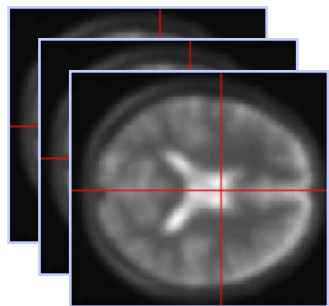


# Contrasts & Statistical Inference

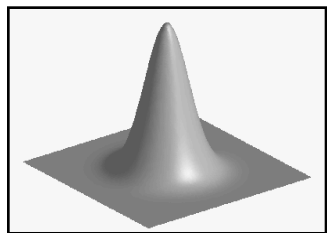
*Christophe Phillips*  
*Slides: Guillaume Flandin*

GIGA – Cyclotron Research Centre *in vivo* imaging  
University of Liège

Image time-series



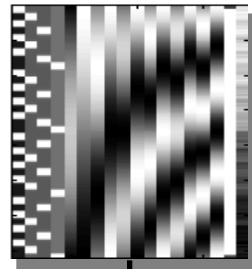
Spatial filter



Realignment

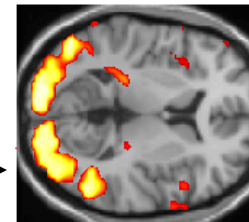
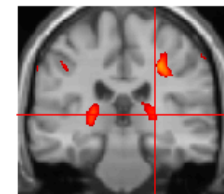
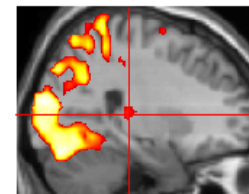
Smoothing

Design matrix



General Linear Model

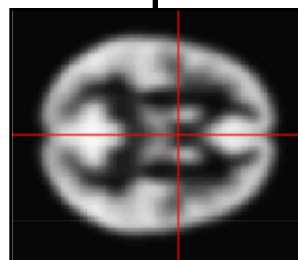
Statistical Parametric Map



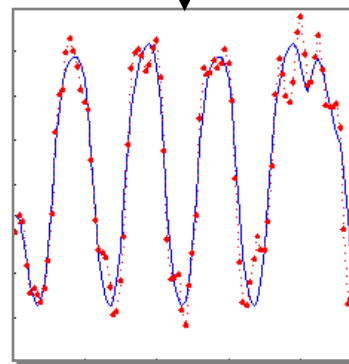
Statistical Inference

RFT

Normalisation

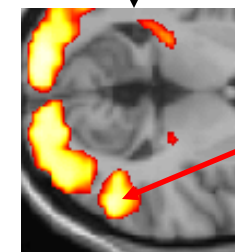


Anatomical reference

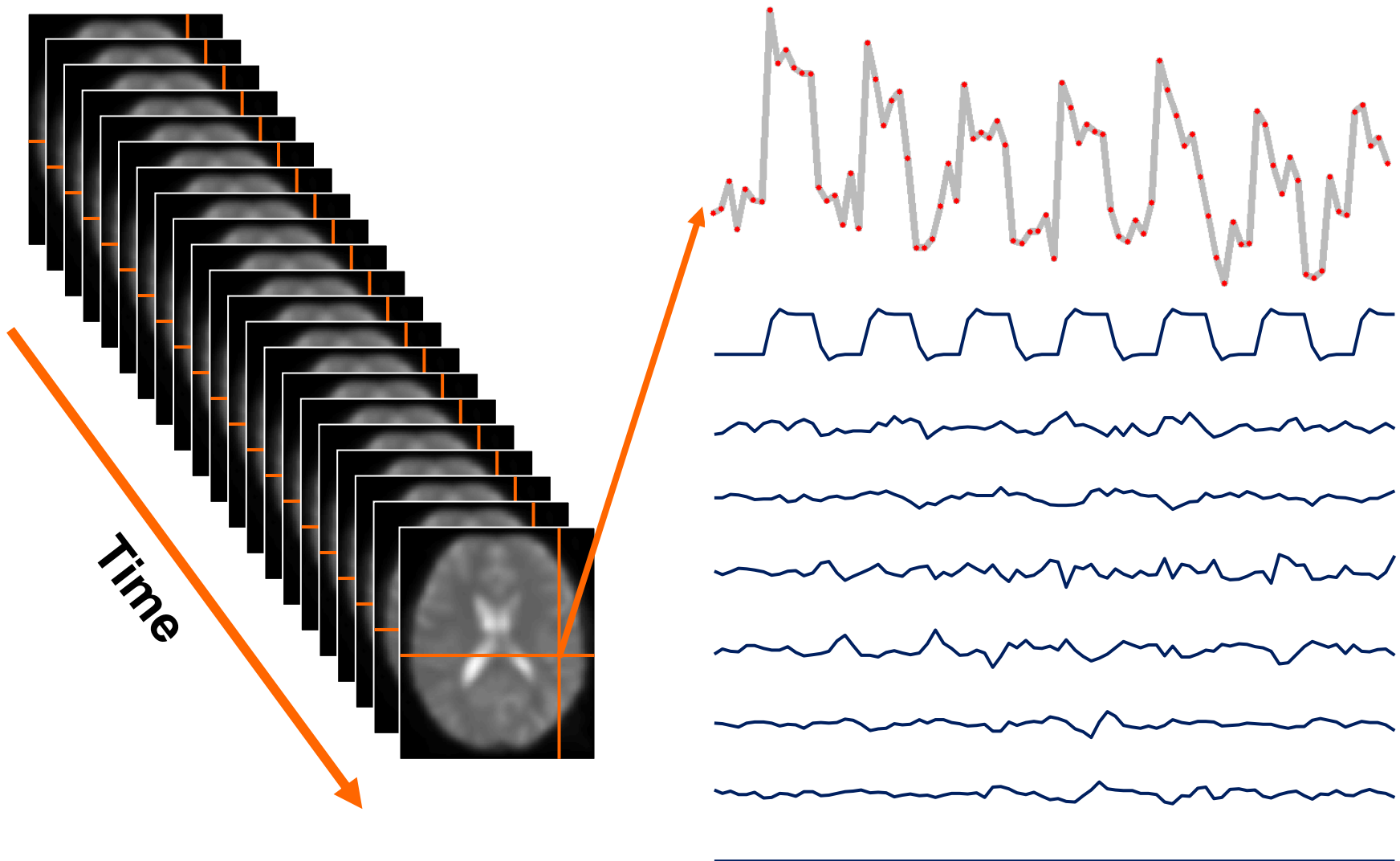


Parameter estimates

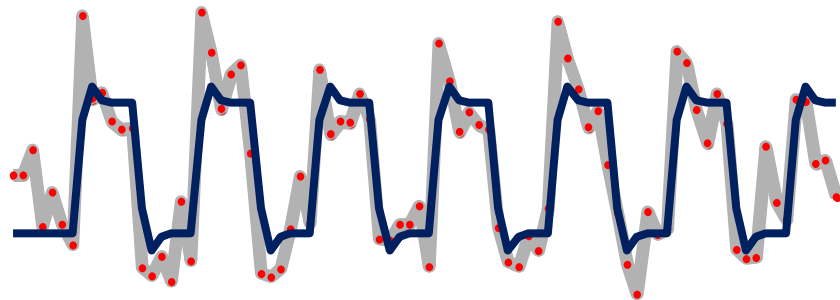
$p < 0.05$



# A mass-univariate approach



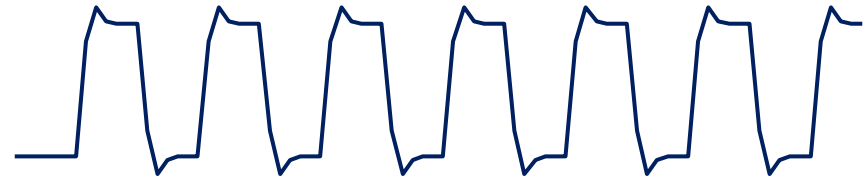
# Estimation of the parameters



i.i.d. assumptions:  $\varepsilon \sim N(0, \sigma^2 I)$

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

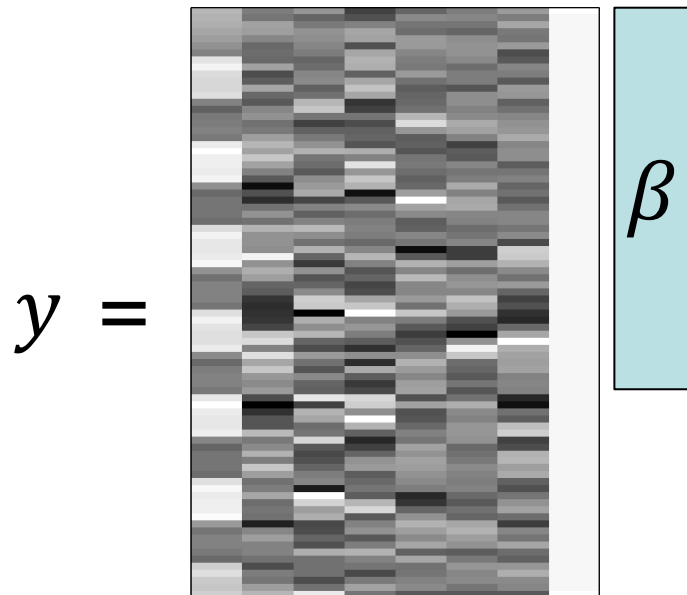
$$\hat{\beta}_1 = 3.9831$$



$$\hat{\beta}_{2-7} = \{0.6871, 1.9598, 1.3902, 166.1007, 76.4770, -64.8189\}$$



$$\hat{\beta}_8 = 131.0040$$



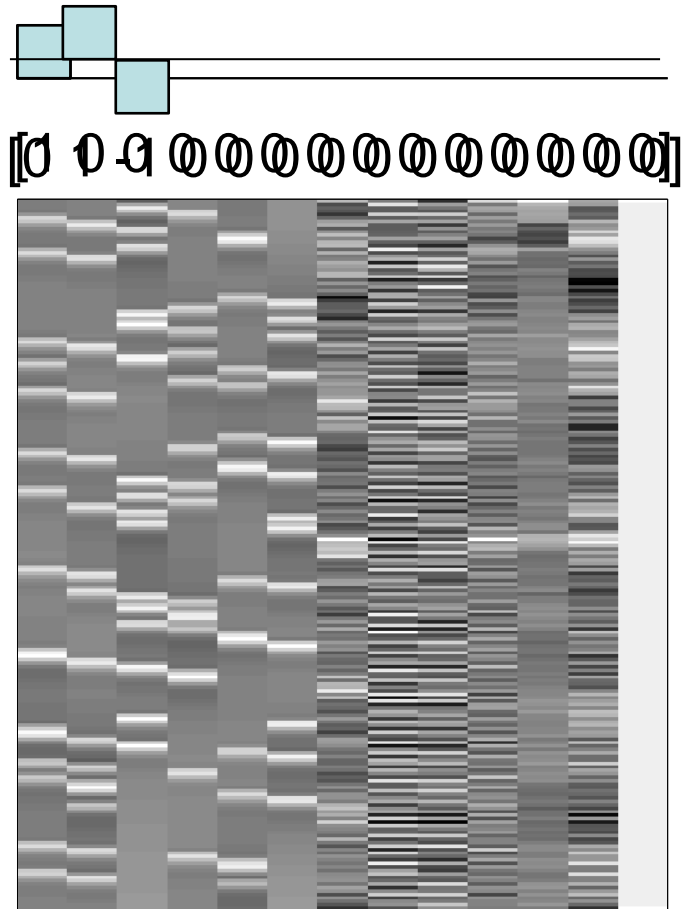
$+\varepsilon$

$$\hat{\varepsilon} =$$


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

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

# Contrasts



□ 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  $\beta$ .

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

$$\begin{aligned} c^T \beta &= \mathbf{1} \times \beta_1 + \mathbf{0} \times \beta_2 + \mathbf{0} \times \beta_3 + \mathbf{0} \times \beta_4 + \dots \\ &= \beta_1 \end{aligned}$$

$$c = [0 \ 1 \ -1 \ 0 \ \dots]^T$$

$$\begin{aligned} c^T \beta &= \mathbf{0} \times \beta_1 + \mathbf{1} \times \beta_2 + \mathbf{-1} \times \beta_3 + \mathbf{0} \times \beta_4 + \dots \\ &= \beta_2 - \beta_3 \end{aligned}$$

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

# Hypothesis Testing

To test a hypothesis, we construct “test statistics”.

## ❑ Null Hypothesis $H_0$

Typically what we want to disprove (no effect).

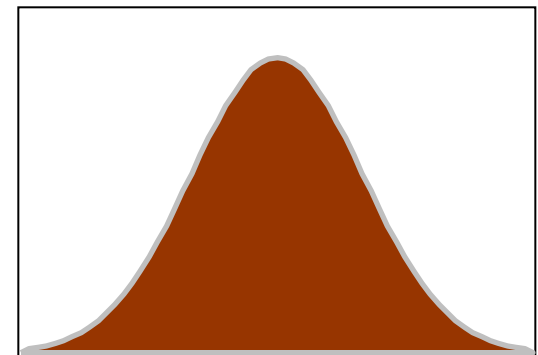
⇒ The Alternative Hypothesis  $H_A$  expresses outcome of interest.

## ❑ 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  $T$

# Hypothesis Testing

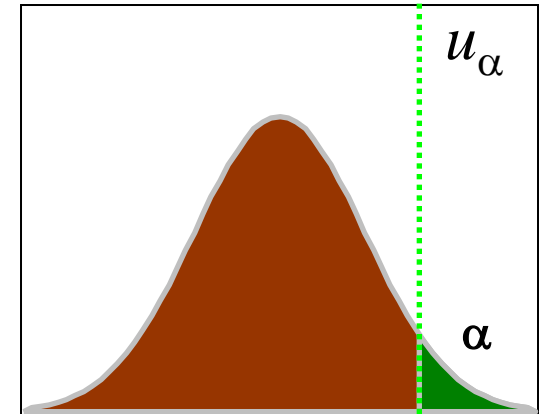
## □ **Significance level $\alpha$ :**

Acceptable *false positive rate*  $\alpha$ .

$\Rightarrow$  threshold  $u_\alpha$

Threshold  $u_\alpha$  controls the false positive rate

$$\alpha = p(T > u_\alpha \mid H_0)$$



Null Distribution of T

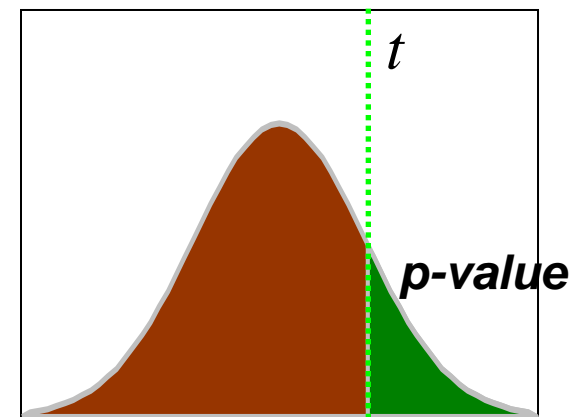
## □ **Conclusion about the hypothesis:**

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.



Null Distribution of T

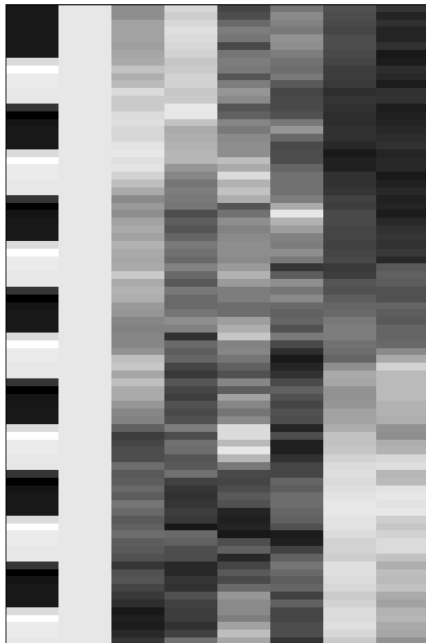
$$p(T > t \mid H_0)$$

# T-test - one dimensional contrasts – SPM{t}

$$c^T = 1 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0$$



$\beta_1 \ \beta_2 \ \beta_3 \ \beta_4 \ \beta_5 \ \dots$



Question: box-car amplitude > 0 ?

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

Null hypothesis:

$$H_0: c^T \beta = 0$$

*contrast of  
estimated  
parameters*

Test statistic:

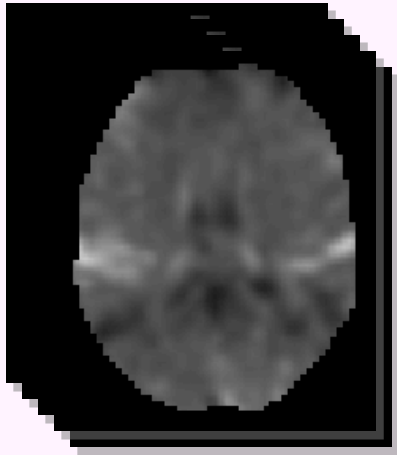
$$T = \frac{\text{contrast of estimated parameters}}{\sqrt{\text{variance estimate}}}$$

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



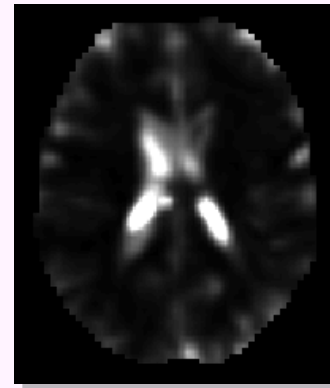
# T-contrast in SPM

□ For a given contrast  $c$ :



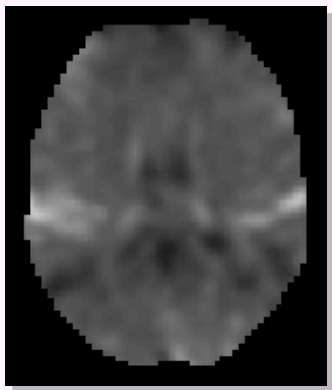
beta\_???? images

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



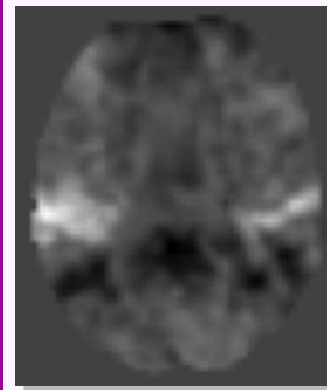
ResMS image

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



con\_???? image

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



spmT\_???? image

SPM $\{t\}$

# T-test: a simple example

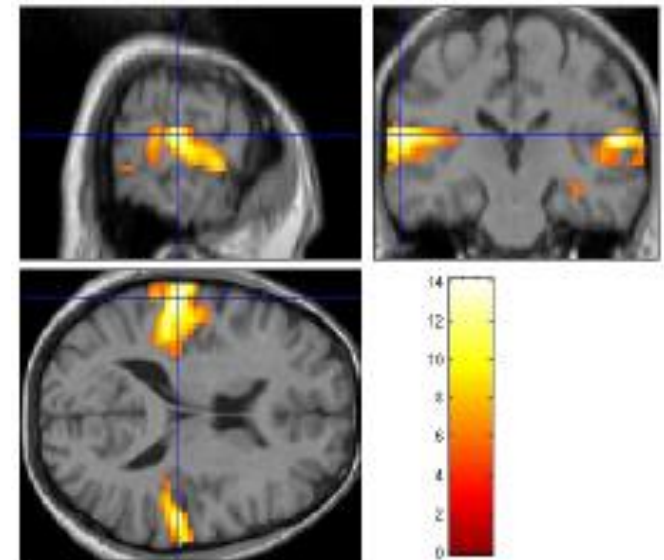
Passive word listening versus rest

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

Q: activation during listening ?

Null hypothesis:  $\beta_1 = 0$

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



SPMresults:

Height threshold  $T = 3.2057$   $\{p < 0.001\}$

voxel-level			mm mm mm		
$T$	( $Z$ )	$p_{\text{uncorrected}}$			
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	42	9
5.44	4.97	0.000	48	27	24
5.32	4.87	0.000	36	-27	42

## T-test: summary

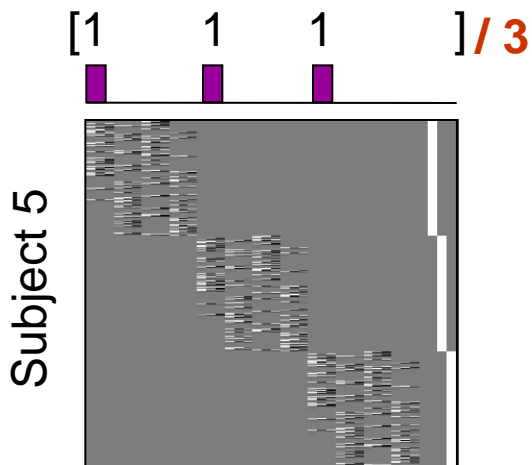
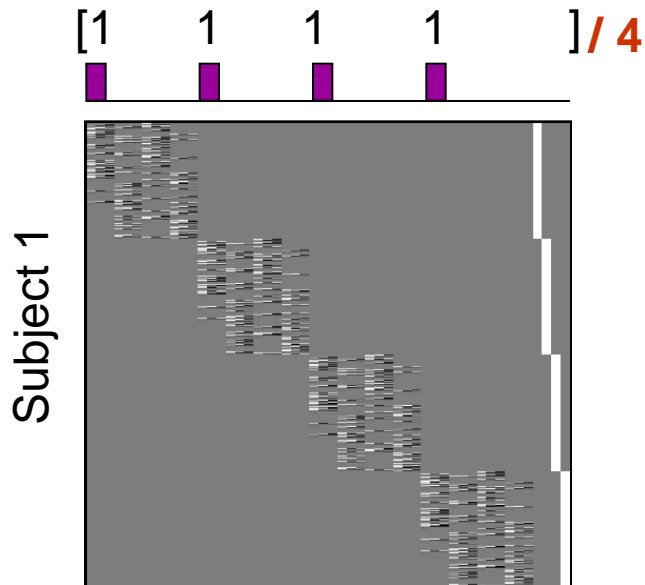
- ❑ T-test is a *signal-to-noise* measure (ratio of estimate to standard deviation of estimate).

- ❑ Alternative hypothesis:

$$H_0: c^T \beta = 0 \quad \text{vs} \quad H_A: c^T \beta > 0$$

- ❑ 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.

# Scaling issue



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

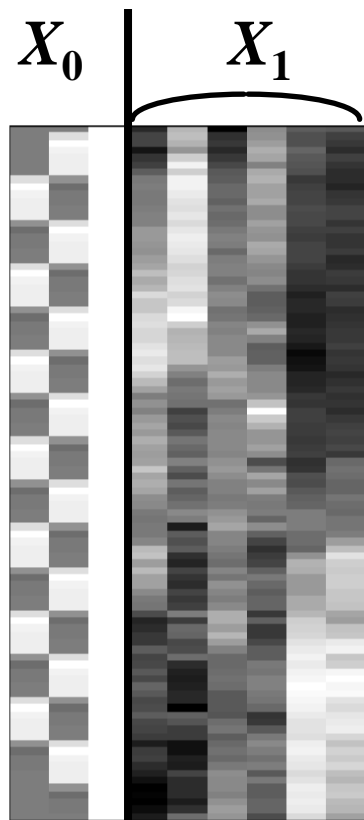
- The  $T$ -statistic does not depend on the scaling of the regressors.
- The  $T$ -statistic does not depend on the scaling of the contrast.
- Contrast  $c^T \hat{\beta}$  depends on scaling.
- Be careful of the interpretation of the contrasts  $c^T \hat{\beta}$  themselves (eg, for a second level analysis):

sum  $\neq$  average

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

□ Model comparison:

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



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



$$\text{RSS}_0 \\ \sum \hat{\varepsilon}_{reduced}^2$$

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

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

$$F \propto \frac{ESS}{RSS} \sim F_{v_1, v_2}$$

$$v_1 = \text{rank}(X) - \text{rank}(X_0) \\ v_2 = N - \text{rank}(X)$$

Full model ?

or Reduced model?

# **F-test** - multidimensional contrasts – $\text{SPM}\{F\}$

❑ Tests multiple linear hypotheses:

$\mathbf{H}_0$ : True model is  $X_0$

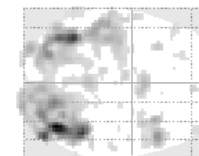
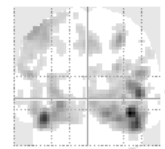
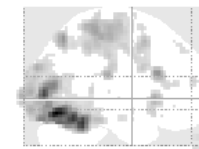
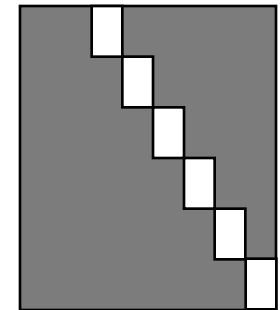
$\mathbf{H}_0$ :  $\beta_4 = \beta_5 = \dots = \beta_9 = 0$

test  $\mathbf{H}_0$ :  $c^T \beta = 0$  ?

$X_0$  |  $X_1$  ( $\beta_{4-9}$ )

$X_0$

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

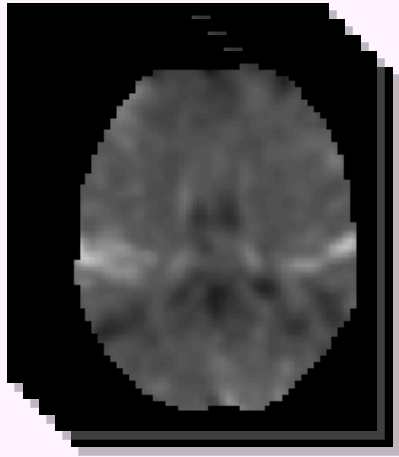


$\text{SPM}\{F_{6,322}\}$

Full model?

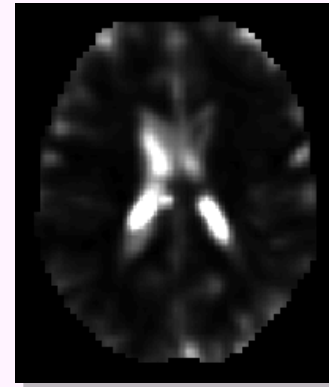
Reduced model?

# F-contrast in SPM



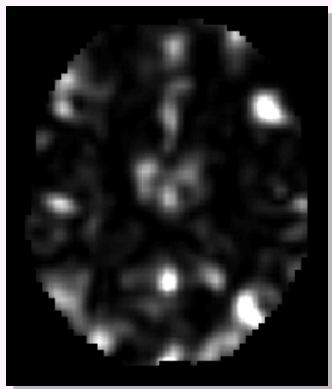
beta\_???? images

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



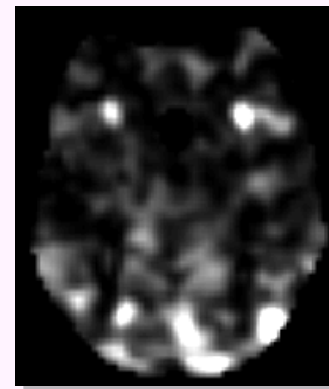
ResMS image

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



ess\_???? images

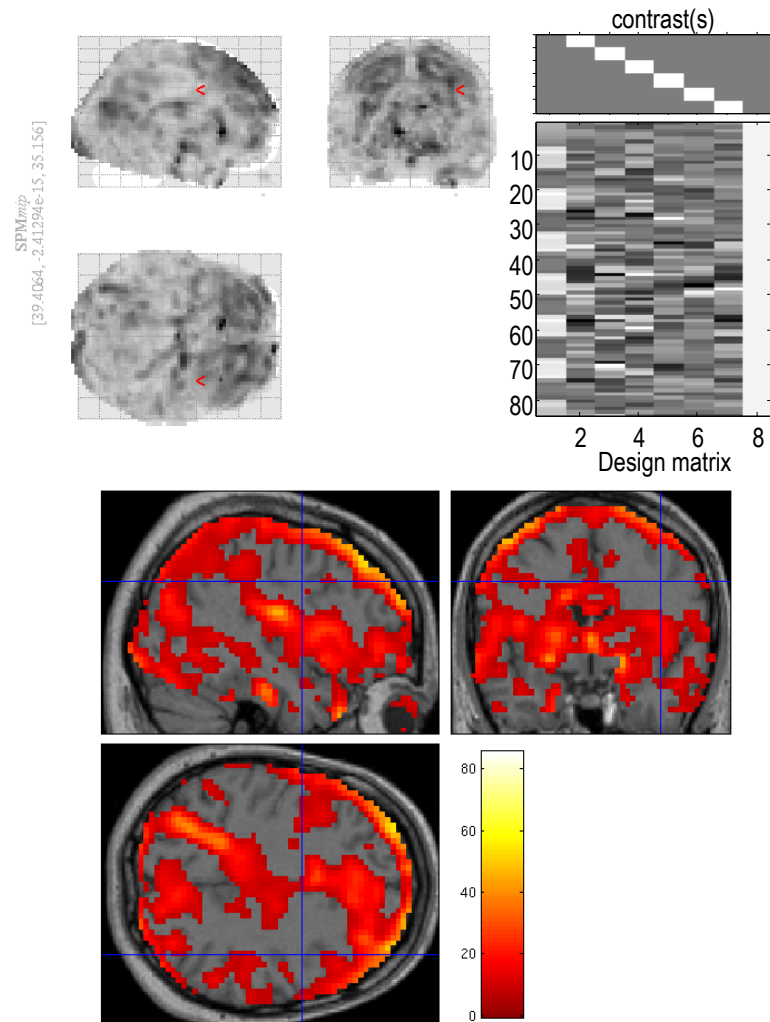
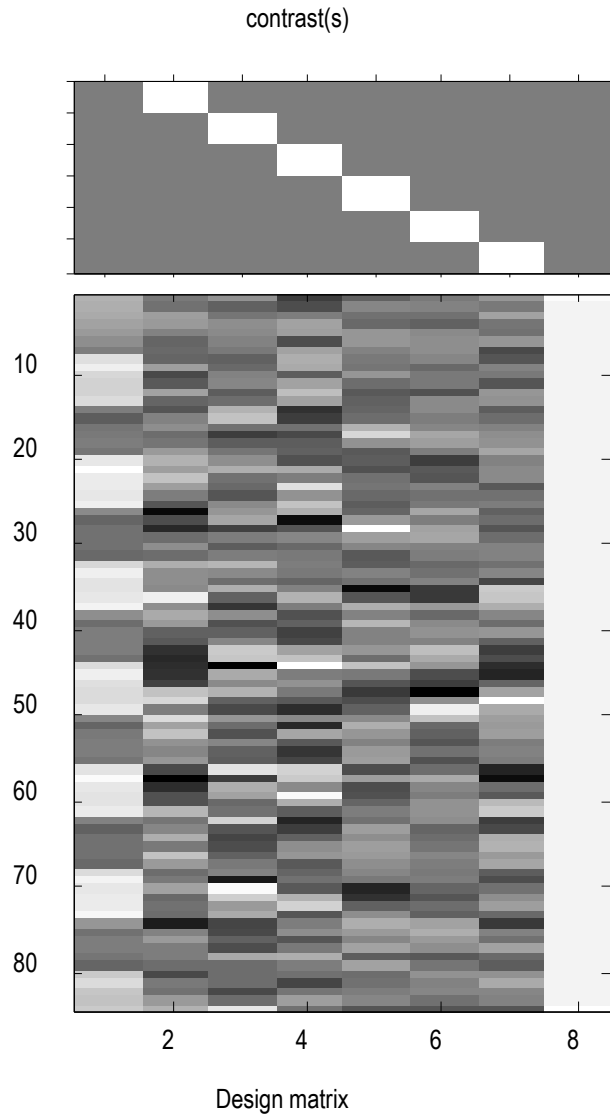
$$(RSS_0 - RSS)$$



spmF\_???? images

$$SPM\{F\}$$

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





## F-test: summary

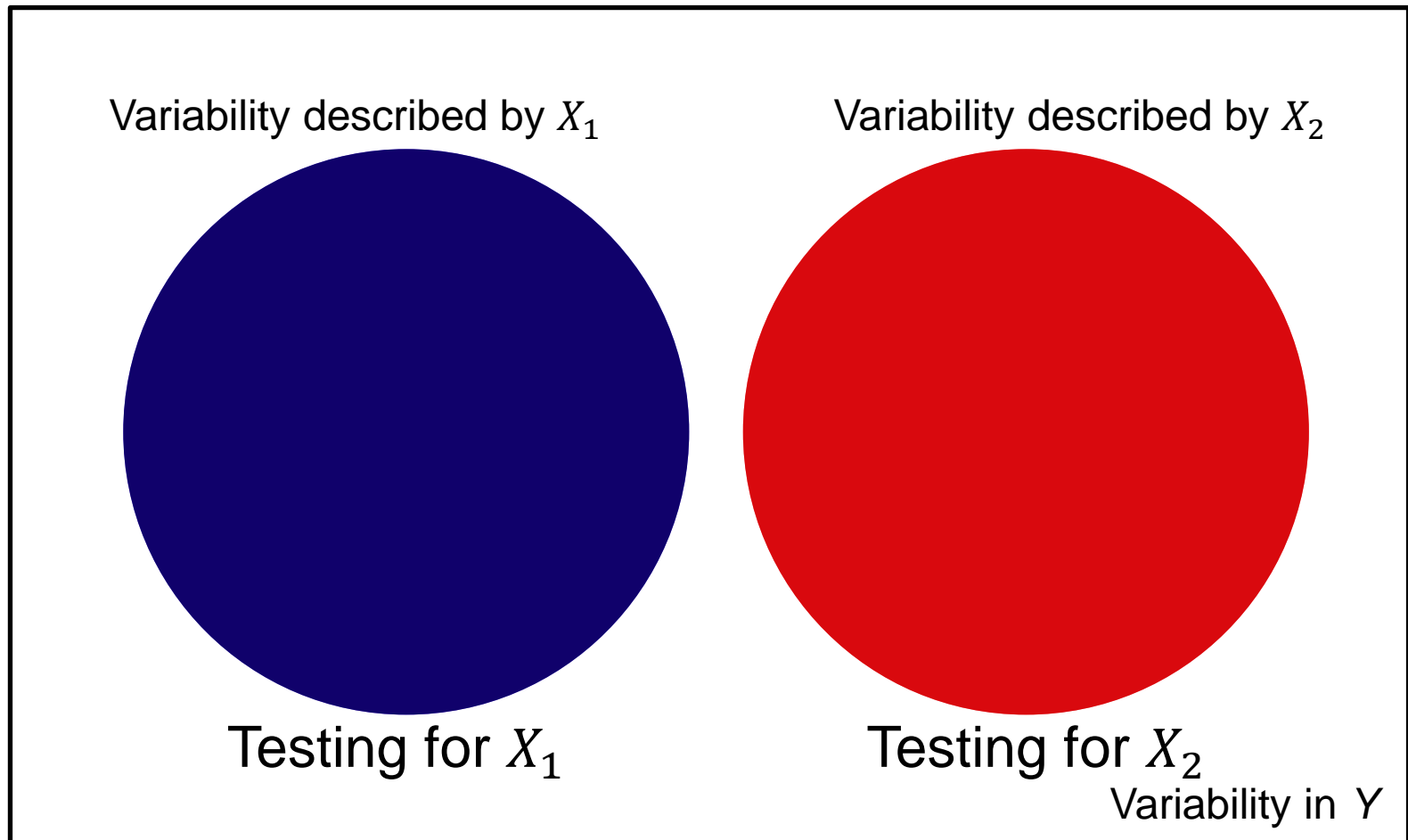
- ❑ F-tests can be viewed as testing for the additional variance explained by a larger model wrt a simpler (***nested***) model  $\Rightarrow$  ***model comparison***.
- ❑ F tests a weighted **sum of squares** of one or several combinations of the regression coefficients  $\beta$ .
- ❑ In practice, we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

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

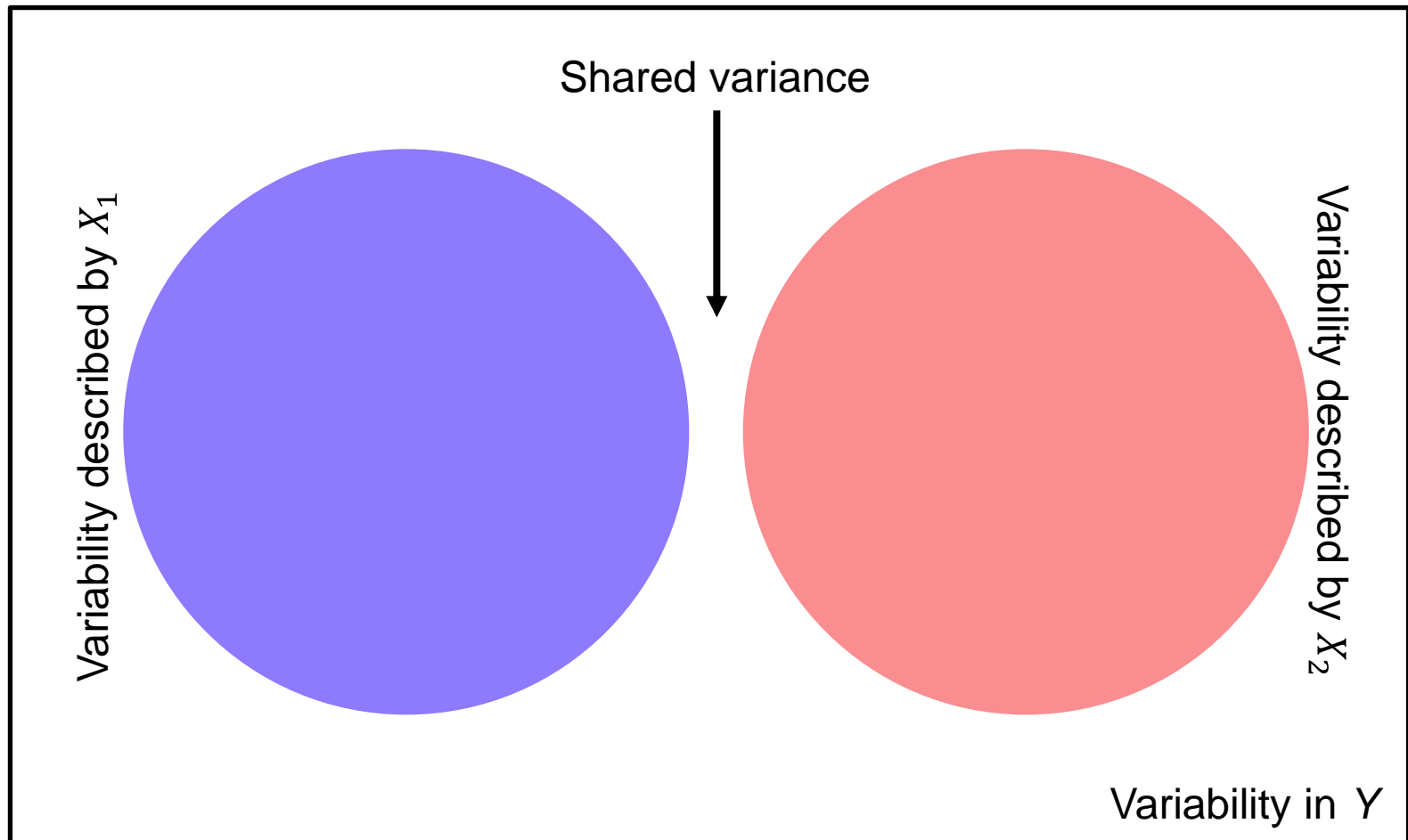
Null Hypothesis  $H_0 : \beta_1 = \beta_2 = \beta_3 = 0$

Alternative Hypothesis  $H_A : \text{at least one } \beta_k \neq 0$
- ❑ 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.

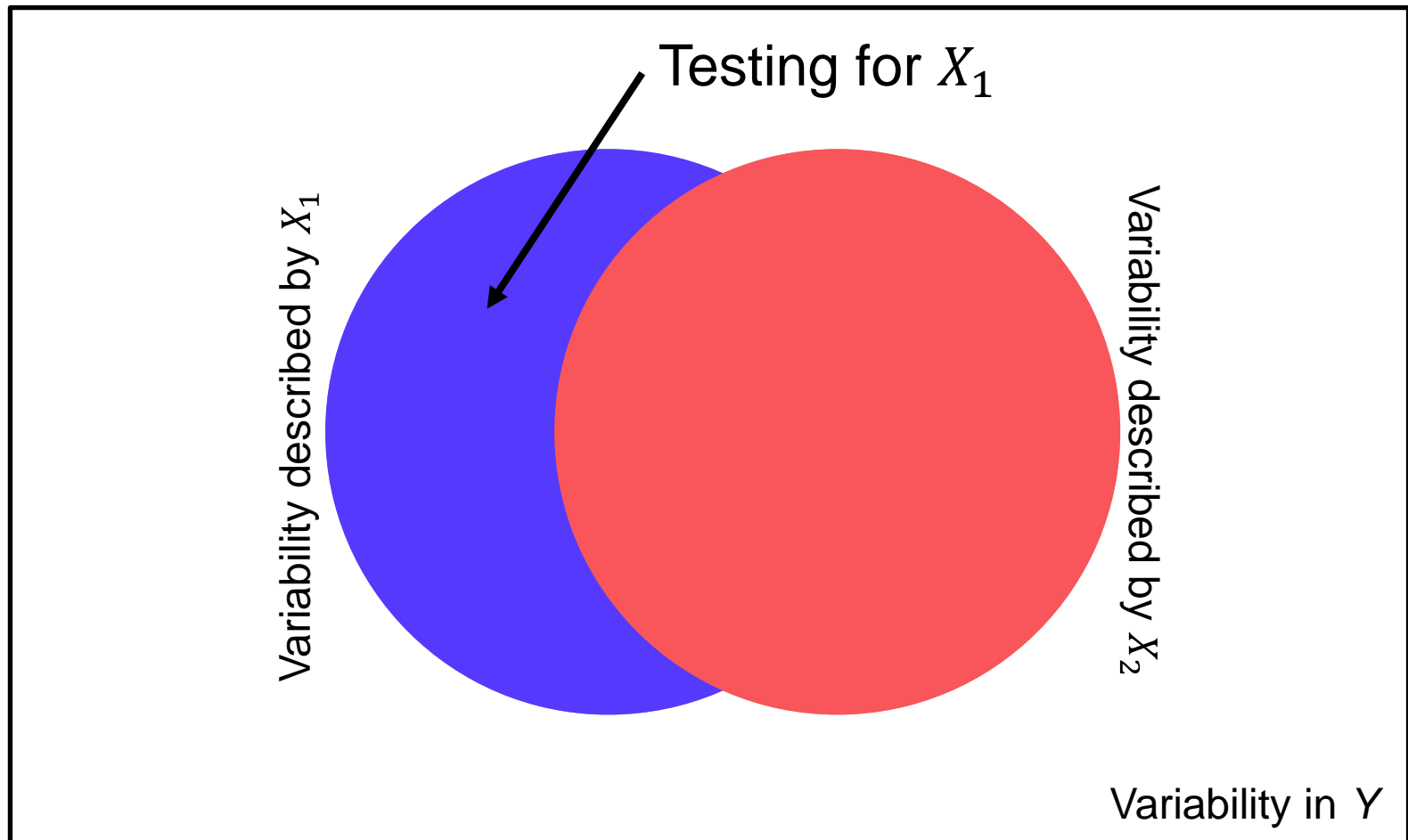
# Orthogonal regressors



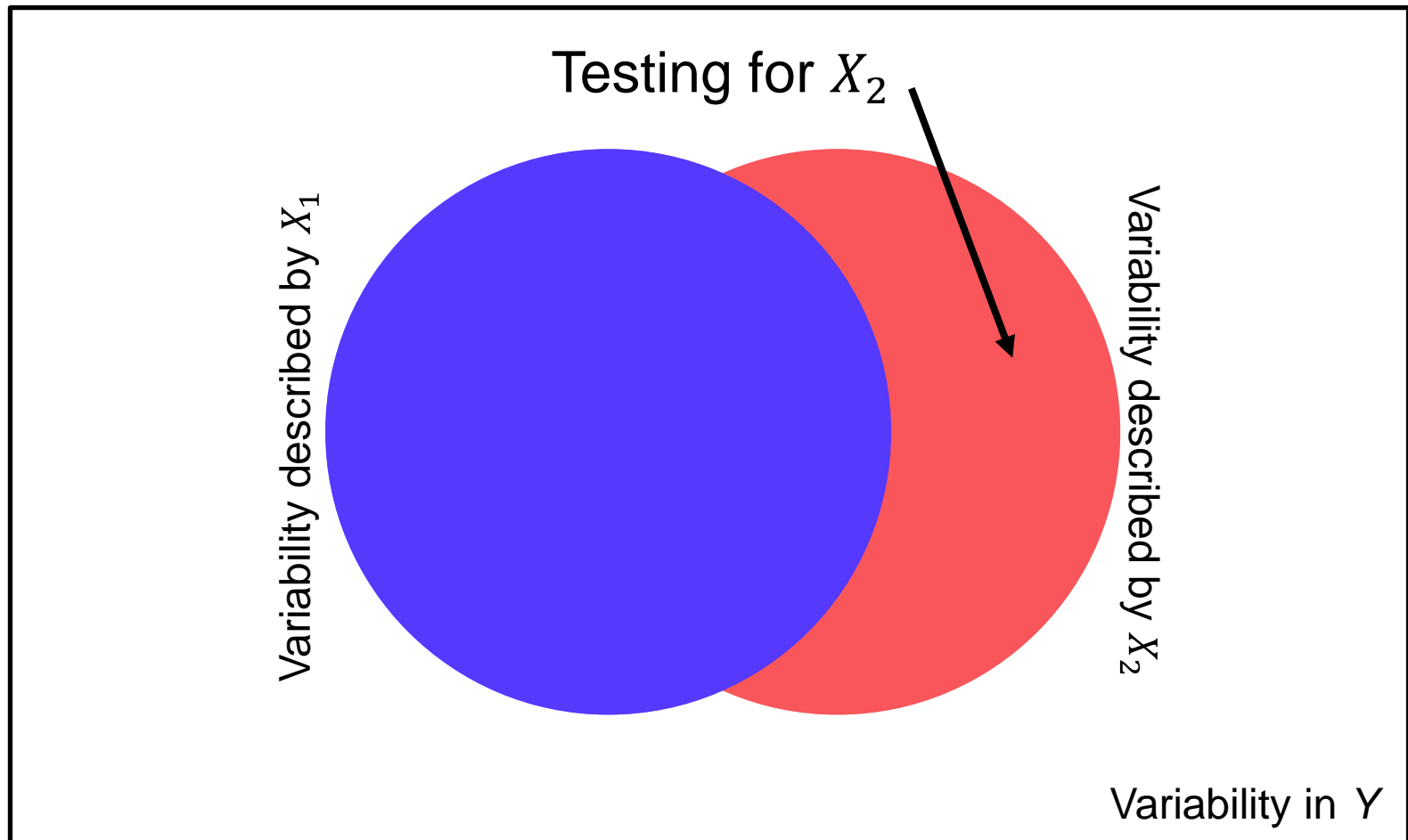
# Correlated regressors



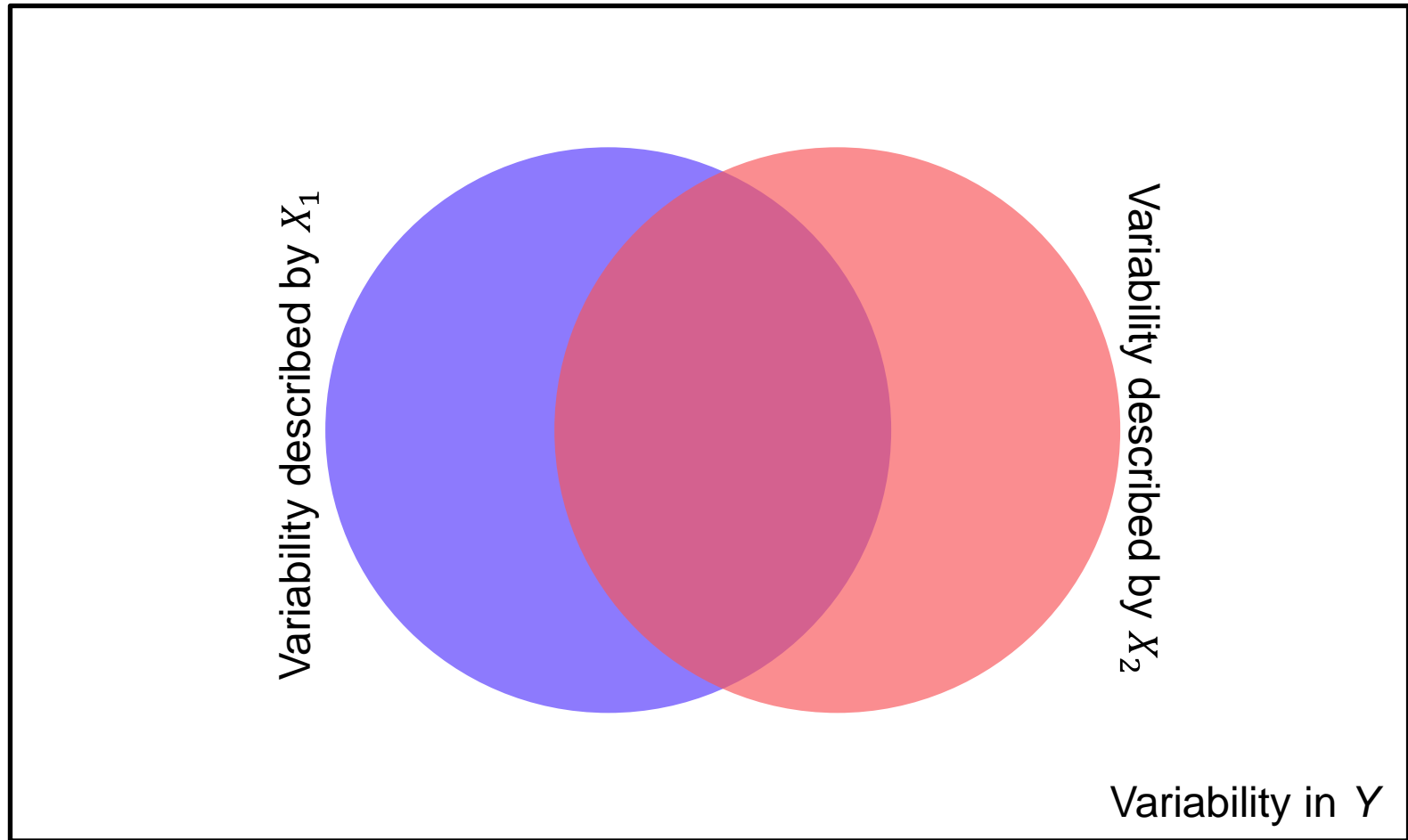
# Correlated regressors



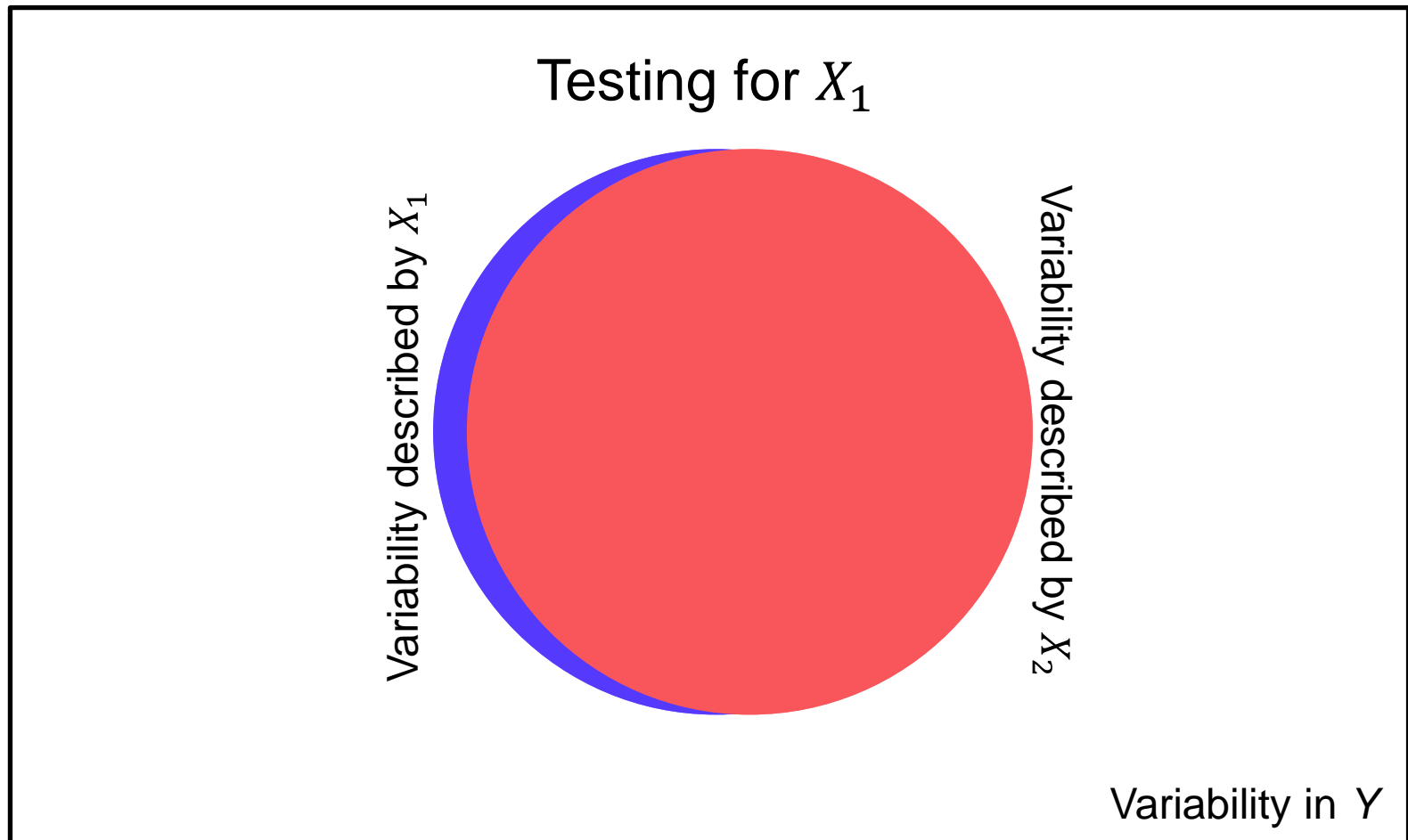
# Correlated regressors



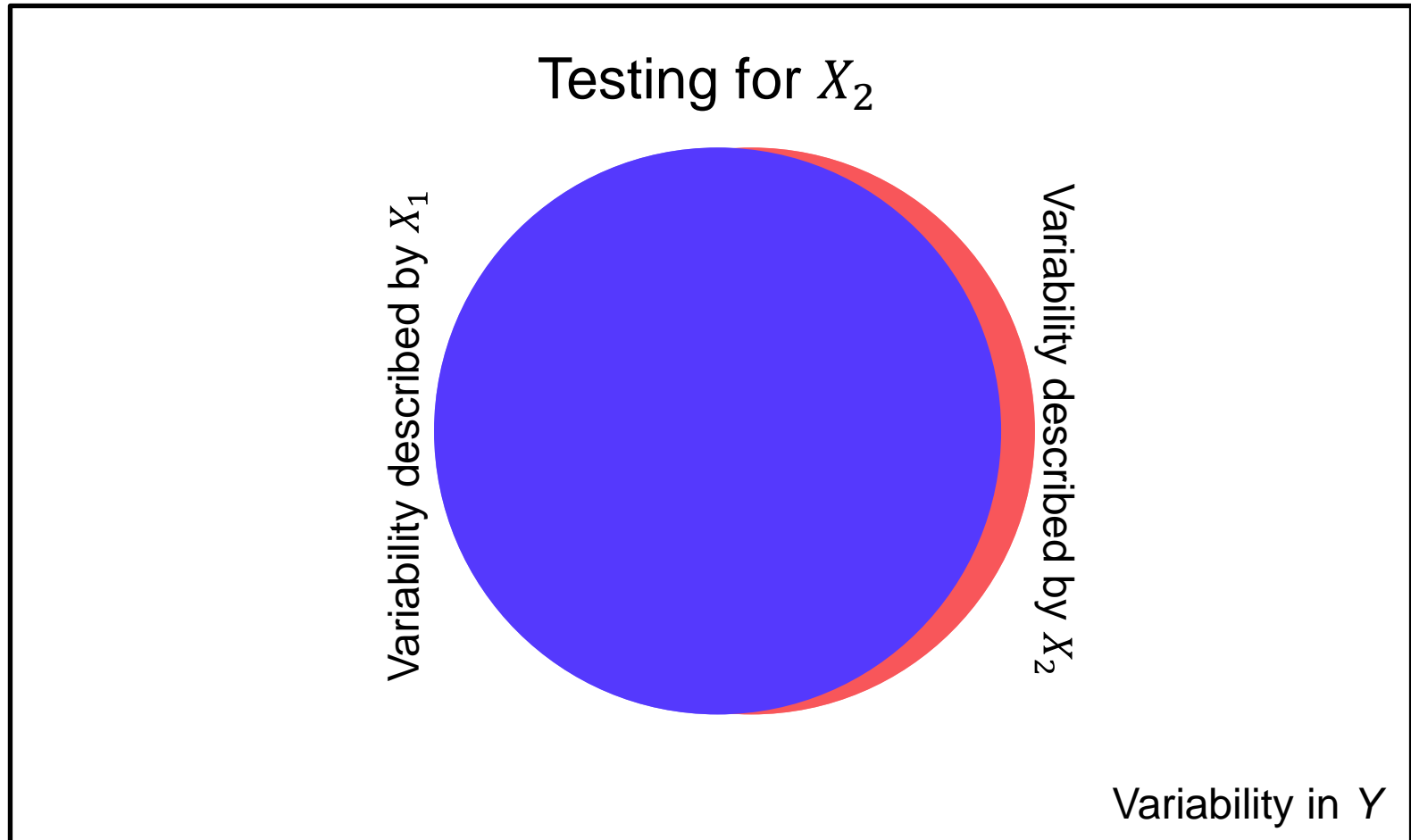
# Correlated regressors



# Correlated regressors

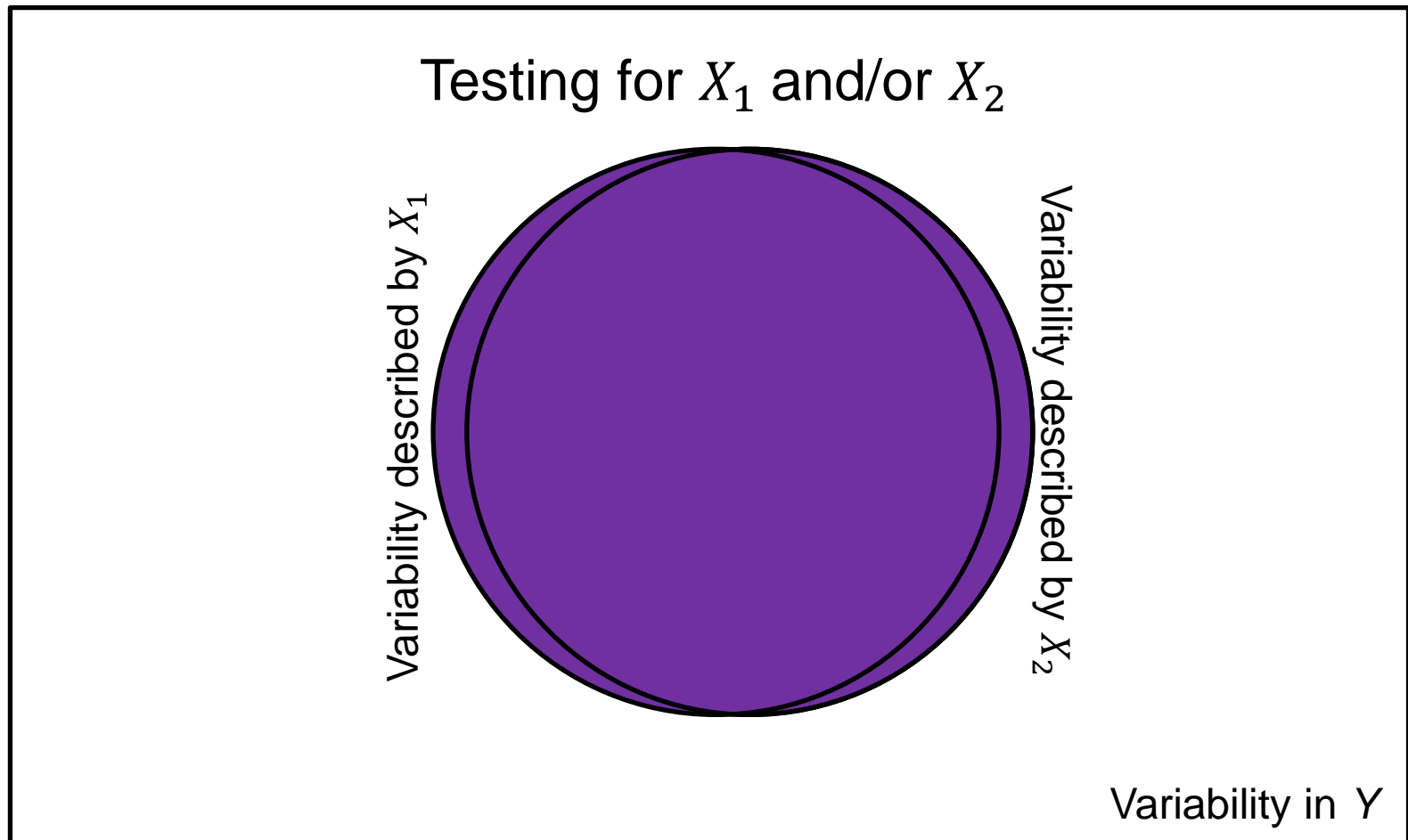


# Correlated regressors

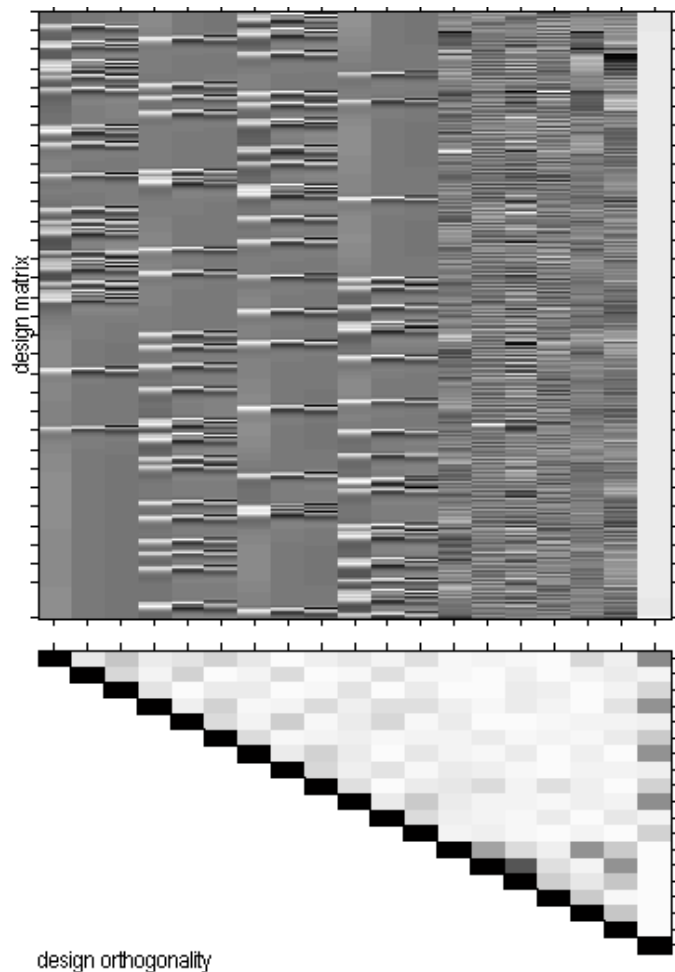




# Correlated regressors



# Design orthogonality



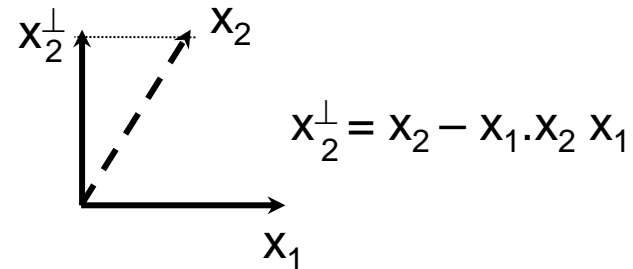
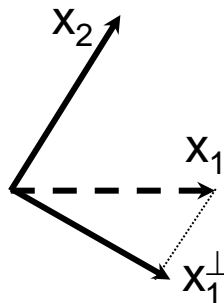
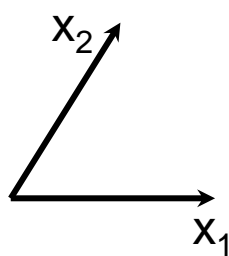
- For each pair of columns of the design matrix, the orthogonality matrix depicts the magnitude of the **cosine of the angle** between them, with the range 0 to 1 mapped from white to black.
- If both vectors have **zero mean** then the cosine of the angle between the vectors is the same as the **correlation** between the two variates.

**Measure** : abs. value of cosine of angle between columns of design matrix  
**Scale** : black - colinear ( $\cos=+1/-1$ )  
 white - orthogonal ( $\cos=0$ )  
 gray - not orthogonal or colinear

## Correlated regressors: summary

- We implicitly test for an **additional** effect only. 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***.



- Orthogonalisation = decorrelation. Parameters and test on the non modified regressor change.

Rarely solves the problem as it requires assumptions about which regressor to uniquely attribute the common variance.

- ⇒ change regressors (i.e. design) instead, e.g. factorial designs.
- ⇒ use F-tests to assess overall significance.

- 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

# Bibliography:

- ❑ *Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Elsevier, 2007.
- ❑ *Plane Answers to Complex Questions: The Theory of Linear Models*. R. Christensen, Springer, 1996.
- ❑ *Statistical parametric maps in functional imaging: a general linear approach*. K.J. Friston et al, Human Brain Mapping, 1995.
- ❑ *Ambiguous results in functional neuroimaging data analysis due to covariate correlation*. A. Andrade et al., NeuroImage, 1999.
- ❑ Estimating efficiency a priori: a comparison of blocked and randomized designs. A. Mechelli et al., NeuroImage, 2003.

