

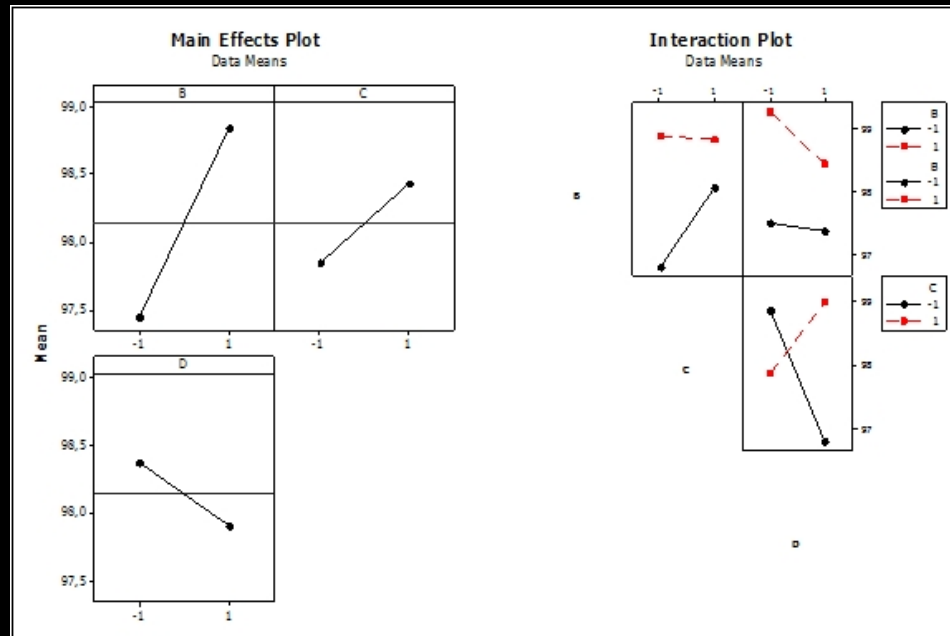
GLM Flex & tools

A toolbox for fMRI analysis

T. Chaminade

Factorial plan

		F ₁ 1		F ₁ 2
F ₂ 1		F ₁ 1 F ₂ 1		F ₁ 2 F ₂ 1
F ₂ 2		F ₁ 1 F ₂ 2		F ₁ 2 F ₂ 2

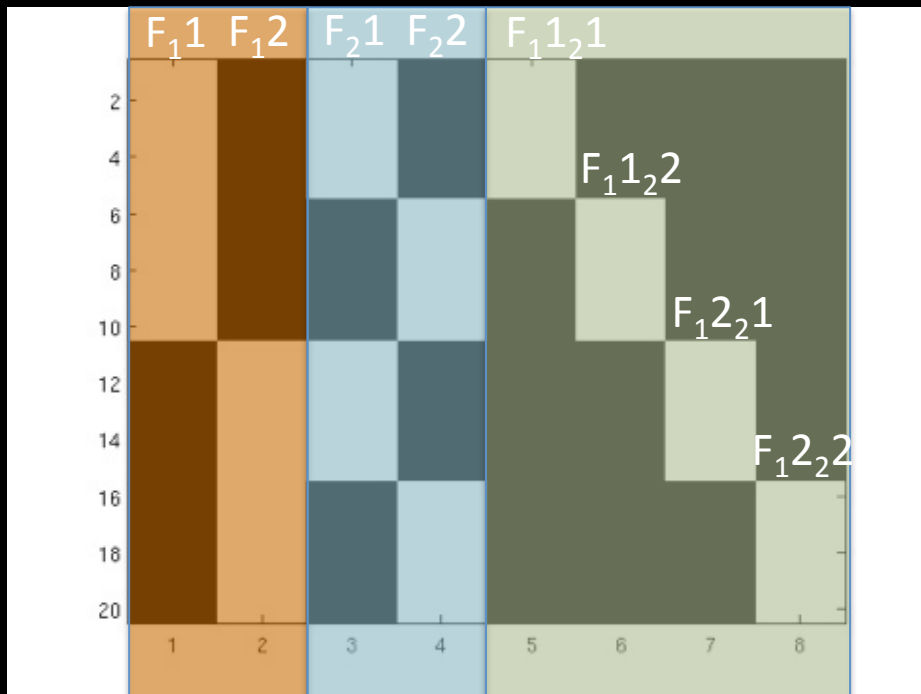


Why using GLM Flex

Copied shamelessly from http://nmr.mgh.harvard.edu/harvardagingbrain/People/AaronSchultz/GLM_Flex_Intro_.html + help from Scott Love

- 1. GLM Flex uses partitioned error terms.

The way this works is through the addition of **additional interaction terms into the GLM model**. For instance, a simple mixed design measures ANOVA **has two error terms**. The **between subjects error term is computed from the total variance of the Subject Factor** (minus any between effects), and the **within factor error term is computed from the Subject by Within-Factor interaction minus all other effects and error terms**. Note that the Subject by Within Factor interaction is an identity matrix and will capture 100% of the variance in the data. After subtracting out the other bits we are left with the model residual which is what SPM uses. In practice I've set things up so that the "Final" interaction term that would result in an identity matrix is left out of the model, and the full model residual is used as is.



You have 2 error terms in your model:

- (1) **Between-subject effects**; and
- (2) **Within-subject effects**

There is never a error term for interactions of the between-subject and within-subject factors. For those interactions, you use the within-subject error for that factor.

You can end up with more error terms when you have multiple within-subject error terms. For example, if there was 2 within-subject factors:

- (1) Between-subject effects;
- (2) Within-subject factor 1 effects;
- (3) Within-subject factor 2 effects; and
- (4) Interaction of factor 1 and factor 2 effects.

Donald McLaren

(shamelessly again, from GLMFlex forum:

https://groups.google.com/forum/#!forum/fmri_matlab_tools)

Why using GLM Flex

- **4. GLM Flex can be used to run analyses with more factors than SPM8 will allow.**

Allows for **up to 6 factors** (SPM8: 3), that can be defined as within-subject or between-subject factors (6-way interactions!)

- **6.Variance (heteroscedasticity=unequal variance) and Independence Corrections;**

I borrowed the methodology from this directly from spm and I use the **spm_reml script to estimate the variance and covariance hyper-parameters**. The variance-covariance correction is computed on the pooled model not the full partitioned model (see previous slide). In general **partitioned model will be more robust against violations of equality of variance and sphericity** (*as all are acquired within subject, experimental paradigm and physical setup; ThC has issues with longitudinal*) . In general, **using these options shouldn't hurt anything, but my impression thus far is that it won't help that much either**. (If you find big differences between corrected and uncorrected models, please drop me a line, I would be interested in knowing in when this correction has a noticeable impact).

Just because something is a within factor does not guarantee equality of variance. A more difficult condition can result in both a change of mean and variance, so when correcting I think it's best to just go ahead and correct for both variance equality and independence. My experience thus far has suggested that performing the var/covar correction tends not to have much of an effect on the results when using partitioned error models, and generally I don't use it.

My recommendation is to run the model twice, once with the var/covar correction and once without. If you don't see much of a difference between the subsequent maps, then I would use the uncorrected model, as is it will be easier to explain, and gives parsimony with what you would get in SPSS, SAS, or R.

I still think that when performing the correction for within subject factors you might as well correct for both variance and independence.

Aaron Schultz

Why using GLM Flex

- **3. GLM Flex can be used to automatically remove outliers.**

To remove outliers we use Cook's distance (put in info on the threshold). Only a single data point is removed from a voxel at one time. If a data point is removed that voxel gets kicked into a set with a smaller size.

- **2. GLM Flex can analyze voxels with missing data.**

The scripts are setup to look for voxels with matching subjects, that is if we are doing a one sample t-test we start with the voxels that aren't missing any data. Then we move on to Voxels that are missing only Subject1, then only Subject2 etc ..., then it's voxels only missing Subject1 and Subject2, then Subject1 and Subject3 etc ... In practice we don't look for every possible combination, rather we sort the data into sets with the same N, and then break those sets into the constituent sets of Subjects. In this way we can iteratively walk through the different sets in a fairly efficient manner without having to analyze each voxel independently.

The tricky bit was pooling variance across voxels when dealing with a sub-model where there are only a few voxels. Luckily all that needed to be done was to take the first pass covariance matrix from voxels without missing data, and simply pool the data from the sub-model with the sub-indexed portions of the original covariance matrix. This way there are always enough voxels entering into the covariance matrix to get reasonably reliable estimates.

- **5. GLM Flex can be used to run second level models on FreeSurfer surface volumes (requires a freesurfer install).**

I simply leverage the MRIread.m and MRIwrite.m to get FS surface volumes into matlab, and then the data can be analyzed in the same manner as typical 3D Volumes.

Summary

Complex factorial designs with correct partitioning of error & modelling of variance/covariance inequality

Removing of single data points (one voxel in one image) without removing this image/subject from analysis

How to use GLM Flex

- No GUI – all is with code
- 3 steps
 - Describe your factorial plan;
 - Parameterize your analysis;
 - Indicate which contrasts you want to calculate;
- Exploration of statistical maps then performed with other toolbox – FIVE provided with GLM Flex, or xjView

Describe your factorial plan

IN.N_subs = [6 6] **number subjects**

IN.Between=[2] **levels of between subject factor F_1 (groups)**

IN.BetweenLabs = {'ASD' 'CTL'} **labels for between**

IN.Within = [2 3] **number of within— ie factors of exp plan**

IN.WithinLabs = {'F₂1' 'F₂2'} {'F₃1' 'F₃2' 'F₃3'} **labels for within**

IN.Interactions = {[1 2] [1 3] [2 3] [1 2 3]} **interactions to calculate**

IN.EqualVar = [1 1 1] **1=IsEqual \Leftrightarrow no correction**

IN.Independent = [1 1 1] **1=IsIndep \Leftrightarrow no correction**

F = CreateDesign(IN);

figure(20); clf

imagesc(F.XX); colormap(gray); shg

Parameterize analysis

I.OutputDir = ['OutputDirectory']

I.F = F output of design specification

I.Scans = {'scans in order of design lines'}

I.RemoveOutliers = 1 cf slide 4

I.DoOnlyAll = 0 if yes, only analyze vowels in which all data is present, if no →

I.minN = 5 min number of observation to analyze the voxels ie if less than 5 observations eliminate voxel from analysis

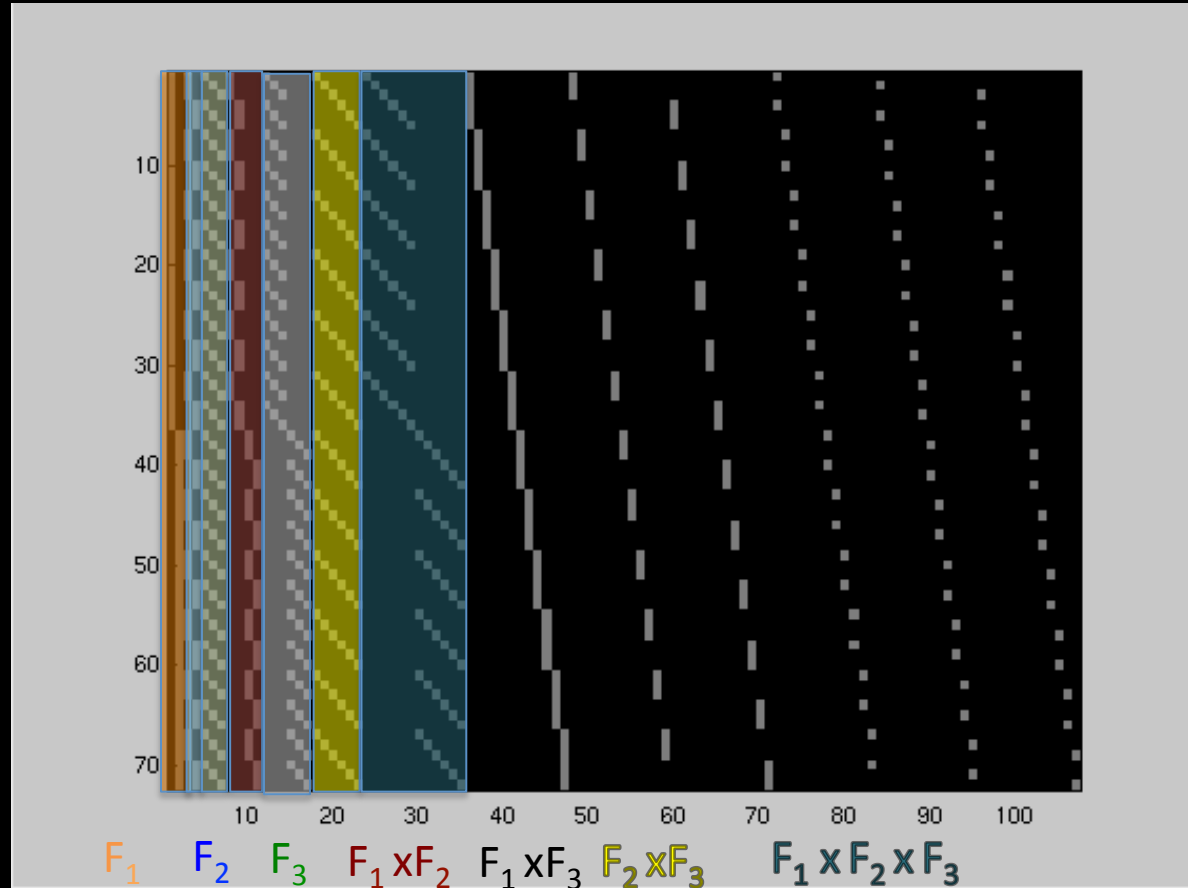
I.CompOpt=0; supposedly run SPM GLM to have .mat

I.Mask= ['mask.nii'];

run analysis with I = GLM_Flex(I)

Factorial plan

```
IN.N_subs = [6 6]
IN.Between=[2]
IN.Within = [2 3]
IN.Interactions =...
  {[1 2] [1 3] [2 3] [1 2 3]}
```



All terms are shown and calculated (even if not all asked in IN.Interactions) !

Calculations

IN.N_subs = [6 6]

IN.Between=[2]

IN.Within = [2 3]

Finished Creating Factor Matrix

Finished Creating Main Effects

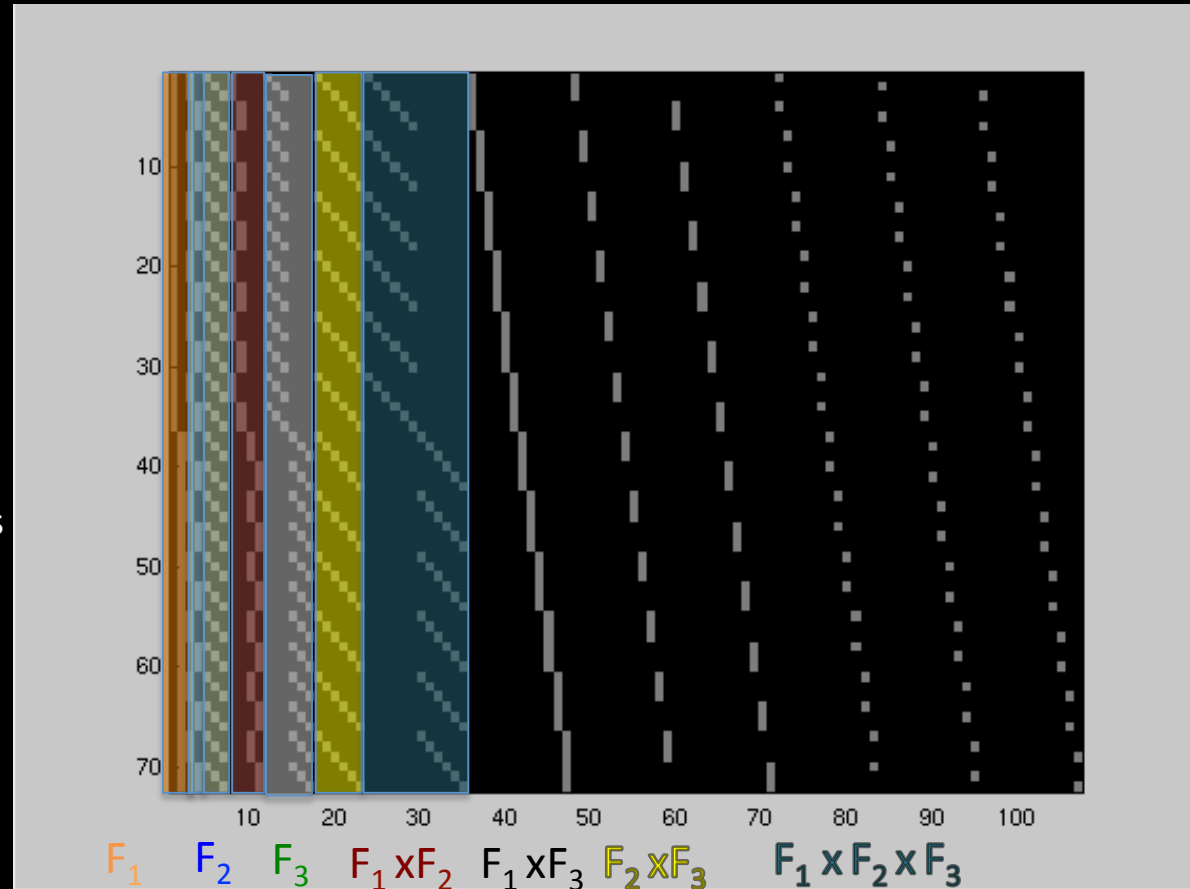
Finished Creating Two Way Interactions

Finished Creating Three Way Interactions

...

Finished Creating Design Matrix.

Finished Other Stuff.

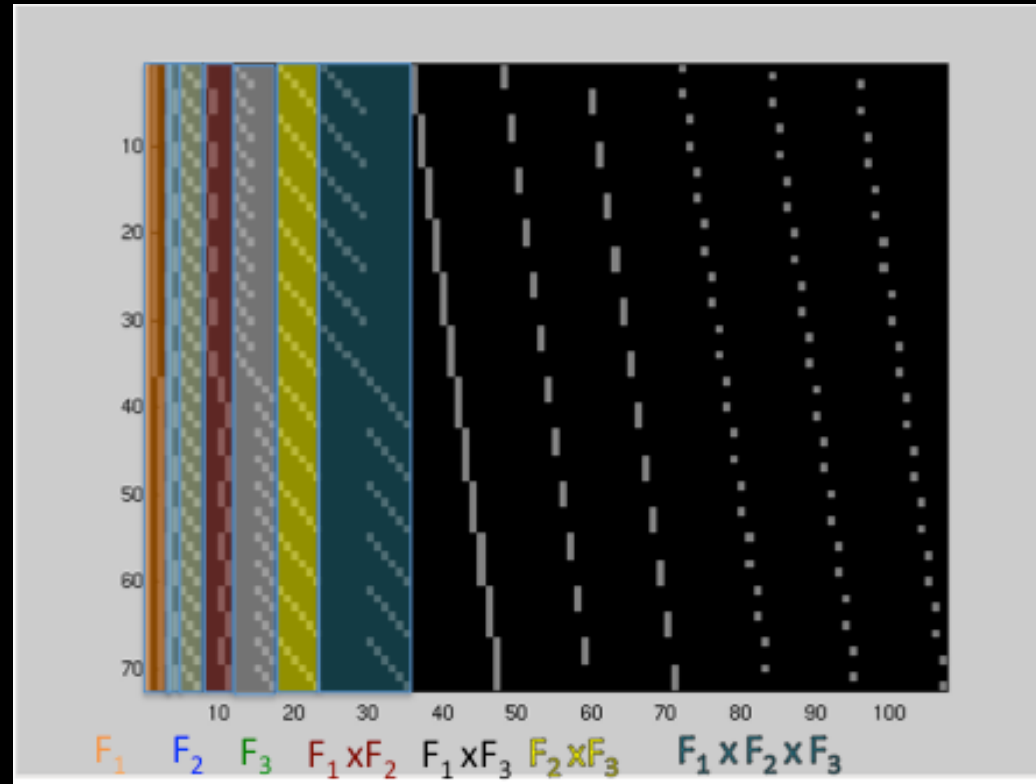


- Covariance terms for all main effects and interaction terms are calculated, always as follows (whether OR NOT there is a between subject factor) : #1: F_1 between subject, used for group effects and t-tests over all conditions
- Then all within subjects main effects, in our case: #2: main effect F_2 , #3: main effect F_3
- Then all within subjects factor interactions interactions , in our case: #4: $F_2 \times F_3$

Specify contrasts

```
IN.N_subs = [6 6]  
IN.Between=[2]  
IN.Within = [2 3]
```

```
I.Cons(1).name = 'Group';  
I.Cons(1).Groups = {1 2};  
I.Cons(1).Levs = [2];  
I.Cons(1).ET = [1]; : #1:F1: between subject  
I.Cons(1).mean = 0;
```



Specify contrasts

```
IN.N_subs = [6 6]
```

```
IN.Between=[2]
```

```
IN.Within = [2 3]
```

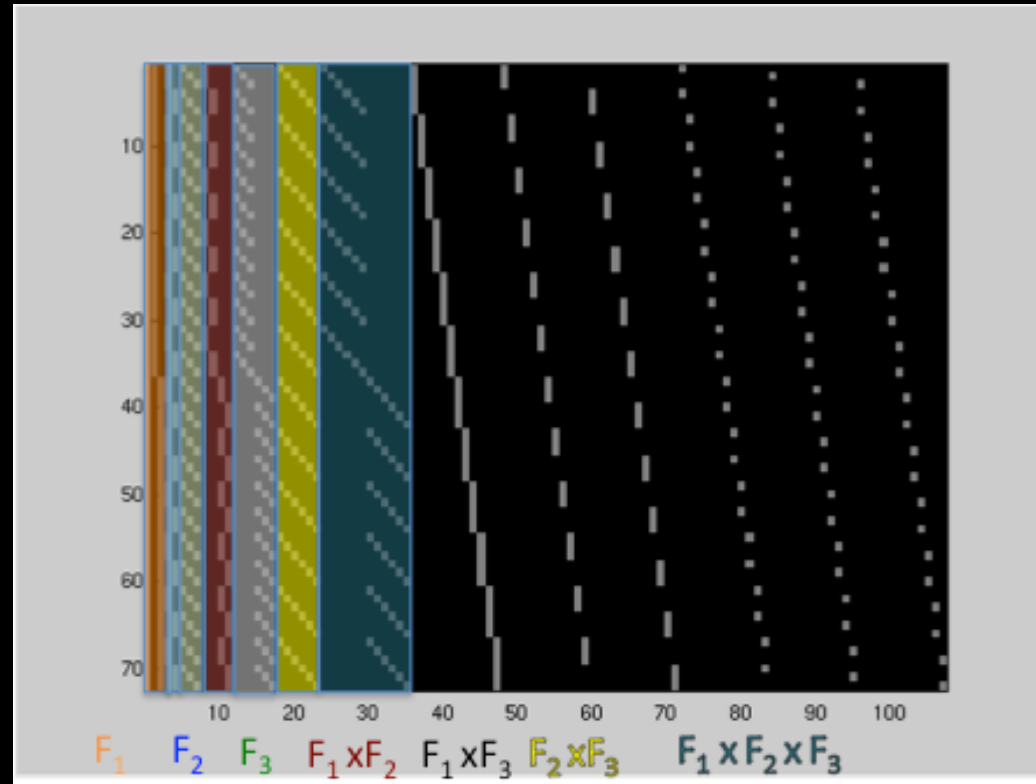
```
I.Cons(2).name = 'F2';
```

```
I.Cons(2).Groups = {3 4};
```

```
I.Cons(2).Levs = [2];
```

```
I.Cons(2).ET = [2]; : #2:F2 error term
```

```
I.Cons(2).mean = 0;
```



Specify contrasts

```
IN.N_subs = [6 6]
```

```
IN.Between=[2]
```

```
IN.Within = [2 3]
```

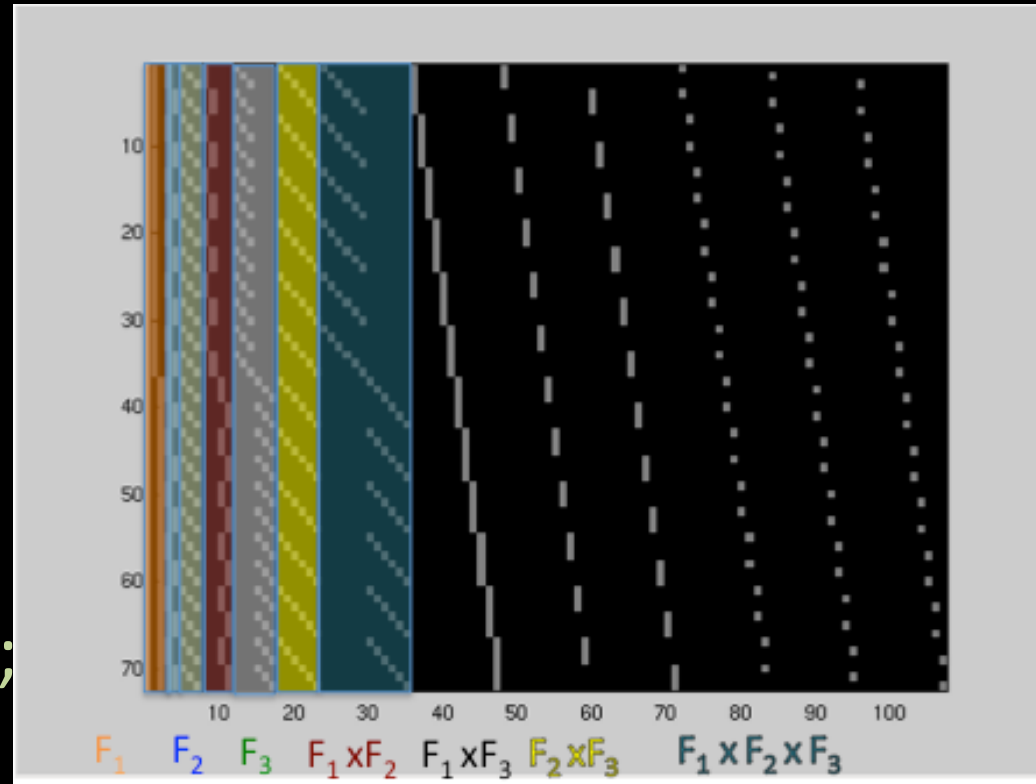
```
I.Cons(3).name = 'F3';
```

```
I.Cons(3).Groups = {5 6 7};
```

```
I.Cons(3).Levs = [3];
```

```
I.Cons(3).ET = [3]; : #3:F3 error term
```

```
I.Cons(3).mean = 0;
```



Specify contrasts

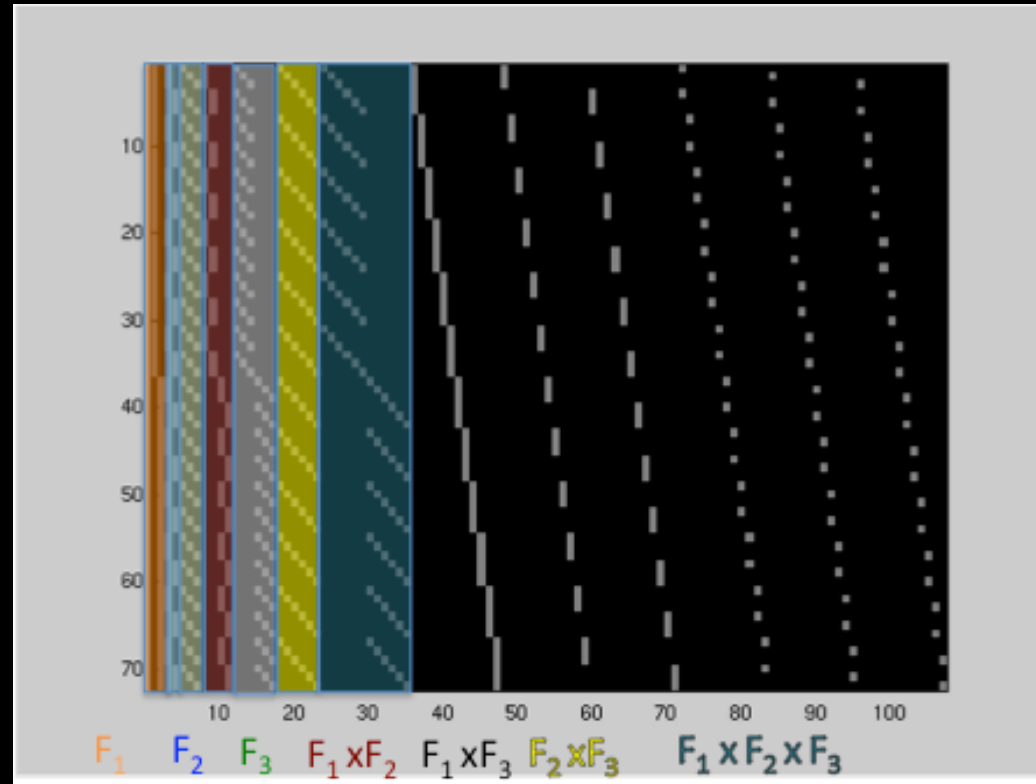
```
IN.N_subs = [6 6]  
IN.Between=[2]  
IN.Within = [2 3]
```

```
I.Cons(4).name = 'F1X F2';  
I.Cons(4).Groups = ...  
{8 9 10 11};
```

```
I.Cons(4).Levs = [2 2];
```

```
I.Cons(4).ET = [2]; : #2:F2 error term
```

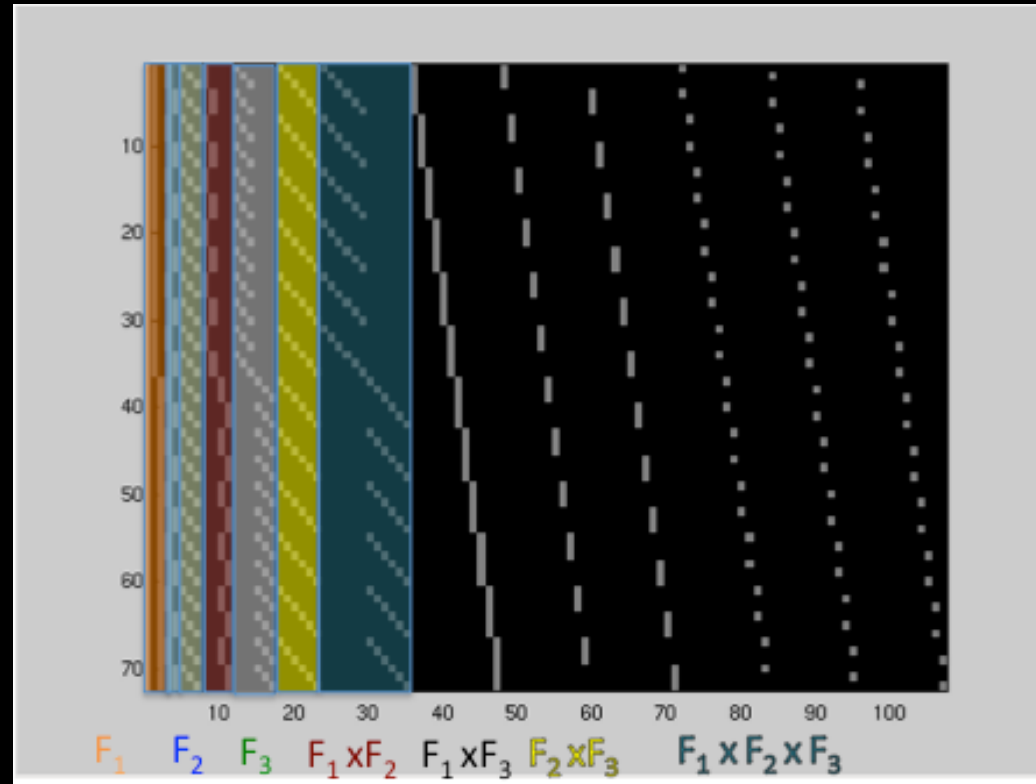
```
I.Cons(4).mean = 0;
```



Specify contrasts

```
IN.N_subs = [6 6]  
IN.Between=[2]  
IN.Within = [2 3]
```

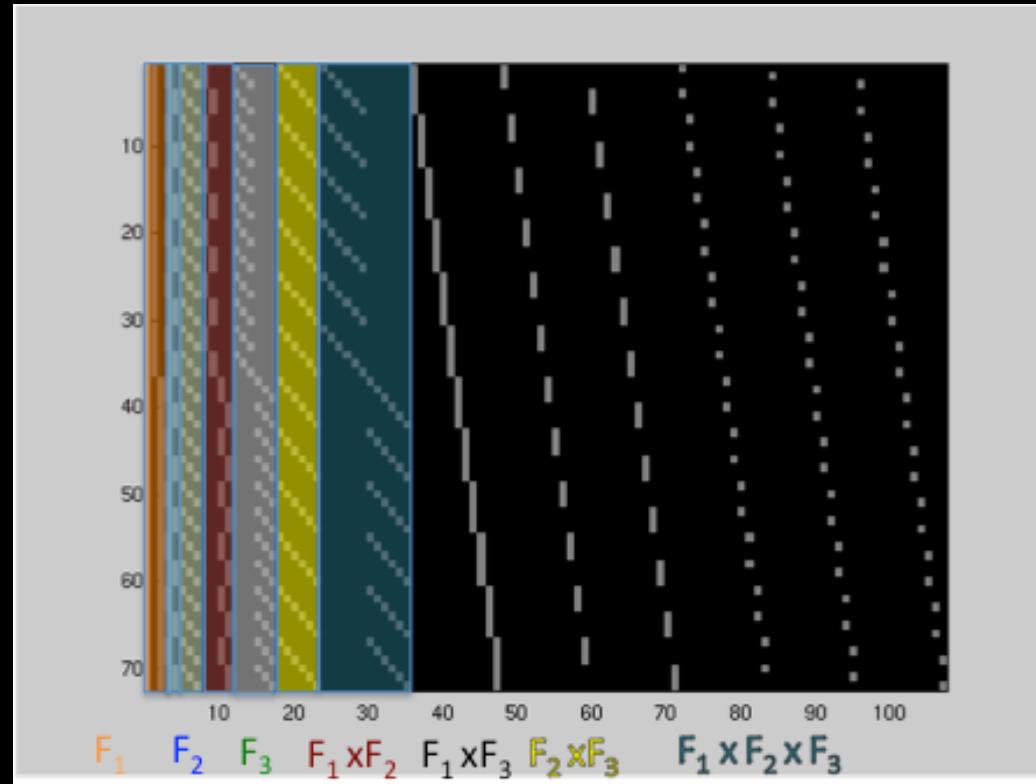
```
I.Cons(5).name = 'F1 x F3';  
I.Cons(5).Groups =  
{12 13 14 15 16 17};  
I.Cons(5).Levs = [2 3];  
I.Cons(5).ET = [3]; : #3:F3 error term  
I.Cons(5).mean = 0;
```



Specify contrasts

```
IN.N_subs = [6 6]  
IN.Between=[2]  
IN.Within = [2 3]
```

```
I.Cons(6).name = 'F2 x F3';  
I.Cons(6).Groups =  
{18 19 20 21 22 23};  
I.Cons(6).Levs = [2 3];  
I.Cons(6).ET = [4]; : #4:F2 x F3 error term  
I.Cons(6).mean = 0;
```



Specify contrasts

```
IN.N_subs = [6 6]
```

```
IN.Between=[2]
```

```
IN.Within = [2 3]
```

```
I.Cons(7).name = 'F1 x F2 x F3';
```

```
I.Cons(7).Groups = ...
```

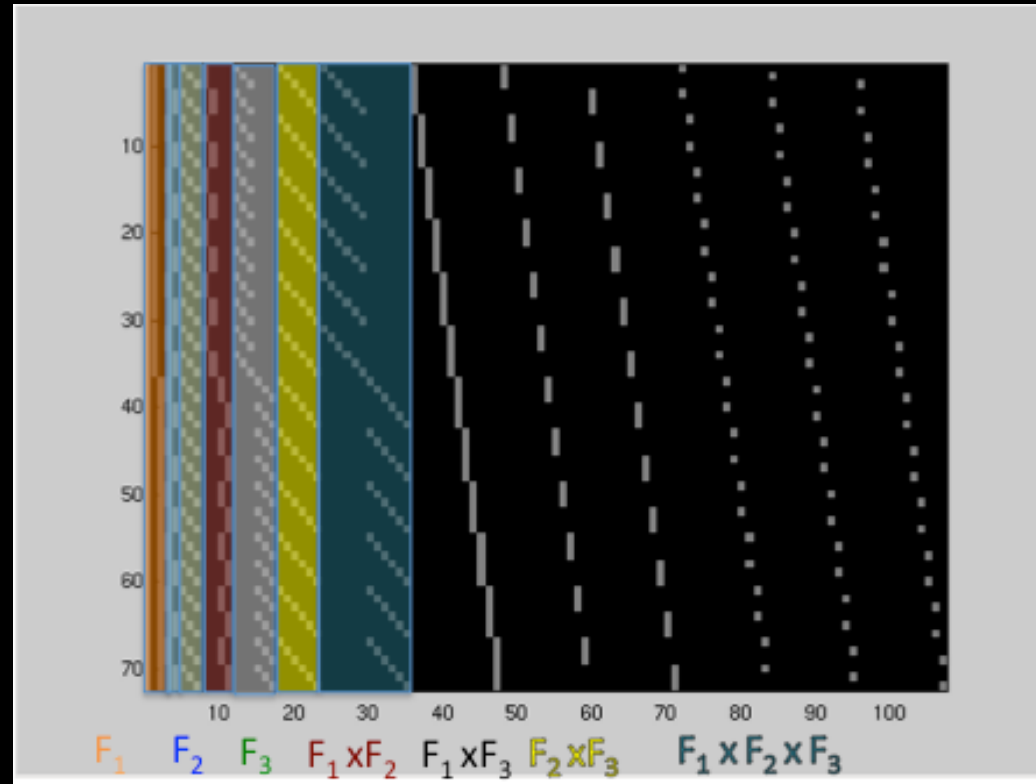
```
{24 25 26 27 28 29 ...
```

```
30 31 32 33 34 25};
```

```
I.Cons(7).Levs = [2 2 3];
```

```
I.Cons(7).ET = [4]; : #4:F2 x F3 error term
```

```
I.Cons(7).mean = 0;
```



Results

- In the analysis folder check the number of ResML images files: these are your error terms and their number should correspond to the number of main effects and interactions
- Contrasts of interest are visible as
 - 0001_T_Group.nii : For 1 or 2 levels, T tests (ie bilateral, + and – values)
 - 0003_F_F3.nii: For more than 2 levels, F tests are presented
- Programs like FIVE and xjView can be used for exploring and further processing the contrasts.

View Results - xjView

xjView: /riou/work/scalp/tchamina/Tool/FlexB/0008_T_All.nii,1

File Edit View Insert Tools Desktop Window Help

// Right Cerebrum // Occipital Lobe // Middle Occipital Gyrus // White Matter // undefined // Occipital_Mid_R (aal)

```
/riou/work/scalp/tchamina/Tool/FlexB/0008_T_All.nii,1
This is a T test image.
mat =
-1.5 0 -7.240352e-17 91.5
1.36305e-16 1.5 4.344211e-16 -127.5
-3.748388e-16 -2.450089e-16 1.5 -73.5
0 0 0 1
dimension =
121 145 121
```

search Middle Occipital Gyrus in xBrain

overlay Amygdala

report volume Small volume common region slice view

display intensity All Only + Only - Render View new

cluster size >= 25 Pick Cluster/Info Select Cluster Clear Selection

pValue= 0.001 FDR p= T= 5.8934 df= 5

co-ordinates x = 30.00 y = -85.50 z = 4.50 statistic 45.05

single T1
avg152PD
avg152T1
avg152T2
avg305T1
ch2
ch2bet
aal
brodmann

other ...
colorbar max
auto

PaperBox
Smart, cloud reference manager for team. <http://paper-box.co>

FIVE

