Group Analyses

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

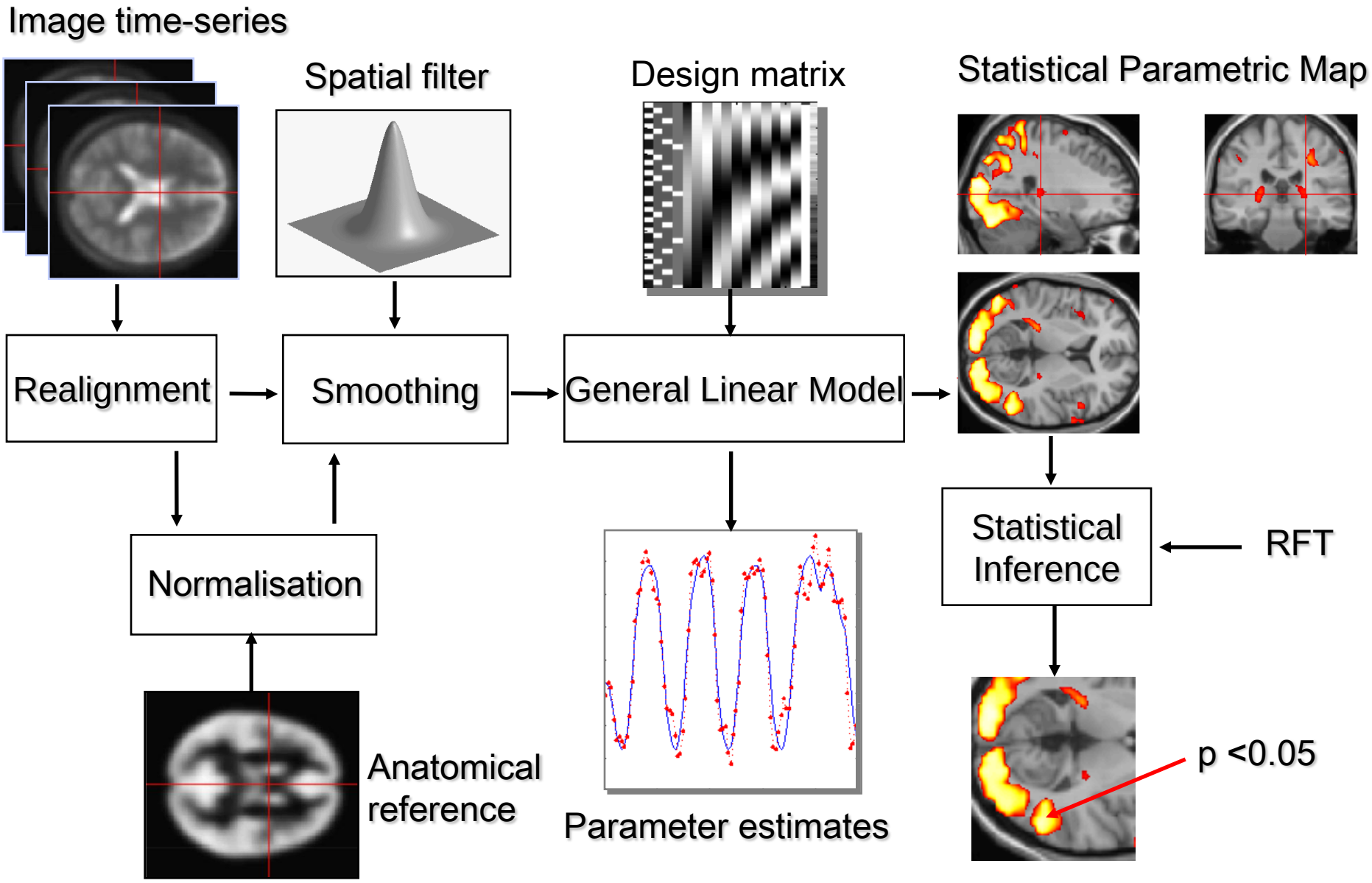
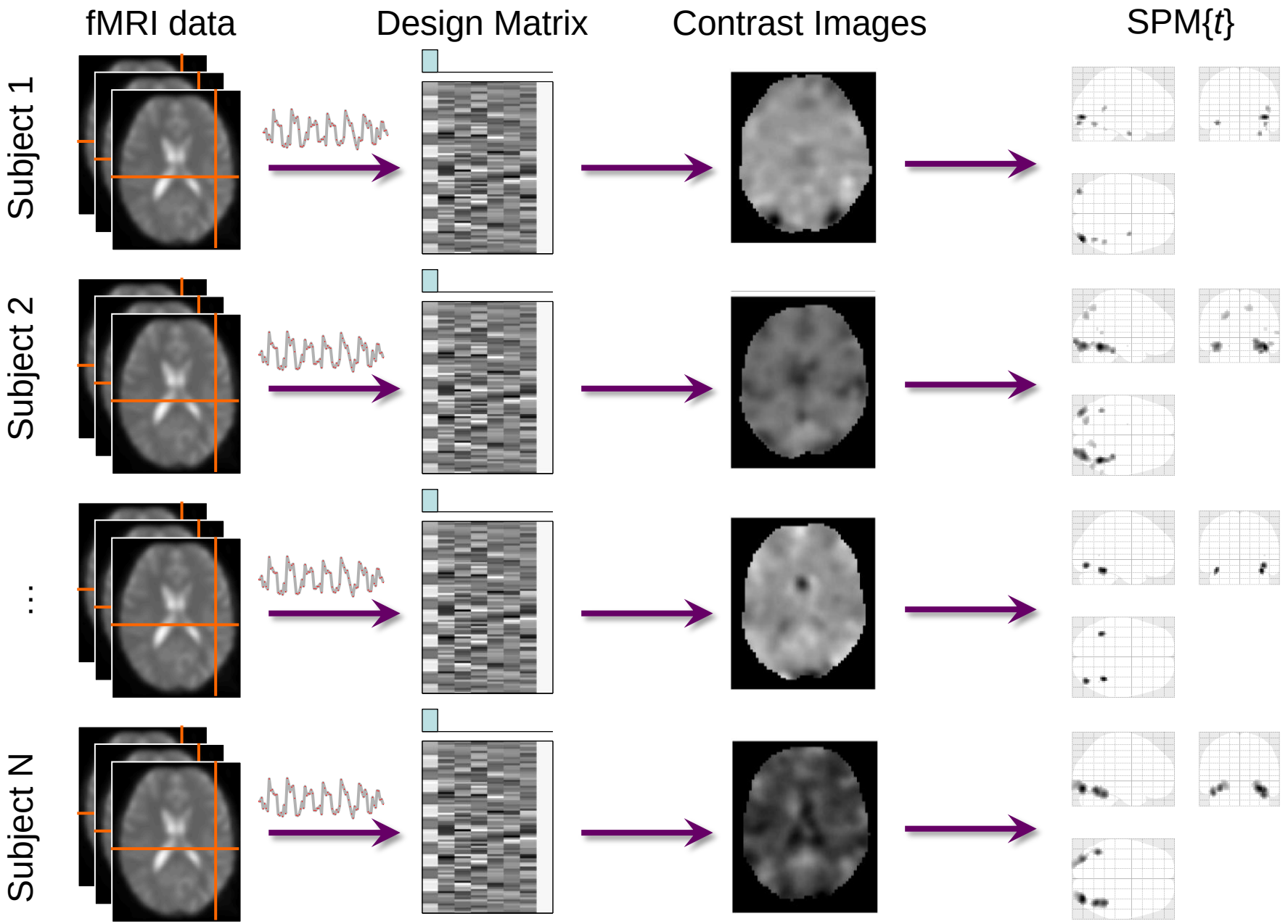
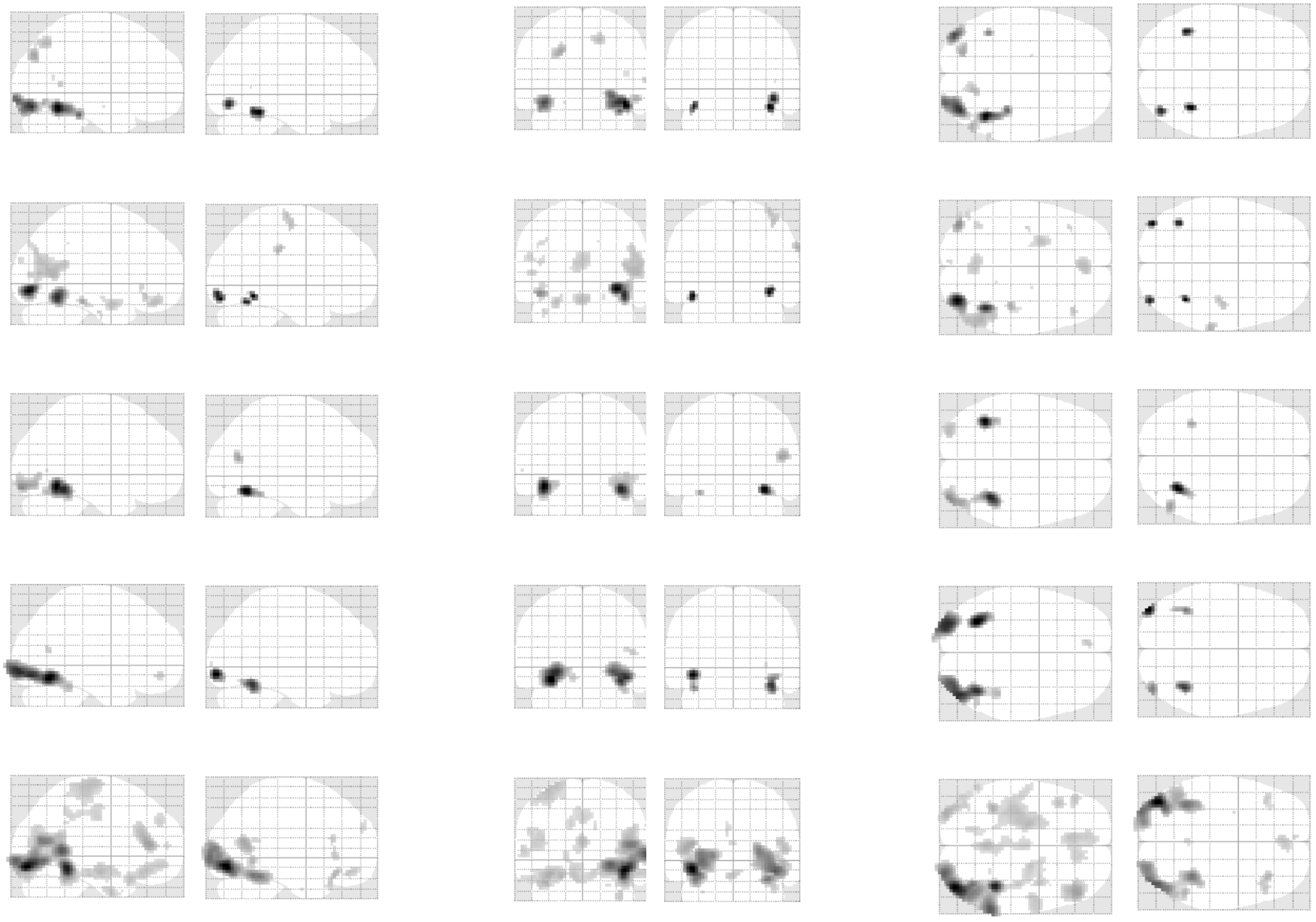


Image time-series
Spatial filter
Design matrix
Statistical Parametric Map
Realignment
Smoothing
General Linear Model
Normalisation
Statistical Inference
RFT
Anatomical reference
Parameter estimates
p <0.05

GLM: repeat over subjects

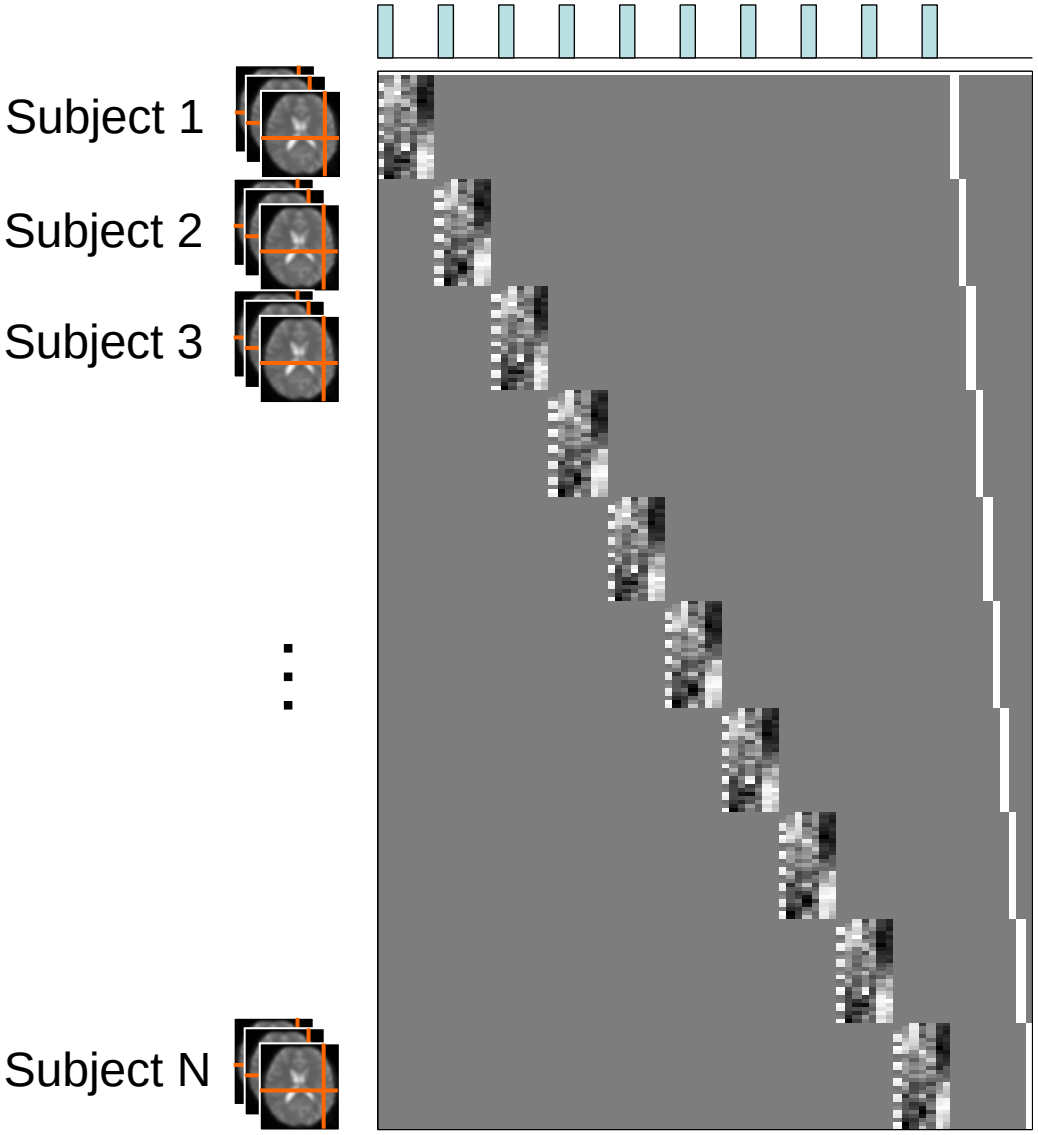


First level analyses (p<0.05 FWE):

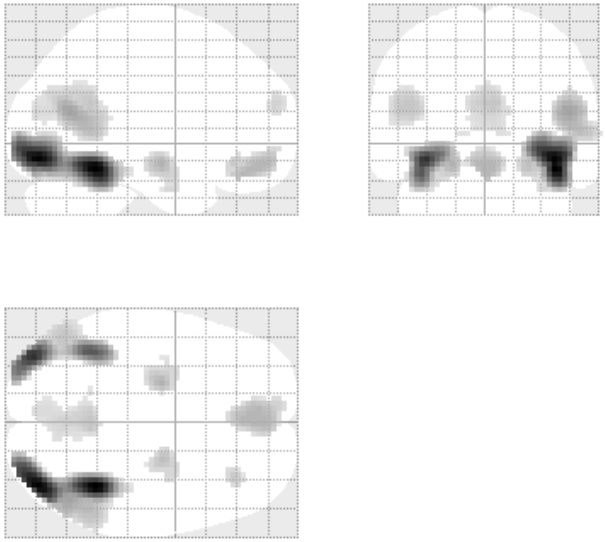


Data from R. Henson

Fixed effects analysis (FFX)



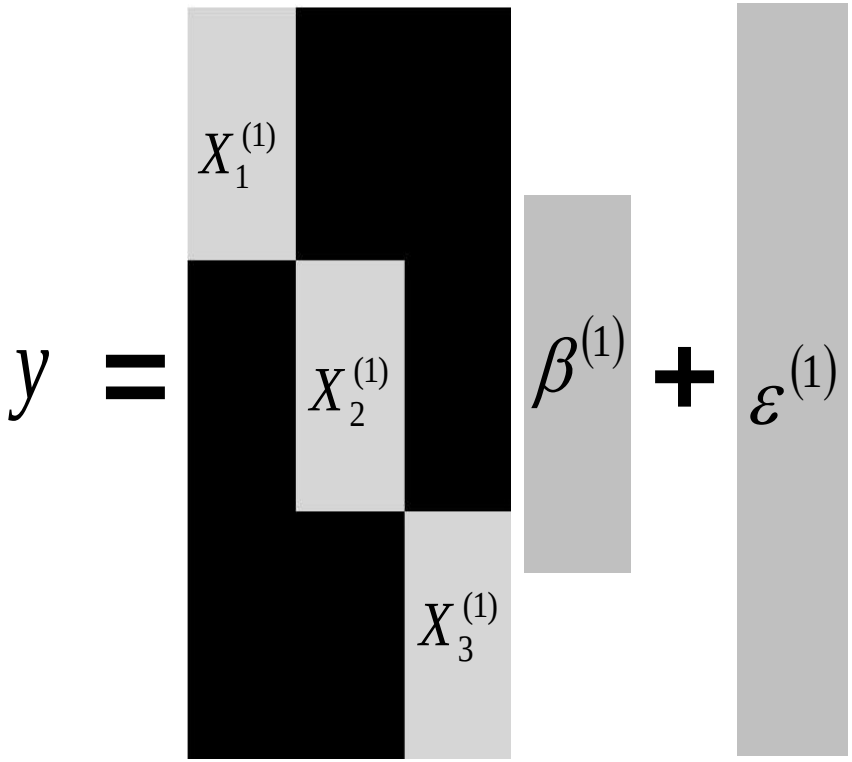
Modelling all subjects at once



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

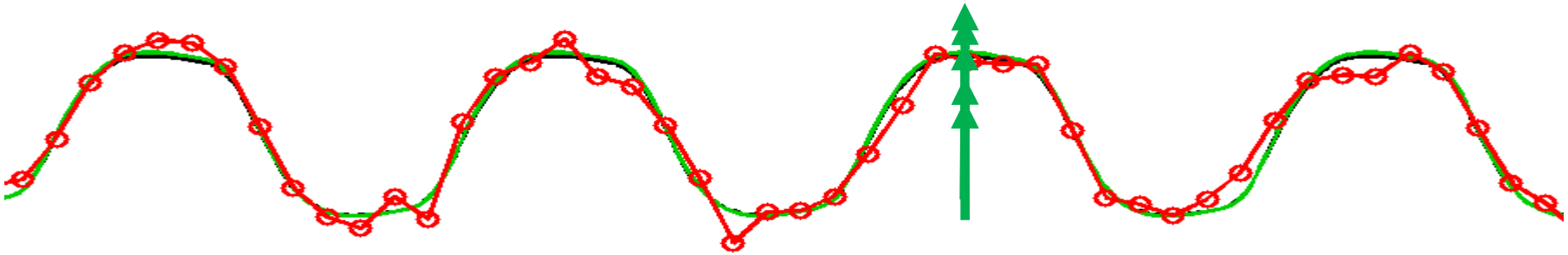
Within-subject Variance

- True response magnitude is *fixed.*

Random effects

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

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

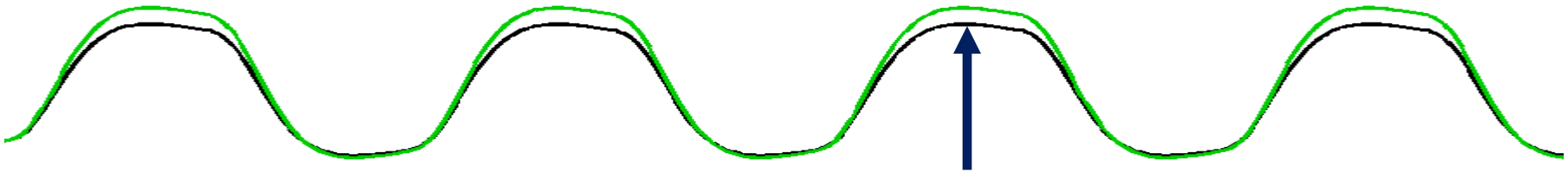


- Two sources of random variation:
  - measurement errors — Within-subject Variance
  - response magnitude (over subjects) — Between-subject Variance
- Response magnitude is *random*
  - each subject/session has random magnitude

Random effects

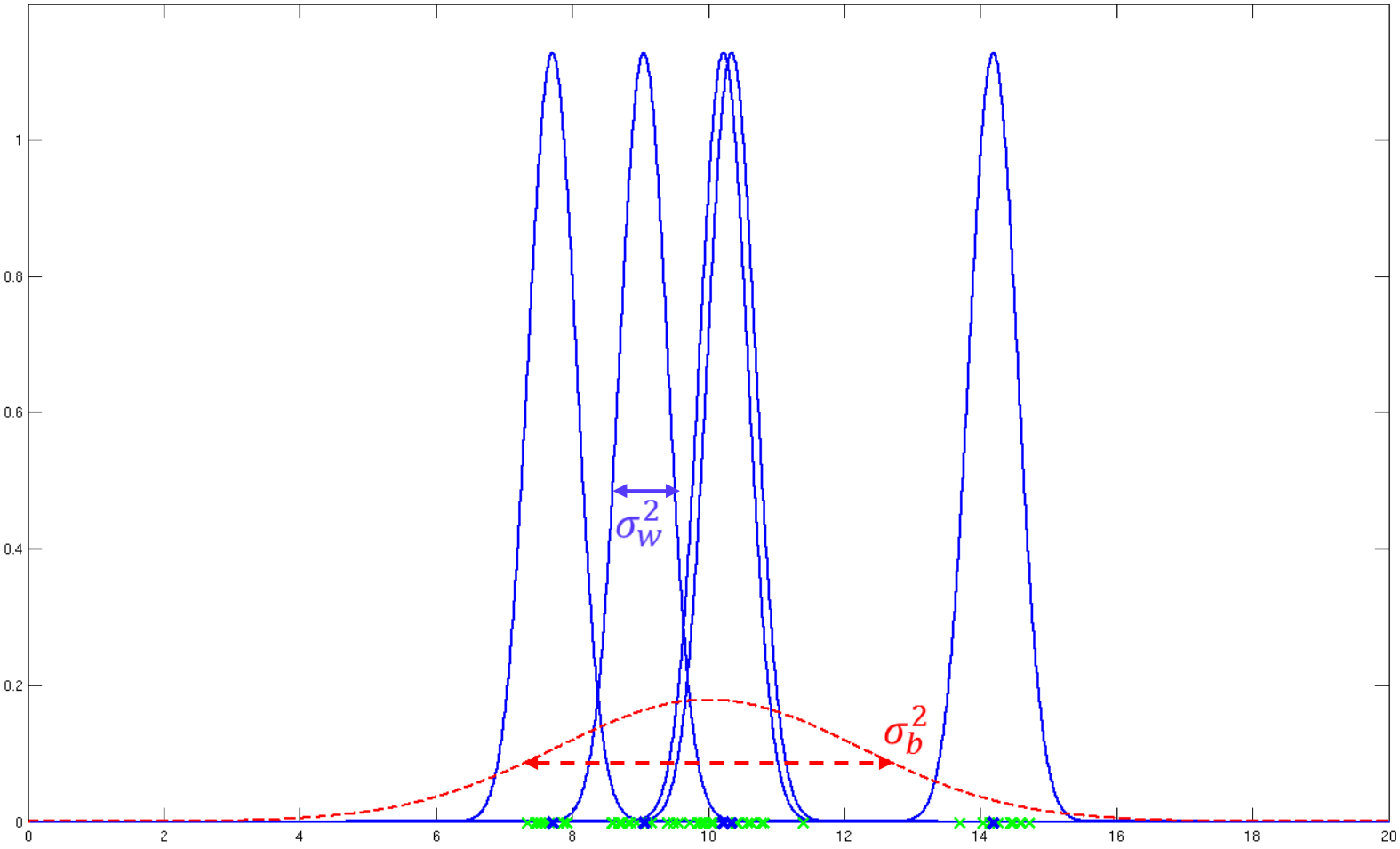
$$y = X^{(1)}\beta^{(1)} + \varepsilon^{(1)}$$

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



- Two sources of random variation:
  - measurement errors — Within-subject Variance
  - response magnitude (over subjects) — 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

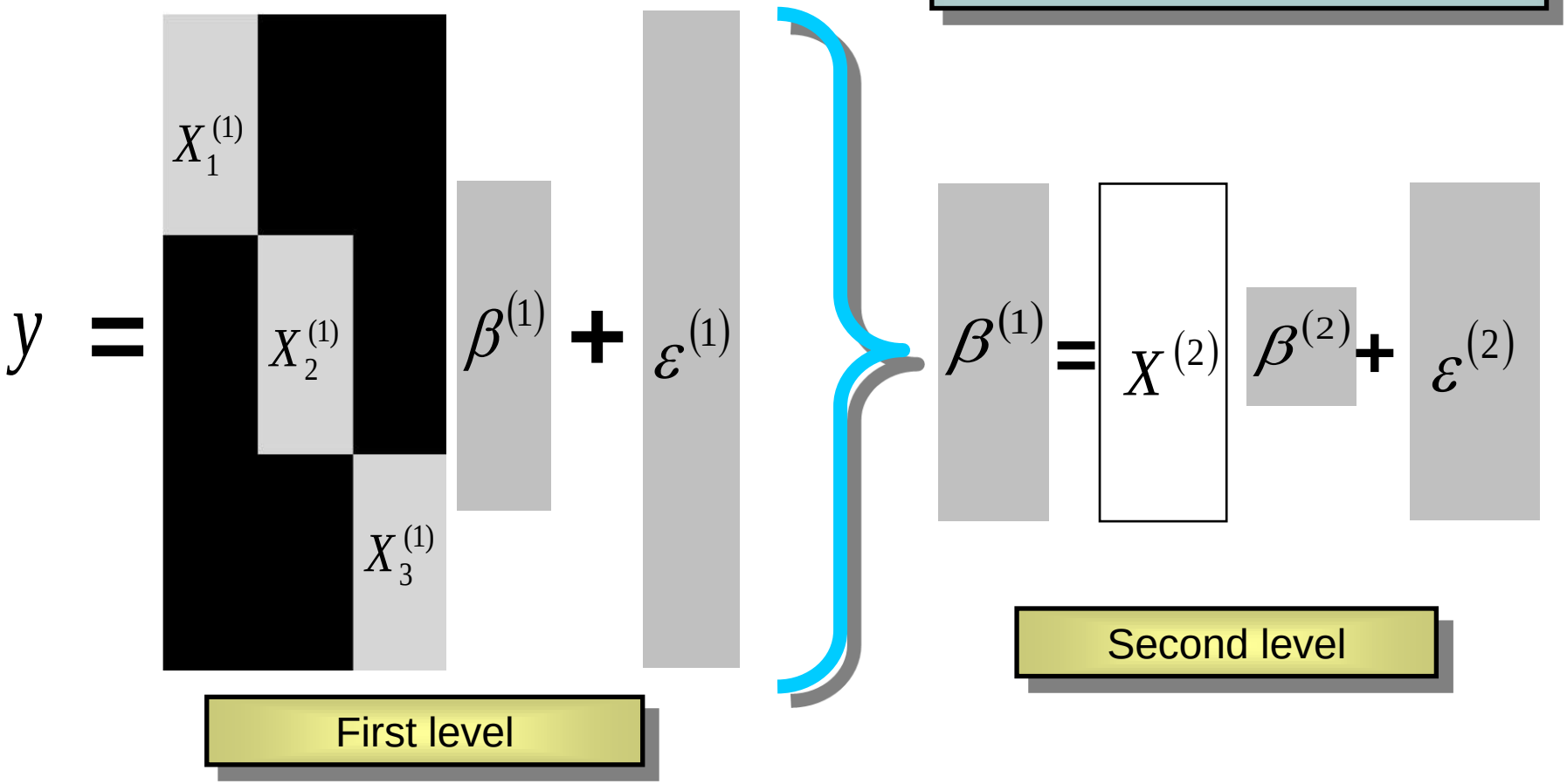
… all the same

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

Hierarchical models

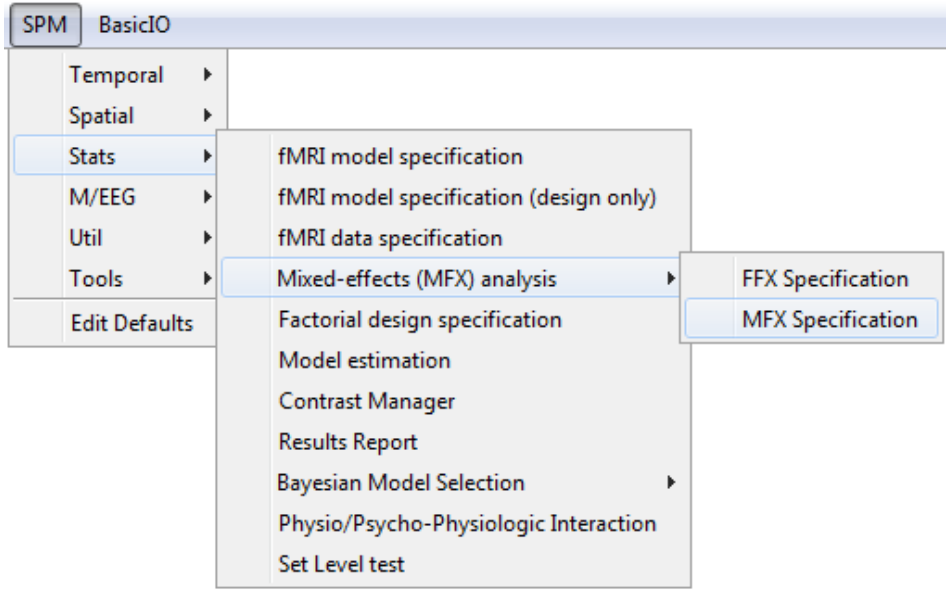
Example: Two level model

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



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

SPM

First level

Second level

fMRI data

Design Matrix

Contrast Images

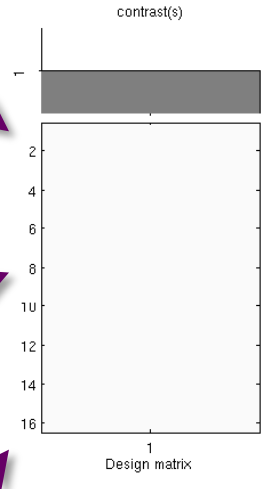
One-sample t-test @ second level

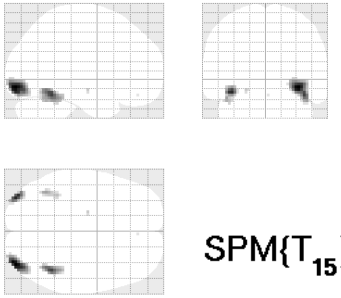
Subject 1

...

Subject N

$$t = \frac{c^T \hat{\beta}}{\sqrt{V\hat{a}r(c^T \hat{\beta})}}$$





SPM{T_{15}}

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

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.

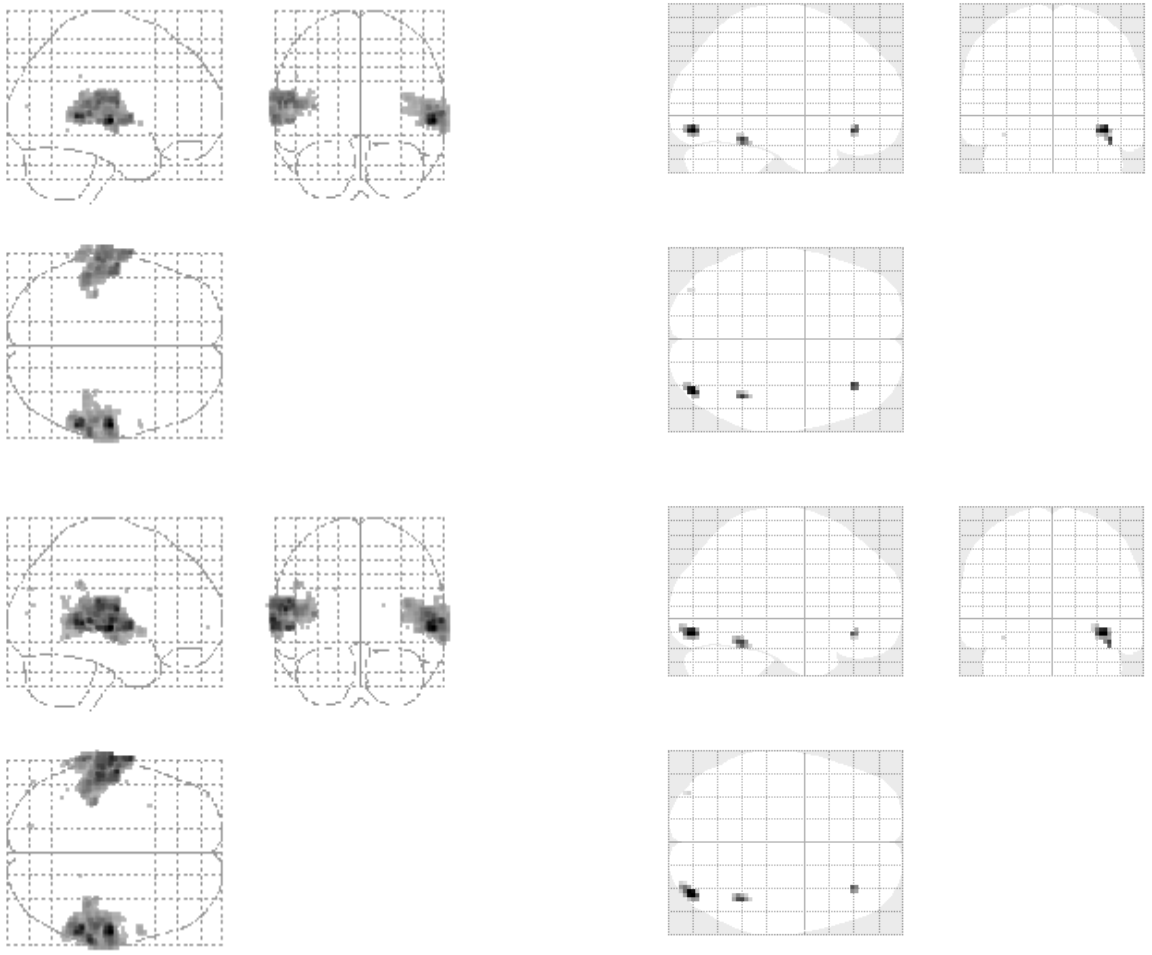
Simple group fMRI modeling and inference. Mumford & Nichols. NeuroImage, 2009.

Summary Statistics RFX Approach

Robustness

Summary statistics

Hierarchical Model



Listening to words

Viewing faces

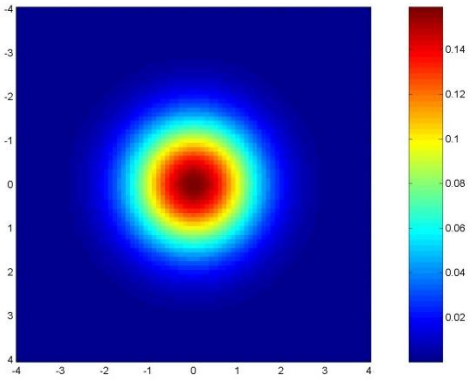
Mixed-effects and fMRI studies. Friston et al., NeuroImage, 2005.

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

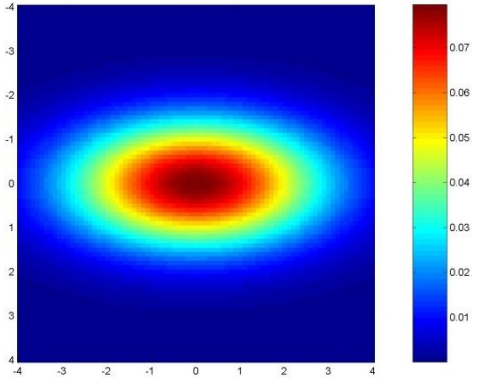
GLM assumes Gaussian "spherical" (i.i.d.) errors

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



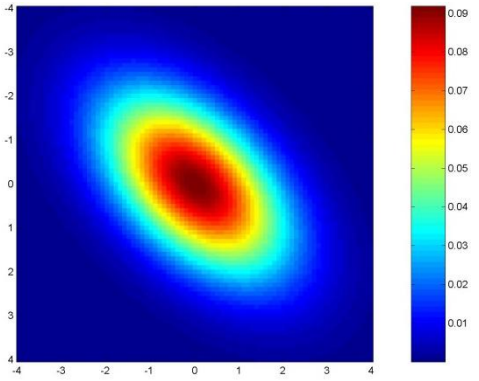
$$Cov(e) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Examples for non-sphericity:



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

non-identically distributed

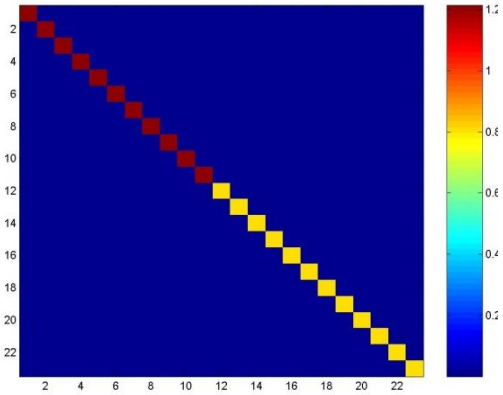


$$Cov(e) = \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix}$$

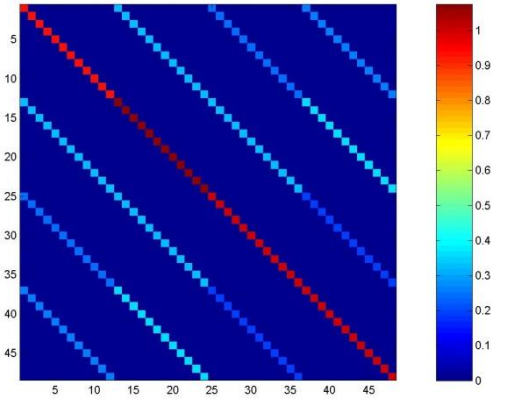
non-independent

2nd level: Non-sphericity

Error covariance matrix



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

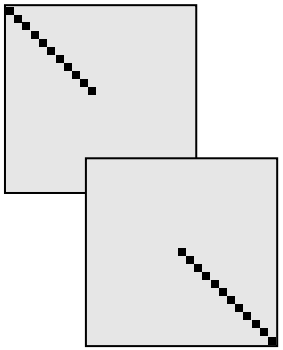


Errors are not independent
and not identical
(e.g. repeated measures for each subject
(multiple basis functions, multiple
conditions, etc.))

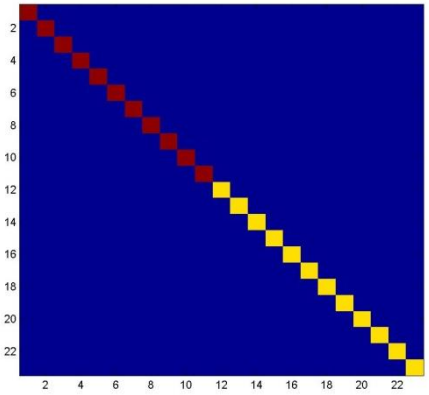
2nd level: Variance components

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

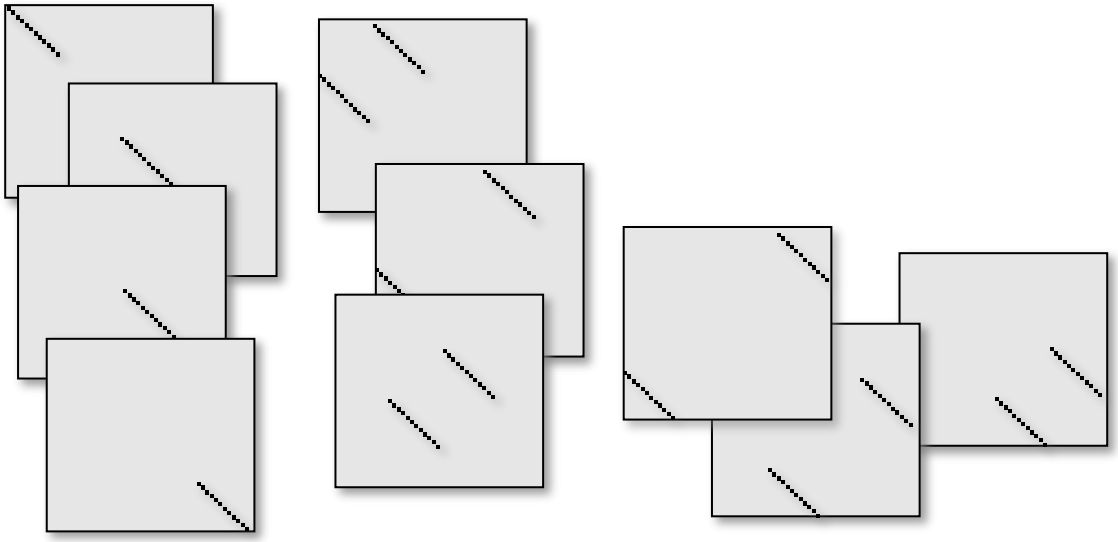
Q_k's:

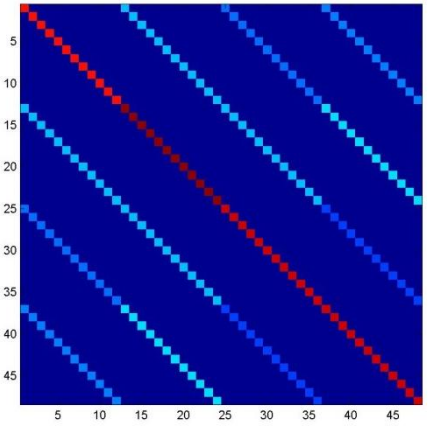


Error covariance matrix



Q_k's:





Example 1: between-subjects ANOVA

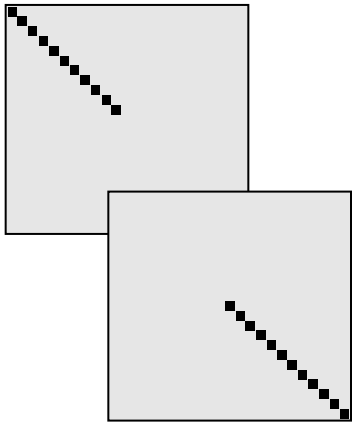
- Stimuli:
  - Auditory presentation (SOA = 4 sec)
  - 250 scans per subject, block design
  - 2 conditions
    - Words, e.g. “book”
    - Words spoken backwards, e.g. “koob”
- Subjects:
  - 12 controls
  - 11 blind people

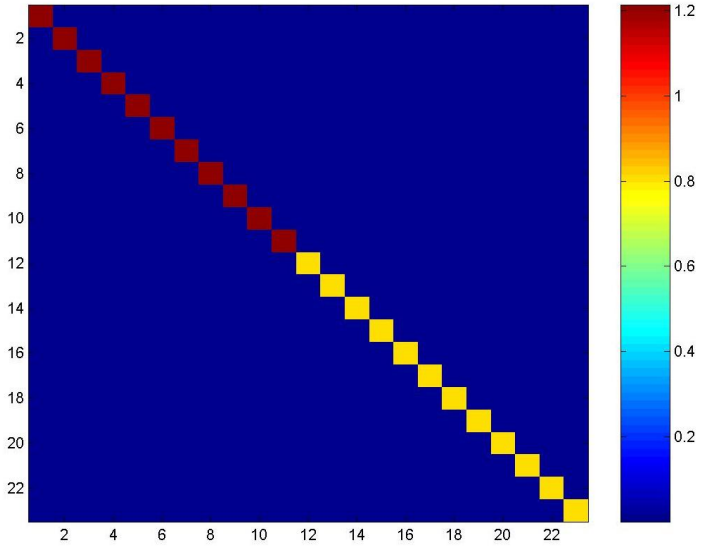
Data from Noppeney et al.

Example 1: Covariance components

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

Q_k's:



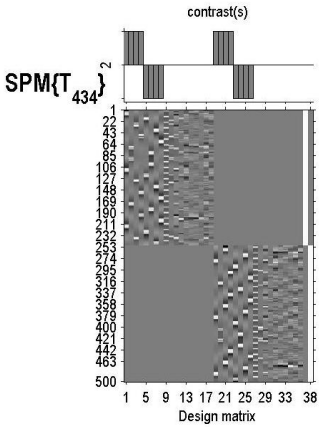


Error covariance matrix

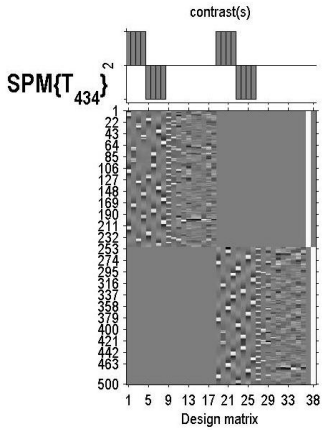
Example 1: Group differences

First Level

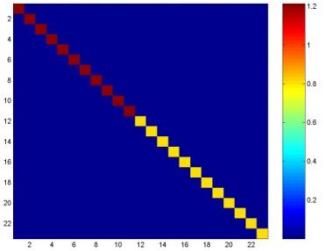
controls



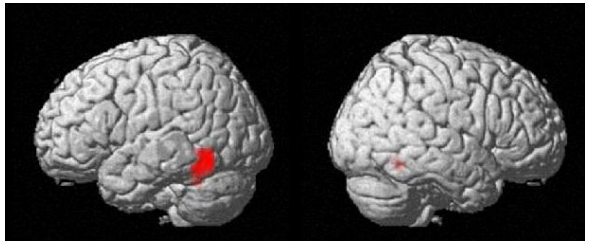
blinds



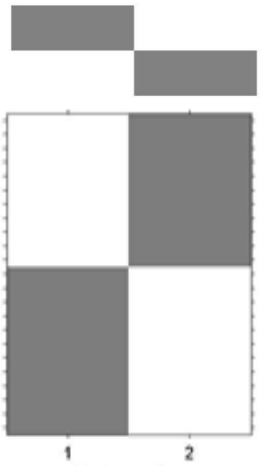
Second Level



$Cov(\varepsilon)$



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



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

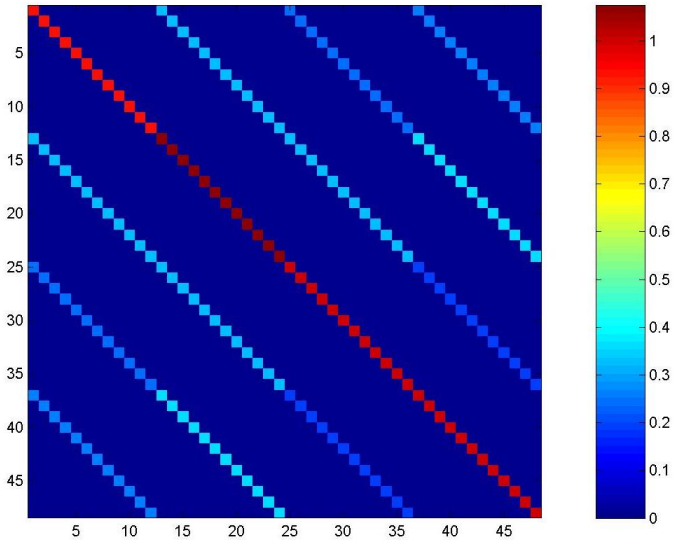
- Question:
  - What regions are generally affected by the semantic content of the words?

Noppeney et al., Brain, 2003.

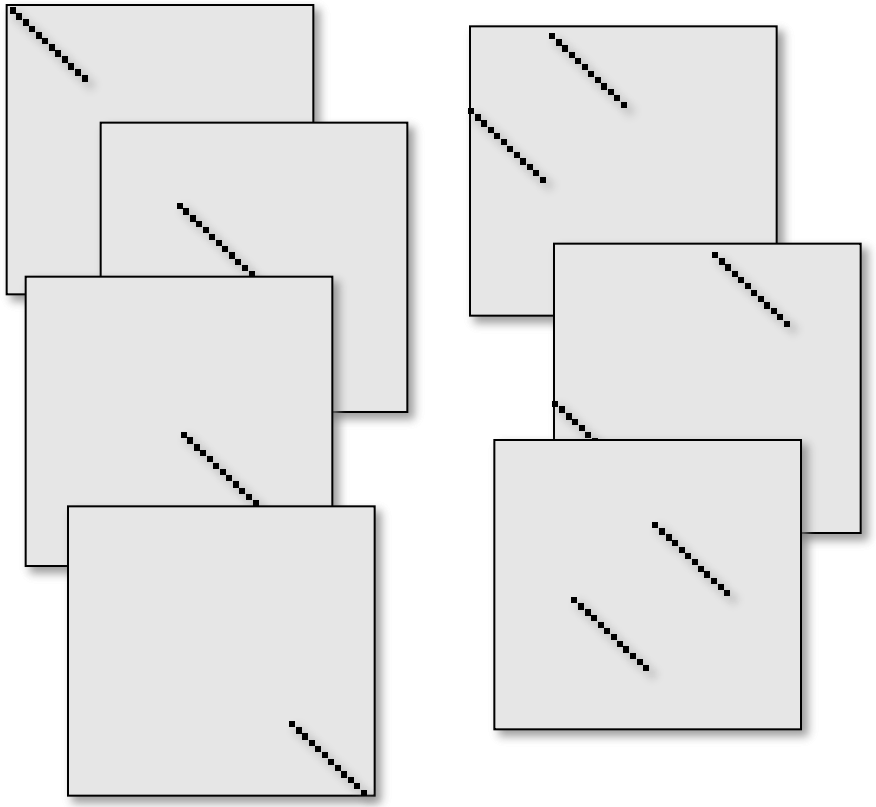
Example 2: Covariance components

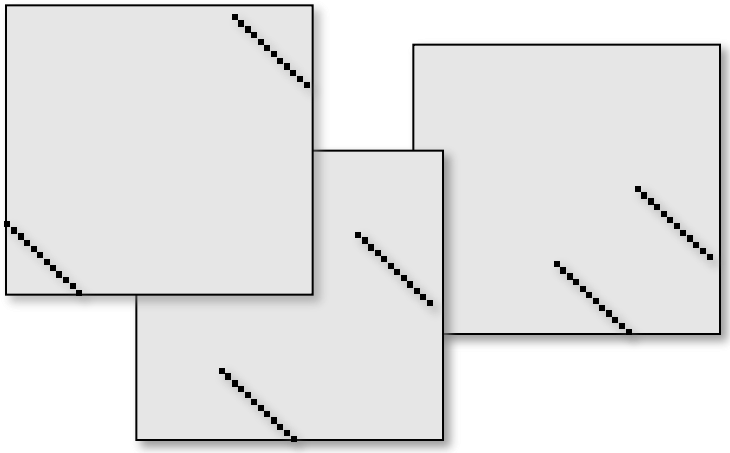
- Errors are not independent and not identical

Error covariance matrix



Q_k's:

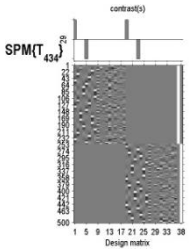




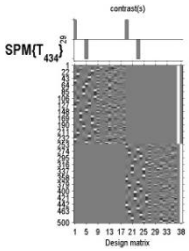
Example 2: Repeated measures ANOVA

Motion | Sound | Visual | Action

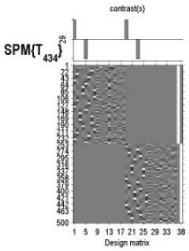
First Level



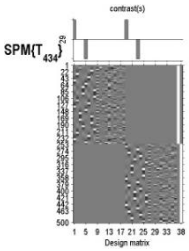
$=$?



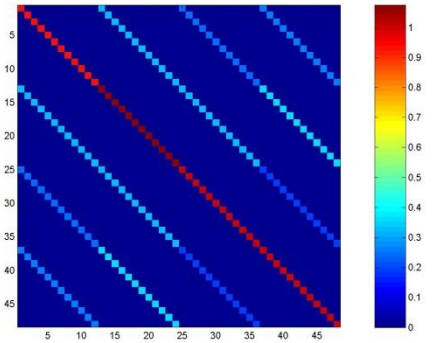
$=$?



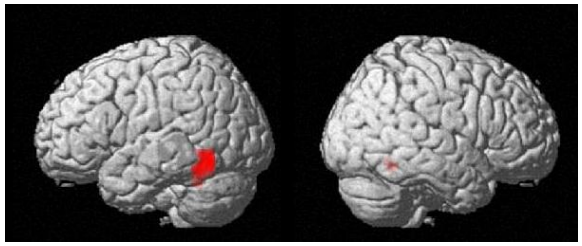
$=$?

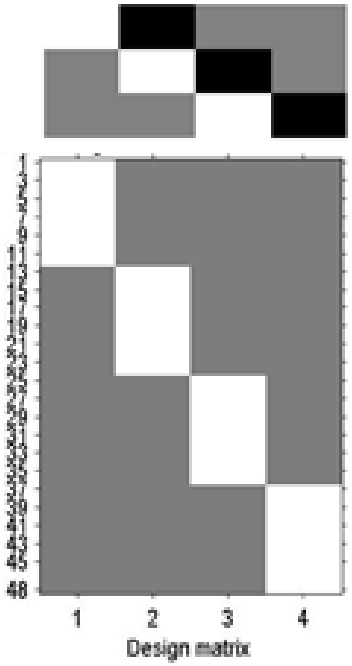


Second Level



$Cov(\varepsilon)$

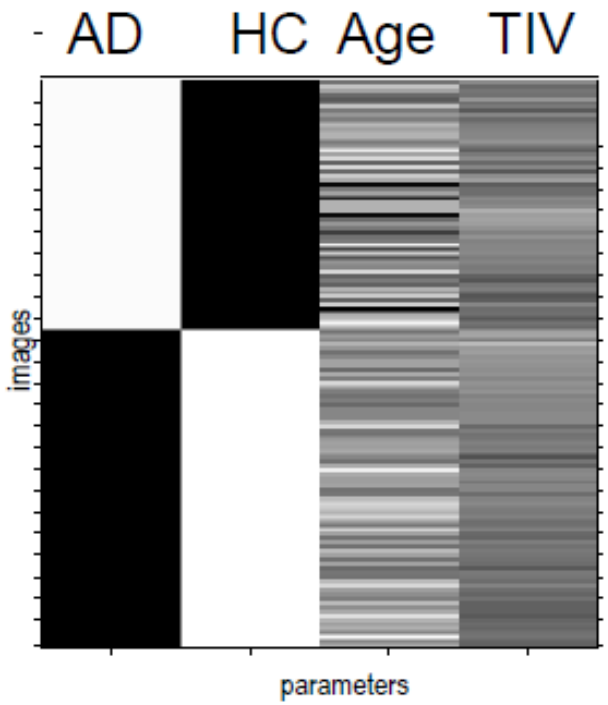


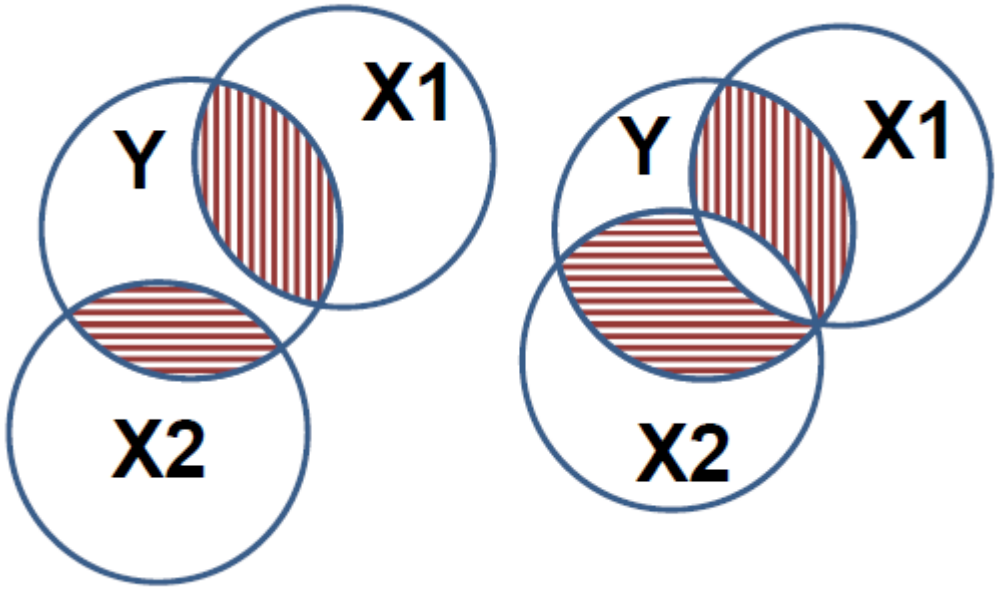


X

$$c^T = \begin{pmatrix} 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{pmatrix}$$

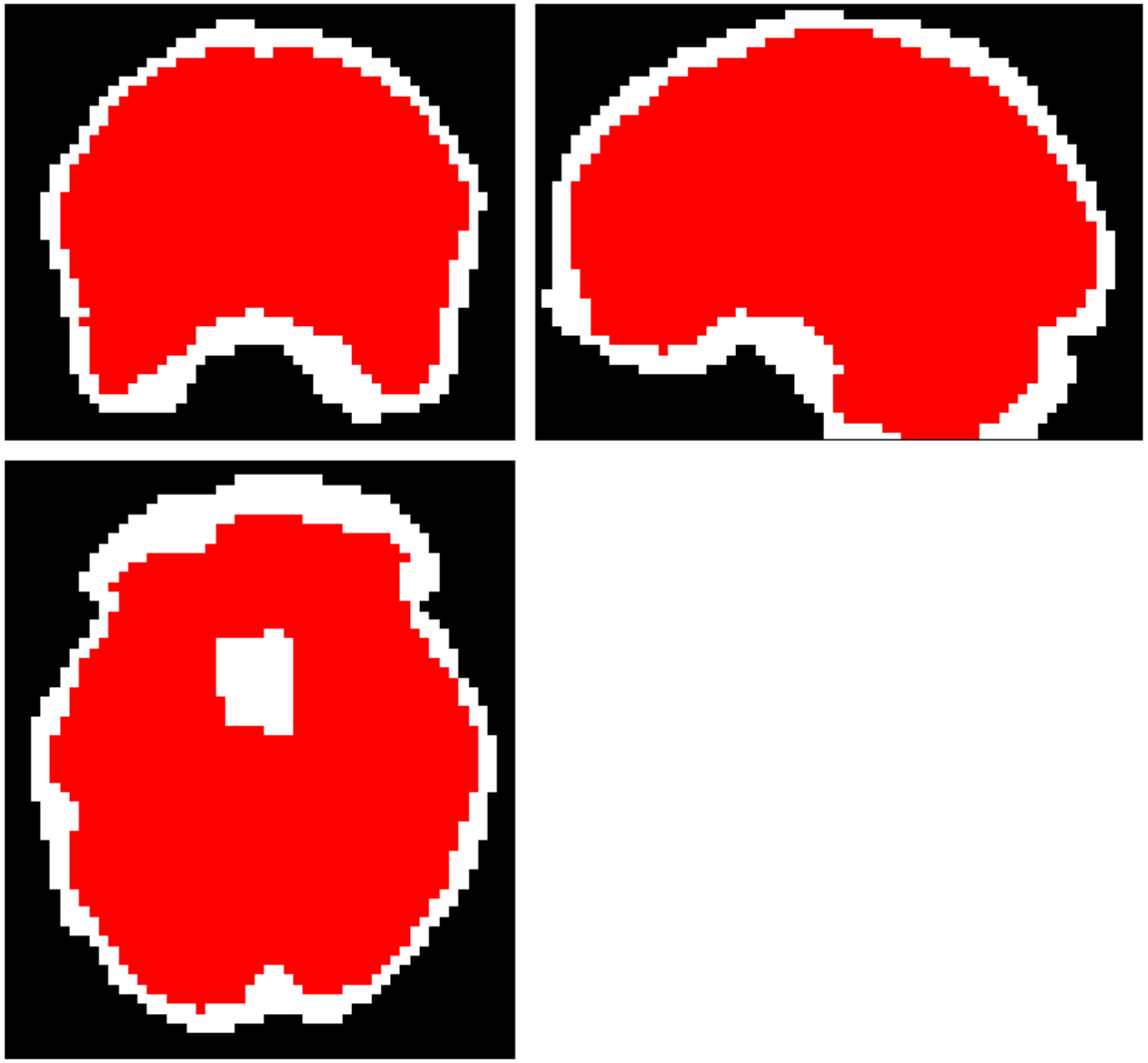
ANCOVA model





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

- 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

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.

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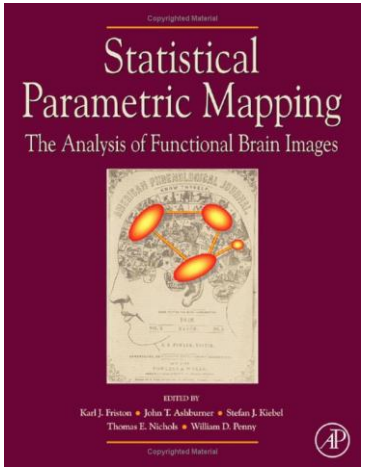
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