Introduction à la statistique médicale

Statistical Parametric Mapping short course

Course 4:

Random Effect Analysis

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GIGA – CRC *In Vivo* Imaging &

GIGA – *In Silico* Medicine

Random effects & variance components

- Fixed effects
  - Are you confident that a new observation from any of subjects 1-3 will be around their mean?
  - Yes! *using within-subjects variance*
  - infer for these subjects – *case study*
- Random effects
  - Are you confident that a new observation from a new subject will be around the mean of first 3?
  - No! *using between-subjects variance*
  - infer for any subject – *population*

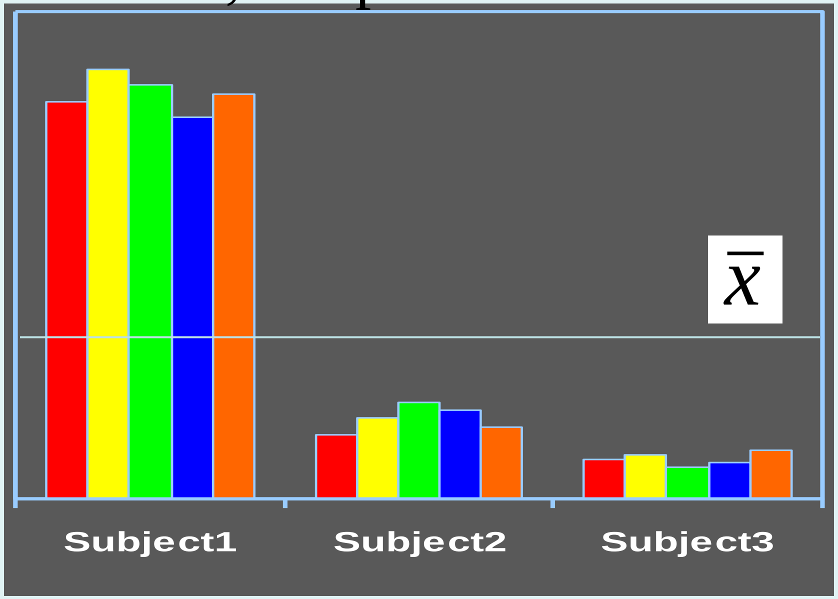
Random Effects Illustration

- Standard linear model

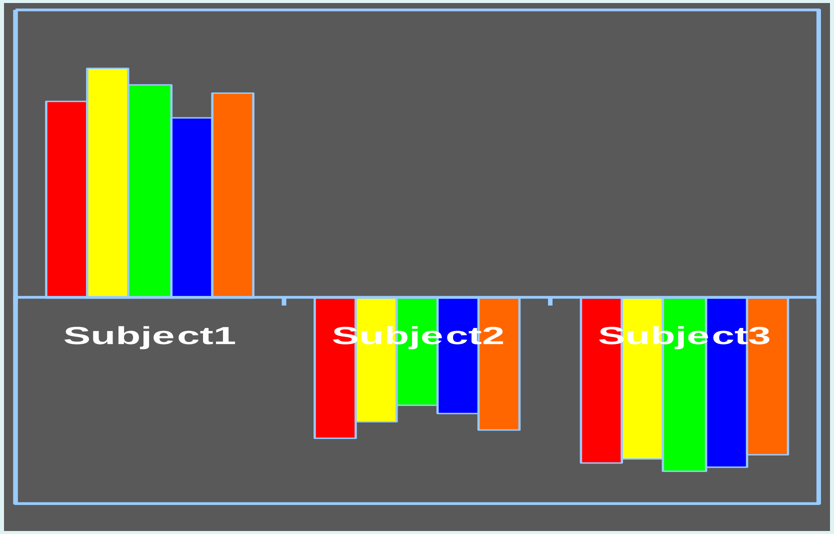
$$Y = X\beta + \varepsilon$$

  assumes only one source of *iid* random variation
- Consider this RT data
- Here, two sources
  - Within subject var.
  - Between subject var.
  - Causes dependence in ε

3 Ss, 5 replicated RT's



Residuals



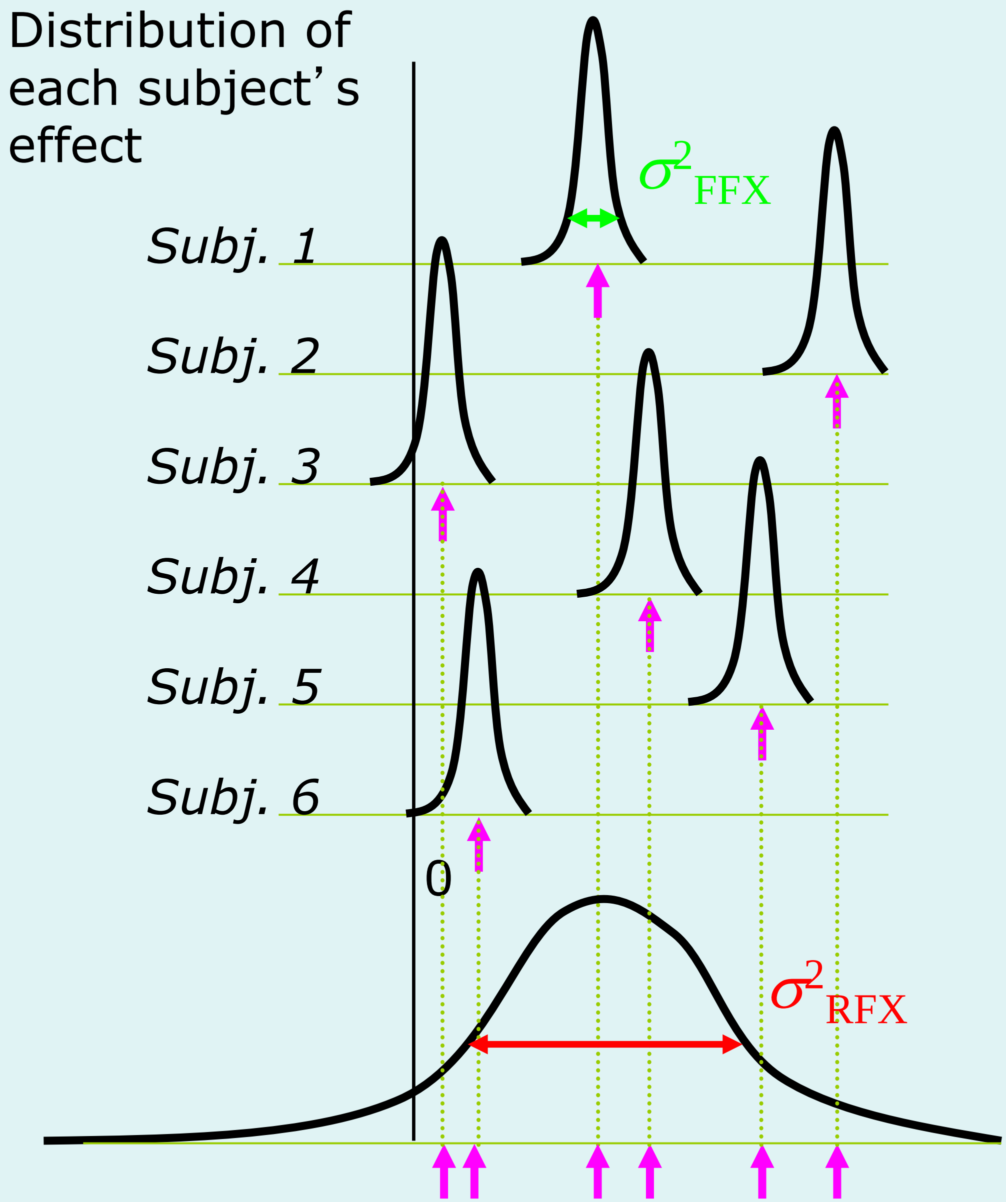
Fixed vs. Random effects

- Fixed Effects

  Intra-subject variation suggests *all these subjects* different from zero

- Random Effects

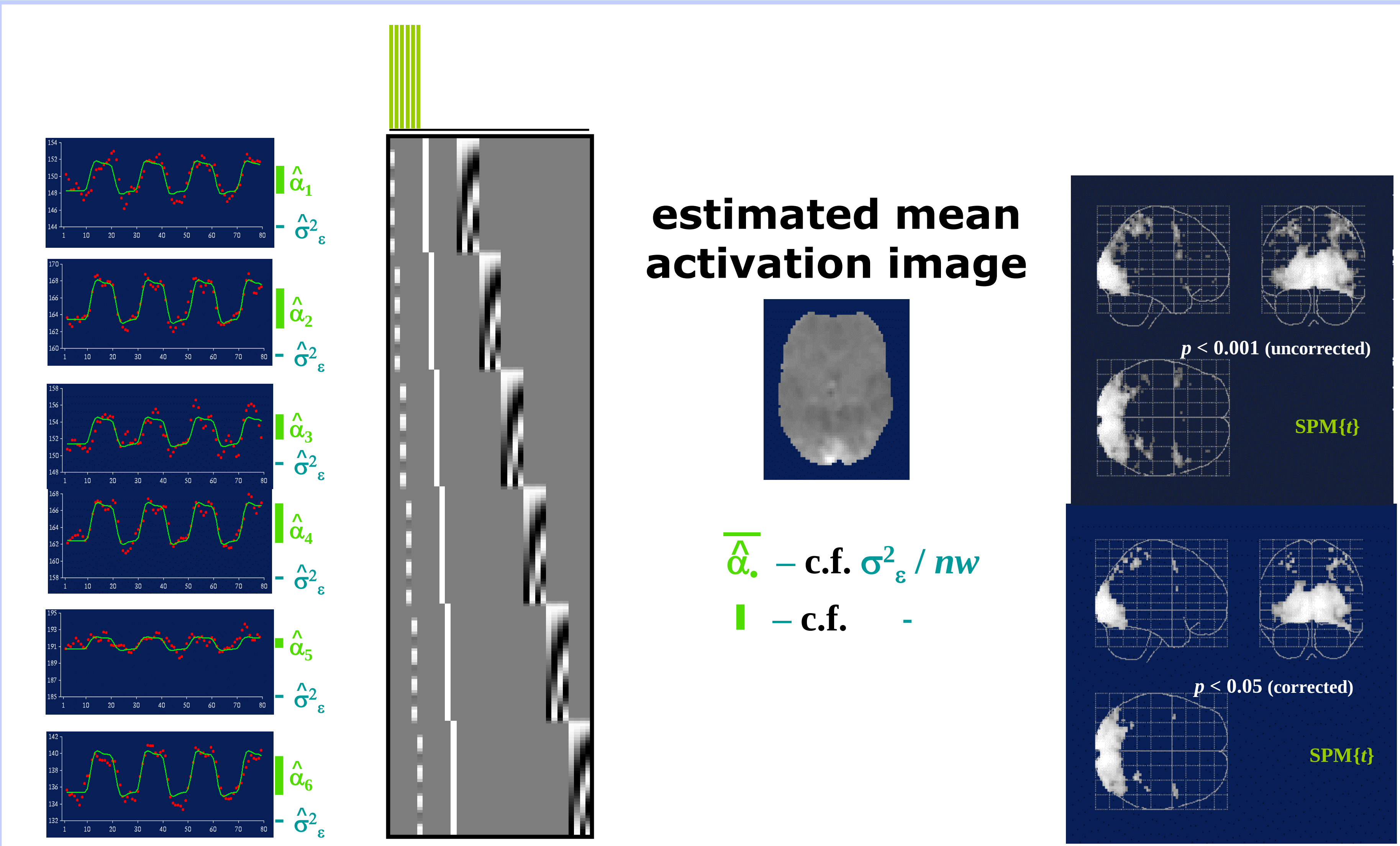
  Intersubject variation suggests *population* not very different from zero



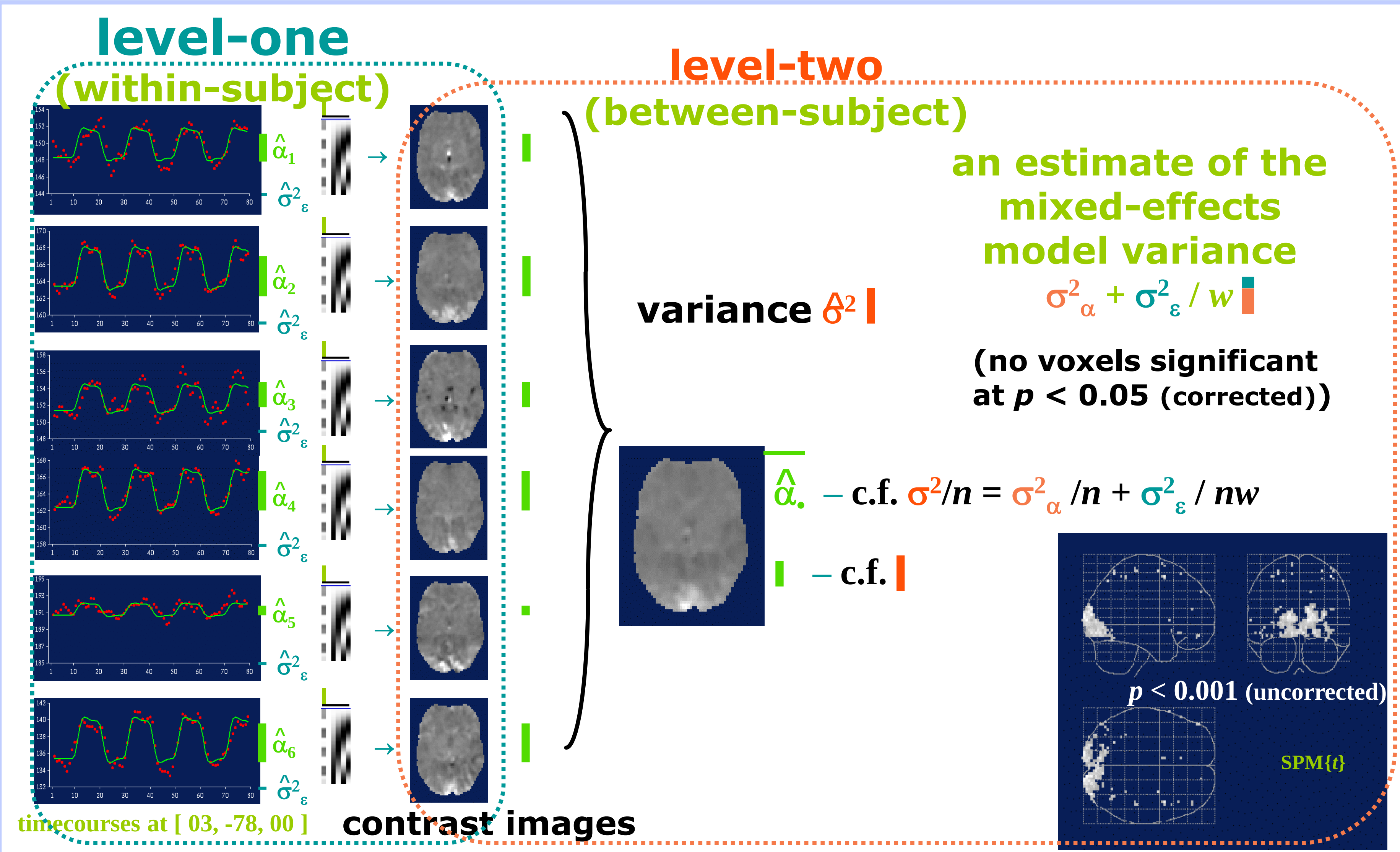
Fixed vs. Random

- Fixed is not "wrong," just usually is not of interest
- Fixed Effects Inference
  - "I can see this effect in this cohort"
- Random Effects Inference
  - "If I were to sample a new cohort from the population I would get the same result"

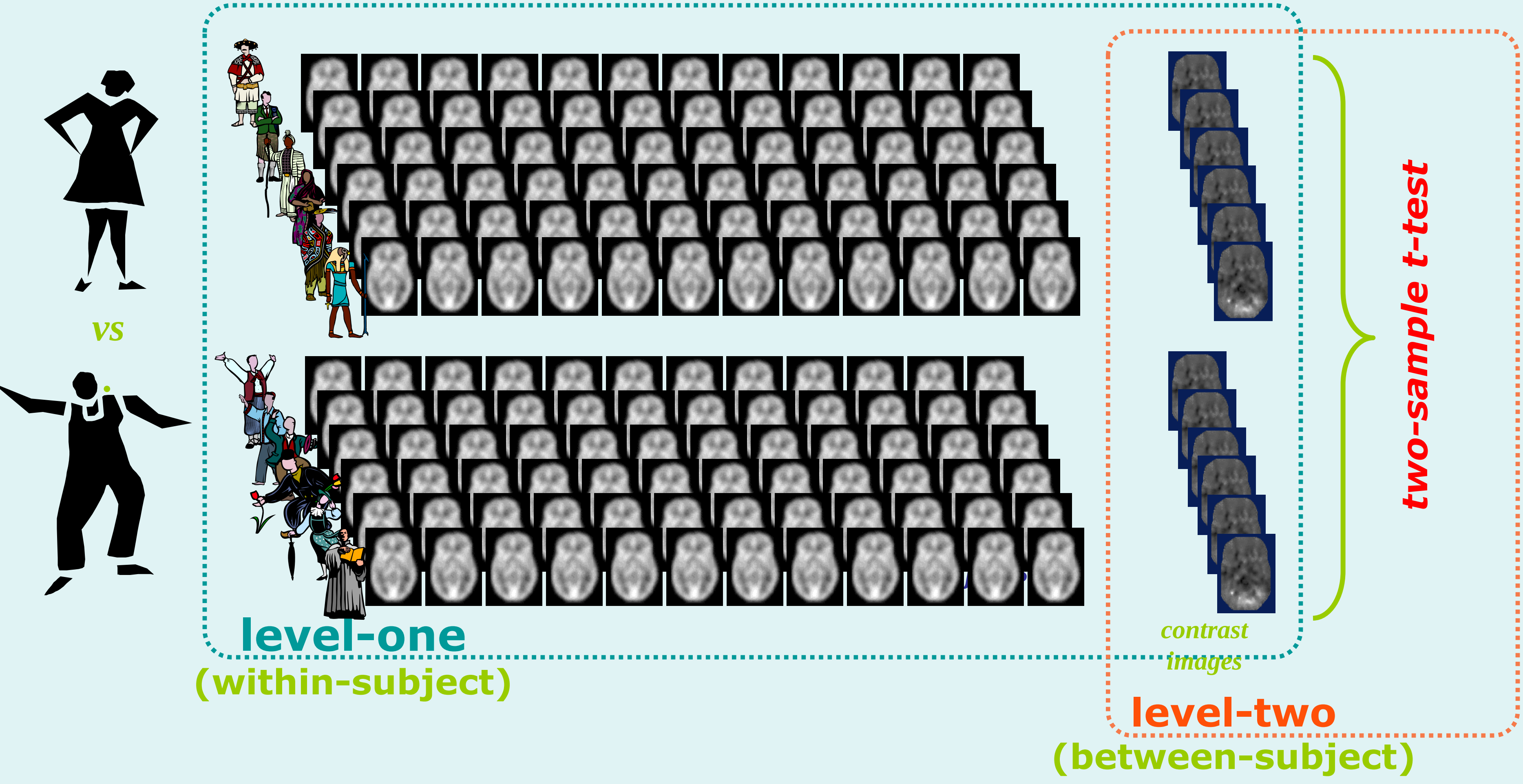
Multi-subject analysis…?



Two-stage analysis of random effect…



Two stage random effects, group comparison

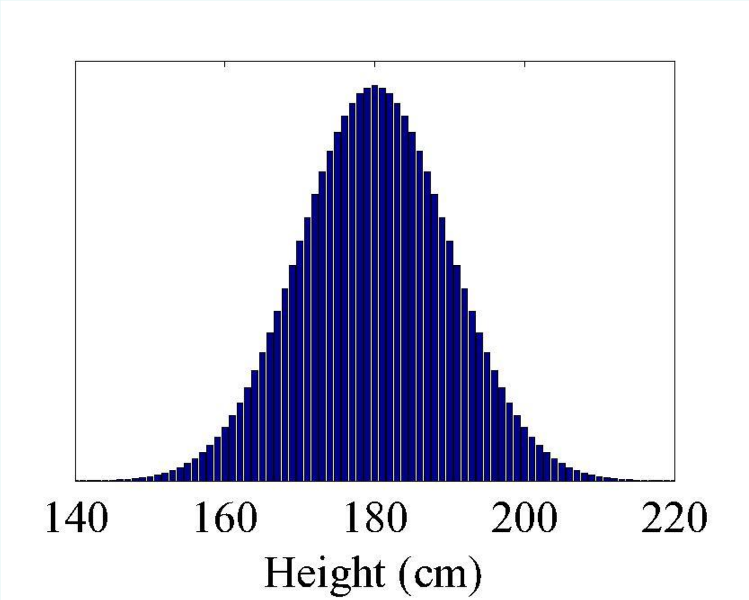


Summary

- Analyse subjects individually
  - Build within-subject models
  - Calculate contrast(s) of interest
- Use contrast images in a 2^{nd} level (Random Effect, RFX) analysis
  - Build between-subject model
  - Calculates SPMs of interest
- Draw conclusions for the population

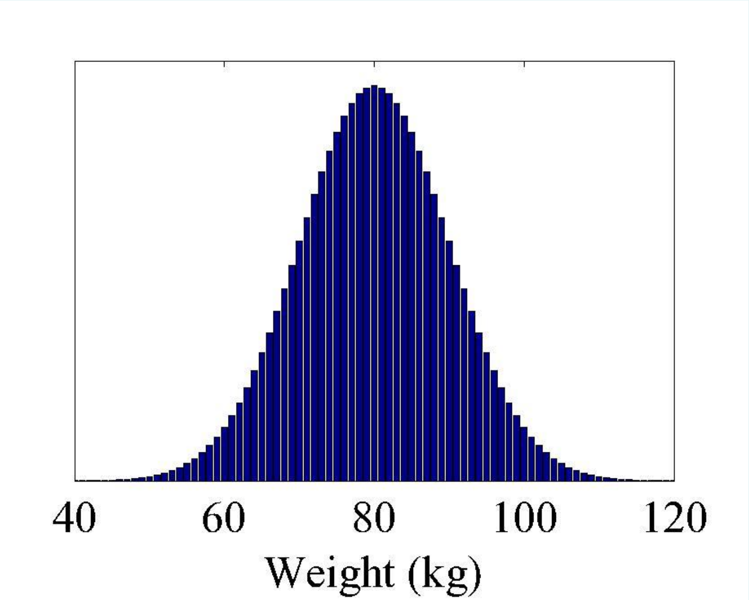
Variance-Covariance matrix

Height of Swedish men



μ=180cm, σ=14cm (σ^2=200)

Weight of Swedish men



μ=80kg, σ=14kg (σ^2=200)

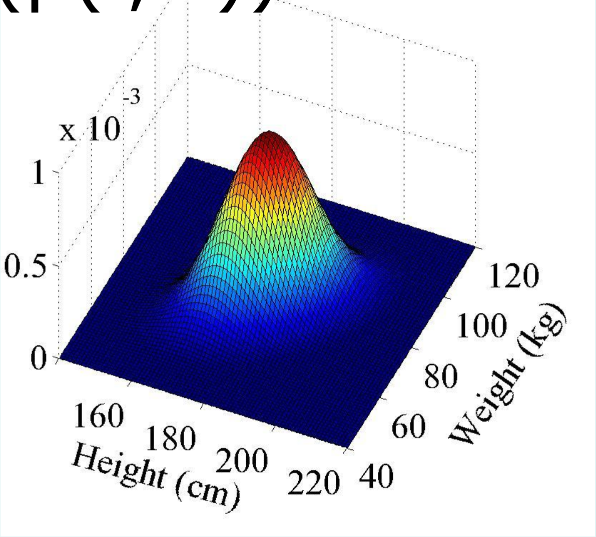
Each completely characterised by μ (mean) and σ^2 (variance),

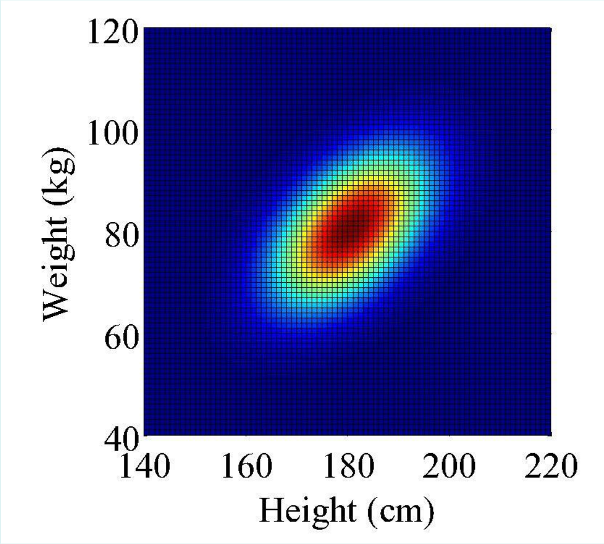
i.e. we can calculate $p(l|\mu,\sigma^2)$ for any l

Source: J. Andersson

Variance-Covariance matrix

- Now let us view height and weight as a 2-dimensional stochastic variable ($p(l,w)$).





$$\boldsymbol{\mu} = \begin{bmatrix} 180 \\ 80 \end{bmatrix} \qquad \boldsymbol{\Sigma} = \begin{bmatrix} 200 & 100 \\ 100 & 200 \end{bmatrix} \qquad p(l,w|\boldsymbol{\mu},\boldsymbol{\Sigma})$$

Source: J. Andersson

Sphericity

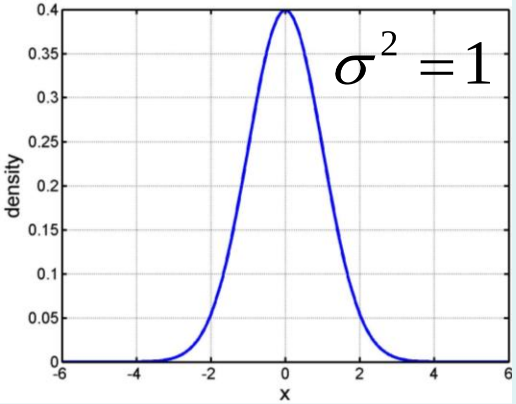
$$y = X\beta + \varepsilon$$

$$C_\varepsilon = Cov(\varepsilon) = E(\varepsilon\varepsilon^T)$$

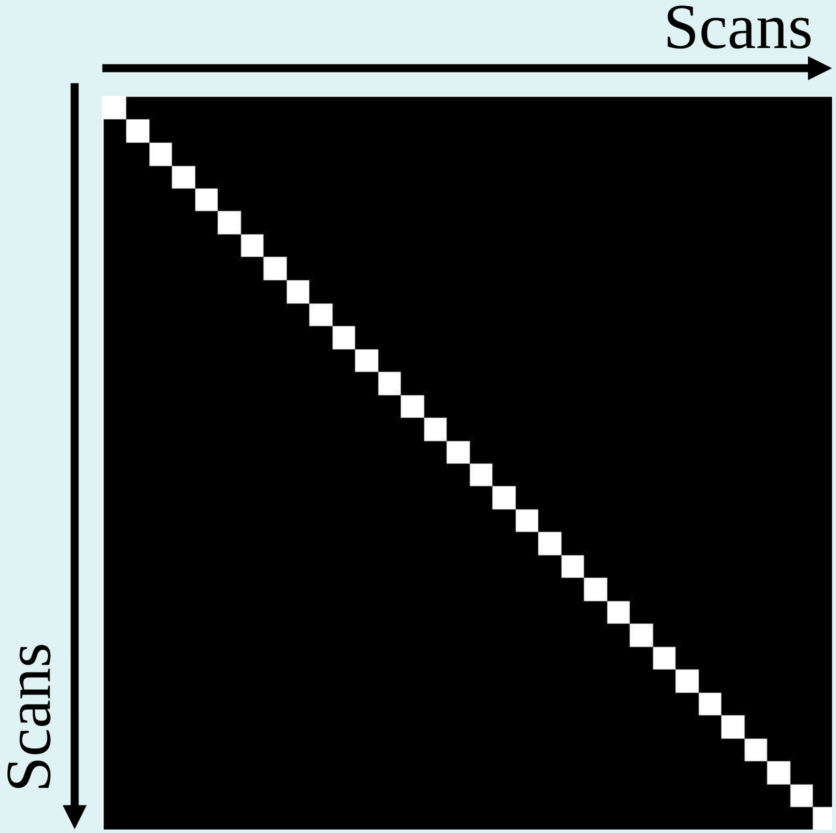
‚sphericity' means:

$$Cov(\varepsilon) = \sigma^2 I$$

i.e. $$Var(\varepsilon_i) = \sigma^2$$

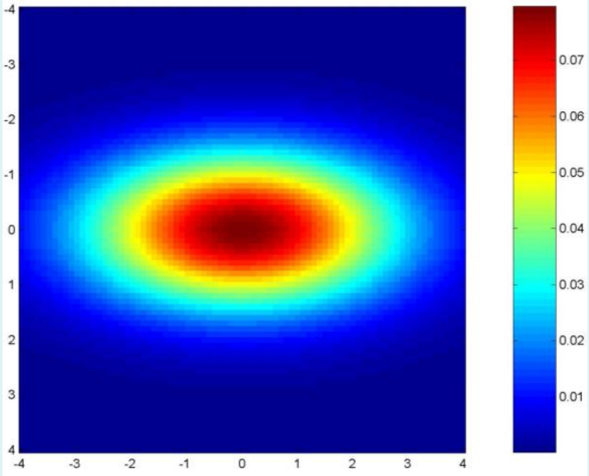


$\sigma^2 = 1$



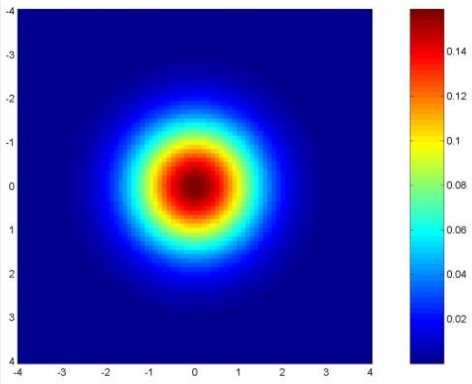
Non-sphericity

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

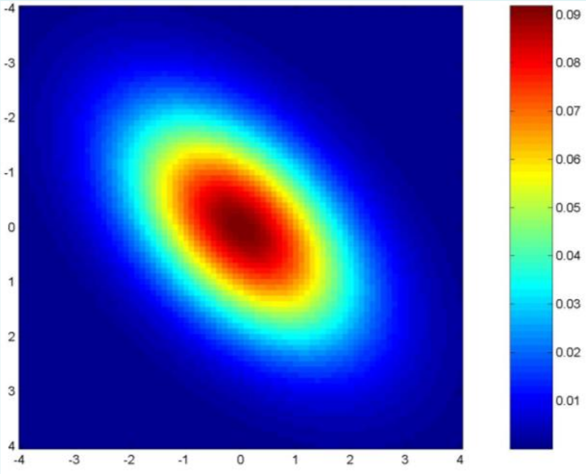


non-sphericity means that the error covariance doesn‘t look like this:

$$Cov(\varepsilon)=\sigma^2 I$$



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



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

Variance quiz

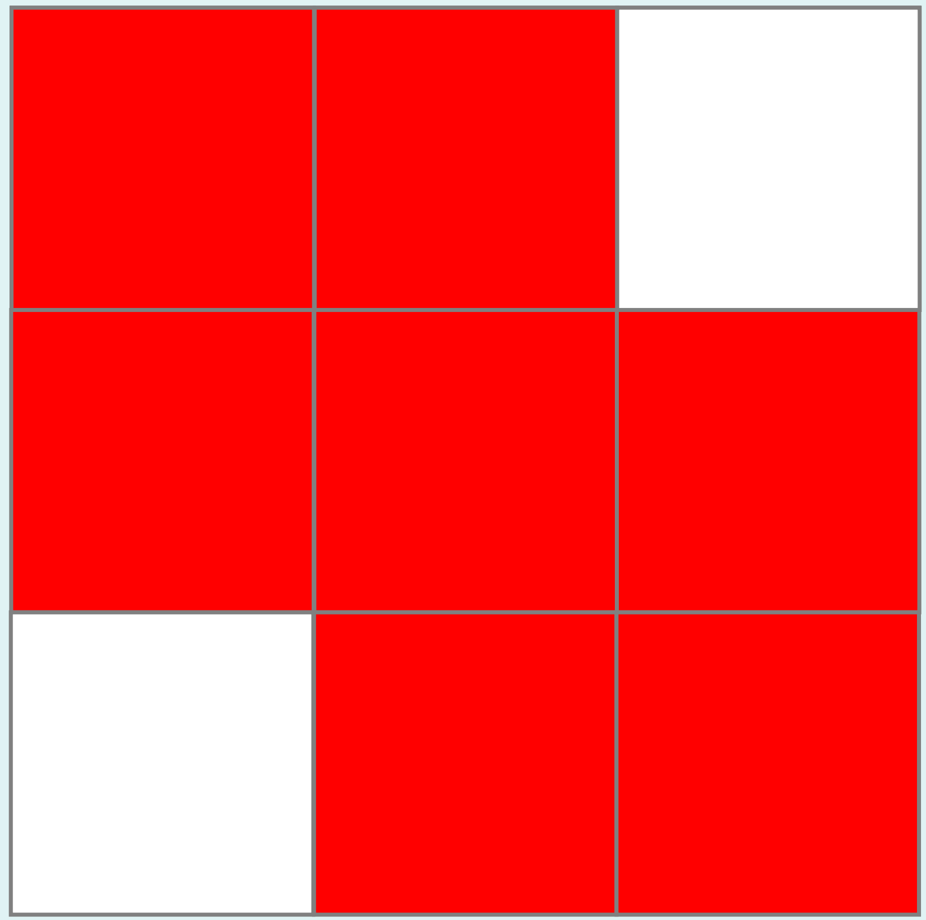
Height			
Weight			
# hours watching telly per day			

Variance quiz

Height

Weight

hours watching telly per day



Variance quiz

Height				
Weight				
# hours watching telly per day				
Shoe size				

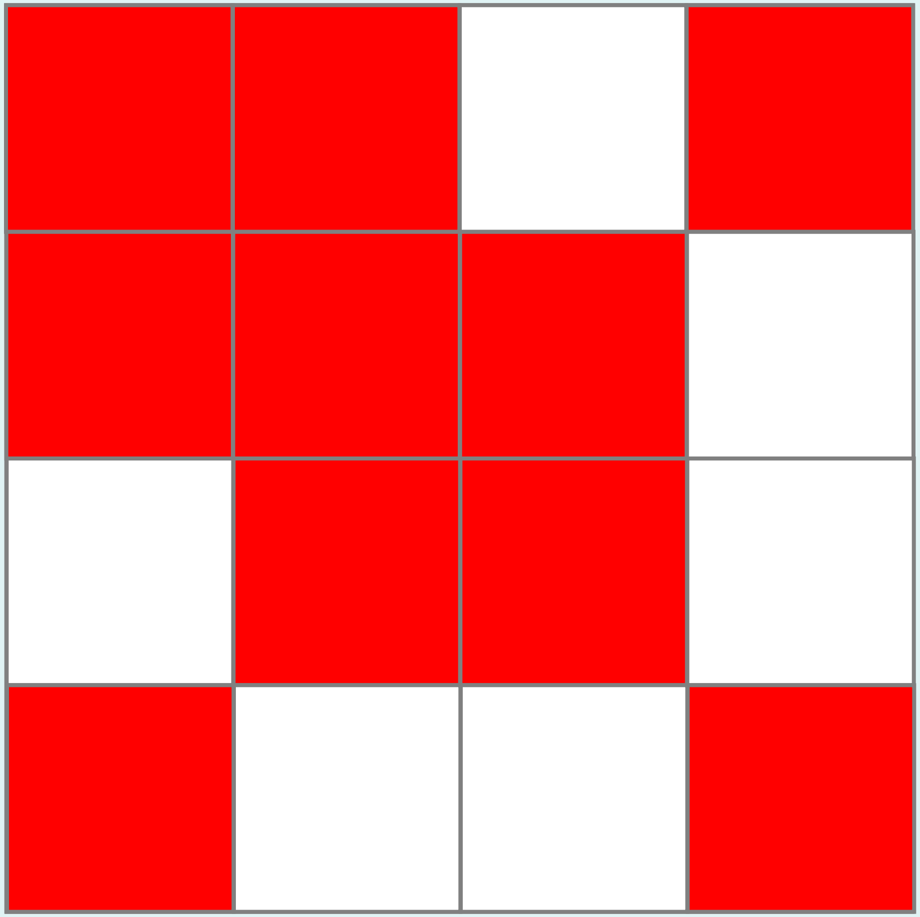
Variance quiz

Height

Weight

hours watching telly per day

Shoe size



Example I

Stimuli:

Auditory Presentation (SOA = 4 secs) of (i) words and (ii) words spoken backwards

e.g. “Book” and “Koob”

Subjects:

(i) 12 control subjects
(ii) 11 blind subjects

Scanning:

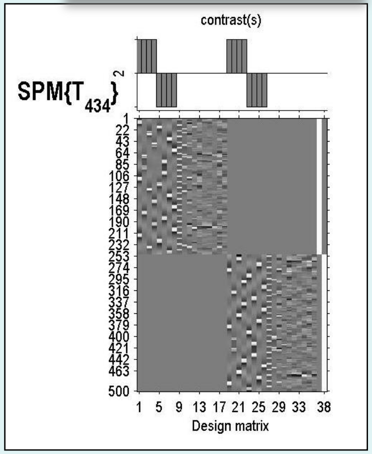
fMRI, 250 scans per subject, block design

U. Noppeney et al.

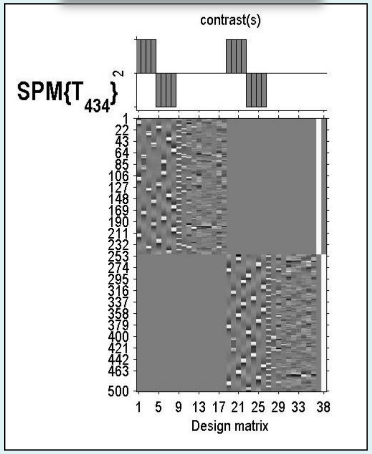
Population differences

1st level:

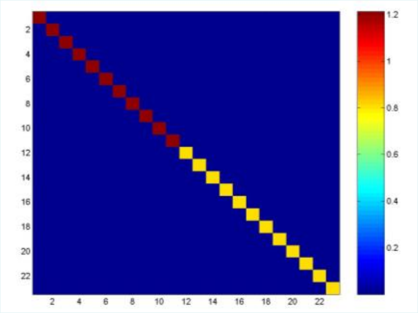
Controls



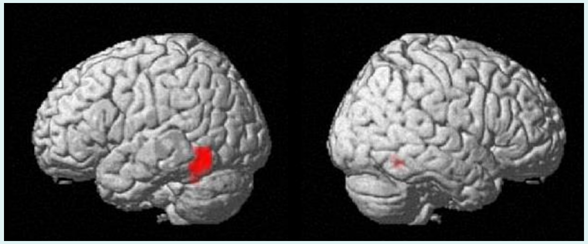
Blinds

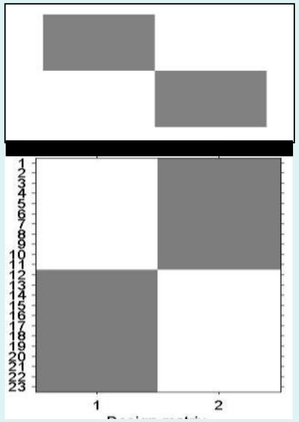


2nd level:



V





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

X

Example II

Stimuli:

Auditory Presentation (SOA = 4 secs) of words

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

Subjects:

(i) 12 control subjects

Scanning:

fMRI, 250 scans per subject, block design

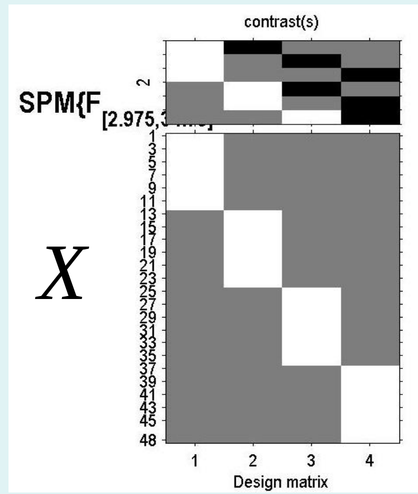
Question:

What regions are affected by the semantic content of the words?

U. Noppeney et al.

SPM Notation: iid case

$$\underset{N\times 1}{y} = \underset{N\times p}{X}\ \underset{p\times 1}{\theta} + \underset{N\times 1}{\varepsilon}$$



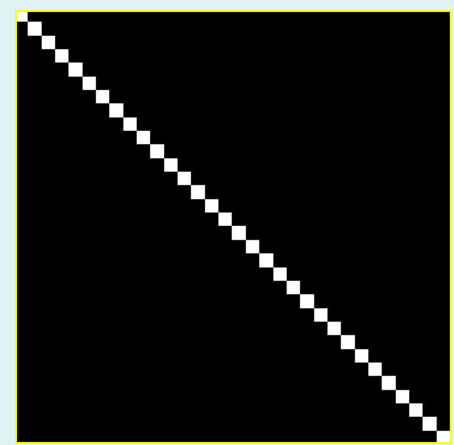
$$\mathrm{Cor}(e) = I$$

- 12 subjects,
  4 conditions
  - Use F-test to find differences btw conditions
- Standard Assumptions
  - Identical distribution
  - Independence
  - “Sphericity”... but here not realistic!

Error covariance

N

N



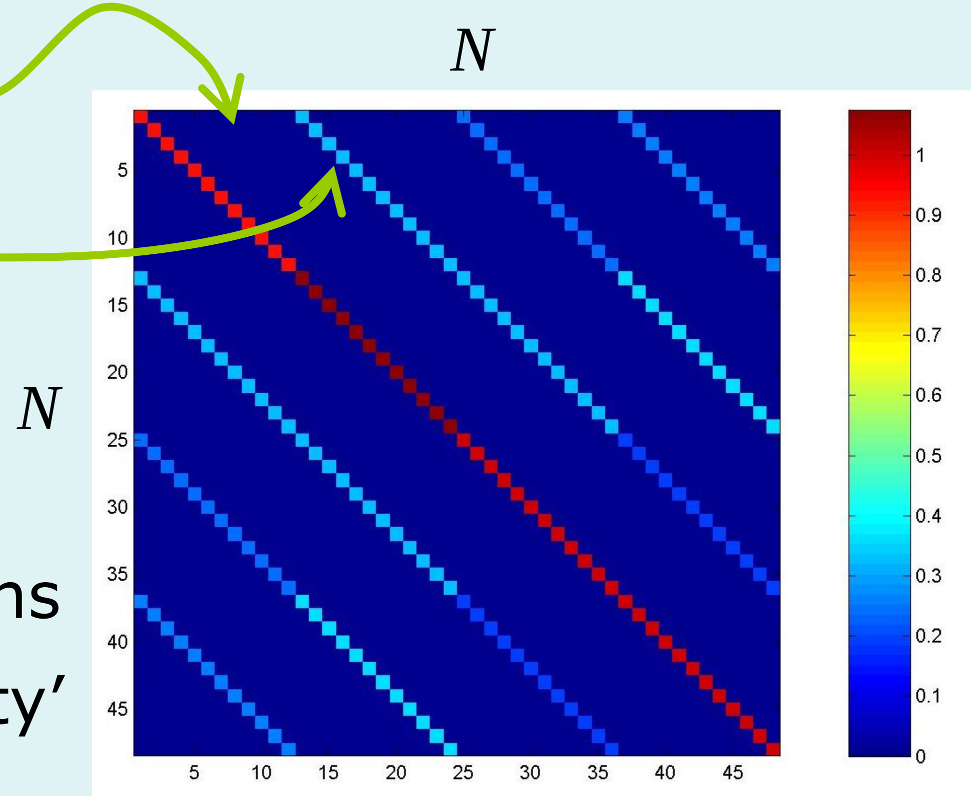
Multiple Variance Components

$$\underset{N\times 1}{y} = \underset{N\times p}{X}\ \underset{p\times 1}{\theta} + \underset{N\times 1}{\varepsilon}$$

- 12 subjects, 4 conditions
- Measurements btw subjects uncorrelated
- Measurements w/in subjects correlated

$$Cor(\varepsilon) = \sum_k \lambda_k Q_k$$

Error covariance



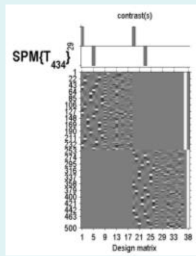
Errors can now have different variances and there can be correlations

Allows for 'nonsphericity'

Repeated measures Anova

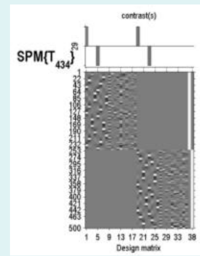
1st level:

Motion



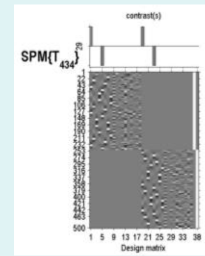
$\stackrel{?}{=}$

Sound



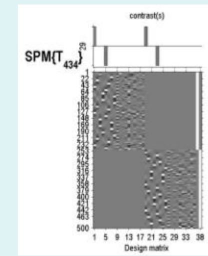
$\stackrel{?}{=}$

Visual

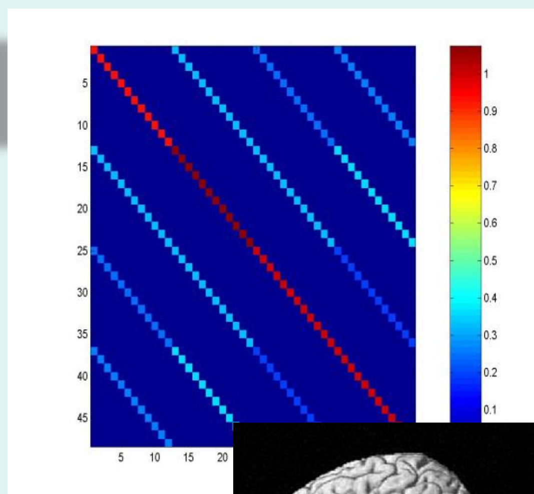


$\stackrel{?}{=}$

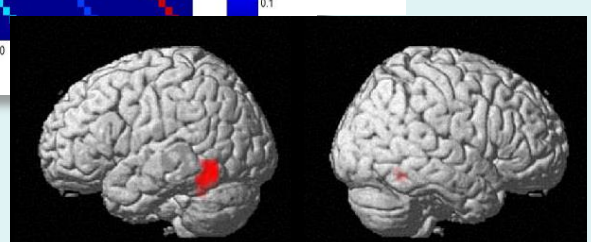
Action



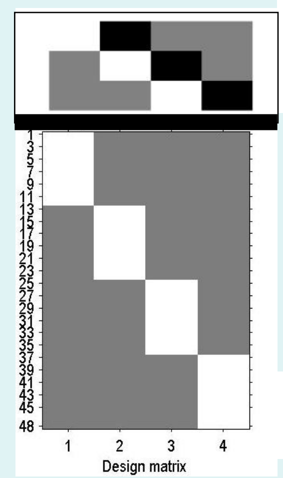
2nd level:



V



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



X