Functional Image Analysis with a General Linear Model (GLM).

a.k.a "spm" for fun and profit

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Image Analysis Goals

1) Does condition X yield a change in function?

2) Where do activations occur?

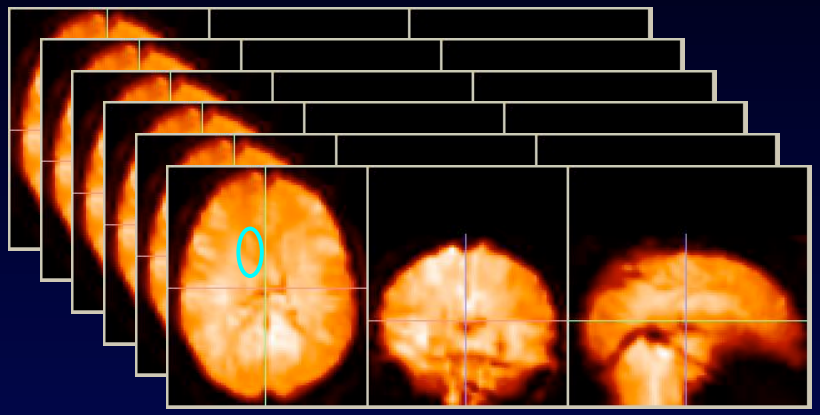
3) Where do interesting activations occur?

4) Are these activations significant?

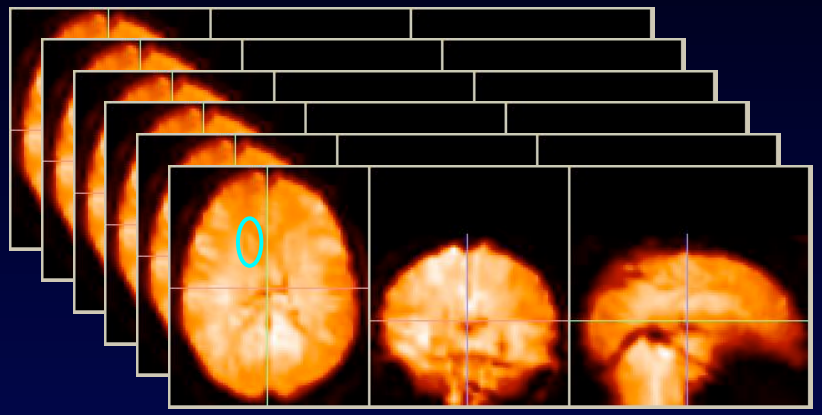
5) How does an activation compare to others for the same condition? Other conditions? Within and across subjects?

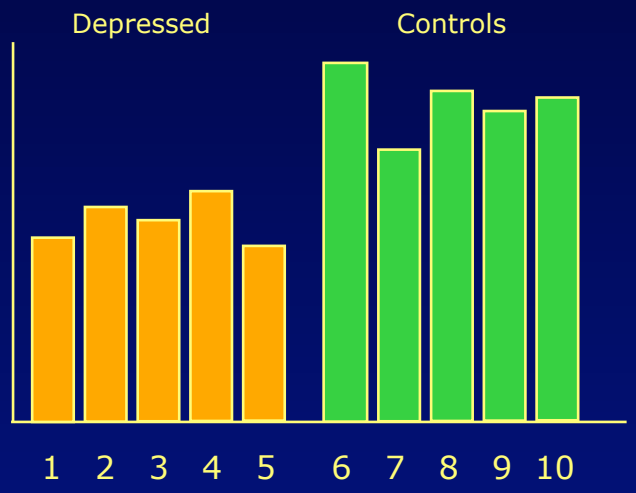
Region of Interest (ROI) Analysis

Depressed



Controls

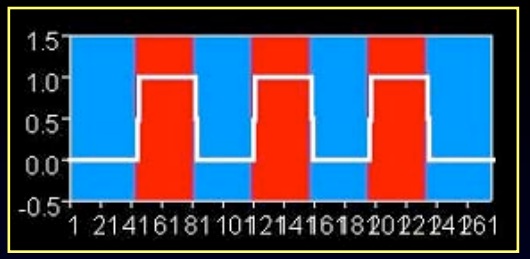


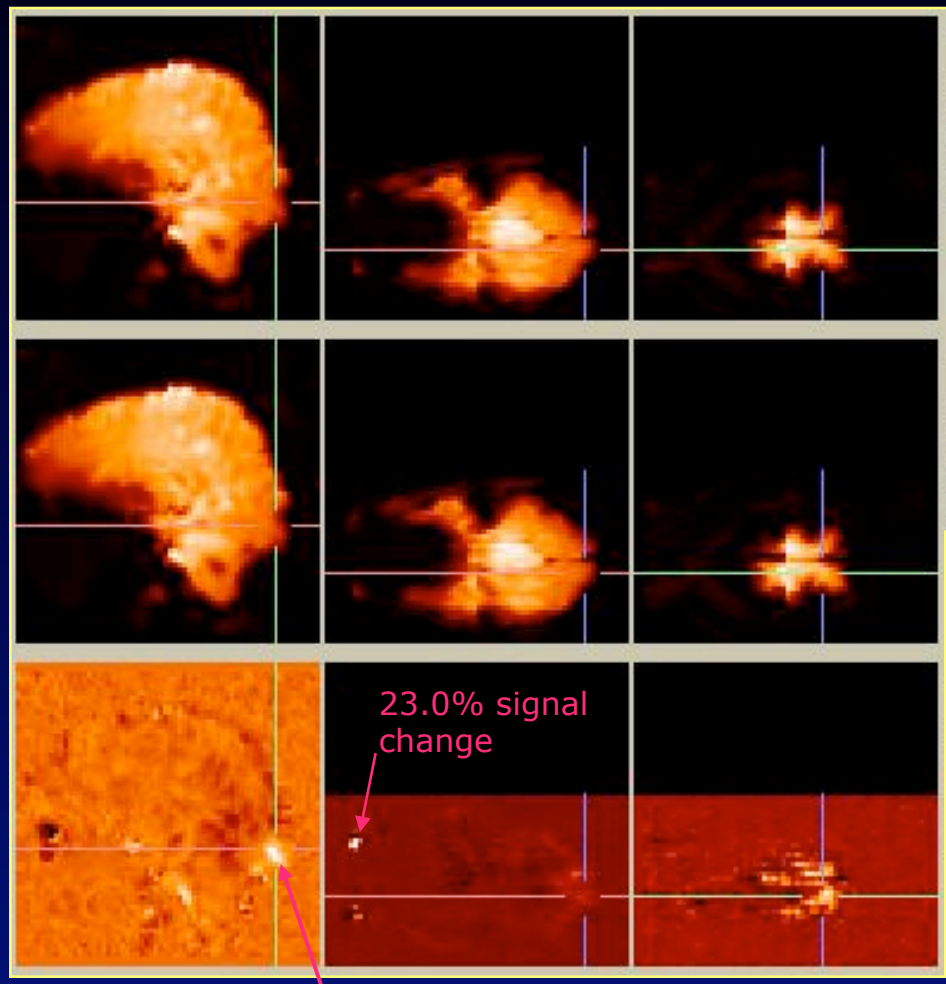


Where to draw ROIs?

How to assign variance?

Subtraction Image: finding differences

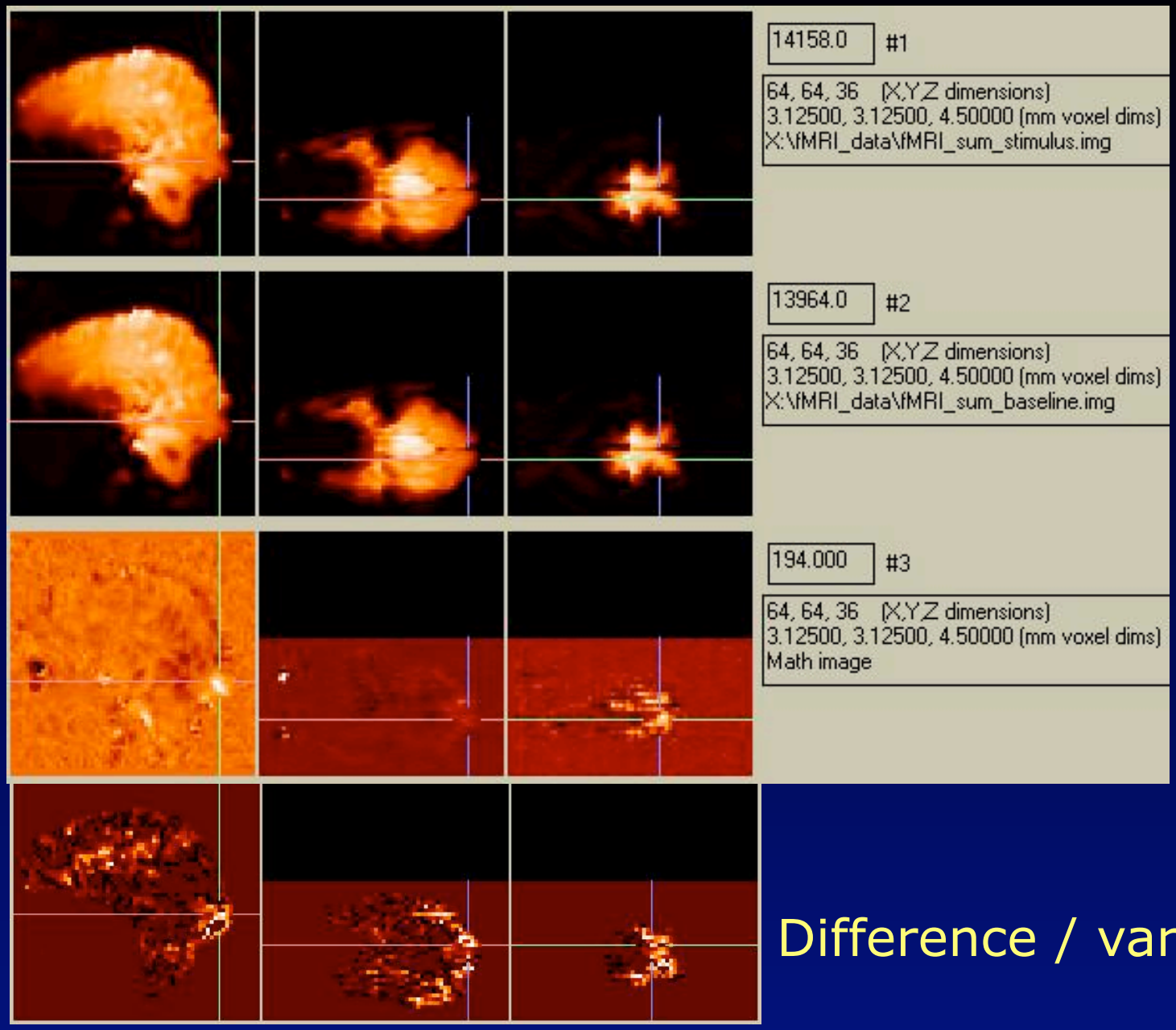




Is the difference in the brain?

Is the difference really due to changes in brain function?

But is it Reliable?



Difference / variance

Hypothesis Driven Research:

A systematic approach to proving hunches.

Most of the time, we find what we are looking for… even when we shouldn't.*

Science can also involve a discovery.

*Steve Kornguth & Frank Siegel

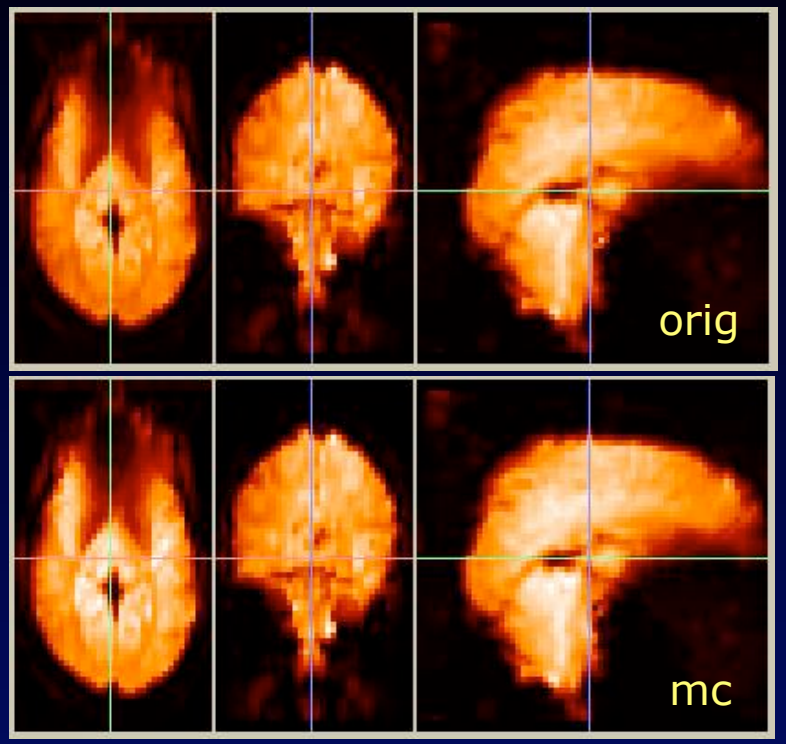
Preprocessing

Goals:

- Focus on structure(s) of interest
- Increase sensitivity, specificity

- Motion correction
- Slice-timing correction
- Coregistration to a template
- Mask the brain
- Spatial, temporal smoothing
- Normalize to a global average

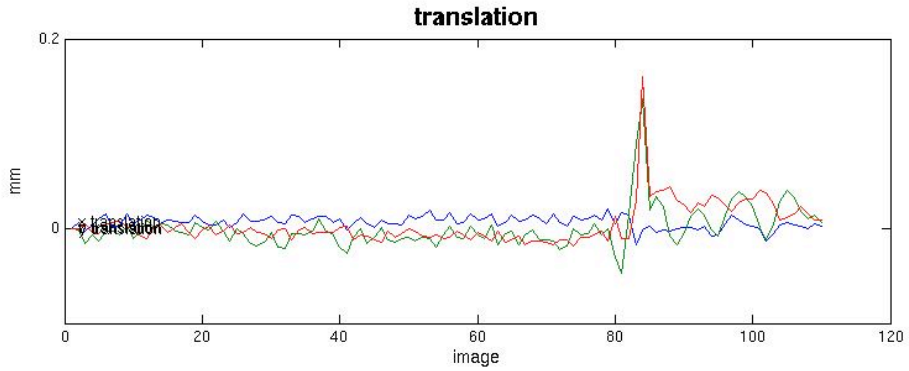
Motion correction

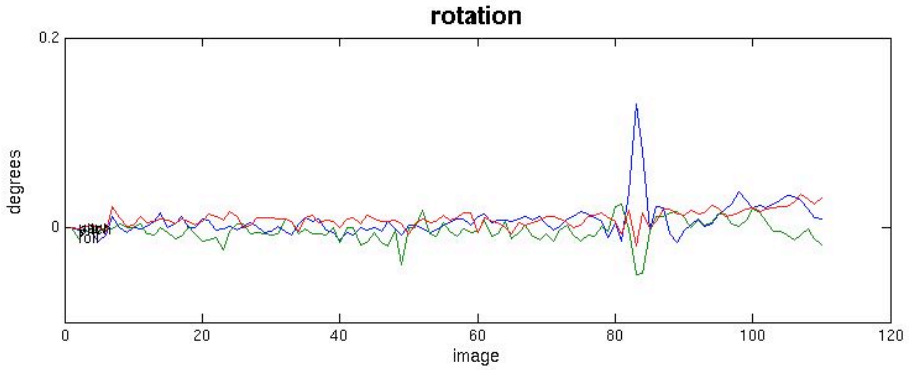


Print | Clear | ColorMap | Effects | cut | move | resize | text | edit

Image realignment

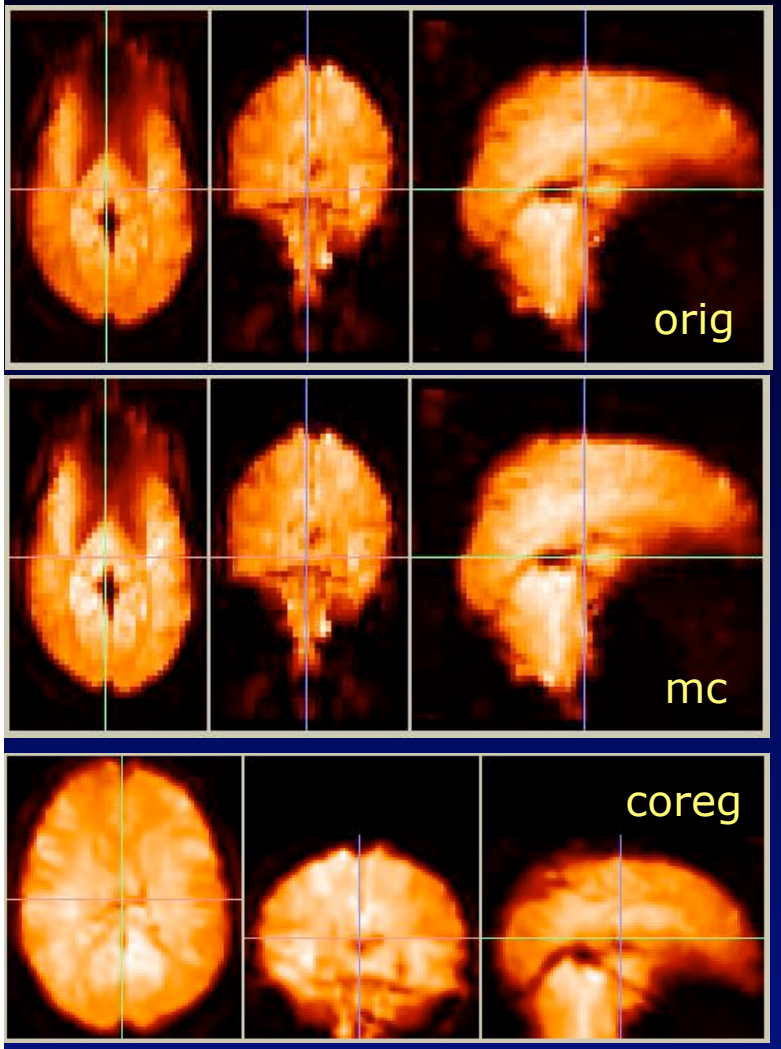
1 /scratch/fMRI_data/data/fMRI_vis_stim_0000.img
2 /scratch/fMRI_data/data/fMRI_vis_stim_0001.img
3 /scratch/fMRI_data/data/fMRI_vis_stim_0002.img
4 /scratch/fMRI_data/data/fMRI_vis_stim_0003.img
5 /scratch/fMRI_data/data/fMRI_vis_stim_0004.img
6 /scratch/fMRI_data/data/fMRI_vis_stim_0005.img
7 /scratch/fMRI_data/data/fMRI_vis_stim_0006.img
8 /scratch/fMRI_data/data/fMRI_vis_stim_0007.img
9 /scratch/fMRI_data/data/fMRI_vis_stim_0008.img
10 /scratch/fMRI_data/data/fMRI_vis_stim_0009.img
11 /scratch/fMRI_data/data/fMRI_vis_stim_0010.img
12 /scratch/fMRI_data/data/fMRI_vis_stim_0011.img
..... etc





SPM99 (oakes): 11:50:56 - 27/02/2002

Coregistration to a template



Print Clear ColorMap Effects cut move resize text edit

Spatial Normalisation

Image : /scratch/fMRI_data/data/meanfMRI_vis_stim_0000.img

Parameters : /scratch/fMRI_data/data/meanfMRI_vis_stim_0000_sn3d

Linear {affine} component – image flipped

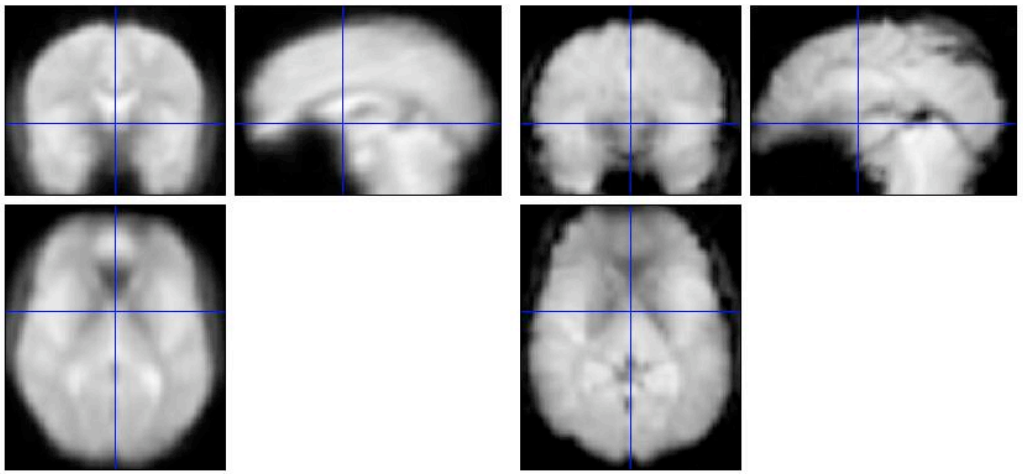
X1 = −0.953*X −0.007*Y +0.039*Z +1.241

Y1 = 0.059*X +0.914*Y +0.035*Z −19.540

Z1 = 0.035*X −0.172*Y +0.941*Z −0.722

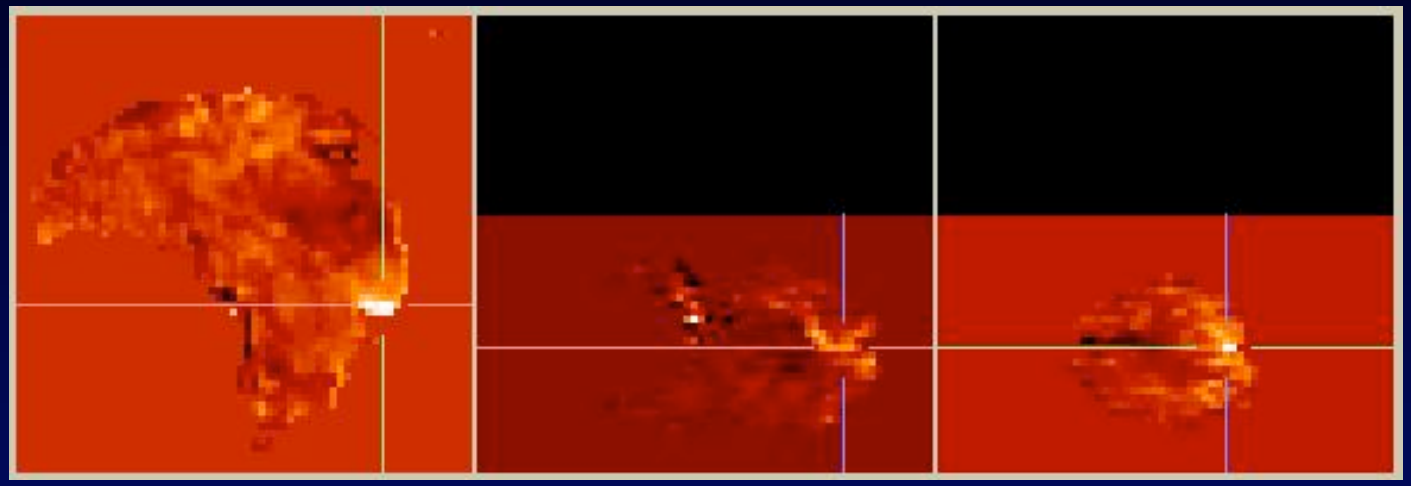
12 nonlinear iterations

7 x 8 x 7 basis functions



(4) Gimp [SPM_analy...] [oakes@ver...] oakes@verv...

Masking



Threshold = 7000 (range = 0-25000)

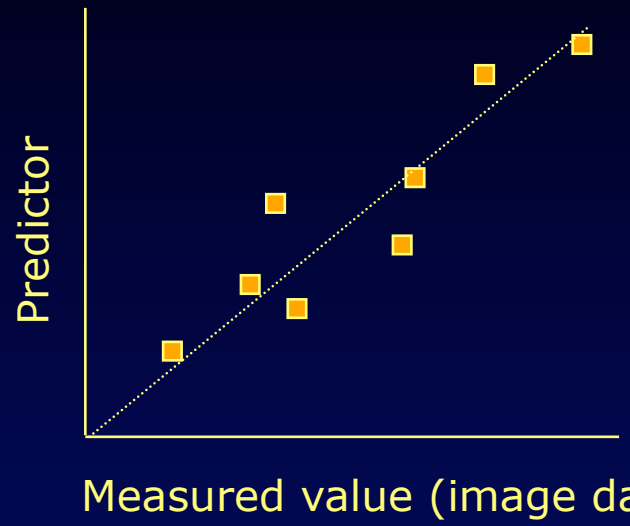
SPM:
statistical parameteric map

A map showing the location, spatial extent, and relative magnitude of statistically significant activations to an experiment.

Software:

- AFNI (fMRI)
- BrainVoyager (fMRI)
- fmristat (fMRI, PET)
- FSL (fMRI)
- SPM2 (fMRI, PET)
- VoxBo (fMRI)

General Linear Model (GLM)



$$Y_i = (\beta * X_i) + c + E_i$$

Effect magnitude

Uncertainty (error)

Student's t-statistic:

$t = \beta / E$

All statistics are calculated voxelwise.

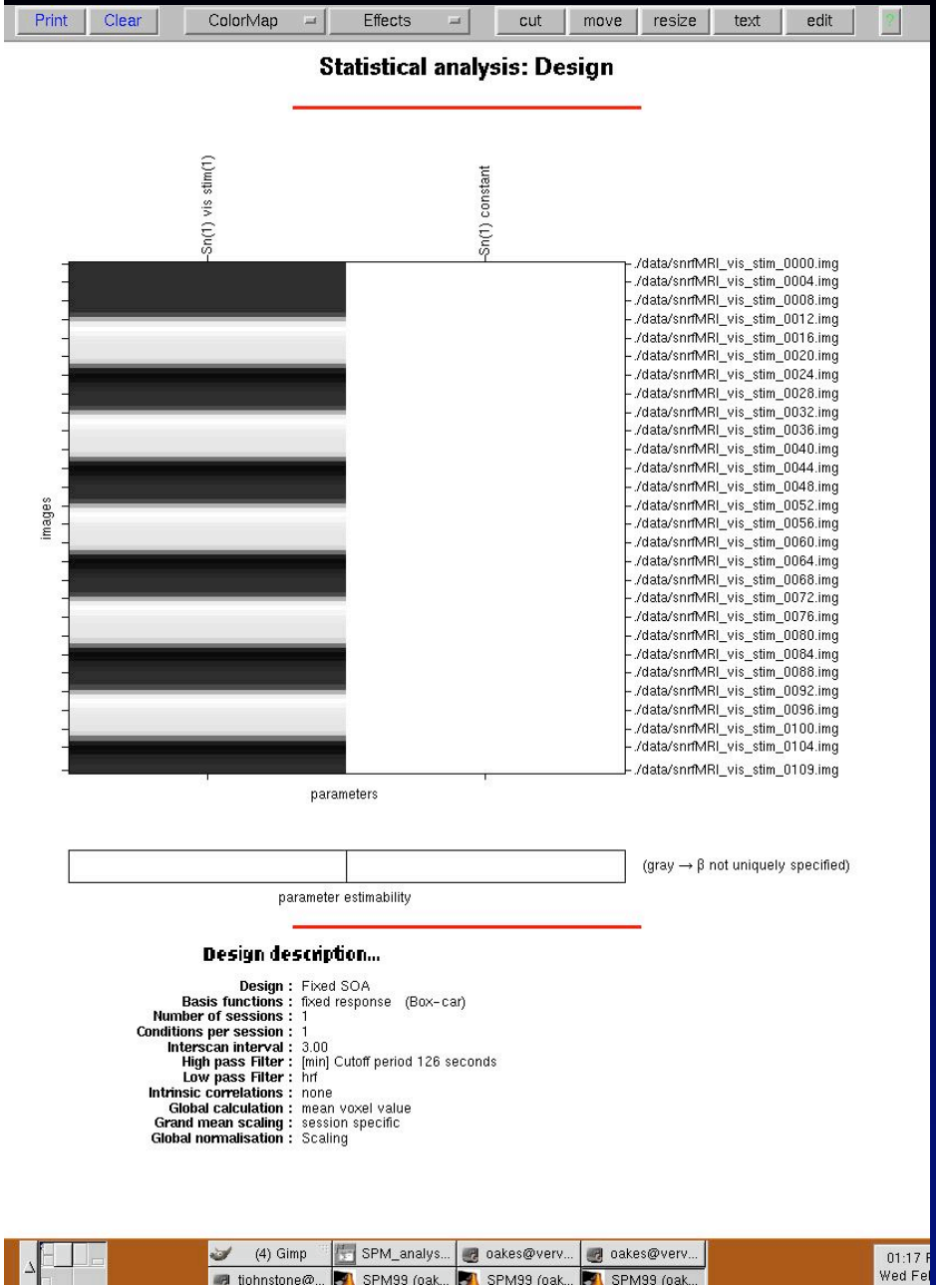
Best GLM explanation: http://www.mrc-cbu.cam.ac.uk/Imaging/Common/spmstats.shtml

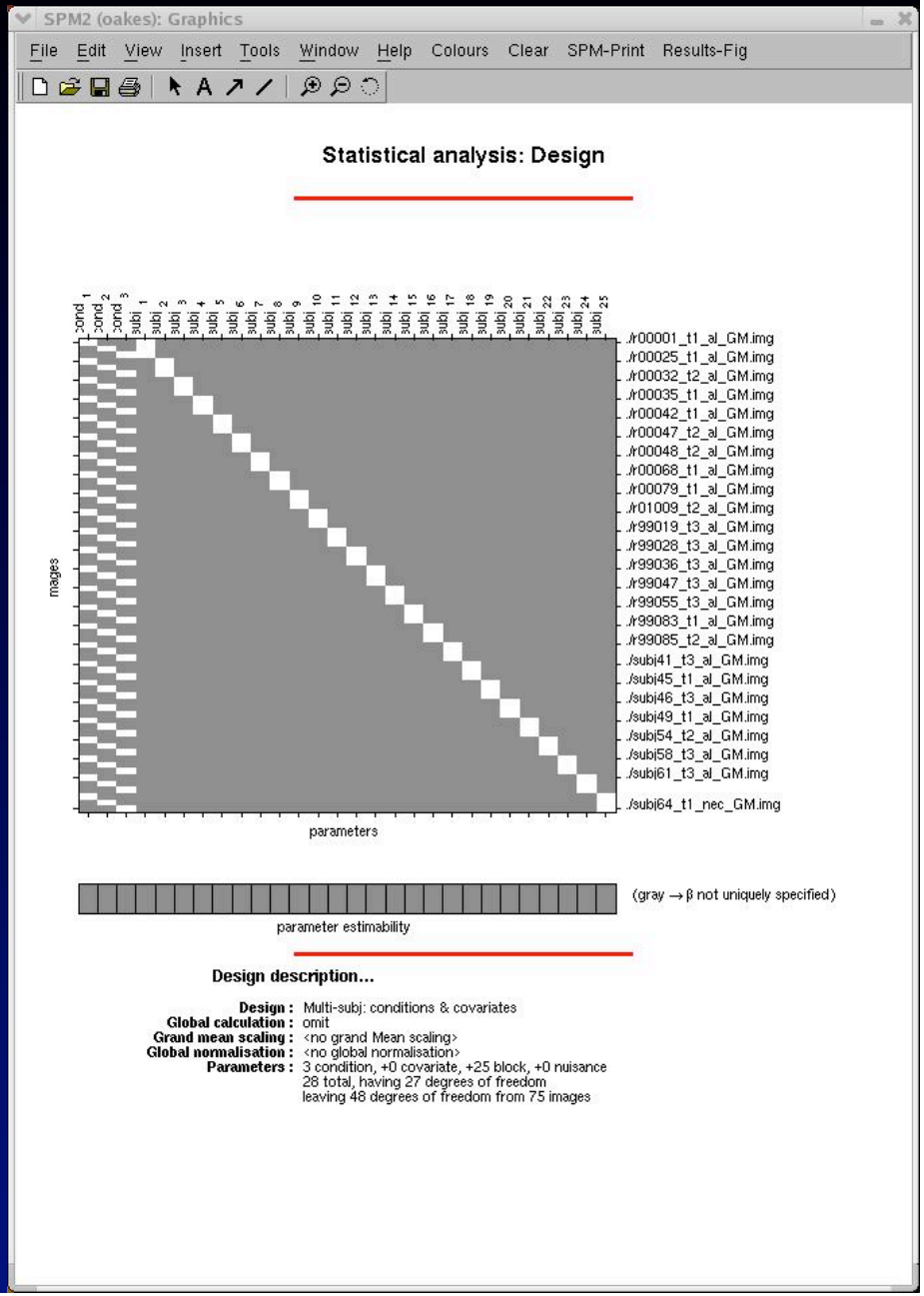
GLM parts

- β-estimates (effect magnitude)
- contrast indicators
- con*** (t-stat) or ess*** (F-stat)
- ResMS (residual error)
- spmT*** or spmF***

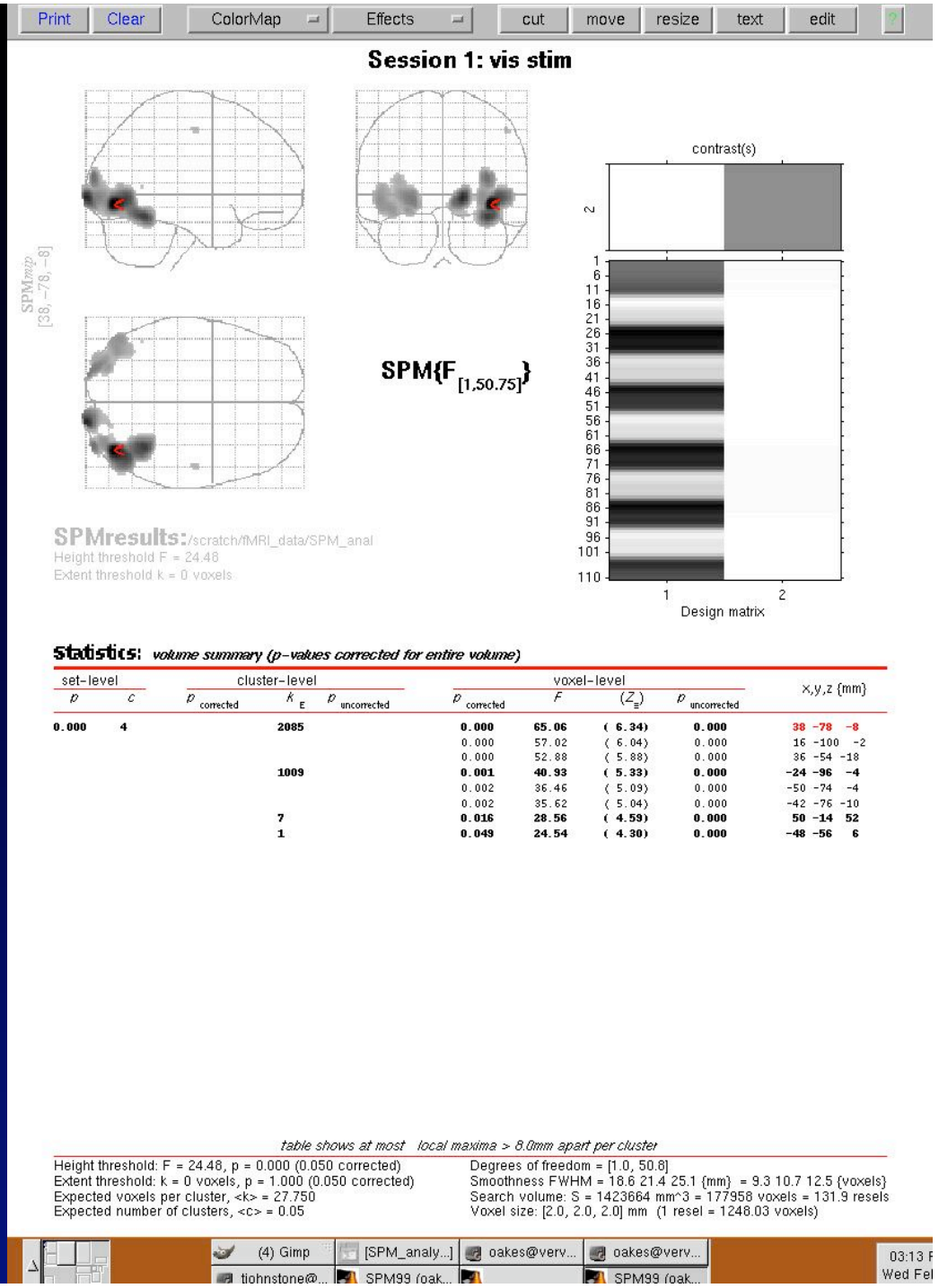
$$Y_i = (\beta * X_i) + c + E_i$$

SPM2 design matrix

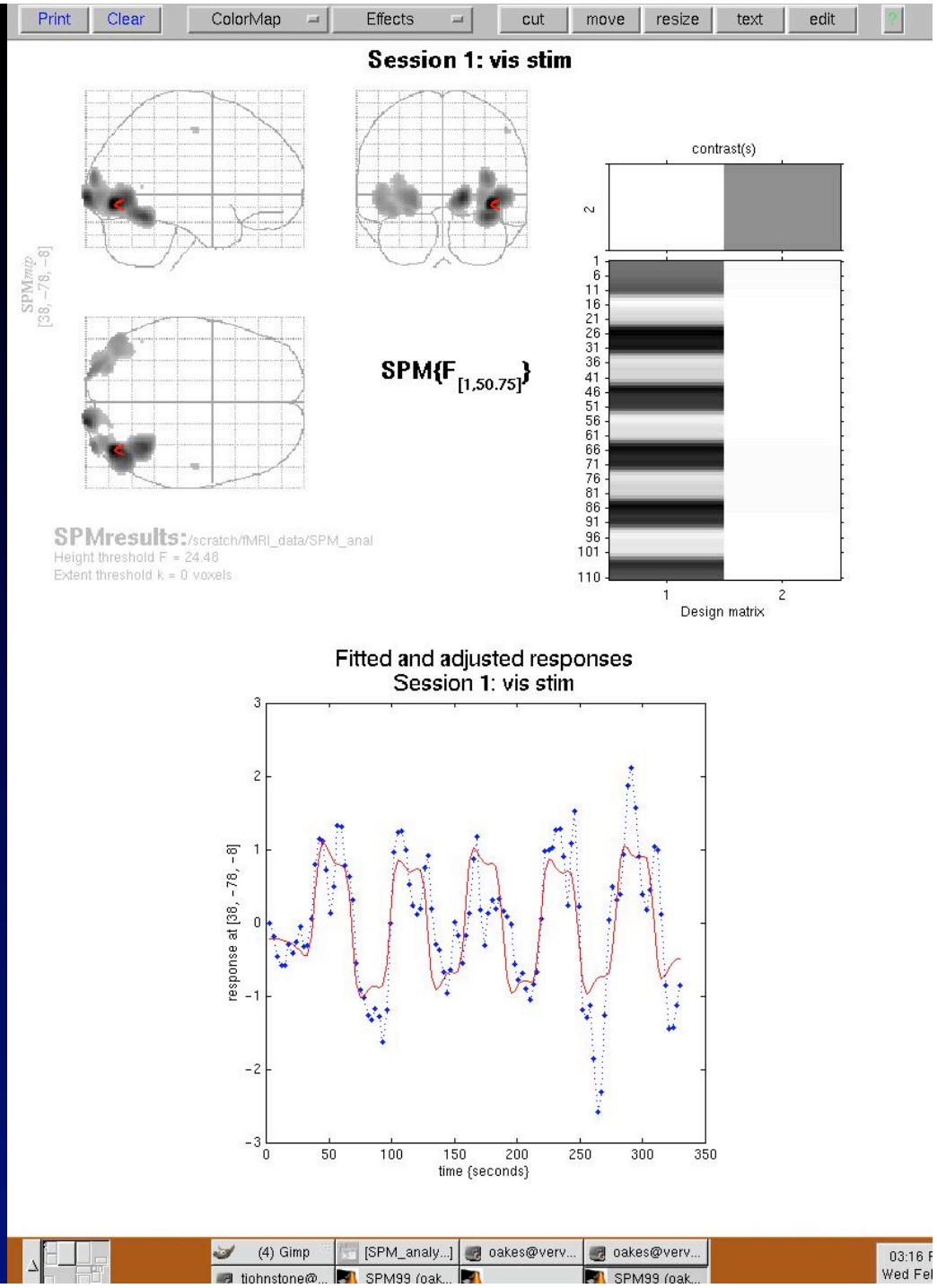




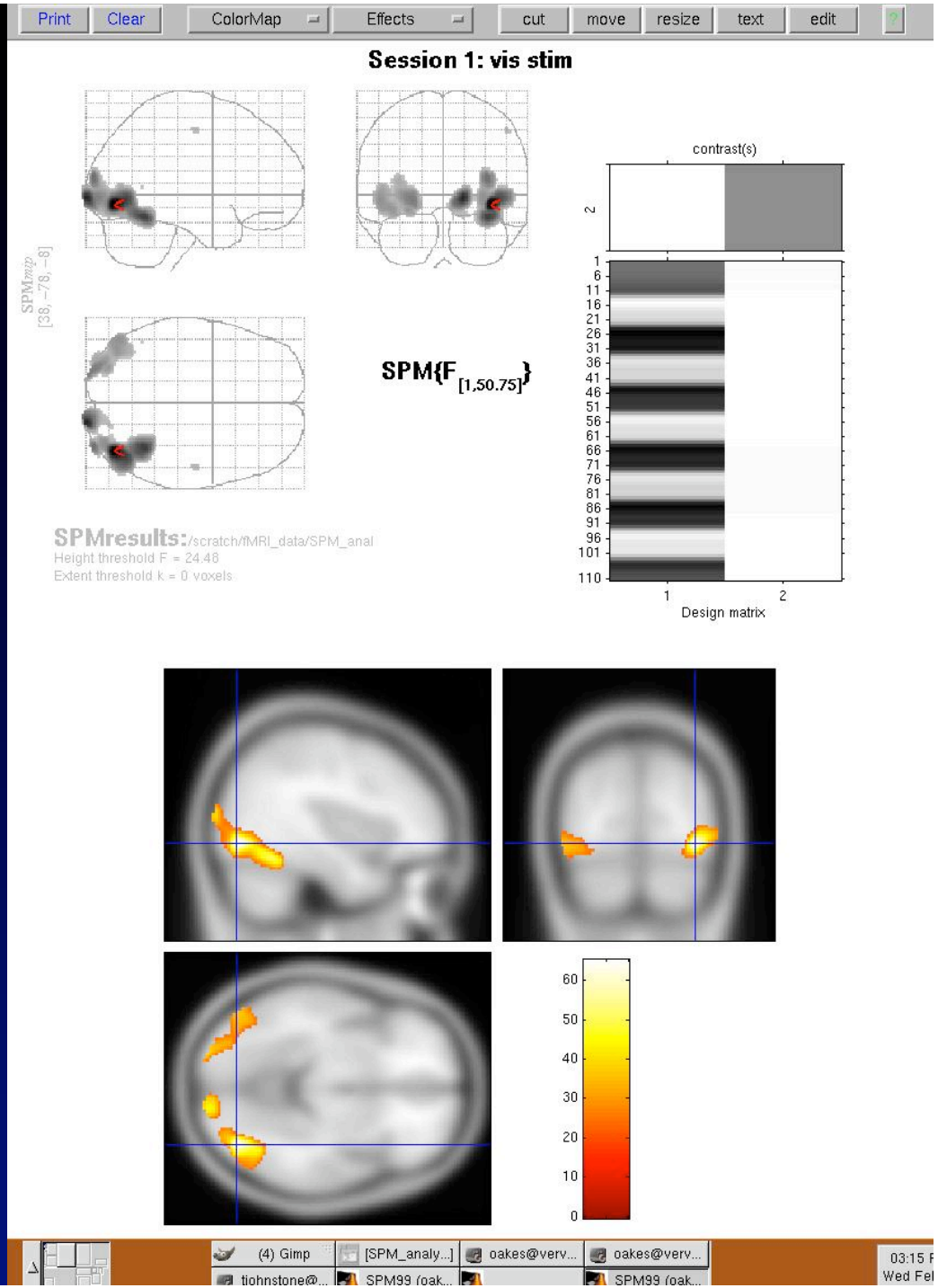
Results example



Plot of data and fit



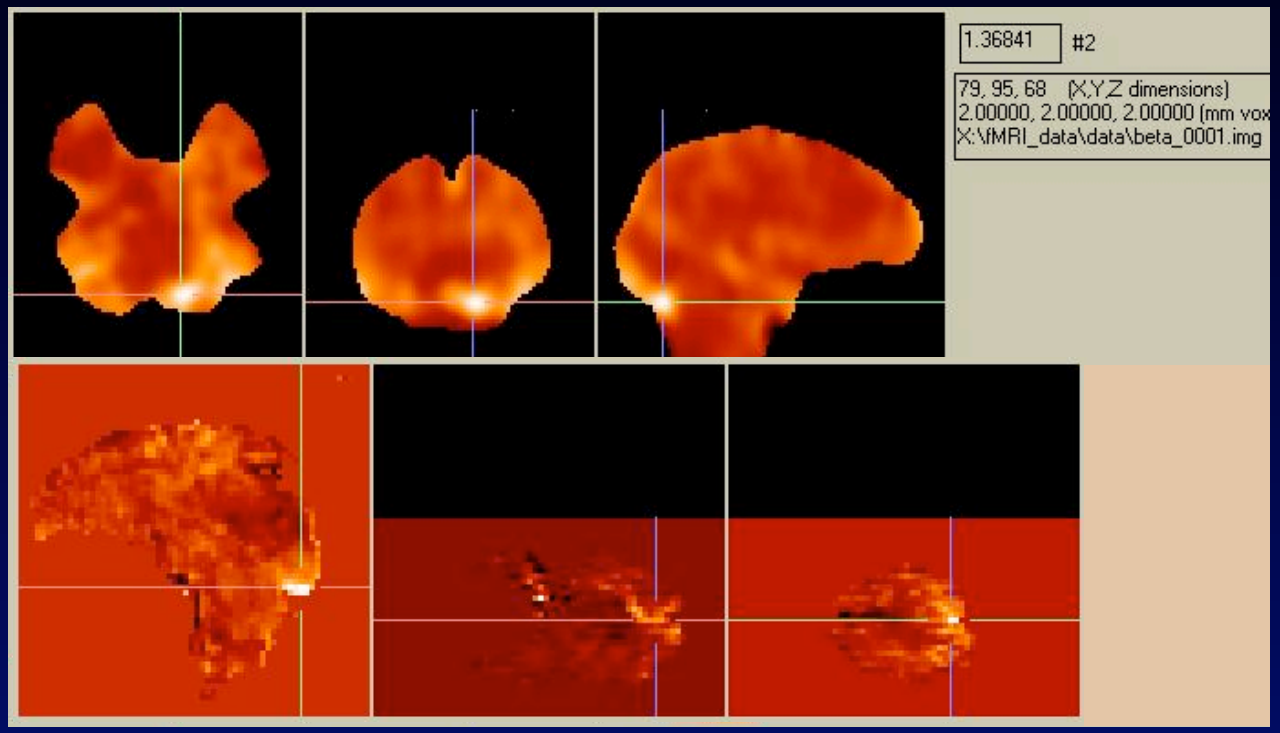
Results: overlay



GLM effect size

SPM β image

Subtraction image



GLM components from SPM

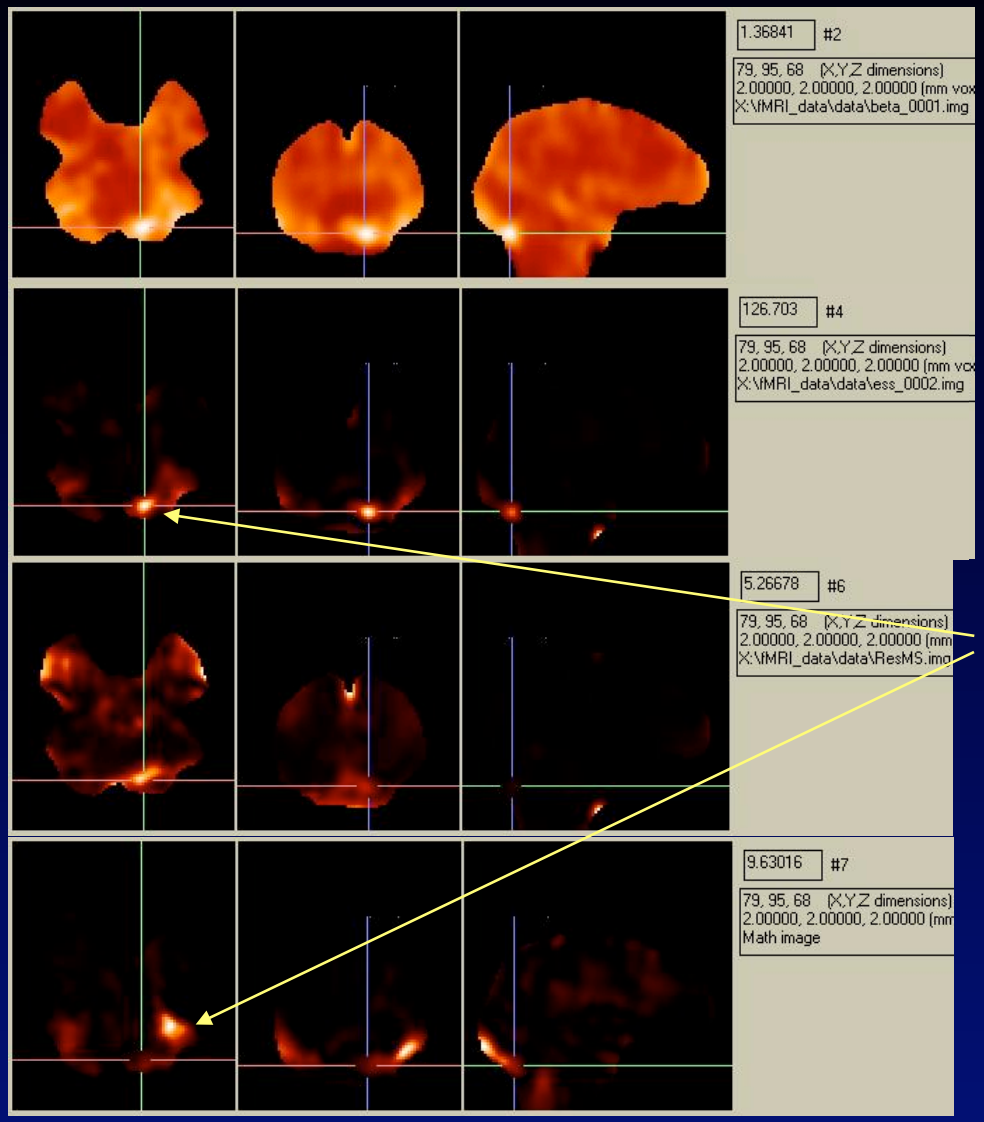
β image

β image weighted with contrast

error estimate

t-statistic map:

$$\frac{\text{weighted } \beta}{\text{error}}$$



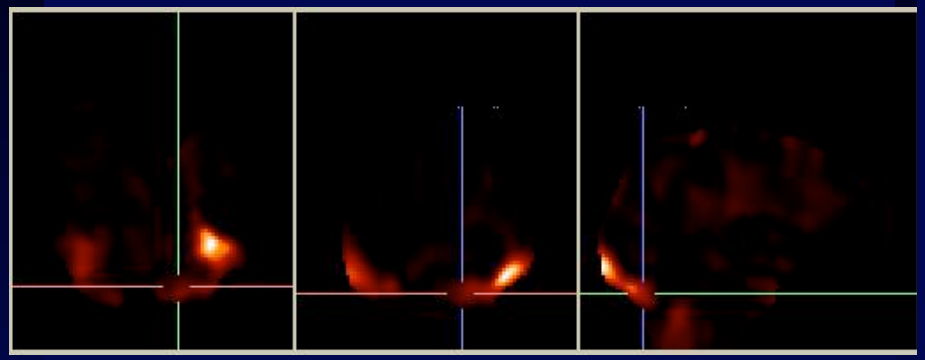
Why the difference?

The spm shows where we are SURE there is a difference.

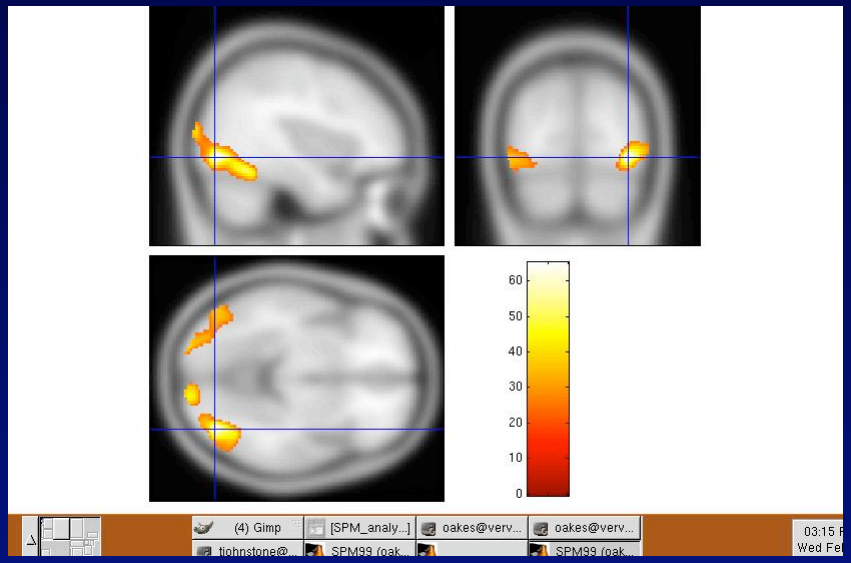
This is different than a subtraction image, which shows areas of large but possibly unreliable differences.

Thresholding

- Localization
- Remove non-significant regions
- Compare cluster sizes



How do we get clusters from a continuous spm?



Statistical threshold:
$p < 0.05$

Limit results to the most significant pixels (95% confidence level).

Approx. 500,000 pixels in the brain!
=> 25,000 significant pixels.

Multiple Comparisons

Bonferroni correction: $p' = p / N$

$p' = 0.05 / 500{,}000 = 1.0e\text{-}7$

Too conservative!

Most image data are not independent.

Challenge: find N which represents the true number of independent data points.

In SPM and fmristat, this is done via Random Field Theory and resolution elements (resels).

Sample GLM script with fmristat

```
hrf_parameters = [5.4 5.2 10.8 7.35 0.35];
frametimes = (0:138)*2;
slicetimes = zeros (1, 30);
onsets = [5 22 39 56 73 90 107 124 141 158 175 192 209 212 217 220 224 230 235 241 244 248 253 257];
eventid = [1 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2];
duration = zeros( 1,24);
height = ones( 1,24);
events = [ eventid', onsets', duration', height' ]

X_cache = fmridesign( frametimes, slicetimes, events, [], hrf_parameters )

imagesc( squeeze( X_cache.X( :,1,1,:) ))        % hrf go
imagesc( squeeze( X_cache.X( :,2,1,:) ))        % hrf nogo
imagesc( squeeze( X_cache.X( :,1,2,:) ))        %hfr deriv go

contrast = [1 0;  % slow only
            0 1;  % fast only
            1 1]; % both

which_stats = [1 1 1 1 1 1 1 1 1];

[mtr_df_016 p] = fmrilm( filename, output_file_base, X_cache, contrast, [], which_stats )

% saves workspace as fmristat.mat to task directory
save /study/fMRI_tools/analysis/fmristat/016/mtr/fmristat.mat

% load workspace & view different stats images
load /study/fMRI_tools/analysis/fmristat/016/mtr/fmristat.mat

t_file = '/study/fMRI_tools/analysis/fmristat/016/mtr/both_Stat_mag_t.img';
view_slices( t_file, maskfile );

blur_file = gauss_blur ( t_file, 8, '/study/fMRI_tools/analysis/fmristat/016/mtr/both_t')

sigT = stat_threshold( 3.75*(64*64)*30*5, 64*64*30, 0, mtr_df_016);
glass_brain( t_file, sigT, maskfile );
```

Web resources

http://brainimaging.waisman.wisc.edu/~oakes/spm/visual_stim_demo/fmri_visual_stim.html

http://www.mrc-cbu.cam.ac.uk/Imaging/Common/spmstats.shtml