SPM course, CRC, Liege, Septembre 2009

Group analysis (RFX)

C. Phillips, Centre de Recherches du Cyclotron, ULg, Belgium

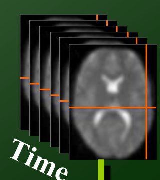
Based on slides from: T. Nichols, S. Kiebel, JB. Poline

Contents

- Introduction & recap
- Variance components
- Hierarchical model
- RFX and summary statistics
- Variance/covariance matrix
- « Take home » message

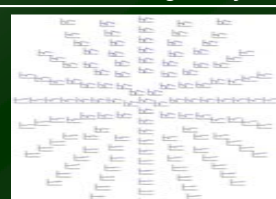
Data

fMRI, single subject



fMRI, multi-subject

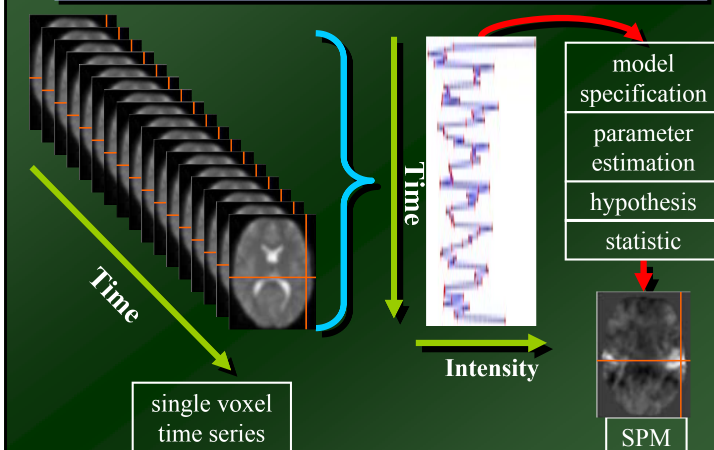
EEG/MEG, single subject



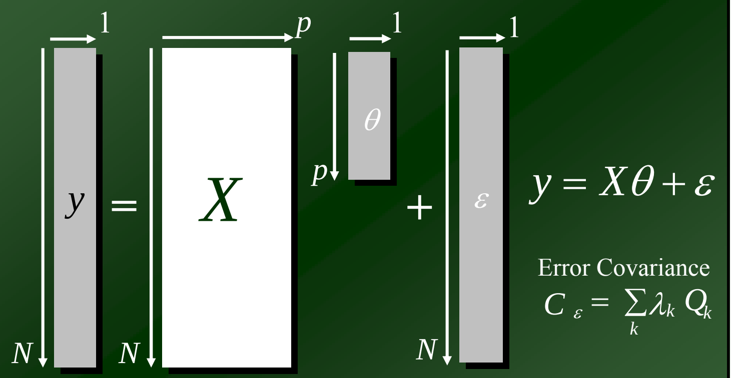
ERP/ERF, multi-subject

Hierarchical model for all imaging data!

Reminder: voxel by voxel analysis



General Linear Model



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

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

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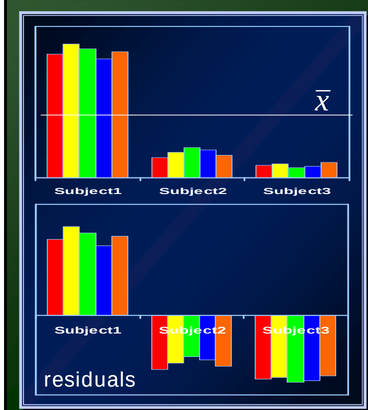
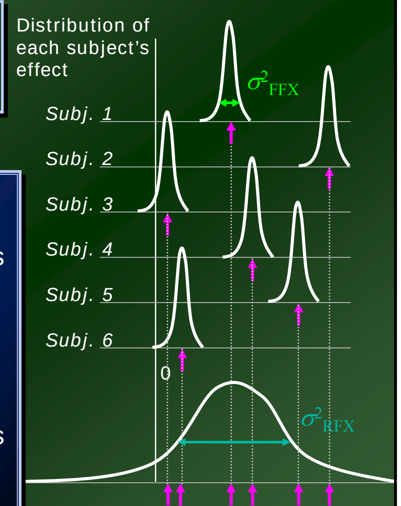
Random effects & variance components



- 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*

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 isn't "wrong," just usually isn't of interest as limited to "case study".
- 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"

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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

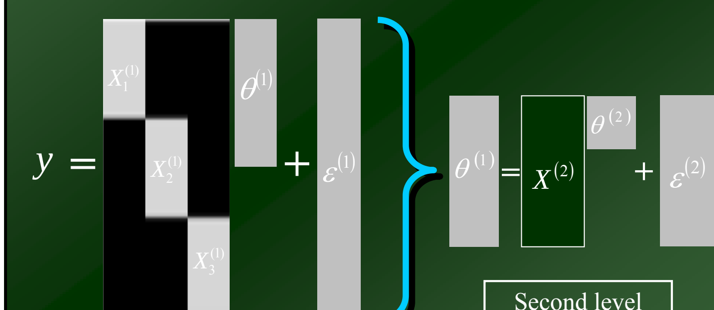
$$C_\varepsilon^{(i)} = \sum_k \lambda_k^{(i)} Q_k^{(i)}$$

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

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

Example: two level model

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



First level

Second level

Estimation

Hierarchical model

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

Single-level model

$$
\begin{aligned}
y \;=\; & \varepsilon^{(1)} + X^{(1)}\varepsilon^{(2)} + \\
& \ldots + \\
& X^{(1)}\ldots X^{(n-1)}\varepsilon^{(n)} + \\
& X^{(1)}\ldots X^{(n)}\theta^{(n)} \\
& = X\theta + e
\end{aligned}
$$

Group analysis in practice

Many 2-level models are just too big to compute.

And even if, it takes a long time!

Is there a fast approximation?

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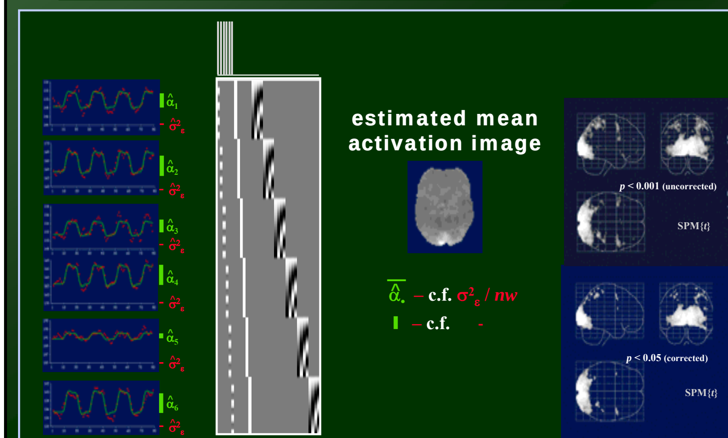
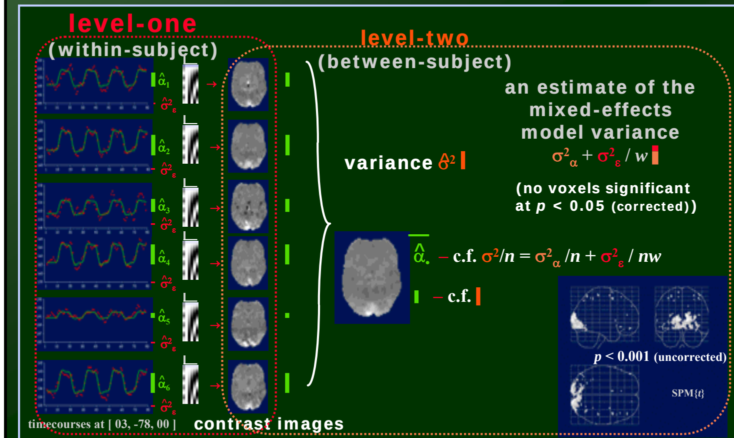
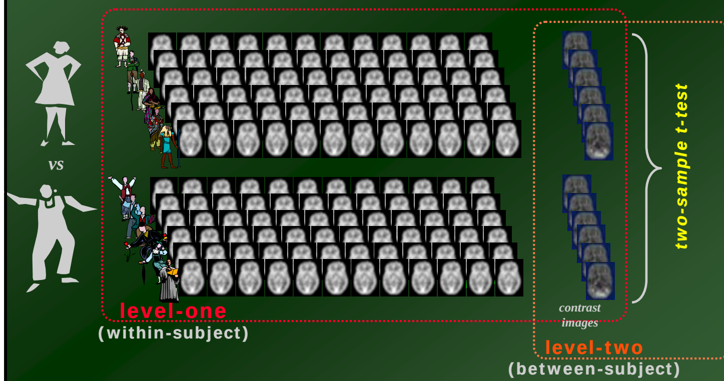
Multi-subject analysis…?



Two-stage analysis of random effect…



Two stage random effects group comparison

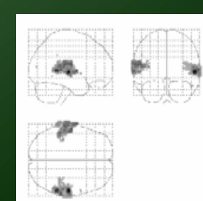


Summary

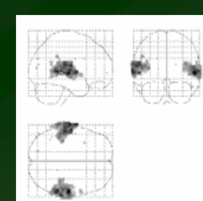
- Analyse subjects individually
  - Build within-subject models
  - Calculate contrast(s) of interest
- Use contrast images in a 2nd level (Random Effect, RFX) analysis
  - Build between-subject model
  - Calculates SPMs of interest
- Draw conclusions for the population

Auditory Data

Summary statistics



Hierarchical Model



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

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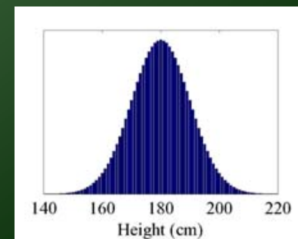
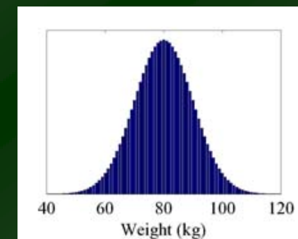
Variance-Covariance matrix

Height of Swedish men



μ=180cm, σ=14cm (σ^2=200)

Weight of Swedish men



μ=80kg, σ=14kg (σ^2=200)

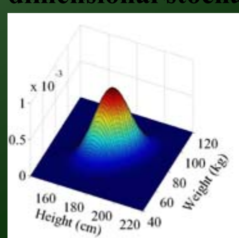
Each completely characterised by μ (mean) and σ^2 (variance),

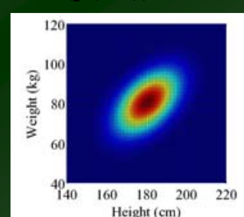
i.e. we can calculate $p(l|\mu,\sigma^2)$ for any l

Source: J. Andersson

Variance-Covariance matrix

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





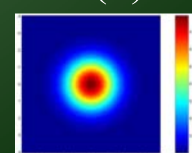
$$\boldsymbol{\mu} = \begin{bmatrix} 180 \\ 80 \end{bmatrix} \qquad \boldsymbol{\Sigma} = \begin{bmatrix} 200 & 100 \\ 100 & 200 \end{bmatrix} \qquad p(l,w|\boldsymbol{\mu},\boldsymbol{\Sigma})$$

Source: J. Andersson

‚non-sphericity'

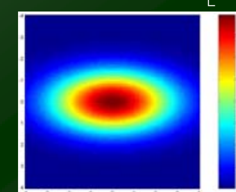
non-sphericity means that the error covariance doesn't look like this:

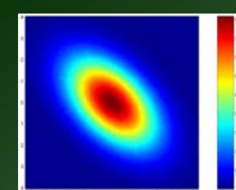
$$Cov(\varepsilon) = \sigma^2 I$$



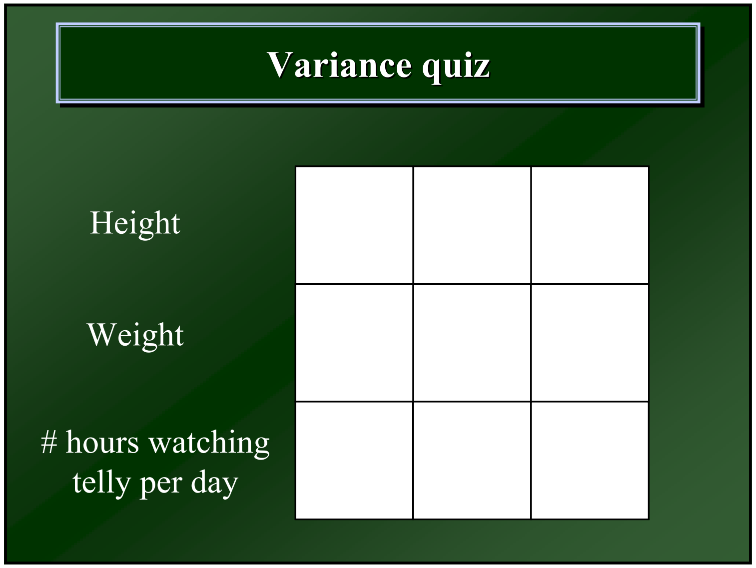
$$Cov(\varepsilon) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

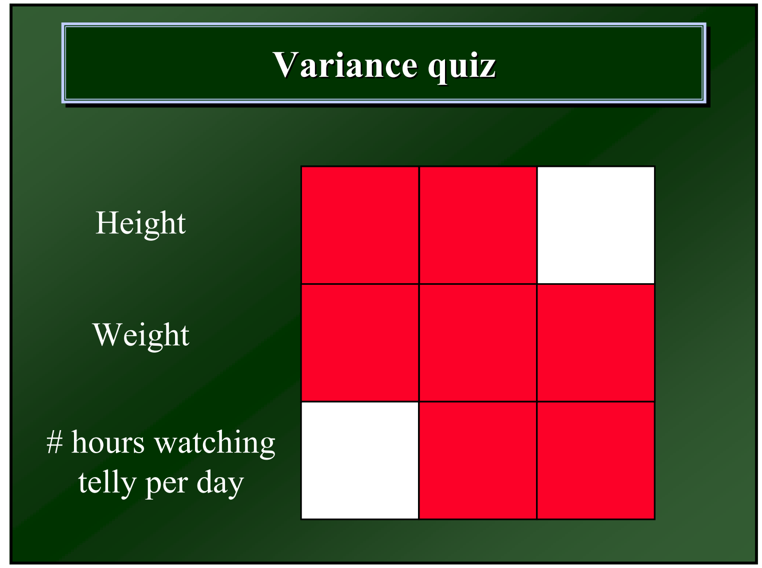
$$Cov(\varepsilon) = \begin{bmatrix} 4 & 0 \\ 0 & 1 \end{bmatrix}$$





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


Variance quiz
Height
Weight
hours watching telly per day


Variance quiz
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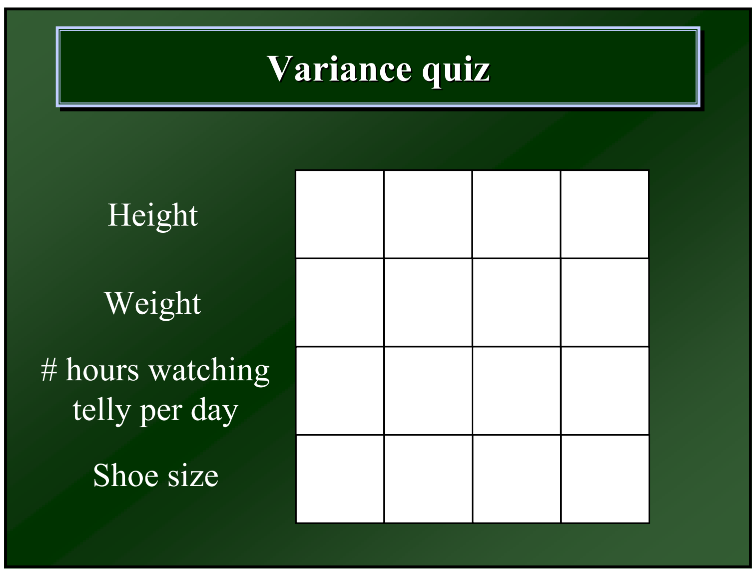
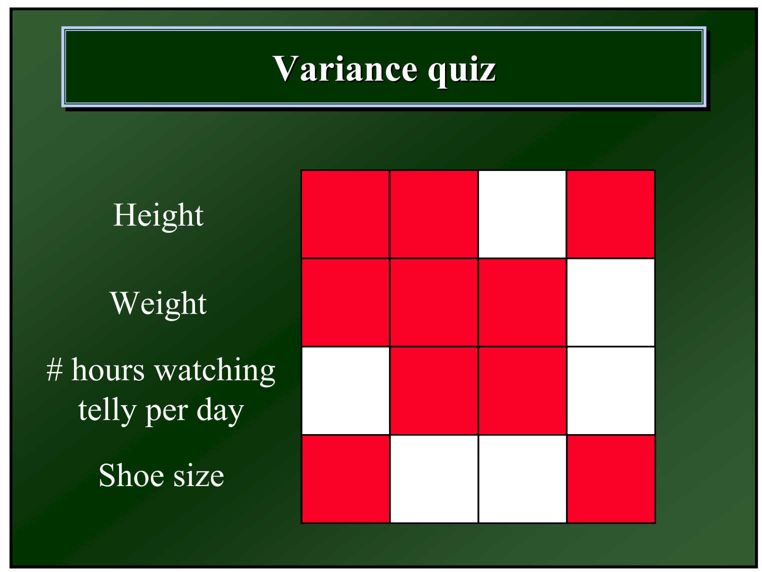

Variance quiz
Height
Weight
hours watching telly per day
Shoe size


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"

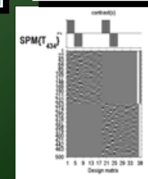
Subjects: (i) 12 control subjects (ii) 11 blind subjects

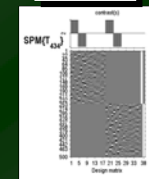
Scanning: fMRI, 250 scans per subject, block design

U. Noppeney et al.

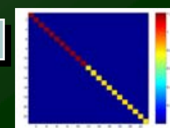
Population differences

1[st] level: Controls | Blinds

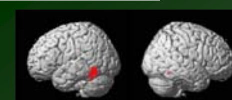




2[nd] level:



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

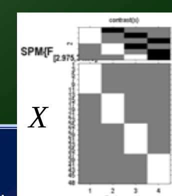
Question: What regions are affected by the semantic content of the words?

U. Noppeney et al.

SPM2 Notation: iid case

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

X



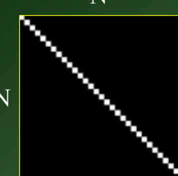
$$\mathrm{Cor}(\varepsilon) = \lambda I$$

- 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



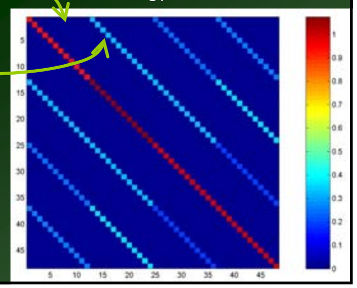
Multiple Variance Components

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

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

Error covariance

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



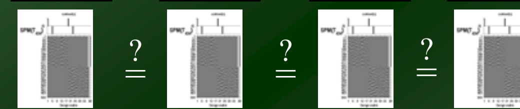
Errors can now have different variances and there can be correlations

Allows for 'nonsphericity'

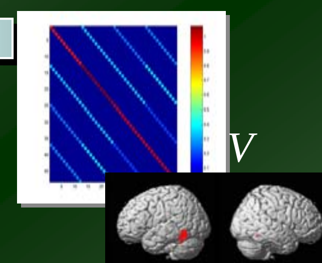
Repeated measures Anova

1st level:

Motion | Sound | Visual | Action



2nd level:



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

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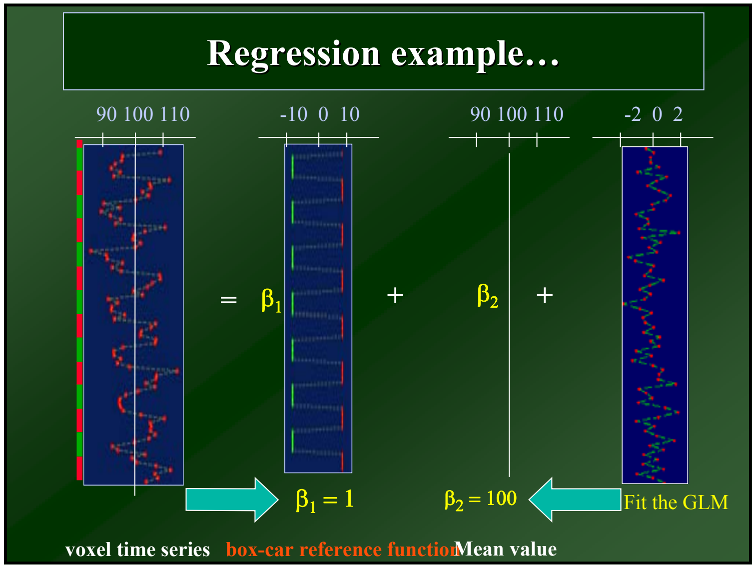
- Design efficiency
- Experimental design
- Random effect analysis
- « Take home » message

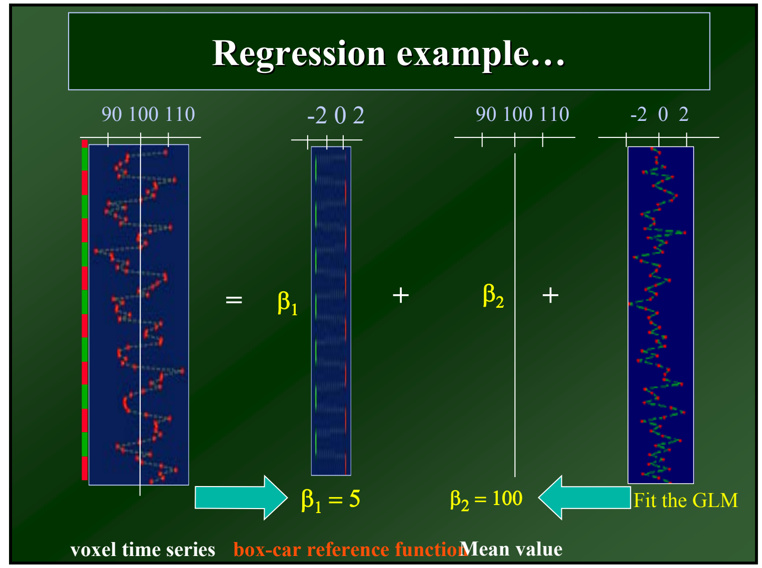
Summary

Linear hierarchical models are general enough for typical multi-subject imaging data (PET, fMRI, EEG/MEG).

Summary statistics are robust approximation for group analysis.

Also accomodates multiple contrasts per subject.





Notes !

- *Coefficients (= parameters) are estimated using the Ordinary Least Squares (OLS) by minimizing the fluctuations, - variability – variance – of the noise – the residuals*
- *Because the parameters depend on the scaling of the regressors included in the model, one should be careful in comparing manually entered regressors*
- *The residuals, their sum of squares and the resulting tests (t,F), do not depend on the scaling of the regressors.*

Top Ten Things Sex and Brain Imaging Have in Common

10. It's not how big the region is, it's what you do with it.
9. Both involve heavy PETting or powerful magnetism.
8. It's important to select regions of interest.
7. Experts agree that timing is critical.
6. Both require correction for motion.
5. Experimentation is everything.
4. You often can't get access when you need it.
3. You always hope for multiple activations.
2. Both make a lot of noise.
1. Both are better when the assumptions are met.