Mapping white matter pathways with Diffusion MRI

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Clinical Case

- 47-y.o. golf professional
- Brain tumor resected in 1999
- Tumor recurrence in 2011

Clinical case courtesy of Dr. Alexandra Golby, Brigham and Women’s Hospital, Harvard Medical School
What does the surgeon want to see?

- Where are the tracts?
- Are they normal?
- Is anything missing?
Pre-op Imaging

T1

T2

DWI
DTI Tractography for Brain Surgery

- Non-invasive 3D visualization of peritumoral white matter anatomy
- Spatial relationship of a tumor with tracts involved in motor, visual or language function
- A potentially clinically useful guide to the location of eloquent tracts for subcortical mapping
Part 1: An Introduction to Diffusion Tensor Imaging
White Matter Exploration

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

\( S_i = S_0 e^{-b\hat{g}_i^T D\hat{g}_i} \)

Stejskal-Tanner (1965)

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

DWI dataset

DTI dataset
DTI Color Map

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

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

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

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

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

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

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

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

\[ = \begin{bmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \end{bmatrix} \]
Diffusion Tensor Shape

\[ \lambda_1 = \lambda_2 = \lambda_3 \]

Isotropic media (CSF, gray matter)

\[ \lambda_1 \gg \lambda_2, \lambda_3 \]

Anisotropic media (white matter)

\[ \lambda_1 \sim \lambda_2 \gg \lambda_3 \]
Diffusion Tensor Imaging (DTI)

A: Anisotropic; B: Isotropic
DTI Tractography
DTI Tractography

Seed Point
DTI Tractography

Seed Point
DTI Tractography

DTI tractography provides 3D reconstruction of the trajectory of white matter pathways
Brain Mapping for Neurosurgery
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 tracts.
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

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Part 1: From DWI images to Tensors
The Diffusion Weighted Imaging (DWI) dataset is composed of 48 volumes acquired with 41 different diffusion-sensitizing gradient directions, and 7 baseline image acquired without diffusion weighting.
Loading the DWI Dataset

First, start Slicer4
Loading the DWI Dataset

In your files archive, locate the file **dwi.nnrd** in the dataset folder for this tutorial.
Loading the DWI Dataset

Drag and drop the file **dwi.nnrd** onto the viewer of the Slicer4 application
Exit the archive folders window, and click **OK** to load the dataset to Slicer.
Loading the DWI Dataset

Welcome

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

Adjust the **Window Level editor presets** with the **Volume** module menu.
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

Diffusion MRI Analysis

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NA-MIC ARR 2012-2016
Estimating the tensor

Click on the Modules menu and select the module **DWI to DTI Estimation**
Estimating the tensor

Select the module **DWI to DTI Estimation** in the modules menu:
- Set the Input DWI volume to ‘dwi’
- Set the Diffusion Tensor Mask to ‘None’
- Select Output DTI Volume ‘Create and Rename New Volume’, and rename it ‘dti’
- Set Output Baseline Volume to ‘baseline’
- Select the Estimation Parameters ‘WLS’ (Weighted Least Squares) and click on **Apply**.
Estimating the tensor

Position your mouse over the **pin icon** and select the volume **dti**
Exploring the DWI Dataset

Slicer displays the DTI volume in color by orientation mode:
- Red: right-left
- Green: anterior-posterior
- Blue: inferior-superior
Diffusion Tensor Data

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

Stejskal-Tanner equation (1965)

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

• The diffusion tensor $D$ 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

\[ \lambda_1 = \lambda_2 = \lambda_3 \]

\[ \lambda_1 \gg \lambda_2, \lambda_3 \]

\[ \lambda_1 \sim \lambda_2 \gg \lambda_3 \]

Isotropic media
(Cerebrospinal Fluid, gray matter)

Anisotropic media
(white matter)
Exploring the DWI Dataset

Use the slider to browse through the dti volume, and try to locate the Corpus Callosum.
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.
Characterizing the Size of the tensor: Trace

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

• 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
Click on the Modules menu and select the module **Diffusion Tensor Scalar Measurements**
Type in the following information in the IO menu:

- select the Operation ‘Trace’
- set Input DTI Volume to ‘dti’
- select Output Scalar Volume ‘Create and Rename new Volume’ and rename it ‘trace’
- click on Apply to calculate the trace map of the tensor volume
The trace image appears in the red viewer
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’ 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

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.
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**
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**.
Set the **Active Volume** to ‘dti’ and the **Scalar Mode** to ‘ColorOrientation’.
Scroll down the module panel and:
- 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.
3D Visualization: Glyphs

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

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

Click on the **fit to screen icon** to adjust the dimensions of the yellow slice viewer to fit the screen.
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

Select the module
Tractography Interactive Seeding
Labelmap Seeding: Step 1: I/O

- Set the Input DTI Volume to ‘dti’
- Set the Input Label Map to ‘fa-label’
- Set Output Fiber Bundle to ‘Create and Rename New Fiber Bundle’ and rename it ‘corpusCallosum’
- Uncheck Enable Seeding Tracks

Change to **Conventional** view
Labelmap Seeding: Step 2: Seeding parameters

Select the default Tractography Seeding parameters:
- Check Use index Space
- Stopping Criteria: Fractional Anisotropy
- Stopping Value: 0.15
Labelmap Seeding: Step 3: Generate Tracts

The tracts generated in the corpus callosum area appear in the 3D viewer.

Check Enable Seeding Tracks
Labelmap Seeding: Step 4: Undesirable track removal

Click on the Modules menu and select the module Tractography Display.
Labelmap Seeding: Step 4: Undesirable track removal

Set ROI for Fiber Select to ‘ROI node’
Labelmap Seeding: Step 4: Undesirable track removal

Adjust the ROI frame to include the undesirable tracks.
Labelmap Seeding: Step 4: Undesirable track removal

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

Uncheck ROI Visibility
Labelmap Seeding: Tracts

Select the module
Tractography Interactive Seeding
Tractography Results

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

Uncheck **Enable Seeing Tracks**.
Fiducial Seeding

Select the module Markups
Click on the arrow icon to create a fiducial
Fiducial Seeding

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

Select the module **Tractography Interactive 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’ and rename it ‘*Cingulum*’
Check **Enable Seeding Tracks**
Part of the left cingulum appears in the 3D viewer. Move the Left Cingulum fiducial to explore the spatial relationship between the left cingulum and the corpus callosum.
Fiducial Seeding

Go to the **Markups** module
Fiducial Seeding

Double click on the Name and change it to **RightCingulum**
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.
Click on the arrow icon to create a new fiducial, and position it in the 3D viewer.
Move the fiducial F-3 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.
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