

NA-MIC National Alliance for Medical Image Computing http://na-mic.org

fMRI Data Analysis

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Surgical Planning Lab, Harvard Medical School Sandy Wells, Steve Pieper, Cindy Wible, Haiying Liu, Carsten Richter

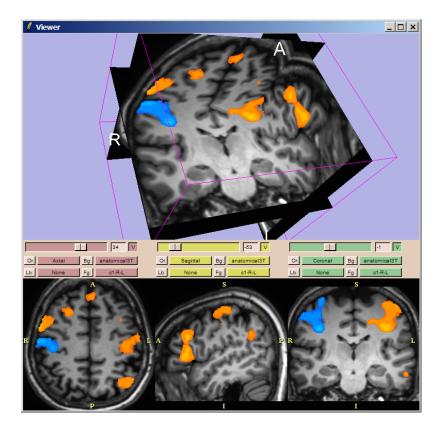


Disclaimer

It is the responsibility of the user of 3DSlicer to comply with both the terms of the license and with the applicable laws, regulations and rules.



Goal of the tutorial



Guiding you step by step through the process of using the fMRIEngine to analyze fMRI data and visualize results within Slicer. A sensory motor paradigm was used for the tutorial dataset.



fMRI engine Module

The fMRIEngine is:

- An open-source package for analyzing and visualizing brain activations supporting the file formats DICOM, ANALYZE, and NIfTI.
- A developing framework for a suite of activation detection algorithms and inference engines; currently it provides a linear modeling detector.
- A research prototype: the full save/reload functionalities are under development. There are no capabilities at this time to do the fMRI pre-processing steps.



Prerequisites

This tutorial assumes that you have already completed Slicer Basics:

- Loading and Viewing Data (Slicer Training 1)
- Saving Data (Slicer Training 7)

Supporting material:

www.na-mic.org/Wiki/index.php/Slicer:Workshops:User_Training_101



Computer Resources

- This tutorial guides you through a full fMRI analysis of a real fMRI timeseries to get users familiar with the interface and workflow.
- You have the option of using either
 - a full-dataset (90 time pts) fMRI-long-dataset.zip for which your computer must have adequate processing speed and RAM (we recommend at least 3GB) or
 - a truncated portion (30 time pts) fMRI-short-dataset.zip of the full dataset, that requires at least 1GB RAM.
- The short dataset contains the first 30 time points of the full dataset.
- Please use the appropriate dataset for your computer.

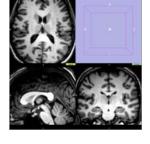


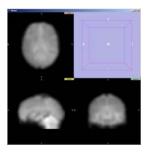
Tutorial datasets

The fMRI tutorial dataset is composed of

Structural scans(anatomical3T.img)

Functional scans.....(functionalxx.img)

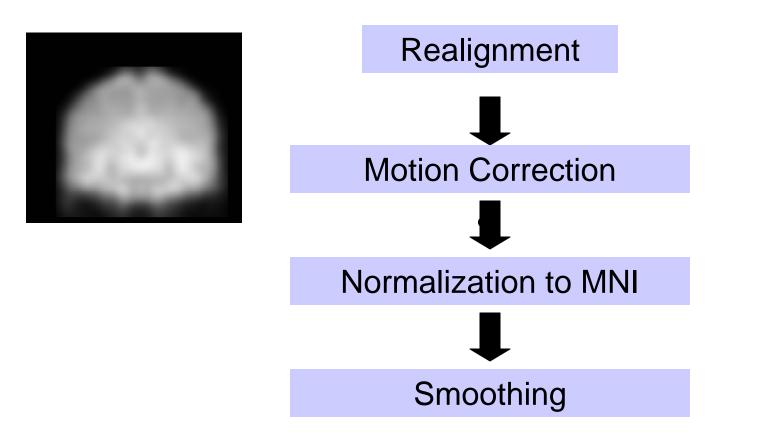




www.na-mic.org/Wiki/index.php/Slicer:Workshops:User_Training_101

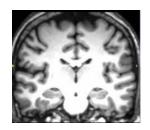


fMRI Data pre-processing (SPM)





Data description



Structural (MPRAGE): ANALYZE format 135 slices 1.0 mm x 1.0 mm x 1.0 mm voxels Normalized to MNI



Pre-processed Functional (EPI): NIfTI format 68 slices 2.0 mm x 2.0 mm x 2.0 mm voxels Repetition Time TR = 2s



Paradigm description

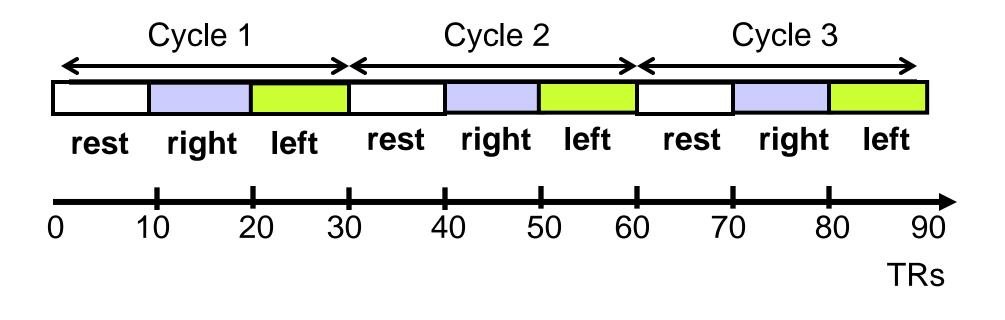
- Finger sequencing fMRI task to elicit activation in the hand regions of the primary sensory motor cortex
- Block design motor paradigm
- Subject touches thumb to fingers sequentially within block (thumb touches first through fourth finger)
- Subject alternates left and right hand



Paradigm design

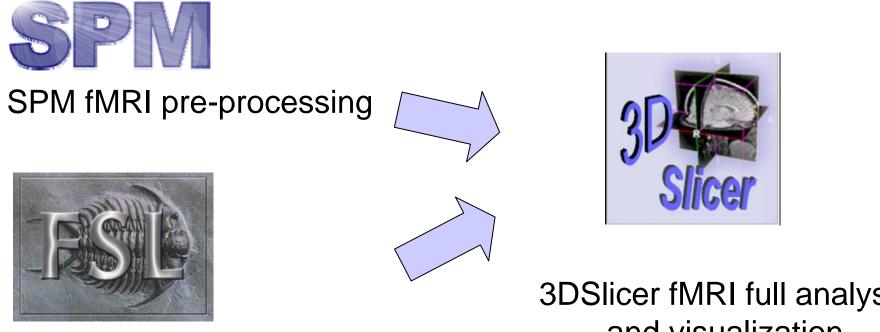
Three cycles

rest | right hand | left hand





fMRI Engine compatibilities



FSL fMRI pre-processing

3DSlicer fMRI full analysis and visualization



fMRI Engine compatibilities



SPM fMRI full analysis



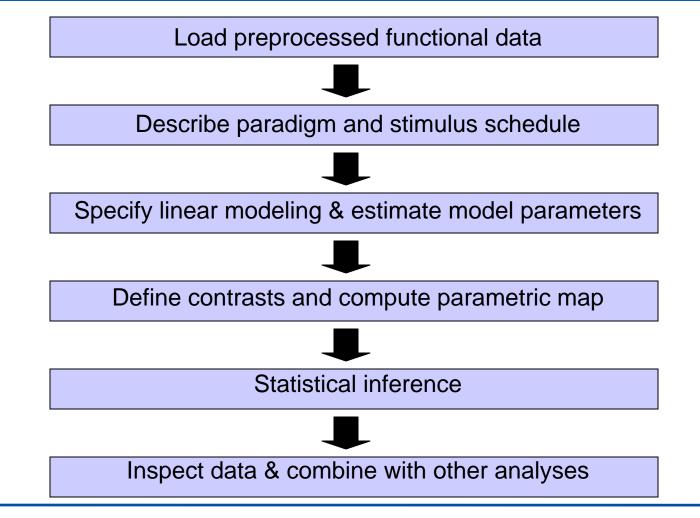
FSL fMRI full analysis



3DSlicer visualization and modeling



fMRIEngine workflow





Overview

Part 1: Loading and Previewing Data Part 2: Describing stimulus schedule Part 3: Linear modeling & estimation Part 4: Contrasts & computing SPMs Part 5: Inference & inspection



Loading the structural dataset



Click on Add Volume in the main menu



Loading the structural dataset



Select the reader **Generic Reader** in the Props Panel of the module **Volumes**.

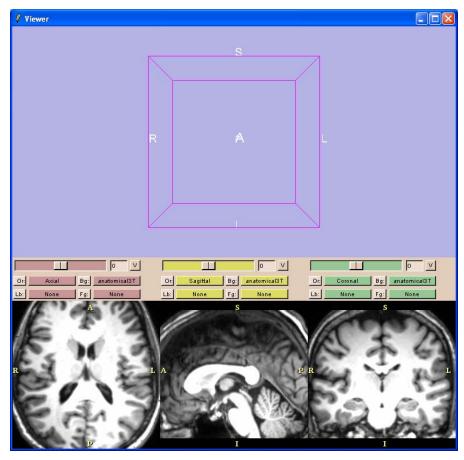
Click on Browse, select the file **Anatomical3T.hdr** in the directory/structural.

The anatomical volume in the short and long datasets are identical.



Loading the structural dataset







fMRI Engine

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Select Modules in the main menu Select Application→fMRIEngine



Load Image Sequence

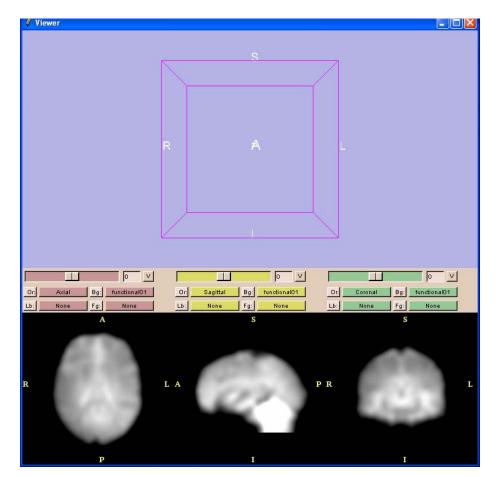
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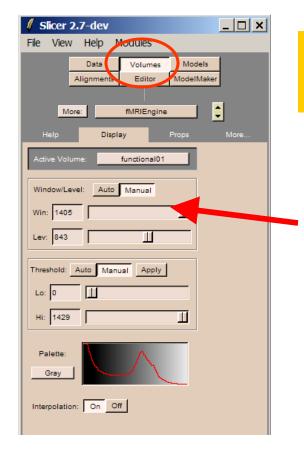
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Slicer loads the functional volumes in the Viewer.



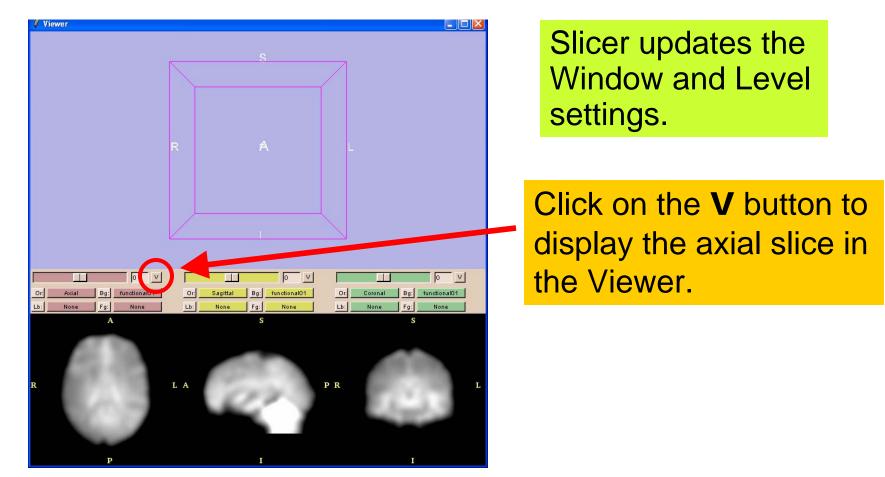


Click on the module **Volumes**, and select the panel **Display**

Adjust **Win** and **Lev** to get best display of image data



Set Image Display





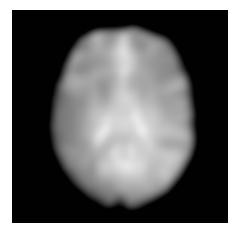
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Click on the letter I in the control window to display the Inferior view.



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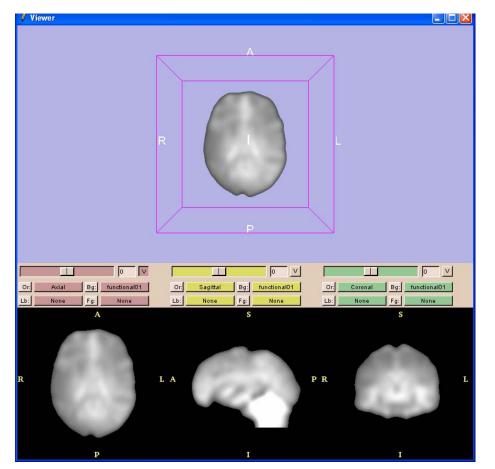
Parallel Slice Opacity: 1



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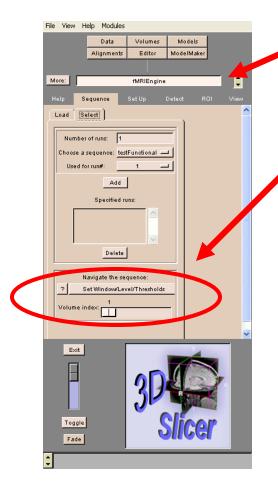
Adjust the low threshold **Lo** to mask out background





The display settings apply to currently viewed image in the sequence only



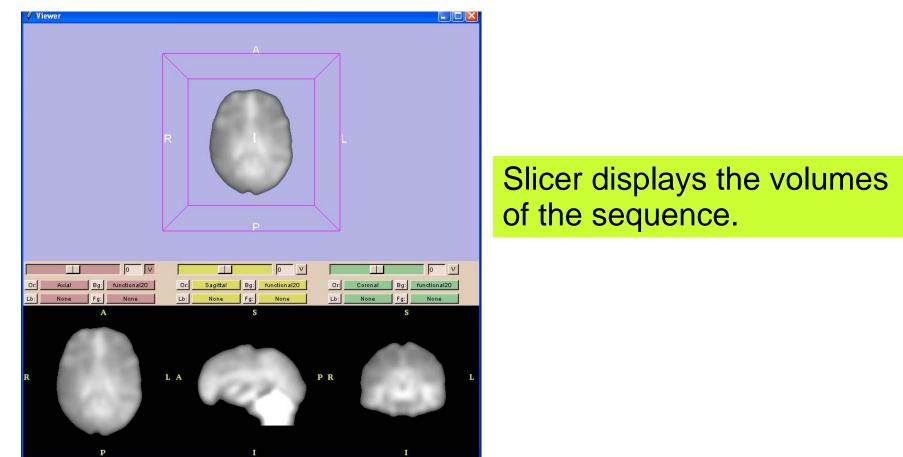


Click on **fMRIEngine**, select the panel **Sequence**, and pick the tab **Select**

Click on Set Window/Level/Thresholds to apply to all volumes in the sequence

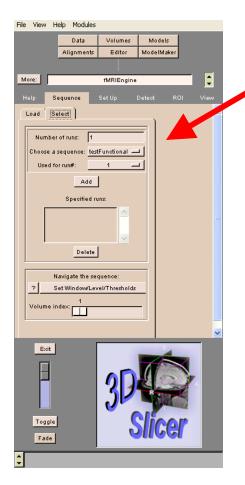
Visually inspect sequence using the **Volume index** to check for intensities aberrations







Select Image Sequence



Specify the **number of runs = 1**, select the sequence **testFunctional**

Click on **Add** to assign the sequence to run 1



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Slicer assigns the sequence to run 1



Overview

Part 1: Loading and Previewing Data Part 2: Describing stimulus schedule Part 3: Linear modeling & estimation Part 4: Contrasts & computing SPMs Part 5: Inference & inspection



Stimulus schedule

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| Defined condition: | s for run#: 1 | | |
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Pick **Set Up** Tab in the fMRIEngine and choose the **Linear Modeling** detector

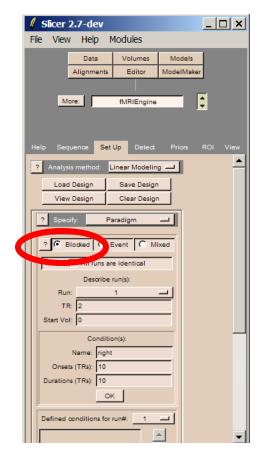


The **General Linear Modeling** is a class of statistical tests assuming that the experimental data are composed of the linear combination of different model factors, along with uncorrelated noise

$\mathbf{Y} = \mathbf{B}\mathbf{X} + \mathbf{e}$

- B = set of experimental parameters
- Y = Observed data
- X = Design Matrix e = noise



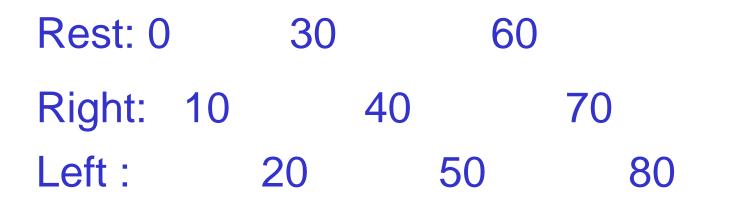


Select the design type **Blocked**



Paradigm timing parameters

- Repetition Time TR = 2s
- Durations: 10 TRs in all epochs
- Onsets (in TRs):





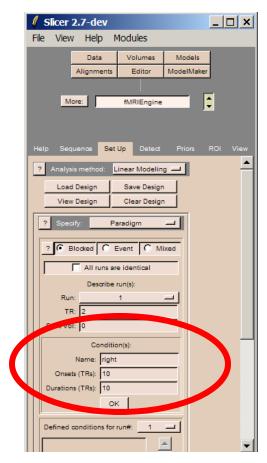
Stimulus schedule

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| All runs are identical | |
| Describe run(s): Run: 1 | |
| TR: 2 | |
| Start Vol: 0 | _ |
| Condition(s): | |
| Name: right | |
| Onsets (TRs): 10 | |
| Durations (TRs): 10 | |
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| Defined conditions for run#: 1 | |
| | |

Enter the characteristics of the run TR = 2 and Start Volume = 0 (ordinal number)



Stimulus schedule



Enter the schedule for the first condition

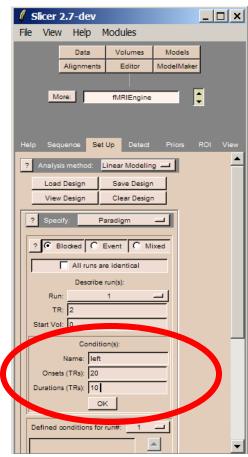
Short dataset: Name = right Onset = 10 Durations = 10

Long dataset: Name = right Onset = 10 40 70 Durations = 10 10 10

Click on **OK** to add this condition to the list of defined conditions



Stimulus schedule

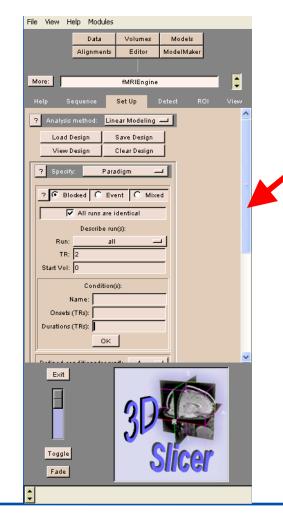


Enter the schedule for the second condition Short dataset: Name = left Onset = 20 Durations = 10

Long dataset: Name = left Onset = 20 50 80 Durations = 10 10 10

Click on **OK** to add this condition to the list of defined conditions





Scroll down in the **Set-up** panel to see the list of defined conditions



Editing the Stimulus schedule

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The list of specified conditions appears in the left panel



Overview

Part 1: Loading and Previewing Data Part 2: Describing stimulus schedule Part 3: Linear modeling & estimation Part 4: Contrasts & computing SPMs Part 5: Inference & inspection

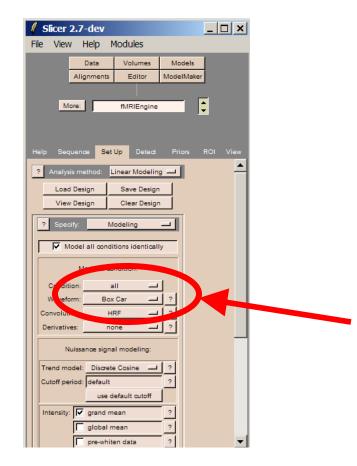


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Select Specify Modeling

Click on Model all conditions identically





Select Condition: **all** Waveform: **BoxCar**

Click on the question mark next to **Waveform** for detailed description of the modeling option.



fMRIEngine information 💶 🗖

Stimulus function

Modeling options include the specification of a stimulus function, which is a basic signal waveform meant to correspond to a stimulus time-course. The *boxcar* function is selected by default, and produces an EV with a sharp 'on-and-off' signal describing each stimulus presentation. The *half-sine* function may be selected instead; it produces an EV signal with a smoother and symmetric shape during each stimulus presentation.

Once a waveform has been selected, additional modeling options may be applied. When signal modeling is complete, clicking the *OK* button will add the resulting EV to a list displayed at the bottom of the GUI panel. Any EV in this list may be selected and either edited or deleted using the associated *edit* and *delete* buttons. By default, an EV that represents the *baseline* for every run will be automatically added to this list. If this EV is not desireable, it mav

close

Slicer displays a detailed description of the Stimulus function.



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Select

- Convolution: HRF
- (Hemodynamic Response Function)
- Derivatives: none



Nuisance Signal Modeling



On the subpanel Nuisance signal modeling, select Trend model: Discrete Cosine Cutoff period: default

Click on use default cutoff

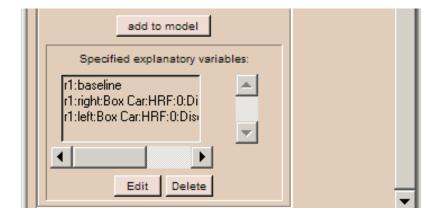


Nuisance Signal Modeling

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Scroll down in the Set Up panel and click on add to model





The list of explanatory variables (EV) appears in the left panel, including the baseline that is automatically added. The string are Slicer specific representation of the modeling.

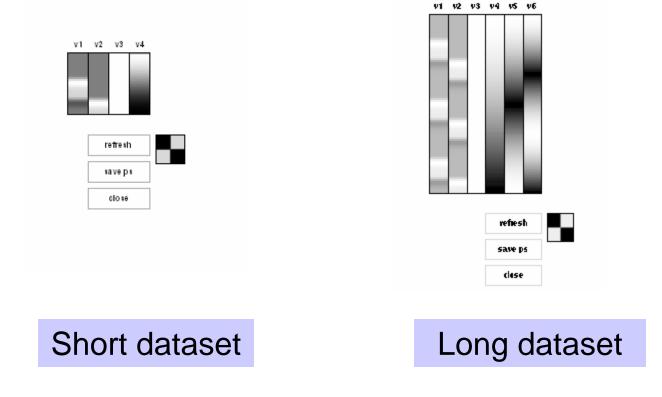


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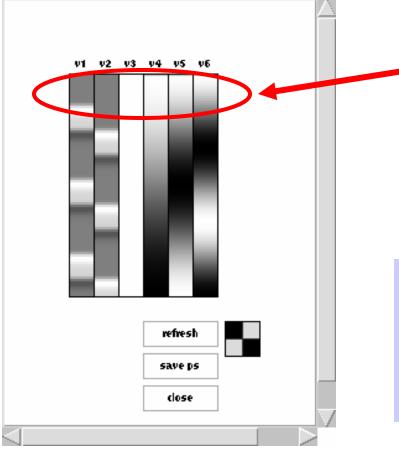
Click View Design to display the design matrix



A window displaying the model design appears.



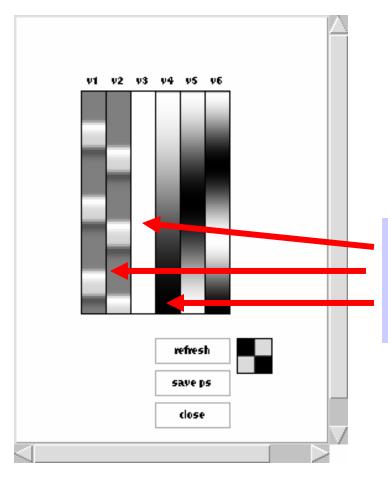




Move the mouse from left to right over the columns of the matrix to display the characteristics of the modeled conditions.

v1 = left modeled condition
v2 = right modeled condition
v3 = baseline
v4,v5,v6 = low frequency noise

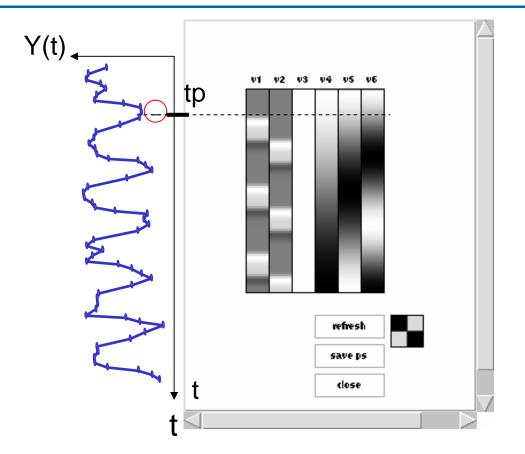




Observe the different values of the signal intensity in the matrix.

White \rightarrow positive signal intensity 1 Mid-Grey \rightarrow null intensity 0 Black \rightarrow negative intensity - 1



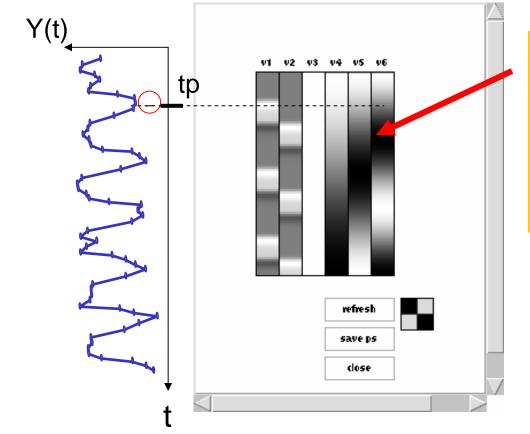


Each column represents the contribution from each condition we might see in a voxel time course.

Modeled Signal

Y(tp) = b1 v1(tp) + b2 v2(tp) + b3 v3 (tp) + b4 v4(tp) + b5 v5(tp) + b6 v6(tp)





Move the mouse up and down to browse the different volumes associated with the time points.



Estimation

| 🦸 Slicer | 2.7-dev | | _ [| L |
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| | Alignments | Editor | ModelMaker | |
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| Help Sec | quence Set | Up Detect | Priors ROI | View |
| ? Analys | sis method: | inear Modelin | ° — | - |
| Load | d Design | Save Design | | |
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| ? Spec | fy: Es | timation | | |
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| Estimate | model: | | | |
| Choos | e run(s): | run1 🗖 | ? | |
| | | Fit Model | ? | |
| | | Save Beta |] | |
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Select **Specify Estimation** to estimate B and e at every voxel: Y = BX + e

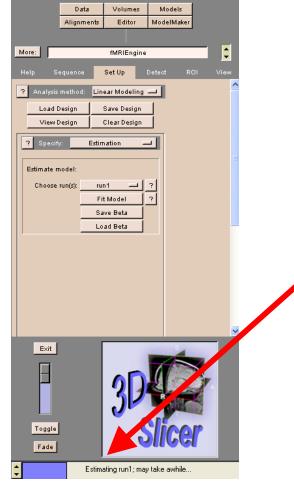


Estimating model parameters

| Slicer 2.7-dev | The Estimation pan appears | el |
|------------------|---------------------------------------|----|
| More: fMRIEngine | Select run1 and click on Fit Model | |



Estimating model parameters



Slicer shows the progress of model estimation



Part 1: Loading and Previewing Data Part 2: Describing stimulus schedule Part 3: Linear modeling & estimation Part 4: Contrasts & computing SPMs Part 5: Inference & inspection



| | 🖉 Slicer 2.7-dev |
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| | File View Help Modules |
| | Data Volumes Models |
| | Alignments Editor ModelMaker |
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| | More: fMRIEngine |
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| | Help Sequence Set Up Detect Priors ROI View |
| | ? Analysis method: Linear Modeling - |
| | Load Design Save Design |
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| (| ? Specify: Estimation |
| | |
| | Estimate model. |
| | Choose run(s): run1 ? |
| | Fit Model ? |
| | Save Beta |
| | Load Beta |
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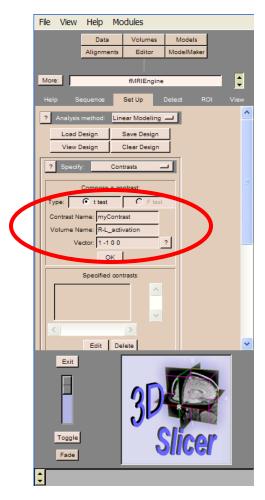
In the SetUp panel, select Specify → Contrasts



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| Fade | | | | | | |

The Panel for the contrasts appears





Choose the contrast type t-test

Enter the contrast name **myContrast**, and the Volume Name **R-L_activation**



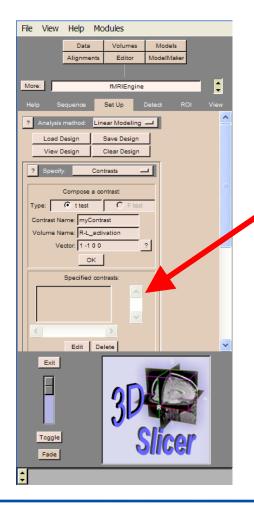
Contrast Vector

- Encoding of the effect that you want to test
- A contrast component per column in the design matrix (trailing zeros may be omitted)

1 0 0 0 0 \rightarrow test for whether there is any effect for the right hand

1 -1 0 0 0 \rightarrow statistically contrast the effect for the right and left hand





Select the statistical test t-test

Specify the contrast vector **1 –1 0 0** (enter a space between the values)

Click **OK** to add this contrast to a list of defined contrasts



Specify Contrasts

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| Type: | Compose a | C F t | act / | |
| | st Name: c1 | | - | |
| | e Name: R-L_ | activation | | |
| | Vector: 1 -1 (| o d | ? | |
| | 0 | | | |
| | Specified | contrasts: | | |
| c1-R | -L_activation | | <u> </u> | |
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| | | | | |
| | Edit | Delete | | - |

The resulting contrast named **myContrast-R-L_activation** appears in the list of specified contrasts.

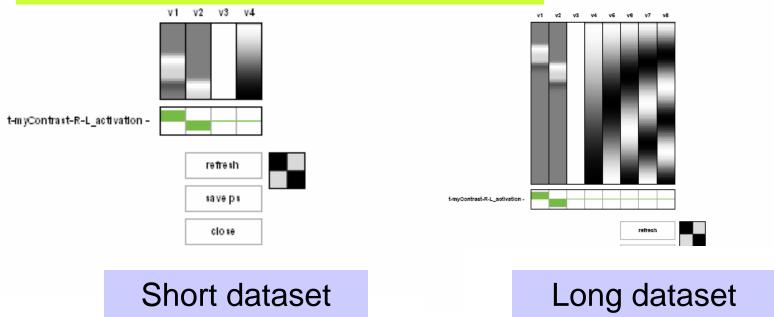


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| | | Spec | ified | contrasts: | | |
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Click on **View Design** to display the Design matrix



A window displaying the design matrix and contrast vector appears.



Check that the contrast and model are correct.



Perform activation detection

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| File \ | /iew Help | Modules | | |
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| More: fMRIEngine | | | | |
| Help | Sequence Set | Up Detect | Priors ROI Vitar | |
| | | | | |
| Select contrast(s): | | | | |
| c1-R-L_activation | | | | |
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| ? Compute | | | | |
| Computing volume for this contrast: | | | | |
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Click on the tab **Detect** and select the contrast **myContrast-R-L_activation**

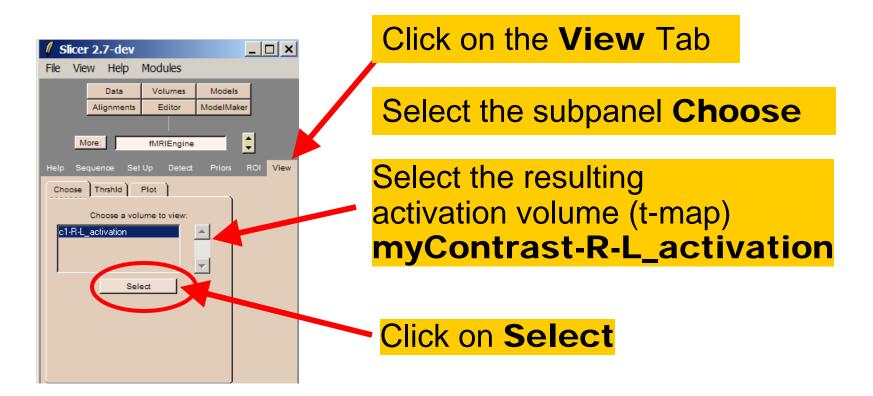
Click on **Compute** to compute the statistical map of activation (t-test)



Part 1: Loading and Previewing Data Part 2: Describing stimulus schedule Part 3: Linear modeling & estimation Part 4: Contrasts & computing SPMs Part 5: Inference & inspection



Select the activation volume



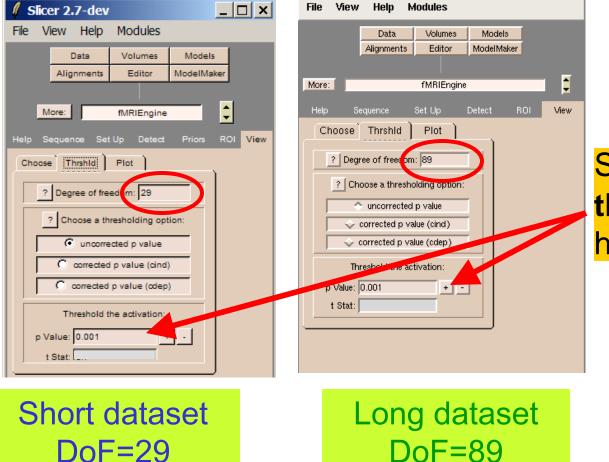


| 🖉 Slicer 2.7-dev | | | | | |
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| Choose a volume to view: | | | | | |
| Select | | | | | |
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Click on the **Thrshold** Tab



Slicer indicates the degree of freedom (DoF): Nvol-1



Specify the **p-Value** threshold 0.001 and hit Enter



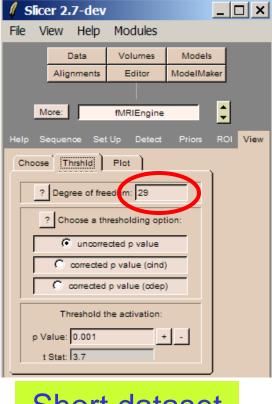
Null hypothesis

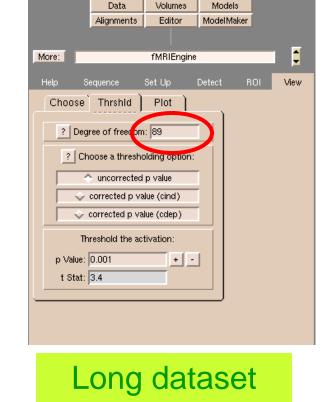
- H0: there is no difference between the right hand condition and left hand condition on the fMRI signal. This is tested at each voxel.
- If the resulting probability is lower than the experiment's alpha value (p <0.001), the null hypothesis can be rejected.



Slicer calculates the corresponding threshold t Stat

File View Help





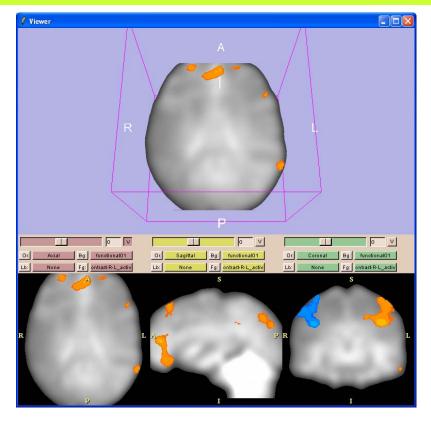
Modules

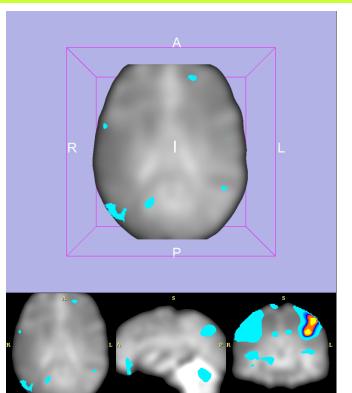
Short dataset t Stat = 3.7

t Stat = 3.4



Slicer displays the activation map overlaid on the fMRI images

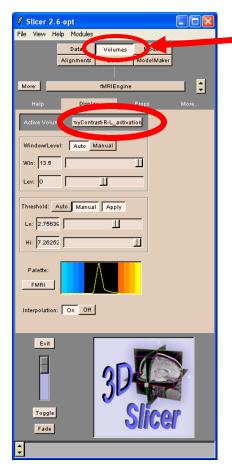




Short dataset



fMRI color palette



Click on the module **Volumes**

Select the panel **Display** and set the Active Volume to be the activation volume **myContrast-R-L_activationMap**

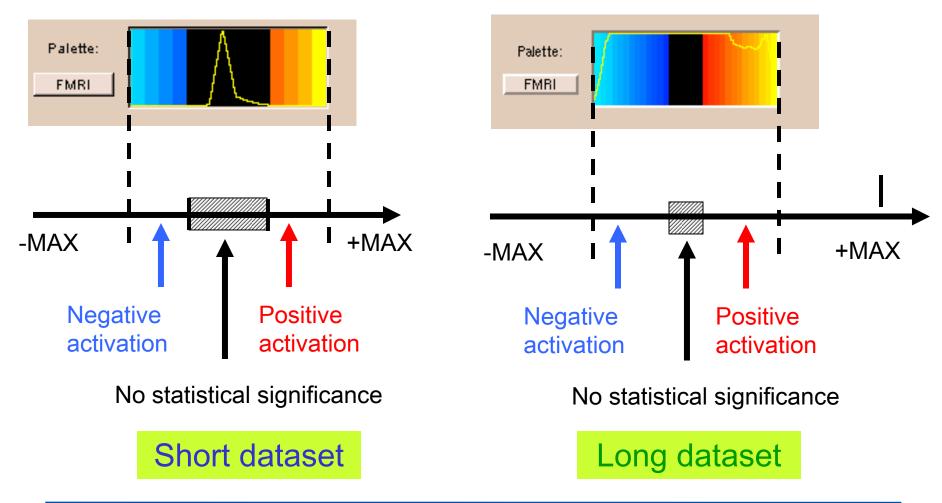


Adjust the **Window** and **Level** of the color palette for the volume **myContrast-R-L_activationMap**



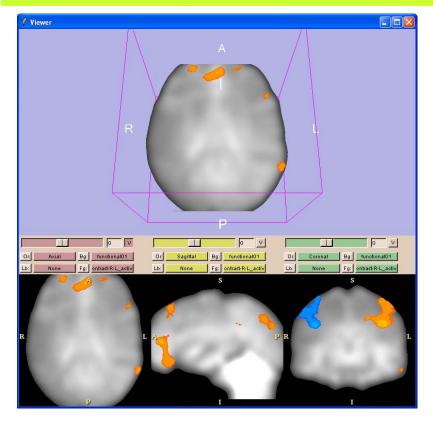


fMRI color palette

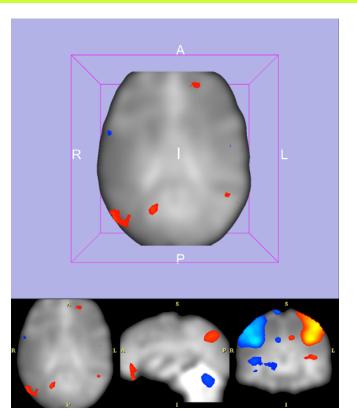




Slicer displays the activation map overlaid on the fMRI images

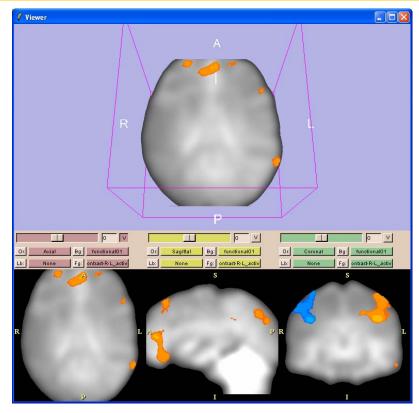


Short dataset

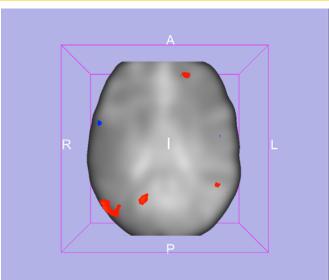


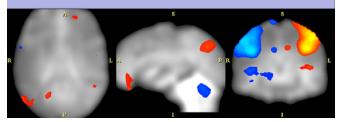


Left click on **Bg** in the 2D anatomical viewers to display the volume **anatomical 3T** in background



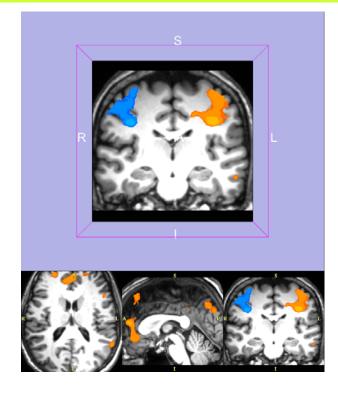
Short dataset



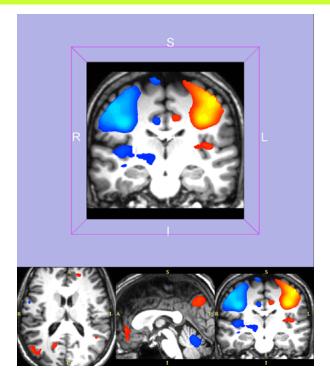




Slicer displays the activation map superimposed on the anatomical images.



Short dataset

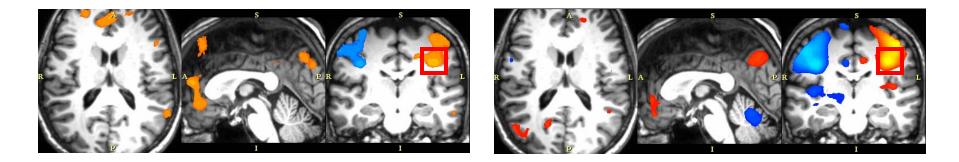




| File View Help Modules | |
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| Data Volumes Models | |
| Alignments Editor ModelMaker | |
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| Help Sequence Set Up Detect ROI View | |
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| ? Cutoff frequency: | |
| Condition: right | Select Timecourse plot option |
| Timecourse | |
| Peristimulus plot | |
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Mouse over labelled area in Slice Window and left click on the pixel $\mathbf{R} = -40 \ \mathbf{A} = \mathbf{0} \ \mathbf{S} = 20$, which is highly significant in the activation map. The left-hemisphere of the subject is shown on the right side of the image, in radiological convention.

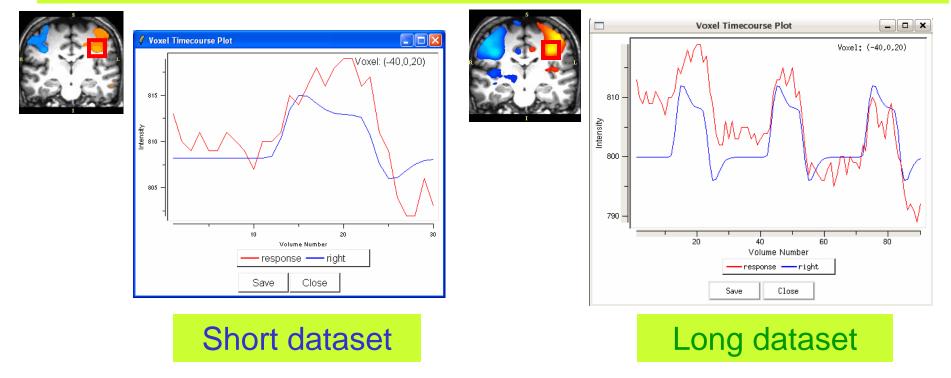


Short dataset

Long dataset



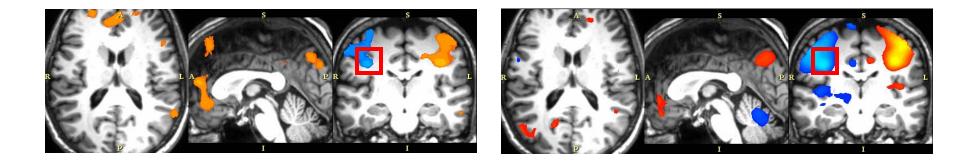
Slicer displays the voxel's actual timecourse (response) plotted with the modeled condition (right *hand*) for the selected voxel.



The graphs show a good correlation between the observed BOLD signal Y(t) and the model.



Mouse over labelled area in Slice Window and left click on the pixel $\mathbf{R} = \mathbf{40} \ \mathbf{A} = \mathbf{0} \ \mathbf{S} = \mathbf{20}$, which is highly significant in the opposite direction.

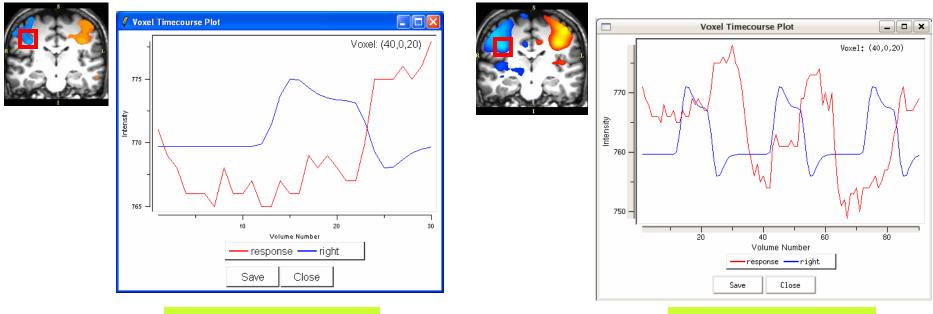


Short dataset

Long dataset



Slicer displays the voxel's timecourse plotted with the modeled condition for the selected voxel



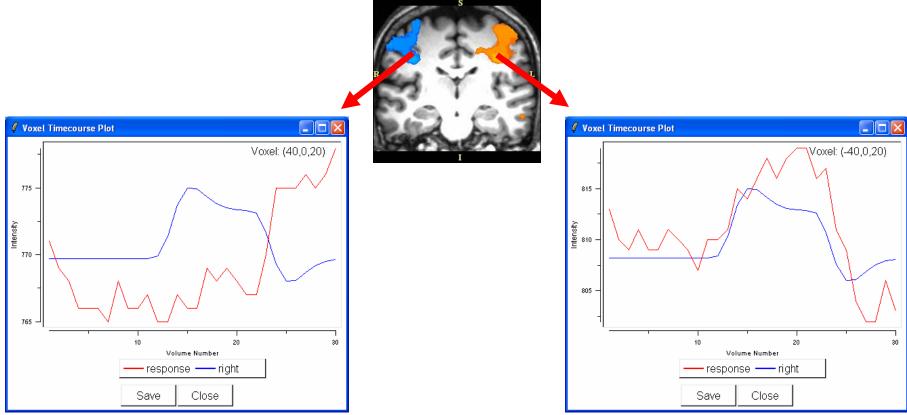
Short dataset

Long dataset

If we were plotting the left hand condition, what correlation would be observed?



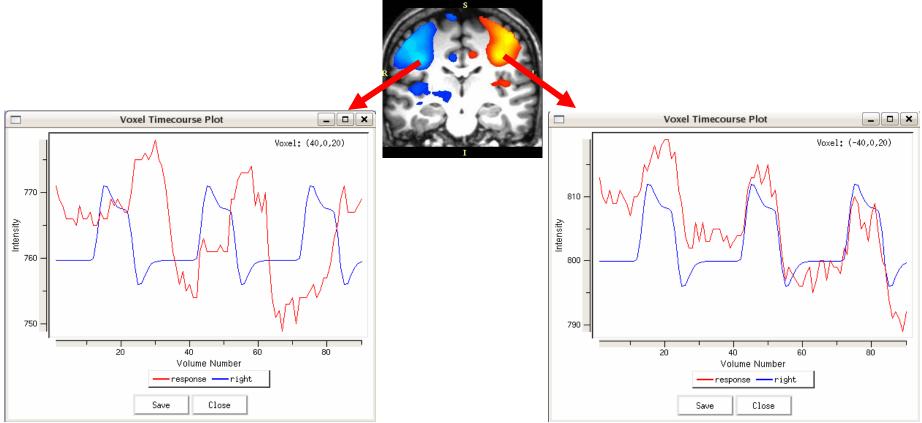
Contralateral side vs Ipsilateral side (short dataset)



During the **right hand condition**, the observed signal decreases in the ipsilateral side and increases on the contralateral side.



Contralateral side vs Ipsilateral side (long dataset)



During the **right hand condition**, the observed signal decreases in the ipsilateral side and increases on the contralateral side.



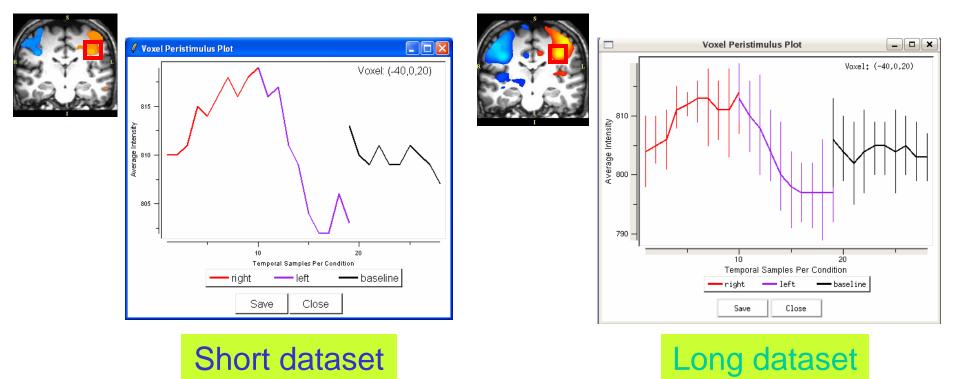
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Select **Peristimulus plot** option and click on the voxel (-40,0,20) in the positive activation region



Voxel Peristimulus Plot

Slicer displays a plot of the mean time course values of the selected voxel in the positive activation region during different blocks.





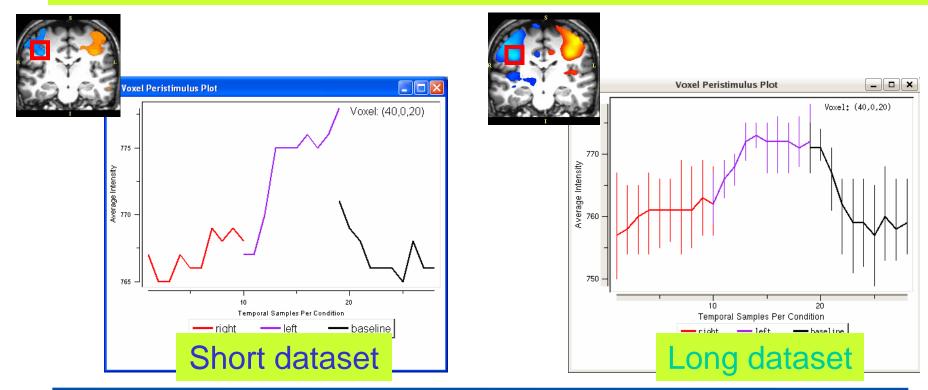
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Select **Peristimulus histogram** option and click on the voxel in the negative activation region (40,0,20)



Voxel Peristimulus Plot

Slicer displays a plot of the mean time course values of the selected voxel in the negative activation region during different blocks.





| Slicer 2.7-dev |
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| File View Help Modules |
| Data Volumes Models Alignments Editor ModelMaker |
| More: fMRIEngine |
| Help Sequence Set Up Detect Priors ROI View |
| RegionMap Stats |
| Label map: Load _ |
| Load a label map: |
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 Select the ROI panel and RegionMap tab
 Choose New Activation from Label map



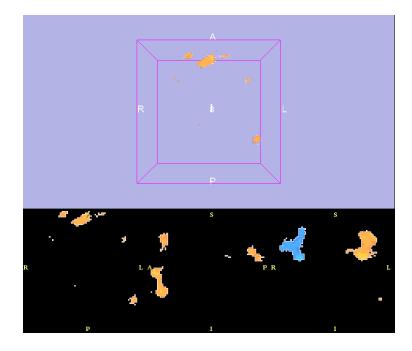
Activation-based region of interest

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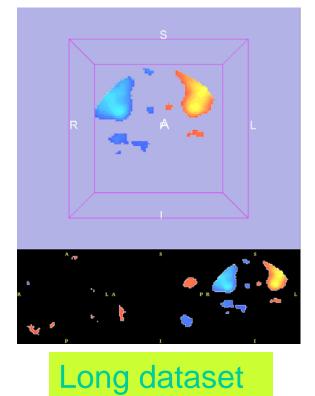
Click Create label map from activation, and wait while activation "blobs" are labelled

Activation-based region of interest

The label map is shown in Foreground, and the activation map is shown in Background.



Short dataset





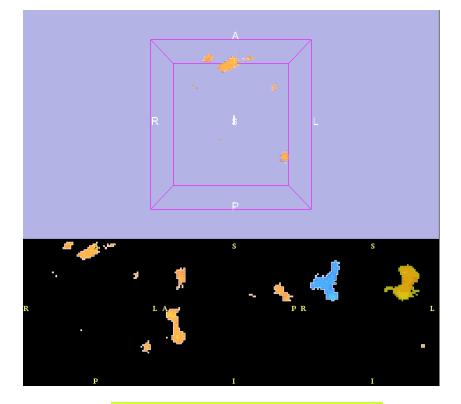
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| | Region statis | tics: | | |
| ? Selec | t label(s) by cli | cking region(s |). | |
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| | Plot time se | ries | | |
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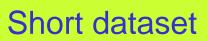
Select the subtab **Stats** Select one or multiple regions in the left hemisphere to include in analysis by clicking in Slice Window.

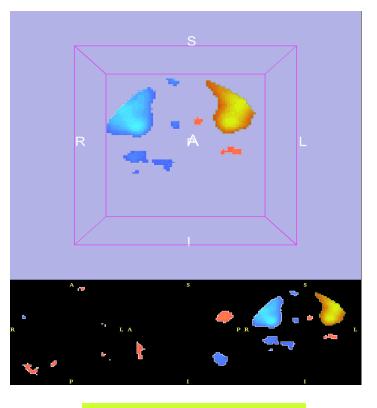
Select the condition right.



The selected regions appear in green.







Long dataset

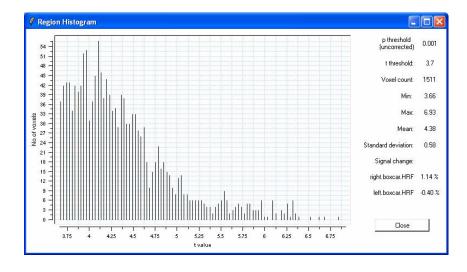


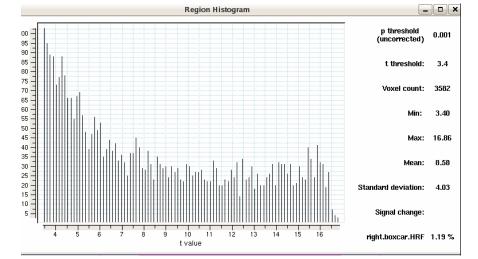
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| More: fMRIEngine | |
| Help Sequence Set Up Detect ROI View RegionMap Stats | |
| Region statistics: ? Select label(s) by clicking region(s). | |
| Show stats | |
| Save region voxels Region plot: | |
| Condition: right | |
| Timecourse Peristimulus plot | |
| Plot time series | |
| Clear selections | |
| | |

Click **Show stats** to display the statistics for the selected regions



Slicer displays the statistics for the selected region(s)





Short dataset



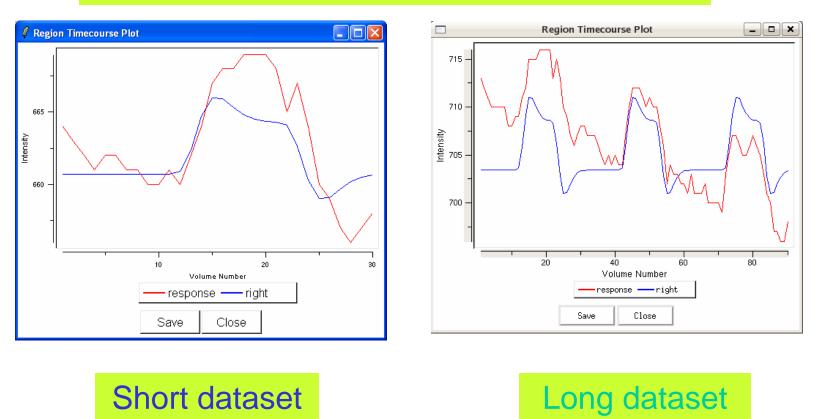


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Select **Timecourse plot** option and click on **Plot time series** for this region.



Slicer displays the region timecourse plot





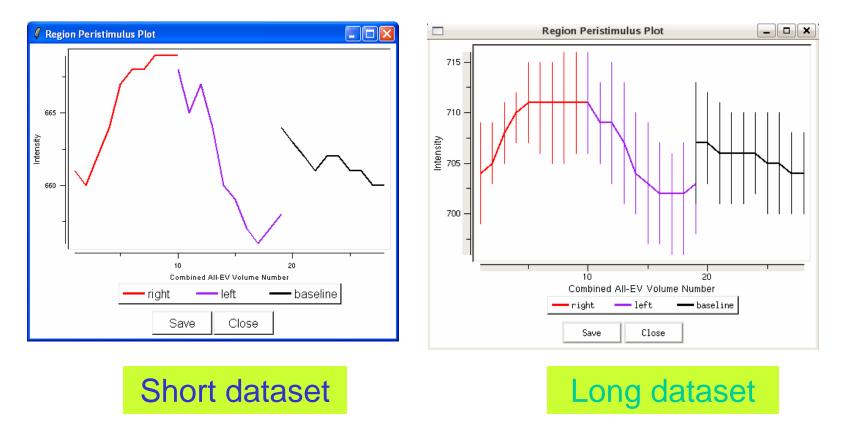
Region Peristimulus Plot

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Select **Peristimulus plot** and click **Plot time series** for this region.



Slicer displays the Region Peristimulus Plot



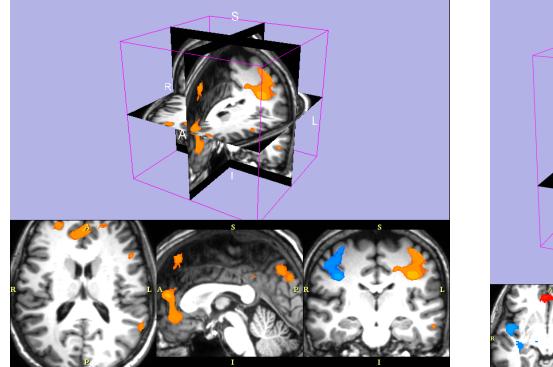


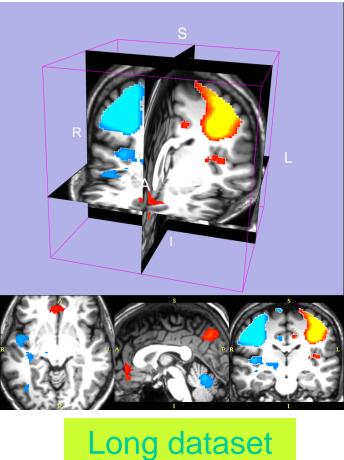
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Click on Clear selections and display the structural volume **anatomical3T** in the background (**Bg**) and the activation map **myContrast-R-L_activation** in the foreground (**Fg**).

Display three anatomical slices in the 3D Viewer.







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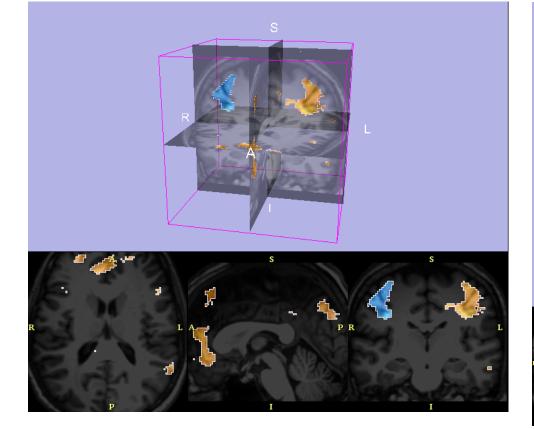
Short dataset

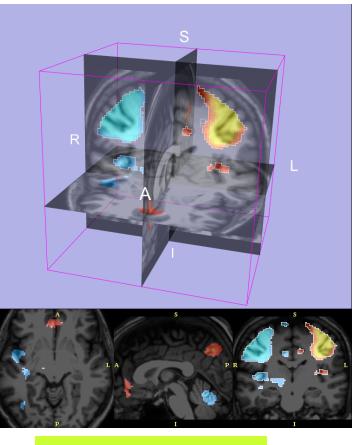




Fade in the activation volume for a good view of combined data







Short dataset

Long dataset



Conclusion

- Analysis and visualization of fMRI data
- Framework activation detection algorithms and inference engines
- Open-Source environment