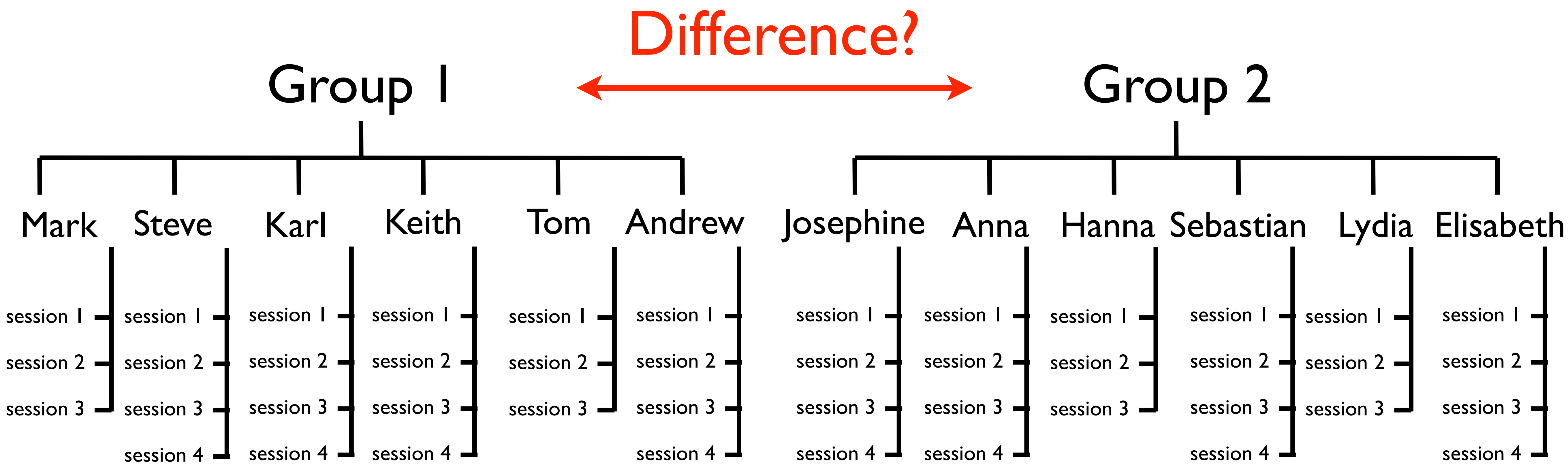
Group-level Analysis in OSL

OHBA Analysis Workshop

Group Analysis

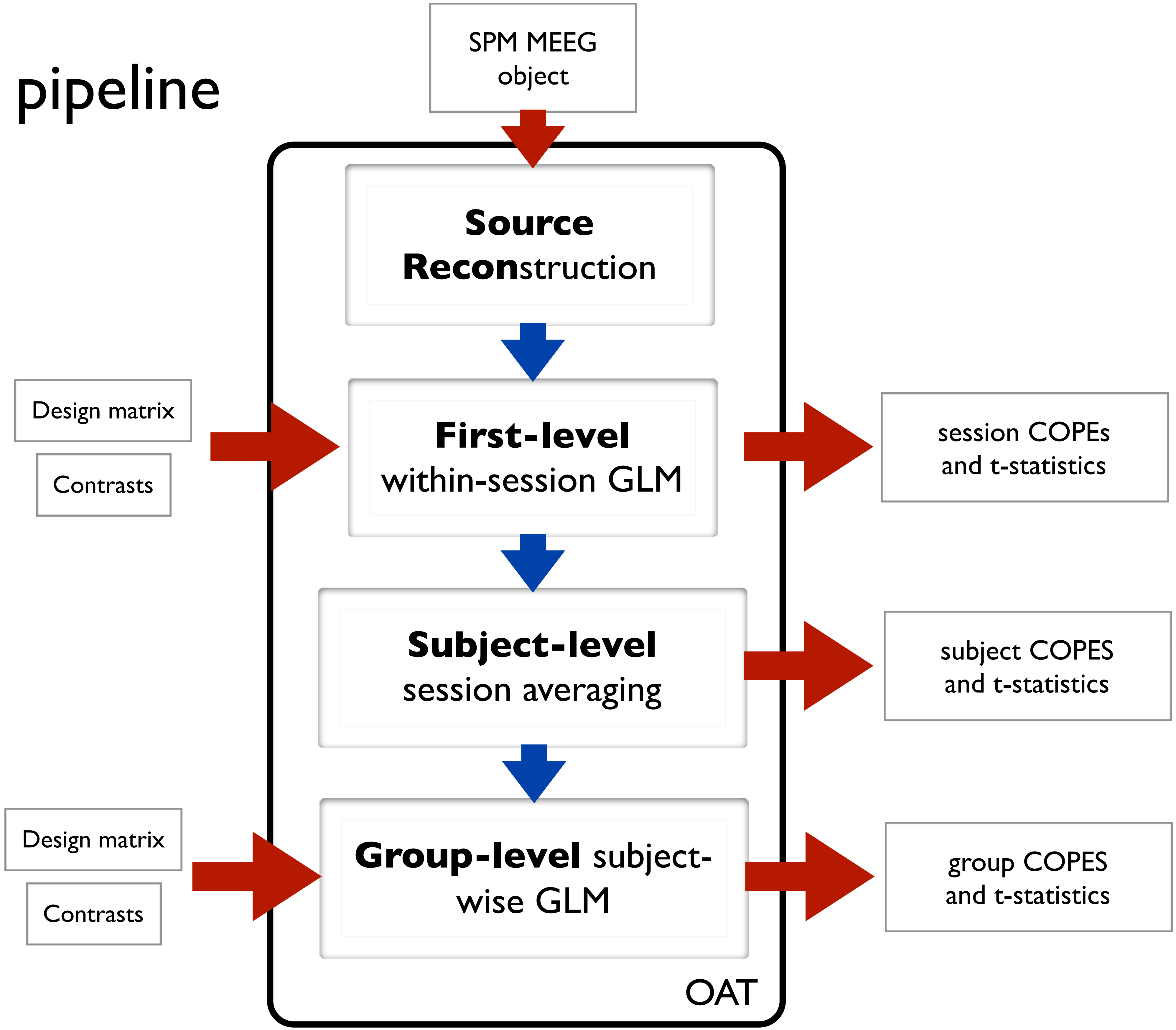
- typically need to infer across multiple subjects, sometimes multiple groups and/or multiple sessions



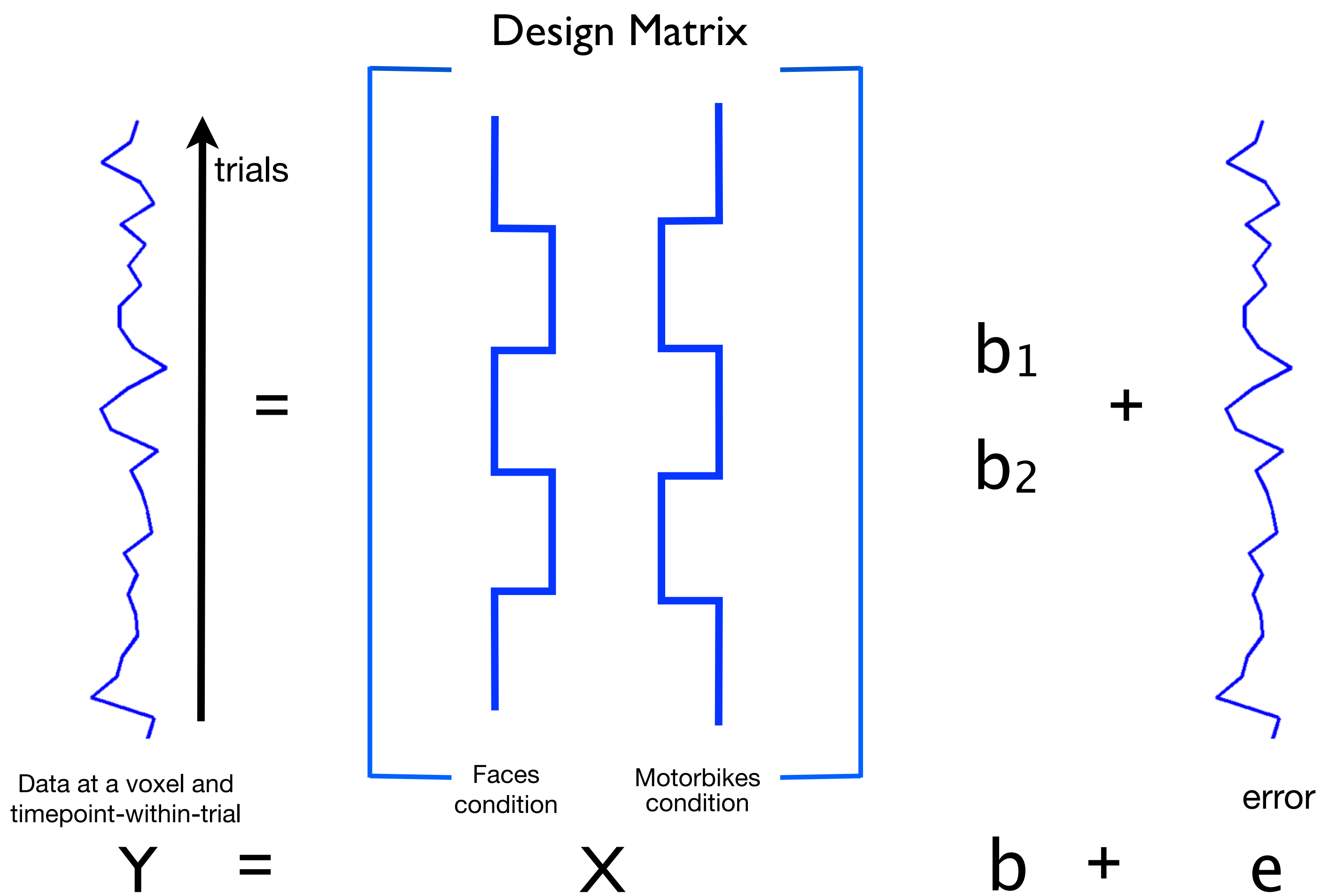
- questions of interest involve tests/comparisons at the group level

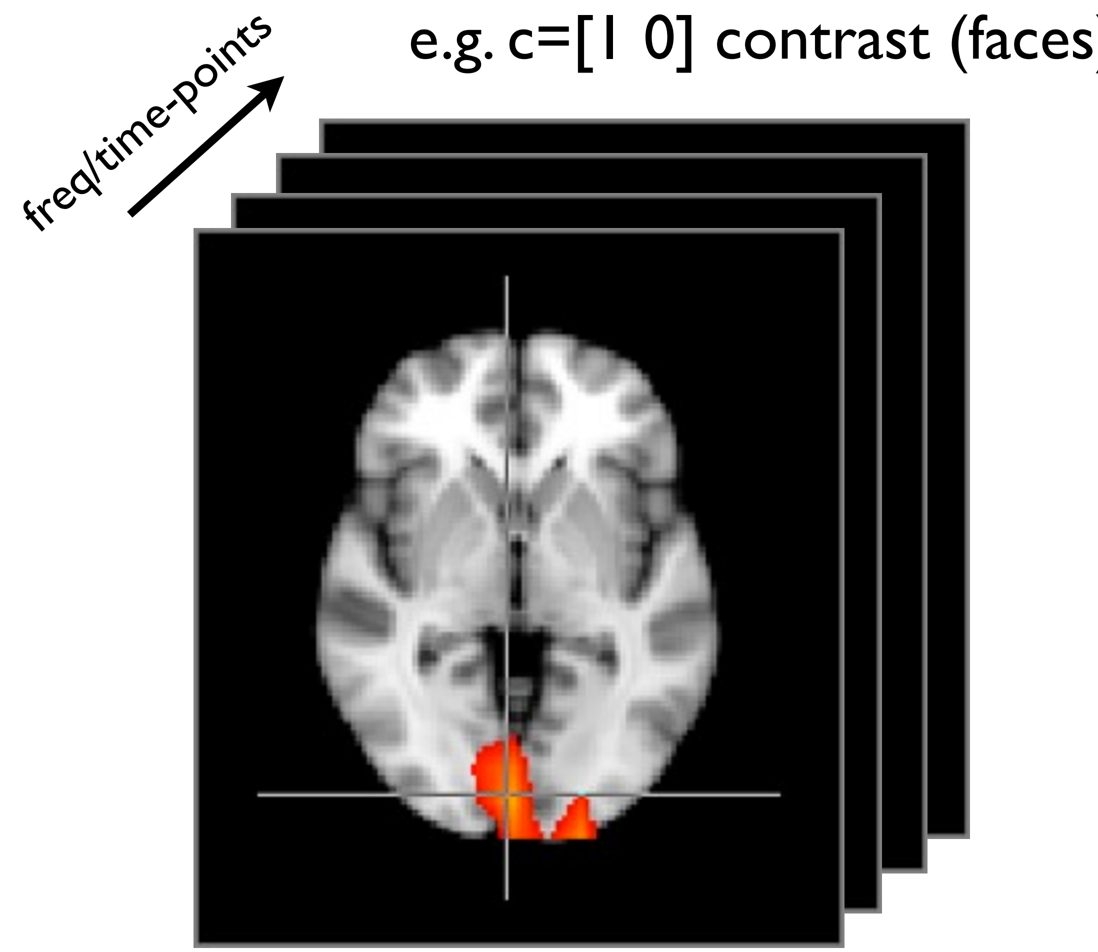
OAT Pipeline Stages

- 4 distinct pipeline stages:



First-Level (Trial-wise) GLM





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

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

B is the Parameter Estimates (PEs) of b

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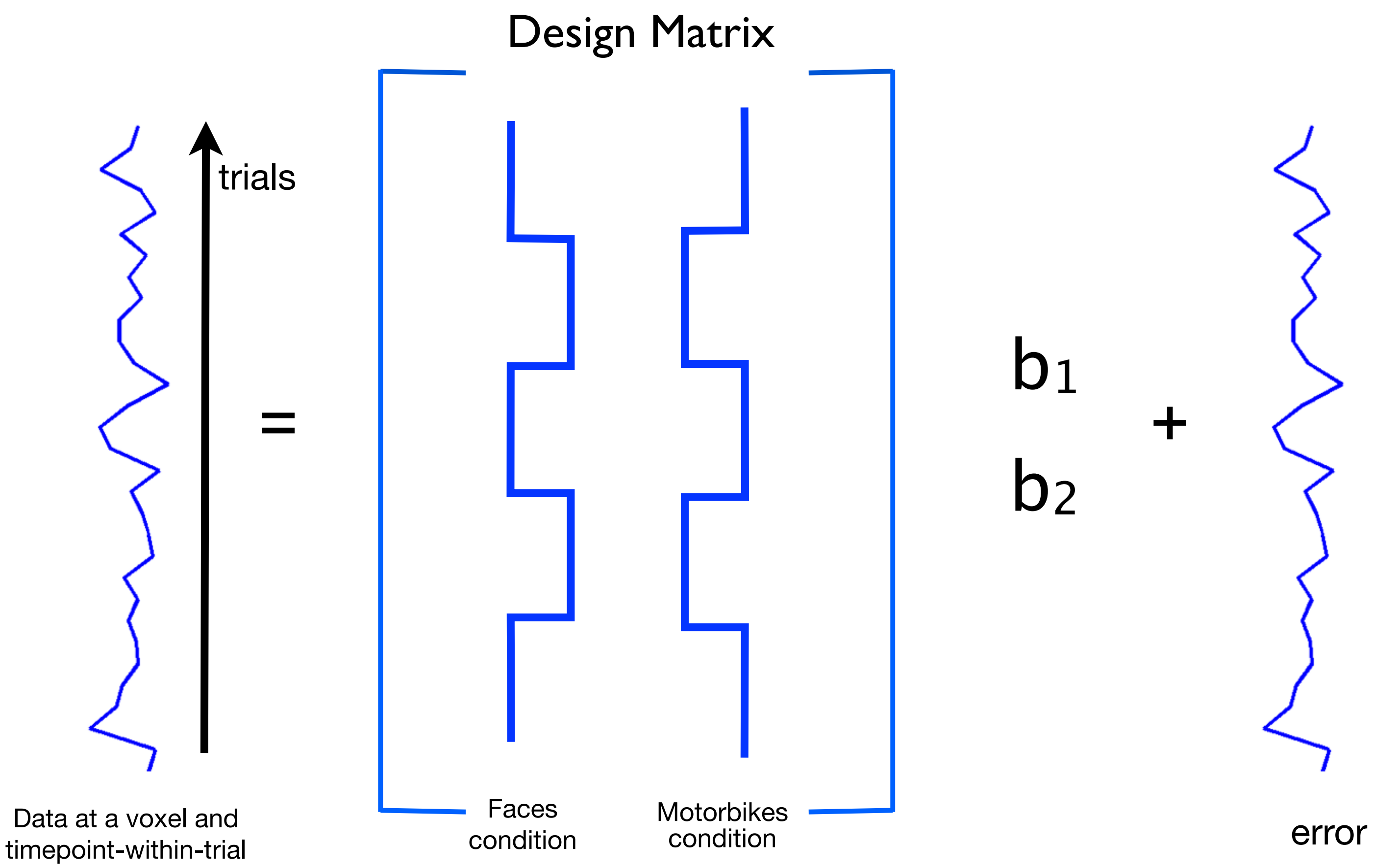
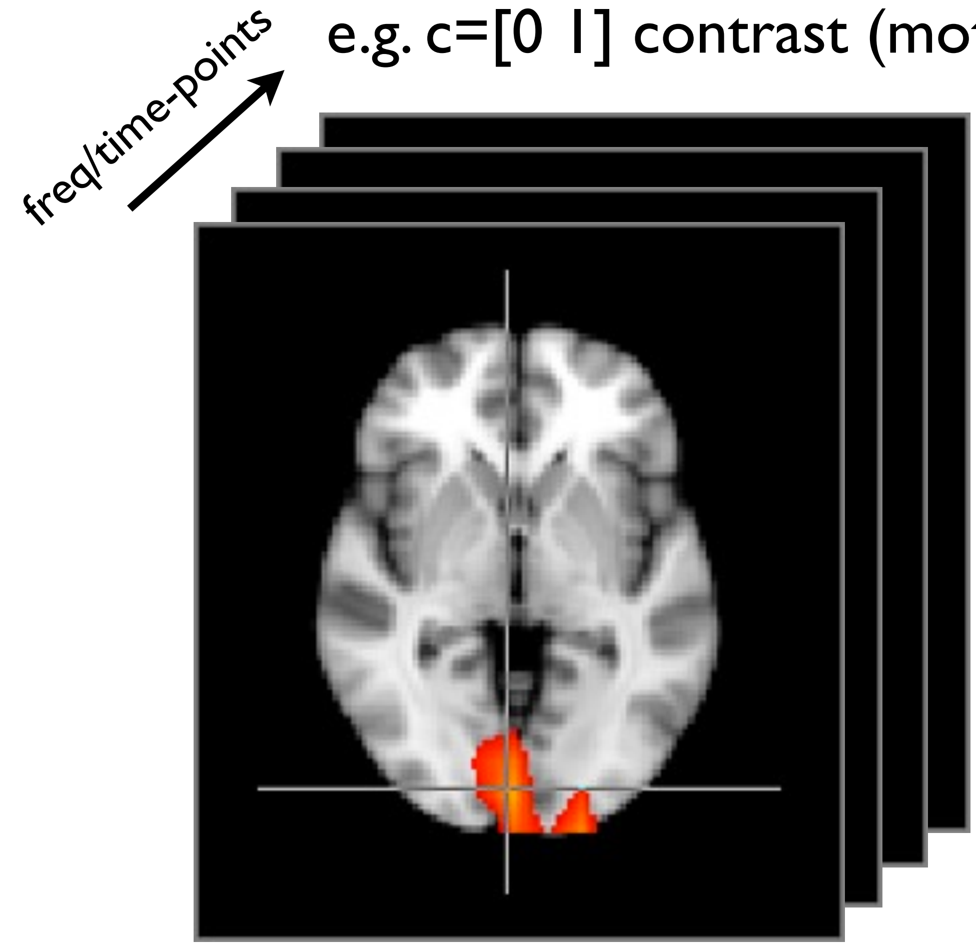


$Y \quad = \quad X \quad b \quad + \quad e$

e.g. c=[0 1] contrast (motorbikes)



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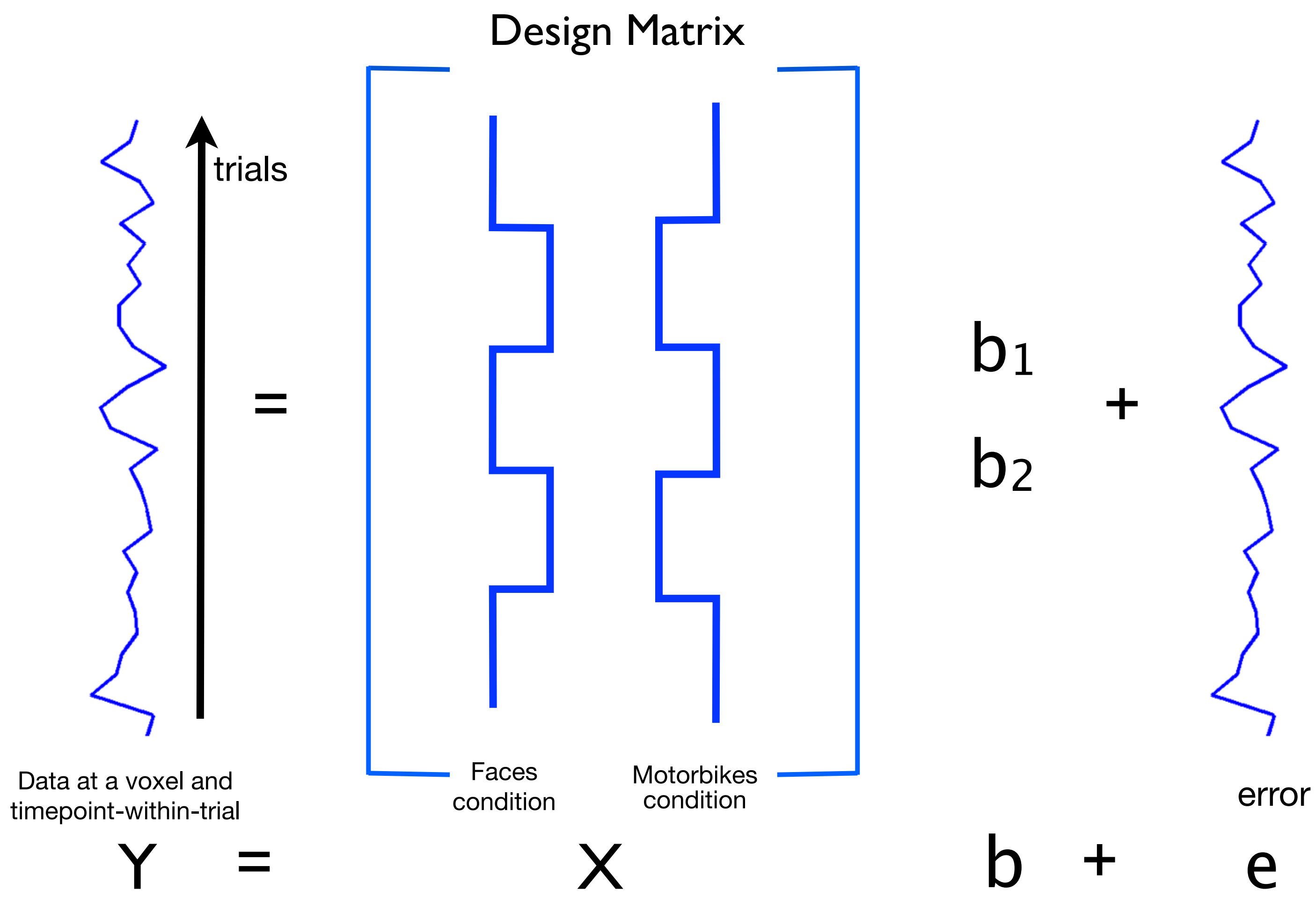

e.g. c=[1 -1] contrast
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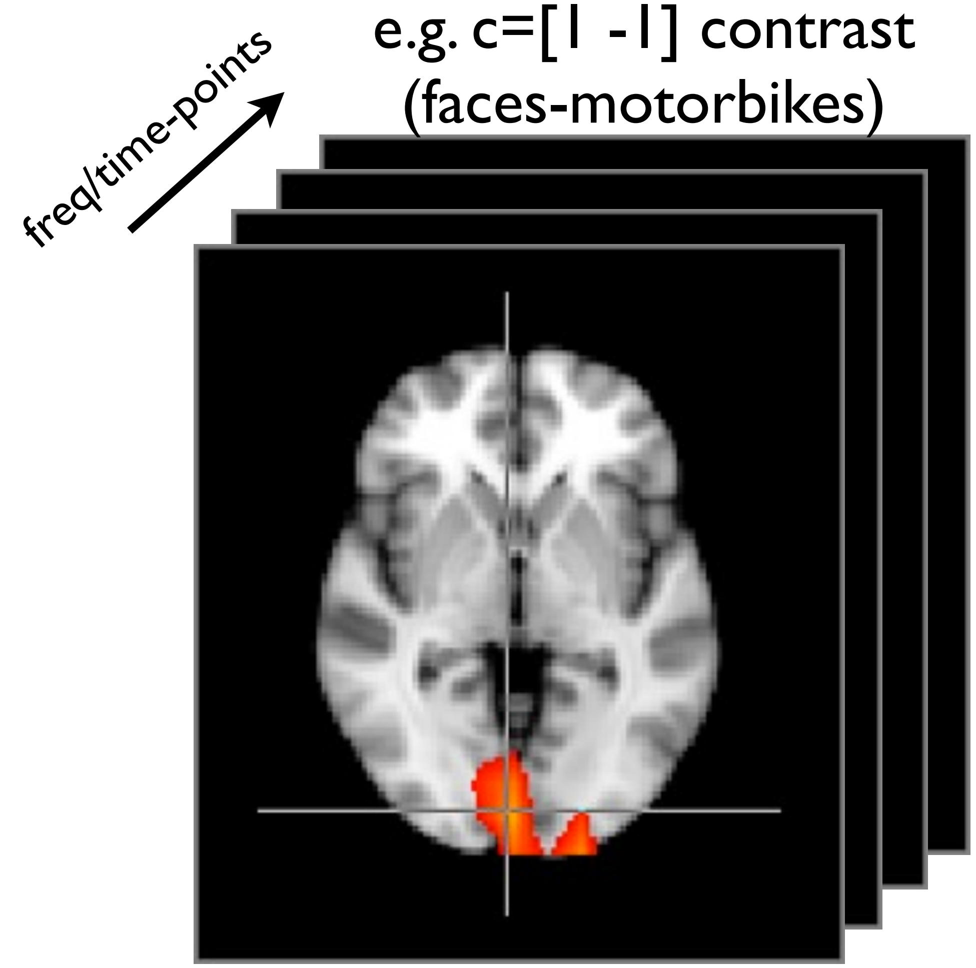

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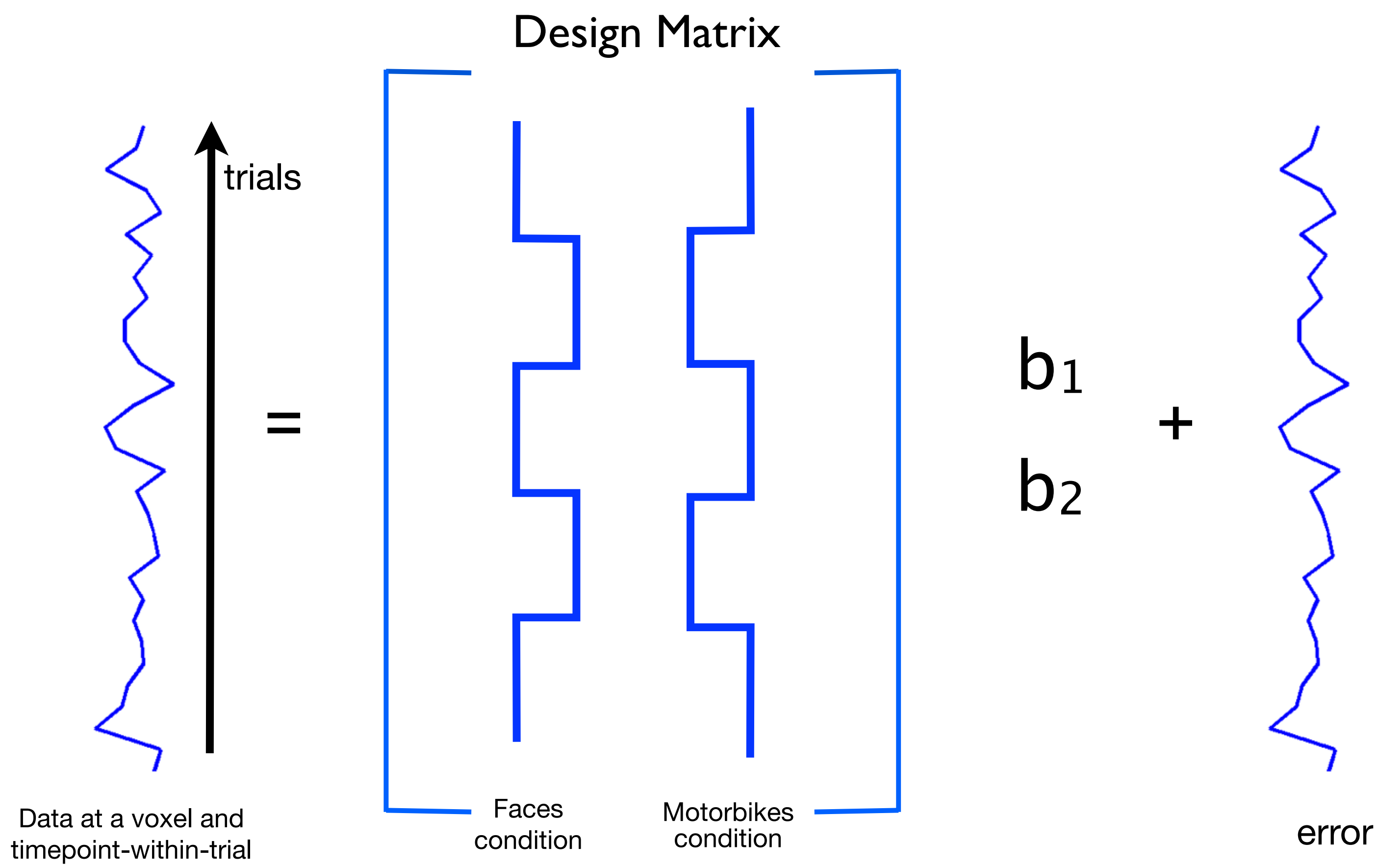
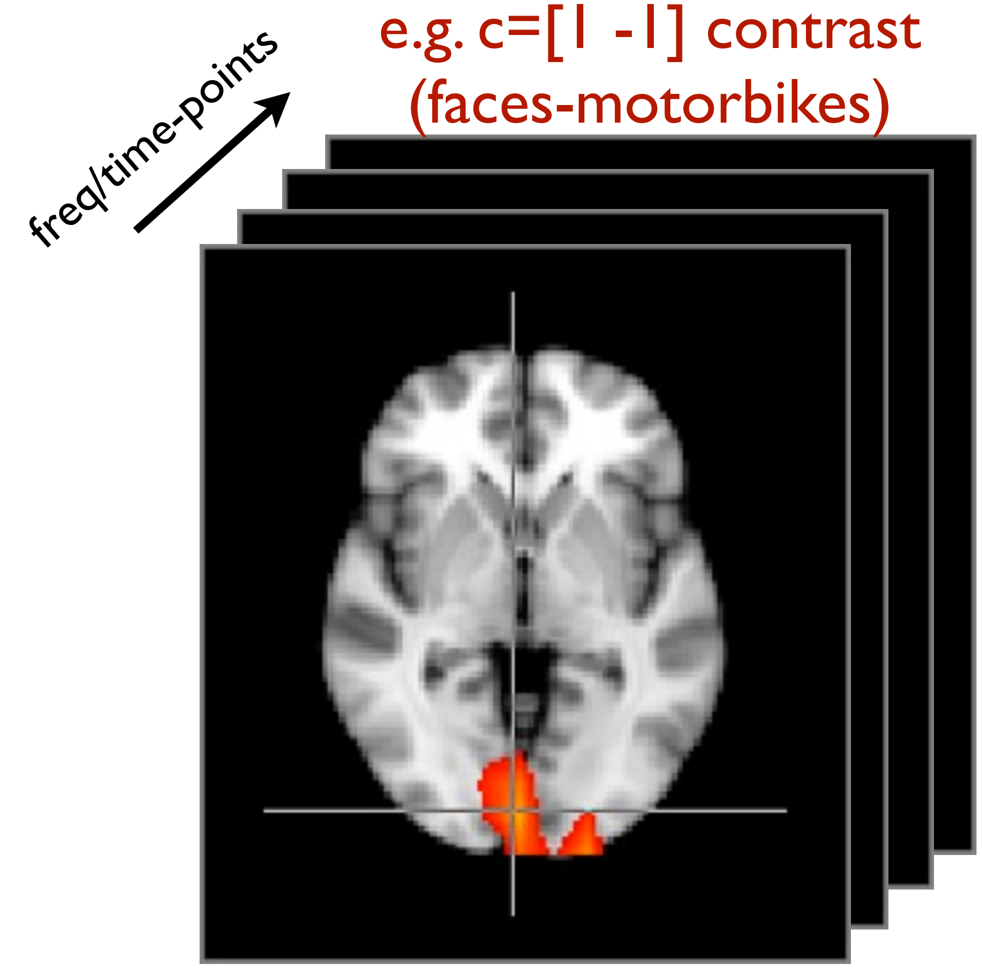
First-Level (Trial-wise) GLM

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

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





Y = X b + e

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

$$Y=Xb+e \longrightarrow B=\mathrm{pinv}(X)Y$$

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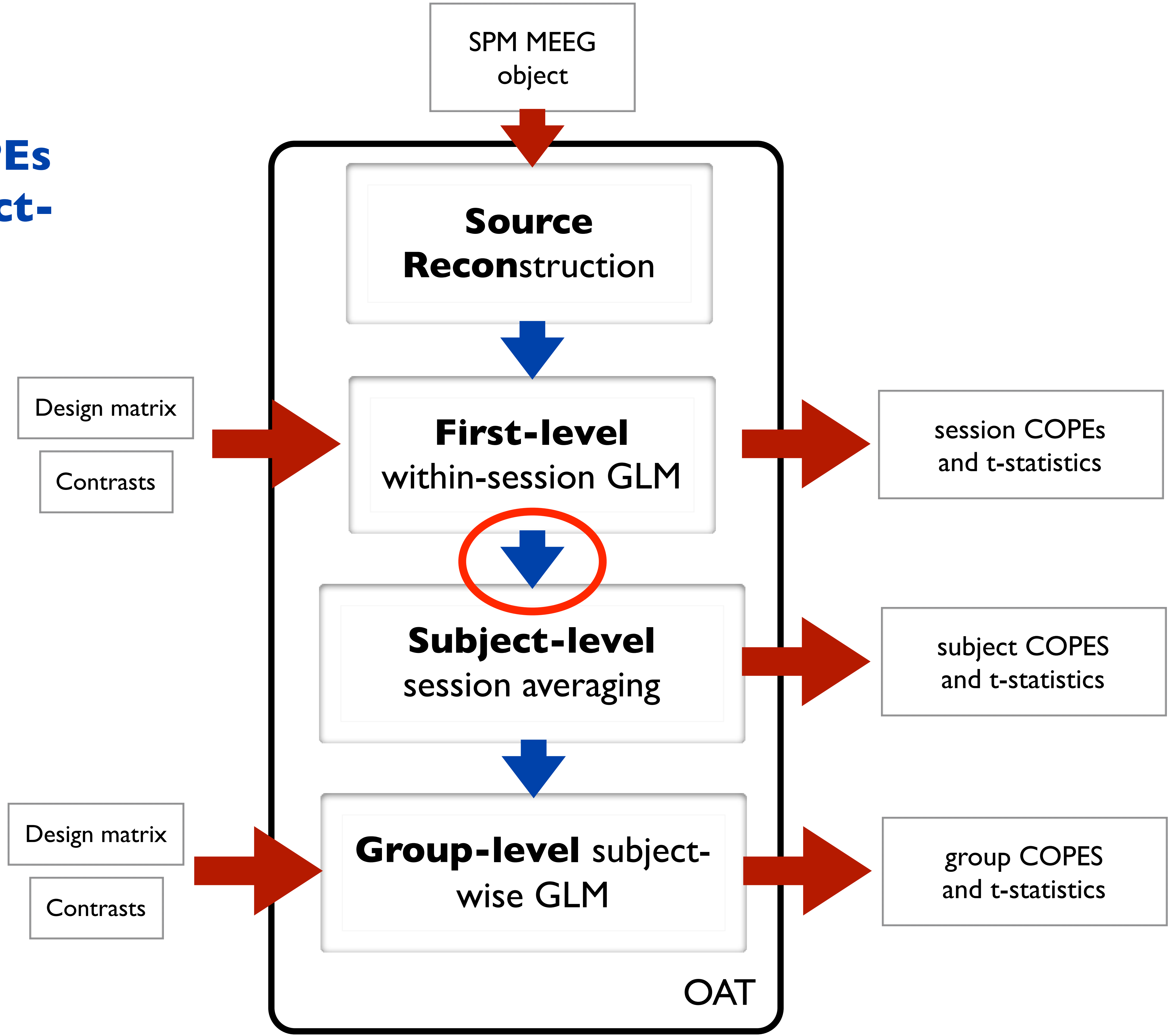
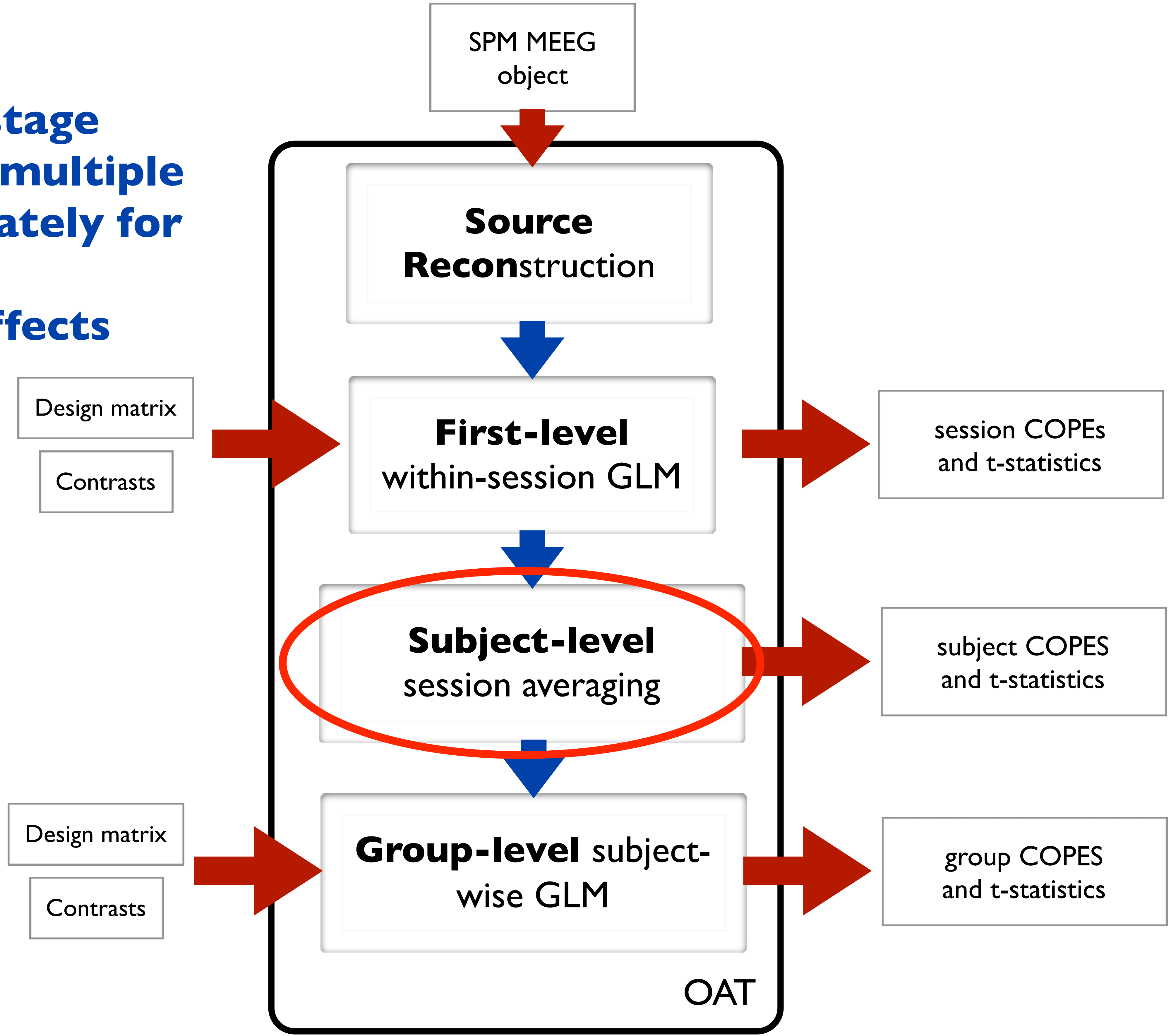
Multiple Session Analysis

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



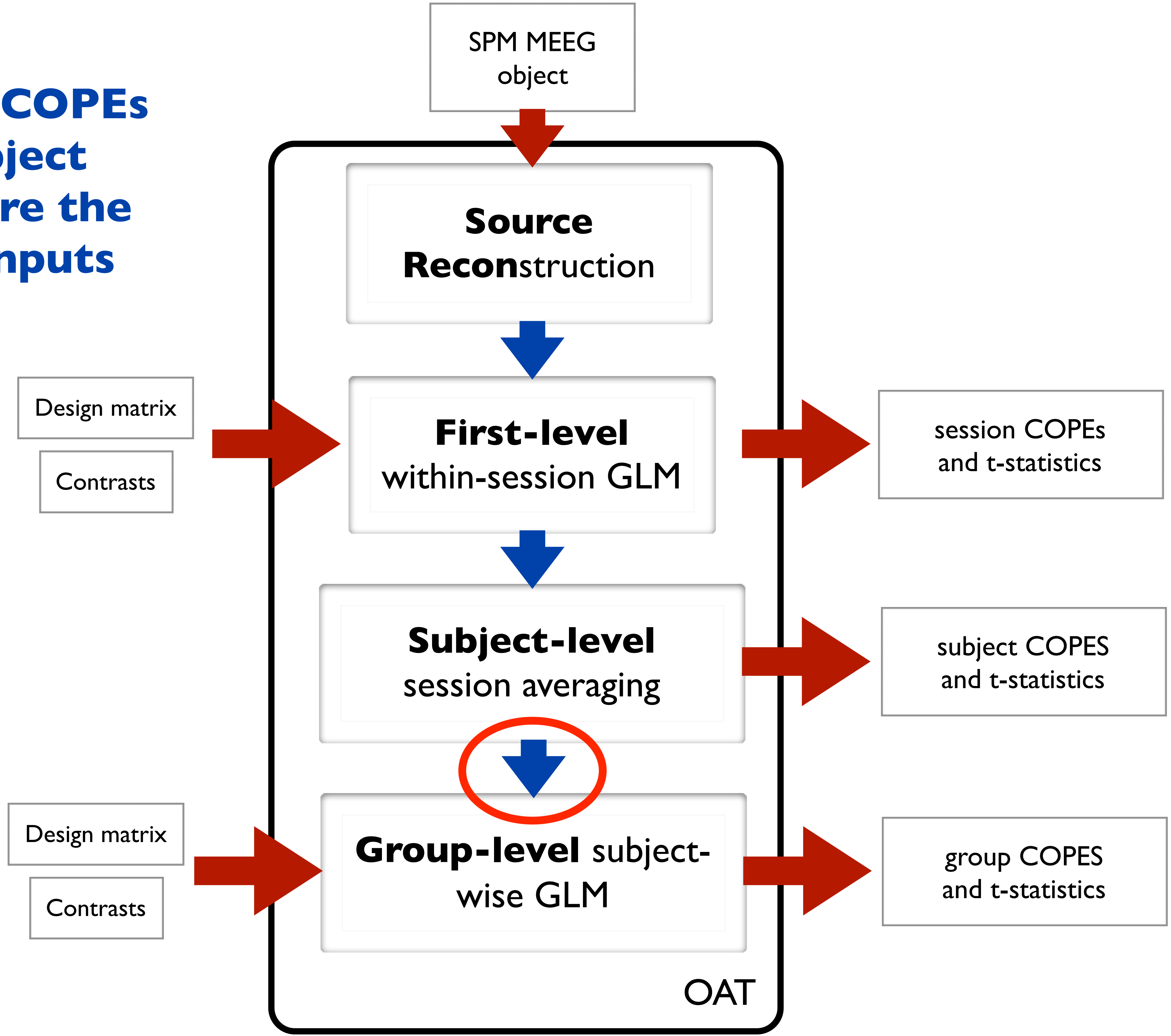
Multiple Session Analysis

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



Multiple Subject Analysis

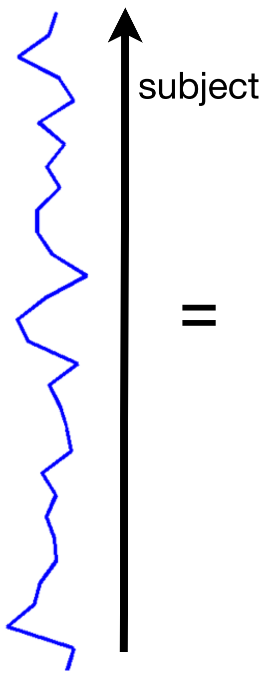
Subject-level COPEs (i.e. mean subject effect sizes) are the Group-level Inputs



Subject-wise GLM (Multiple Regression)

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

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



$$
= \begin{array}{c}
\text{Design Matrix} \\
\left[\begin{array}{cc}
1 & 0 \\
1 & 0 \\
1 & 0 \\
1 & 0 \\
1 & 0 \\
1 & 0 \\
1 & 0 \\
0 & 1 \\
0 & 1 \\
0 & 1 \\
0 & 1 \\
0 & 1 \\
0 & 1 \\
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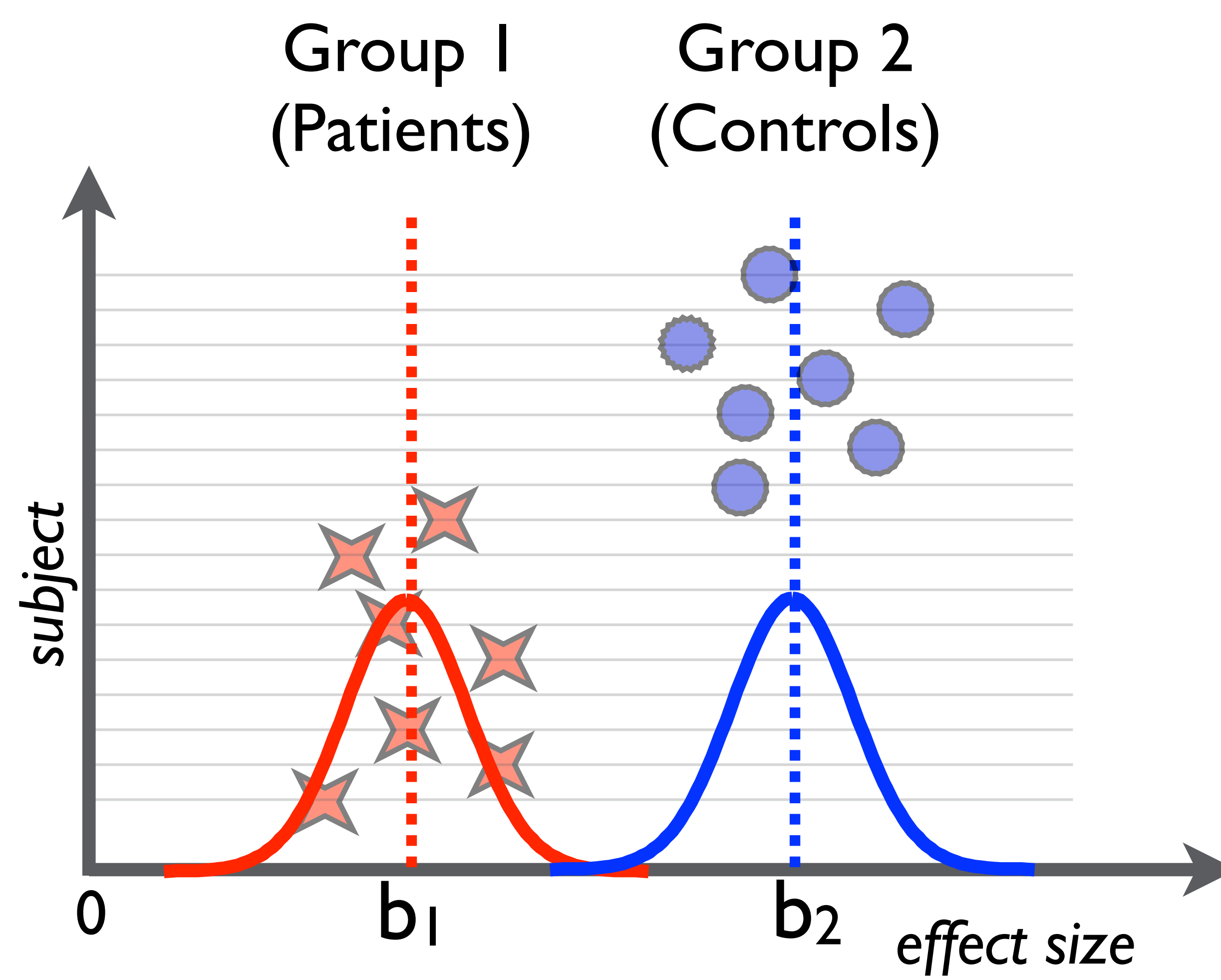
\end{array}\right] \\
\text{Patients} \quad \text{Controls}
\end{array}
\begin{array}{c} b_1 \\ b_2 \end{array} +
$$

error

$$Y \quad = \quad X \quad b \quad + \quad e$$

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

$$Y=Xb+e$$



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\text{Group 2 (Controls)} \\ \\ \\ \\ \\ \\ \\
\end{array}
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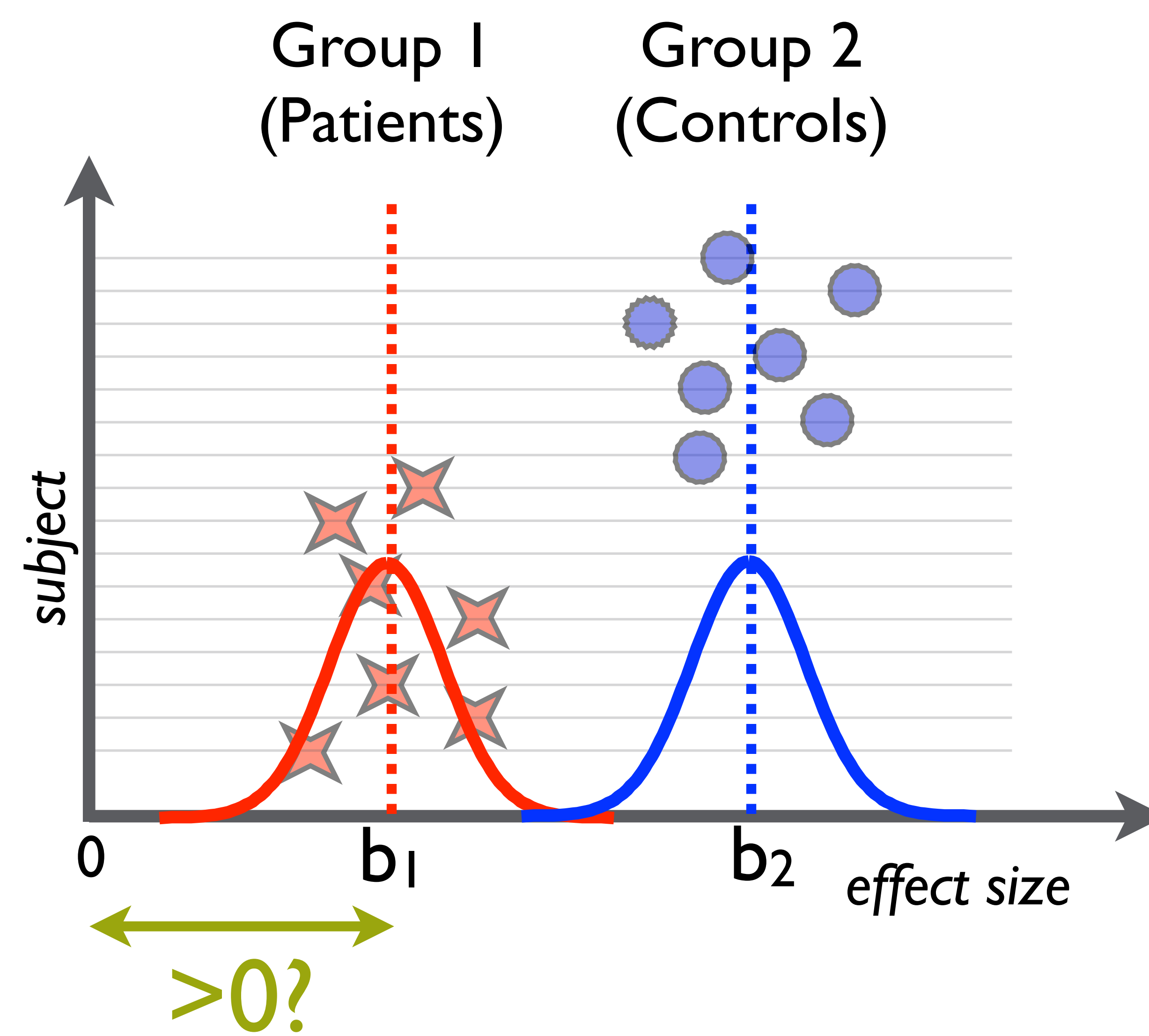
\end{bmatrix}
$$

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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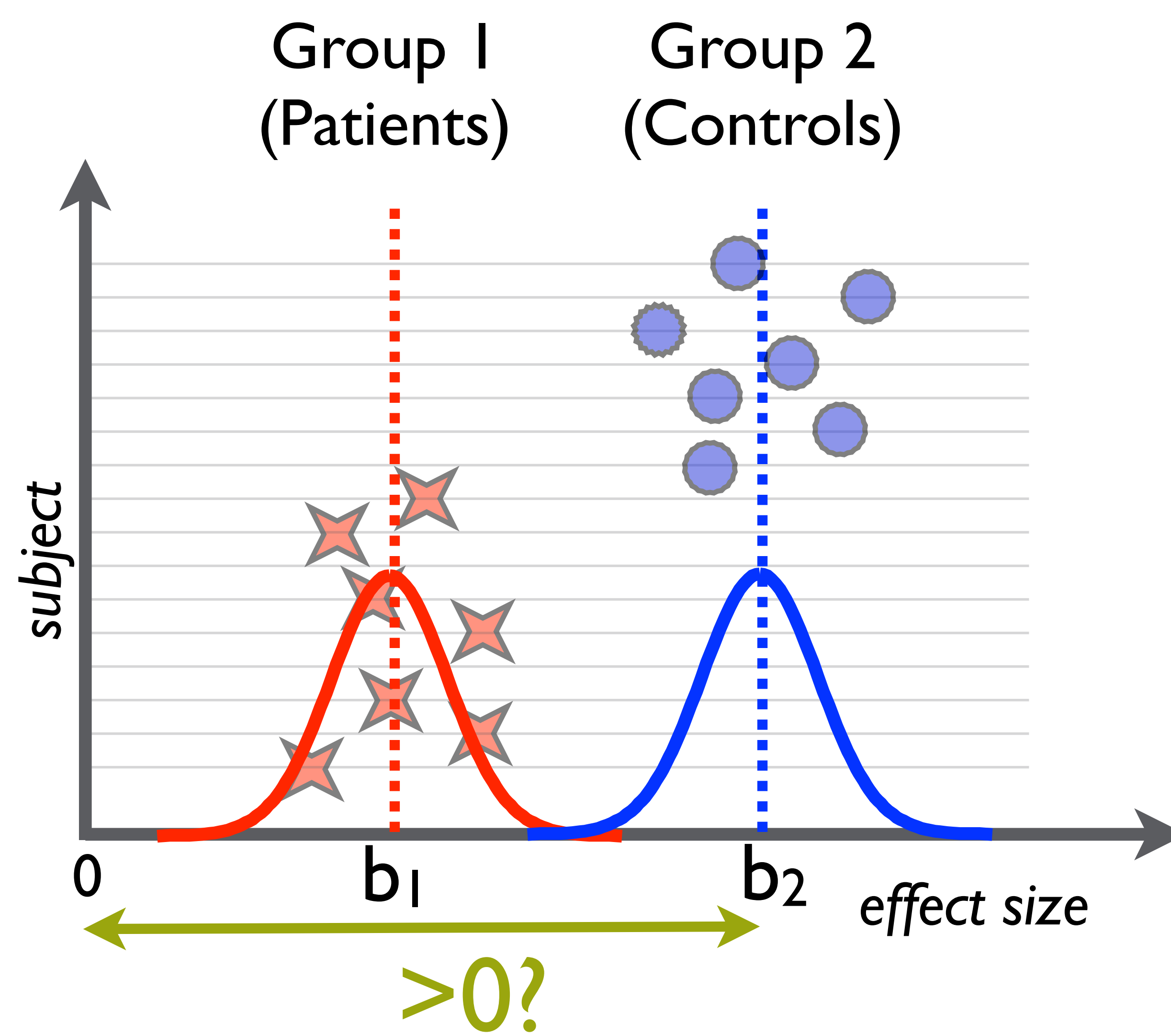

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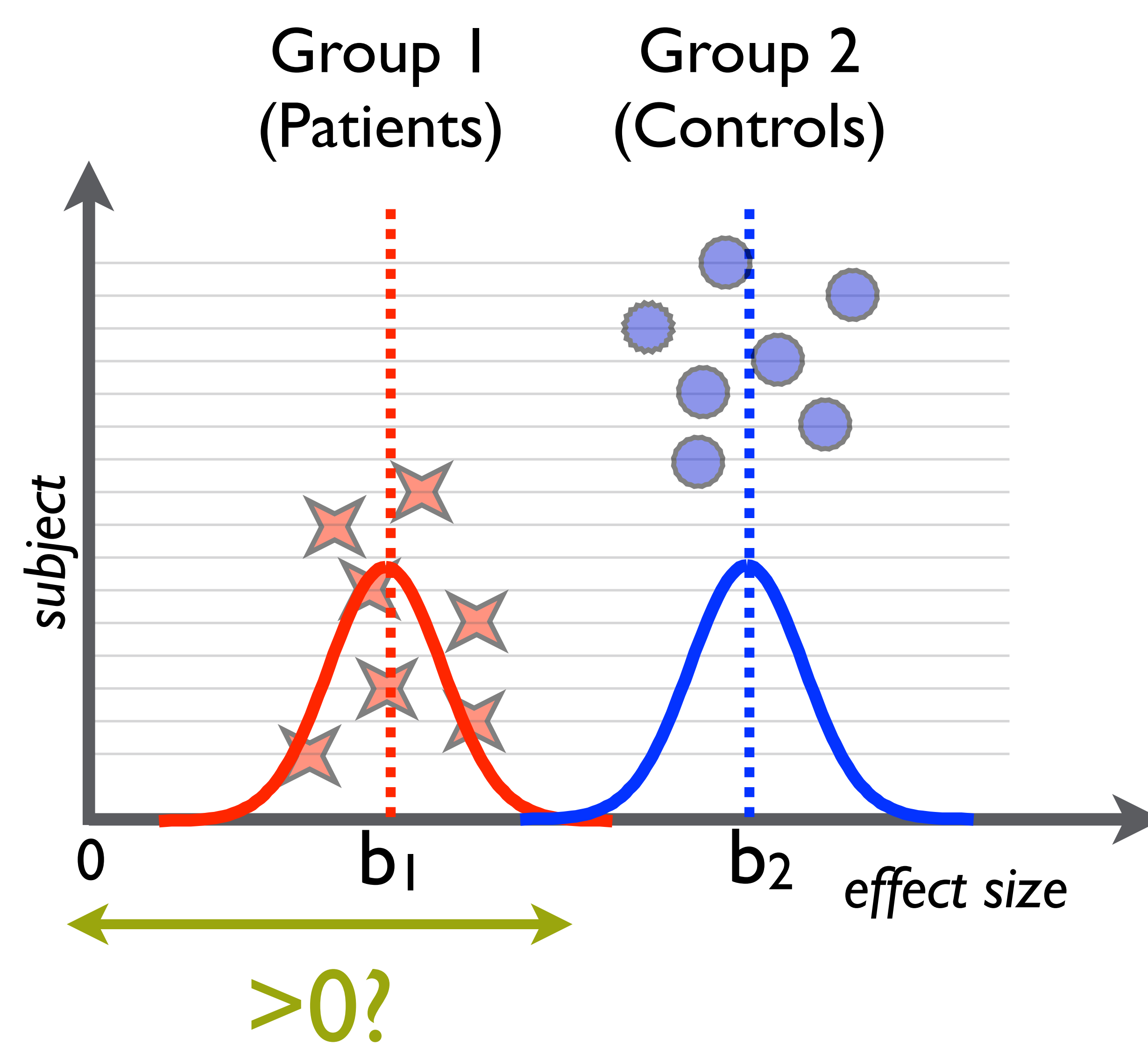

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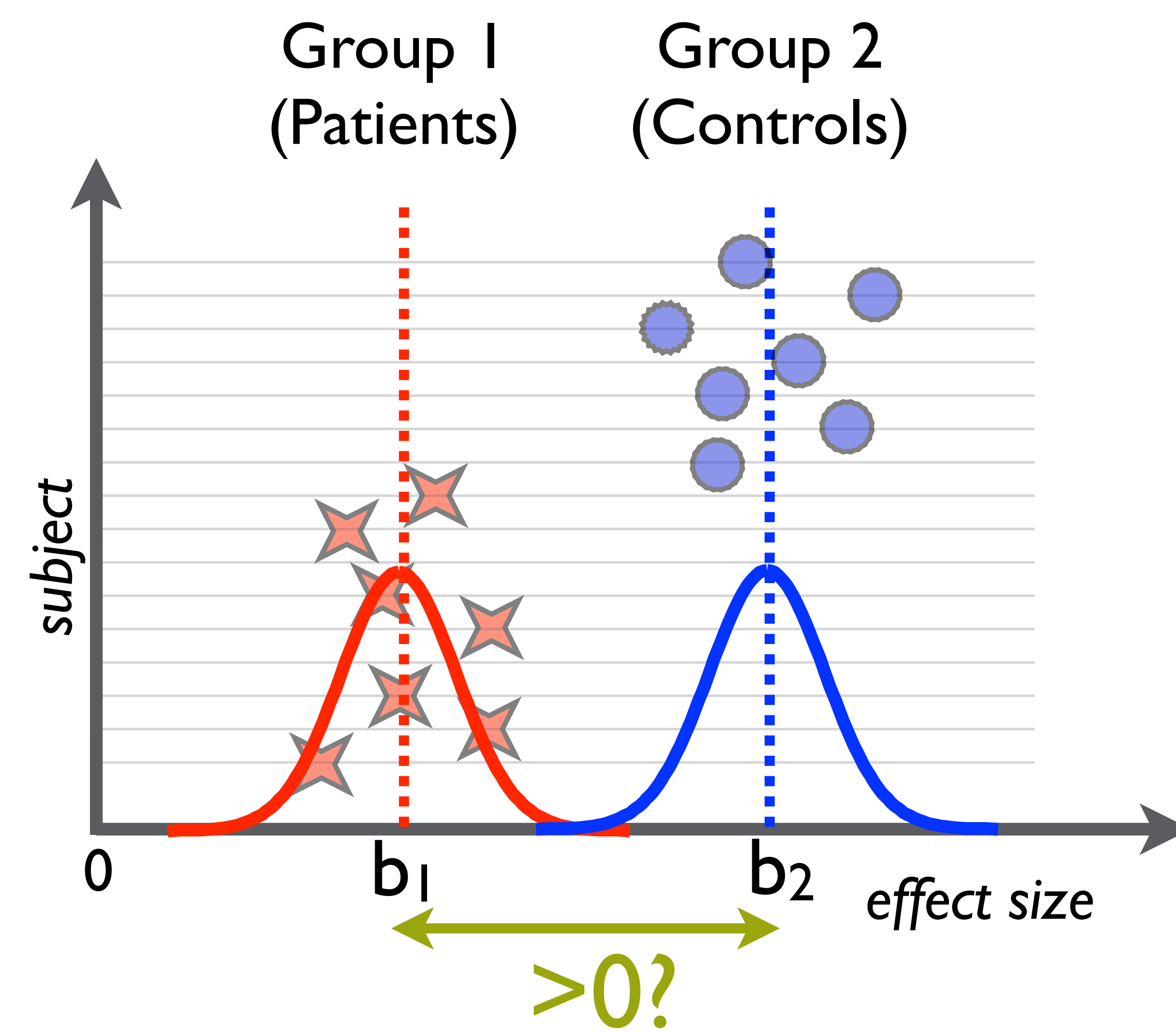

Subject-wise GLM (Multiple Regression)

Design Matrix

$$
Y = \begin{array}{c} \\ \left[\begin{array}{cc} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{array}\right] \\ \text{Patients} \quad \text{Controls} \end{array} \begin{array}{c} b_1 \\ b_2 \end{array} + e
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subjects

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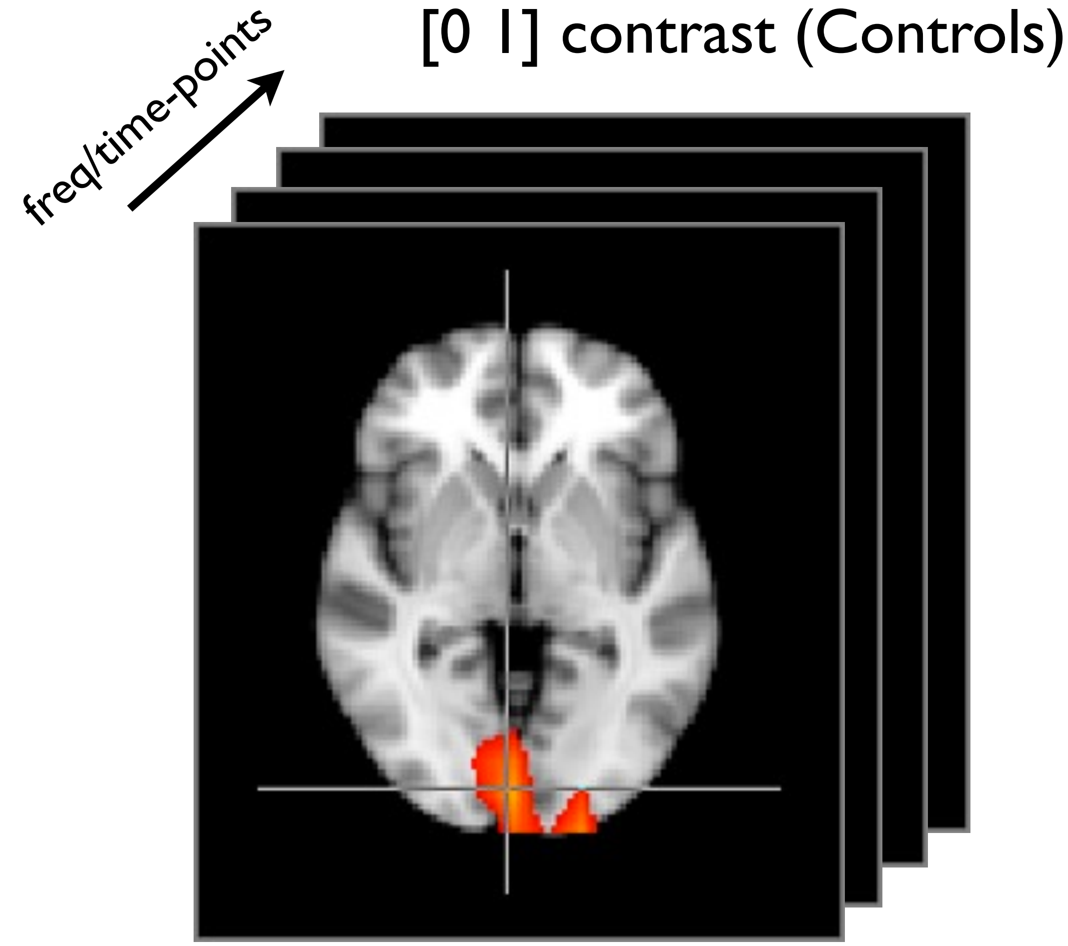
$Y \;=\; X \;\; b \; + \; e$

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



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

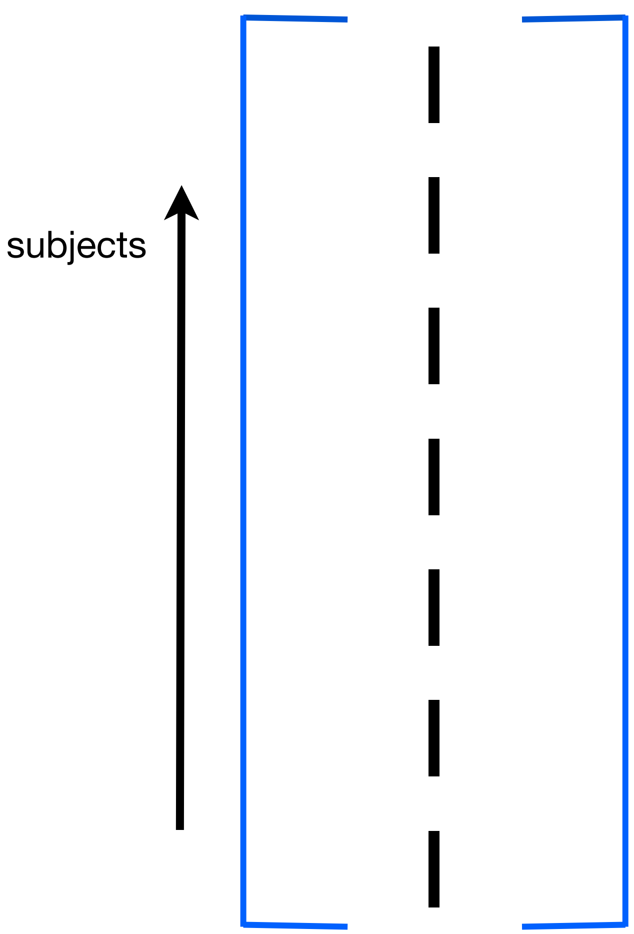
$Y=Xb+e$ → Fit GLM

- This is also all repeated for ALL first-level contrasts (COPES)

Single Group Average

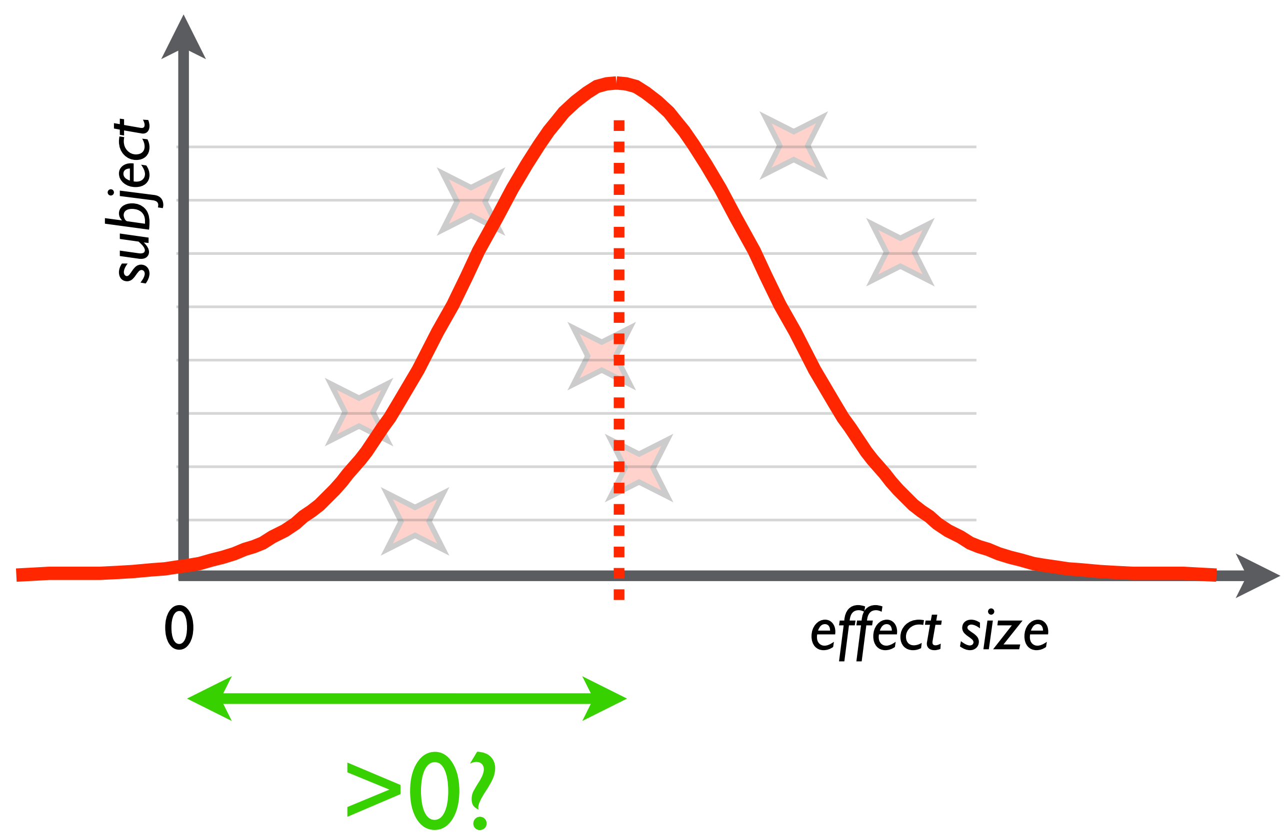
- We have 7 subjects - all in one group - and want the mean group average:

Design Matrix



Contrast 1: [1]

Does the group activate on average?



Behavioural Variables

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

Design Matrix

subjects

$$\begin{bmatrix} 1 & 3 \\ 1 & 1 \\ 1 & 0 \\ 1 & 1 \\ 1 & 0 \\ 1 & -1 \\ 1 & -4 \end{bmatrix}$$

- 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)

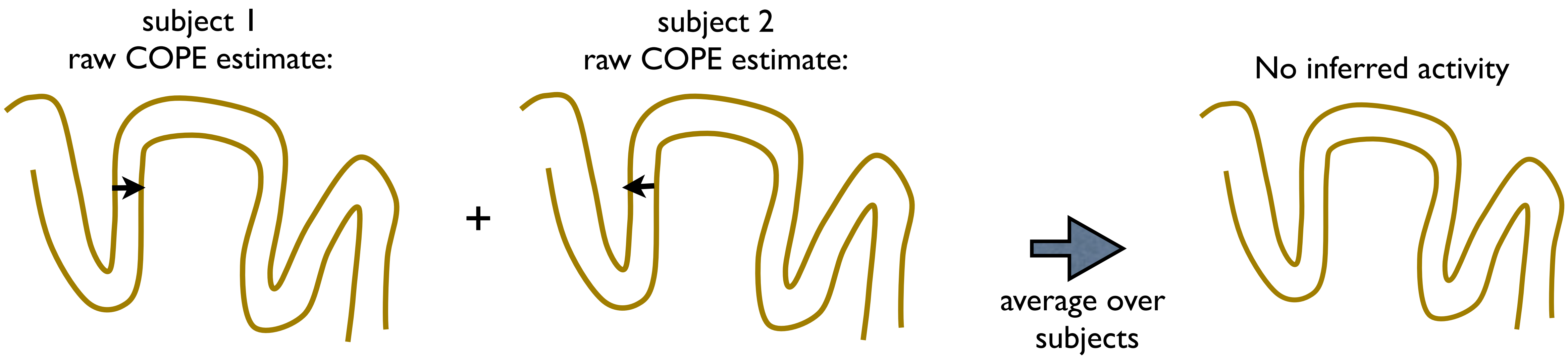
Other things you can do with the Group GLM

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

- Time-frequency power analysis. Note: if whole brain then do these a band at a time (for speed)
- Sensor space

Note on ERF “rectification”

For ERF analysis, in OSL we rectify (take the absolute value of) the first-level COPEs and baseline correct



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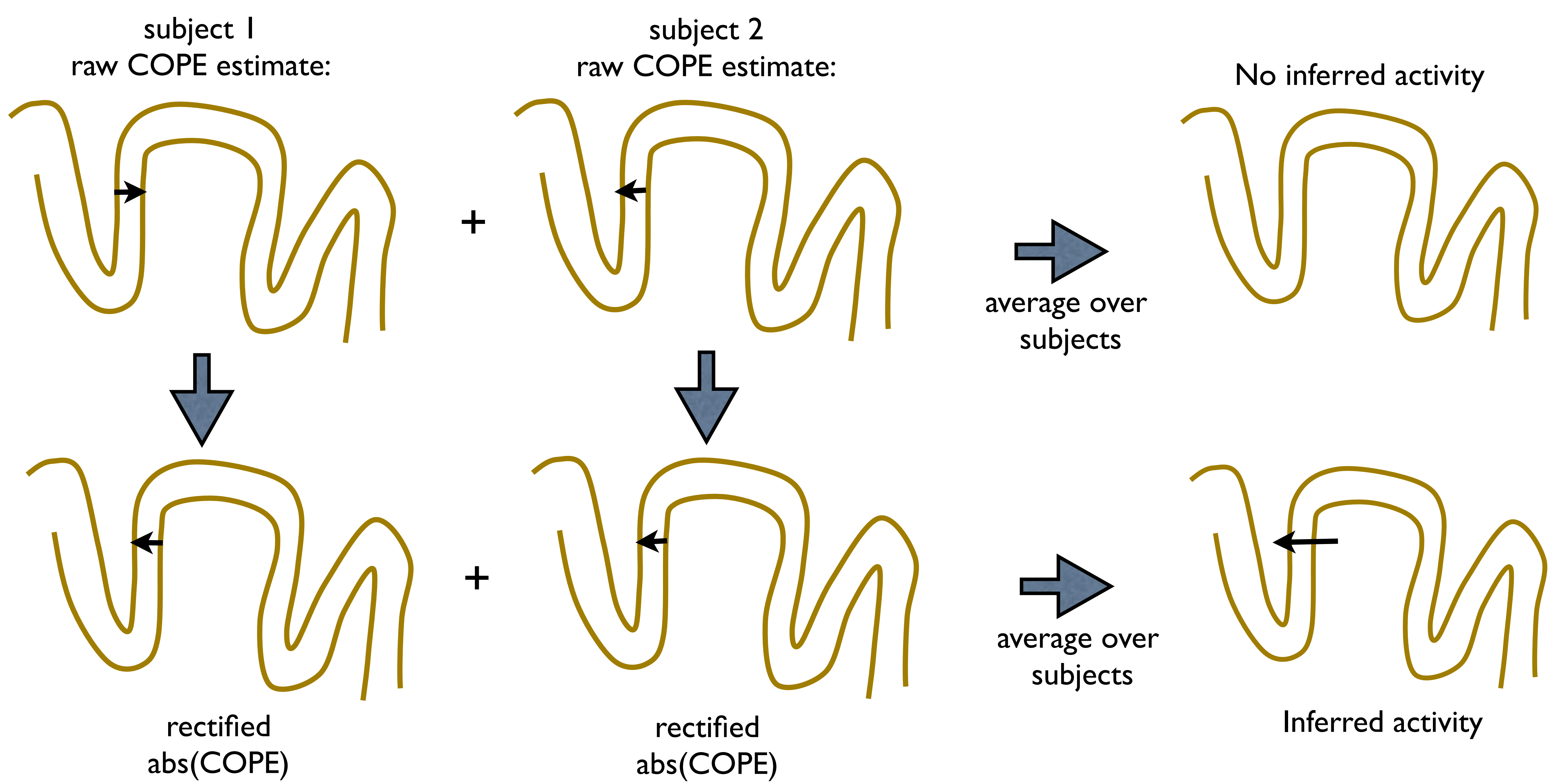

Multiple Comparison Problem

- We could carry out a null hypothesis test for each voxel using a chosen false positive rate (FPR)
- However, if we used FPR=0.05 with 20,000 brain voxels then we would get 1000 FPs

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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

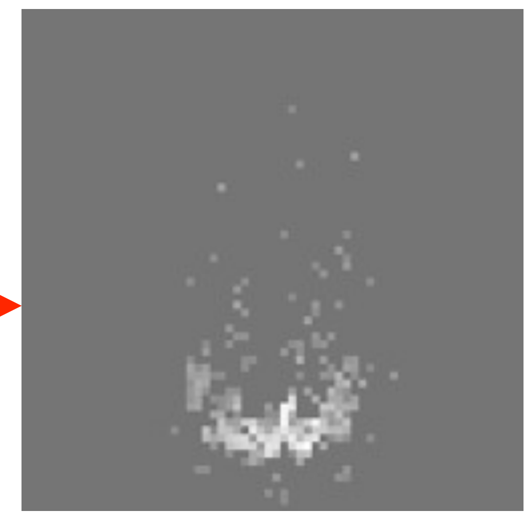
  $0.05 / 20{,}000 = 0.0000025$

Thresholding: Clustering

What about testing significance on clusters?

stat image

Threshold at
(arbitrary!) level



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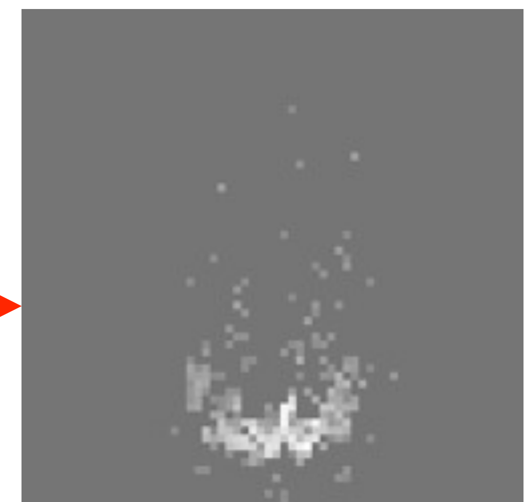


- Form clusters from surviving voxels.

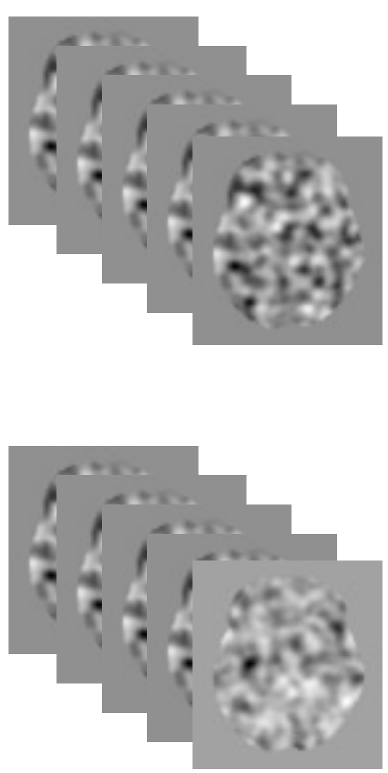
- **BUT**, what is the probability of getting a cluster, given its spatial extent (no. of voxels in cluster) and z threshold, under the null hypothesis?
- Can use Random Field Theory, but involves dodgey assumptions, instead ...

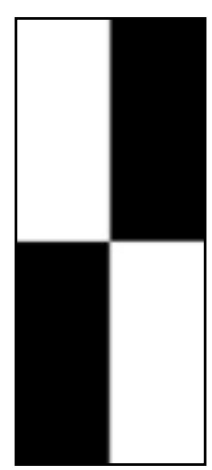
Permutation Testing

We can record the cluster sizes from our dataset

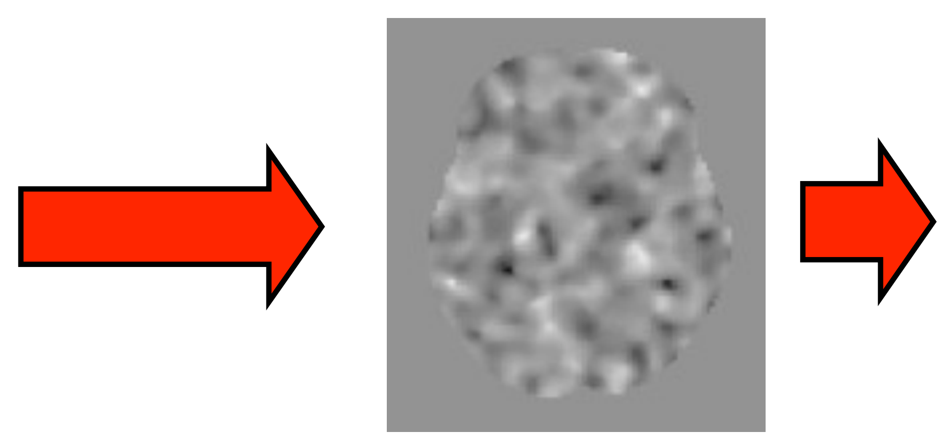
Group 1

Group 2





Our actual 2nd level model

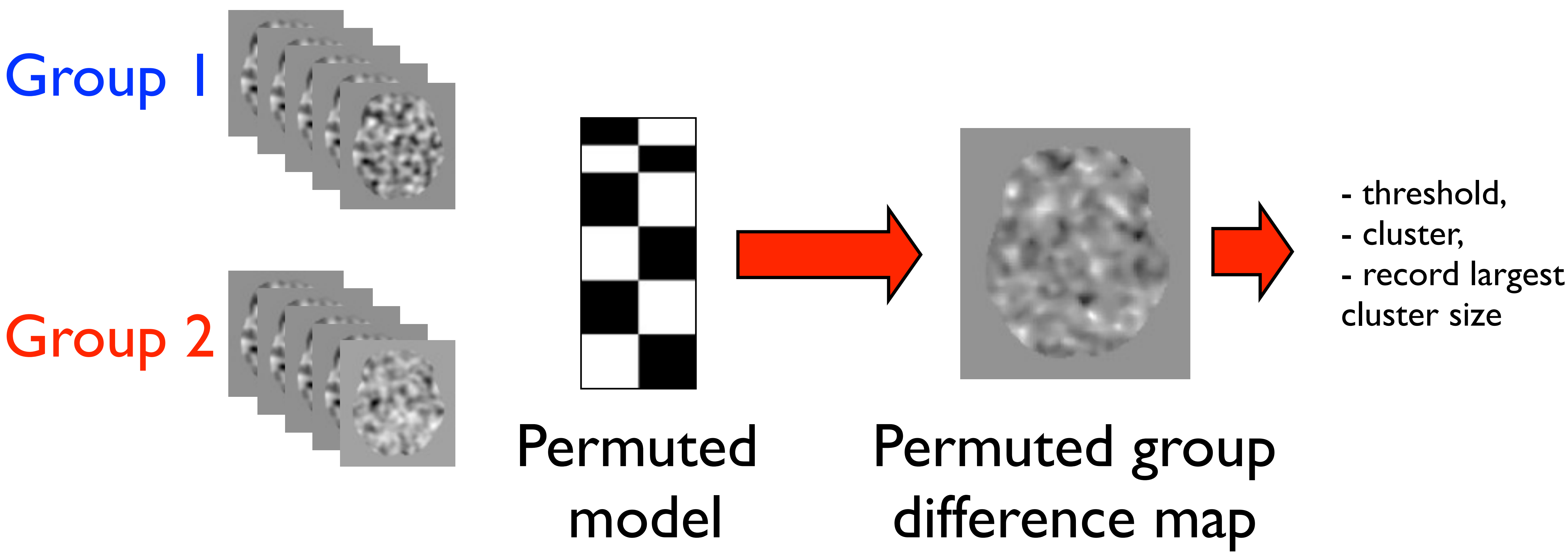


Our actual group difference map

- 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



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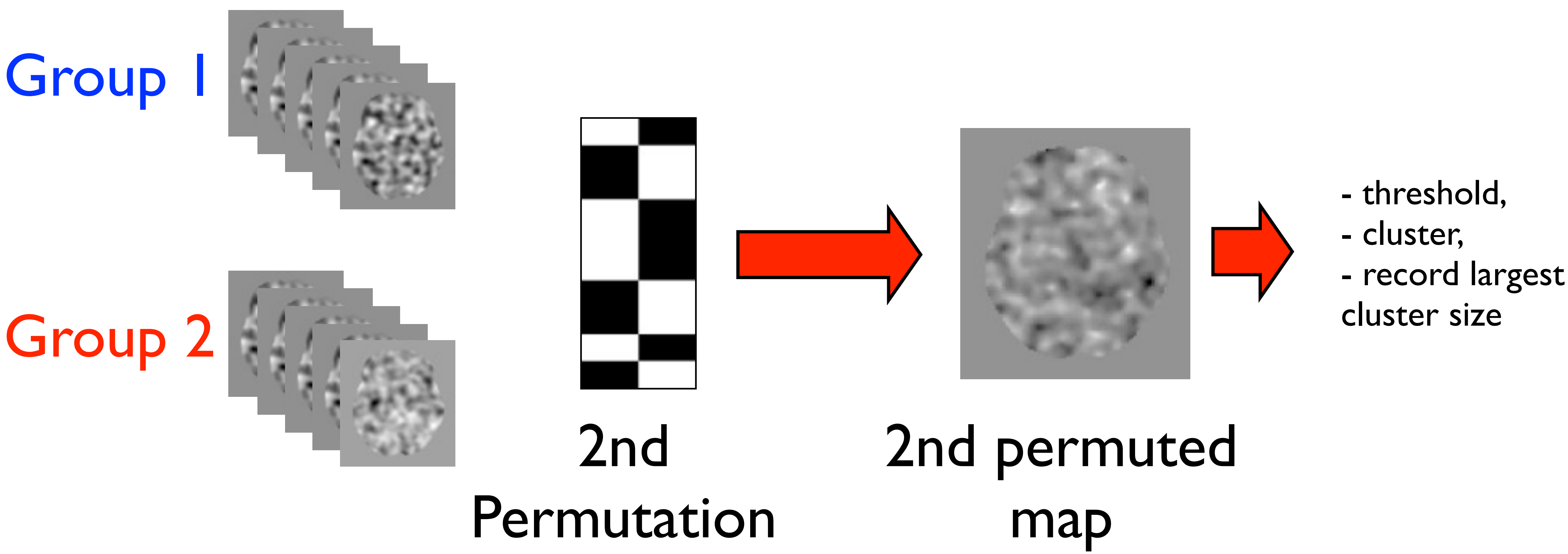

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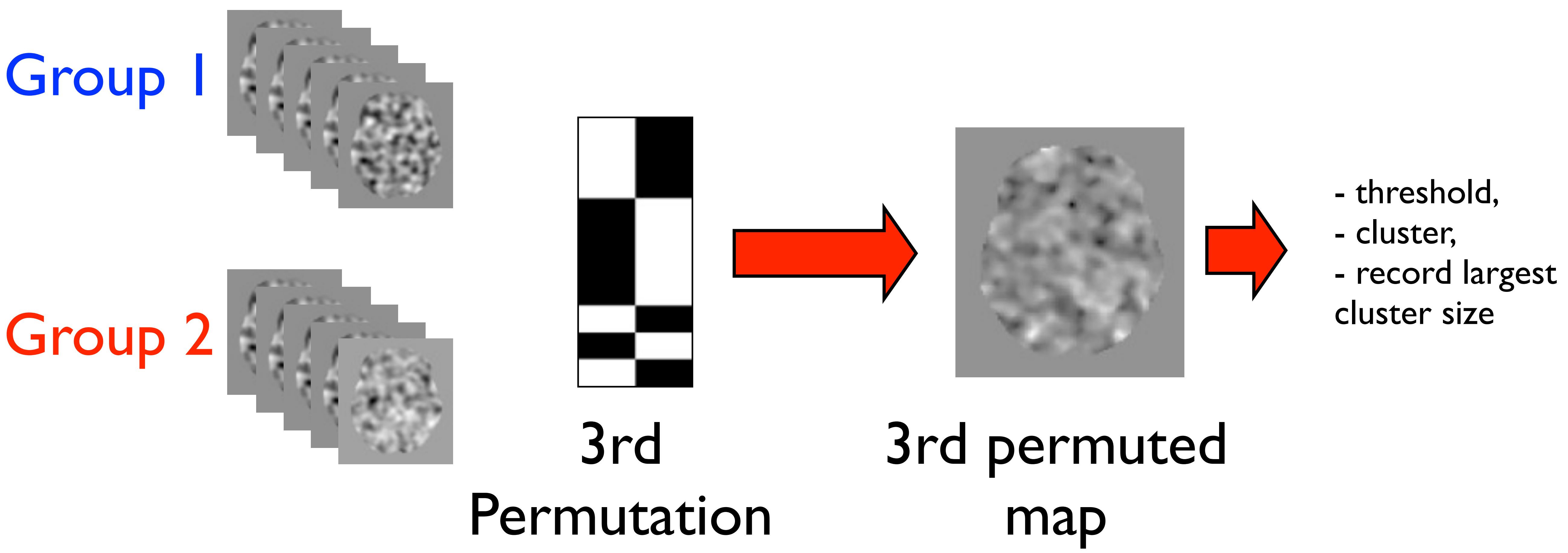

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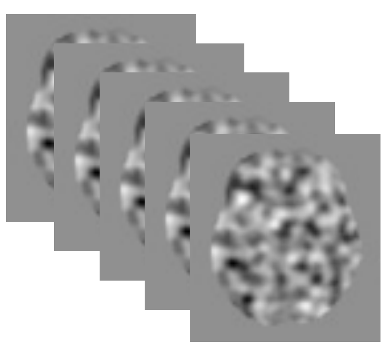
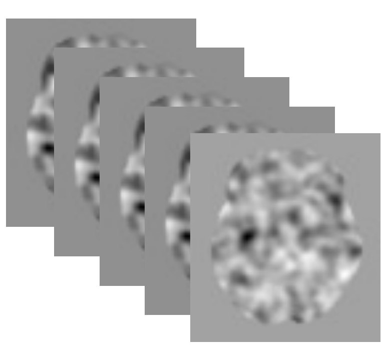
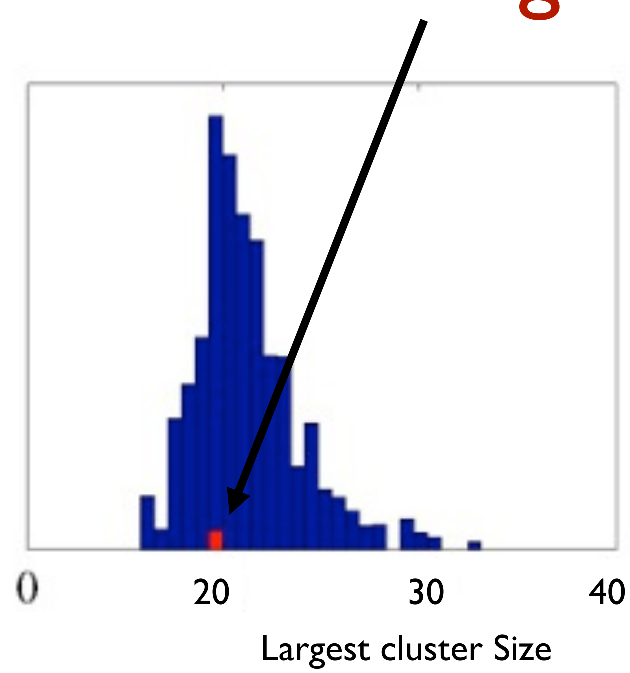


Group 2



Original group labellings



- 3925 permutations yielded larger clusters than original group labellings.
- We cannot reject the null-hypothesis in this case

5000 permutations

Permutation Testing

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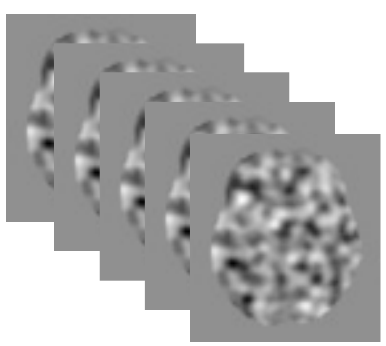
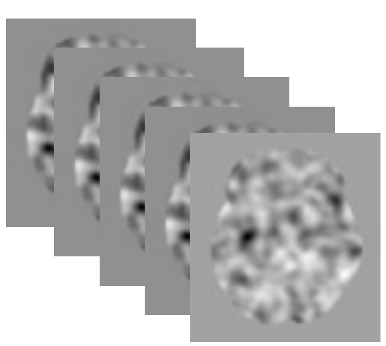


Group 2



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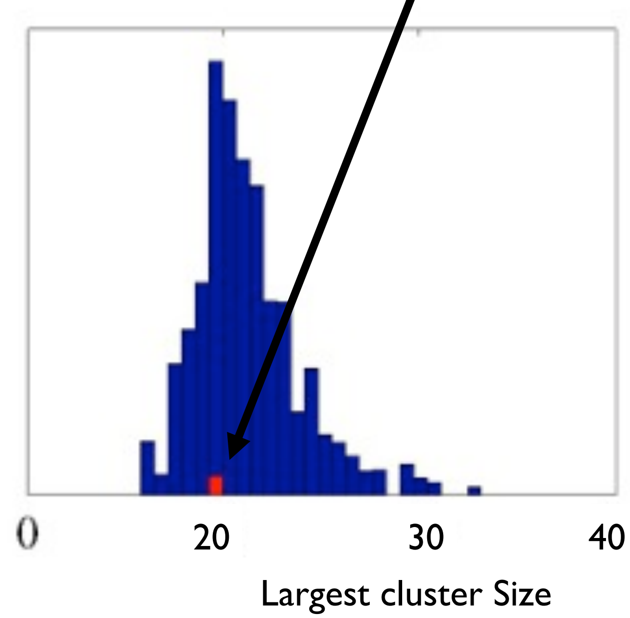
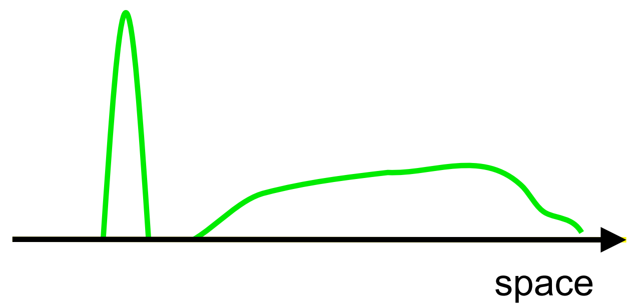


5000 permutations

- OSL has the facility to test clusters in:
  - 2-D (time-frequency)
  - 3-D (space)
  - 4-D (space and e.g. time)
- Note: 4D is very slow!!

How do we choose the (arbitrary!) cluster forming threshold?

This is arbitrary and a trade-off



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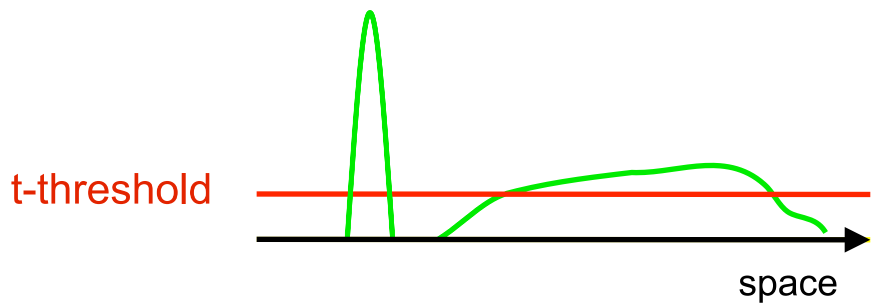
1. **Low threshold** - can detect clusters with large spatial extent and low t-statistic



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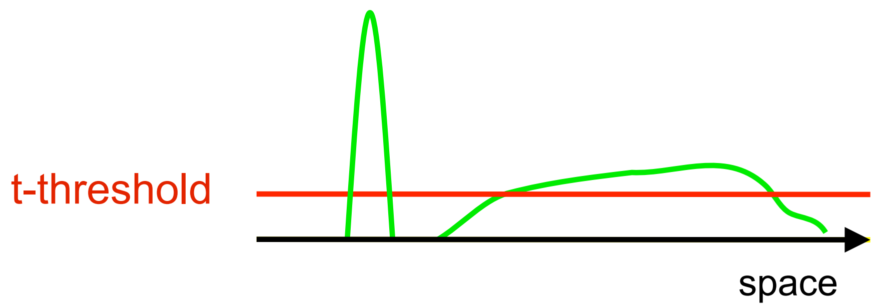
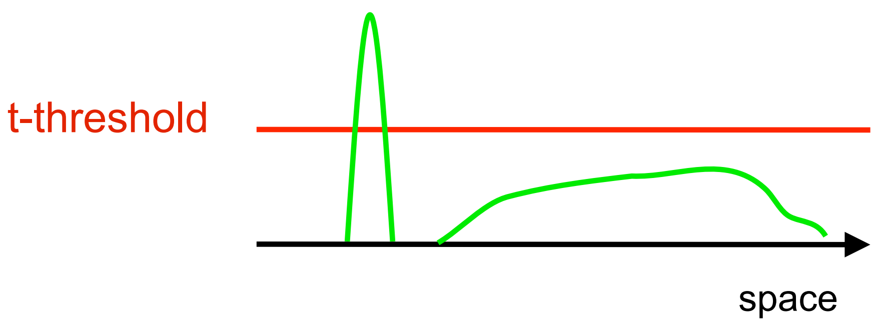


2. **High threshold** - gives more power to clusters with small spatial extent and high t-statistic



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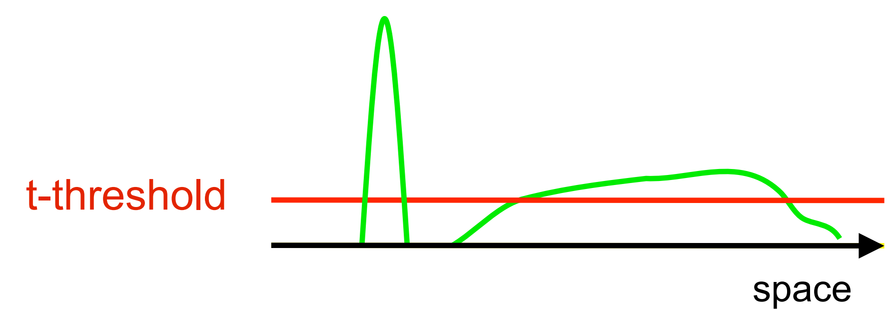

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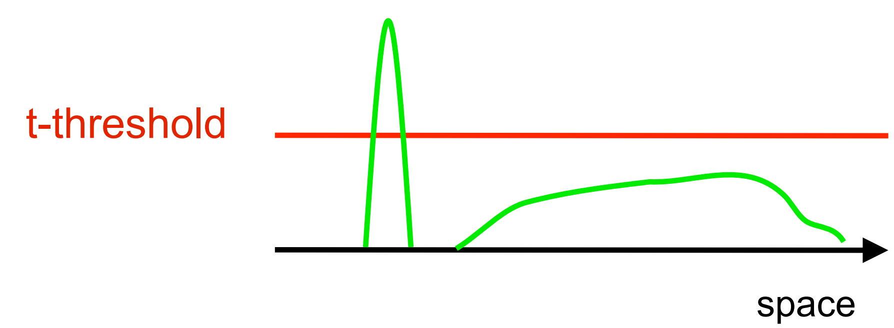

Variance Smoothing

- 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