

Medical Image Analysis

Instructor: Moo K. Chung

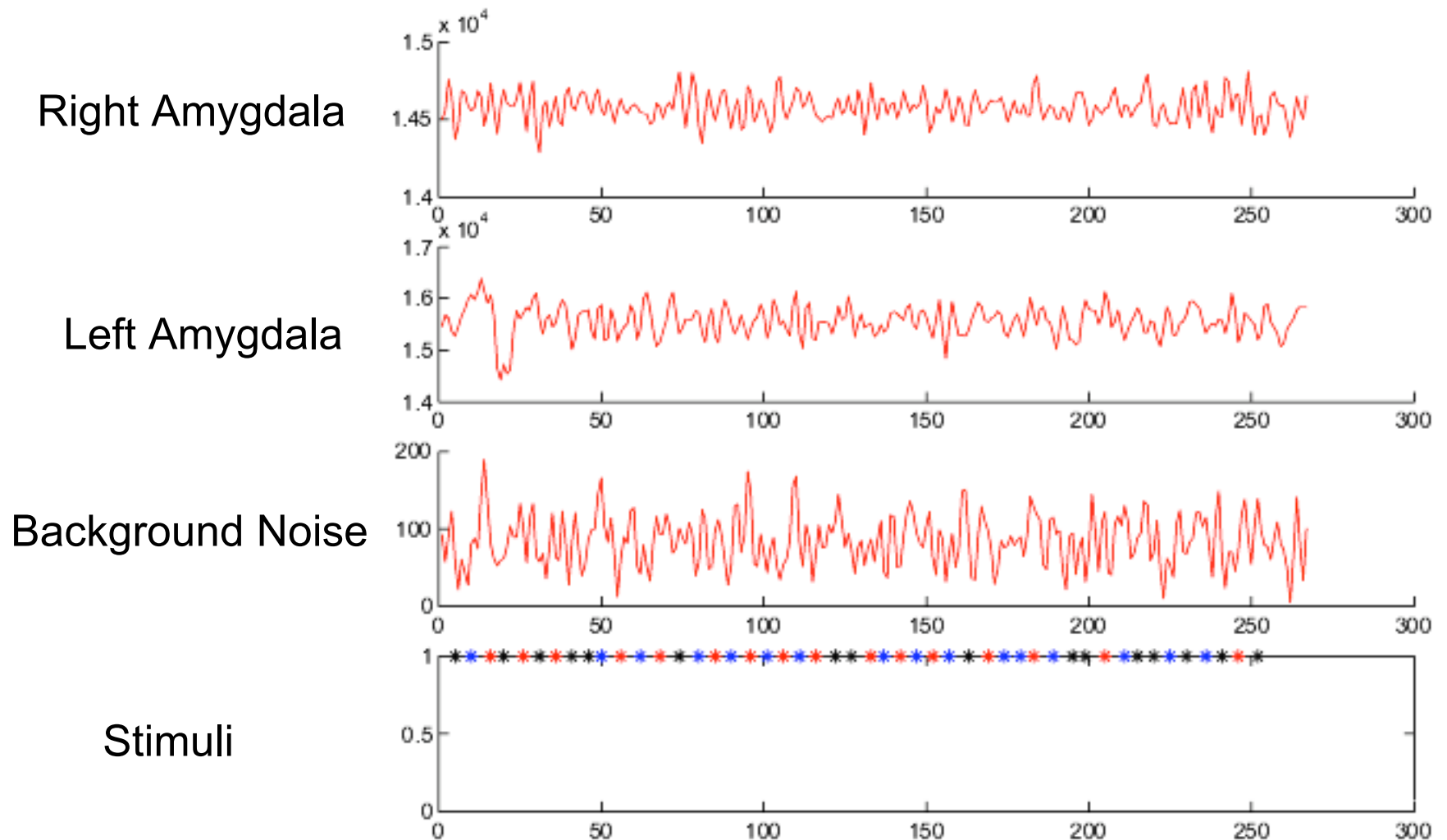
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Lecture 14.

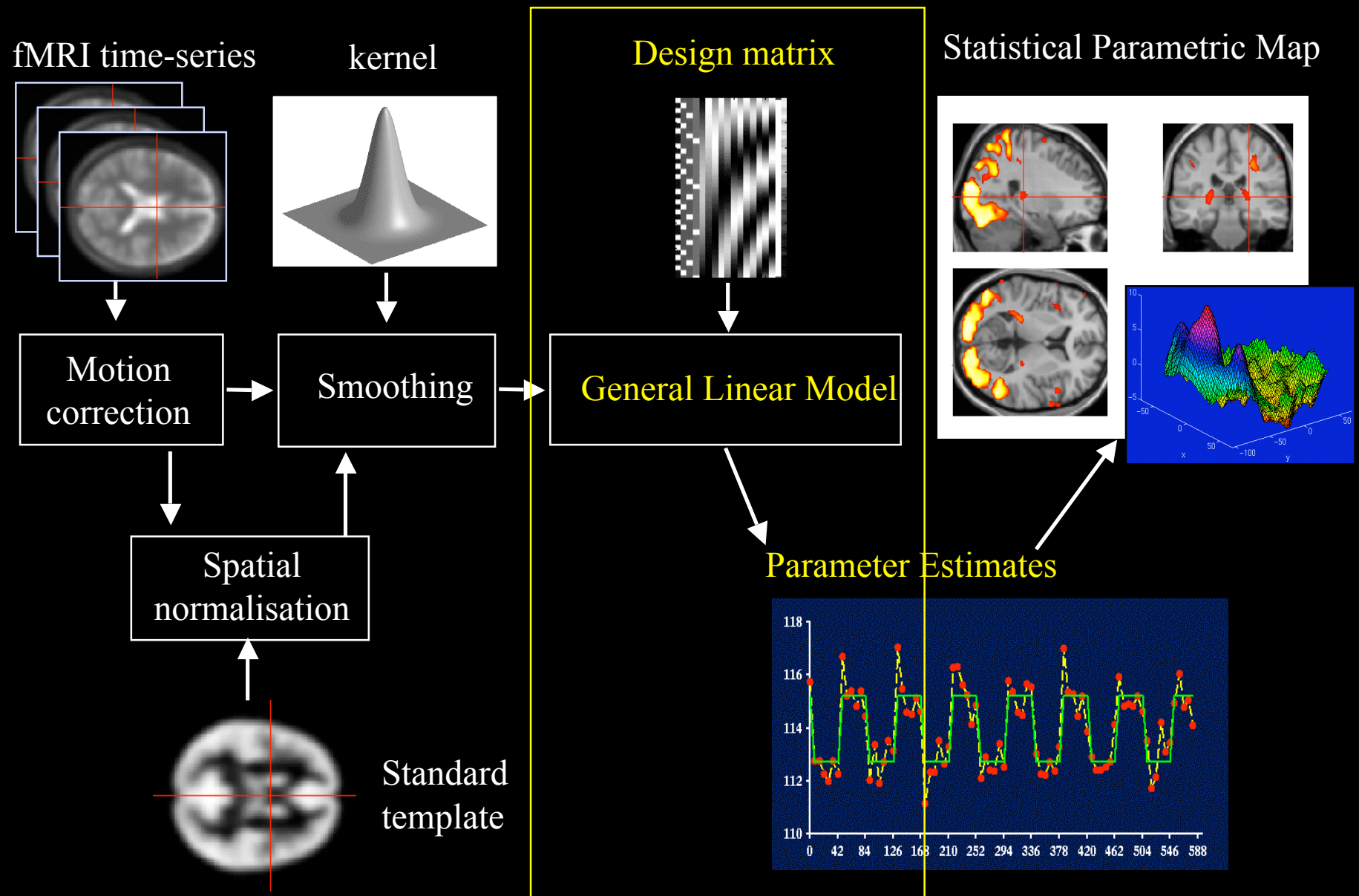
fMRI time series analysis

March 27, 2007

Example of fMRI: functional MRI in amygdala in picture showing experiment



fMRI analysis framework

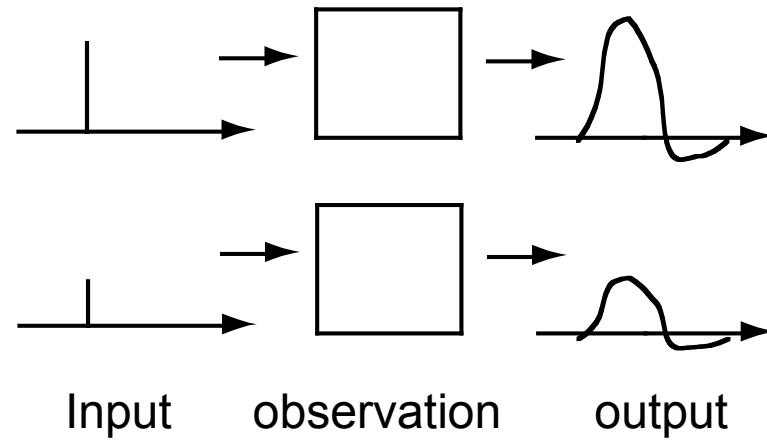


Source: Gary Huang

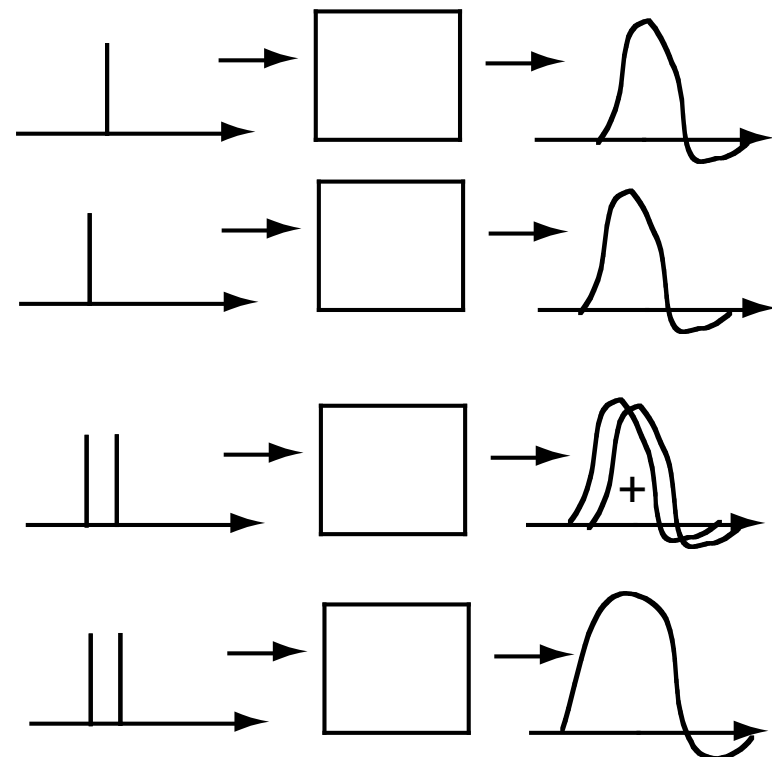
Linear systems

- System = input --> output
Stimulus or Neural activity
--> functional MRI responses
- System is linear if shows two properties
Homogeneity (Scalability) & Superposition

Homogeneity

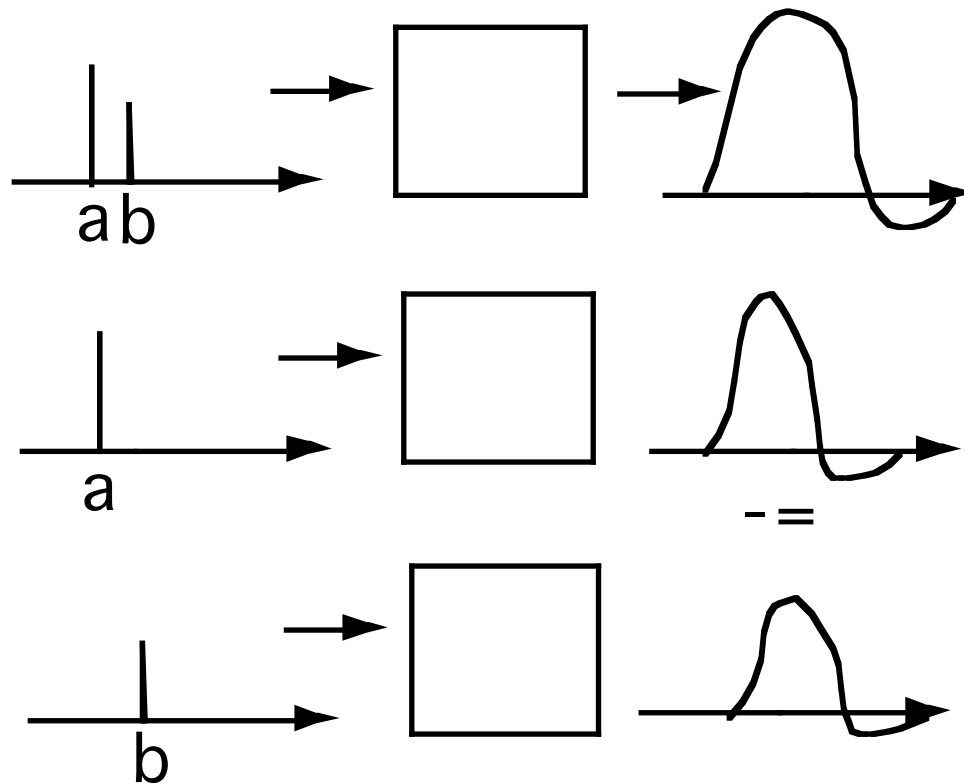


Superposition

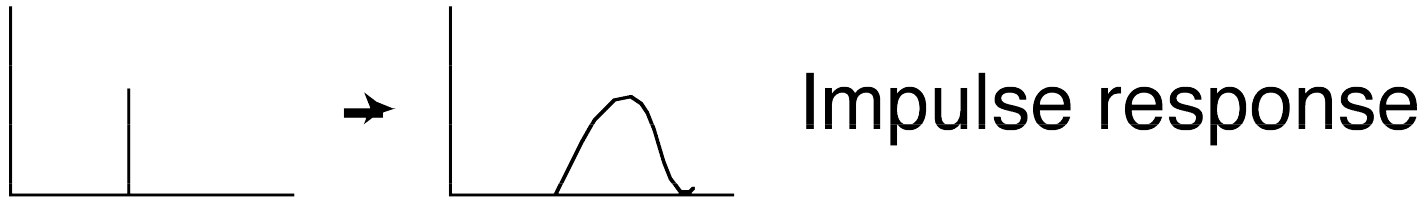


Source: Stephen Engel

Subtracting responses



Modeling linear system



$$y(t) = \int_0^t H(t-s)f(s)ds + e(t)$$

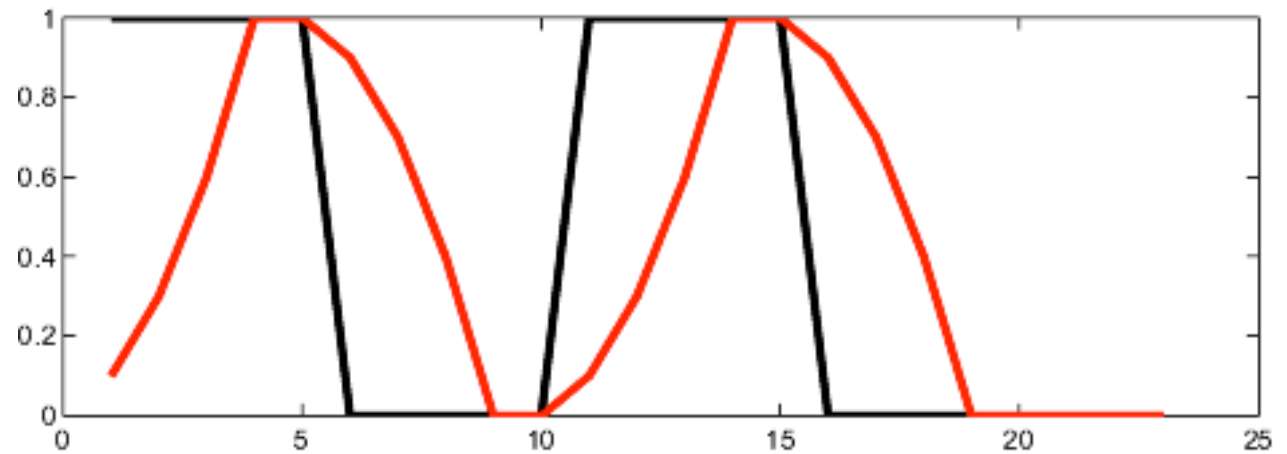
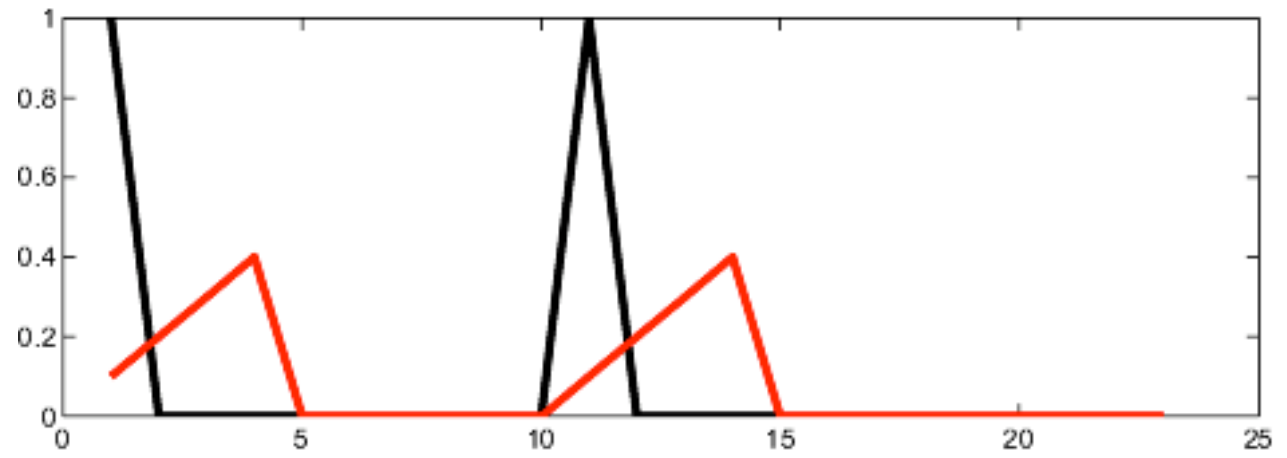
Observed fMRI signal $y(t)$

HRF(hemodynamic response function) $H(t)$

Gaussian random process $e(t)$

Example: Impulse and HRF relation

black: stimuli
red: response



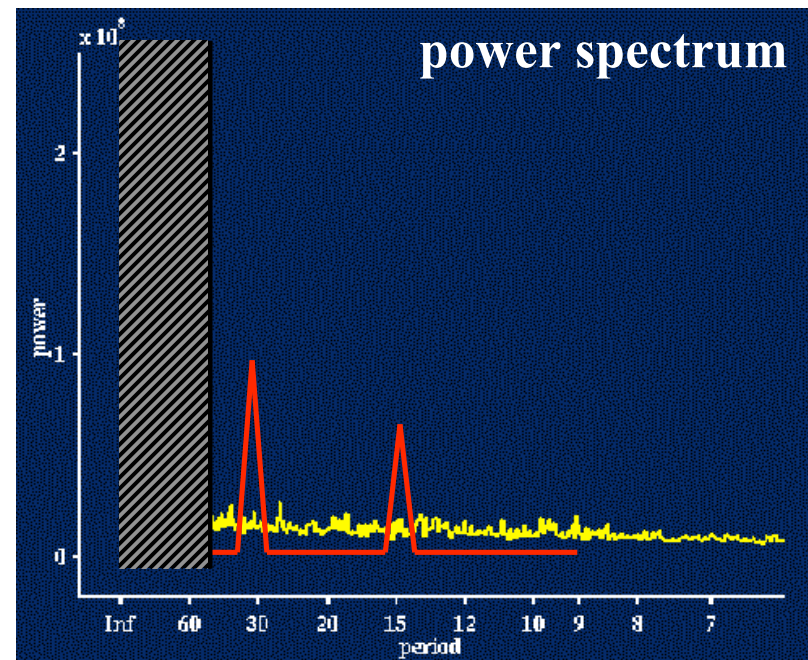
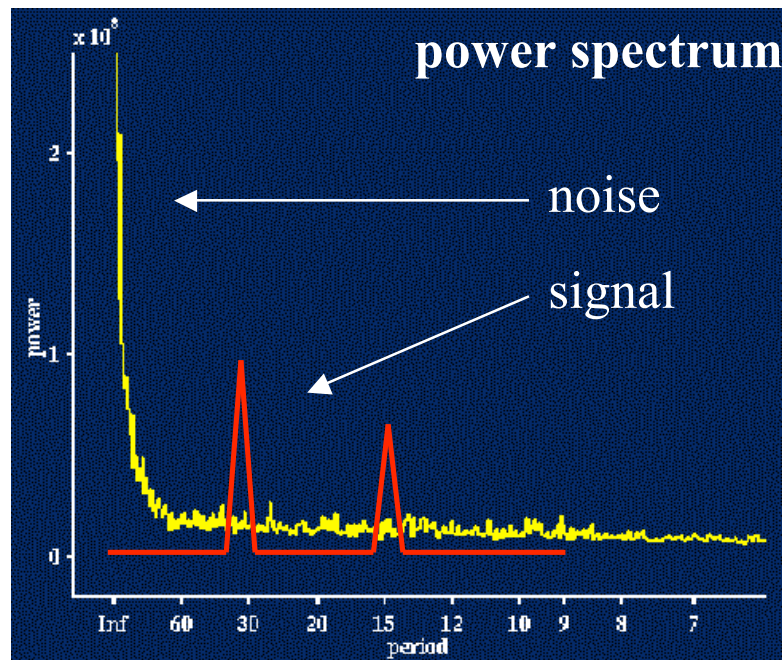
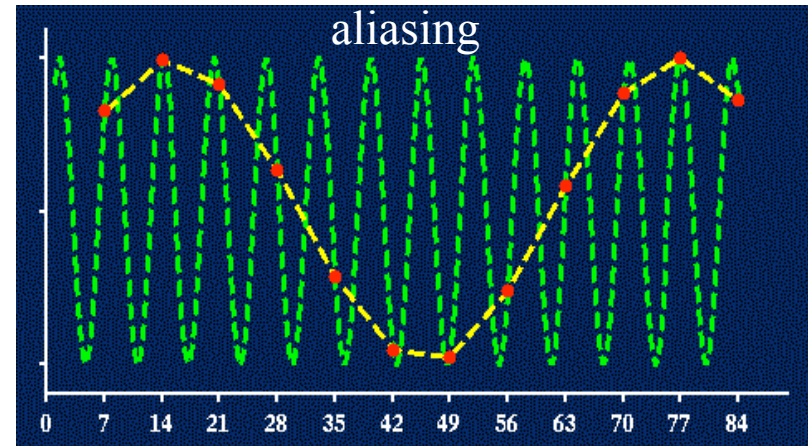
Drift of magnetic fields

$$y(t) = \int_0^t H(t-s)f(s)ds + e(t)$$

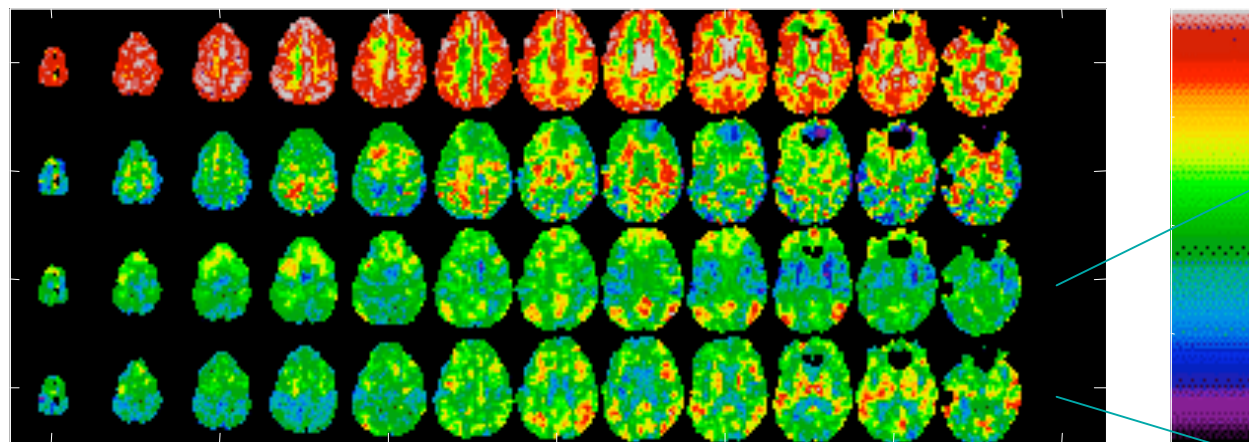
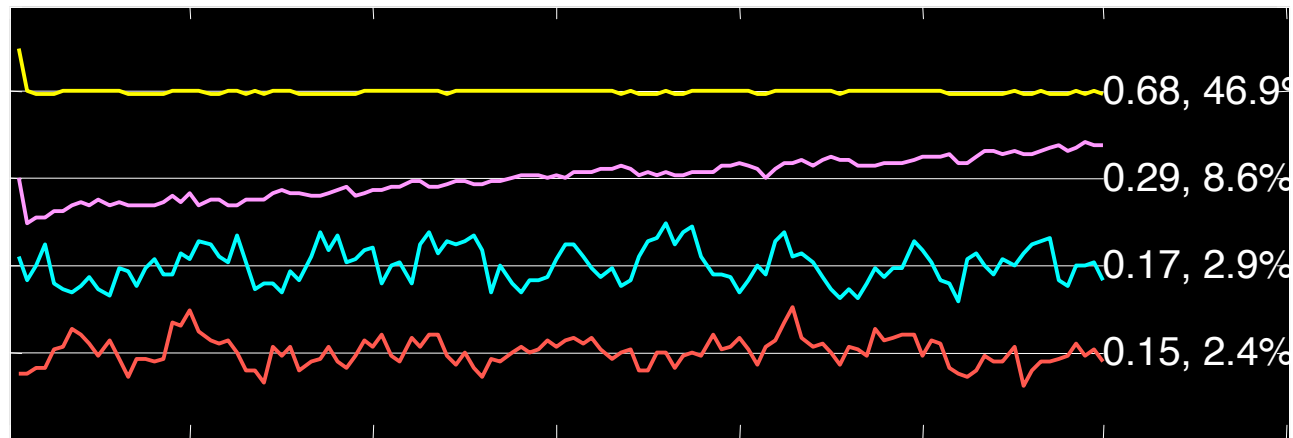
To account for slow drift of magnetic fields, we can add a linear drift term **$at+b$**

Low frequency noise

- Low frequency noise:
 - Physical (scanner drifts)
 - Physiological (aliased)
 - cardiac (~ 1 Hz)
 - respiratory (~ 0.25 Hz)



PCA of time series



3: long-range correlation or anatomical effect: remove by converting to % of brain

4: signal?

Modeling HRF

$$y(t) = \int_0^t H(t-s)f(s)ds + e(t)$$

Various models for HRF:

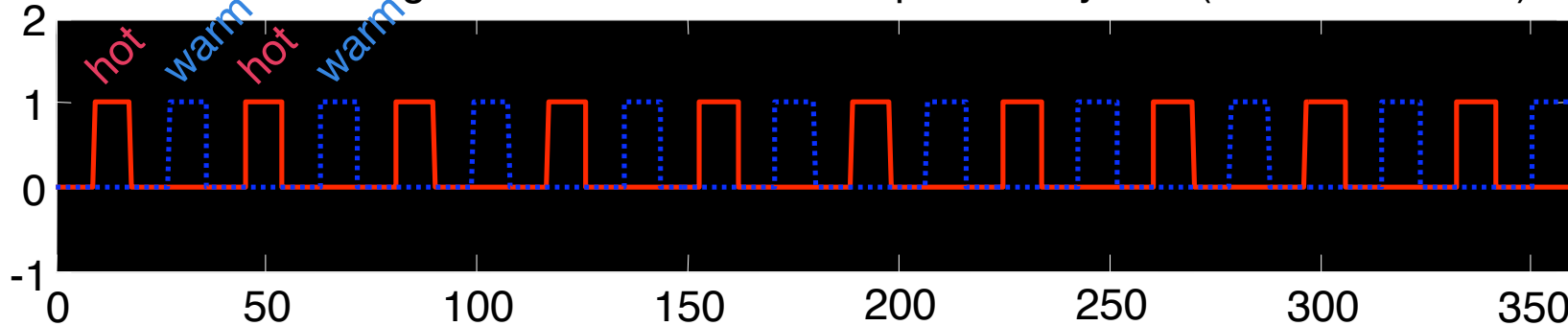
Lange and Zeger (1997): a gamma function

Friston (1998): difference of two gamma functions

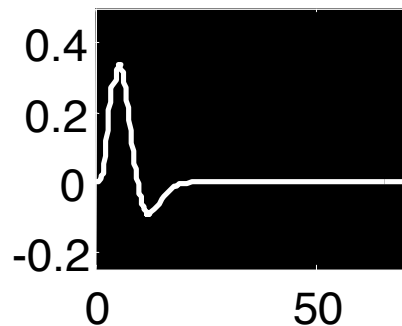
Example: pain perception

Source: Keith Worsley

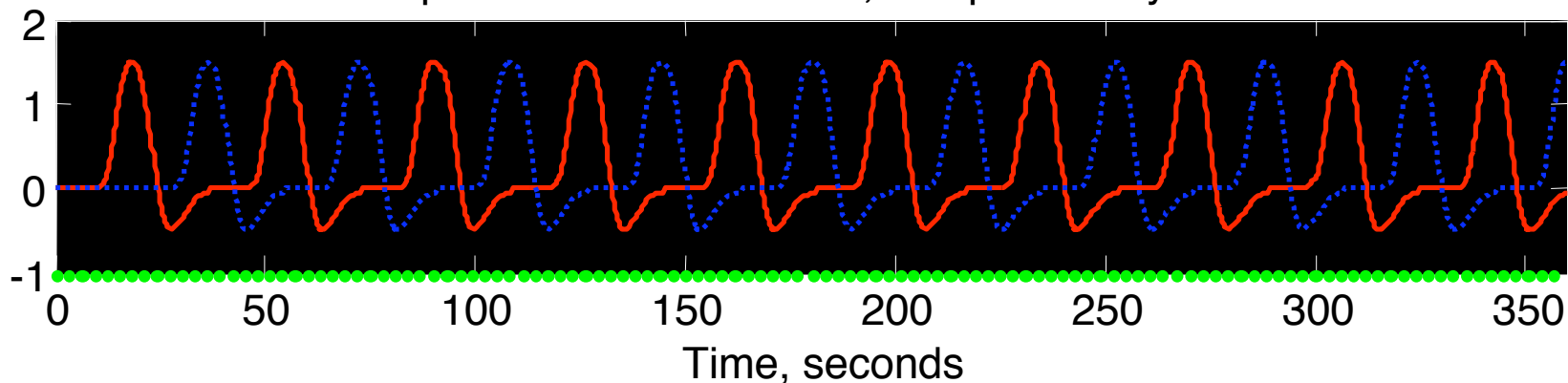
Alternating hot and warm stimuli separated by rest (9 seconds each).



Hemodynamic response function: difference of two gamma densities

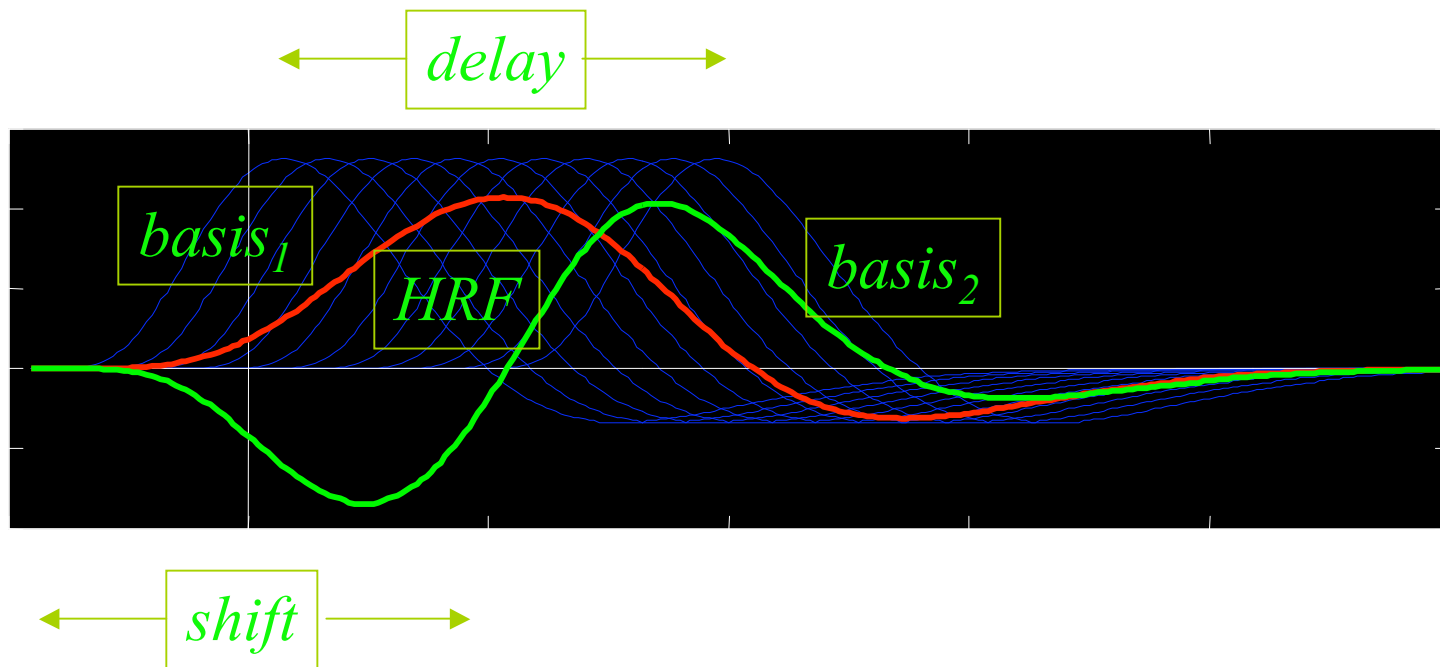


Responses = stimuli * HRF, sampled every 3 seconds



Modeling the delay of the response: Keith Worsley

- Delay or latency to the peak of the HRF is approximated by a linear combination of two *optimally* chosen basis functions:



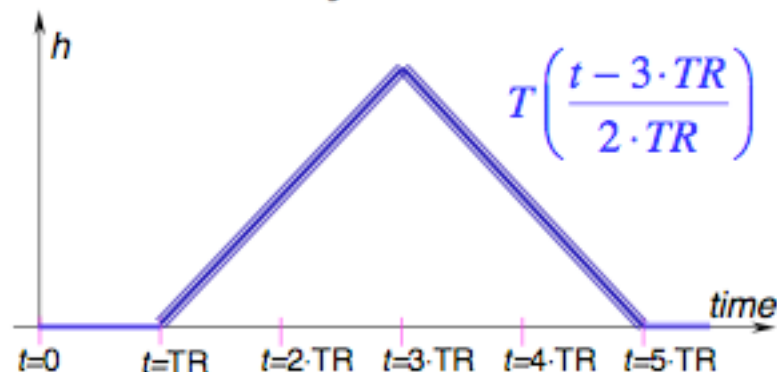
$$HRF(t + shift) \sim basis_1(t) w_1(shift) + basis_2(t) w_2(shift)$$

- Convolve *bases* with the stimulus, then add to the linear model

HRF modeling using the tent function

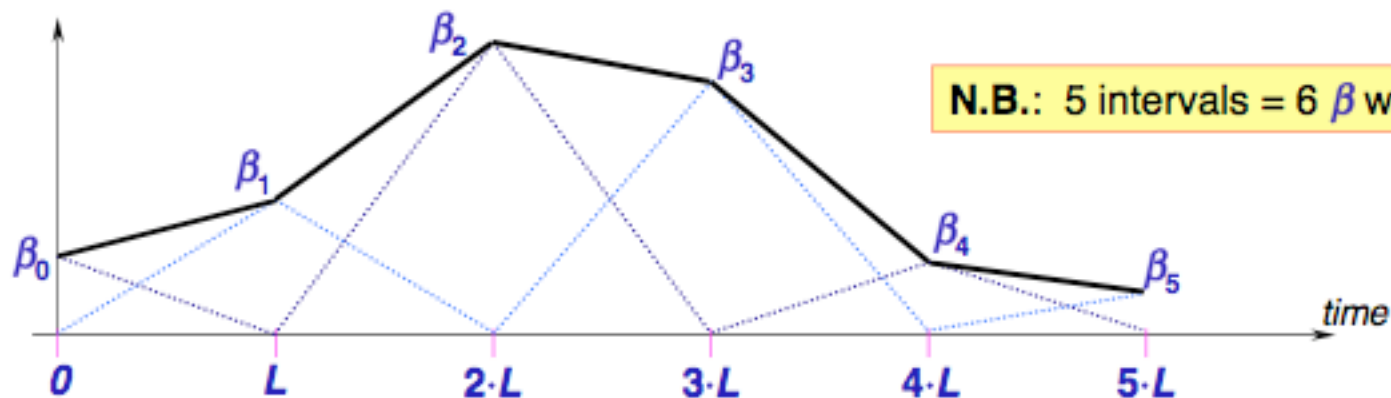
- Simplest set of such functions are closely related to stick functions: **tent functions**

$$T(x) = \begin{cases} 1 - |x| & \text{for } -1 < x < 1 \\ 0 & \text{for } |x| > 1 \end{cases}$$



- Expansion in a set of spaced-apart tent functions is the same as linear interpolation

$$\beta_0 \cdot T\left(\frac{t}{L}\right) + \beta_1 \cdot T\left(\frac{t-L}{L}\right) + \beta_2 \cdot T\left(\frac{t-2 \cdot L}{L}\right) + \beta_3 \cdot T\left(\frac{t-3 \cdot L}{L}\right) + \dots$$



N.B.: 5 intervals = 6 β weights

Discretizing integral

$$y(t) = \int_0^t H(t-s)f(s)ds + e(t)$$


$$y(t) = \sum_{t_j \leq t} H(t-t_j)f(t_j) + e(t)$$


$$y(j) = H(j)f(0) + H(j-1)f(1) + H(j-2)f(2) \cdots + H(j-p)f(p) + \epsilon(j)$$

Assumption: HRF decays to zero after time lag p .

Matrix formulation

$$y(0) = H(0)f(0)$$

$$y(1) = H(1)f(0) + H(0)f(1) + e(1)$$

$$y(2) = H(2)f(0) + H(1)f(1) + H(0)f(2) + e(2)$$

$$y(3) = H(3)f(0) + H(2)f(1) + H(1)f(2) + H(0)f(3) + e(3)$$



$$\mathbf{y} = \mathbf{XH} + \mathbf{e}$$

$$\mathbf{X} = \begin{pmatrix} f(0) & 0 & \cdots & 0 \\ f(1) & f(0) & \cdots & 0 \\ f(2) & f(1) & f(0) & 0 \\ \cdots & \cdots & \cdots & \cdots \\ f(m) & f(m-1) & \cdots & f(m-p) \end{pmatrix} \quad \text{:Toeplitz matrix}$$

MATLAB

```
>> toeplitz(1:10)
```

```
ans =
```

1	2	3	4	5	6	7	8	9	10
2	1	2	3	4	5	6	7	8	9
3	2	1	2	3	4	5	6	7	8
4	3	2	1	2	3	4	5	6	7
5	4	3	2	1	2	3	4	5	6
6	5	4	3	2	1	2	3	4	5
7	6	5	4	3	2	1	2	3	4
8	7	6	5	4	3	2	1	2	3
9	8	7	6	5	4	3	2	1	2
10	9	8	7	6	5	4	3	2	1

periodic impulse function

```
>> toeplitz([1 0 0 0 0 1 0 0 0 0 1 0 0 0 0])
```

```
ans =
```

1	0	0	0	0	1	0	0	0	0	1	0	0	0	0
0	1	0	0	0	0	1	0	0	0	0	1	0	0	0
0	0	1	0	0	0	0	1	0	0	0	0	1	0	0
0	0	0	1	0	0	0	0	1	0	0	0	0	1	0
0	0	0	0	1	0	0	0	0	1	0	0	0	0	1
1	0	0	0	0	1	0	0	0	0	1	0	0	0	0
0	1	0	0	0	0	1	0	0	0	0	1	0	0	0
0	0	1	0	0	0	0	1	0	0	0	0	1	0	0
0	0	0	1	0	0	0	0	1	0	0	0	0	1	0
0	0	0	0	1	0	0	0	0	1	0	0	0	0	1
1	0	0	0	0	1	0	0	0	0	1	0	0	0	0
0	1	0	0	0	0	1	0	0	0	0	1	0	0	0
0	0	1	0	0	0	0	1	0	0	0	0	1	0	0
0	0	0	1	0	0	0	0	1	0	0	0	0	1	0
0	0	0	0	1	0	0	0	0	1	0	0	0	0	1

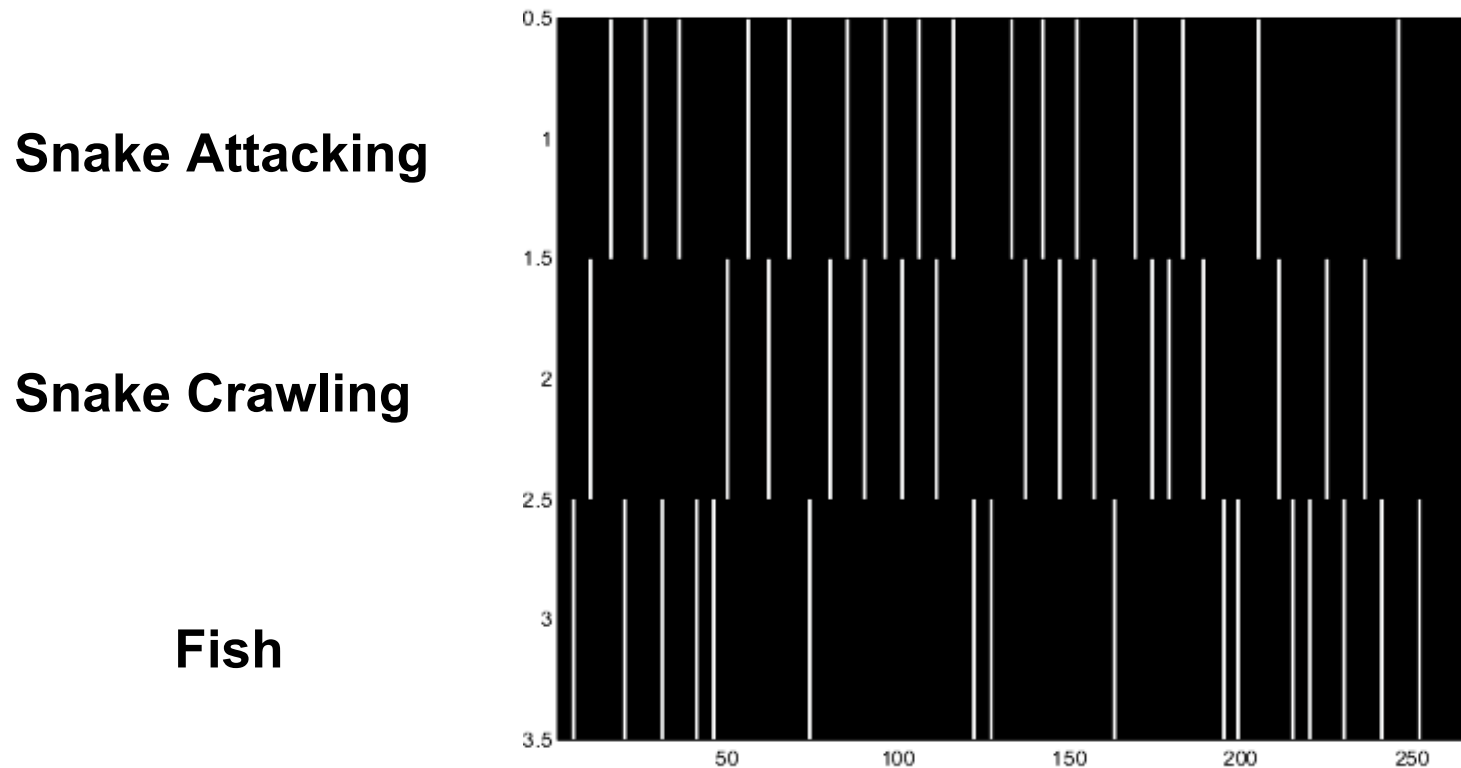
Simple linear model approach

$$\mathbf{y} = \mathbf{X}\mathbf{H} + \mathbf{e}$$

$$\hat{\mathbf{H}} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{y}$$

- This estimation gives us the height of HRF at each time point.
- Nonparametric HRF estimation technique: estimates HRF as a linear combination of smooth basis functions.

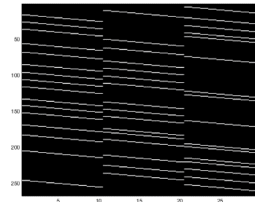
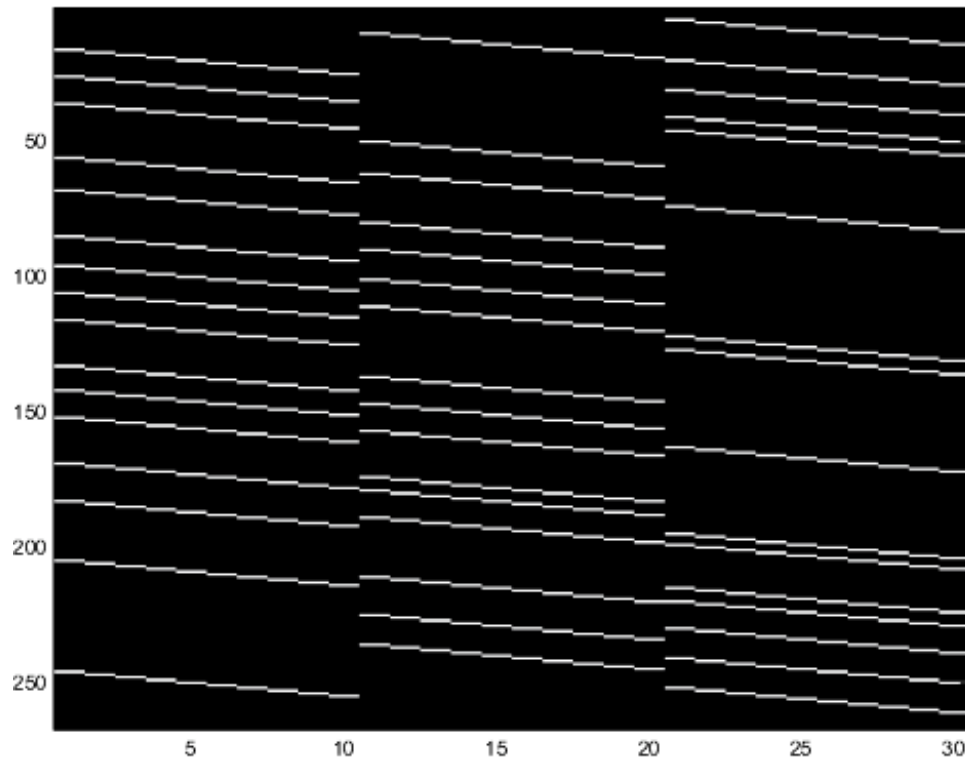
Event related design: Multiple stimuli



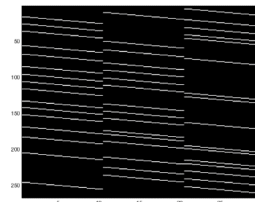
$$y = X_1 H_1 + X_2 H_2 + X_3 H_3 + e$$

Design Matrix

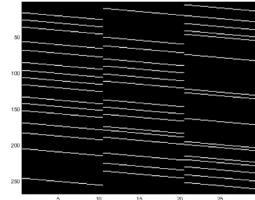
easy to incorporate different runs and subjects



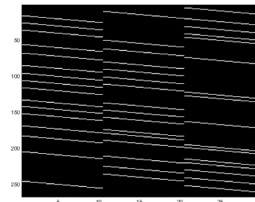
subject 1



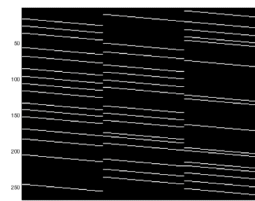
subject 2



subject 3



subject 4



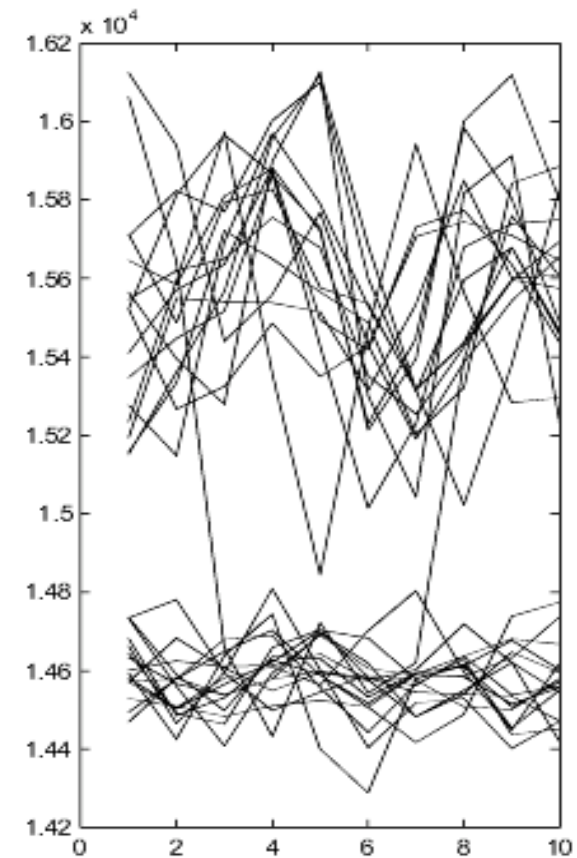
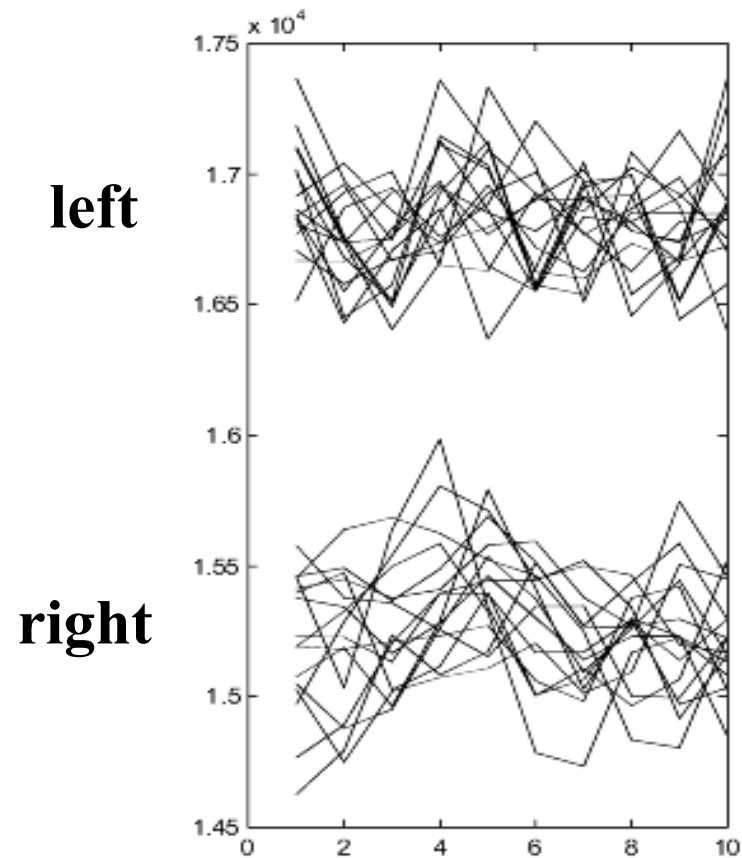
subject 5

fMRI experiment of picture showing

Snake attacking

subject 1

subject 2

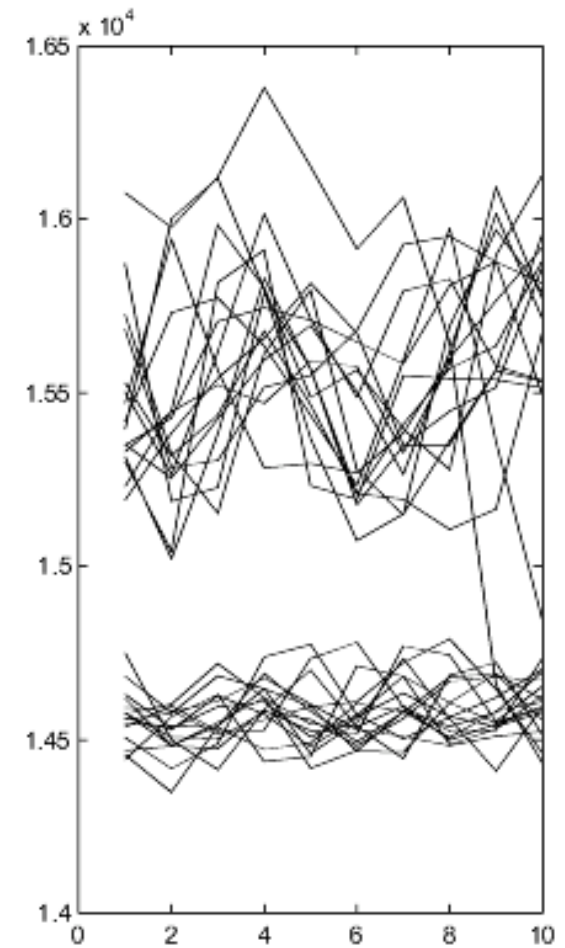
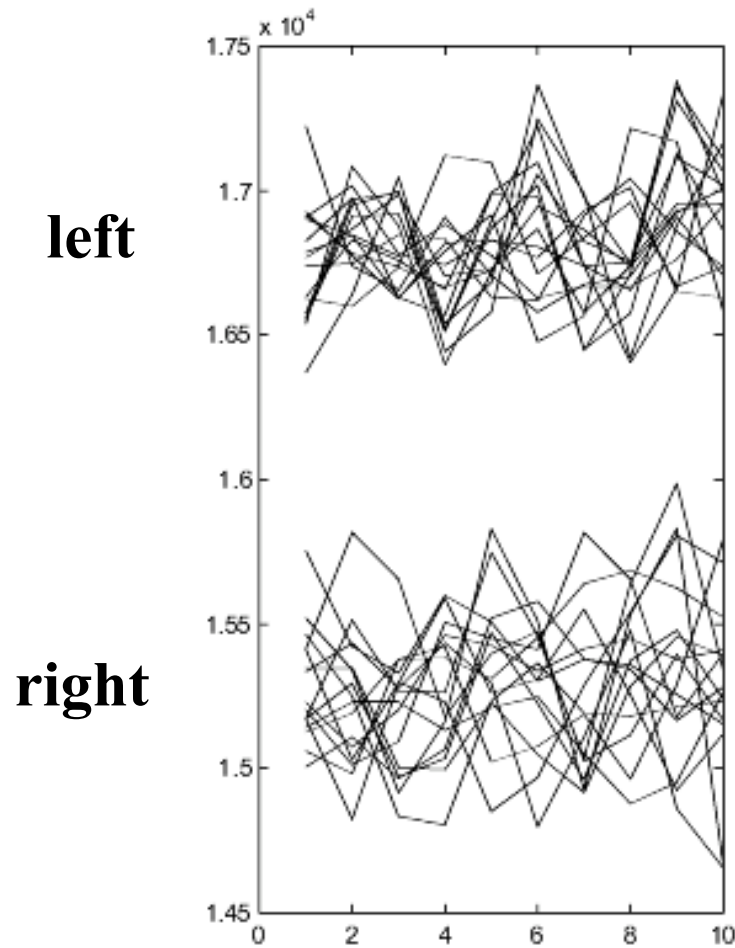


Are you seeing any pattern?

Snake crawling

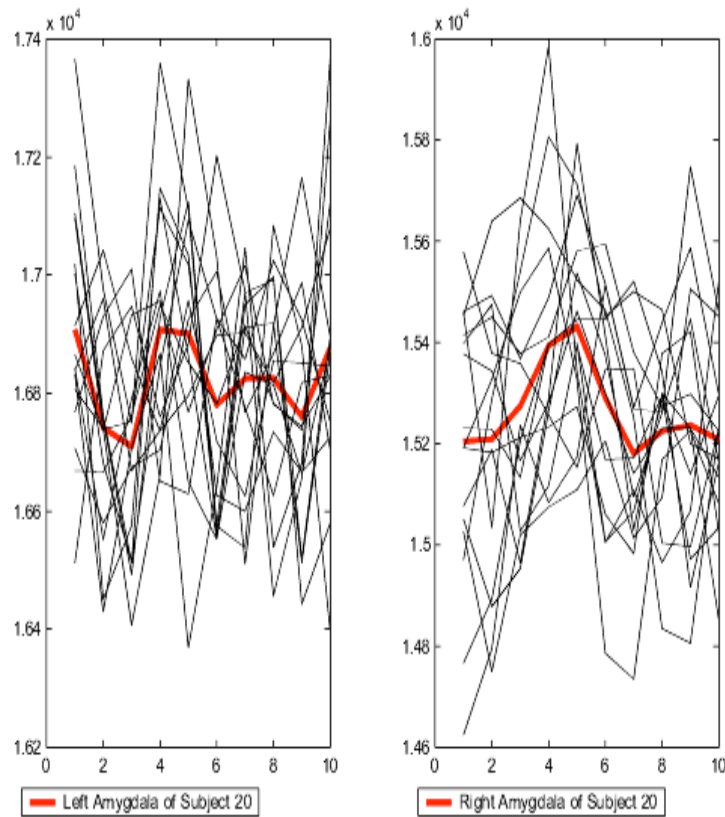
subject 1

subject 2



Now we are see something

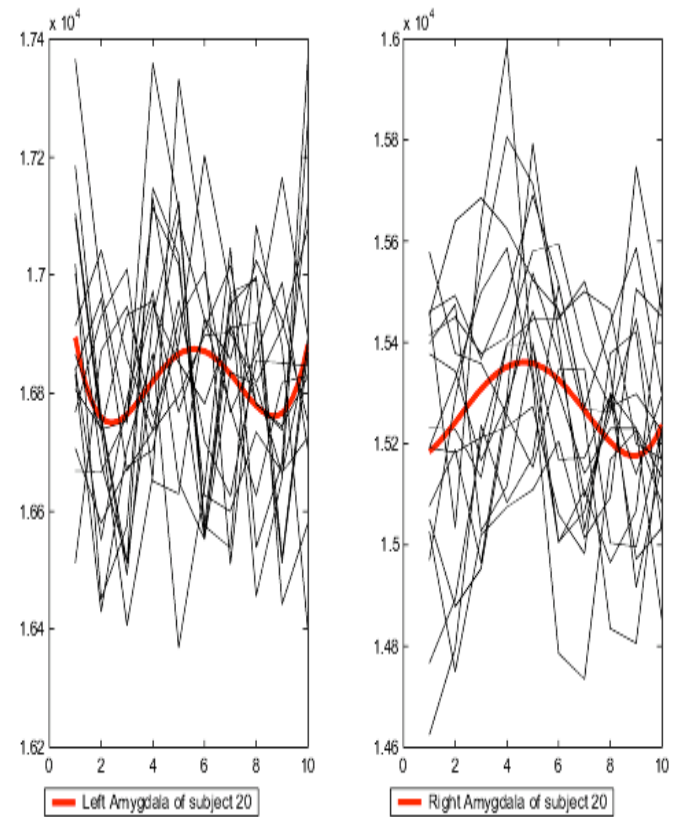
Subject 1



left

right

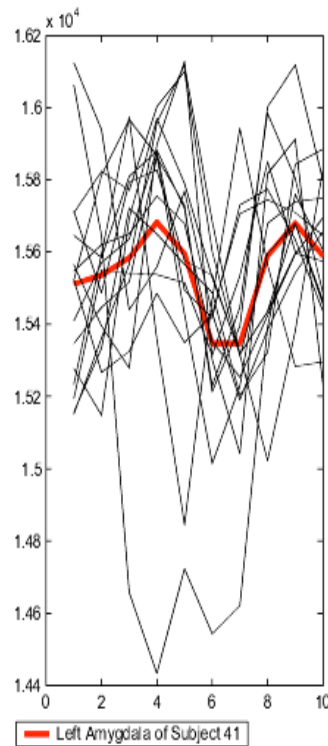
Kernel smoothing



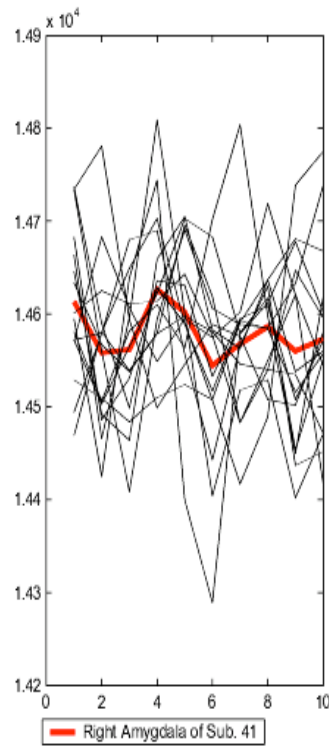
left

right

subject 2

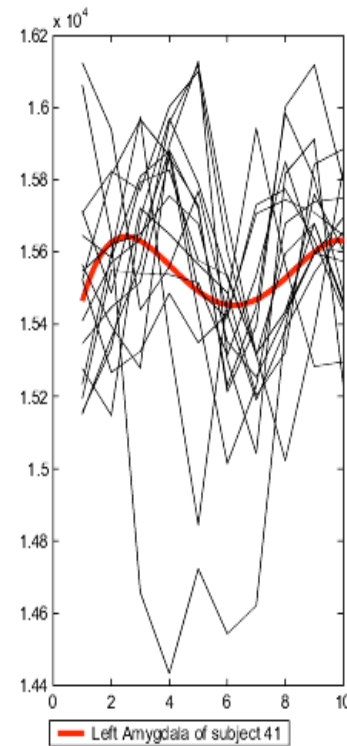


left

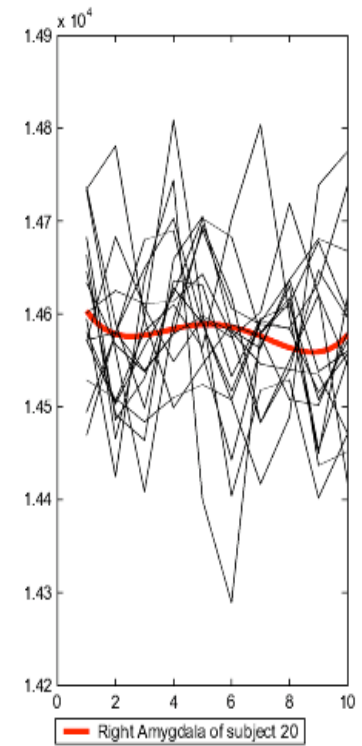


right

Kernel smoothing



left



right

Problem with Ordinary Least Squares (OLS) Estimation

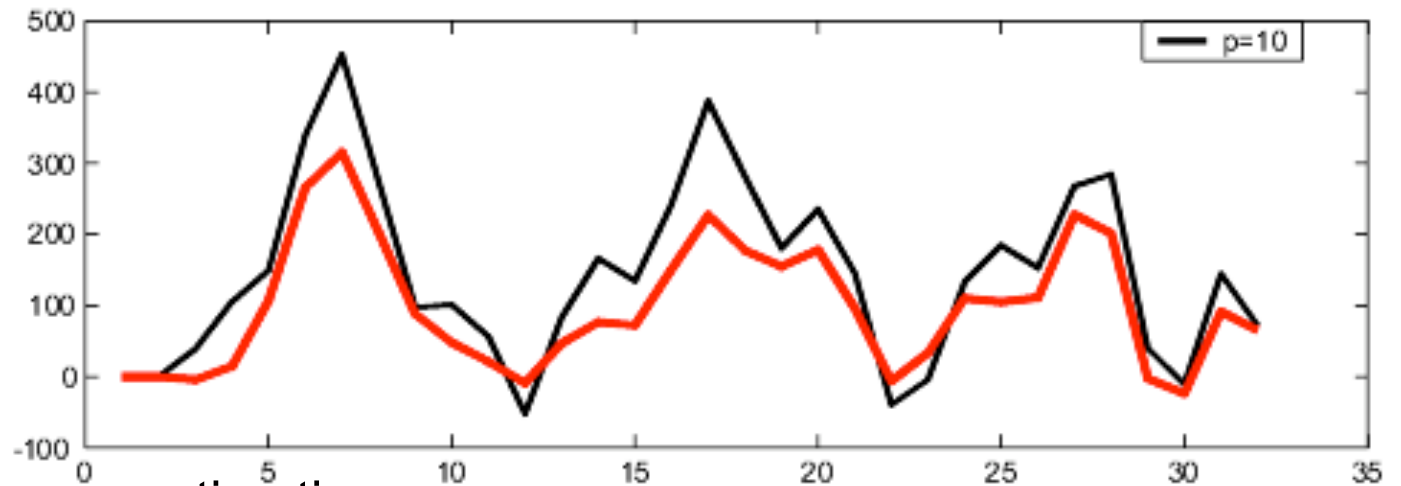
- OLS is inefficient since it does not take care of temporal correlation.
- More false positives (Burock et al., 1998; Dale, 1999, Woolrich et al., 2001; Purdon et al., 2001; Wicker and Ponlupt, 2003)
- To address these problems, we model temporal correlation via the *whitening process*.

HRF

snake attacking

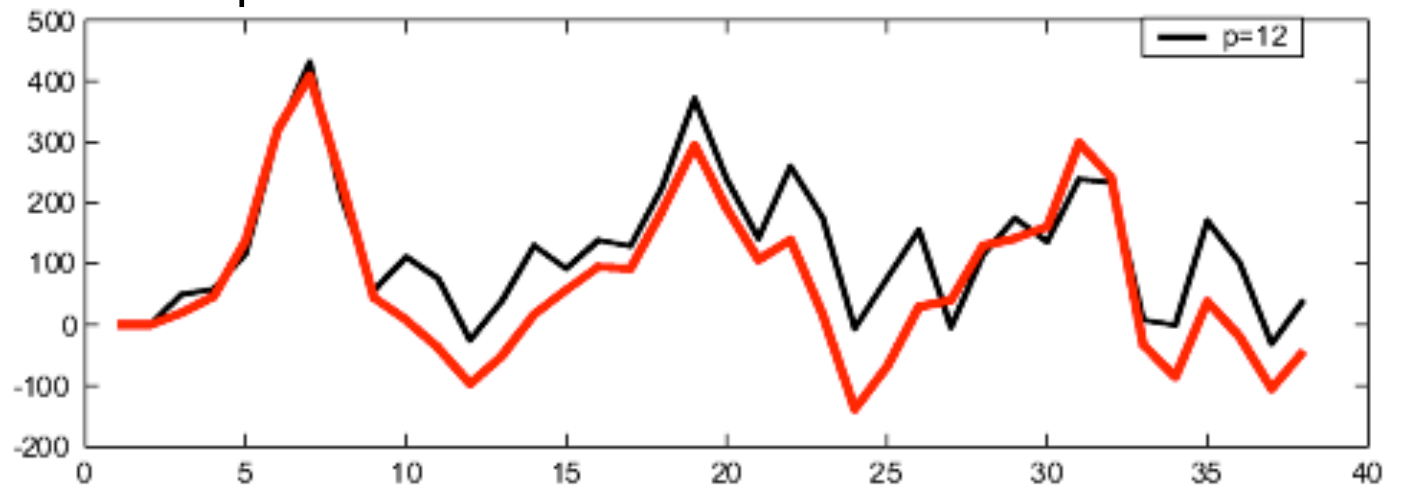
snake crawling

fish swimming



Black: least squares estimation

Red: generalized least squares estimation



Modeling correlated error

$$y(t) = \int_0^t H(t-s)f(s)ds + e(t)$$

Autoregressive model (AR) models

- AR(1) : Bullmore et al. (1999), Burock and Dale (2000), Purdon et al. (2001).
- AR(3) : Bullmore et al., (1996)

AR(p) model

$$e(t) = c_1 e(t-1) + \cdots + c_p e(t-p) + \epsilon(t)$$

White noise with zero mean and finite variance

- Time series $e(t)$ is called an autoregressive (AR) process of order p and denoted AR(p)
- This model correlates the time series up to p lags.

AR(1) model

$$e(t) = \rho e(t-1) + \epsilon(t)$$

Gaussian white noise $\epsilon(t) \approx N(0, \sigma^2)$

$$E[e(t)] = 0 \quad V[e(t)] = \frac{\sigma^2}{1 - \rho^2}$$

(auto) covariance: $Cov[e(t), e(t-p)] = \frac{\sigma^2}{1 - \rho^2} \rho^p$

(auto) correlation: $corr[e(t), e(t-p)] = \rho^p$

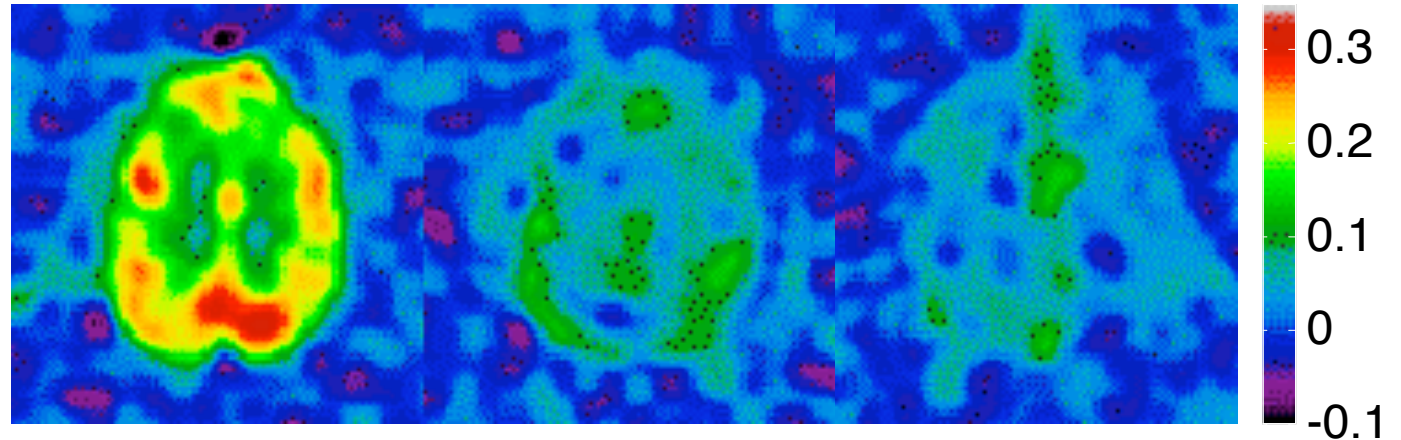
Higher order AR model?

c_1

c_2

c_3

AR(1) seems
to be adequate



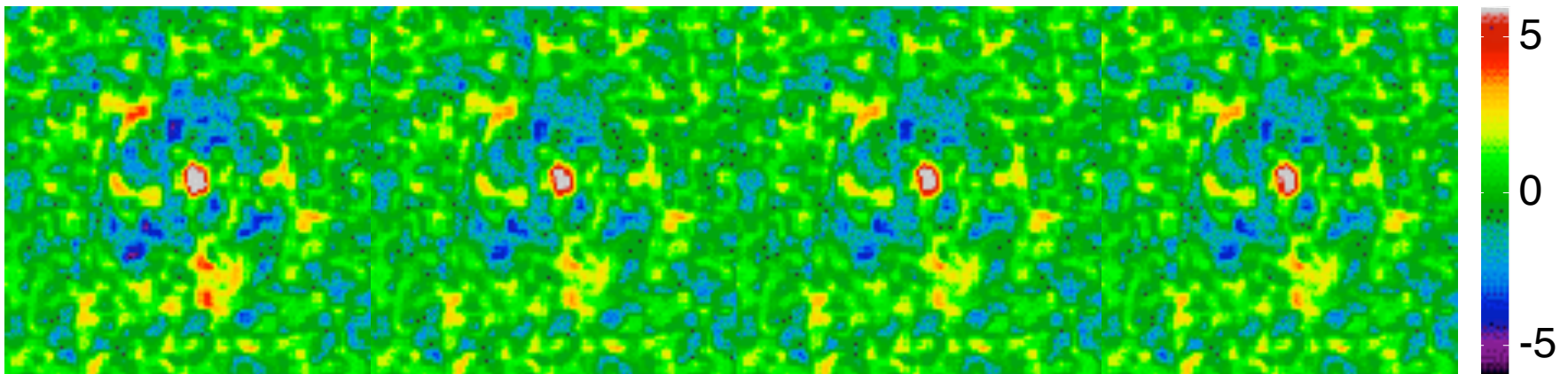
... has little effect on the T statistics:

No correlation

AR(1)

AR(2)

AR(3)



Covariance matrix of noise

Multivariate normal $N(0, V)$

$$y = \mathbf{X}\mathbf{H} + \mathbf{e}$$

- Estimate residual from LSE: $e = y - X(X'X)^{-1}X'y$
- Estimate covariance matrix: $V = (V_{ij}) = E(ee')$

$$V_{ij} = \text{Var}[e(1)] \text{corr}[e(i), e(j)]$$

For AR(1) model, the covariance matrix has a special form:

$$\frac{\sigma^2}{1 - \rho^2}$$

$$\rho^{|i-j|}$$

Covariance matrix = Toeplitz matrix

$$V_{ij} = \text{Var}[e(1)]\text{corr}[e(i), e(j)]$$

$$V = \frac{\sigma^2}{1 - \rho^2} \begin{pmatrix} 1 & \rho & \rho^2 & \ddots \\ \rho & 1 & \rho & \rho^2 \\ \rho^2 & \rho & 1 & \rho \\ \ddots & \rho^2 & \rho & 1 \end{pmatrix}$$

Variance

autocorrelation

- Estimating autocorrelation at lag l

$$\text{corr}[e(t), e(t - l)] = \frac{E[e(t)e(t - l)]}{Ee^2(t)}$$

- Sample autocorrelation at lag l

$$\frac{\sum_{j=l}^n [e(j)e(j - l)]}{\sum_{j=1}^n e^2(j)}$$

Generalized Least Squares (GLS) Estimation

$$y = XH + e$$

- Whitening process:

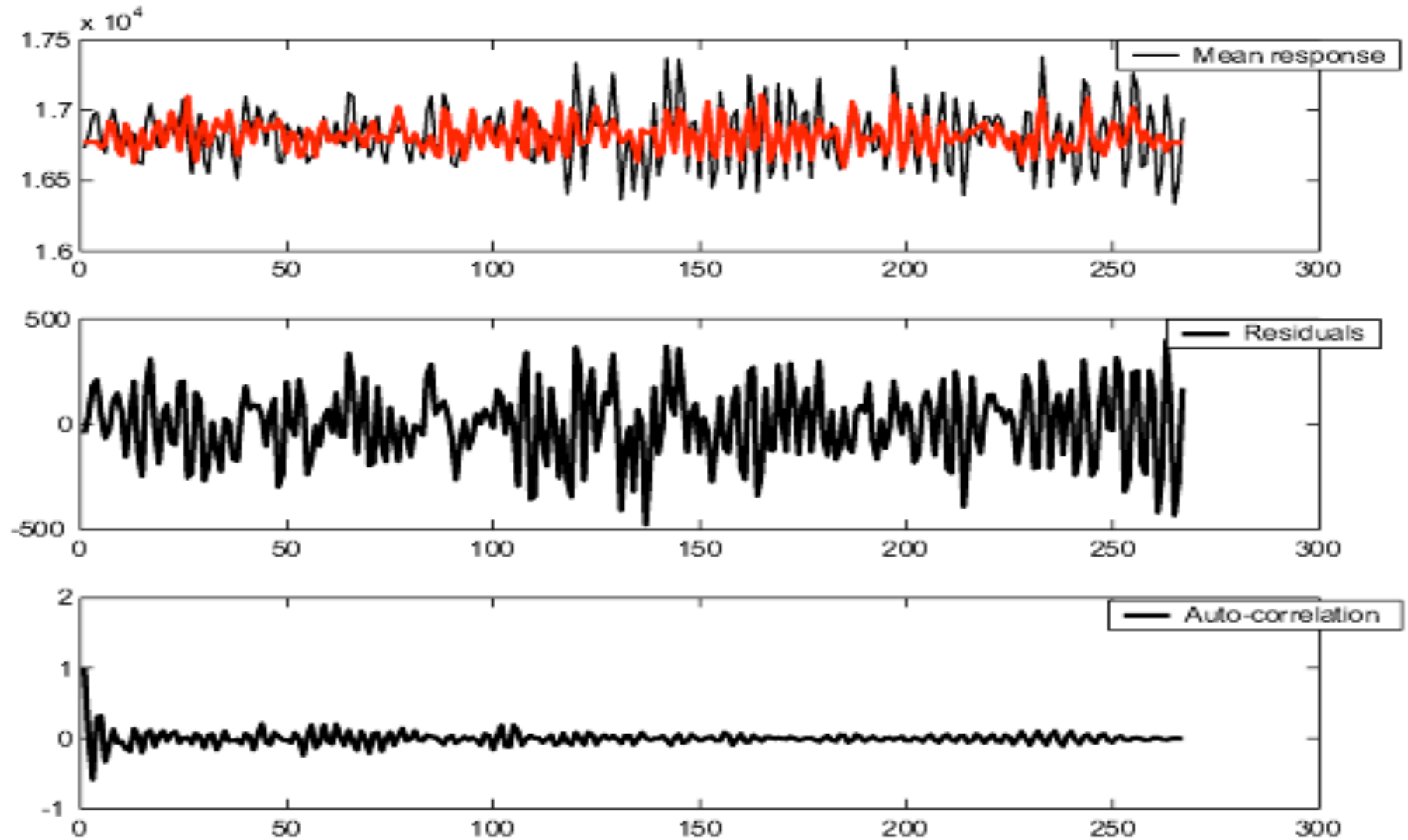
$$V^{-1/2}y = V^{-1/2}XH + \boxed{V^{-1/2}e}$$

Noise is uncorrelated now

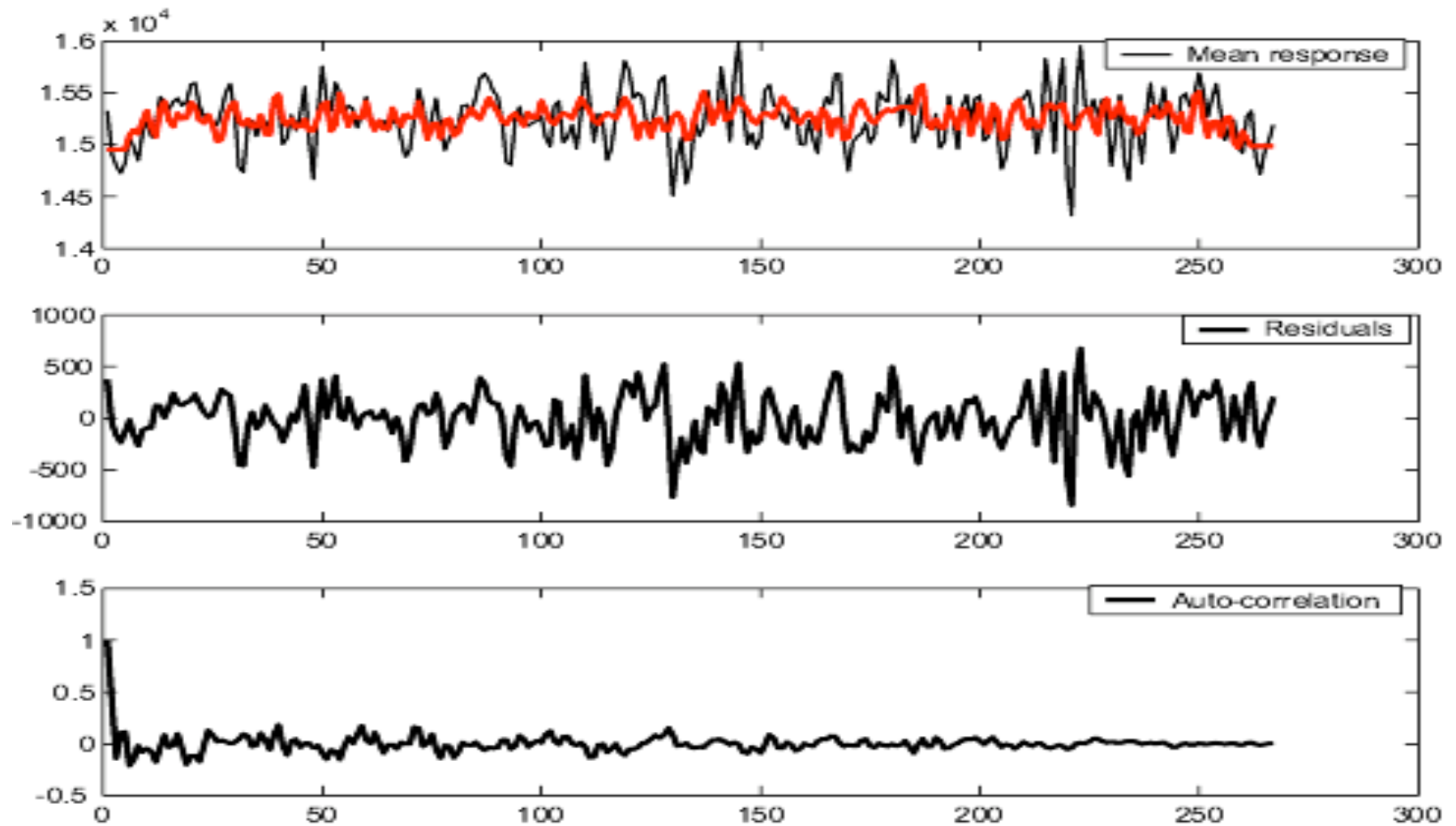
- GLS estimation:

$$\hat{H} = (X'V^{-1}X)^{-1}X'V^{-1}y$$

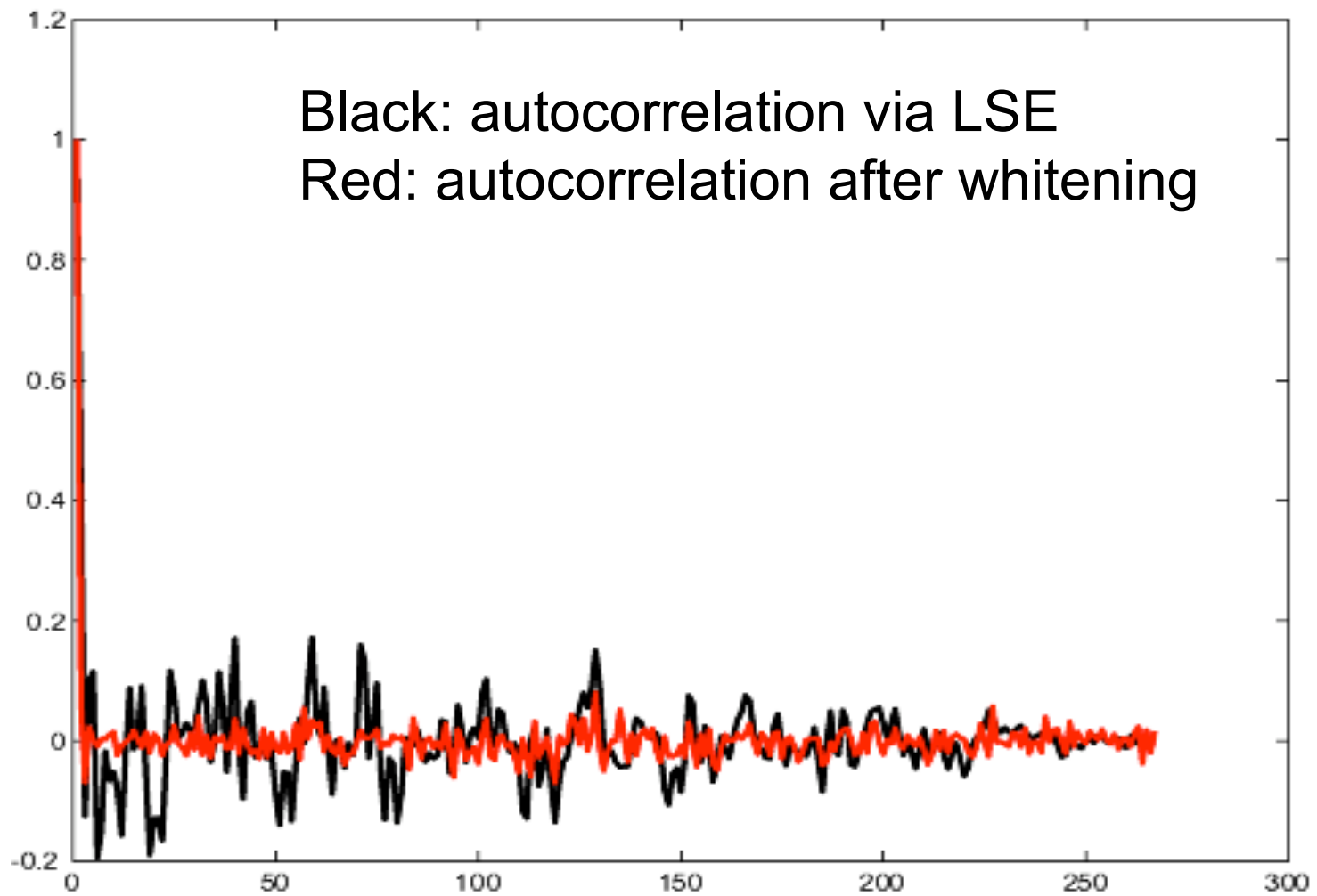
Estimating autocorrelation at the left amygdala



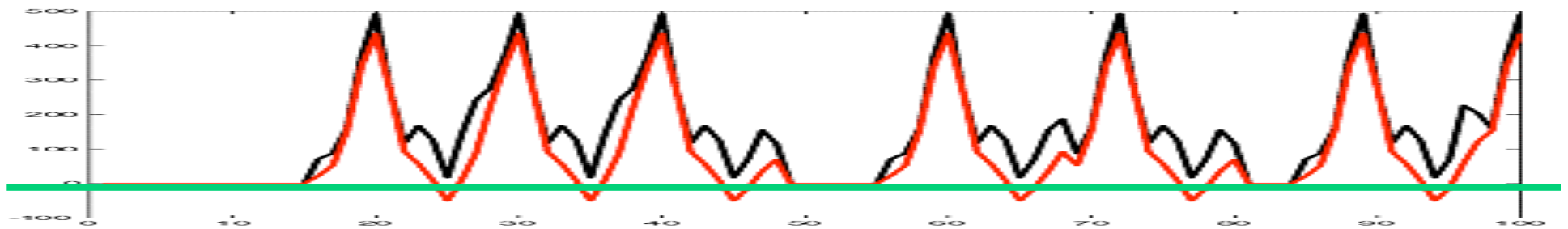
Estimating autocorrelation at the right amygdala



Whitening of noise by GLS



HRF reconvolved with the initial stimuli



- Black: HR based on LSE
Red: HR based on GLE
- GLE can get the dip while LSE can not obtain the dip.

What do we do with the HRF estimation ?

- 1. Inference on the height of HRF**
- 2. Inference on the area under HRF**



Group comparisons via GLM (t or F tests)

Other issues in fMRI analysis:

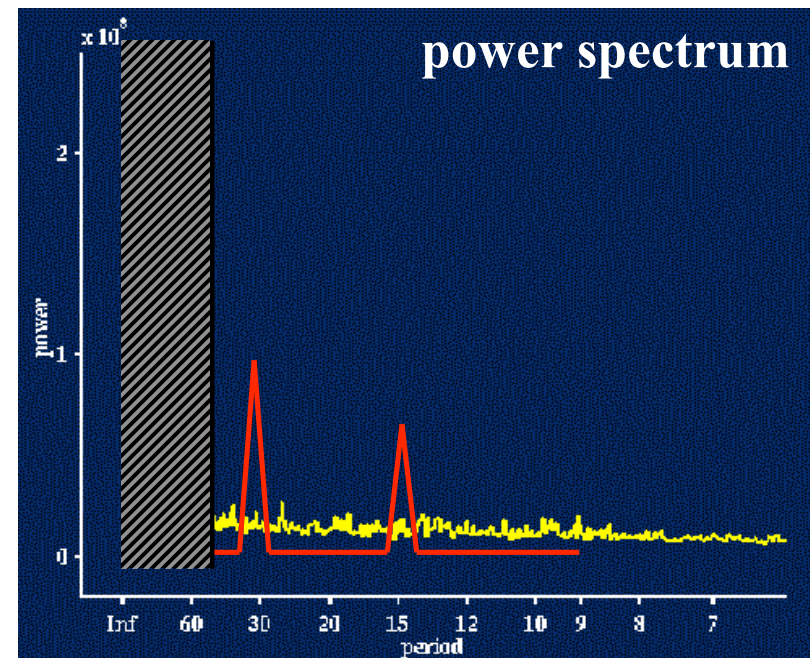
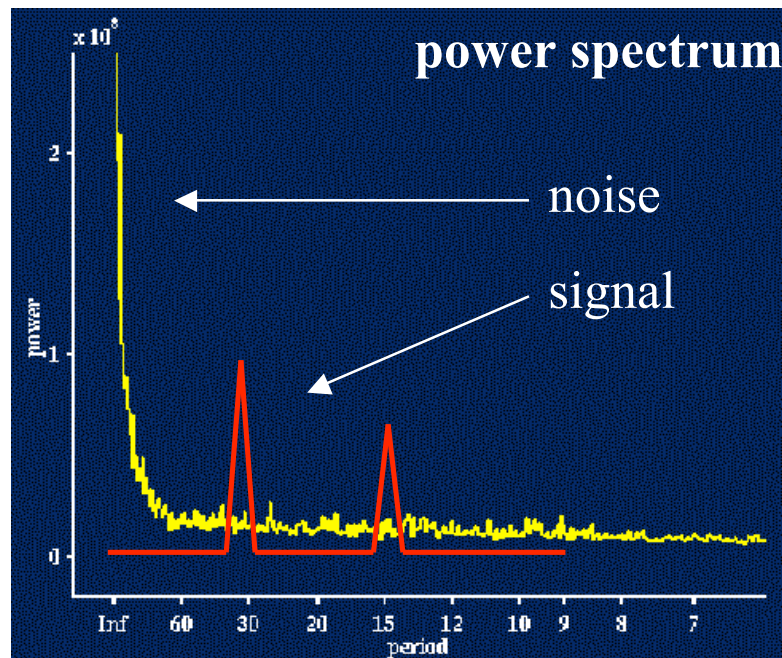
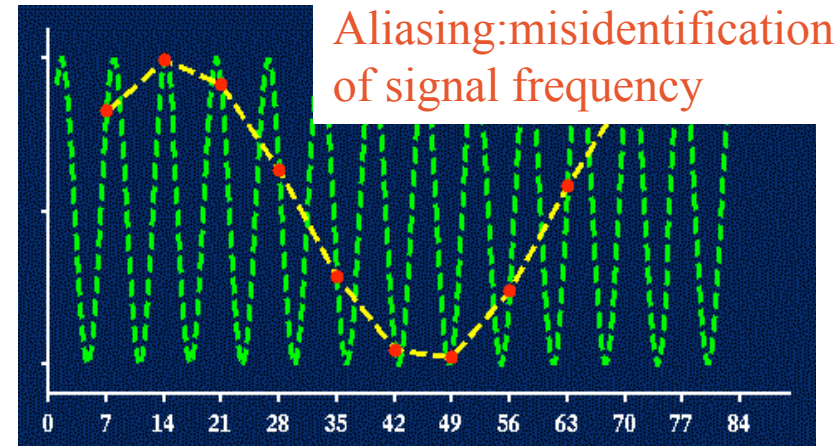
Fourier analysis of fMRI

Signal filtering/smoothing

Effect of tissue volume to fMRI analysis

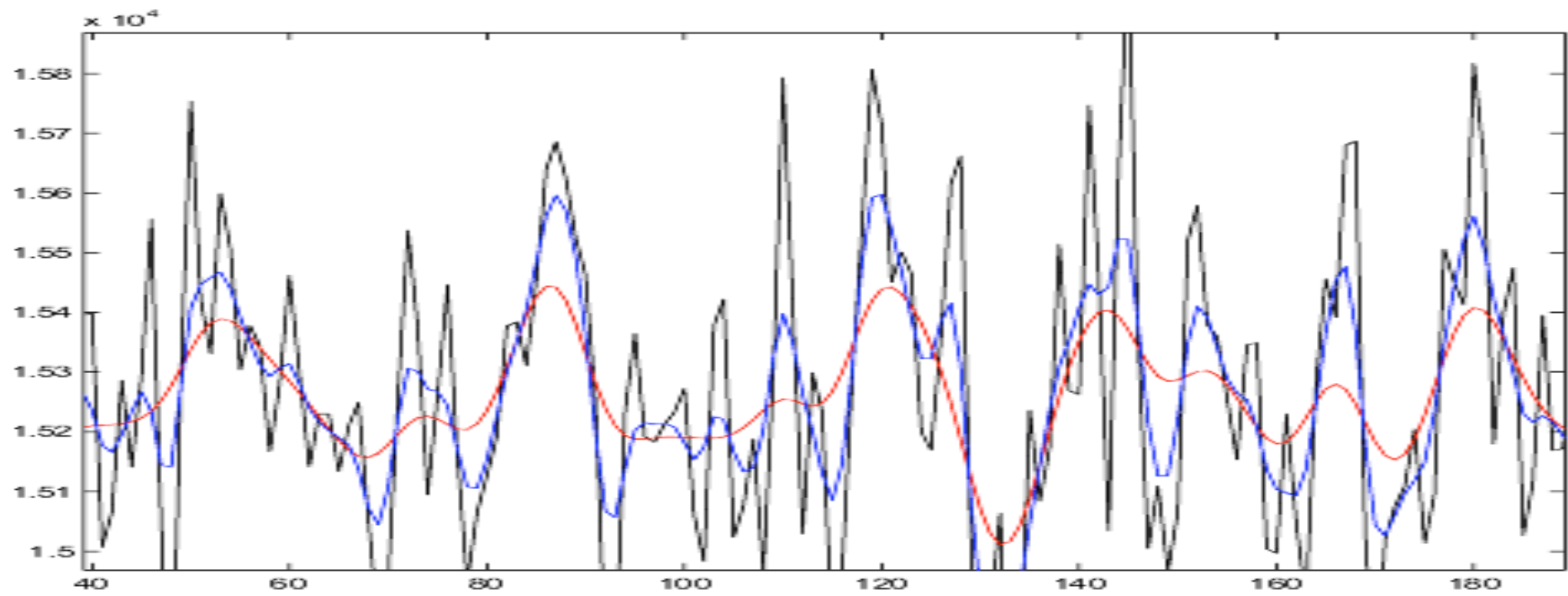
Low frequency noise reduction via Fourier transform

- Low frequency noise:
 - Physical (scanner drifts)
 - Physiological (aliased)
 - cardiac (~ 1 Hz)
 - respiratory (~ 0.25 Hz)



Diffusion smoothing/filtering

- generalization of Gaussian kernel smoothing
- spatially and temporally adaptive filter



Effect of tissue density on fMRI analysis



NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 24 (2005) 1–11

The relationship between cerebral blood flow and volume in humans

Egill Rostrup,^{a,*} Gitte M. Knudsen,^b Ian Law,^{b,c} Søren Holm,^c
Henrik B.W. Larsson,^a and Olaf B. Paulson^{a,b}



NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 34 (2007) 500–508

Technical Note

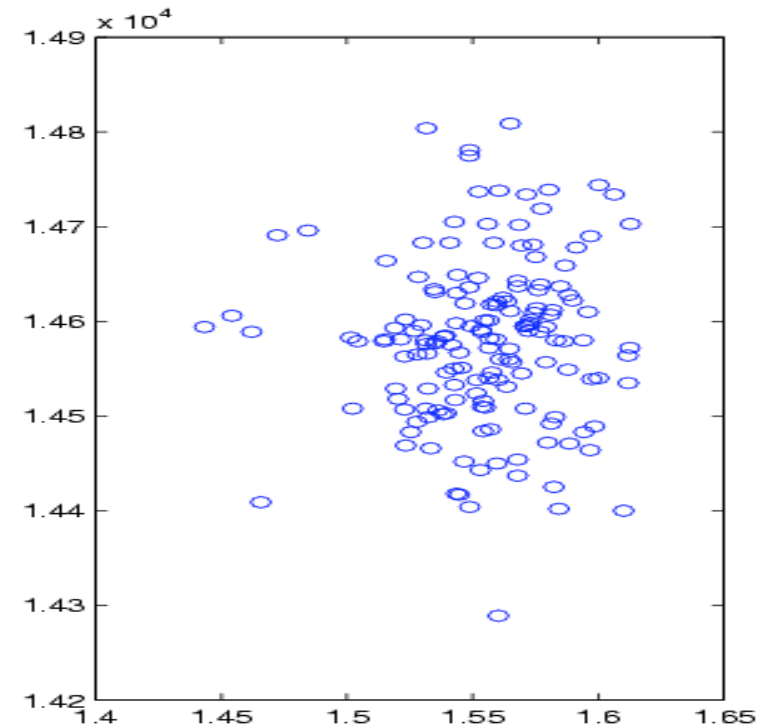
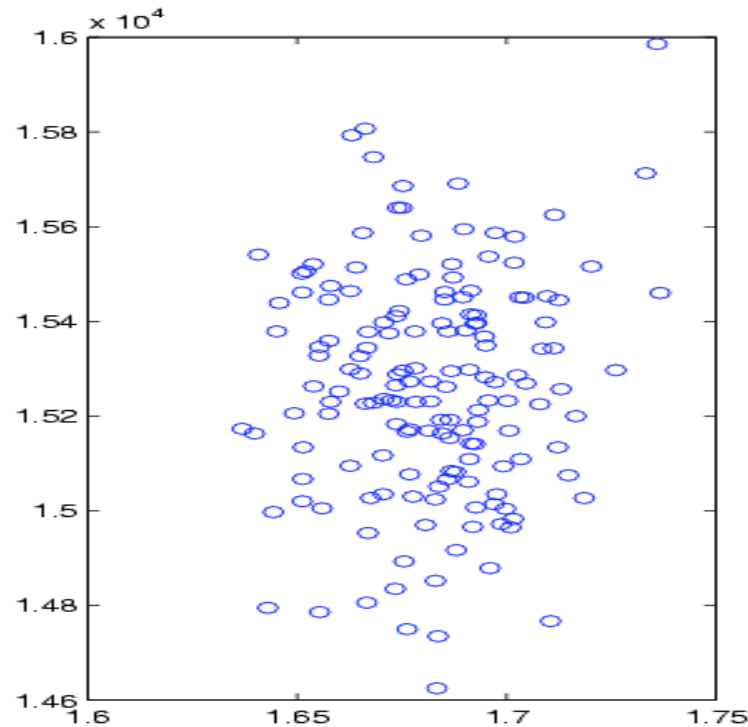
Integrating VBM into the General Linear Model with voxelwise anatomical covariates

Terrence R. Oakes,^{a,*} Andrew S. Fox,^{a,b} Tom Johnstone,^a Moo K. Chung,^c
Ned Kalin,^{a,b,d} and Richard J. Davidson^{a,b,d}

Publicly available fMRI data analysis tools

- SPM5
- AFNI+SUMA package (SUMA enables surface-based fMRI analysis)
- FMRISTAT (Keith Worsley's own MATLAB tools)

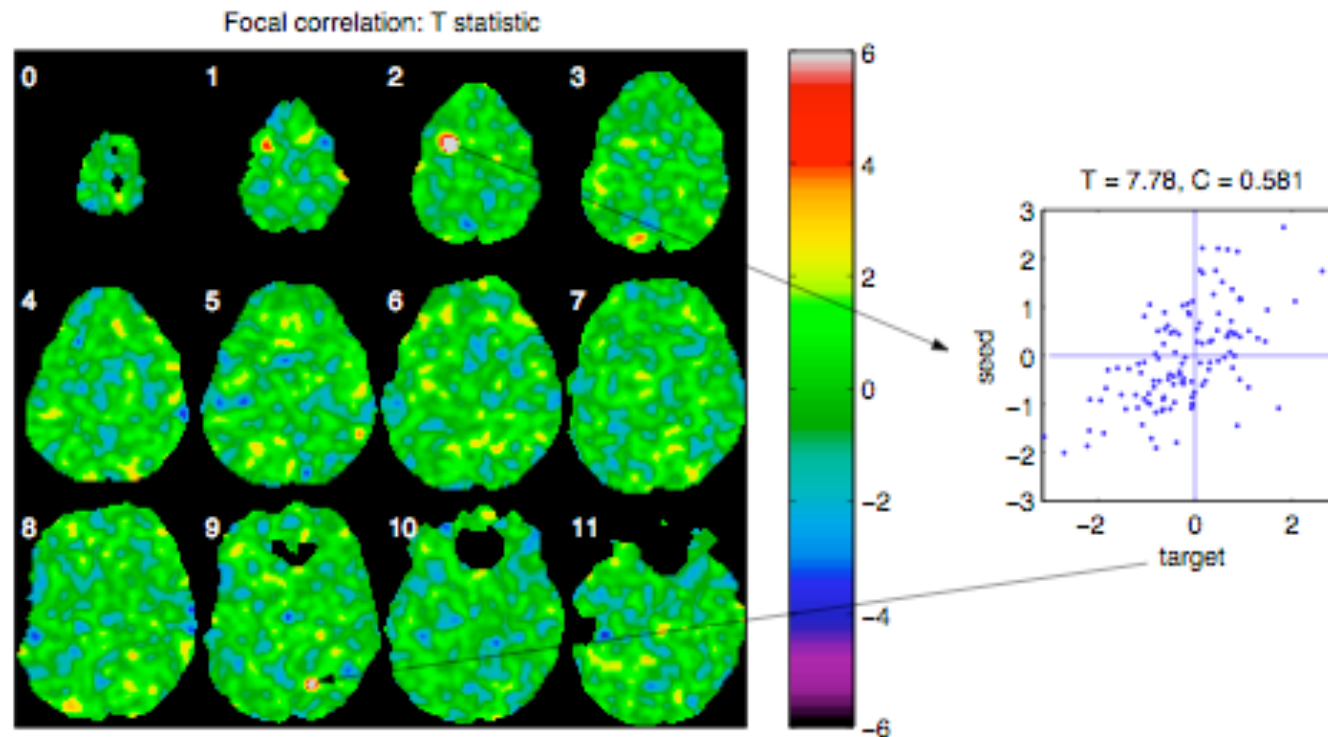
Connectivity/correlation analysis in fMRI analysis



scatter plot of left and right amygdala fMRI for two subjects
Basic scientific question: how two fMRI time series are related ?

Single seed functional connectivity analysis

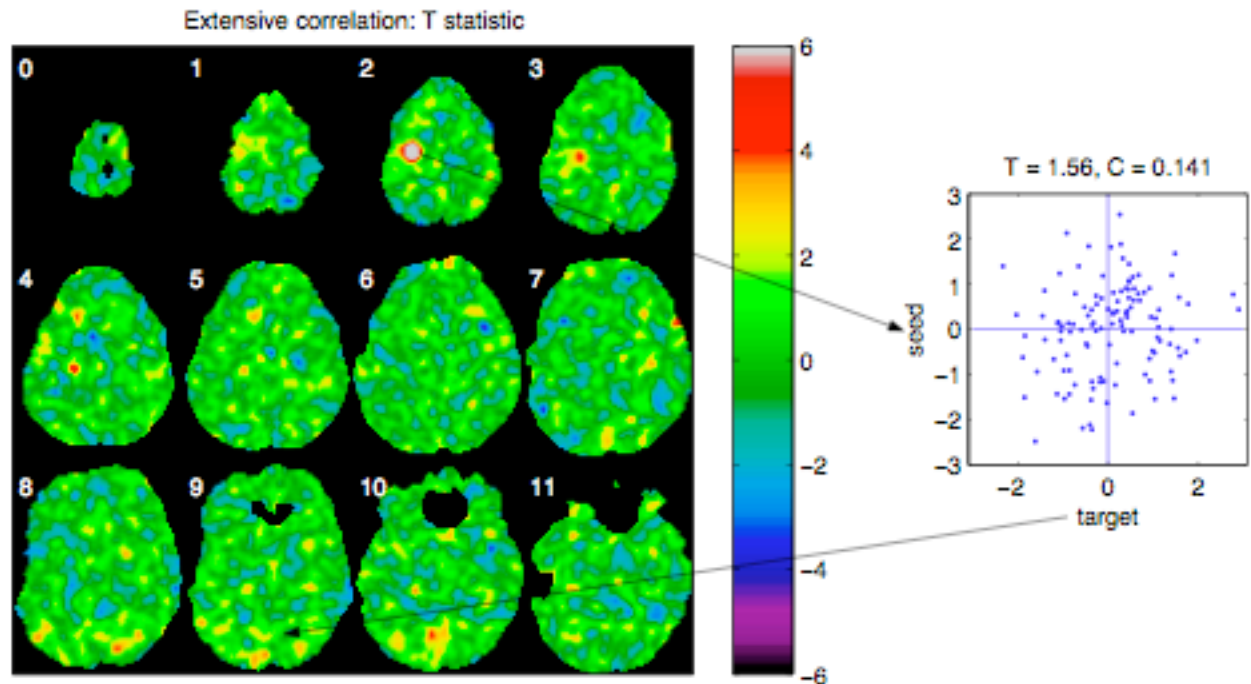
From a single seed, we compute correlation for every other voxels



High correlation

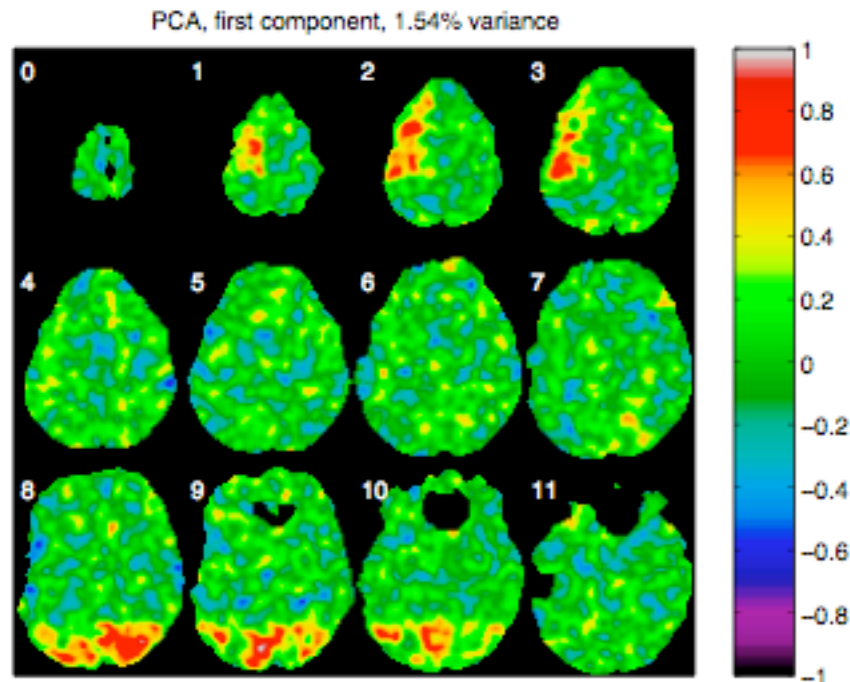
Source: Keith Worsley

Correlation analysis showing no connection

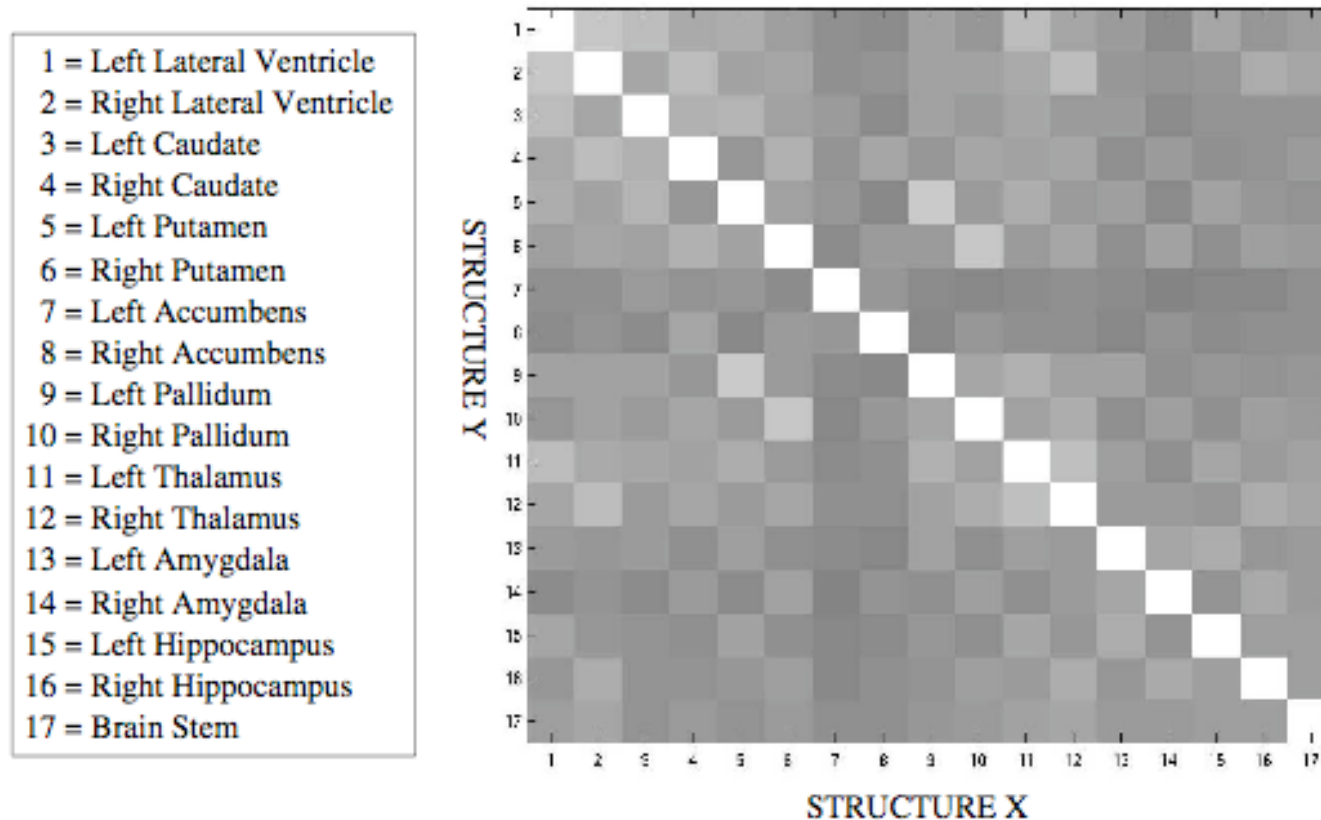


PCA showing connection

(PCA constructed out of correlation matrix)



Multiseed functional connectivity analysis



Partial correlation, partial multiple correlation and canonical correlation can be used.

Lecture 15 Topics

Similarity Measures in Image