Physics Tutorial 6: Diffusion MRI

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The purpose of this tutorial is to cover material related to Diffusion MRI, using a simple diffusion acquisition simulator. Questions without any asterisks are those that should be attempted by everyone, whereas more challenging questions are marked with one (*) or two (**) asterisks, and should be considered optional. Take these opportunities to think about these questions, and then discuss your answers with your tutor.

At the end of the tutorial period, you will receive a "take-home tutor", which is an annotated version of this tutorial guide that will help you complete the tutorial at home if you don't manage to make it all the way through with your tutor, or if you missed the tutorial session.

Attendance will be taken by the tutors, and marks will be given by participation. If you would like additional feedback or clarification on the tutorial material, you are welcome to submit your questions or comments to Weblearn, and a tutor will provide written feedback for you. Those unable to attend the tutorial must submit answers to all unstarred questions to receive credit for the tutorial.

Part 0 – Getting Started

Download and unzip the file containing the tutorial resources from Weblearn, or if you have access to the FMRIB internal network, copy them into your current directory from here:

~mchiew/GradCourse/6_Diffusion

Start MATLAB, and make sure you're inside the tutorial directory (i.e., the folder containing all the tutorial files).

Note to jalapeno00 users: please start with the -nojvm option, "matlab -nojvm"; *this should reduce server CPU load if lots of people are trying to use jalapeno00 simultaneously*

Part 1 – The Diffusion Simulator and the Tensor Model

This tutorial uses a diffusion MRI MATLAB tool that simulates the acquisition and simple inspection of diffusion weighted MRI under semi-realistic conditions.

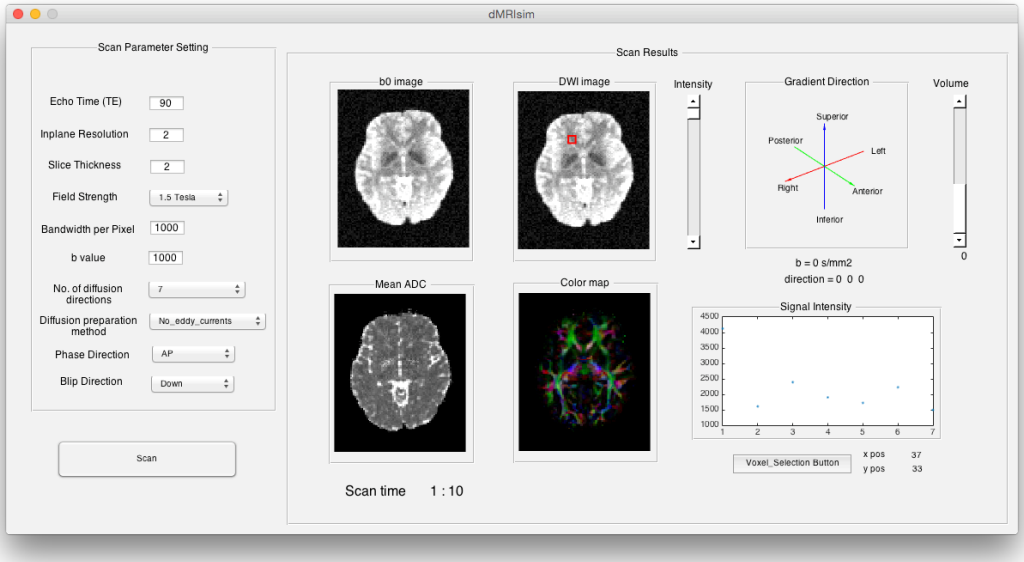

Figure 1

The simulator is able to realistically demonstrate the effects of changing:

- Echo time (TE)
- In-plane image resolution (Δx, Δy)
- Slice thickness (Δz)
- Magnetic field strength (B0)
- Acquisition Bandwidth
- Diffusion-weighting (b-value)
- Number of diffusion directions acquired
- Diffusion encoding method (type of diffusion encoding gradients)
- Phase encoding direction
- Phase encoding blip direction

The effects of modifying these parameters is reflected in the various output measures provided:

No diffusion weighting reference "b=0" image

The b=0 image is the reference image for all the subsequent directional, diffusion weighted images. It is an image acquired in the absence of any diffusion encoding gradients, with all other parameters the same. This produces the "S_0" image.

Diffusion weighted images (one for each direction acquired)

When diffusion gradients are applied in a given direction, with a given b-value, the signals from the image that is produced can be expressed relative to the reference b=0 data as:

$$S_i = S_0 e^{-bD_i}$$

where S_i is the diffusion-weighted signal in the i^{th} direction, and D_i is the apparent diffusion coefficient in that same direction.

Question 1.1
Why is it necessary to measure diffusion weighting relative to a reference "b=0" image?

Estimated mean apparent diffusion coefficient (ADC) image

The mean ADC represents the average diffusion coefficient computed after estimation of the diffusion tensor:

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

where mean ADC = $(D_{xx} + D_{yy} + D_{zz})/3$. This represents the *overall*, net effect of diffusion in all directions. A higher mean ADC represents a case where water molecules are able to produce larger net displacements in the same amount of time, compared to more restricted displacement in voxels with lower ADC.

Extra Information
Estimation of the diffusion tensor is performed by solving a uniquely determined (6 direction measurement) or an over-determined (more than 6 directions) linear system. Each measurement of diffusion in a different direction provides the following linear constraint to the variables D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{xz}, D_{yz}:

$$\ln\left(\frac{S_i}{S_0}\right) = -b \cdot (u \quad v \quad w) \cdot \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} \cdot \begin{pmatrix} u \\ v \\ w \end{pmatrix}$$

where $\begin{pmatrix} u \\ v \\ w \end{pmatrix}$ is a unit vector denoting the direction of the diffusion encoding gradient.

Estimated colour map fractional anisotropy (FA) image
The mean ADC does not provide any information of preferential diffusion directions. Instead colour-coded FA maps provide information about the primary diffusion direction, by colouring left-right directions red, anterior-posterior directions green, and inferior-superior directions red.

Extra Information
The eigen-decomposition of the diffusion tensor is:

$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix} = [V_1 \quad V_2 \quad V_3] \begin{bmatrix} \lambda_1 & & \\ & \lambda_2 & \\ & & \lambda_3 \end{bmatrix} [V_1 \quad V_2 \quad V_3]'$$

where V_1, V_2, and V_3 are column vectors associated with the axes of the diffusion tensor ellipsoid (see Fig. 2). V_1 corresponds to the primary diffusion direction (and V_2 to the secondary, V_3 to the tertiary), and the colour assigned to the voxel in the FA colour map is determined by what degree V_1 is aligned with the left-right, anterior-posterior, or inferior-superior directions.

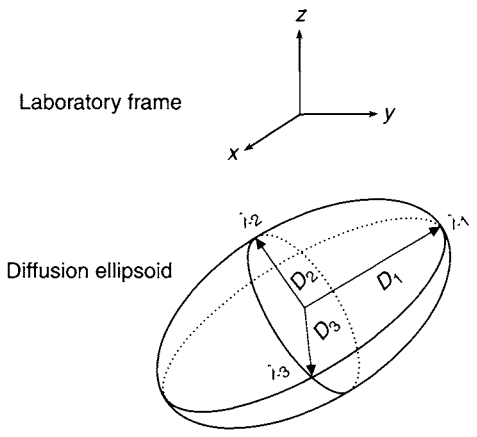

Figure 2 (*source: Bernstein et al., Handbook of MRI Pulse Sequences 2004*)

Start the diffusion simulator by typing:
`>> dMRISim`
into the MATLAB command window. Change the field strength to 7T and the number of diffusion directions to 21, then hit the "Scan" button. Use the voxel selection button to select a voxel in white matter where the fibres run anterior to posterior (i.e. they appear green in the colour map).

Now scroll through the different diffusion weighted images using the "Volume" scroll bar at the top right. You may wish to use the "intensity" scroll bar to show the diffusion-weighted images more clearly.

Question 1.4
Using **only** the diffusion weighted images and the signal intensity plot, state which volume numbers correspond to the following cases and how you deduced this:
a) no diffusion weighting (b = 0).
b) diffusion weighting in approximately the anterior-posterior direction.

Part 2 –Diffusion Acquisition Parameters

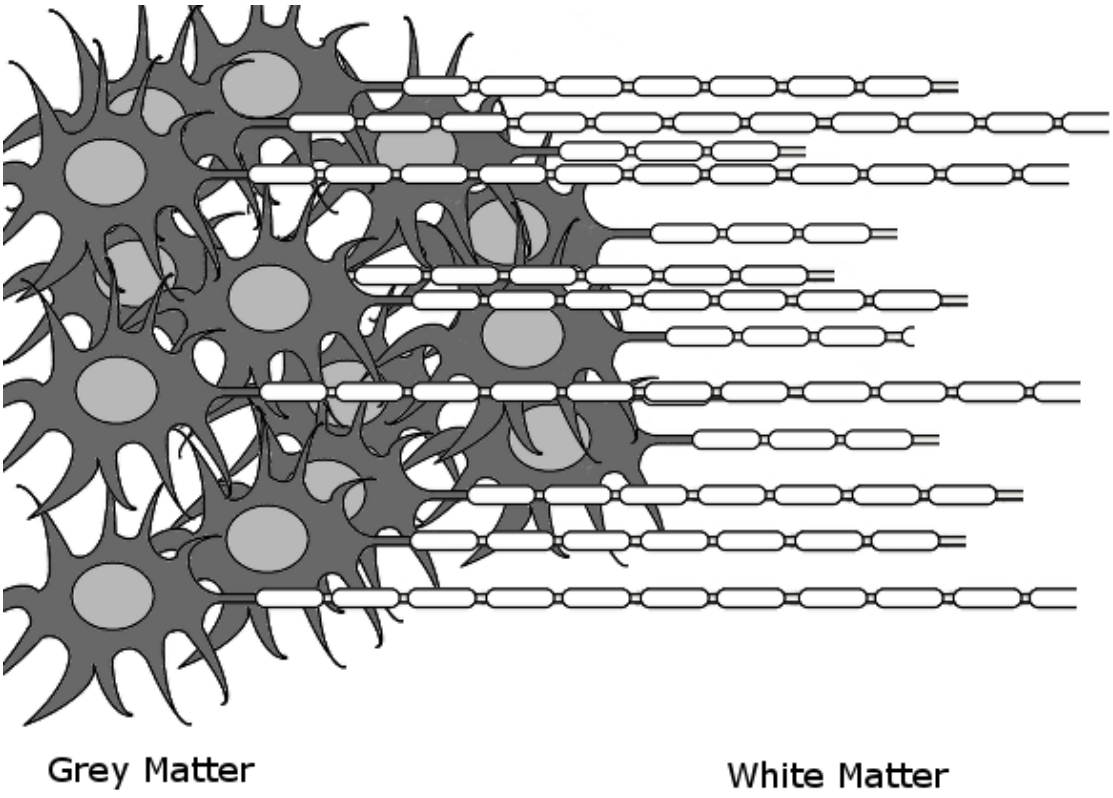

Figure 3

Diffusion-weighted measurements are designed to reveal information about the microstructural properties of the tissues under investigation. Grey matter (neuron bodies), white matter (neuron projections, or axons) and cerebral-spinal fluid all have distinct diffusion tensor signatures that reflect their respective structures (or lackthereof).

Question 2.1
How might diffusion change in WM axons with increasing radius?

The high degree of fractional anisotropy in white matter is what people are often interested in when acquiring diffusion data for the purpose of axonal fibre characterisation. There are many choices of acquisition parameters that can be made to balance the quality of the diffusion tensor estimates with scan time and image quality.

One parameter is the number of diffusion directions. At a bare minimum, the diffusion tensor has 6 free parameters, so 6 non-collinear directions must be acquired (in addition to the directionless b=0 reference image). In practice, measurements can be made on up to *hundreds* of different directions.

Another parameter is the b-value, or strength of diffusion encoding. Increasing the b-value increases the diffusion contrast, but can often result in increasing TE. The optimal b-value for measuring diffusion in the human brain is around b=1000 s/mm^2, which is large enough to ensure diffusion has a strong impact on the signal intensity, but not so large as to cause too much signal loss.

Question 2.2
What effect does increasing TE have on the diffusion data?

Question 2.3**
Estimate the optimal b-value for measuring diffusion contrast

Other parameters can include field strength, and image resolution.

Part 3 – Artefacts and Complications

3.1 Distortion and Eddy Currents

In a typical diffusion imaging protocol a spin-echo EPI readout is used.

Question 3.1.1
How much do dropout and distortion affect the images produced in the simulator (you may like to change the TE and bandwidth to test this)? Can you explain why this is?

Distortion in diffusion acquisitions also arises due to eddy current effects from the diffusion encoding gradients.

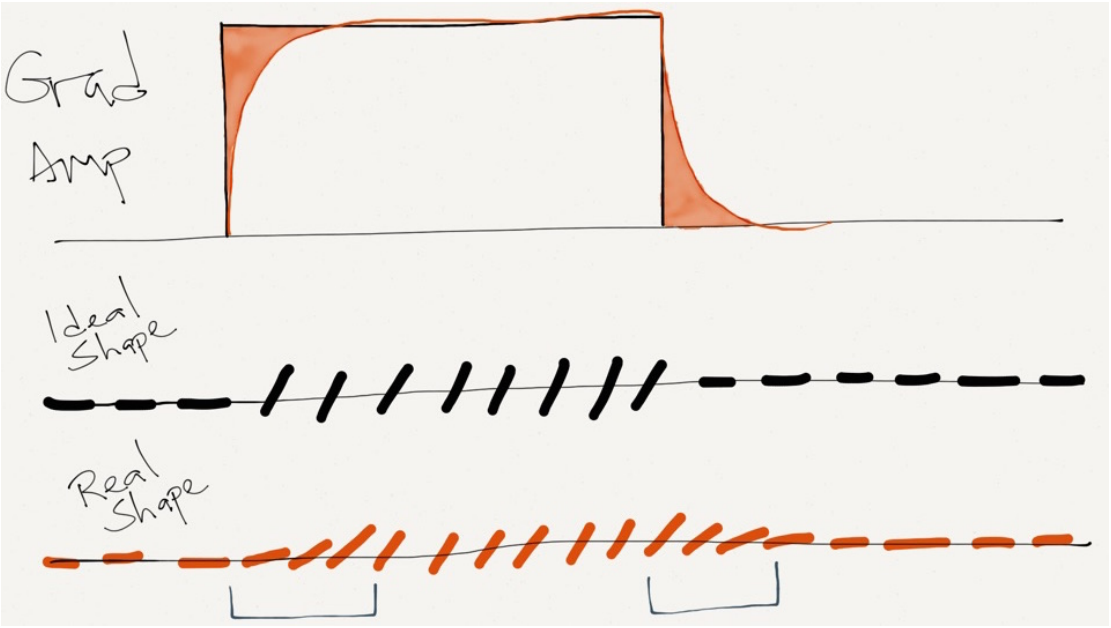

Figure 4

Eddy currents cause the gradient waveforms to deform, where the effect can be understood as a "resistance to change" behaviour of the magnetic field gradients. Fig. 4 illustrates the principle with a simple gradient pulse, showing the sluggish response of the orange, realistic gradients to being turned on and off, relative to the ideal gradient pulse (controlled by the input current to the gradient coil).

Because eddy currents alter the strength of the gradient, but do not affect the direction, eddy current effects follow the same directional dependence as the diffusion encoding. Therefore, different diffusion-weighted images will each have unique image distortions depending on the direction of diffusion encoding. This distortion is also dependent on the EPI phase-encoding and blip directions.

Question 3.1.2
Turn on the eddy current simulation by selecting the monopolar diffusion encoding gradients. Examine the effect of eddy currents on the FA colour maps. How might you explain the bright "ring" artefact you see?

Question 3.1.3*
Why are eddy currents specific to diffusion-encoding gradients?

Question 3.1.4**
Ideally, magnetic field gradient strength would be directly proportional to the current in the gradient coil. In practice, eddy current effects cause the gradient strength to have characteristic delayed and smoothed responses to change. Where do the eddy currents come from, and what do they tell you about the impulse response of the gradient system?

One way of mitigating eddy current effects is by trying to design gradient waveforms in a way that accounts for the anticipated eddy-current delays (known as "pre-emphasis") or by trying to design gradient pulses that elicit eddy currents which tend to cancel each other out.

Bipolar diffusion encoding gradients (i.e. those with both positive and negative lobes) are designed to produce the latter effect, in order to minimise eddy current distortion in images.

Question 3.1.5
Why aren't bipolar gradients always used?

3.2 Multiple Fibres

Figure 5 shows a colour map of the primary diffusion direction (left) and the FA map (right) from the same coronal slice. Notice how the white matter tracts appear bright, e.g. the corpus callosum running left-right between hemispheres appears red in the colour map and bright in the FA map. We usually observe high FA in WM tracts due to the strong dependence of the measured signal on a particular diffusion encoding direction – i.e. the signal decreases (diffusion contrast increases) as the gradient direction becomes closer to the tract orientation.

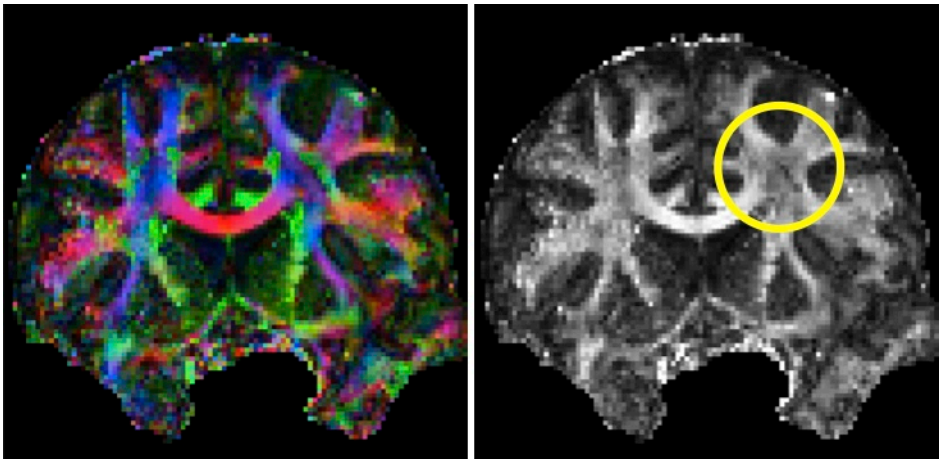

Figure 5

Question 3.2.1
The region highlighted by the yellow circle in the FA map is a white matter region, however it has low FA. Why do you think is?

It can be useful to think about what the tensor model assumes about how diffusion behaves within a voxel, and how this can be insufficient to capture more complex diffusion geometries, like cases with crossing fibres or "kissing" fibres.

Models other than the tensor model are used to describe the dependence of diffusion signals on measurement orientation and how this reflects the underlying internal voxel geometry, which you will learn about in the Analysis Course next term.