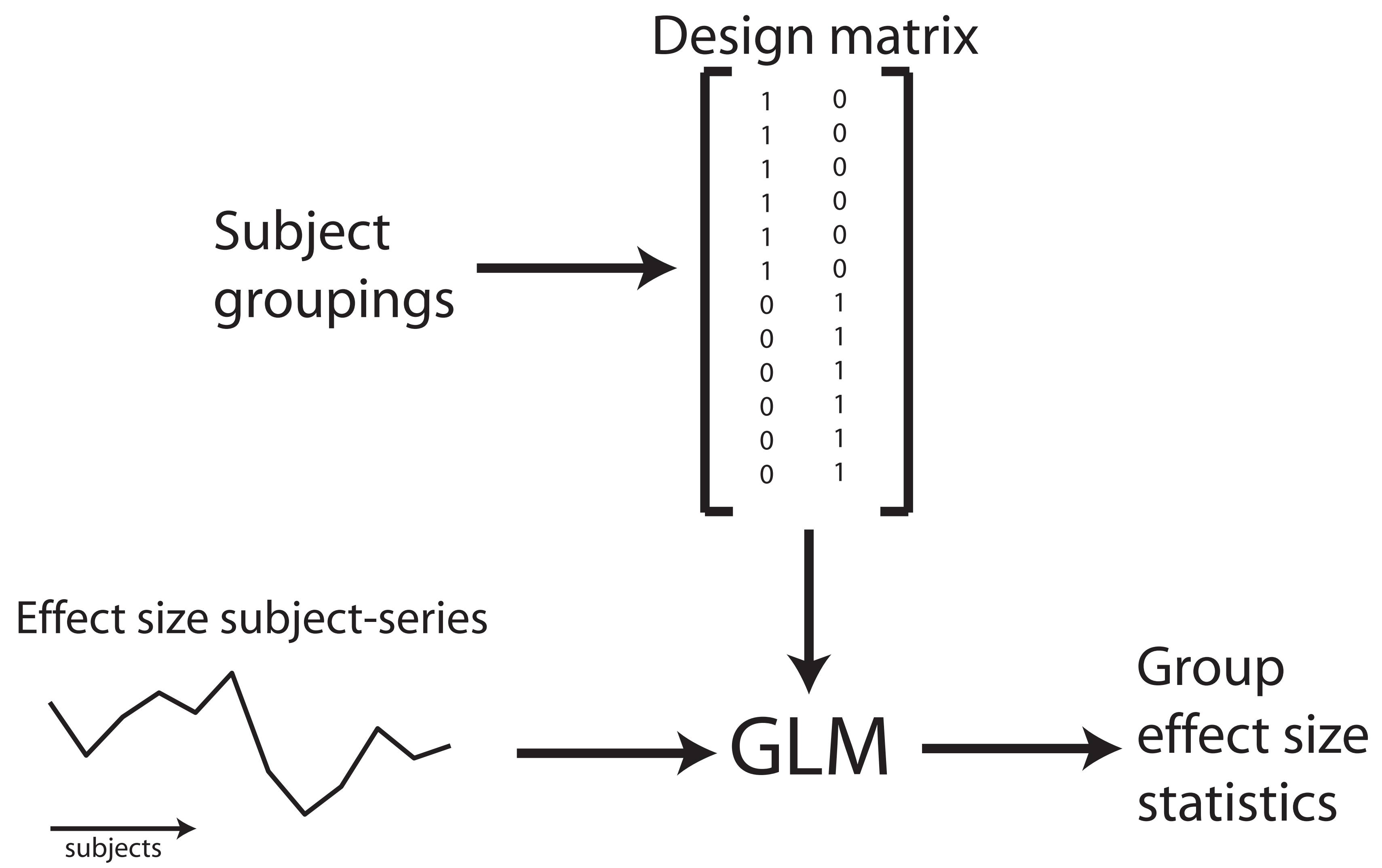
FMRI group analysis

- Overview
- Fixed versus mixed effects
- Multiple sessions per subject



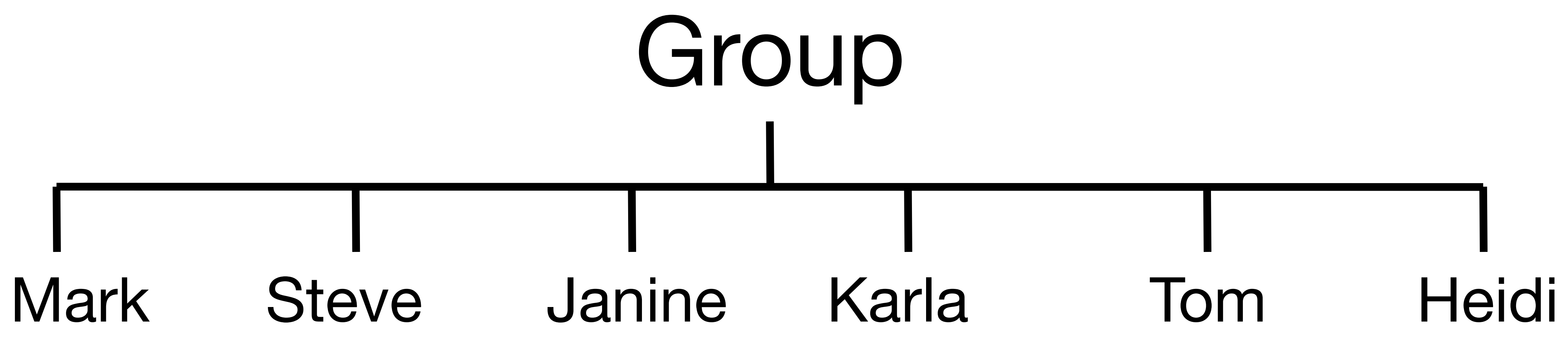
Similarities across modalities

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

Same across modalities (steps 1–2 and 4–5)

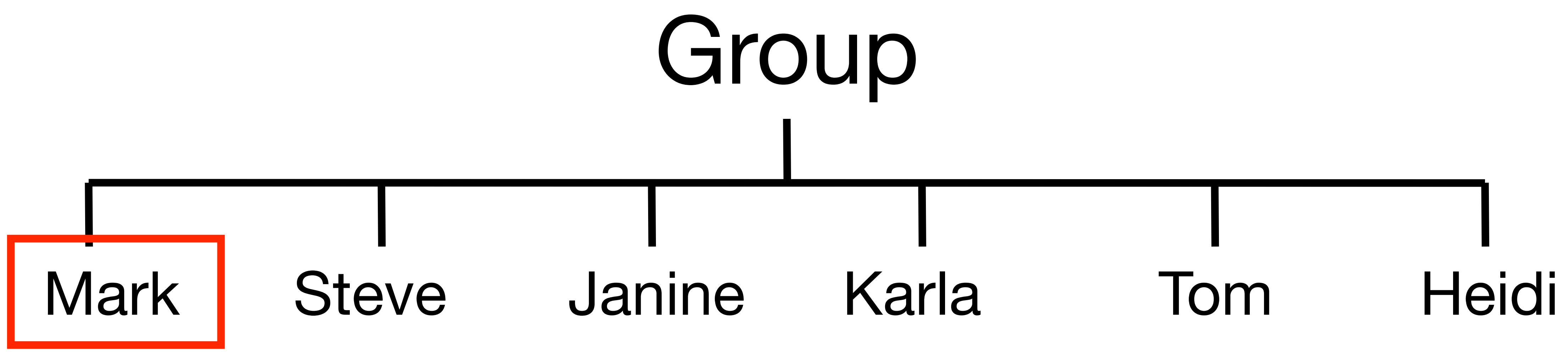
Different across modalities (step 3)

A simple example



Does the group activate on average?

A simple example



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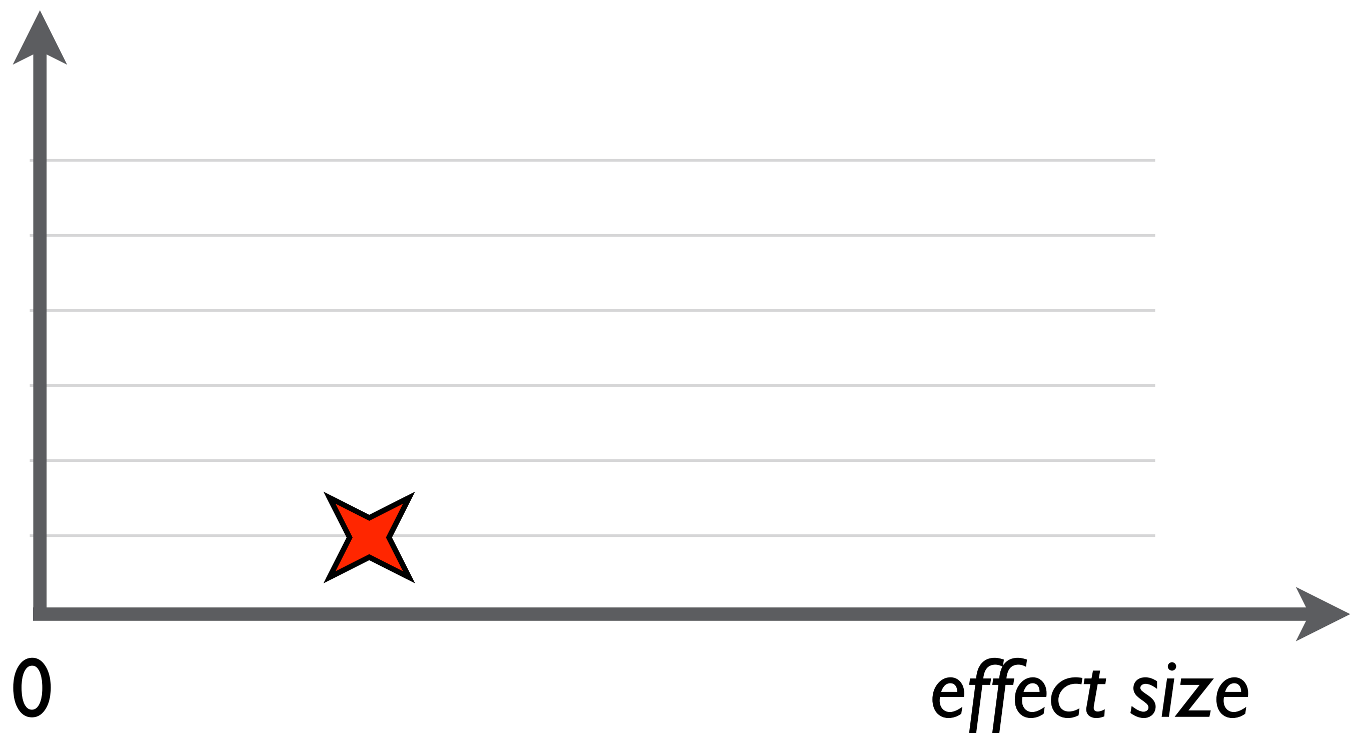

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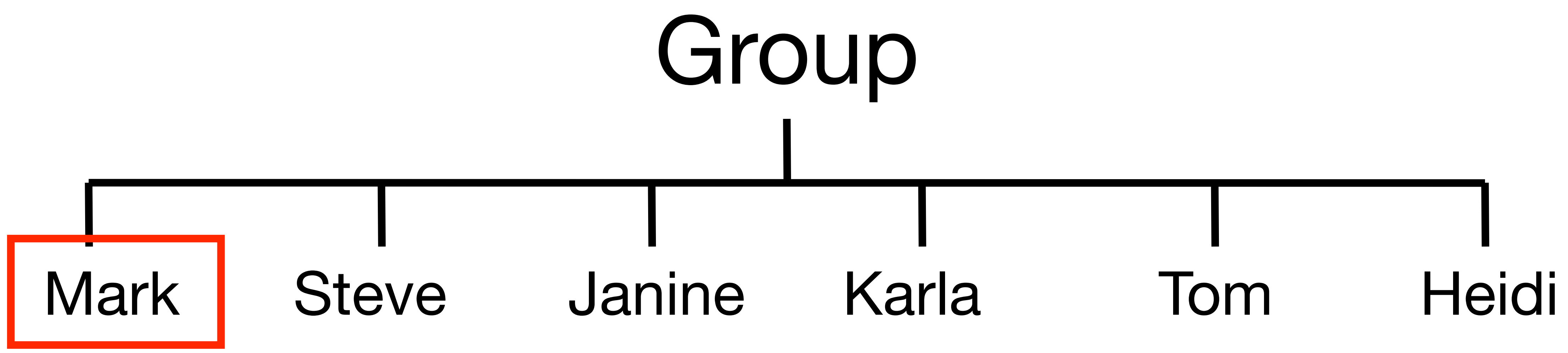
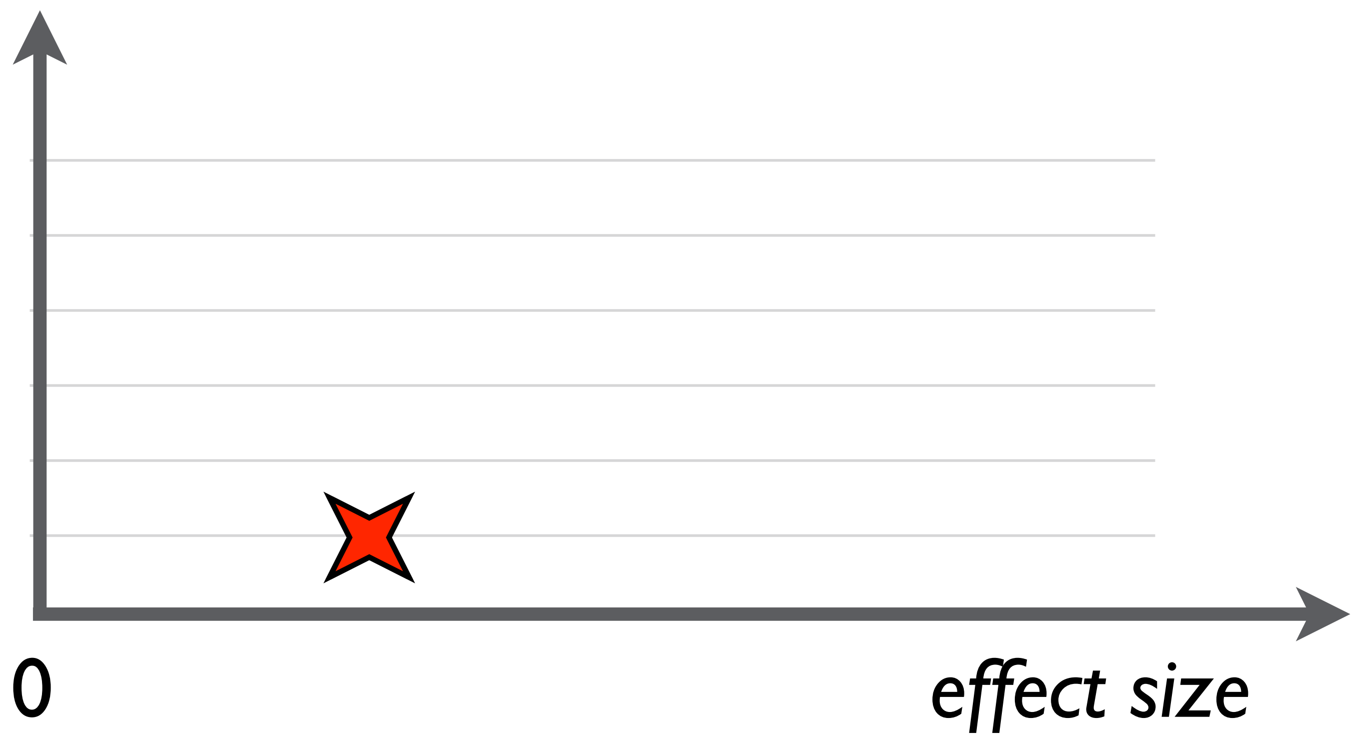


Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

First-level GLM
on Mark's 4D FMRI
data set



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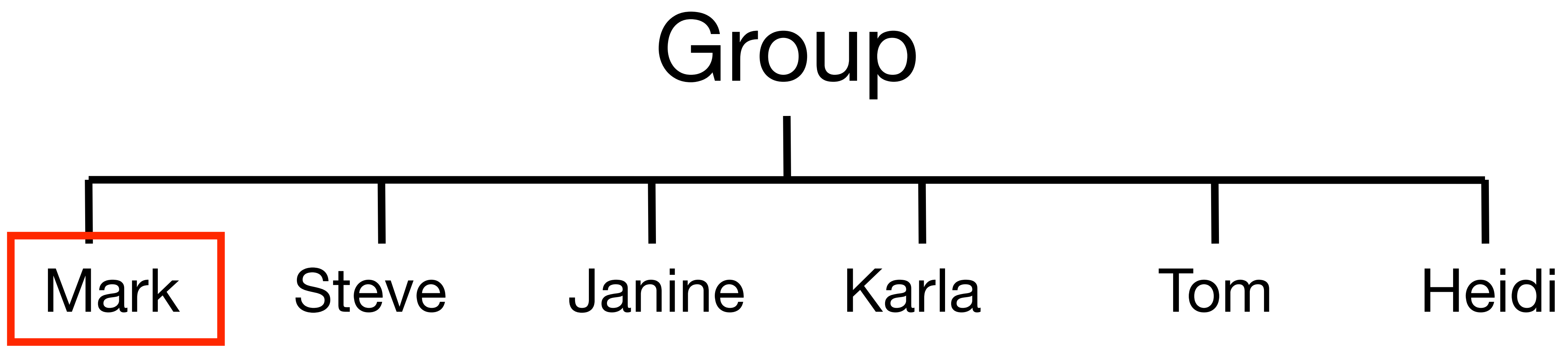
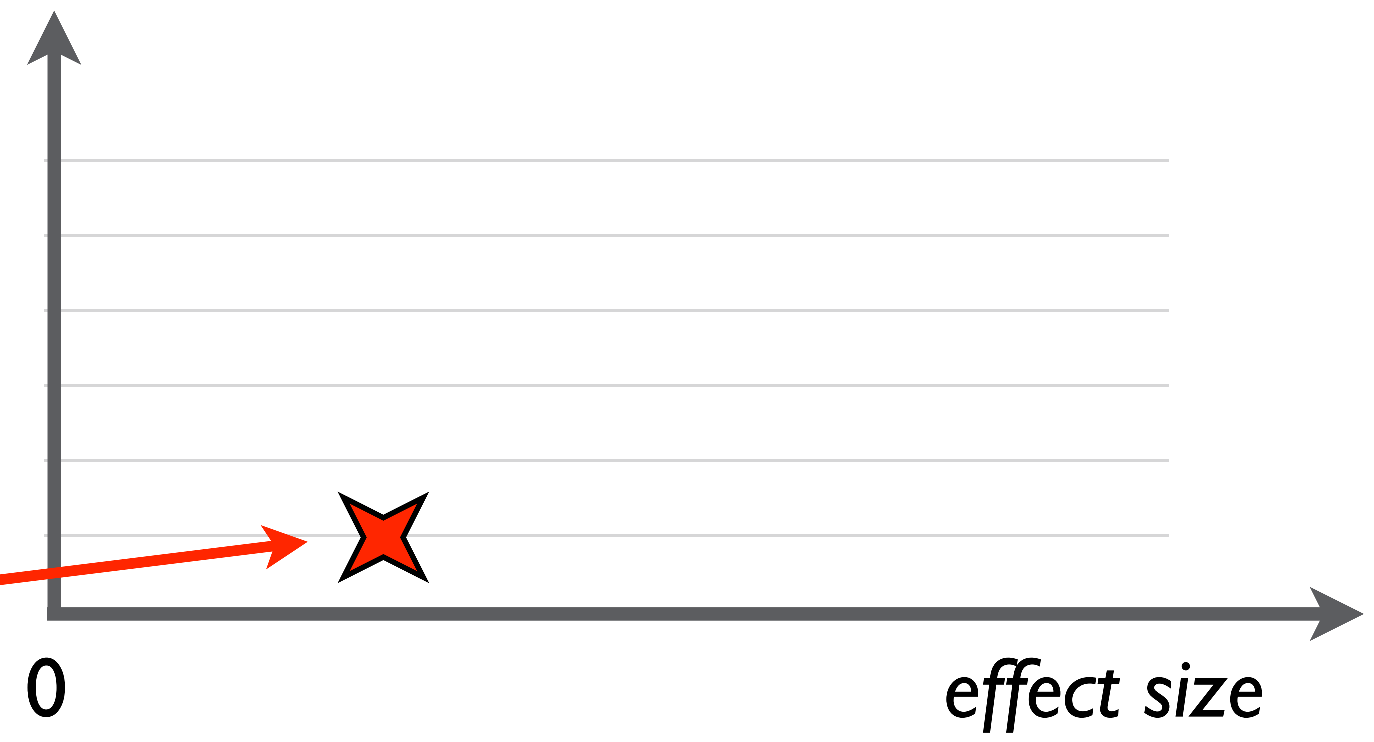


Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

Mark's
effect size



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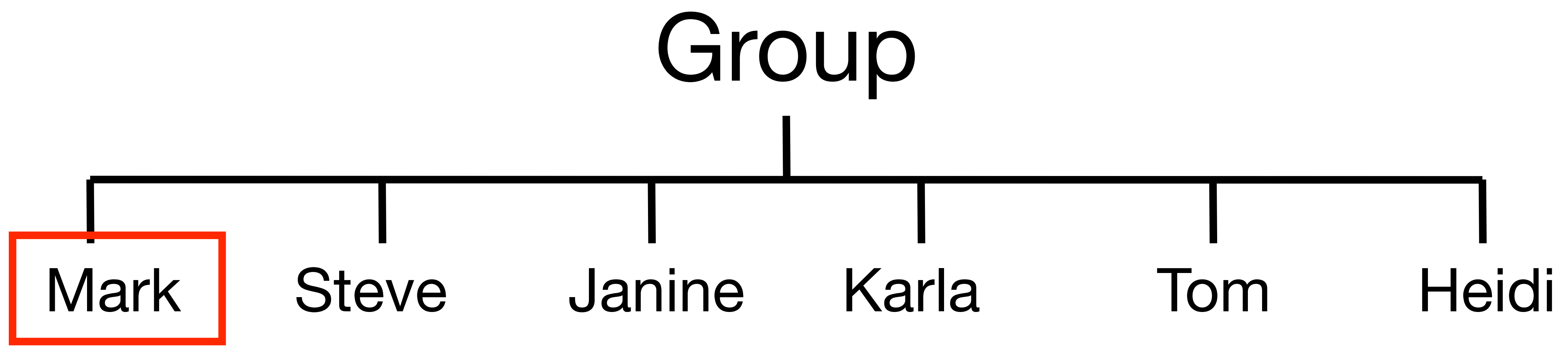
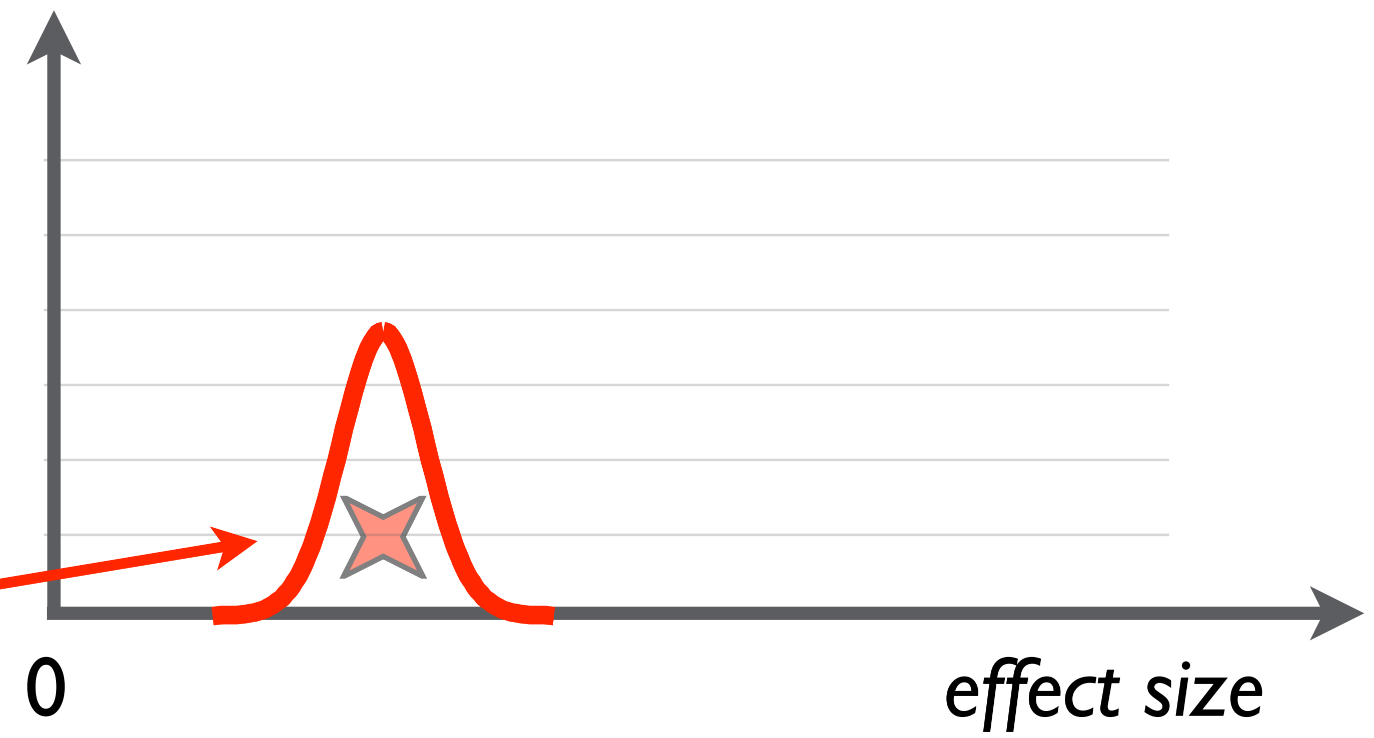


Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

Mark's within-subject variance



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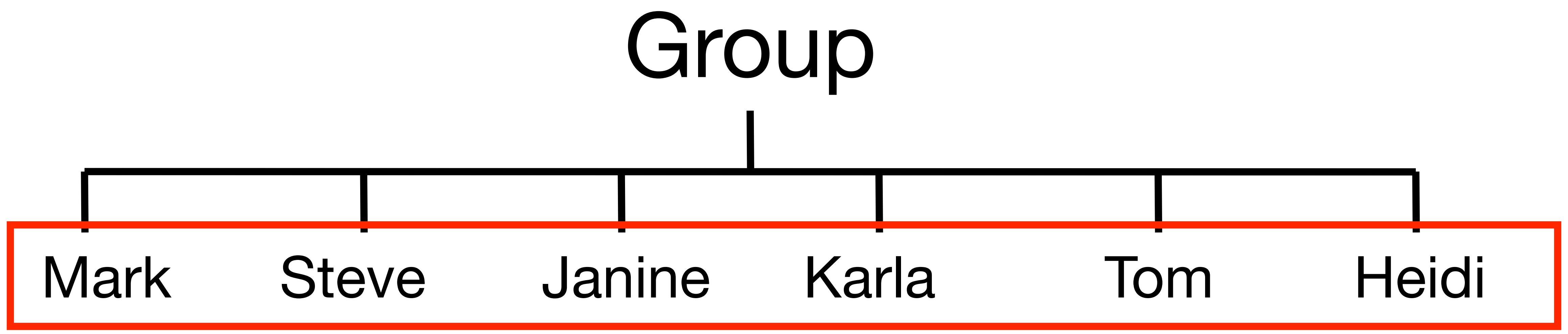
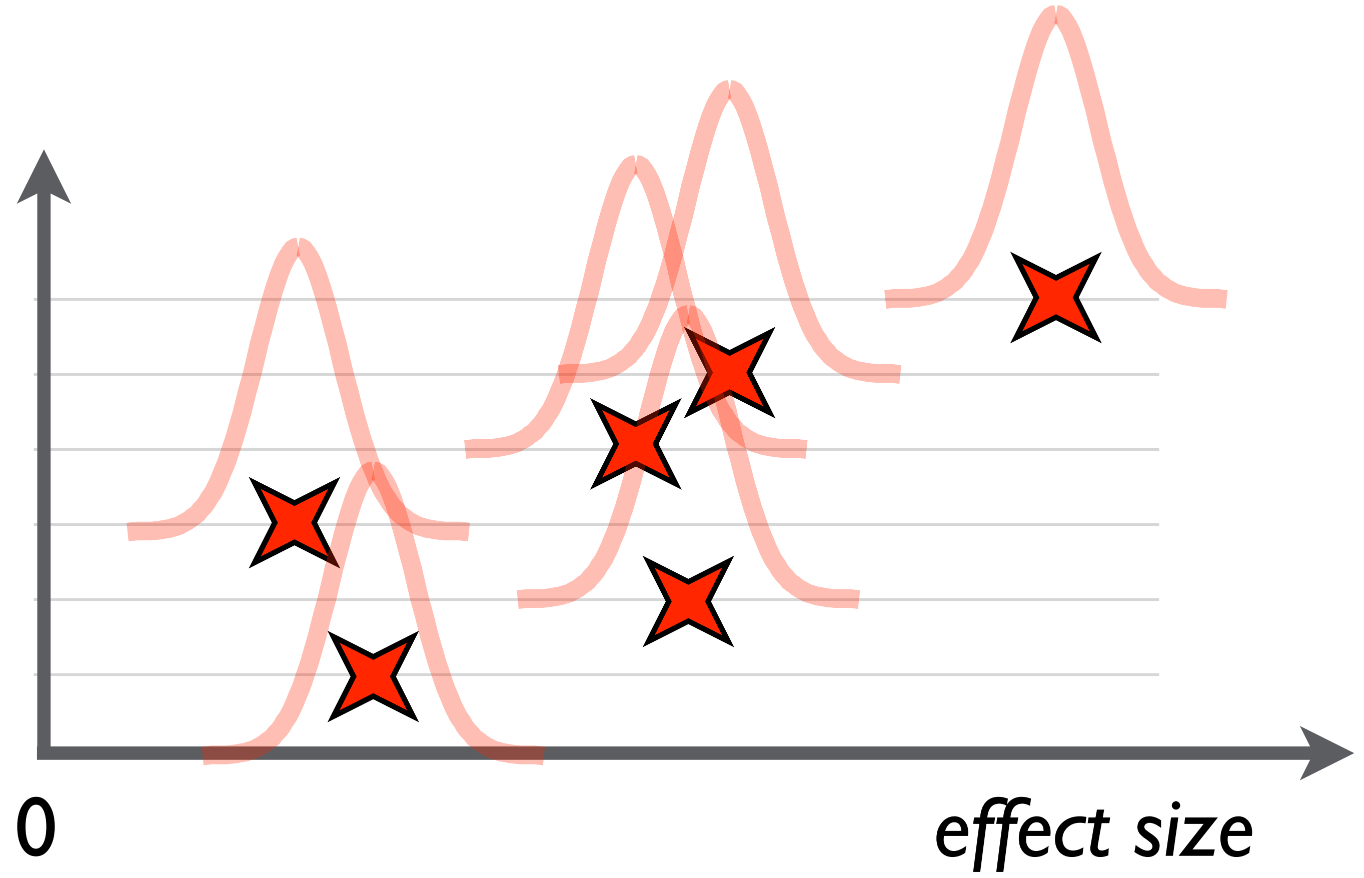


Does the group activate on average?

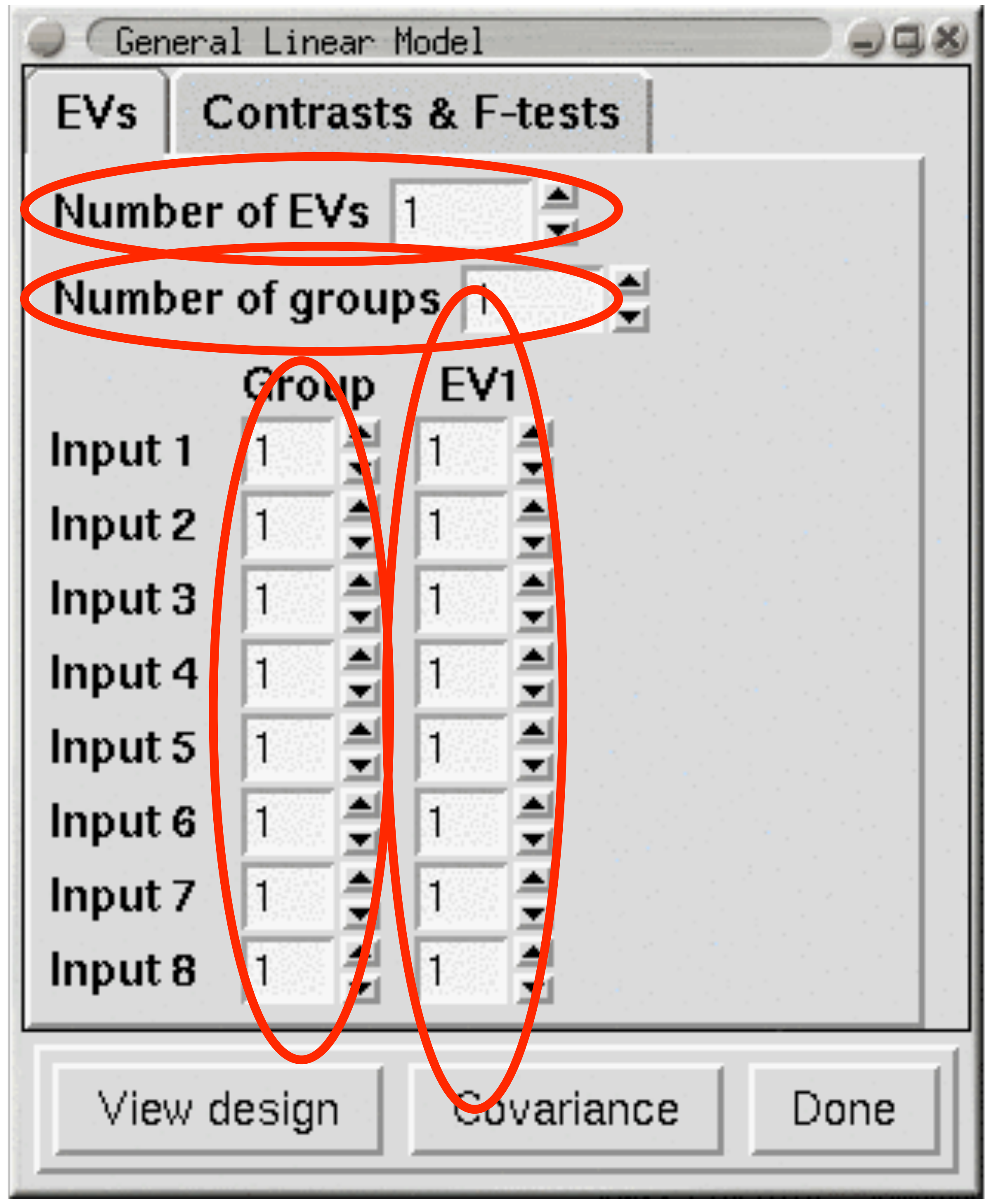
$$Y_k = X_k \beta_k + \epsilon_k$$

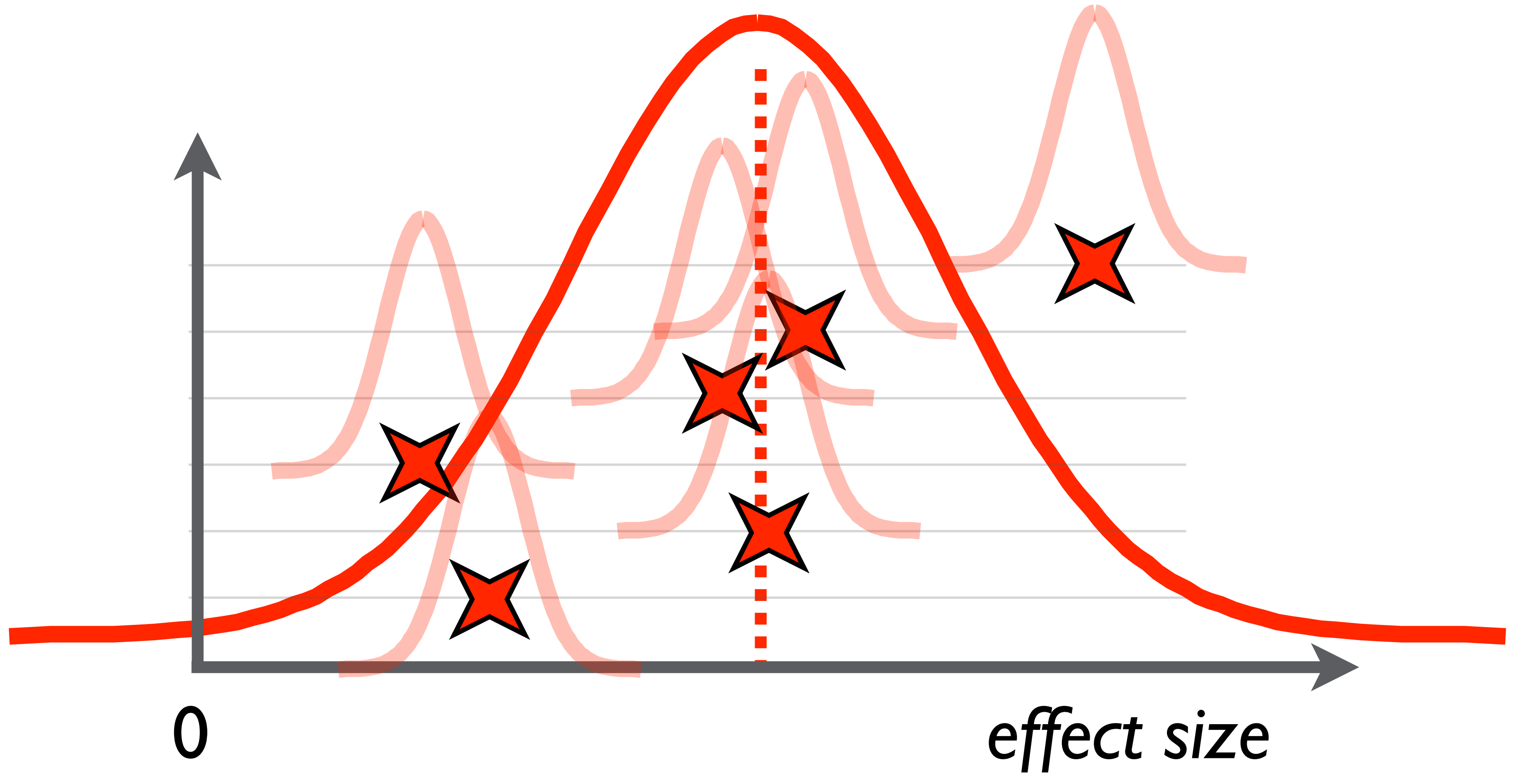
All first-level GLMs
on 6 FMRI data set



Single Group Average

Does the group activate on average?





Single Group Average

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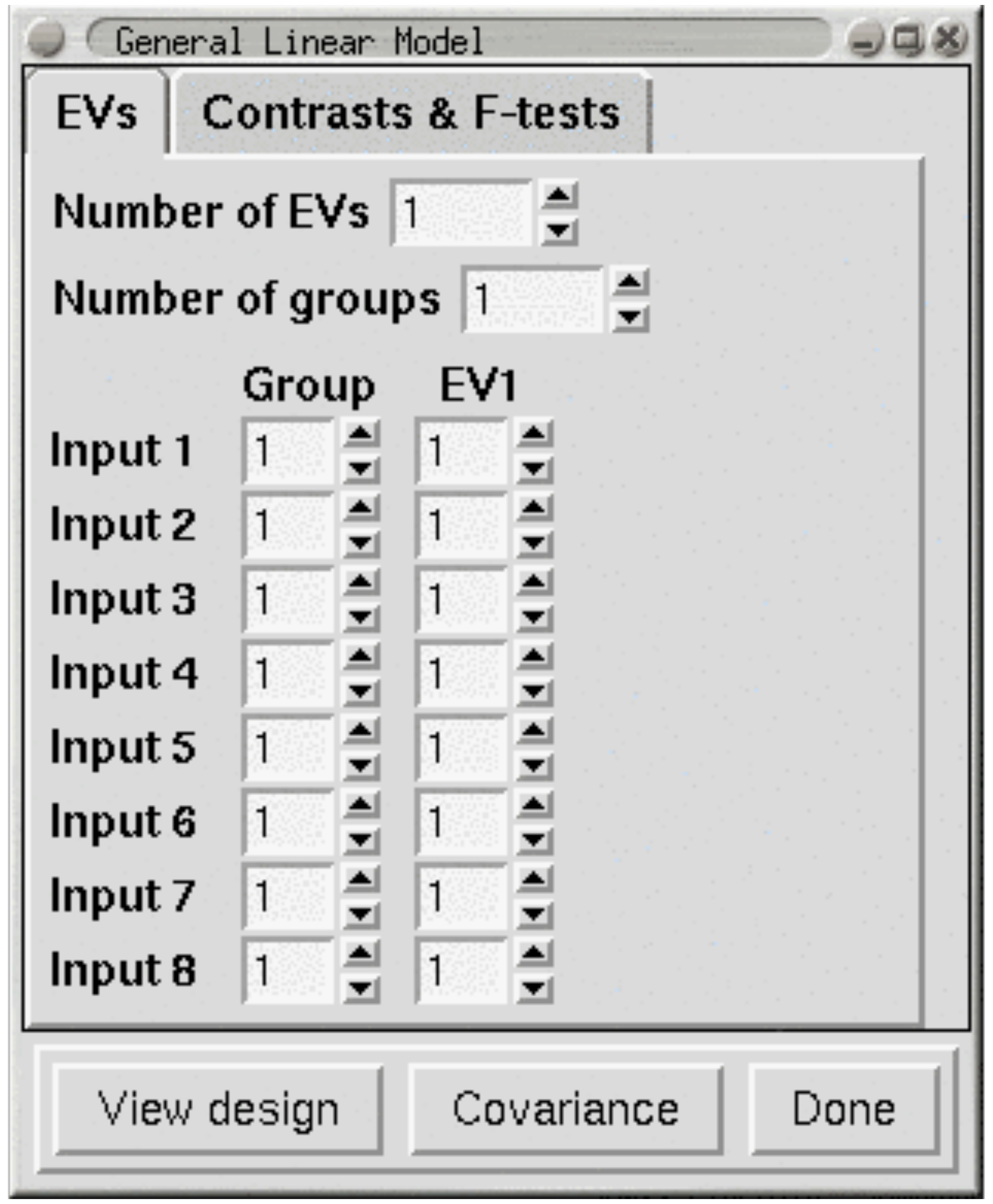
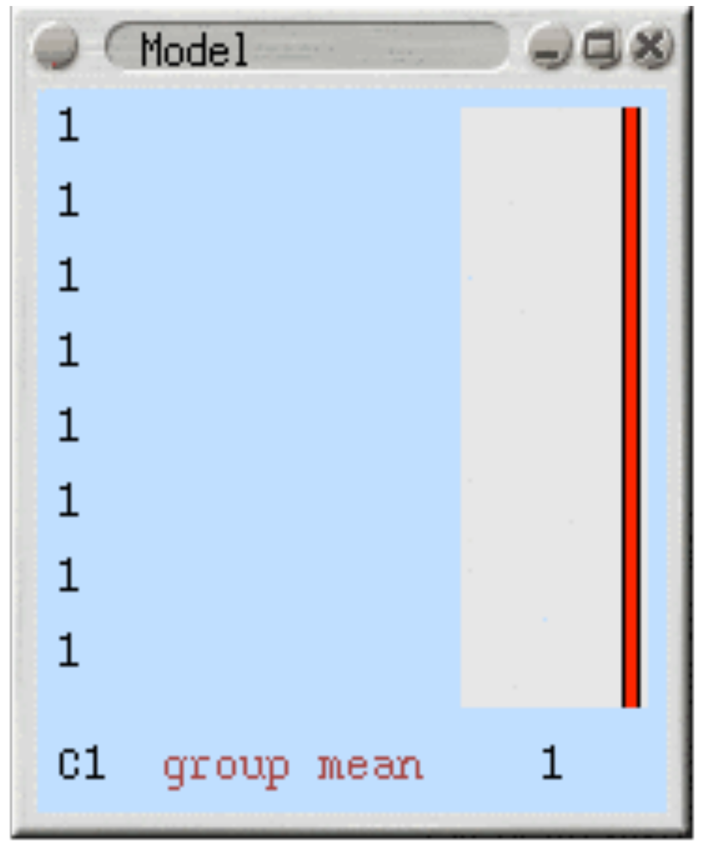
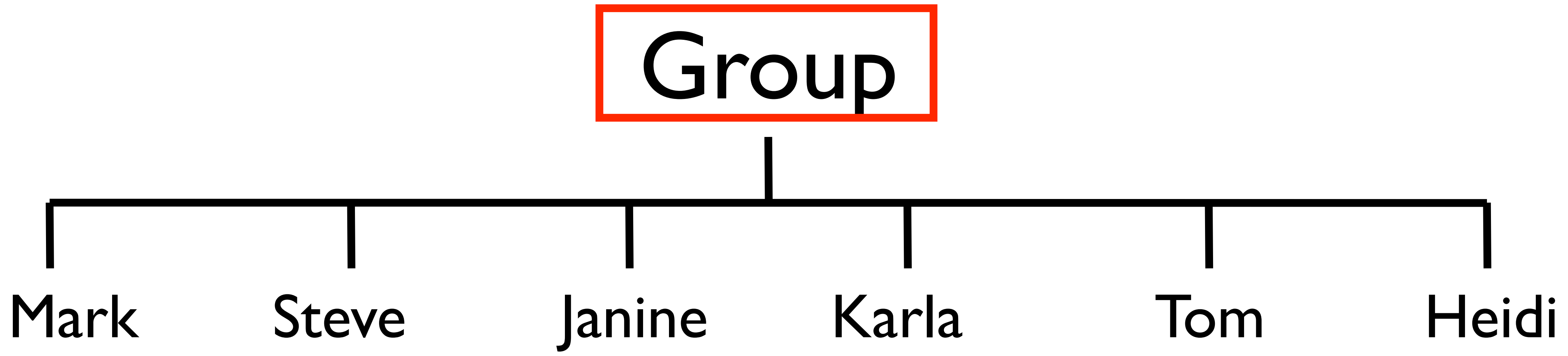




Fixed versus mixed effects

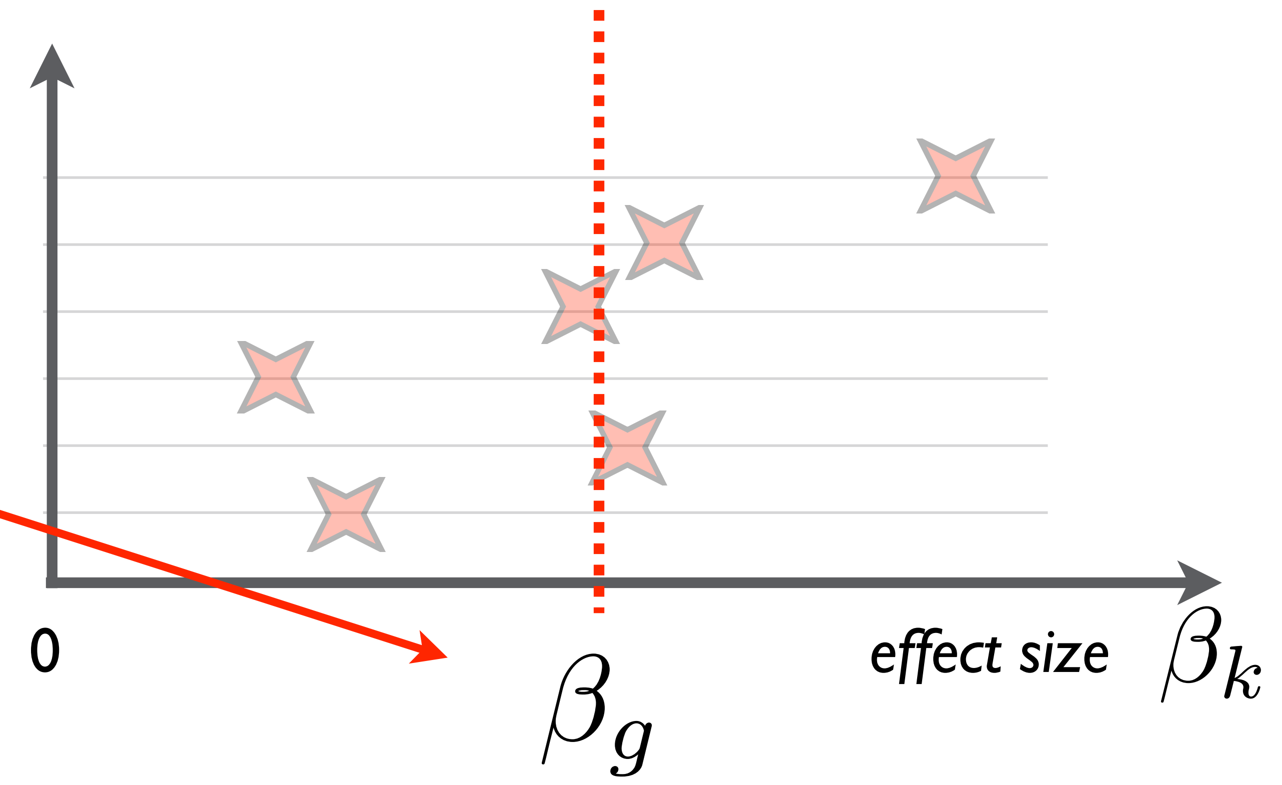
Fixed-Effects Analysis

Do these exact 6 subjects activate on average?



$$Y_K = X_K \beta_K + \epsilon_K$$
$$\beta_K = X_g \beta_g$$

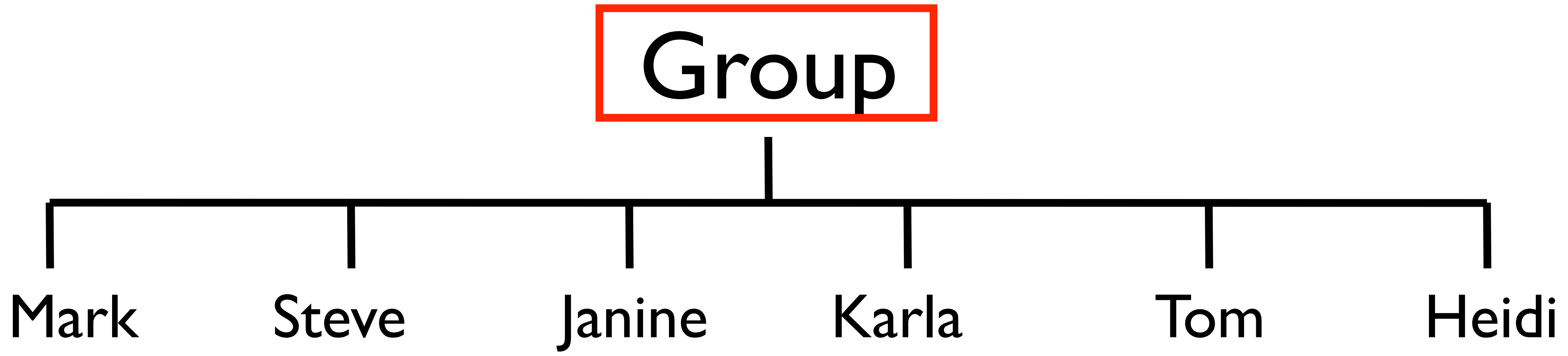
Fixed Effects Analysis:



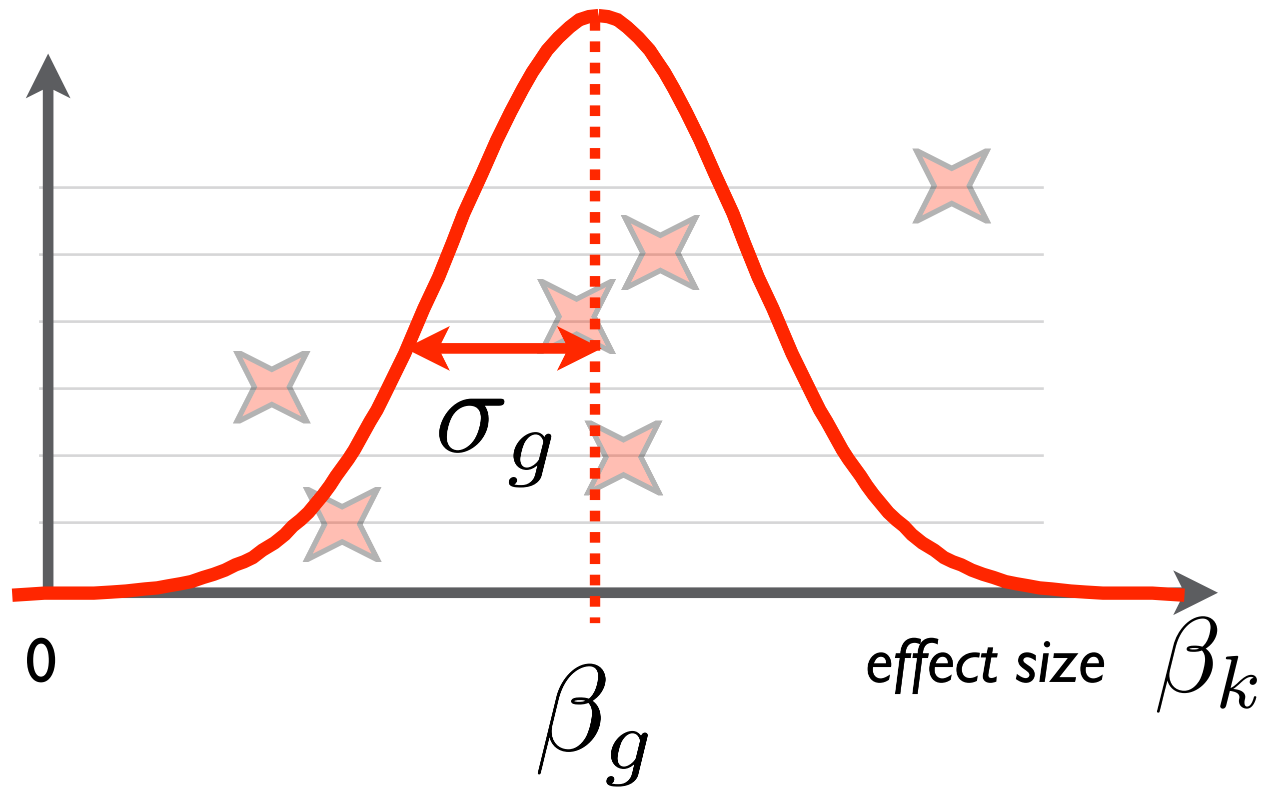
- *Consider only these 6 subjects*
  - *estimate the mean across these subject*
  - *only variance is within-subject variance*

Mixed-Effects Analysis

Does the population activate on average?



$$Y_K = X_K \beta_K + \epsilon_K$$
$$\beta_K = X_g \beta_g + \epsilon_g$$

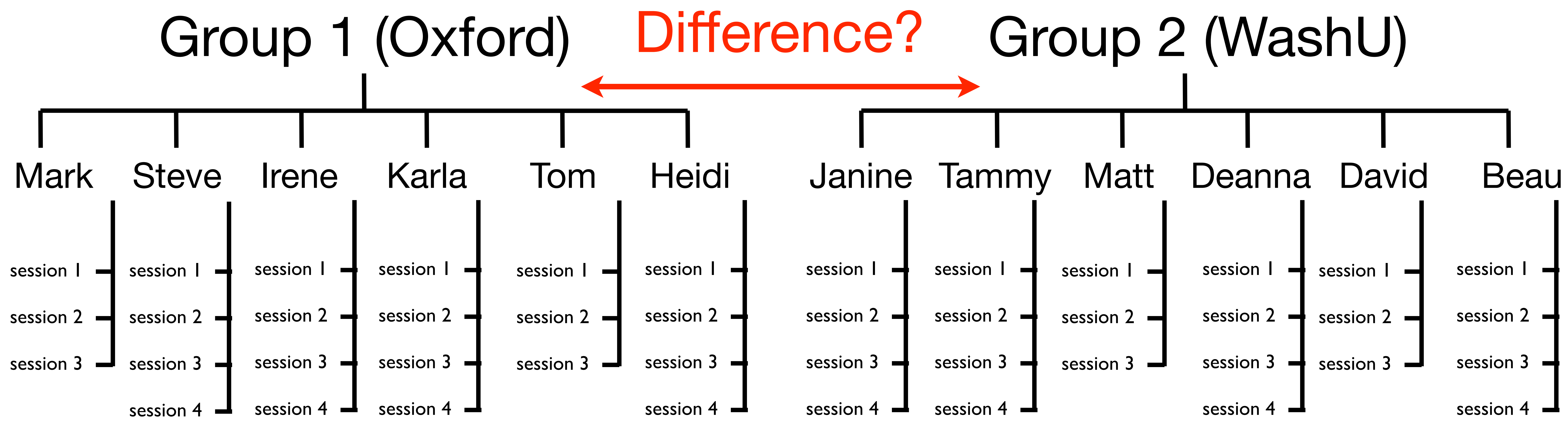


Mixed-Effects Analysis:

- *Consider the 6 subjects as samples from a wider population*
  - *estimate the mean across the population*
  - *between-subject variance accounts for random sampling*

Multiple sessions per subject

All-in-One Approach

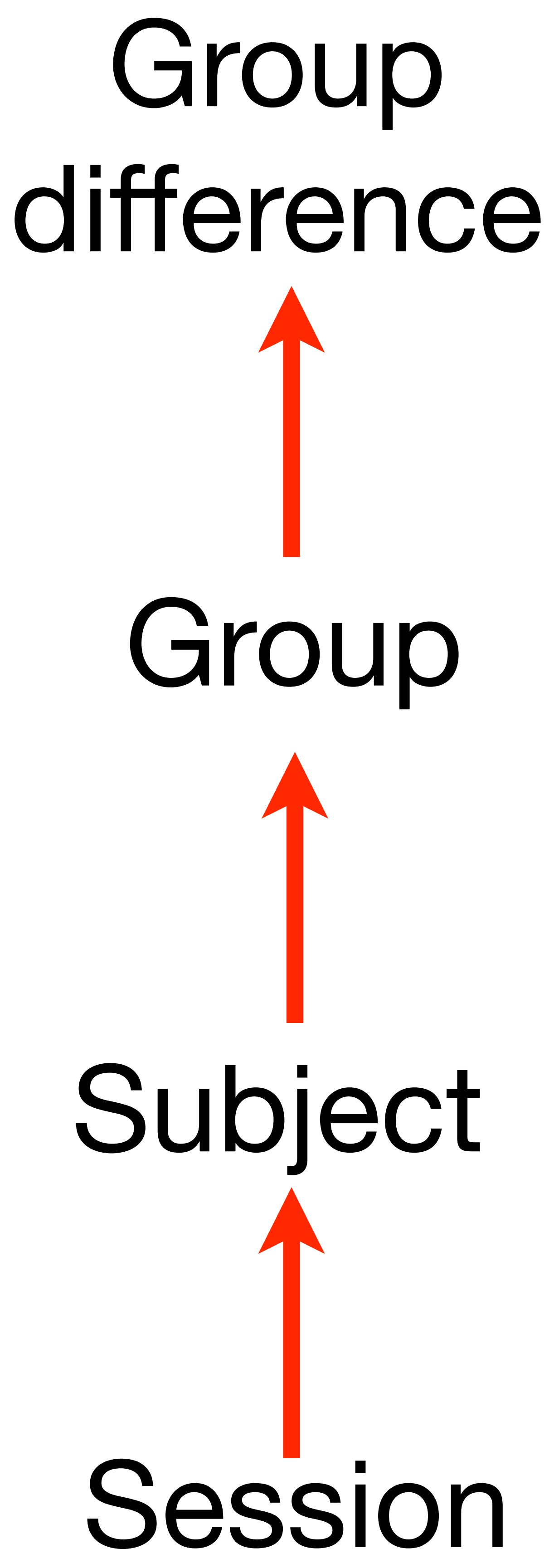


- Could use one (huge) GLM to infer group difference
  - difficult to ask sub-questions in isolation
  - computationally demanding
  - need to process again when new data is acquired

Summary Statistics Approach

In FEAT estimate levels one stage at a time

- At each level:
  - Inputs are summary stats from levels below (or FMRI data at the lowest level)
  - Outputs are summary stats or statistic maps for inference
- Need to ensure formal equivalence between different approaches!

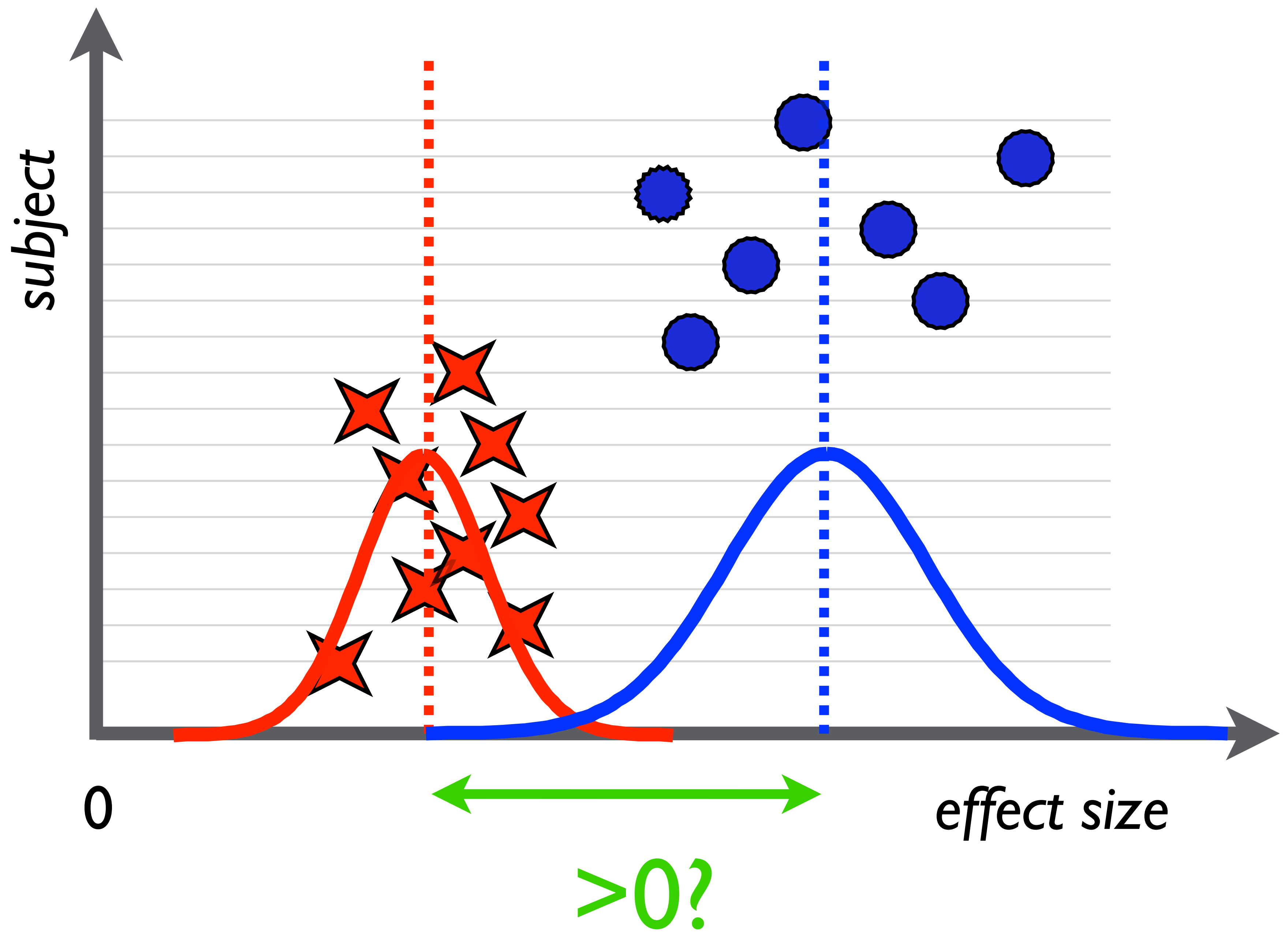


Unpaired Two-Group Difference

- We have two groups (e.g. 9 WashU, 7 Oxford) with different between-subject variance

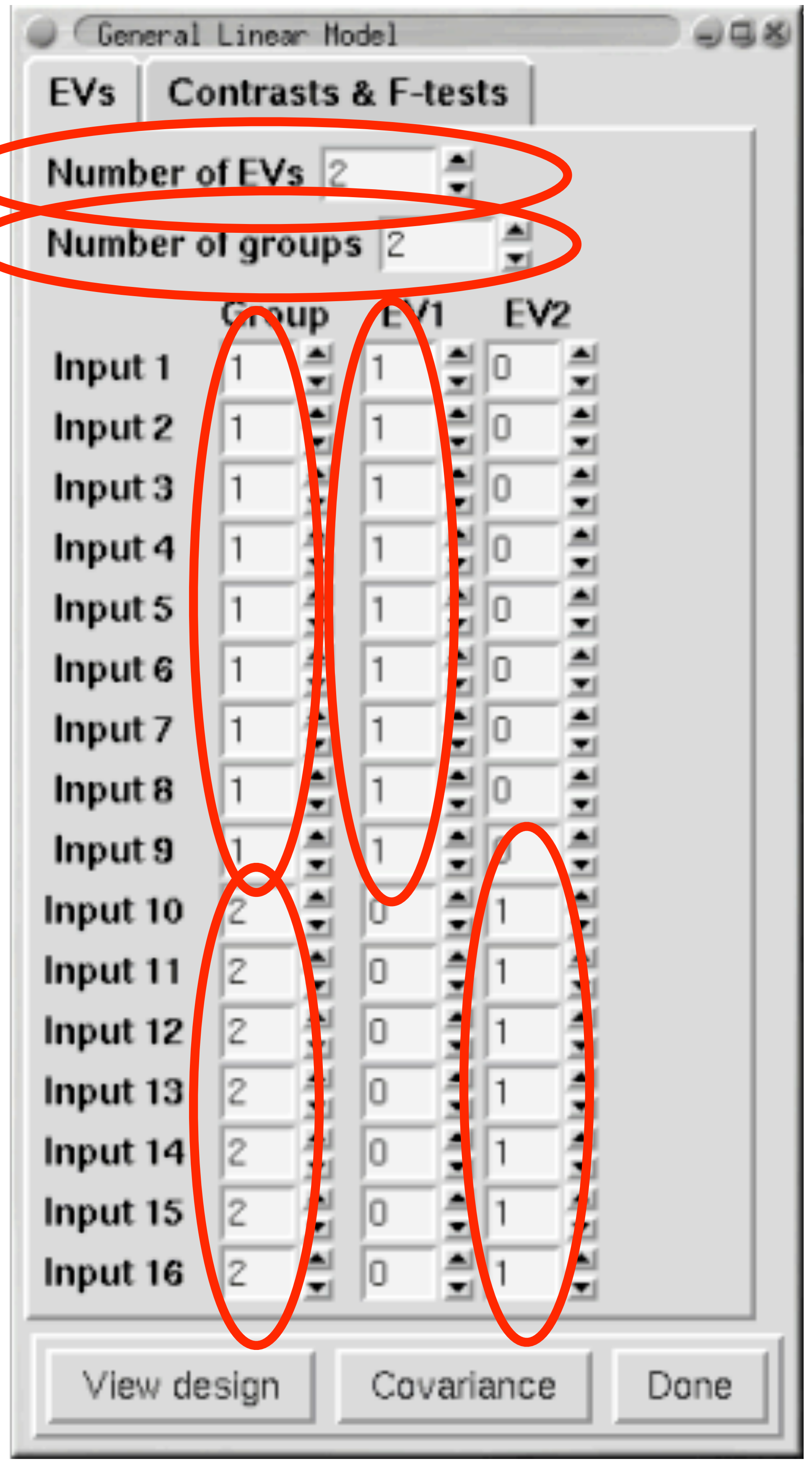
  Is there a significant group difference?

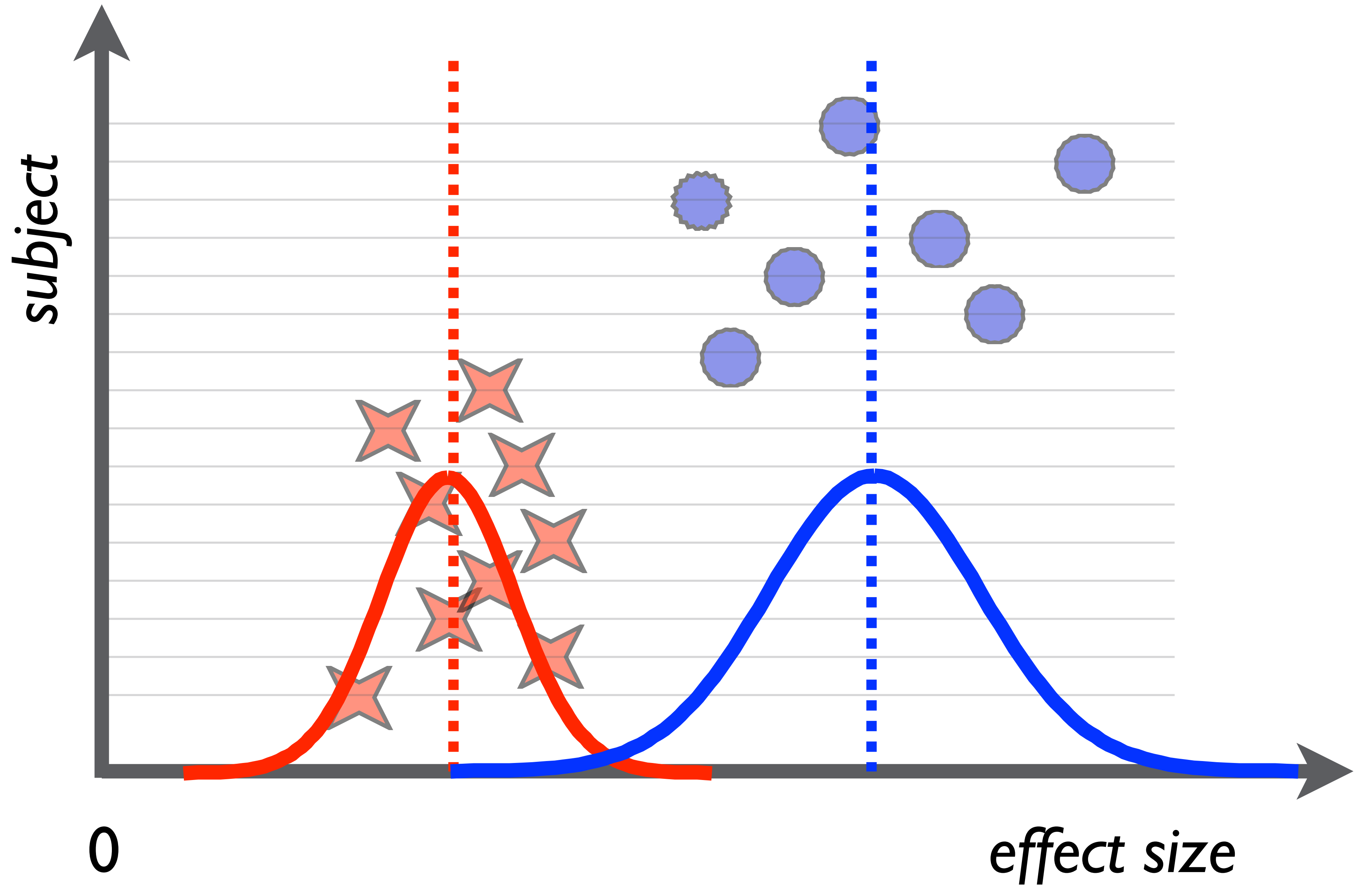
- estimate means
- estimate std-errors (FE or ME)
- test significance of difference in means



Unpaired Two-Group Difference

Is there a significant group difference?





Unpaired Two-Group Difference

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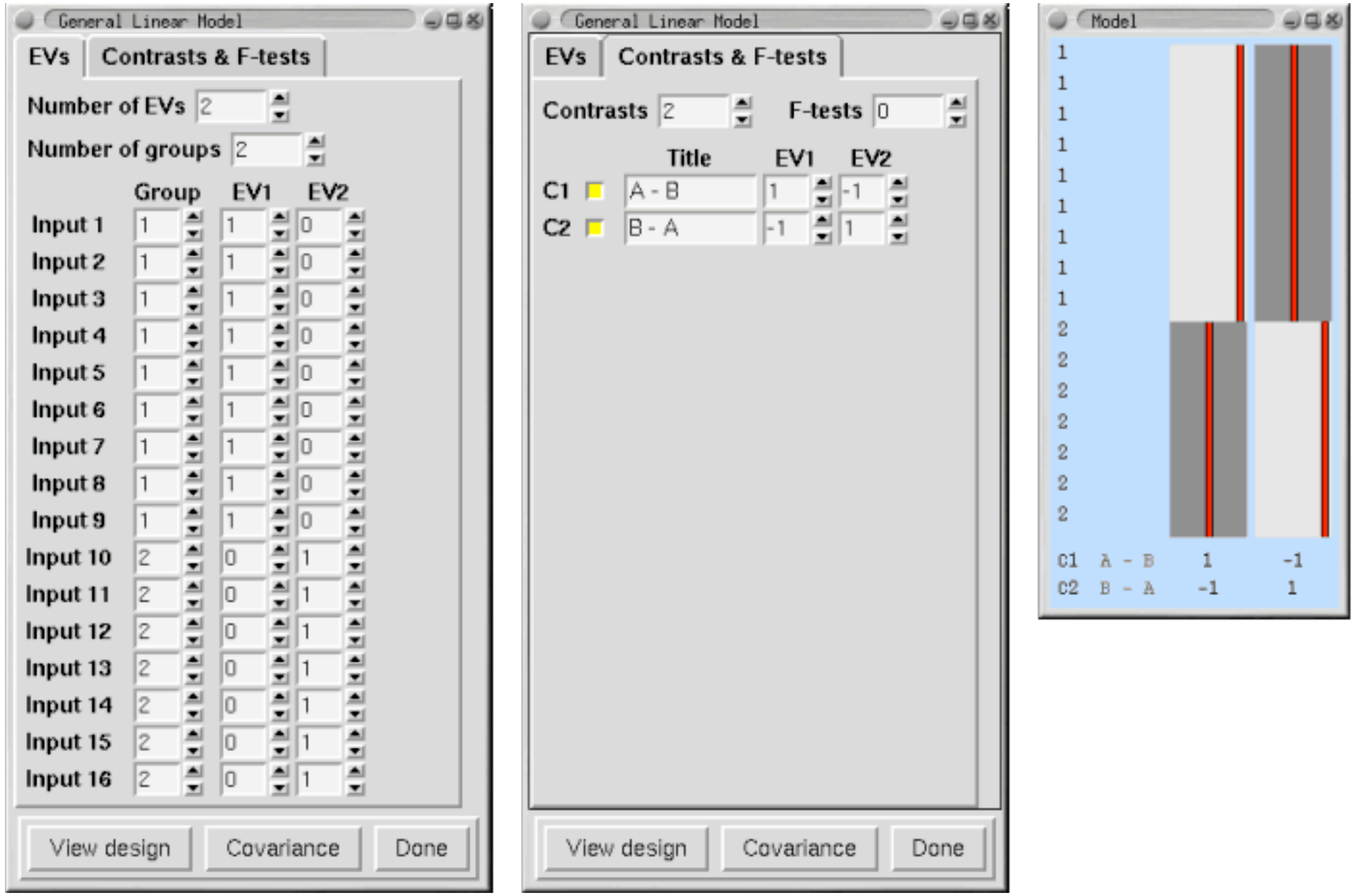
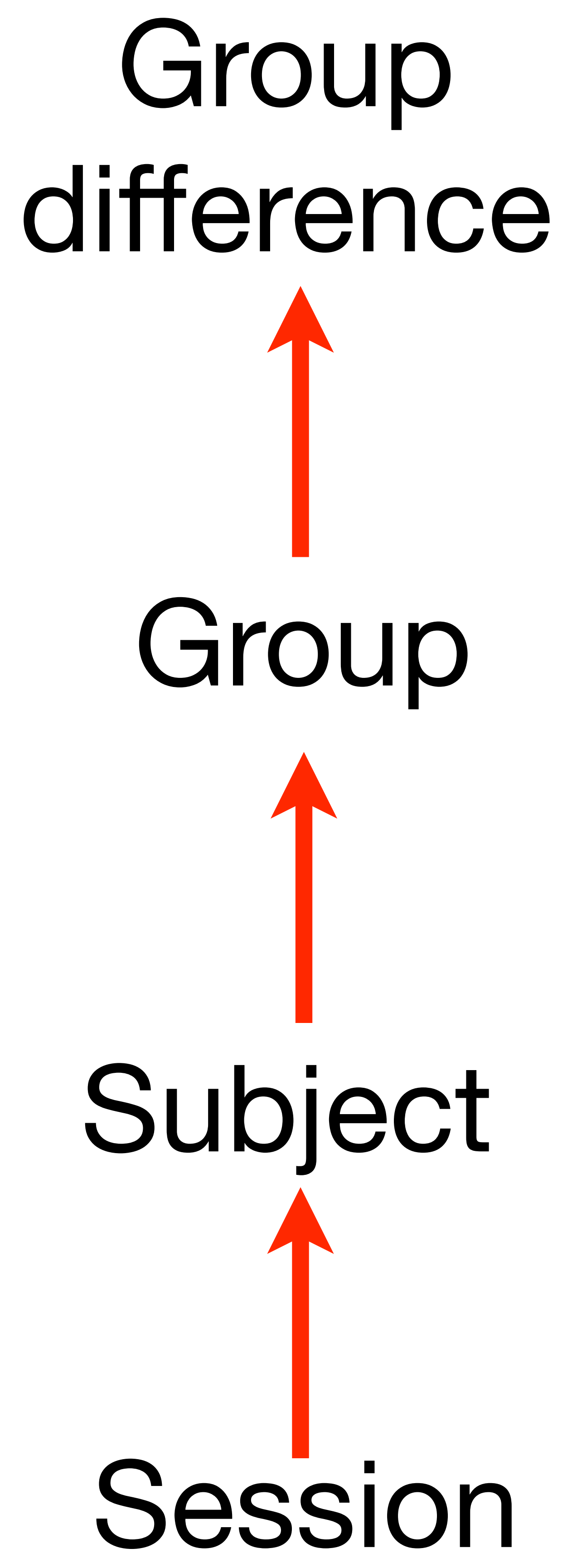


FLAME

FMRIB's Local Analysis of Mixed Effects

- Fully Bayesian framework
  - Input COPES, VARCOPES & DOFs from lower-level
  - estimate COPES, VARCOPES & DOFs at current level
  - pass these up
- Infer and threshold at top level (Z-stat)
- Equivalent to All-in-One approach



FLAME Inference

- Default is:
  - FLAME1: fast approximation for all voxels
- Optional slower, slightly more accurate approach:
  - FLAME1+2:
    - FLAME1 for all voxels, FLAME2 for voxels close to threshold
    - FLAME2: MCMC sampling technique

Choosing Inference Approach

1. Fixed Effects

   Use for intermediate/top levels

2. Mixed Effects - OLS

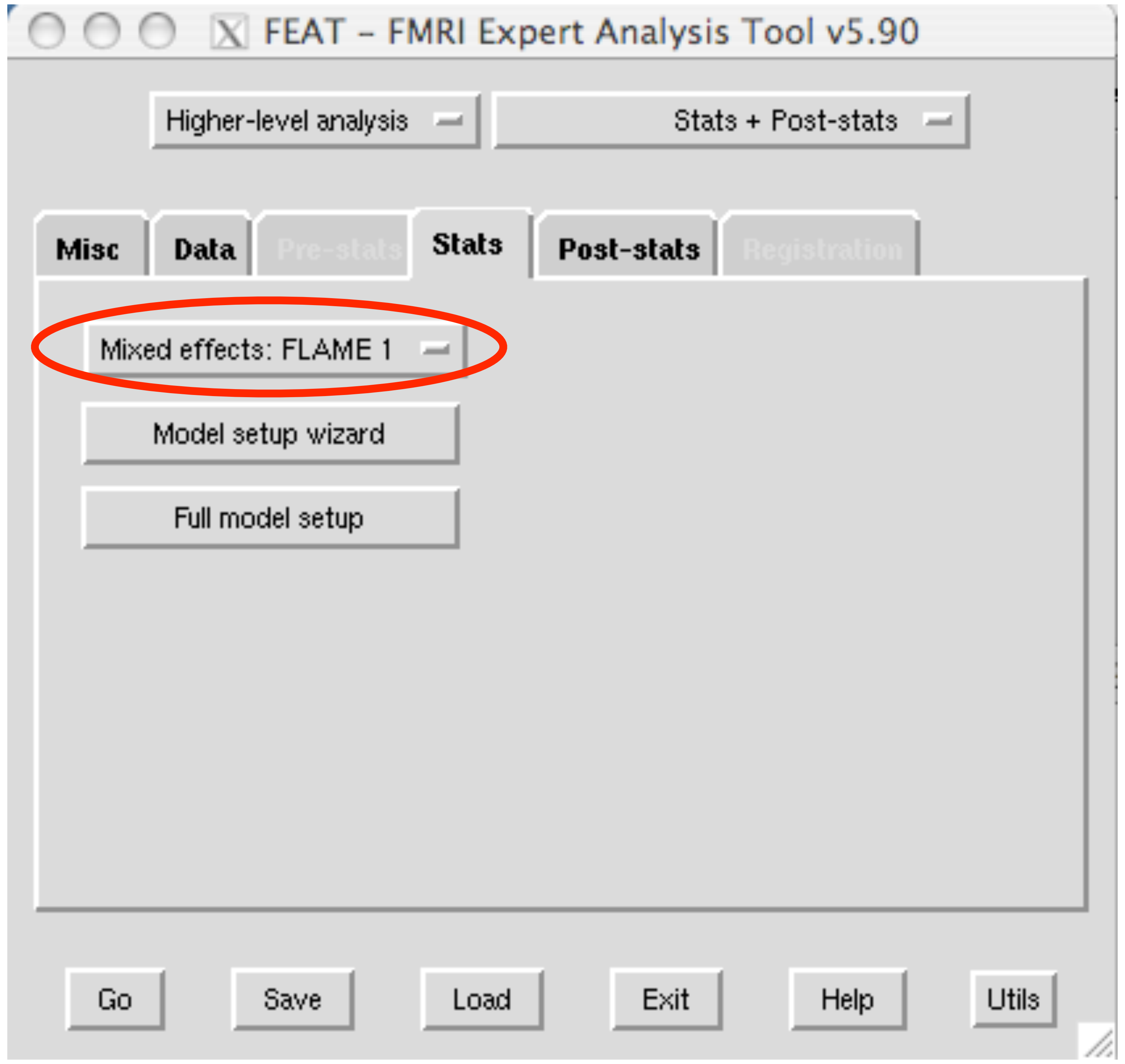
   Use at top level: quick and less accurate

3. Mixed Effects - FLAME 1

   Use at top level: less quick but more accurate

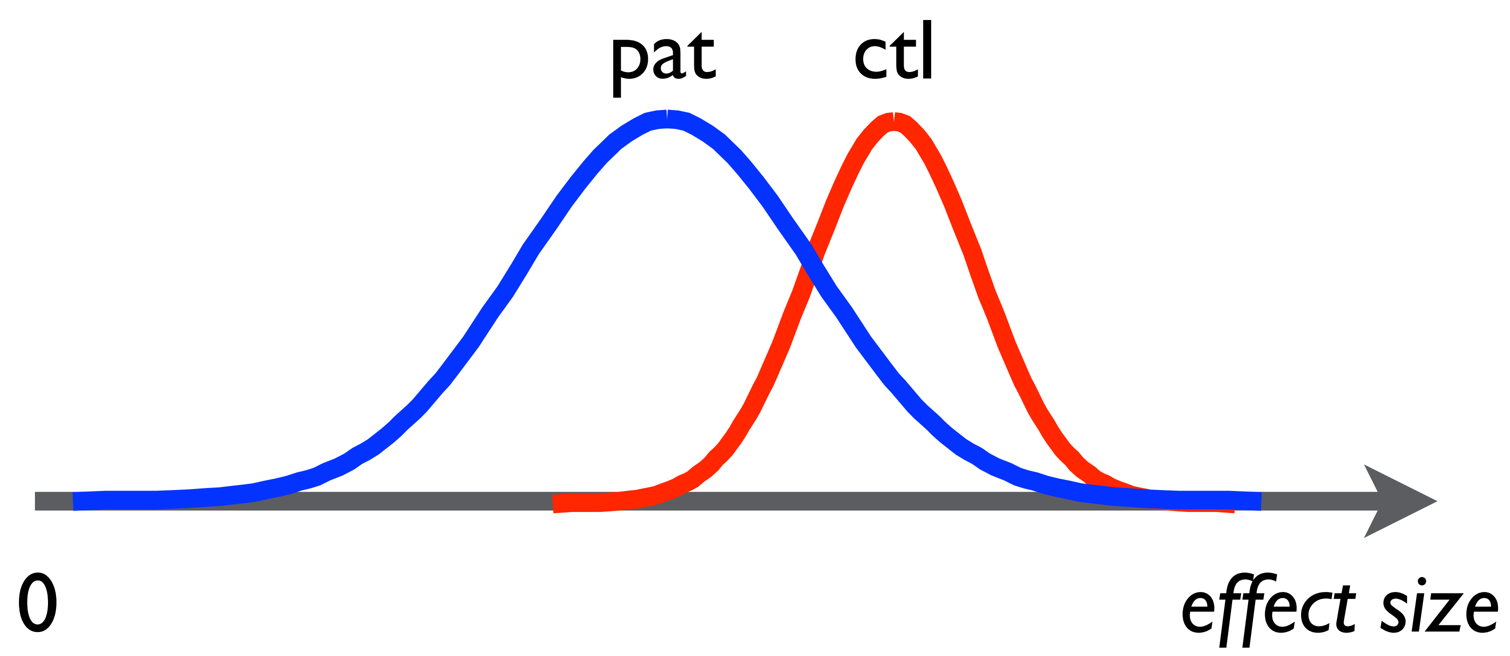
4. Mixed Effects - FLAME 1+2

   Use at top level: slow but even more accurate

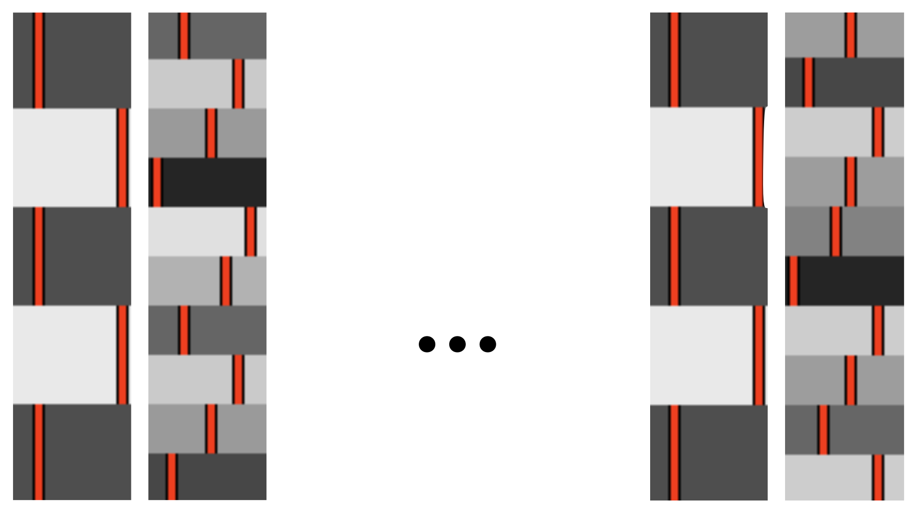


FLAME vs. OLS

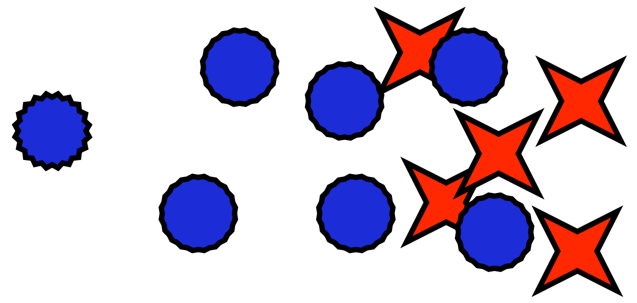
- allow different within-level variances (e.g. patients vs. controls)



- allow non-balanced designs (e.g. containing behavioral scores)

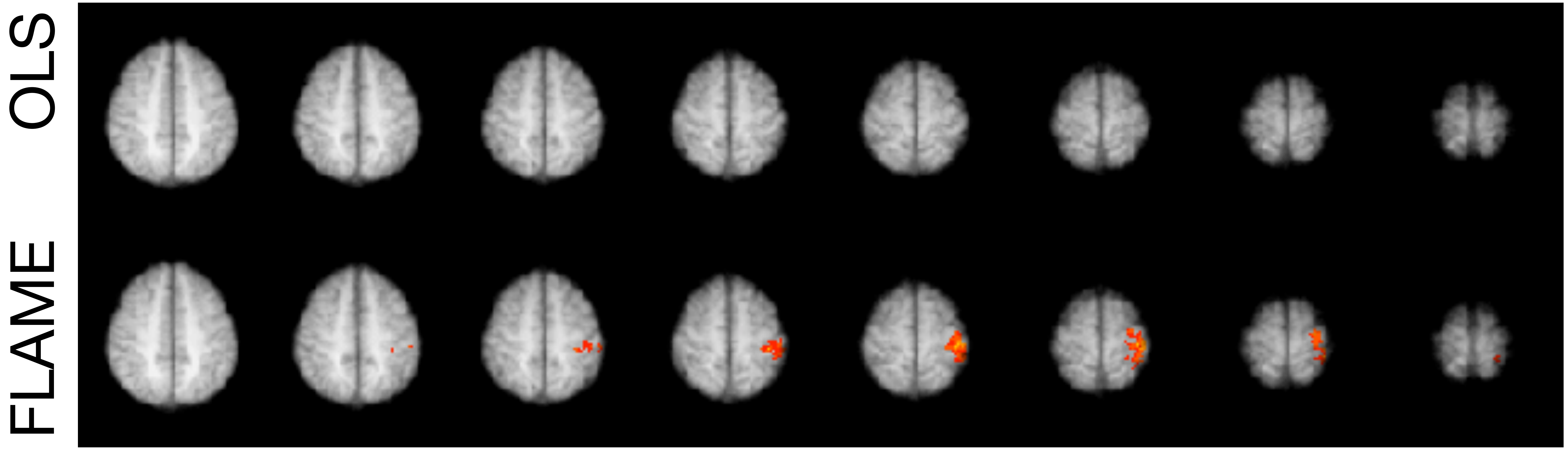


- allow un-equal group sizes



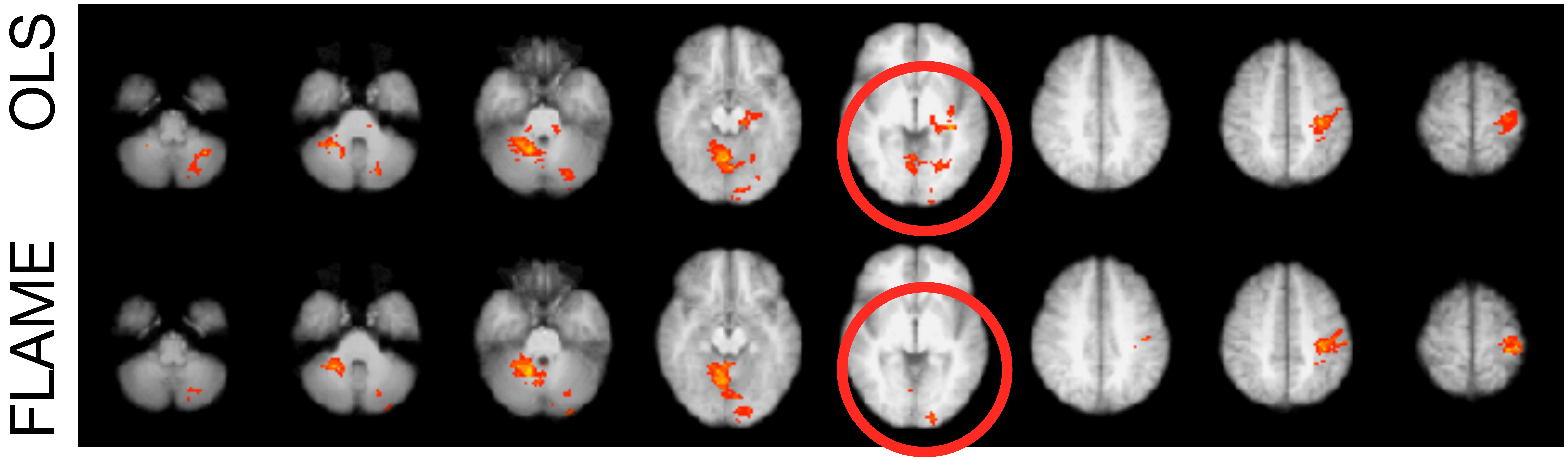
FLAME vs. OLS

- Two ways in which FLAME can give different Z-stats compared to OLS:
  - *higher Z* due to increased efficiency from using lower-level variance heterogeneity

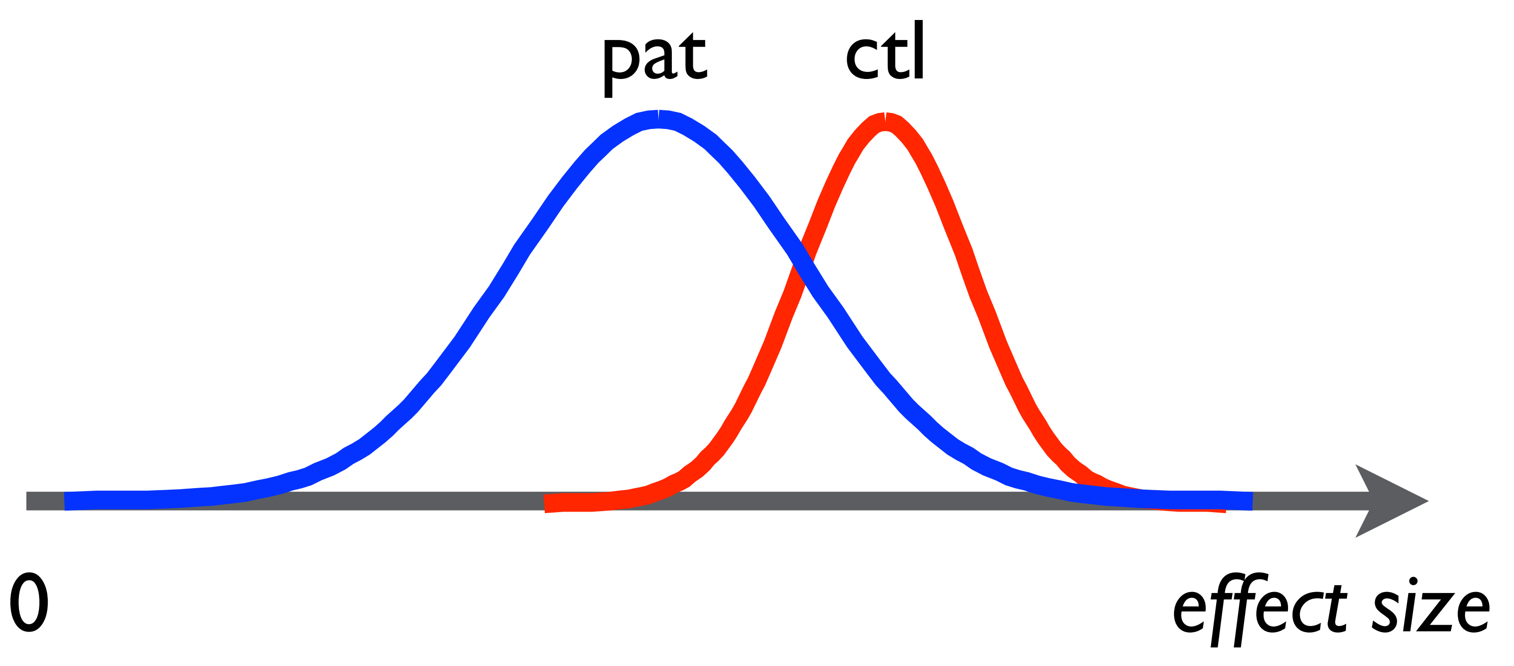


FLAME vs. OLS

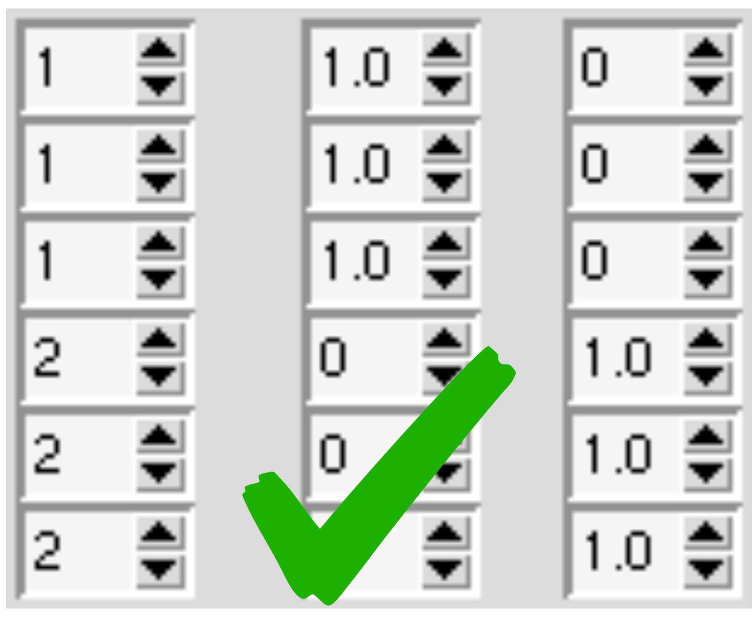
- Two ways in which FLAME can give different Z-stats compared to OLS:
  - *Lower Z* due to higher-level variance being constrained to be positive (i.e. solve the implied negative variance problem)

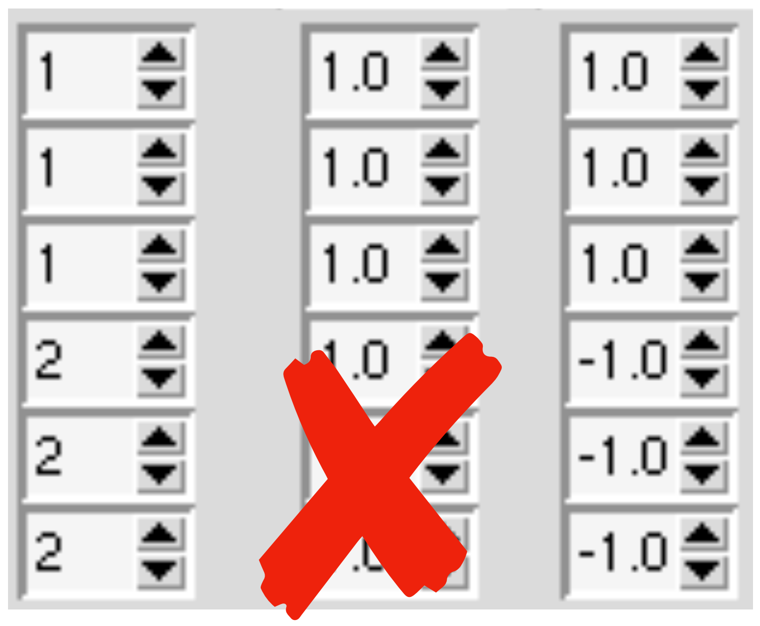


Multiple Group Variances



- can deal with multiple group variances
- separate variance will be estimated for each variance group (be aware of #observations for each estimate, though!)
- EVs can only have non-zero values for a single group



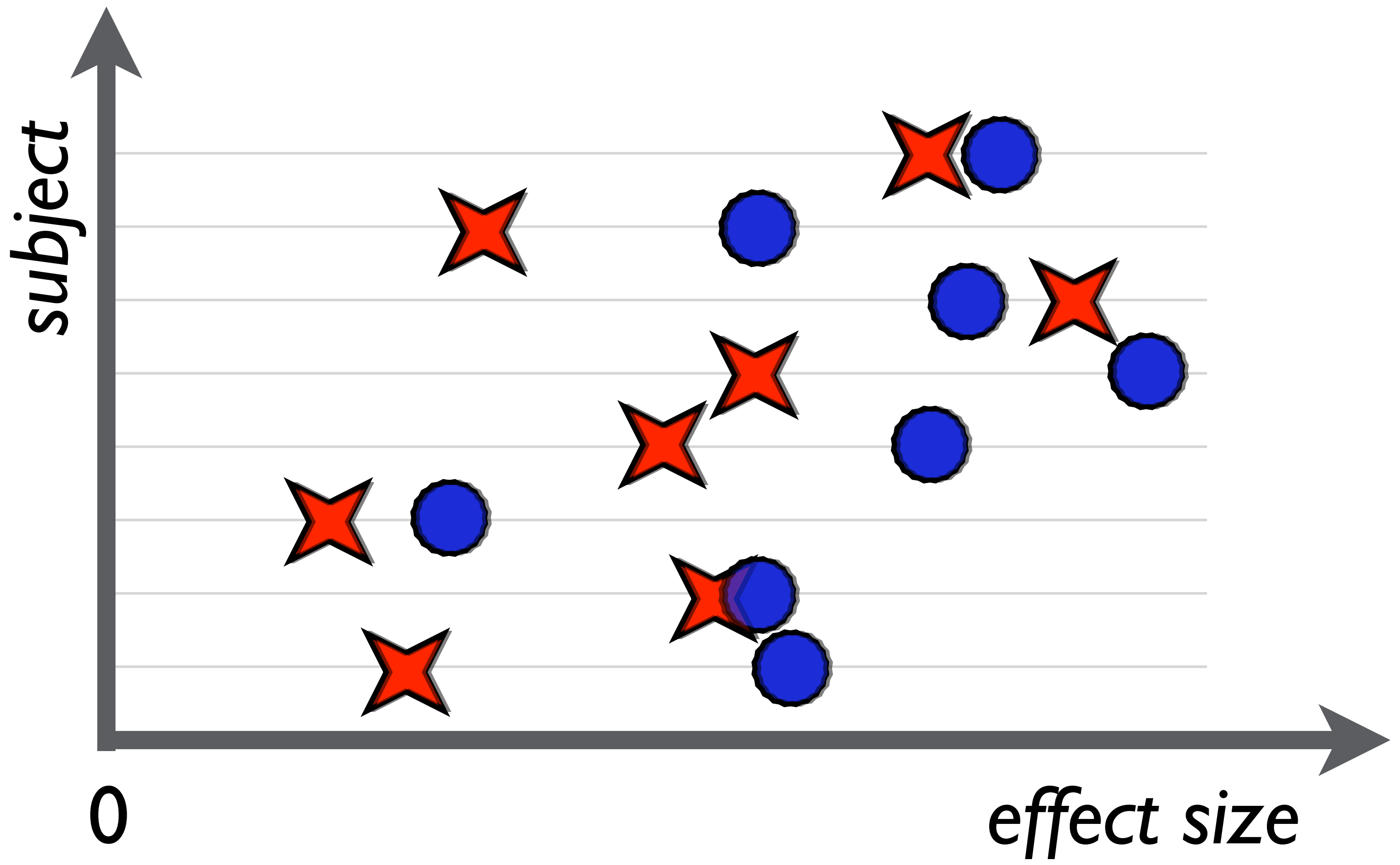


Paired T-test

Paired T-Test

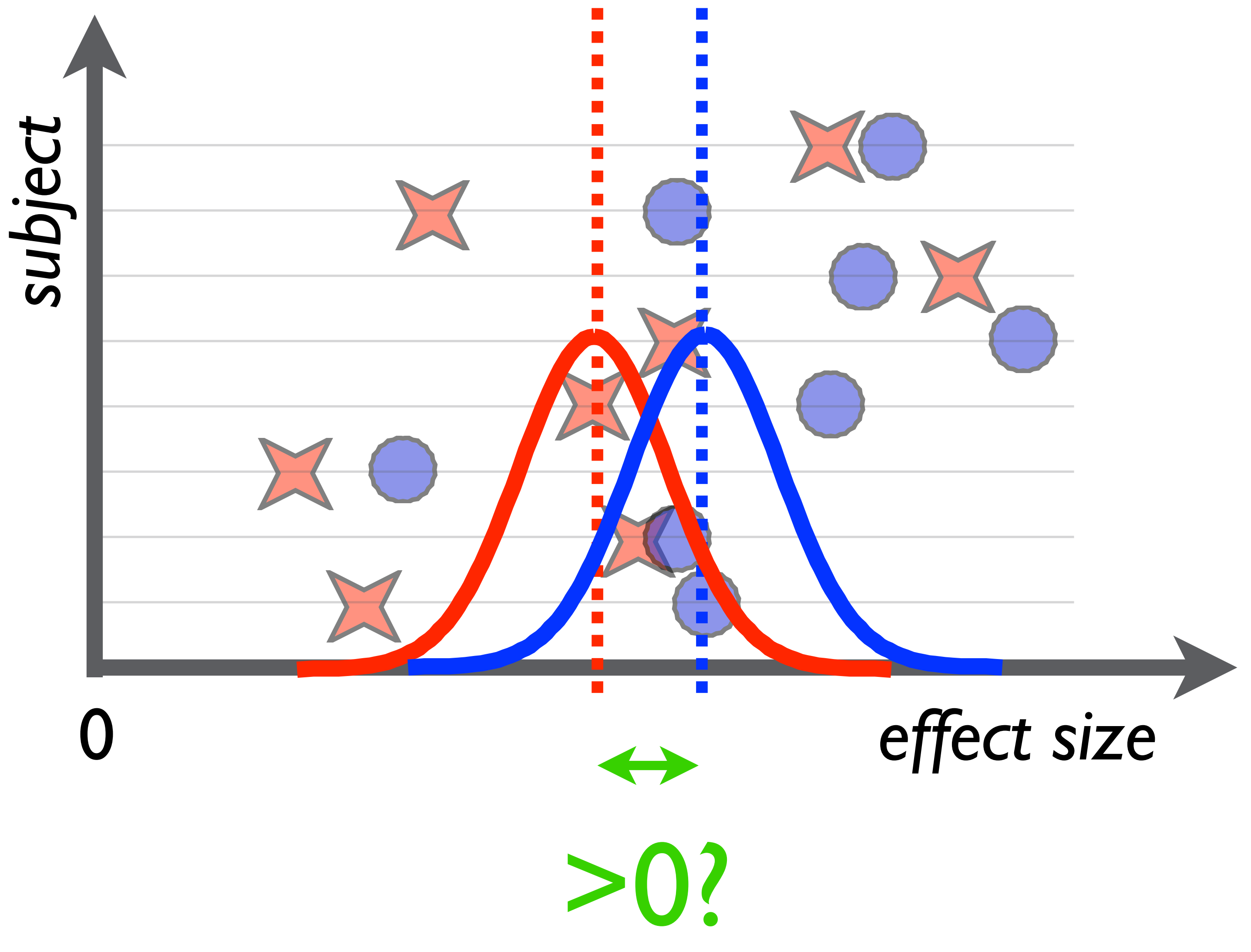
- 8 subjects scanned under 2 conditions (A,B)

  Is there a significant difference between conditions?



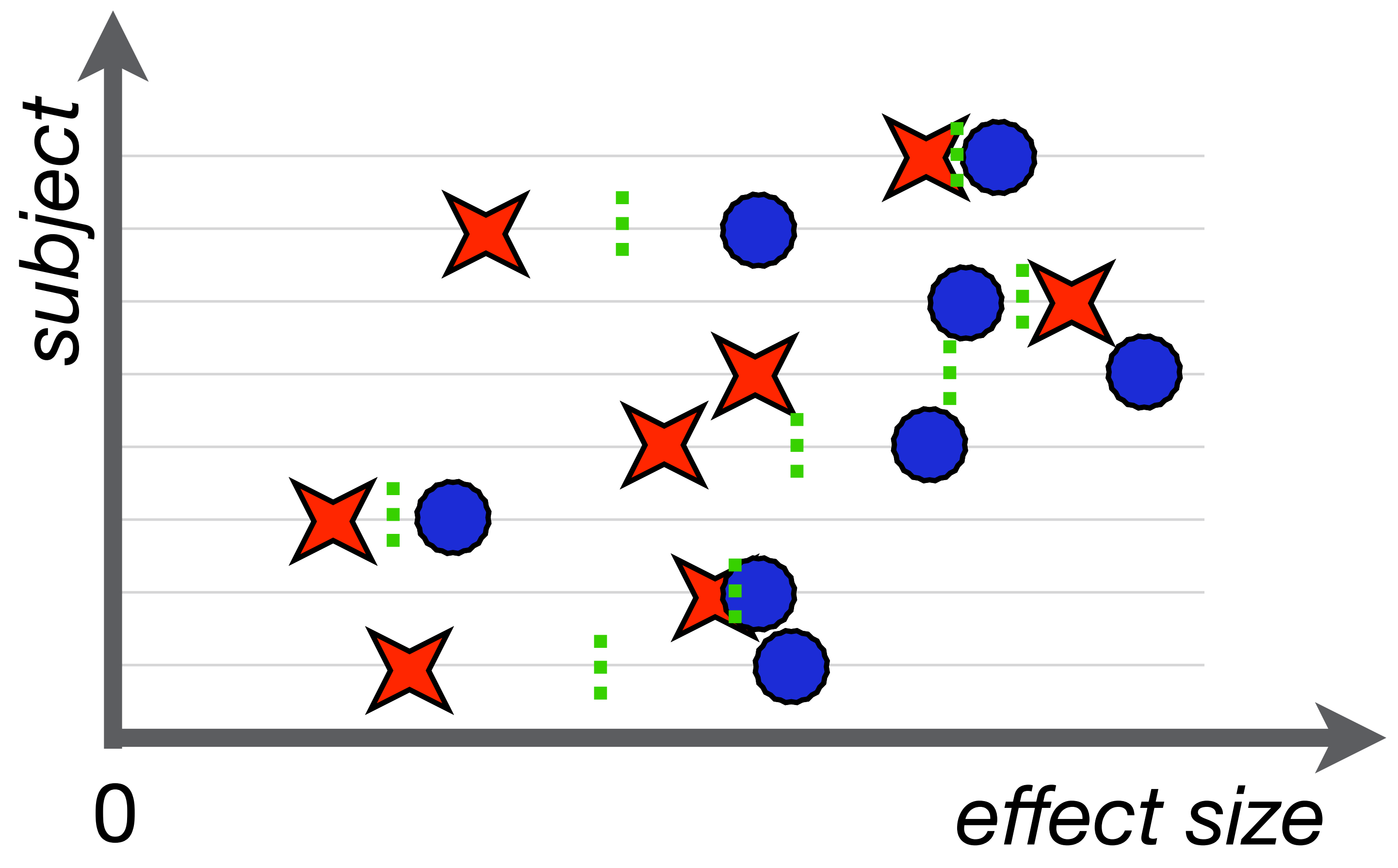
Paired T-Test

First, let's try an unpaired T-test



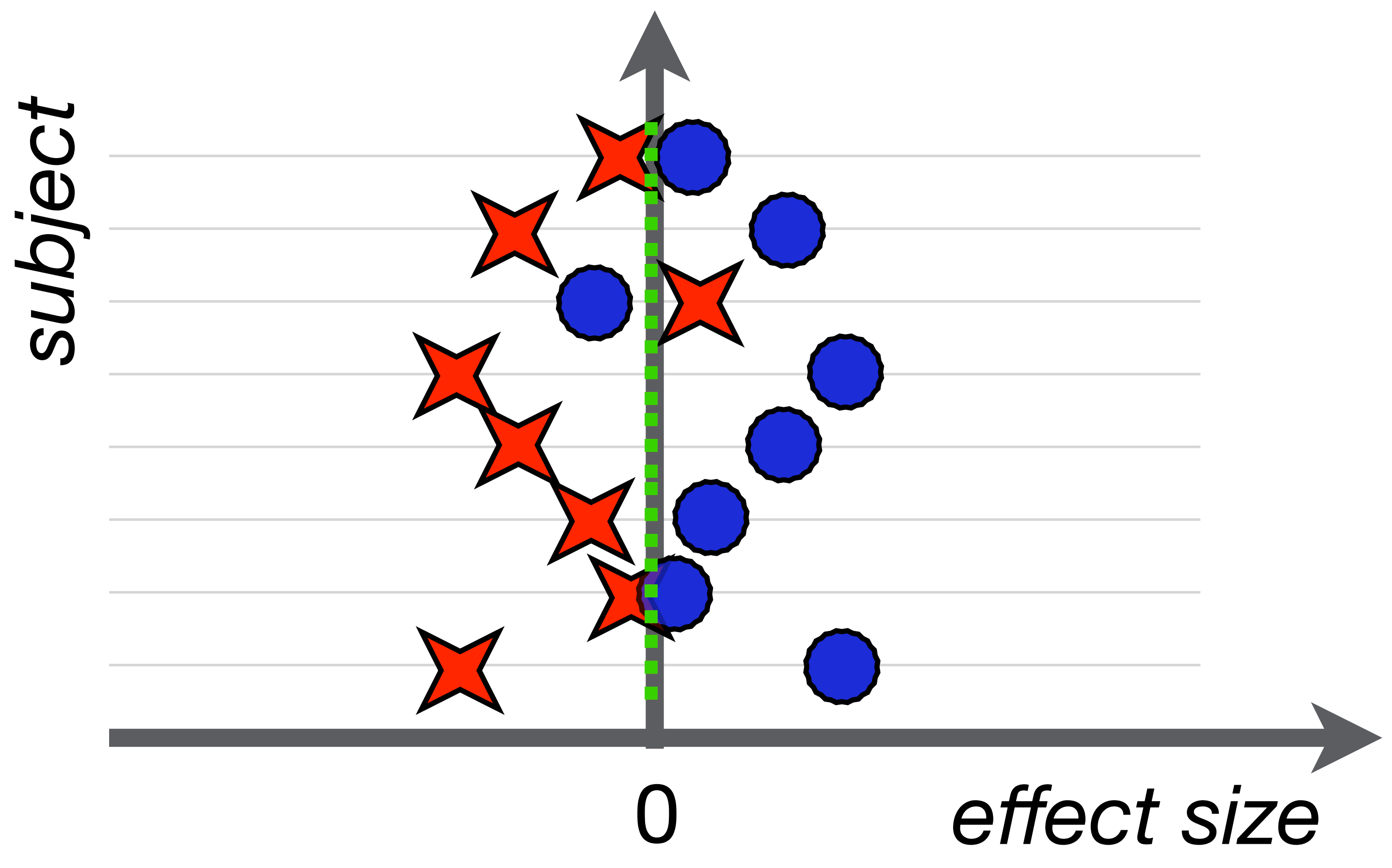
Paired T-Test

data

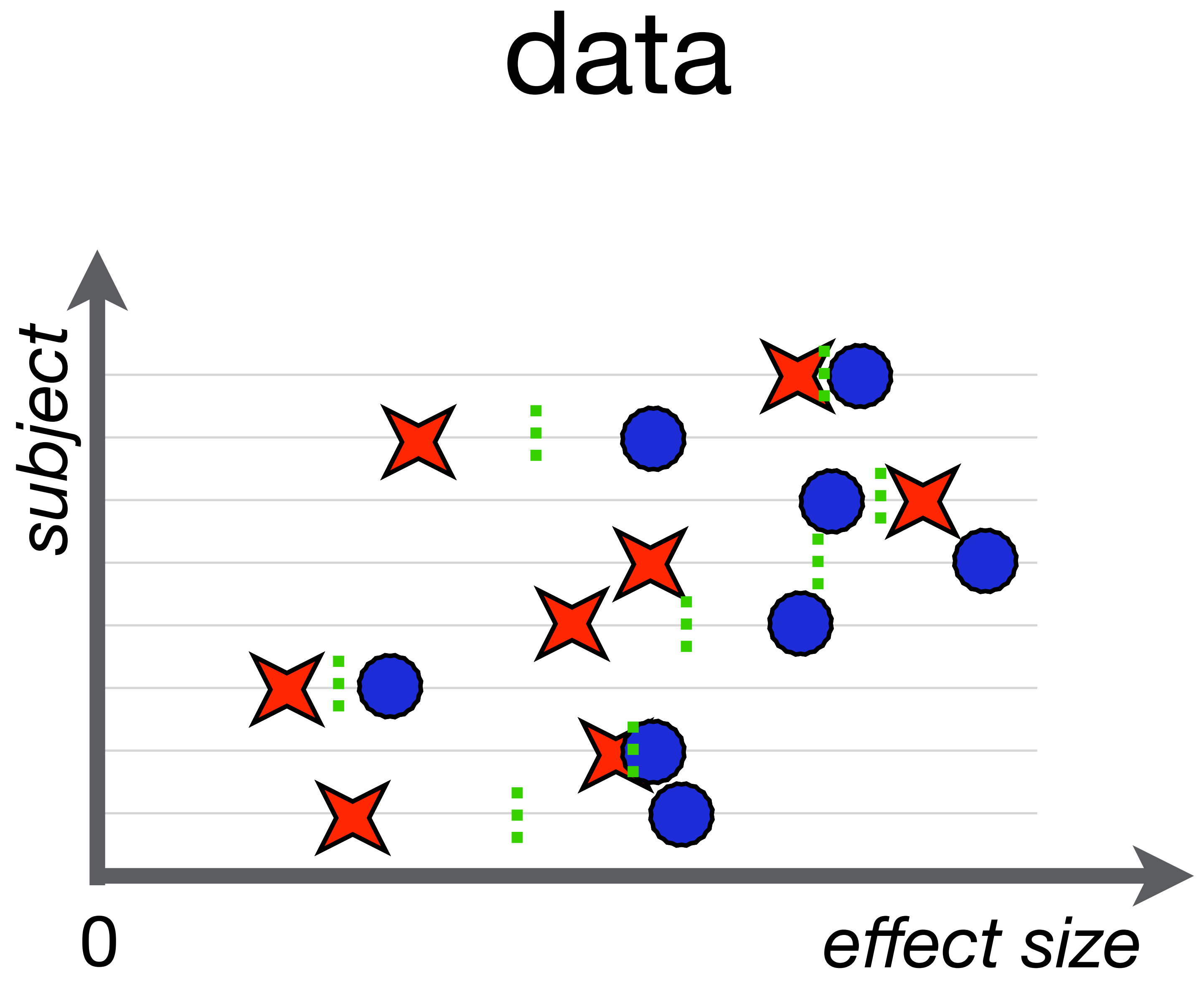


subject mean
accounts for large prop.
of the overall variance

de-meaned data



Paired T-Test



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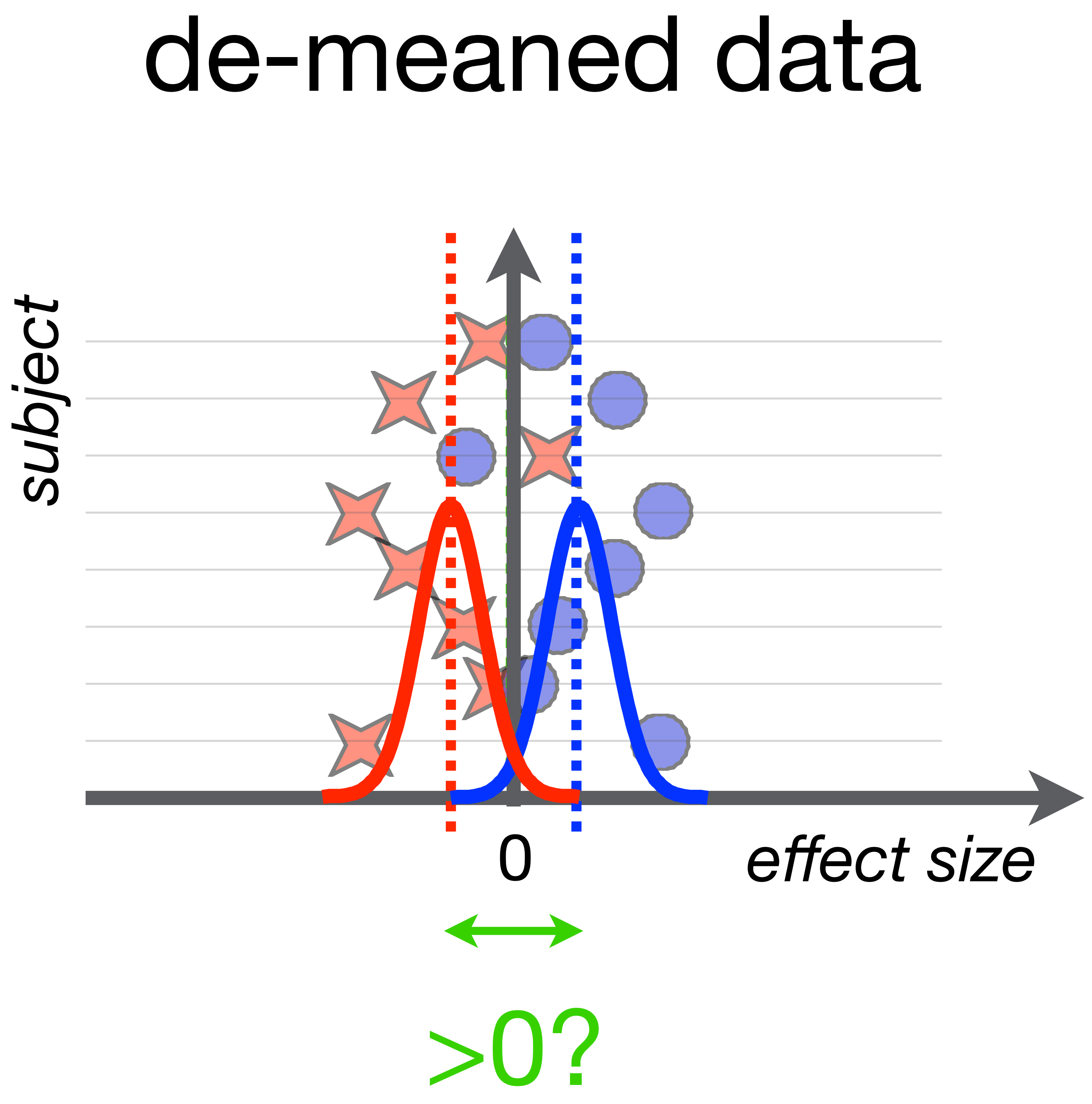
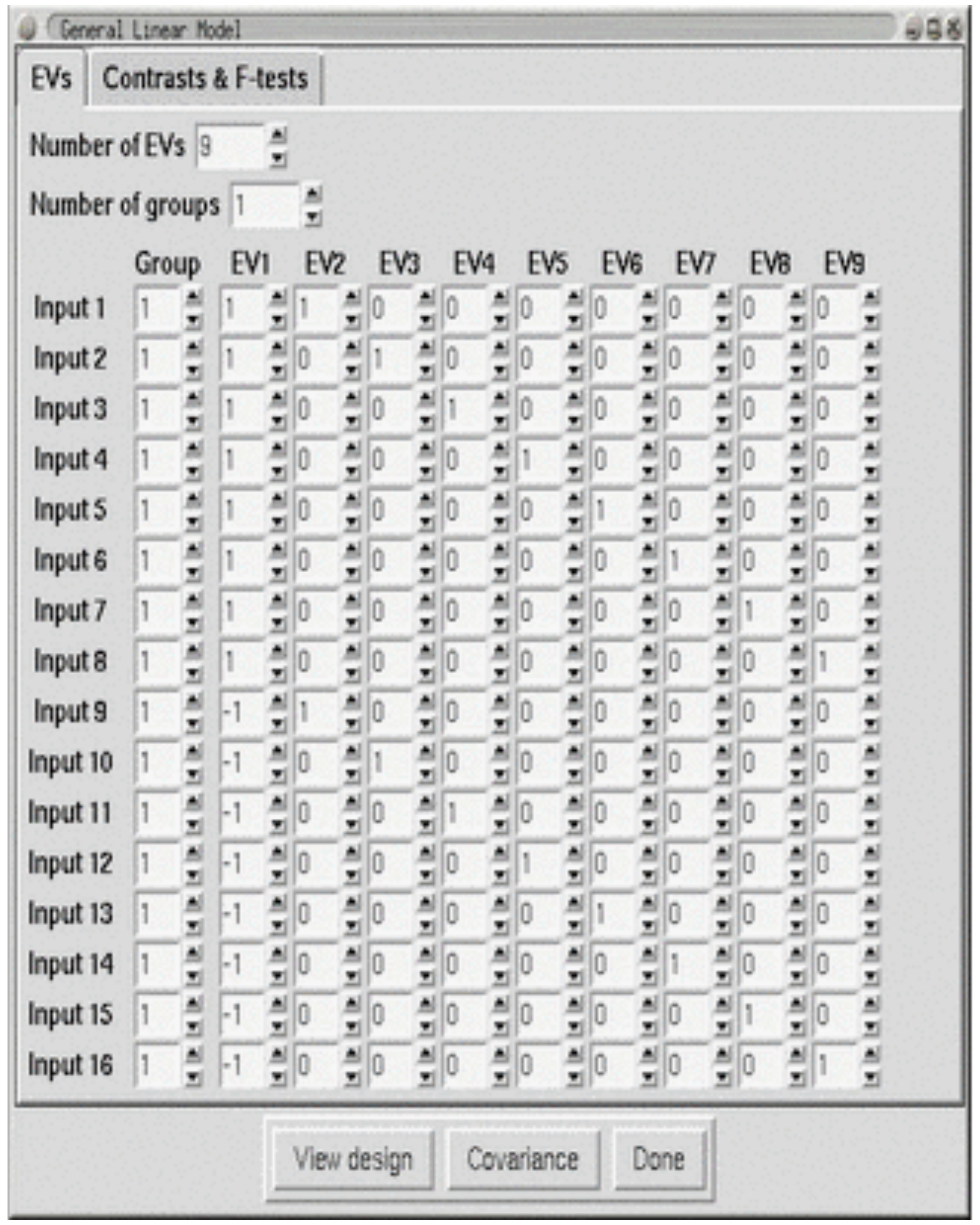
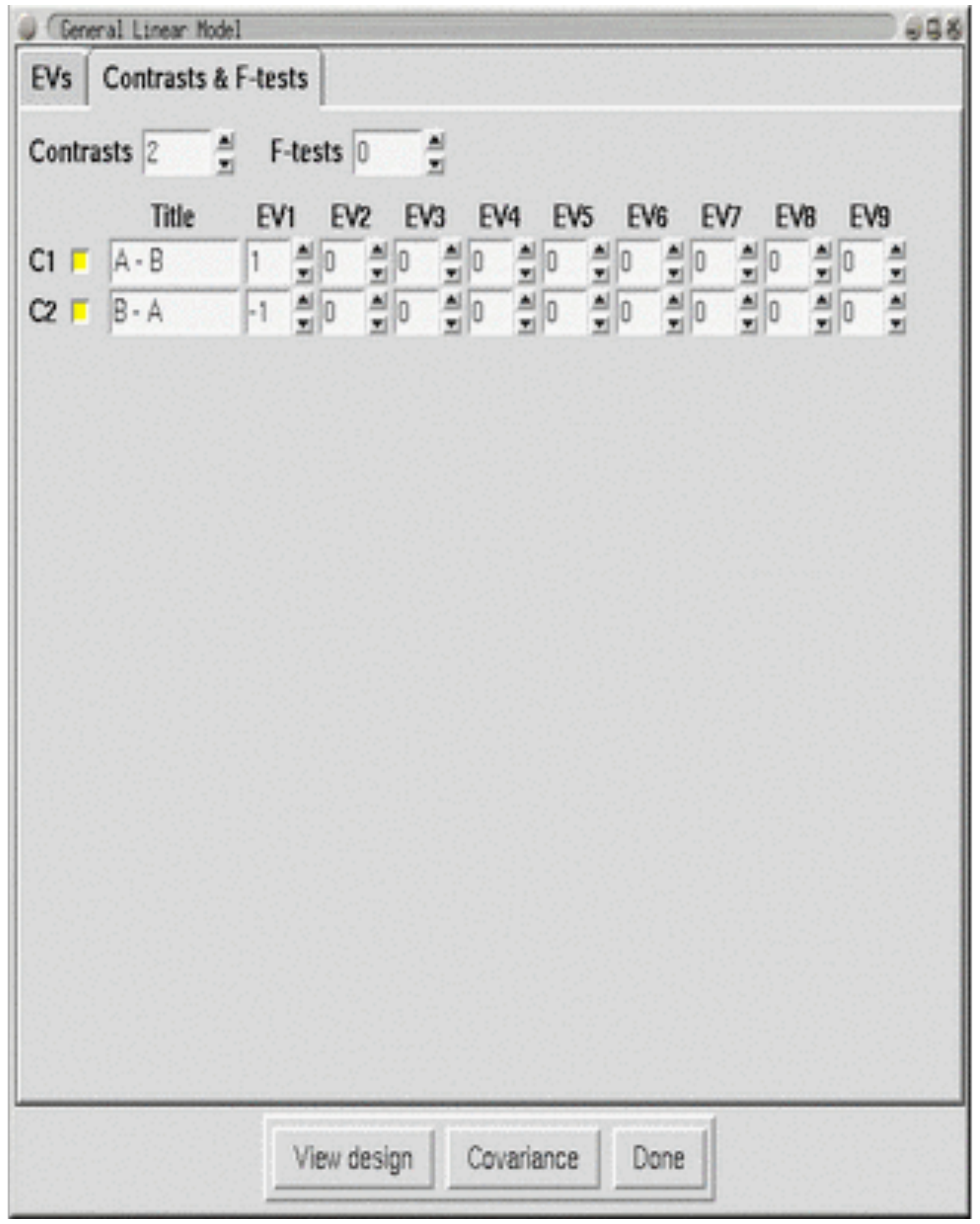
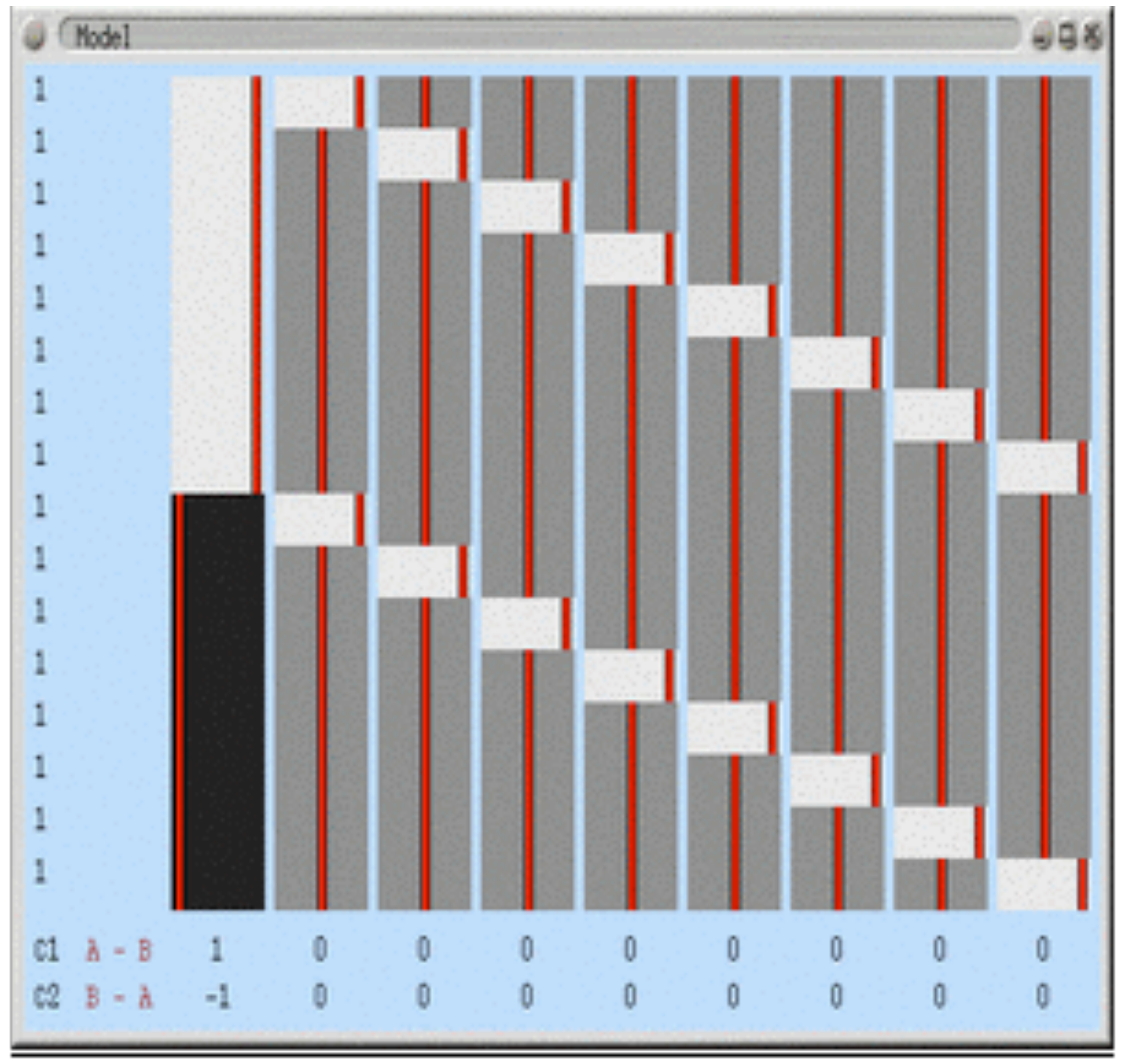


Paired T-Test

Model out each subject's mean



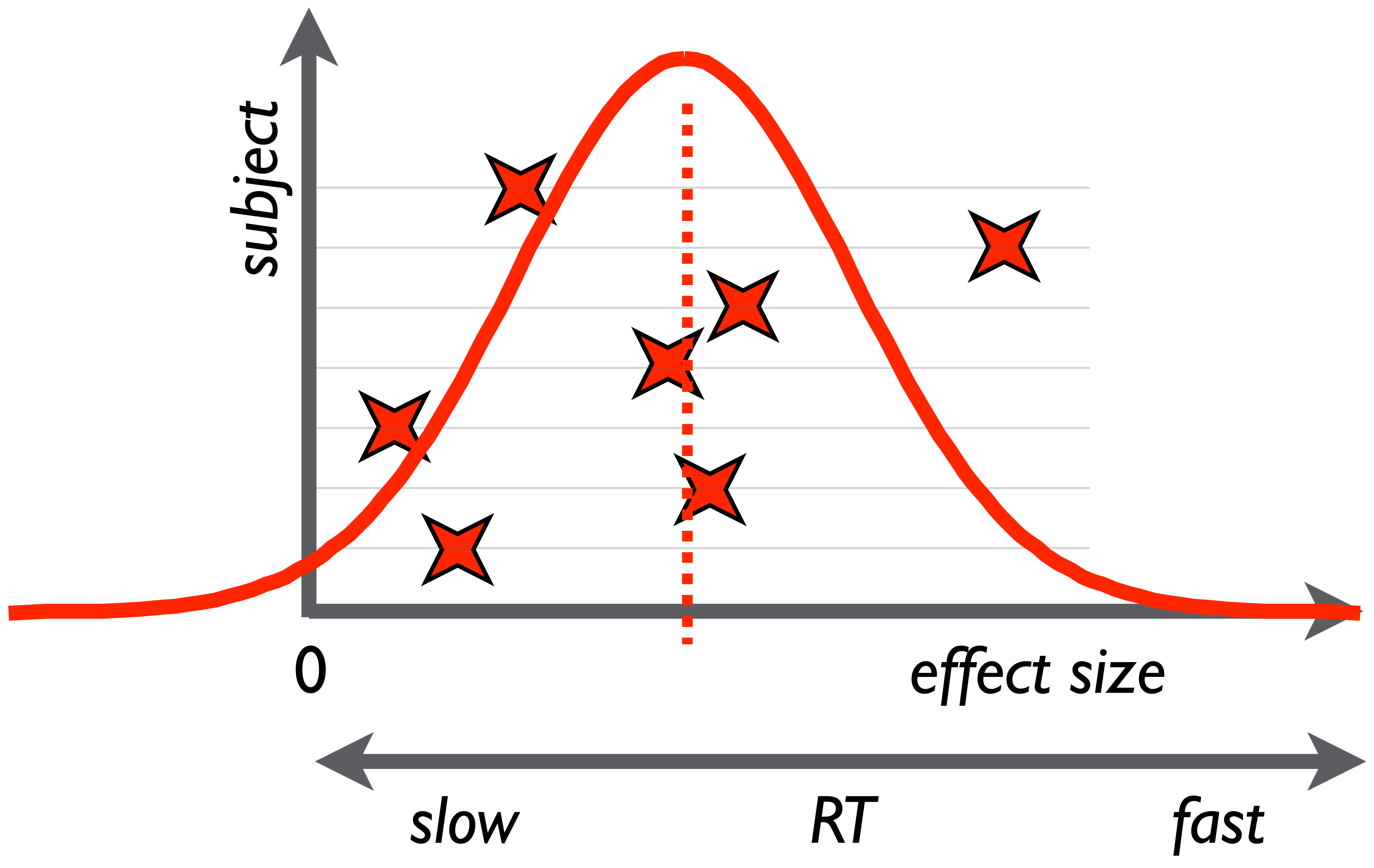




Group average with covariate

Group average with covariate

- Additional measurements (e.g. age; disability score; behavioral measures like reaction times)
- use covariates to ‘explain’ variation



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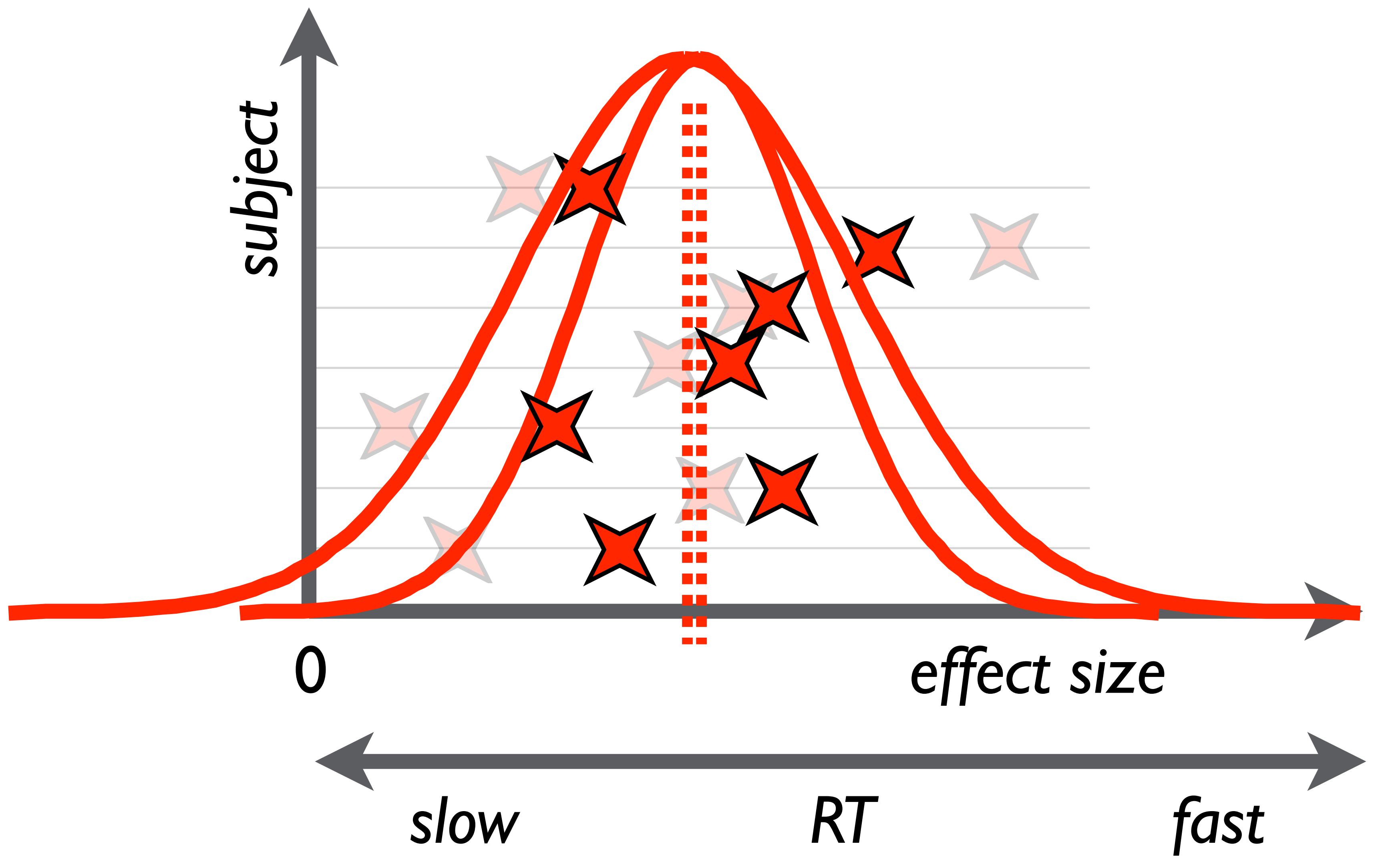
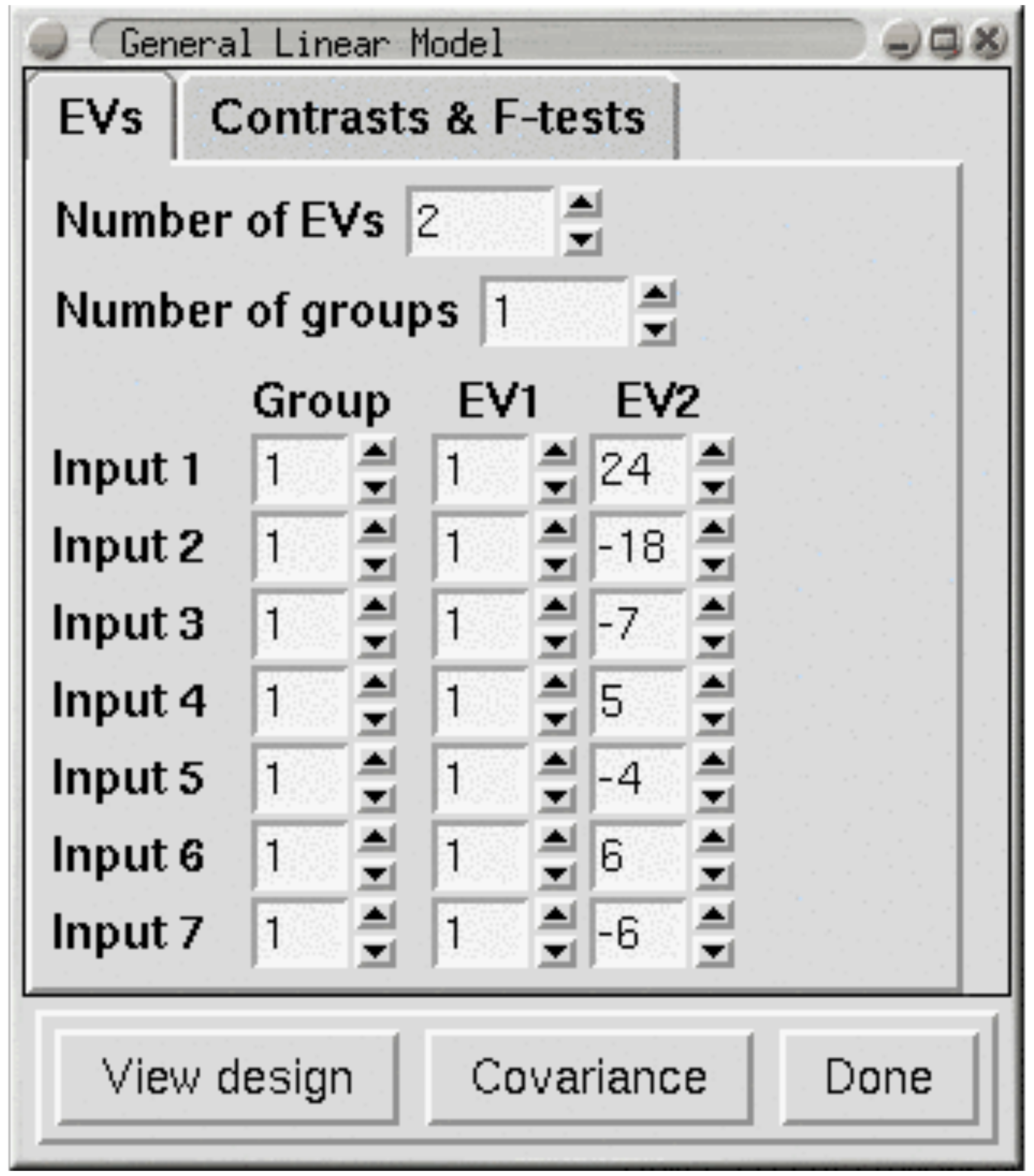
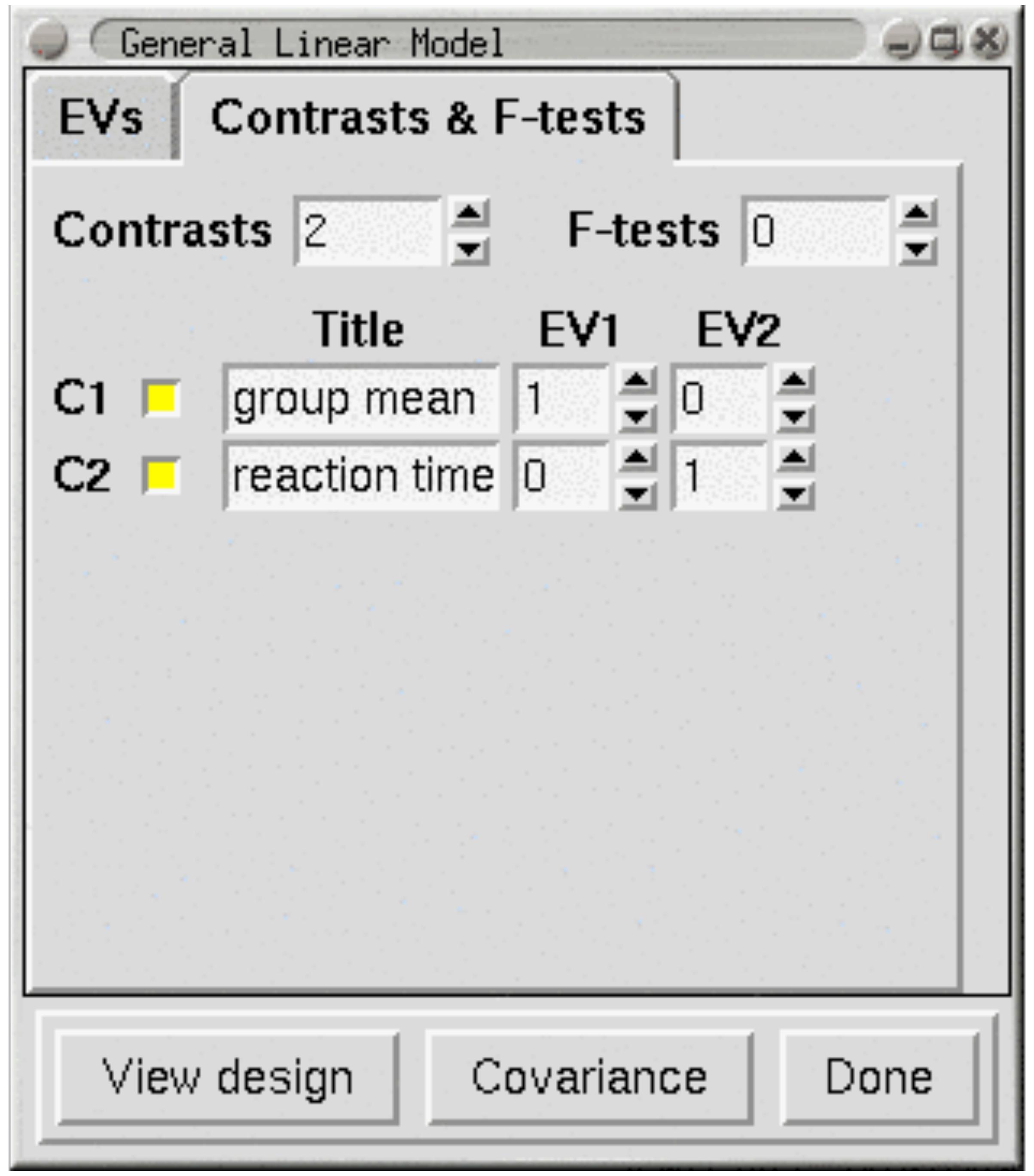
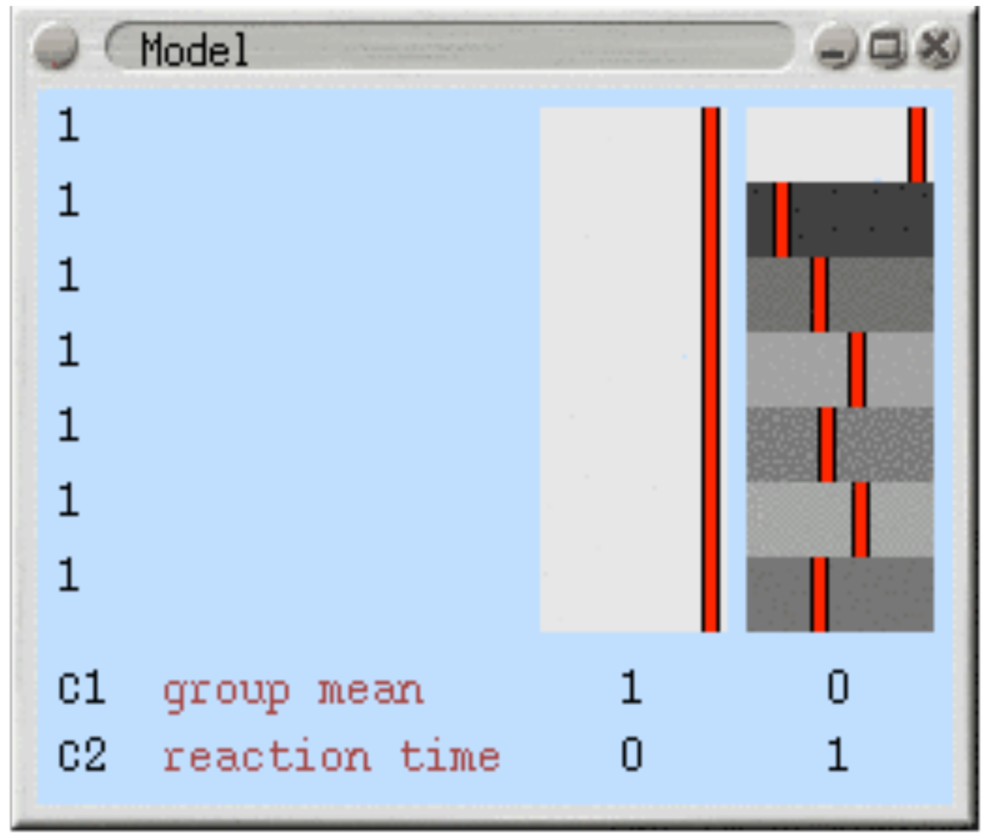


Group average with covariate

Need to demean covariates







Break Time!