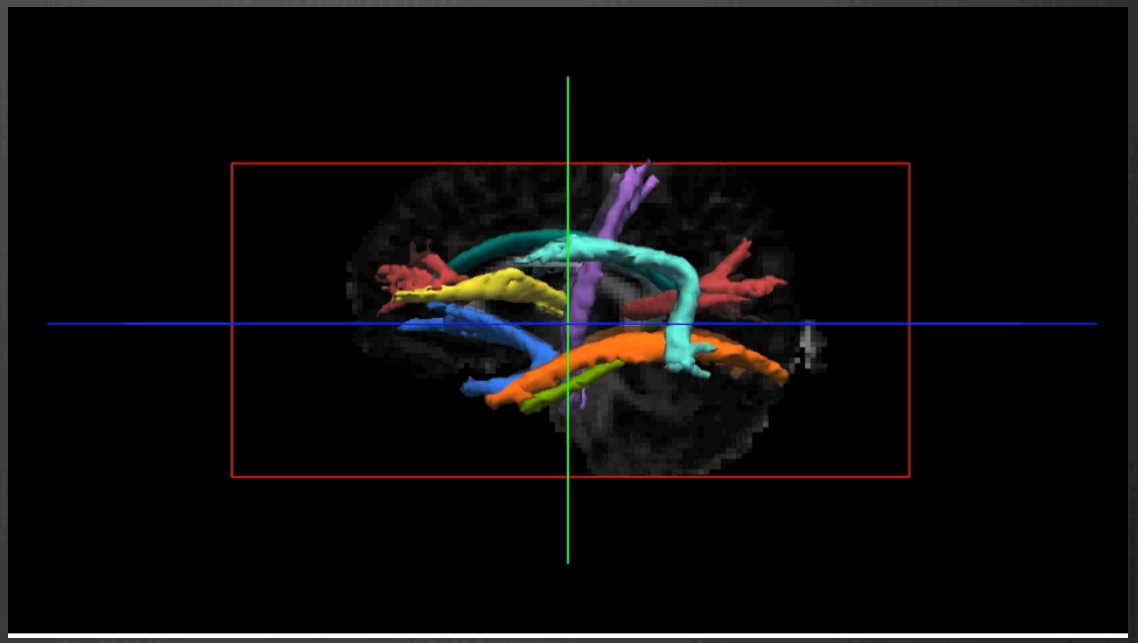
- Multiple fibers only if they are supported by data

Schizophrenia study

Data courtesy of Dr. Randy Gollub and MIND Institute





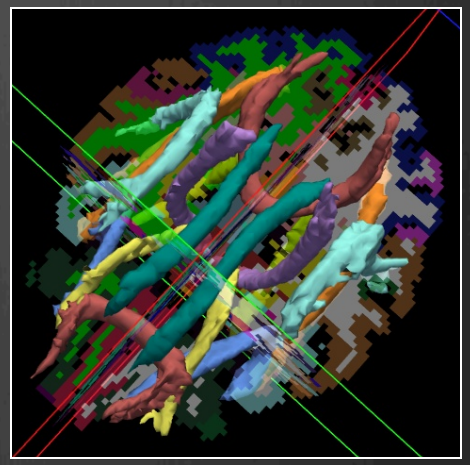


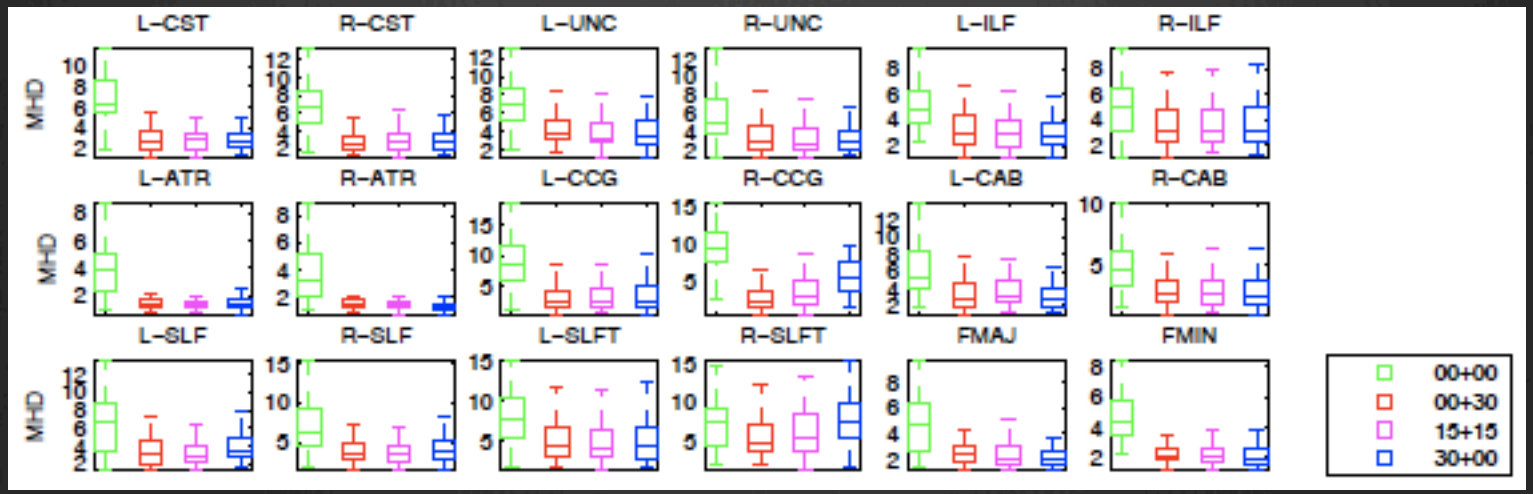
Pathway distributions reconstructed automatically in a SZ patient using 30 healthy training subjects

Schizophrenia study

Data courtesy of Dr. Randy Gollub and MIND Institute

- Reconstruct pathways in 34 SZ patients and 23 healthy controls 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





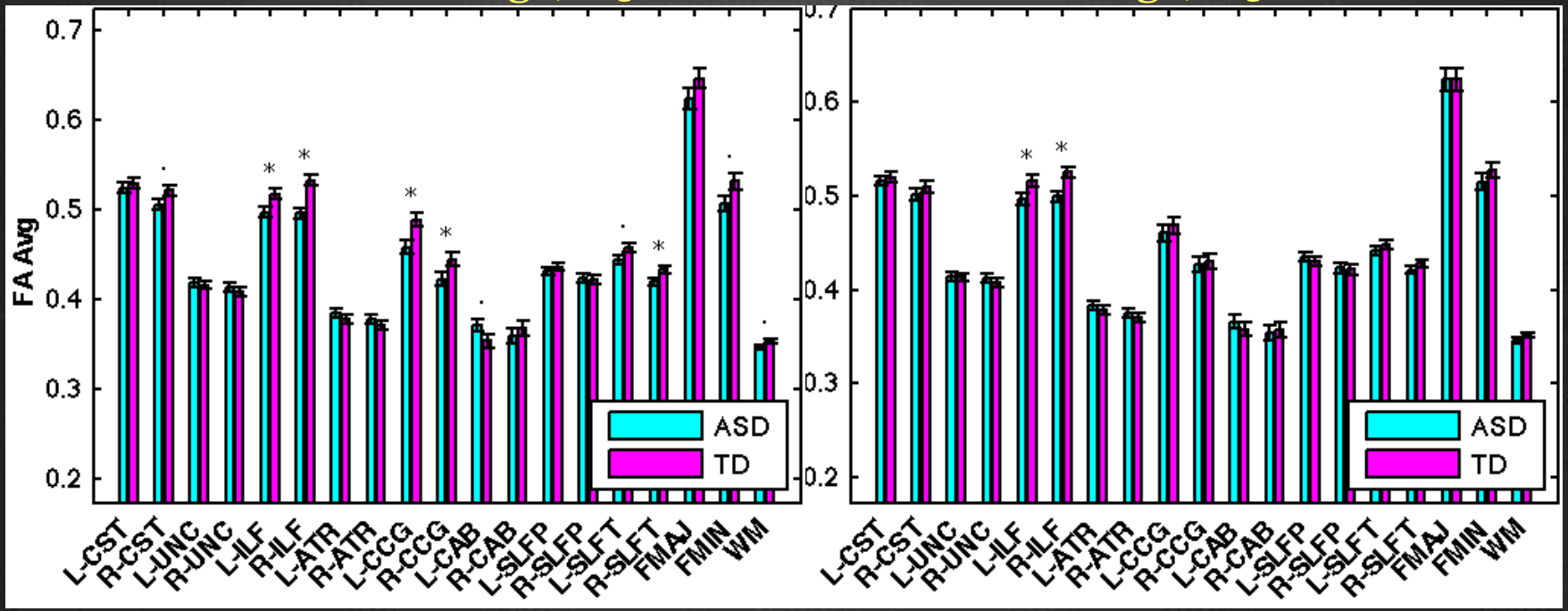
Beware of motion!

Data courtesy of Dr. Nancy Kanwisher and Ellison autism study

- 50 children with autism spectrum disorder (ASD) vs. 50 typically developing children (TD)
- Some children scanned twice, so scans can be matched for motion

Matched for age, IQ

Matched for age, IQ & motion



[Yendiki *et al,* OHBM 2013]

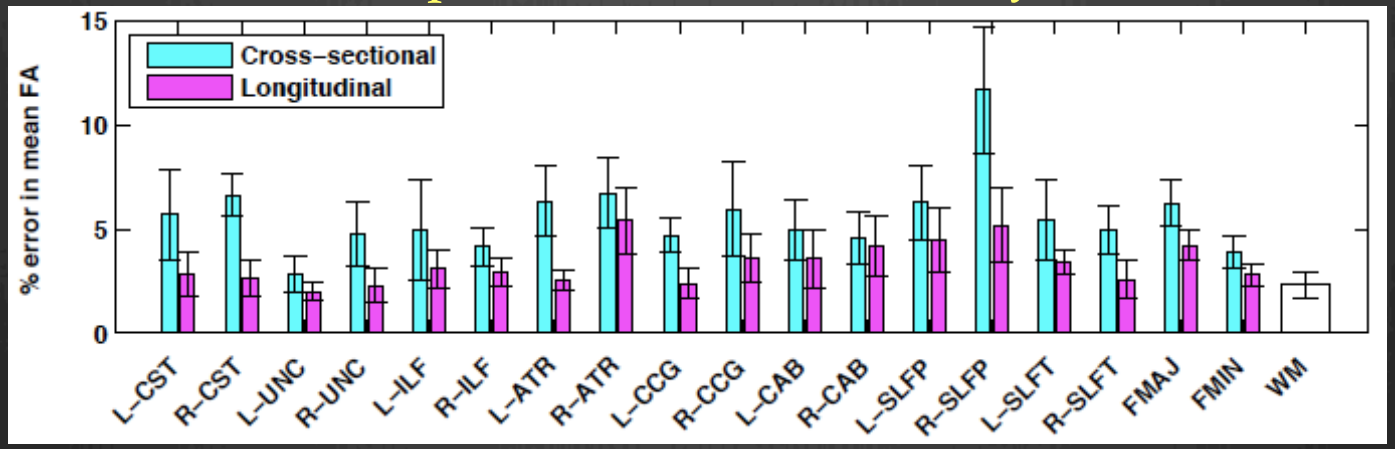
Usage

- 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`

New development: Longitudinal

- Reconstruct a subject's pathways simultaneously in all time points
- Ensures better spatial correspondence (avoid getting different parts of the pathway in different time points due to degeneration)

Improved test-retest reliability



Longitudinal

- Define `baselist` in config file
- Paths saved under `dpathlong/`

Cross-sectional

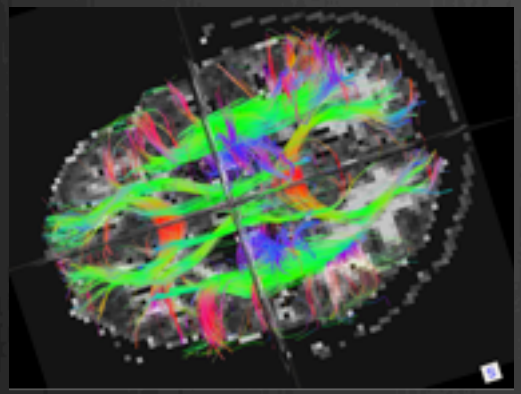
- Do not define `baselist`
- Paths saved under `dpath/`

Future development: A better atlas

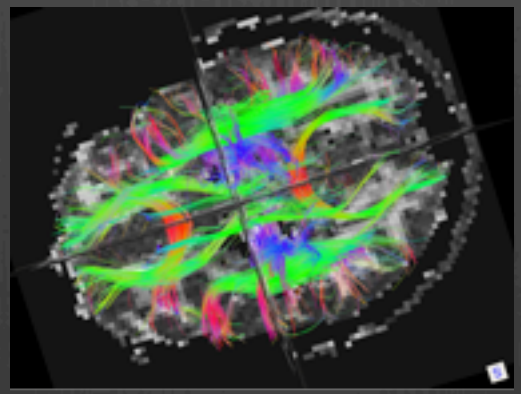
GFA

- Need high SNR, high angular resolution, tolerable scan time
- Combine advances in hardware and sequences:
  - *Connectom* scanner with 8 times stronger gradients
  - Accelerated simultaneous multi-slice acquisition (Setsompop ‘11)

1x-slice DSI (45 min)

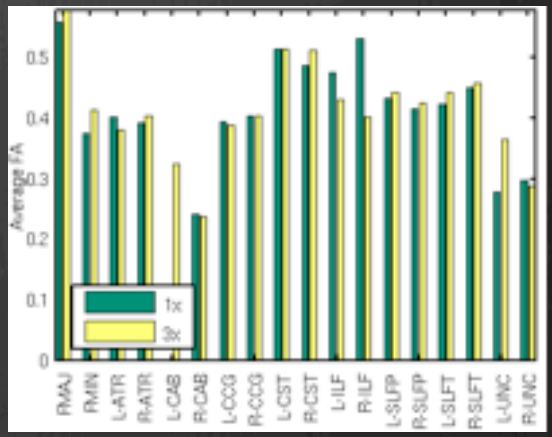


3x-slice DSI (15 min)



[Images from Setsompop ‘12]

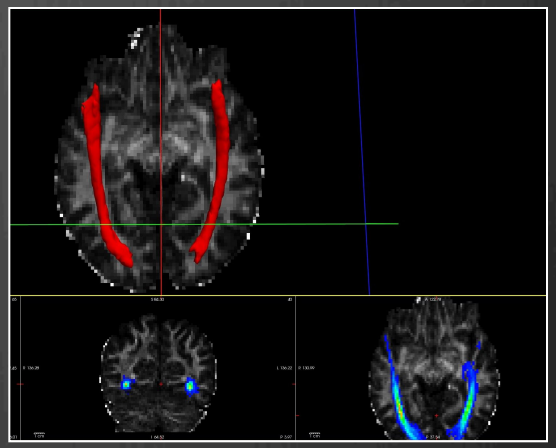
Comparable tracts and FA



- Goal:
  - Create a gold standard atlas from this data
  - Use it to do tractography in *conventional data*

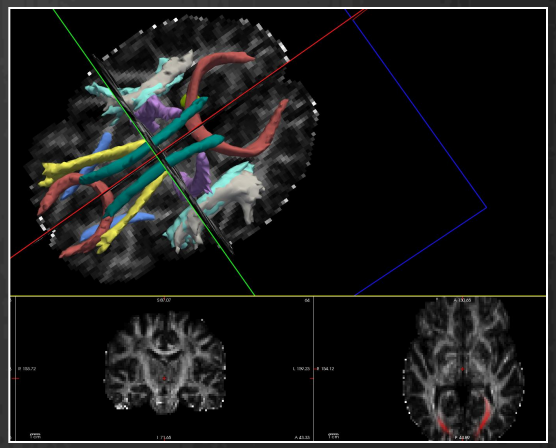
Tutorial

- How to run TRACULA and view outputs:
  - Set up configuration file (input images, gradient directions, b-values, registration method, etc.)
  - "Run" trac-all (*don't actually run it!*)
  - Look at pathways in freeview
  - Look at FA, MD, and other stats for each pathway



```
# subjectname Diff001
# pathwayname lh.cst
#
Count 1000
Volume 327
Len_Min 35
Len_Max 70
Len_Avg 53.119
Len_Center 48
AD_Avg 0.00106102
AD_Avg_Weight 0.00108794
AD_Avg_Center 0.00105527
RD_Avg 0.000438781
RD_Avg_Weight 0.000430744
RD_Avg_Center 0.000441464
MD_Avg 0.000646195
MD_Avg_Weight 0.000649809
MD_Avg_Center 0.000646067
FA_Avg 0.519271
FA_Avg_Weight 0.539241
FA_Avg_Center 0.511358
```

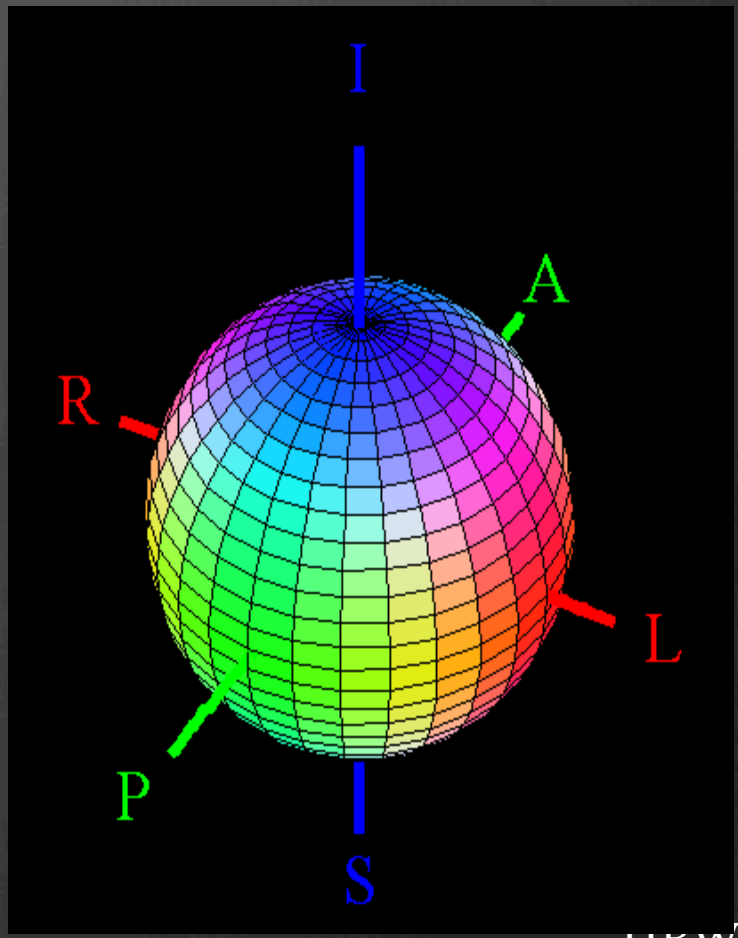
```
# subjectname Diff001
# pathwayname lh.cst
#
# pathway start
x y z AD RD MD FA
66 63 13 0.00103657 0.000574918 0.000728804 0.374774
66 63 14 0.00100453 0.000480365 0.000655088 0.478045
67 64 15 0.000816154 0.000359865 0.000511961 0.547635
67 64 16 0.000946625 0.000421327 0.000596426 0.521222
68 64 17 0.000967142 0.000305692 0.000526175 0.646745
68 64 18 0.00114626 0.000333594 0.000604484 0.658591
69 65 19 0.00152806 0.000740932 0.00100331 0.426333
69 65 20 0.00126399 0.000470638 0.000735089 0.57121
69 65 21 0.00140243 0.000482392 0.000789071 0.611696
70 65 21 0.00143949 0.000480912 0.000800438 0.618516
70 65 22 0.00116007 0.000156374 0.000490939 0.858895
70 66 23 0.00138642 0.000415134 0.000738896 0.650657
71 66 24 0.00134187 0.000385197 0.000704089 0.678151
71 66 25 0.00108983 0.000289931 0.000556565 0.729769
71 66 26 0.00111074 0.000307493 0.000575241 0.693343
72 66 27 0.00117242 0.000398032 0.00065616 0.619191
72 66 28 0.00118738 0.000448541 0.000694819 0.568624
```



Diffusion direction visualization

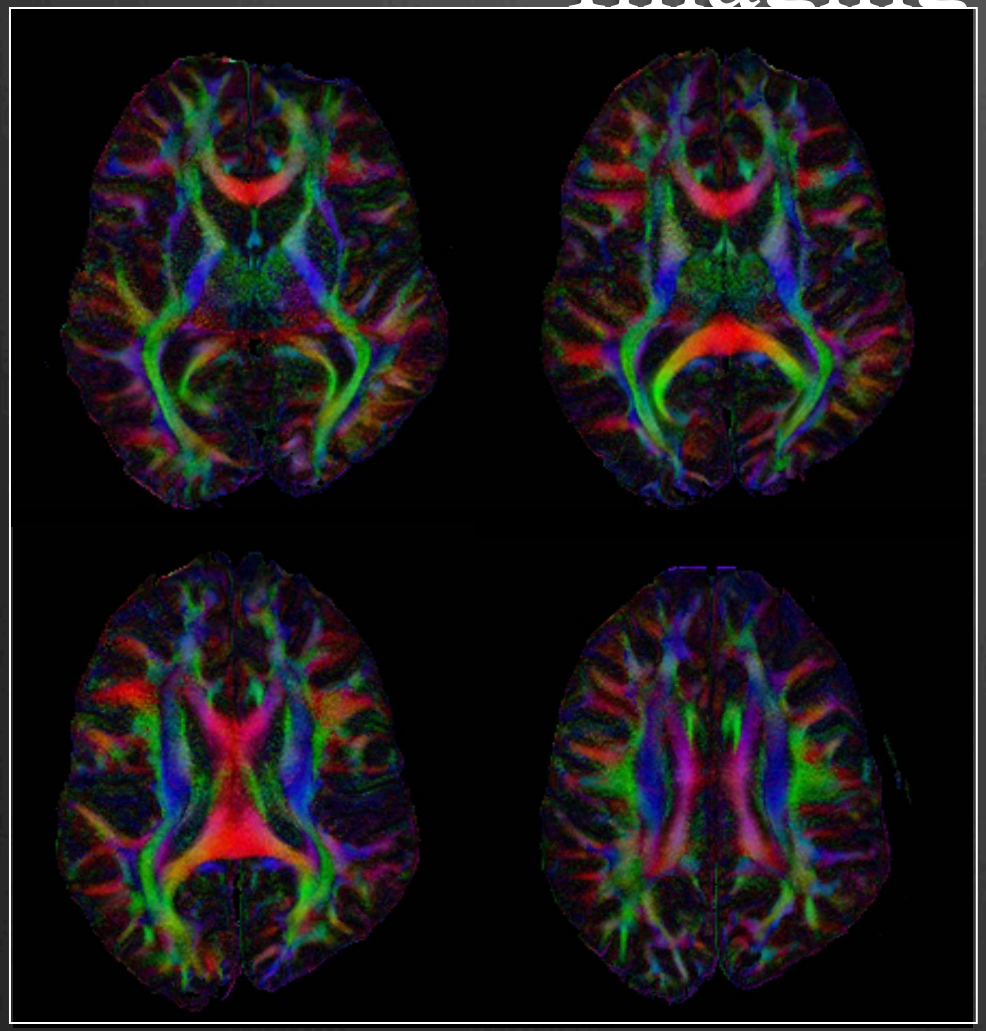
Image brightness by anisotropy indices (FA, 1-2 difference, 2-3 difference)

Orientation of the eigenvectors was represented by use of RGB color coding.



HBW
L

Intera 3.0T: Diffusion Tensor Imaging



SENSE-DTI
High res FA-maps:
(256x256), 4mm

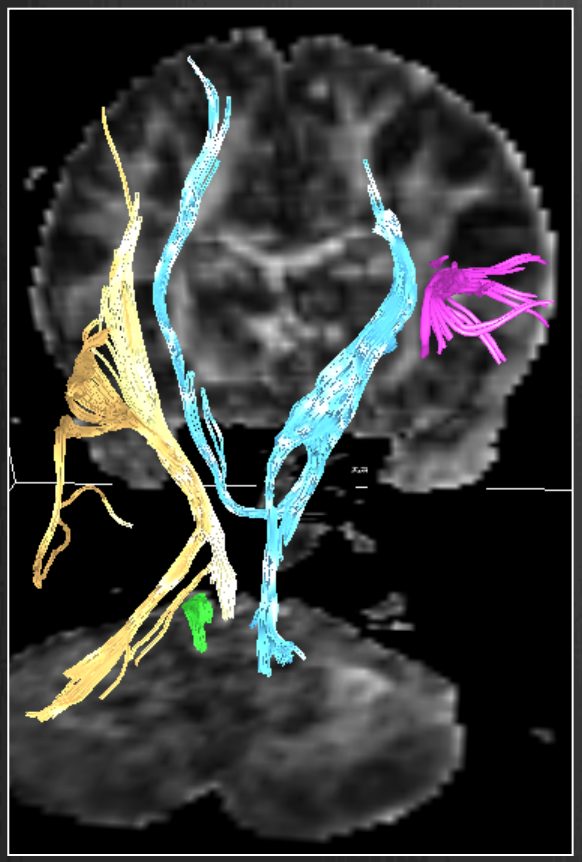
SENSE fact.= 2.5

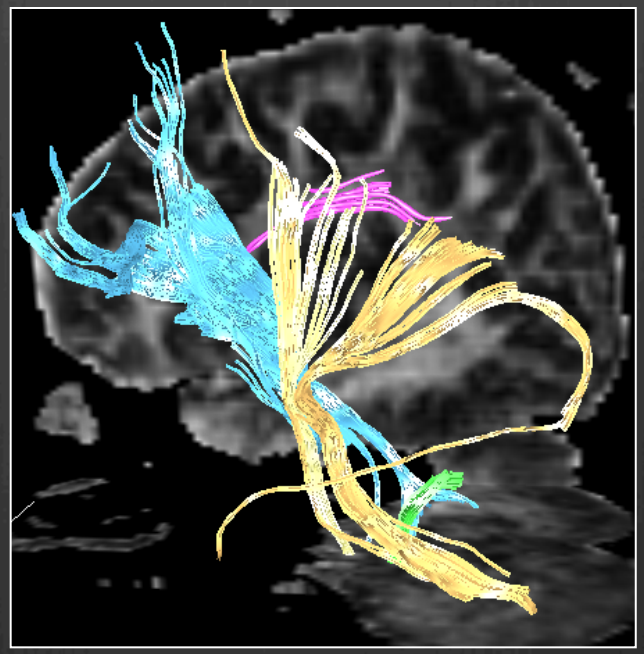
Directions:
red: RL
green: AP
blue: FH

HBWL

Fiber Tracking

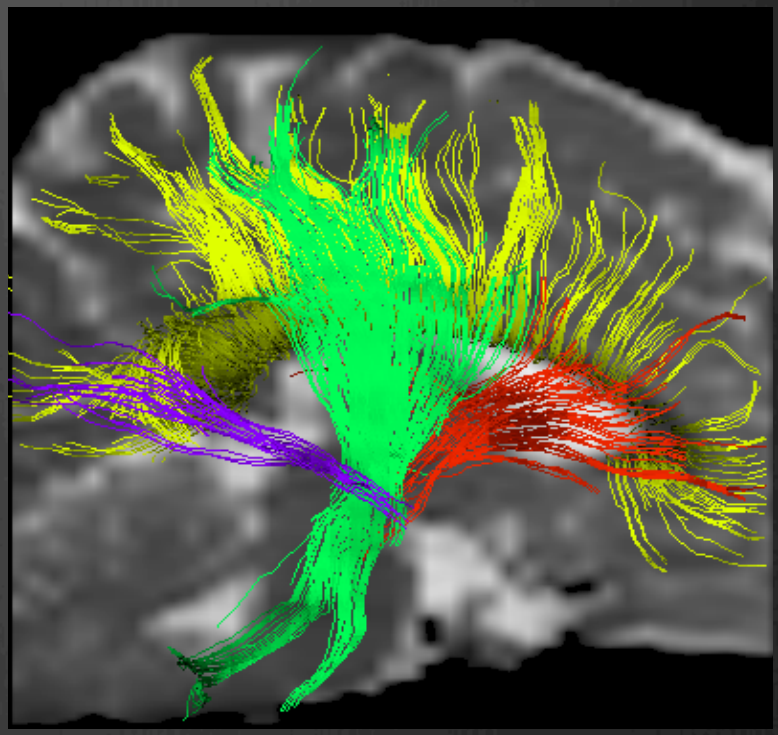
- Corticospinal Tract
- Inferior Cerebellar Peduncle
- Superior Cerebellar Peduncle
- Anterior Thalamic Radiation
- Superior Longitudinal Fasciculus





HBWL

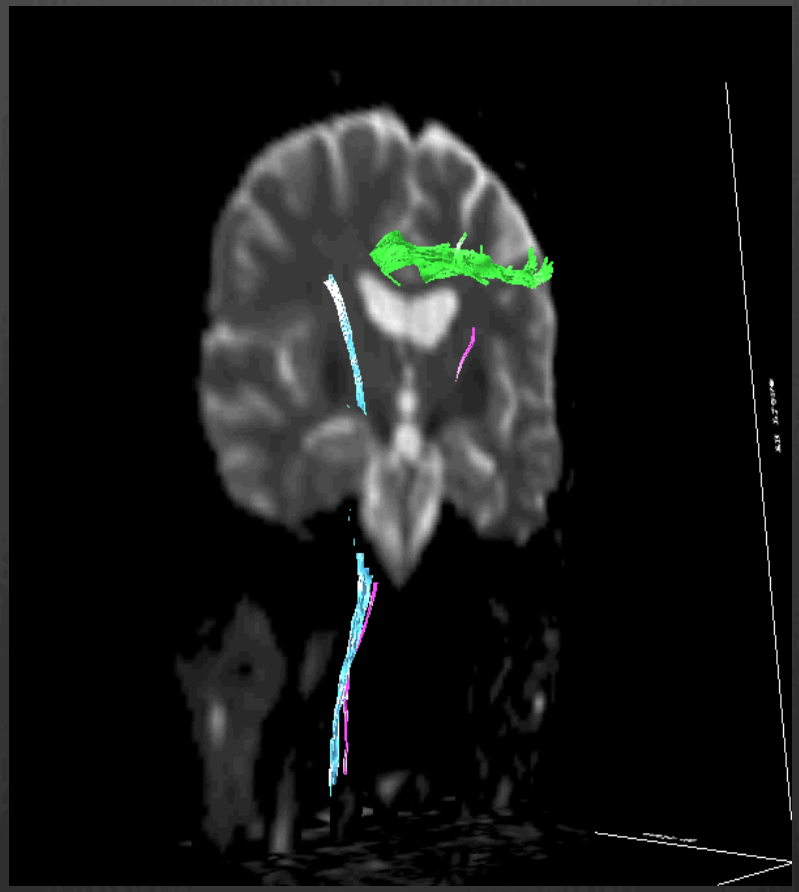
Comparison with anatomical preparation



S. Mori, B. Stieltjes, R. Xue, M. Solaiyappan, W. Kaufmann & P. van Zijl,
F.M. Kirby research center, Johns Hopkins University, Baltimore.

HBWL

Diffusion tensor imaging tractography



HBWL

Applications

- Ischemia
- Fiber direction
- Demyelinations
- Tumor delimitation
- Others