The General Linear Model (GLM)

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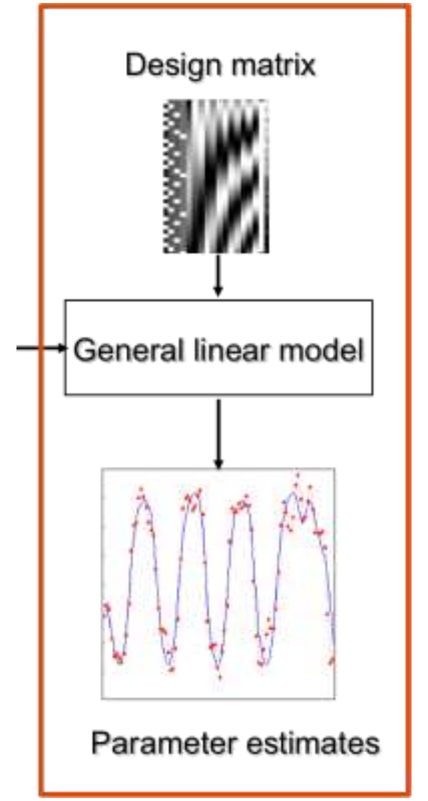


With many thanks for slides & images to:

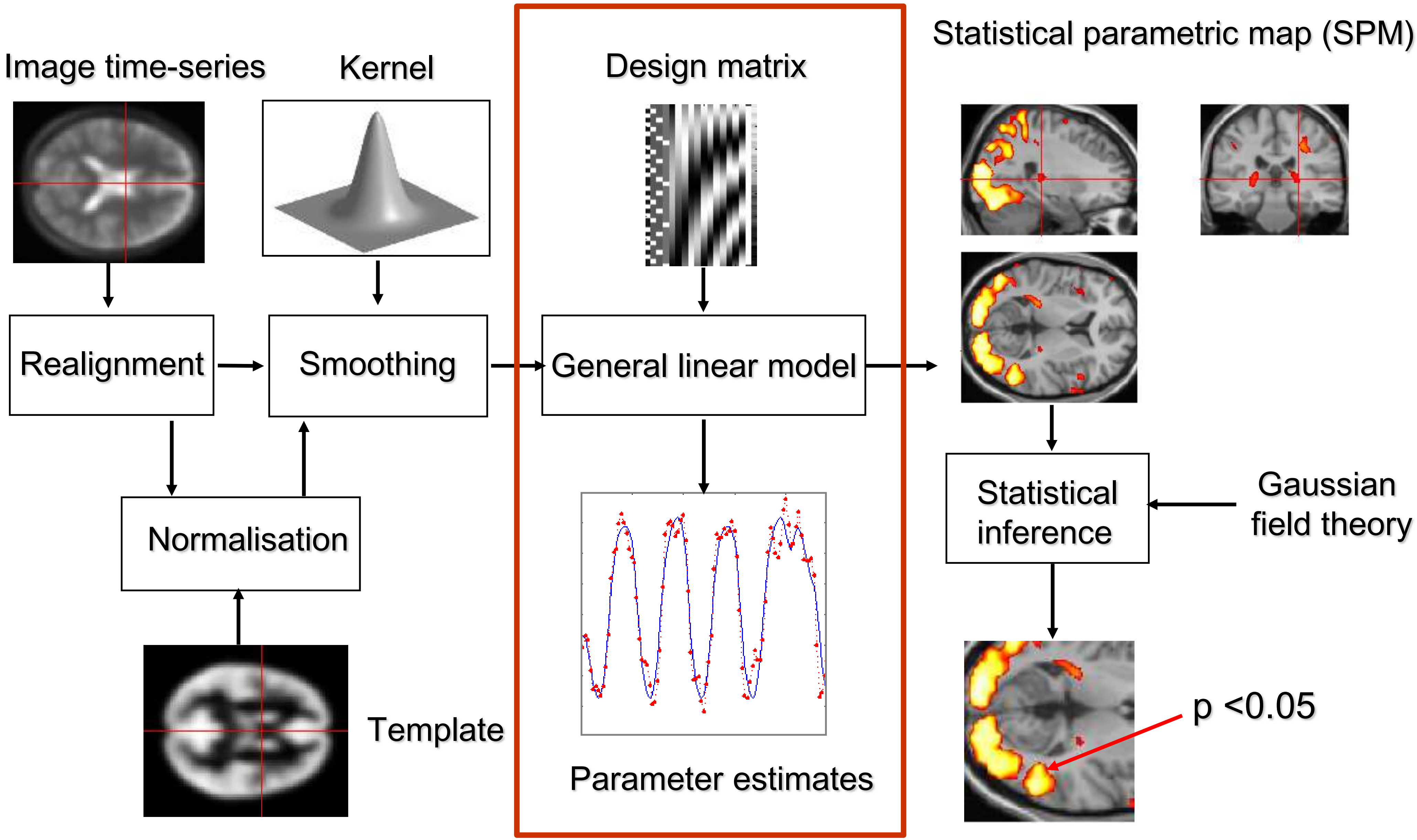
FIL Methods group, Virginia Flanagin and Klaas Enno Stephan

Translational Neuromodeling Unit

University of Zurich[UZH]

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

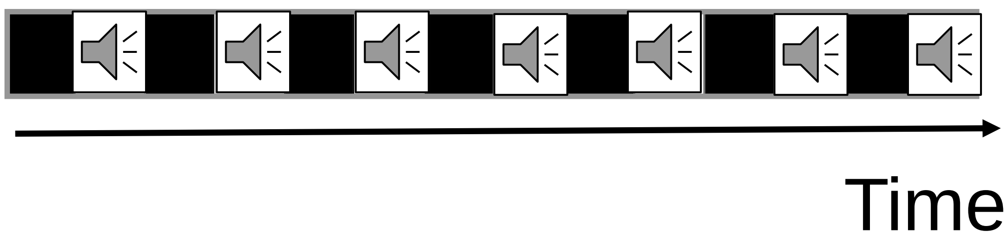
Overview of SPM



Research Question:

Where in the brain do we represent listening to sounds?

Image a very simple experiment…



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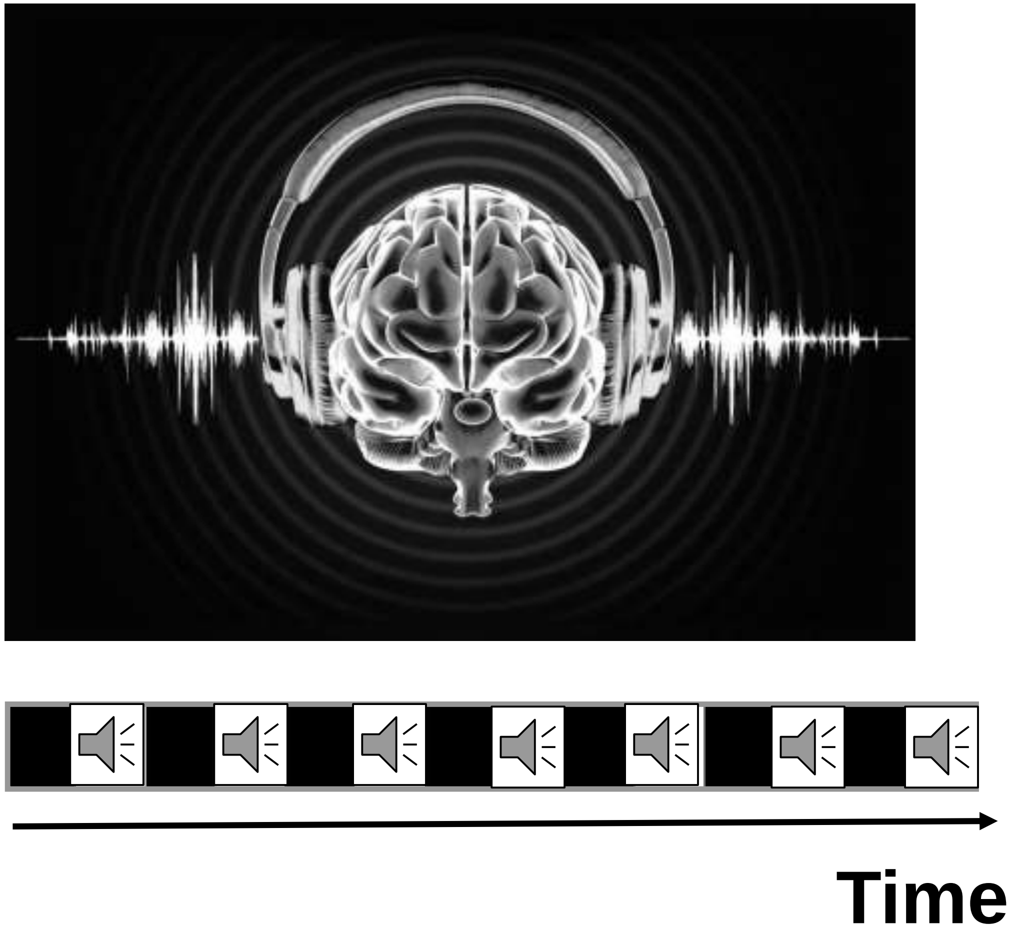


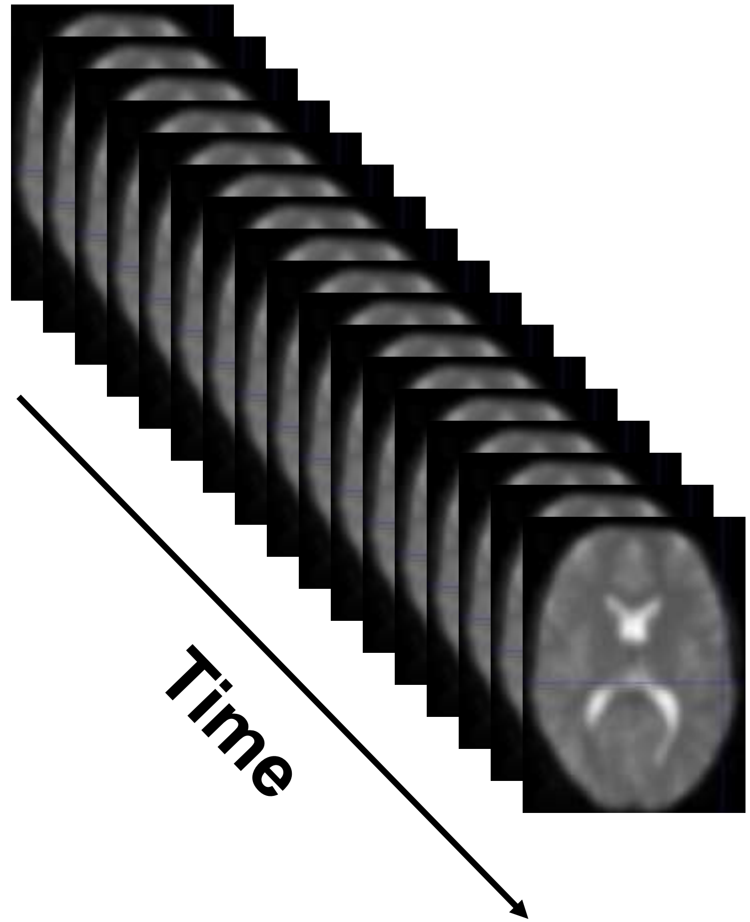


Image a very simple experiment…

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

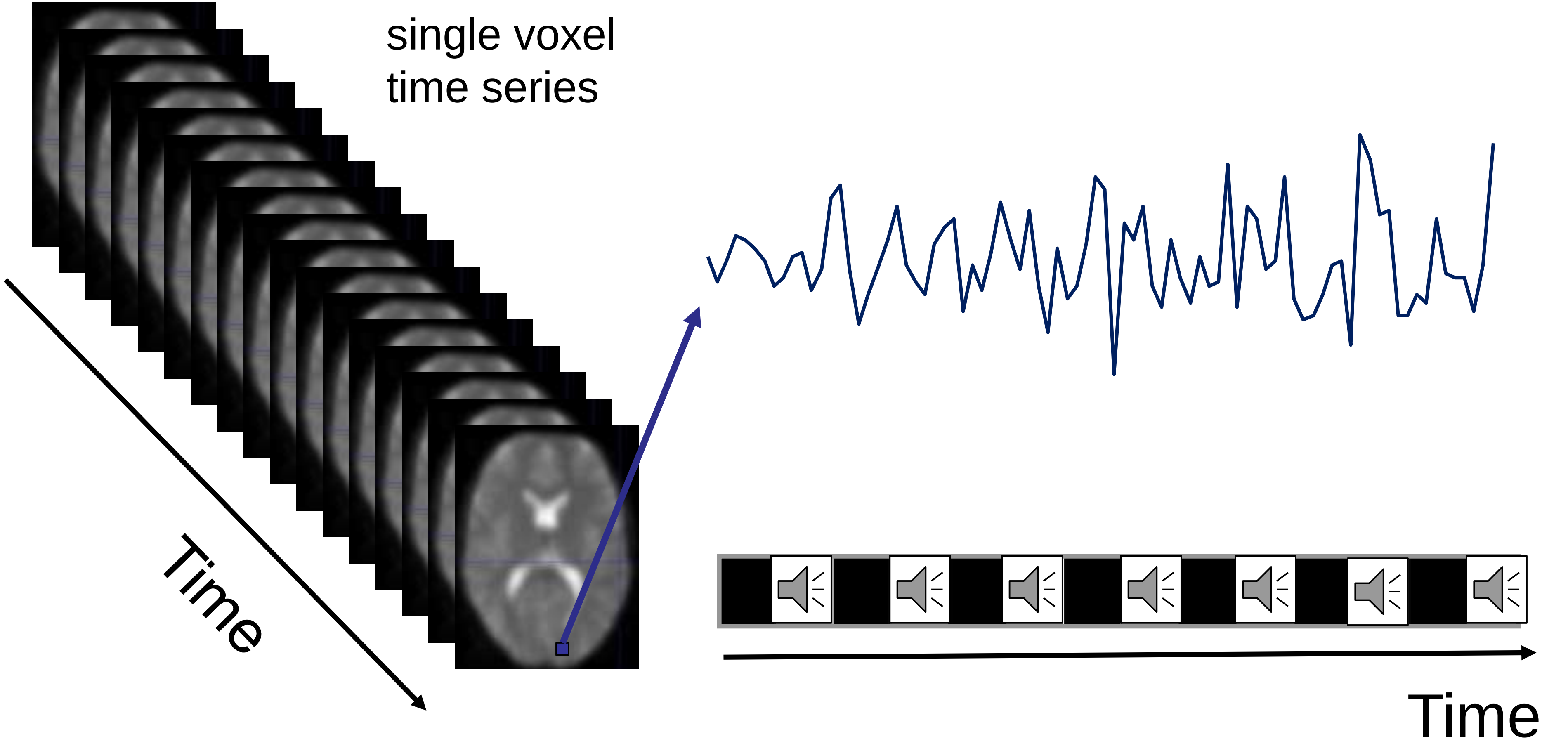
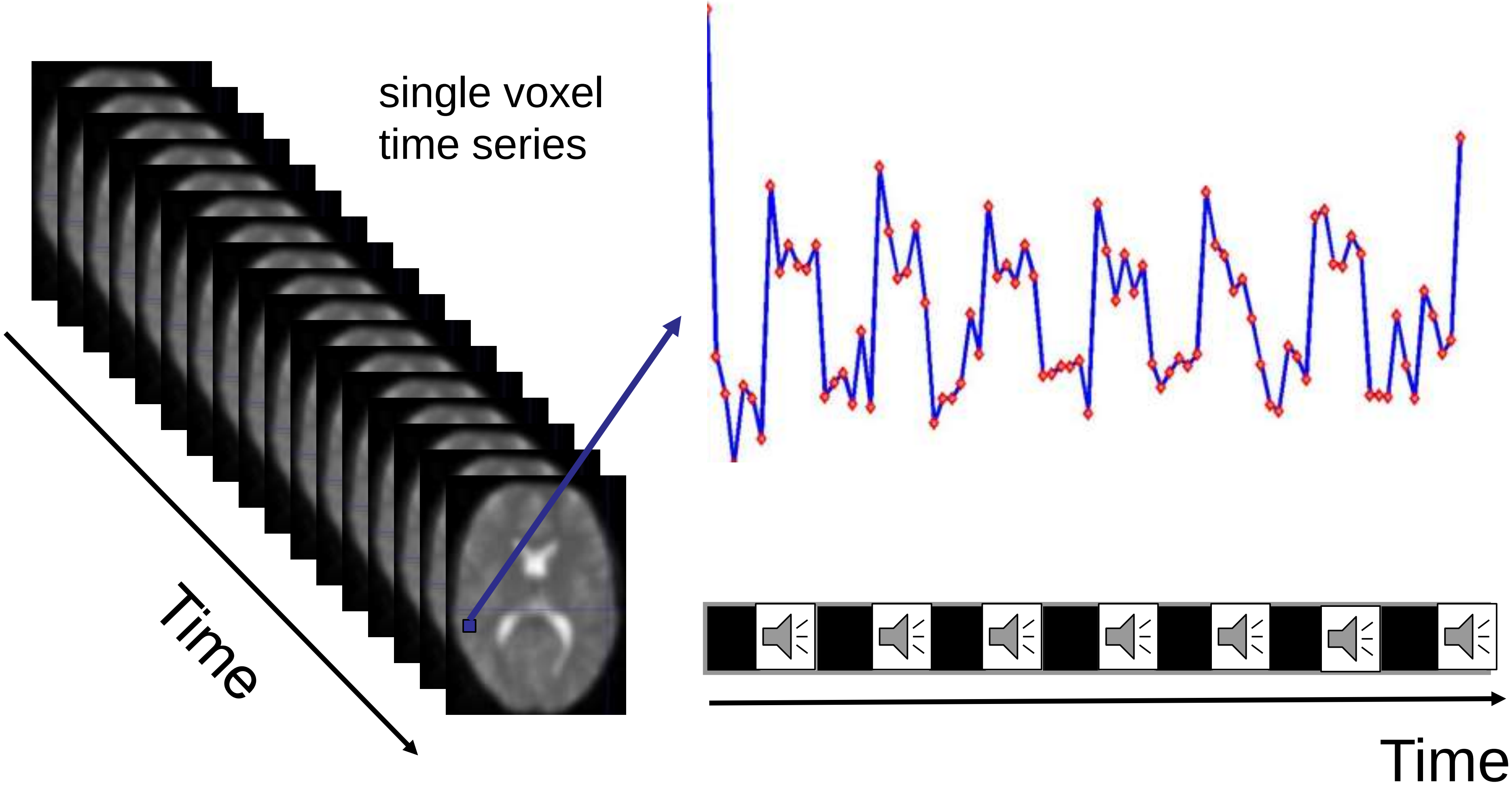
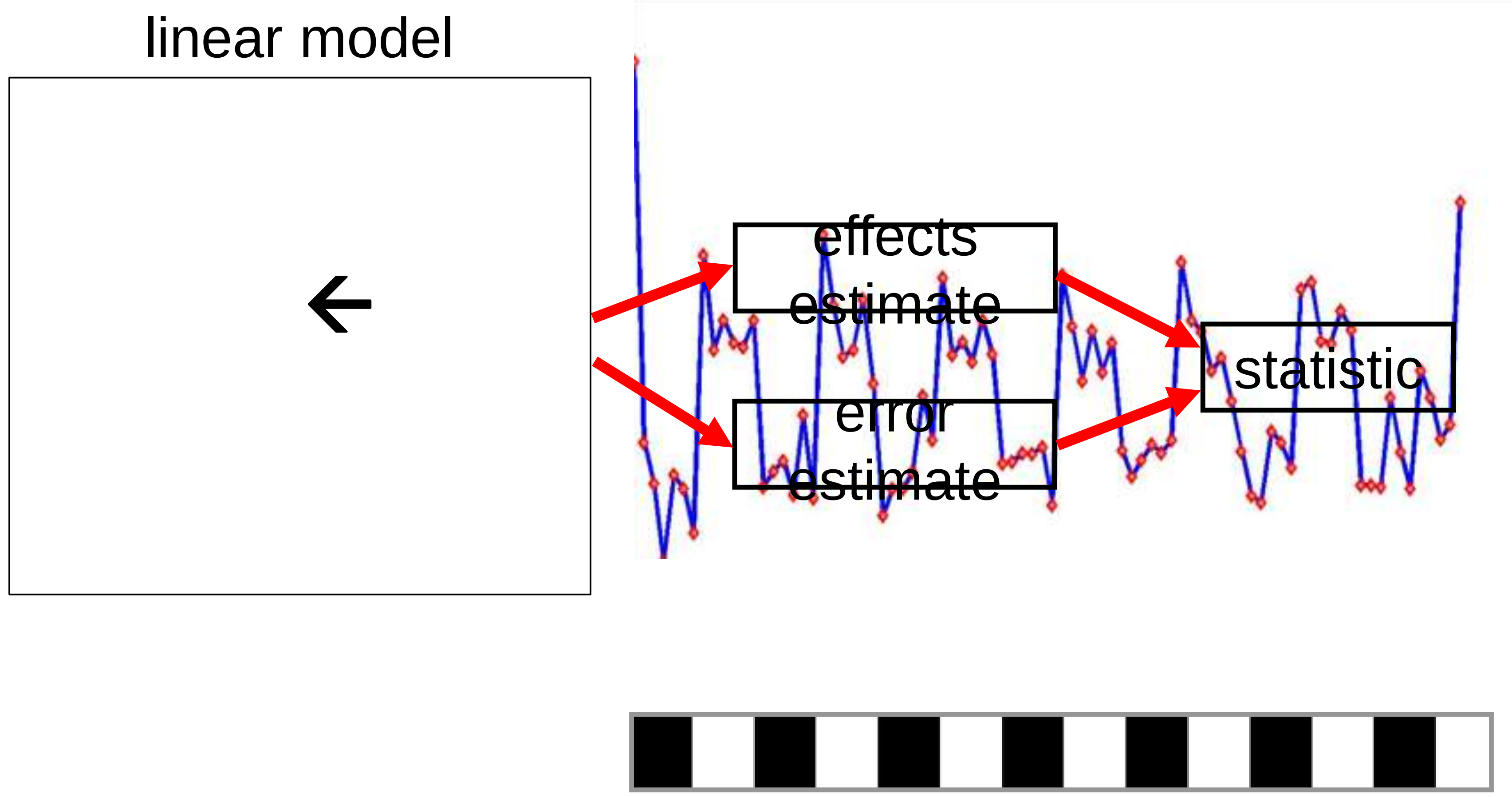


Image a very simple experiment…

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

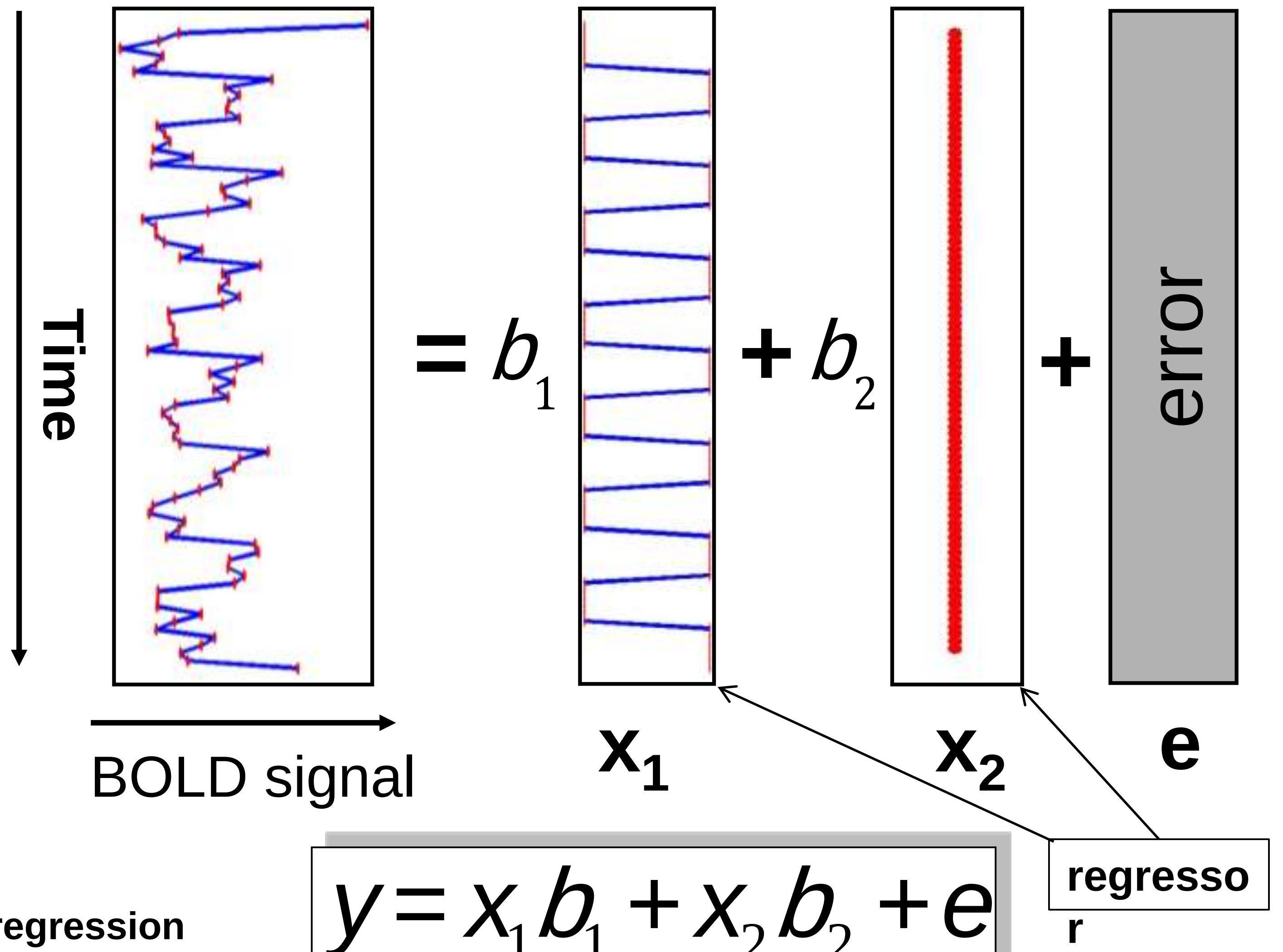


You need a model of your data…



Explain your data…

as a combination of experimental manipulation, confounds and errors

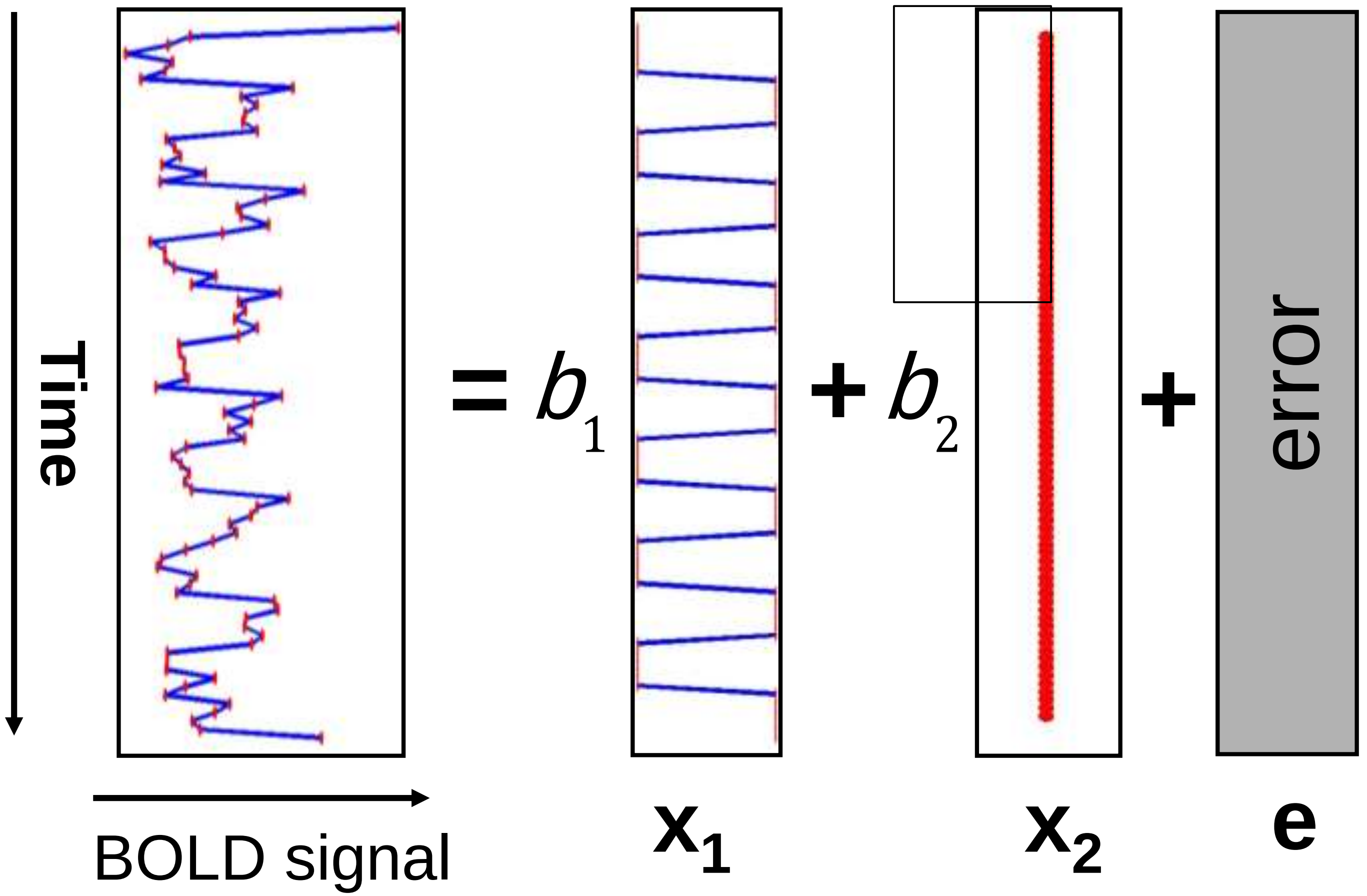


Single voxel regression model:

$$y = x_1 b_1 + x_2 b_2 + e$$

Explain your data…

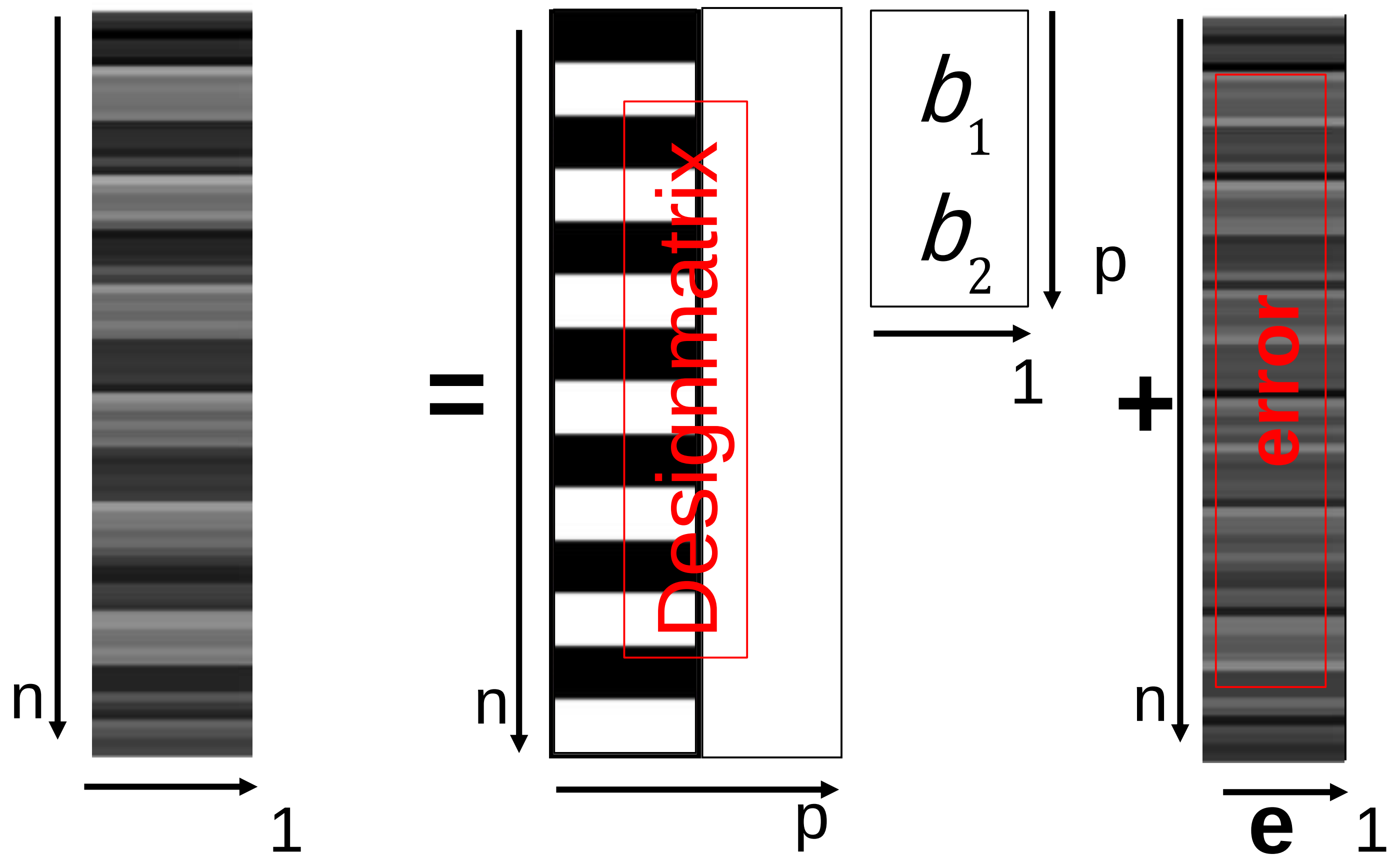
as a combination of experimental manipulation,confounds and errors



Single voxel regression model:

$$y = X\beta + e$$

The black and white version in SPM



$$y = X\beta + e$$

n: number of scans
p: number of regressors

Model assumptions

Designmatrix

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

→ Talk: Experimental Design Wed 9:45 – 10:45

error

You want to estimate your parameters such that you minimize:

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

This can be done using an **Ordinary least squares** estimation (OLS) assuming an i.i.d. error

error

GLM assumes identical and independently distributed errors

i.i.d. = error covariance is a scalar multiple of the identity matrix

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

$$Cov(e) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

(columns: t1, t2; rows: t1, t2)

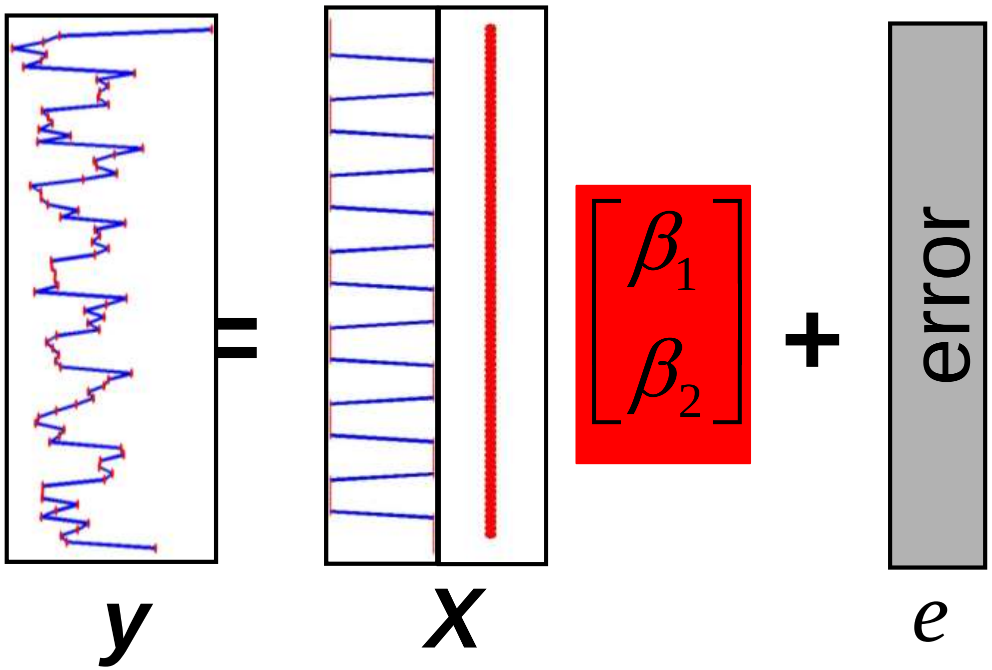
non-identity

$$Cov(e) = \begin{bmatrix} 4 & 0 \\ 0 & 1 \end{bmatrix}$$

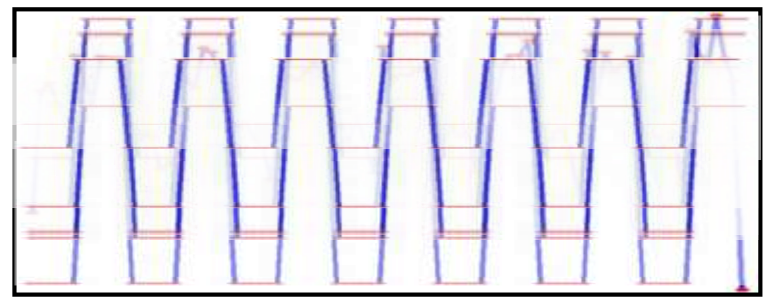
non-independence

$$Cov(e) = \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix}$$

How to fit the model and estimate the parameters?



„Option 1": Per hand



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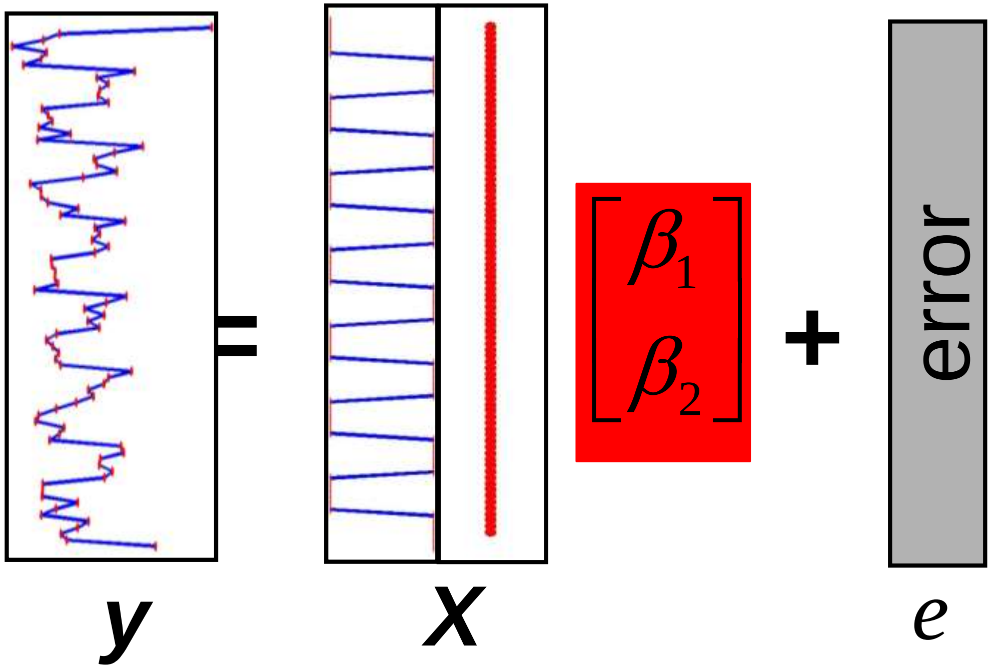

OLS (Ordinary Least Squares)

$$\hat{y} = X\hat{b}$$

Data predicted by our model

$$e = y - \hat{y}$$

Error between predicted and actual data

$$e = y - X\hat{b}$$

Goal is to determine the betas such that we minimize the quadratic error

$$\min(e^T e) = \min((y - X\hat{b})^T (y - X\hat{b}))$$

OLS (Ordinary Least Squares)

$$e^T e = (y - X\hat{b})^T (y - X\hat{b})$$

The goal is to minimize the quadratic error between data and model

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$$e^T e = (y^T - \hat{b}^T X^T)(y - X\hat{b})$$

This is a scalar and the transpose of a scalar is a scalar ☺

$$e^T e = y^T y - y^T X\hat{b} - \hat{b}^T X^T y + \hat{b}^T X^T X\hat{b}$$

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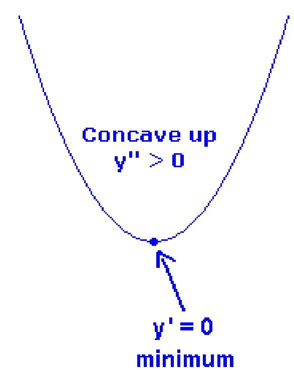
$$e^T e = y^T y - 2\hat{b}^T X^T y + \hat{b}^T X^T X\hat{b}$$

$$\frac{\partial e^T e}{\partial \hat{b}} = -2X^T y + 2X^T X\hat{b}$$

$$0 = -2X^T y + 2X^T X\hat{b}$$

You find the extremum of a function by taking its derivative and setting it to zero



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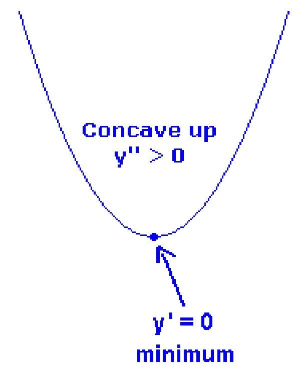


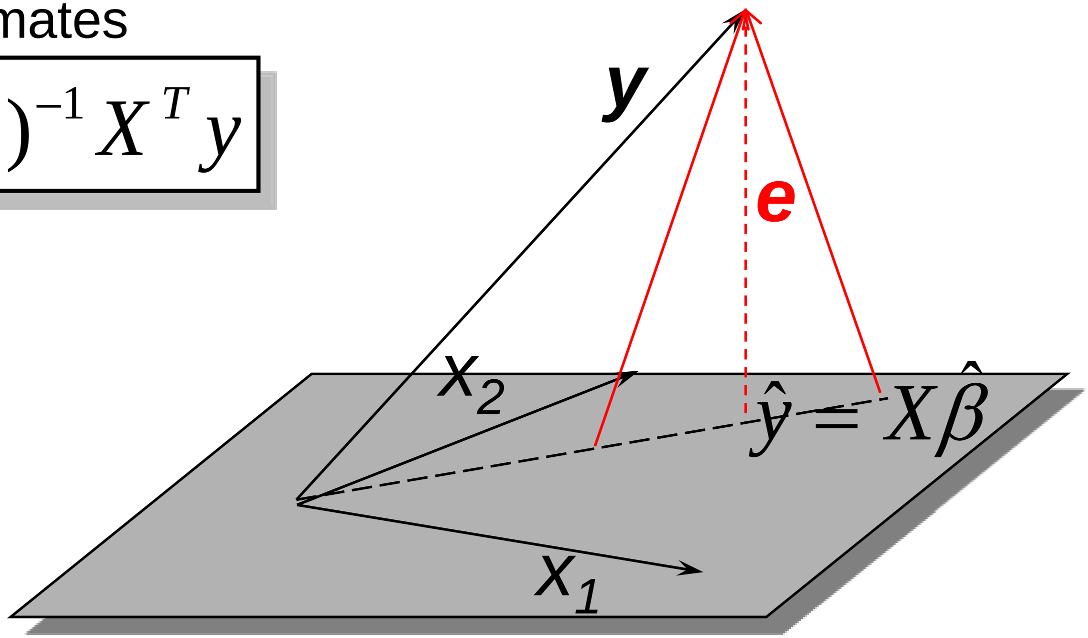
$$\hat{b} = (X^T X)^{-1} X^T y$$

SOLUTION: OLS of the Parameters

A geometric perspective on the GLM

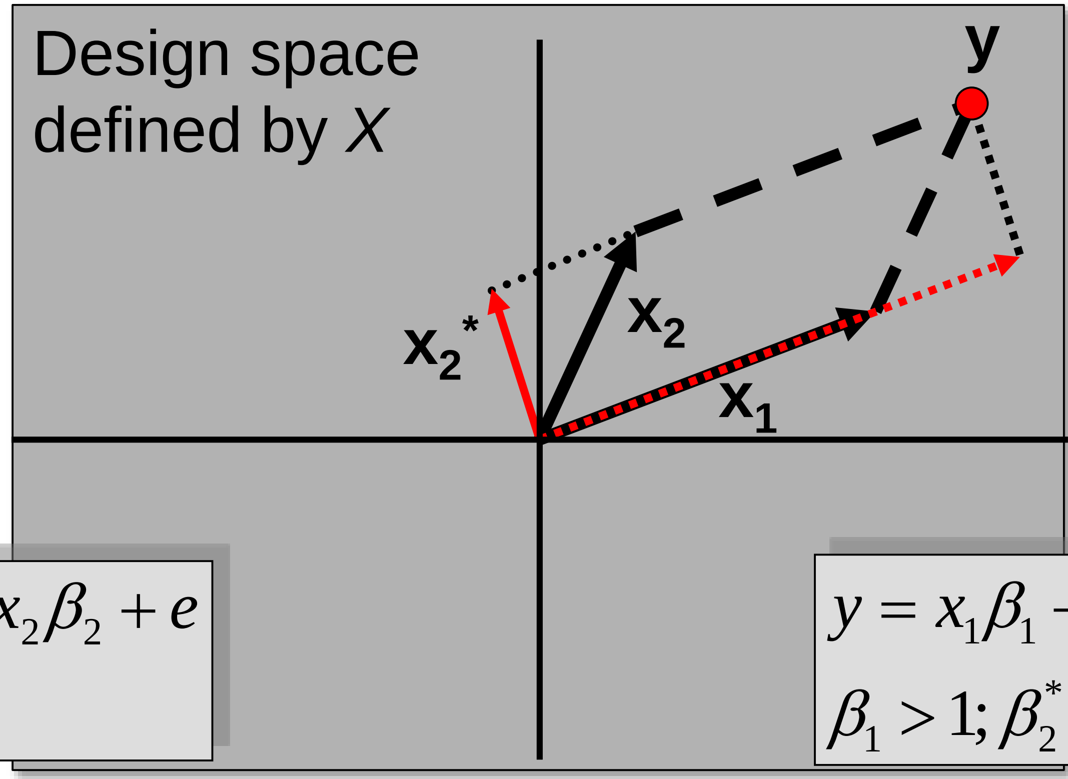
OLS estimates

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



Design space
defined by *X*

Correlated and orthogonal regressors



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

$$\beta_1 = \beta_2 = 1$$

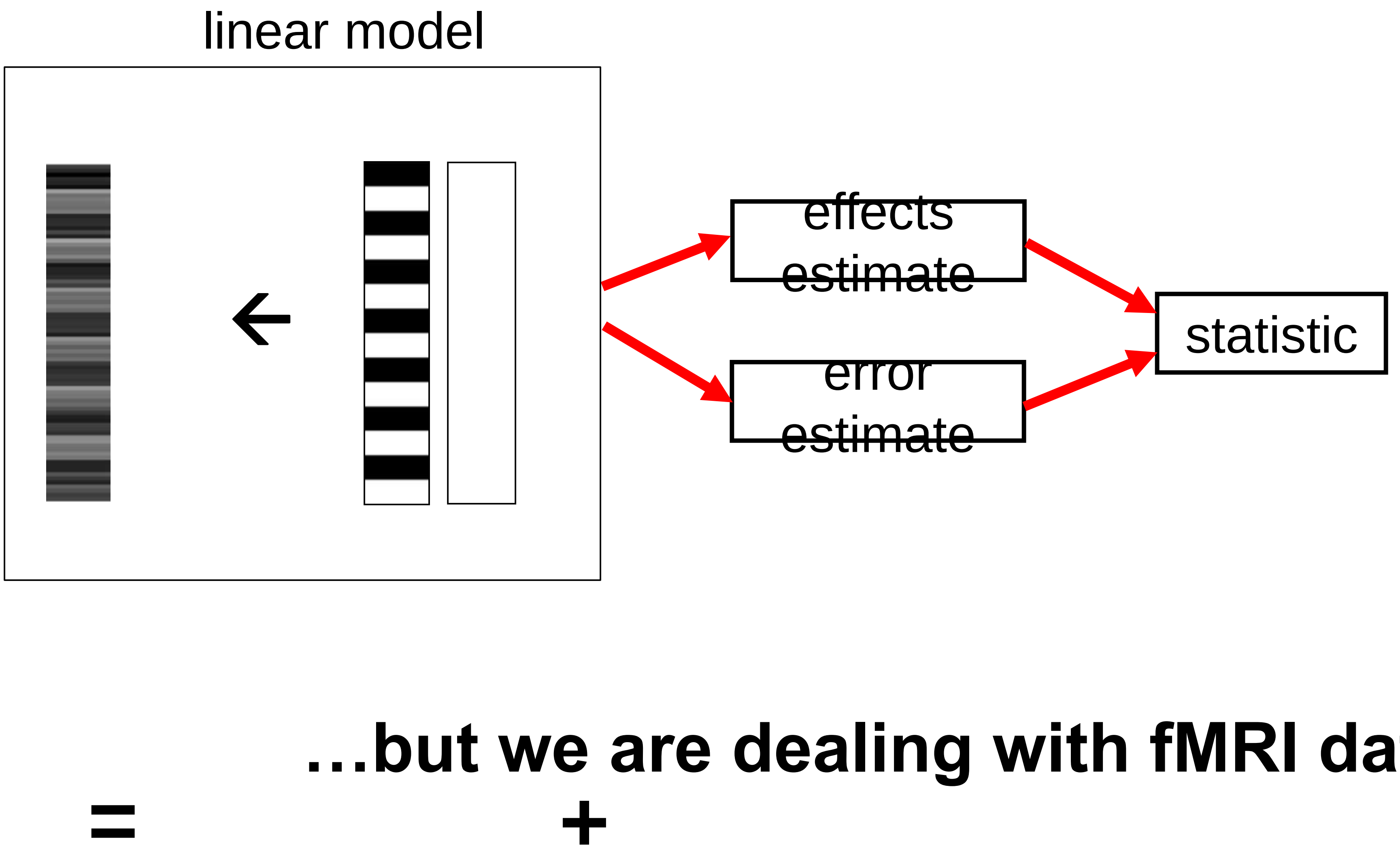
$$y = x_1\beta_1 + x_2^*\beta_2^* + e$$

$$\beta_1 > 1; \beta_2^* = 1$$

Correlated regressors = explained variance is shared between regressors

When x_2 is orthogonalized with regard to x_1, only the parameter estimate for x_1 changes, not that for x_2!

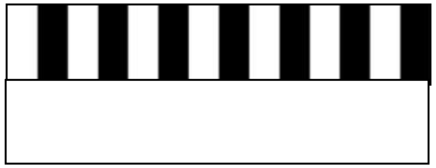
We are nearly there…



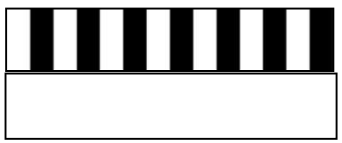
…but we are dealing with fMRI data

What are the problems?

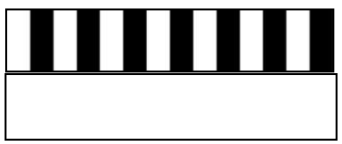
Design



Error



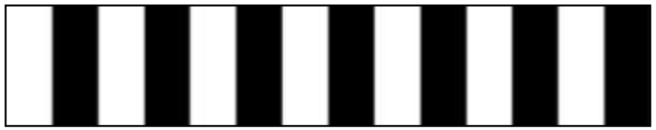
1. BOLD responses have a delayed and dispersed form.

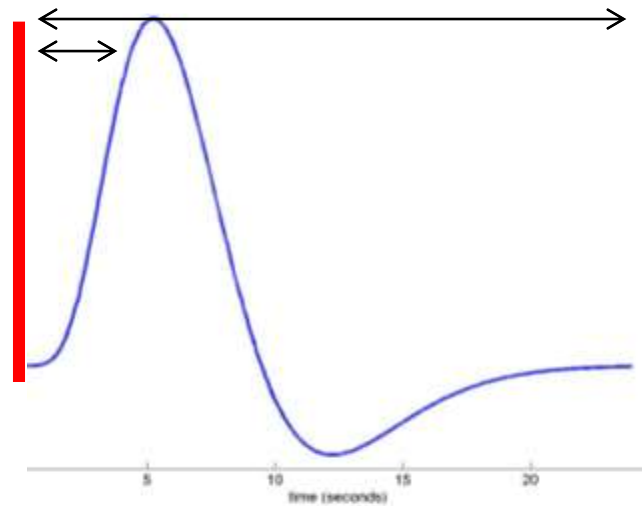


2. The BOLD signal includes substantial amounts of low-frequency noise.

3. The data are serially correlated (temporally autocorrelated). This violates the assumptions of the noise model in the GLM

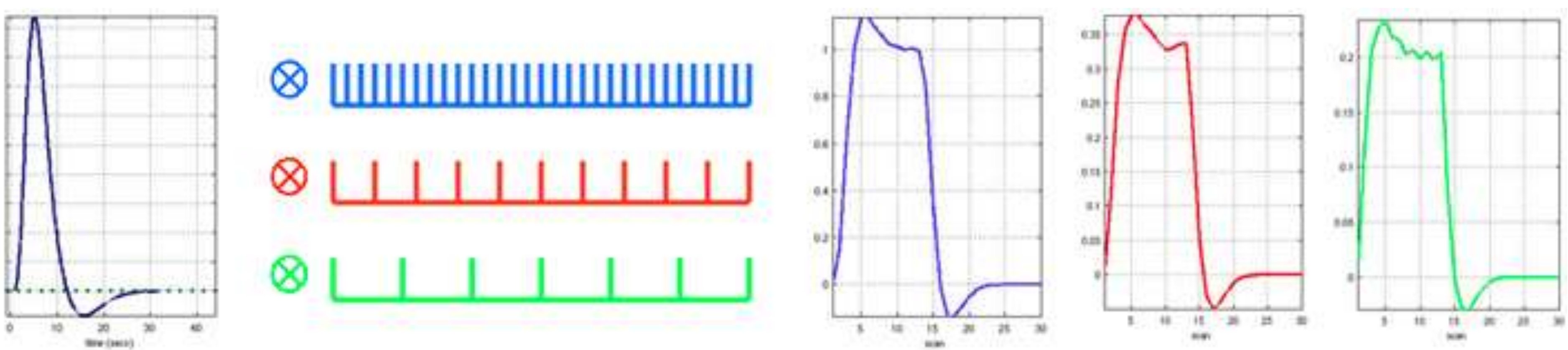
Problem 1: Shape of BOLD response





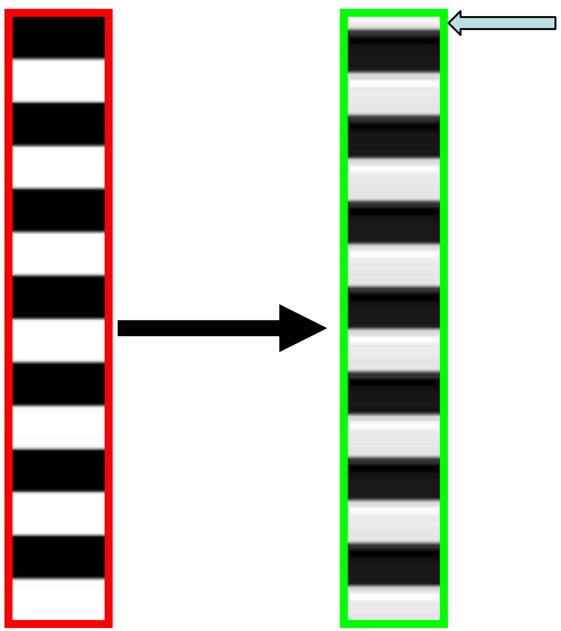
$$f \otimes g(t) = \int_0 f(\tau)g(t-\tau)d\tau$$

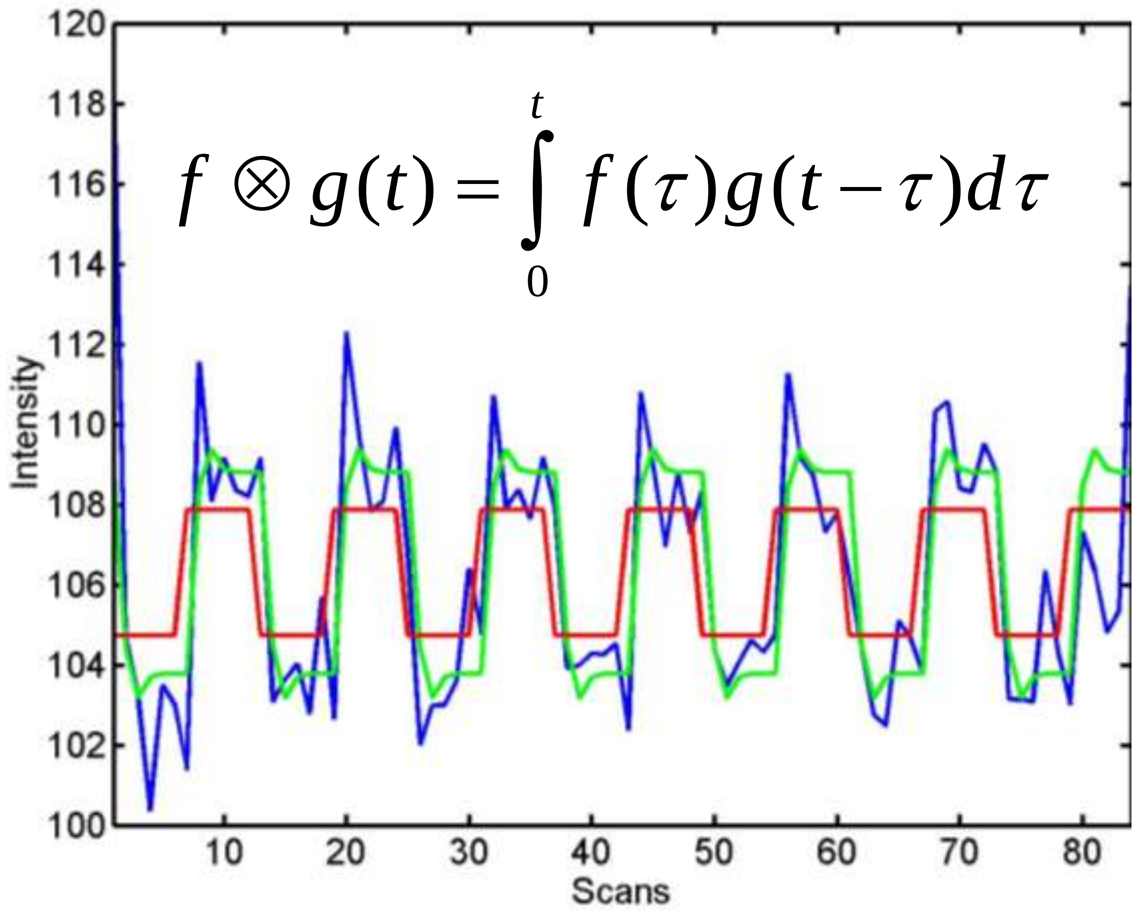
The response of a linear time-invariant (LTI) system is the convolution of the input with the system's response to an impulse (delta function).



Solution: Convolution model of the BOLD response

expected BOLD response
= input function x impulse response function (HRF)

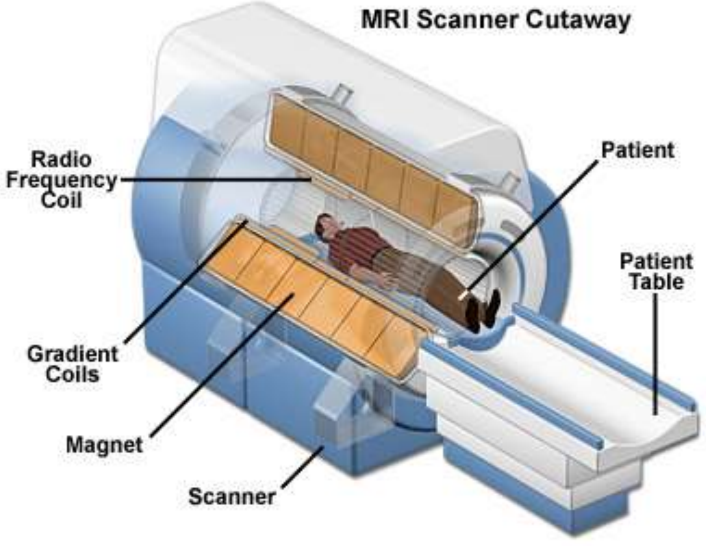


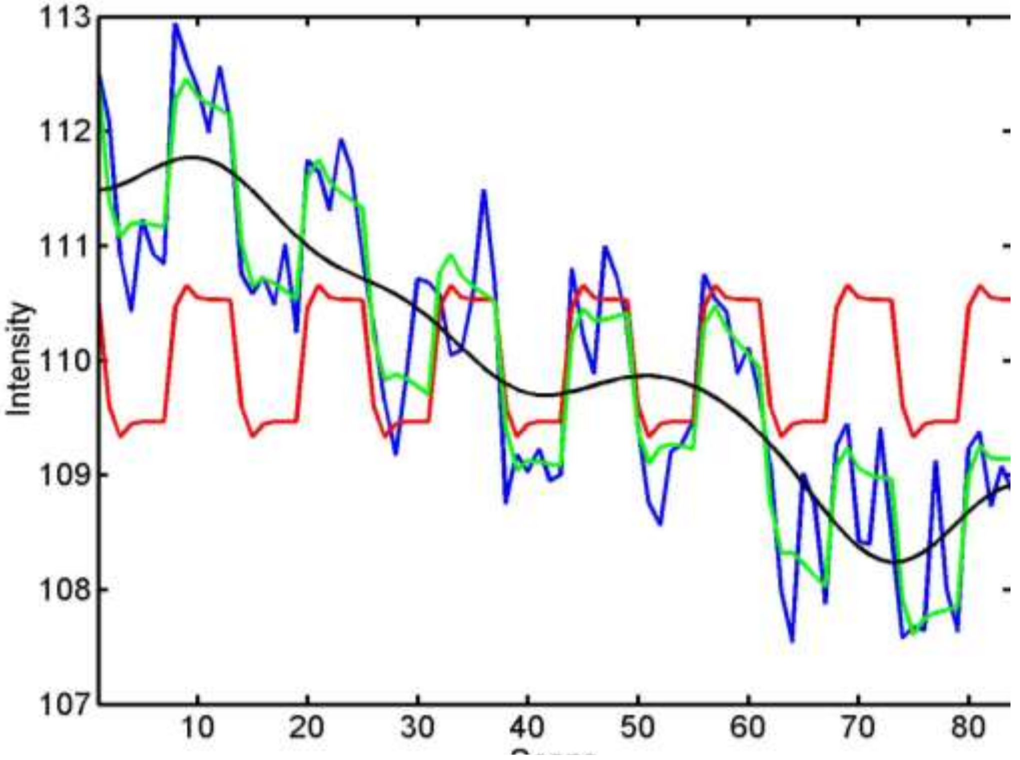


$$f \otimes g(t) = \int_0^t f(\tau) g(t-\tau) d\tau$$

blue = data
green = predicted response, taking convolved with HRF
red = predicted response, NOT taking into account the HRF

Problem 2: Low frequency noise





blue = data

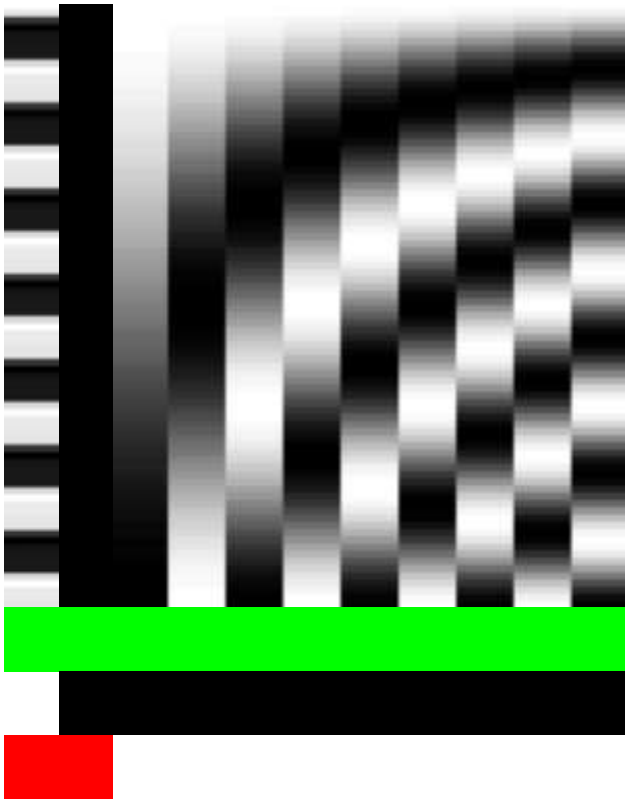
black = mean + low-frequency drift

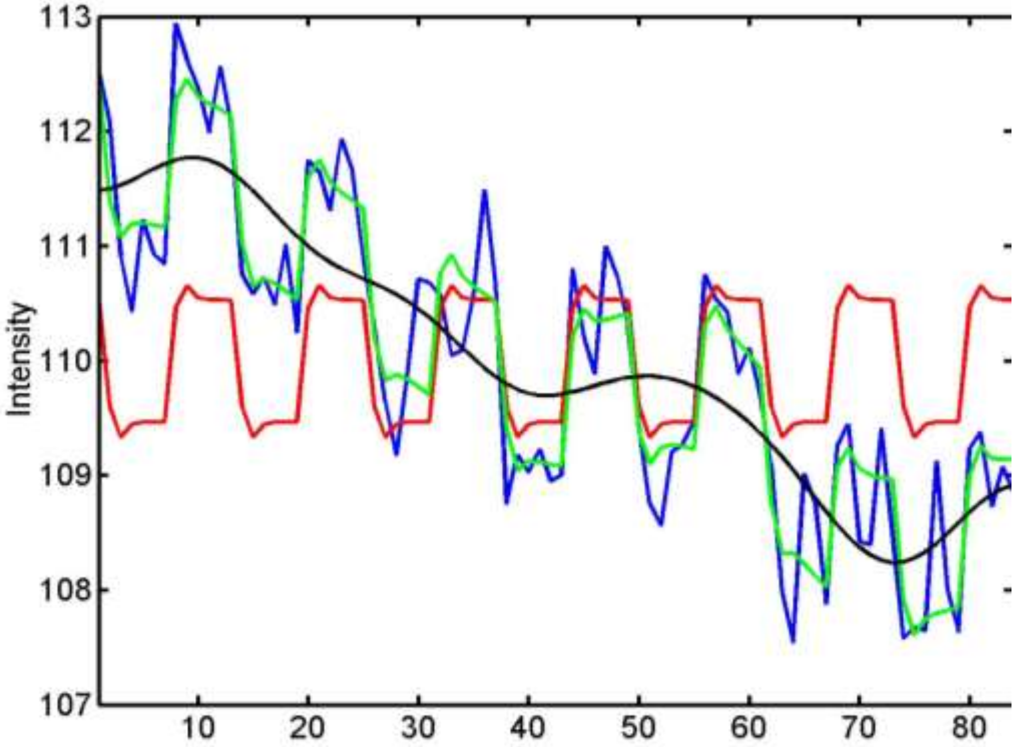
green = predicted response, taking into account low-frequency drift

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

Problem 2: Low frequency noise

Linear model





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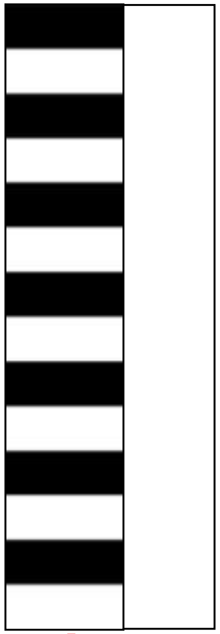
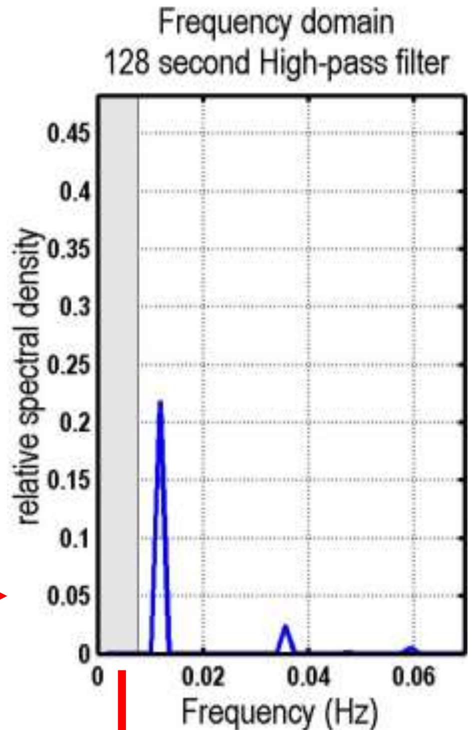
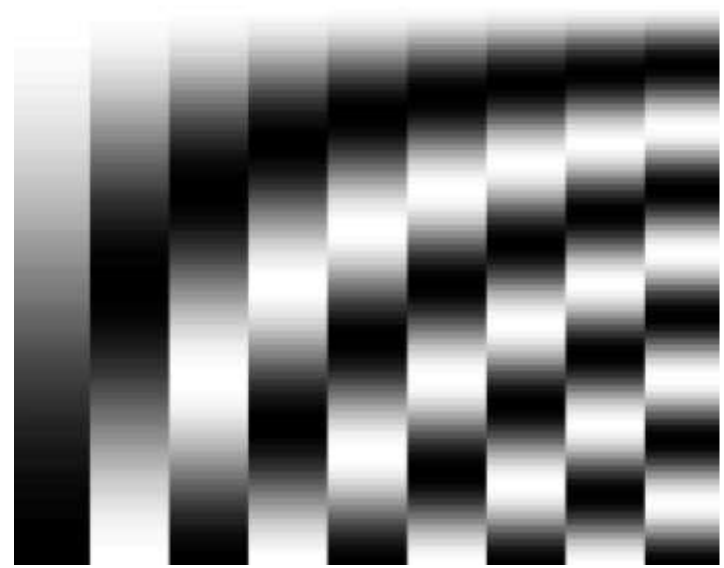
Solution 2: High pass filtering





discrete cosine transform (DCT) set



Problem 3: Serial correlations

i.i.d

$$Cov(e) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

(columns: t1, t2; rows: t1, t2)

non-identity

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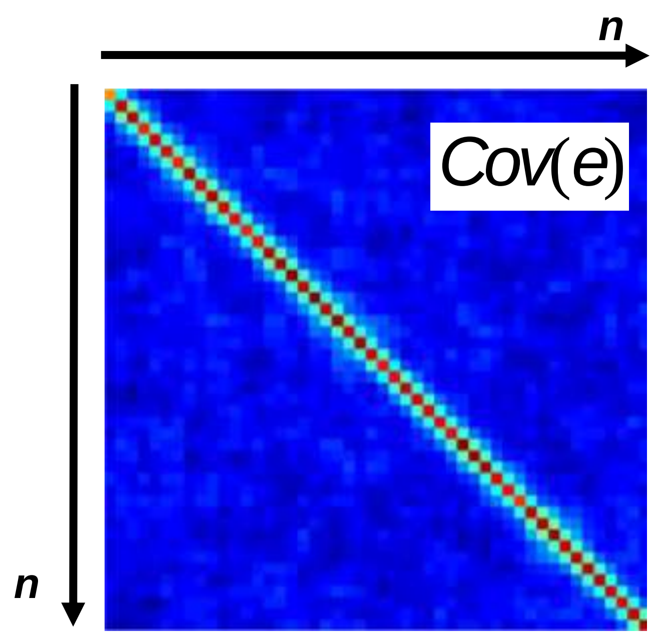
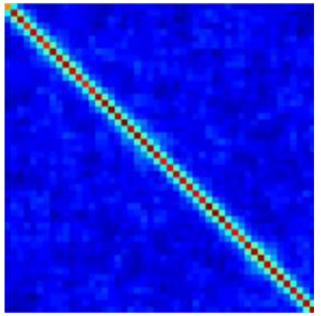


n: number of scans

Problem 3: Serial correlations



- **Transform the signal into a space where the error is iid**

This is i.i.d (brace over We)

$$Wy = WX\beta + We$$

- ***Pre-whitening***:

  1. Use an enhanced noise model with multiple error covariance components, i.e. e ~ $N(0,\sigma^2 V)$ instead of e ~ $N(0, \sigma^2 I)$.

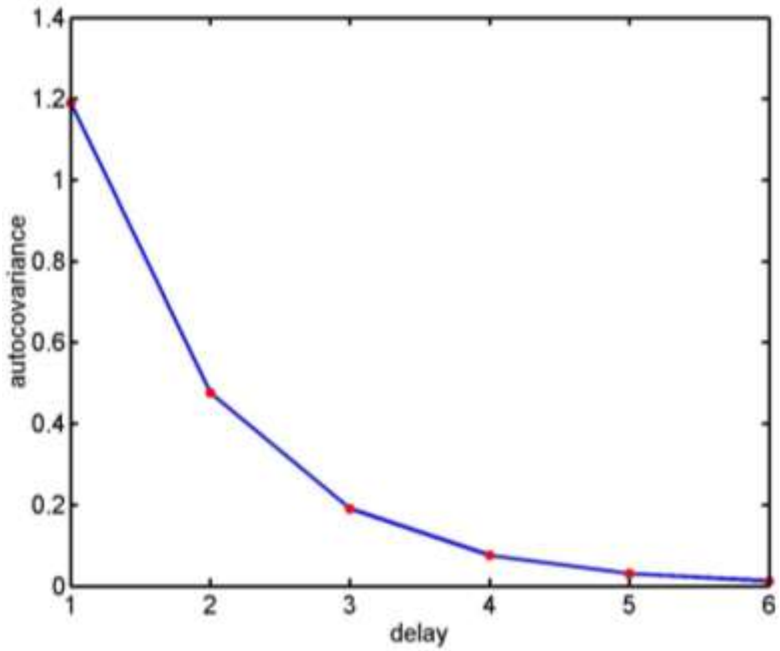
  2. Use estimated serial correlation to specify filter matrix W for whitening the data.

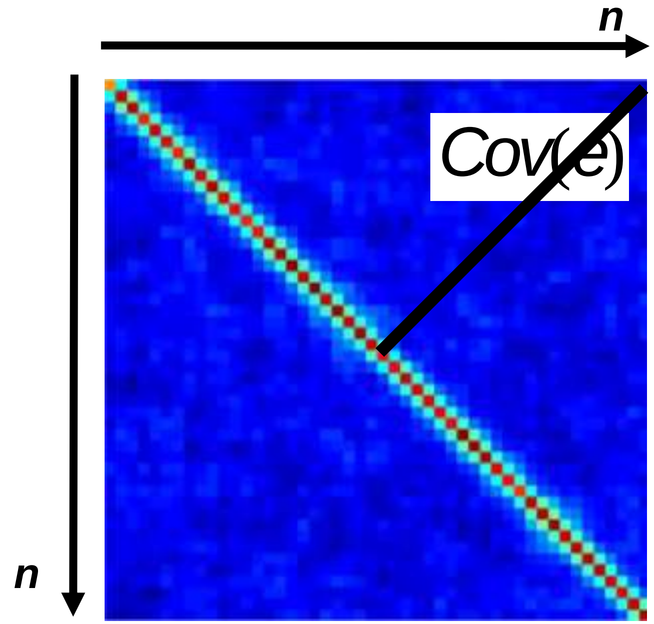
Problem 3: How to find W → Model the noise

$$e_t = ae_{t-1} + \varepsilon_t \text{ with } \varepsilon_t \sim N(0, \sigma^2)$$

1st order autoregressive process: AR(1)

autocovariance function





n: number of scans

Model the noise: Multiple covariance components

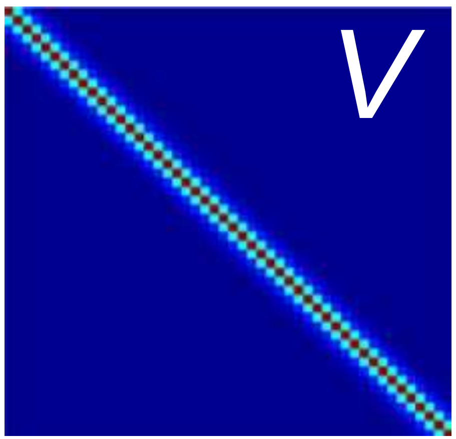
$$e \sim N(0, \sigma^2 V)$$

enhanced noise model

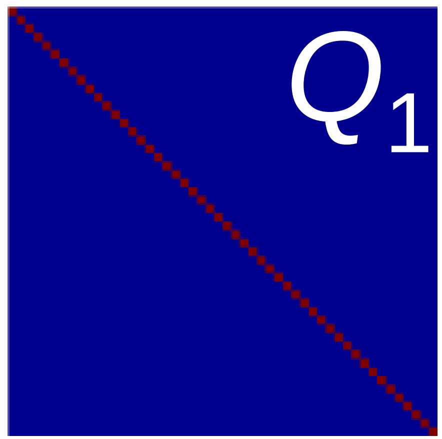
$$V \propto Cov(e)$$

$$V = \sum \lambda_i Q_i$$

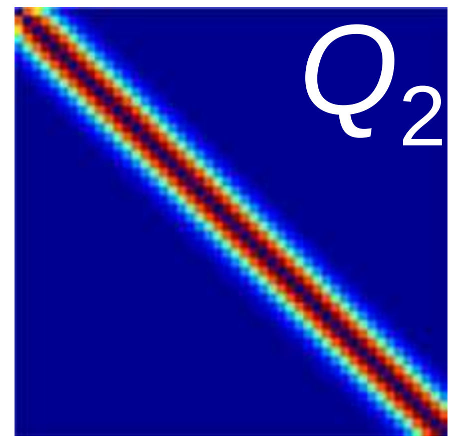
error covariance components *Q* and hyperparameters



$= /_1$



$+ /_2$



Estimation of hyperparameters with EM (expectation maximisation) or ReML (restricted maximum likelihood).

How do we define *W* ?

- Enhanced noise model

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

- Remember linear transform for Gaussians

$$x \sim N(\mu, \sigma^2), y = ax$$
$$\Rightarrow y \sim N(a\mu, a^2\sigma^2)$$

- Choose *W* such that error covariance becomes spherical

$$We \sim N(0, \sigma^2 W^2 V)$$
$$\Rightarrow W^2 V = I$$
$$\Rightarrow W = V^{-1/2}$$

- **Conclusion:** *W* **is a simple function of** *V*

$$Wy = WX\beta + We \rightarrow y_s = X_s b + e_s$$

We are there…

- the GLM models the effect of your experimental manipulation on the acquired data

- GLM includes all known experimental effects and confounds

- estimates effects an errors on a voxel-by-voxel basis

Because we are dealing with fMRI data there are a number of problems we need to take care of:

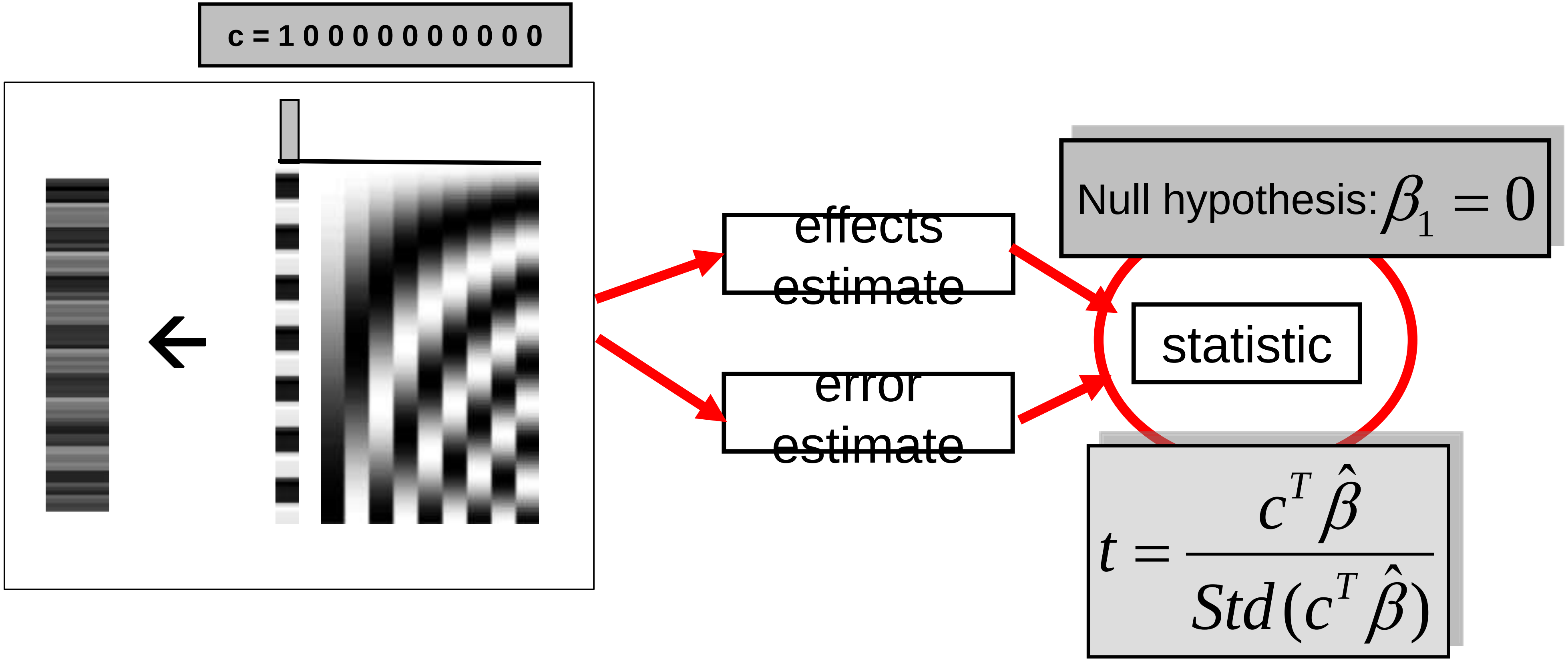
- Convolution with a canonical HRF

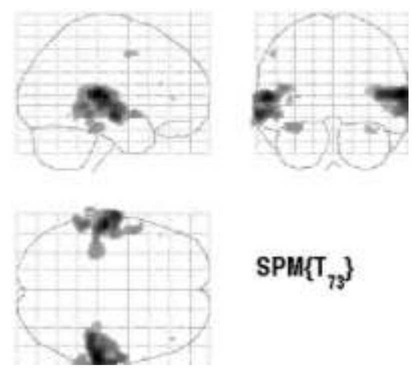
- High-pass filtering to account for low-frequency drifts

- Estimation of multiple variance components (e.g. to account for serial correlations)

= +

We are there…



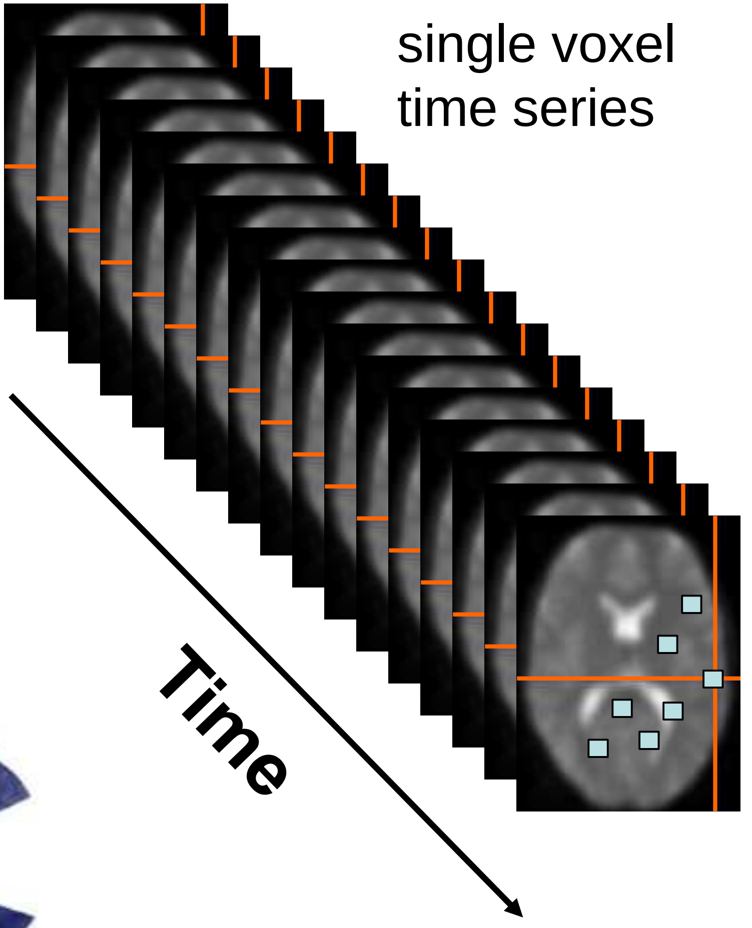


→ Talk: Statistical Inference and design efficiency. Next Talk

So far we have looked at a single voxel…

- Mass-univariate approach:
  GLM applied to > 100,000 voxels

- Threshold of p<0.05 more than 5000 voxels significant by chance!



- Massive problem with multiple comparisons!

- Solution: Gaussian random field theory

Outlook: further challenges

- correction for multiple comparisons → Talk: Multiple Comparisons Wed 8:30 – 9:30
- variability in the HRF across voxels → Talk: Experimental Design Wed 9:45 – 10:45
- limitations of frequentist statistics → Talk: entire Friday
- GLM ignores interactions among voxels → Talk: Multivariate Analysis Thu 12:30 – 13:30

Thank you for listening!

- **Friston, Ashburner, Kiebel, Nichols, Penny (2007)** ***Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Elsevier.**

- Christensen R (1996) *Plane Answers to Complex Questions: The Theory of Linear Models*. Springer.

- Friston KJ et al. (1995) Statistical parametric maps in functional imaging: a general linear approach. *Human Brain Mapping* 2: 189-210.