



Diffusion MRI Analysis

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Harvard University

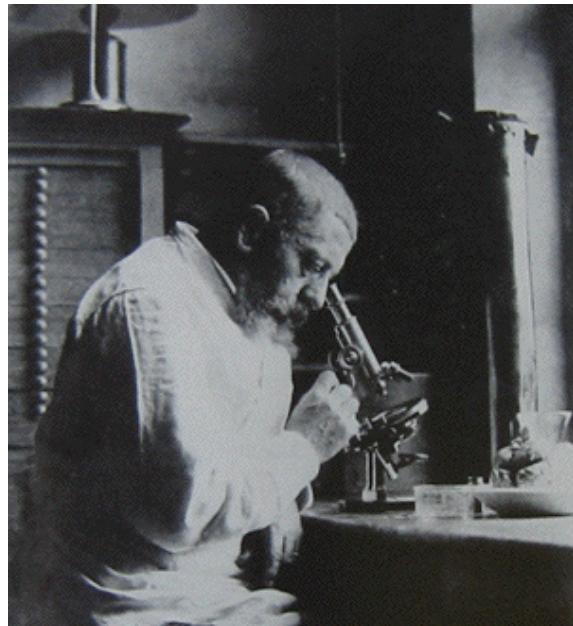
Director of Training, National Alliance
for Medical Image Computing

Brain Anatomy



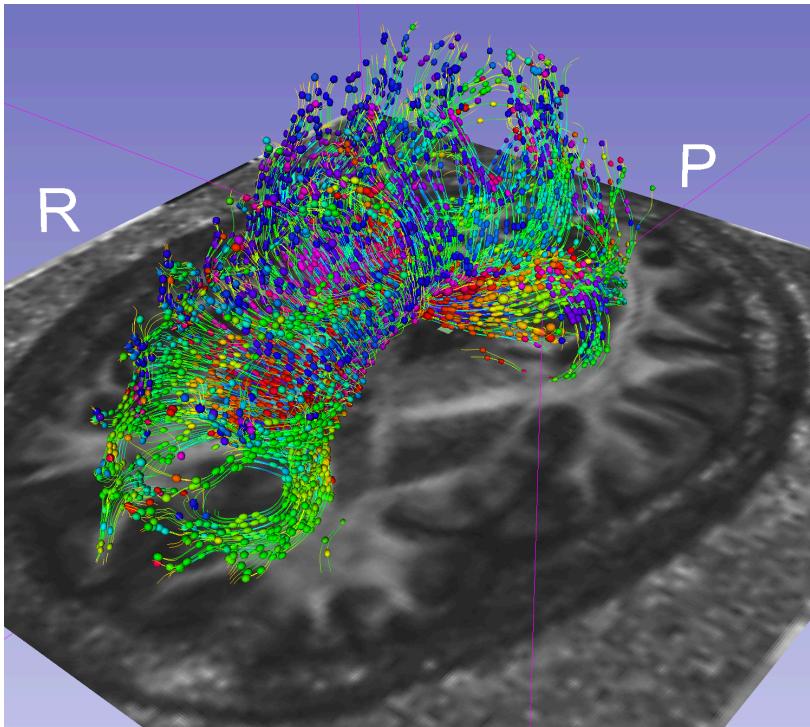
- White matter ~45% of the brain
- Myelinated nerve fibers (~ 10 μm axon diameter)

White Matter Exploration



Jules Joseph Dejerine (*Anatomie des centres nerveux* (Paris, 1890-1901): Atlas of Neuroanatomy based on myelin stained preparation

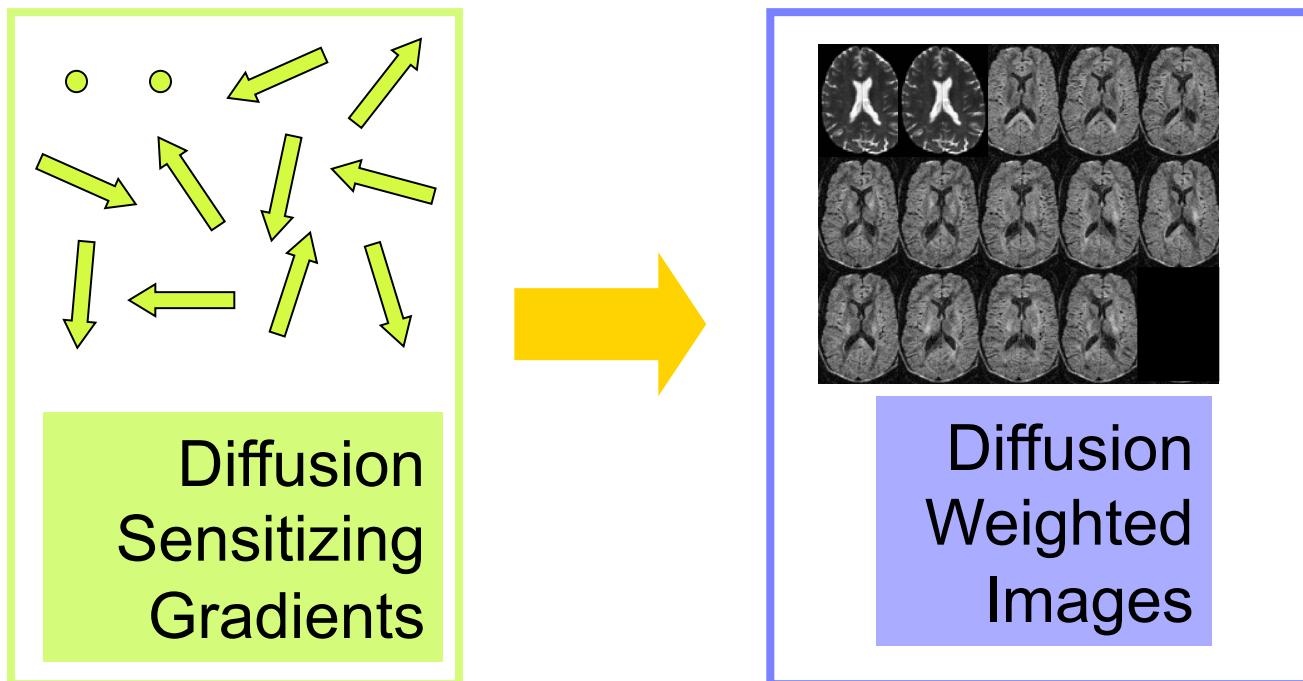
Tutorial Outline



This tutorial is an introduction to the fundamentals of Diffusion MRI analysis, from the estimation of diffusion tensors to the interactive 3D visualization of fiber tracts.

Tutorial dataset

The tutorial dataset is a Diffusion Weighted MR scan of the brain acquired with 42 gradient directions and one baseline.

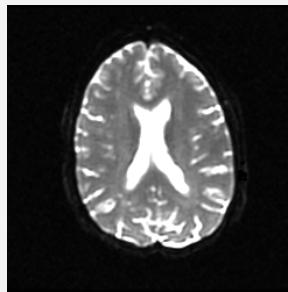


Learning Objectives

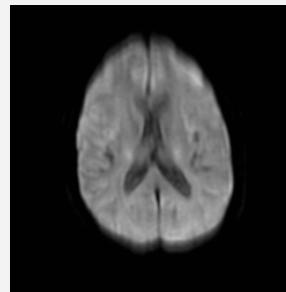
Following this tutorial, you'll be able to

- 1) Estimate a tensor volume from a set of Diffusion Weighted Images
- 2) Understand the shape and size of the diffusion ellipsoid
- 3) Reconstruct DTI tracts from a pre-defined region of interest
- 4) Interactively visualize DTI tracts seeded from a fiducial

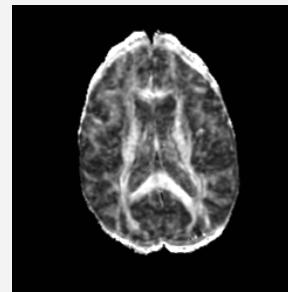
MR Diffusion Analysis Pipeline



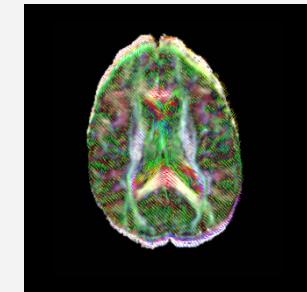
DWI
Acquisition



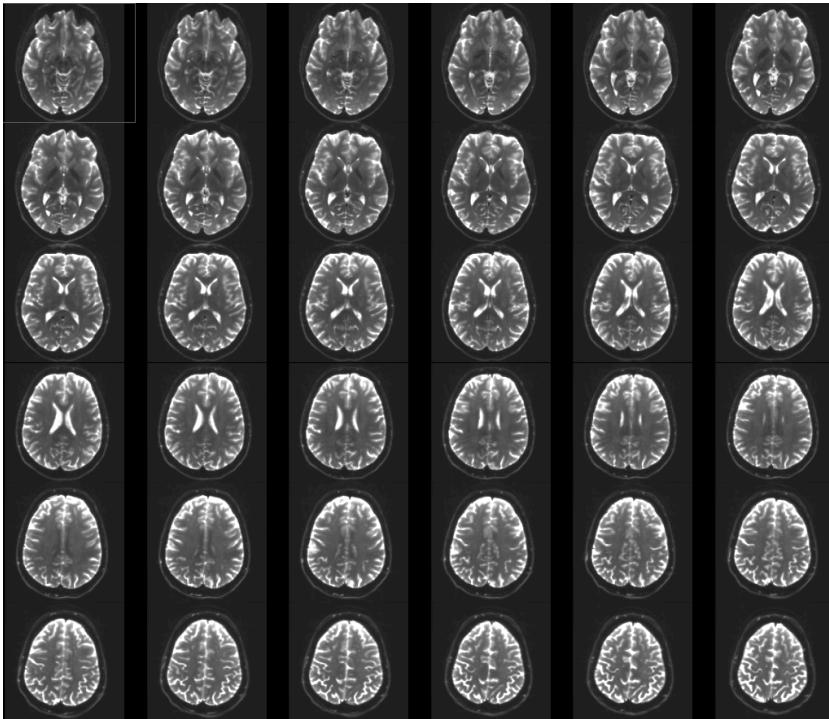
Tensor
Calculation



Scalar
Maps

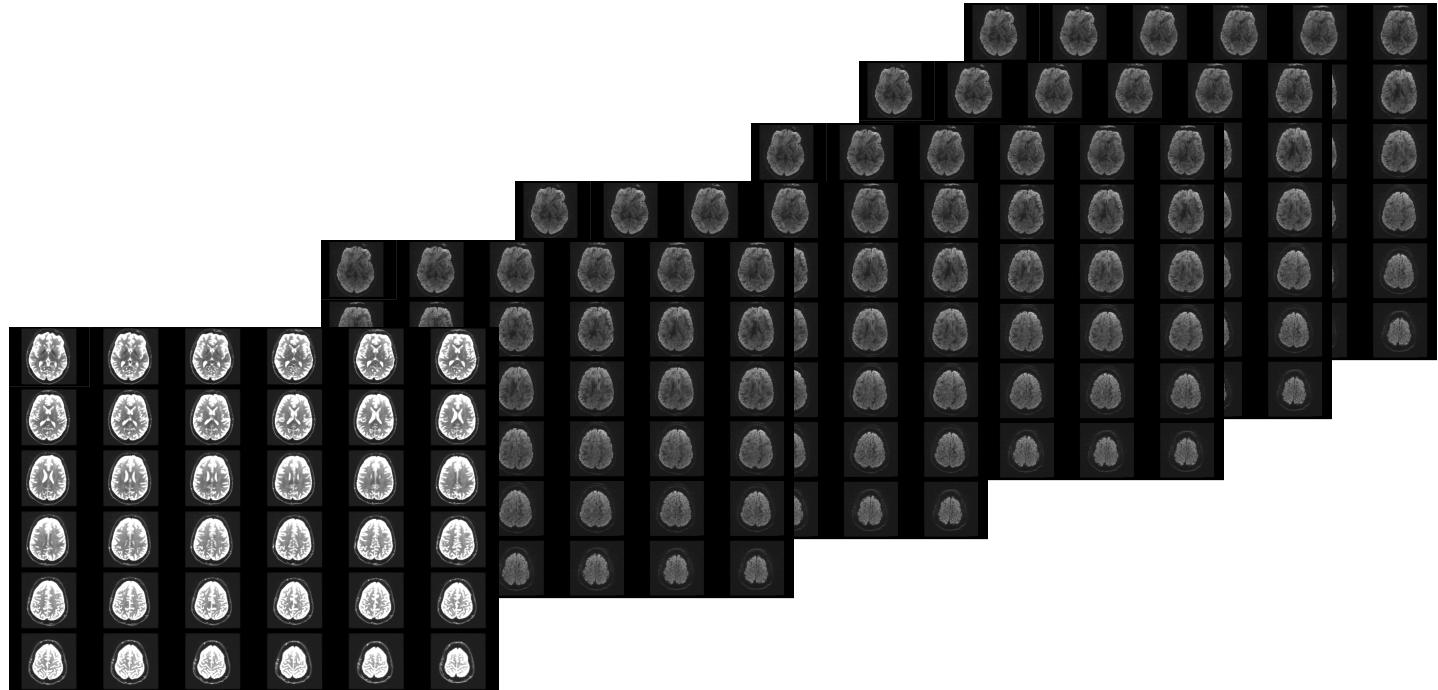


3D
Visualization



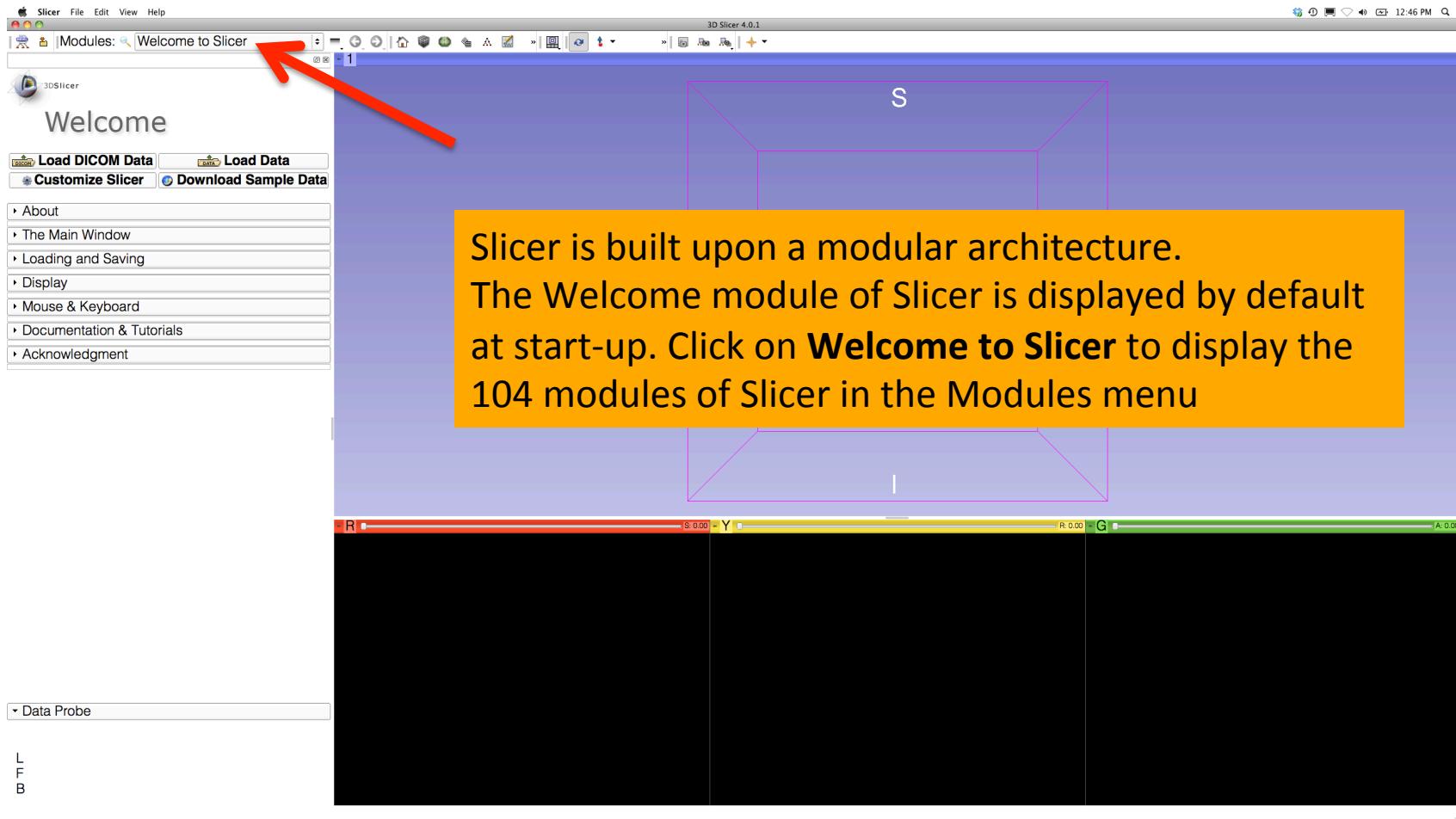
Part 1: From DWI images to Tensors

Understanding the DWI dataset

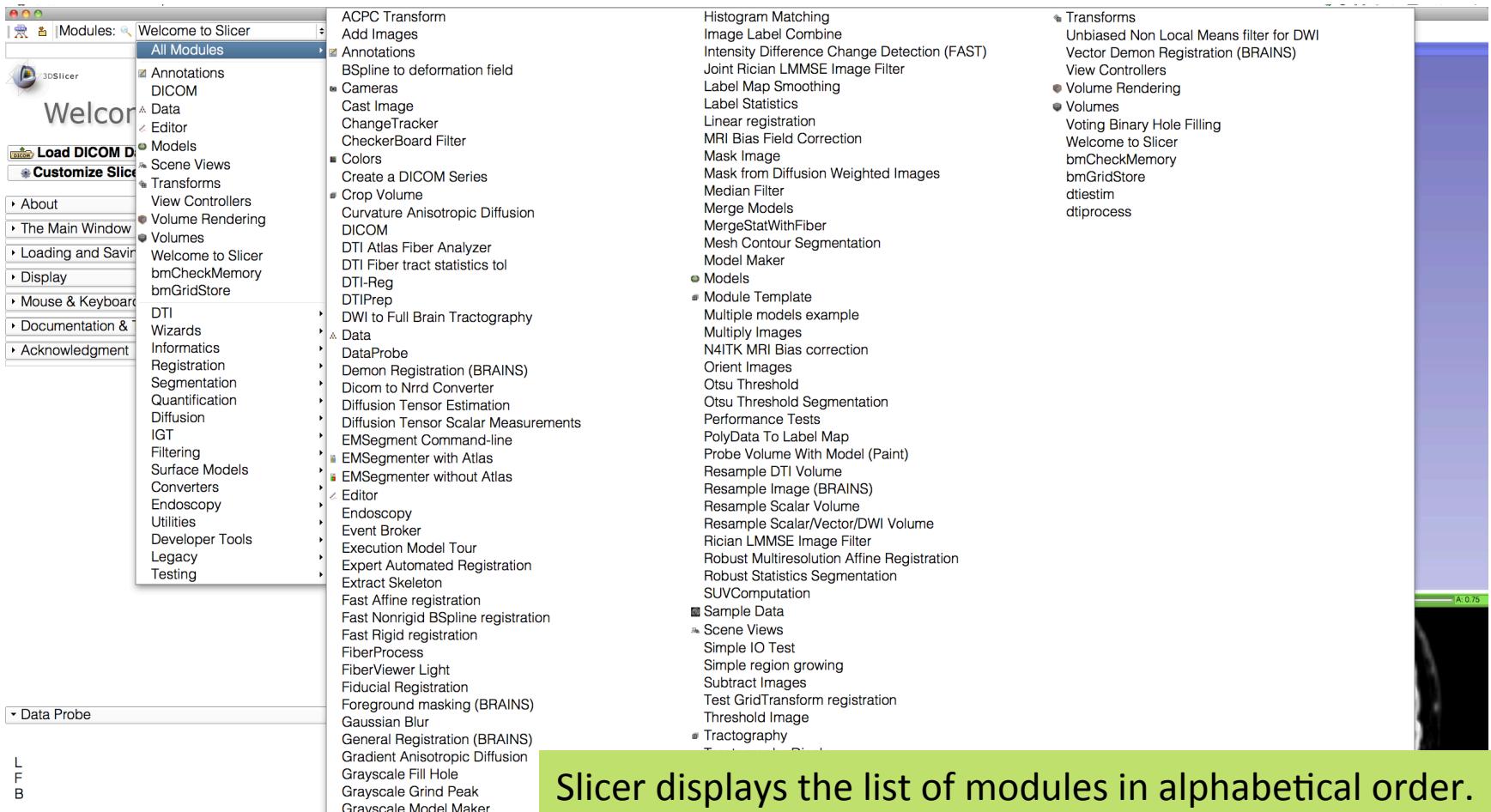


The DWI dataset is composed of one volume acquired without diffusion-sensitizing gradient, and 42 volumes acquired with 42 different diffusion-sensitizing gradients.

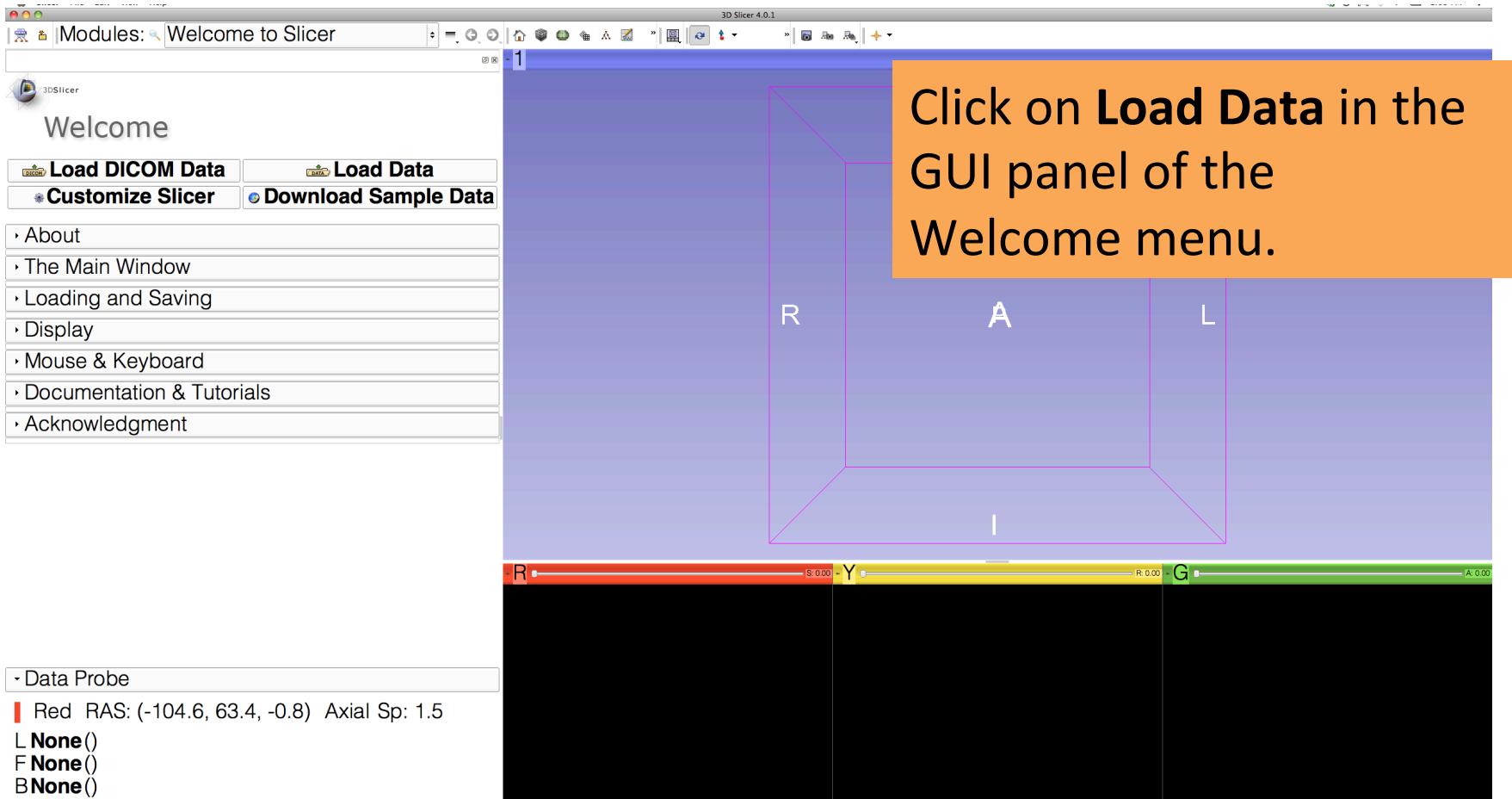
Loading the DWI dataset



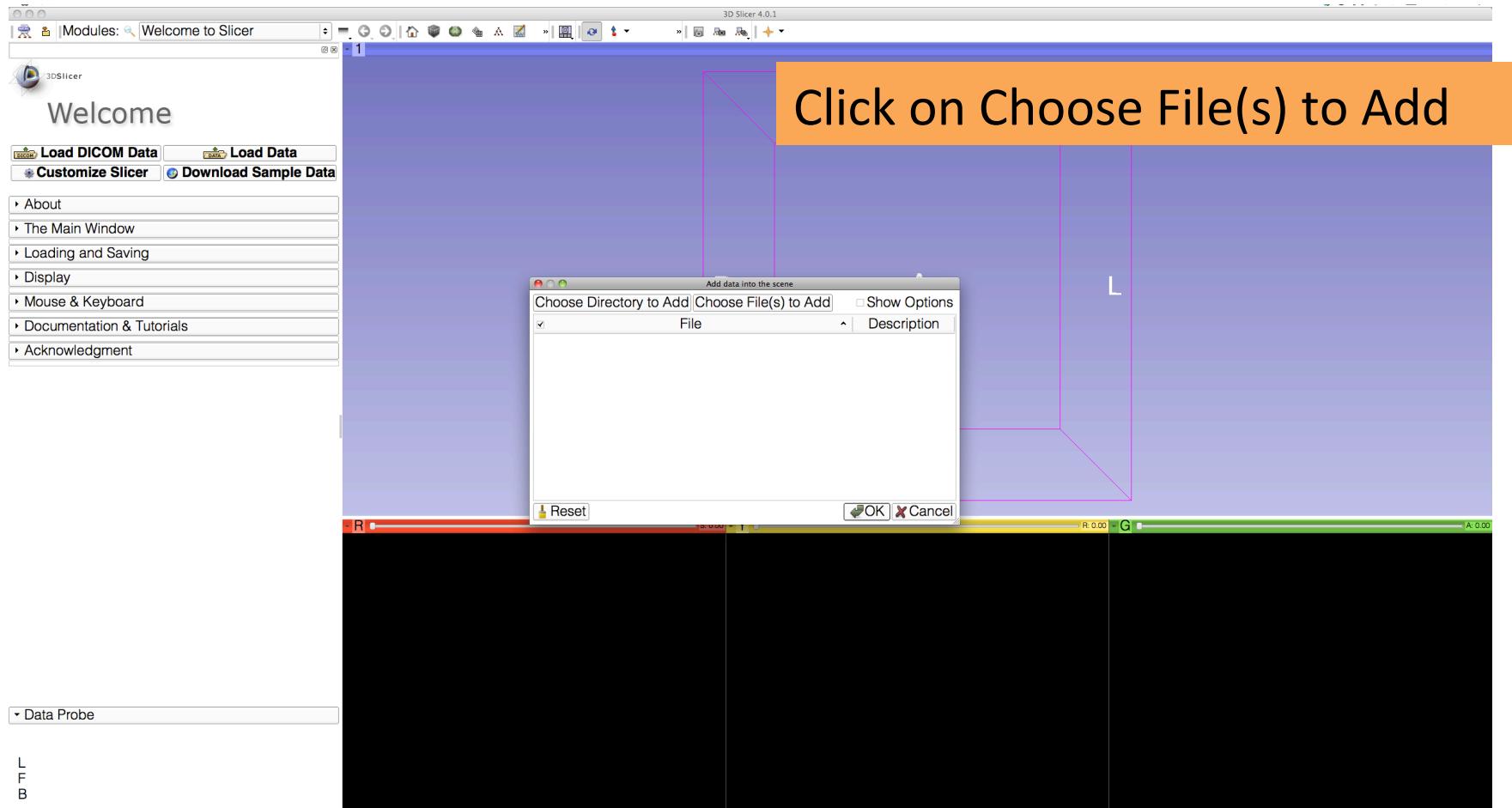
Start the Slicer software



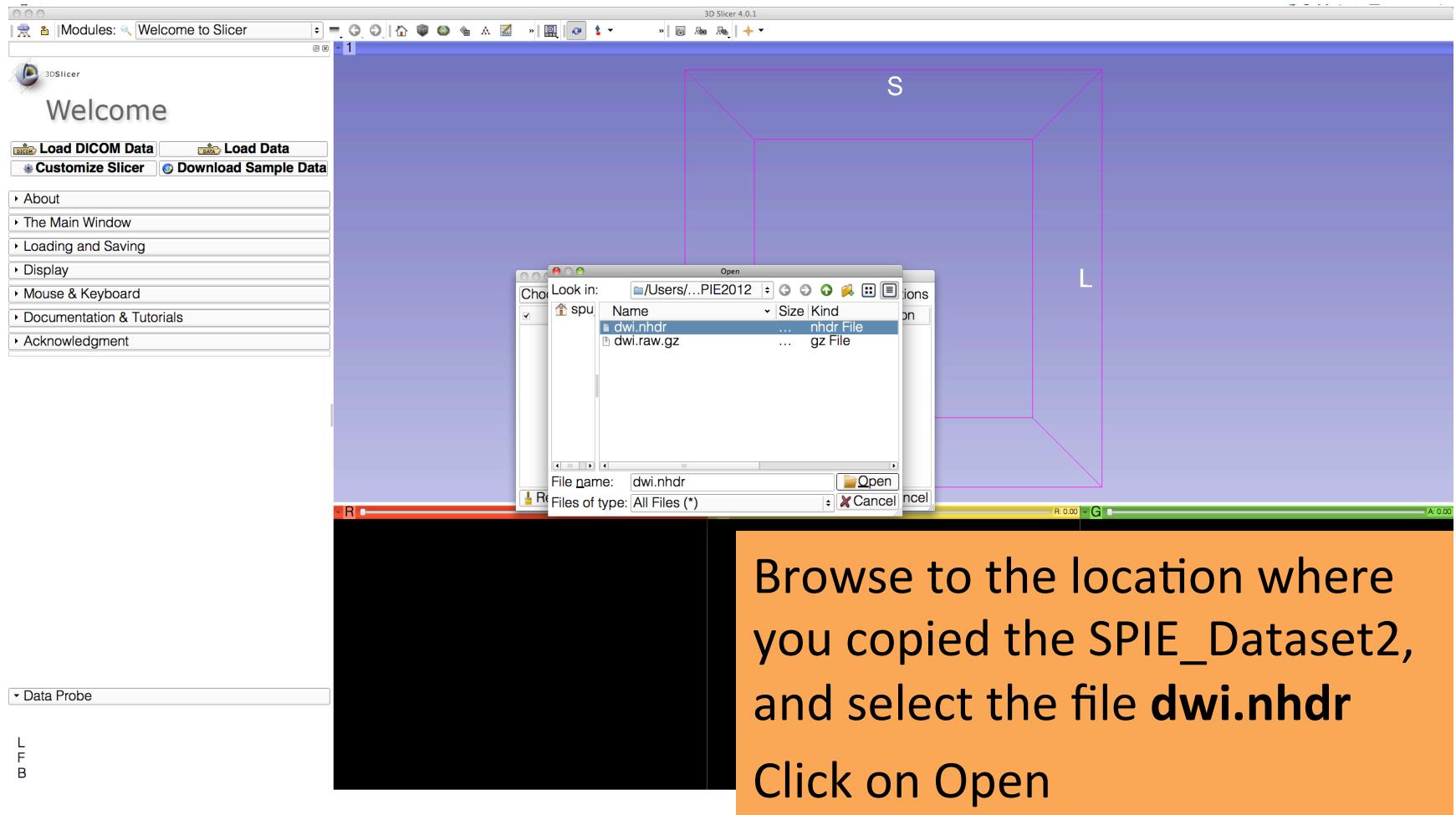
Loading the DWI dataset



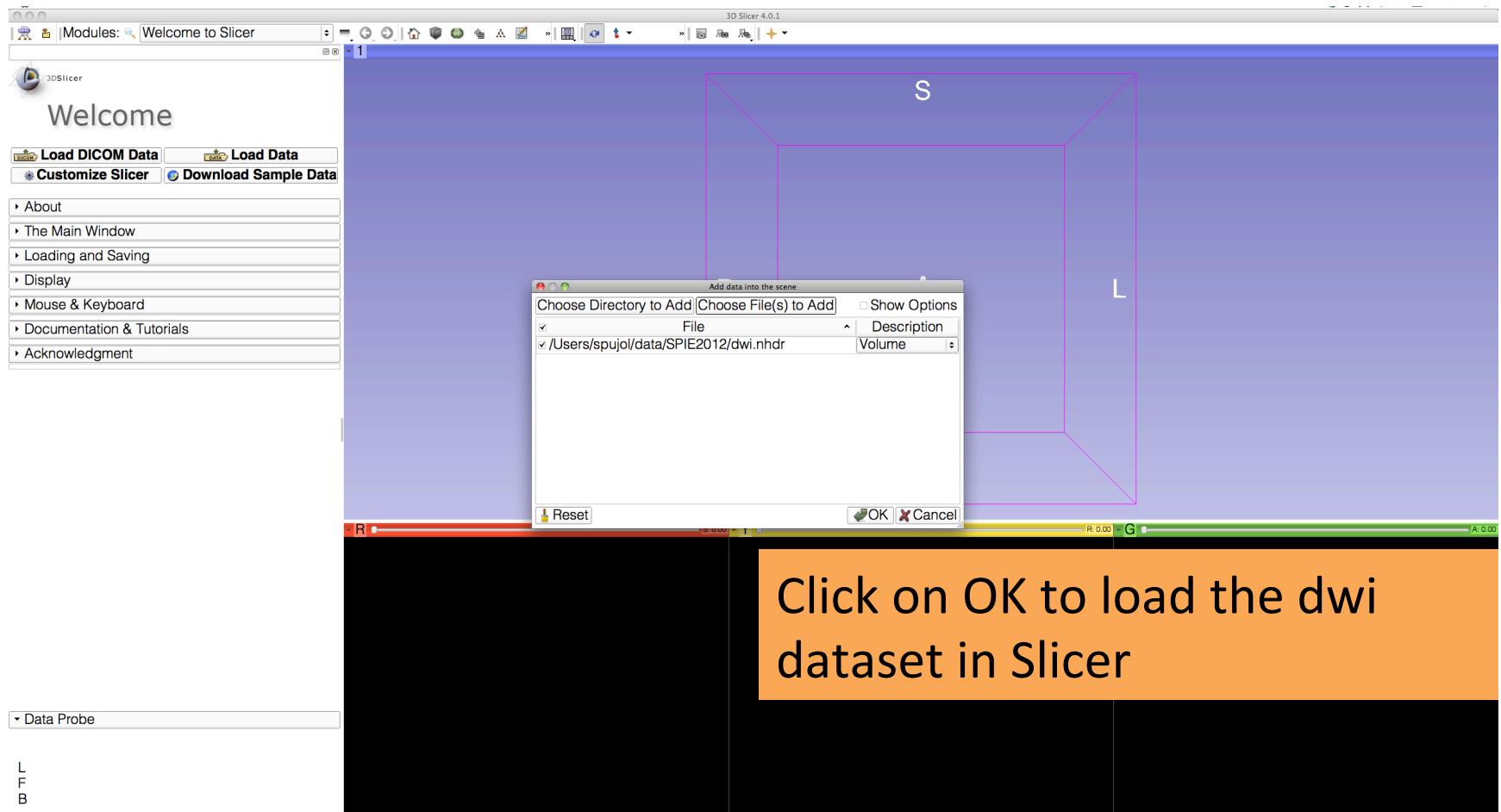
Loading the DWI dataset



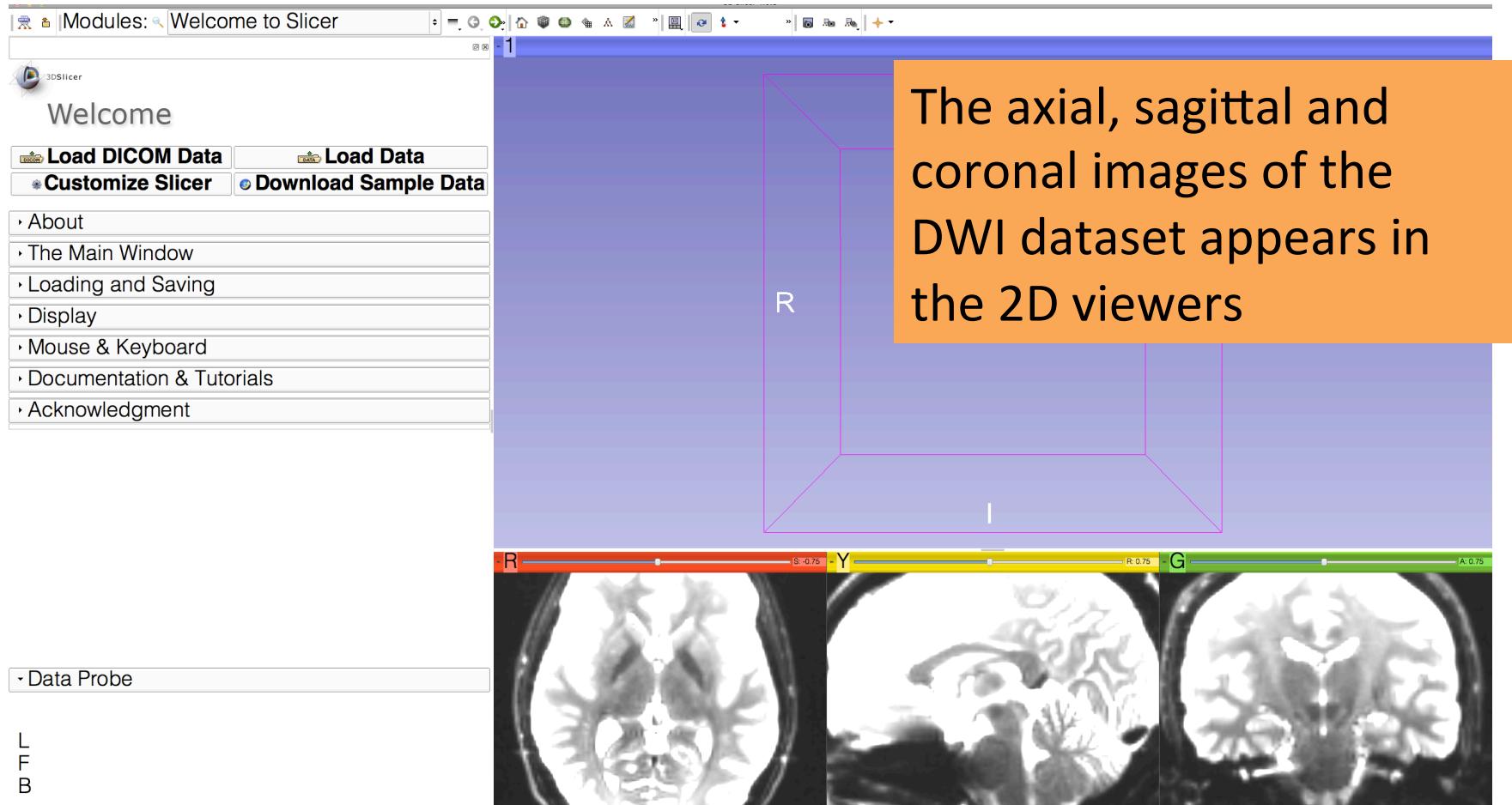
Loading the DWI dataset



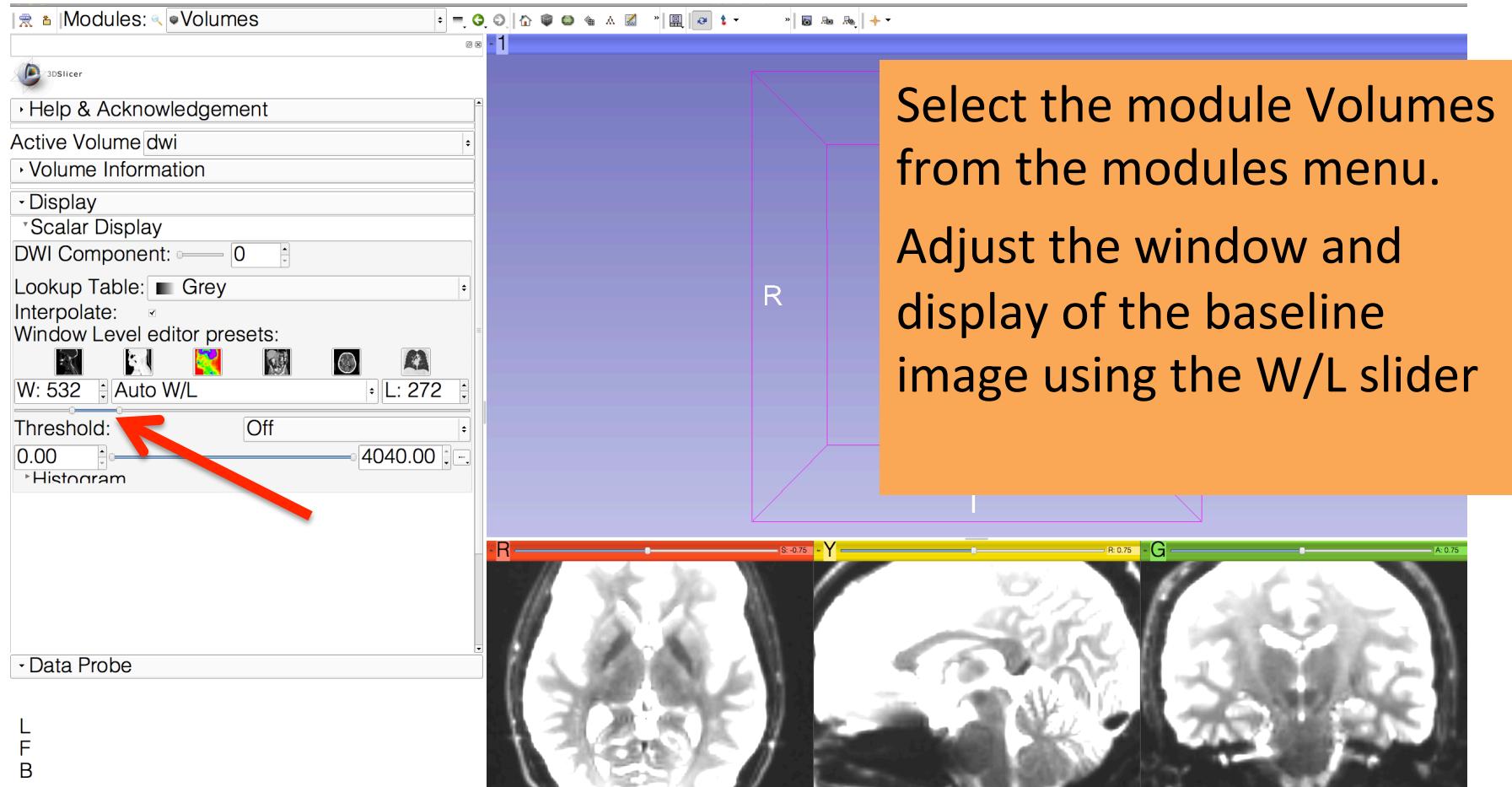
Loading the DWI dataset



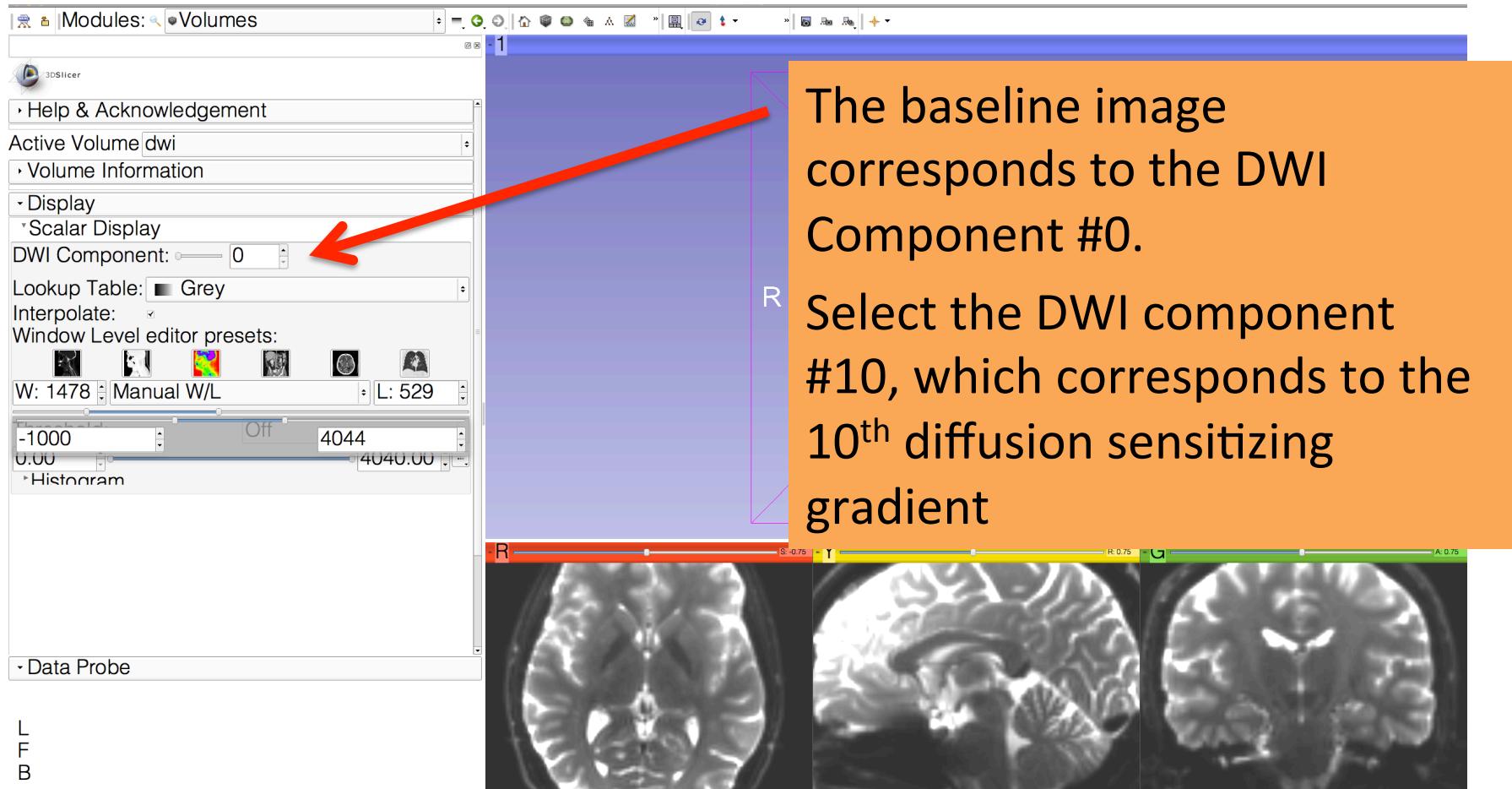
Loading the DWI dataset



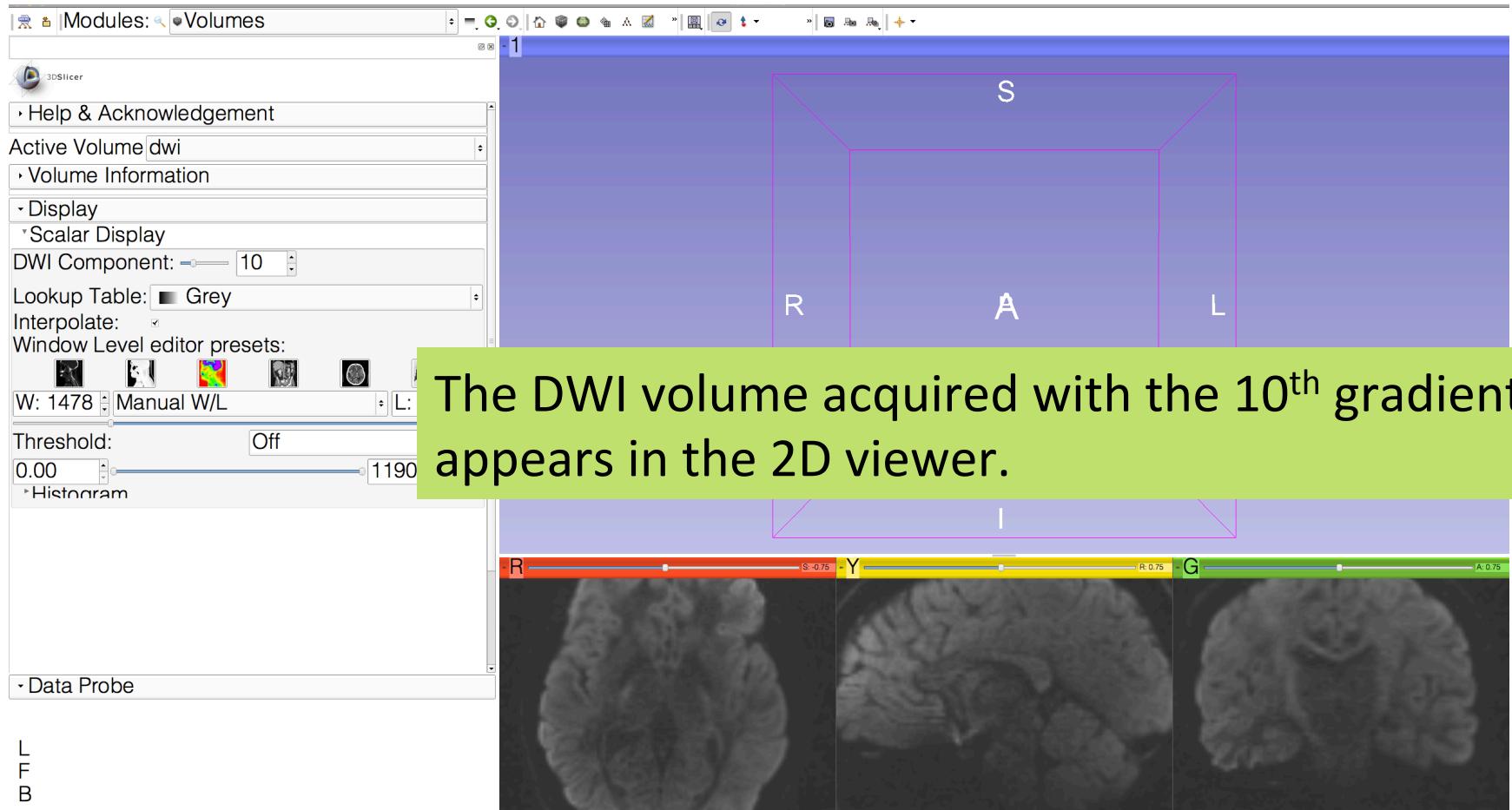
Adjusting Window and Level



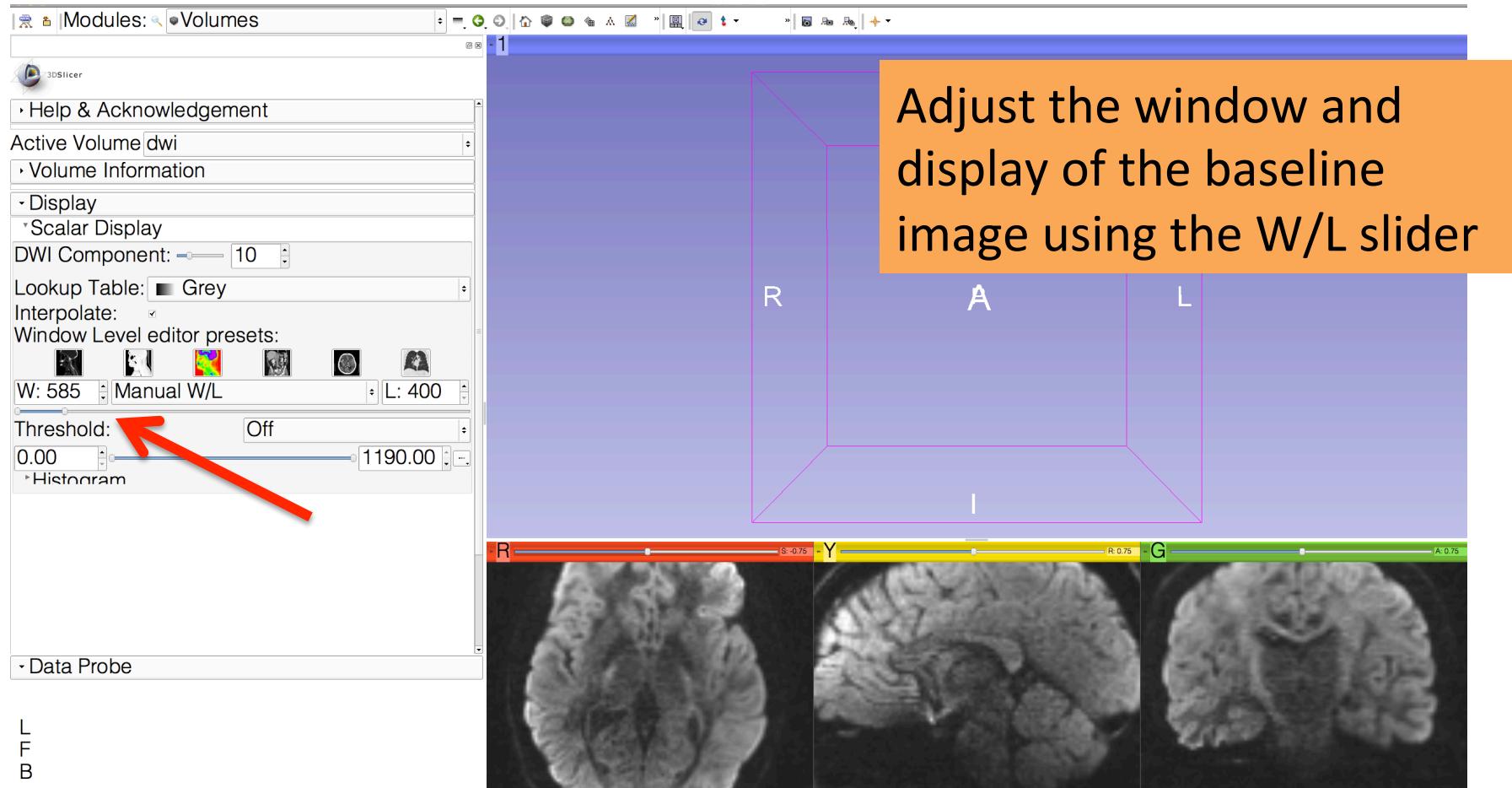
Exploring the DWI dataset



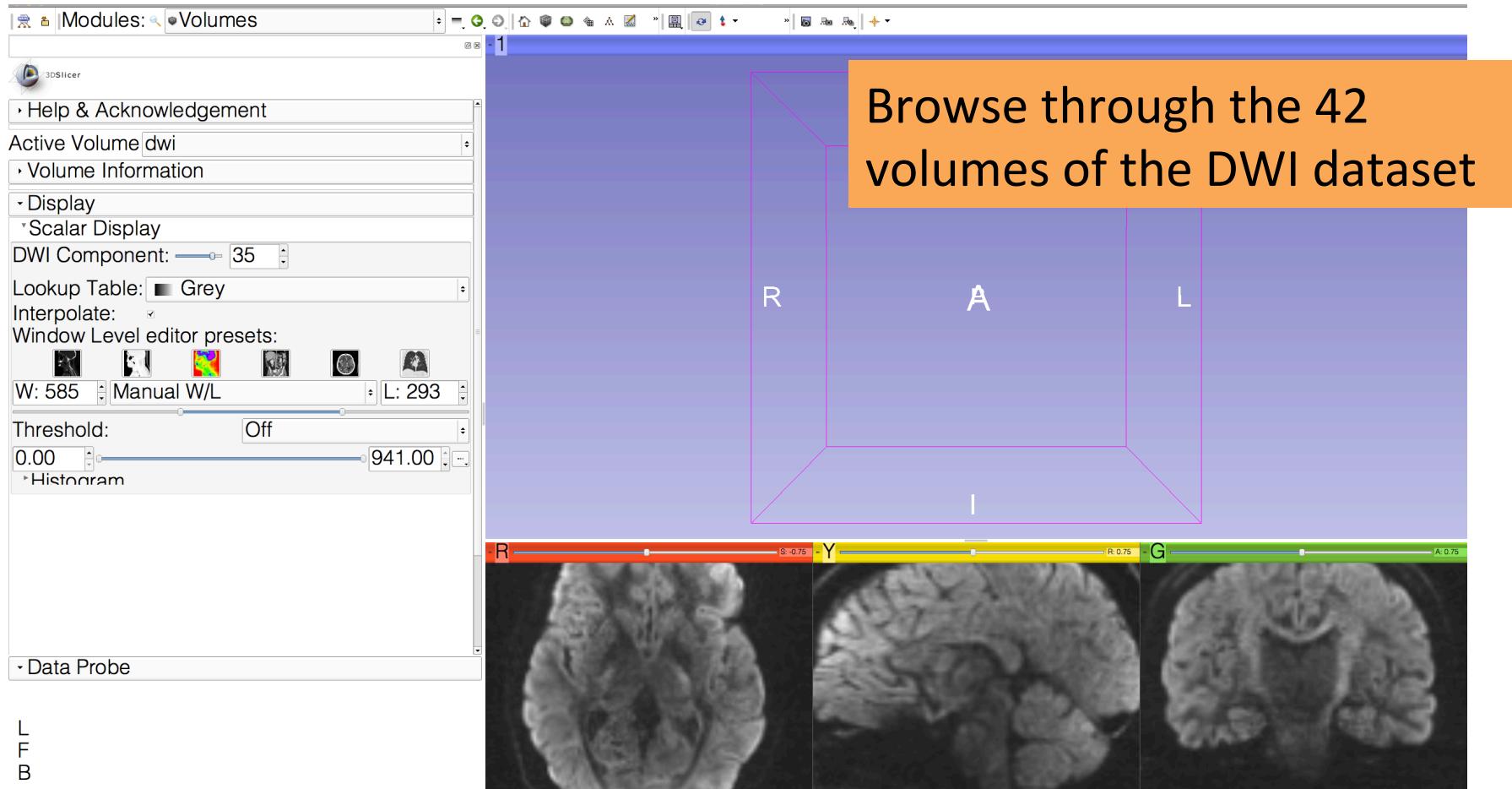
Exploring the DWI dataset



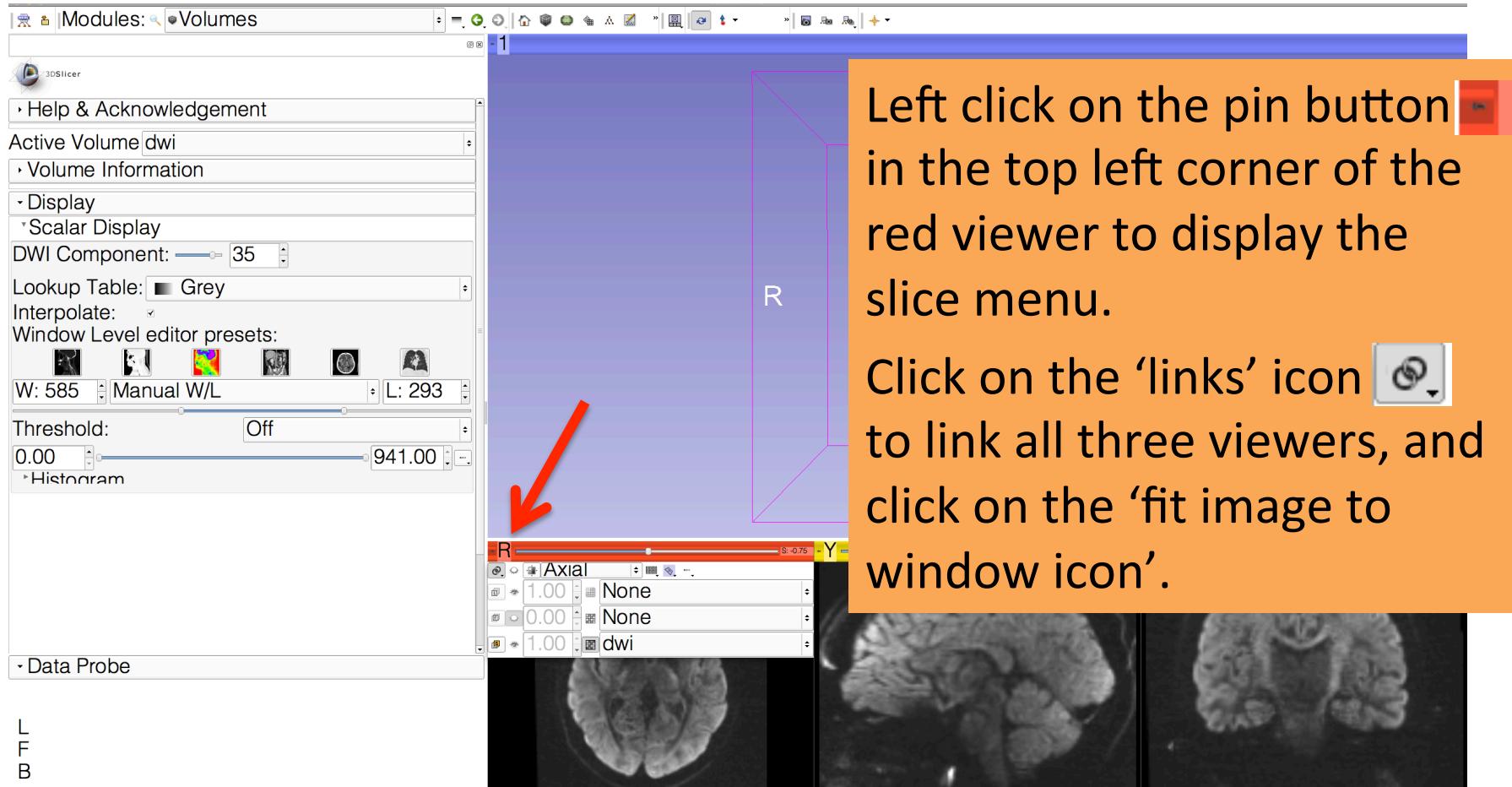
Exploring the DWI dataset



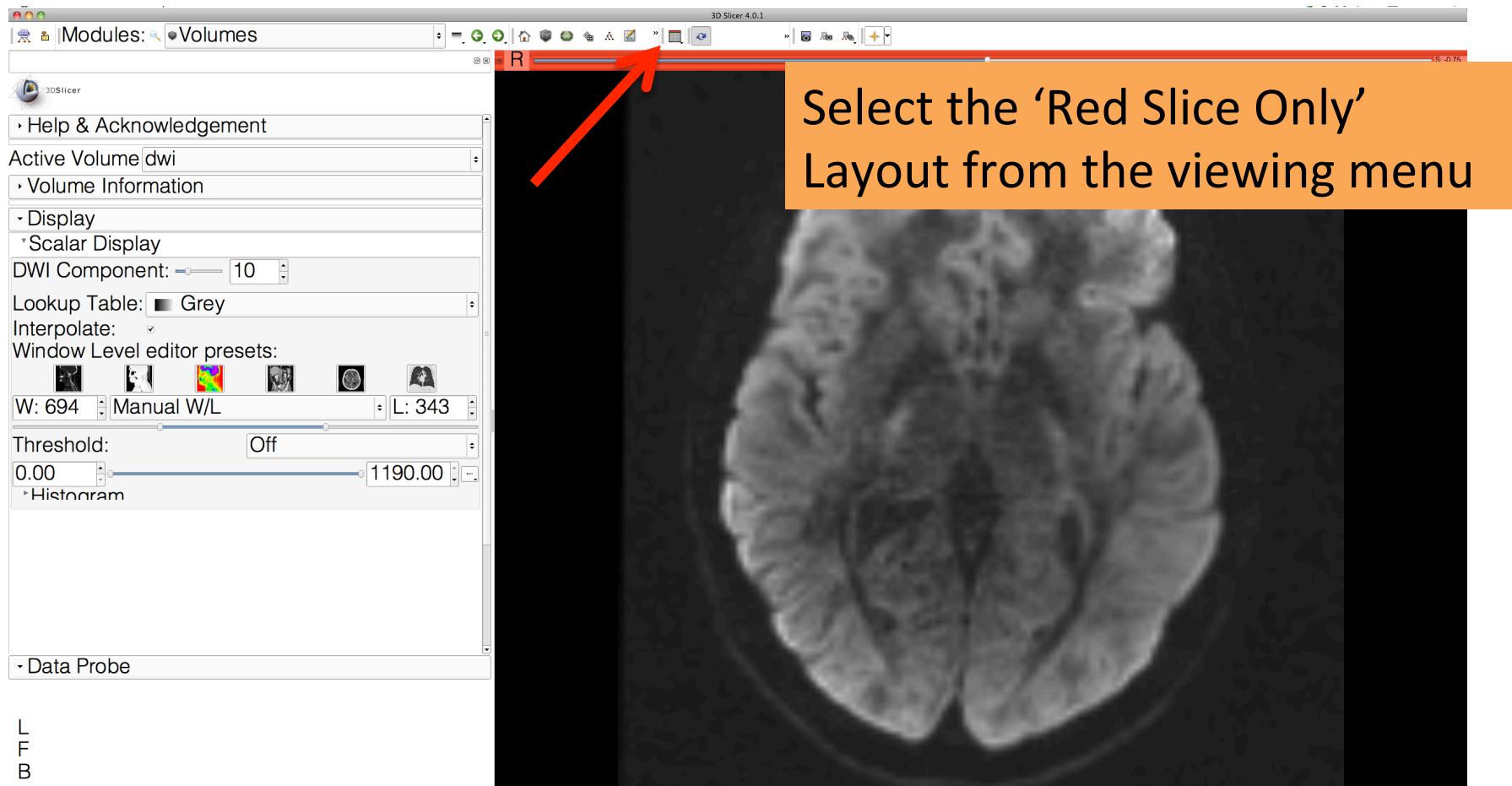
Exploring the DWI dataset



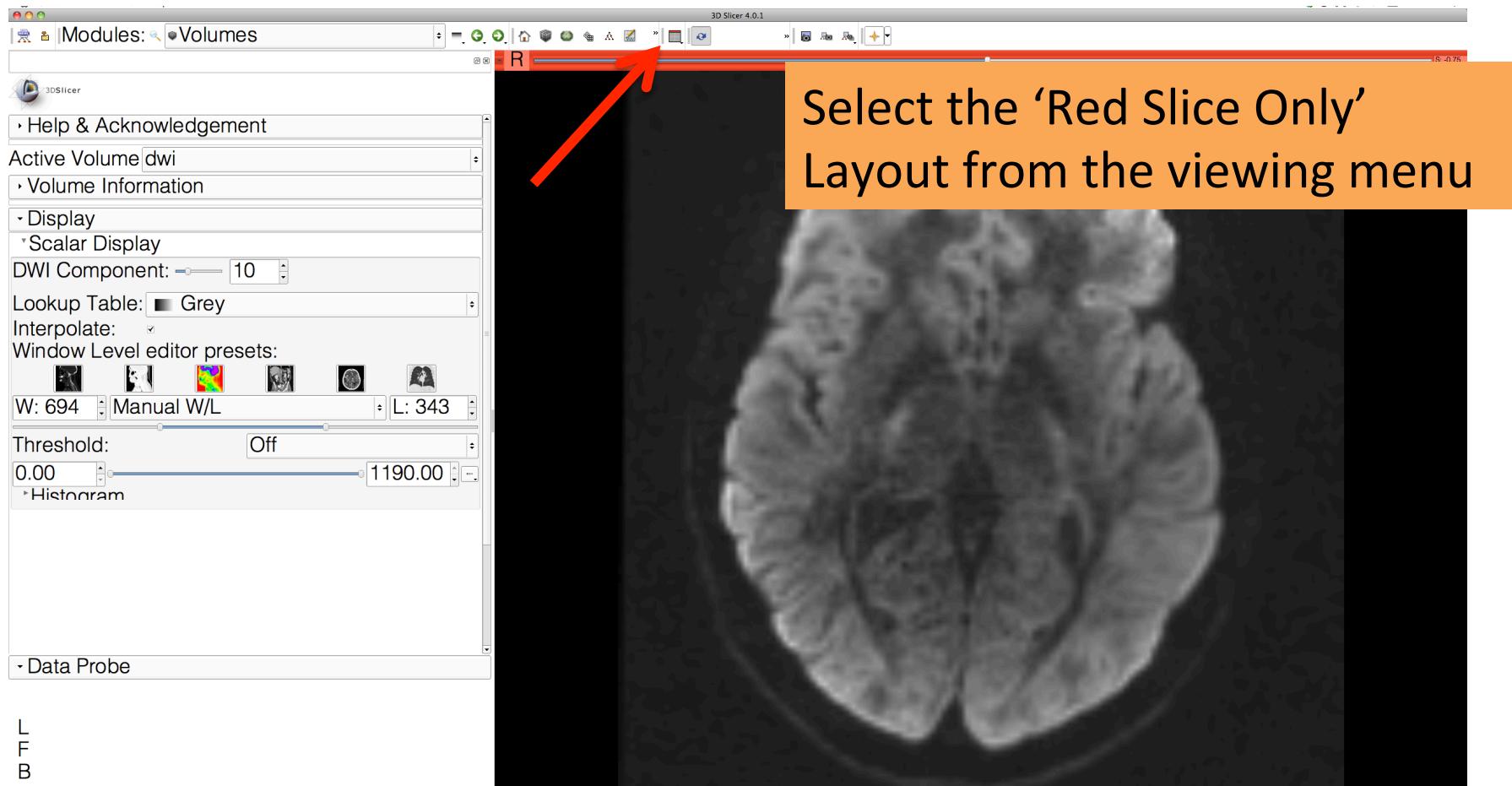
Exploring the DWI dataset



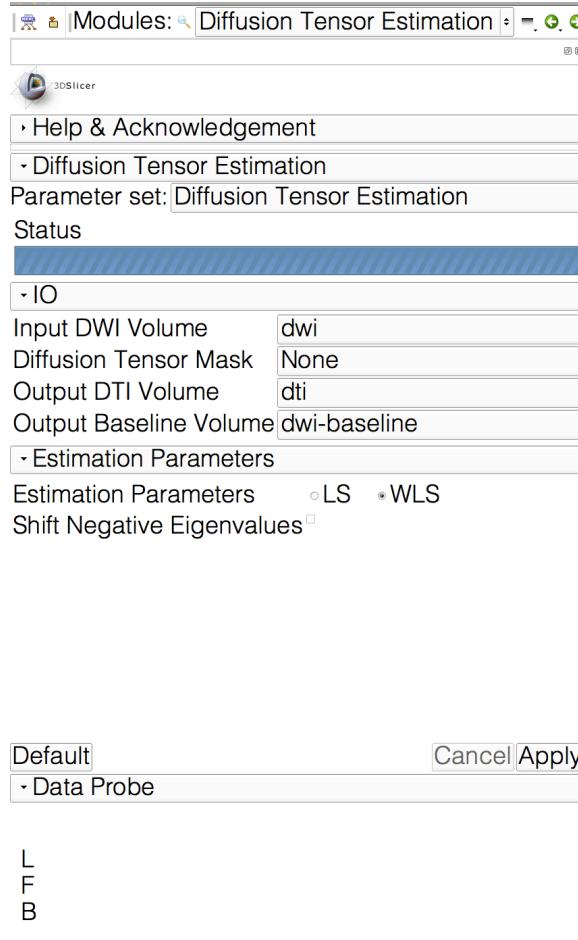
Exploring the DWI dataset



Exploring the DWI dataset



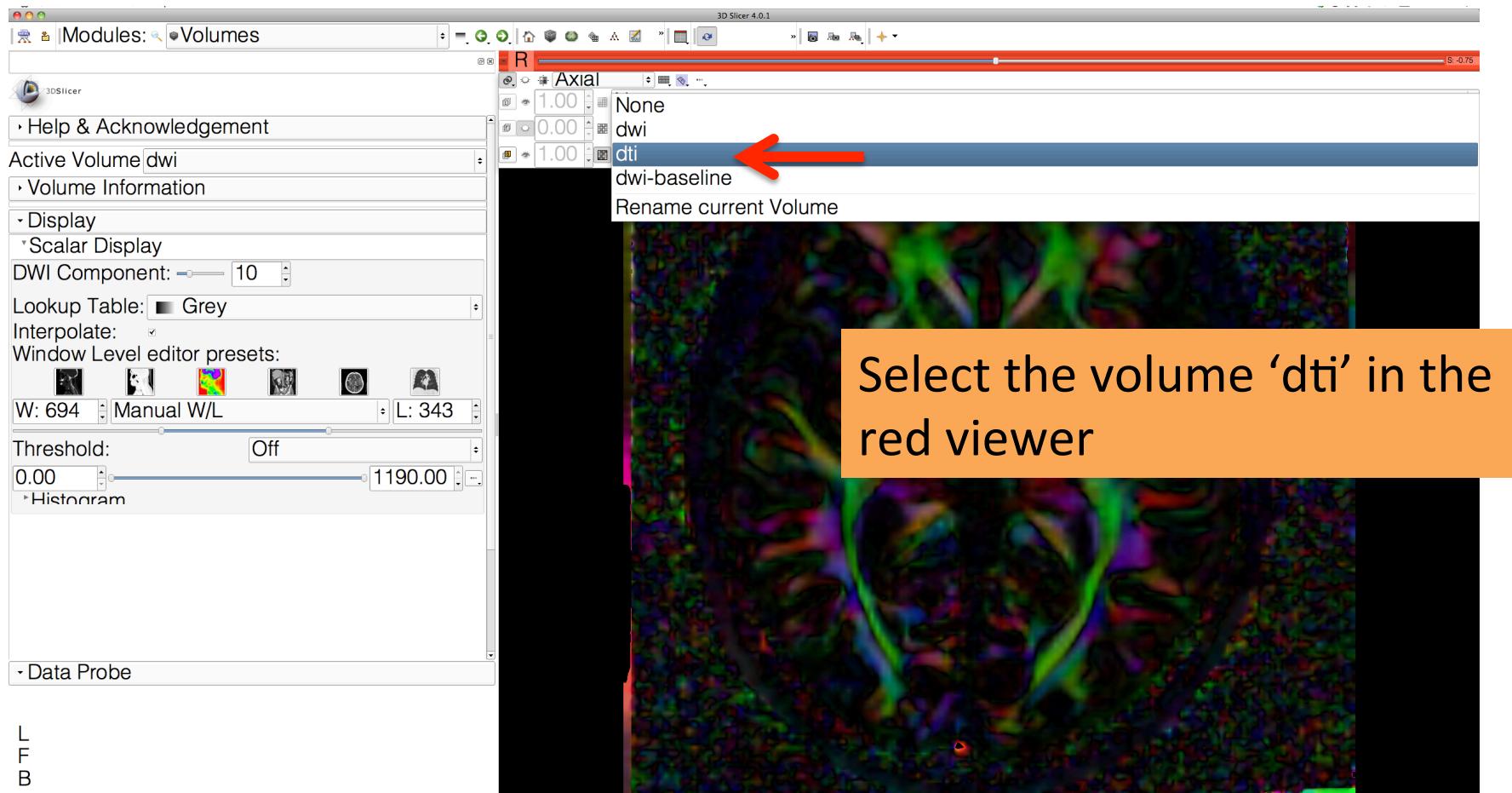
Diffusion Tensor Estimation



Select the module **Diffusion Tensor Estimation** in the modules menu:

- select the Input DWI volume 'dwi'
- select Output DTI Volume 'Create New Diffusion Tensor Volume', and rename it 'dti'
- select Output Baseline Volume ' Create new Volume', and rename it 'dwi-baseline'
- select the Estimation Method 'WLS' (Weighted Least Squares) and click on Apply.

Diffusion Tensor Estimation



Diffusion Tensor Estimation

Slicer displays the DTI volume in color by orientation mode:

Red: right-left

Green: anterior-posterior

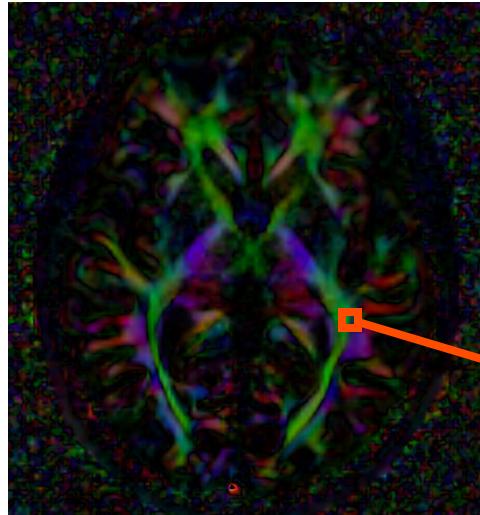
Blue: inferior-superior

Default Cancel Apply

Red RAS: (-86.1, 69.2, -0.8) Axial Sp: 1.5

L None()
F None()
B dti (121, 18, 47) ColorOrientation 0

Diffusion Tensor Data



$$S_i = S_0 e^{-b\hat{g}^T \underline{D} \hat{g}_i}$$

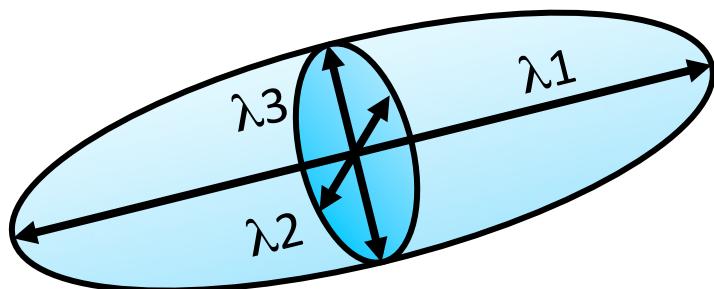
Stejskal-Tanner equation (1965)

$$\underline{\mathbf{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

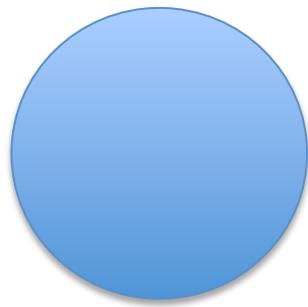
The diffusion tensor $\underline{\mathbf{D}}$ in the voxel (I,J,K) is a 3x3 symmetric matrix.

Diffusion Tensor

- The diffusion tensor D in the voxel (I,J,K) can be visualized as an ellipsoid, with the eigenvectors indicating the directions of the principal axes, and the square root of the eigenvalues defining the ellipsoidal radii.
- Scalar maps can be derived from the rotationally invariant eigenvalues λ_1 , λ_2 , λ_3 to characterize the size and shape of the diffusion tensor.

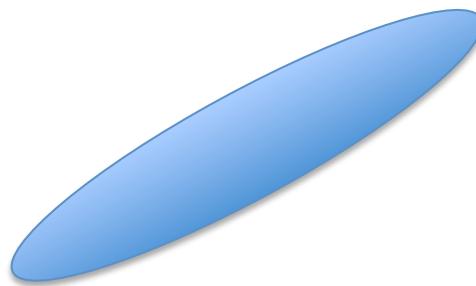


Diffusion Tensor Shape



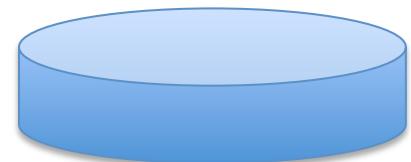
$$\lambda_1 = \lambda_2 = \lambda_3$$

Isotropic media
(CSF, gray matter)



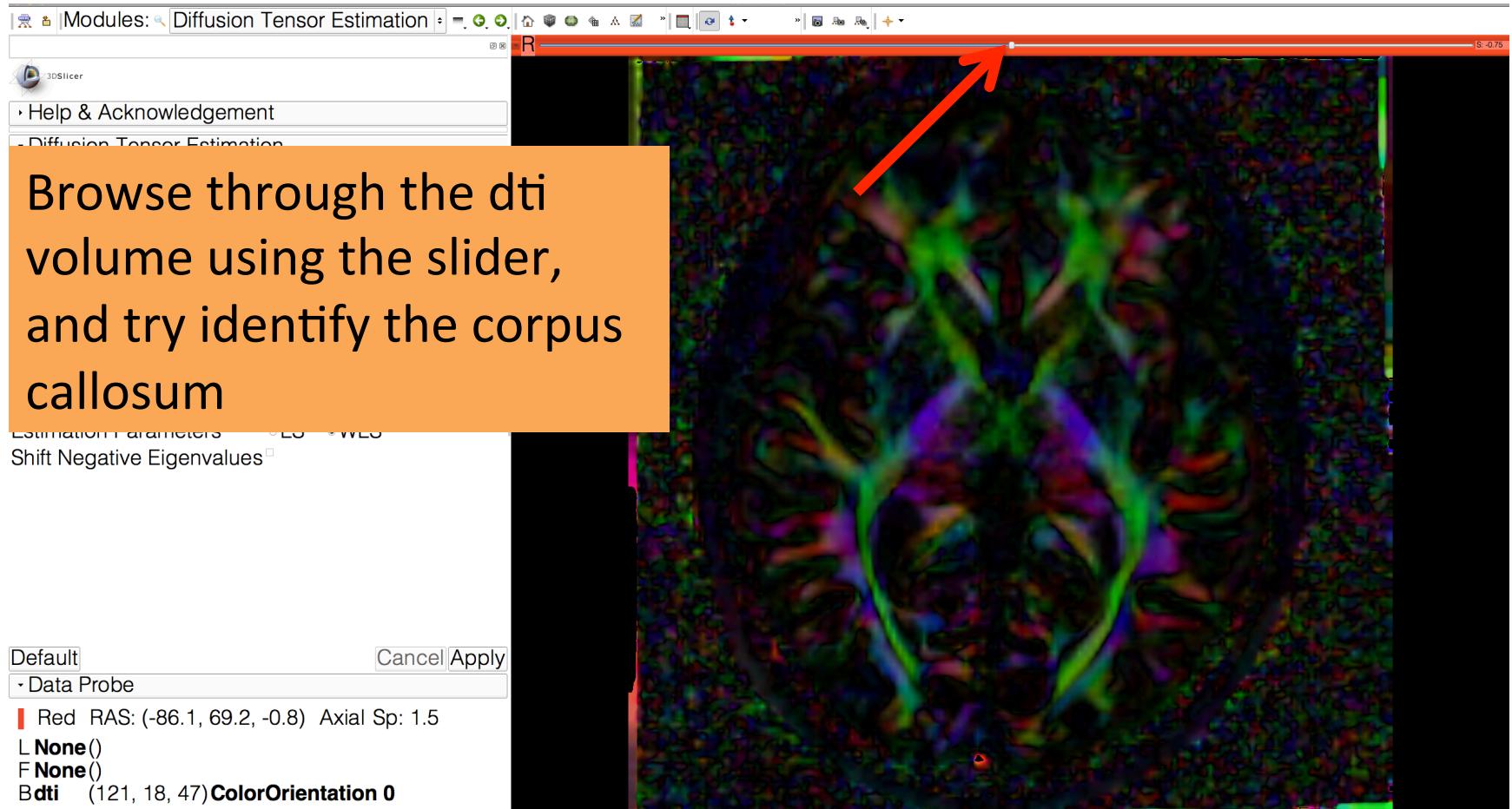
$$\lambda_1 >> \lambda_2, \lambda_3$$

Anisotropic media
(white matter)



$$\lambda_1 \sim \lambda_2 >> \lambda_3$$

Exploring the Diffusion Tensor Data



Corpus Callosum

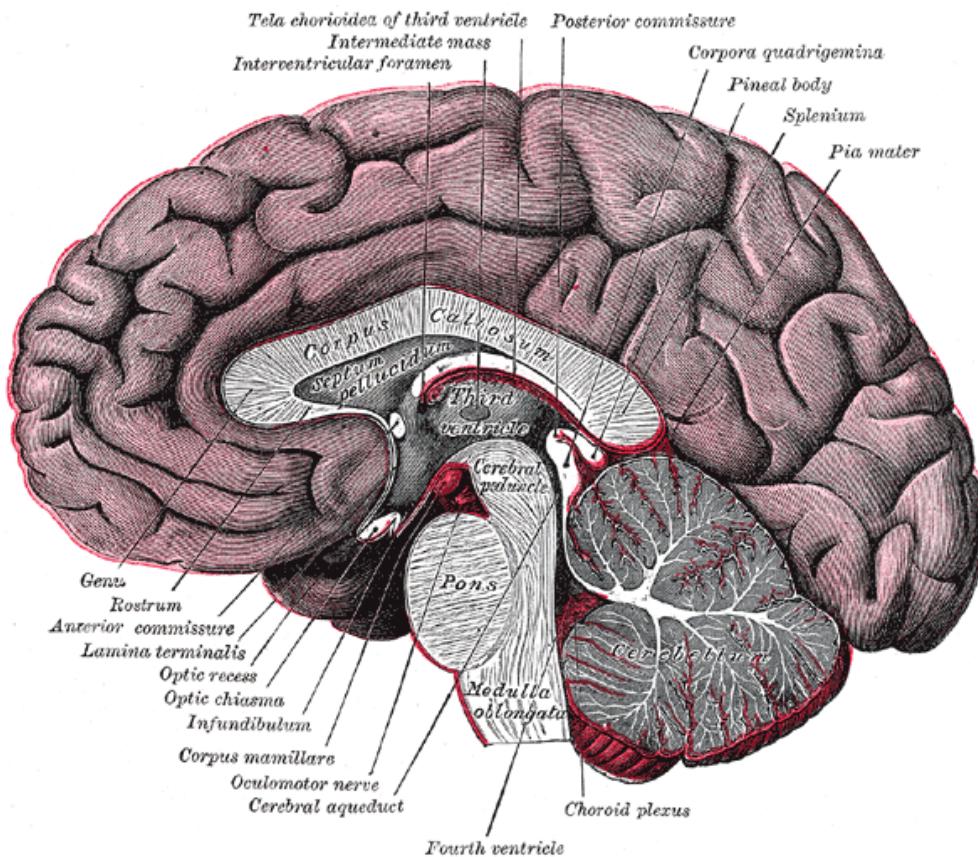
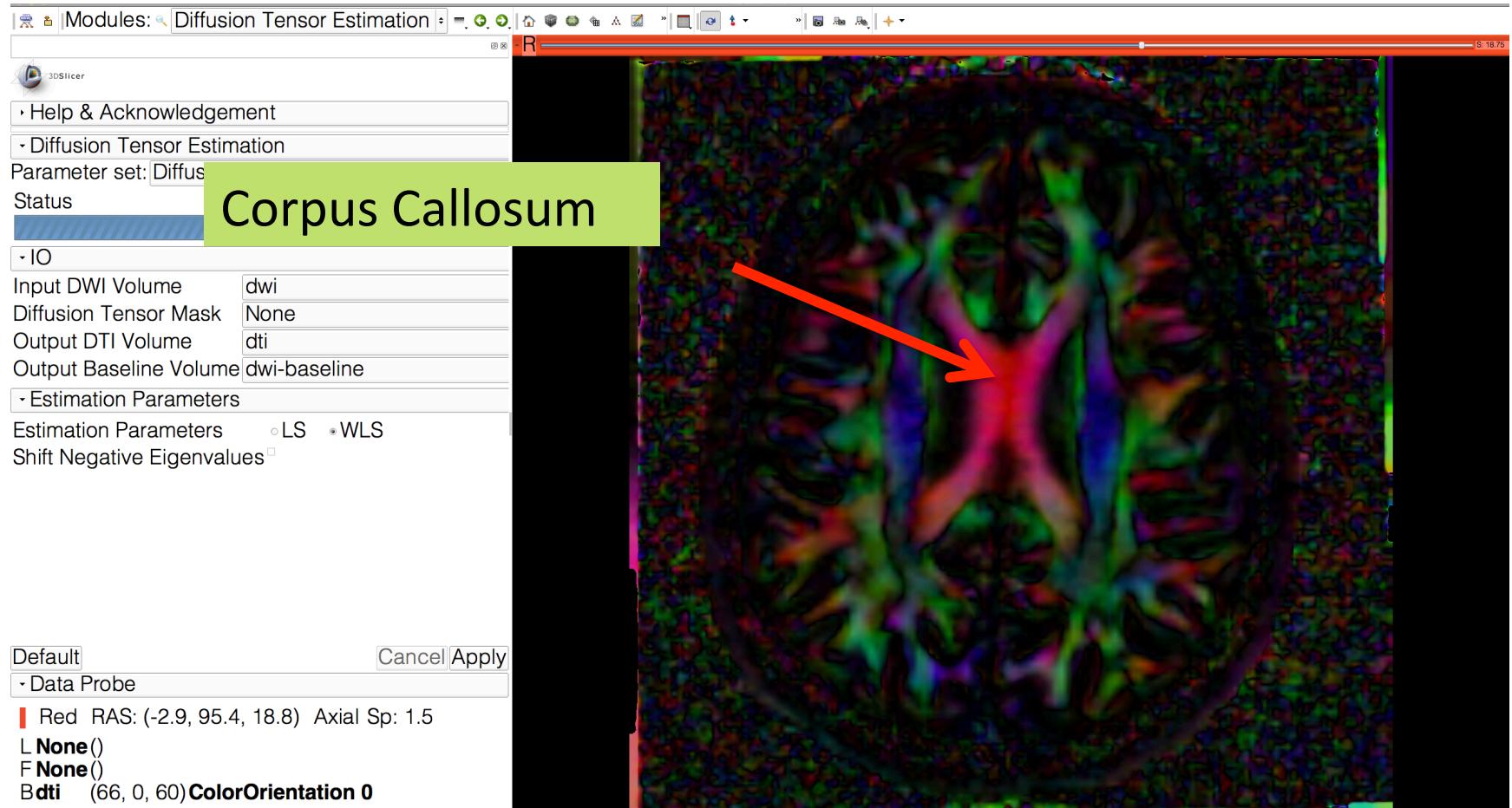


Image from Gray's Anatomy

Diffusion MRI Analysis – Sonia Pujol, Ph.D.
NA-MIC ARR 2012

The corpus callosum is a broad thick bundle of dense myelinated fibers that connect the left and right hemisphere. It is the largest white matter structure in the brain

Exploring the Diffusion Tensor Data

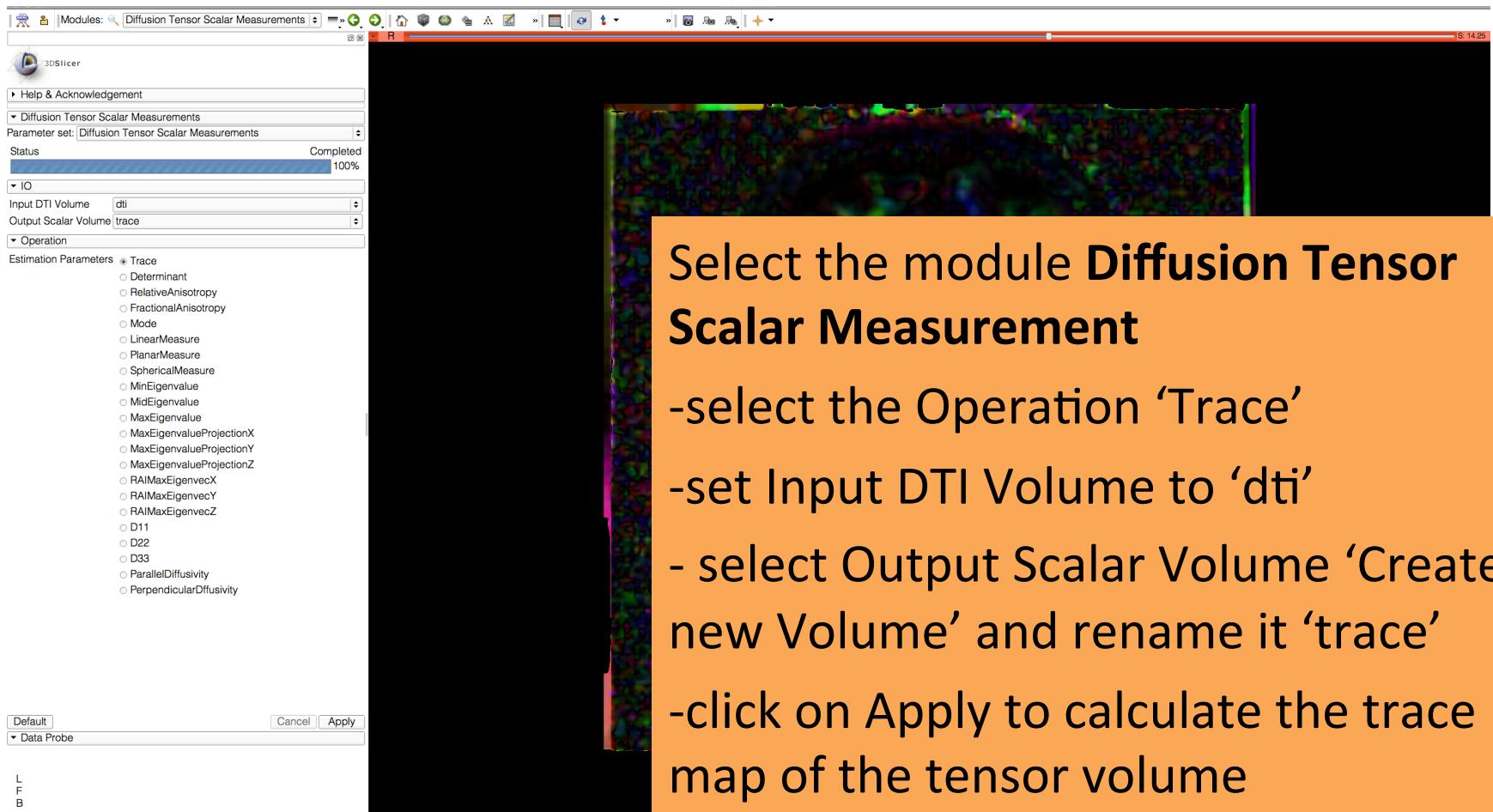


Characterizing the Size of the tensor: Trace

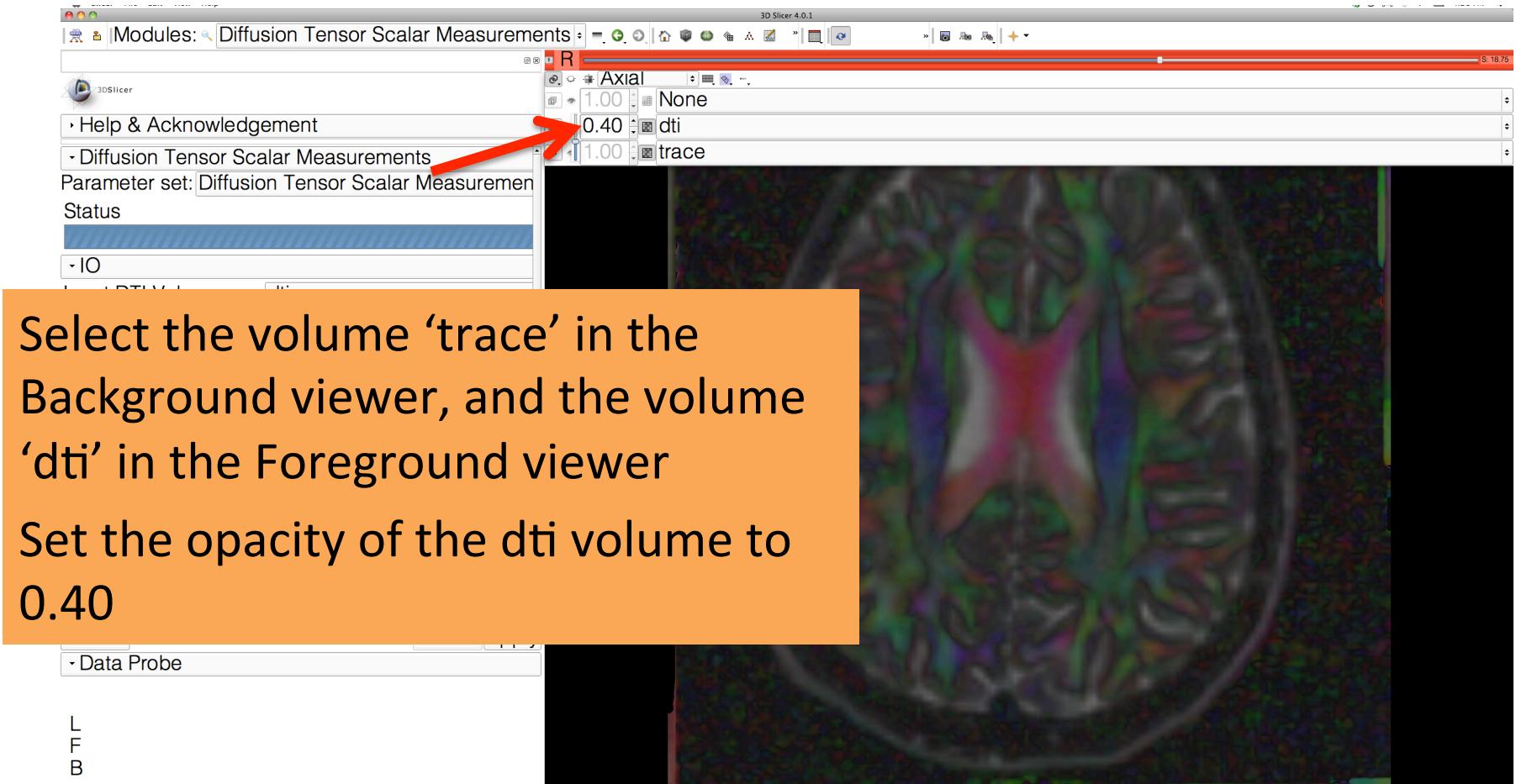
$$\text{Trace}(D) = \lambda_1 + \lambda_2 + \lambda_3$$

- $\text{Trace}(D)$ is intrinsic to the tissue and is independent of fiber orientation, and diffusion sensitizing gradient directions
- $\text{Trace}(D)$ is a clinically relevant parameter for monitoring stroke and neurological condition
- $\text{Trace}(D)$ is useful to characterize the size of the diffusion ellipsoid

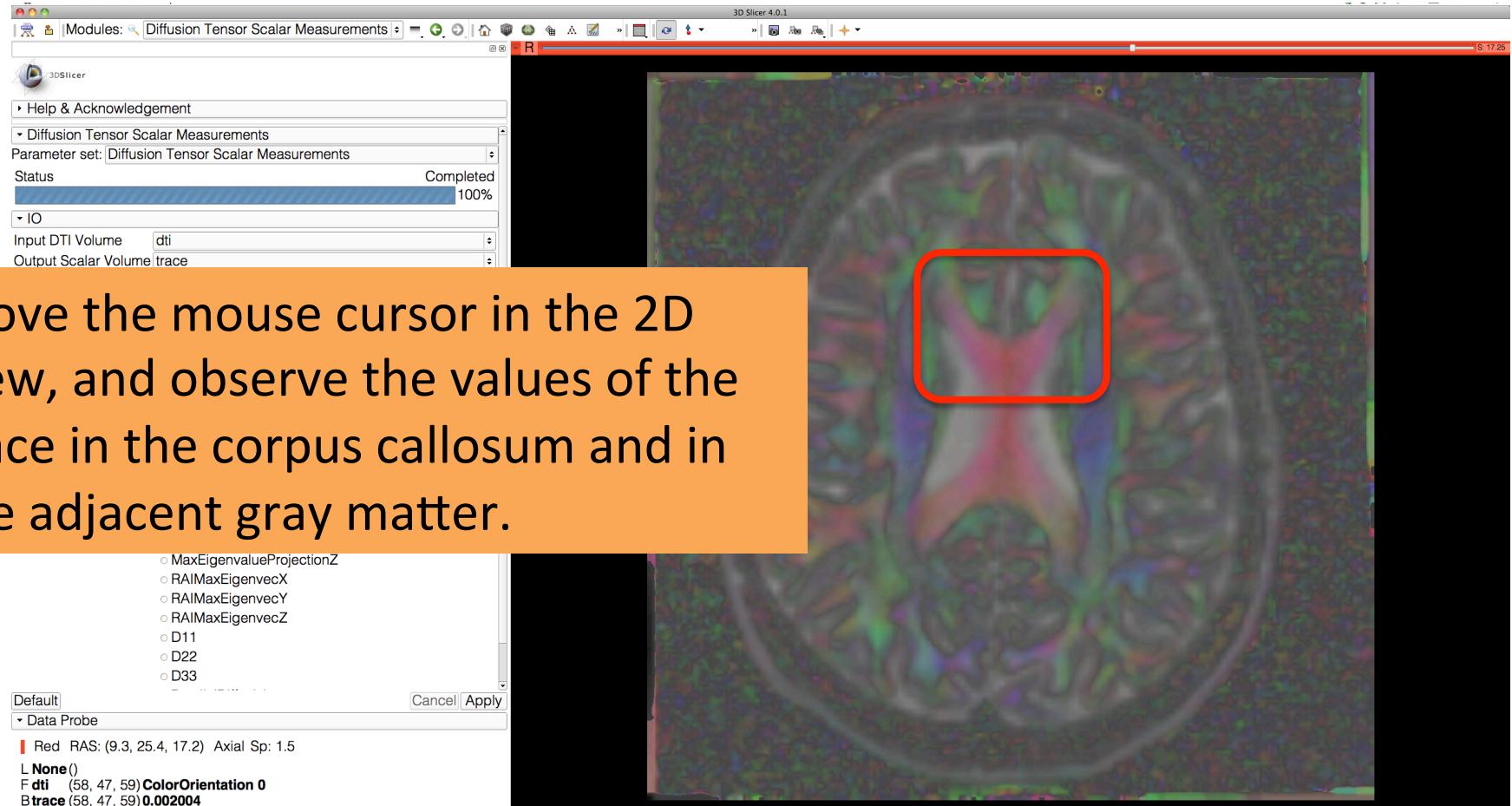
Characterizing the Size of the tensor: Trace



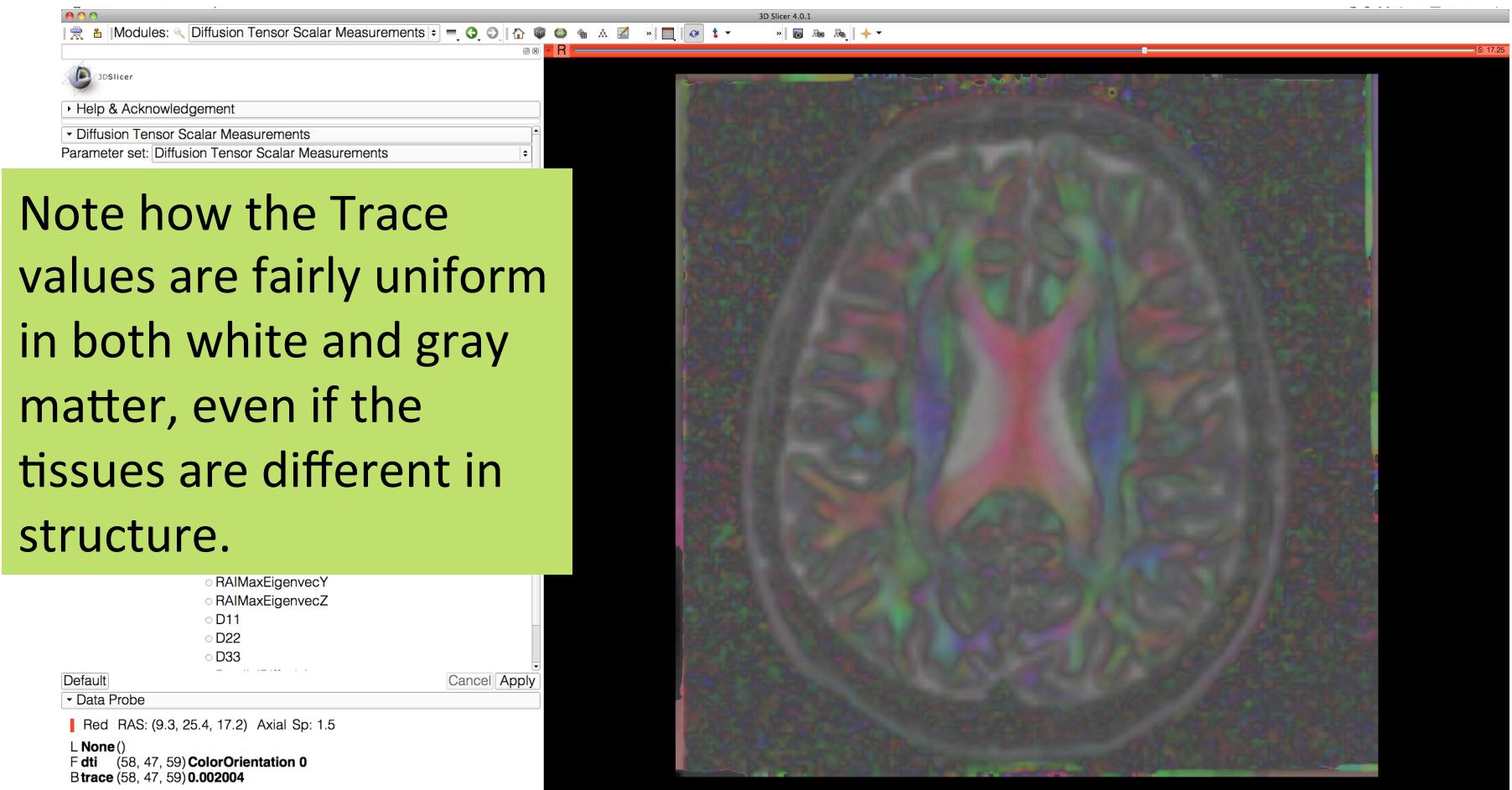
Exploring the Diffusion Tensor Data



Exploring the Diffusion Tensor Data



Characterizing the Size of the tensor: Trace

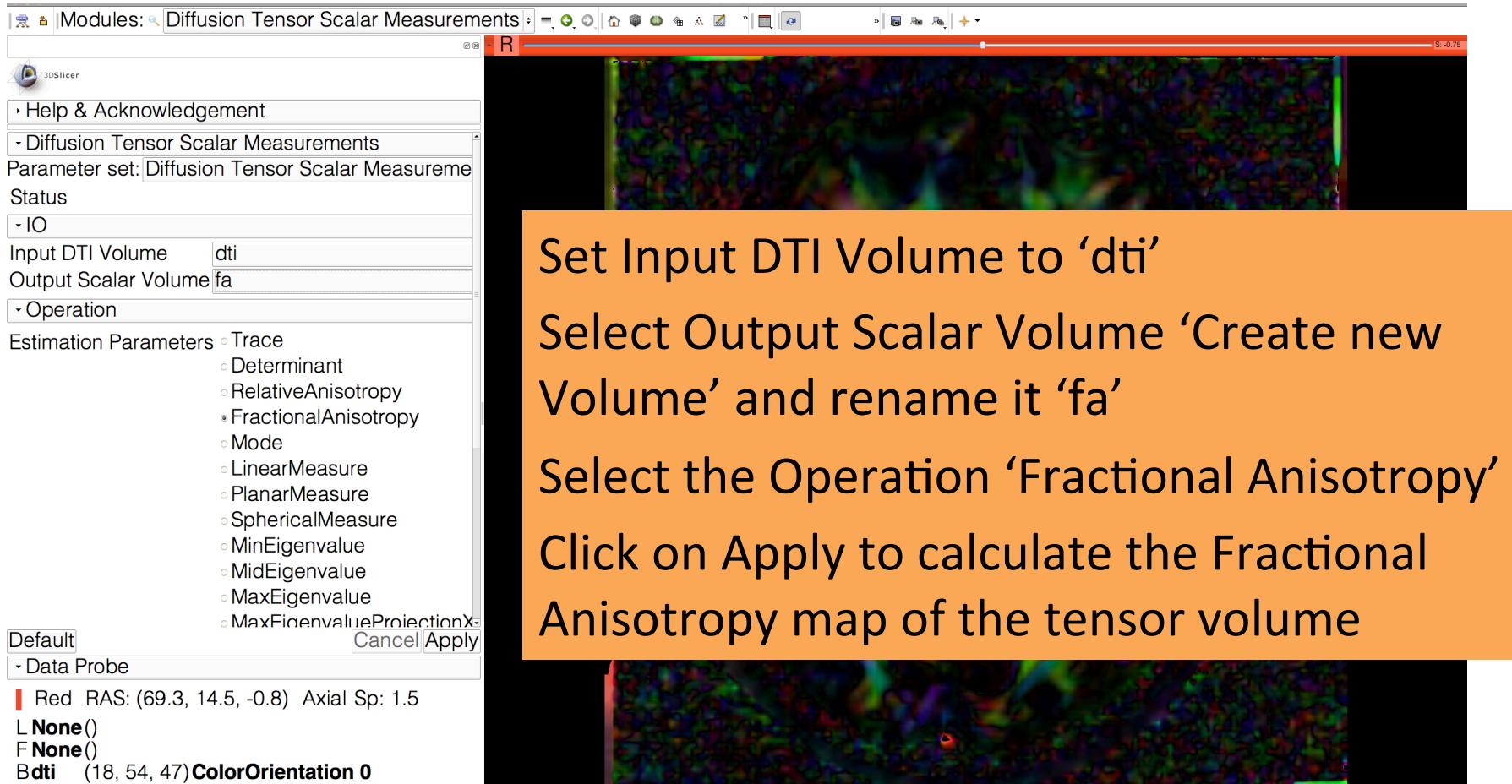


Scalar Maps: Fractional Anisotropy

$$FA(D) = \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\sqrt{2} \sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

- FA(D) is intrinsic to the tissue and is independent of fiber orientation, and diffusion sensitizing gradient directions
- FA(D) is useful to characterize the shape (degree of ‘out-of-roundness’) of the diffusion ellipsoid’
- Low FA:  → High FA: 

Characterizing the Shape of the tensor: Fractional Anisotropy



Set Input DTI Volume to 'dti'

Select Output Scalar Volume 'Create new Volume' and rename it 'fa'

Select the Operation 'Fractional Anisotropy'

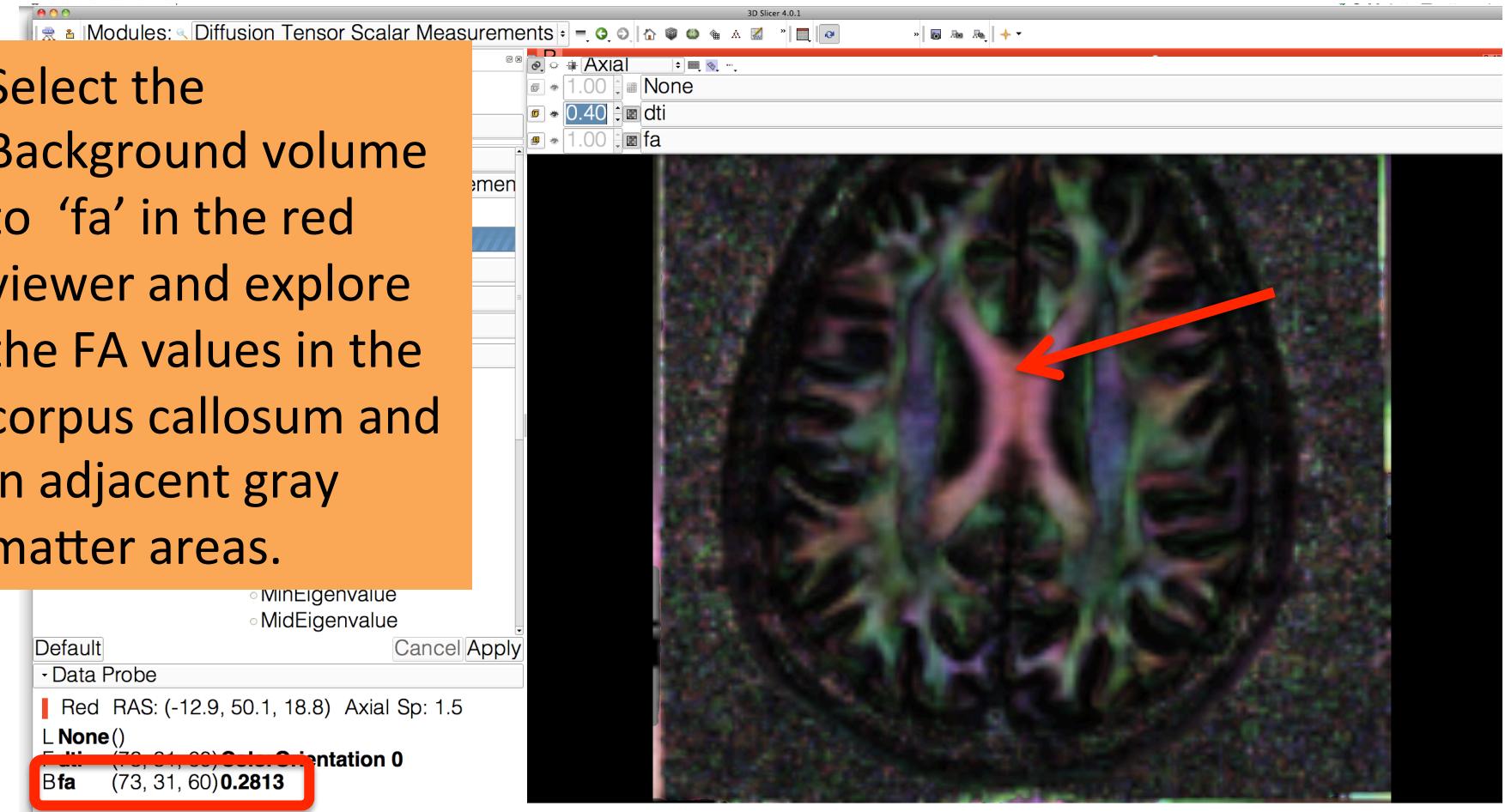
Click on Apply to calculate the Fractional Anisotropy map of the tensor volume

Red RAS: (69.3, 14.5, -0.8) Axial Sp: 1.5

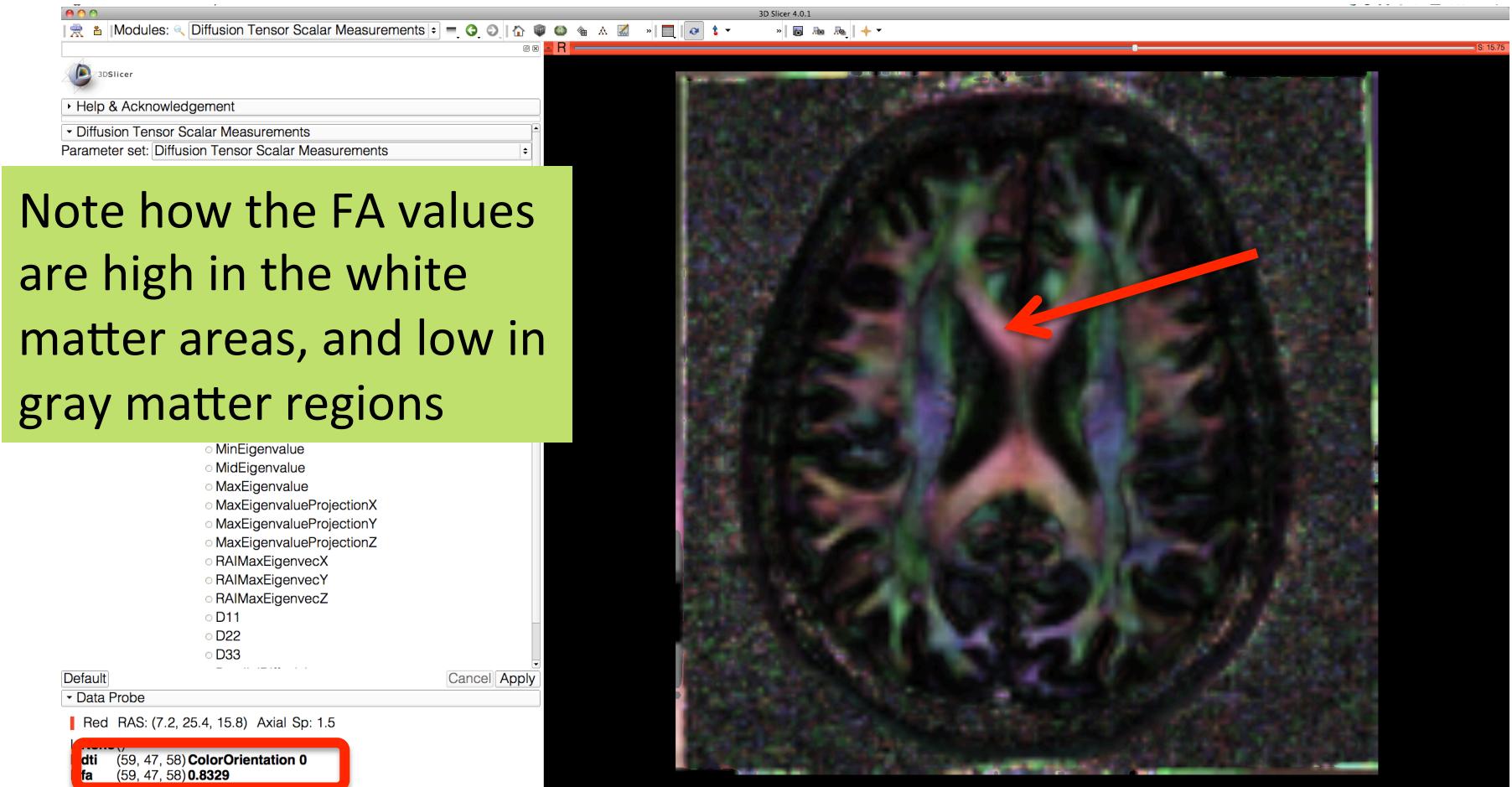
L **None()**
F **None()**
B **dti** (18, 54, 47) **ColorOrientation 0**

Fractional Anisotropy

Select the Background volume to 'fa' in the red viewer and explore the FA values in the corpus callosum and in adjacent gray matter areas.



Fractional Anisotropy

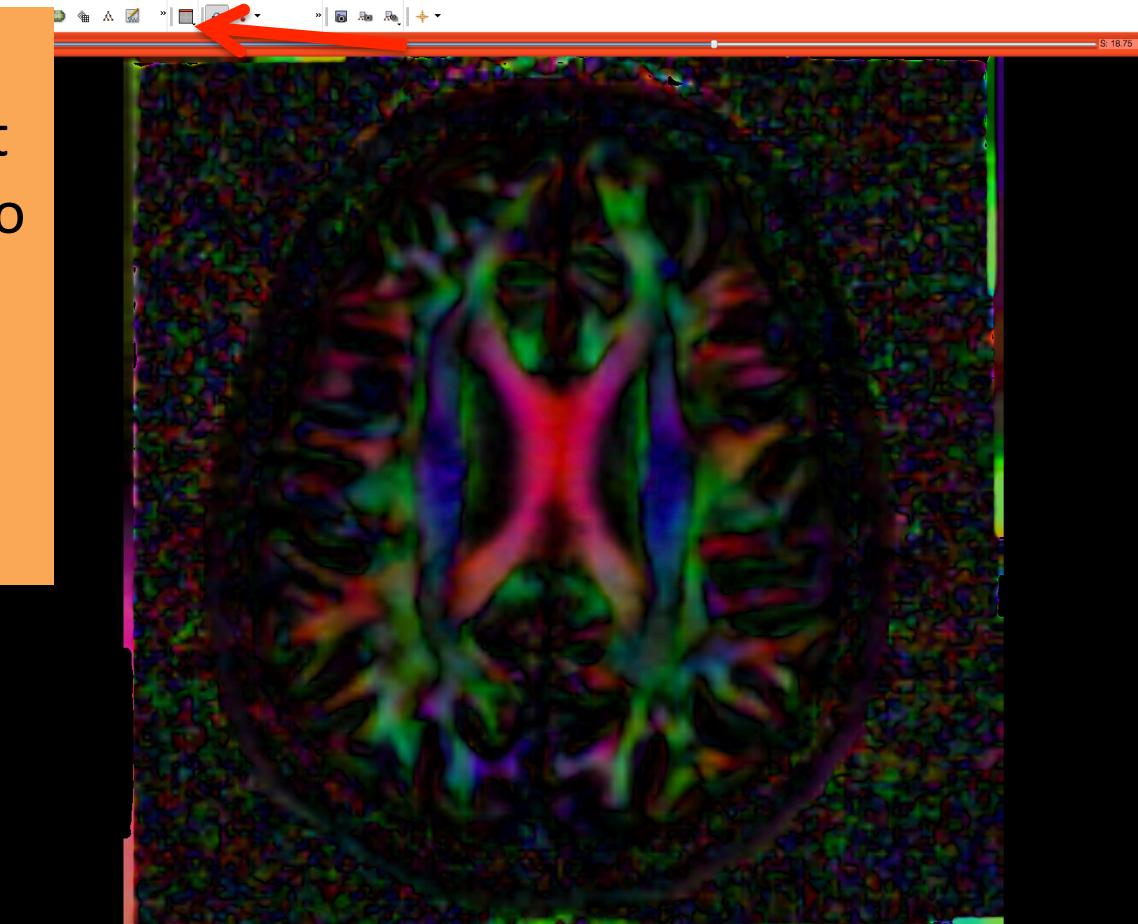


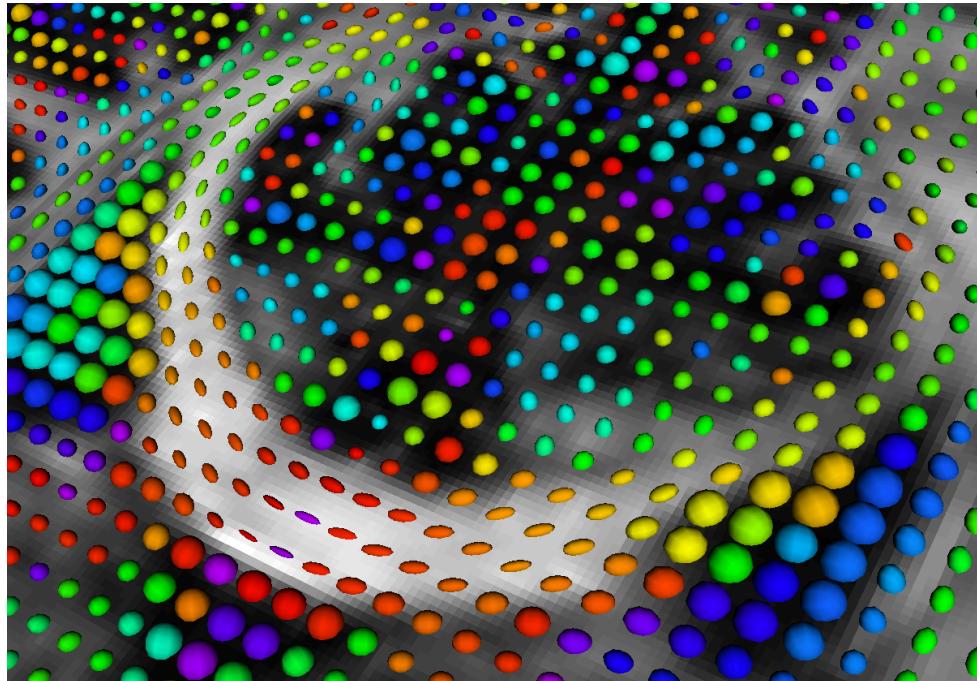
Fractional Anisotropy

Set the Foreground volume to 'None', and set the Background volume to 'dti' in the red viewer menu.

Go back to conventional layout

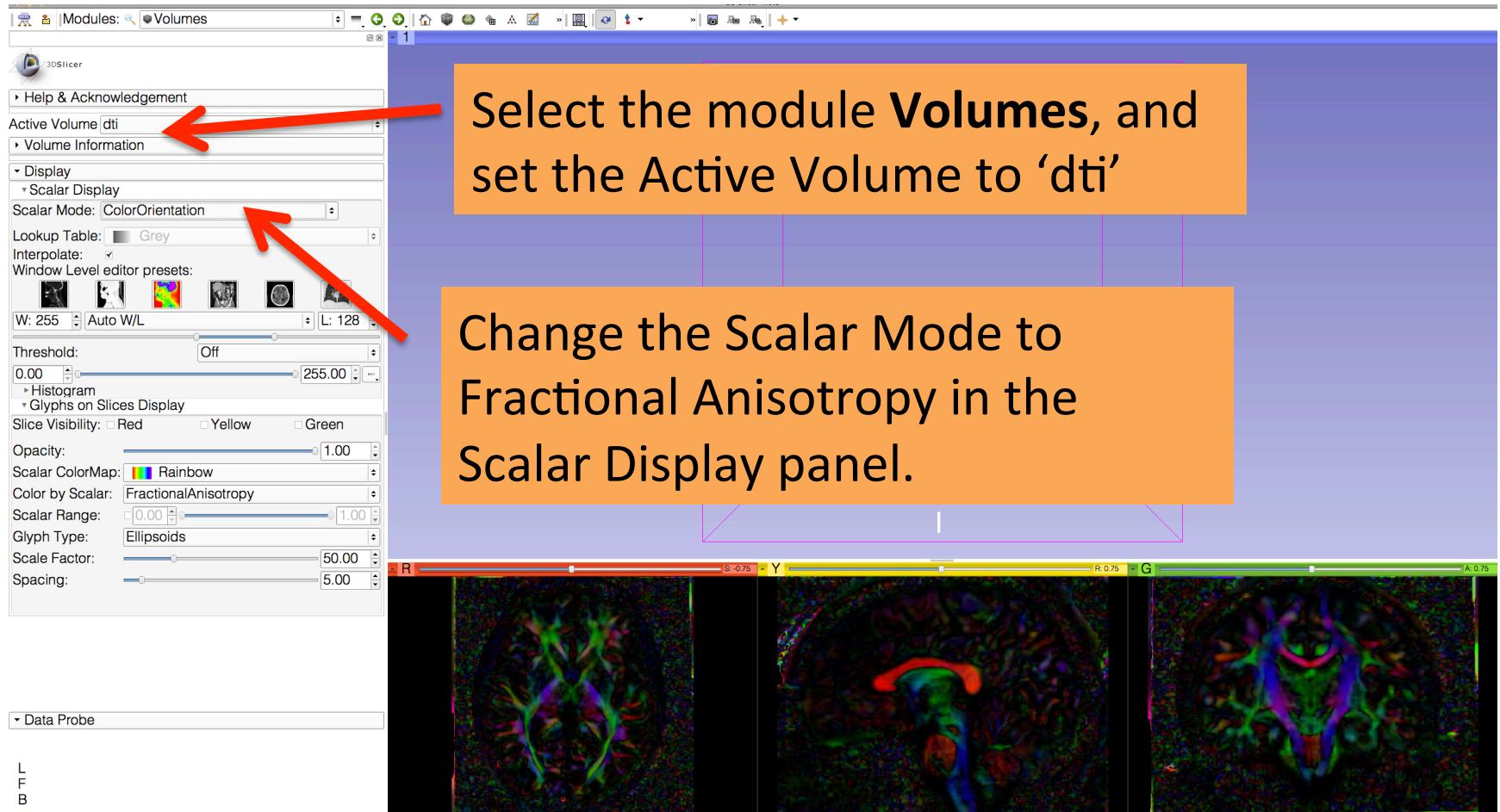
Default	Cancel	Apply
Data Probe		
Red RAS: (-2.9, 95.4, 18.8) Axial Sp: 1.5		
L None()		
F None()		
B dti (66, 0, 60)	ColorOrientation	0



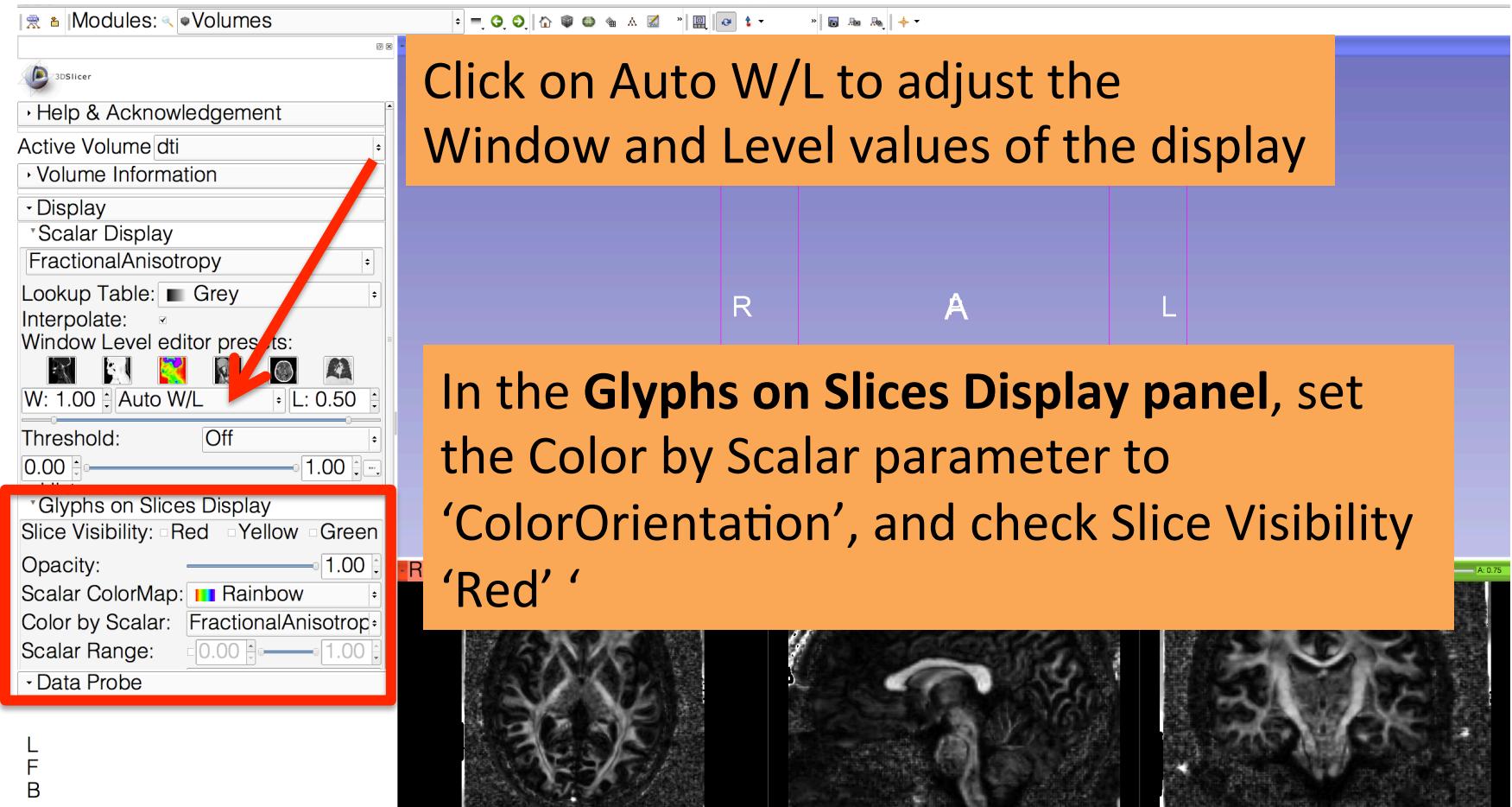


Part 2: Visualizing the tensor data

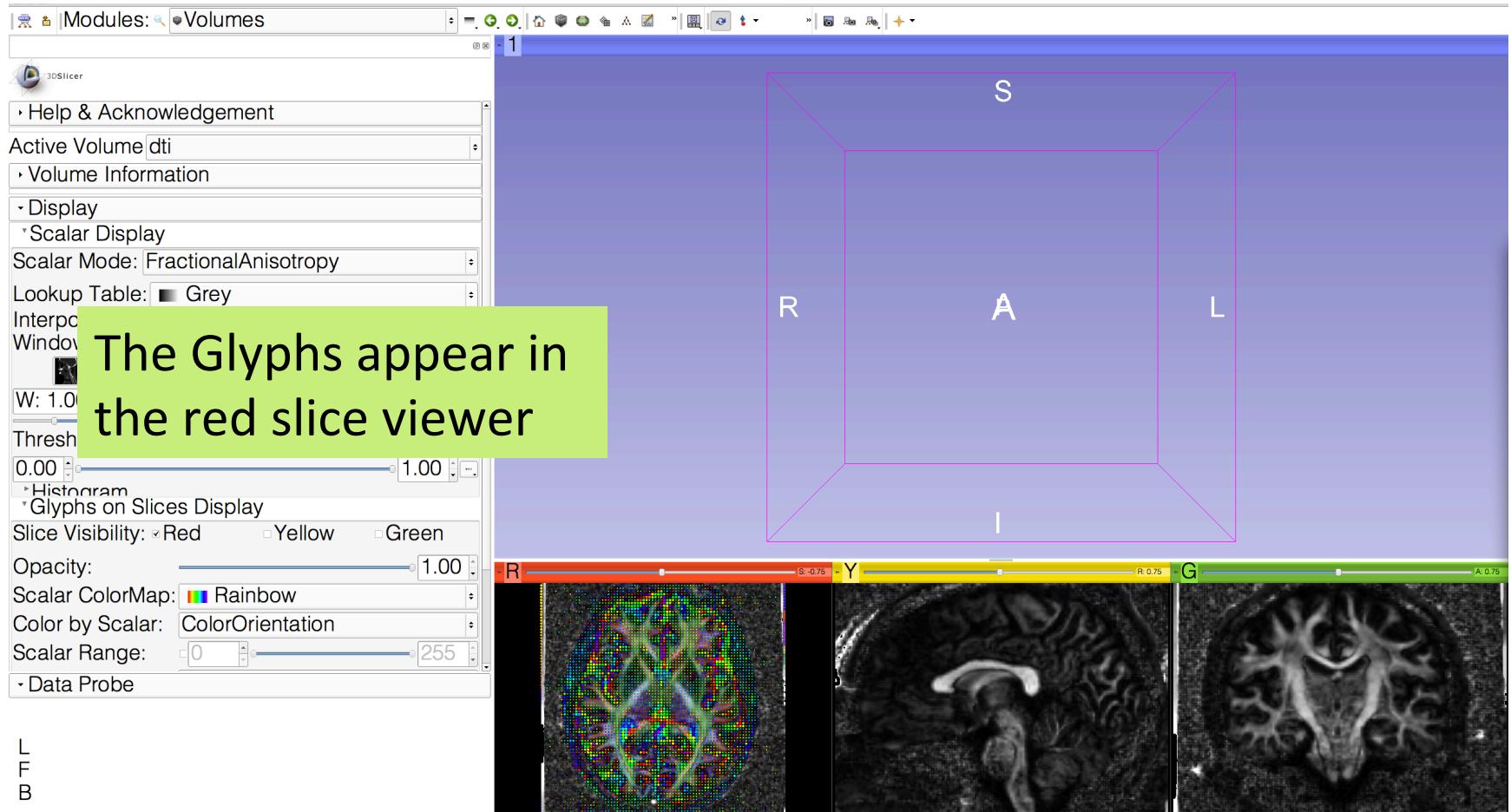
3D Visualization: Glyphs



3D Visualization: Glyphs



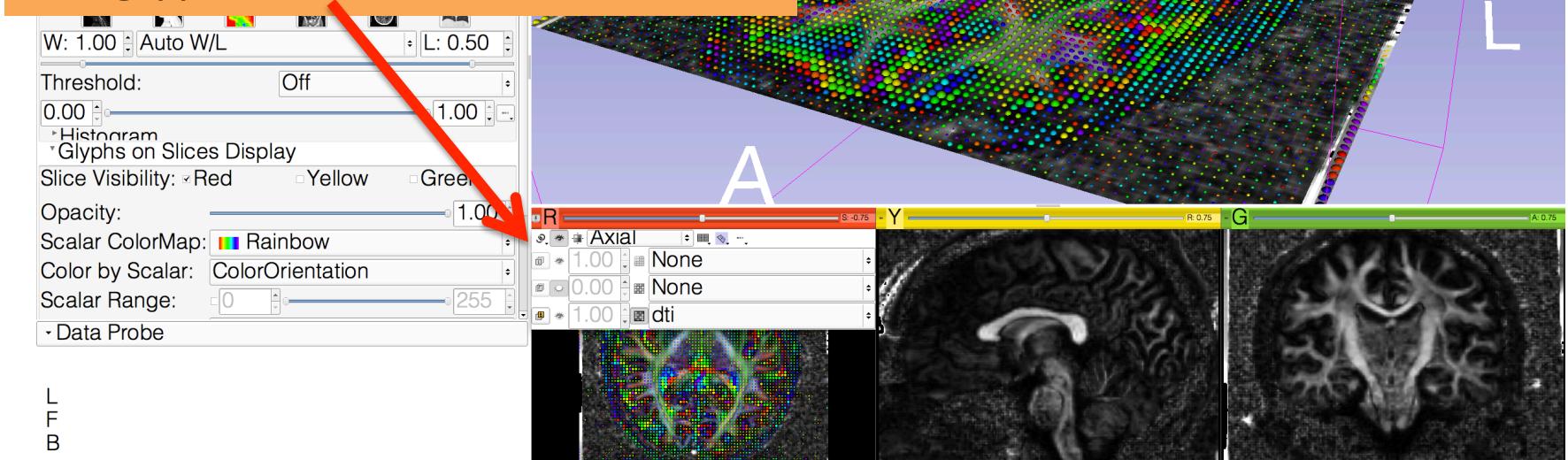
3D Visualization: Glyphs



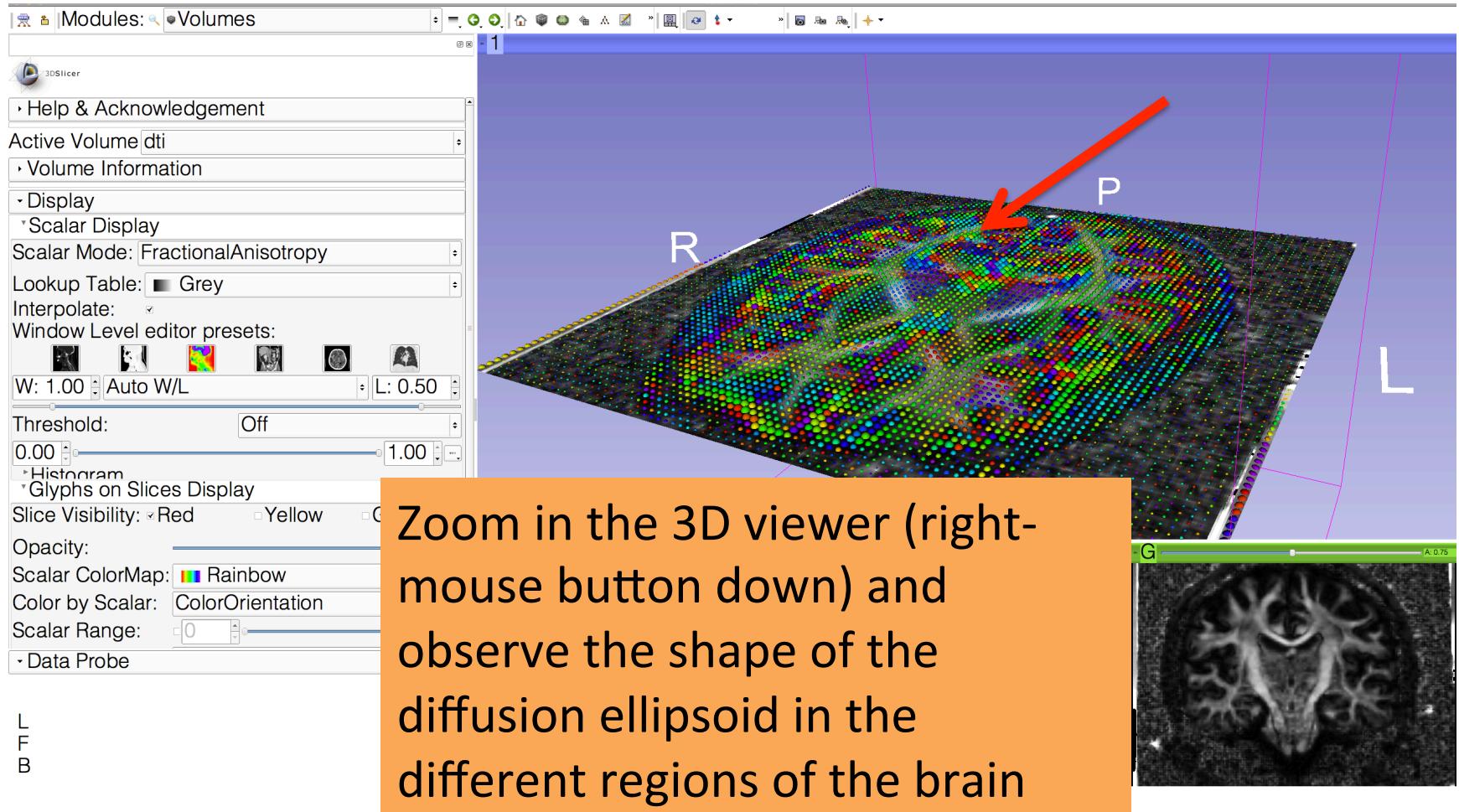
3D Visualization: Glyphs

Click on the link icon in the red slice viewer to unlink the three viewers.

Click on the eye icon to display the glyphs in the 3D Viewer

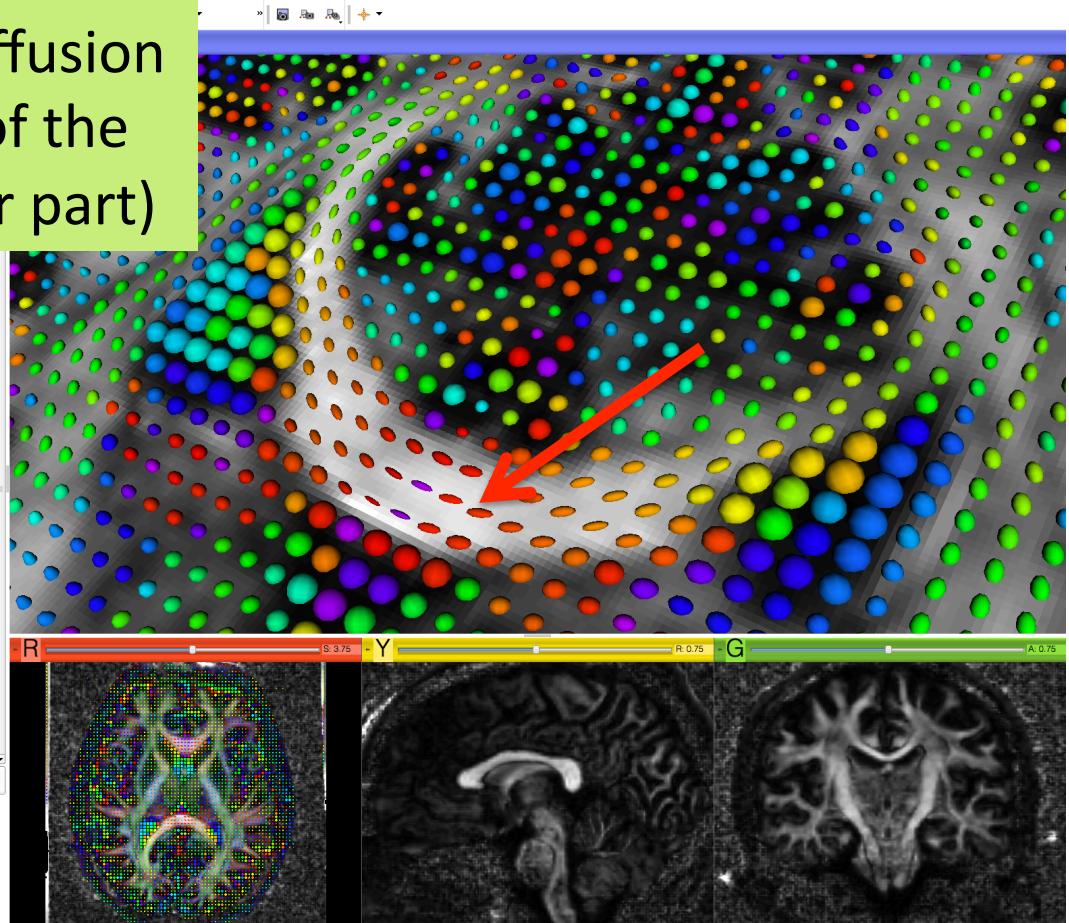
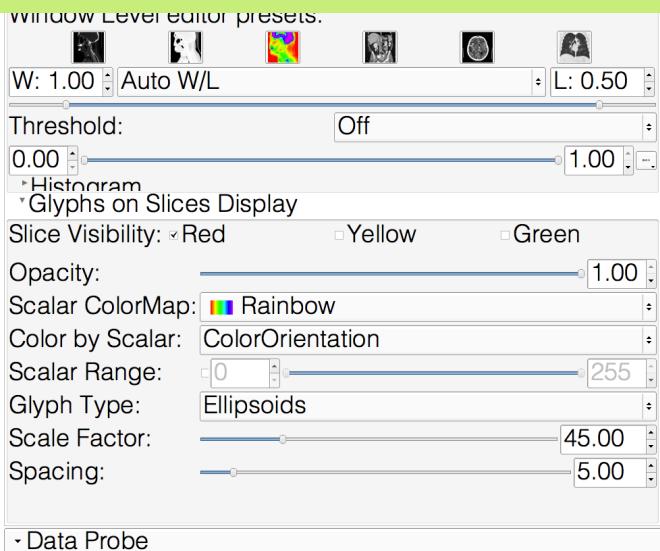


3D Visualization: Glyphs



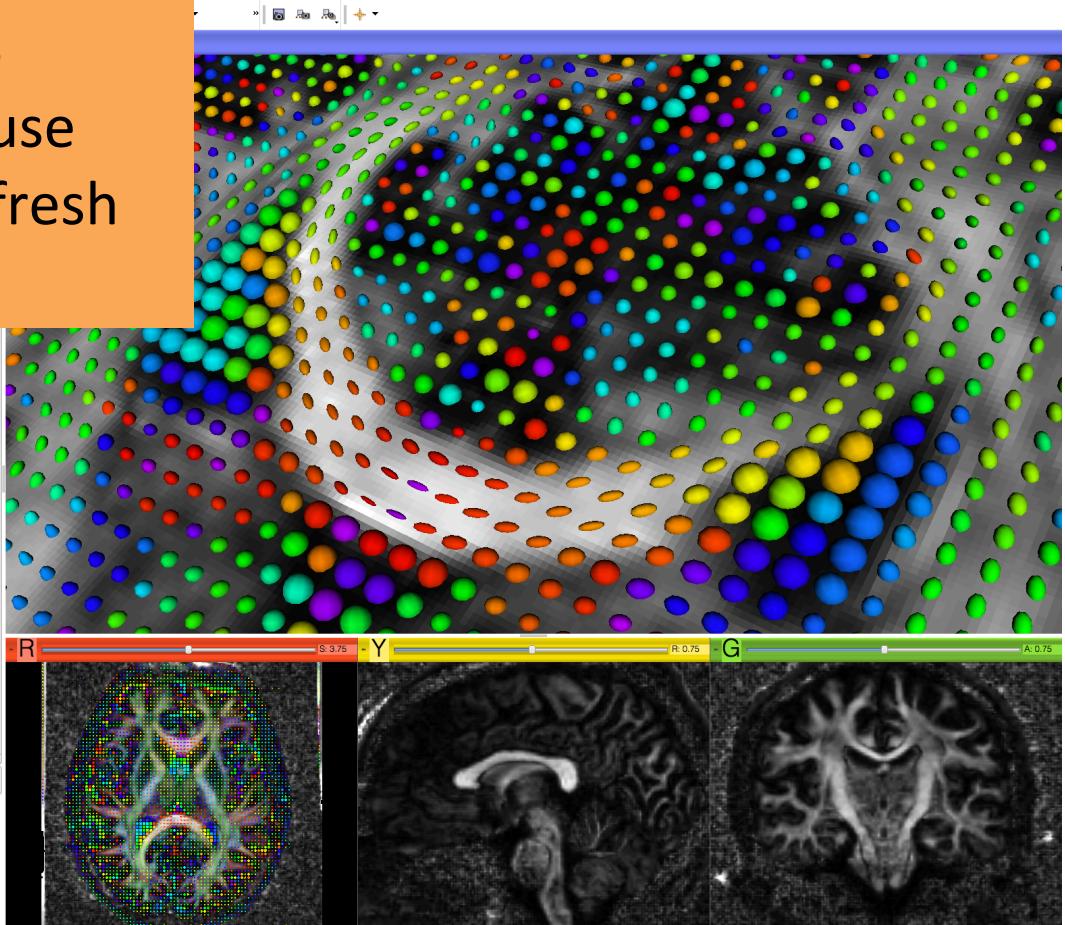
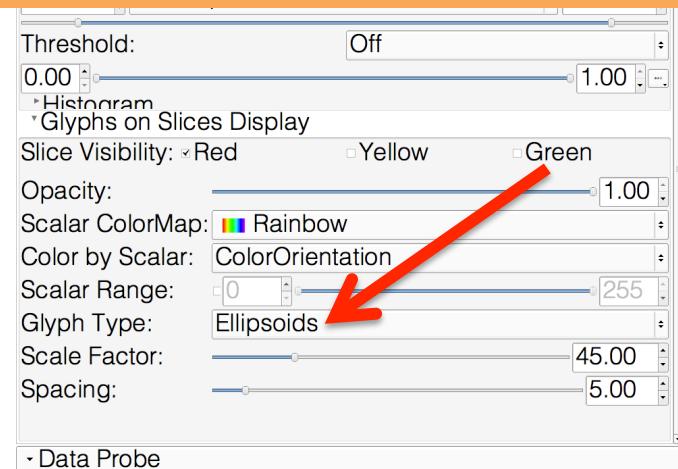
3D Visualization: Glyphs

Note the orientation of diffusion ellipsoid of the splenium of the corpus callosum (posterior part)



3D Visualization: Glyphs

Change the Glyph Type to 'Lines', and move the mouse inside the 3D viewer to refresh the display.



L
F
B

3D Visualization: Glyphs

Slicer displays the glyphs as lines that represent the principal direction of diffusion (main eigenvector)

Threshold: Off
0.00 0.00

Histogram
• Glyphs on Slices Display

Slice Visibility: Red Yellow Green

Opacity: 1.00

Scalar ColorMap: Rainbow

Color by Scalar: ColorOrientation

Scalar Range: 0 255

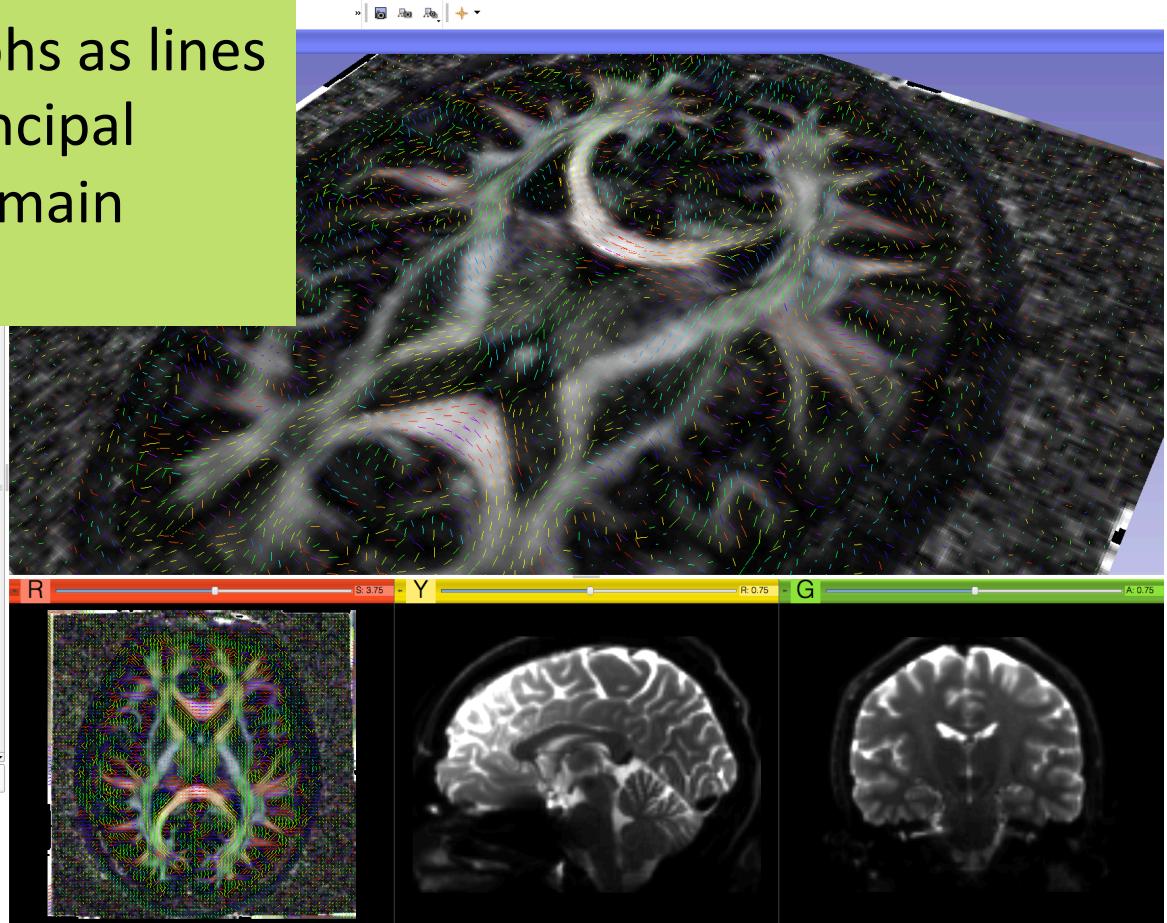
Glyph Type: Lines

Scale Factor: 45.00

Spacing: 5.00

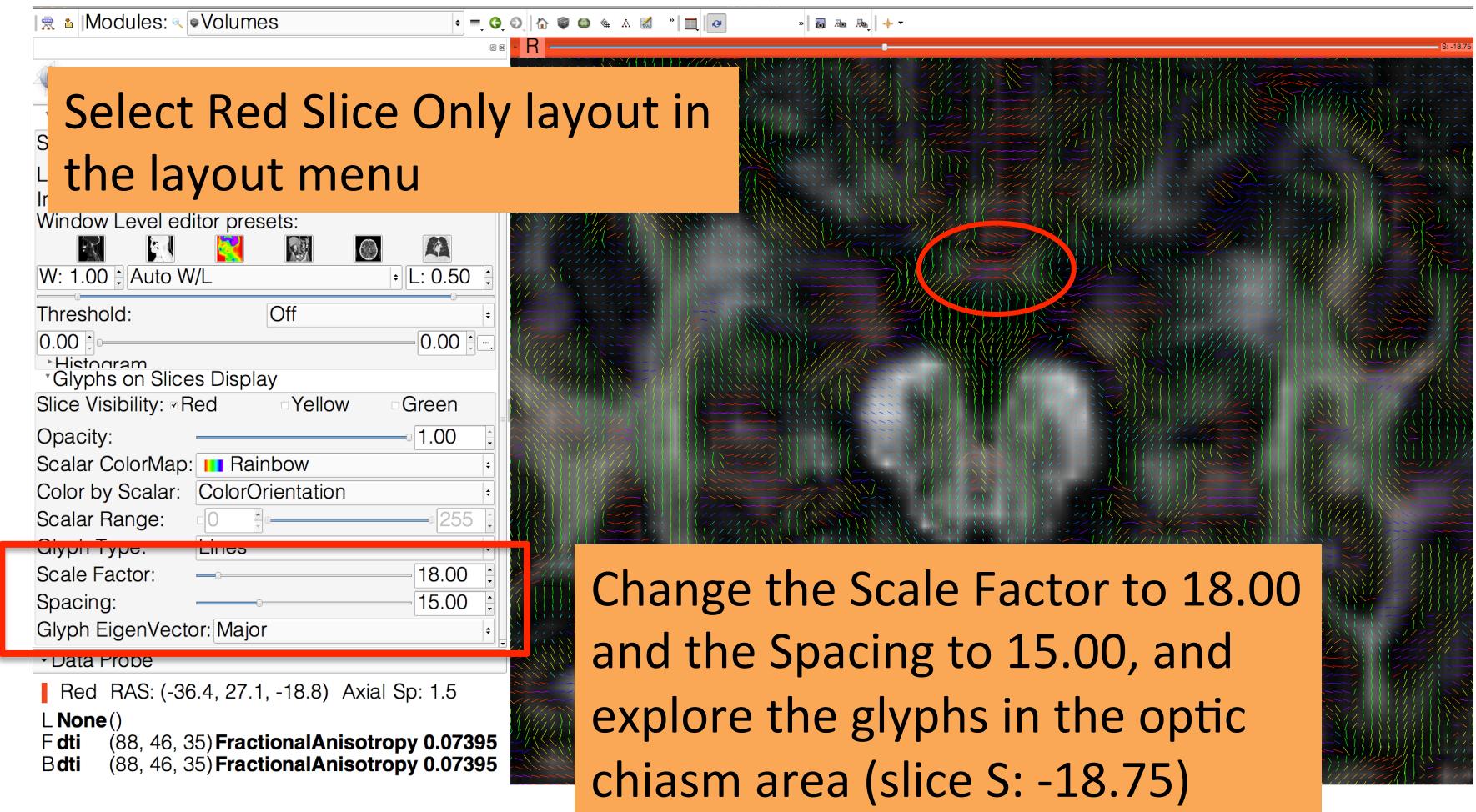
Glyph EigenVector: Major

• Data Probe

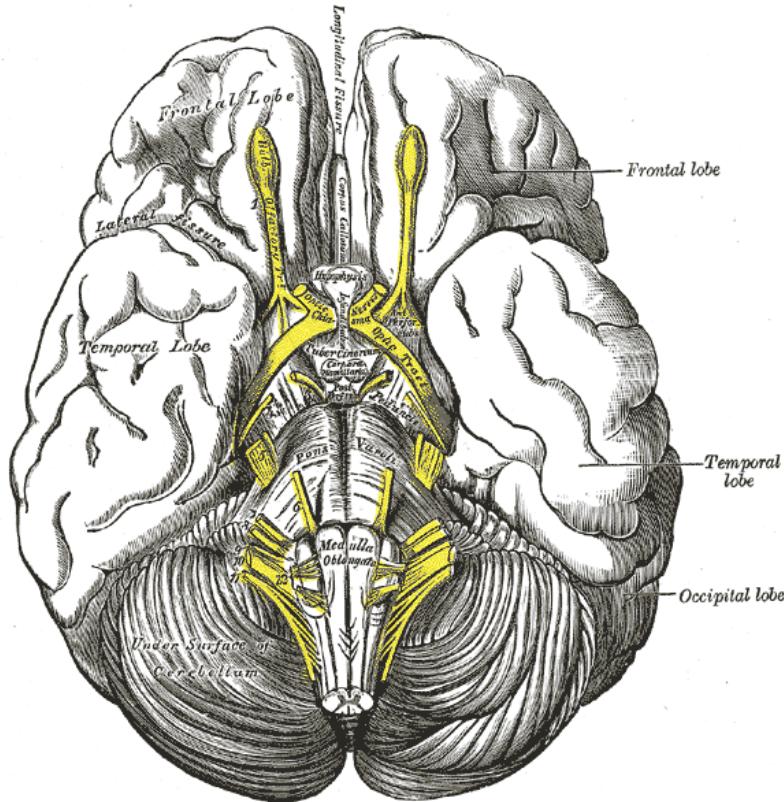


L
F
B

3D Visualization: Glyphs



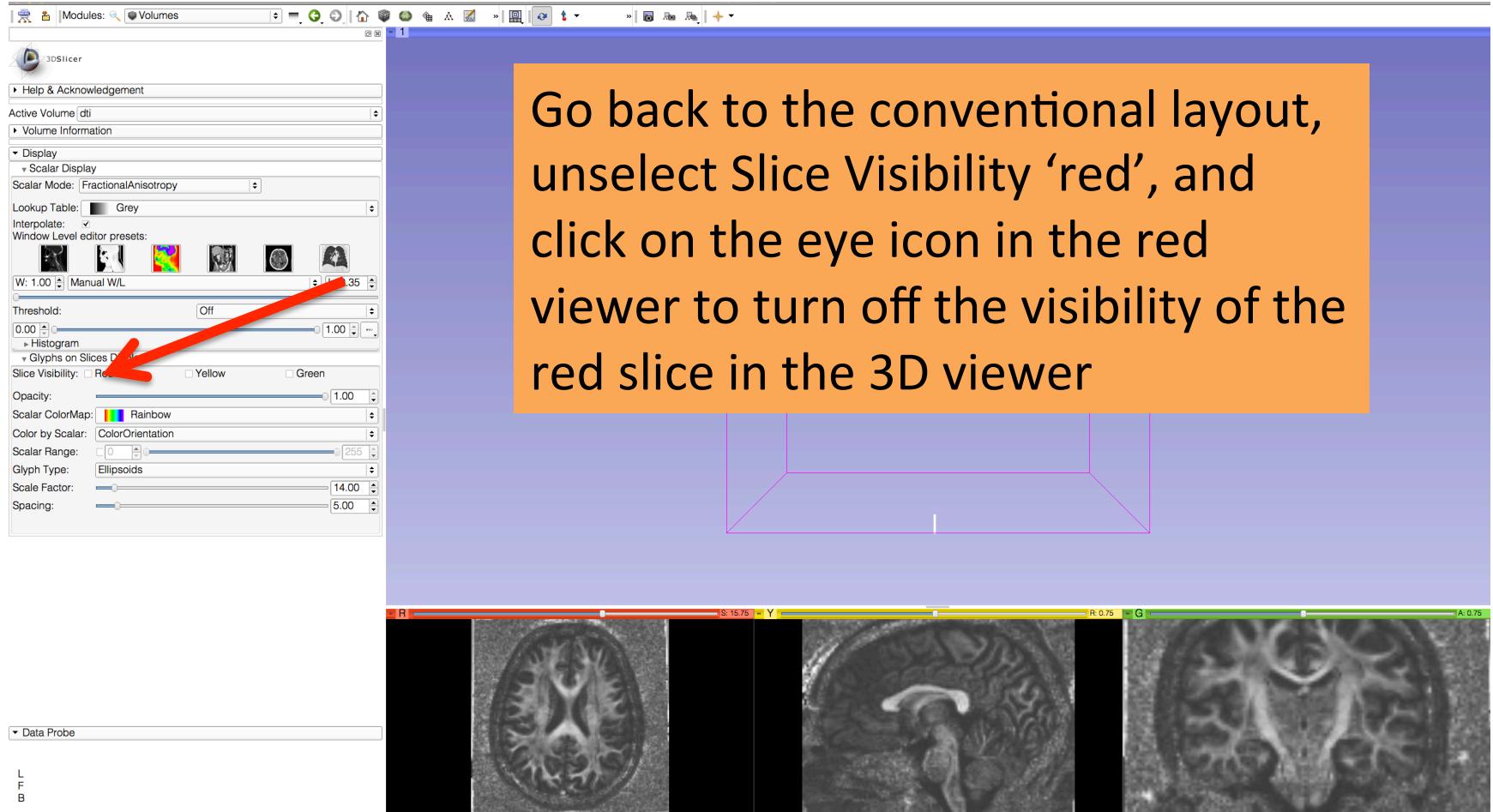
Optic Chiasm

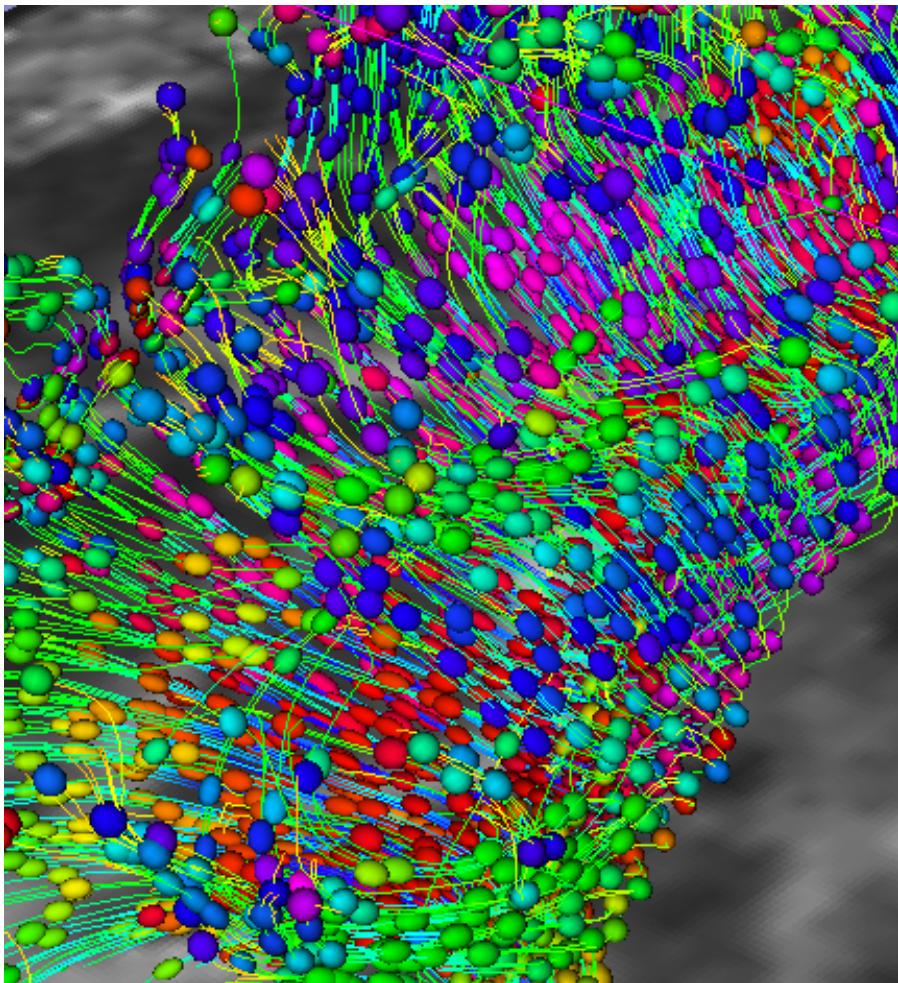


The optic chiasm corresponds to the part of the brain where the optic nerves cross.

Image from Gray's Anatomy

3D Visualization: Glyphs



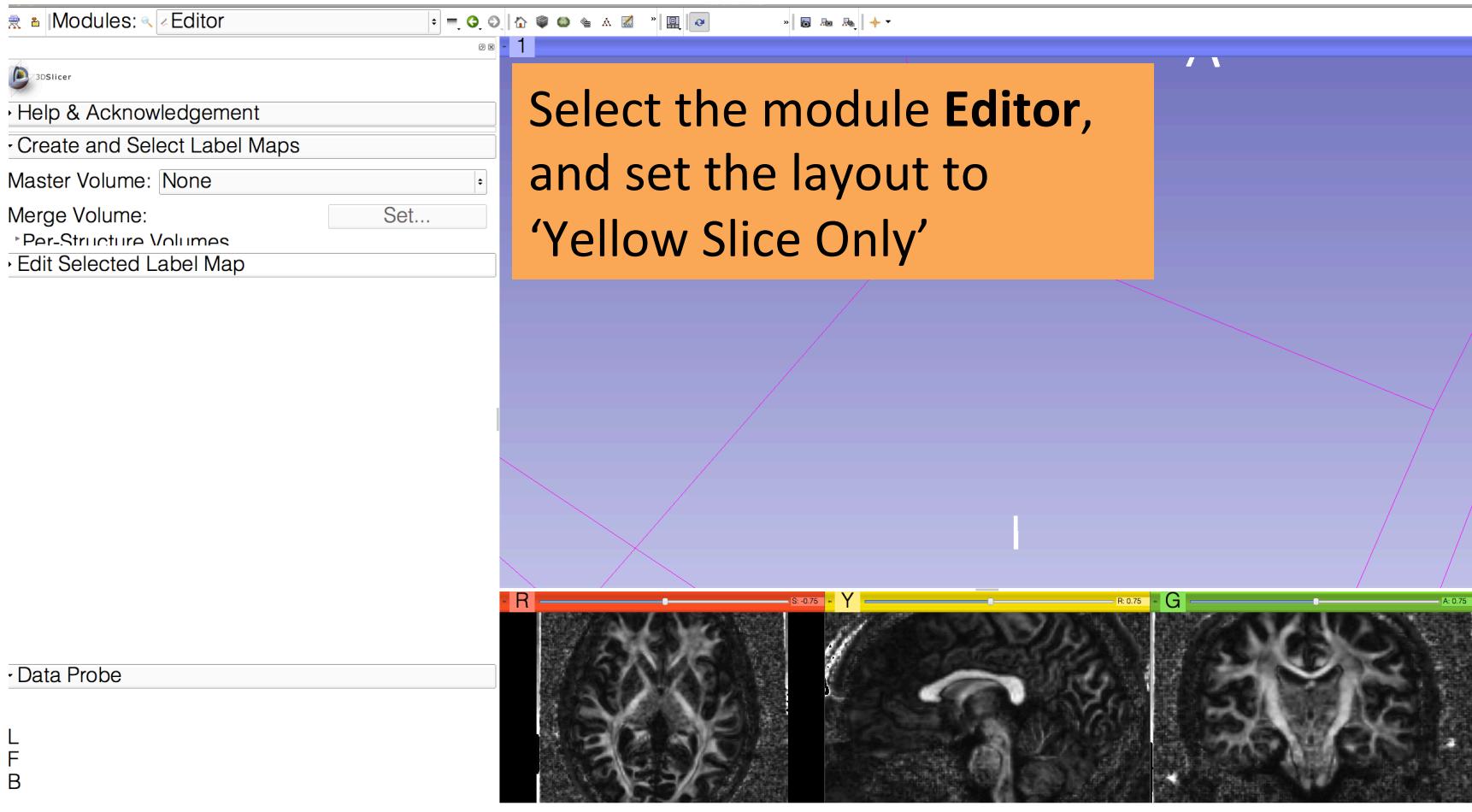


Part 3: From tensors to tracts

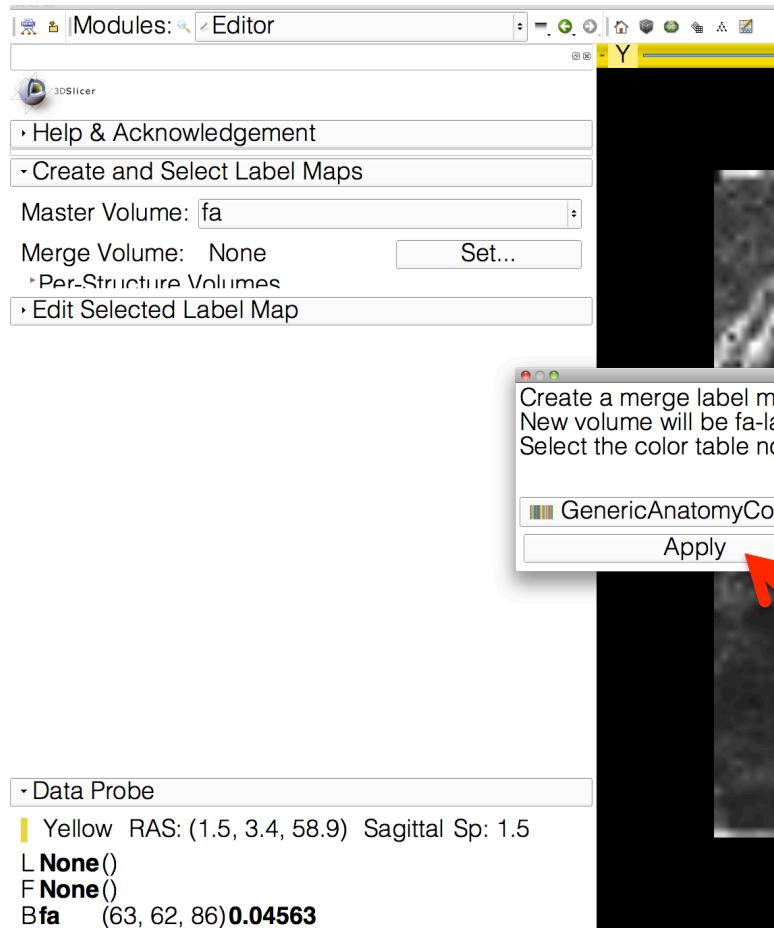
Diffusion MRI tractography

- Tractography can be defined as the virtual reconstruction of the trajectory of water molecules along white matter bundles.
 - DTI tracts provide a mathematical representation of the underlying white matter anatomy.
 - Each voxel contains hundreds of thousands of axon fibers: size of a voxel $\sim 1\text{-}5 \text{ mm}$; diameter of an axon $\sim 0.1\text{-}10 \mu\text{m}$
- A DTI tract is not equivalent to a real fiber.

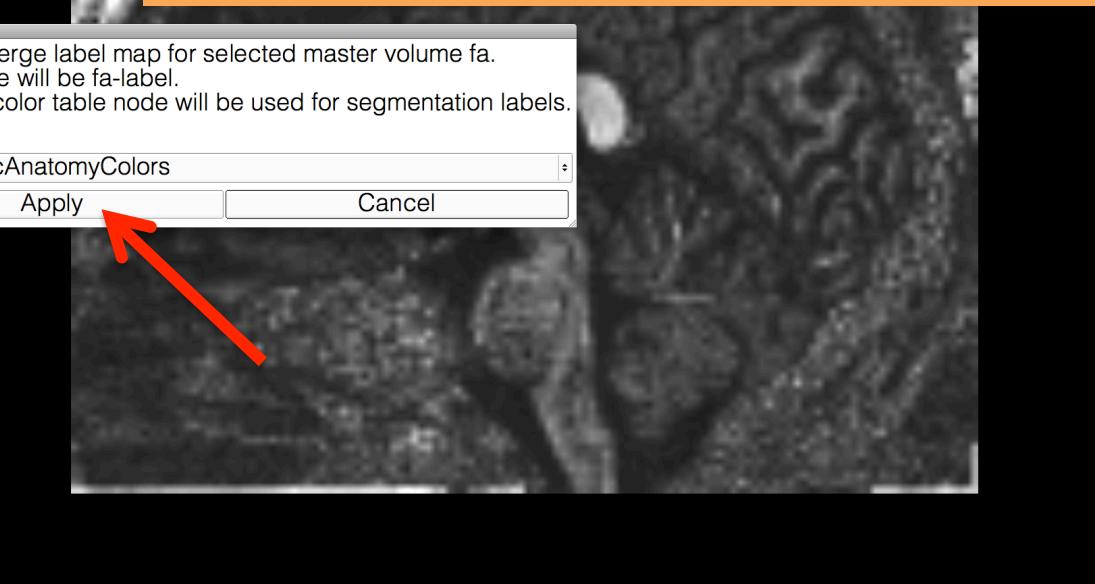
Tractography Seeding: ROI definition



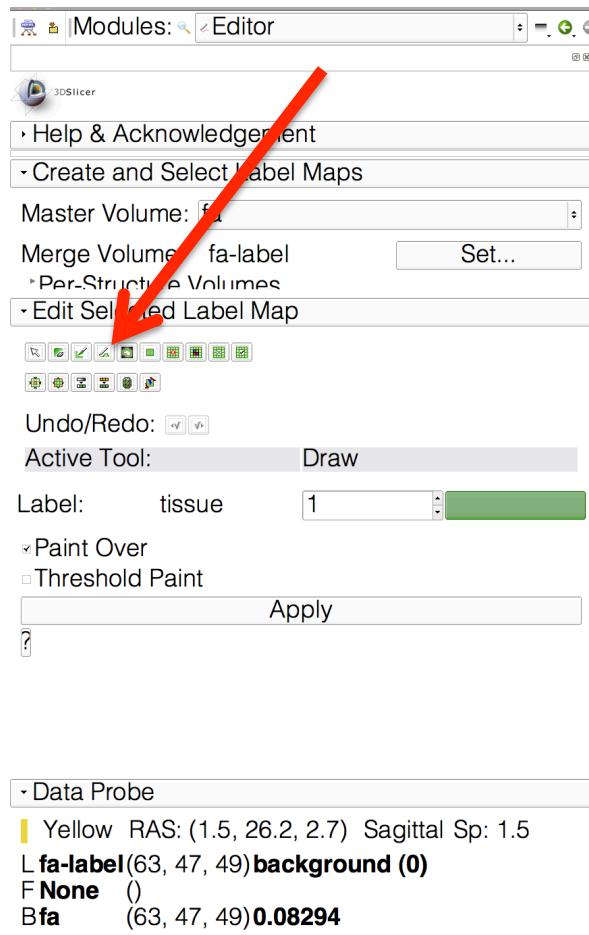
ROI Definition



Set the Master Volume to 'fa'
Click on Apply in the pop-up
window to create an empty
labelmap 'fa-label'

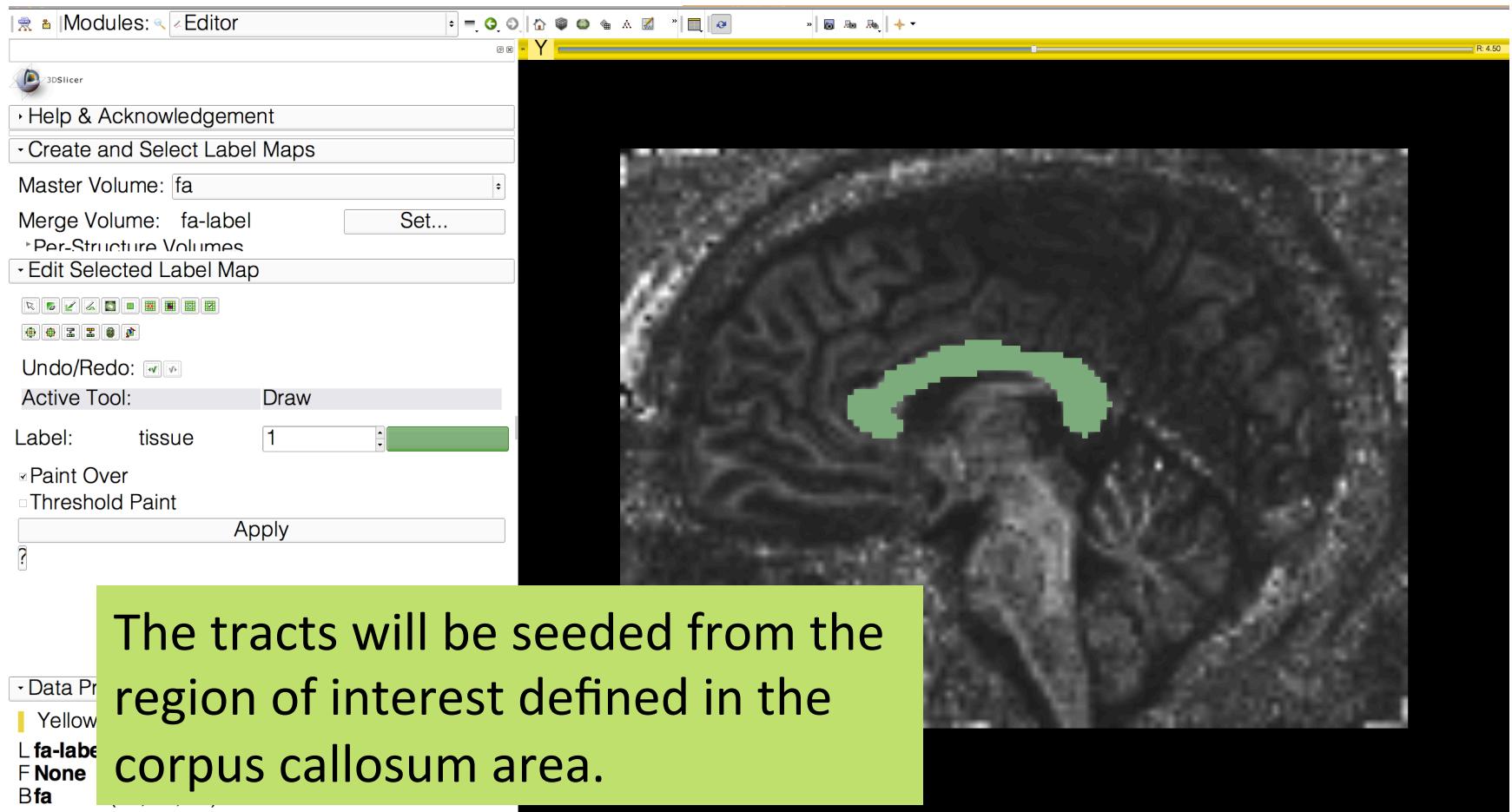


ROI Drawing



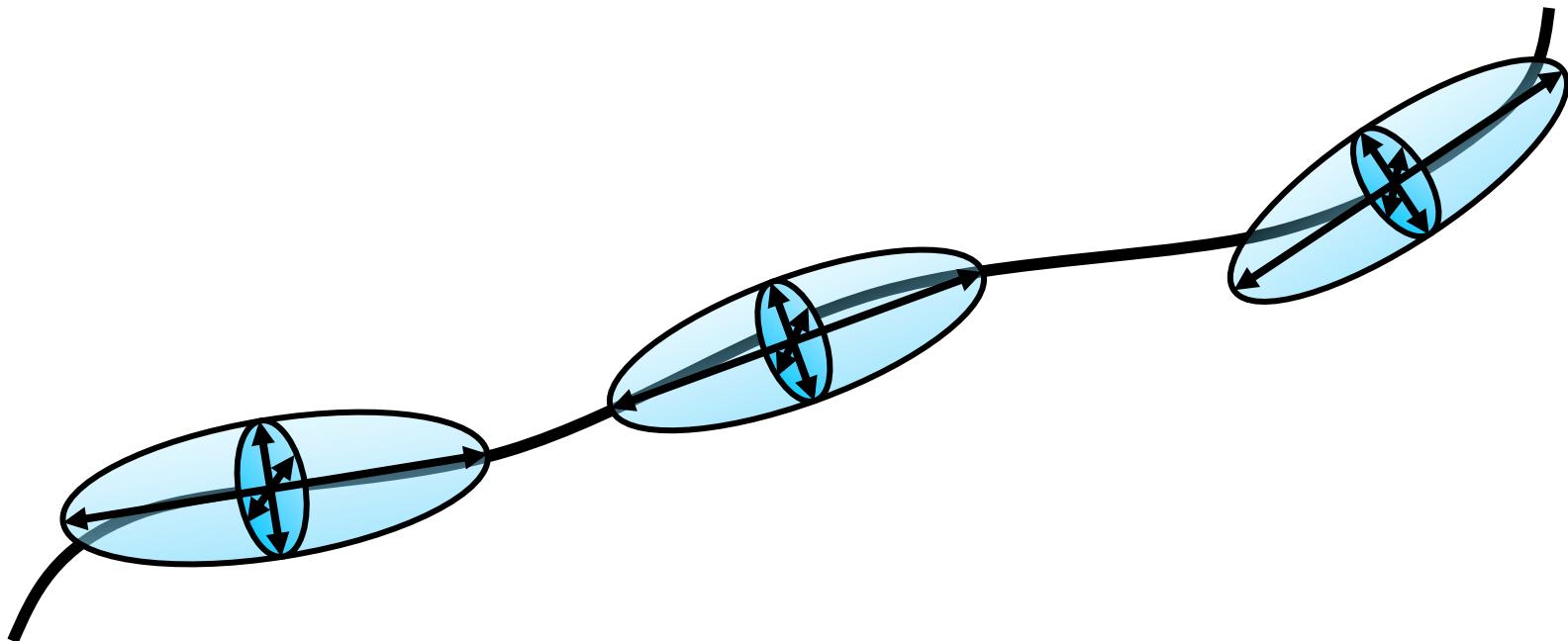
Use the draw tool to outline the contour of the corpus callosum in the sagittal slice, and press Enter.
Repeat the same operation on 3 adjacent sagittal slices.

ROI Drawing

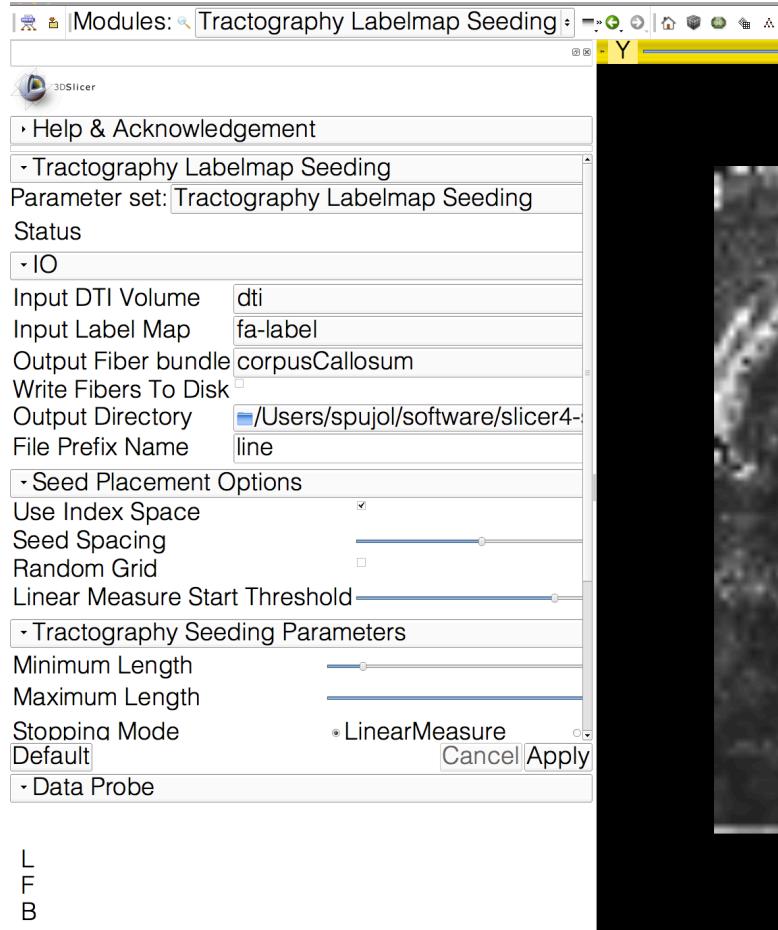


Streamline tractography

Underlying Assumption: the orientation of the fibers is collinear with the direction of the principal eigenvector



Labelmap Seeding: I/O



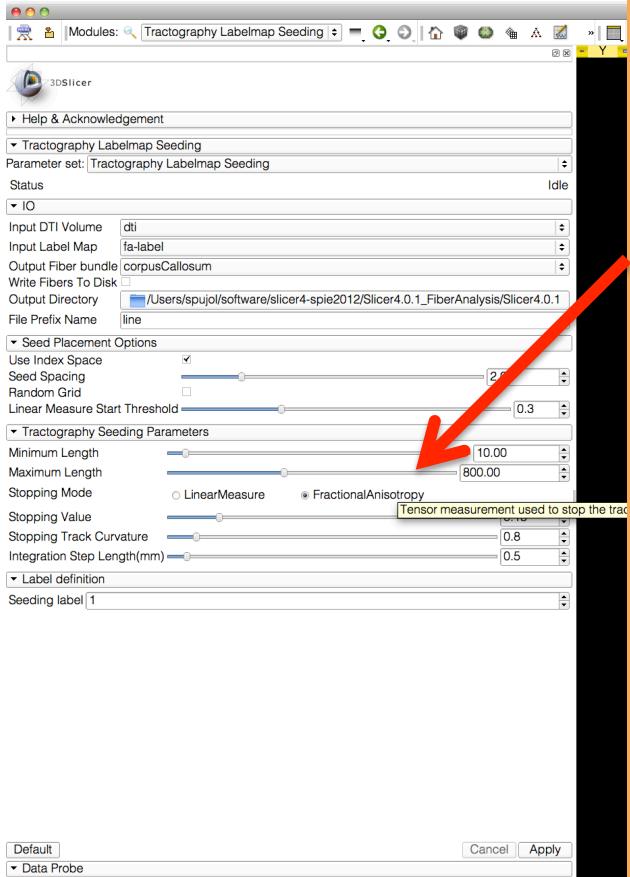
Select the module **Tractography Labelmap Seeding**

Set the Input DTI Volume to 'dti'

Set the Input Label Map to 'fa-label'

Set Output Fiber Bundle to 'Create New Fiber Bundle' and rename it 'corpusCallosum'

Labelmap Seeding: parameters



Select the Seed Placement Options to 'Use Index Space'.

Select Stopping Mode 'Fractional Anisotropy'

Select the default tractography Seeding parameters:

-Minimum length: 10 mm

-Maximum length: 800 mm

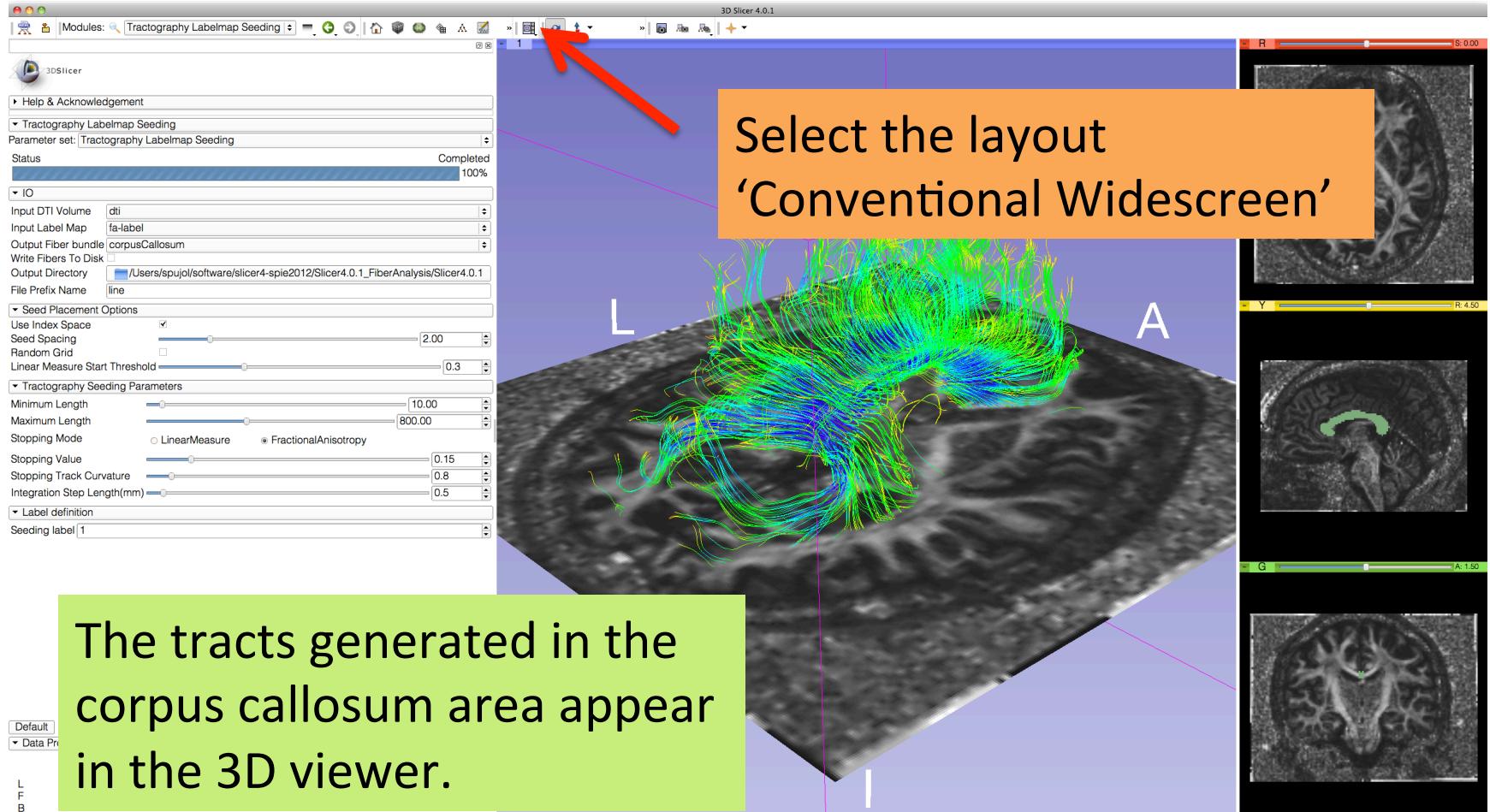
-Stopping value: 0.15

-Stopping track curvature: 0.8

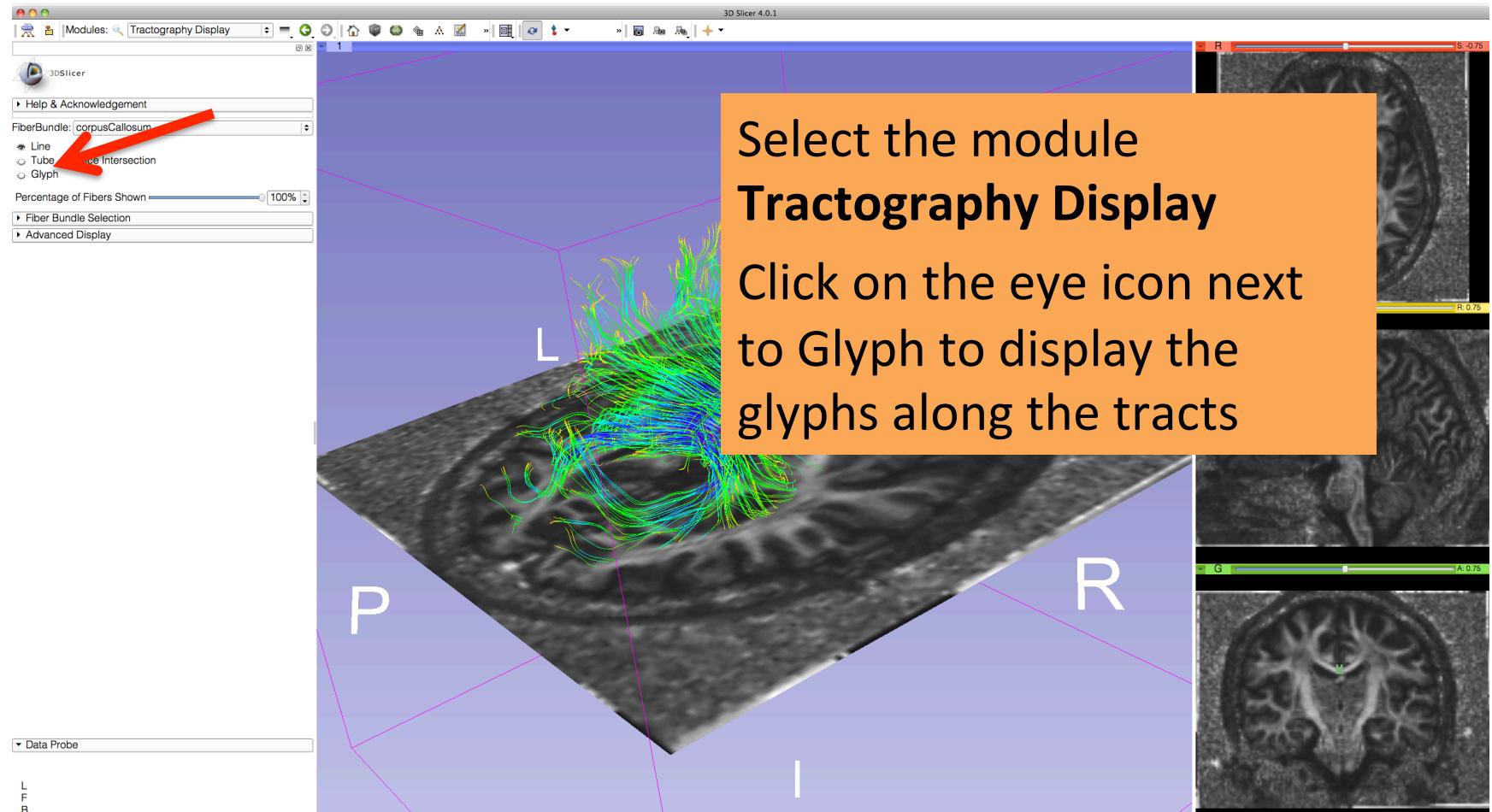
-Integration step length: 0.5 mm

Click on **Apply**

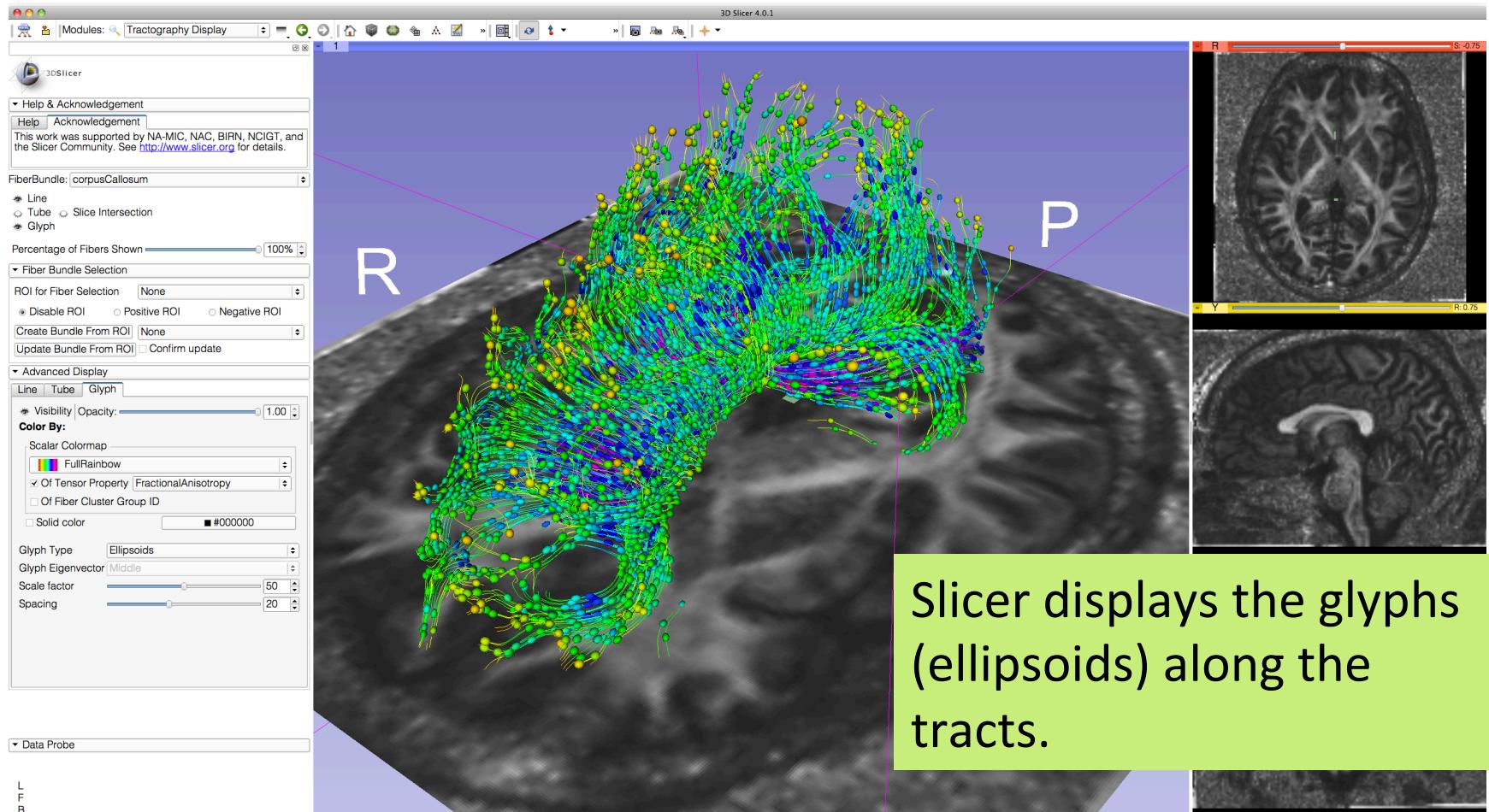
Labelmap Seeding: Tracts



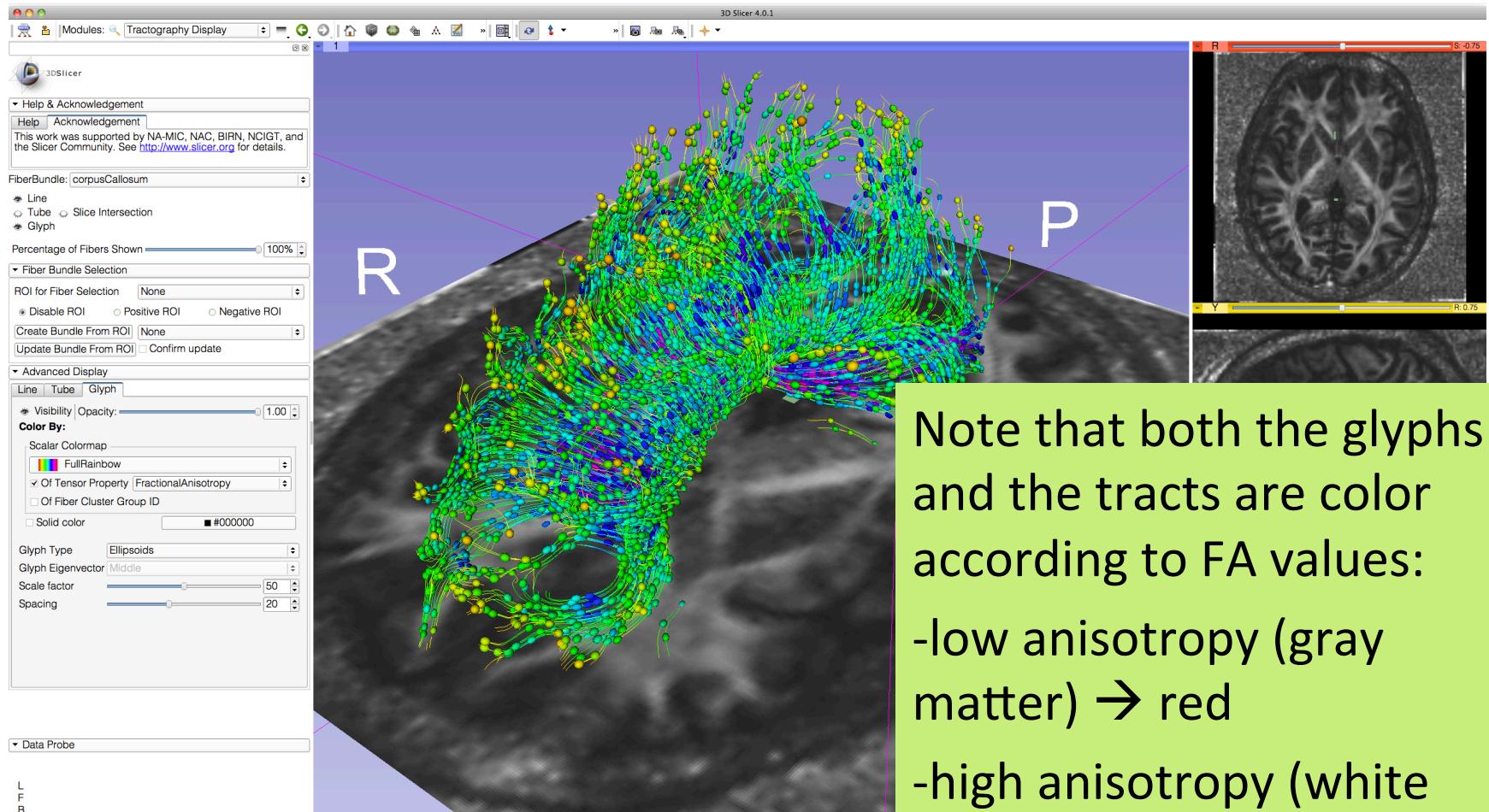
Labelmap Seeding: Tracts



Tractography Results



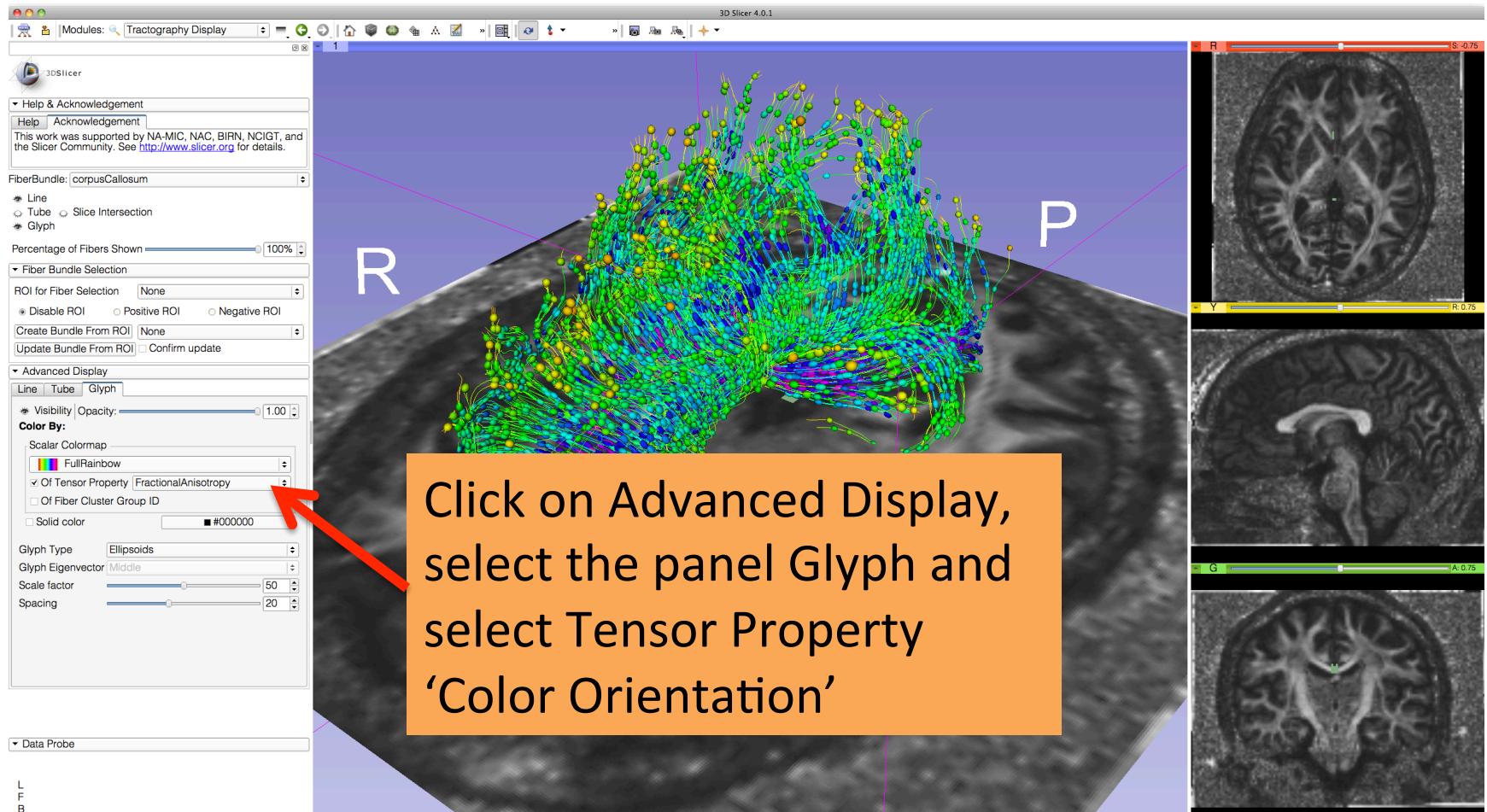
Tractography Results



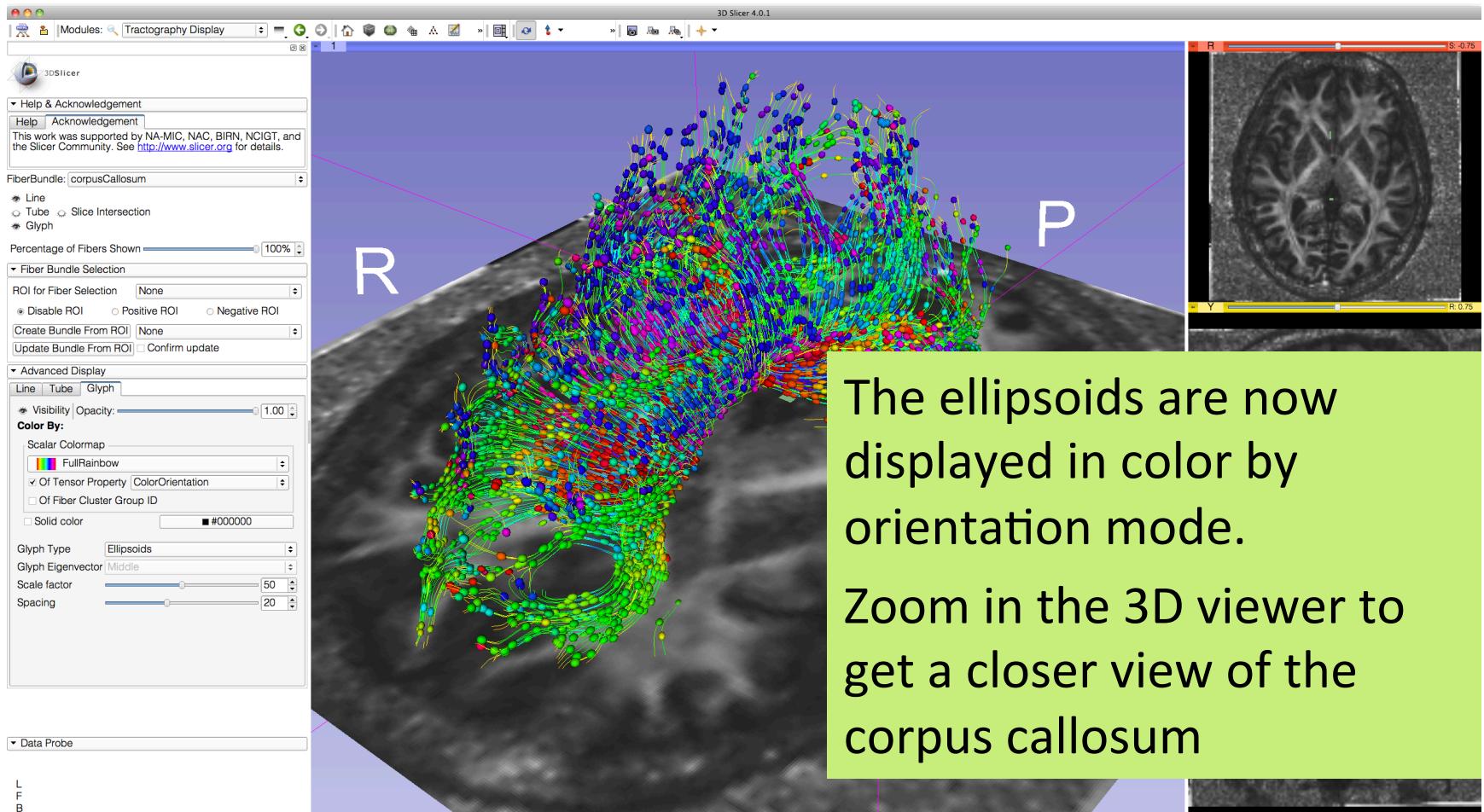
Note that both the glyphs and the tracts are color according to FA values:

- low anisotropy (gray matter) → red
- high anisotropy (white matter) → blue

Tractography Results



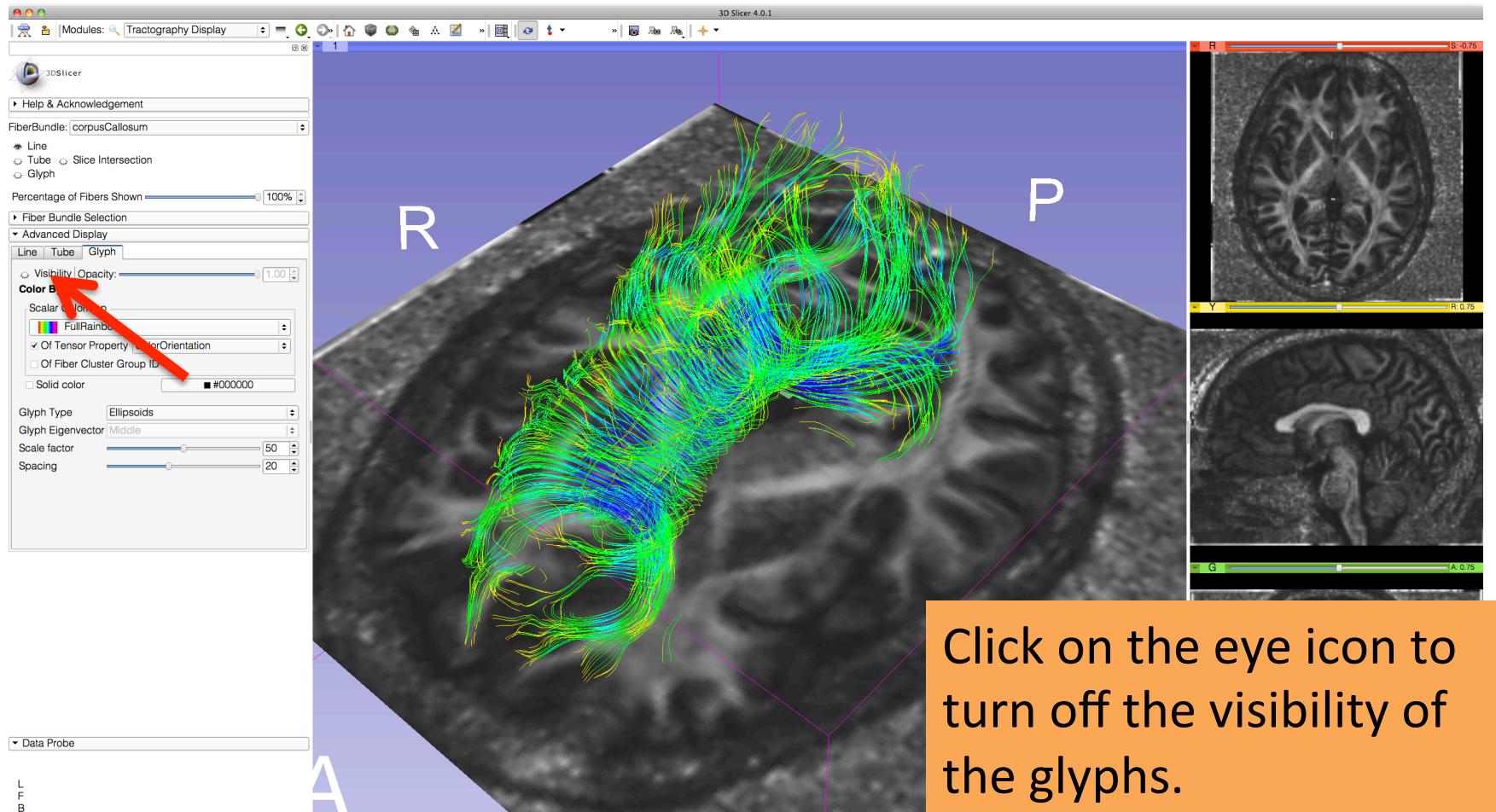
Tractography Results



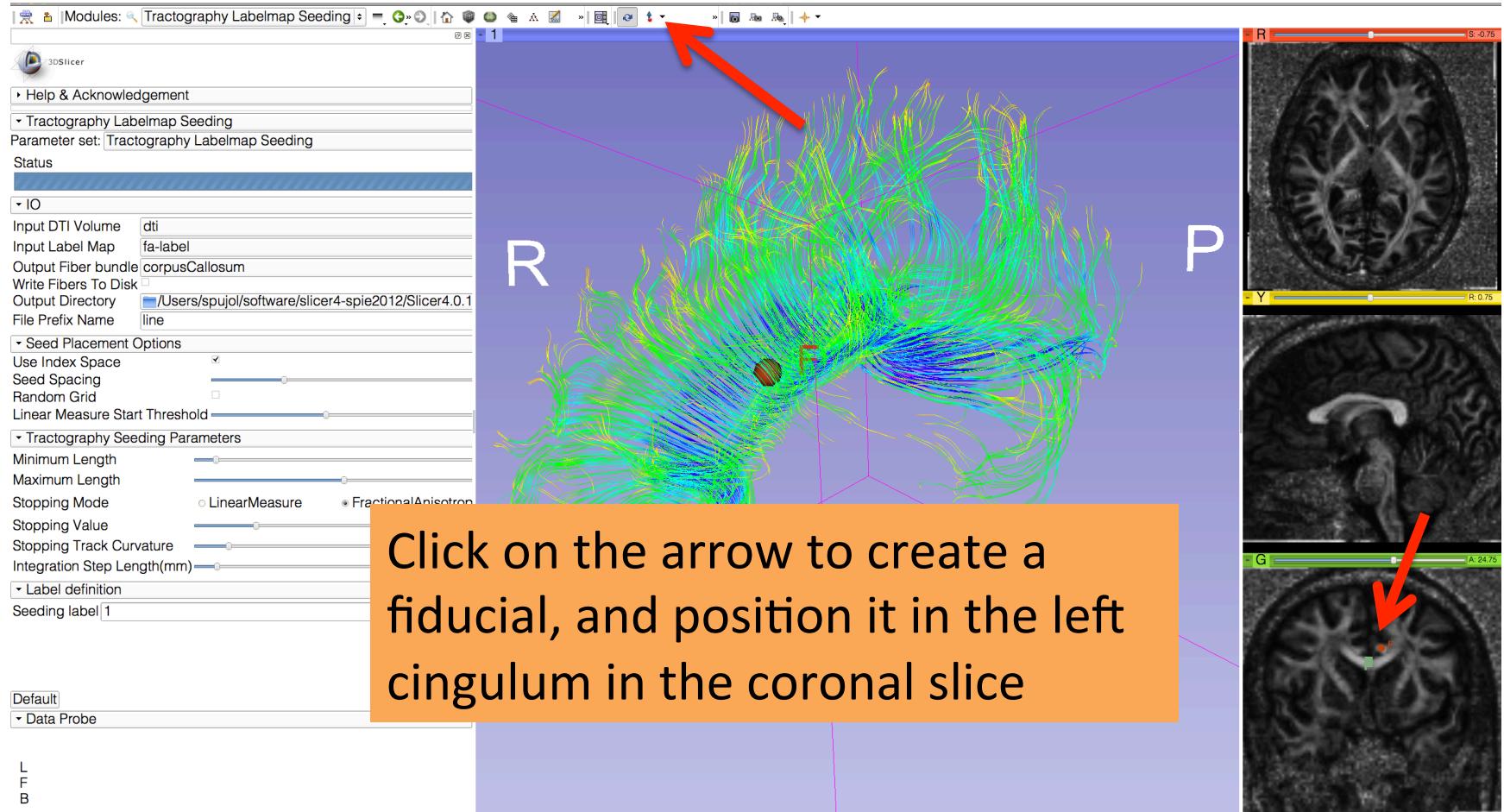
Tractography Results



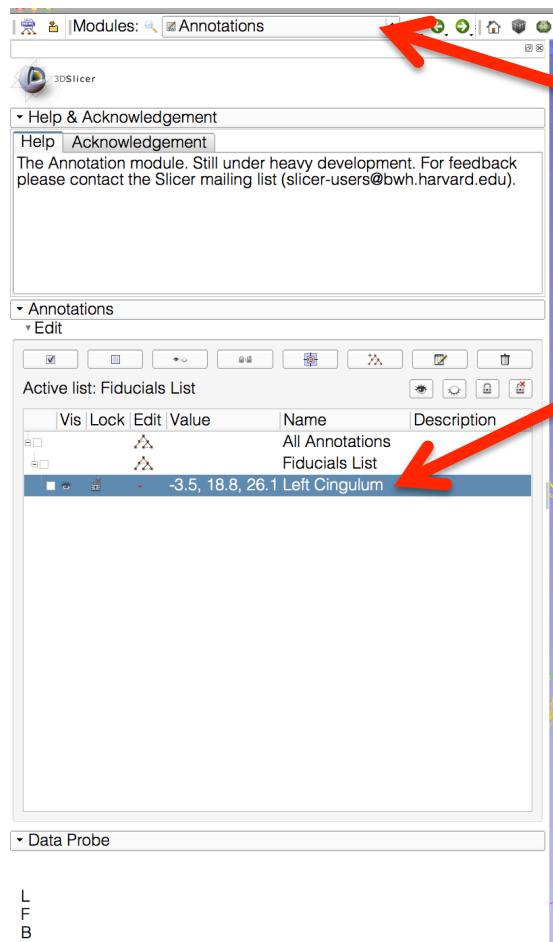
Tractography Results



Fiducial Seeding

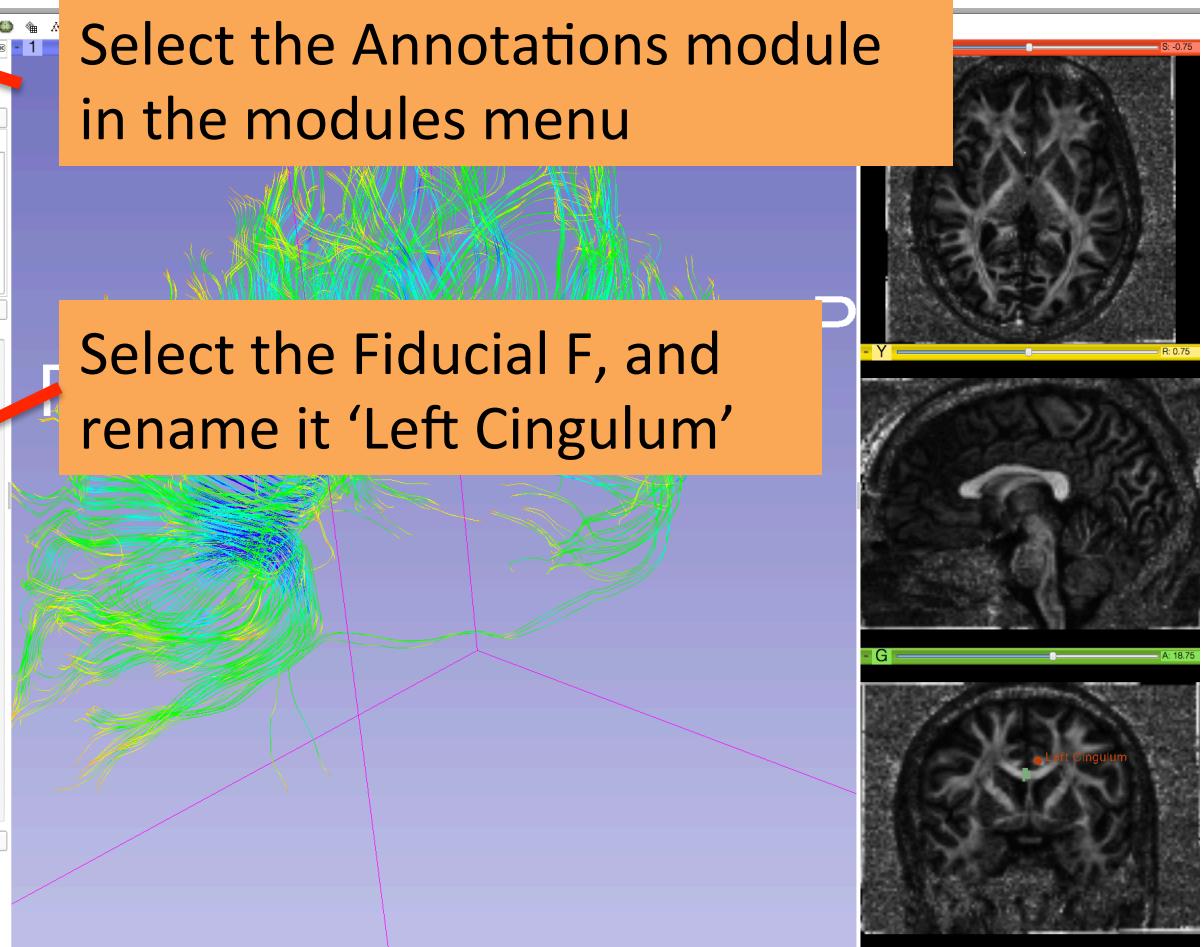


Fiducial Seeding

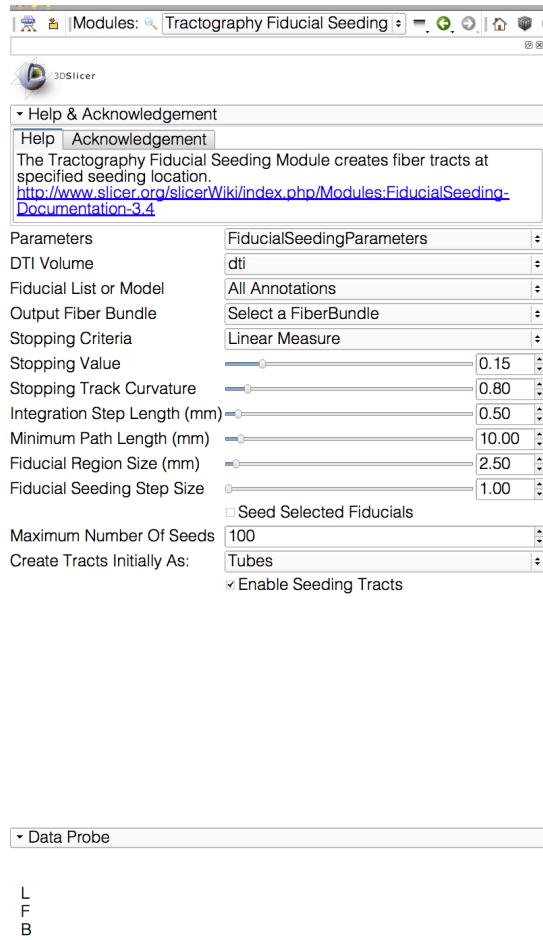


Select the Annotations module in the modules menu

Select the Fiducial F, and rename it 'Left Cingulum'



Fiducial Seeding



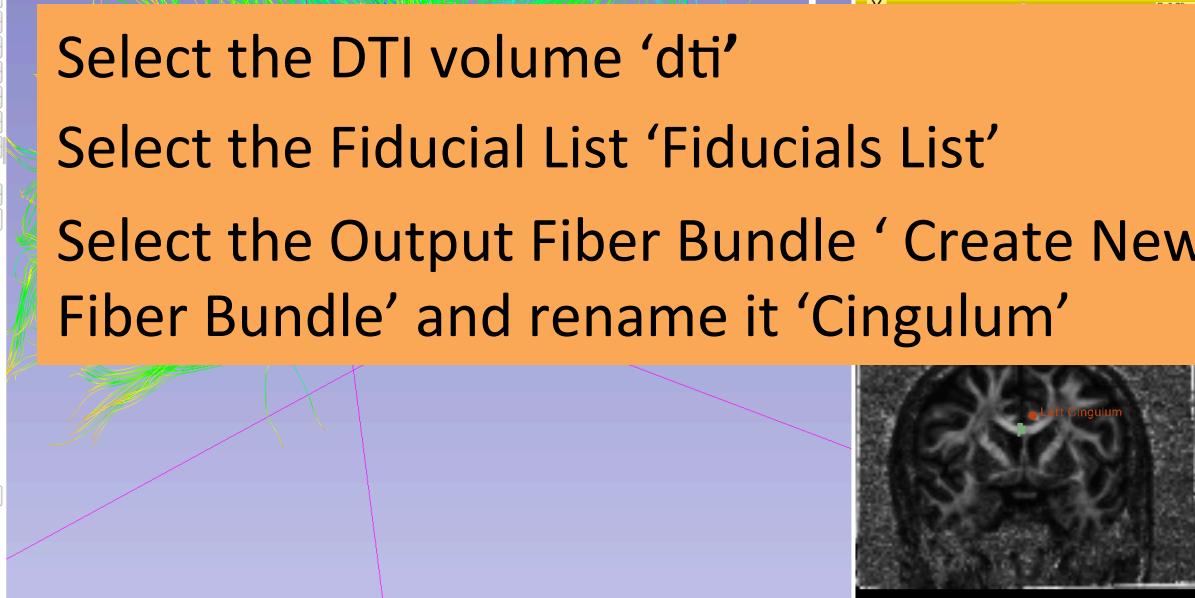
Select the module **Tractography Fiducial Seeding**



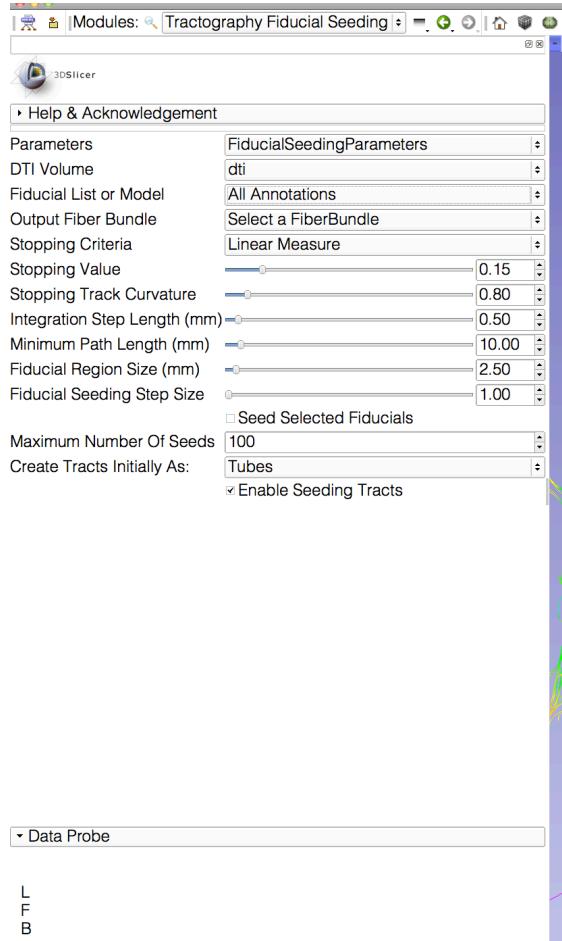
Select the DTI volume 'dti'

Select the Fiducial List 'Fiducials List'

Select the Output Fiber Bundle 'Create New Fiber Bundle' and rename it 'Cingulum'



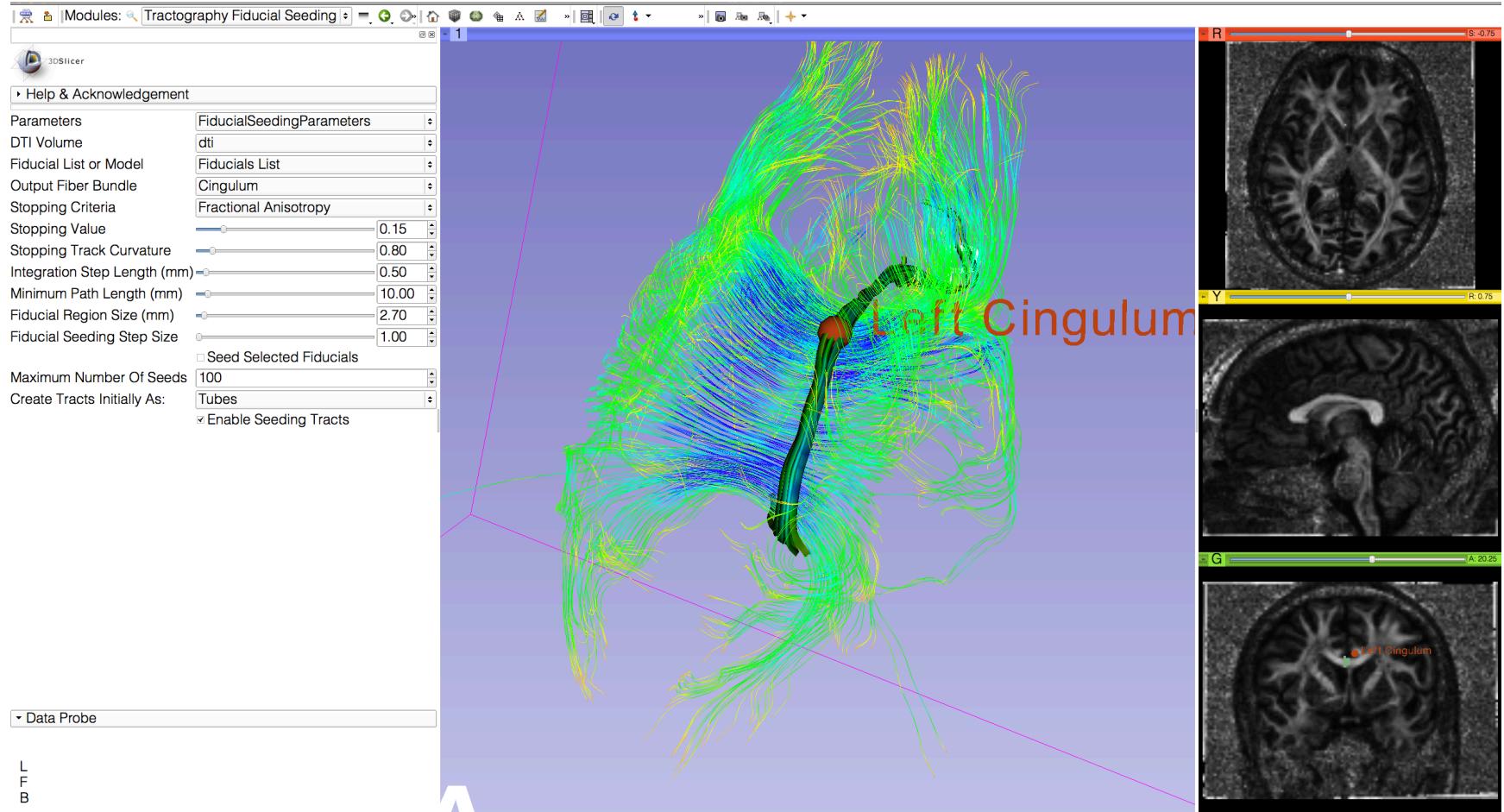
Fiducial Seeding



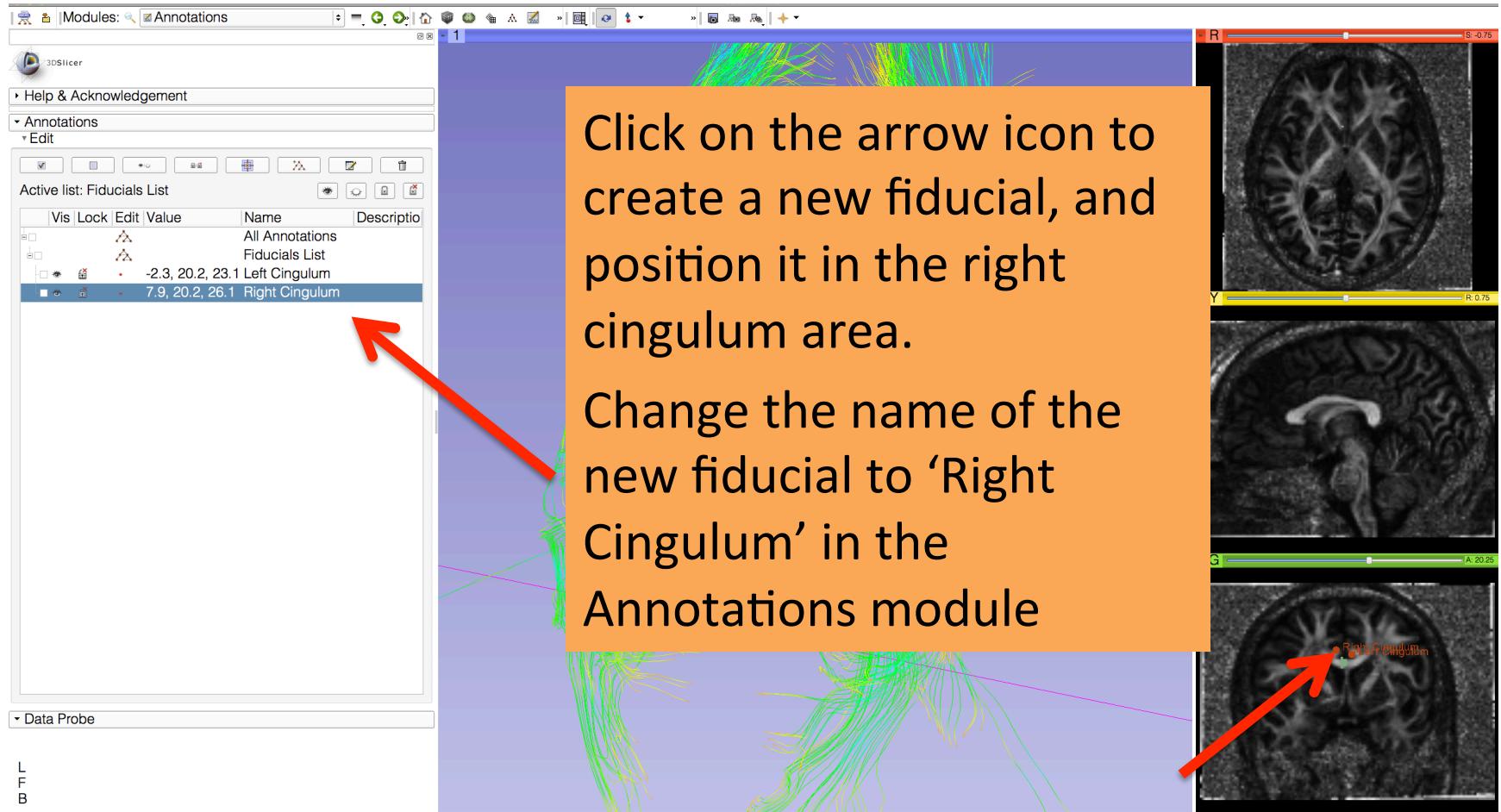
Set the tractography parameters as follows:

- Stopping Criteria: Fractional Anisotropy
- Stopping Value: 0.15
- Stopping Track Curvature: 0.8
- Integration step length: 0.5 mm
- Minimum length: 10 mm
- Fiducial regions size: 2.5 mm
- Fiducial step size: 1.0
- Maximum number of seeds: 100
- Create Tracts Initially as Tubes

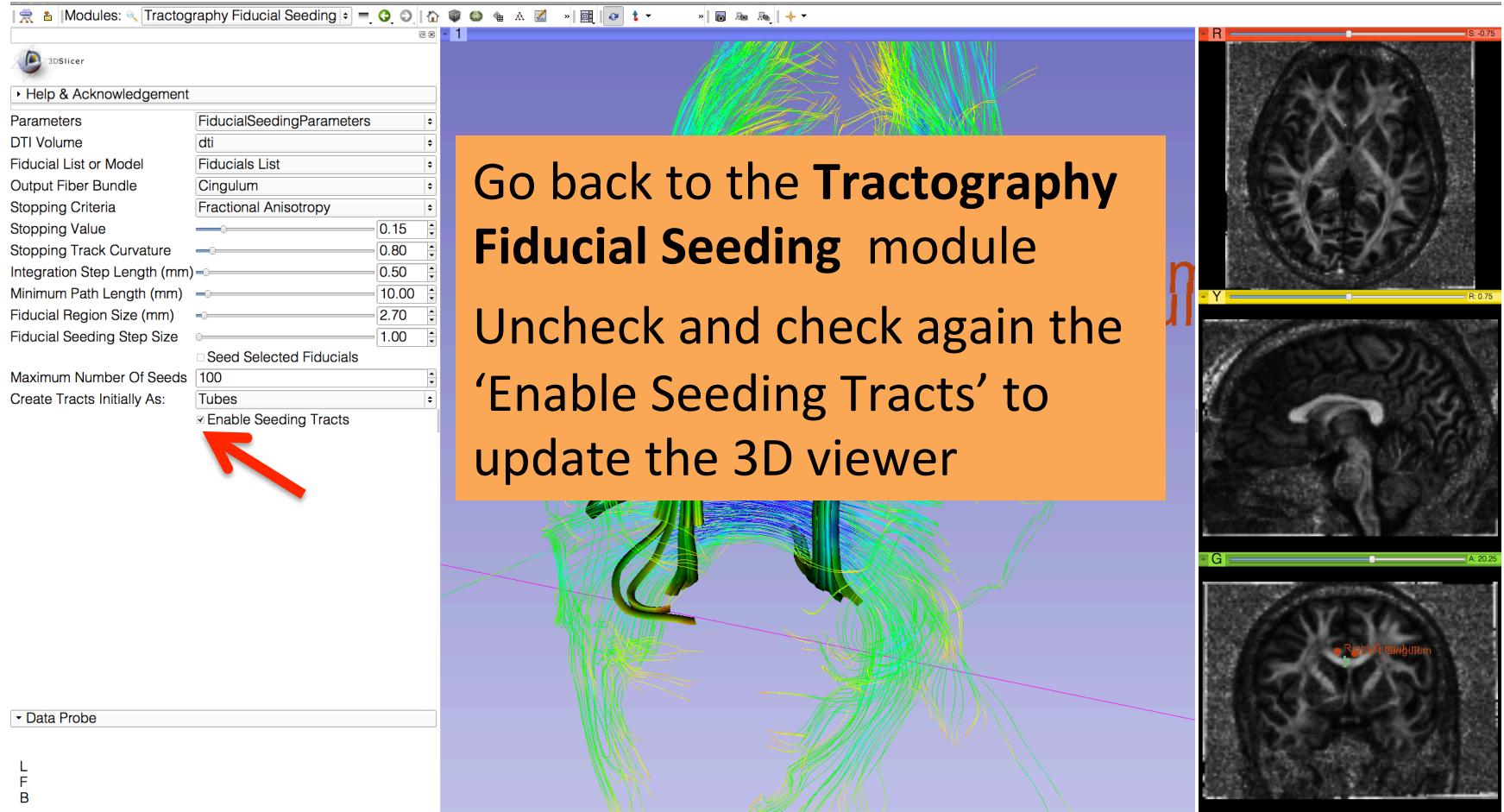
Fiducial Seeding



Fiducial Seeding



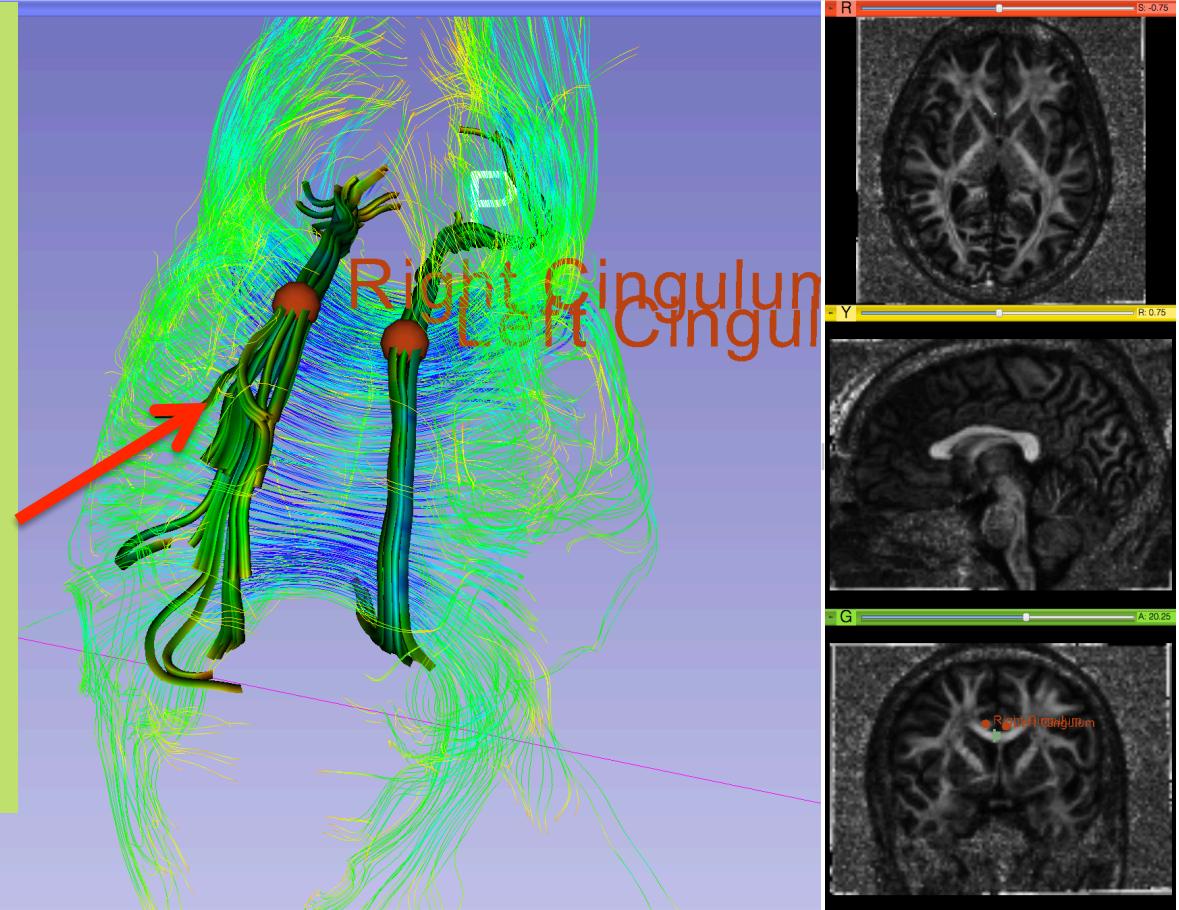
Fiducial Seeding



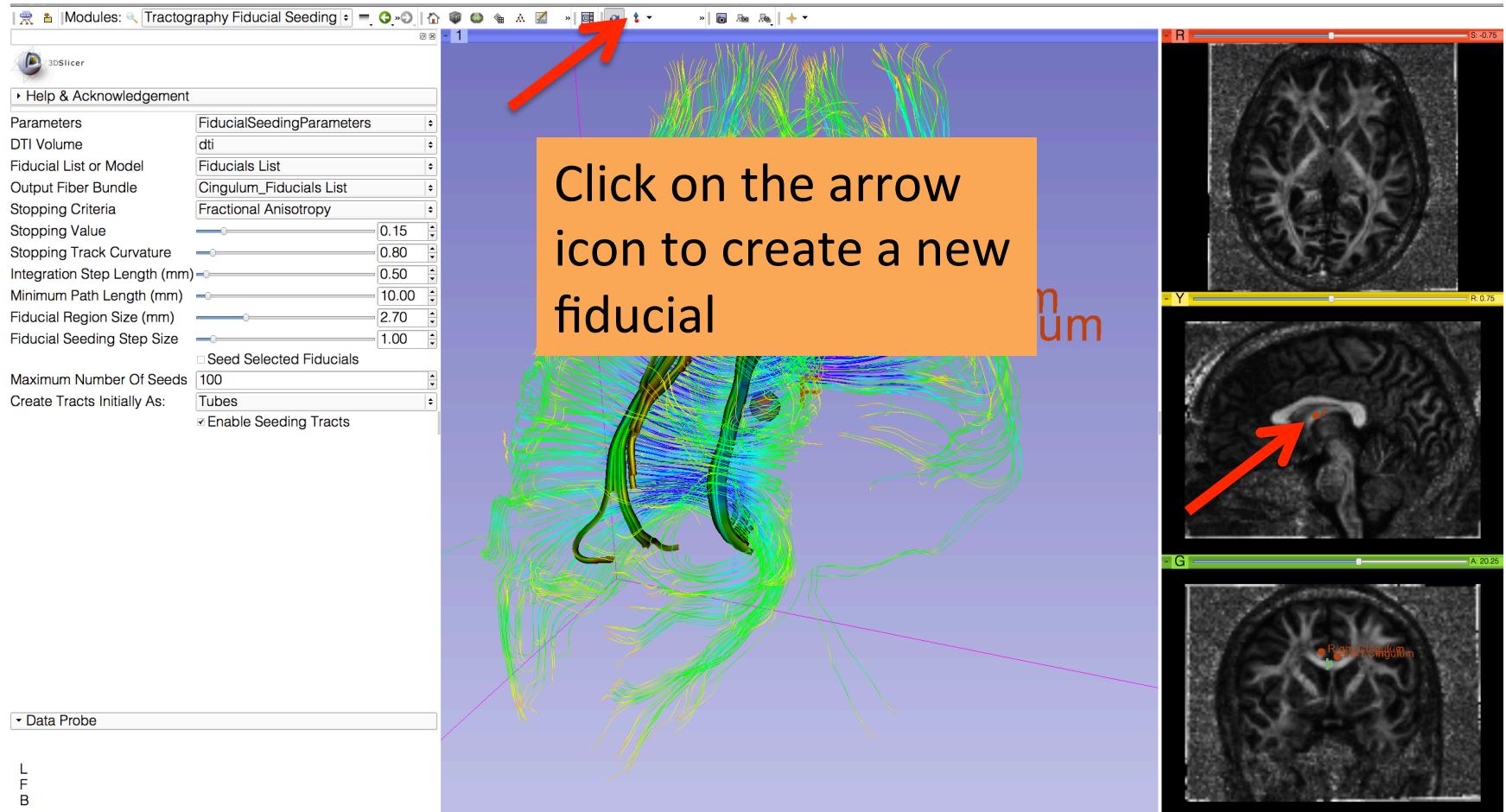
Fiducial Seeding

Part of the left and right cingulum appear in the 3D viewer.

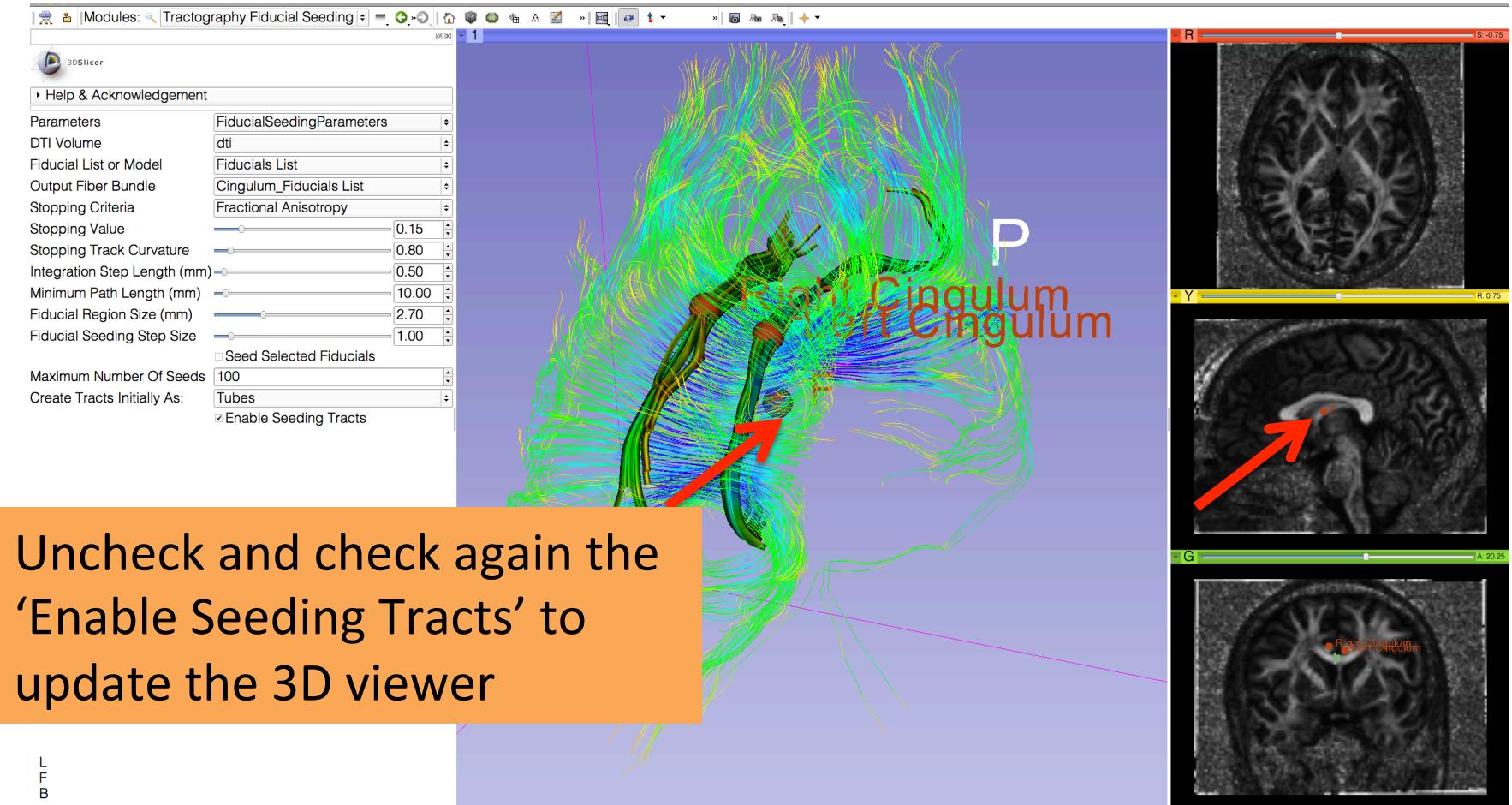
Move the fiducials to explore the spatial relationship between the cingulum and the corpus callosum



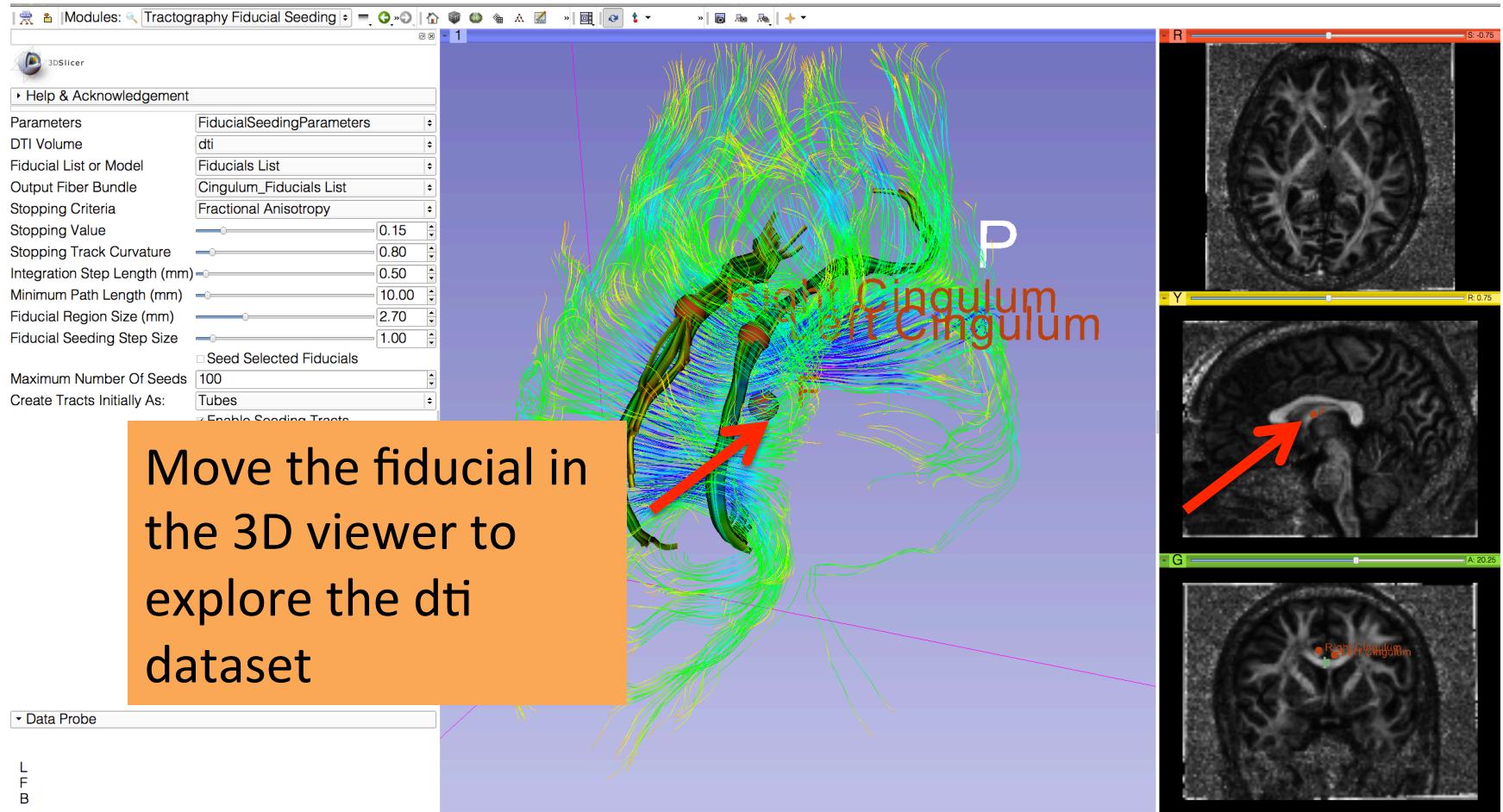
Fiducial Seeding



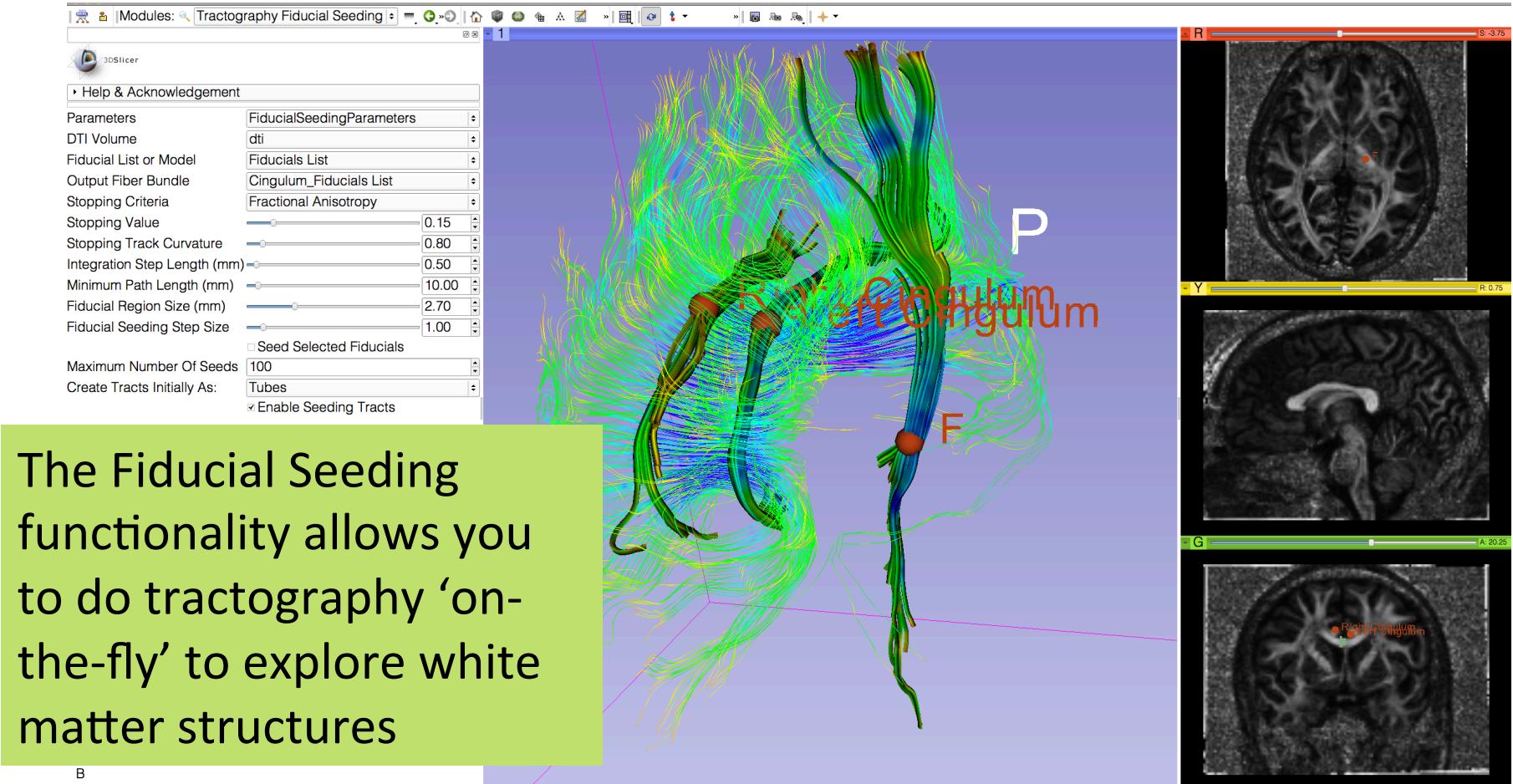
Fiducial Seeding



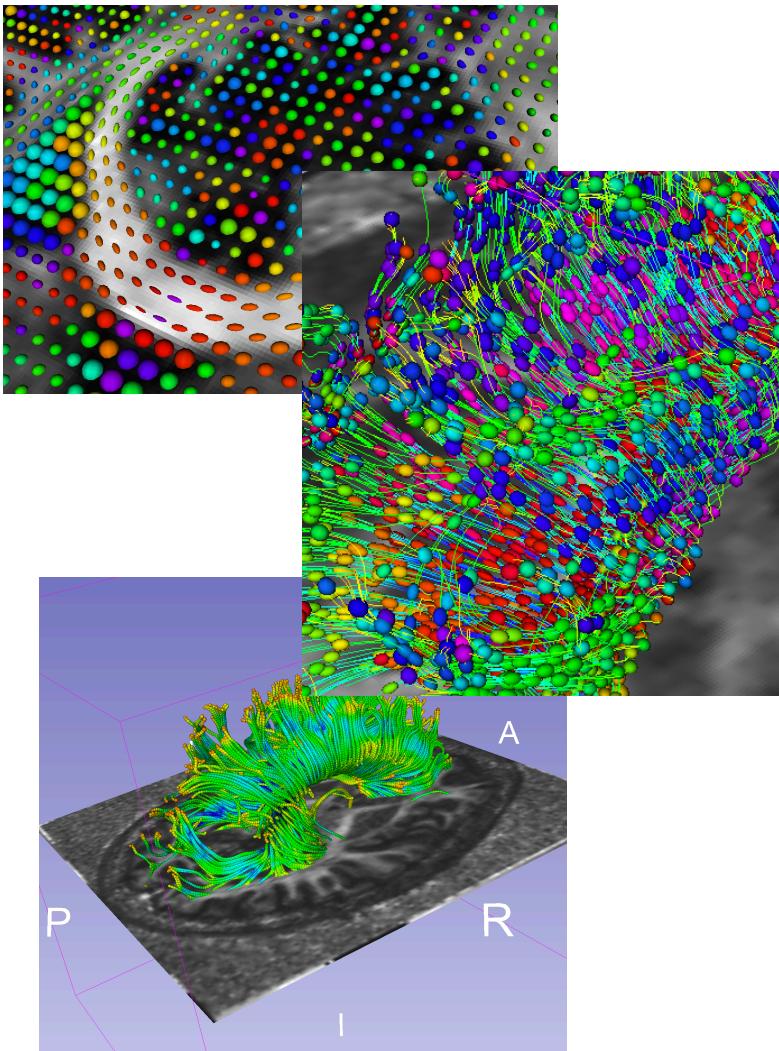
Fiducial Seeding



Tractography ‘on-the-fly’



Conclusion



This tutorial guided you through the different steps of a Diffusion MR Analysis pipeline, from tensor estimation to 3D tracts visualization, for exploring and studying the brain white matter pathways.

Acknowledgments



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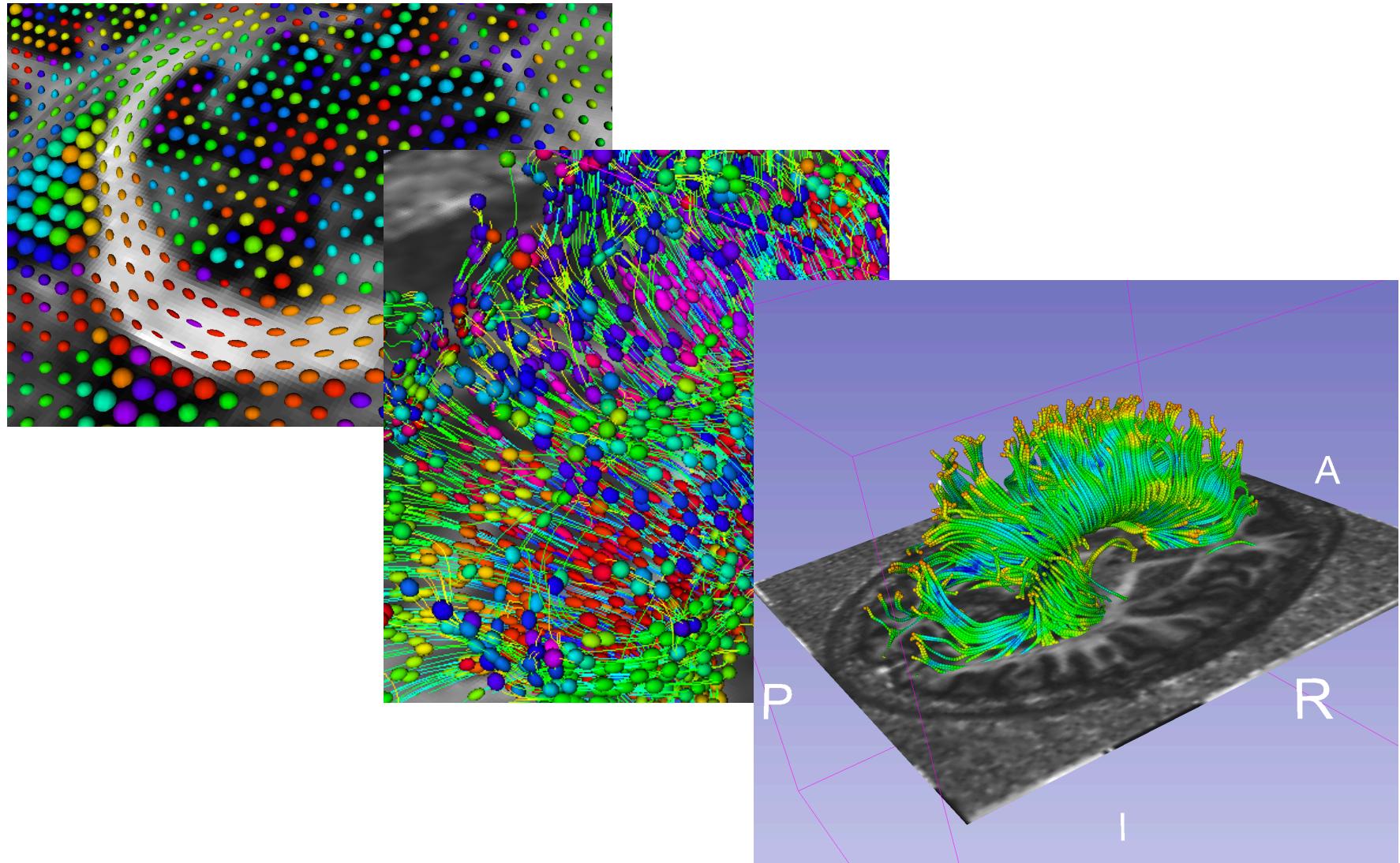
Slicer Community

- www.slicer.org

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