SPM

The General Linear Model

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Thank you to Guillaume Flandin for the slides

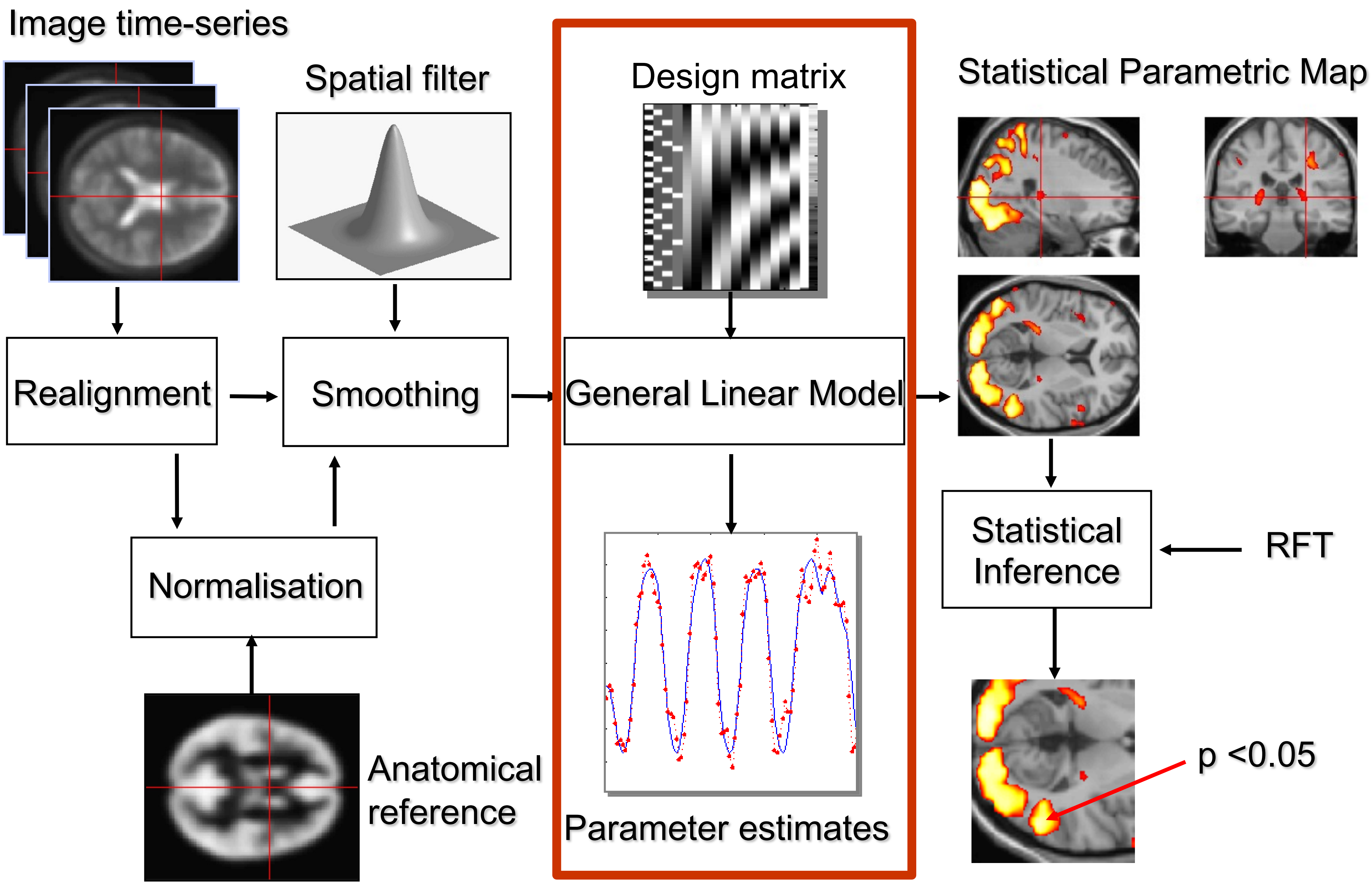


Image time-series
Spatial filter
Design matrix
Statistical Parametric Map
Realignment
Smoothing
General Linear Model
Normalisation
Statistical Inference
RFT
Anatomical reference
Parameter estimates
p <0.05

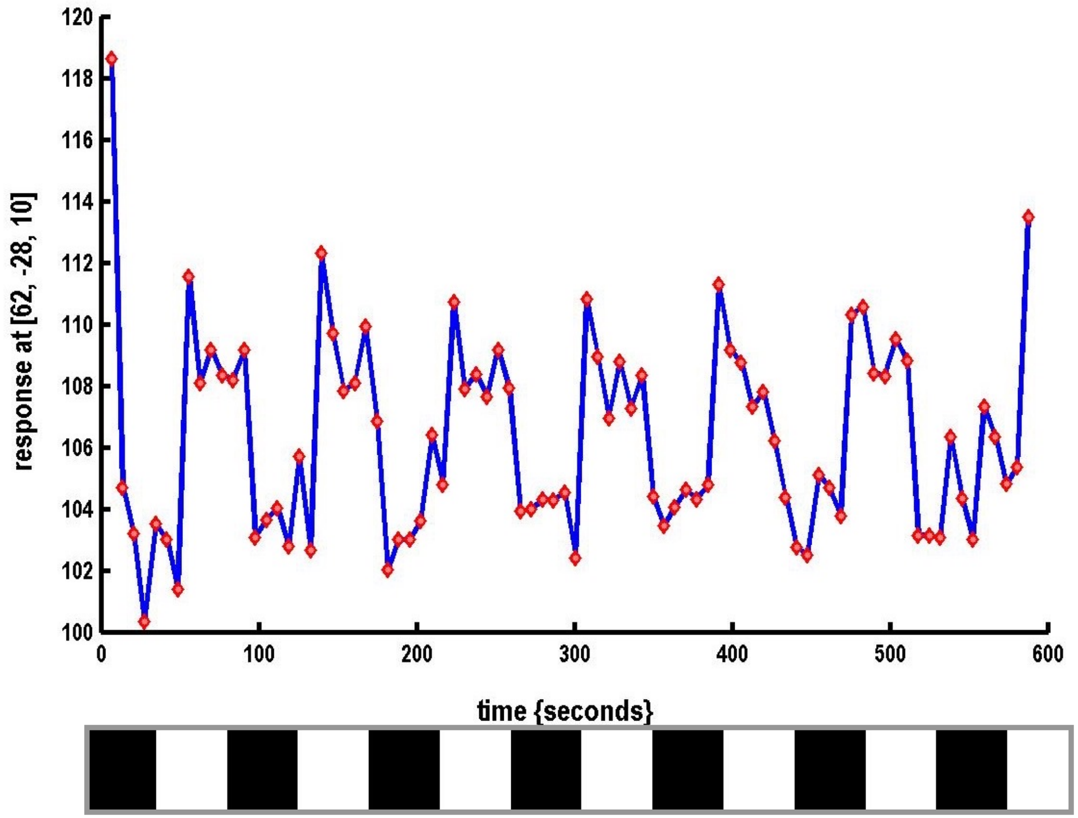
A very simple fMRI experiment

One session

Passive word listening versus rest

7 cycles of rest and listening

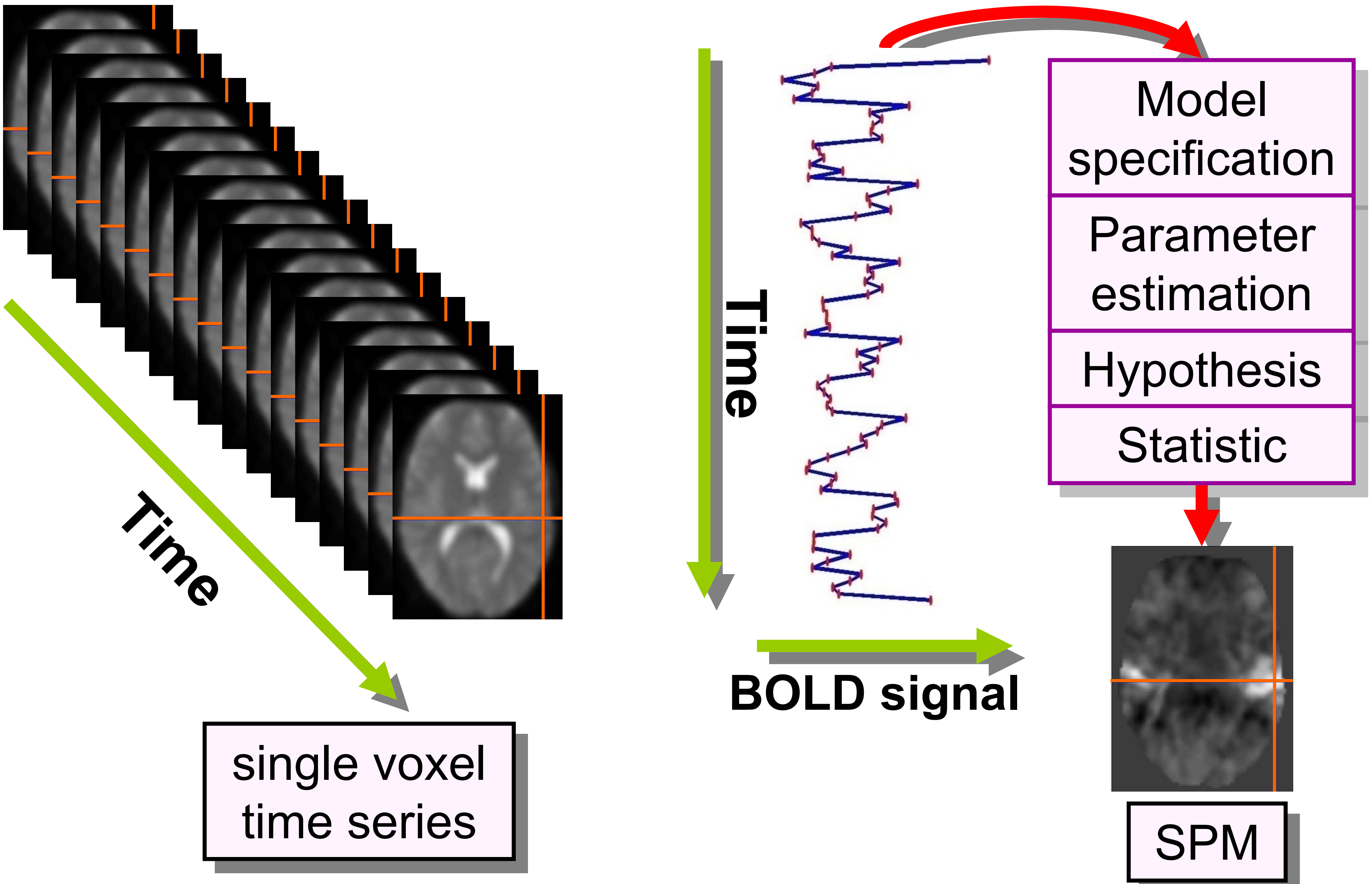
Blocks of 6 scans with 7 sec TR



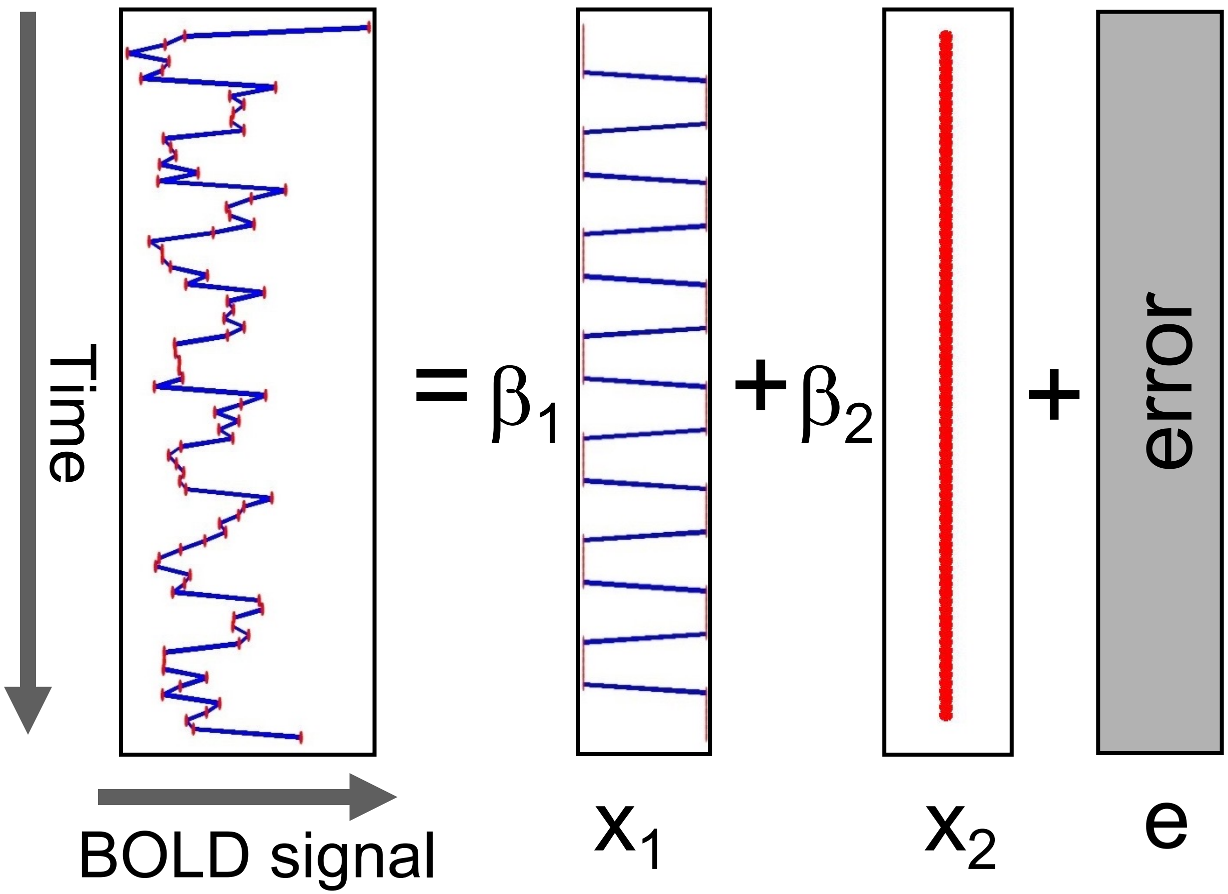
Stimulus function

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

Voxel-wise time series analysis

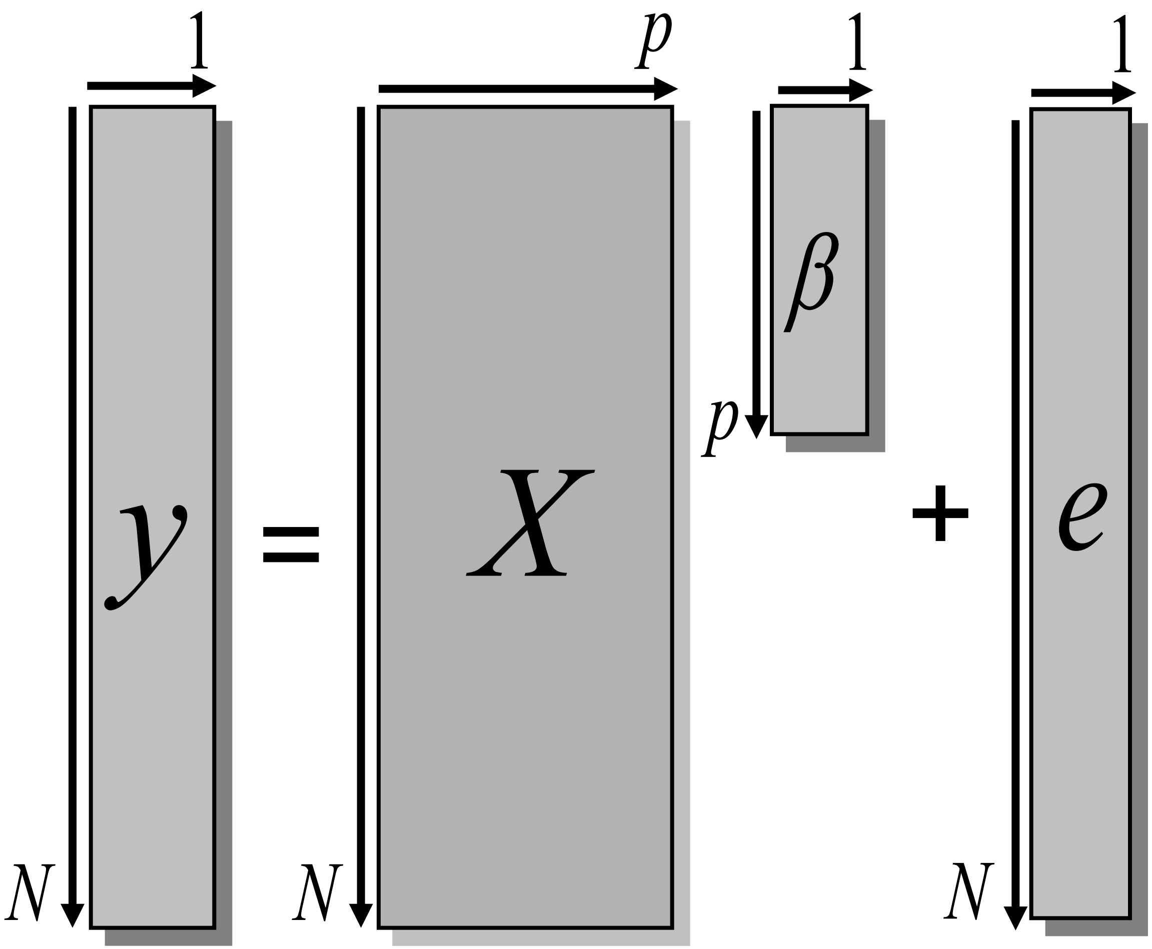


Single voxel regression model



$$y = x_1\beta_1 + x_2\beta_2 + e$$

Mass-univariate analysis: voxel-wise GLM



$$y = X\beta + e$$

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

Model is specified by
1. Design matrix X
2. Assumptions about e

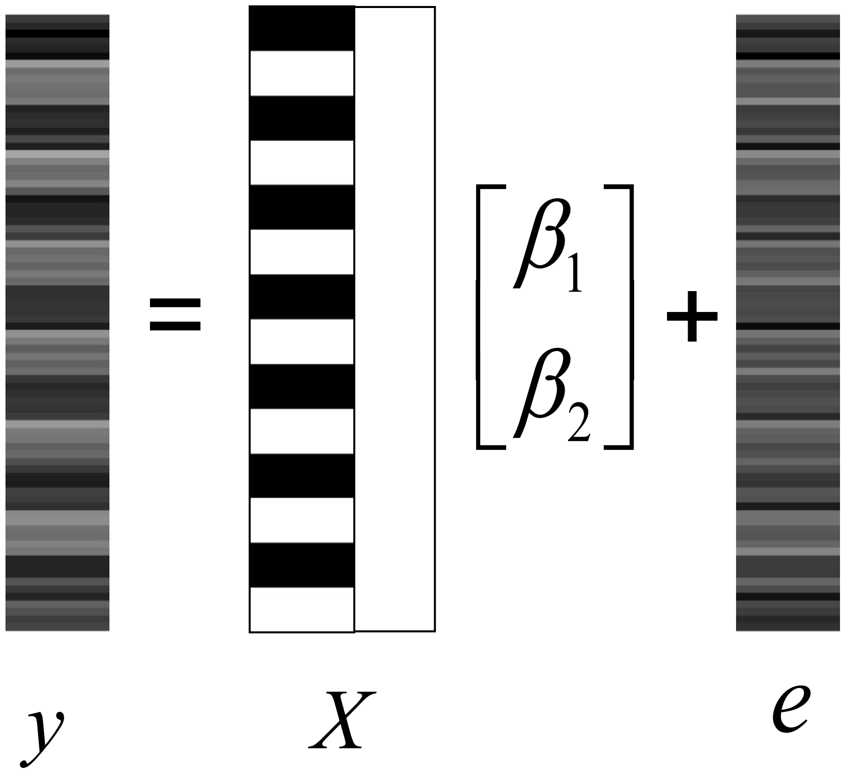
N: number of scans
p: number of regressors

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

GLM: a flexible framework for parametric analyses

- one sample *t*-test
- two sample *t*-test
- paired *t*-test
- Analysis of Variance (ANOVA)
- Analysis of Covariance (ANCoVA)
- correlation
- linear regression
- multiple regression

Parameter estimation



$$y = X\beta + e$$

Objective: estimate parameters to minimize

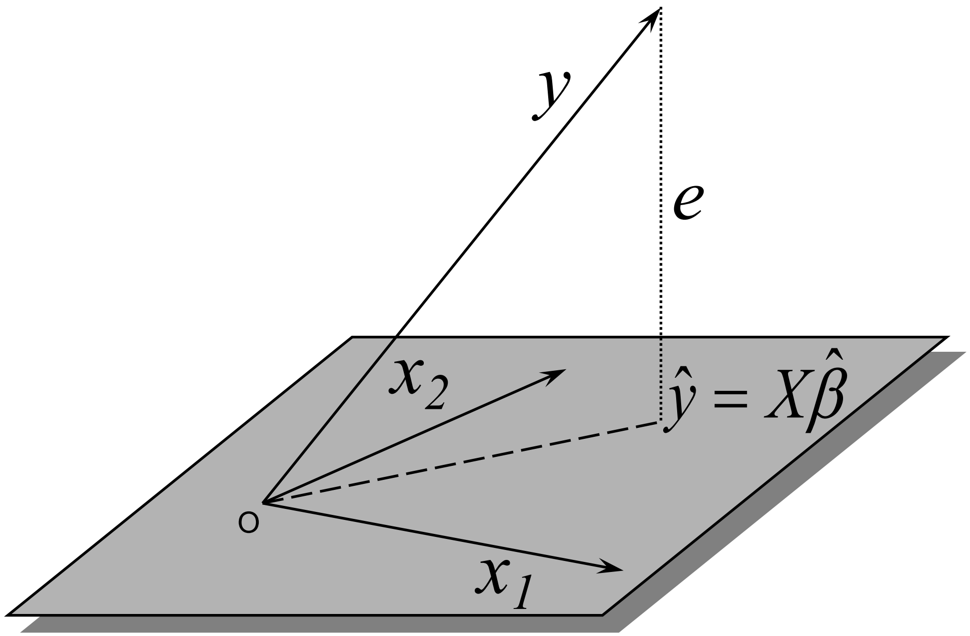
$$\sum_{t=1}^{N} e_t^2$$

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

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

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

A geometric perspective on the GLM



Design space defined by X

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

$$X^T e = 0$$

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

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

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

Ordinary Least Squares (OLS)

Problems of this model with fMRI time series

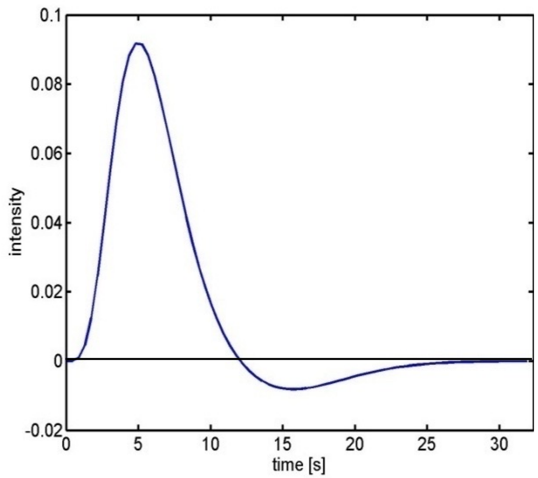
1. The *BOLD response* has a delayed and dispersed shape.

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

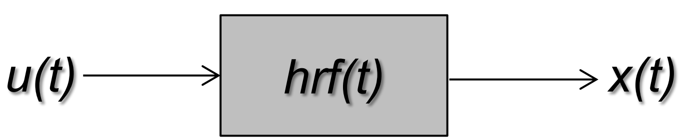
3. Due to breathing, heartbeat & unmodeled neuronal activity, the *errors are serially correlated*. This violates the assumptions of the noise model in the GLM.

Problem 1: BOLD response

Hemodynamic response function (HRF):

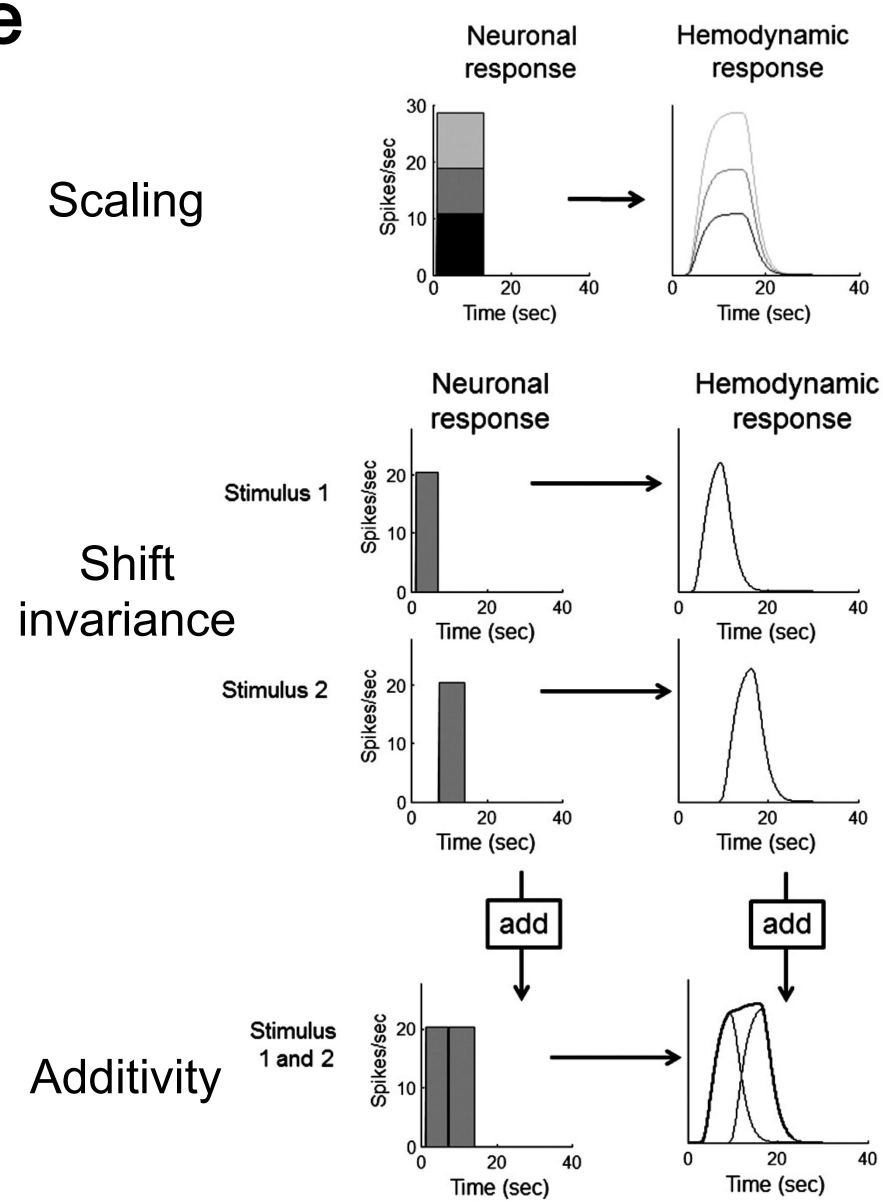


Linear time-invariant (LTI) system:



Convolution operator:

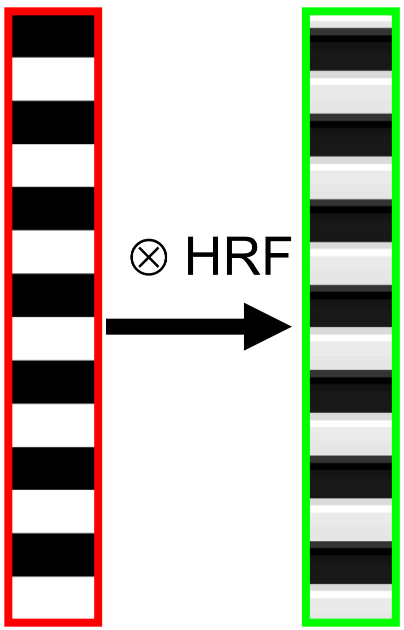
$$x(t) = u(t) * hrf(t)$$
$$= \int_0^t u(\tau) hrf(t-\tau) d\tau$$

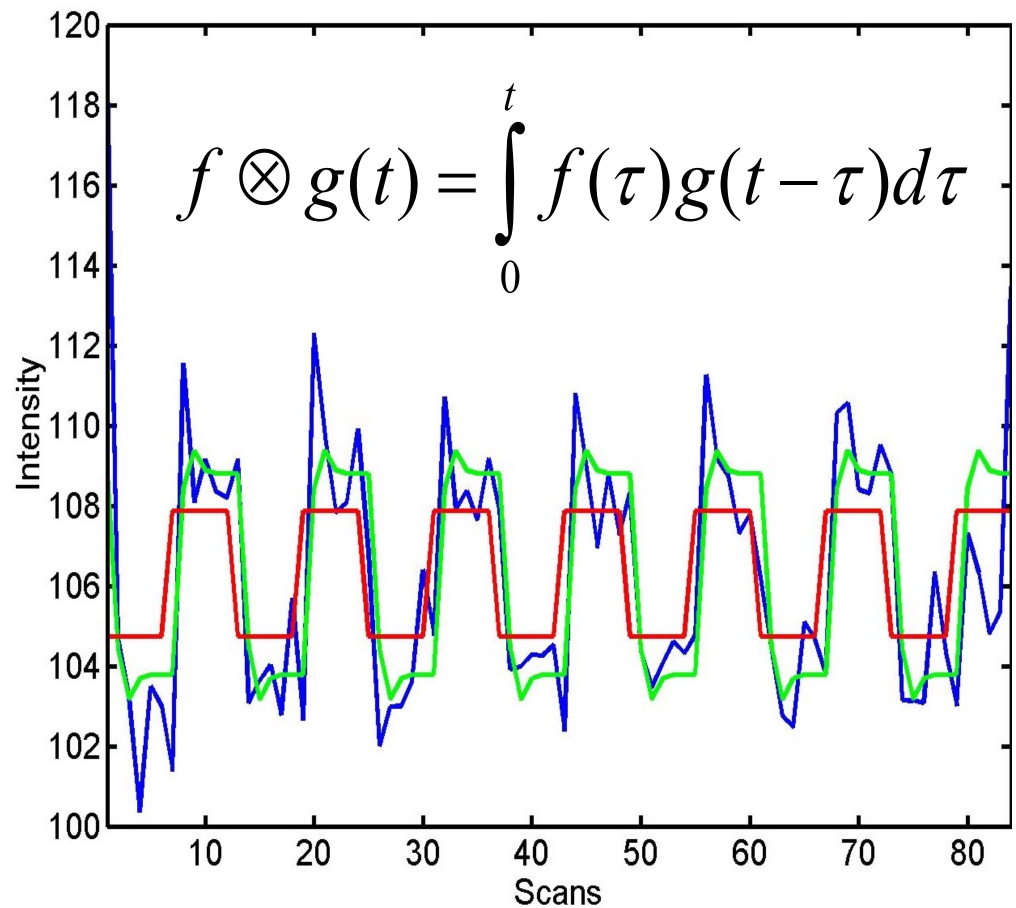


Boynton et al, NeuroImage, 2012.

Convolution model of the BOLD response

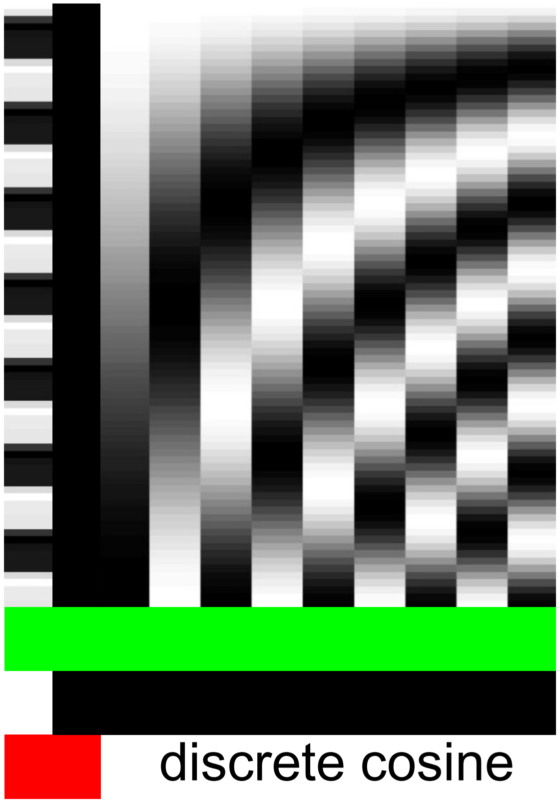
Convolve stimulus function with a canonical hemodynamic response function (HRF):



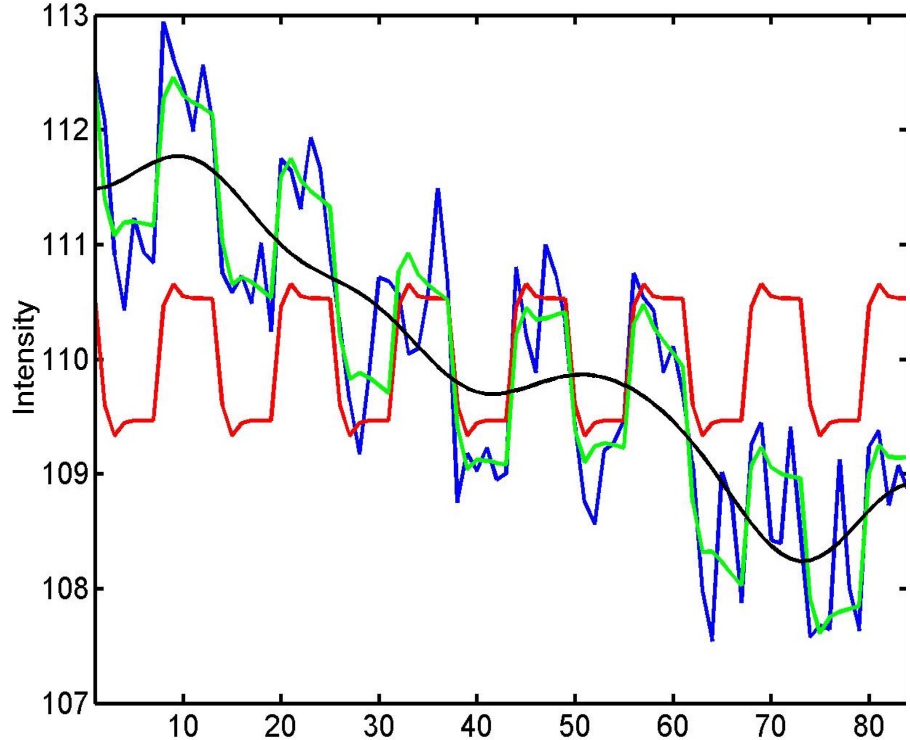


Problem 2: Low-frequency noise

Solution: High pass filtering



discrete cosine transform (DCT) set



blue = data

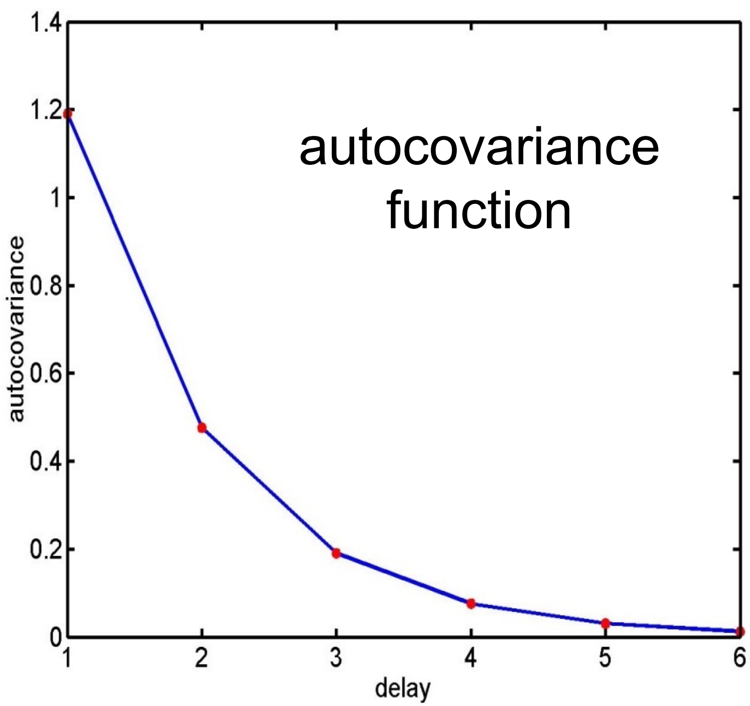
black = mean + low-frequency drift

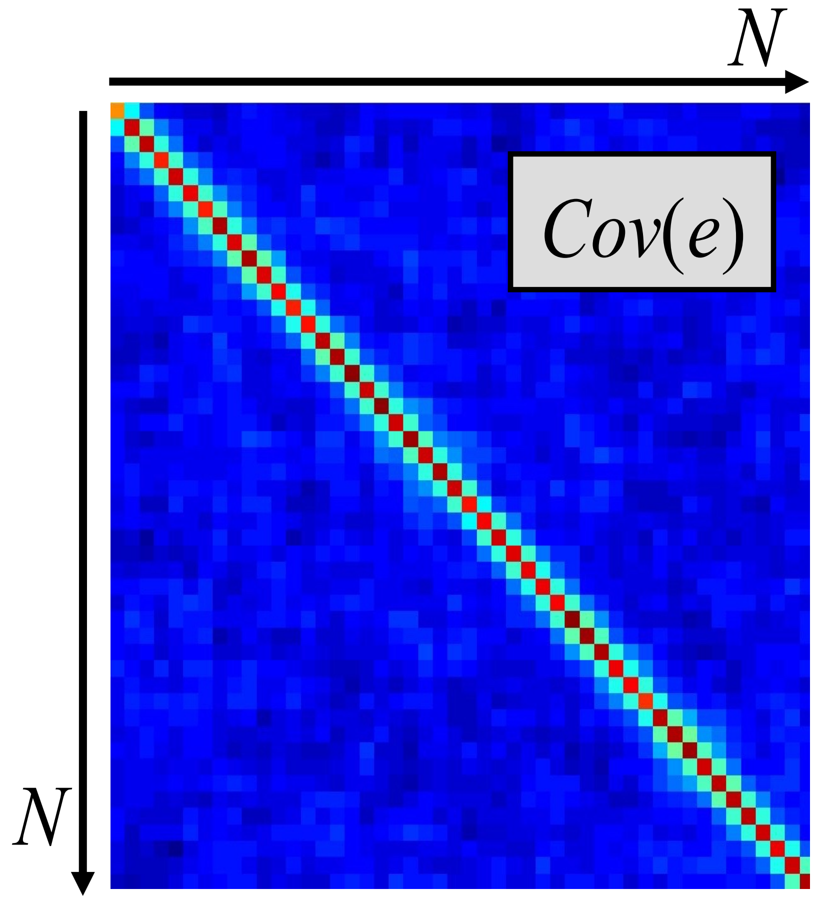
green = predicted response, taking into account low-frequency drift

red = predicted response, NOT taking into account low-frequency drift

Problem 3: Serial correlations

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



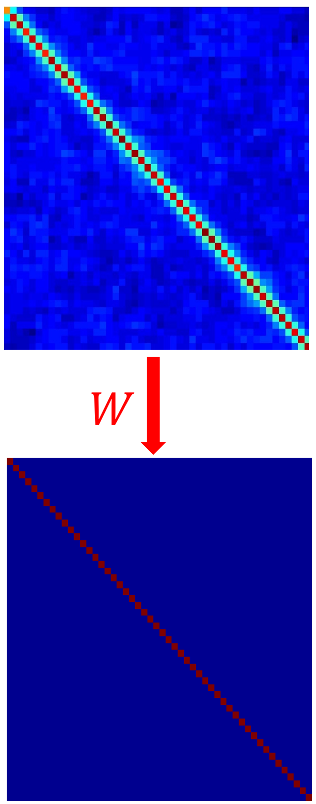


$$y = X\beta + e \qquad e \sim \mathcal{N}(0, \sigma^2 V)$$

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

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

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



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

Multiple covariance components

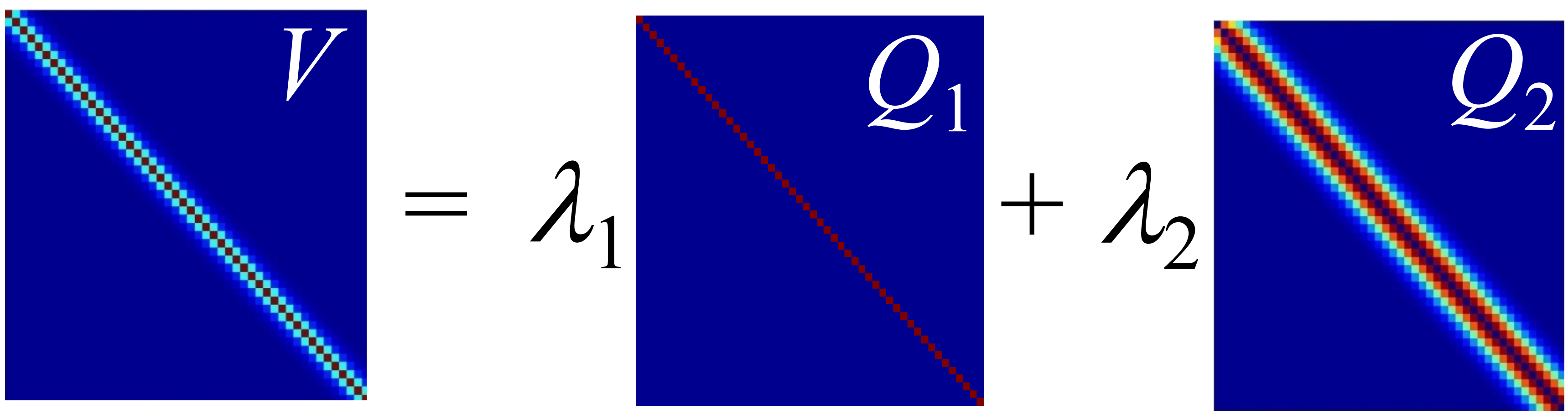
enhanced noise model at voxel *i*

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

$$C_i = \sigma_i^2 V$$

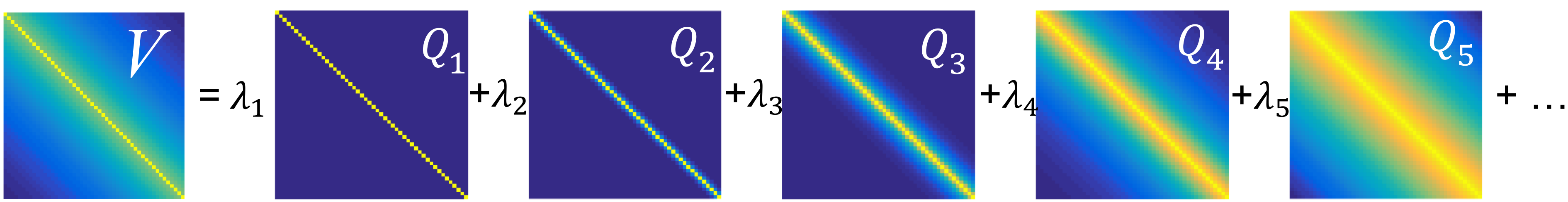
$$V = \sum \lambda_j Q_j$$

error covariance components Q
and hyperparameters λ



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

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

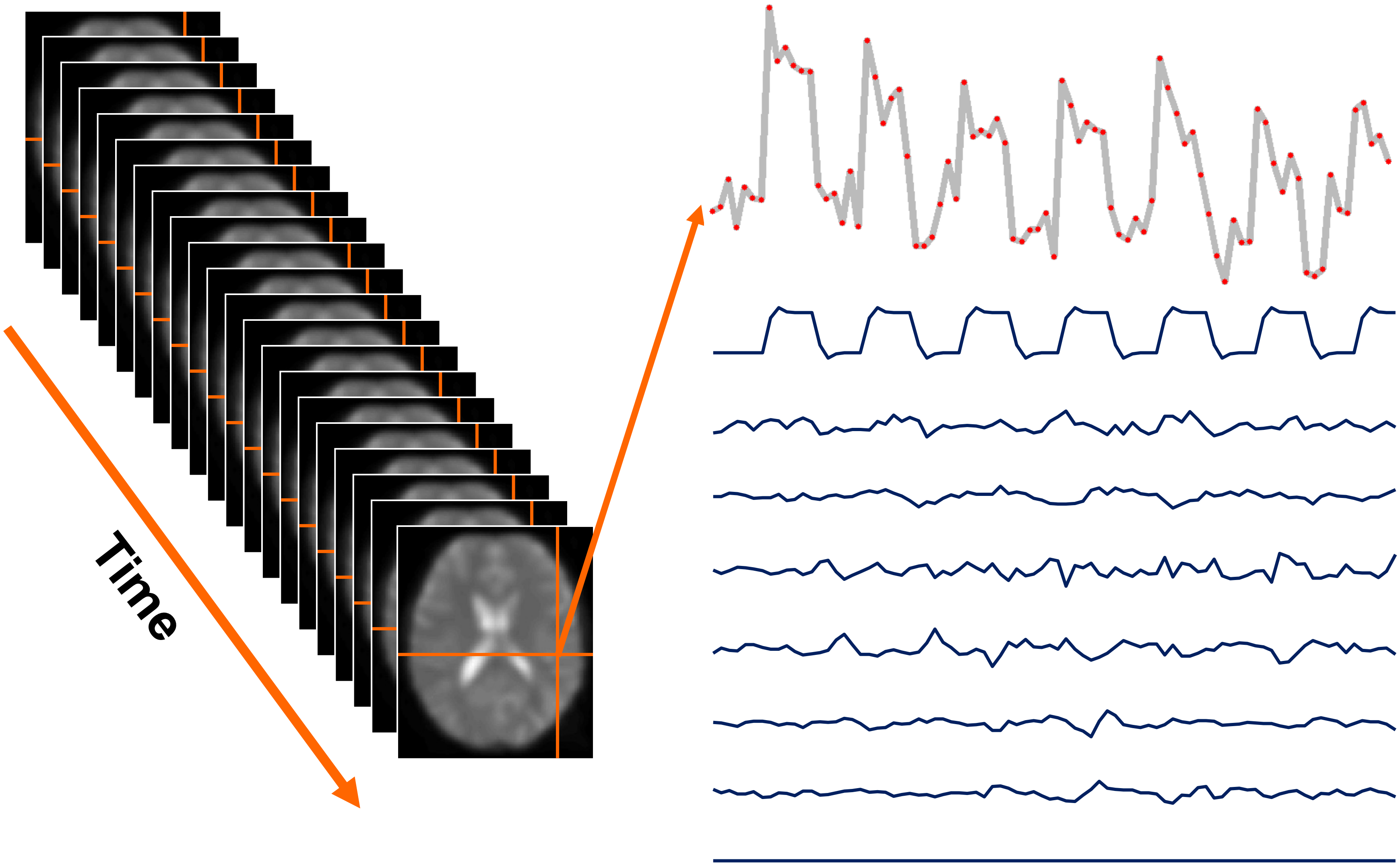


The flexibility of the ReML enables the use of any number of components of any shape

Summary

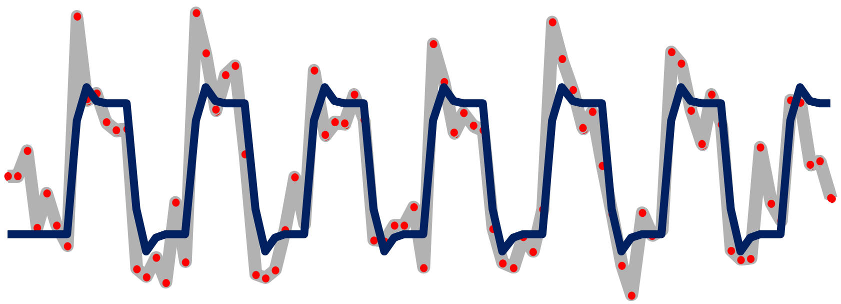
- Mass univariate approach.
- Fit GLMs with design matrix, X, to data at different points in space to estimate local effect sizes, β
- GLM is a very general approach
- Hemodynamic Response Function
- High pass filtering
- Temporal autocorrelation

A mass-univariate approach



SPM

Estimation of the parameters



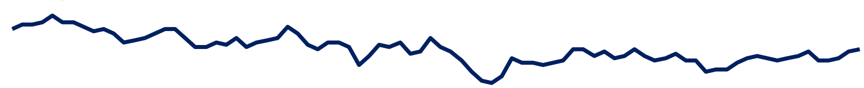
noise assumptions: $\varepsilon \sim N(0, \sigma^2 V)$

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

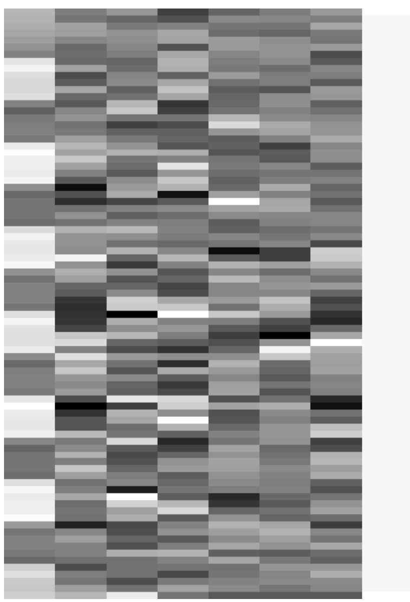
$$\hat{\beta} = (X_s^T X_s)^{-1} X_s^T y_s$$

$\hat{\beta}_1 = 3.9831$

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



$\hat{\beta}_8 = 131.0040$

$y =$  $\beta + \varepsilon$

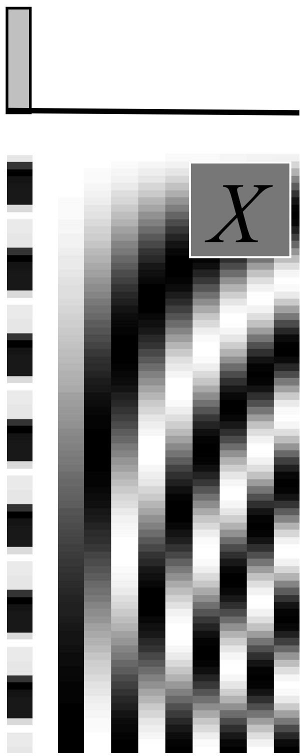
$\widehat{\varepsilon_s} =$ 

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

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

Contrasts & statistical parametric maps

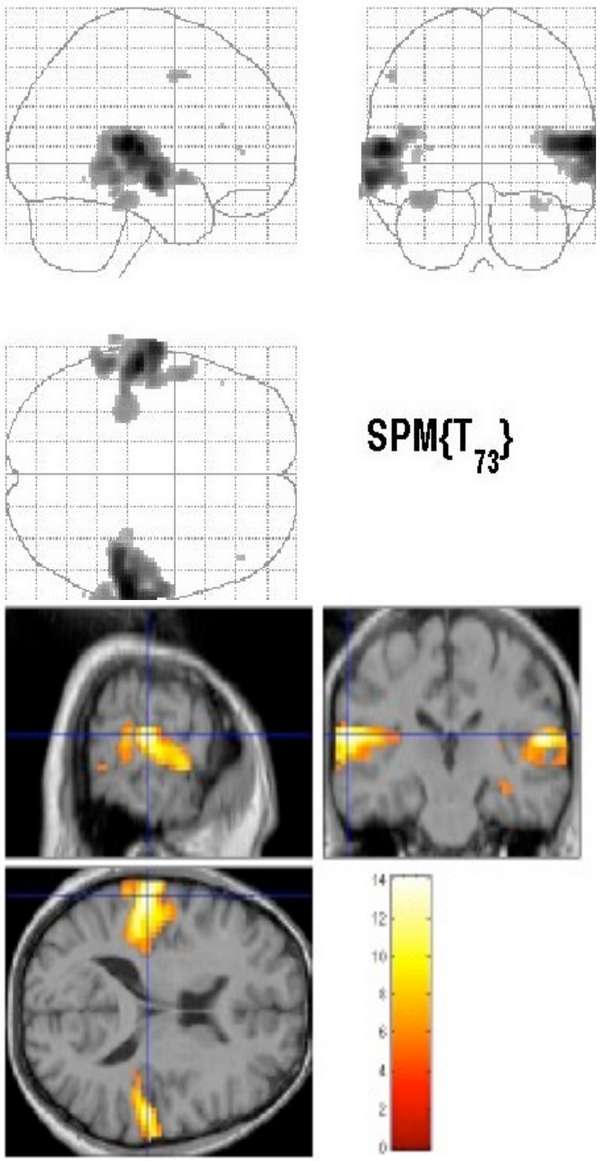
c = 1 0 0 0 0 0 0 0 0 0 0 0



Q: activation during listening ?

Null hypothesis: $\beta_1 = 0$

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



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.