SNSS Diffusion Module: Tutorial 2

3DSlicer for Diffusion Tensor Analysis
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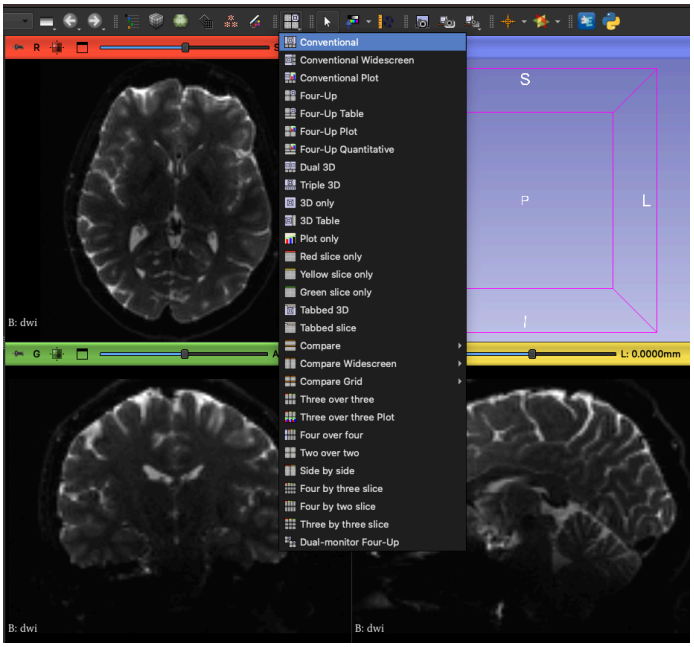
This tutorial will cover diffusion data inspection and DTI analysis using 3D Slicer.

Preparation

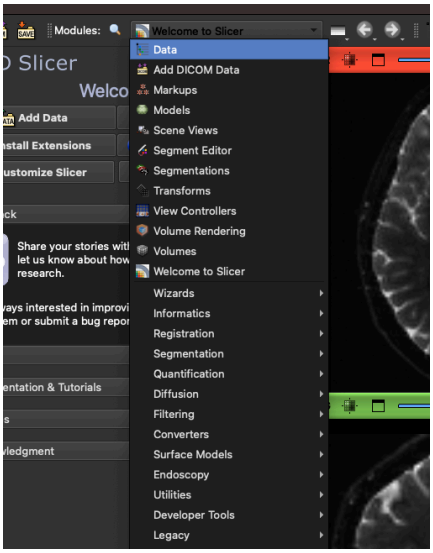
1. Download and install the stable release of 3DSlicer for your OS from https://download.slicer.org/
2. You will also need the SlicerDMRI extension. Open 3DSlicer and go to the View menu at the top. Select Extensions Manager. On the page that opens, install SlicerDMRI. You may need to select the Diffusion category to see it.
3. Go to https://dmri.slicer.org/docs/ and download the “test data” for the Slicer DTI tutorial. Unzip the data so that you can access the file dwi.nrrd. You may also wish to save the pdf for the Slicer DTI Tutorial itself, which covers some of the material below, as well as tractography.

Data Loading and 3DSlicer Basics

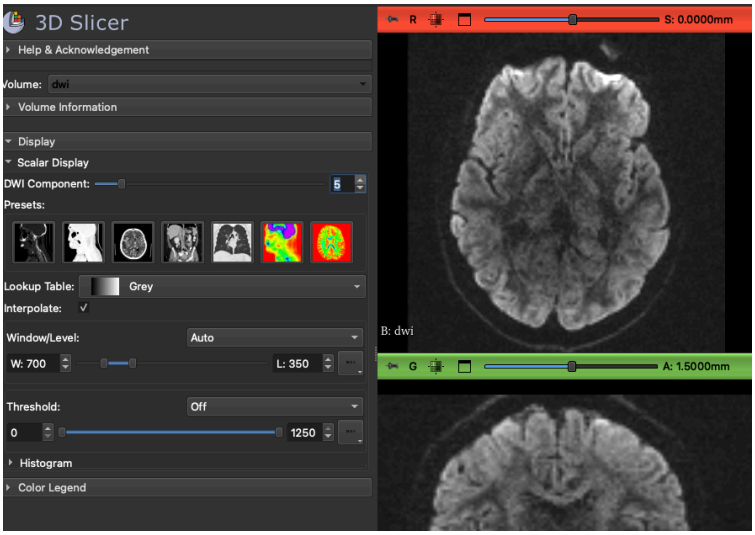
1. Open 3DSlicer and click on “Add Data” and Choose File(s) to Add. Select the dwi.nrrd file that you downloaded and click OK.
2. You should see an unweighted brain image. The View layout icon on the toolbar can be used to change the window layout. Choose a view like Conventional or Four-Up that allows you to easily see all three directions.



3. Slicer is organized into modules, listed in a dropdown. Some useful modules for data inspection include Data and Volumes.

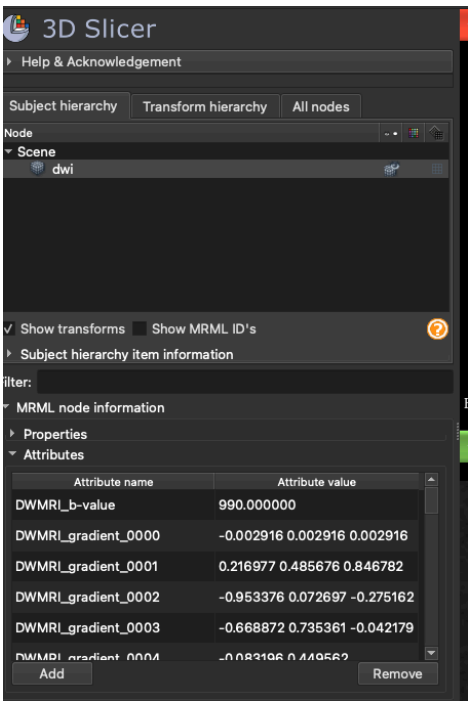


4. Open the Volumes Module. Under Display, move through the DWI components to look at the data. You can also use the sliders over the images or the scroll wheel to scroll through different slices within a volume.
   If Window/Level is Auto, you should see good contrast, regardless of diffusion weighting. However, the intensities in different DWI components will not be directly comparable. If you set Window/Level to Auto, you can see how the contrast in an area changes between DWI components, but either low diffusion weighting will appear very bright or high diffusion weightings may be difficult to see.



5. This data was likely converted from its original dicom format to nrrd. Information about the b-values and b-vectors is in the header of this file. You can view it if you open the Data module. Select “dwi” under Scene. Then open the MRML node information section. Under Attributes,

you should see the b-value and a list of gradient directions.



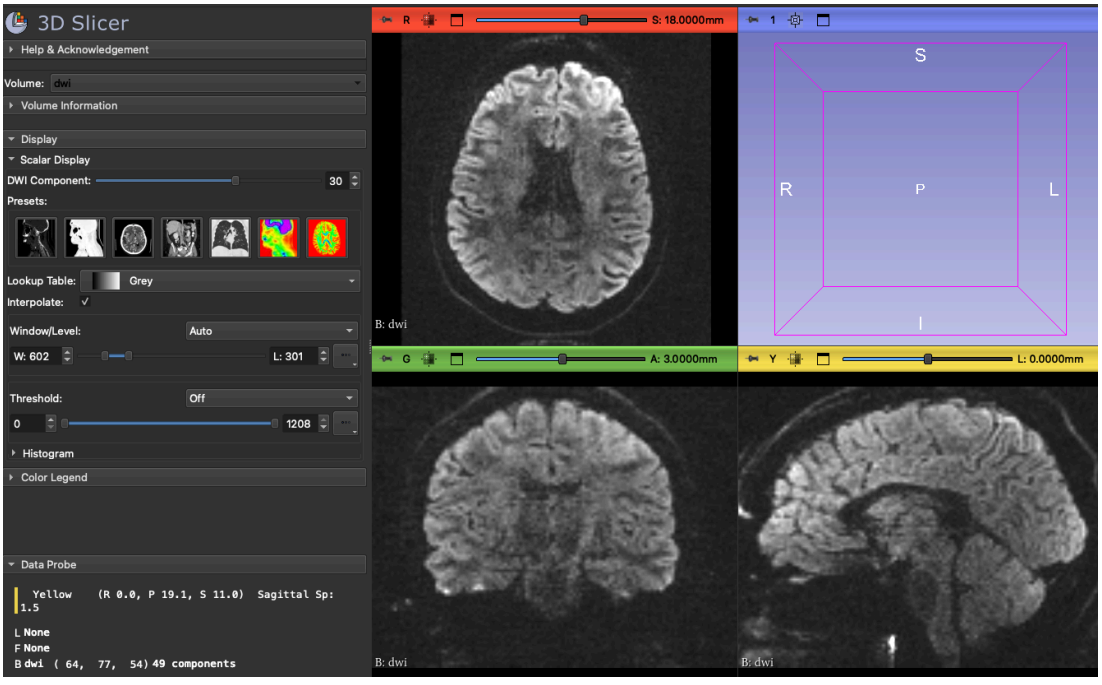
Data Inspection Exercises

1. Can you identify the unweighted (b=0 s/mm^2) diffusion volumes using the attributes? Does this match up with what you expect from scrolling through the volumes?
2. If you scroll to the bottom of the attributes, you should see a “space” attribute that tells you that the data is in a “right-anterior-superior” orientation. The components of the diffusion vector should follow this order. Find a gradient direction where the gradient is strong in the left-right direction. Would you expect the corpus callosum to be lighter or darker relative to other white matter in this volume? Go to that volume in the image viewer to check your answer.
3. Scroll through the volumes to look for distortion and other artefacts. Do the distortions change between the unweighted and diffusion-weighted volumes? What does that tell you? Which direction is the phase encode direction? How might you correct any distorted data (you do not need to actually run the correction)?

Answers on the next page

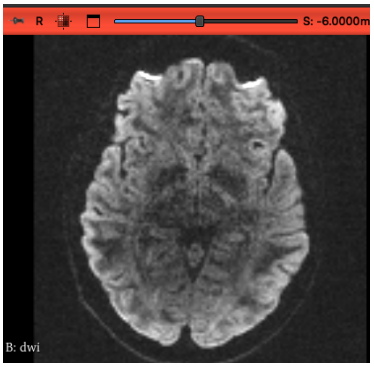
Data Inspection Answers

1. The unweighted volumes are the vectors in the list where *all three* components are near zero. These include DWMRI_gradient_0000, DWMRI_gradient_0007, DWMRI_gradient_0014, etc. These values may not be exactly zero because there is some small amount of diffusion weighting even in “unweighted” diffusion images due to slice selection gradients and crushers around the radiofrequency pulses. For other directions, the sum of the squares of the three components of the vector should be near 1. This dataset has 42 directions with significant diffusion weighting and 8 (nearly) unweighted images. The unweighted images can be easily identified by the bright signal intensity in the ventricles, which is attenuated to nearly zero in the b=990 s/mm^2 volumes.
2. Any volume where the first number in the 3-element vector is above 0.95 will be mostly weighted in the left-right direction. For example, volume 30 has a vector in the direction (-0.982764 -0.140853 0.065272).
   Since the fibres in the corpus callosum mainly run in the left-right direction, water should move more in this direction and the signal should be more attenuated relative fibres oriented in other directions. You can see this clearly in the dark region of the sagittal image. You can also see it in the axial image, but the nearby ventricles will also appear dark because of the fast water diffusion in all directions in the ventricle.
   This is a good check to run on your data, especially if you have complex analysis that takes a long time to run. This data was set up to be easily loaded into 3DSlicer. If you convert your own dicom data off of the scanner, there can occasionally be errors in the data orientation and diffusion directions that may swap the order of the directions around. This can result in odd DTI eigenvectors or colour maps where the colours look wrong.

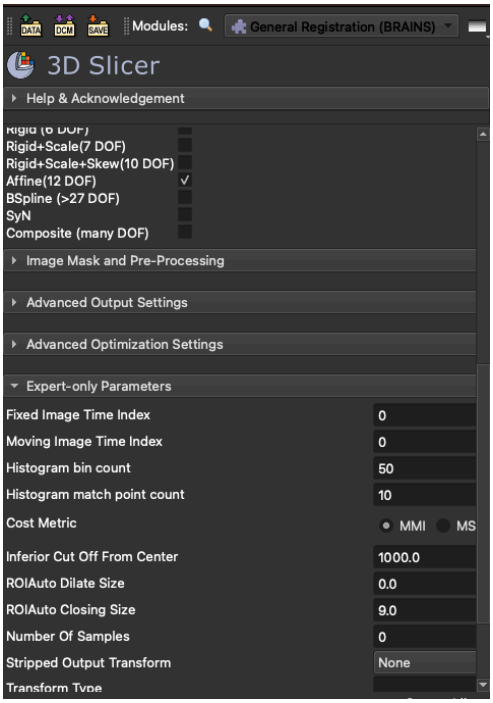


4. There is some distortion near the anterior of the image in some of the lower slices. You can see some “signal pileup” along what appears as the edge of the brain and then the brain itself appears to be the wrong shape, with signal voids where you expect the brain near the skull. This distortion is similar between the unweighted and diffusion-weighted volumes, which

means that it is likely a susceptibility-induced distortion (a distortion caused by eddy current effects would be larger in the diffusion-weighted image). You might also have guessed that it is a susceptibility-based distortion because it doesn't seem to be a global transformation of the whole slice but is located near the air-tissue interface just air-tissue interface just above the sinuses.
Since the distortion appears to be compressing signal toward the posterior and because it is symmetric on both sides of the brain, the phase encode direction is likely to be the anterior-posterior direction.

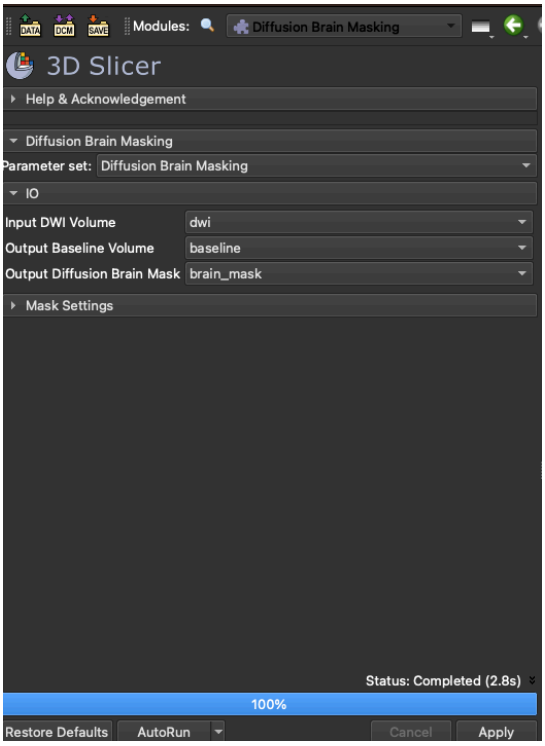


To do a correction for a susceptibility-based distortion, we would need a B0 map or reverse blip image, which we do not have. In addition, Slicer does not currently have a module for this correction. The software is open source, so one could become available in the future. For eddy current distortions, there is a Registration module that performs affine registration and a cost metric like max mutual information could be used to register the diffusion weighted images to one of the unweighted images even though they have different contrast. However, each volume would need to be registered individually and we would not be able to distinguish true patient motion from eddy current-based distortions. Tools like eddy or topup from FSL are preferable because they use the diffusion directions and diffusion encoding information to correct for effects in all volumes.

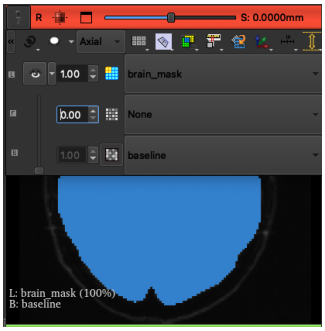


Diffusion Analysis

1. Create a brain segmentation. Open the Diffusion Brain Masking module under the Diffusion - Process menu. Select dwi as the input volume. For Output Baseline Volume, select Create new Volume as: baseline. For Output Diffusion Brain Mask, Create New LabelMapVolume as brain_mask. Click Apply.

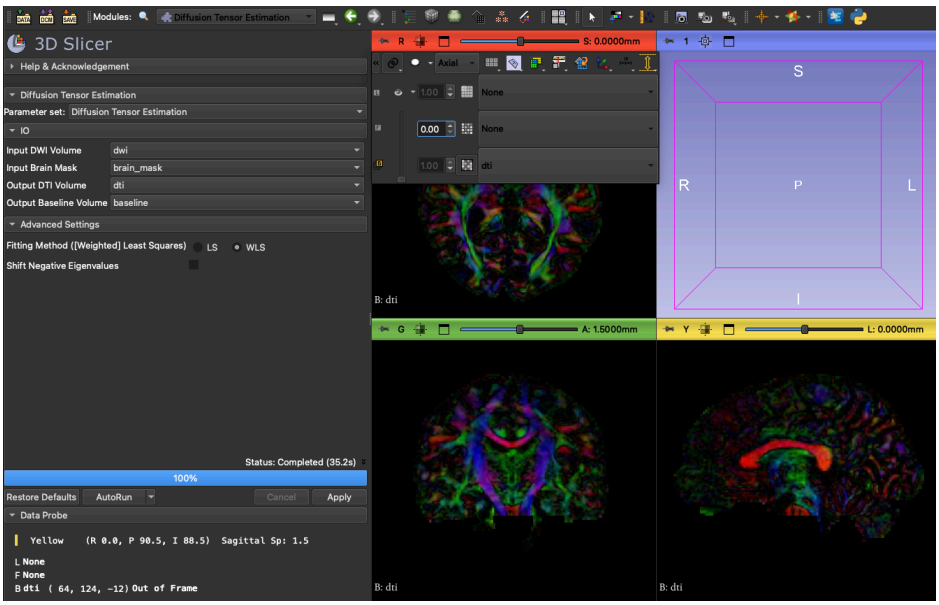


2. The segmentation should appear over the previous image. To turn it off, you can mouse over the pin icon, then click on the double arrows to expand the menu. Change the selection beside L (label) to None to turn off mask visibility.

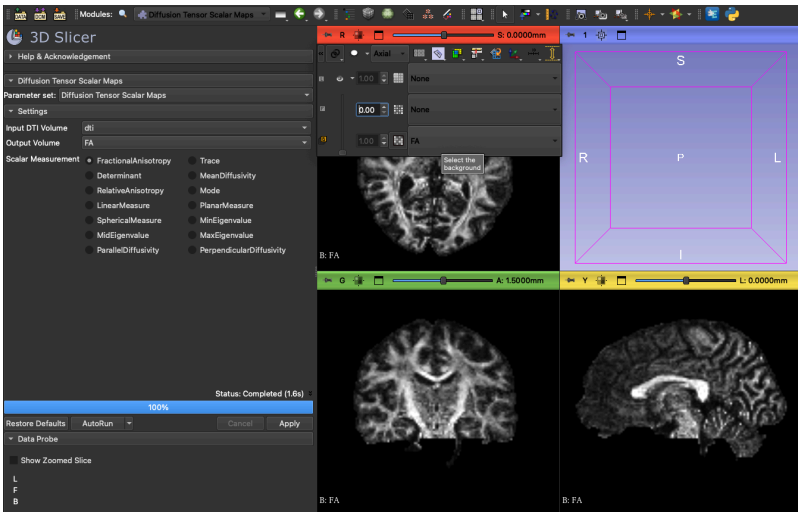


3. Now open the Diffusion Tensor Estimation module under the Diffusion - Process menu. Select DWI as the Input DWI Volume, brain_mask as the Input Brain Mask, create a new Output DTI volume named dti and an Output Baseline Volume as baseline. Under Advanced Settings, you can choose WLS for a weighted least squares fit (takes longer to process) or LS for least squares. Click Apply. When the fit has finished running, open up the display options and turn off brain_mask in the label display, then set the background (B) image to dti. The display will show the tensor fit as a colour map, with intensity based on anisotropy, a left-right orientation

as red, anterior-posterior as green and superior-inferior as blue.

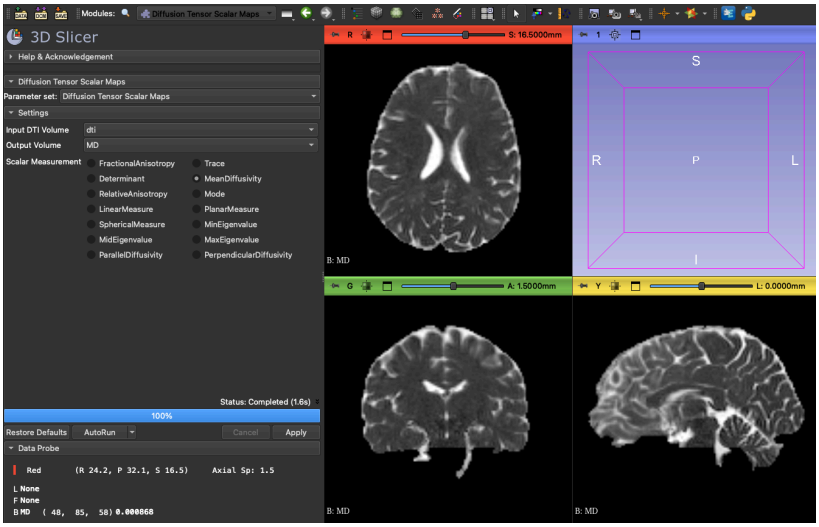


4. Scroll through the slices. Identify the corpus callosum. Does the colour agree with what you expect? Can you identify other white matter regions?
5. Open the Diffusion Tensor Scalar Maps module under the Diffusion - Quantify menu. Select dti as the Input DTI Volume. Create a new Output Volume called FA. Select the FractionalAnisotropy measurement and click Apply. You may need to turn off the brain_mask in the L display to view the result.



6. Do the same for MeanDiffusivity. If you move your mouse over the resulting image, you can see the values for the mean diffusivity in any voxel in the Data Probe section in the bottom left of the window. What do you expect the mean diffusivity to be in the ventricles? What is the mean diffusivity in white matter versus grey matter? Open the FA map that you calculated in

the last step and check the values for the same three regions.



7. Feel free to explore other Scalar Measurement maps. FA is the most common measure of anisotropy, but it can be less sensitive than some other anisotropy metrics.
8. That's the end of the tutorial. When you exit, you will be prompted to Save. You can save all of the volumes that you have generated or just selected ones as nrrd files or in other formats. If you save all folders to one directory, you can re-open them all using the Add Data button with Choose Directory To Add.

Answers for Diffusion Analysis

You should see that the ventricles have a mean diffusivity near 0.003. The units are mm^2/s. This is close to what you would expect for free water near 37 degrees celsius since the water in the CSF is nearly free. In grey matter and white matter, diffusivity will be lower, likely somewhere between 0.0005 mm^2/s and 0.001 mm^2/s. The grey matter and white matter are not easily distinguished by mean diffusivity.

In the FA map, you should see that the ventricles have low anisotropy, near zero. The white matter has a fairly high value, around 0.8 in regions where the fibres are aligned, although it may be lower in regions where fibres cross (0.4). Grey matter has quite low anisotropy, around 0.1, and CSF should be nearly 0.