Neuroimaging for Machine Learners

Validation and inference

PRoNTo course
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Univariate analysis:

- Introduction: within & between subjects analysis
- GLM, contrasts & Statistical inference
- Multiple comparison problem & other inference levels
- Conclusion

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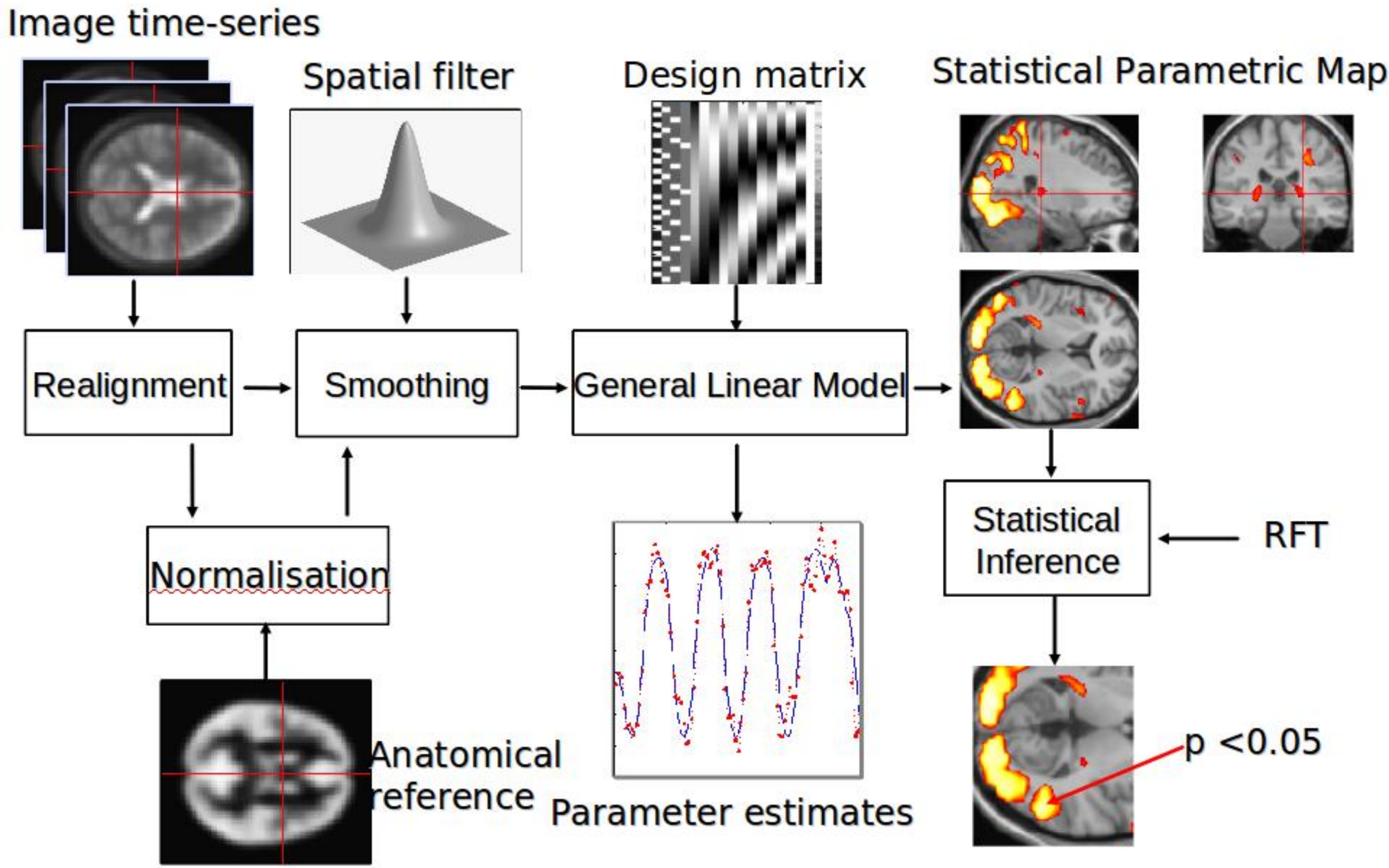
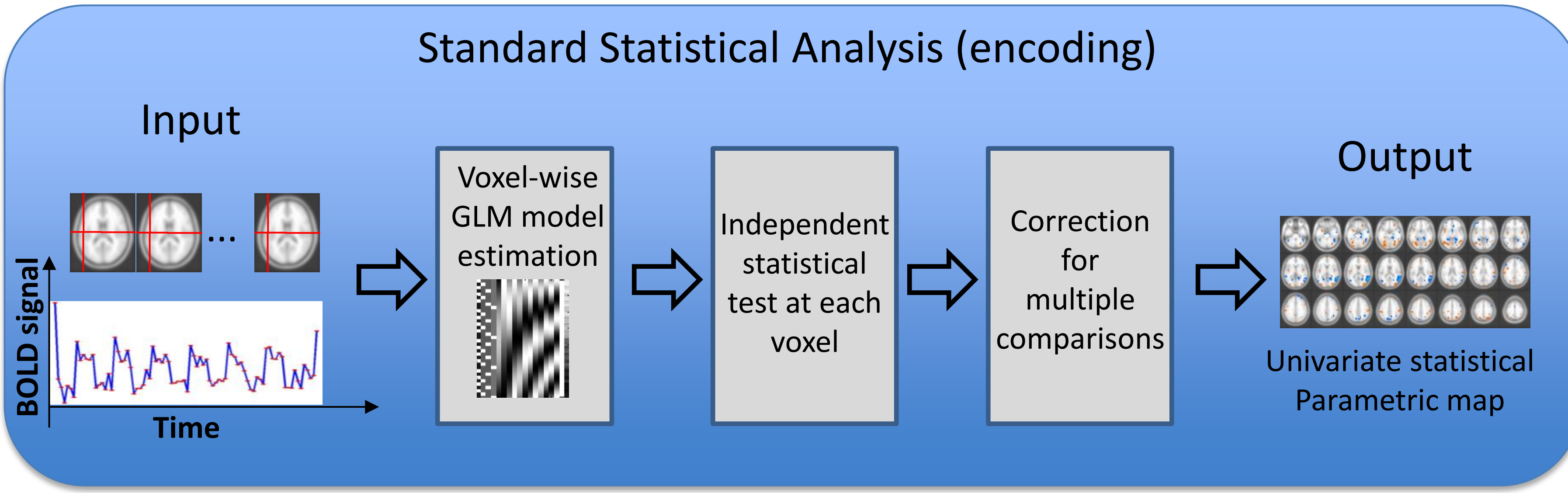


Image time-series
Spatial filter
Design matrix
Statistical Parametric Map
Realignment
Smoothing
General Linear Model
Normalisation
Statistical Inference
RFT
Anatomical reference
Parameter estimates
p <0.05

Standard univariate approach



Find the mapping g from explanatory variable X to observed data Y

g: X ➔ Y

Within subject analysis :

- « first level » analysis
- data = series of measurements from 1 subject, typically « functional MRI » (fMRI)
- modelling BOLD response time series
  ➔ activation task or resting connectivity
- sometimes with parametric modulation and/or confounding regressor
- output = contrast images, statistical maps, connectivity maps, and « cleaned » signal

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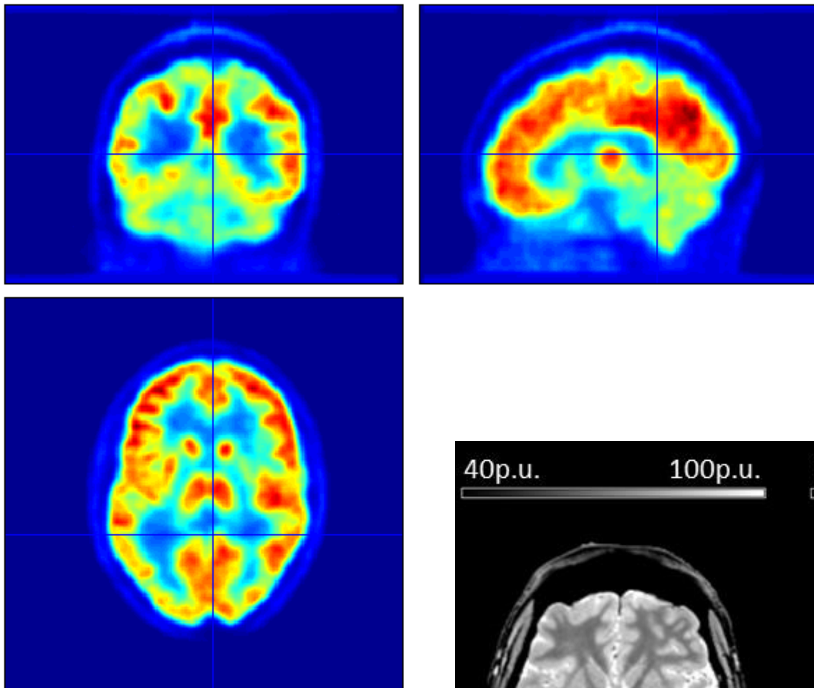
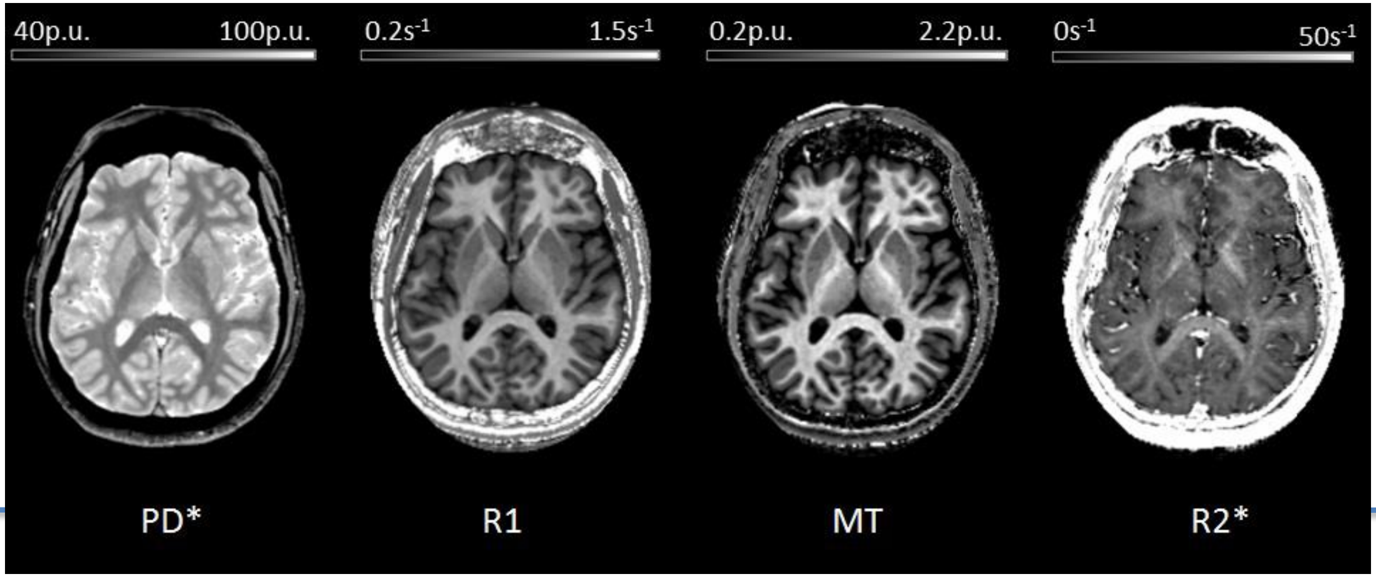
Between subjects analysis :

- « second level » analysis
- data = 1 (or few) image(s)/subject from group(s) of subjects, e.g. contrast image, tissue density, deformation map, FDG-PET scan,…
- modelling group effect/differences or regressing subjects' score (confound/interest)
- output = « raw » signal, contrast images and statistical maps

FDG-PET scan



Quantitative MRI



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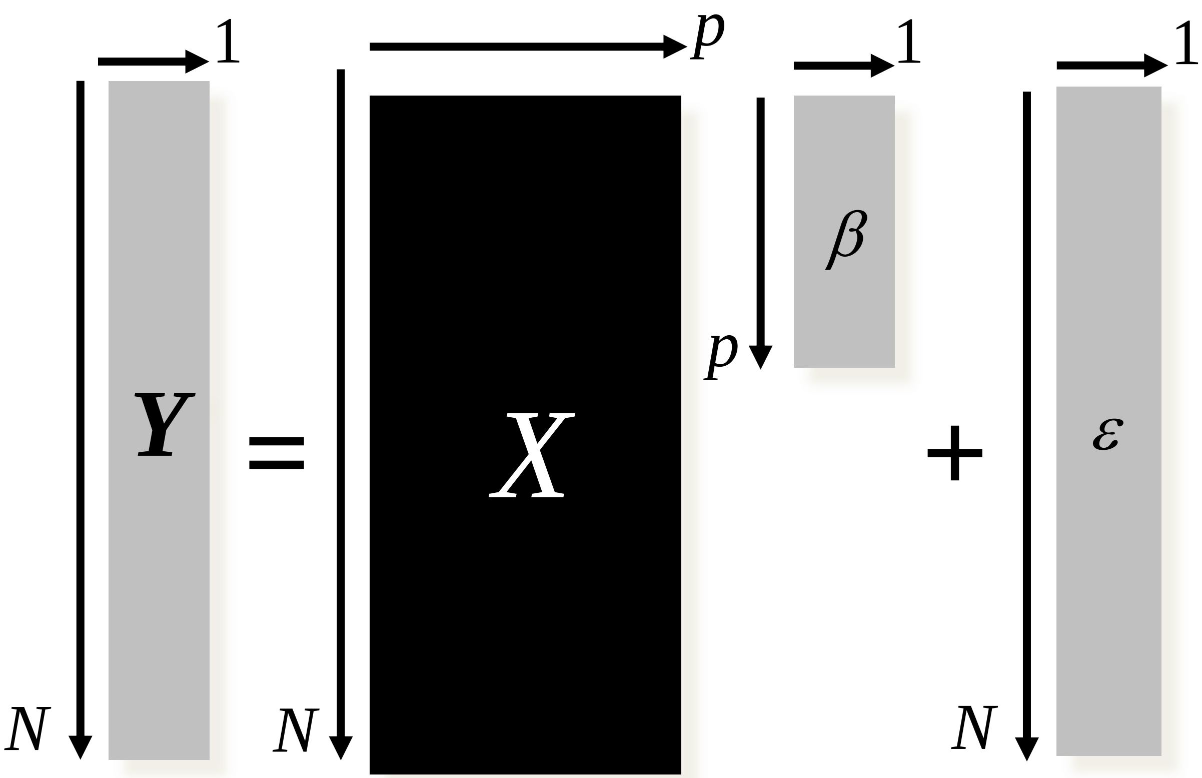
General Linear Model



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

N: # images

p: # regressors

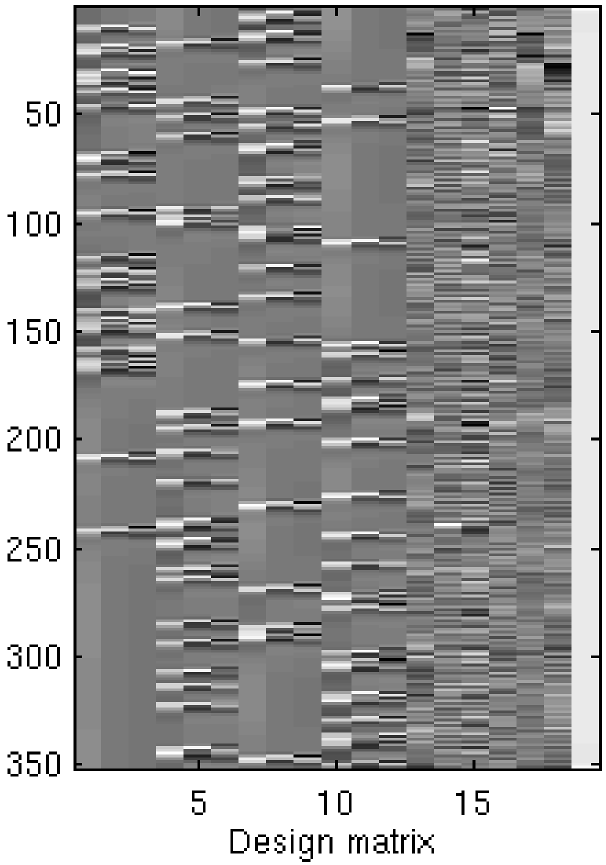
GLM defined by:

- design matrix X
- error term ε distribution

$$\varepsilon \sim N(0, \sigma V)$$

Design matrix example

Single subject
fMRI time series



<u>Aim:</u>

model BOLD signal variation over time/scans, with

- 4 conditions + movement parameters + mean
- each condition event modelled by HRF with 2 derivatives (≈Taylor expansion)

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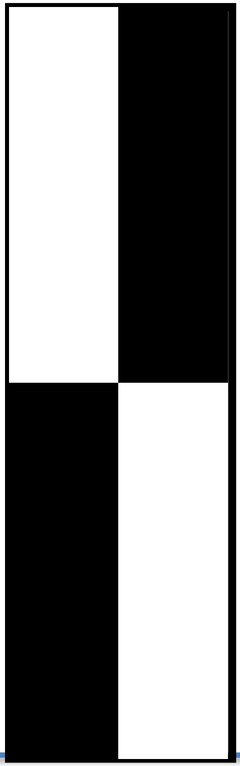
Design matrix example

Group comparison
with two-sample t-test

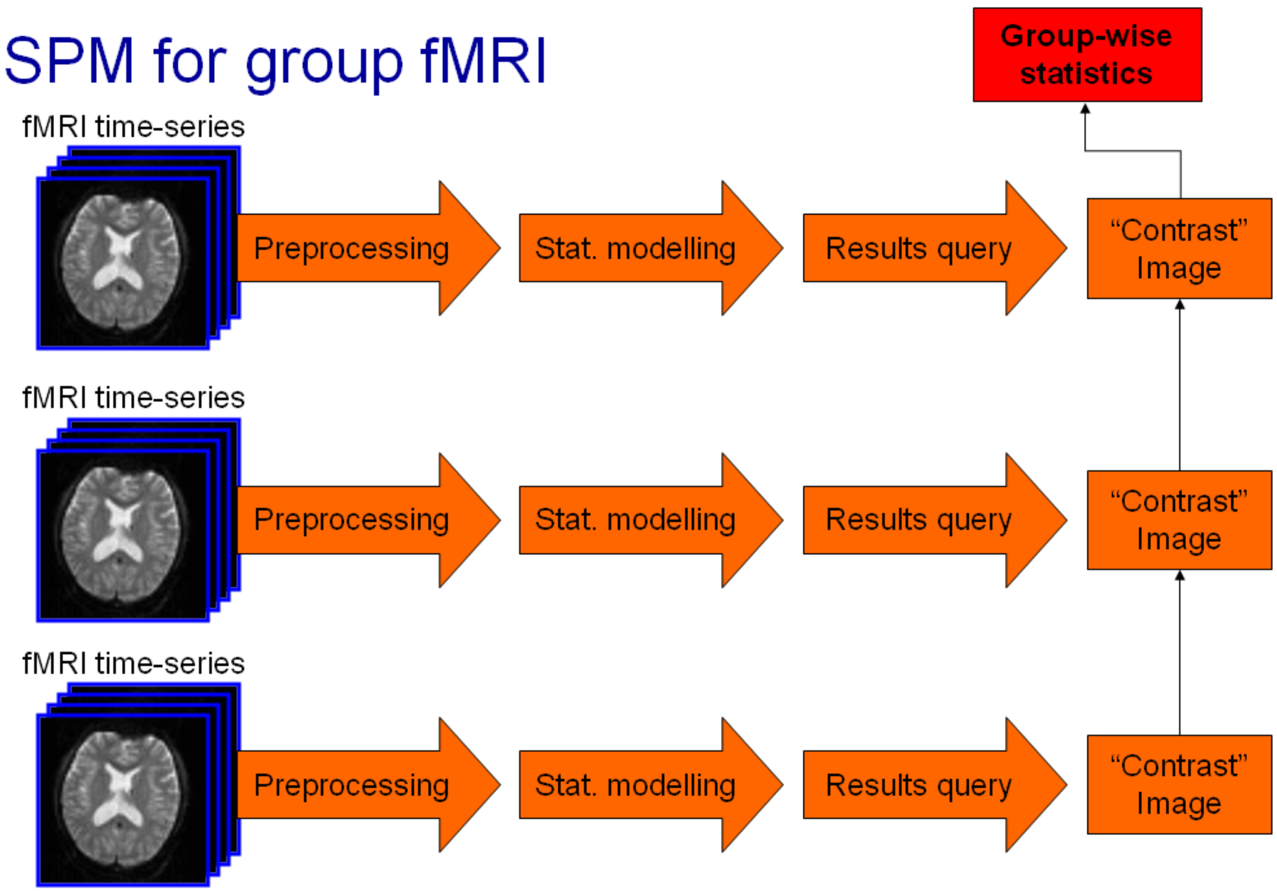


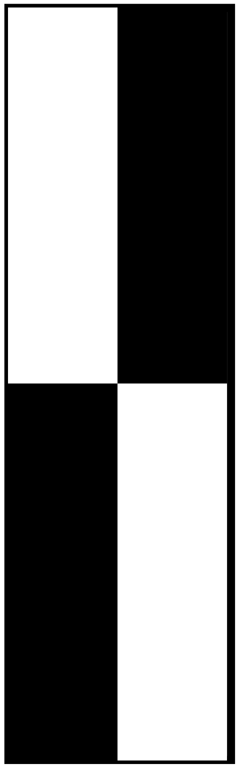
Aim:

model “group effect“ with:

- Separate group averages

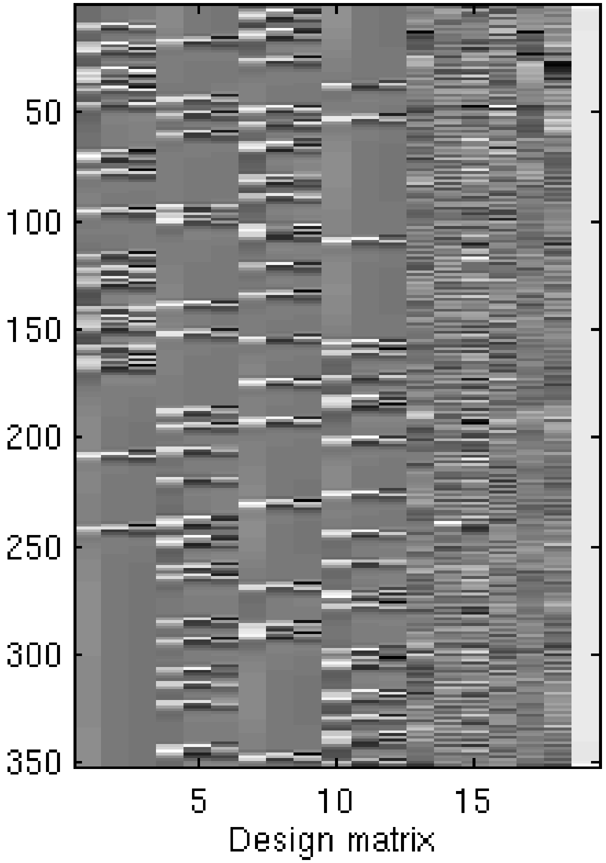
Design matrix example



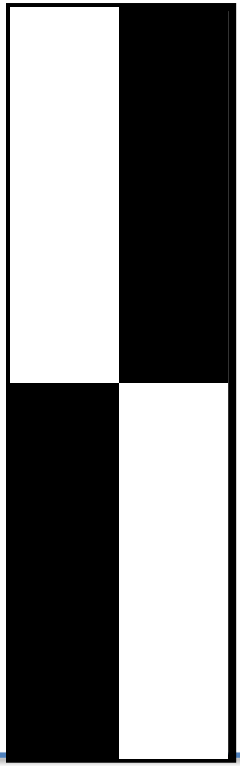


Design matrix example

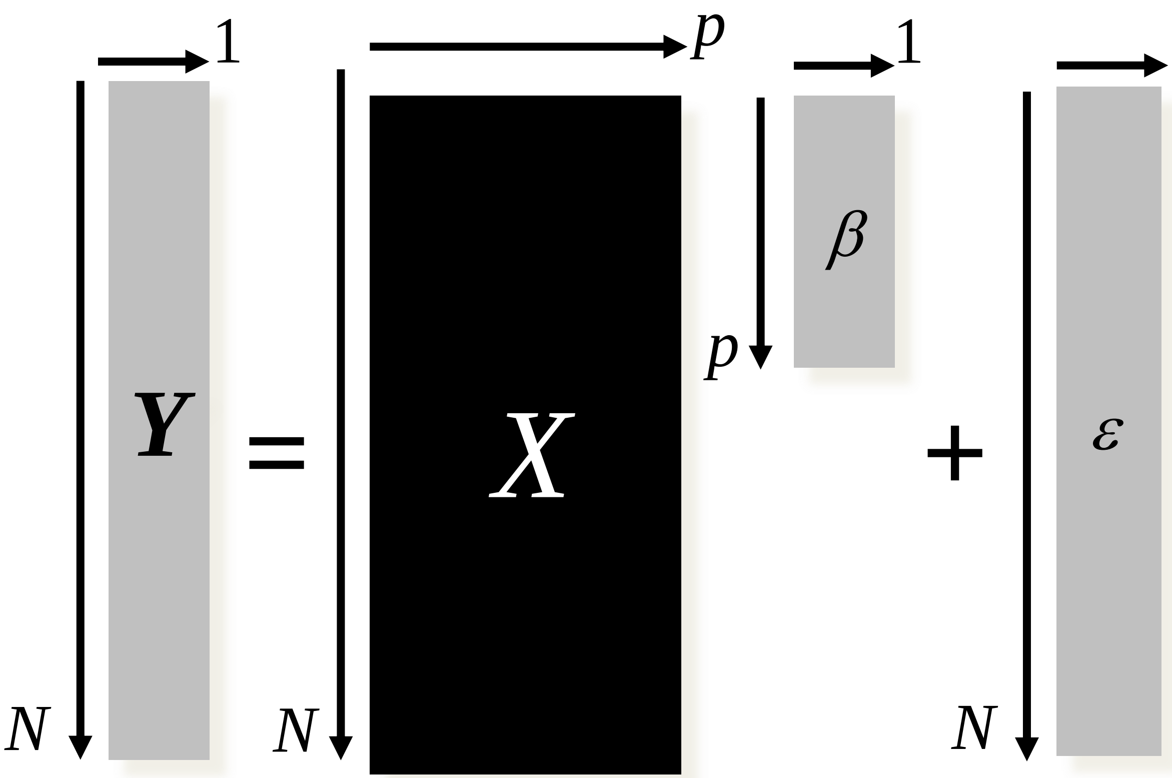
Single subject
fMRI time series



Group comparison
with two-sample t-test



General Linear Model



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

$$\varepsilon \sim N(0, \sigma V)$$

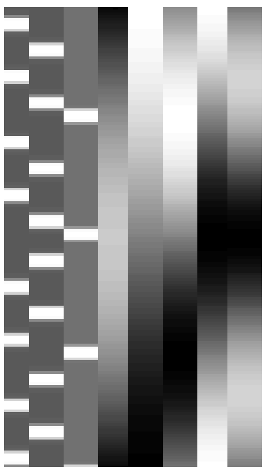
<u>NOTE</u>:

- GLM applied to each and every voxel *individually*!
- Estimation of the β's in a (weighted) least-square sense.

T-test & contrast

A contrast selects a specific effect of interest:

- ⇨ contrast *c* = vector of length *p.*
- ⇨ $c^T\beta$ = linear combination of regression coefficients β.



c^T = [1 0 0 0 0 …]

$$c^T\beta = \mathbf{1}\text{x}\beta_1 + \mathbf{0}\text{x}\beta_2 + \mathbf{0}\text{x}\beta_3 + \mathbf{0}\text{x}\beta_4 + \mathbf{0}\text{x}\beta_5 + \ldots$$

c^T = [0 -1 1 0 0 …]

$$c^T\beta = \mathbf{0}\text{x}\beta_1 + \mathbf{-1}\text{x}\beta_2 + \mathbf{1}\text{x}\beta_3 + \mathbf{0}\text{x}\beta_4 + \mathbf{0}\text{x}\beta_5 + \ldots$$

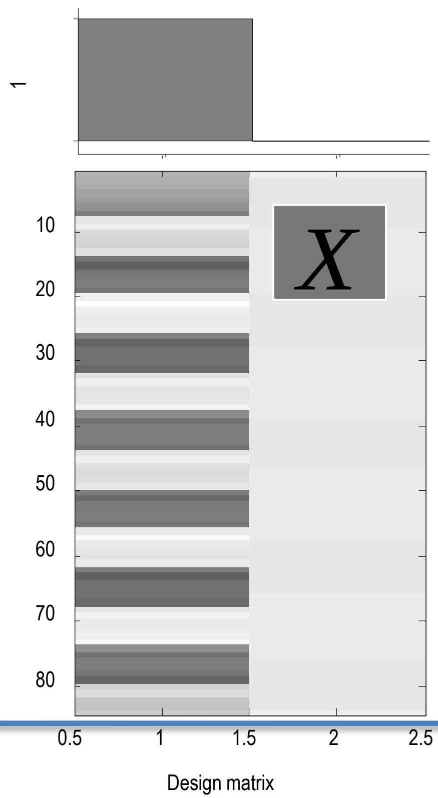
Under i.i.d assumptions $\varepsilon \sim N(0, \sigma I)$

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

***t*-test** example:

Passive word listening versus rest

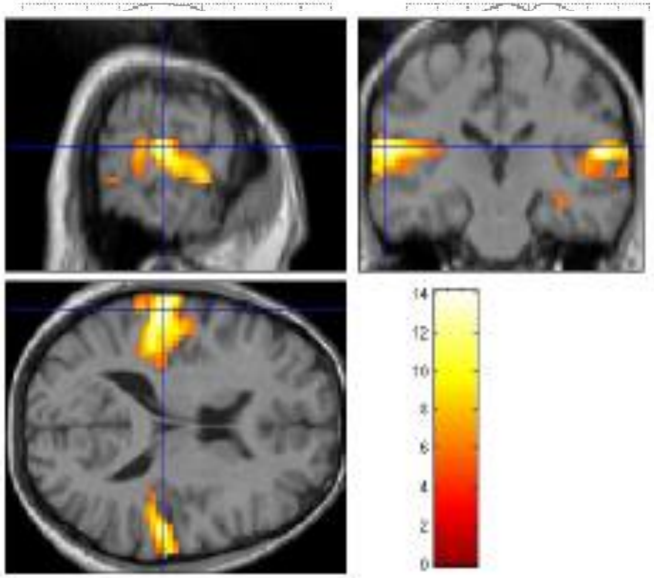
$c^T = [\,1 \quad 0\,]$



Q: activation during listening ?

Null hypothesis: $\beta_1 = 0$

$$t = \frac{c^T \hat{\beta}}{Std(c^T \hat{\beta})}$$



SPMresults:

Height threshold T = 3.2057 {p<0.001}

voxel-level			mm mm mm		
T	(Z)	p uncorrected			
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	9	42
5.44	4.97	0.000	48	27	24
5.32	4.87	0.000	36	-27	42

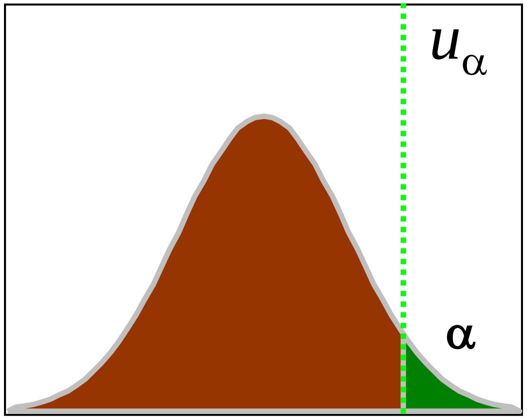
Classical inference

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

Significance level α: $\alpha = p(T > u_\alpha \mid H_0)$

Acceptable *false positive rate α*.

⇨ threshold u_α

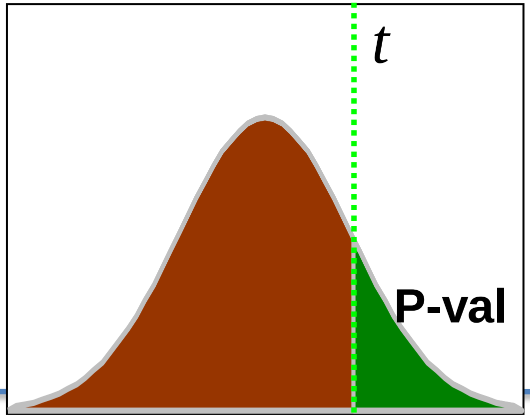


Null Distribution of T

Observation of test statistic t
= a realisation of T

⇨ Reject H_0 in favour of H_A if $t > u_\alpha$

p-value = evidence against H_0. $p(T > t \mid H_0)$

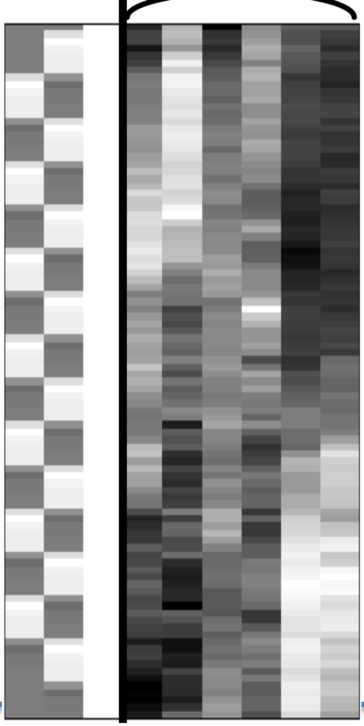


Null Distribution of T

F-test & contrast

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

X_0 X_1



Full model ?

→ **RSS** $\sum \hat{\varepsilon}^2_{full}$

X_0

or Reduced model?

→ **RSS_0** $\sum \hat{\varepsilon}^2_{reduced}$

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

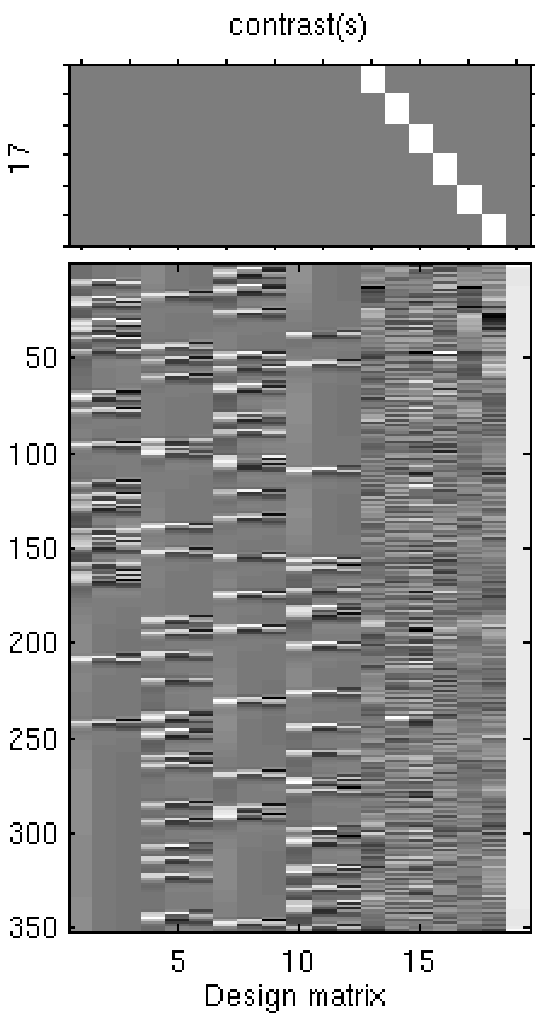
$$F \propto \frac{RSS_0 - RSS}{RSS}$$

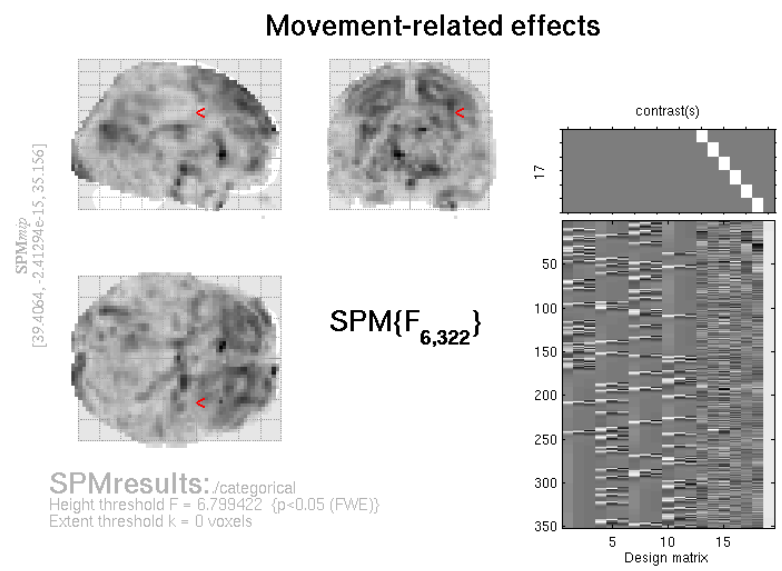
$$F \propto \frac{ESS}{RSS} \sim F_{\nu_1,\nu_2}$$

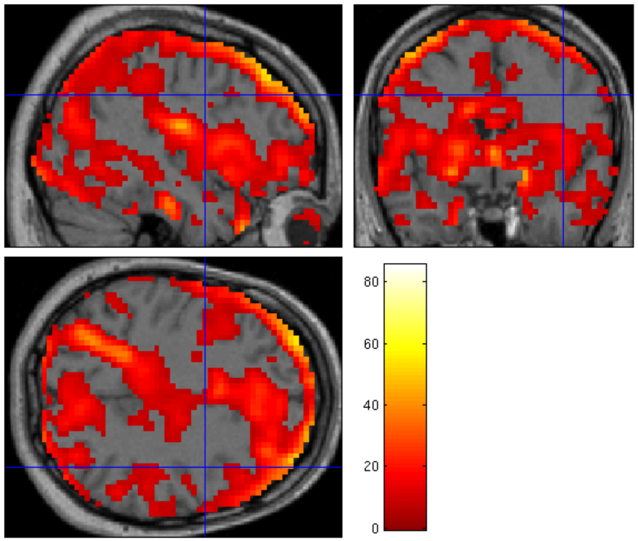
$\nu_1 = \text{rank}(X) - \text{rank}(X_0)$

$\nu_2 = N - \text{rank}(X)$

***F*-test** example:
movement related effects







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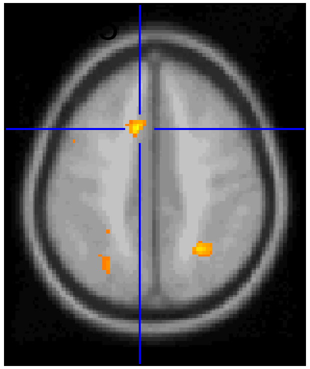
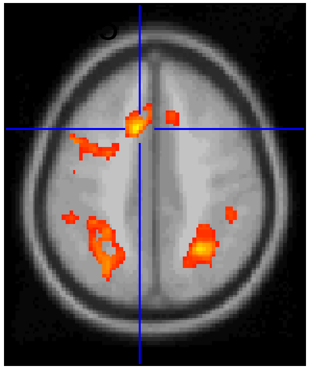
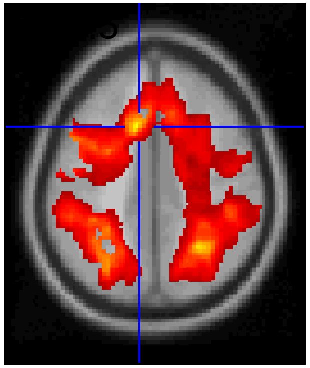
Multiple comparison problem

High Threshold → Med. Threshold → Low Threshold







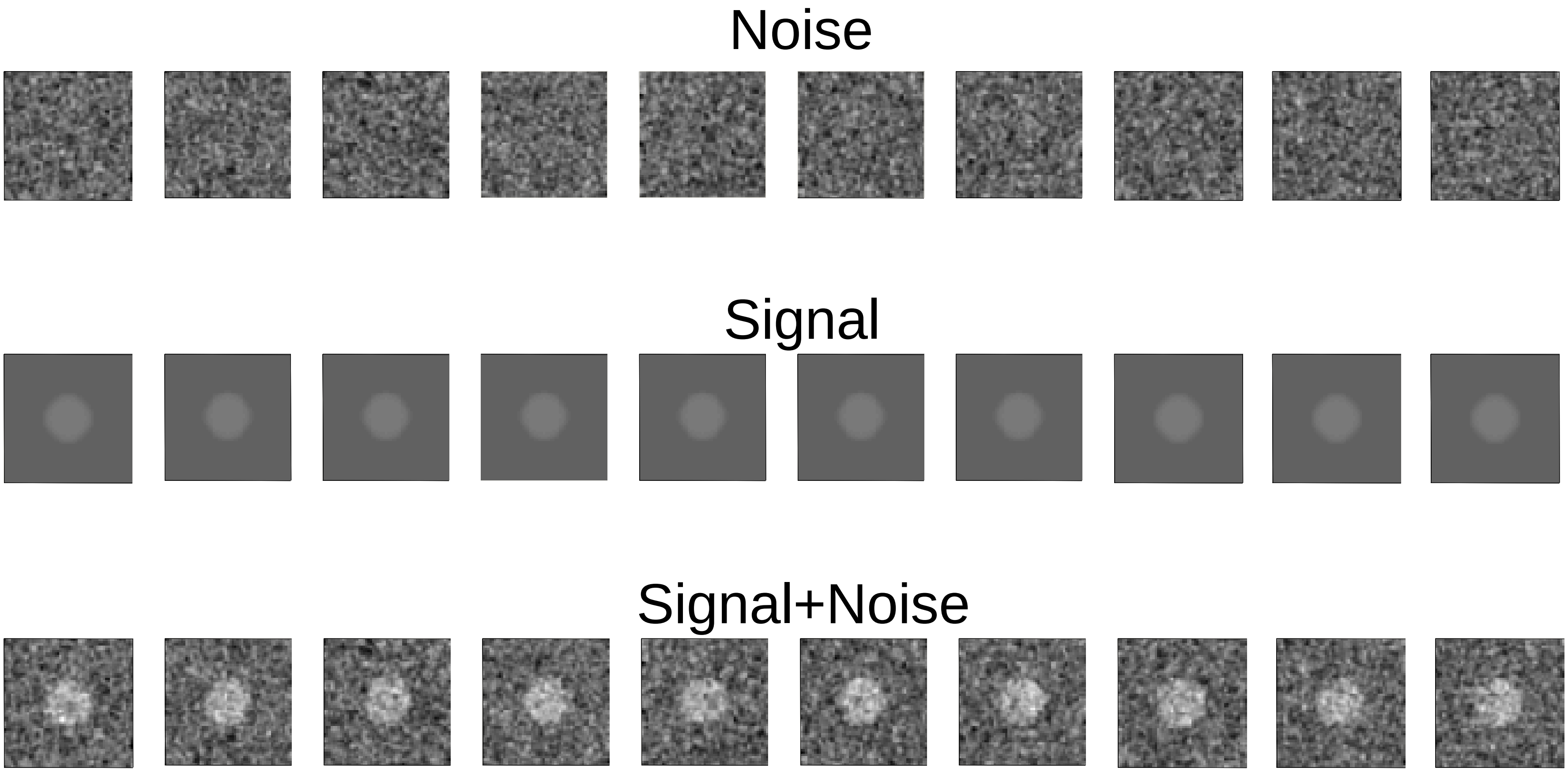
Good Specificity

Poor Power
(risk of false
negatives)

Poor Specificity
(risk of false
positives)

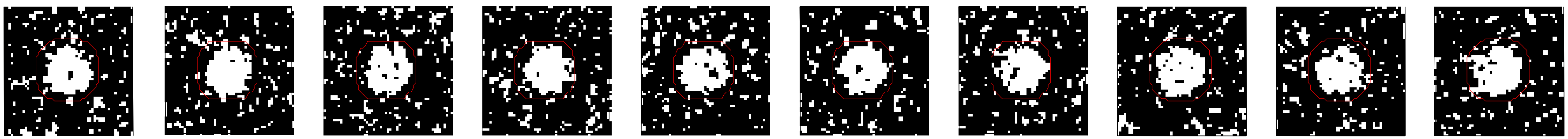
Good Power

Multiple comparison problem



Multiple comparison problem

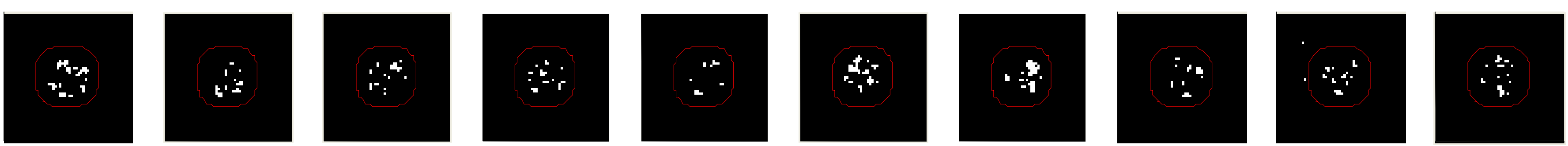
Use of '*uncorrected*' p-value, $\alpha = 0.1$



11.3% 11.3% 12.5% 10.8% 11.5% 10.0% 10.7% 11.2% 10.2% 9.5%

Percentage of Null Pixels that are False Positives

Use of '*corrected*' p-value, $\alpha=0.1$



FWE

Multiple comparison problem

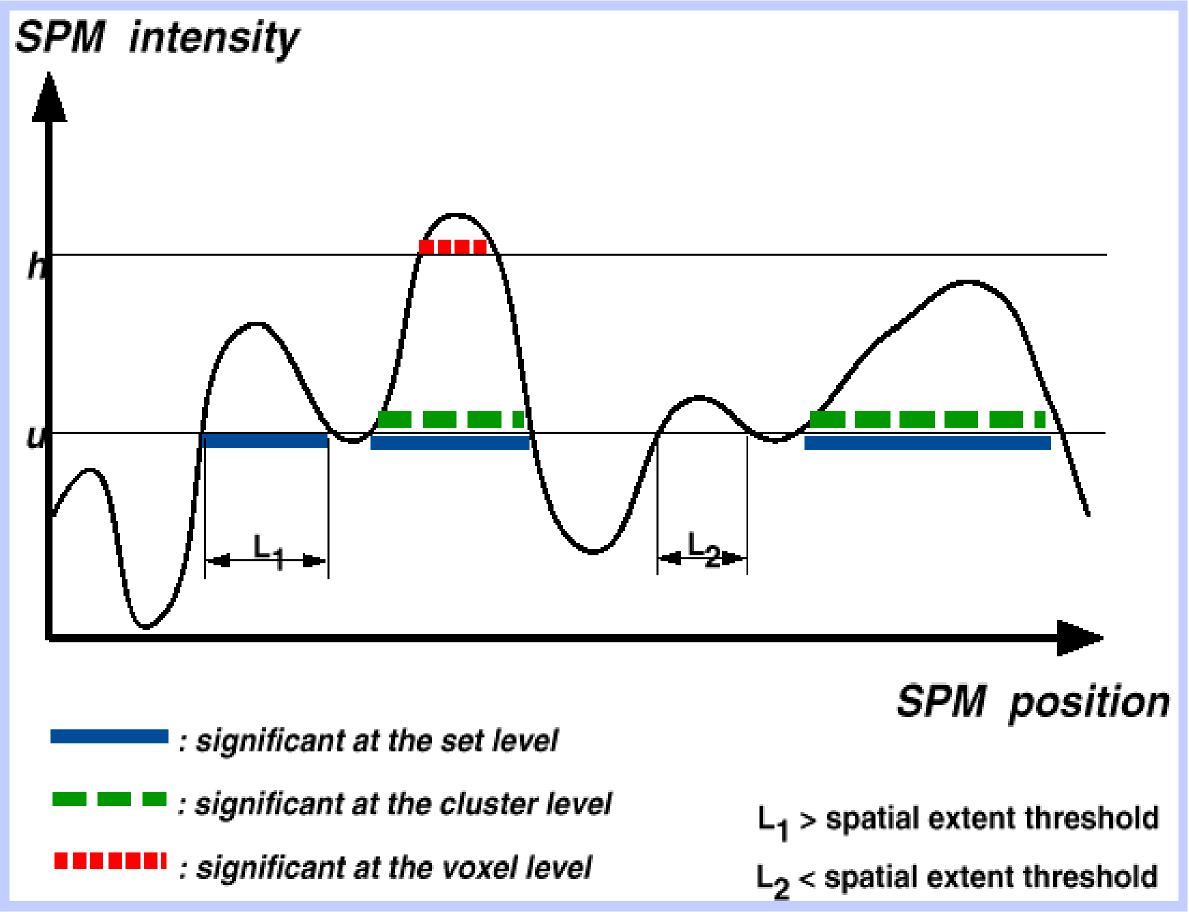
Inference with multiple comparison in neuroimaging depends on:

- search volume = # tests performed
- smoothness of the data
- size & shape of volume of interest
- statistics employed (t- or F-)

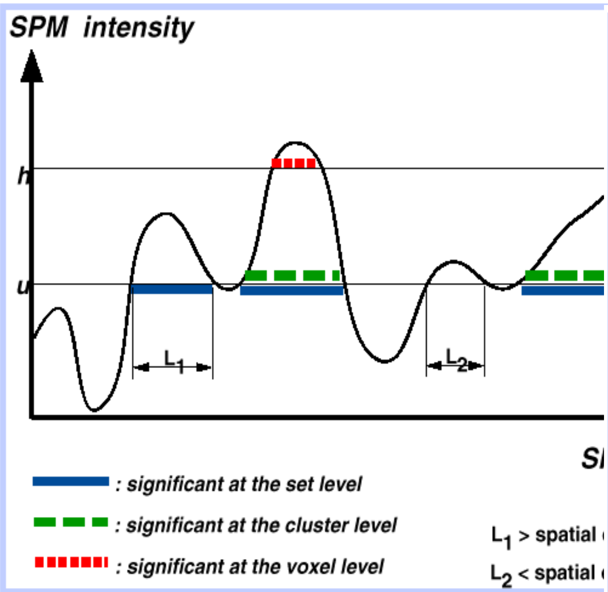
  + degrees of freedom

➔ usually derived from data and test performed

More inference levels



More inference levels



Sensitivity	Test based on	Parameters set by the user	Regional specificity
−	The intensity of a voxel	• Low pass filter	+
	The spatial extent above u or the spatial extent and the maximum peak height	• Low pass filter • intensity threshold u	
	The number of clusters above u with size greater than n	• Low pass filter • intensity thres. u • spatial threshold n	
+	The sum of square of the SPM or a MANOVA	• Low pass filter	−

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Conclusion

From a ‘neuroimager’ perspectives, GLM is useful for:

- Localising an effect of interest, while accounting for
  - effects of no interest
  - confounding effects
  - HRF shape (for fMRI)
- Clean signal & functional connectivity

Conclusion

From a ‘machine learner’ perspectives, GLM is useful for:

- Check for « *is there any effect?* »
- Data filtering (e.g. confound removal)
- HRF deconvolution for fMRI (single event modeling) or subject’s response extraction (contrast building)
- Feature selection/masking

Thank you for your attention!

Any question?

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