Why & How: Introduction to fMRI

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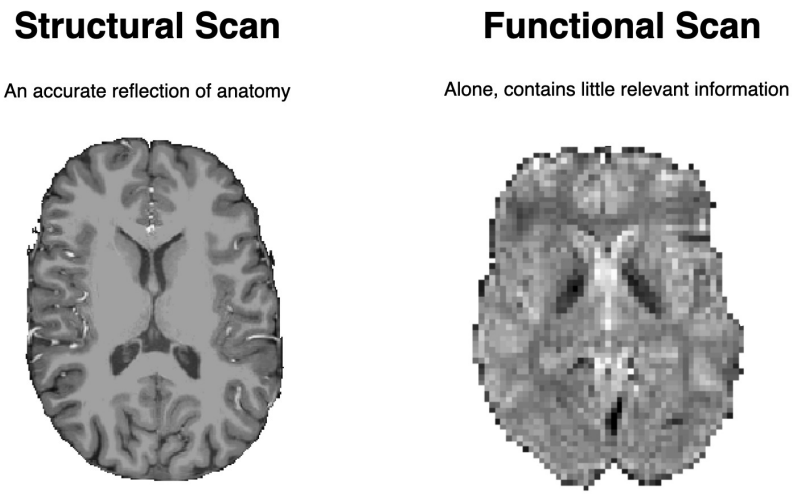
1 Fundamental Concepts

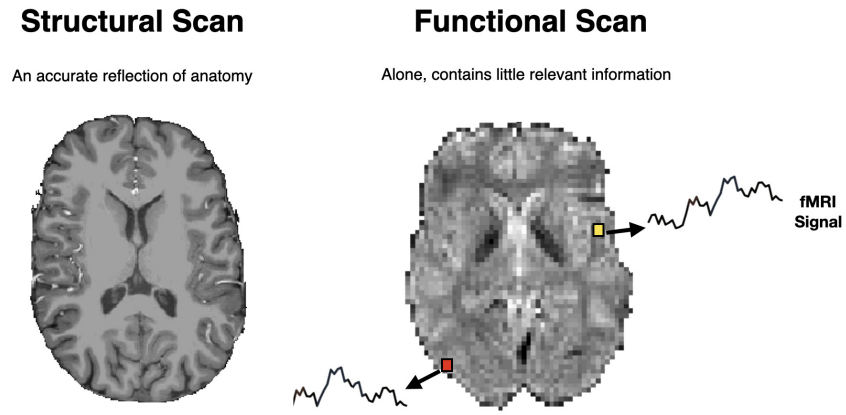
1.1 Functional MRI is about time

1.1.1 Unlike a structural image, a functional image is worthless alone



1.1.2 The functional information is encoded in the time domain

Functional MRI scans **always** have a temporal dimension.



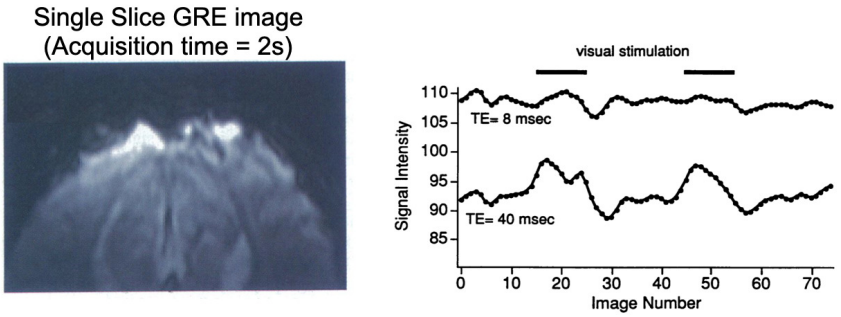
1.2 We infer function from MR signal intensity fluctuations

1.2.1 Signal intensity depends on magnetic properties of the tissue

$$S(\mathrm{TE}) = S_0(\rho, T_1, \mathrm{TR}, \theta)e^{-\frac{\mathrm{TE}}{T_2^*}}$$

Spin density (ρ) and T1

T2*



(Ogawa et al. 1992)

See also (Poser et al. 2006) for a discussion on how to exploit the TE dependence of the signal to improve image quality.

1.2.2 T2* depends on blood oxygenation

But what is the relation between T2* and brain activity?

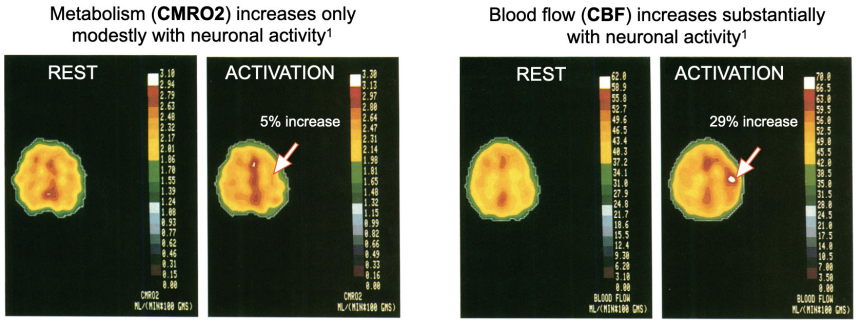
oxyhemoglobin diamagnetic

deoxyhemoglobin paramagnetic

> The presence of deoxyhemoglobin in a blood vessel causes a **susceptibility difference between the microvessel and the surrounding tissue** inducing microscopic magnetic field gradients that cause dephasing of the MR signal, leading to a reduction in the value of T2*.

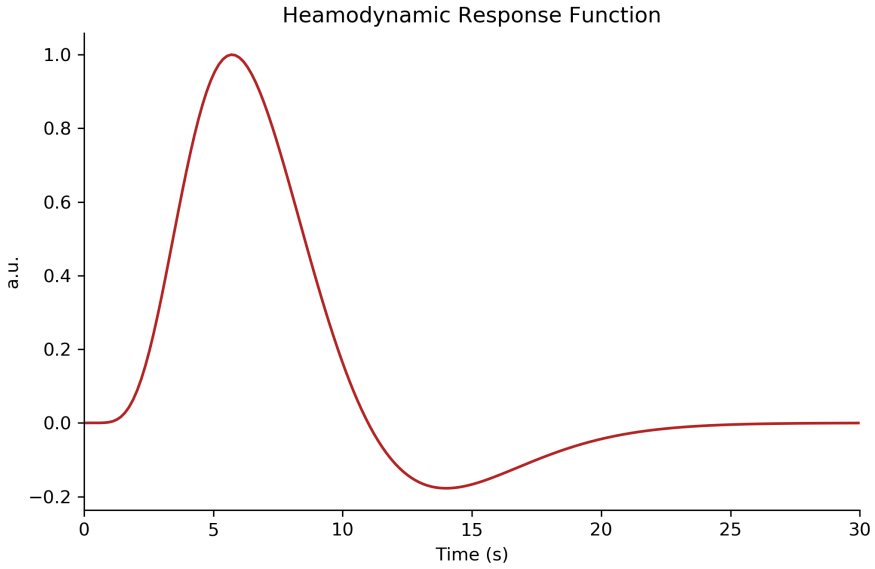
Recommended reading for those interested in MR physics: (Norris 2006)

1.2.3 And functional activity relates to blood via a mechanism called "Neurovascular Coupling"



PET study that demonstrated functional hyperemia: (Fox and Raichle 1986) Because the relative flow increase is larger than metabolism, we get a "washout" of deoxyhemoglobin, and T2* increases.

1.2.4 We simplify Neurovascular Coupling by assuming a Heamodynamic Response



Two main features of the response: delayed peak and undershoot.

An influencial work that led to the concept of a "Canonical Haemodynamic Response Function" (Glover 1999)

1.2.5 And we then fit a response model to our data

Here in this example we are trying to estimate the effect size of the response to two different events (one in green, the other in red). By fitting a model to each voxel in the image, we can use estimates and the residual errors to search for regions that are statistically significantly correlated with our task.

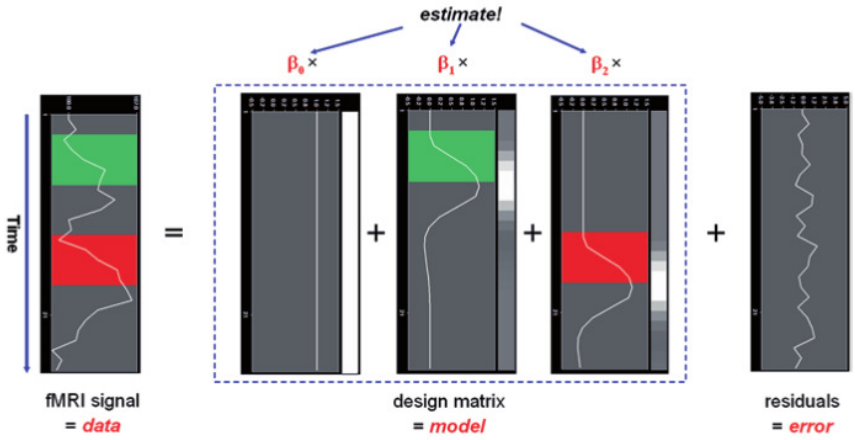
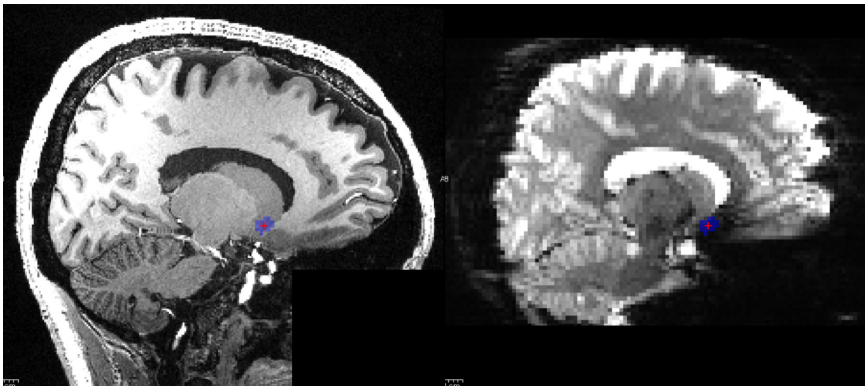


image credit: Rainer Goebel; brain voyager documentation.

1.3 Artefacts and confounds

1.3.1 Images have artefacts

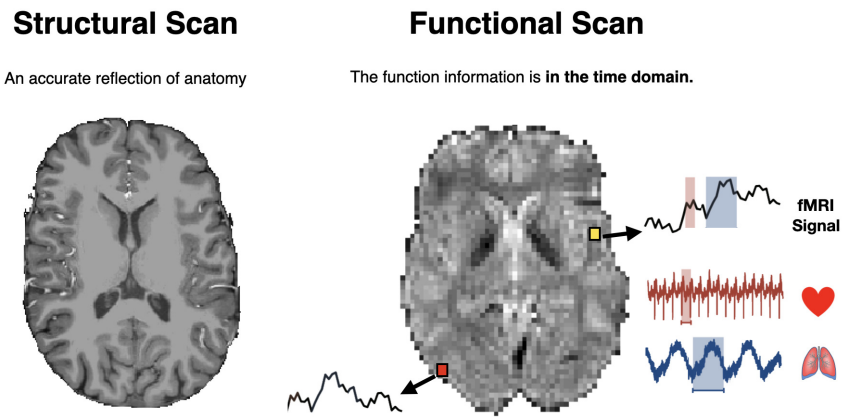
As in "artificial": fictious, not real.



Right: MPRAGE anatomical scan; Left: EPI functional scan

We see distortions, dropouts and some blurring. The echo-planar-imaging (EPI) sequence can acquire images in seconds, but we pay a price for all that speed.

1.3.2 And many other things change with time



The signals are influenced by respiration and cardiac pulsation, but also other factors.

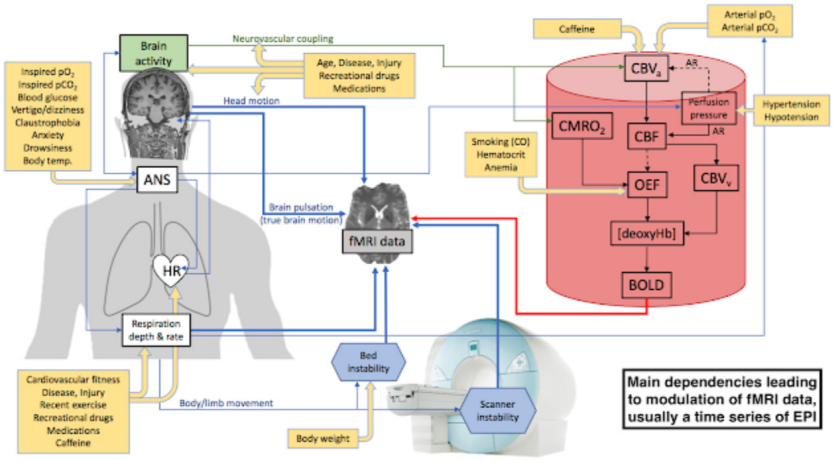
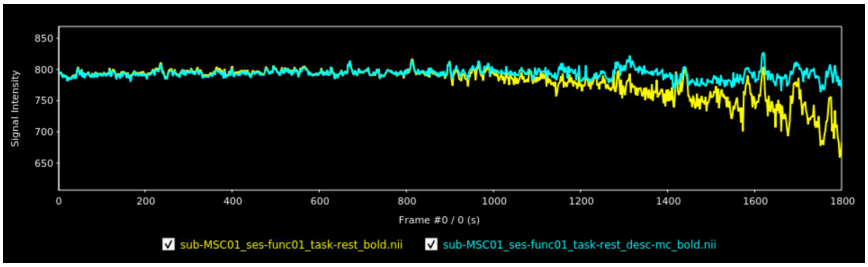


Image adapted from (Krainik et al. 2013), as seen in fMRI data modulators; practical fMRI blog.

1.3.3 Motion artefacts

- Introduces signal changes that are unrelated to BOLD



- Introduces spurious correlations amongst voxels

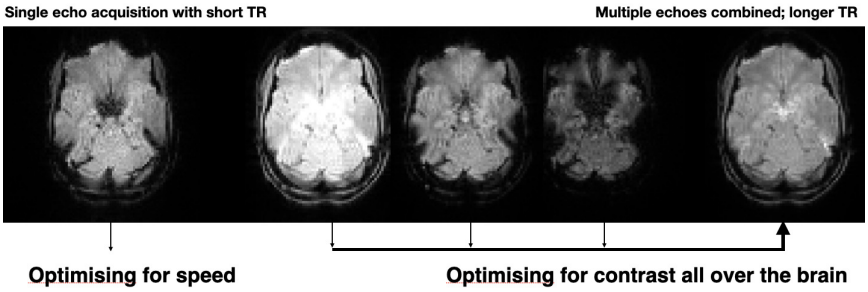
Motion correction cannot undo the damage of motion. Example of a correlation matrix between regions, before and after motion confound regression.

For generating such correlation matrices, see the python library nilearn.

1.4 The art of fMRI acquisition is compromising

1.4.1 We can optimise for different goals

We can optimise for speed, to help removing confounds. Or we could optimise for image quality, to reduce artefacts.



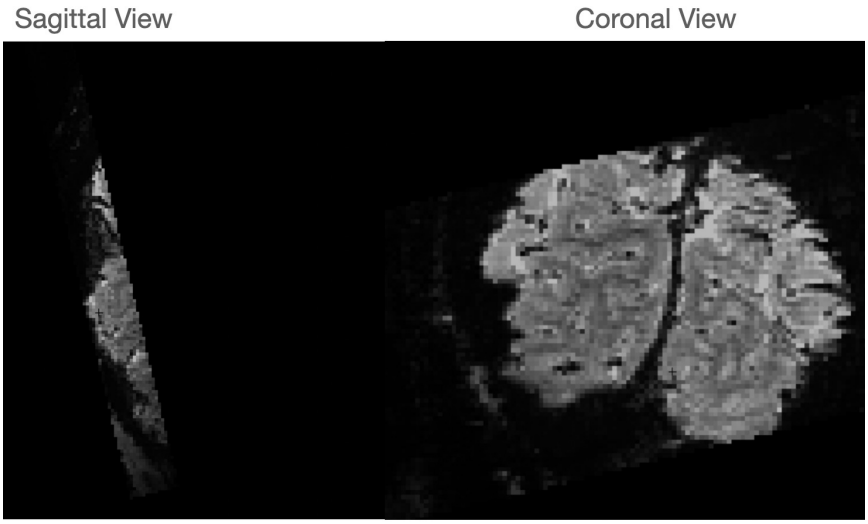
Both images have the same spatial resolution of 2.5mm isotropic, and are both sampling information as fast and efficiently as possible.

	Fast TR	Short TR
Repetition Time	584ms	1260ms
Number of Echoes	1	3
Echo Time	38ms	15,26,54ms
Length of time series	820	380

1.4.2 But how do we decide where to compromise?

Acquisition protocols are best tailored to the project at hand.

In our group we are optimising for high spatio-temporal resolution, to look at signal differences between large draining veins and the gray matter tissue.



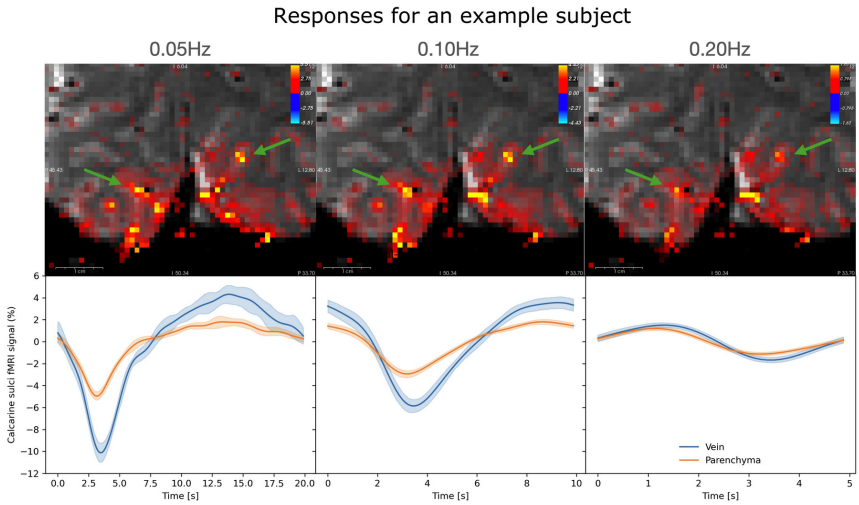
Resolution = 1 millimeter isotropic. TR= 874ms.

We compromise on brain coverage, only acquiring 18 slices over the visual cortex. This choice allows us to acquire data just fast enough to observe rapid dynamics, but brings challenges when analysing the data across runs and participants.

1.5 Task and rest fMRI - the two most common fMRI apps

1.5.1 Task fMRI measures responses to an external stimulus

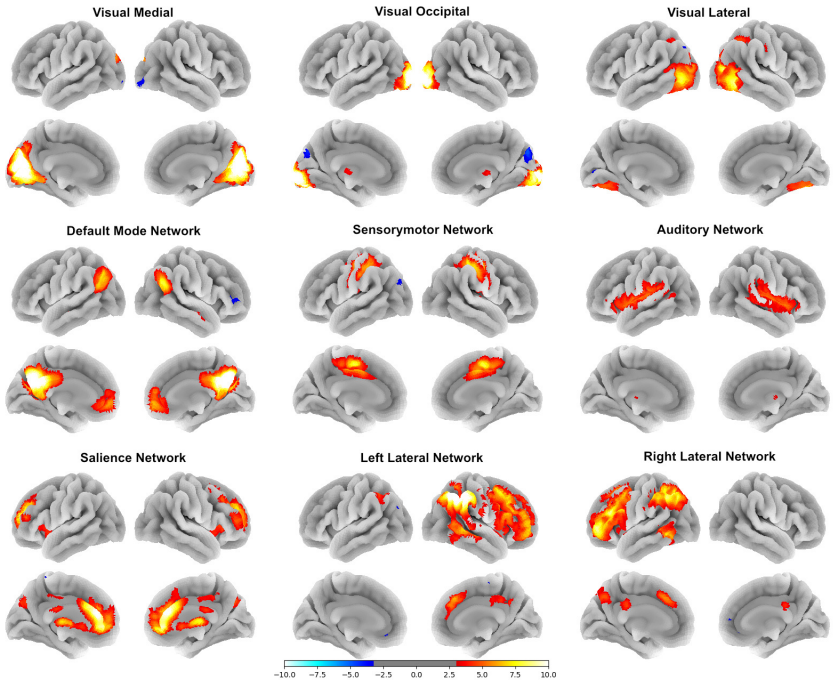
- (neuroscience) Does any particular region of the brain correlate with a given stimulus?
- (physiology) How precise and localized are blood oxygenation and flow changes happening in the brain?



Work that I've been doing with Dr. Laura Lewis and Dr. Jonathan Polimeni

1.5.2 Resting-state is used to investigate spontaneous activity

These maps can be obtained by clustering the voxel time-series. In the example below the clustering was done based on independent component analysis (ICA).



See (Smith et al. 2009) for an overview.
Example questions that resting-state can help investigate:

- Are there differences in the spontaneous activity of healthy controls and individuals diagnosed with depression?
- Does brain activity change during awake and sleep?

1.6 Where to find more information?

- Jingyuan and Saskia's Why and How Introduction to fMRI
- Why and How series also has talks on MR Physics (by Avery Berman)
- Huettel, Song & McCarthy's Functional MRI book
- NeuroImage 20 years of fMRI Special Edition
- Nilearn documentation contains hundreds of simple fMRI analysis examples.
- NeuroStars for questions about preprocessing and analysis

- Mumford Brain Stats - Jeanette Mumford answers questions on fMRI stats.
- The Martinos Community!

2 Interactive Session - Hands on fMRI

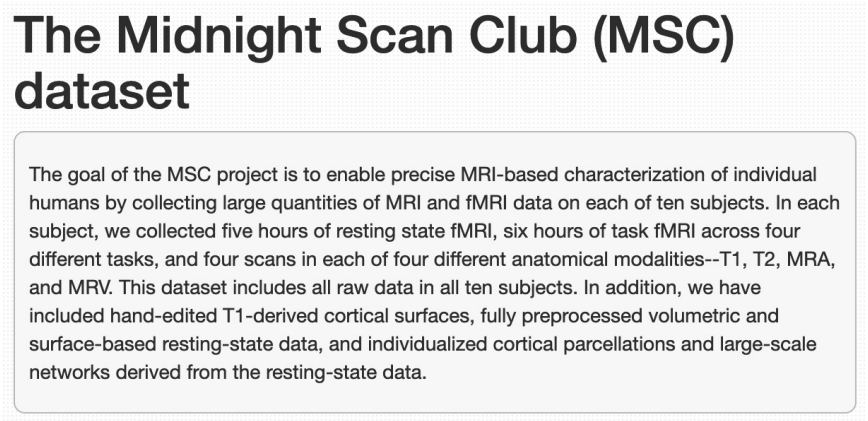
2.1 Good practices when piloting an fMRI experiment.

- Minimal preprocessing - motion correction and detrending
- ICA to search for "invisible" time-series artefacts

Look at publicly available qdata, so if anyone is curious, they can try the analysis themselves.

The Midnight Scan Club

`https://legacy.openfmri.org/dataset/ds000224/`



2.2 What does an fMRI dataset look like?

We'll first look at the data in a data viewer called `freeview`.

```
DATA1="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_bold.nii.gz"
freeview $DATA1 &
```

What do we see in space, and in time?

2.2.1 What happens to the signal if we motion correct the image?

To motion correct we can use a tool from FreeSurfer that wraps the AFNI motion correction, `mc-afni2`.

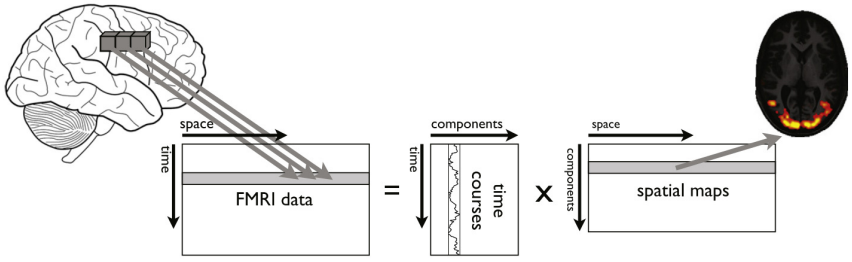
```
DATA_IN="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_bold.nii.gz"
DATA_OUT="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_desc-mc_bold.nii.gz
mc-afni2 --i $DATA_IN --o $DATA_OUT
```

And we can look at the input and output:

```
DATA_IN="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_bold.nii.gz"
DATA_OUT="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_desc-mc_bold.nii.gz
freeview $DATA_IN $DATA_OUT &
```

2.2.2 Exploratory analysis using FSL Melodic

Melodic is an excellent tool for quality control, since it allows us to look at spatio-temporal patterns in the data that are not readily visible with the naked eye.




```
Melodic &
```

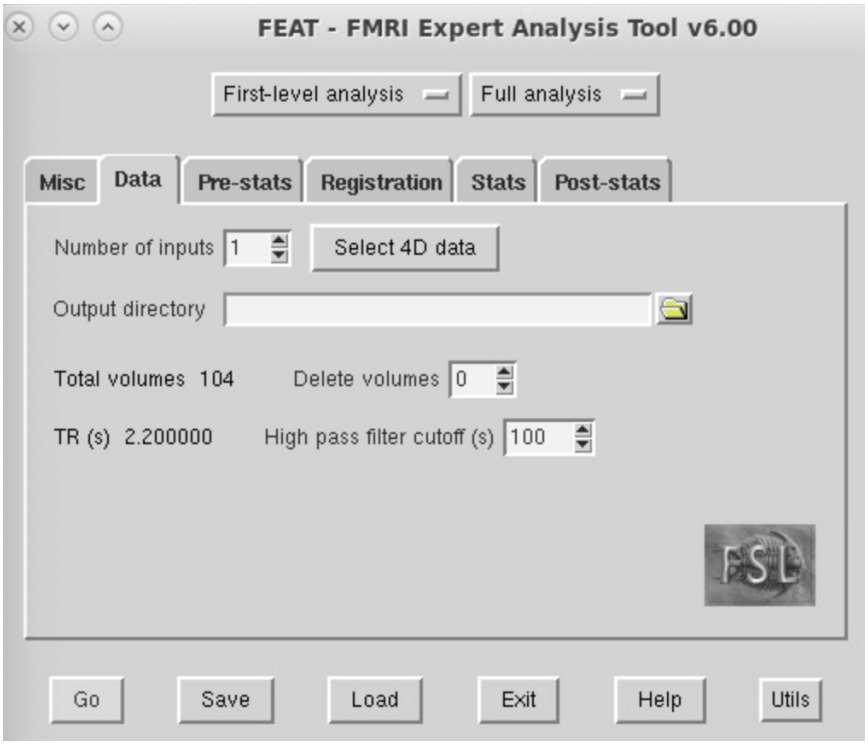
`https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/MELODIC`

2.2.3 Looking for activation with FSL FEAT

FEAT FMRI Expert Analysis Tool

`https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT`

Simple "black-box" tool that does both preprocessing and analysis of task fMRI datasets.



Can we find activation?

```
Feat &
```

2.3 What does a fMRI study look like?

Using as example the Midnight Scan Club open dataset.

```
gio open midnight-scan-club &
```

2.4 Considerations of multi-session scanning

Here we look at two datasets of the same task, but acquired in different sessions

```
SES1="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_bold.nii.gz"
SES2="sub-MSC01/ses-func02/func/sub-MSC01_ses-func02_task-rest_bold.nii.gz"
freeview $SES1 $SES2 &
```

Some points that we immediately notice is that **the artefacts are run-dependent.** Even if we were to put both images into space, they will never exactly align with each other. The question is: is this big enough a problem, or can we live with it?

2.5 Considerations of multi-participant scanning

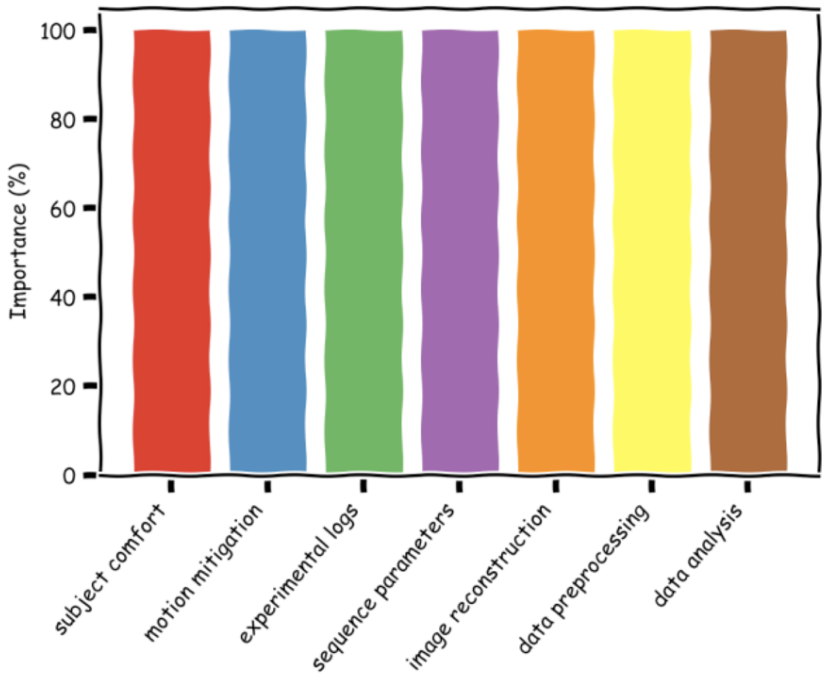
- Brains are different: size, shape and topography

```
SUB1="sub-MSC01/ses-func01/func/sub-MSC01_ses-func01_task-rest_bold.nii.gz"
SUB2="sub-MSC02/ses-func01/func/sub-MSC02_ses-func01_task-rest_bold.nii.gz"
freeview $SUB1 $SUB2 &
```

Here we can make a decision whether to normalize all brains into a common space, or whether we extract features from each subject and then compare the features at the group level.

3 Conclusion

- Functional information is encoded in time
- Image acquisition is a balancing act
- Always important to look at the data for artefacts
- Fixing problems in the acquisition is better than in analysis



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