



#### **Diffusion MRI Analysis**

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#### **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

#### White Matter Exploration



First non-invasive window on the organization of brain white matter pathways *in-vivo* 

# **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 DiffusionMRI\_tutorialData is a Diffusion Weighted MR scan of the brain acquired with 41 gradient directions and one baseline.



The dataset is available on the Slicer Training Compendium (www.slicer.org)

#### **Tutorial software**



#### The tutorial uses the 3DSlicer version 4.1 software available at www.slicer.org

#### Disclaimer

It is the responsibility of the user of 3DSlicer to comply with both the terms of the license and with the applicable laws, regulations and rules. Slicer is a tool for research, and is not FDA approved.

# **3DSlicer**



3D Slicer is a multi-institution effort supported by the National Institutes of Health.

- An end-user application for image analysis
- An open-source environment for software development
- A software platform that is both easy to use for clinical researchers and easy to extend for programmers

# 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**



Calculation

Acquisition

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Maps

Visualization



#### Part 1: From DWI images to Tensors

# Understanding the DWI dataset



The Diffusion Weighted Imaging (DWI) dataset is composed of 1 volume acquired without diffusion-sensitizing gradient, and 41 volumes acquired with 41 different diffusion-sensitizing gradient directions.

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Mouse & Keyboard	DWI to Full Brain Tractography
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Tractography Display Tractography Fiducial Seeding Tractography Label Map Seeding Transform MRML Files to New EMSegmenter Standard Transforms Vector Demon Registration (BRAINS) View Controllers Volume Rendering Volumes Voting Binary Hole Filling Image Filter WebGL Export Welcome to Slicer

Slicer displays the list of 103 modules in alphabetical order.

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Left click on the pin button in the top left corner of the red viewer to display the slice menu.

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Click on the 'links' icon . to link all three viewers, and click on the 'fit image to window icon'.



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#### **Diffusion Tensor Estimation** 📷 📸 Modules: 🔍 DWI to DTI Estimation

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Default Data Probe

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Select the module **DWI to DTI 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 'baseline'

-select the Estimation Method 'WLS' (Weighted Least Squares) and click on Apply.

#### **Diffusion Tensor Estimation**

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#### **Diffusion Tensor Estimation**



Green: anterior-posterior

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#### **Diffusion Tensor Data**



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

#### **Diffusion Tensor**

- The diffusion tensor <u>D</u> 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 λ1, λ2, λ3 to characterize the size and shape of the diffusion tensor.



# **Diffusion Tensor Shape**

 $\lambda 1 = \lambda 2 = \lambda 3$   $\lambda 1 >> \lambda 2, \lambda 3$   $\lambda 1^{\sim} \lambda 2 >> \lambda 3$ 

Isotropic media (CSF, gray matter) Anisotropic media (white matter)

### **Exploring the Diffusion Tensor Data**

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Browse through the dti volume using the slider, and try identify the corpus callosum

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#### **Corpus Callosum**



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

Image from Gray's Anatomy

#### **Exploring the Diffusion Tensor Data**

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▼ Data Probe

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#### Characterizing the Size of the tensor: Trace

Trace(D) =  $\lambda 1 + \lambda 2 + \lambda 3$ 

- Trace(D) is intrinsic to the tissue and is independent of fiber orientation, and diffusion sensitizing gradient directions
- Trace(D) is a clinically relevant parameter for monitoring stroke and neurological condition (degree of structural coherence in tissue)
- Trace(D) is useful to characterize the size of the diffusion ellipsoid
#### Characterizing the Size of the tensor: Trace



#### Trace

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#### Scalar Maps: Fractional Anisotropy

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

- 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

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IO     Input DTI Volume dti     Output Scalar Volume fa	Set Input DTI Volume to 'dti'
Operation  Estimation Parameters      Trace     Determinant     RelativeAnisotropy     FractionalAnisotropy	Select Output Scalar Volume 'Create new Volume' and rename it 'fa'
∘ Mode ∘ LinearMeasure ∘ PlanarMeasure	Select the Operation 'Fractional Anisotropy'
<ul> <li>SphericalMeasure</li> <li>MinEigenvalue</li> <li>MidEigenvalue</li> <li>MaxEigenvalue</li> <li>MaxFigenvalue</li> </ul>	Click on Apply to calculate the Fractional Anisotropy map of the tensor volume
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#### **Fractional Anisotropy**

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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.

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Data Probe

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#### **Fractional Anisotropy**



#### **Fractional Anisotropy**

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

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# Go back to conventional layout







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#### Part 2: Visualizing the tensor data



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#### Click on Auto W/L to adjust the Window and Level values of the display

#### In the **Glyphs on Slices Display panel**, set the Color by Scalar parameter to 'ColorOrientation', and check Slice Visibility 'Red' '

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

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





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different regions of the brain

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





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

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#### **Optic Chiasm**



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

Image from Gray's Anatomy

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Go back to the conventional layout, unselect Slice Visibility 'red', and click on the eye icon in the red viewer to turn off the visibility of the red slice in the 3D viewer



▼ Data Probe

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#### 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 ~ 1-5 mm is <u>very different</u> from the diameter of an axon~0.1-10 μm
- $\rightarrow$  A DTI tract is not equivalent to a real fiber.

#### Tractography Seeding: ROI definition

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Master Volume: fa	\$				35.
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Per-Structure Volumes					100
· Edit Selected Label Map					77.

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

Create a merge label map for selected master volume fa. New volume will be fa-label. Select the color table node will be used for segmentation labels.

Cancel





- Data Probe Yellow RAS: (1.5, 3.4, 58.9) Sagittal Sp: 1.5 L None() F None() Bfa (63, 62, 86) 0.04563

#### **ROI** Drawing

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B <b>fa</b>	(63, 47, 49) <b>0.08294</b>

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**

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#### Streamline tractography

<u>Underlying Assumption</u>: the orientation of the fibers is collinear with the direction of the principal eigenvector



## Labelmap Seeding: I/O

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<ul> <li>Help &amp; Acknowled</li> </ul>	gement	
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Stopping Value		0.15 🖨
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<ul> <li>Label definition</li> </ul>		
Seeding label 1 Default		Cancel Apply
<ul> <li>Data Probe</li> </ul>		

F B Modules: 🔍 Tractography Label Map Seeding 😫 💻 🧿 🕘 🛛 🏠 🌒 🚳

Select the module **Tractography Label Map Seeding** Set the Input DTI Volume to 'dti' Set the Input Label Map to 'falabel'

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



#### Labelmap Seeding: parameters

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	FractionalAnisotropy	
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▼ Label definition		
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Select the Seed Placement Options to 'Use Index Space'. Select Stopping Criteria '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

NA-MIC ARR 2012

#### Labelmap Seeding: Tracts

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Help & Acknowledgement	N/S
Input DTI Volume dti	Select the layout
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Output Fiber Bundle corpusCallosum	'Conventional Widescreen'
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Stopping Value	
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in the 3D viewer.

#### Labelmap Seeding: Tracts

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3DSlicer		ALVA.
Help & Acknowledgement   Input DTI Volume   dti   Input Label Map   fa-label   Output Fiber Bundle corpusCallosum   Write Fibers To Disk   Output Directory	Select the module Tractography Display	
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FractionalAnisotropy Stopping Value     0.15  Stopping Track Curvature     0.8  Integration Step Length(mm)     0.5		A: 0.75
Label definition Default Cancel Apply Data Probe		

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#### **Tractography Results**





Slicer displays the glyphs (ellipsoids) along the tracts.

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#### **Tractography Results**

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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**

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Click on Advanced Display, select the panel Glyph and select Tensor Property 'Color Orientation'





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# **Tractography Results**

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The ellipsoids are now displayed in color by orientation mode. Zoom in the 3D viewer to get a closer view of the

corpus callosum

## **Tractography Results**



## **Tractography Results**



Select the module
Annotations

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	A	Fiducials
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Click on the arrow to create a fiducial, and position it in the left cingulum in the coronal slice



Data Probe

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Help & Acknowledgeme	nt		_
Parameter set FiducialSeec	dingParameters		1
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Input DTI Volume	Select a Dien	sorVolume	¢
Input Fiducial List or Model	Fiducials List		\$
Output Fiber Bundle	Select a FiberBu	undle	\$
<ul> <li>Seed Placement Options</li> </ul>	6		
Fiducial Region Size		= 2.50mm	4
Fiducial Seeding Step Size	-0	= 1.00mm	4
Seed Selected Fiducials			
Max Number of Seeds	100		4
<ul> <li>Tractography Seeding P</li> </ul>	arameters		
Minimum Path Length		20.00mm	4
Stopping Criteria	Fractional Anisotr	ору	\$
Stopping Value		0.25	4
Stopping Track Curvature	0	0.70	4
Integration Step Length		0.50mm	4
<ul> <li>Enabling Options</li> </ul>			
Create Tracts Initially As T	ubes		\$
Enable Seeding Tracts			

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#### 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'

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Output Fiber Bundle	Cingulum	
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Seed Selected Fiducials		
Max Number of Seeds	100	
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Create Tracts Initially As Tu	ubes	
Enable Seeding Tracts		

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Data Probe

L F B Set the tractography parameters as follows:

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- -Fiducial region size: 2.5 mm
- -Fiducial Seeding Step Size: 1.0 mm

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

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🔍 Tractography Fiducial Seeding 🗧 🧿 🕘 🟠

Part of the left cingulum appears in the 3D viewer.

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Move the Left Cingulum fiducial to explore the spatial relationship between the left cingulum and the corpus callosum

Data Probe

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		<b>-</b> 8.5, <sup>-</sup>	12.9, 24	I.9 Rig	htCin.	

🛯 🚵 🚵 Modules: 🔍 🗹 Annotations

Click on the arrow icon to create a new fiducial, and position it in the right cingulum area.

Change the name of the new fiducial to 'Right Cingulum' in the Annotations module







#### **Fiducial Seeding** 👩 🜆 👧 🔶 🔻

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

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

В







# Tractography 'on-the-fly'



matter structures interactively

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# **DTI Analysis**

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Scene Model: Transform

Display MRML ID's
 Show Hidden nodes

Filter:

Load & Add Scenes Or Individual Datasets

Data Probe

L F B Select the module Data to display the list of elements that have been generated in this tutorial

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# 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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### Neuroimage Analysis Center NIH P41RR013218

# **Questions and Comments**

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