# fMRI Course, Day 5 1st-Level Analysis

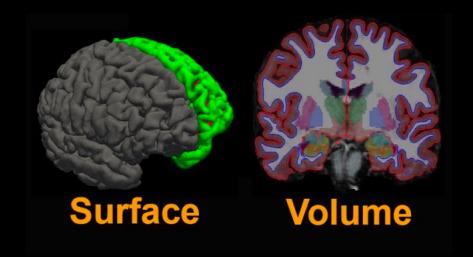
August 5<sup>th</sup>, 2022

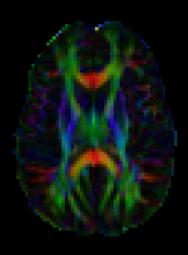
# **About Me**

## **Neuroimaging Initiative (NII)**

## Consulting for anyone who does neuroimaging





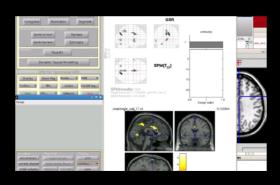


## Goals

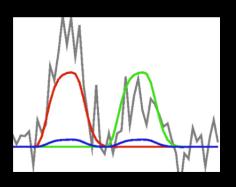
- 1. Understand how to do the steps
- 2. Understand why we did the steps



#### **Both Remember Steps and Apply Concepts**







## **Problem**

How to accommodate dozens of labs spread across three campuses?

How to stay current with the latest methods and tools?

How to make sure the ideas "stick"?

### **Solutions**

Illustrations and demonstrations using data

Goal is for you to analyze your own data

Feedback is highly appreciated!

# **About Me**

Andy's Brain Book

latest

Search docs

INSTALI

Overview

UNIX FOR NEUROIMAGERS

What is Unix?

Unix Tutorial #1: Navigating the directory tree

Unix Tutorial #2: Copying and Removing

Unix Tutorial #3: Reading Text Files

Unix Tutorial #4: Shells and Path Variables

Unix Tutorial #5: For-Loops

Unix Tutorial #6: Conditional Statements

Unix Tutorial #7: Scripting

Unix Tutorial #8: The Sed Command

Unix Tutorial #9: Automating The Analysis

FMRI SHORT COURSE WITH FSL

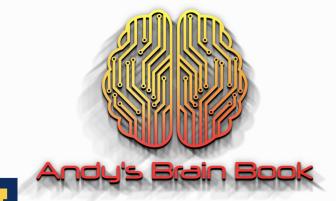
Introduction

fMRI Tutorial #1: Downloading the Data

Docs » Welcome to Andy's Brain Book!

C Edit on GitHub

#### Welcome to Andy's Brain Book!



UNIVERSITY OF MICHIGAN

This resource is sponsored by the University of Michigan.

This book, *Andy's Brain Book*, is the ReadTheDocs companion to Andy's Brain Blog. It is intended for fMRI beginners, with more advanced imaging techniques being added later on. If this is your first

# **Overview of The Schedule**

Friday		8:30 AM –	Level Analysis &	Andy Jahn	
8/5/2022		12:30 PM	Experimental Design	University of Michigan	
Monday	8:30 AM –		Contrasts, Group Analysis & Double Dissociations	Andy Jahn	
8/8/2022	12:30 PM			University of Michigan	
	4:00 PM		Pattern Analysis & Classification via MVPA-virtual but live	Stephen LaConte Virginia Tech	
Tuesday	8:30 AM -		Pitfalls in fMRI Research	Andy Jahn	
8/9/2022	12:30 PM			University of Michigan	
Wednesday 8/10/2022	8:30 AM – 12:30 PM		Network Analysis & Tools	Scott Peltier University of Michigan Alex Iordan University of Michigan	
Thursday 8/11/2022	8:30 AM – 12:30 PM		Part 1- Introduction to Open Science Part 2- BIDS, MRIQC & fMRI Prep	Andy Jahn University of Michigan Scott Peltier University of Michigan	
Friday	8:30 AM –		Reproducibility	Andy Jahn	
8/12/2022	12:30 PM			University of Michigan	

## **Overview of The Schedule**

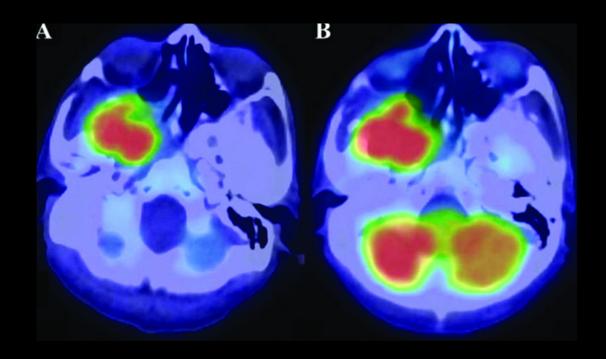
At regular intervals, I will be asking you to download software and data

This is just to help with the demonstrations; don't worry if you are unable to download or install these!

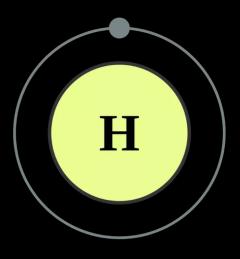
# Today's Agenda

- 1. Brief review of fMRI
- 2. The BOLD Response
- 3. Model Fitting and 1<sup>st</sup>-Level Analysis
- 4. Other Modeling Options: Parametric Modulation and Finite Impulse Response

**Neuroimaging Scene: The Early 1990's** 



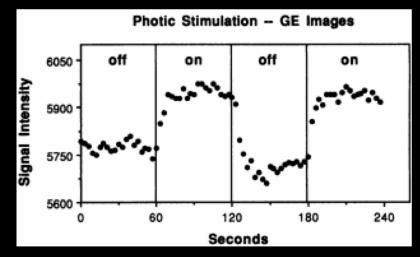
MRIs: More powerful & More widespread

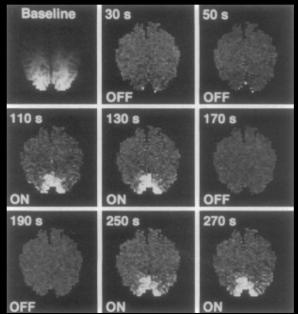


Deoxygenated blood = Lower signal

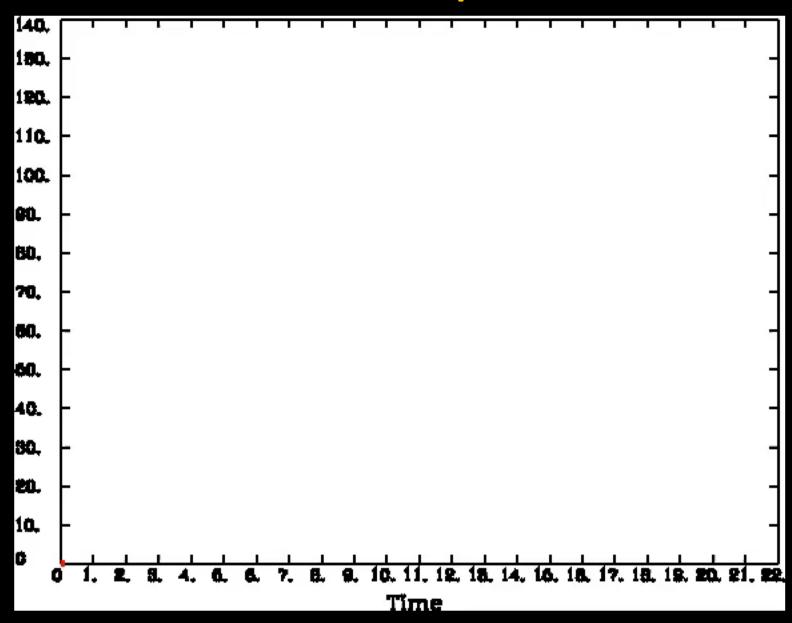
Oxygenated blood = Higher signal

**Blood Oxygenation Level Dependent Signal (BOLD Signal)** 

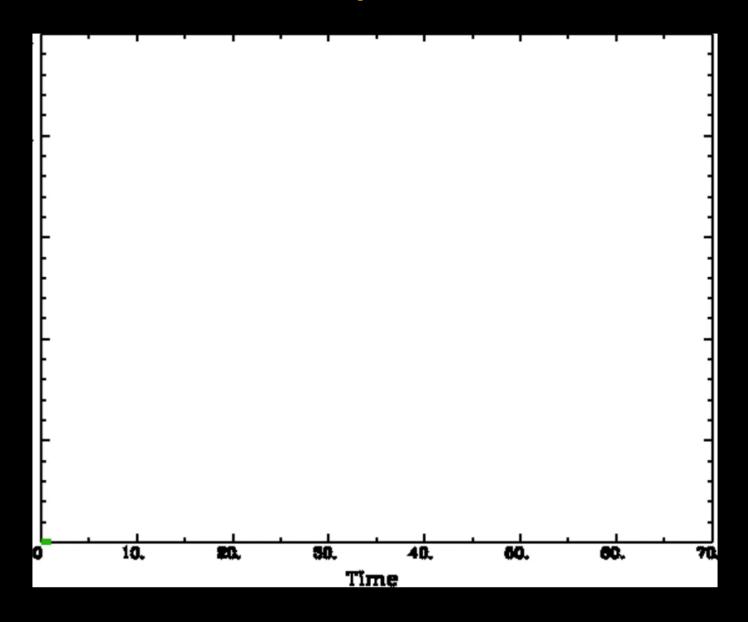




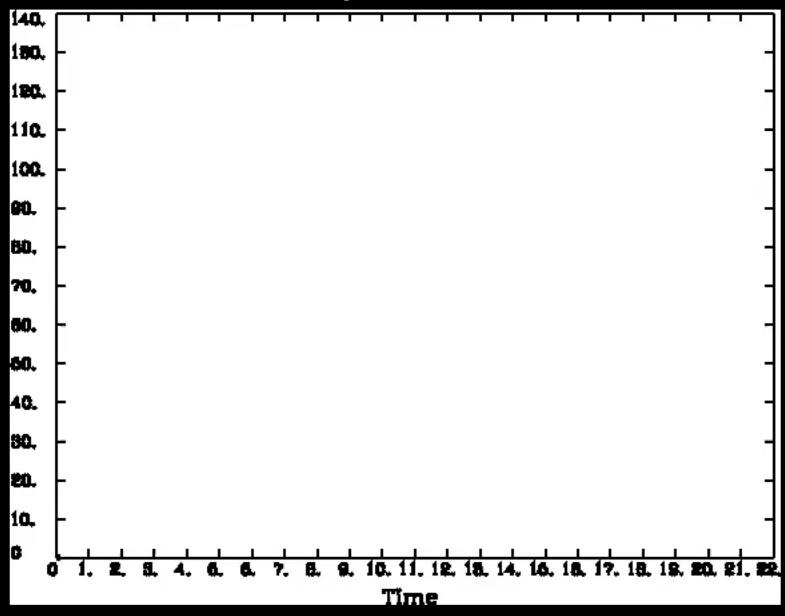
# The BOLD Response



## The BOLD Response: Duration



## **The BOLD Response: Convolution**



#### **Applet Demonstration of Convolution**

https://phiresky.github.io/convolution-demo/

#### **Interim Summary**

- 1. Stimulus transducted into neural firing
- 2. More neural firing = more oxygen consumption
- 3. More oxygen consumption = more blood flow
  - 4. More blood flow = greater measured signal

Observed signal is a few steps removed from actual neural activity

#### What We've Done So Far...

- 1. Overview of fMRI
- 2. Preprocessing the individual subject
  - 3. Experimental Designs
    - 4. Timing Files
- 5. Creating the general linear model (GLM)

Flanker task: Behavioral task adapted for fMRI analysis

**Behavioral** 

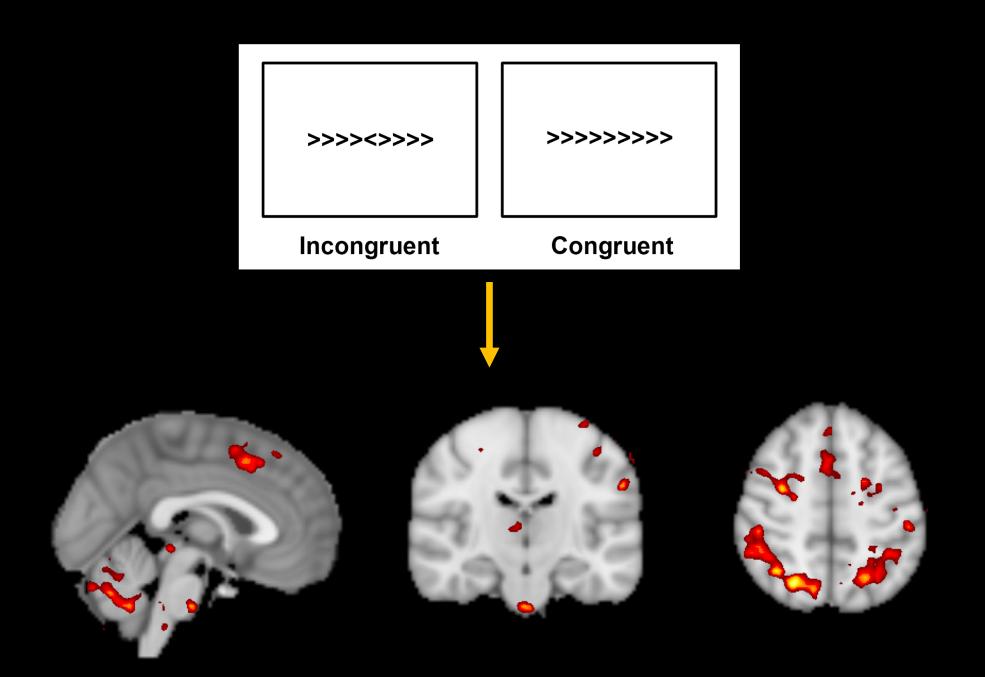
\* Dependent measure of interest is reaction time

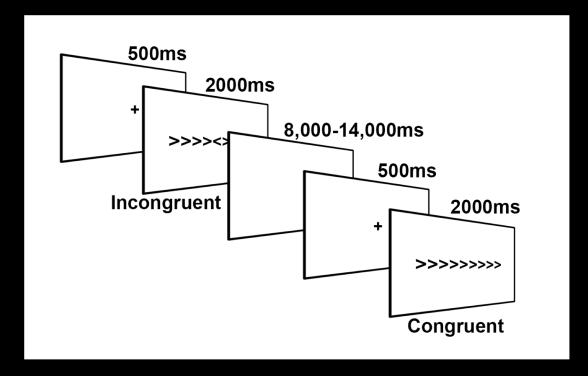
\* Can have the same amount of time between trials

**fMRI** 

\* Two dependent measures:
reaction time & the BOLD
response

\* Will need differing amounts of time between trials





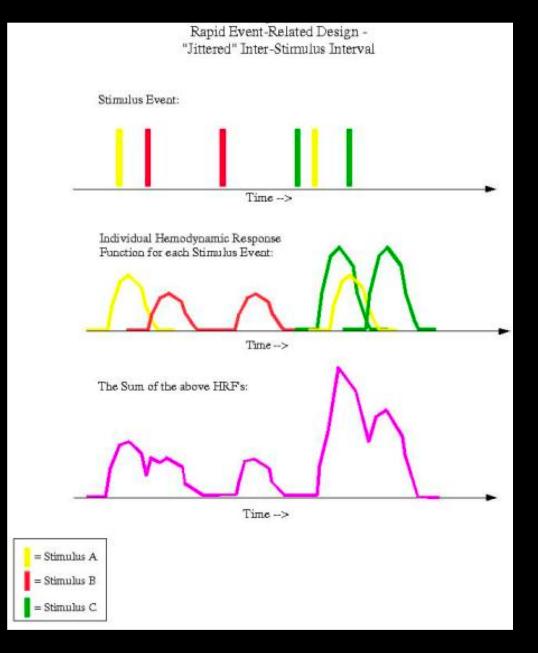
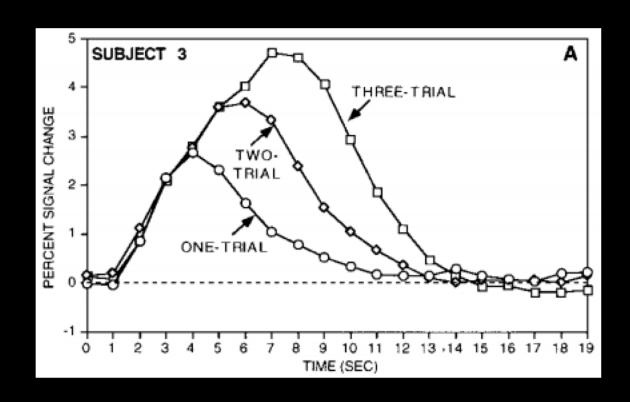
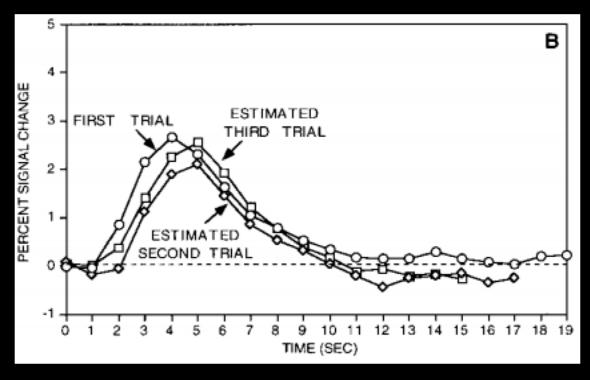


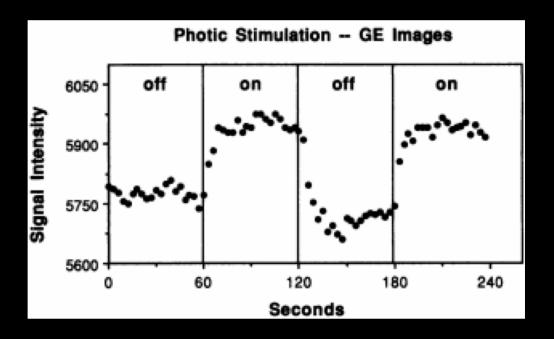
Image from Bob Cox

#### Linearity





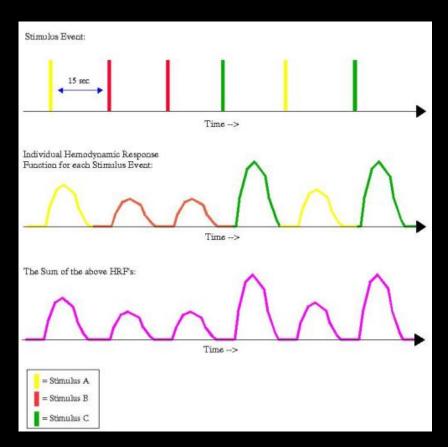
1. Block design (e.g., Kwong et al., 1992)

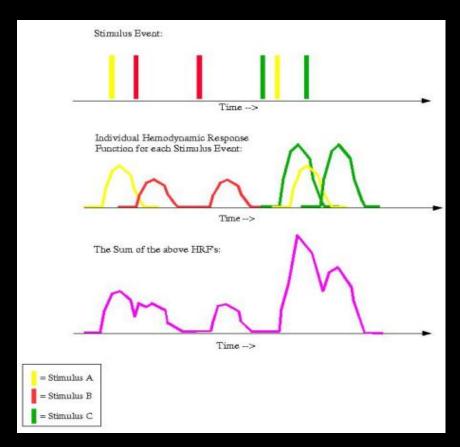


Advantages: Powerful, easy to design

Disadvantages: Boring, predictable, cannot use complex designs

#### 2. Event-related designs

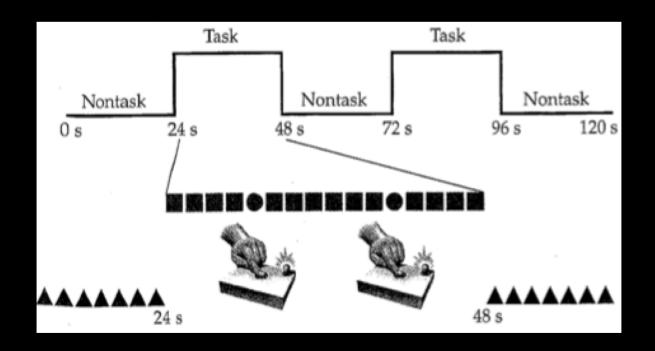




Advantages: More engaging, can use more complex designs

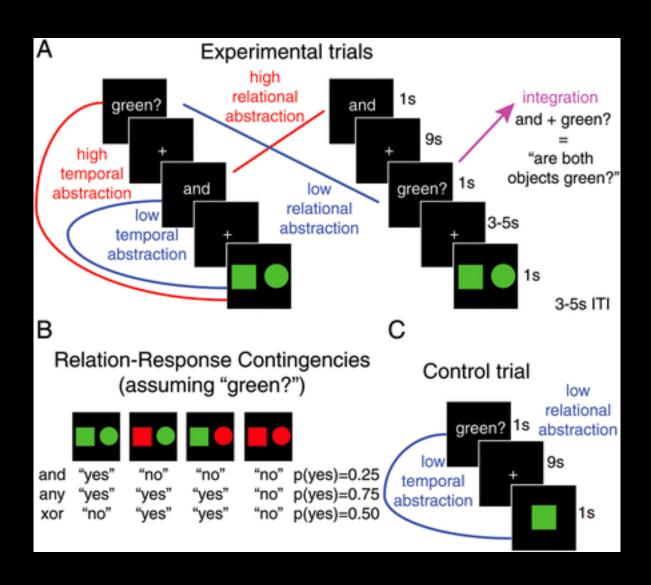
Disadvantages: Less power, susceptible to collinearity

**Mixed Designs** 

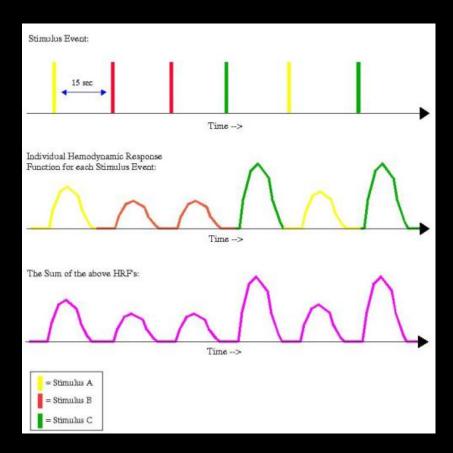


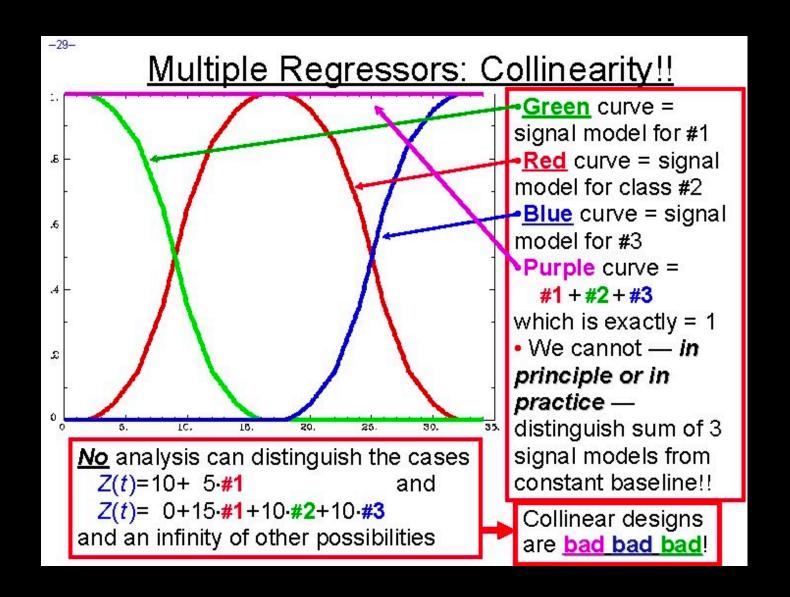
Block: State effects; trial: item-related effects

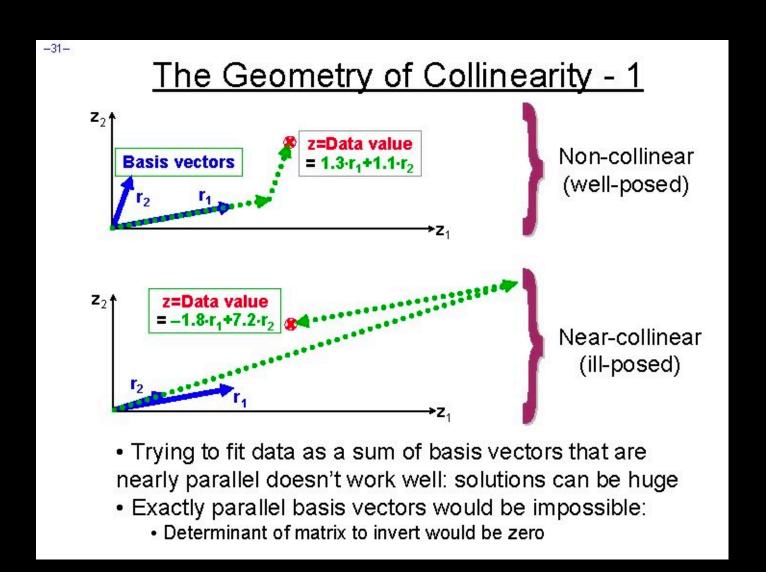
Disadvantages: Very sensitive to errors in HRF modeling



Differing amounts of time between trials (i.e., jitter) are needed to avoid collinearity







# **Questions?**

# **Demonstration of viewing the time-series**

# **Timing Files**

SUB-O1_TASK-FLANKER_RUN-1_EVENTS.TSV & DOWNLOAD						
onset \$	duration <b>♦</b>	tri	‡res…	co <b>\$</b>		
0.0	2.0	incongrue	1.095	correct		
10.0	2.0	incongrue	0.988	correct		
20.0	2.0	congruent	0.591	correct		
30.0	2.0	congruent	0.499	correct		
40.0	2.0	incongrue	0.719	correct		
52.0	2.0	congruent	0.544	correct		
64.0	2.0	congruent	0.436	correct		
76.0	2.0	incongrue	0.47	correct		

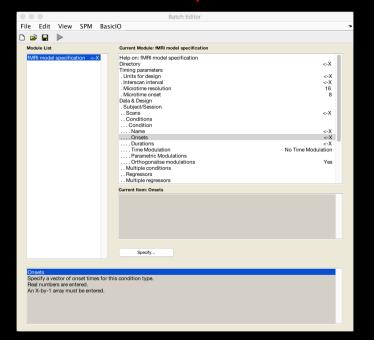
congruent... 0.409

correct

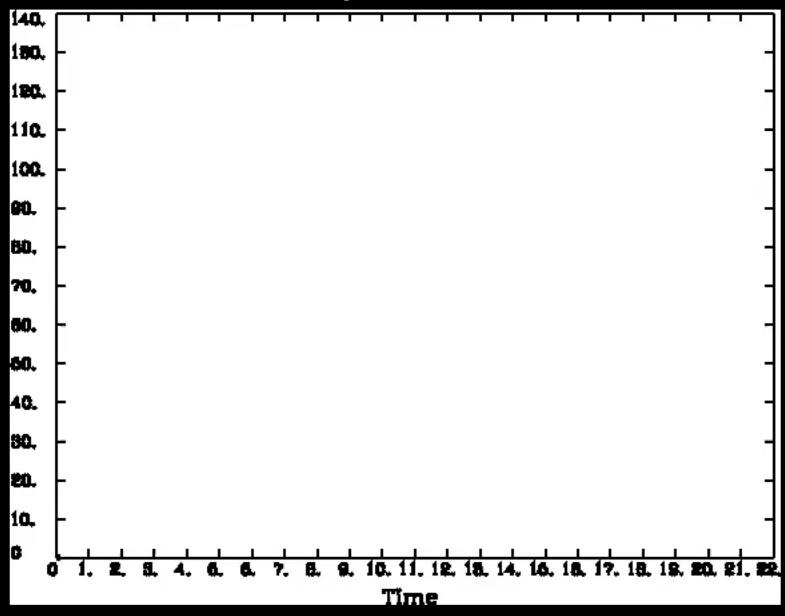
88.0

2.0

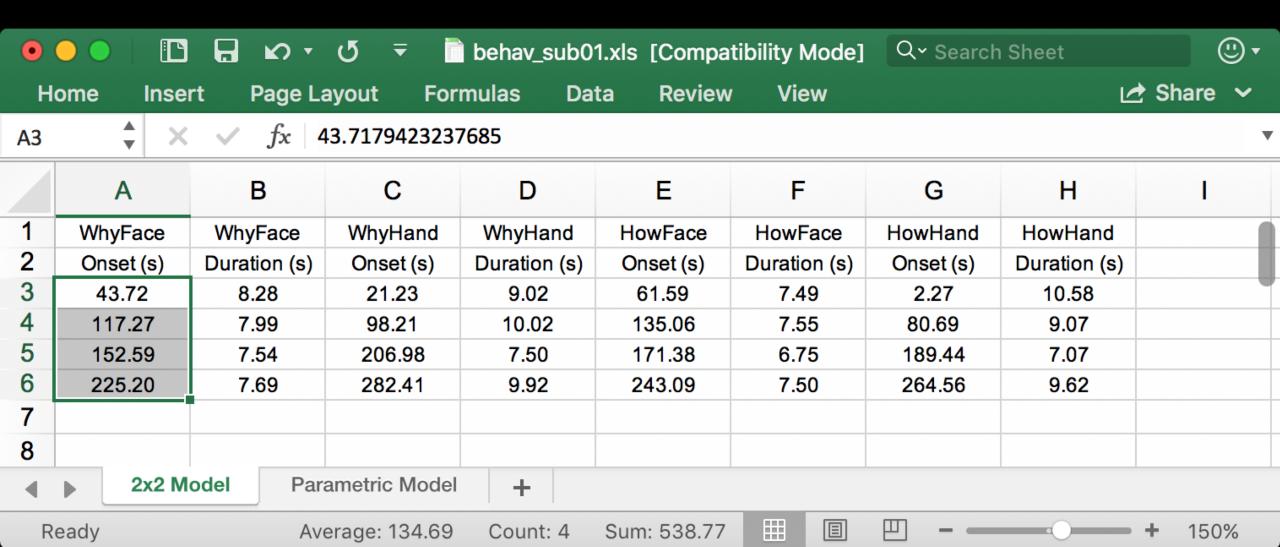
onset	duration	ı trial_type
0.0	2.0	incongruent_correct
10.0	2.0	incongruent_correct
20.0	2.0	incongruent_correct
32.0	2.0	congruent_correct
42.0	2.0	congruent_correct
52.0	2.0	incongruent_correct
64.0	2.0	congruent_correct
76.0	2.0	congruent_correct
88.0	2.0	incongruent_correct
102.0	2.0	congruent_correct
116.0	2.0	congruent_correct



## **The BOLD Response: Convolution**



#### **How to Write out Timings?**

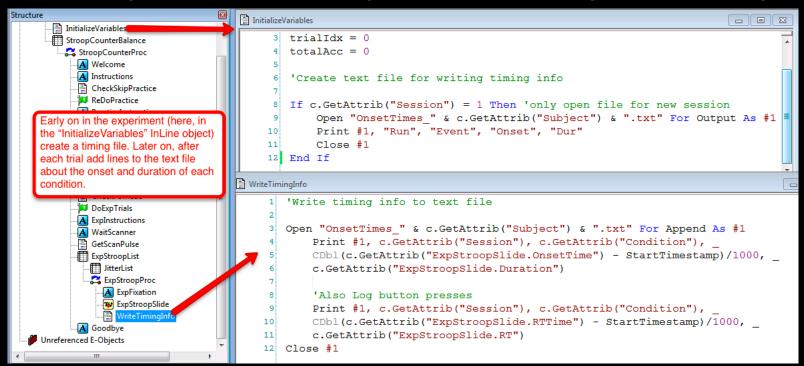


#### **How to Write out Timings?**

Depends on what stimulus presentation software you use

My advice: Write the timings in BIDS format (Onset, Duration, Trial Type, etc)

These can be easily edited and imported into any of the major packages



### **How to Write out Timings?**

DS000102 - 🗁 SUB-01 - 🗁 FUNC - 🖰 SUB-01\_TASK-FLANKER\_RUN-1\_EVENTS.TSV



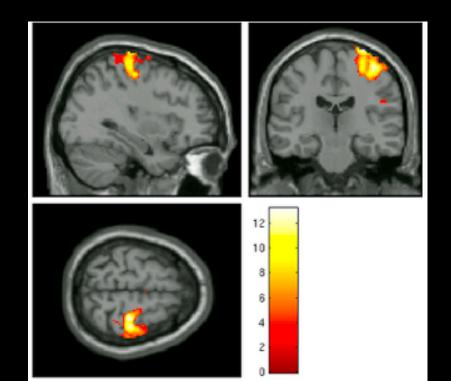
-									
	ONSET	DURATION	TRIAL_TYPE	RESPONSE_T	CORRECTNESS	STIMVAR	RSPONSE	STIMULUS	COND
	0.0	2.0	incongruen	1.095	correct	2	1	incongruent	cond003
	10.0	2.0	incongruen	0.988	correct	2	1	incongruent	cond003
	20.0	2.0	congruent	0.591	correct	1	1	congruent	cond001
	30.0	2.0	congruent	0.499	correct	1	1	congruent	cond001
	40.0	2.0	incongruen	0.719	correct	2	1	incongruent	cond003
	52.0	2.0	congruent	0.544	correct	1	1	congruent	cond001
	64.0	2.0	congruent	0.436	correct	1	1	congruent	cond001
	76.0	2.0	incongruen	0.47	correct	2	1	incongruent	cond003
	88.0	2.0	congruent	0.409	correct	1	1	congruent	cond001
	102.0	2.0	incongruen	0.563	correct	2	1	incongruent	cond003
	116.0	2.0	congruent	0.493	correct	1	1	congruent	cond001
	130.0	2.0	congruent	0.398	correct	1	1	congruent	cond001
	140.0	2.0	congruent	0.466	correct	1	1	congruent	cond001
	150.0	2.0	incongruen	0.518	correct	2	1	incongruent	cond003
	164.0	2.0	incongruen	0.56	correct	2	1	incongruent	cond003
	174.0	2.0	incongruen	0.533	correct	2	1	incongruent	cond003
	184.0	2.0	congruent	0.439	correct	1	1	congruent	cond001

#### **Onset Times Recommendations**

No matter how you choose to write them out, you need to verify them

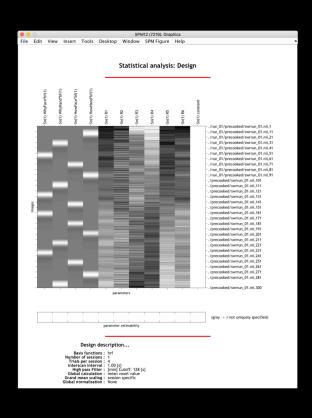
Some scanners acquire a few "dummy scans" at the beginning

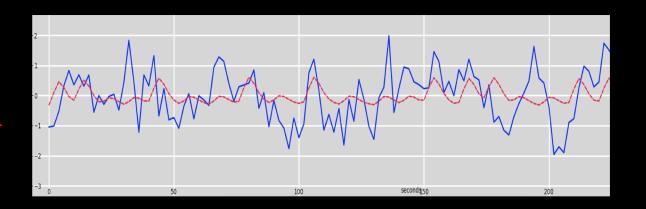
If the experiment has a motor response, check that contrast first

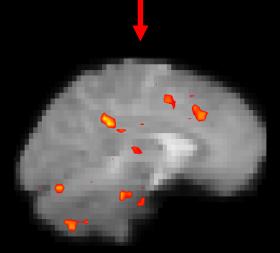


### **Overview of model fitting**

Fit the Model at each voxel ("mass univariate")







Uses one or more regressors (independent variables) to predict an outcome measure (dependent variable)

$$Y = \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \varepsilon$$

**Y**= Outcome variable

 $\beta$  = Beta Weights (parameter estimates)

*X*= Regressor

 $\varepsilon$  = Residual

$$Y = \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \varepsilon$$

Assume that:

$$Y = \text{GPA}$$
,  $X_1 = \text{IQ}$ ,  $X_2 = \text{Drinks per week}$ ,  $X_3 = \text{Height}$ 

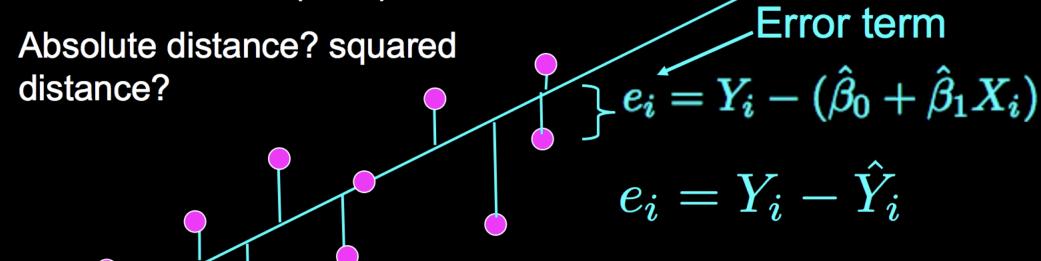


$$GPA = (\beta_1 * IQ) + (\beta_2 * Drinks) + (\beta_3 * Height) + \varepsilon$$

$$m{\beta}_1 = 0.05^*, m{\beta}_2 = -0.07^*, m{\beta}_3 = 0.01 \ (not \ significant)$$

IQ and drinks per week contribute to GPA; height doesn't

Minimize the distance between the data and the line (error).



We can use these numbers to calculate the variance

$$SSE = \sum \left(Y_i - \hat{Y}_i
ight)^2 = \sum e_i^2$$

$$\mathsf{S}^2 = rac{\sum e_i^2}{N-2}$$

#### Test statistic

$$t = (\bar{x} - \mu_0) / (s / \sqrt{n})$$

#### where:

- x = the sample mean
- μ<sub>0</sub> = the hypothesized population mean
- s = the sample standard deviation
- n = the sample size

Deriving a beta weight (β) can be calculated by using linear algebra:

$$Y = X\hat{eta}$$
 
$$X'Y = (X'X)\hat{eta}$$
 
$$(X'X)^{-1}X'Y = \hat{eta}$$

$$\widehat{\operatorname{Var}}[\hat{eta}] = \hat{\sigma}^2 (X'X)^{-1}$$

t-statistics in fMRI are conceptually similar, but computed slightly differently:

$$t = \frac{c(X'X)^{-1}X'Y}{\sqrt{\hat{\sigma}^2 c(X'X)^{-1}c'}}$$

$$\hat{\sigma}^2 = \frac{e'e}{N-p}$$

where 
$$e = Y - X\hat{eta} = Y - \hat{Y}$$

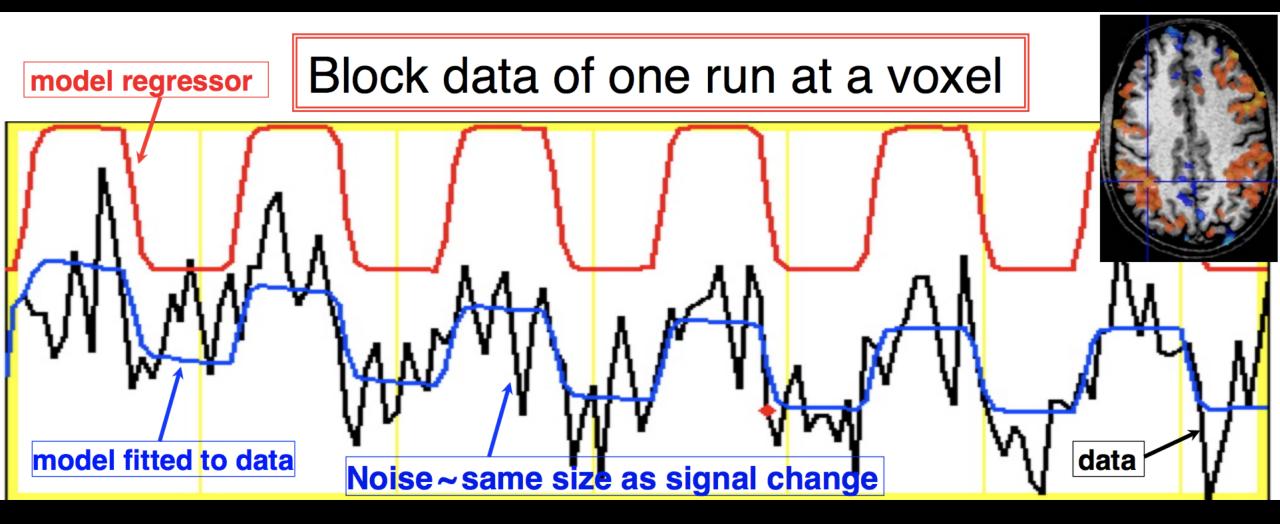
N = Number of time-points

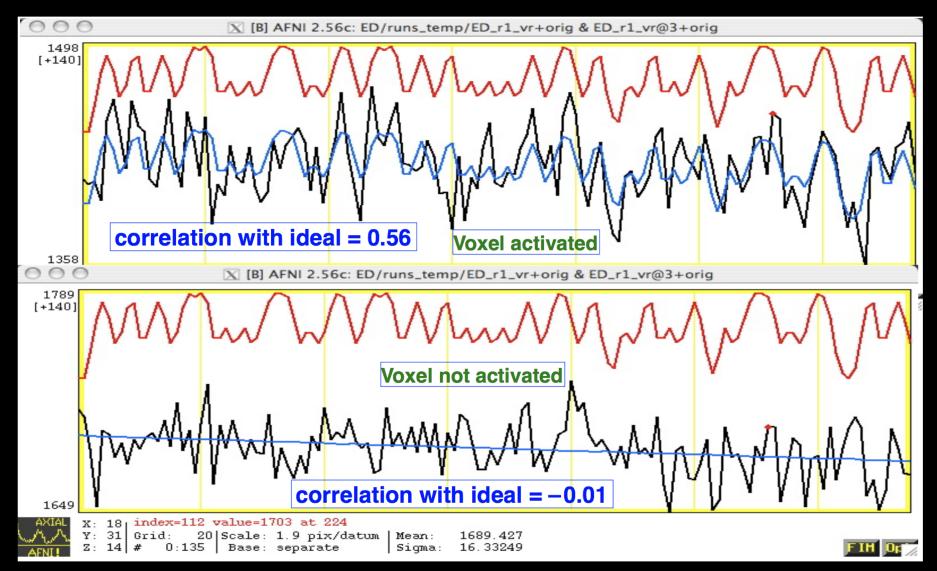
p = Number of regressors

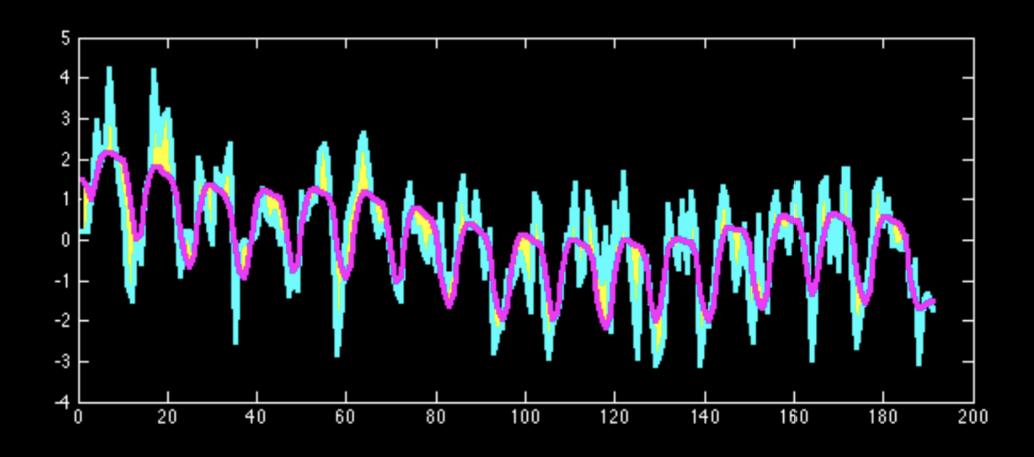
Note: t-statistics are calculated at the 1<sup>st</sup>-level, but usually aren't carried into the 2nd-level analysis

In other words: Magnitude is carried to the group-level, not variance

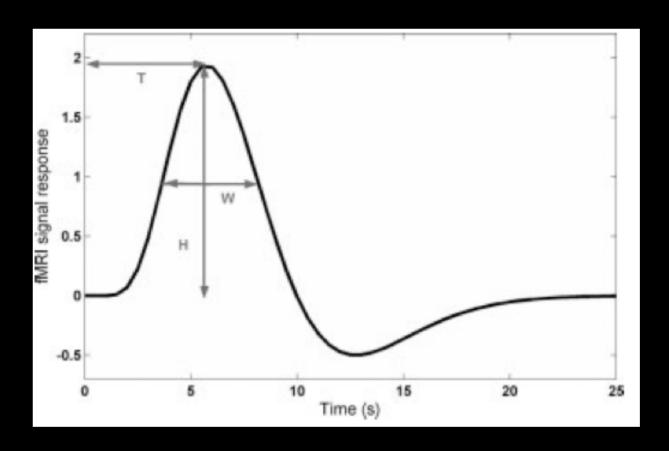
This can be done in other programs, e.g. AFNI's 3dMEMA





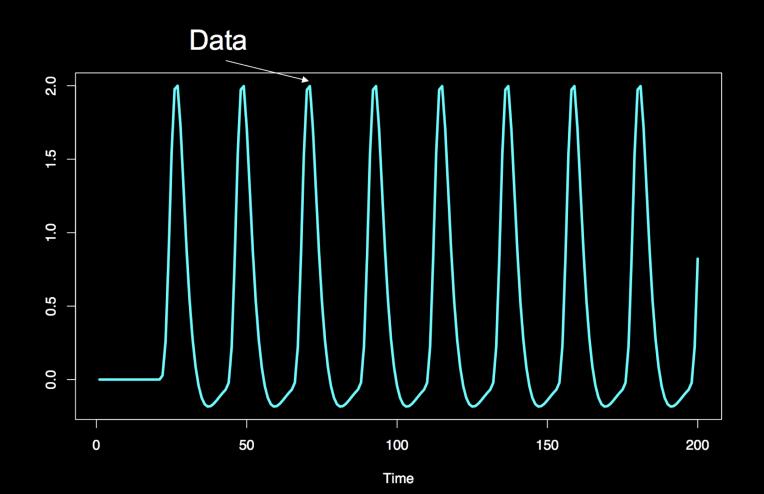


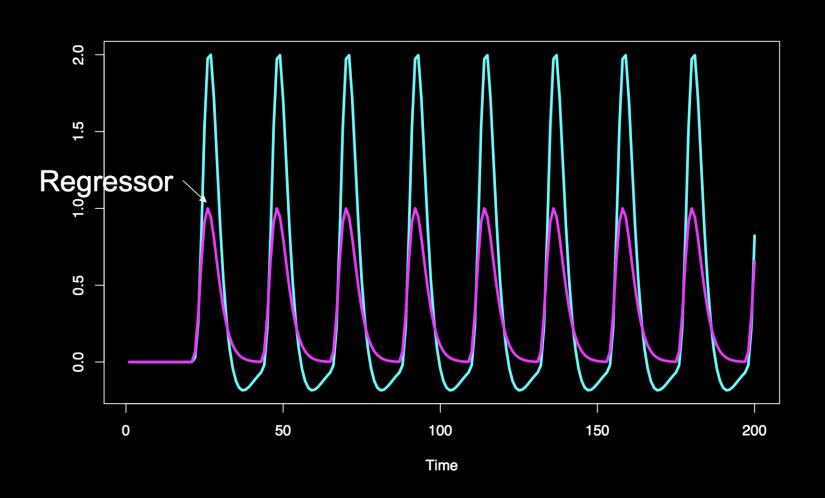
#### **Revisiting the HRF**

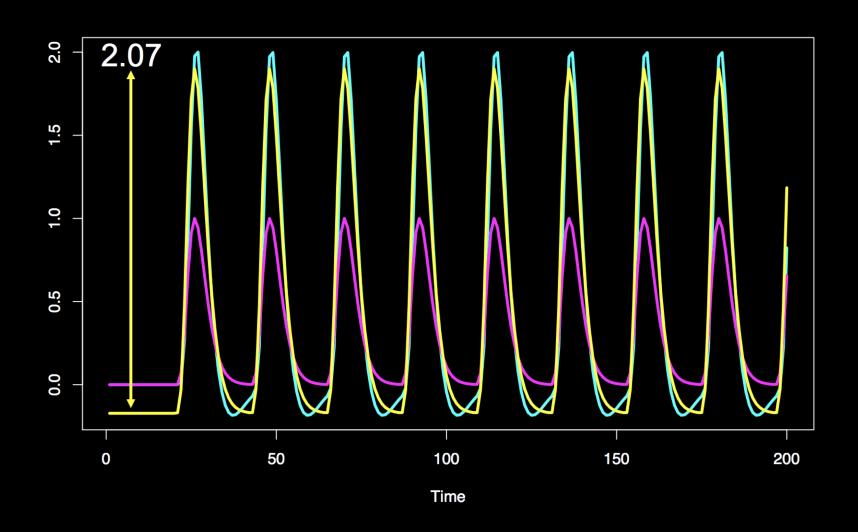


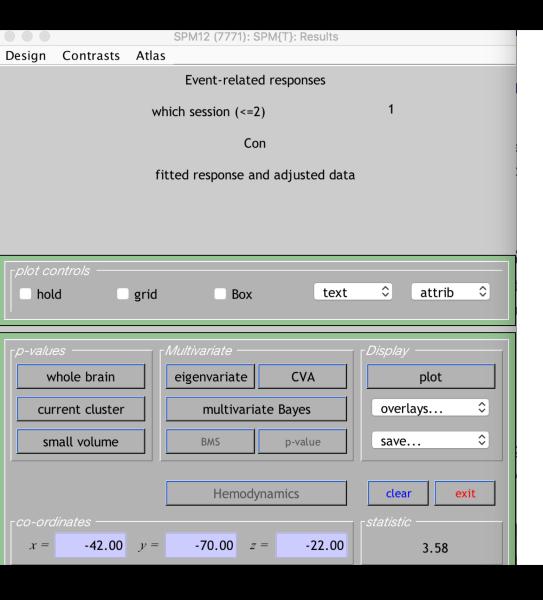
Canonical HRF: Width and delay are fixed, height is estimated as a beta

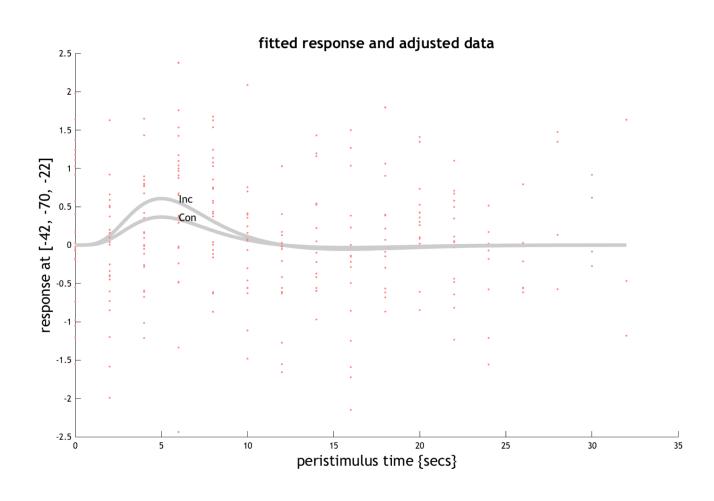
Why use a double-gamma (e.g., model the undershoot?)

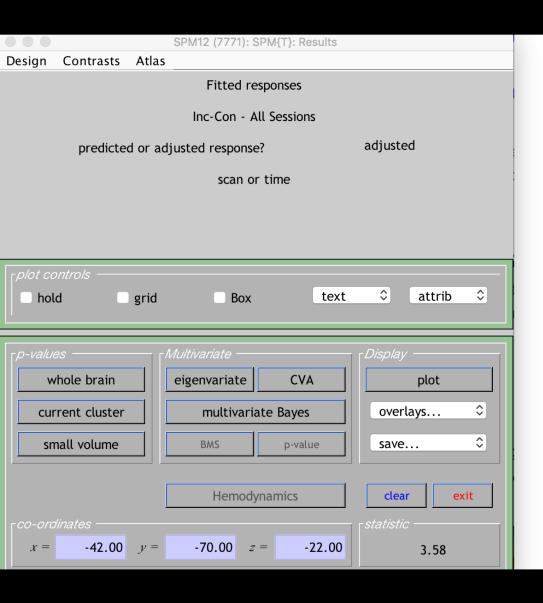


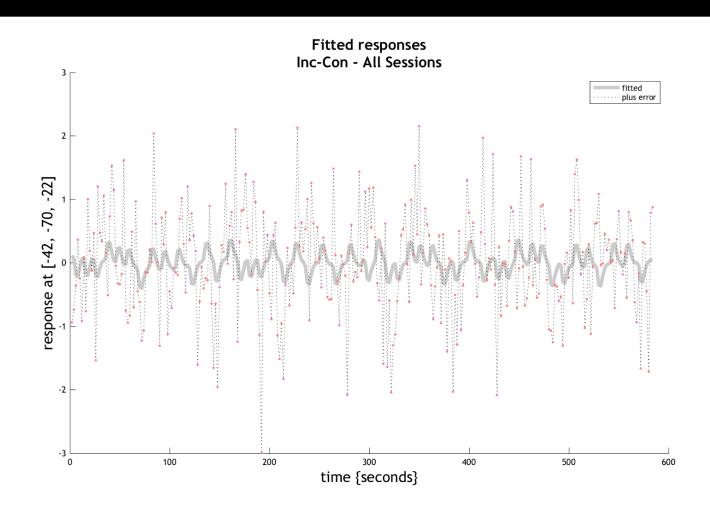


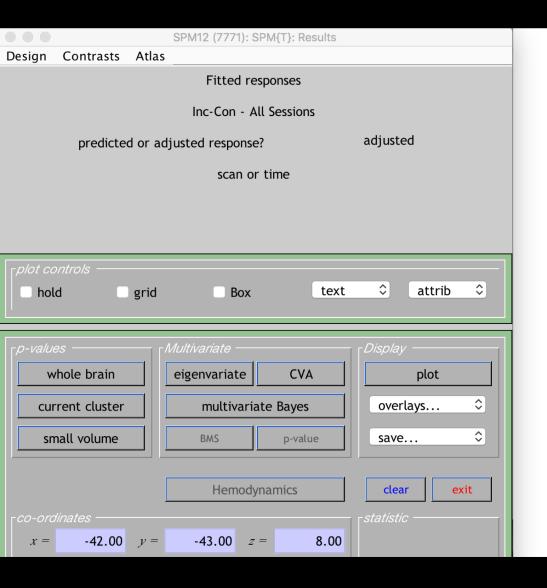


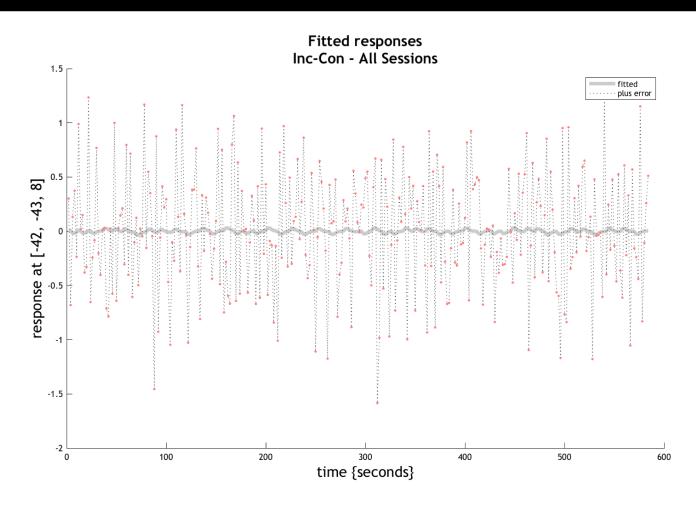


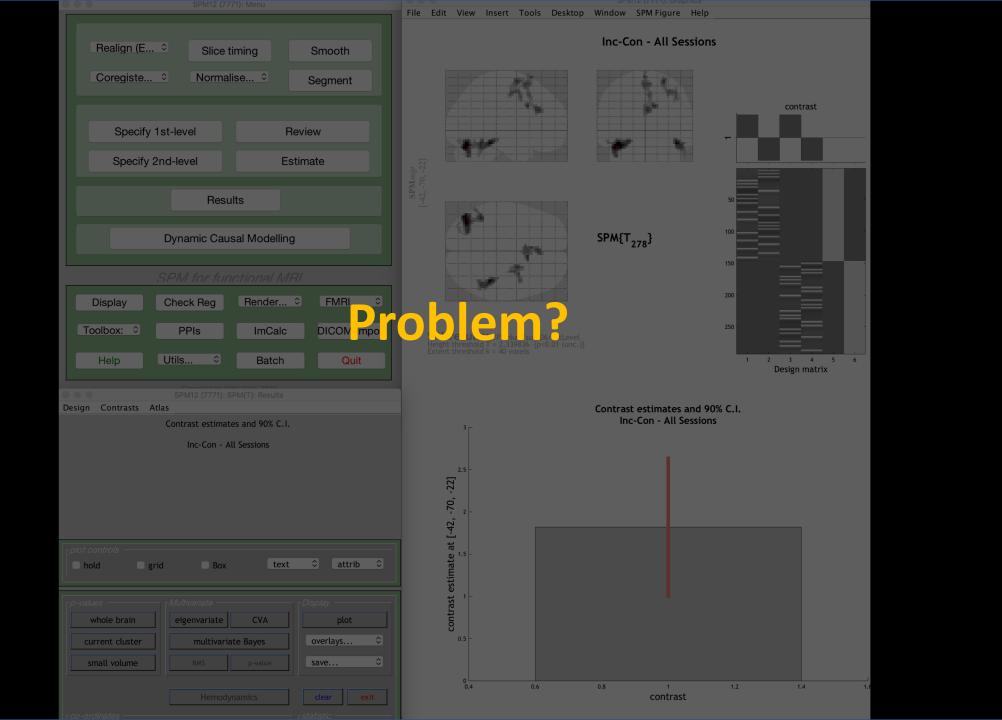












#### **Other options**

Grand mean scaling: Removes intersession variance, allows for combining data across subjects

Intensity normalization: Forces each volume to have the same mean (not recommended)

$$g_s = \frac{\sum_{n=1}^{N} g_{ns}}{N}$$

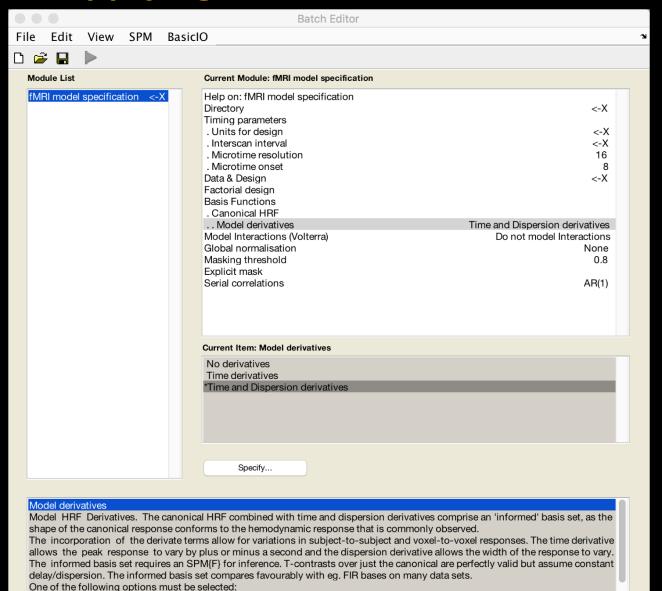
Session-specific grand mean scaling: Multiplies each volume in session s by 100/g<sub>s</sub>

### **Percent Signal Change**

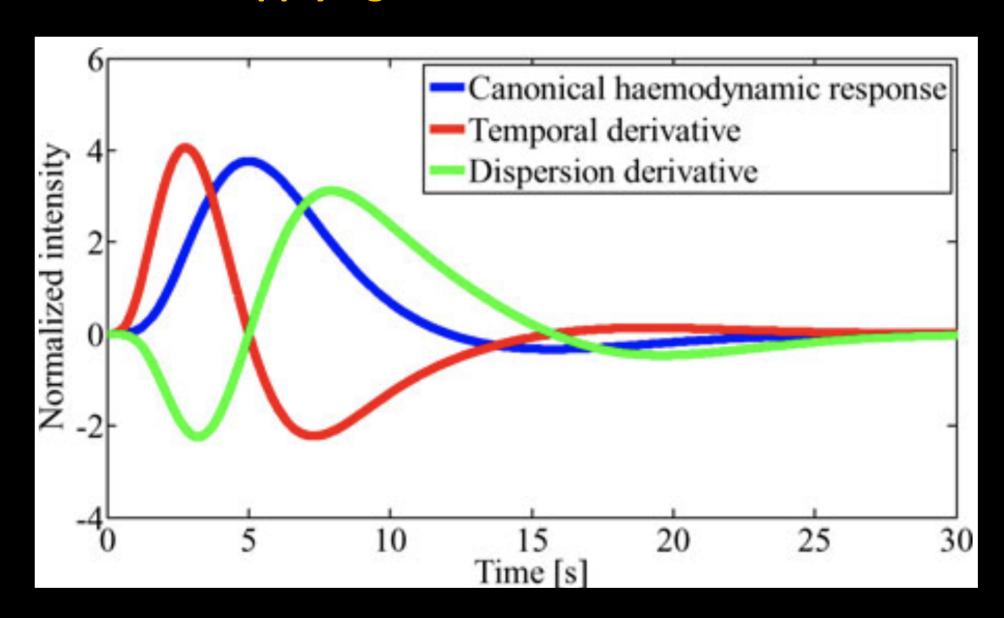
Some recommend reporting percent signal change instead of beta weights

More accurate reflection of effect size, more comparable between studies

ROI tool like Marsbar will scale by the overall mean of the voxels in the region



\* No derivatives

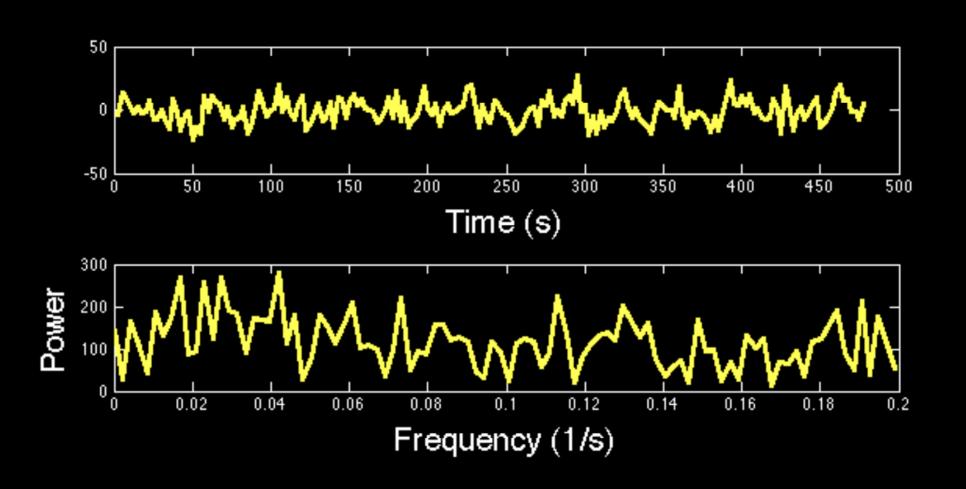


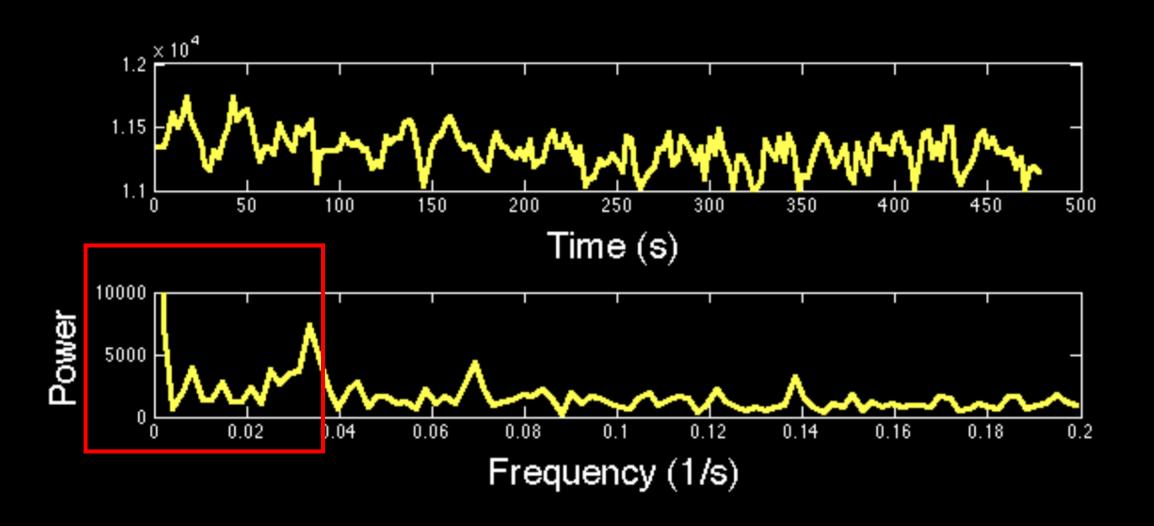
**Benefits of time derivative** 

No interpolation of raw data, may capture variability in BOLD response

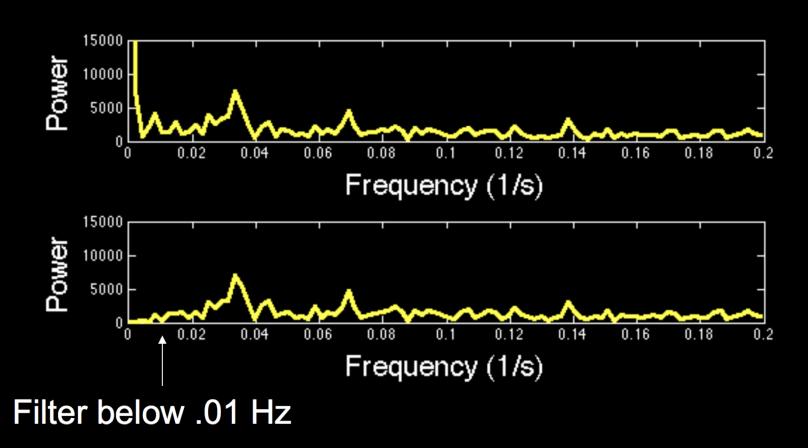
Cons: Requires an additional regressor in the model per condition

#### Other options: Highpass filtering and prewhitening



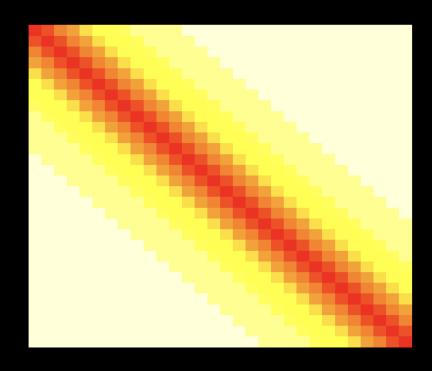


Highpass filter removes frequencies below a certain threshold



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

$$Cov(\epsilon) =$$



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

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

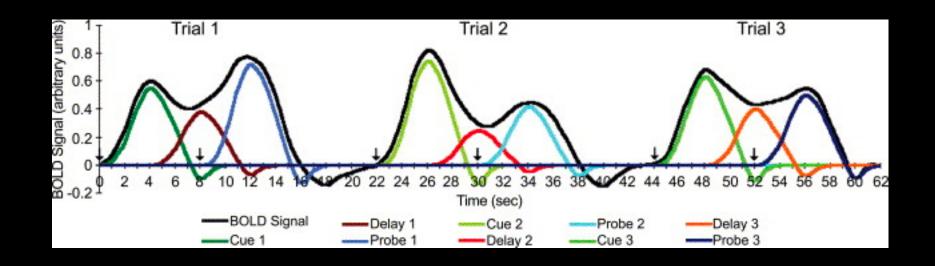
#### **Prewhitening**

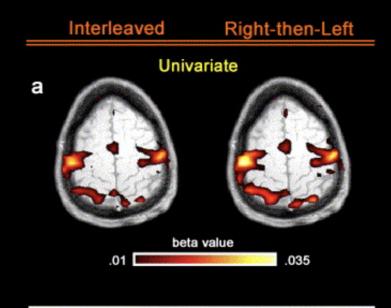
Gauss-Markov assumptions: Normally distributed errors, constant variance, and no temporal autocorrelation

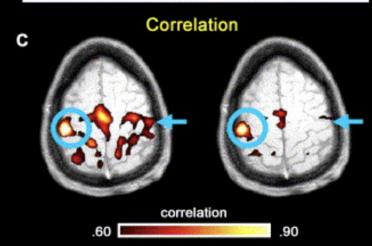
Are fMRI data temporally autocorrelated?

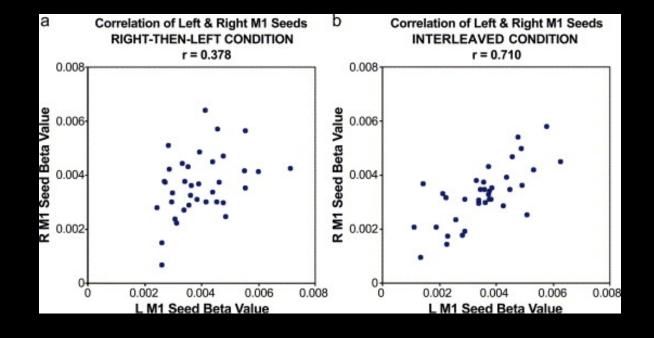
#### **Other options: Individual Modulation**

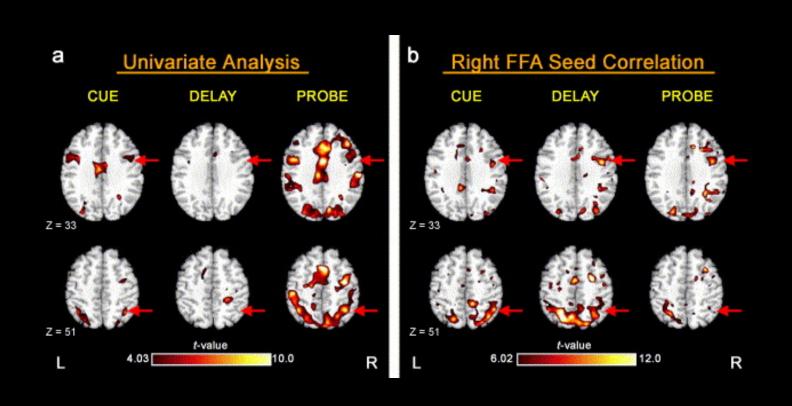
#### Useful for beta-series correlation, MVPA classification

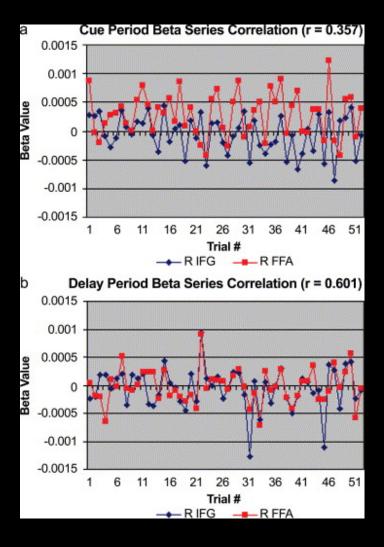










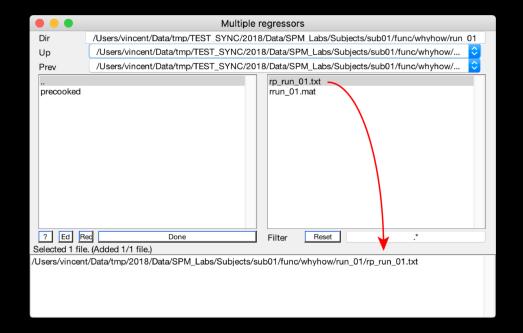


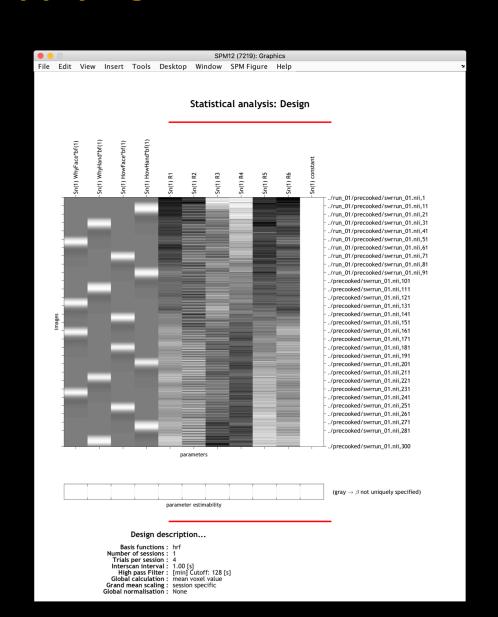
**Drawback: Very tedious to implement without scripting!** 

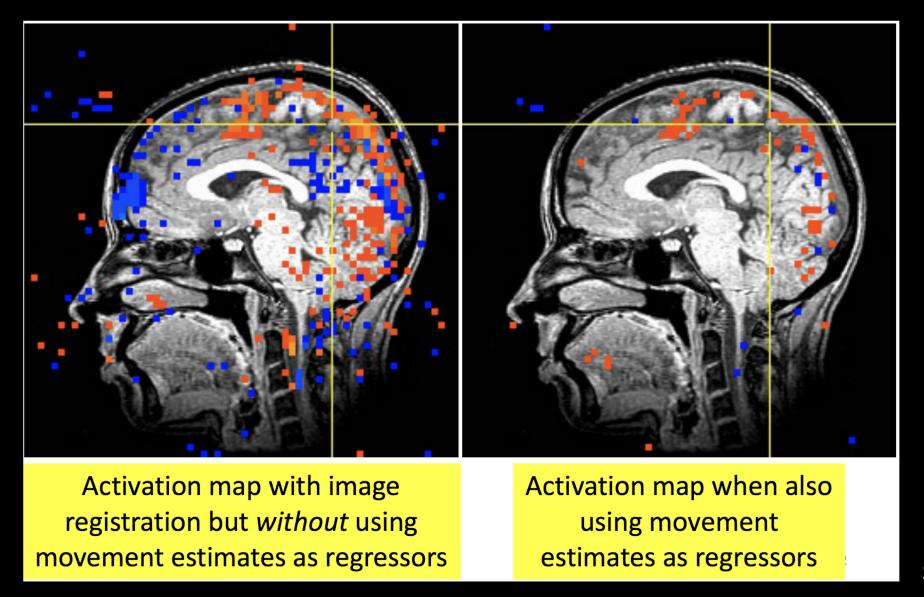
For AFNI users: Can use 'IM' basis function in 3dDeconvolve

#### What about nuisance regressors, such as motion?

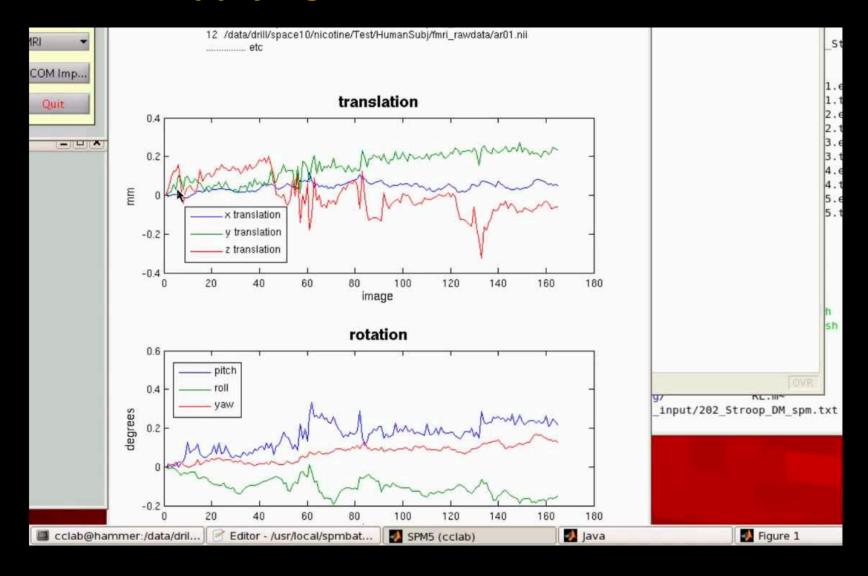








Source: AFNI



**Perennial Question: How much is too much?** 

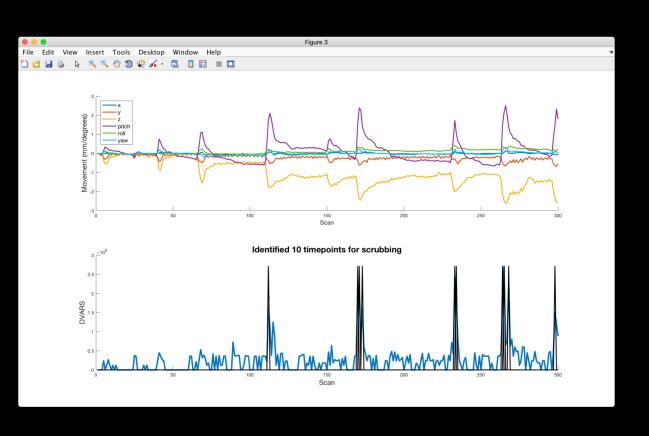
Guideline from days of yore: >1 voxel over entire run, >0.5 voxel between volumes

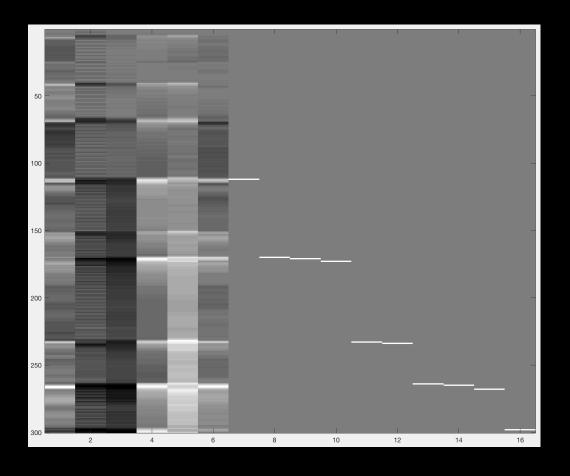
More important: Does motion correlate with your task?

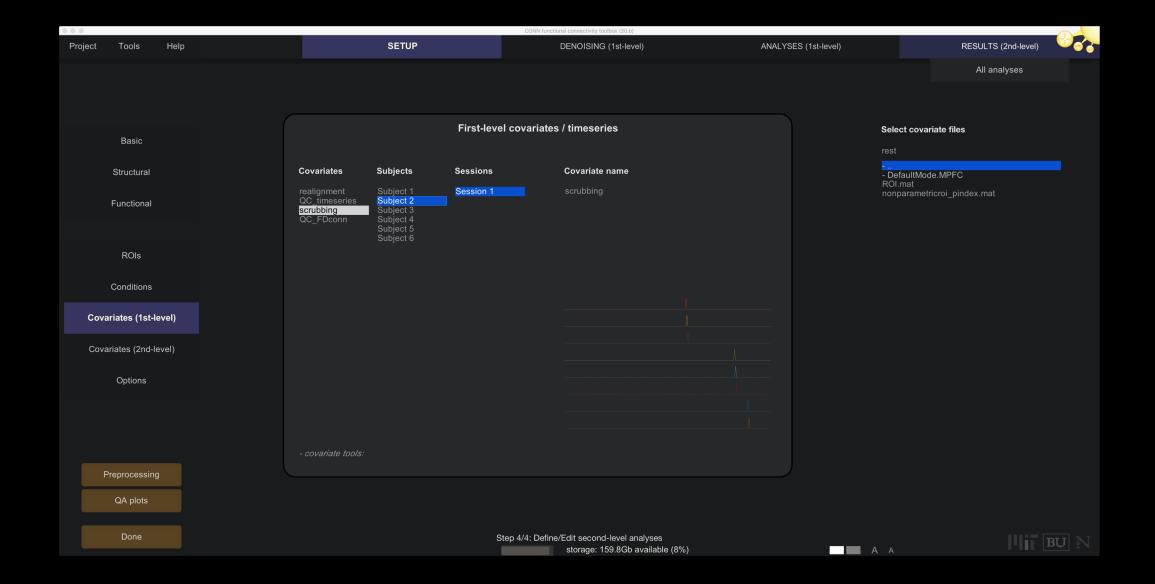
Other nuisance regressors: DVARS, Framewise Displacement (FD)

Derivative Variance (DVARS) measures abrupt global signal changes from volume to volume (Power et al., 2011)

Volumes that exceed a specified threshold are flagged for scrubbing: Inserting that volume as a regressor into the GLM







#### Before we begin the Demo: SPM Terms for Analysis

1<sup>st</sup>-Level Analysis: Individual subject (all runs within the subject)

2nd-Level Analysis: Group-Level Analysis (all subjects within the experiment)

A contrast is simply one condition's beta weight subtracted from another

e.g., A-B

General recommendations: Model everything that is related to the task, and don't model any baseline events (e.g., implicit baseline)

. Subject/Session		
Scans	300 files	
Conditions		
Condition		
Name	WhyFace	
Onsets	9169 117.2590563 152.5798844 225.1941691]	
Durations	9262 7.674989138 8.015399588 8.542317722]	
Time Modulation	No Time Modulation	
Parametric Modulations		
Orthogonalise modulations	Yes	

#### **Example: Pos/Neg/Neu images**



Onset time (s)	Duration (s)	Description
11	4	Negative
17	.5	Face
27.5	4	Neutral
33.5	.5	Face

**Example: Where is Pos activation greater than Neg activation?** 

Contrast weights for each side should sum to +1 and -1

	Pos IAPS	Neg IAPS	Neu IAPS	Face after Pos	Face after Neg	Face after Neu
PosIAPS > NegIAPS	1	-1	0	0	0	0

#### Where is Pos activation greater than Neu activation?

	Pos IAPS	Neg IAPS	Neu IAPS	Face after Pos	Face after Neg	Face after Neu
PosIAPS > NegIAPS	1	-1	0	0	0	0

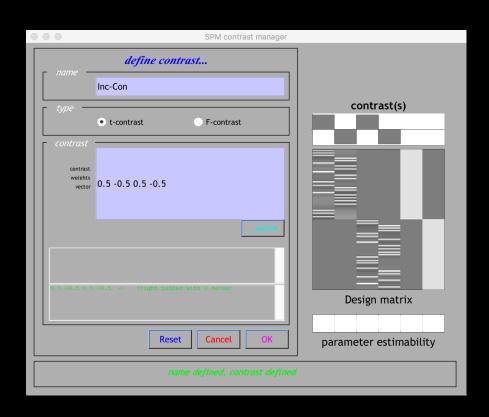
#### Where is both Pos and Neg activation greater than Neu activation?

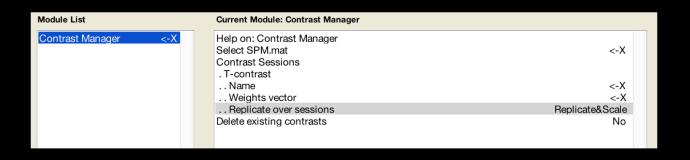
	Pos IAPS	Neg IAPS	Neu IAPS	Face after Pos	Face after Neg	Face after Neu
PosIAPS > NegIAPS	1	-1	0	0	0	0

#### Where is average face activation greater than baseline?

	Pos IAPS	Neg IAPS	Neu IAPS	Face after Pos	Face after Neg	Face after Neu
PosIAPS > NegIAPS	1	-1	0	0	0	0

Contrast weights need to be weighted for number of runs as well





#### **Module List**

Named File Selector	
Realign: Estimate & Reslice	DEP
Slice Timing	DEP
Coregister: Estimate & Reslice	DEP
Segment	DEP
Normalise: Write	DEP
Smooth	DEP
File Set Split	DEP
fMRI model specification	DEP
Model estimation	DEP
Contrast Manager	DEP

#### **Current Module: Contrast Manager**

Help on: Contrast Manager	
Select SPM.mat	DEP Model estimation: SPM.mat File
Contrast Sessions	
. T-contrast	
Name	Inc-Con
Weights vector	[1 -1]
Replicate over sessions	Replicate&Scale
. T-contrast	
Name	Con-Inc
Weights vector	[-1 1]
Replicate over sessions	Replicate&Scale
. T-contrast	
Name	Inc
Weights vector	[1 0]
Replicate over sessions	Replicate&Scale
. T-contrast	
Name	Con
Weights vector	[0 1]
Replicate over sessions	Replicate&Scale
Delete existing contrasts	No

# 1<sup>st</sup>-level setup: Demonstration

# Other Experimental Modeling Options

**Parametric Modulation** 

Finite Impulse Response (FIR)

Why do these types of analyses?

### **Parametric Modulation**

**Uses Auxiliary Behavioral Information (ABI)** 

Continuous (or several finely graded) ABI levels

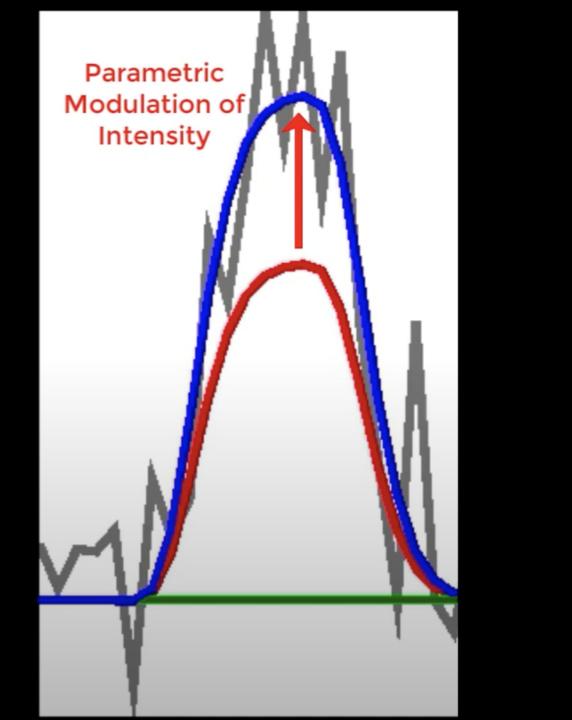
Parametric modulators are estimated in addition to the regressor they modulate

### **Parametric Modulation**

**Example: Light intensity** 

Regressor for a "Light" trial, and also a regressor for the intensity of the light





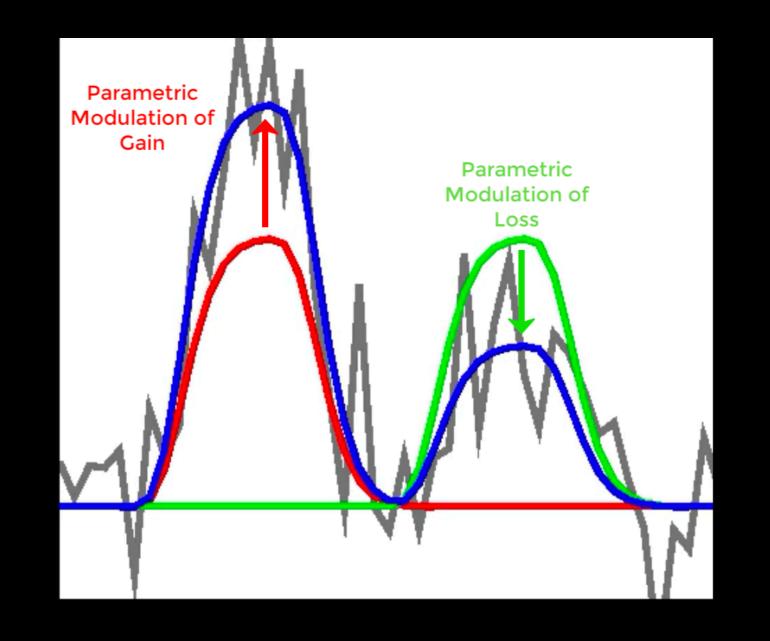
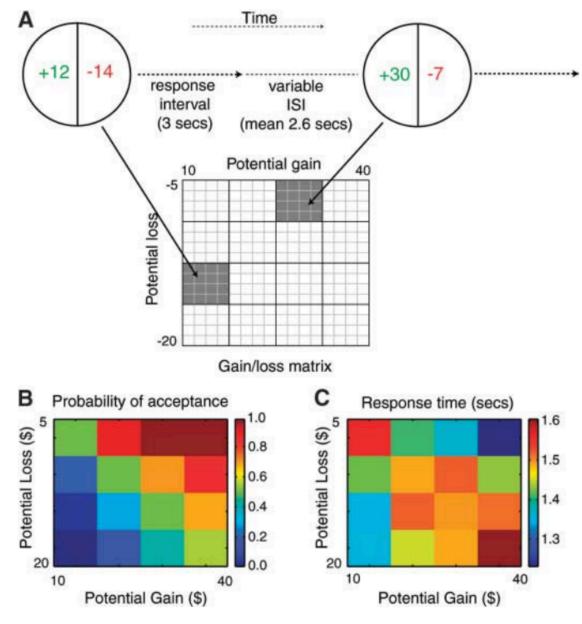


Fig. 1. (A) An illustration of the event-related task design. During each trial, the participant was presented for 3 s with a display showing the size of the potential gain (in green) and loss (in red). After the accept or reject response, a variable interval was presented to allow for optimal deconvolution of fMRI responses to each trial (27). Gambles were not resolved during scanning. The values of gain loss for each trial were sampled from the gain/loss matrix, as shown here for two example gambles; a gamble from each cell in this  $16 \times 16$ matrix was presented during scanning, but the data were collapsed into a 4 × 4 matrix for analysis. All combinations of gains and losses were presented. ISI,



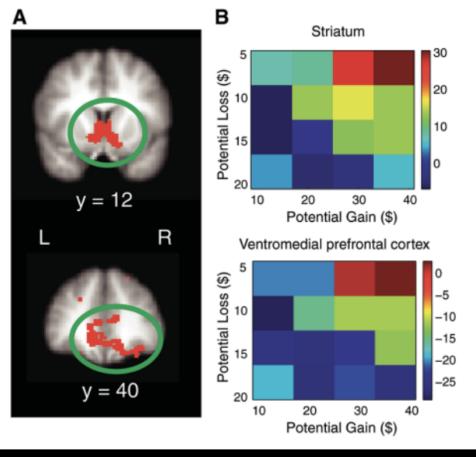
interstimulus interval. (B) Color-coded heatmap of probability of gamble acceptance at each level of gain/loss (red indicates high willingness to accept the gamble, and blue indicates low willingness to accept the gamble). (C) Color-coded heatmap of response times (red indicates slower response times, and blue indicates faster response times).

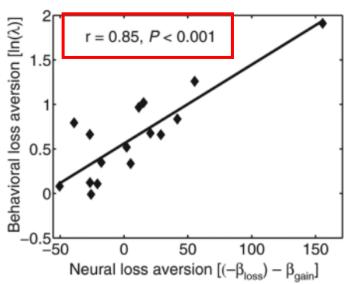
tion (22).

Examination of regions of interest in the striatum and VMPFC from the gain/loss conjunction analysis (Fig. 3) revealed that these

sitivity to losses versus gains) is highly correlated across risky and riskless contexts (23). Therefore, we surmise that a similar mechanism may contribute to other manifestations of loss aversion.

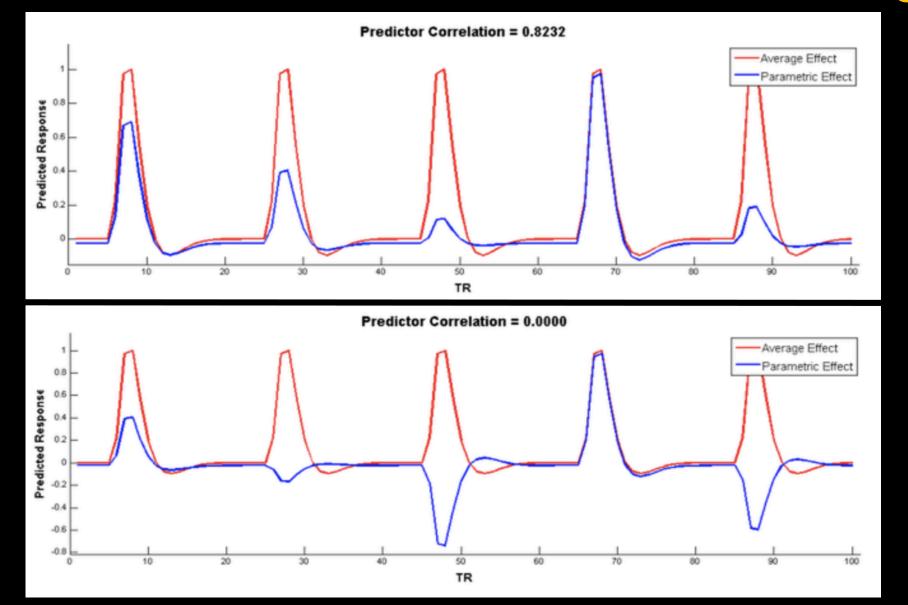
Fig. 3. Conjunction analysis results. (A) Map showing regions with conjointly significant positive gain response and negative loss response (P < 0.05, whole-brain corrected, in each individual map) (see also table S1). Red pixels indicate regions showing significant conjunction; green circles highlight clusters included in the respective heatmaps to the right. L, left; R, right. (B) Heatmaps were created by averaging parameter estimates versus baseline within each cluster in the conjunction map for each of the 16 cells (of 16 gambles each) in the gain/loss matrix; color coding reflects strength of neural response for each condition, such that dark red represents the strongest activation and dark blue represents the strongest deactivation.





**Fig. 4.** Scatterplot of correspondence between neural loss aversion and behavioral loss aversion in ventral striatum [Montreal Neurological Institute coordinates (x, y, z): 3.6, 6.3, 3.9; center of gravity in millimeters]. Regression line and P value were computed with the use of robust regression by iteratively reweighted least squares to prevent the influence of outliers; however, this regression also remained highly significant (P = 0.004) when the extreme data point (top right-hand corner) was removed from the analysis.  $\beta_{loss}$  and  $\beta_{gain}$  are the unstandardized regression coefficients for the loss and gain variables, respectively.

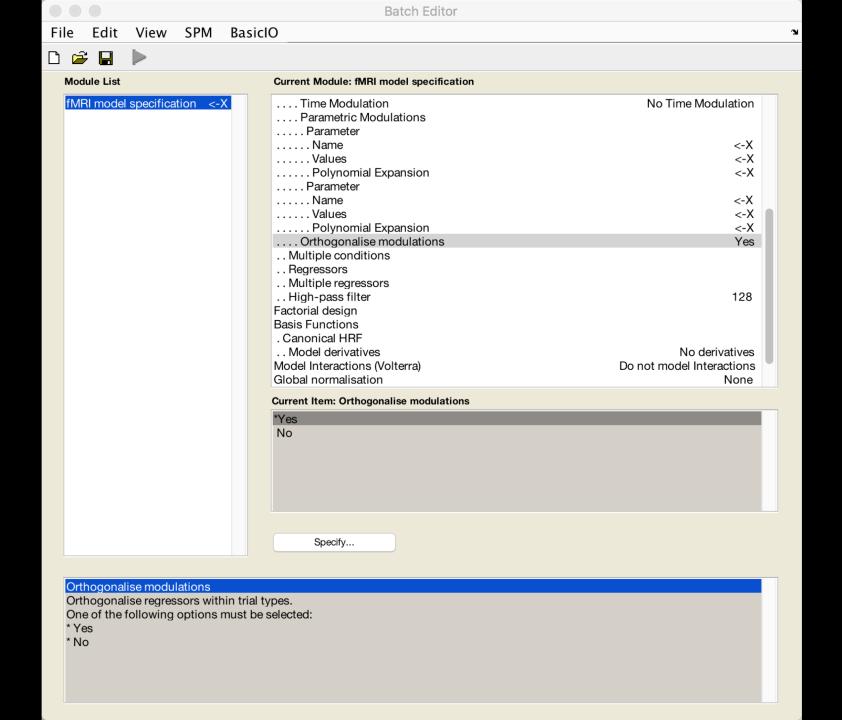
# Parametric Modulation: Mean Centering



### **Parametric Modulation: Other Considerations**

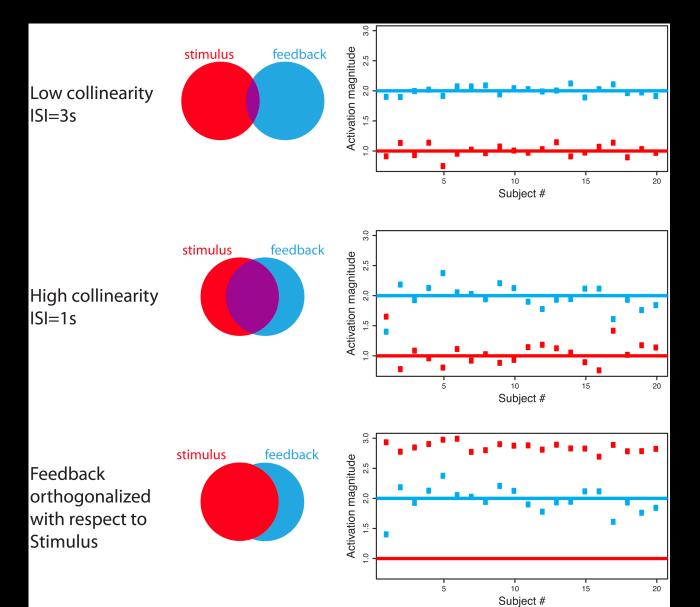
Orthogonalizing the regressors as part of the design

Orthogonalizing as part of the GLM



Should be set

# Why?



# Why?

Regressors without orthogonalization

Unmodulated RT Intensity

Correct orthogonalization for interpretable Unmodulated



RT wrt Unmod Intensity wrt Unmod

SPM RT first Intensity second



RT wrt Unmod Intensity wrt Unmod and RT

SPM Intensity first RT second



RT wrt Unmod and Intensity Intensity wrt Unmod

# **Demonstration of Parametric Modeling Setup**

# Other Experimental Modeling Options

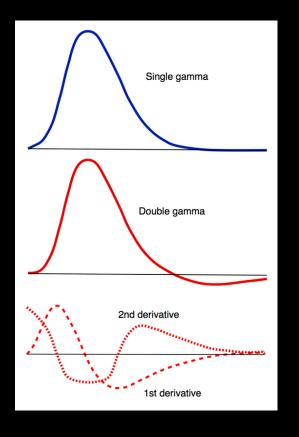
**Parametric Modulation** 

Finite Impulse Response (FIR)

## Other Experimental Modeling Options

**Parametric Modulation** 

Basis functions such as the HRF assume a stereotypical shape



Source: mri-q.com

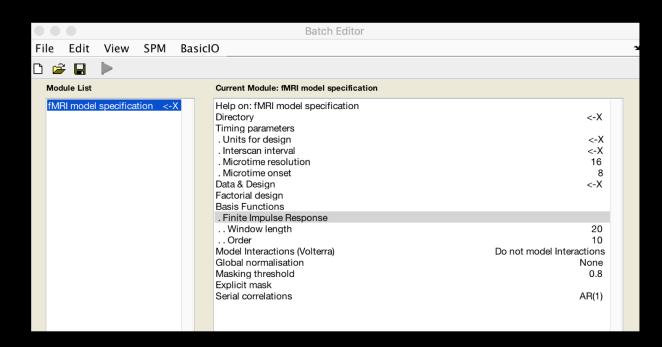
But what if we don't want to assume a shape?

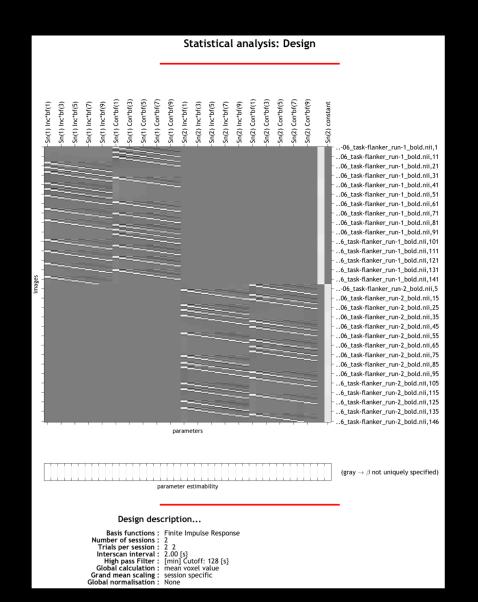
Example: You want to see whether the peak for condition A is later than the peak for condition B

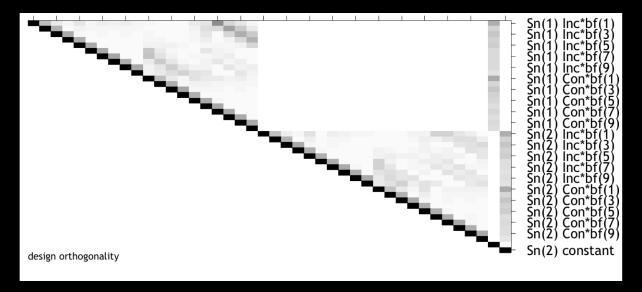
Another example: You think the overall shape of the BOLD response is different between patients and controls, even though the amplitude is the same

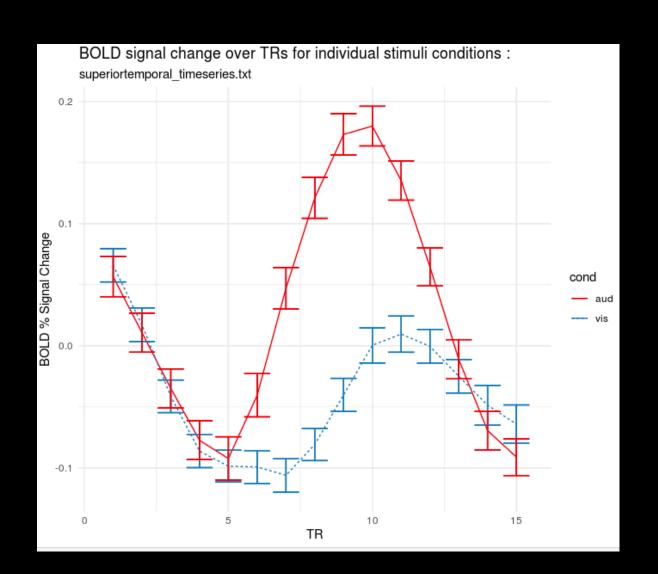
You specify the window length and number of timepoints

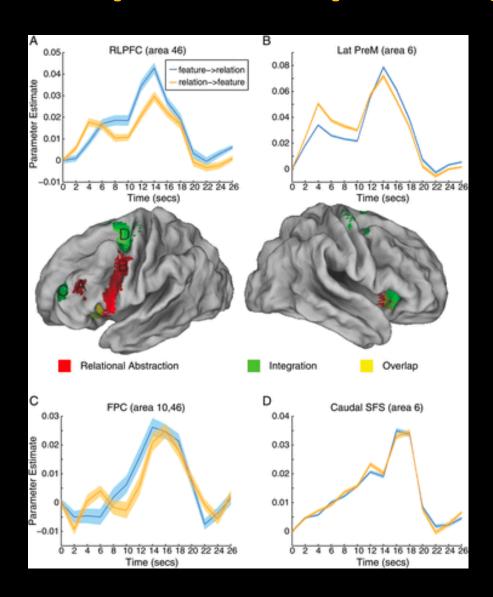
#### e.g.: 20s window, 10 timepoints











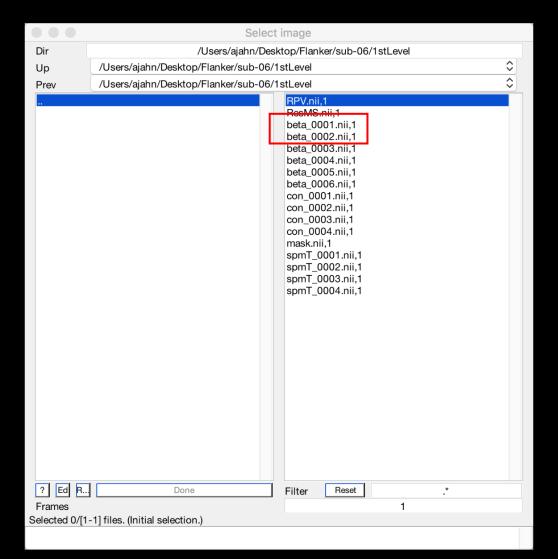
# **Demonstration of FIR Modeling Setup**

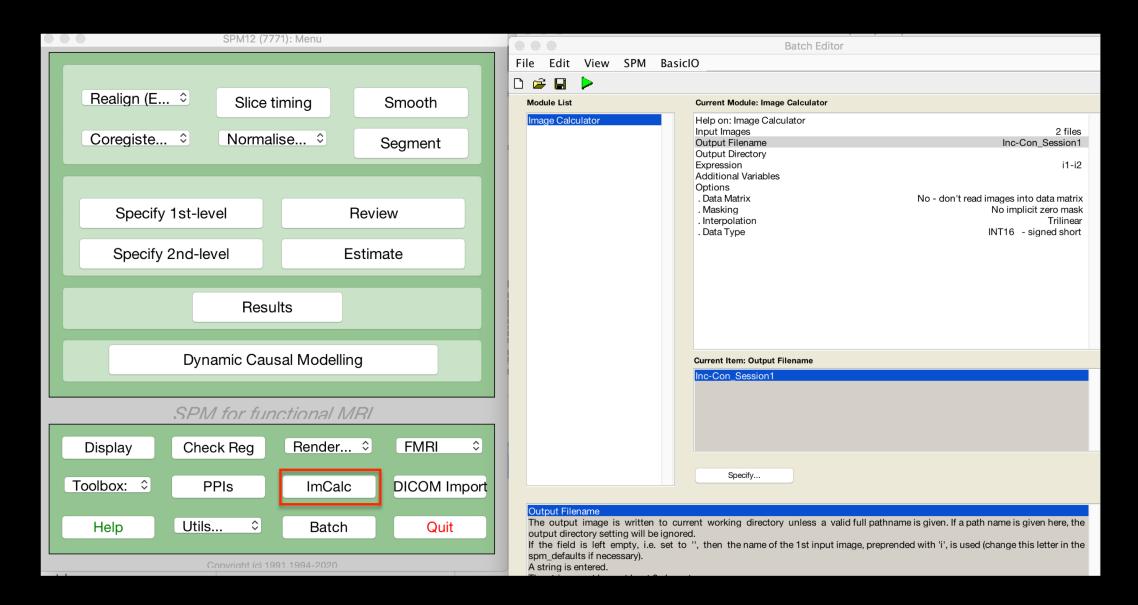
One of the most versatile tools is the image calculator

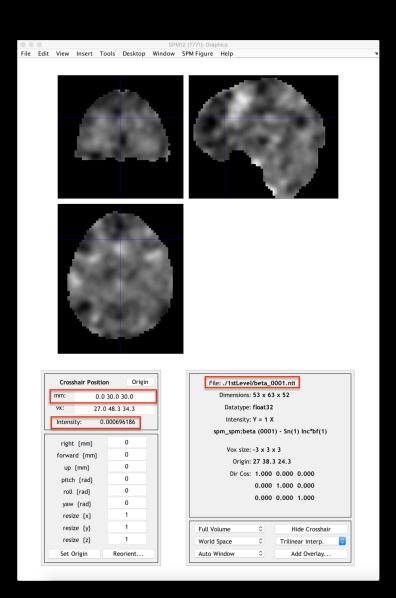
Every package has one (AFNI, FSL, MRtrix, etc.)

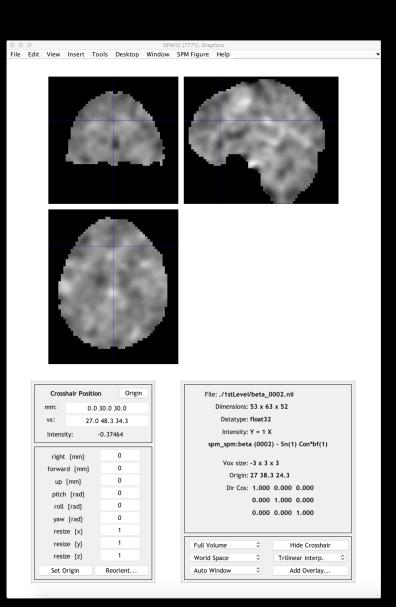
Simple to do basic arithmetic on a 3D image

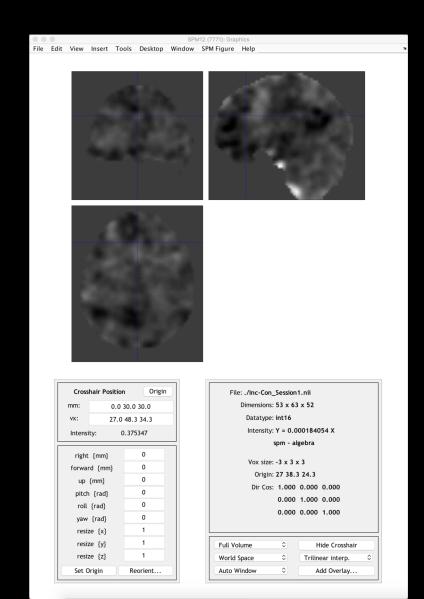








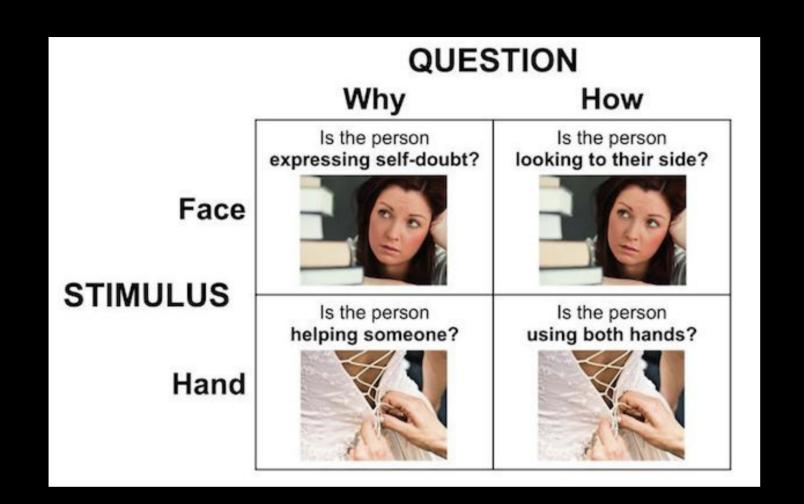




## **Demonstration**

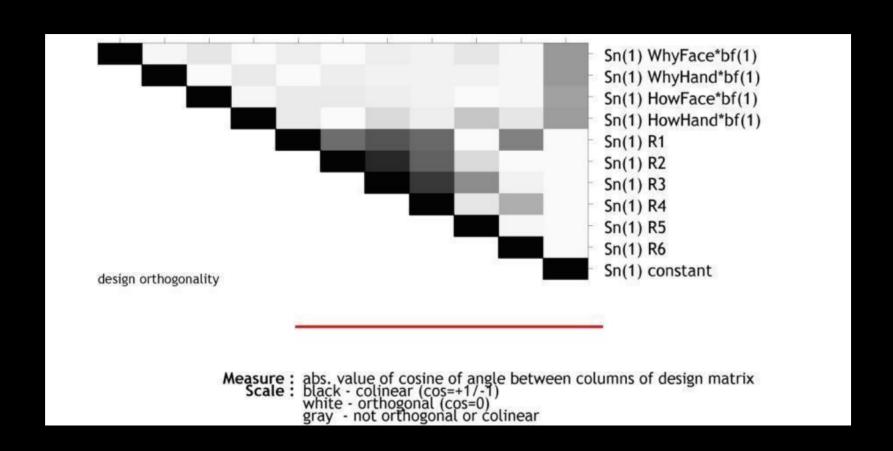
### **Preview of Today's Lab**

#### Dataset collected by Emily Falk; 2x2 factorial design



#### **Preview of Today's Lab**

#### **Block design**



### **Preview of Today's Lab**

ourrent module. Imili model specification

Name Onsets Durations Time Modulation Parametric Modulations	HowFace 284 135.0593544 171.3800147 243.0883199] 4532 10.7859291 8.894711134 9.210554915] No Time Modulation
Orthogonalise modulations	Yes
ConditionNameOnsetsDurationsTime Modulation	HowHand 6296 80.6916593 189.4403629 264.5608179] 313 10.45648544 9.137848595 10.19211621] No Time Modulation
Parametric Modulations Orthogonalise modulations Multiple conditions Regressors	Yes
Multiple regressors High-pass filter	eLab/sub05/func/whyhow/run_01/rp_run_01.txt 128
Factorial design Basis Functions . Canonical HRF Model derivatives Model Interactions (Volterra) Global normalisation Masking threshold	No derivatives Do not model Interactions None 0.8
Explicit mask Serial correlations	AR(1)
Current Item: Directory	

## **Questions?**