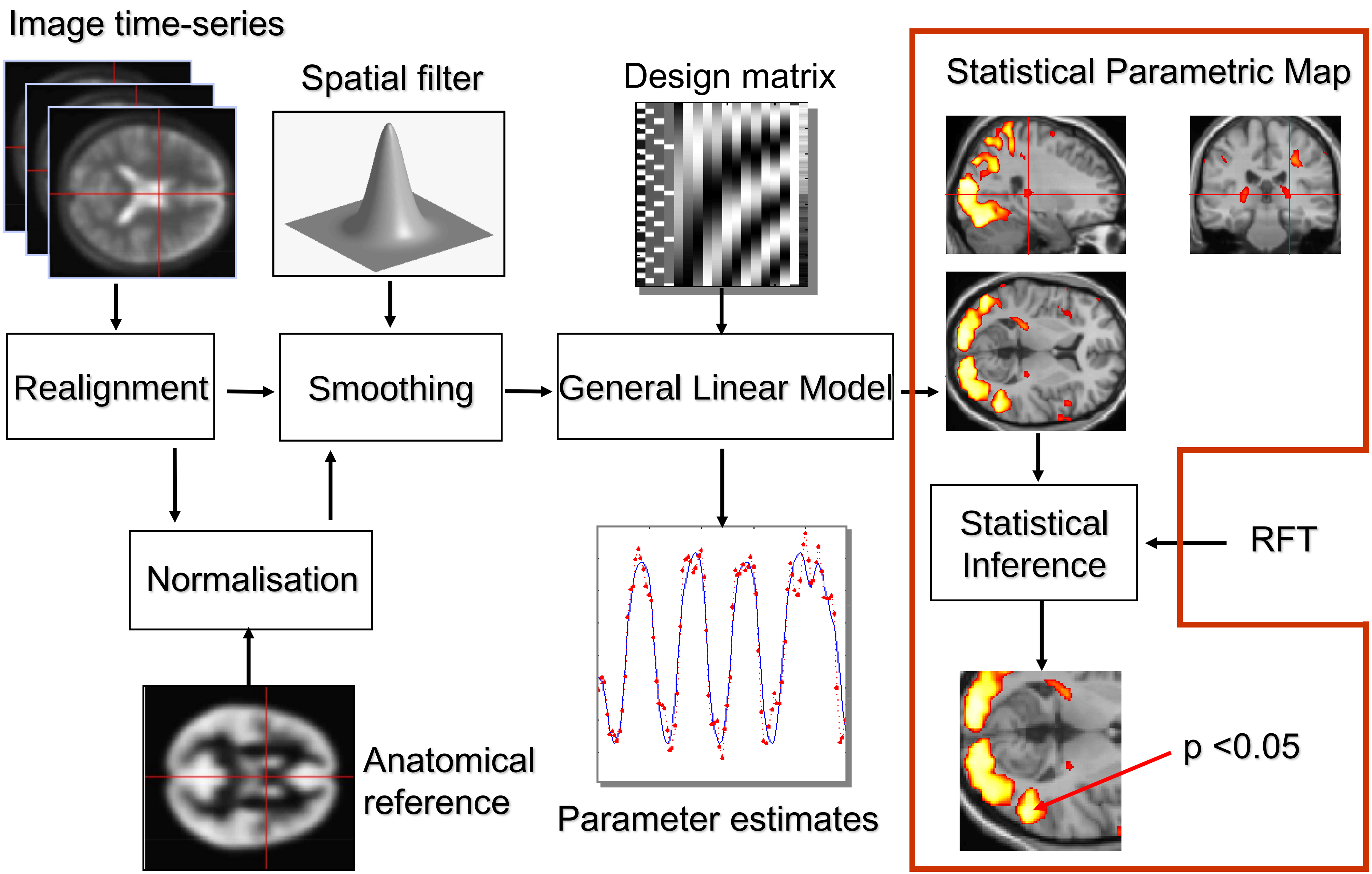
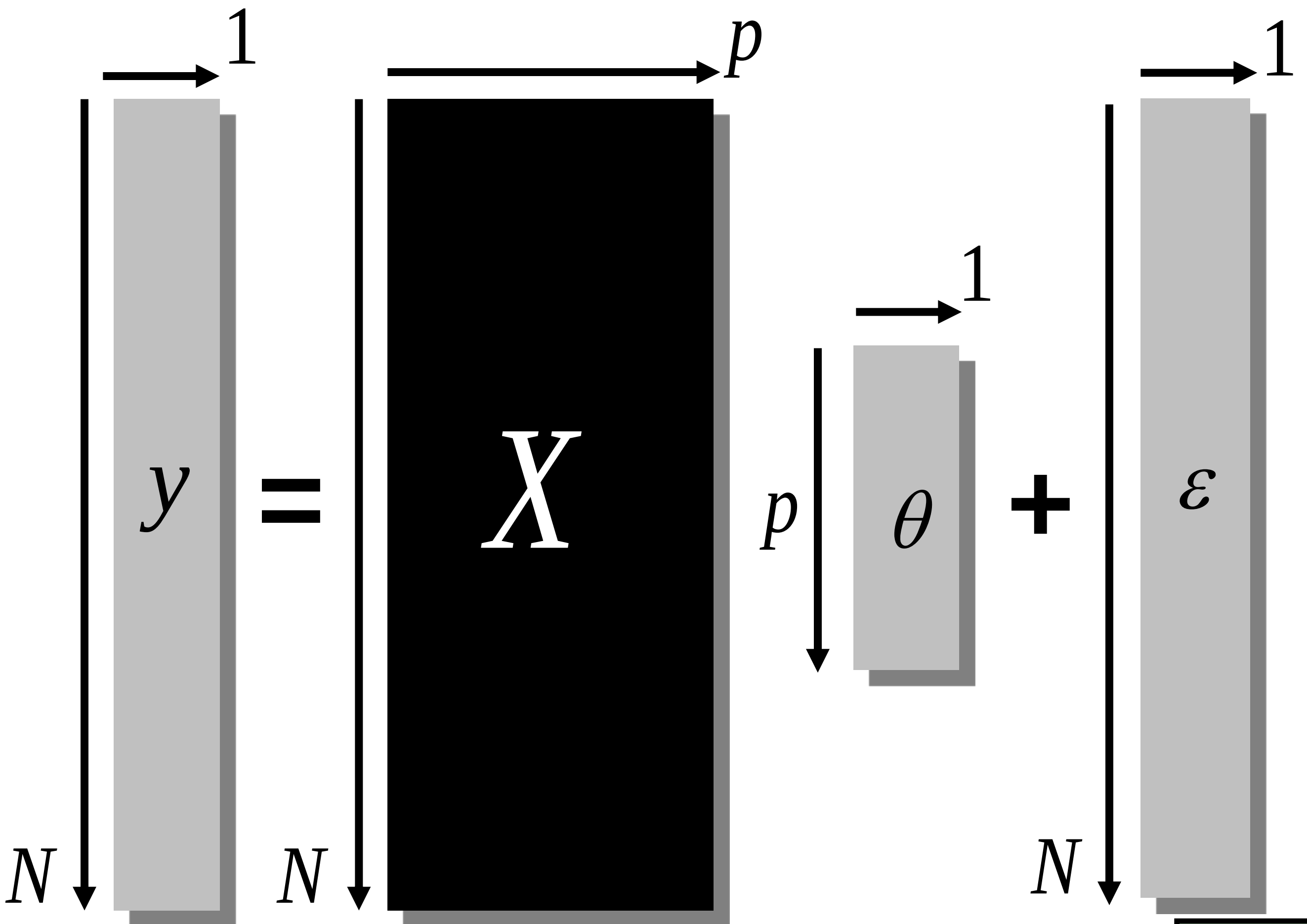
Group analysis

Kherif Ferath
LREN

GLM : individual level



GLM : individual level



$$y = X\theta + \varepsilon$$

Error Covariance

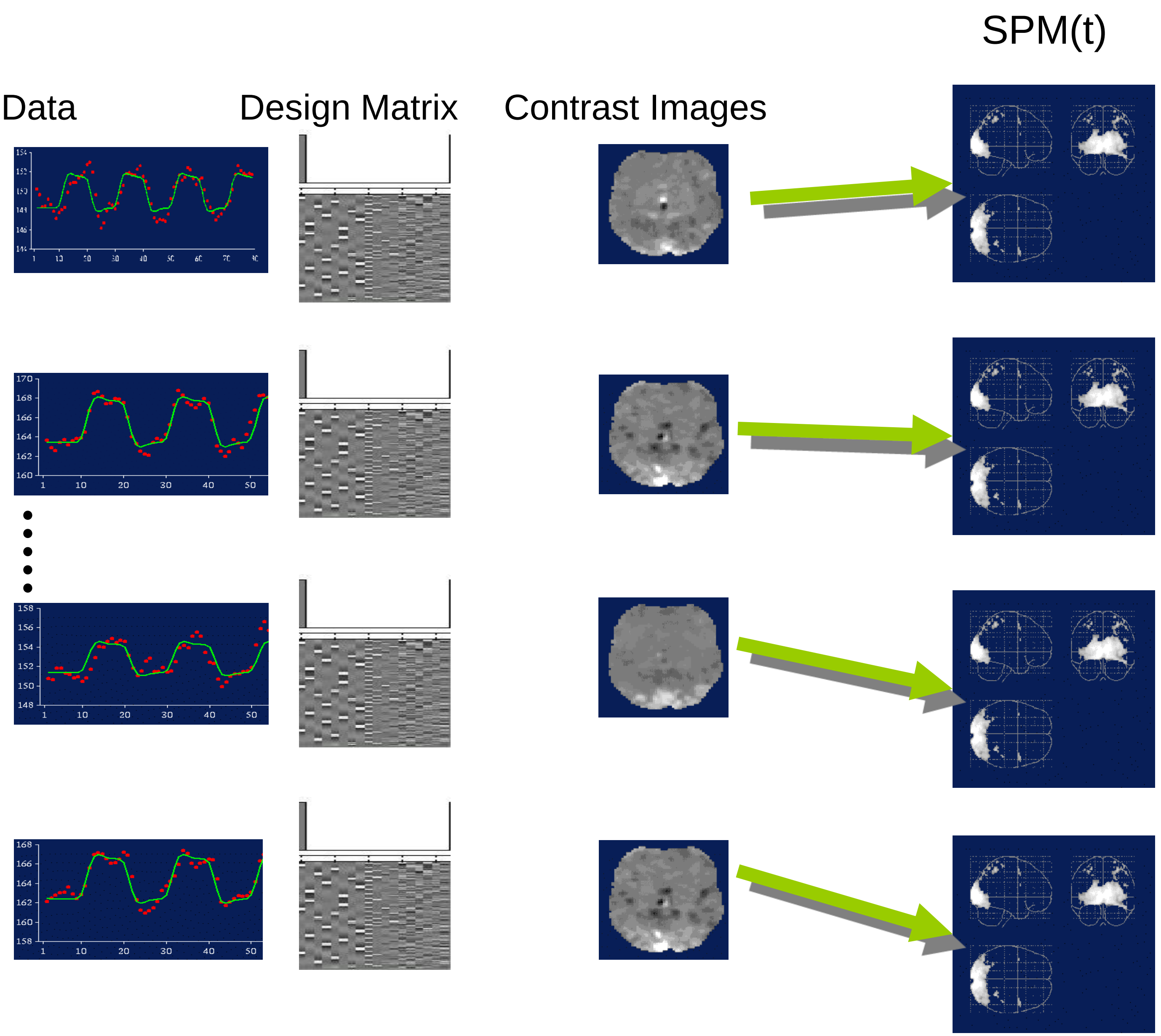
$$C_{\varepsilon} = \sum_k \lambda_k Q_k$$

N: number of scans
p: number of regressors

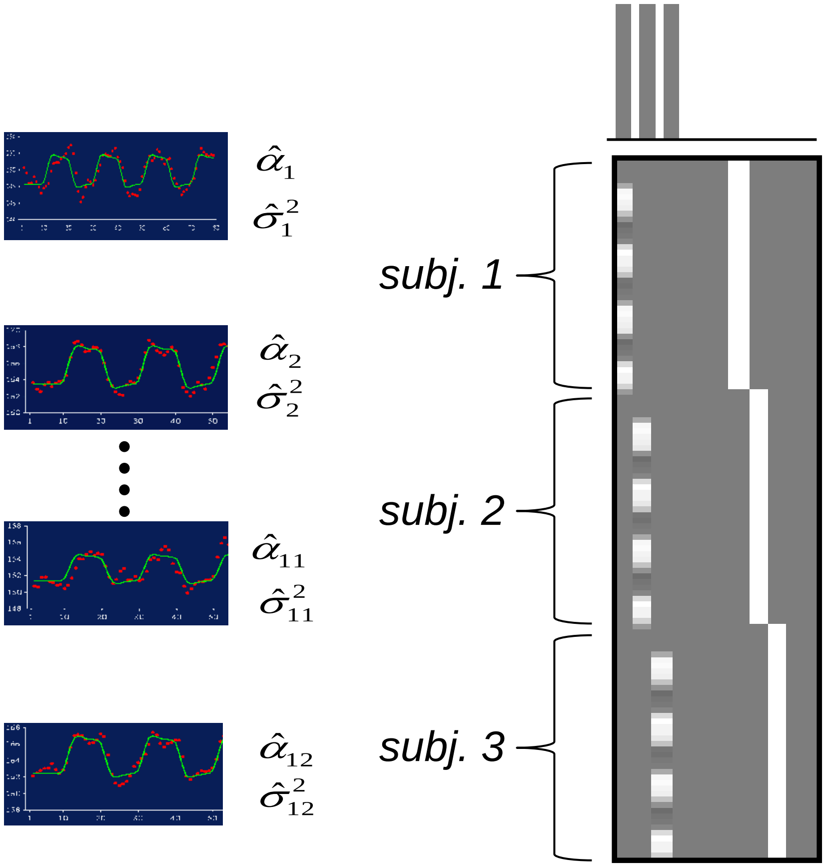
Model is specified by
1. Design matrix *X*
2. Assumptions about ε

GLM : Several individuals

$\hat{\alpha}_1$	$\hat{\sigma}_1^2$
3	***0.9***
4	***1.2***
2	***1.5***
1	***0.5***
1	***0.4***
2	***0.7***
3	***0.8***
3	***2.1***
3	***1.8***
2	***0.8***
4	***0.7***
4	***1.1***



Fixed effect



SPM(t)

T=m/SEM_W=62.7
p=10^{-51}

$\hat{\alpha}_1$	$\hat{\sigma}_1^2$
3	*0.9*
4	*1.2*
2	*1.5*
1	*0.5*
1	*0.4*
2	*0.7*
3	*0.8*
3	*2.1*
3	*1.8*
2	*0.8*
4	*0.7*
4	*1.1*

Mean effect, m=2.67

SEM_W = s_w /sqrt(N)=0.04

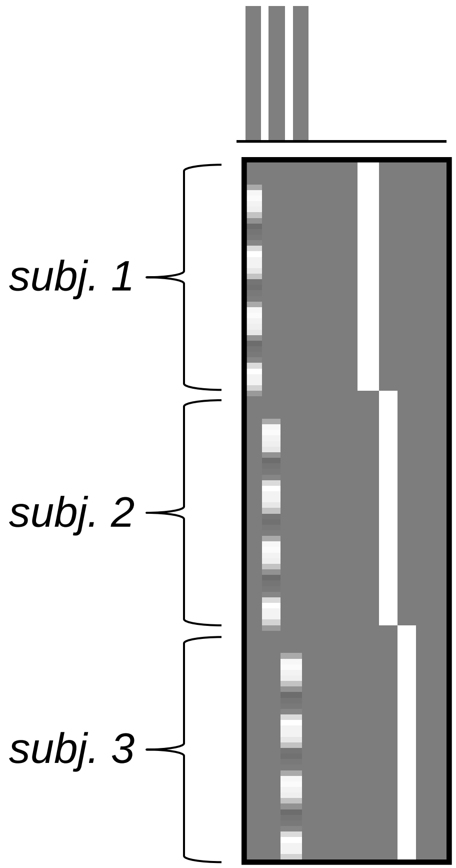
- Grand GLM approach

  (model all subjects at once)

SPM

Fixed effect modelling in SPM

- Grand GLM approach
  (model all subjects at once)



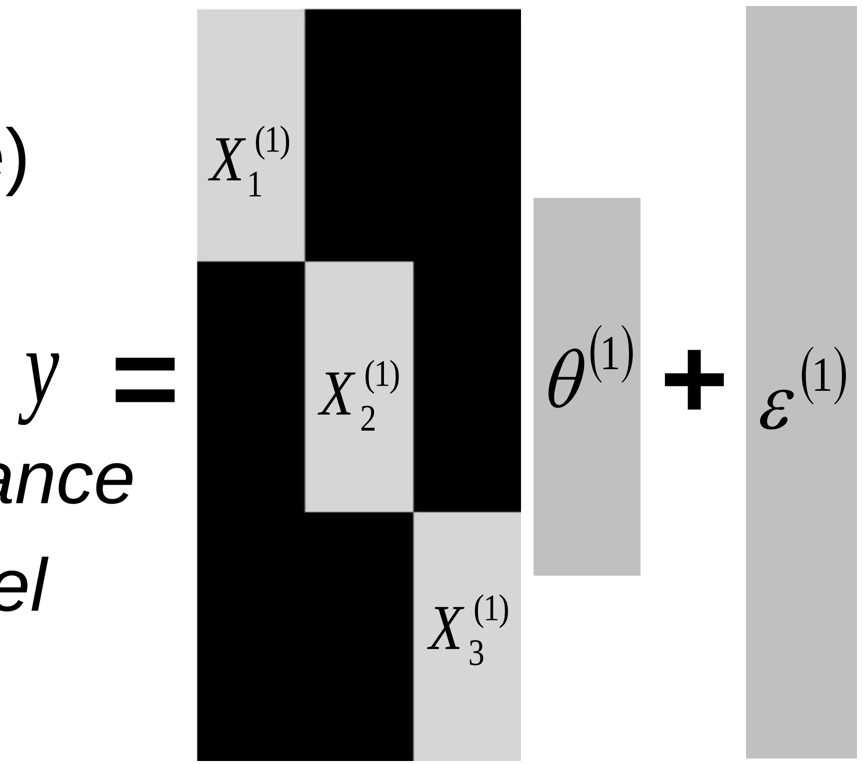
- Good:
  - *max dof*
  - *simple model*

Fixed effect

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

- Grand GLM approach
  (model all subjects at once)

- Bad:
  - *assumes common variance over subjects at each voxel*



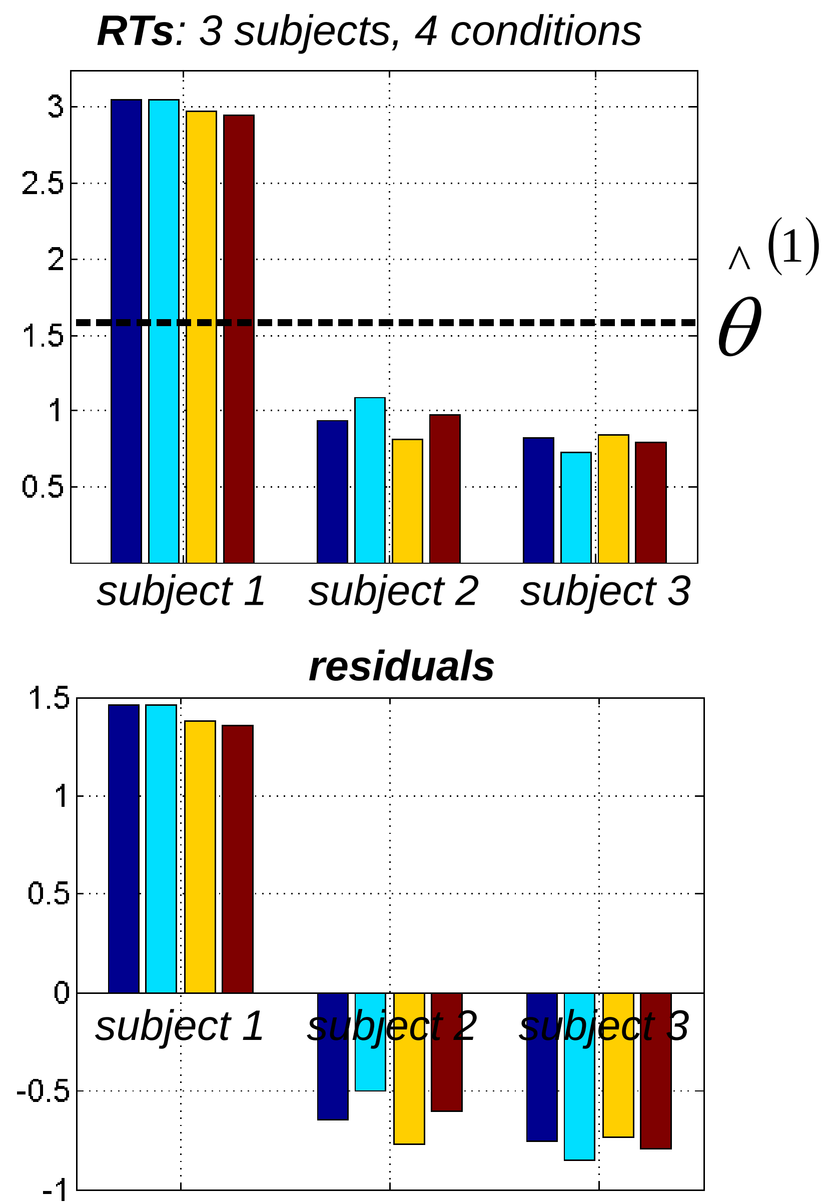
Between subjects variability

- Standard GLM

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

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



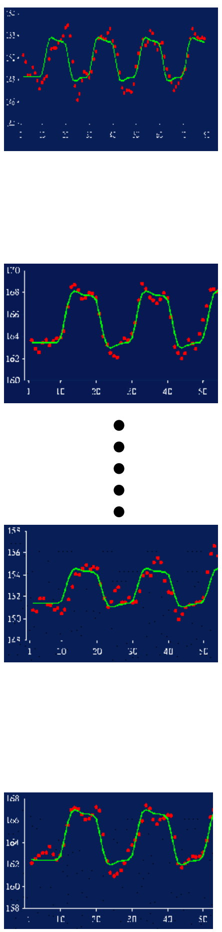
Summary Statistics approach

First level

Data

Design Matrix

Contrast Images

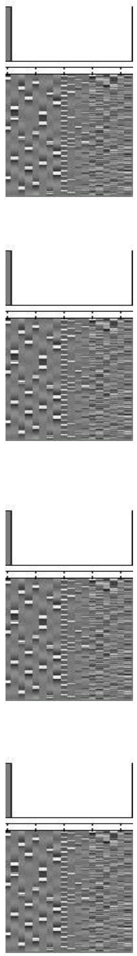


$\hat{\alpha}_1$ $\hat{\sigma}_1^2$

$\hat{\alpha}_2$ $\hat{\sigma}_2^2$

$\hat{\alpha}_{11}$ $\hat{\sigma}_{11}^2$

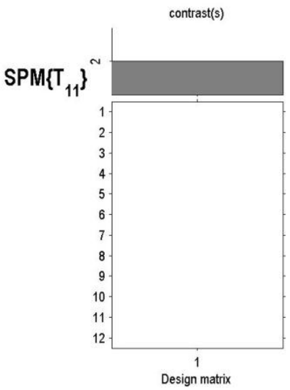
$\hat{\alpha}_{12}$ $\hat{\sigma}_{12}^2$

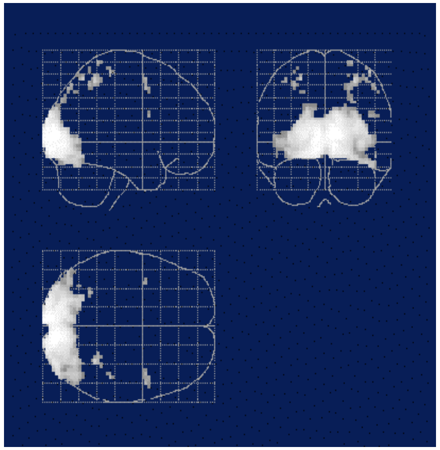


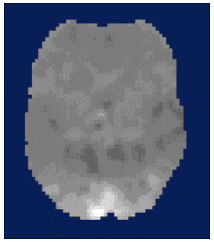
$$y = X^{(1)}\theta^{(1)} + \varepsilon^{(1)}$$

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

SPM(t)







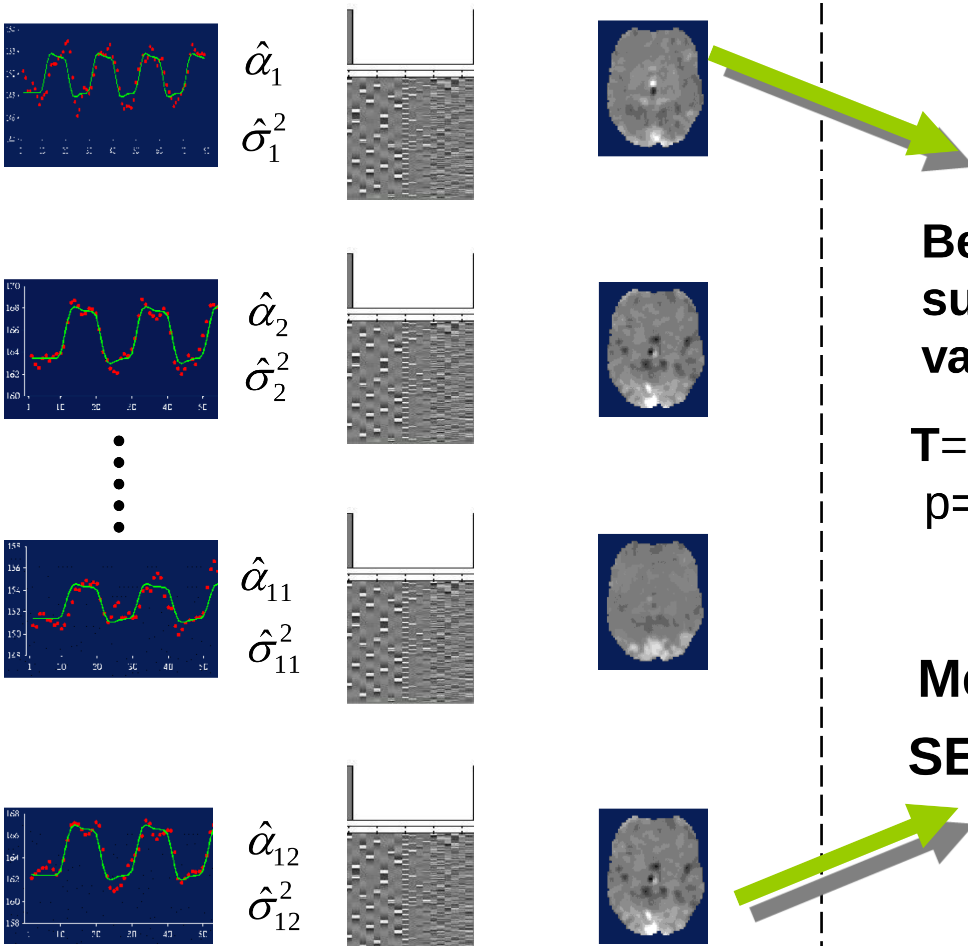
Second level

Summary Statistics approach

SPM

First level

Data | Design Matrix | Contrast Images



$\hat{\alpha}_1$	$\hat{\sigma}_1^2$
3	0.9
4	1.2
2	1.5
1	0.5
1	0.4
2	0.7
3	0.8
3	2.1
3	1.8
2	0.8
4	0.7
4	1.1

Between subject variability

T=m/SEM_b=8.61
p=10^{-6}

Mean effect, m=2.67

SEM_b = s_b /sqrt(N)=0.31

Hierarchical model

Hierarchical model

$$y = X^{(1)}\theta^{(1)} + \varepsilon^{(1)}$$
$$\theta^{(1)} = X^{(2)}\theta^{(2)} + \varepsilon^{(2)}$$
$$\vdots$$
$$\theta^{(n-1)} = X^{(n)}\theta^{(n)} + \varepsilon^{(n)}$$

Multiple variance components at each level

$$C_{\varepsilon}^{(i)} = \sum_k \lambda_k^{(i)} Q_k^{(i)}$$

At each level, distribution of parameters is given by level above.

What we don't know: distribution of parameters and variance parameters.

Lexicon

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

… all the same

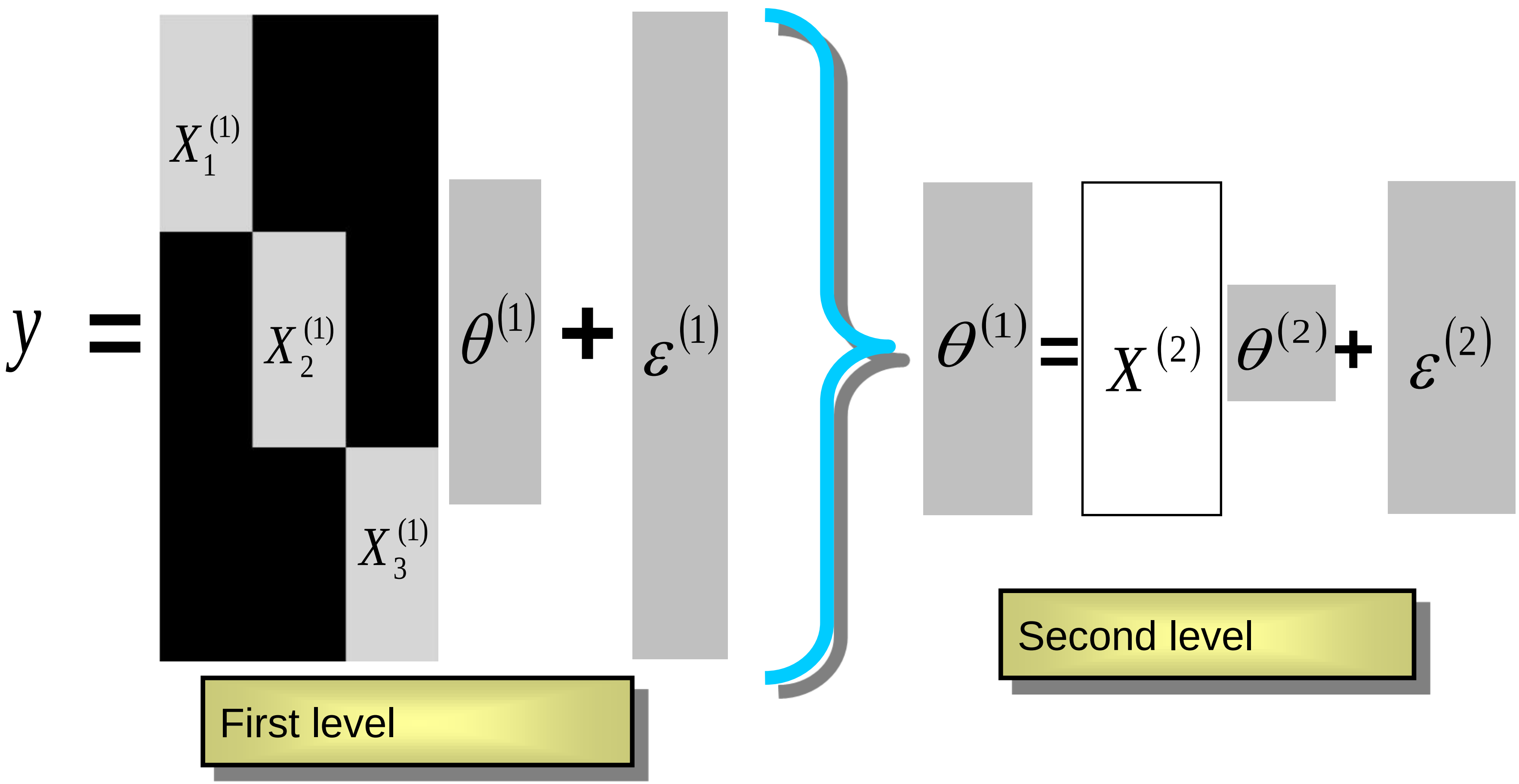
… all alluding to multiple sources of variation
(in contrast to fixed effects)

Hierarchical model

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

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

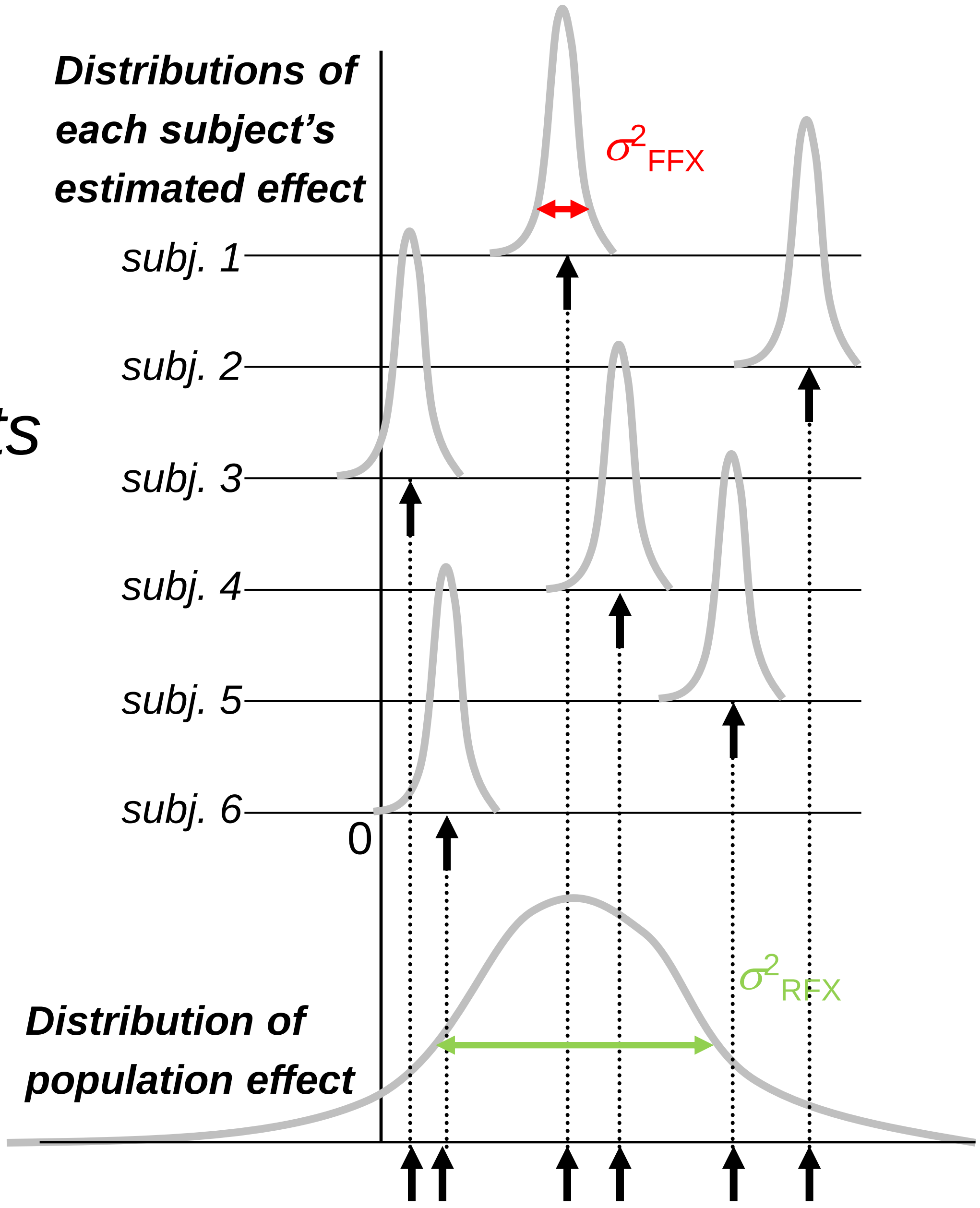
Example: Two level model



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*

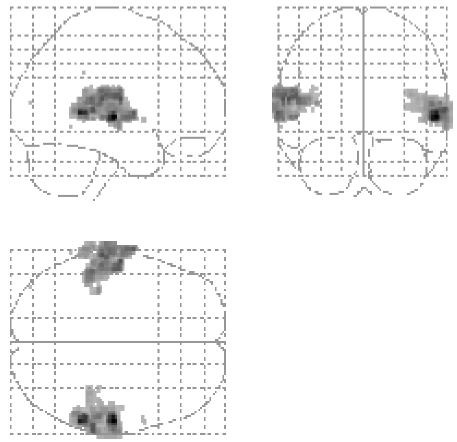


Summary Statistics approach

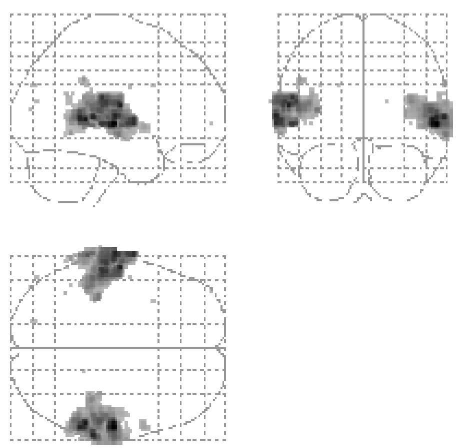
SPM

Robustness

Summary statistics



Hierarchical Model



Friston et al. (2004) Mixed effects and fMRI studies, Neuroimage

Summary Statistics approach

- 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)

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

Summary Statistics approach

Assumptions

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

Non sphericity modelling – basics

- 1 effect per subject
  - Summary statistics approach

- >1 effects per subject
  - non sphericity modelling
  - Covariance components and ReML

***Example 1**: data*

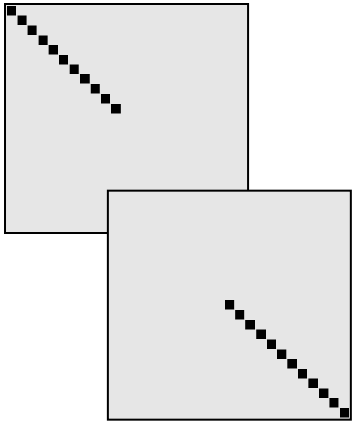
- Stimuli:
  - Auditory presentation (SOA = 4 sec)
  - 250 scans per subject, block design
  - Words, e.g. “book”
  - Words spoken backwards, e.g. “koob”

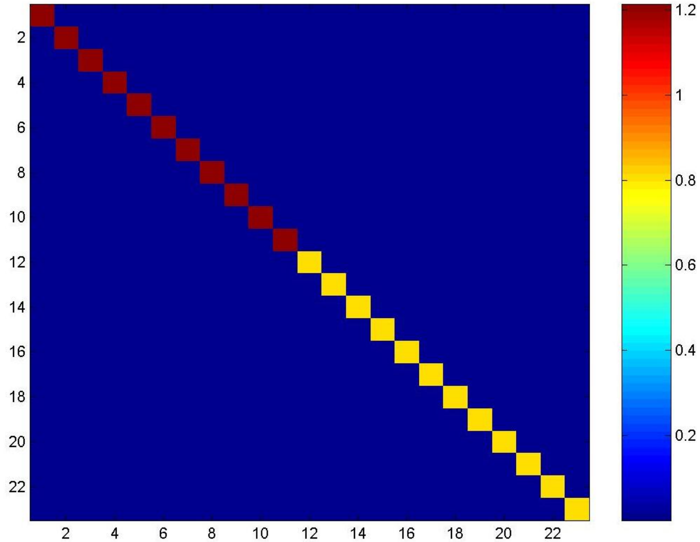
- Subjects:
  - 12 controls
  - 11 blind people

Multiple covariance components (I)

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

Q_k's:

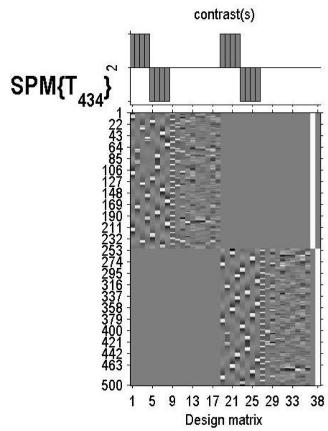




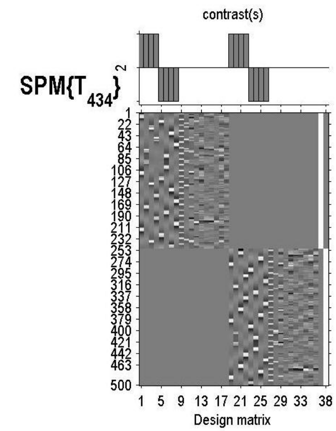
residuals covariance matrix

***Example 1**: population differences*

controls

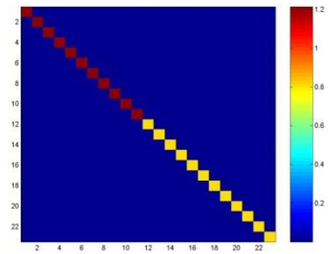


blinds

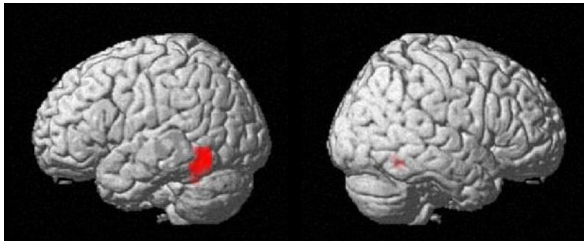


- 1st level

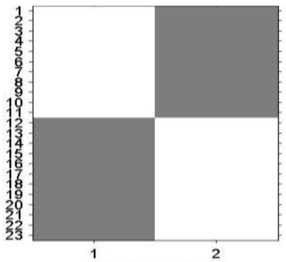
- 2nd level



$$Cov(\varepsilon)$$



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



$$X$$

design matrix

SPM

Example 2

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

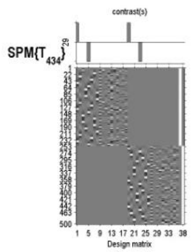
Motion	Sound	Visual	Action
“jump”	“click”	“pink”	“turn”

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

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

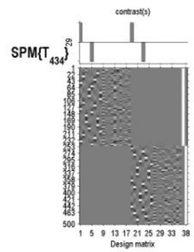
- 1st level
- 2nd level

1: motion



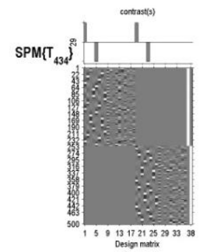
?=

2: sounds



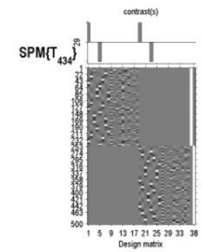
?=

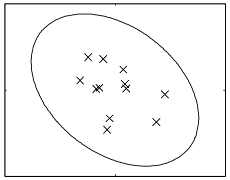
3: visual



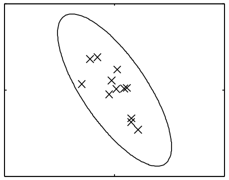
?=

4: action

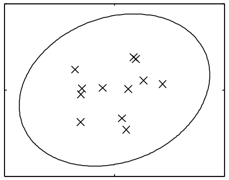




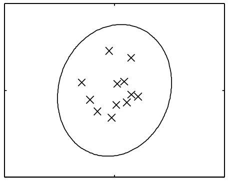
2,1



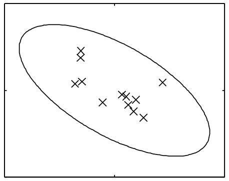
3,1



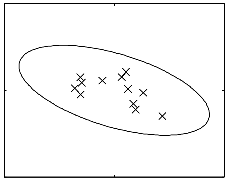
4,1



3,2



4,2

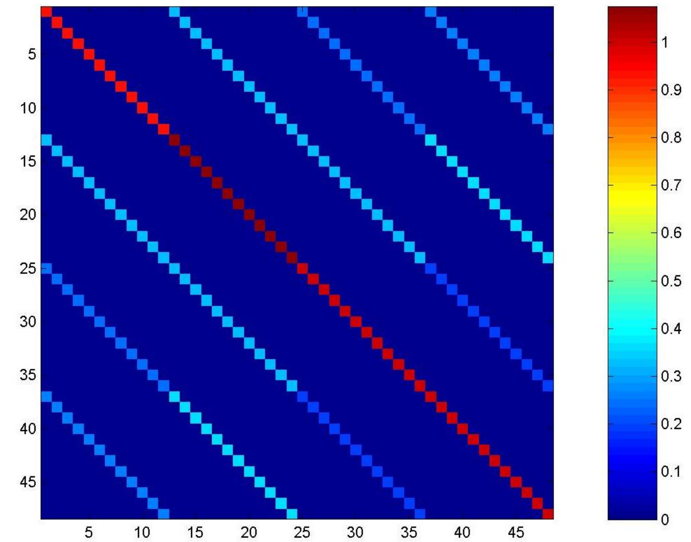


4,3

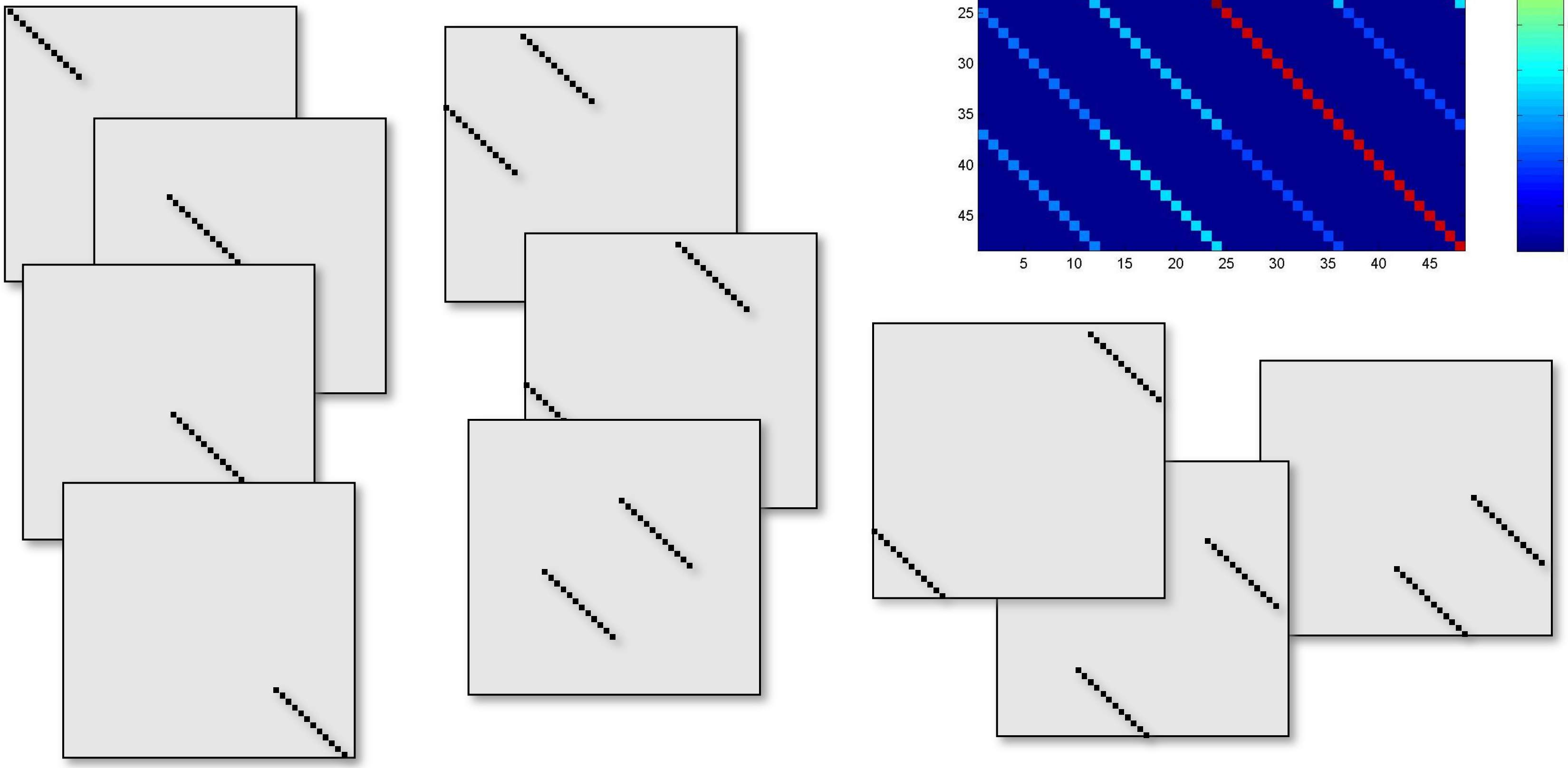
Multiple covariance components (II)

- Errors are not independent and not identical

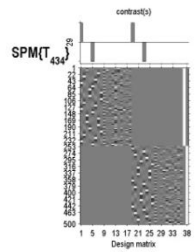
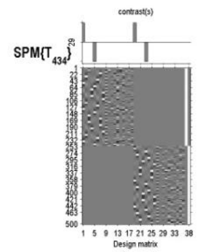
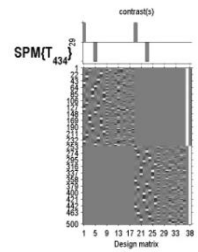
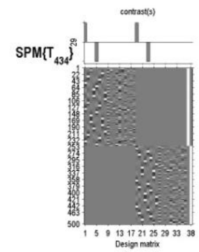
residuals covariance matrix



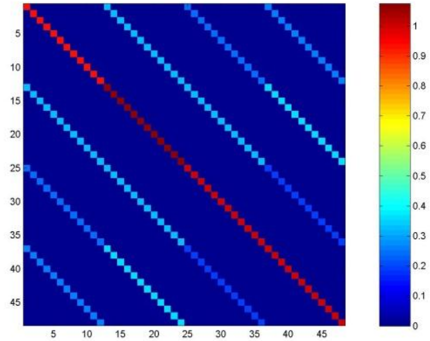
Q_k's:



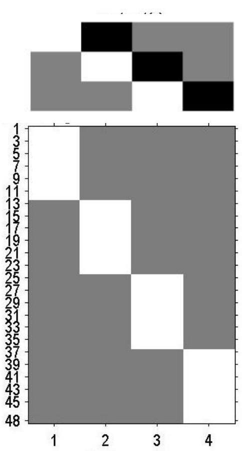
***Example 2**: repeated measures ANOVA*

	1: motion		2: sounds		3: visual		4: action
❑ 1st level		$\overset{?}{=}$		$\overset{?}{=}$		$\overset{?}{=}$	

❑ 2nd level



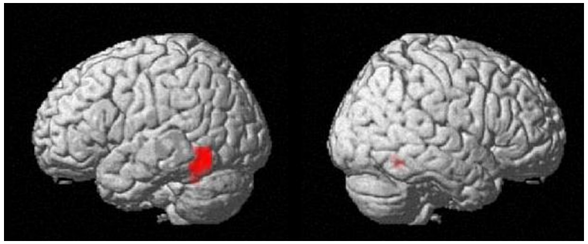
$$Cov(\varepsilon)$$



design matrix

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

$$X$$



SPM

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**:

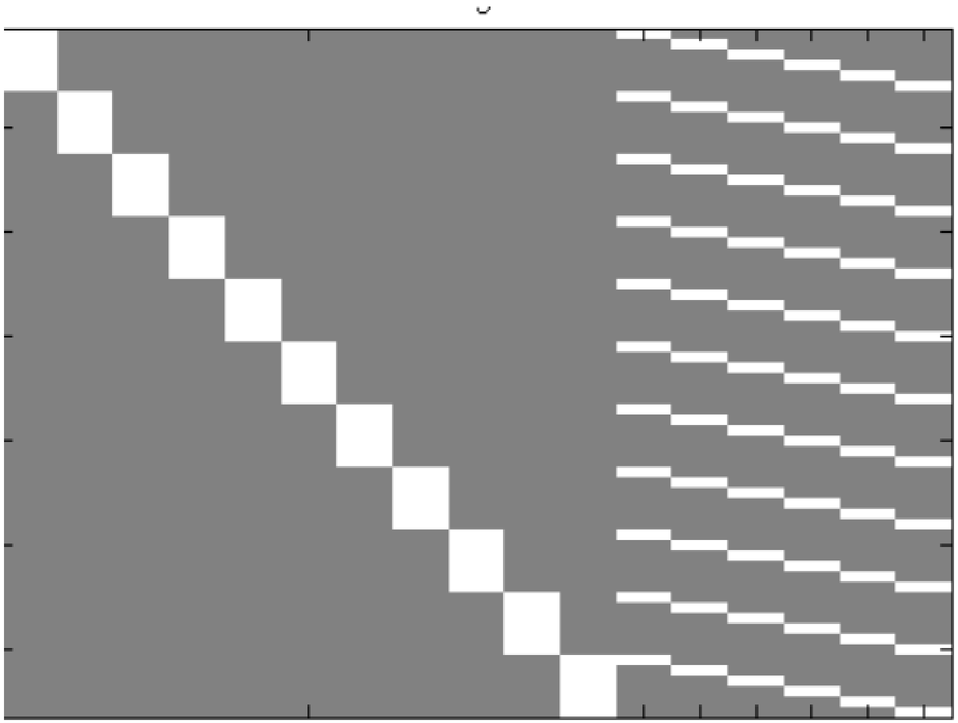
    "If I were to sample a new cohort from the same population I would get the same result"

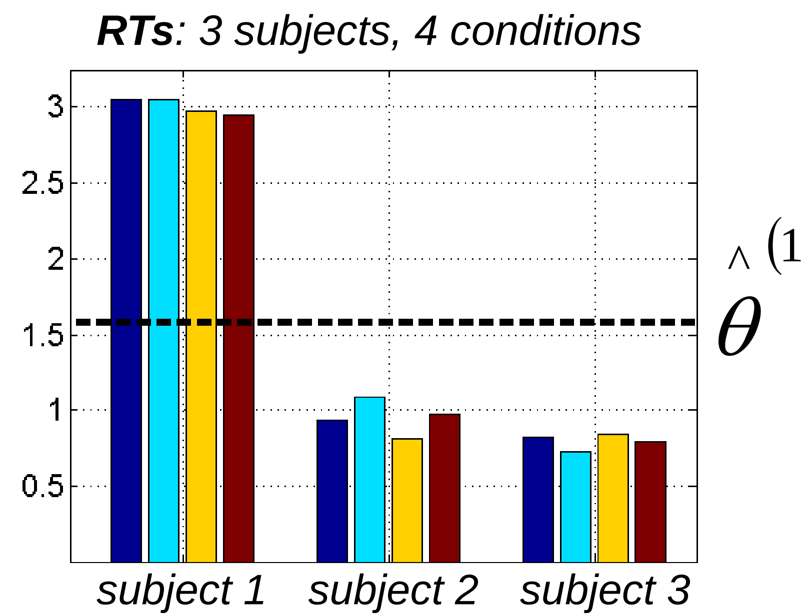
Group analysis: efficiency and power

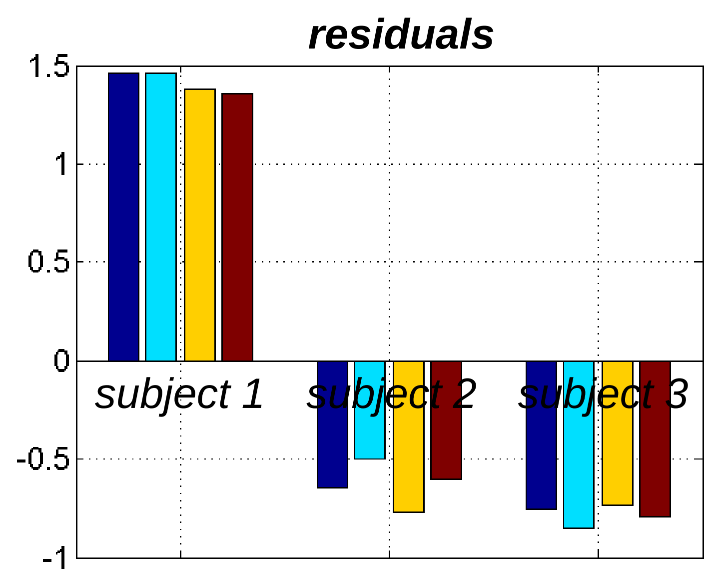
- Efficiency = 1/ [estimator variance]
  - goes up with *n* (number of subjects)
  - c.f. “experimental design” talk

- Power = chance of detecting an effect
  - goes up with degrees of freedom (*dof* = *n*-*p*).

Individual differences



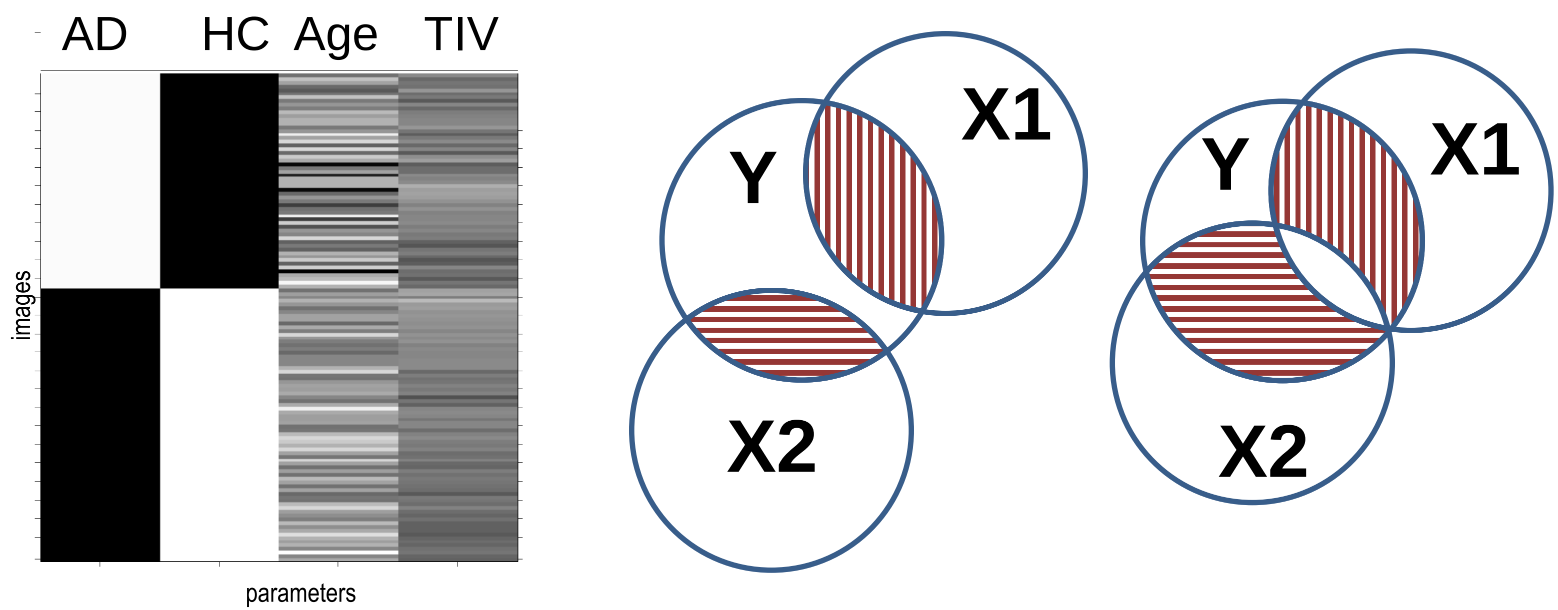




Add a subject factor

Model specification

❑ Orthogonal regressors (=*uncorrelated*):



❑ Non-orthogonal regressors (=*correlated*):

When testing for the first regressor, we are effectively removing the part of the signal that can be accounted for by the second regressor ⇨ *implicit orthogonalisation.*

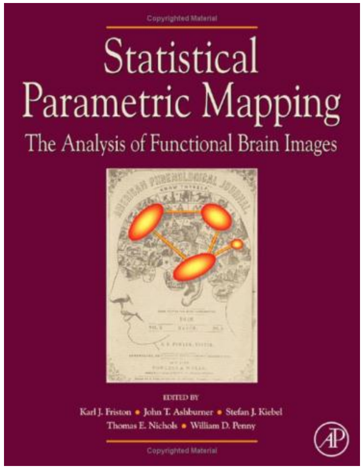
Group analysis

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

… all the same

Alternative multivariate (MAN(C)OVA) …

Bibliography:



- *Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Elsevier, 2007.
- *Generalisability, Random Effects & Population Inference*. Holmes & Friston, NeuroImage,1999.
- *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.
- Simple group fMRI modeling and inference. Mumford & Nichols, *Neuroimage*, 2009.

With many thanks to G. Flandin, W. Penny, J.-B. Poline and Tom Nichols for slides.