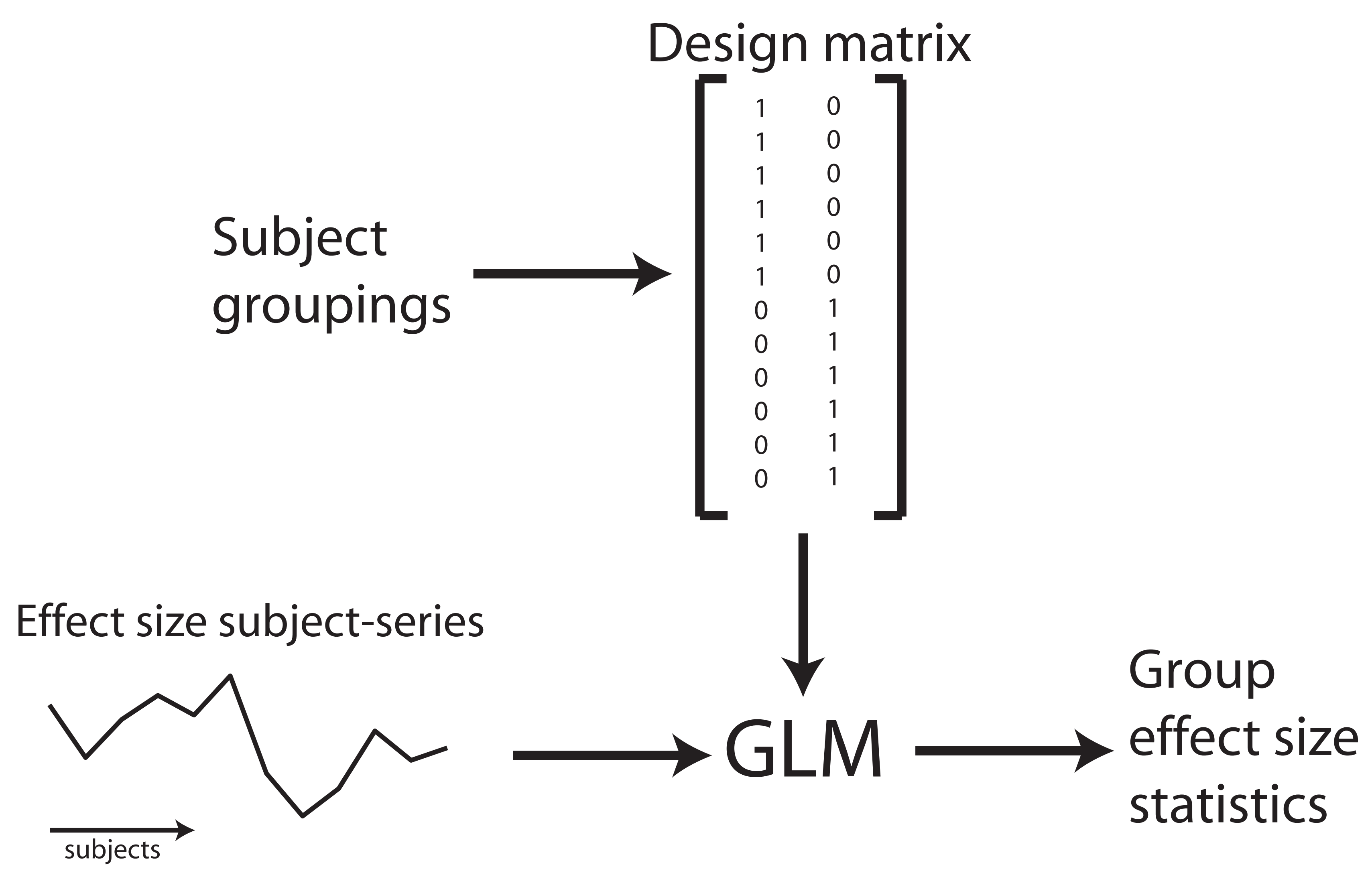
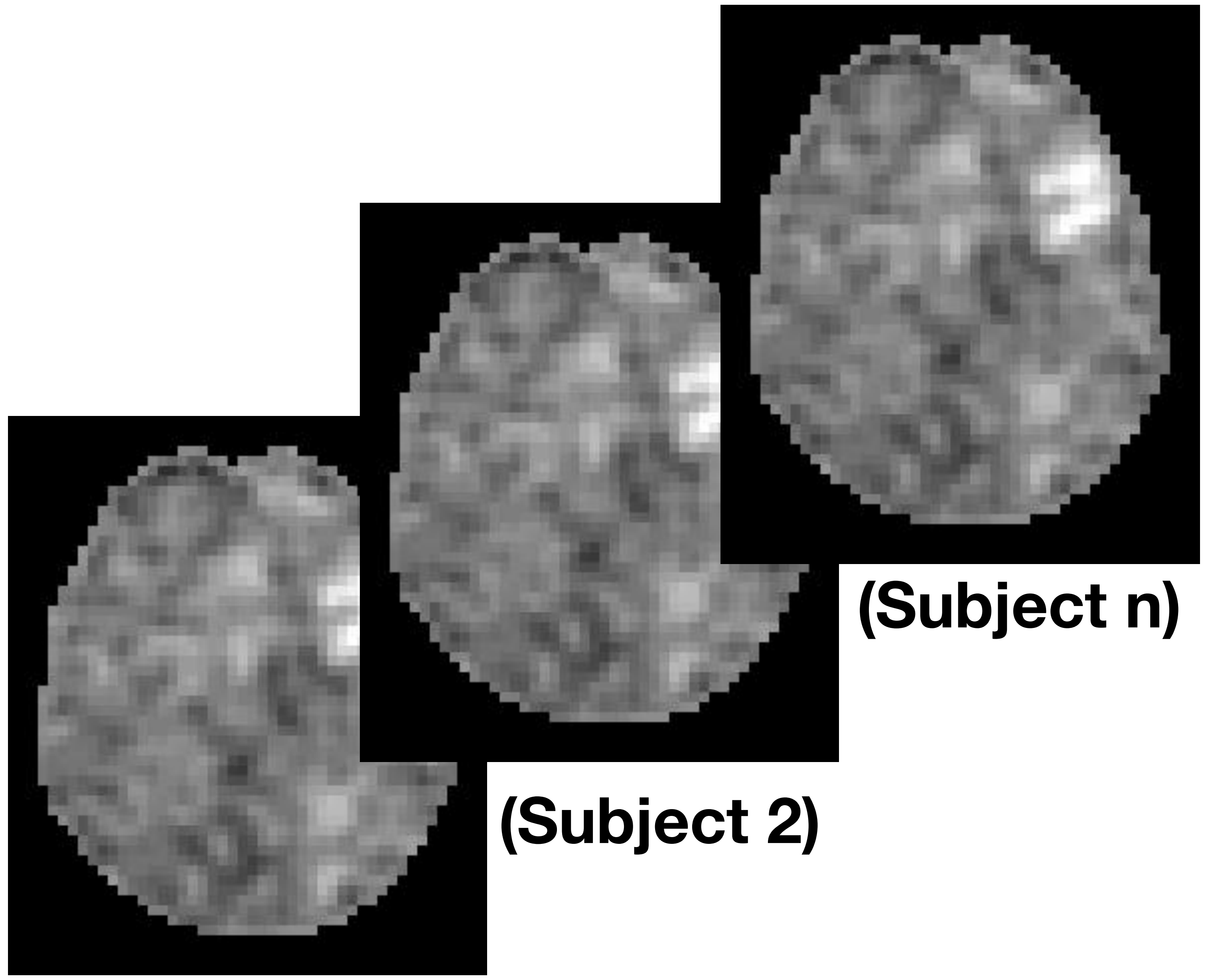
FMRI group analysis

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



The GLM for group analysis



(Subject n)

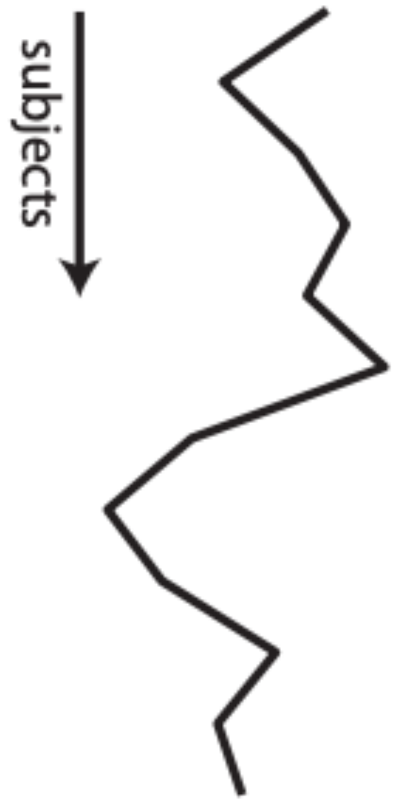
(Subject 2)

COPE from single subject analysis (Subject 1)

OUTPUTS from single subject analysis are INPUT for group analysis

Regressor, Explanatory Variable (EV)

Regression parameters, Effect sizes



$$
= \begin{array}{cc} \mathbf{x}_1 & \mathbf{x}_2 \end{array}
$$

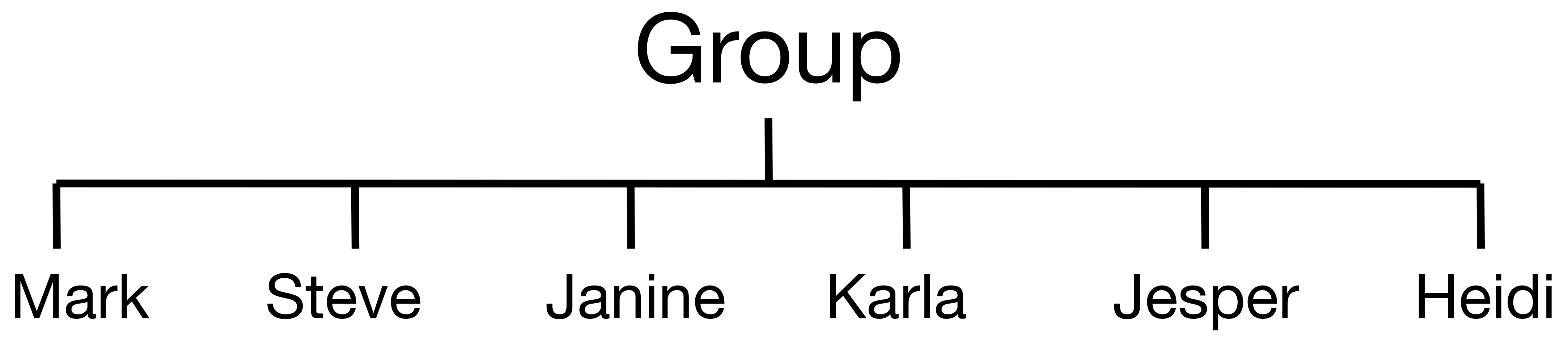
$$
= \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix}
$$

$$
\mathbf{y} = \mathbf{X} \quad \boldsymbol{\beta} + \mathbf{e}
$$

COPEs from a voxel across subjects

Design Matrix

A simple example



Does the group activate on average?

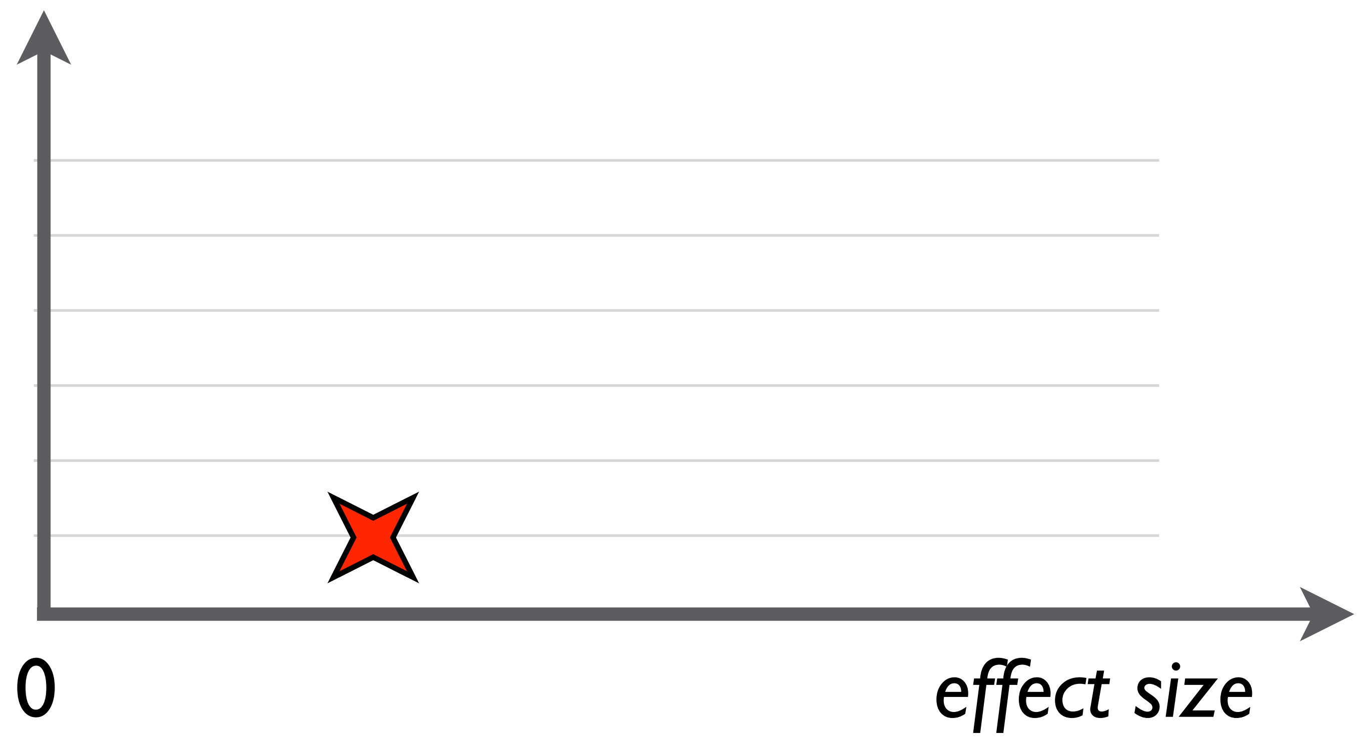
For a specific PE/contrast from the first level analysis,
which part of the brain were significantly activated across all subjects?

A simple example

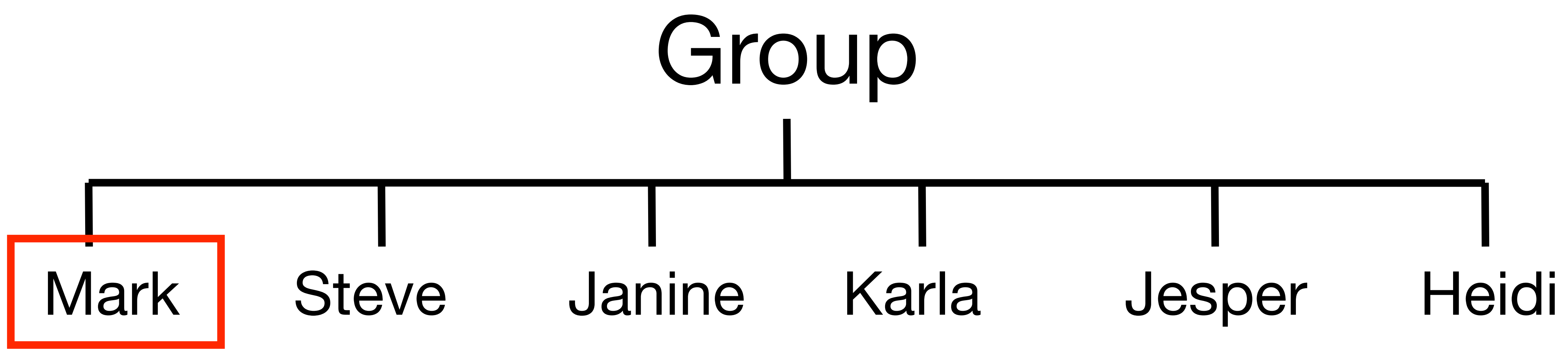
Group

Mark Steve Janine Karla Jesper Heidi

Does the group activate on average?



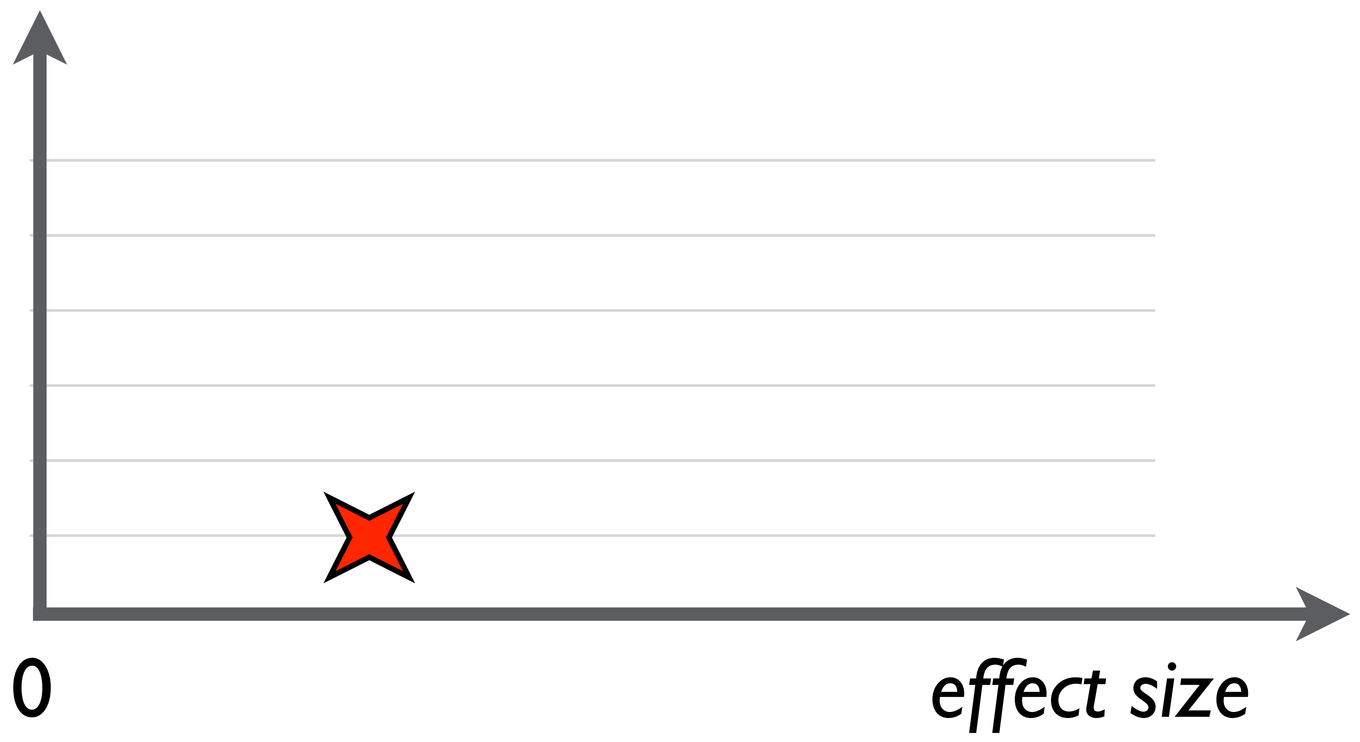
A simple example



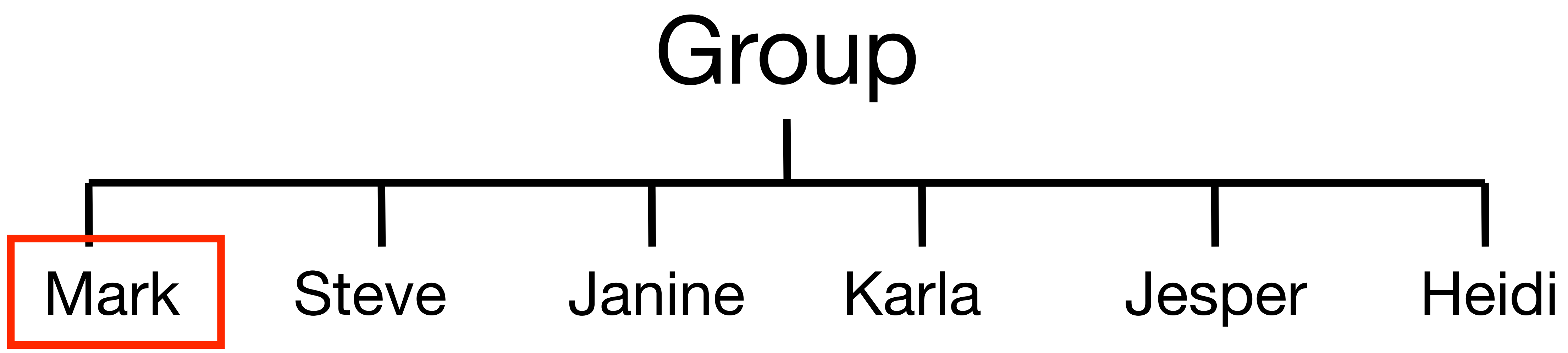
Does the group activate on average?

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

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



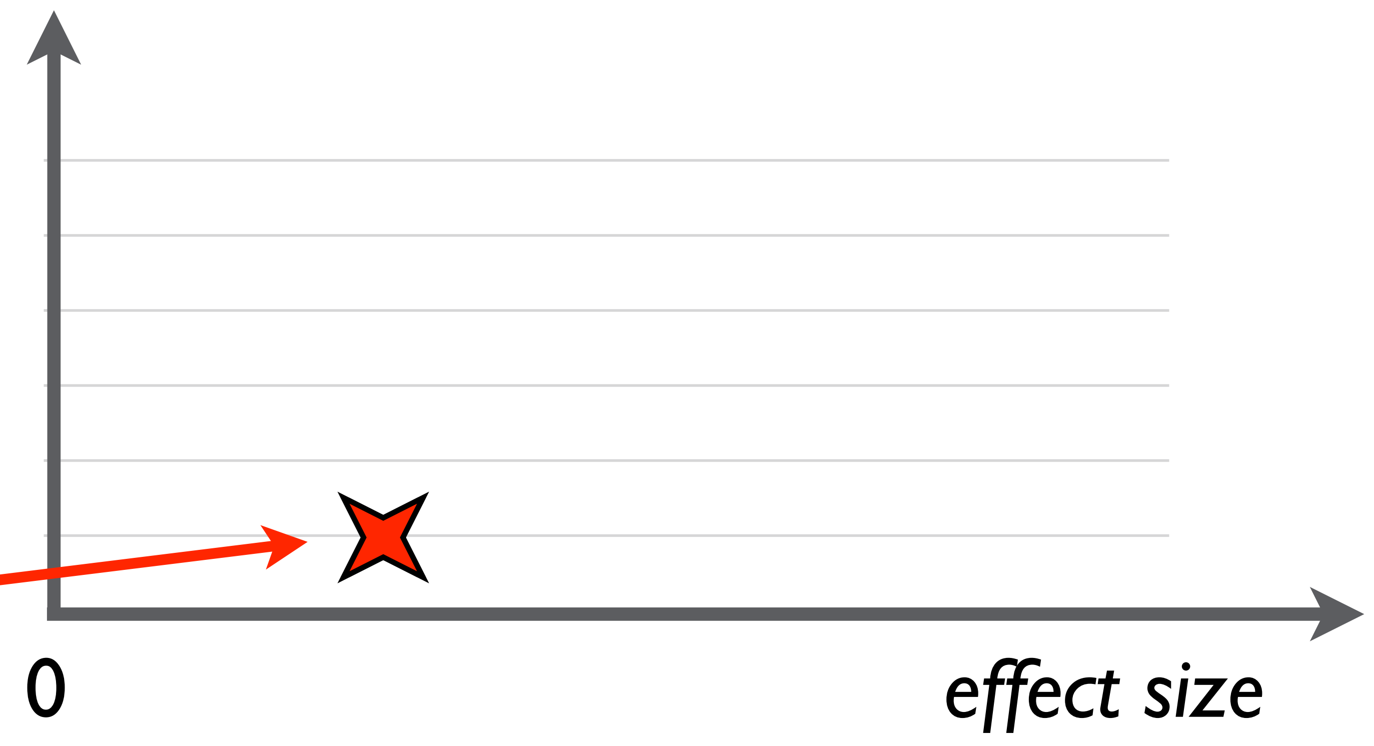
A simple example



Does the group activate on average?

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

Mark's
effect size



A simple example

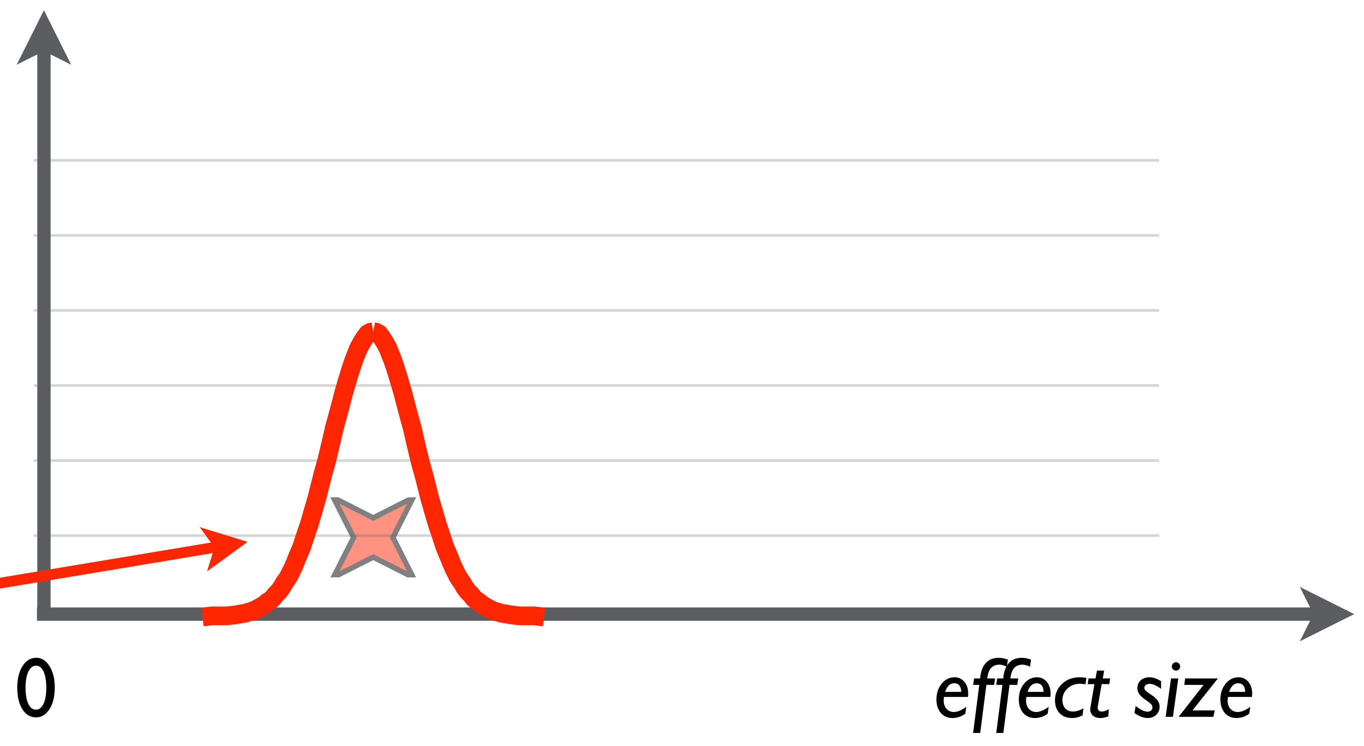
Group

Mark Steve Janine Karla Jesper Heidi

Does the group activate on average?

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

Mark's within-subject variance



A simple example

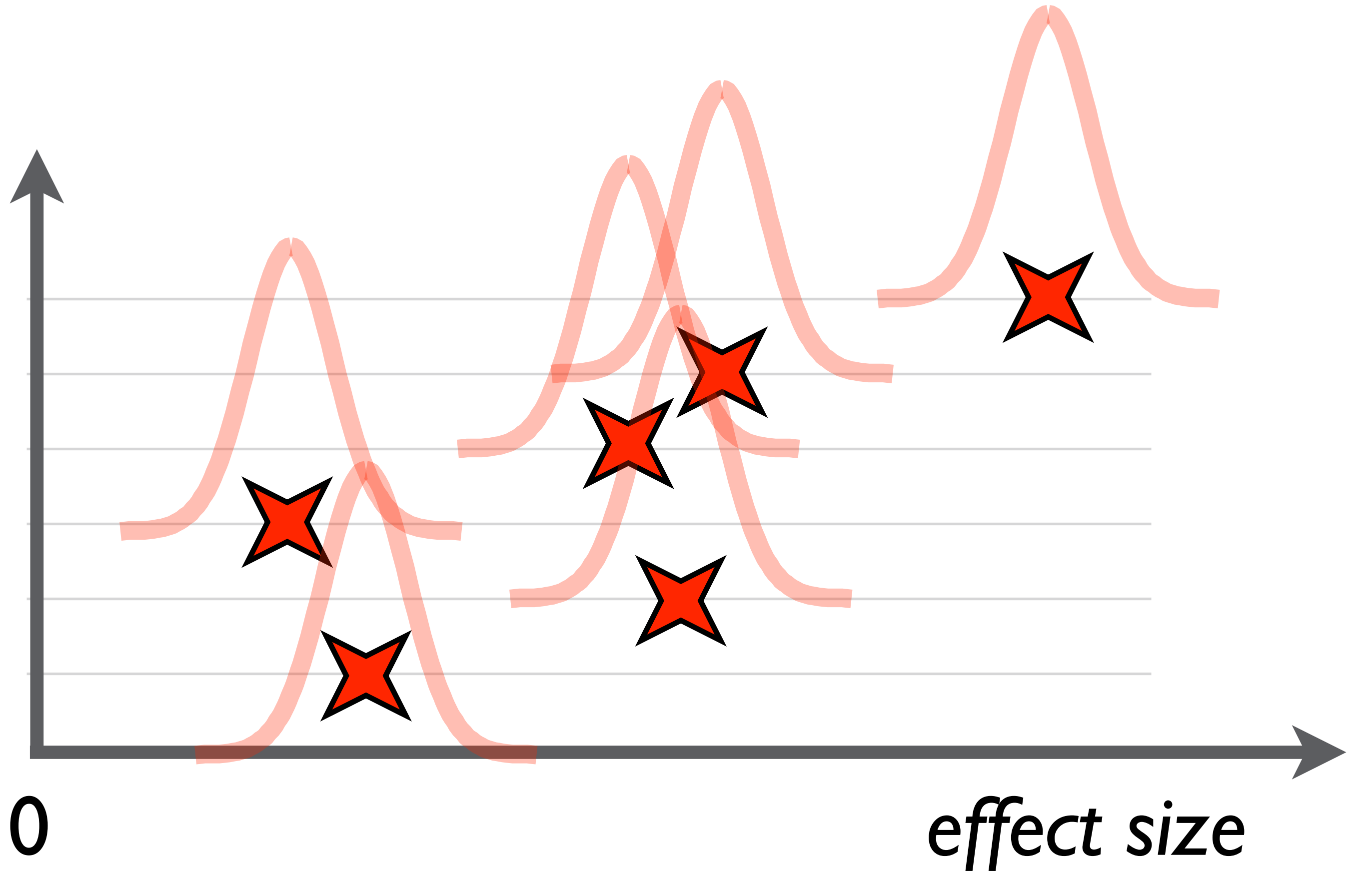
Group

Mark Steve Janine Karla Jesper Heidi

Does the group activate on average?

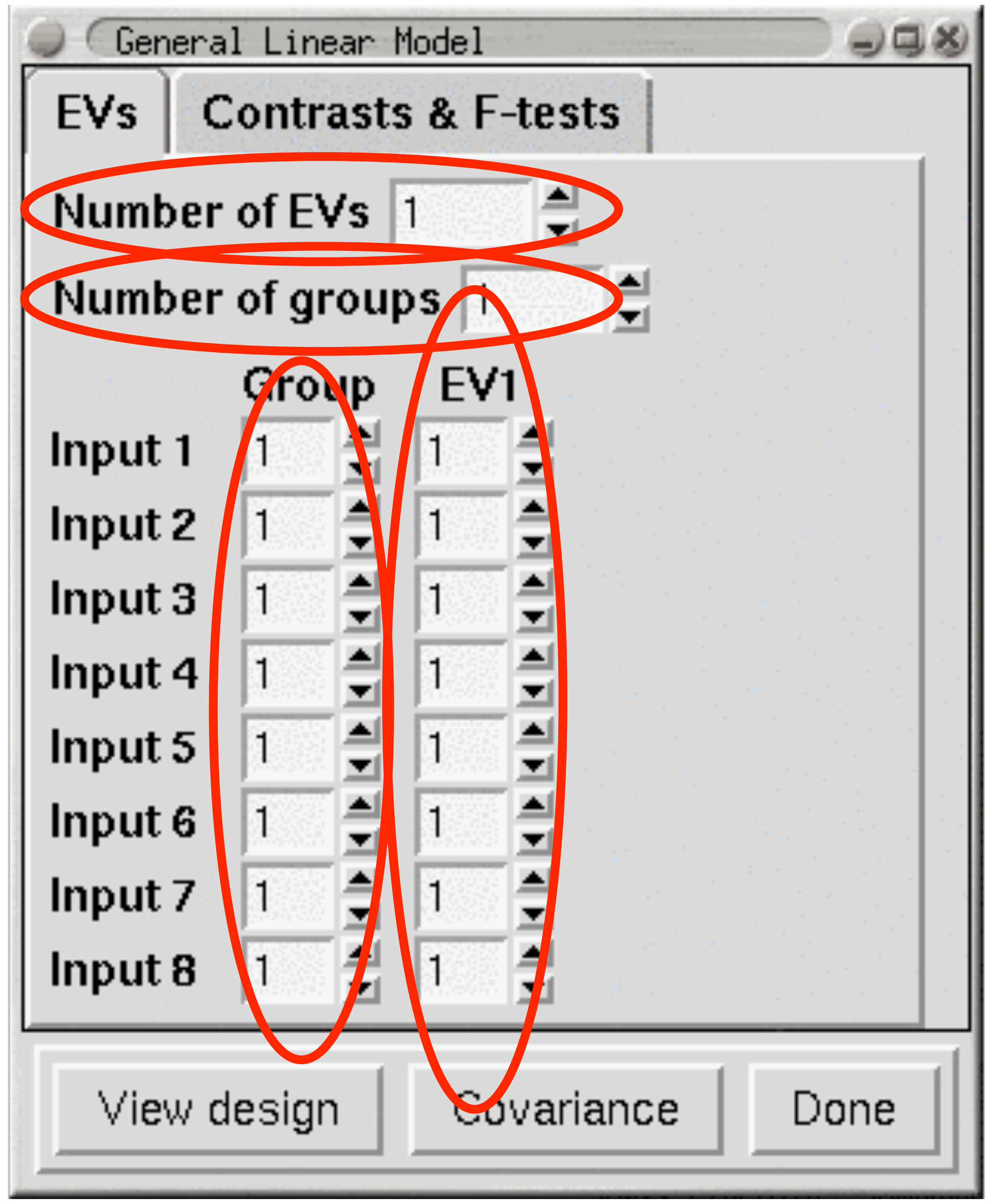
$$Y_k = X_k \beta_k + \epsilon_k$$

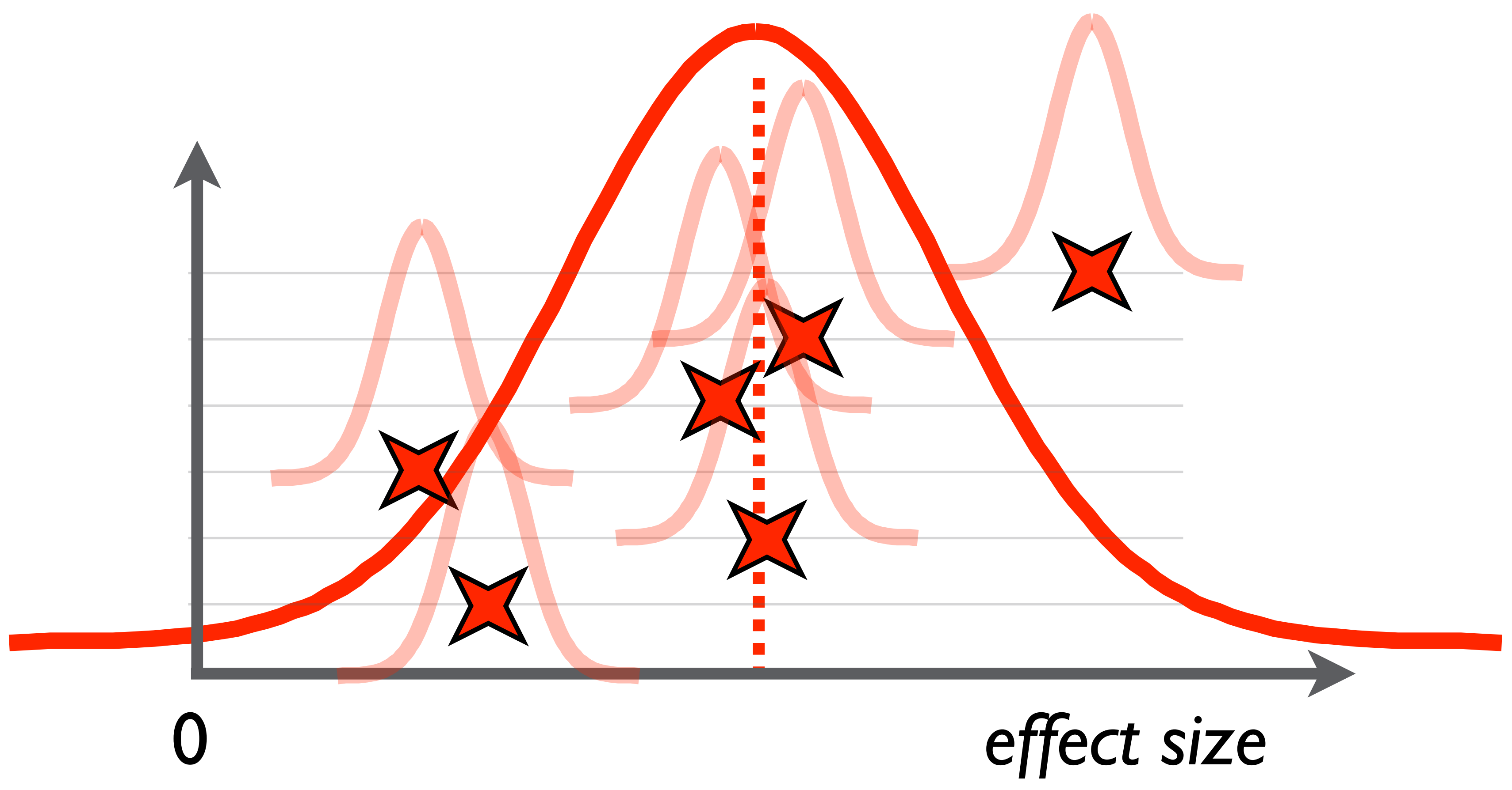
All first-level GLMs
on 6 FMRI data set



Single Group Average

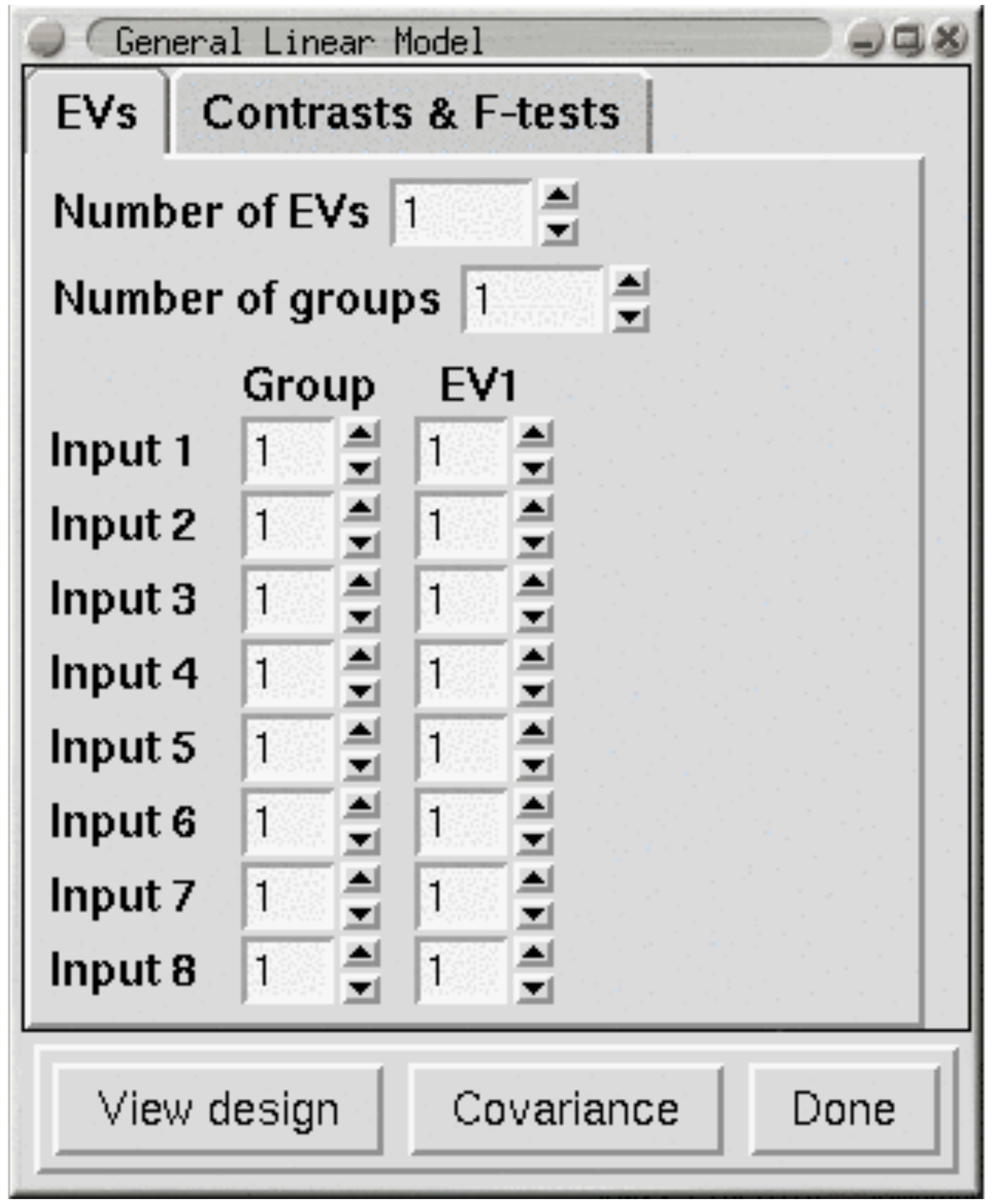
Does the group activate on average?

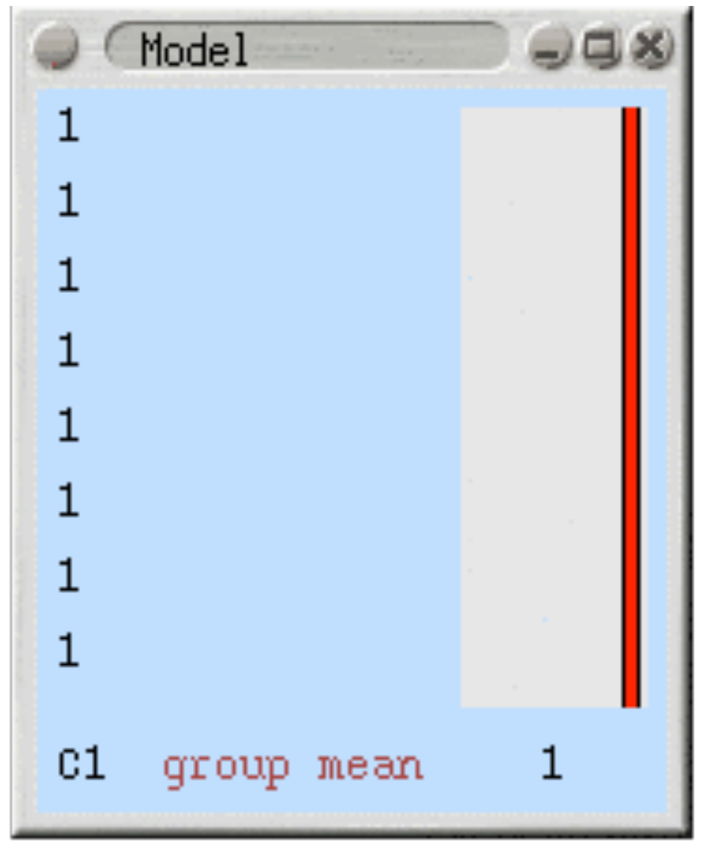




Single Group Average

Does the group activate on average?





Fixed versus mixed effects

Fixed-Effects Analysis

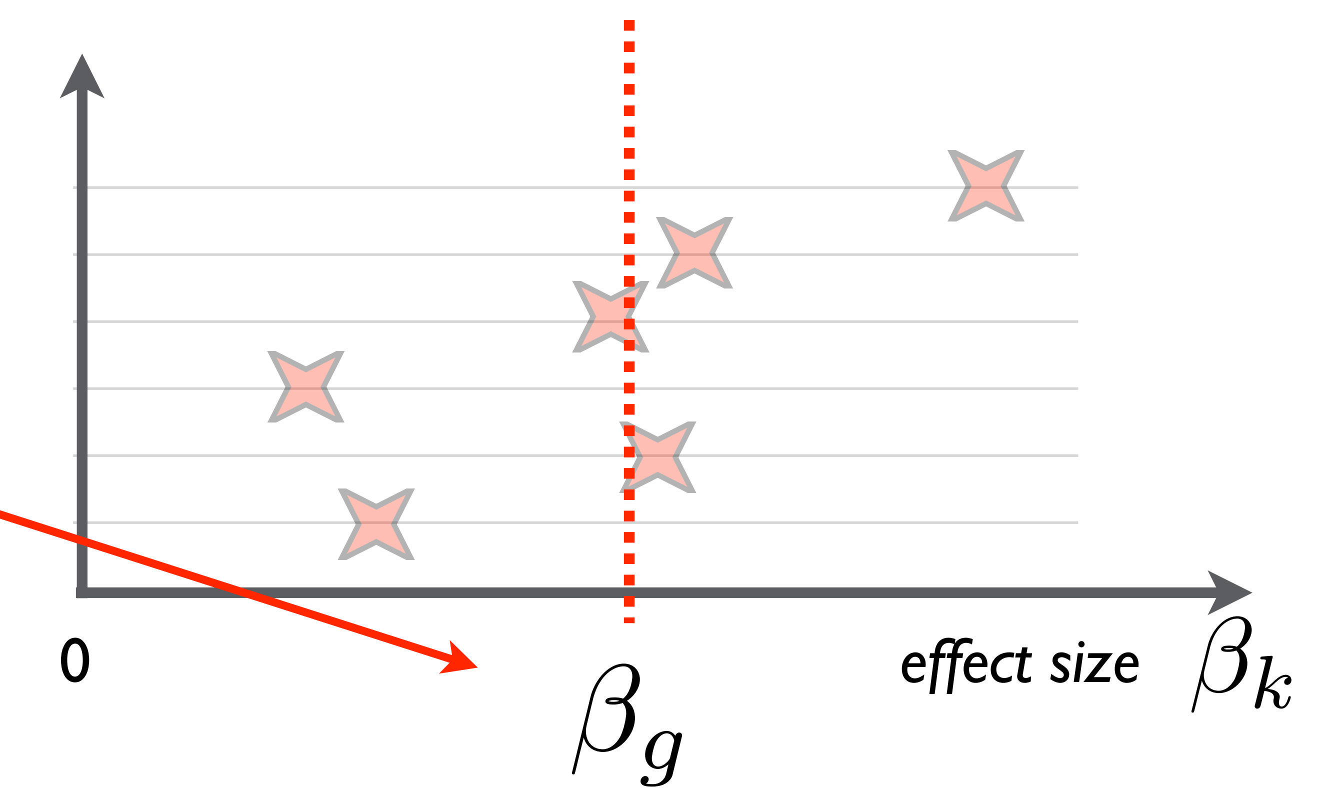
Do these exact 6 subjects activate on average?

Group

Mark Steve Janine Karla Jesper Heidi

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

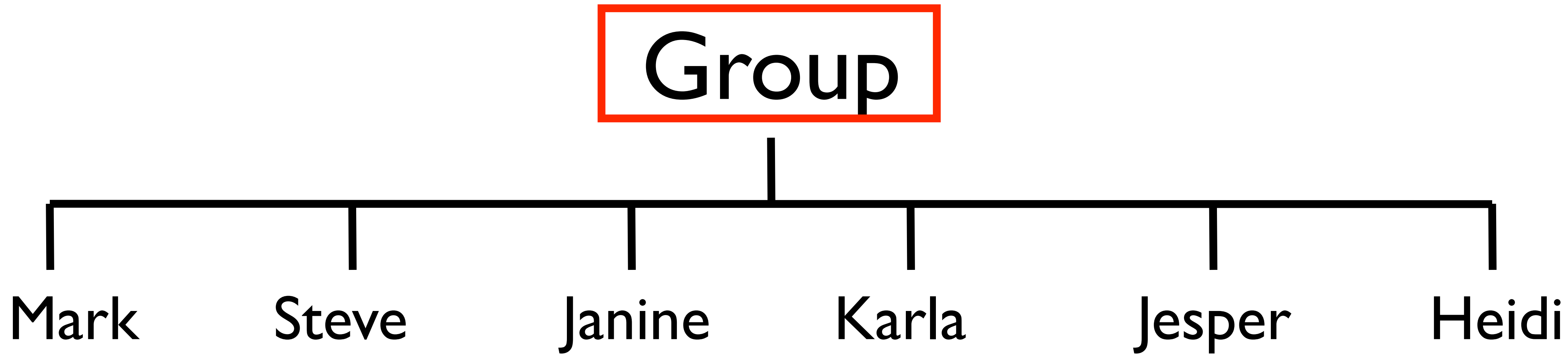
Fixed Effects Analysis:



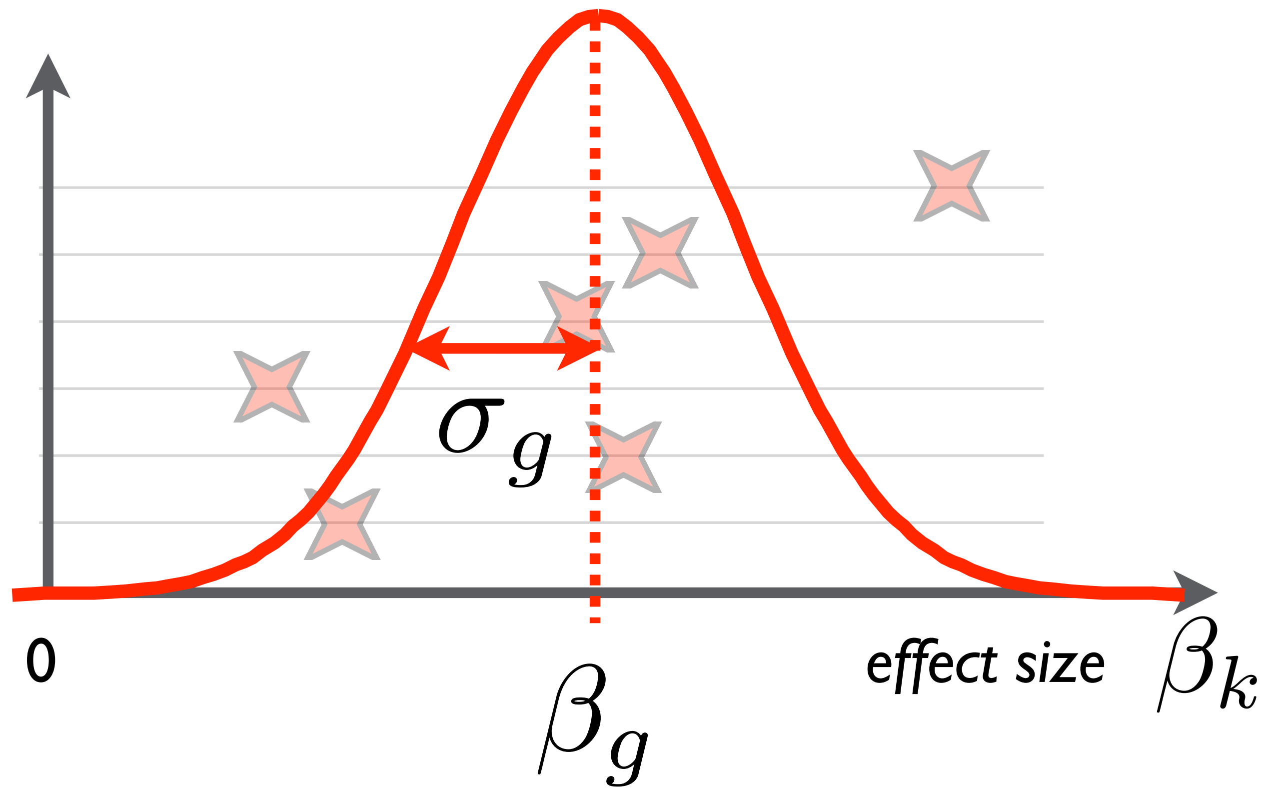
- *Consider only these 6 subjects*
  - *estimate the mean across these subject*
  - *only variance is within-subject variance*

Mixed-Effects Analysis

Does the population activate on average?



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

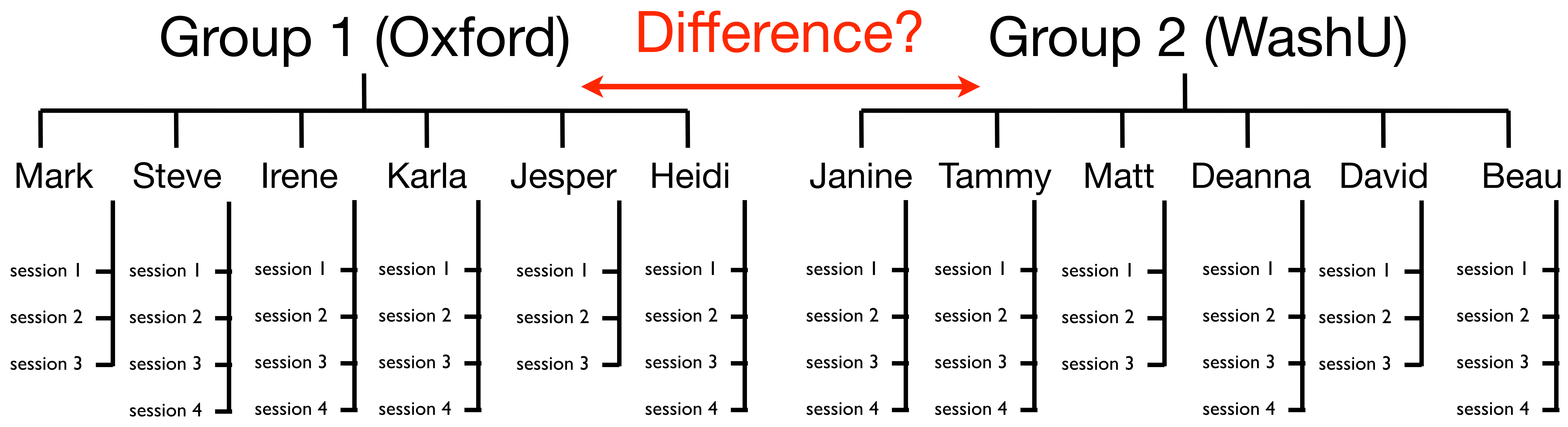


Mixed-Effects Analysis:

- *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!

Group difference

↑

Group

↑

Subject

↑

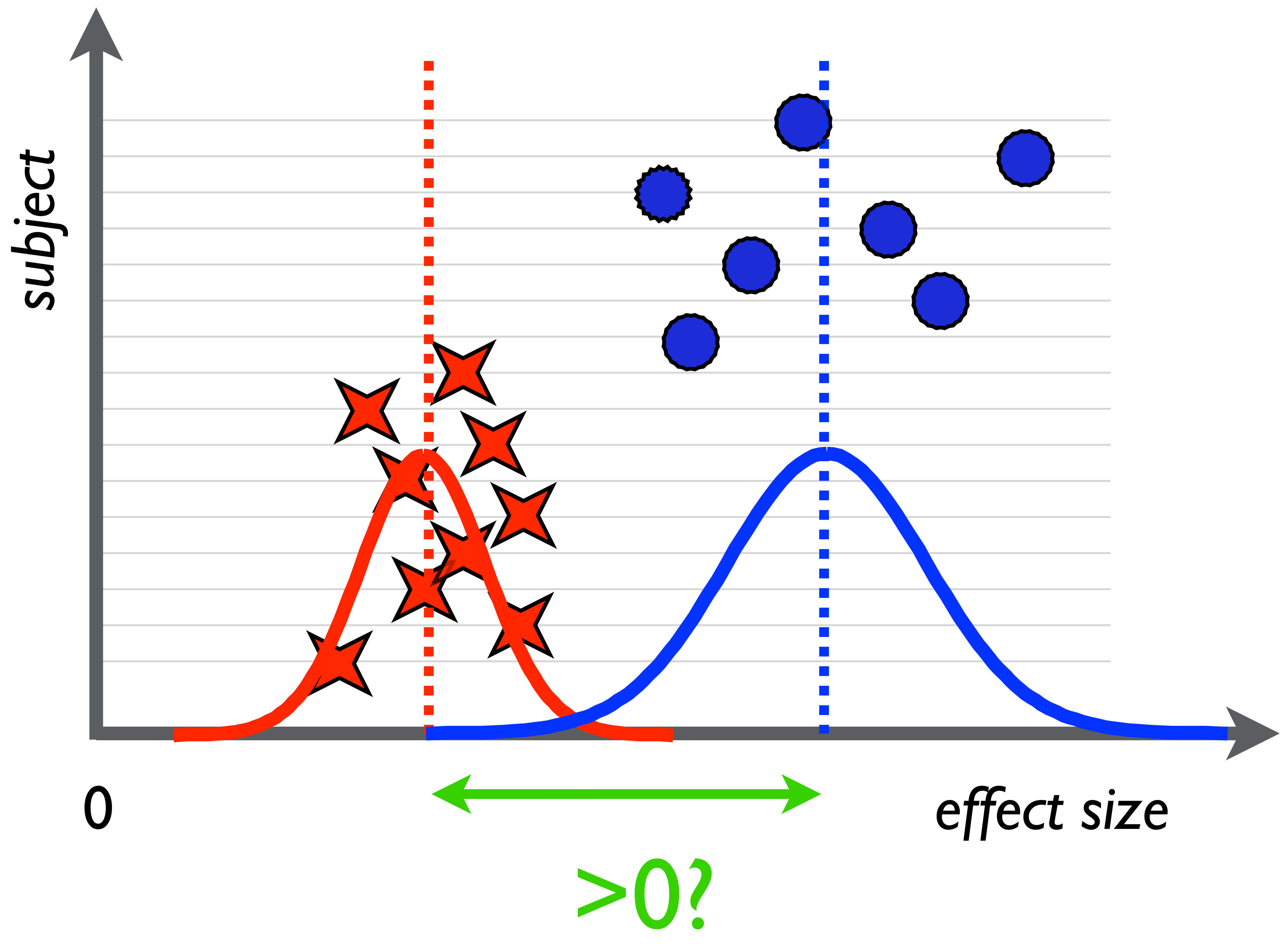
Session

Unpaired Two-Group Difference

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

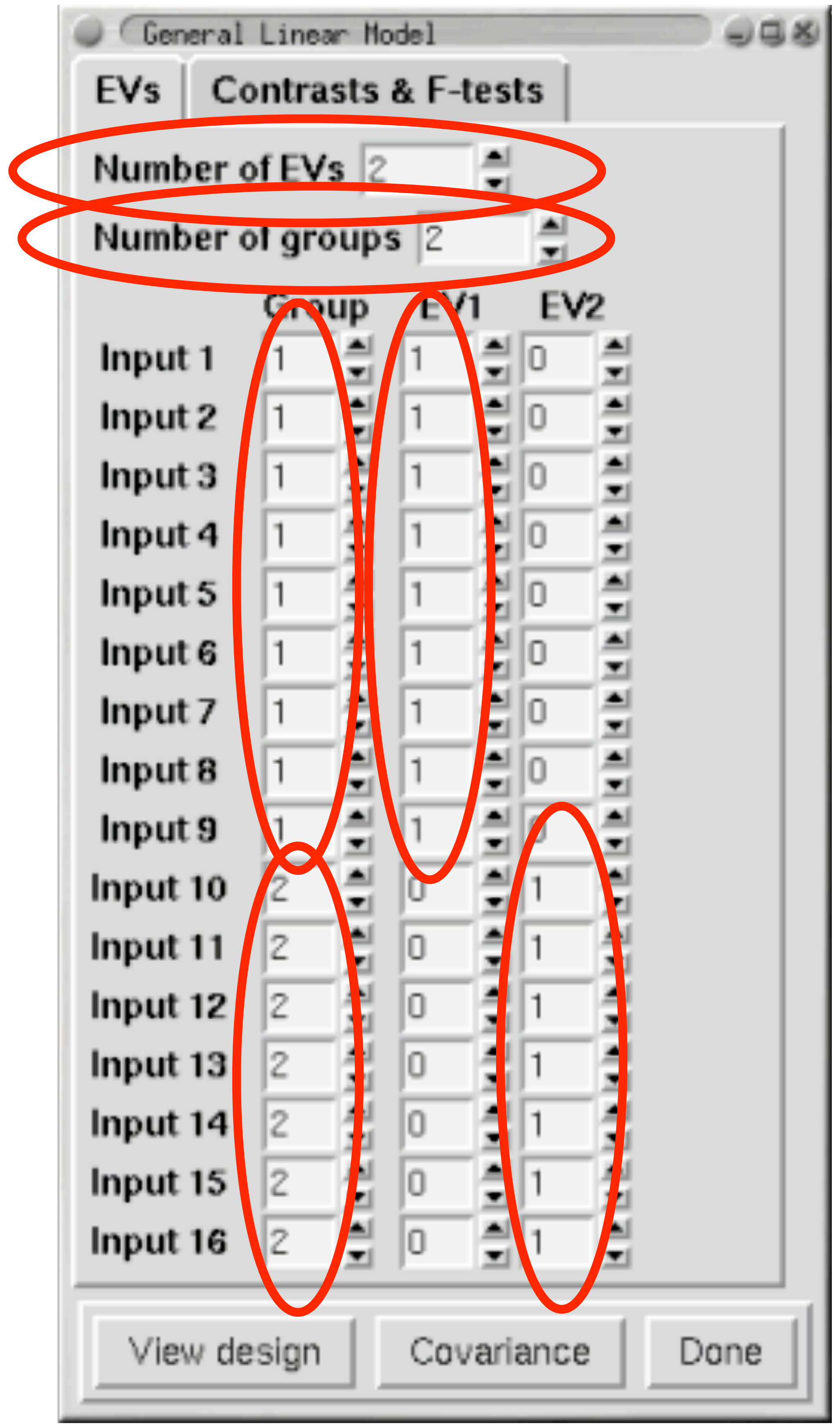
  Is there a significant group difference?

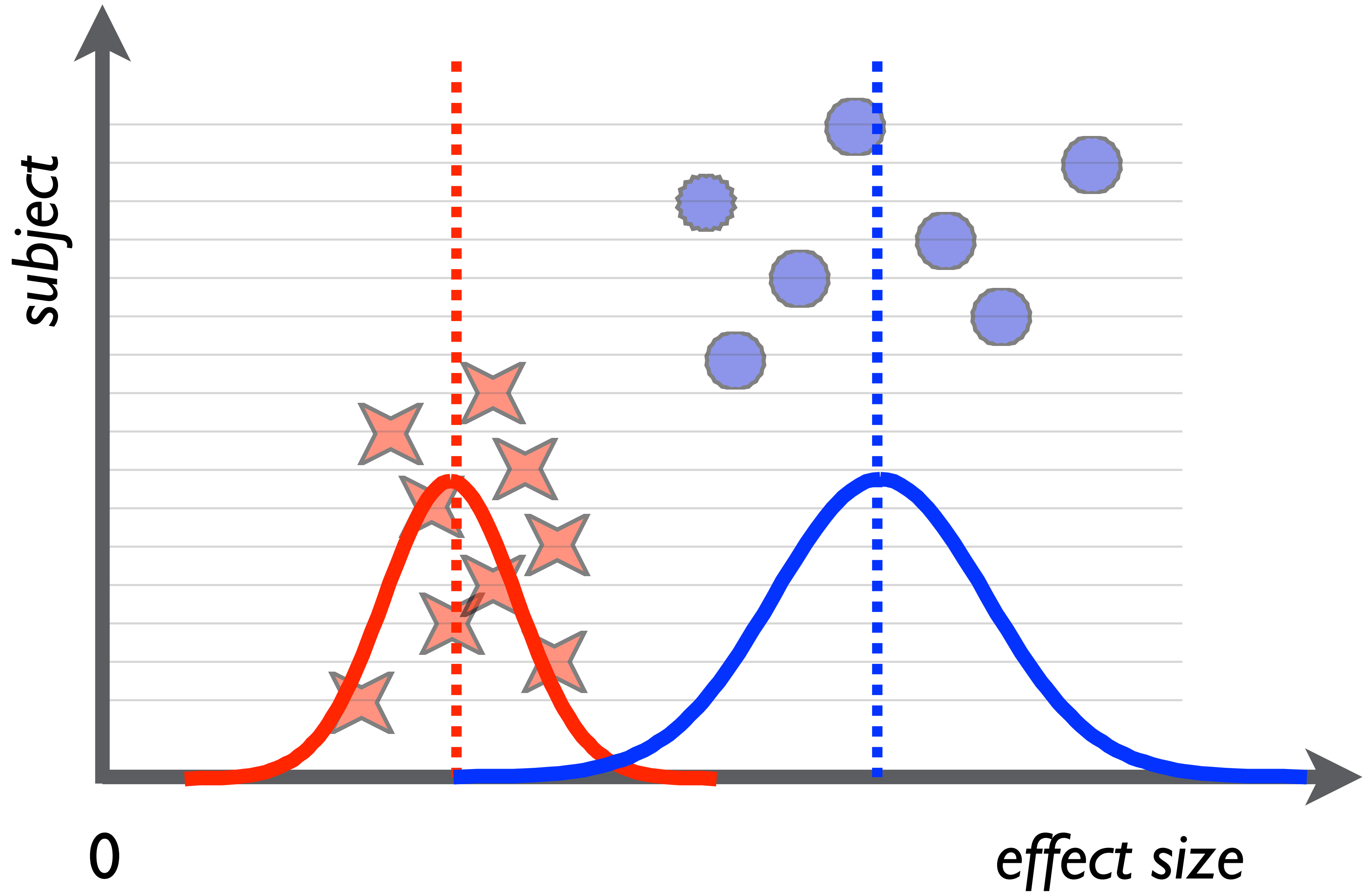
- estimate means
- estimate std-errors (FE or ME)
- test significance of difference in means



Unpaired Two-Group Difference

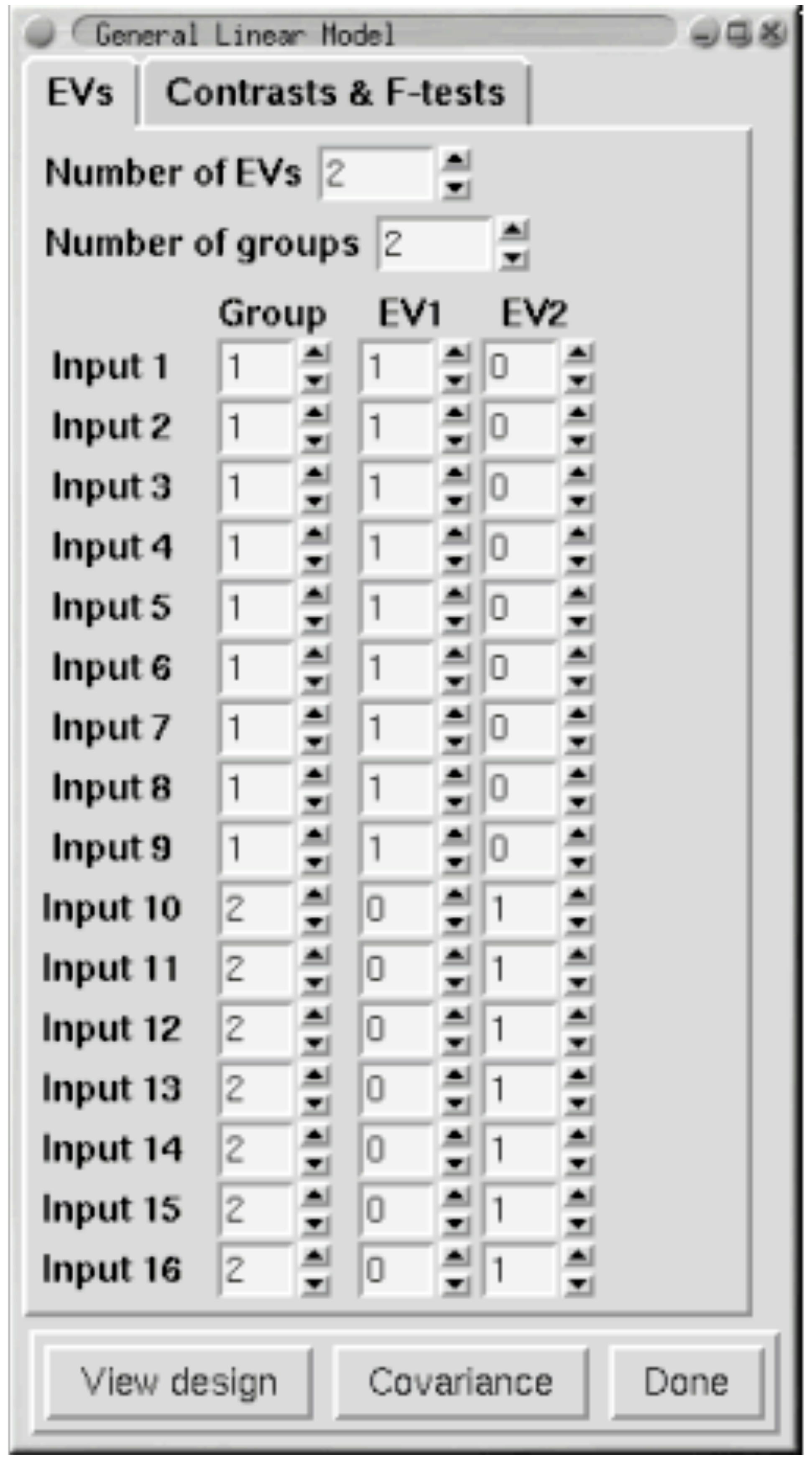
Is there a significant group difference?

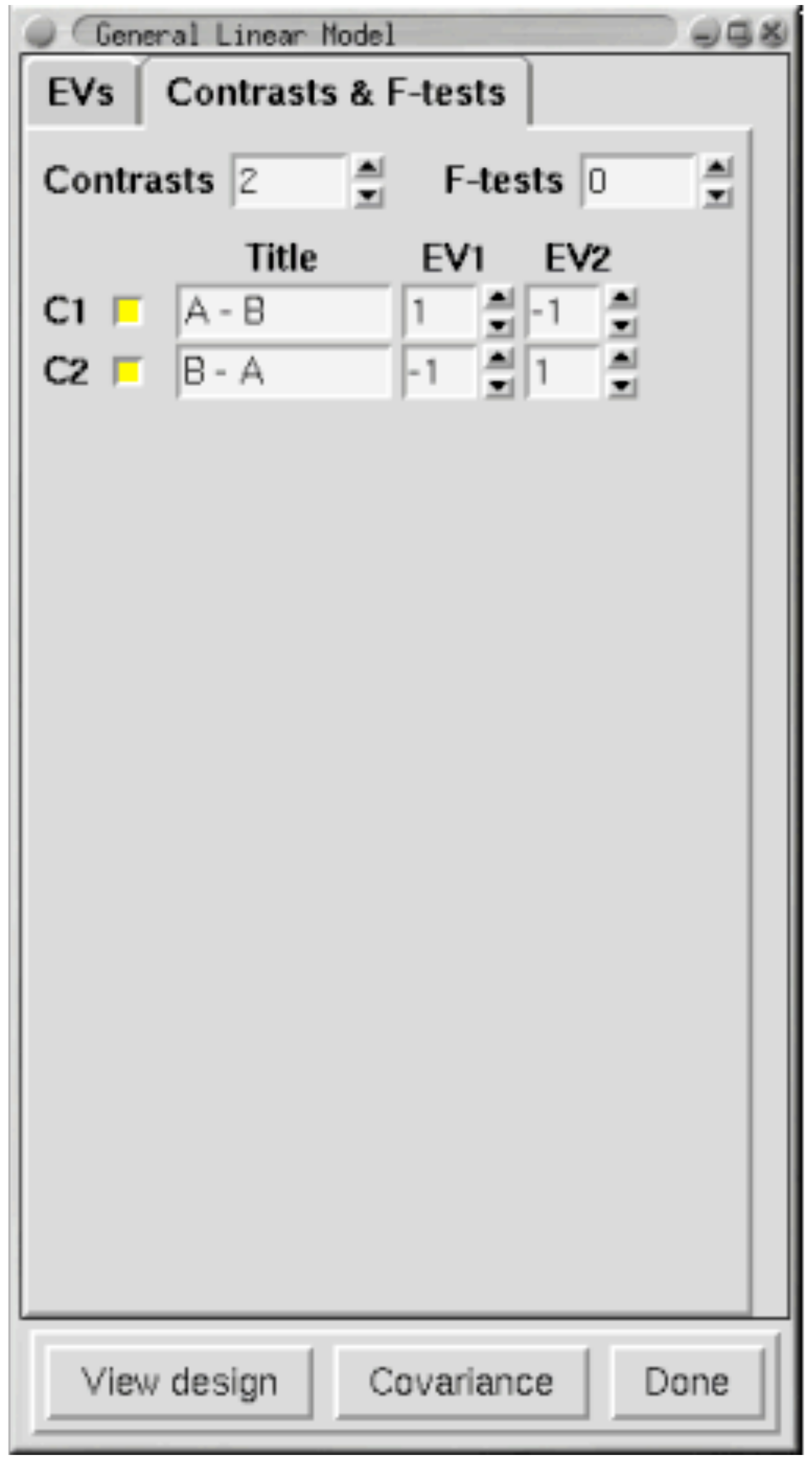


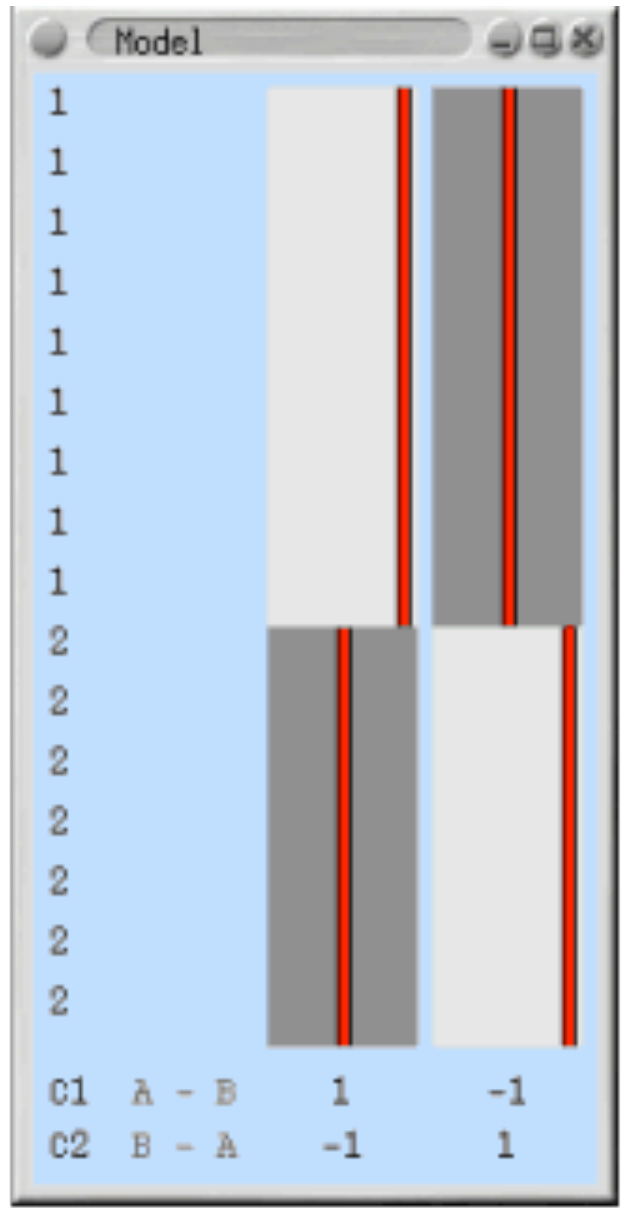


Unpaired Two-Group Difference

Is there a significant group difference?



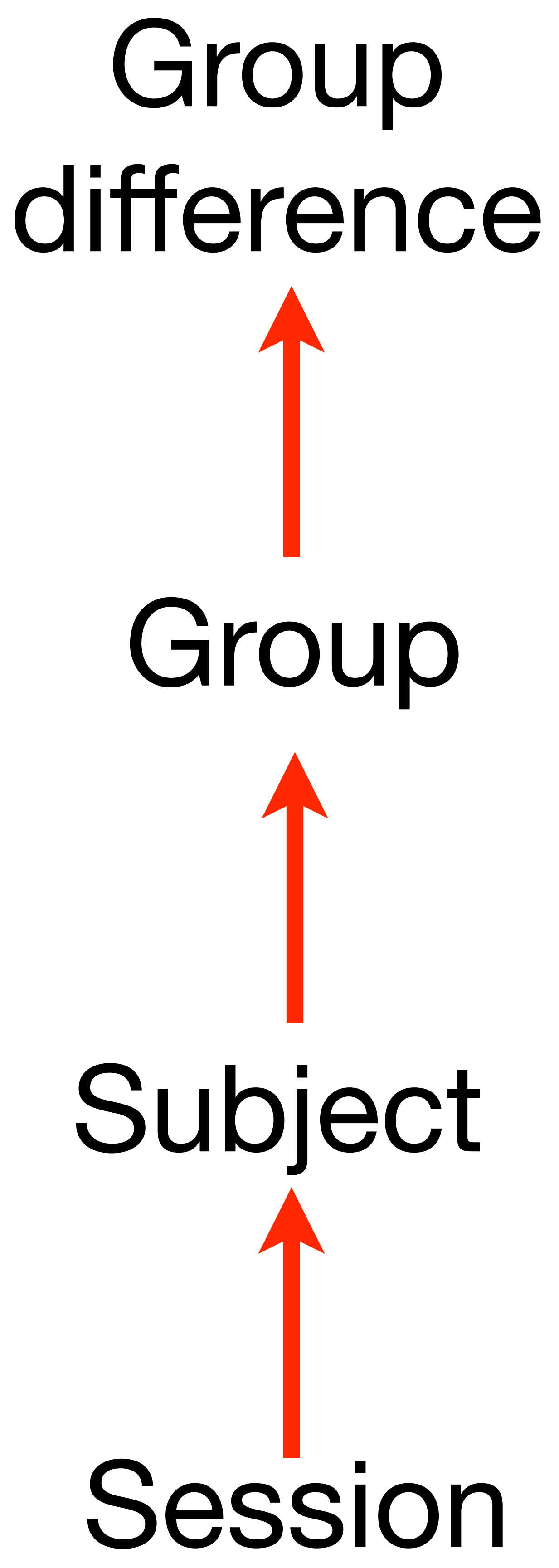




FLAME

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

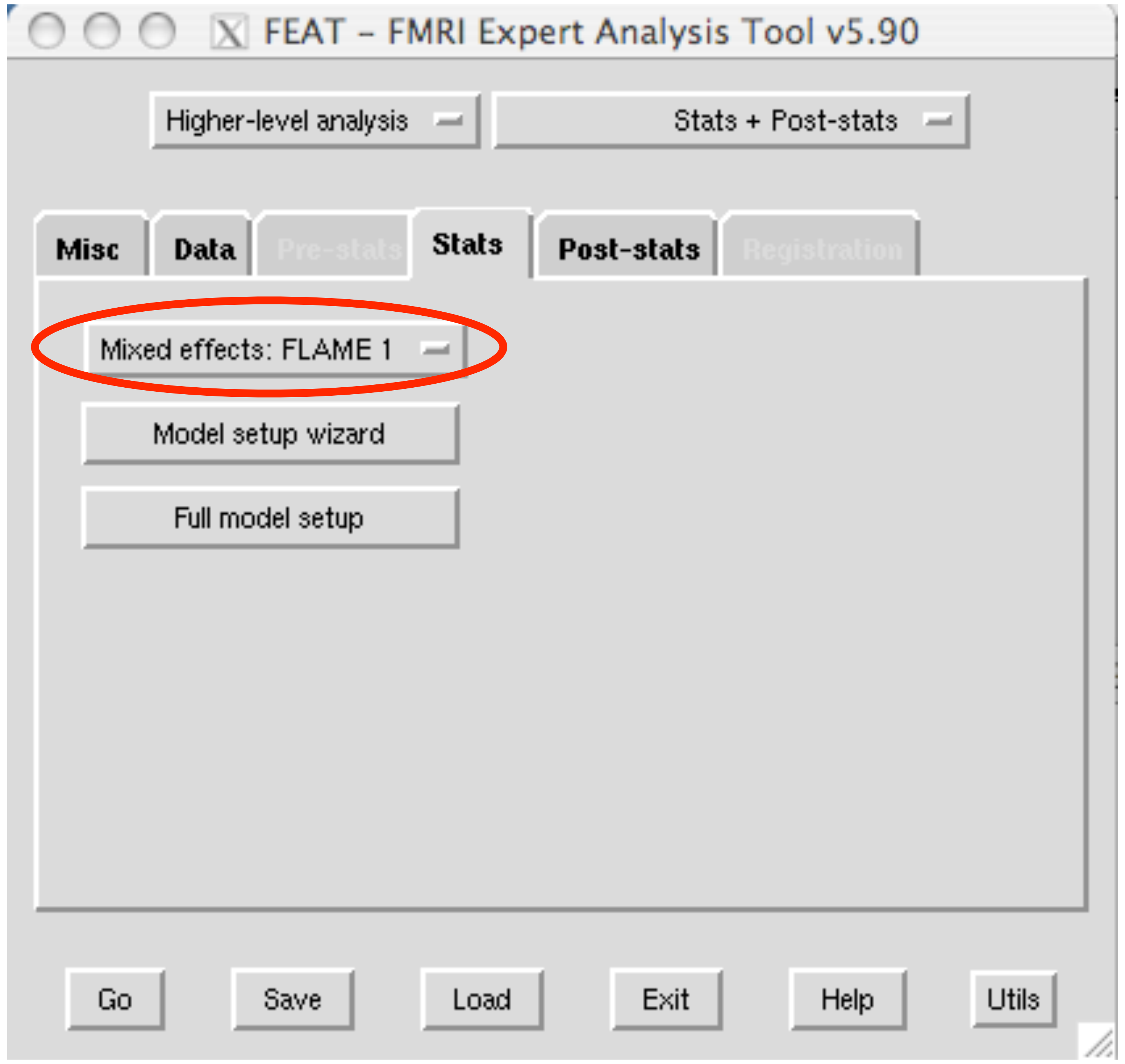
   Use at top level: quick and less accurate

3. Mixed Effects - FLAME 1

   Use at top level: less quick but more accurate

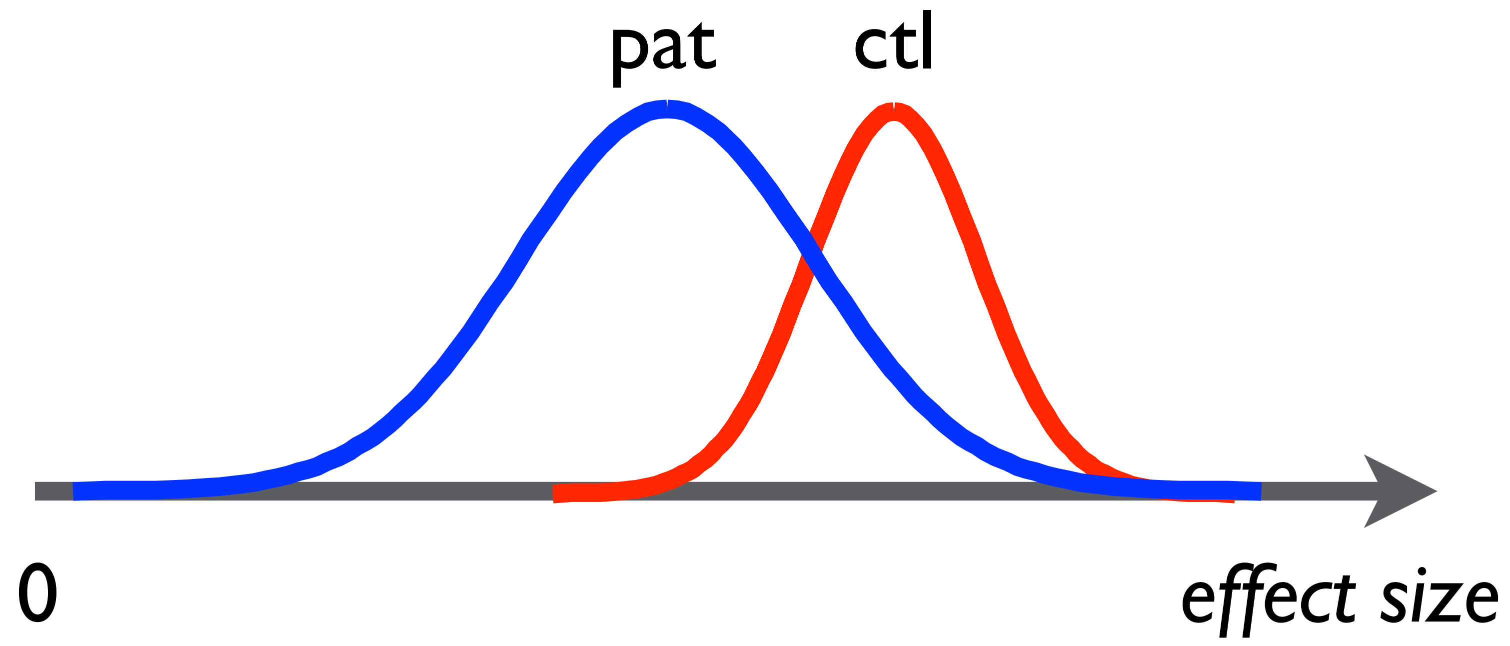
4. Mixed Effects - FLAME 1+2

   Use at top level: slow but even more accurate

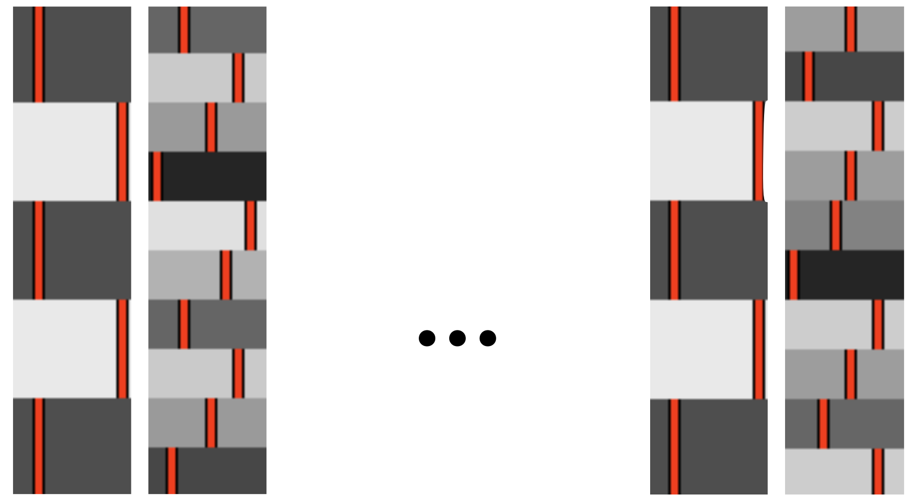


FLAME vs. OLS

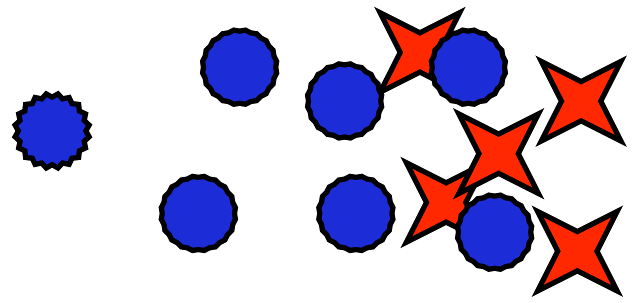
- allow different within-level variances (e.g. patients vs. controls)



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

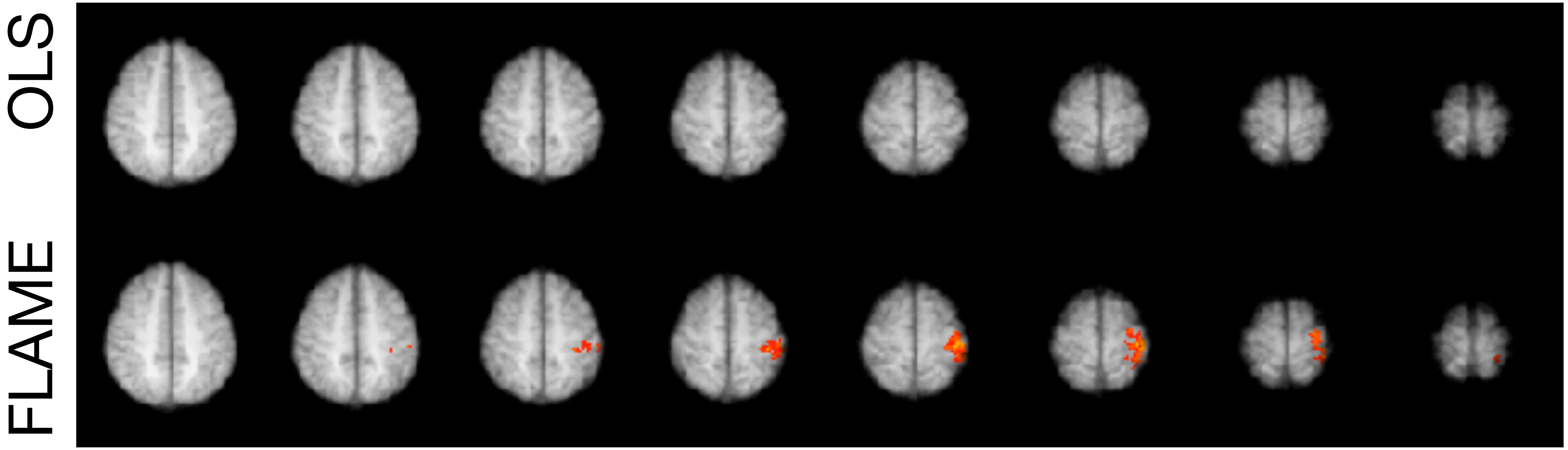


- allow un-equal group sizes



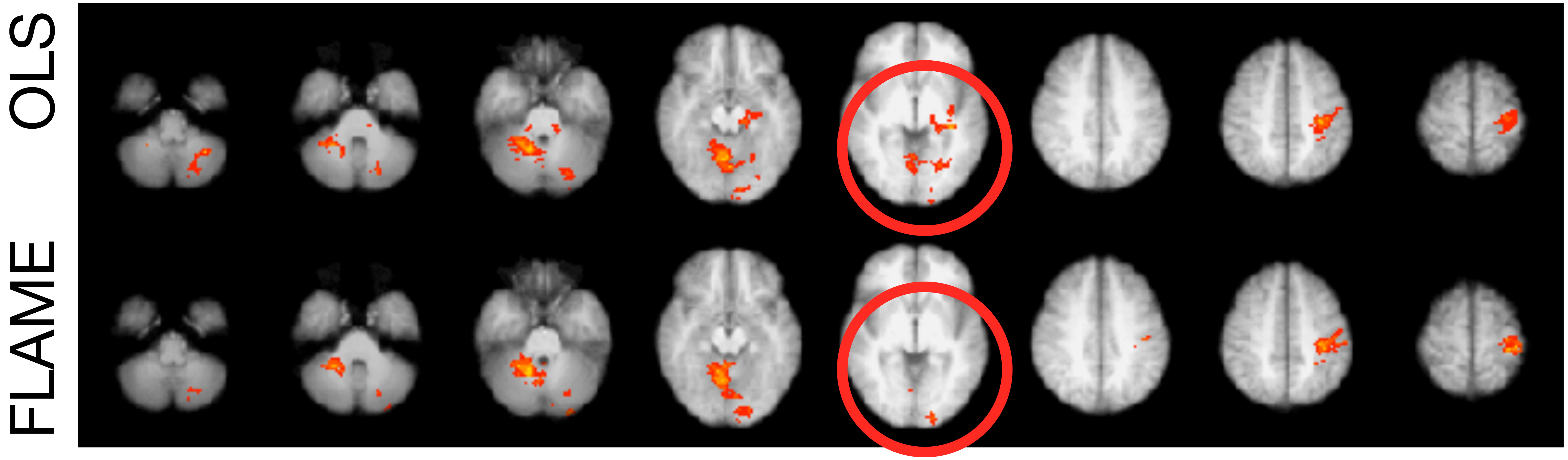
FLAME vs. OLS

- 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

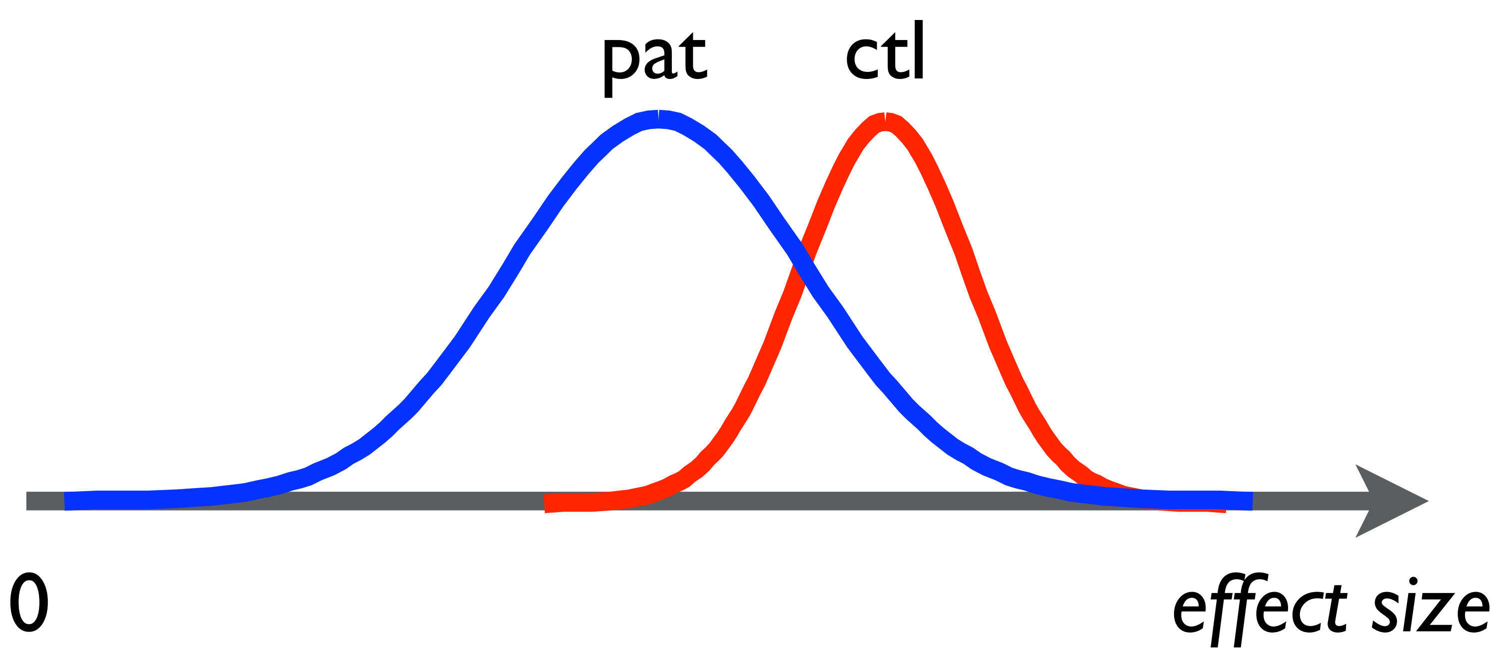


FLAME vs. OLS

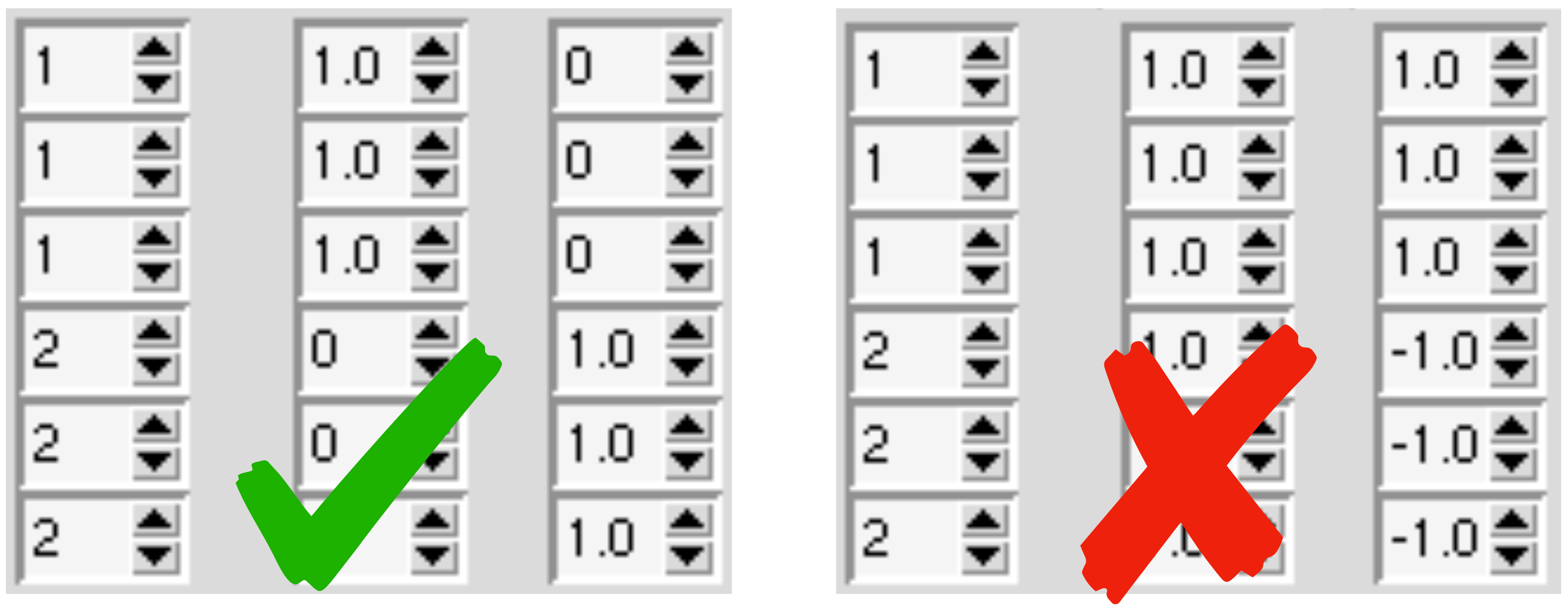
- Two ways in which FLAME can give different Z-stats compared to OLS:
    - *Lower Z* due to higher-level variance being constrained to be positive (i.e. solve the implied negative variance problem)



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

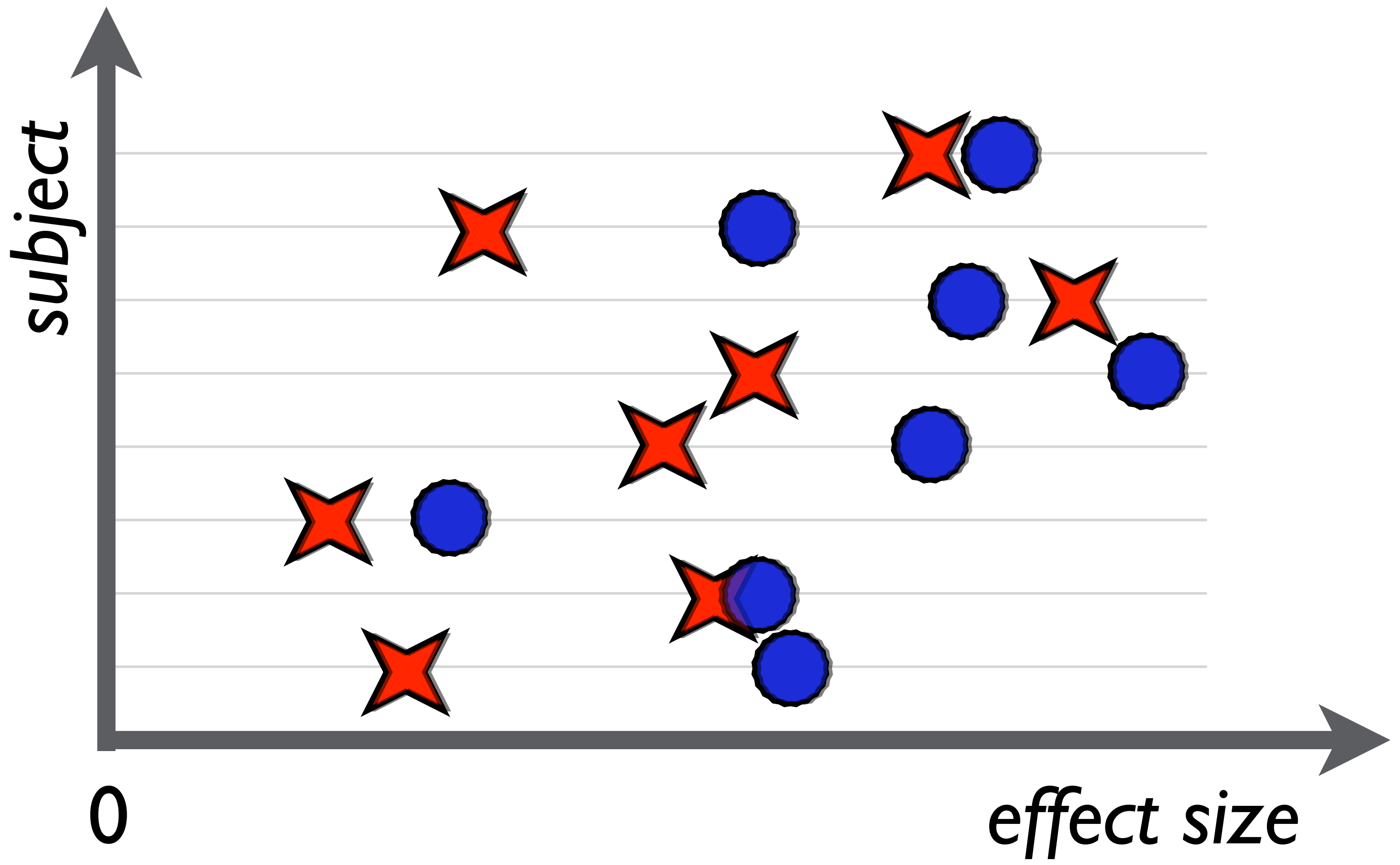


Paired T-test

Paired T-Test

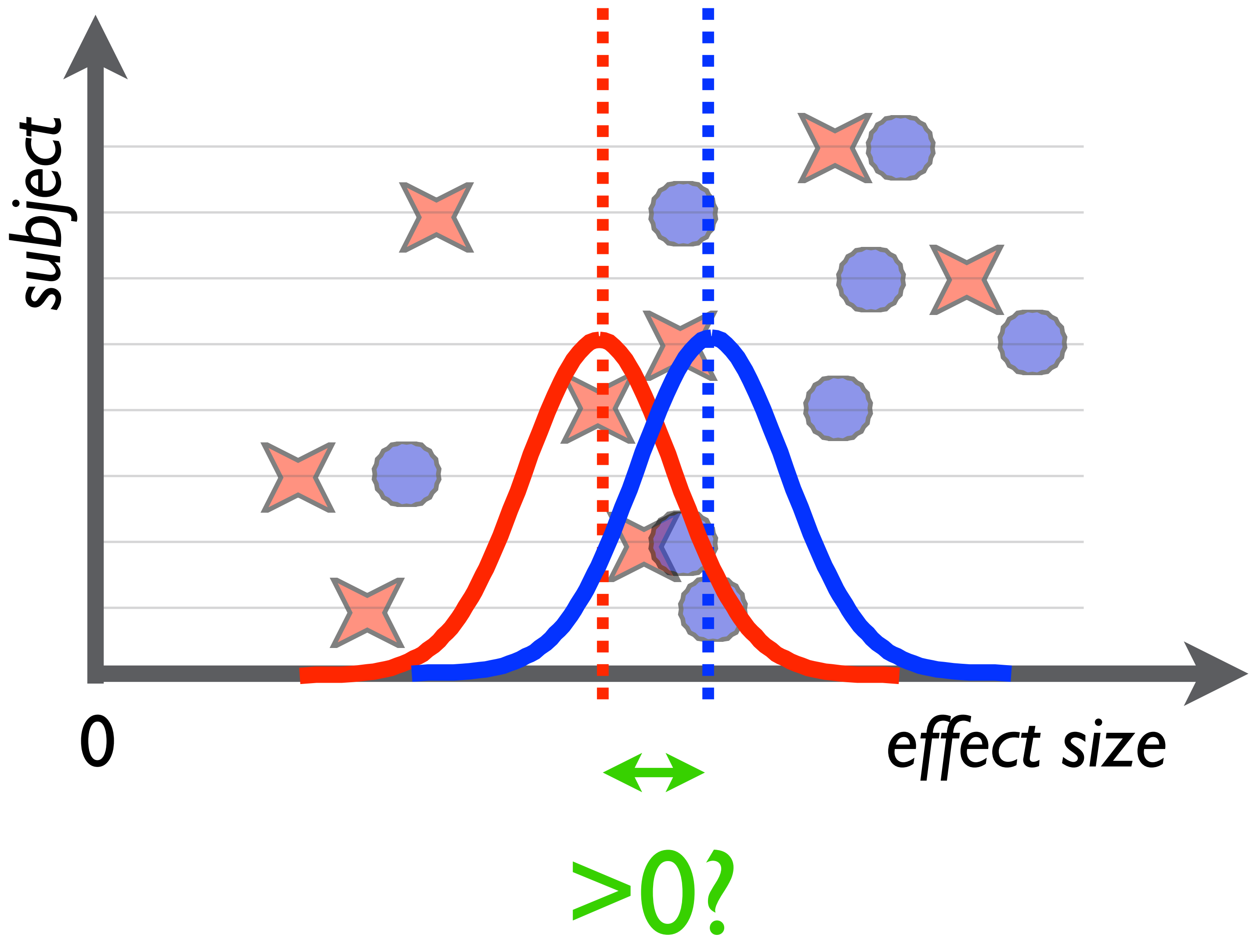
- 8 subjects scanned under 2 conditions (A,B)

  Is there a significant difference between conditions?

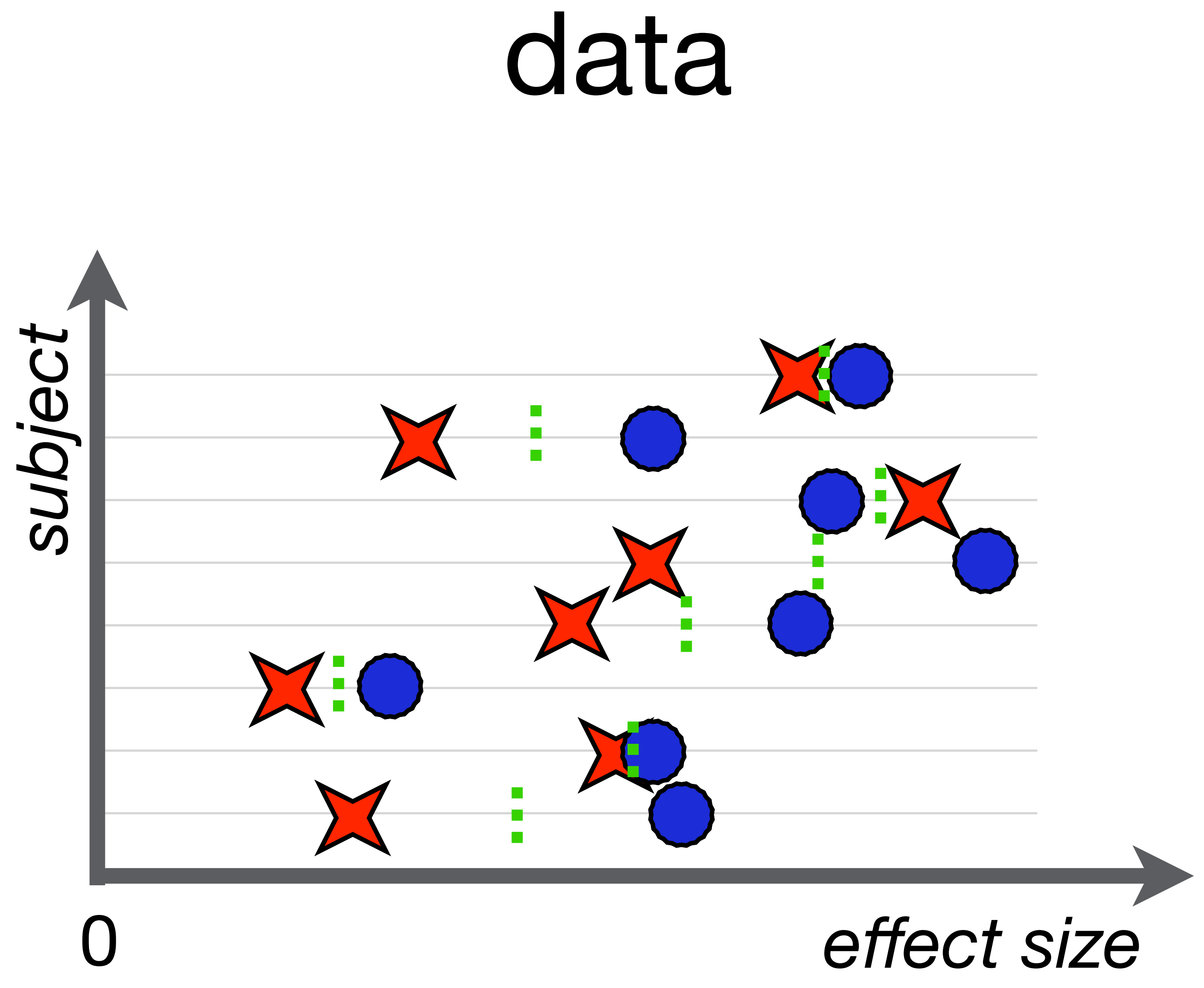


Paired T-Test

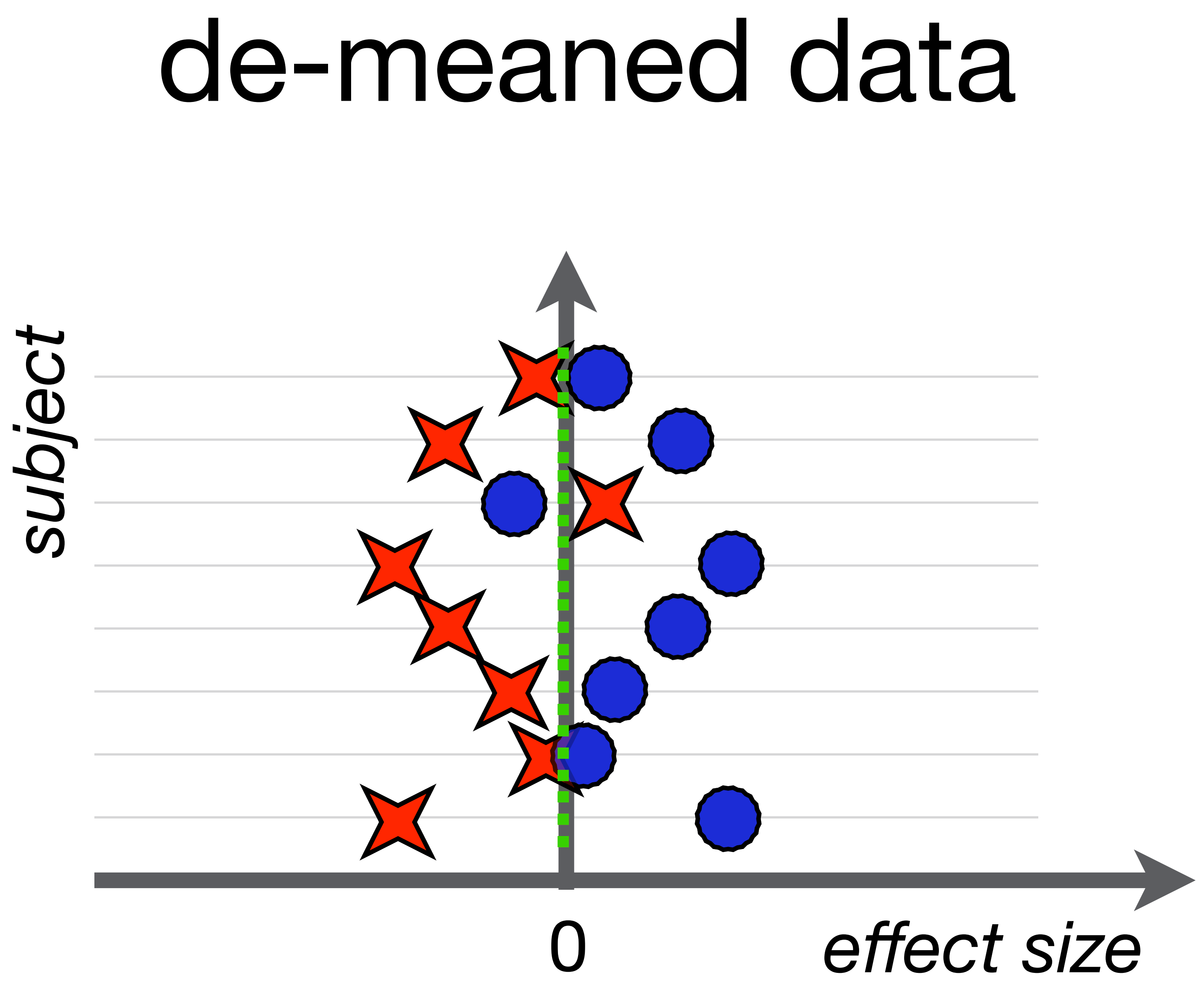
First, let's try an unpaired T-test



Paired T-Test

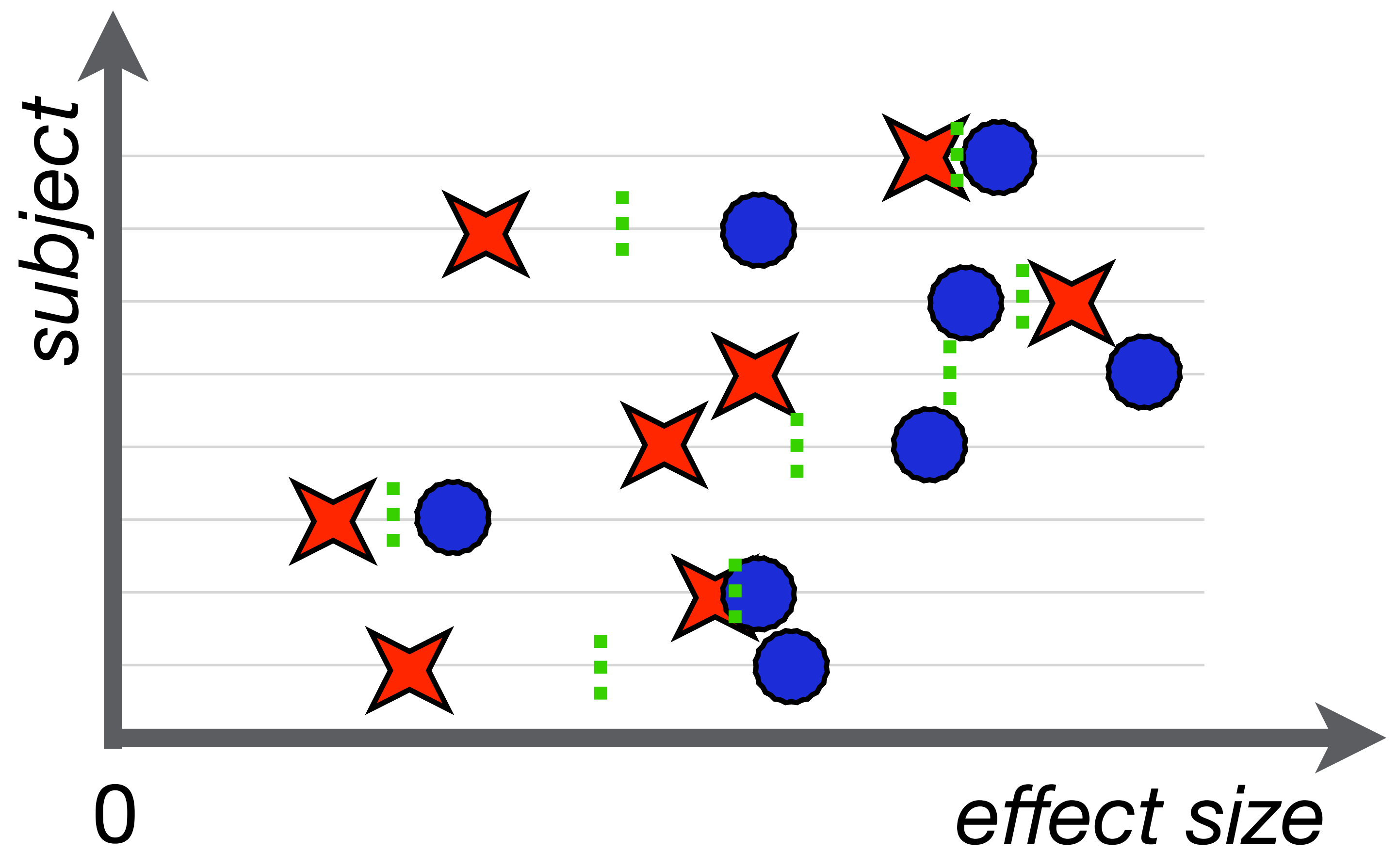


subject mean accounts for large prop. of the overall variance



Paired T-Test

data



subject mean
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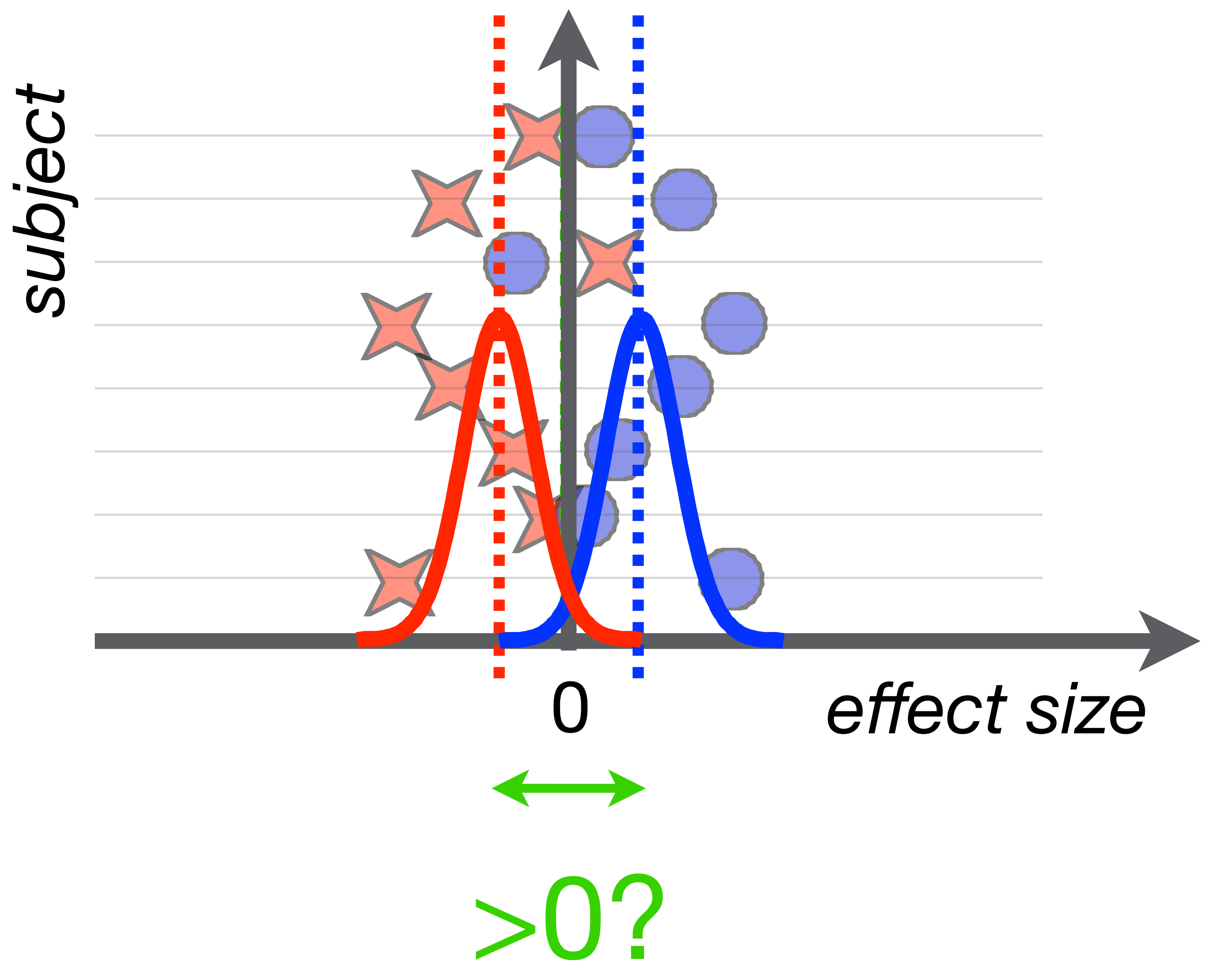
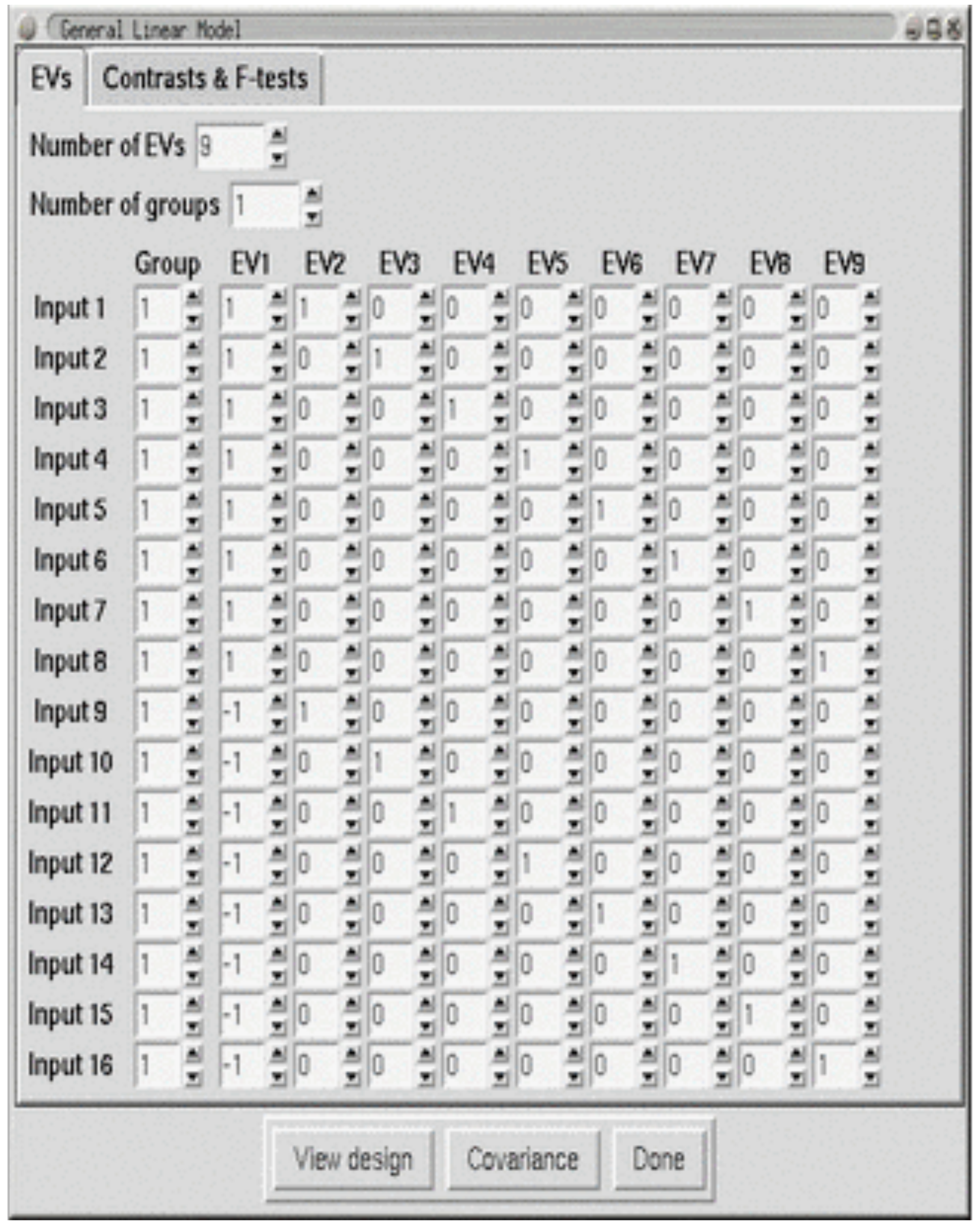
of the overall variance

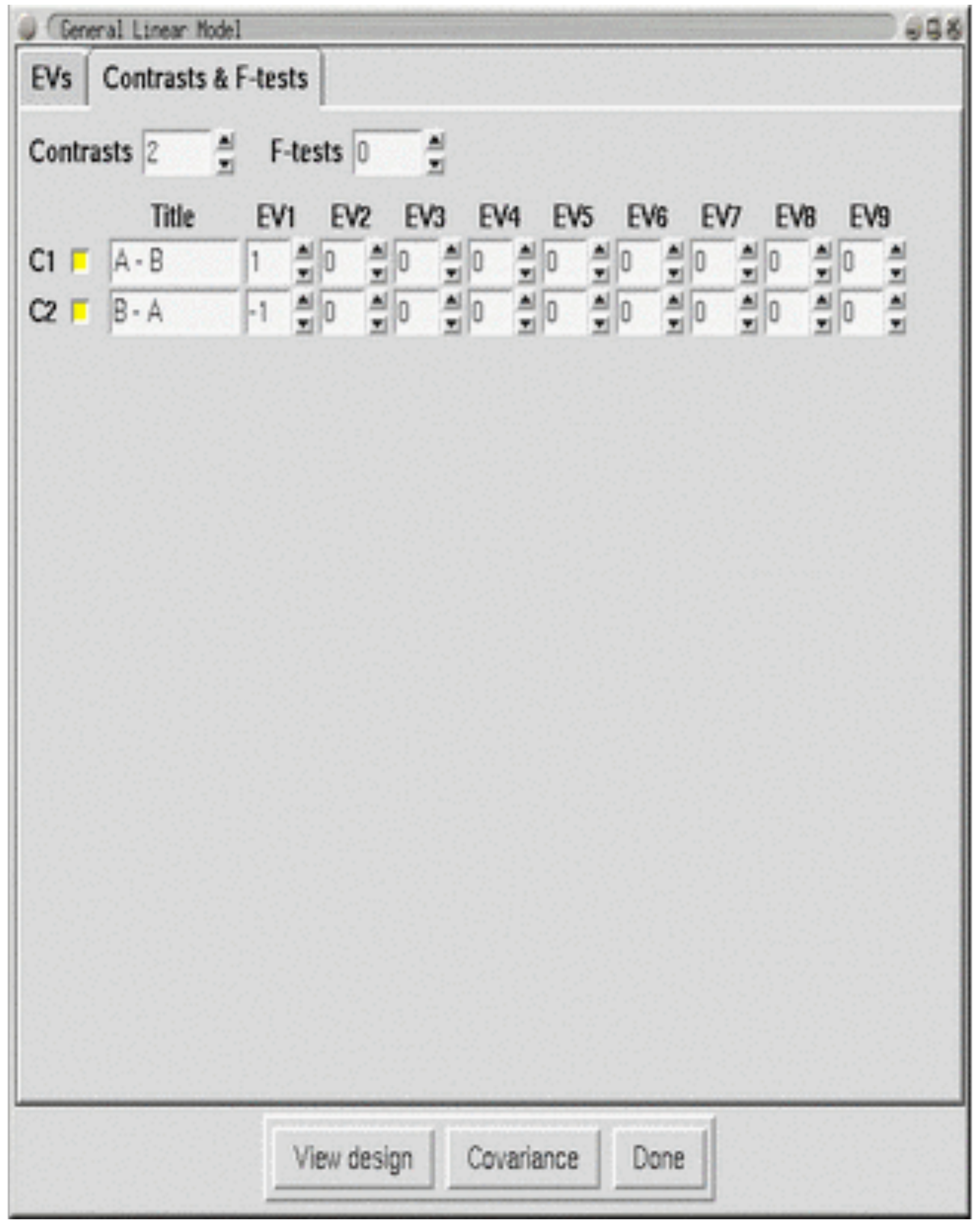
de-meaned data

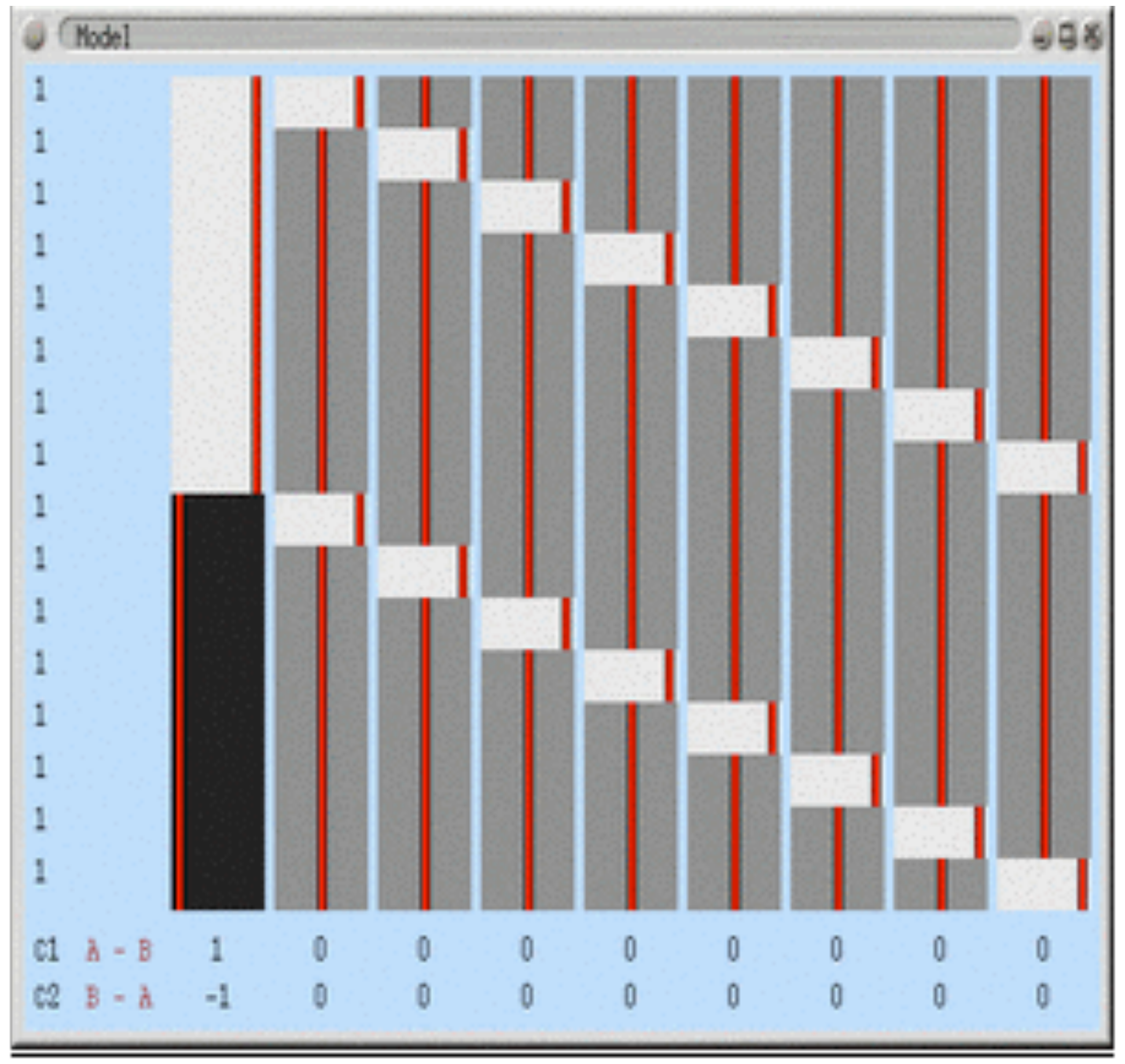


Paired T-Test

Model out each subject's mean



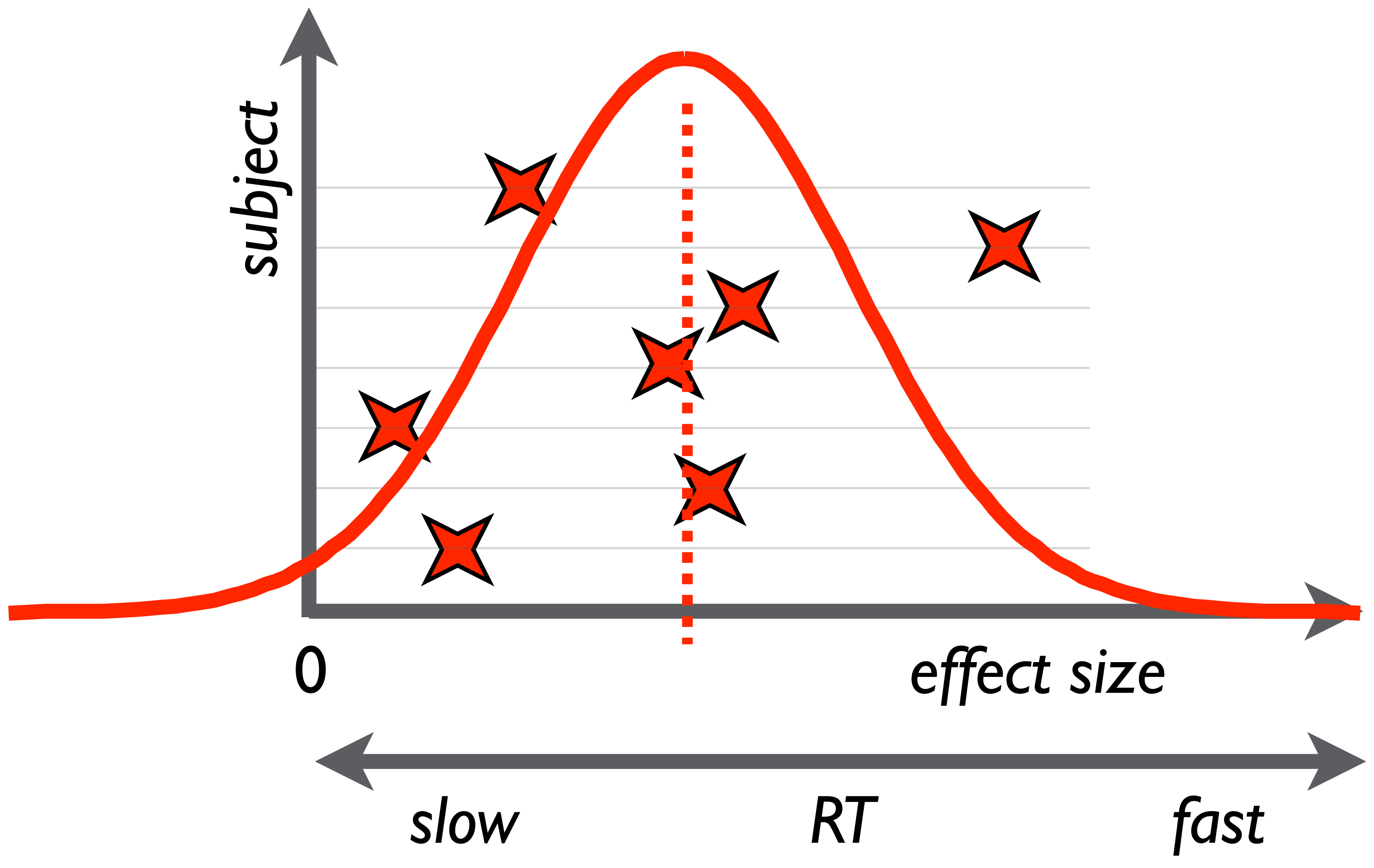




Group average with covariate

Group average with covariate

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



Group average with covariate

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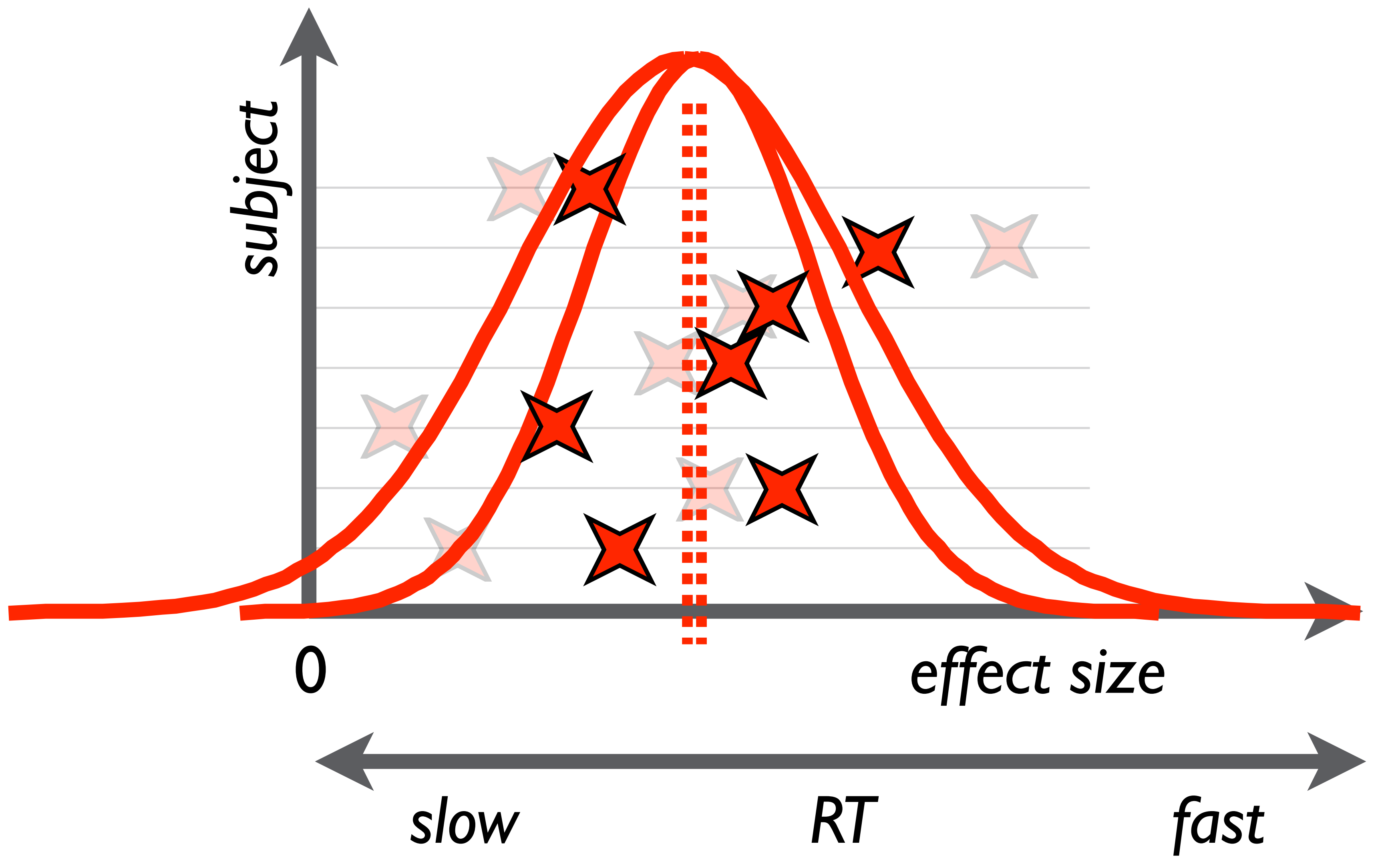
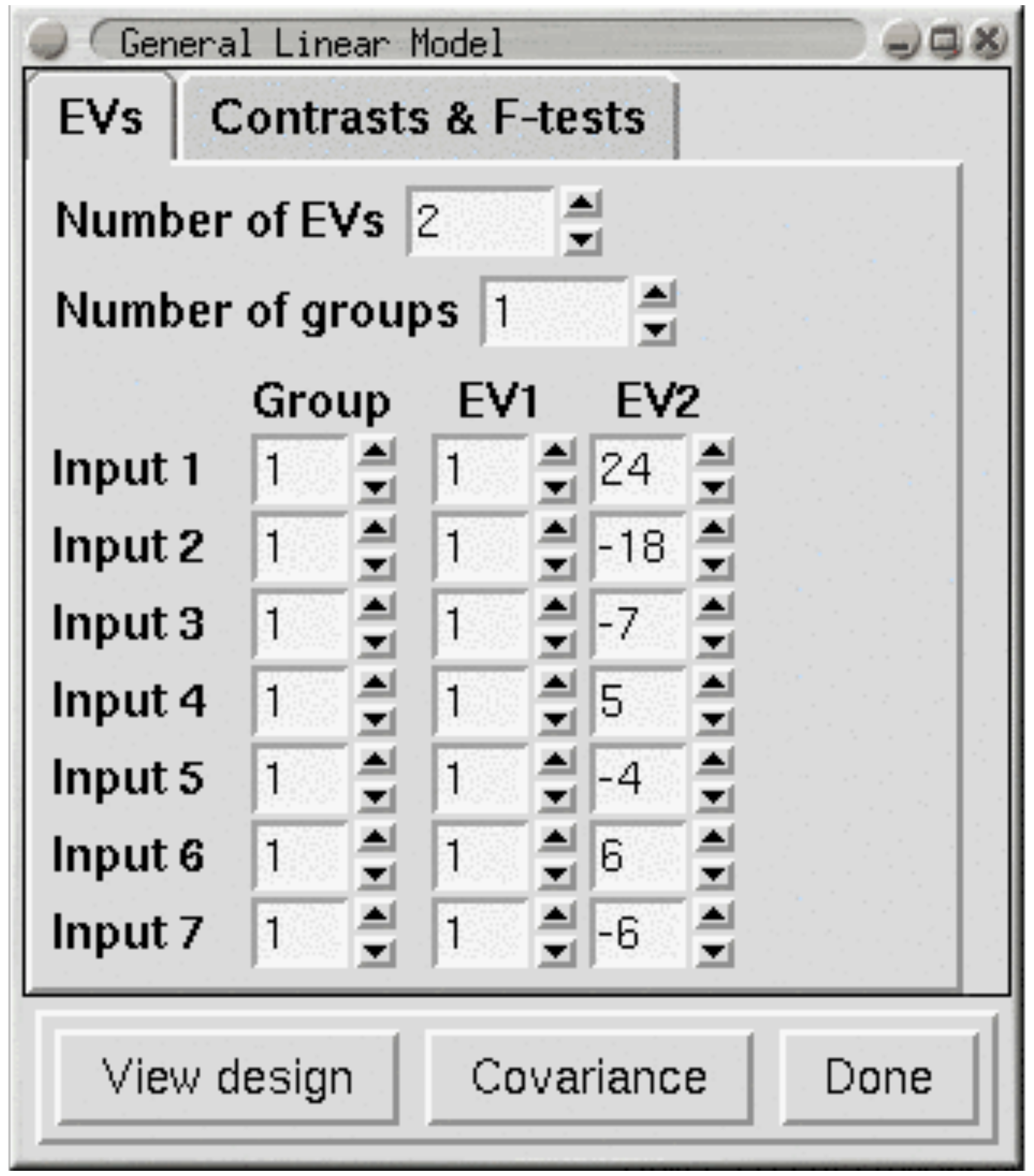
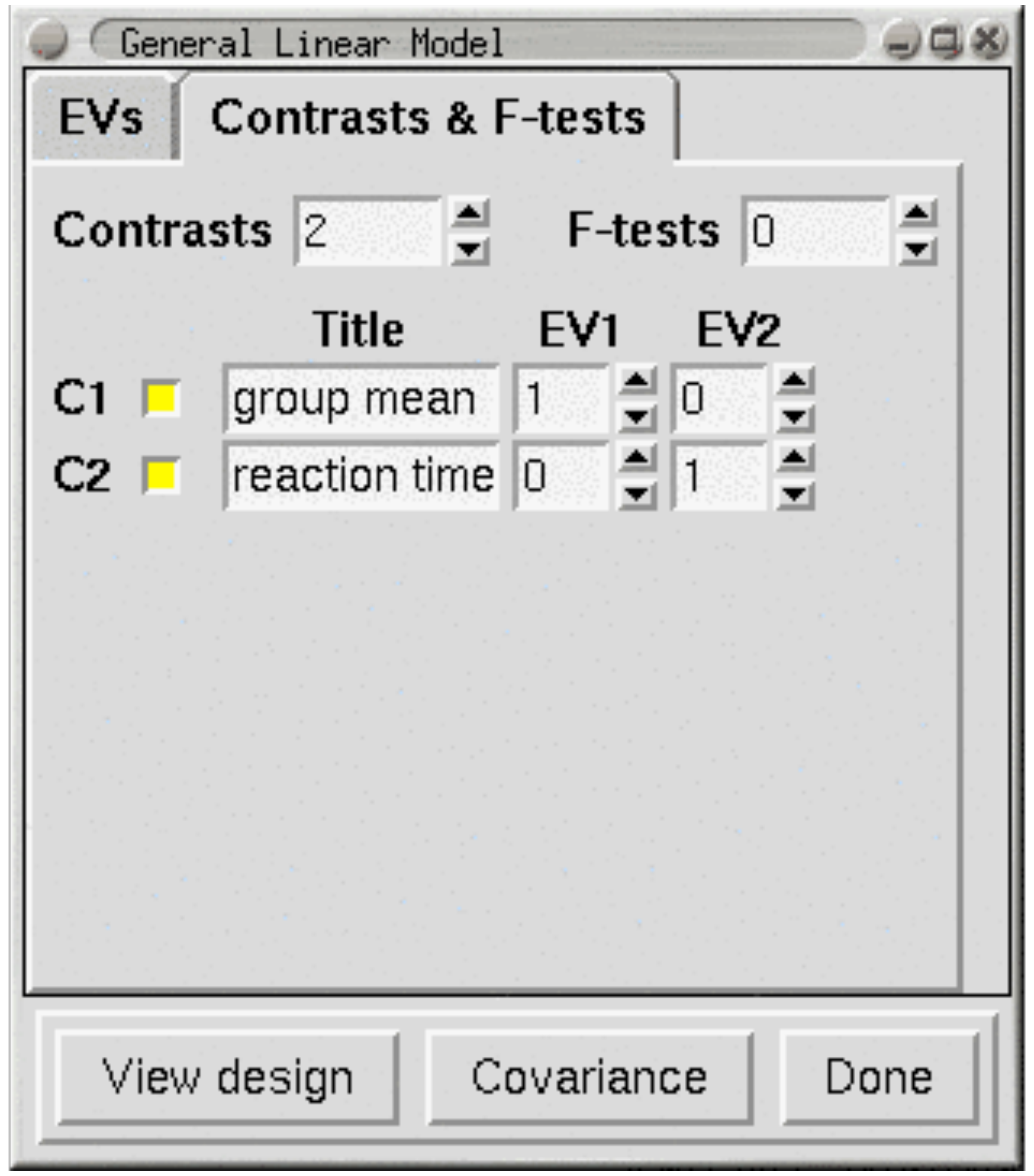
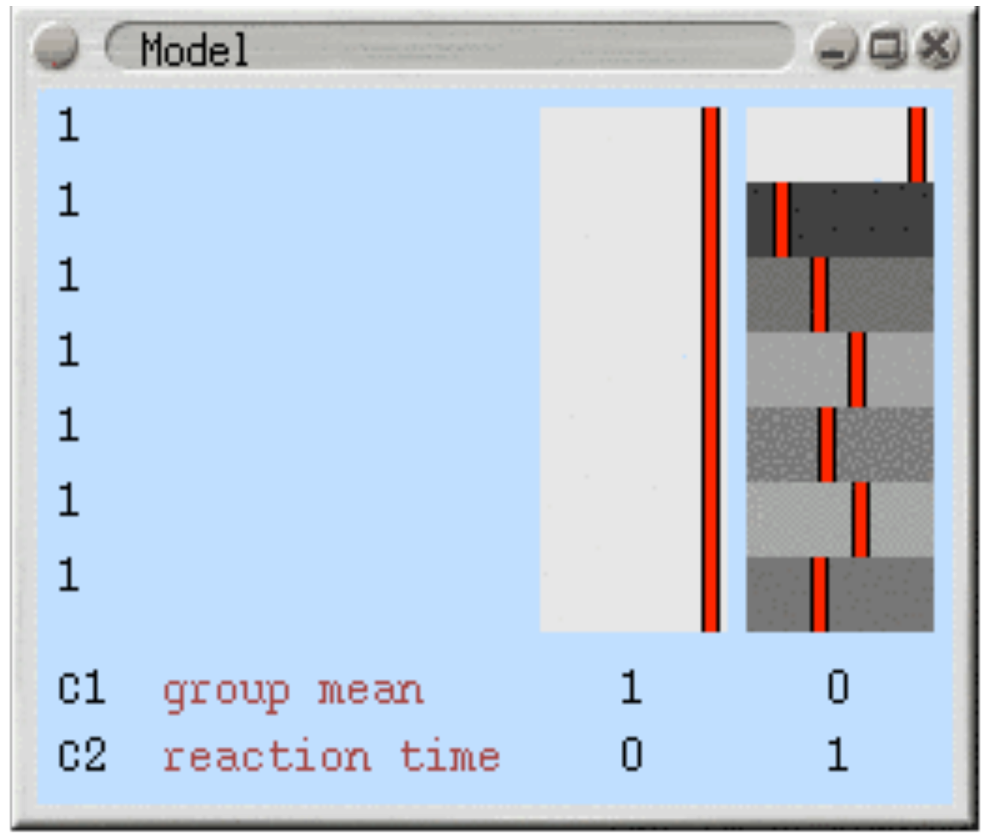


Group average with covariate

Need to demean covariates







Break Time!