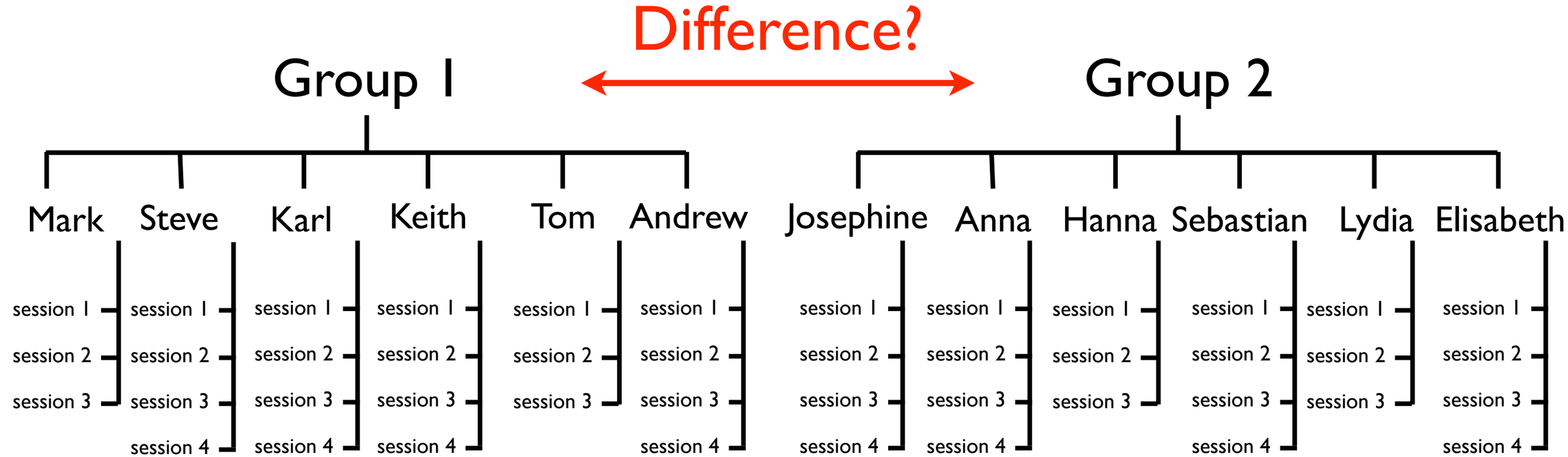
Group-level Analysis in OSL

OHBA Analysis Workshop

Group Analysis

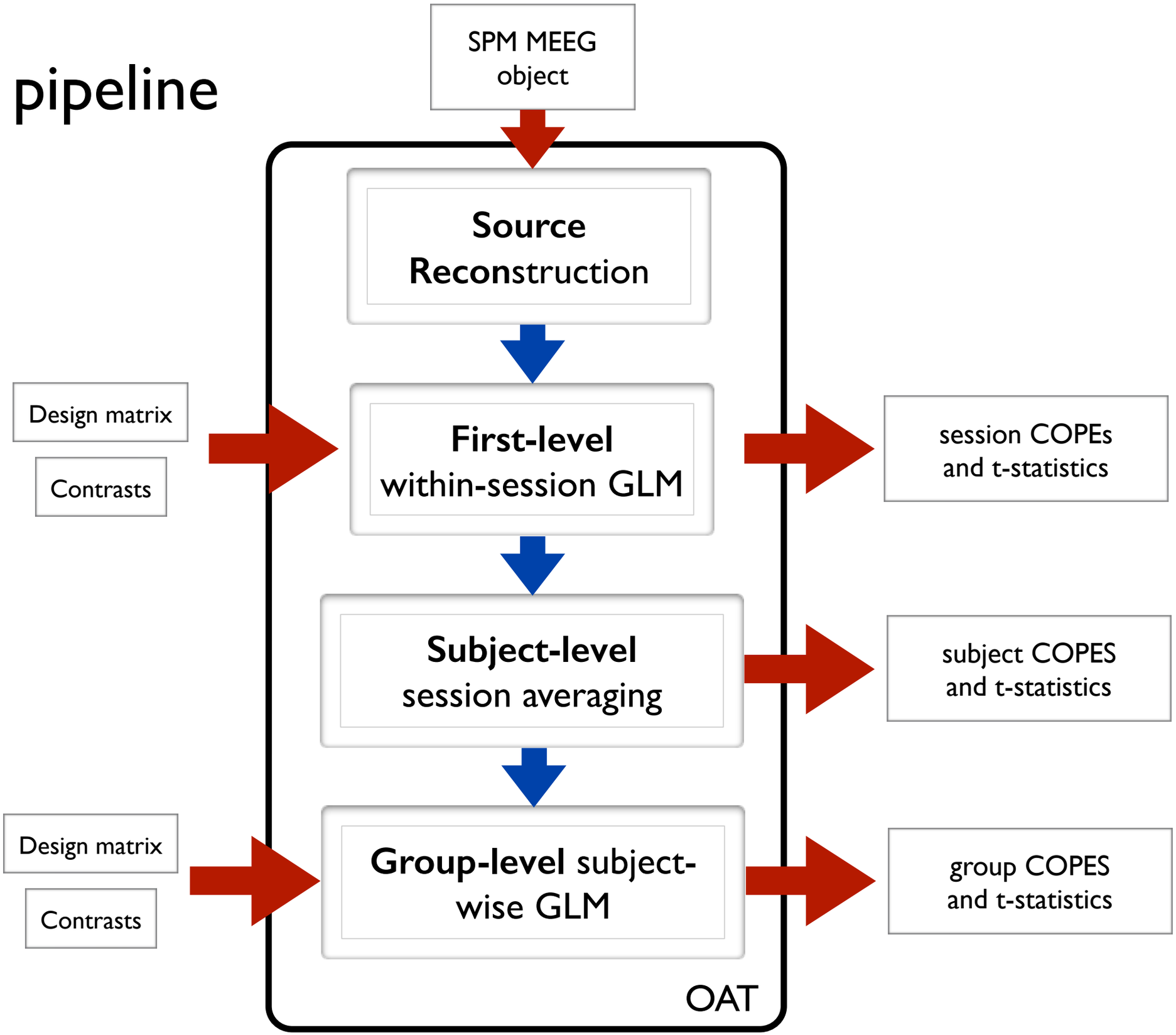
- typically need to infer across multiple subjects, sometimes multiple groups and/or multiple sessions



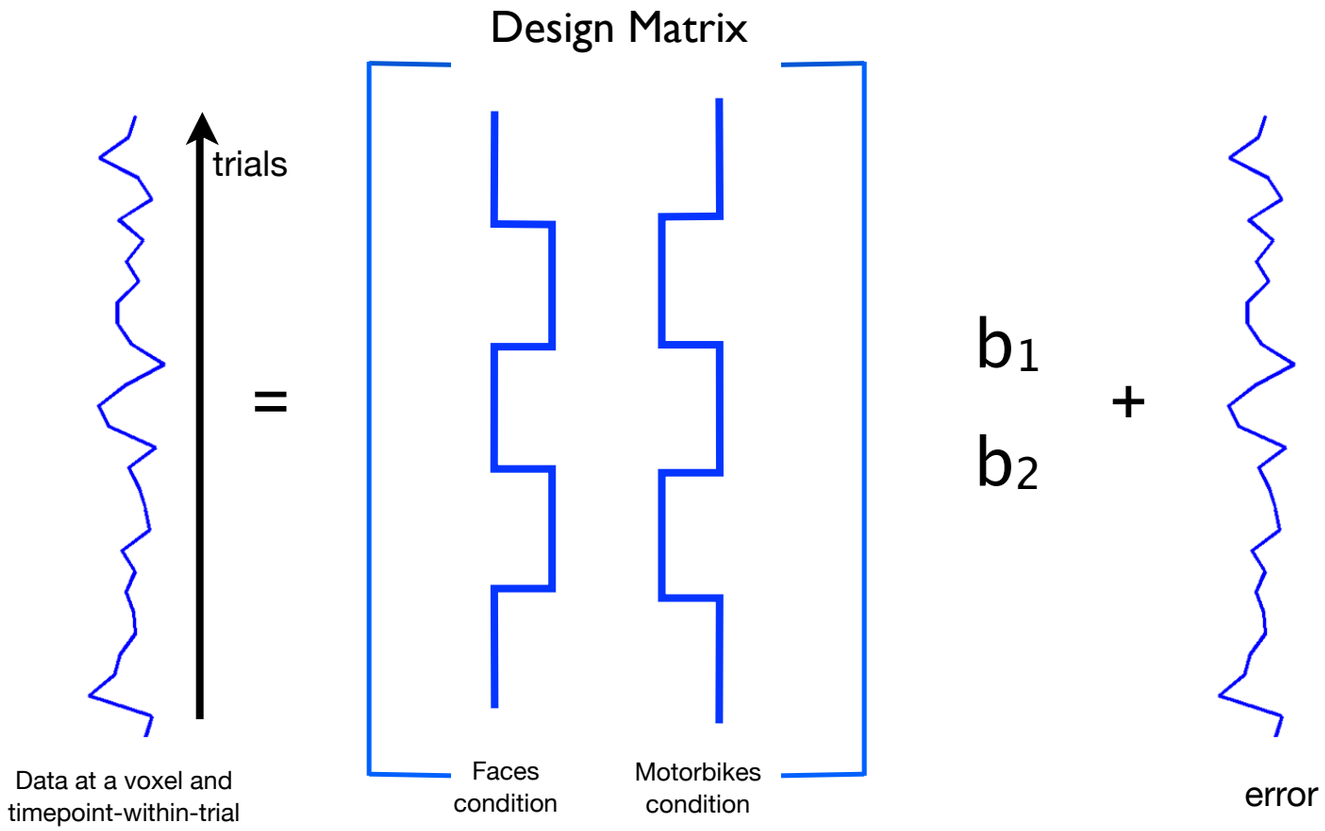
- questions of interest involve tests/comparisons at the group level

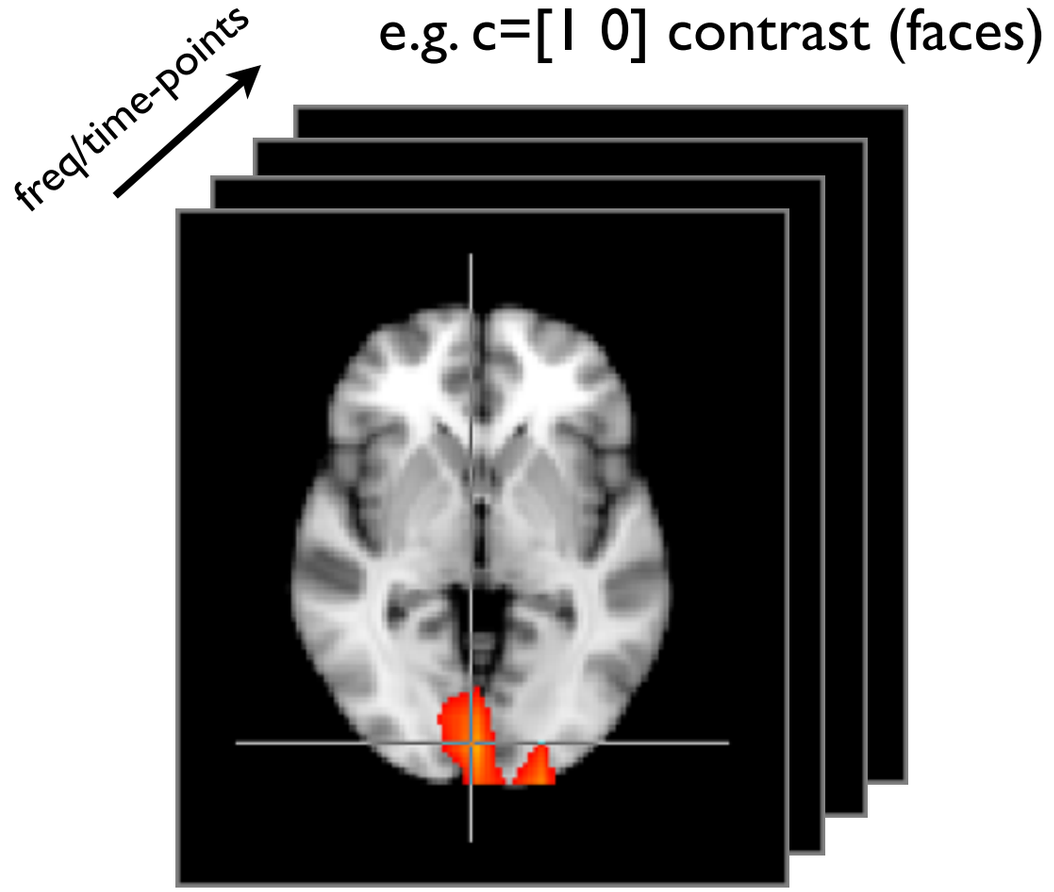
OAT Pipeline Stages

- 4 distinct pipeline stages:



First-Level (Trial-wise) GLM



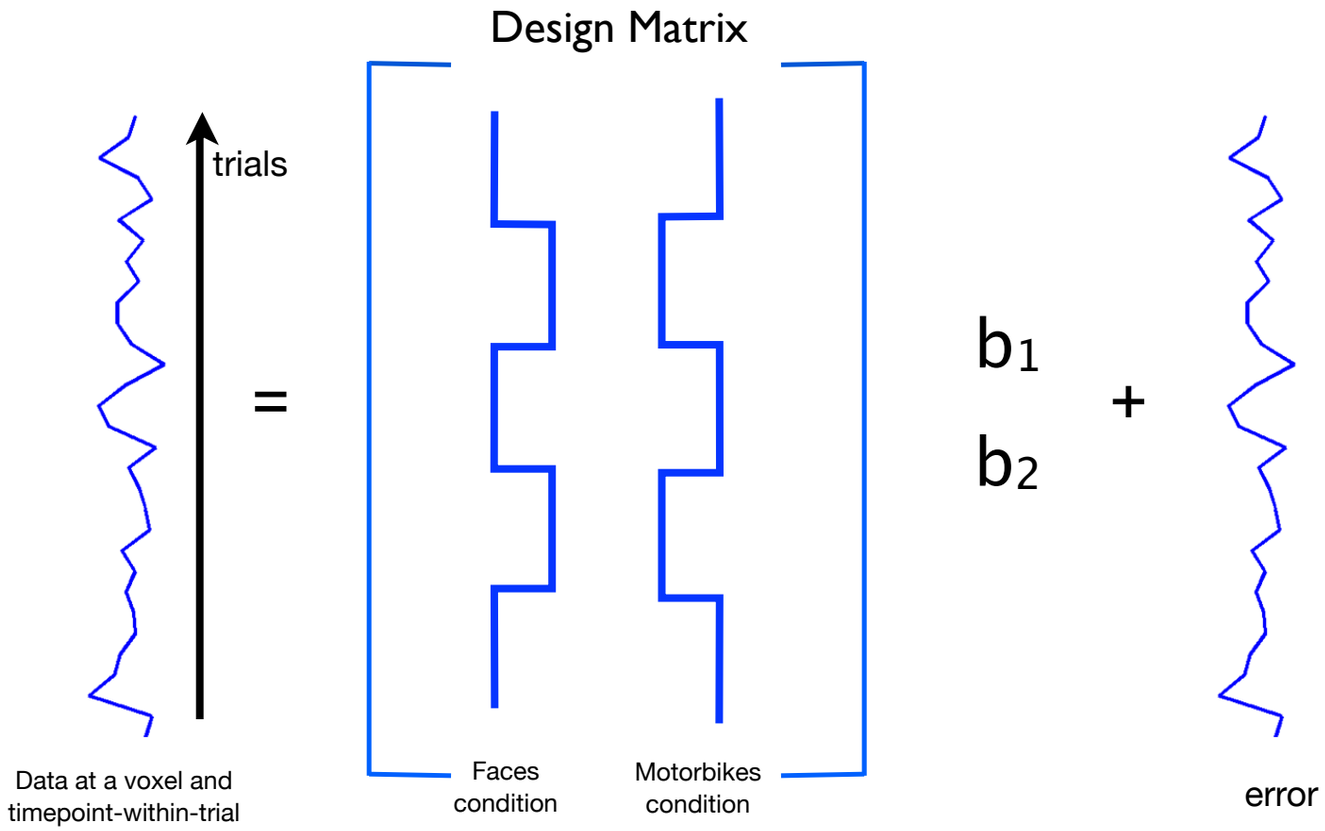


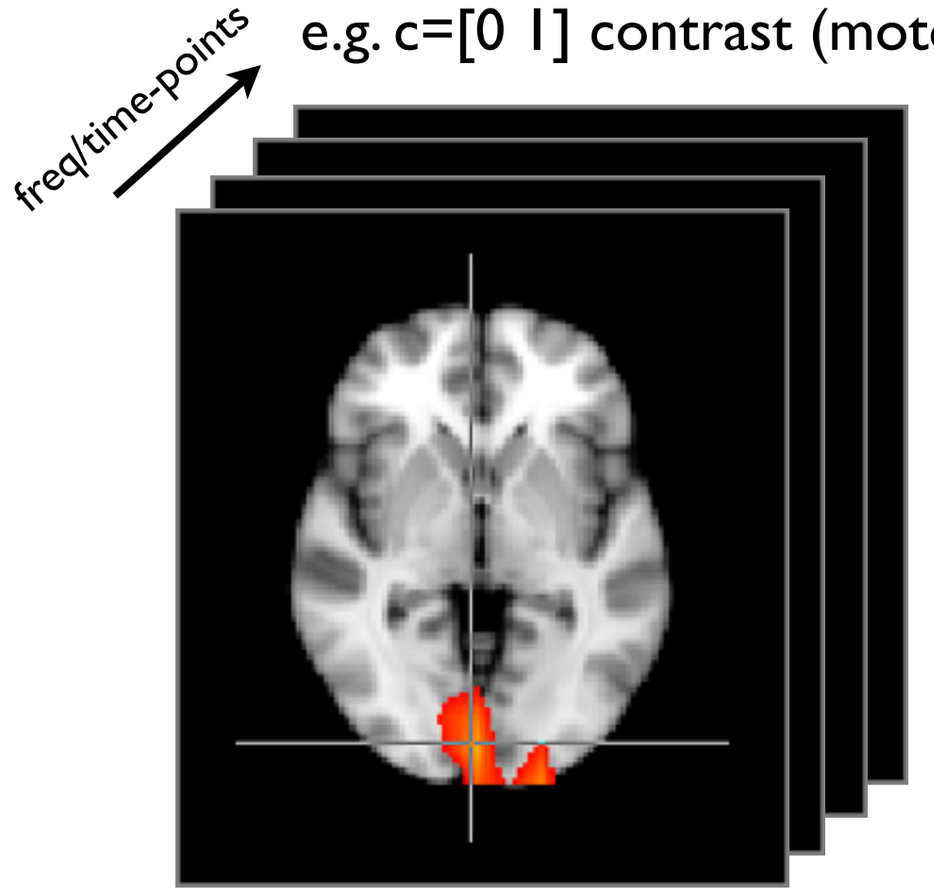
Repeat for all voxels/ freq/time-points, then compute contrasts: COPE=c*B

$$Y=Xb+e \rightarrow B=pinv(X)Y$$

B is the Parameter Estimates (PEs) of b

First-Level (Trial-wise) GLM





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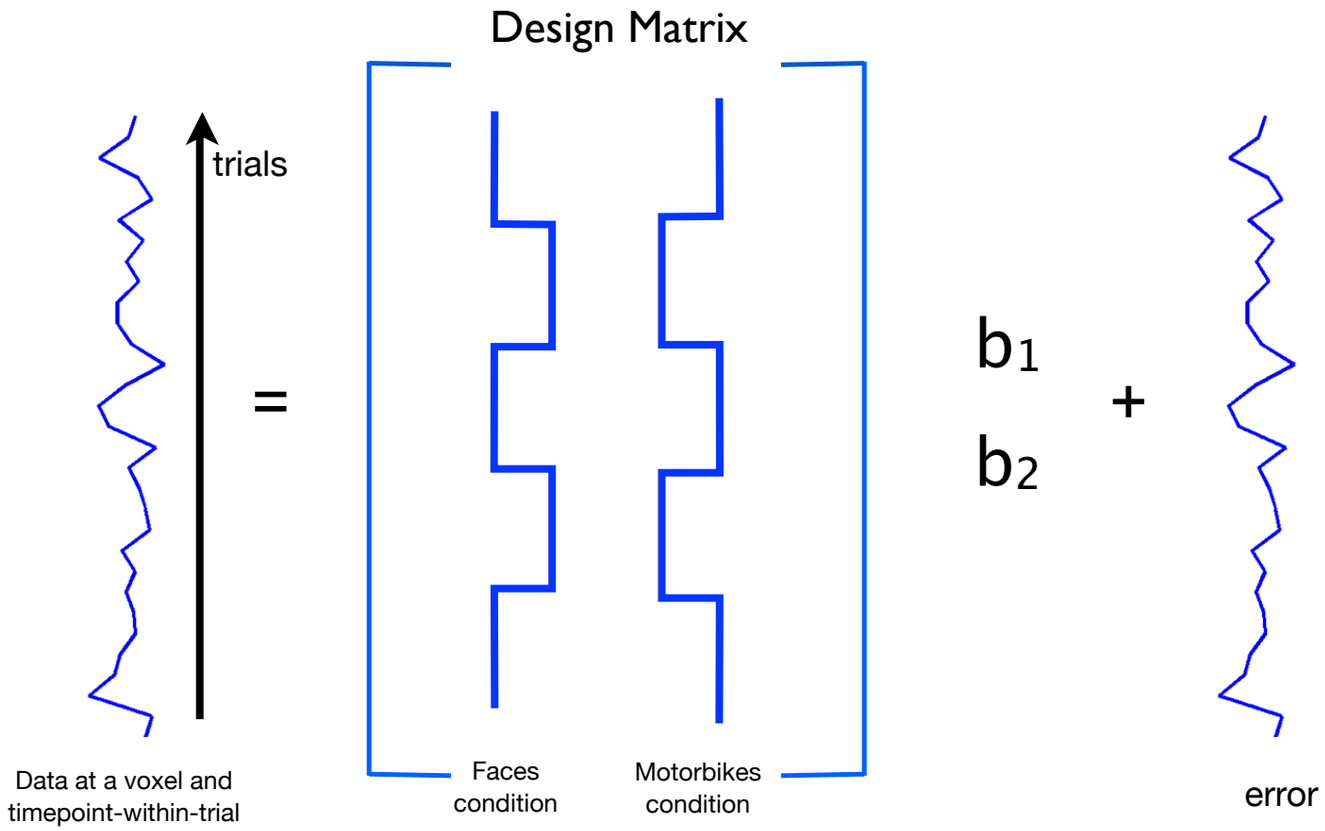

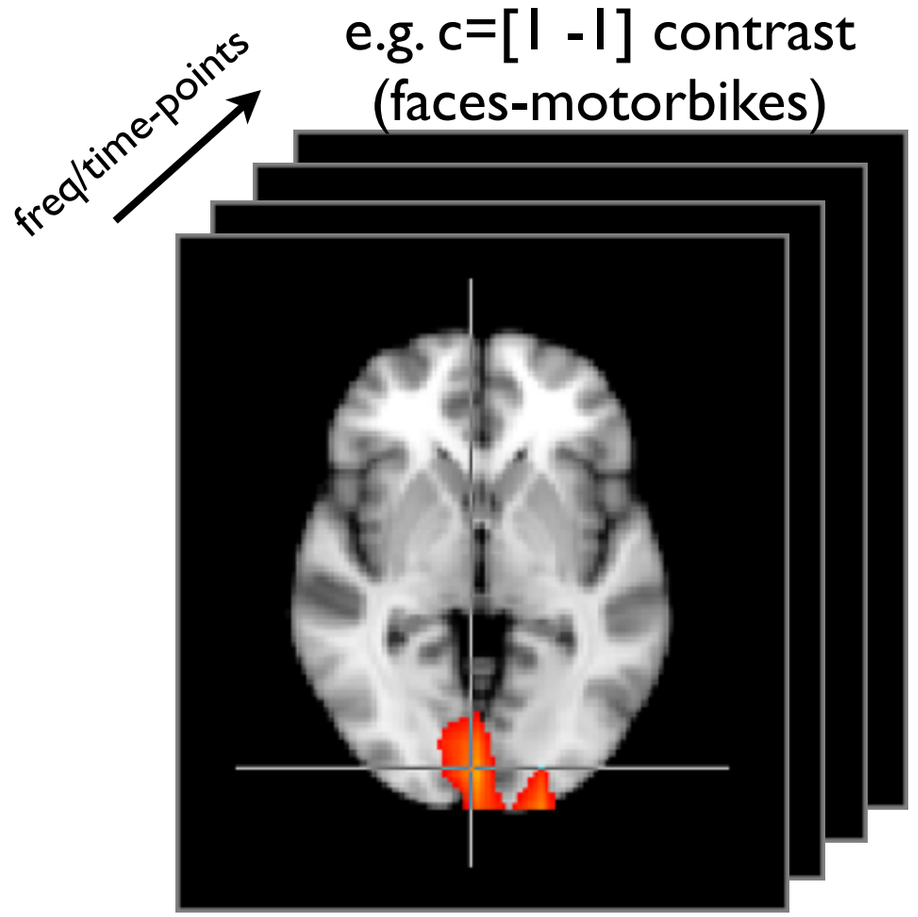

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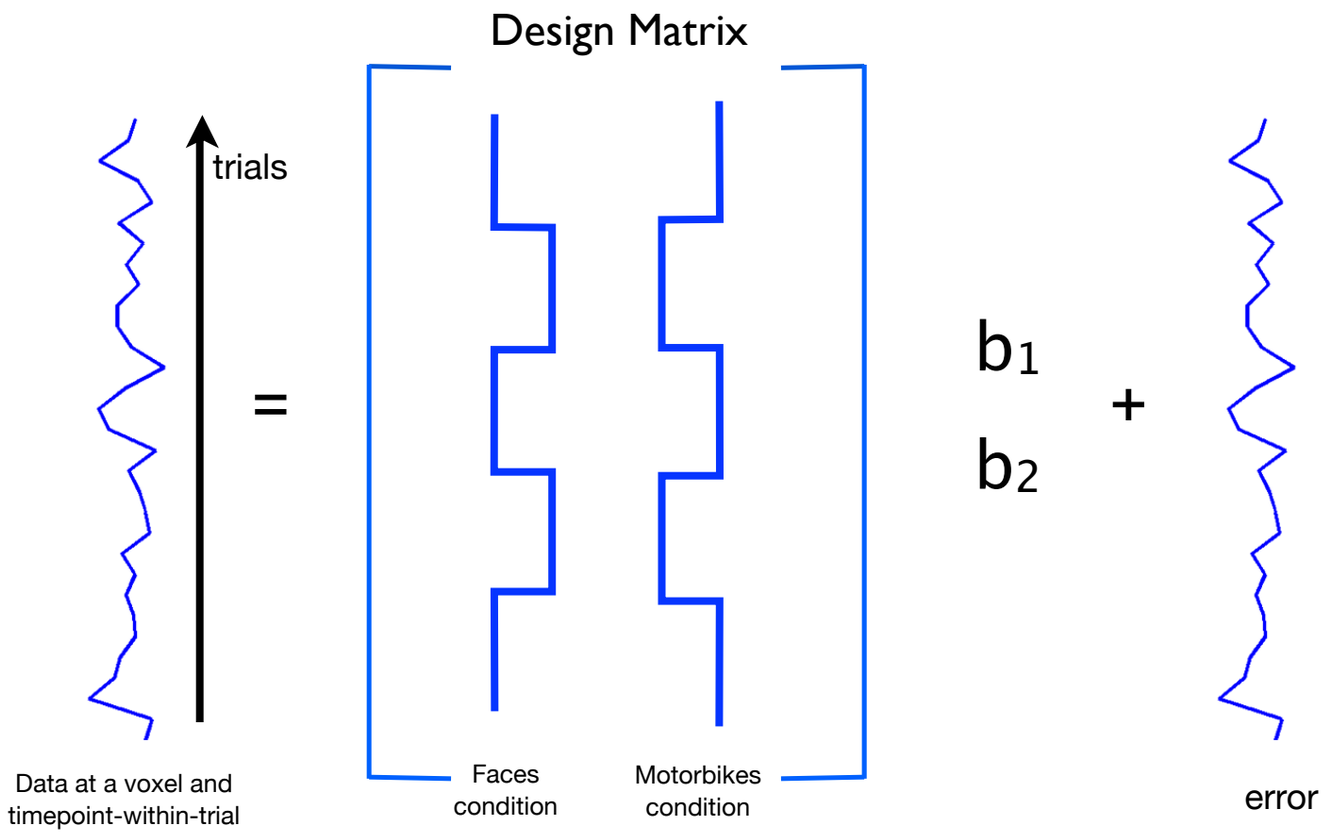
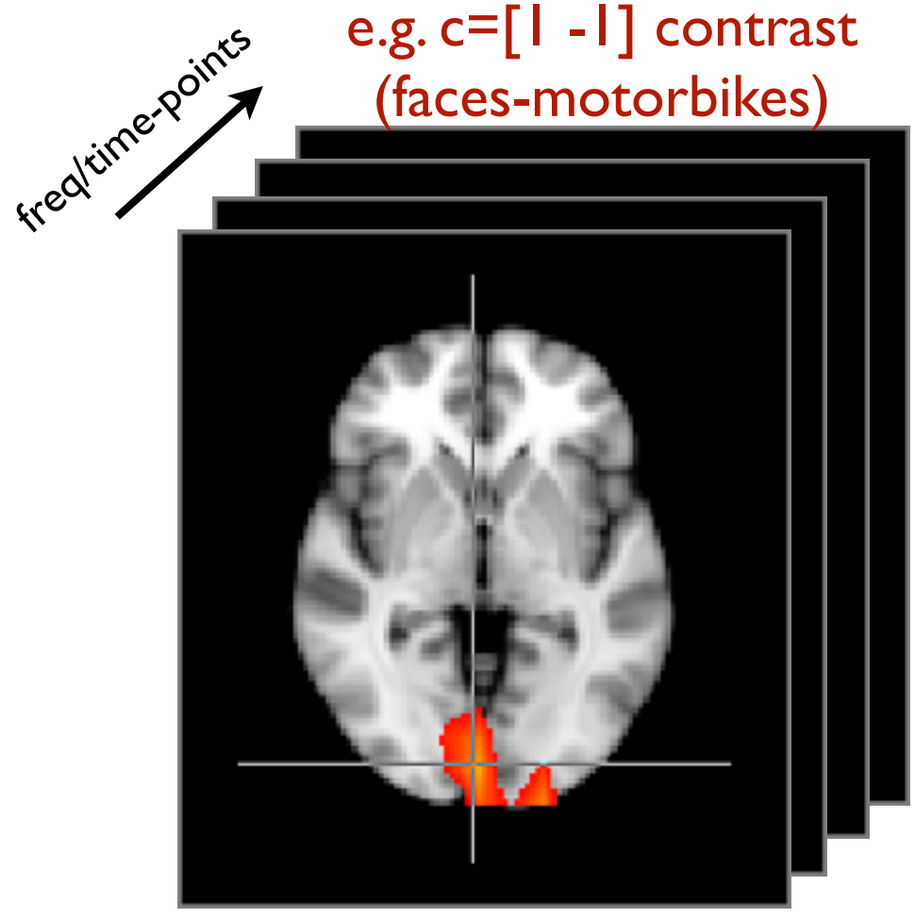
First-Level (Trial-wise) GLM

first-level COPEs are the INPUTS (data) in the Group Analysis:

e.g. c=[1 -1] contrast
(faces-motorbikes)





Repeat for all voxels/
freq/time-points, then
compute contrasts:
COPE=c*B

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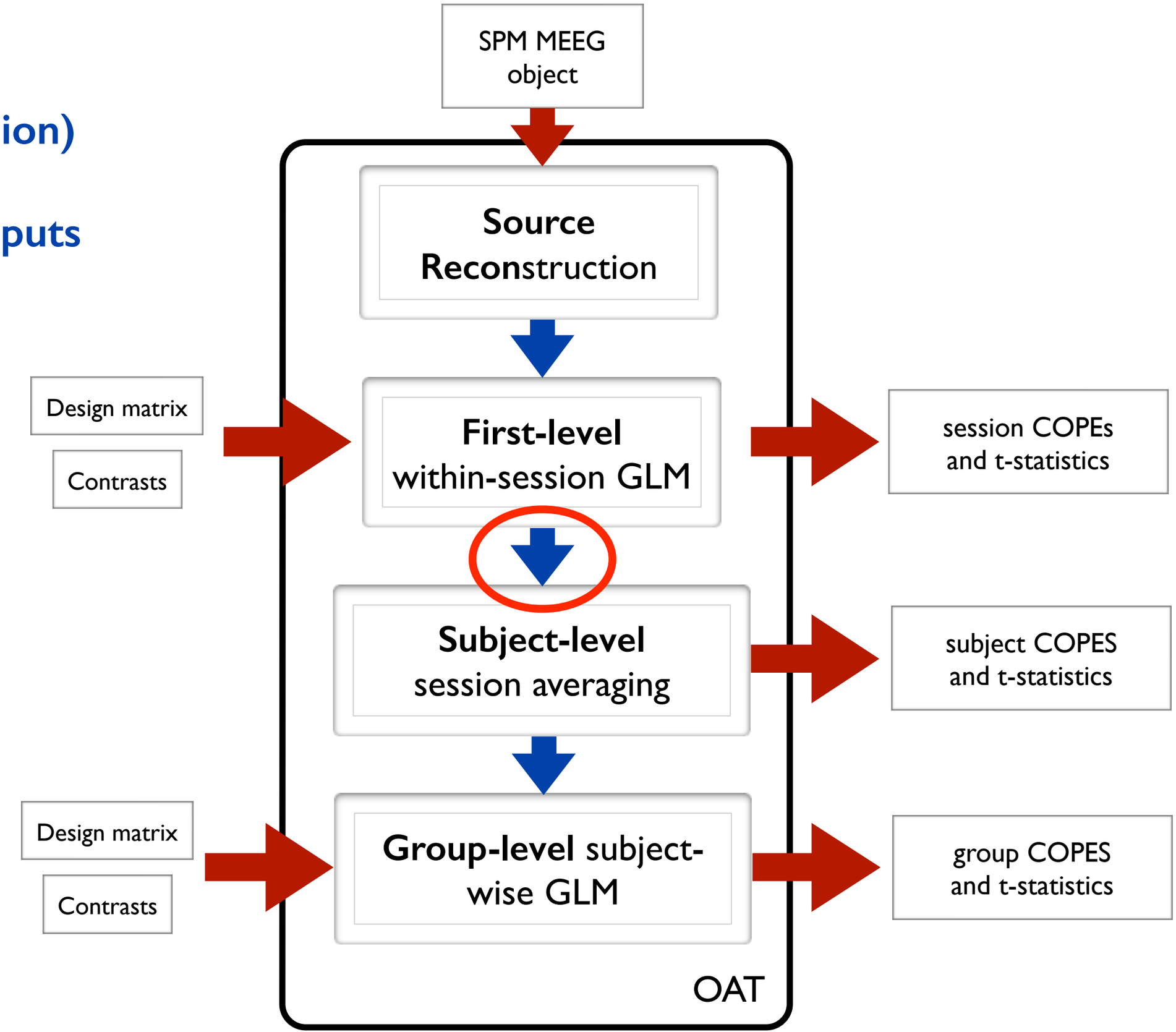
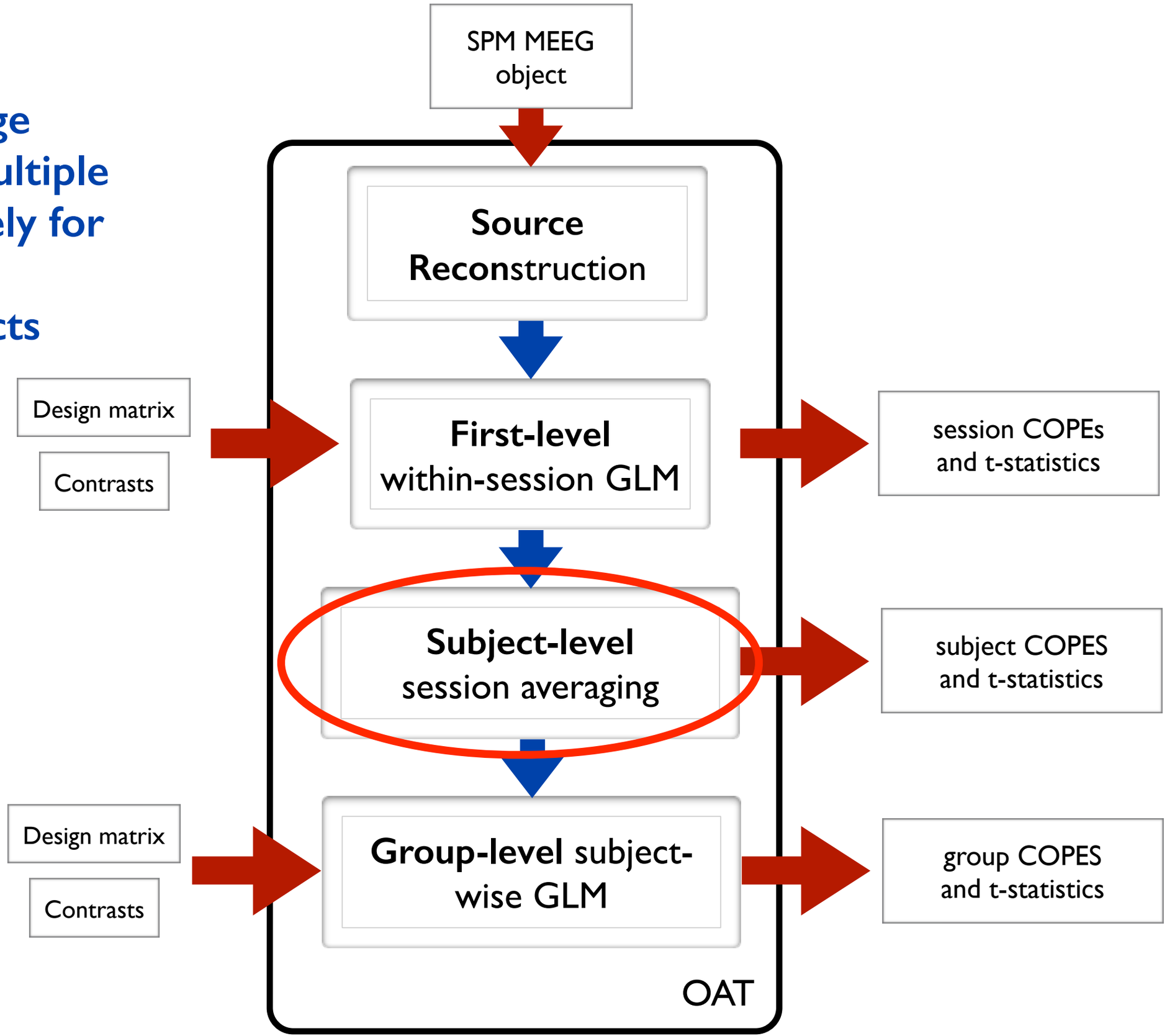
Multiple Session Analysis

First-level (session) COPEs are the Subject-level Inputs



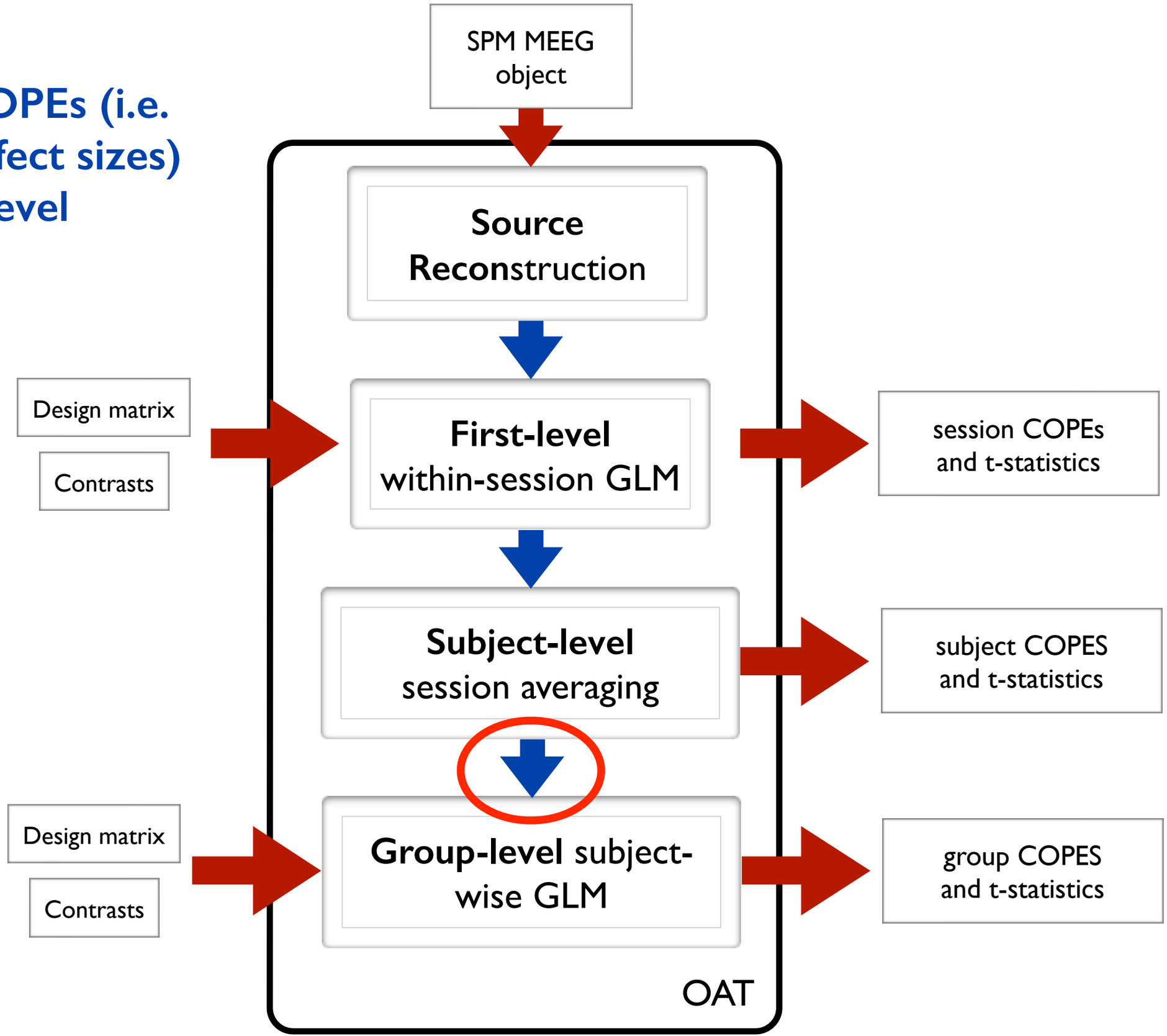
Multiple Session Analysis

Subject-level stage averages over multiple sessions separately for each subject
- using fixed effects



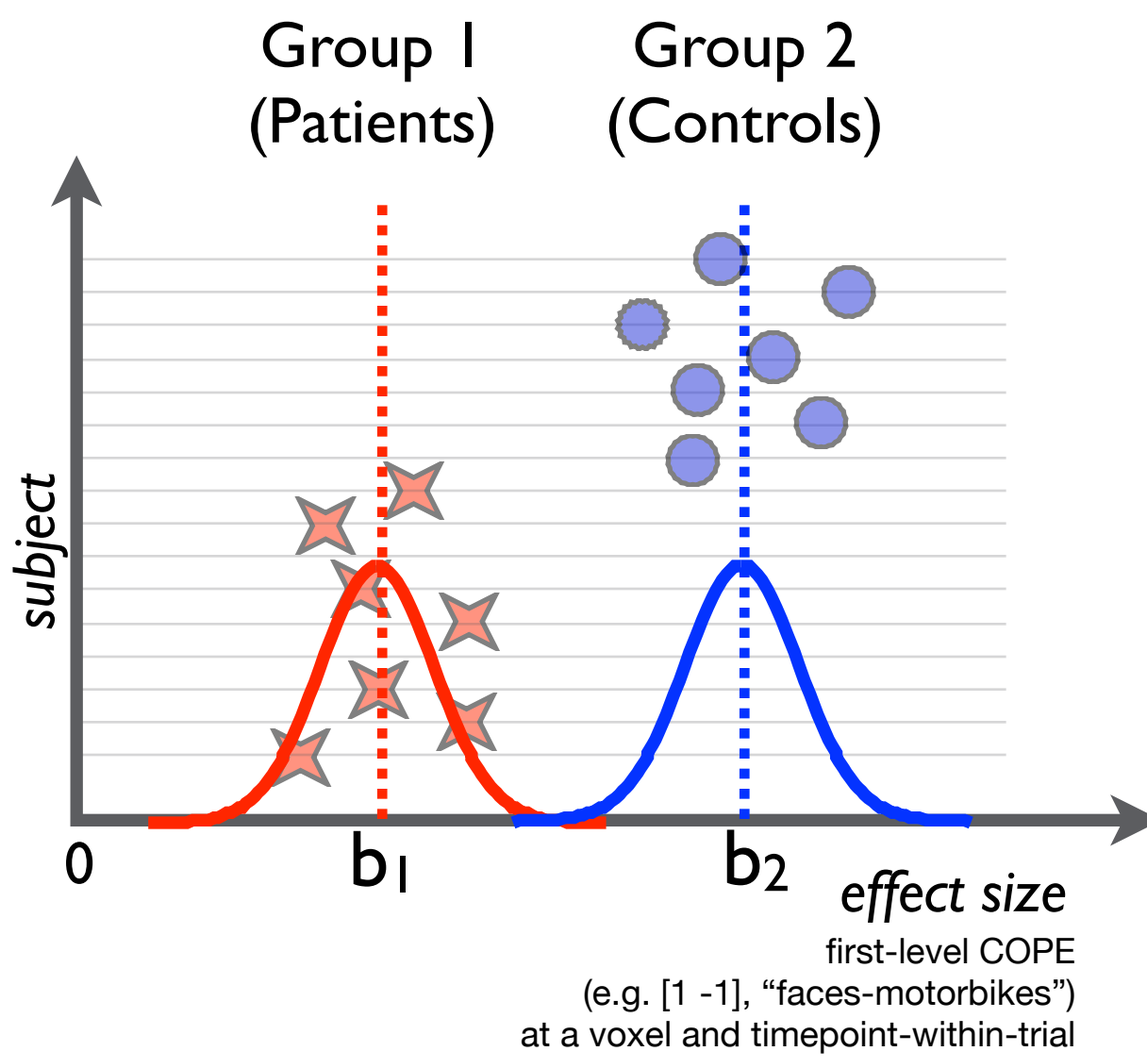
Multiple Subject Analysis

Subject-level COPEs (i.e. mean subject effect sizes) are the Group-level Inputs



Subject-wise GLM (Multiple Regression)

- We have two groups (e.g. 7 patients, 7 controls)



first-level COPE
(e.g. [1 -1], “faces-motorbikes”)
at a voxel and timepoint-within-trial

Subject-wise GLM (Multiple Regression)

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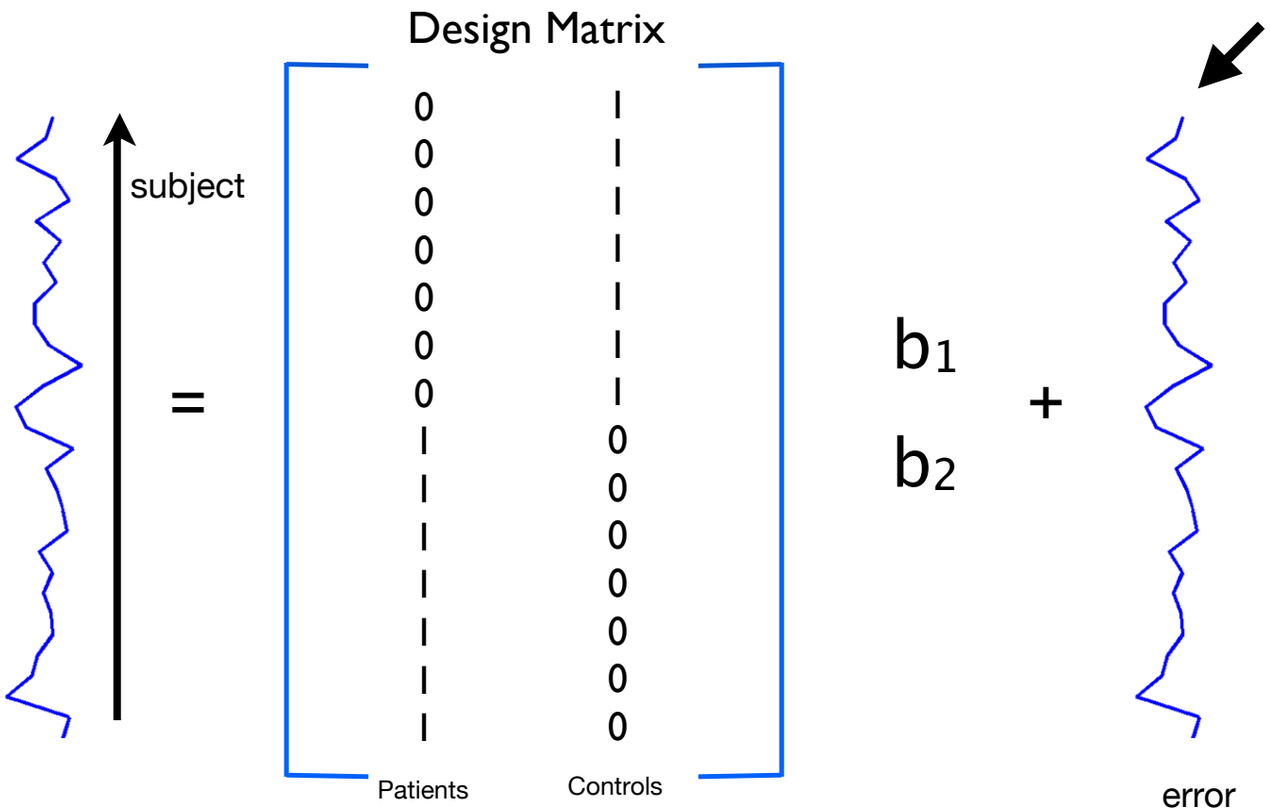
We model the between-subject variance giving inference on the populations (i.e. mixed-effects)



$Y = X b + e$

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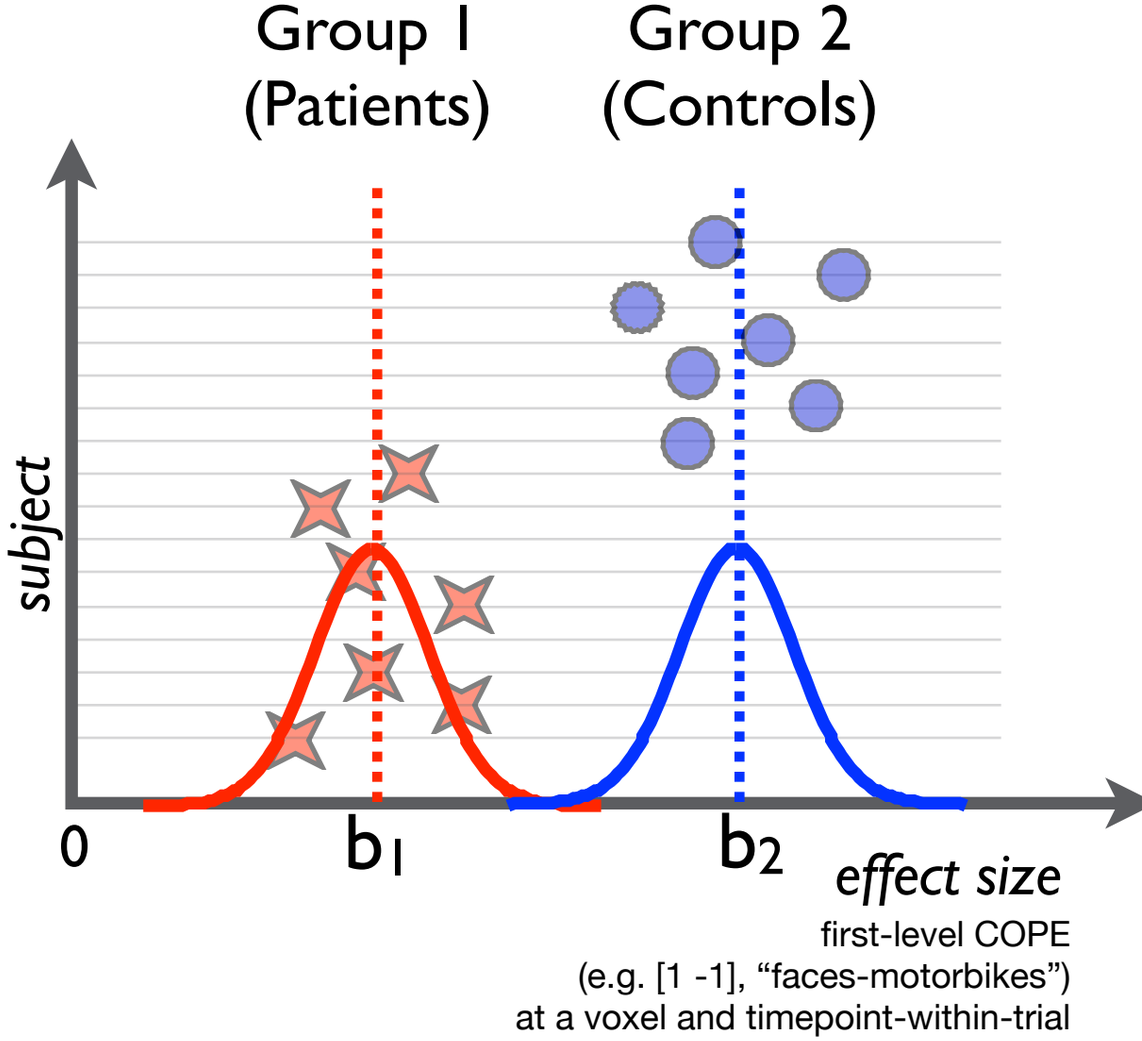

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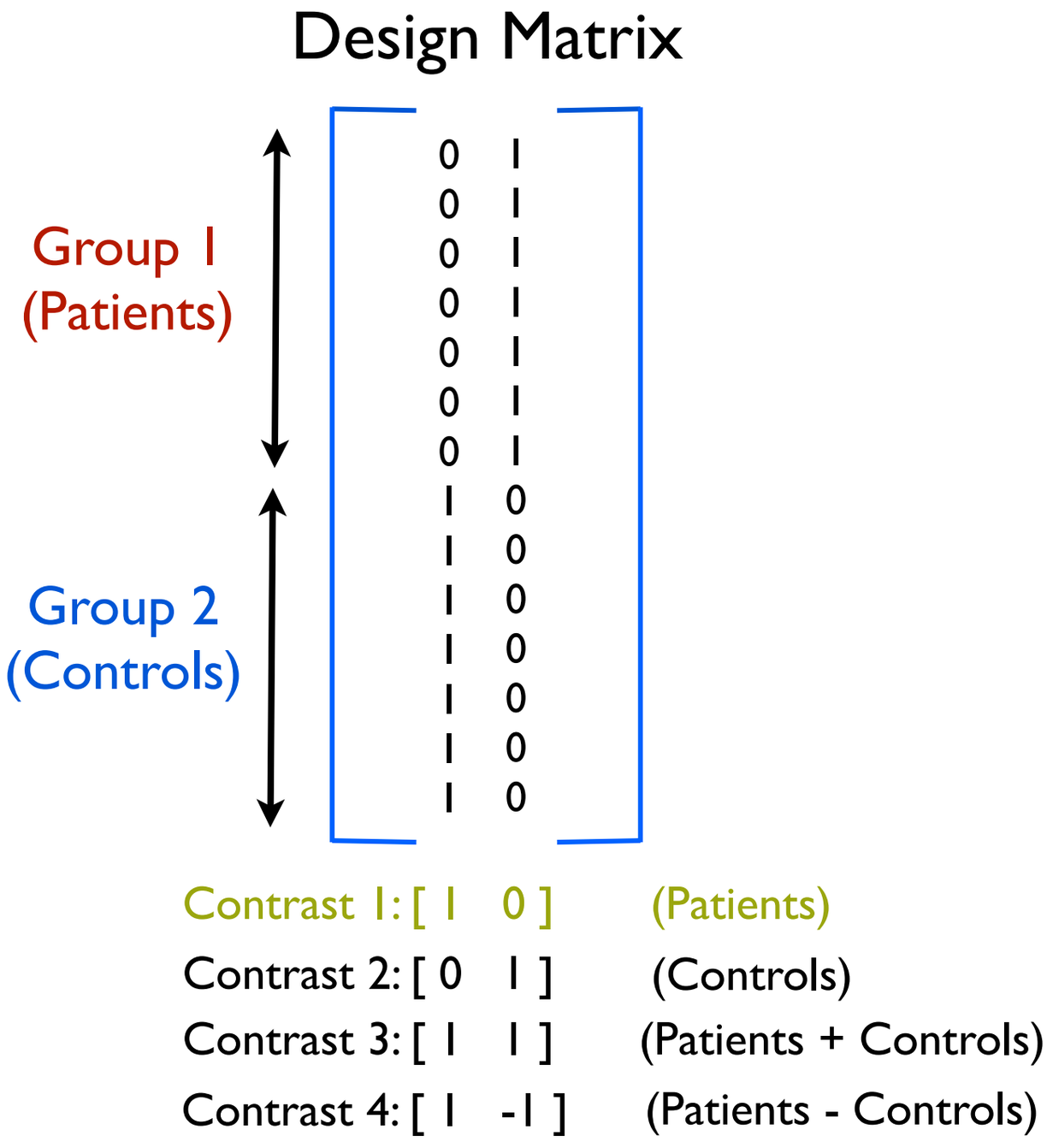

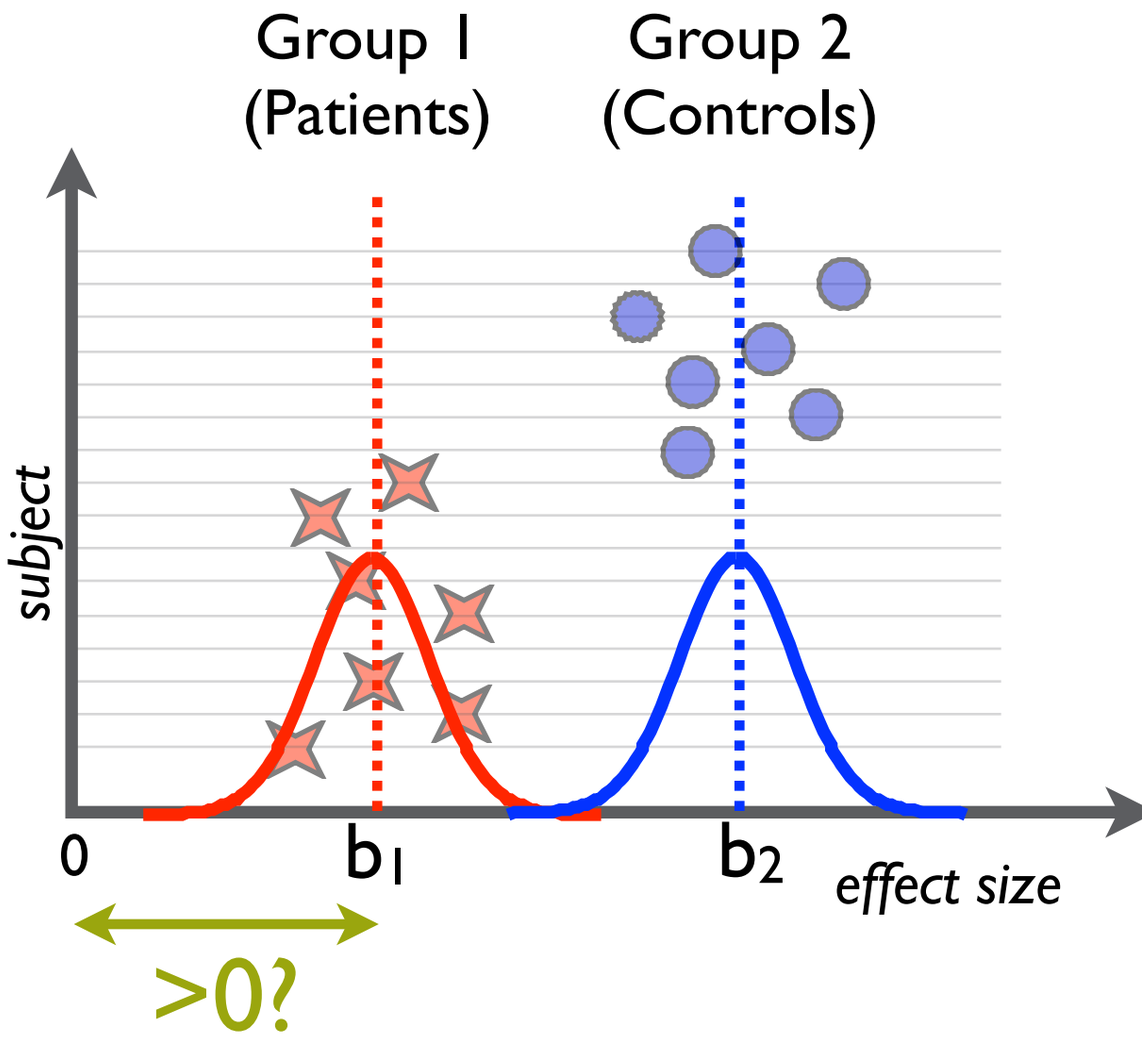

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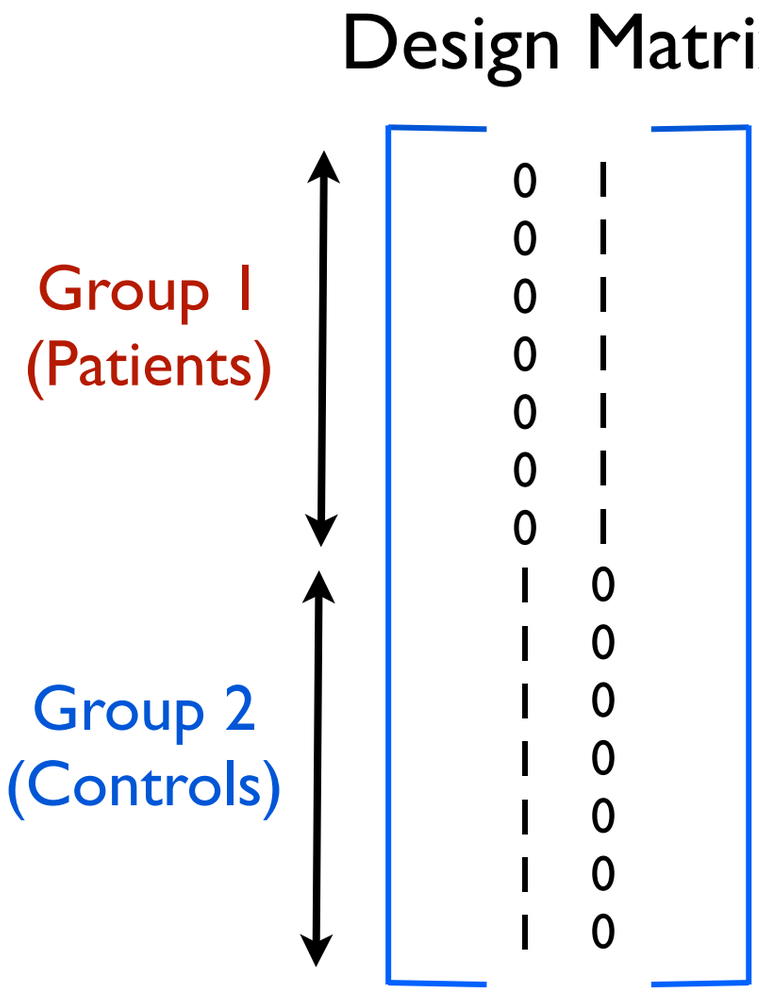
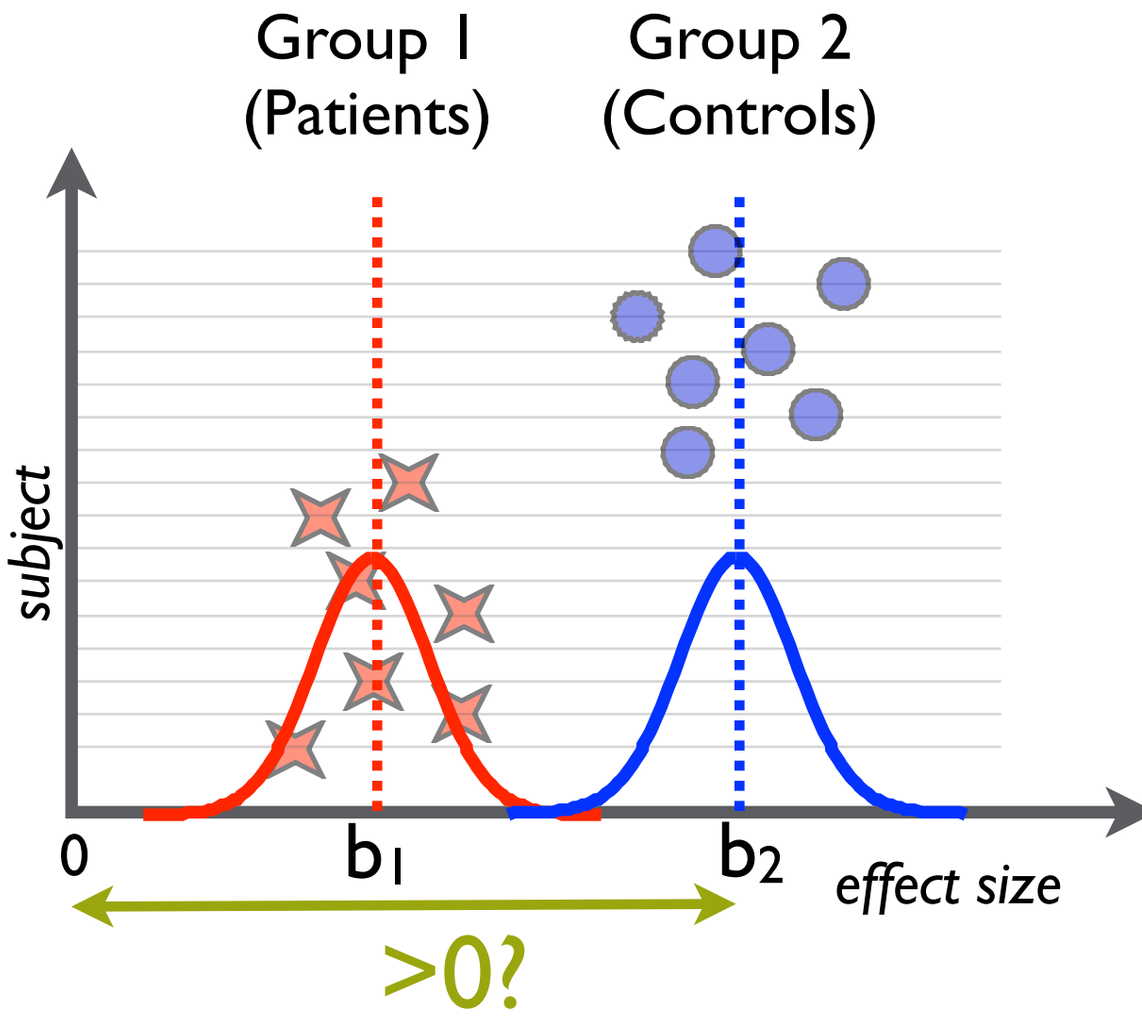


Contrast 1: [1 0] (Patients)

Contrast 2: [0 1] (Controls)

Contrast 3: [1 1] (Patients + Controls)

Contrast 4: [1 -1] (Patients - Controls)



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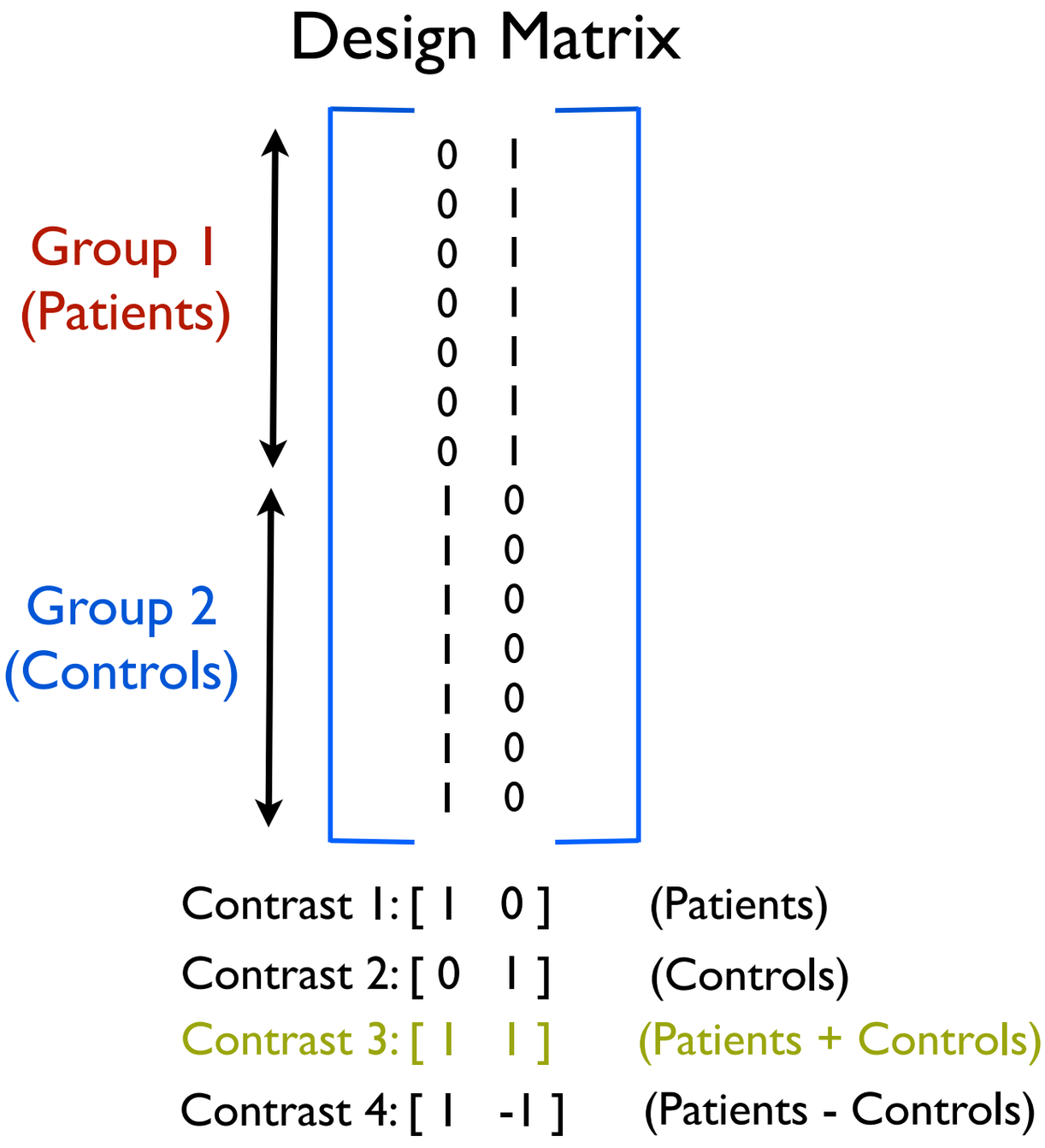

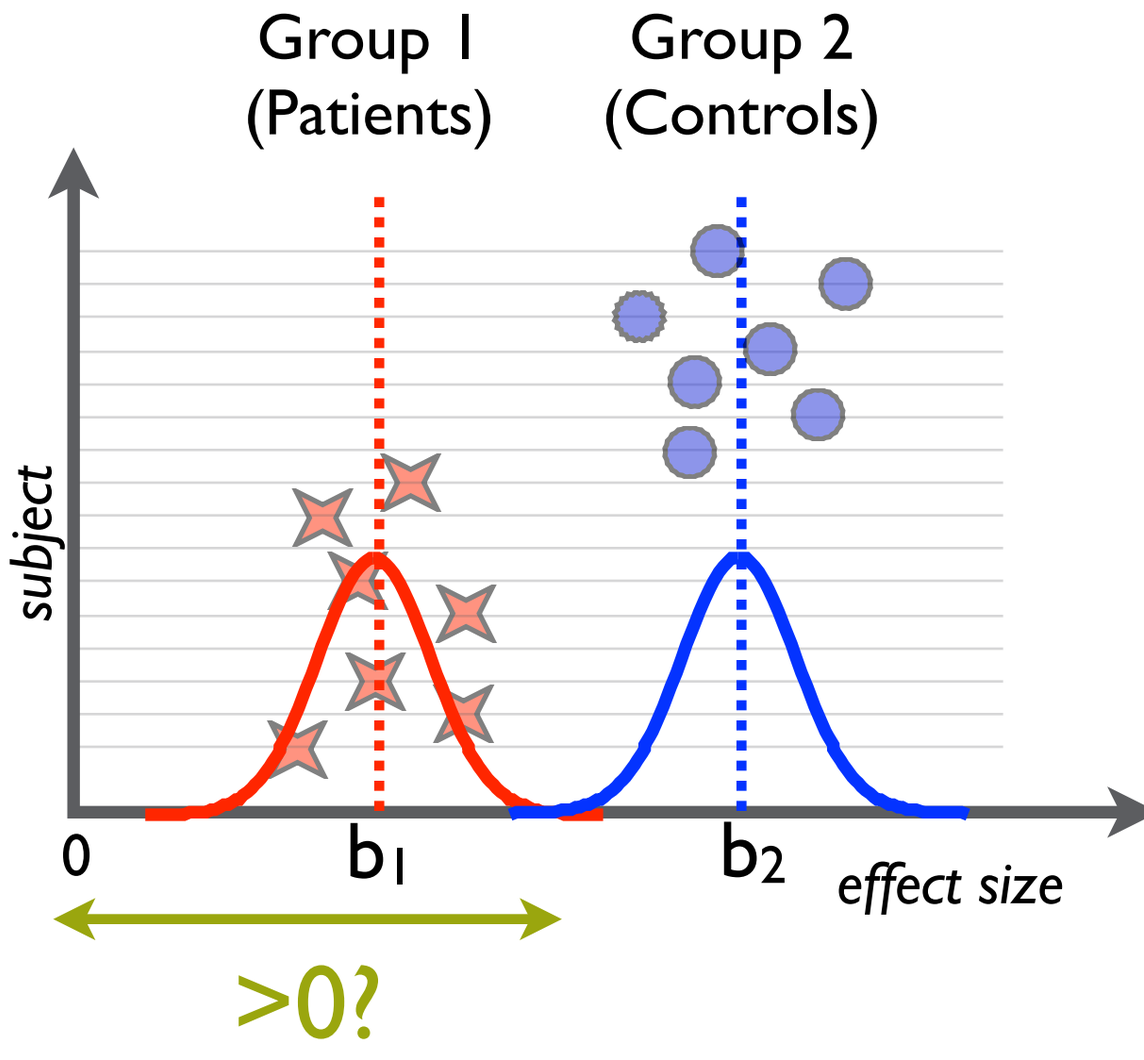

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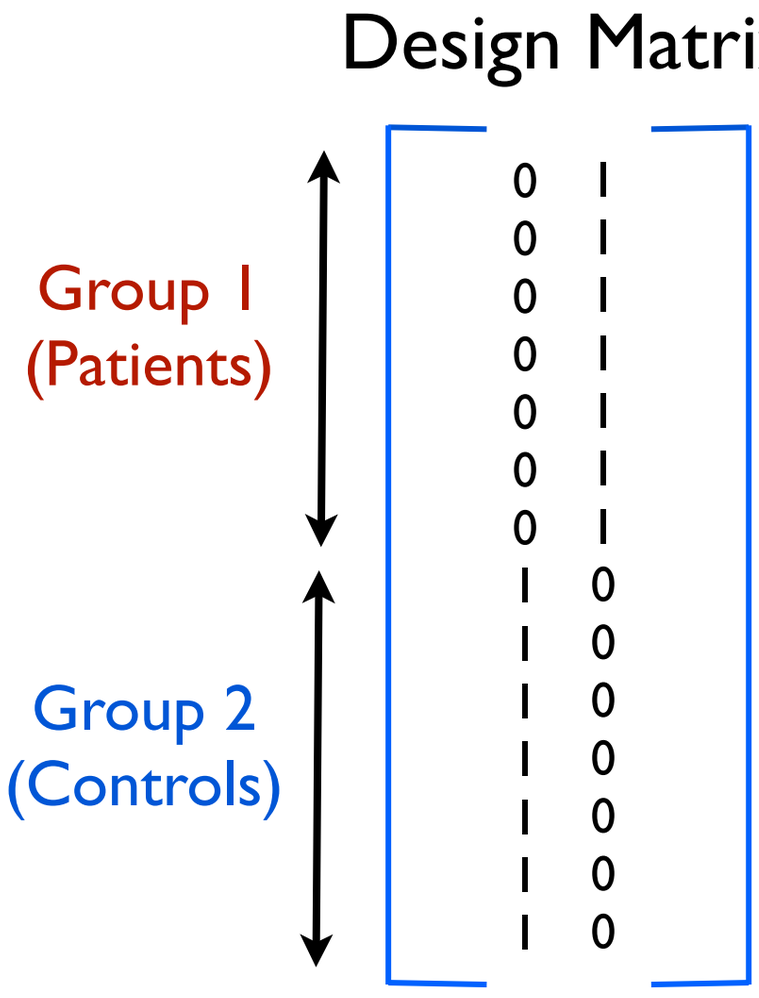

Contrast 1: [1 0] (Patients)

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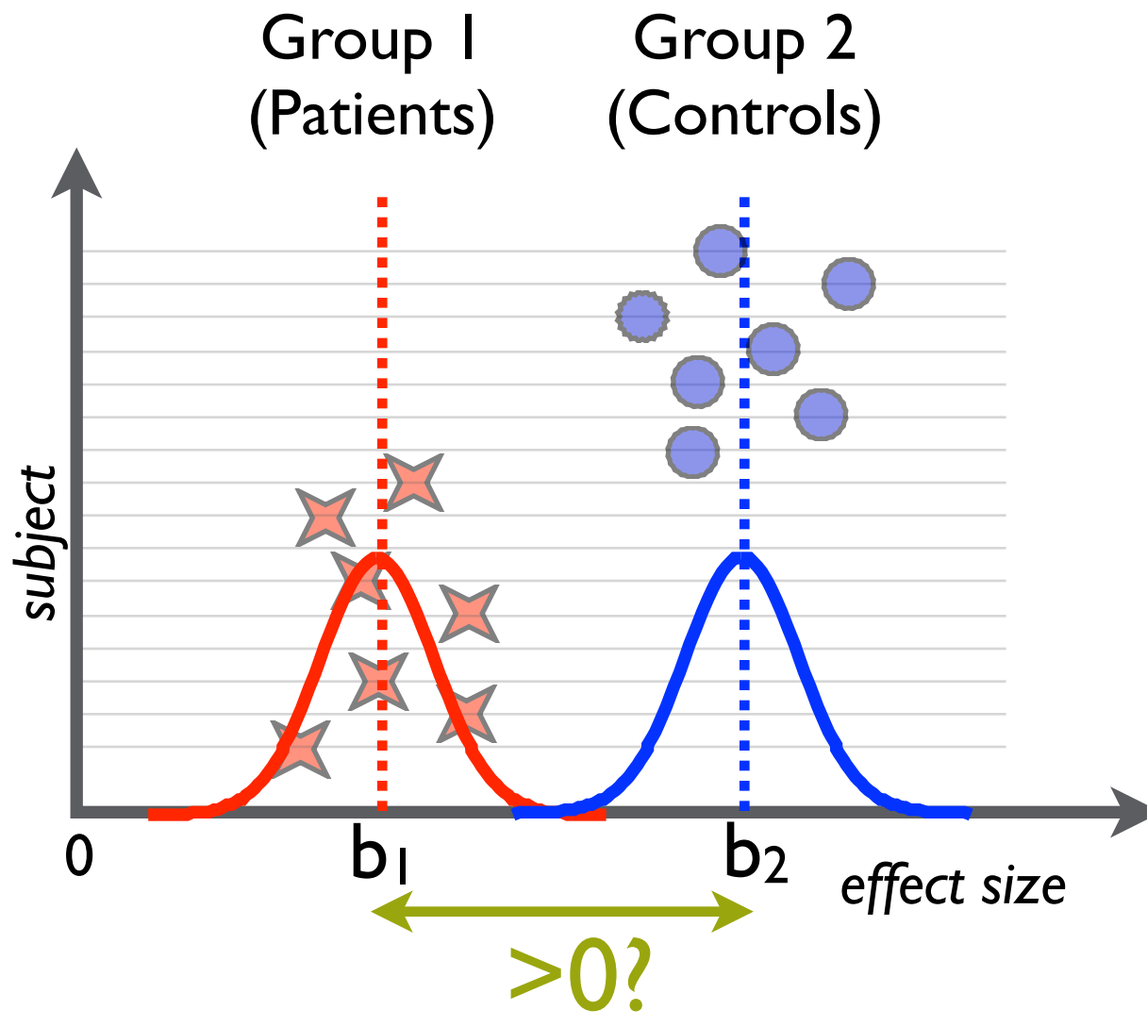

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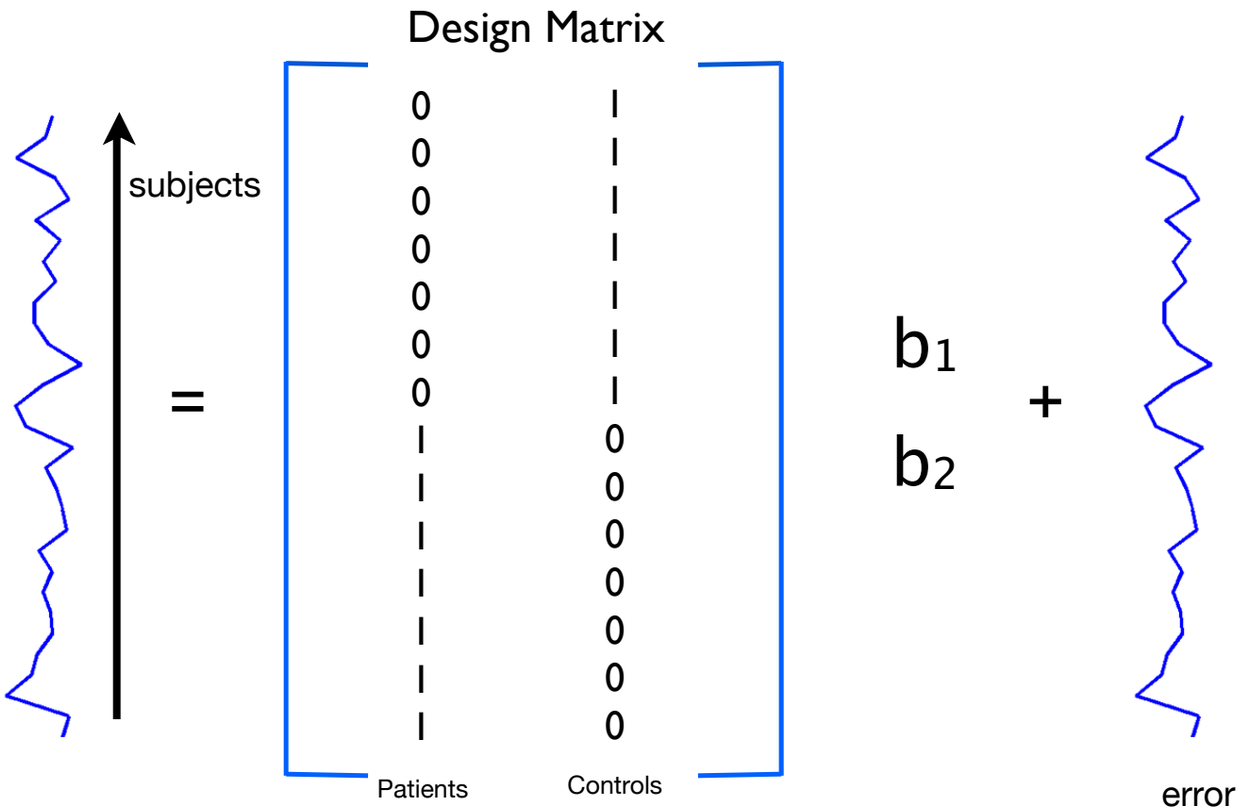
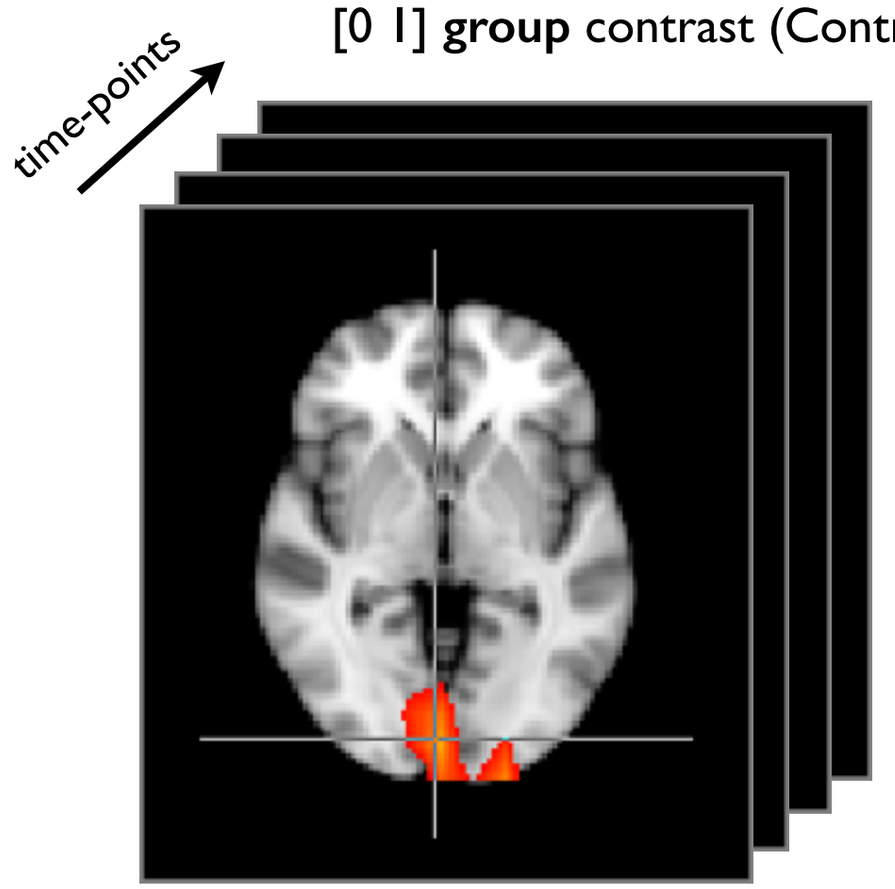


Y = X b + e

First-level COPE (e.g. [1 -1], “faces-motorbikes”) at a voxel and timepoint-within-trial

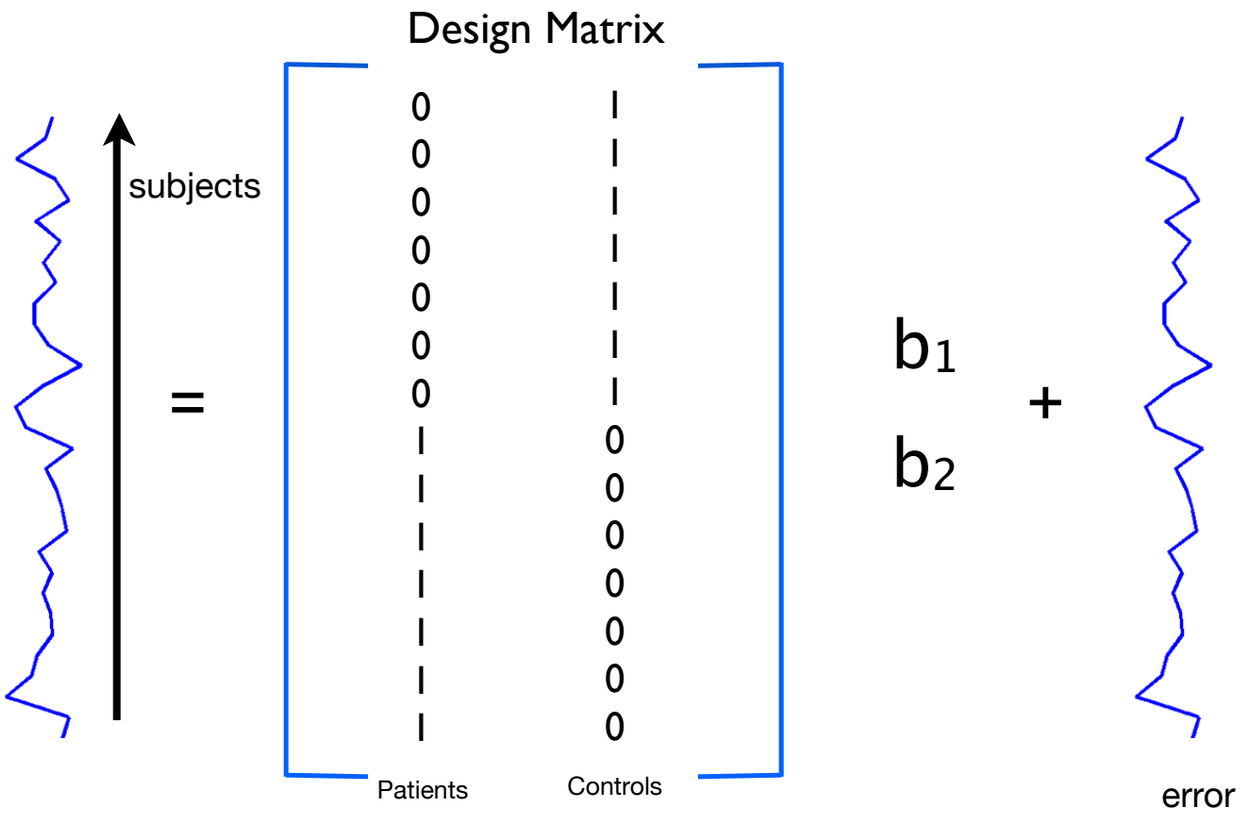
[0 1] **group** contrast (Controls)

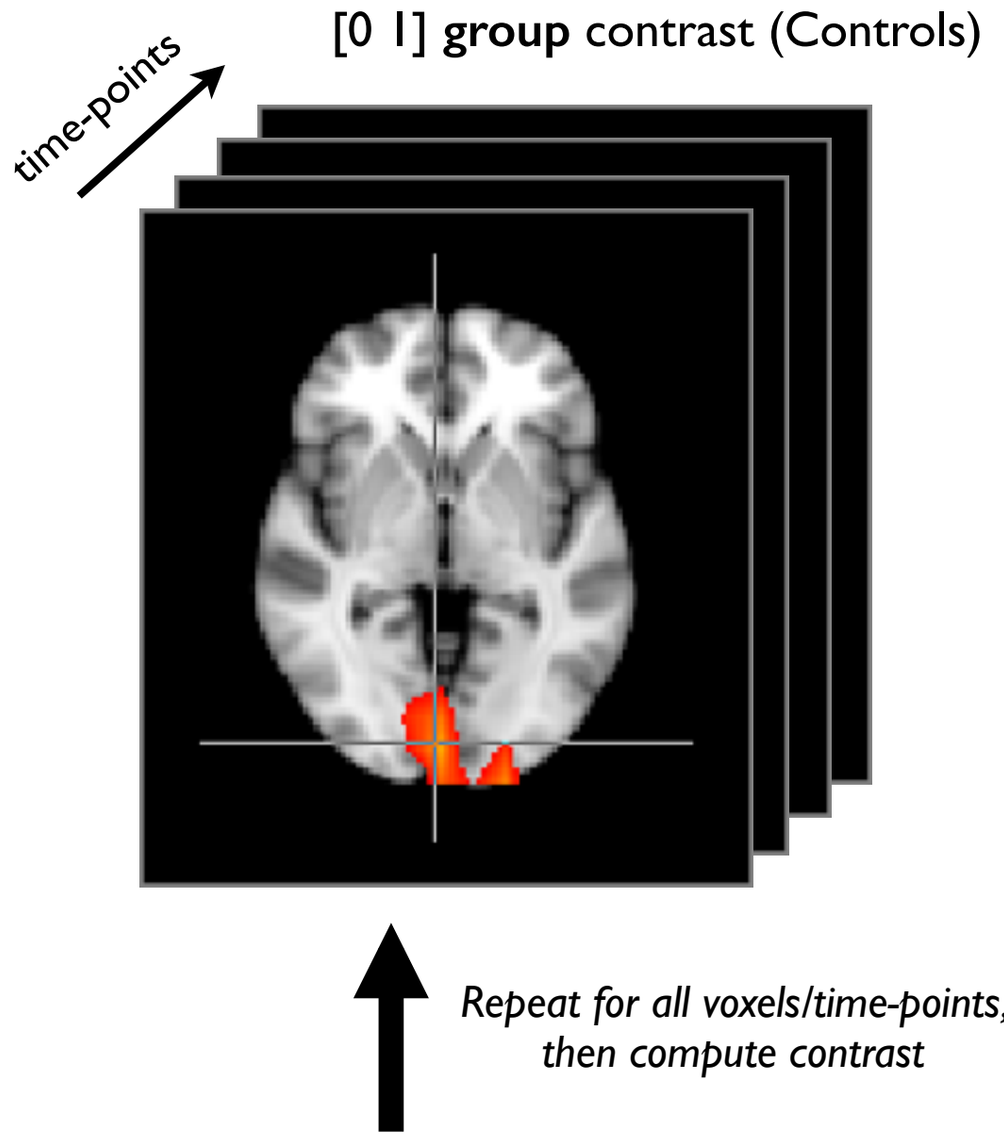


Repeat for all voxels/time-points, then compute contrast

Y=Xb+e → Fit GLM

Subject-wise GLM (Multiple Regression)



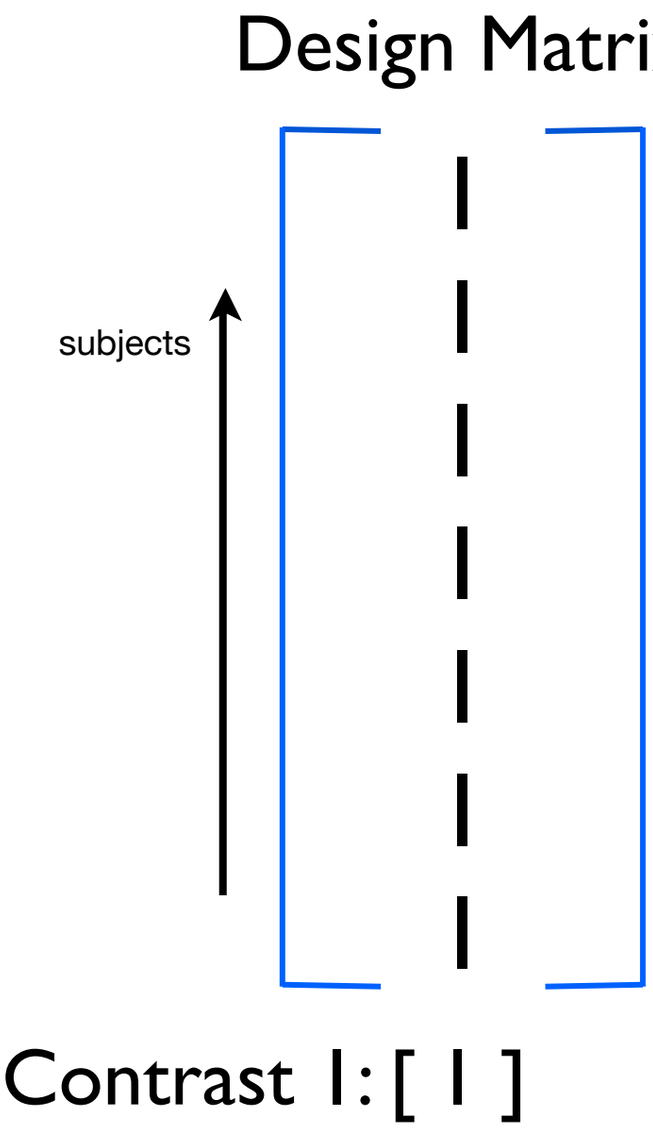


Y=Xb+e → Fit GLM

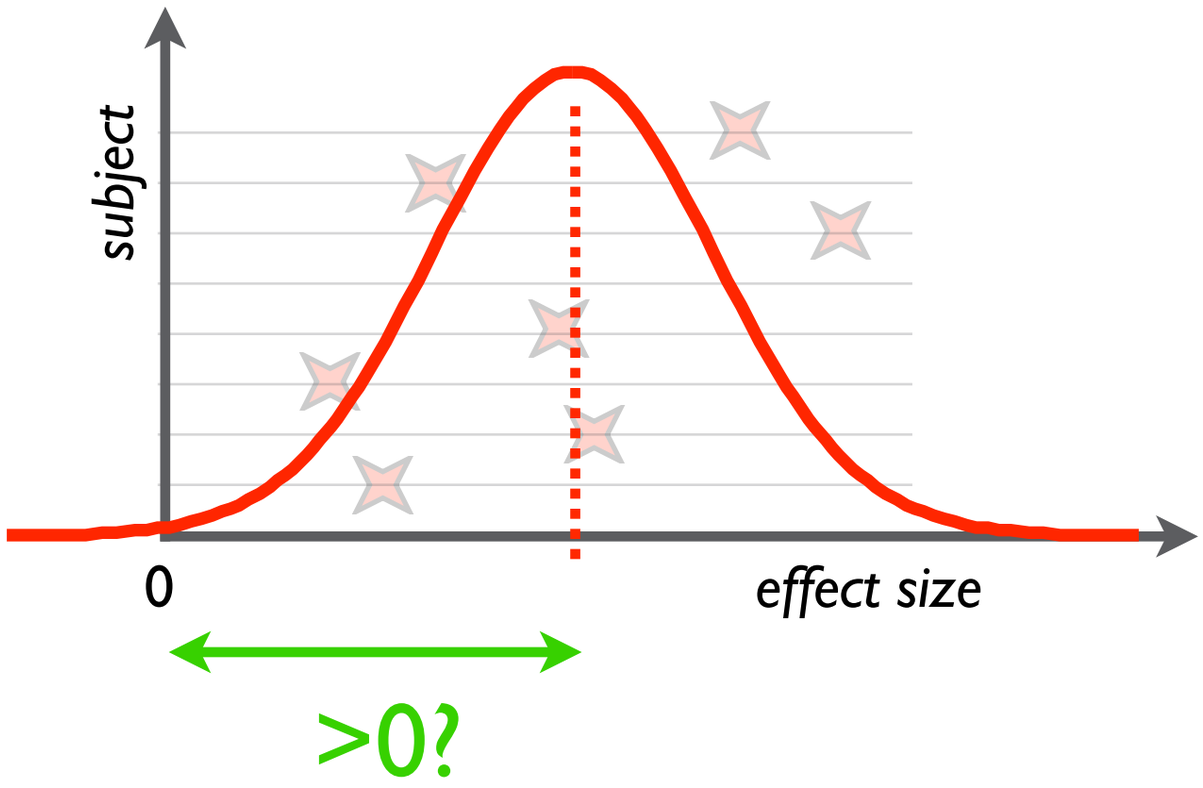
- **The whole group analysis can be repeated for ANY first-level contrast**

Single Group Average

- We have 7 subjects - all in one group - and want the mean group average:

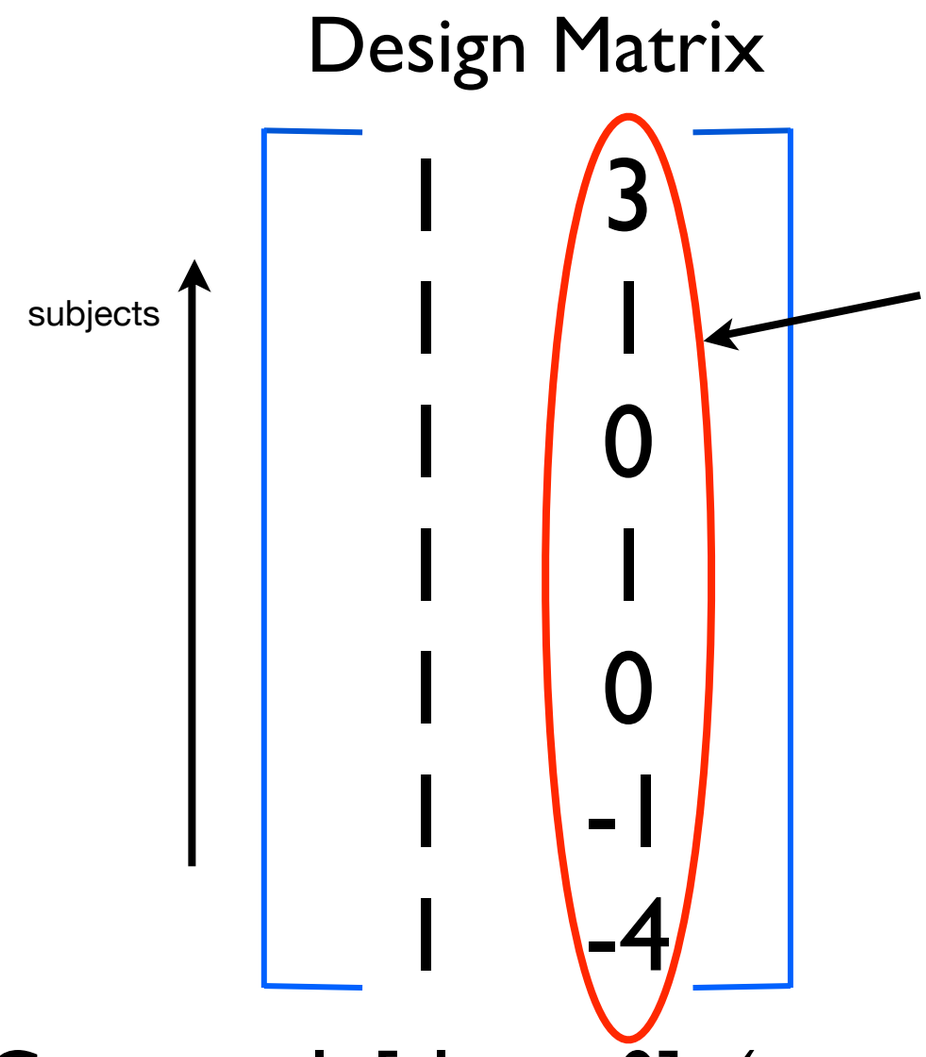


Does the group activate on average?



Behavioural Variables

- We have 7 subjects - all in one group - and want to investigate a behavioural effect



- Behavioural scores for each subject
- (Make sure this regressor is demeaned if you want to interpret the first regression parameter as the group average)

Contrast 1: [1 0] (group average)

Contrast 2: [0 1] (behavioural effect)

Other things you can do with the Group GLM

- Paired t-tests
- Behavioural Regressors
- Interactions
- For more see:
  - *http://www.fmrib.ox.ac.uk/fslcourse/lectures/inference.pdf*

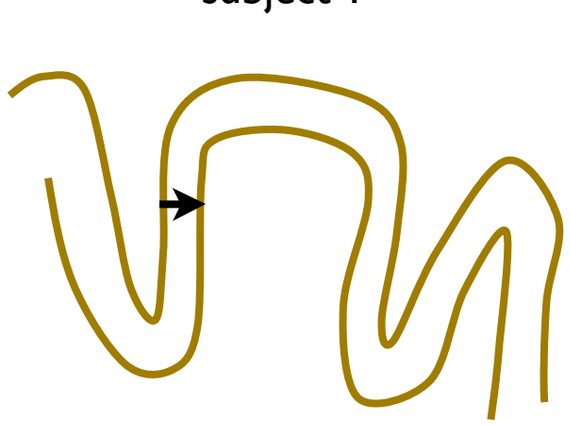
ERF rectification

- Problem:

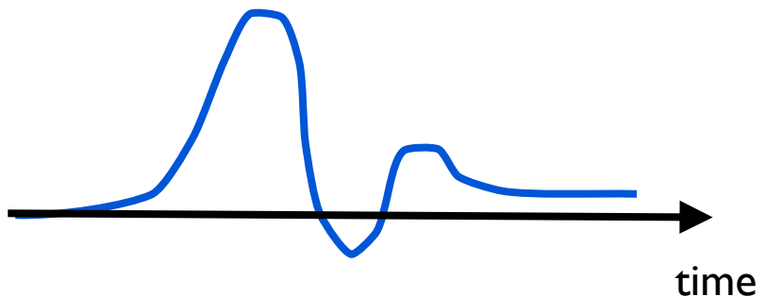
➡ there is an ***ambiguity*** between the reconstructed dipole direction and the sign of the reconstructed time series

➡ not trivial to resolve this, e.g.

subject 1

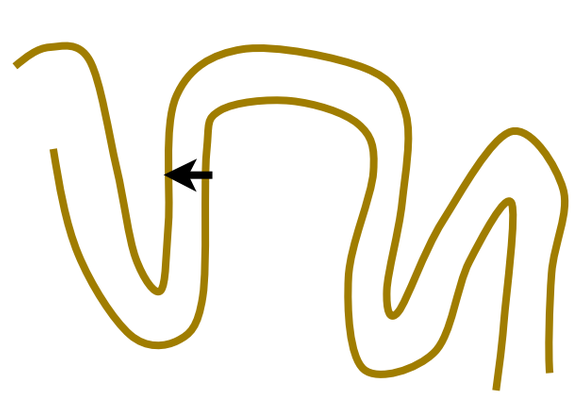


raw COPE estimate:



will cancel out

subject 2



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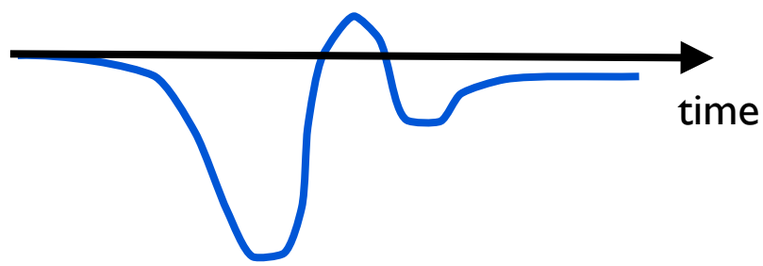
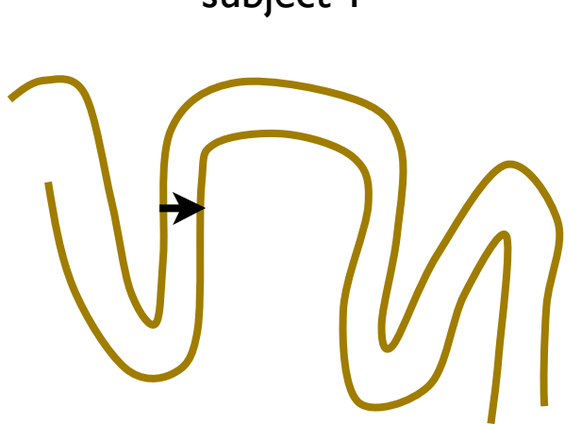


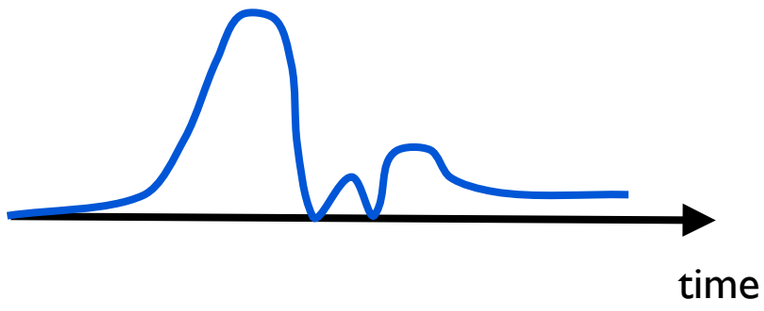
ERF rectification

- Solution: use abs(COPE)

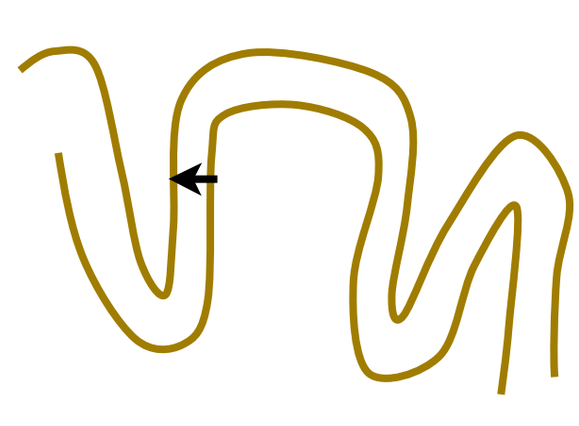
subject 1



abs(COPE) estimate:



subject 2



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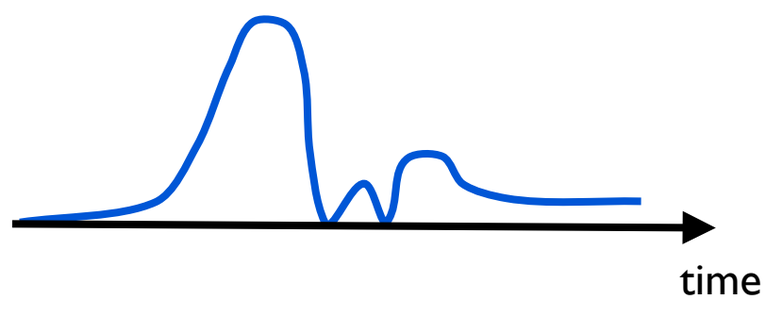

Multiple Comparison Problem

- We could carry out a null hypothesis test for each voxel using a chosen false positive rate (FPR)
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Multiple Comparison Problem

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- However, if we used FPR=0.05 with 20,000 brain voxels then we would get 1000 FPs
- Not good - we would really like the FPR to correspond to the probability of getting one FP in the entire brain

Bonferroni Correction

- Bonferroni: divide uncorrected p-threshold by number of voxels before thresholding

- E.g. 20,000 brain voxels:

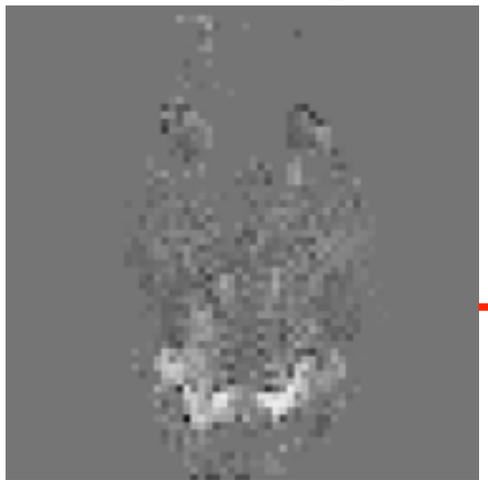
an uncorrected p-threshold of 0.05 becomes

0.05 / 20,000 = 0.0000025

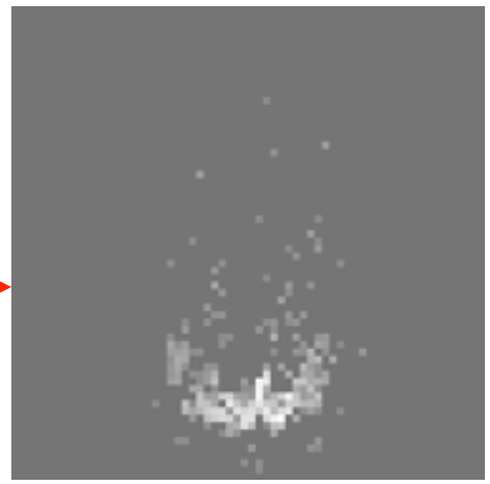
Thresholding: Clustering

What about testing significance on clusters?

stat image



Threshold at
(arbitrary!) level



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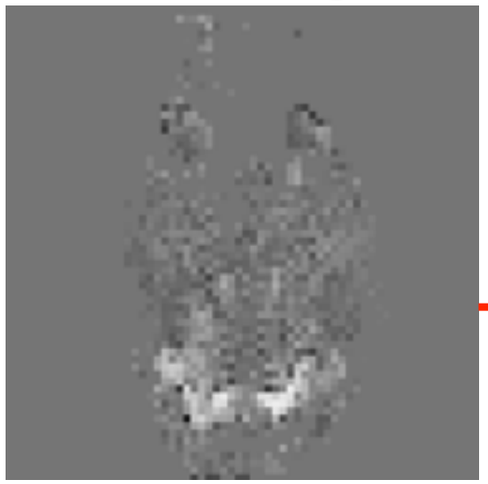

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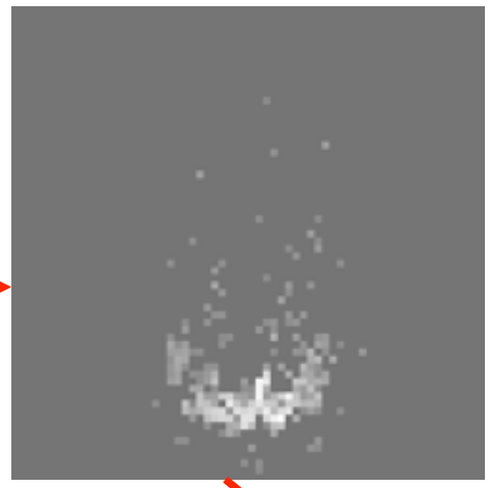


- Form clusters from surviving voxels.

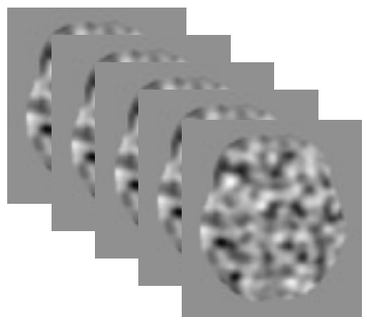
- **BUT**, what is the probability of getting a cluster, given its spatial extent (no. of voxels in cluster) and threshold, under the null hypothesis?
- Can use Random Field Theory, but involves dodgey assumptions, instead ...

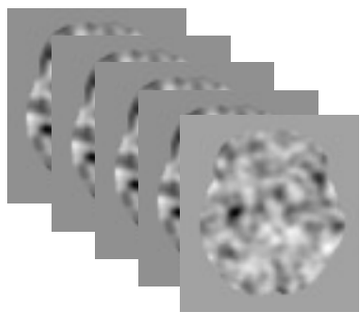
Permutation Testing

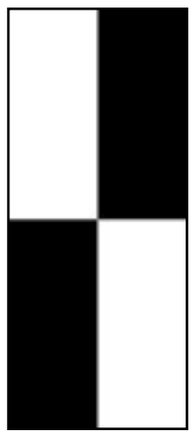
We can record the cluster sizes from our dataset

Group 1

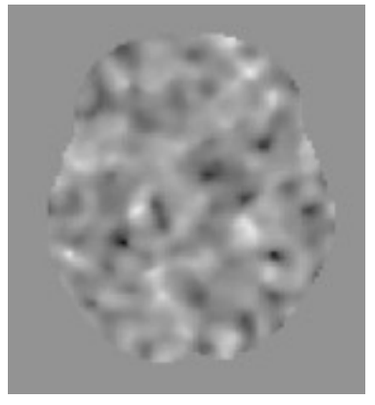
Group 2







Our correct group model

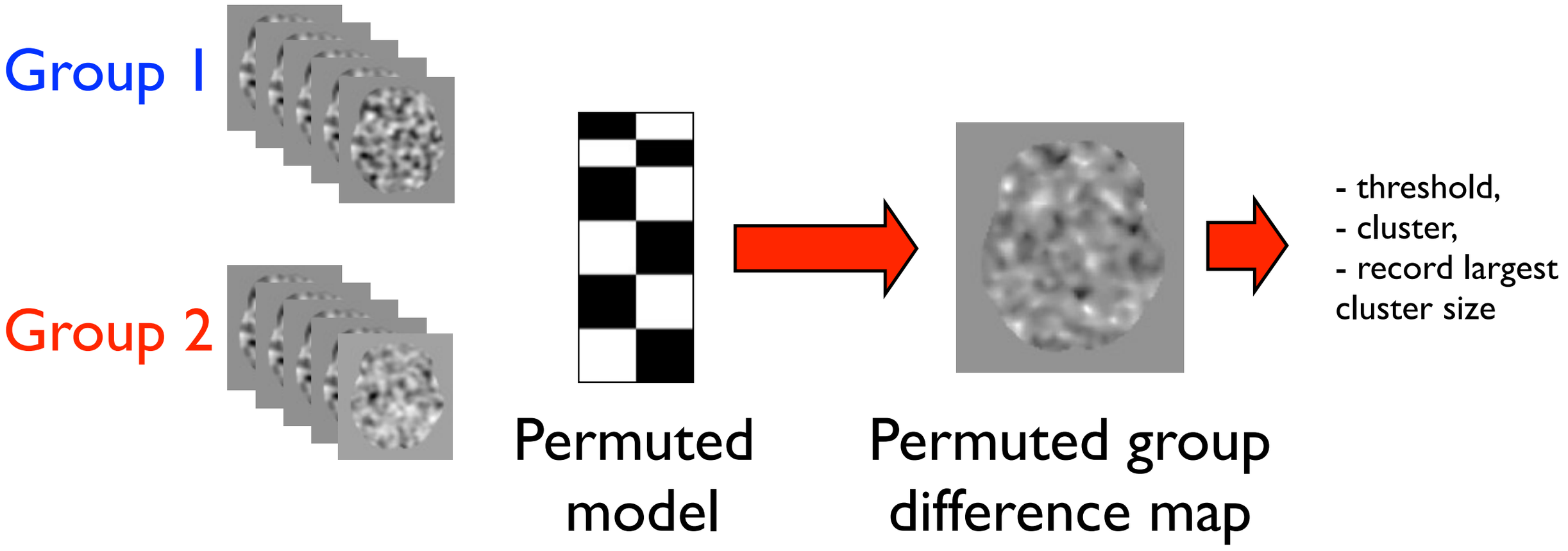


Our actual group difference map

- threshold,
- cluster,
- record **our actual** cluster sizes (but are they significant?)

Permutation Testing

We can then permute the design matrix group labellings to get the null distribution of the maximum cluster size



Permutation Testing

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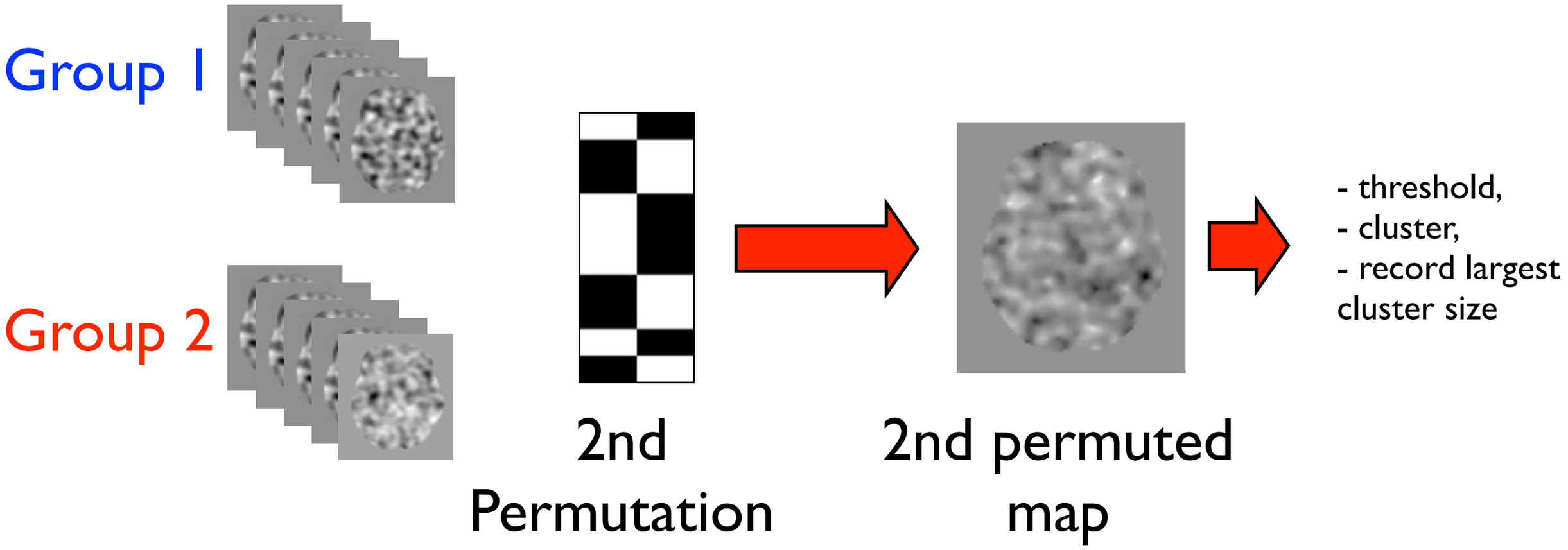

Permutation Testing

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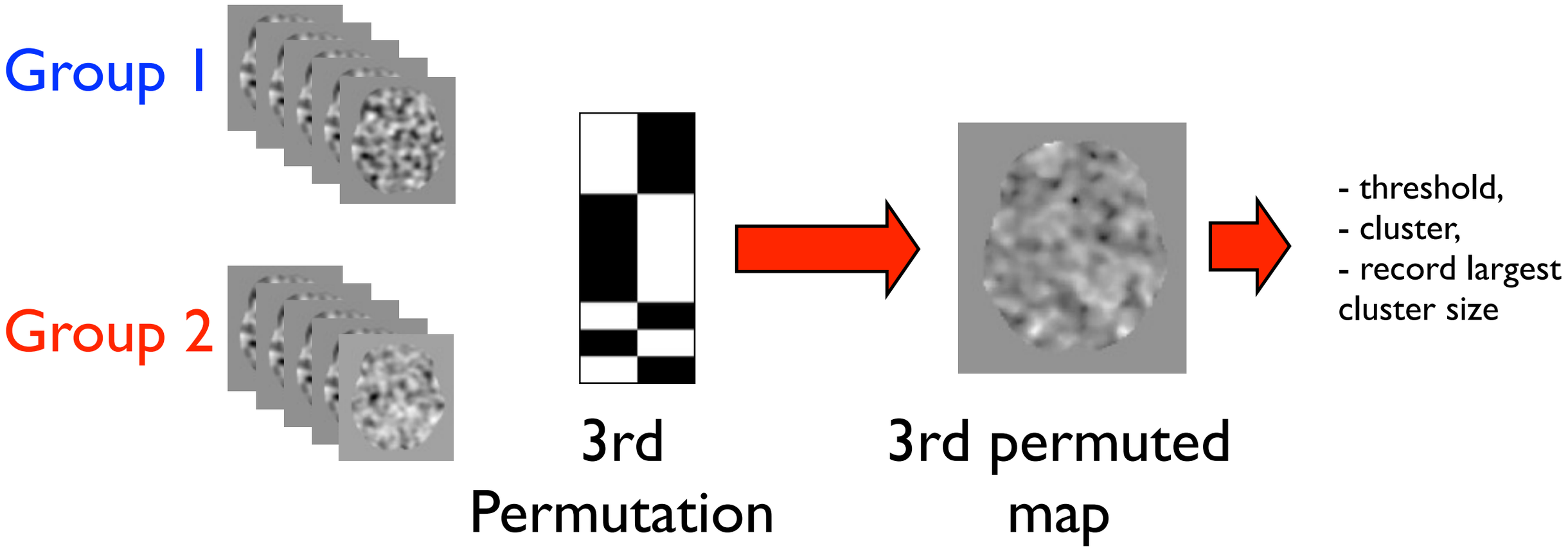
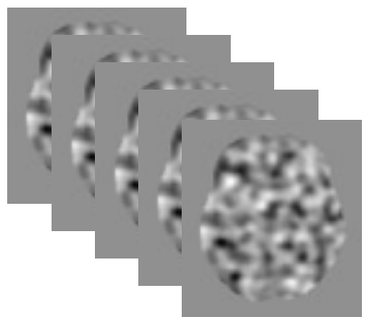


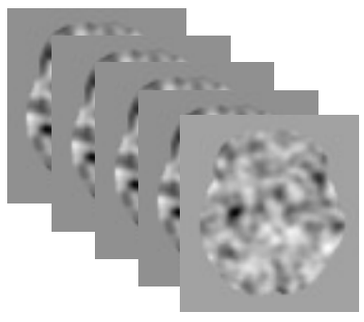
Permutation Testing

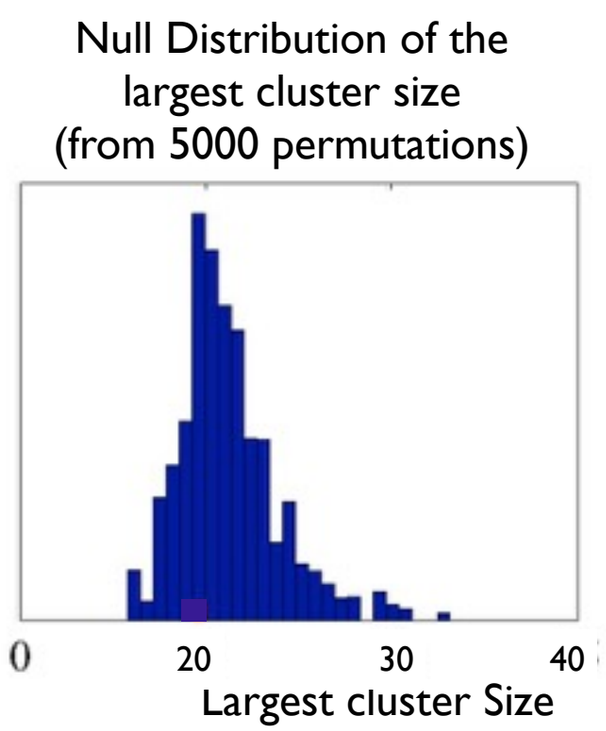
We can then permute the design matrix group labellings to get the null distribution of the maximum cluster size

Group 1



Group 2

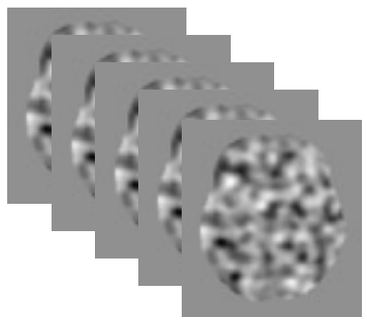




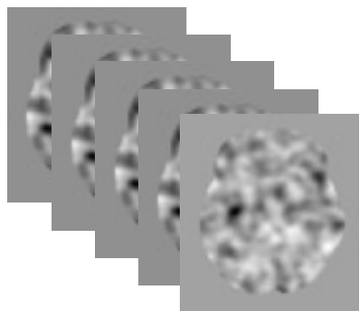
Permutation Testing

We can then permute the design matrix group labellings to get the null distribution of the maximum cluster size

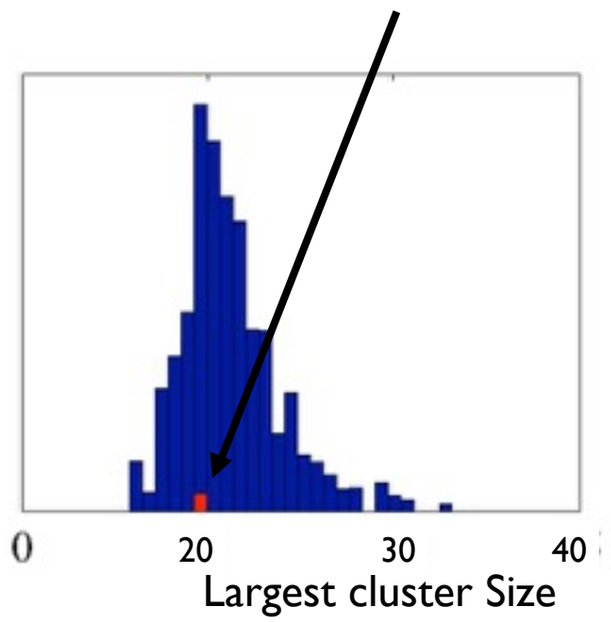
Group 1



Group 2



Cluster size from our correct group model



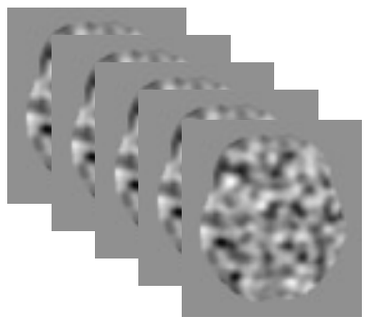
- 3925 permutations yielded larger clusters than original group labellings.

- We CANNOT reject the null-hypothesis in this case

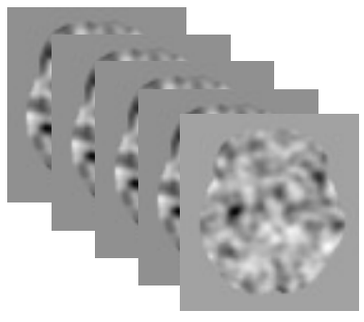
Permutation Testing

We can then permute the design matrix group labellings to get the null distribution of the maximum cluster size

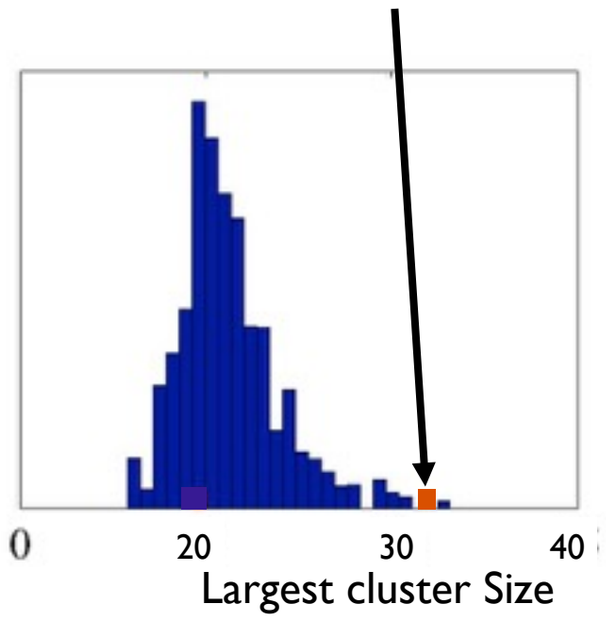
Group 1



Group 2



Cluster size from our correct group model



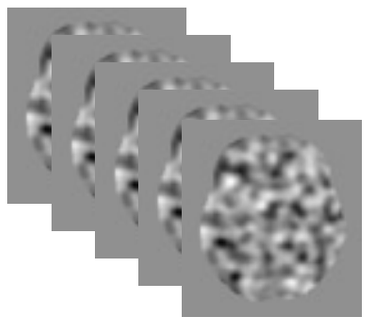
- Only 5 permutations yielded larger clusters than original group labellings:
[Corrected P-Value=5/5000=0.001]

- We CAN reject the null-hypothesis in this case

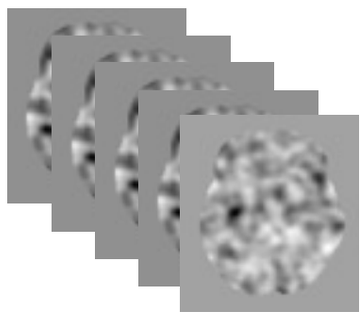
Permutation Testing

We can then permute the design matrix group labellings to get the null distribution of the maximum cluster size

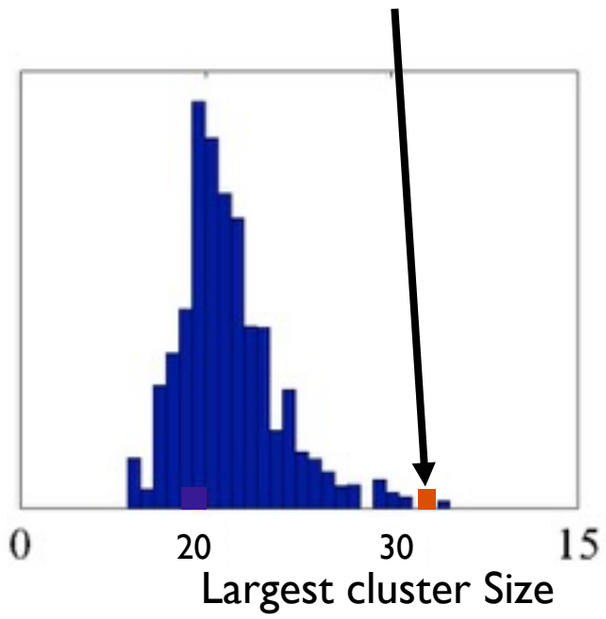
Group 1



Group 2



Cluster size from our correct group model



- OSL has the facility to test clusters in:

  - 1-D (time)
  - 2-D (time-frequency)
  - 2-D/3-D (space)
  - 3-D/4-D (space and time)

- Note: 4D is very slow!!

Variance Smoothing

- It is advantageous to smooth the group (between-subject) variance (VARCOPE)
- This preserves the effect size (COPE) spatial resolution, while increases the degrees of freedom for the VARCOPE estimation
- Permutation testing adjusts accordingly to keeps stats valid

$$\text{tstat} = \frac{\text{COPE}}{\text{sqrt(VARCOPE)}}$$

Practical

Beamformer group analysis, for which source_recon, first_level and subject_level OAT stages have already been run.

Includes:

a) Wholebrain (ERF) analysis
b) Spatial ROI analysis
c) Time window (spatial map) analysis
- Using (3D) permutation testing
d) ROI time-freq analysis using (2D) perm testing