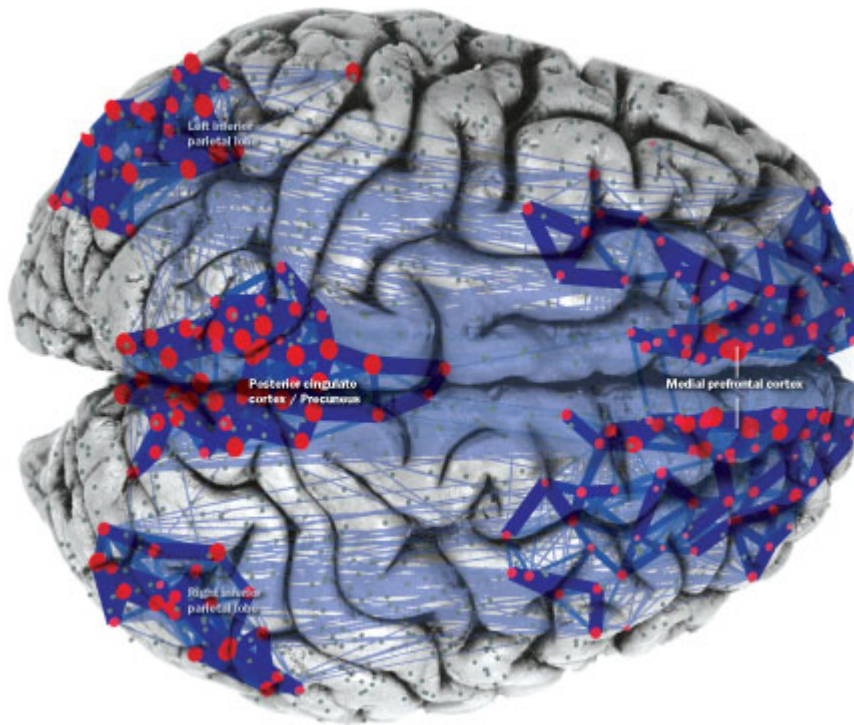


Resting state analysis with SPM



Hamburg SPM course 2012

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- Resting state activity is interesting *per se*

Aims

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- To know what SPM cannot easily do and apply self-made MATLAB scripts to do it
- To extend SPM using the Brain Connectivity Toolbox (<http://www.brain-connectivity-toolbox.net>), which allows graph theoretical analysis of functional connectivity networks

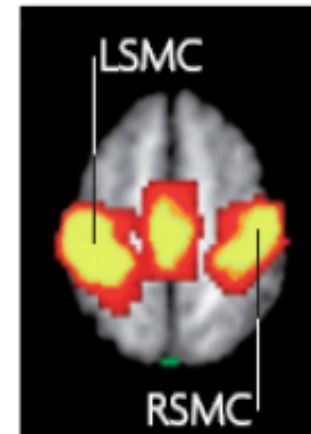
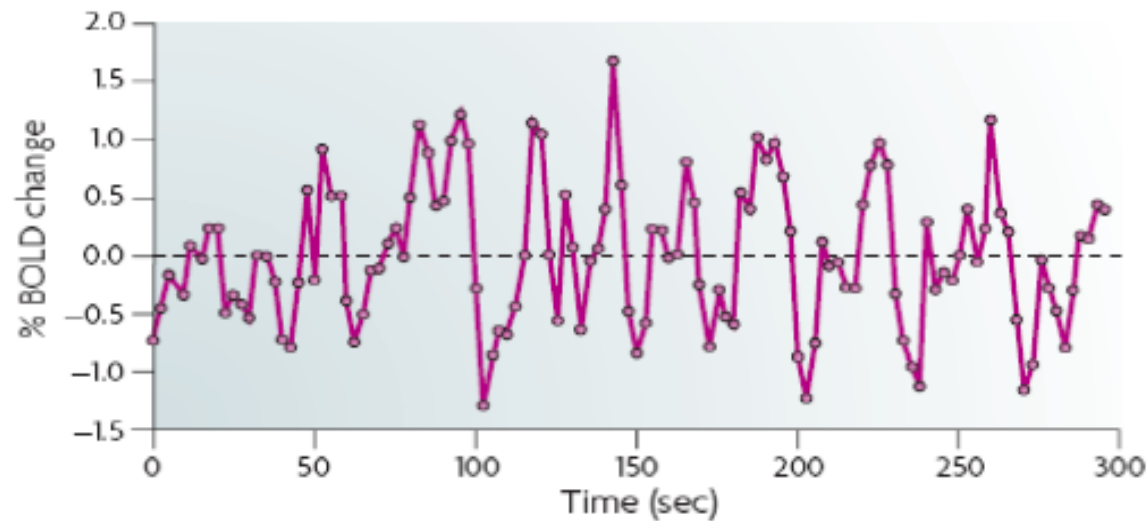
First part: seed correlation

Methods I: Seed correlation

- Functional connectivity between a BOLD timeseries from a given location and the rest of the brain is assessed

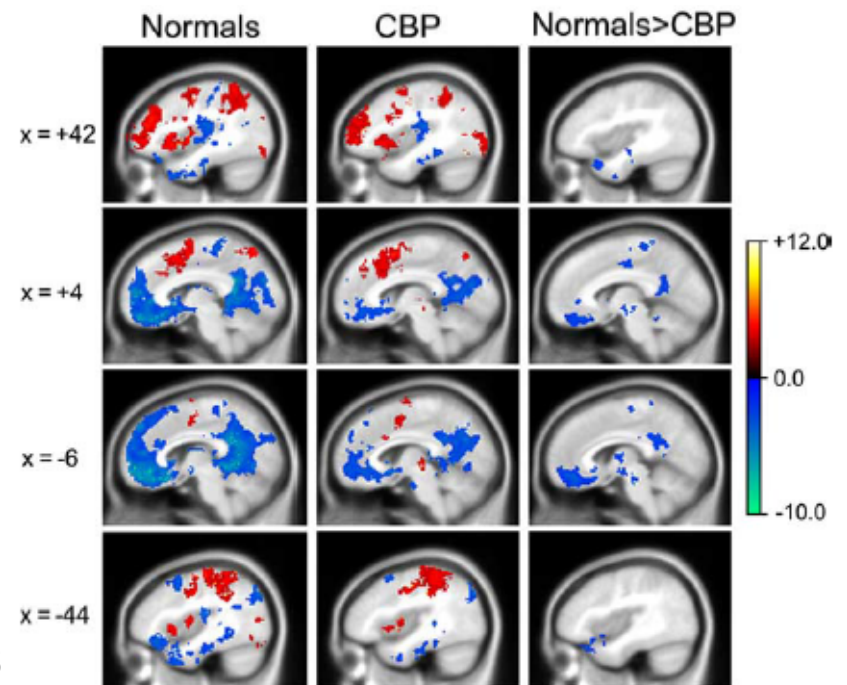
Methods I: Seed correlation

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Methods I: Seed correlation

- Functional connectivity between a BOLD timeseries from a given location and the rest of the brain is assessed
- It is common to apply it individually for each subject (*first level analysis*) and then perform analysis at the group level or inter-group comparisons between different populations (*second level analysis*)



How to do it

- First, extract a BOLD time course from a voxel or a ROI
(*tools/extract_BOLD_regressor.m*)

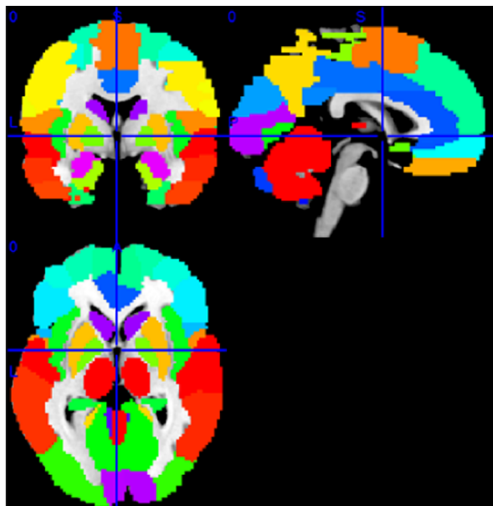
How to do it

- First, extract a BOLD time course from a voxel or a ROI (*tools/extract_BOLD_regressor.m*)
- This can be done from a voxel or from a region in a given template, in this case we use the AAL template

```
Y = spm_vol('aal_atlas.img'); aal = spm_read_vols(Y);
```



Code to open an fMRI volume using SPM



90 cortical and sub-cortical regions + 26 cerebellar regions

How to do it

- First, extract a BOLD time course from a voxel or a ROI (*tools/extract_BOLD_regressor.m*)
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- Then, construct any other regressors you might want to include in the analysis: motion time series, derivatives of motion time series, cardiac and respiratory noise.

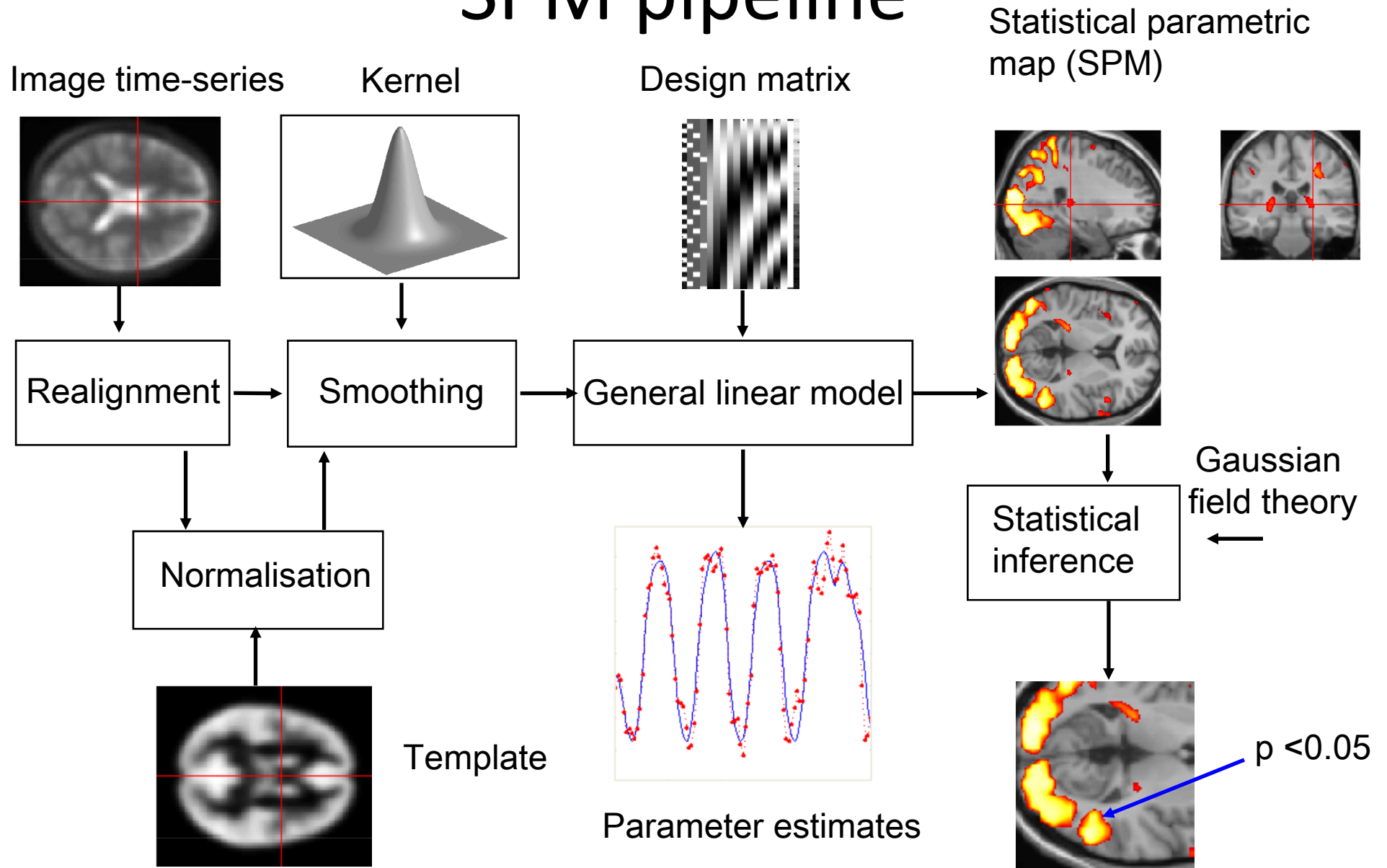
 **RETROICOR method** (Glover et al, 2000)

RETROICOR

How to do it

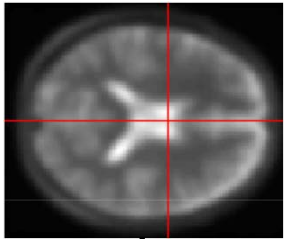
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- Then, construct any other regressors you might want to include in the analysis: motion time series, derivatives of motion time series, cardiac and respiratory noise.
- Put the BOLD regressor in the design matrix, together with the other regressors, and run a first level analysis for each subject you want in the analysis

SPM pipeline

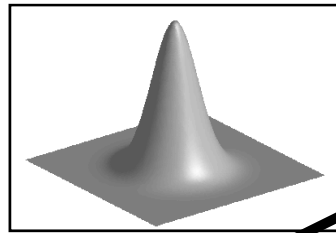


SPM pipeline

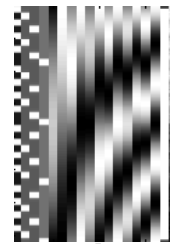
Image time-series



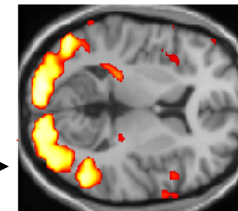
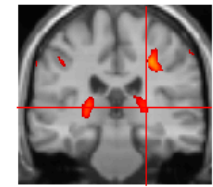
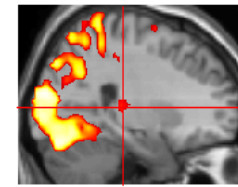
Kernel



Design matrix

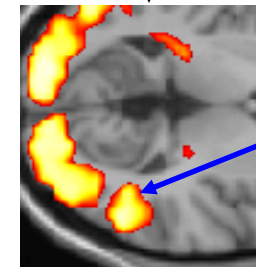


Statistical parametric map (SPM)



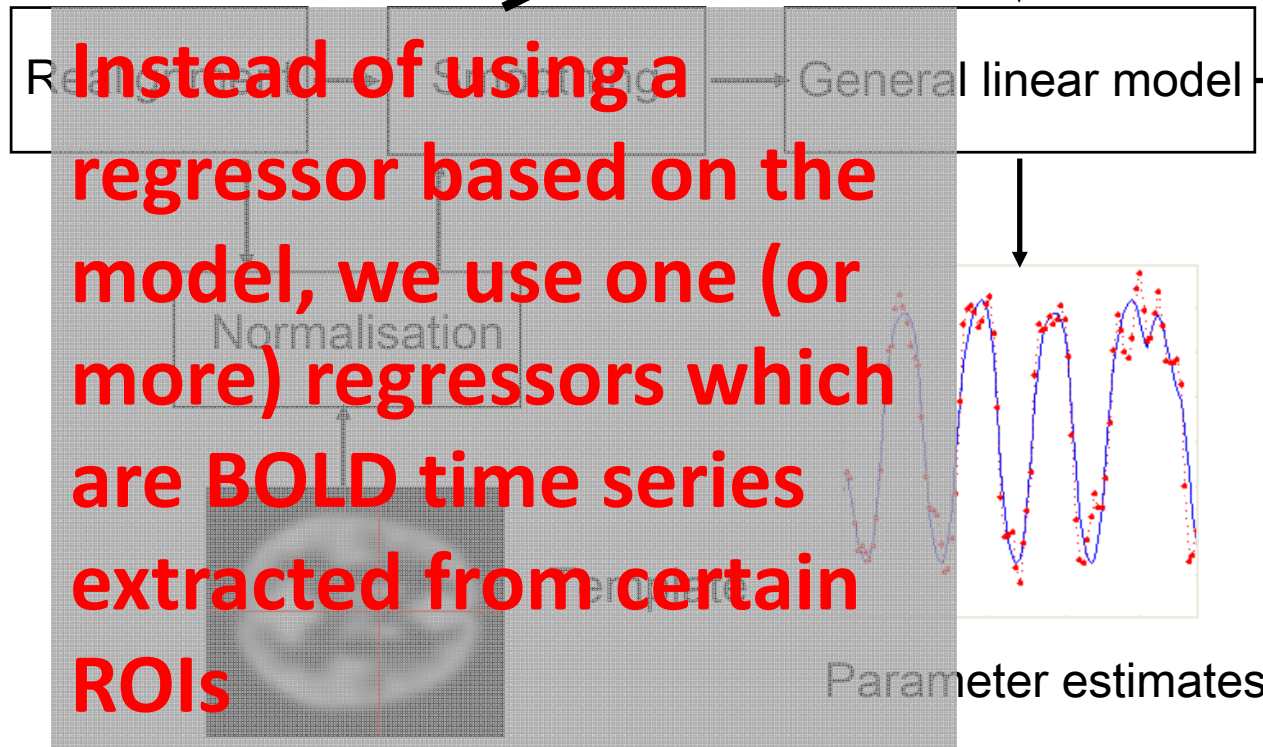
Gaussian field theory

Statistical inference



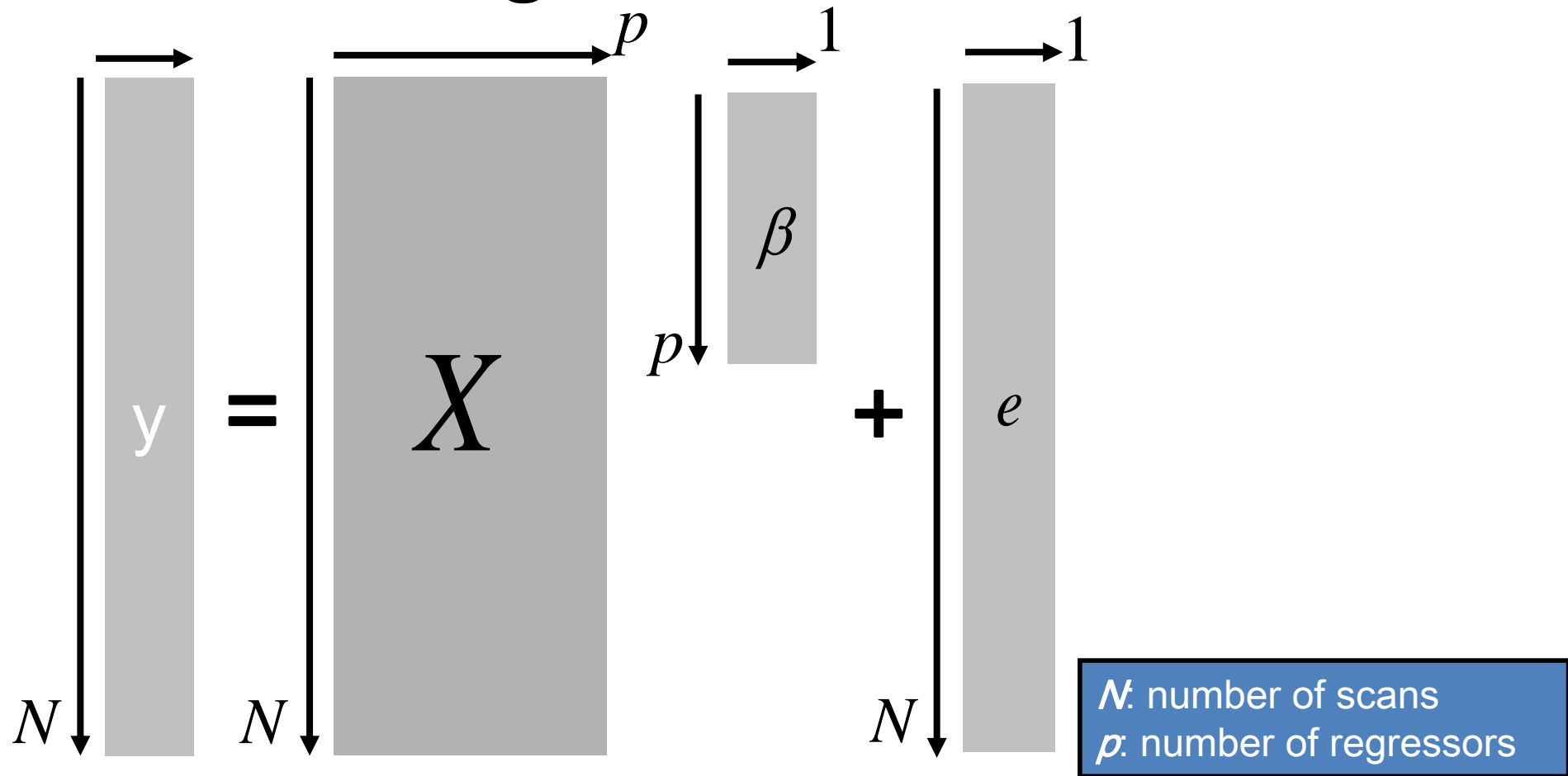
$p < 0.05$

Instead of using a regressor based on the model, we use one (or more) regressors which are BOLD time series extracted from certain ROIs



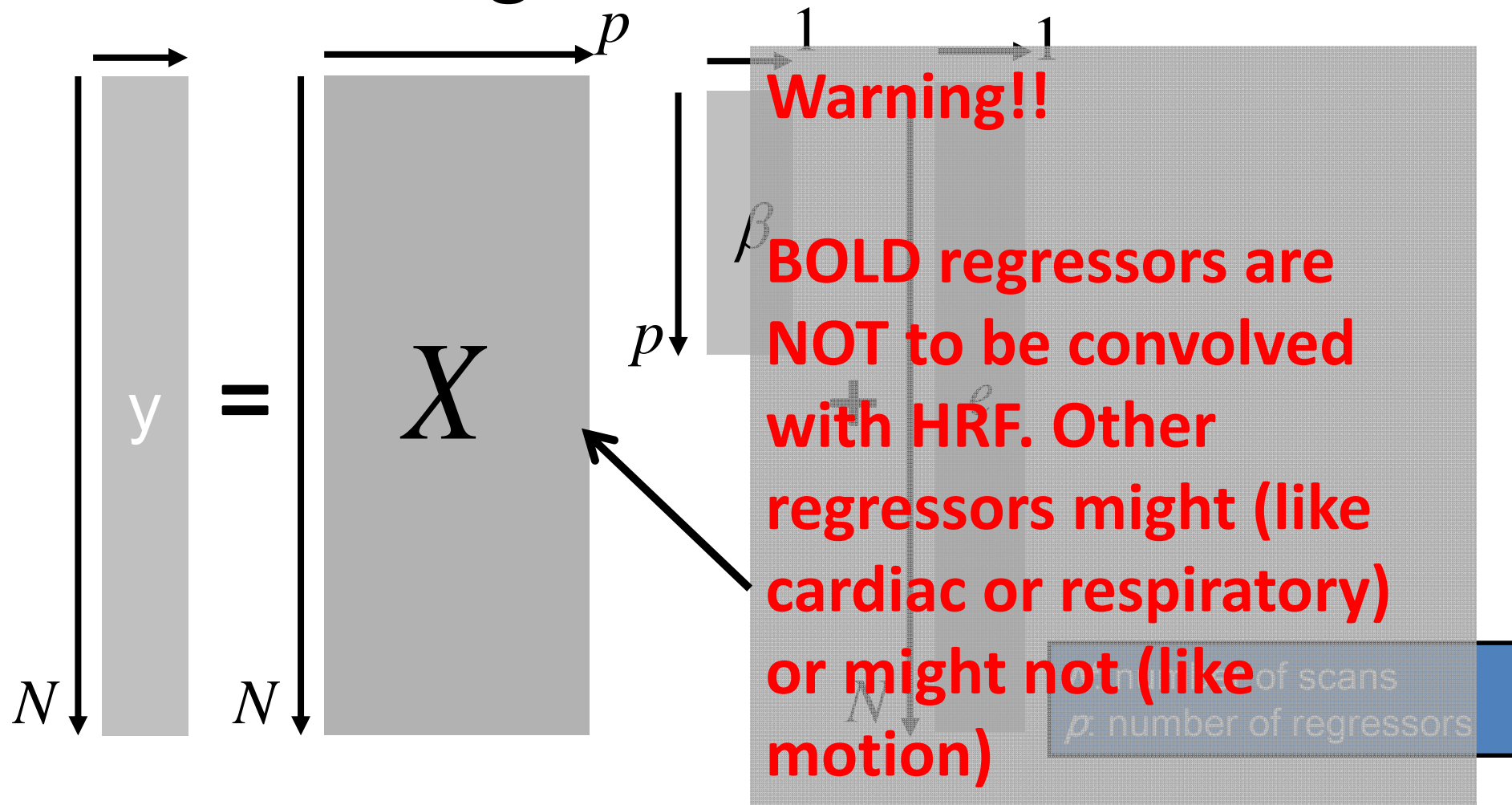
Parameter estimates

Design matrix and GLM



$$y = X\beta + e \quad e \sim N(0, \sigma^2 I)$$

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Dataset

- Five subjects in two groups (50 volumes, 79 x 95 x 68 voxels)

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Dataset

- Five subjects in two groups (50 volumes, 79 x 95 x 68 voxels)
- First group has increased connectivity between left thalamus and both left and right pre-frontal cortex
- Second group has increased connectivity between left thalamus and left pre-frontal cortex only

Steps (first level)

- Load the AAL atlas, which will be necessary to extract the thalamus BOLD timecourse

```
Y = spm_vol('aal_atlas.img'); aal = spm_read_vols(Y);
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```

- Create BOLD regressors running the *extract_BOLD_regressor.m* script (**Check path!**). This will create a .mat file in each subject directory with the corresponding regressor

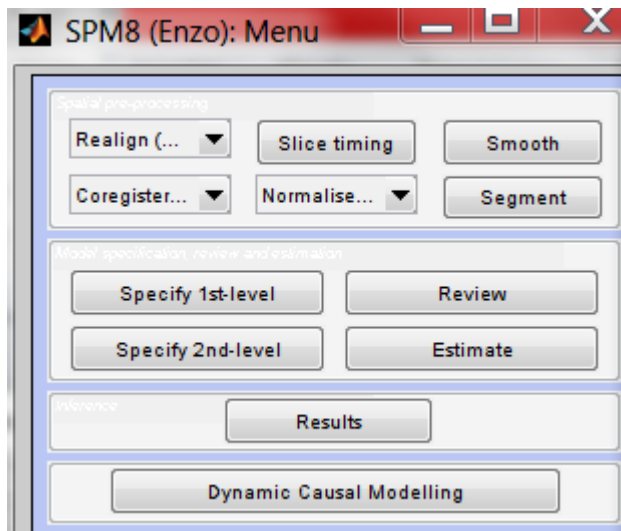
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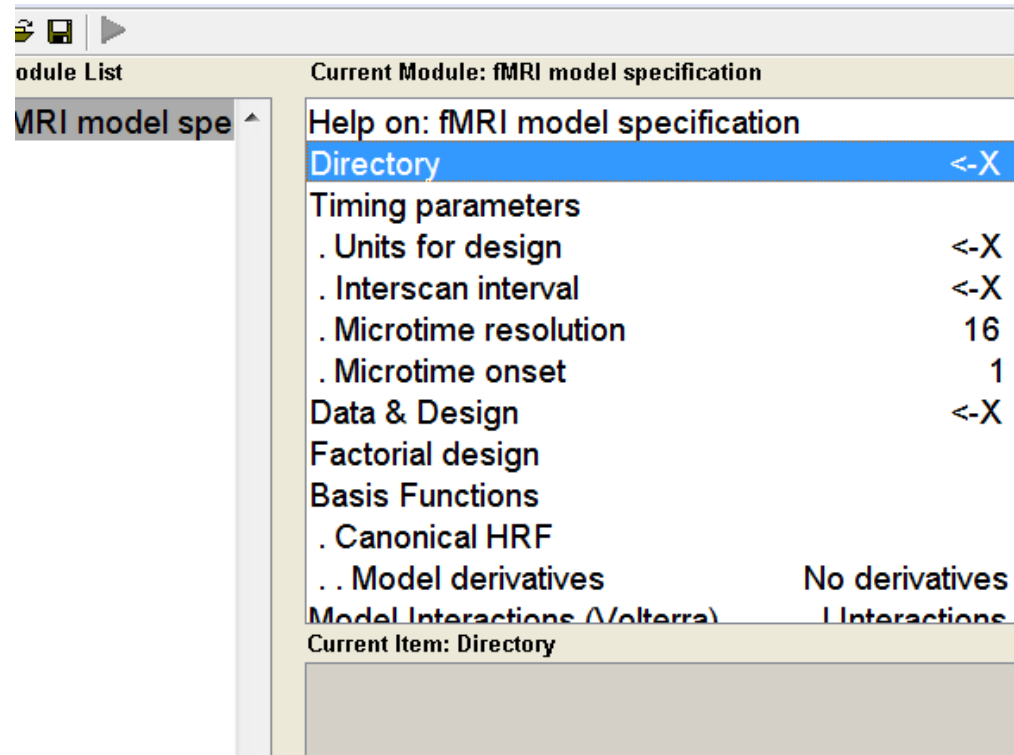
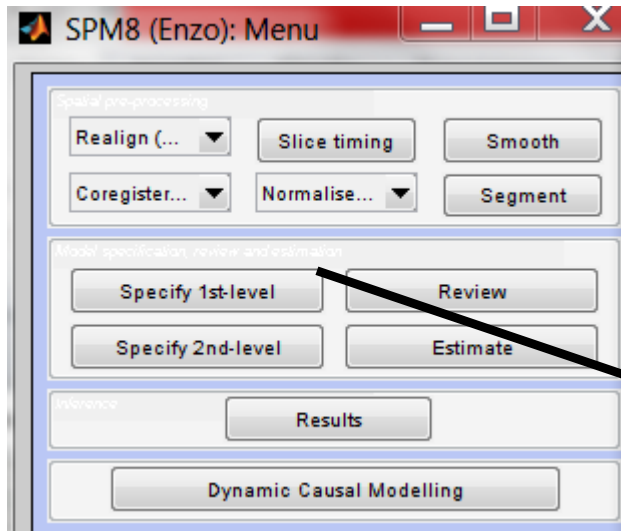
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```

- Create BOLD regressors running the *extract_BOLD_regressor.m* script (**Check path!**). This will create a .mat file in each subject directory with the corresponding regressor
- In each subject file there is a file with noise regressors (*noise_regressors.mat*). These can be combined to form all the regressors to be included in the design matrix using the *create_all_regressors.m* script (**Check path!**).

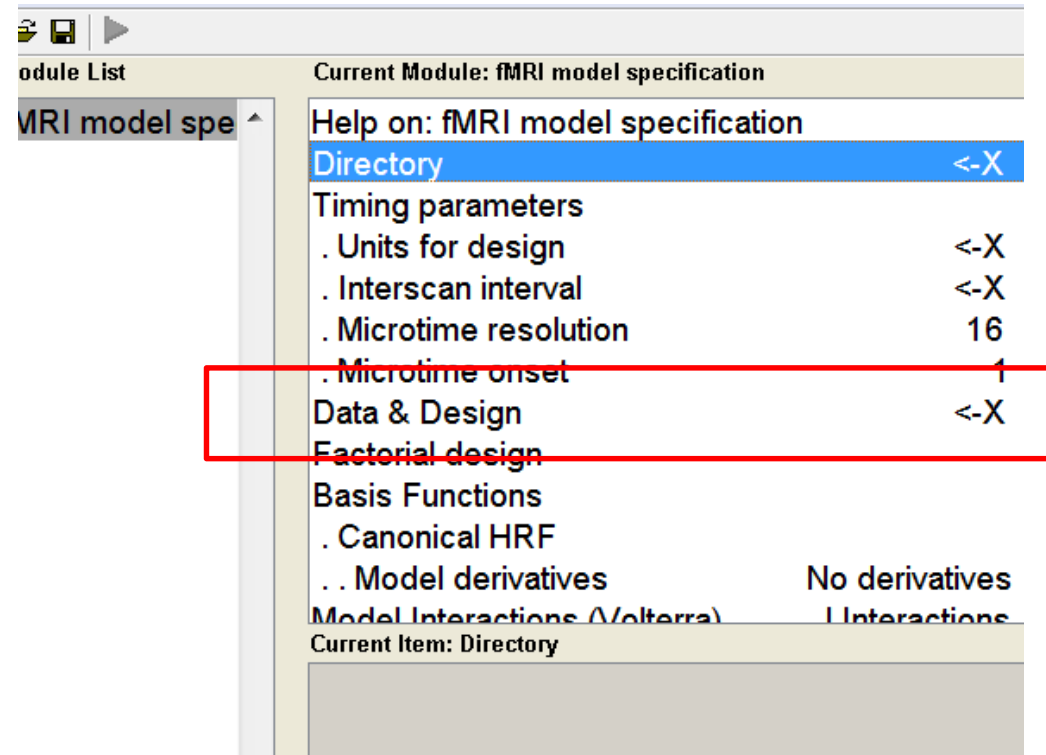
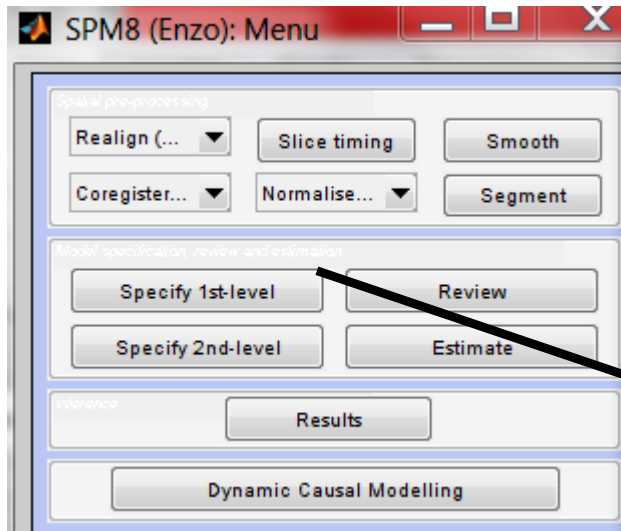
Set up model (first level)



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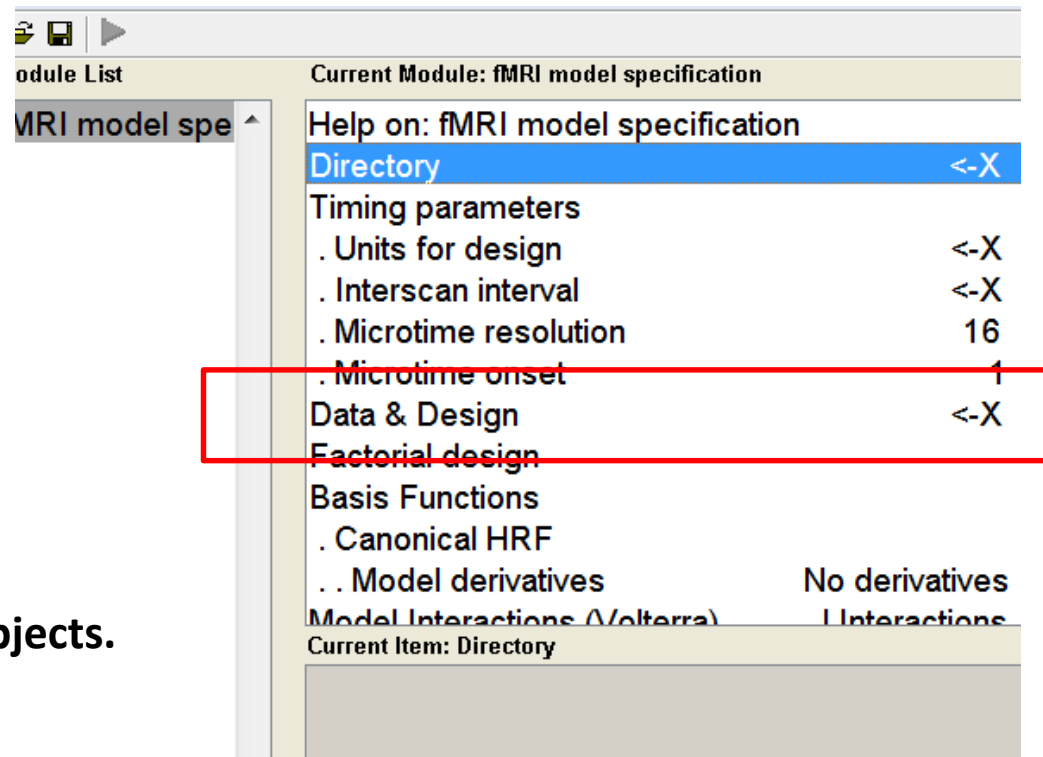
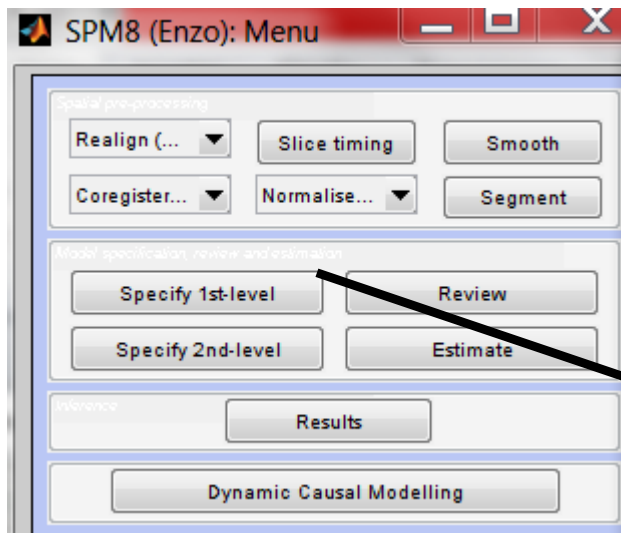
Set up model (first level)



Click Data & Design, add volumes (**careful! Check file order!!**) and add regressors using the Multiple Regressors option.

Select TR (2.08 s.) and select directory. **Model details do not concern us** (we defined our regressor)

Set up model (first level)



Use the batch script
first_level_analysis_job.m for all subjects.
Change directory paths in the file!!

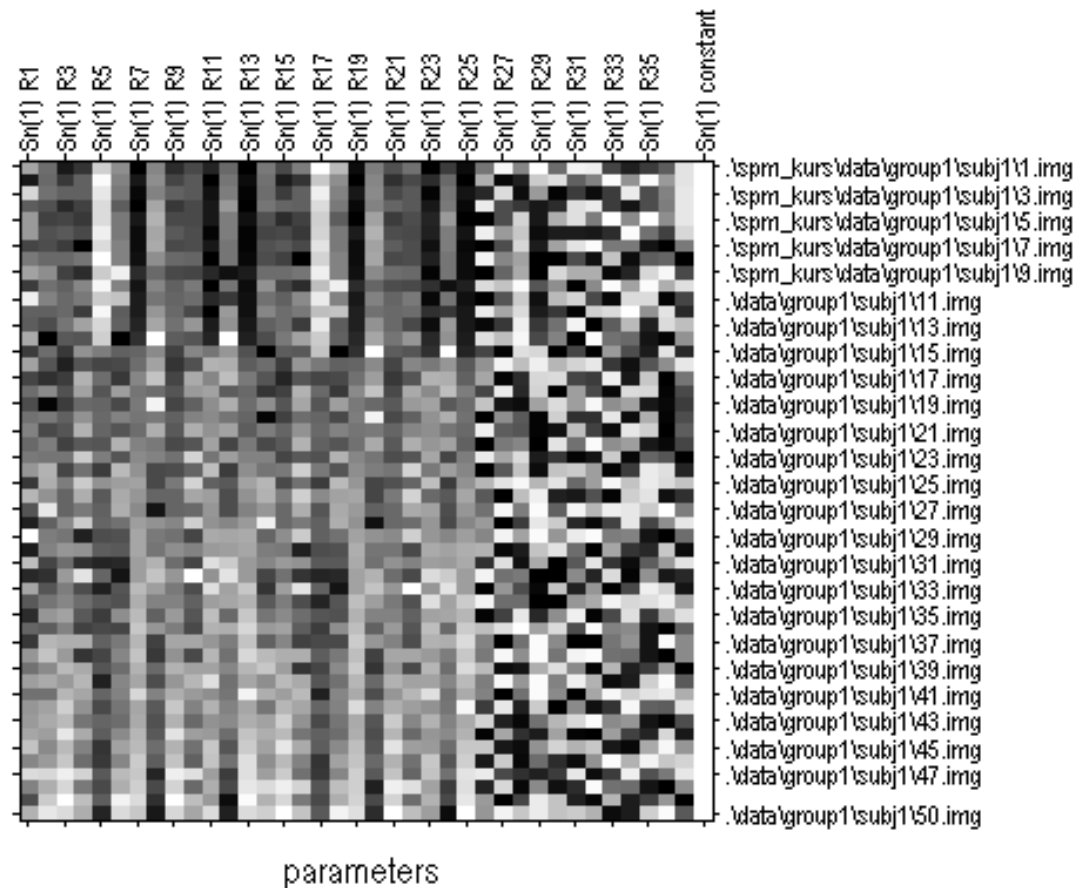
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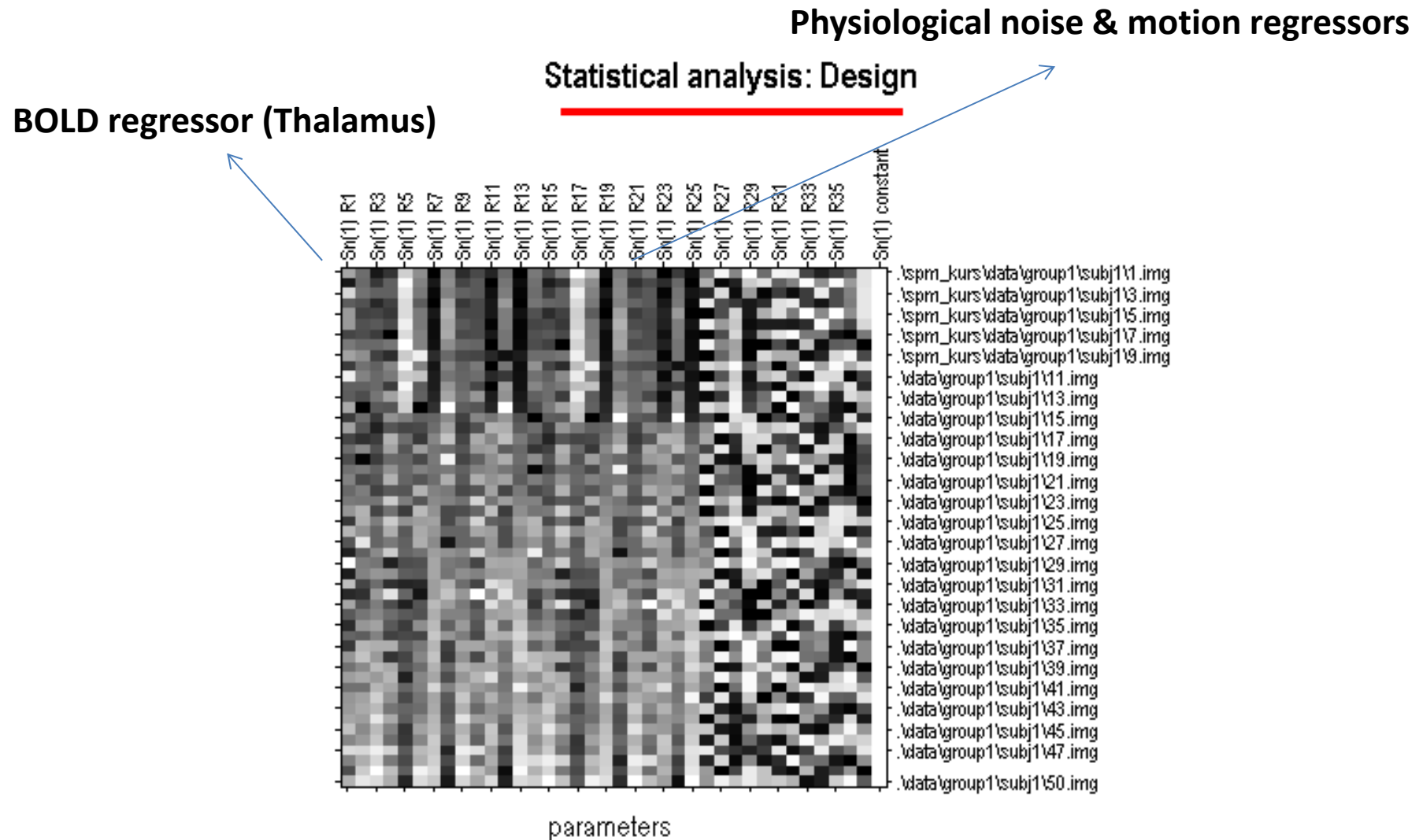
Design matrix (example)

Statistical analysis: Design

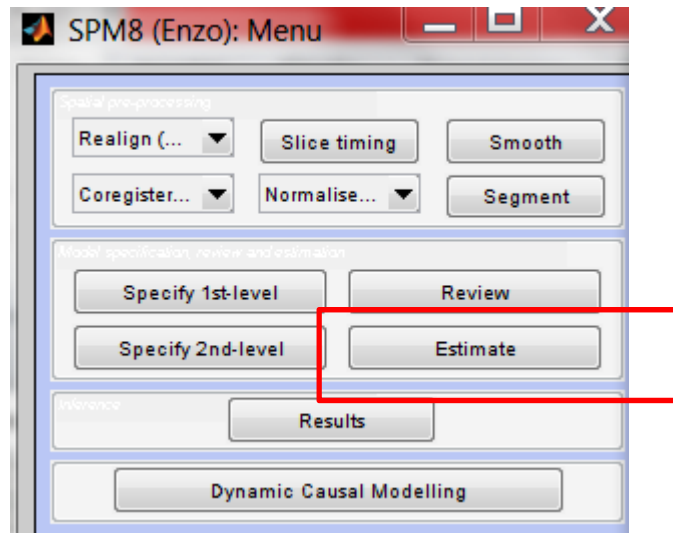
BOLD regressor (Thalamus)



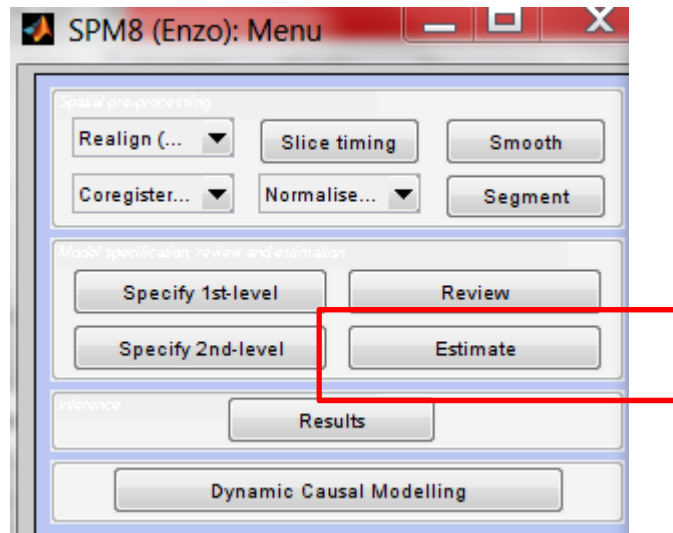
Design matrix (example)



Estimate model (first level)



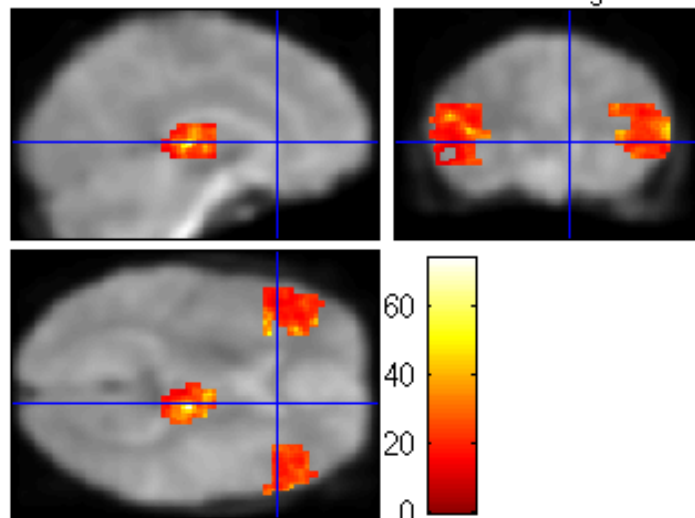
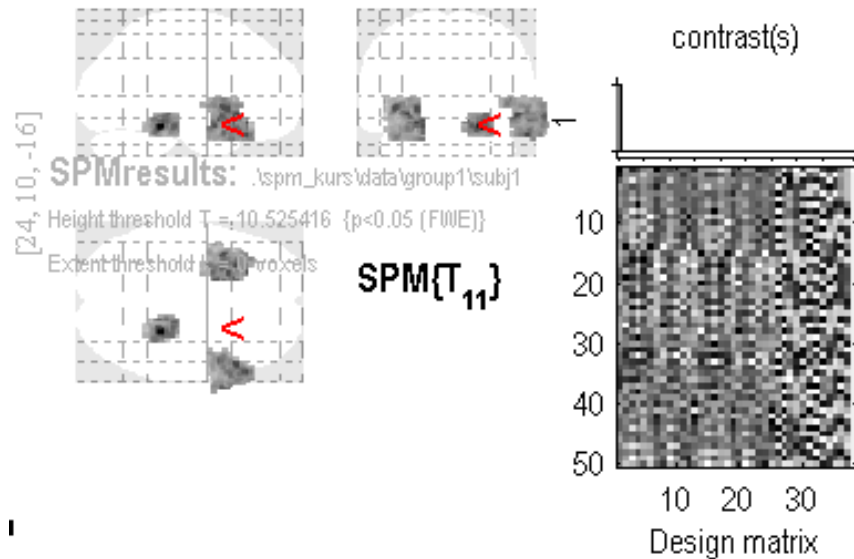
Estimate model (first level)



Use the batch script *estimate_model_first_level_job.m* for all subjects. **Change directory paths in the file!!**

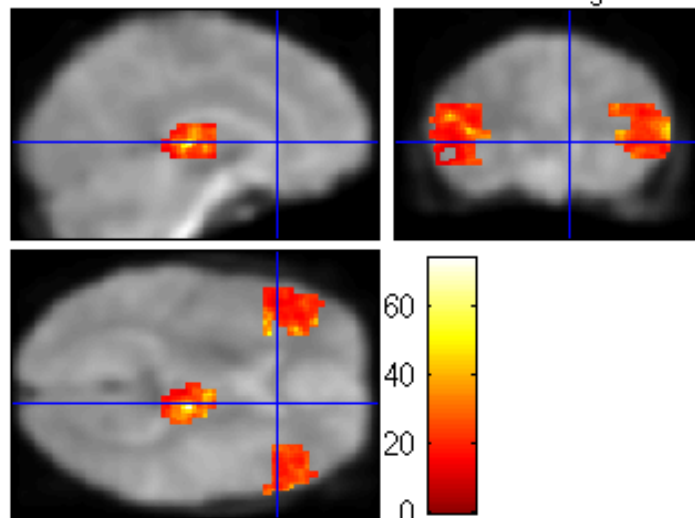
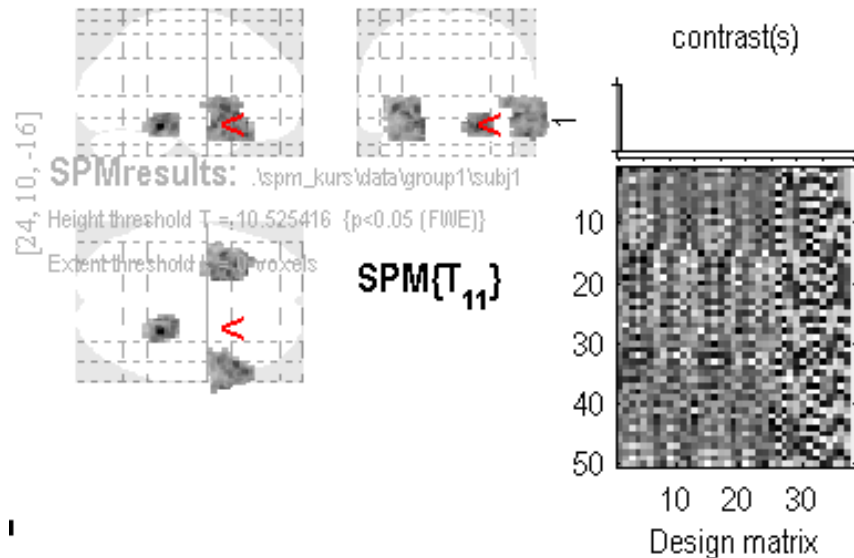
Results (first level)

Thalamic BOLD regressor

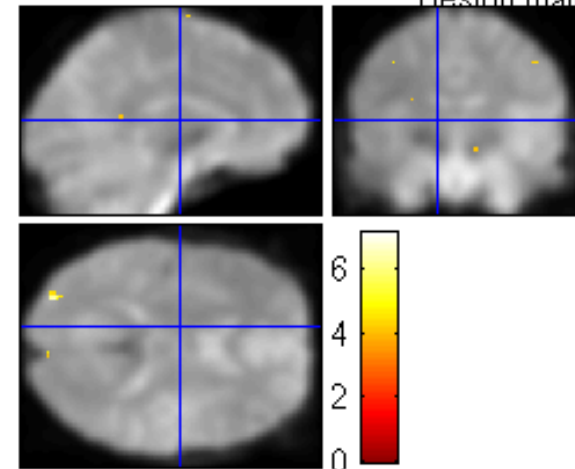
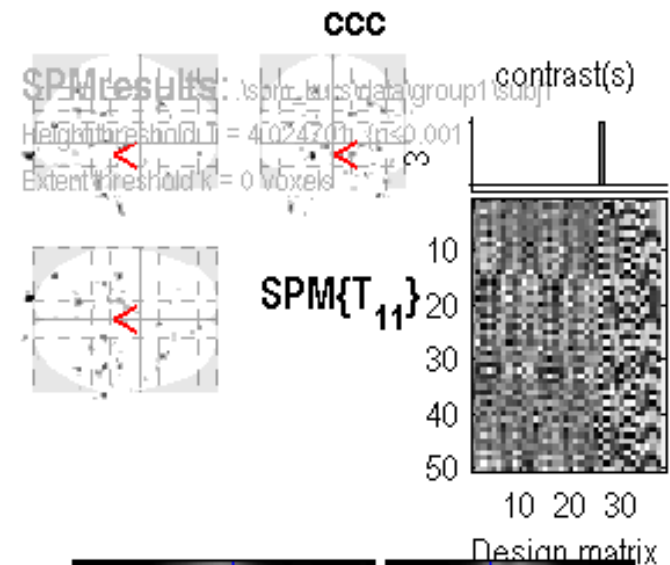


Results (first level)

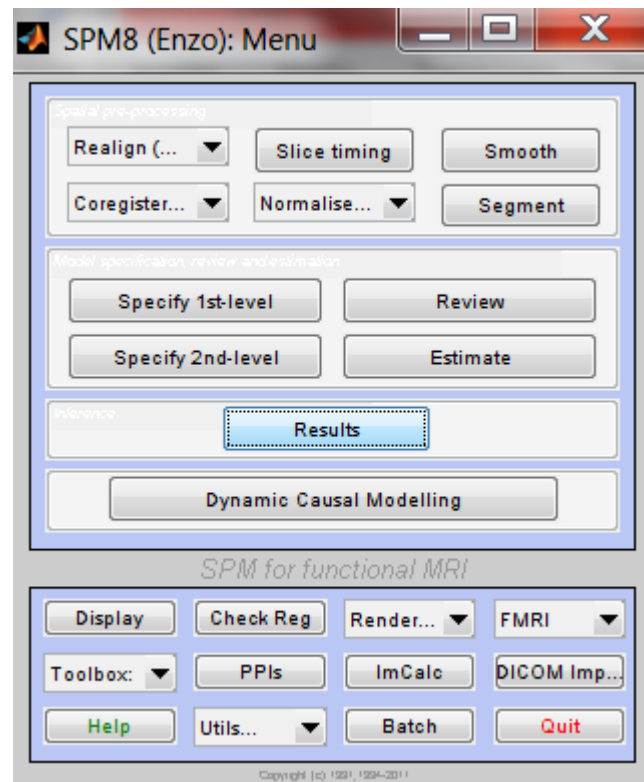
Thalamic BOLD regressor



Cardiac regressor

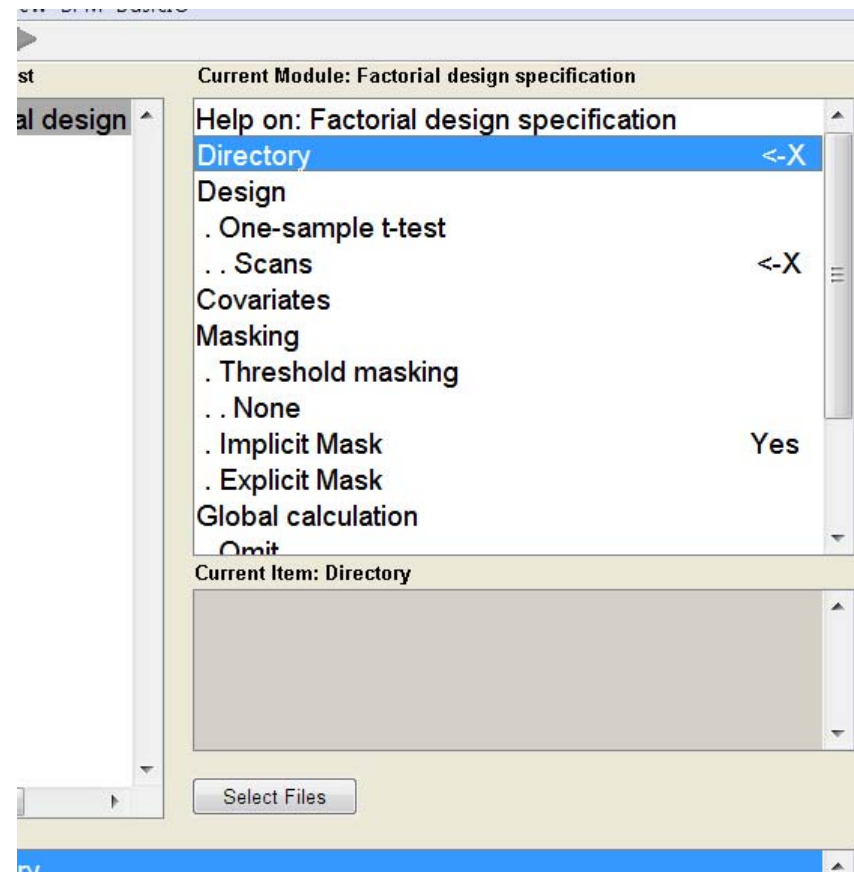
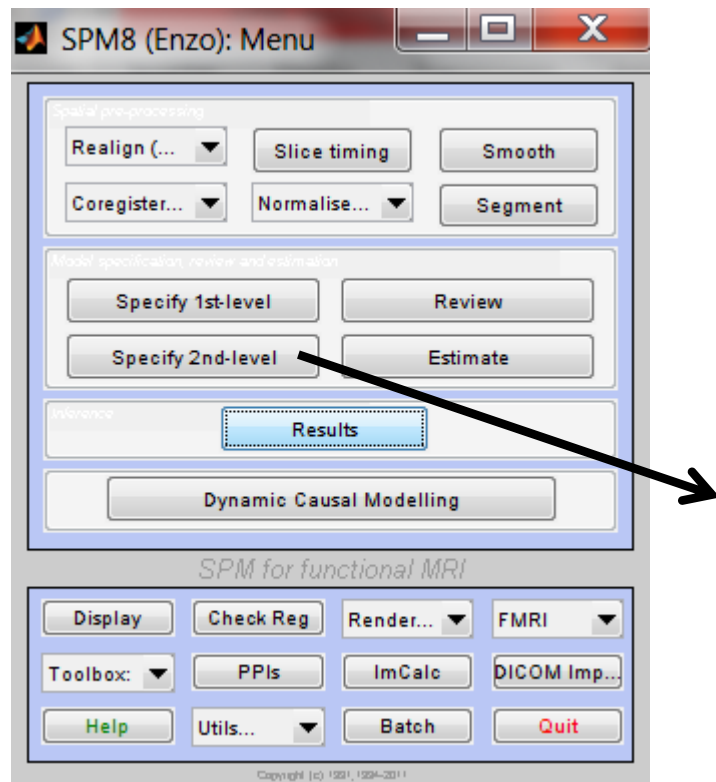


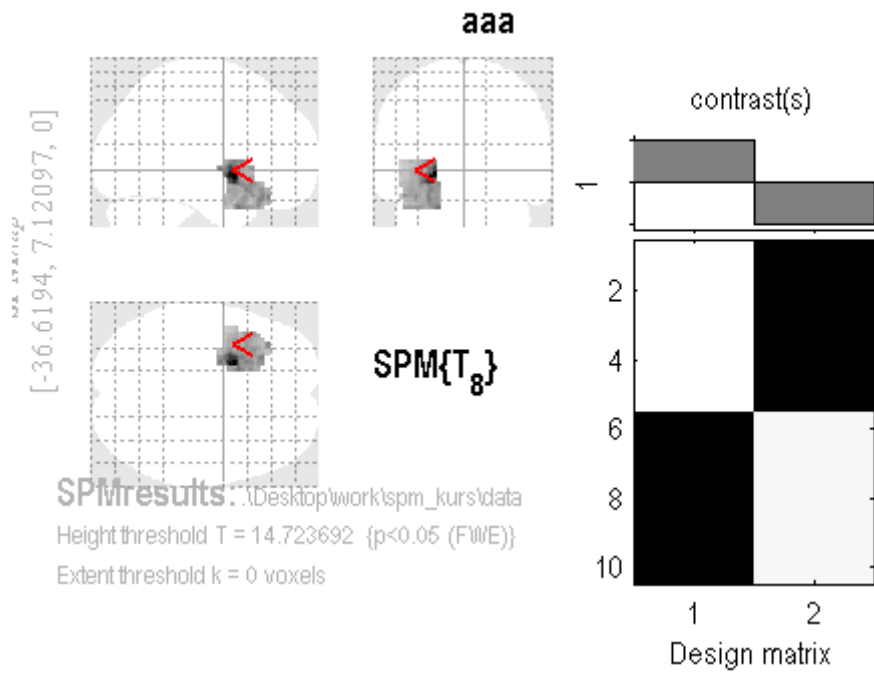
Second level analysis



Second level analysis

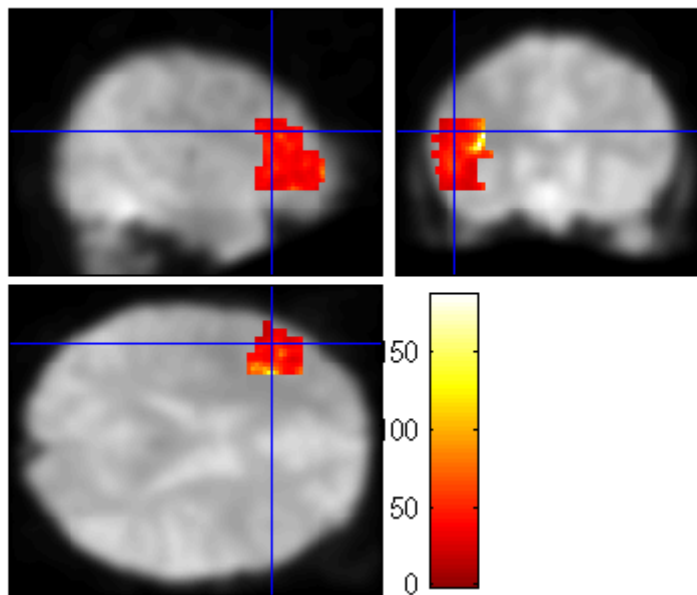
Select two-sample t-test and the Beta_0001.img as „scans“ for each subject in group1 and group 2





Results (second level)

group 1 > group 2



Interim summary

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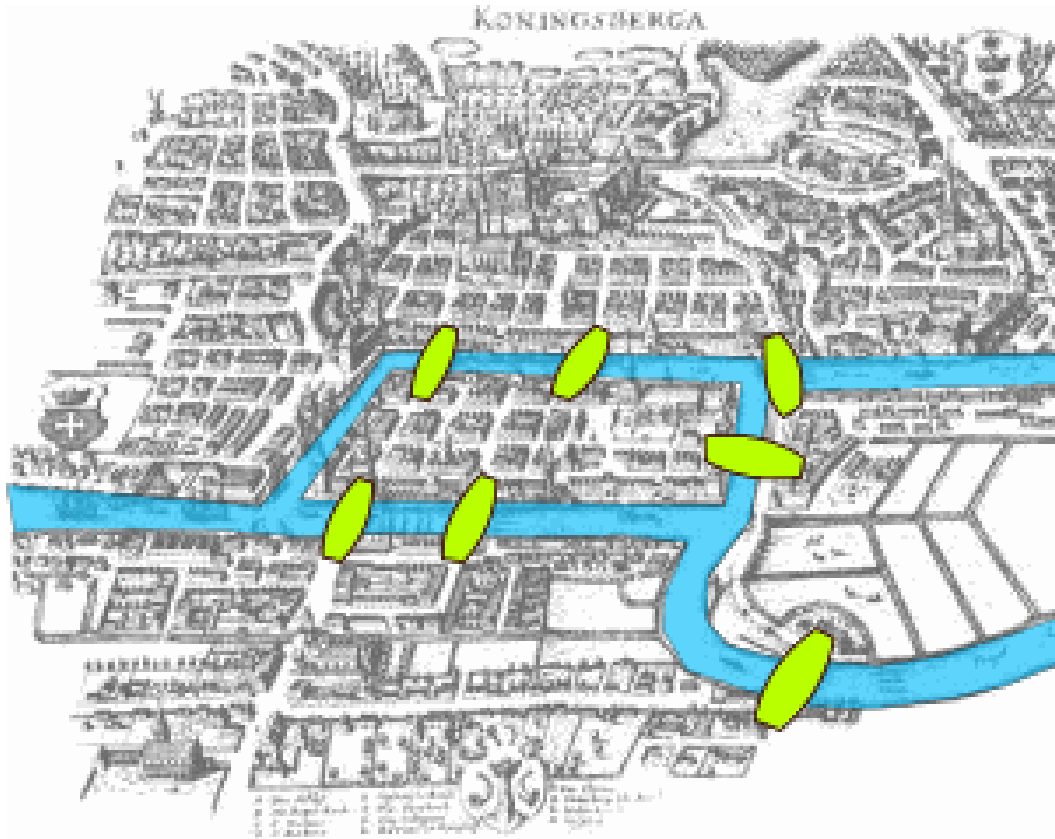
- Seed correlation can be performed in SPM by introducing a BOLD regressor in the Design Matrix, together with other physiological and motion confounds
- At the group level, seed correlation can be used to detect functional connectivity between populations (increasingly used as a candidate „biomarker“ for disease)
- When used that way, it is very important to account for all possible confounds specific to each populations (e.g., drugs? Depression? Motion? Vigilance?????)

What else to do...

- Play with seed correlation in this dataset (for example, using different seeds)
- Play with a longer (200 vols) single subject data set (single_subj/) using different seeds
- **This subject also has EEG regressors, which can be added to the design matrix to study BOLD correlates of different rhythms.**

Second part: graph analysis

Graph analysis of functional connectivity networks



Is it possible to cross all bridges without crossing one more than once?

Graph analysis of functional connectivity networks

- Graphs are simply a representation of **objects** and the **connections** between them

The language of interactions

A graph is a group of **nodes** (*persons, brain regions, soccer players, actors, etc*) and a group of **edges** representing relationships (*love, hate, neuronal coordination, movie co-starring, etc*)

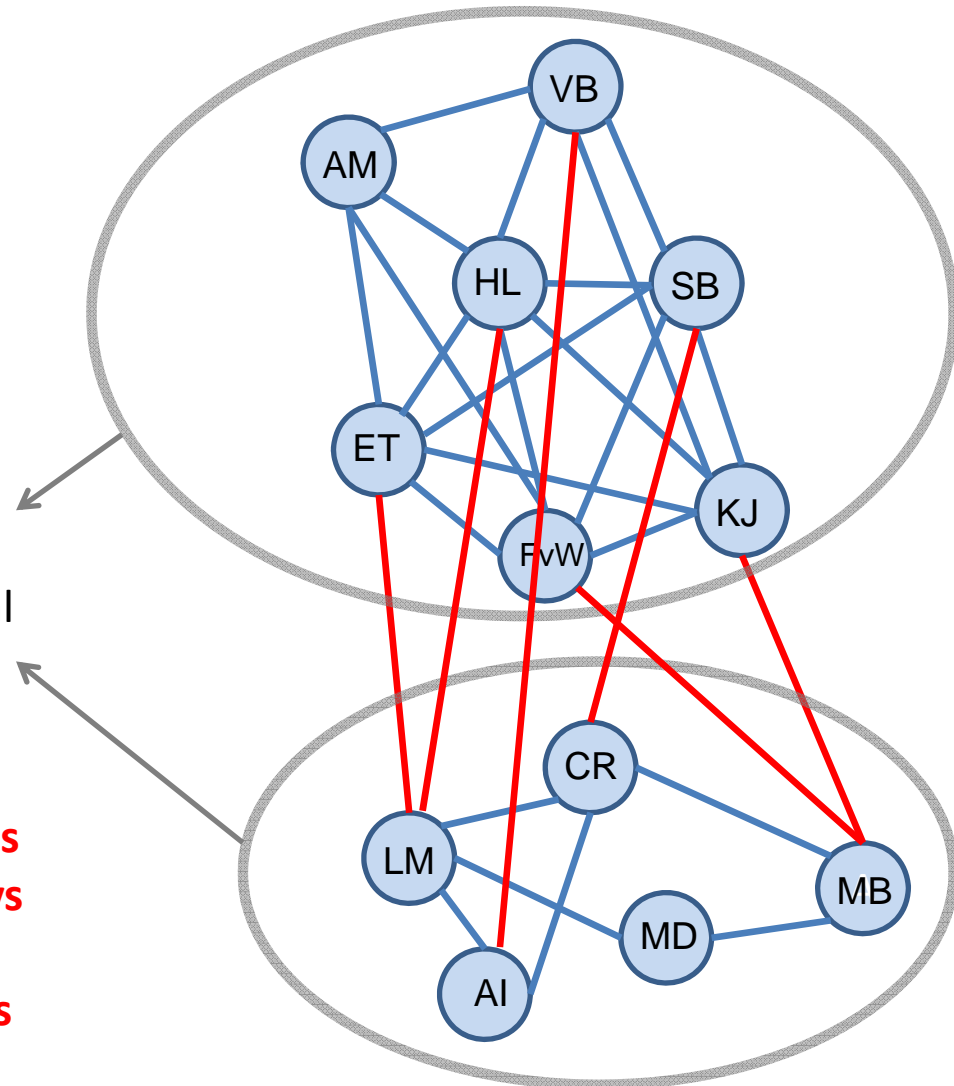


twitter

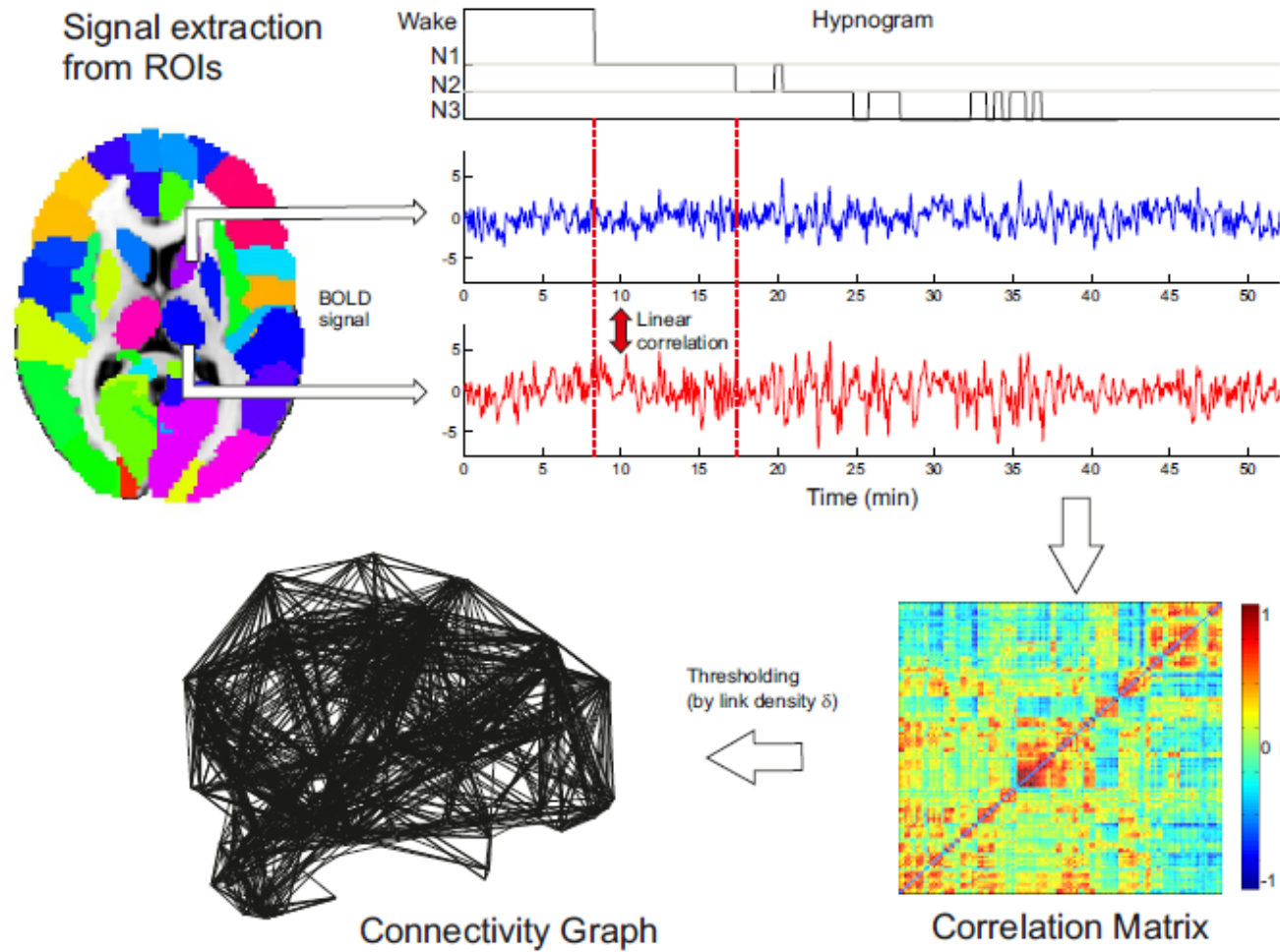


Separated (but interacting) social groups

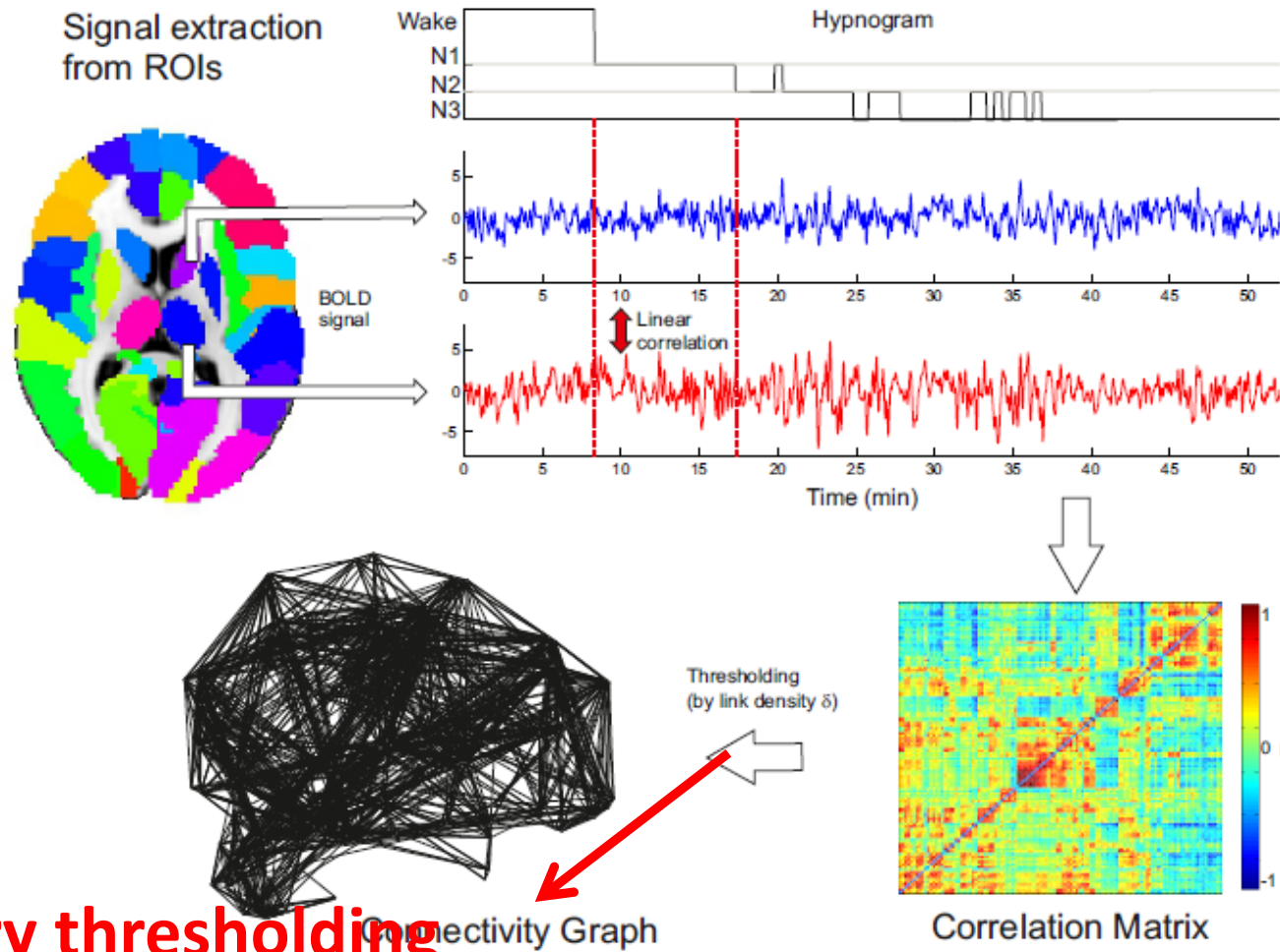
More interactions gradually destroys the identity of separed modules



From BOLD time series to graphs



From BOLD time series to graphs



**Arbitrary thresholding
of functional connectivity**

What to study in a graph?

(see *Bullmore and Sporns, Nat Rev Neurosci 2009* for a review)

- Average path length (L) : mean distance between each pair of nodes

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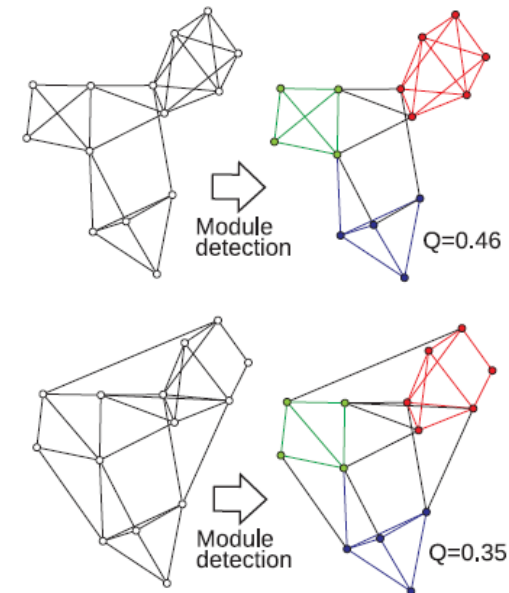
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The arbitrary threshold in FC used to define a connection is selected to match a given density of links. Properties are studied along a range of density of links!!

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- Add the Brain Connectivity Toolbox (BCT) to the path
- Run *network_analysis_first_level_script.m*. This will create in each subject folder a .mat file (network_analysis.mat) containing the results of the first level. (open AAL template!)

How to do it? First level

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- Run *network_analysis_first_level_script.m*. This will create in each subject folder a .mat file (network_analysis.mat) containing the results of the first level. (open AAL template!)
- Note that this script invokes a function (*network_measures_aal.m*) which uses the BCT and gives all the network metrics provided the BOLD time courses in all ROI (in this case, the AAL template)

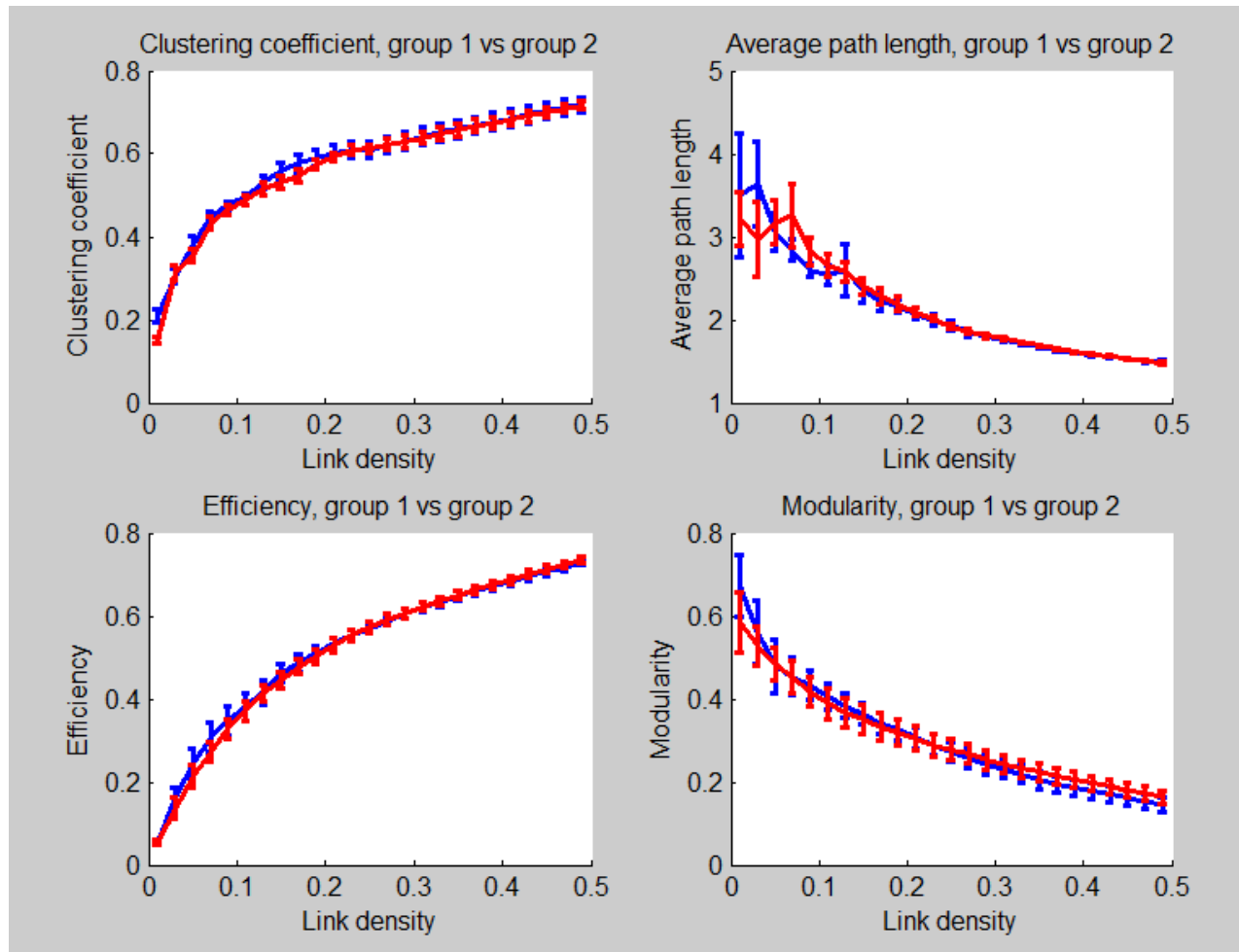
How to do it? Second level

- Run the script *network_analysis_second_level_script.m*, which computes statistics (using Students t-test and Bonferroni corrections).

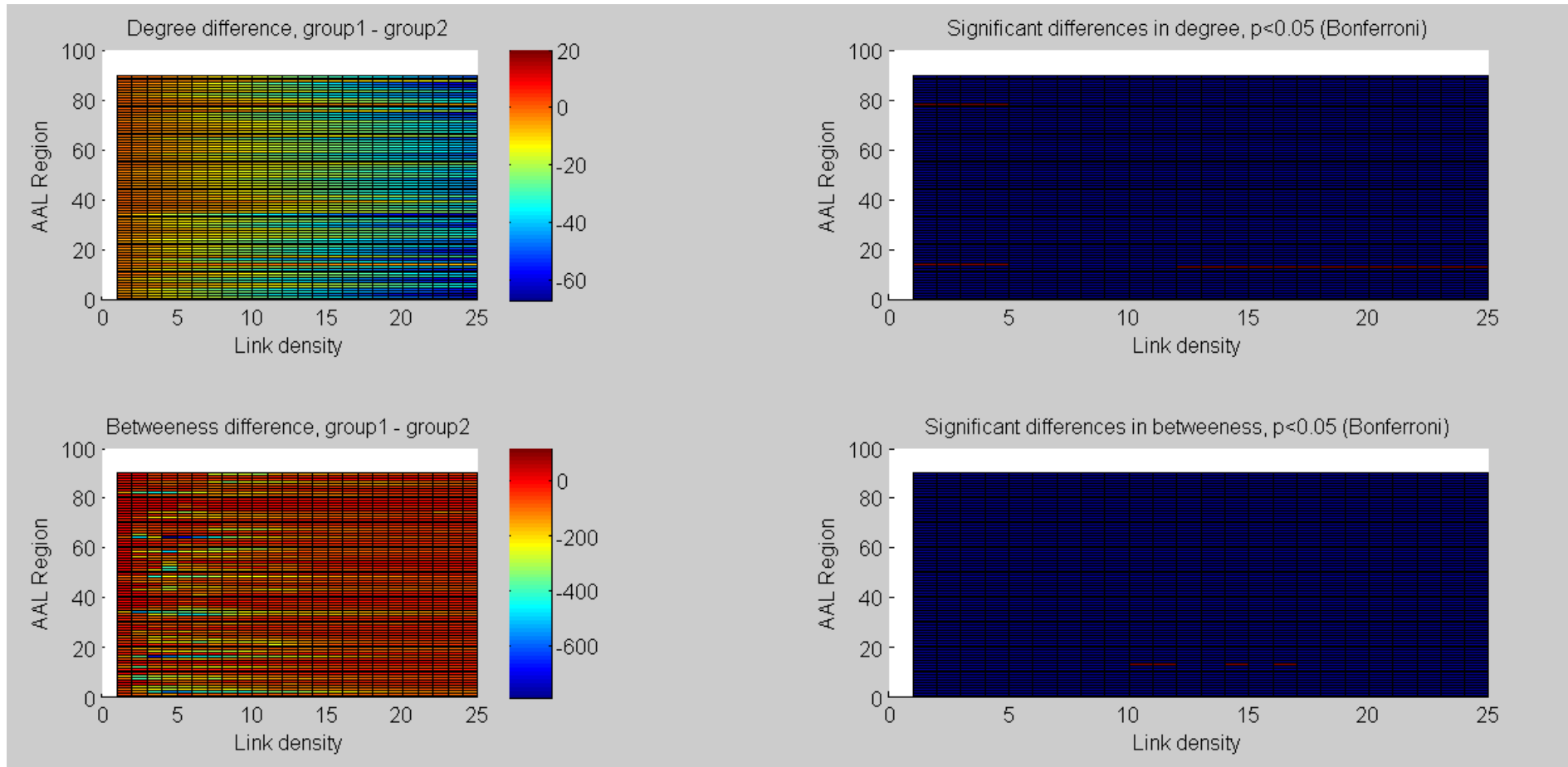
How to do it? Second level

- Run the script *network_analysis_second_level_script.m*, which computes statistics (using Students t-test and Bonferroni corrections).
- Plots are produced automatically

Results - I

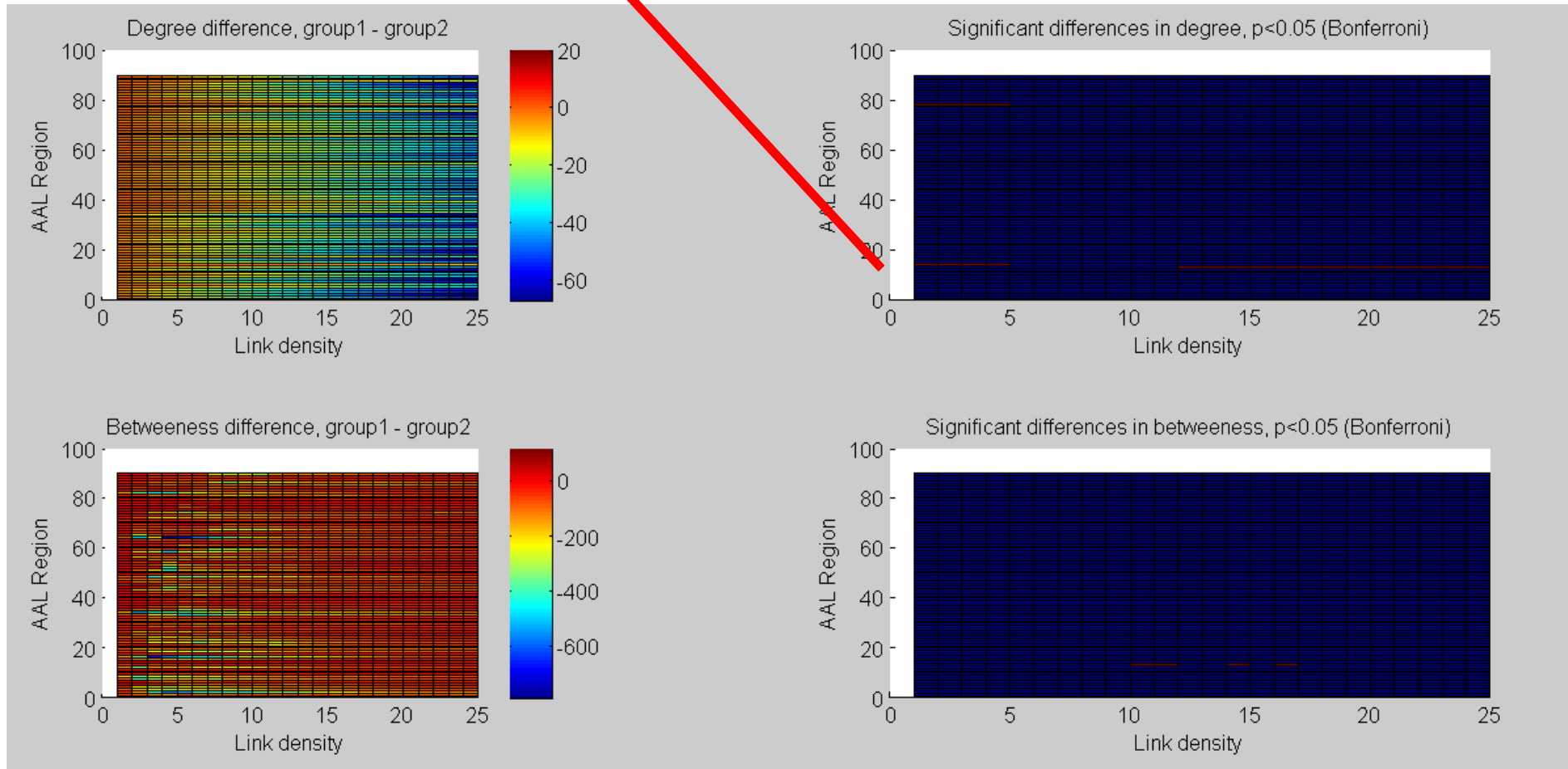


Results - II



Increased prefrontal degree
in group 1
(more connected to the
thalamus!)

Results - II



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- Graph methods allows the study of interactions between *all* pairs of regions
- They provide indexes summarizing the large-scale organization of functional networks
- They constitute an exploratory, multivariate method, as opposed to the seed-based, mass univariate approach of seed correlation.
- In other words, if we did not know a priori that there was something different in pre-frontal areas between both populations, graph methods allow us to explore and find the difference.