The Art and Pitfalls of fMRI Preprocessing

FSL Pre-Processing Pipeline

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FSL Pre-Processing Pipeline

Standard pre-processing:

- Task fMRI
- Resting-state fMRI

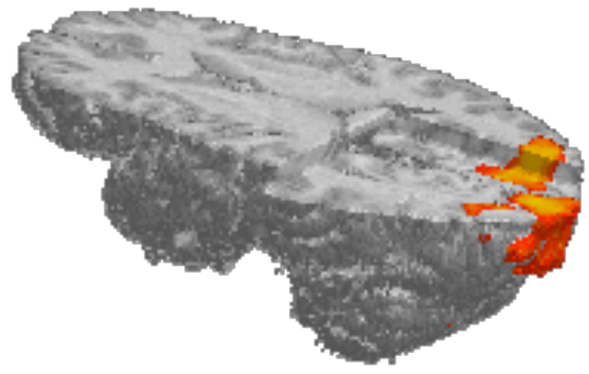
Quality Assessment

Alternatives

- Other pre-processing options
- GLM-based or ICA-based "pre-processing"

Complications

- Spatial and temporal interactions
- HRF variation



HCP Pipeline

FSL Pre-Processing Pipeline

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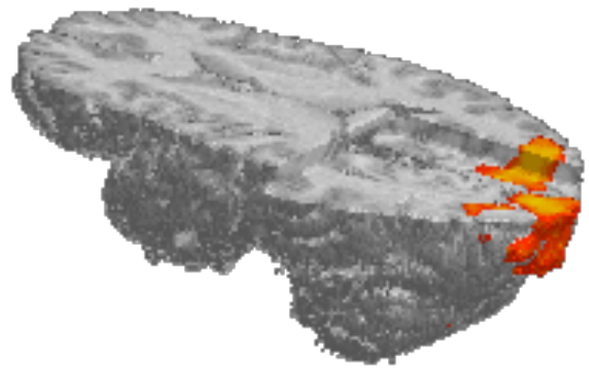
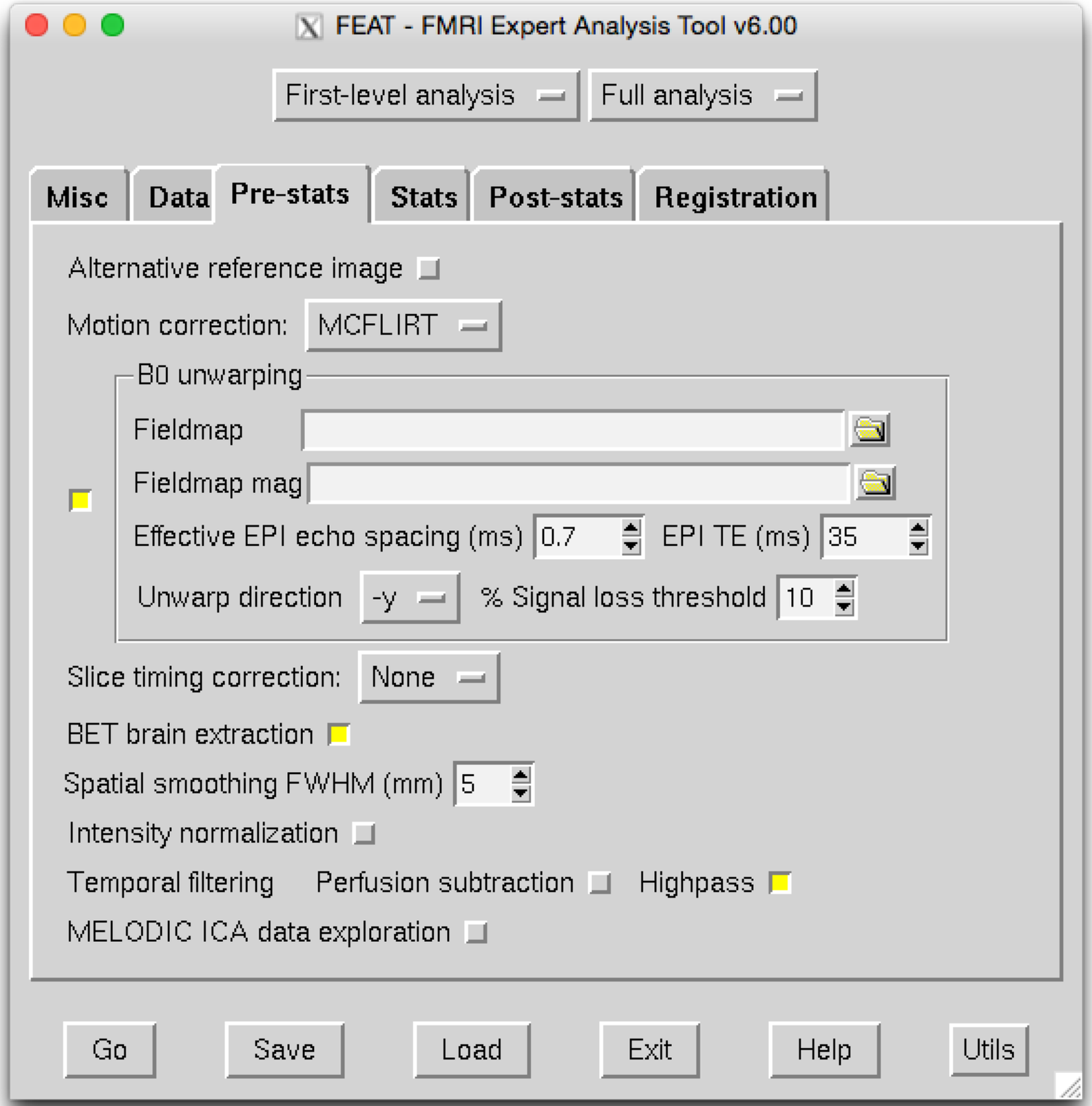
HCP Pipeline



Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)



Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

Motion Correction

Distortion Correction

Spatial Smoothing

Temporal Filtering

GLM

Resampling to Standard Space

Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

- 6 DOF
- Whole-volume
- Normalised correlation
- First volume is reference (or can select other)

Motion Correction

Distortion Correction

Spatial Smoothing

Temporal Filtering

GLM

Resampling to Standard Space

Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

- Requires fieldmaps
- Uses BBR
- Makes a substantial difference to group-level results even in non-distorted areas

Motion Correction

Distortion Correction

Spatial Smoothing

Temporal Filtering

GLM

Resampling to Standard Space

Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

- De-weights different tissues (esp. CSF)
- SUSAN algorithm
- Very similar to Gaussian within GM & WM
- Recommend small FWHM

Motion Correction

Distortion Correction

Spatial Smoothing

Temporal Filtering

GLM

Resampling to Standard Space

Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

- Highpass only
- Tool for calculating cutoff based on design matrix

Motion Correction

Distortion Correction

Spatial Smoothing

Temporal Filtering

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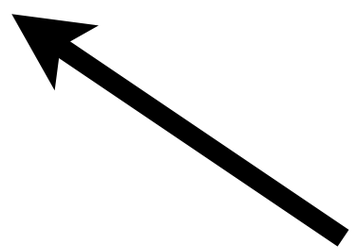
Resampling to Standard Space

Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

- Slice-timing effects modelled with temporal derivatives
- Related to basis functions and HRF variability *(see later)*



Motion Correction

Distortion Correction

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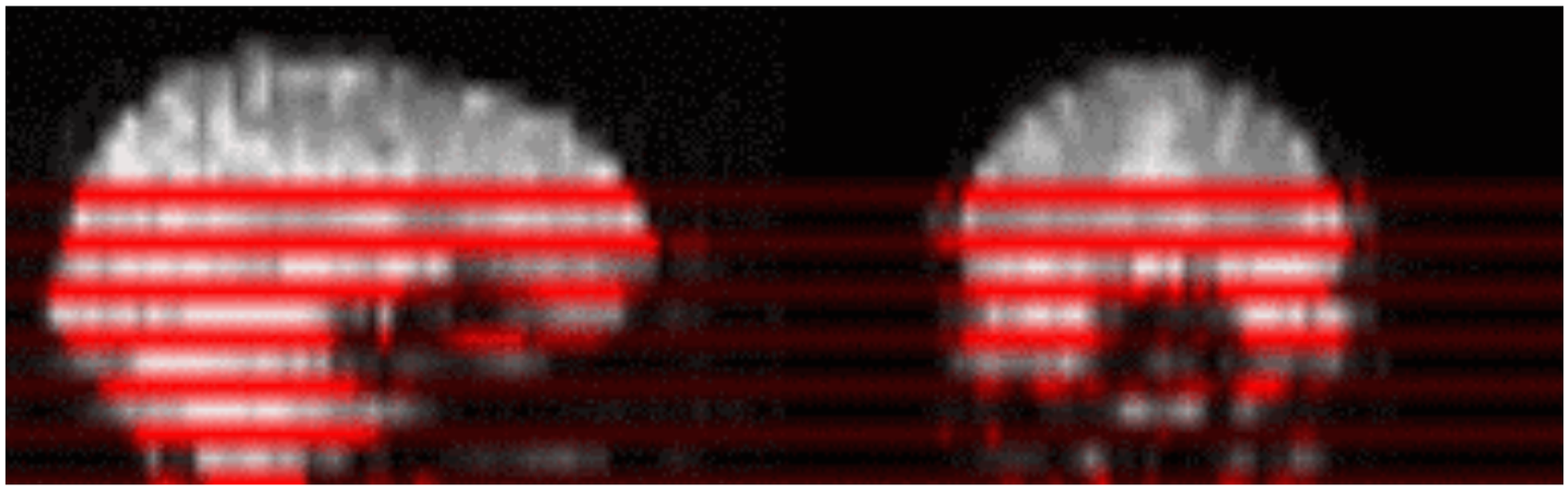
Temporal Filtering

GLM

Resampling to Standard Space

Slice Timing



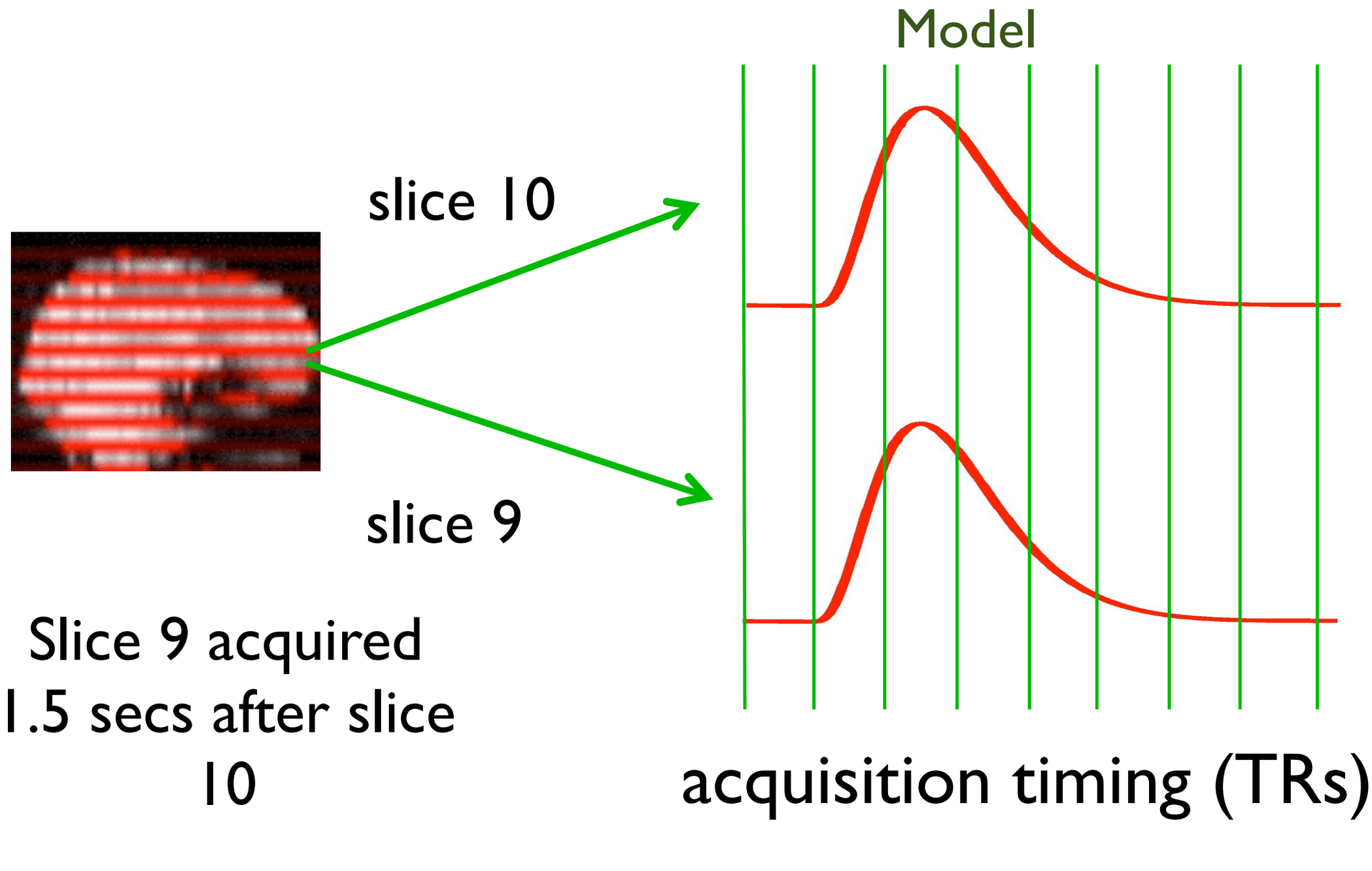
Almost all FMRI scanning takes each slice separately

Each slice is scanned at a slightly different time

Slice order can be interleaved (as shown) or sequential (up or down)

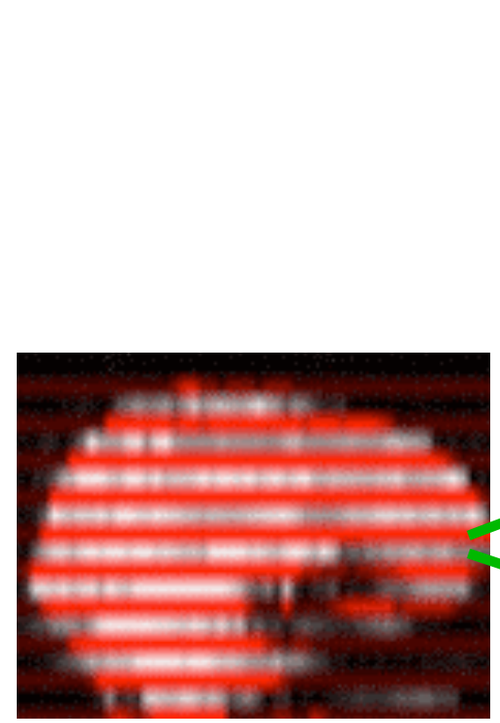
Slice Timing

Without any adjustment, the model timing is always the same



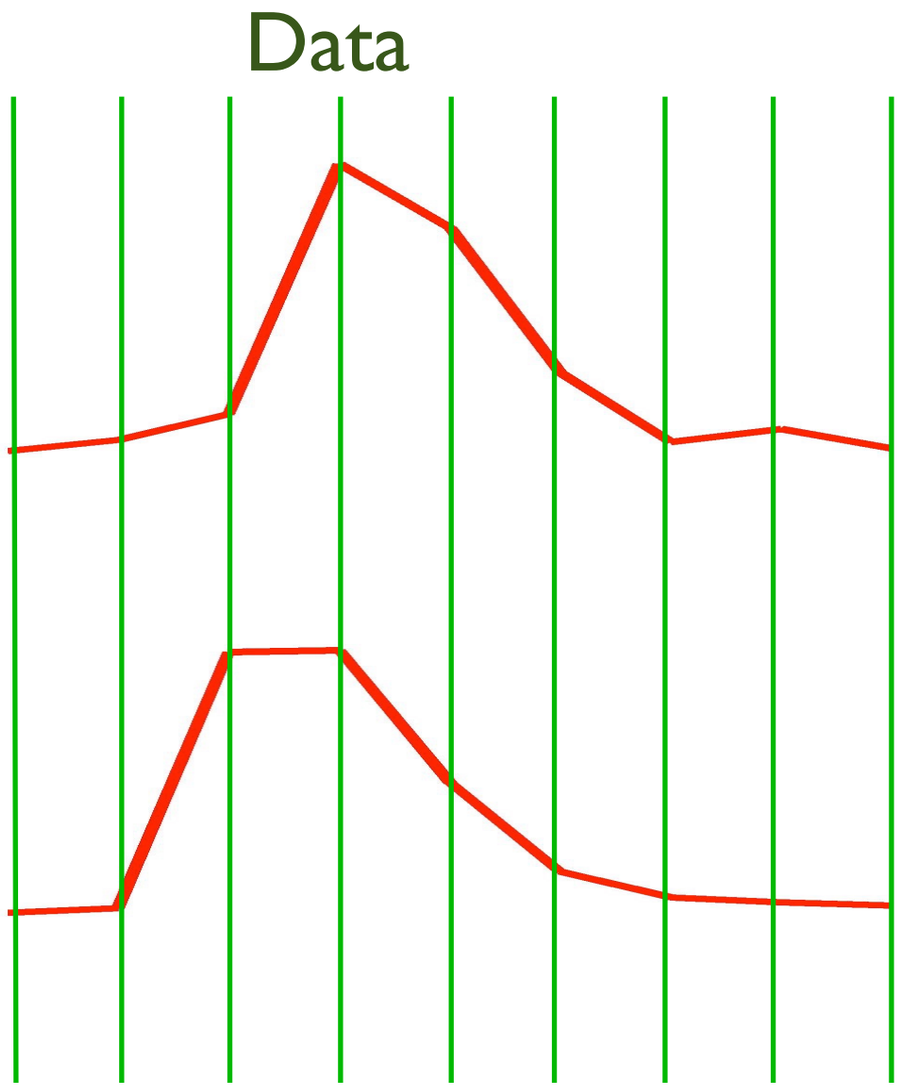
Slice Timing

... but the timing of each slice's data is *different*



slice 10

slice 9

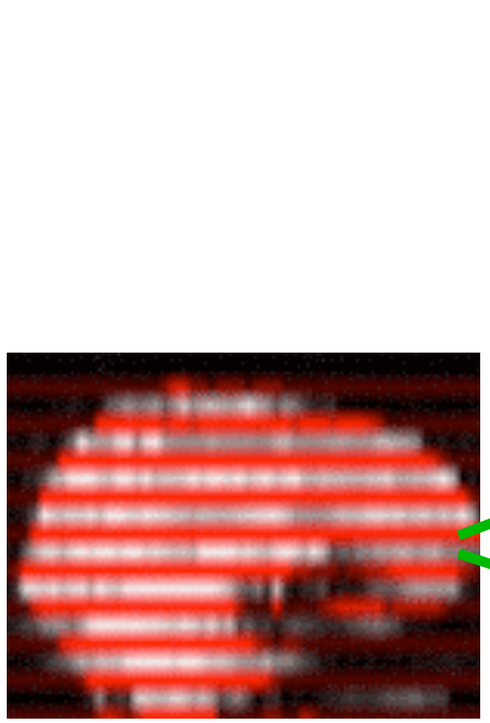


Slice 9 acquired 1.5 secs after slice 10

acquisition timing (TRs)

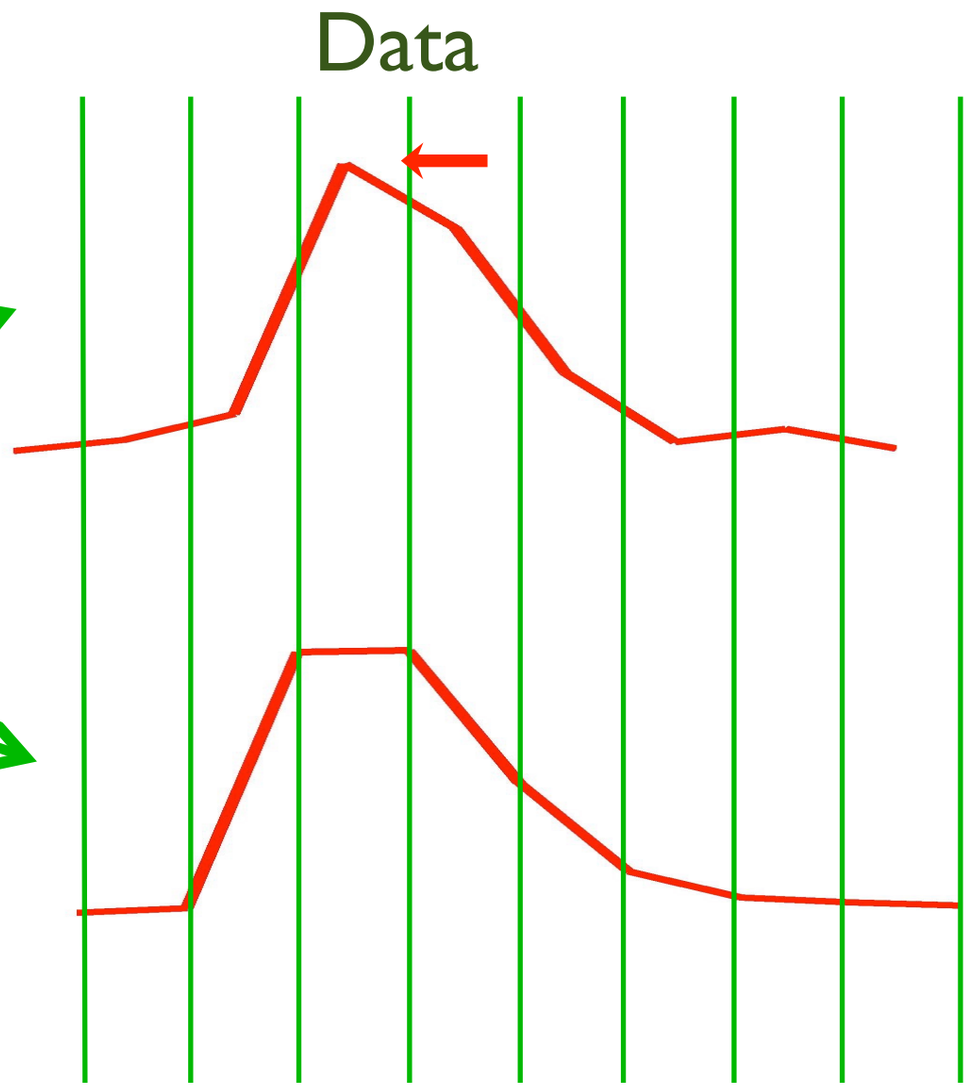
Slice Timing

Can get consistency by shifting the *data*



slice 10

slice 9



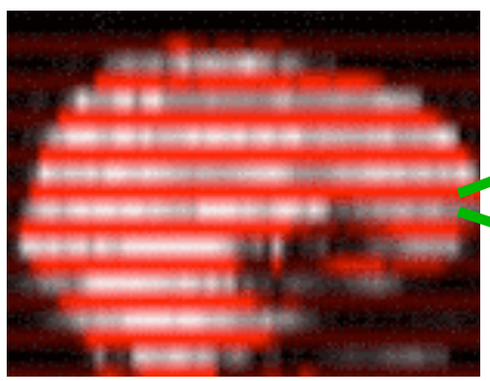
Slice 9 acquired 1.5 secs after slice 10

acquisition timing (TRs)

Slice Timing

... and then interpolating the data =

slice timing correction



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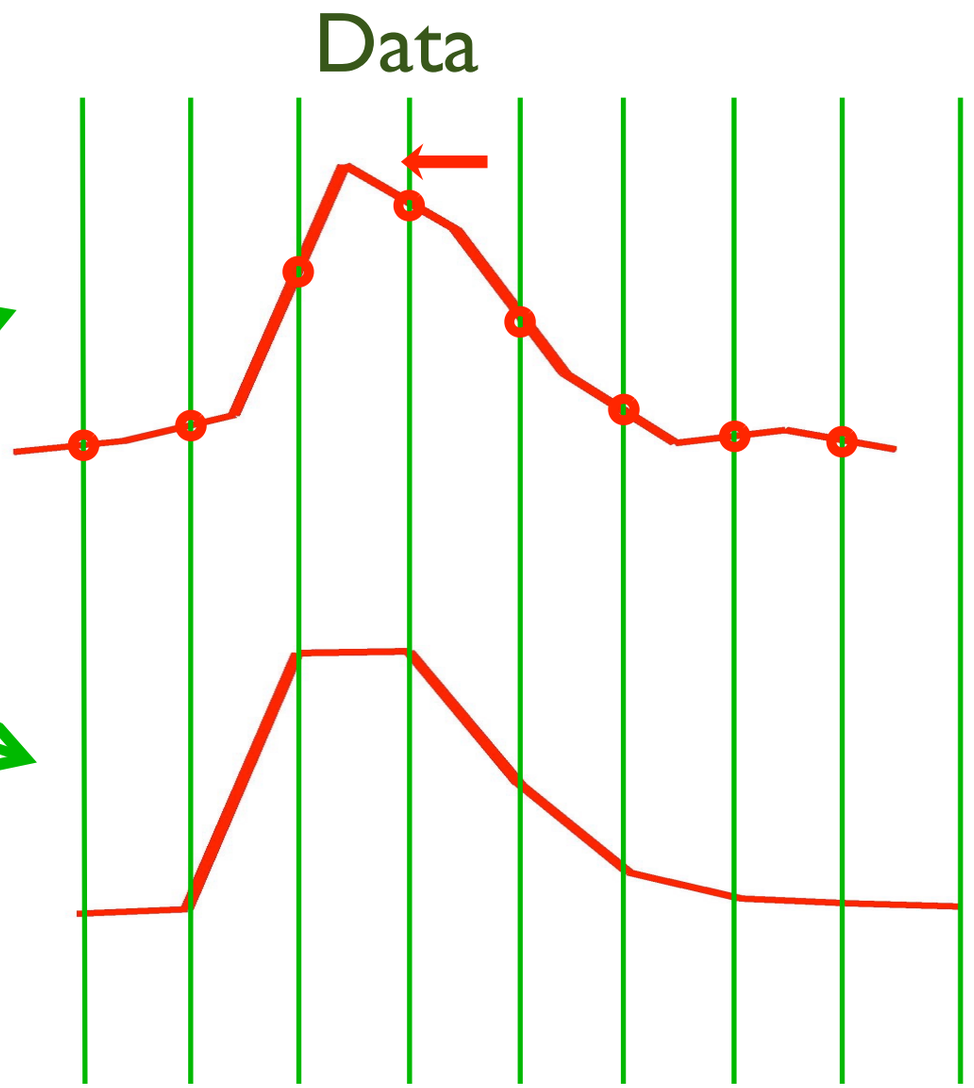
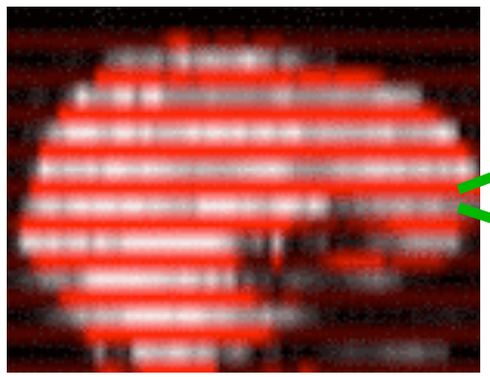


Slice Timing

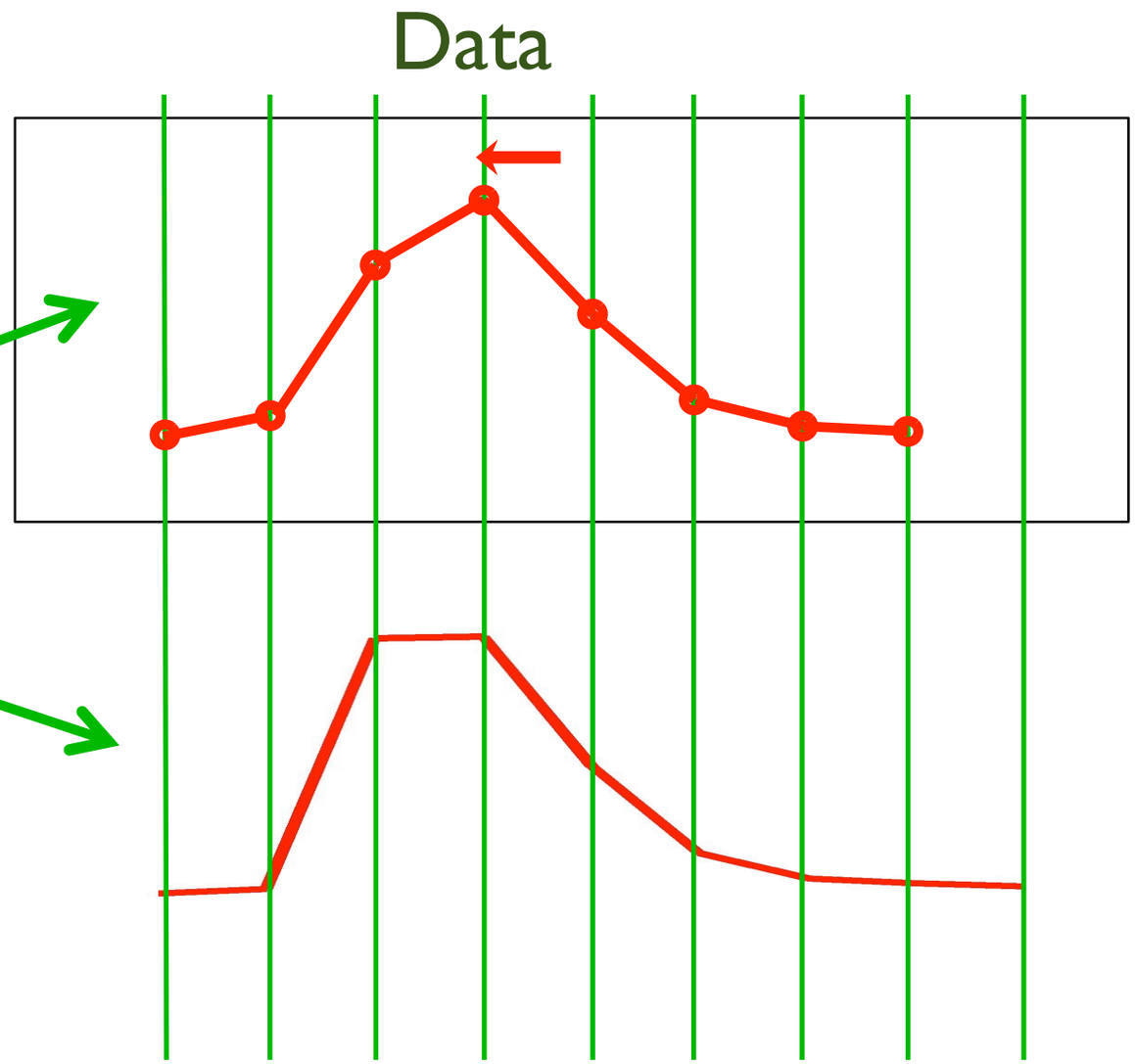
... and then interpolating the data =

slice timing correction



slice 10

slice 9

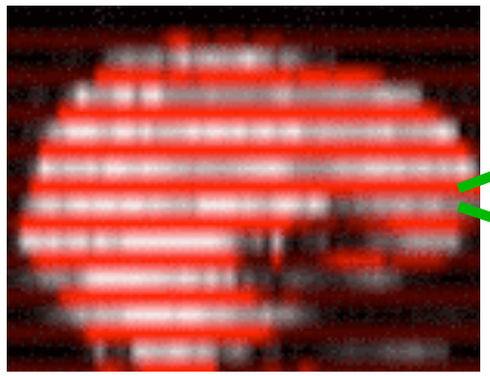


Slice 9 acquired 1.5 secs after slice 10

Slice Timing

... and then interpolating the data =

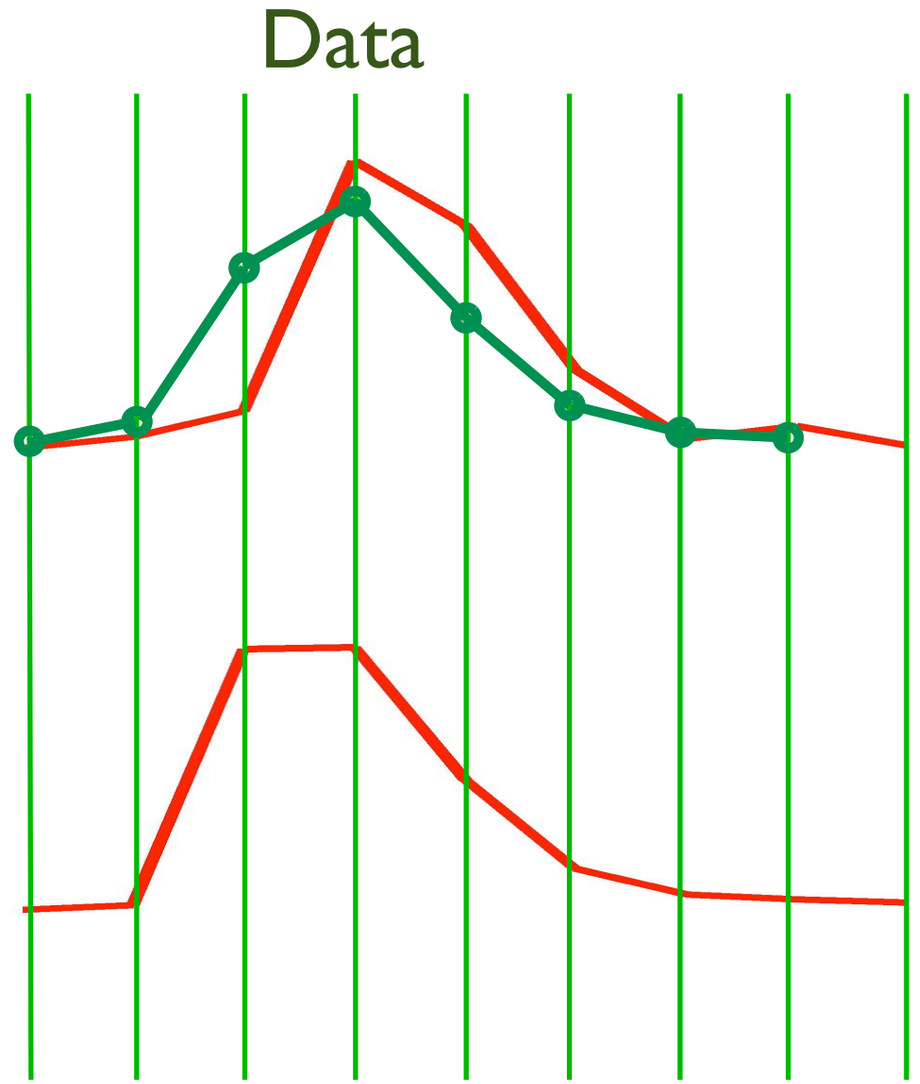
slice timing correction



slice 10

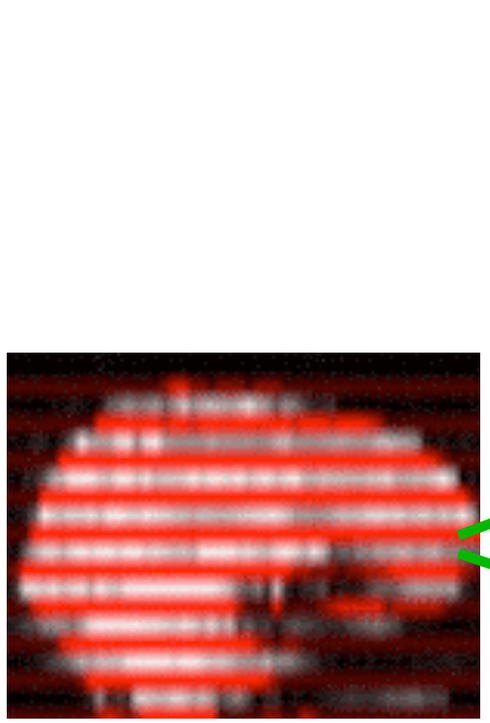
slice 9

Slice 9 acquired 1.5 secs after slice 10



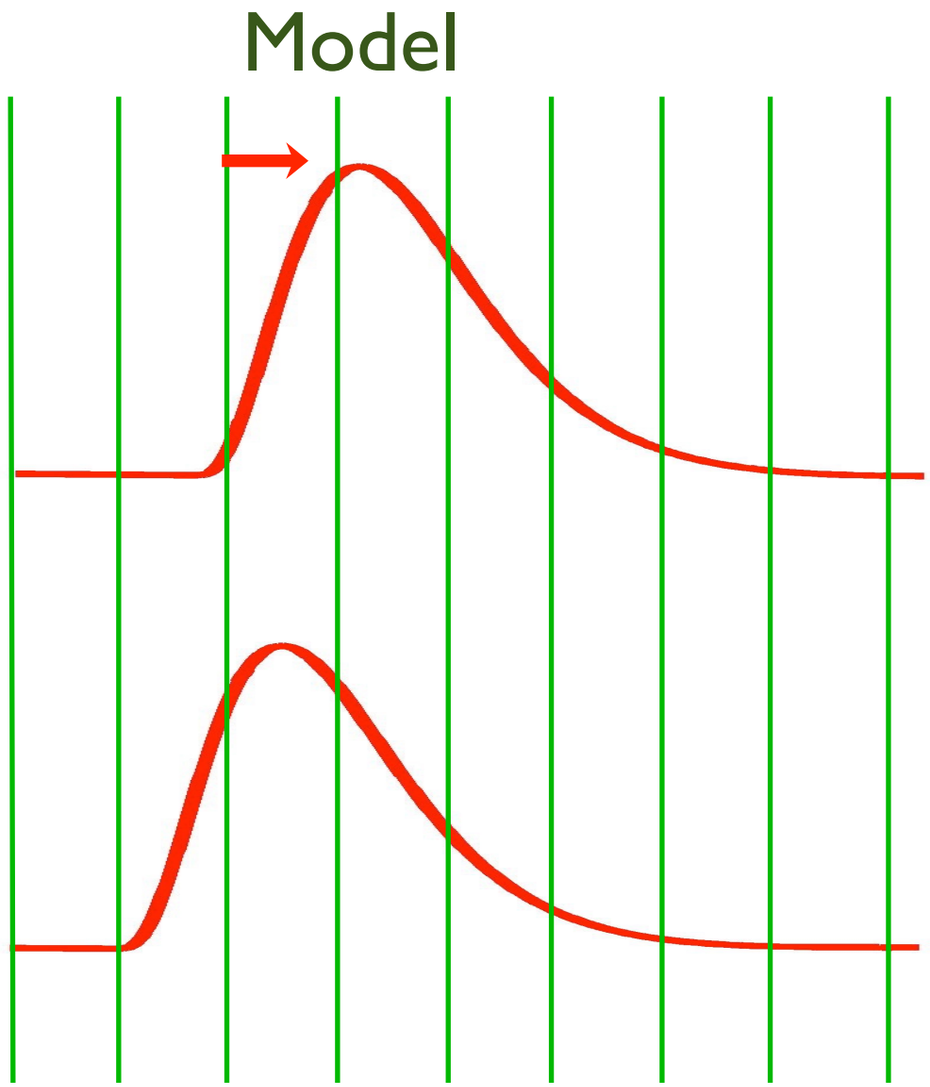
Slice Timing

Alternatively, can get consistency by shifting the *model*



slice 10

slice 9



Slice 9 acquired 1.5 secs after slice 10

acquisition timing (TRs)

Slice Timing

One way to shift the model is to use the *temporal derivative in the GLM*

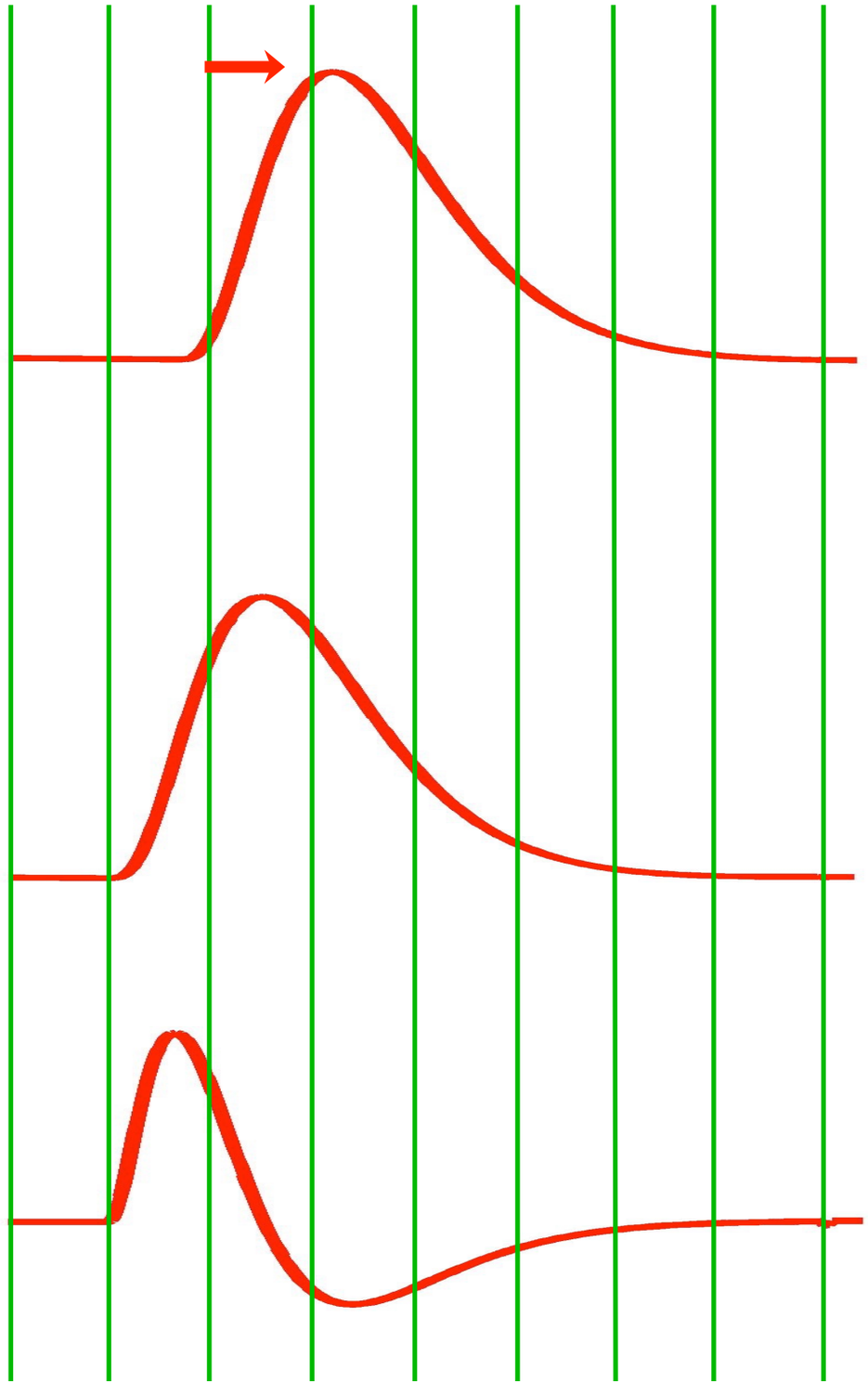
Shifted Model

=

Original Model

-

Temporal Derivative



Based on Taylor approx:

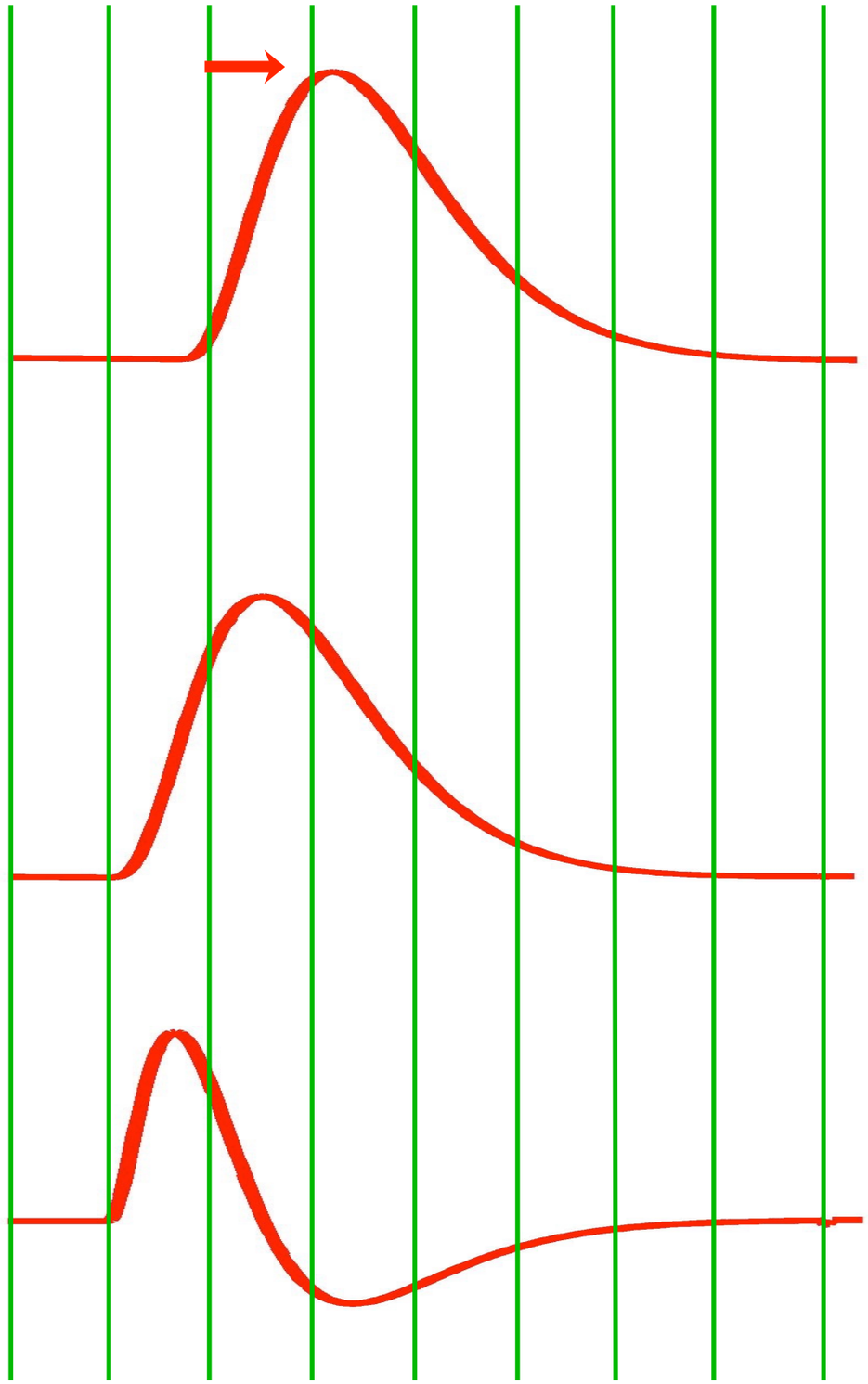
$m(t+a) = m(t) + a.m'(t)$

Slice Timing

Shifting the model can also account for variations in the HRF delay

- as the HRF is known to vary between subjects, sessions, etc.

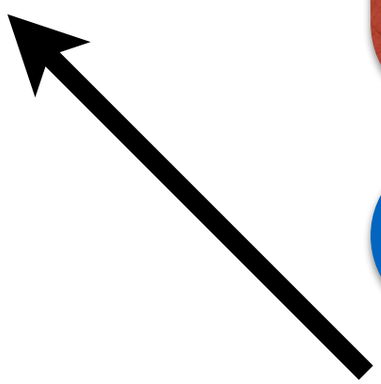
This is an alternative to slice timing correction



Standard Pre-Processing Pipeline

Task-fMRI
(GLM-based)

- Done just before higher-level analysis
- Non-linear registration to MNI152 by default



Motion Correction

Distortion Correction

Spatial Smoothing

Temporal Filtering

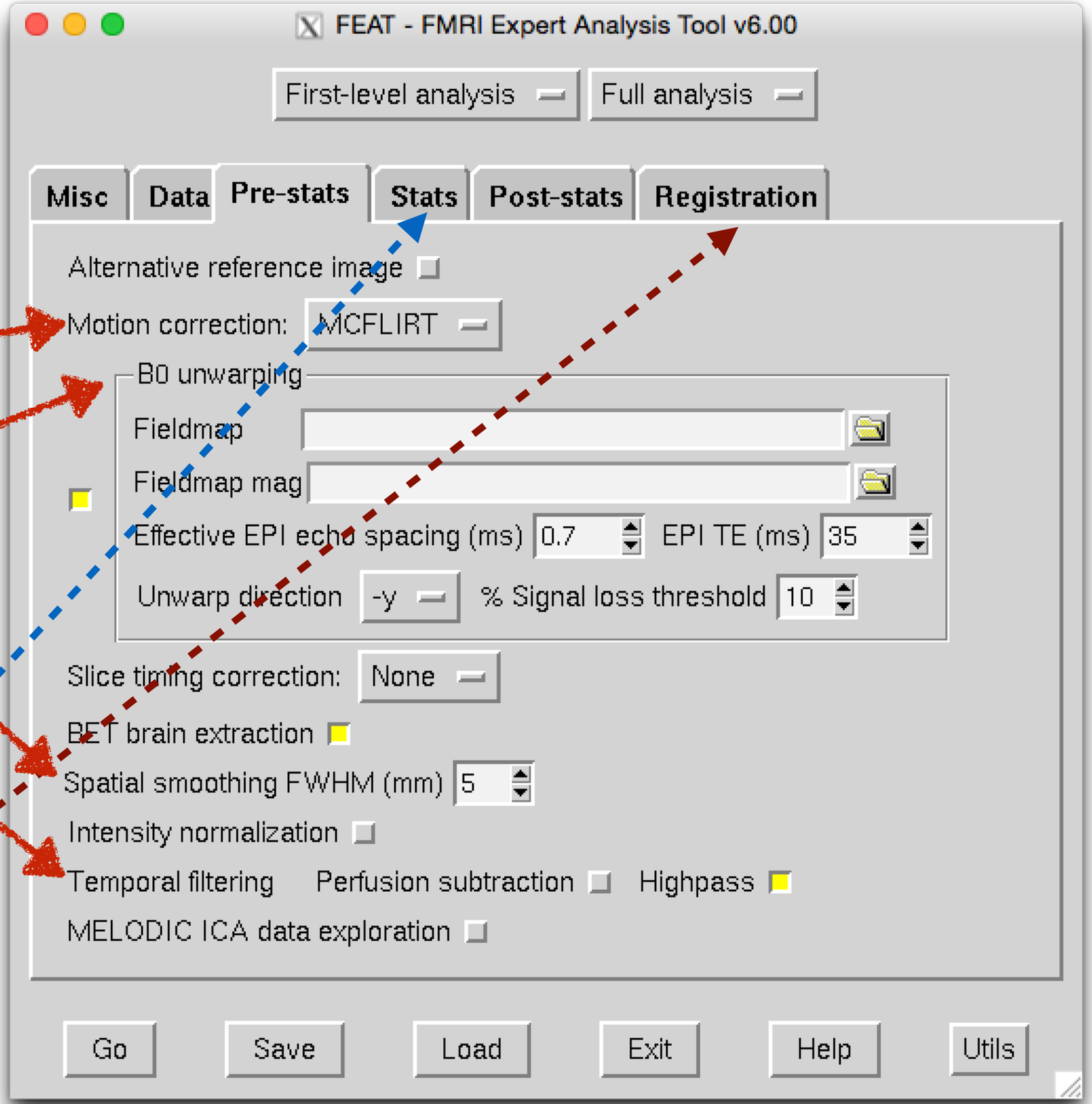
GLM

Resampling to Standard Space

Standard Pre-Processing Pipeline

Task-fMRI *(GLM-based)*

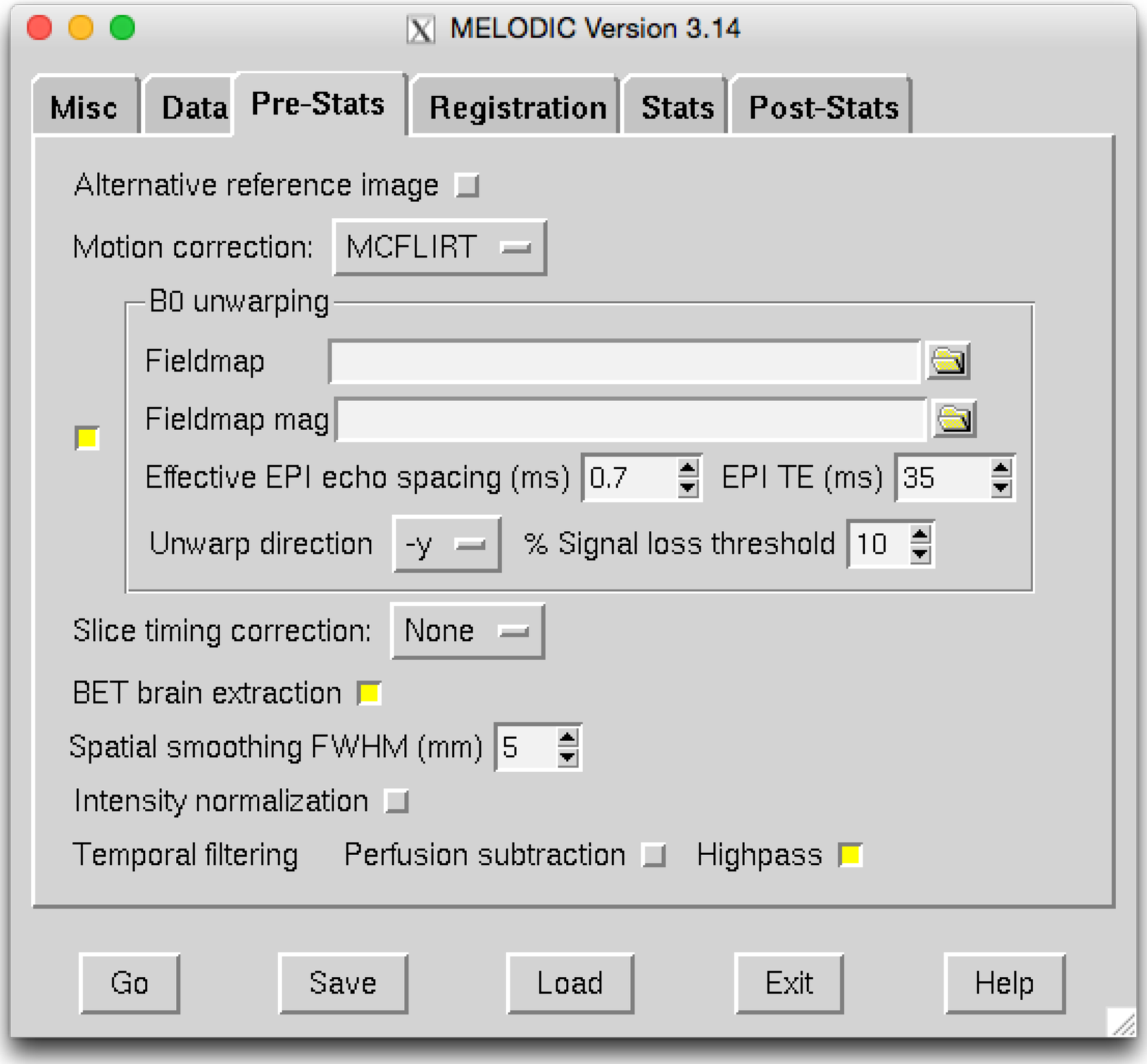
- Motion Correction
- Distortion Correction
- Spatial Smoothing
- Temporal Filtering
- **GLM**
- Resampling to Standard Space



Standard Pre-Processing Pipeline

Resting-State fMRI

(ICA-based)



Standard Pre-Processing Pipeline

Resting-State fMRI
(ICA-based)

- Motion Correction
- Distortion Correction
- Temporal Filtering
- Spatial Smoothing
- ICA-Cleanup
- Resampling to Standard Space
- Group ICA

Standard Pre-Processing Pipeline

Resting-State fMRI
(ICA-based)

- Highpass only
- Cutoff around 100-200 sec = 0.005-0.01 Hz
- There is still some useful power in high frequencies, so these are kept

Motion Correction

Distortion Correction

Temporal Filtering

Spatial Smoothing

ICA-Cleanup

Resampling to Standard Space

Group ICA

Standard Pre-Processing Pipeline

Resting-State fMRI *(ICA-based)*

- Minimal amount recommended
- On high quality data can avoid smoothing completely

Motion Correction

Distortion Correction

Temporal Filtering

Spatial Smoothing

ICA-Cleanup

Resampling to Standard Space

Group ICA

Standard Pre-Processing Pipeline

Resting-State fMRI *(ICA-based)*

- Individual subject ICA used to split data into noise and signal components
- Automatic and manual classification options *(see later)*
- Aggressive or soft cleanup options

Motion Correction

Distortion Correction

Temporal Filtering

Spatial Smoothing

ICA-Cleanup

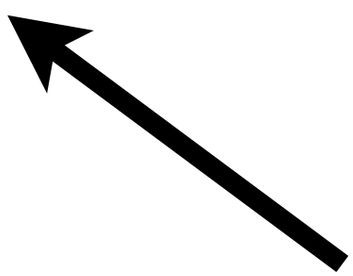
Resampling to Standard Space

Group ICA

Standard Pre-Processing Pipeline

Resting-State fMRI *(ICA-based)*

- Done before group analysis
- Non-linear registration to MNI152 by default
- Resampled in lower-res (e.g. 4mm)



Motion Correction

Distortion Correction

Temporal Filtering

Spatial Smoothing

ICA-Cleanup

Resampling to Standard Space

Group ICA

Standard Pre-Processing Pipeline

Resting-State fMRI
(ICA-based)

Note:
- in FSL slice-timing-correction usually skipped as low frequency signals drive correlations

- Motion Correction
- Distortion Correction
- Temporal Filtering
- Spatial Smoothing
- ICA-Cleanup
- Resampling to Standard Space
- Group ICA

FSL Pre-Processing Pipeline

Standard pre-processing:

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Quality Assessment

Alternatives

- Other pre-processing options
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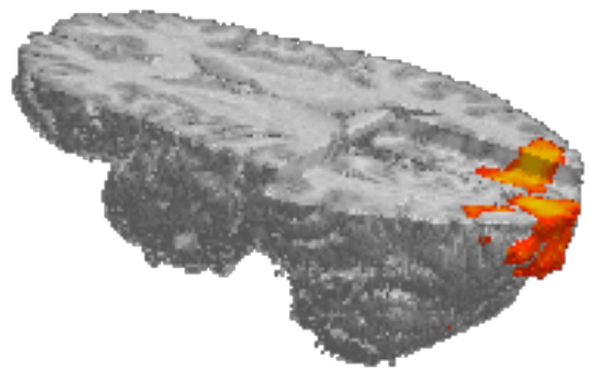
Complications

- Spatial and temporal interactions
- HRF variation

HCP Pipeline



Web Page Output

FEAT Report

/Users/mark/presentations/Graduate/MT08/Analysis/fmri.feat
Finished at Fri 16 Oct 2009 10:14:45 BST

Pre-stats - Stats - Post-stats - Registration - Log

Pre-stats

Analysis methods

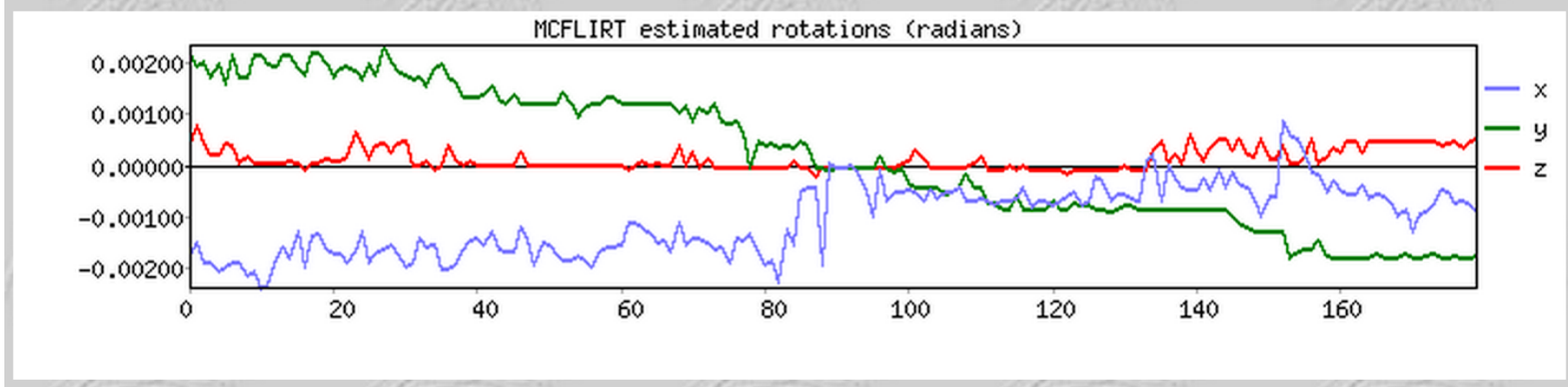
FMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.98, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied; motion correction using MCFLIRT [Jenkinson 2002]; non-brain removal using BET [Smith 2002]; spatial smoothing using a Gaussian kernel of FWHM 5mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma=90.0s).

References

[Jenkinson 2002] M. Jenkinson and P. Bannister and M. Brady and S. Smith. Improved optimisation for the robust and accurate linear registration and motion correction of brain images. NeuroImage 17:2(825-841) 2002.
[Smith 2002] S. Smith. Fast Robust Automated Brain Extraction. Human Brain Mapping 17:3(143-155) 2002.

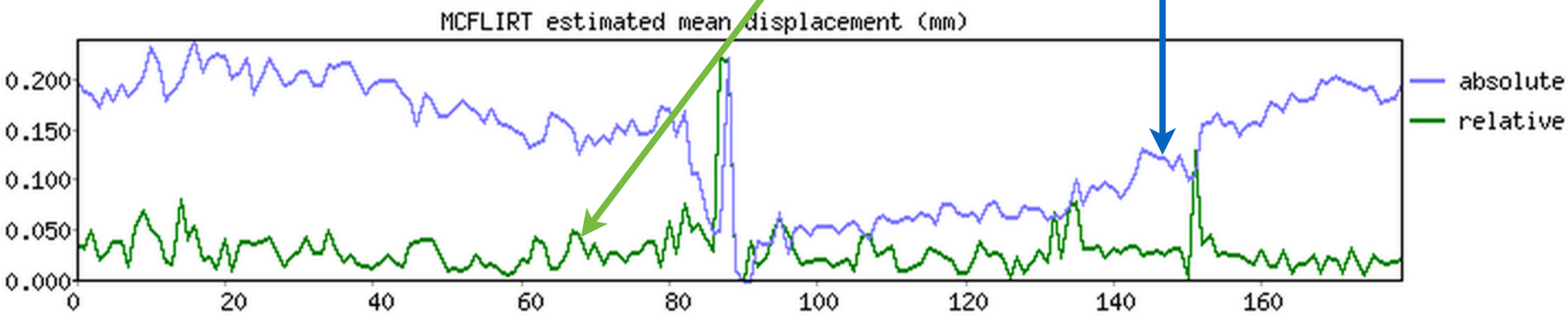
MCFLIRT Motion correction

Mean displacements: absolute=0.13mm, relative=0.03mm



Web Page Output: Motion

Summary of total motion (relative and absolute)

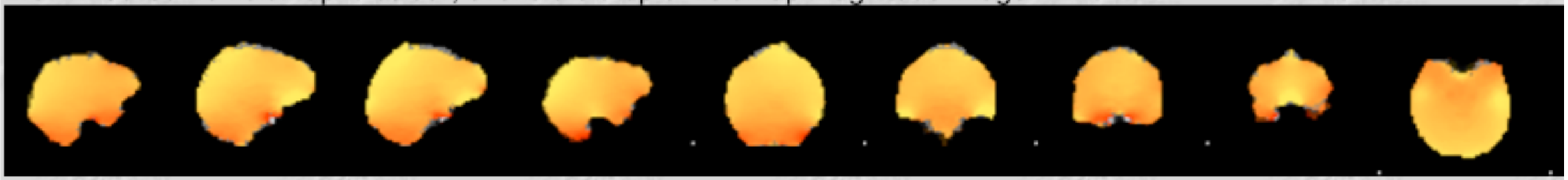


Relative = time point to next time point - shows jumps
Absolute = time point to reference - shows jumps & drifts

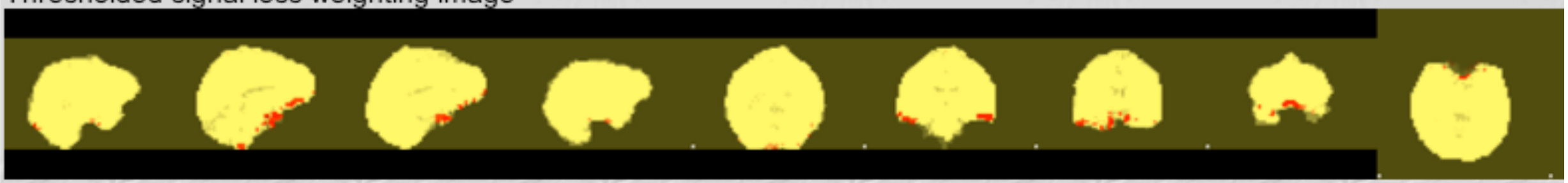
Note that large jumps are more serious than slower drifts, especially in the relative motion plot

Web Page Output: Distortion

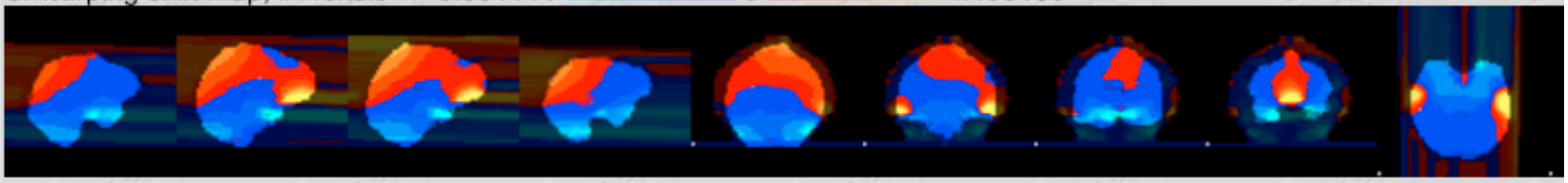
Brain-masked B0 fieldmap in colour, overlaid on top of fieldmap magnitude image



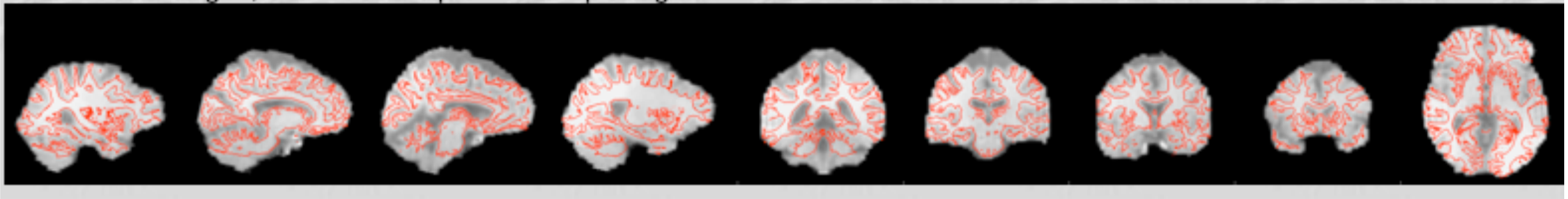
Thresholded signal loss weighting image



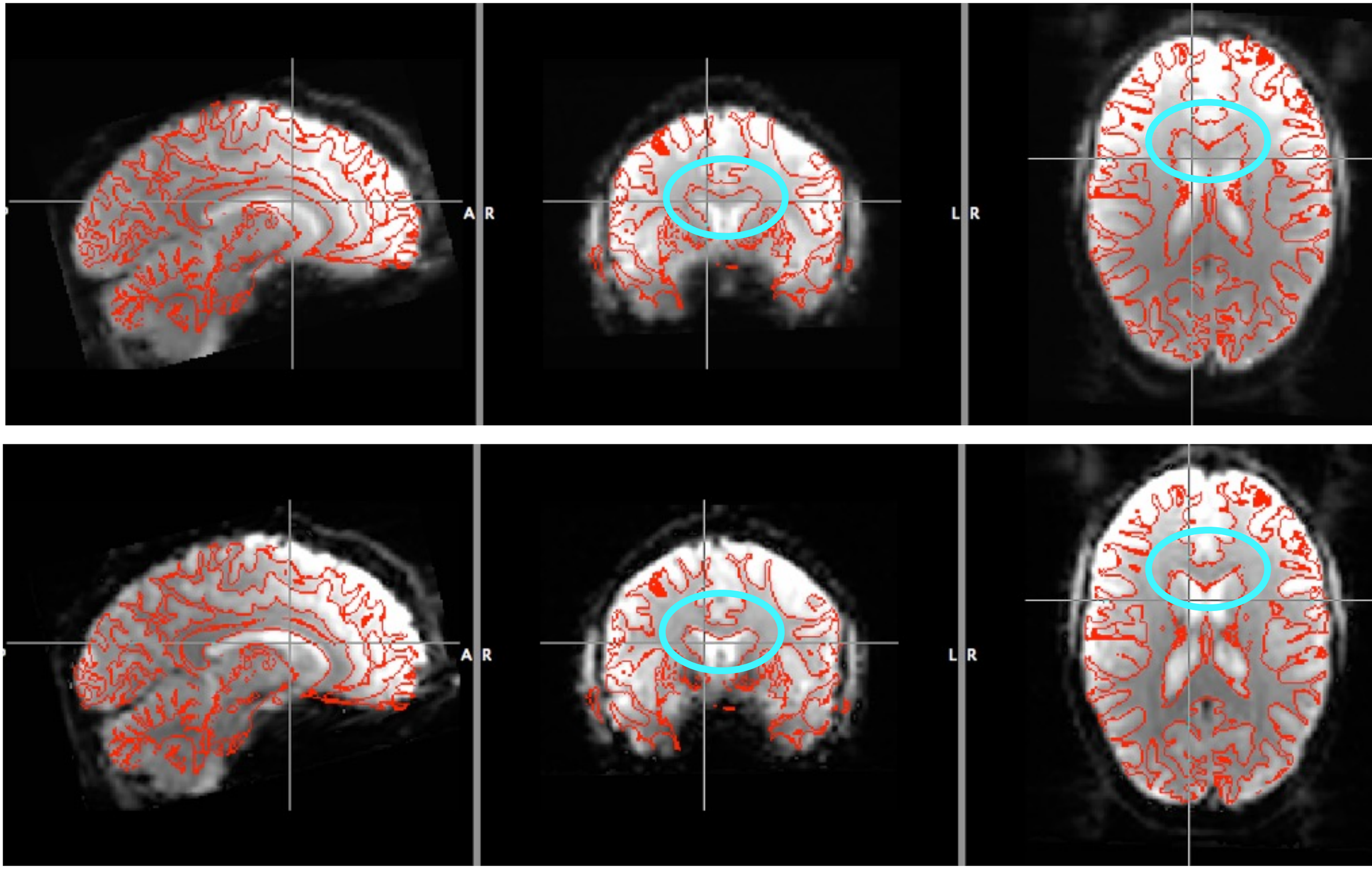
Unwarping shift map, in voxels -3.661111 0 4.190160



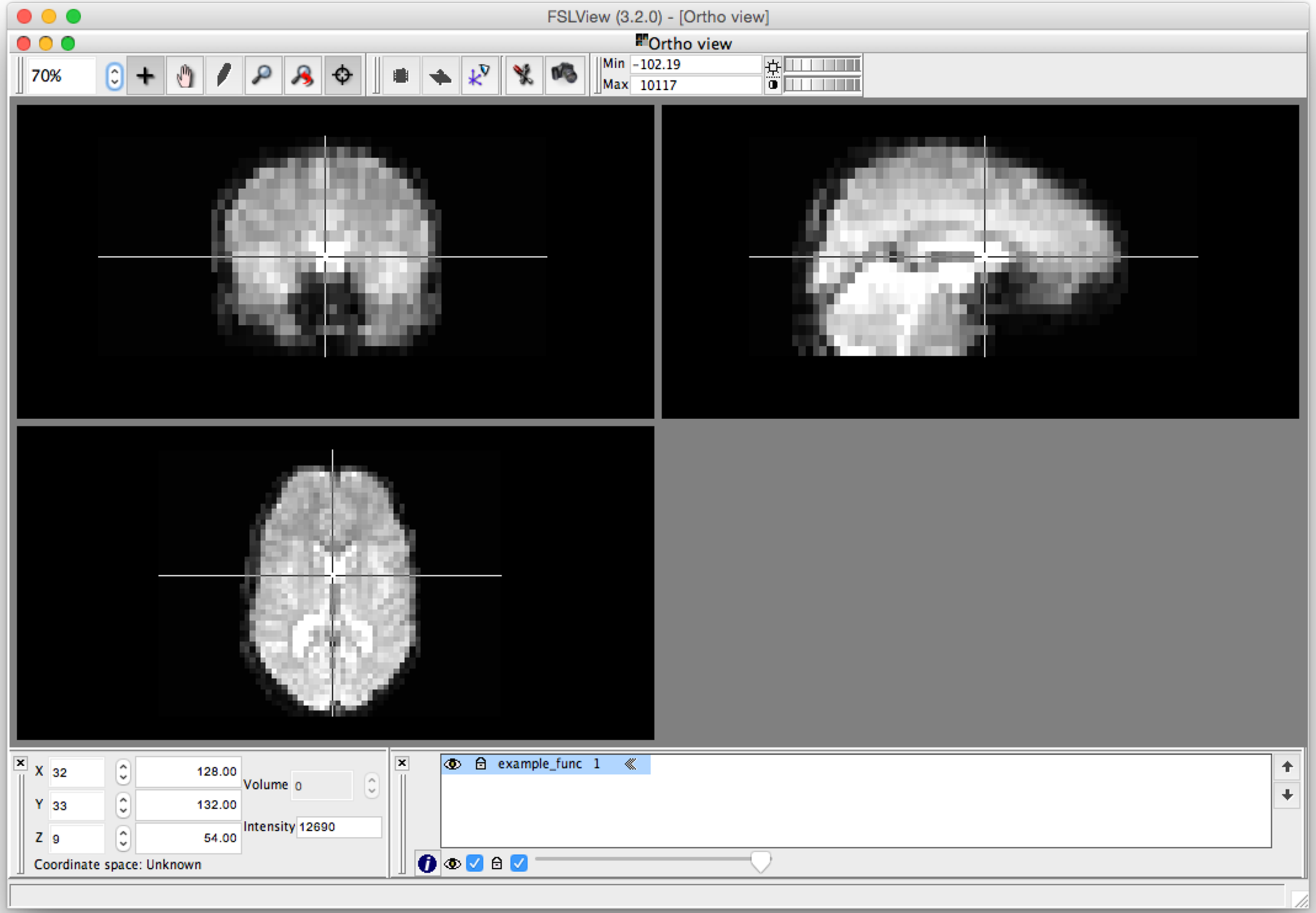
White matter edges, overlaid on top of fieldmap image



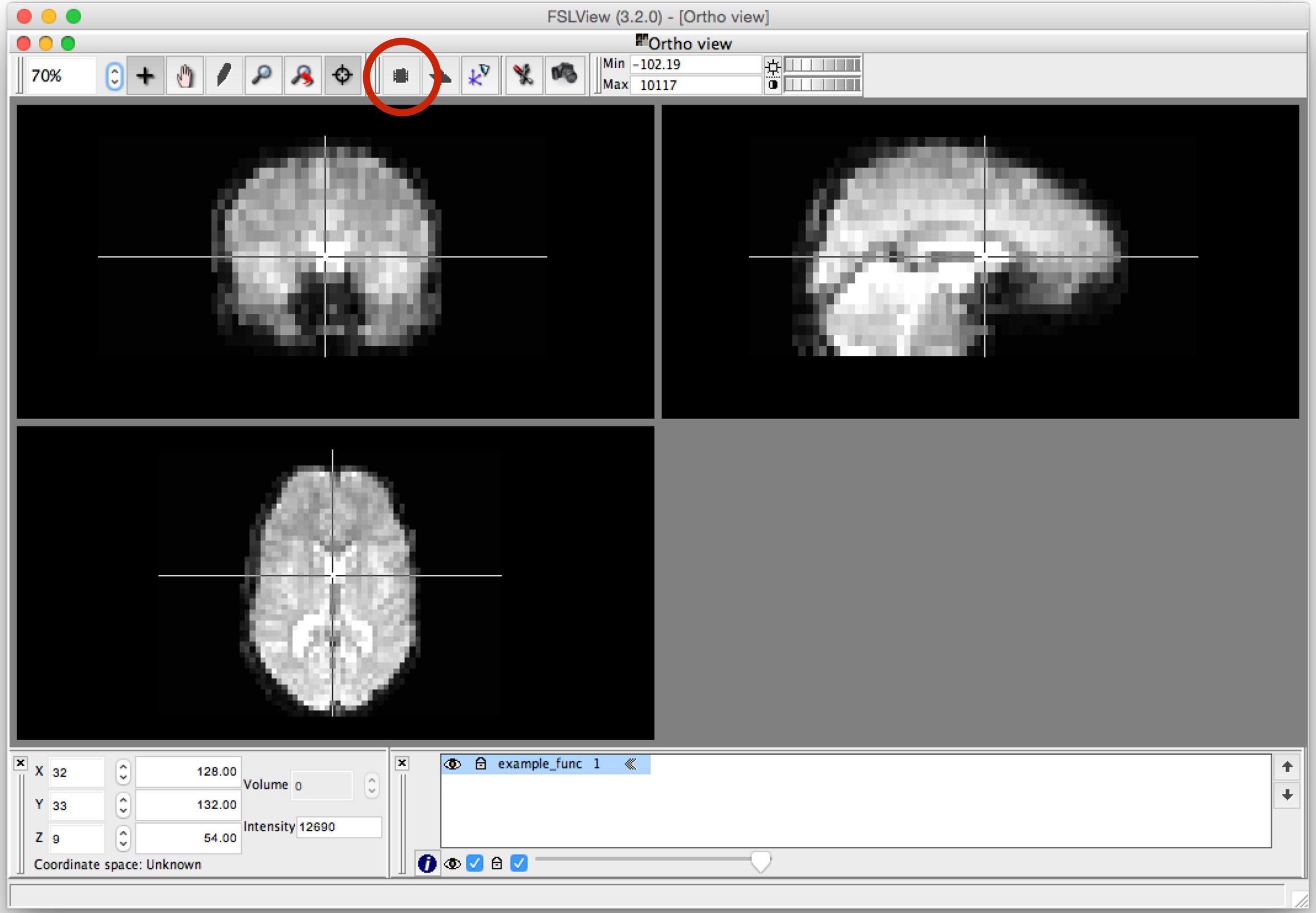
Web Page Output: Distortion



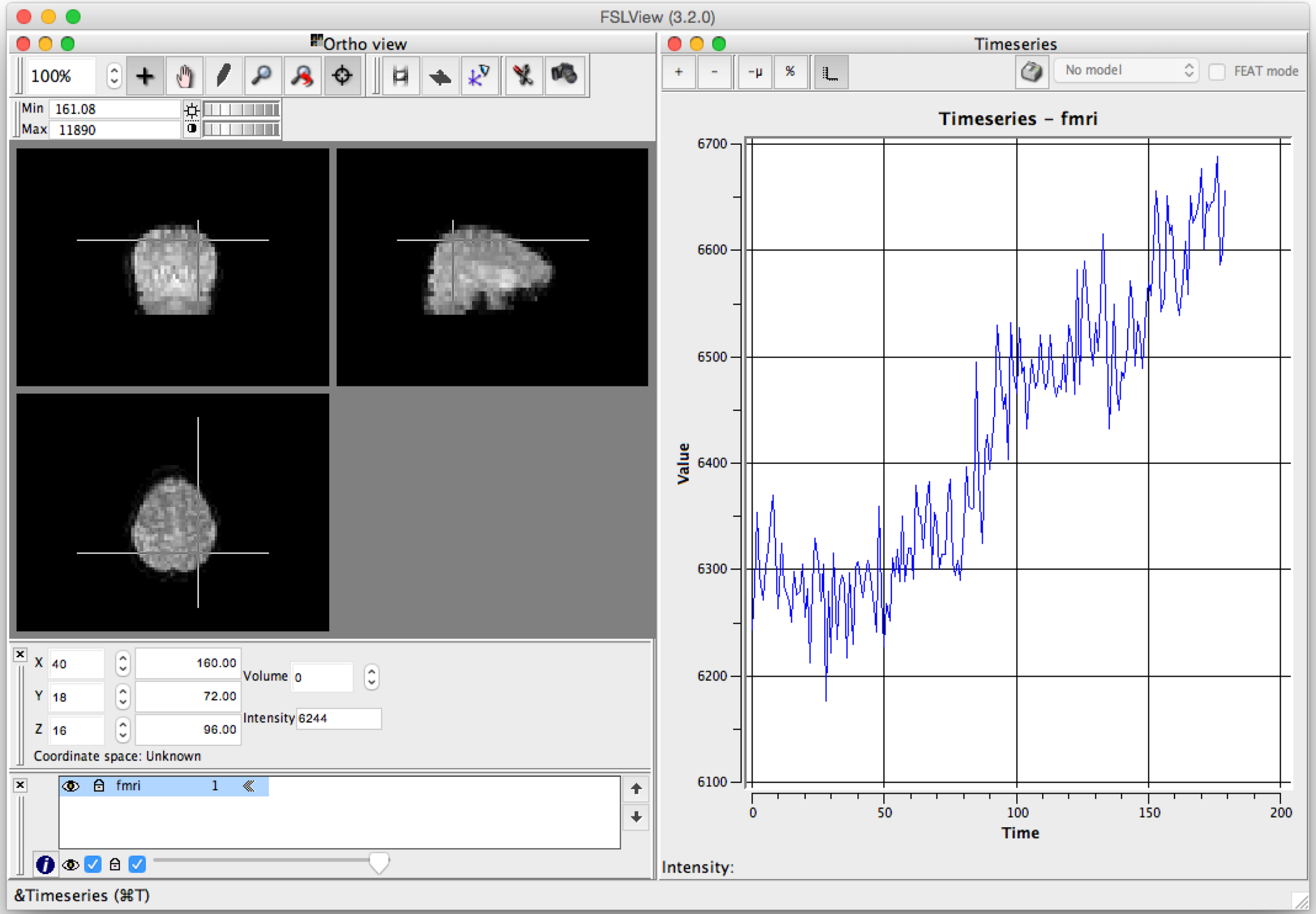
FSLView


FSLView (3.2.0) - [Ortho view]
Ortho view
70%
Min -102.19
Max 10117
X 32 128.00
Y 33 132.00
Z 9 54.00
Volume 0
Intensity 12690
Coordinate space: Unknown
example_func 1

FSLView: Movie Mode



FSLView: Timeseries



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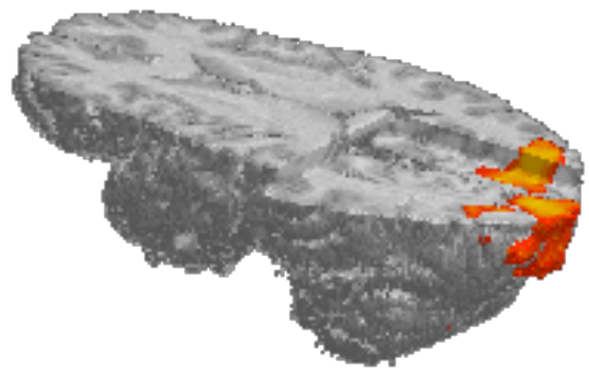
- HRF variation

HCP Pipeline



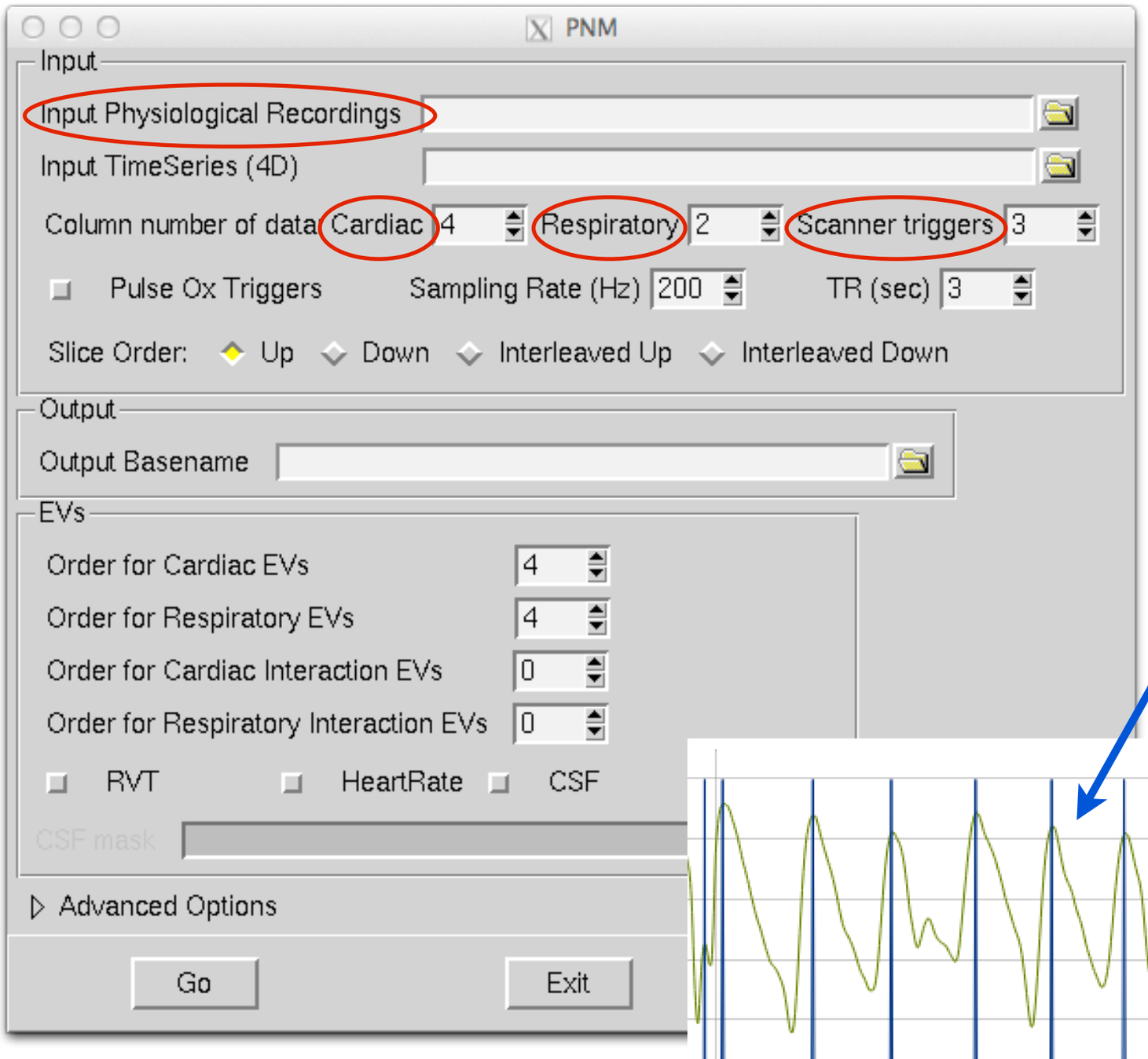
Options in Pre-Processing

- The "standard" pre-processing is not the only option available in FSL
- It is not always the best approach
- Other options are better with different data and subjects
- Alternatives include:
  - slice-timing-correction
  - lowpass filtering (outside of GUI)
  - other reference image for motion/distortion correction (multi-band often needs this)

- Also have other cleanup options (using GLM or ICA):
  - physiological noise modelling
  - confound regressors (e.g. motion parameters)
  - motion-outlier detection (fsl_motion_outliers)
  - ICA-based (FIX, AROMA, manual classification)

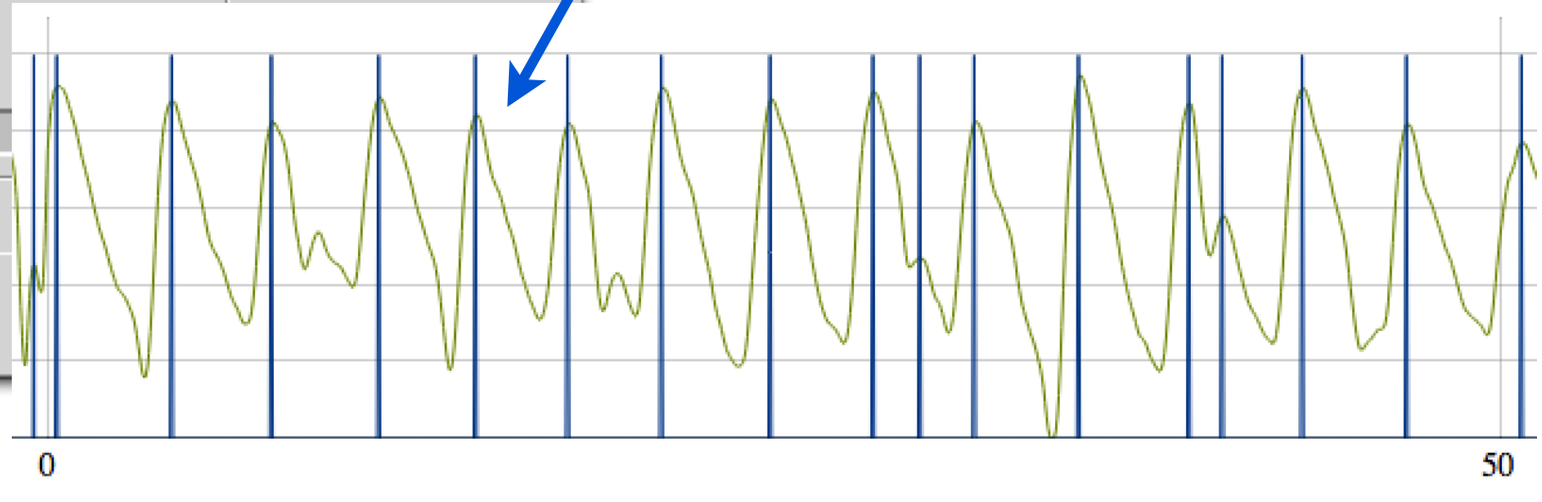
Physiological Noise Model

PNM (GUI)



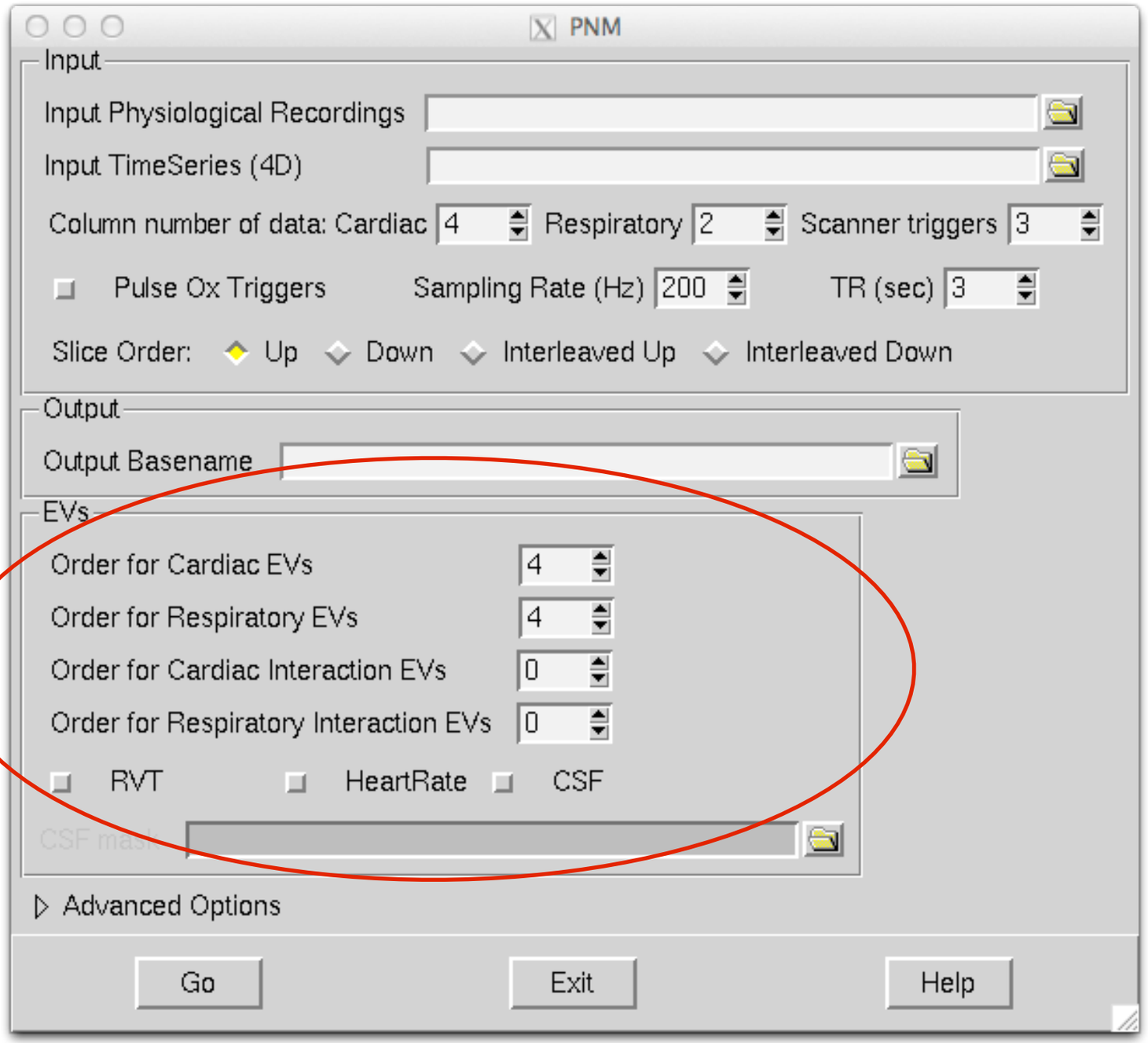
Requires **text file with physiological recordings** (cardiac, respiratory, triggers)

Peak detection in physiological trace needs manual checking via webpage



Physiological Noise Model

PNM (GUI)



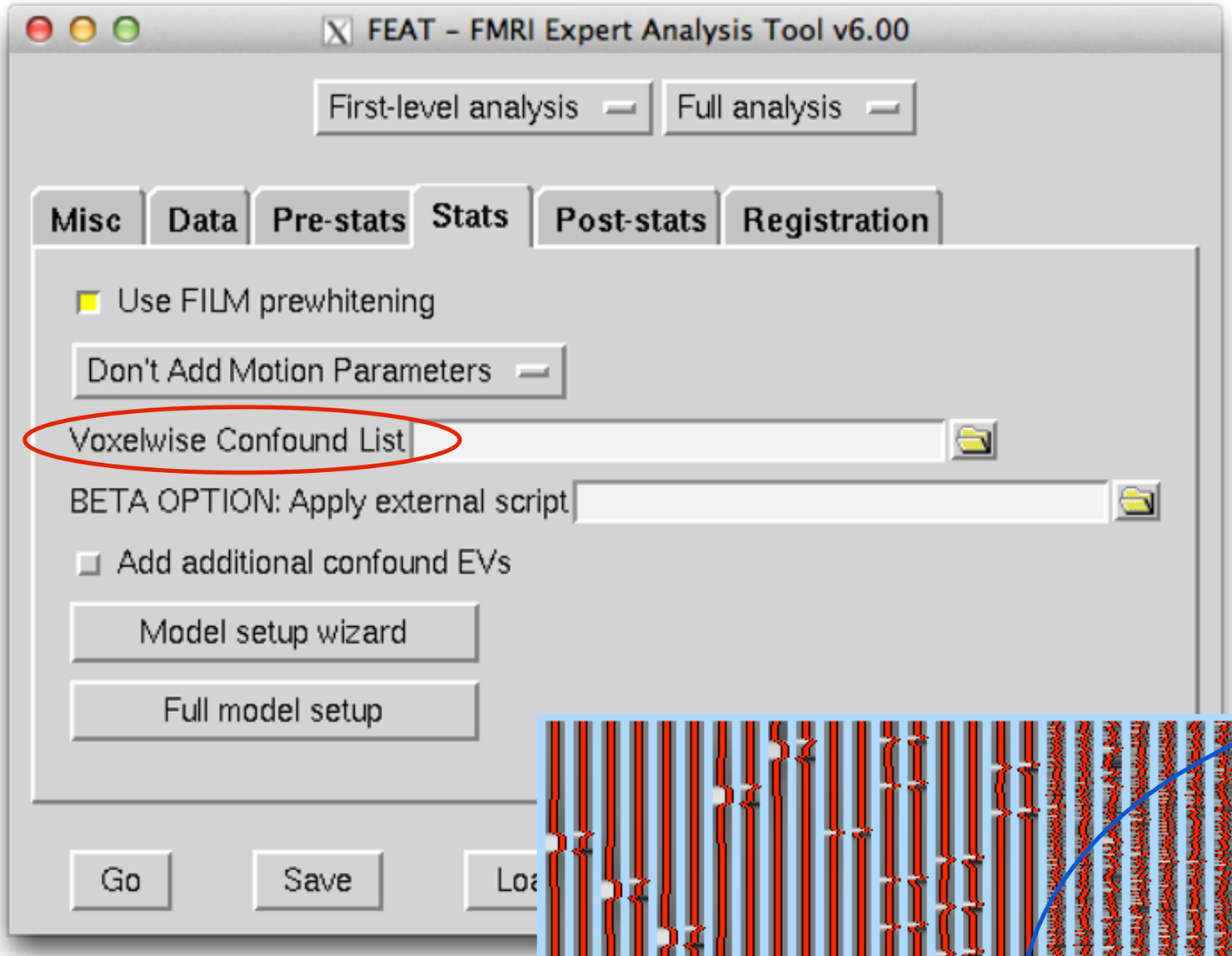
Need to specify what type of corrections:

- Fourier series
  (harmonics / shape)
- Interactions
  (resp x cardiac)

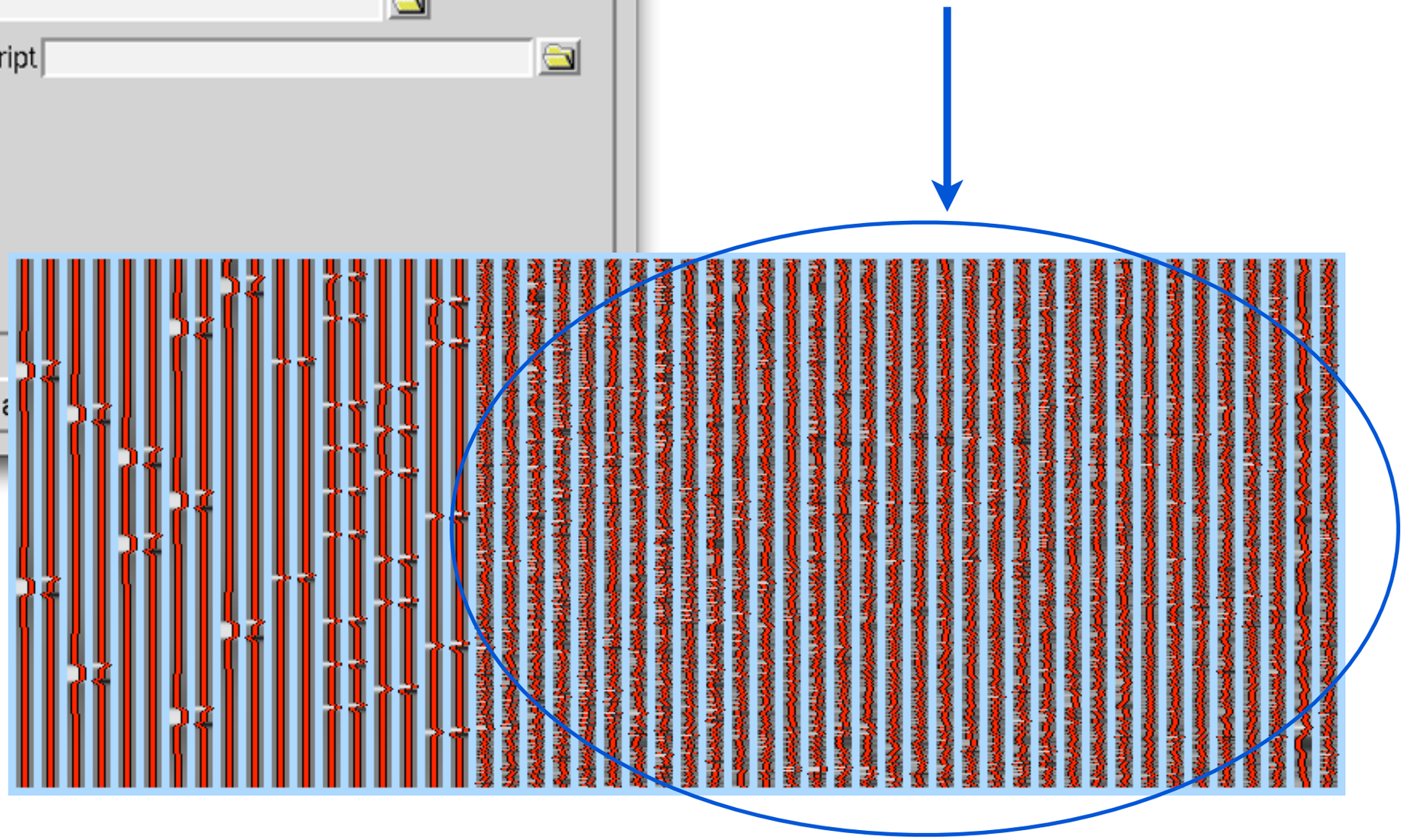
NB: higher orders = better fit to shape, but many more EVs and so less DOF

- RVT
  (resp volume per time)
- HeartRate
- CSF

Physiological Noise Model: GLM

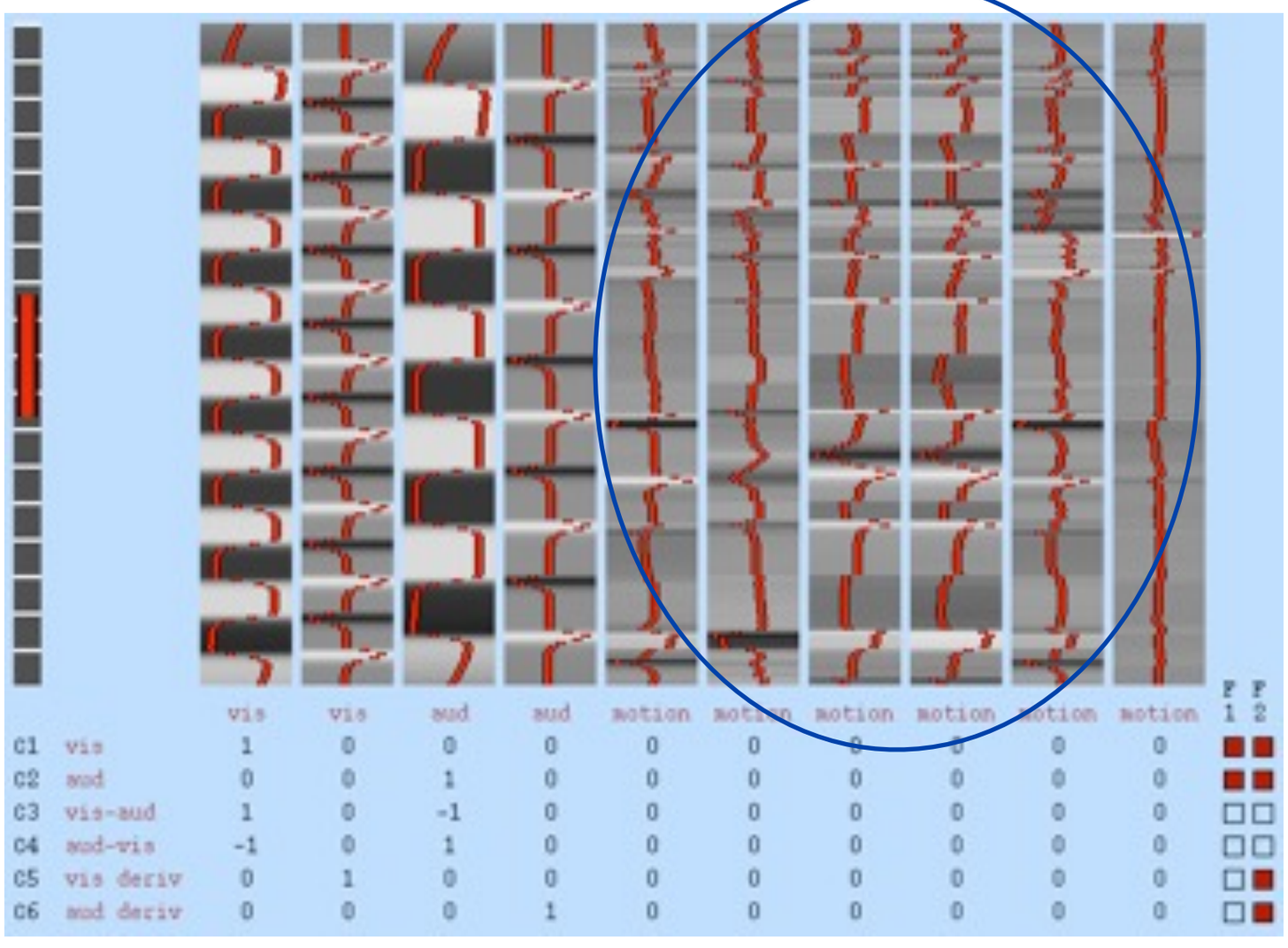


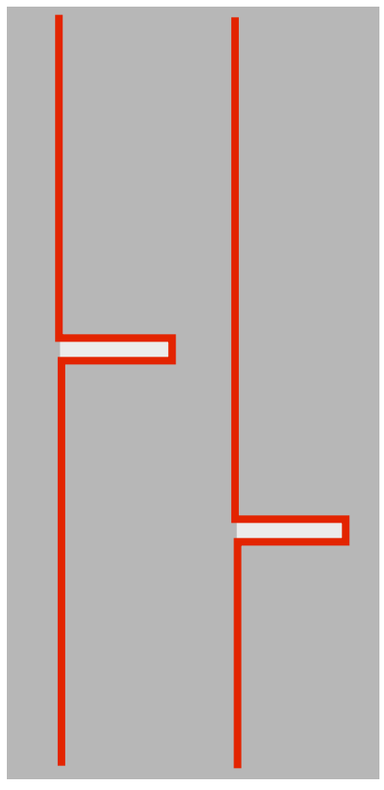
PNM GUI creates files for ***Voxelwise Confounds*** in the GLM



Motion Regressors

Two options (can be combined) both of which work within GLM





Example of 2 outlier timepoints to remove

Motion Parameters

- use button in GUI
- 6 or 24 regressors (EVs)

Motion Outliers

- uses fsl_motion_outliers on command line

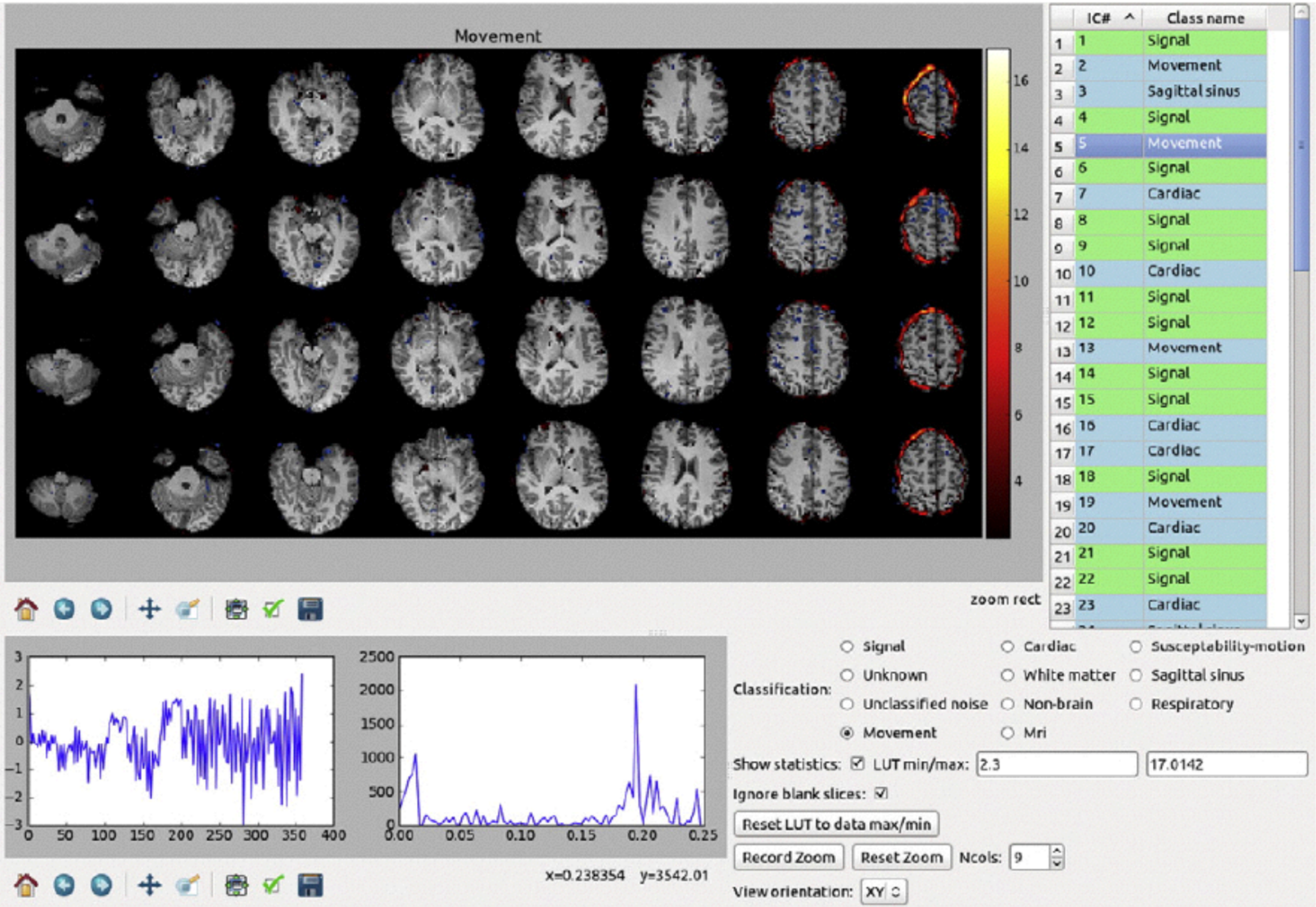
ICA-Based Cleanup

- Principle is simple:
  - use ICA to find components then remove ones that are considered "noise"

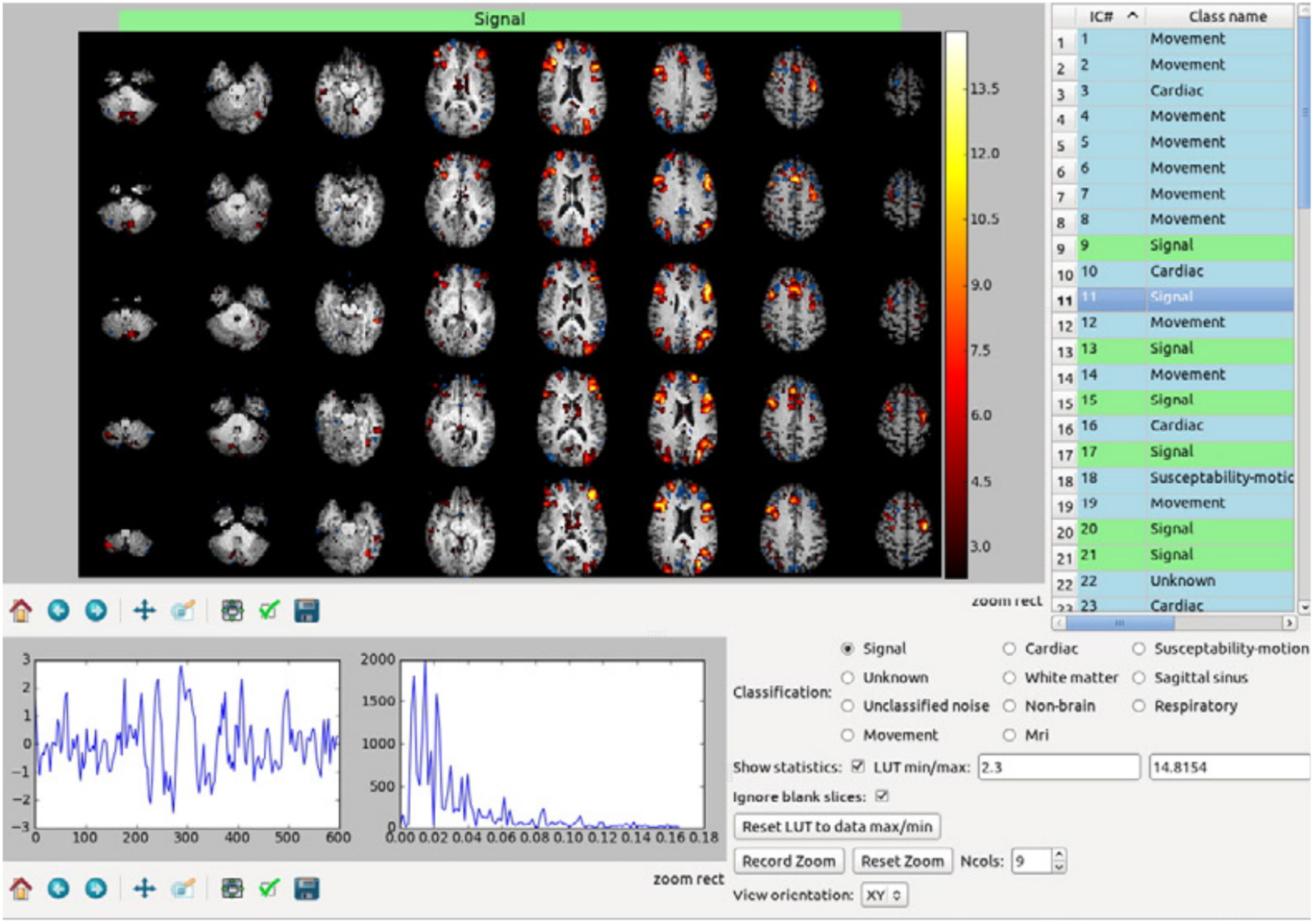
- Can classify noisy ones in three ways:
  - by hand
  - FIX (fully automated and requires ***good training data***)
  - AROMA (fully automated, does not need training data, but often more conservative - *i.e.* leaves more noise)

- Often the most powerful way of removing things such as motion effects and scanner artefacts

Example of a "noise" component

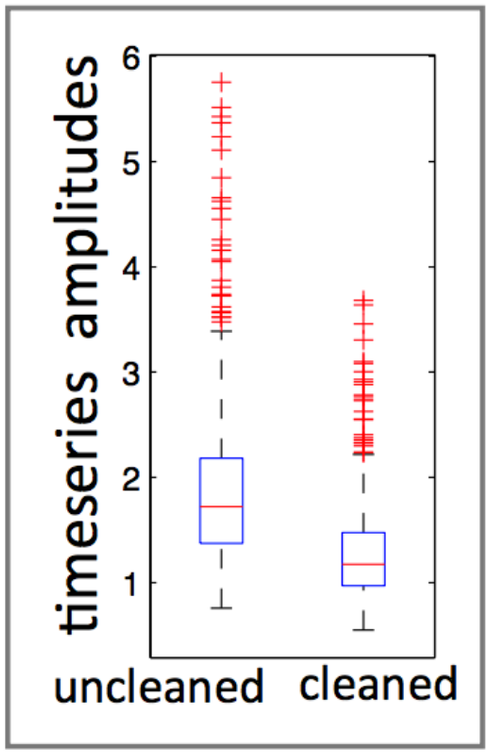


Example of a “non-noise” component

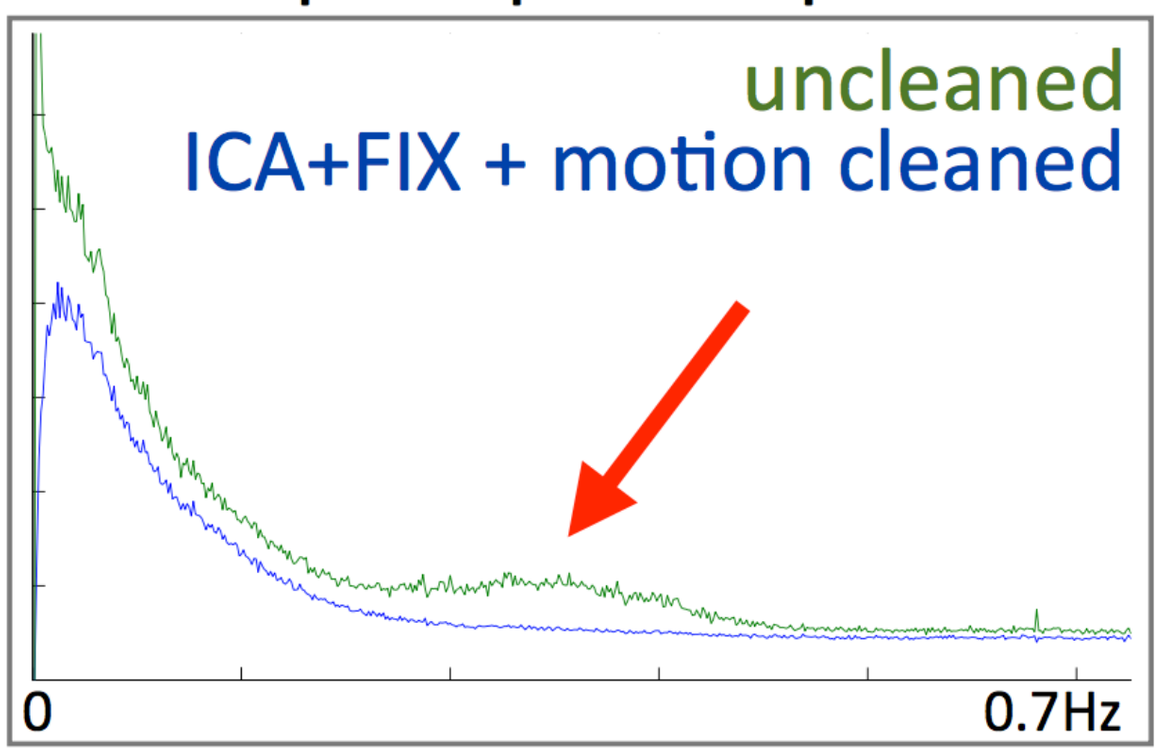


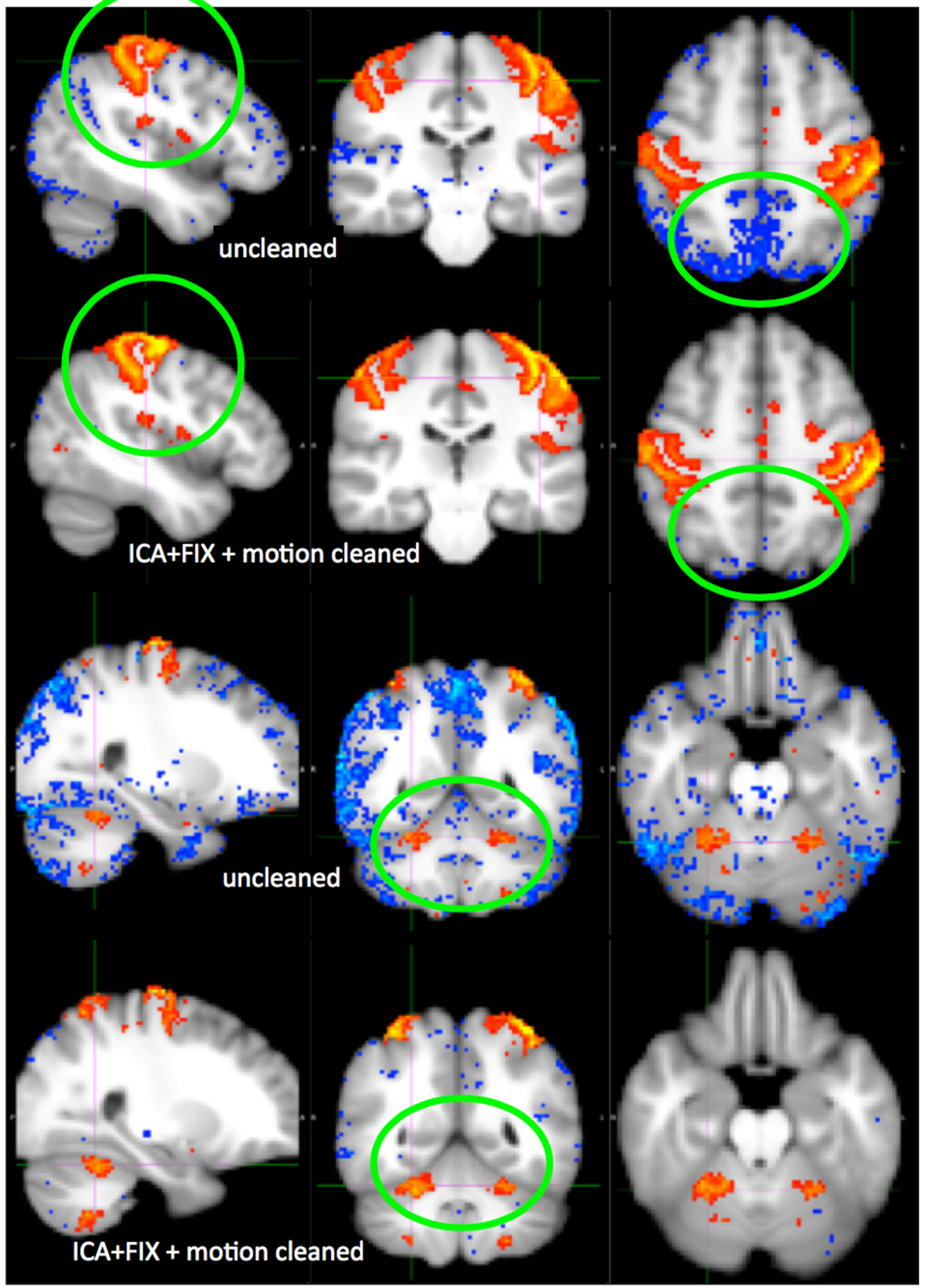
HUMAN Connectome PROJECT

Smith et al., 2013



temporal power spectra





FSL Pre-Processing Pipeline

Standard pre-processing:

- Task fMRI
- Resting-state fMRI

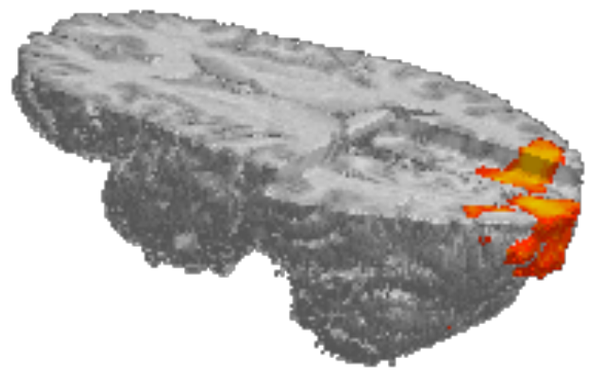
Quality Assessment

Alternatives

- Other pre-processing options
- GLM-based or ICA-based "pre-processing"

Complications

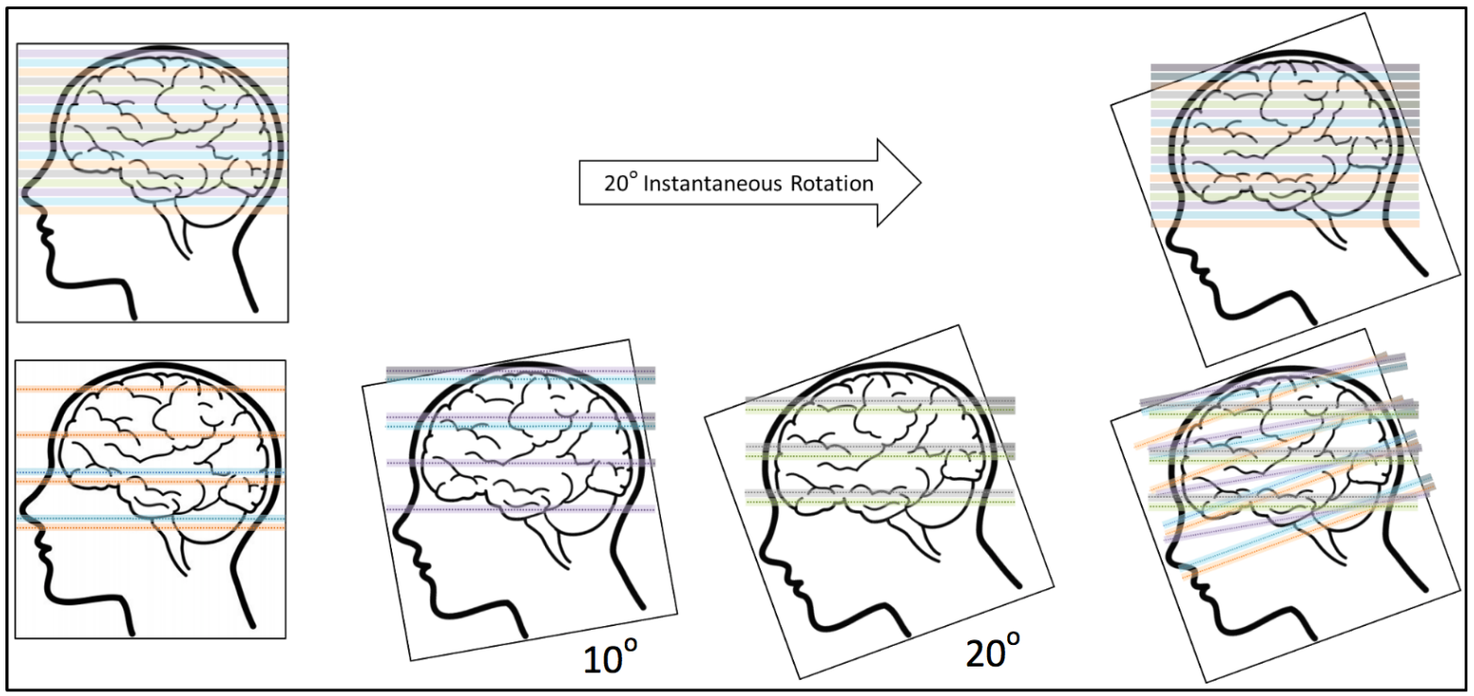
- Spatial and temporal interactions
- HRF variation



HCP Pipeline

Spatial and Temporal Interactions

Acquiring a slice at a time leads to complicated interactions between motion and slice-timing.



Ray Razlighi

- *Motion correction* moves signals between slices (6 DOF)
- *Slice-timing-correction* assumes spatial alignment of voxels
- *Spatial smoothing* mixes slices (problem for derivative modelling)
- *HRF delays* typically vary (problem for slice-timing-correction)
  - These aspects are all inter-related
- Interleaved sequences (incl. multi-band) are harder to correct
- "Best" answer doesn't yet exist (i.e. integrating all together)
- Choice between current options depends on data and subjects
- Strong results will not depend too much on these details

FSL Pre-Processing Pipeline

Standard pre-processing:

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- Resting-state fMRI

Quality Assessment

Alternatives

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Complications

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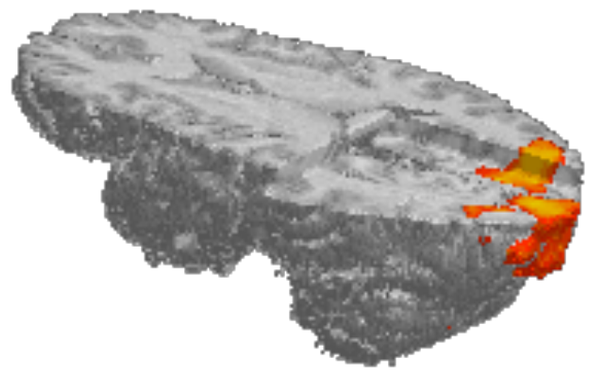
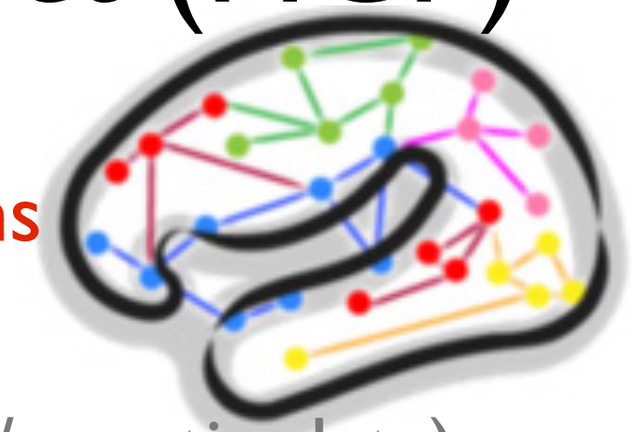


HCP Pipeline

NIH Human Connectome Project (HCP)



$30 million, 5-year project

- Characterize connectivity of healthy adult humans
- 1200 subjects:
  - 22-35 yrs in sibling/twin groups (+ behavioural/genetic data)
- Includes Structural-MRI, Task-FMRI & Resting-FMRI
- Data + network models made freely available
- Provide user-friendly informatics platform

- High quality data:
  - 1 hour of task-FMRI and 1 hour of Resting-FMRI
  - Structural data: 0.7mm isotropic T1-w and T2-w
  - FMRI data: 2mm isotropic / TR=0.72s / Multiband 8
- 8 institution collaboration (>70 investigators) from:
  - Washington U (Van Essen) / U Minnesota (Ugurbil)
  - FMRIB, Oxford / Donder Institute, Nijmegen

HCP Pipeline Overview*

Pre FreeSurfer

FreeSurfer

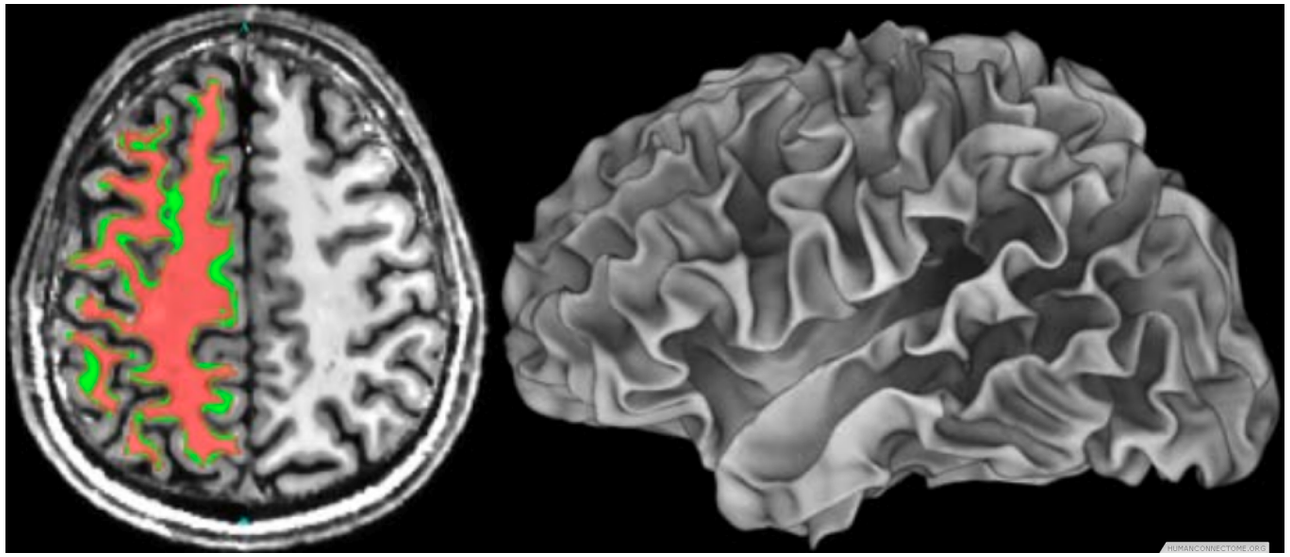
Post FreeSurfer

fMRIVol

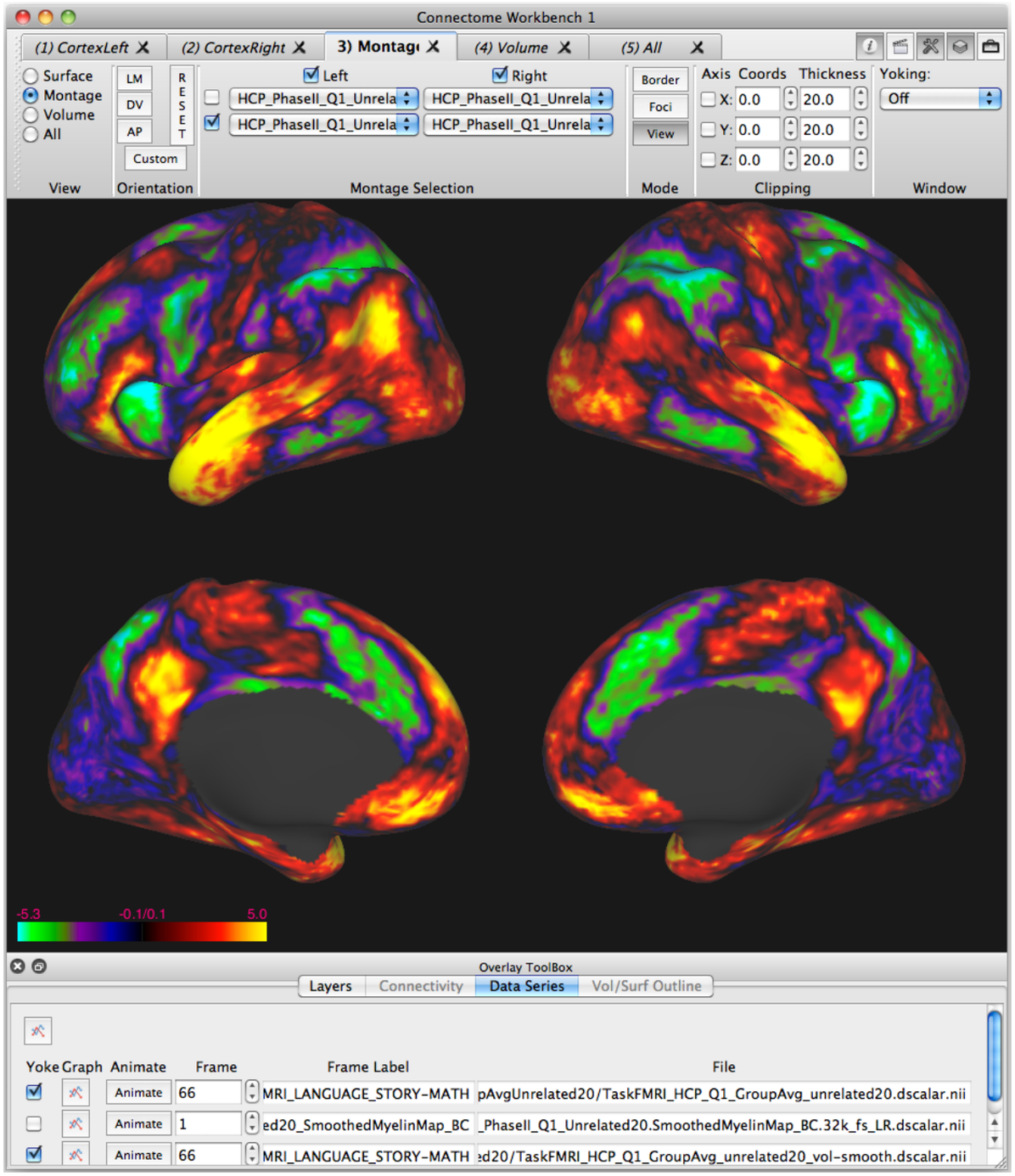
fMRISurf

* see Glasser et al, NeuroImage, 80 (2013): 105-124

HCP Pipeline Overview*



Surface-based analysis



HCP Pipeline Overview*

Pre FreeSurfer

FreeSurfer

Post FreeSurfer

fMRIVol

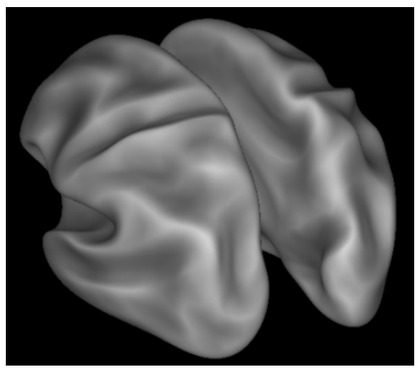
fMRISurf

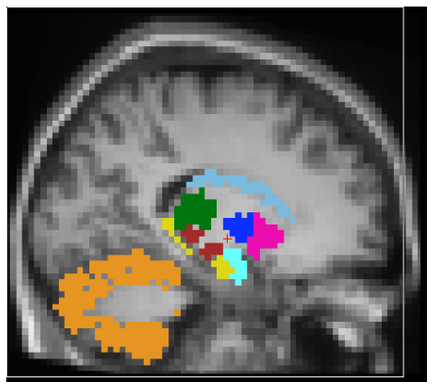
Both volume and surface streams

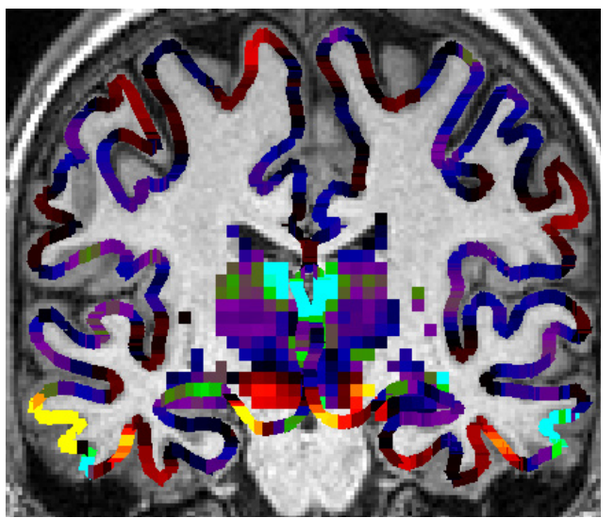
* Glasser et al, NeuroImage, 80 (2013): 105-124

CIFTI

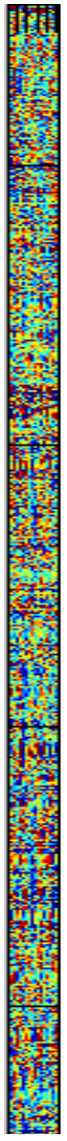
CIFTI Data Format



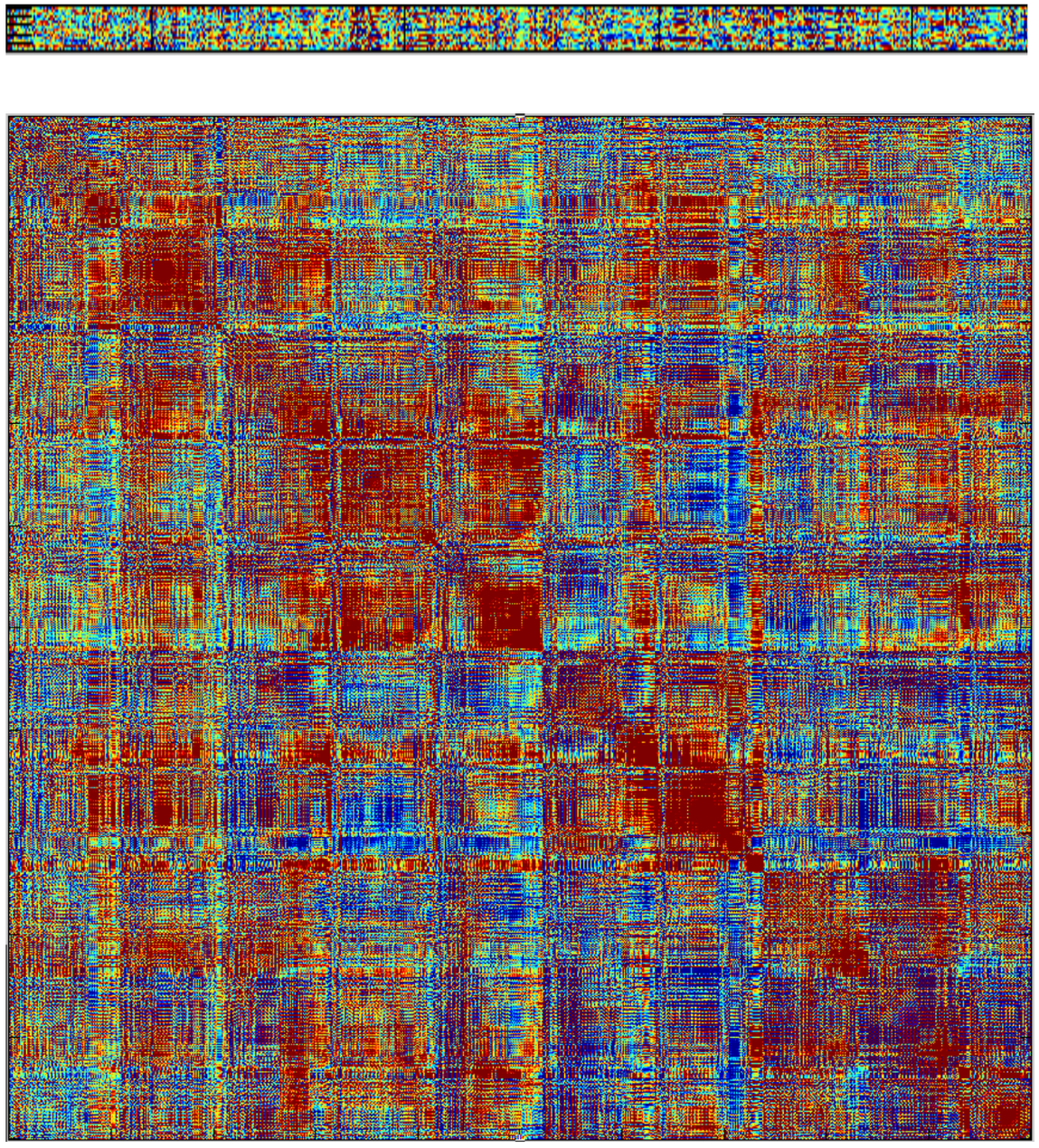




Grayordinates



Time points



Grayordinates

functional connectivity matrix

HCP Pipeline Overview*

Pre FreeSurfer

FreeSurfer

Post FreeSurfer

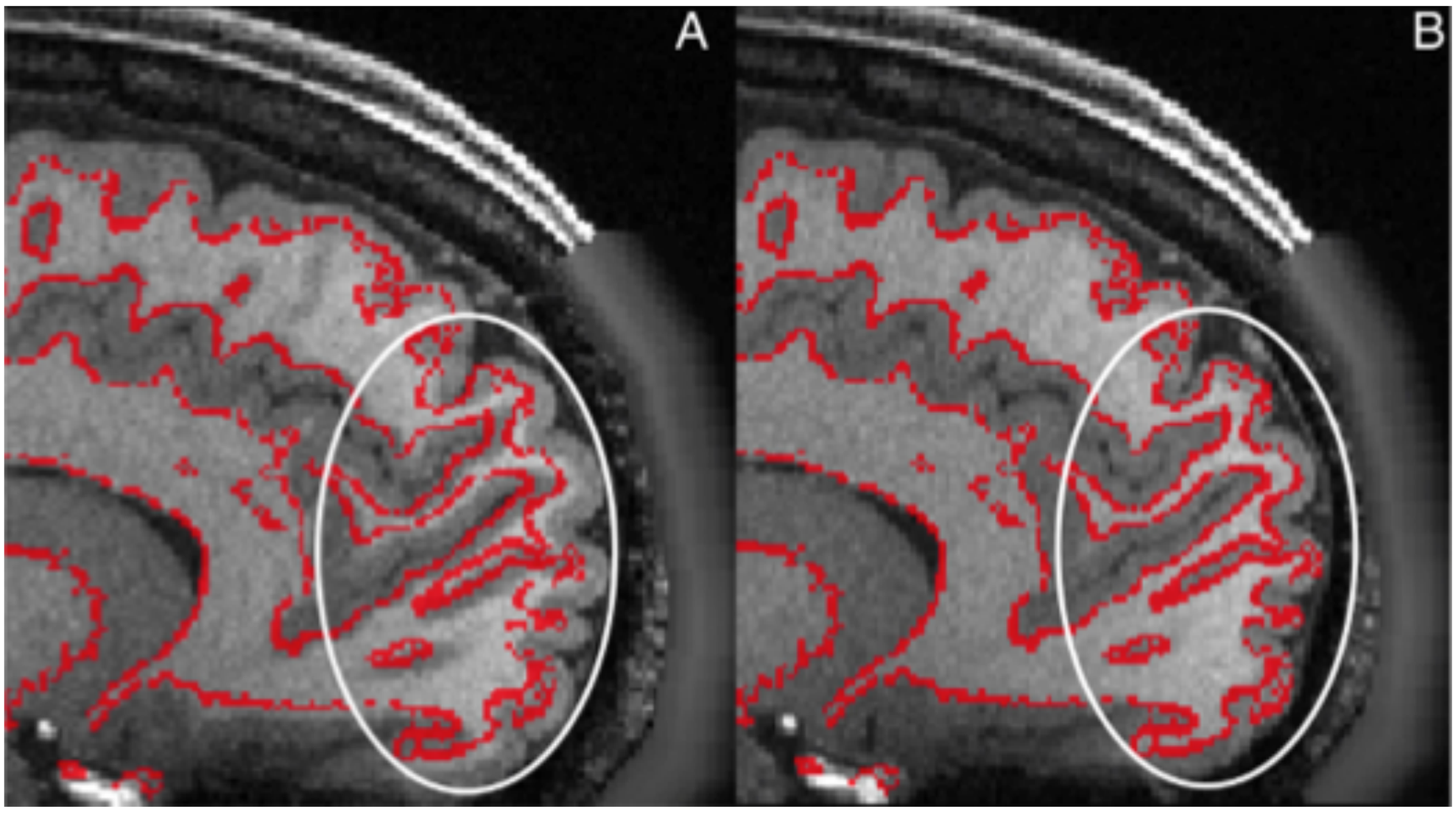
fMRIVol

fMRISurf

* Glasser et al, NeuroImage, 80 (2013): 105-124

Gradient Non-Linearity Distortion

- Correction method (based on MGH code and Siemens coil coefficients) works well



HCP Pipeline Overview*

Pre FreeSurfer

FreeSurfer

Post FreeSurfer

fMRIVol

fMRISurf

* Glasser et al, NeuroImage, 80 (2013): 105-124

Pipeline Overview

- Conversion of DICOM to NIfTI
- Anonymise images
- Reorienting to "standard" orientation (MNI) - swapping axes

Pre FreeSurfer

- Gradient Non-Linearity Correction
- Averaging of separate T1w (and T2w) scans
  - using BBR (topup is an alternative)
- ACPC alignment (via MNI registration)
- Brain Extraction (via non-linear registration)
- T2w to T1w registration (BBR)
- Bias correction (B1 inhomog.) - via sqrt(T1w*T2w)
- Atlas (MNI) Registration

Combine all warps together to avoid repeated interpolation

Pipeline Overview

FreeSurfer - creates surfaces

- Create 1mm version
- Run initial FreeSurfer stages (autorecon 1 & 2)
- Fine tune WM intensity normalisation and registration to T2w
- Run intermediate FreeSurfer stages (inflation, etc.)
- Adjustments to Pial surface (using T2w)
- Run final FreeSurfer stages

Post FreeSurfer

- Non-linear registration to fsLR
- Create ribbon
- Complete myelin mapping

Much of this is necessary for the myelin mapping (T1w/T2w)

HCP Pipeline Overview*

Pre FreeSurfer

FreeSurfer

Post FreeSurfer

fMRIVol

fMRISurf

* Glasser et al, NeuroImage, 80 (2013): 105-124

Pipeline Overview

fMRIVol

- Gradient Non-Linearity Correction
- Motion Correction
- Registration of EPI to T1w
  - with B0 distortion correction (fieldmap)
- Bias field (B1) correction (taken from structural)

fMRISurface

- Extract ribbon from fMRI with voxel outlier exclusion
- Surfaced-based smoothing (2mm FWHM)
- SubCortical processing
  - smooth in volume (same FWHM as on surface)
- Create dense time series (CIFTI)

Acknowledgements

Stephen Smith
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Jon Brooks *(Bristol, UK)*

Doug Greve *(MGH, Harvard)*

… and many others