# Group Analyses

*With many thanks to Guillaume Flandin, W. Penny, S. Kiebel, T. Nichols, R. Henson, J.-B. Poline, F. Kherif*

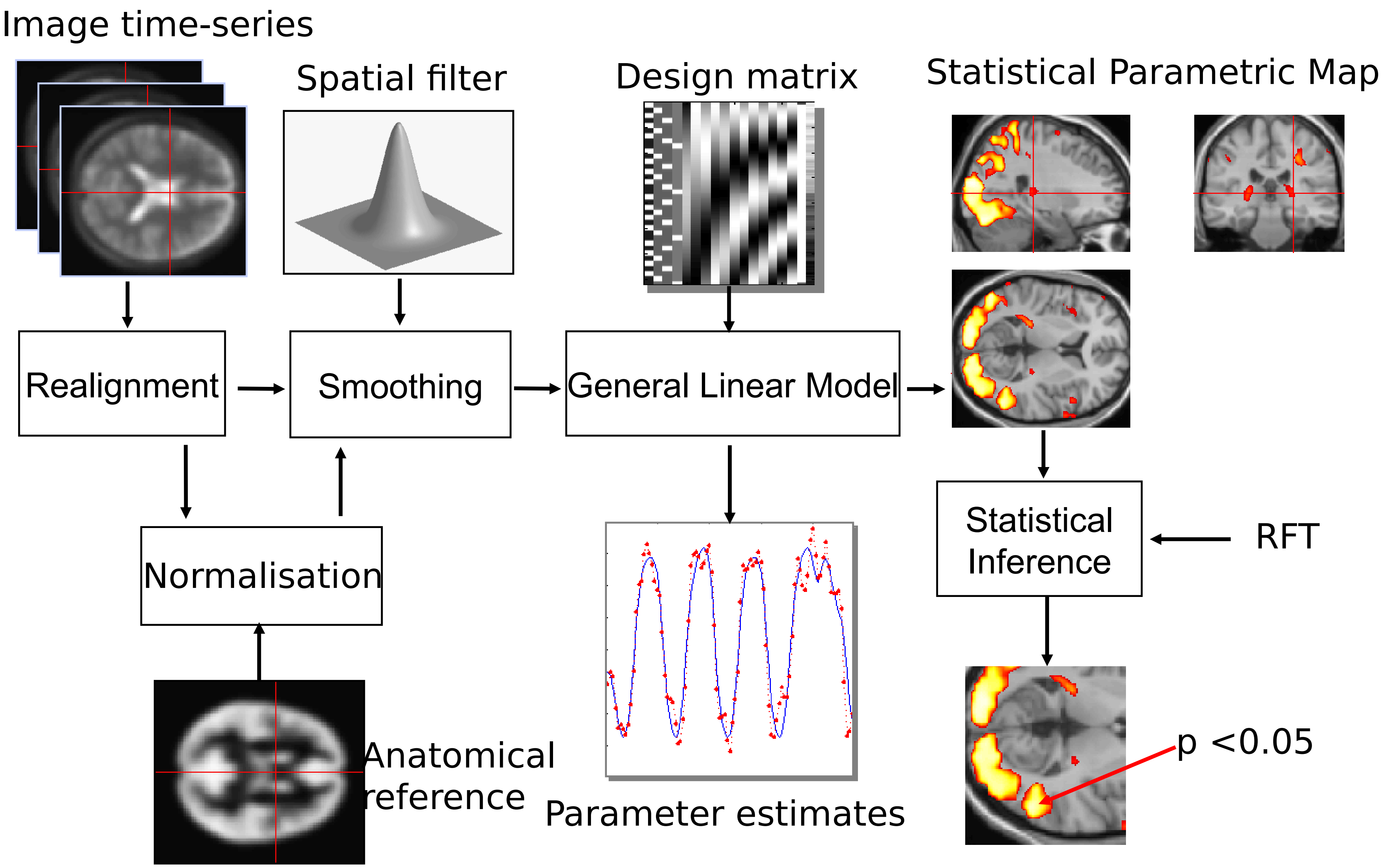
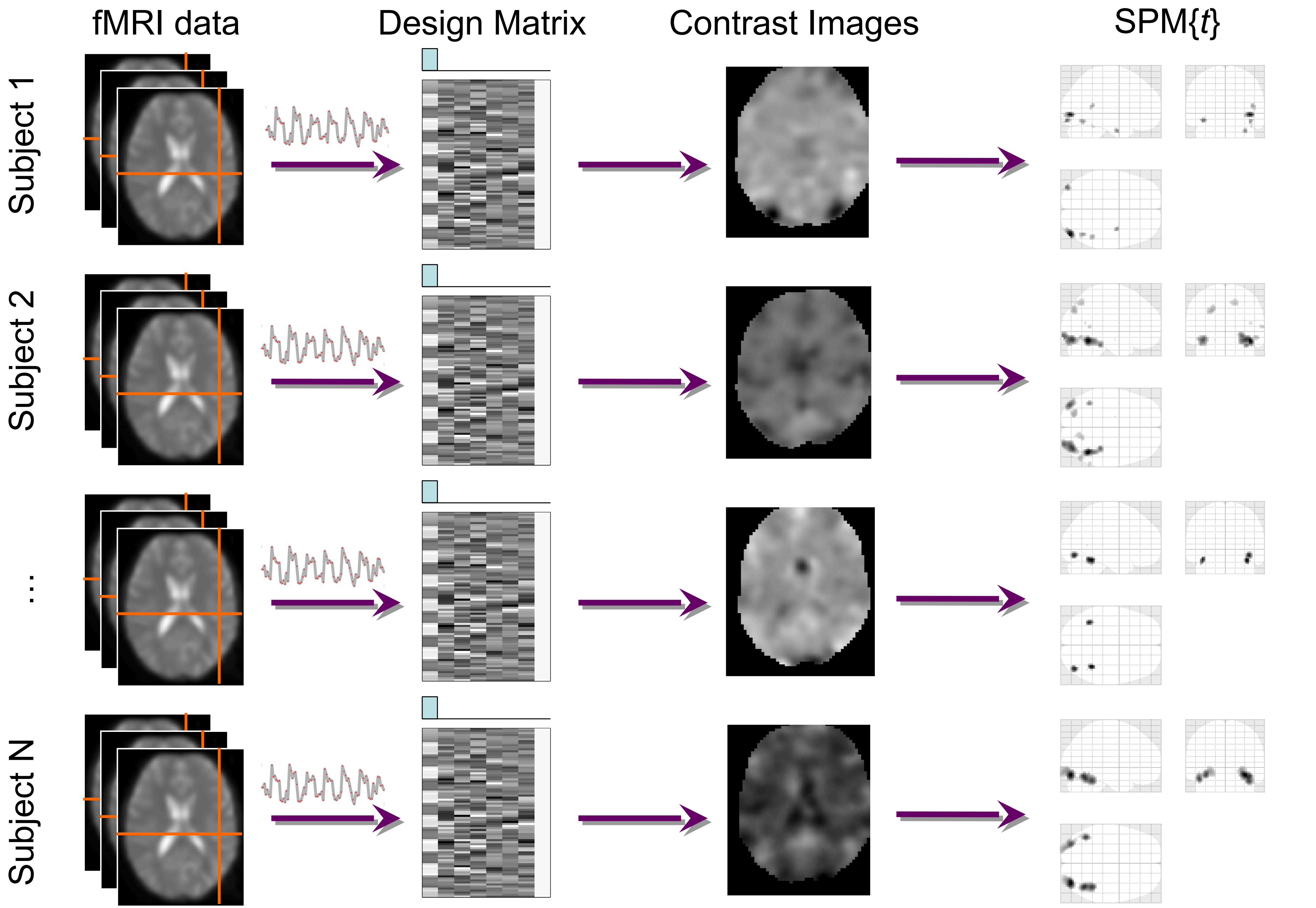
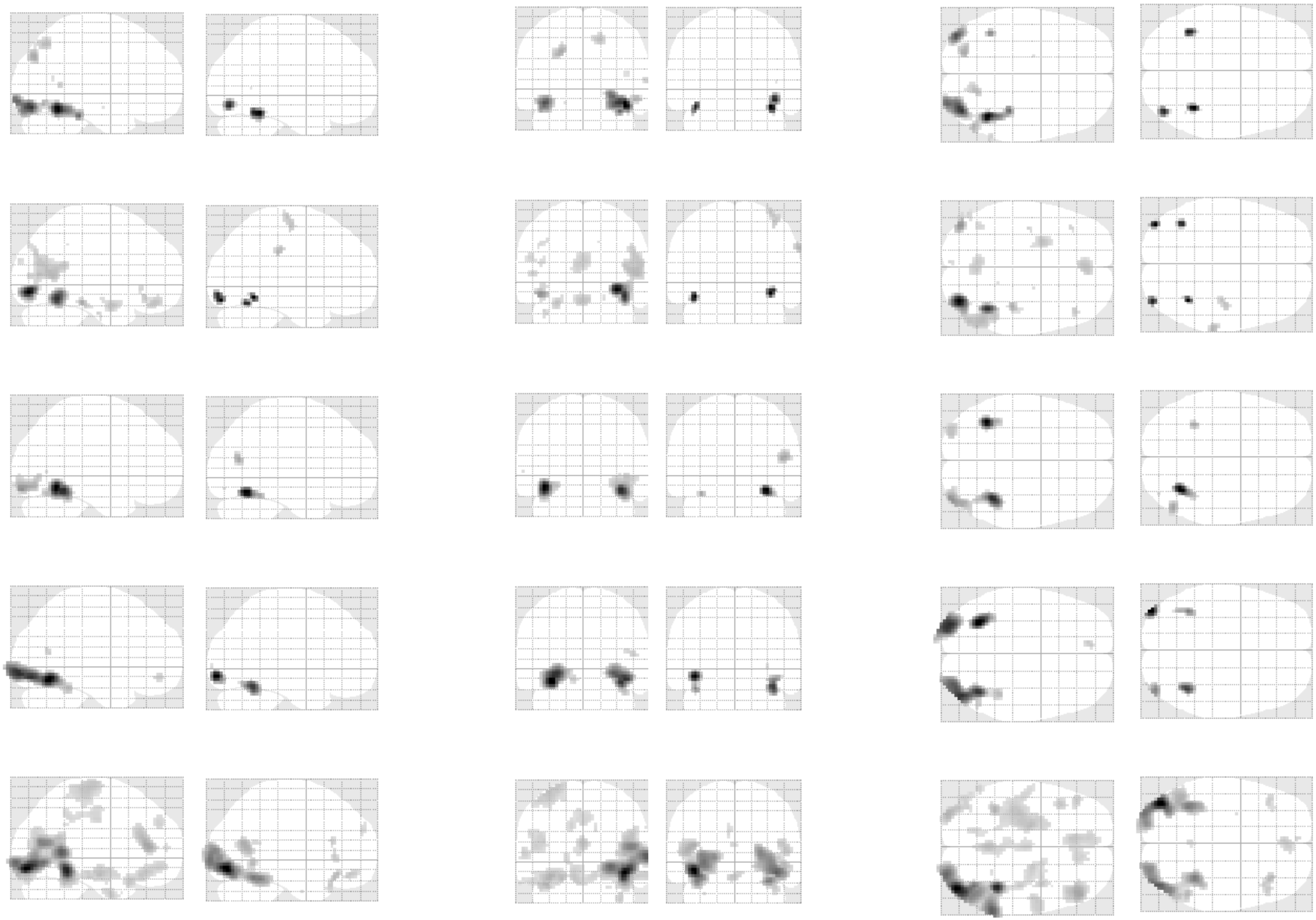


Image time-series
Spatial filter
Design matrix
Statistical Parametric Map
Realignment
Smoothing
General Linear Model
Normalisation
Anatomical reference
Parameter estimates
Statistical Inference
RFT
p <0.05

# GLM: repeat over subjects



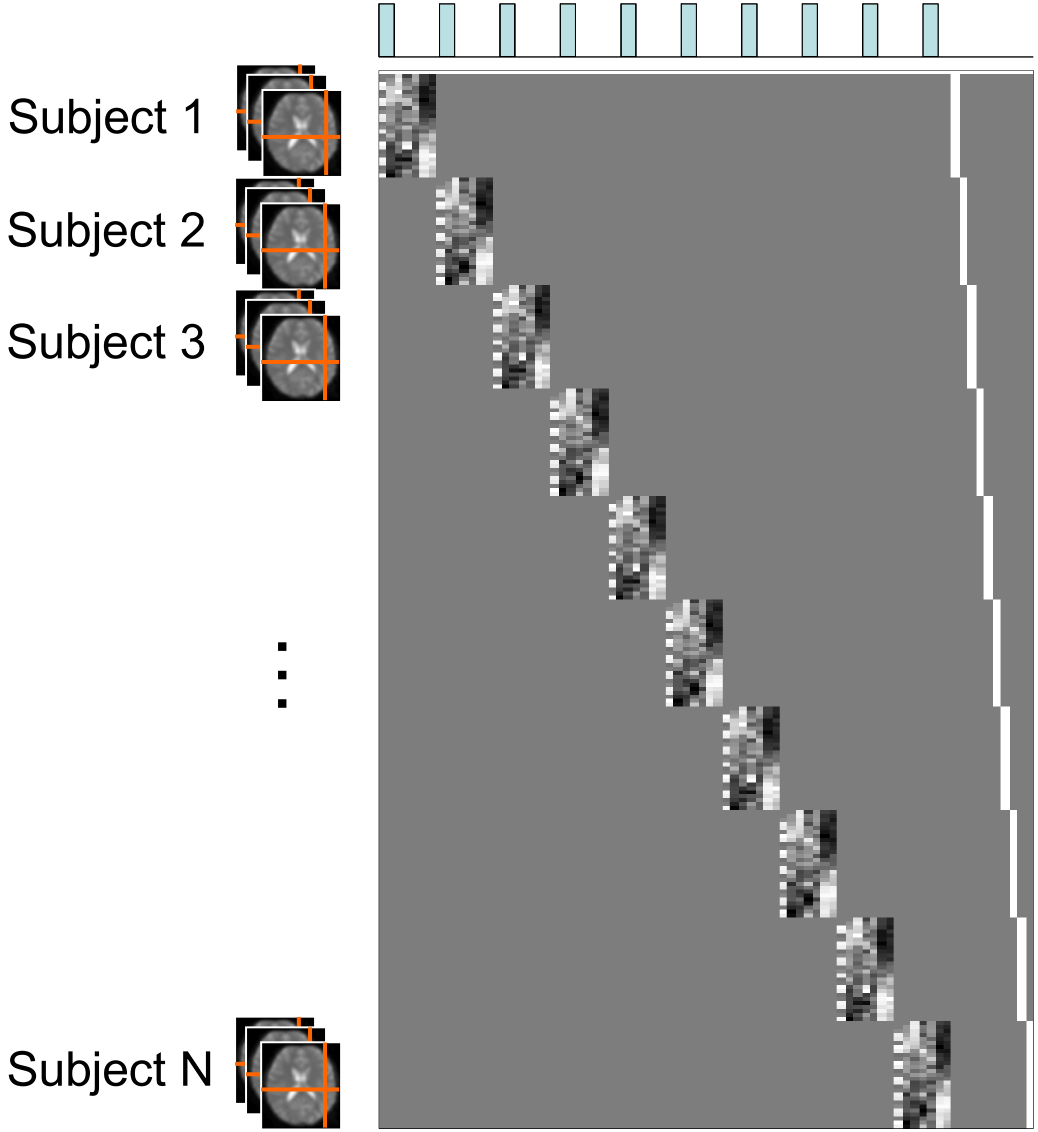
# First level analyses ($p<0.05$ FWE):



Data from R. Henson

# Fixed effects analysis (FFX)

Implicit HM: Strong pooling across rows and columns (contrast).



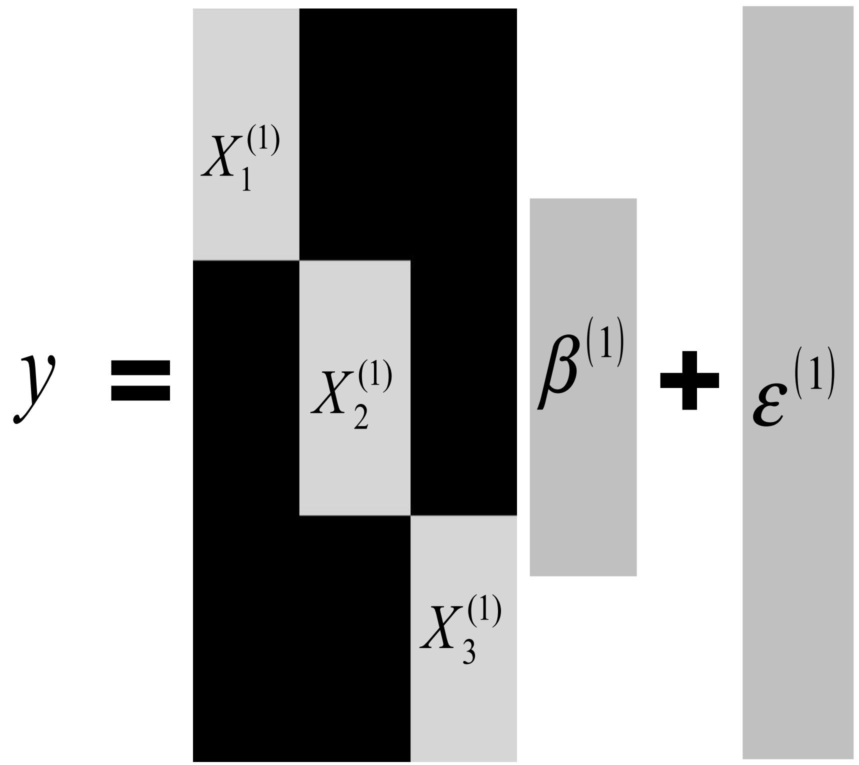

## Modelling all subjects at once

- ☑ Simple model
- ☑ Lots of degrees of freedom

- ☒ Large amount of data
- ☒ Assumes common variance over subjects at each voxel

# Fixed effects analysis (FFX)

$$y = X^{(1)}\beta^{(1)} + \varepsilon^{(1)}$$

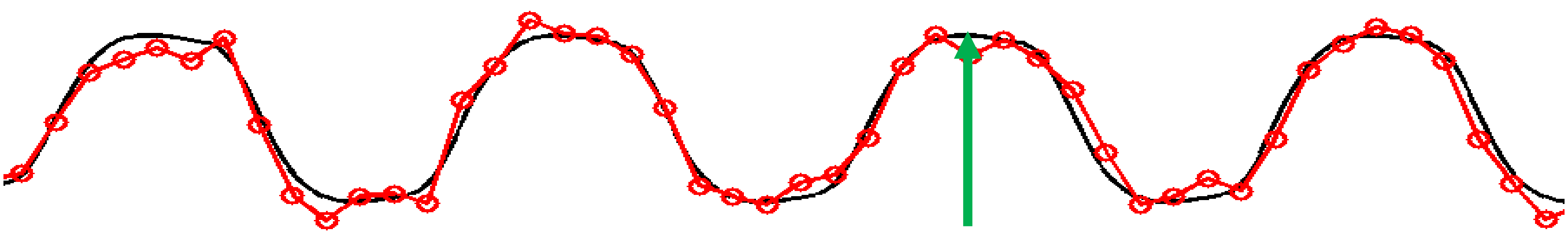



Modelling all subjects at once

- ☑ Simple model
- ☑ Lots of degrees of freedom
- ☒ Large amount of data
- ☒ Assumes common variance over subjects at each voxel

# Fixed effects

$$y = X^{(1)}\beta^{(1)} + \varepsilon^{(1)}$$



- Only one source of random variation (over sessions):
  - measurement error

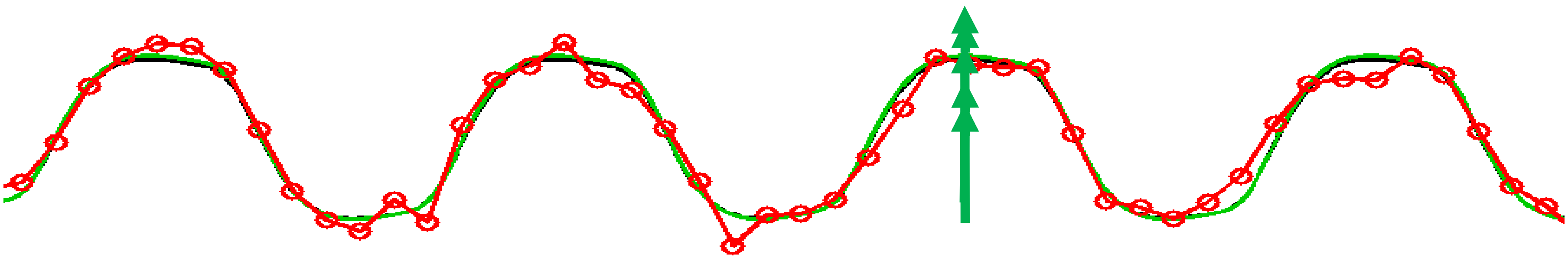
Within-subject Variance

- True response magnitude is *fixed.*

# Random effects

$$y = X^{(1)}\beta^{(1)} + \varepsilon^{(1)}$$

$$\beta^{(1)} = X^{(2)}\beta^{(2)} + \varepsilon^{(2)}$$



- Two sources of random variation:
  - measurement errors
  - response magnitude (over subjects)

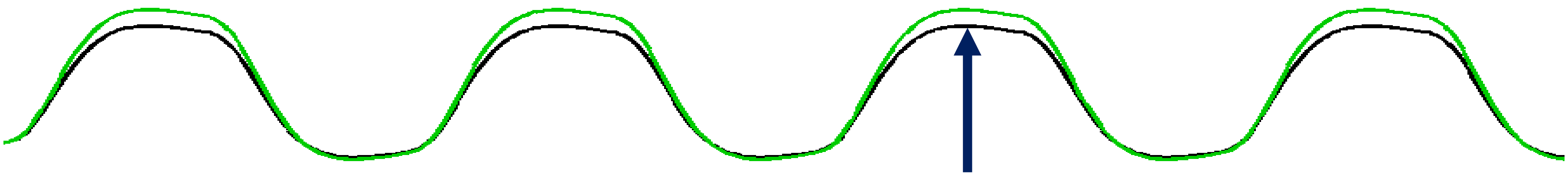
Within-subject Variance

Between-subject Variance

- Response magnitude is *random*
  - each subject/session has random magnitude

# Random effects

$$y = X^{(1)}\beta^{(1)} + \varepsilon^{(1)}$$
$$\beta^{(1)} = X^{(2)}\beta^{(2)} + \varepsilon^{(2)}$$



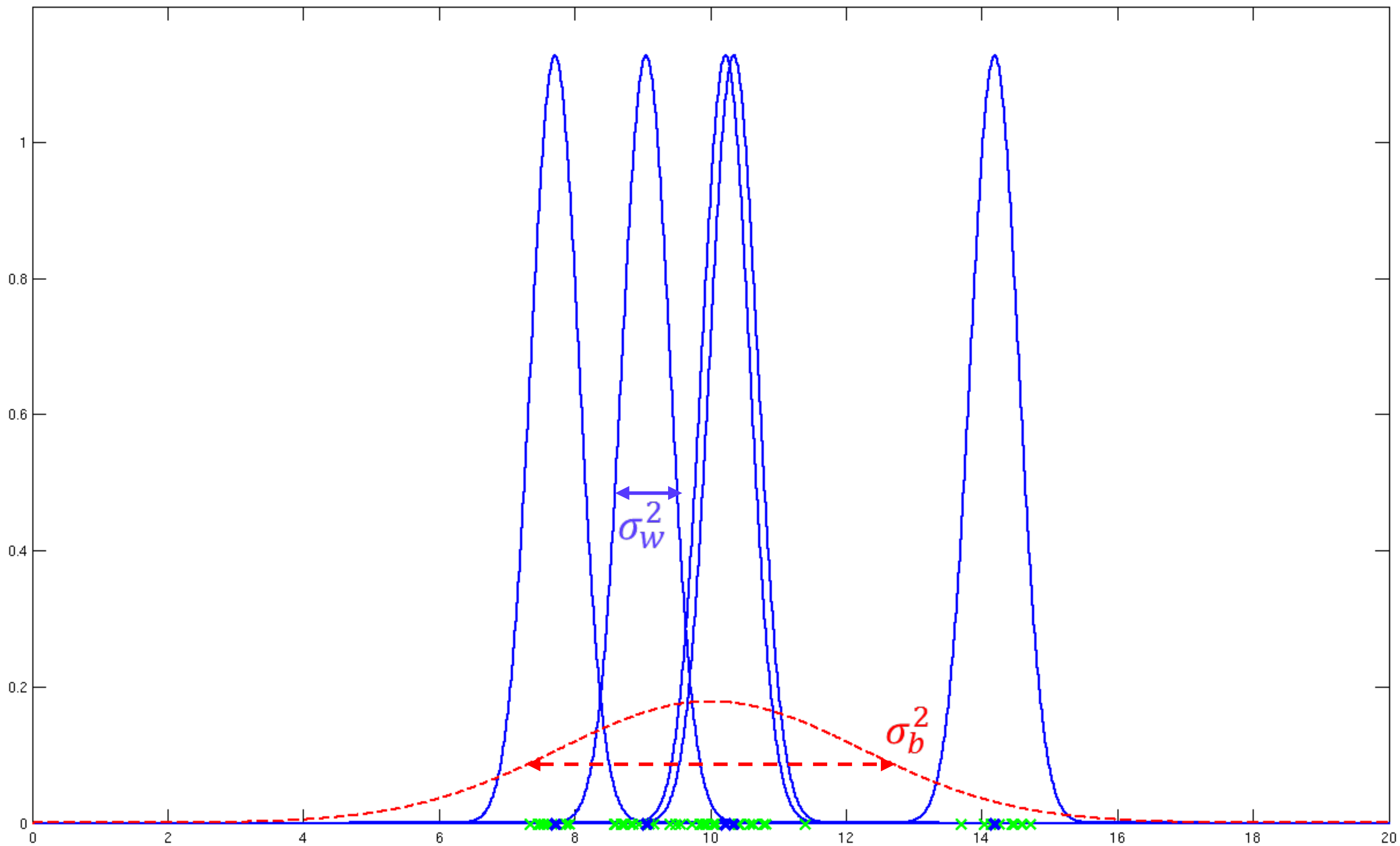
- Two sources of random variation:
  - measurement errors
  - response magnitude (over subjects)

Within-subject Variance

Between-subject Variance

- Response magnitude is *random*
  - each subject/session has random magnitude
  - but population mean magnitude is *fixed*.

# Random effects




Probability model underlying random effects analysis

# Fixed vs random effects

With **Fixed Effects Analysis (FFX)** we compare the group effect to the *within-subject variability*. It is not an inference about the population from which the subjects were drawn.

With **Random Effects Analysis (RFX)** we compare the group effect to the *between-subject variability*. It is an inference about the population from which the subjects were drawn. If you had a new subject from that population, you could be confident they would also show the effect.

# Fixed vs random effects

- Fixed isn't "wrong", just usually isn't of interest.

- Summary:
  - **Fixed effects inference**:
  *"I can see this effect in this cohort"*

  - **Random effects inference**:
  *"If I were to sample a new cohort from the same population I would get the same result"*

# Terminology

**Hierarchical linear models:**

- Random effects models
- Mixed effects models
- Nested models
- Variance components models

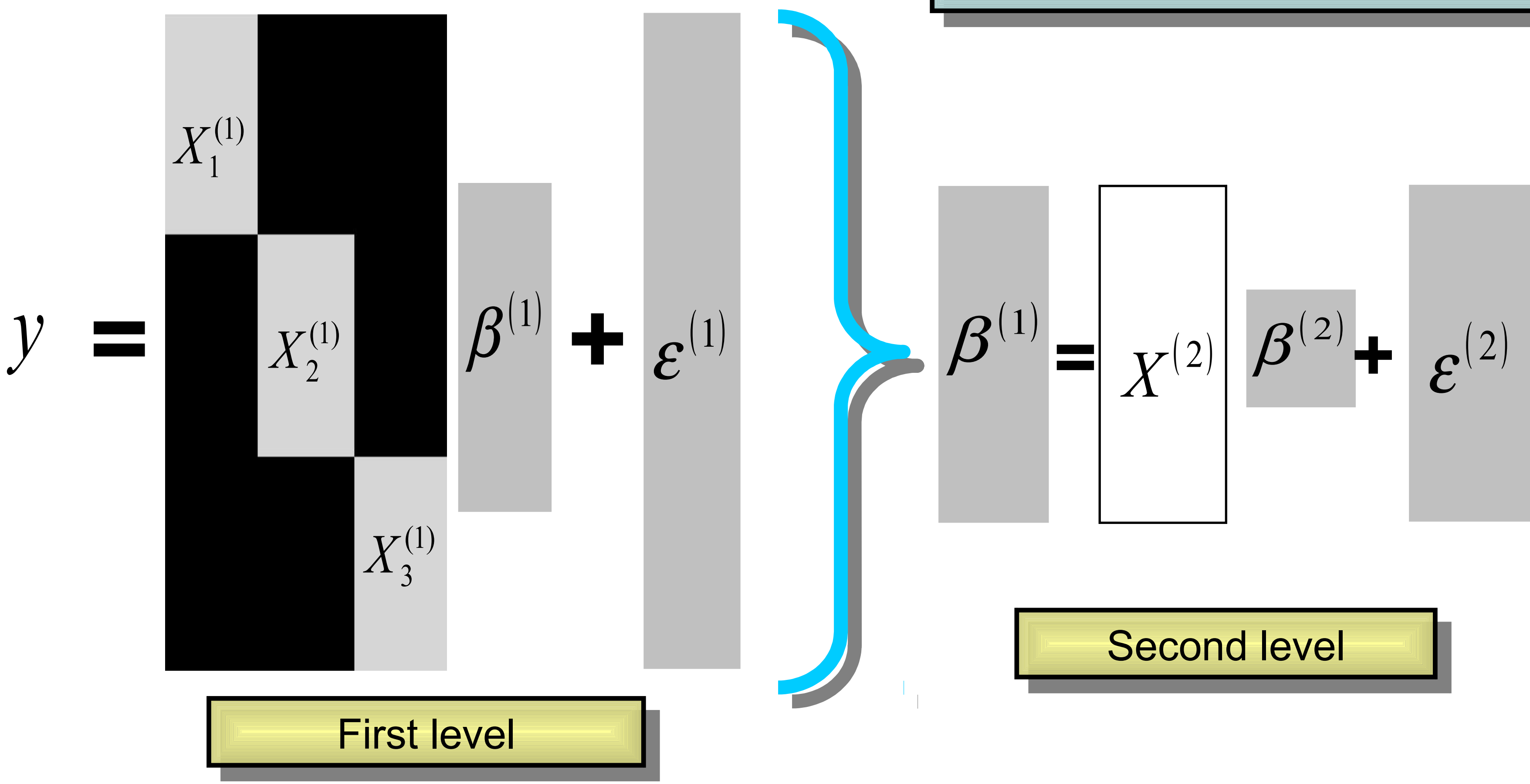
… all the same

… all alluding to multiple sources of variation
(in contrast to fixed effects)

# Hierarchical models

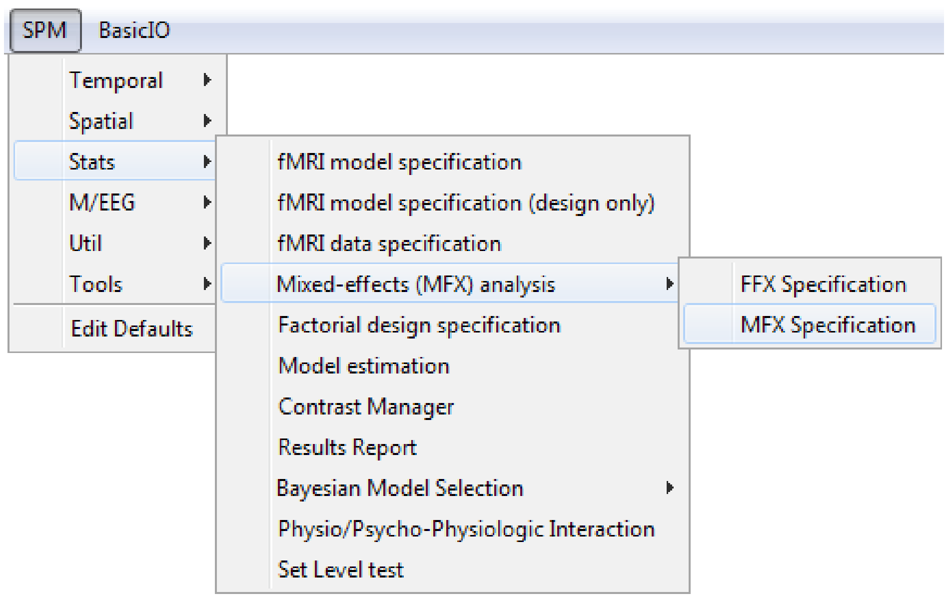
Example: Two level model

$$y = X^{(1)}\beta^{(1)} + \varepsilon^{(1)}$$
$$\beta^{(1)} = X^{(2)}\beta^{(2)} + \varepsilon^{(2)}$$



# Hierarchical models

- Restricted Maximum Likelihood (ReML)
- Parametric Empirical Bayes
- Expectation-Maximisation Algorithm



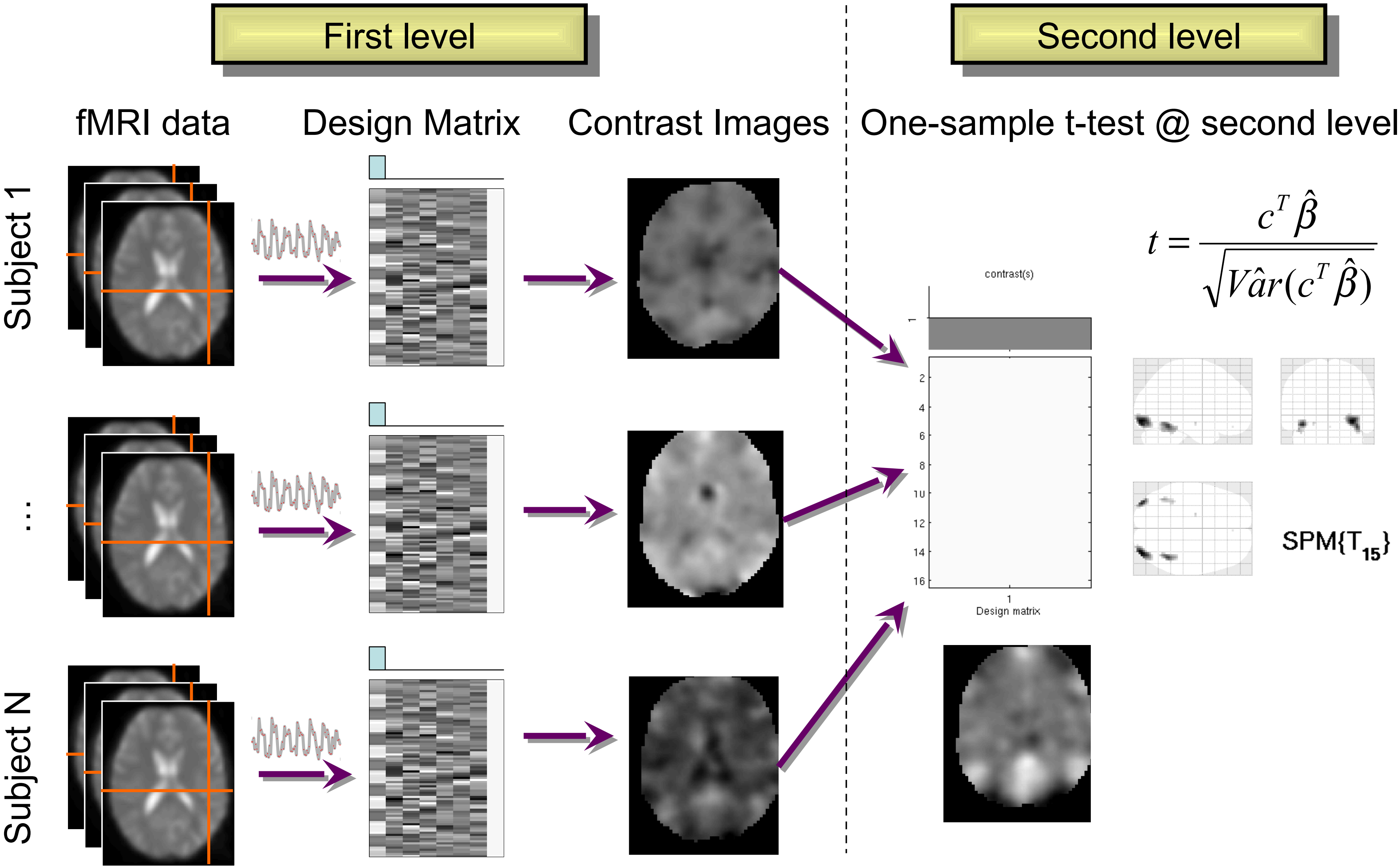

`spm_mfx.m`

**But:**

- Many two level models are just too big to compute.
- And even if, it takes a long time!
- Any approximation?

*Mixed-effects and fMRI studies*. Friston et al., NeuroImage, 2005.

# Summary Statistics RFX Approach




*Generalisability, Random Effects & Population Inference*. Holmes & Friston, NeuroImage,1998.

# Summary Statistics RFX Approach

## Assumptions

- The summary statistics approach is exact if for each session/subject:
  - Within-subjects variances the same
  - First level design the same (e.g. number of trials)
- Other cases: summary statistics approach is robust against typical violations.


*Mixed-effects and fMRI studies*. Friston et al., NeuroImage, 2005.

*Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Elsevier, 2007.

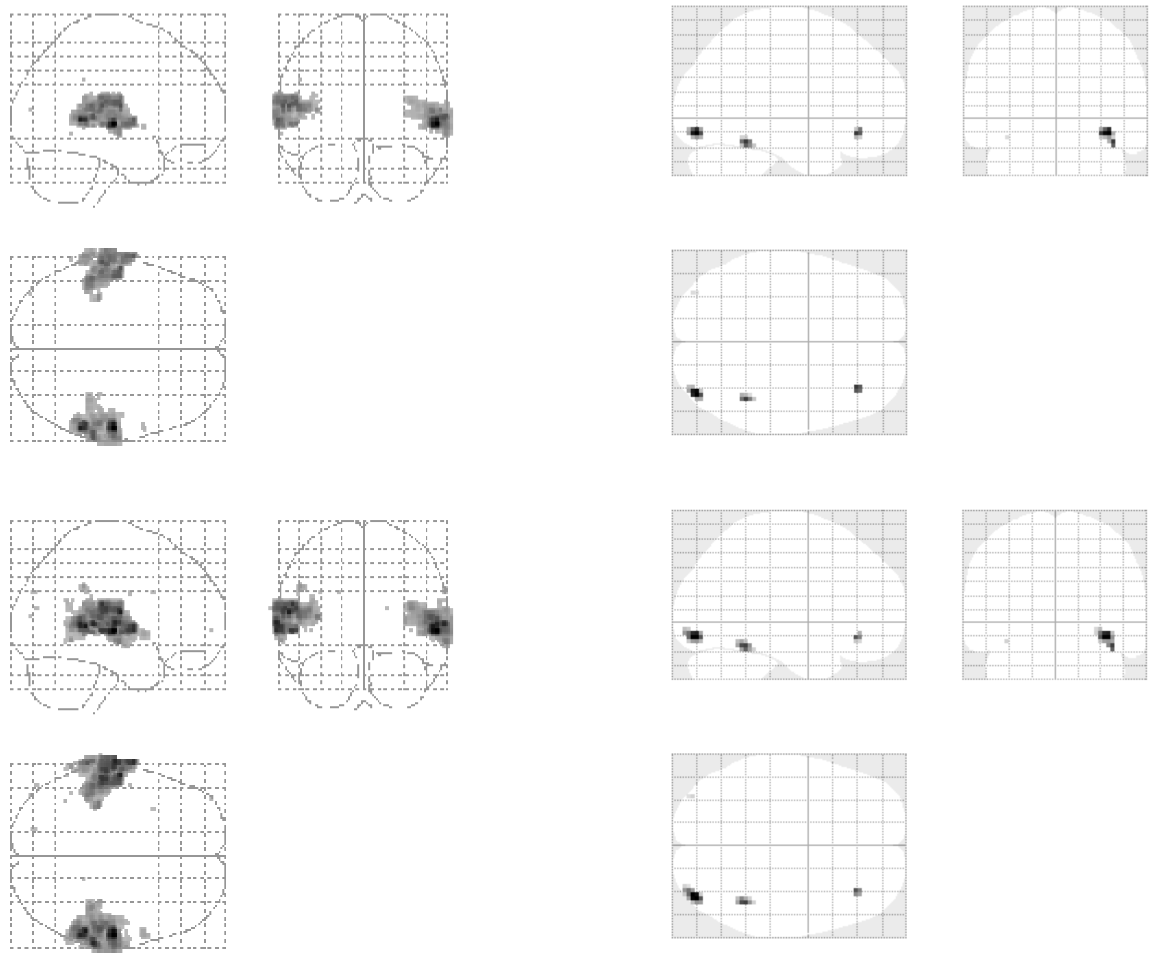
*Simple group fMRI modeling and inference*. Mumford & Nichols. NeuroImage, 2009.

# Summary Statistics RFX Approach

## Robustness

Summary statistics

Hierarchical Model



Listening to words

Viewing faces

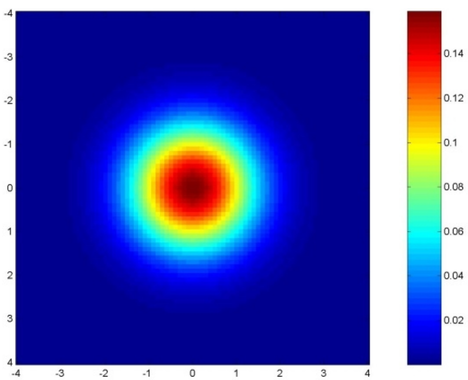
*Mixed-effects and fMRI studies*. Friston et al., NeuroImage, 2005.

# ANOVA & non-sphericity

- **One effect per subject:**
  - Summary statistics approach
  - One-sample t-test at the second level
- **More than one effect per subject or multiple groups:**
  - Non-sphericity modelling
  - Covariance components and ReML

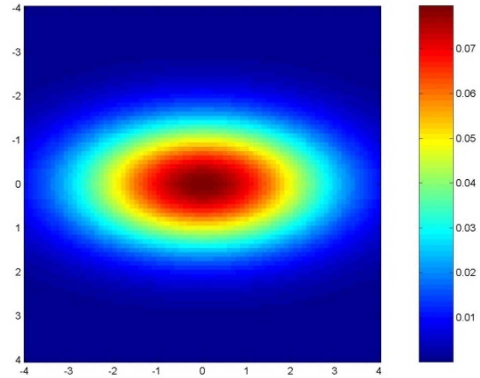
# GLM assumes Gaussian “spherical” (i.i.d.) errors

**sphericity = iid:**
error covariance is
scalar multiple of
identity matrix:
**Cov(e) = $\sigma^2$I**



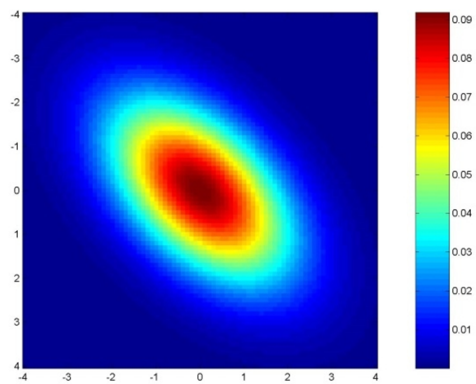

$$Cov(e) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

## Examples for non-sphericity:




$$Cov(e) = \begin{bmatrix} 4 & 0 \\ 0 & 1 \end{bmatrix}$$

non-identically distributed



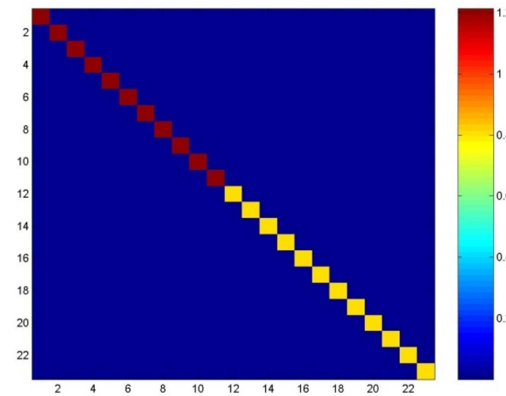

$$Cov(e) = \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix}$$

non-independent

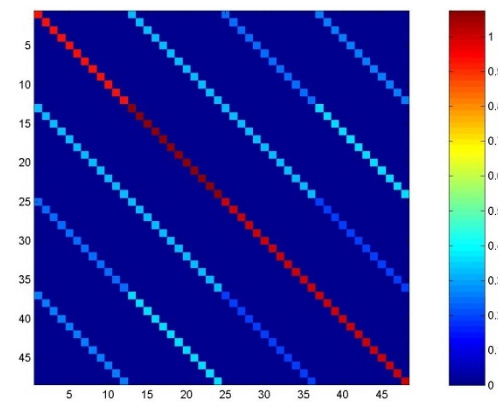
# 2nd level: Non-sphericity

Error covariance matrix

Errors are independent
but not identical
(e.g. different groups (patients, controls))



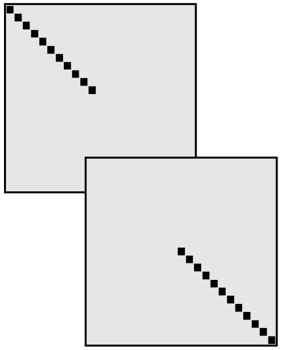
Errors are not independent
and not identical
(e.g. repeated measures for each subject
(multiple basis functions, multiple
conditions, etc.))



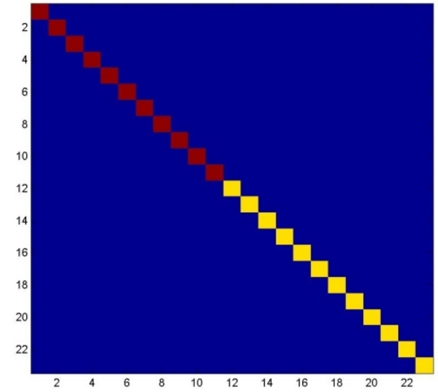
# $2^{nd}$ level: Variance components

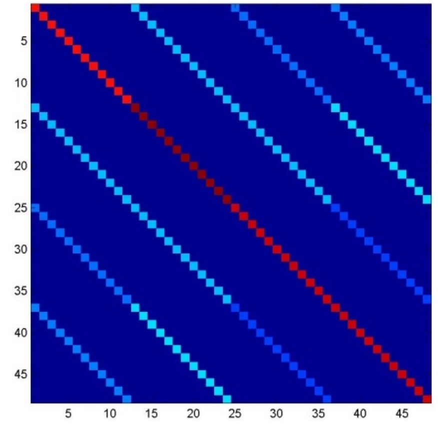
$$\mathrm{Cov}(\varepsilon) = \sum_k \lambda_k Q_k$$

$Q_k$'s:

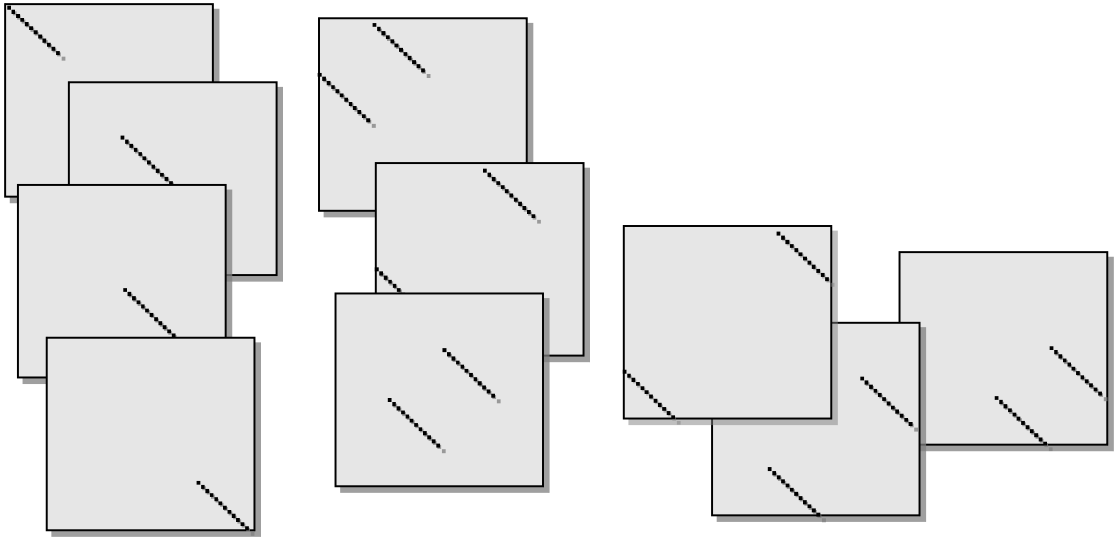


Error covariance matrix




$Q_k$'s:



# Example 1: between-subjects ANOVA

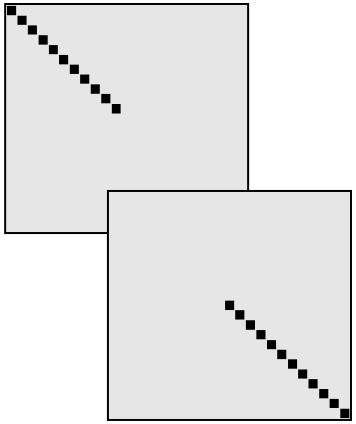
- Stimuli:
  - Auditory presentation (SOA = 4 sec)
  - 250 scans per subject, block design
  - 2 conditions
    - Words, e.g. “book”
    - Words spoken backwards, e.g. “koob”
- Subjects:
  - 12 controls
  - 11 blind people

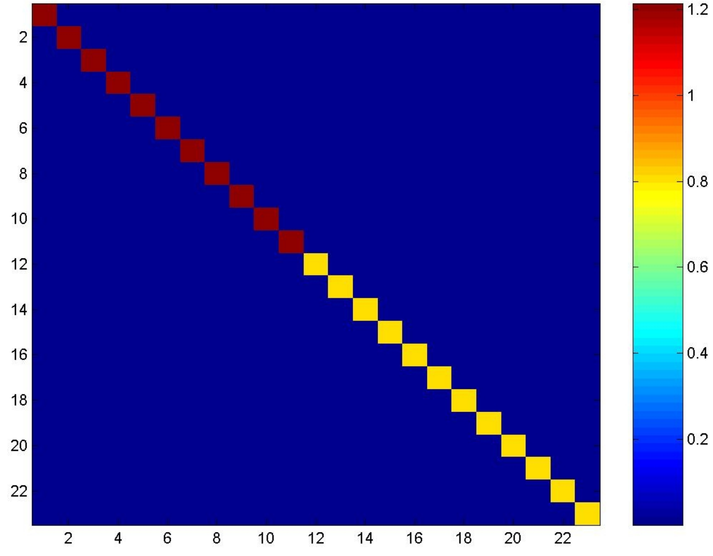
Data from Noppeney et al.

# Example 1: Covariance components

- Two-sample t-test:
  - Errors are independent but not identical.
  - 2 covariance components

$Q_k$'s:



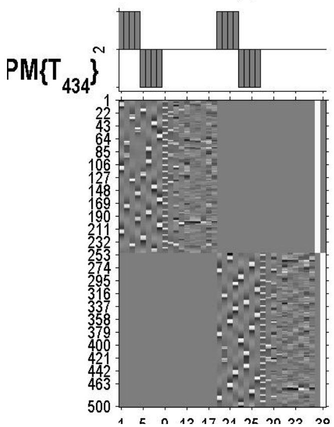



Error covariance matrix

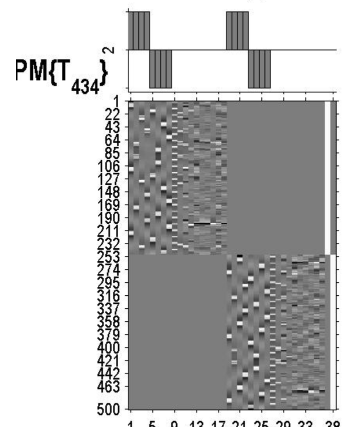
# Example 1: Group differences

First Level

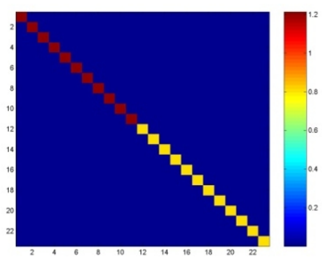
controls



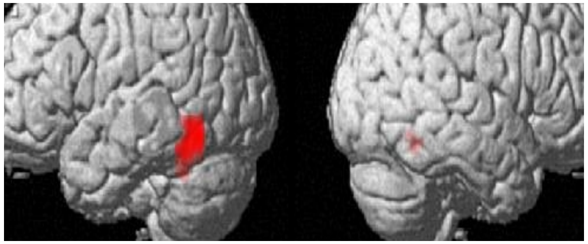

blinds



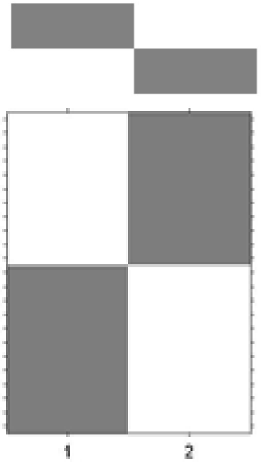

Second Level



$$Cov(\varepsilon)$$



$$c^T = [1 \quad -1]$$



design matrix

$$X$$

# Example 2: within-subjects ANOVA

- Stimuli:
  - Auditory presentation (SOA = 4 sec)
  - 250 scans per subject, block design
  - Words:

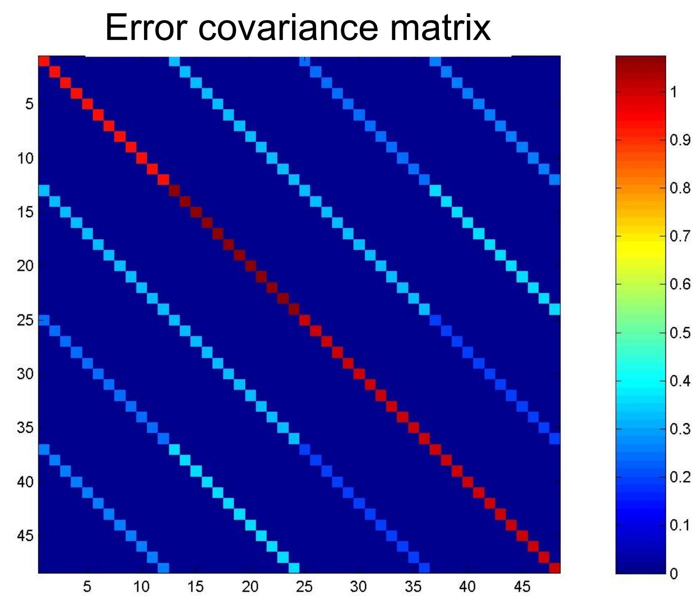
| Motion | Sound | Visual | Action |
|---|---|---|---|
| “jump” | “click” | “pink” | “turn” |

- Subjects:
  - 12 controls
- Question:
  - What regions are generally affected by the semantic content of the words?

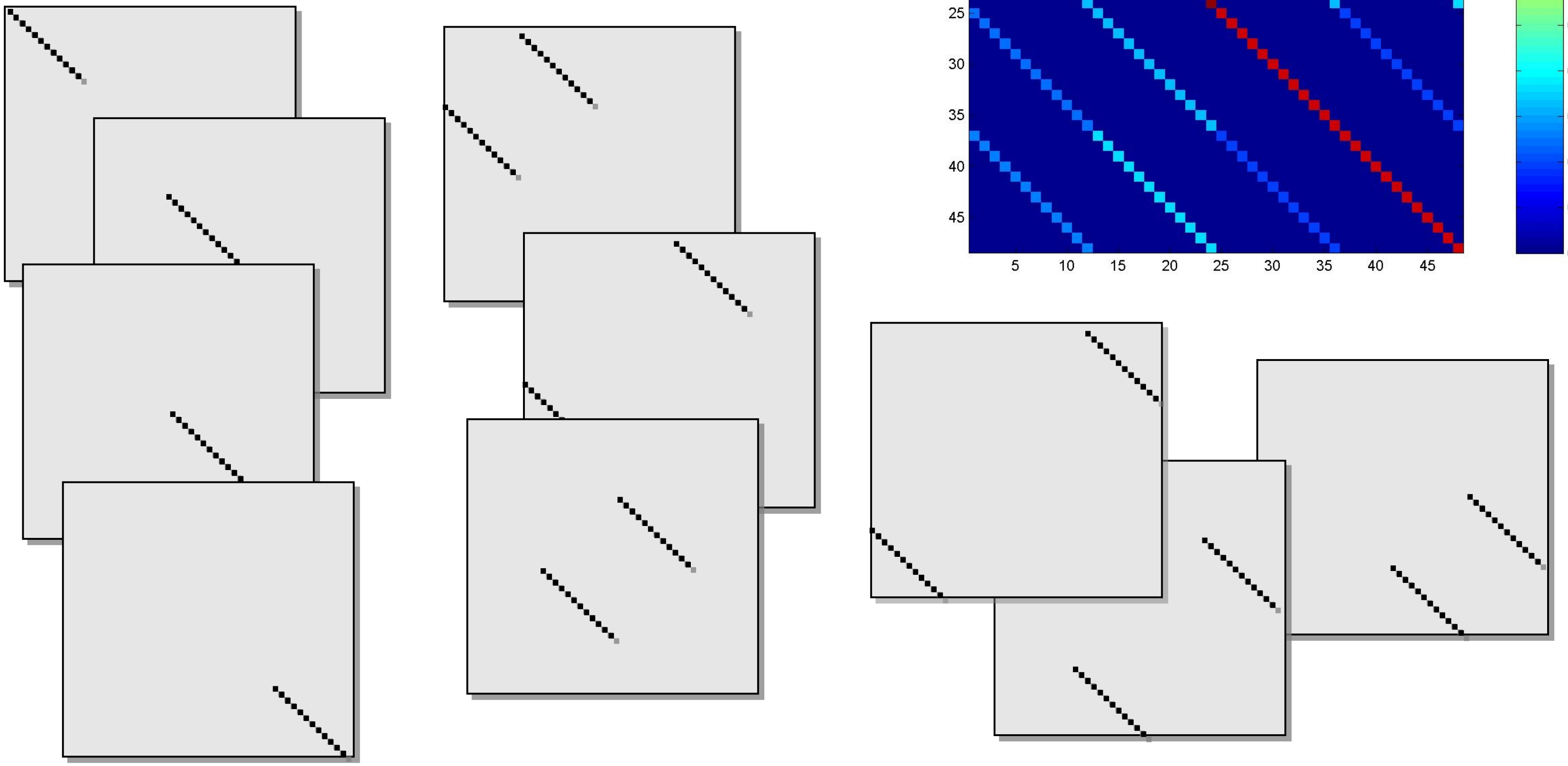
Noppeney et al., Brain, 2003.

# Example 2: Covariance components

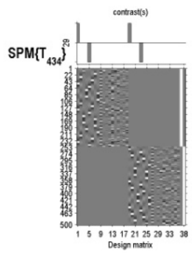
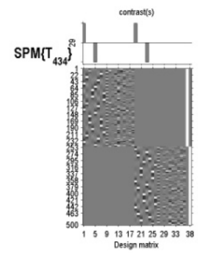
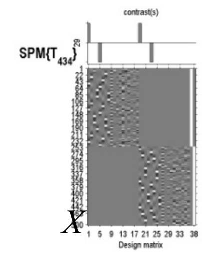
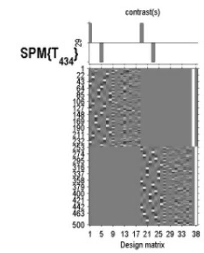
- Errors are not independent and not identical




$Q_k$'s:

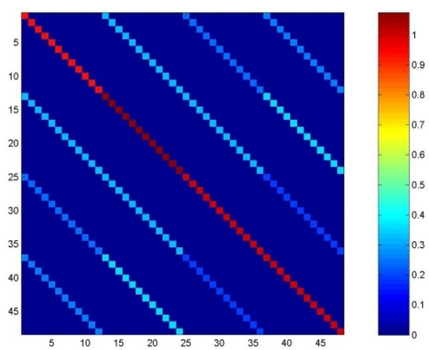


# Example 2: Repeated measures ANOVA

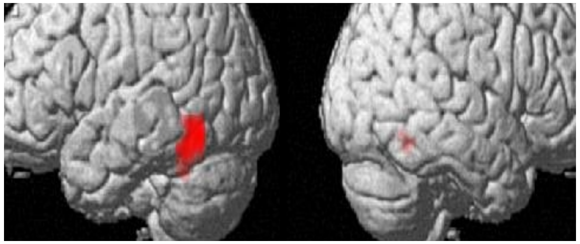
| | Motion | | Sound | | Visual | | Action |
|---|---|---|---|---|---|---|---|
| First Level |  | $\overset{?}{=}$ |  | $\overset{?}{=}$ |  | $\overset{?}{=}$ |  |

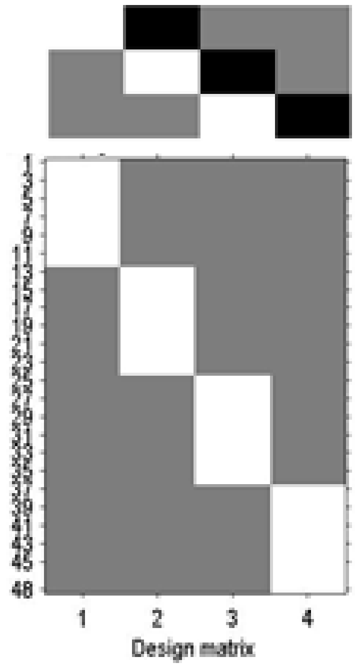


Second Level



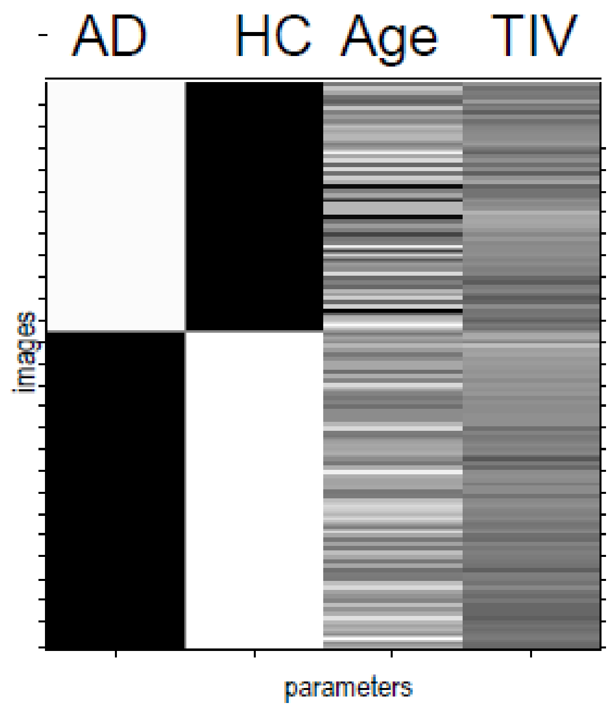
$Cov(\varepsilon)$

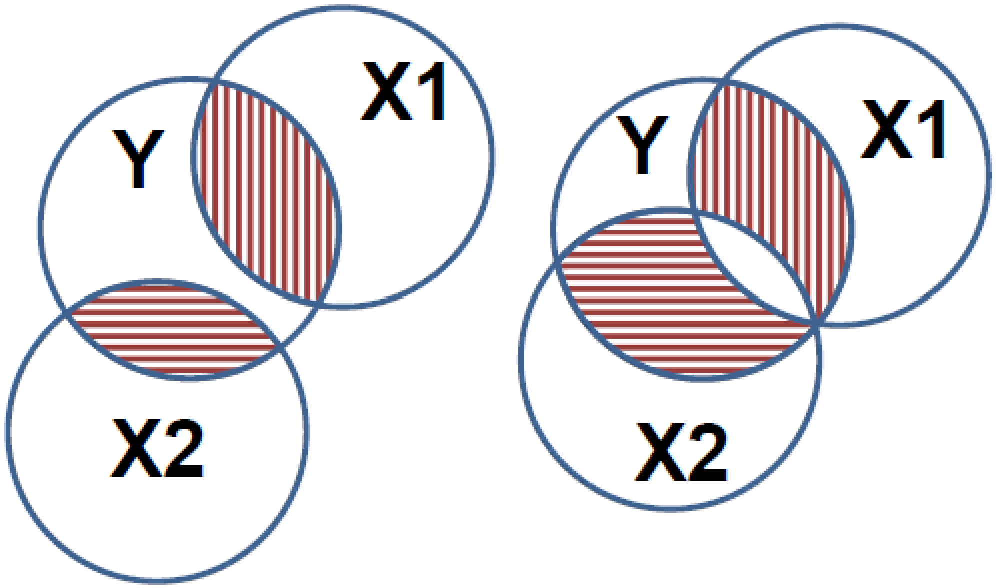





$X$

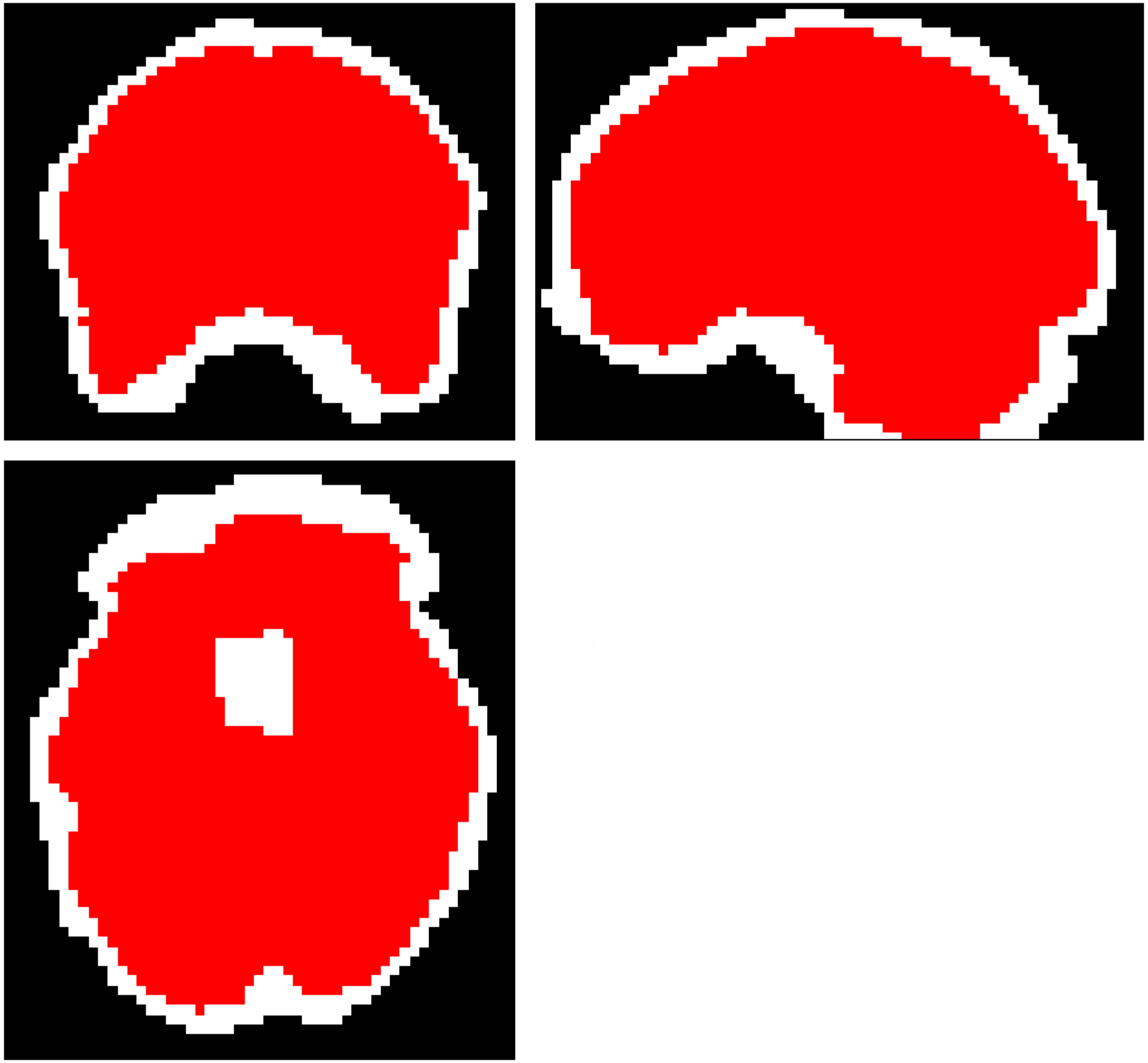
# ANCOVA model




Mean centering continuous covariates for a group fMRI analysis, by J. Mumford: http://mumford.fmripower.org/mean_centering/

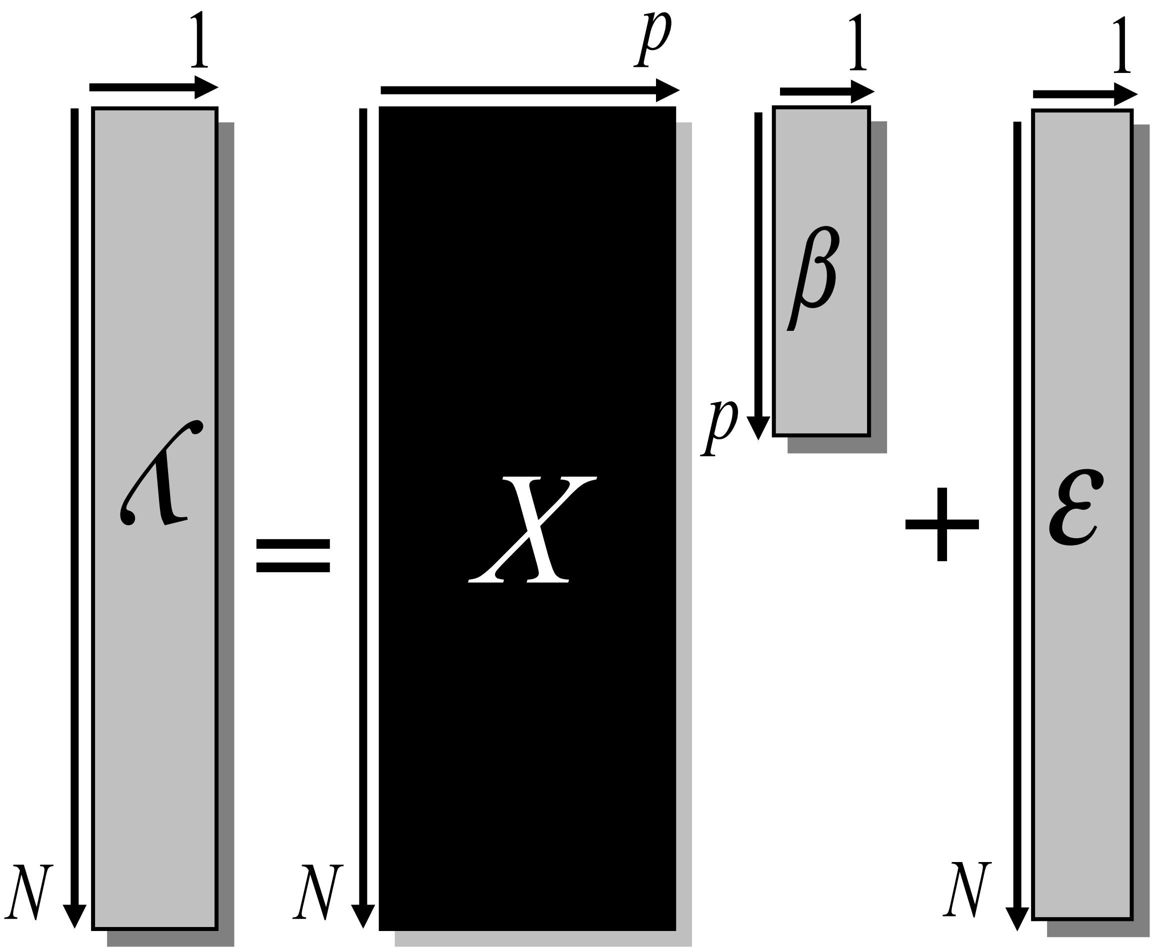
# Analysis mask: logical AND



# SPM interface: factorial design specification

- Many options…
  - One-sample t-test
  - Two-sample t-test
  - Paired t-test
  - Multiple regression
  - One-way ANOVA
  - One-way ANOVA – within subject
  - Full factorial
  - Flexible factorial

# General Linear Model



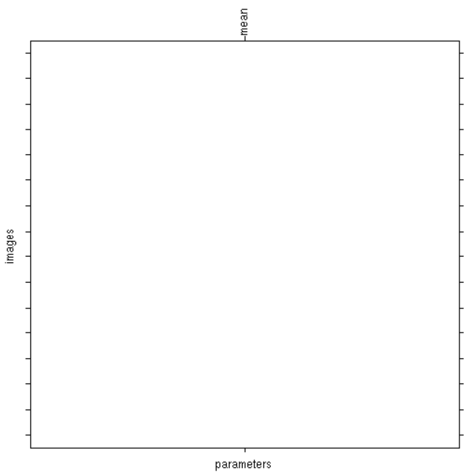

$$\boxed{y = X\beta + \varepsilon}$$

$$\boxed{\varepsilon \sim N(0, \sigma^2 C_\varepsilon)}$$

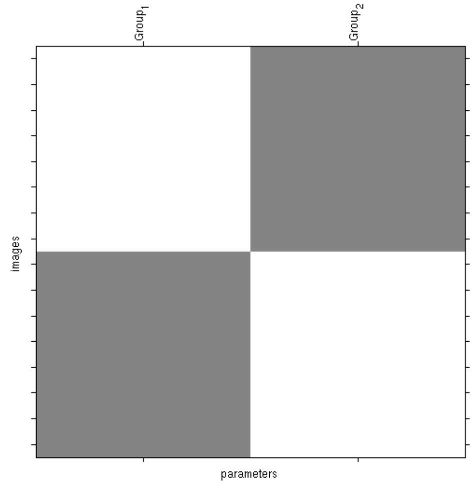
$$\boxed{C_\varepsilon = \sum_k \lambda_k Q_k}$$

Model is specified by
1. Design matrix $X$
2. Assumptions about $\varepsilon$

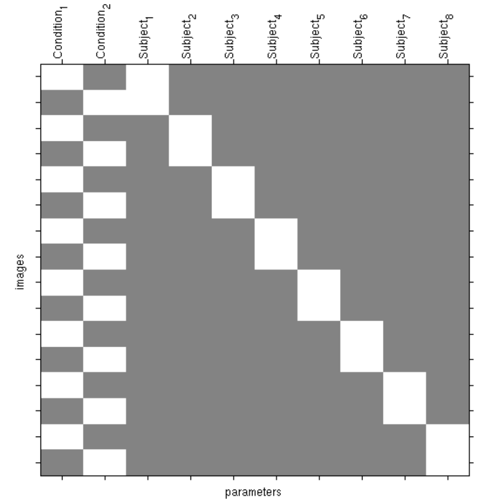
## One-sample t-test



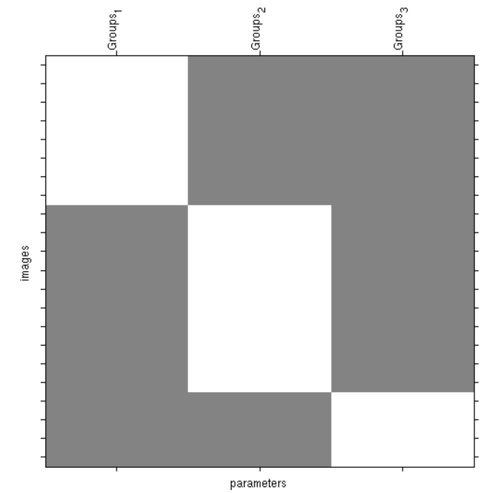

## Two-sample t-test



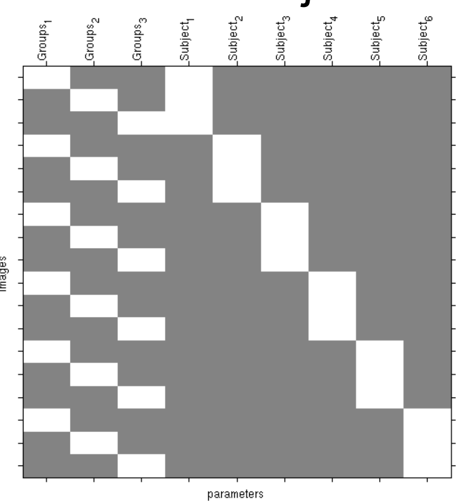

## Paired t-test



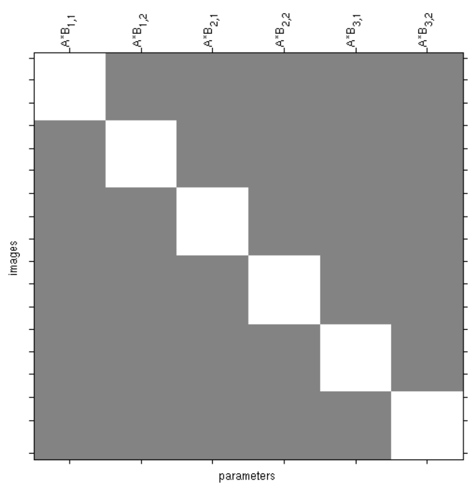

## One-way ANOVA



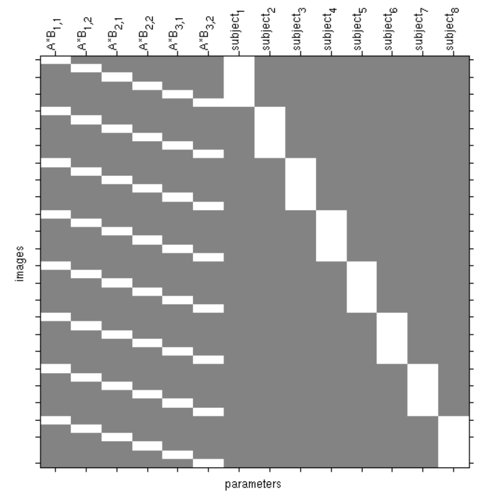

## One-way ANOVA within-subject



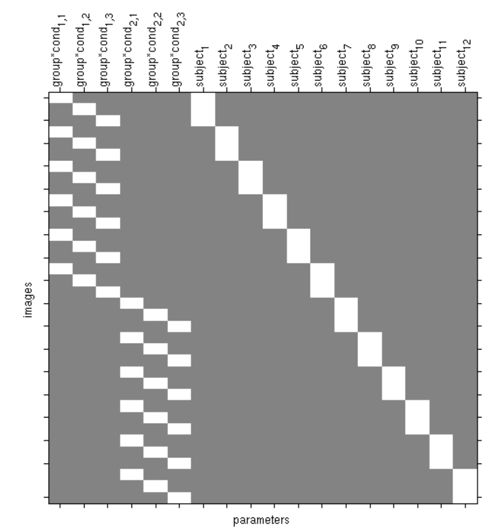

## Full Factorial




## Flexible Factorial




## Flexible Factorial



# Summary

- Group Inference usually proceeds with **RFX analysis**, not FFX. Group effects are compared to between rather than within subject variability.
- **Hierarchical models** provide a gold-standard for RFX analysis but are computationally intensive.
- **Summary statistics** approach is a robust method for RFX group analysis.
- Can also use **‘ANOVA’ or ‘ANOVA within subject’** at second level for inference about multiple experimental conditions or multiple groups.

# Bibliography:


- *Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Elsevier, 2007.
- *Generalisability, Random Effects & Population Inference*. Holmes & Friston, NeuroImage,1998.
- *Classical and Bayesian inference in neuroimaging: theory*. Friston et al., NeuroImage, 2002.
- *Classical and Bayesian inference in neuroimaging: variance component estimation in fMRI*. Friston et al., NeuroImage, 2002.
- *Mixed-effects and fMRI studies*. Friston et al., NeuroImage, 2005.
- *Simple group fMRI modeling and inference.* Mumford & Nichols, NeuroImage, 2009.