Physics Tutorial 5: Functional MRI

Originally Written by Tom Okell and Mike Germuska
Last Modified: Mark Chiew, Hannah Hare, Tom Okell, Alan Stone, Oct 2014

The purpose of this tutorial is to cover material related to functional MRI (FMRI), focusing on some of the basic underlying blood oxygenation level dependent (BOLD) physiology, simulating FMRI data acquisition and simple data analysis. 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/5_FMRI

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 – Introduction to BOLD Physiology

Haemoglobin (Hb) is the component of blood that carries oxygen from the respiratory organs to the rest of the body, including the brain. In its fully oxygenated state Hb is diamagnetic whereas deoxygenated Hb (dHb) is paramagnetic. The presence of dHb increases the magnetic susceptibility difference between vessels and extravascular tissue causing magnetic field gradients.

Question 1.1
Why might the dHb concentration in a vessel change?

Question 1.2
What effect does a reduction in dHb concentration in a vessel have on the T_2^* of surrounding tissue?

When neurons become more active, the local energy demand increases and more oxygen is extracted from the blood. As brain cells use oxygen to produce energy (in the form of ATP) and brain cells do not have a store of energy (or oxygen), the supply of available oxygen in the blood to this region must increase to meet the increased energy demand.

This haemodynamic response to a localised increase in neuronal activity results in a change in local dHb concentration (i.e. oxygen levels). This in turn leads to a measurable change of the MR signal, referred to as the BOLD (blood oxygenation level dependent) response.

Question 1.3*
From what vessels would you expect the BOLD signal to be most prominent: [arteries & arterioles], [capillaries] or [veins & venules]?

Question 1.4
Would you expect dHb to increase or decrease with neuronal activation? In practice what happens to T_2* and why?

Extra Information
In a BOLD FMRI experiment we are correlating changes in a signal time-courses caused by fluctuations in local dHb concentration that can be related to neuronal activation. These changes however, are measured from an unknown baseline.

Interpretation of BOLD signal changes can become difficult and uncertain as we cannot quantify the baseline state of the brain. For example in a standard BOLD experiment we have no way of accounting for changes in baseline signal which may occur between, or even within a scan session. This may become problematic when the baseline state of the brain is altered due to drug (e.g. caffeine) or disease influences or when comparing groups which may have systematic differences in baseline state (comparing a disease cohort with healthy controls). These are all important factors when considering the design of a BOLD FMRI experiments.

The interpretability of BOLD signal changes could be improved by making direct quantitative measures of the underlying haemodynamic effects that contribute towards the BOLD signal, i.e. CBF and oxygen extraction fraction (OEF). These measurements would need to be combined with a mathematical model of BOLD signal responses and their relationship with CBF, OEF and other neurovascular measures to extract quantitative information.

Part 2 – FMRI Simulator

Warnings: Please note that we have made a number of simplifications to create this simulator and allow it to run in a reasonably short time. It will show you approximately the right trends when varying parameters but it will not accurately predict the z-stats you will achieve for a given protocol. In particular many of the processing steps performed in FEAT have been neglected here (e.g. pre-whitening, smoothing, clustering etc.). For convenience, any z-stat greater than 9 is set to 9.

In this part of the tutorial we explore how various scanner parameters are likely to affect the functional activation that can be observed using BOLD-based functional MRI.

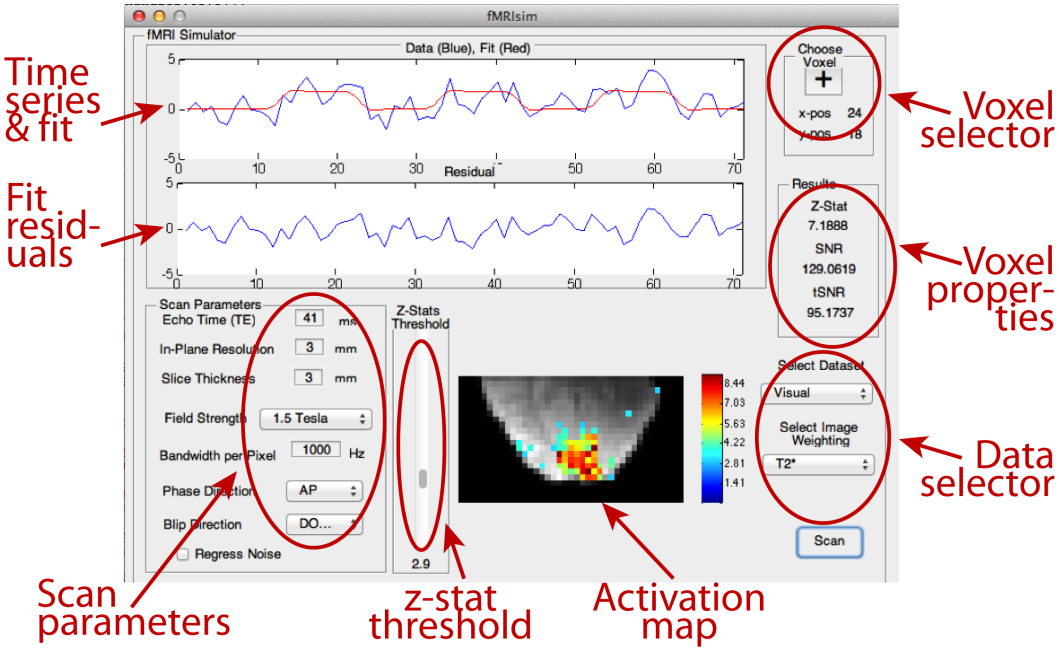

Figure 1

2.1 Visual Cortex Activation

Consider the simulated FMRI dataset, with a 10 s off / 10 s on visual stimulus.

The choice of TE in an FMRI experiment is important for determining how sensitive the acquisition is to BOLD signal fluctuations. Recall that gradient-echo BOLD contrast is maximised when TE ~ T2*. Also, it is sometimes useful to think of z-stats like a contrast-to-noise ratio (CNR) measure, where higher z-stats mean greater signal contrast relative to noise levels. In the simulator, it is evident that the z-statistics change when the TE parameter is changed, and that they peak in the range of 30 – 50 ms.

Question 2.1.1
Using a TE = 30 ms, examine the effect on the z-stats when slice thickness is varied from 2 – 12 mm. What happens to the z-stats initially? At what point does this behaviour change? Why might this be?

In addition to TE and slice thickness, choices of in-plane resolution, bandwidth per pixel, and field strength also affect the output z-statistics (and often not independently!).

Exercise 2.1.2
As a group, try to find an optimal protocol (set of parameters) for this simulated visual FMRI experiment. With your tutor, discuss how each change makes the z-statistic image better or worse.

2.2 Noise in FMRI

Noise in FMRI is distinct from noise in structural MRI, because a time-series of images are taken, meaning that noise *between* images is just as important as the noise *within* images. Temporal SNR (tSNR) is a term developed to express the SNR with respect to the *between* images noise, whereas SNR refers to the familiar *within*

image noise. As you recall, SNR is affected by many different sequence parameter choices. Similarly, tSNR is affected by parameter choices, but also depends on SNR.

Question 2.2.1
Why does tSNR not equal SNR at each point?

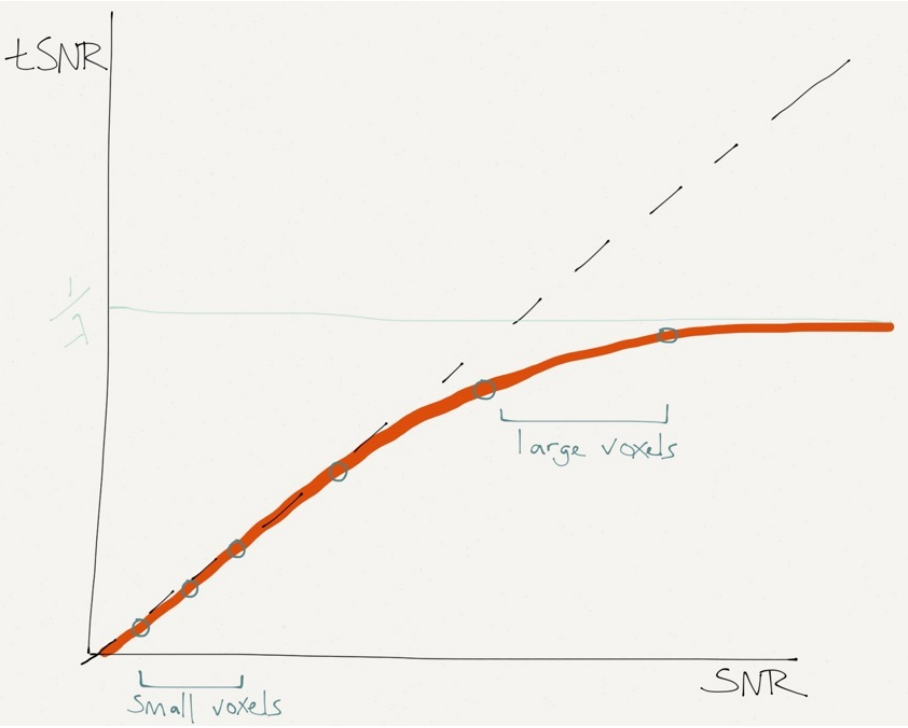

Figure 2

Question 2.2.2**
Given the shape of the tSNR vs. SNR curve in Fig. 2, assuming that $SNR = S/\sigma_0$, that the physiological noise $\sigma_P = \lambda S$, and that $\lim_{SNR\to\infty} tSNR = 1/\lambda$, try to express tSNR as a function of SNR and λ. (Hint, noise terms add in quadrature)

Physiological noise is primarily caused by physical fluctuations like breathing and cardiac pulsation. Breathing can induce changes in the local magnetic field homogeneity (by changing the size of the chest cavity), and gross motion of the head with the respiratory cycle is often observed. Cardiac pulsations can lead to variations in signals near blood vessels and fluid cavities (ventricles) due movement and tissue displacement.

When cardiac and respiratory cycles are measured using physiological monitoring equipment (e.g. resipiratory bellows or pulse oximeter), these signals can be used to remove signal components that fluctuate in a similar manner before running FMRI statistical analysis (i.e., the "RETROICOR" method, see Glover et al., *MRM* 2000).

Question 2.2.3
When regressing out the physiological noise, why does the tSNR not have exactly the same value as the SNR?

2.3 Frontal & Visual Cortex Activation

Different regions of the brain may need different considerations when planning an FMRI experiment. The brain and head anatomy in visual areas of the brain (occipital

lobe) are very different to the structural properties in frontal brain regions.

In addition to BOLD contrast and noise considerations, care must be taken in FMRI acquisitions to minimise the impact of magnetic field inhomogeneity on image dropout (*within-voxel* field variation) and distortion (*between-voxel* field variation). As a general rule, decreasing TE reduces signal dropout, and increasing bandwidth reduces image distortion. However, do not forget that these parameters also affect BOLD contrast and noise.

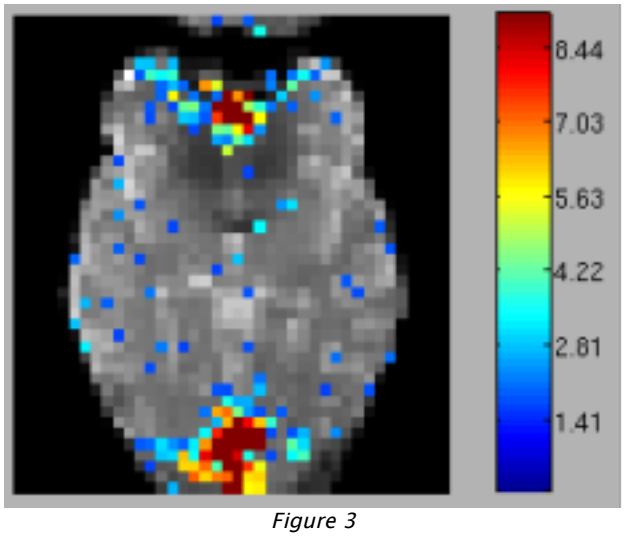

Figure 3

Question 2.3.1
Keeping the protocol the same, we can still see the strong activation at the back of the brain, but why can't we see the frontal activation as clearly? Hint: Depending on your protocol, you may not see any frontal activation at first, but with some parameter tweaking, you should be able to get activation like that shown in Fig. 3. It will probably help to display the activation on top of the T2* image, rather than the T1.

Image artefacts due to magnetic field inhomogeneity are affected by the way the image is encoded in k-space. For example, switching the phase-encoding direction will alter the direction of the artefact, and similarly for “blip-up” vs. “blip-down” encoding.

Exercise 2.3.2
As a group, try to find an optimal protocol (set of parameters) for this simulated frontal & visual FMRI experiment. With your tutor, discuss how each change makes the z-statistic image better or worse, this time taking into account artefacts.

Question 2.3.3*
Given the problems you have seen with EPI, why don’t we use other types of pulse sequences to do fMRI?