NeuroImaging Data Processing

aka. Statistical Parametric Mapping short course

Course 3:

General Linear Model, p.1

LIÈGE université
GIGA
CRC Human Imaging

Christophe Phillips

fnrs LA LIBERTÉ DE CHERCHER

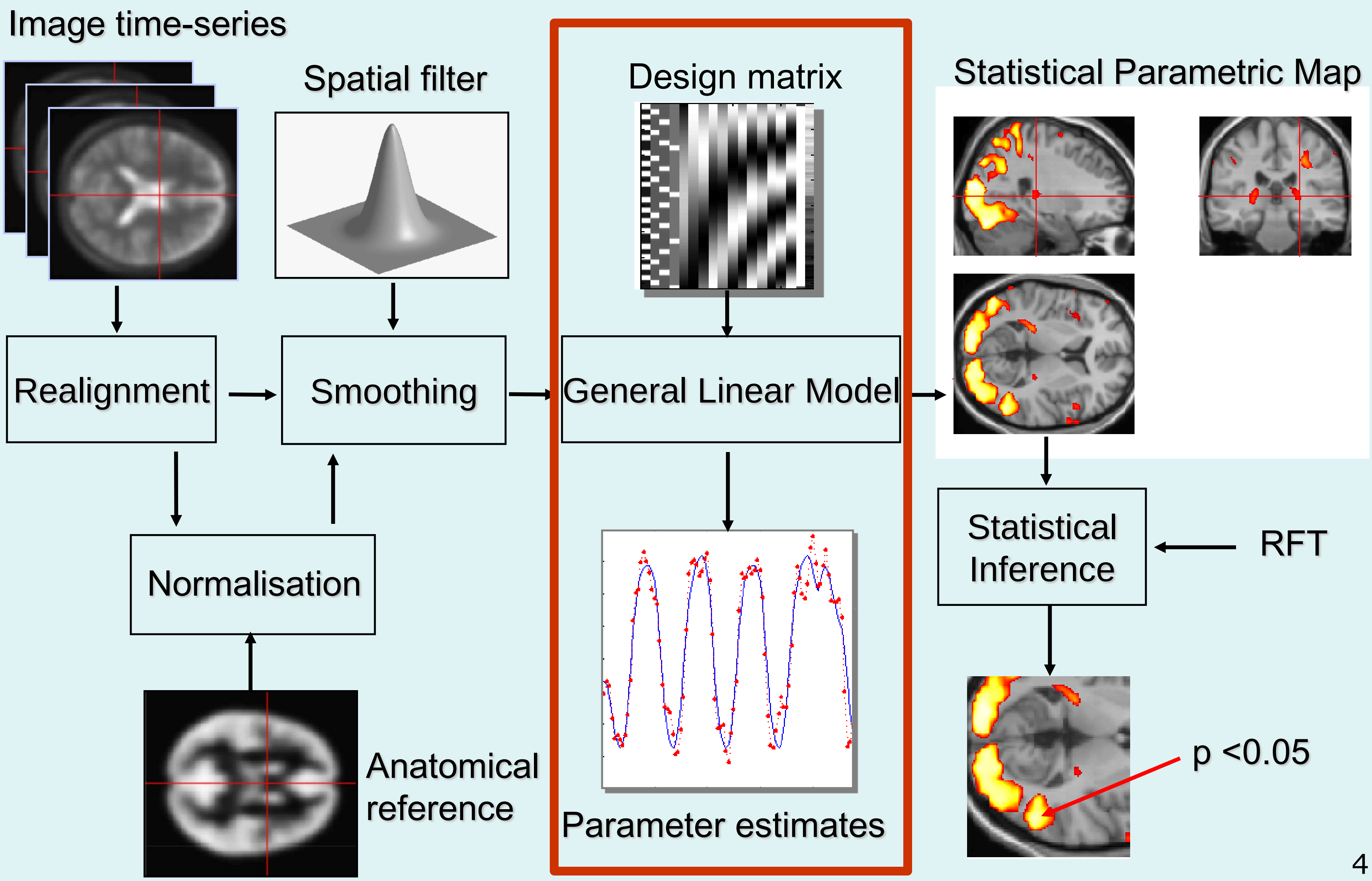
Content

- **Introduction**
- **General Linear Model**
- **Parameter estimation**
- **Improved model**
- **Conclusion**

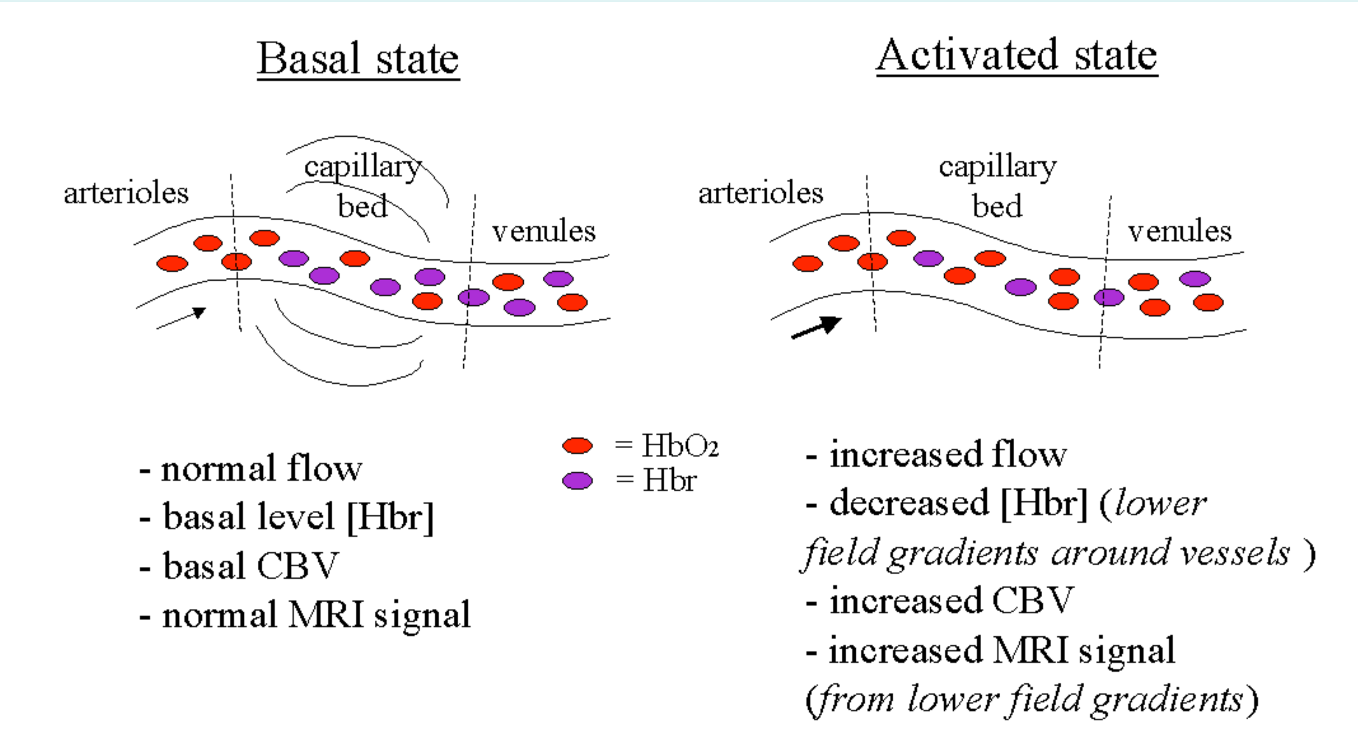
Content

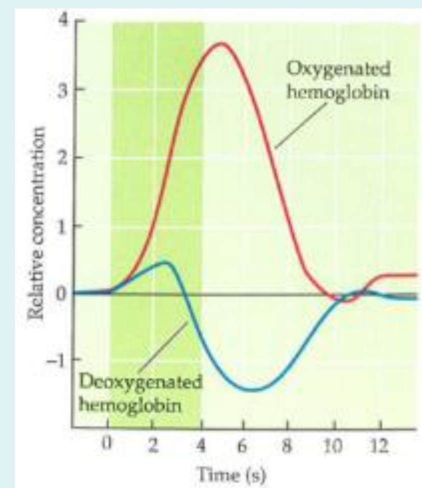
- **Introduction**
- **General Linear Model**
- **Parameter estimation**
- **Improved model**
- **Conclusion**

SPM work flow



fMRI & BOLD signal

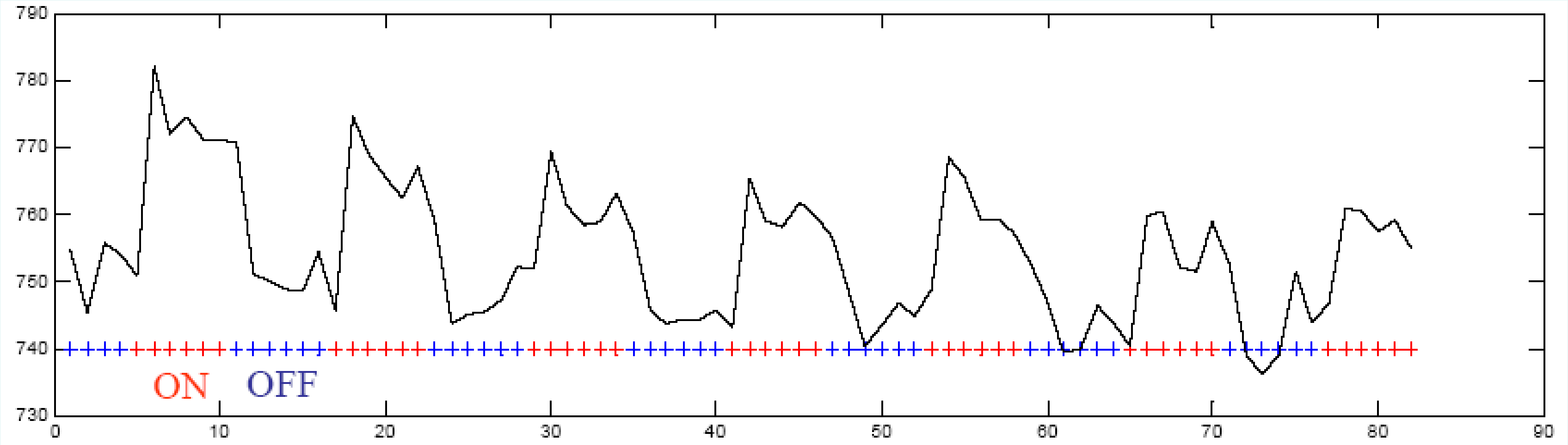




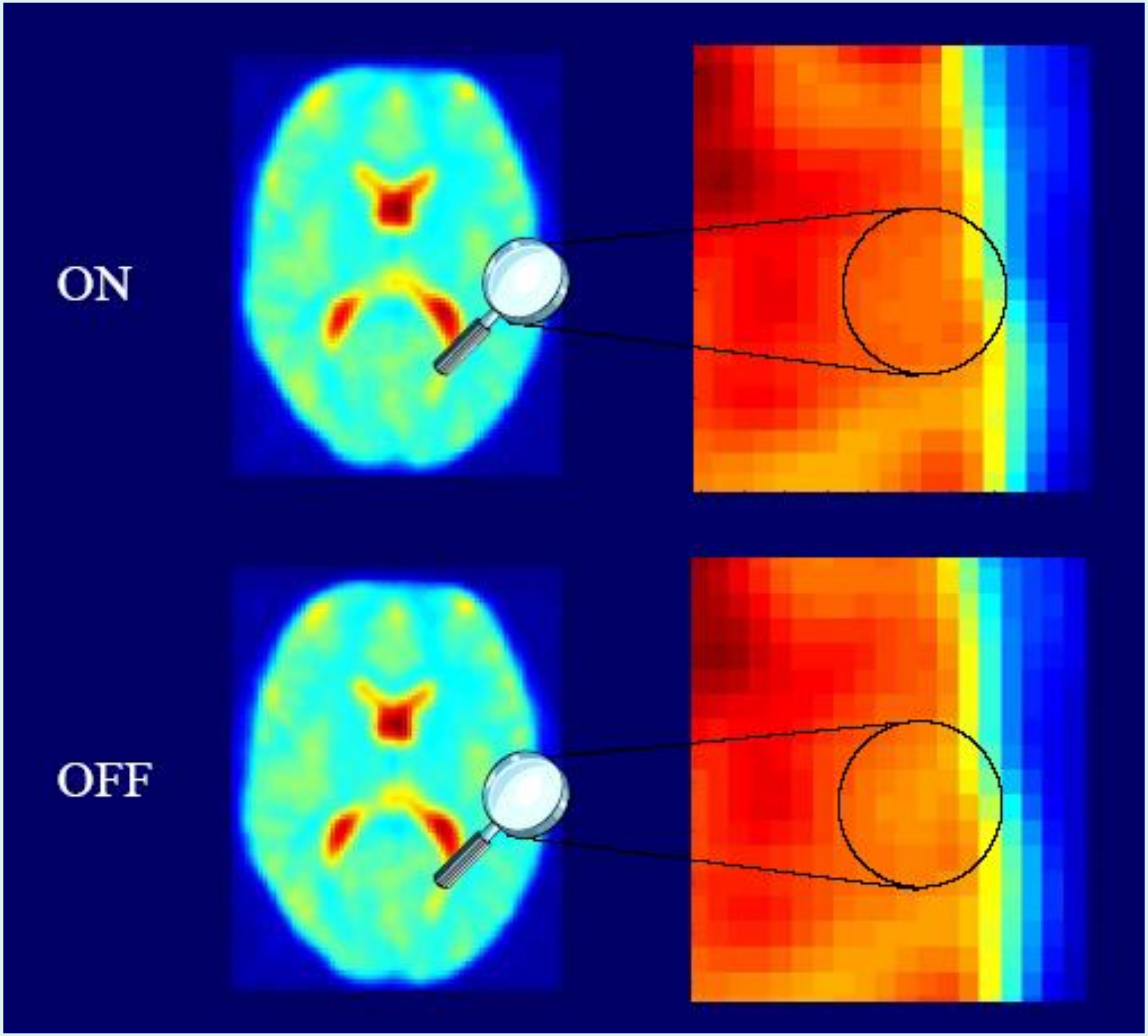
A simple fMRI experiment

Stimuli: passive word listening versus rest

BOLD response in the primary auditory cortex

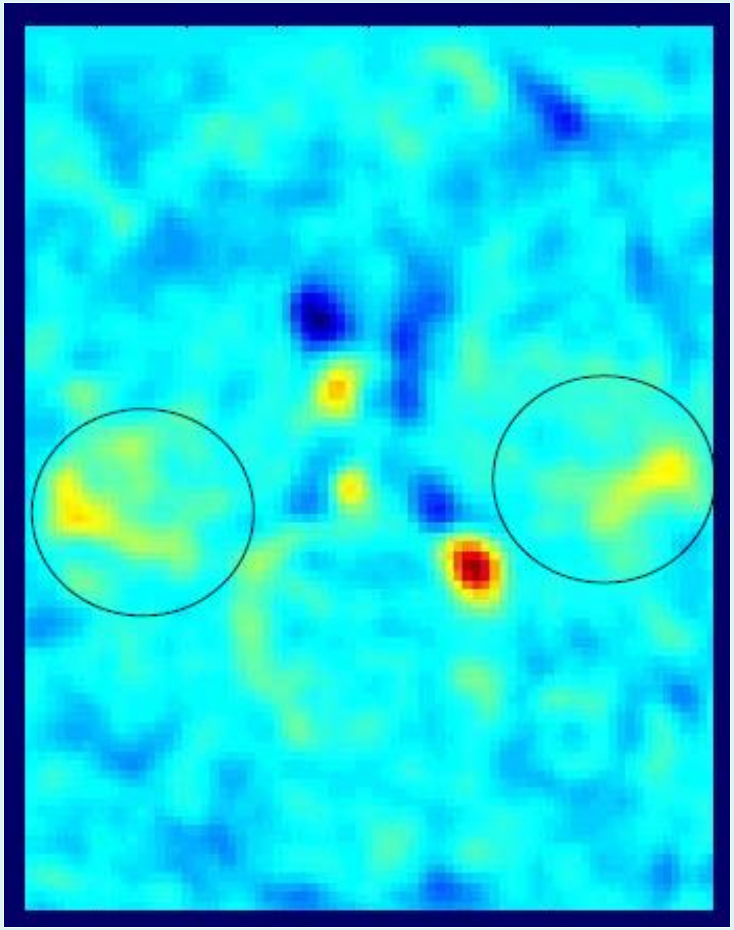


Looking at 2 scans



Looking at 2 scans

ON-OFF, just one scan per condition



Simple *f*MRI example dataset

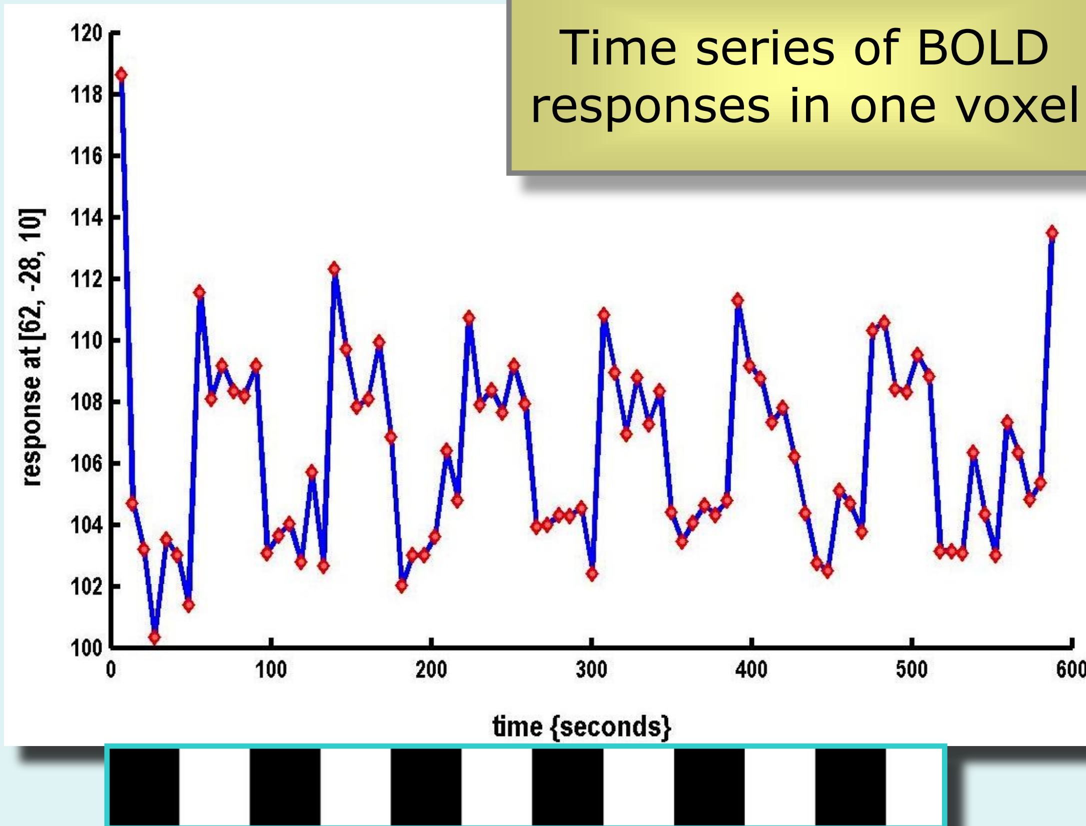
One session, one subject

Passive word listening versus rest

7 cycles of rest and listening

Each epoch 6 scans with 7 sec TR

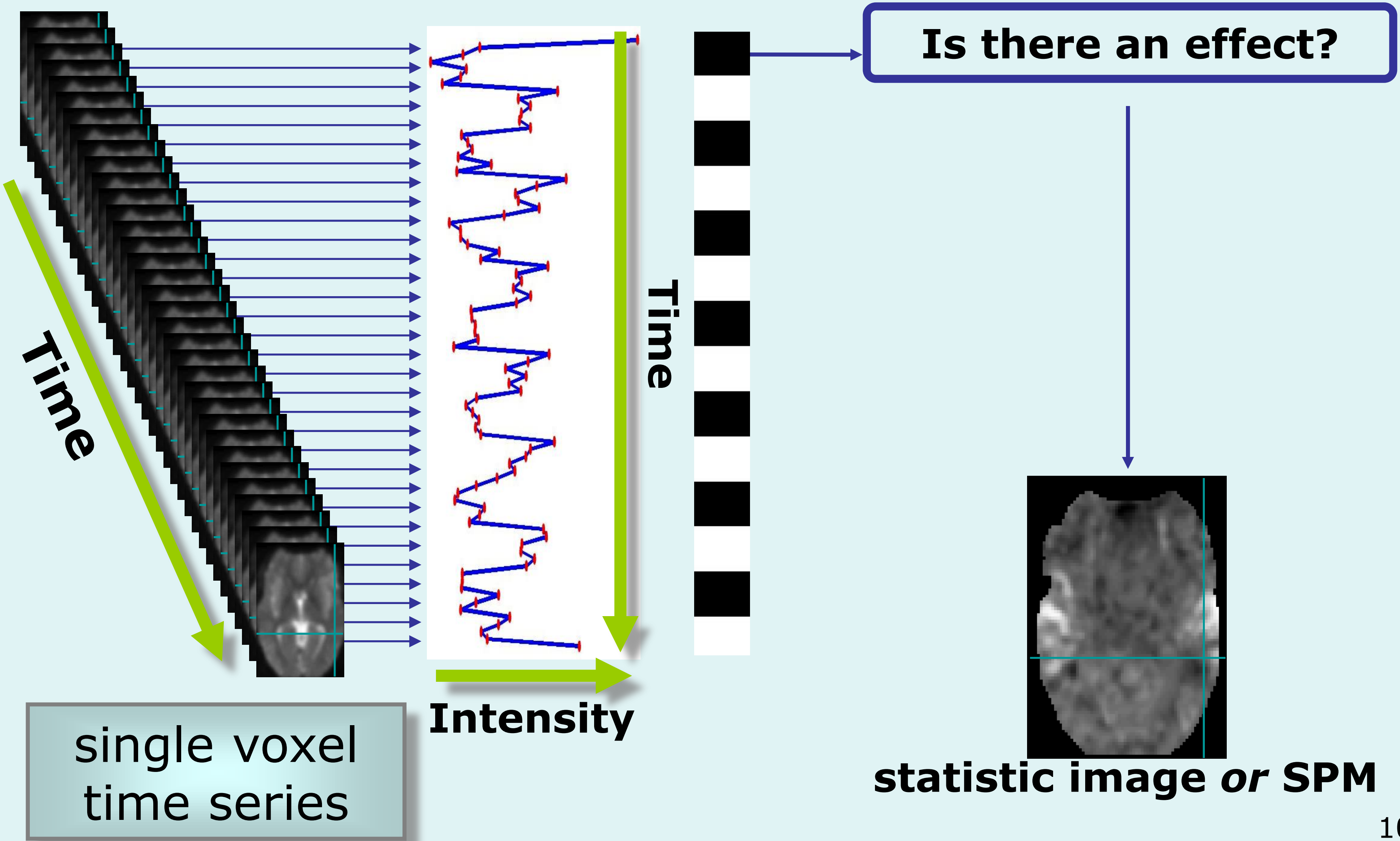
Time series of BOLD responses in one voxel



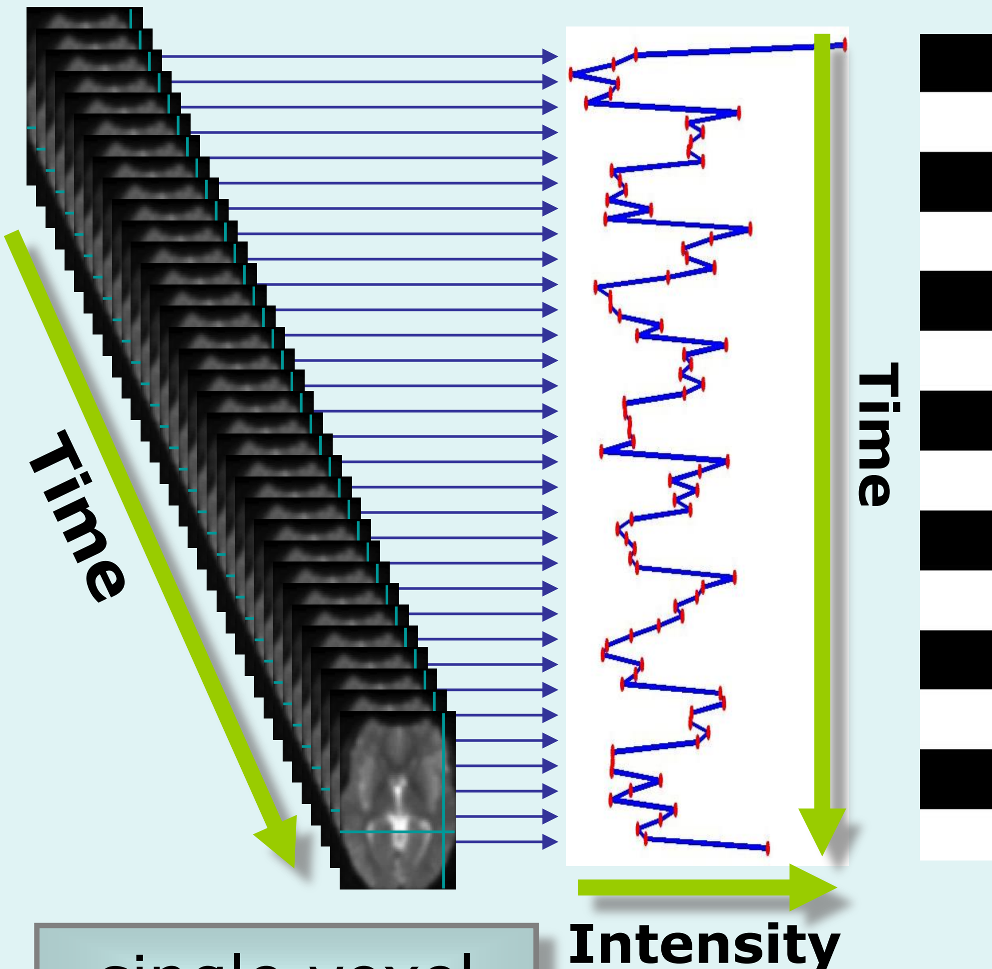
Stimulus function

Question: Is there a change in the BOLD response between listening and rest?

Voxel by voxel statistics

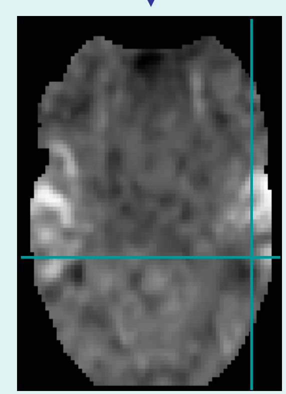


Voxel by voxel statistics



single voxel
time series

- **model specification**
- **parameter estimation**
- **hypothesis test**
- **statistic**



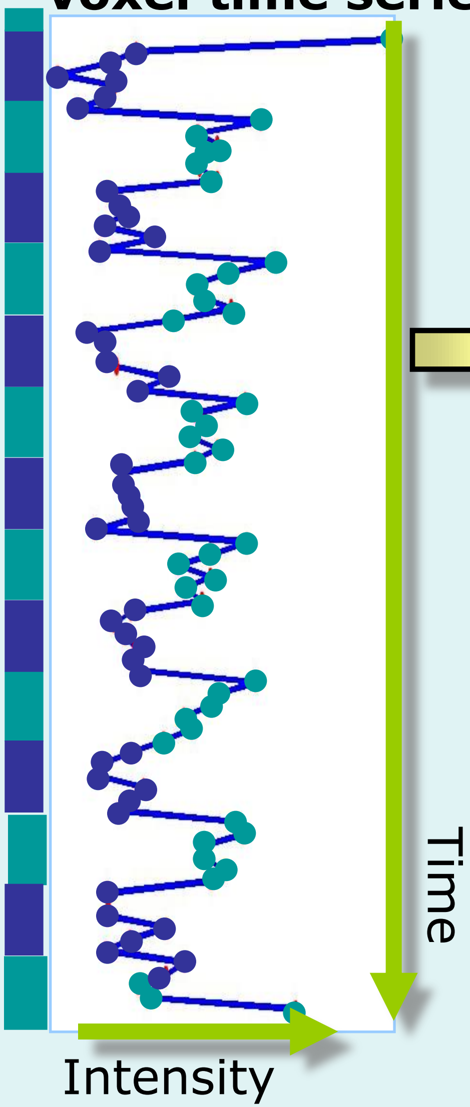
statistic image *or* SPM

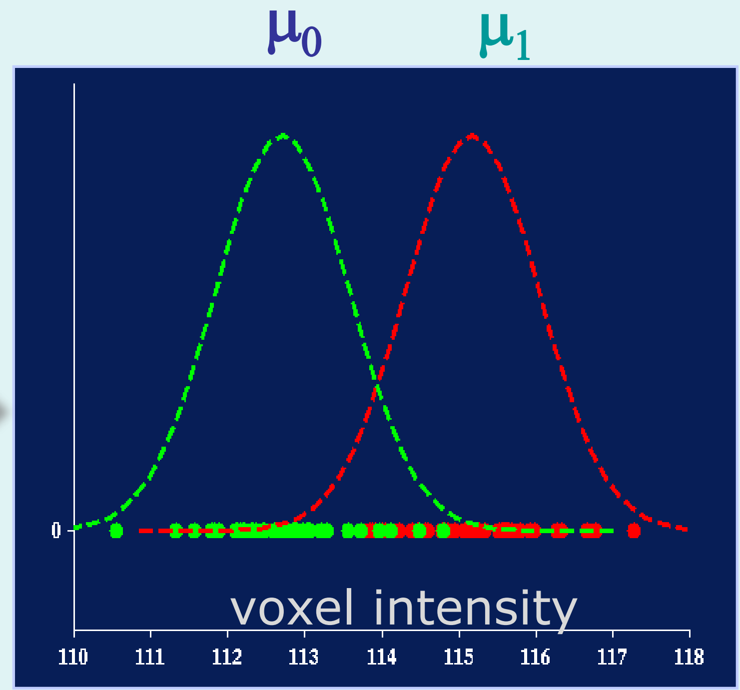
Content

- **Introduction**
- **General Linear Model**
- **Parameter estimation**
- **Improved model**
- **Conclusion**

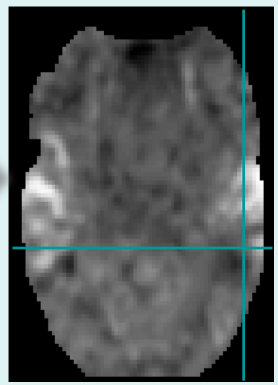
Single voxel, two-sample t-test

voxel time series





$$t = \frac{\mu_1 - \mu_0}{\sqrt{\sigma^2\left({}^1/_{n_1} + {}^1/_{n_0}\right)}}$$

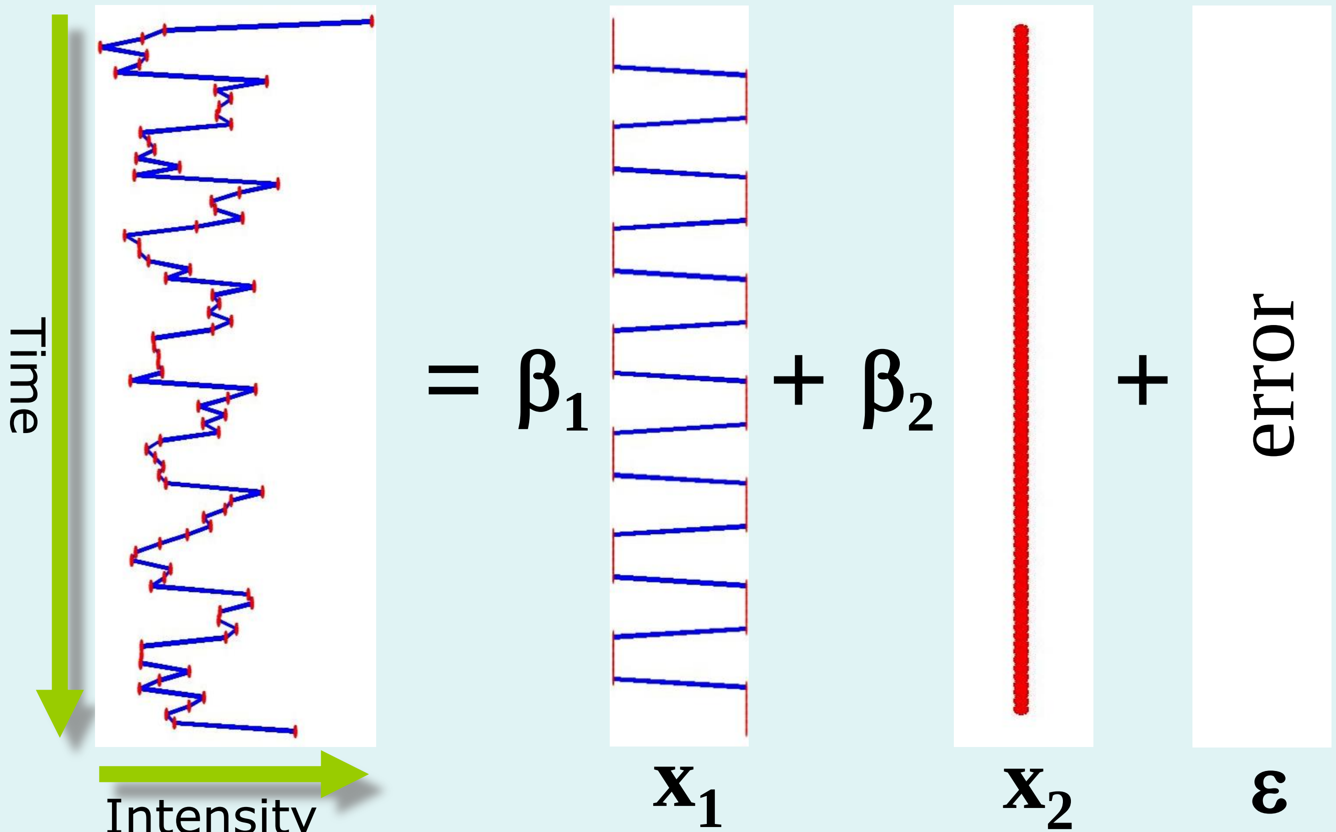


***t*-statistic image**
SPM{*t*}

compares size of effect to its error standard deviation

Question: Is there a change in the BOLD response between listening and rest?

Single voxel, regression model



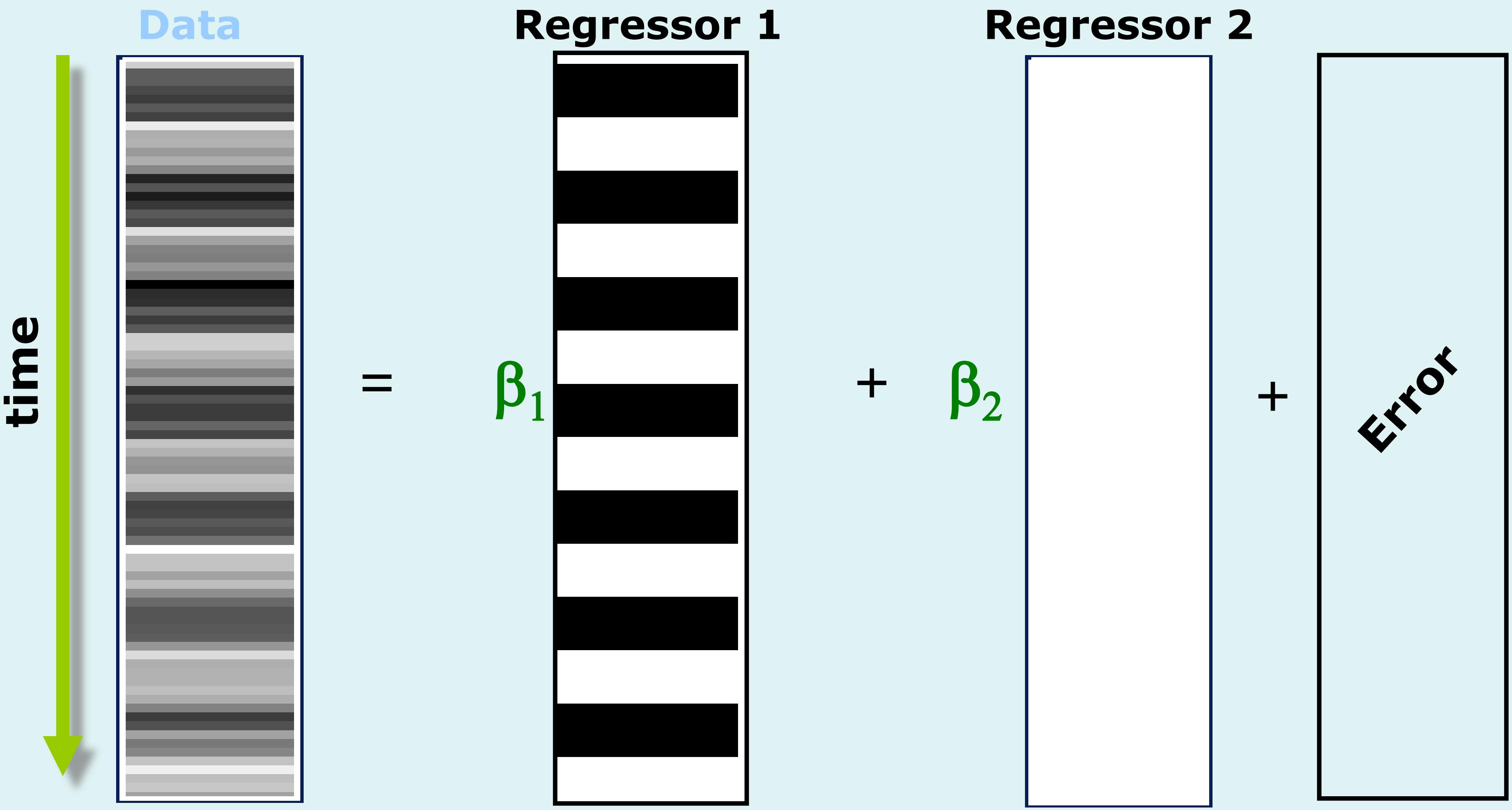
$$\varepsilon \sim N(0, \sigma^2 I)$$

(error is normal and independently and identically distributed)

Question: Is there a change in the BOLD response between listening and rest?

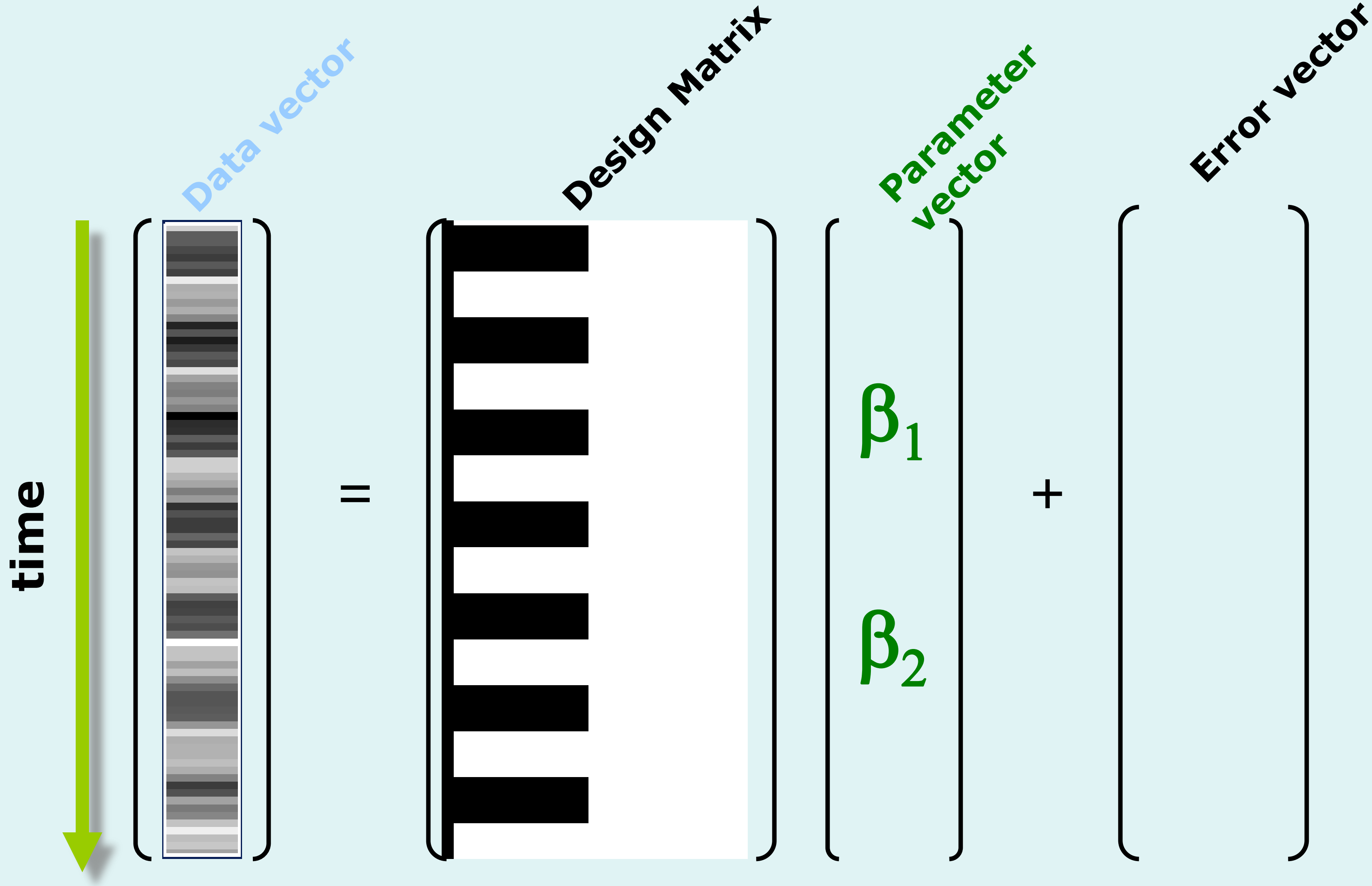
Hypothesis test: $\beta_1 = 0$? (using t-statistic)

Model as basis functions



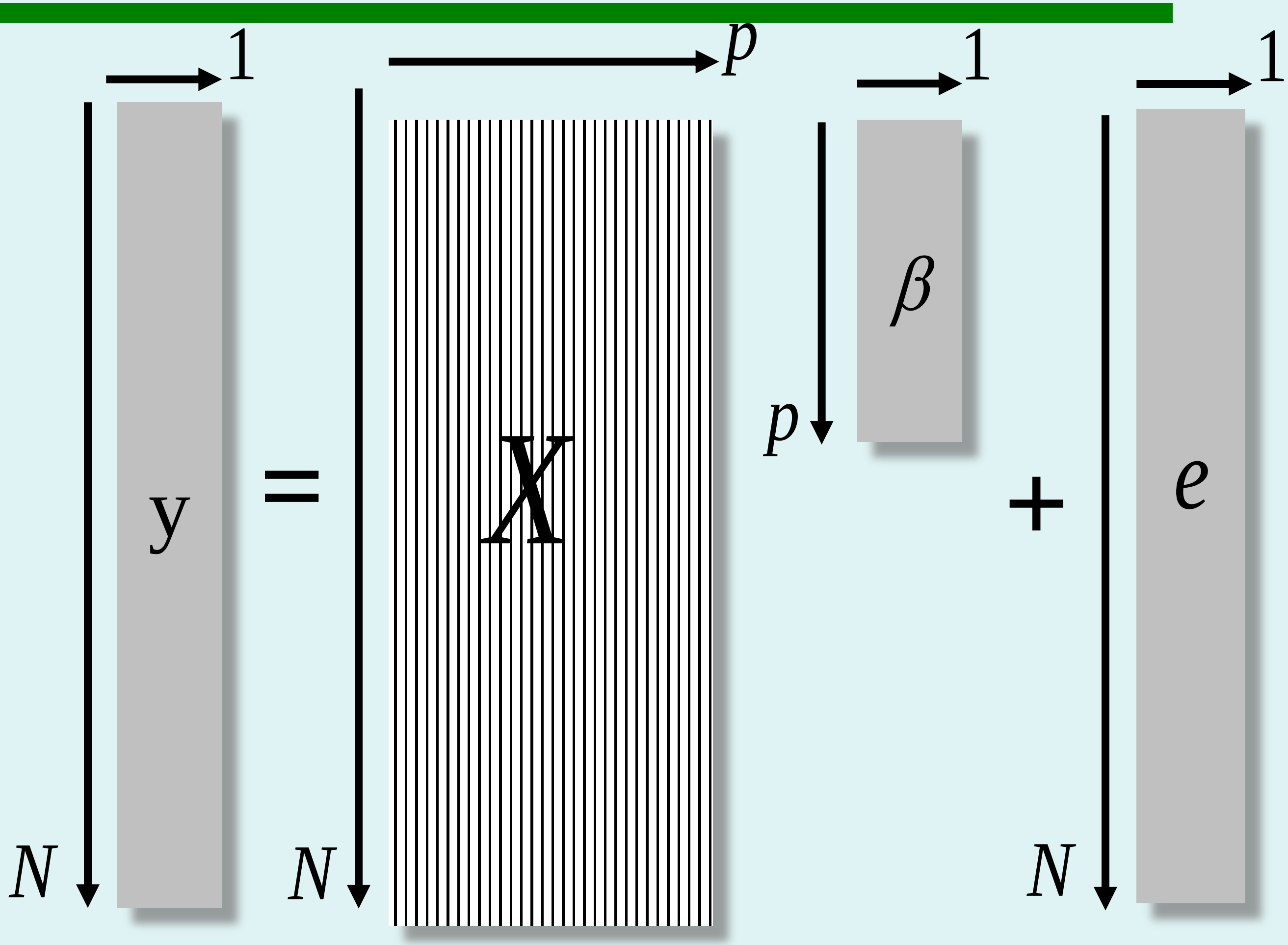
$$y = \beta_1 \cdot X_1 + \beta_2 \cdot X_2 + \varepsilon$$

Design matrix



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

General Linear Model



$$y = X\beta + e$$

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

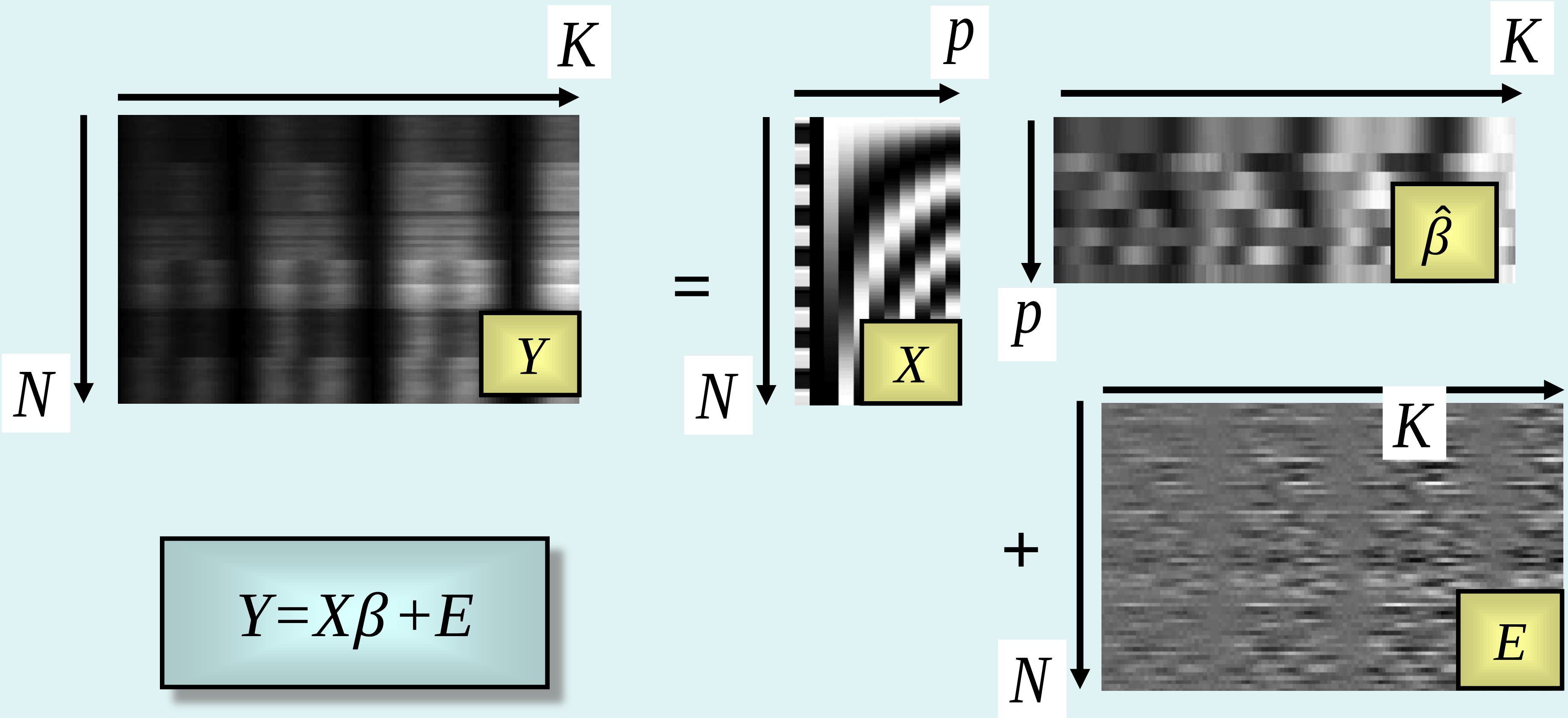
N: number of scans

p: number of regressors

Model is specified by

1. Design matrix **X**
2. Assumptions about **ε**

GLM & Mass univariate approach



$$Y = X\beta + E$$

The design matrix embodies all available knowledge about experimentally controlled factors and potential confounds.

Classical statistics

- parametric
  - one sample *t*-test
  - two sample *t*-test
  - paired *t*-test
  - Anova
  - AnCova
  - correlation
  - linear regression
  - multiple regression
  - *F*-tests
  - etc…

all cases of the

General Linear Model

assume normality

to account for serial correlations:

Generalised Linear Model

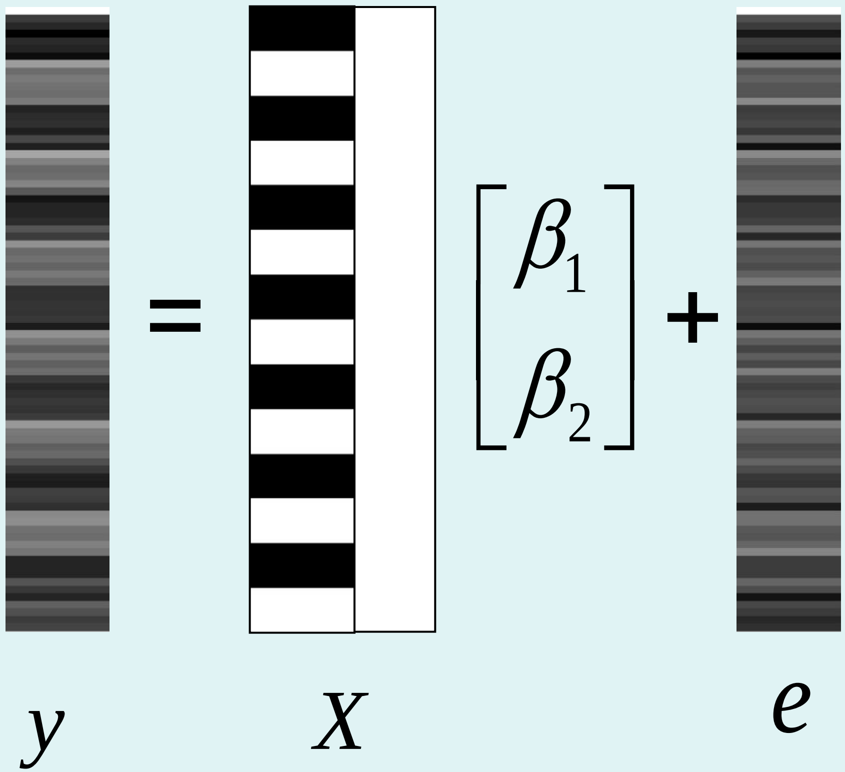
- non-parametric?

$\rightarrow$ **SnPM**

Content

- **Introduction**
- **General Linear Model**
- **Parameter estimation**
- **Improved model**
- **Conclusion**

Parameter estimation



$$\begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix}$$

$$y = X\beta + e$$

Objective: estimate parameters to minimize

$$\sum_{t=1}^{N} e_t^2$$

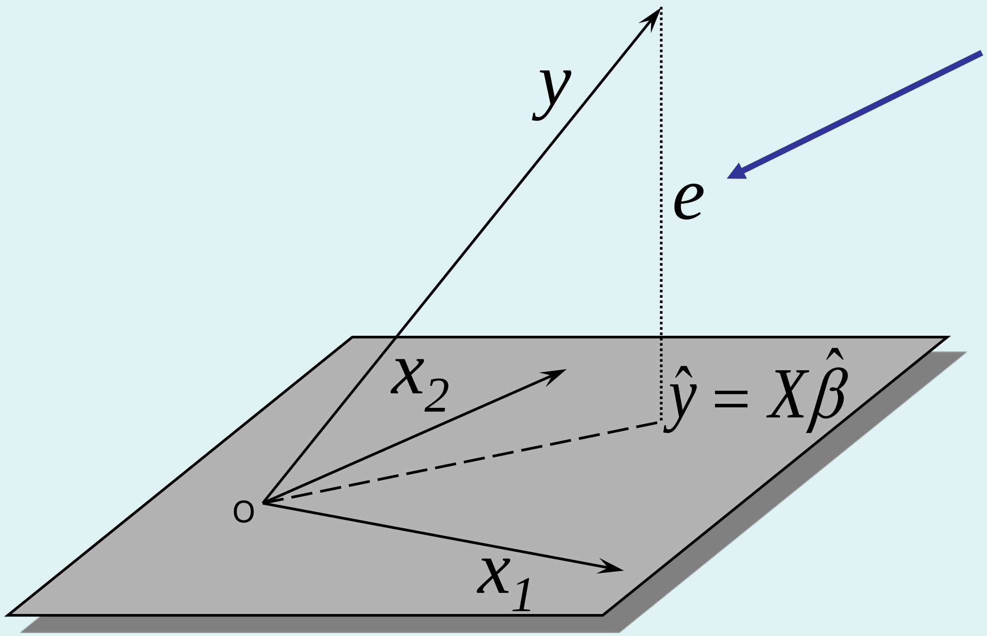
Ordinary least squares estimation (OLS) (assuming i.i.d. error):

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

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

Geometric perspective on the GLM

Ordinary Least Squares (OLS)



Smallest errors (shortest error vector) when e is *orthogonal* to X

$$X^T e = 0$$

$$X^T (y - X\hat{\beta}) = 0$$

$$X^T y = X^T X\hat{\beta}$$

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

Design space defined by X

N data points → N dimension space !

Content

- **Introduction**
- **General Linear Model**
- **Parameter estimation**
- **Improved model**
- **Conclusion**

Problems with fMRI time series

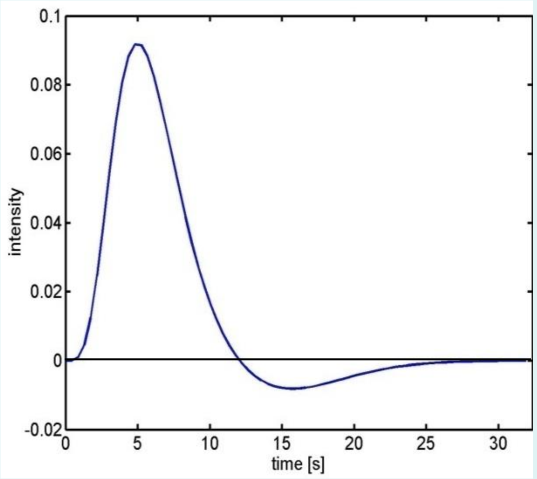
1. The ***BOLD response*** has a delayed and dispersed shape.

2. The BOLD signal includes substantial amounts of ***low-frequency noise*** (e.g. due to scanner drift).

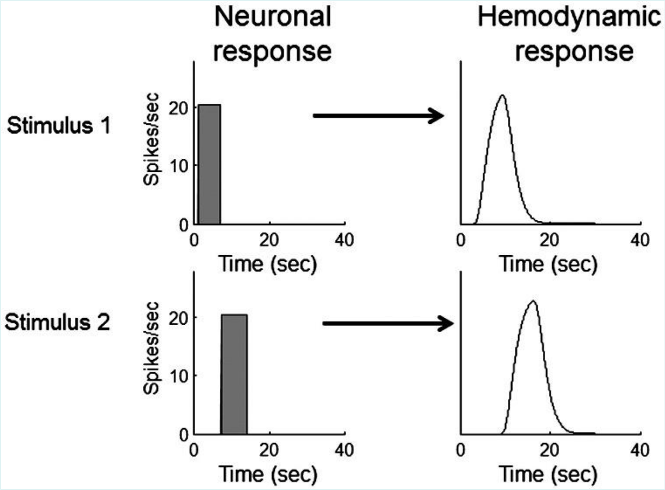
3. Due to breathing, heartbeat & unmodeled neuronal activity, the ***errors are serially correlated***. This violates the assumptions of the noise model in the GLM.

Problem 1: BOLD response

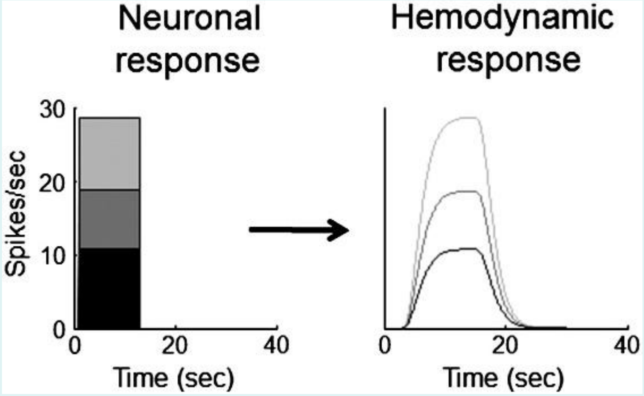
Hemodynamic response function (HRF):



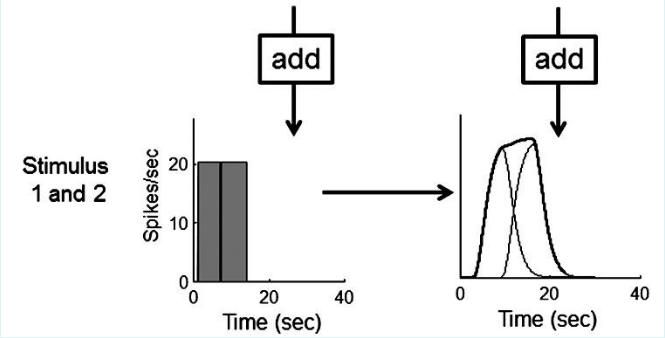
Shift invariance



Scaling



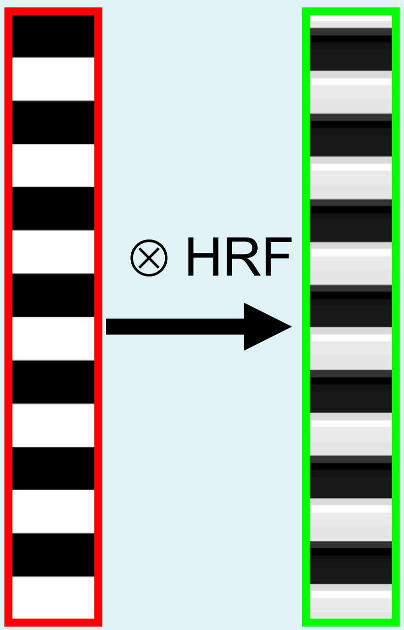
Additivity

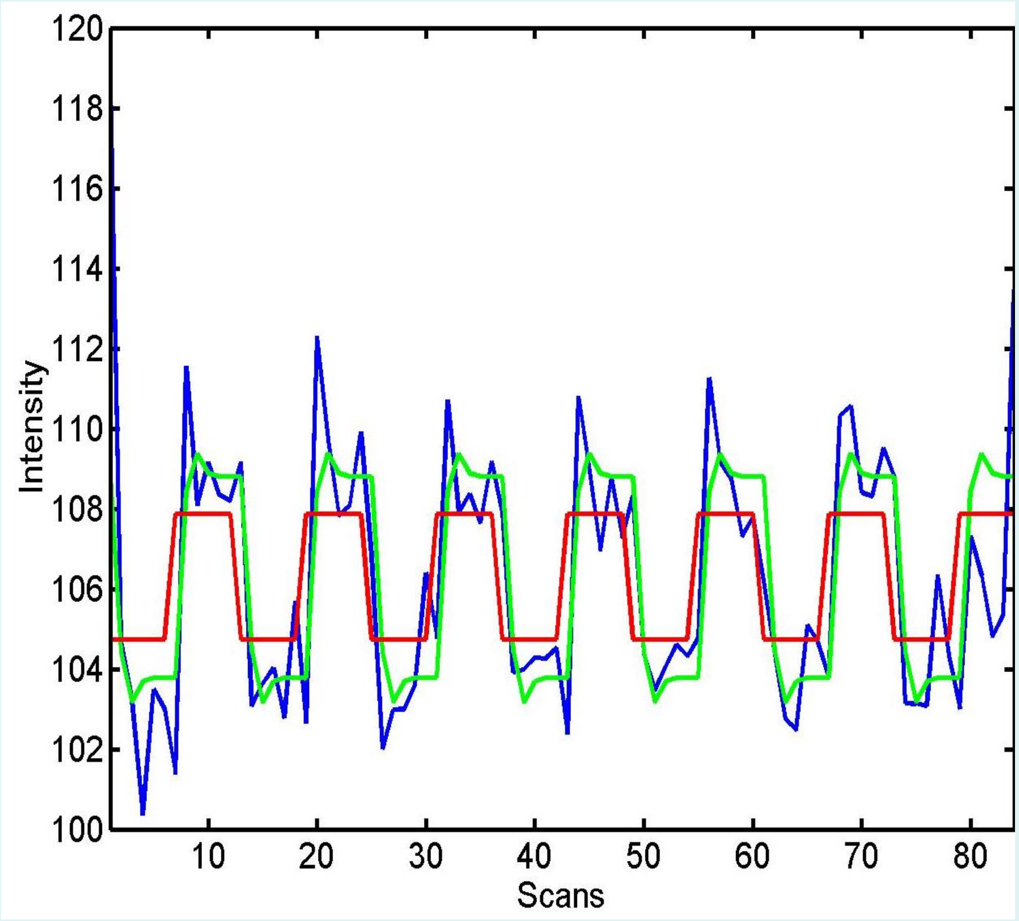


Boynton et al, NeuroImage, 2012.

Solution for the BOLD response

Convolve stimulus function with a canonical hemodynamic response function (HRF):

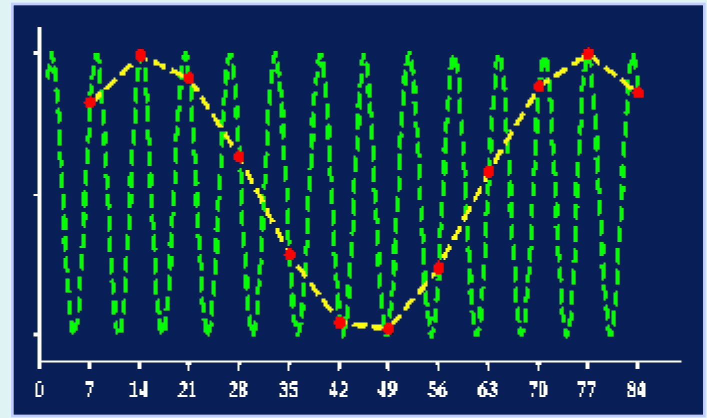


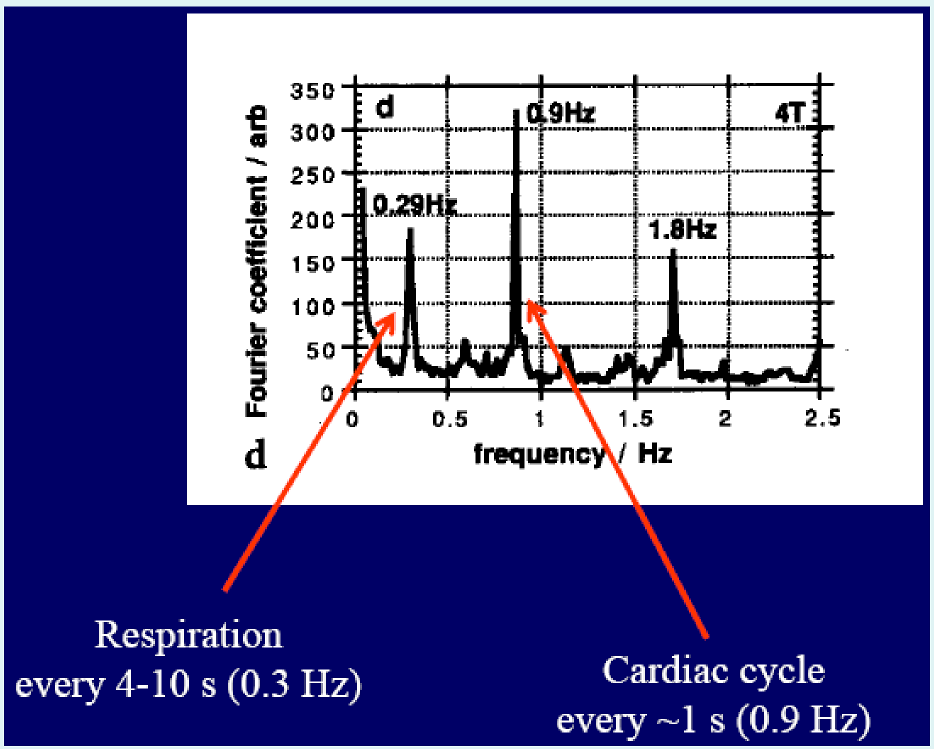


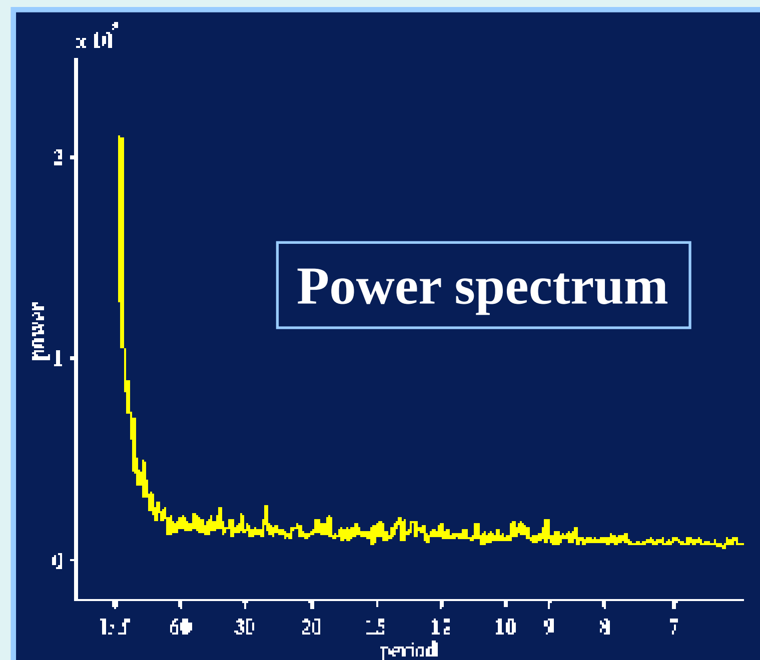
Problem 2: Low frequency noise

- Physiological noise + scanner drift
- Aliased high frequency effects

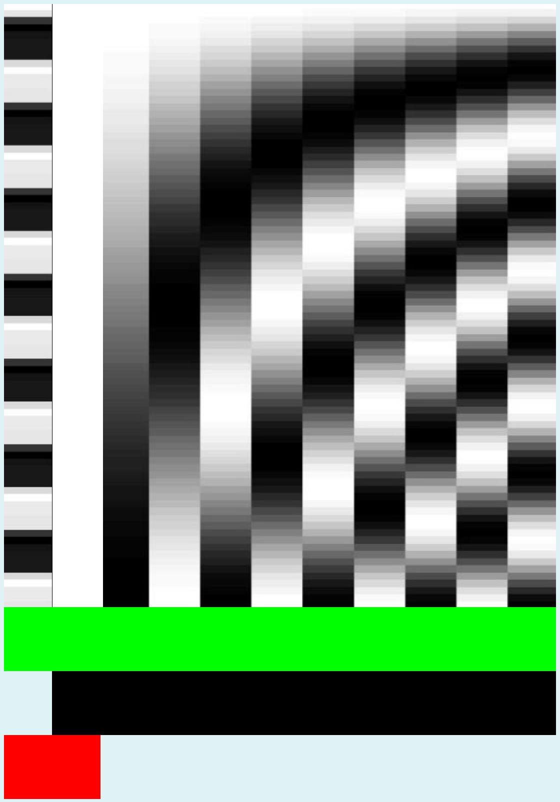
⇒ Power in the low frequencies



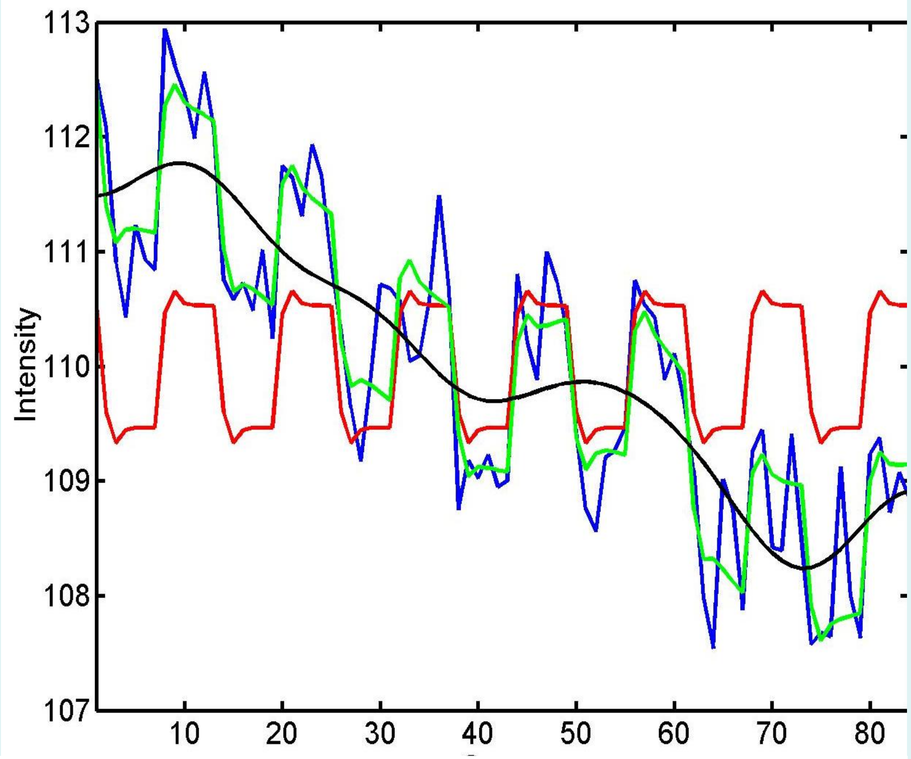




Solution with high pass filtering



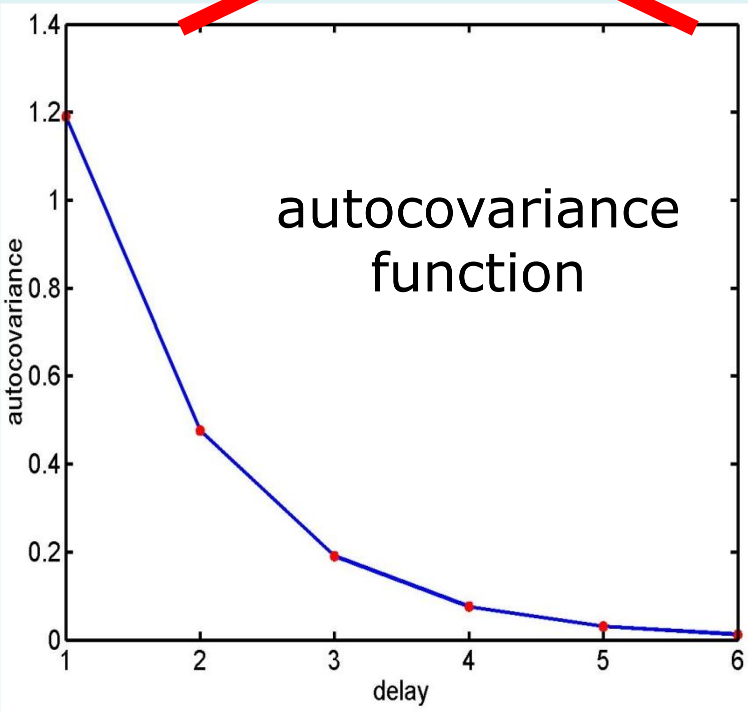
discrete cosine transform (DCT) set

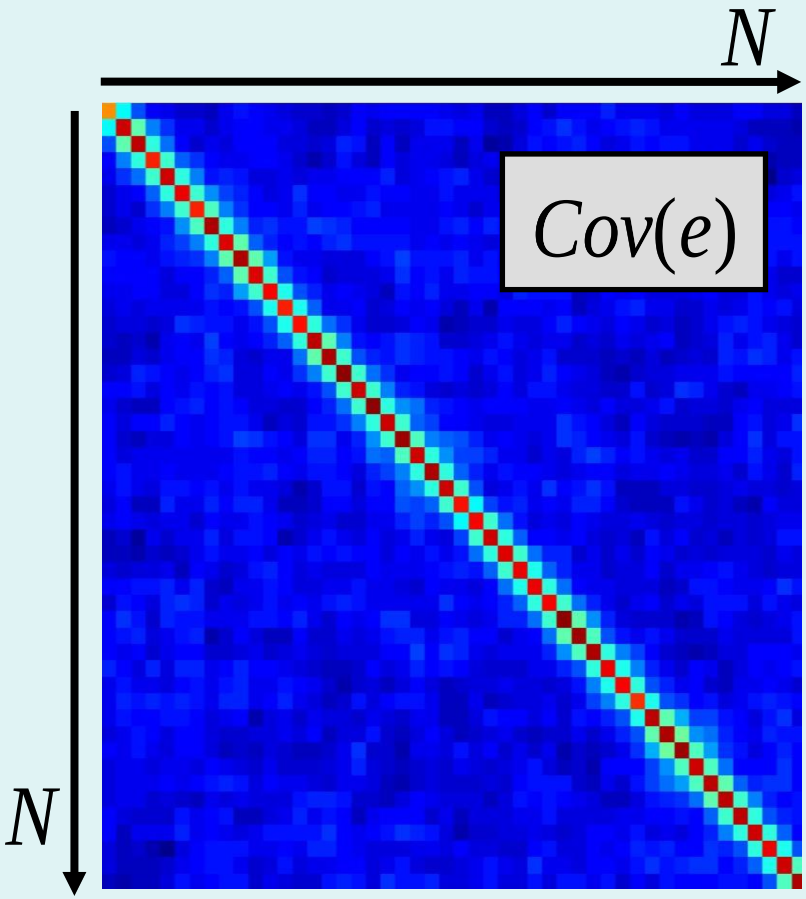


blue =	data
black =	mean + low-frequency drift
green = account	predicted response, taking into low-frequency drift
red = into	predicted response, NOT taking account low-frequency drift

Problem 3: Serial correlations

i.i.d: $e \sim \mathcal{N}(0, \sigma^2 I)$





$e \sim \mathcal{N}(0, \sigma^2 V)$

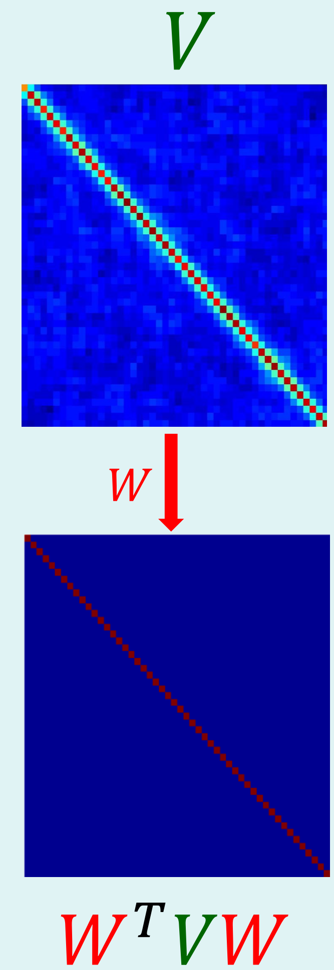
Solution for serial correlations

$y = X\beta + e \qquad e \sim \mathcal{N}(0, \sigma^2 V)$

Let $\quad W^T W = V^{-1}$

$Wy = WX\beta + We \qquad We \sim \mathcal{N}(0, \sigma^2 \underbrace{W^T V W}_{I})$

$\boldsymbol{y_s}$ $\quad$ $\boldsymbol{X_s}$ $\quad$ $\boldsymbol{e_s}$



Solution : Whitening the data
BUT this requires an estimation of V

Equivalent to the Weighted Least Square estimator

Multiple covariance components

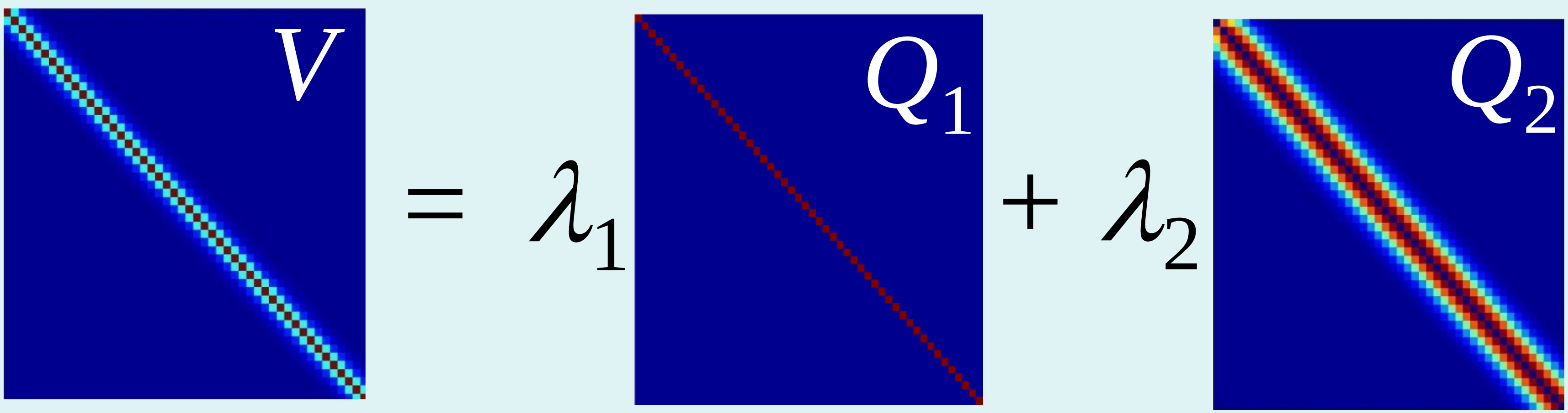
enhanced noise model at voxel *i*

$$e_i \sim N(0, C_i)$$

$$C_i = \sigma_i^2 V$$

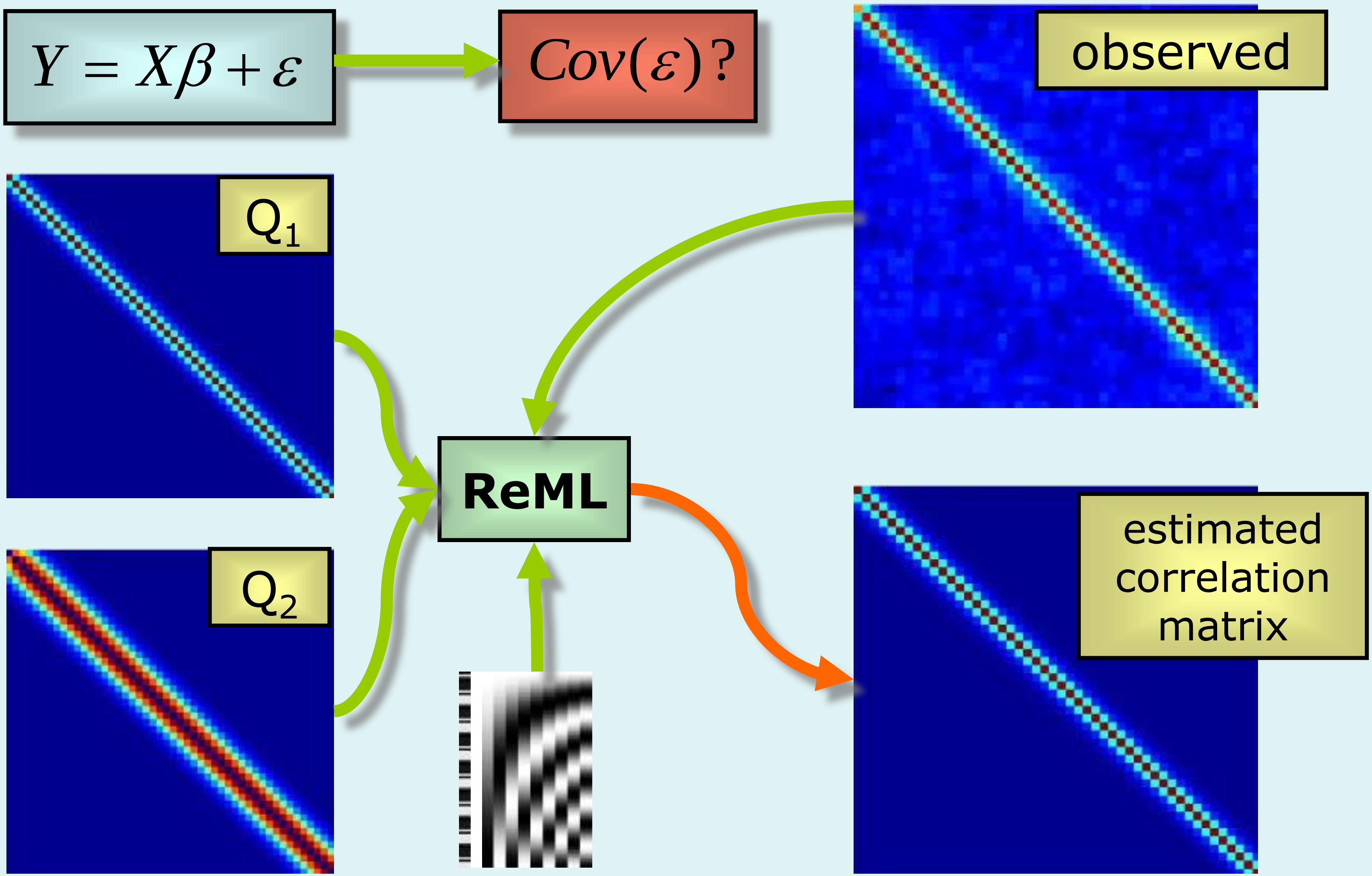
$$V = \sum \lambda_j Q_j$$

error covariance components
Q and hyperparameters λ



Estimation of hyperparameters λ with ReML (Restricted Maximum Likelihood).

Restricted Maximum Likelihood



Estimation in SPM

$$y_j = X\theta_j + \varepsilon_j$$

$$\hat{C}_\varepsilon = \hat{Cov}(\varepsilon) = \mathrm{ReML}\left(\sum_{voxel\ j} y_j y_j^T, X, Q \right)$$

ReML (pooled estimate)

$$\hat{\theta}_{j,OLS} = X^+ y_j$$

$$\hat{\theta}_{j,ML} = (X^T V^{-1} X)^{-1} X^T V^{-1} y_j$$

Ordinary least-squares ⟷ Maximum Likelihood

- 2 passes (first pass for selection of voxels)
- more accurate estimate of *V*

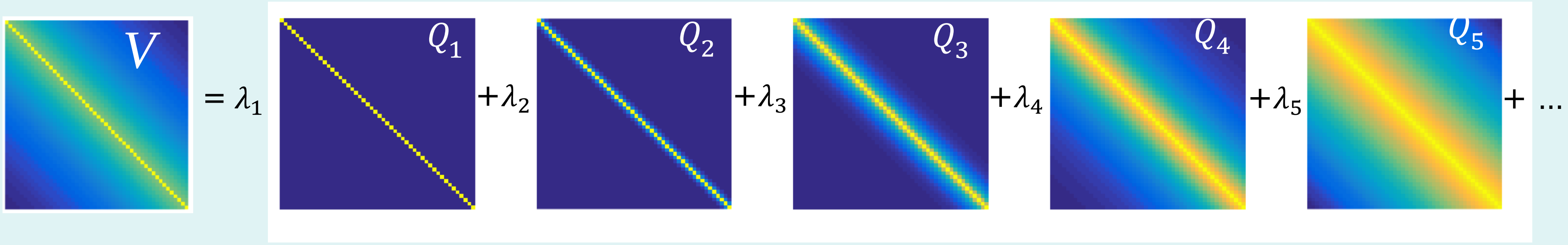
Assume, at voxel *j*: $C_{\varepsilon,j} = \sigma_j V$

$$t = \frac{c^T \theta}{\mathrm{SE}(c^T \theta)}$$

$$\mathrm{SE}(c^T \theta) = \sqrt{\hat{\sigma}^2 c^T (V^{-1/2} X)^- (V^{-1/2} X)^{-T} c}$$

Limitations

The AR(1)+white noise model may not be enough for short TR (<1.5 s)

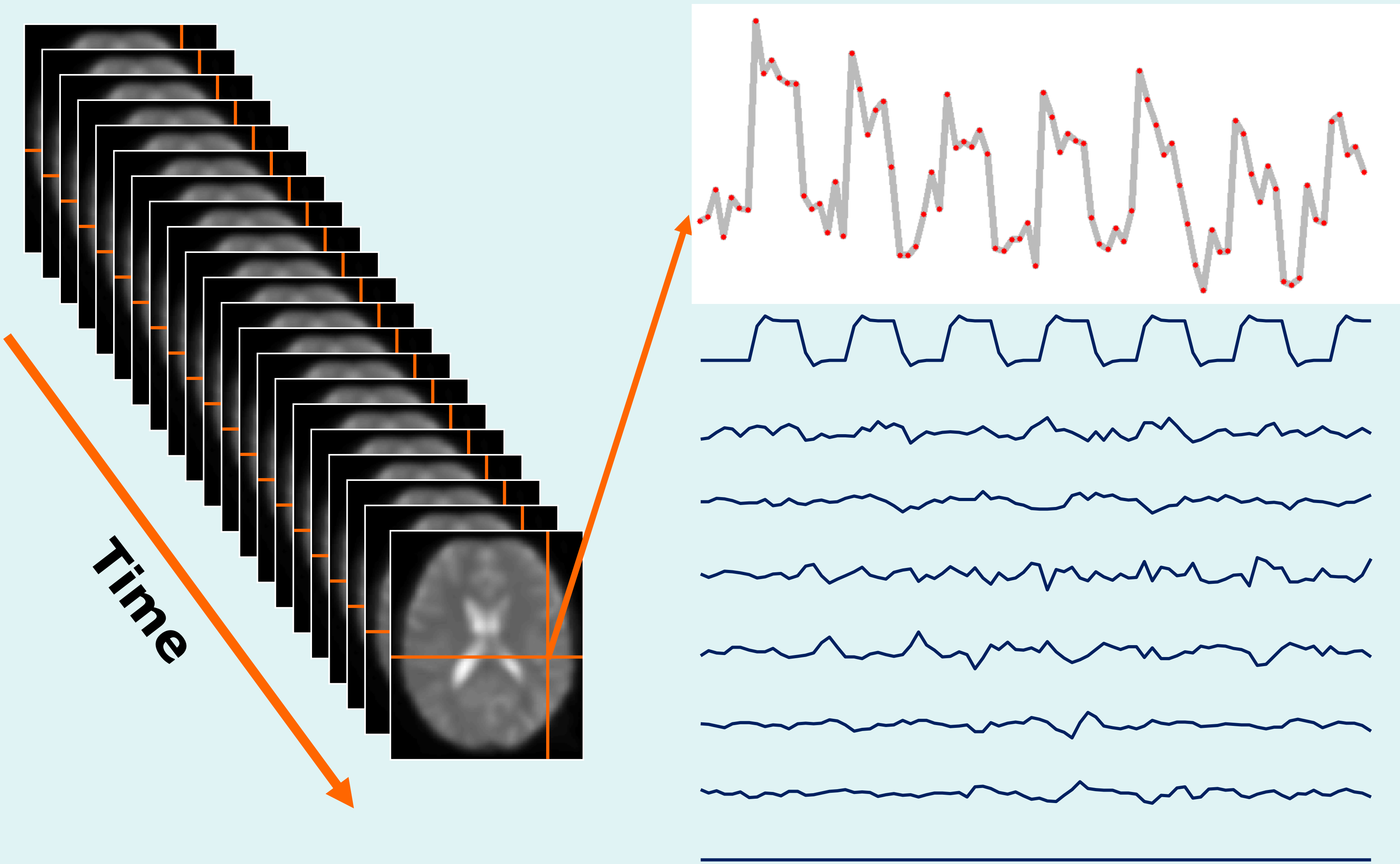


The flexibility of the ReML enables the use of any number of components of any shape

Content

- **Introduction**
- **General Linear Model**
- **Parameter estimation**
- **Improved model**
- **Conclusion**

A mass univariate approach

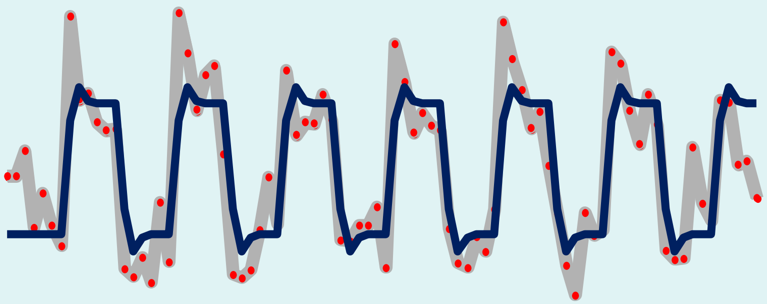


Summary

Mass univariate approach:

- Fit GLMs with
  - design matrix, X,
  - to data at different points in space
  - to estimate local effect sizes, β
- GLM, a very general approach that accommodates
  - Hemodynamic Response Function
  - Nuisance effects, e.g. high pass filtering
  - Error term covariance, e.g. temporal autocorrelation

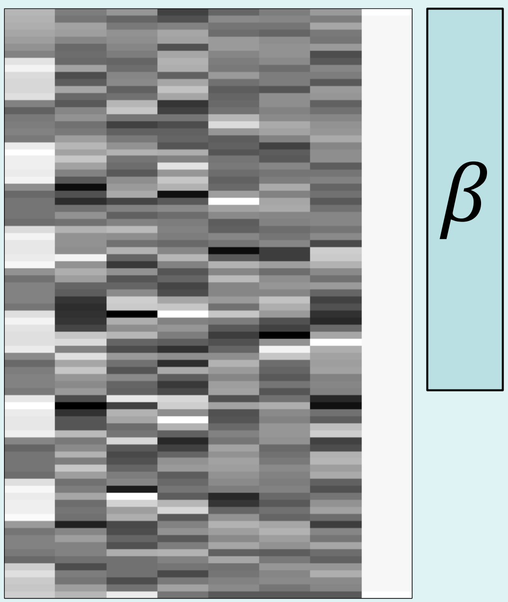
Summary



noise assumptions: $\varepsilon \sim N(0, \sigma^2 V)$

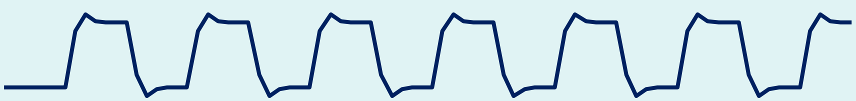
Pre-whitening: $X_s = WX \quad y_s = Wy \quad \varepsilon_s = W\varepsilon$

$$\hat{\beta} = (X_s^T X_s)^{-1} X_s^T y_s$$

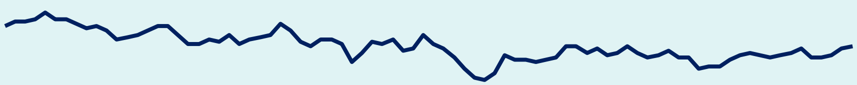
$y =$ 

$+\varepsilon$

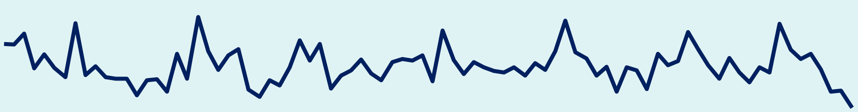
$\hat{\beta}_1 = 3.9831$



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



$\hat{\beta}_8 = 131.0040$

$\widehat{\varepsilon_s} =$ 

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

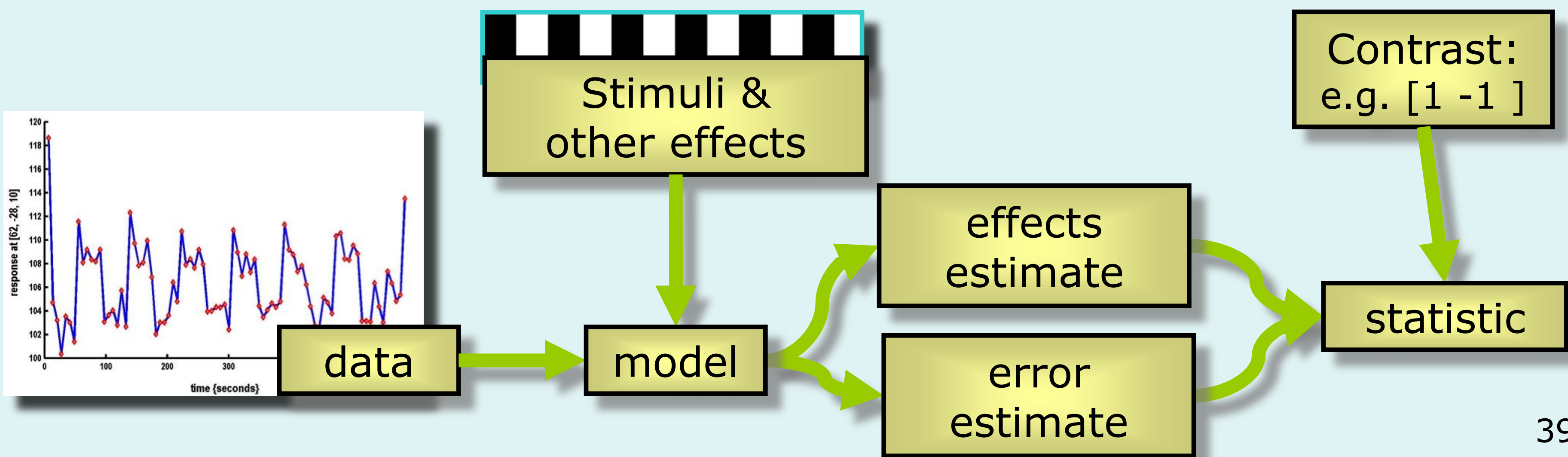
$$\hat{\sigma}^2 = \frac{\widehat{\varepsilon_s}^T \widehat{\varepsilon_s}}{N-p}$$

Why modelling?

Why? — Make inferences about effects of interest

How?
1. Decompose data into effects and error
2. Form statistic using estimates of effects and error

Model? — Use any available knowledge



References

- Statistical parametric maps in functional imaging: a general linear approach, K.J. Friston et al, Human Brain Mapping, 1995.
- Analysis of fMRI time-series revisited – again, K.J. Worsley and K.J. Friston, NeuroImage, 1995.
- The general linear model and fMRI: Does love last forever?, J.-B. Poline and M. Brett, NeuroImage, 2012.
- Linear systems analysis of the fMRI signal, G.M. Boynton et al, NeuroImage, 2012.