Group analysis

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SPM Course
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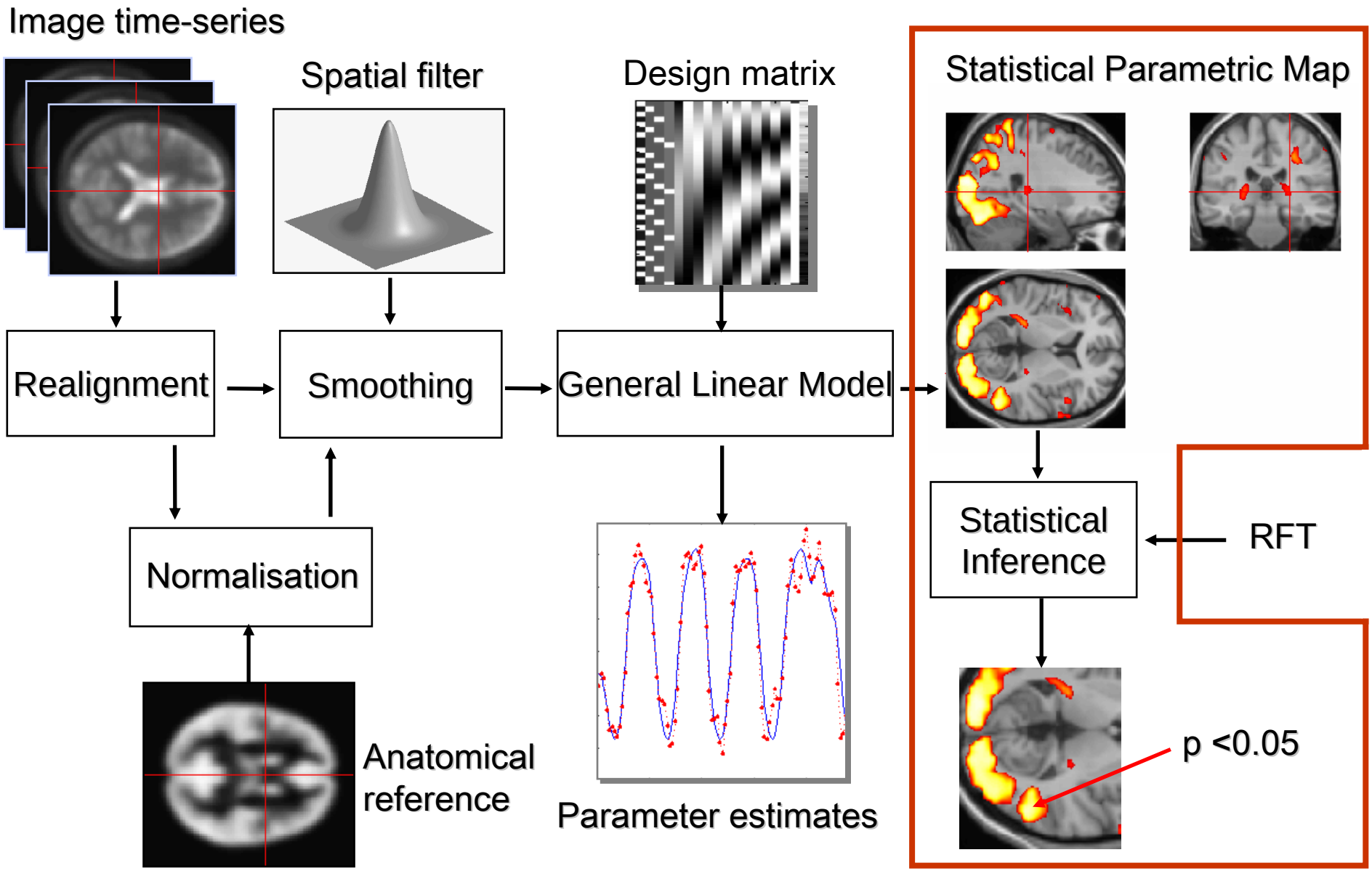


Image time-series
Spatial filter
Design matrix
Statistical Parametric Map
Realignment
Smoothing
General Linear Model
Normalisation
Statistical Inference
RFT
Anatomical reference
Parameter estimates
p <0.05

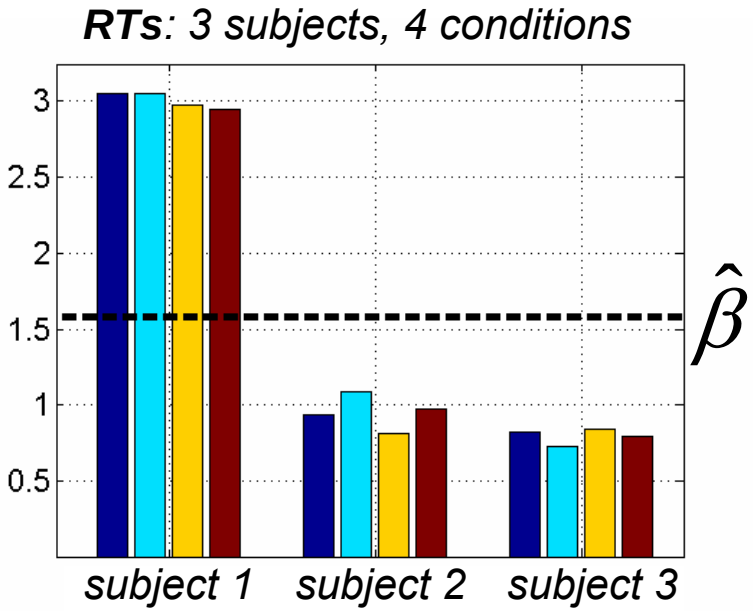
Between subjects variability

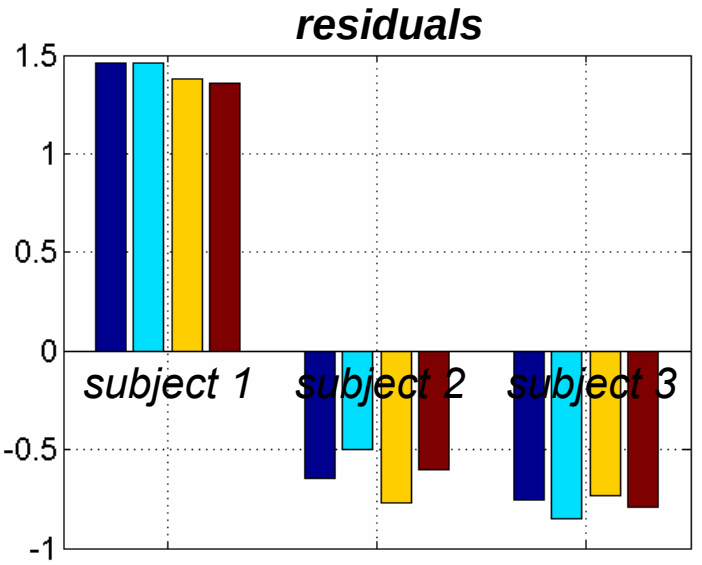
- Standard GLM

$$y = X\beta + \varepsilon$$

assumes only one source of i.i.d. random variation

- But, in general, there are at least two sources:
  - *within subj. variance*
  - *between subj. variance*
- Causes dependences in ε





Lexicon

- Hierarchical models
- Mixed effect models
- Random effect (RFX) models
- Components of variance

… all the same

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

Overview

- Group analysis: fixed versus random effects
- Two RFX methods:
  - *summary statistics approach*
  - *non-sphericity modelling*
- Examples

Overview

- Group analysis: fixed versus random effects
- Two RFX methods:
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Fixed vs random effects

- Fixed effects:

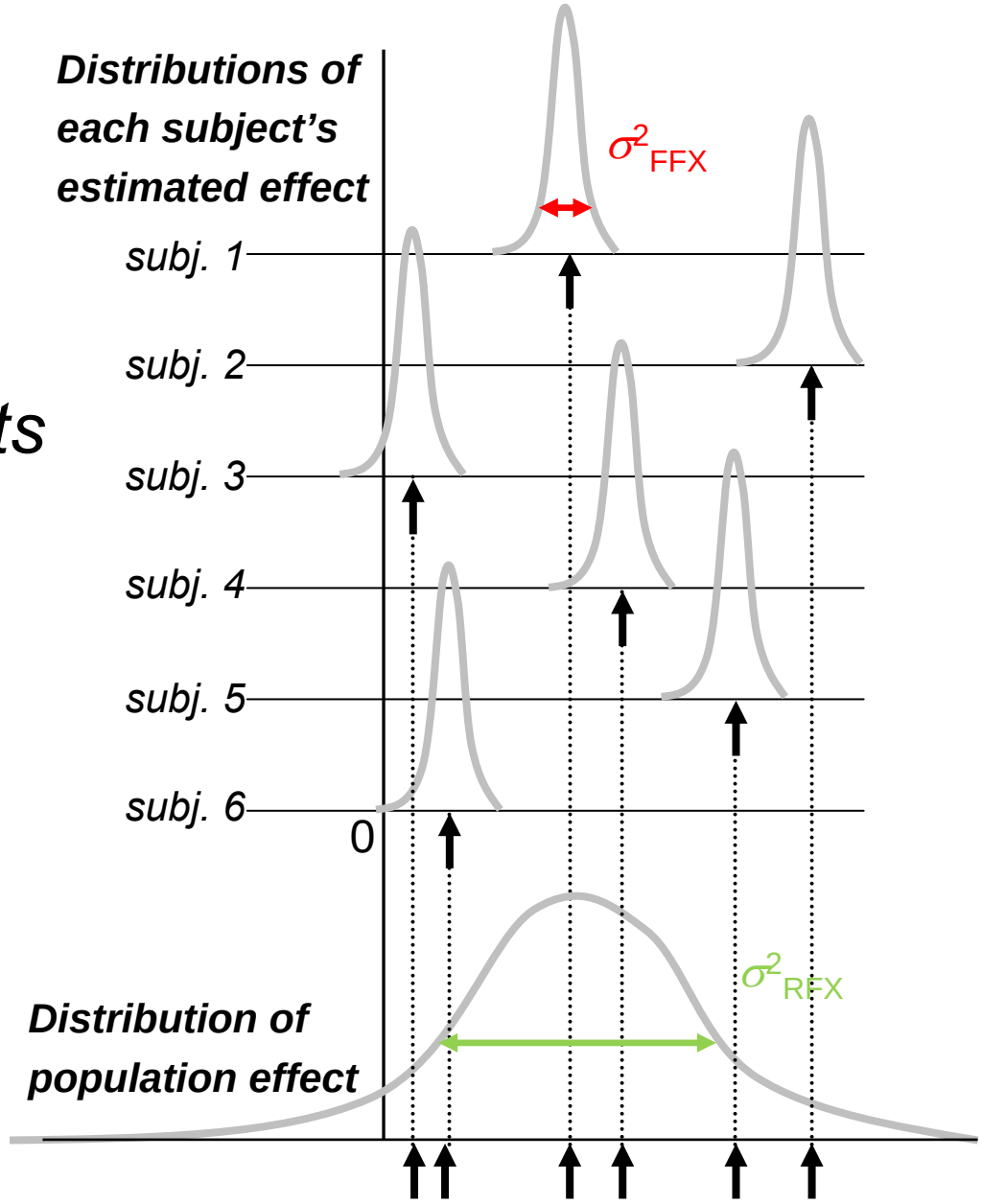
Intra-subjects variation

suggests *all these subjects different from zero*

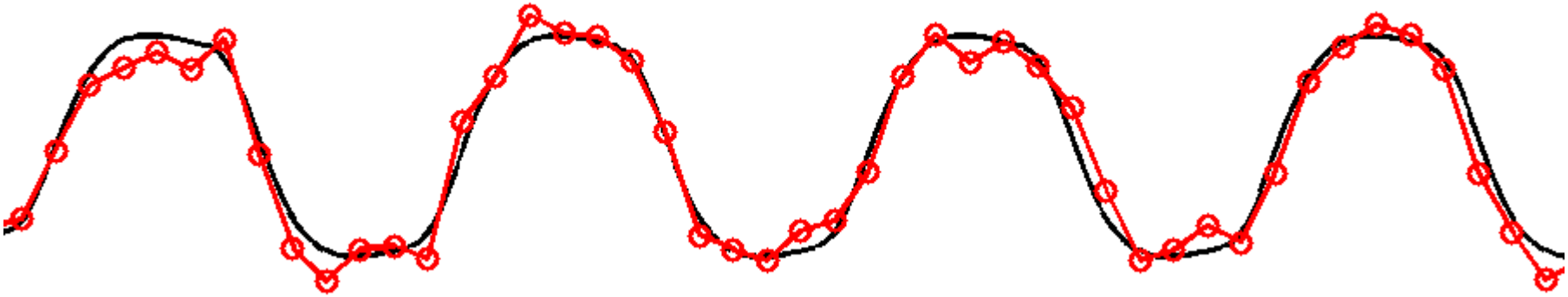
- Random effects:

Inter-subjects variation

suggests *population not different from zero*

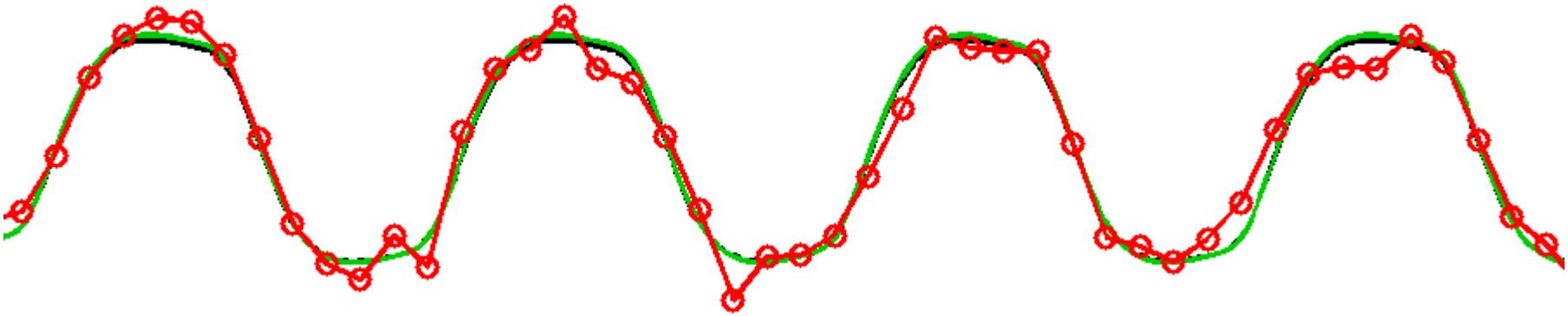


Fixed effects



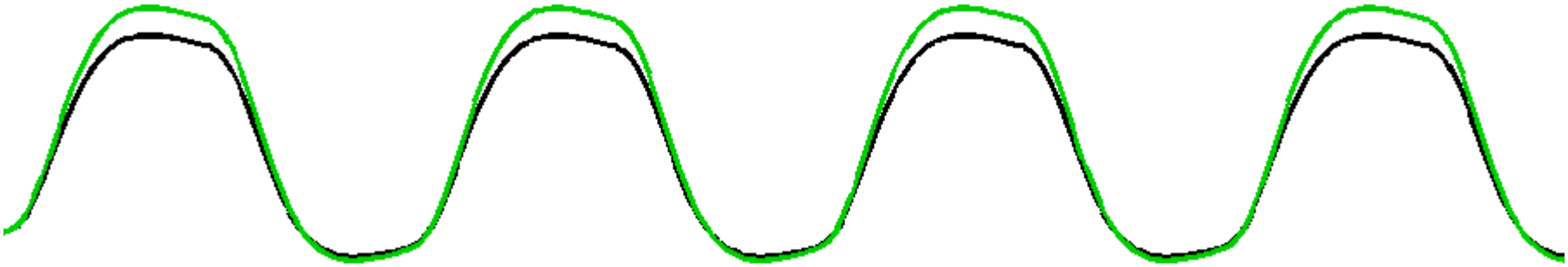
- Only source of variation (over sessions) is measurement error
- True response magnitude is *fixed*

Random effects



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

Random effects



- Two sources of variation
  - measurement errors
  - response magnitude (over subjects)
- Response magnitude is *random*
  - each subject/session has random magnitude
  - but note, population mean magnitude is *fixed*

Fixed vs random effects

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

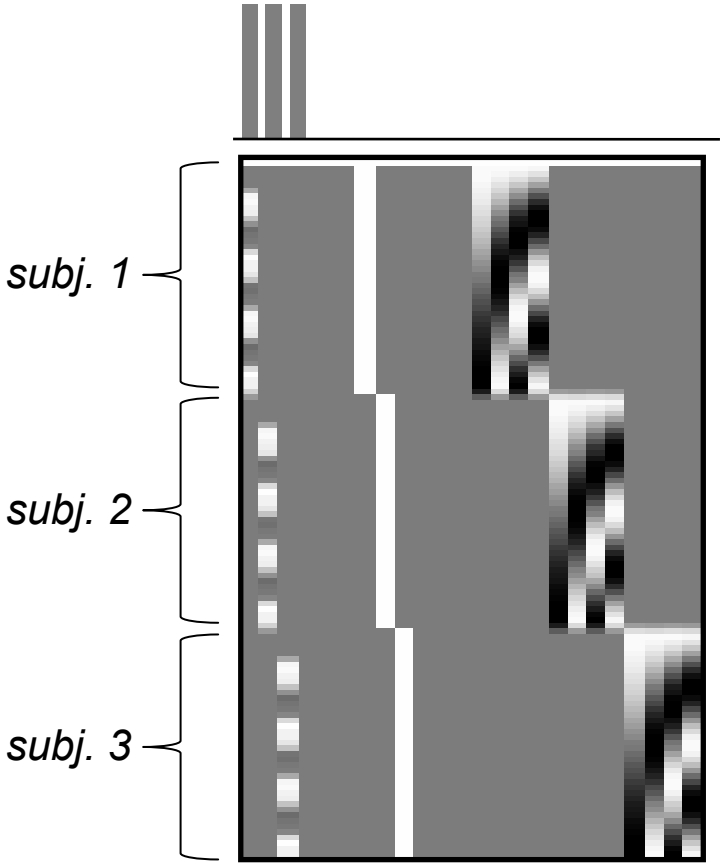
- Summary:
  - **Fixed effect inference**:

  "I can see this effect in this cohort"
  - **Random effect inference**:

  "If I were to sample a new cohort from the same population I would get the same result"

Fixed effect modelling in SPM

- Grand GLM approach
  (model all subjects at once)
- Good:
  - *max dof*
  - *simple model*
- Bad:
  - *assumes common variance over subjects at each voxel*



Group analysis: efficiency and power

- Efficiency = 1/ [estimator variance]
  - goes up with *n* (number of subjects)
  - c.f. “experimental design” talk

- Power = chance of detecting an effect
  - goes up with degrees of freedom (*dof* = *n*-*p*).
  - I reject the null when *P<0.05*. Is my risk of false positive rate (FPR) controlled at 5%?

    Well, not exactly, but valid control: $FPR \leq \alpha$.

    This is potentially conservative.

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  - *summary statistics approach*
  - *non-sphericity modelling*
- Examples

Summary statistics approach

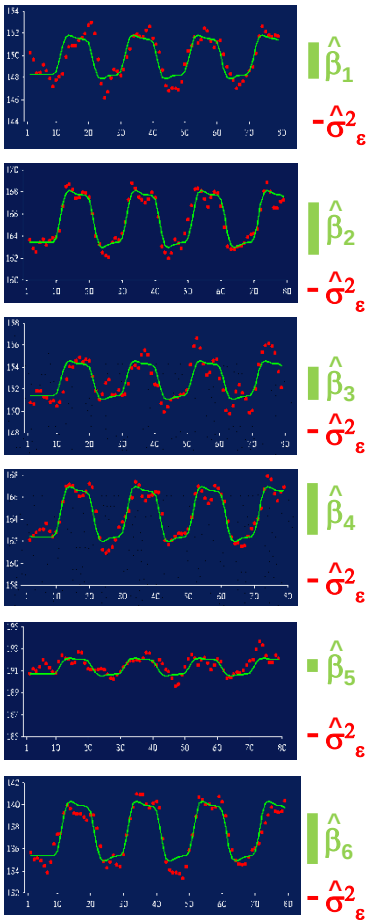
- Proposed by Holmes and Friston

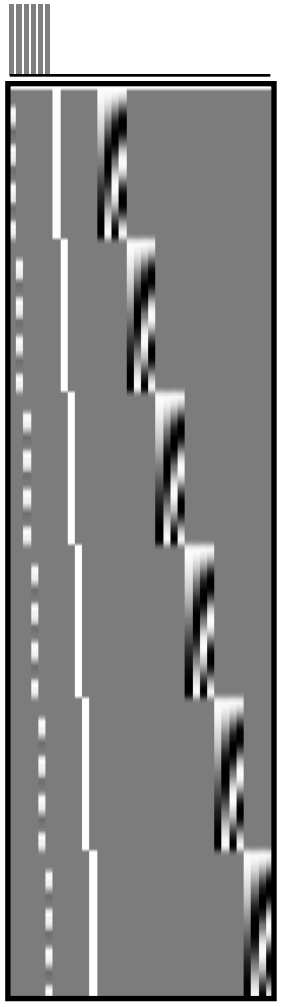
- 1- or 2- sample *t* test on contrast image
  - intra-subject variance not used

- Procedure:
  - Fit GLM for each subject i
    and compute contrast estimate $c\hat{\beta}_i$ (first level)
  - Analyze $\left\{c\hat{\beta}_i\right\}_{i=1,\ldots,n}$ (second level)

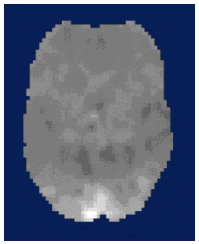
HF approach: motivation (I)

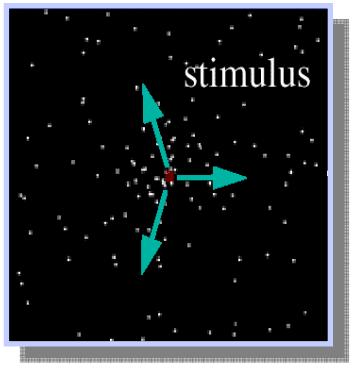
Fixed effects...





estimated mean activation image…



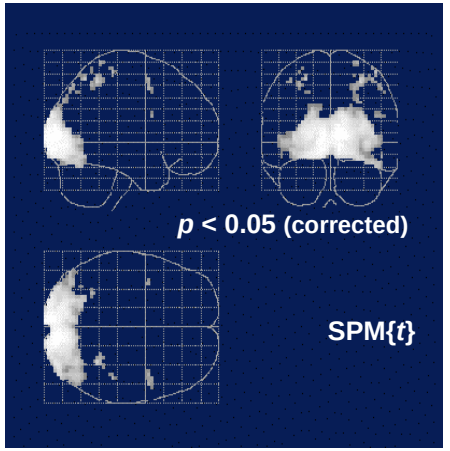


…to be compared with residuals variance:

- $\sigma^2_\varepsilon / nw$

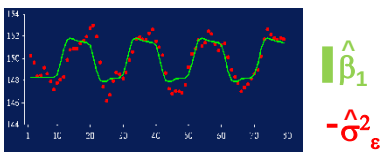
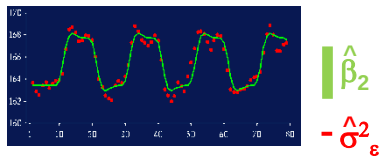
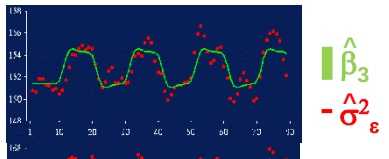
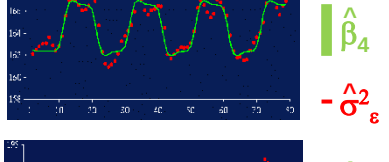
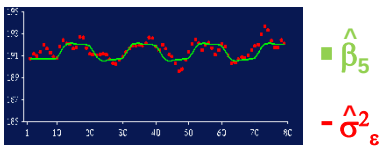
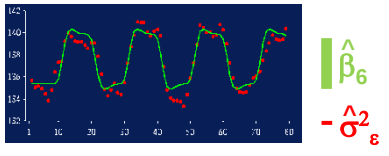
n – subjects

w – error dof

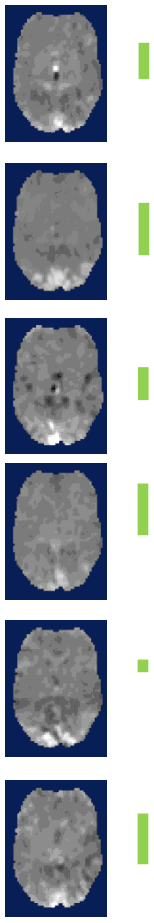


HF approach: motivation (II)

1st level (within subjects) **2nd level** (between-subject)

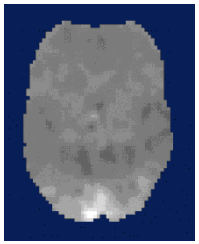







$\hat{\beta}_1$ $-\hat{\sigma}^2_\varepsilon$
$\hat{\beta}_2$ $-\hat{\sigma}^2_\varepsilon$
$\hat{\beta}_3$ $-\hat{\sigma}^2_\varepsilon$
$\hat{\beta}_4$ $-\hat{\sigma}^2_\varepsilon$
$\hat{\beta}_5$ $-\hat{\sigma}^2_\varepsilon$
$\hat{\beta}_6$ $-\hat{\sigma}^2_\varepsilon$



contrasts

estimated mean activation image…

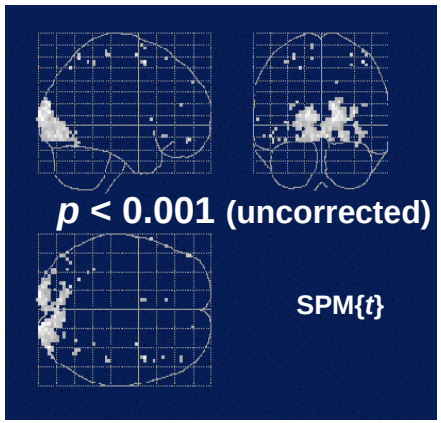


$\overline{\hat{\alpha}}$

…to be compared with RFX variance:

$$\sigma^2 = \sigma^2_\alpha + \sigma^2_\varepsilon / w$$

no voxels significant at $p < 0.05$ (corrected)

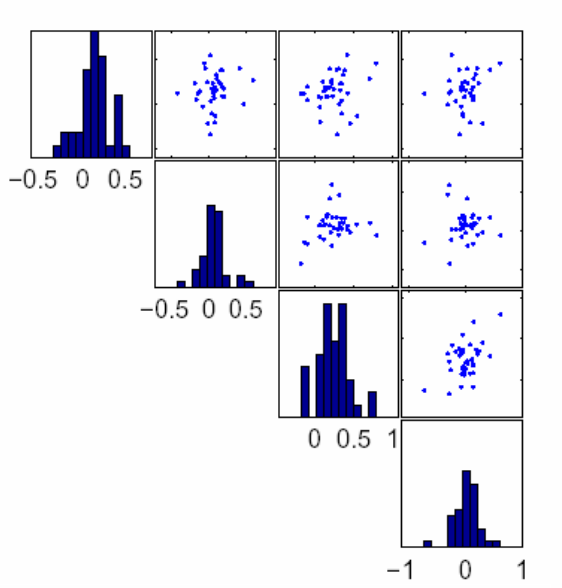


HF approach: assumptions

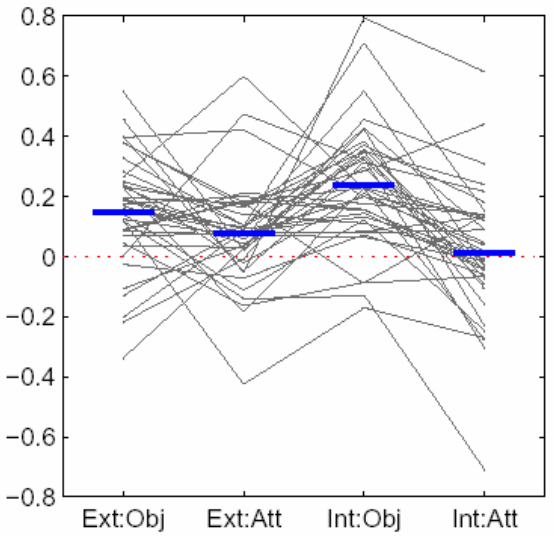
- Distribution
  - Normality
  - Independent subjects
- Homogeneous variance:
  - Residual error the same for all subjects
  - Balanced designs

HF approach: limitations

- Limitations
  - Only single image per subject
  - If 2 or more conditions, must fit separate model for each contrast



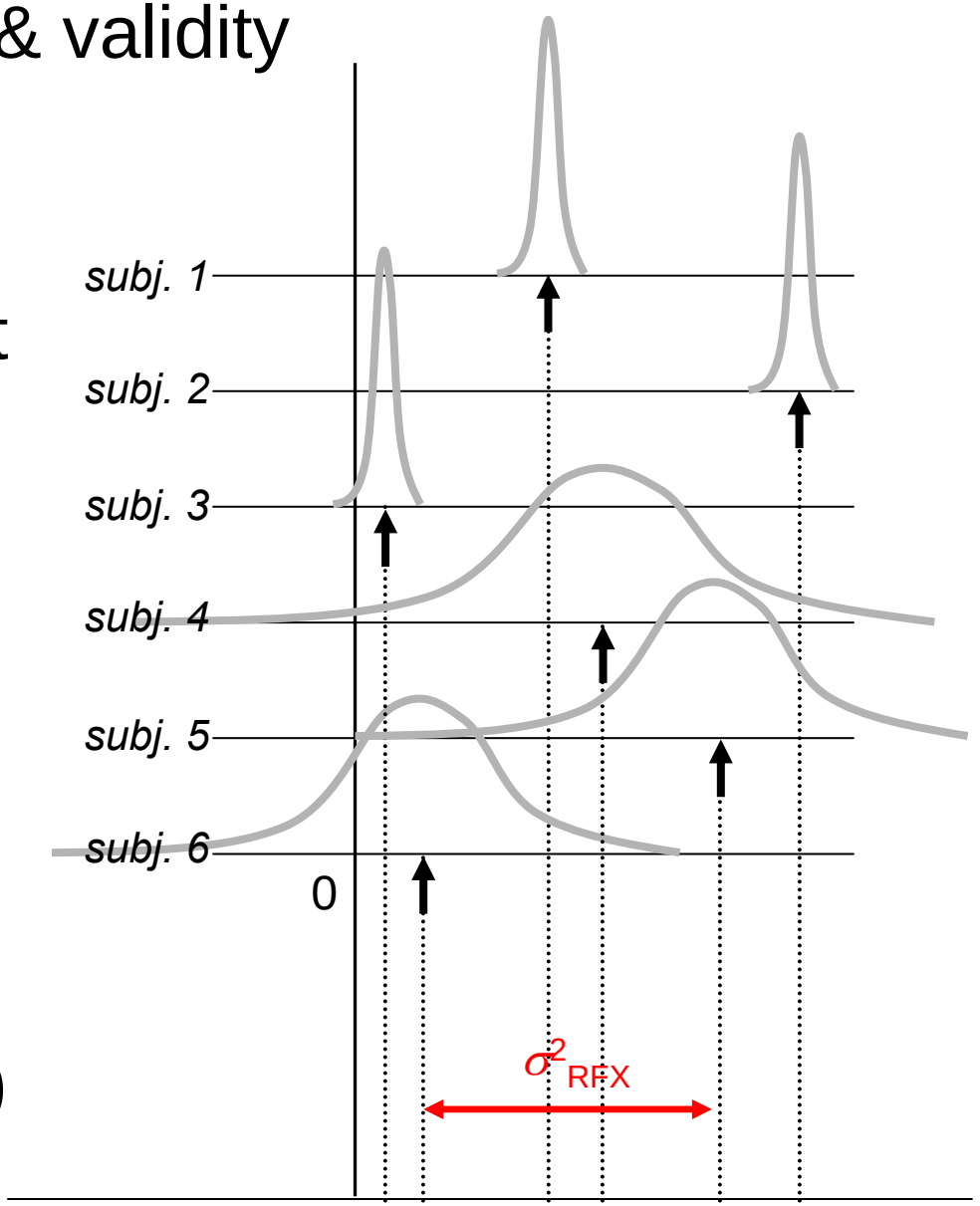
- Limitation a strength!
  - No sphericity assumption made on different conditions when fitting separate models



HF approach: efficiency & validity

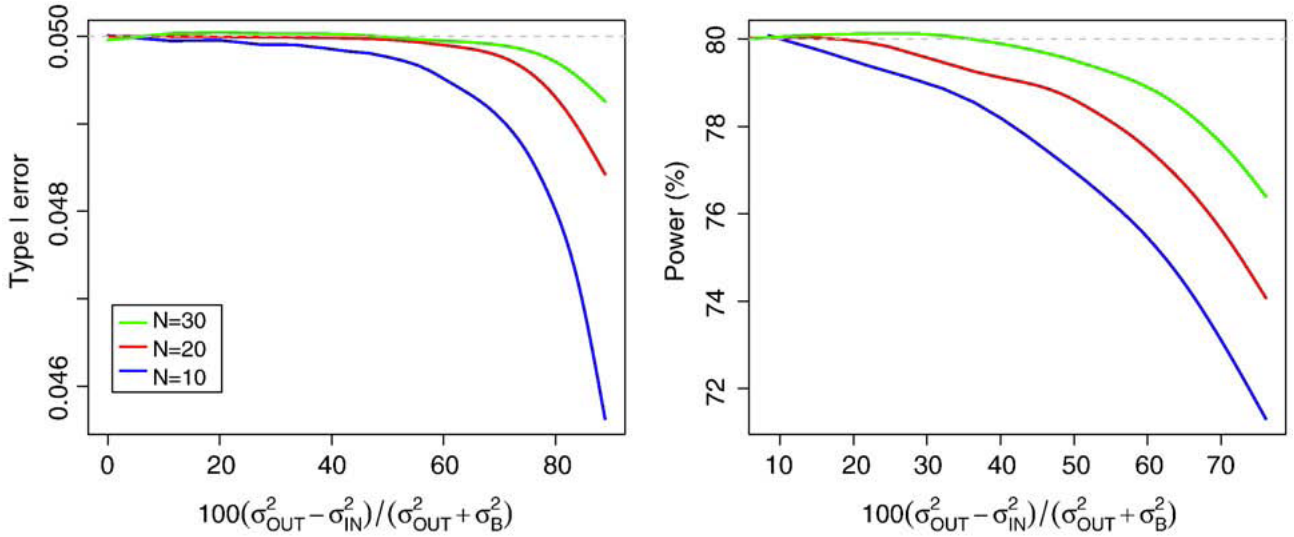
- If assumptions true
  - Optimal, fully efficient
  - Exact p-values
- If σ^2_{FFX} differs btw subj.
  - Reduced efficiency
  - Biased σ^2_{RFX}
  - Liberal dof

  (here 3 subj. dominate)



HF approach: robustness

- In practice, validity and efficiency are excellent
  - For 1-sample case, HF impossible to break



Mumford & Nichols. Simple group fMRI modeling and inference. *Neuroimage*, 47(4):1469--1475, 2009.

- 2-sample and correlation might give trouble
  - Dramatic imbalance and/or heteroscedasticity

Overview

- Group analysis: fixed versus random effects
- Two RFX methods:
  - *summary statistics approach*
  - *non-sphericity modelling*
- Examples

Non sphericity modelling – basics

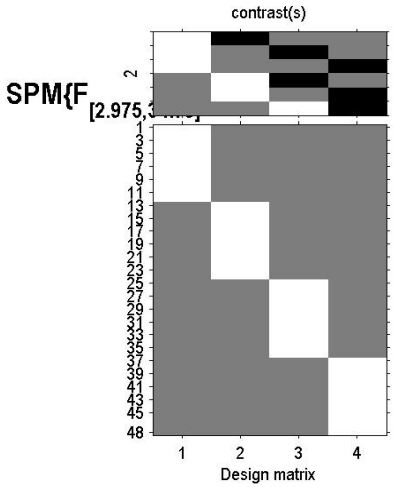
- 1 effect per subject
  - Use Holmes & Friston approach
- >1 effects per subject
  - Can't use HF, must use non sphericity modelling
  - Covariance components and ReML

  (c.f. "Bayesian inference" talk)

The i.i.d. case

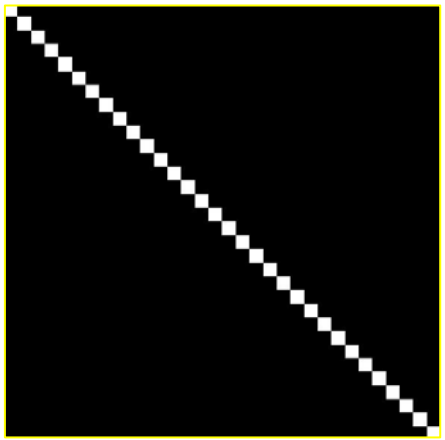
$$y = X \beta + e$$

$n \times 1 \quad n \times p \quad p \times 1 \quad n \times 1$



design matrix

$$\mathrm{Cov}(\varepsilon) = \lambda I$$



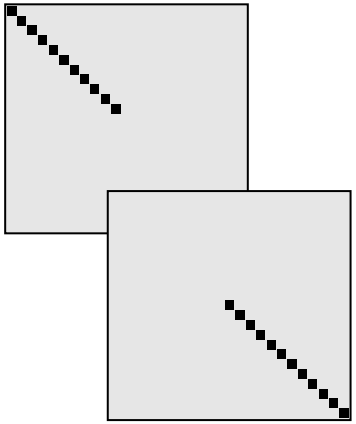
residuals covariance matrix

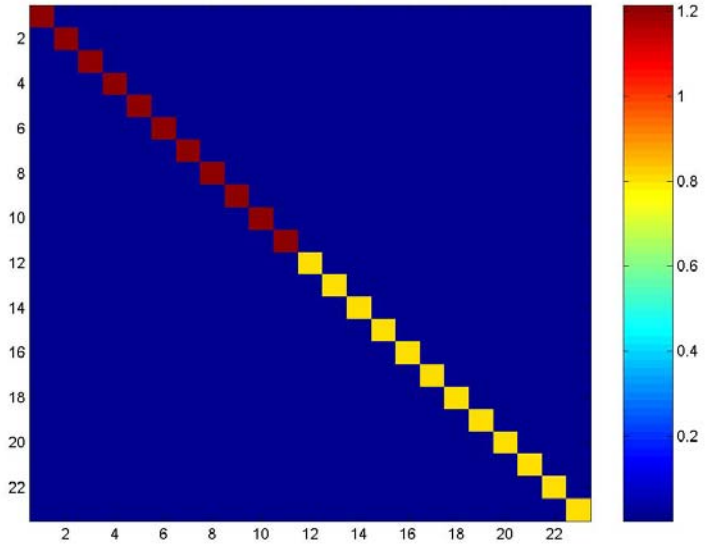
- 12 subjects, 4 conditions
  - Use F-test to find differences btw conditions
  - Underlying assumption: residuals i.i.d.

Multiple covariance components (I)

- E.g., 2-sample t-test
  - Errors are independent but not identical.
  - 2 covariance components

Q_k's:



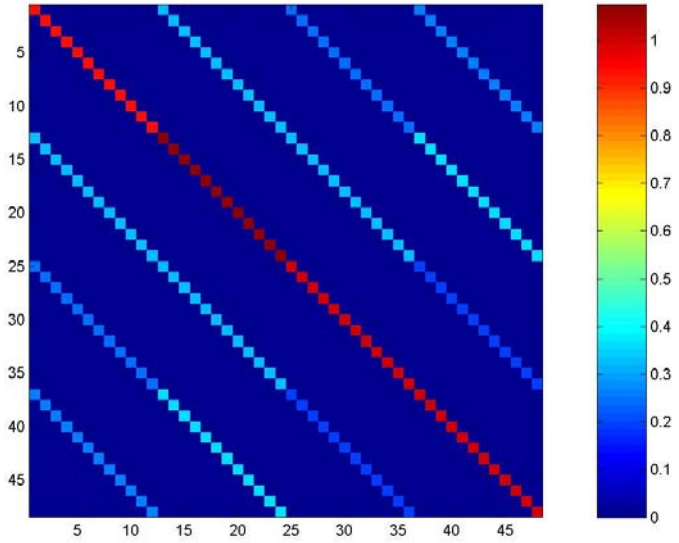


residuals covariance matrix

Multiple covariance components (II)

- Errors are not independent and not identical

residuals covariance matrix



Q_k's:

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***Example 1**: data*

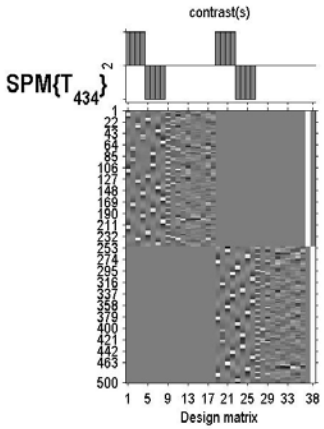
- Stimuli:
  - Auditory presentation (SOA = 4 sec)
  - 250 scans per subject, block design
  - Words, e.g. “book”
  - Words spoken backwards, e.g. “koob”

- Subjects:
  - 12 controls
  - 11 blind people

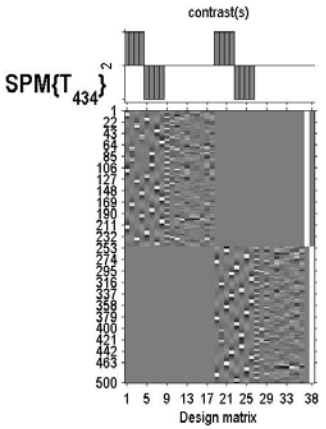
***Example 1**: population differences*

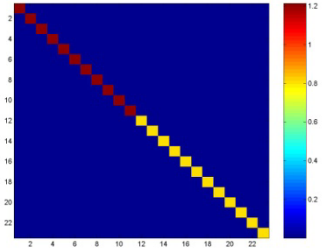
- 1st level
- 2nd level

controls

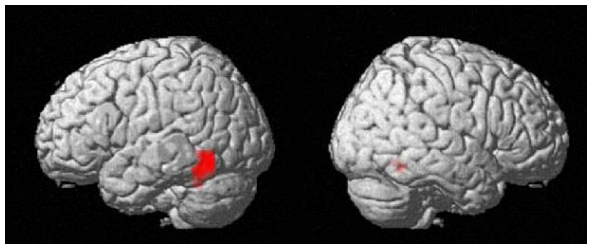


blinds

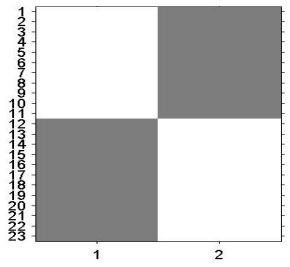




$$Cov(\varepsilon)$$



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



$$X$$

design matrix

Example 2

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

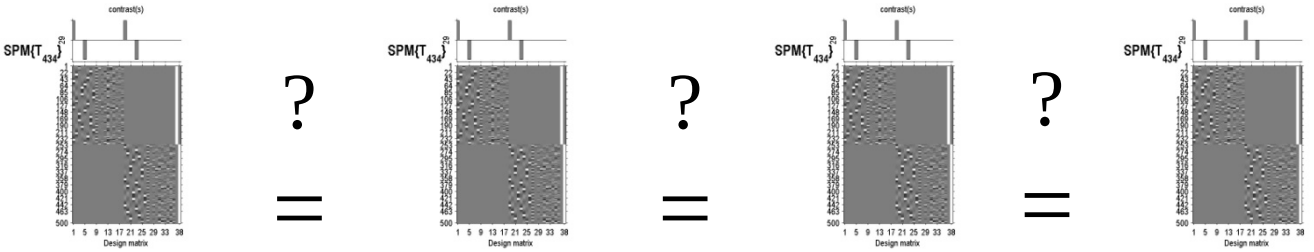
Motion	Sound	Visual	Action
“jump”	“click”	“pink”	“turn”

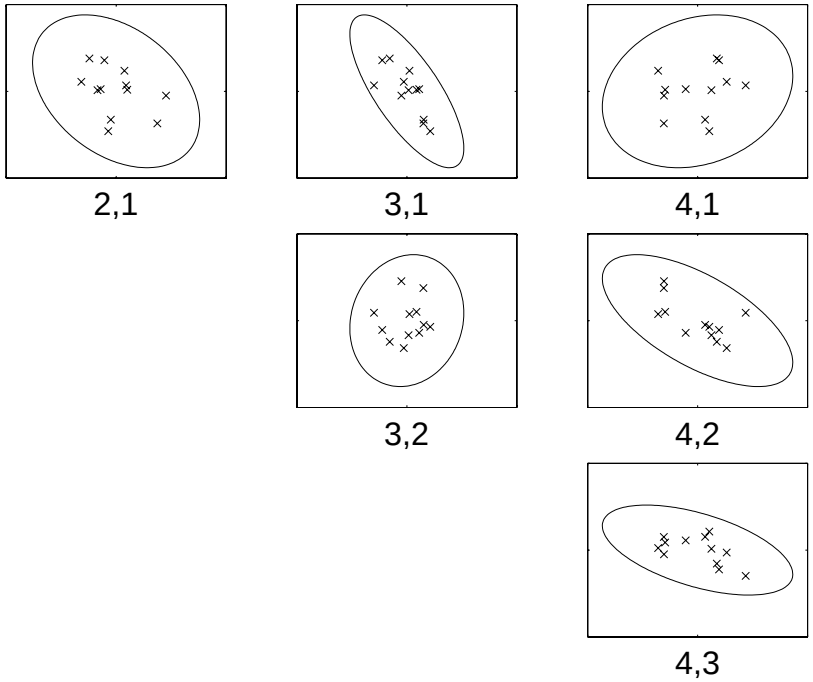
- Subjects:
  - 12 controls
- Question:
  - What regions are affected by the semantic content of the words?

***Example 2**: repeated measures ANOVA*

- 1st level
- 2nd level

1: motion 2: sounds 3: visual 4: action

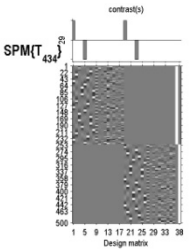




***Example 2**: repeated measures ANOVA*

- 1st level

1: motion



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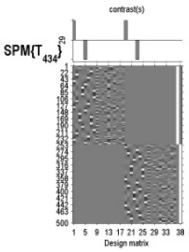
2: sounds



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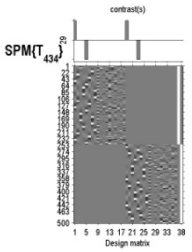
3: visual



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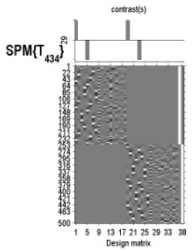
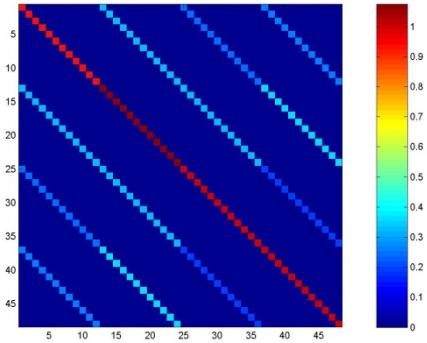
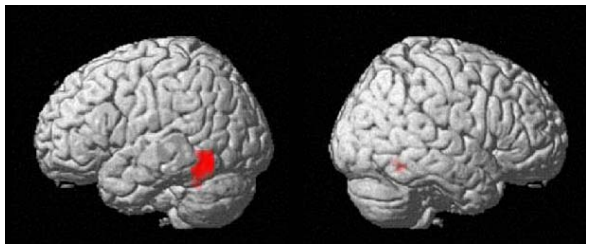
4: action

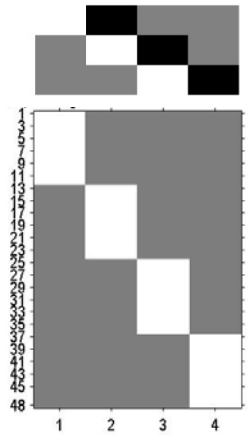


- 2nd level



$Cov(\varepsilon)$



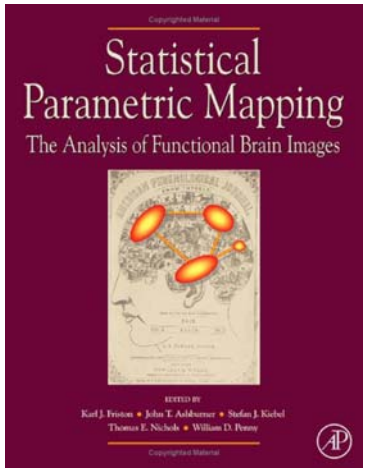


design matrix

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

X

Bibliography:



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