Statistical Inference

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SPM Course
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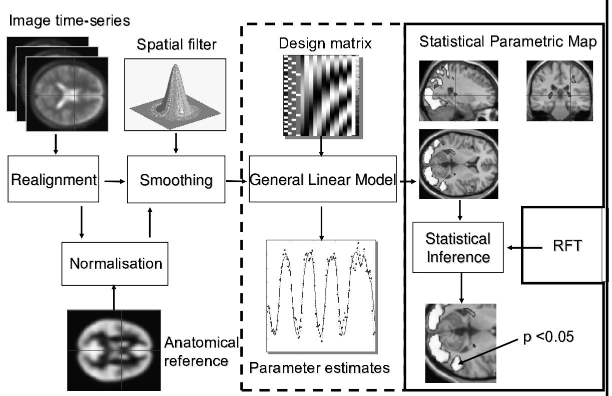
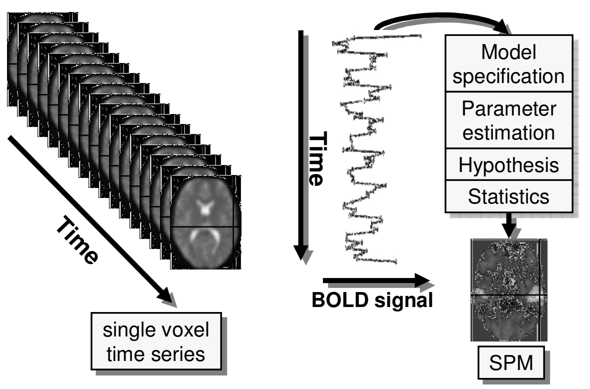


Voxel-wise time series analysis



Overview

- ❑ Model specification and parameters estimation
- ❑ Hypothesis testing
- ❑ Contrasts
  - ➢ *T*-tests
  - ➢ *F*-tests
- ❑ Contrast estimability
- ❑ Correlation between regressors
  - ➢ Example(s)
- ❑ Design efficiency

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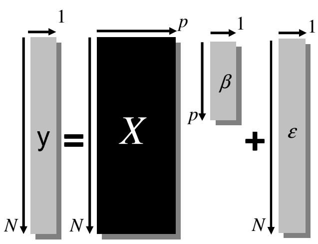
The GLM



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

Sphericity assumption:
Independent and identically distributed (i.i.d.) error terms

$$\varepsilon \sim N(0, \sigma^2 I)$$

N: number of scans, p: number of regressors

❑ The General Linear Model is an equation that expresses the observed response variable in terms of a linear combination of explanatory variables *X* plus a well behaved error term. Each column of the design matrix corresponds to an effect one has built into the experiment or that may confound the results.

Parameter estimation: OLS

- Find $\hat{\beta}$ that minimises $\boxed{\left\| y - X\beta \right\|^2 = \varepsilon^T \varepsilon}$
- The Ordinary Least Estimates are:

$$\boxed{\hat{\beta} = (X^T X)^{-1} X^T y}$$

- Under i.i.d. assumptions, the Ordinary Least Squares estimates are Maximum Likelihood.

$$\varepsilon \sim N(0, \sigma^2 I) \longrightarrow Y \sim N(X\beta, \sigma^2 I)$$

$$\varepsilon \sim N(0, \sigma^2 I) \longrightarrow \hat{\beta} \sim N(\beta, \sigma^2 (X^T X)^{-1})$$

$$\boxed{\hat{\sigma}^2 = \frac{\hat{\varepsilon}^T \hat{\varepsilon}}{N - p}}$$

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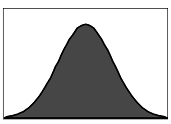
Hypothesis testing

To test an hypothesis, we construct "test statistics".

- **The Null Hypothesis H_0**
  Typically what we want to disprove (no effect).
  ⇨ The Alternative Hypothesis H_A expresses outcome of interest.

- **The Test Statistic T**
  The test statistic summarises evidence about H_0.
  Typically, test statistic is small in magnitude when the hypothesis H_0 is true and large when false.
  ⇨ We need to know the distribution of T under the null hypothesis.



Null Distribution of T

Significance level and p-value

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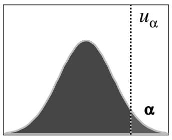
- ❑ ***Significance level α:***
  Acceptable *false positive rate α*.
  ⇨ threshold u_α
  Threshold u_α controls the false positive rate
  $$\alpha = p(T > u_\alpha \mid H_0)$$

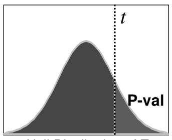


Null Distribution of T

Observation of test statistic t, a realisation of T

- ❑ **The conclusion about the hypothesis:**
  We reject the null hypothesis in favour of the alternative hypothesis if $t > u_\alpha$

- ❑ ***P*-value:**
  A *p*-value summarises evidence against H_0.
  This is the chance of observing value more extreme than *t* under the null hypothesis.
  $$\boxed{p(T > t \mid H_0)}$$



Null Distribution of T

Type I and II errors

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- ❑ Neyman-Pearson lemma:
  - ➢ the likelihood ratio...
  $$\Lambda = \frac{p(Y|H_1)}{p(Y|H_0)} \geq u$$
  - ➢ ...is the most powerful test of size (FPR)
  $$\alpha = p(\Lambda \geq u | H_0)$$
- ❑ Increasing the FPR decreases power
  - ➢ Type I error is more serious than type II error
  - ➢ We choose to keep the type I error low (5%)

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Contrasts

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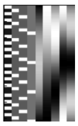
- We are usually not interested in the whole β vector.

- A contrast selects a specific effect of interest:
  - ⇨ a contrast c is a vector of length p.
  - ⇨ $c^T\beta$ is a linear combination of regression coefficients β.



$c^T = [1\ 0\ 0\ 0\ 0\ \ldots]$

$c^T\beta = \mathbf{1}\times\boldsymbol{\beta}_1 + \mathbf{0}\times\boldsymbol{\beta}_2 + \mathbf{0}\times\boldsymbol{\beta}_3 + \mathbf{0}\times\boldsymbol{\beta}_4 + \mathbf{0}\times\boldsymbol{\beta}_5 + \ldots$

$c^T = [0\ \text{-}1\ 1\ 0\ 0\ \ldots]$

$c^T\beta = \mathbf{0}\times\boldsymbol{\beta}_1 + \mathbf{-1}\times\boldsymbol{\beta}_2 + \mathbf{1}\times\boldsymbol{\beta}_3 + \mathbf{0}\times\boldsymbol{\beta}_4 + \mathbf{0}\times\boldsymbol{\beta}_5 + \ldots$

- Under i.i.d assumptions:

$$\boxed{c^T\hat{\beta} \sim N(c^T\beta, \sigma^2 c^T (X^T X)^{-1} c)}$$

T-test: one dimensional contrasts

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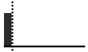
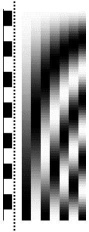
$\boldsymbol{c^T} = \mathbf{1\ 0\ 0\ 0\ 0\ 0\ 0\ 0}$



$\boldsymbol{\beta}_1\ \boldsymbol{\beta}_2\ \boldsymbol{\beta}_3\ \boldsymbol{\beta}_4\ \boldsymbol{\beta}_5\ \ldots$

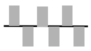


Question: box-car amplitude > 0 ?

=

$\beta_1 = c^T\beta > 0$?

Null hypothesis: $\boxed{H_0\text{: } c^T\beta = 0}$



Test statistic:

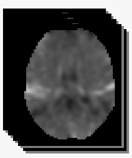
$$T = \frac{\textbf{\textit{contrast} of estimated parameters}}{\sqrt{\textbf{variance estimate}}}$$

$$\boxed{T = \frac{c^T\hat{\beta}}{\sqrt{\mathrm{var}(c^T\hat{\beta})}} = \frac{c^T\hat{\beta}}{\sqrt{\hat{\sigma}^2 c^T (X^T X)^{-1} c}} \sim t_{N-p}}$$

T-contrast in SPM

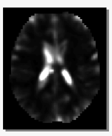
SPM

- For a given contrast c:



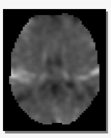
beta_???? images

$$\hat{\beta} = (X^T X)^{-1} X^T y$$



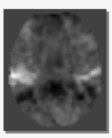
ResMS image

$$\hat{\sigma}^2 = \frac{\hat{\varepsilon}^T \hat{\varepsilon}}{N - p}$$



con_???? image

$$c^T\hat{\beta}$$



spmT_???? image

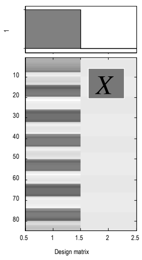
SPM{*t*}

T-test: a simple example

SPM

- ❑ Passive word listening versus rest

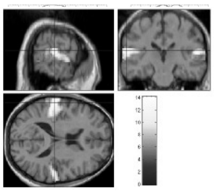
Q: activation during listening ?



X

H0: $\beta_1 = 0$

c^T = [1 0]



SPMresults:
Height threshold T = 3.2057 {p<0.001}

voxel-level *T*	($Z_\equiv$)	$p_{uncorrected}$	mm	mm	mm
13.94	Inf	0.000	−63	−27	15
12.04	Inf	0.000	−48	−33	12
11.82	Inf	0.000	−66	−21	6
13.72	Inf	0.000	57	−21	12
12.29	Inf	0.000	63	−12	−3
9.89	7.83	0.000	57	−39	6
7.39	6.36	0.000	36	−30	−15
6.84	5.99	0.000	51	0	48
6.36	5.65	0.000	−63	−54	−3
6.19	5.53	0.000	−30	−33	−18
5.96	5.36	0.000	36	−27	9
5.84	5.27	0.000	−45	42	9
5.44	4.97	0.000	48	27	24
5.32	4.87	0.000	36	−27	42

T-test: a few remarks

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- ❑ *T*-test is a signal-to-noise measure (ratio of estimate to standard deviation of estimate).
- ❑ *T*-contrasts are simple combinations of the betas; the T-statistic does not depend on the scaling of the regressors or the scaling of the contrast.
- ❑ Unilateral test:

H$_0$: $c^T\beta = 0$ vs H$_A$: $c^T\beta > 0$

Scaling issue

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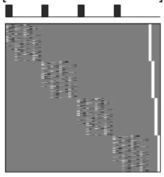
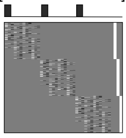
[1 1 1 1] / **4**

Subject 1



[1 1 1] / **3**

Subject 5



$$T = \frac{c^T\hat{\beta}}{\sqrt{\mathrm{var}(c^T\hat{\beta})}} = \frac{c^T\hat{\beta}}{\sqrt{\hat{\sigma}^2 c^T (X^T X)^{-1} c}}$$

- ❑ The *T*-statistic does not depend on the scaling of the regressors.
- ❑ The *T*-statistic does not depend on the scaling of the contrast.
- ❑ Contrast $c^T\hat{\beta}$ depends on scaling.
- ➢ Be careful of the interpretation of the contrasts $c^T\hat{\beta}$ themselves (eg, for a second level analysis):

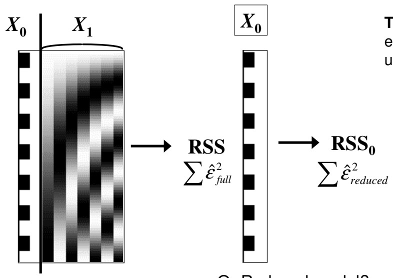
sum ≠ average

F-test: the extra sum-of-squares principle

SPM

- Model comparison: *Full vs. Reduced model?*

Null Hypothesis H_0: True model is X_0 (reduced model)



Test statistic: ratio of explained variability and unexplained variability (error)

$$F \propto \frac{RSS_0 - RSS}{RSS}$$

$$F \propto \frac{ESS}{RSS} \sim F_{\nu_1,\nu_2}$$

ν_1 = rank(X) – rank(X_0)
ν_2 = N – rank(X)

F-test: multidimensional contrats

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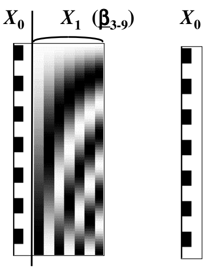
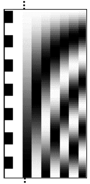
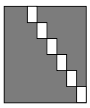
- Tests multiple linear hypotheses:

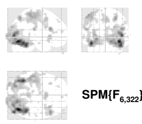
H_0: True model is X_0 | **H_0:** $\beta_3 = \beta_4 = ... = \beta_9 = 0$ | **test H_0 :** $c^T\beta = 0$?



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



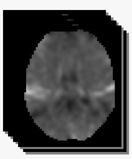




SPM{$F_{6,322}$}

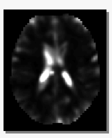
F-contrast in SPM

SPM



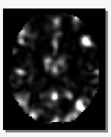
beta_???? images

$$\hat{\beta} = (X^T X)^{-1} X^T y$$



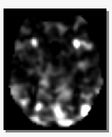
ResMS image

$$\hat{\sigma}^2 = \frac{\hat{\varepsilon}^T \hat{\varepsilon}}{N - p}$$



ess_???? images

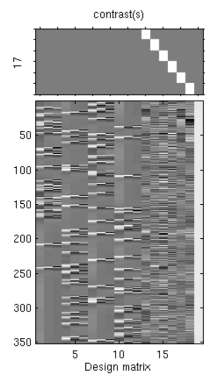
$(RSS_0 - RSS)$

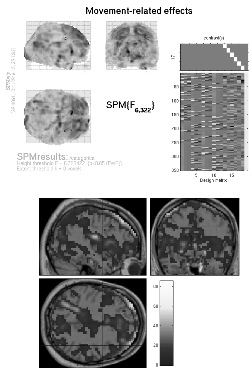


spmF_???? images

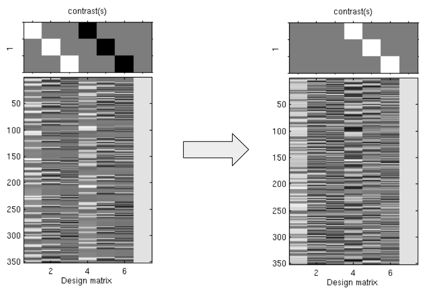
SPM{F}

F-test example: movement related effects





Multidimensional contrasts



Think of it as constructing 3 regressors from the 3 differences and complement this new design matrix such that data can be fitted in the same exact way (same error, same fitted data).

F-test: a few remarks

- F-tests can be viewed as testing for the additional variance explained by a larger model wrt a simpler (nested) model ⇨ Model comparison.
- F tests a weighted sum of squares of one or several combinations of the regression coefficients β.
- In practice, we don't have to explicitly separate X into $[X_1 X_2]$ thanks to multidimensional contrasts.
- Hypotheses:

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad \begin{array}{l} \text{Null Hypothesis } H_0: \ \beta_1 = \beta_2 = \beta_3 = 0 \\ \text{Alternative Hypothesis } H_A: \ \text{at least one } \beta_k \neq 0 \end{array}$$

- In testing uni-dimensional contrast with an *F*-test, for example $\beta_1 - \beta_2$, the result will be the same as testing $\beta_2 - \beta_1$. It will be exactly the square of the *t*-test, testing for both positive and negative effects.

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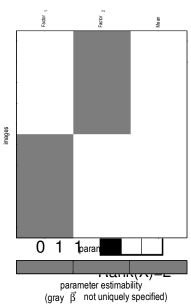
Estimability of a contrast

- If X is not of **full rank** then we can have $X\beta_1 = X\beta_2$ with $\beta_1 \neq \beta_2$ (different parameters).
- The parameters are **not** therefore 'unique', 'identifiable' or '**estimable**'.
- For such models, $X^T X$ is not invertible so we must resort to generalised inverses (SPM uses the **pseudo-inverse**).
- Example:



[1 0 0], [0 1 0], [0 0 1] are not estimable.
[1 0 1], [0 1 1], [1 -1 0], [0.5 0.5 1] are estimable.

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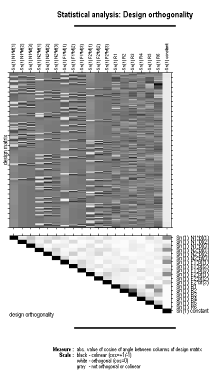
Design orthogonality



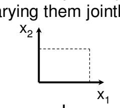
- For each pair of columns of the design matrix, the orthogonality matrix depicts the magnitude of the **cosine of the angle** between them, with the range 0 to 1 mapped from white to black.
- The cosine of the angle between two vectors *a* and *b* is obtained by:

$$\cos\alpha = \frac{a \cdot b}{\|a\|\|b\|}$$

- If both vectors have **zero mean** then the cosine of the angle between the vectors is the same as the **correlation** between the two variates.

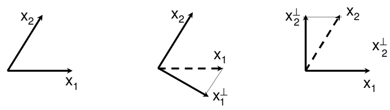
Multicollinearity

- Contrast covariance matrix: $Var(c^T\hat{\beta}) = \sigma^2 c^T (X^T X)^{-1} c$
- Orthogonal regressors (=*uncorrelated*):
  By varying each separately, one can predict the combined effect of varying them jointly.



$(X^T X)^{-1}$ is diagonal

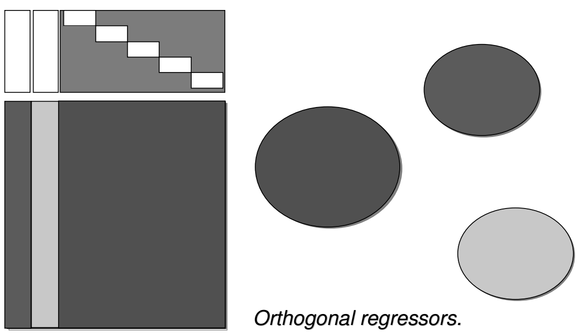
- Non-orthogonal regressors (=*correlated*):
  When testing for the first regressor, we are effectively removing the part of the signal that can be accounted for by the second regressor ⇨ *implicit orthogonalisation.*



$x_2^{\perp} = x_2 - x_1.x_2\ x_1$

It does not reduce the predictive power or reliability of the model as a whole.

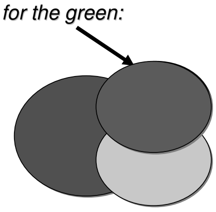
Shared variance



Orthogonal regressors.

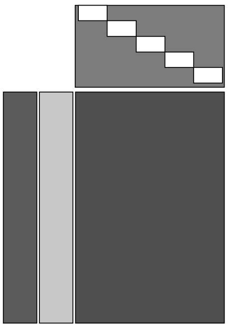
Shared variance

Testing for the green:

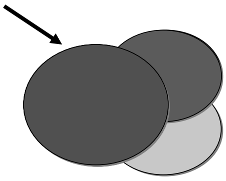


Correlated regressors, for example:
green: subject age
yellow: subject score

Shared variance

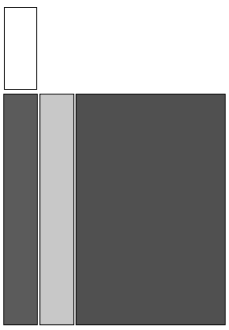


Testing for the red:

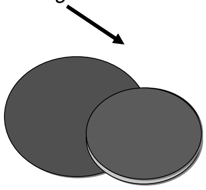


Correlated regressors.

Shared variance



Testing for the green:

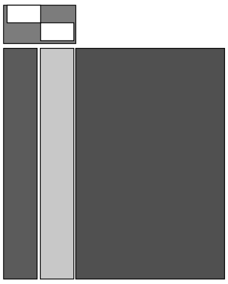


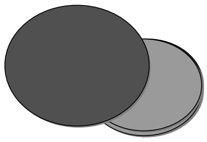
Highly correlated.
Entirely correlated⇨ non estimable

SPM

Shared variance

Testing for the green and yellow





If significant, can be G and/or Y

Examples

SPM

A few remarks

- ❑ We implicitly test for an <u>additional</u> effect only, be careful if there is correlation
  - \- Orthogonalisation = decorrelation : not generally needed
  - \- Parameters and test on the non modified regressor change

- ❑ It is always simpler to have orthogonal regressors and therefore designs.

- ❑ In case of correlation, use F-tests to see the overall significance. There is generally no way to decide to which regressor the « common » part should be attributed to.

- ❑ Original regressors may not matter: it's the contrast you are testing which should be as decorrelated as possible from the rest of the design matrix

SPM

Overview

- ❑ Model specification and parameters estimation
- ❑ Hypothesis testing
- ❑ Contrasts
  - ➢ *T*-tests
  - ➢ *F*-tests
- ❑ Contrast estimability
- ❑ Correlation between regressors
  - ➢ Example(s)
- ❑ Design efficiency

Design eficiency

- The aim is to minimize the standard error of a *t*-contrast (i.e. the denominator of a t-statistic).

$$T = \frac{c^T \hat{\beta}}{\sqrt{\mathrm{var}(c^T \hat{\beta})}}$$

$$\mathrm{var}(c^T \hat{\beta}) = \hat{\sigma}^2 c^T (X^T X)^{-1} c$$

- This is equivalent to maximizing the efficiency *e*:

$$e(\hat{\sigma}^2, c, X) = (\underbrace{\hat{\sigma}^2}_{\text{Noise variance}} c^T \underbrace{(X^T X)}_{\text{Design variance}}{}^{-1} c)^{-1}$$

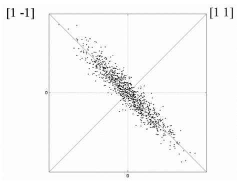
- If we assume that the noise variance is independent of the specific design:

$$e(c, X) = (c^T (X^T X)^{-1} c)^{-1}$$

- This is a relative measure: all we can really say is that one design is more efficient than another (for a given contrast).

Design efficiency

- The efficiency of an estimator is a measure of how reliable it is and depends on error variance (the variance not modeled by explanatory variables in the design matrix) and the design variance (a function of the explanatory variables and the contrast tested).
- $X^T X$ represents covariance of regressors in design matrix; high covariance increases elements of $(X^T X)^{-1}$.
- High correlation between regressors leads to low sensitivity to each regressor alone.



$$\begin{bmatrix} 1 & -0.9 \\ -0.9 & 1 \end{bmatrix}$$

$$c^T (X^T X)^{-1} c$$

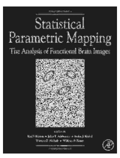
c^T=[1 0]: 5.26

c^T=[1 1]: 20

c^T=[1 -1]: 1.05

Bibliography

- *Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Elsevier, 2007.



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