The general linear model and Statistical Parametric Mapping

II: GLM for fMRI

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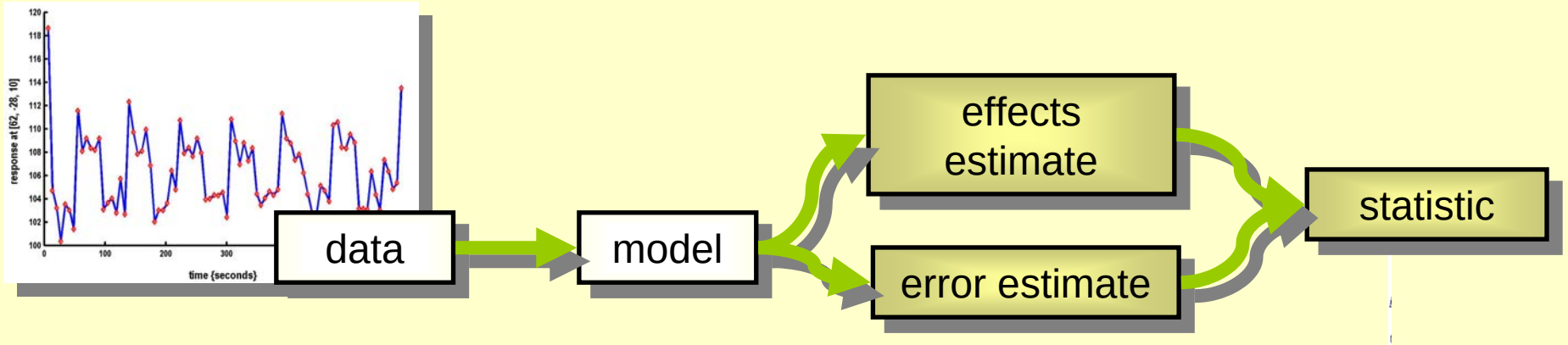
Overview

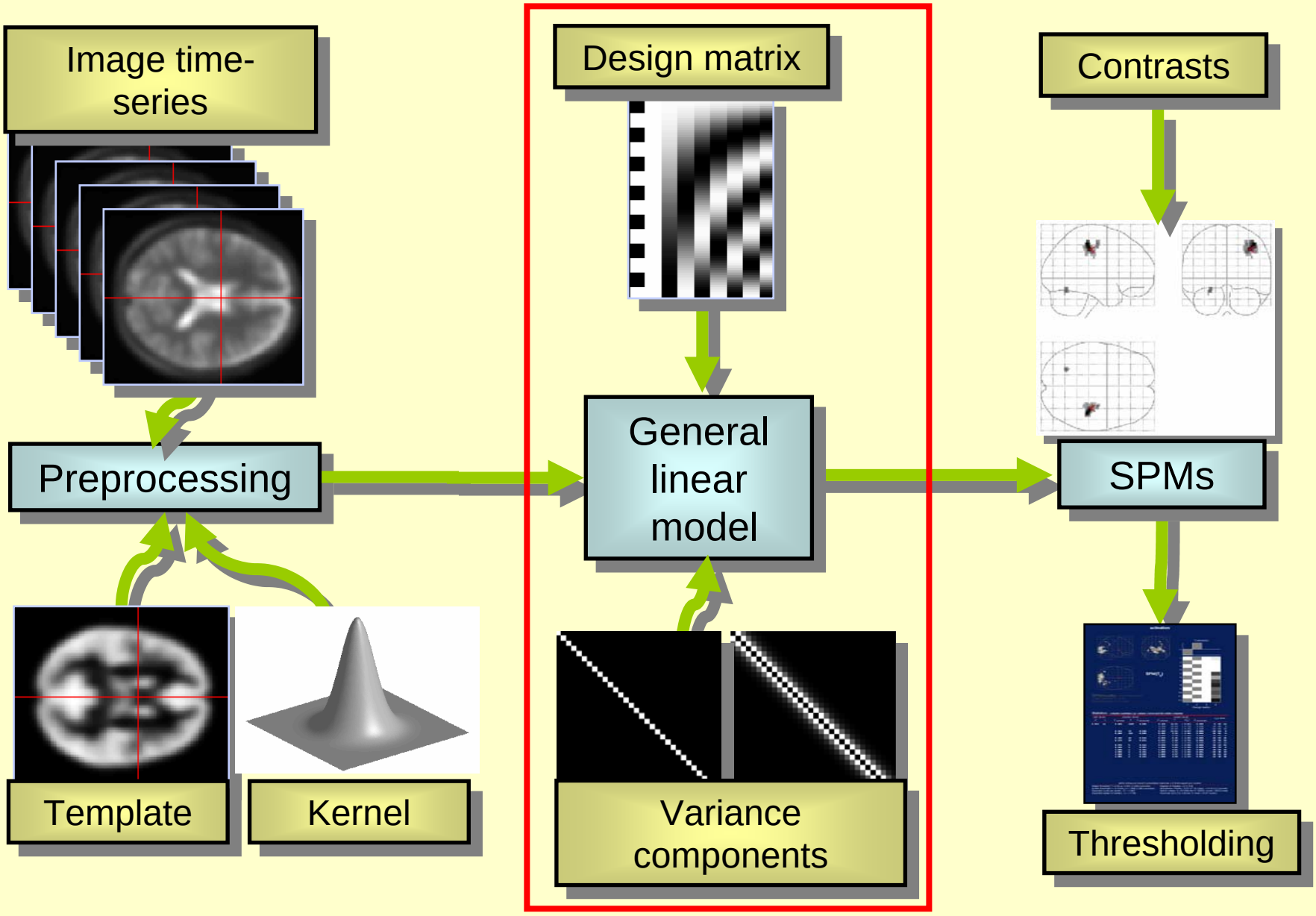
- Introduction
  - Two GLMs in 2-stage procedure
- General linear model(s) for fMRI
  - Low frequency noise
  - Haemodynamic response
  - Temporal basis functions
  - Time series

Modelling fMRI data

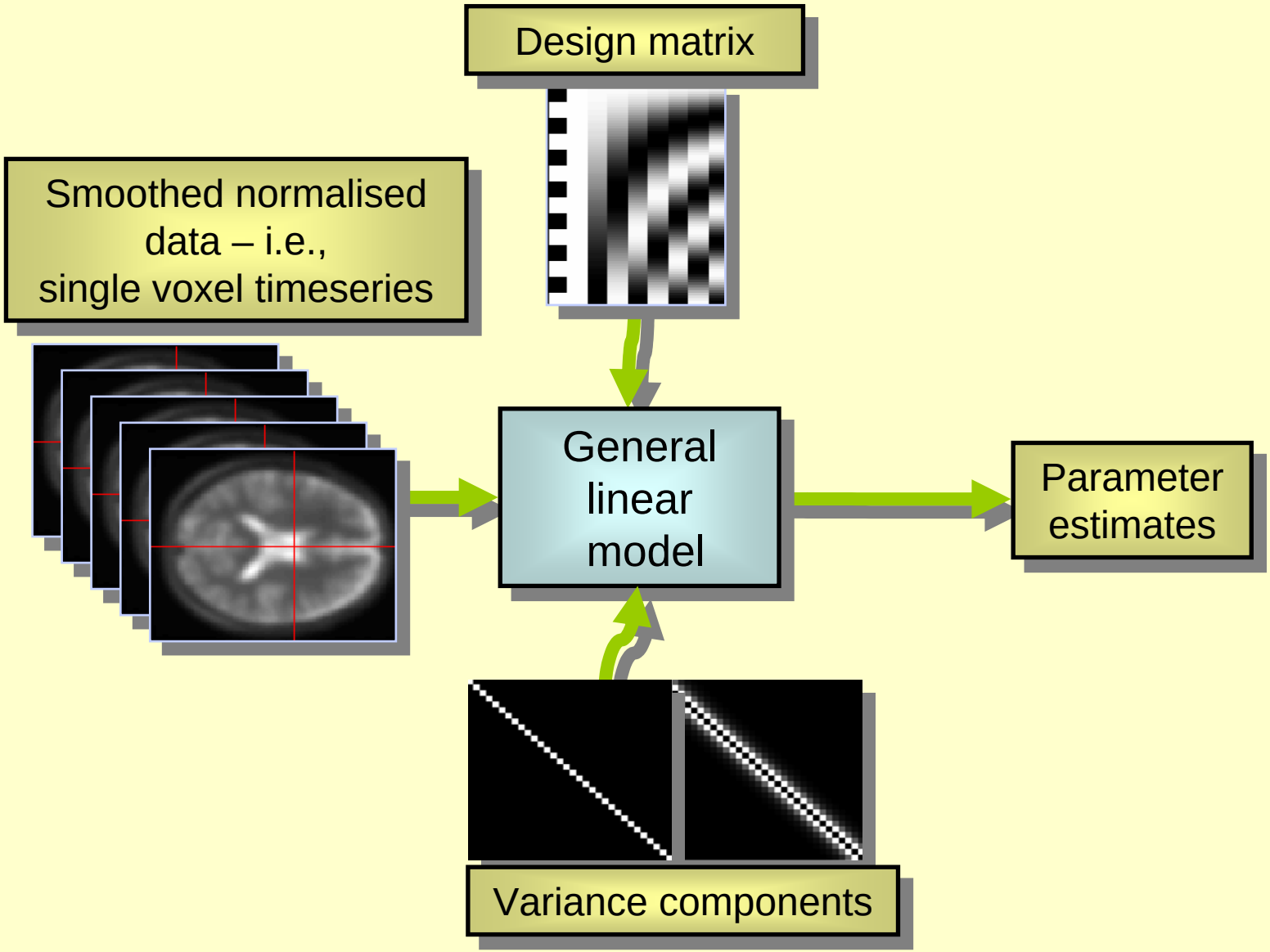
Why?	Make inferences about effects of interest
How?	1. Decompose data into effects and error 2. Form statistic using estimates of effects and error
Model?	Use any available knowledge



Overview of SPM



Modelling in SPM



2-stage GLM

'Summary statistic' random effects method

Single subject

Each has an independently acquired set of data
These are modelled separately
Models account for **within subjects variability**
Parameter estimates apply to individual subjects

1st level

Single subject **contrasts of parameter estimates** taken forward to 2nd level as (spm_con*.img) **'con images'**

Group/s of subjects

To make population inferences, 2nd level models account for **between subjects variability**
Parameter estimates apply to group effect/s

2nd level

Statistics compare **contrasts of 2nd level parameter estimates to 2nd level error**

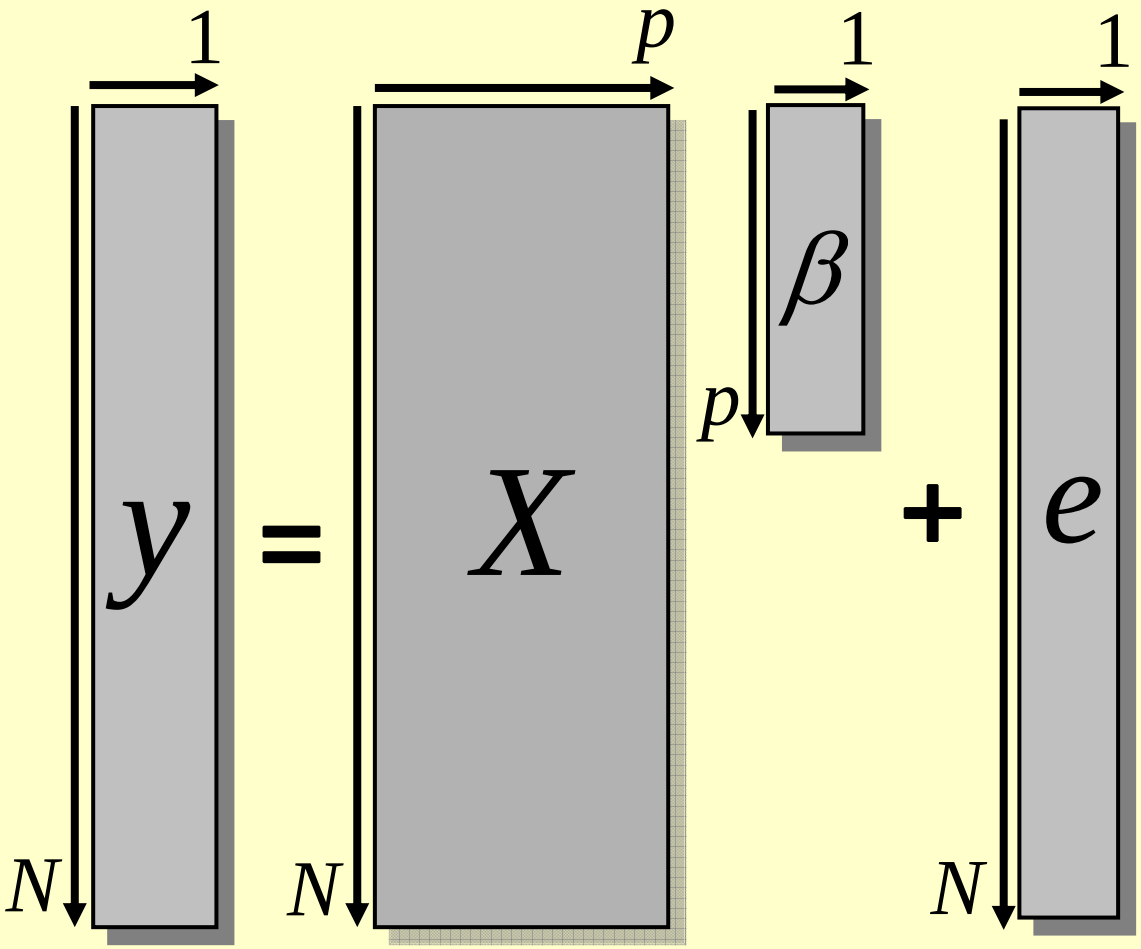
2-stage GLM

Single subject

Each has an independently acquired set of data
These are modelled separately
Models account for **within subjects variability**
Parameter estimates apply to individual subjects

1st level

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

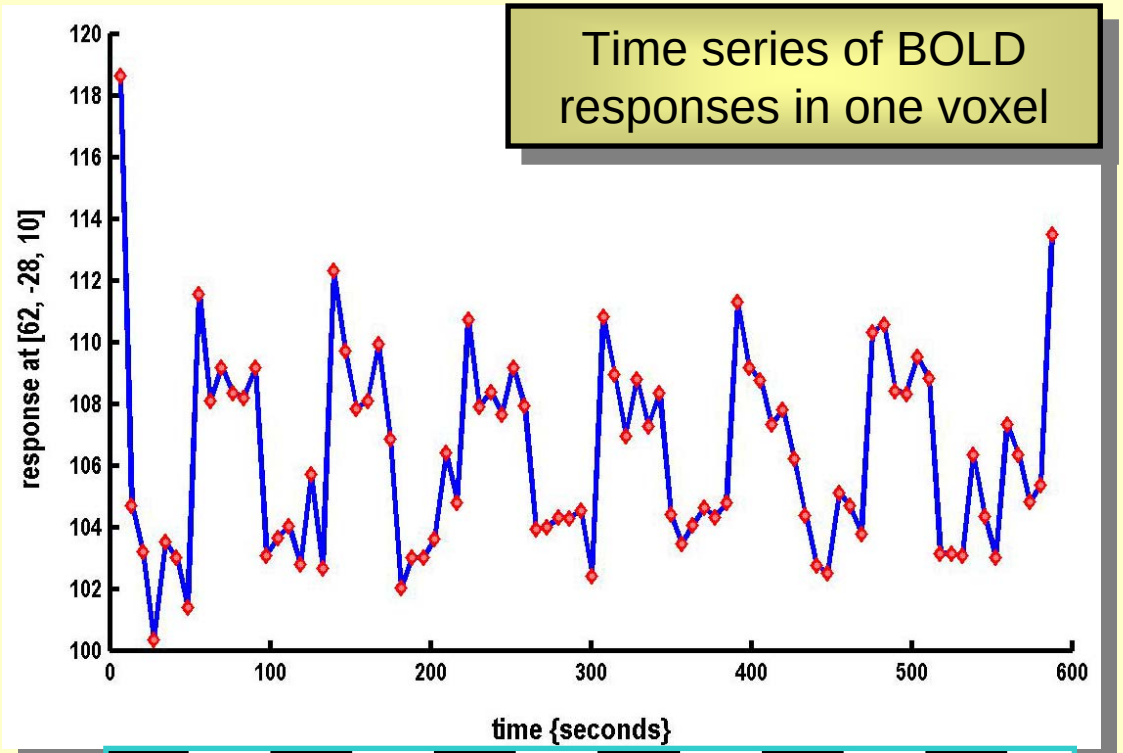
fMRI example

One session

Passive word listening versus rest

7 cycles of rest and listening

Each epoch 6 scans with 7 sec TR



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

The GLM applied to fMRI

What are the problems?

1. The BOLD signal includes substantial amounts of low-frequency noise.
2. BOLD responses have a delayed and dispersed form ('sluggish')
3. The data are a timeseries, so are serially correlated (temporally autocorrelated; for TR < ~8s)

→ Therefore they are not independent observations - violates the assumptions of the GLM's noise model

The GLM applied to fMRI

What are the solutions?

1. The data can be filtered to remove low-frequency (1/f) noise
2. Effects are convolved with haemodynamic (BOLD) response function (HRF), to capture the sluggish nature of the response
3. The data are modelled as a timeseries, taking account of temporal autocorrelation

The GLM applied to fMRI

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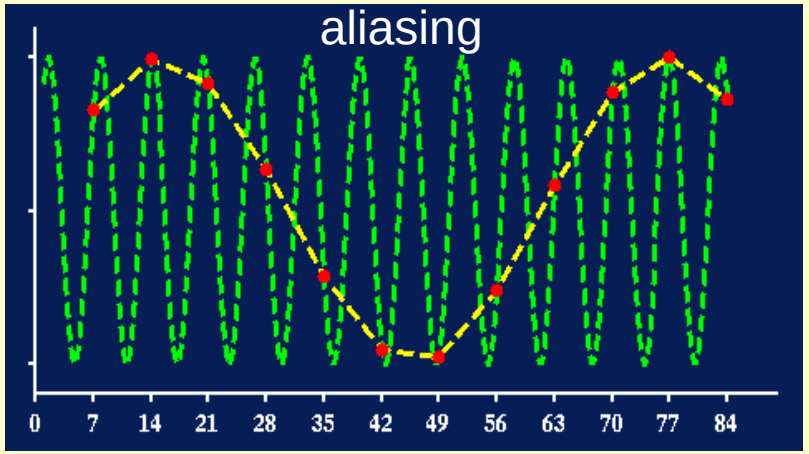
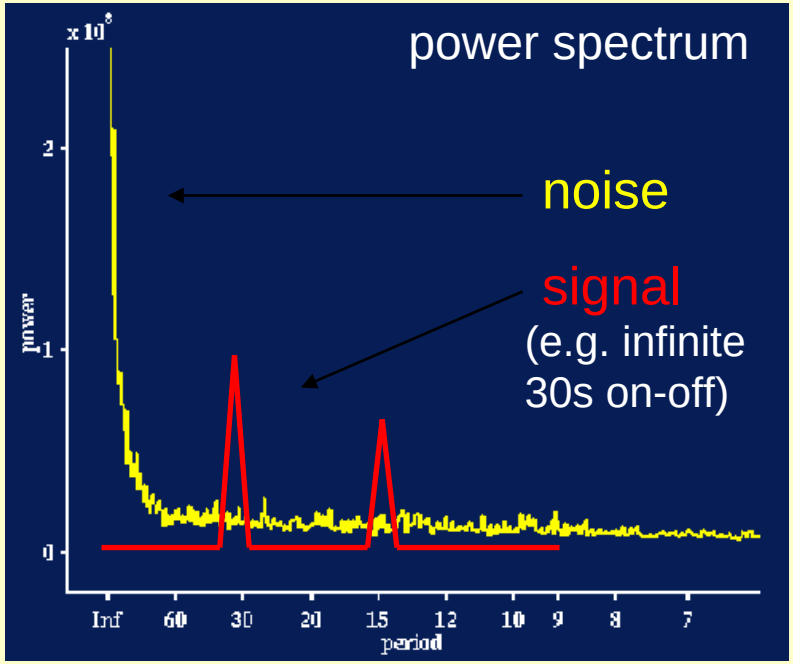
1. Low frequency noise

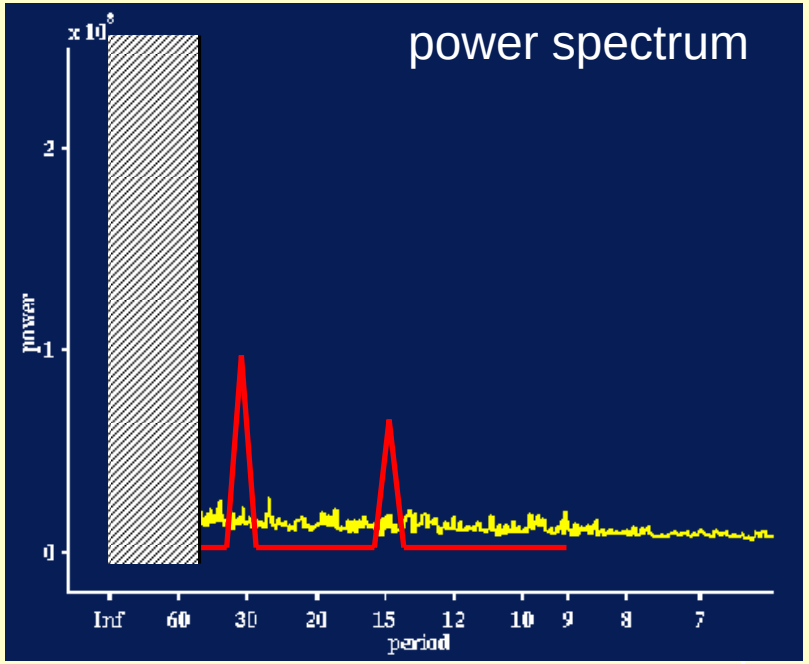
Physical (scanner drifts)

Physiological (aliased)

- cardiac (~1 Hz)
- respiratory (~ 0.25 Hz)

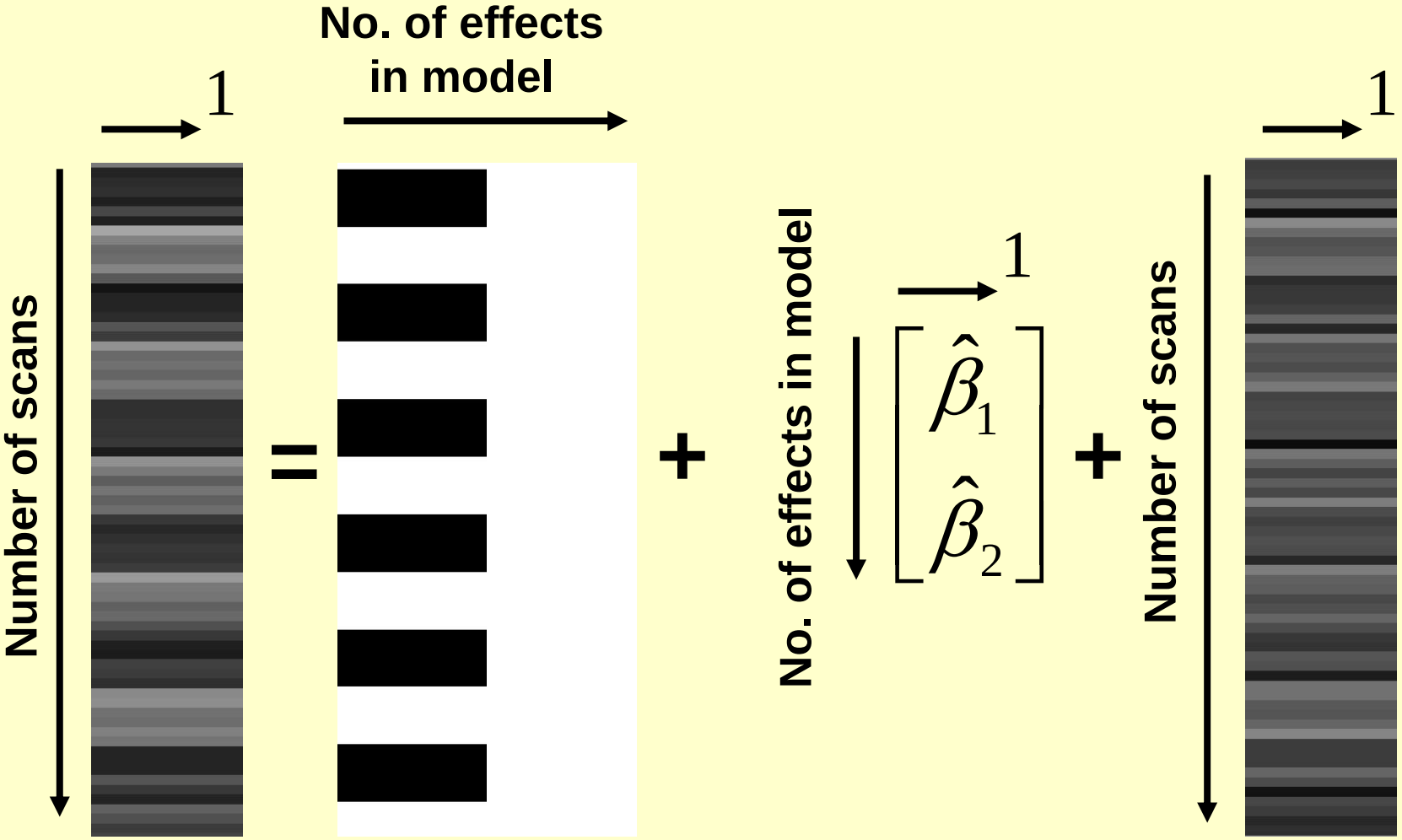






Regression model

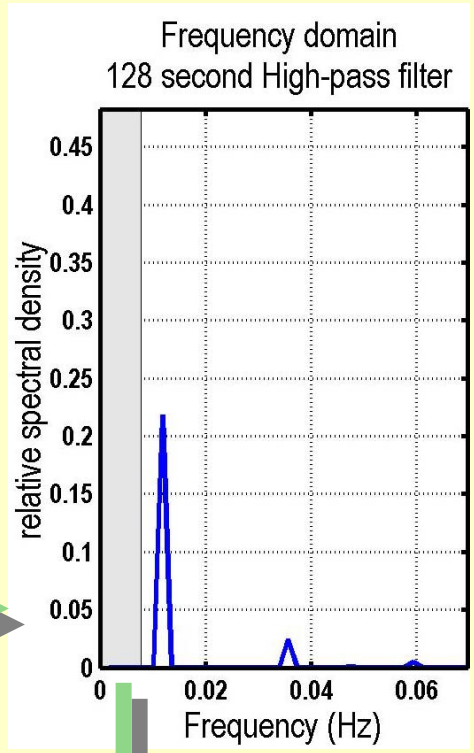
Single subject



$$Y = X_1 * \hat{\beta}_1 + \hat{\varepsilon}_1$$

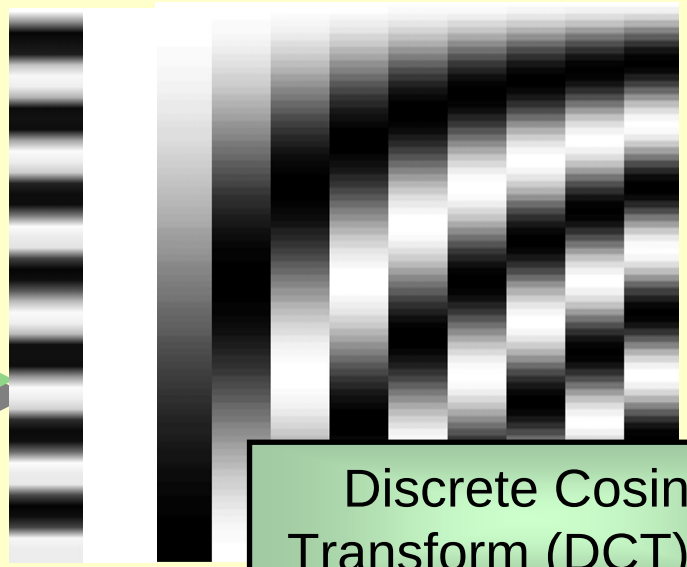
Add high pass filter

Single subject



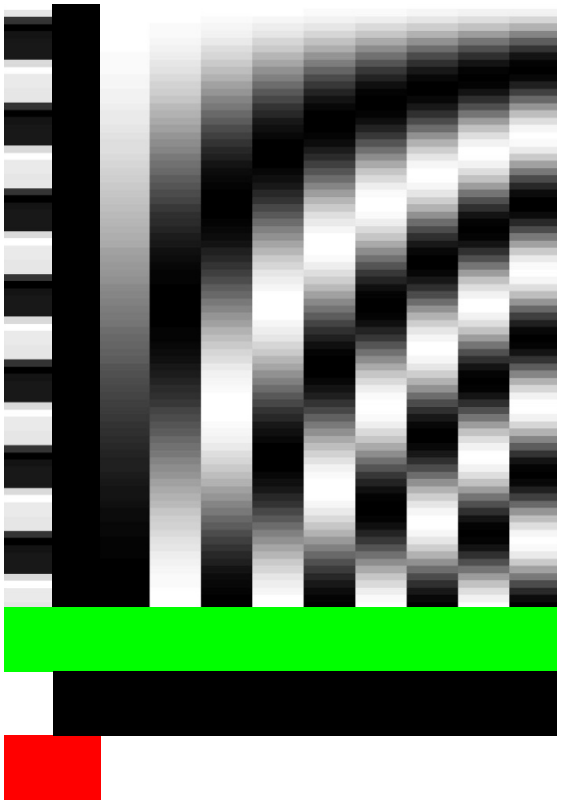
This means 'taking out' fluctuations below the specified frequency

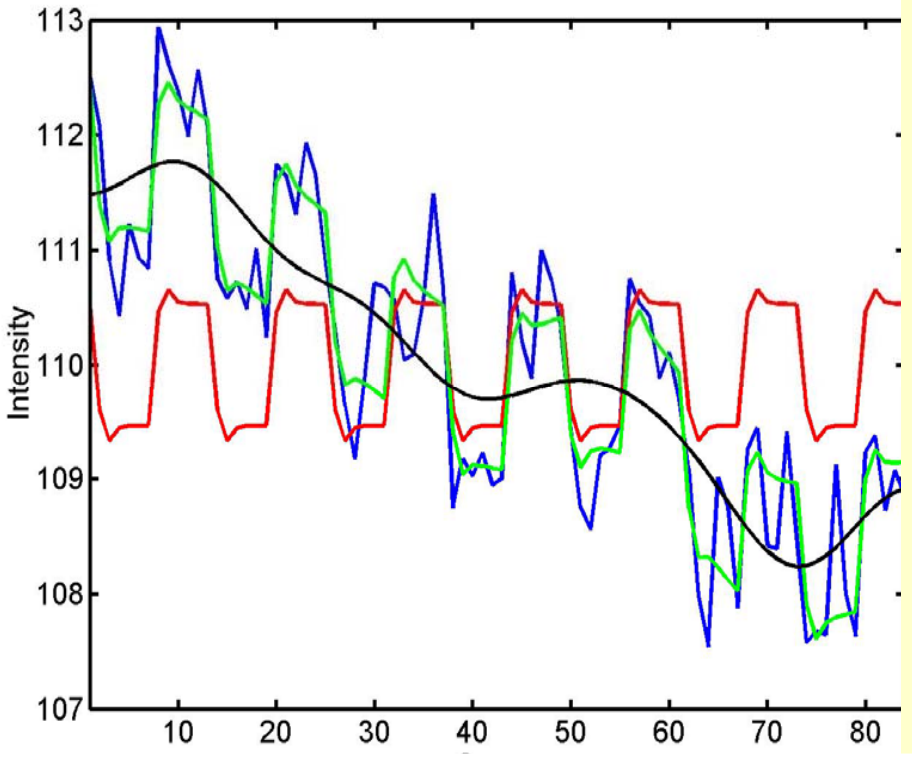
SPM implements by fitting low frequency fluctuations as effects of no interest



Discrete Cosine Transform (DCT) set

High pass filtering: example





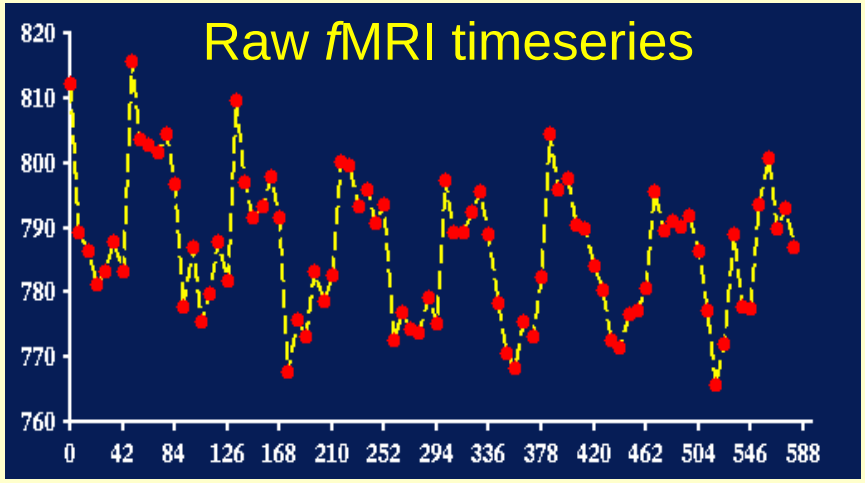
blue = data

black = mean + low-frequency drift

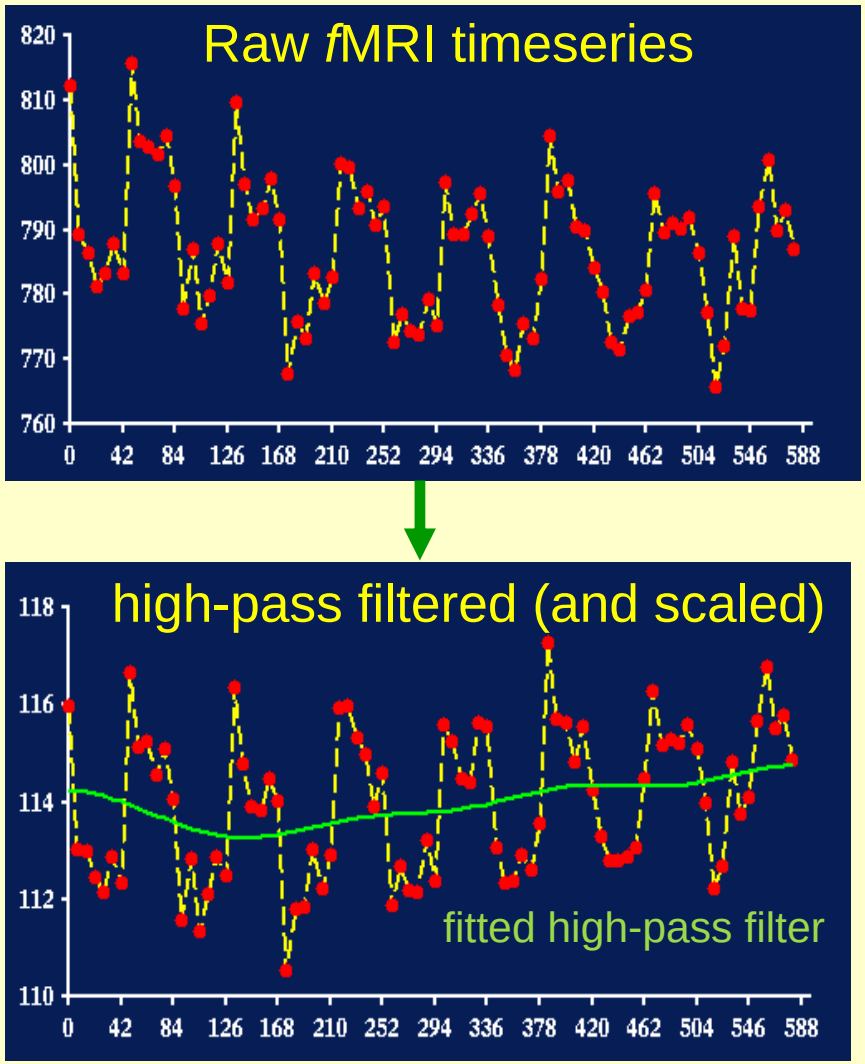
green = predicted response, taking into account low-frequency drift

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

Fitted & adjusted data



Fitted & adjusted data



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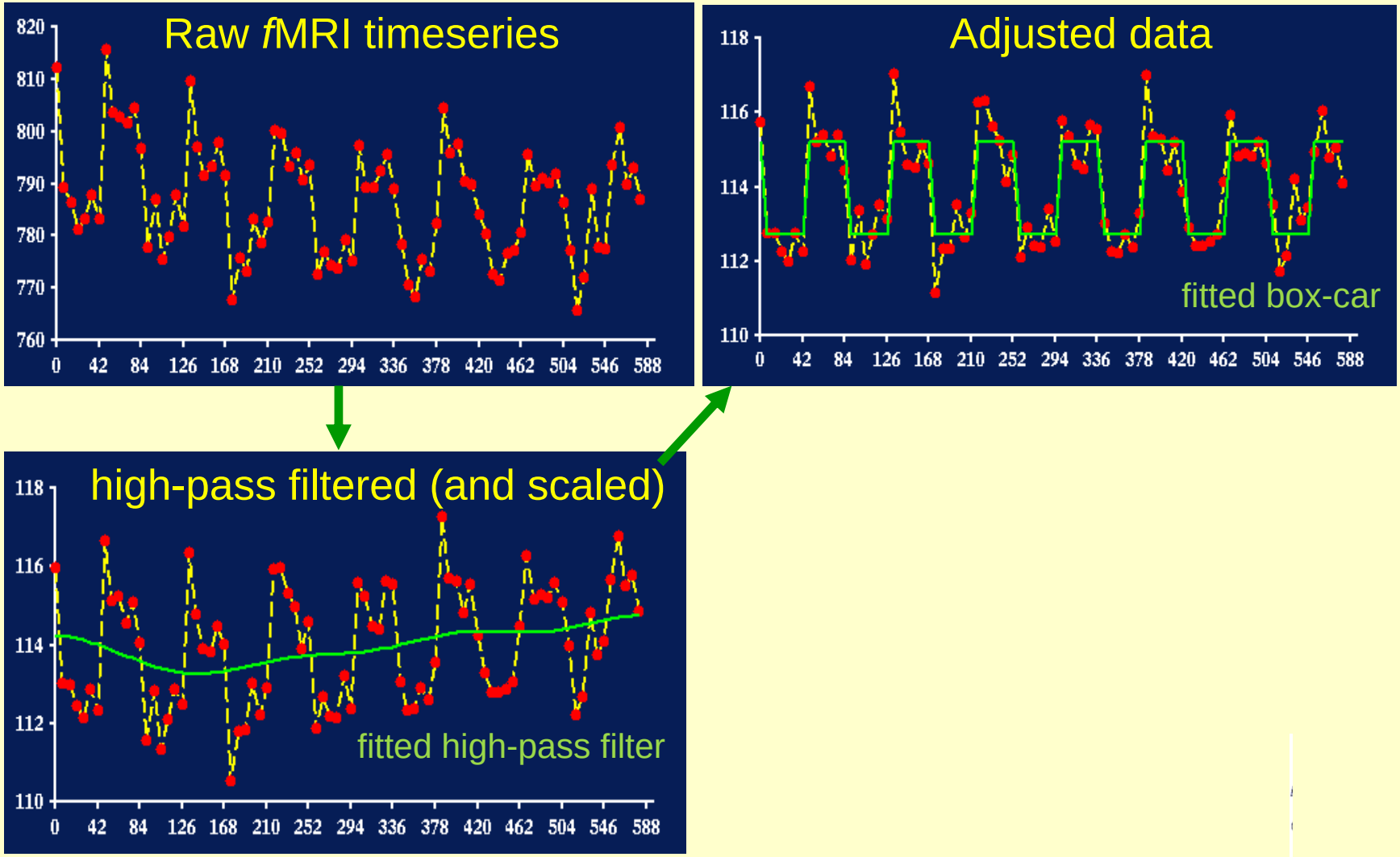

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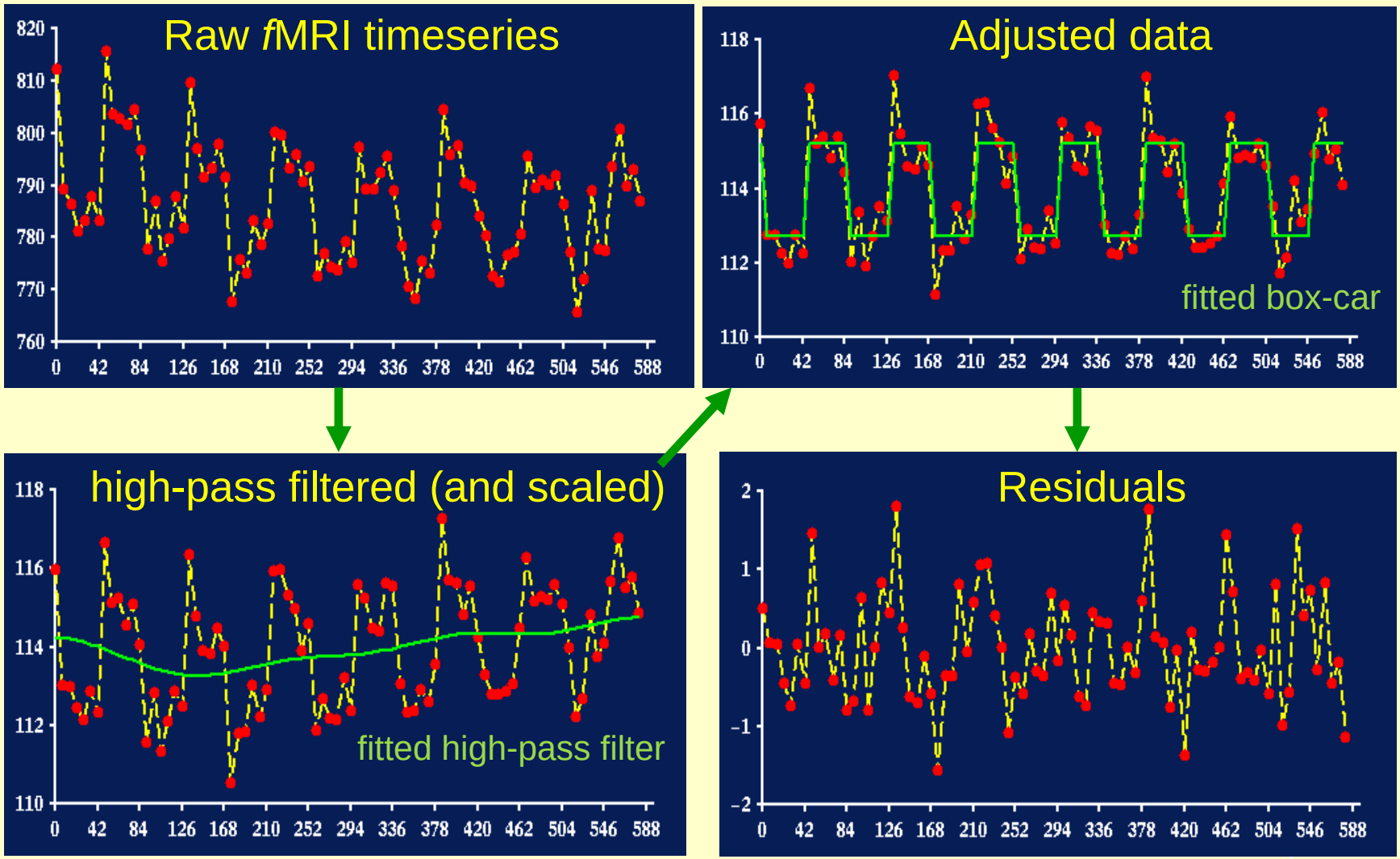
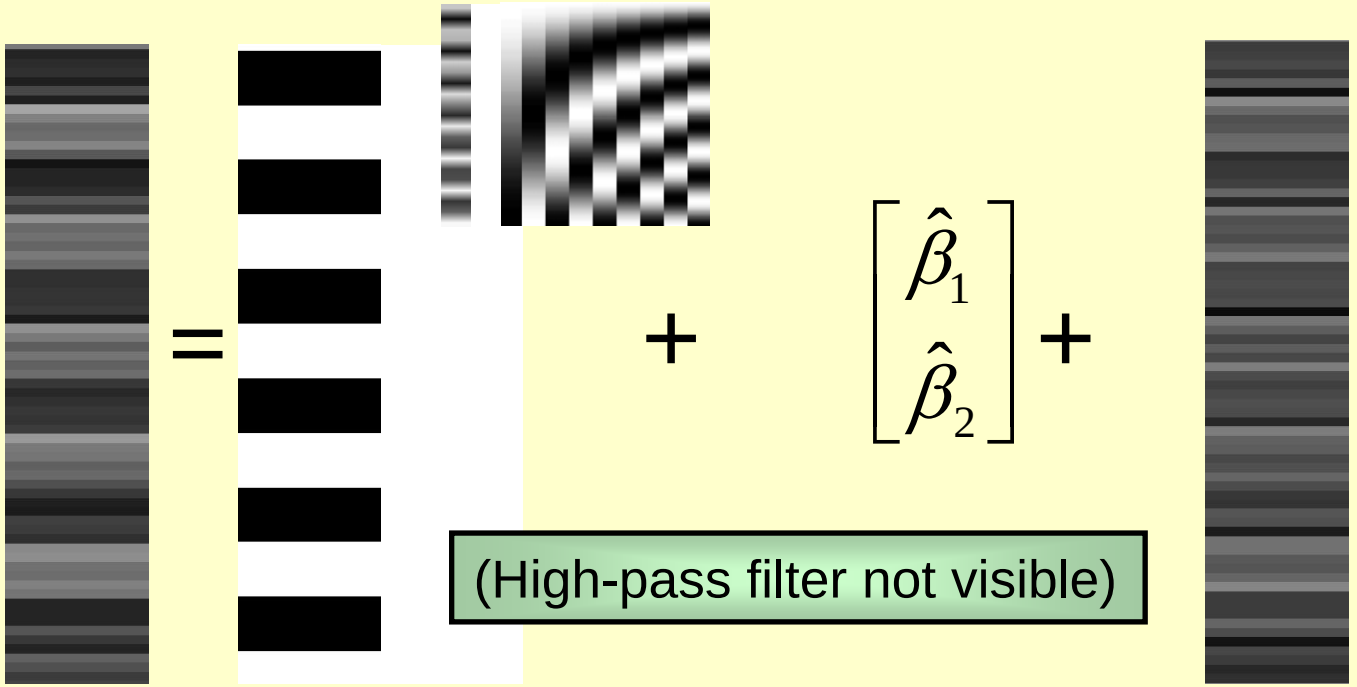


Regression model

Single subject

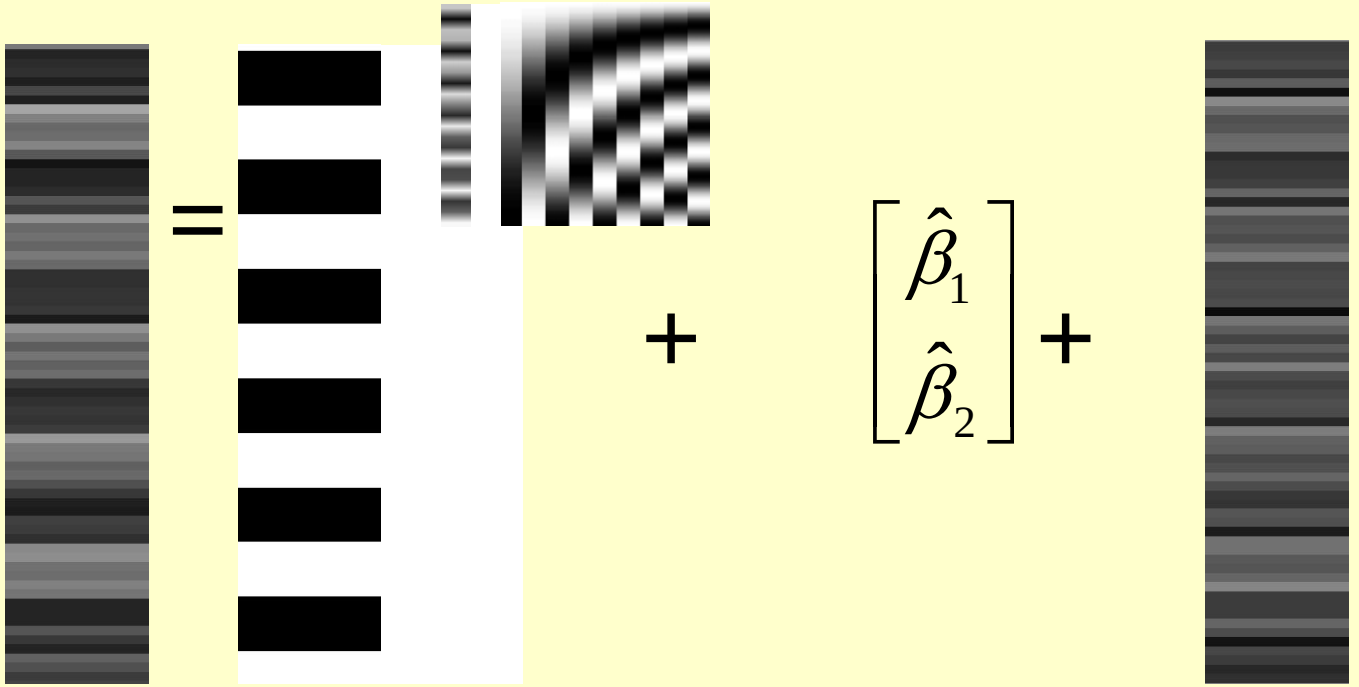


(High-pass filter not visible)

$$Y = X_1 * \hat{\beta}_1 + \hat{\varepsilon}_1$$

Regression model

Single subject



$$Y = X_1 * \hat{\beta}_1 + \hat{\varepsilon}_1$$

What's wrong with this model?

1. Stimulus function is not expected BOLD response
2. Data are serially correlated

The GLM applied to fMRI

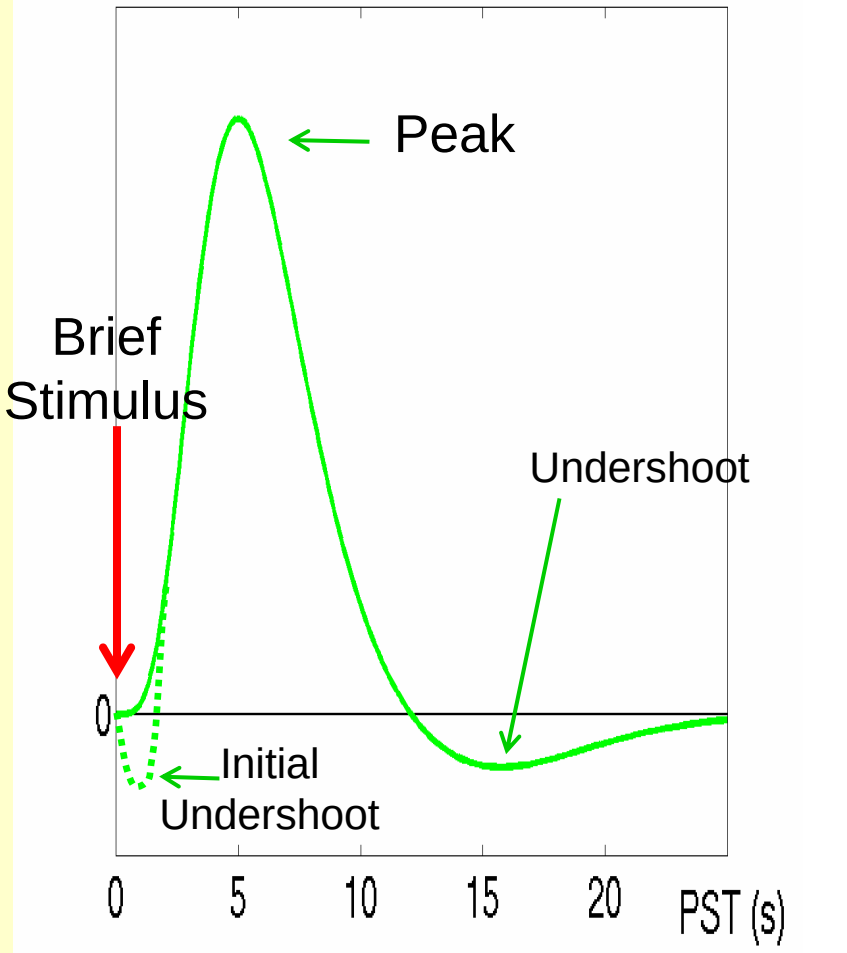
What are the solutions?

1. The data can be filtered to remove low-frequency (1/f) noise
2. **Effects are convolved with haemodynamic (BOLD) response function (HRF), to capture the sluggish nature of the response**
3. The data are modelled as a timeseries, taking account of temporal autocorrelation

2. The BOLD Haemodynamic Response

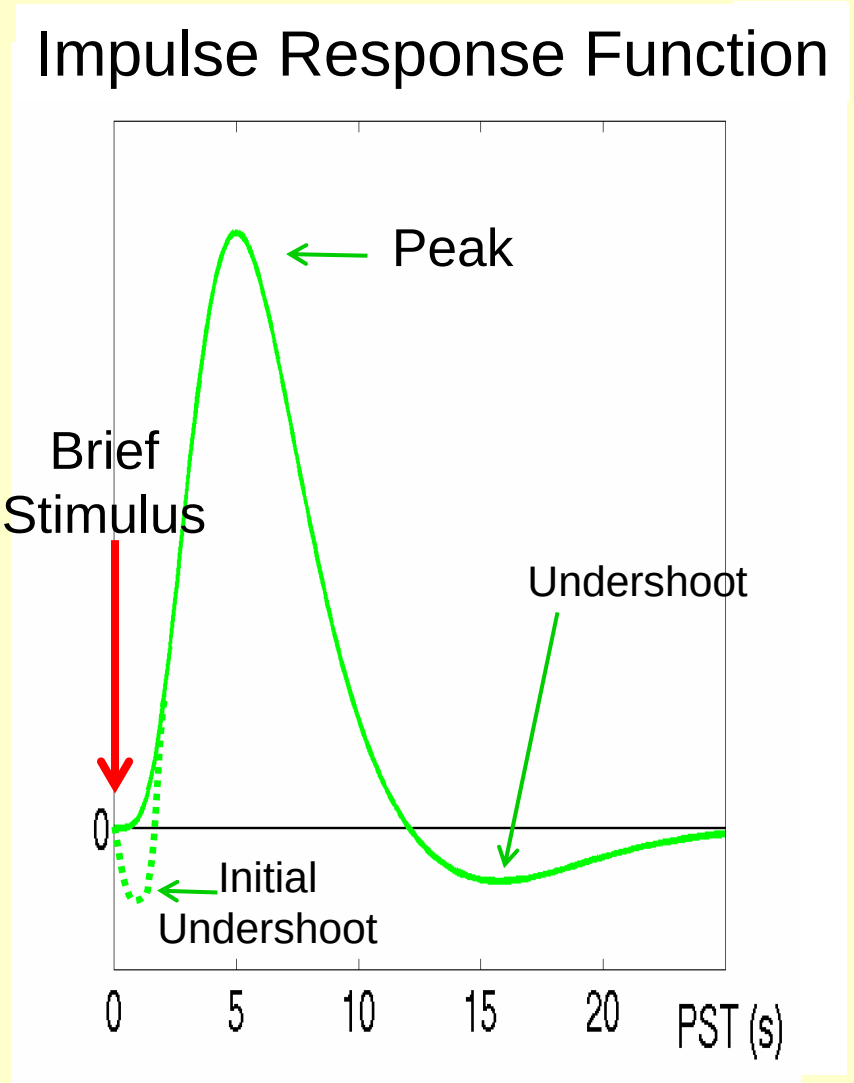
- Function of blood oxygenation, flow, volume (Buxton et al, 1998)
- Peak (max. oxygenation) 4-6s post stimulus; baseline after 20-30s
- May observe an initial undershoot
- Similar across V1, A1, S1
- May differ across other regions
- Differs across individuals (Aguirre et al, 1998)

Impulse Response Function



2. The BOLD Haemodynamic Response

- Particularly important for event-related fMRI
- Early studies used long Stimulus Onset Asynchrony (SOA) to allow BOLD to return to baseline
- But can accommodate overlap of successive responses at short SOAs if the BOLD response is explicitly modeled (esp. if responses assumed to combine linearly)



The General Linear (Convolution) model

GLM for a single voxel:

$y(t) = u(t) \otimes h(\tau) + \varepsilon(t)$

$u(t)$ = neural causes

(stimulus train)

$u(t) = \sum \delta(t - nT)$

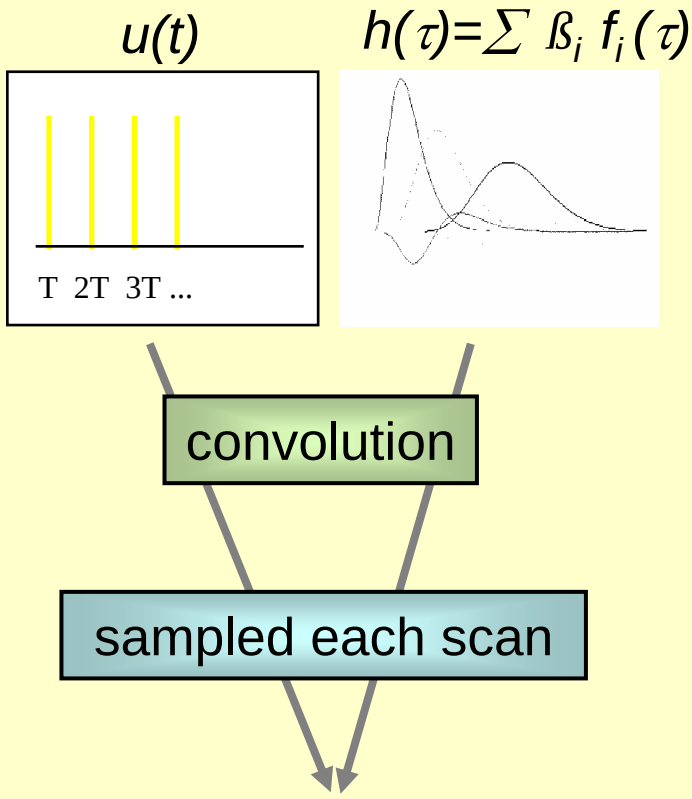
$h(\tau)$ = hemodynamic (BOLD) response

$h(\tau) = \sum \beta_i f_i(\tau)$

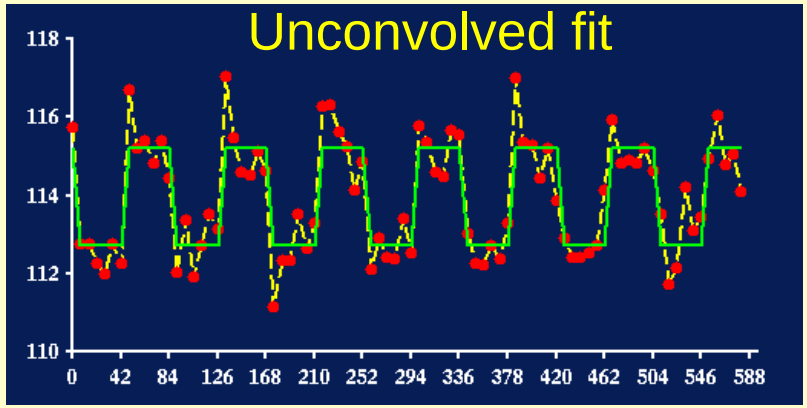
$f_i(\tau)$ = temporal basis functions

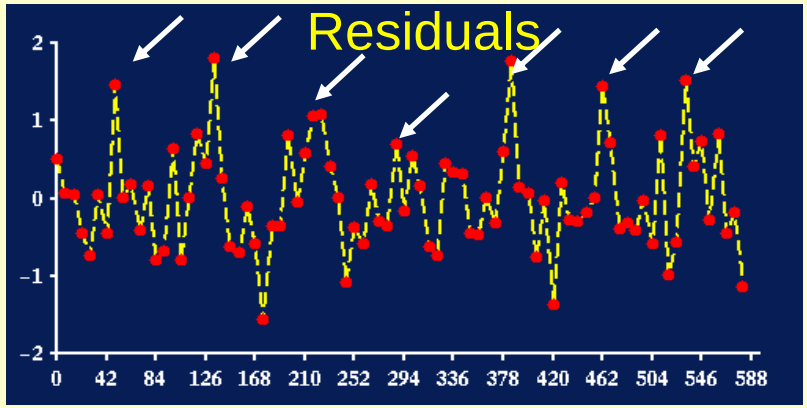
$y(t) = \sum\sum \beta_i f_i(t - nT) + \varepsilon(t)$

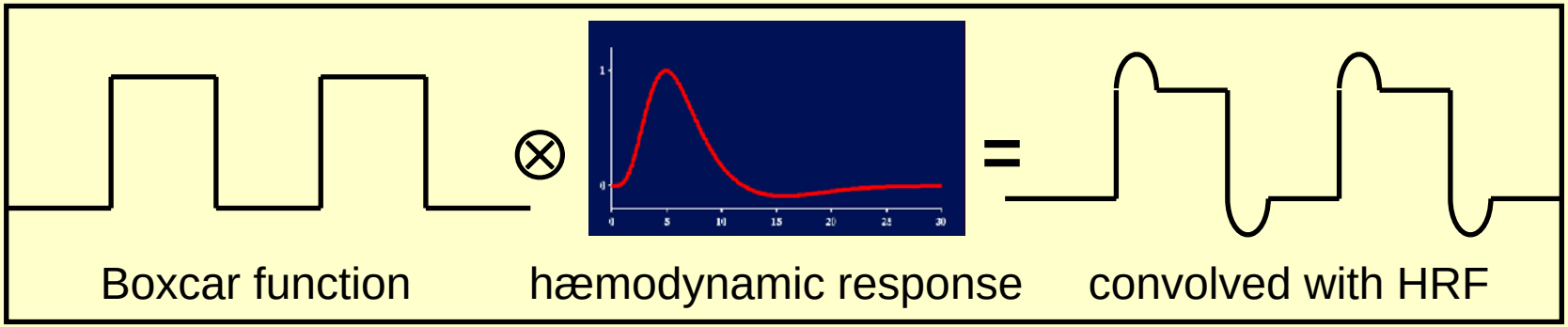
$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{\varepsilon}$



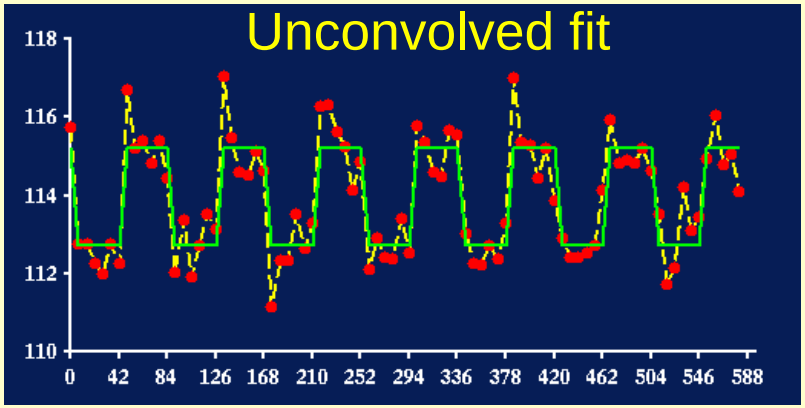
Convolution with the HRF

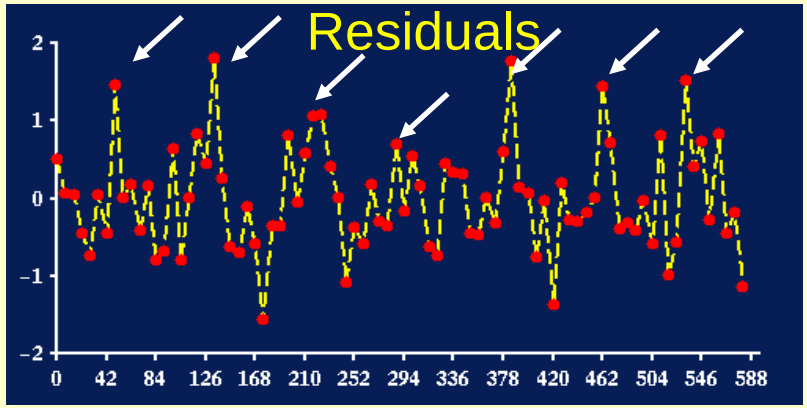


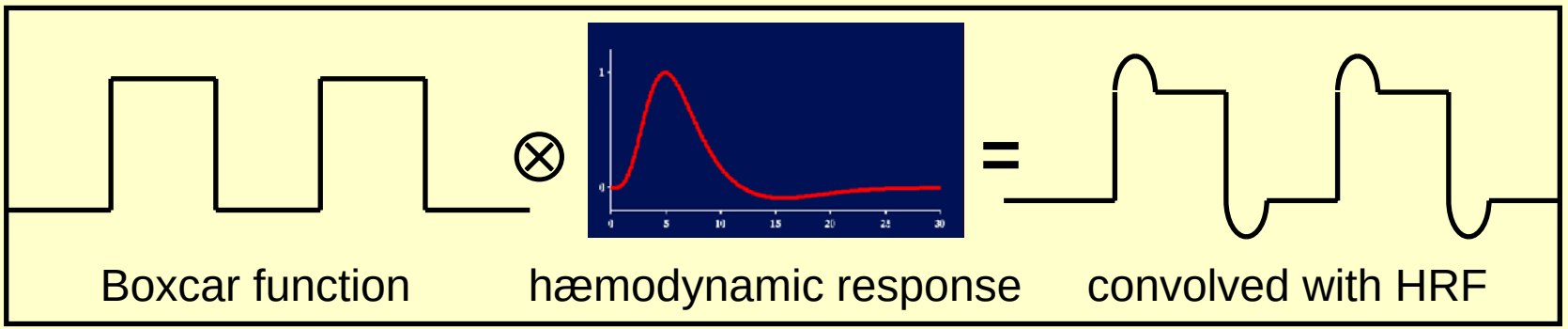


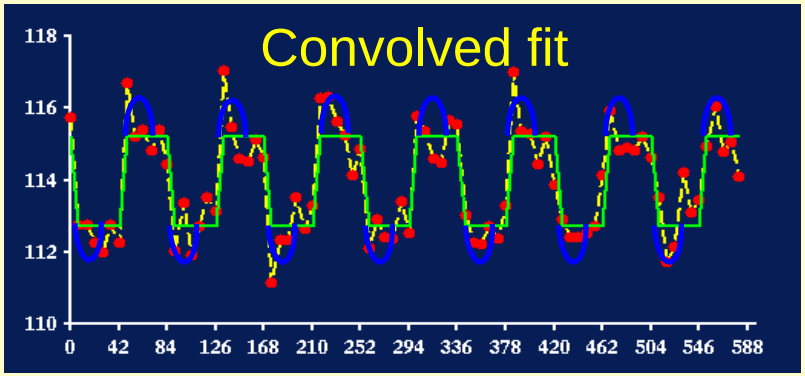


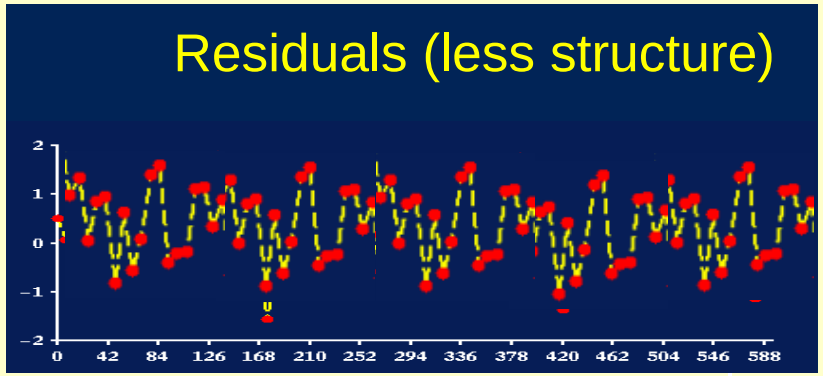
Convolution with the HRF





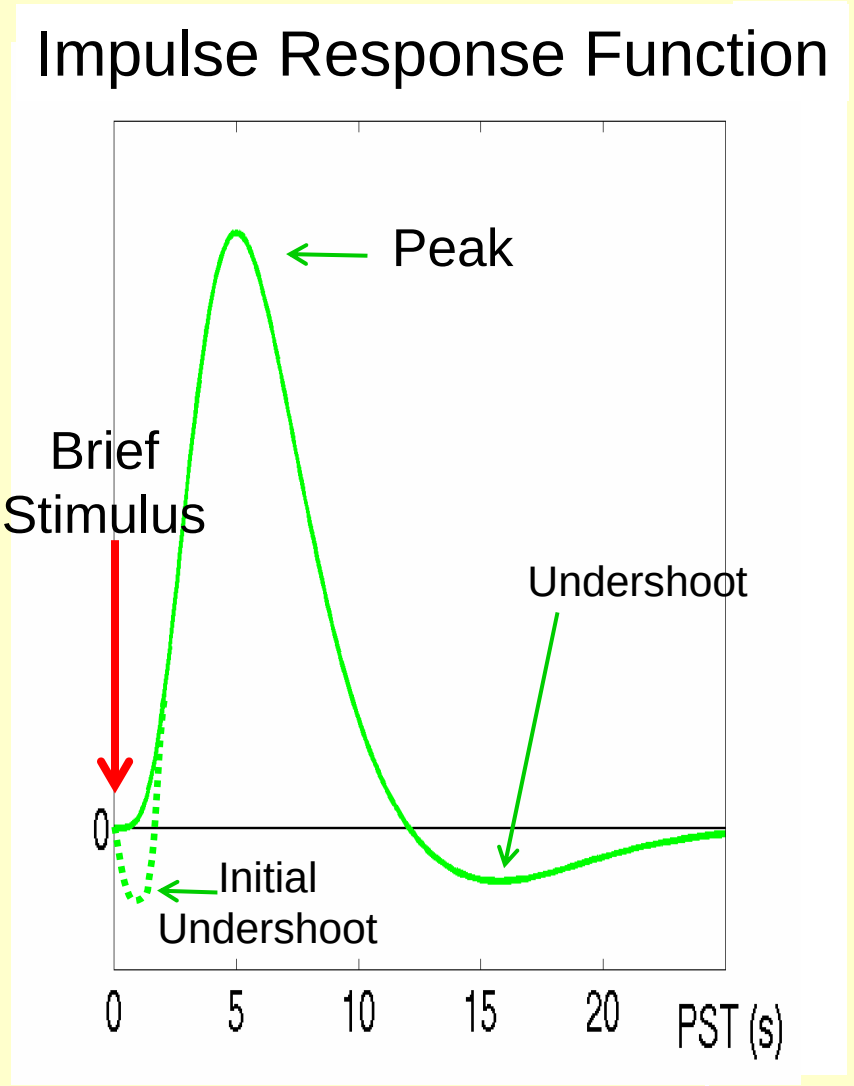




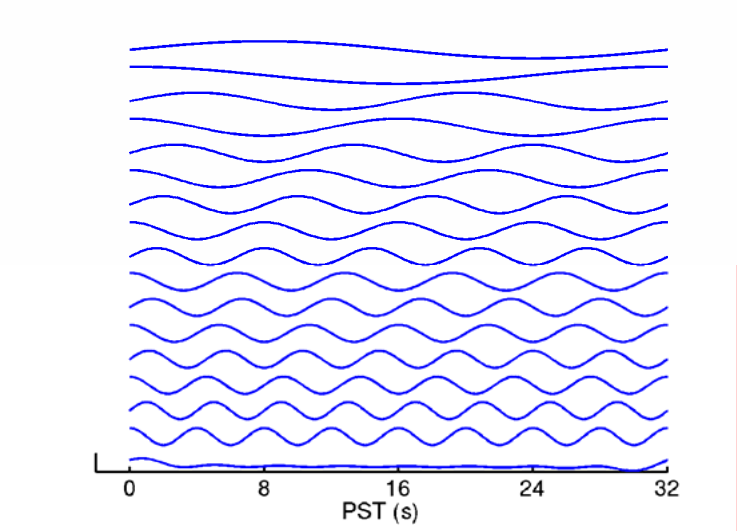


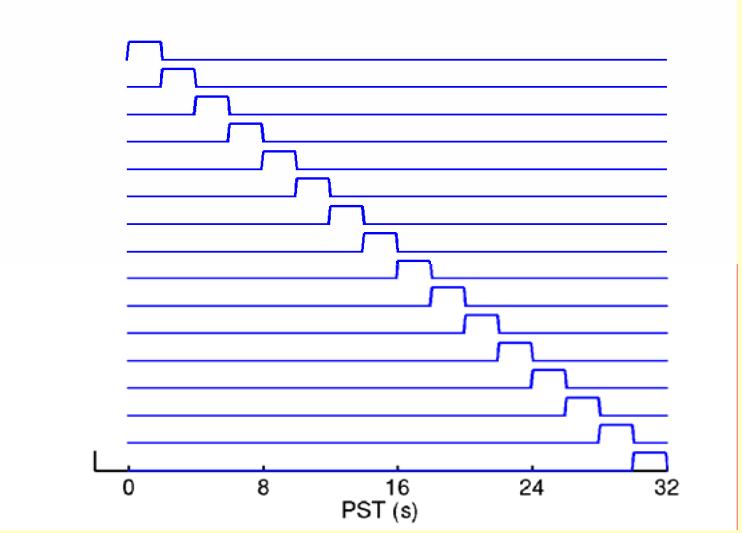
The BOLD Haemodynamic Response

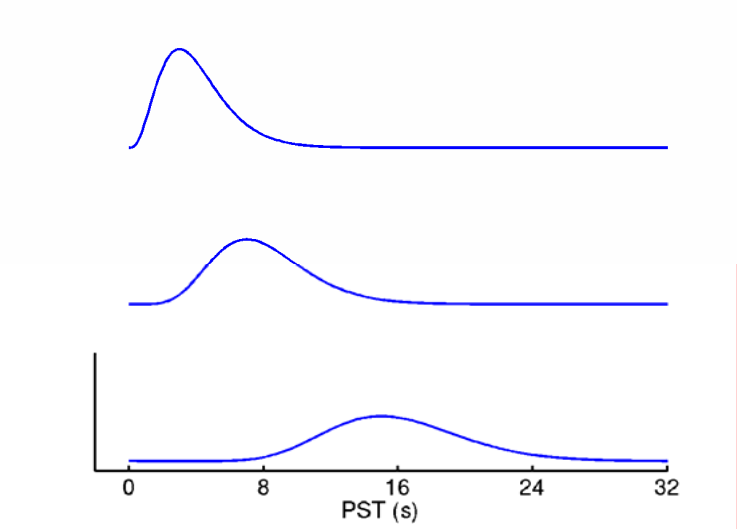
- May differ across regions
- Differs across individuals
- This matters in event-related fMRI
- Different possible shapes are modelled using multiple *temporal basis functions*
- Each is entered separately in the GLM and each is fitted separately (separate parameter estimates)

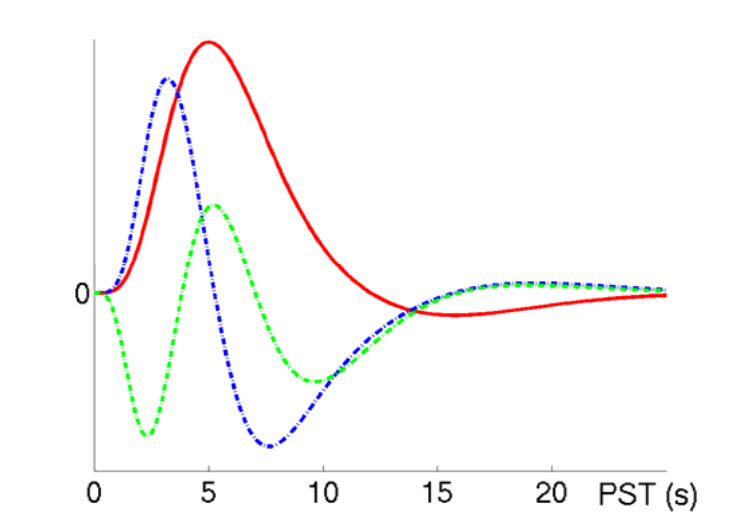


Temporal basis functions



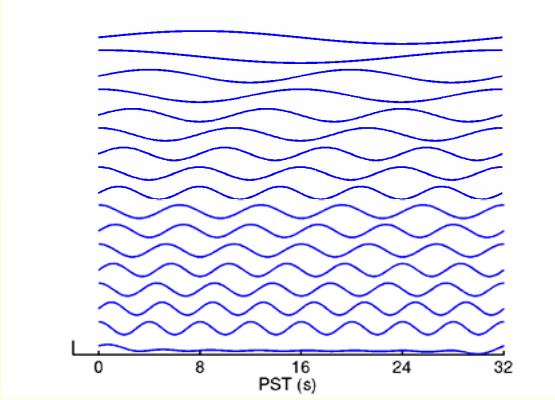






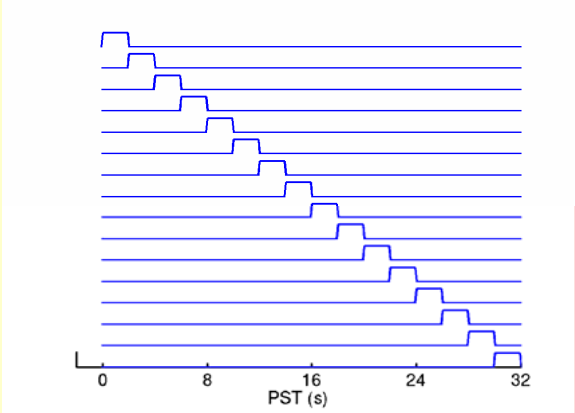
Temporal basis functions

- Fourier Set
  - Windowed sines & cosines
  - Any shape (up to frequency limit)
  - Inference via F-test



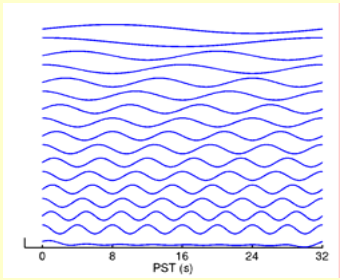
Temporal basis functions

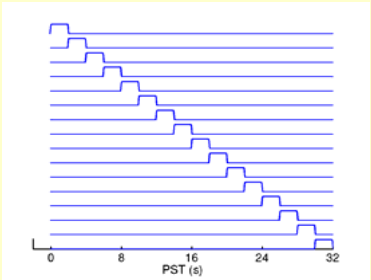
- Finite Impulse Response (FIR)
  - Mini “timebins” (selective averaging)
  - Any shape (up to bin-width)
  - Inference via F-test

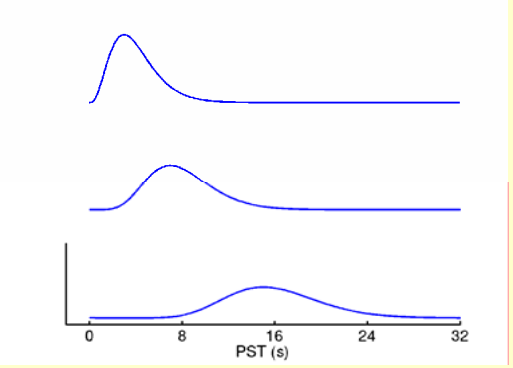


Temporal basis functions

- Fourier Set/ FIR
  - Any shape (up to frequency limit / bin width)
  - Inference via F-test
- Gamma Functions
  - Bounded, asymmetrical (like BOLD)
  - Set of different lags
  - Inference via F-test

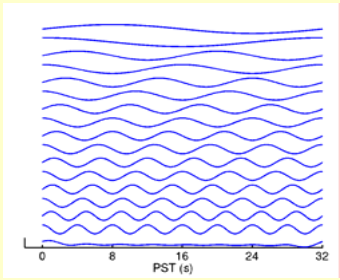


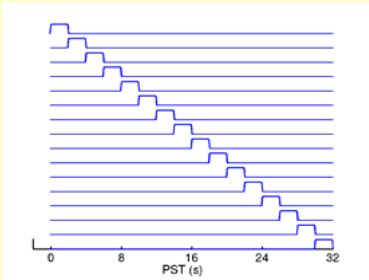


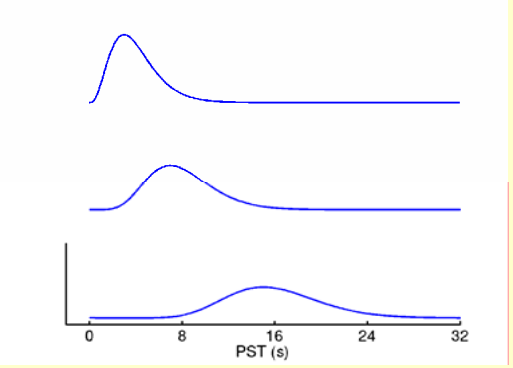


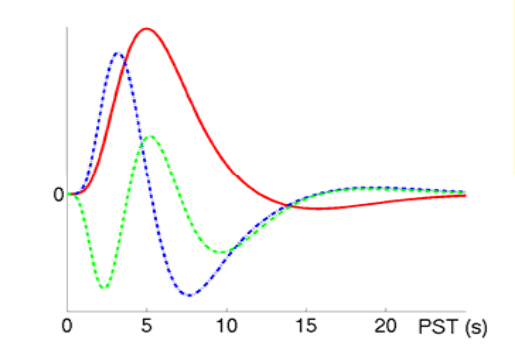
Temporal basis functions

- Fourier Set / FIR
  - Any shape (up to frequency limit / bin width)
  - Inference via F-test
- Gamma Functions
  - Bounded, asymmetrical (like BOLD)
  - Set of different lags
  - Inference via F-test
- ‘Informed Basis Set’
  - Best guess of canonical BOLD response
  - Variability captured by Taylor expansion
  - ‘Magnitude’ inference via t-test…?

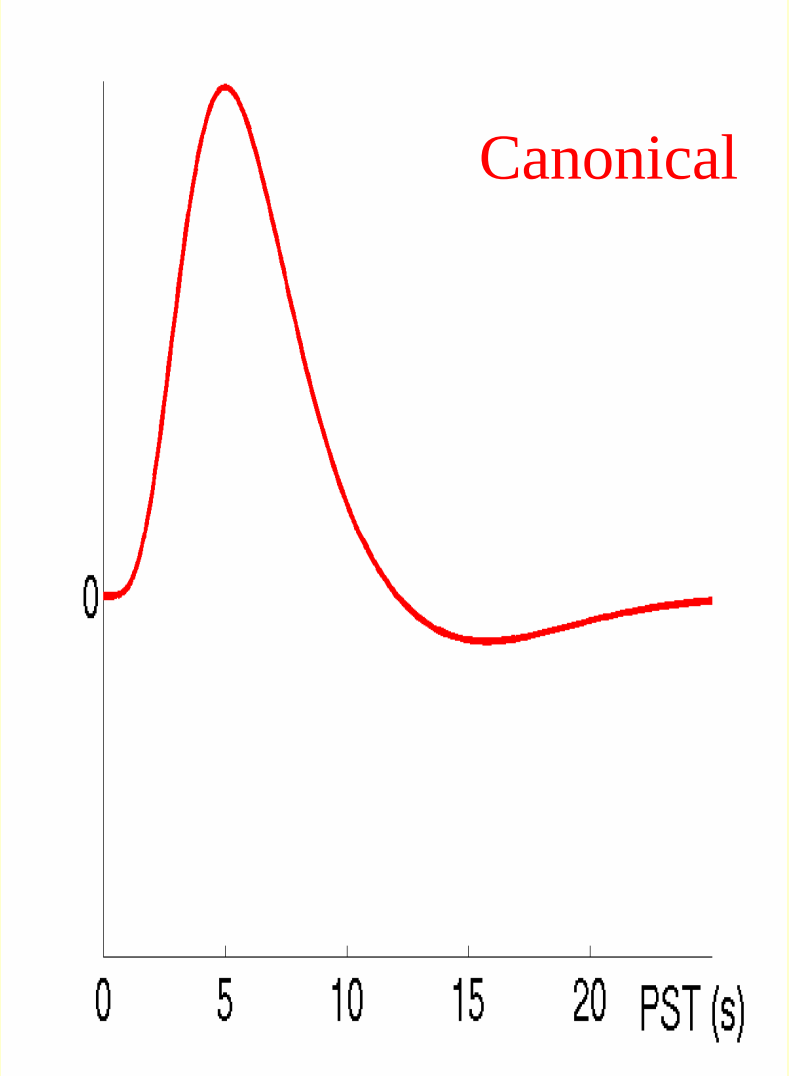








Temporal basis functions

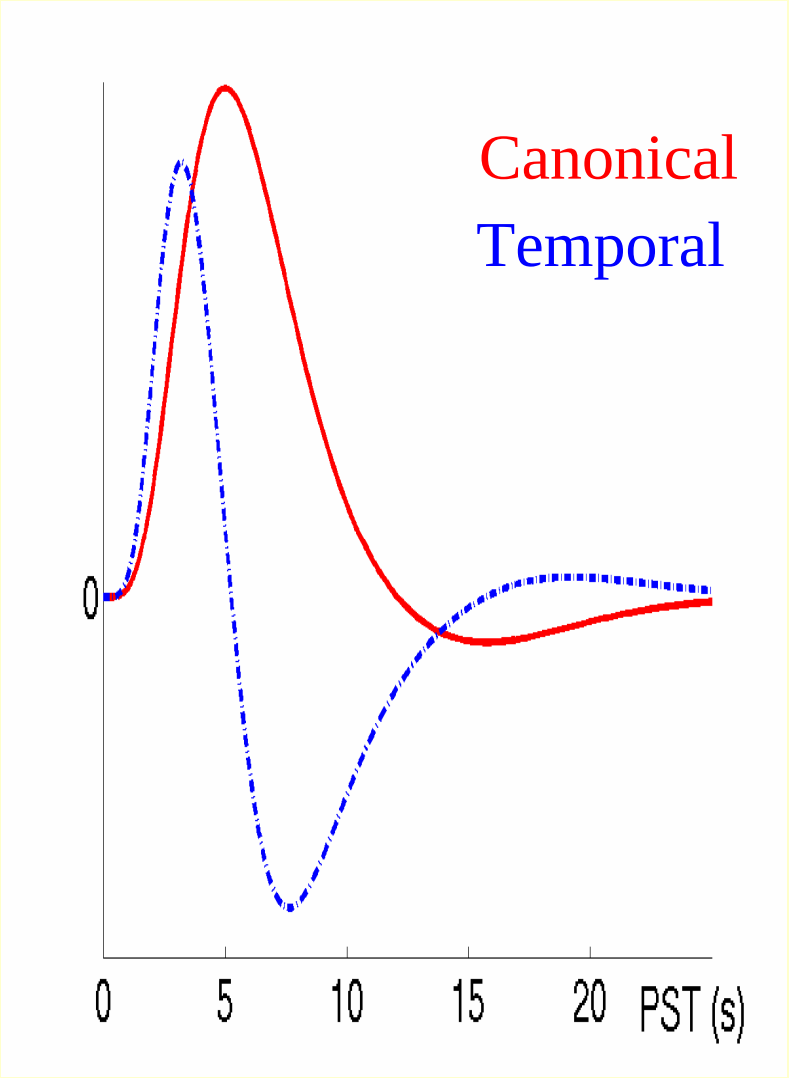


‘Informed’ Basis Set

(Friston et al. 1998)

- Canonical HRF (2 gamma functions)

Temporal basis functions



‘Informed’ Basis Set

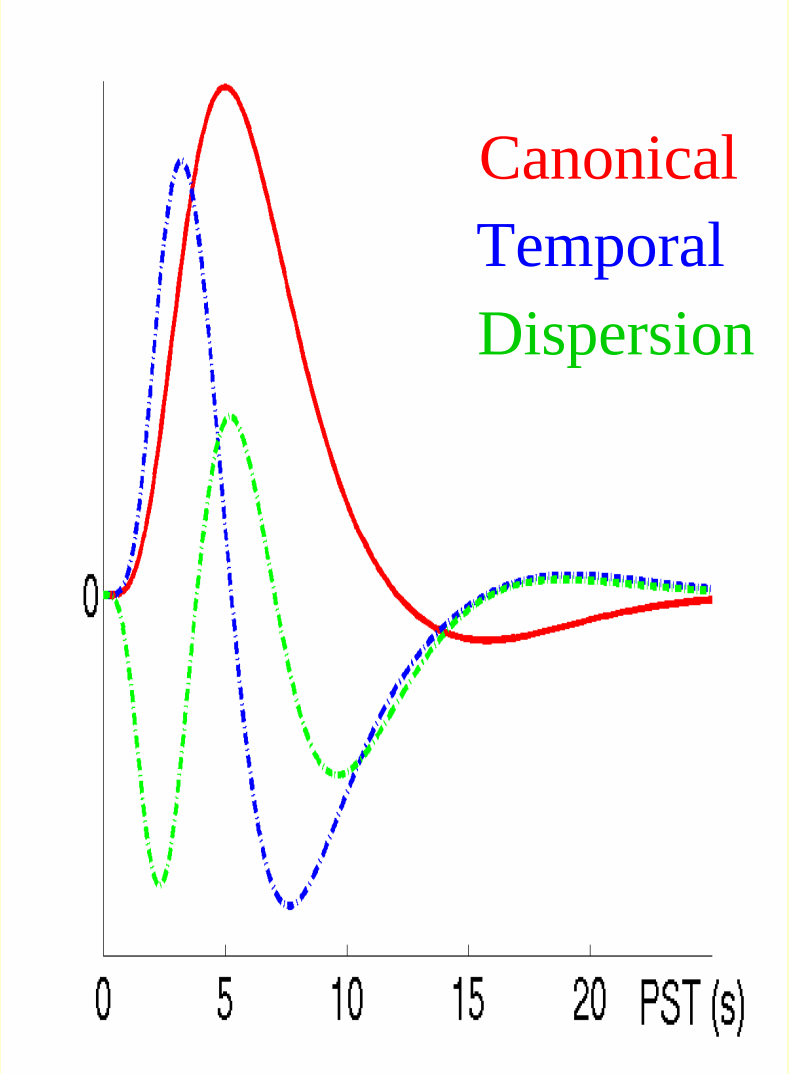
(Friston et al. 1998)

- Canonical HRF (2 gamma functions)

plus Multivariate Taylor expansion in:

time (*Temporal Derivative*)

Temporal basis functions



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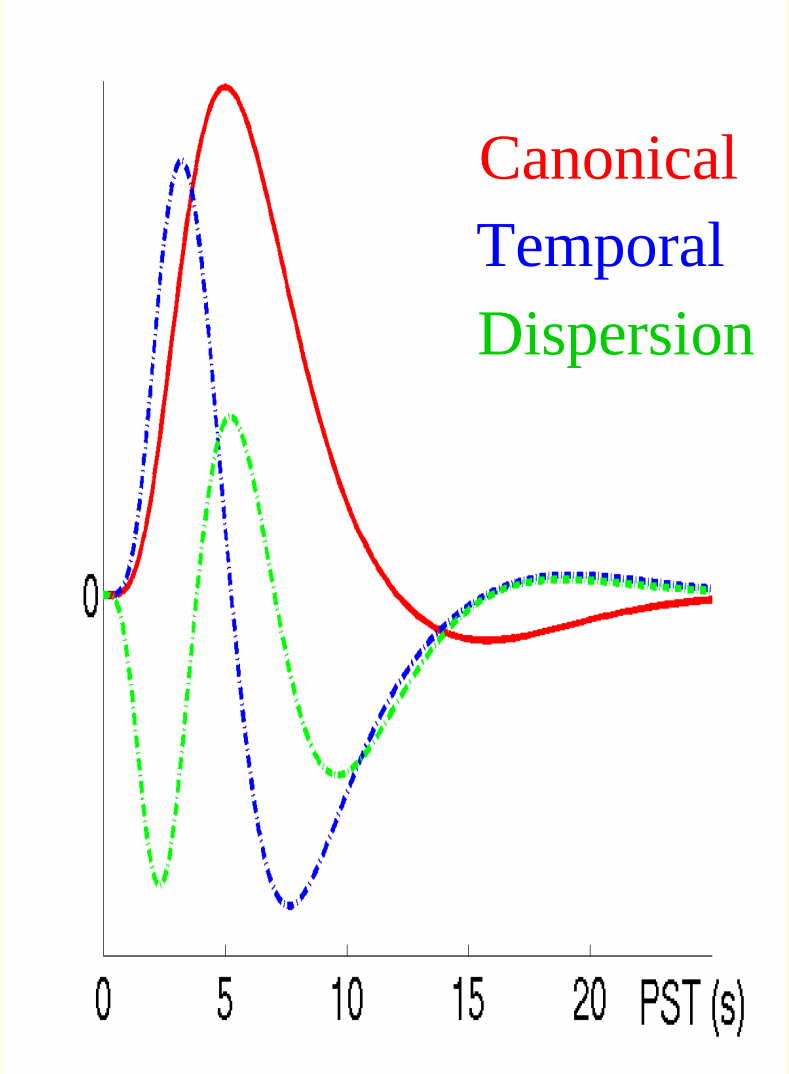

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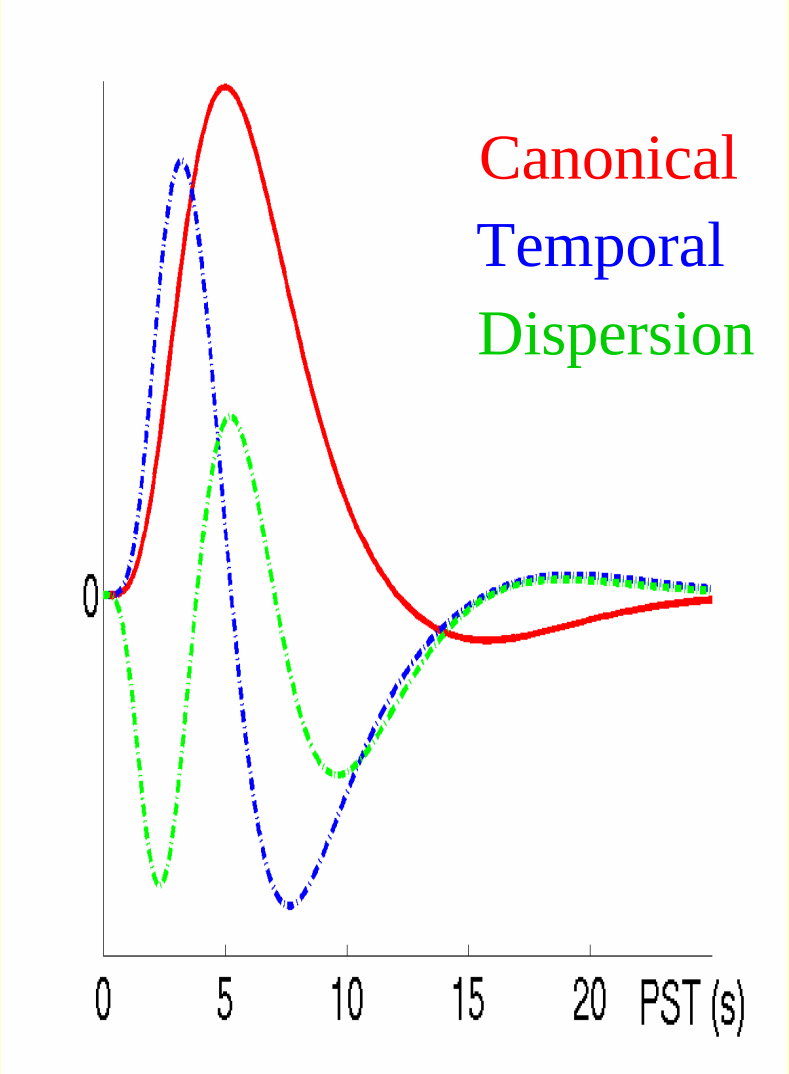
Temporal basis functions



‘Informed’ Basis Set

(Friston et al. 1998)

- Canonical HRF (2 gamma functions)

  plus Multivariate Taylor expansion in:

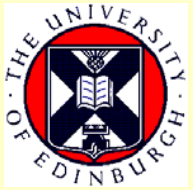
  time (*Temporal Derivative*)

  width (*Dispersion Derivative*)
- Magnitude’ inference via t-test on canonical parameters (provided canonical is a reasonable fit)
- ‘Latency’ inference via tests on *ratio* of derivative : canonical parameters

The GLM applied to fMRI

What are the solutions?

1. The data can be filtered to remove low-frequency (1/f) noise
2. Effects are convolved with haemodynamic (BOLD) response function (HRF), to capture the sluggish nature of the response
3. **The data are modelled as a timeseries, taking account of temporal autocorrelation**

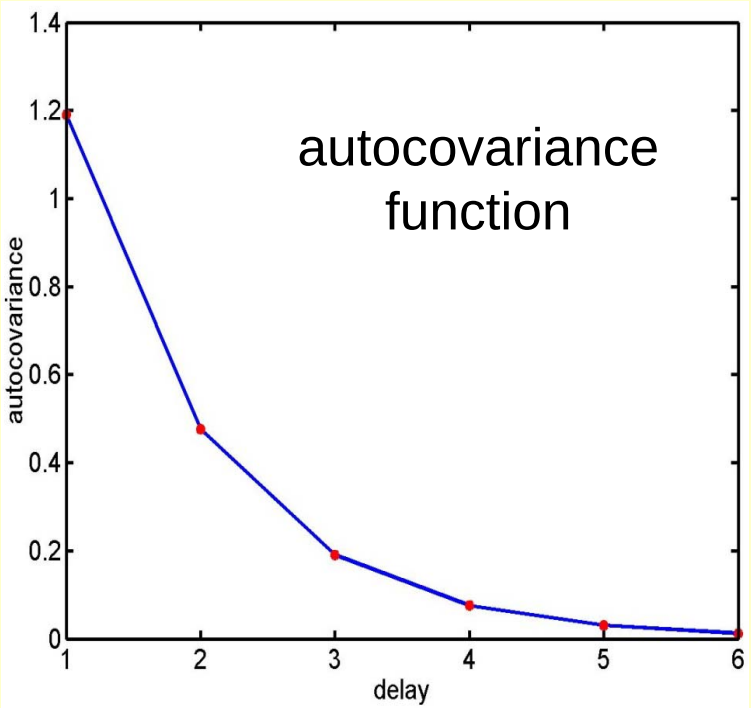


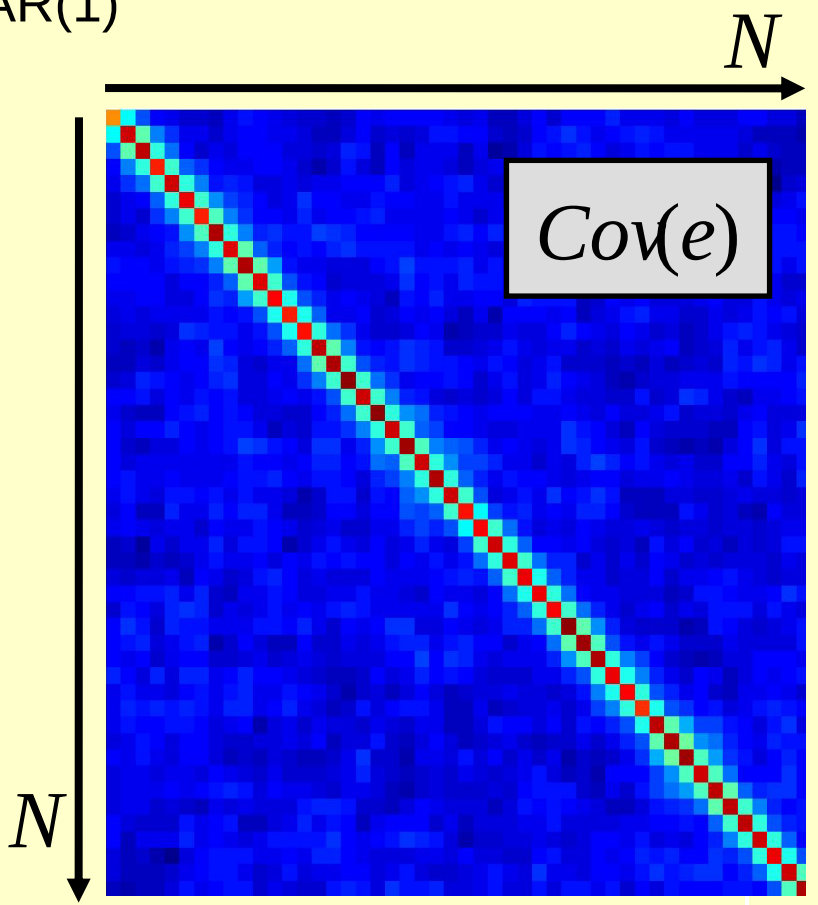
3. Serial correlations

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

Each observation is related to adjacent observations

1st order autoregressive process: AR(1)



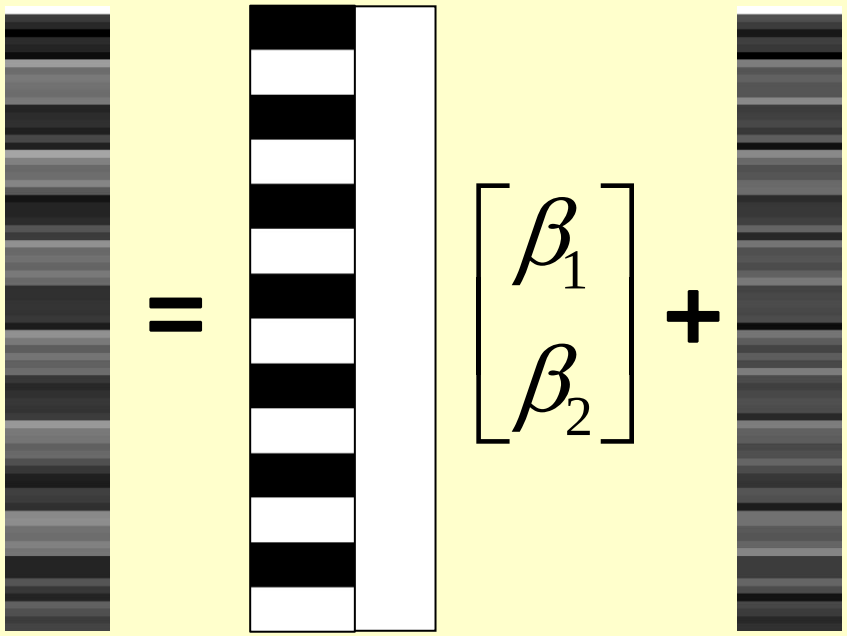


3. Serial correlations

- Why are they a problem?
- If we have fewer independent observations than we think, this affects degrees of freedom and statistical inference (see RFX lecture)
- But this is a single subject model and our inference will likely be at group level
- …we still want to optimise parameter estimation in 2-stage procedure

(see also RFX, Covariance Components lectures)

Parameter estimation (OLS)



$$y = X\beta + e$$

Objective:

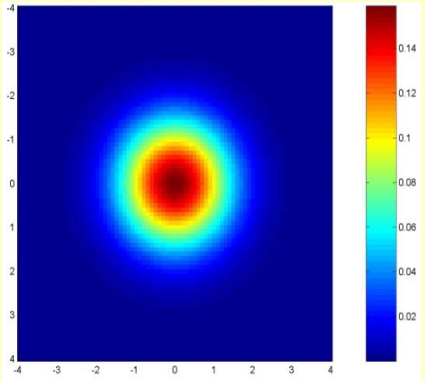
estimate parameters to minimize $\sum_{t=1}^{N} e_t^2$

Ordinary least squares estimation (OLS):

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

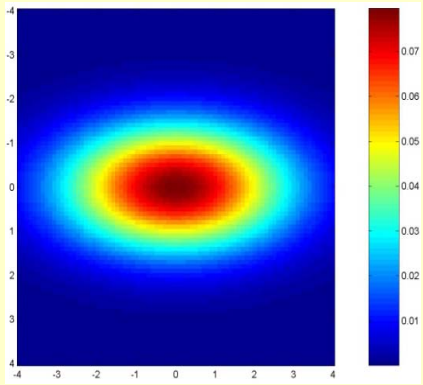
Assumes Gaussian 'spherical' (i.i.d.) errors

sphericity = i.i.d.
error covariance is a multiple of the identity matrix:
Cov(e) = $\sigma^2 I$



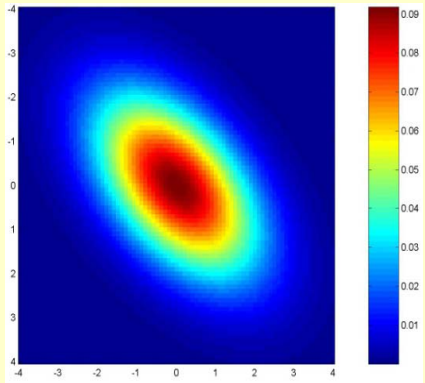
$$Cov(e) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Examples of non-sphericity:



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

non-identity



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

non-independence

Dealing with serial correlations

Pre-whitening

- Use an enhanced noise model with multiple error covariance components

  i.e. $e \sim N(0, \sigma^2 V)$ instead of $e \sim N(0, \sigma^2 I)$

  V is modelled using an AR (1) + white noise model estimated across all active voxels

- Use the estimated V to specify a filter matrix *W* for whitening the data – *'undoing'* the serial correlations

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

$$Wy = WX\beta + We$$

Dealing with serial correlations

- Once data are ‘pre-whitened’, estimation can proceed using Ordinary Least Squares
- The parameter estimates are again maximum likelihood
- This is Weighted Least Squares (WLS)
- (see Covariance Components lecture)
- The parameter estimates are ready to be used for statistical inference

Summary: GLM for fMRI

- Mass-univariate approach: same GLM for each voxel
- 2-stage procedure: single subject then group level
- GLM includes all known experimental effects and confounds
- High-pass filter to account for low-frequency noise
- Convolution with an HRF

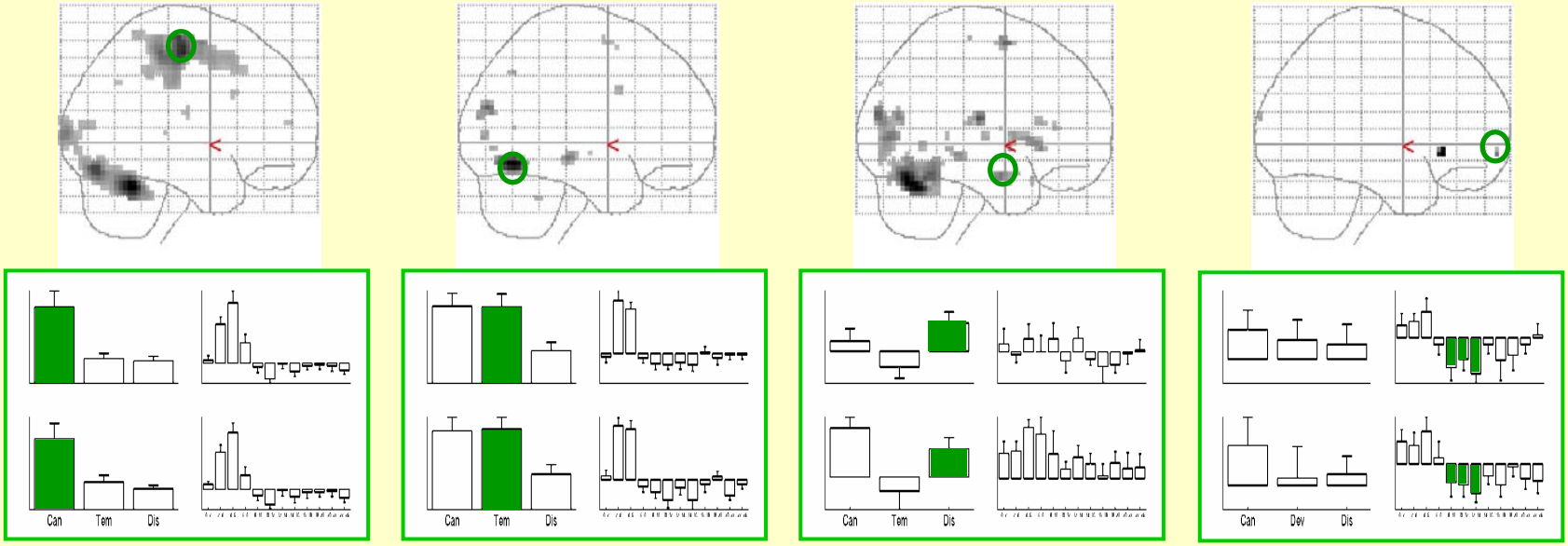
  → both have design implications: later lectures
- Prewhiten the data to account for serial correlations

  → Covariance component estimation: later lecture

Many thanks to R Henson, A Holmes, S Kiebel,
C Ruff, JB Poline and K Stephan for slides

Which temporal basis set?

In this example (rapid motor response to faces; Henson et al, 2001)



Canonical + Temporal + Dispersion + FIR

Canonical + 2 derivatives appear sufficient to capture most activity

For more complex trials (e.g. stimulus-prolonged delay (>~2 s)-response) better modelled with separate *neural* components (i.e., activity no longer delta function) + constrained HRF (Zarahn, 1999)