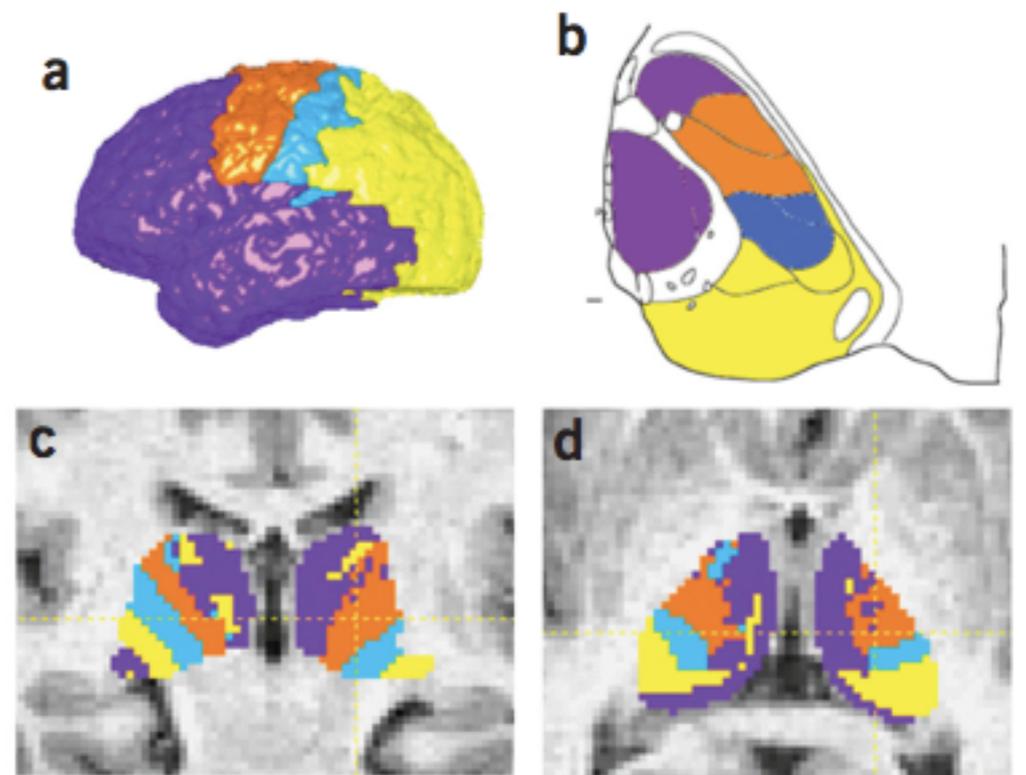
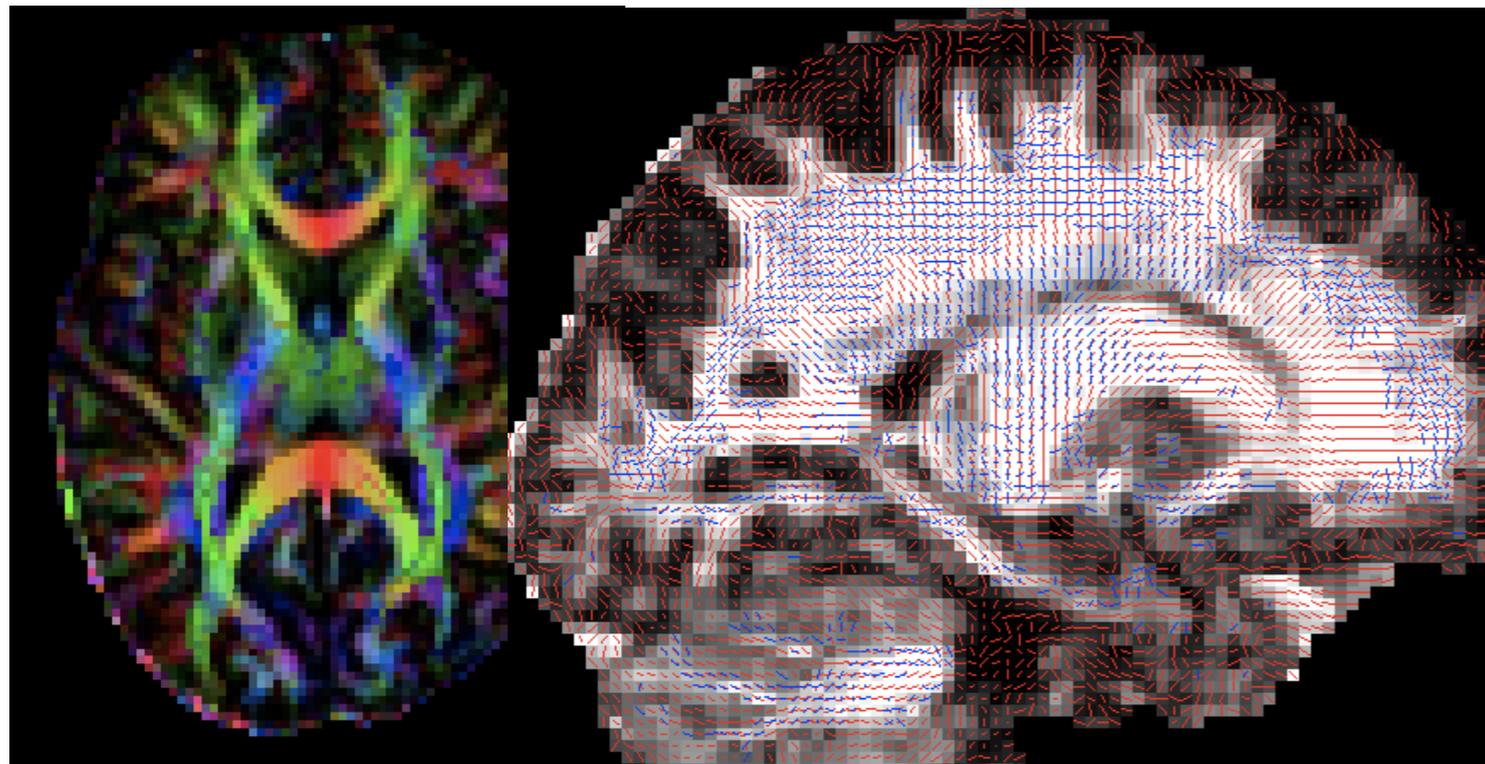




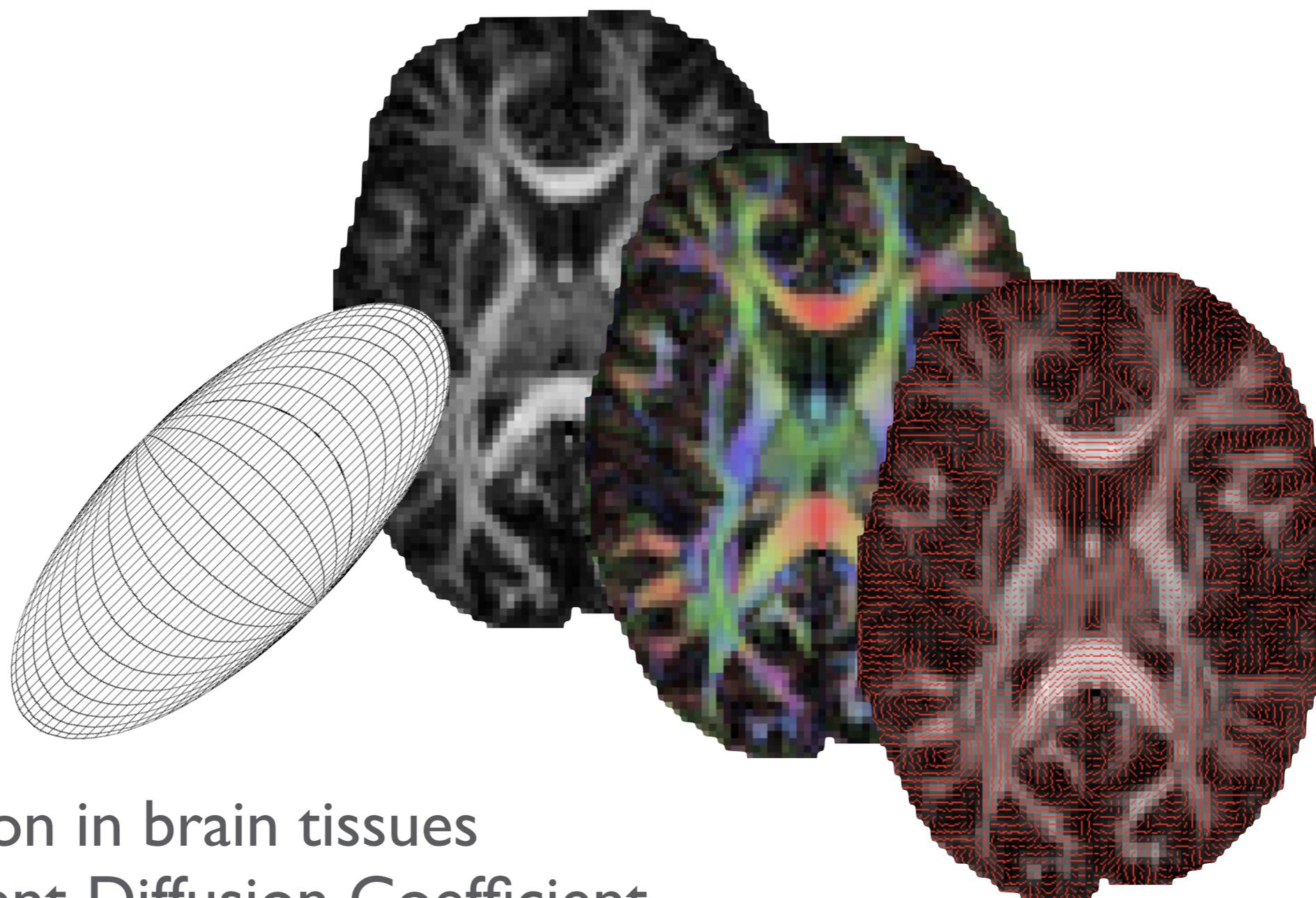
# FMRIB Diffusion Toolbox

- DTI model fit
- Eddy current correction
- Voxel-Based diffusion analysis (TBSS)
- BEDPOSTX modelling crossing fibres
- PROBTRACKX propagating uncertainty in tractography





# Diffusion Tensor Imaging - basic principles



- Diffusion in brain tissues
- Apparent Diffusion Coefficient
- Diffusion Tensor model
- Tensor-derived measures

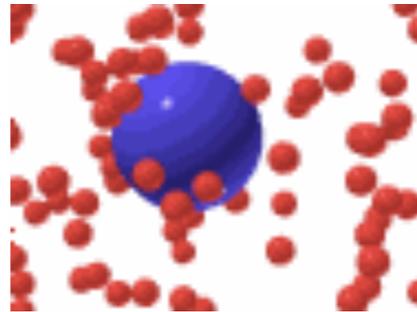


# Brownian motion

Molecules are in constant motion



Robert Brown (1773-1858)



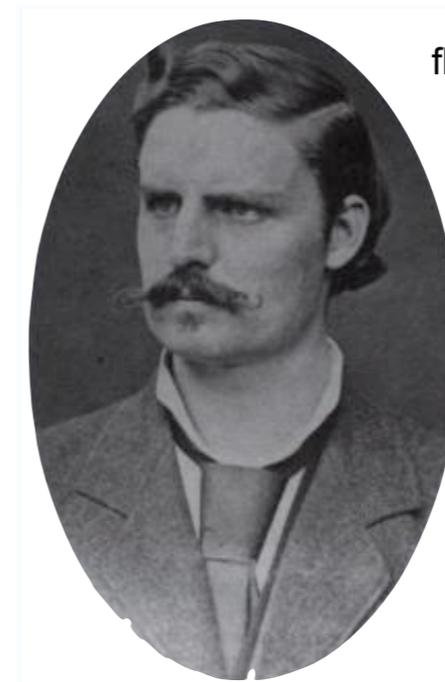
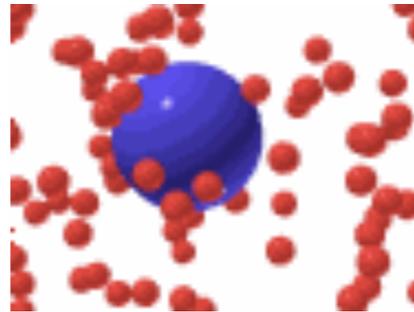


# Brownian motion

Molecules are in constant motion



Robert Brown (1773-1858)



Adolf Fick (1829-1901)

diffusion coefficient

flux

concentration

$$J = -D \nabla \phi.$$
$$\frac{\partial \phi}{\partial t} = D \frac{\partial^2 \phi}{\partial x^2}$$

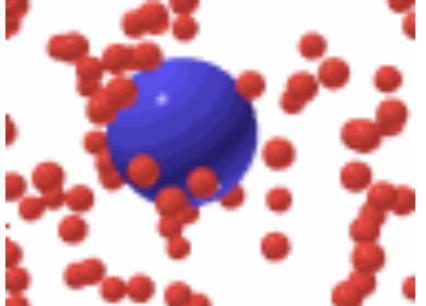


# Brownian motion

## Molecules are in constant motion



Robert Brown (1773-1858)



Adolf Fick (1829-1901)

diffusion coefficient

flux

concentration

$$J = -D \nabla \phi.$$

$$\frac{\partial \phi}{\partial t} = D \frac{\partial^2 \phi}{\partial x^2}$$



Albert Einstein (1879-1955)

$$\langle x^2 \rangle = 2nDt$$

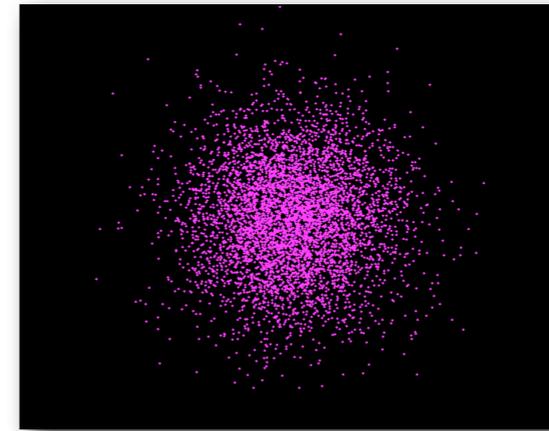
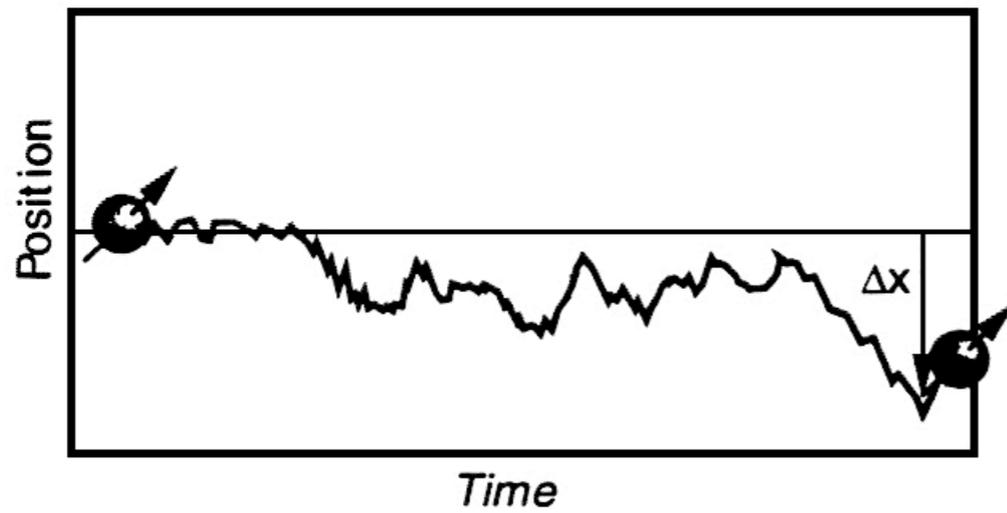
displacement

time

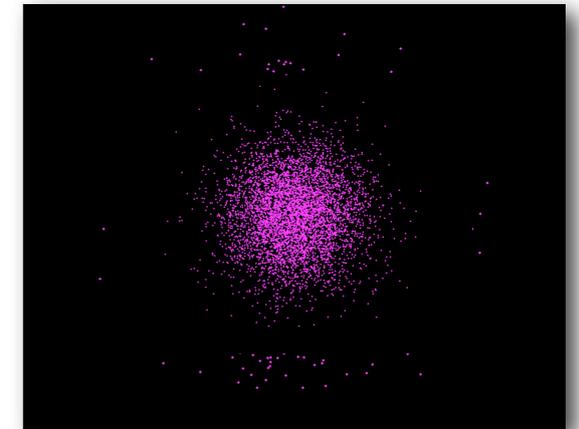
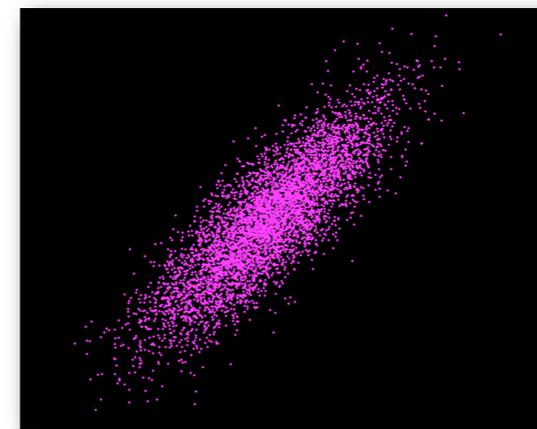
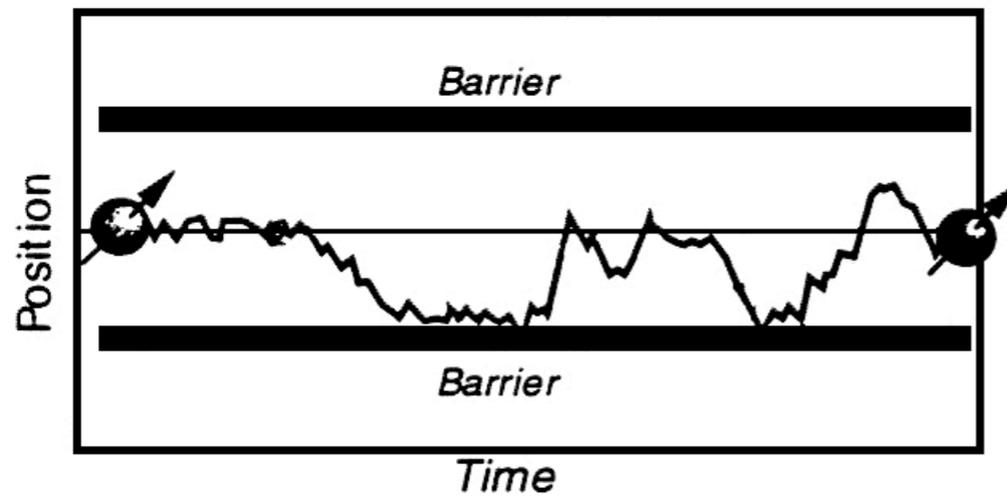


# Diffusion in tissues

Free Diffusion

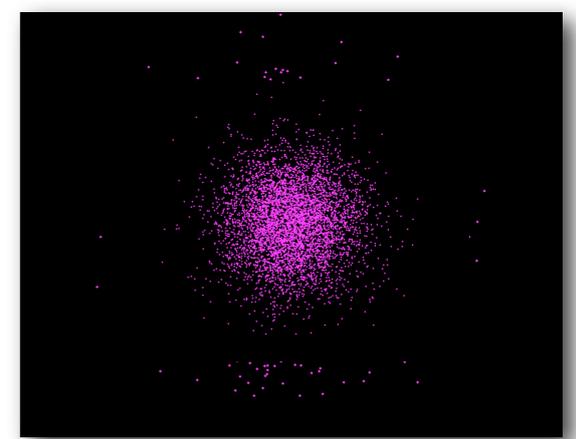
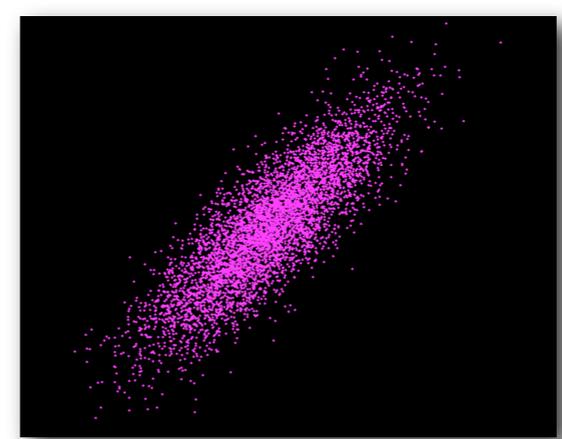
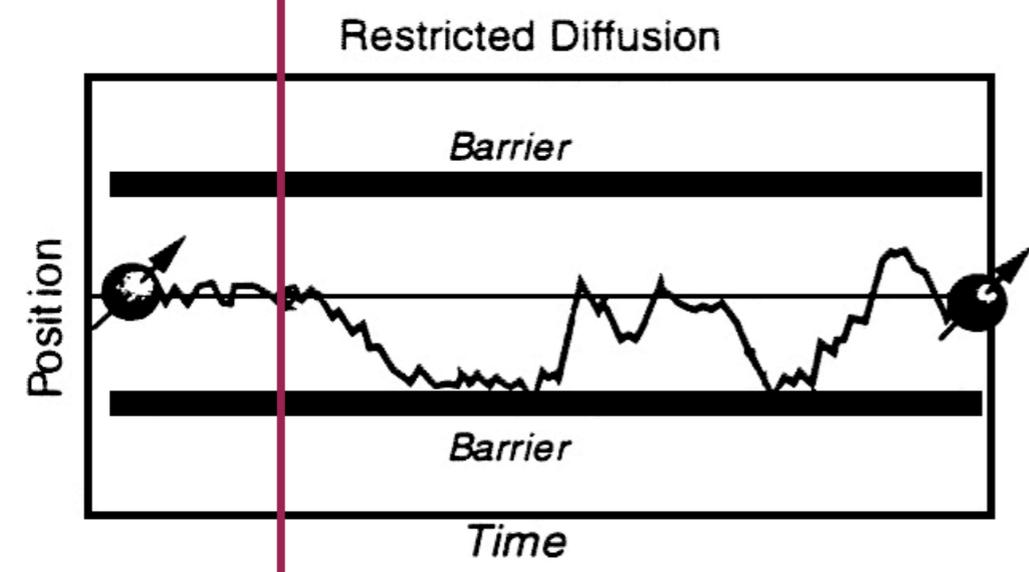
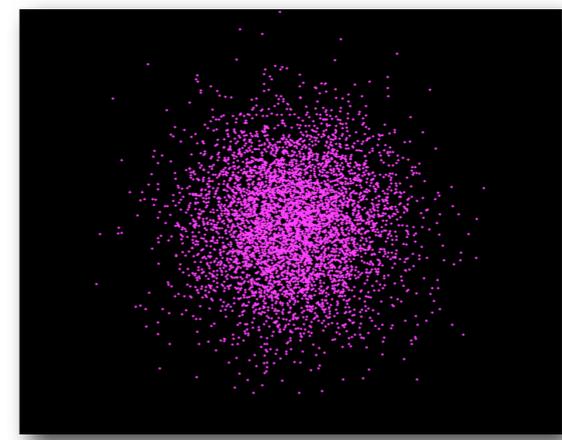
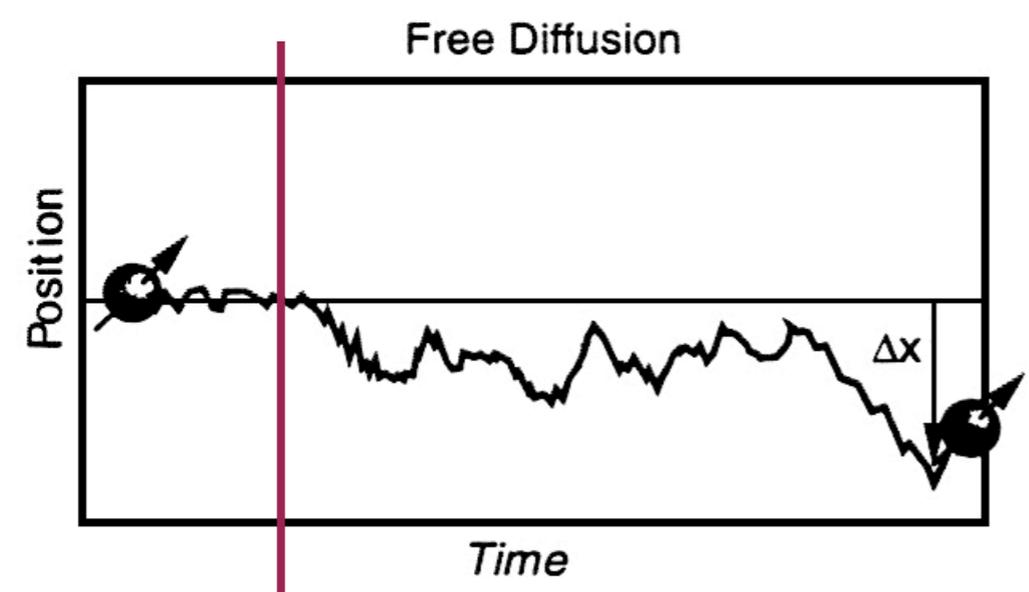


Restricted Diffusion





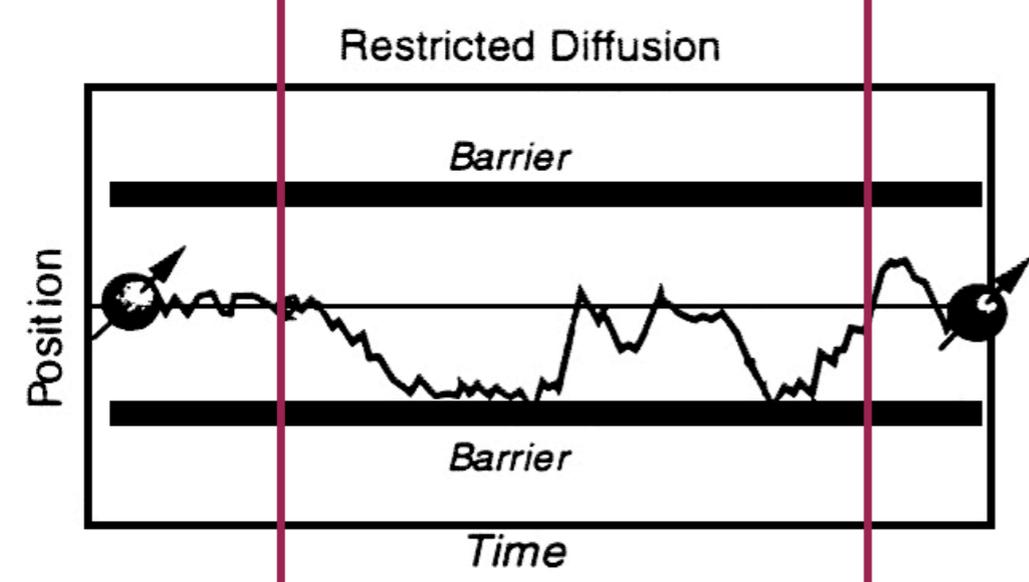
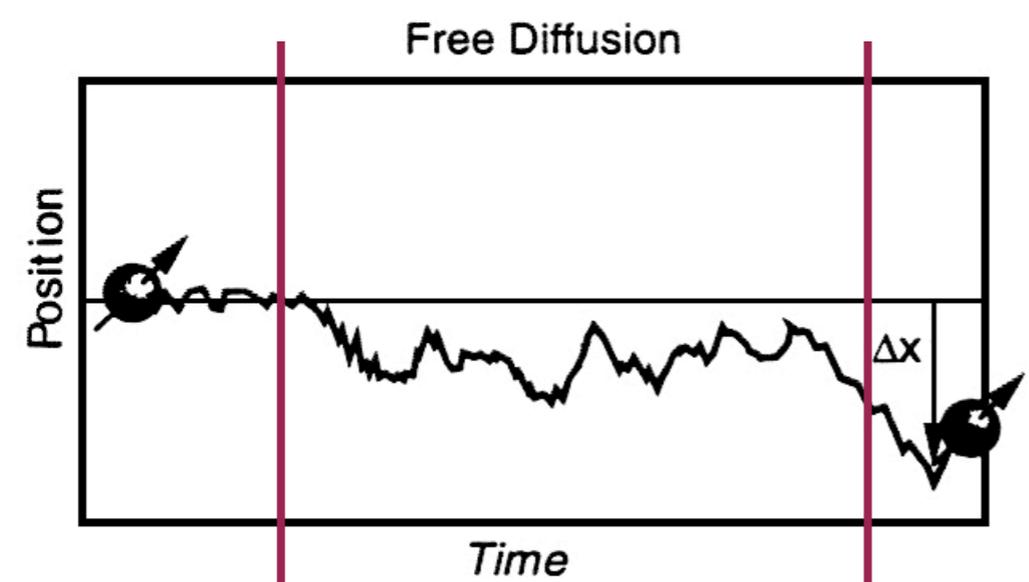
# Diffusion in tissues



“Looks” like free diffusion

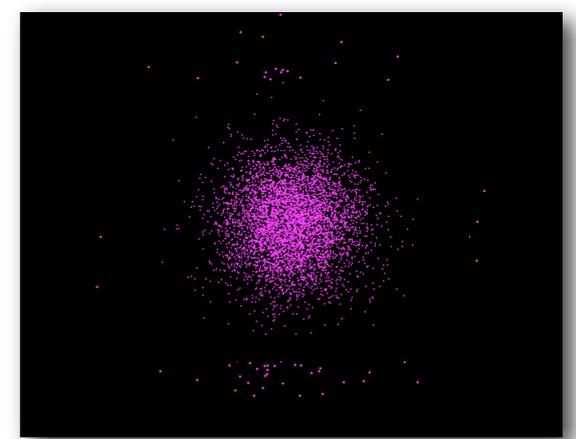
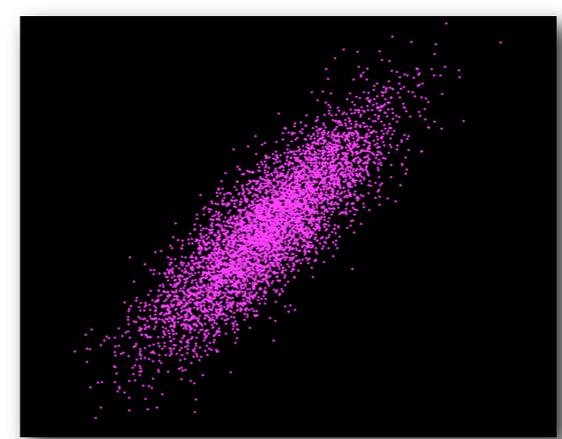
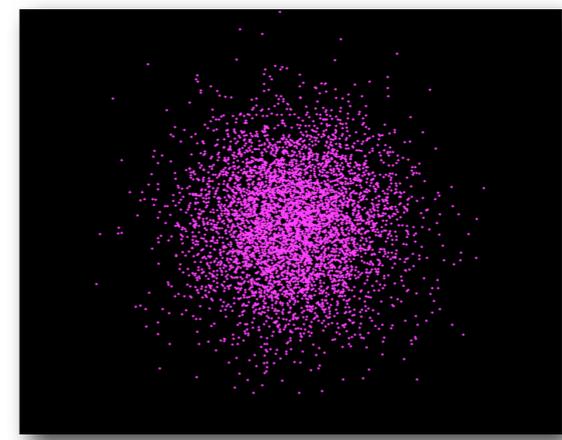


# Diffusion in tissues



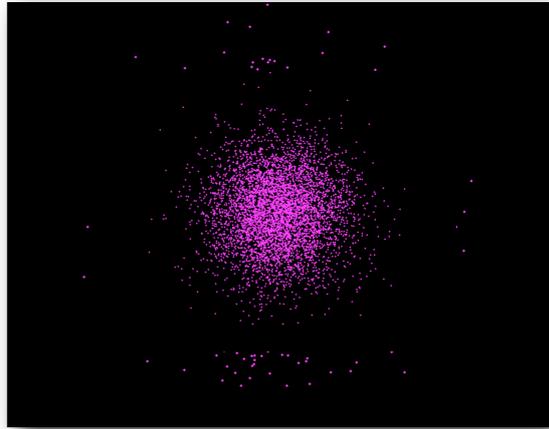
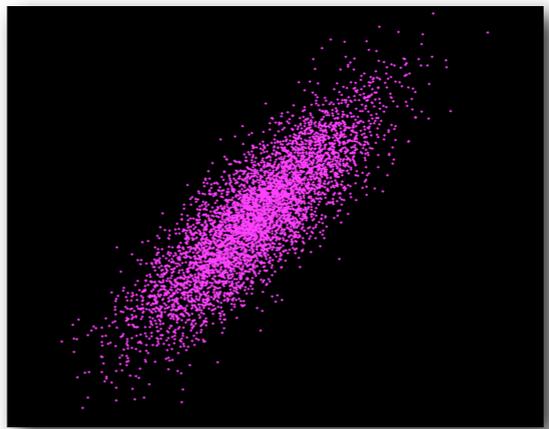
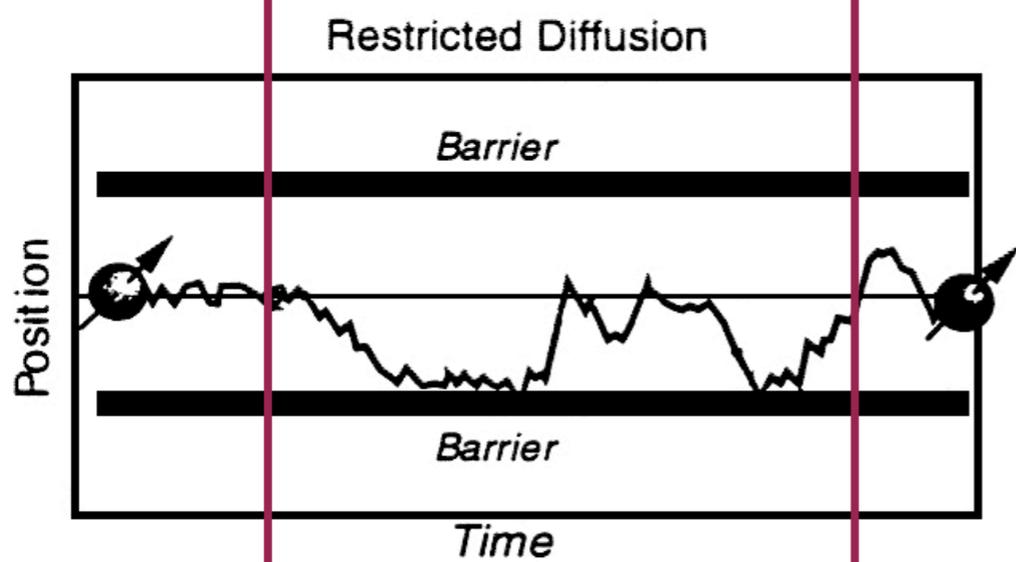
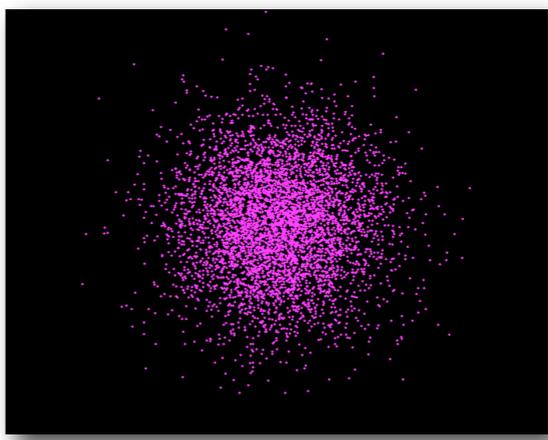
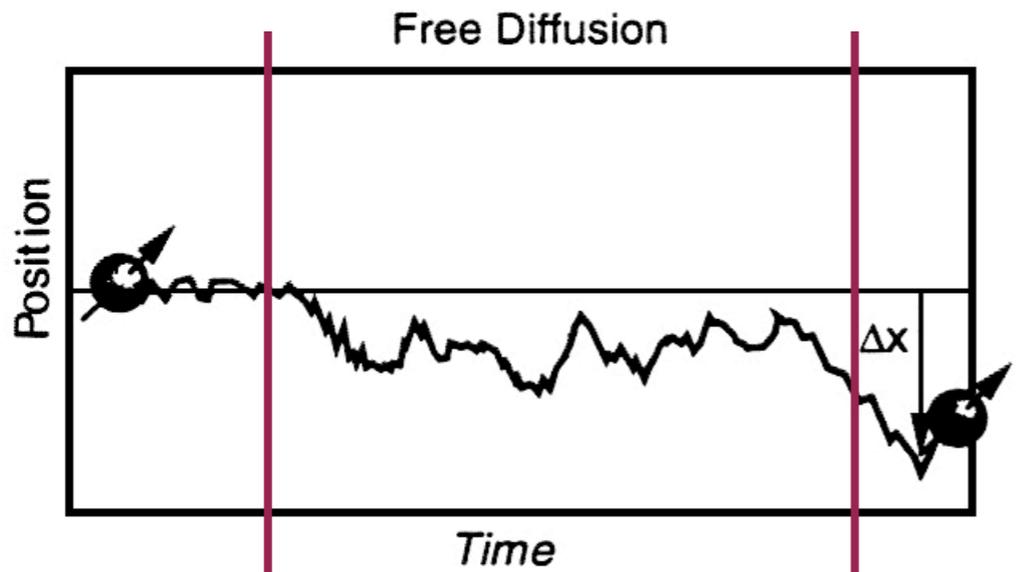
“Looks” like free diffusion

“Doesn’t look” like free diffusion





# Diffusion in tissues



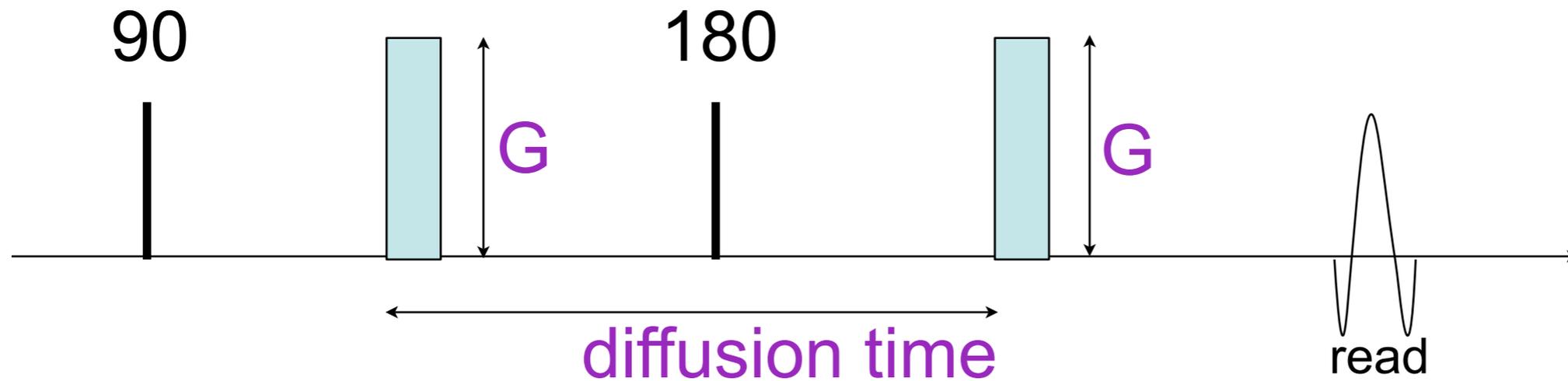
“Looks” like free diffusion

“Doesn’t look” like free diffusion

“Apparent” diffusion coefficient (ADC) depends on the diffusion experiment!

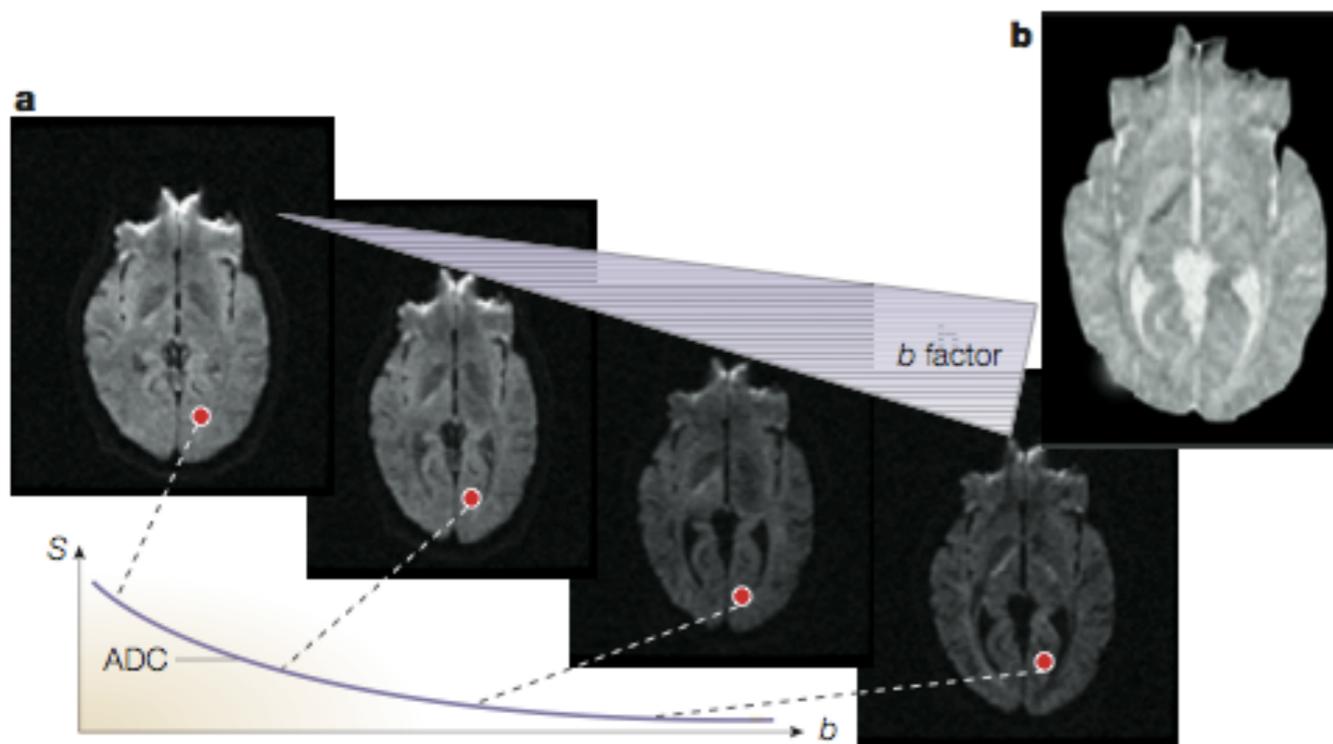


# Measuring diffusion with MRI



Diffusion contrast is modulated by:

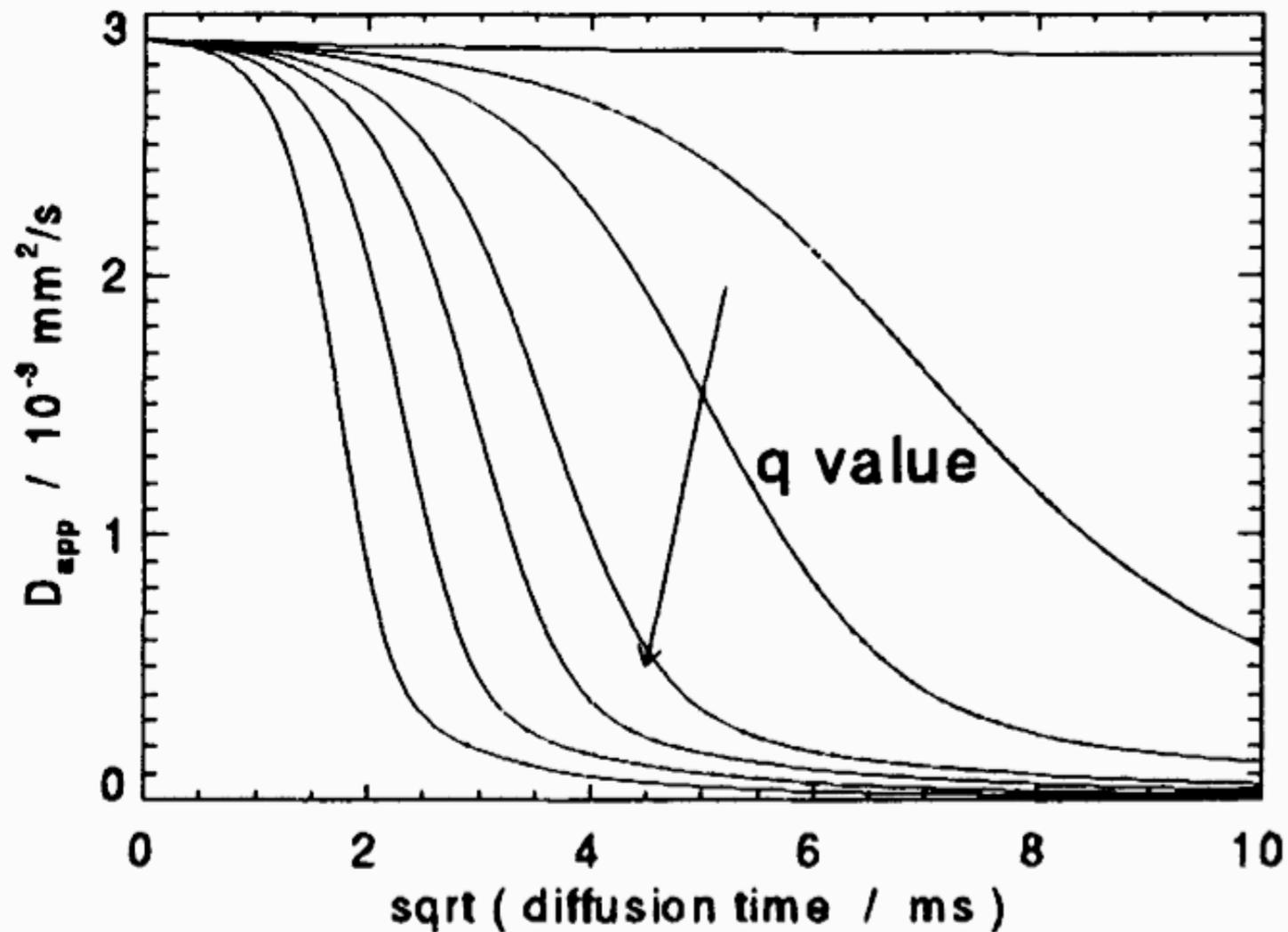
- . Gradient **strength**
- . Gradient **orientation**
- . Diffusion **time**





# Apparent diffusion coefficient

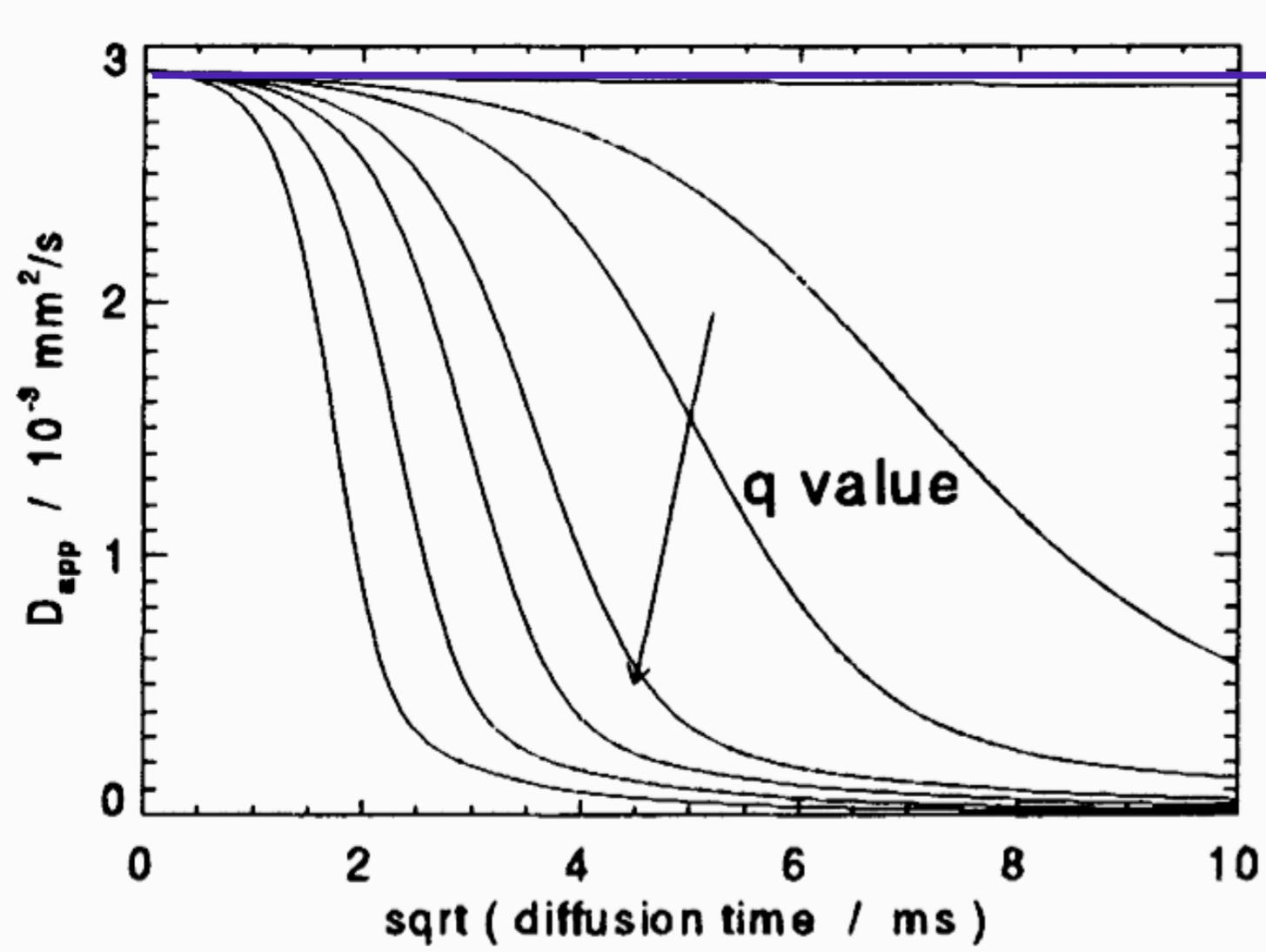
Remember:  
 $q \sim$  gradient strength





# Apparent diffusion coefficient

Remember:  
 $q \sim$  gradient strength



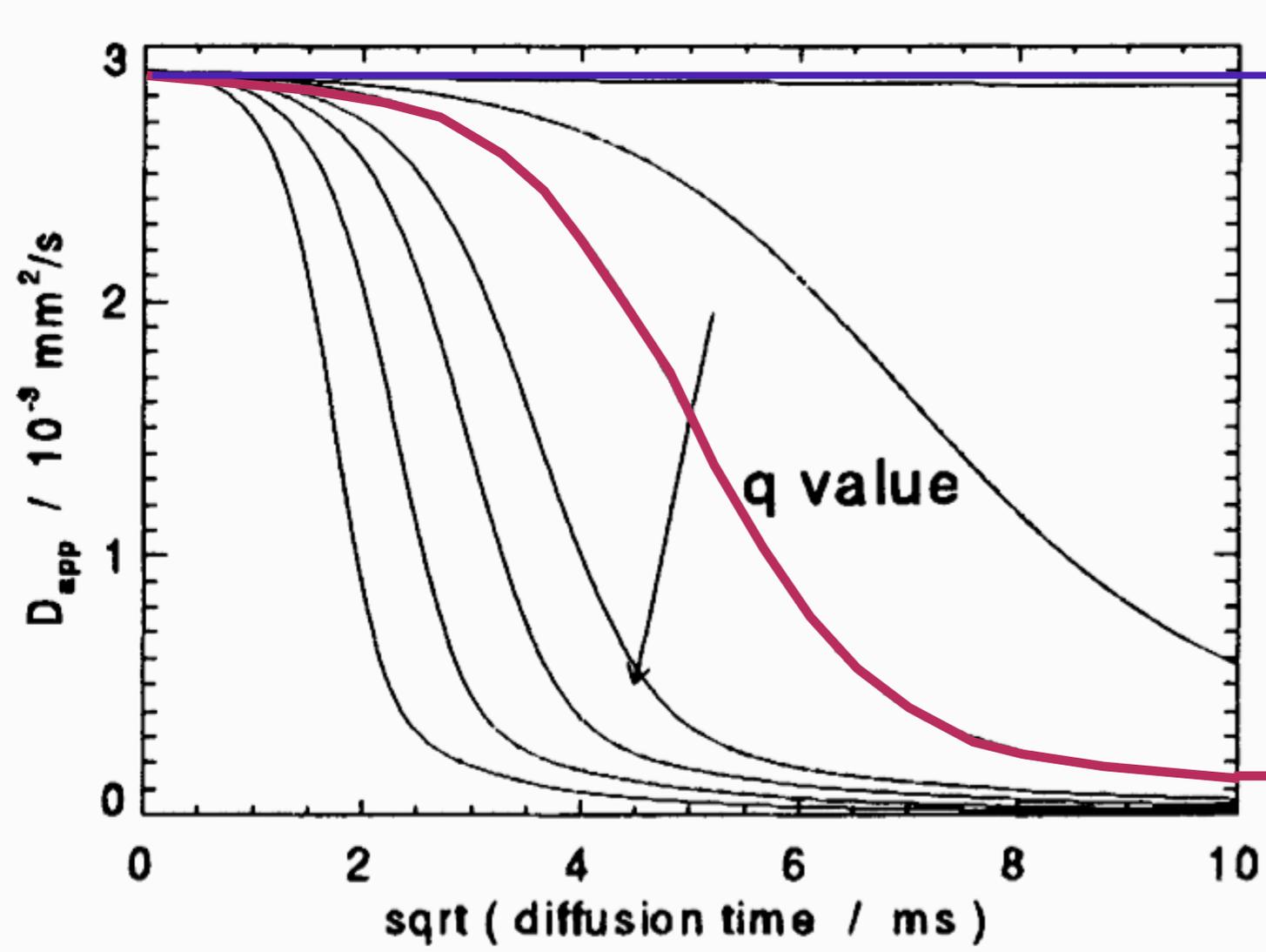
"intrinsic" diffusion coefficient

Pfeuffer et al, NMR Biomed 1998



# Apparent diffusion coefficient

Remember:  
 $q \sim$  gradient strength



“intrinsic” diffusion coefficient

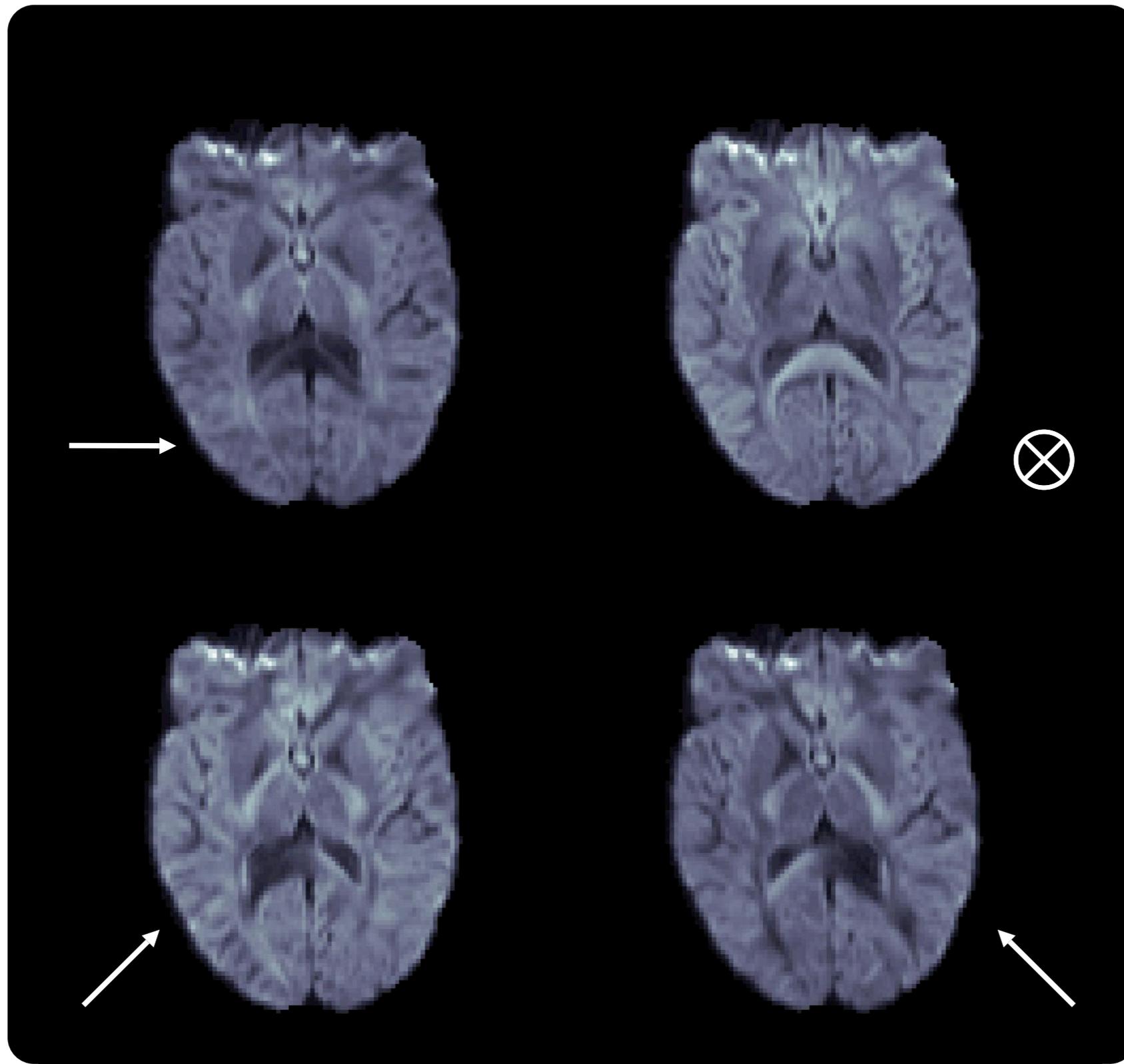
“apparent” diffusion coefficient

Typical experiment (50-100 ms)

Pfeuffer et al, NMR Biomed 1998

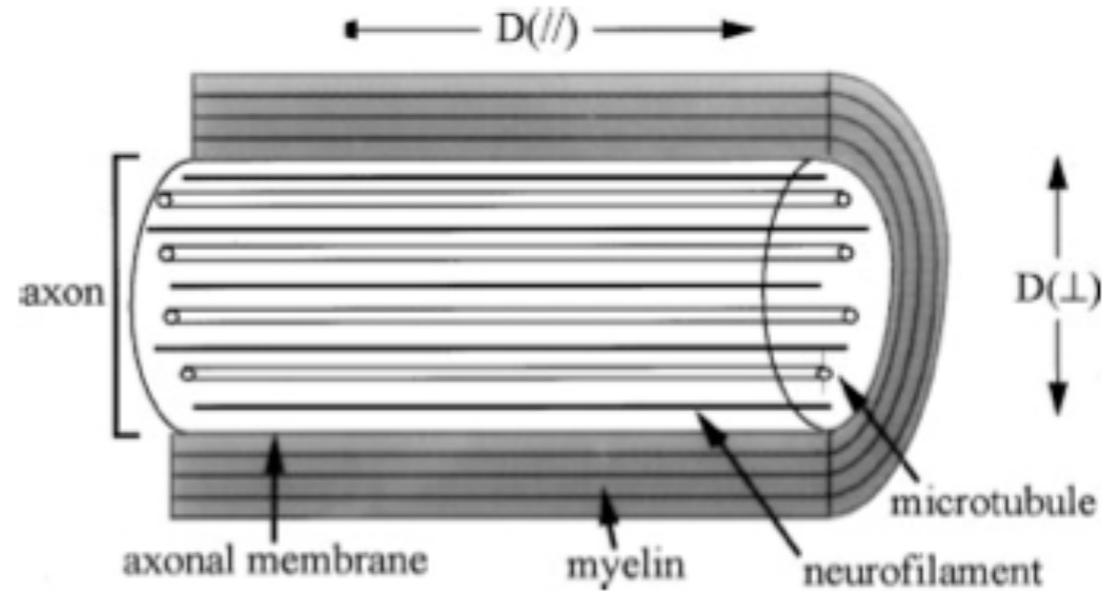
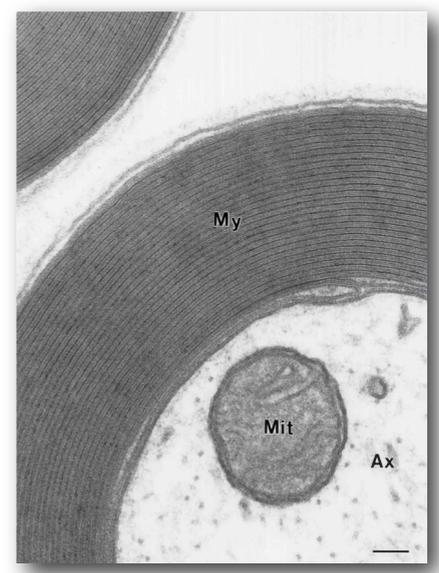
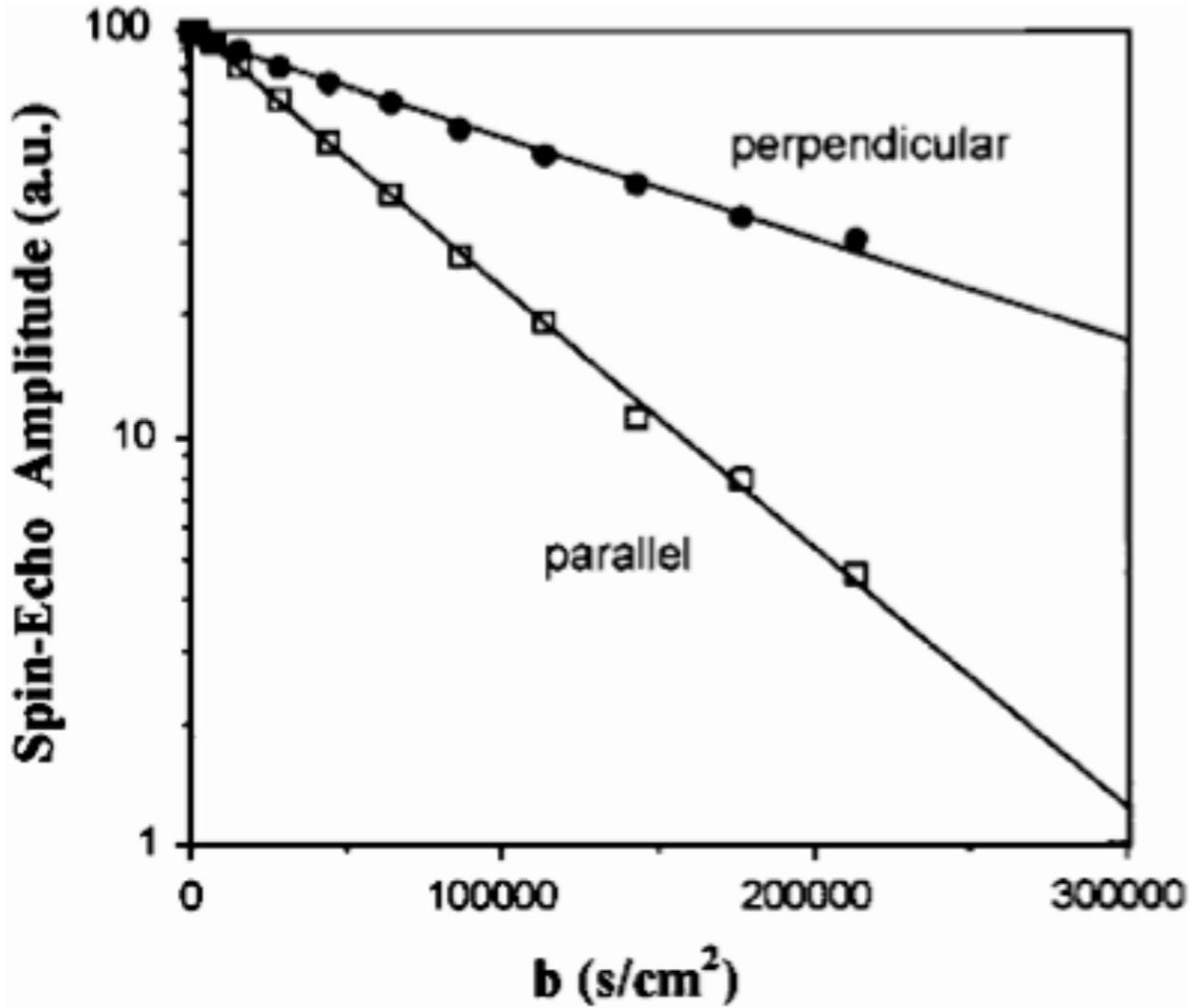


# Orientation contrast in Diffusion MR





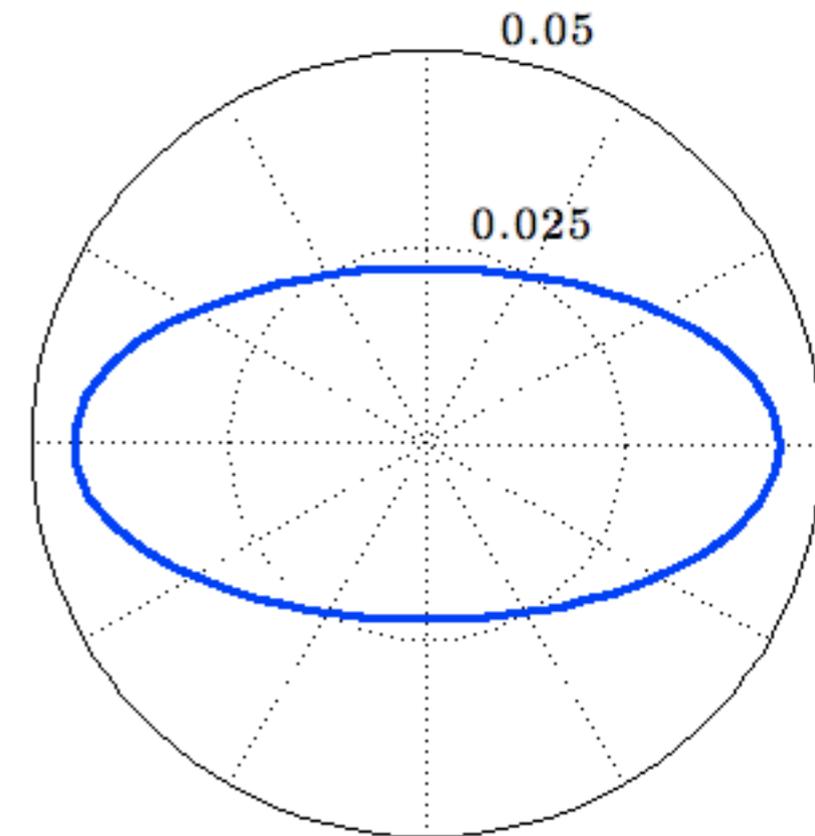
# Anisotropy of the Apparent diffusion coefficient



Beaulieu, NMR Biomed 2002



# Diffusion tensor model



Iso-probability contour

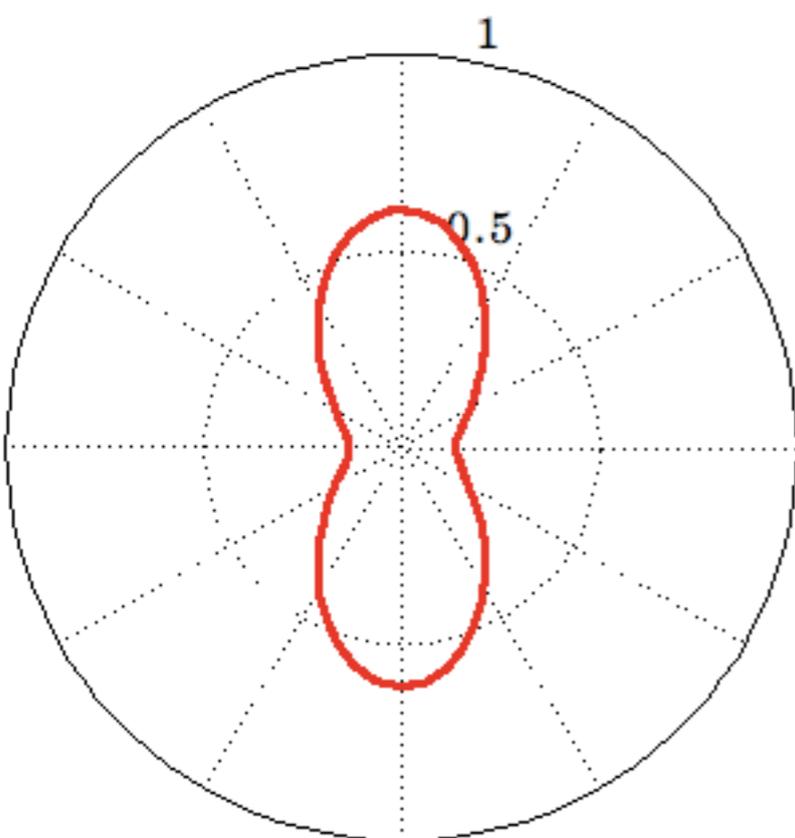
$$\mathcal{N}(0, 2\tau\mathbf{D})$$

mean squared displacement





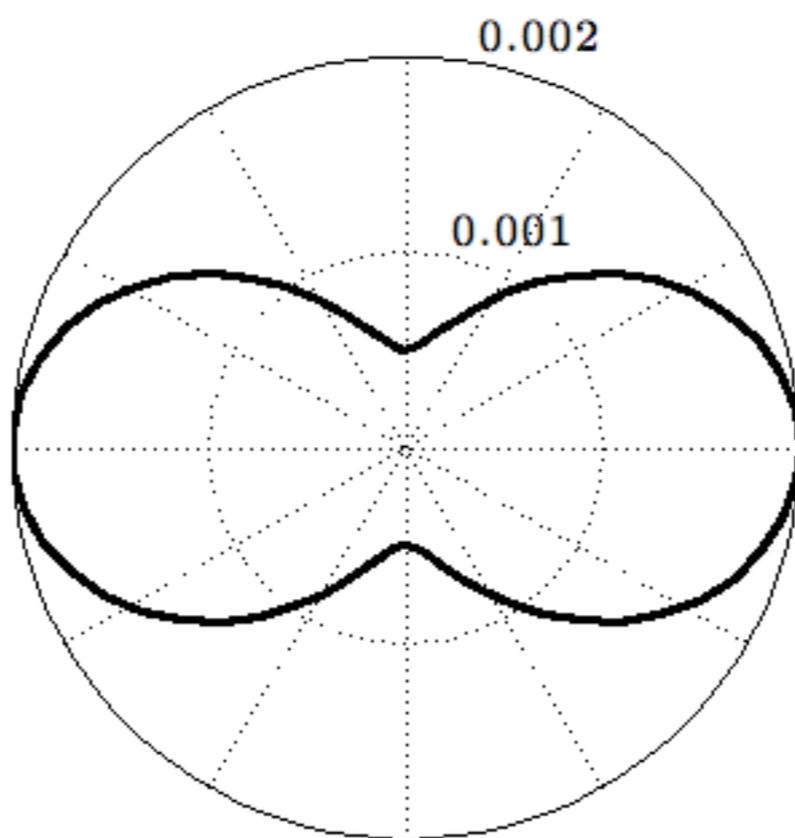
# Diffusion tensor model



diffusion MRI signal

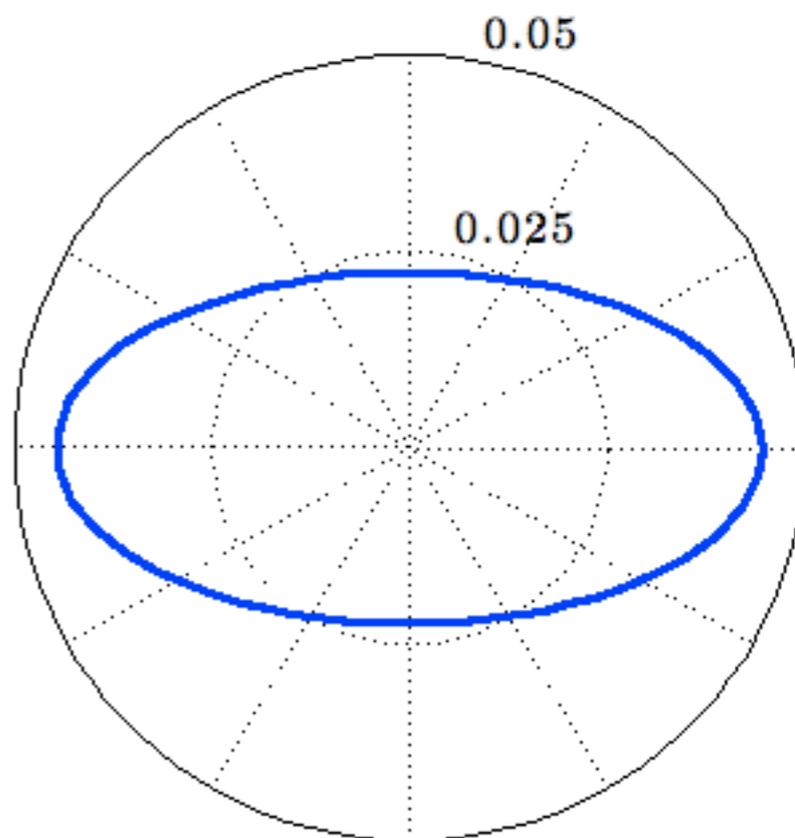
$$\exp(-b\mathbf{x}^T\mathbf{D}\mathbf{x})$$

↑  
signal attenuation



ADC profile  
(mm<sup>2</sup>/s)

$$\mathbf{x}^T\mathbf{D}\mathbf{x}$$



Iso-probability contour

$$\mathcal{N}(0, 2\tau\mathbf{D})$$

↑  
mean squared displacement

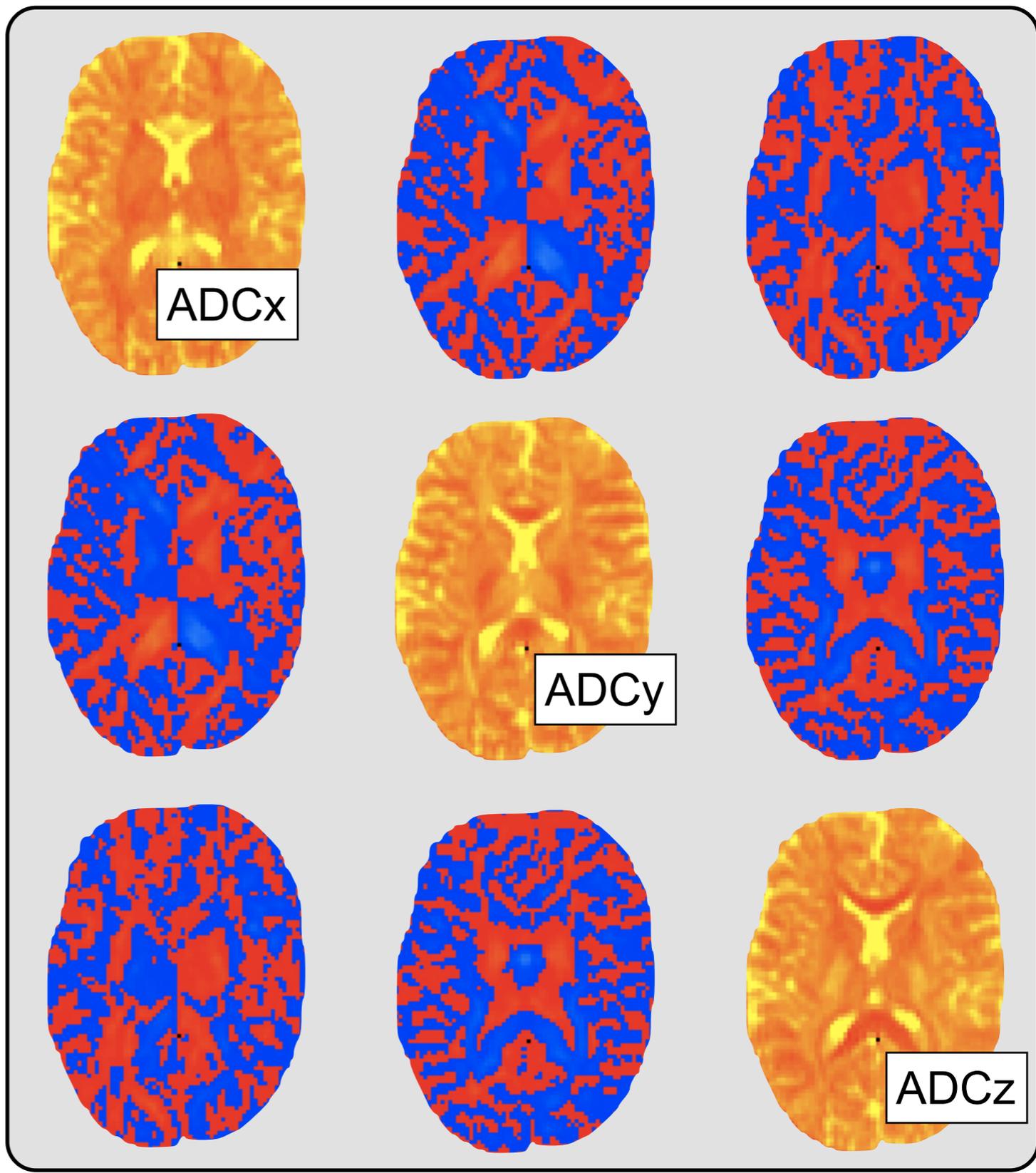
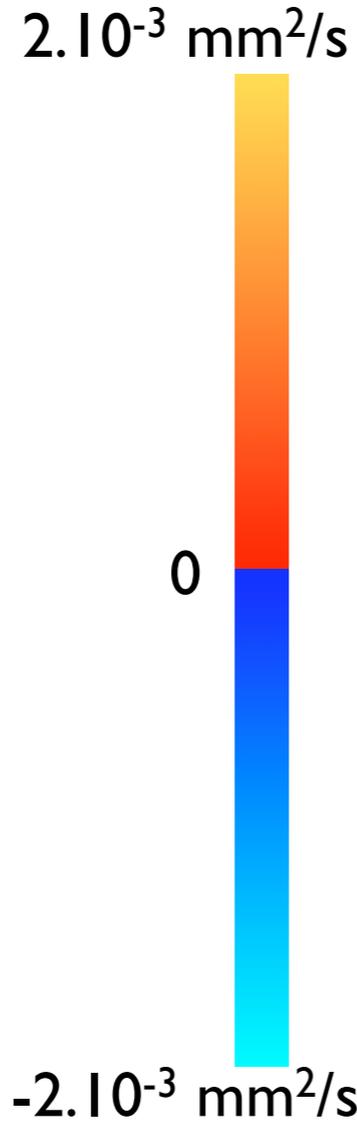




# Diffusion tensor model

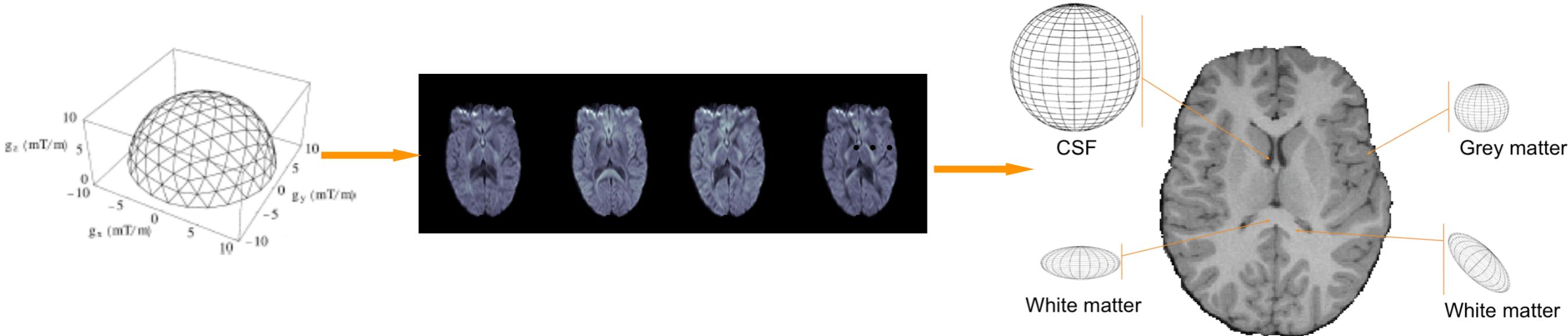
$$\exp(-b\mathbf{x}^T \mathbf{D} \mathbf{x})$$

↑





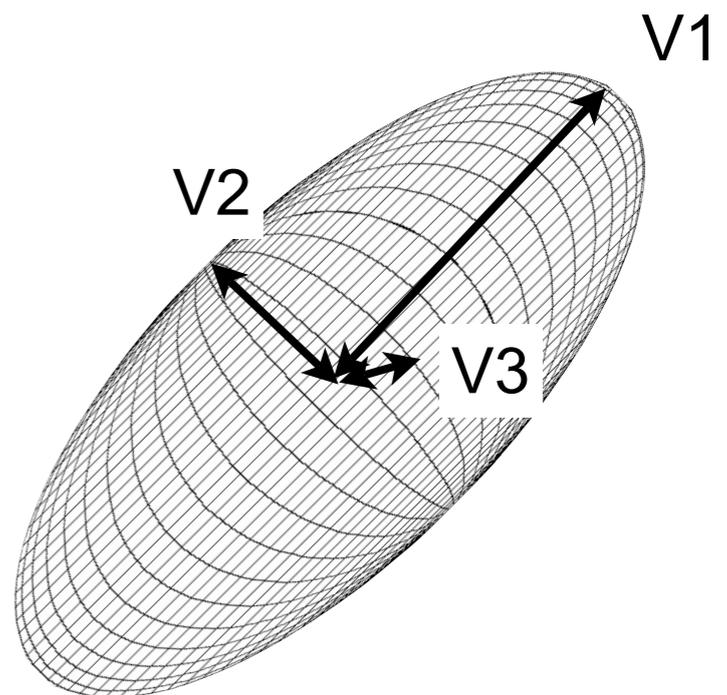
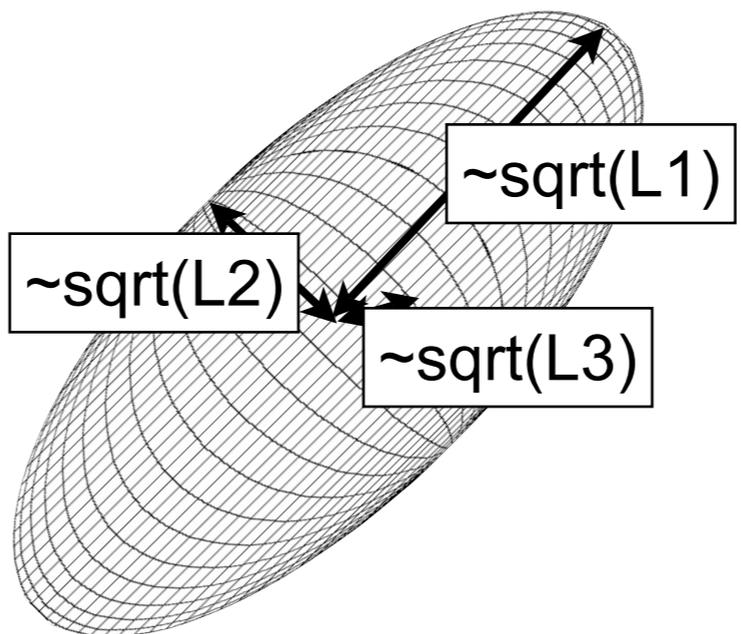
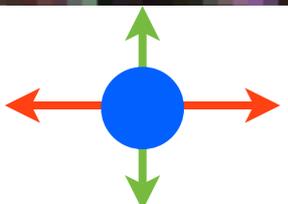
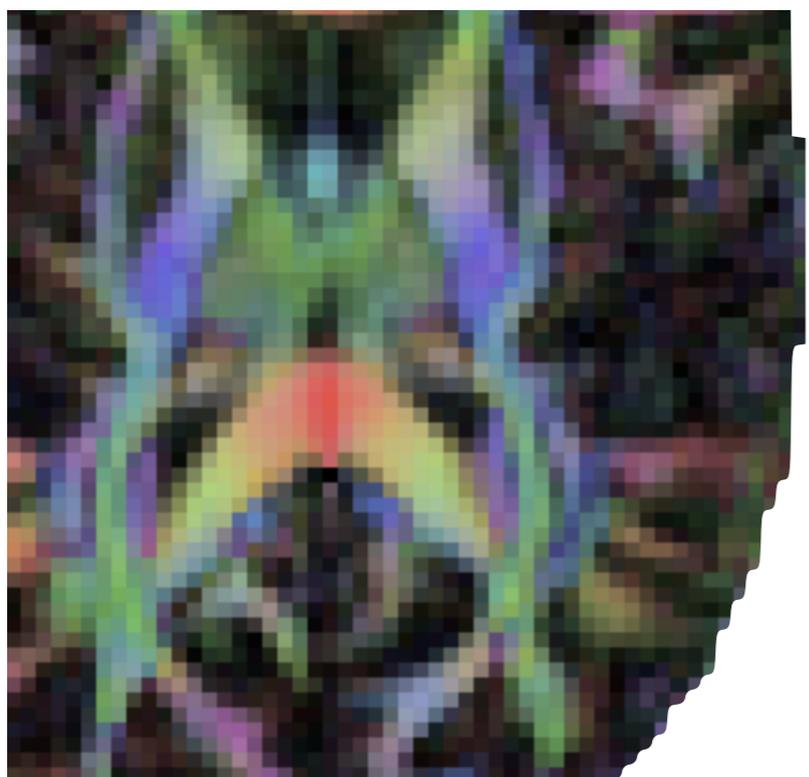
# Diffusion tensor model Estimation





# Diffusion tensor model eigenspectrum

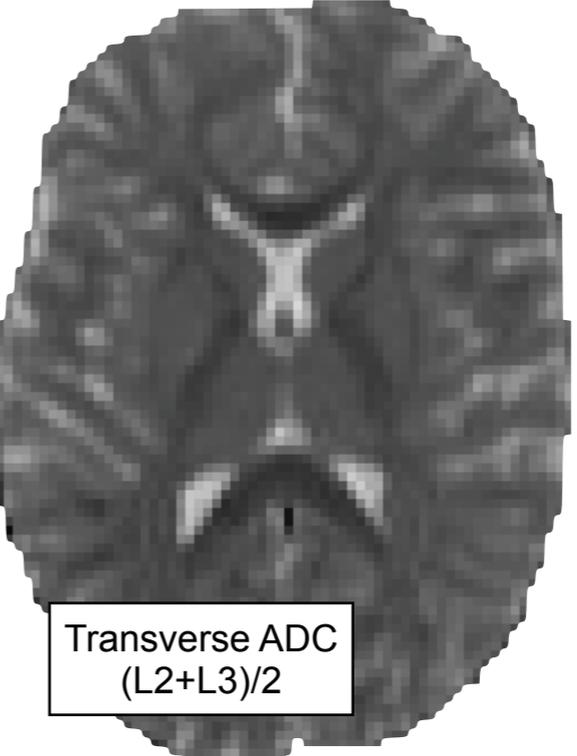
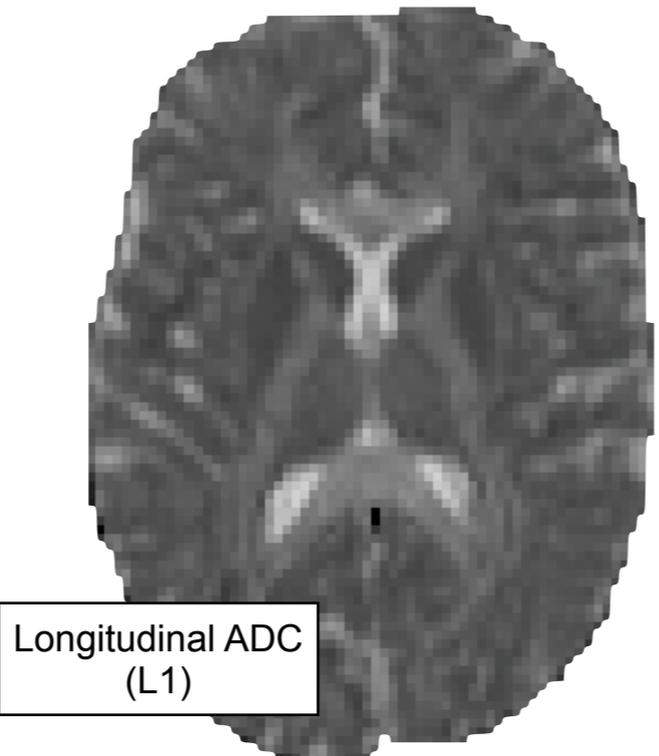
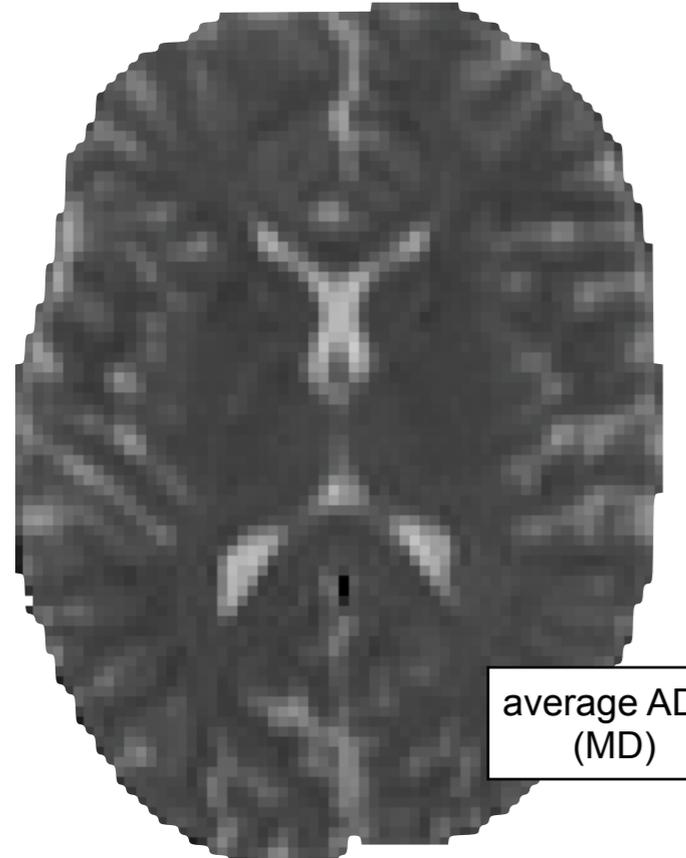
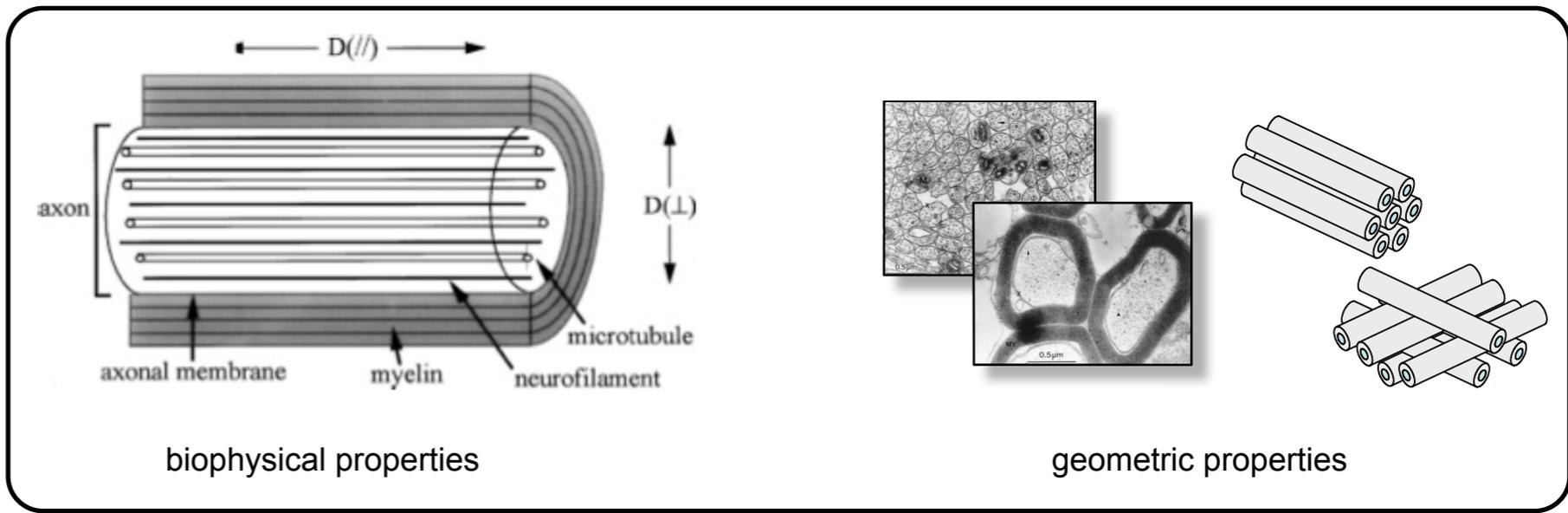
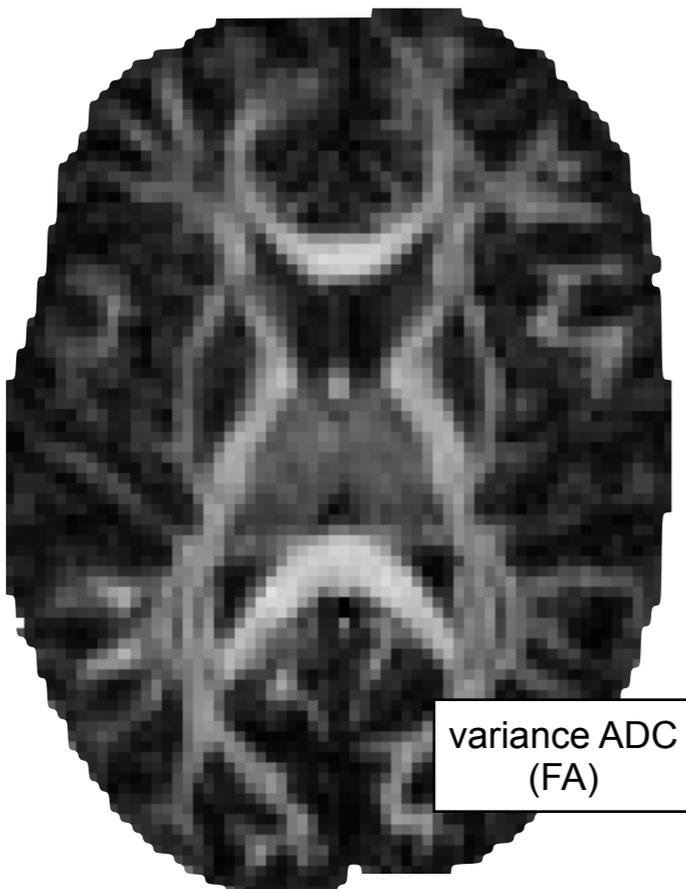
V1 map



L1=ADCmax  
L3=ADCmin  
L1+L2+L3 = 3x(average ADC)

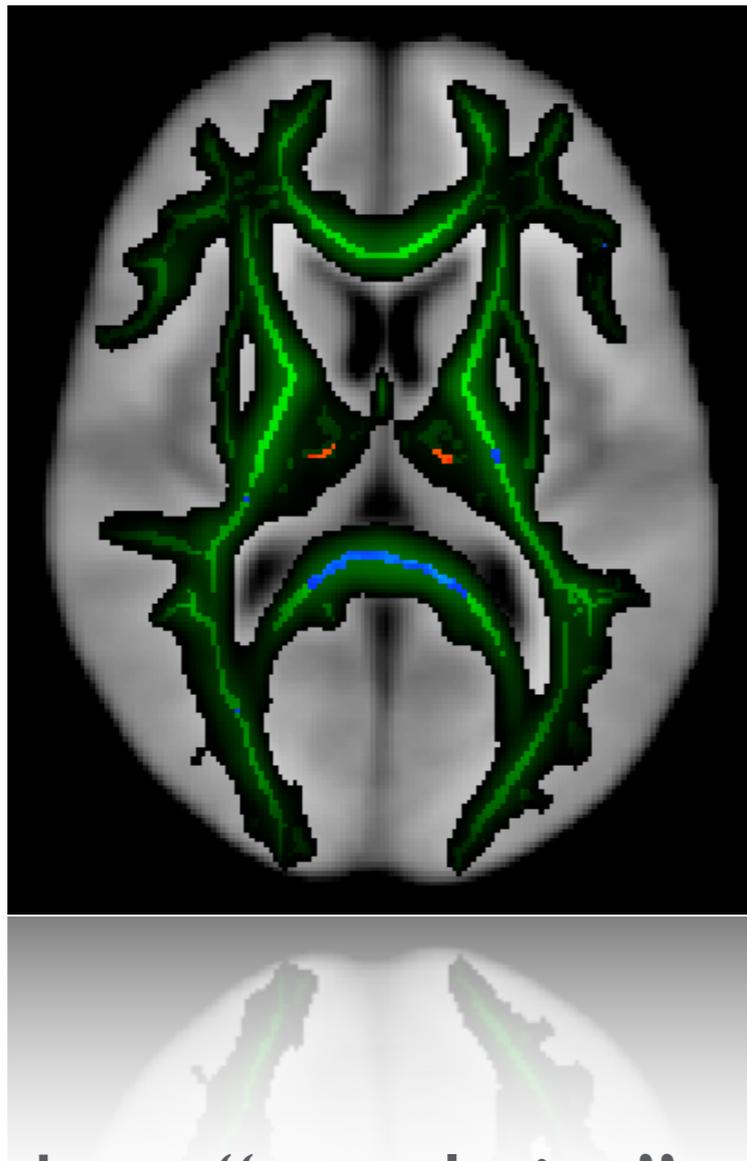


# Tensor-derived measures





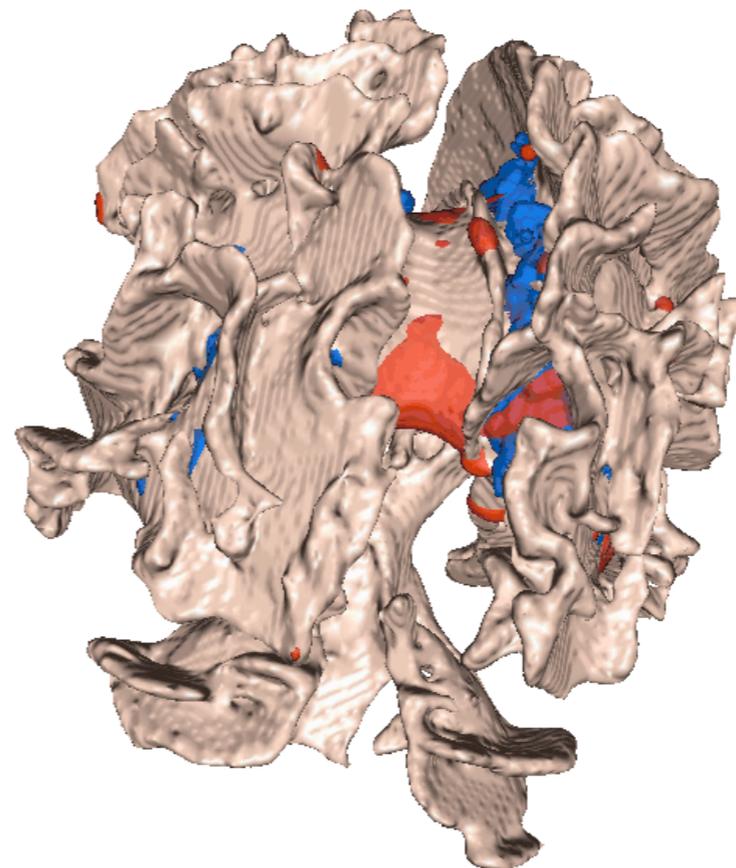
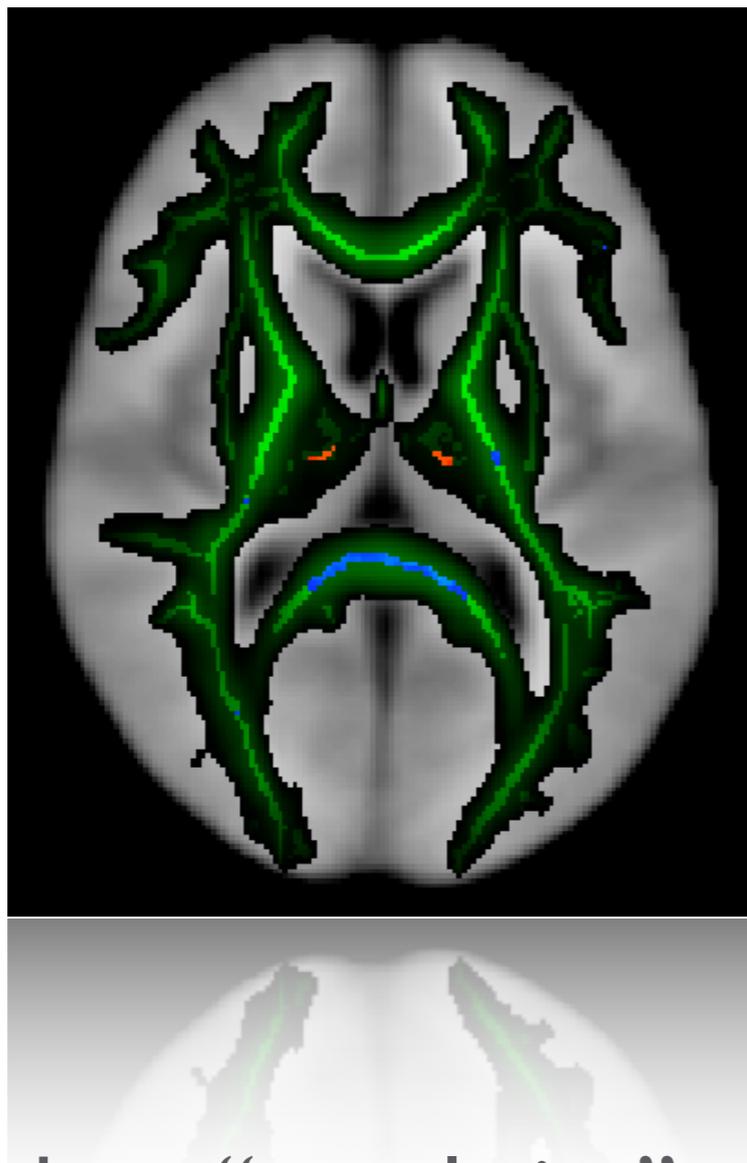
# TBSS : Tract-Based Spatial Statistics



- Need: robust “voxelwise” cross-subject stats on DTI
- Problem: alignment issues confound valid local stats
- TBSS: solve alignment using alignment-invariant features:
- Compare FA taken from tract centres (via skeletonisation)



# TBSS : Tract-Based Spatial Statistics



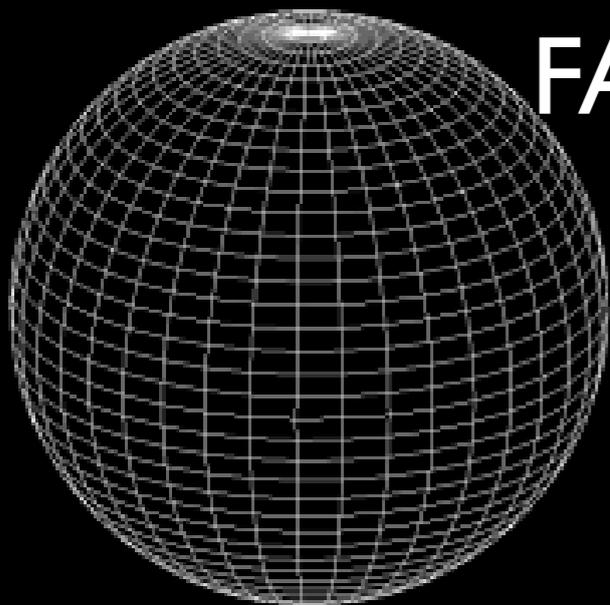
- Need: robust “voxelwise” cross-subject stats on DTI
- Problem: alignment issues confound valid local stats
- TBSS: solve alignment using alignment-invariant features:
- Compare FA taken from tract centres (via skeletonisation)



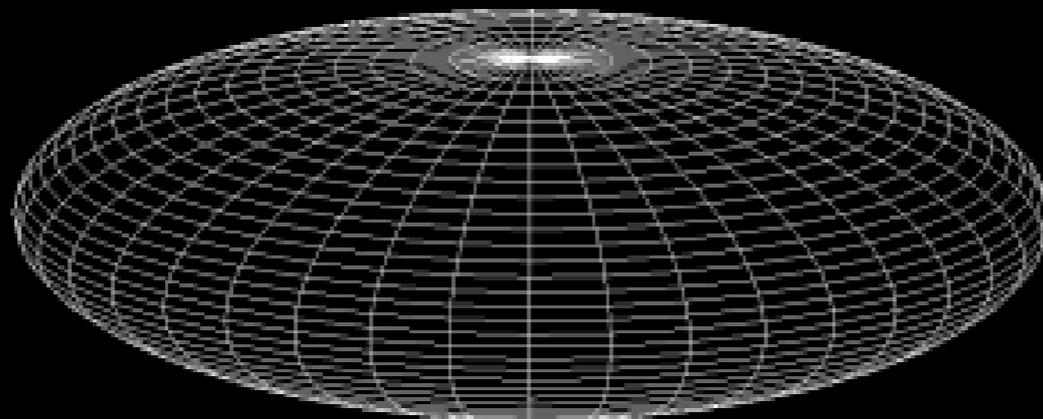
# Tensor-derived parameters: Fractional Anisotropy

- FA encodes how strongly directional diffusion is
  - (derived from diffusion tensor eigenvalues)
- Hence good marker for WM integrity
  - i.e., good marker for disease, development, etc.

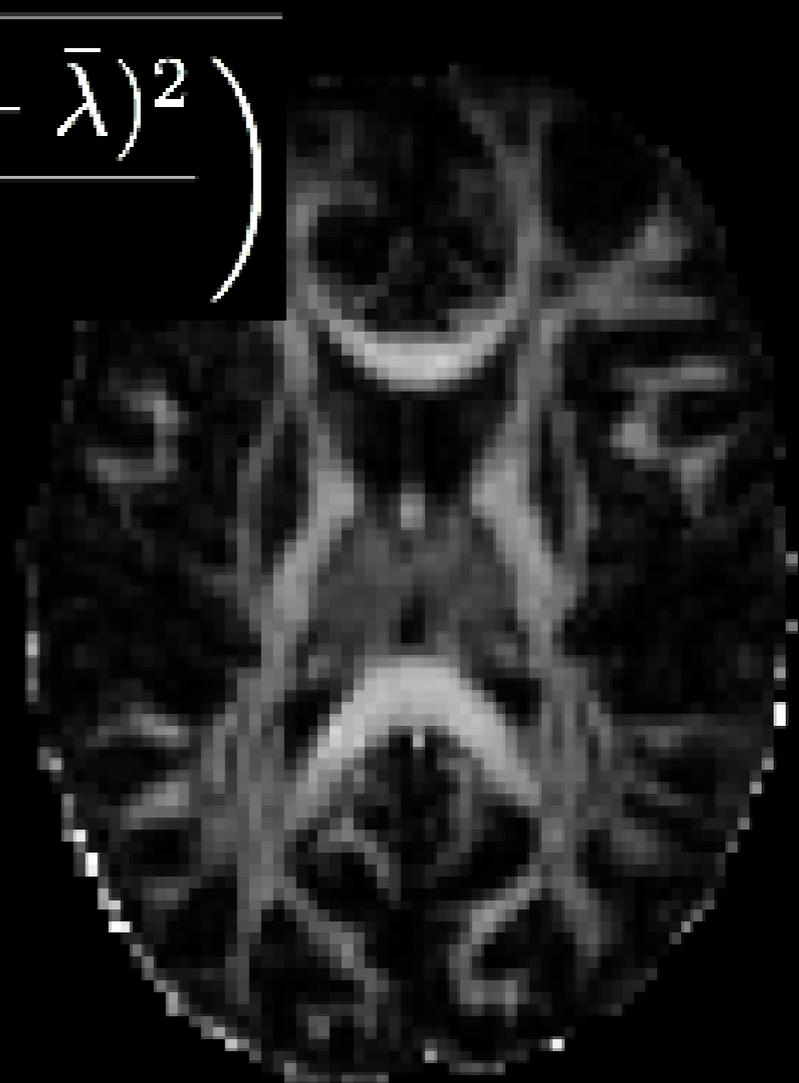
$$FA = \sqrt{\frac{3}{2} \left( \frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2} \right)}$$



FA=0



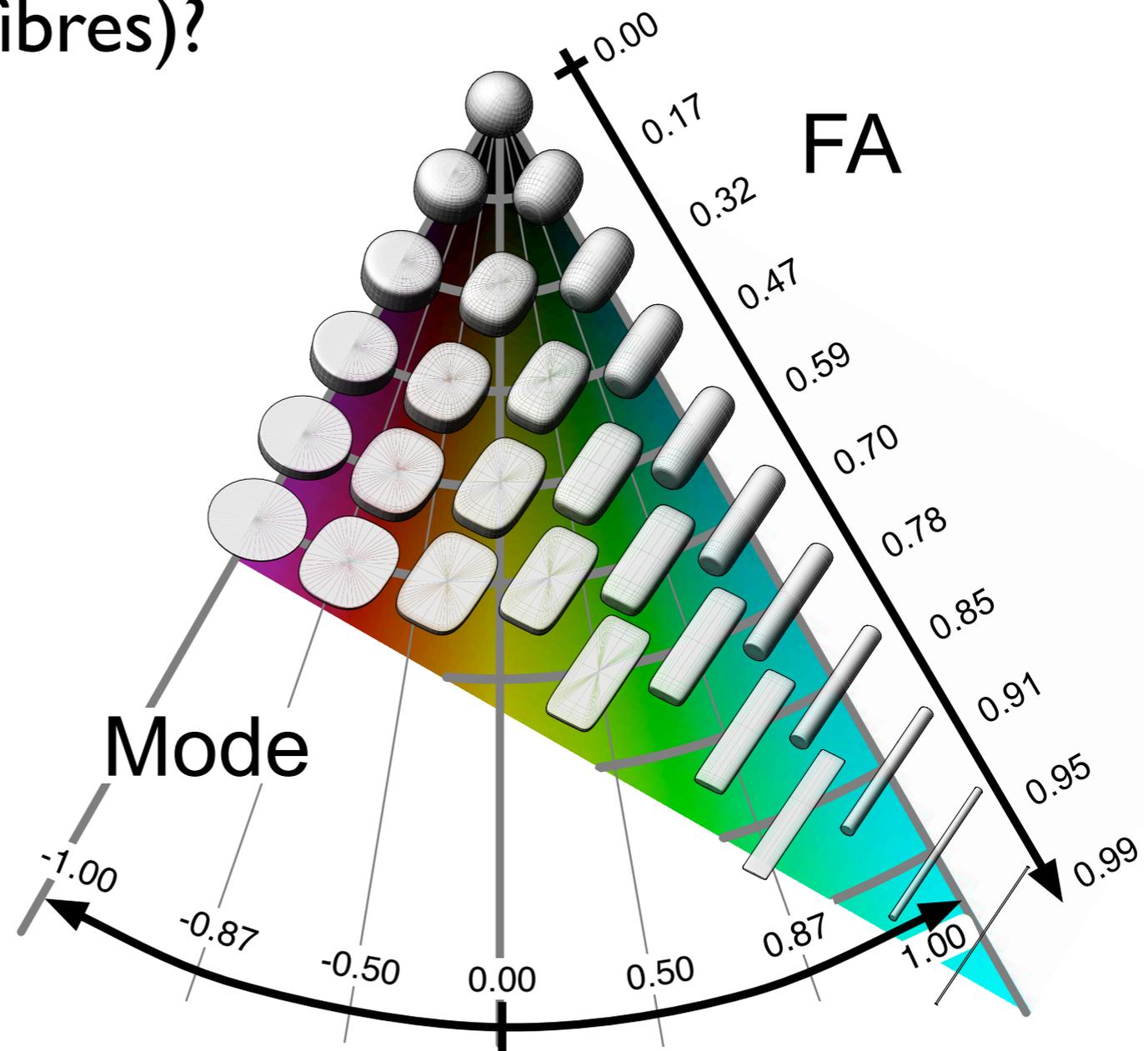
FA=0.8



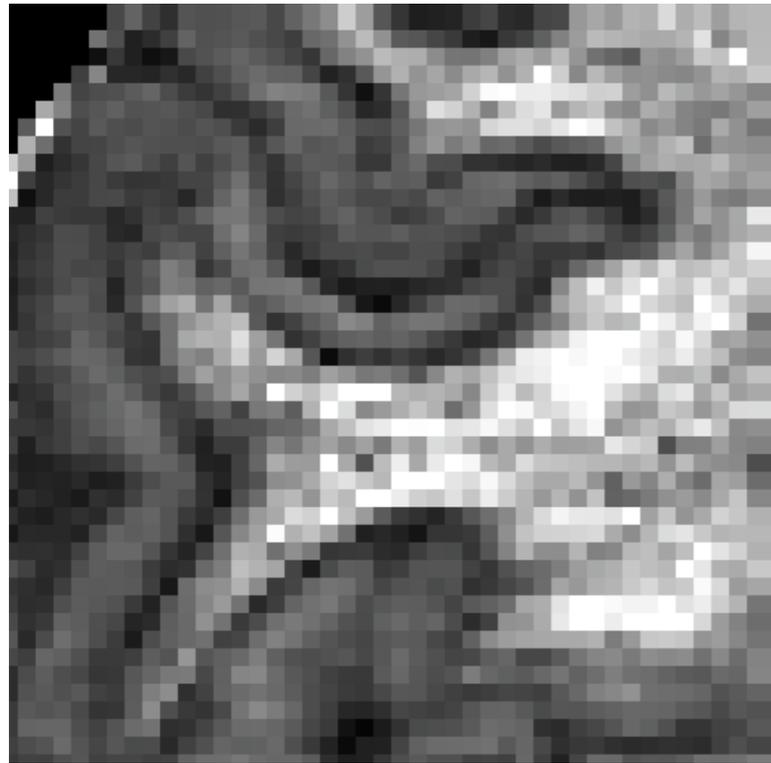


# Orthogonal Tensor Invariants (Kindlmann, TMI 2007)

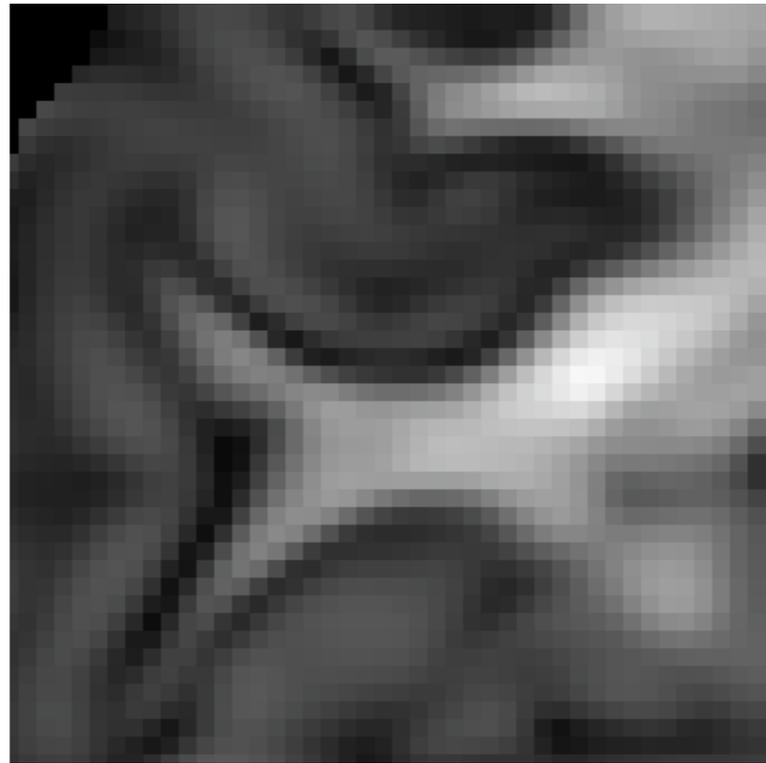
- Nice to have 3 orthogonal (independent) tensor-derived measures: MD, FA & “Mode”
- Mode: is the tensor tubular (one strong fibre) or flat-cylindrical (two strong fibres)?



At “normal” resolutions, tracts appear thinner than they really are primarily because of the interference between orthogonal anisotropy in GM and WM



original 0.7mm data -> FA



data smoothed to match  
2mm data -> FA



data smoothed to match  
3.5mm data -> FA

*high-resolution ex-vivo diffusion data:  
McNab & Miller (FMRIB)*

*computation resources:  
Jones, Stathakis & Wise (CUBRIC cluster)*





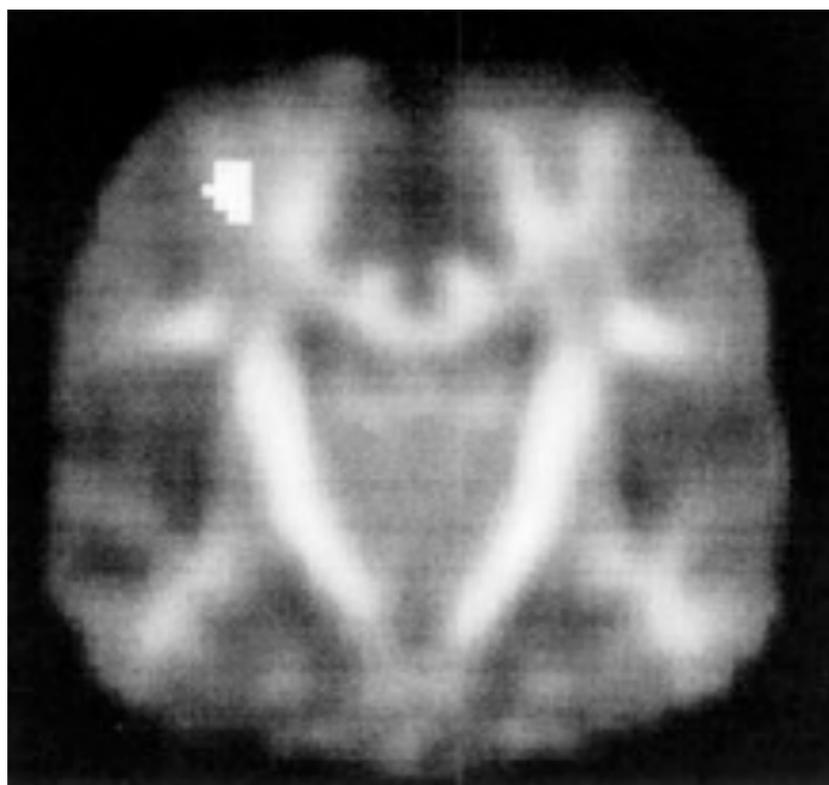
# VBM-style Analysis of FA

- VBM [Ashburner 2000, Good 2001]
  - Align all subjects' data to standard space
  - Segment -> grey matter segmentation
  - Smooth GM
  - Do voxelwise stats (e.g. controls-patients)
- 
- VBM on FA [Rugg-Gunn 2001, Büchel 2004, Simon 2005]
  - Like VBM but no segmentation needed

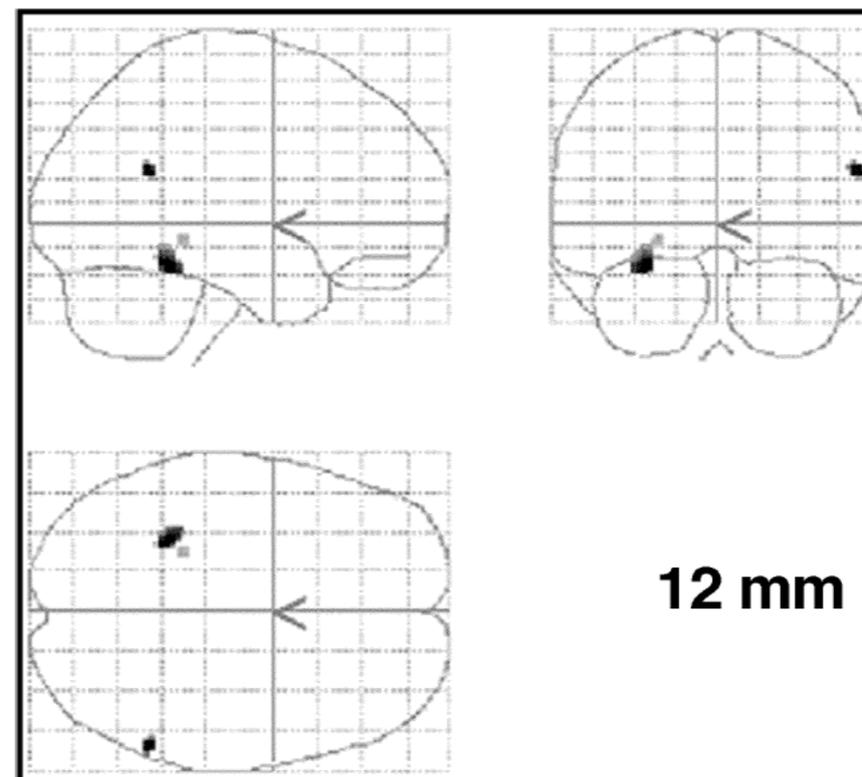


# VBM-style Analysis of FA

- VBM [Ashburner 2000, Good 2001]
  - Align all subjects' data to standard space
  - Segment -> grey matter segmentation
  - Smooth GM
  - Do voxelwise stats (e.g. controls-patients)
- 
- VBM on FA [Rugg-Gunn 2001, Büchel 2004, Simon 2005]
  - Like VBM but no segmentation needed



Büchel 2004

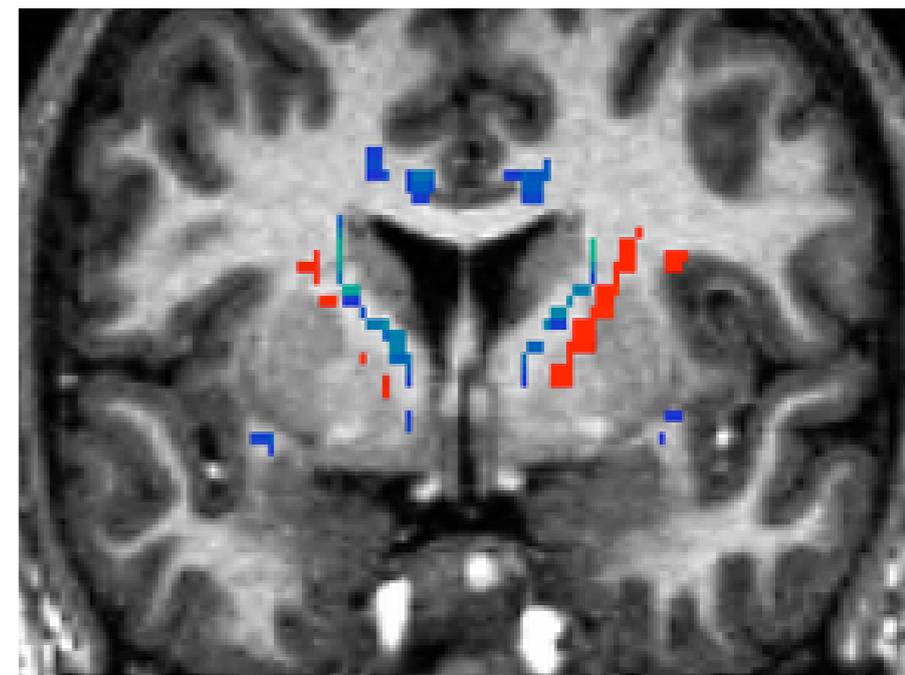
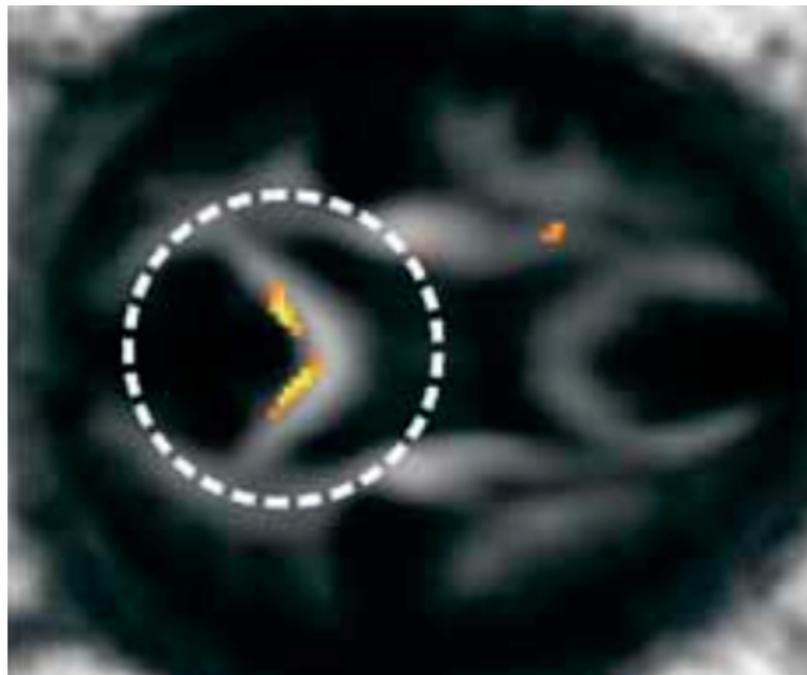
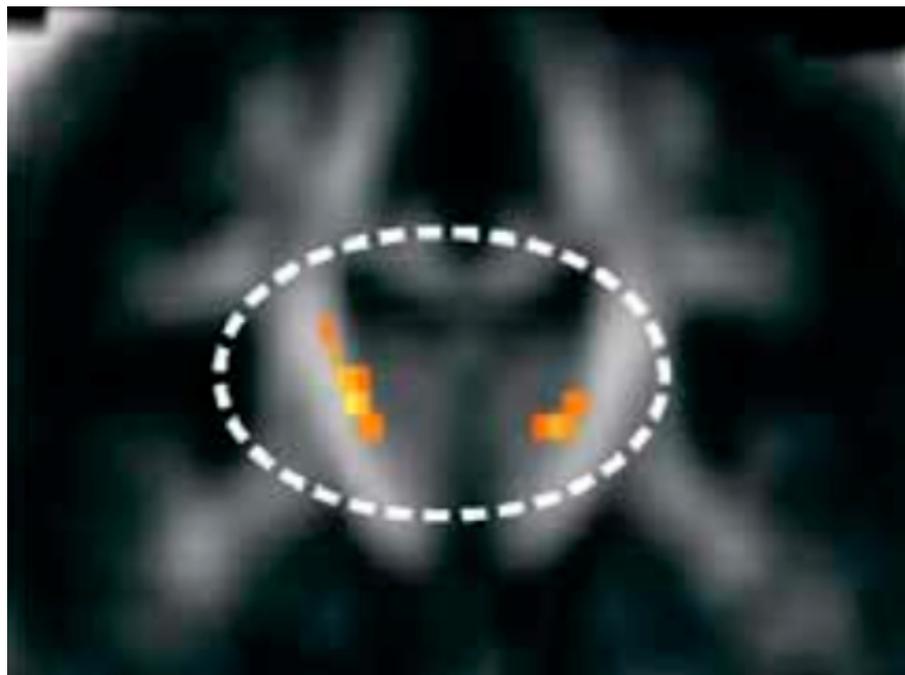


Jones 2005



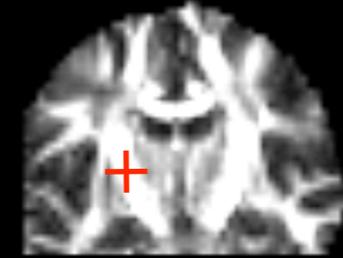
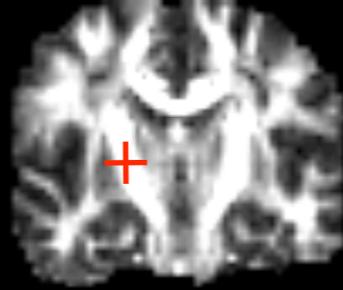
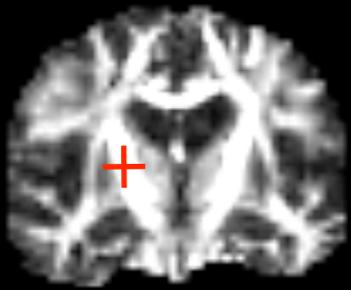
# VBM-style Analysis of FA

- Strengths
  - Fully automated & quick
  - Investigates whole brain
- Problems [Bookstein 2001, Davatzikos 2004, Jones 2005]
  - Alignment difficult; smallest systematic shifts between groups can be incorrectly interpreted as FA change
  - Needs smoothing to help with registration problems
  - No objective way to choose smoothing extent

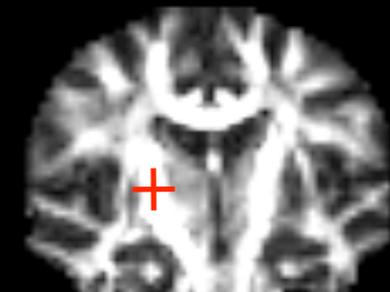
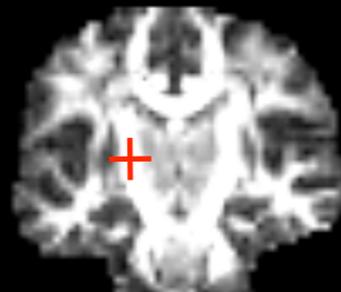
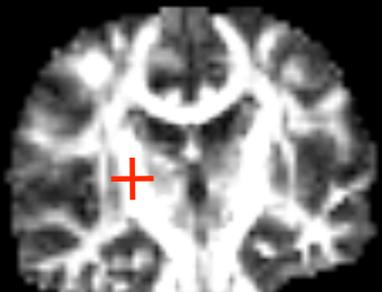
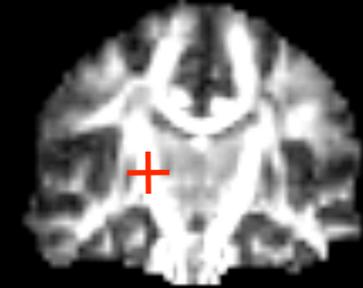
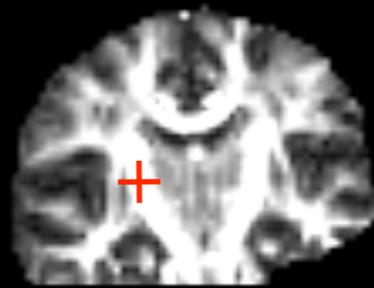
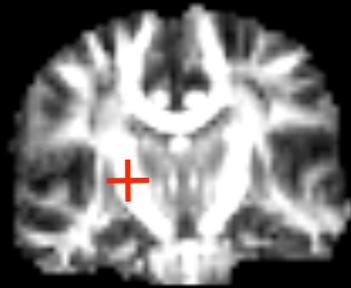




# Hand-placed voxel/ROI-based FA Comparison

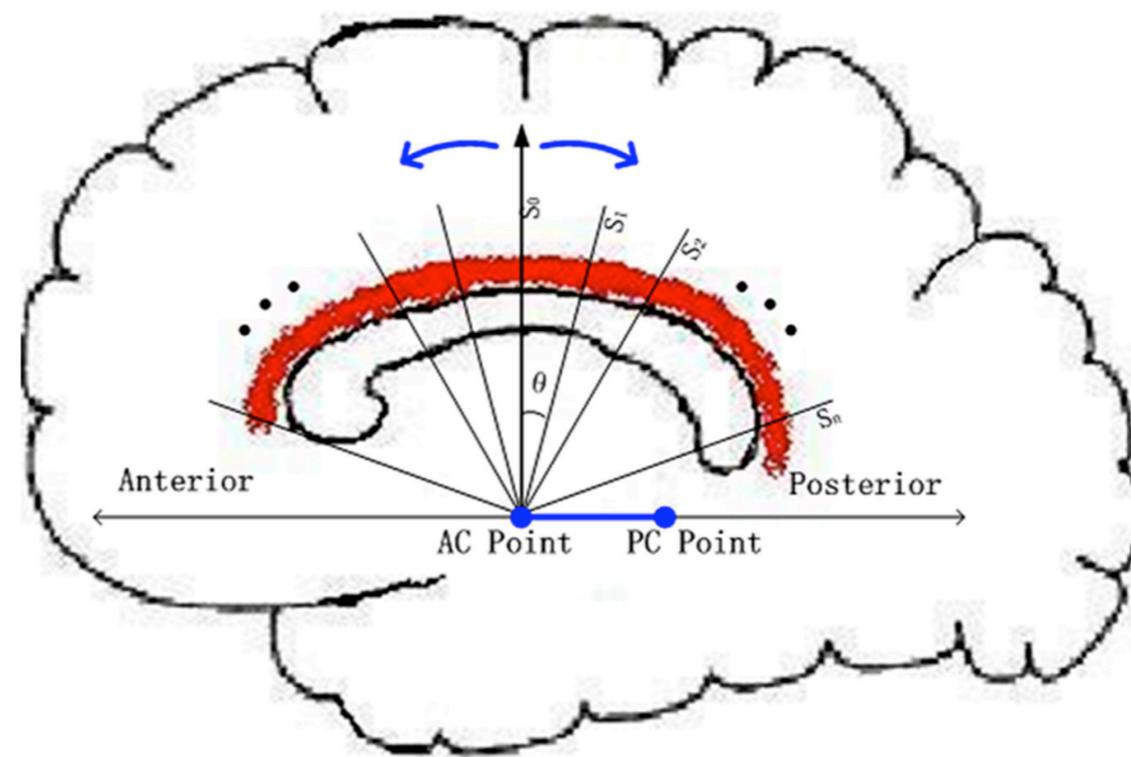
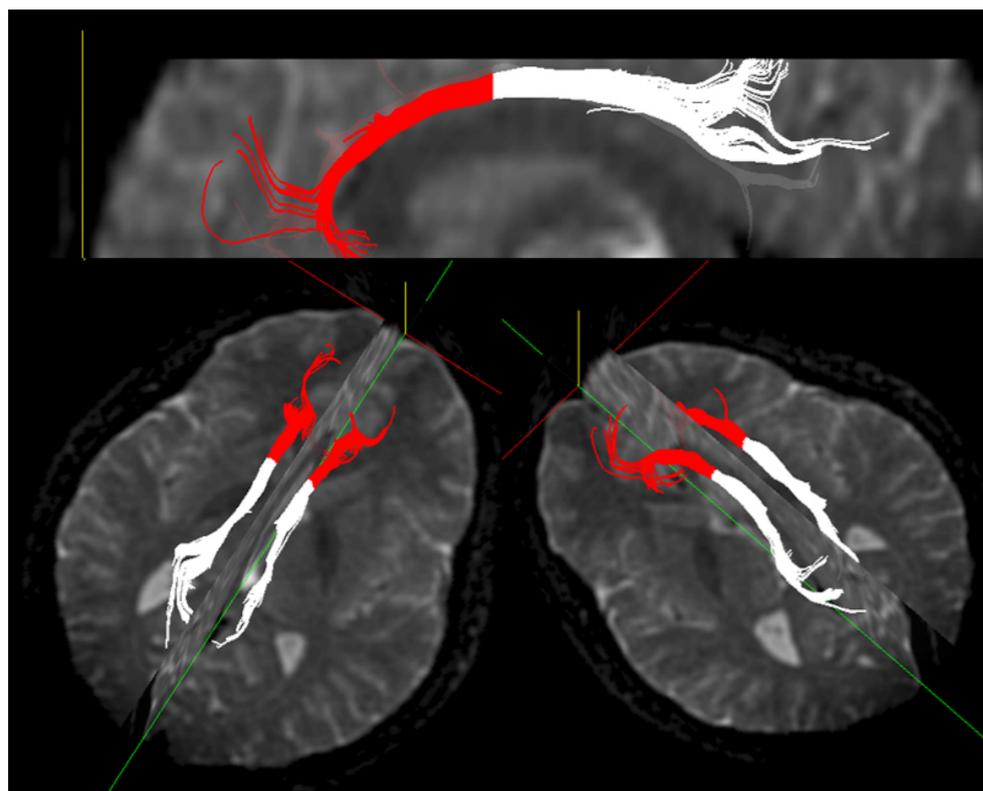


labour-intensive, subjective, potentially inaccurate, doesn't investigate whole brain





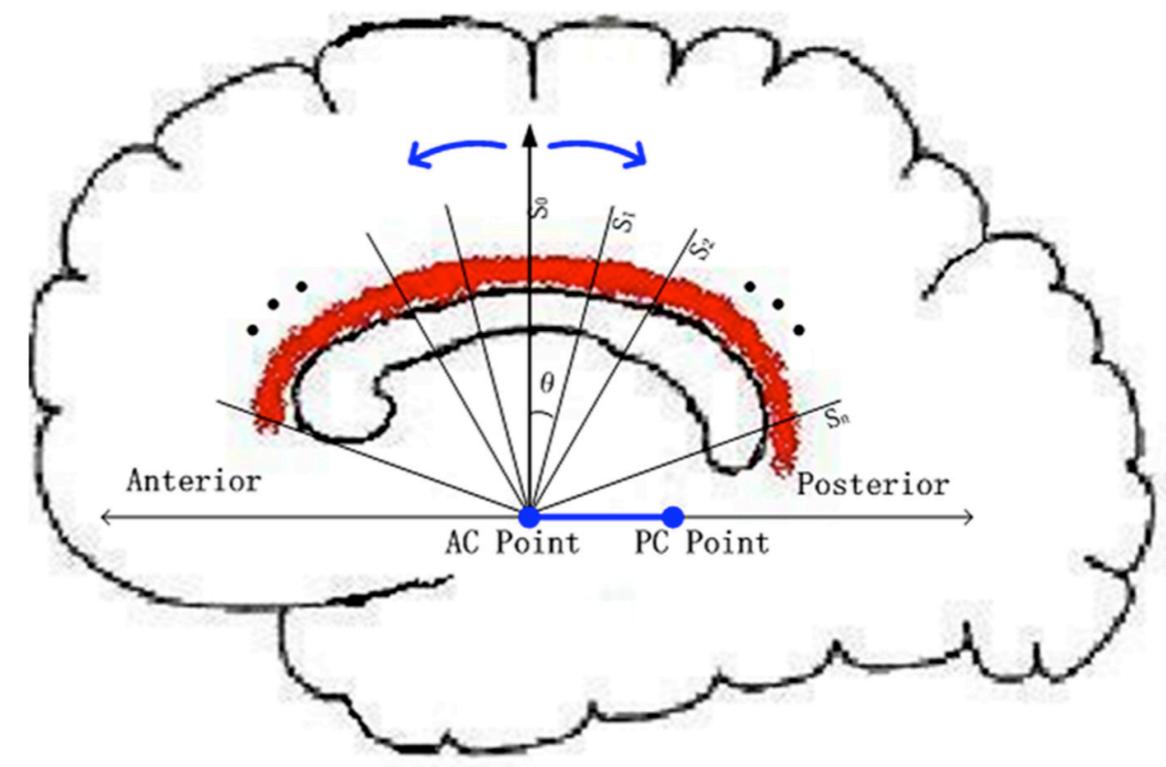
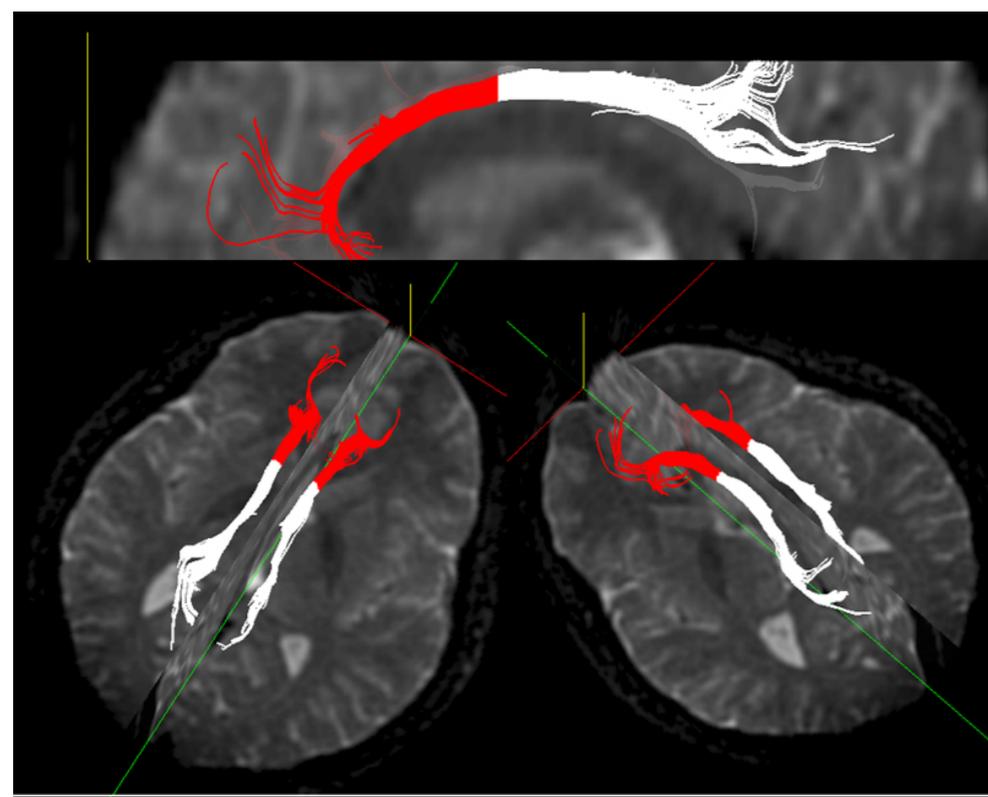
# Tractography-Based FA Comparison



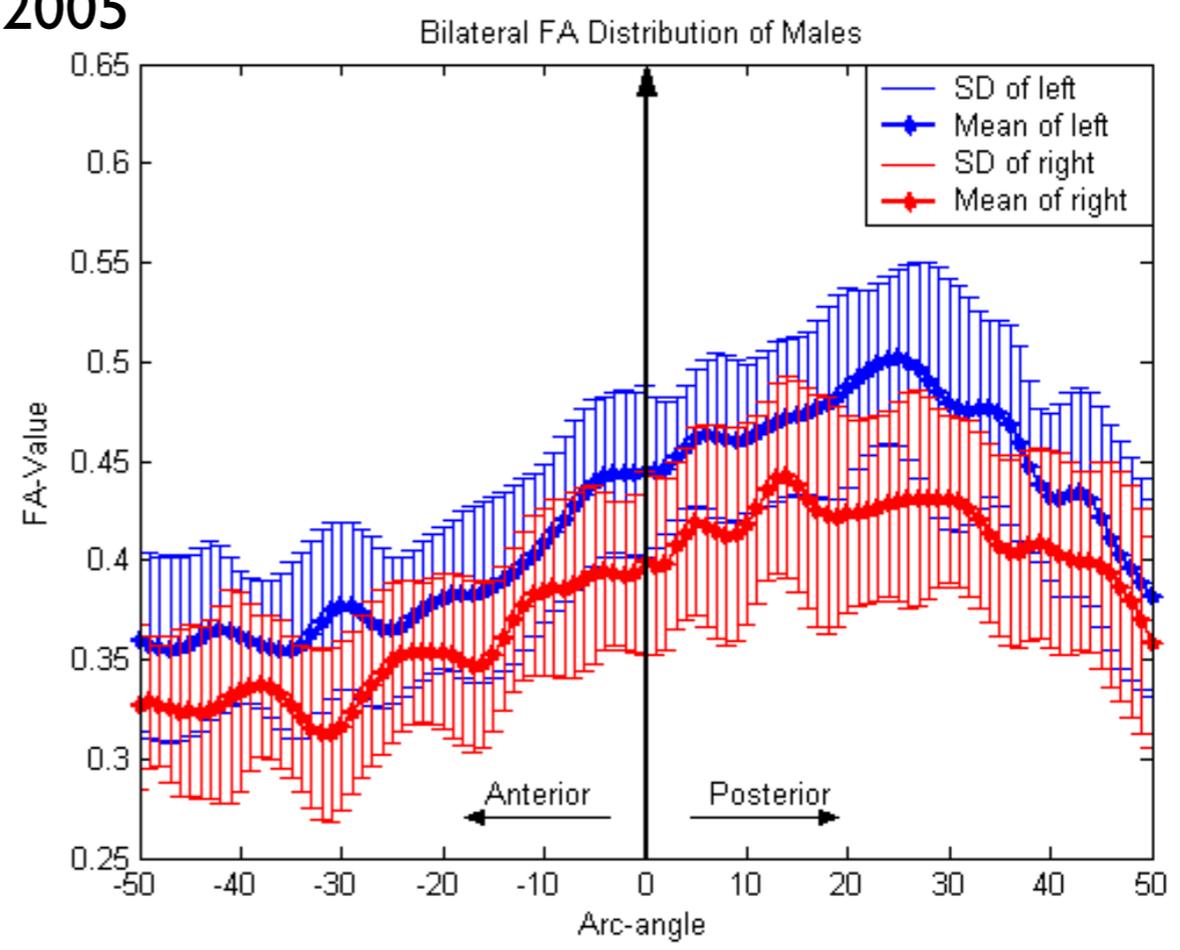
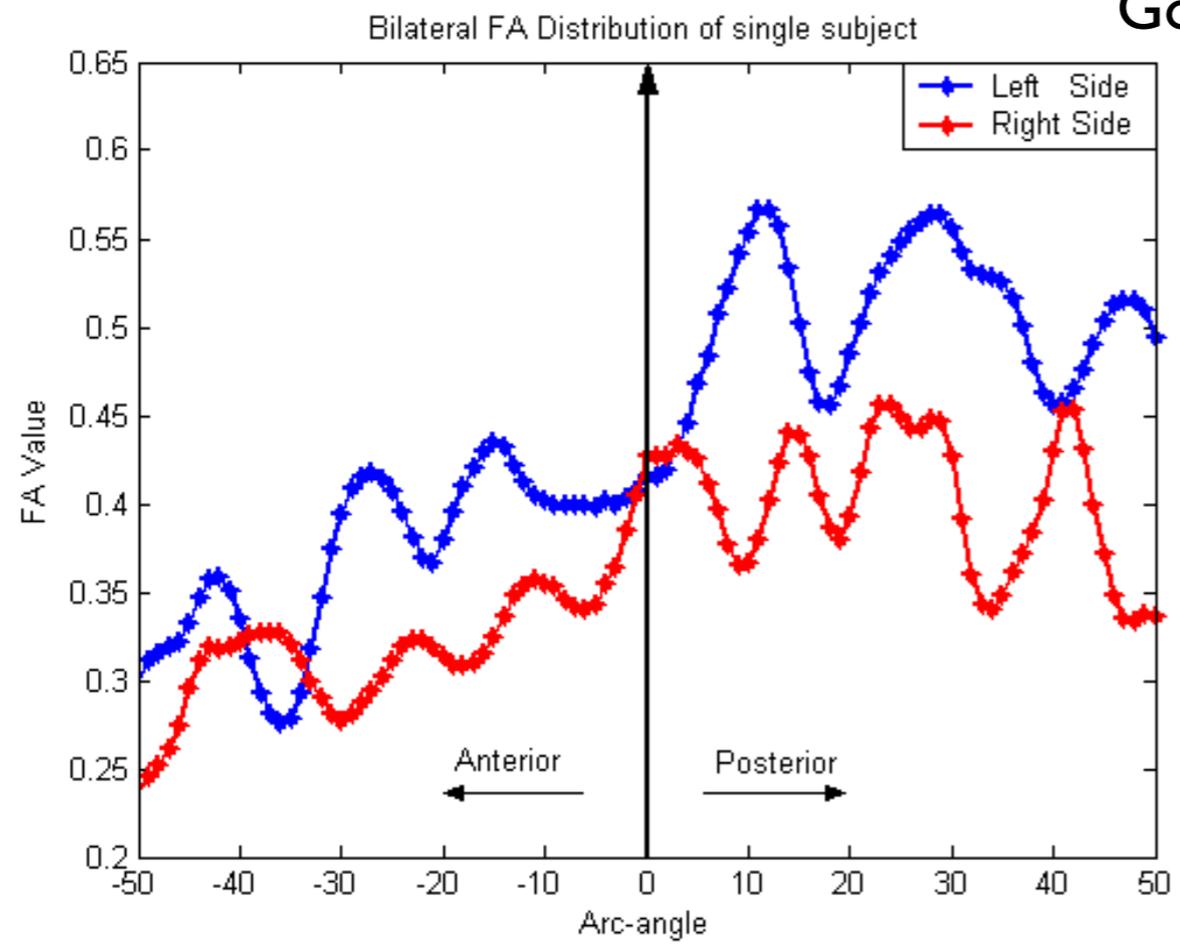
- Method [Gong 2005, Corouge 2006]
  - Define a given tract in all subjects
  - Parameterise FA along tract
  - Compare between subjects
- Strength: correspondence issue hopefully resolved
- Problems
  - Currently requires manual intervention to specify tract
  - Hence doesn't investigate whole brain
  - Projection of FA onto tract needs careful thought



# Tractography-Based FA Comparison

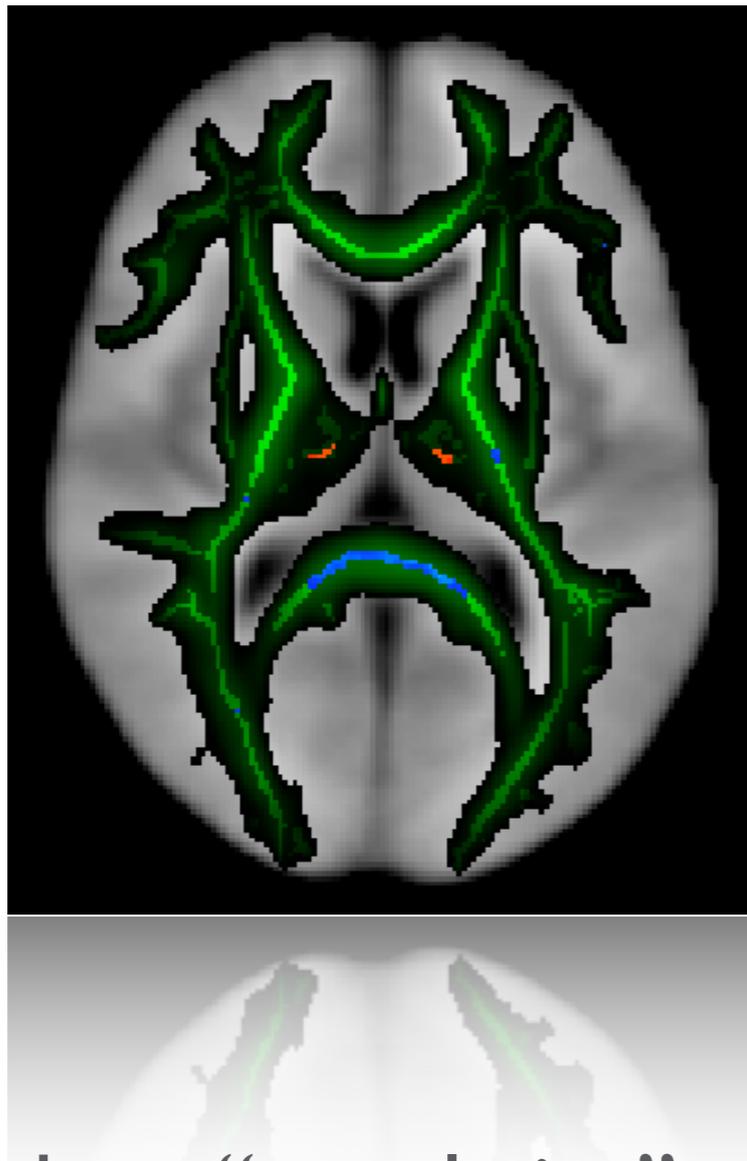


Gong 2005





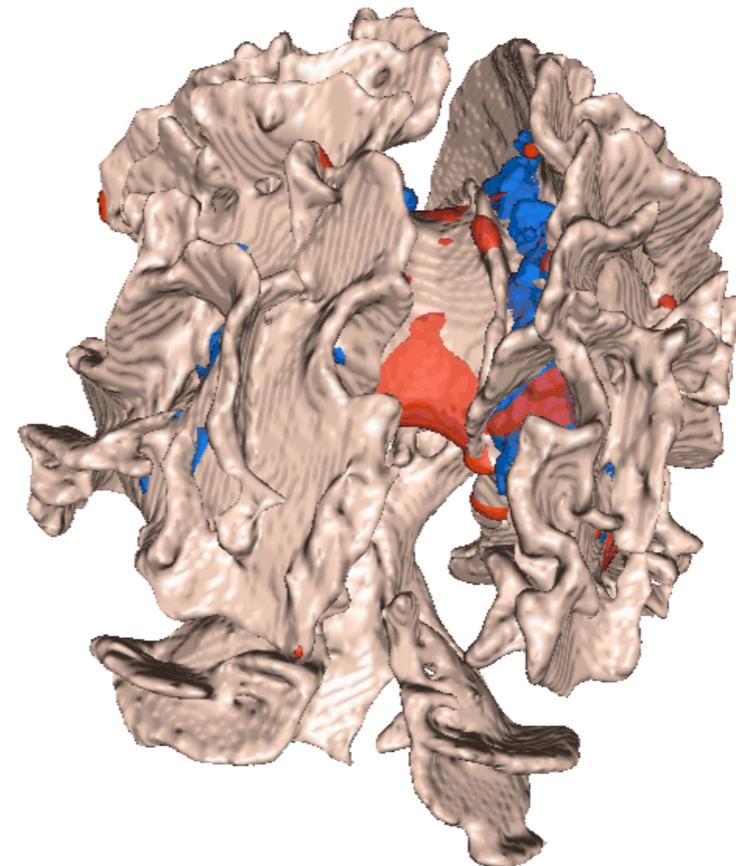
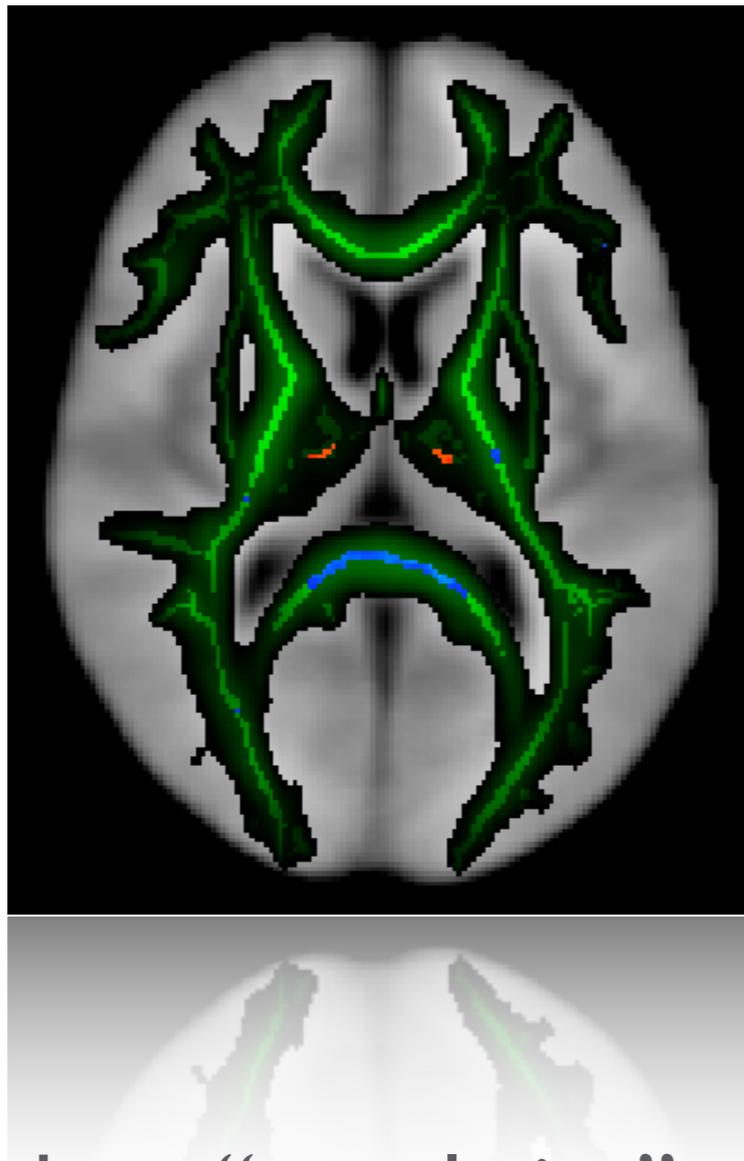
# TBSS : Tract-Based Spatial Statistics



- Need: robust “voxelwise” cross-subject stats on DTI
- Problem: alignment issues confound valid local stats
- TBSS: solve alignment using alignment-invariant features:
- Compare FA taken from tract centres (via skeletonisation)



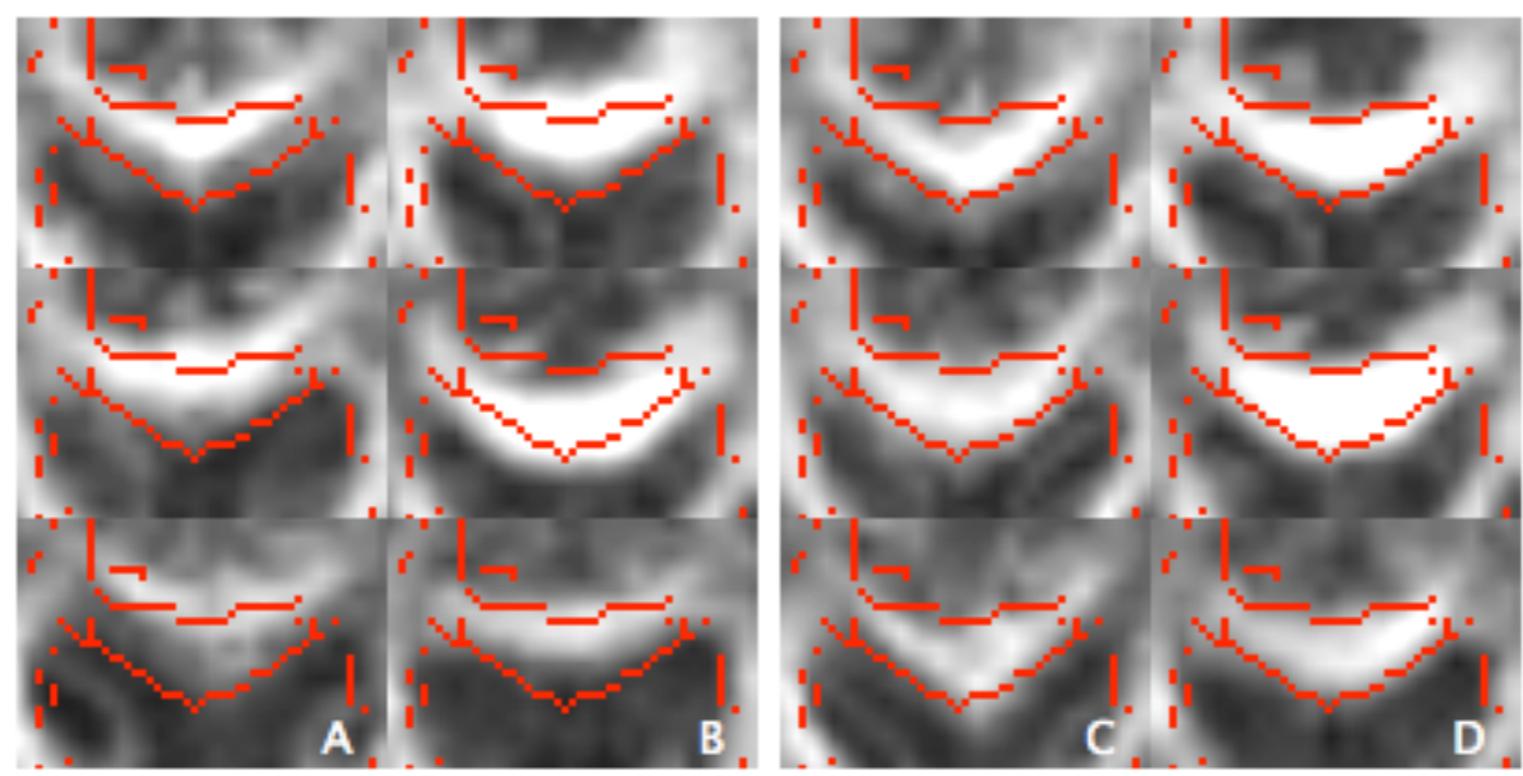
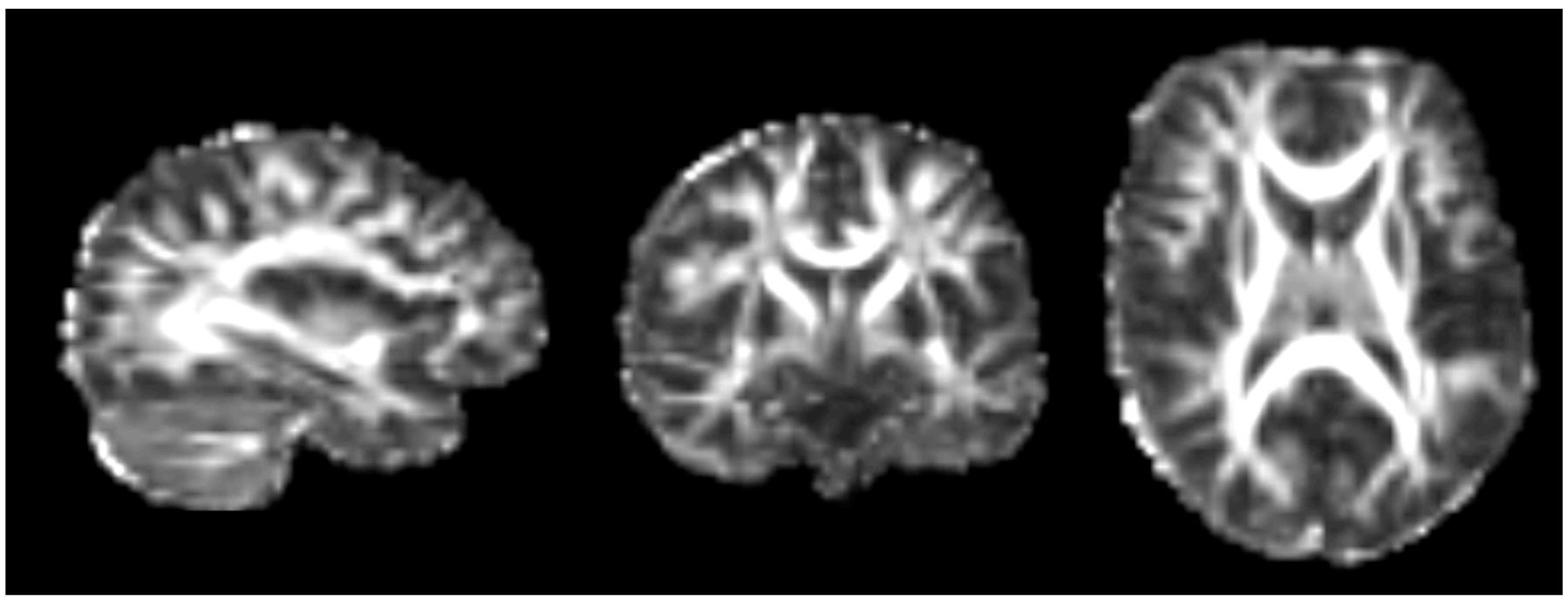
# TBSS : Tract-Based Spatial Statistics



- Need: robust “voxelwise” cross-subject stats on DTI
- Problem: alignment issues confound valid local stats
- TBSS: solve alignment using alignment-invariant features:
- Compare FA taken from tract centres (via skeletonisation)

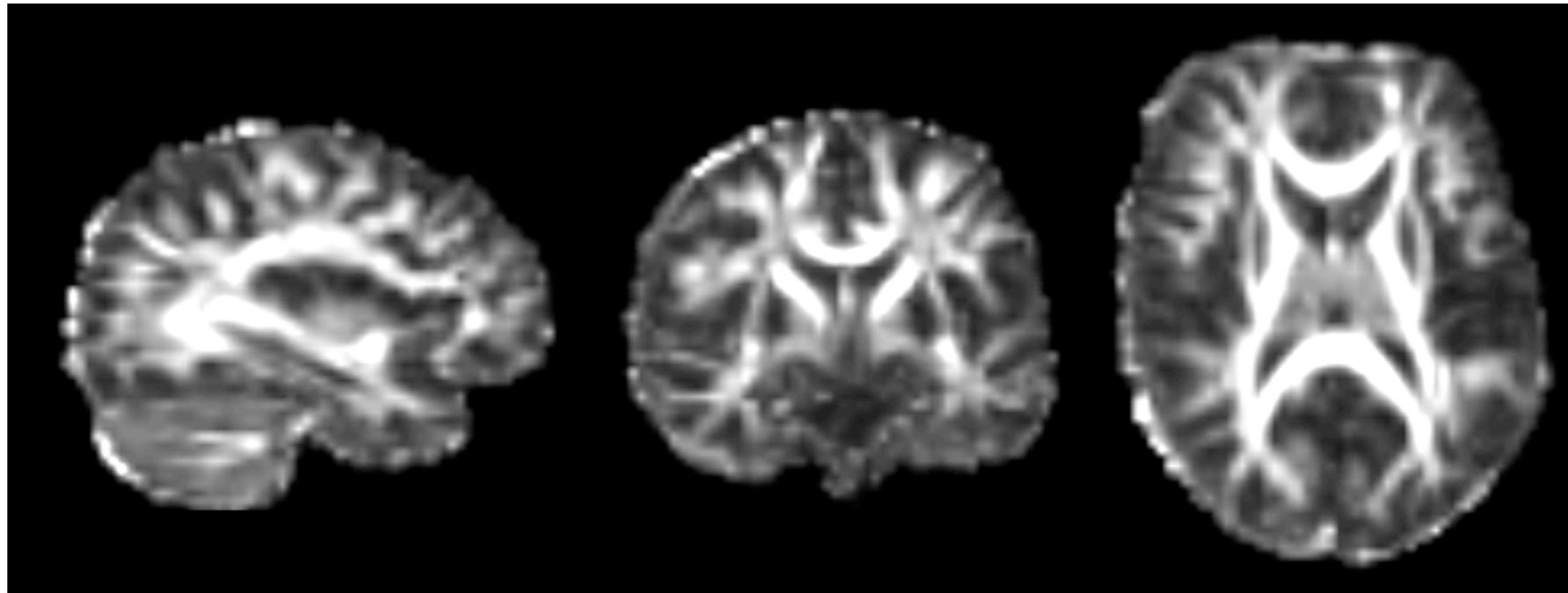


# I. Use medium-DoF nonlinear reg to pre-align all subjects' FA (nonlinear reg: FNIRT)

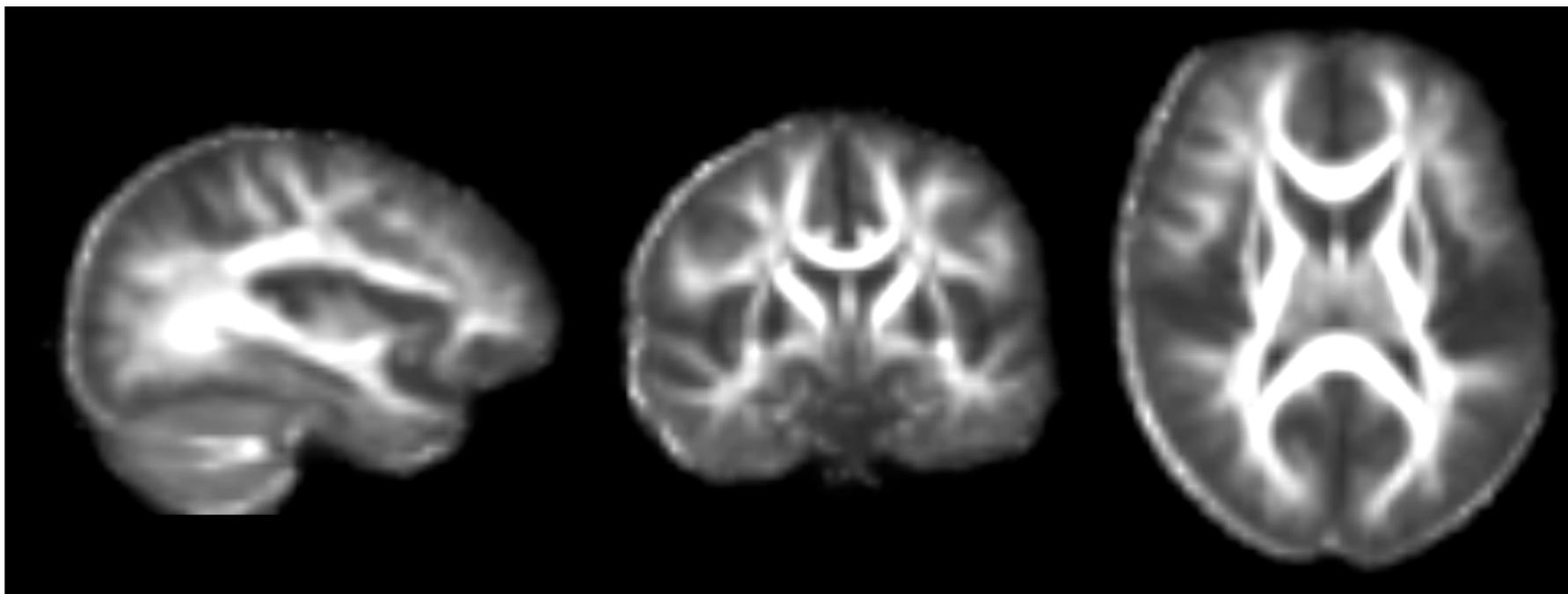




1. Use medium-DoF nonlinear reg to pre-align all subjects' FA (nonlinear reg: FNIRT)

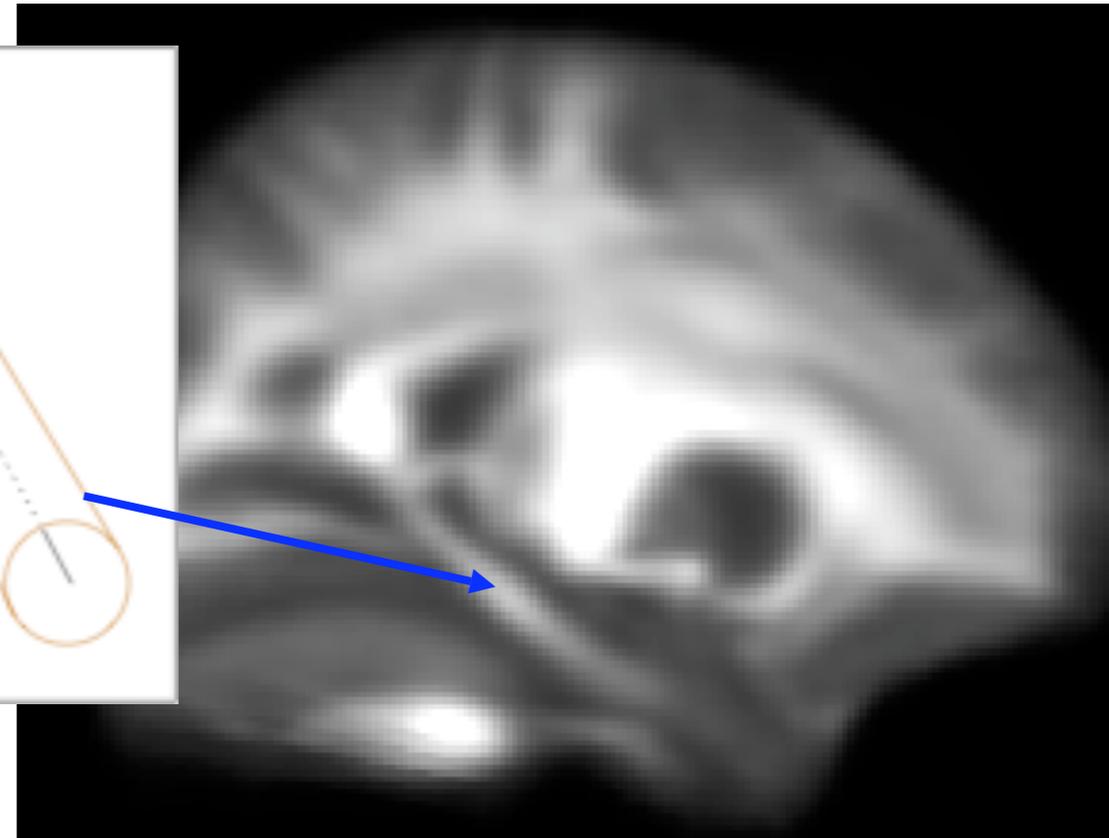
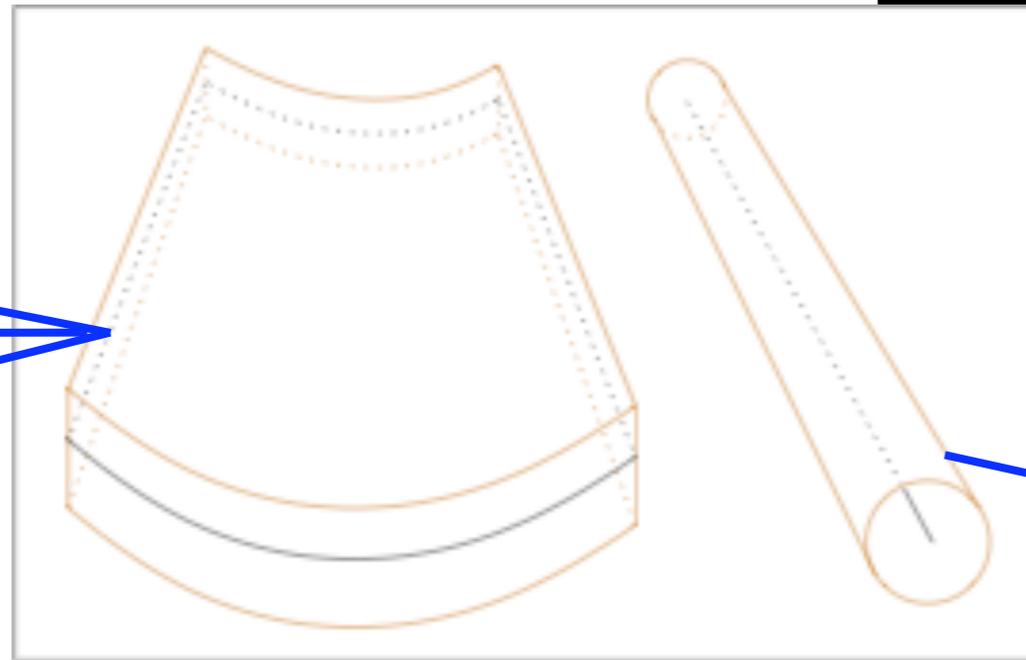
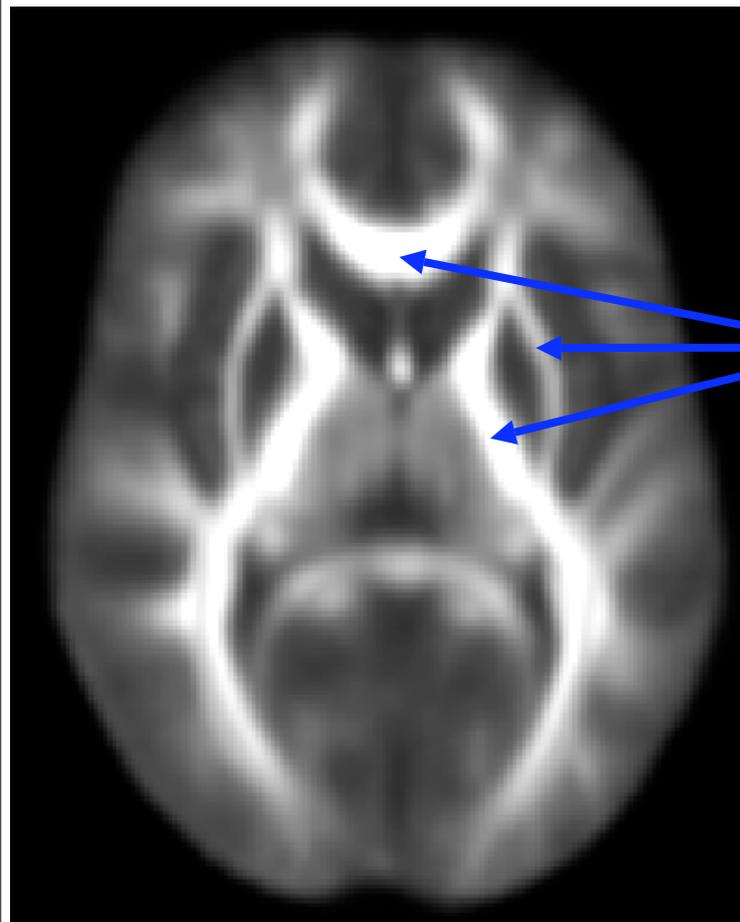


2. Create mean FA image (no smoothing)



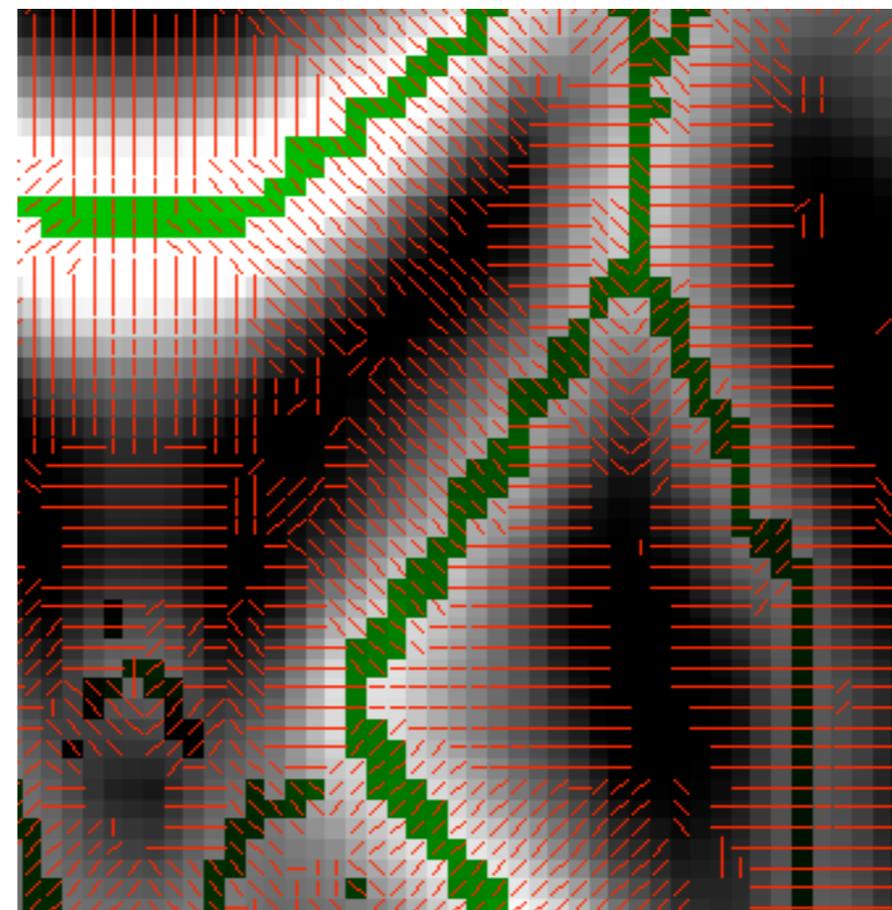
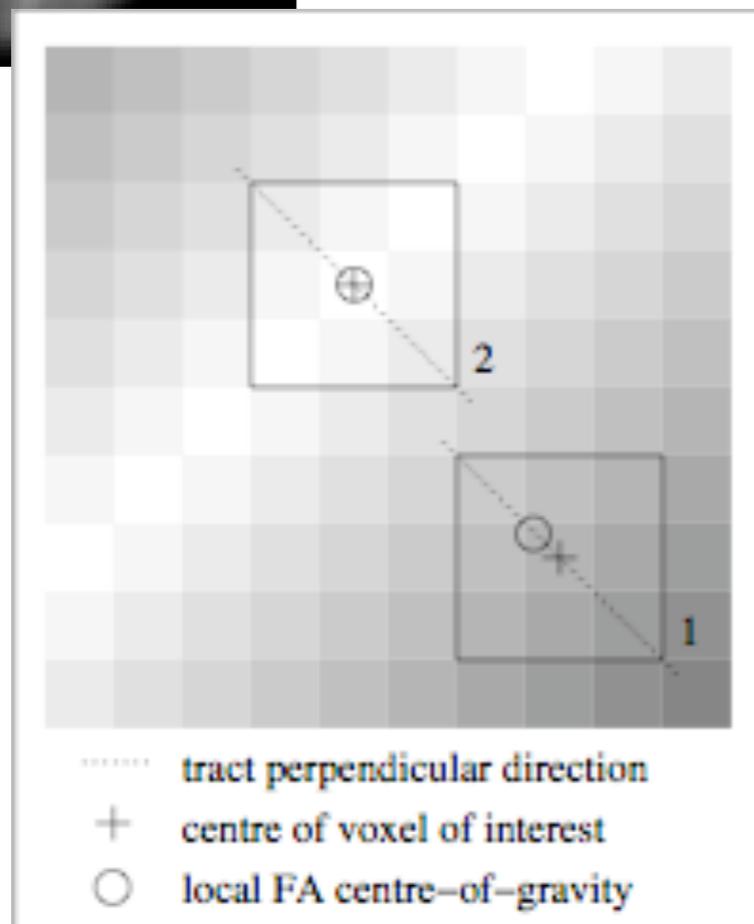
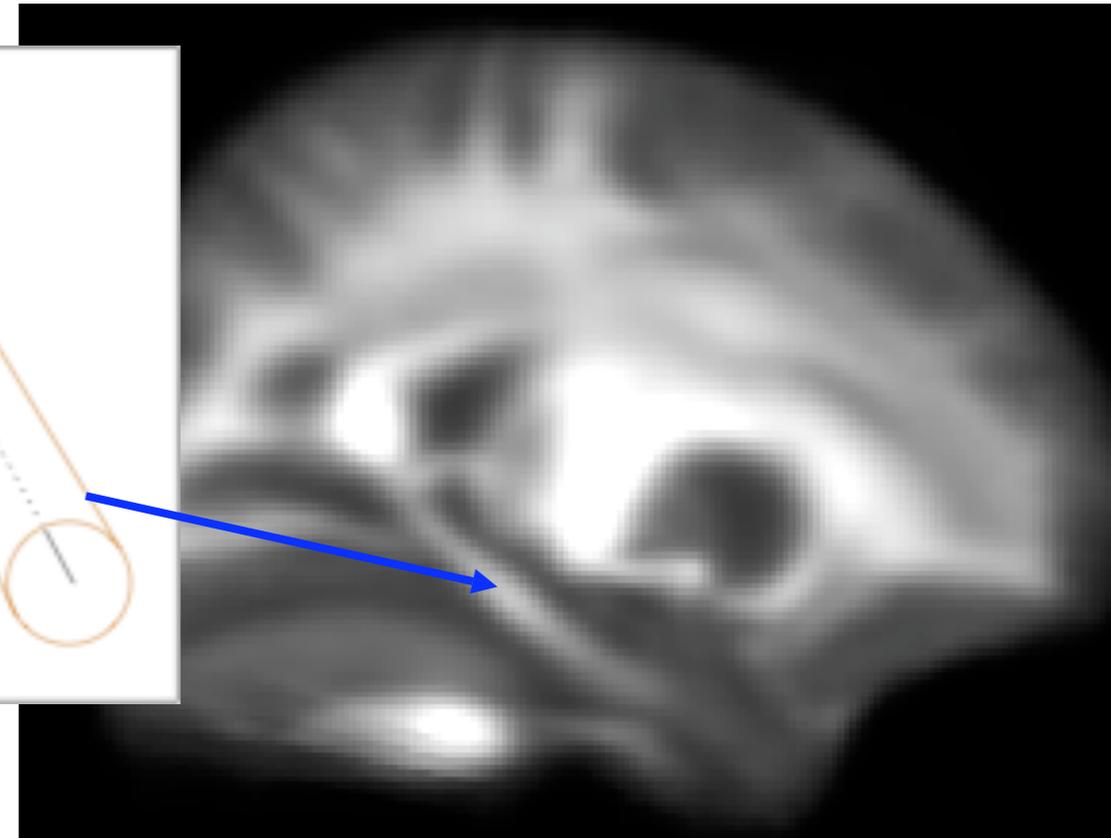
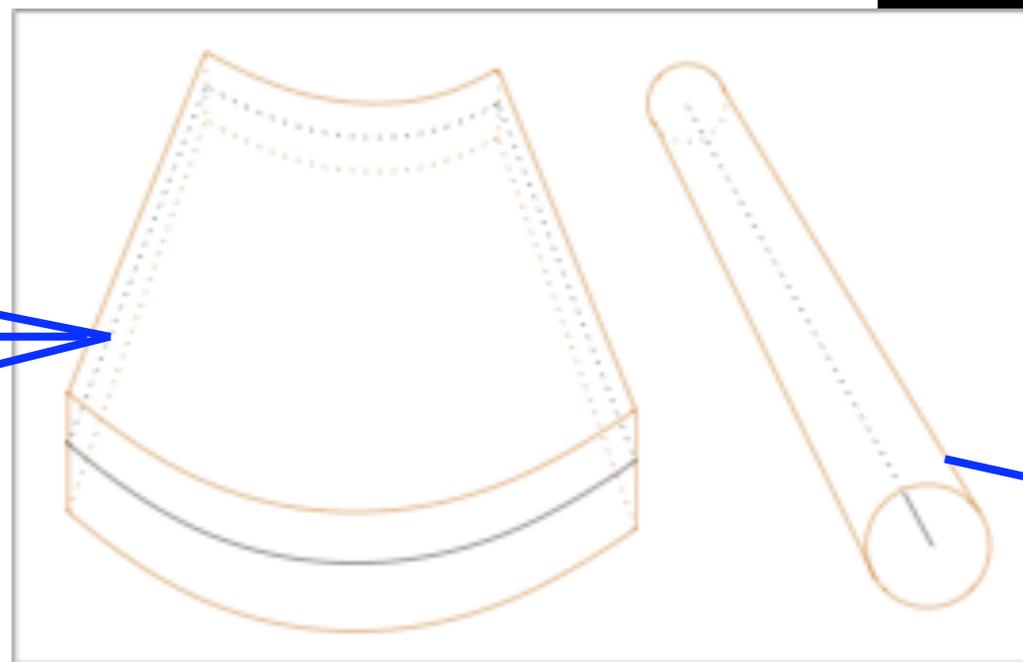
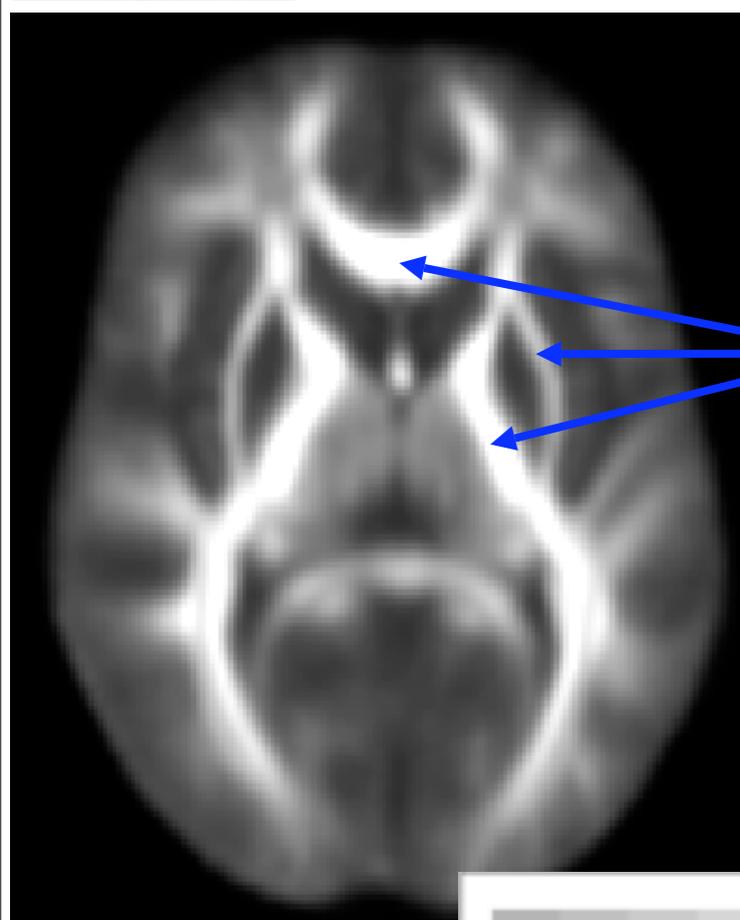


## 2. "Skeletonise" Mean FA





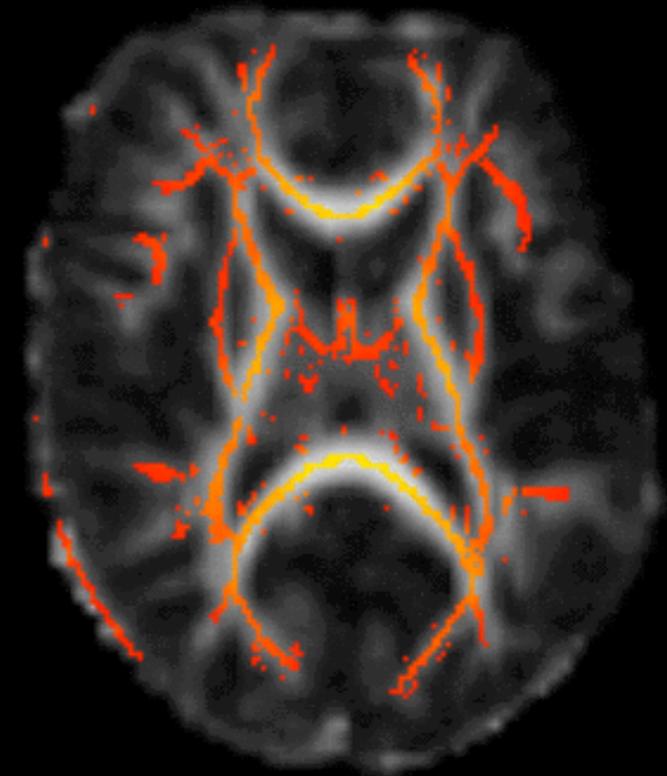
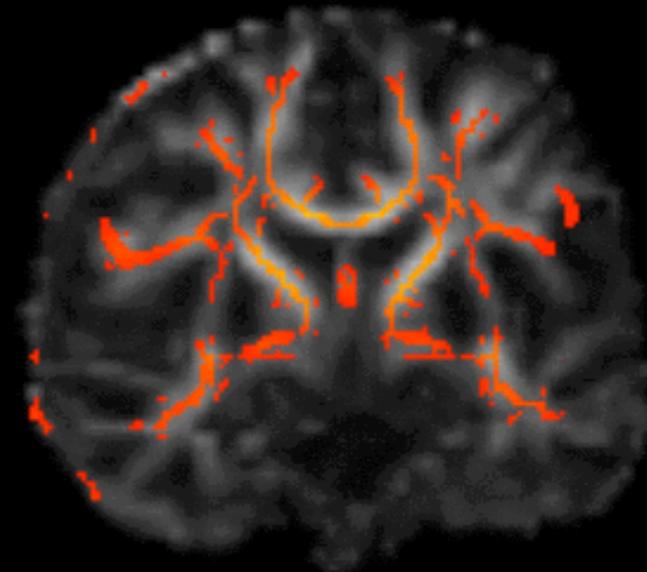
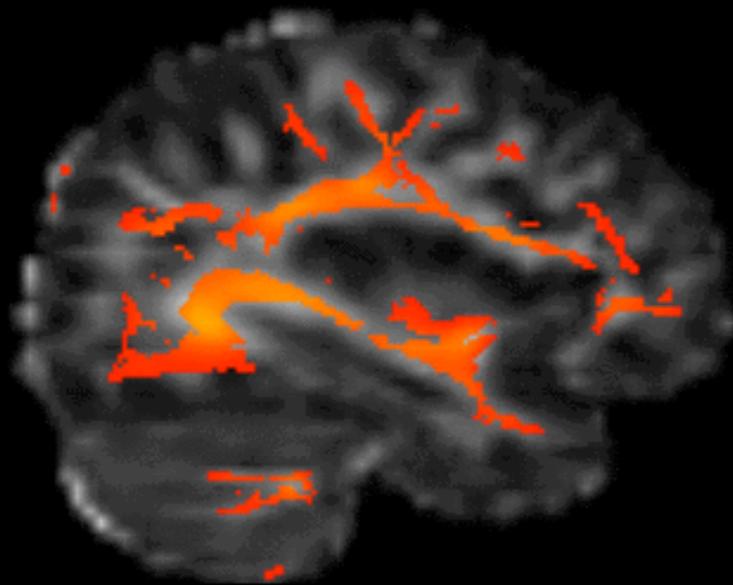
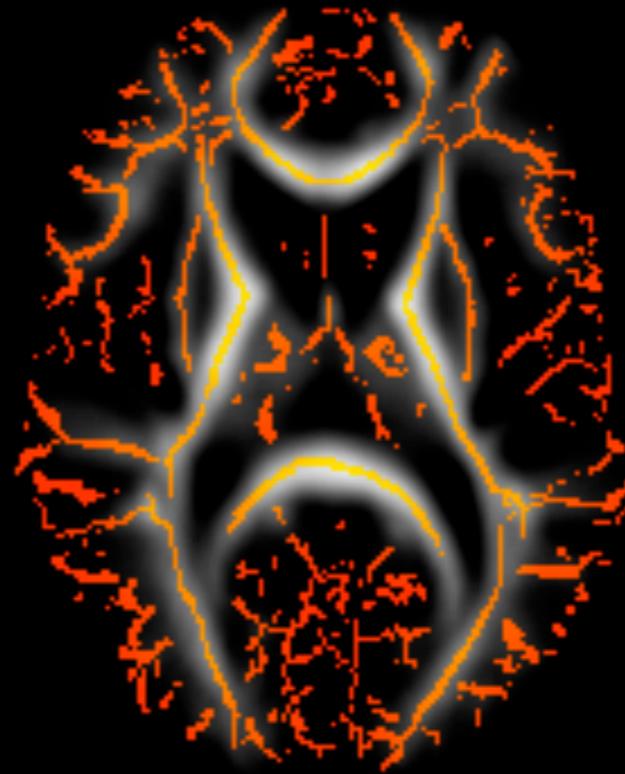
## 2. "Skeletonise" Mean FA





# 3. Threshold Mean FA Skeleton

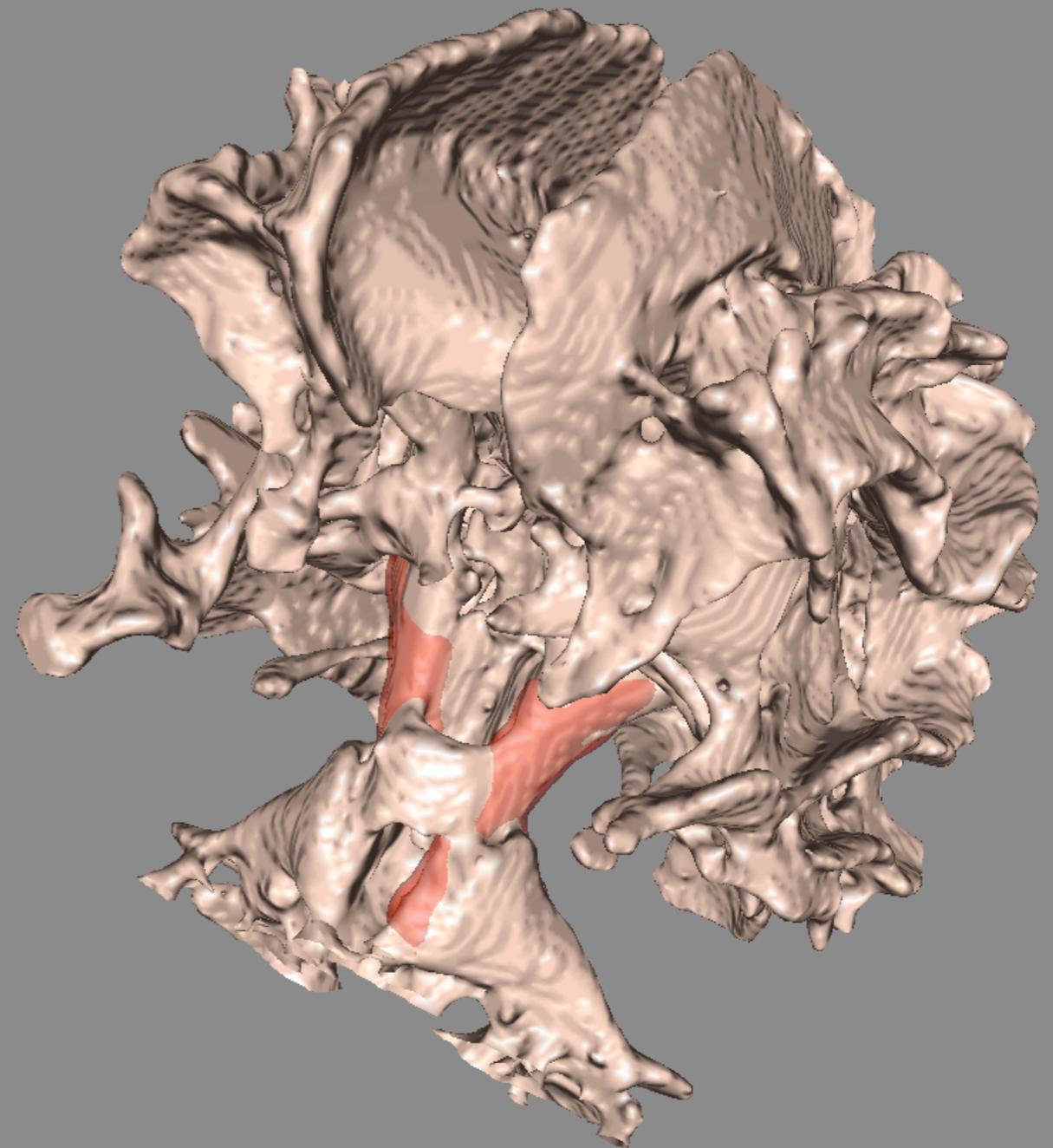
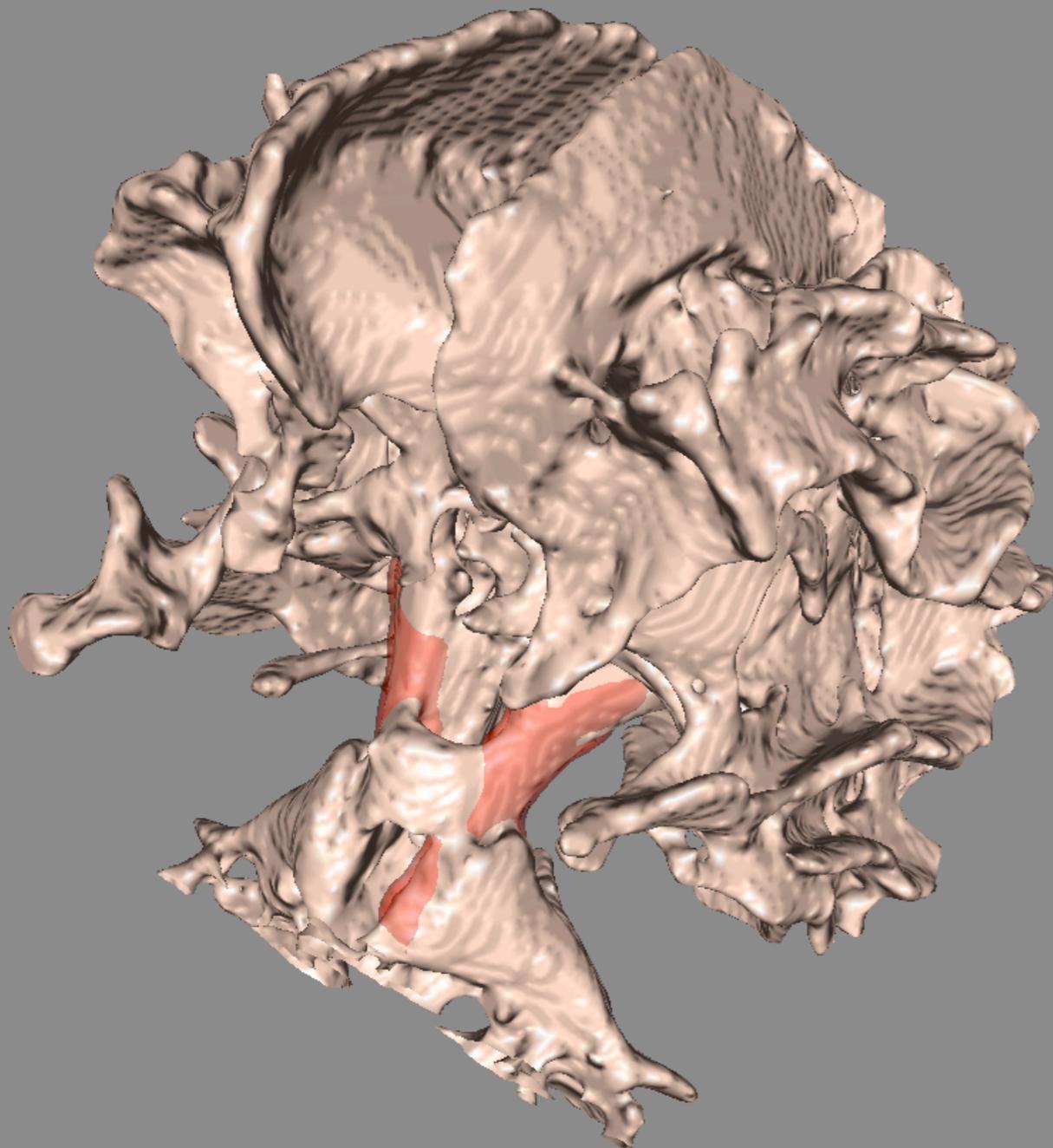
giving “objective” tract map





# 3. Threshold Mean FA Skeleton

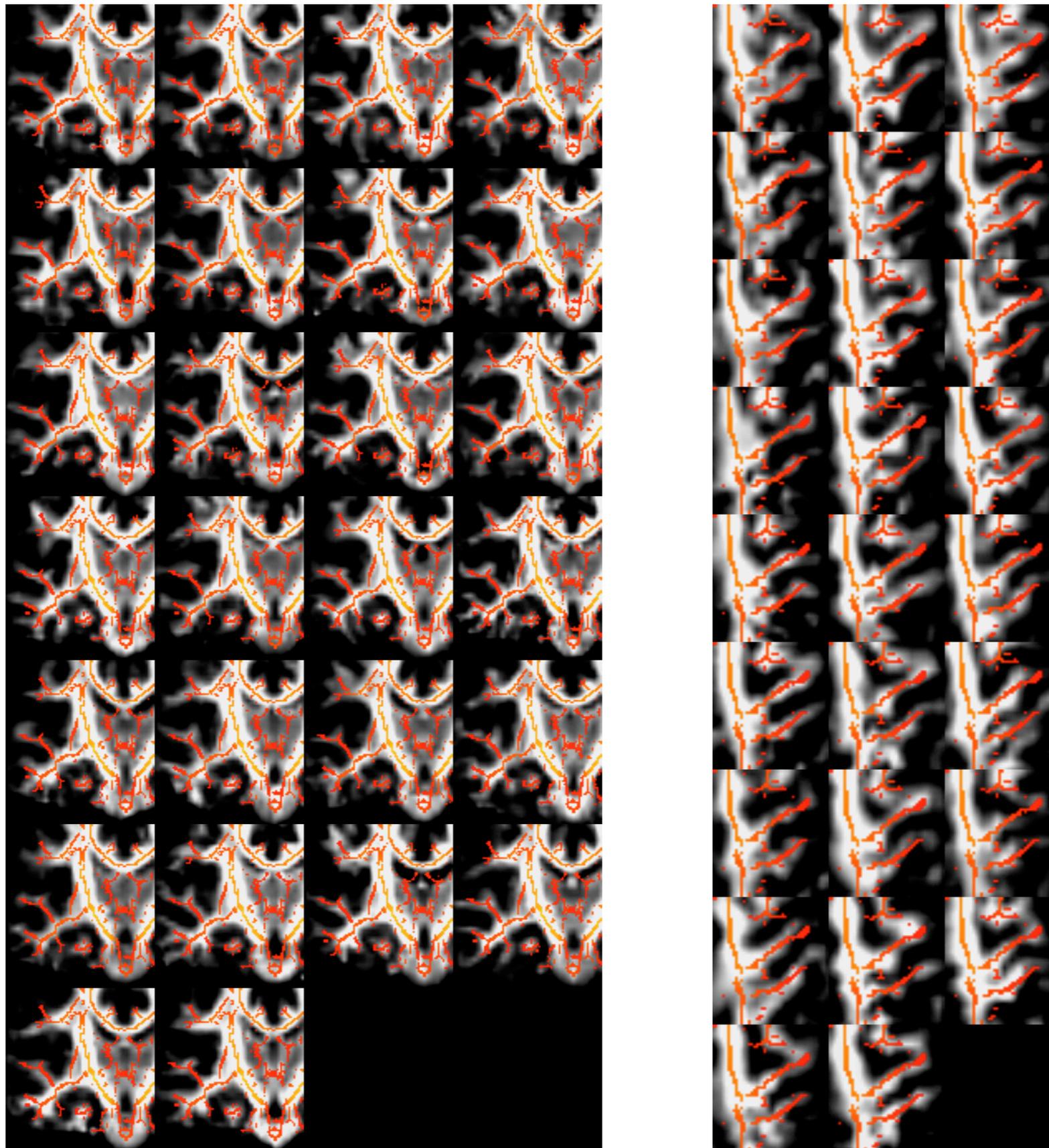
giving “objective” tract map





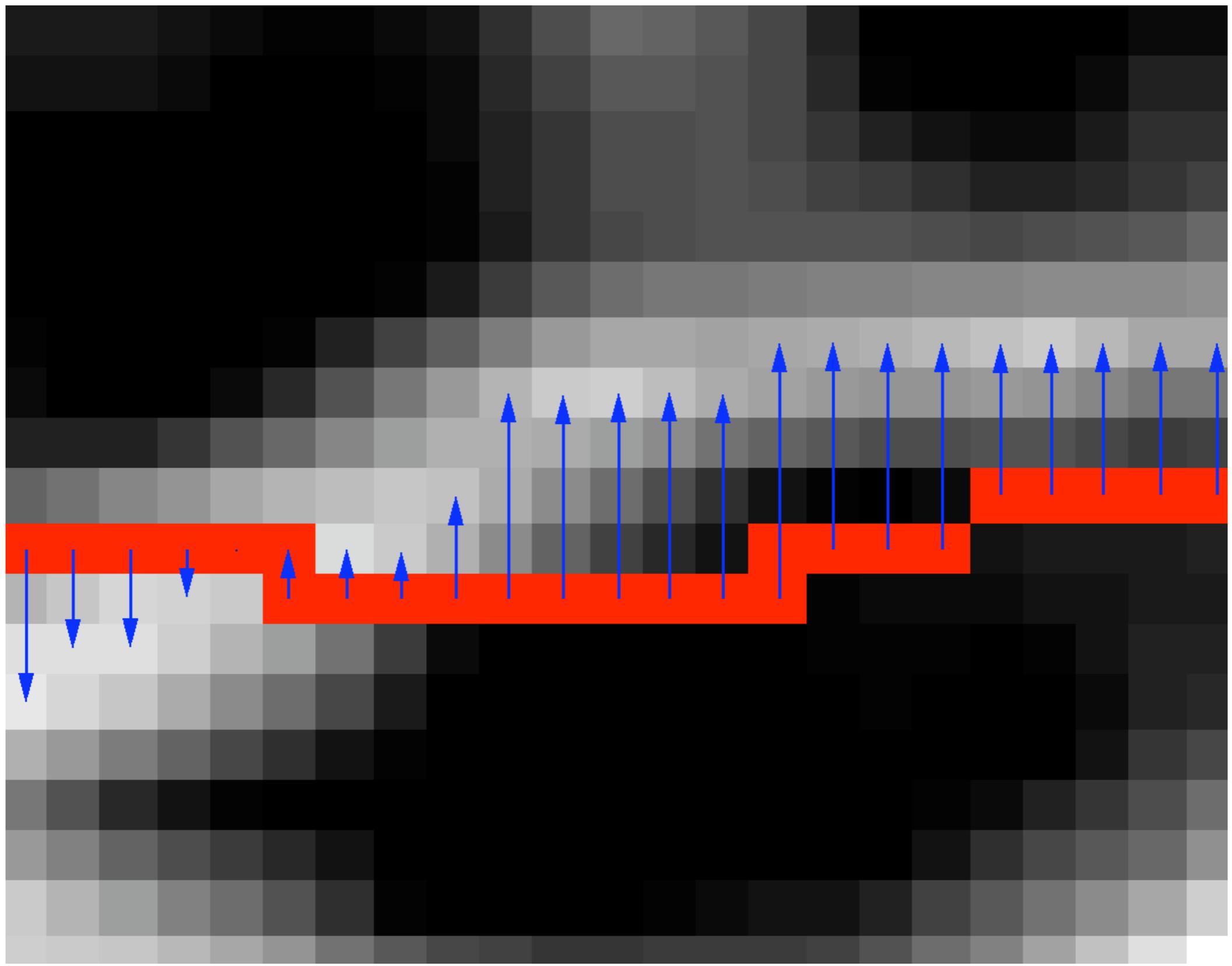
# 3. Threshold Mean FA Skeleton

giving “objective” tract map



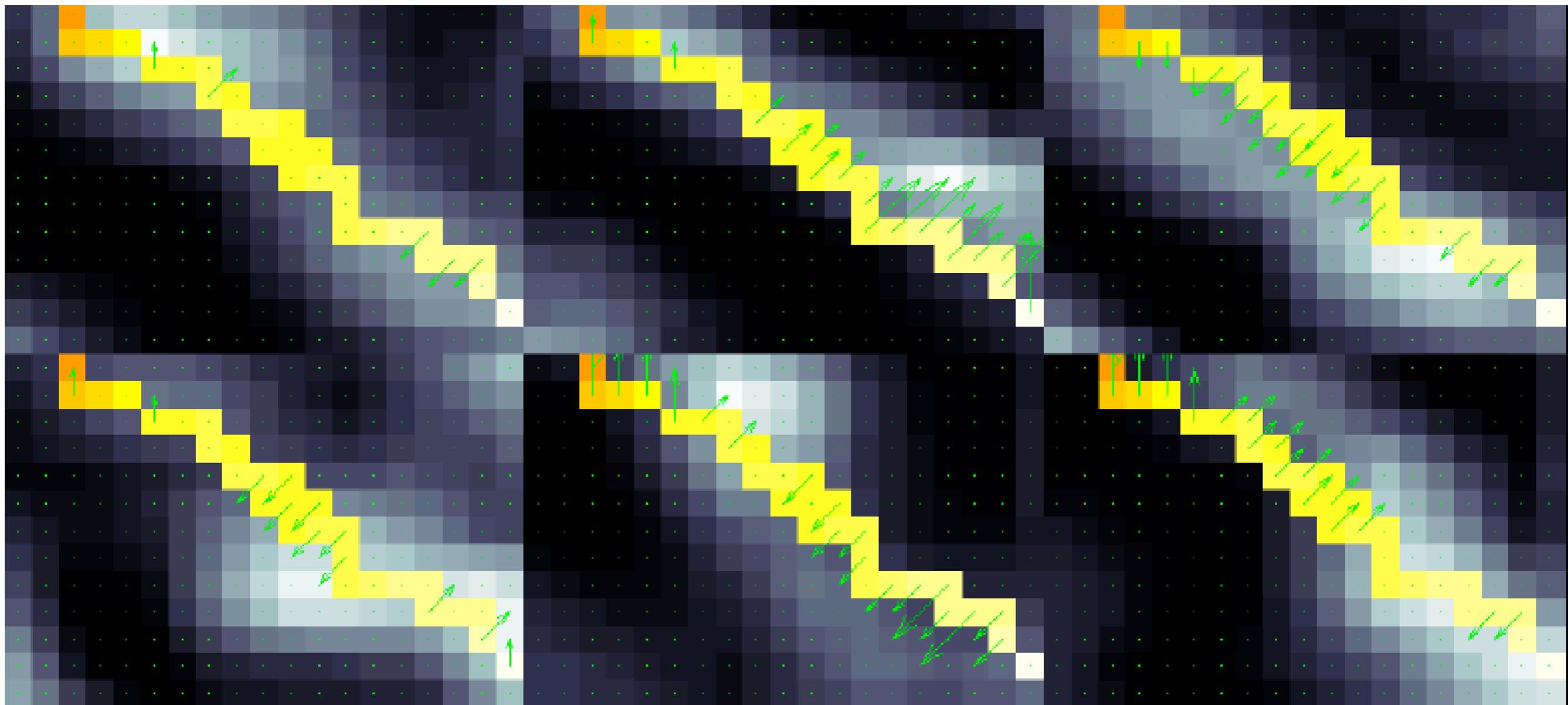


4. For each subject's warped FA, fill each point on the mean-space skeleton with nearest maximum FA value (i.e., from the centre of the subject's nearby tract)





4. For each subject's warped FA, fill each point on the mean-space skeleton with nearest maximum FA value (i.e., from the centre of the subject's nearby tract)





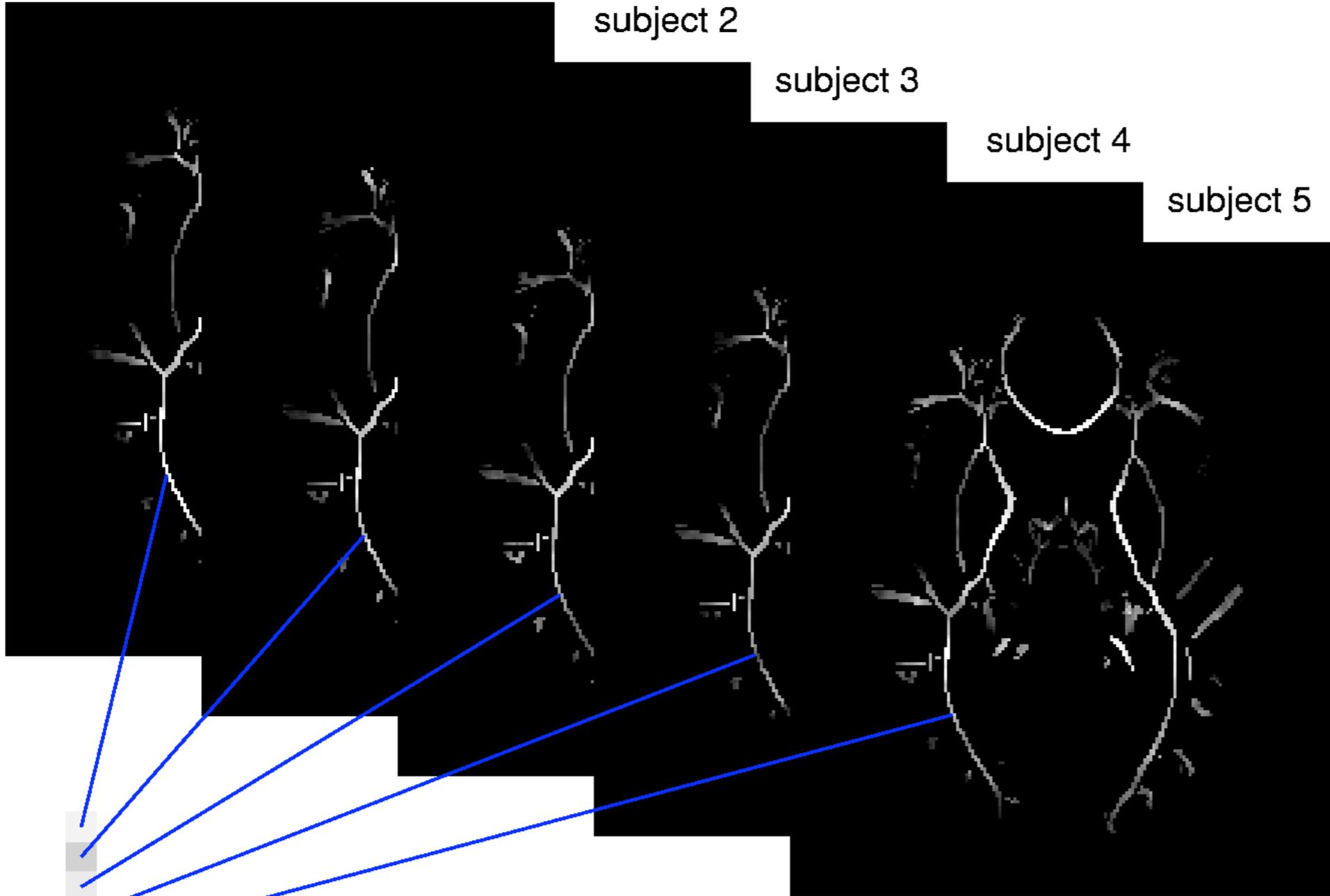
subject 1

subject 2

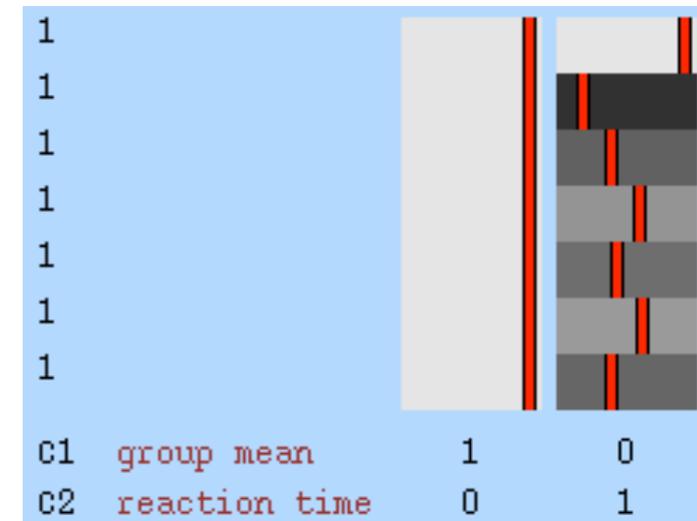
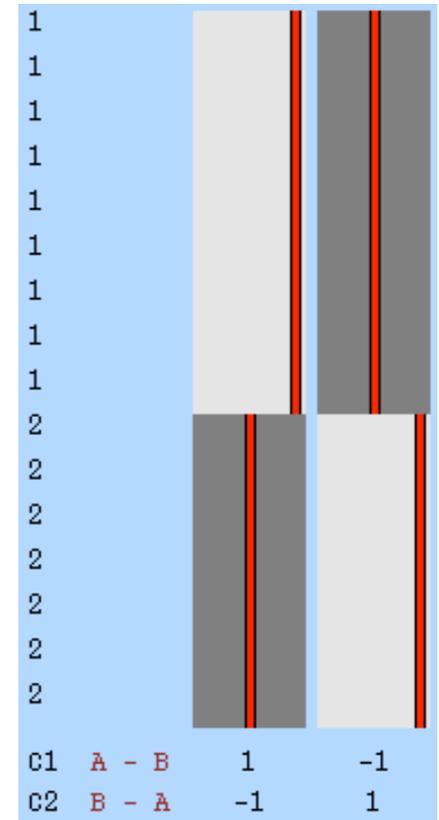
subject 3

subject 4

subject 5



one skeleton voxel's data vector (to be fed into GLM)





# 5. Do cross-subject voxelwise stats on skeleton-projected FA

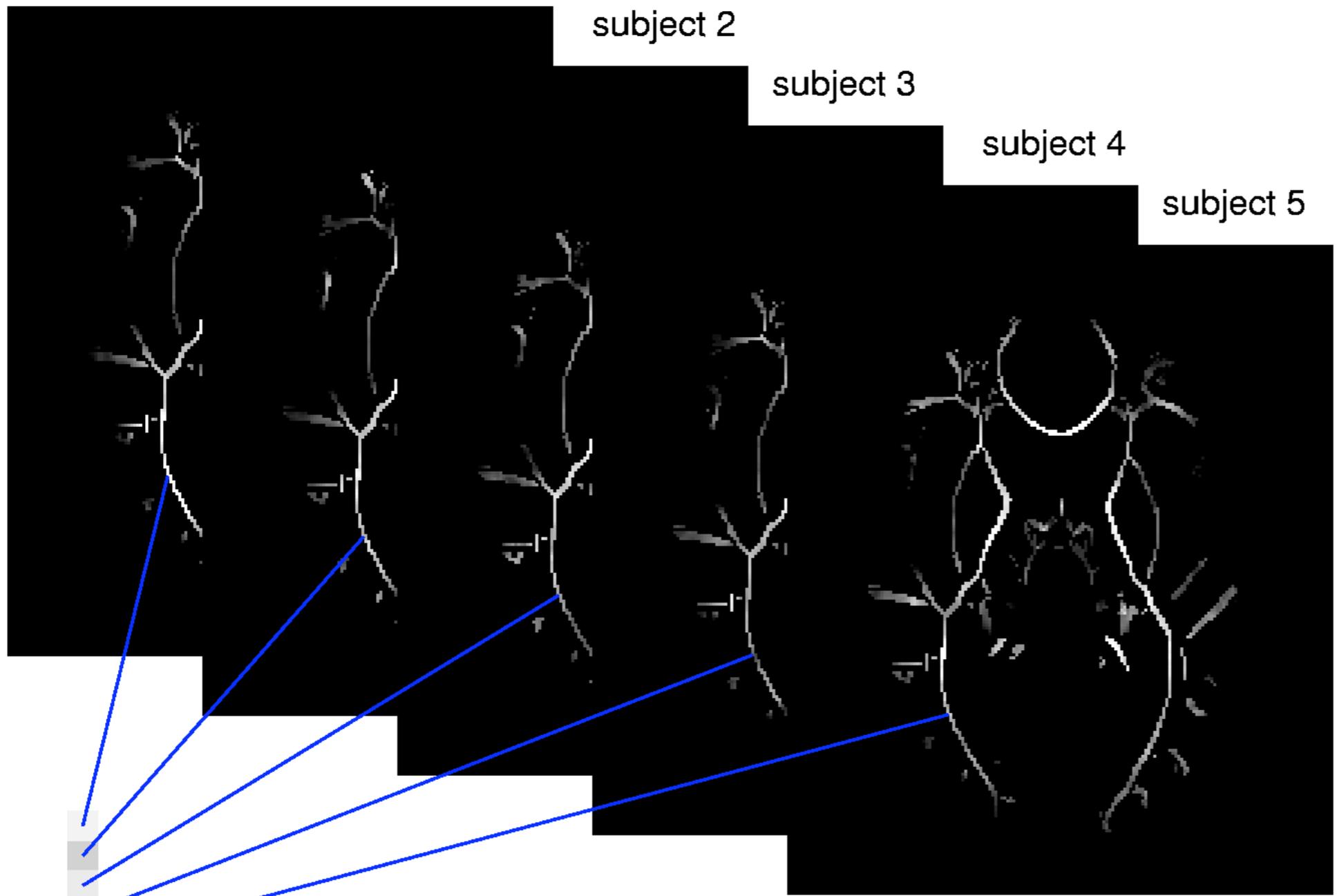
subject 1

subject 2

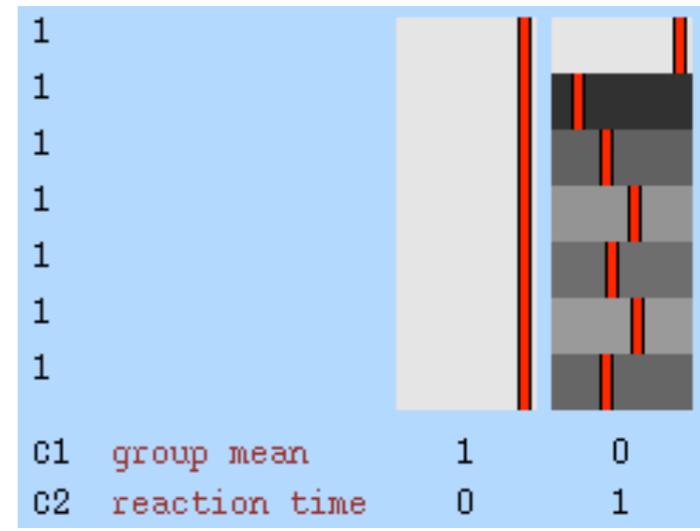
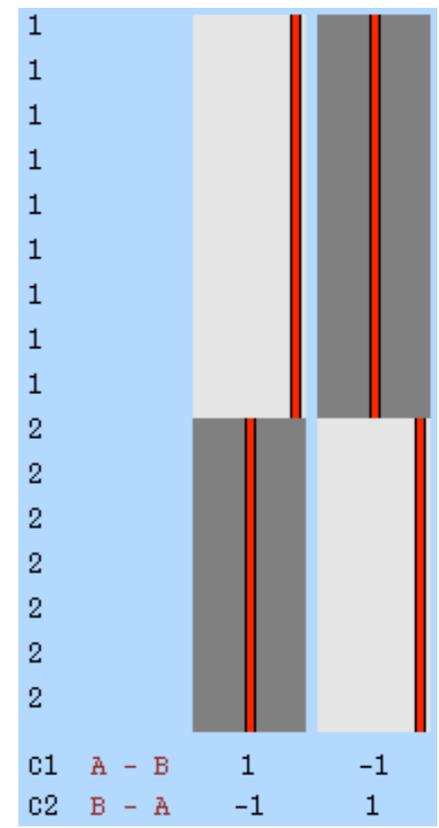
subject 3

subject 4

subject 5

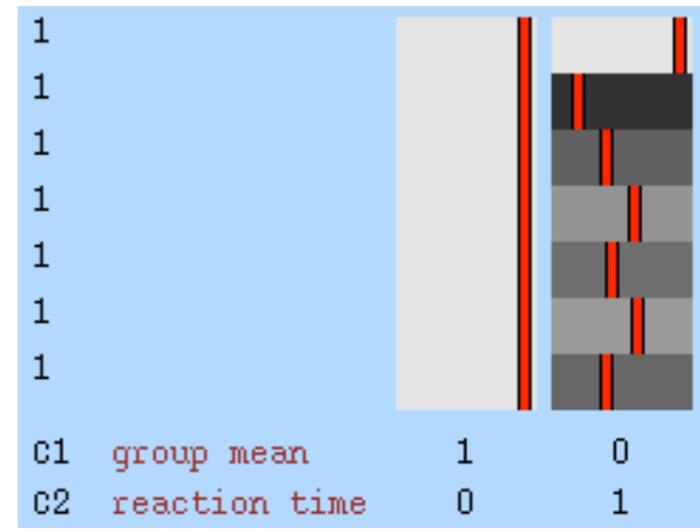
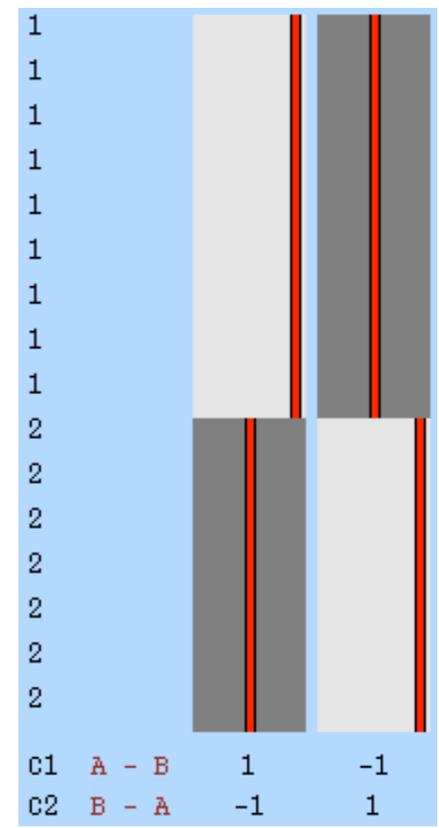
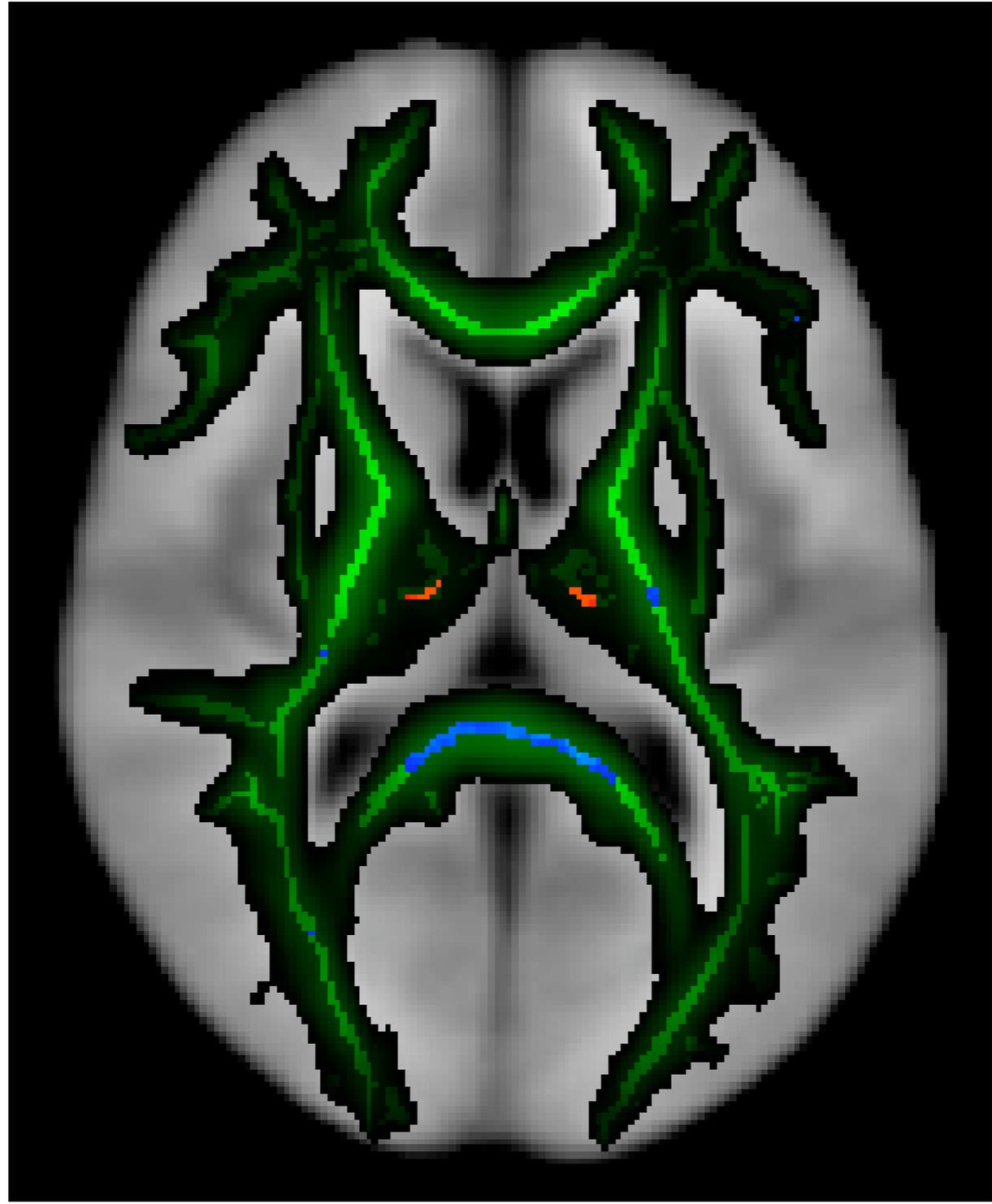


one skeleton voxel's data vector (to be fed into GLM)





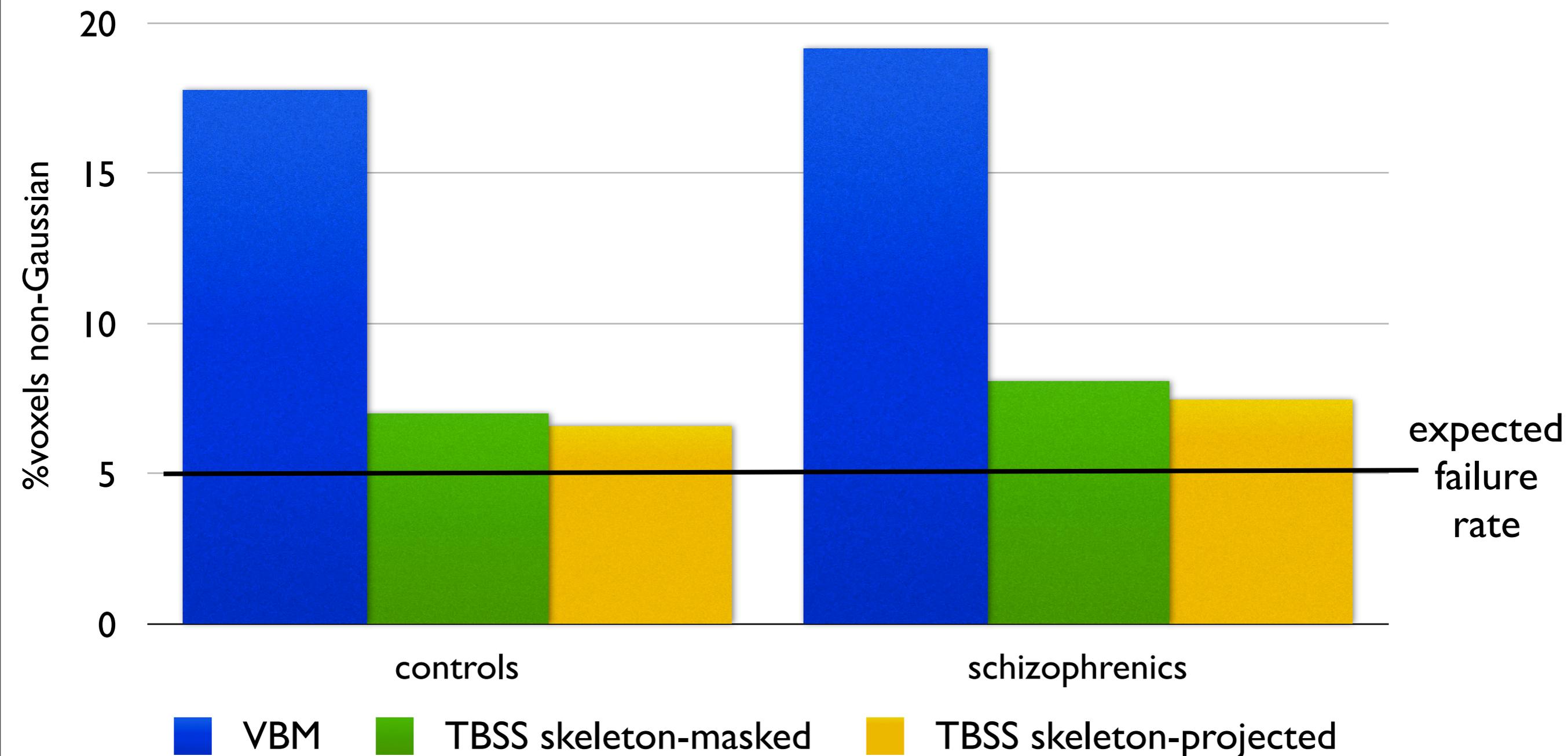
- 5. Do cross-subject voxelwise stats on skeleton-projected FA
- 6. Threshold, (e.g., permutation testing, including multiple comparison correction)





# Testing for Gaussianity

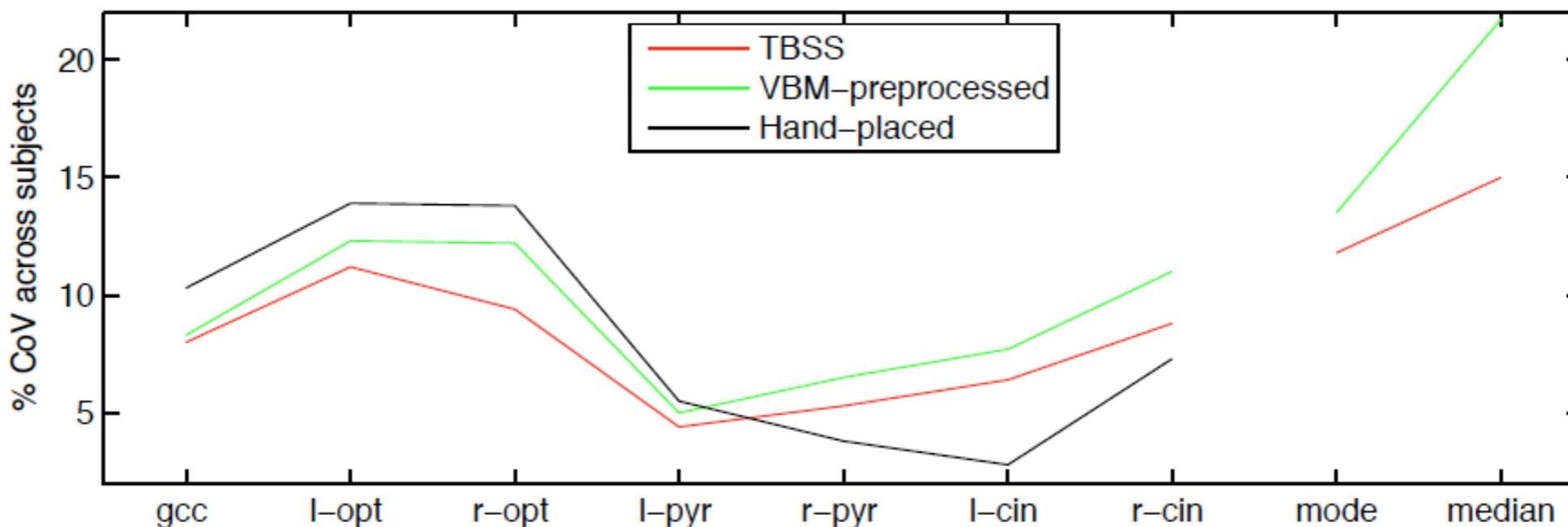
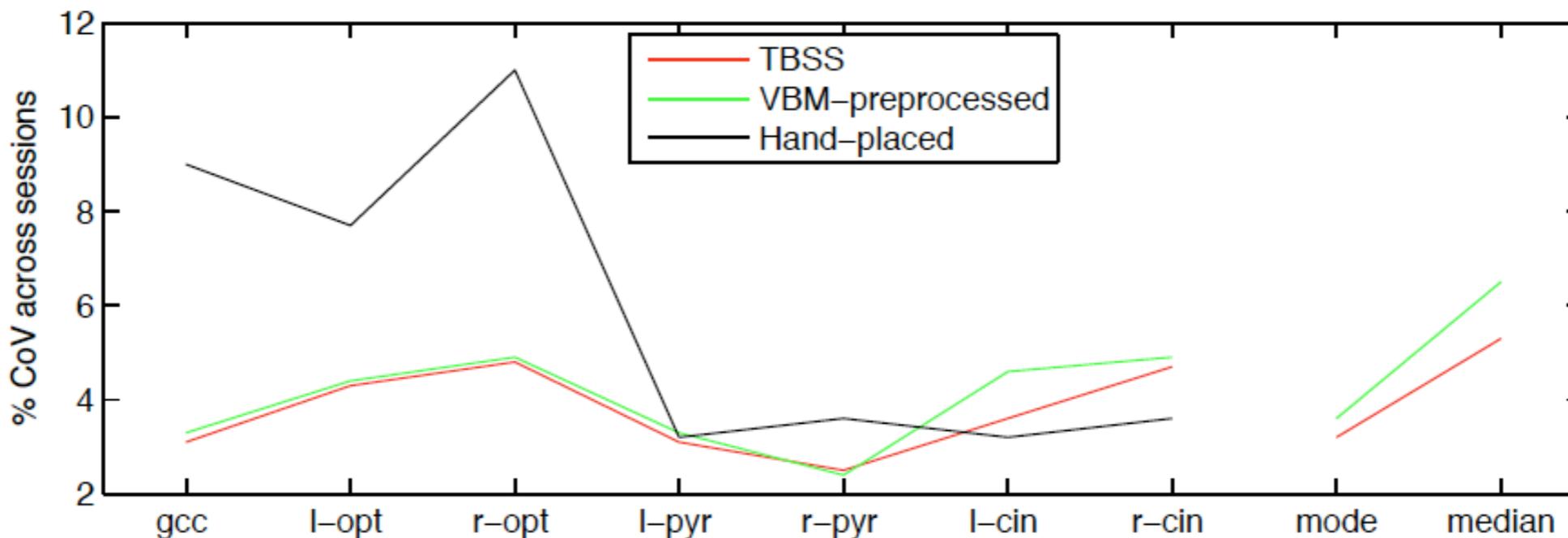
- 36 controls & 33 schizophrenics (Mackay)
- Test each voxel across subjects for Gaussianity using Lilliefors at 5%
- No smoothing with any preprocessing method





# Repeatability Tests

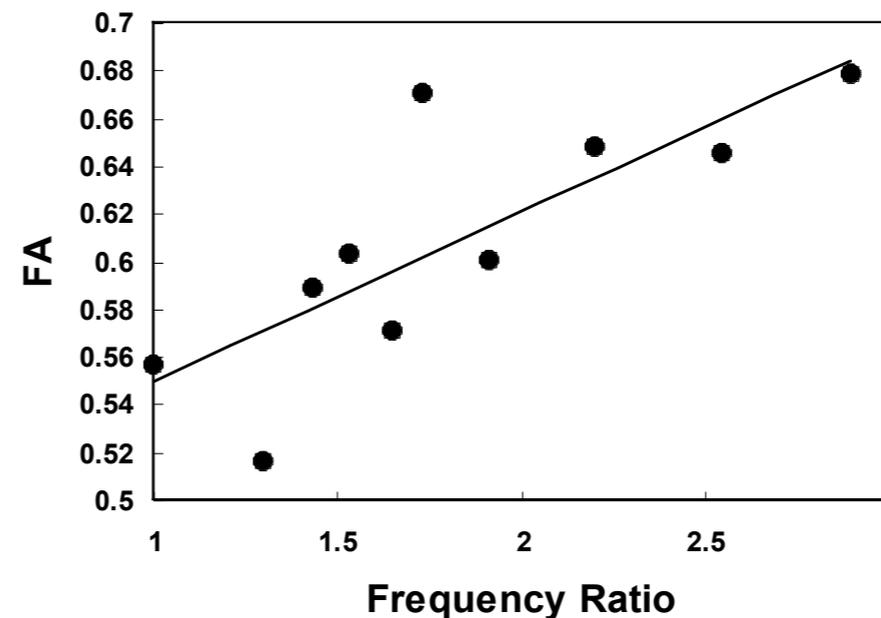
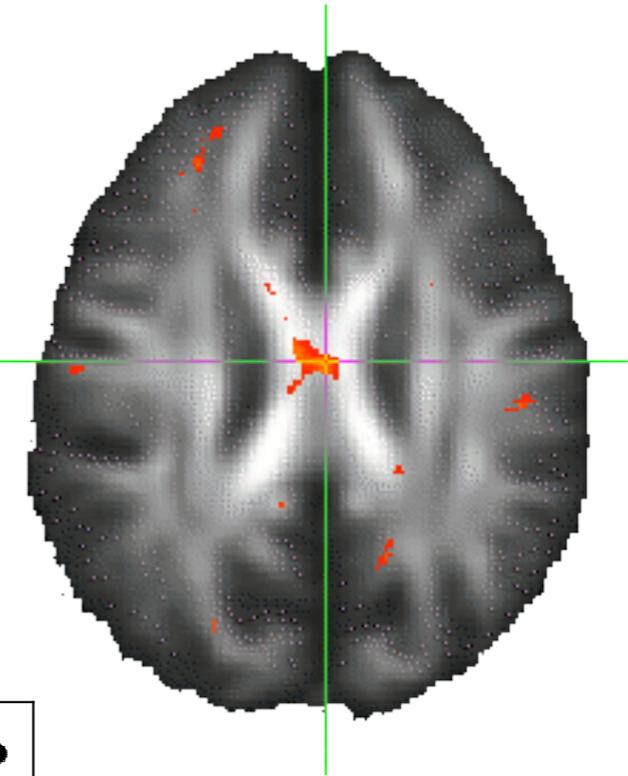
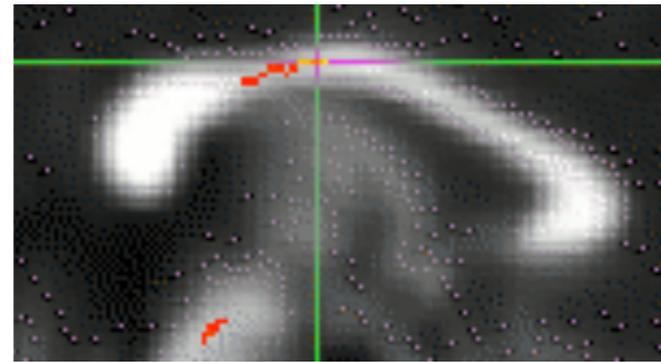
- 8 controls scanned twice each
- Measure %CoV across sessions & subjects
- Test hand-placed points and global mode & median





# Differences in healthy controls

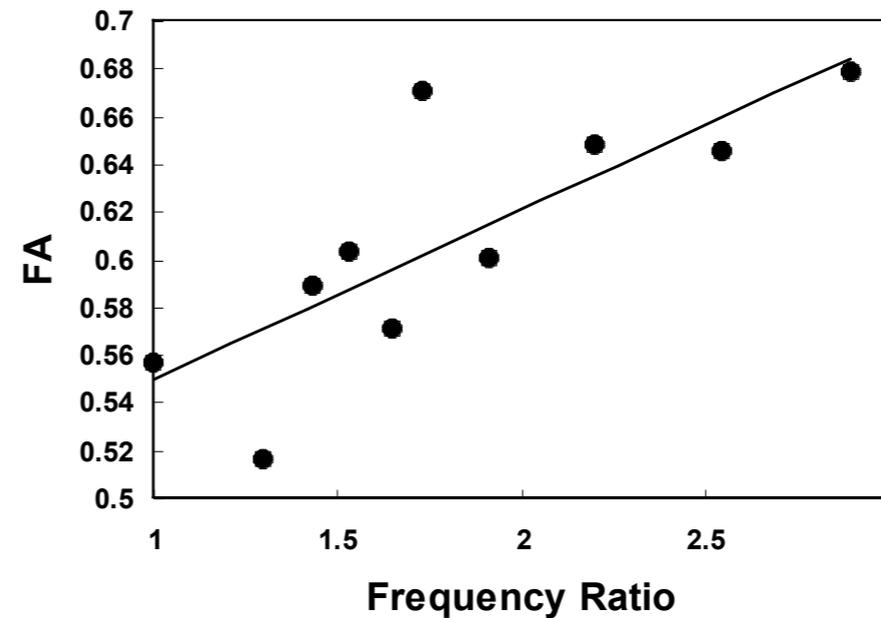
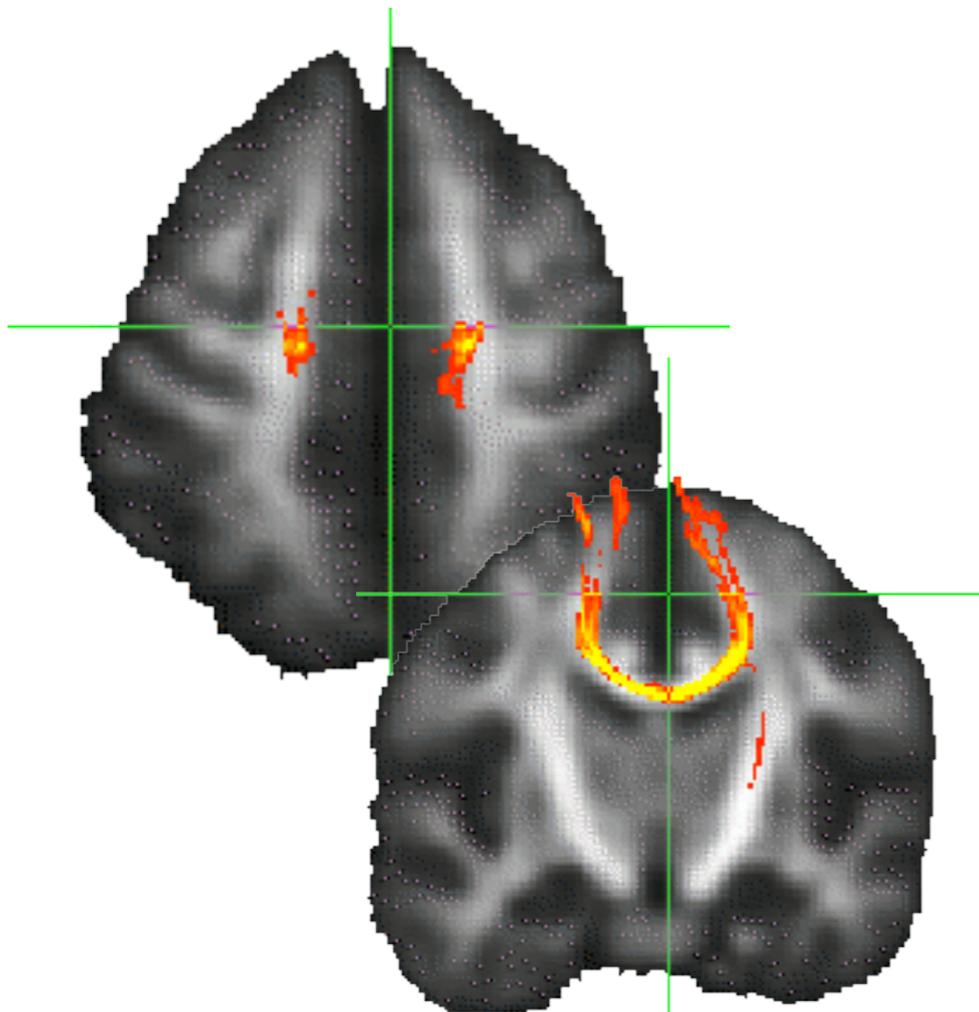
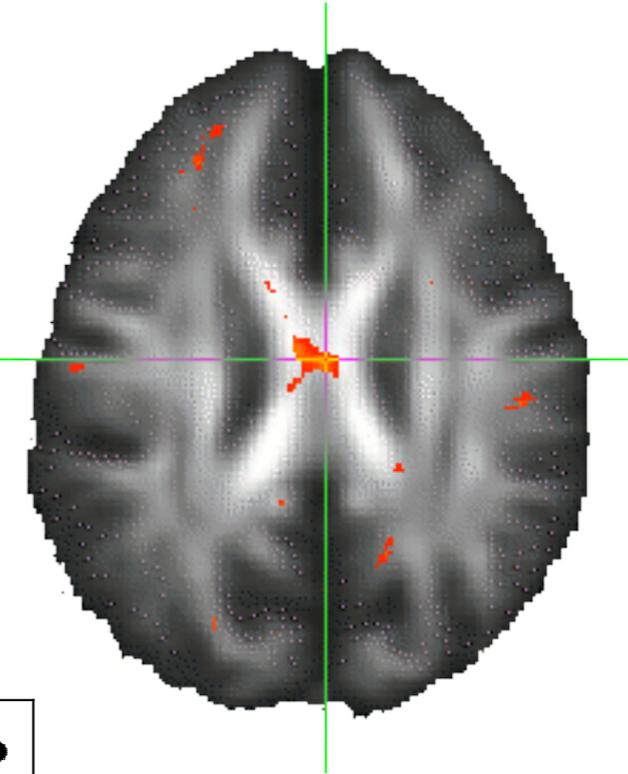
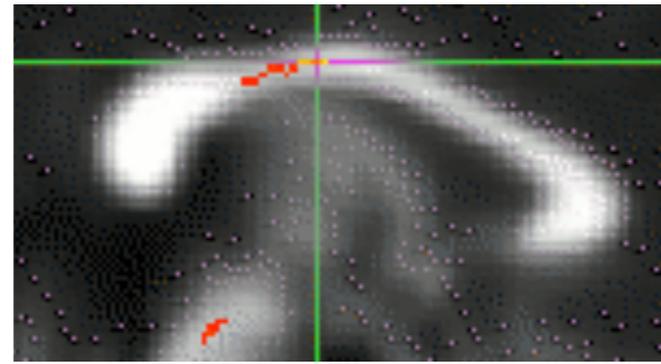
Normal variation in bimanual co-ordination skill



- Inter-individual variation in FA along a specific motor pathway is related to variation in motor skill
- Experience-dependent structural changes?

# Differences in healthy controls

Normal variation in bimanual co-ordination skill



- Inter-individual variation in FA along a specific motor pathway is related to variation in motor skill
- Experience-dependent structural changes?





# Schizophrenia (Mackay)

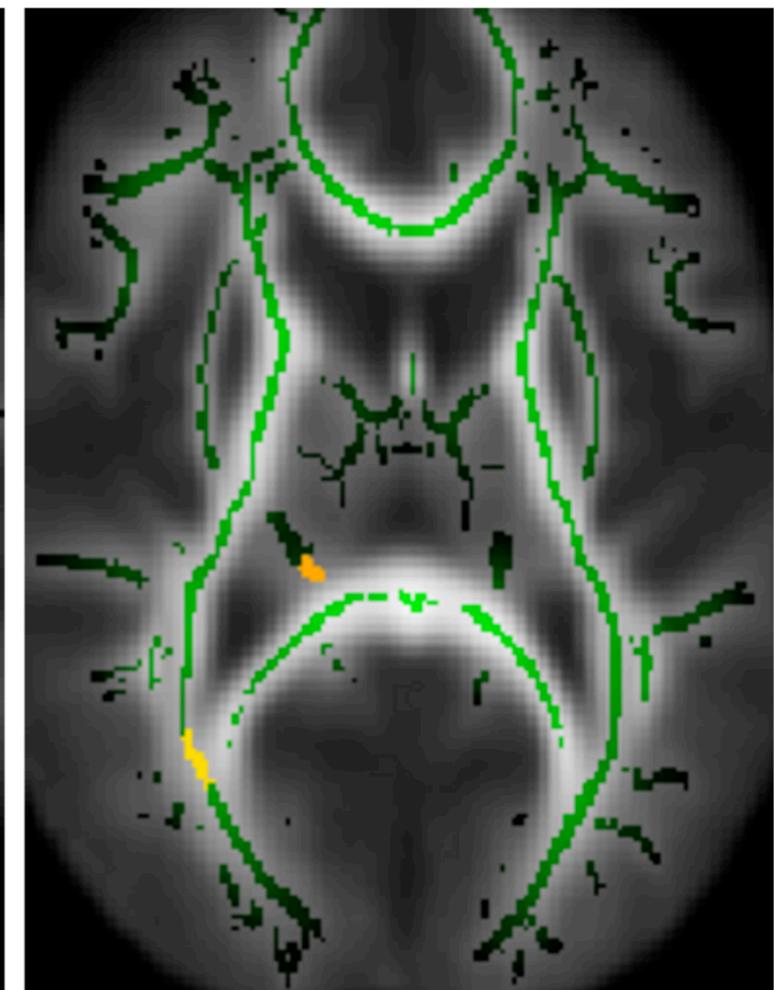
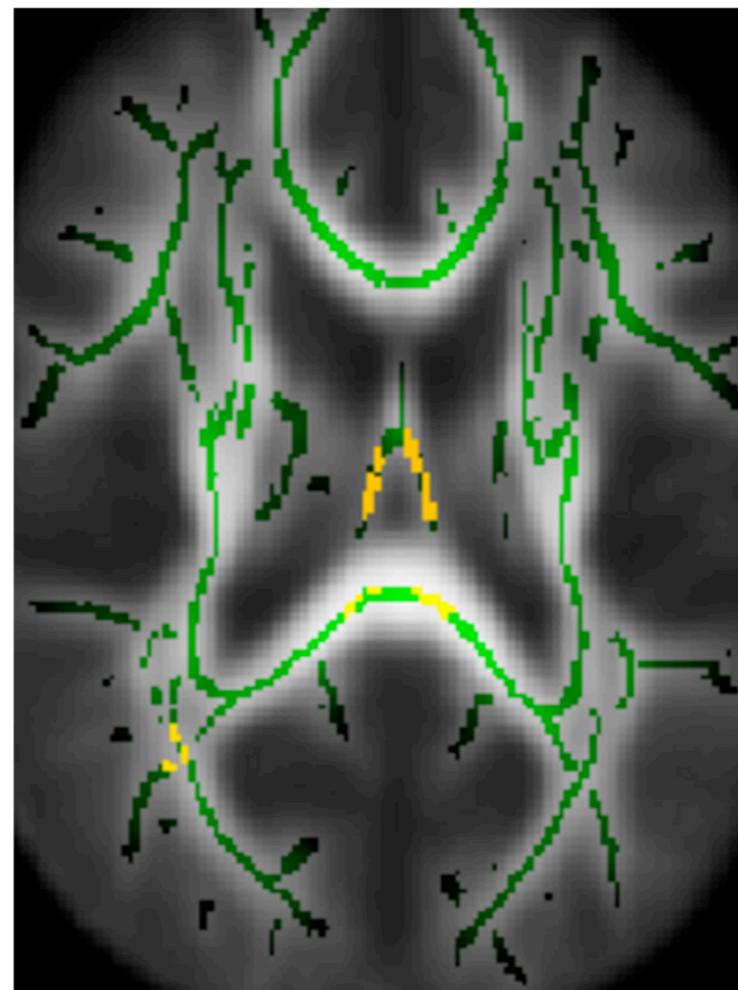
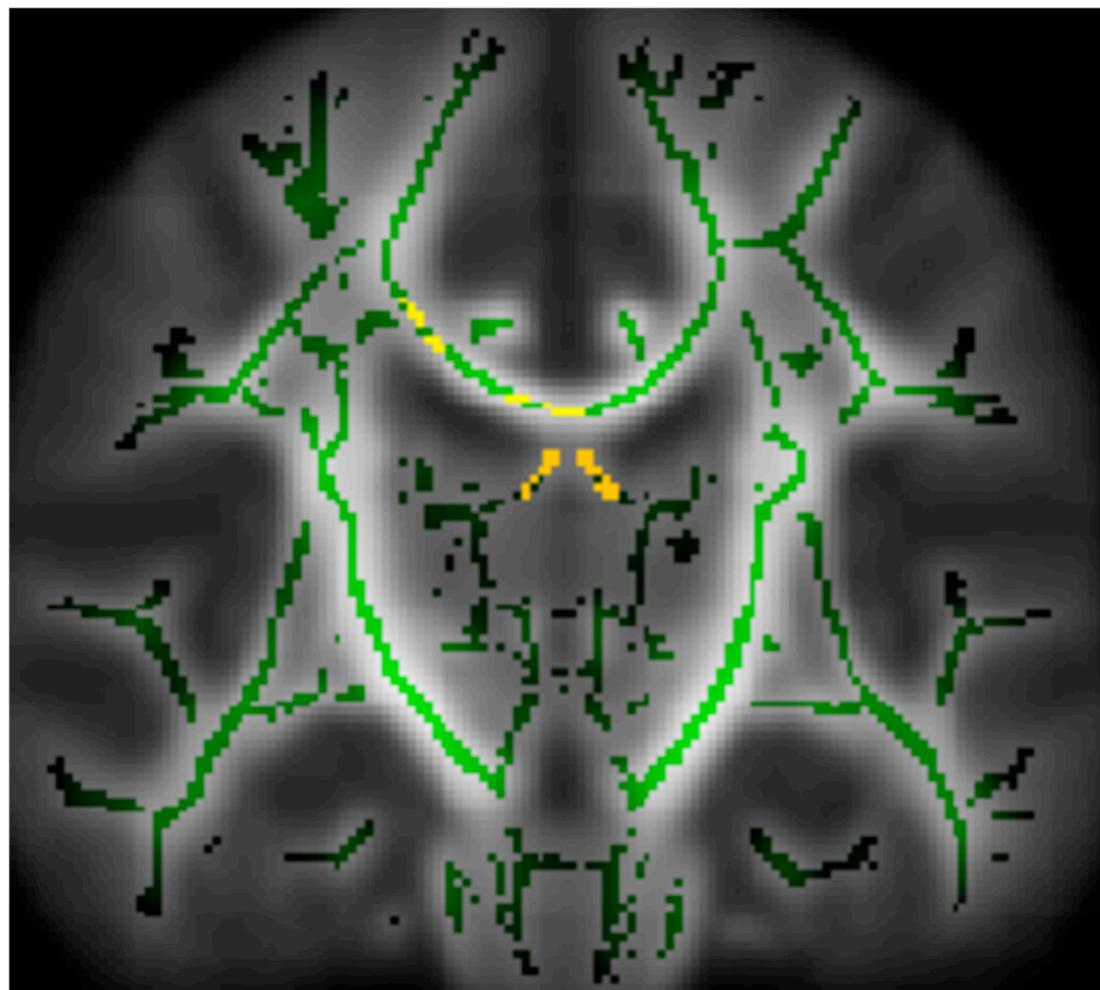
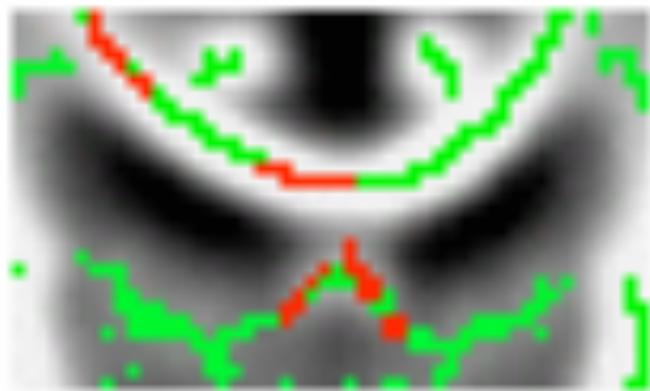
TBSS & VBM show reduced FA in corpus callosum & fornix  
VBM shows spurious result in thalamus due to increased ventricles in schiz.

TBSS

VBM

mean FA (controls)

mean FA (schiz.)

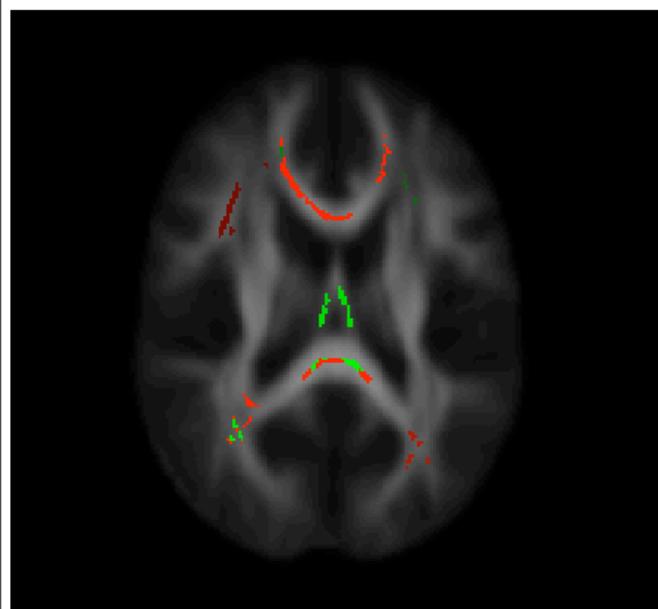
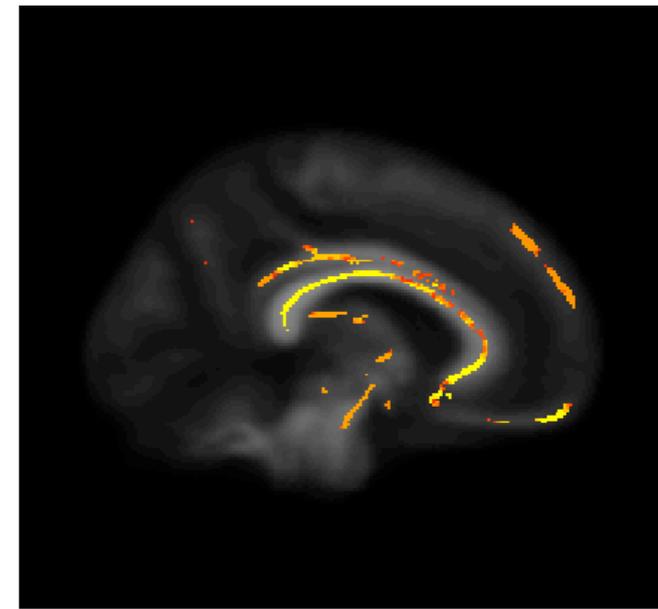
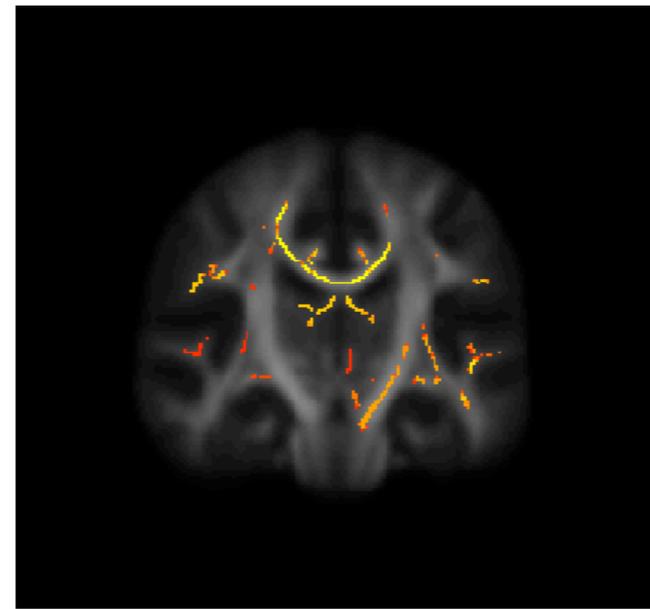
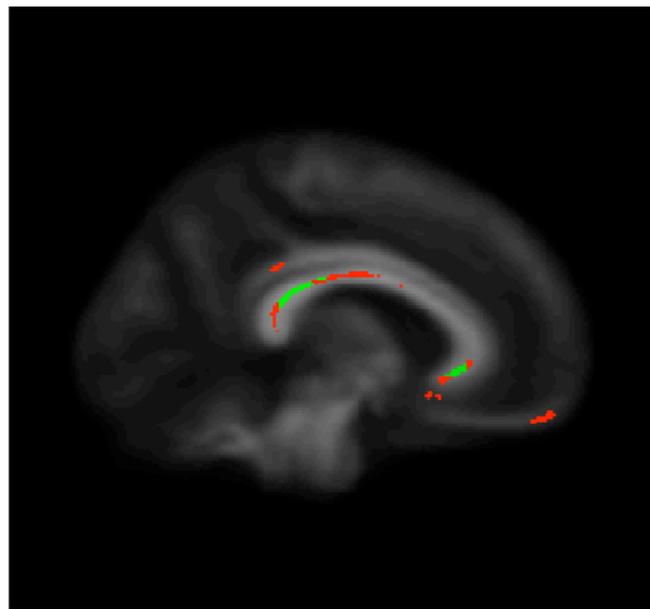
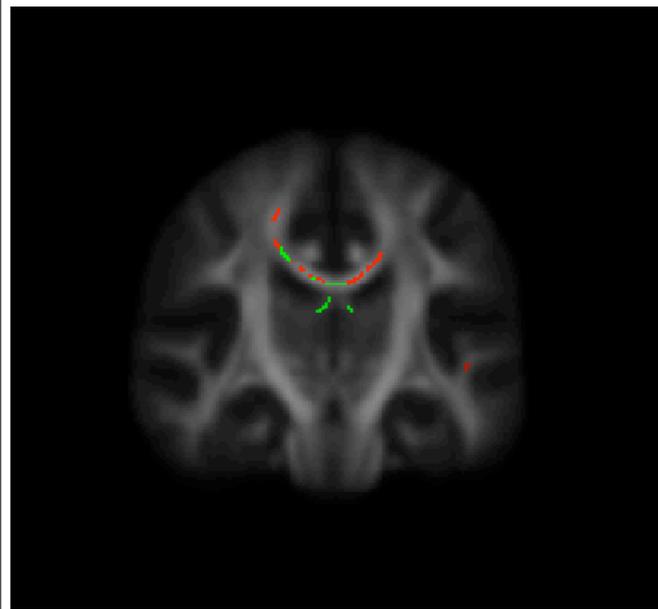




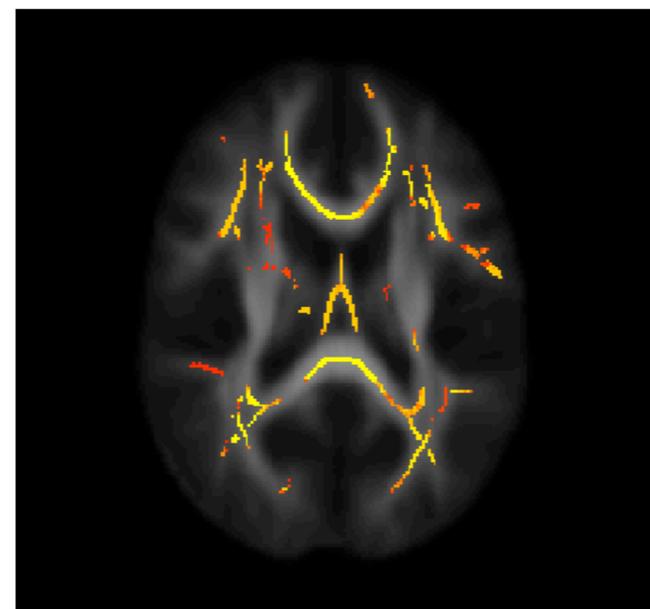
# TFCE for TBSS

controls > schizophrenics

$p < 0.05$  corrected for multiple comparisons across space,  
using randomise



cluster-based:  
cluster-forming  
threshold =  
2 or 3

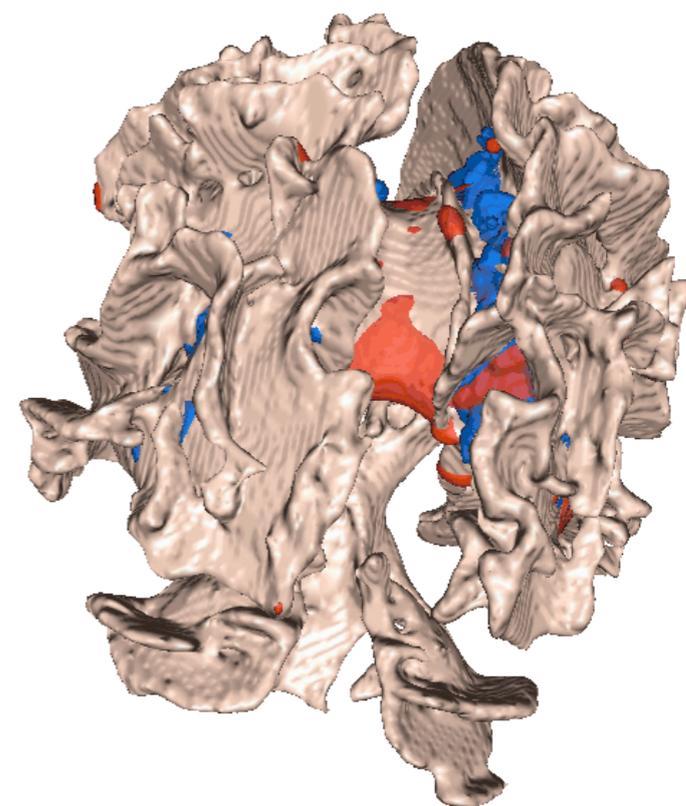
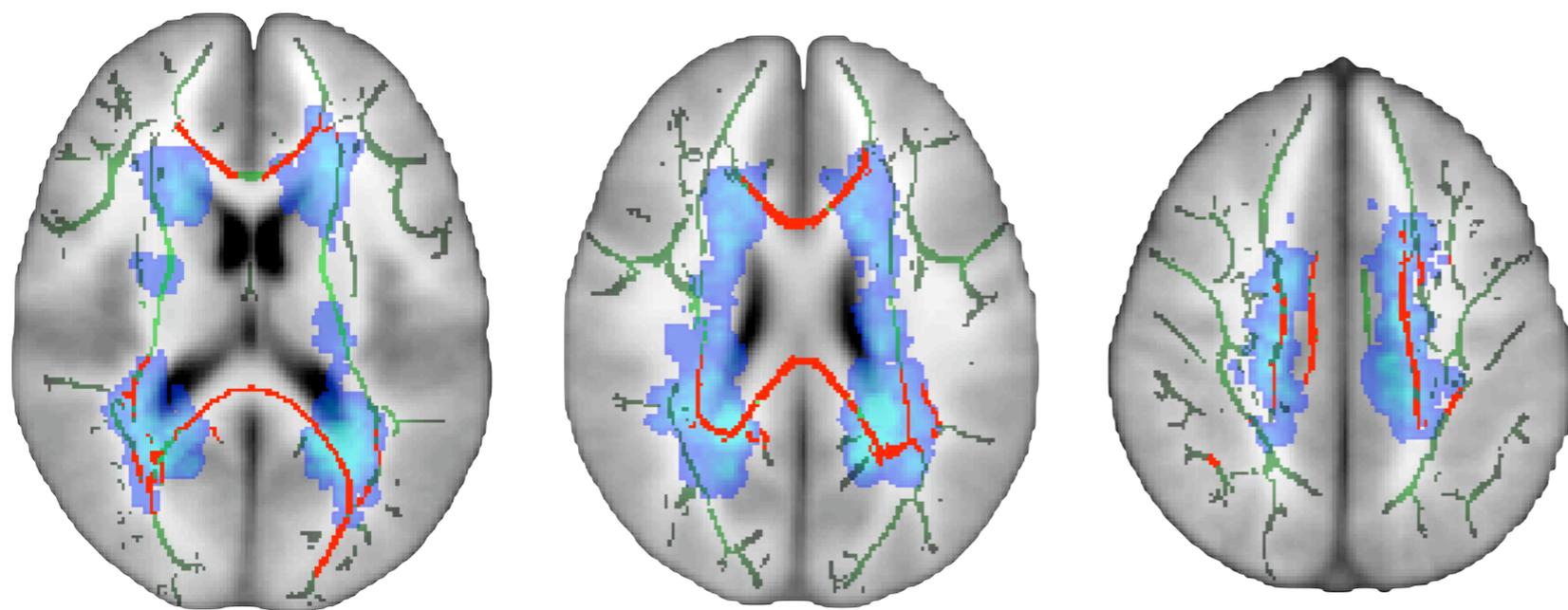
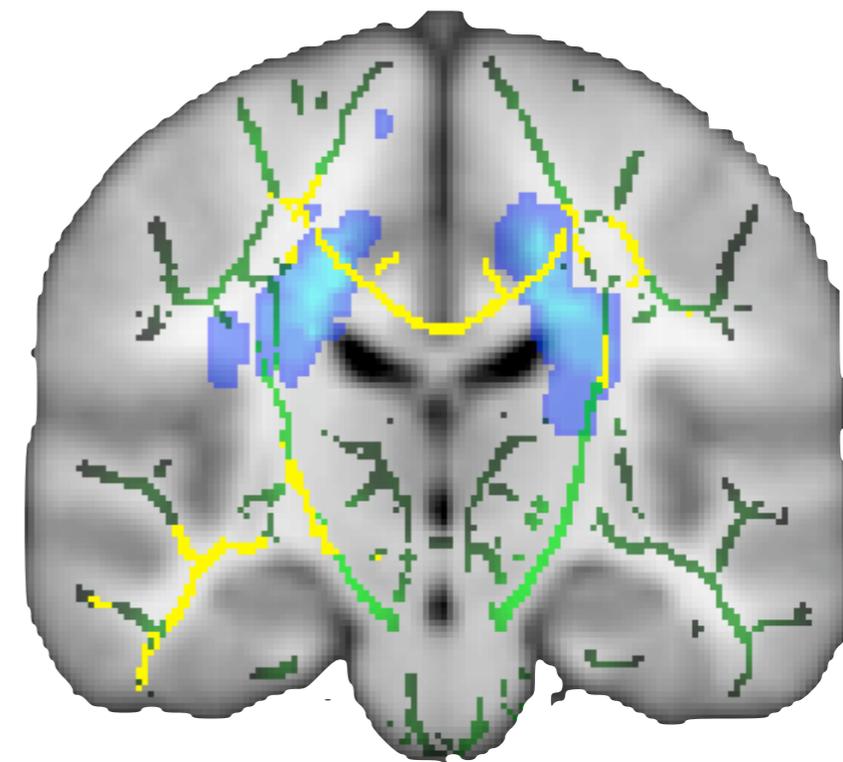


TFCE



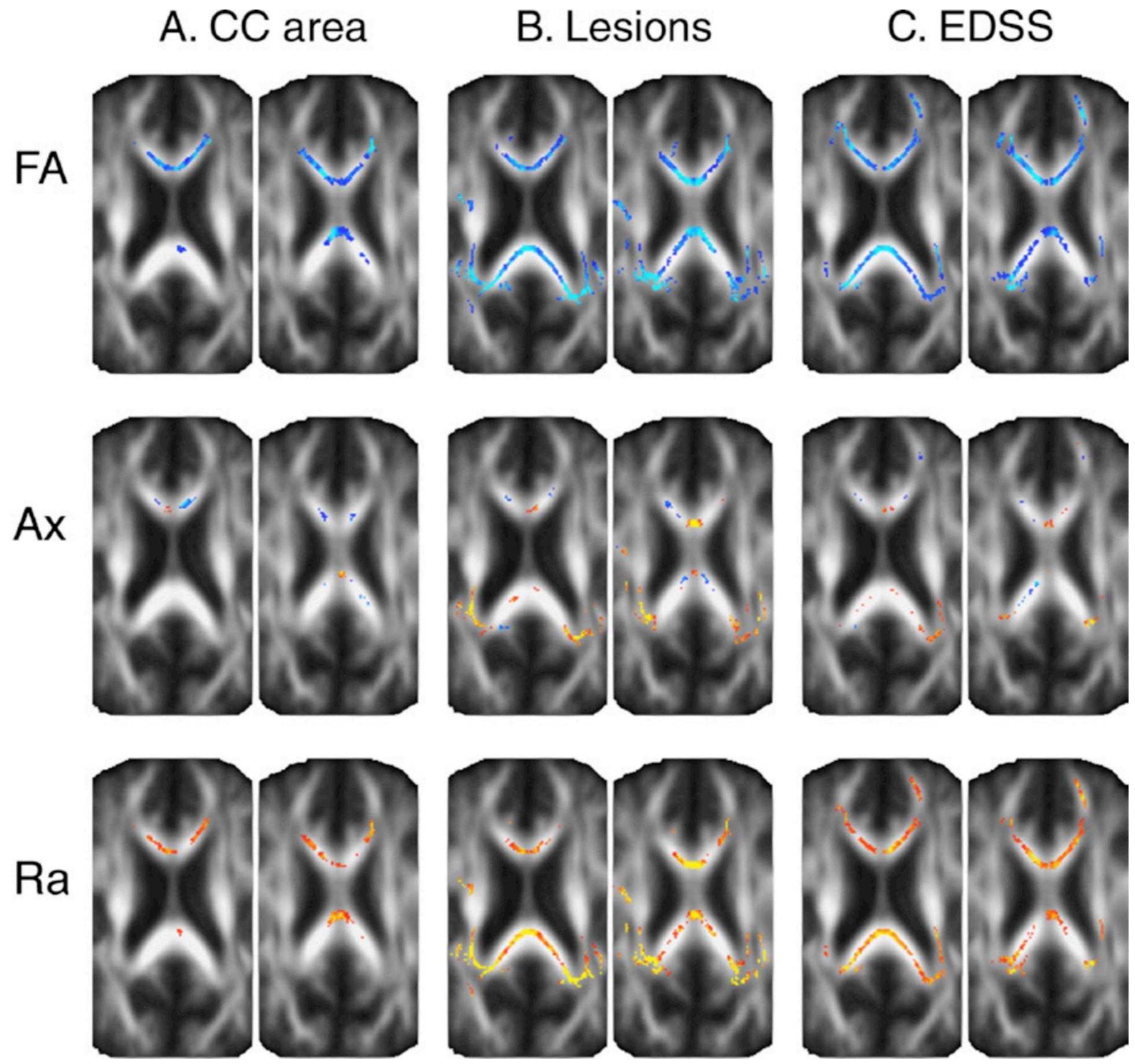
# Multiple Sclerosis (Cader, Johansen-Berg & Matthews)

- 15 MS patients
  - **Yellow** = -ve corr. FA vs EDSS
  - **Blue** = group lesion probability (50%)
  - **Red** = -ve corr. FA vs lesion volume
- Note reduced FA away from lesions





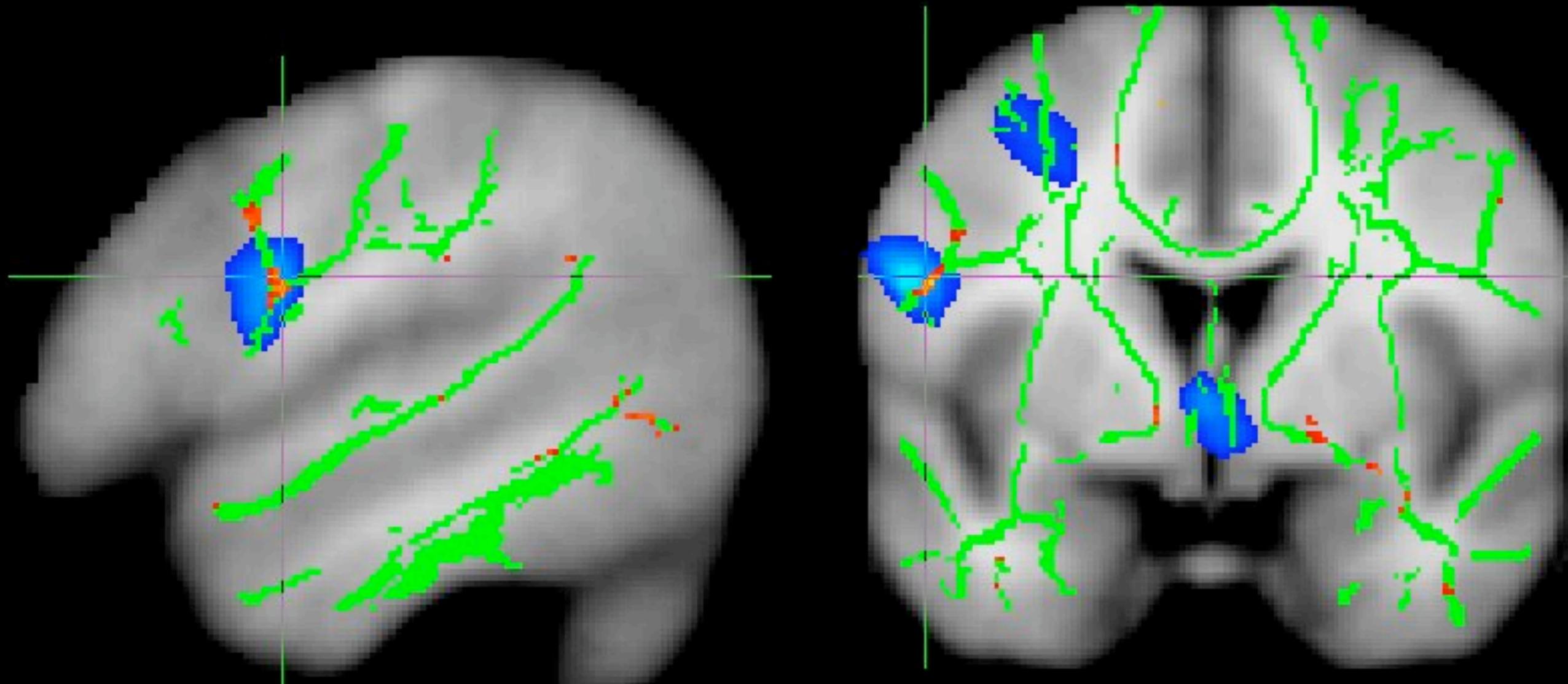
# Multiple Sclerosis (Cader, Johansen-Berg & Matthews)





# Lower FA in Stutterers in ventral-premotor *(Watkins)*

**Right**



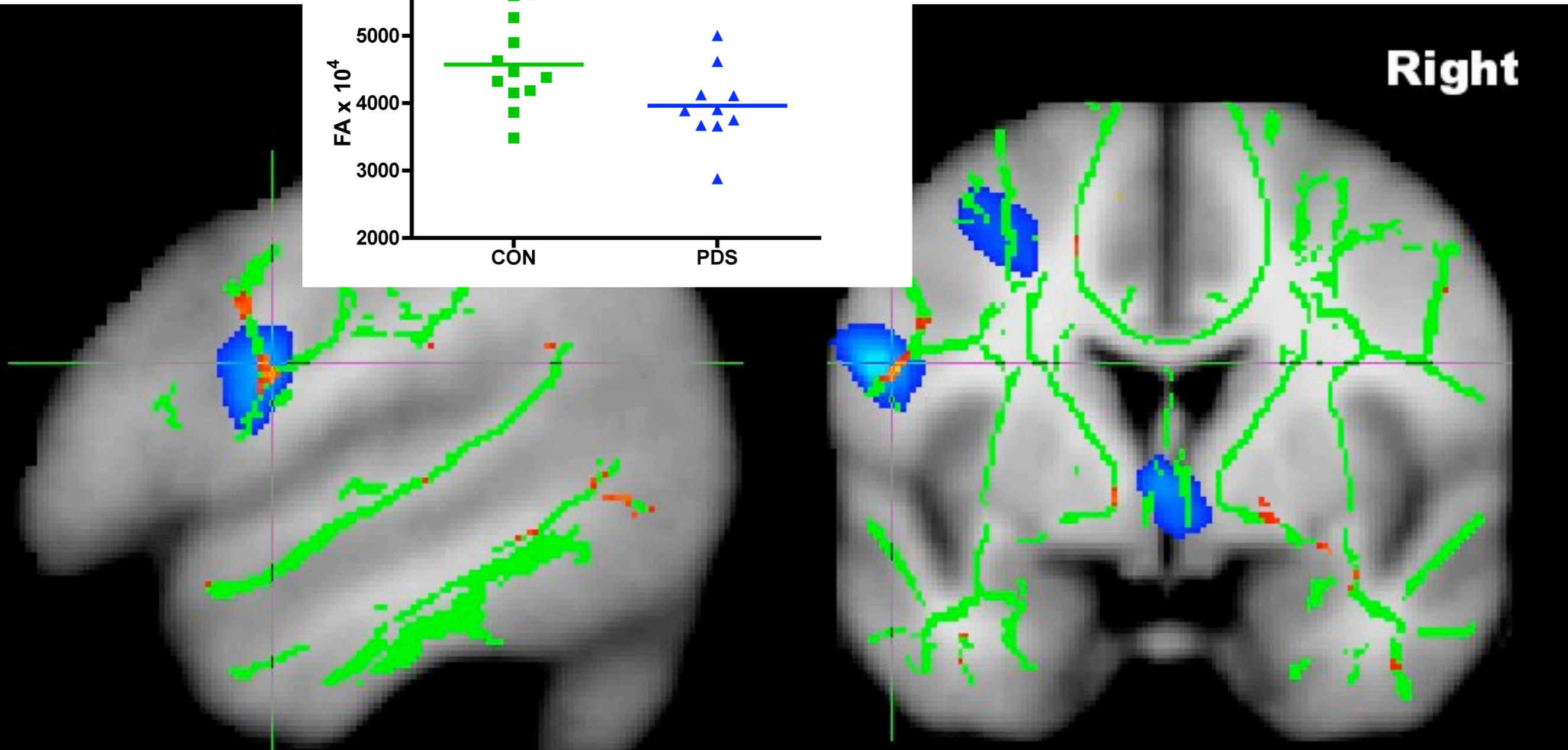
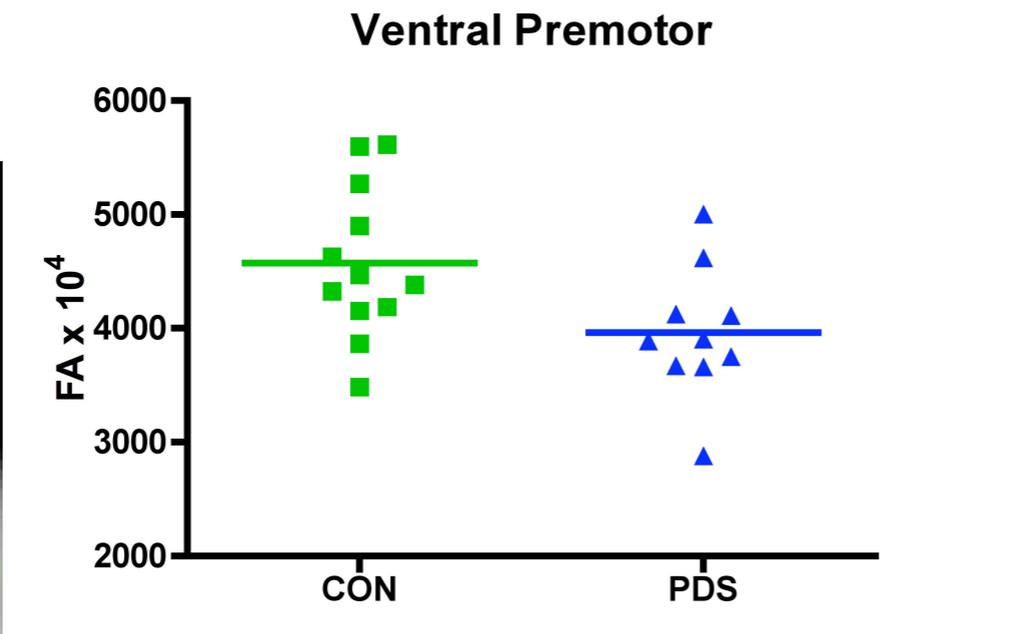
**Blue - FMRI contrast of Controls > PWS during speech production**

**Green - FA tract skeleton**

**Red - FA contrast of Controls > PWS**



# Lower FA in Stutterers in ventral-premotor *(Watkins)*



**Blue - FMRI contrast of Controls > PWS during speech production**

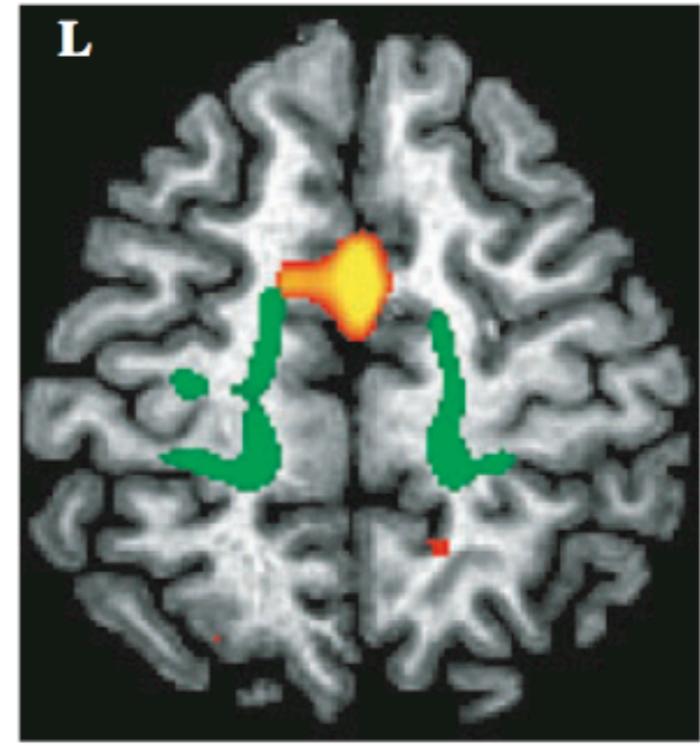
**Green - FA tract skeleton**

**Red - FA contrast of Controls > PWS**

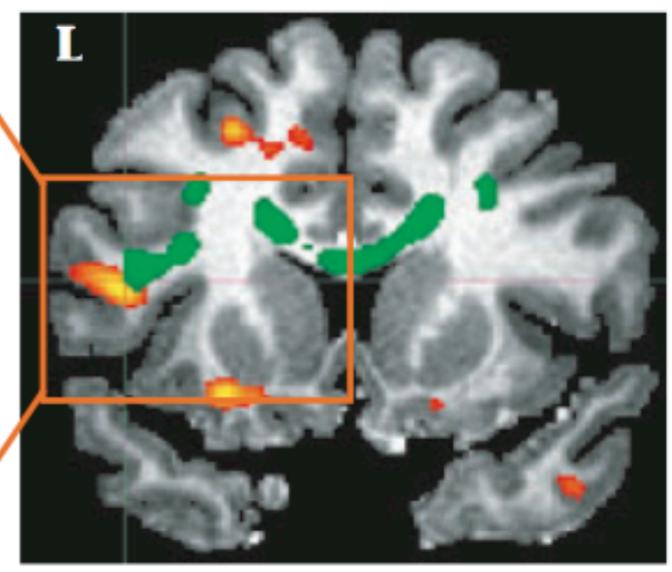
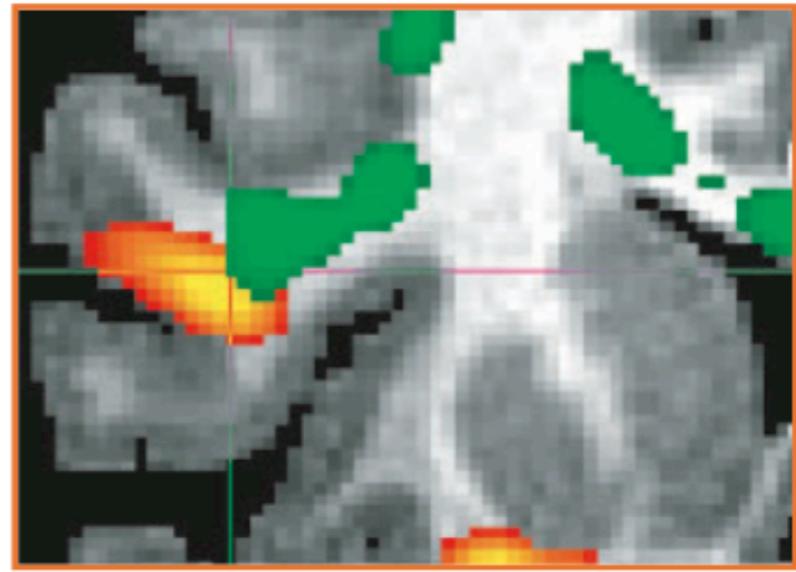
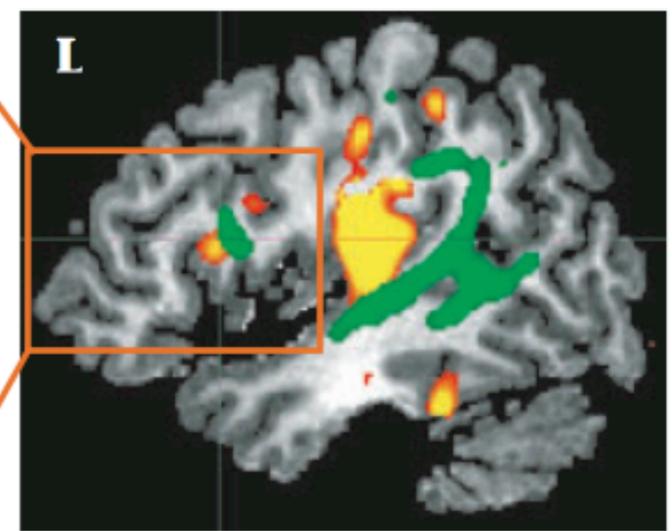
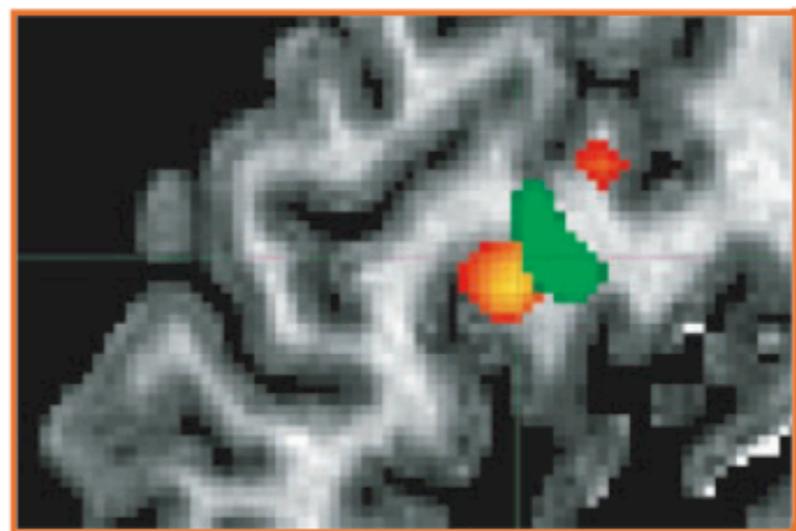


# TBSS & FSL-VBM in adolescent-onset schizophrenia

Douaud & James, Brain 2007



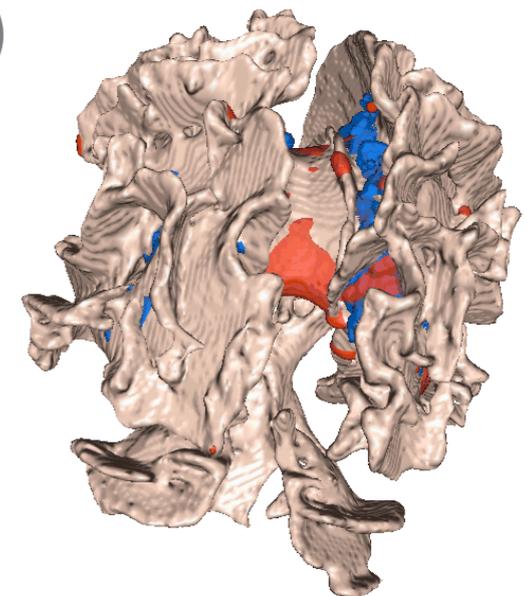
FA reduction  
GM reduction





# TBSS - Conclusions

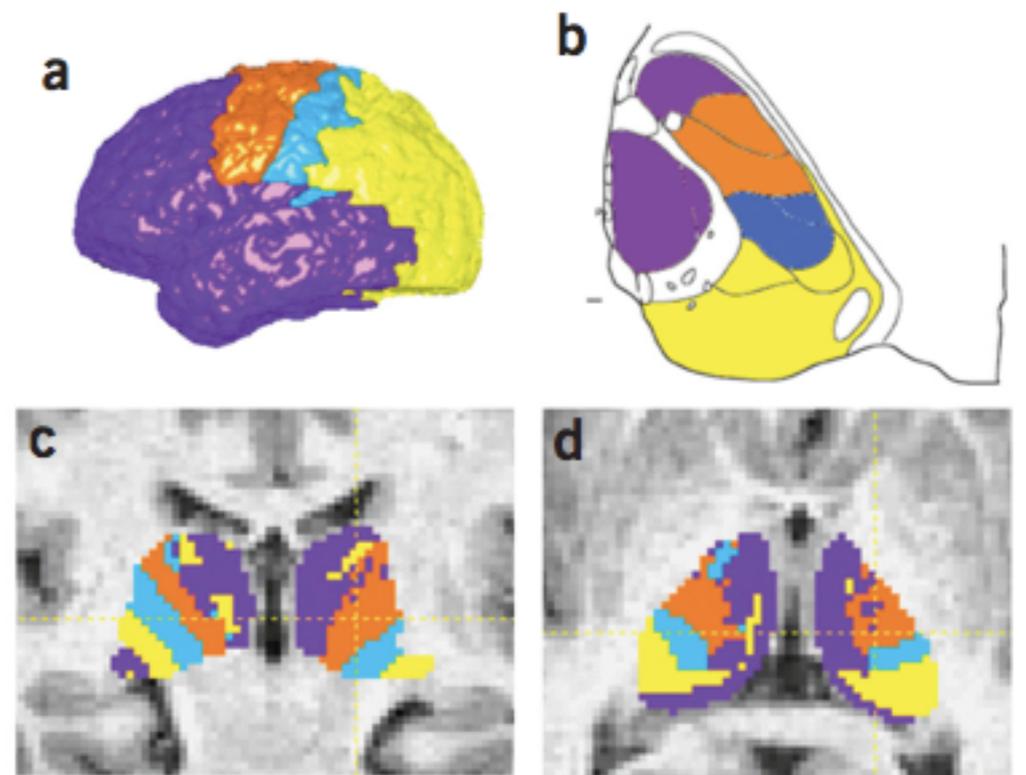
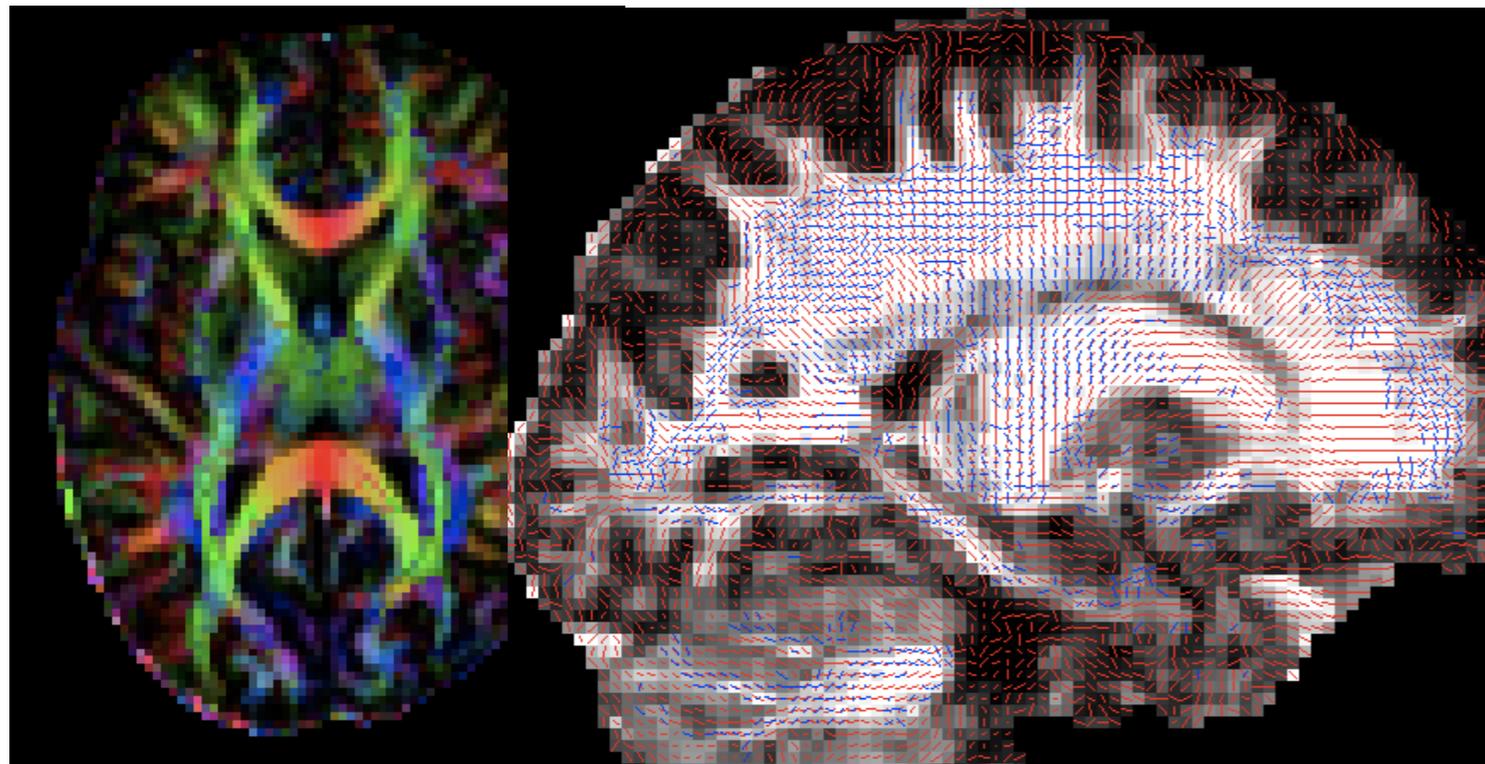
- Attempting to solve correspondence/smoothing problems
- Less ambiguity of interpretation / spurious results than VBM
- Easier to test whole brain than ROI / tractography
- Limitations & Dangers
  - Interpretation of partial volume tracts still an issue
  - Crossing tracts?
- Future work
  - Use full tensor (for registration and test statistic)
  - Use other test statistics (MD, PDD, width)
  - Multivariate stats (across voxels and/or different diffusion measures) & discriminant (ICA, SVM)





# FMRIB Diffusion Toolbox

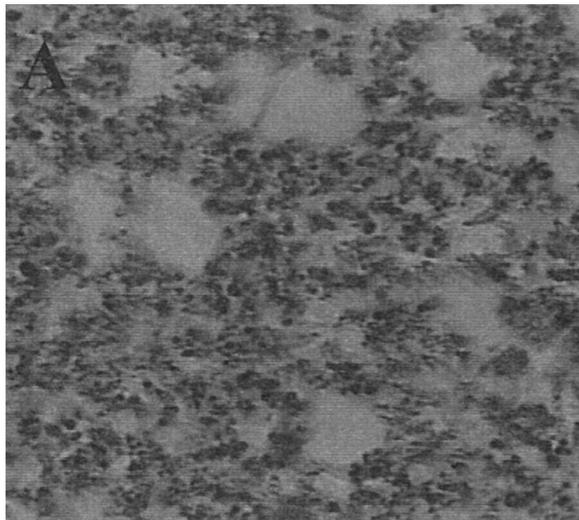
- DTI model fit
- Eddy current correction
- Voxel-Based diffusion analysis (TBSS)
- BEDPOSTX modelling crossing fibres
- PROBTRACKX propagating uncertainty in tractography





# Connectivity - Why do we care?

- Clinical measurements
  - White matter (dys)connectivity is thought to form the substrate for many different neurological and psychiatric disorders.



E.g. axonal degeneration/  
demyelination in MS.

Evangelou et al. 2000

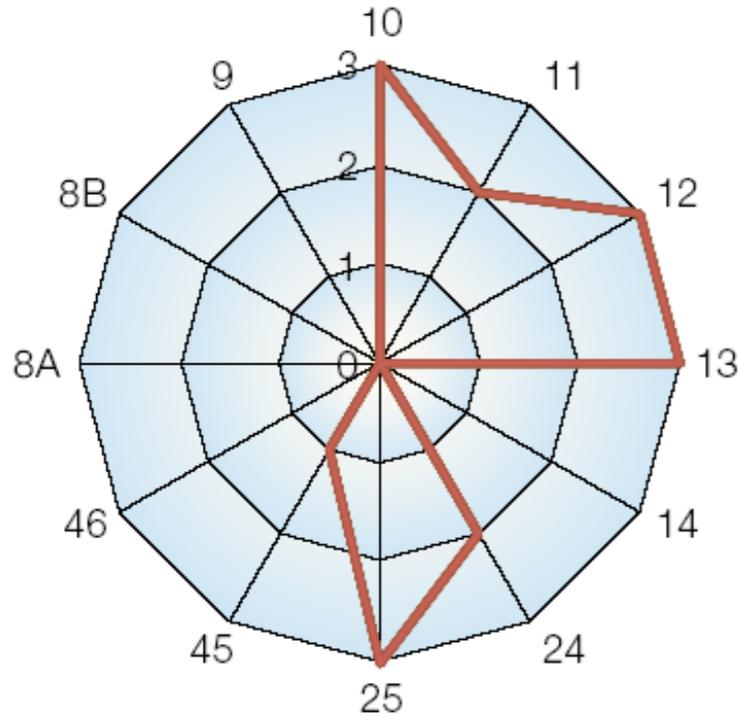
- Diffusion tractography allows in-vivo measurements specific to different connections.



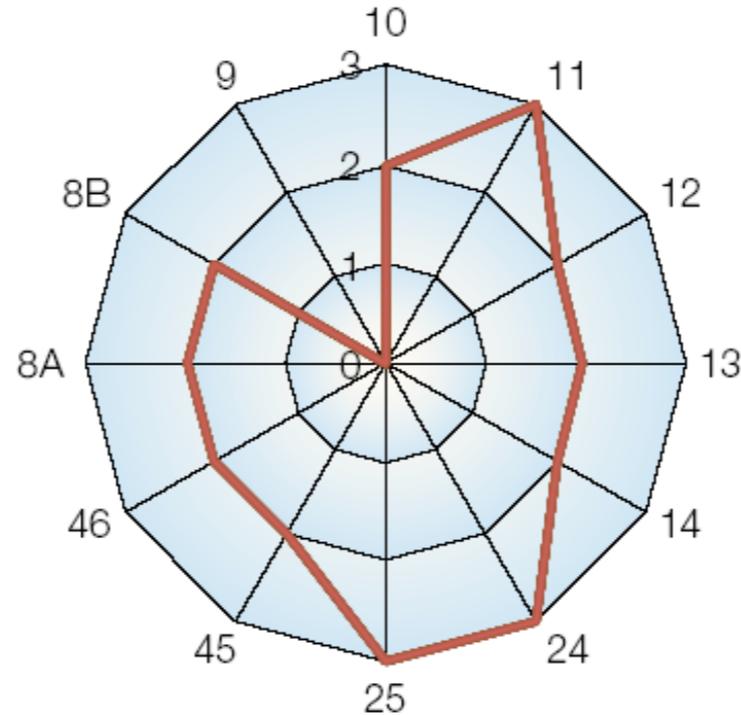
# Basic Science - Connections

## constrain function

Afferents of area 14

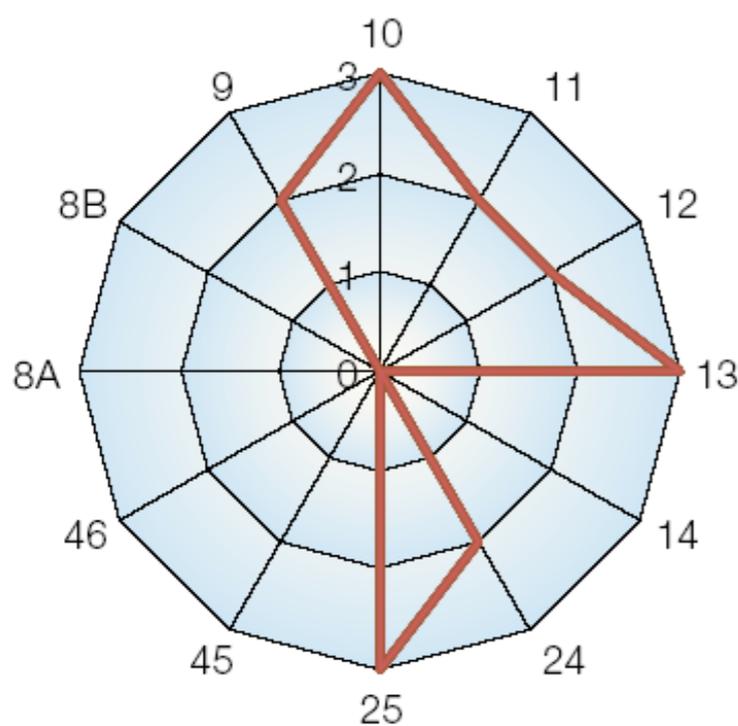


Afferents of area 9

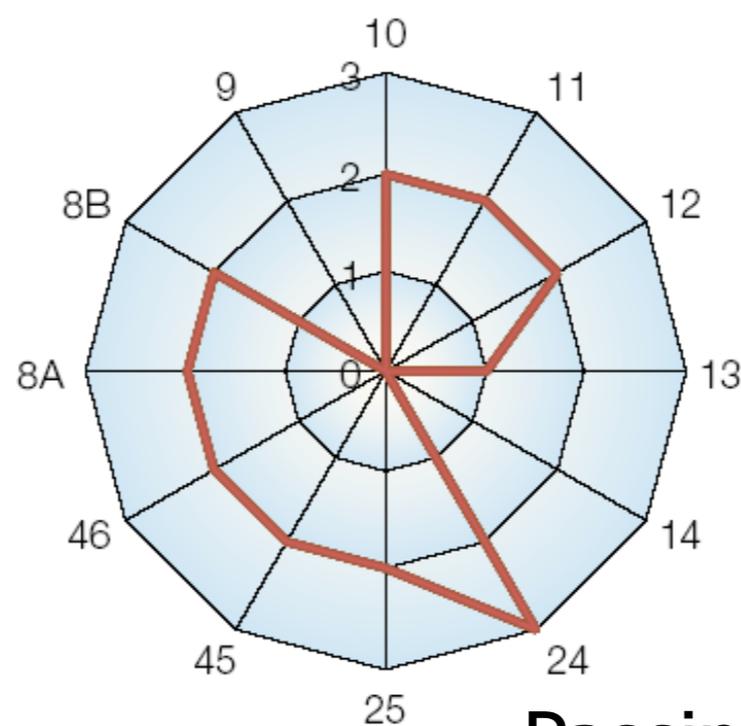


Different regions  
have distinct  
connectivity  
fingerprints

Efferents of area 14



Efferents of area 9

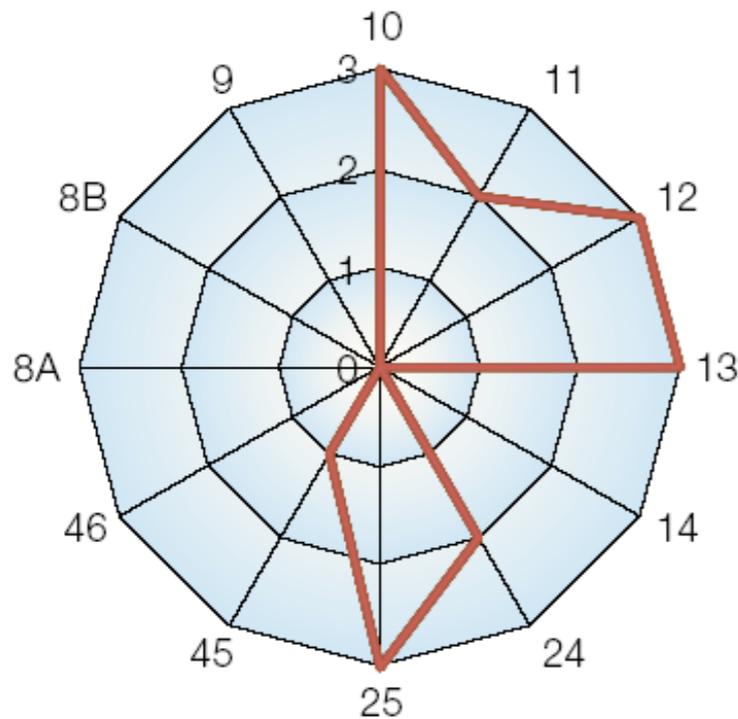




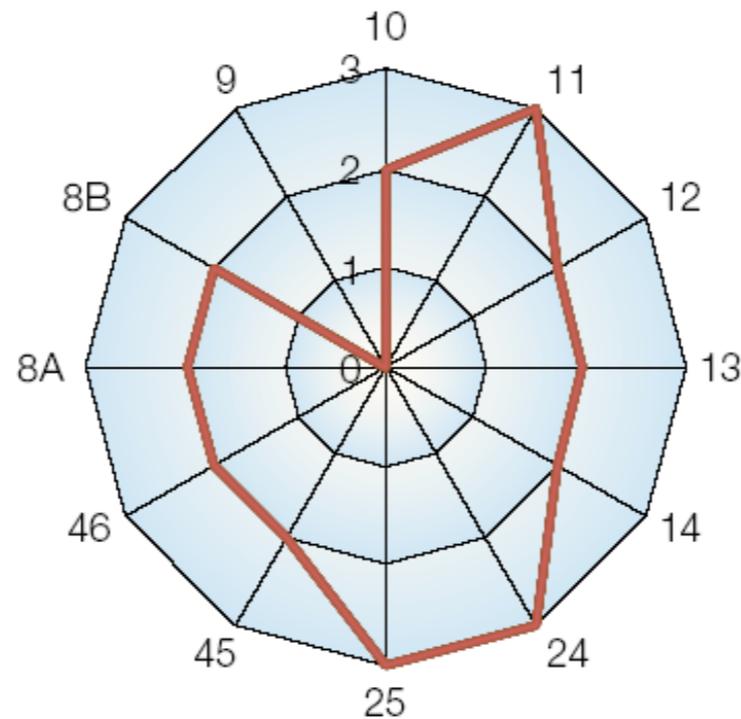
# Basic Science - Connections

## constrain function

Afferents of area 14

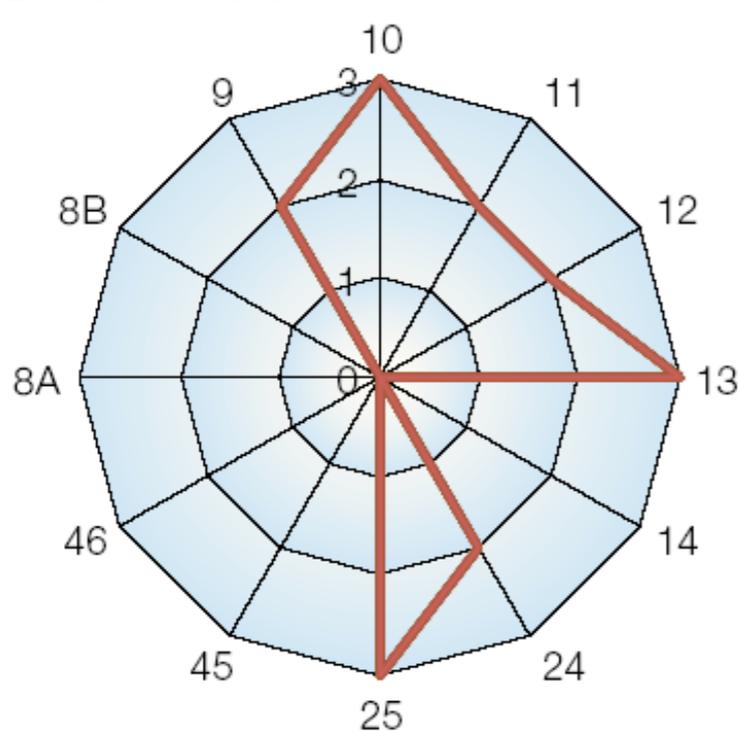


Afferents of area 9

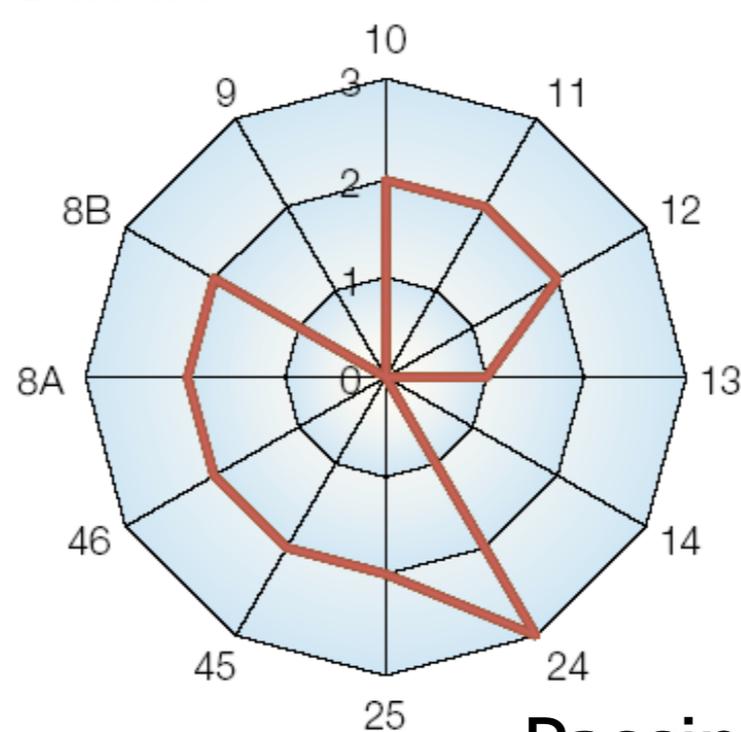


Different regions have distinct connectivity fingerprints

Efferents of area 14



Efferents of area 9



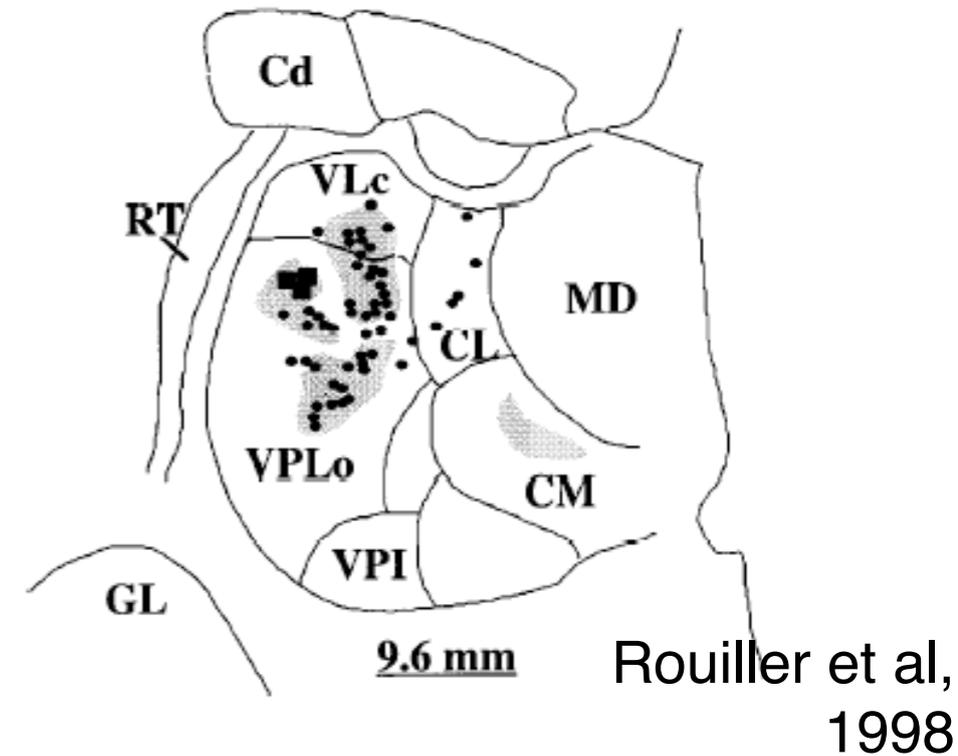
Understanding regional connectivity will be essential for our understanding of systems neuroscience.



# Investigating connectivity

# Investigating connectivity

- Tracer studies in non-human animals



Post-mortem

- In human
  - Post-mortem dissection reveals large tracts
  - Post-mortem histology shows degeneration after remote lesions

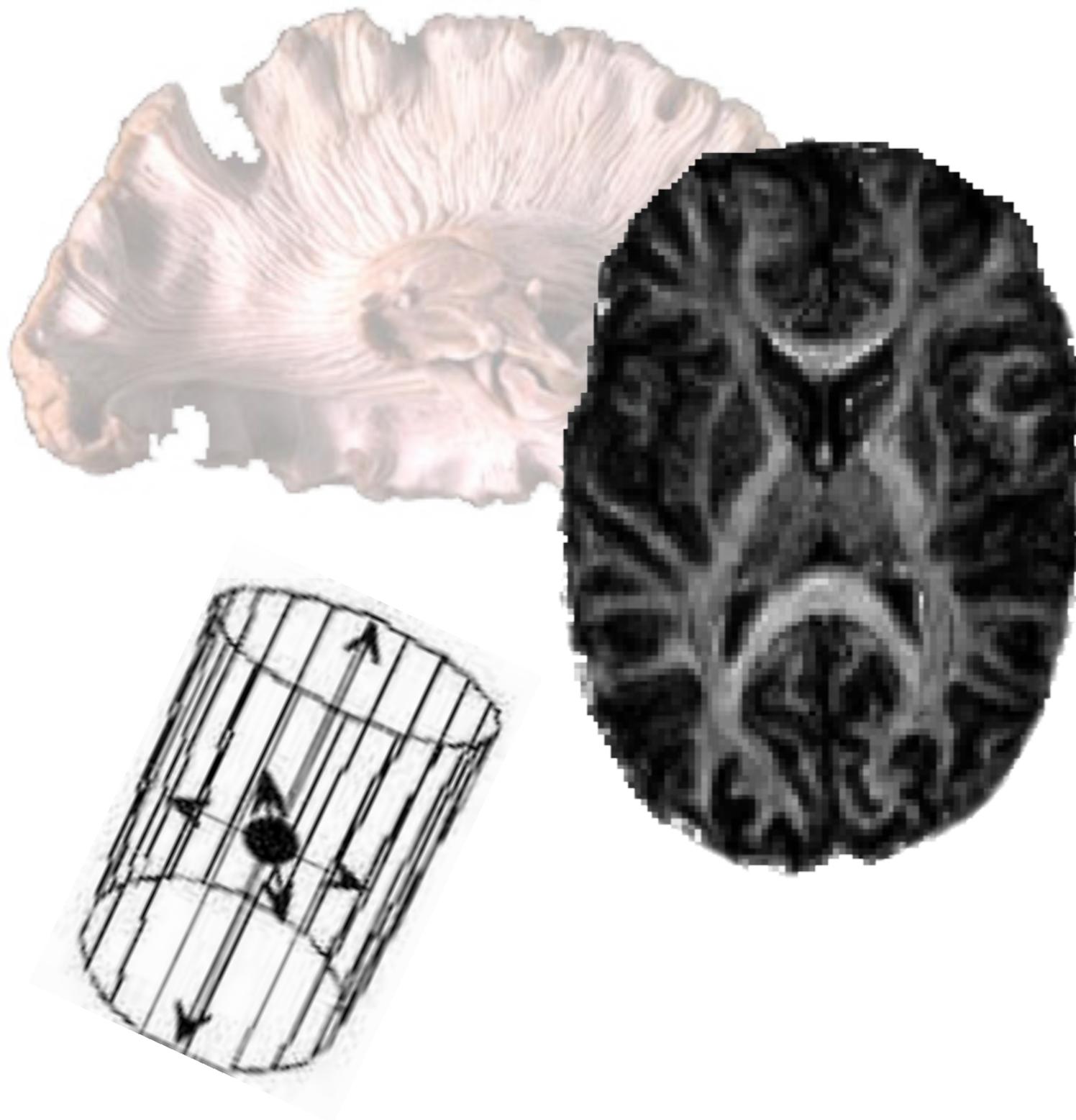


# Investigating human brain connectivity





# Investigating human brain connectivity

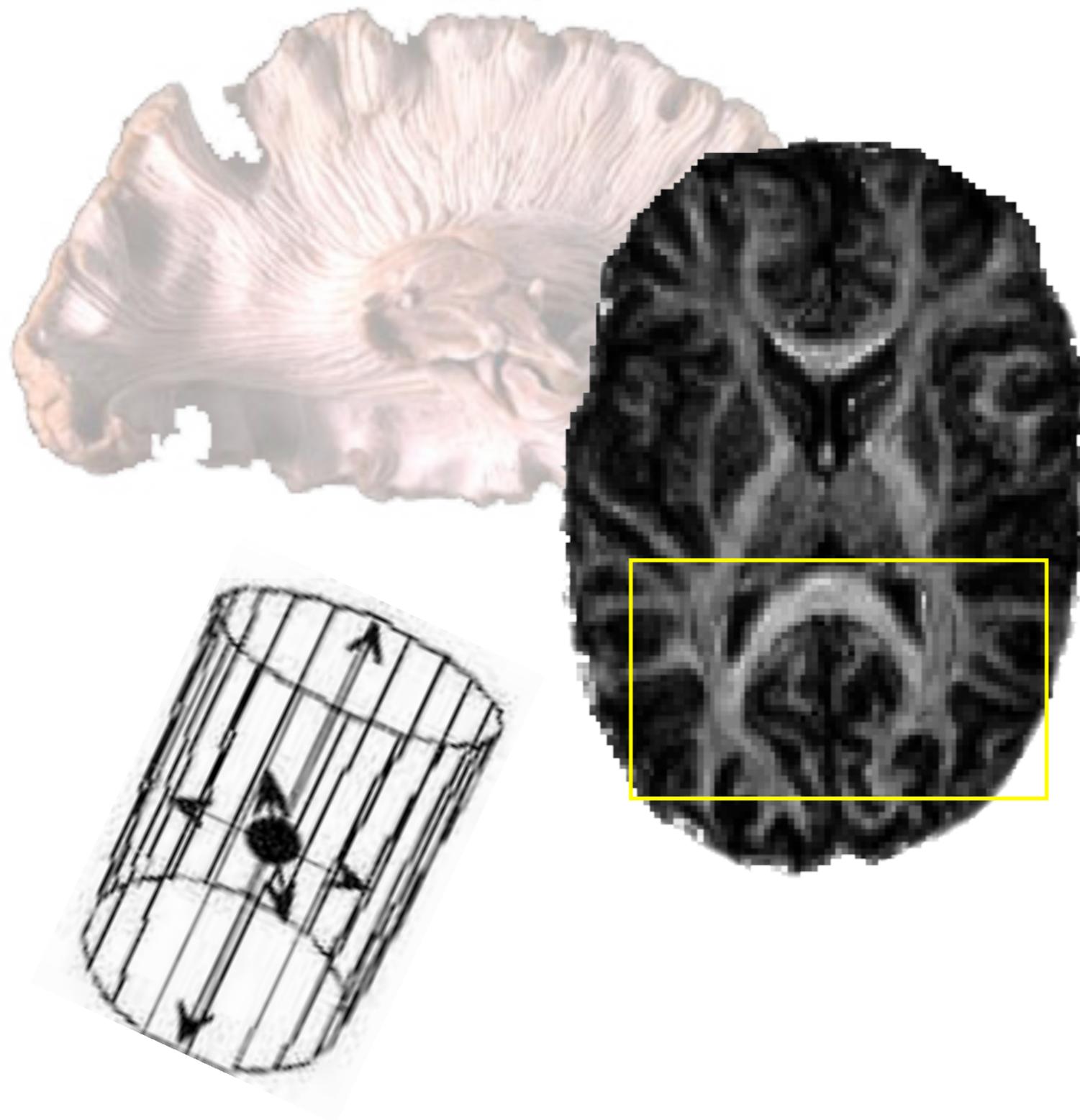


## Diffusion-weighted MR imaging

- Fractional anisotropy
- Principal diffusion direction



# Investigating human brain connectivity

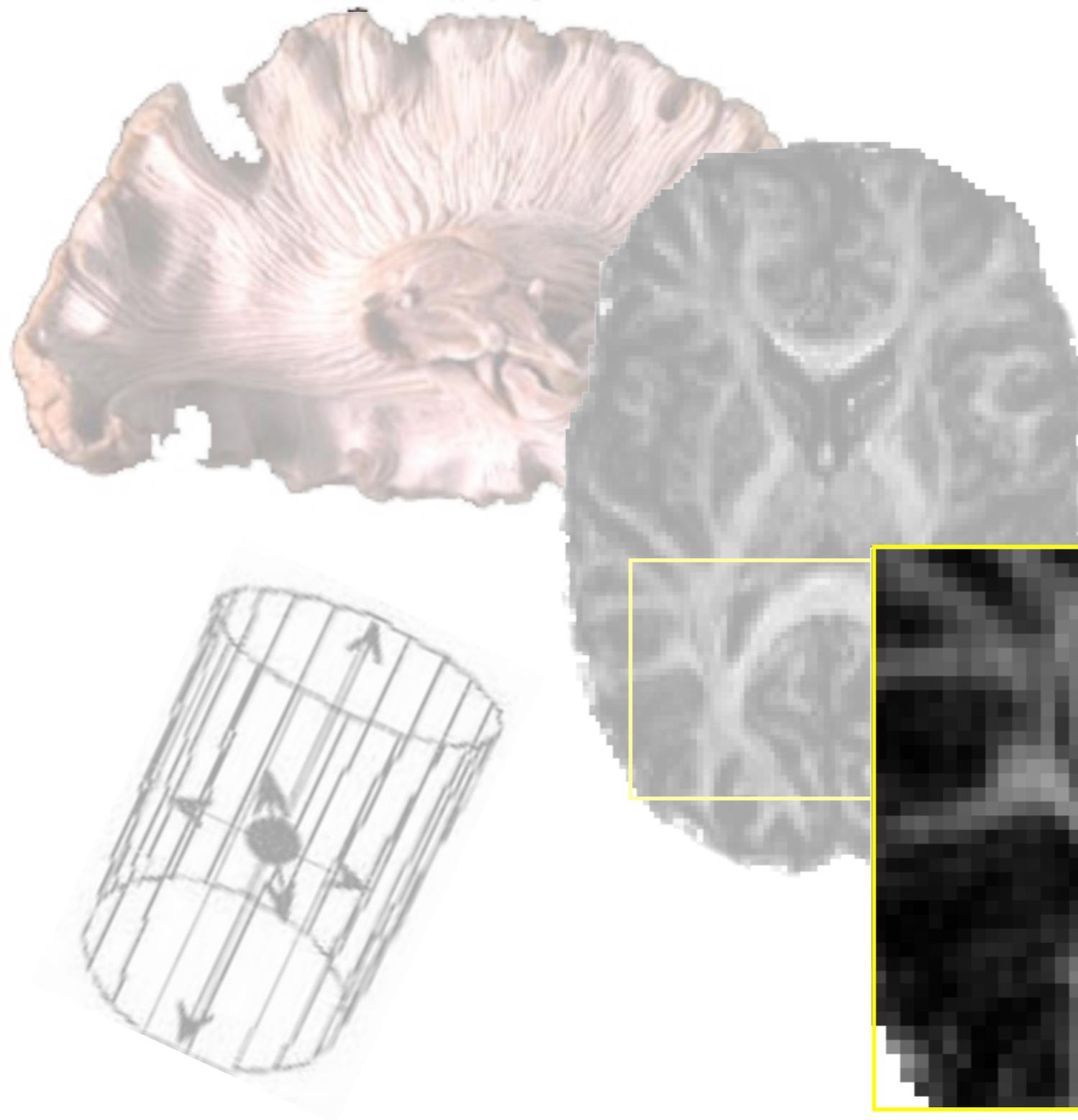


## Diffusion-weighted MR imaging

- Fractional anisotropy
- Principal diffusion direction



# Investigating human brain connectivity



## Diffusion-weighted MR imaging

- Fractional anisotropy
- Principal diffusion direction

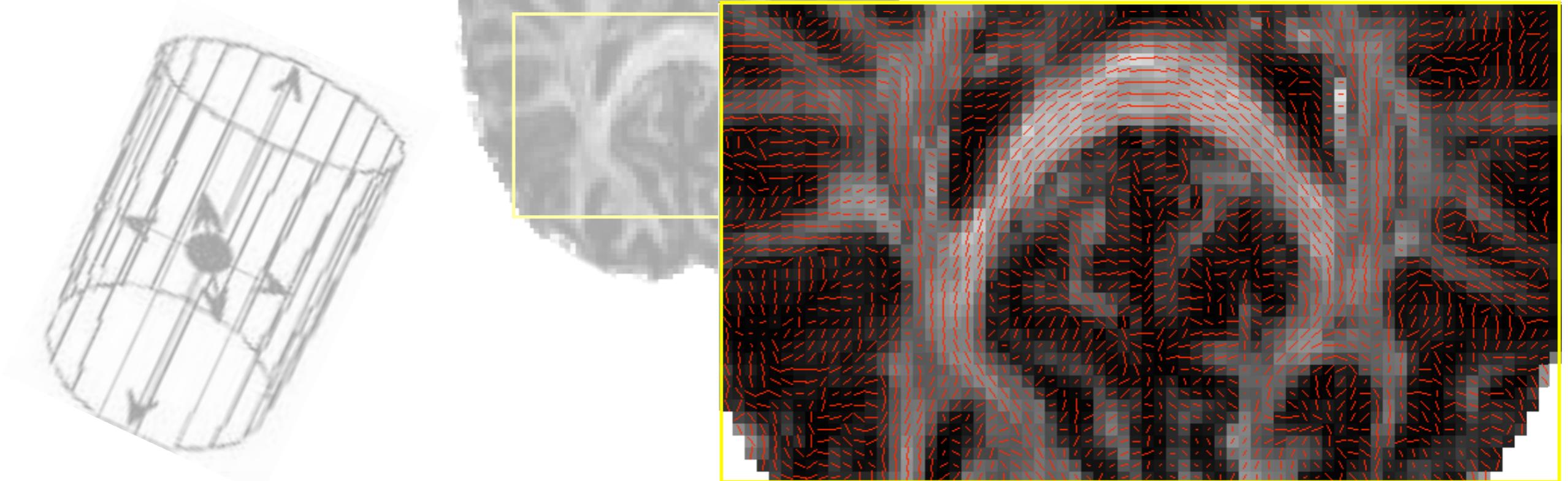


# Investigating human brain connectivity



## Diffusion-weighted MR imaging

- Fractional anisotropy
- Principal diffusion direction



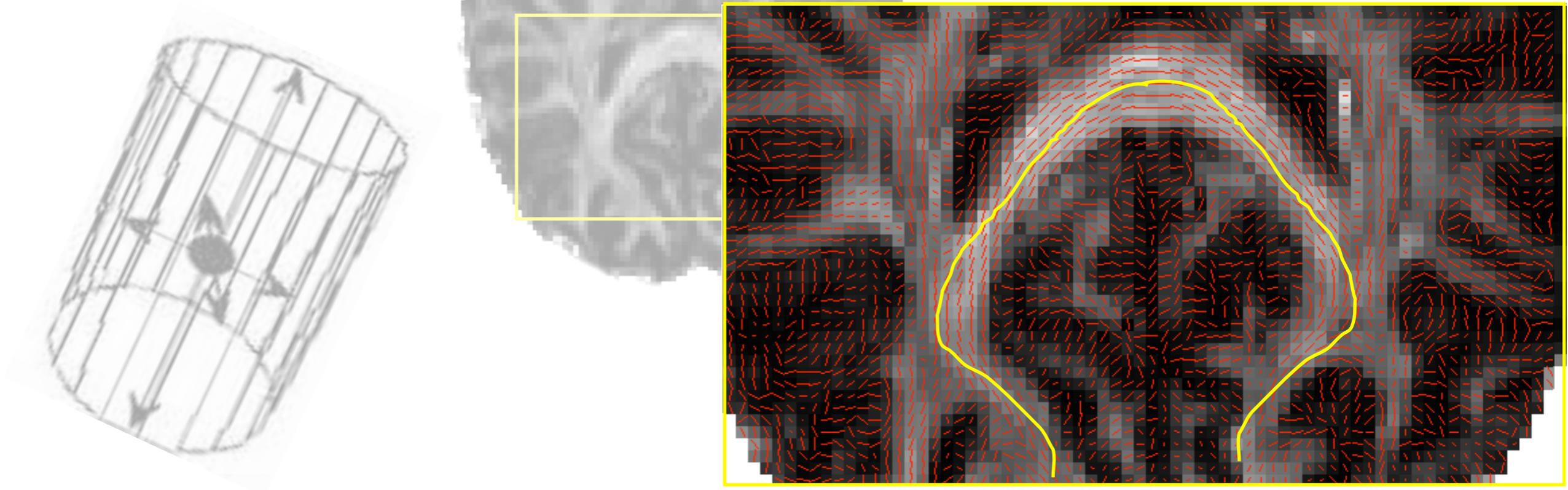


# Investigating human brain connectivity



## Diffusion-weighted MR imaging

- Fractional anisotropy
- Principal diffusion direction



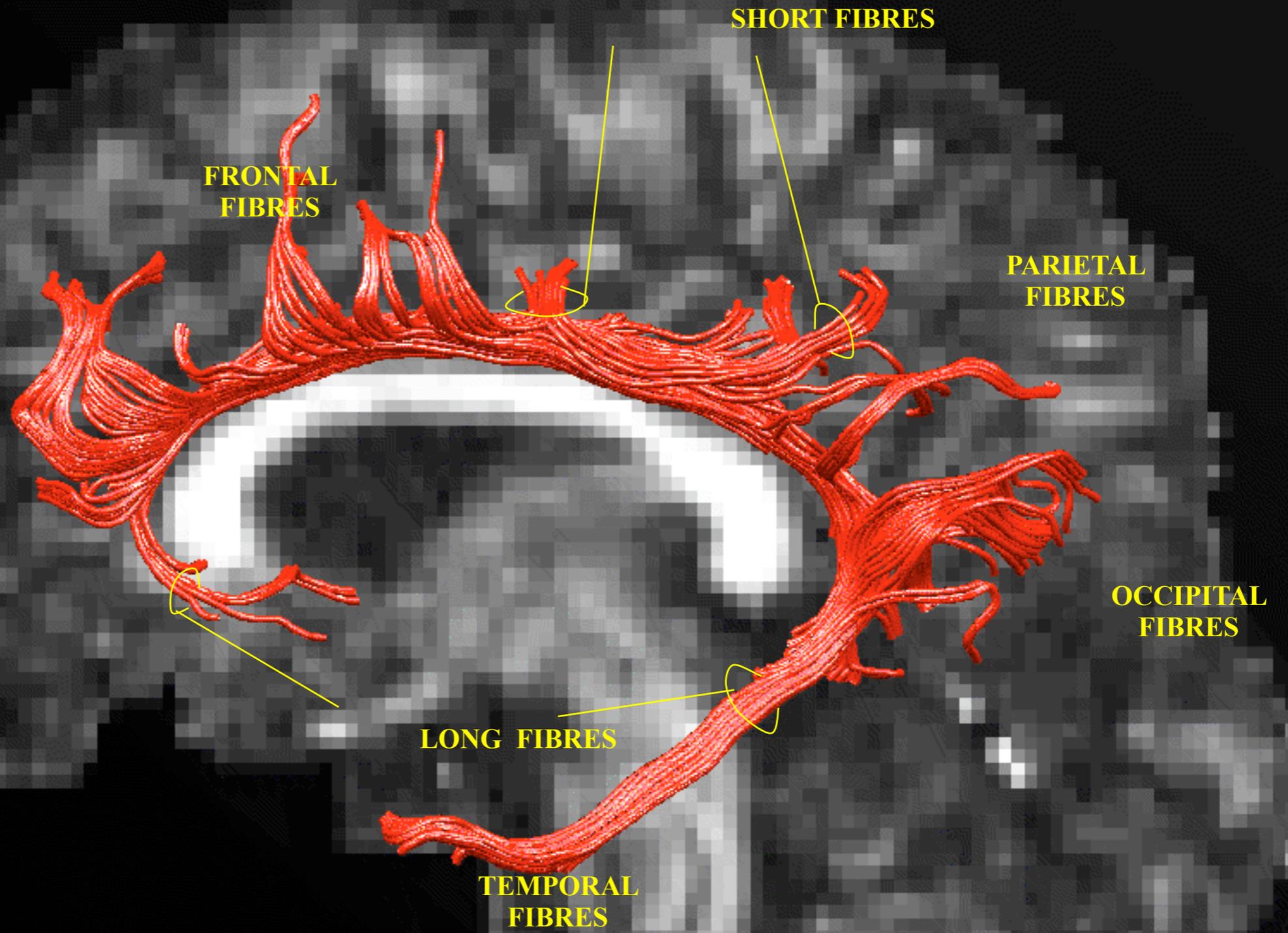


# Streamline tractography can dissect major bundles



**Cingulum**

**Derek Jones**



**Cingulum**

**Derek Jones**



# But elsewhere...Uncertainty in fibre orientation.

Measured from repeated datasets

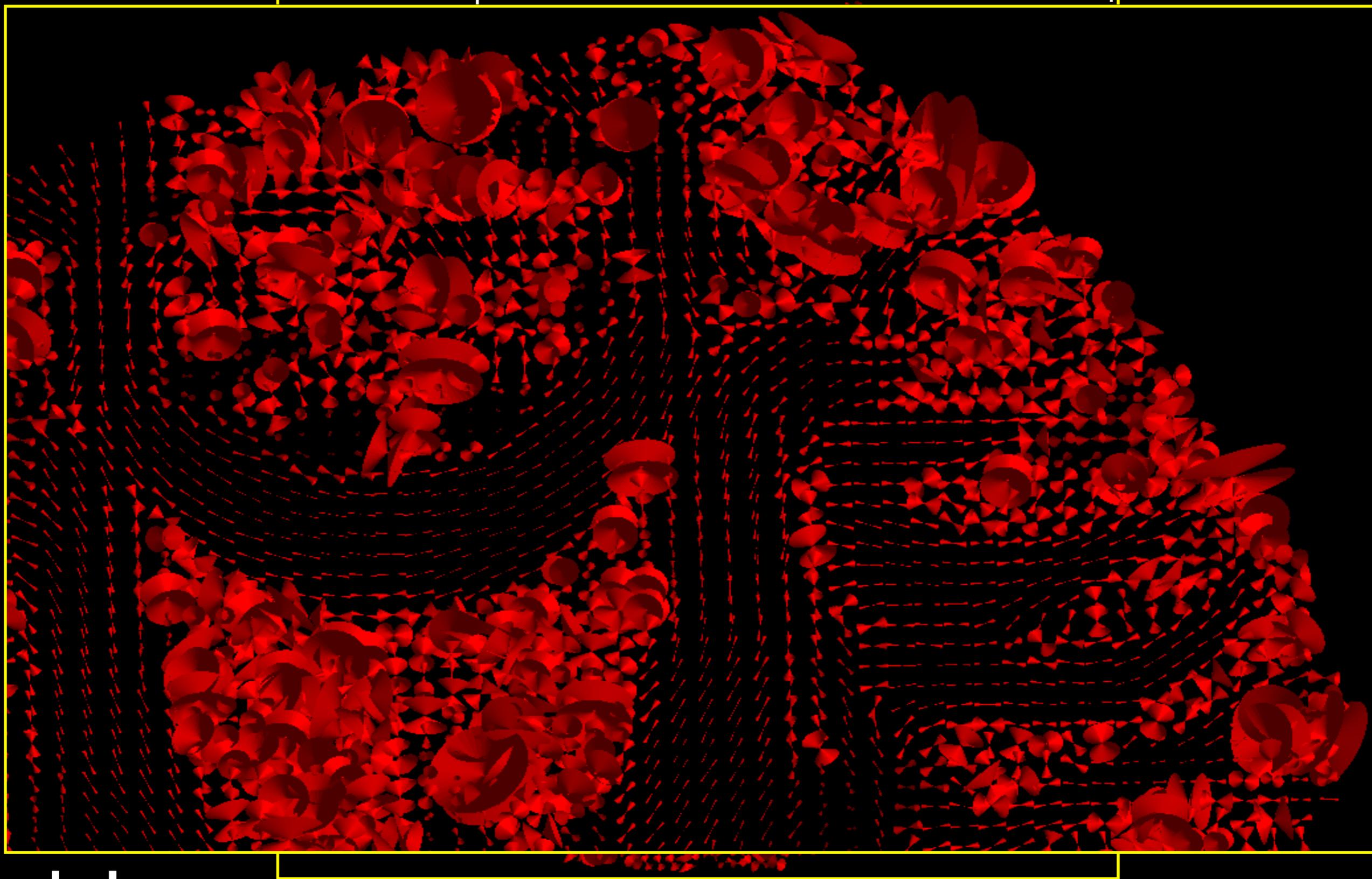


Derek Jones



# But elsewhere...Uncertainty in fibre orientation.

Measured from repeated datasets



Derek Jones



# So what can we do?



# So what can we do?

- Remember ... a long time ago in the world of fMRI ...



# So what can we do?

- Remember ... a long time ago in the world of fMRI ...
- We estimated two things:
  - A cope file (the parameters)
  - A varcope file (uncertainty in these parameters)



# So what can we do?

- Remember ... a long time ago in the world of fMRI ...
- We estimated two things:
  - A cope file (the parameters)
  - A varcope file (uncertainty in these parameters)
- We estimated our parameters, and their uncertainty from a single dataset.

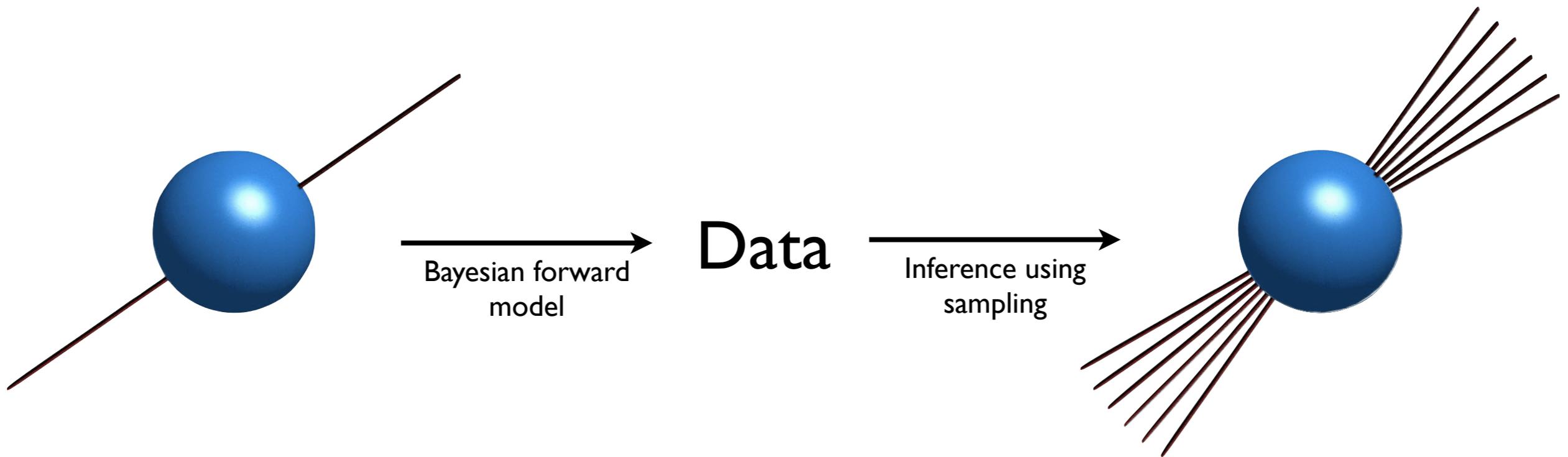


# So what can we do?

- Remember ... a long time ago in the world of fMRI ...
- We estimated two things:
  - A cope file (the parameters)
  - A varcope file (uncertainty in these parameters)
- We estimated our parameters, and their uncertainty from a single dataset.
- Can we do a similar thing with Diffusion parameters?



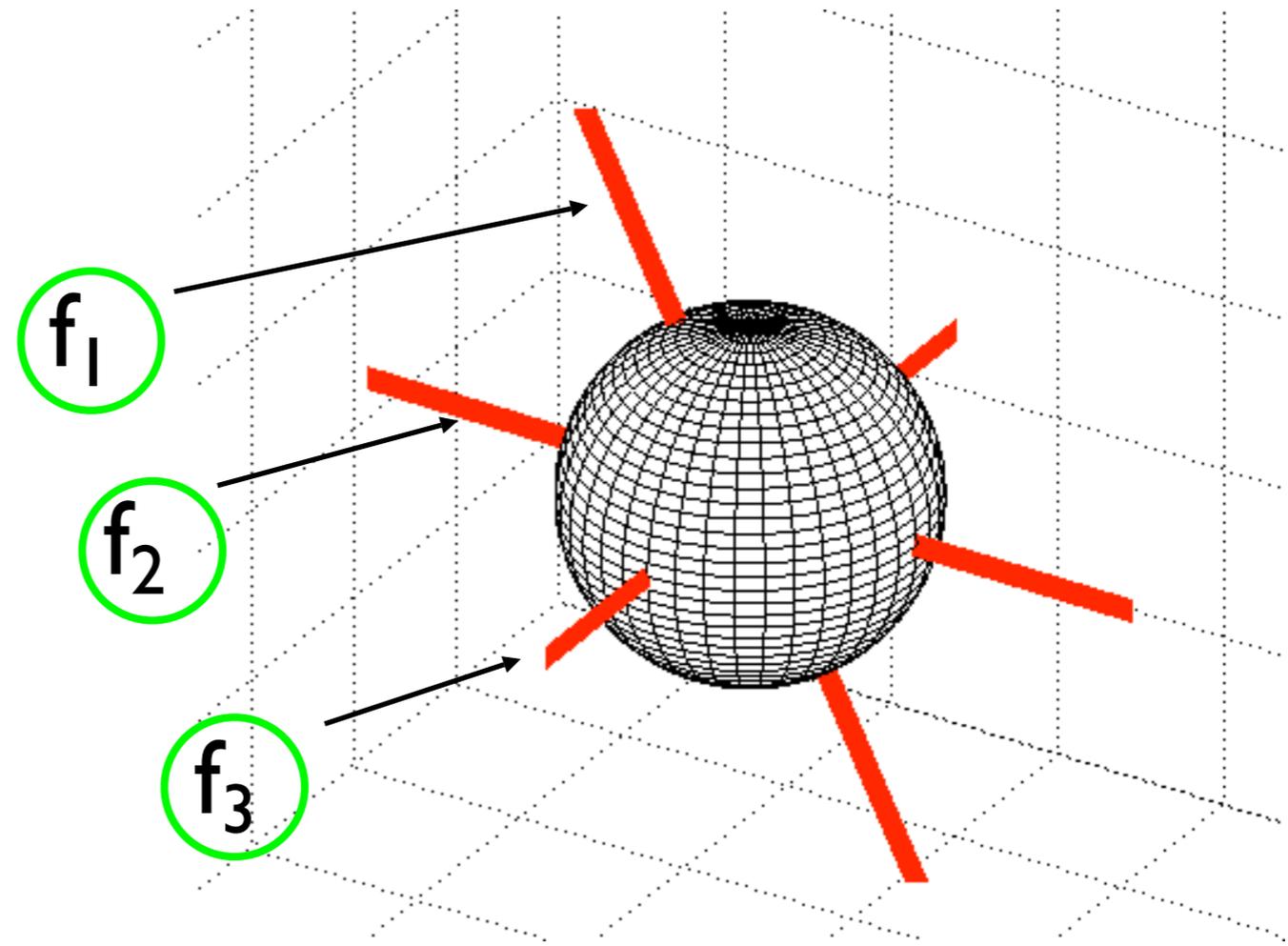
# Diffusion Model in FDT tractography



- \* FDT tractography uses a simple model of local diffusion
  - o A single anisotropic direction with isotropic background diffusion
- \* Reasons:
  - o No ambiguity between ADC profile and uncertainty
  - o Avoid errors due to sorting eigenvectors in DTI
  - o Simplifies extensions to multiple fibre orientations



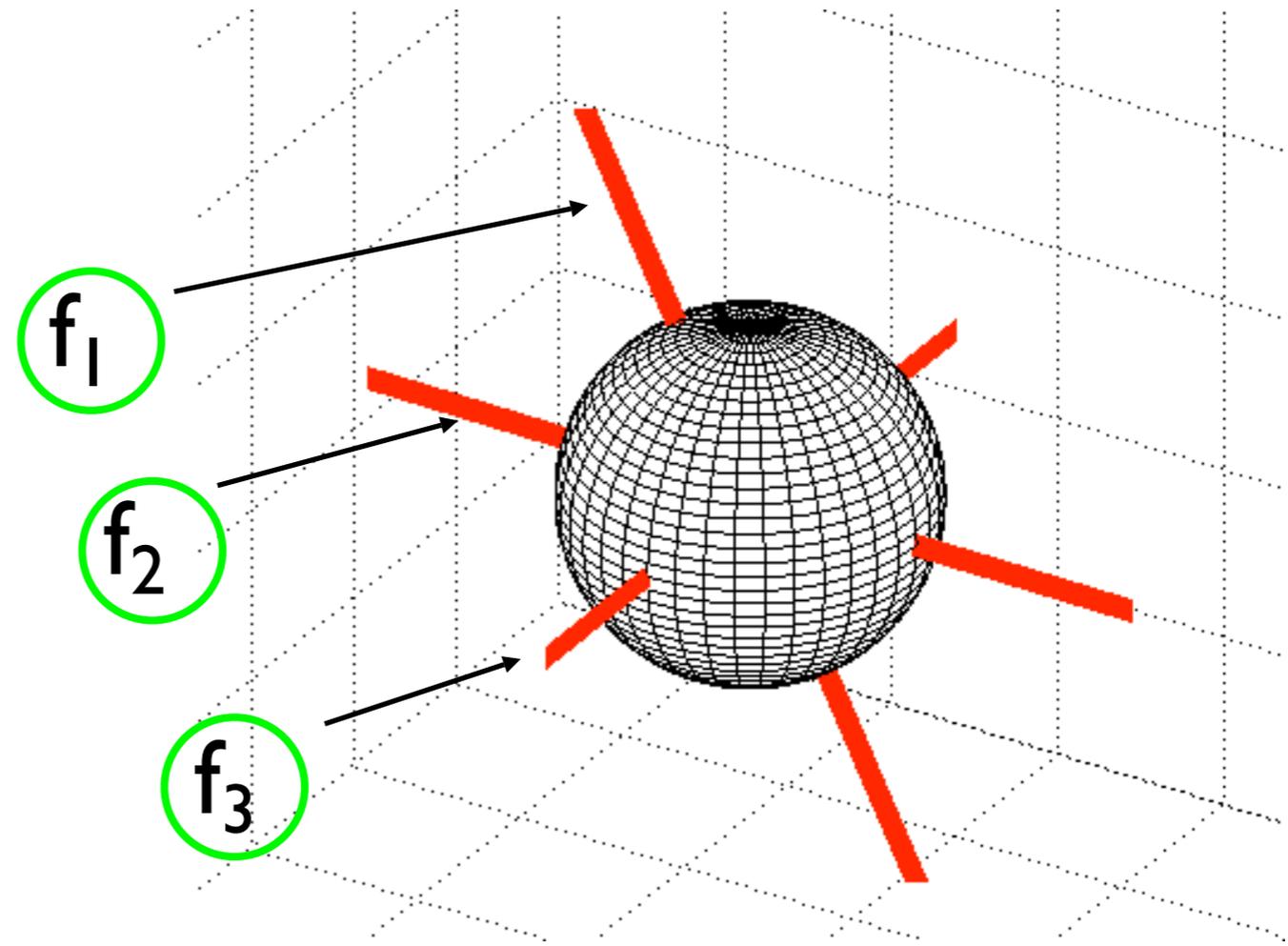
# Modelling complex architecture





# Modelling complex architecture

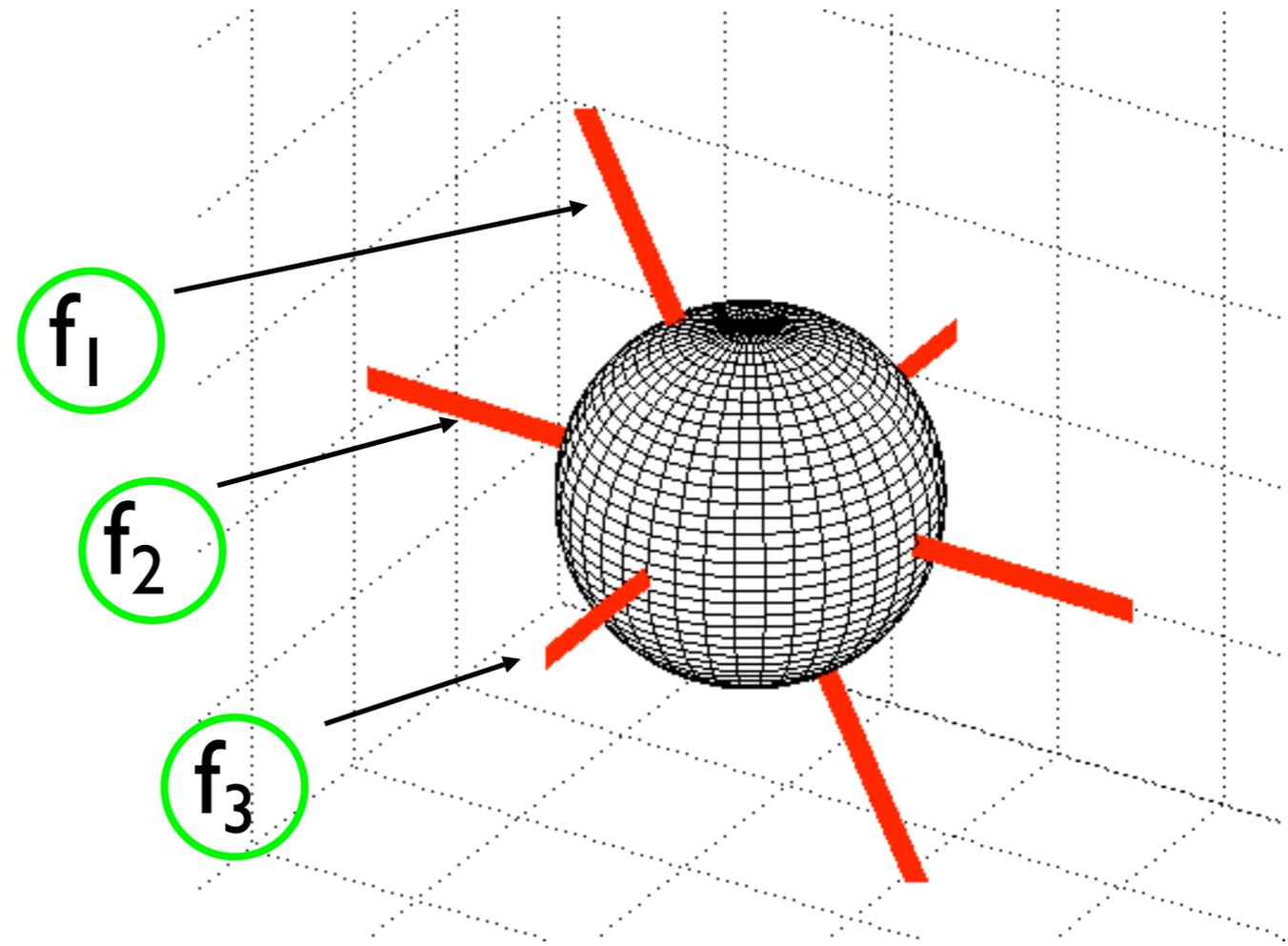
- Form testable hypotheses.
- Ask questions about parameters of interest





# Modelling complex architecture

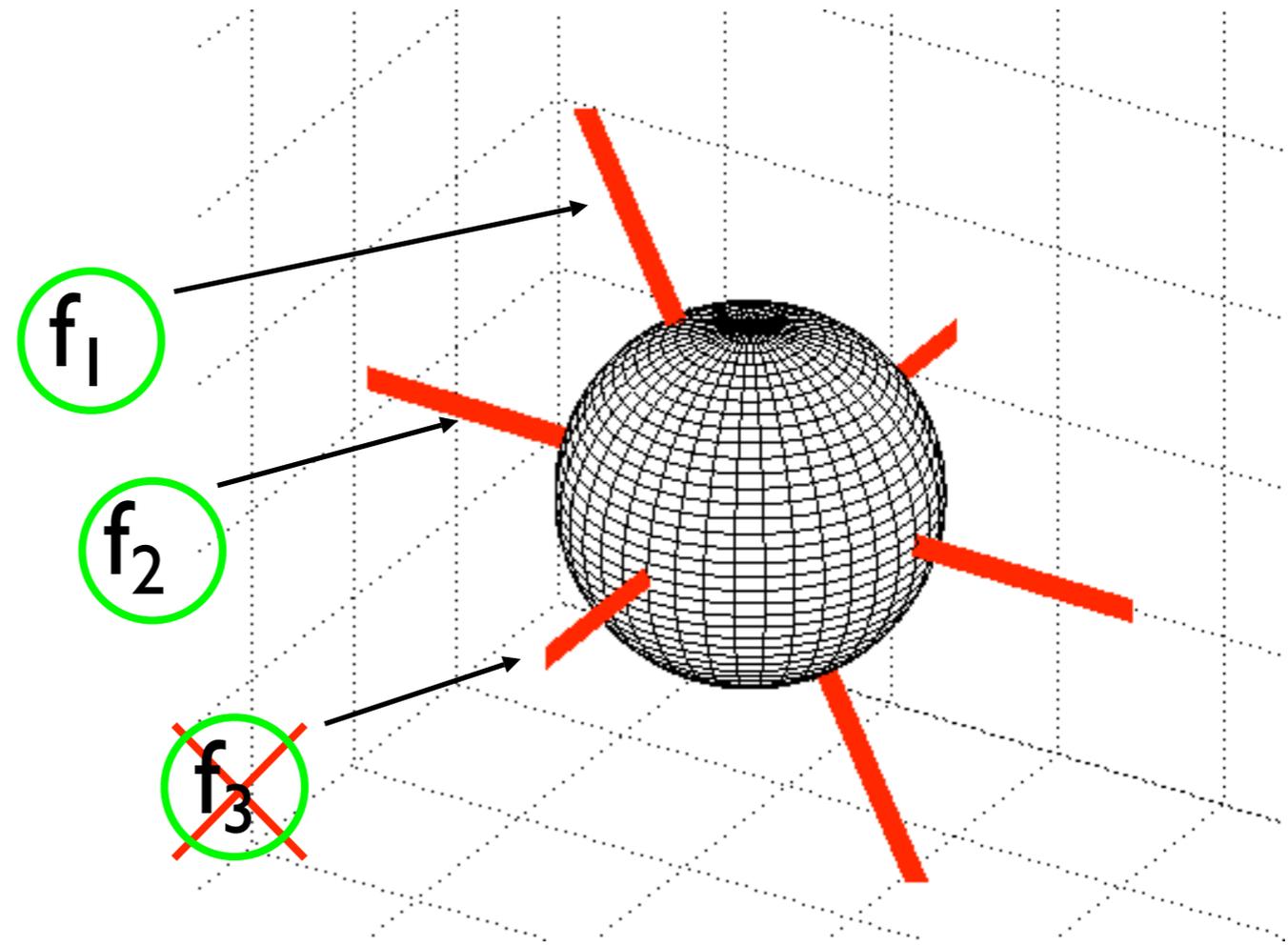
- Form testable hypotheses.
- Ask questions about parameters of interest
- Extra sensitivity gained from assumptions





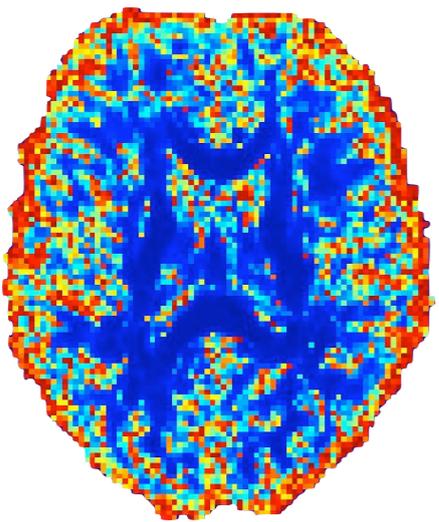
# Modelling complex architecture

- Form testable hypotheses.
- Ask questions about parameters of interest
- Extra sensitivity gained from assumptions
- Only estimate complexity that is supported by the data

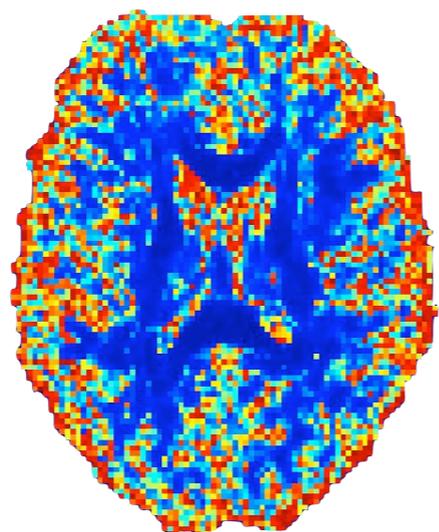




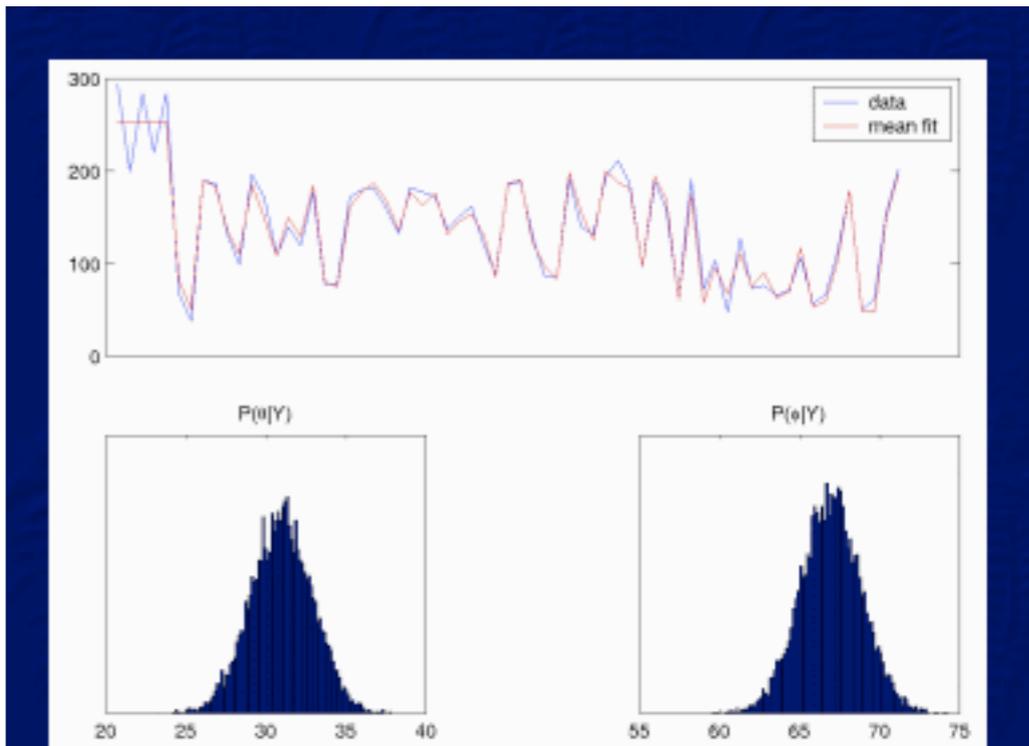
# Uncertainty from a single dataset



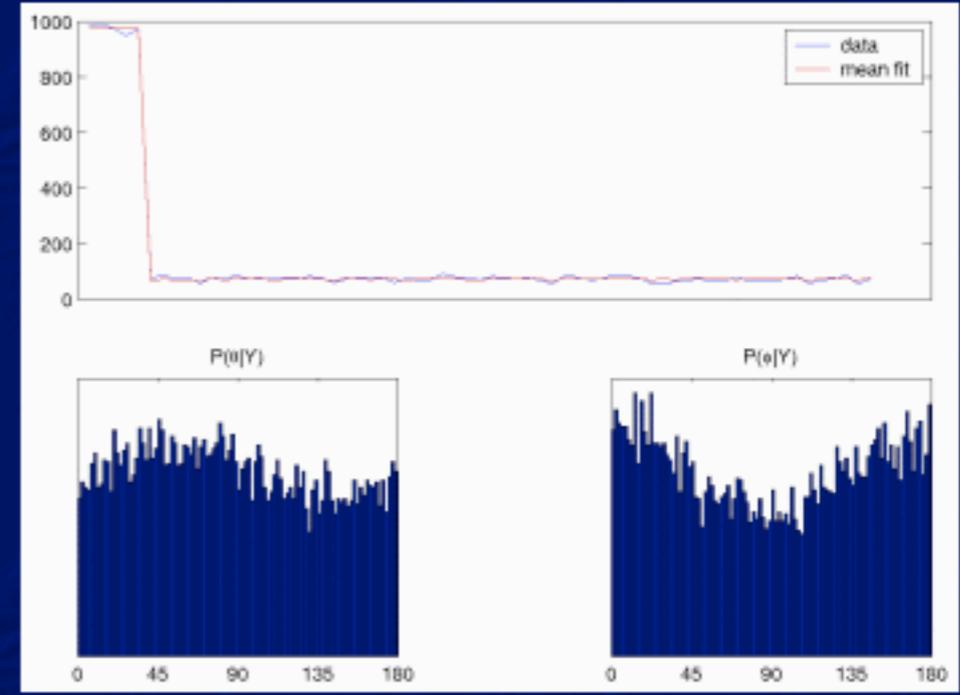
Empirical



Bayesian



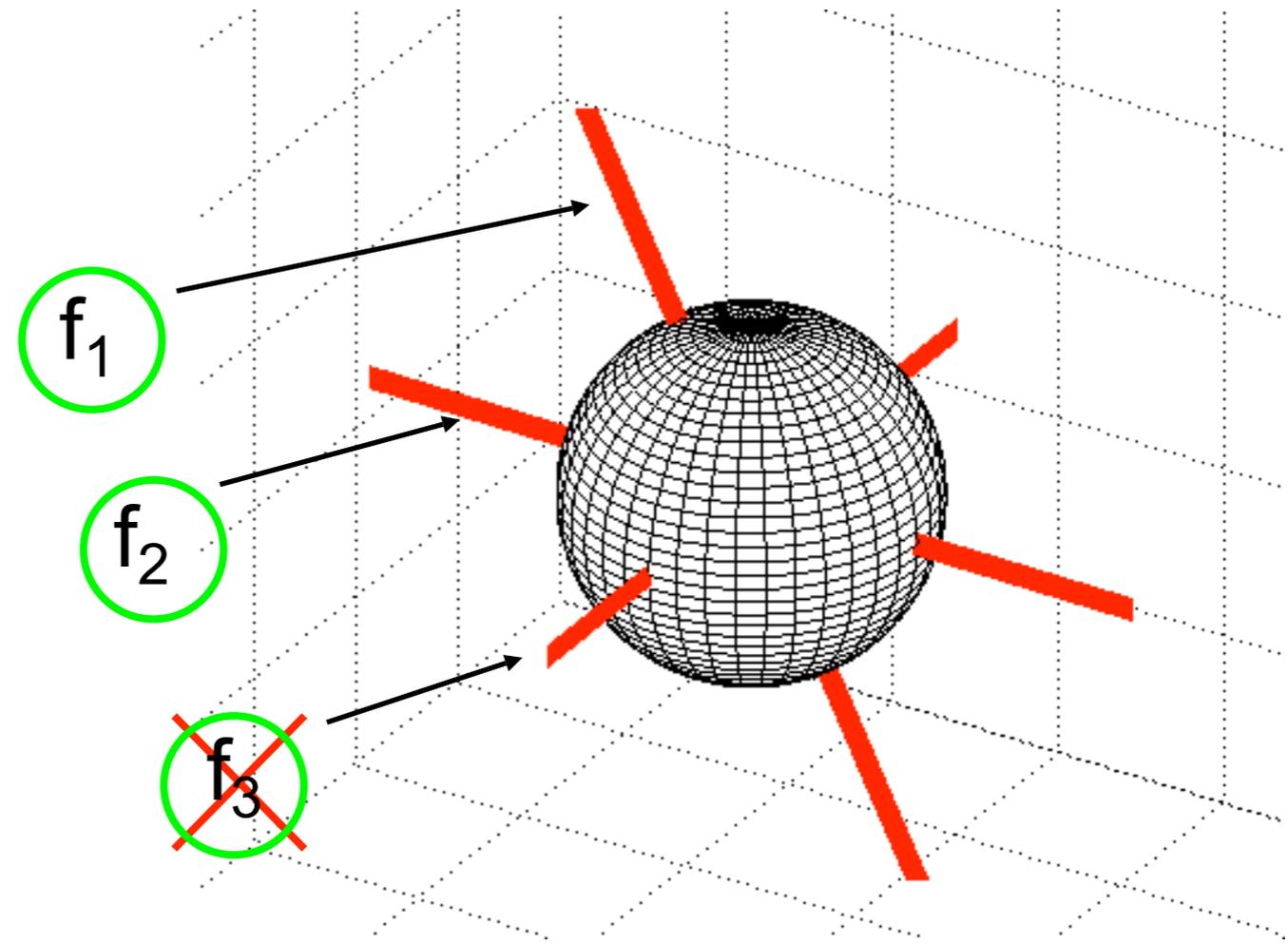
White Matter Voxel

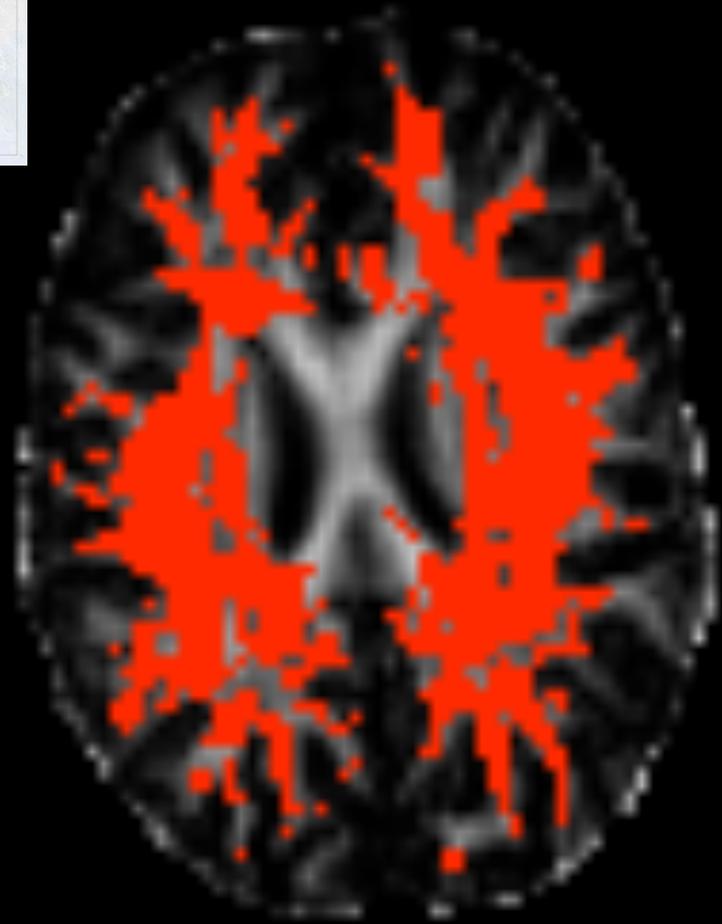


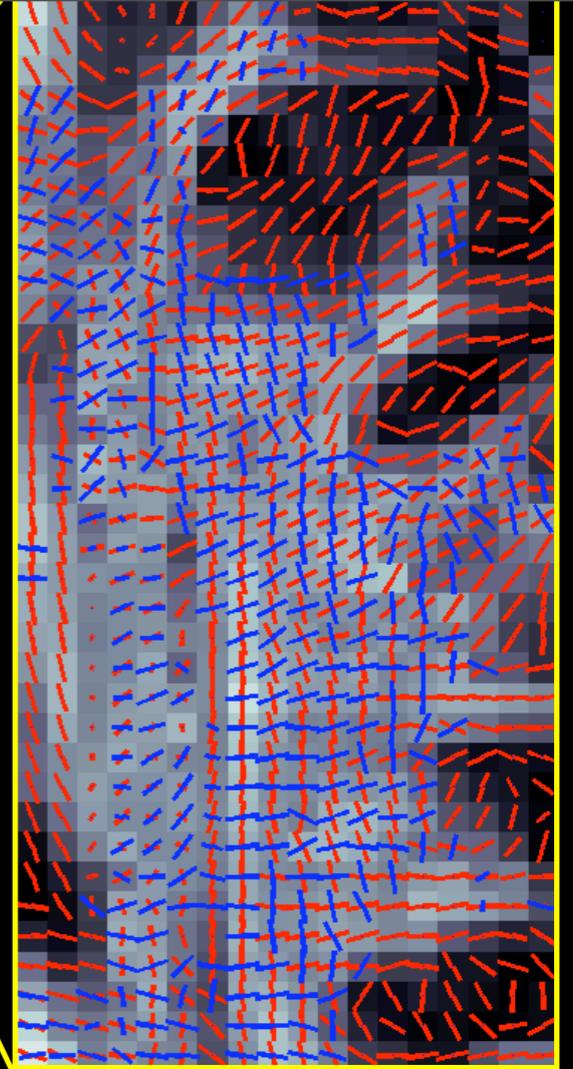
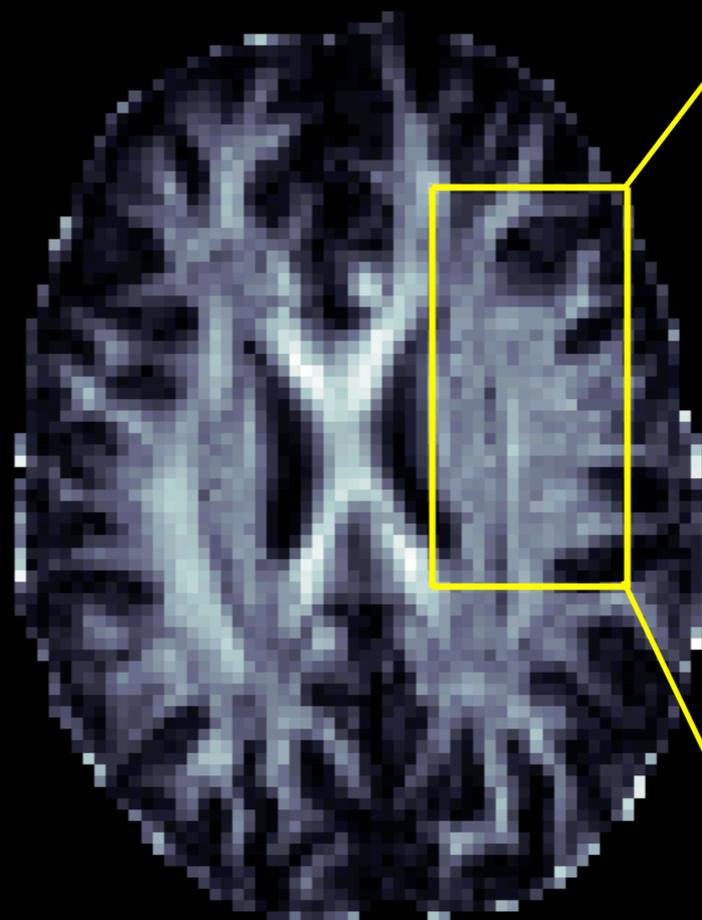
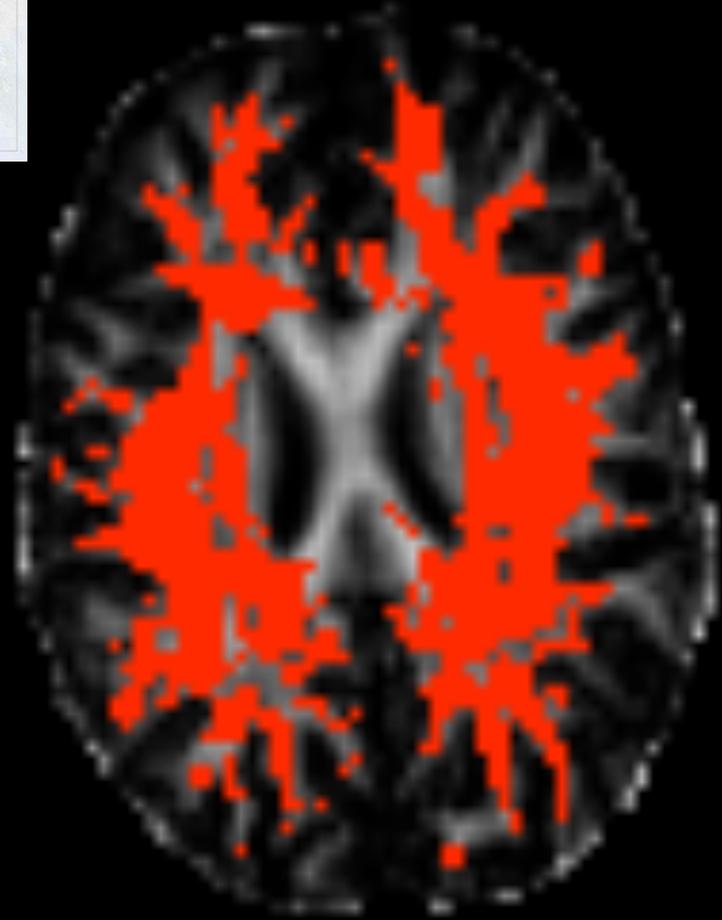
CSF Voxel

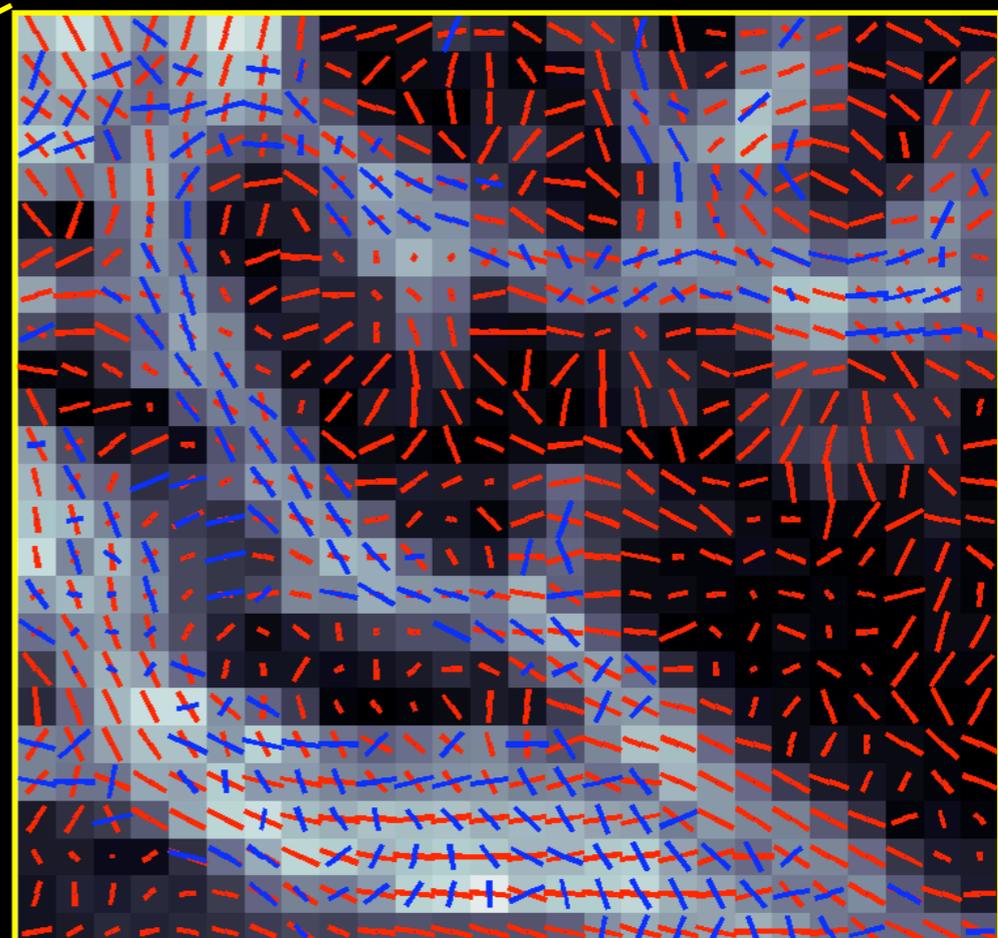
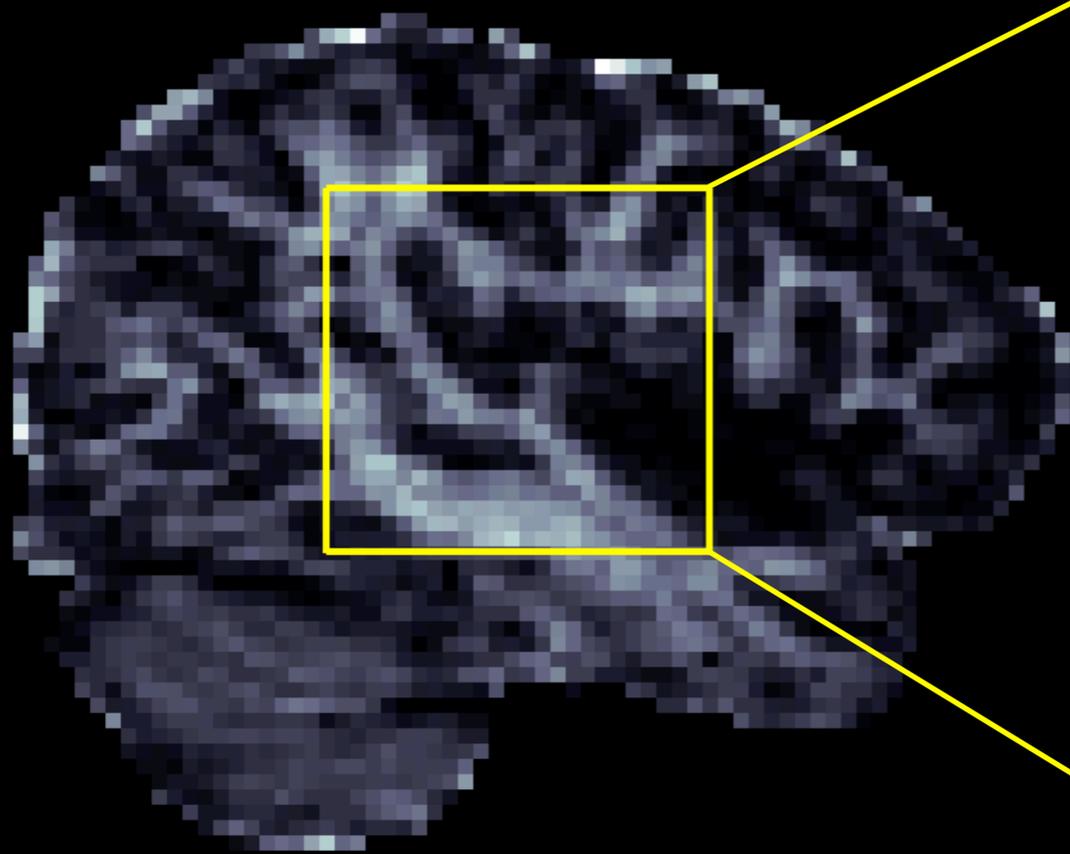
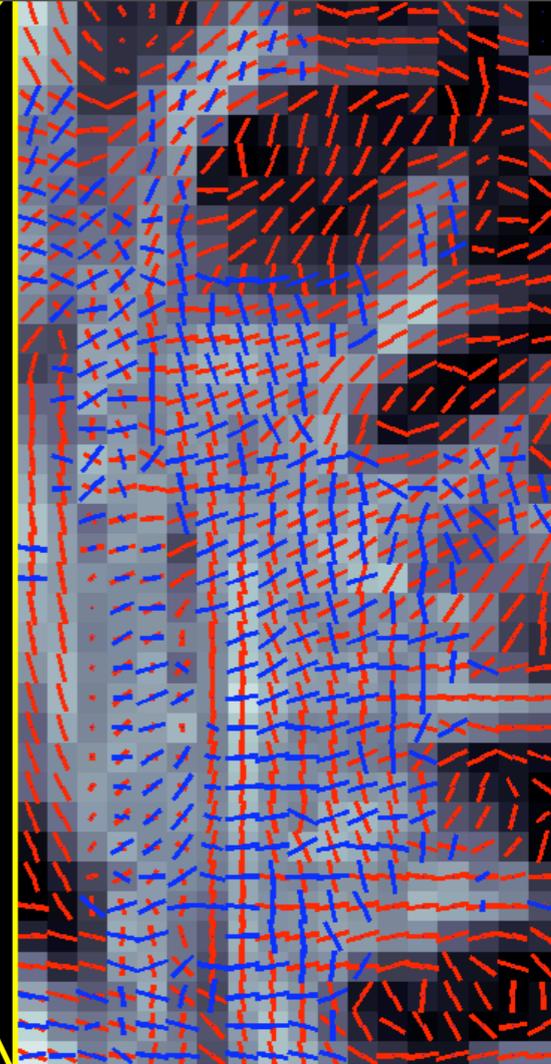
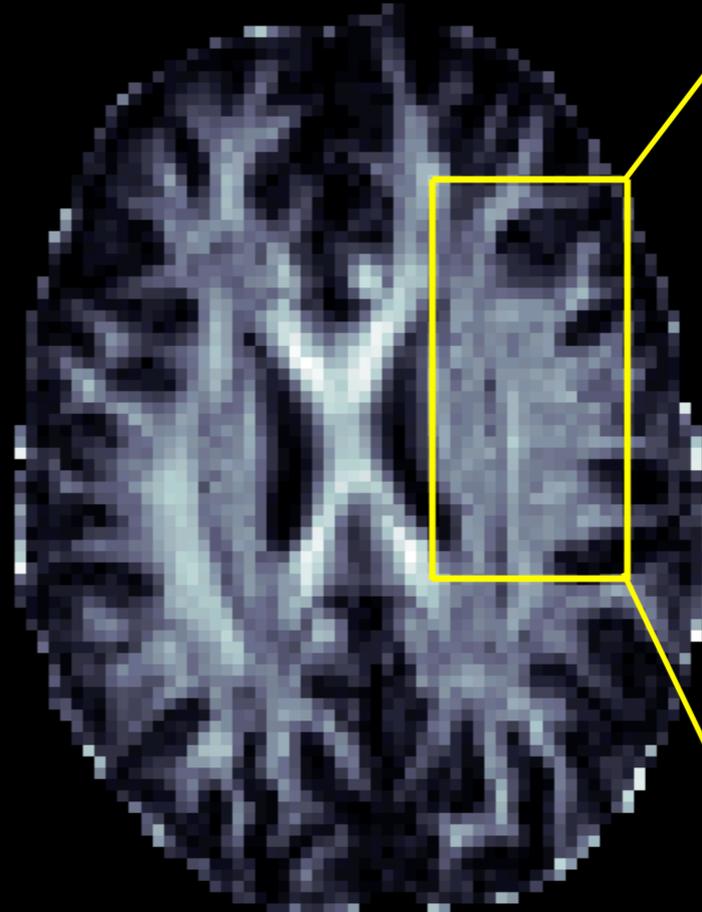
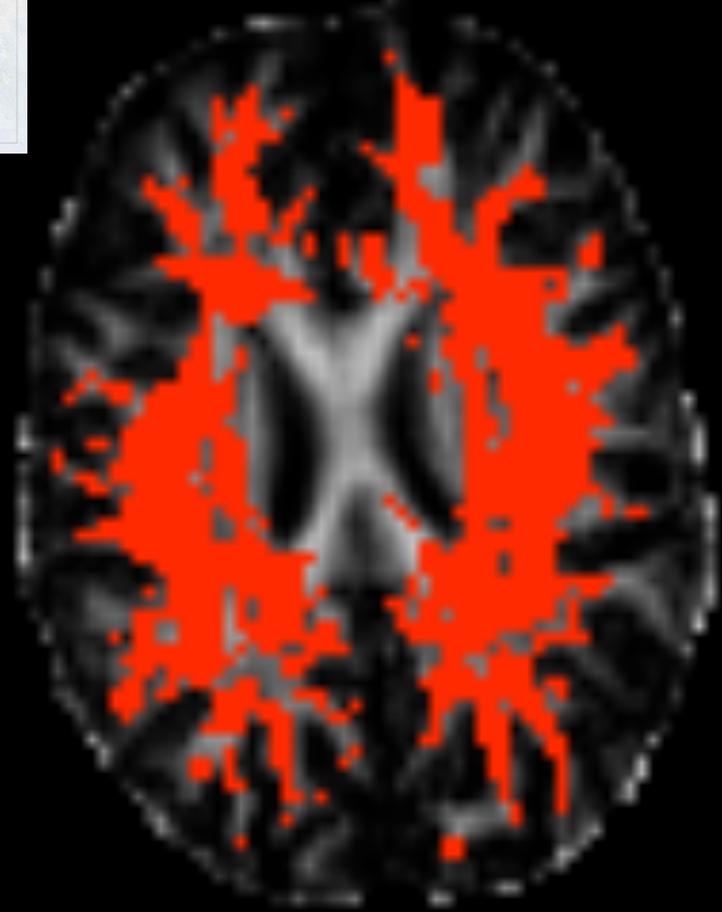
# Modelling complex architecture

- Form testable hypotheses.
  - Ask questions about parameters of interest
- Extra sensitivity gained from assumptions
- Only estimate complexity that is supported by the data





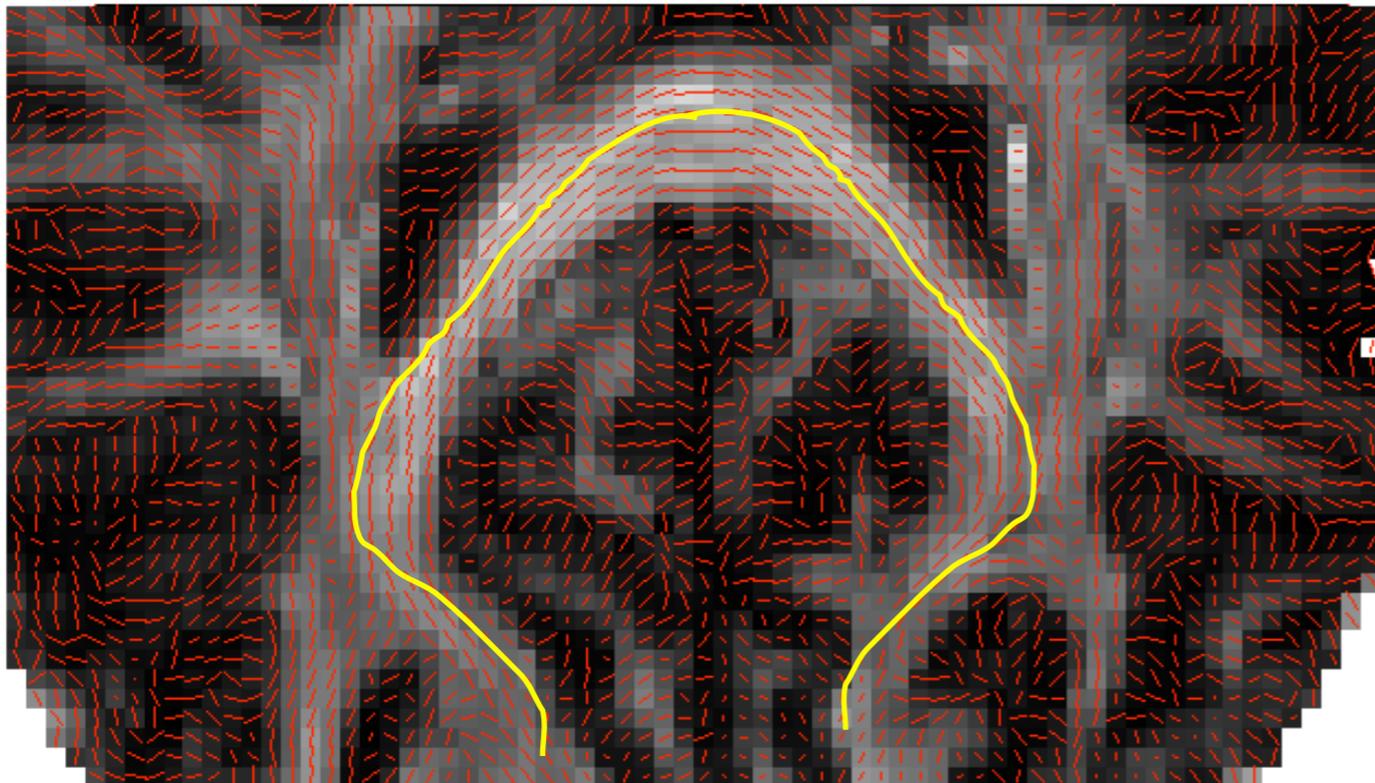




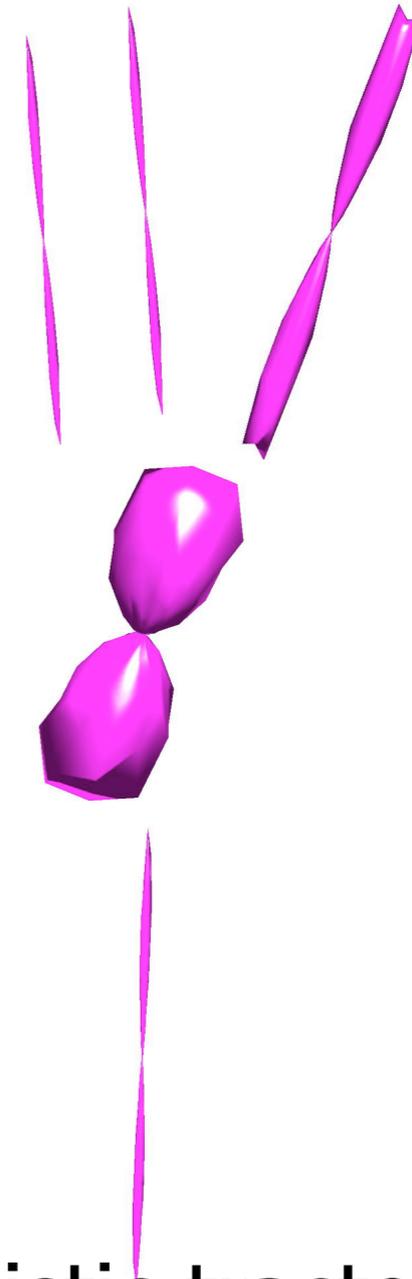


# Probabilistic tractography

- But now, we no longer have a single direction at each voxel. How can we do tractography?



'Streamlining'



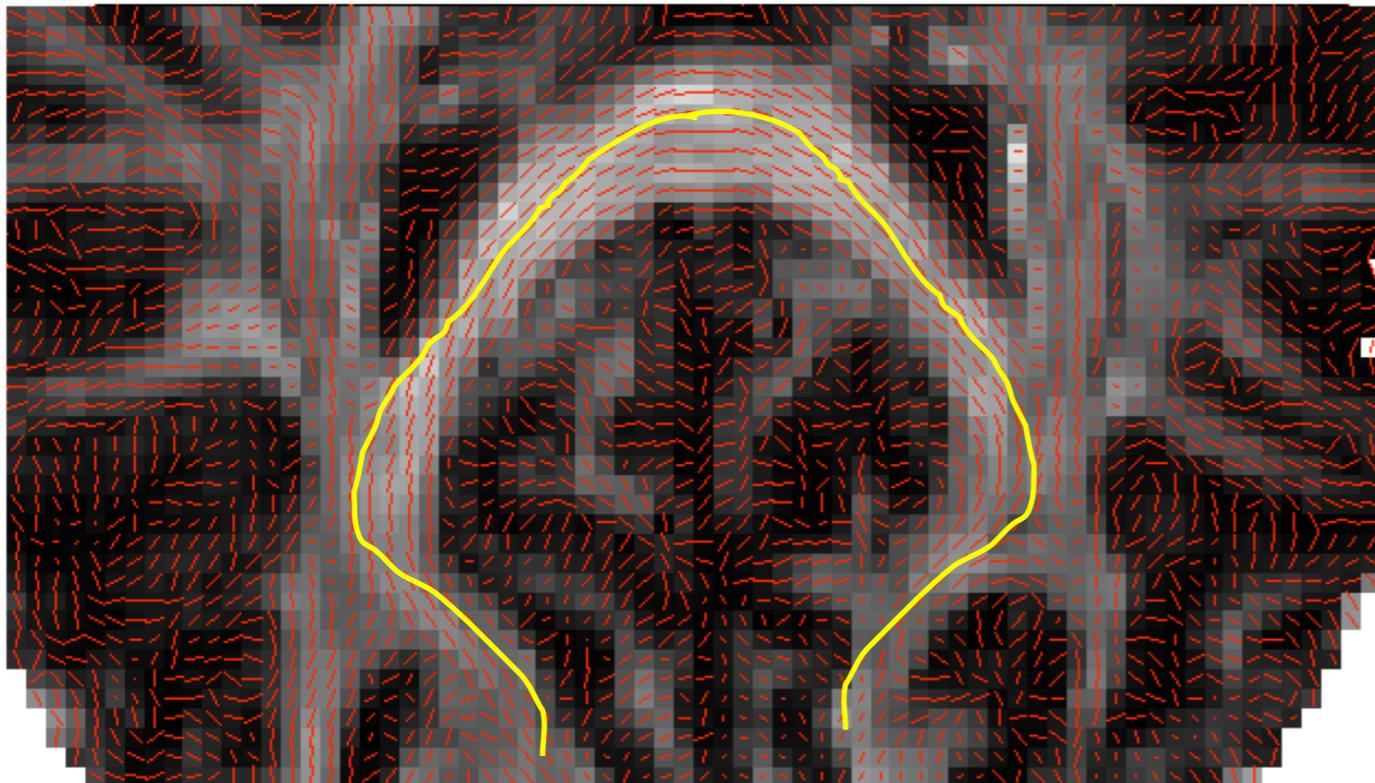
Probabilistic tractography

Behrens et al, 2003, Parker et al. 2003,  
Hagmann et al 2003, Jones et al. 2004

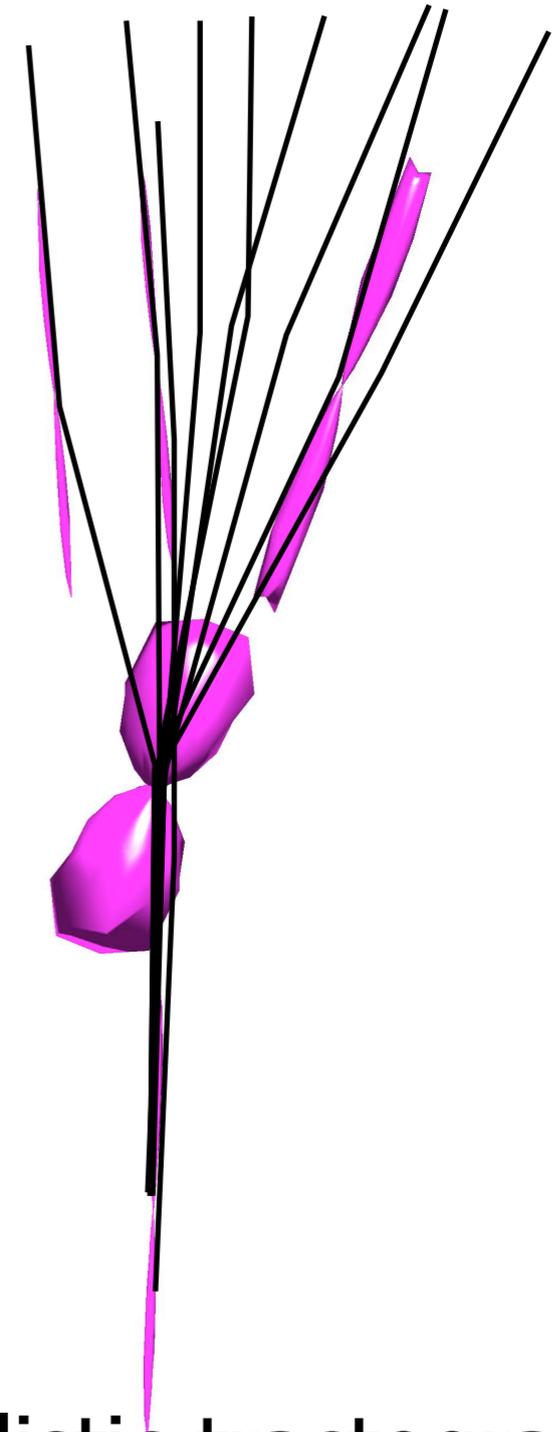


# Probabilistic tractography

- But now, we no longer have a single direction at each voxel. How can we do tractography?



'Streamlining'

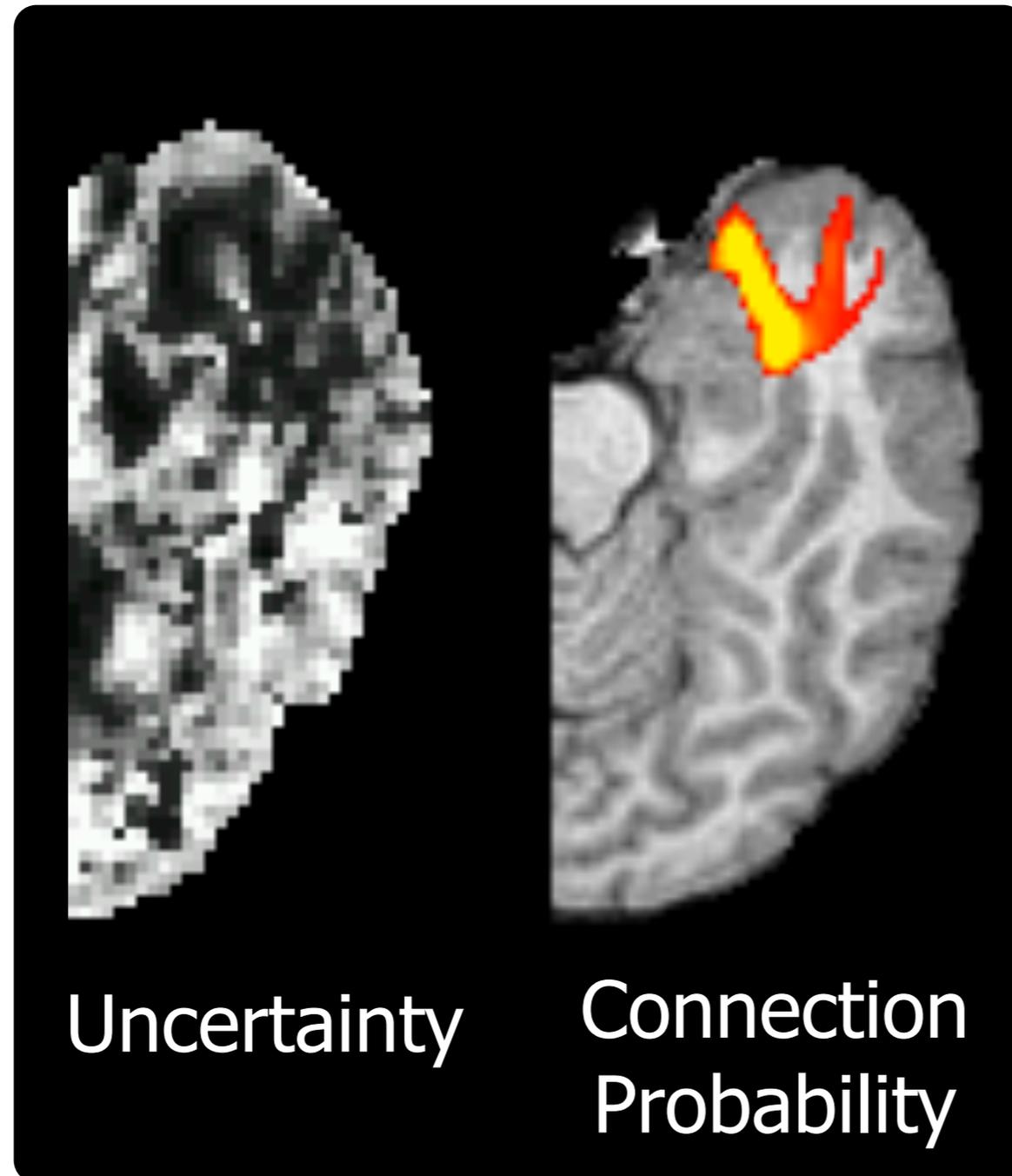
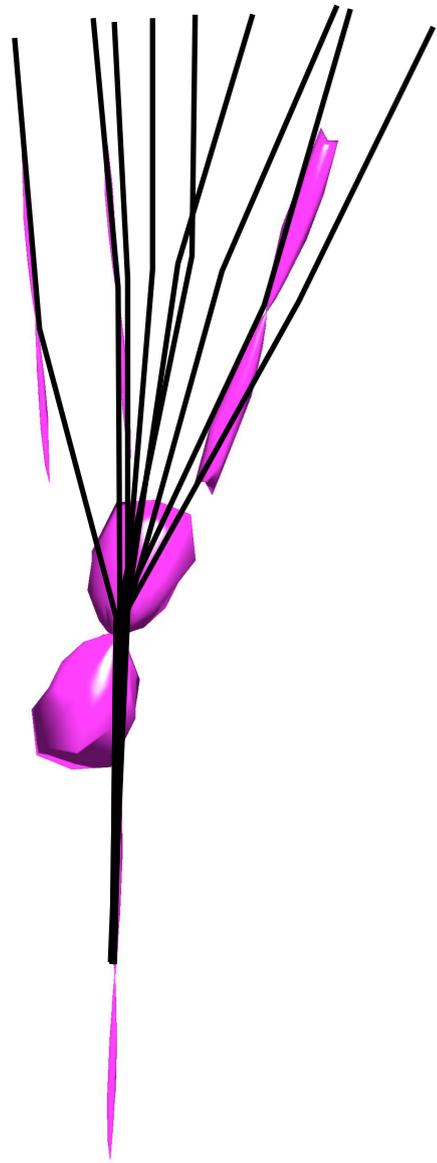


Probabilistic tractography

Behrens et al, 2003, Parker et al. 2003,  
Hagmann et al 2003, Jones et al. 2004



# Probabilistic Tractography

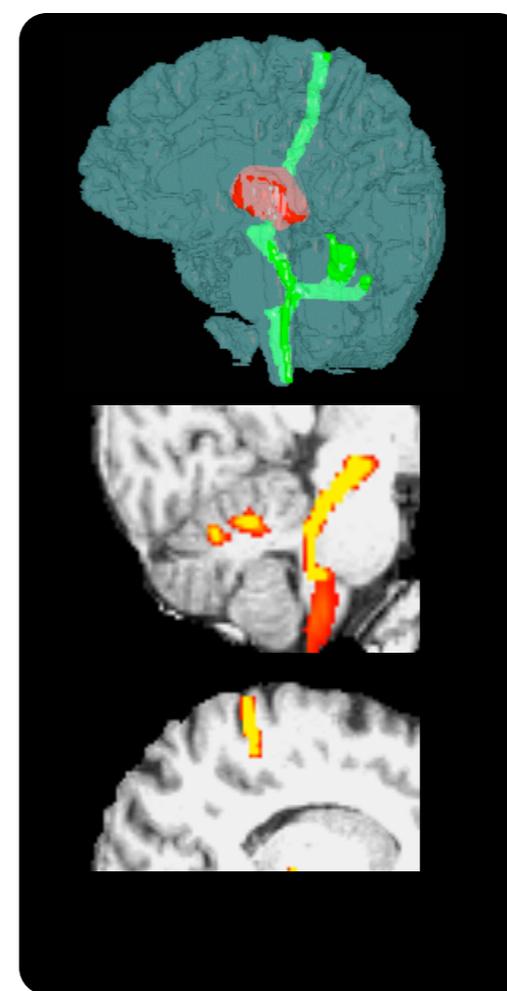
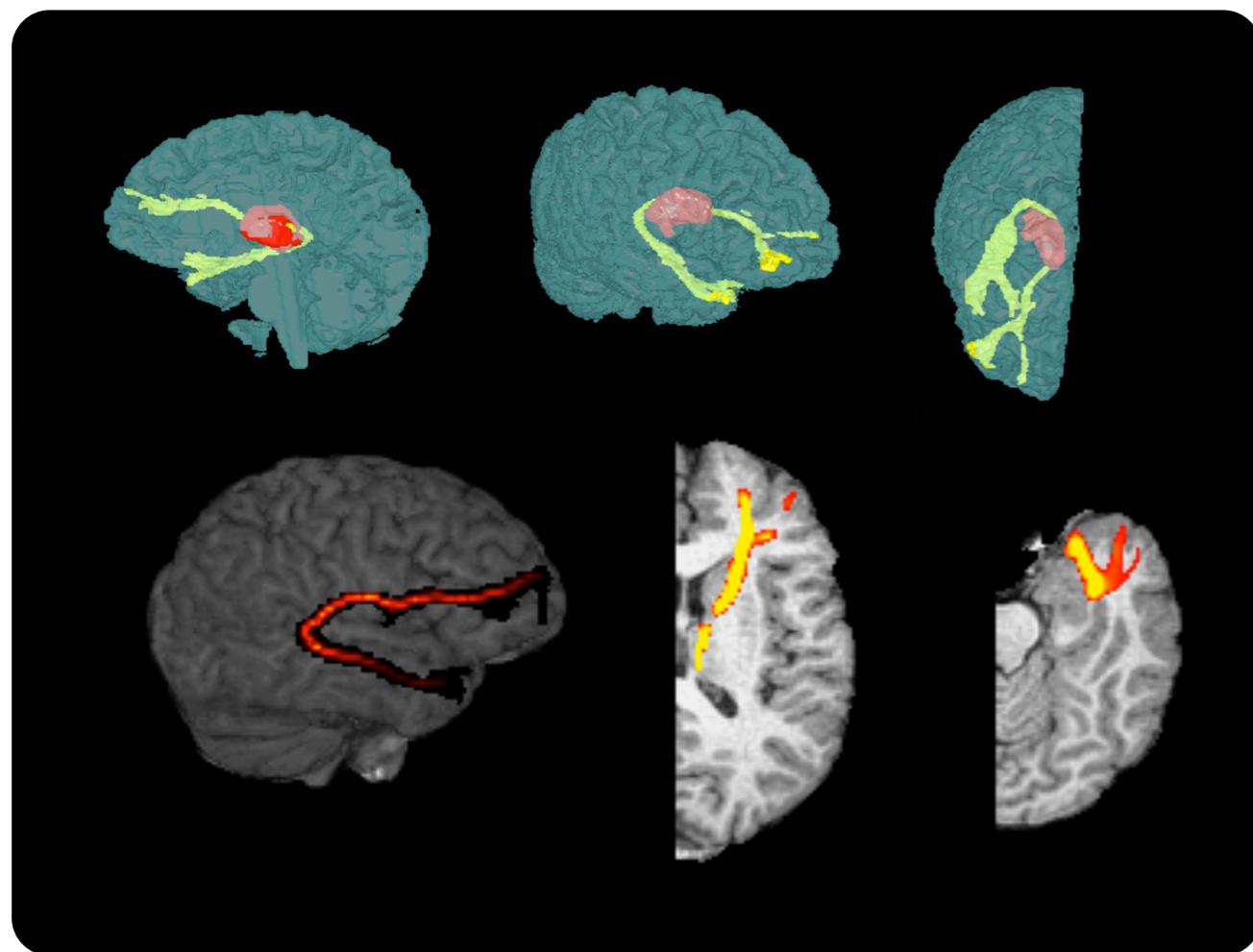
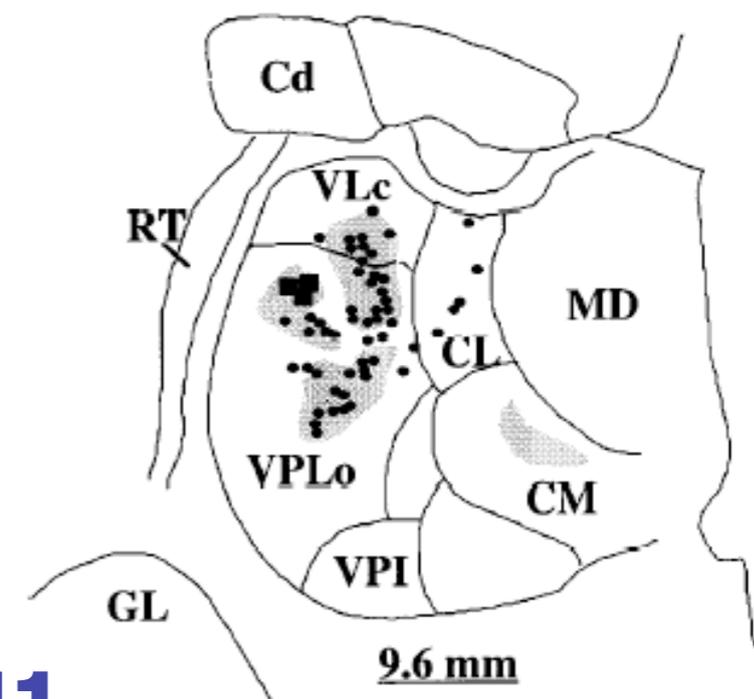


- Allows you to track into regions of low anisotropy, eg **grey matter**
- Provides **quantitative (see later)** probability of connection from A to B

# Thalamic connections with cortex

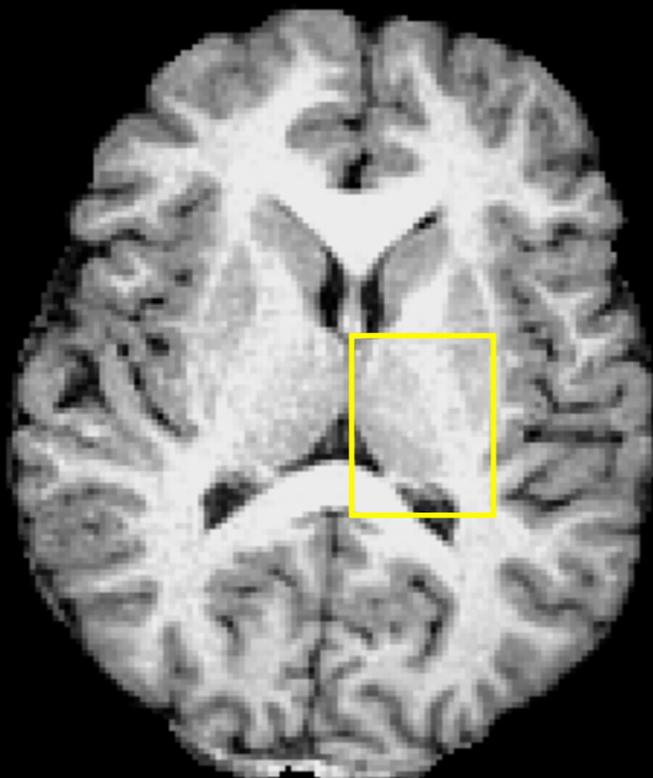
**MD -> PFC**

**VL -> M1**





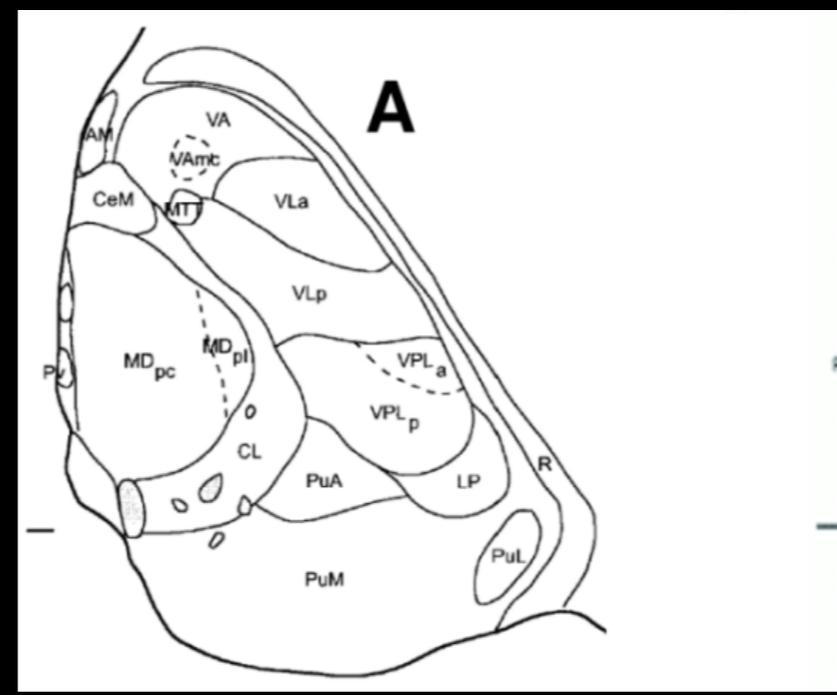
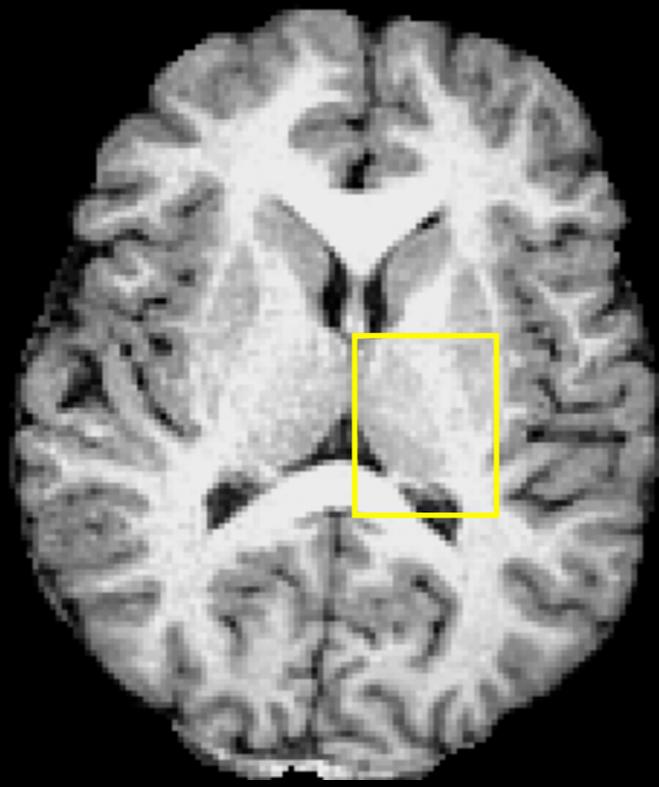
# Connectivity-based classification of thalamic voxels produces clusters



Behrens, Johansen-Berg et al, Nature Neuroscience, 2003

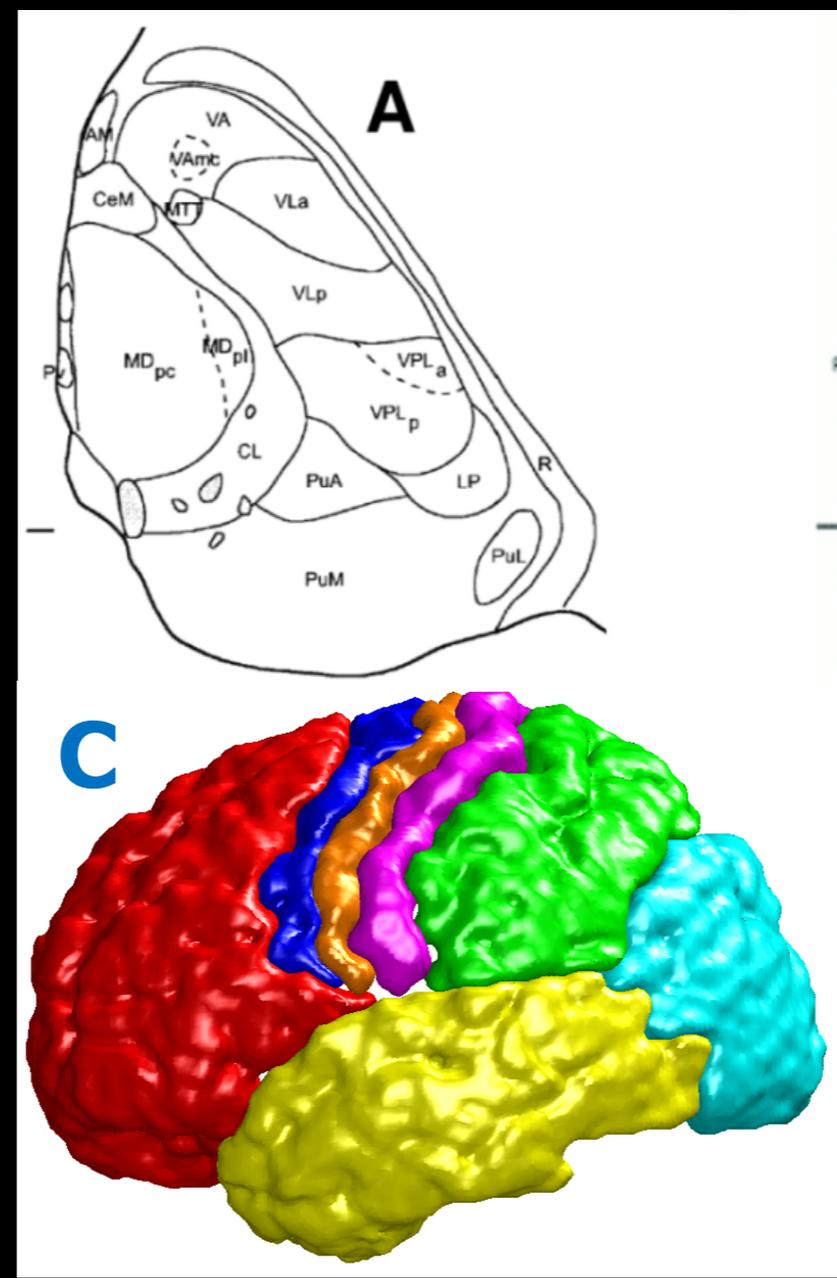
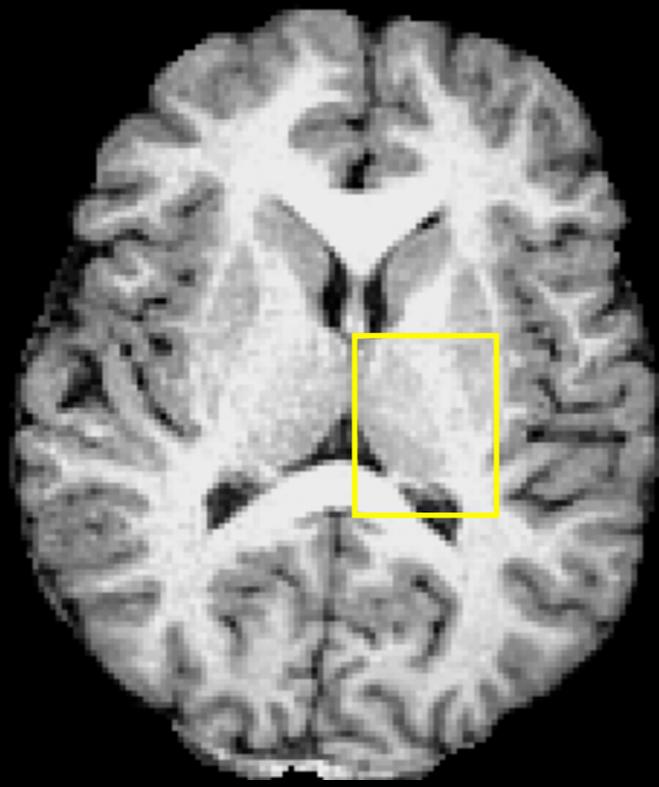


# Connectivity-based classification of thalamic voxels produces clusters



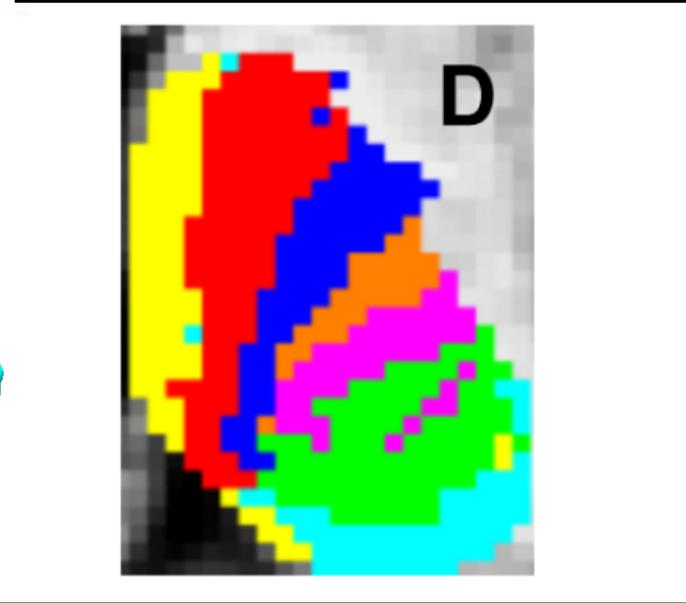
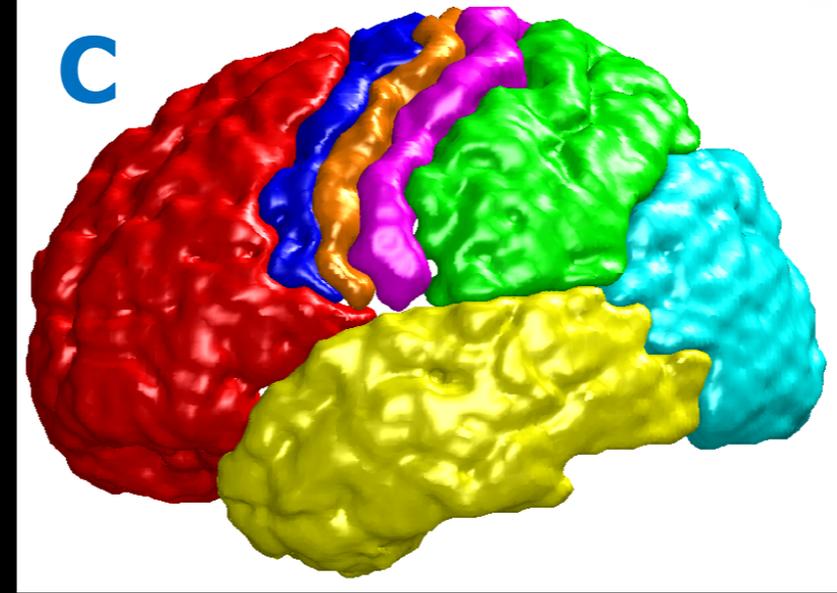
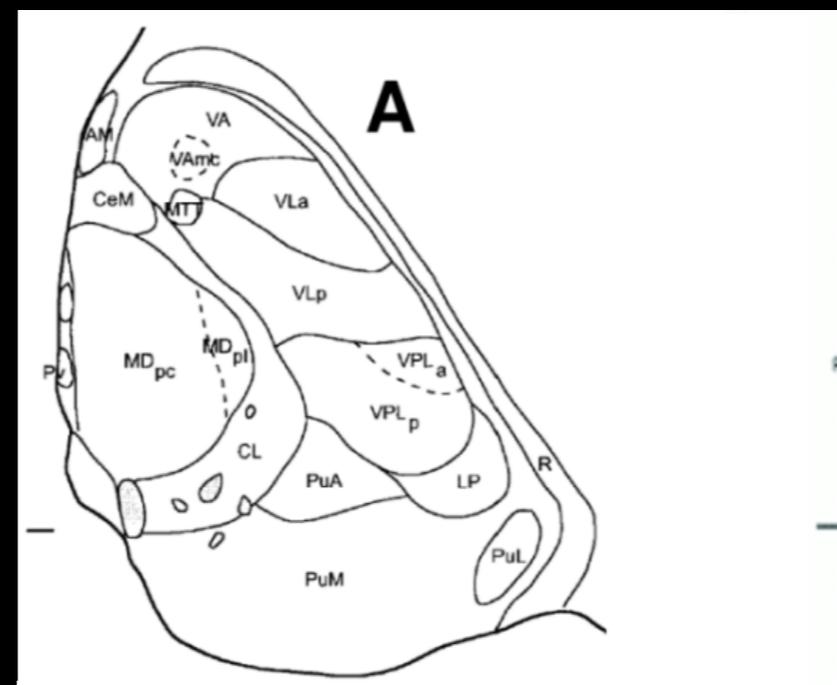
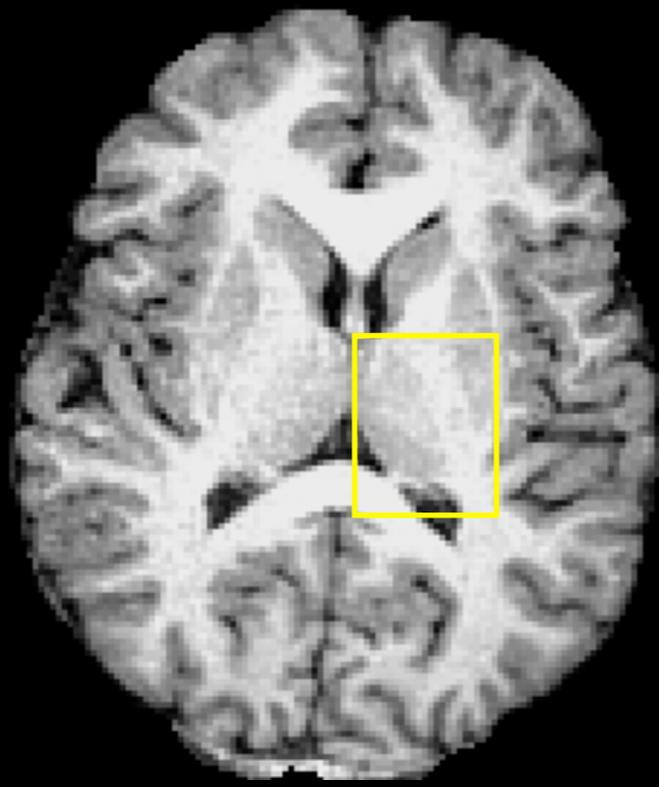


# Connectivity-based classification of thalamic voxels produces clusters



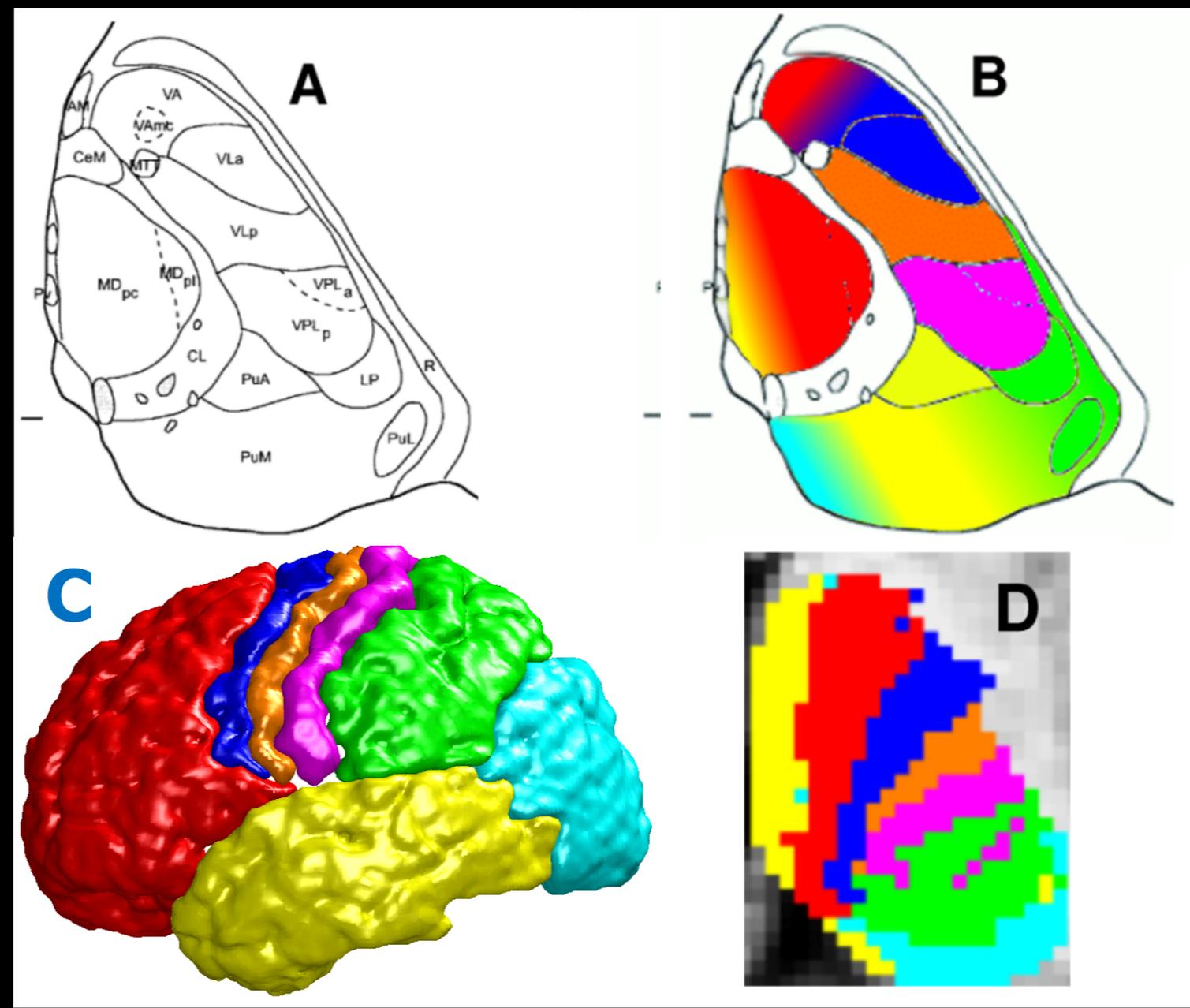
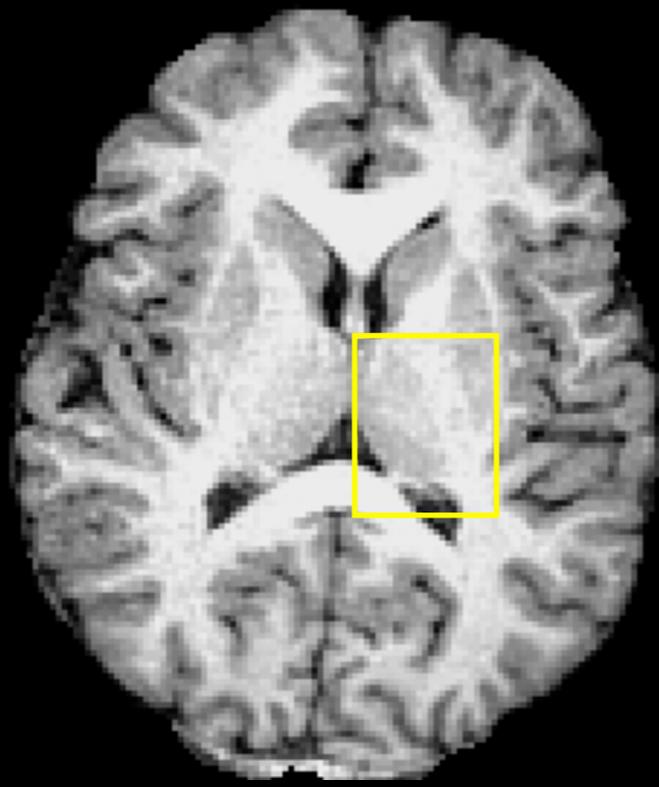


# Connectivity-based classification of thalamic voxels produces clusters



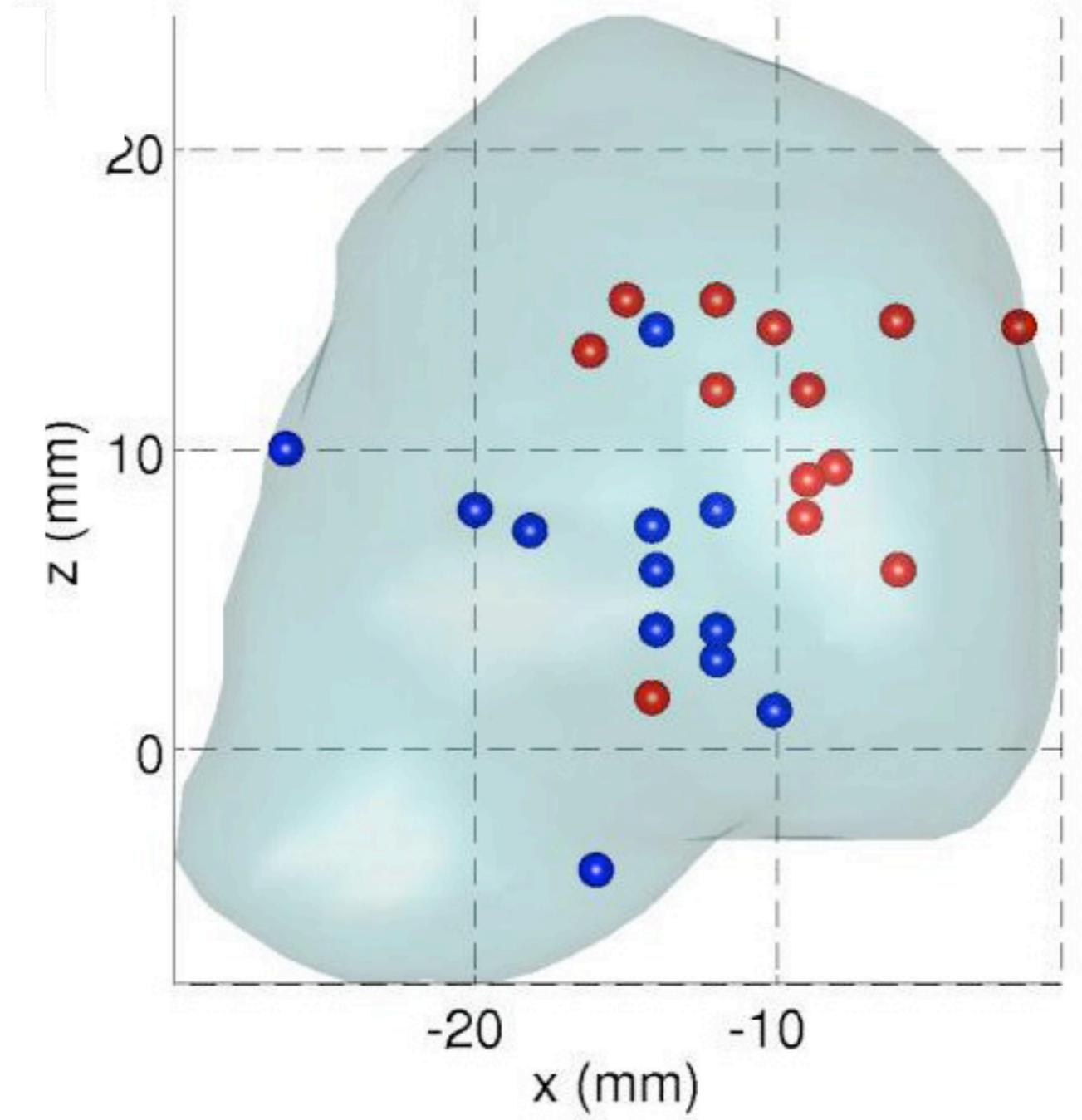
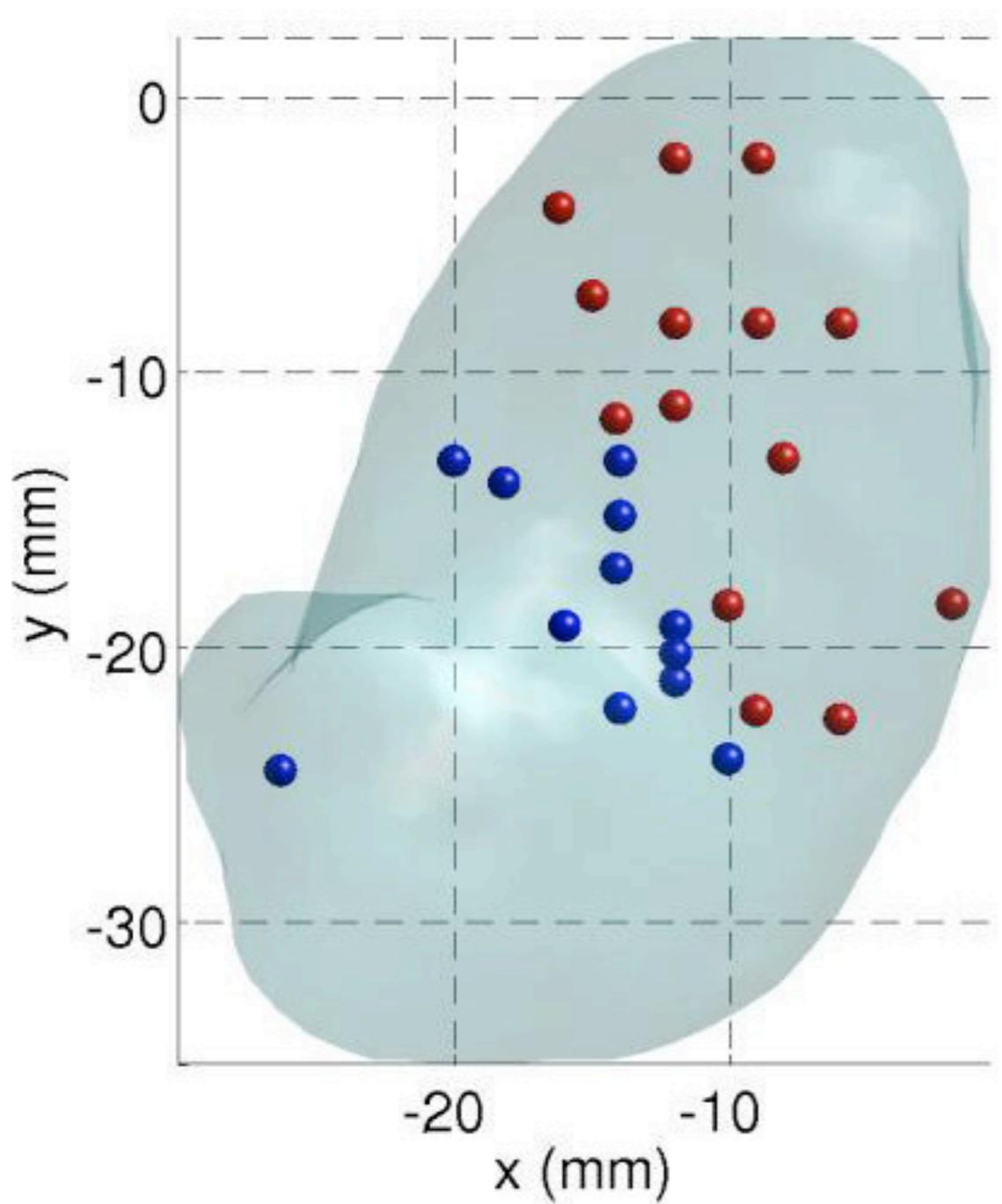


# Connectivity-based classification of thalamic voxels produces clusters





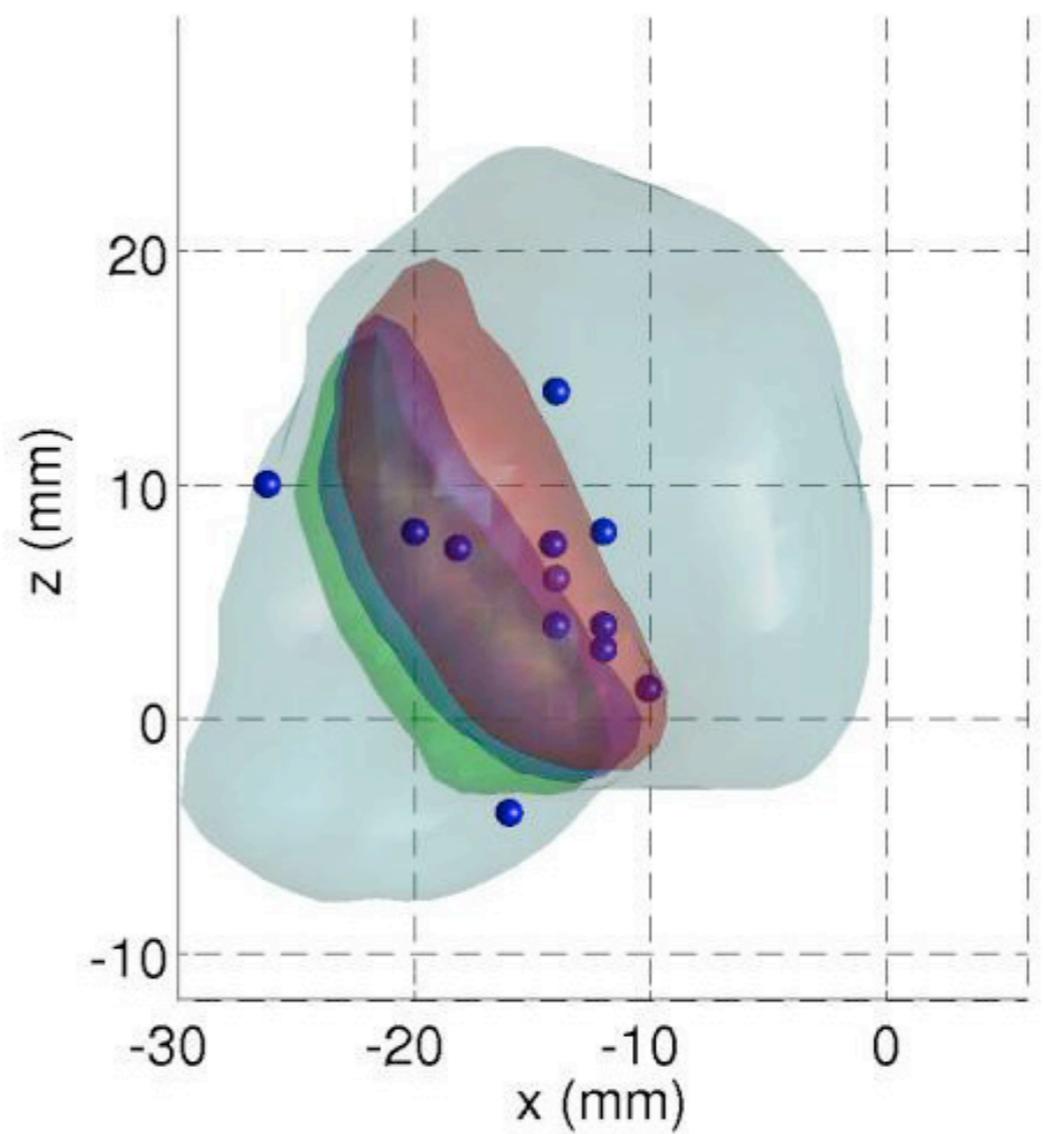
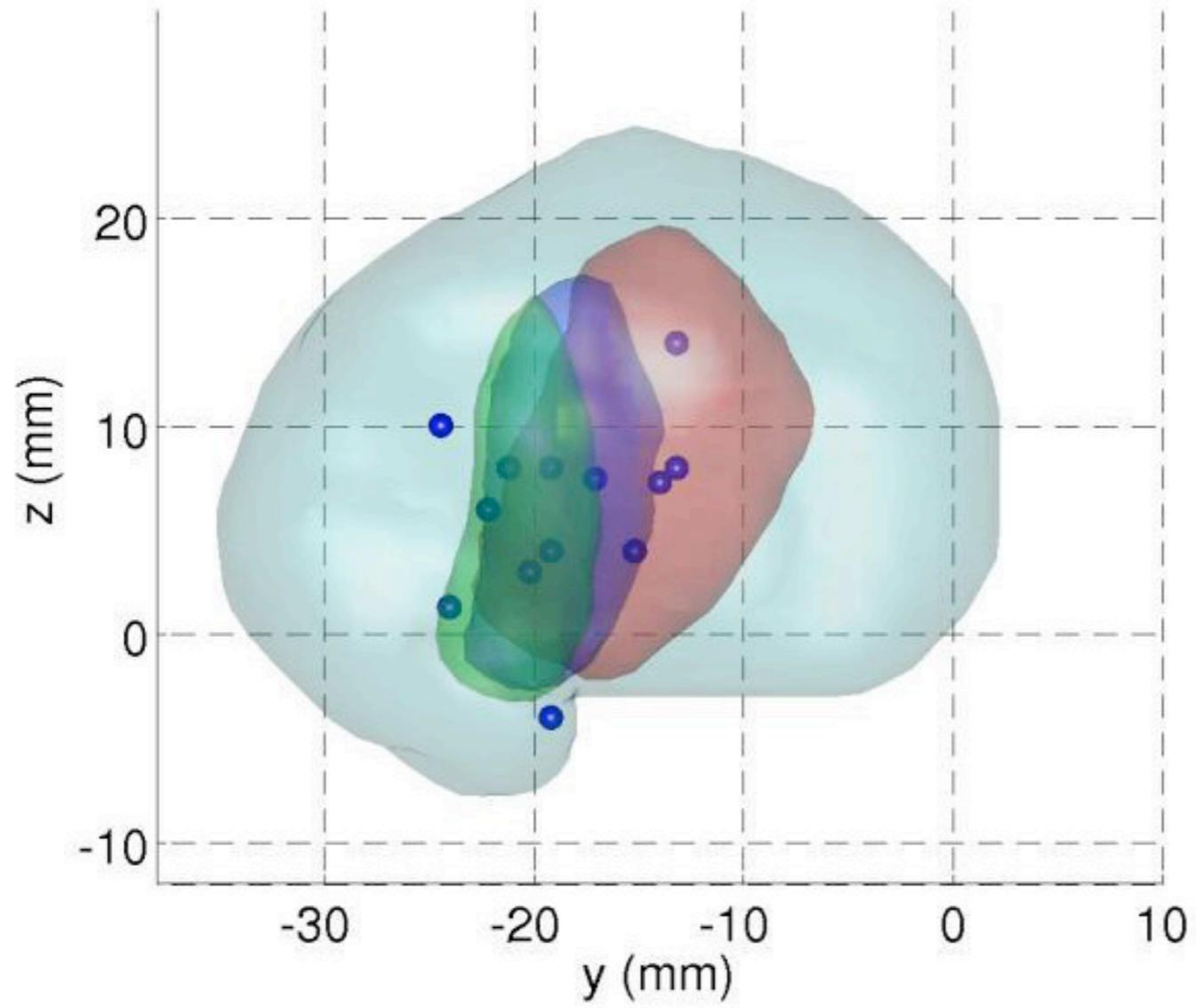
# Functional validation: meta-analysis of FMRI activations within thalamus



- Executive tasks
- Motor tasks

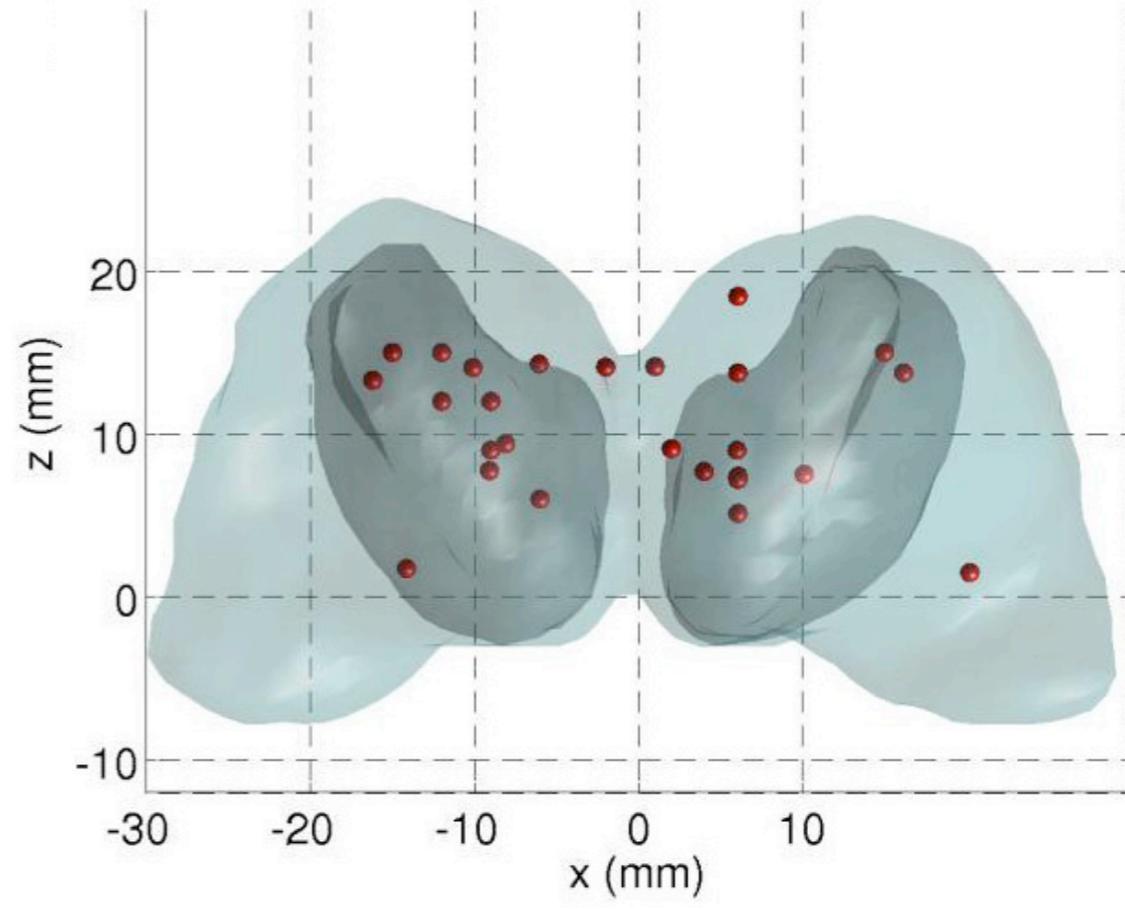
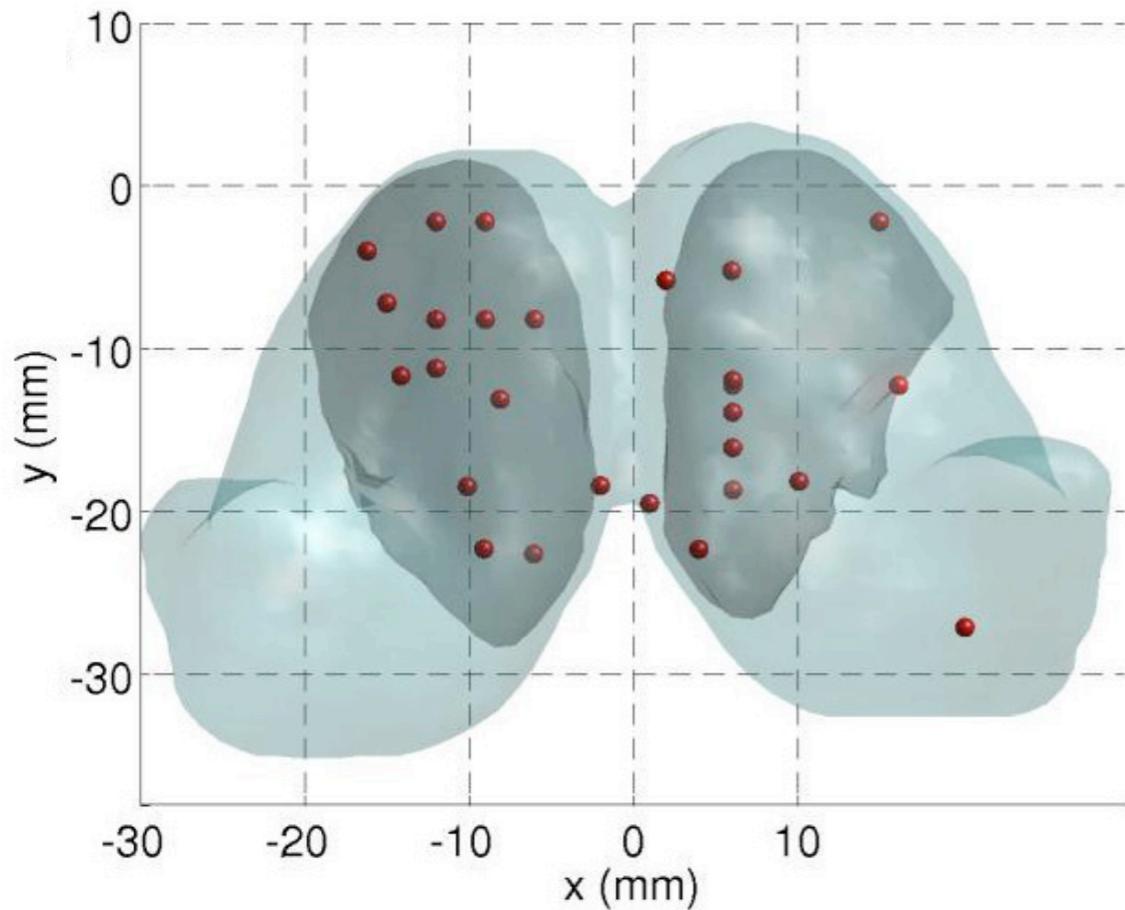


# Correspondence between functional activations and connectivity-defined volumes: motor tasks



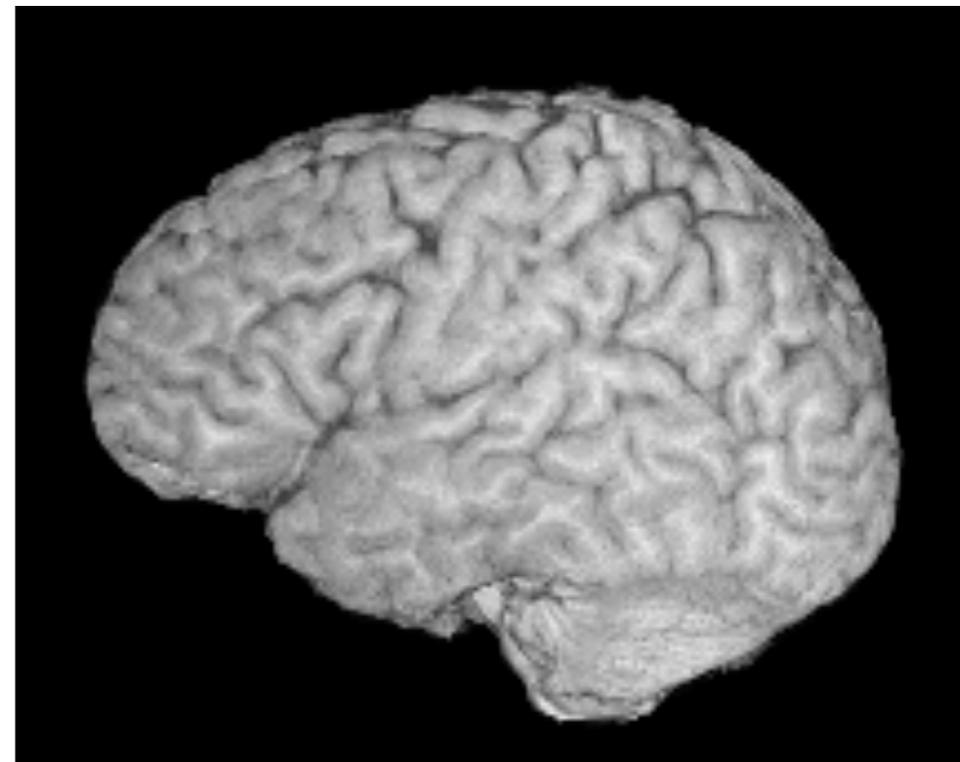
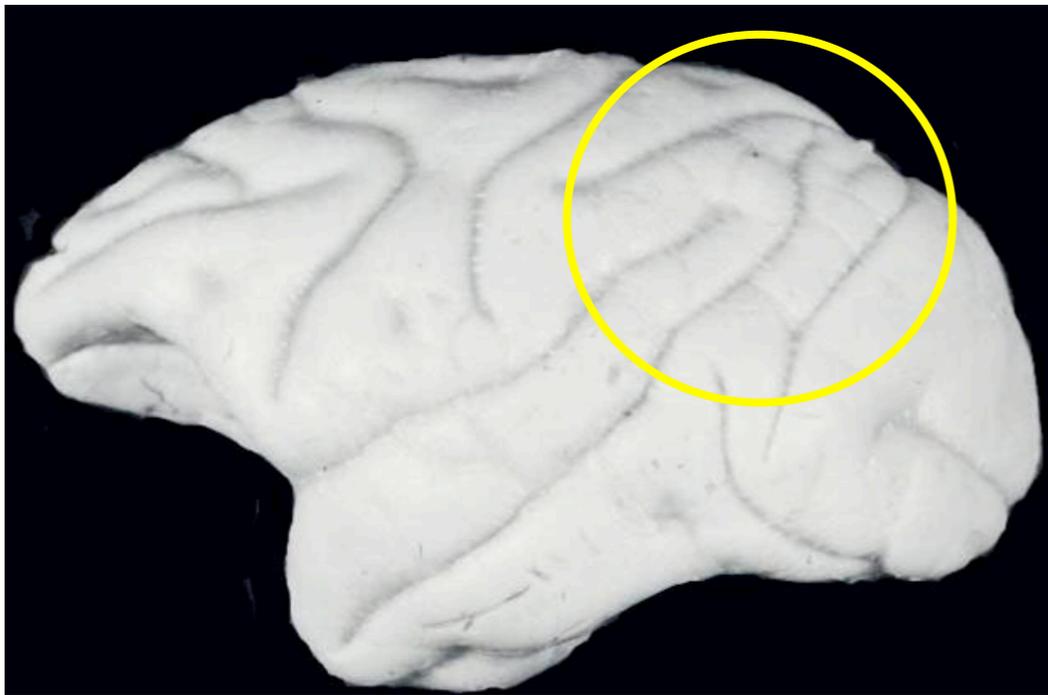


# Correspondence between functional activations and connectivity-defined volumes: executive tasks





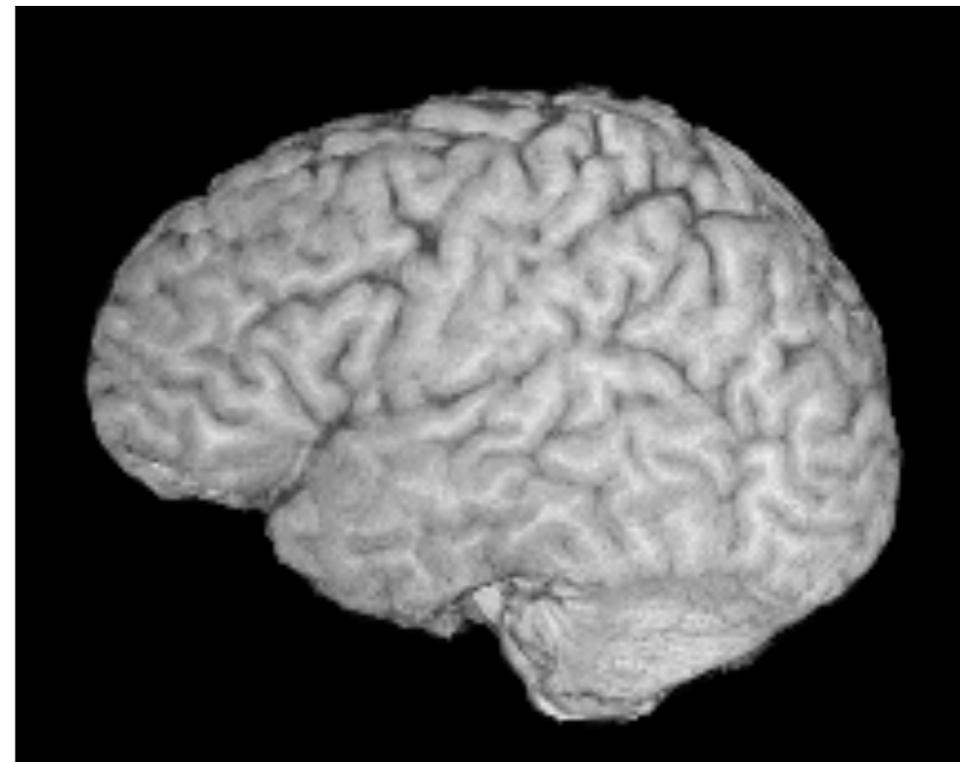
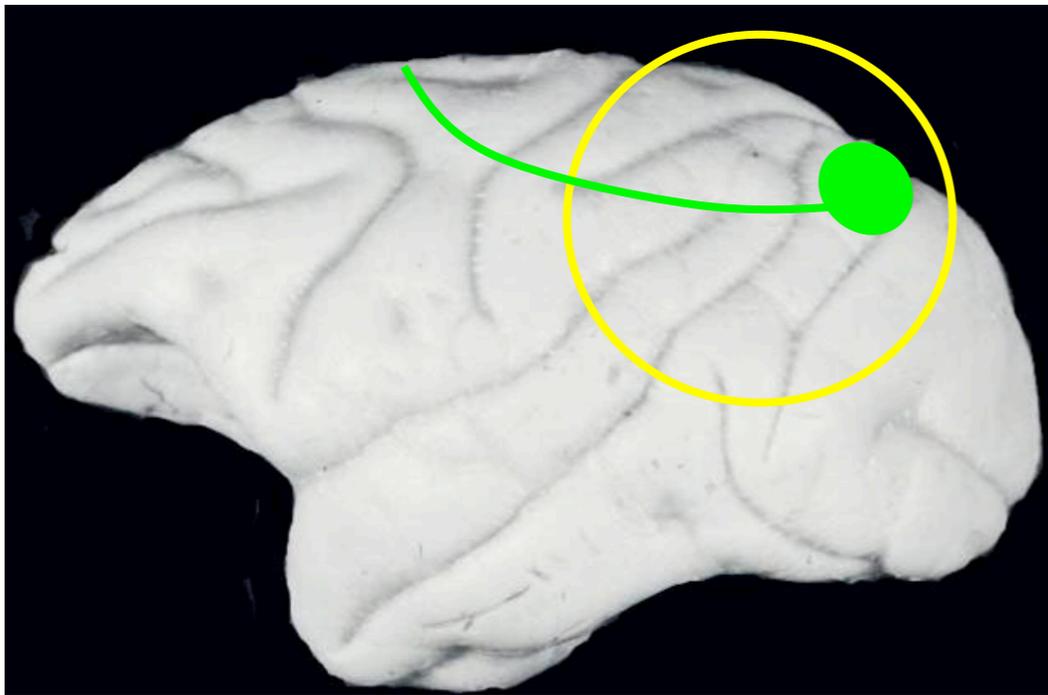
# Parieto-premotor connections



Behrens and Rushworth



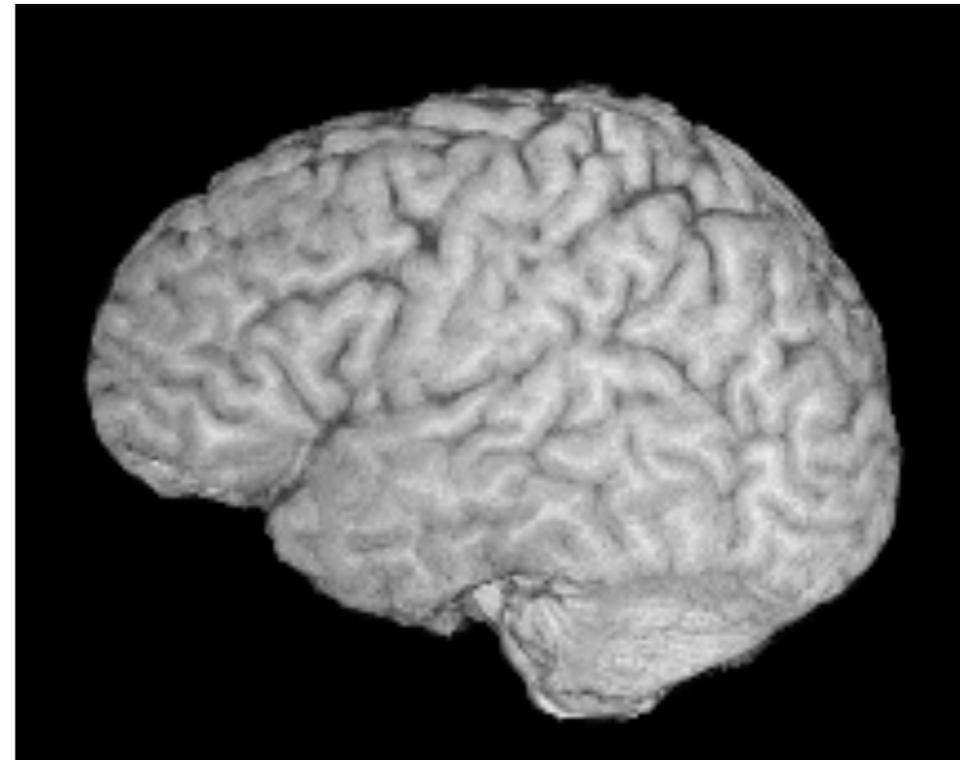
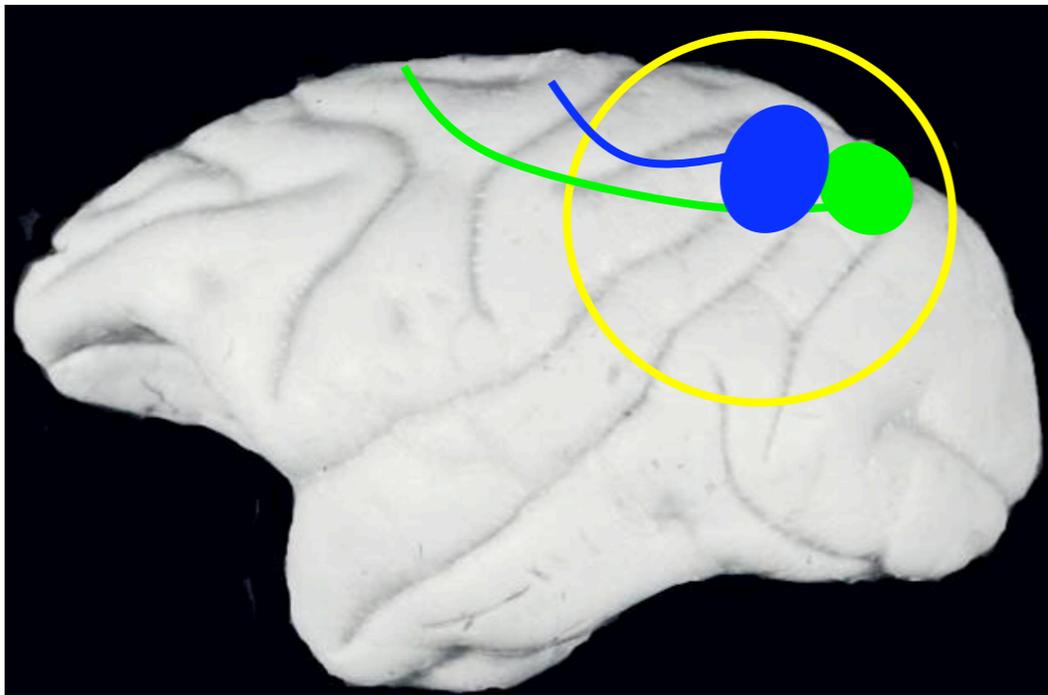
# Parieto-premotor connections



Posterior PL  $\leftrightarrow$  Anterior PMC



# Parieto-premotor connections

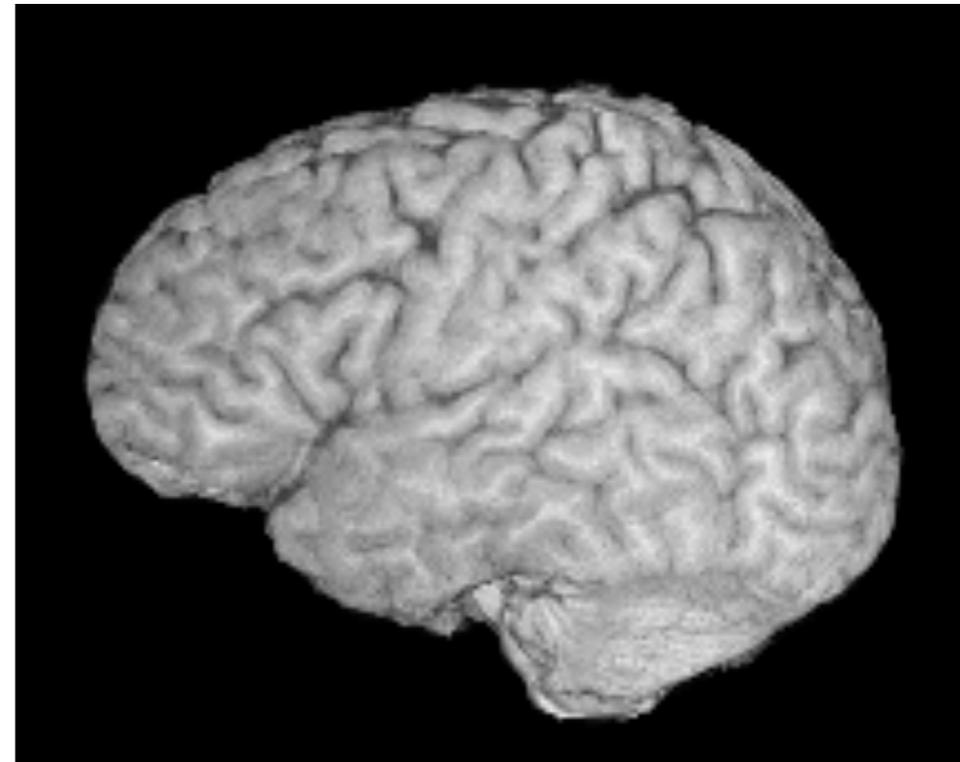
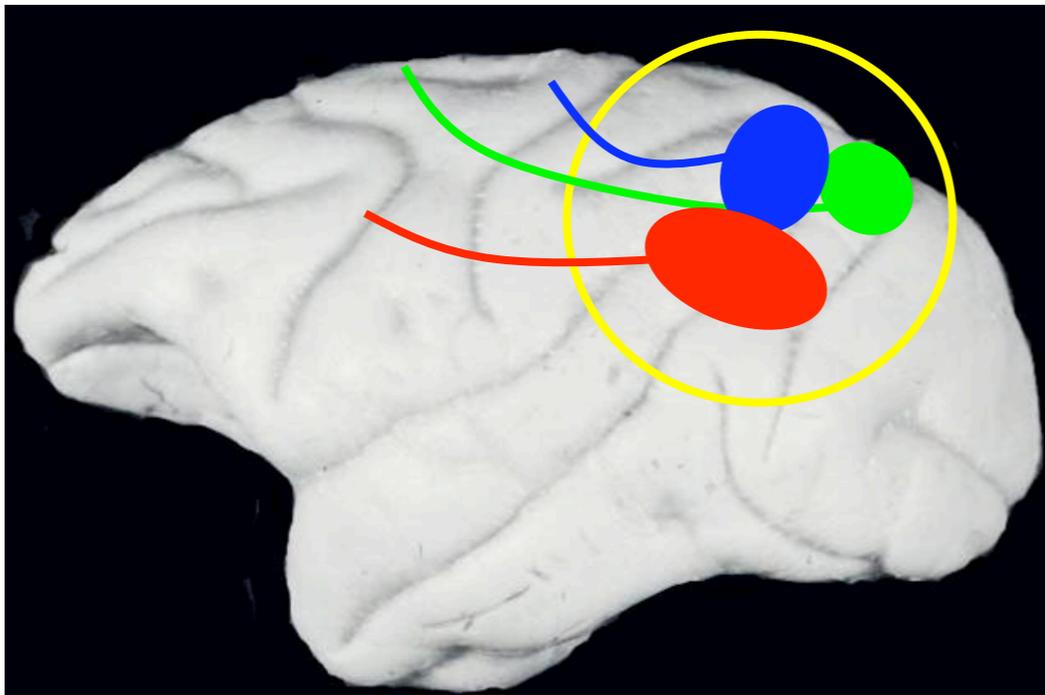


Posterior PL  $\leftrightarrow$  Anterior PMC

Anterior PL  $\leftrightarrow$  Posterior PMC



# Parieto-premotor connections



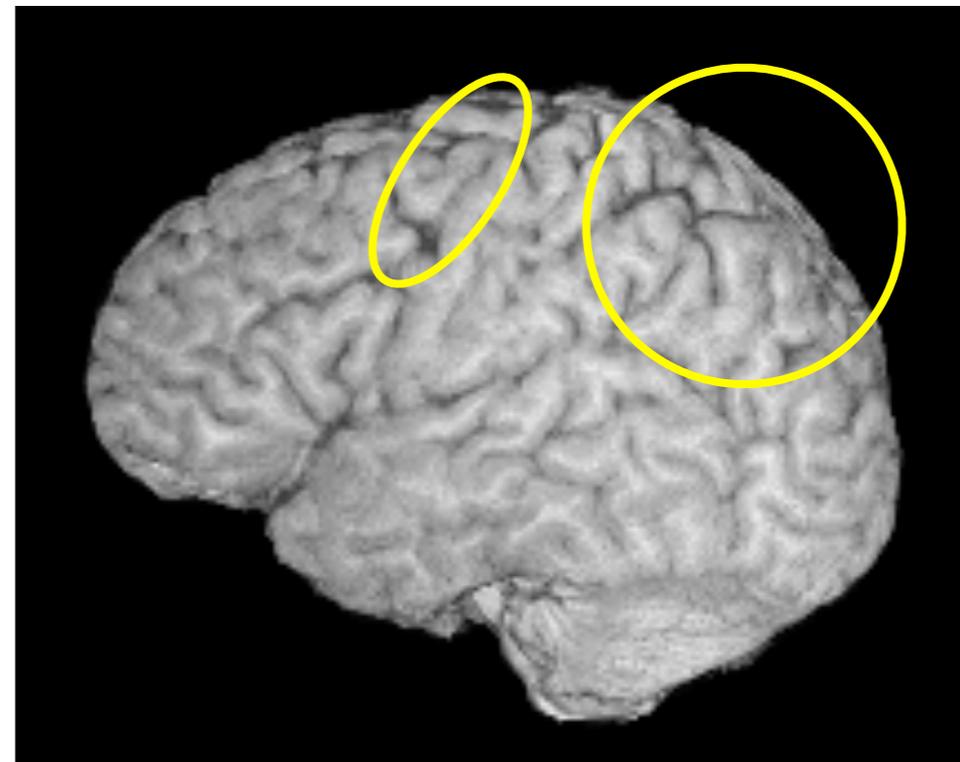
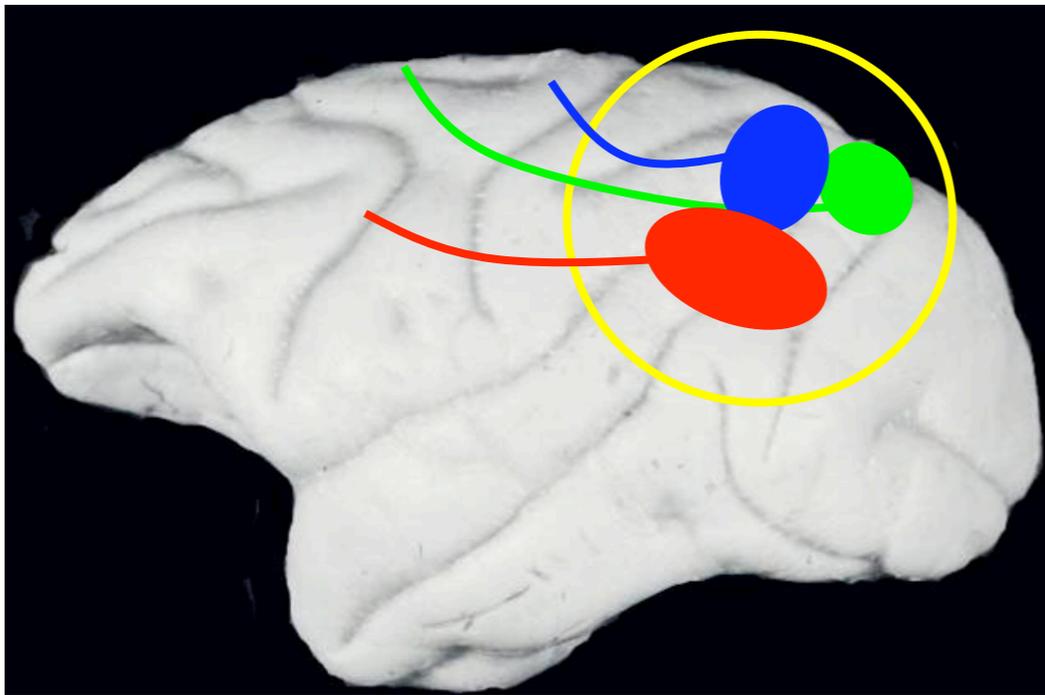
Posterior PL  $\leftrightarrow$  Anterior PMC

Anterior PL  $\leftrightarrow$  Posterior PMC

Lateral PL  $\leftrightarrow$  Frontal Eye Fields



# Parieto-premotor connections



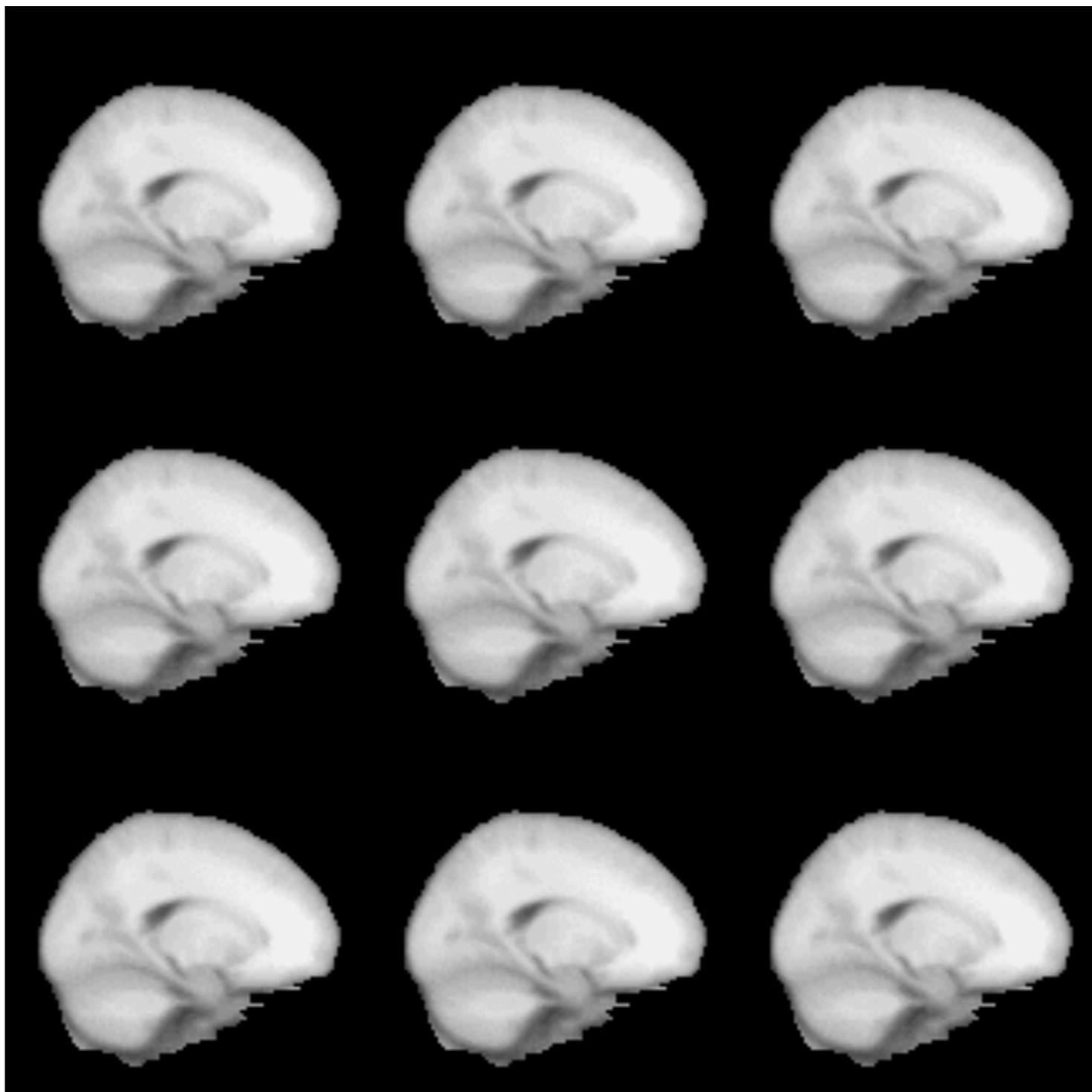
Posterior PL  $\leftrightarrow$  Anterior PMC

Anterior PL  $\leftrightarrow$  Posterior PMC

Lateral PL  $\leftrightarrow$  Frontal Eye Fields



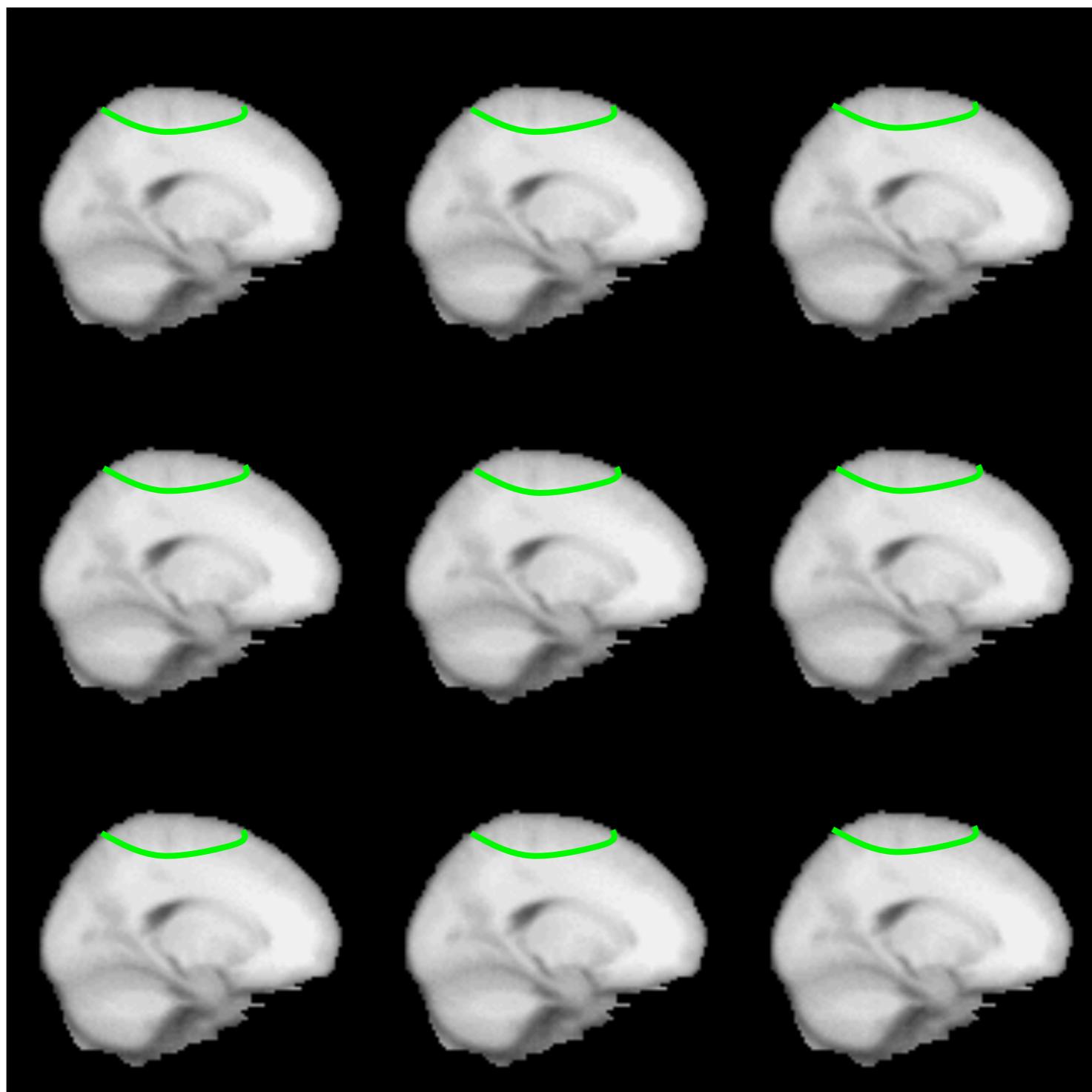
# But....



Tracking Parietal -> Medial premotor regions in 9 subjects



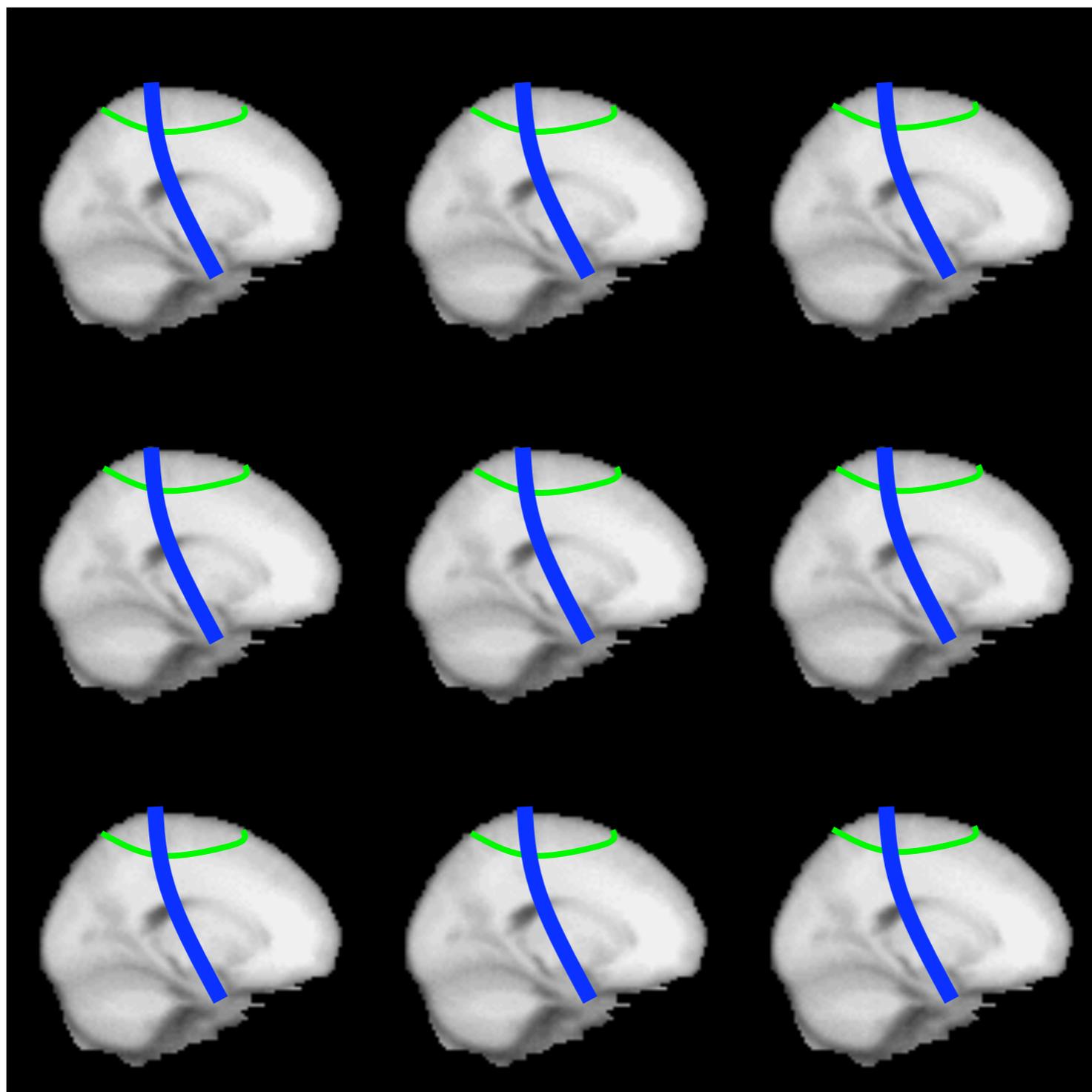
But....



Tracking Parietal -> Medial premotor regions in 9 subjects



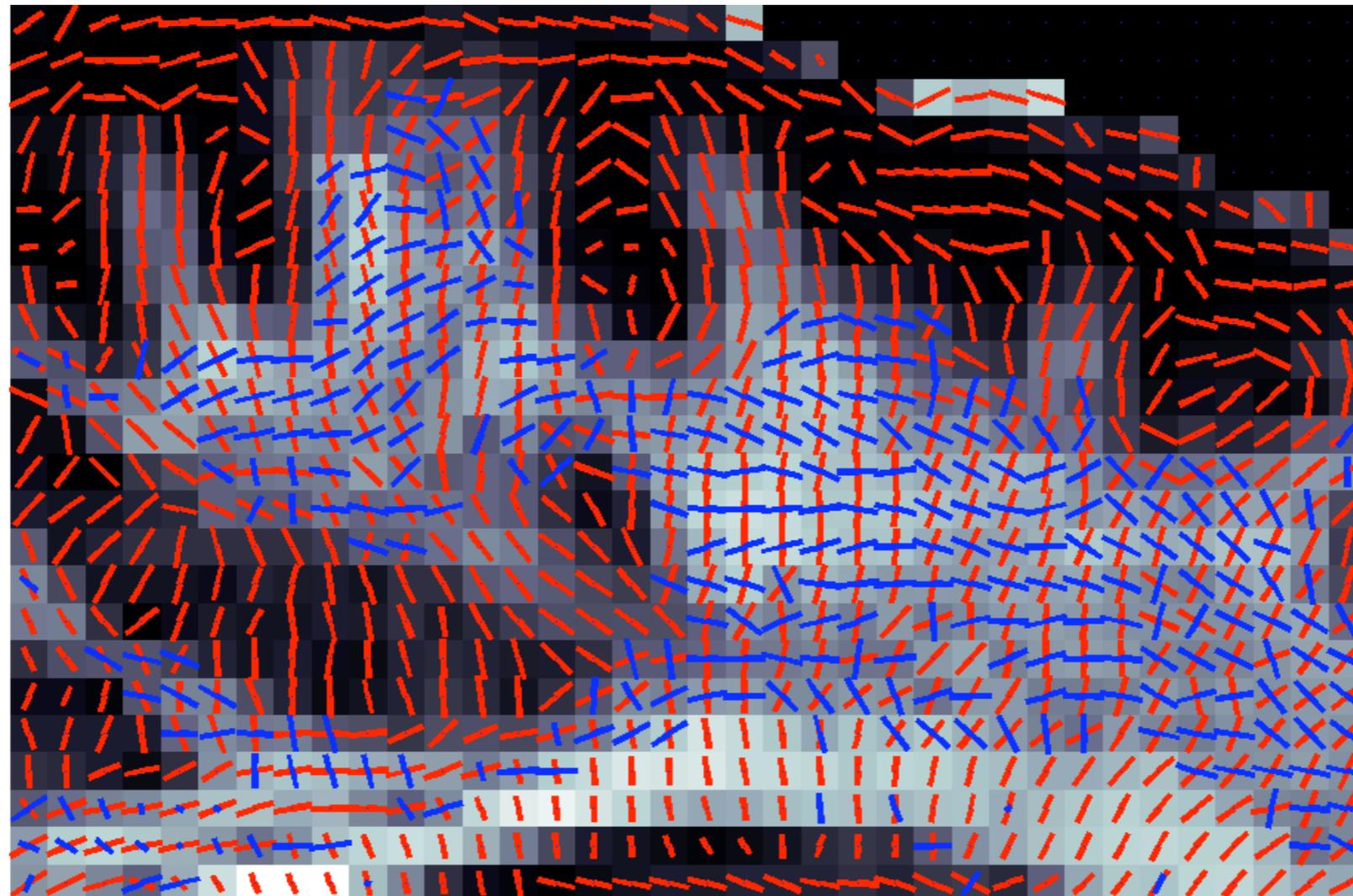
# But....



Tracking Parietal -> Medial premotor regions in 9 subjects

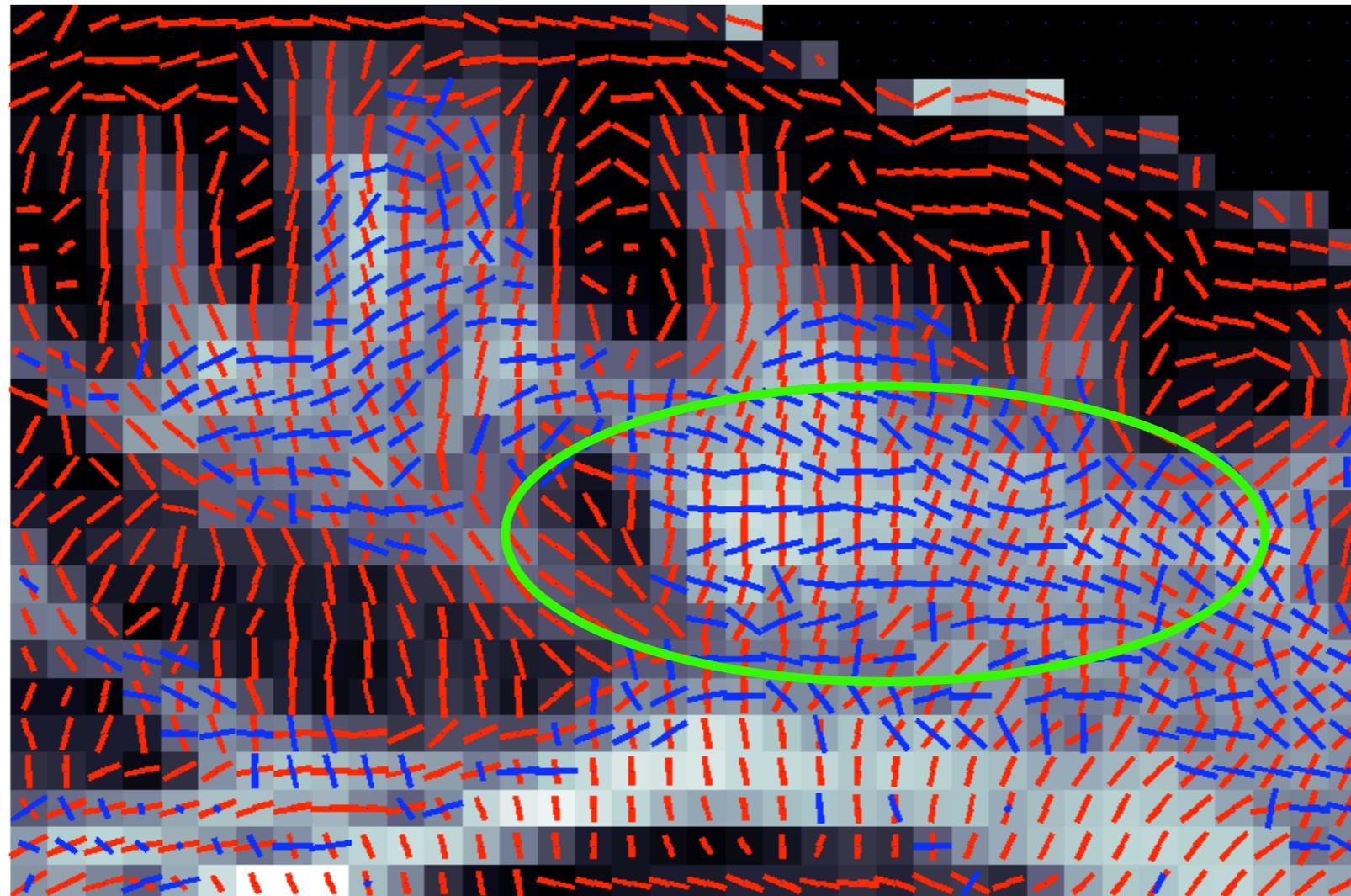


# Using multi-fibre modelling.



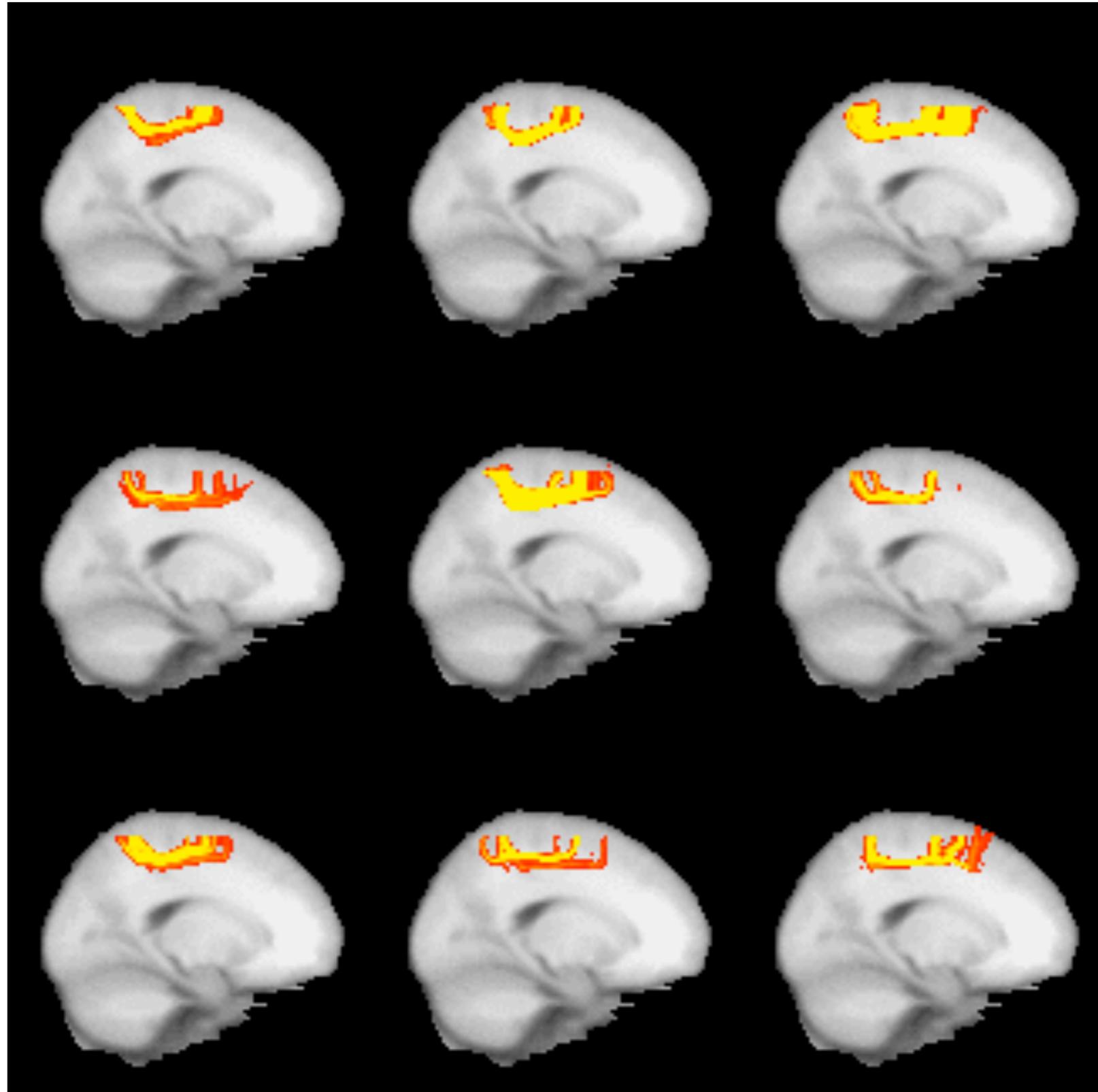


# Using multi-fibre modelling.



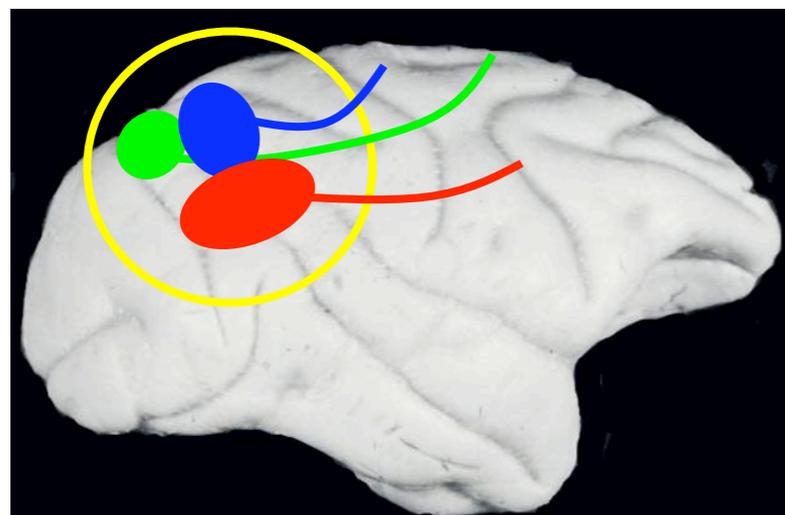


# Using multi-fibre modelling.





# Topography of premotor connections in parietal lobe.



Average of 9 subjects.  
Tracking from parietal  
To:

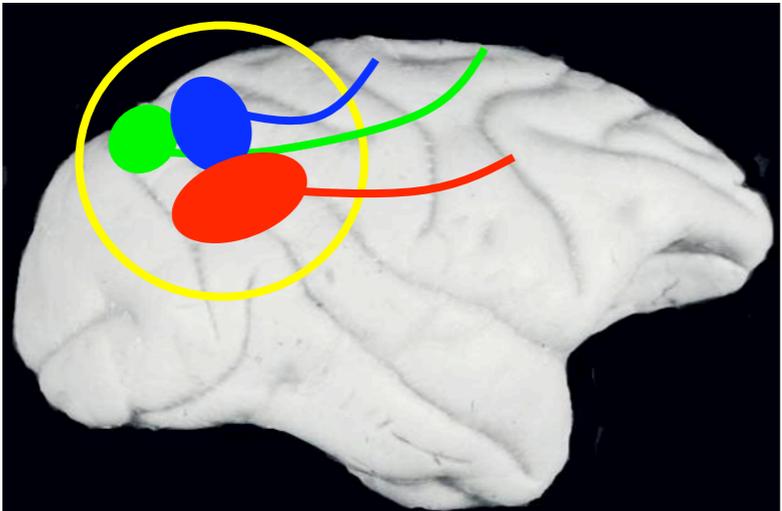
Anterior Premotor

Posterior Premotor

Frontal Eye Fields

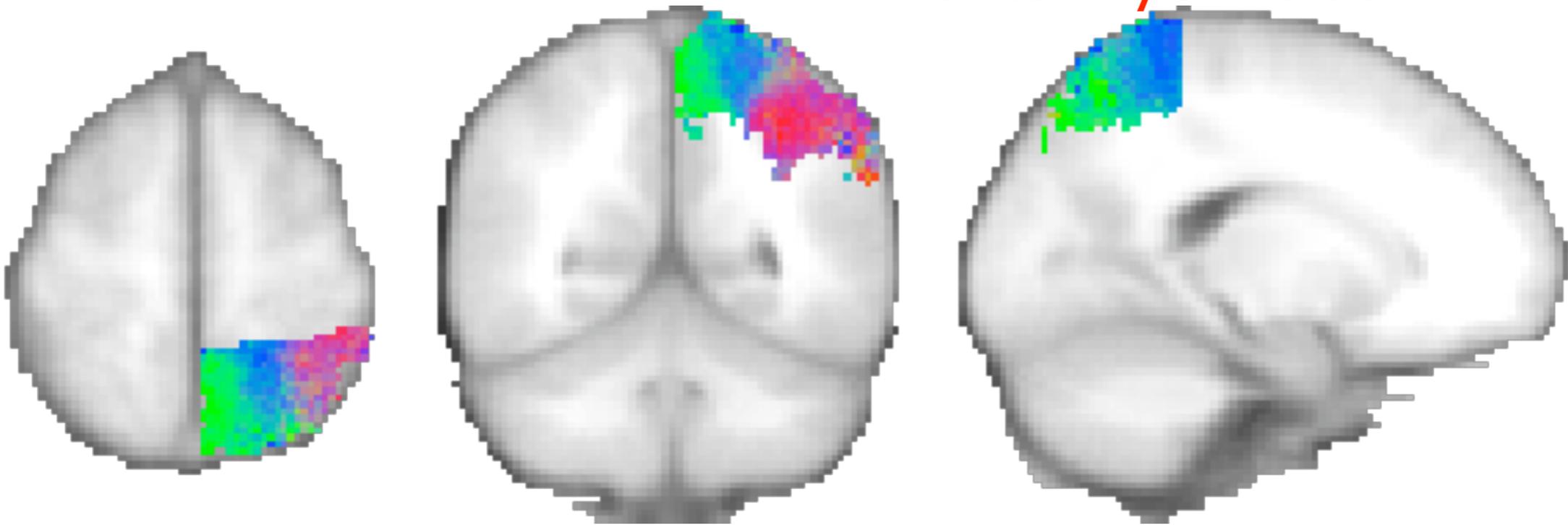


# Topography of premotor connections in parietal lobe.



Average of 9 subjects.  
Tracking from parietal  
To:

- Anterior Premotor
- Posterior Premotor
- Frontal Eye Fields



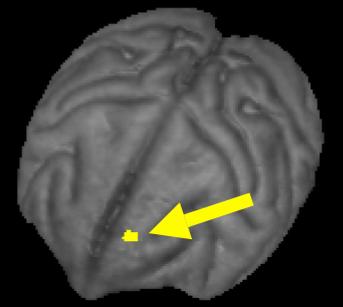
Behrens and Rushworth



# Connectivity of prefrontal cortex

DWI

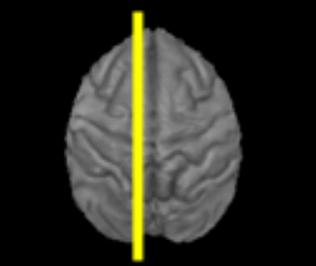
Mn



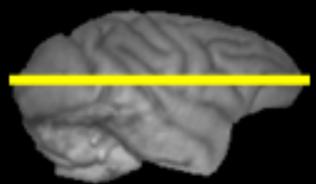
24h 48h 72h 96h 168h

BA9

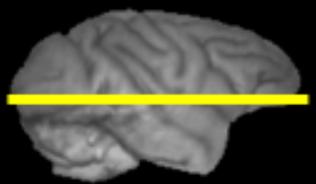
BA9



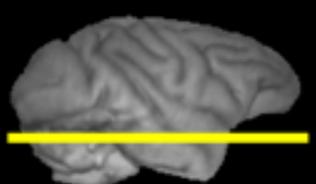
X= -4.0mm



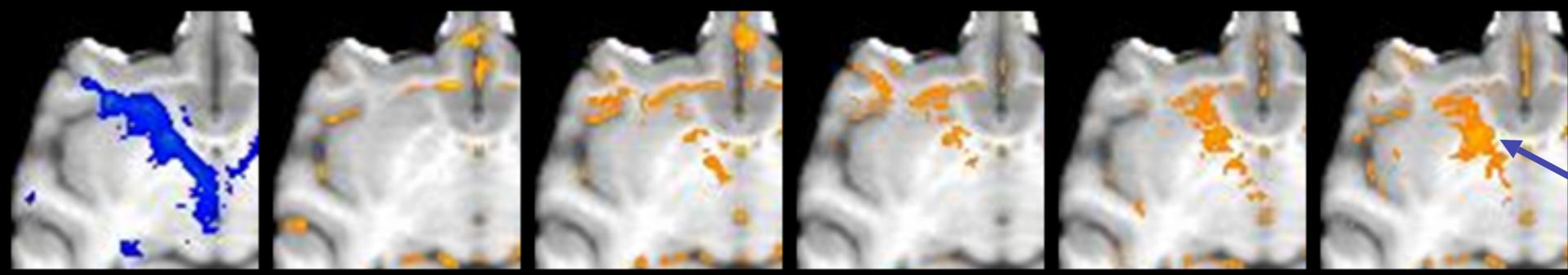
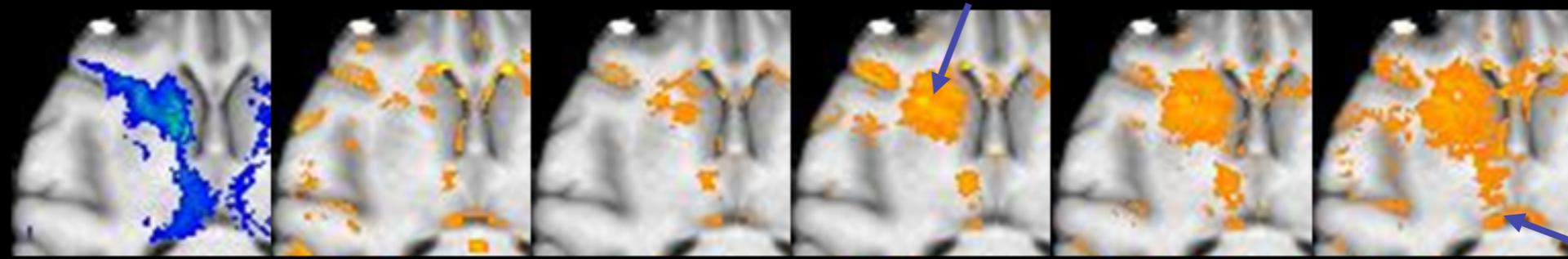
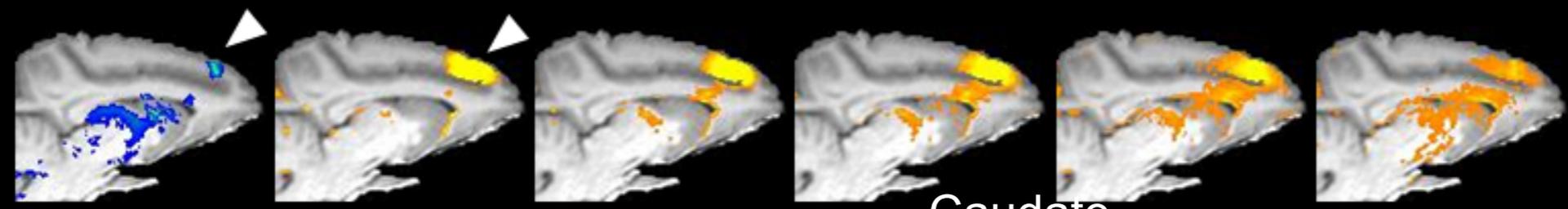
Z=5.5mm



Z=1.0mm



Z=-6.5mm



Thalamus

Pallidum

Midbrain peduncle



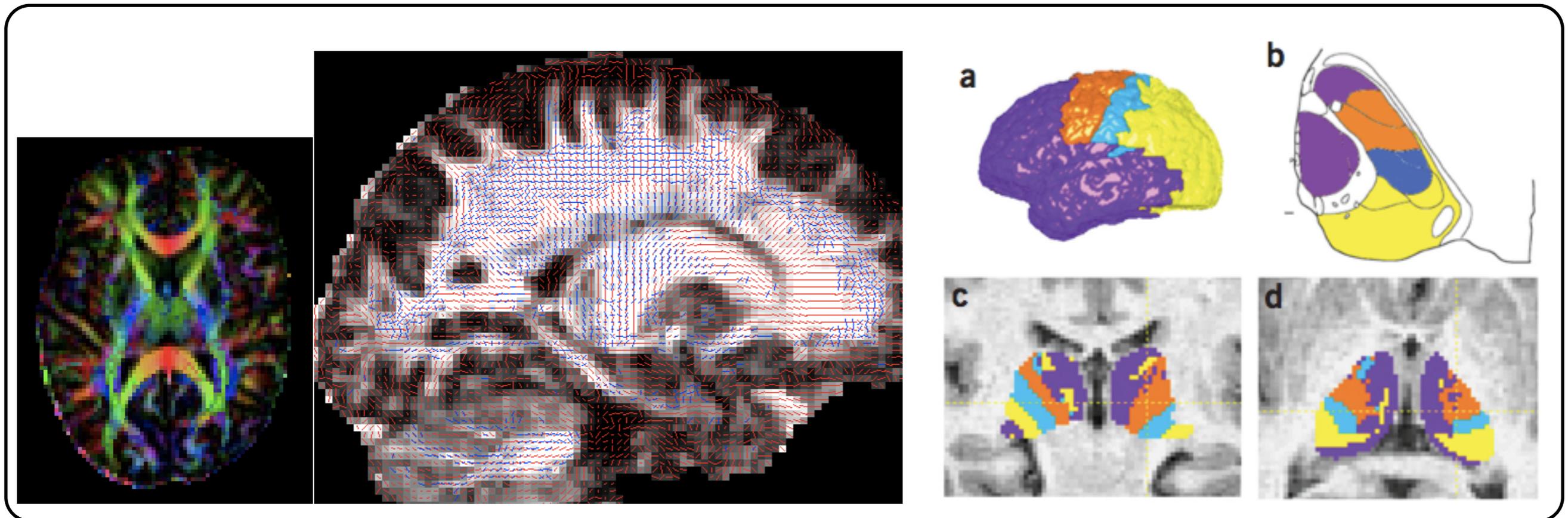
# What is a quantitative measure of connectivity?

- Number of axons connecting 2 areas?
- Proportion of axons from a seed that reach a target?
- “Integrity” of the connecting white matter ...
  - Effective conductivity?
  - Degree of myelination?
  - Packing density?
- What are we measuring?
  - The probability that the **dominant** path through the diffusion field passes through this region.



# FMRIB Diffusion Toolbox

- DTI model fit
- Eddy current correction
- Voxel-Based diffusion analysis (TBSS)
- BEDPOSTX modelling crossing fibres
- PROBTRACKX propagating uncertainty in tractography

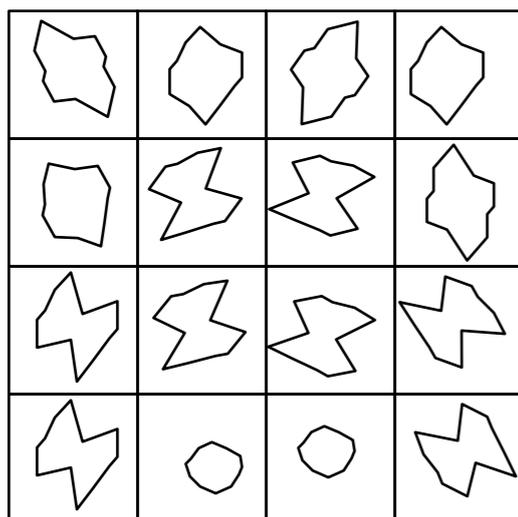
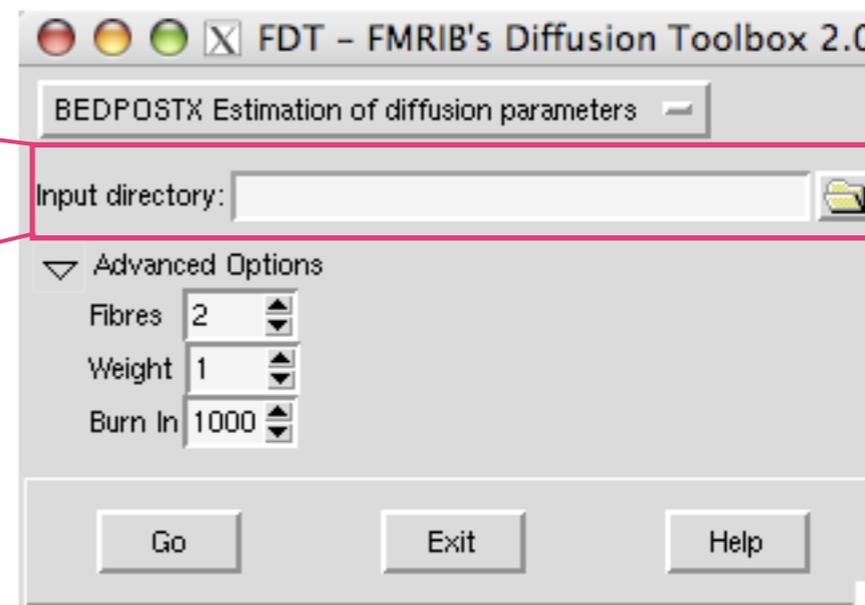




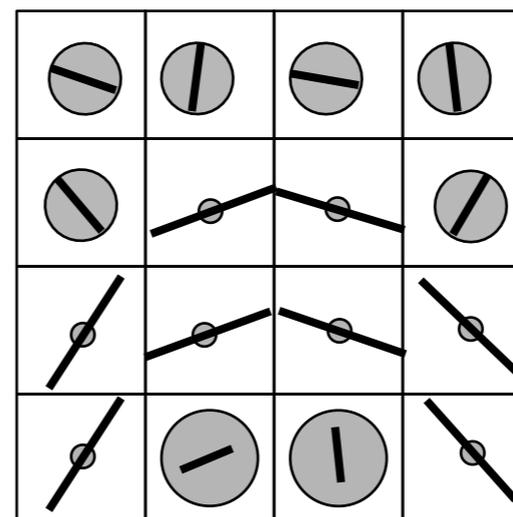
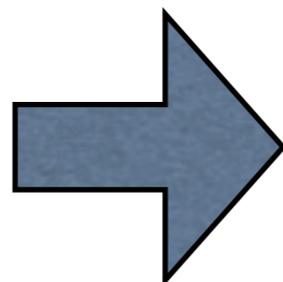
# BEDPOSTX

## GUI options

data.nii.gz  
nodif\_brain\_mask.nii.gz  
bvecs  
bvals



Data

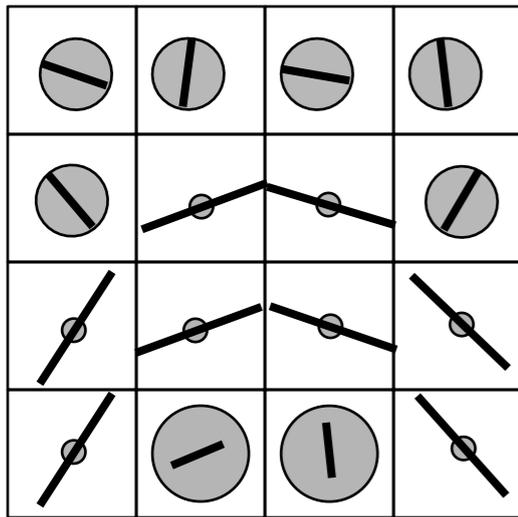


Model parameters



# BEDPOSTX

## Results



- Sample orientations



merged\_th1samples.nii.gz  
merged\_ph1samples.nii.gz  
merged\_th2samples.nii.gz  
merged\_ph2samples.nii.gz

- Sample fractional volumes



merged\_f1samples.nii.gz  
merged\_f2samples.nii.gz

- Mean orientation



dyads1.nii.gz  
dyads2.nii.gz

- Mean fractional volumes



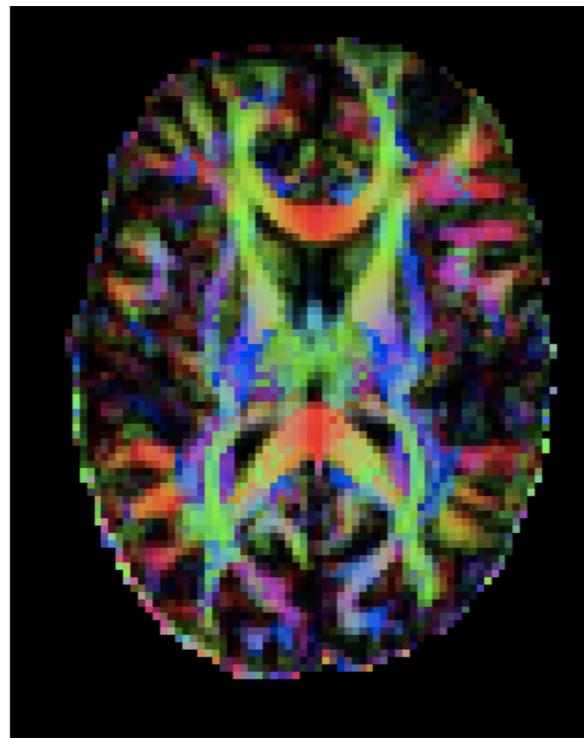
mean\_f1samples.nii.gz  
mean\_f2samples.nii.gz



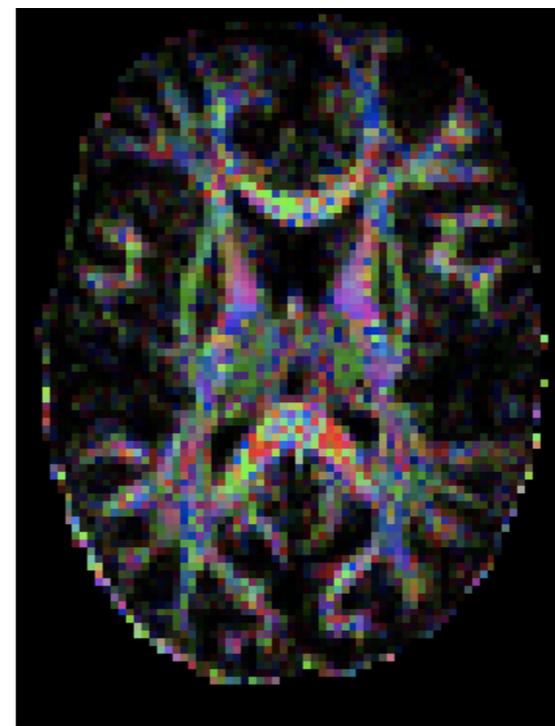
# BEDPOSTX

## Results

- Mean orientation



dyads1.nii.gz



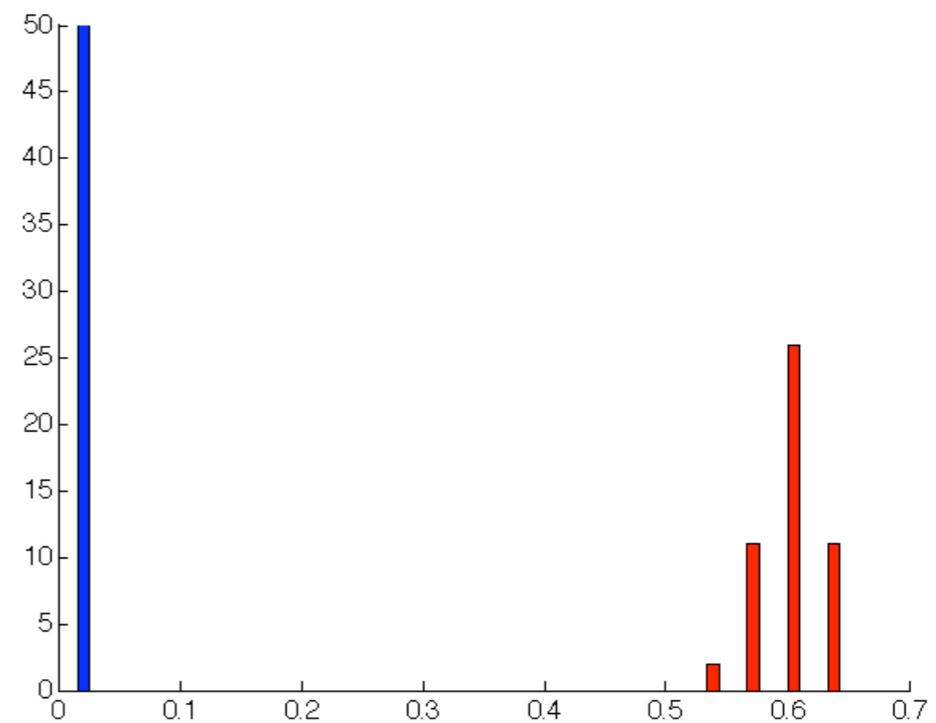
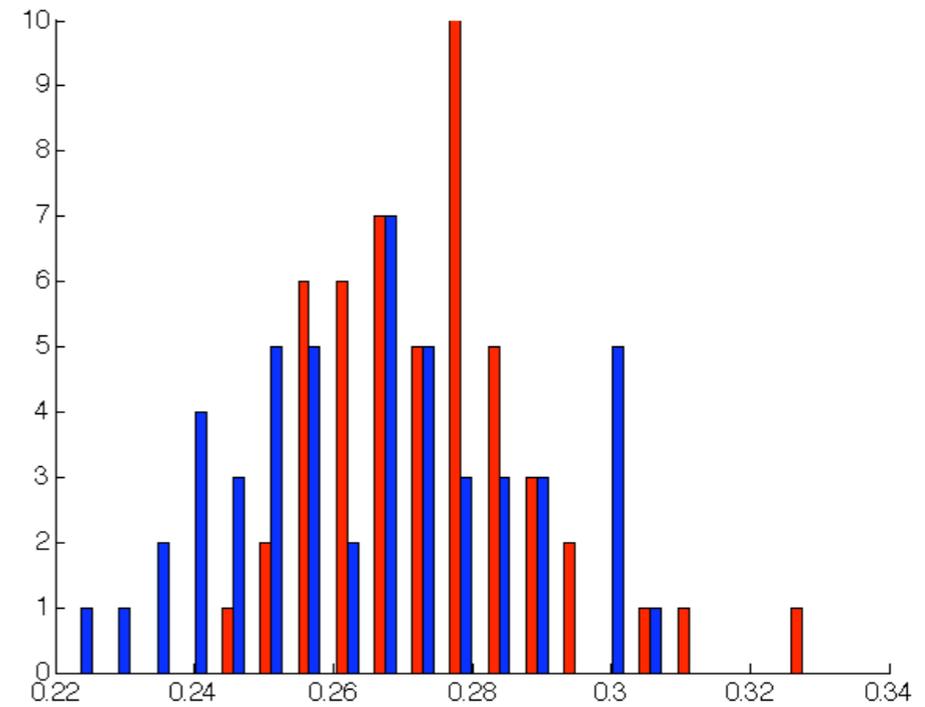
dyads2.nii.gz



# BEDPOSTX

## Results

- Mean fractional volumes

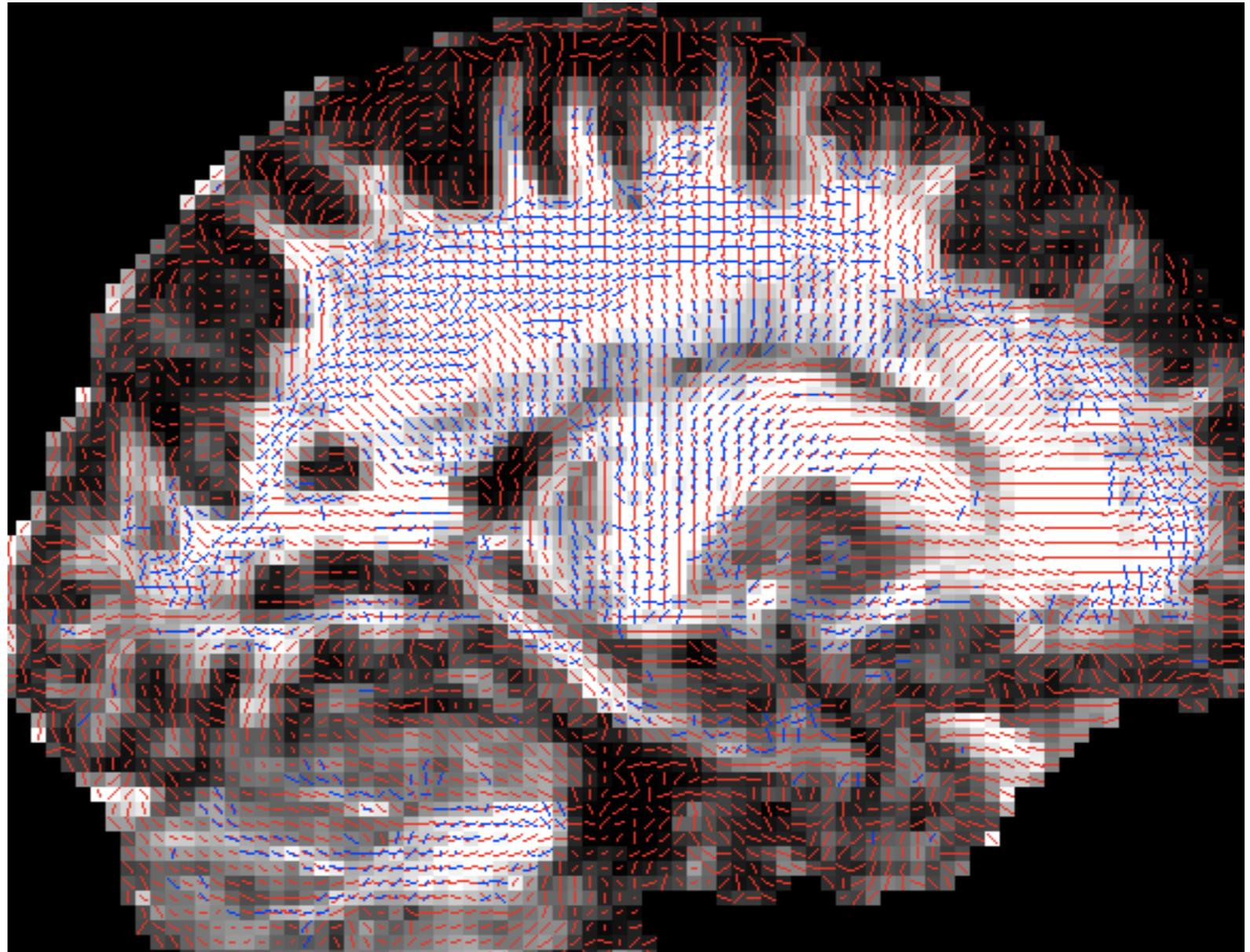




# BEDPOSTX

## Results

- Mean orientation



---

maskdyads dyads2 mean\_f2samples

[dyads1.nii.gz](#)

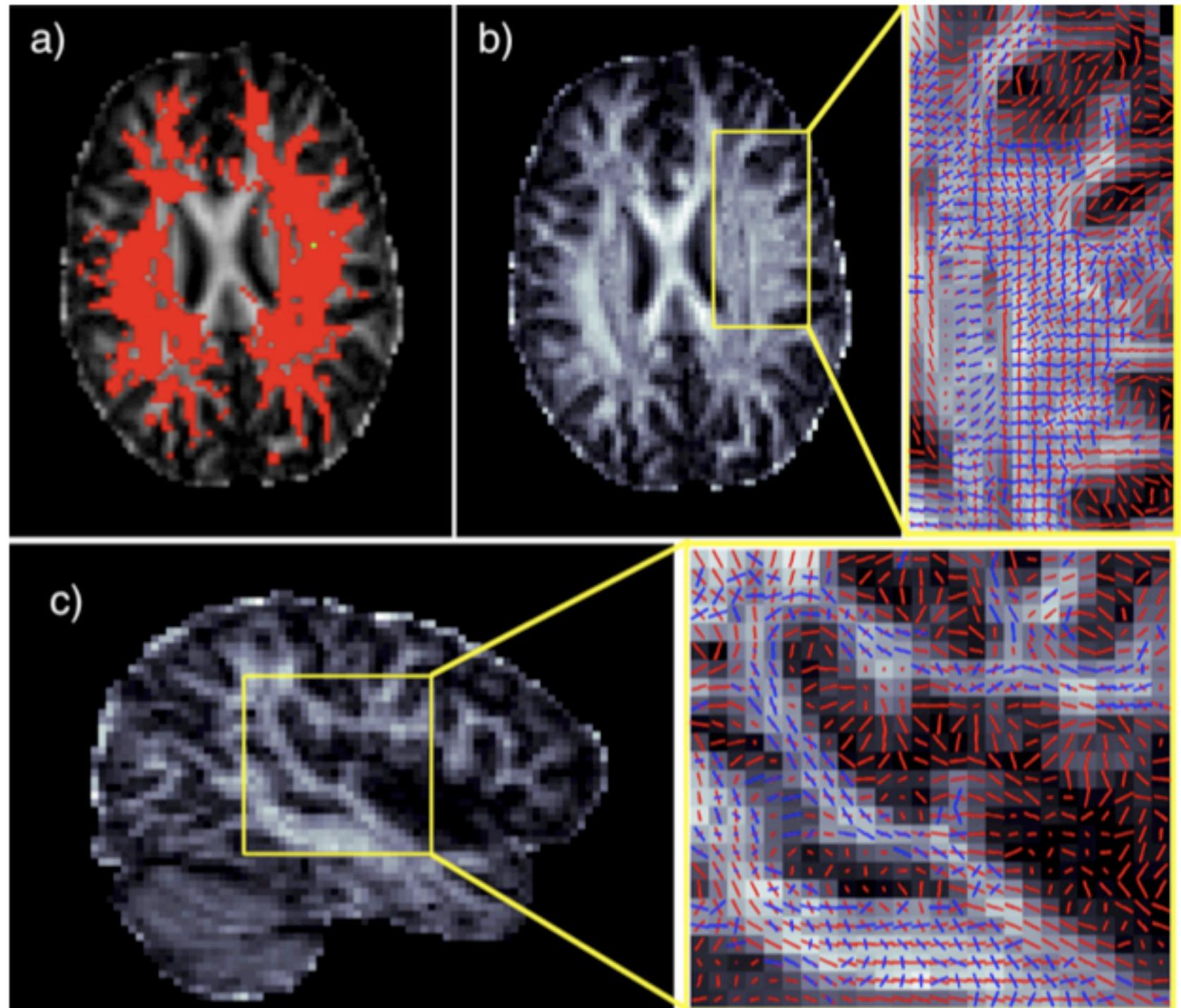
[dyads2.nii.gz](#)



# BEDPOSTX

## Modelling crossing fibres

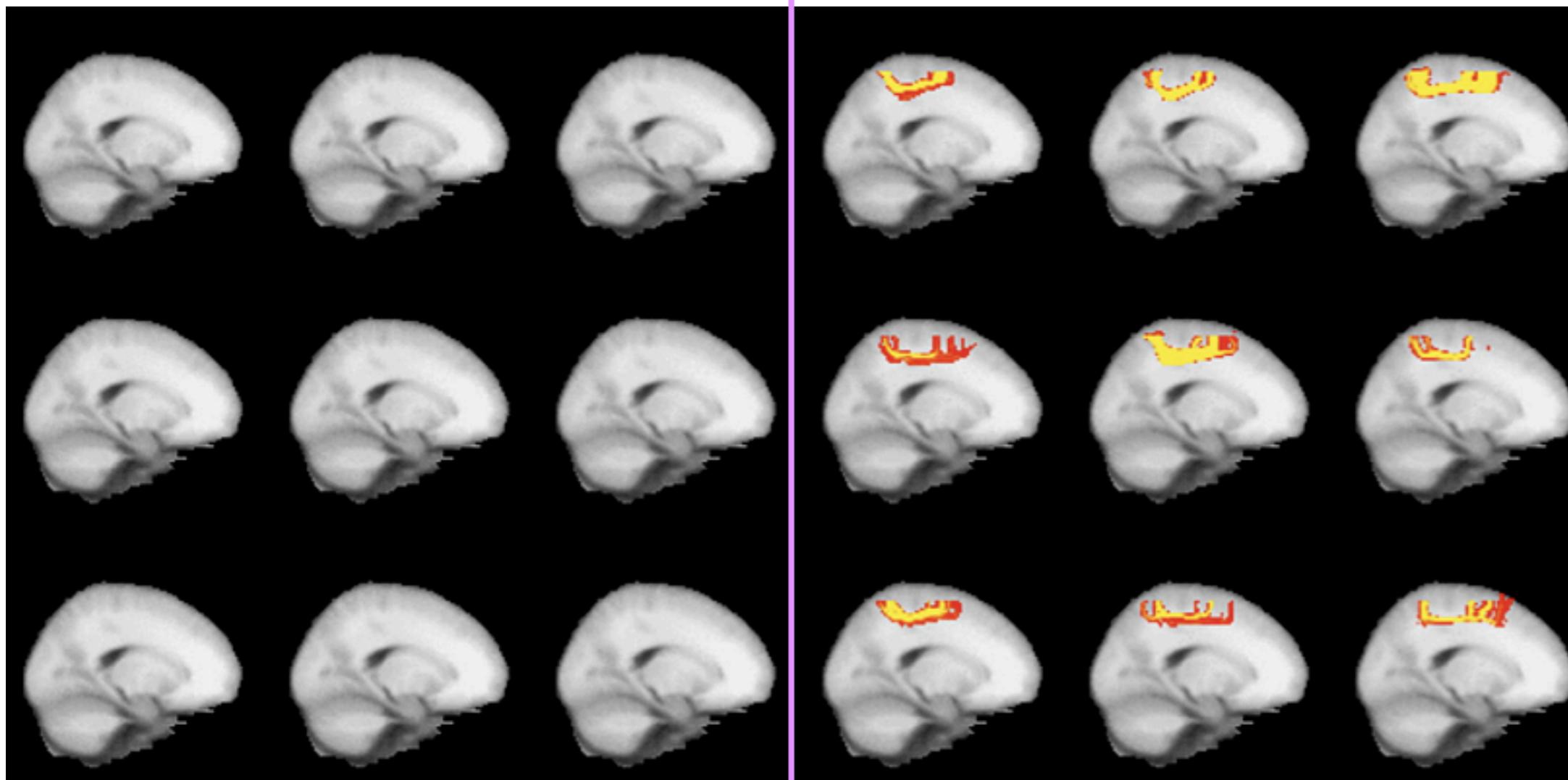
- large portion of the white matter voxels has two fibres
- Crossing fibres form form coherent bundles





# BEDPOSTX

Modelling crossing fibres



1 fibre

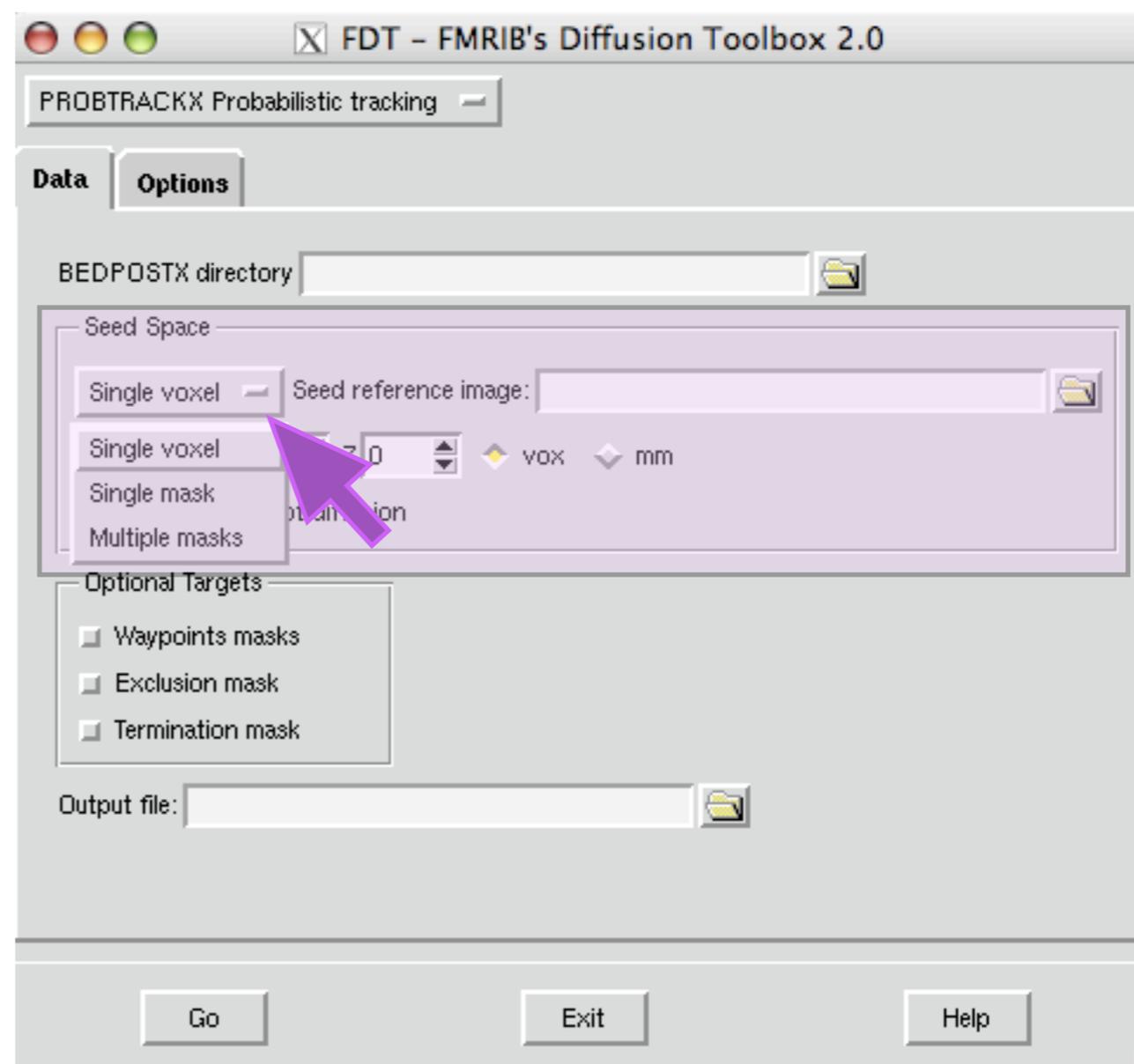
2 fibres



# PROBTRACKX

## Seed specification

- Different ways of specifying seeds
- Allow seed specification in a different space





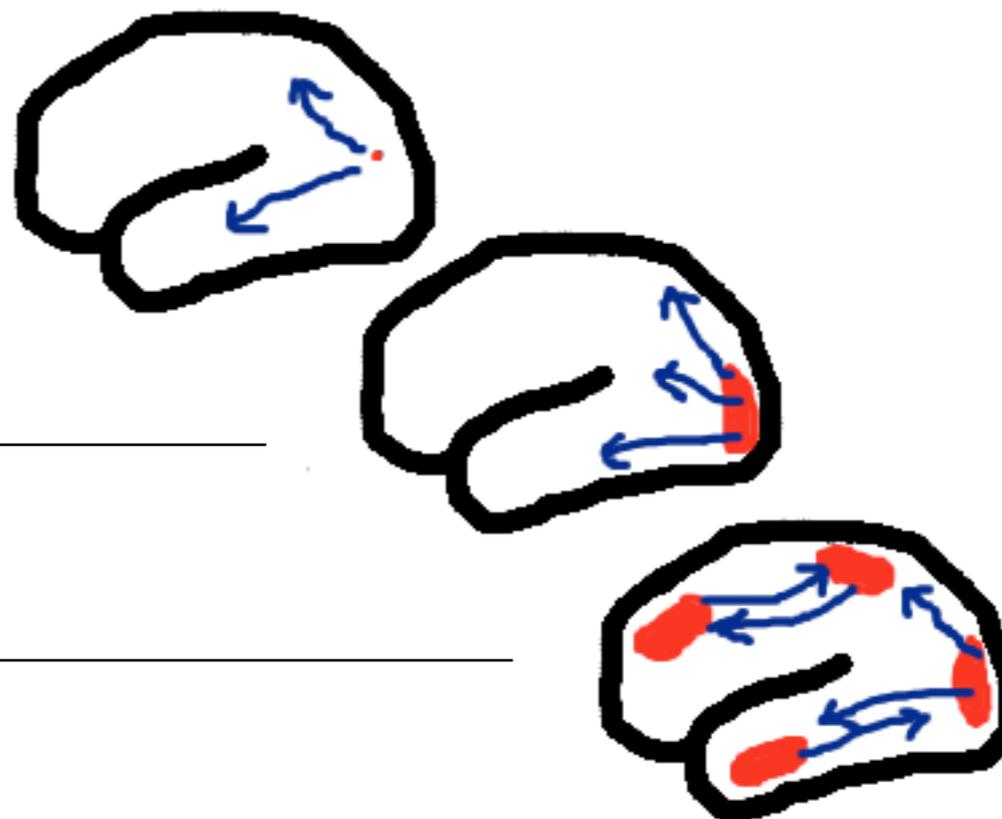
# PROBTRACKX

## Seed specification

- single voxel \_\_\_\_\_

- single mask \_\_\_\_\_

- multiple masks \_\_\_\_\_

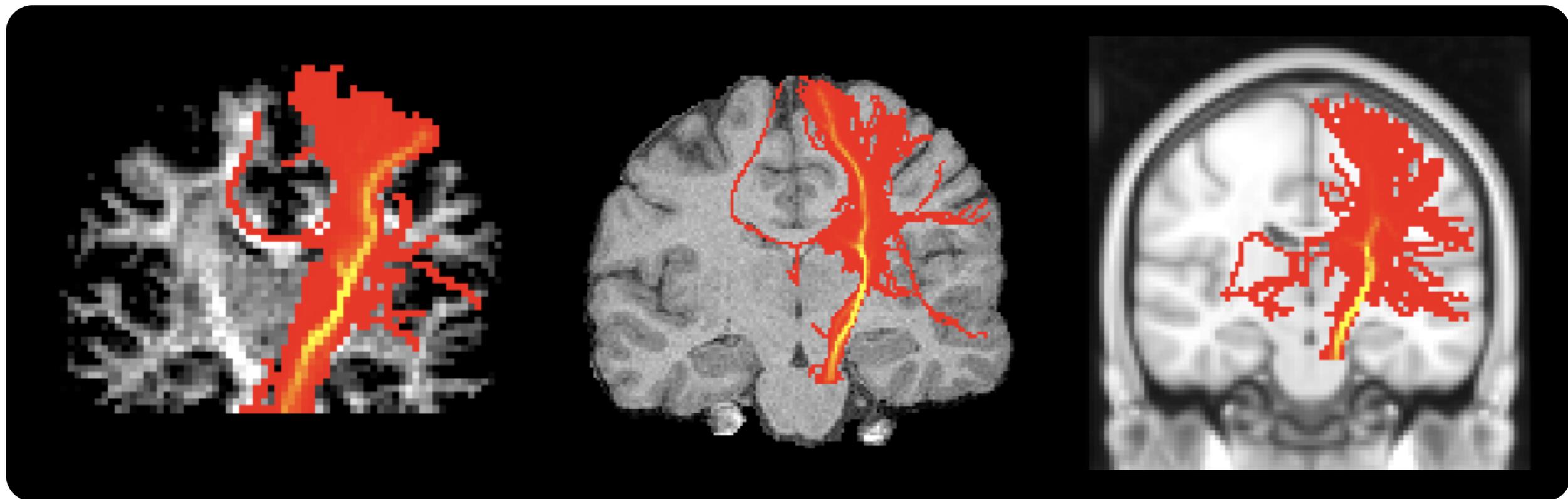




# PROBTRACKX

## Seed specification

- Different seed spaces



Diffusion space

Structural space

Standard space



# PROBTRACKX

(optional) Targets specification

- Waypoints
  - Exclusion
  - Termination
  - Classification
- Dissecting specific tracts
- Quantification of connectivity



# PROBTRACKX

(optional) Targets specification

- Waypoints
  - Exclusion
  - Termination
  - Classification
- Dissecting specific tracts
- Quantification of connectivity

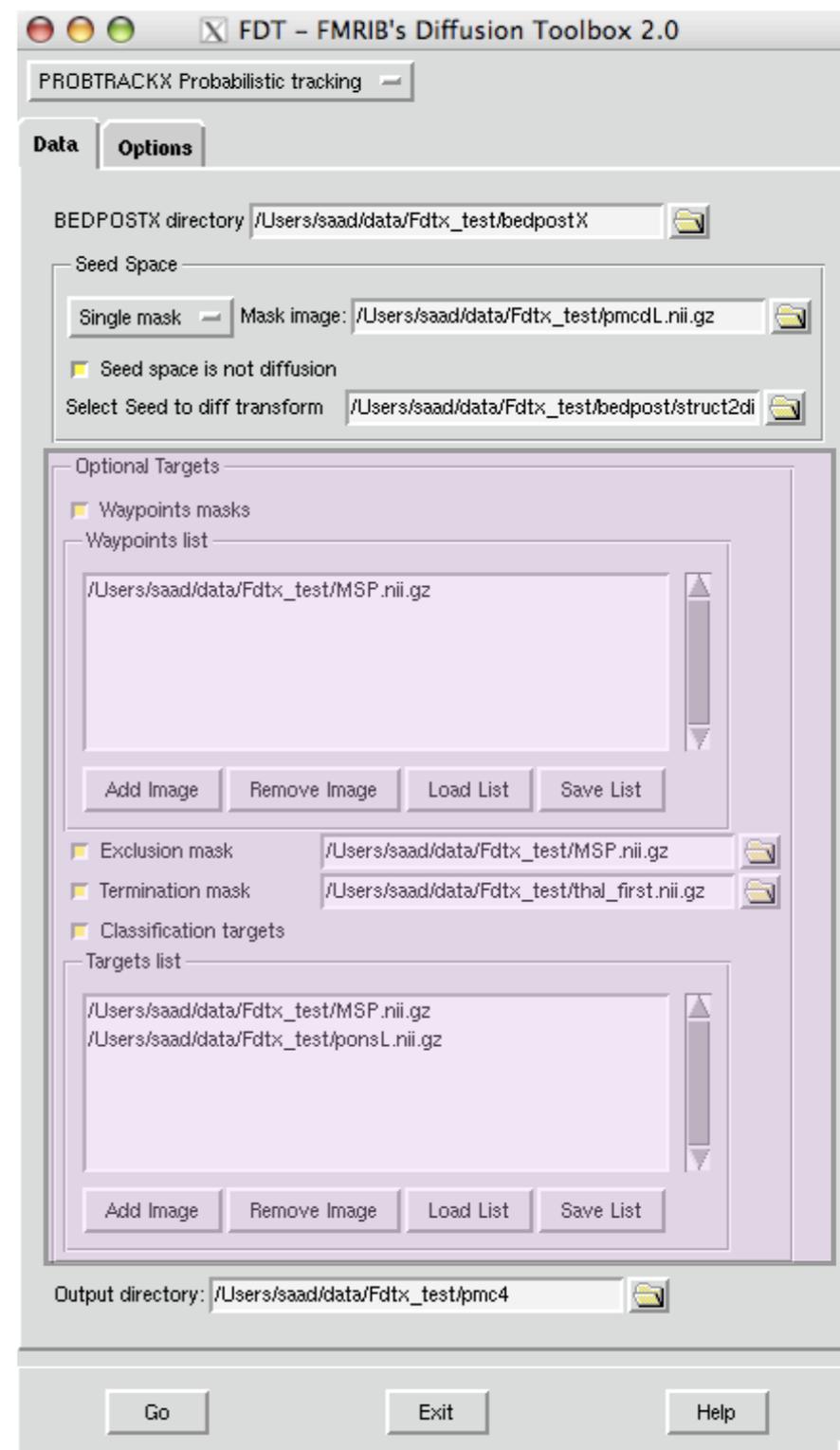
**ALL THE TARGETS IN THE SAME SPACE AS THE SEEDS**



# PROBTRACKX

(optional) Targets specification

- Waypoints
- Exclusion
- Termination
- Classification

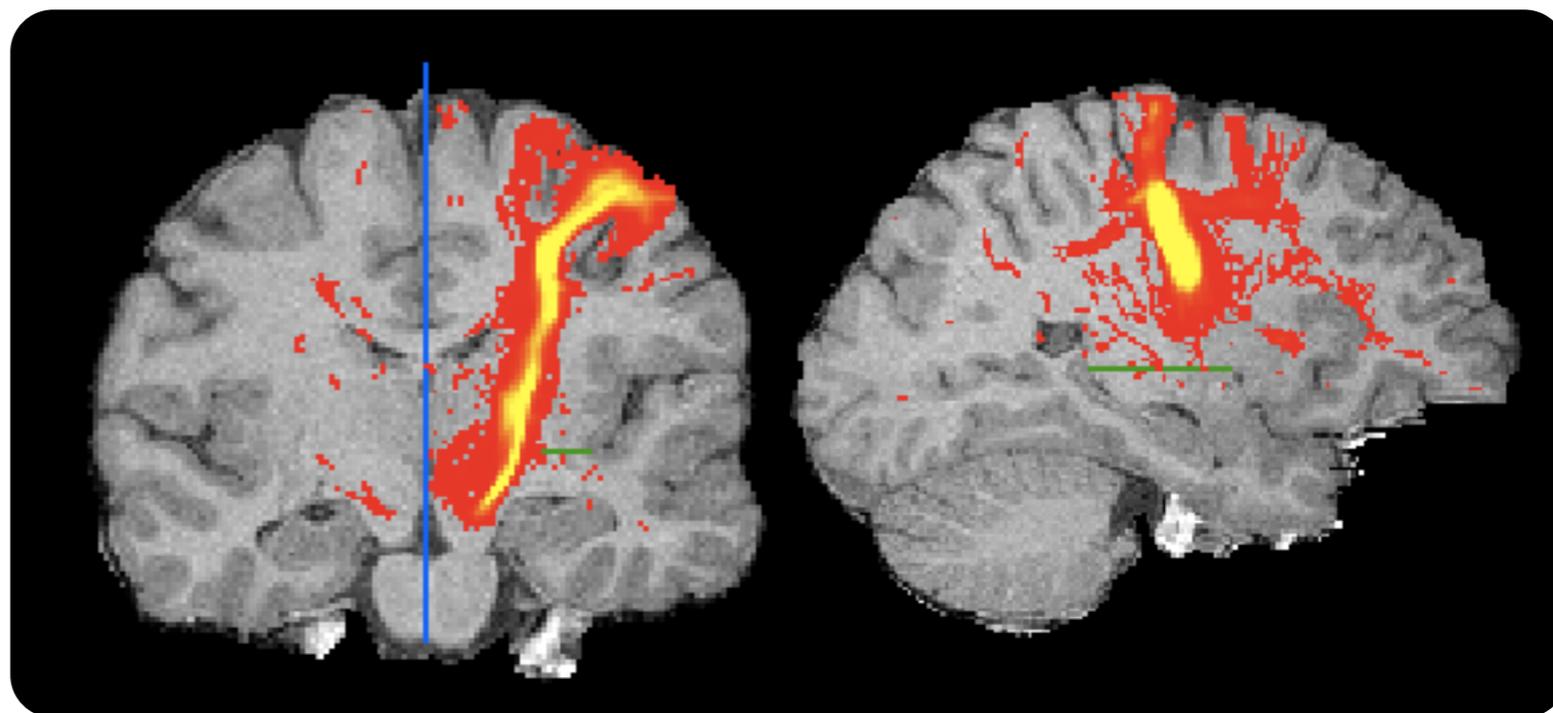
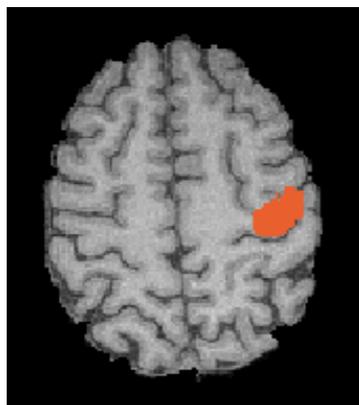




# PROBTRACKX

Dissecting a specific tract  
Cortico-spinal tract

Seed: M1, hand area



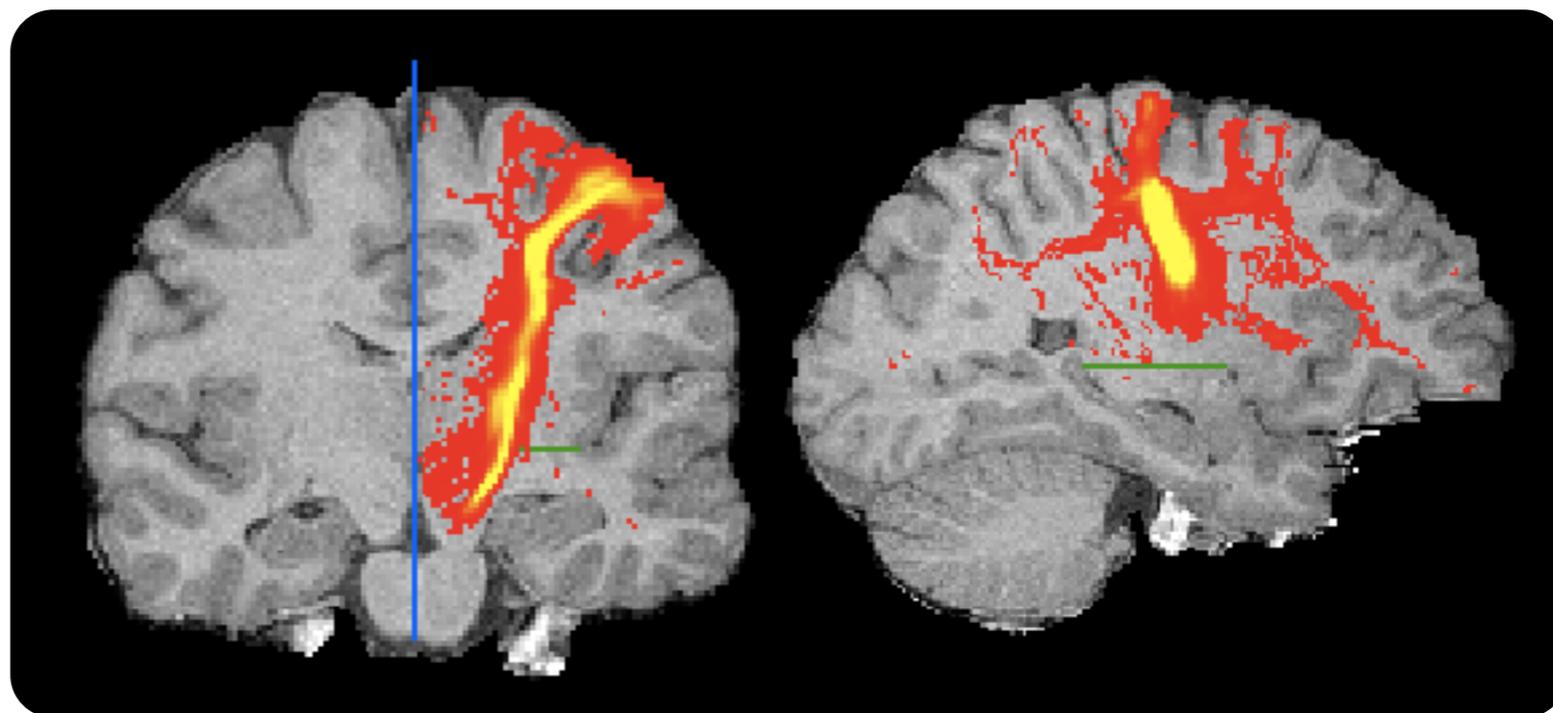
No targets



# PROBTRACKX

Dissecting a specific tract  
Cortico-spinal tract

Seed: M1, hand area



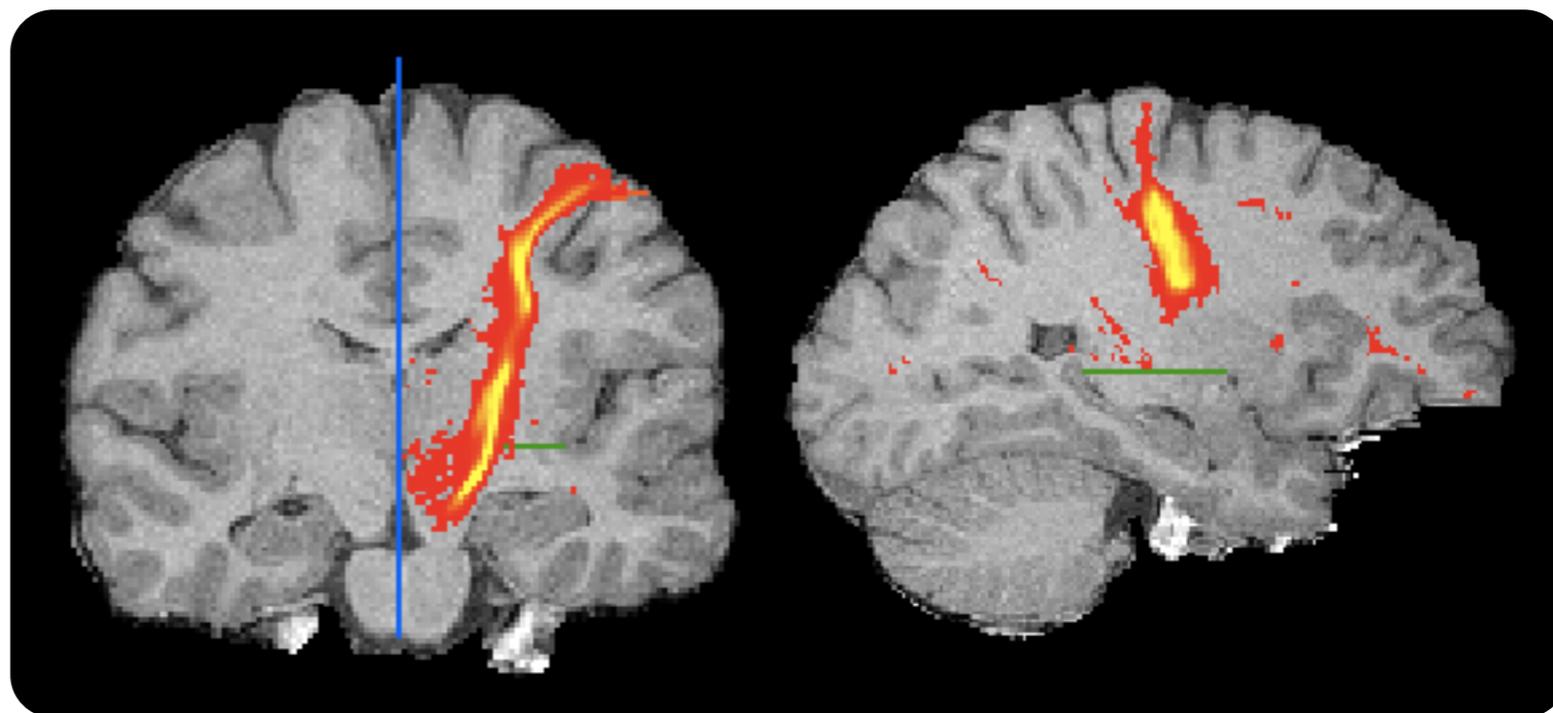
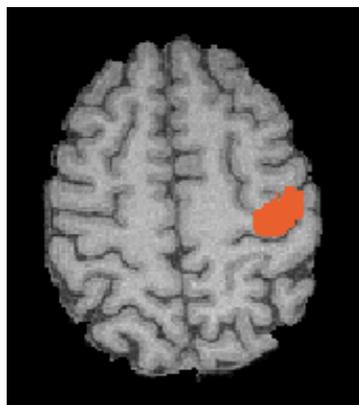
Exclusion: Mid-Sagittal plane



# PROBTRACKX

Dissecting a specific tract  
Cortico-spinal tract

Seed: M1, hand area



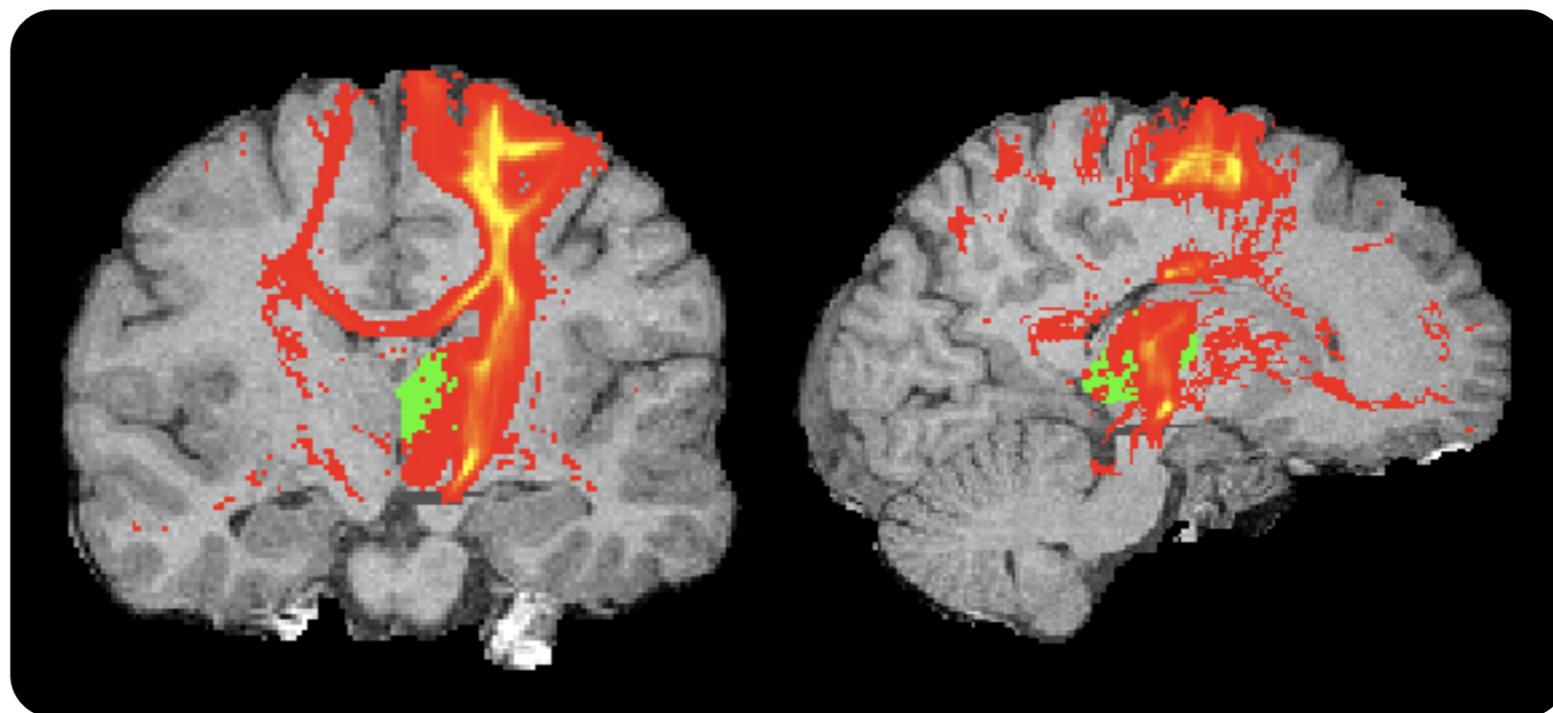
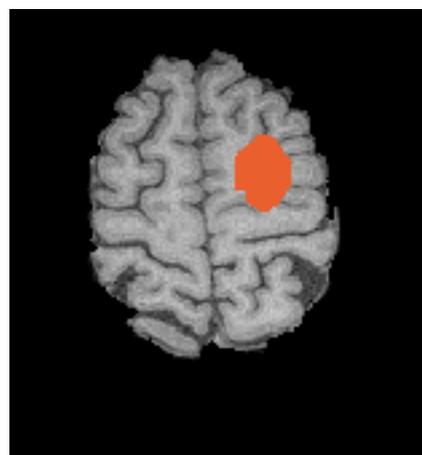
Waypoint: Internal Capsule



# PROBTRACKX

Dissecting a specific tract  
Cortico-spinal tract

Seed: dorsal PMC



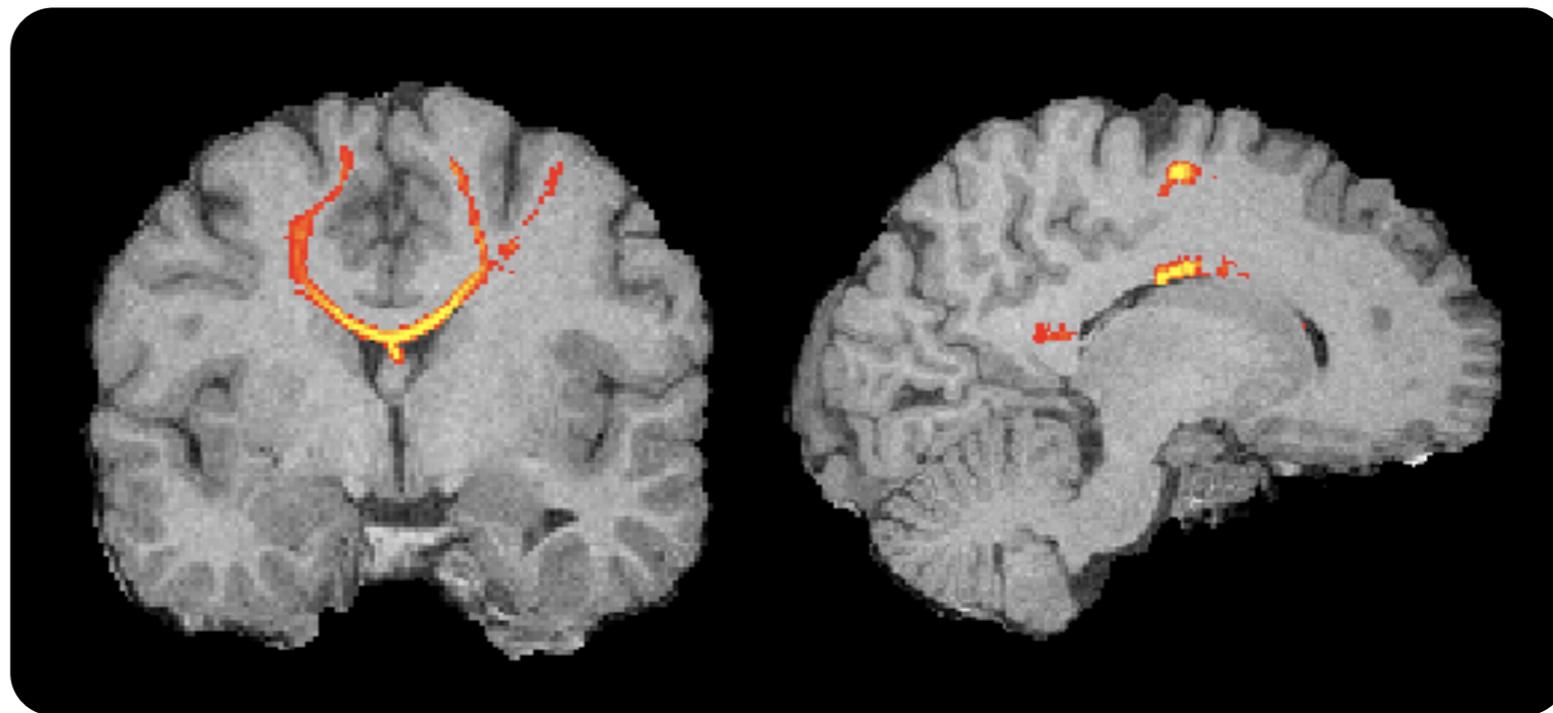
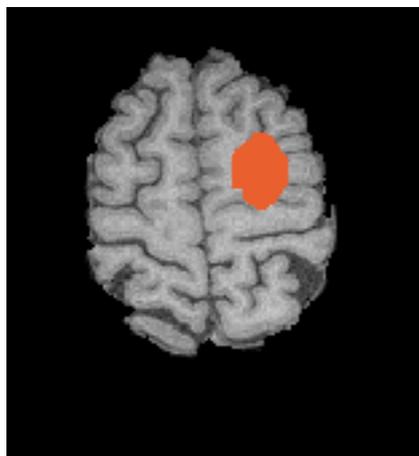
No targets



# PROBTRACKX

Dissecting a specific tract  
Cortico-spinal tract

Seed: dorsal PMC



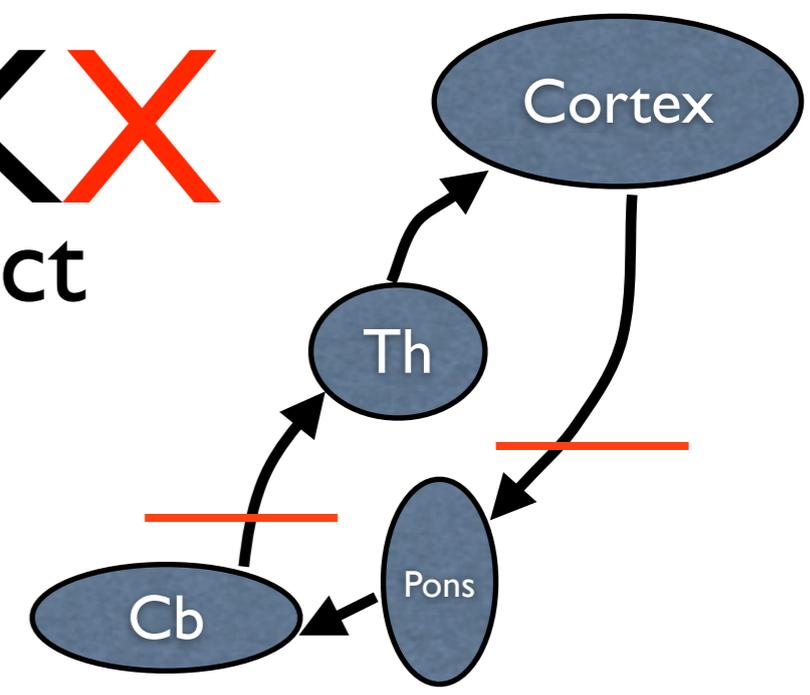
Waypoint: Corpus Callosum



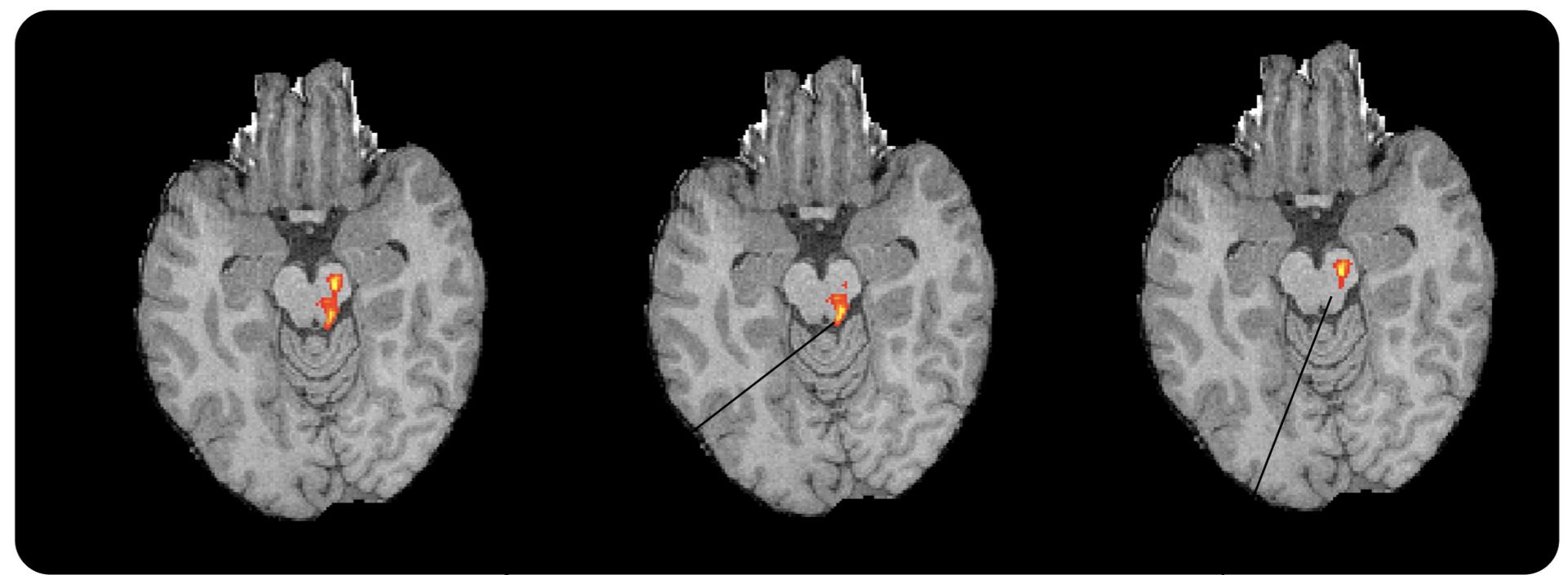
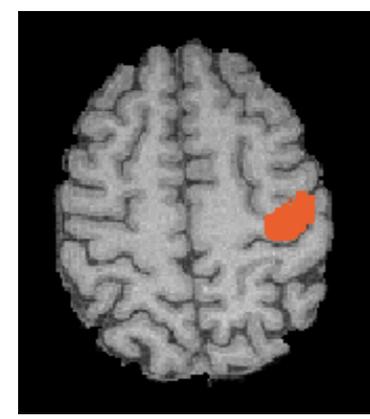
# PROBTRACKX

Dissecting a specific tract

Cortico-cerebellar  
projections



Seed: M1 hand



Waypoint: Thalamus

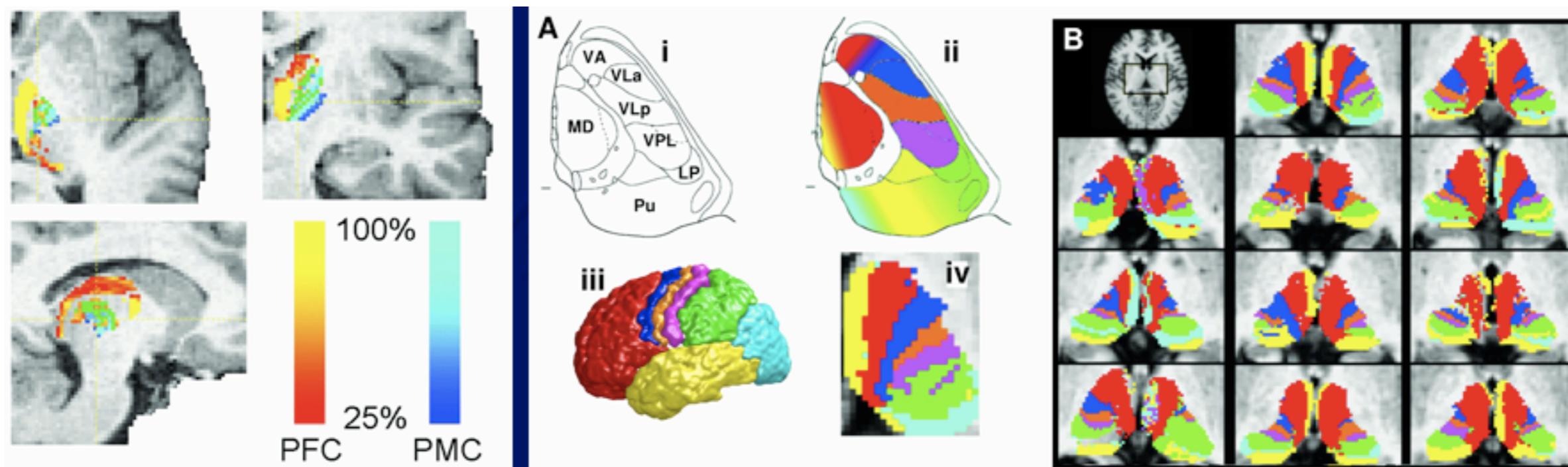
Termination: Thalamus



# PROBTRACKX

## Connectivity-based seed classification

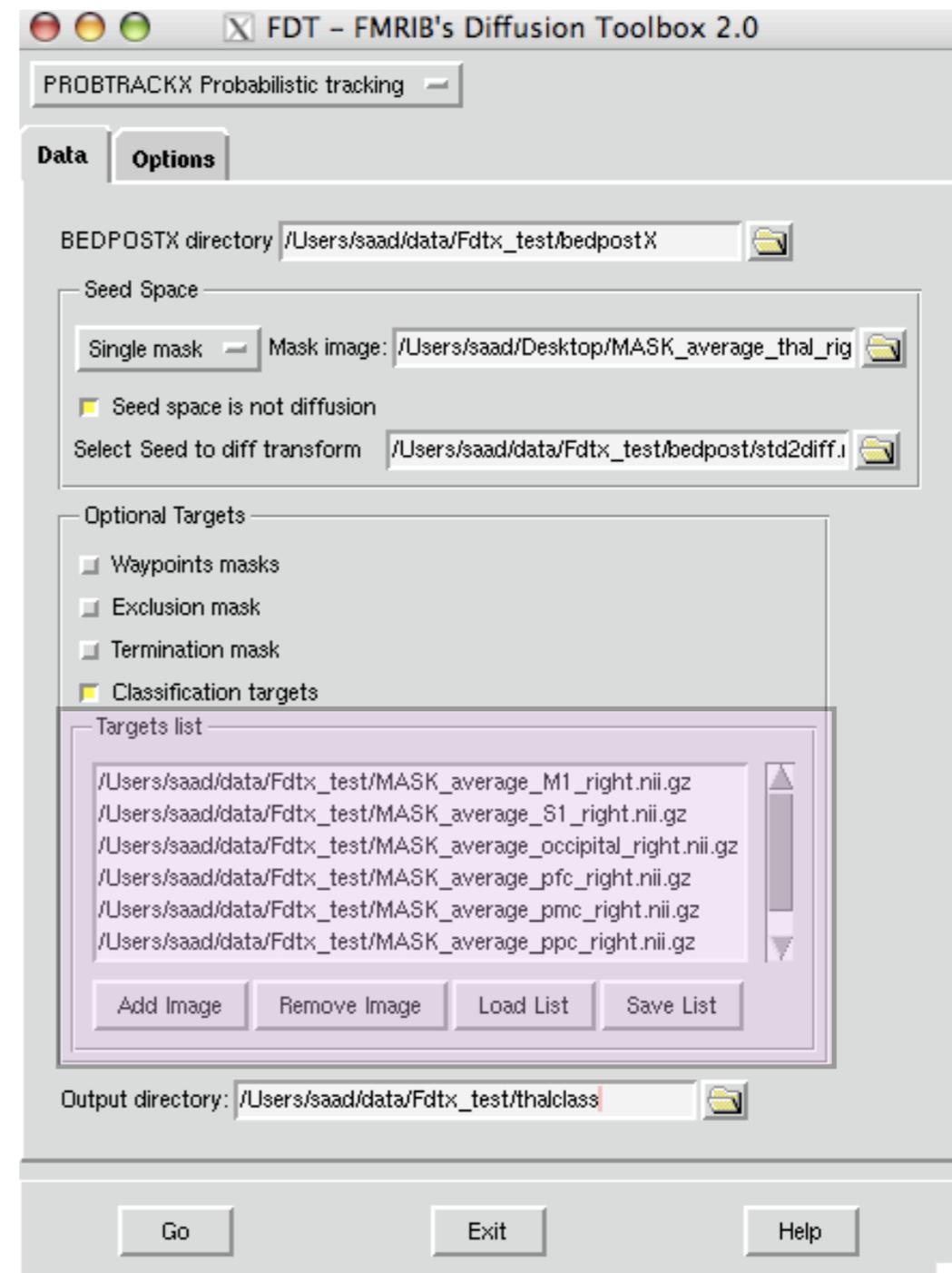
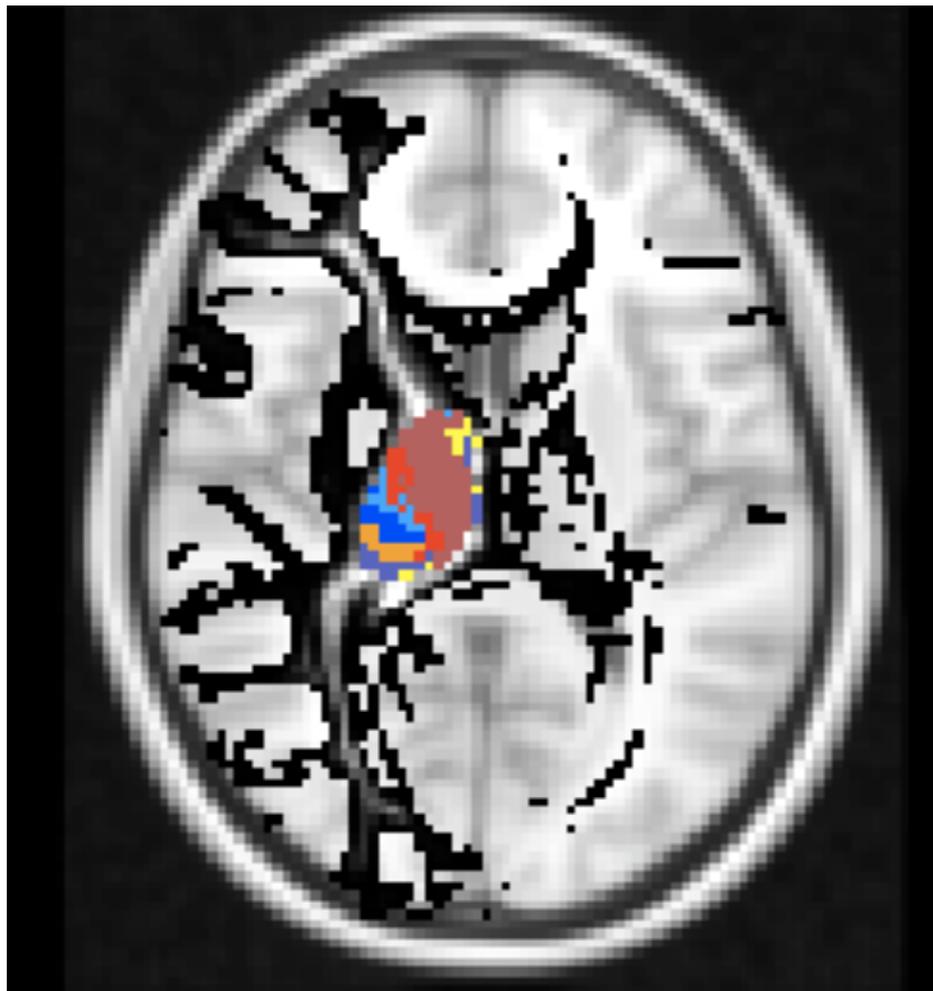
- Quantify the connectivity of seed regions to target regions
- e.g. thalamic voxels can be classified according to their probability of connection to specific cortical targets





# PROBTRACKX

Connectivity-based seed classification  
Thalamic segmentation





# Discussion

## What are we (not) measuring?

- Distribution of a fibre orientation rather than distribution of fibre orientations
- Thresholding tract distribution is tricky
- Bins (voxels) are arbitrary
- Favour seed classification for quantitative analysis (masks are meaningful)



# FMRIB Diffusion Toolbox

- DTI model fit
- Eddy current correction
- Voxel-Based diffusion analysis (TBSS)
- BEDPOSTX modelling crossing fibres
- PROBTRACKX propagating uncertainty in tractography

