Diffusion MRI Analysis

Sonia Pujol, Ph.D.

Surgical Planning Laboratory
Harvard University
Brain Anatomy

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

Jules Joseph Dejerine
Diffusion Tensor Imaging (DTI)

- First non-invasive window on white matter anatomy
- Measurement of the motion of water molecules using MRI techniques.
- Three-dimensional reconstruction of the trajectory of white matter bundles
In this example, the DWI scan was acquired with 12 diffusion sensitizing gradient directions (S1-S12) and 2 non-diffusion sensitizing gradients (S0).
From DWI to DTI

DWI

DTI

\[ S_i = S_0 e^{-b \hat{g}^T D \hat{g}_i} \]

Stejskal-Tanner (1965)

Si: DWI volume acquired with ith gradient
So: Baseline volume
Diffusion Tensor Imaging

\[ S_i = S_0 e^{-b\hat{g}_i^T \hat{D} \hat{g}_i} \]
Diffusion Tensor Imaging

\[ S_i = S_0 e^{-b \hat{g}_i^T \hat{D} \hat{g}_i} \]

\[ \hat{D} = \begin{bmatrix}
  D_{xx} & D_{xy} & D_{xz} \\
  D_{yx} & D_{yy} & D_{yz} \\
  D_{zx} & D_{zy} & D_{zz}
\end{bmatrix} \]
Diffusion Tensor Imaging

\[ S_i = S_0 e^{-b\hat{g}_i^T D\hat{g}_i} \]

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

\[ \lambda_1 \geq \lambda_2 \geq \lambda_3 \]
DTI tractography provides 3D reconstruction of the trajectory of white matter pathways
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.

Download the dataset at: https://www.slicer.org/w/images/e/e6/Dti_tutorial_data.zip
3D Slicer

The tutorial uses the 3D Slicer (Version 4.8.1, revision 26813, Stable Release) software available at:

http://download.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.
SlicerDMRI

An open-source project to improve and extend diffusion magnetic resonance imaging software in 3D Slicer:

http://dmri.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.
Install SlicerDMRI

First, start Slicer4
Install SlicerDMRI

Click on the Modules menu

Click on the Diffusion menu; then, click on Install Slicer Diffusion Tools
Install SlicerDMRI

Click on the **Open Extension Manager** menu
Install SlicerDMRI

Search for SlicerDMRI in Extension Manager

Click on SlicerDMRI to install
Install SlicerDMRI

Click Yes to install UKFTractography
Install SlicerDMRI

Restart Slicer to finish installation
Install SlicerDMRI

Related modules appear in the Diffusion menu.
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
The Diffusion Weighted Imaging (DWI) dataset is composed of 41 volumes acquired with 41 different diffusion-sensitizing gradient directions, and one baseline image acquired without diffusion weighting.
Loading the DWI Dataset

In your files archive, locate the file `dwi.nrrd` in the dataset folder for this tutorial.

Drag and drop the file `dwi.nrrd` onto the viewer of the Slicer application.
Exit the archive folders window, and click **OK** to load the dataset to Slicer.
Loading the DWI Dataset

Slicer displays DWI volume of the brain
Loading the DWI Dataset

Click on the Modules menu and select the module Volumes.
Loading the DWI Dataset

The baseline image corresponds to the DWI Component #0. Select the DWI Component #10, which corresponds to the 10th diffusion sensitizing gradient.
Loading the DWI Dataset

For image contrast adjustment, you may use the Manual W/L slider.
Loading the DWI Dataset

Position your mouse over the **pin icon**, then click on the **link icon** and the **fit image to window icon**
Loading the DWI Dataset

Click on the Slicer layout menu and select the **Red slice only** layout.
Loading the DWI Dataset

Slicer displays only the Axial anatomical slice in the Viewer
Creating a brain mask

Click on the **Modules** menu, then select **Diffusion -> Process -> Diffusion Brain Masking**
Creating a brain mask

- select the **Input DWI volume** ‘dwi’
- select **Output Baseline Volume** ‘Create new Volume as…’, and name it ‘baseline’
- select **Output Diffusion Brain Mask** ‘Create new LabelMapVolume as…’, and name it ‘brain_mask’
- click on **Apply**.
Creating a brain mask

Slicer displays the edited brain mask
Creating a brain mask

Change the label layer to None to make the mask invisible.
Estimating the tensor

Click on the Modules menu, then select Diffusion -> Process -> Diffusion Tensor Estimation
Estimating the tensor

- Set the Input DWI volume to ‘dwi’
- Set the Input Brain Mask to ‘brain_mask’
- Select Output DTI Volume ‘Create DiffusionTensorVolume as ...’, and name it ‘dti’
- Set Output Baseline Volume to ‘baseline’
- Under ‘Advanced Settings’, set Fitting Methods to ‘WLS’ (Weighted Least Squares)
- Click on Apply.
Estimating the tensor

Position your mouse over the **pin icon**, click on the **double arrow** and select the **dti** in the **B** field, set the **F** and **L** to none.
Exploring the DWI Dataset

Slicer displays the DTI volume in color by orientation mode:
Red: right-left
Green: anterior-posterior
Blue: inferior-superior
The diffusion tensor \( \mathbf{D} \) in the voxel \((I,J,K)\) is a 3x3 symmetric matrix.

\[
S_i = S_0 e^{-b \hat{g}^T \mathbf{D} \hat{g}_i}
\]

Stejskal-Tanner equation (1965)
Diffusion Tensor

• The diffusion tensor $\mathbf{D}$ in each voxel can be visualized as a diffusion ellipsoid, with the eigenvectors indicating the directions of the principal axes, and the ellipsoidal proportional to the square root of the eigenvalues defining the.

• Scalar maps can be derived from the rotationally invariant eigenvalues $\lambda_1, \lambda_2, \lambda_3$ to characterize the size and shape of the diffusion tensor.
Diffusion Tensor Shape

Isotropic media
(Cerebrospinal Fluid, gray matter)

Anisotropic media
(white matter)

\( \lambda_1 = \lambda_2 = \lambda_3 \)

\( \lambda_1 >> \lambda_2, \lambda_3 \)

\( \lambda_1 \sim \lambda_2 >> \lambda_3 \)
Click on the Slicer layout menu and select the **Yellow slice only** layout.
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.
Corpus Callosum
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 (degree of structural coherence in tissue).
- \( \text{Trace}(D) \) is useful to characterize the size of the diffusion ellipsoid.
Click on the Modules menu, then select Diffusion -> Quantify -> Diffusion Tensor Scalar Maps
Type in the following information in the IO menu:
- select the Operation ‘Trace’
- set Input DTI Volume to ‘dti’
- select Output Volume ‘Create new Volume as...’ and name it ‘trace’
- click on Apply to calculate the trace map of the tensor volume
Trace

Set L as none.

The trace image appears in the yellow viewer.
Trace

Adjust window level by right-dragging up and down.
Trace

Position your mouse over the **pin icon** and then select the ‘>>’ icon to display this table and fill in the following information:

- Select the volume ‘**trace**’ in the Background viewer
- Select the volume ‘**dti**’ in the Foreground viewer
- Set the **opacity** of the **dti** volume to **0.40**
Position your mouse within the region of the Corpus Callosum and observe the trace values in the Data Probe.
Note how the Trace values are fairly uniform in both white and gray matter, even if the tissues are different in structure.
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:
Fractional Anisotropy

Fill in the following information:
- Set Input DTI Volume to ‘dti’
- Select Output Scalar Volume ‘Create new Volume as ...’ and name it ‘fa’
- In ‘Scalar Measurement’, select ‘Fractional Anisotropy’
- Click on Apply to calculate the Fractional Anisotropy map of the tensor volume
Fractional Anisotropy

Set L as none.

The FA image appears in the yellow viewer.
Fractional Anisotropy

Position your mouse over the **pin icon** and click the ‘>>’ icon to display this table. Set the background volume to ‘fa’ and be sure the foreground volume is still set to ‘dti’ with **opacity** at 0.40.
Fractional Anisotropy

Explore the FA values in the Corpus Callosum and in adjacent gray matter areas. Note how the FA values are high in the white matter areas, and low in gray matter regions.
Fractional Anisotropy

Change to Conventional view
Part 2: Visualizing the tensor data
Click on the Modules menu and select the module *Volumes*.
3D Visualization: Glyphs

Position the mouse over the pin icon and select the ‘<<’ icon to display the axial slice toolbar. Set the Foreground to ‘fa’ and the Background to ‘dti’, with the Foreground opacity set to 1.00.
3D Visualization: Glyphs

Set the **Active Volume** to ‘dti’ and the **Scalar Mode** to ‘ColorOrientation’
3D Visualization: Glyphs

Scroll down the module panel and in the **Glyphs on Slices Display** section:
- Check off the option for **Red, Yellow, and Green Slice Visibility**
- Set the **Color by Scalar** parameter to ‘ColorOrientation’
- Set the **Glyph Type** to ‘Ellipsoids’
3D Visualization: Glyphs

The glyphs appear in all 3 slice viewers.
3D Visualization: Glyphs

Position your mouse over the **pin icon** select the **eye icon** to display the axial, coronal, and sagittal slices in the 3D viewer.
Slicer displays the anatomical slices in the 3D viewer.
3D Visualization: Glyphs

Zoom in to observe the glyphs. The ellipsoids represent the principal direction of diffusion (main eigenvector).
Diffusion MRI tractography

Deselect the option for **Red**, **Yellow**, and **Green** **Slice Visibility**, and deselect the eye icon.
Diffusion MRI tractography

Click L to reset the 3D view to left

Position your mouse over the pin icon and change the Foreground to ‘None’ and the background to ‘fa’
Part 3: From tensors to tracts
DTI tractography

• Definition of a region of interest (ROI) for seeding tract in an FA map (Editor module)

• Single-tensor tractography (Tractography Interactive Seeding module)

• Fiducial-seeding tractography (Tractography Interactive Seeding module)
Diffusion MRI tractography

Select the module Editor
Diffusion MRI tractography

Click on OK
Diffusion MRI tractography

Select the **Yellow slice only** layout
Diffusion MRI tractography

Select the **DrawEffect** tool
Outline the contour of the Corpus Callosum with the **DrawEffect tool** and press enter. Repeat this step with 3 adjacent sagittal slices.
In the next section, we will seed tracts from this anatomical region of interest.
Diffusion MRI tractography

Click on the Modules and then select Diffusion -> Tractography -> Tractography Seeding.
Step 1: I/O

- Set the Input DTI Volume to ‘dti’
- Set Output Fiber Bundle to ‘corpusCallosum’ by renaming the default parameter ‘Fiber Bundle’
- Set the Input Fiducials, Model or Label Map to ‘fa-label’

Change to Conventional view
Step 2: Seeding parameters

Select the default Tractography Seeding parameters:
- Threshold Type: Fractional Anisotropy
- Seeding Threshold: 0.30
- Stopping Threshold: 0.25

Click **Update** to generate tractography.
Step 3: Generate Tracts

The tracts generated in the corpus callosum area appear in the 3D viewer.
Step 4: Undesirable track removal

Click on the Modules menu, then select **Diffusion** -> **Tractography** -> **Tractography Display**
Step 4: Undesirable track removal

Click Fiber Bundle Selection
Step 4: Undesirable track removal

In ‘Fiber Bundle Selection’, under ROI for Fiber Select, create a new AnnotationROI as ‘ROI node’ and select Disable ROI.
Step 4: Undesirable track removal

Adjust the ROI frame to include the undesirable tracks, using the colorful spheres provided.
Step 4: Undesirable track removal

Click on **Negative ROI** to finish
Step 4: Undesirable track removal

Uncheck ROI Visibility
Fiducial Seeding

Click on the Modules and then select Diffusion -> Tractography -> Tractography Seeding.
Fiducial Seeding

Position the mouse over the **pin icon** and click on the **eye icon** to display the axial slice in the 3D viewer.

Unlink the **link icon**
Fiducial Seeding

Select the module **Markups**
Fiducial Seeding

Click on the arrow icon to create a fiducial.
Position the fiducial in the left cingulum of the coronal slice
Double click on the fiducial and change the name to **LeftCingulum**
Fiducial Seeding

Click on the **Modules** and then select **Diffusion -> Tractography -> Tractography Seeding**.

Set the Input DTI volume to `dti`
Set the Input **Fiducials, Model or Label Map** to `F`
Select the Output Fiber Bundle `Create New Fiber Bundle as ...` and name it **Cingulum**
Click **Update**
Part of the left cingulum appears in the 3D viewer.

Move the fiducial and update the Left Cingulum fiducial to explore the spatial relationship between the left cingulum and the corpus callosum.
Tractography ‘on-the-fly’

Select the module **Markups**
Tractography ‘on-the-fly’

Select the List ‘Create new MarkupsFiducial’

Click on the arrow icon to create a new fiducial, and position it in the 3D viewer.
Tractography ‘on-the-fly’

Click on the **Modules** and then select **Diffusion -> Tractography->Tractography Seeding.**

Set the Input DTI volume to ‘**dti**’
Set the Input **Fiducials, Model or Label Map** to ‘**F_1**’
Select the Output Fiber Bundle ‘Create New Fiber Bundle as ...’ and name it ‘**TractOnTheFly**’
Check **Update (check for interactive)**
Tractography ‘on-the-fly’

Move the fiducial F_1-1 in the 3D viewer to explore the dti dataset
Tractography ‘on-the-fly’

The Fiducial Seeding functionality allows you to do tractography ‘on-the-fly’ to explore white matter structures interactively.
Select the module **Data** to display the list of elements that have been generated in this tutorial.
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

• Open Source Diffusion MRI Technology For Brain Cancer Research NIH U01CA199459

• National Center for Image Guided Therapy (NCIGT)
  NIH P41EB015898

• Neuroimage Analysis Center (NAC)
  NIH P41EB015902

• Fan Zhang, Ph.D.
  Brigham and Women’s Hospital, Harvard Medical School