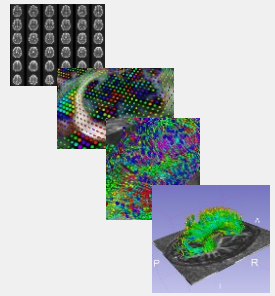
Diffusion MRI Analysis of the Human Brain

Sonia Pujol, Ph.D.

Director of Outreach, Neuroimage Analysis Center
Director of Training, 3D Slicer
Brigham and Women's Hospital
Harvard Medical School

Tutorial Outline



This tutorial is an introduction to the fundamentals of Diffusion MRI analysis, from computation of DTI data to 3D visualization of fiber tracts.

Tutorial Outline

- Part 1: Basics of Diffusion MRI mapping of white matter pathways
- Part 2: Hands-on Diffusion MRI analysis using 3D Slicer

Learning Objectives

Following this tutorial, you will be able to

1) Compute a **diffusion tensor imaging** (DTI) volume from a diffusion weighted MRI scan

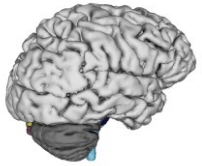
2) Understand the **shape of the diffusion tensor ellipsoid** in different regions of the brain

3) Reconstruct the **3D trajectory of white matter tracts** from DTI data

Tutorial Outline

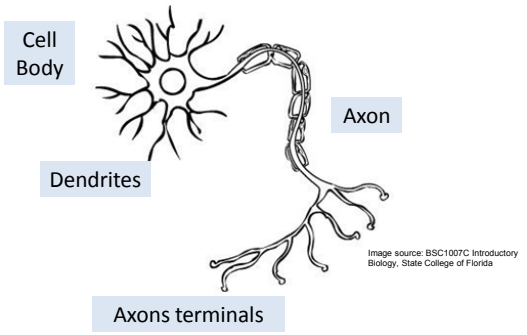
- **Part 1: Basics of Diffusion MRI mapping of white matter pathways**
- Part 2: Hands-on Diffusion MRI analysis using 3D Slicer

Human Brain

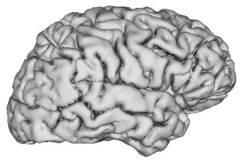


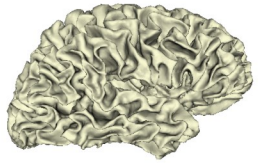
The human brain weighs between 1,300 and 1,400 g and contains **100, 000,000, 000 (100 billions)** neurons.

Neuron



Human Brain

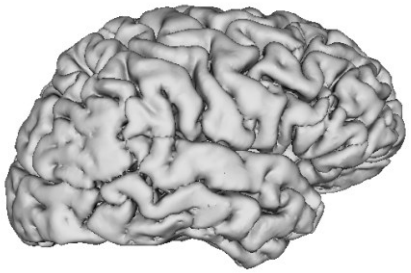




Grey Matter
(neuron cell bodies)

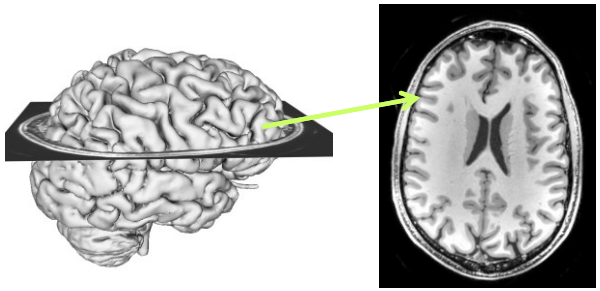
White Matter
(neurons axons)

Cerebral Cortex

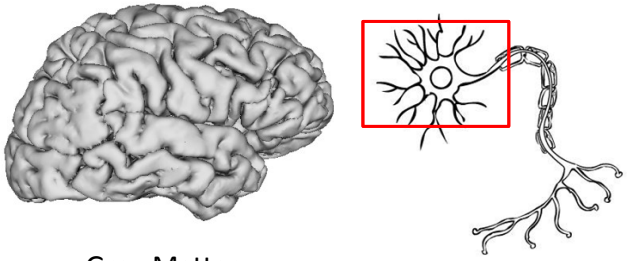


The cerebral cortex is composed of folded **grey matter**

Cerebral Cortex



Cerebral Cortex

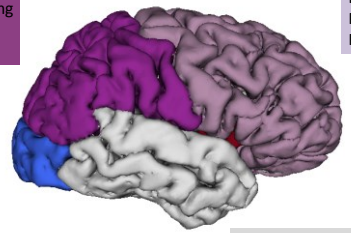


Grey Matter
(neuron cell bodies)

Cerebral Cortex

Parietal Lobe:
Reception and processing of sensory information from the body

Frontal Lobe:
Decision making
Problem solving
Planning

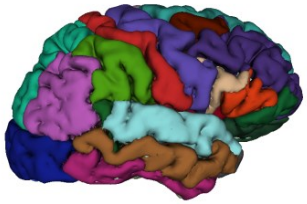


Occipital Lobe:
Vision

The cortex is divided into four sections called **lobes**.

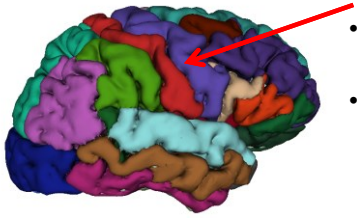
Temporal Lobe:
Memory
Emotion
Hearing
Language

Cerebral Cortex



The lobes can be divided into functional areas involved in **movement, vision**, **hearing**, **touch**, **smell**, **thinking** and **reasoning**.

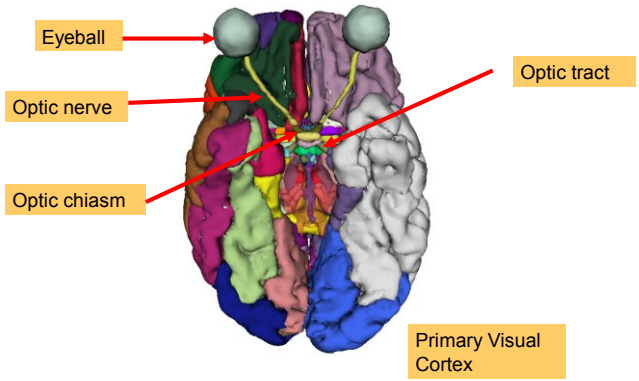
Motor System



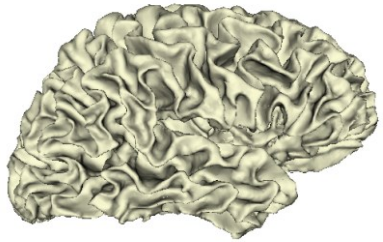
Primary Motor Cortex:

- Located in pre-central gyrus of the frontal lobe
- Responsible for voluntary movement

Visual System

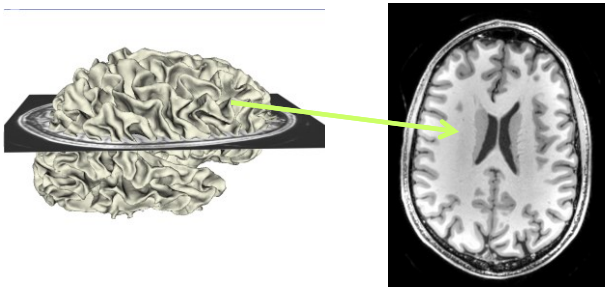


Cerebral White Matter

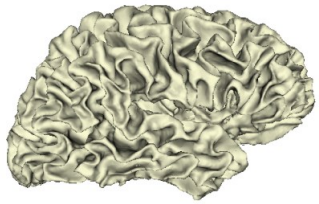


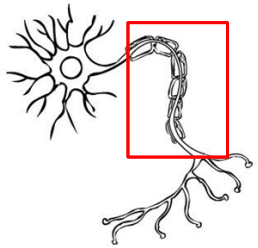
The human brain white matter is composed of myelinated axons.

Cerebral White Matter



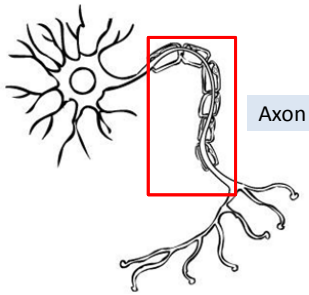
Cerebral White Matter





White Matter
(neurons axons)

Neuron

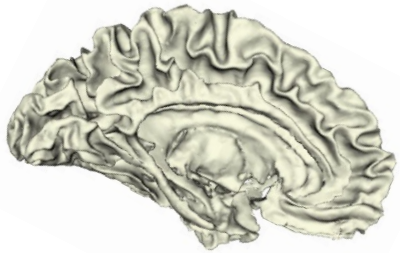


Axon

- Axons are coated with electrical insulation called **myelin**
- Myelin increases the **speed of electrical communication** between neurons

Image source: BSC1007C Introductory Biology. State College of Florida

White Matter Structure



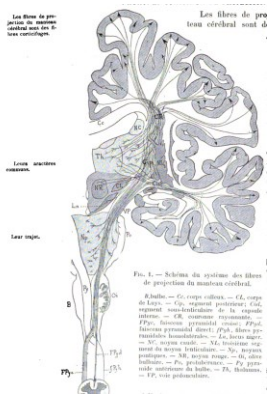
White Matter Structure

Human White Matter Exploration

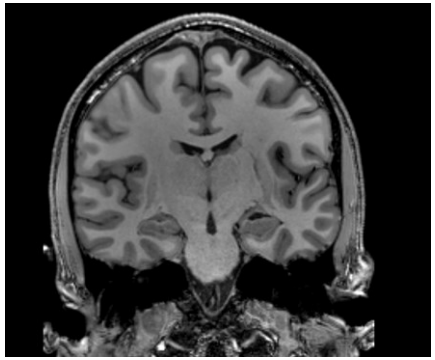
Joseph Jules and Augusta Dejerine: Neuroanatomy atlas based on myelin-stained preparations

(Anatomie des centres nerveux, Paris, 1895-1901)

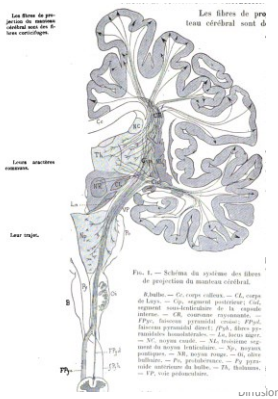
Dejerine Atlas

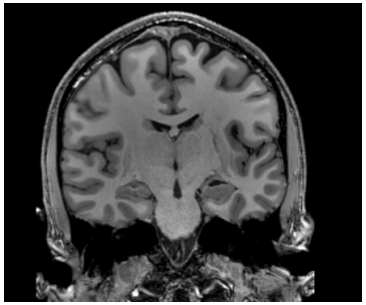


Structural MRI



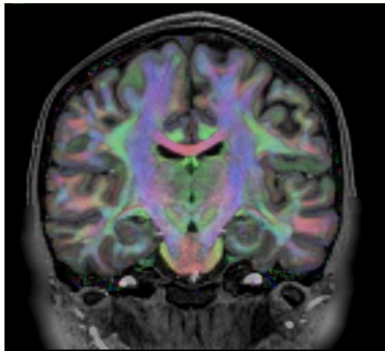
Structural MRI





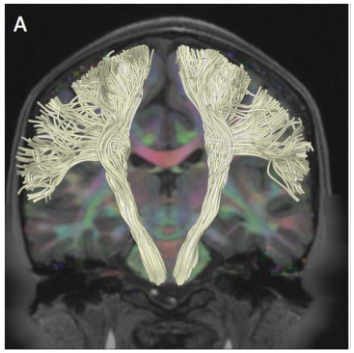
Diffusion MRI Analysis of the Human Brain,
S.Pujol, ARR 2012-2017

Diffusion-weighted MRI



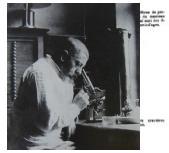
Diffusion MRI Analysis of the Human Brain,
S.Pujol, ARR 2012-2017

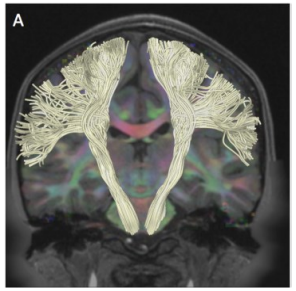
Tractography



Diffusion MRI Analysis of the Human Brain,
S.Pujol, ARR 2012-2017

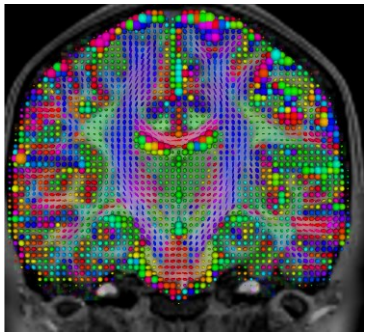
White Matter Exploration





Diffusion MRI Analysis of the Human Brain,
S.Pujol, ARR 2012-2017

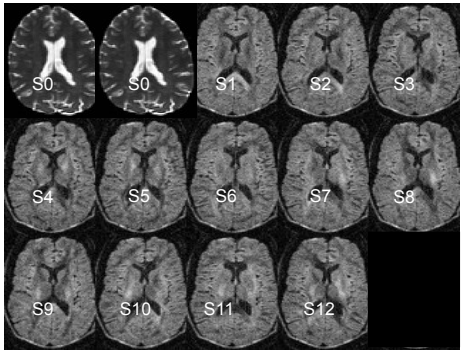
Diffusion Weighted MRI



- First **non-invasive** window on white matter anatomy
- Measurement of the diffusion of water molecules in the brain using diffusion sensitizing gradients

Diffusion MRI Analysis of the Human Brain, S.Pujol, ARR 2012-2017

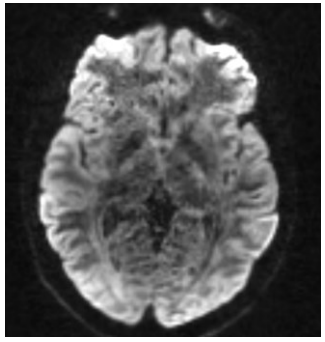
Diffusion Weighted MRI



In this example, the DWI scan was acquired with 12 diffusion sensitizing gradient directions (S1-S12) and 2 non-diffusion sensitizing gradients (S0)

Diffusion MRI Analysis of the Human Brain, S.Pujol, ARR 2012-2017

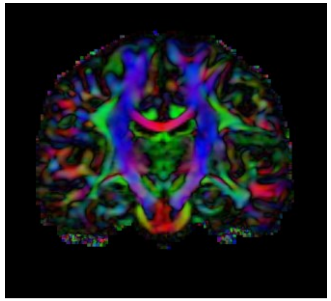
Diffusion Weighted MRI



- In **grey matter and cerebrospinal fluid**, the displacement of water molecules is identical in all directions: the diffusion is **isotropic**
- In **white matter**, myelin sheets and axonal membranes act as barriers: the diffusion is **anisotropic**

Diffusion MRI Analysis of the Human Brain, S.Pujol, ARR 2012-2017

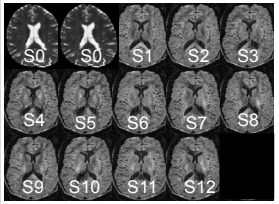
Diffusion Tensor Imaging



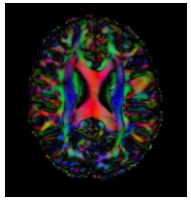
Diffusion Tensor Imaging (DTI) is a **mathematical framework** that was developed to model the **anisotropic diffusion** of water molecules in the brain.

From DWI to DTI

DWI



DTI

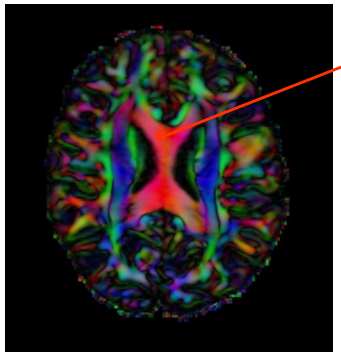


Stejskal-Tanner (1965) $S_i = S_0 e^{-b\hat{g}i^T \underline{D}\hat{g}_i}$

Si: DWI volume acquired with ith gradient
S0: Baseline volume

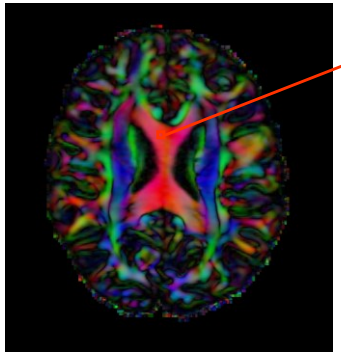
Diffusion MRI Analysis of the Human Brain, S.Pujol, ARR 2012-2017

Diffusion Tensor Imaging



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

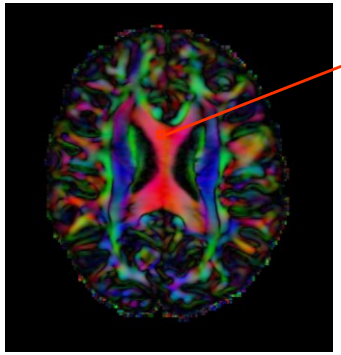
Diffusion Tensor Imaging



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

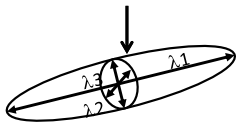
$$\underline{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

Diffusion Tensor Imaging

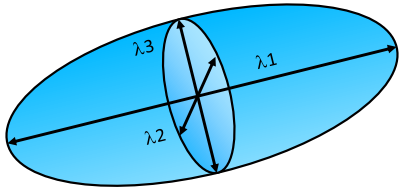


$S_i = S_0 e^{-b\hat{g}i^T \underline{D}\hat{g}_i}$

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

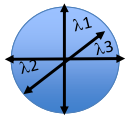


Diffusion Tensor



- The **diffusion tensor** in each voxel can be visualized as an ellipsoid.
- The **principal directions of diffusion** of water molecules correspond to the axis of the ellipsoid.

Diffusion Tensor



λ1= λ2= λ3

λ1>> λ2, λ3

λ1~λ2>> λ3

Isotropic media
(CSF, grey matter)

Anisotropic media
(white matter)

Corpus Callosum

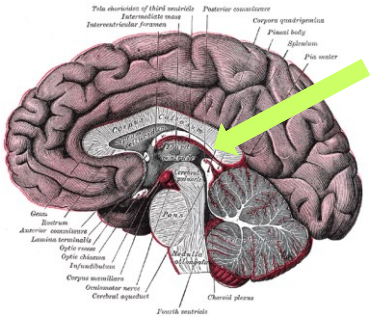


Image from Grey's Anatomy

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

Corpus Callosum

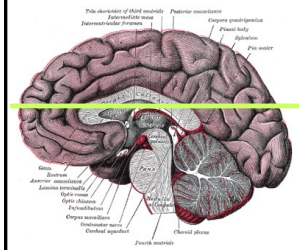
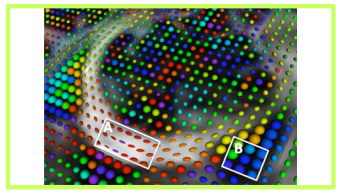
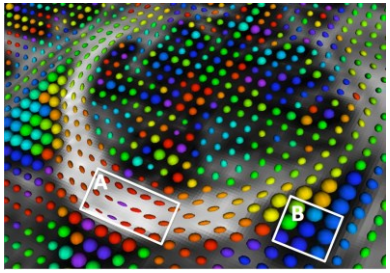


Image from Grey's Anatomy



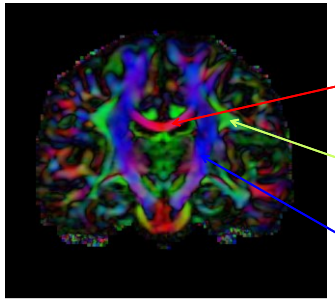
Diffusion Tensor Ellipsoid



A: White Matter: Anisotropic Diffusion

B: CSF: Isotropic Diffusion

DTI Color Map



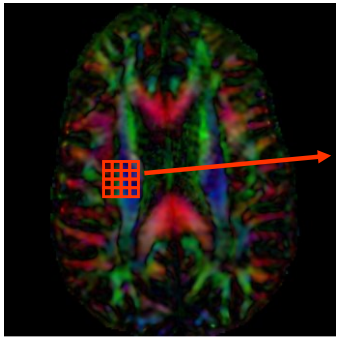
Color coding:

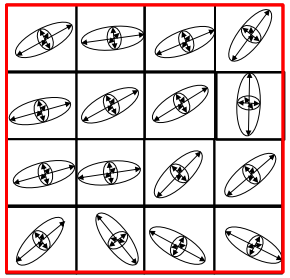
Red: left-right
(e.g. corpus callosum)

Green: anterior-posterior (e.g superior portion of cingulum)

Blue: inferior-superior (e.g. corticospinal tract)

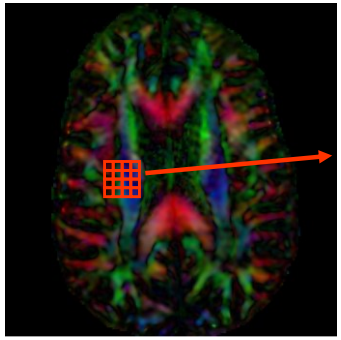
DTI Tractography

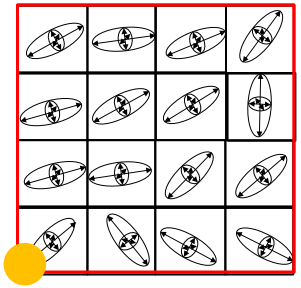




43

DTI Tractography

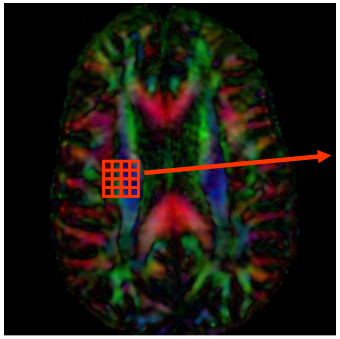


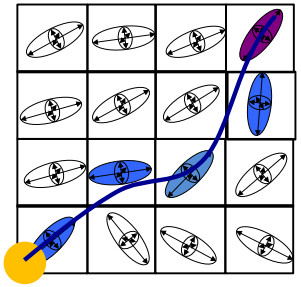


Seed Point

44

DTI Tractography

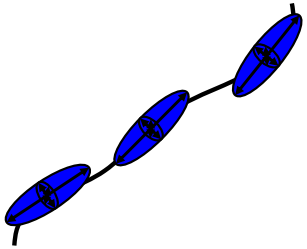


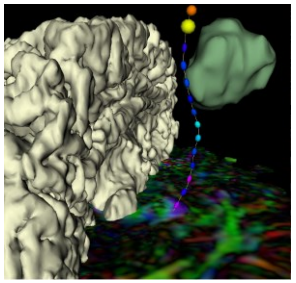


Seed Point

45

DTI Tractography





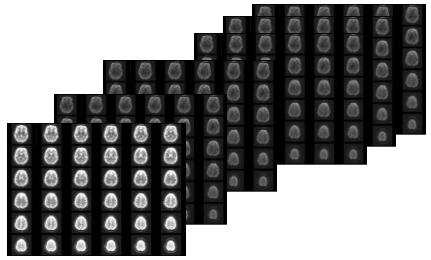
DTI tractography provides 3D reconstruction of the trajectory of white matter pathways

Tutorial outline

- Part 1: Basics of Diffusion MRI mapping of white matter pathways

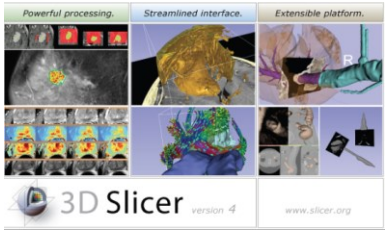
- **Part 2: Hands-on Diffusion MRI analysis using 3D Slicer**

Tutorial DWI Dataset



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

Tutorial Software

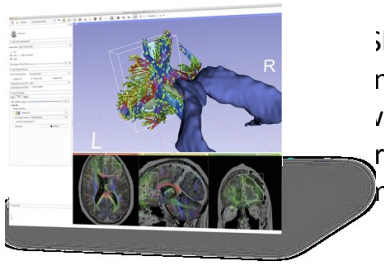


The tutorial uses the 3D Slicer software version 4.3

Disclaimer

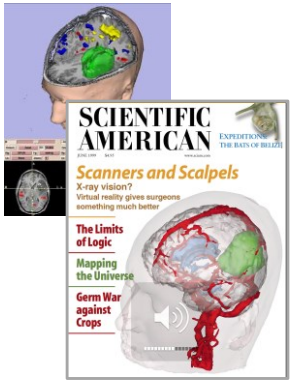
It is the responsibility of the user of 3DSlicer to comply with both the terms of the license and with the applicable laws, regulations and rules. Slicer is a tool for research, and is not FDA approved.

3D Slicer



ɨlicer or ‘Slicer’ is an n-source platform for ving, analyzing and racting with nedical imaging data

3D Slicer History



- 1997: Slicer starts as a Master’s thesis project between Harvard Medical School and the MIT in Boston, MA

3D Slicer History

- 1997: Slicer starts as a Master’s thesis project between Harvard Medical School and the MIT in Boston, MA
- 2017: Slicer is an open-source software platform for medical research used around the world

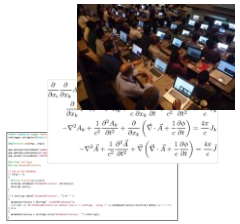
A multi-disciplinary platform

An open-source platform for imaging scientists

An end-user application for clinicians

A software platform that is both easy to extend for scientists & easy to use for clinicians

Bridging the gap to accelerate translational research



Algorithm Development

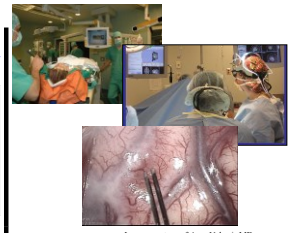


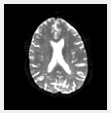
Image courtesy of Arya Nabavi, MD

Problem solving

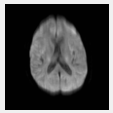
3D Slicer Community

- Clinicians
- Clinical researchers
- Engineers
- Postdoctoral fellows
- Medical Students
- Engineering students
- Software developers
- Staff researchers
- MR Technologists

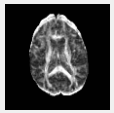
MR Diffusion Analysis Pipeline



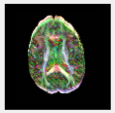
DWI Acquisition



Tensor Calculation

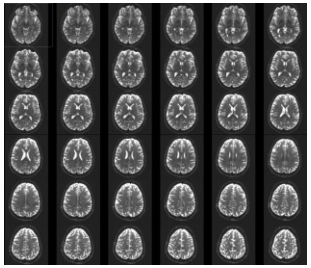


Scalar Maps



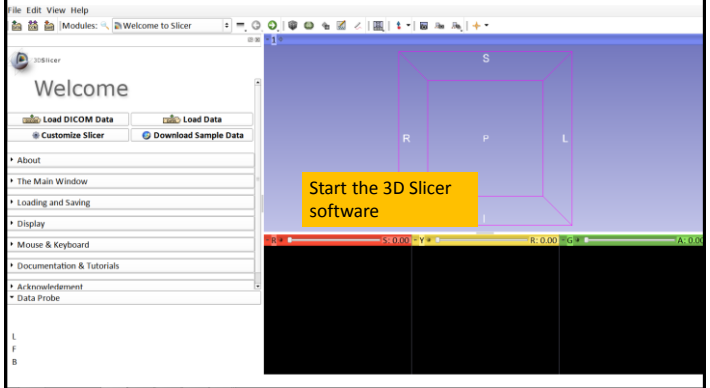
3D Visualization

Diffusion MRI Analysis of the Human Brain, S.Pujol, ARR 2012-2017

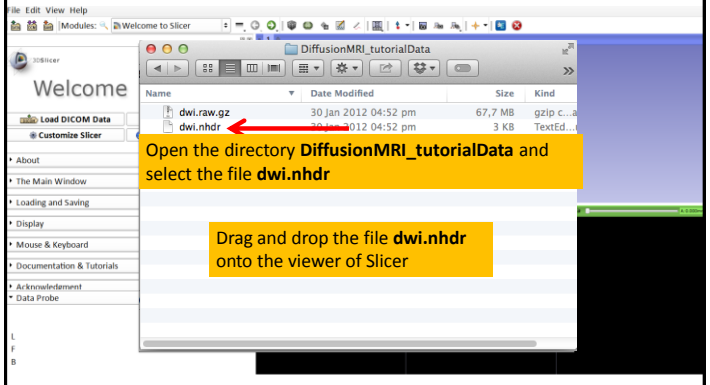


Step 1:
Loading the DWI dataset and mask

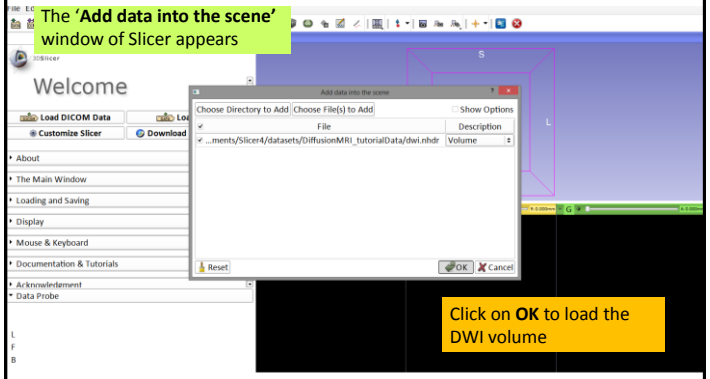
Loading the DWI Dataset



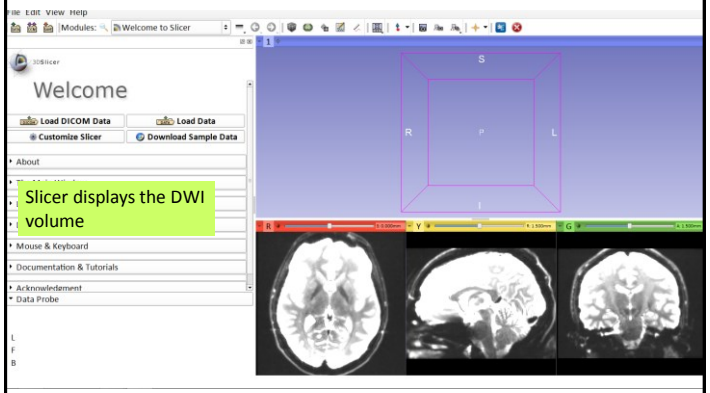
Loading the DWI Dataset



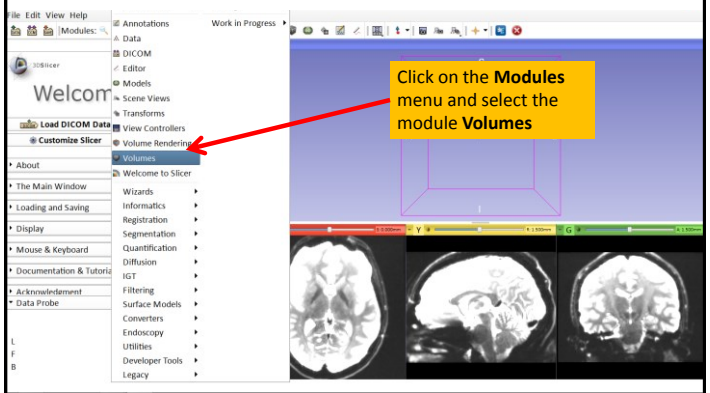
Loading the DWI Dataset



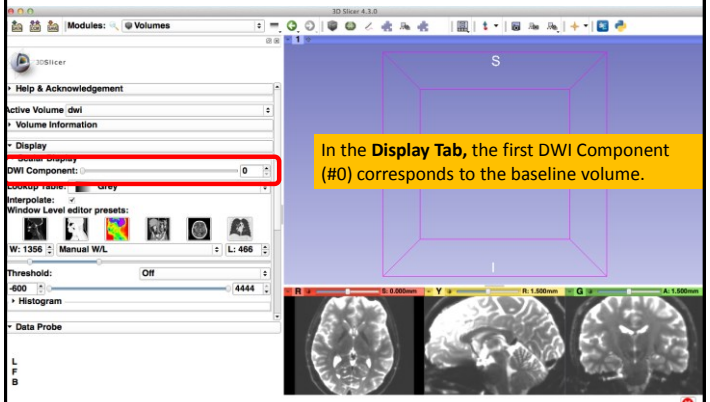
Loading the DWI Dataset



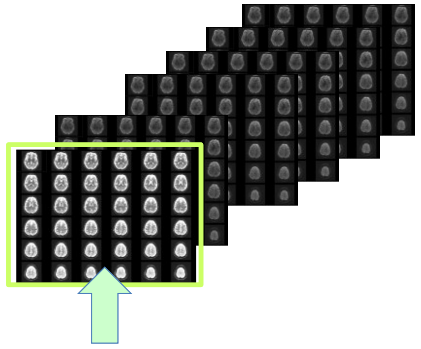
Loading the DWI Dataset



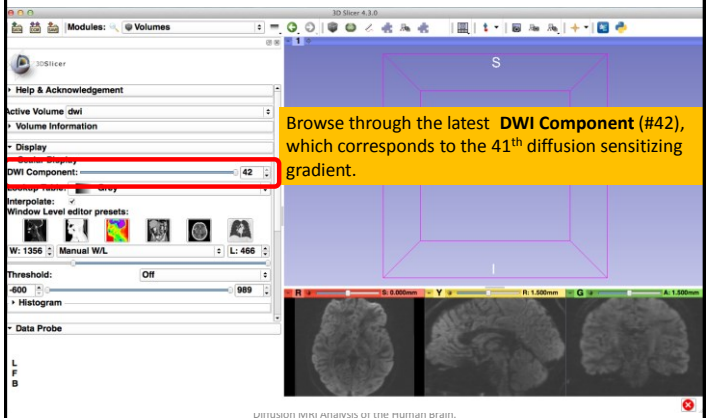
Loading the DWI dataset



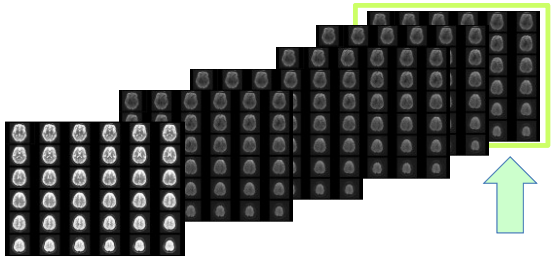
Tutorial DWI Dataset



Loading the DWI dataset

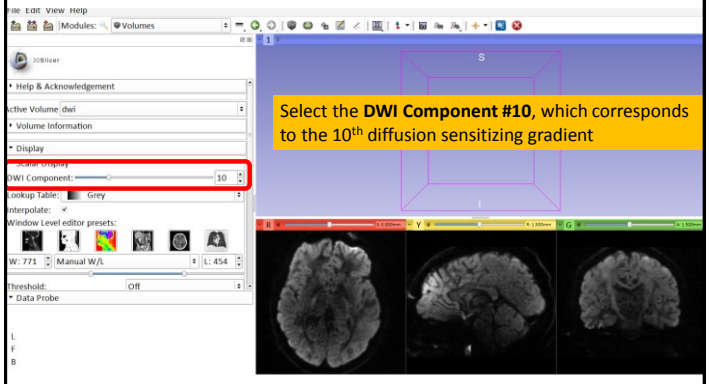


Tutorial DWI Dataset

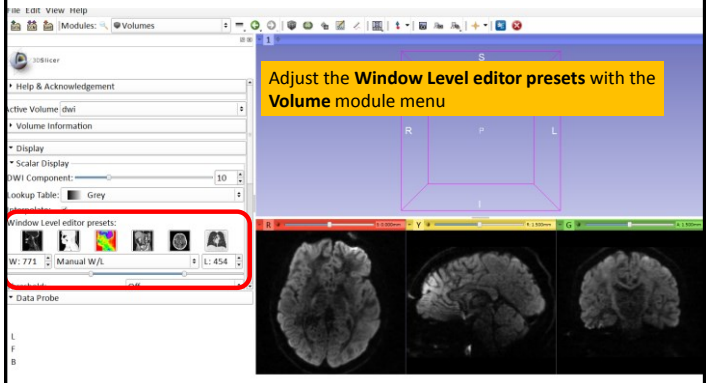


42th diffusion sensitizing gradient

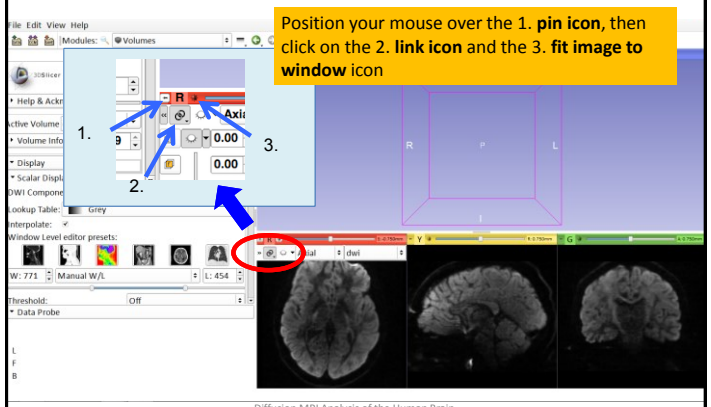
Loading the DWI Dataset



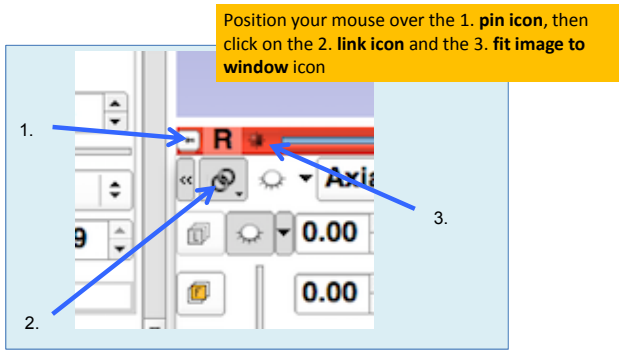
Loading the DWI Dataset



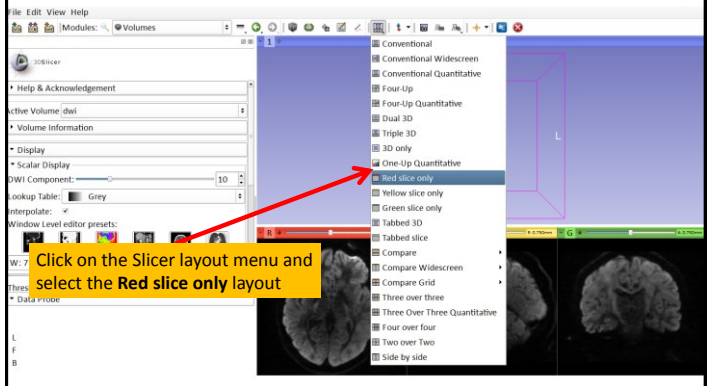
Loading the DWI Dataset



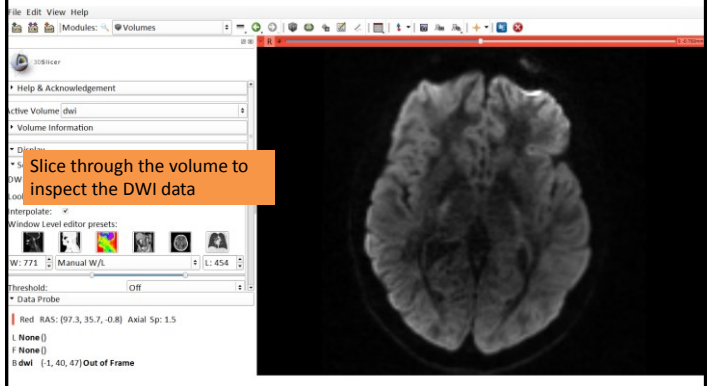
Loading the DWI Dataset



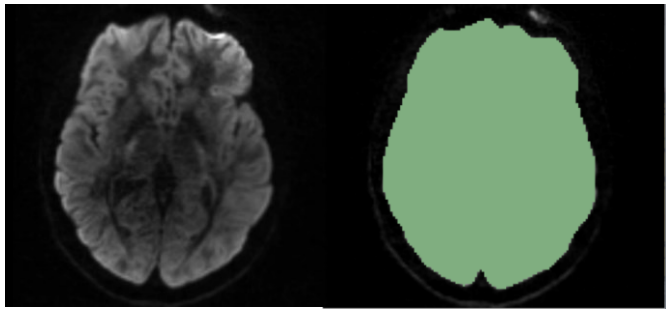
Loading the DWI Dataset



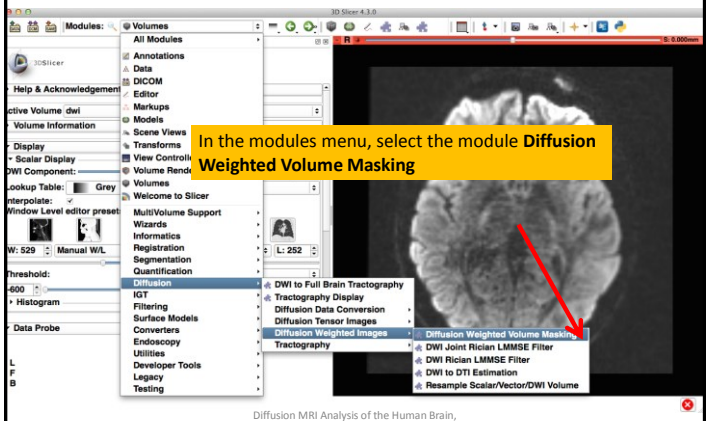
Loading the DWI Dataset



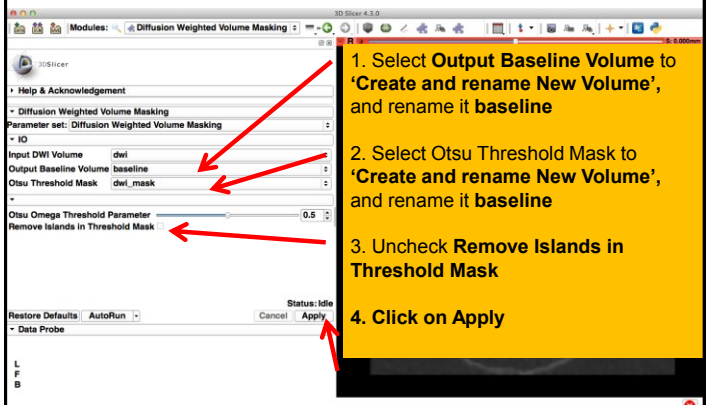
DWI Dataset and DWI Mask



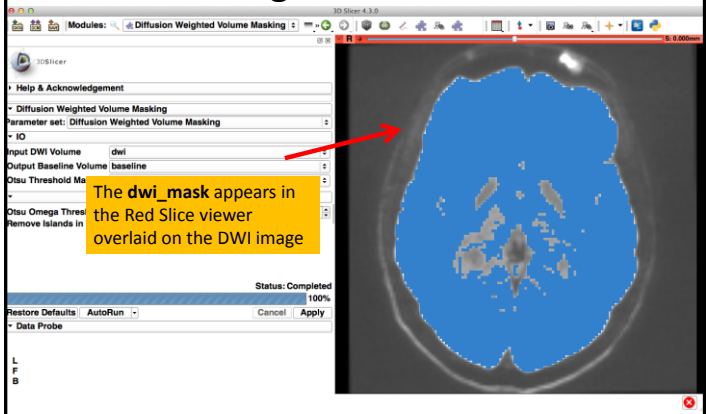
Creating the DWI Mask



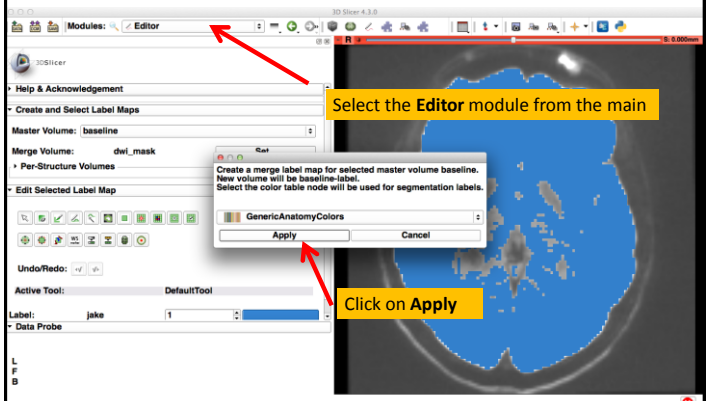
Creating the DWI Mask



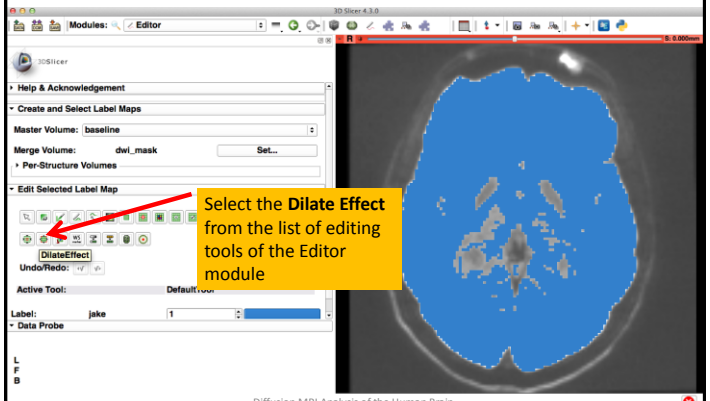
Loading the DWI Mask



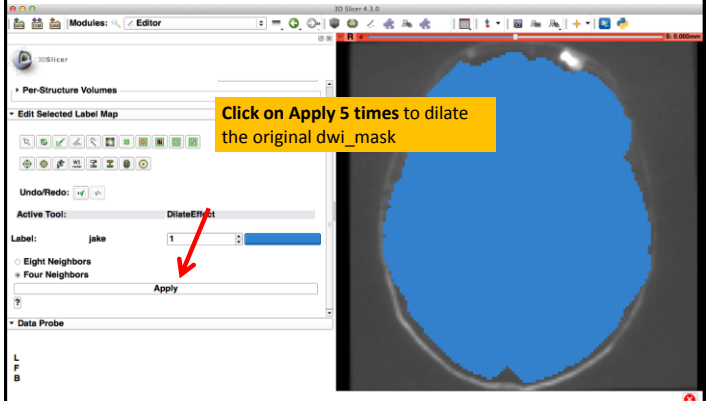
Loading the DWI Mask



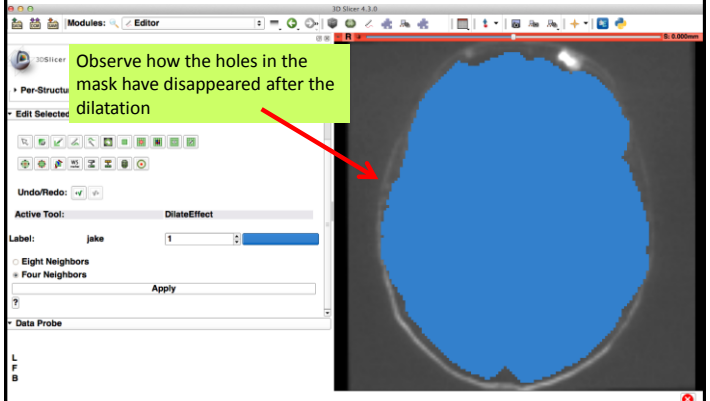
Loading the DWI Mask



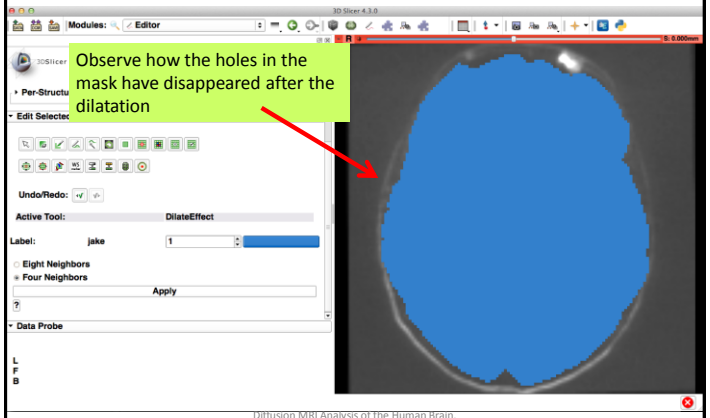
Loading the DWI Mask



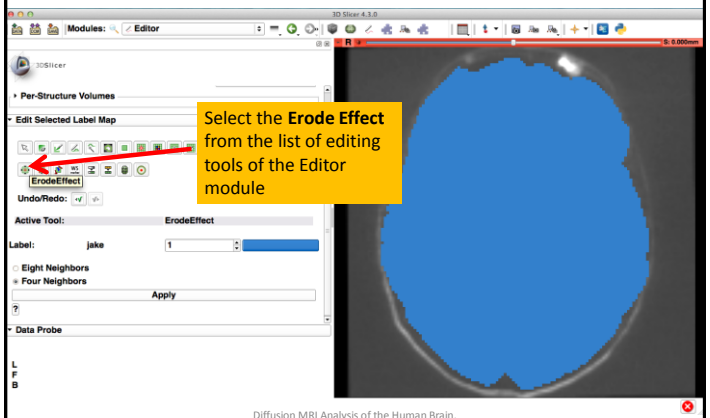
Loading the DWI Mask



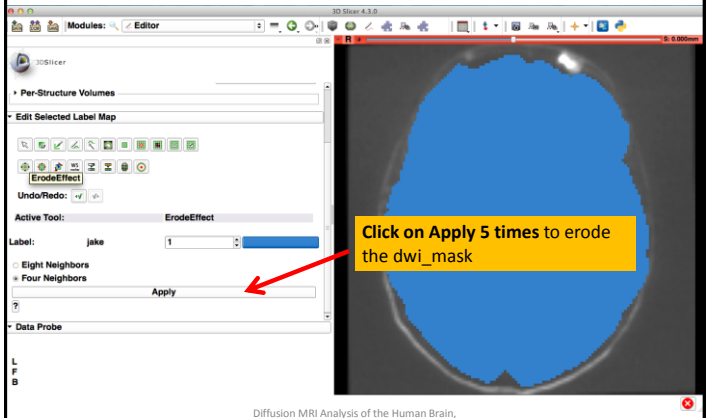
Loading the DWI Mask



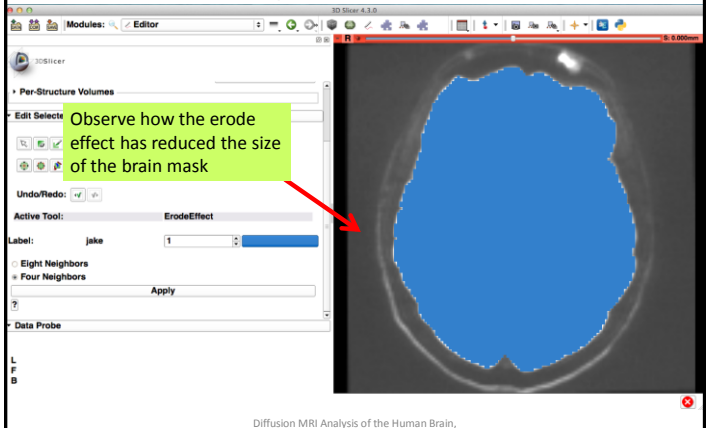
Loading the DWI Mask

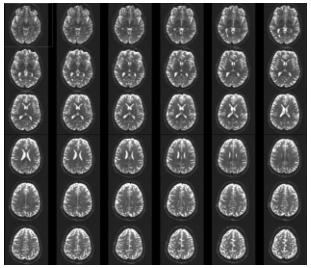


Loading the DWI Mask



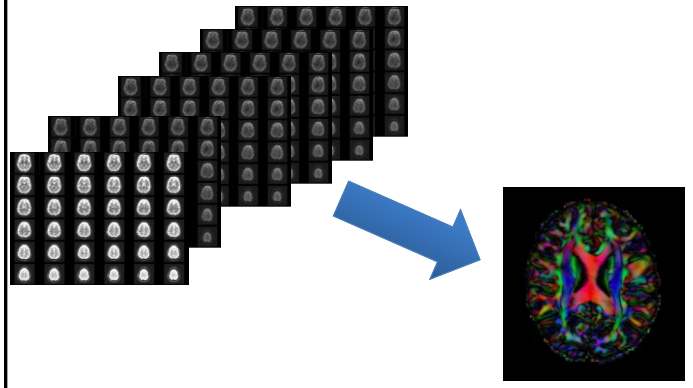
Loading the DWI Mask



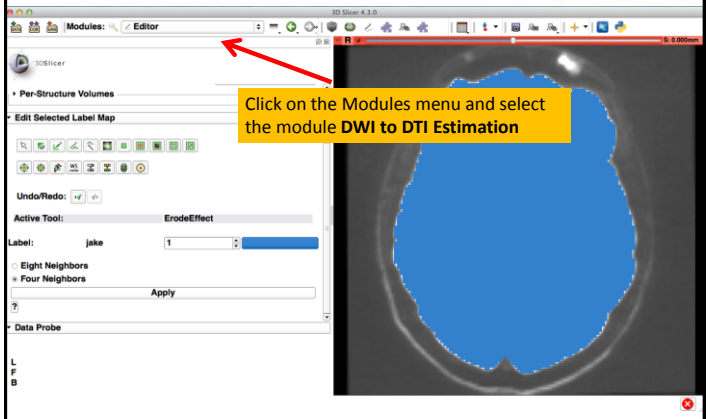


Step 2:
Computing the DTI dataset

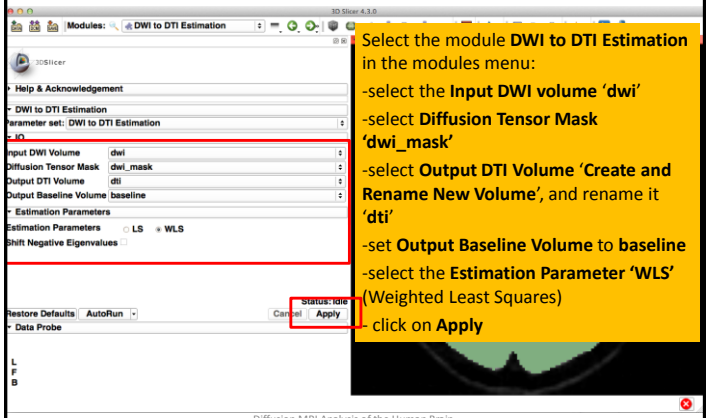
From DWI to DTI



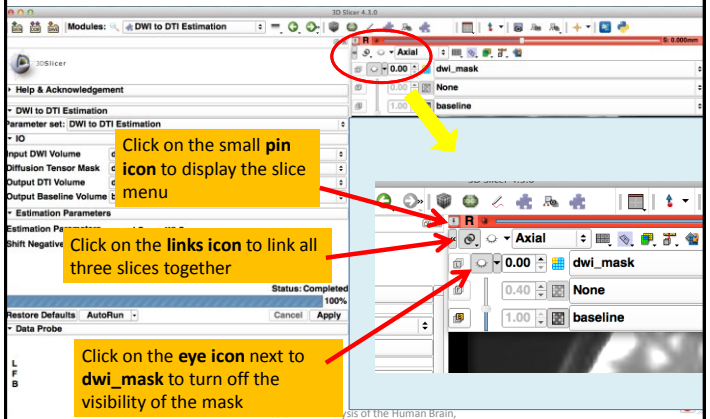
From DWI to DTI



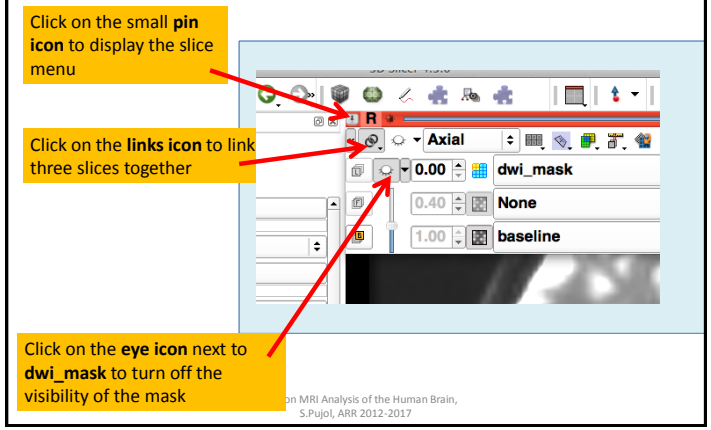
From DWI to DTI



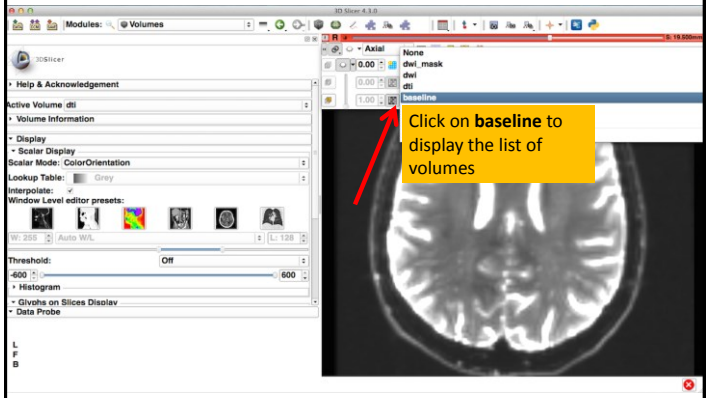
From DWI to DTI



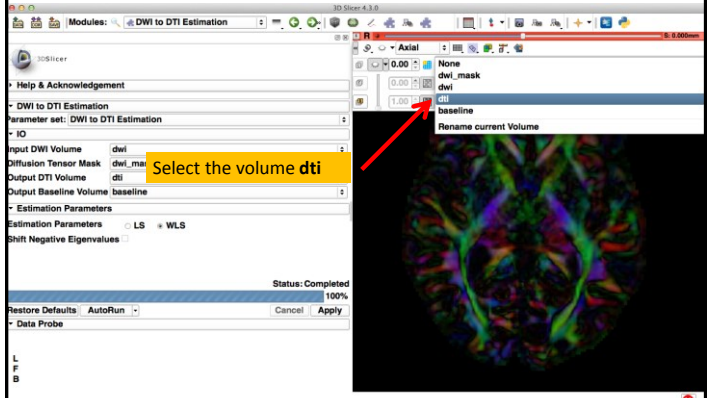
From DWI to DTI



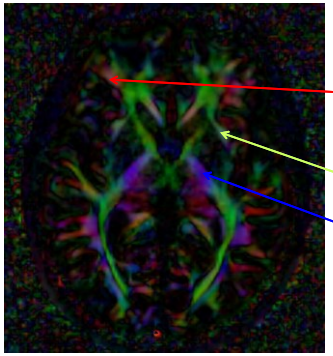
From DWI to DTI



From DWI to DTI



DTI Color Map



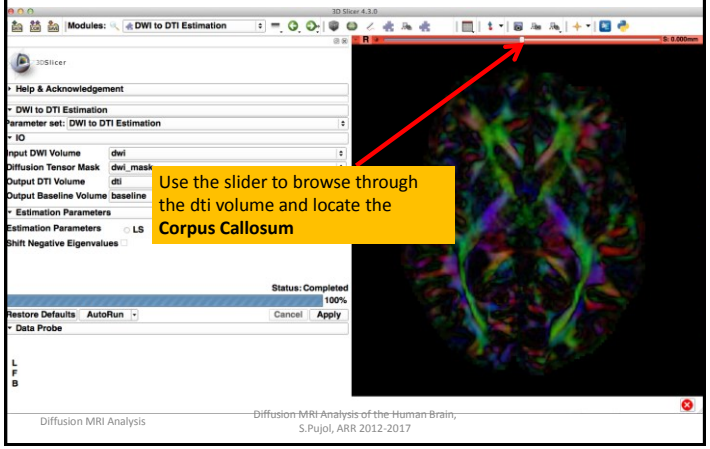
Color coding:

Red: left-right

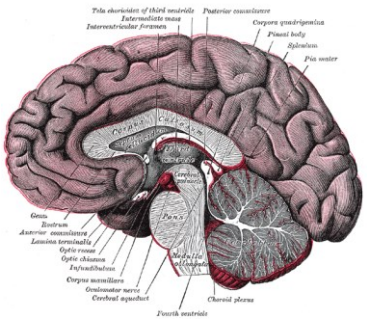
Green: anterior-posterior

Blue: inferior-superior

Exploring the DWI Dataset



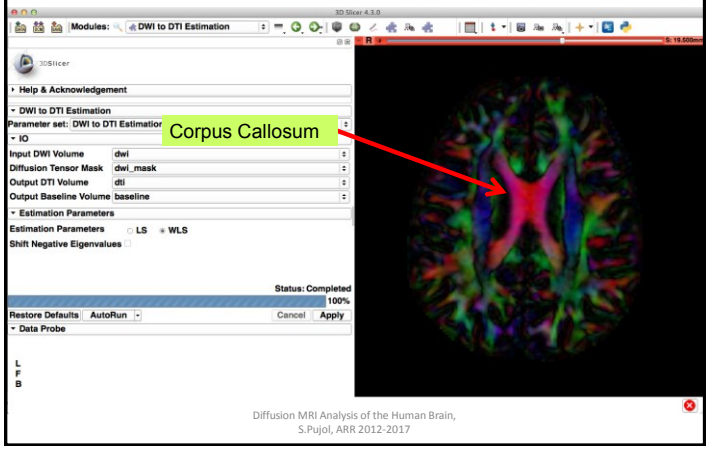
Corpus Callosum



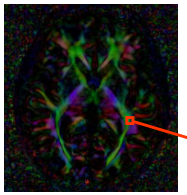
The corpus callosum is a broad thick bundle of dense myelinated fibers that connect the left and right hemisphere. It is the largest white matter structure in the brain

Image from Grey's Anatomy

Corpus Callosum



Diffusion Tensor Data



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

Stejskal-Tanner equation (1965)

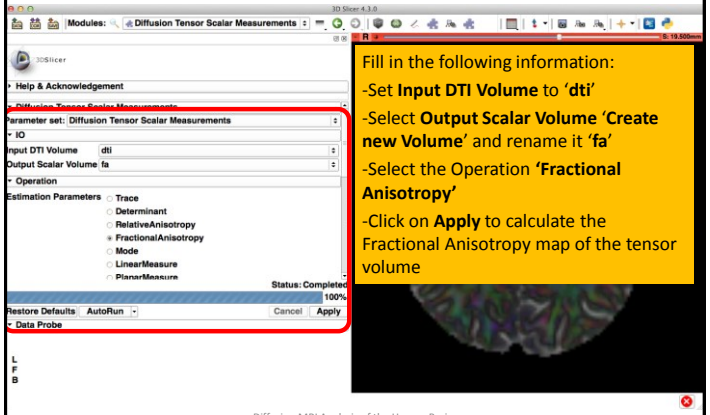
$$\underline{\mathbf{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

The diffusion tensor D in the voxel (I,J,K) is a 3x3 symmetric matrix.

Scalar Maps: Fractional Anisotropy

- FA(D) is intrinsic to the tissue and is independent of the direction of the diffusion sensitizing gradients.
- FA(D) can be used to characterize the shape (degree of 'out-of-roundness') of the diffusion ellipsoid
- Low FA: → High FA:

Fractional Anisotropy



Fill in the following information:

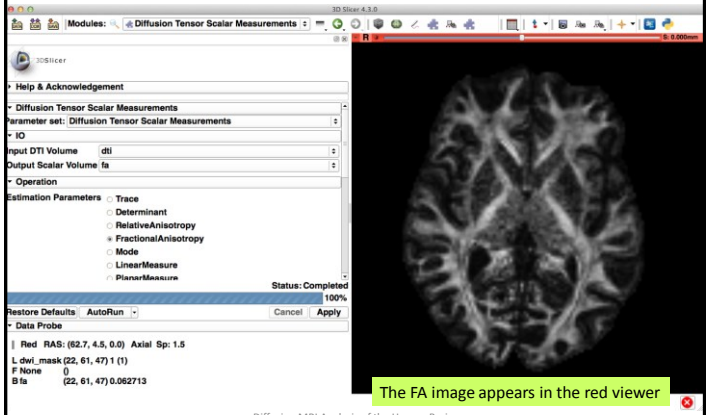
-Set **Input DTI Volume** to '**dti**'

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

-Select the Operation **'Fractional Anisotropy'**

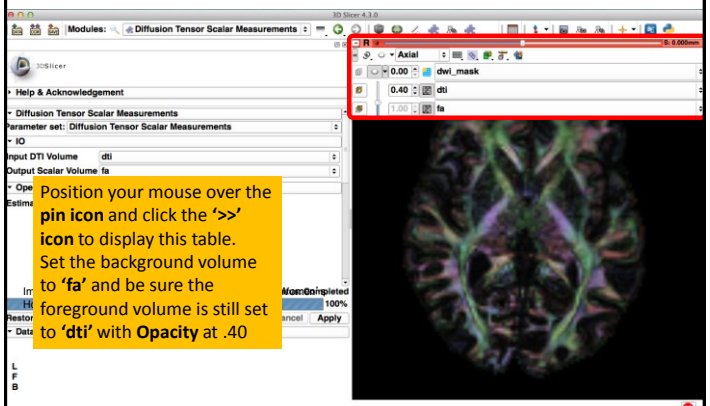
-Click on **Apply** to calculate the Fractional Anisotropy map of the tensor volume

Fractional Anisotropy

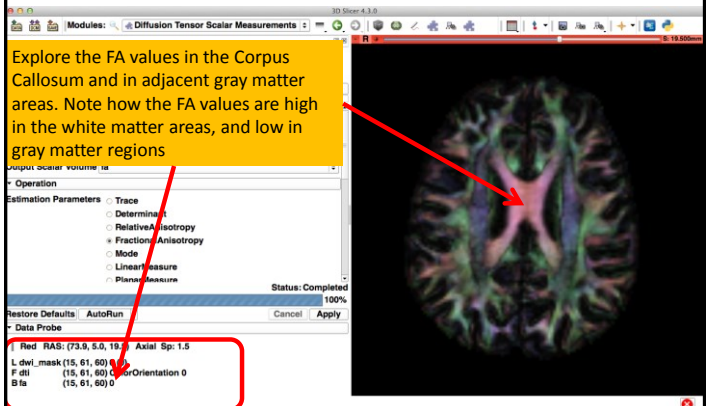


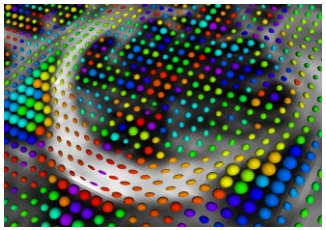
The FA image appears in the red viewer

Fractional Anisotropy



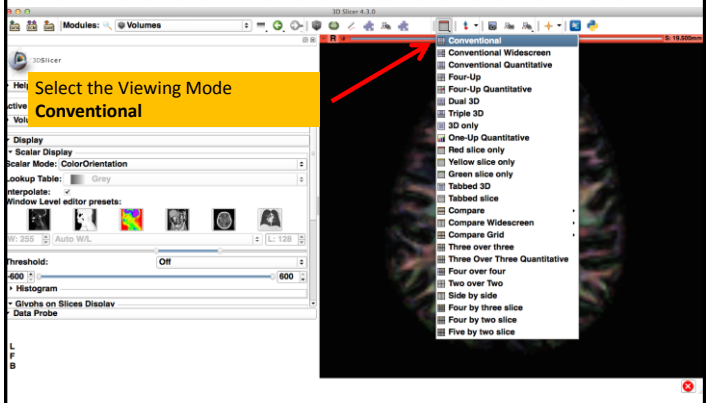
Fractional Anisotropy



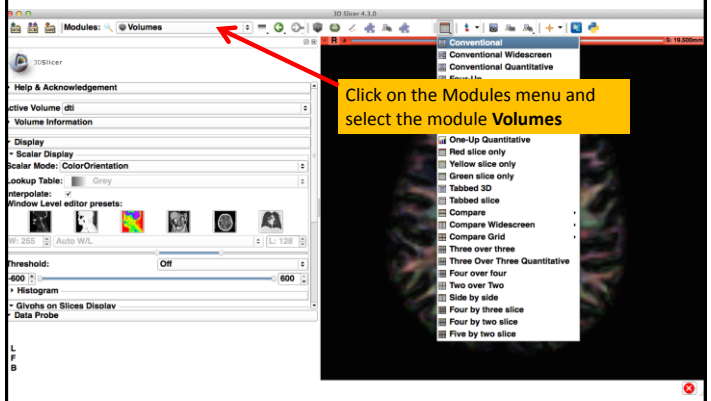


Step 3:
Visualizing the diffusion tensor data

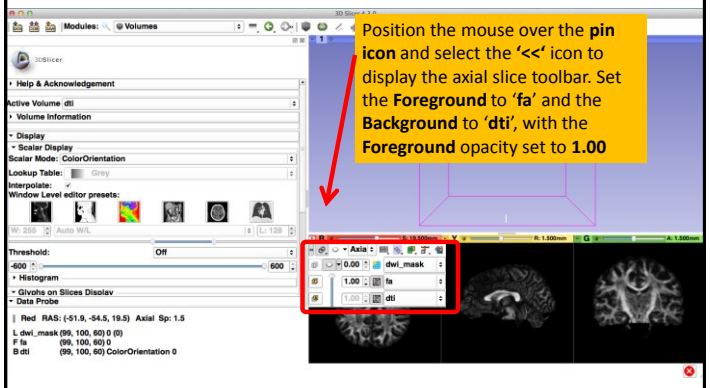
3D Visualization: Glyphs



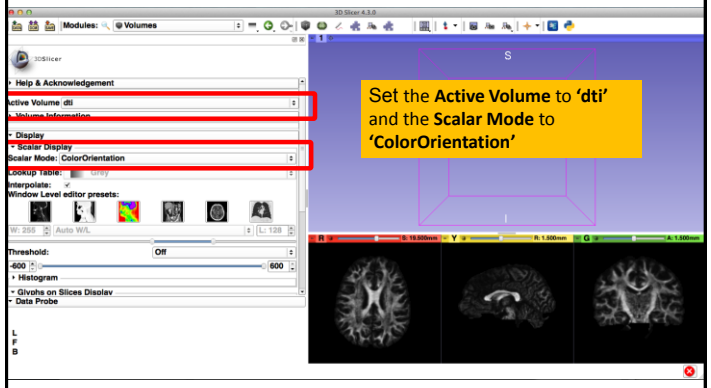
3D Visualization: Glyphs



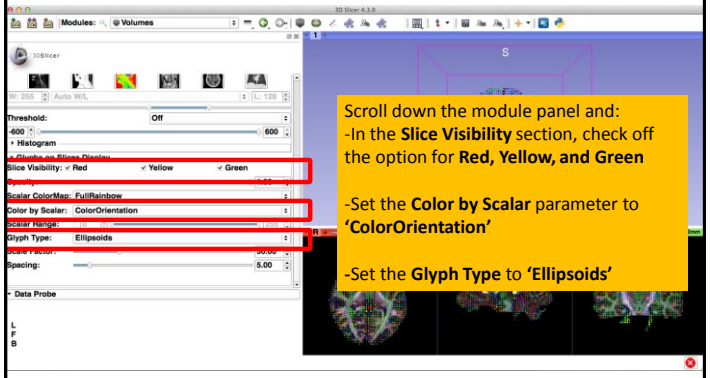
3D Visualization: Glyphs



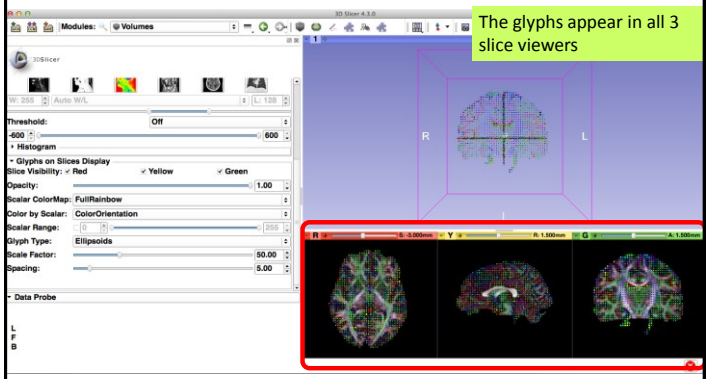
3D Visualization: Glyphs



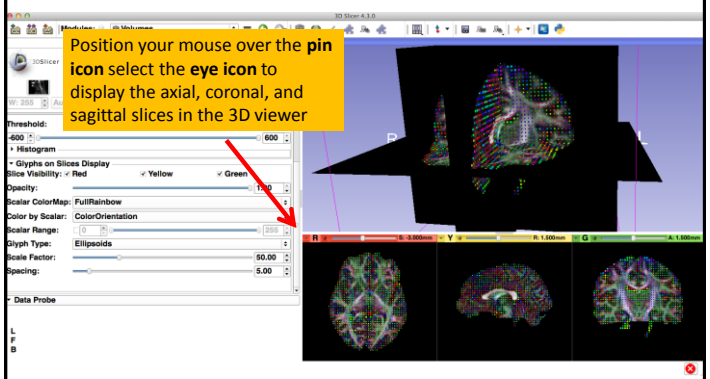
3D Visualization: Glyphs



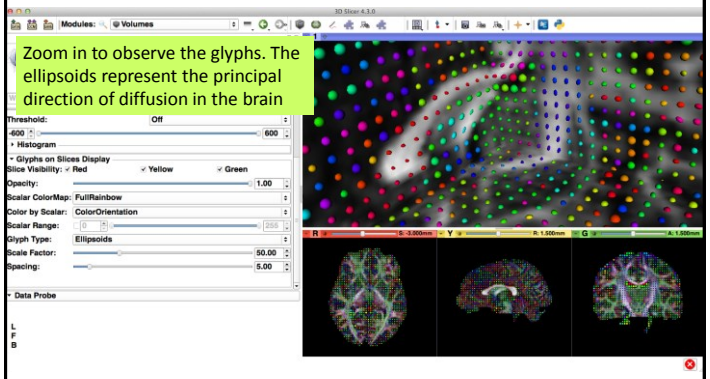
3D Visualization: Glyphs

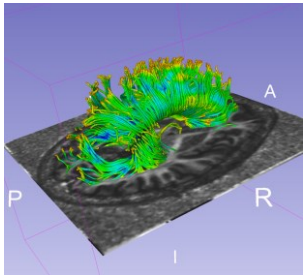


3D Visualization: Glyphs



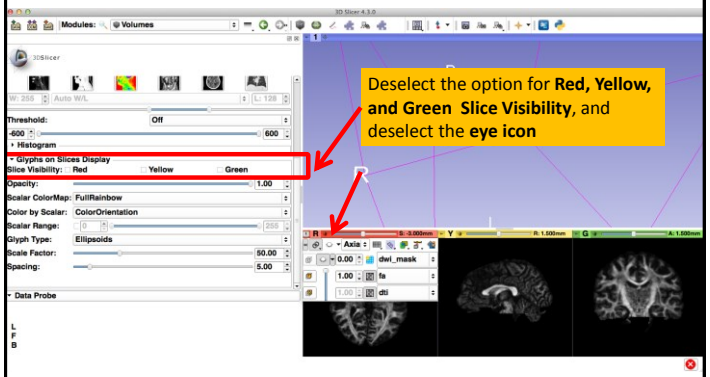
3D Visualization: Glyphs



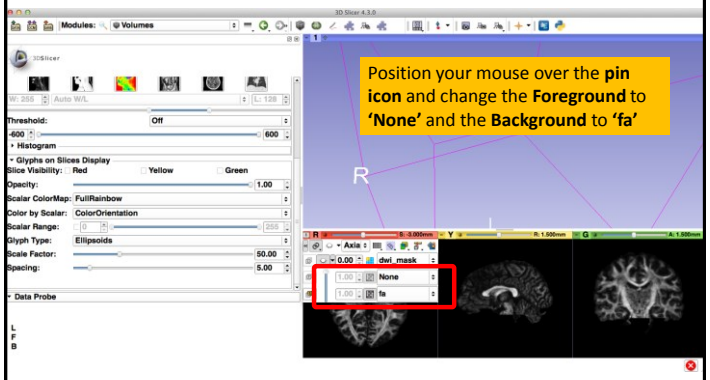


Step 4: Generating fiber tracts

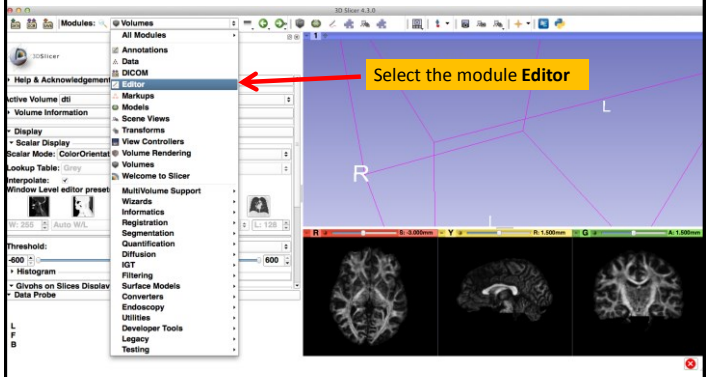
Diffusion MRI tractography



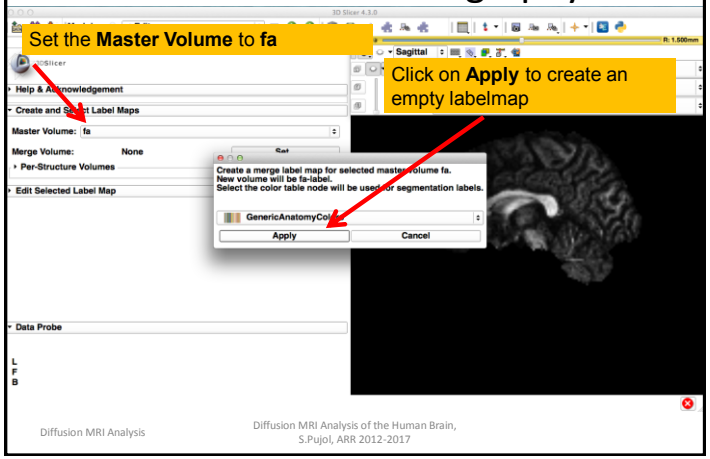
Diffusion MRI tractography



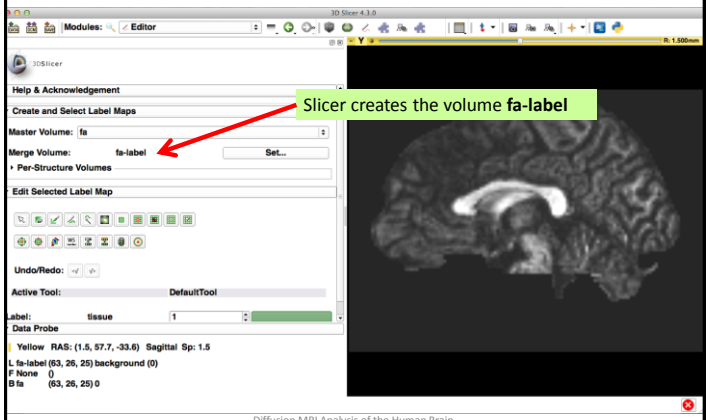
Diffusion MRI tractography



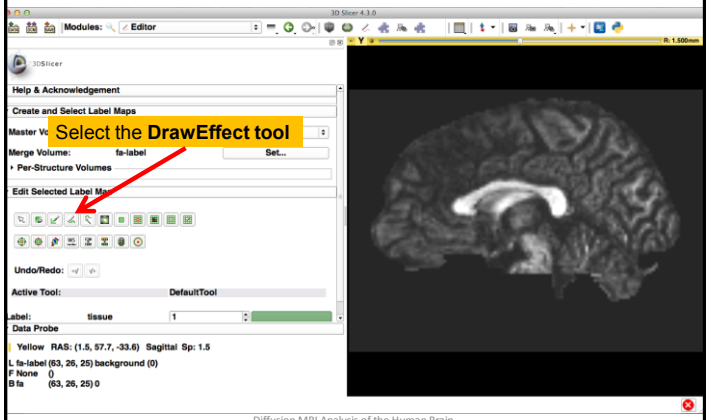
Diffusion MRI tractography



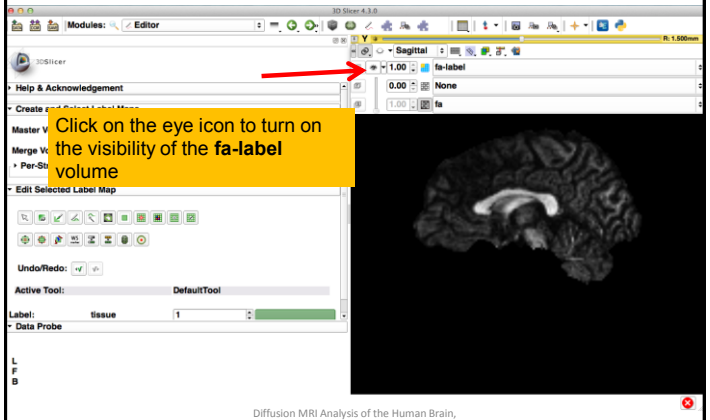
Diffusion MRI tractography



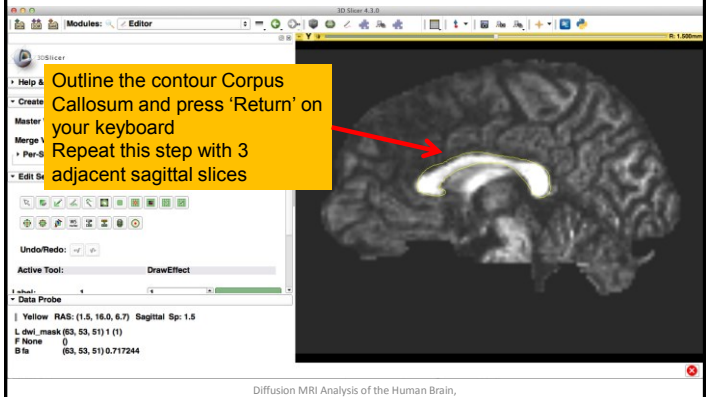
Diffusion MRI tractography



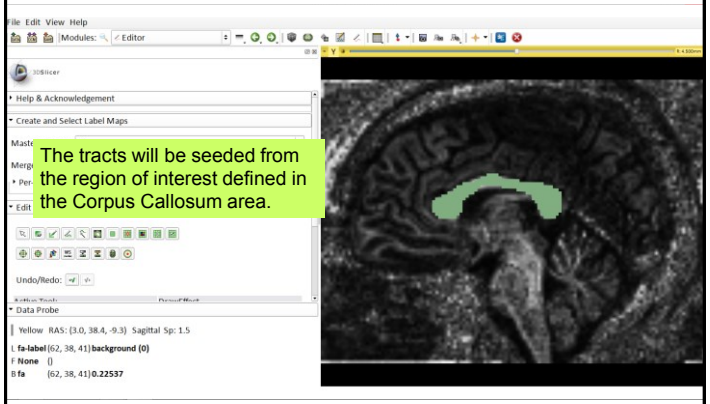
Diffusion MRI tractography



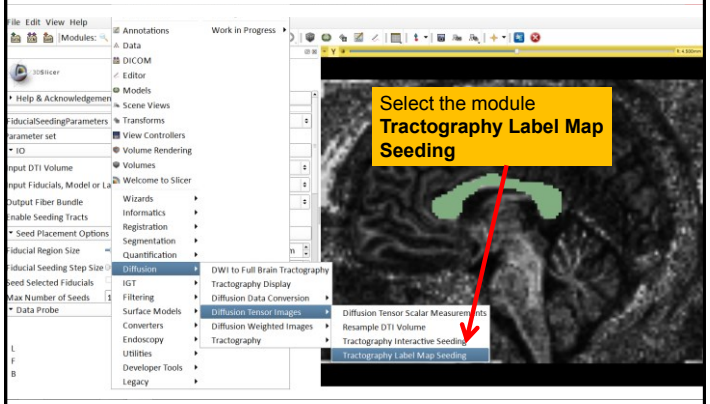
Diffusion MRI tractography



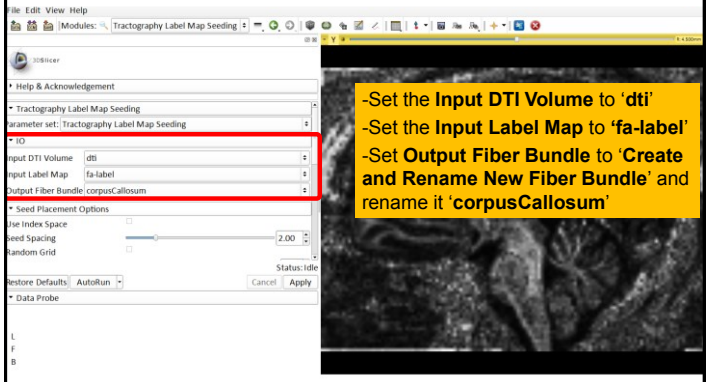
Diffusion MRI tractography



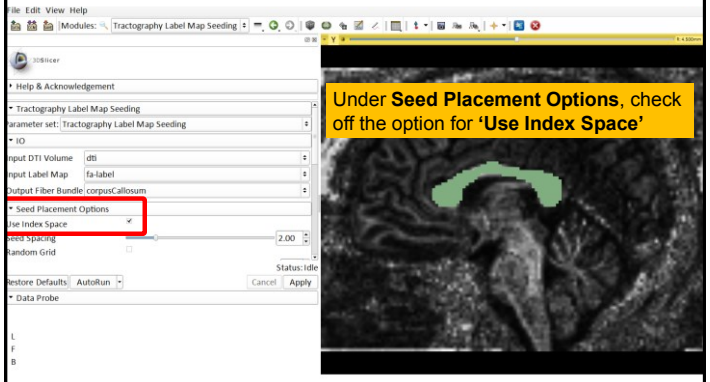
Diffusion MRI tractography



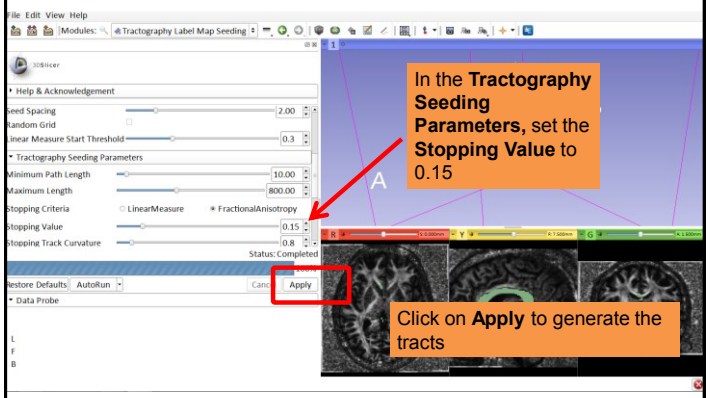
Diffusion MRI tractography



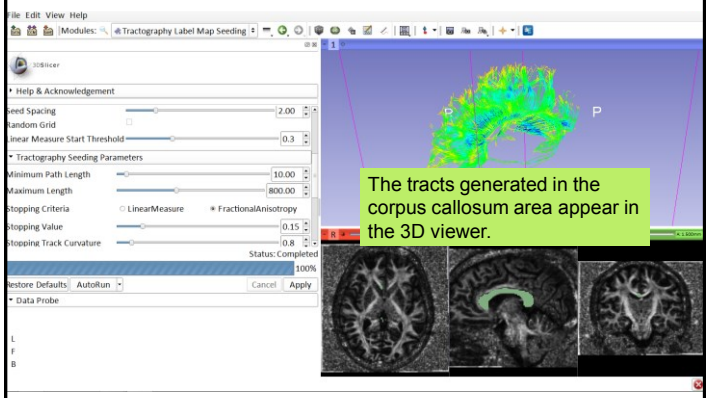
ROI Drawing



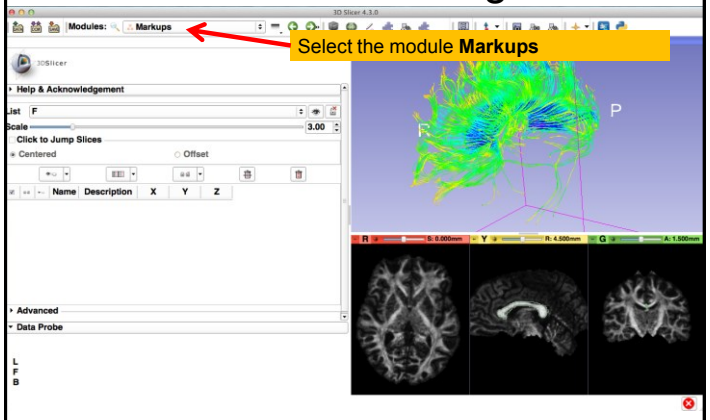
Labelmap Seeding: Tracts



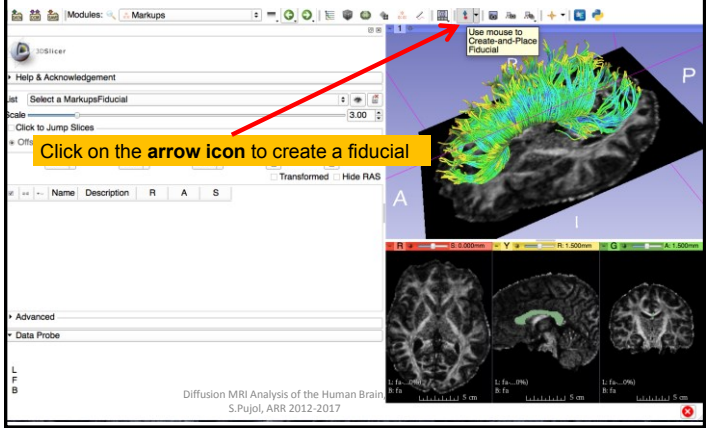
Labelmap Seeding: Tracts



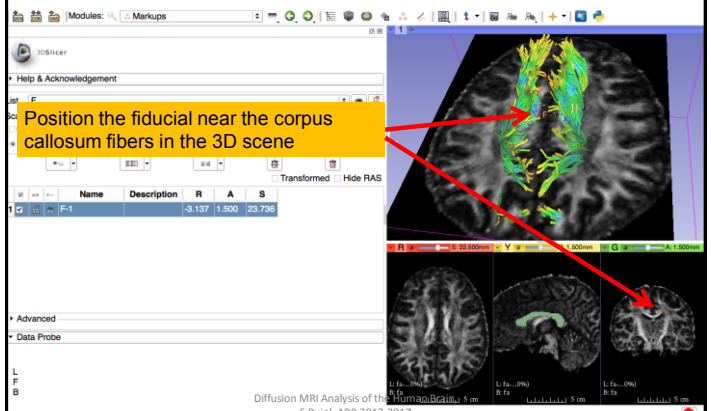
Fiducial Seeding



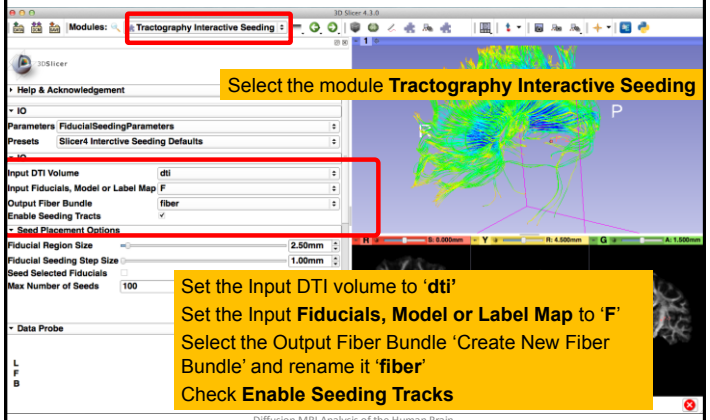
Fiducial Seeding



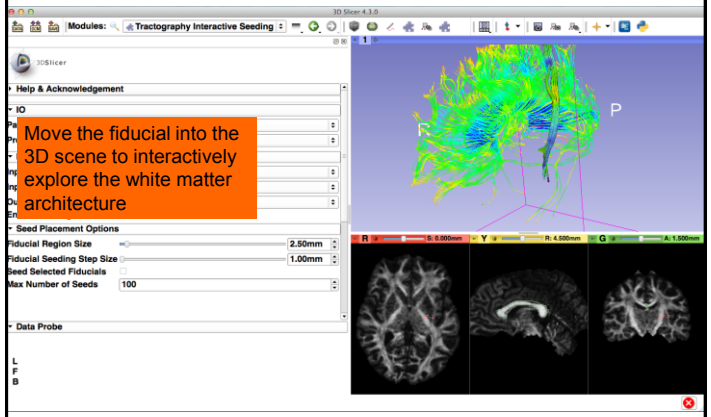
Fiducial Seeding



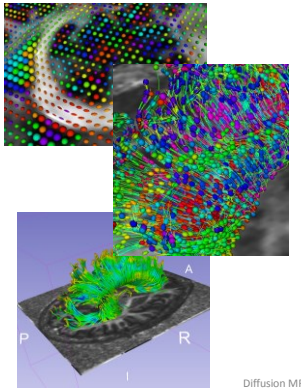
Fiducial Seeding



Fiducial Seeding



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 3D architecture of the brain white matter.

Acknowledgments

- National Alliance for Medical Image Computing (NA-MIC)
  NIH U54EB005149

- Neuroimage Analysis Center (NAC)
  NIH P41RR013218