

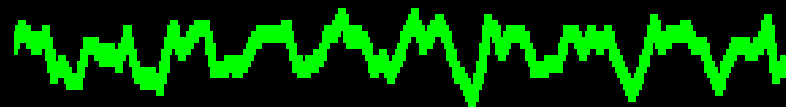
# First-level fMRI modeling

Jeanette Mumford

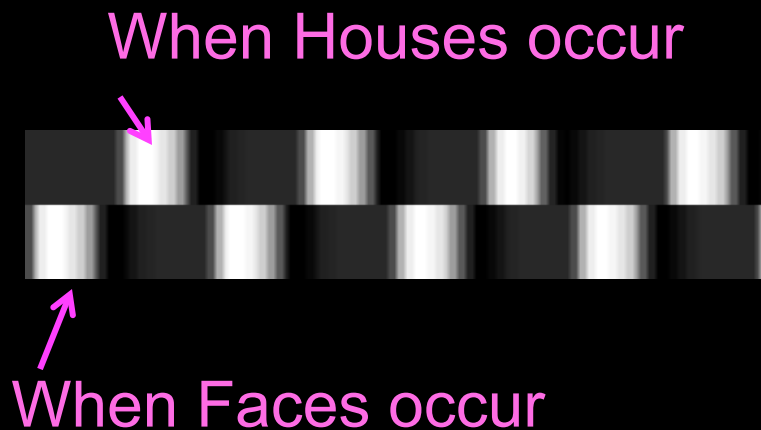
University of Wisconsin - Madison

# Quick GLM overview

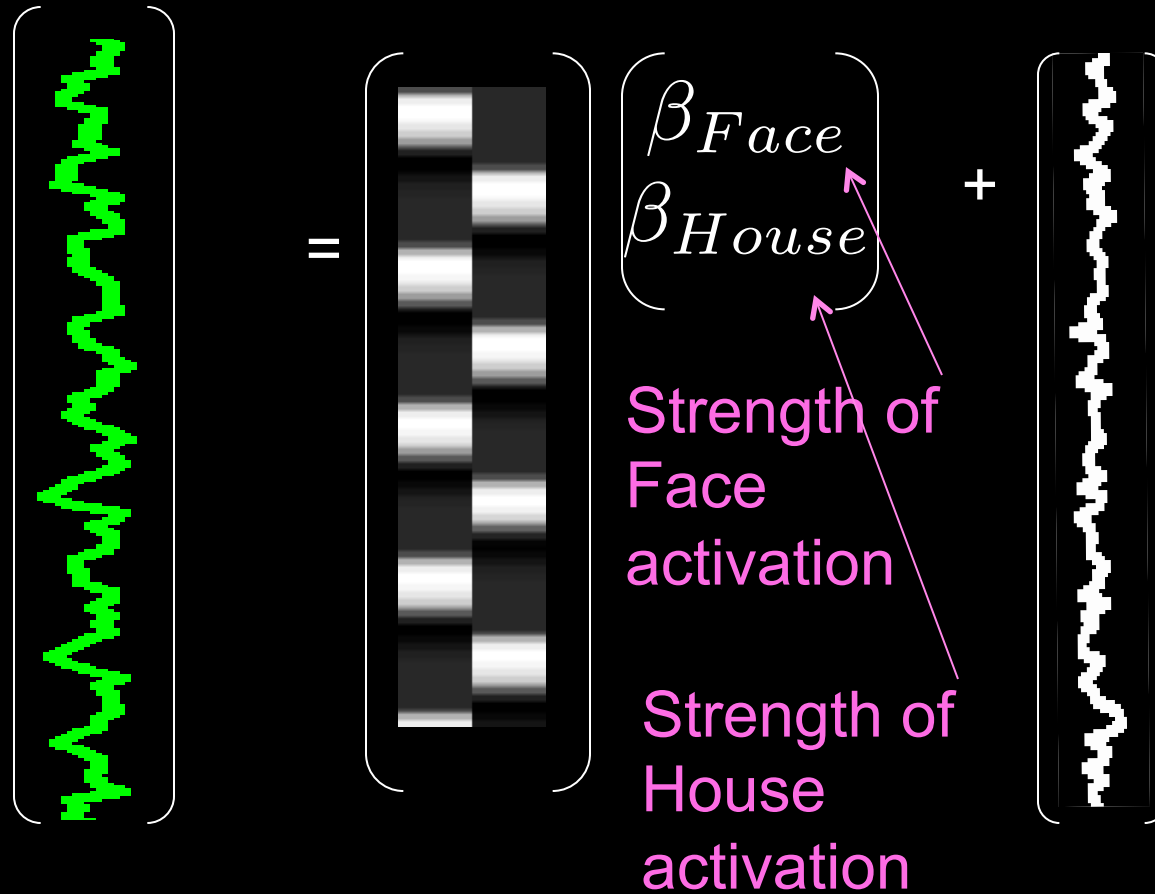
Data: BOLD  
time series



Model: Expected  
BOLD response  
for 2 blocked  
tasks



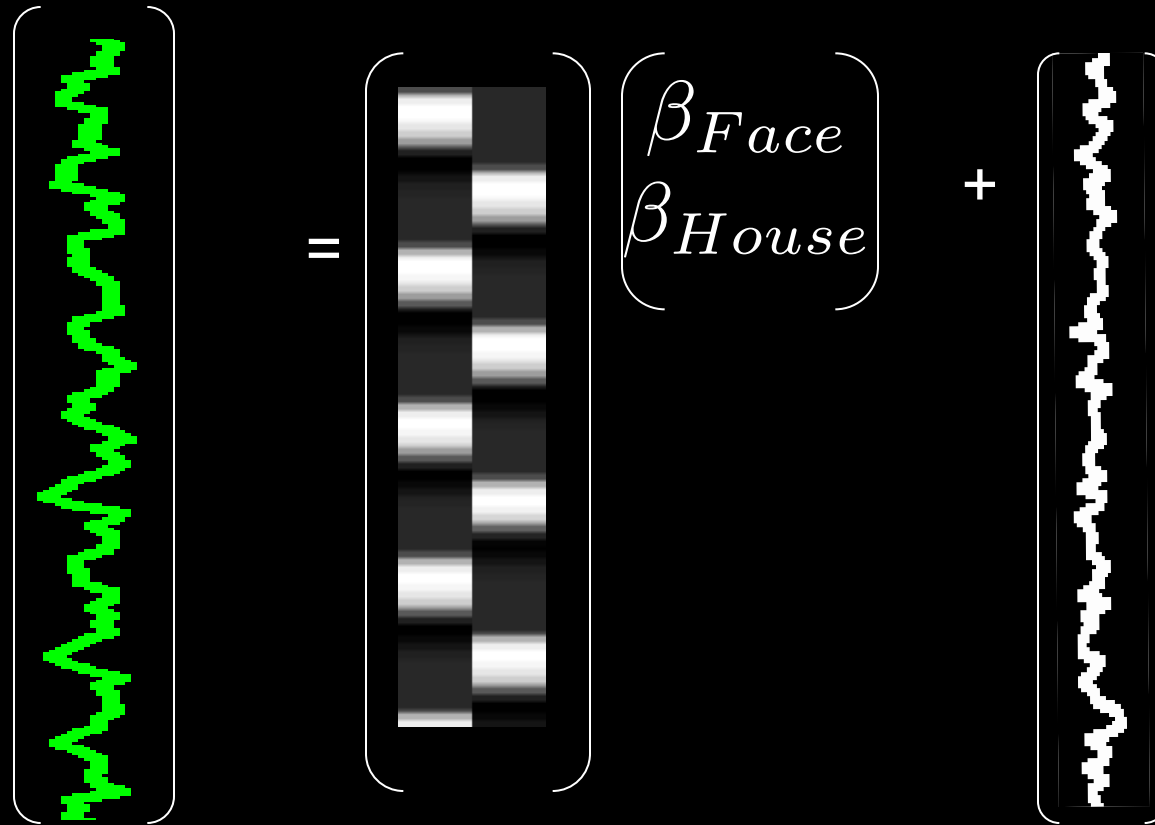
# Quick GLM overview



# Quick GLM overview

$$\begin{matrix} \left[ \text{Green signal} \right] & = & \left[ \text{Grayscale checkerboard} \right] & \begin{pmatrix} \beta_{Face} \\ \beta_{House} \end{pmatrix} & + & \left[ \text{White noise} \right] \\ Y & & X & \beta & & \epsilon \end{matrix}$$

# Quick GLM overview



How do we find the FFA?

$$\beta_{Face} > \beta_{House} \rightarrow \beta_{Face} - \beta_{House} > 0$$

# Quick GLM overview

The diagram shows a green waveform on the left, followed by an equals sign. To the right of the equals sign is a grayscale waveform, then a vector in parentheses containing  $\beta_{Face}$  and  $\beta_{House}$ , followed by a plus sign and a white noise waveform.

$$\begin{bmatrix} 1 & -1 \end{bmatrix} \begin{bmatrix} \beta_{Face} \\ \beta_{House} \end{bmatrix} > 0$$

# What do we need to know?

- What is the general structure of a t-statistic?
- What are the assumptions we make with the linear model (Gauss Markov)?
- What is the residual?

# T-statistic structure

contrast you are estimating

---

$\sqrt{\text{estimated variance of contrast you are estimating}}$

contrast you are estimating

---

$= \frac{\text{contrast you are estimating}}{\sqrt{(\text{variance contribution from model})(\text{residual variance})}}$

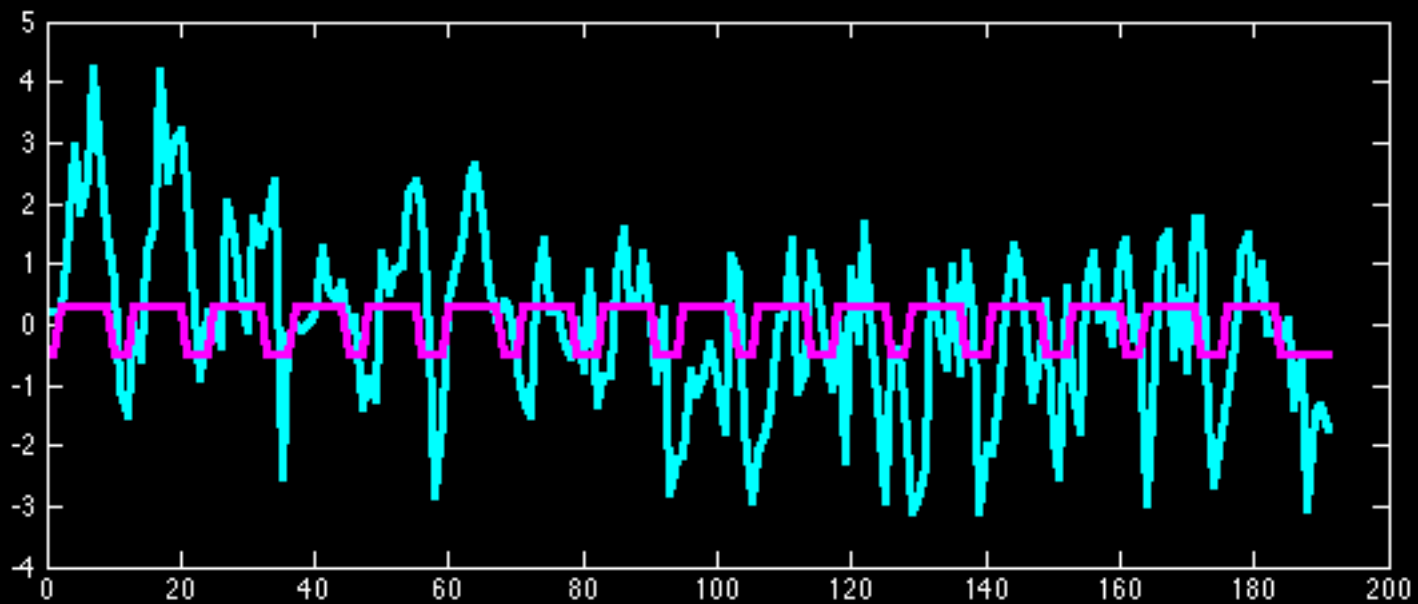
$$= \frac{c(X'X)^{-1}X'Y}{\sqrt{c(X'X)^{-1}c'\hat{\sigma}}}$$



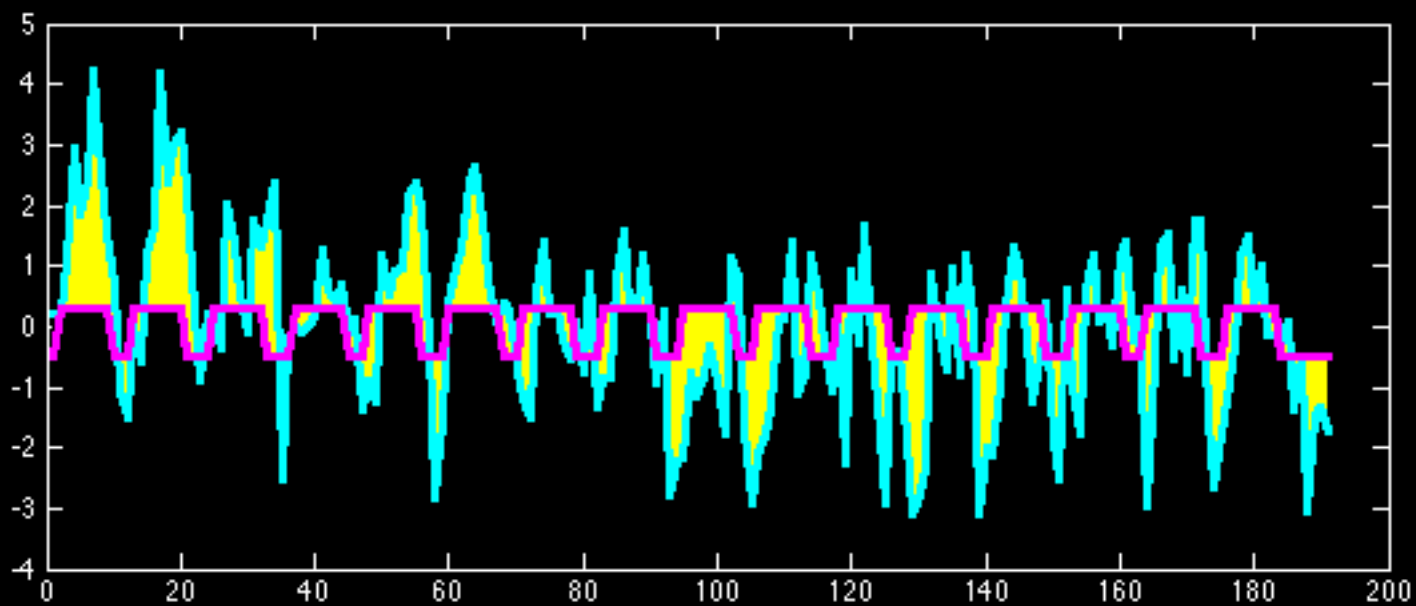
# Gauss Markov Theorem

- If the errors
  - Have mean 0
  - Are uncorrelated
  - Have the same variance
- The least squares estimates are unbiased and have minimum variance among all unbiased estimators!

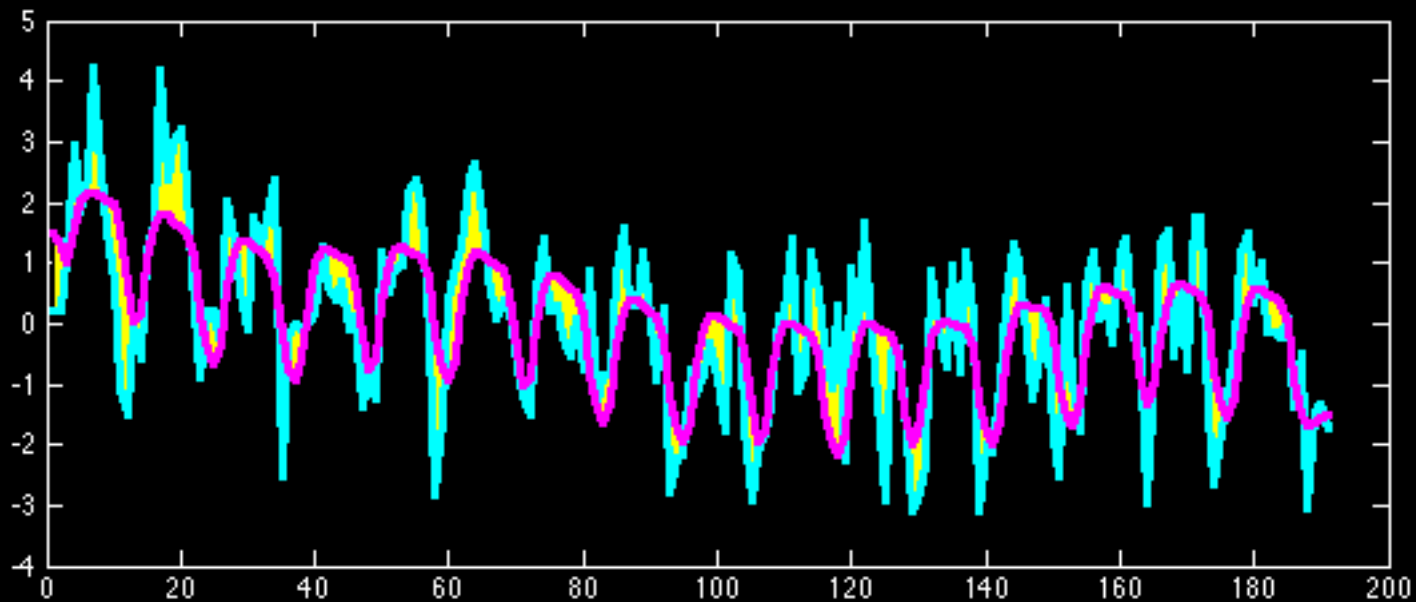
# Goal



# Goal

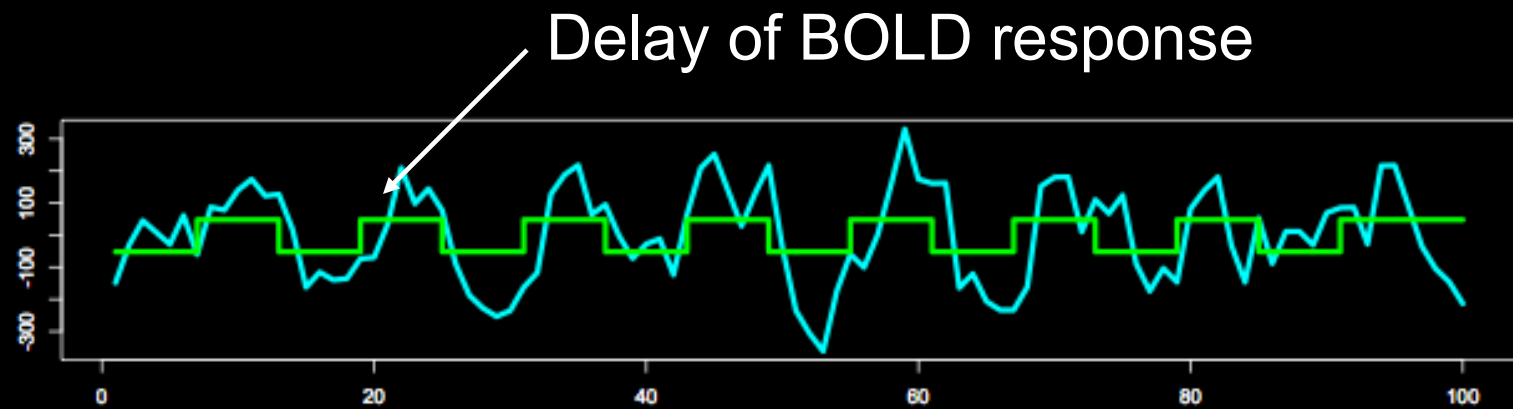


# Goal

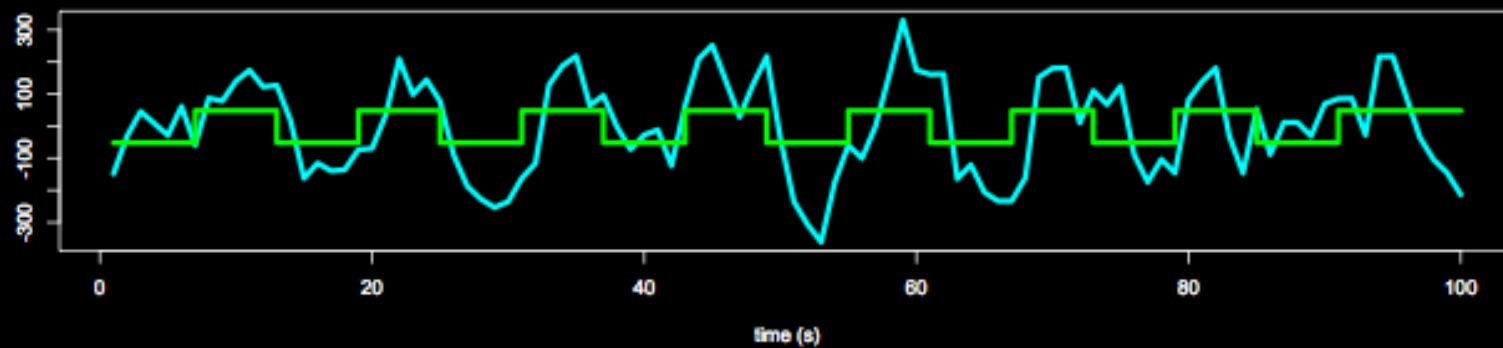


Who wants smaller residuals??  
You do!!

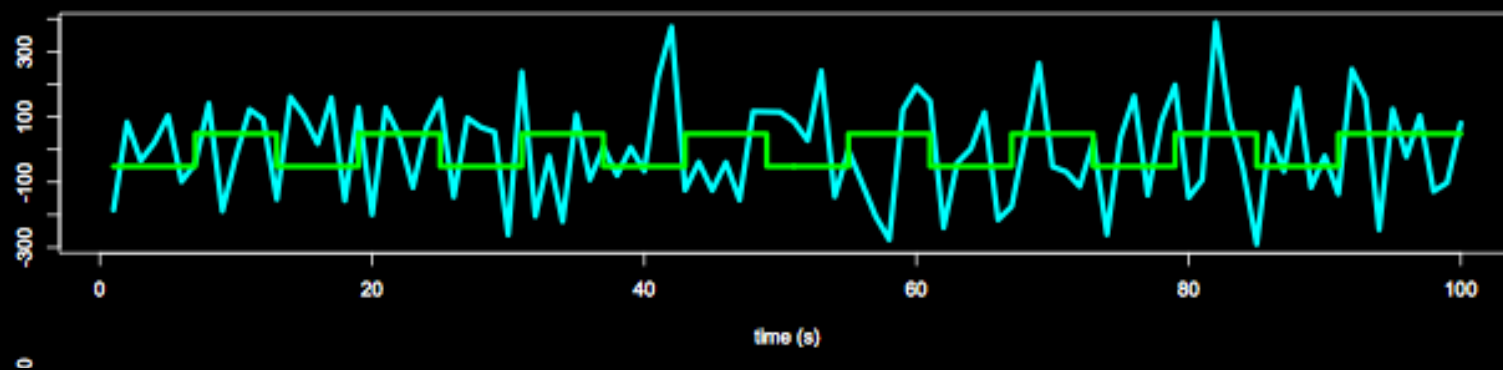
Voxel  
with  
signal



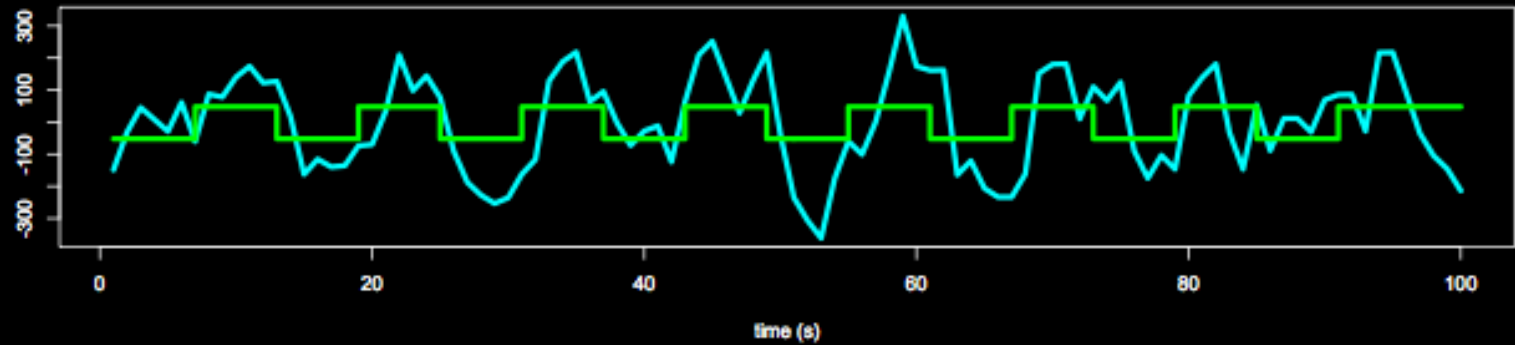
Voxel  
with  
signal



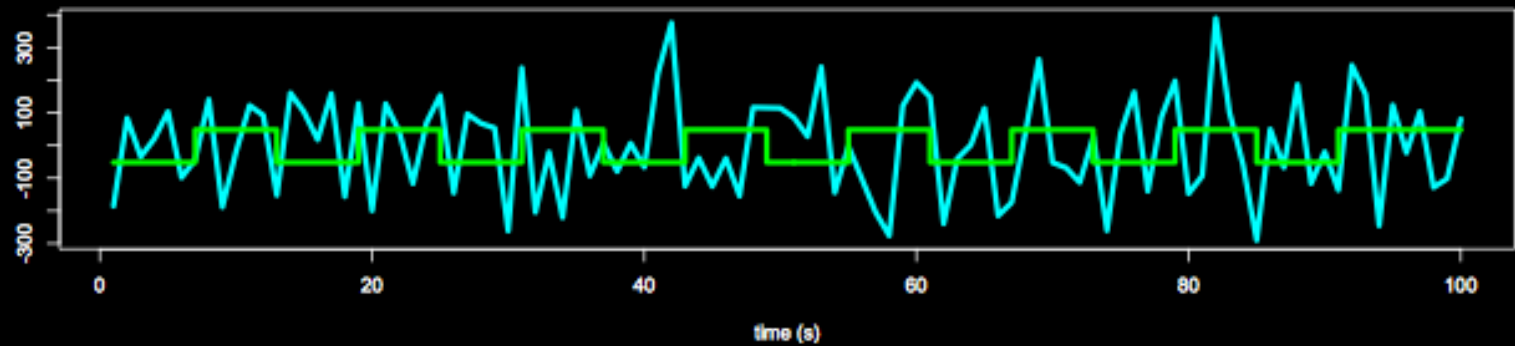
Voxel  
no  
signal



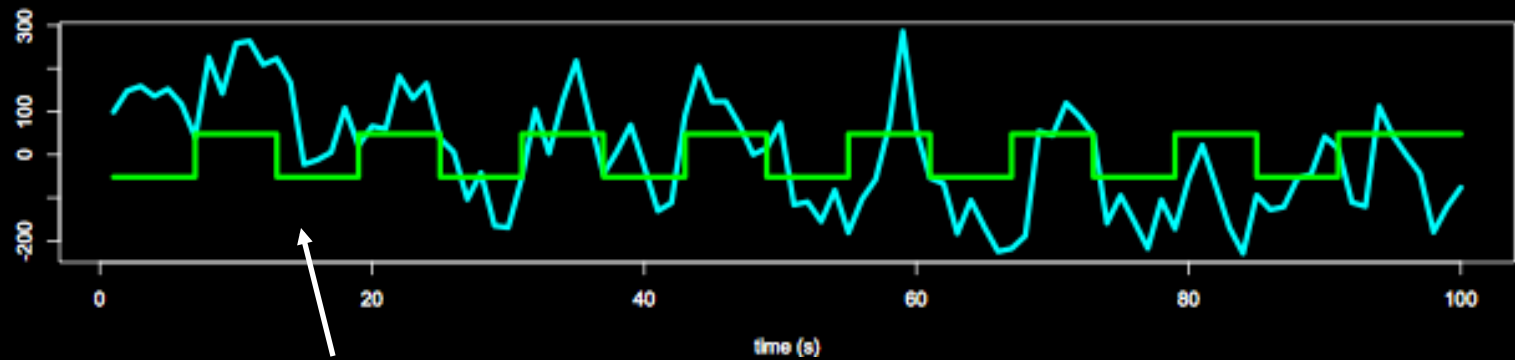
Voxel  
with  
signal



Voxel  
no  
signal



Voxel  
signal  
and drift



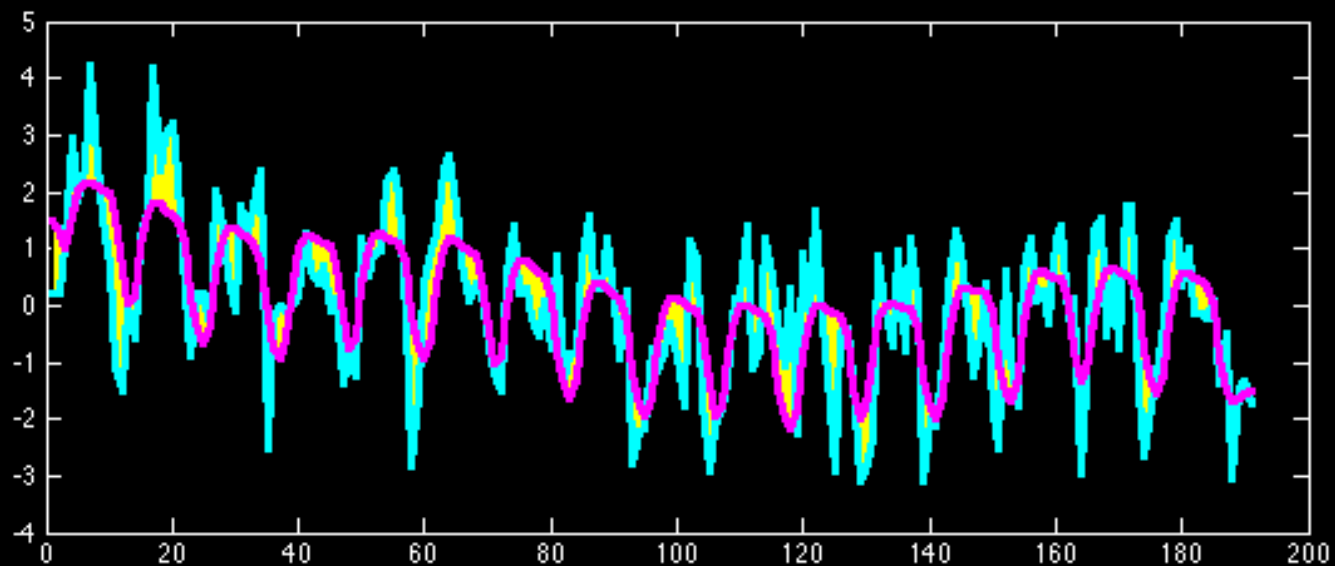
Starts off high

# BOLD issues

- BOLD response is delayed
  - Convolution
  - FIR modeling
- BOLD time series suffer from low frequency noise
  - Highpass filtering
  - Prewhitening
- Scaling the data
  - Grand mean scaling
  - Intensity normalization

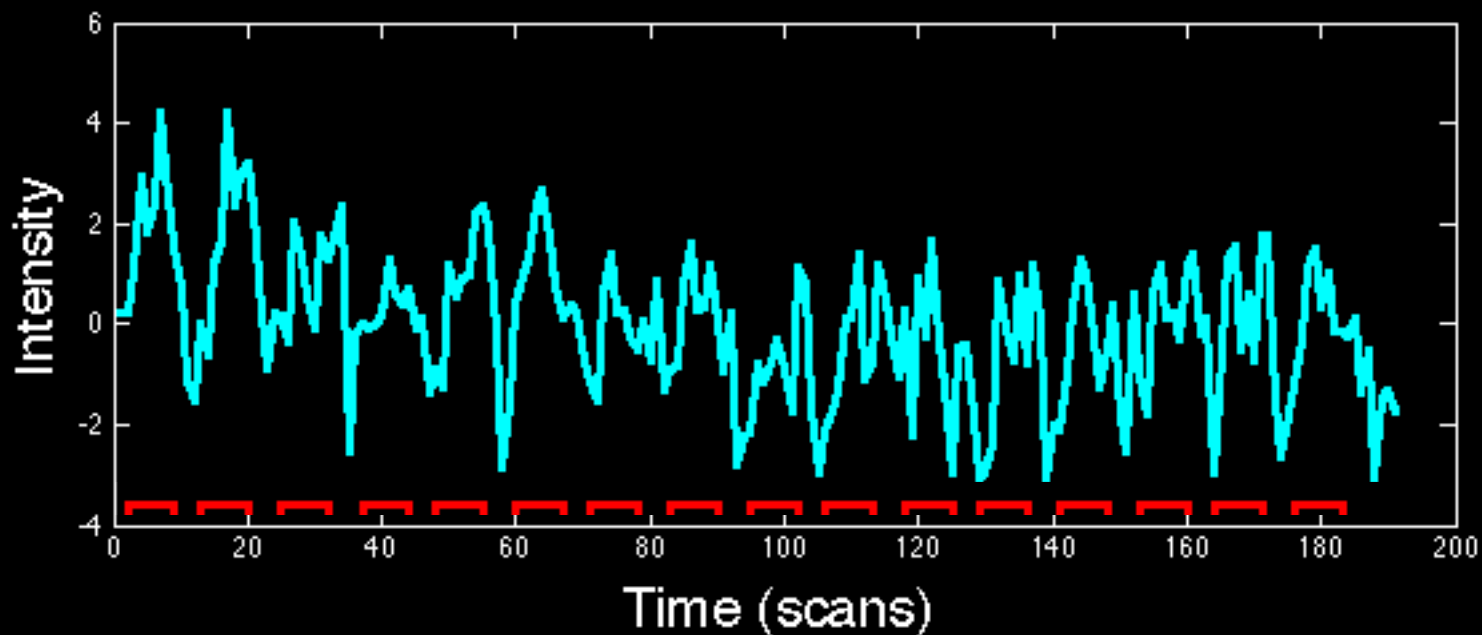


# How to make a good model



Big residuals  $\Rightarrow$  Big variance  $\Rightarrow$  Small t stat

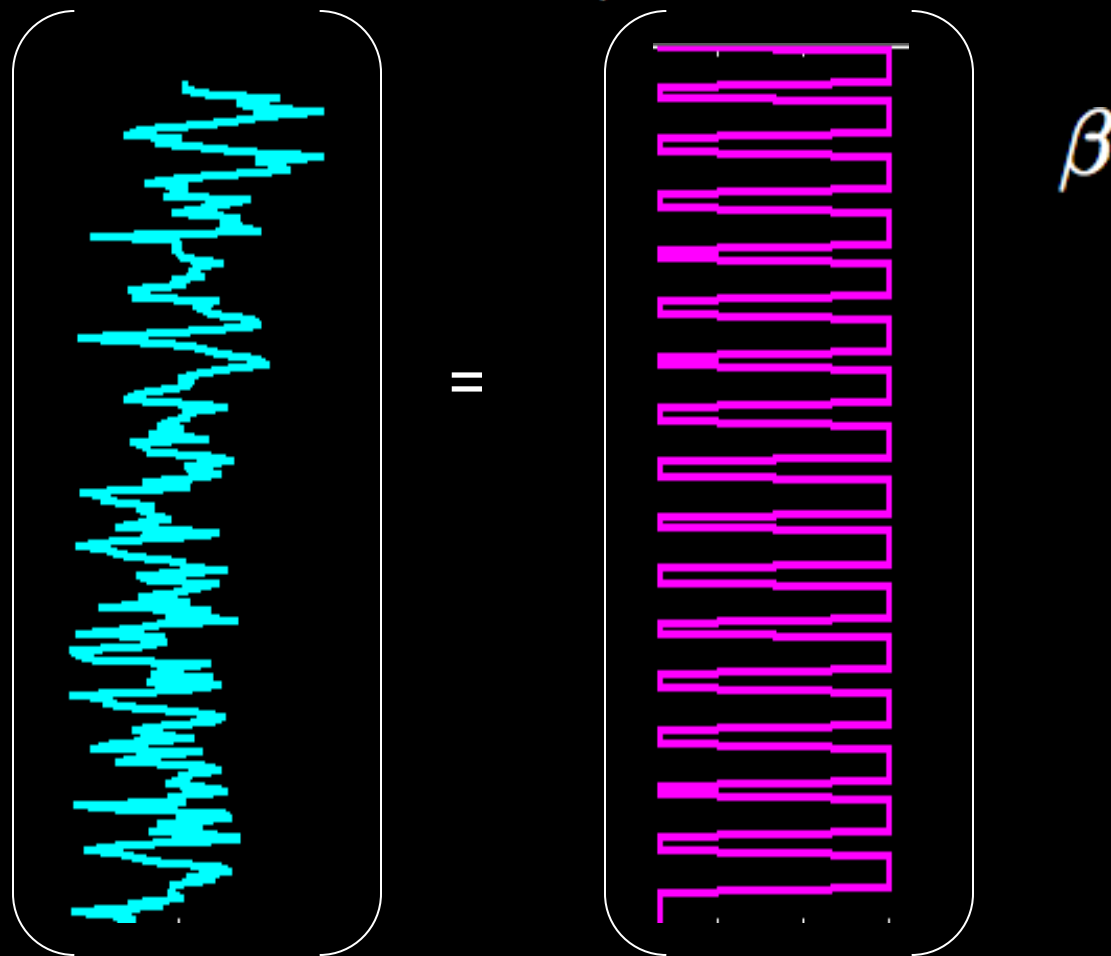
# Understanding the data



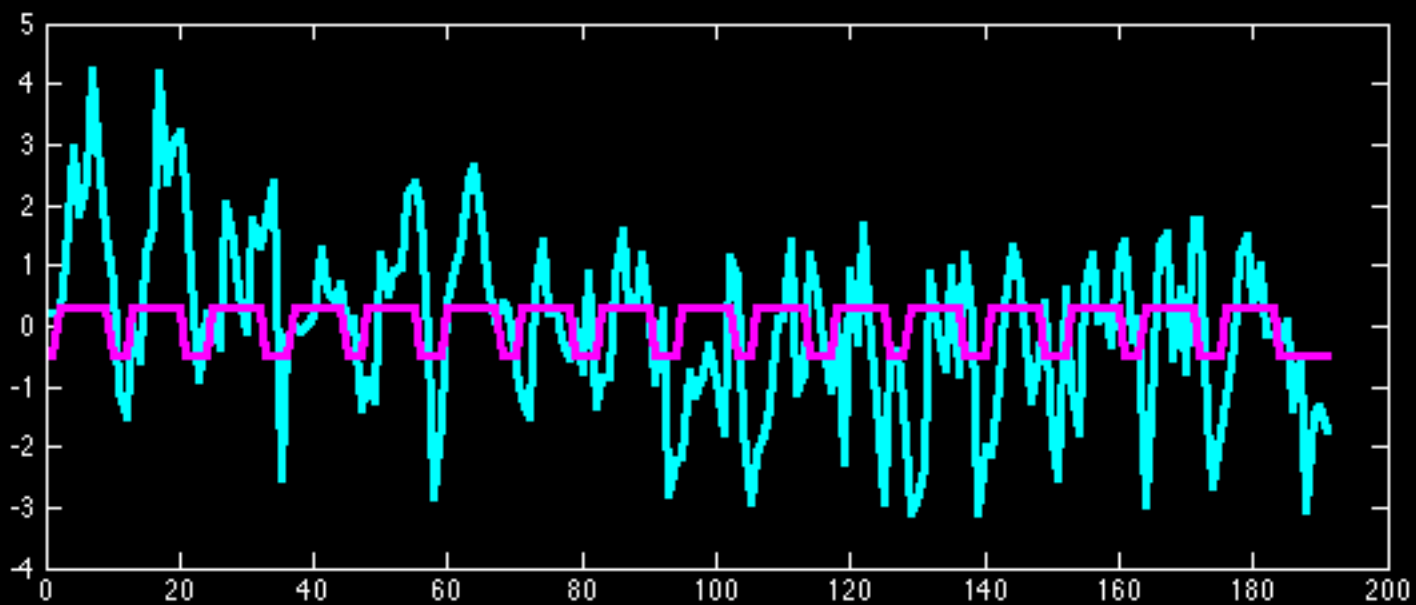
- Time series drifts down in beginning
- BOLD response is delayed

# Simplest Model

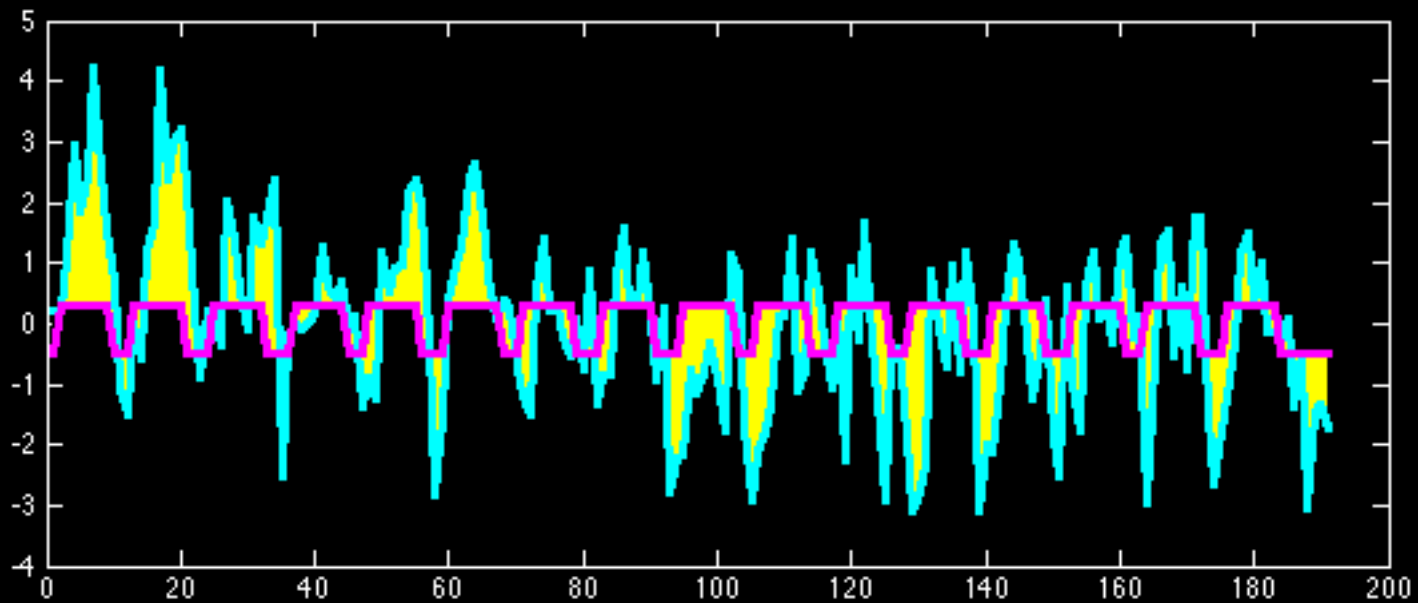
$$Y = X\beta$$



# Simplest Model



# Simplest Model



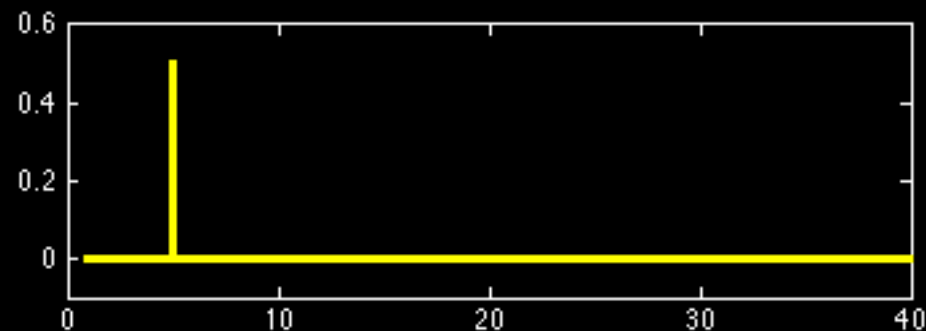
$$t = \frac{\underline{c}(X'X)^{-1}X'Y}{\hat{\sigma}\sqrt{\underline{c}(X'X)^{-1}\underline{c}'}}$$

$$t = \frac{0.3}{1.41 \times 0.06} = 3.55$$

# Modeling the delay

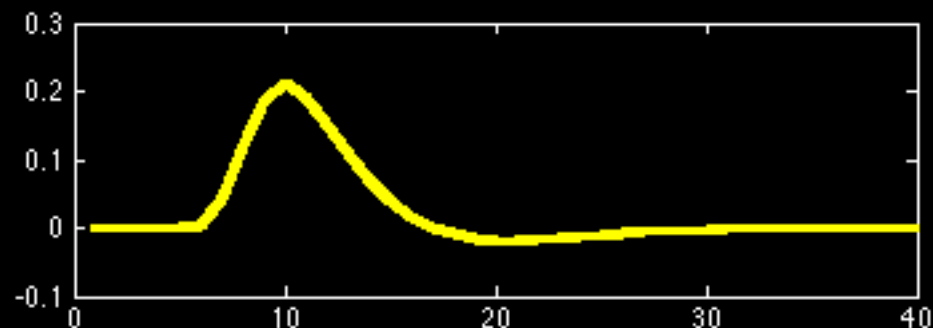
- Hemodynamic response function
  - Real data was used to find good models for the hemodynamic response

Stimulus



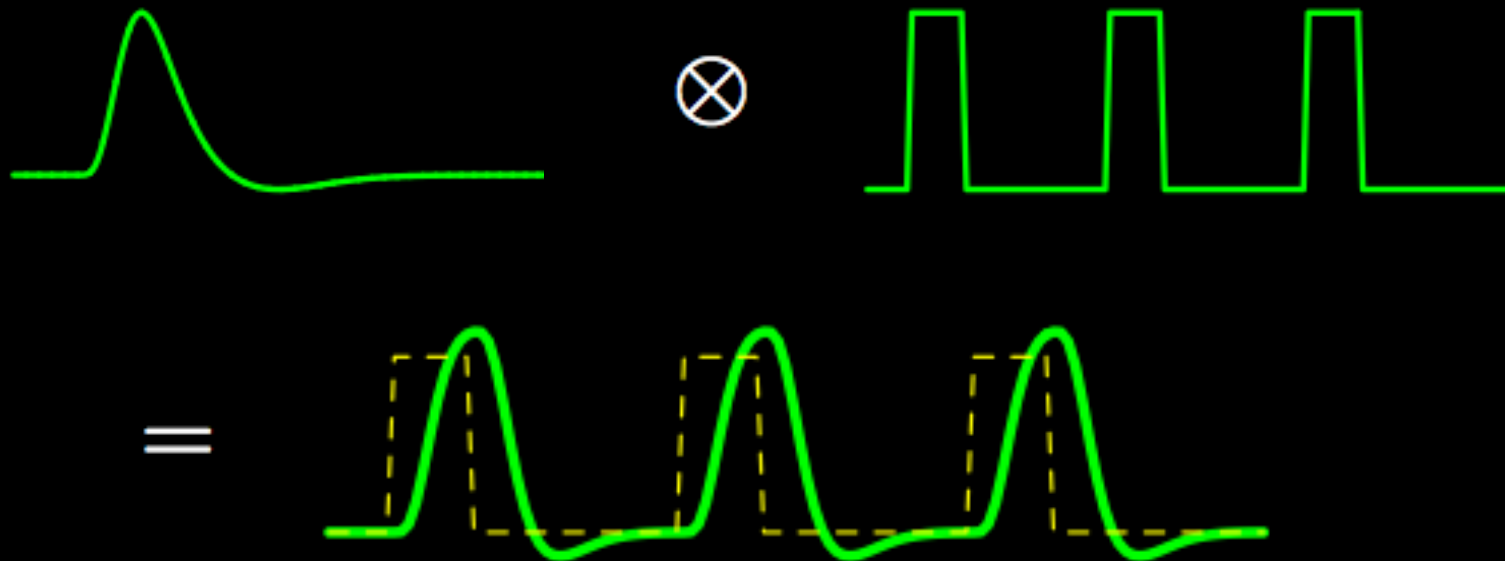
HRF

(double gamma)



# Convolution

- Combine HRF and expected neural response



Typically model derivative of convolved HRF to adjust for small differences in onset (<1s)

# Different HRF's

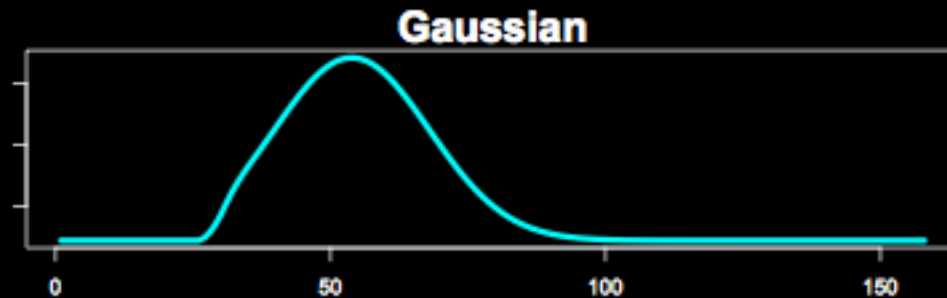
Too symmetric



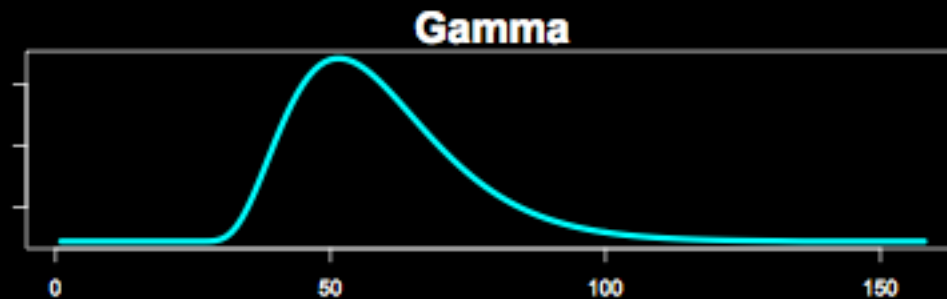


# Different HRF's

Too symmetric

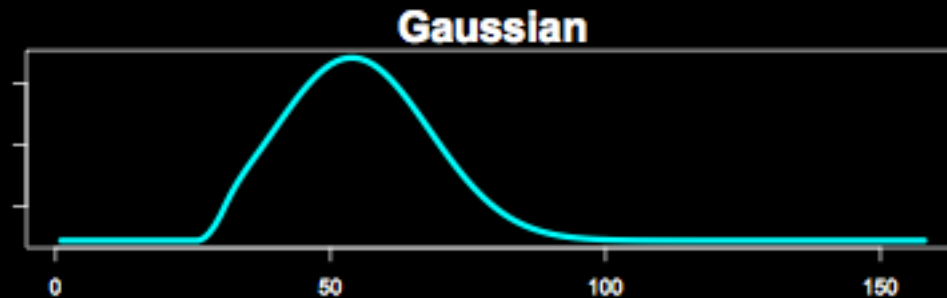


Basic shape okay,  
but no post stimulus  
undershoot

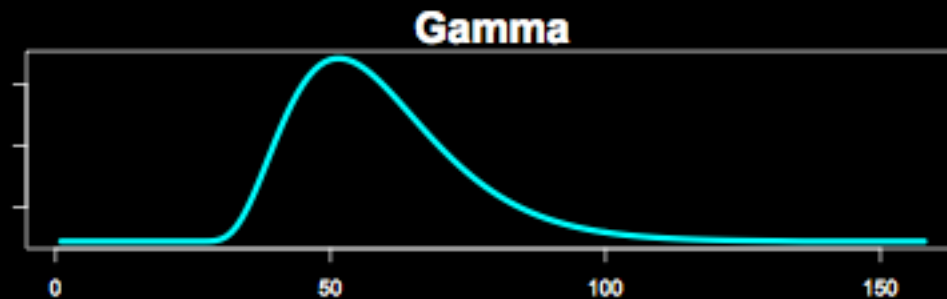


# Different HRF's

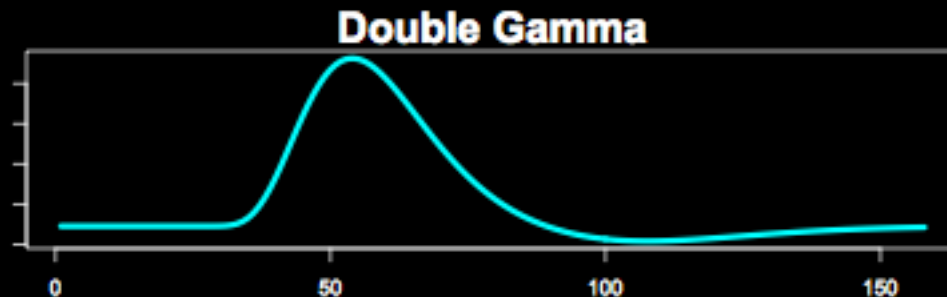
Too symmetric



Basic shape okay,  
but no post stimulus  
undershoot

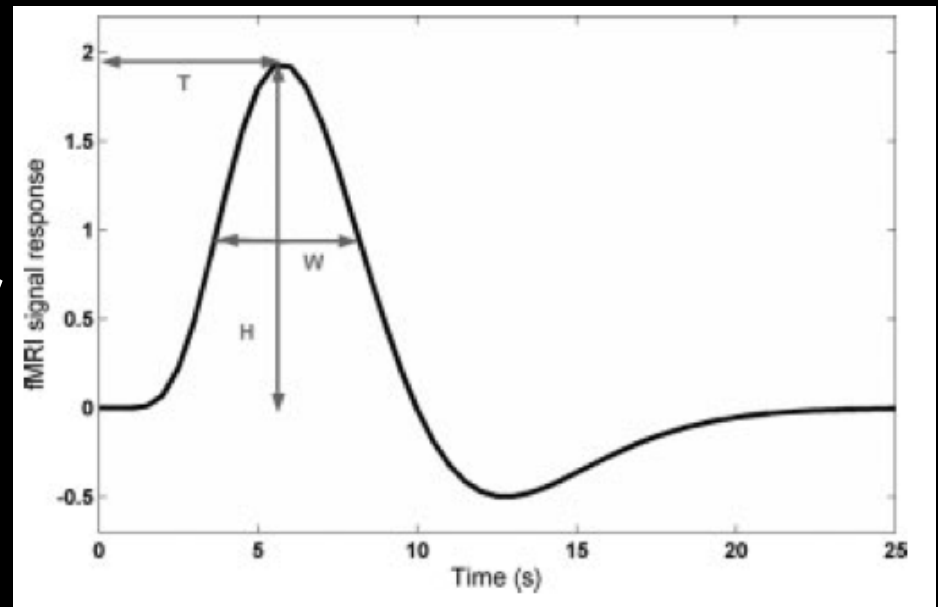


Includes post  
stimulus  
undershoot



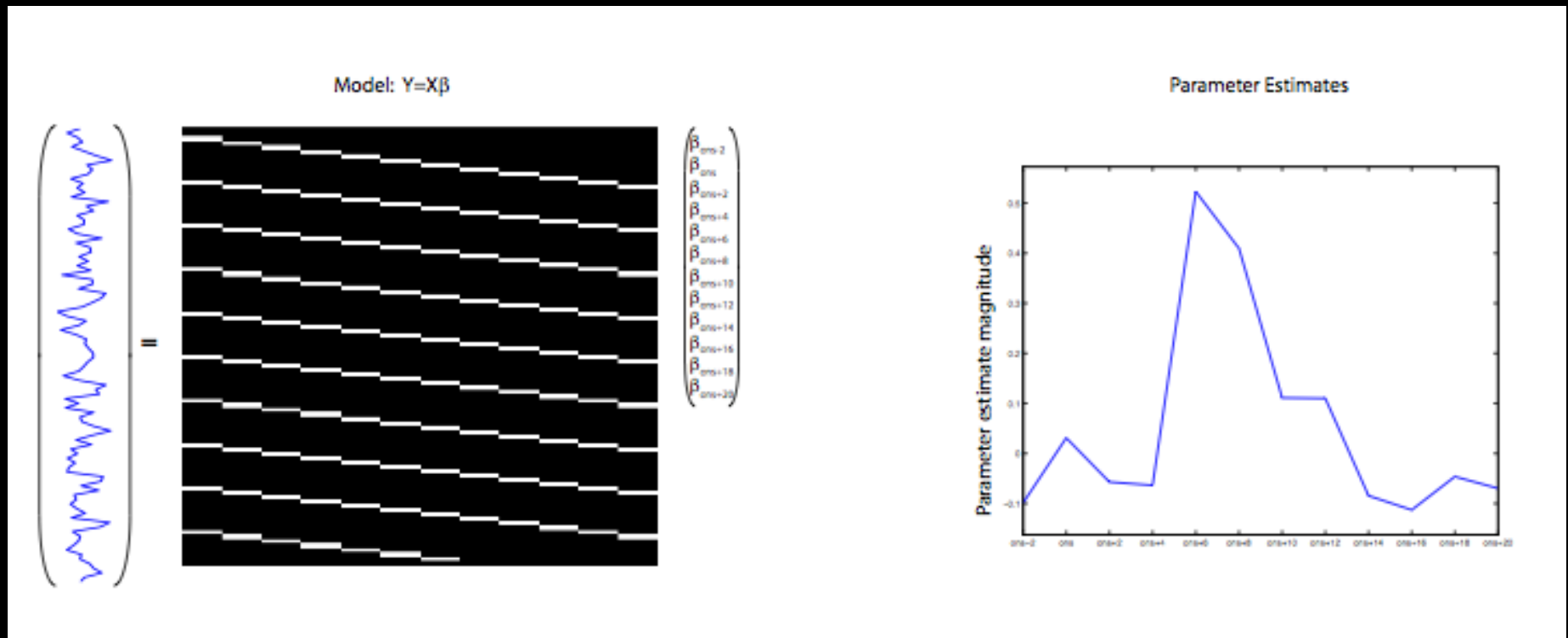
# Assumptions of canonical HRF

- The width, height and delay are correct
- Lindquist & Wager (2007)
  - Fit H/W/T separately
  - Works okay-ish



# Finite impulse response model

- FIR
  - Make no assumption about the shape of the HRF

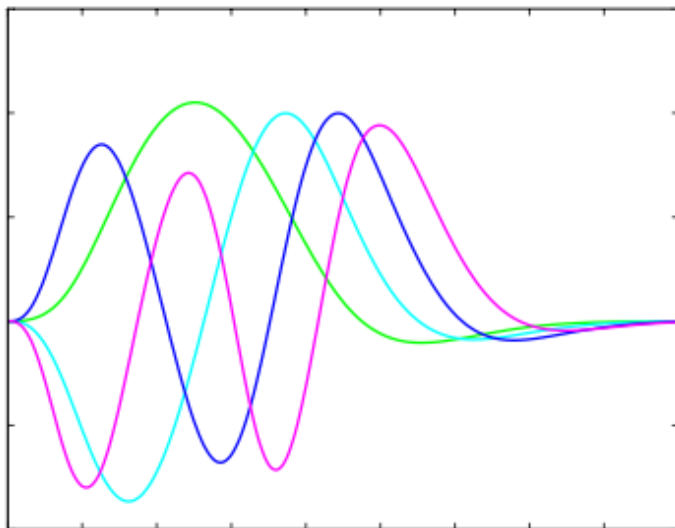


# Constrained basis set

- Lower the number of regressors in the model by using a basis set
- Constrained to shapes that are reasonable for HRF shapes

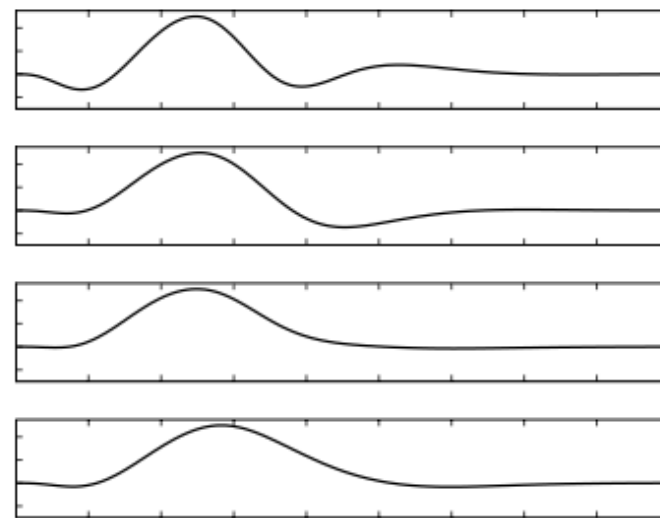
# Constrained basis set

A



Basis set

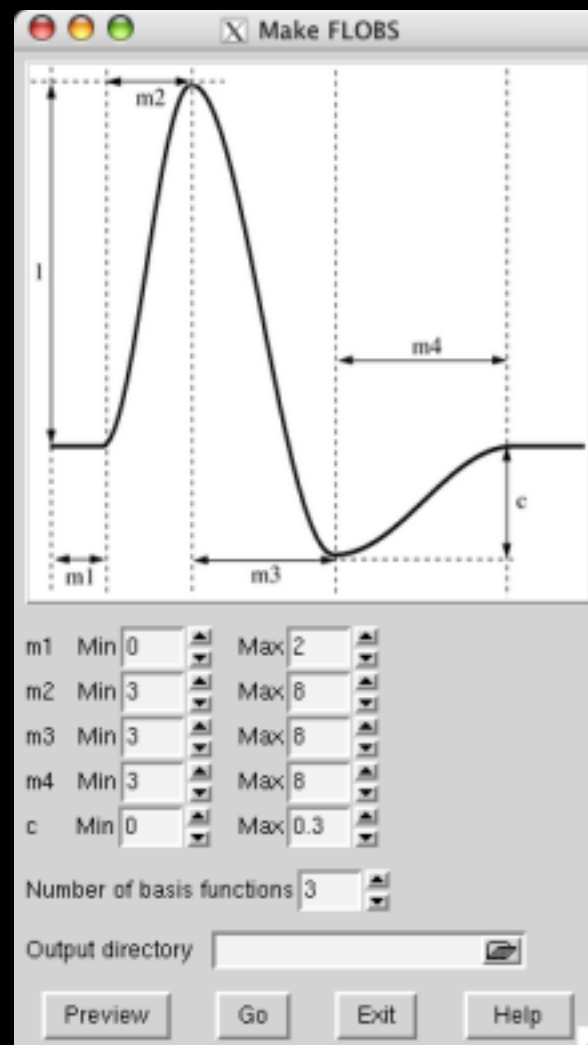
B



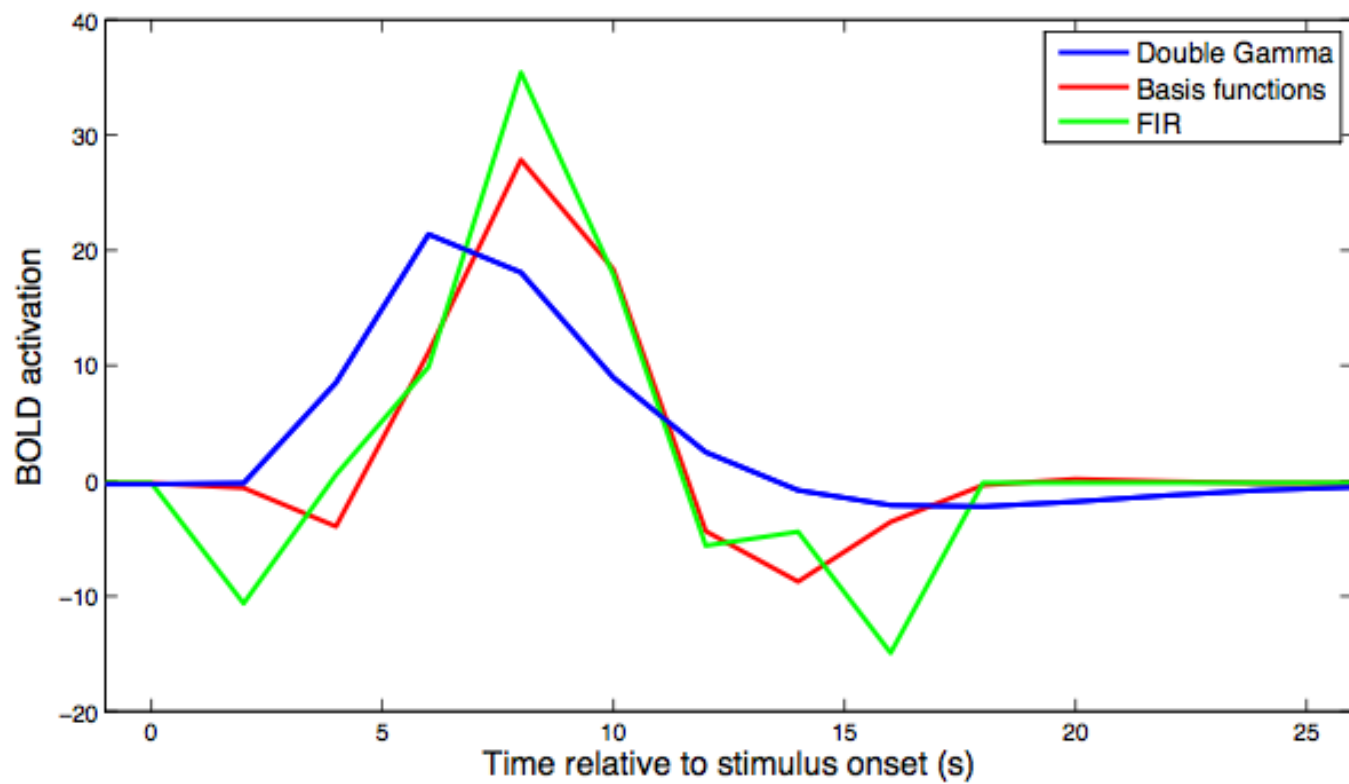
HRF possibilities

# FLOBS

- fMRIB Linear Optimal Basis Sets
  - Generates a set of basis sets to model signal
  - Specify ranges for different portions of the hrf



# Comparison





# More thoughts about canonical HRF

- Advantages:
  - Simpler analysis
  - Easily interpretable outcome
  - Simplifies group analysis
- Disadvantages
  - Biased if canonical HRF is incorrect

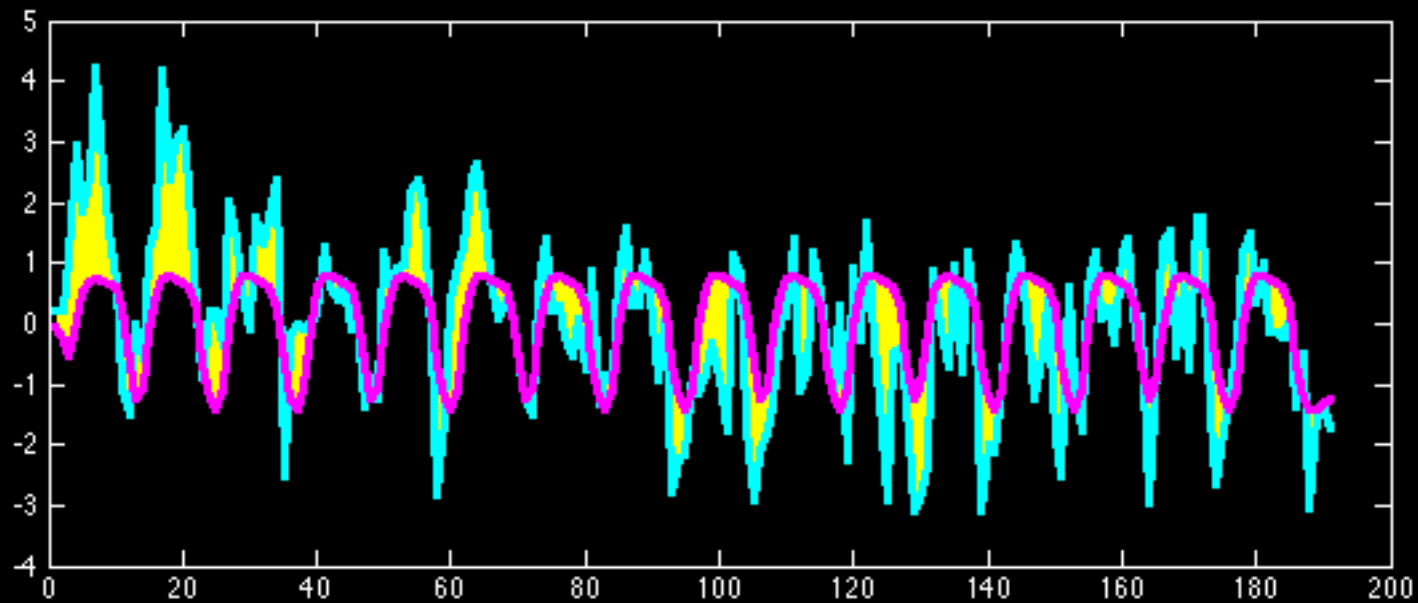
# Unbiased basis sets

- Advantages
  - Not biased towards a particular shape
  - Allows testing of hypotheses about specific HRF parameters
- Disadvantages
  - Less powerful
  - Makes group analysis more difficult
  - Tend to overfit the data (i.e., fit noise)

# We can make a design matrix!

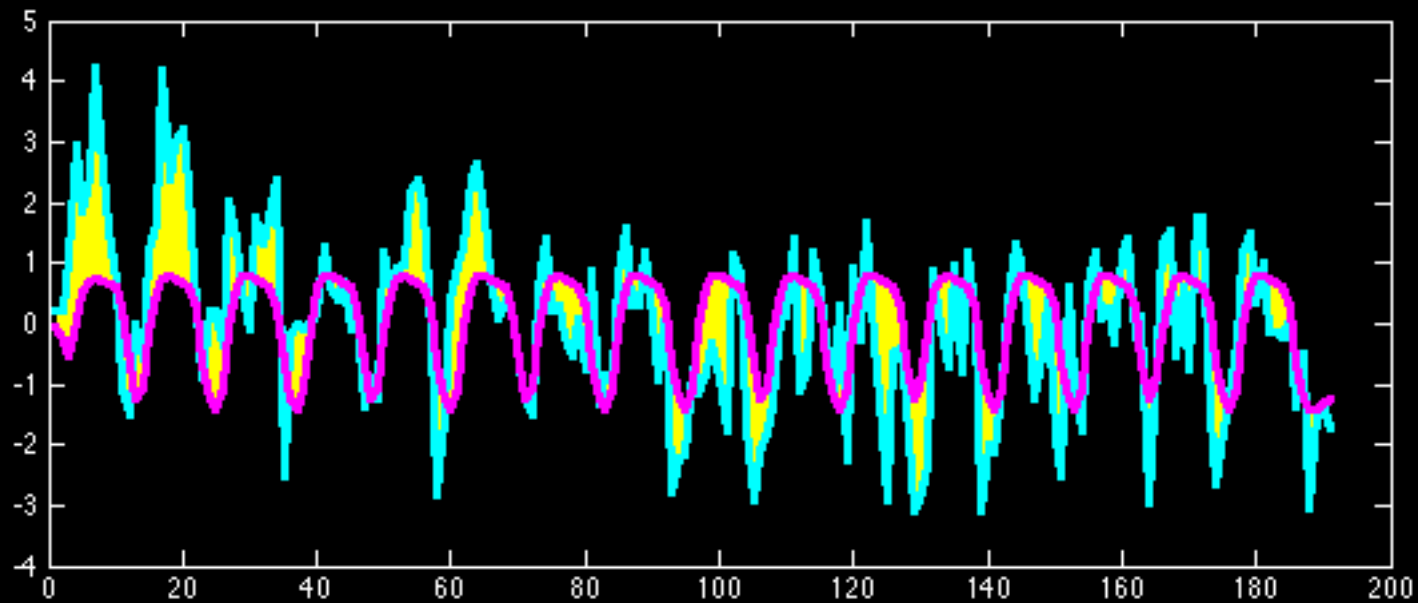
- Start with task blocks or delta functions
- Convolve
- Estimate the GLM and carry out hypothesis!

# Convolved Boxcar



$$t = \frac{0.66}{1.22 \times 0.06} = 9.02$$

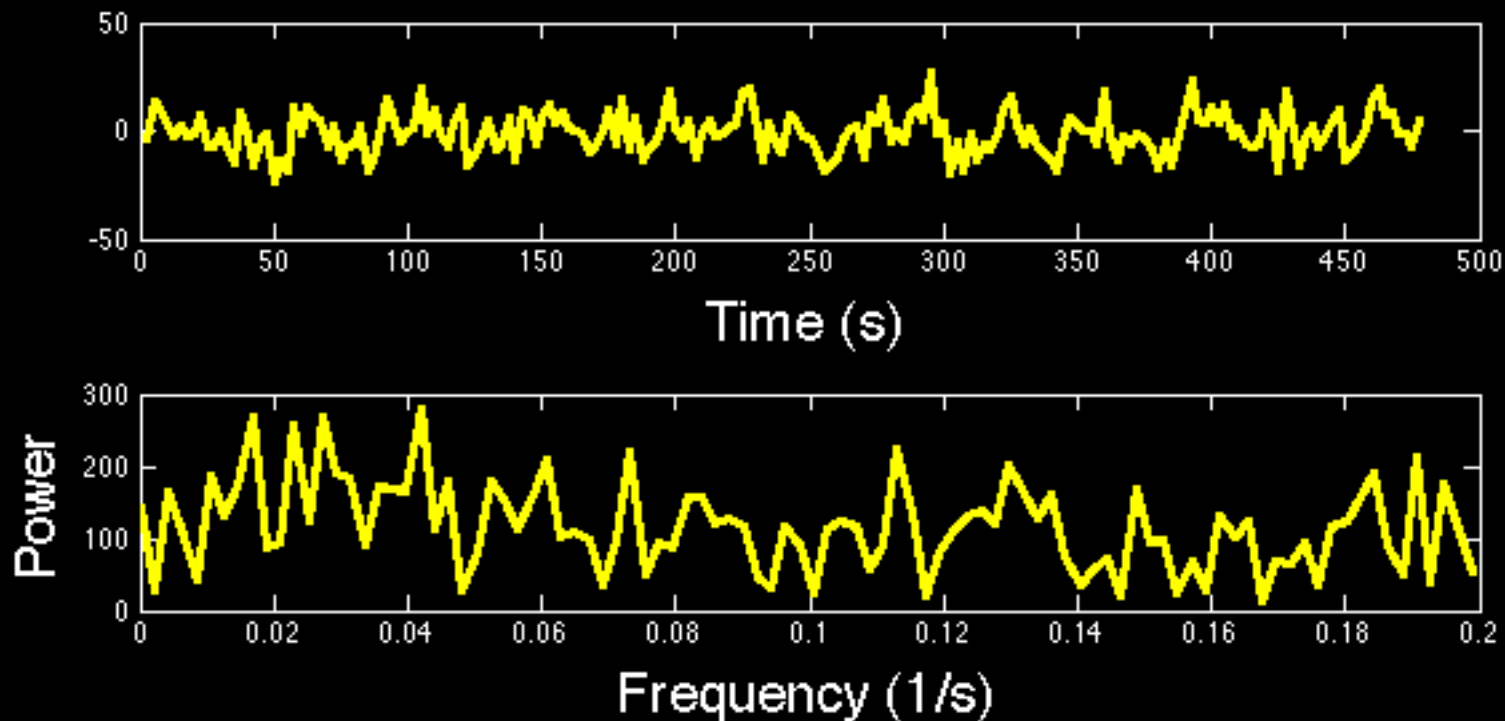
# Convolved Boxcar



$$t = \frac{0.66}{1.22 \times 0.06} = 9.02$$

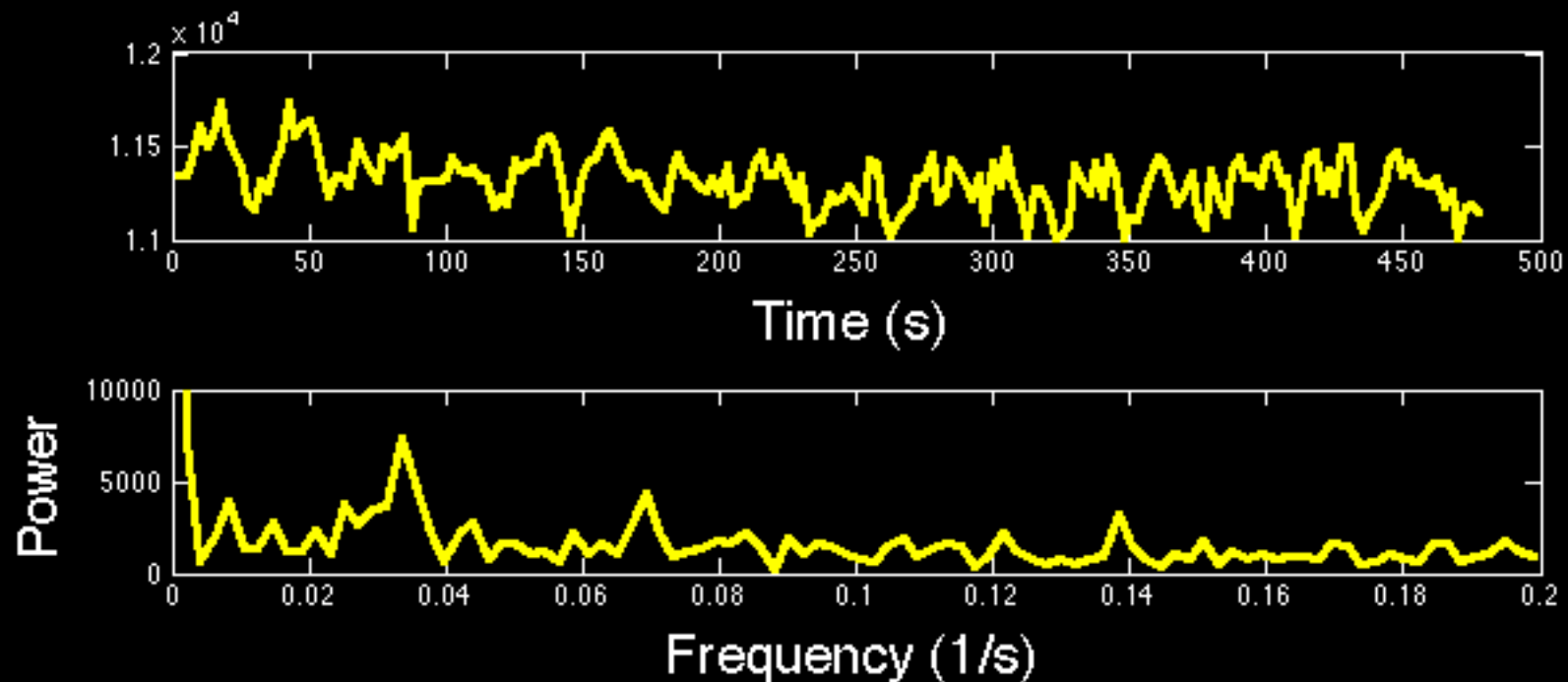
# The Noise

- White noise
  - All frequencies have similar power
  - Not a problem for OLS



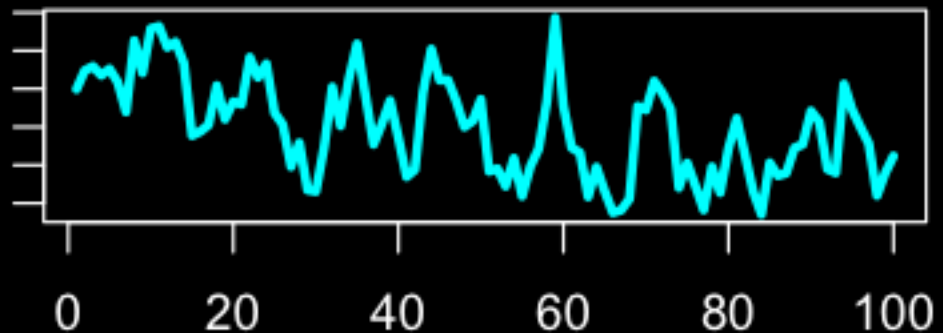
# More Noise

- Colored noise
  - Has structure
  - OLS needs help!



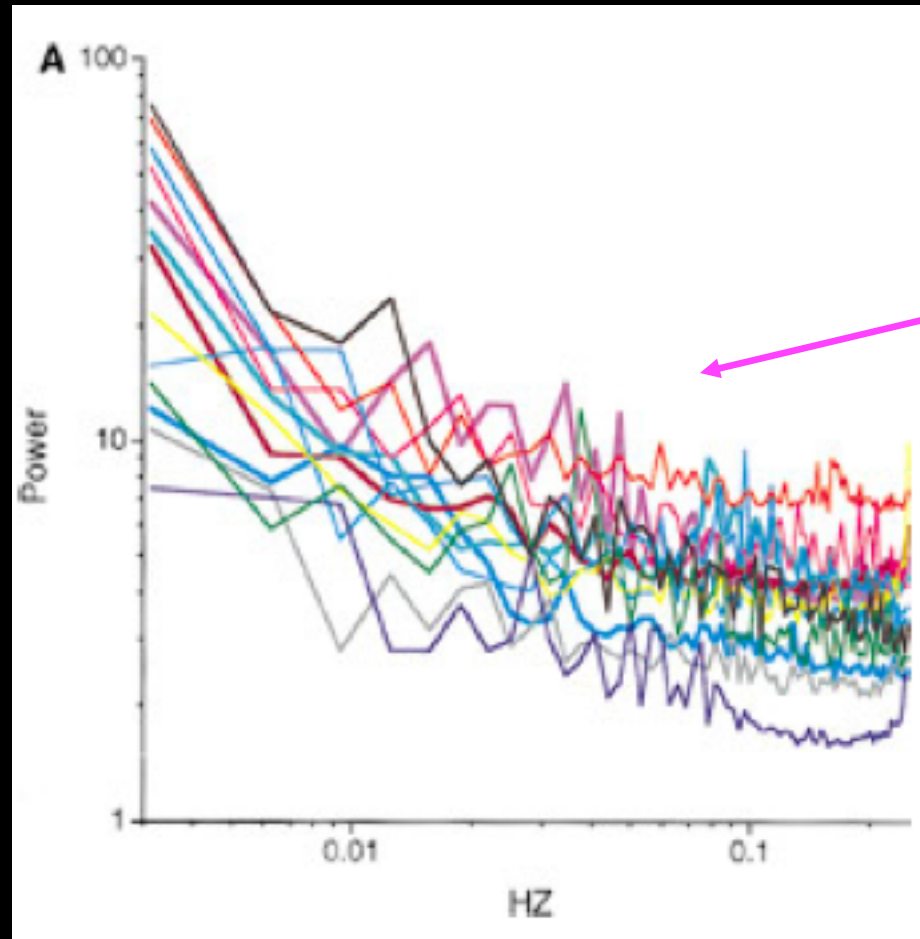
# What about the drift?

- Sources
  - Head motion
  - Cardiac noise
  - Respiratory noise
  - Scanner noise



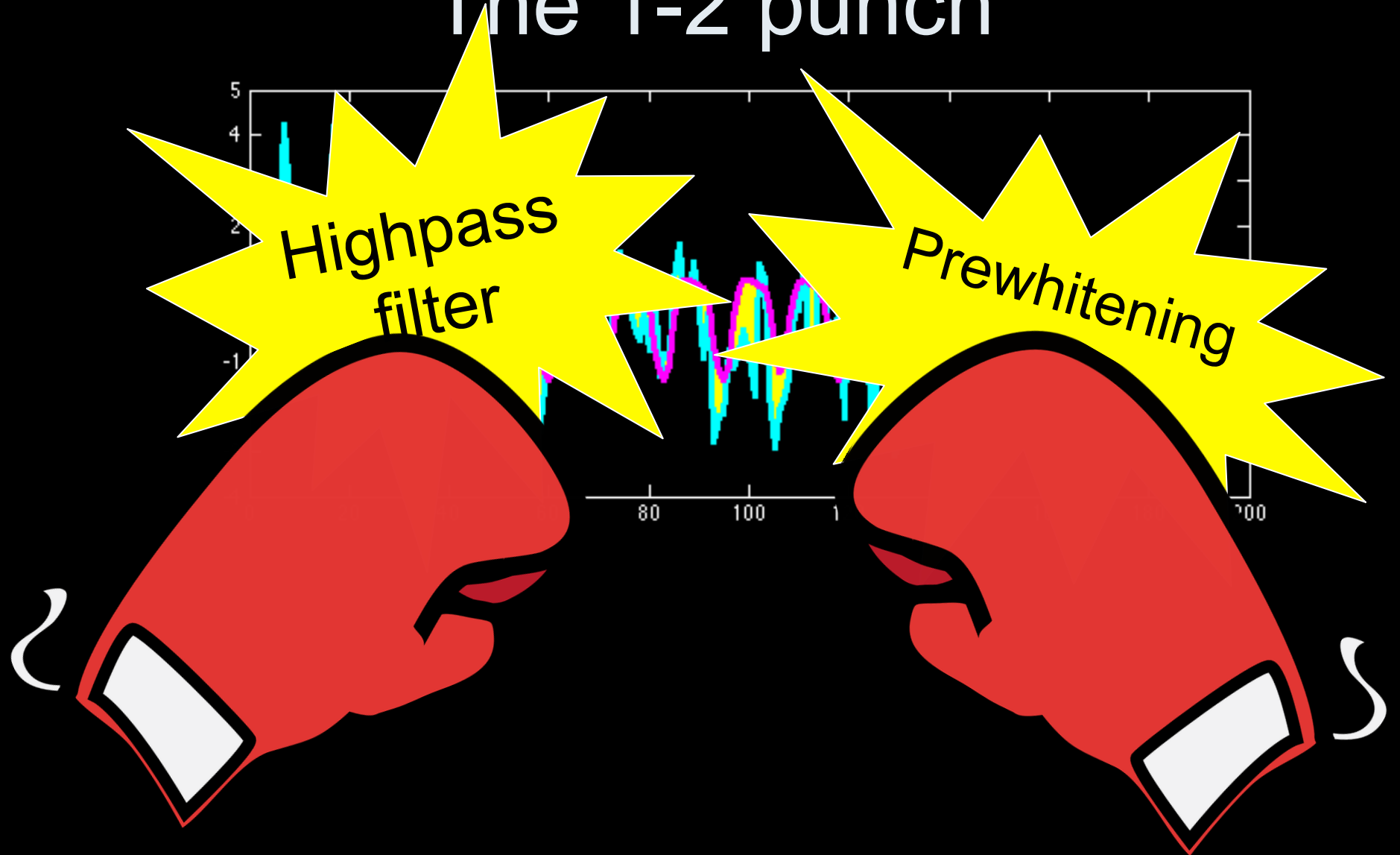


# What the noise looks like

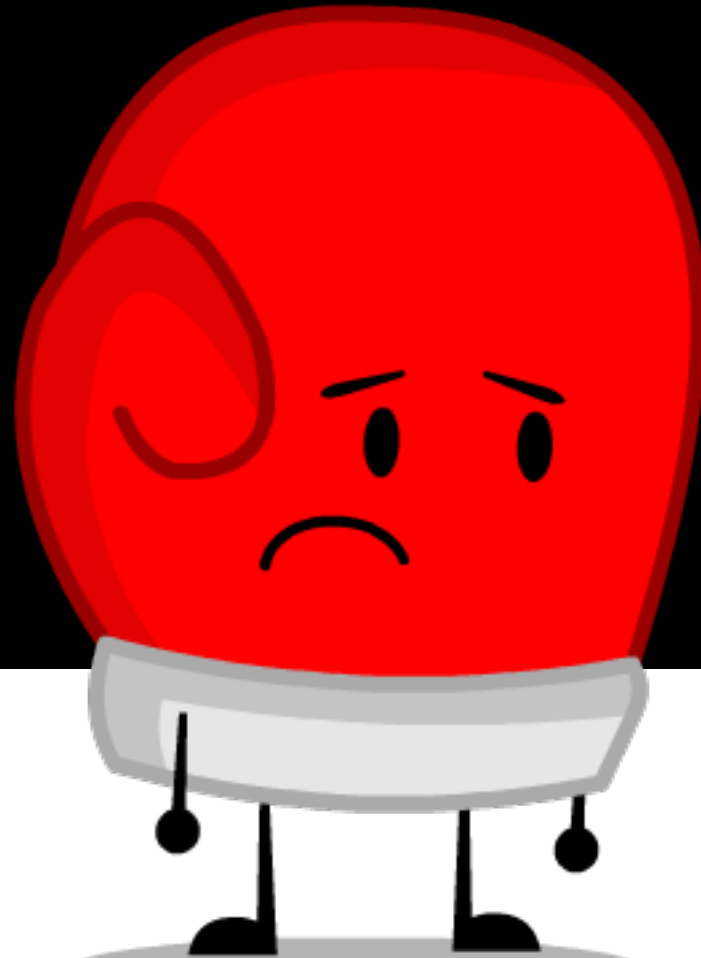


Power spectra of noise data  
(Zarahn, Aguirre, D'Esposito, NI, 1997)

# The 1-2 punch



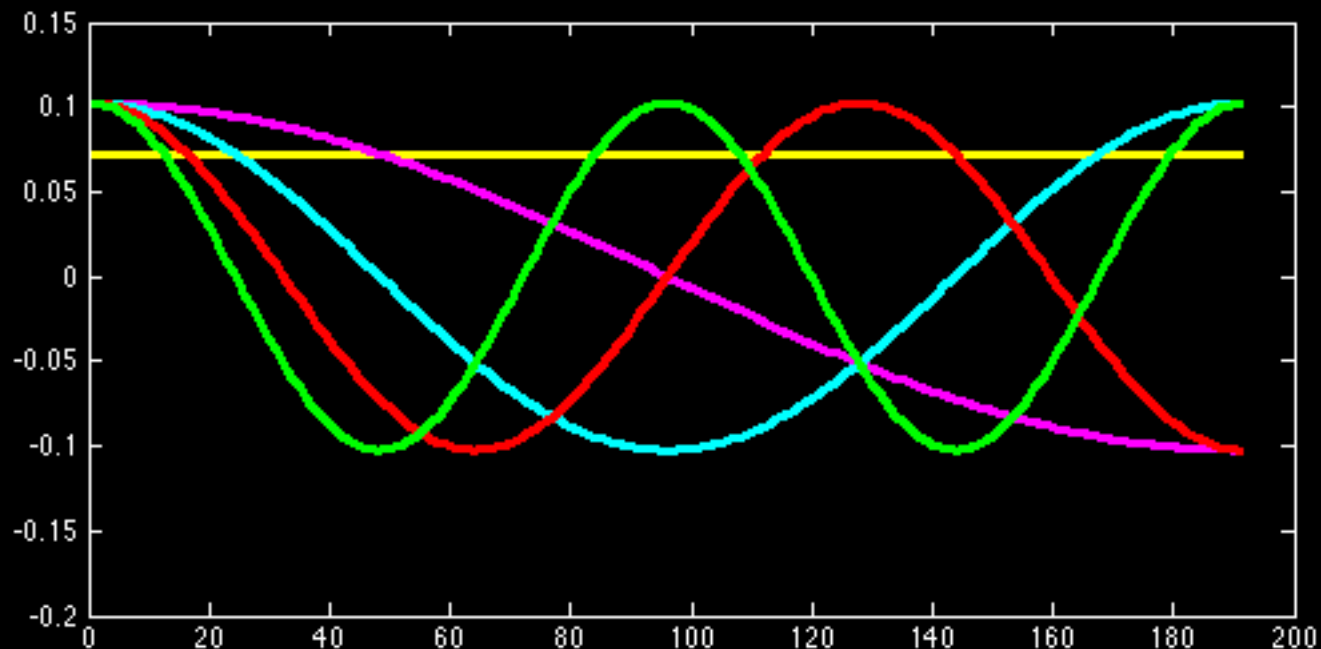
Typically not used



Lowpass filter

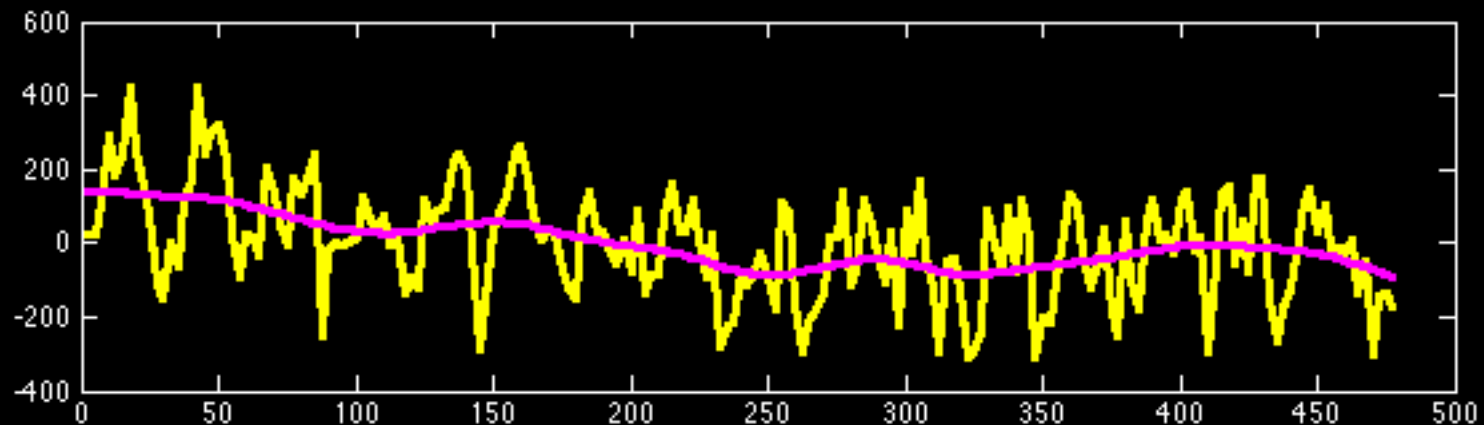
# Highpass filtering

- Remove low frequency noise
  - SPM: Adds a discrete cosine transform basis set to design matrix



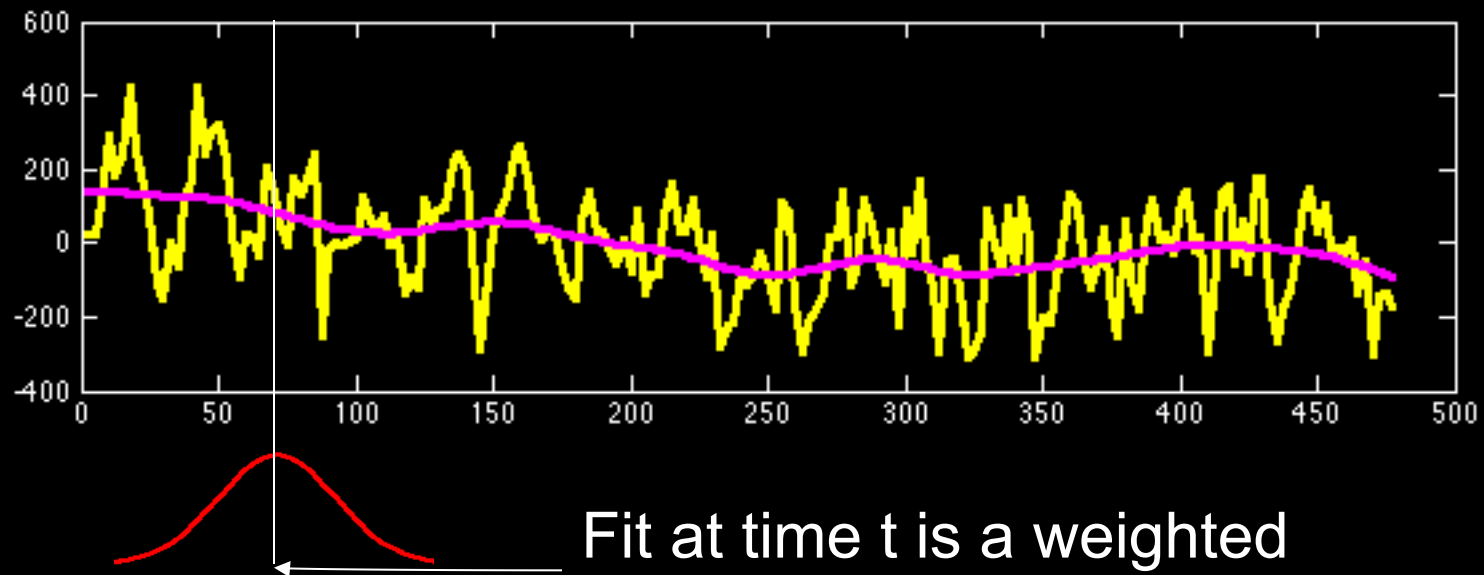
# Highpass filtering

- FSL: Gaussian-weighted running line smoother
  - Step 1: Fit a Gaussian weighted running line



# Highpass filtering

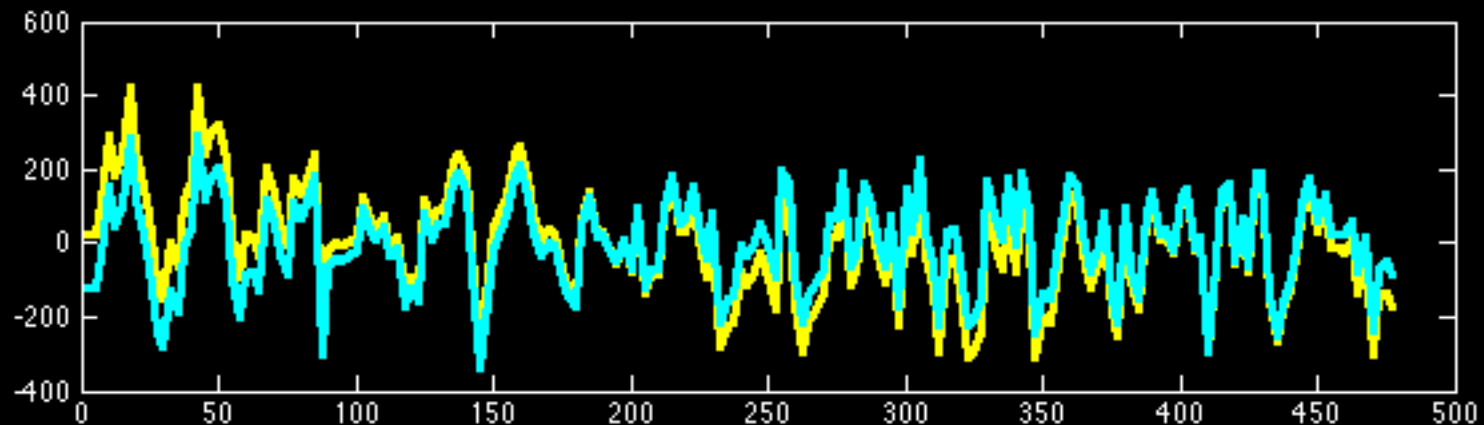
- FSL: Gaussian-weighted running line smoother
  - Step 1: Fit a Gaussian weighted running line



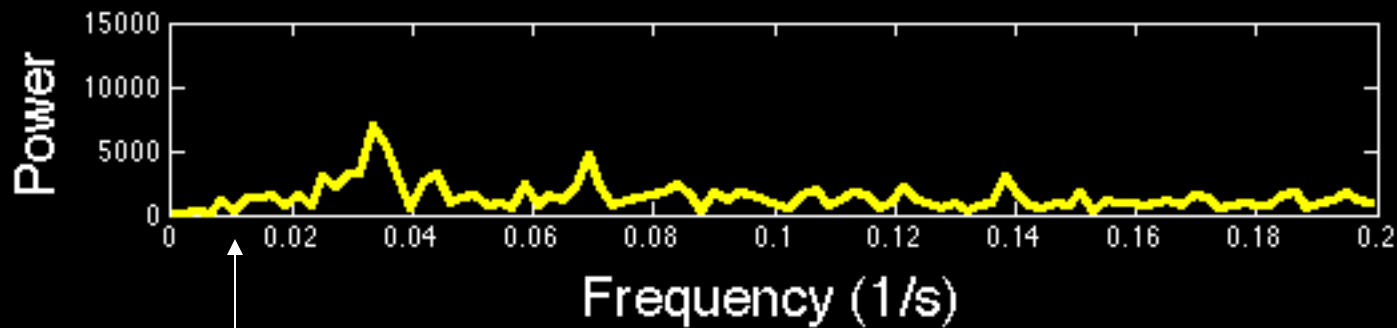
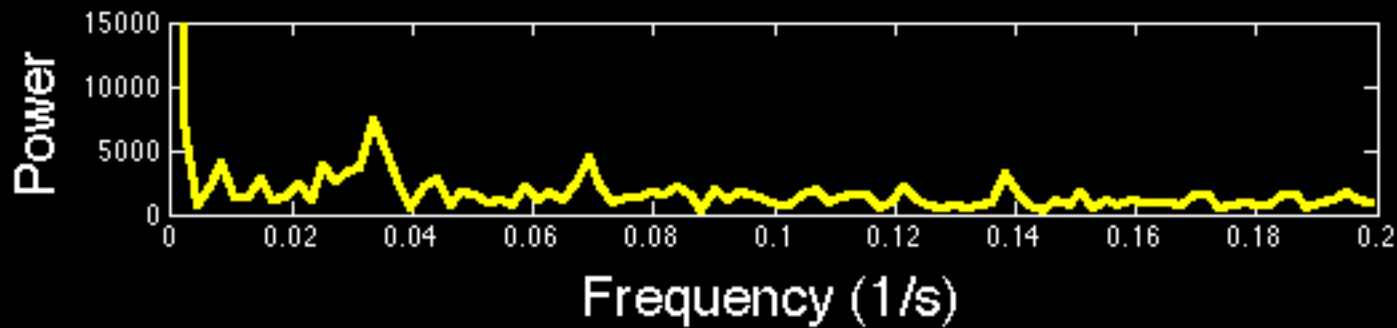
Fit at time  $t$  is a weighted average of data around  $t$

# Highpass filtering

- Step 2: Subtract Gaussian weighted running line fit



# Highpass filtering



Filter below .01 Hz

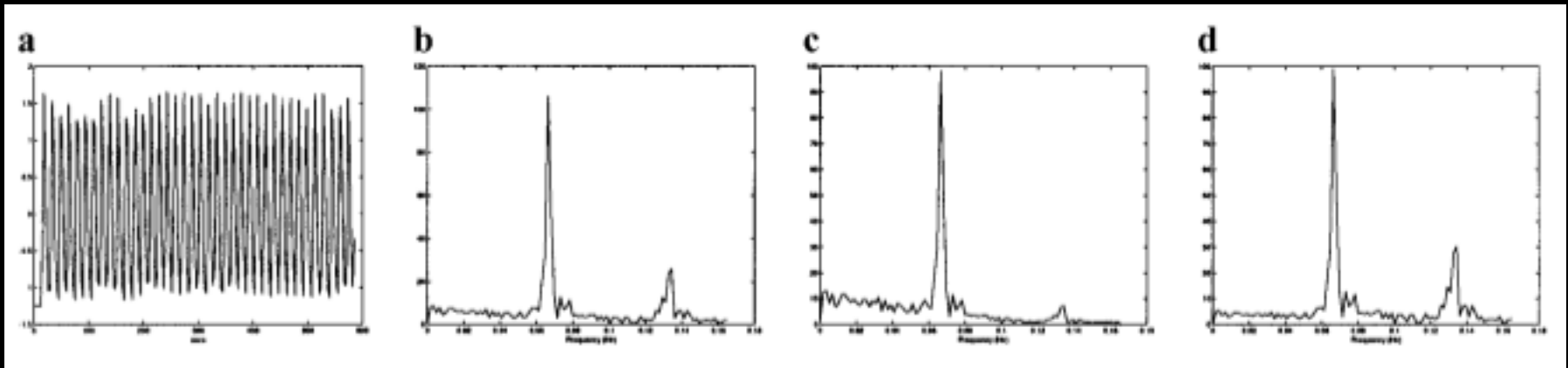


# Filter cutoff

- High, but not higher than paradigm frequency
  - Look at power spectrum of your design and base cutoff on that
  - Block design: Longer than 1 task cycle... usually twice the task cycle
  - Event related design: Larger than 66 s (based on the power spectrum of a canonical HRF of a single response)

# Highpass vs lowpass filtering

- What does it do to the signal??



Signal

Power  
spectrum

Lowpass  
filter

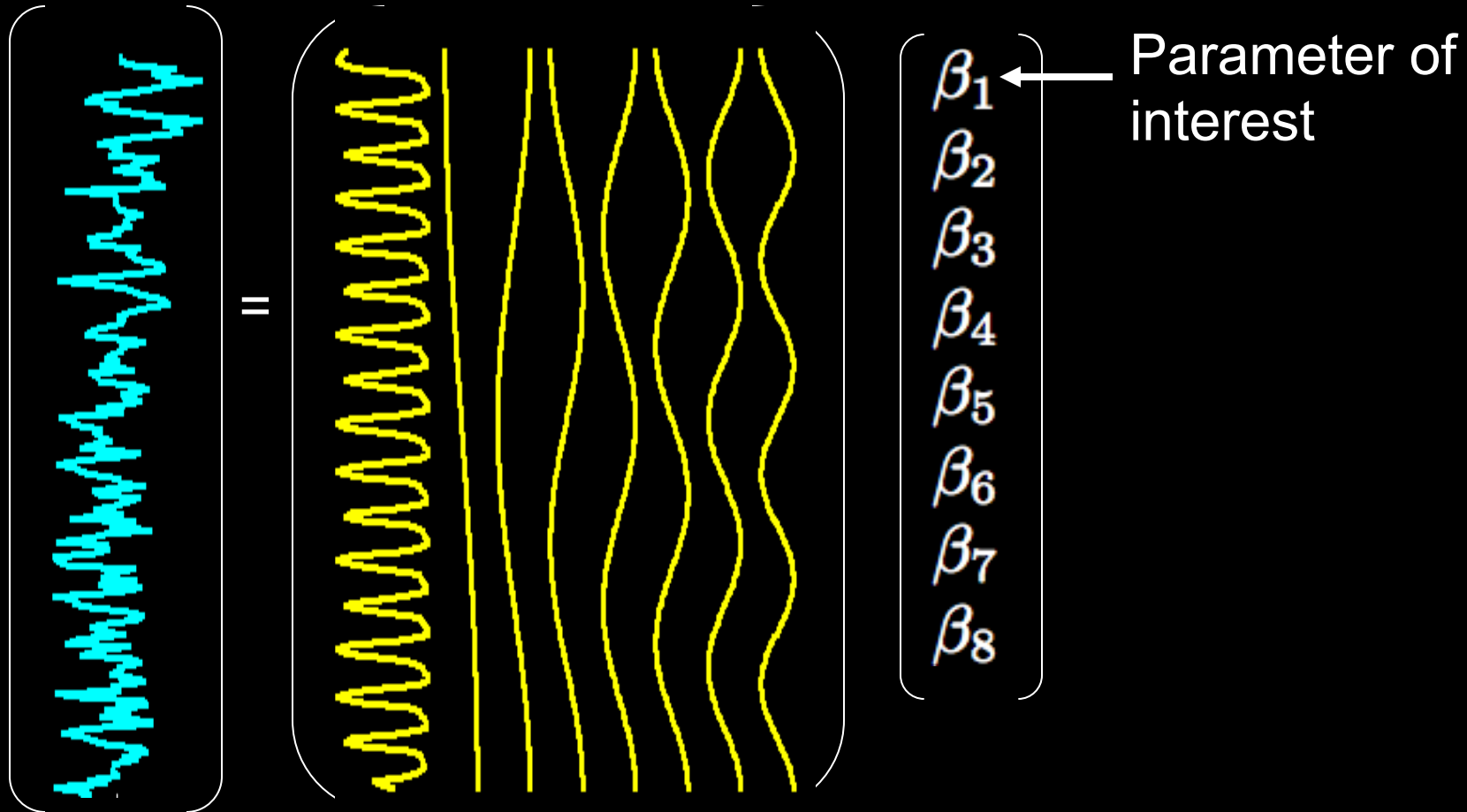
Highpass  
filter

# Filtering Conclusions

- Highpass filter
  - Yes!
  - Just don't remove your signal
- Lowpass filter
  - No (typically)
  - Tends to remove signal

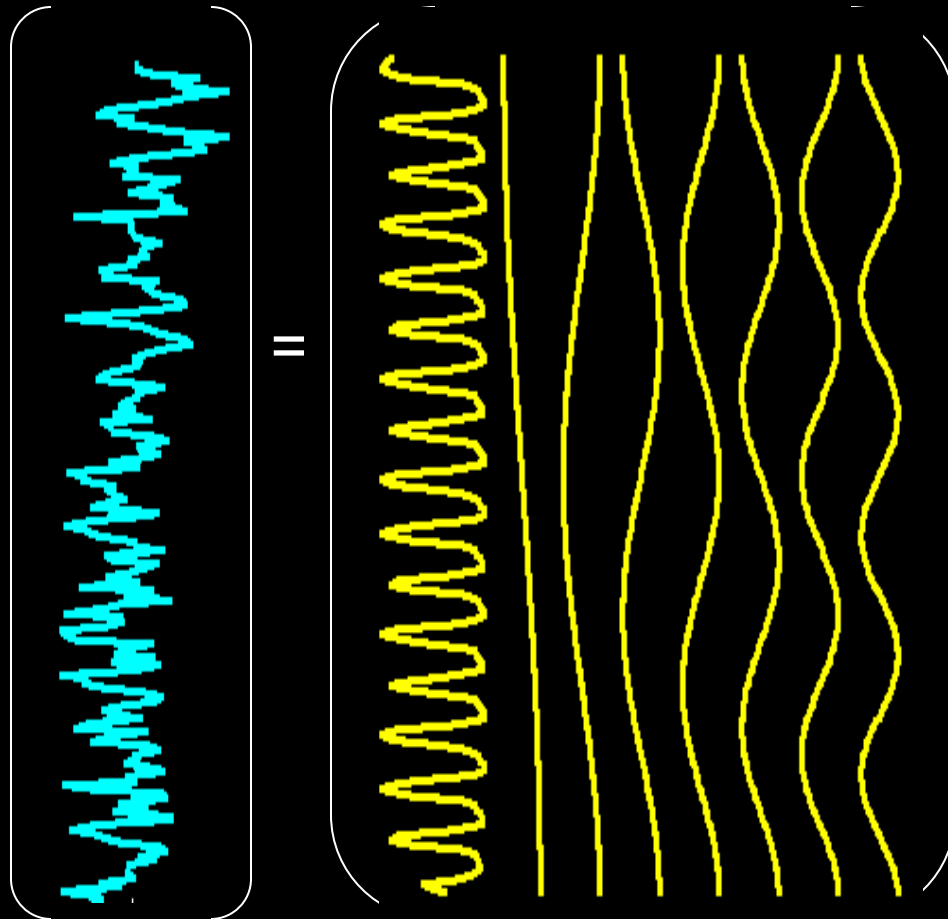
# Model with HP filter

$$Y = X\beta$$



# Model with HP filter

$$Y = X\beta$$



$$\begin{bmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \\ \beta_6 \\ \beta_7 \\ \beta_8 \end{bmatrix}$$

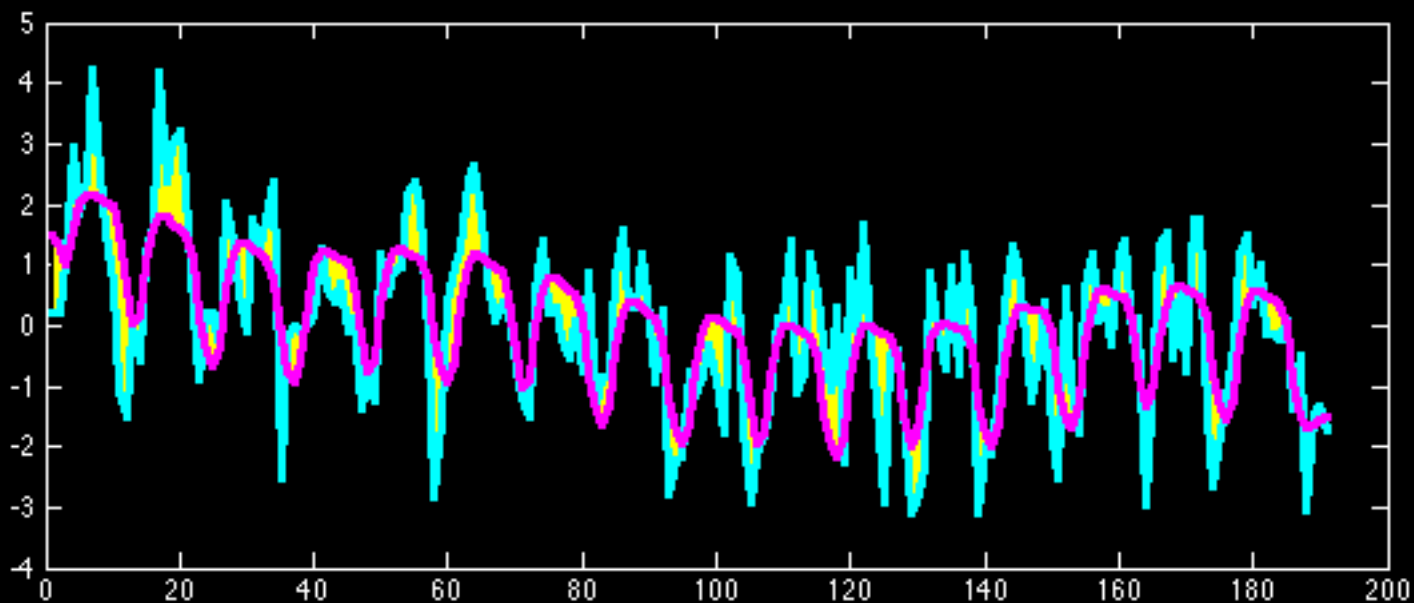
Parameter of interest

$$H_0 : c\beta = 0$$

Use contrast

$$c = (1 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0)$$

# Convolution & HP filter

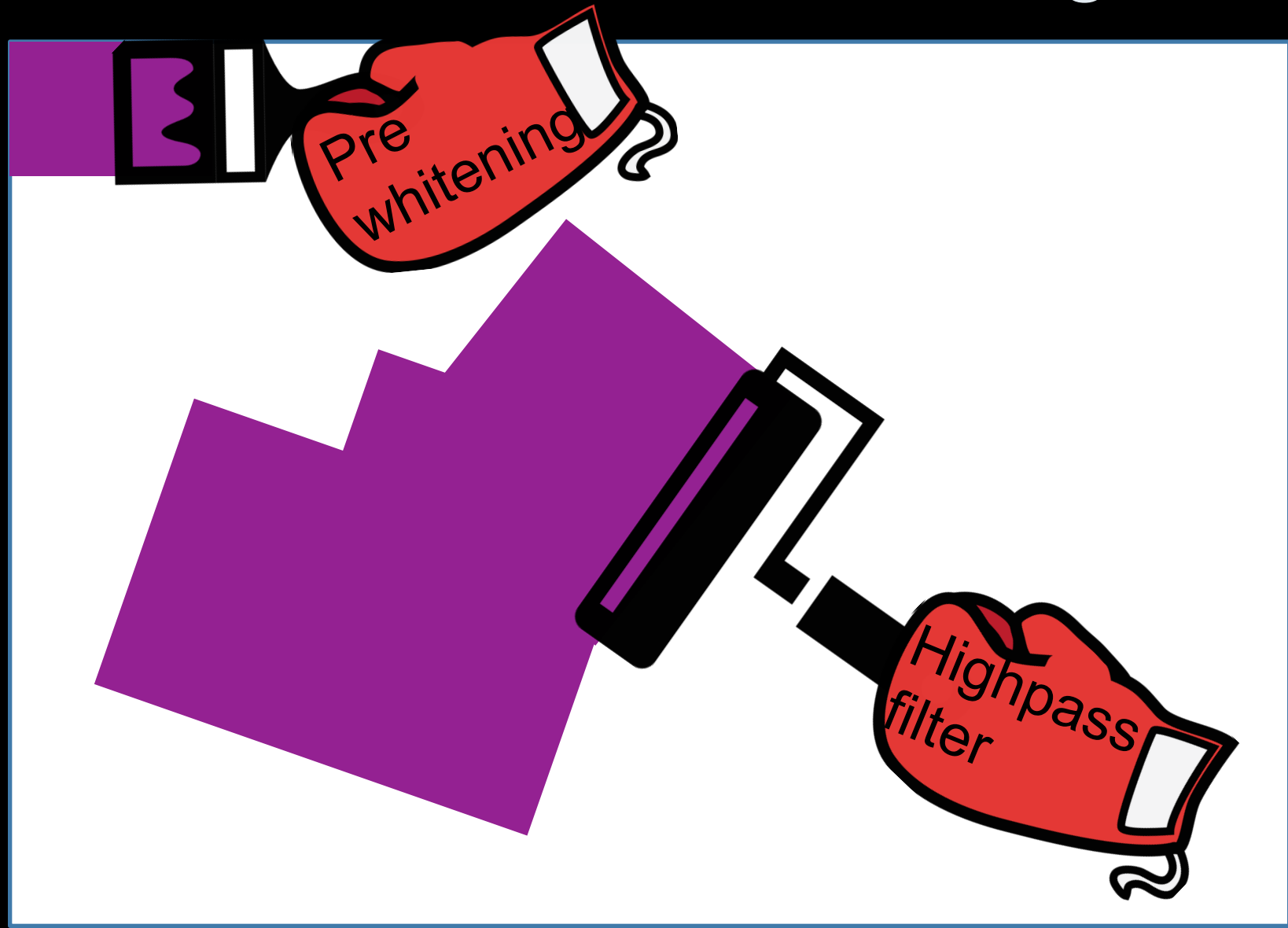


$$t = \frac{0.64}{1.04 \times 0.06} = 10.26$$

Diagrammatic annotations for the equation above:

- A green arrow points down to the numerator  $0.64$ .
- A green arrow points down to the denominator  $1.04 \times 0.06$ .
- A green arrow points up to the result  $10.26$ .
- A green horizontal line is positioned below the denominator  $1.04 \times 0.06$ .

# Punch 2: Prewhitening



# Prewhitening

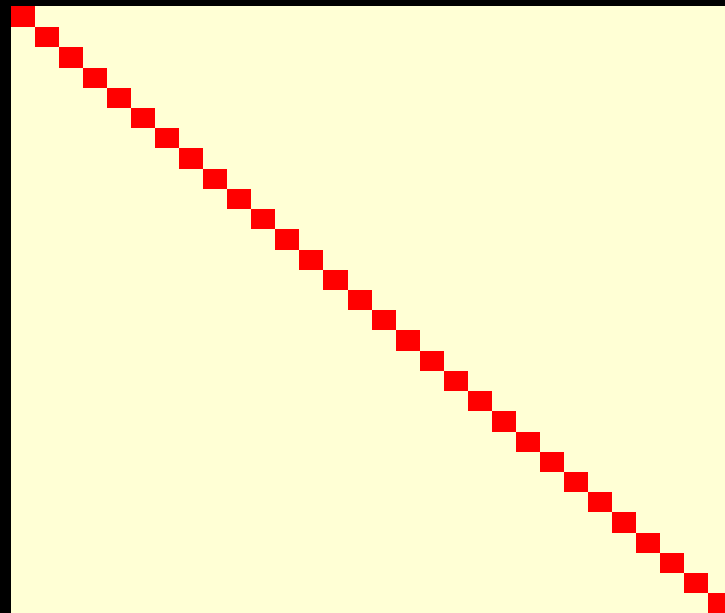
- Remember Gauss Markov?
  - If our errors are distributed with mean 0, constant variance and **not temporally autocorrelated** then our estimates are unbiased and have the smallest variance of all unbiased estimators.
  - Uh oh,



# Prewhitening

$$Y = X\beta + \epsilon$$

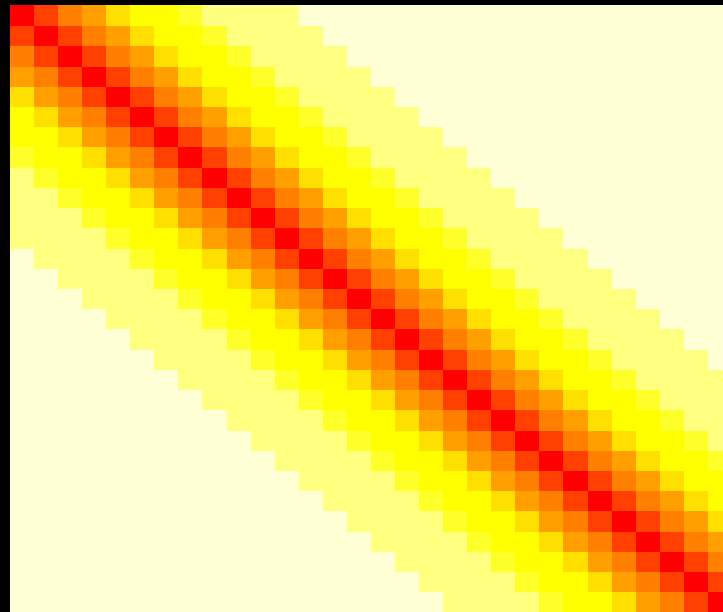
$$\text{Cov}(\epsilon) =$$



# Prewhitening

$$Y = X\beta + \epsilon$$

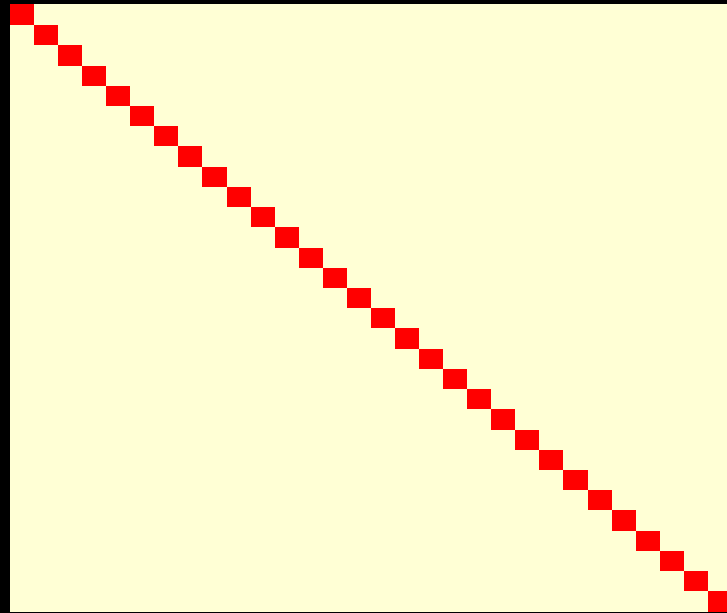
$$\text{Cov}(\epsilon) =$$



# Prewhitening

- Matrix magic
  - Find a matrix  $K$  such that

$$\text{Cov}(K\epsilon) =$$



# Prewhitening

- Estimate this GLM

$$KY = KX\beta + K\epsilon$$

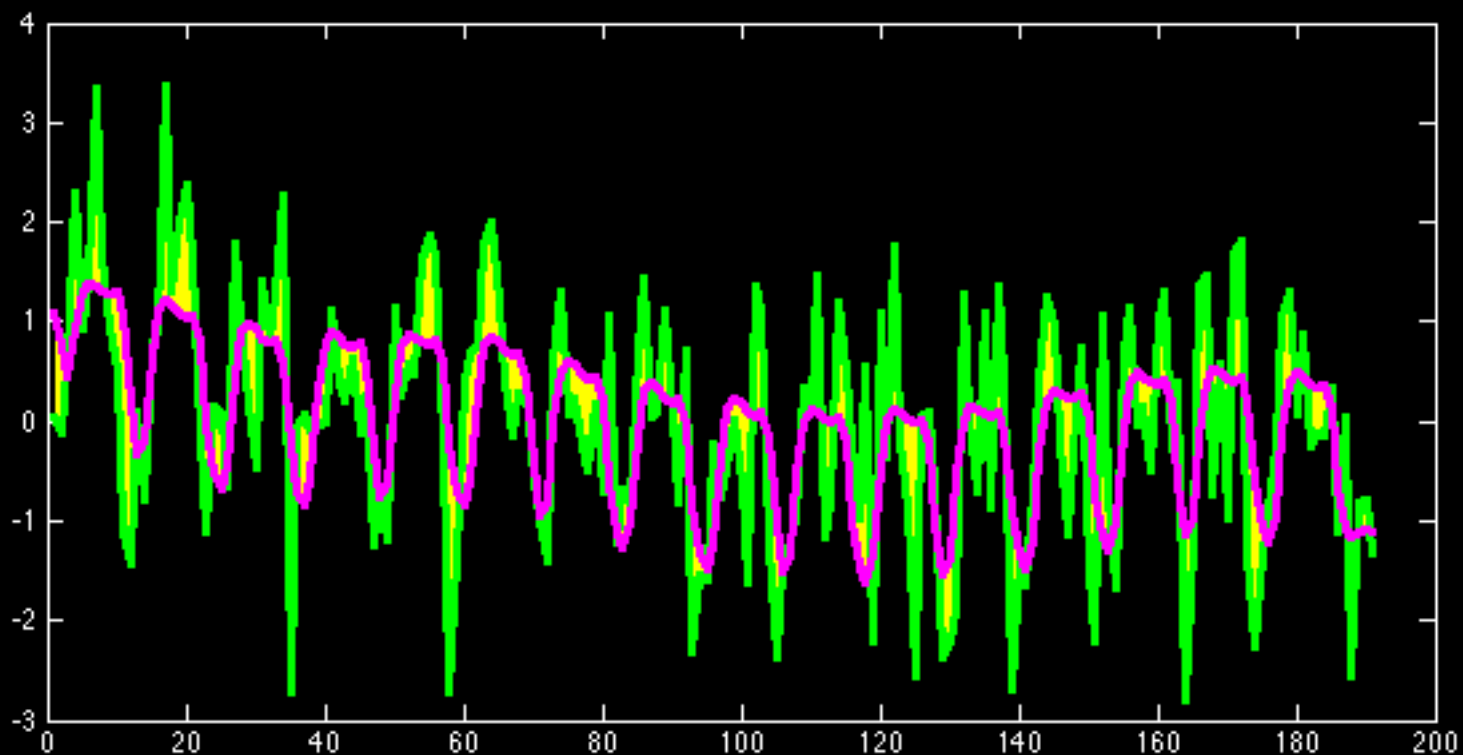
# Prewhitening

- Step 1: Fit the linear regression ignoring temporal autocorrelation
- Step 2: Use residuals from first regression to estimate temporal autocorrelation to obtain  $K$
- Step 3: Create prewhitened model and estimate in usual way

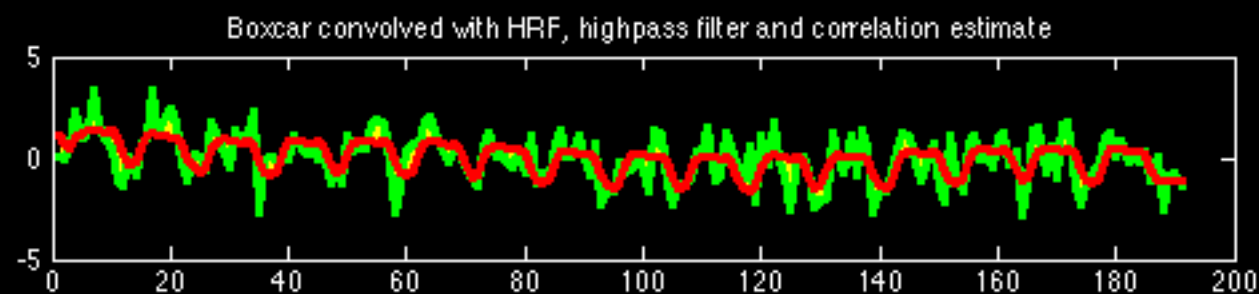
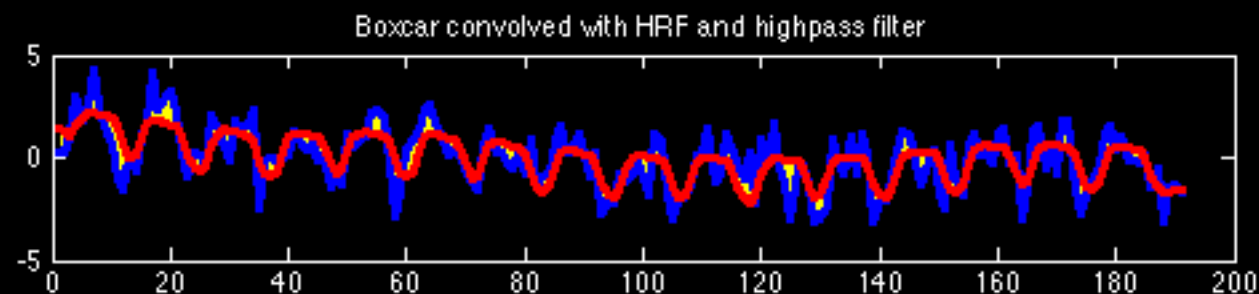
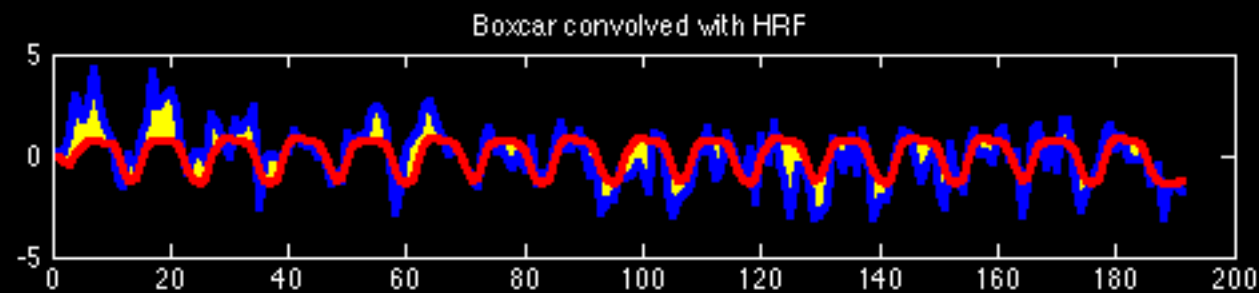
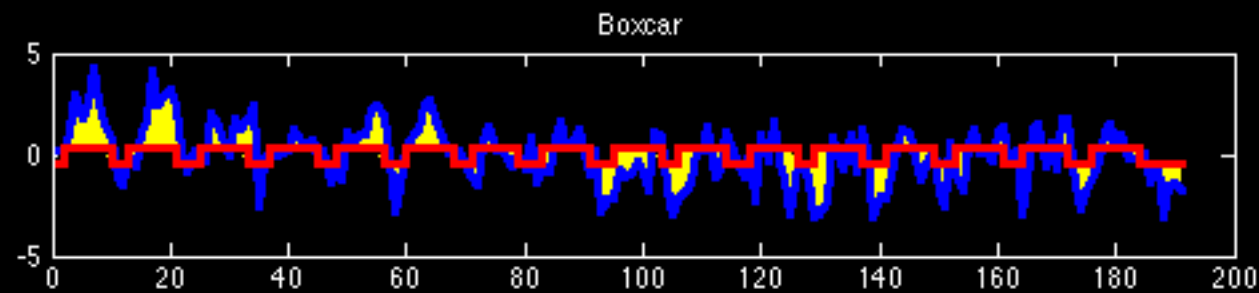
# Estimating $V$

- There's a bias problem....
  - SPM uses a global covariance estimate to help with this
  - FSL uses a local estimate, but smoothes it

# Convolution, HP filter, Whitening



$$t = \frac{0.66}{0.954 \times 0.08} = 8.65$$





# Scaling

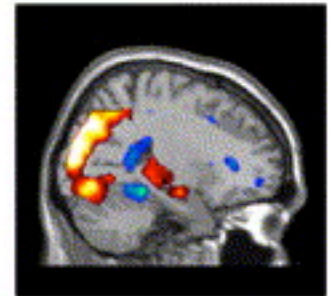
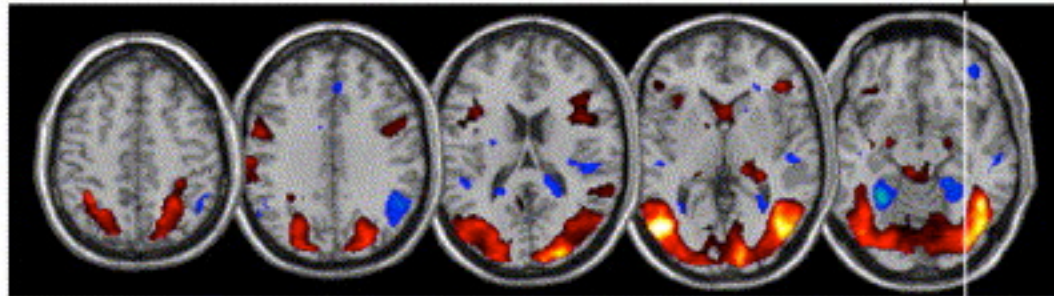
- Grand Mean Scaling (good)
  - Removes intersession variance
  - Allows us to combine data across subjects
  - Whole 4D data set is scaled by a single number
  - Automatically done in software packages

# Scaling

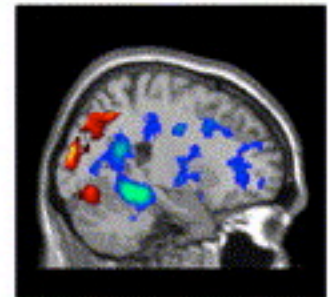
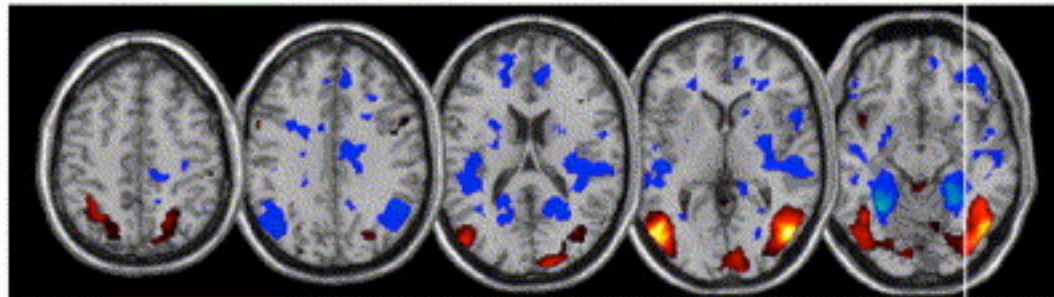
- Proportional scaling aka Intensity normalization (not good)
  - Forces each volume of 4D dataset to have the same mean
  - Also done by modeling the global signal
  - Idea is to remove background activity

# Intensity Normalization

without



with



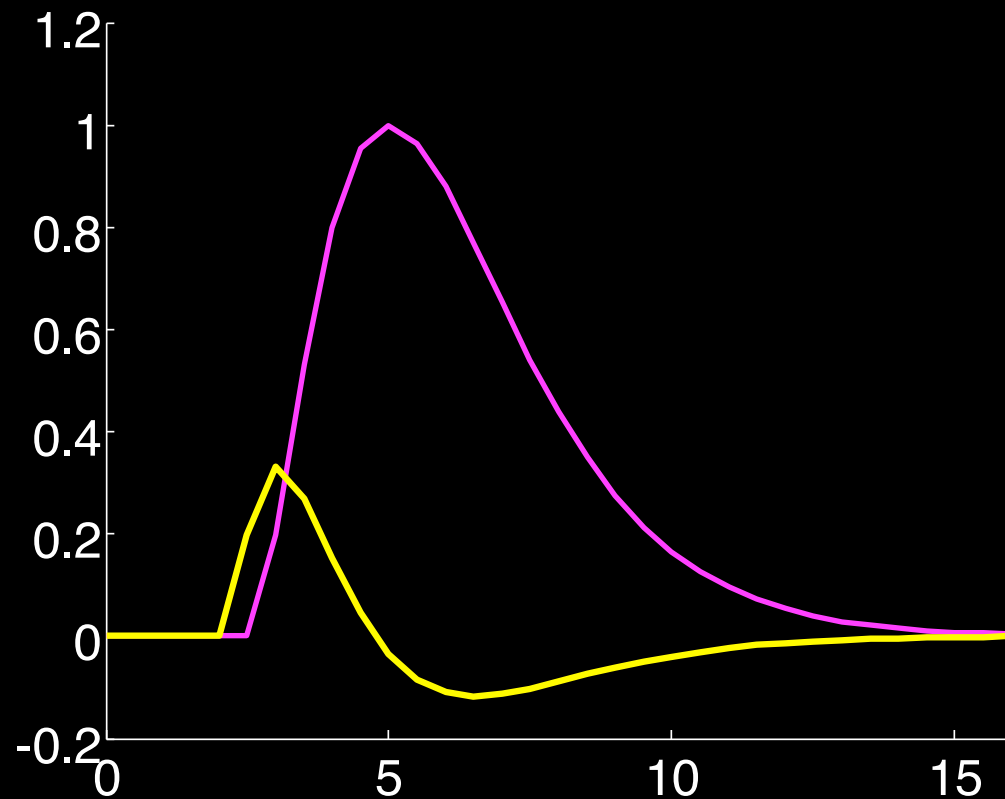
Junghofer et al, 2004, NI

Signal is lost and negative activation artifacts

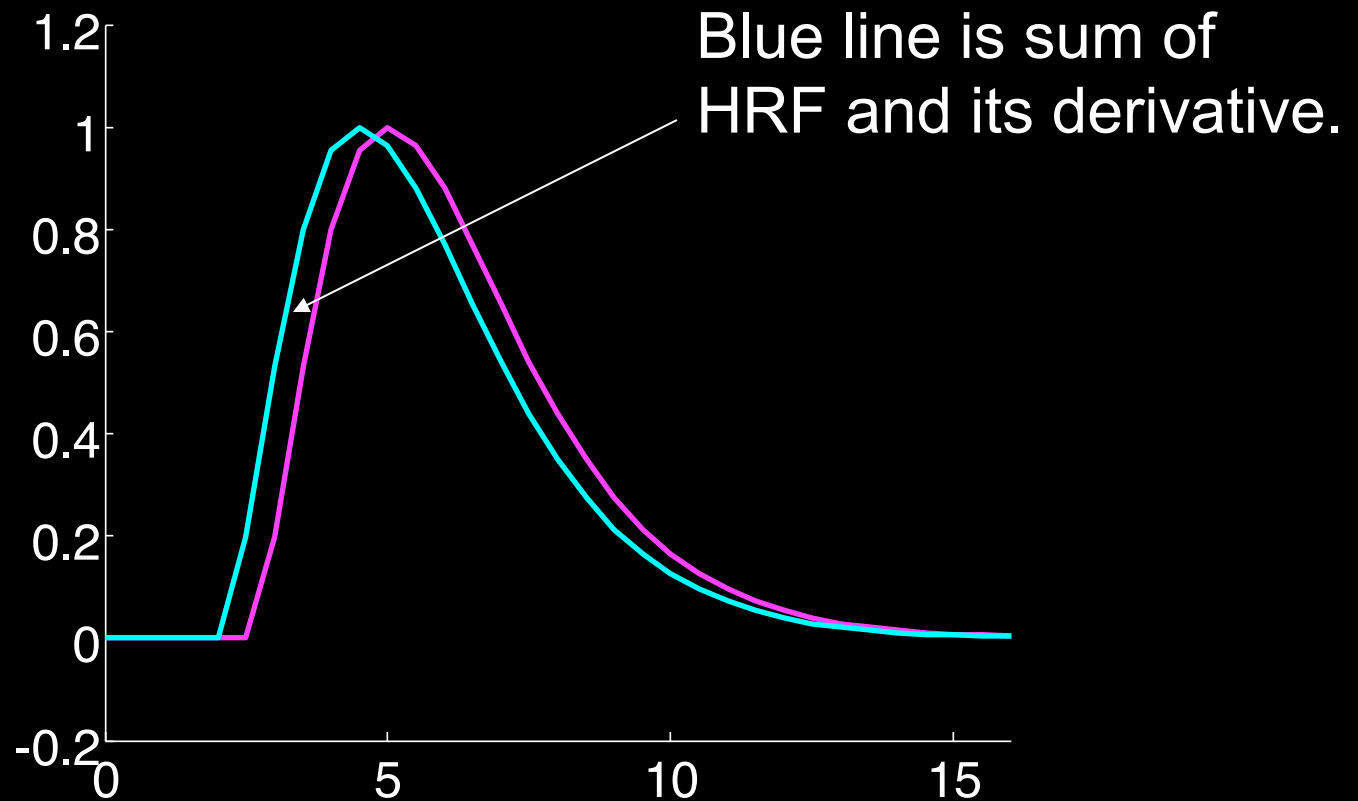
# Other modeling considerations

- Adding the derivative of the HRF
- Adding motion parameters to the model

# Model HRF & Derivative



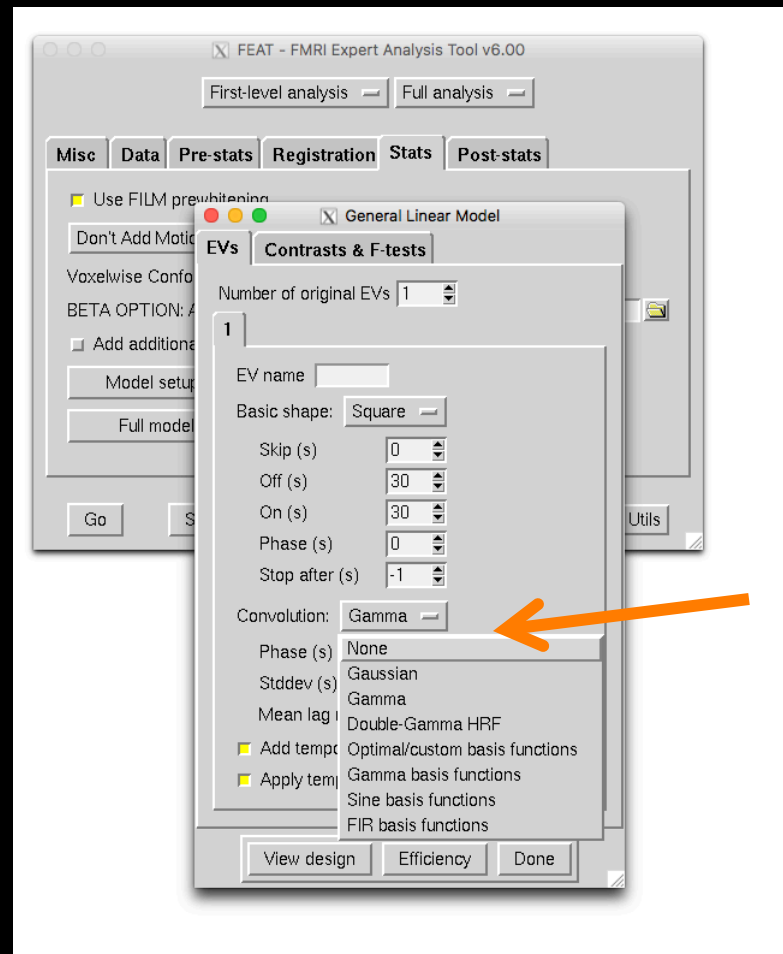
# “Shifted” HRF



# Temporal derivative

- We model the derivative, but don't study inferences of it
  - Lindquist, et al (NI, 2008) suggest this is a bad idea...may lead to bias

# Where are these options in the Feat GUI?

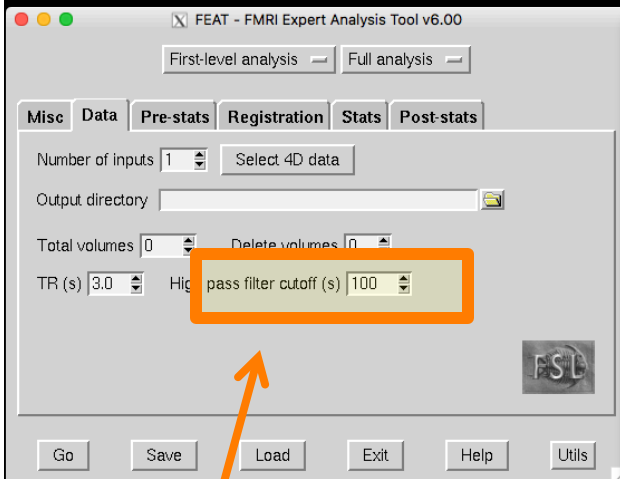


Convolution  
option . . .  
which one should  
you use?

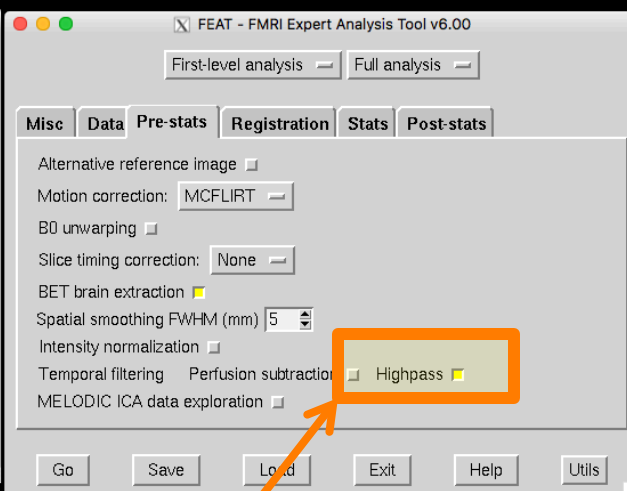


# Where are these options in the Feat GUI?

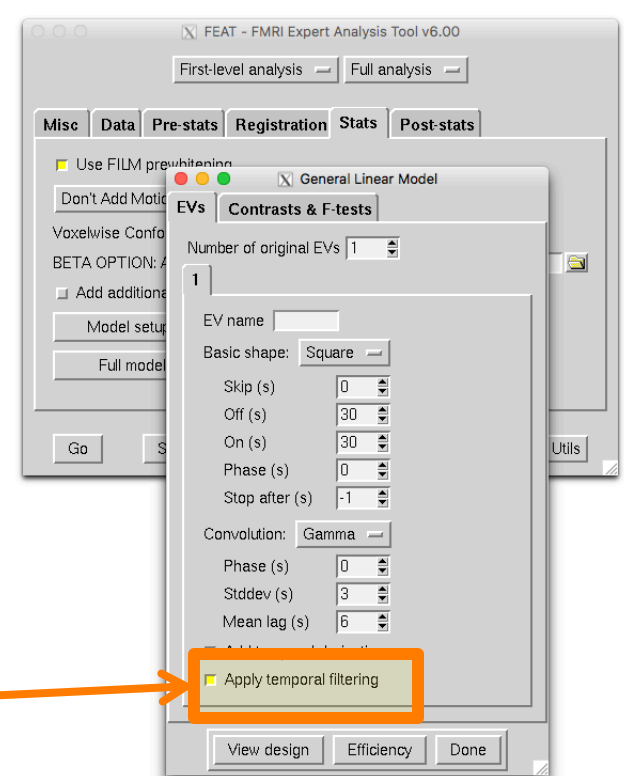
- Highpass filter (3 places!!)



Sets cutoff for data and design

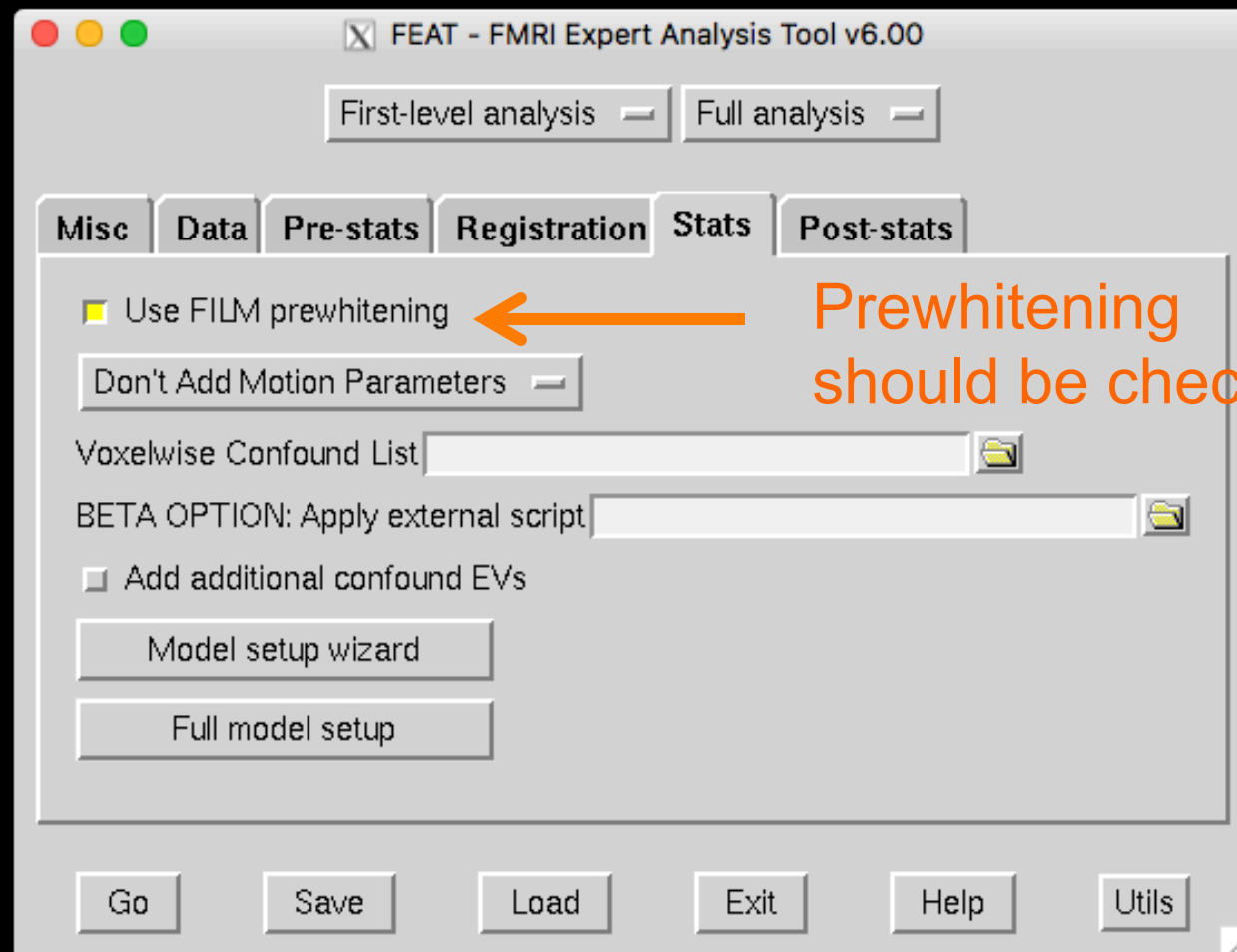


Turns it on for data



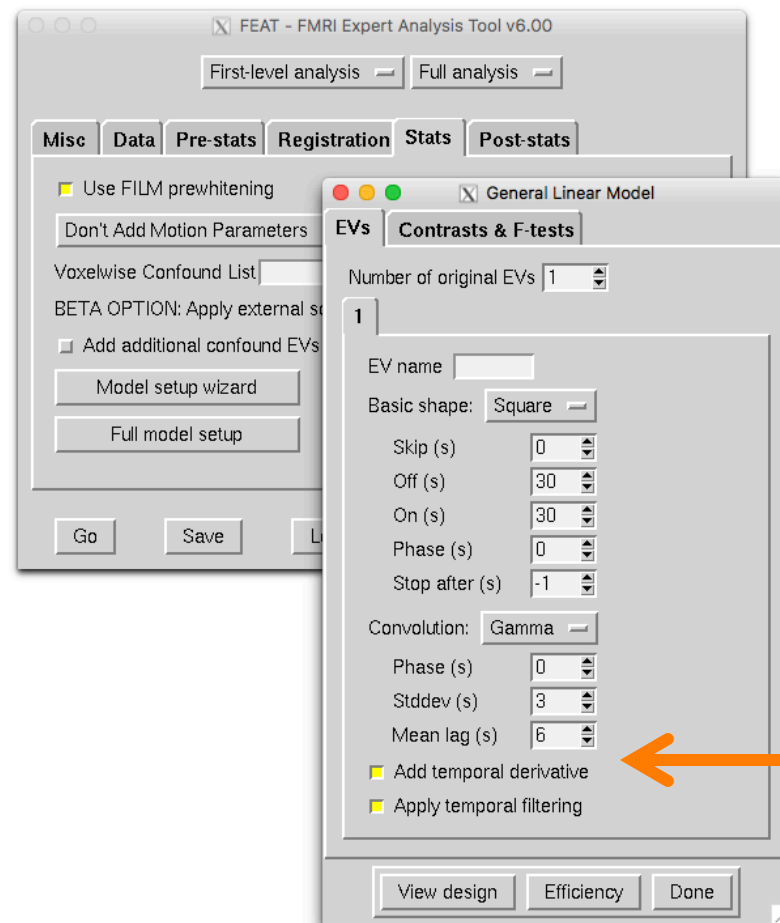
Turns it on for design

# Where are these options in the Feat GUI?



Prewhitening  
should be checked

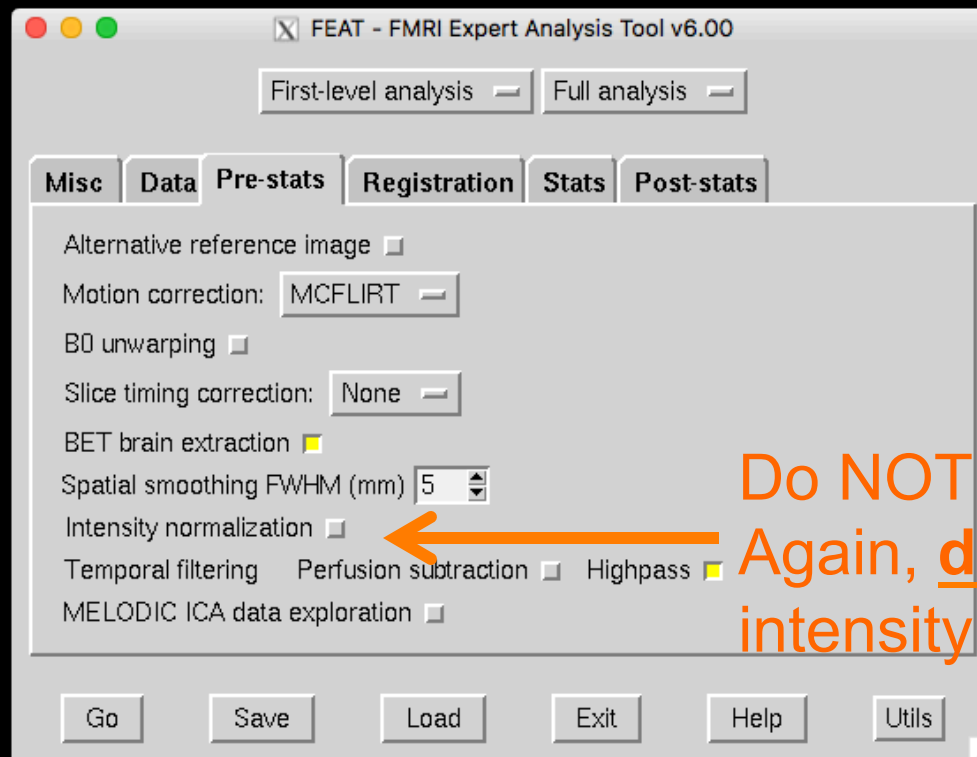
# Where are these options in the Feat GUI?



Derivative

# Where are these options in the Feat GUI?

- Intensity normalization



Do NOT check this.  
Again, don't use  
intensity normalization

Questions?