fMRI Course, Day 8:
Design Optimization and 2nd-Level Analysis

August 7th, 2023

Overview of PSY808 Course

Questions from previous lecture?

How did the lab go?

Did the contrasts make sense?

What was the most confusing part of the lab?

Questions:

1. How to increase the size of the t-statistic?
2. How to deal with low-frequency noise?
3. Should we lowpass filter fMRI data?

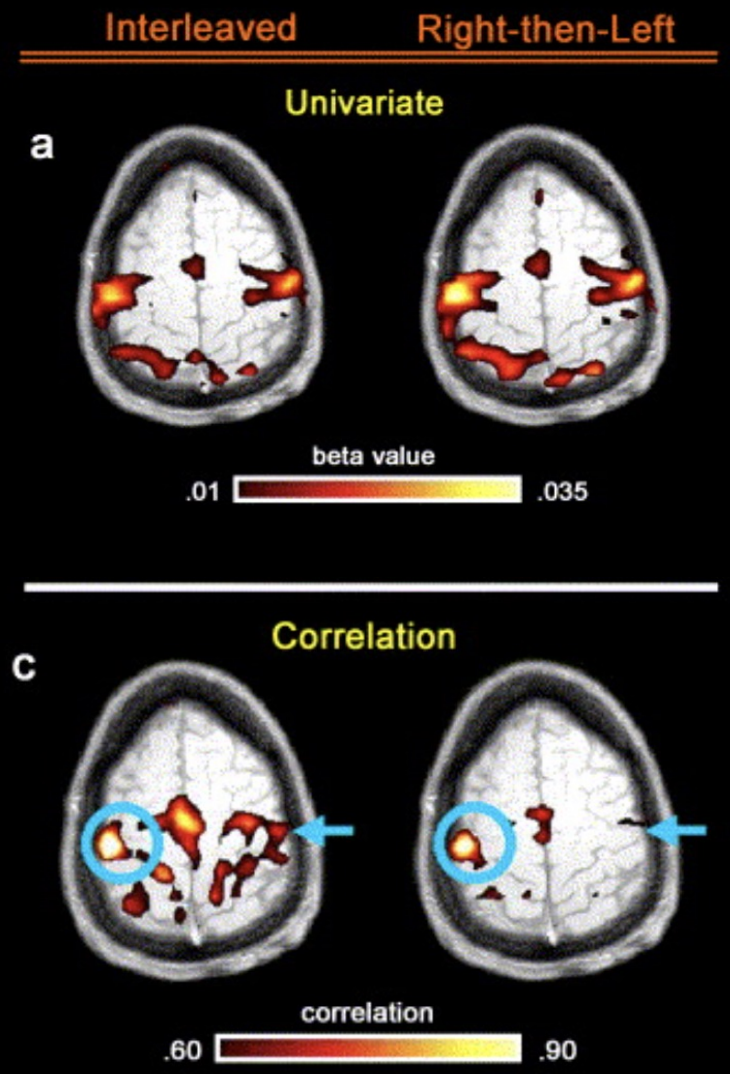
Slides from Yesterday

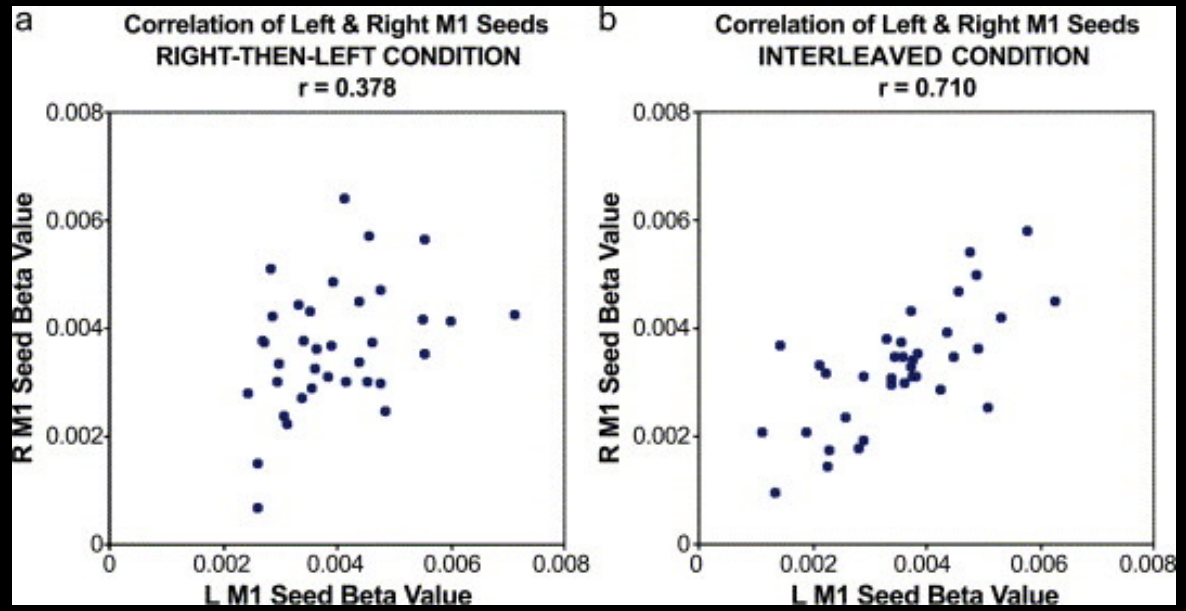
Applying the GLM to fMRI Data

Other options: Individual Modulation

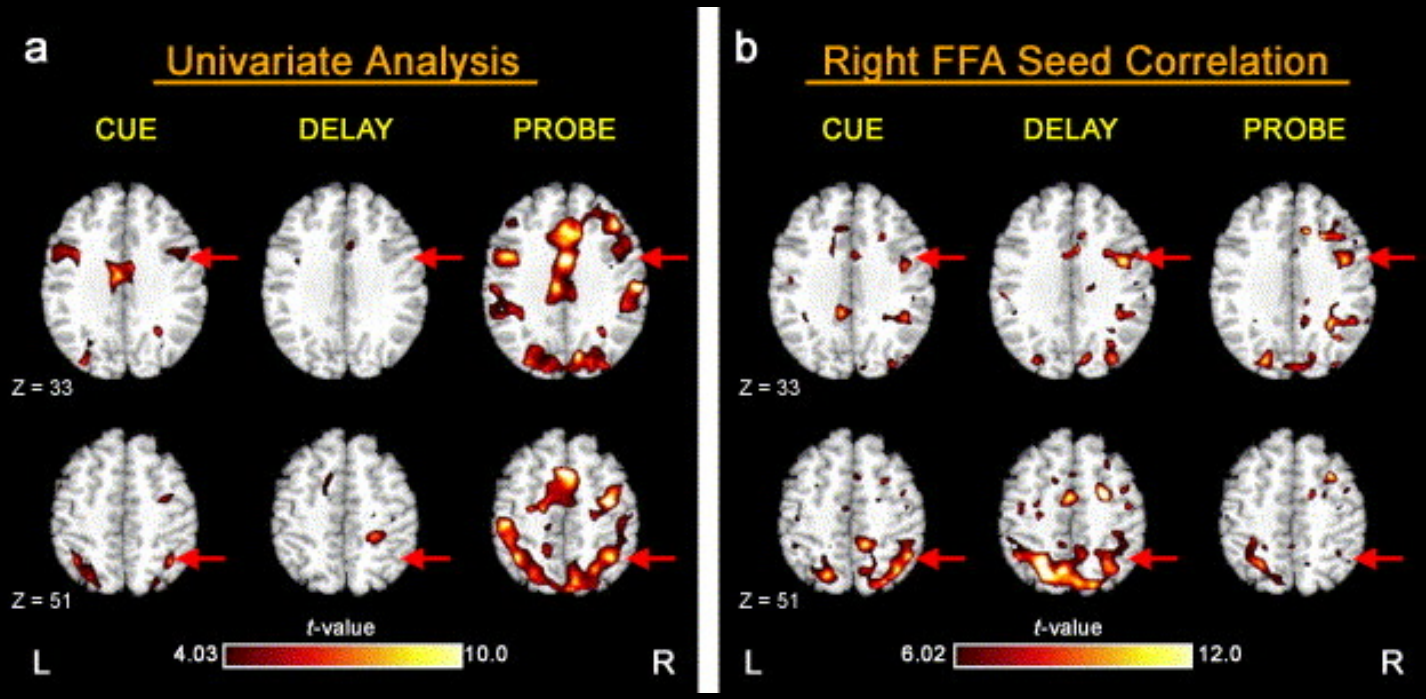
Useful for beta-series correlation, MVPA classification

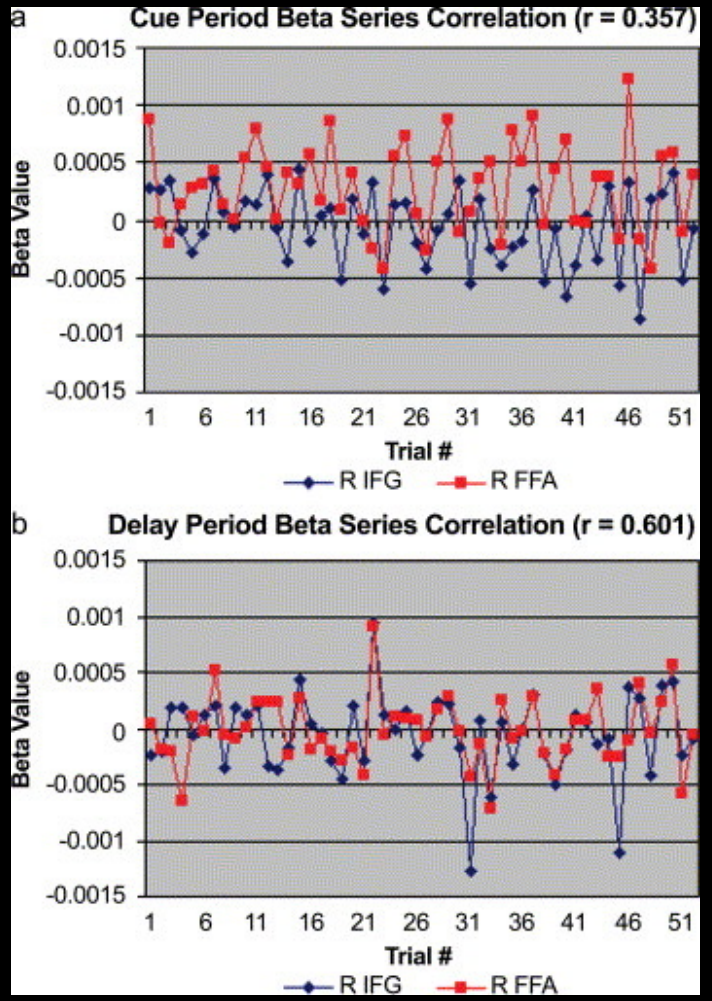
Applying the GLM to fMRI Data





Applying the GLM to fMRI Data





Applying the GLM to fMRI Data

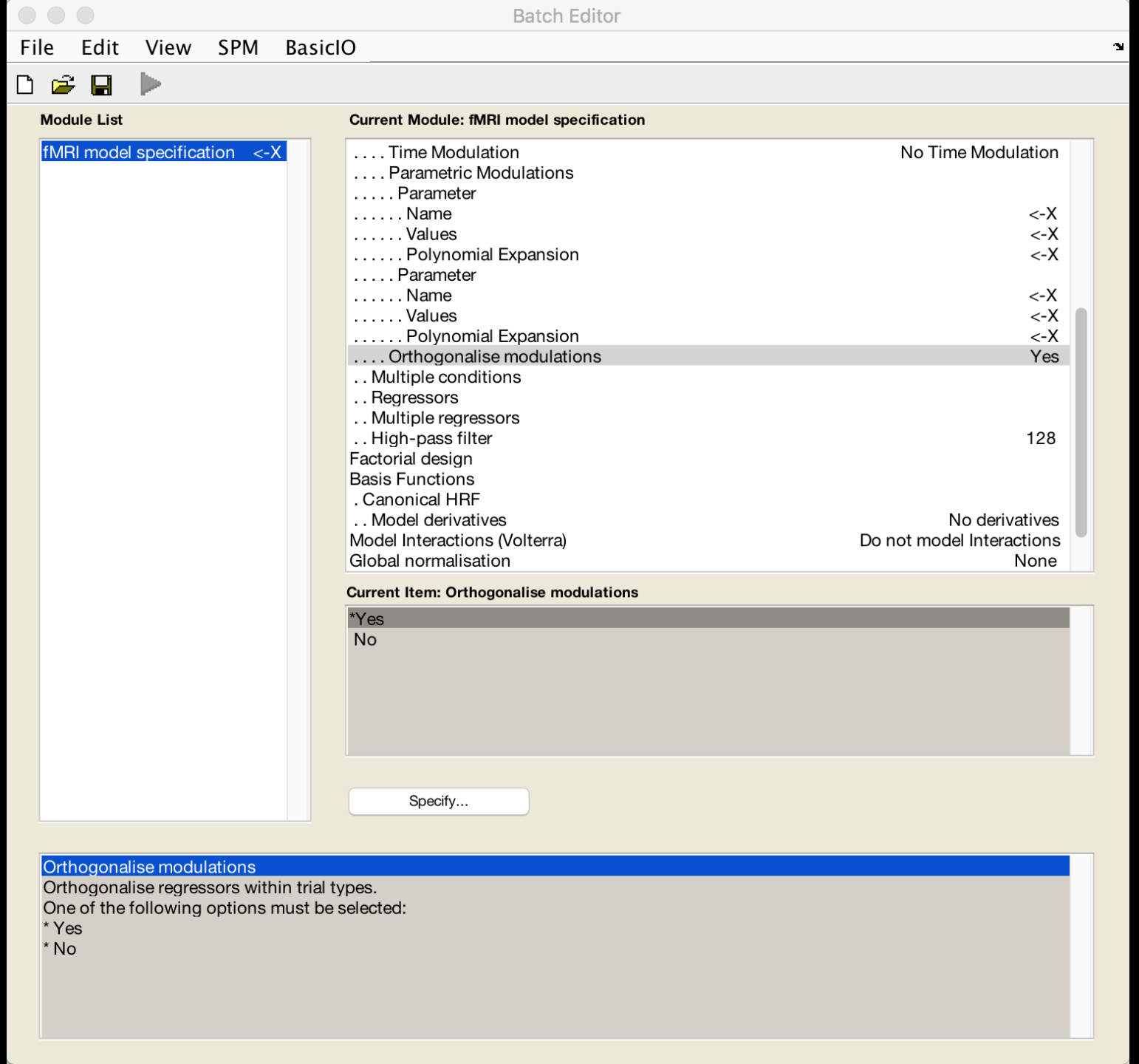
Drawback: Very tedious to implement without scripting!

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

Parametric Modulation: Other Considerations

Orthogonalizing the regressors as part of the design

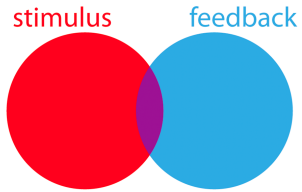
Orthogonalizing as part of the GLM

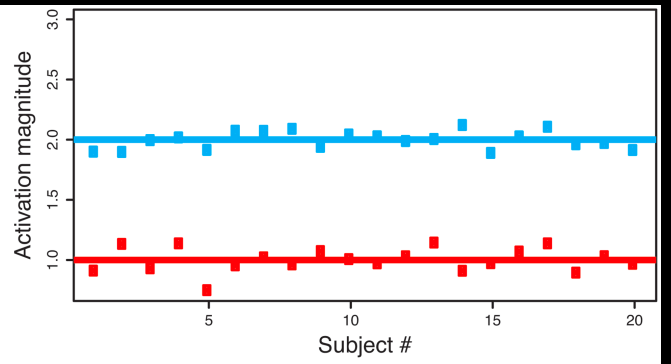


Should be set to “No”

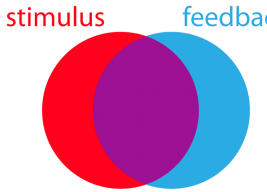
Why?

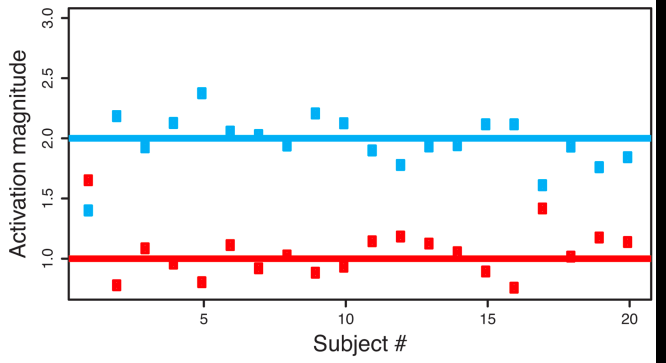
Low collinearity
ISI=3s



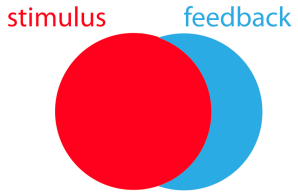


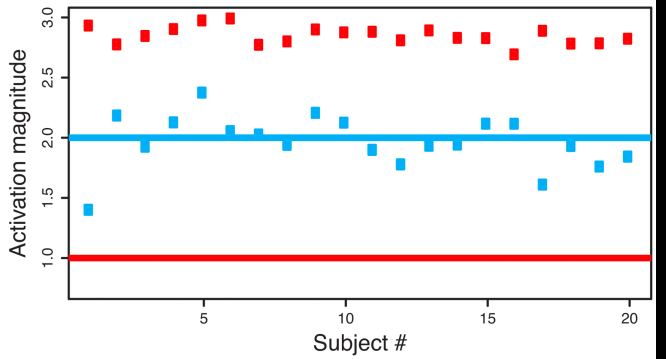
High collinearity
ISI=1s





Feedback orthogonalized with respect to Stimulus

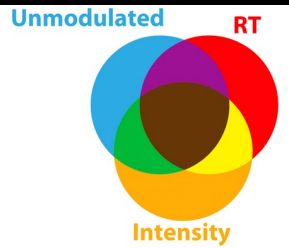




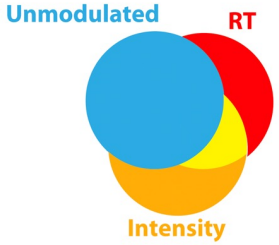
Mumford et al., 2015

Why?

Regressors without orthogonalization

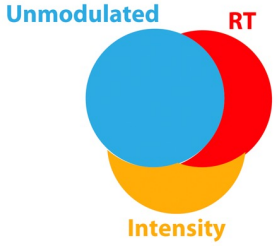


Correct orthogonalization for interpretable Unmodulated



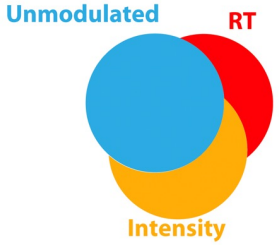
RT wrt Unmod
Intensity wrt Unmod

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)

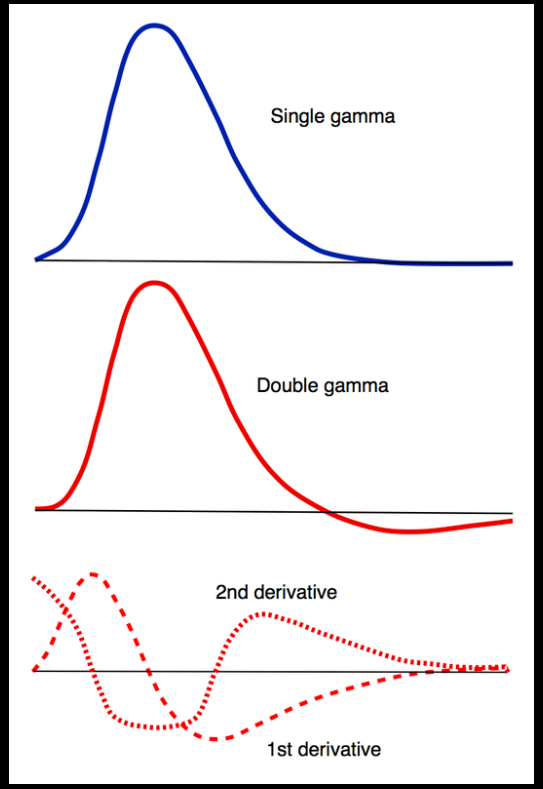
Other Experimental Modeling Options

Parametric Modulation

Finite Impulse Response (FIR)

Finite Impulse Response (FIR)

Basis functions such as the HRF assume a stereotypical shape



Source: mri-q.com

Finite Impulse Response (FIR)

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

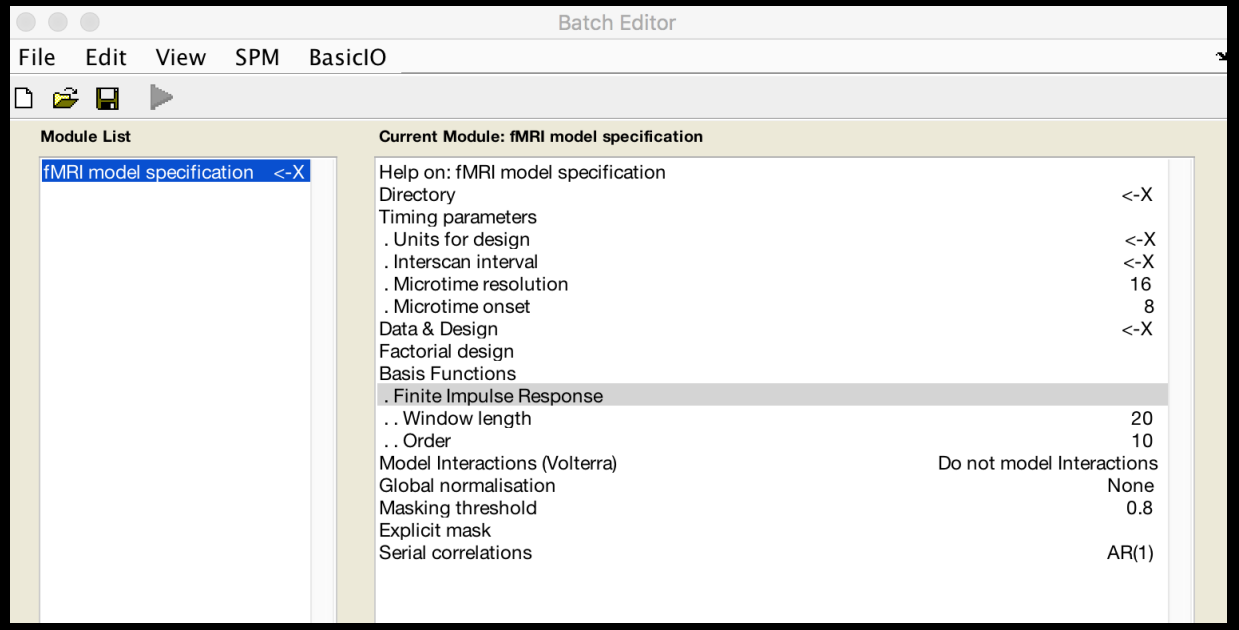
Example: You want to see whether the peak for condition A is later than the peak for condition B

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

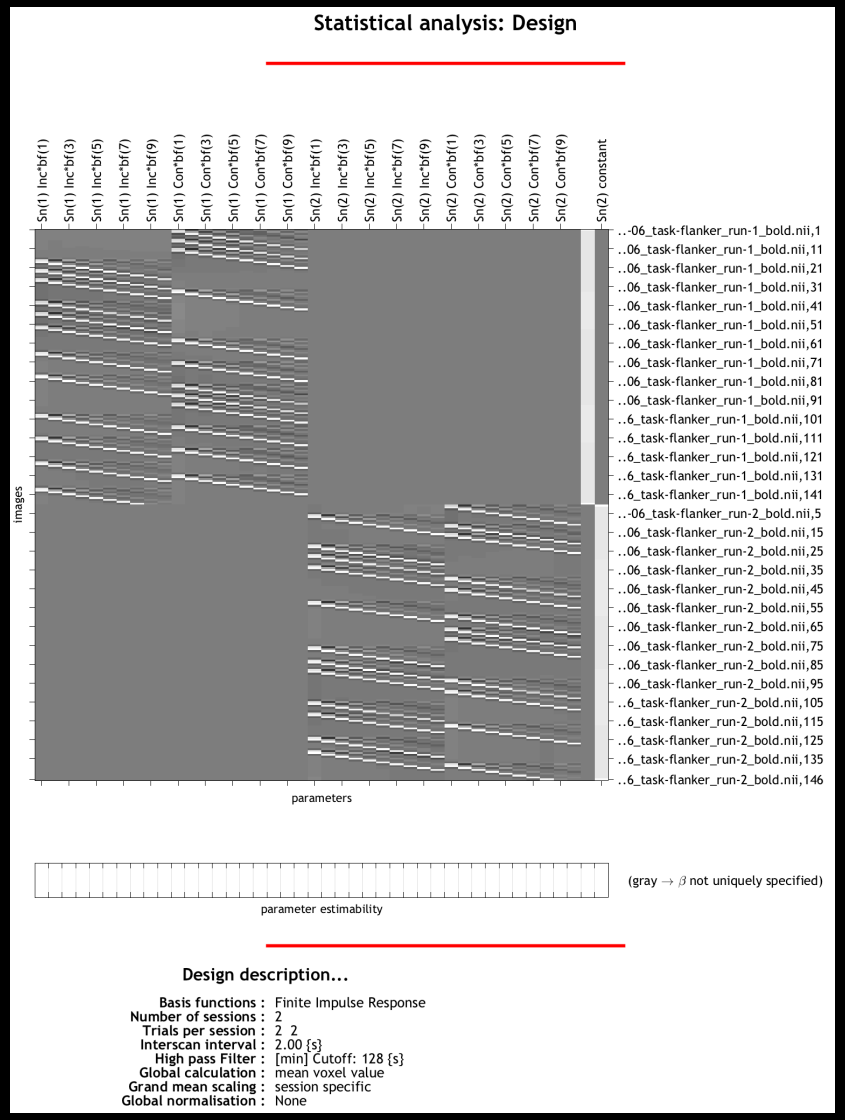
Finite Impulse Response (FIR)

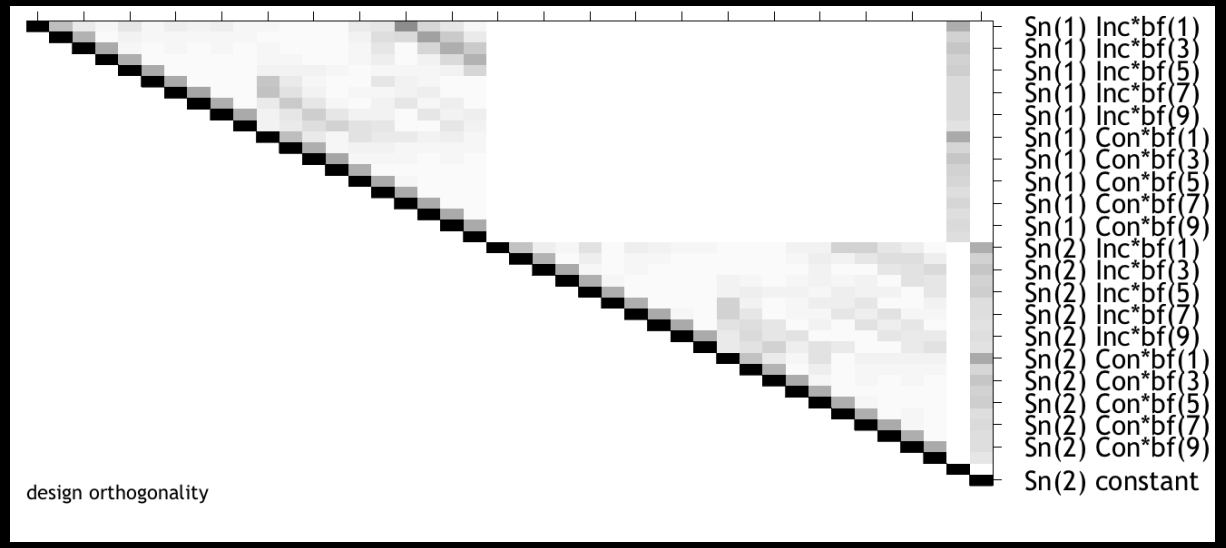
You specify the window length and number of timepoints

e.g.: 20s window, 10 timepoints



Finite Impulse Response (FIR)





Finite Impulse Response (FIR)

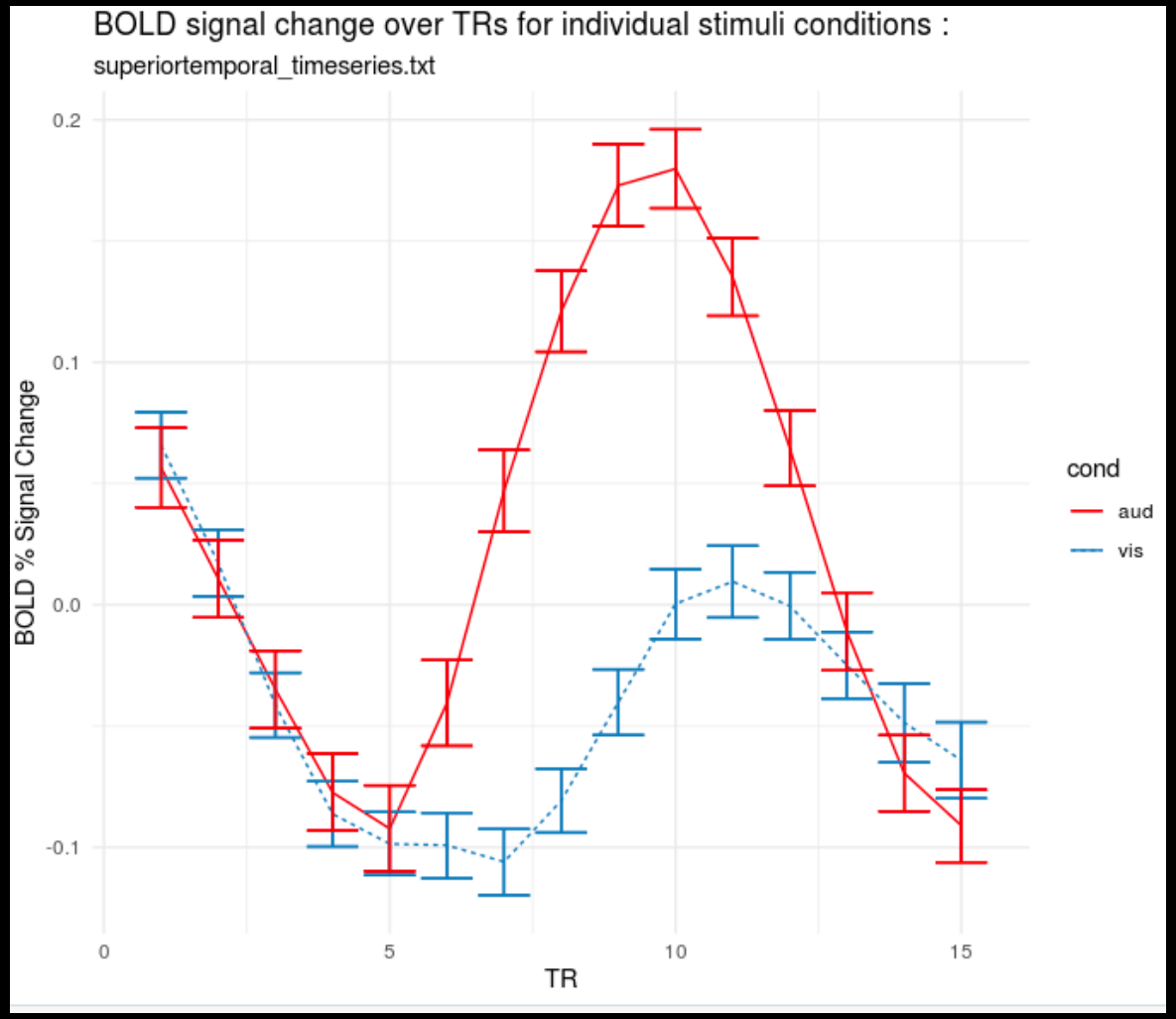
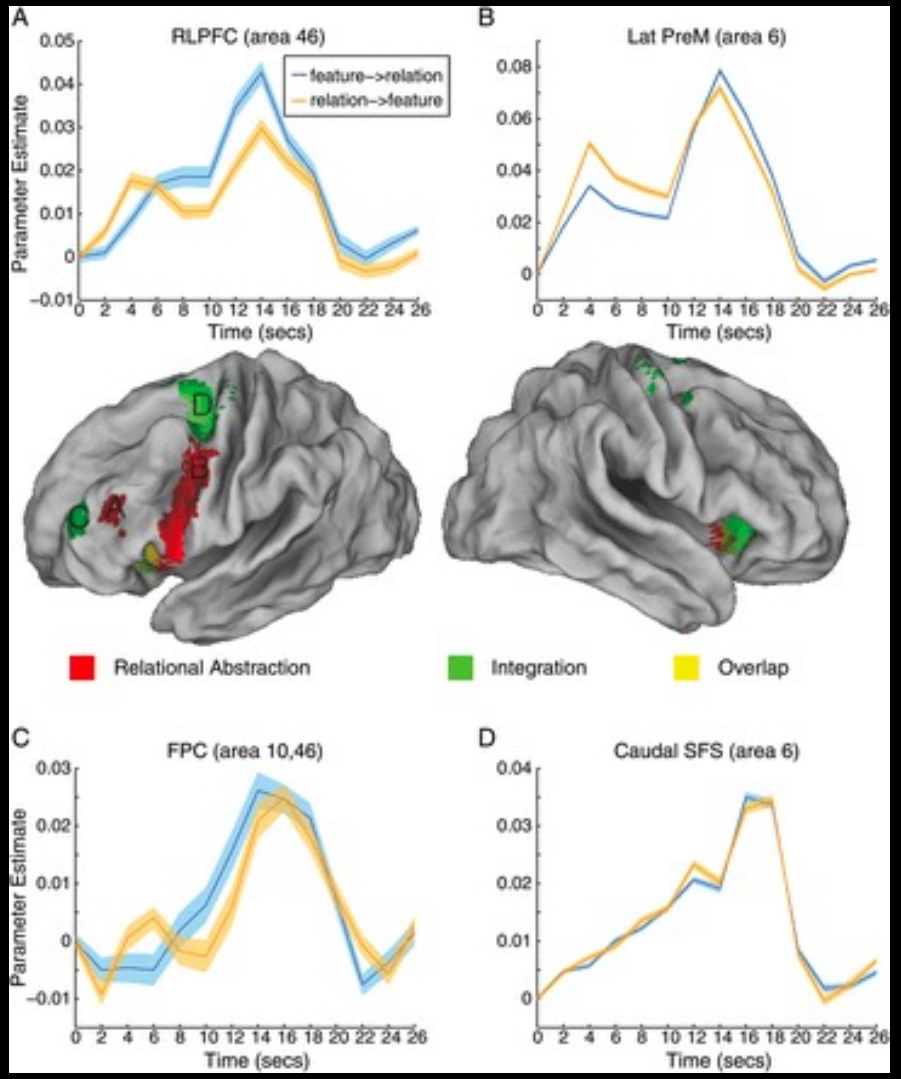


Image by Karthik Ganesan

Finite Impulse Response (FIR)



Nee et al., 2013

Demonstration of FIR Modeling Setup

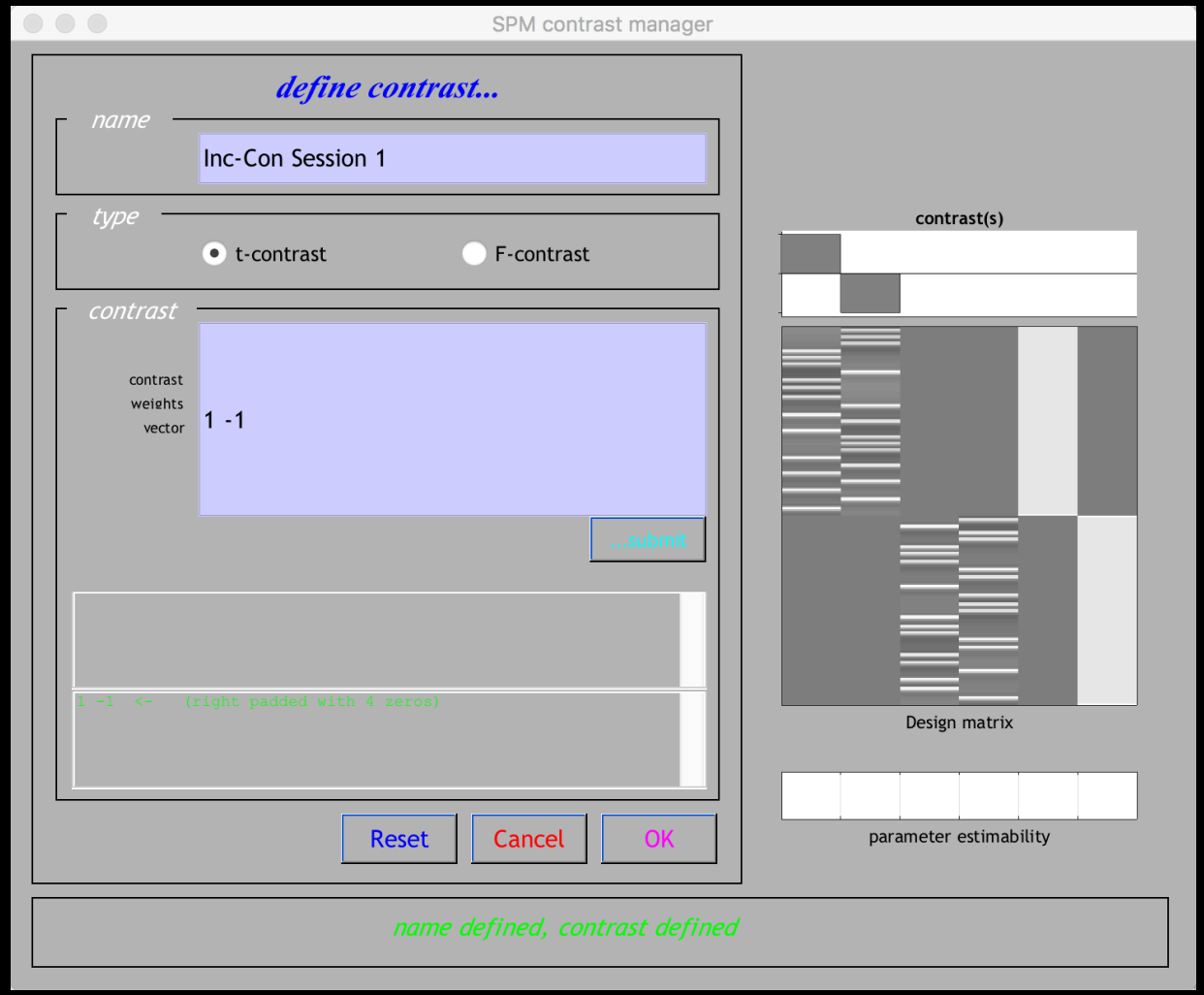
ImCalc: The Image Calculator

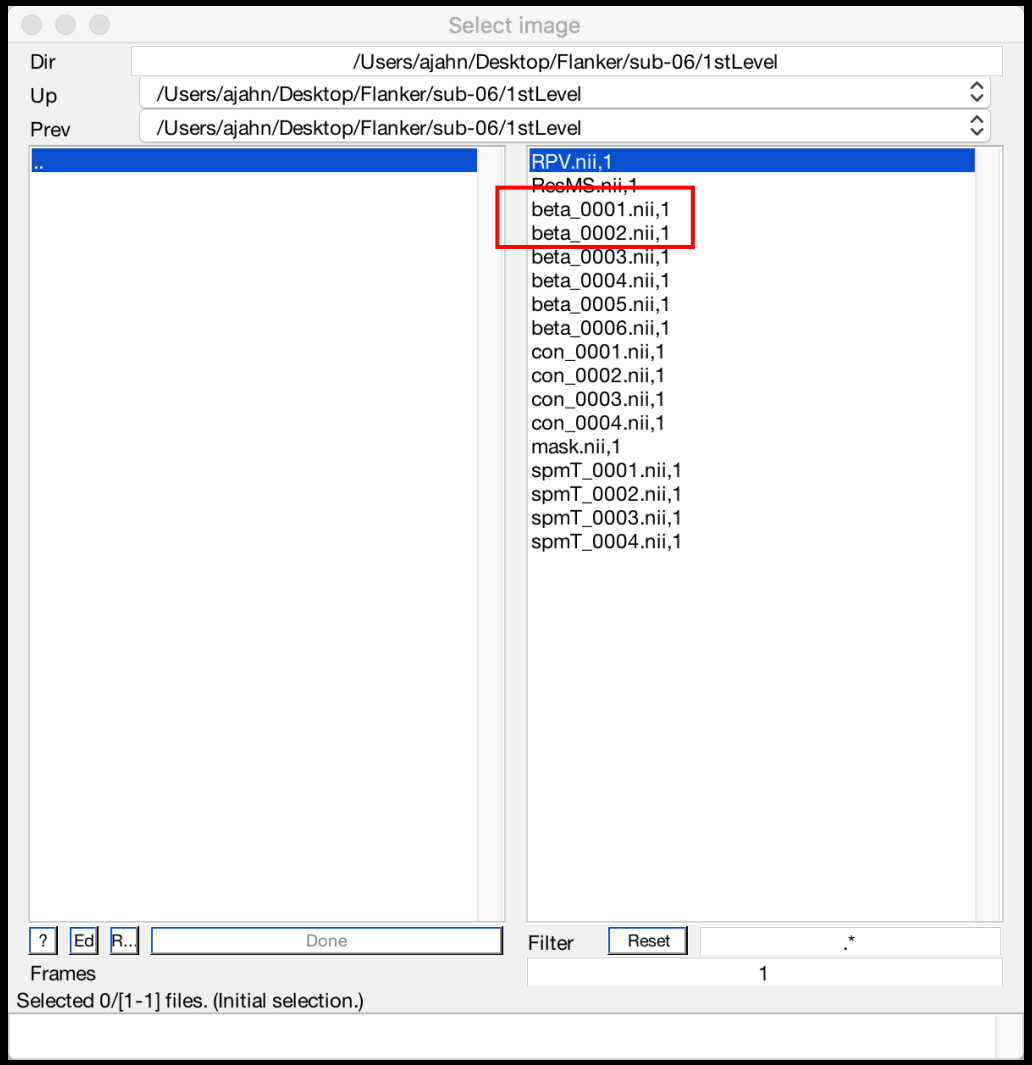
One of the most versatile tools is the image calculator

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

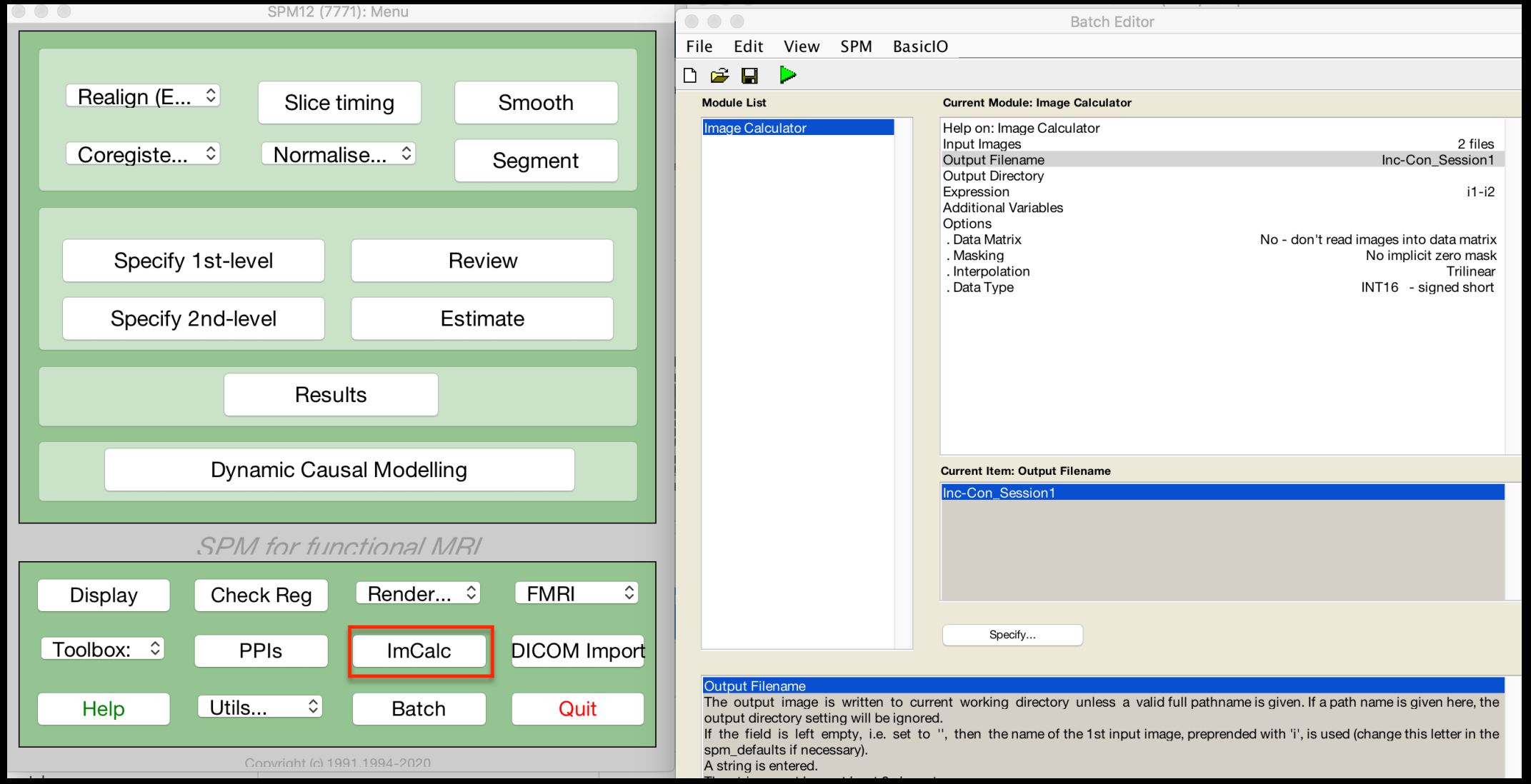
Simple to do basic arithmetic on a 3D image

ImCalc: The Image Calculator

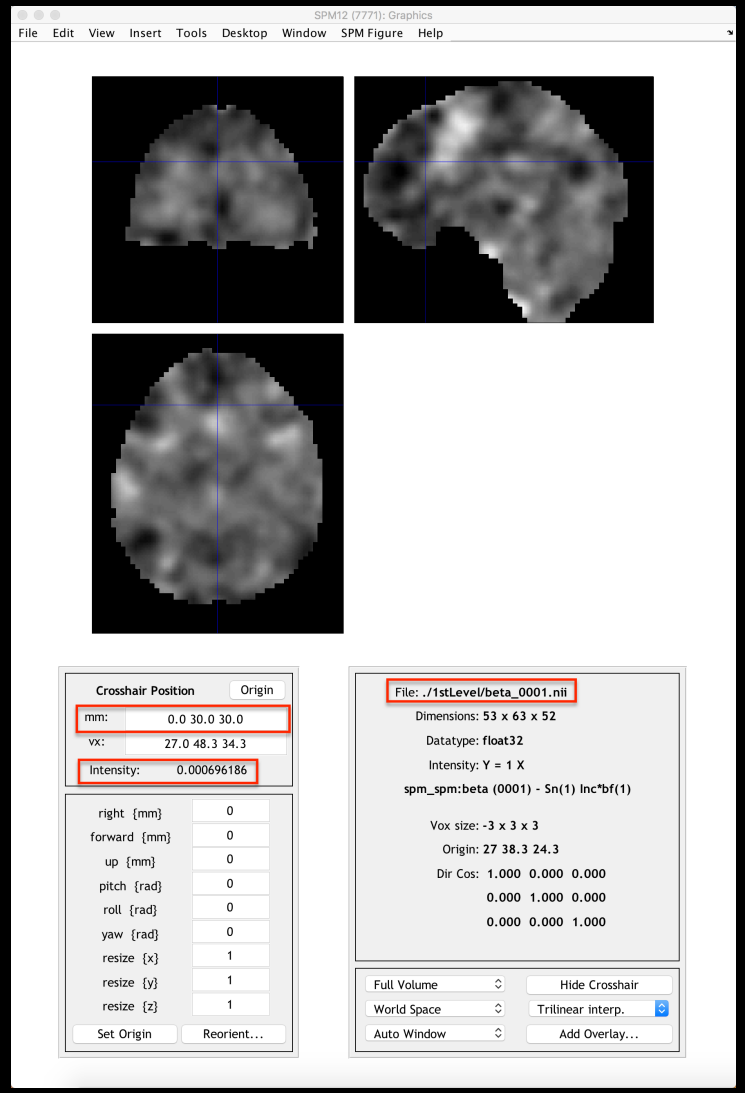


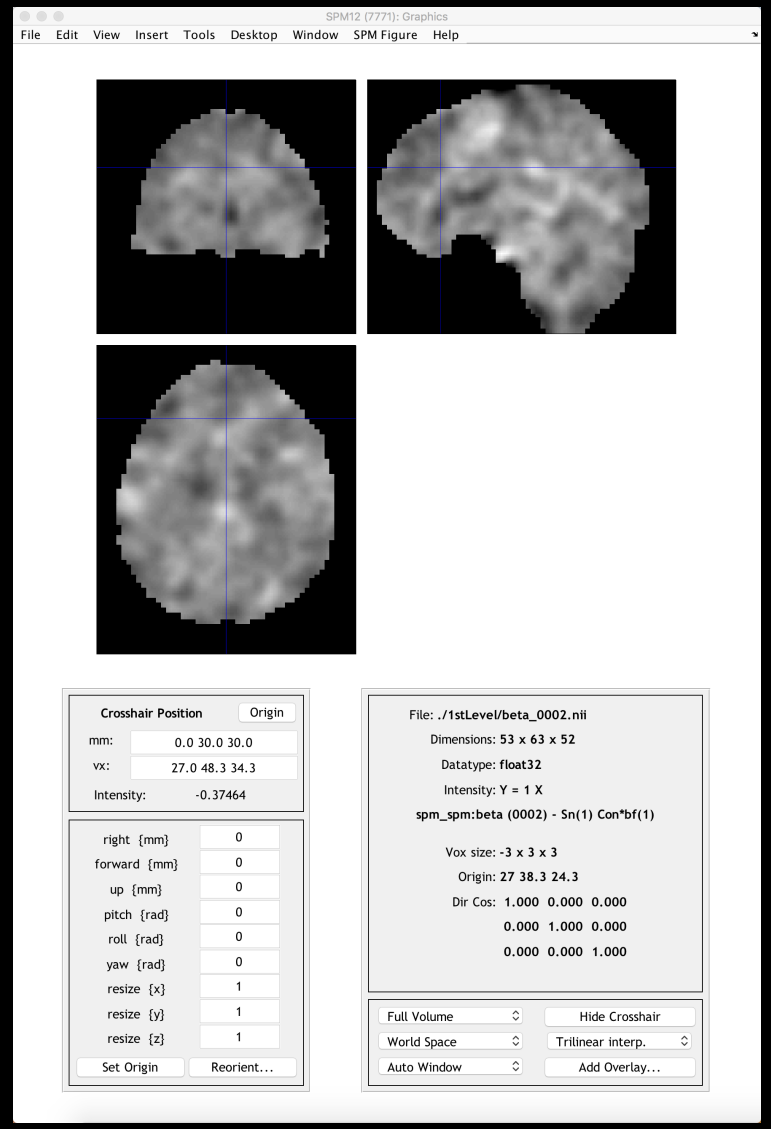


ImCalc: The Image Calculator

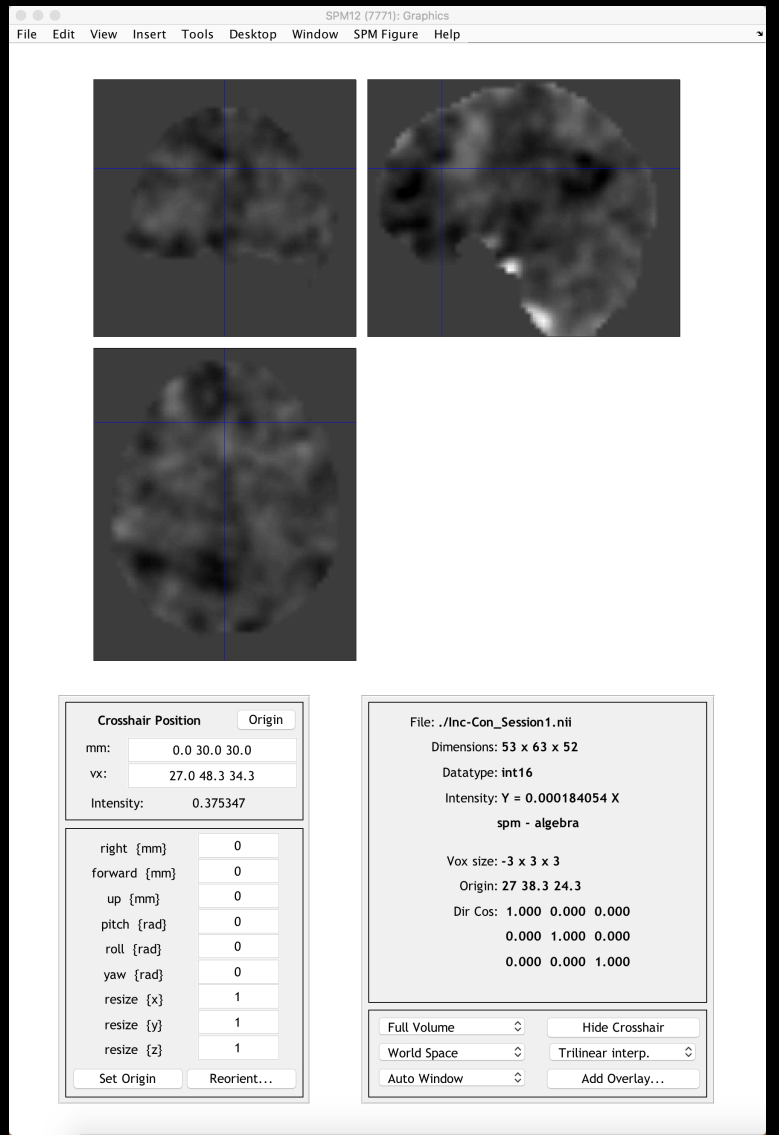


ImCalc: The Image Calculator





ImCalc: The Image Calculator



Today's Lecture

Design optimization and power analysis

OptimizeX and optseq (optimization), Gpower (power analysis)

Group-level analysis options

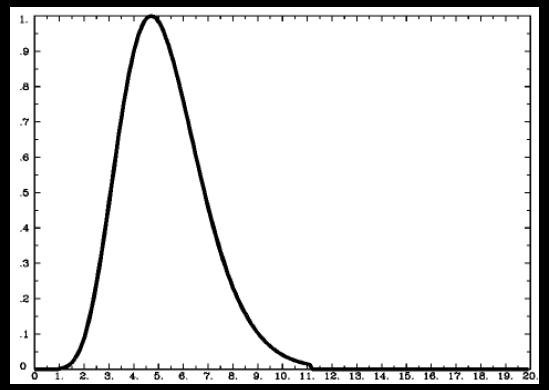
Other Statistical Scenarios

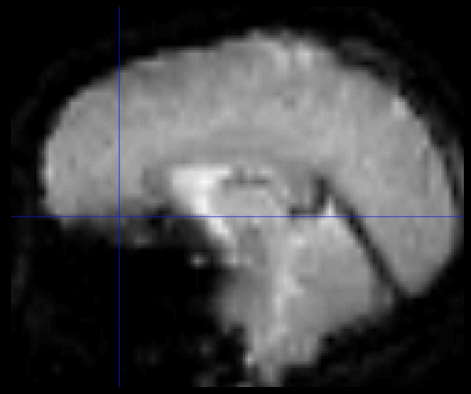
Review So Far

From stimulus to the BOLD response

How tissue properties, blood flow, and magnetic properties interact

Creating contrast images from T1- and T2-weightings





Preprocessing Steps

Brain extraction (or “skull stripping”)

Motion Correction

Slice Timing Correction

Smoothing

Registration

Normalization

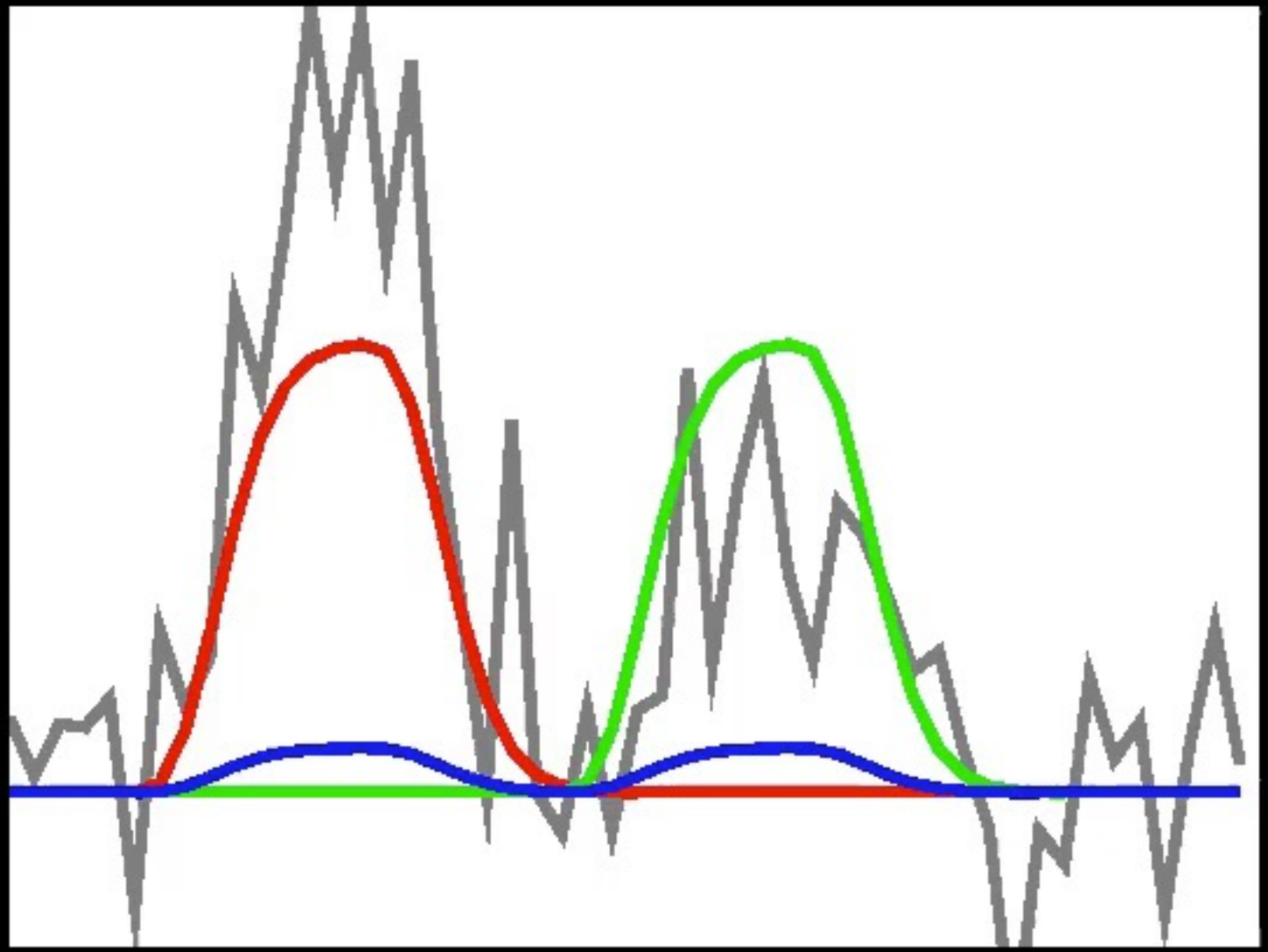
Temporal Filtering

Review So Far

Overview of the General Linear Model

Parameter Estimates

Creating beta maps and contrast maps



Fit at each voxel (“mass univariate” approach)

Bob Cox, AFNI

Questions

Let’s look at some GLMs, and see if you can identify each part!

ming
Smooth
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Review
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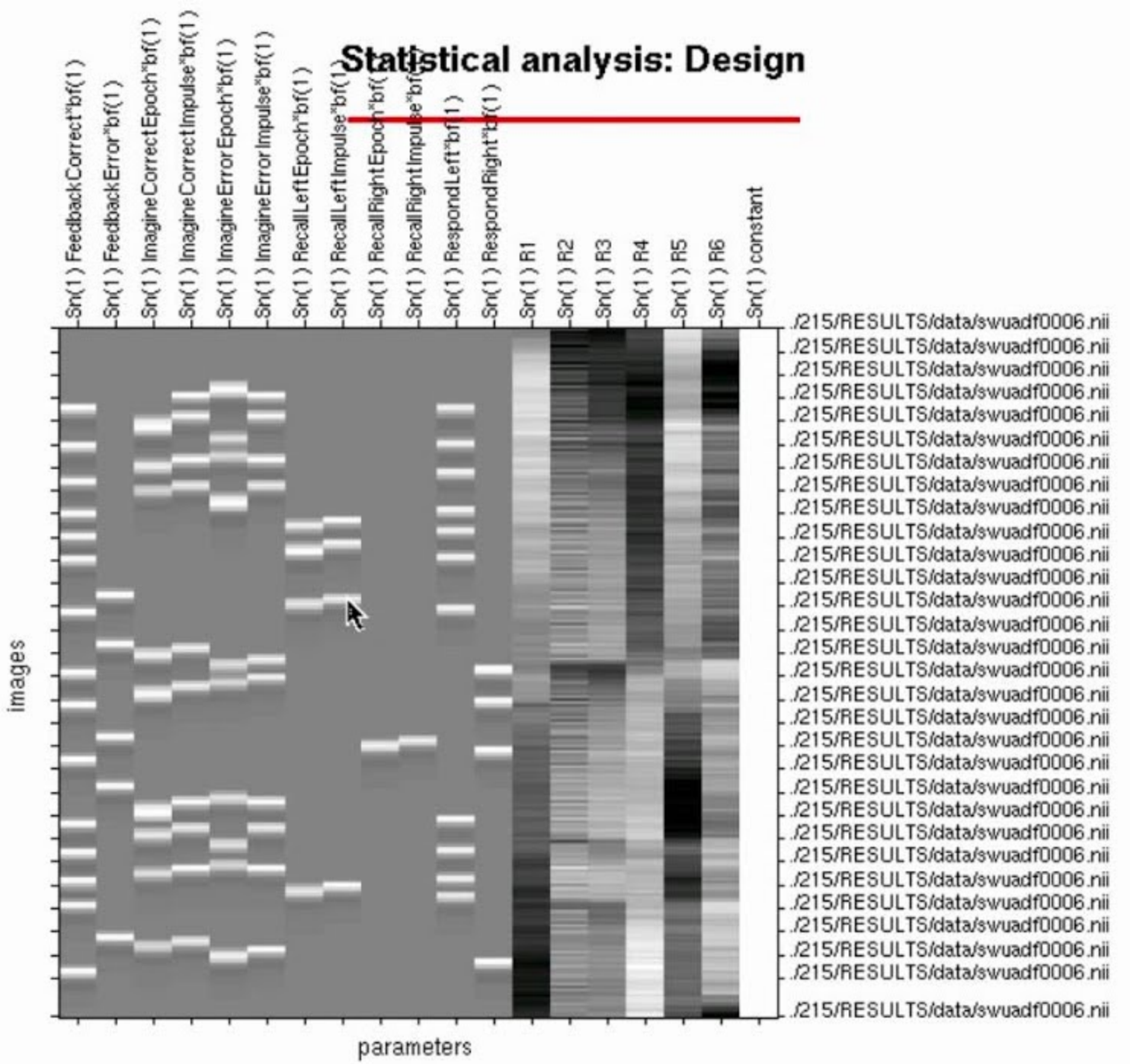
Render.....
FMRI
ImCalc
DICOM Imp...
Defaults
Quit
03,2005-2008

SPM5: spm_fmri_spm_
==========
Mapping files
Calculating globals

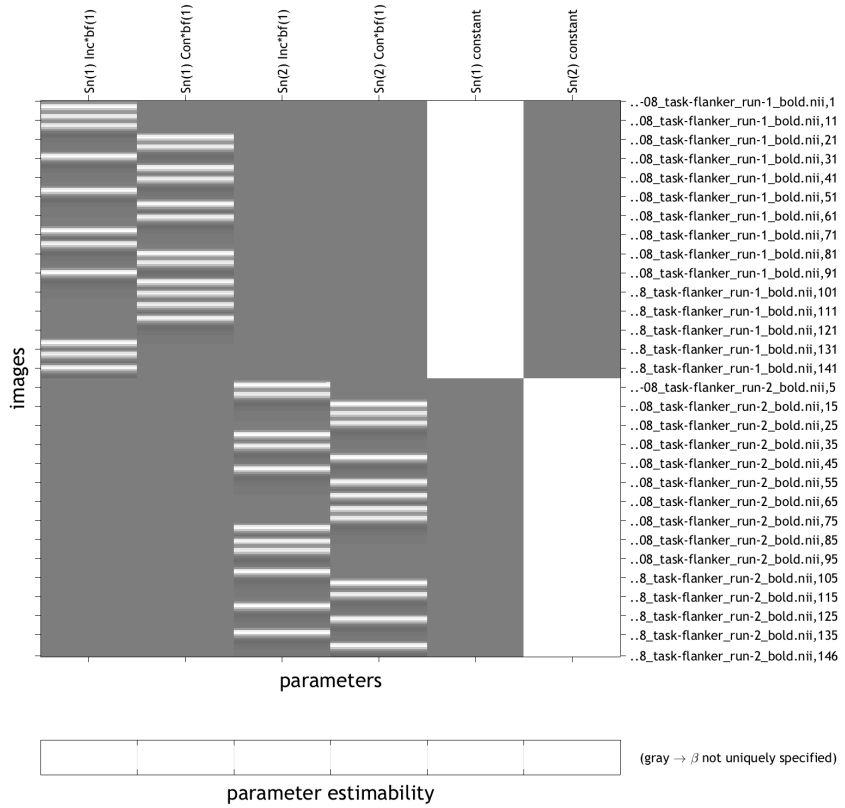


ultis_2
ultis_2/

SPM12 (7219): Graphics

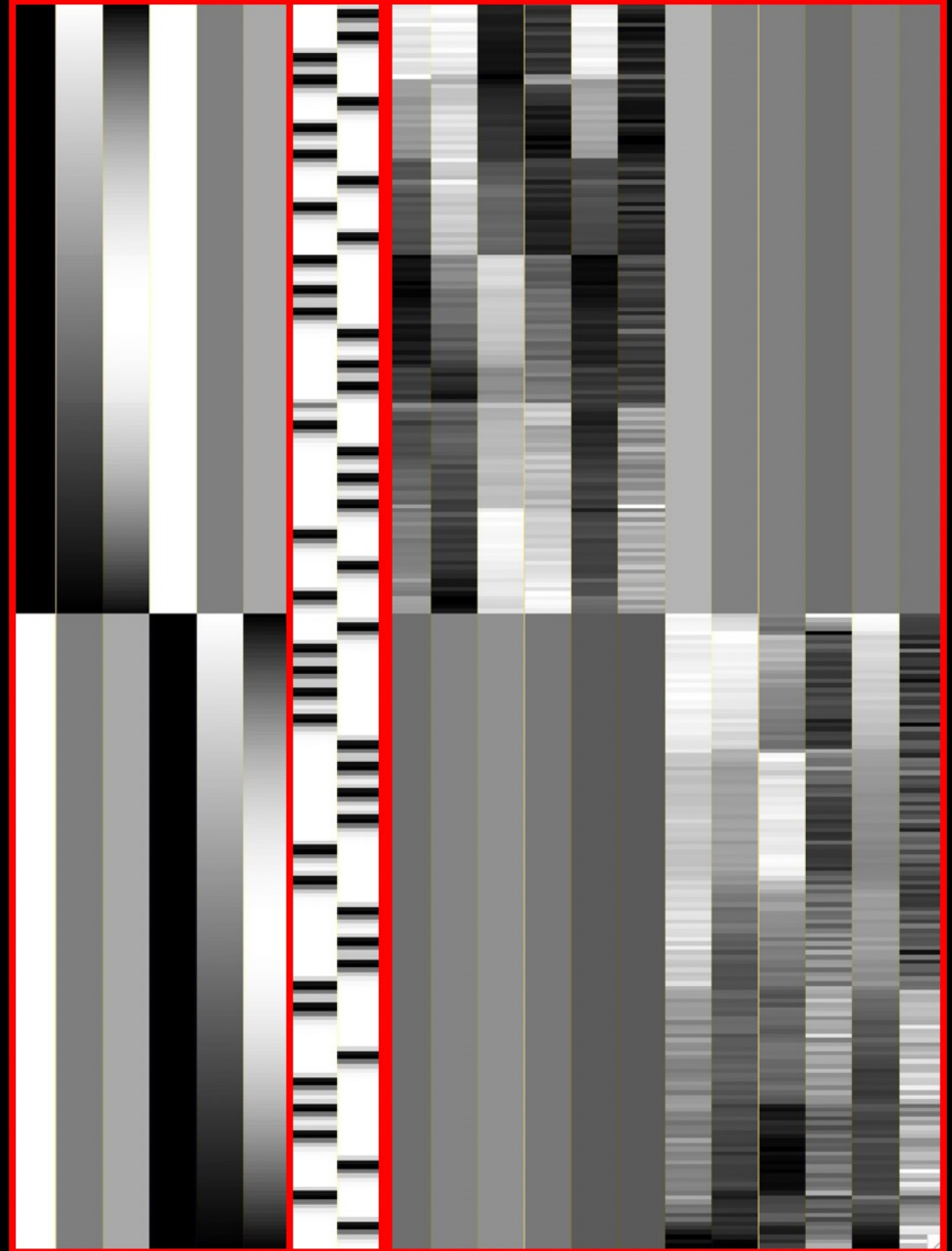
File Edit View Insert Tools Desktop Window SPM Figure Help

Statistical analysis: Design



Design description...

Basis functions : hrf
Number of sessions : 2
Trials per session : 2 2
Interscan interval : 2.00 {s}
High pass Filter : [min] Cutoff: 128 {s}
Global calculation : mean voxel value
Grand mean scaling : session specific
Global normalisation : None



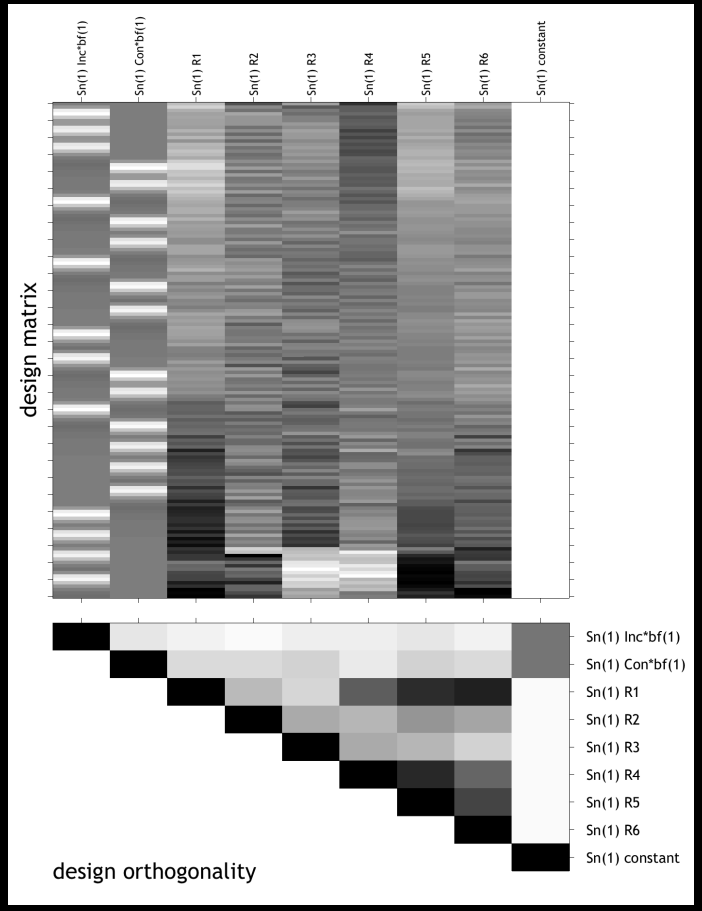
Review: SPM Terms for Analysis

1st-Level Analysis: Individual subject (all trials across runs)

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

Review of Collinearity

Last week, we looked at a correlation matrix



SPM12 (7771): Menu

Realign (E...
Slice timing
Smooth
Coregiste...
Normalise...
Segment

Select your SPM.mat file

Specify 1st-level
Review
Specify 2nd-level
Estimate

Results

Dynamic Causal Modelling

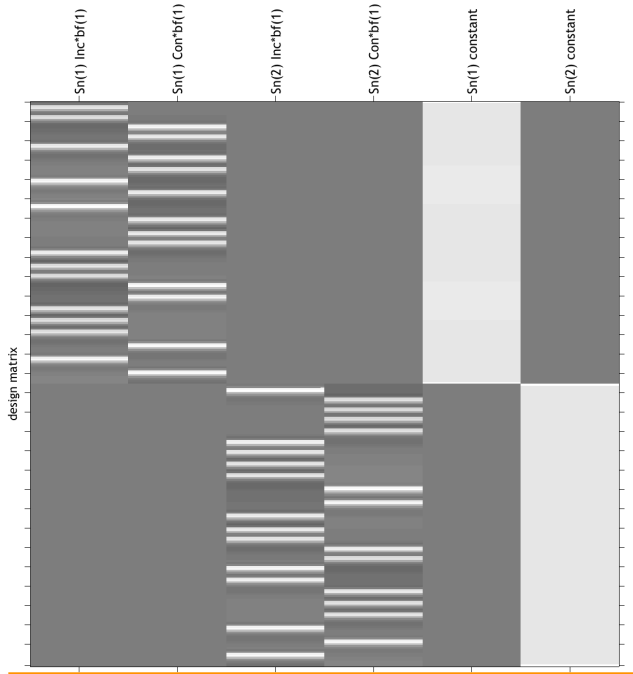
SPM for functional MRI

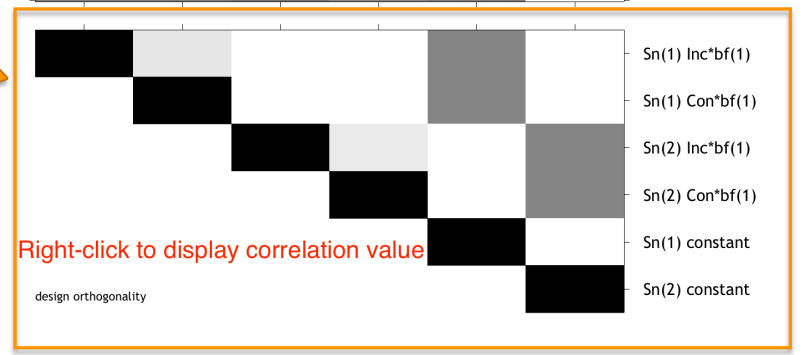
Display
Check Reg
Render...
FMRI
Toolbox:
PPIs
ImCalc
DICOM Import
Help
Utils...
Batch
Quit

Design

File Edit View Insert Tools Desktop Window SPM Figure Help

Statistical analysis: Design orthogonality





Measure : abs. value of cosine of angle between columns of design matrix
Scale : black - colinear (cos=+1/-1)
white - orthogonal (cos=0)
gray - not orthogonal or colinear

PUBLISH VIEW

Breakpoints | Run | Run and Advance | Run Section | Advance | Run and Time

EDIT BREAKPOINTS RUN

Flanker ▸ sub-01 ▸ 1stLevel

Editor - /Users/ajahn/Downloads/fmridata/LIPREAD/Subjects/Decoding_audOnly_RSA_ROI.m

convertOnsetTimes.m | Decoding_audOnly_RSA_ROI.m | Haxby_RSA.m | Haxby_MVPA_ROI.m | decoding.m | decoding_generate_

```
67
68    %% Decide whether you want to see the searchlight/ROI/... durin
69    cfg.plot_selected_voxels = 500; % 0: no plotting, 1: every step
70
71    %% Add additional output measures if you like
72    % See help decoding_transform_results for possible measures
73
74    % cfg.results.output = {'accuracy_minus_chance', 'AUC'}; % 'acc
75
76    % You can also use all methods that start with "transres_", e.g
77    %   cfg.results.output = {'SVM_pattern'};
78    % will use the function transres_SVM_pattern.m to get the patte
79    % linear svm weights (see Haufe et al, 2015, Neuroimage)
80
81    %% Nothing needs to be changed below for a standard leave-one-r
82    %% validation analysis.
83
84    % The following function extracts all beta names and correspond
85    % numbers from the SPM.mat
86    regressor_names = design_from_spm(['/Users/ajahn/Downloads/fmri
87
88    % Extract all information for the cfg.files structure (labels w
89    cfg = decoding_describe_data(cfg,labelnames,labels,regressor_na
90
91    % This creates the leave-one-run-out cross validation design:
92    cfg.design = make_design_cv(cfg);
```

Command Window

```
ans =
    1.0000   -0.0925         0         0    0.4635         0
   -0.0925    1.0000         0         0    0.4625         0
         0         0    1.0000   -0.0655         0    0.4588
         0         0   -0.0655    1.0000         0    0.4655
    0.4635    0.4625         0         0    1.0000         0
         0         0    0.4588    0.4655         0    1.0000

fx >>
```

Statistical analysis: Design orthogonality

Measure : abs. value of cosine of angle between columns of design matrix
Scale : black - colinear (cos=+1/-1)
white - orthogonal (cos=0)
gray - not orthogonal or colinear

Review of Collinearity

Rule of thumb: Correlations of 0.4 or greater are considered "moderate" (source: AFNI command xmat_tool.py)

However, a high correlation between one set of regressors may not matter, given the regressors you are focused on

The challenge is to include as many regressors as is reasonable, without overfitting or introducing collinearity

Variance Inflation Factor

What what if one regressor is a linear sum of two or more other regressors? Pairwise correlations don't show this

e.g., does $X_1=X_2+X_3$?

Variance Inflation Factor

$$X_1 = \beta_0 + \beta_1 X_2 + \beta_2 X_3 + \epsilon$$

R = $Cor(X_1, \hat{\beta}_0 + \hat{\beta}_1 X_2 + \hat{\beta}_2 X_3) = Cor(X_1, \widehat{X_1})$

Example

X_1	X_2	X_3
1	1	0
2	2	0
3	3	0
4	4	0
5	5	0
1	0	1
2	0	2
3	0	3
4	0	4
5	0	5

$cor(X_1, X_2) = cor(X_1, X_3) = .39$

$$X_1 = \beta_1 X_2 + \beta_2 X_3$$

What's the solution for the betas?

$$X_1 = \widehat{X_1} \implies cor\left(X_1, \widehat{X_1}\right) = 1$$

Example

$$VIF = \frac{1}{1 - R^2} = \frac{1}{1 - [cor(X_1, \widehat{X_1})]^2}$$

Goal: VIF < 5

What is a cutoff? VIF no greater than 10

Repeat the same process for each regressor in the model

VIF: Summary

Detects any collinearity from any combination of regressors

Matlab code: vif = diag(inv(corrcoef(X)))’;

Where “X” is the design matrix

VIF: Summary

Useful for checking whether a design has high collinearity

Solutions: Remove the regressor, or change the design

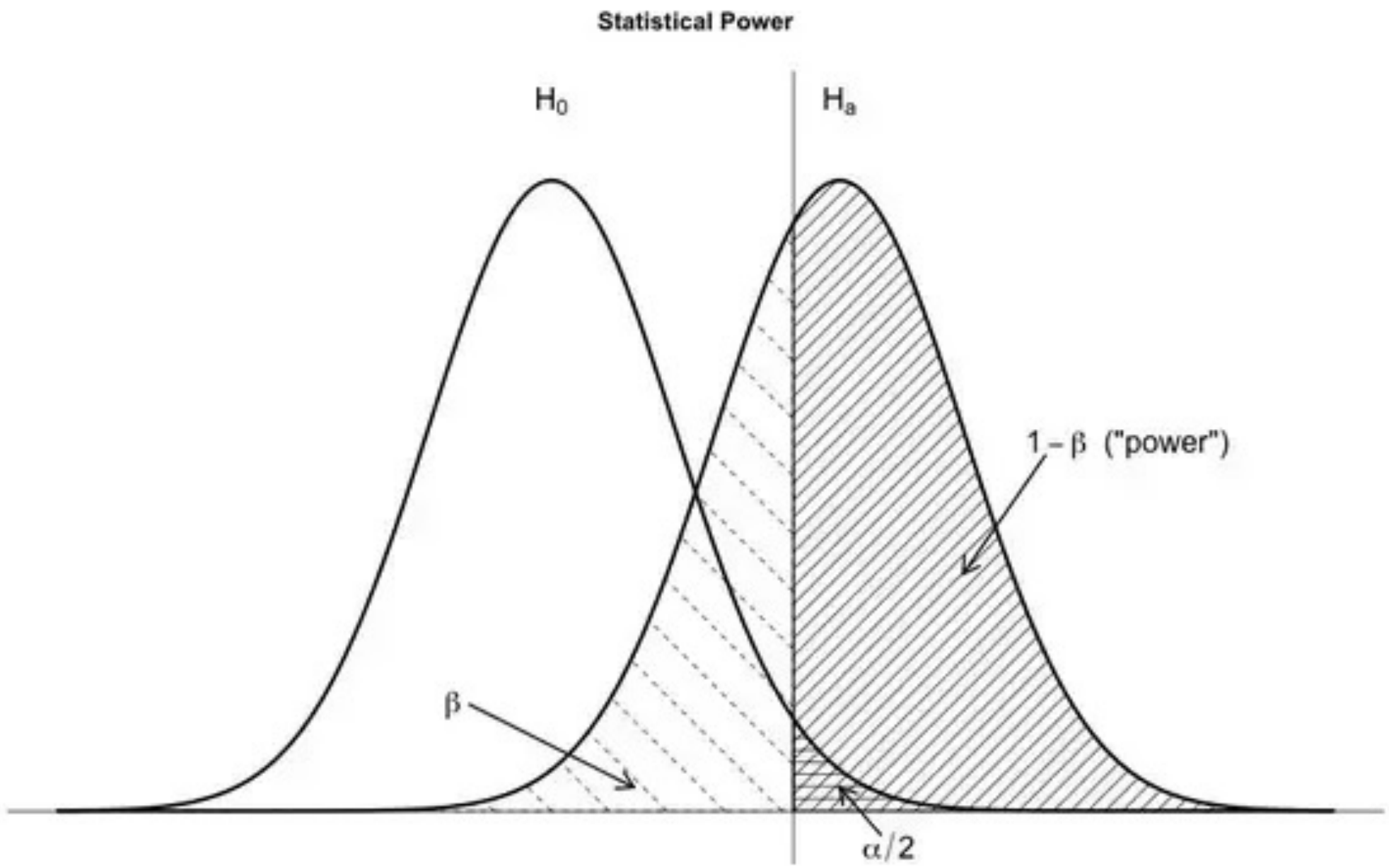
These edits can be done before scanning

Efficiency vs. Power

Two terms you will come across are Efficiency and Power

Let's begin with Power: Can you detect an effect if it is actually there?

As variance increases, power decreases


Statistical Power
H_0
H_a
$1-\beta$ ("power")
β
$\alpha/2$

Efficiency vs. Power

Efficiency is inversely proportional to variance

$$\frac{1}{c(X'X)^{-1}c'}$$

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

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

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

All measures of efficiency are relative

Efficiency vs. Power

Example: You have a fixed number of subjects that you can scan (due to budget, population, etc.)

Options:

1. Scan longer
2. Include more trials
3. Increase ITI
4. Create a more efficient experiment

Efficiency vs. Power

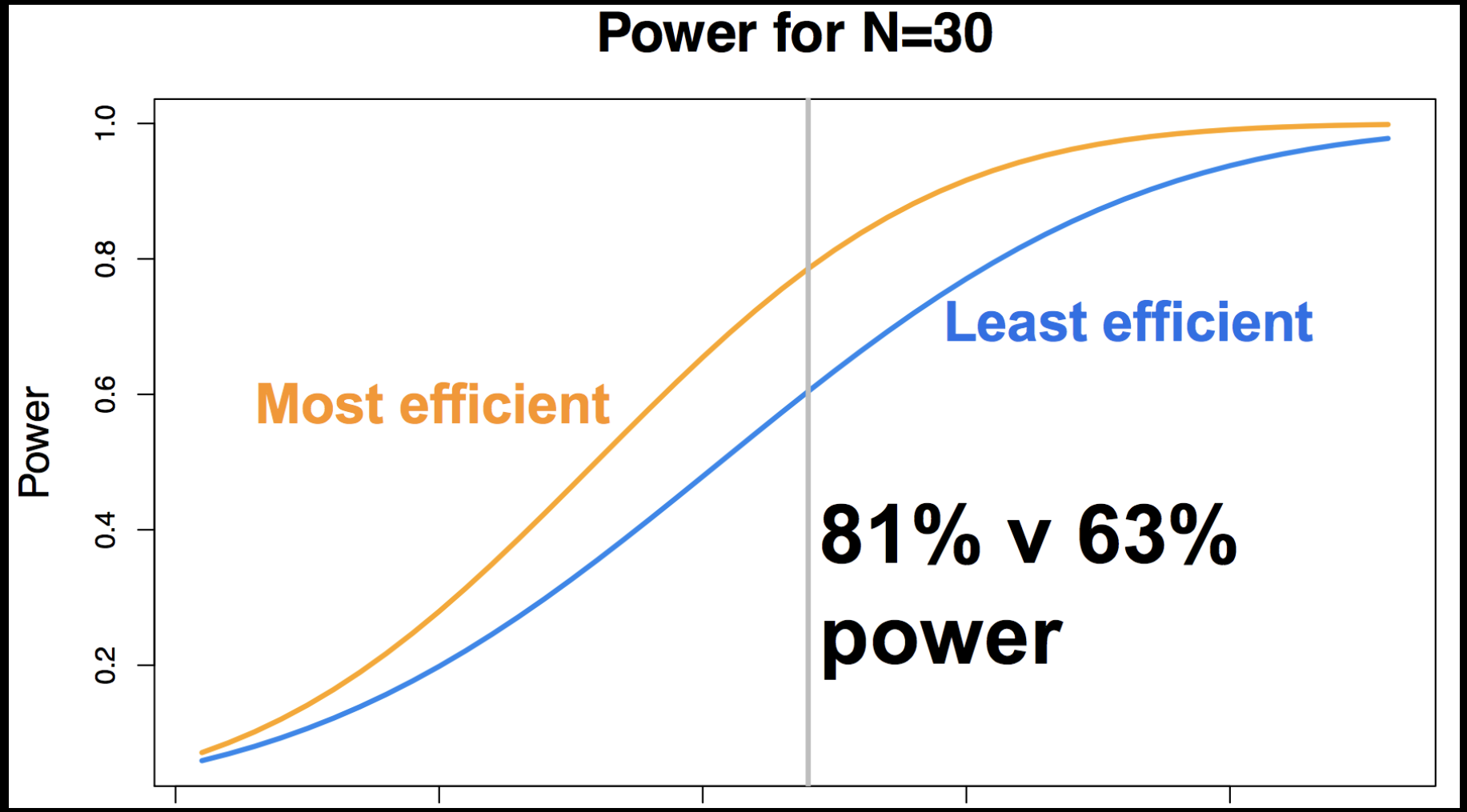
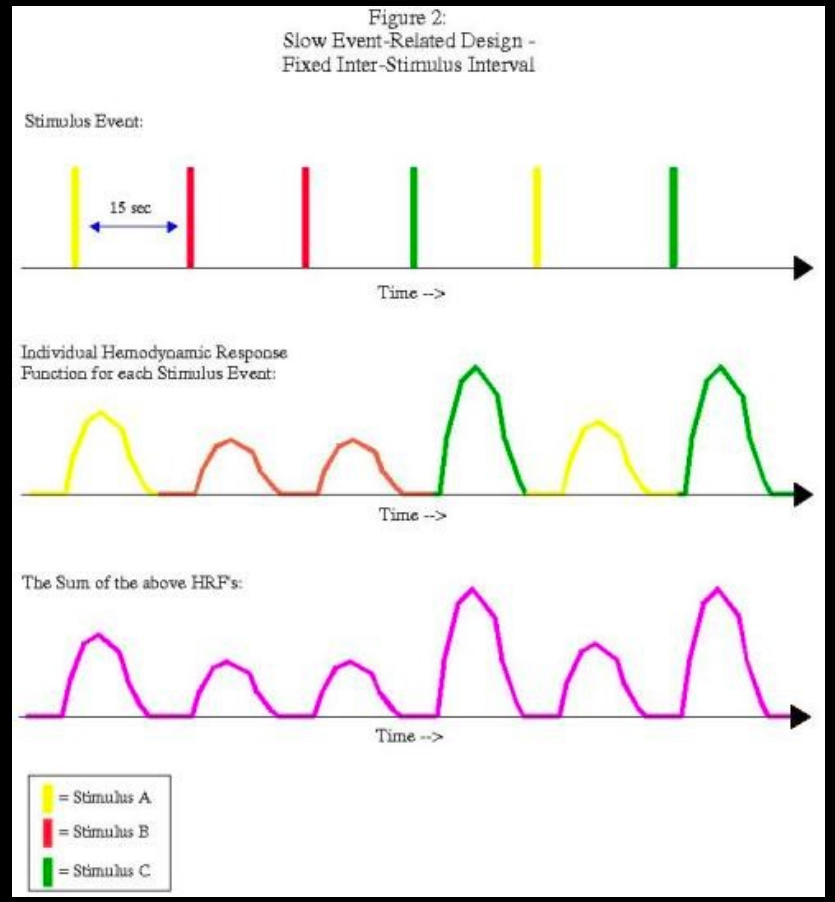
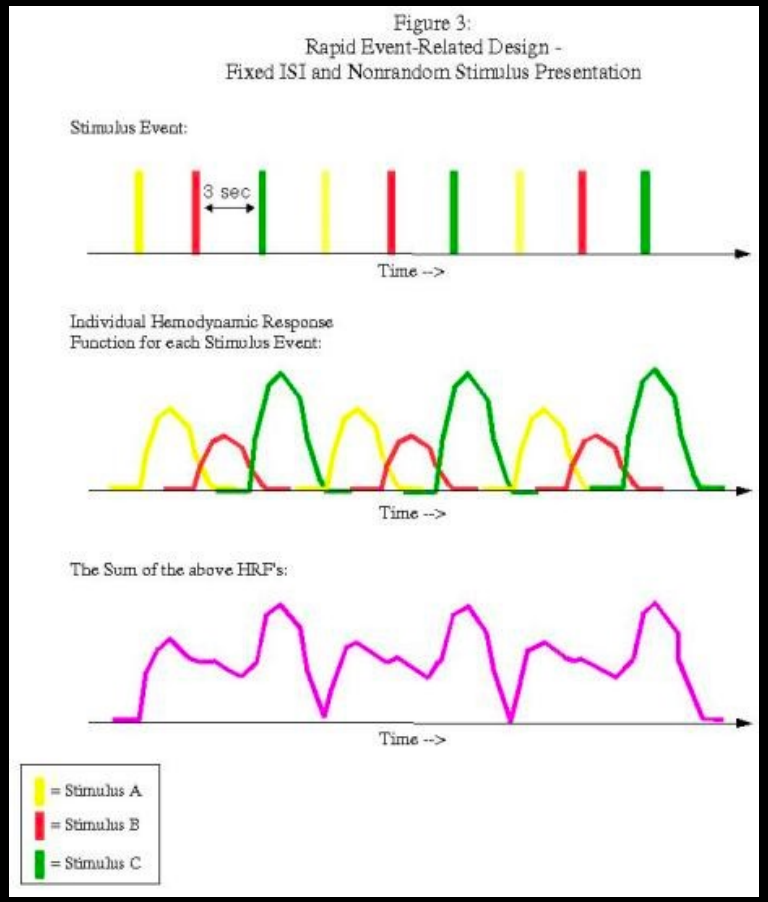
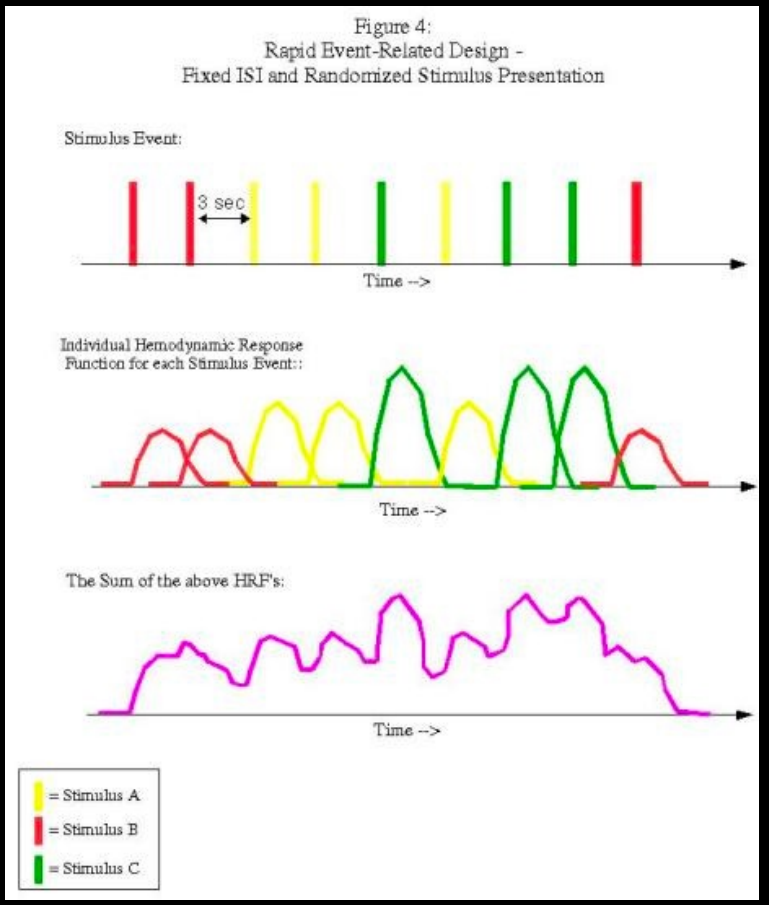


Figure from Jeanette Mumford

Efficiency vs. Power







Slides from AFNI

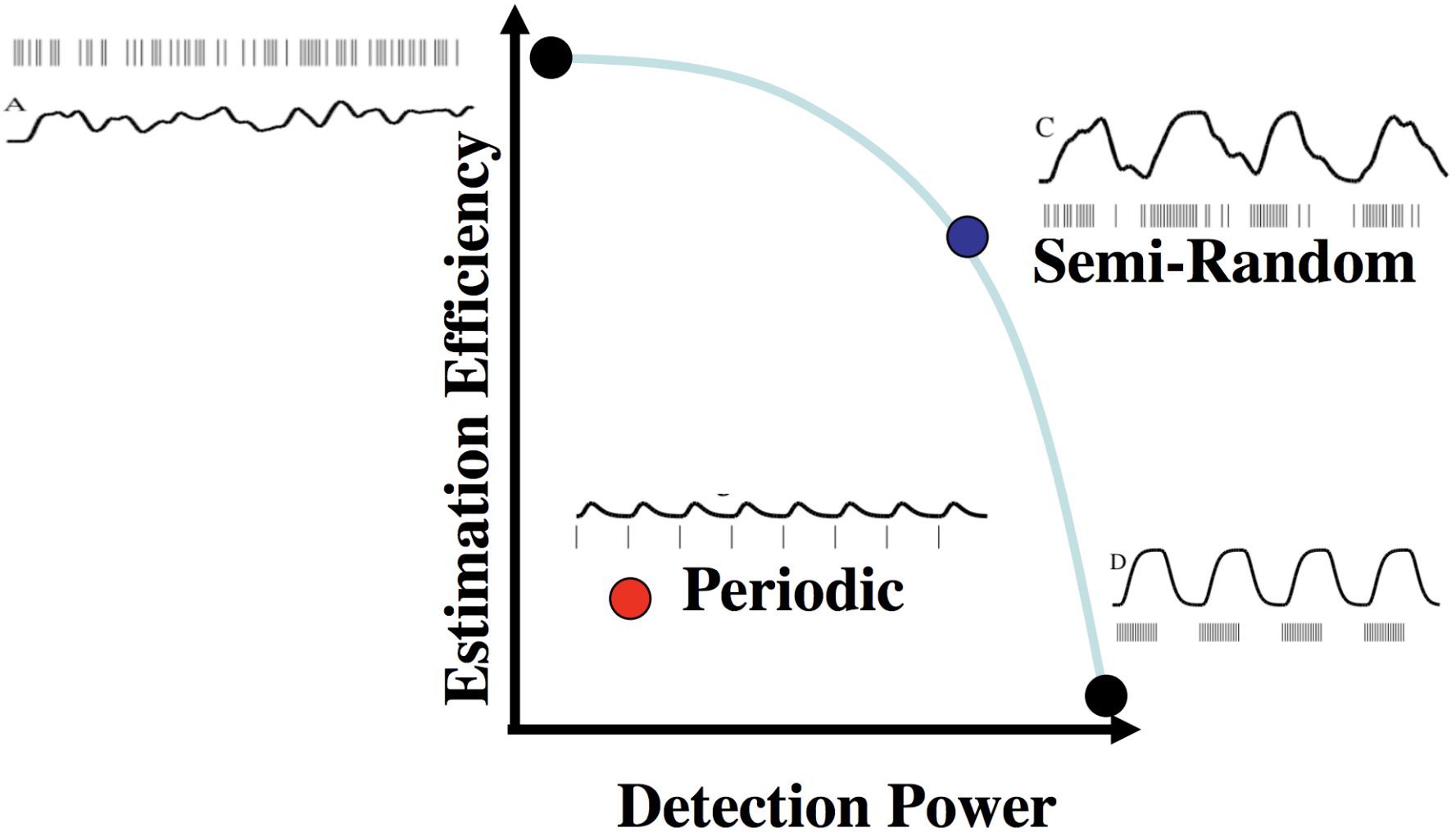
Estimation vs. Detection

Detection is observing a signal if it is really there

Estimation is the analysis of the finer details of the signal, such as the shape of the BOLD response

There tends to be a tradeoff between the two

Fundamental Trade-off



Slide courtesy of Tom Liu

Optimization Strategies

Let’s say we just want to increase our efficiency;
how to choose?

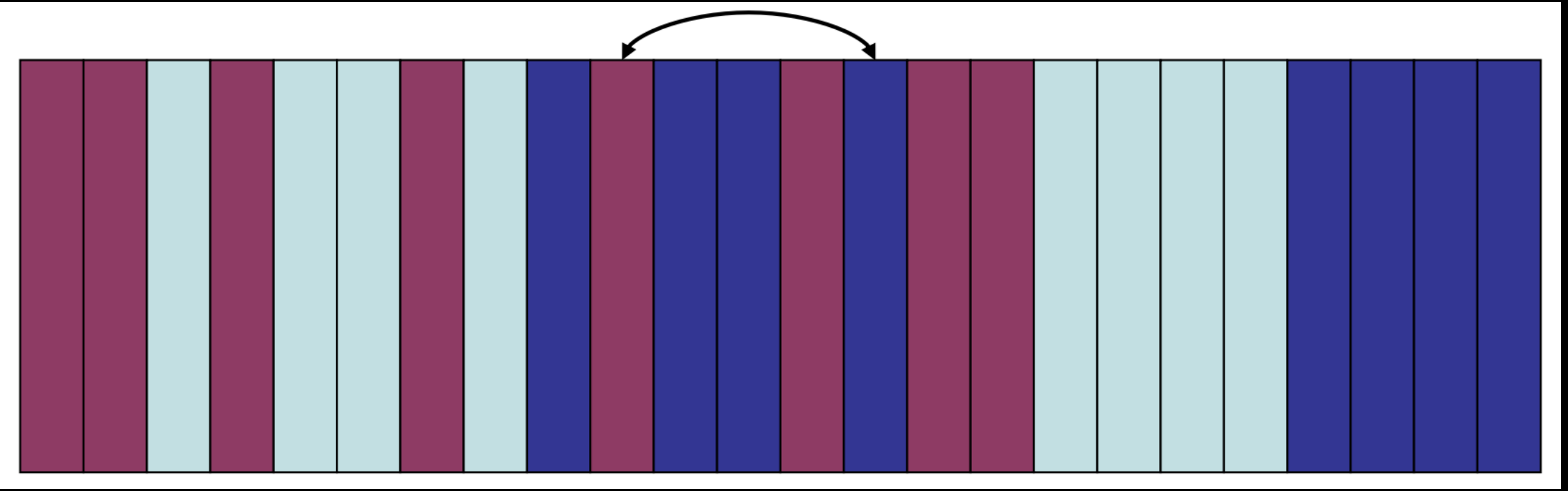
You could just create designs, calculate efficiency, and repeat

Drawbacks of this approach?

Optimization Strategies

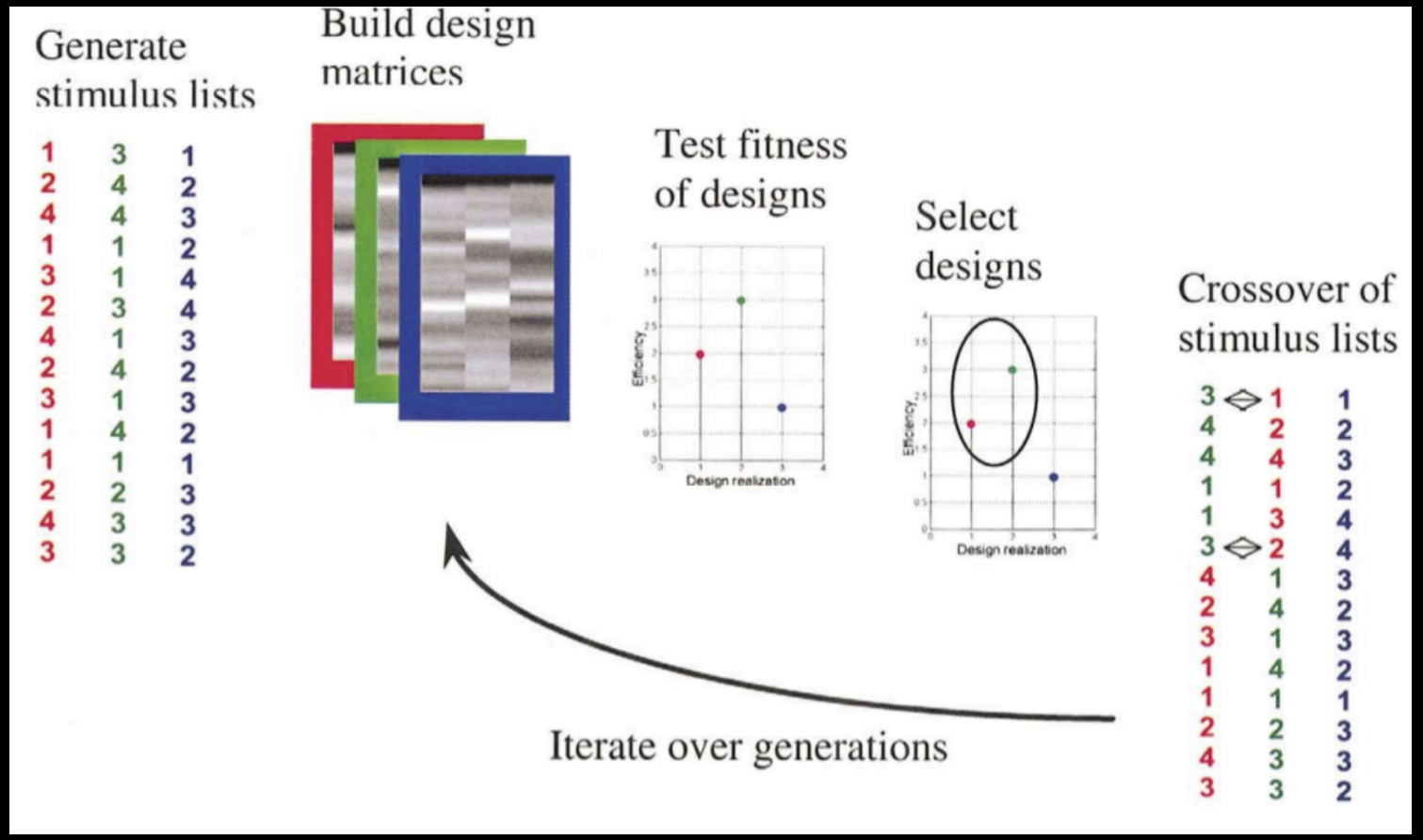
Permuted block design

Start with stimuli blocked and then randomly permute



Optimization Strategies

Genetic algorithm



Optimization Strategies

Resources

Welcome to the Optseq Home Page

optseq2 is a tool for automatically scheduling events for rapid-presentation event-related (RPER) fMRI experiments (the schedule is the order and timing of events). Events in RPER are presented closely enough in time that their hemodynamic responses will overlap. This requires that the onset times of the events be jittered in order to remove the overlap from the estimate of the hemodynamic response. RPER is highly resistant to habituation, expectation, and set because the subject does not know when the next stimulus will appear or which stimulus type it will be. RPER is also more efficient than fixed-interval event related (FIER) because more stimuli can be presented within a given scanning interval at the cost of assuming that the overlap in the hemodynamic responses will be linear. In SPM parlance, RPER is referred to as 'stochastic design'.

The flexibility of RPER means that there are a huge number of possible schedules, and they are not equal. optseq2 randomly samples the space of possible schedules and returns the 'best' one, where the user can control the definition of 'best'. Cost functions include: average efficiency, average variance reduction factor (VRF), and a weighted combination of average and stddev of the VRF. The user can also specify that the first order counter-balancing of the sequence of stimuli be pre-optimized.

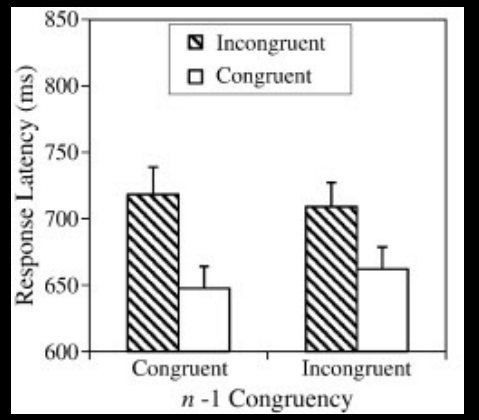
Download the Linux version of optseq2.
Download the Linux x86_64 version of optseq2.
Download the MacOSX-PowerPC version of optseq2.
Download the MacOSX-Intel version of optseq2.
Download the Cygwin version of optseq2.

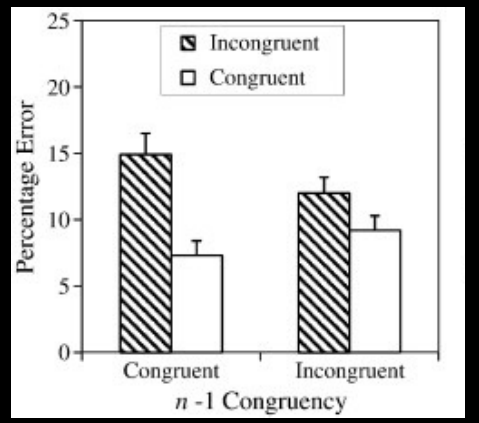
Optimization Strategies

```
(base) ajahn:~/Desktop/Flanker/2ndLevel_Inc-Con$ optseq2 --ntp 160 --tr 2 --psdwin 0 20 2
--ev disgustingPic 2 20 --ev attractivePic 2 15 --ev neutralPic 2 30 --evc 1 -1 0 --nkeep
3 --o IAPS --tnullmin 2 --tnullmax 8 --nsearch 1000
```

Why not just use the best one?

0.0000	2	2.000	1.0000	attractivePic
2.0000	0	2.000	1.0000	NULL
4.0000	2	2.000	1.0000	attractivePic
6.0000	0	2.000	1.0000	NULL
8.0000	1	2.000	1.0000	disgustingPic
10.0000	0	2.000	1.0000	NULL
12.0000	3	2.000	1.0000	neutralPic
14.0000	0	4.000	1.0000	NULL
18.0000	1	2.000	1.0000	disgustingPic
20.0000	0	2.000	1.0000	NULL
22.0000	3	2.000	1.0000	neutralPic
24.0000	0	2.000	1.0000	NULL
26.0000	1	2.000	1.0000	disgustingPic
28.0000	0	2.000	1.0000	NULL
30.0000	3	2.000	1.0000	neutralPic
32.0000	0	2.000	1.0000	NULL





Optimization Strategies

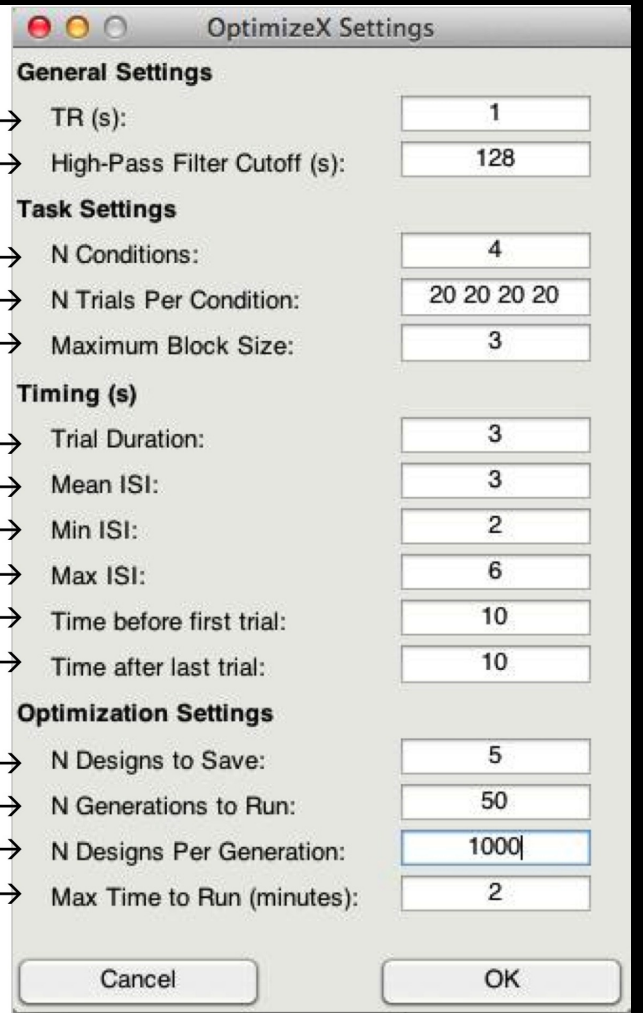
OptimizeX

TR you will use to acquire images →
High-pass filter you will use to analyze images →

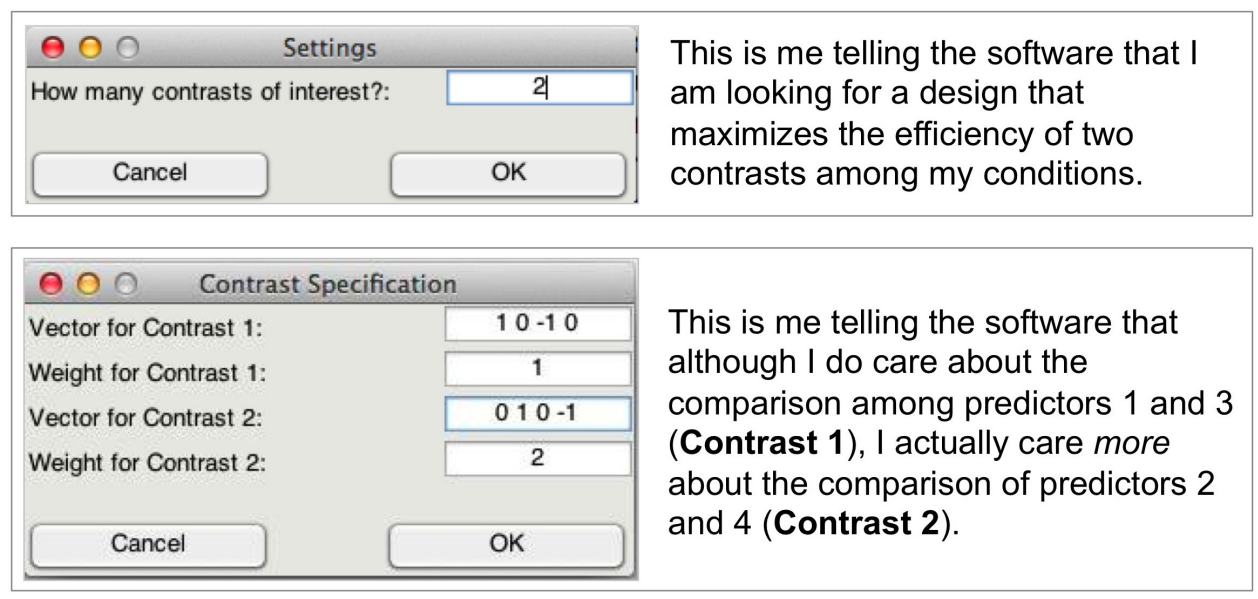
# of conditions in your design →
# of trials per condition (unbalanced OK, e.g. 25 20 15 25) →
blocks = trials from same condition occurring in a row →

duration of your trials (0 for purely event-related) →
mean interstimulus interval →
minimum value for interstimulus interval →
maximum value for interstimulus interval →
“rest” interval to add to beginning of scan →
“rest” interval to add at end of scan →

number of “optimal” designs to save →
number of generations to test →
# of designs to include in each generation →
maximum amount of time to run the program →

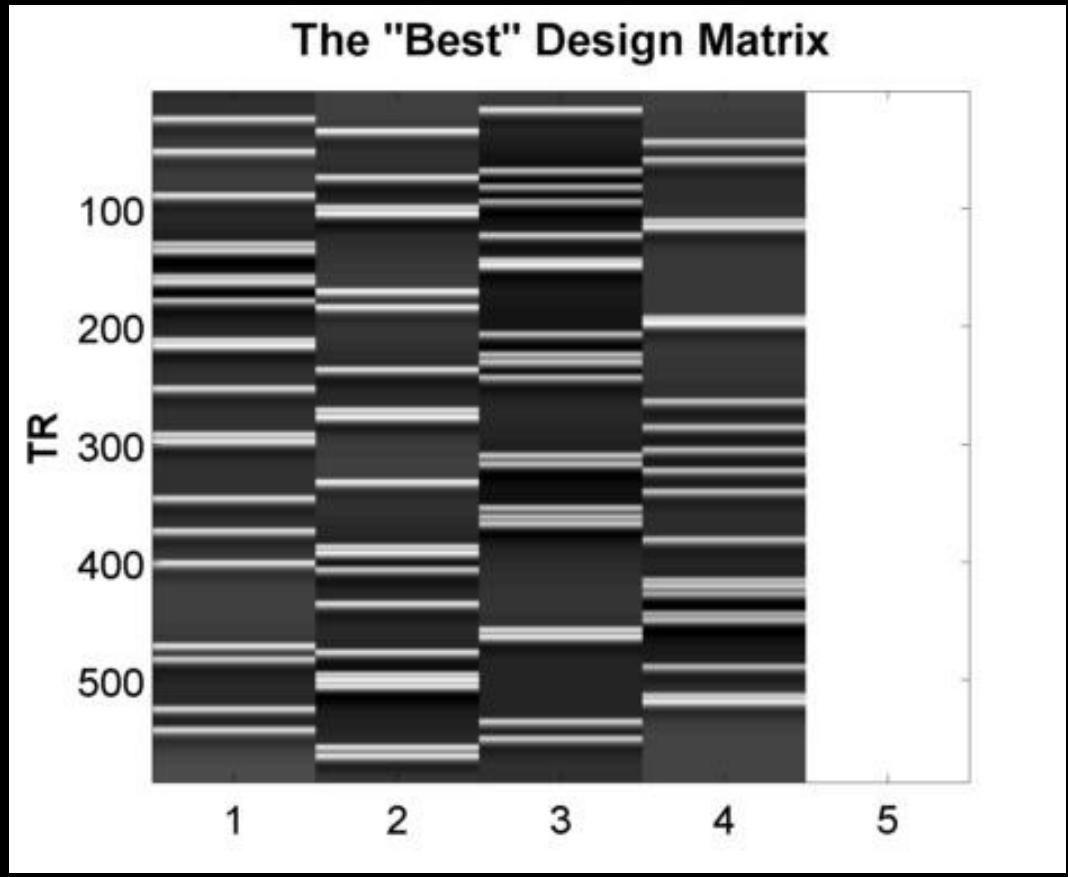


Optimization Strategies



This is me telling the software that I am looking for a design that maximizes the efficiency of two contrasts among my conditions.

This is me telling the software that although I do care about the comparison among predictors 1 and 3 (**Contrast 1**), I actually care *more* about the comparison of predictors 2 and 4 (**Contrast 2**).



Optimization Strategies

	A	B	C	D	E
1	Trial	Condition	Onset	Duration	ISI
2	1	3	10.00	3.00	4.77
3	2	1	17.77	3.00	7.32
4	3	2	28.10	3.00	6.03
5	4	4	37.13	3.00	5.20
6	5	1	45.33	3.00	4.04
7	6	4	52.37	3.00	6.31
8	7	3	61.68	3.00	2.69
9	8	2	67.37	3.00	4.92
10	9	3	75.29	3.00	4.45
11	10	1	82.74	3.00	2.13
12	11	3	87.88	3.00	2.04
13	12	2	92.91	3.00	2.87
14	13	2	98.78	3.00	2.56
15	14	4	104.35	3.00	2.59
16	15	4	109.93	3.00	3.53
17	16	3	116.46	3.00	4.43
18	17	1	123.88	3.00	3.10
19	18	1	129.99	3.00	4.77

Optimization Strategies: Summary

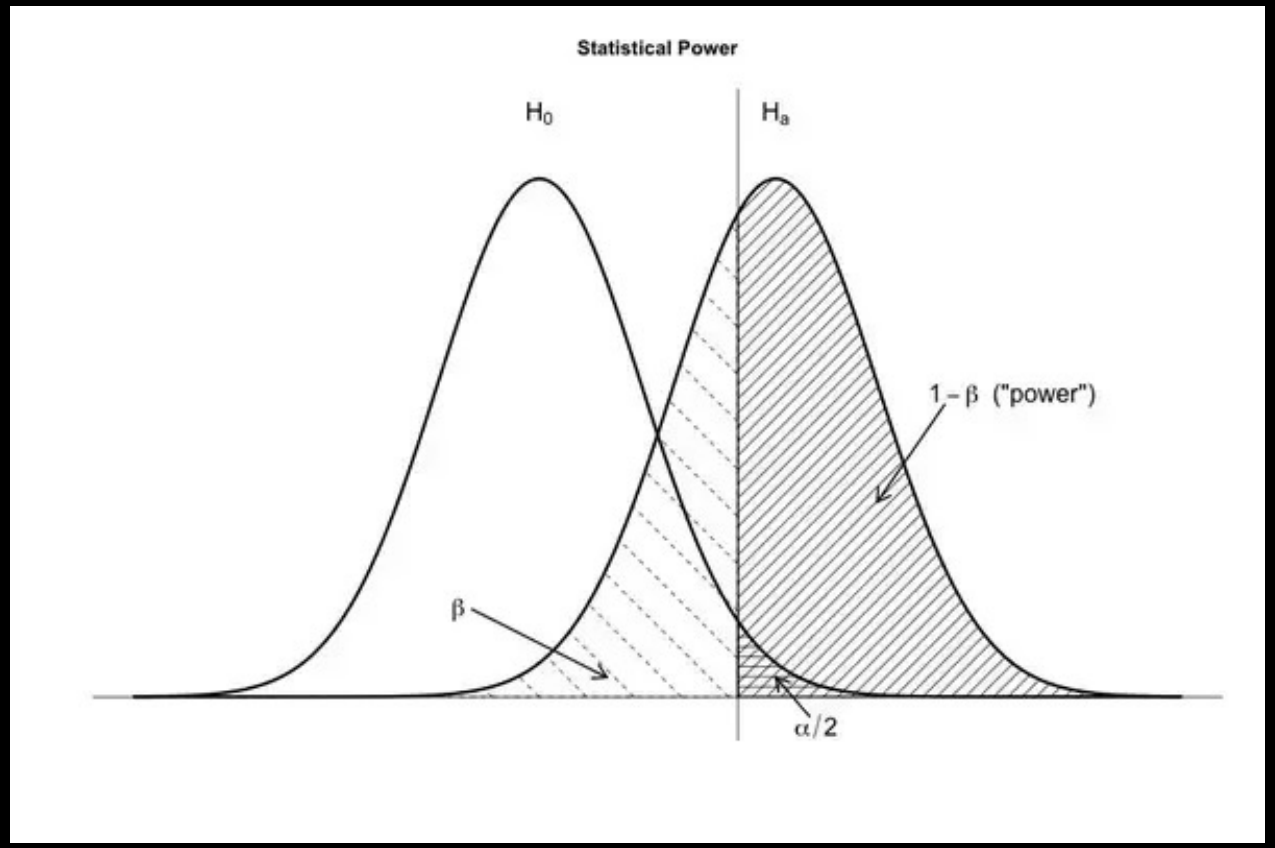
Each resource generates multiple designs

There is no best design; all efficiencies are relative!

Also need to consider whether the design “feels” right

Power Analysis

Remember this?



Power Analysis

Power analyses for behavioral studies are simpler:

Easier to recruit large N

Relatively inexpensive to run lots of subjects

Behavioral effects can be very strong

Power Analysis

Now for imaging studies:

More difficult to recruit large N (e.g., >50 per study)

Expensive to run lots of subjects ($500-$900 per hour)

Imaging effects can be very weak

Several sources of noise

Power Analysis

What happens during grant writing?

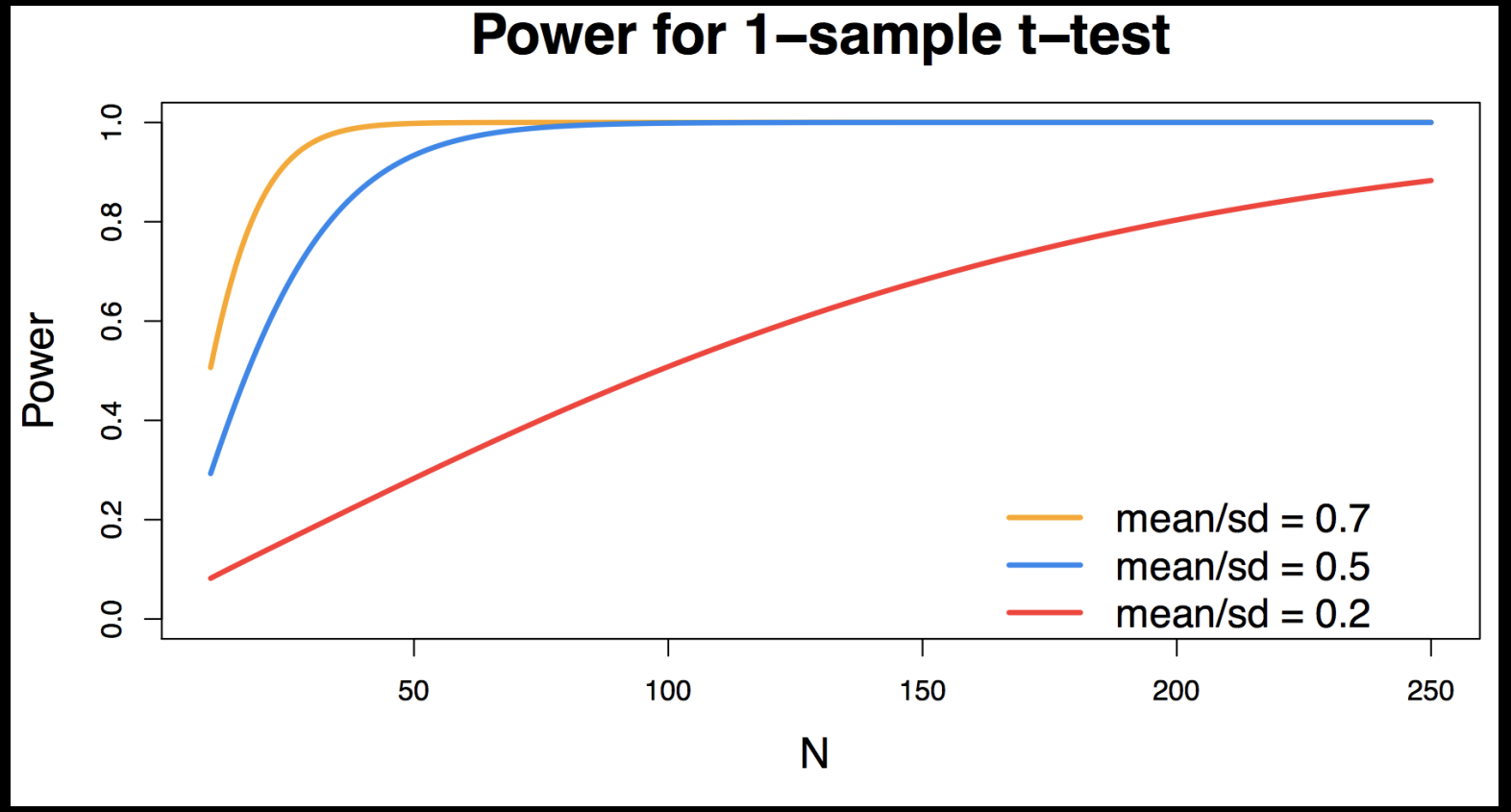
Becomes a hunt for 80% power

Most fMRI studies won't have this kind of power,
for the reasons listed above

Does that mean we shouldn't even do it in the first place?

Power Analysis

What are reasonable ranges for power, given effect size?



Power Analysis

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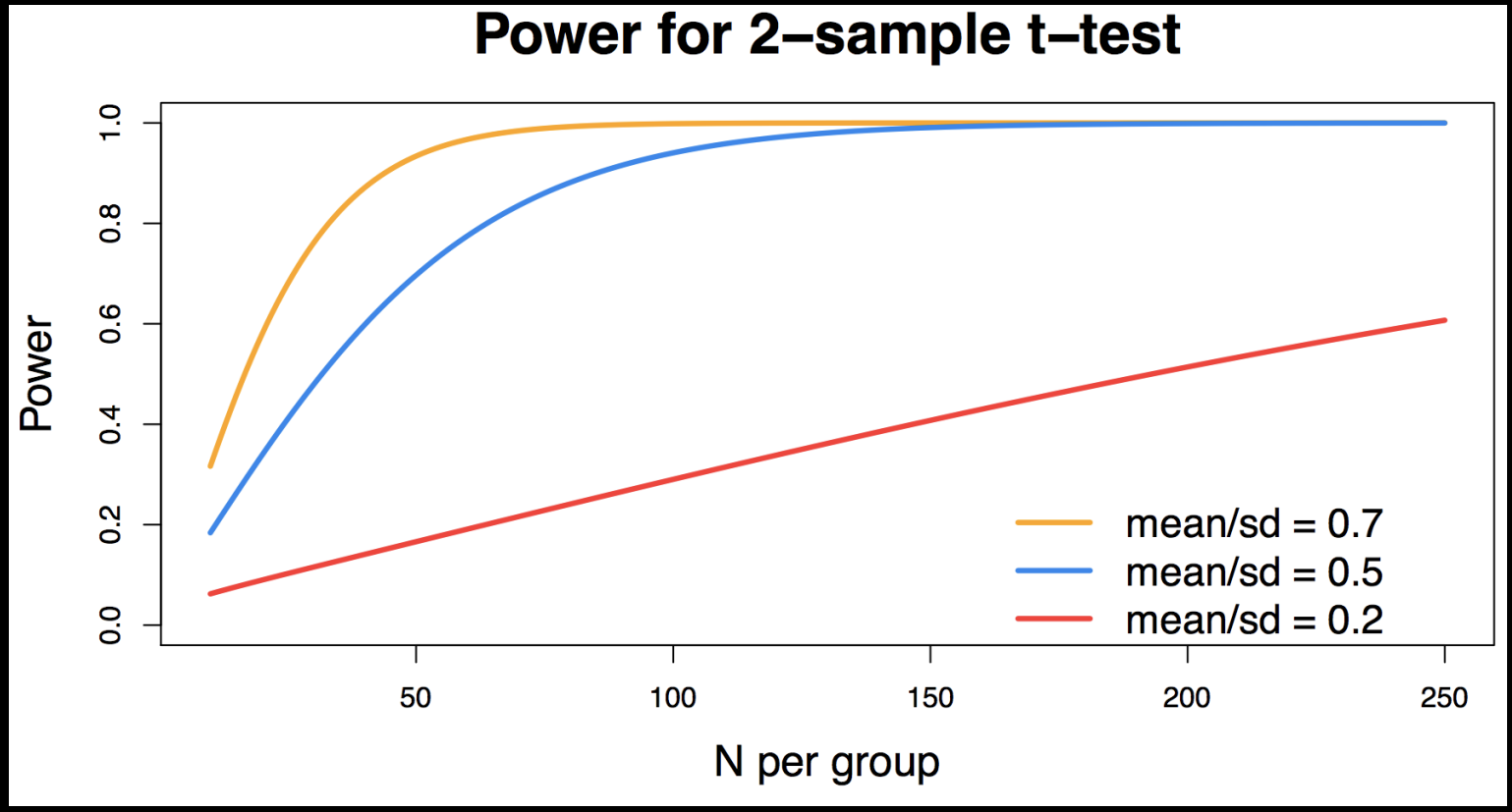

Power Analysis

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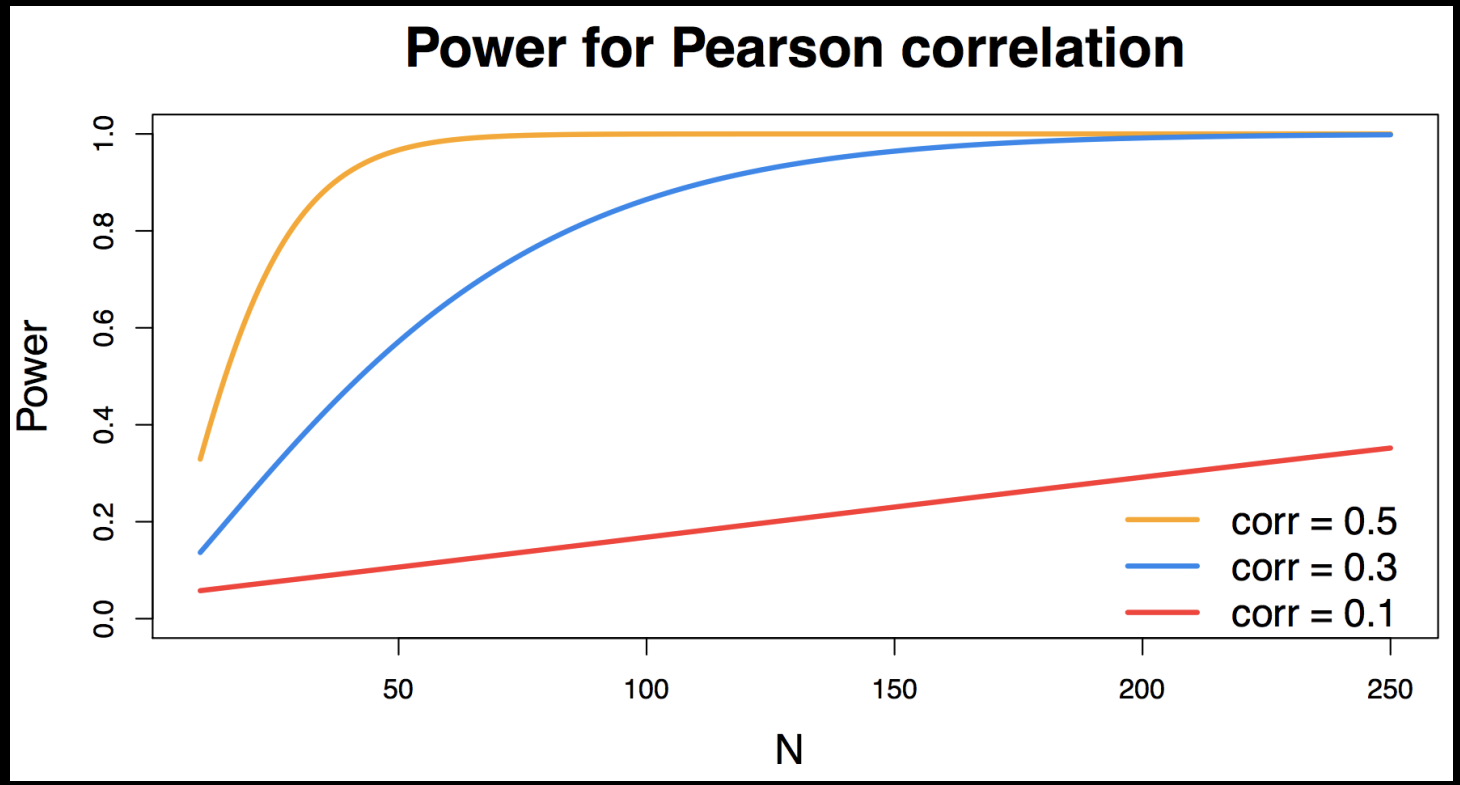
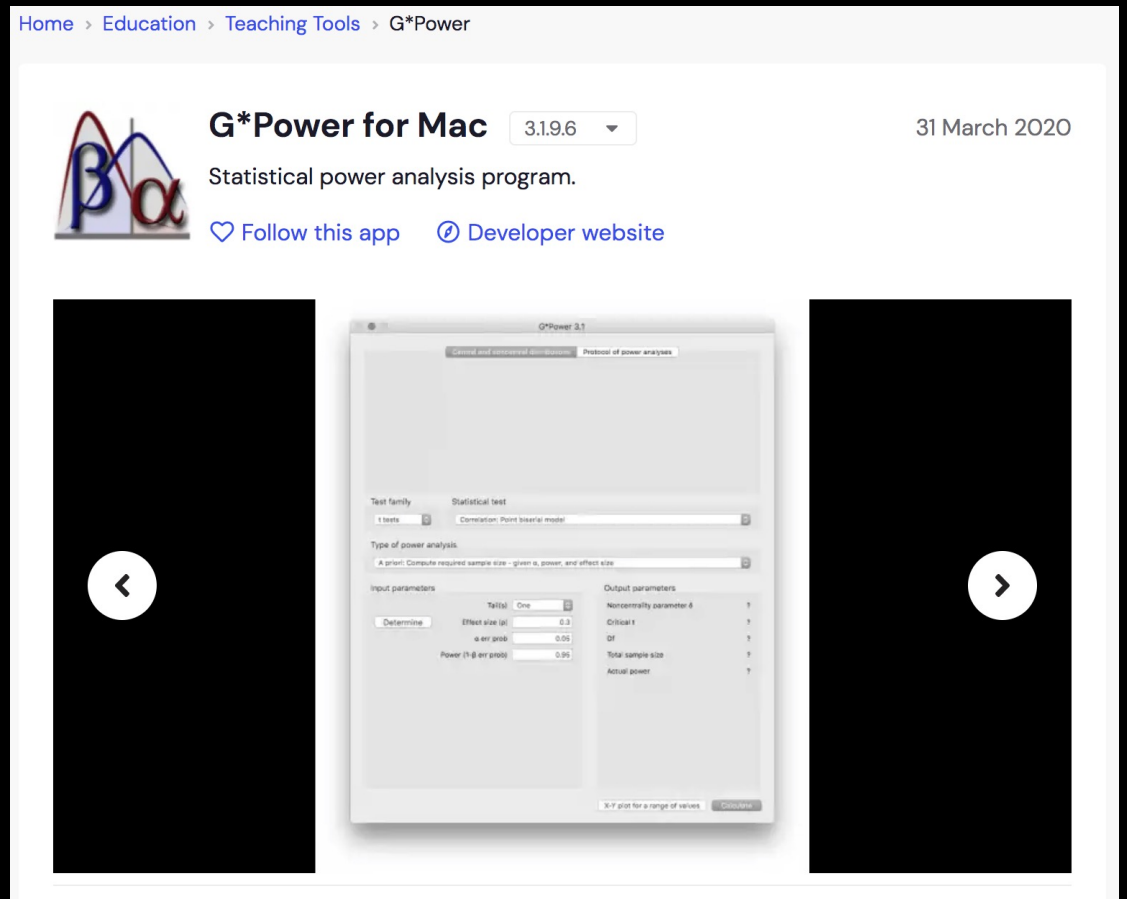
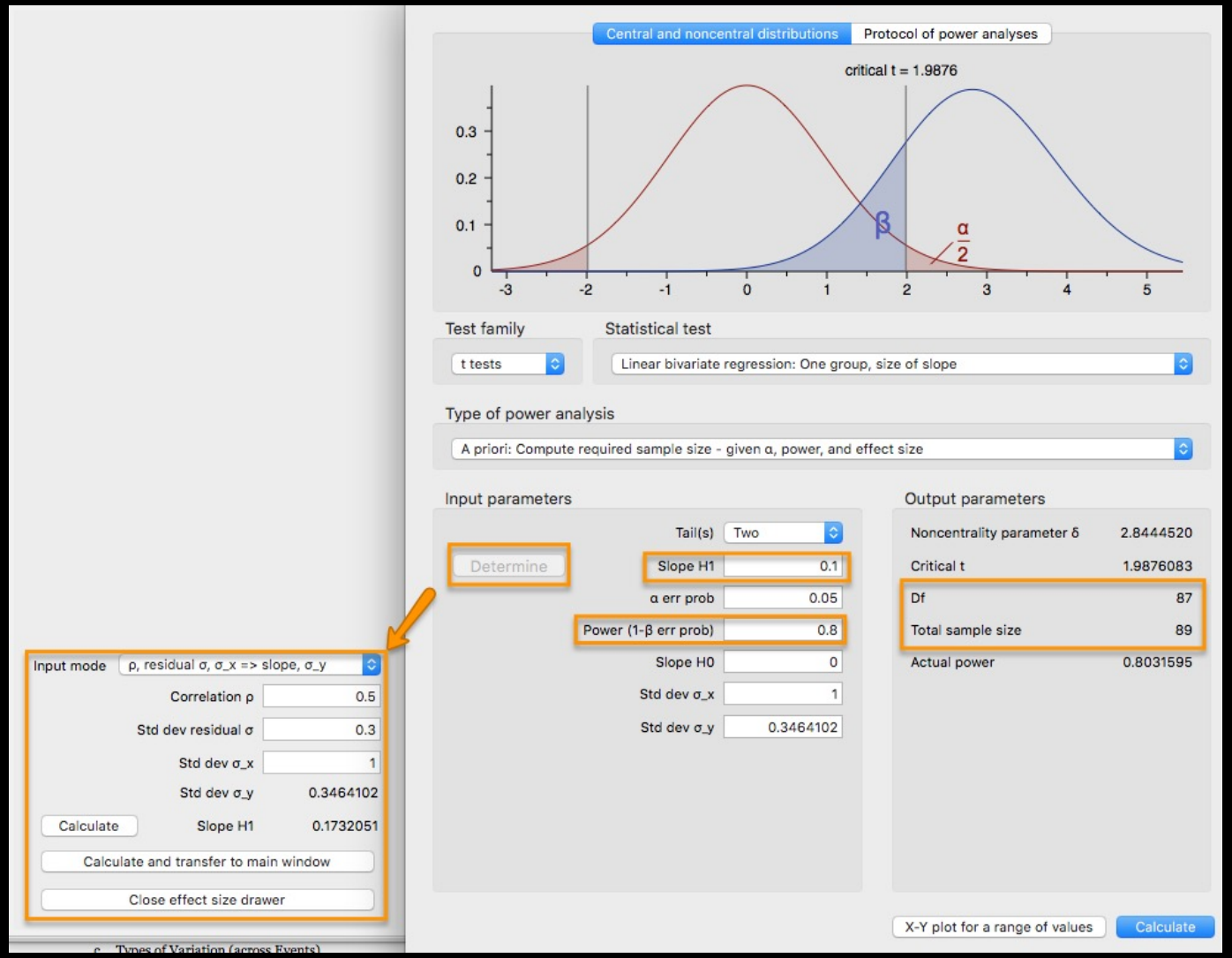


Power Analysis

What is the best way to estimate power?



Power Analysis



Power Analysis

What about estimating power from another published study?

Keep in mind that only significant results are usually published; this may just contribute to the file drawer problem (to be discussed more on Tuesday)

Power Analysis

What about calculating power after a study is run? (e.g., post-hoc power analysis?)

This is a statistical fallacy, since the null hypothesis has already been either rejected or not rejected; there is no "power" to calculate!

Power Analysis

Statistical Practice

The Abuse of Power: The Pervasive Fallacy of Power Calculations for Data Analysis

John M. HOENIG and Dennis M. HEISEY

It is well known that statistical power calculations can be valuable in planning an experiment. There is also a large literature advocating that power calculations be made whenever one performs a statistical test of a hypothesis and one obtains a statistically nonsignificant result. Advocates of such post-experiment power calculations claim the calculations should be used to aid in the interpretation of the experimental results. This approach, which appears in various forms, is fundamentally flawed. We document that the problem is extensive and present arguments to demonstrate the flaw in the logic.

culations as a matter of policy (Anon. 1995; Anon. 1998). We emphasize that these calculations are sought primarily with the thought that they are useful for explaining the observed data, rather than for the purpose of planning some future experiment. We even found statistical textbooks that illustrate the flawed approach (e.g., Rosner 1990; Winer, Brown, and Michels 1991; Zar 1996). Researchers need to be made aware of the shortcomings of power calculations as data analytic tools and taught more appropriate methodology.

It is important to understand the motivation of applied scientists for using power analysis to interpret hypothesis tests with nonsignificant results. The traditional, widely ac-

Power Analysis

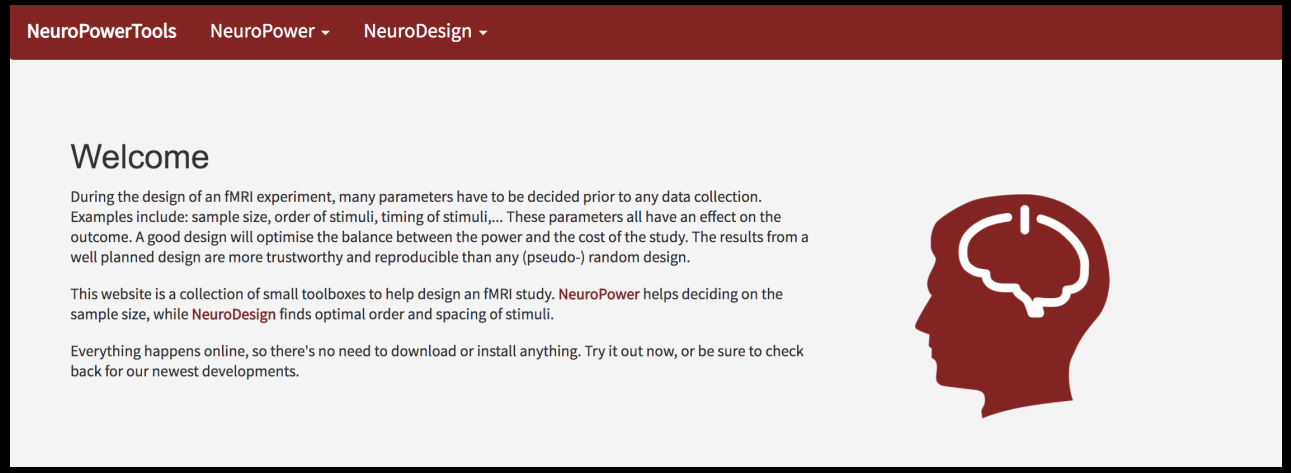
Tools for power analysis

Fmripower

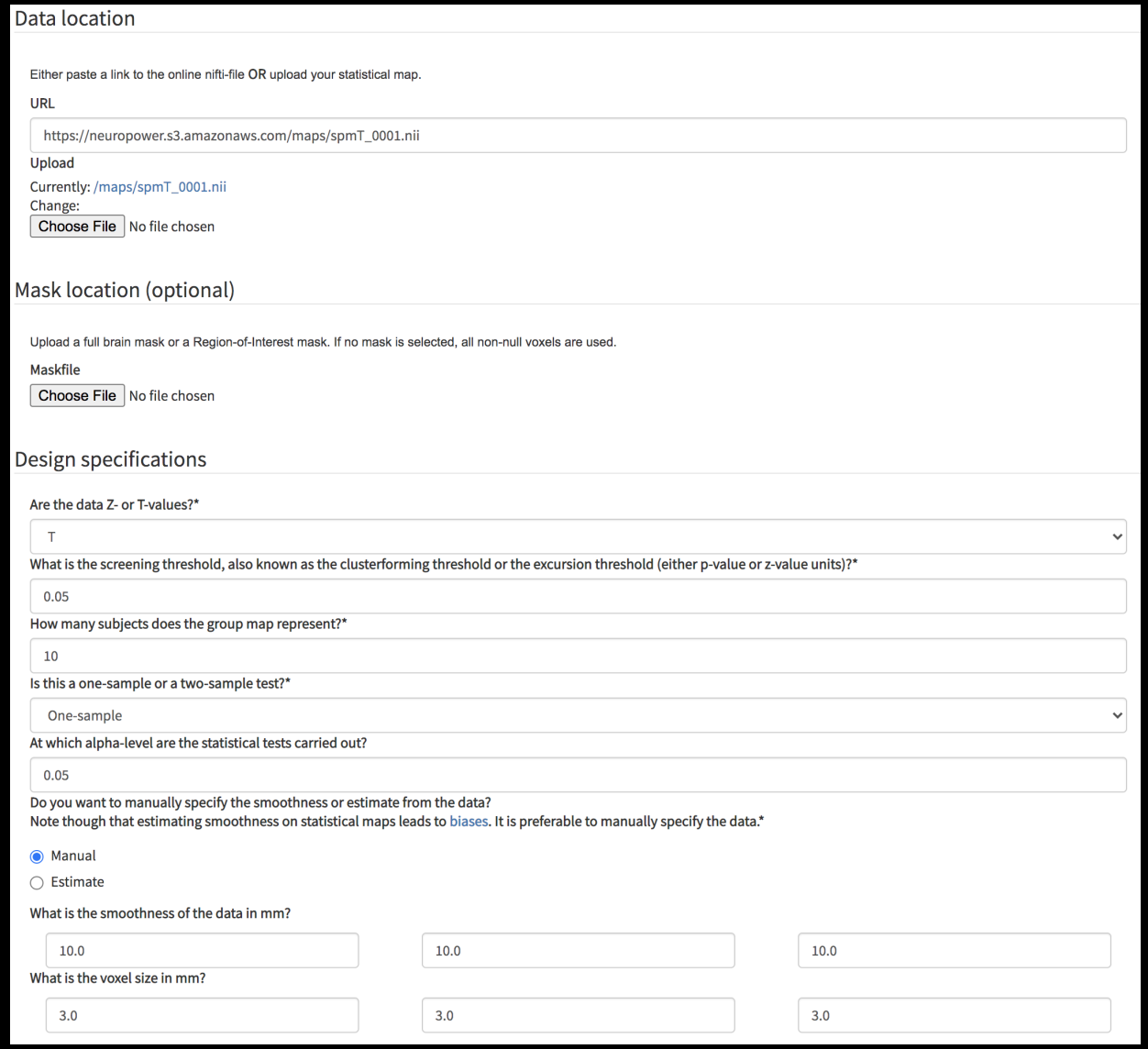
What happened to the fmripower tool?

The fMRIPower tool hit old age and was starting to have quite a few issues. I have chosen to replace the tool with a set of instructions so you can carry out power analyses on your own. I will post that information soon! In a nutshell, all you really need to do is perform an ROI analysis, get your effect size and carry out a power analyis using that effect size. Of course, don't forget, you must use an a priori ROI. I realize it is super frustrating, but you cannot use the ROI that was active in the same data set from which you are running the power analysis.

Hopefully that's enough for now, but I will make a video and blog post with instructions soon.



Power Analysis



Power Analysis

NeuroPowerTools NeuroPower NeuroDesign

OVERVIEW START PEAK TABLE MODEL FIT POWER CALCULATION POWER TABLE RESET

There is not enough power to estimate a threshold for BH.

Power

To see the power for a certain sample size or vice versa, please fill out either the minimal power or the sample size.

MCP*

Random Field Theory

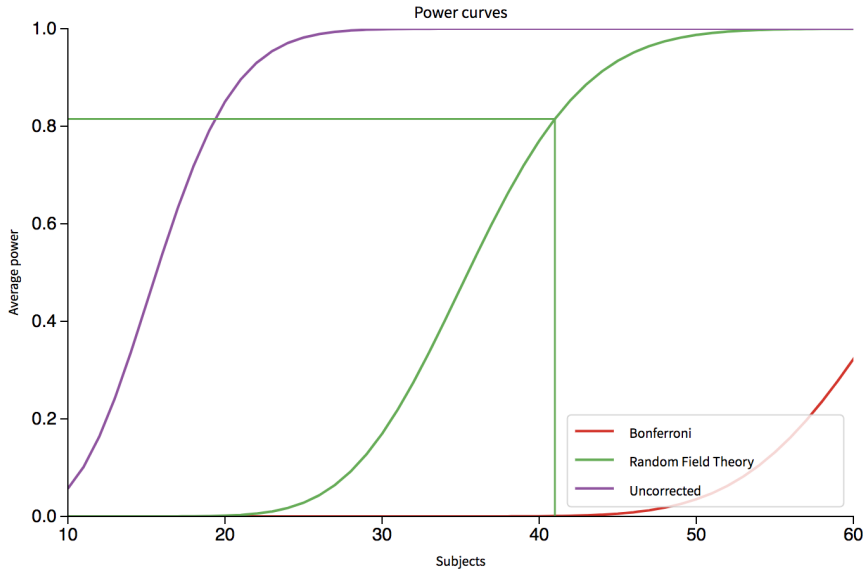
Sample size

Power

.8

Submit parameters

Hover over the lines to see detailed power predictions



save svg

To obtain a statistical power of 0.8 this study would require a sample size of 41 subjects.

Power Analysis

When evaluating a power analysis, make sure that the estimates seem to fall within reasonable bounds, and that the parameters were clearly defined

Questions?

Group-Level Analysis

Once we have estimated a model for each individual subject (1st-level analysis), we combine them into a 2nd-level analysis

In SPM: Usually focus on just the mean of the parameter estimate; variance is discarded at the group level

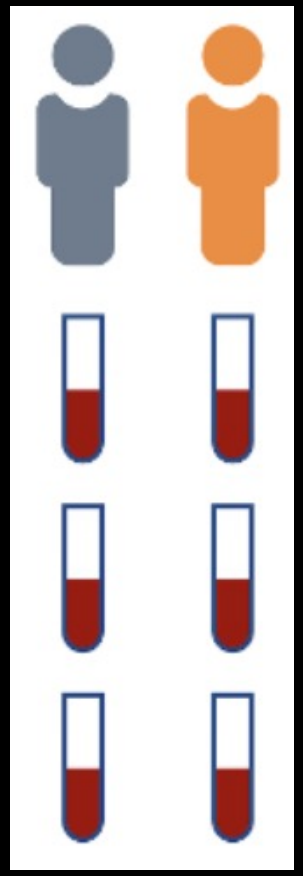
Group-Level Analysis

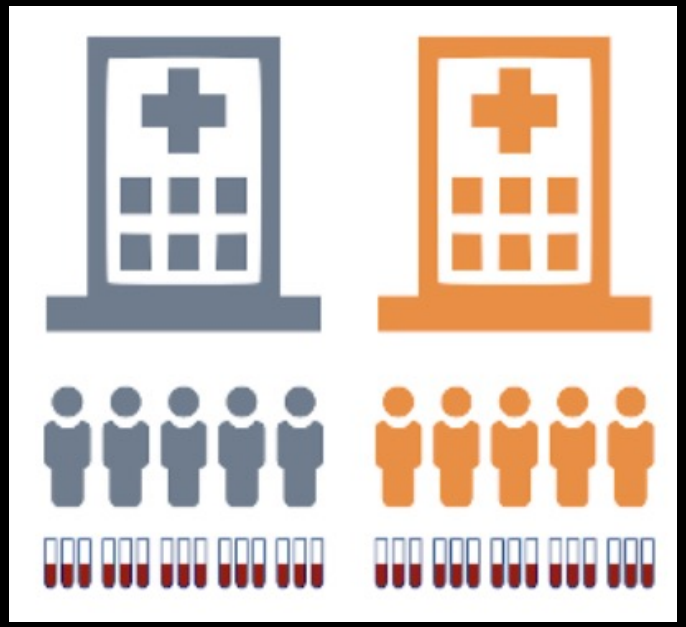
N.B.: The way that betas are calculated in the 1st-level is different than how they are estimated at the 2nd-level

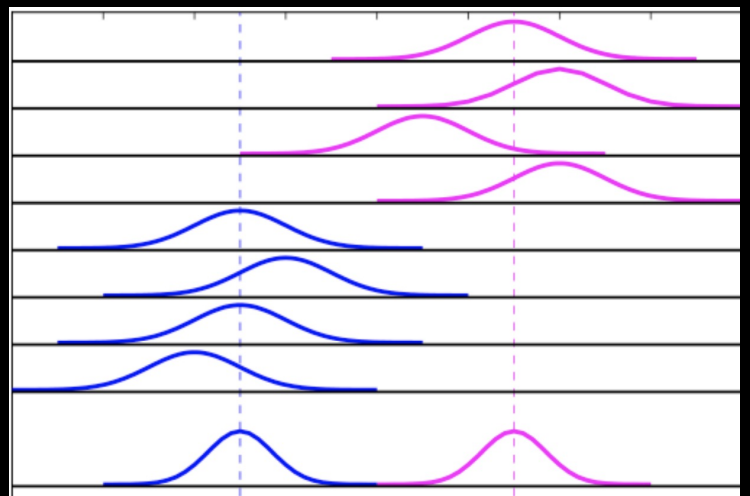
The difference can be expressed as "Fixed-Effects" vs. "Random-Effects"

Combining both generates "Mixed-Effects"

Group-Level Analysis

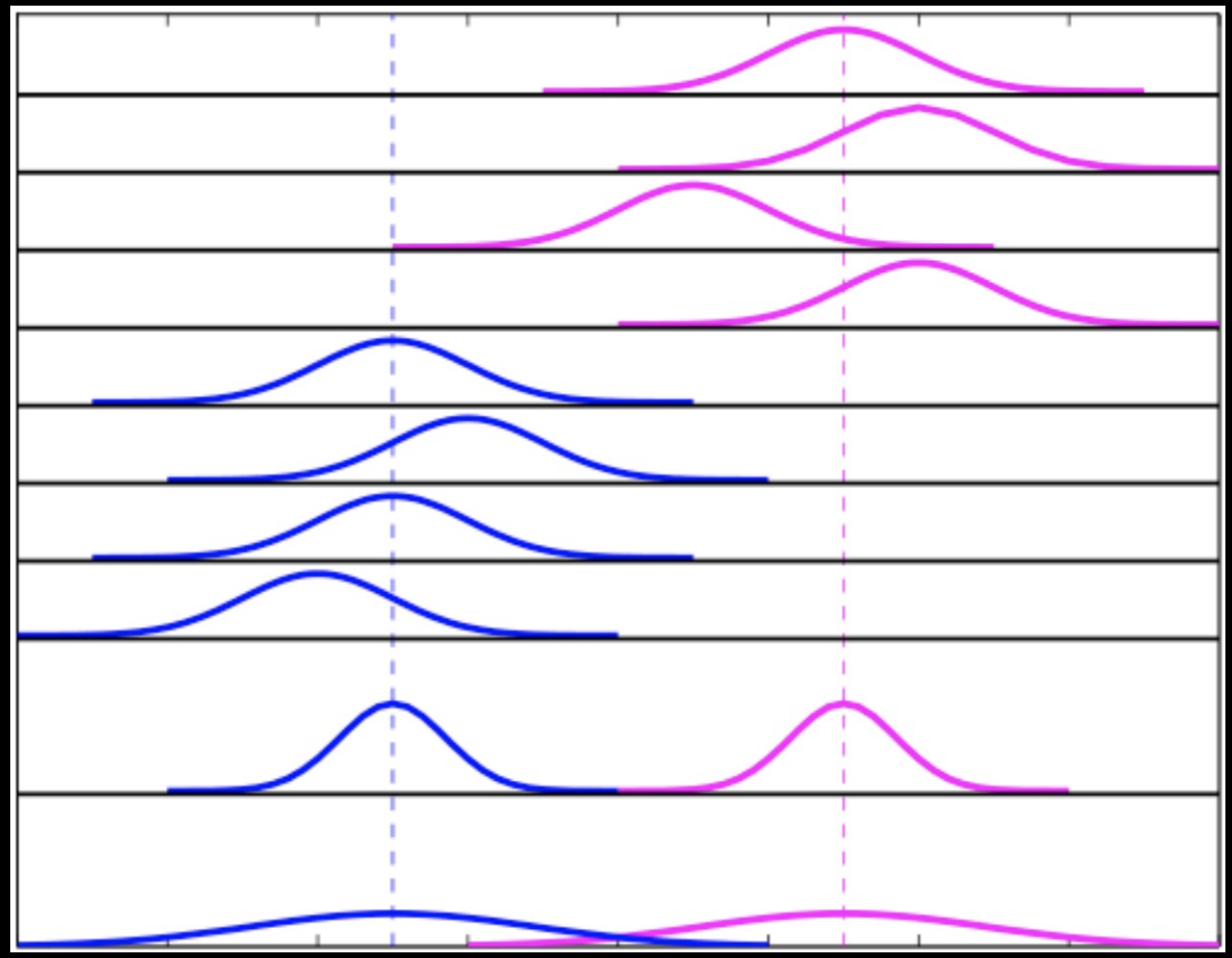






Fixed Effects

Group-Level Analysis



Fixed Effects

Mixed Effects

Group-Level Analysis

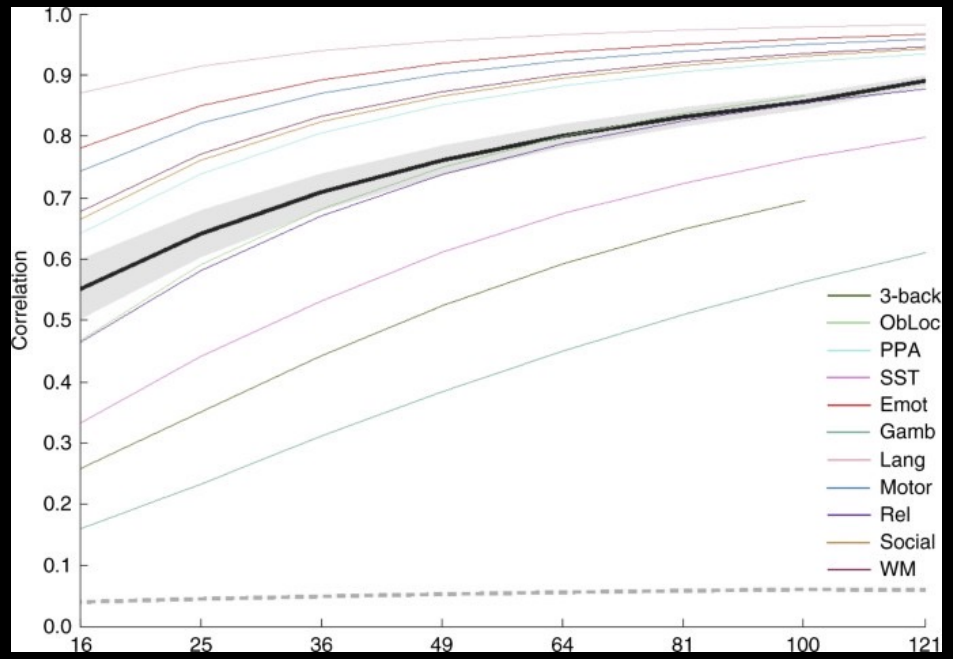
Summary: Fixed Effects applies only to the subjects you sampled

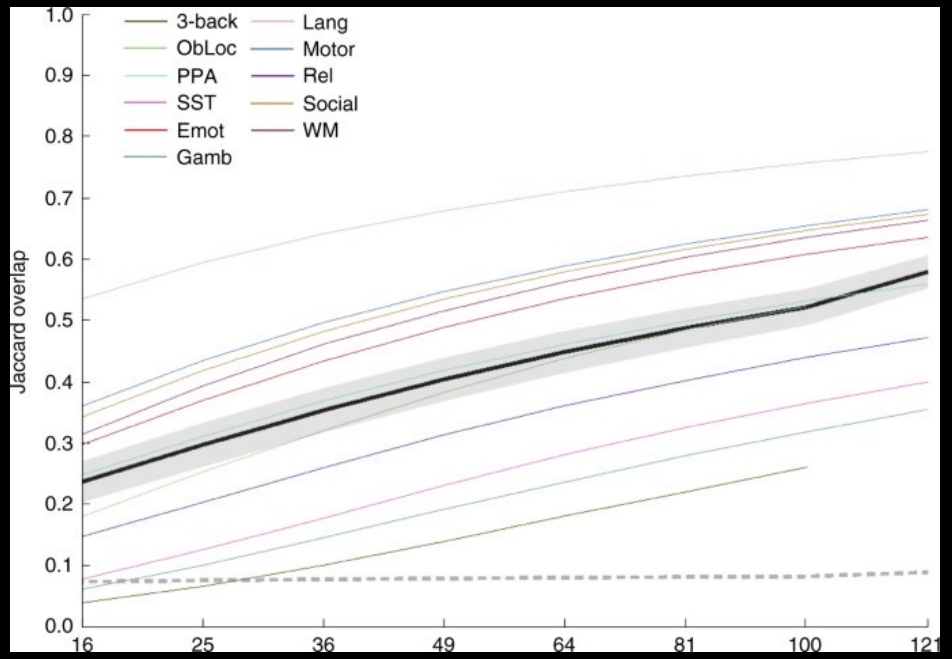
Random effects assumes that the subjects were randomly sampled from the population, and that you're trying to make an inference about the population (i.e., parameters)

Mixed effects combines the two

Question: To reduce overall variance, should we collect more samples, or more subjects?

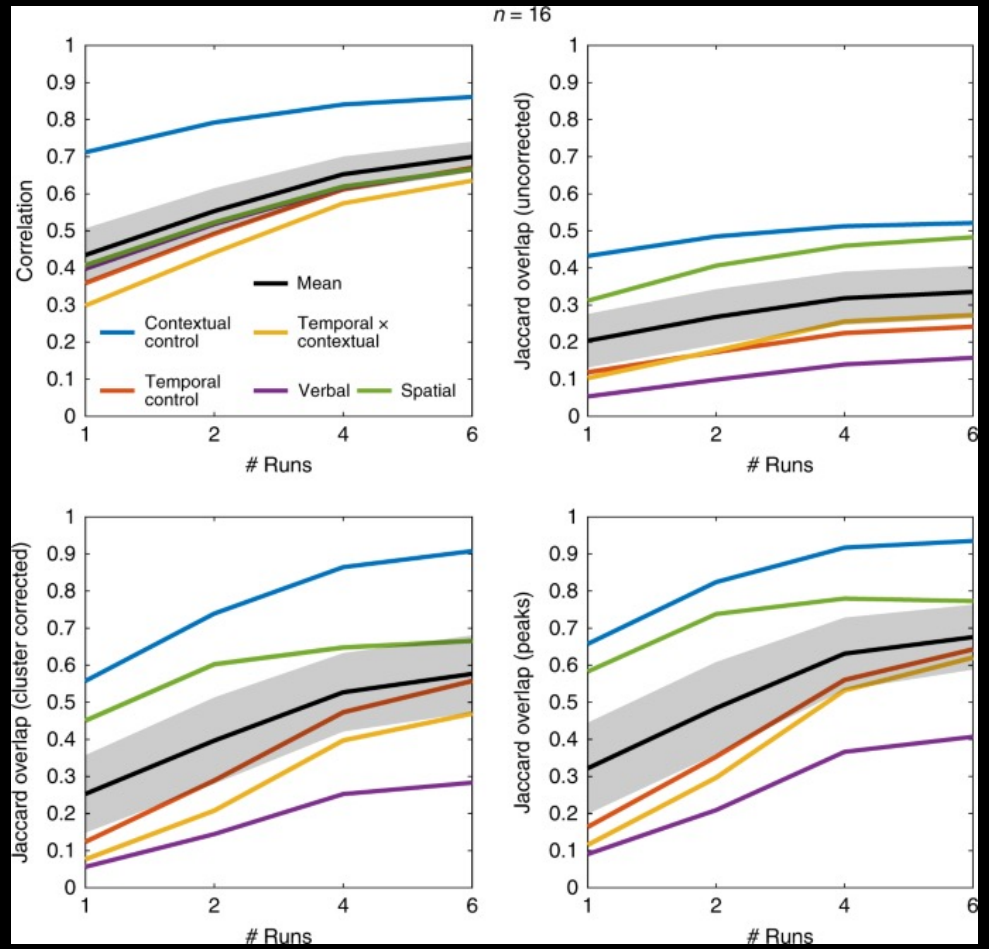
Group-Level Analysis

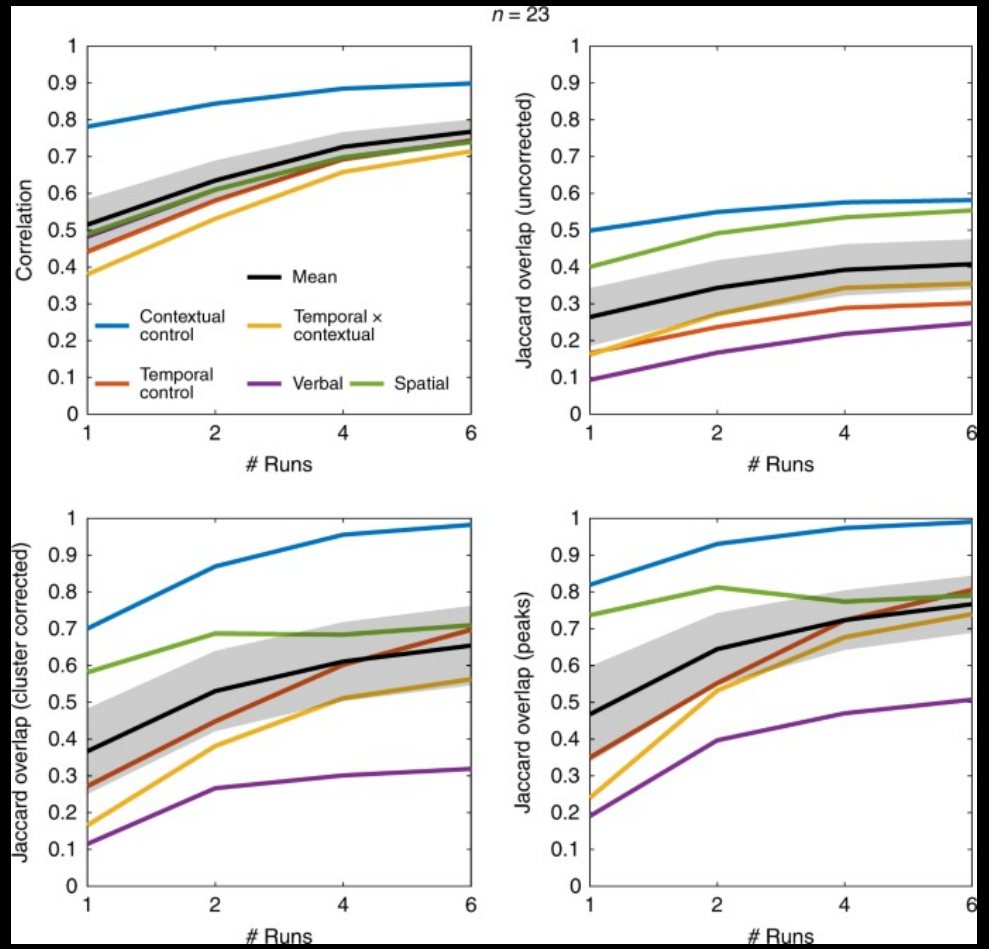




Turner et al., 2018

Group-Level Analysis





Nee, 2019

Group-Level Analysis

Simplest model: 1-sample t-test

A parameter estimate (or contrast of parameter estimates, also called a contrast estimate) is submitted to a t-test

Is the average of the parameter (or contrast) estimates significantly different from zero?

Group-Level Analysis

However, this typically isn't very interesting

Since fMRI signal is arbitrary, it is more useful
to contrast one condition to another

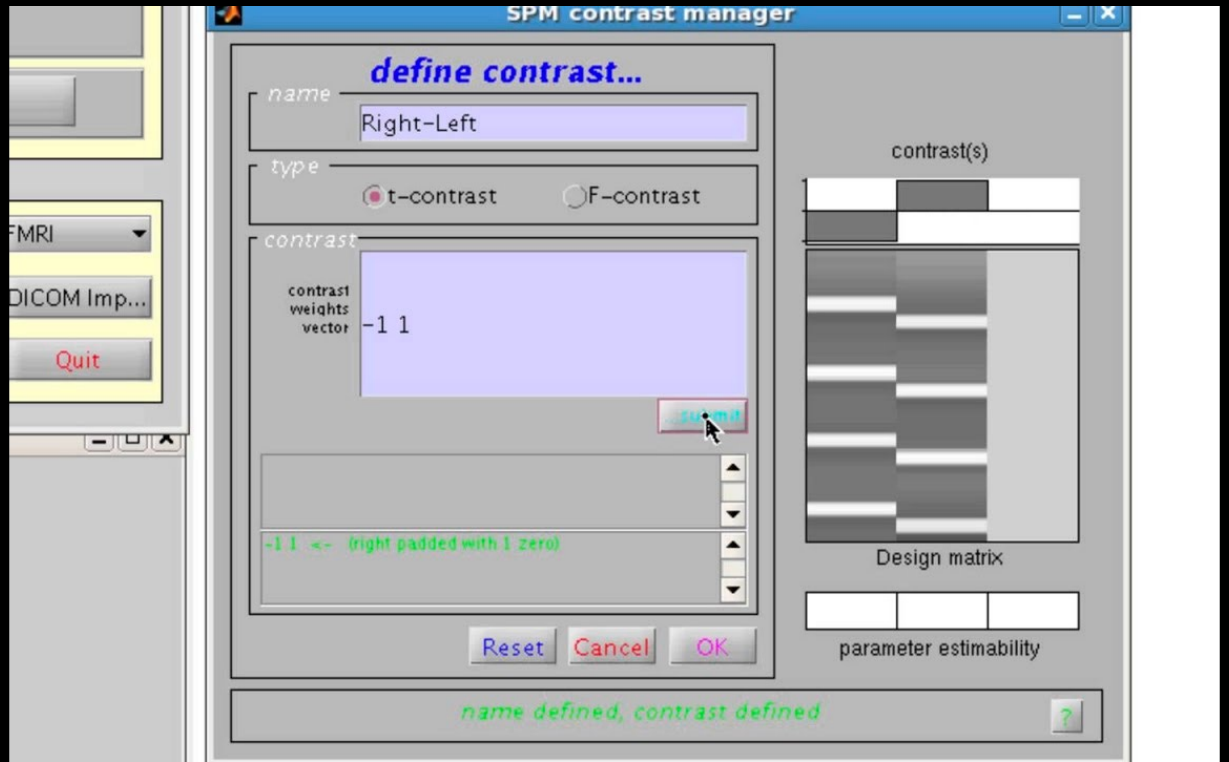
You can then run a one-sample t-test on this contrast
(to be discussed in a little bit)

Group-Level Analysis

e.g., button presses

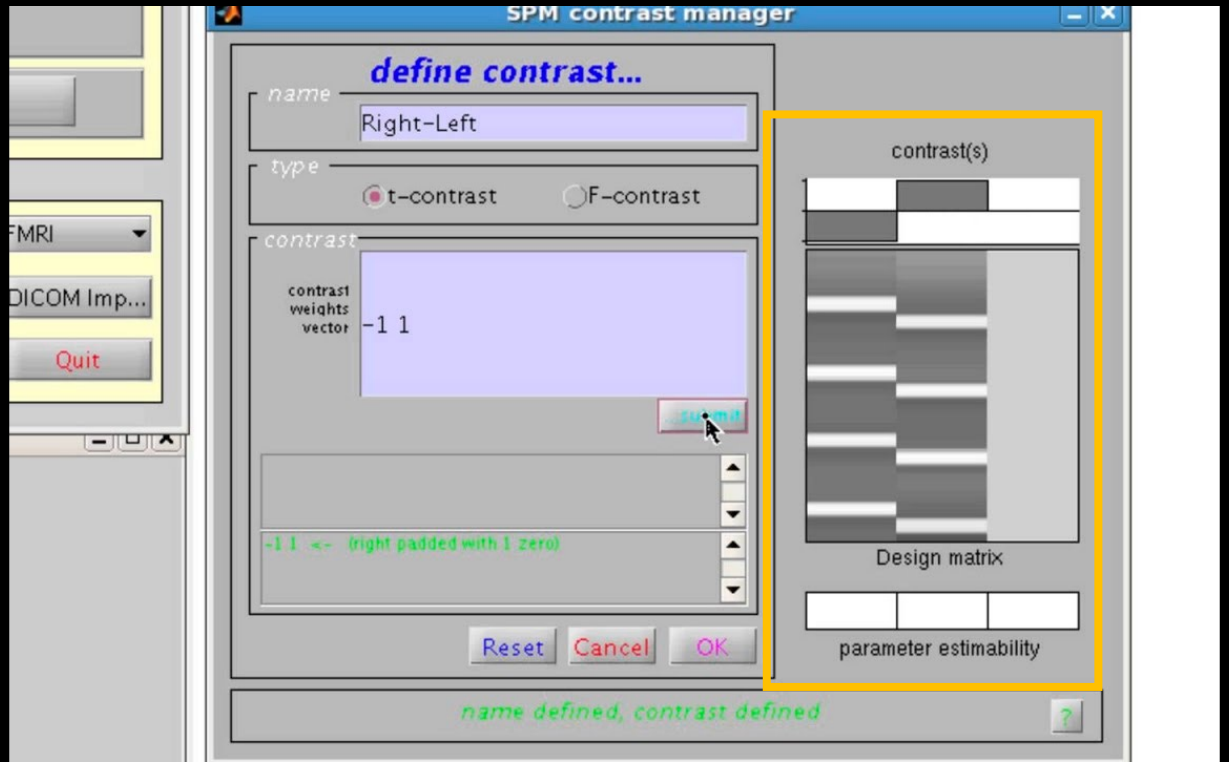
Group-Level Analysis

Very simple contrast (and useful to check whether your timings are correct!)



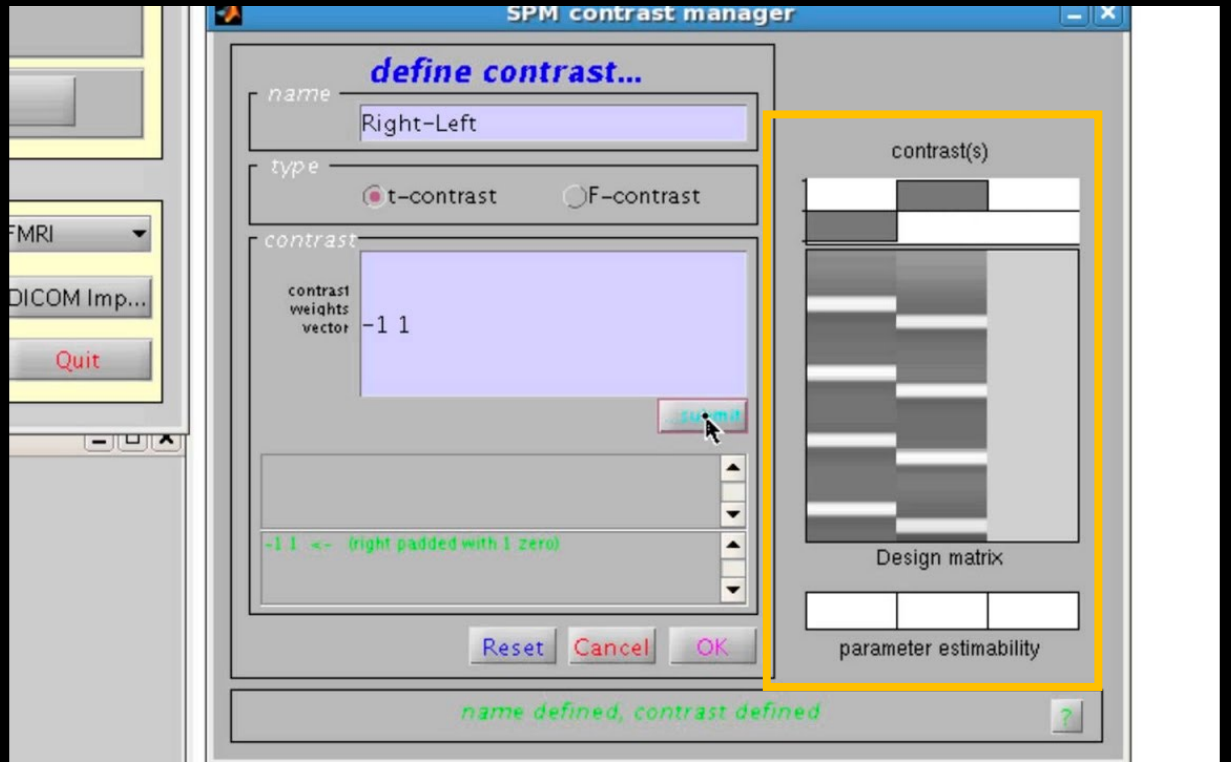
Group-Level Analysis

What is this?



Group-Level Analysis

How you specify the contrast weights depends on the order of the regressors

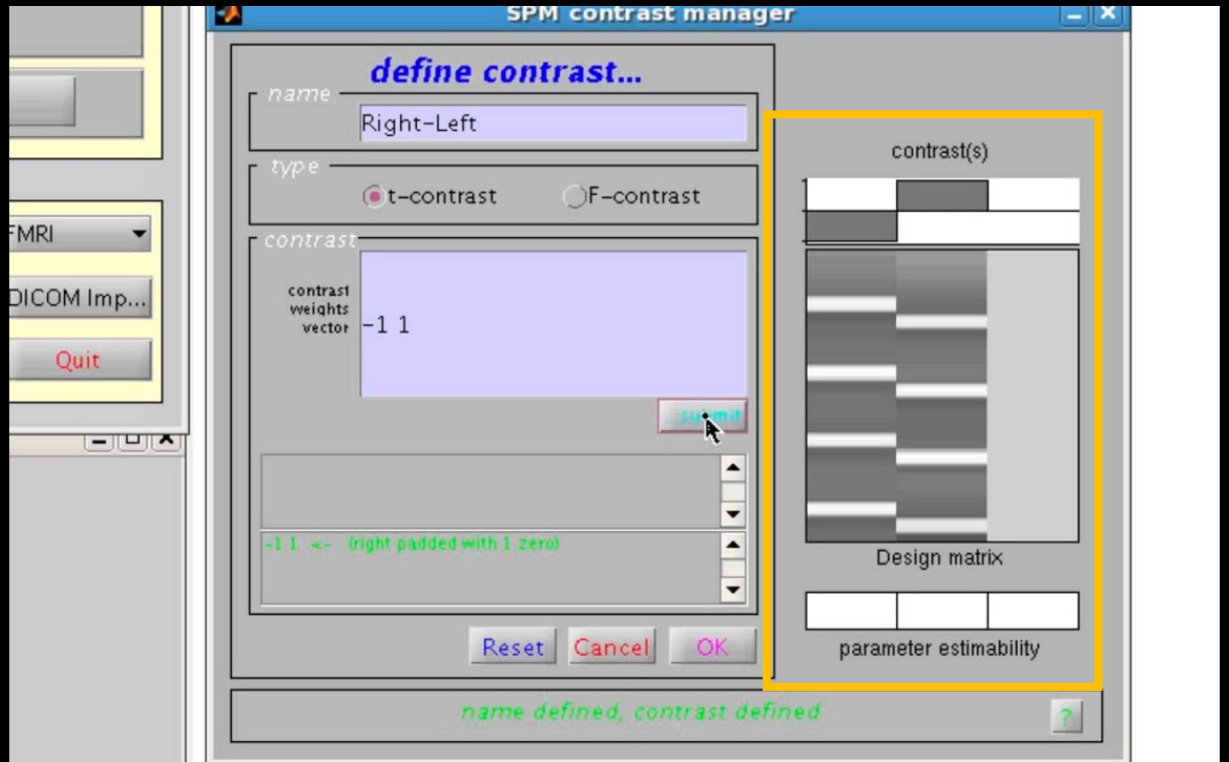


c = [-1 1]

Group-Level Analysis

In this example: Left was first, Right was second

How would I specify the contrast of Left-Right?



c = [-1 1]

Group-Level Analysis

In a group-level context

One-sample:

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_N \end{bmatrix} = \begin{bmatrix} \beta_0 \\ \beta_0 \\ \vdots \\ \beta_0 \end{bmatrix} + \epsilon$$

Group-Level Analysis

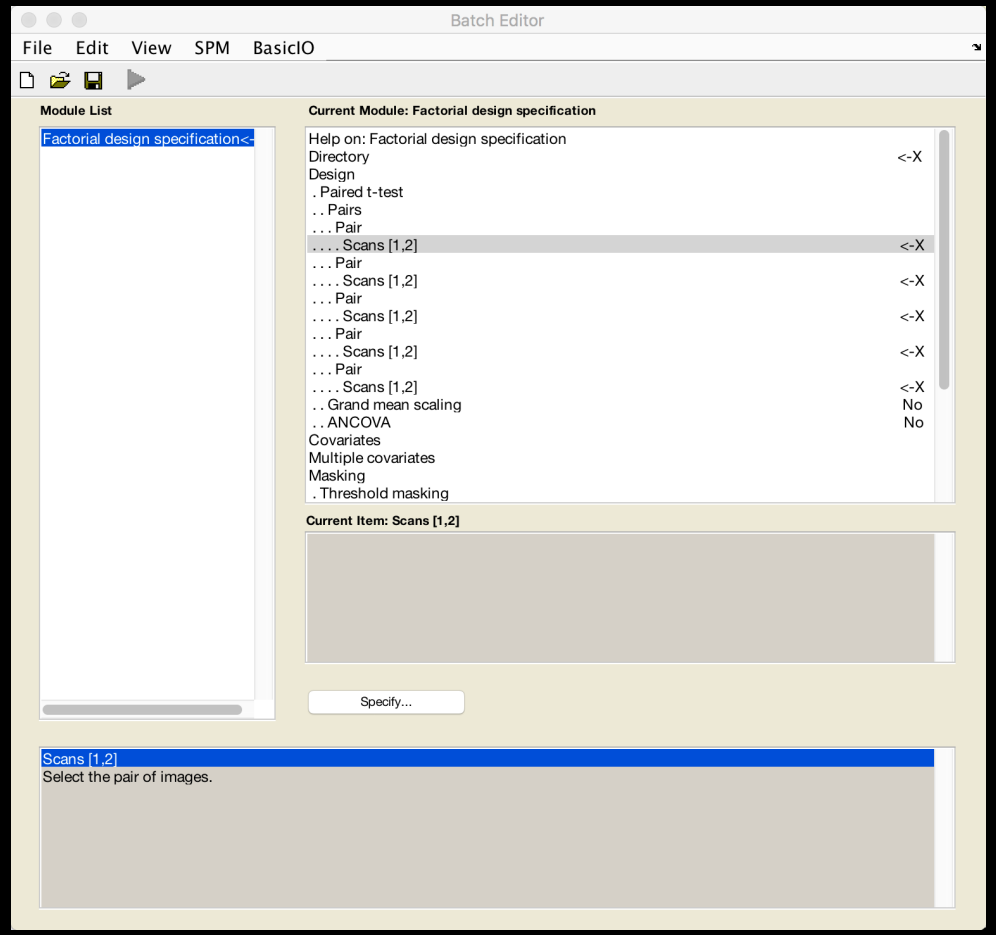
In a group-level context

Two-sample:

$$\begin{bmatrix} Y_1 \\ Y_2 \\ Y_3 \\ Y_4 \\ Y_5 \\ Y_6 \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} + \epsilon$$

Group-Level Analysis

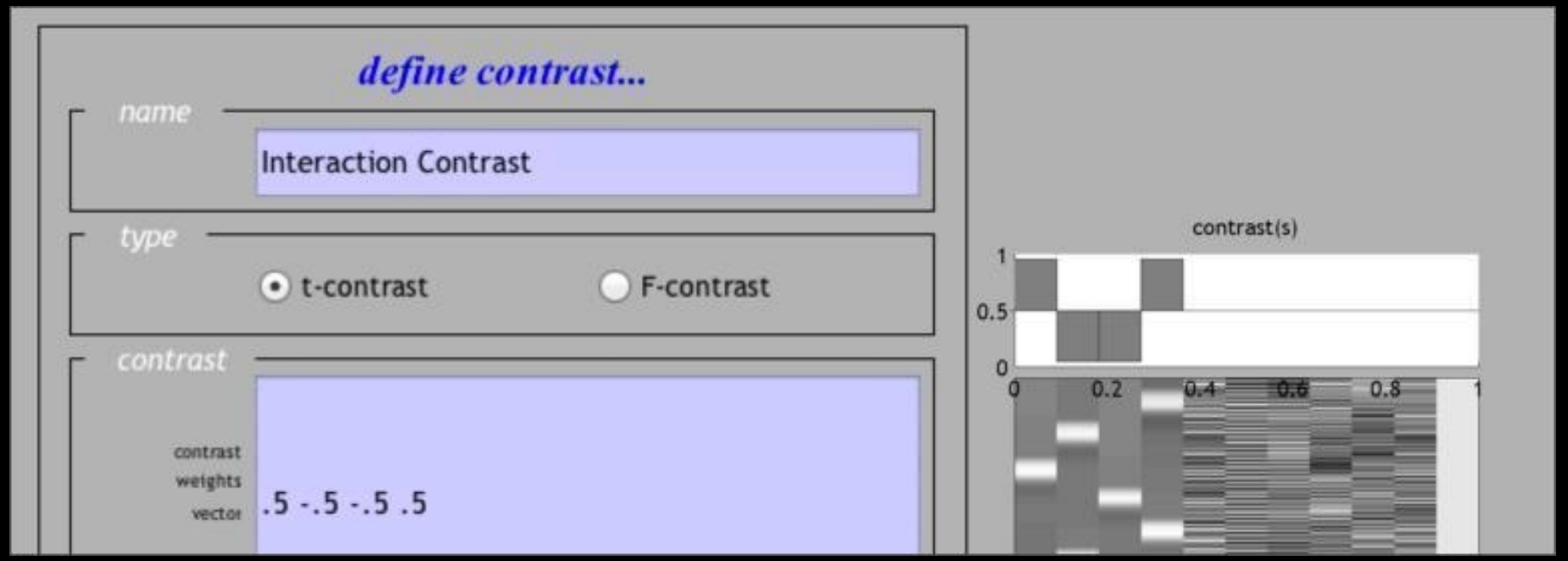
What about a paired t-test?



Group-Level Analysis

What about an interaction?

If each subjects has two conditions (A,B) with two levels (1,2) then you can do the following contrast:



Group-Level Analysis

What if we perform a one-sample t-test on contrasts?

e.g., calculate A-B for each of 10 subjects, to create 10 contrasts

Is this valid?

Summary Statistics

The above is called a “summary statistics” approach

Valid if the intra-subject variabilities are relatively similar across subjects

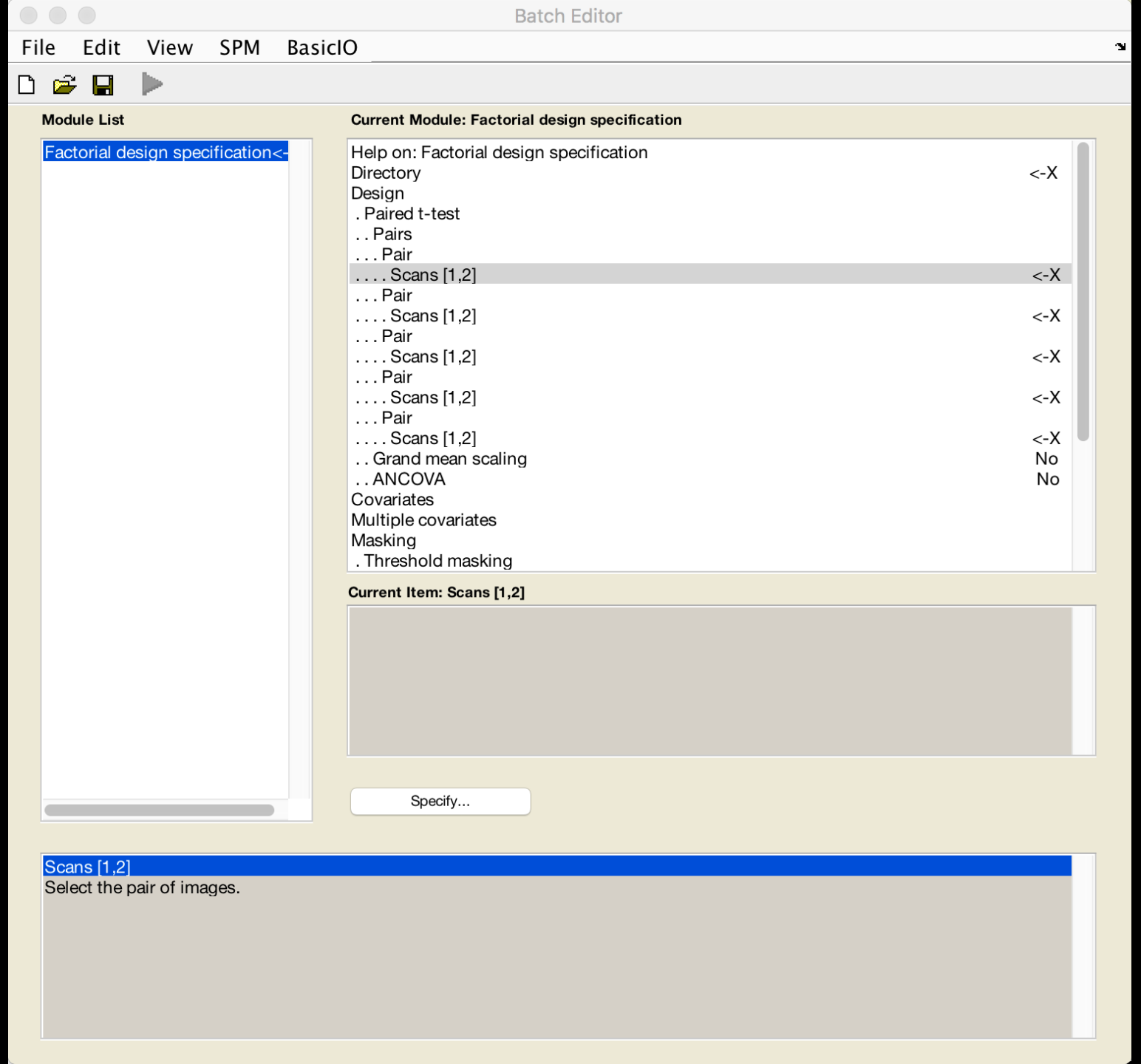
For most studies, this assumption is true
(Penny & Holmes, 2004)

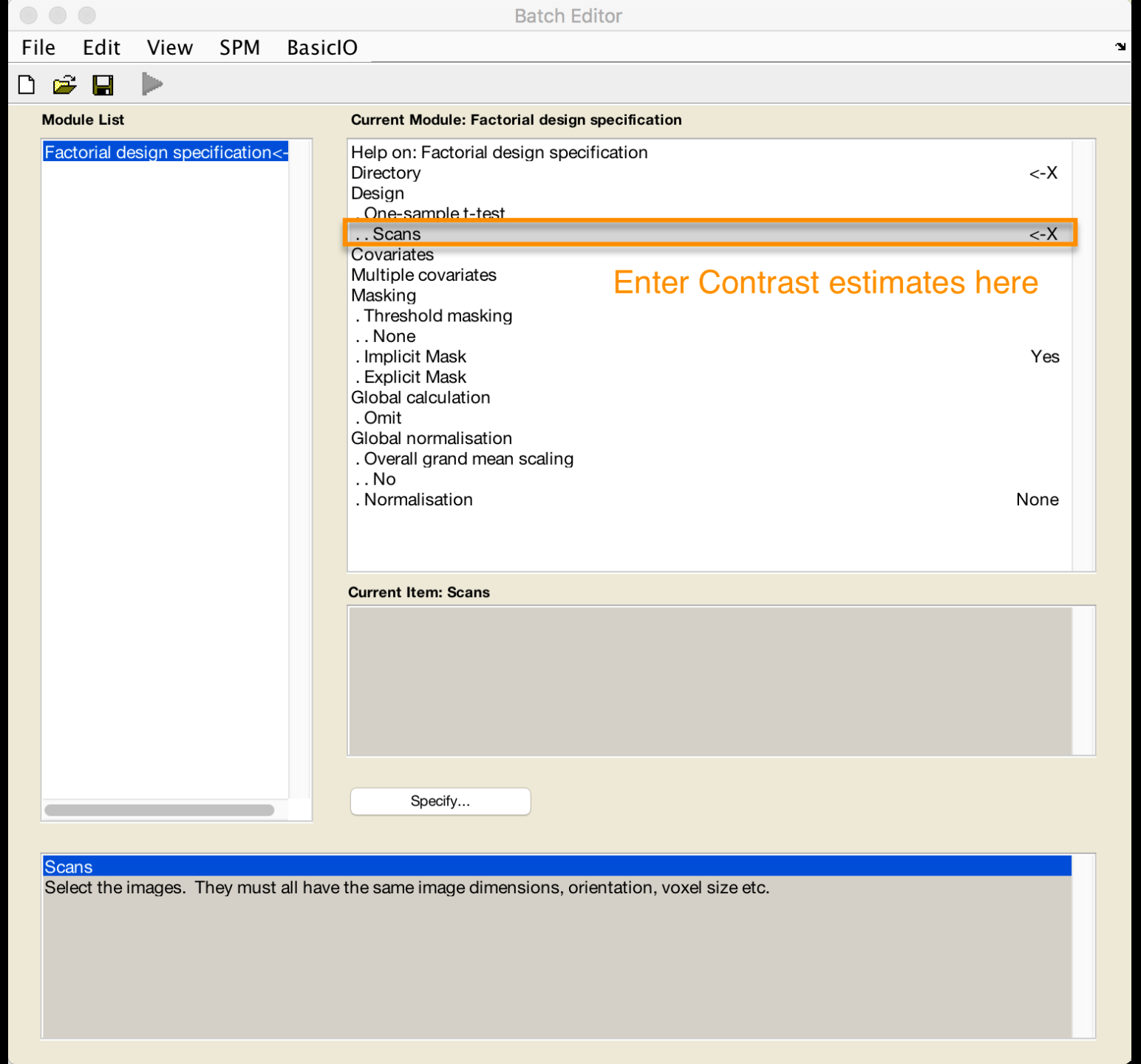
Summary Statistics

Pros: Easy to implement, simplifies interactions

Cons: Assumptions may not be valid; check whether the variance and number of runs is similar for each subject

Example: Using Summary Statistics to run a one-sample t-test on an interaction term


Batch Editor
File
Edit
View
SPM
BasicIO
Module List
Factorial design specification<-
Current Module: Factorial design specification
Help on: Factorial design specification
Directory <-X
Design
. Paired t-test
. . Pairs
. . . Pair
. . . . Scans [1,2] <-X
. . . Pair
. . . . Scans [1,2] <-X
. . . Pair
. . . . Scans [1,2] <-X
. . . Pair
. . . . Scans [1,2] <-X
. . . Pair
. . . . Scans [1,2] <-X
. . Grand mean scaling No
. . ANCOVA No
Covariates
Multiple covariates
Masking
. Threshold masking
Current Item: Scans [1,2]
Specify...
Scans [1,2]
Select the pair of images.


Batch Editor
File Edit View SPM BasicIO
Module List
Factorial design specification<-
Current Module: Factorial design specification
Help on: Factorial design specification
Directory <-X
Design
. One-sample t-test
. . Scans <-X
Covariates
Multiple covariates
Masking
. Threshold masking
. . None
. Implicit Mask Yes
. Explicit Mask
Global calculation
. Omit
Global normalisation
. Overall grand mean scaling
. . No
. Normalisation None
Enter Contrast estimates here
Current Item: Scans
Specify...
Scans
Select the images. They must all have the same image dimensions, orientation, voxel size etc.

F-tests

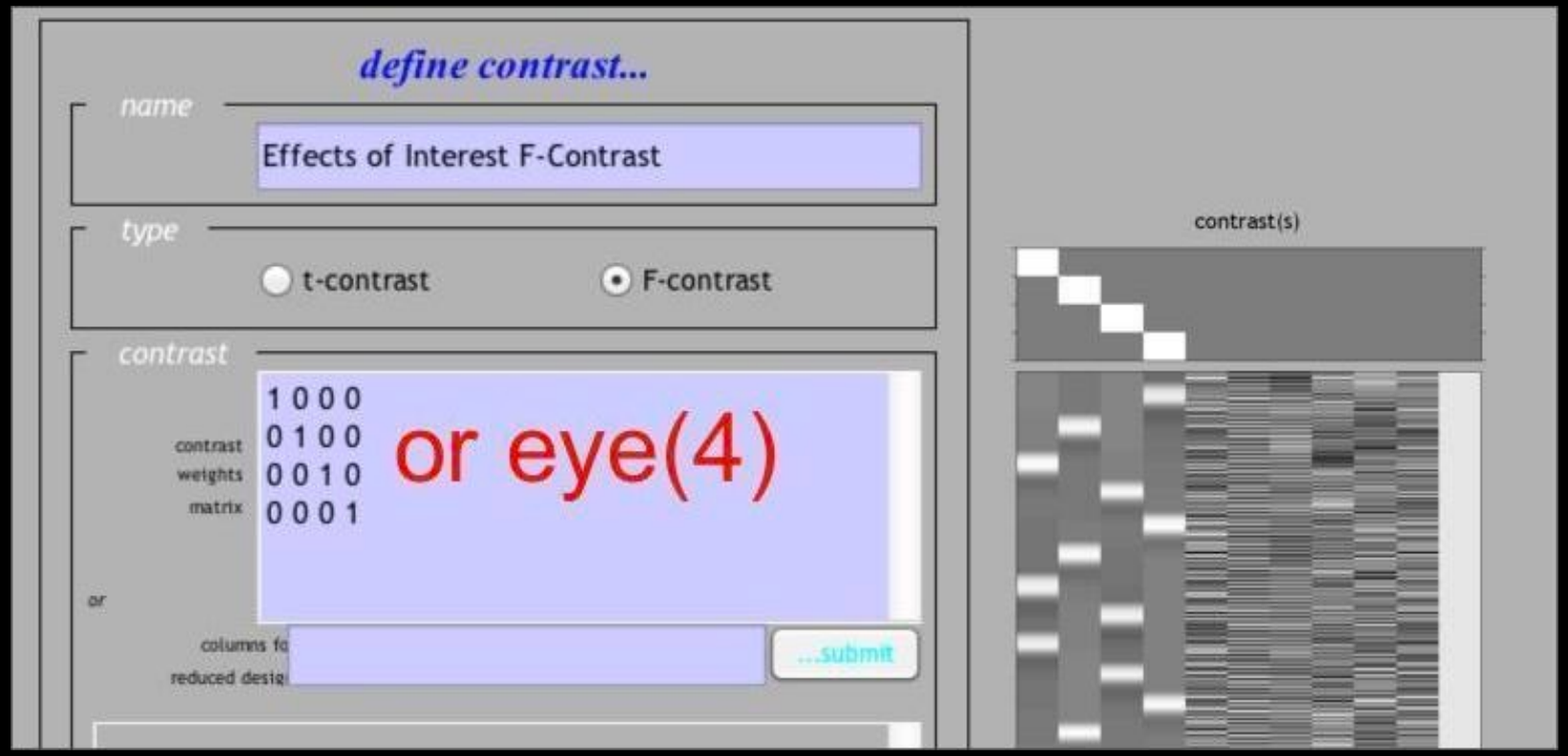
Also called ”omnibus” tests

Tests whether one or more contrasts is significant

Question: Does this maximize Detection or Estimation?

F-tests

Instead of a contrast vector, F-tests require contrast matrices



F-tests

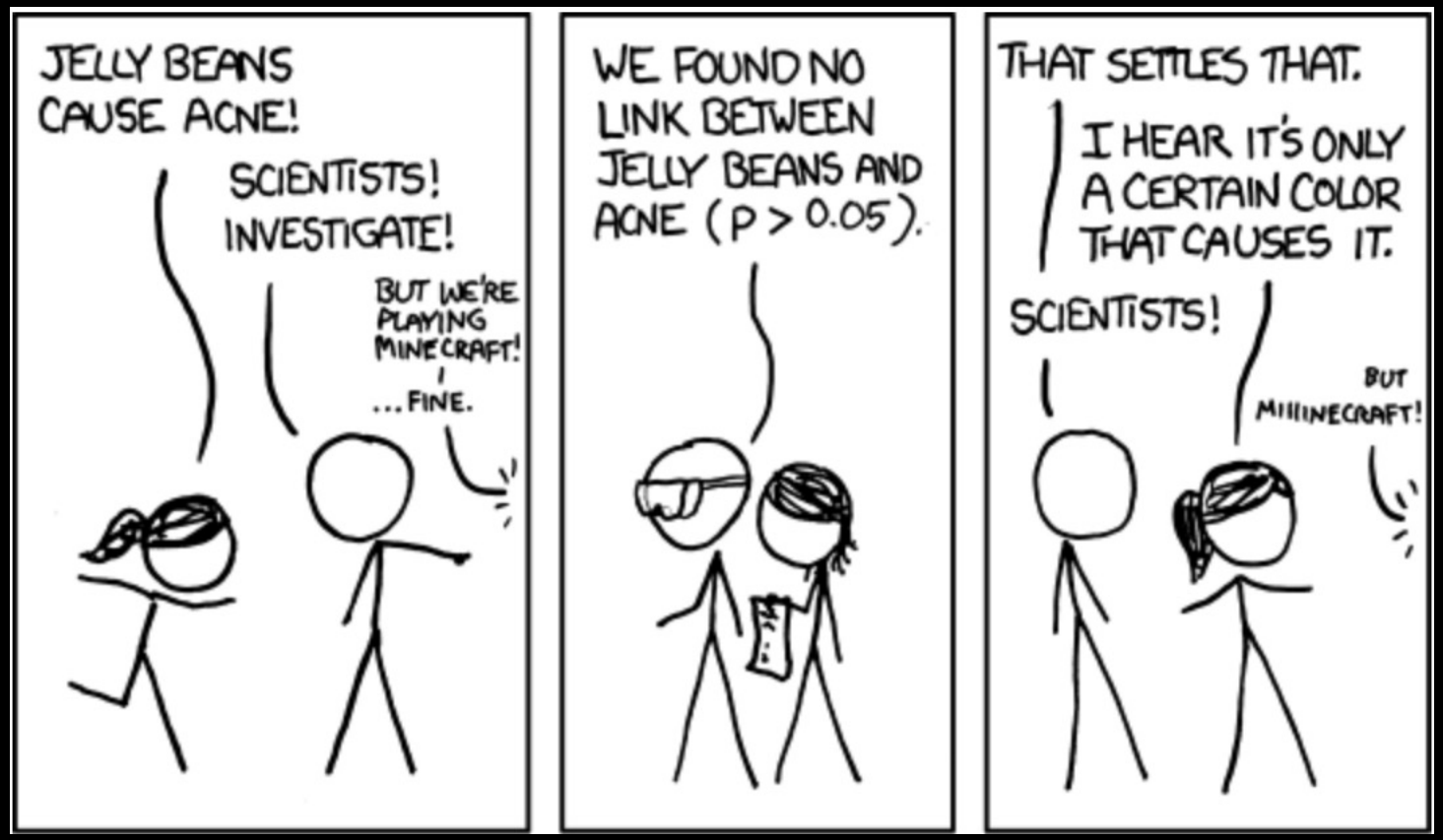
You can also specify multiple contrasts, e.g.:

[1 -1 0 0
-1 1 0 0
0 0 1 -1
0 0 -1 1
0 1 -1 0
0 -1 1 0]

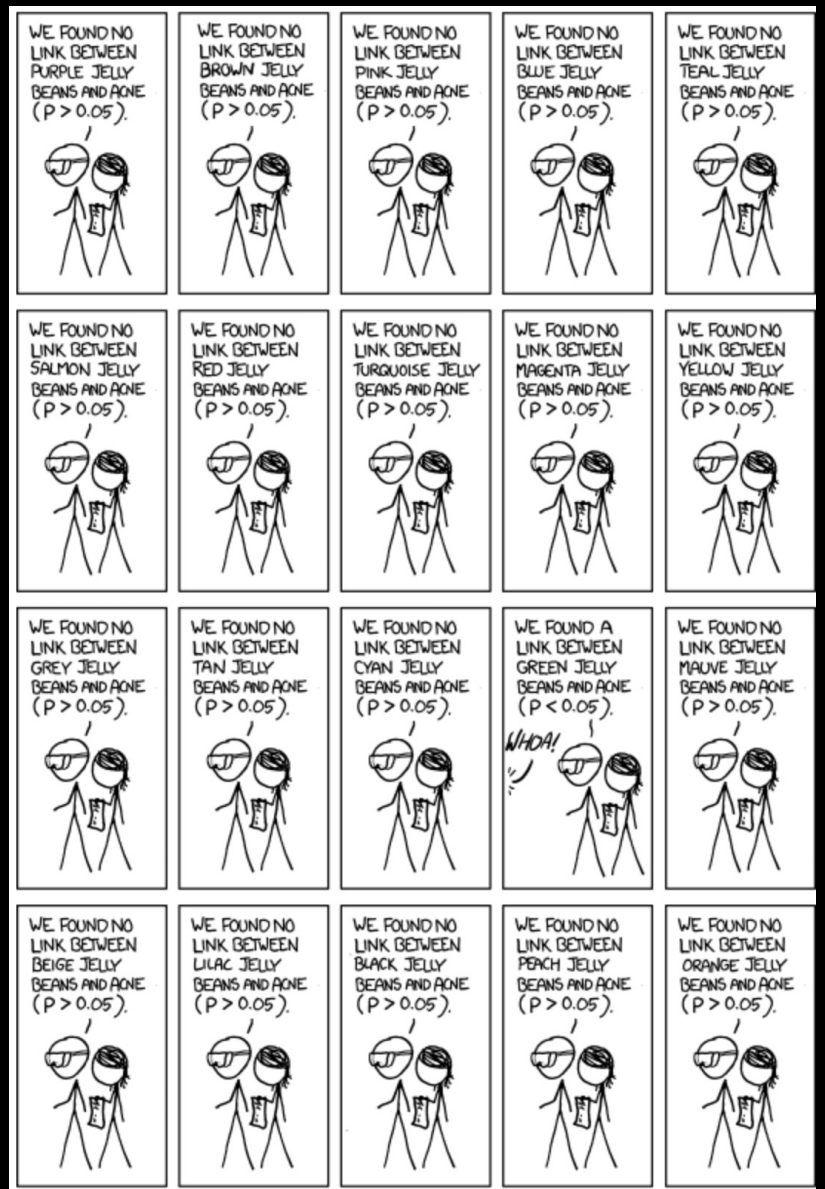
Demonstration of Group-Level Analysis

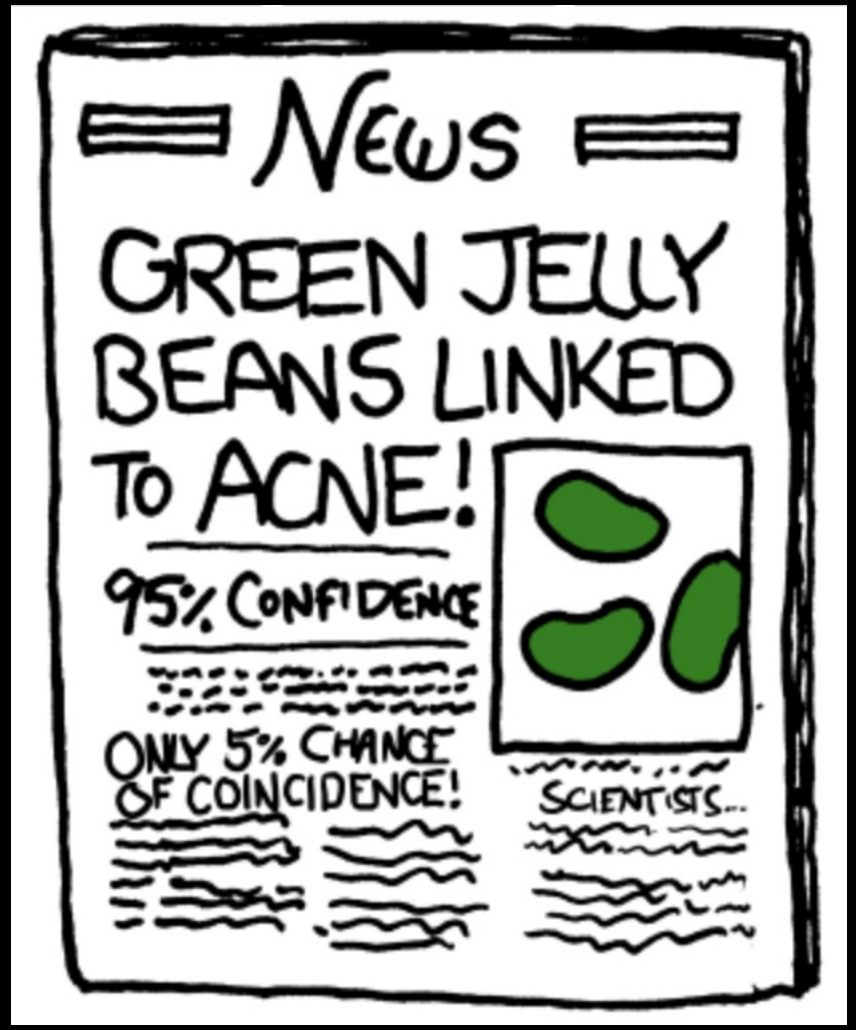
Correcting for Multiple Comparisons

Correcting for Multiple Comparisons



Correcting for Multiple Comparisons



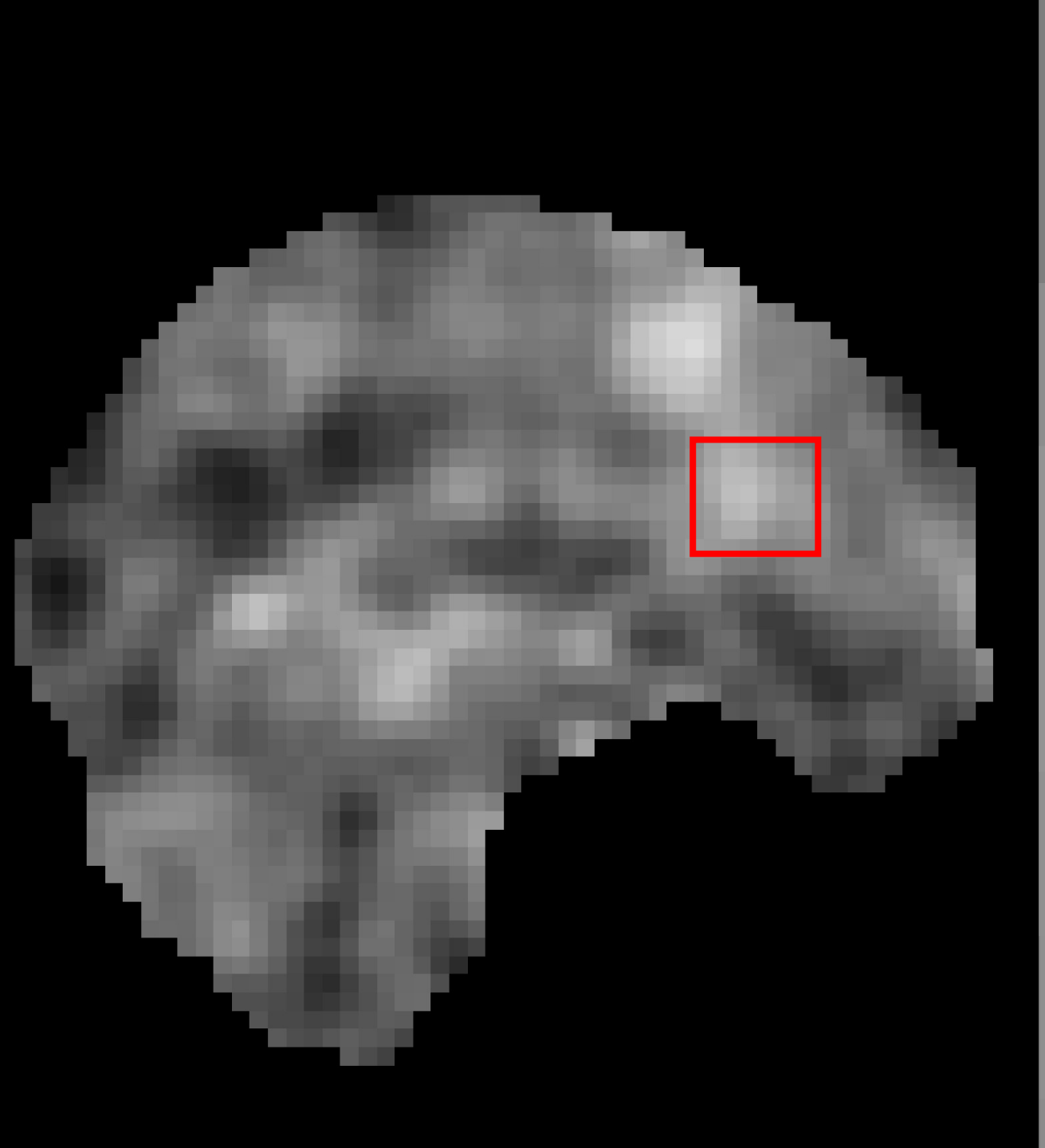


Correcting for Multiple Comparisons

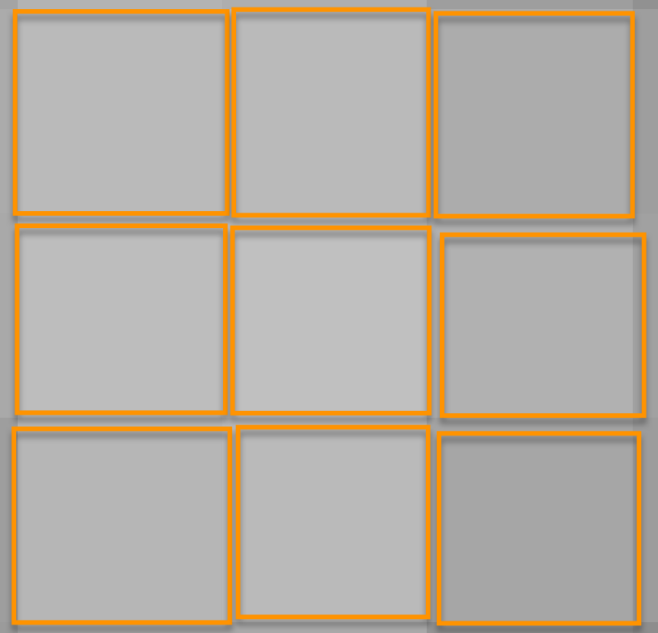
Now consider an fMRI dataset

Quick poll: How many voxels in a typical volume?

Depends on voxel size, but usually between 100k-300k



Test for significance in each voxel



Correcting for Multiple Comparisons

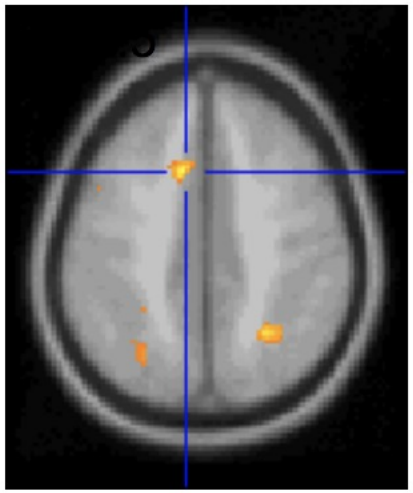
Balancing act between Type I and Type II errors

Legal Errors

		Actual Criminal	
		Yes Alternate Hypo	No Null Hypothesis
Decision on the basis of Case Trial	Punish (Criminal)	Good Decision	Convicting the Innocent
	Acquit (Innocent)	Acquit Guilty	Good Decision

Correcting for Multiple Comparisons

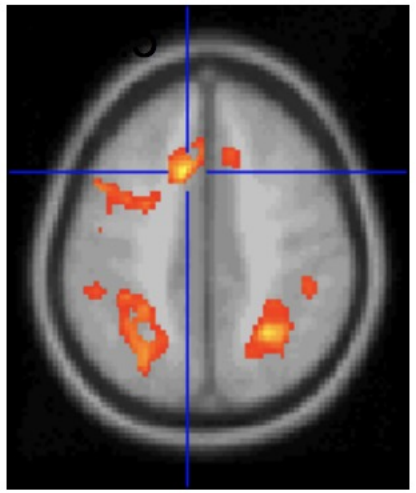
High Threshold



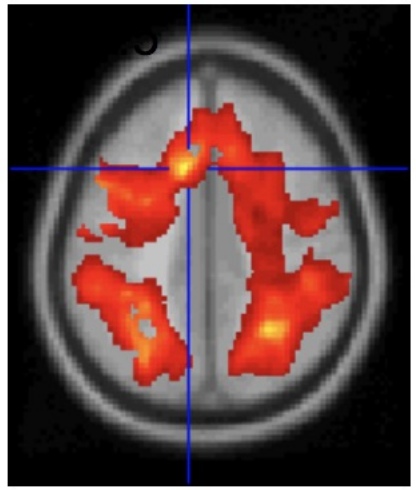
Good Specificity

Poor Power
(risk of false negatives)

Med. Threshold



Low Threshold



Poor Specificity
(risk of false positives)

Good Power

Correcting for Multiple Comparisons

What can be done?

Bonferroni correction

FDR correction

Cluster correction

Bonferroni Correction

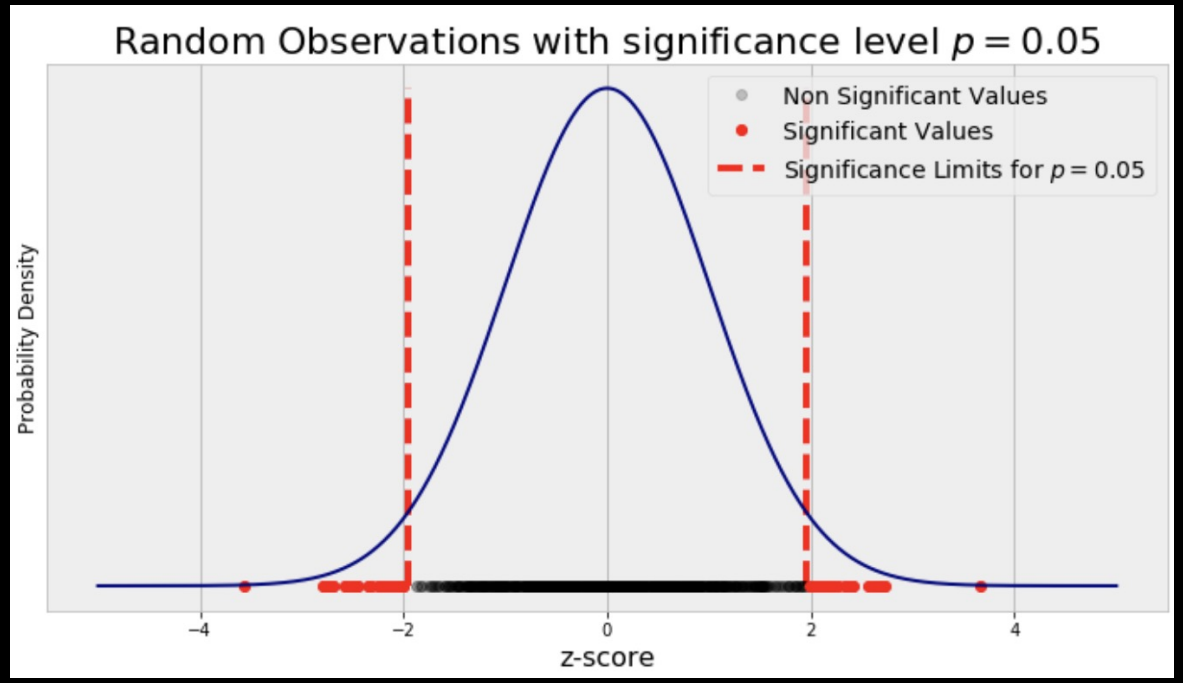
Simplest correction method to understand and calculate

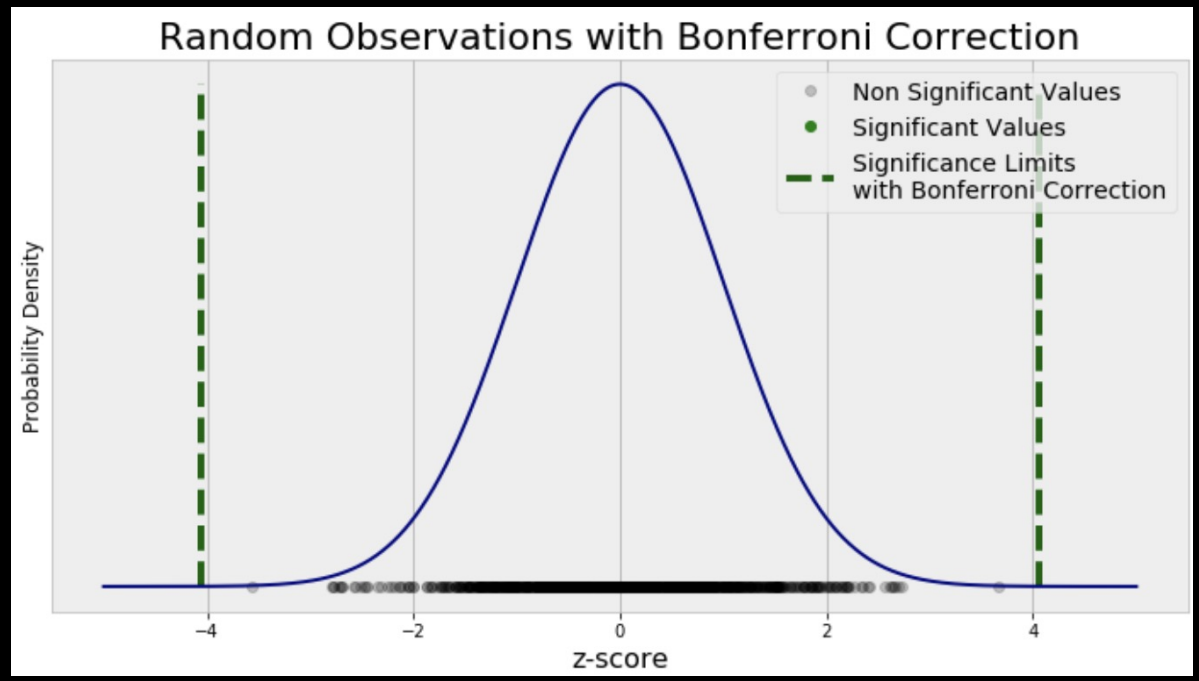
Given an alpha level α and number of tests n,
the corrected alpha level can be found by α/n

Example: $\alpha=0.05$, $n=10$

$\alpha = 0.005$

Bonferroni Correction





Source: towardsdatascience.com

Bonferroni Correction

Example: α=0.05, n=100,000

α =0.000005 (!)

This revised alpha is then used at each voxel in the analysis

Bonferroni Correction

Pros: Easy to understand, easy to use

Excellent for guarding against Type I error

Cons: Conservative, too severe for fMRI

Inflates the probability of Type II errors

Alternative: False Discovery Rate (FDR)

Bonferroni and other correction methods control for the Probability of observing a single false positive

FDR: Control the fraction of false positives

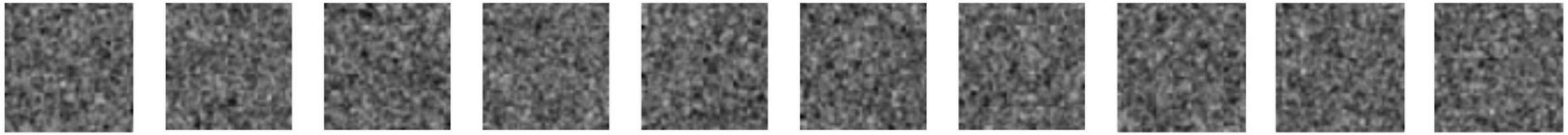
i.e.: You know there will a a certain percentage of false positives, but you can live with it

Alternative: False Discovery Rate (FDR)

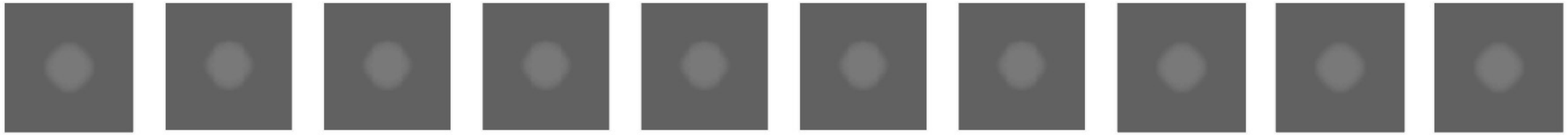
- FDR
  - E (# of true null declared active / # voxels declared active)

	Declared active	Fail to Declare active	Total
Non-active	50	950	1000
Active	80	20	100
Total	130	970	1100

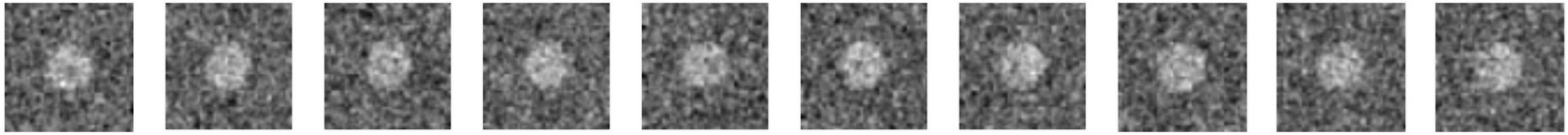
Noise



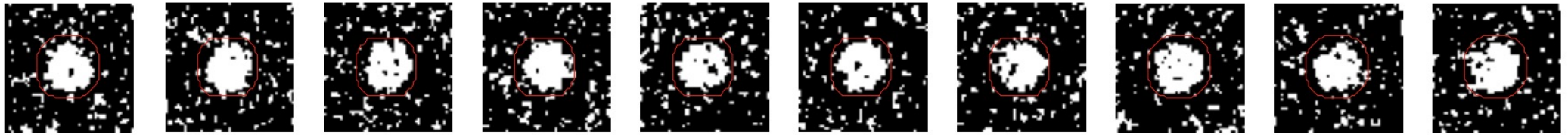
Signal



Signal+Noise



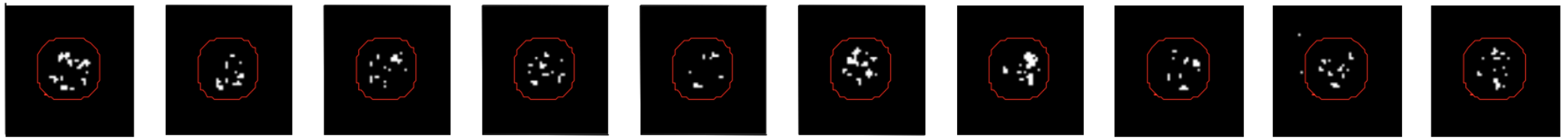
Control of Per Comparison Rate at 10%



11.3% 11.3% 12.5% 10.8% 11.5% 10.0% 10.7% 11.2% 10.2% 9.5%

Percentage of Null Pixels that are False Positives

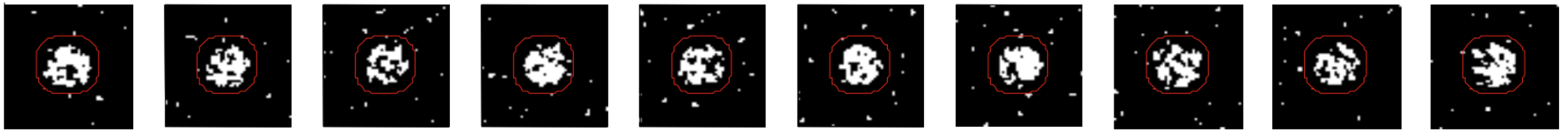
Control of Familywise Error Rate at 10%



FWE

Occurrence of Familywise Error

Control of False Discovery Rate at 10%



6.7% 10.4% 14.9% 9.3% 16.2% 13.8% 14.0% 10.5% 12.2% 8.7%

Percentage of Activated Pixels that are False Positives

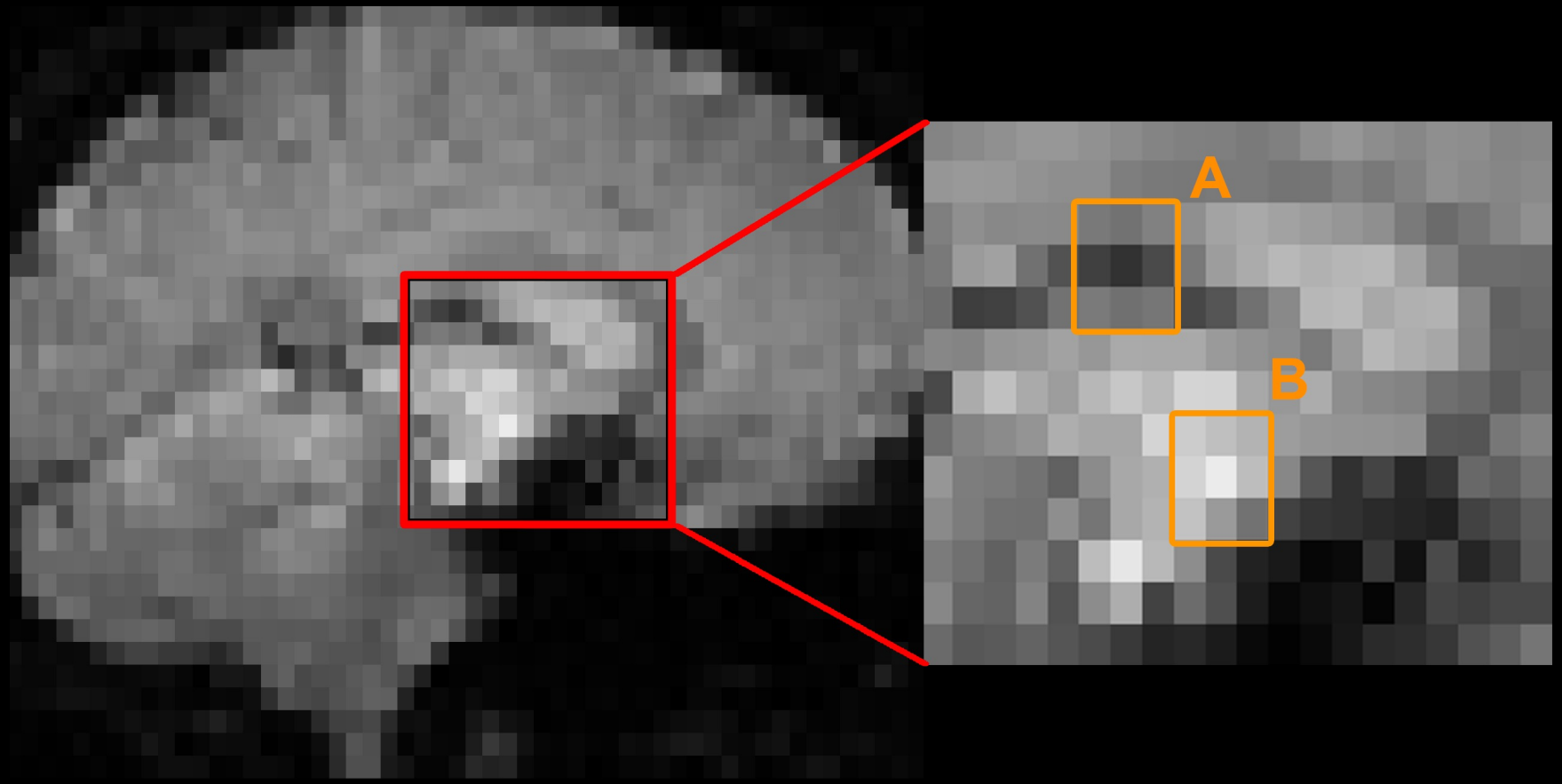
Cluster Correction

Bonferroni might be appropriate if each voxel were independent

But are they? Consider how the brain is designed

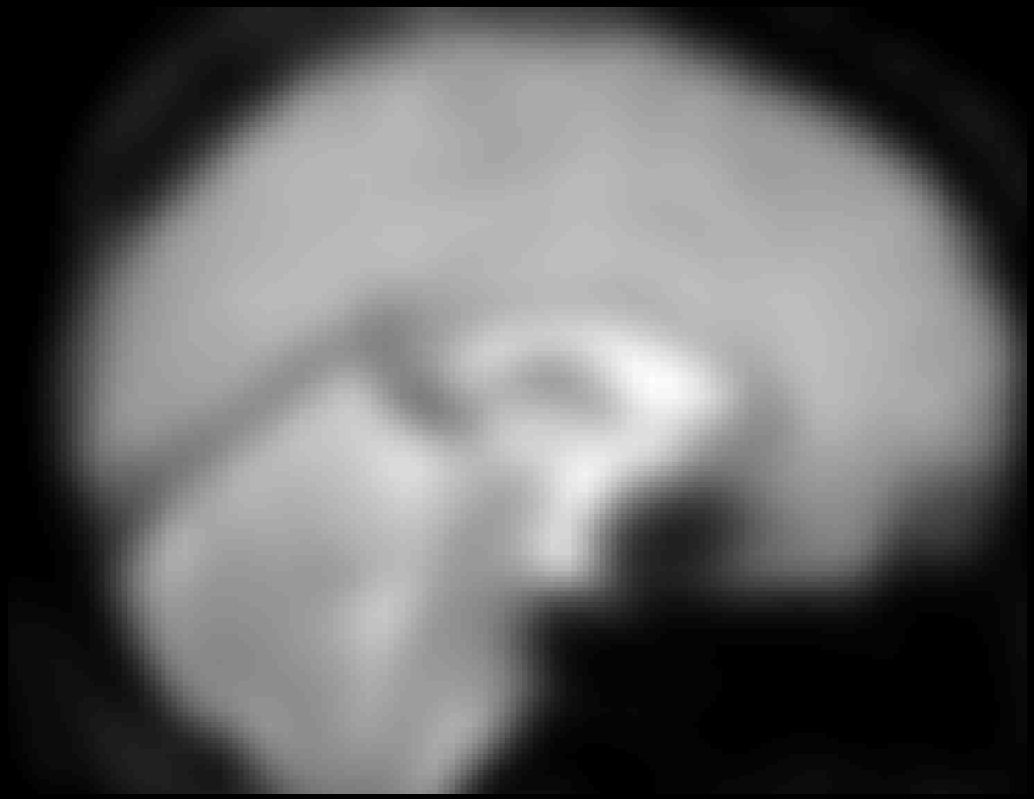
Cluster Correction

Functional image, unsmoothed



Cluster Correction

Functional image, smoothed



Cluster Correction

In SPM, cluster correction thresholds are calculated with Random Field Theory (RFT)

Accounts for the spatial smoothness of the data

Based on the estimated FWHMx (not the same as applied FWHMx!)

Cluster Correction

Example after 8mm smoothing kernel

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 2.34, p = 0.010 (1.000)
Extent threshold: k = 30 voxels, p = 0.107 (0.999)
Expected voxels per cluster, <k> = 11.965
Expected number of clusters, <c> = 7.21
FWEp: 4.869, FDRp: Inf, FWEc: 198, FDRc: 198

Degrees of freedom = [1.0, 278.0]
FWHM = 10.5 10.5 10.2 mm mm mm; 3.5 3.5 3.4 {voxels}
Volume: 1811403 = 67089 voxels = 1431.6 resels
Voxel size: 3.0 3.0 3.0 mm mm mm; (resel = 41.85 voxels)

Cluster Correction

Statistics: *p-values adjusted for search volume*

set-level		cluster-level			
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}
0.846	5	0.026	0.024	198	0.000
		0.537	0.175	85	0.011
		0.999	0.794	31	0.102
		0.489	0.175	89	0.010
		0.105	0.050	146	0.002

Multiple Comparisons Correction: Summary

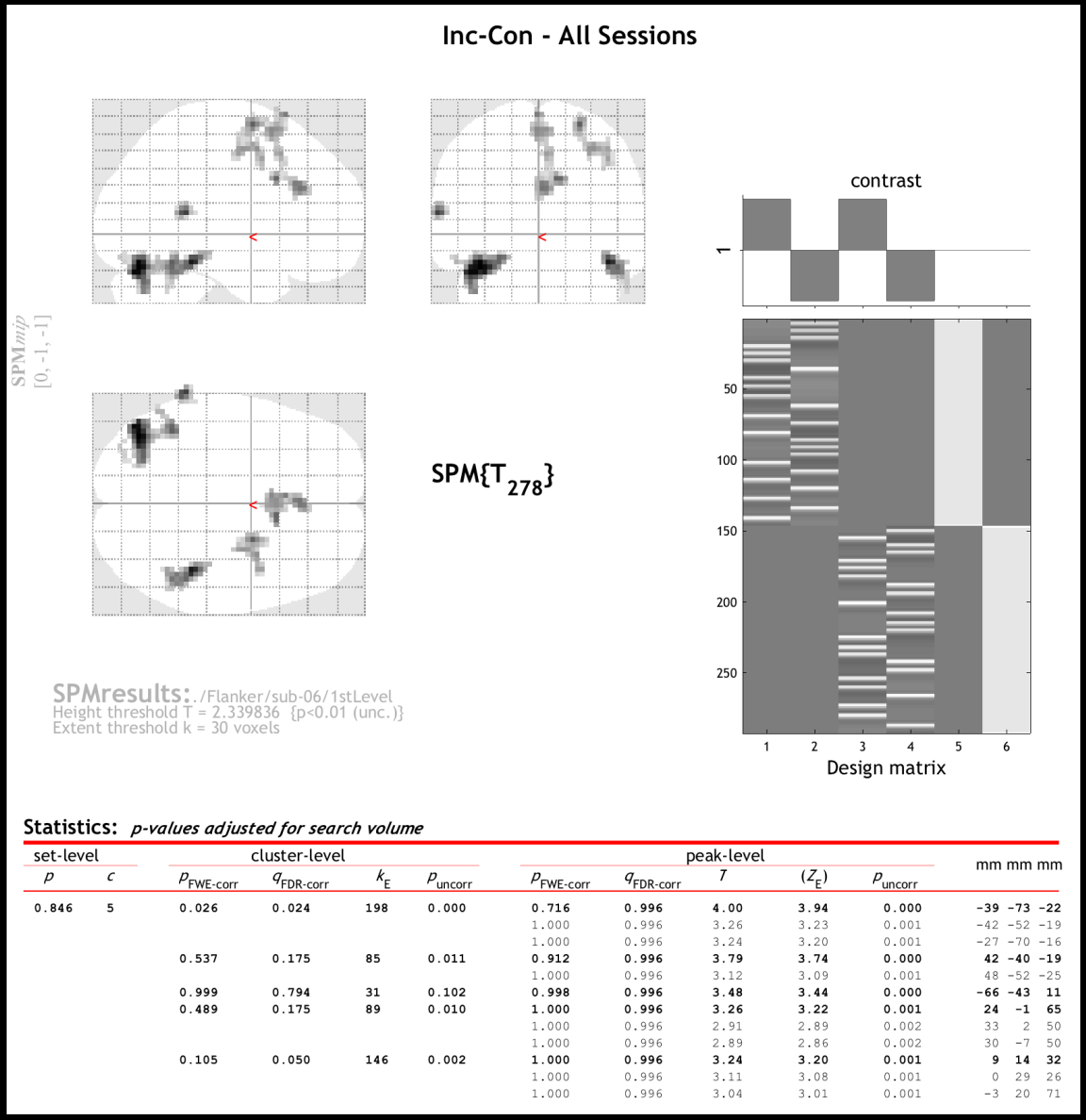
Most common method is cluster-wise thresholding

Cons: Loss of spatial specificity

As we will see tomorrow, you should use a Cluster-forming threshold of p=0.001 for most experiments

Non-parametric options seem to be getting more popular

Applying this to a dataset



Statistics: *p-values adjusted for search volume*

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	(Z_E)	p_{uncorr}	
0.846	5	0.026	0.024	198	0.000	0.716	0.996	4.00	3.94	0.000	-39 -73 -22
						1.000	0.996	3.26	3.23	0.001	-42 -52 -19
						1.000	0.996	3.24	3.20	0.001	-27 -70 -16
		0.537	0.175	85	0.011	0.912	0.996	3.79	3.74	0.000	42 -40 -19
						1.000	0.996	3.12	3.09	0.001	48 -52 -25
		0.999	0.794	31	0.102	0.998	0.996	3.48	3.44	0.000	-66 -43 11
		0.489	0.175	89	0.010	1.000	0.996	3.26	3.22	0.001	24 -1 65
						1.000	0.996	2.91	2.89	0.002	33 2 50
						1.000	0.996	2.89	2.86	0.002	30 -7 50
		0.105	0.050	146	0.002	1.000	0.996	3.24	3.20	0.001	9 14 32
						1.000	0.996	3.11	3.08	0.001	0 29 26
						1.000	0.996	3.04	3.01	0.001	-3 20 71

Applying this to a dataset

Set-level: Probability of finding that many clusters

Cluster-level: Probability of finding a cluster of a given size

Peak-level: Probability of a statistic that size in that voxel

Applying this to a dataset

Statistics: *p-values adjusted for search volume*

set-level		cluster-level				peak-level					mm	mm	mm
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	(Z_E)	p_{uncorr}			
0.846	5	0.026	0.024	198	0.000	0.716	0.996	4.00	3.94	0.000	-39	-73	-22
						1.000	0.996	3.26	3.23	0.001	-42	-52	-19
						1.000	0.996	3.24	3.20	0.001	-27	-70	-16
		0.537	0.175	85	0.011	0.912	0.996	3.79	3.74	0.000	42	-40	-19
						1.000	0.996	3.12	3.09	0.001	48	-52	-25
		0.999	0.794	31	0.102	0.998	0.996	3.48	3.44	0.000	-66	-43	11
		0.489	0.175	89	0.010	1.000	0.996	3.26	3.22	0.001	24	-1	65
						1.000	0.996	2.91	2.89	0.002	33	2	50
						1.000	0.996	2.89	2.86	0.002	30	-7	50
		0.105	0.050	146	0.002	1.000	0.996	3.24	3.20	0.001	9	14	32
						1.000	0.996	3.11	3.08	0.001	0	29	26
						1.000	0.996	3.04	3.01	0.001	-3	20	71

Demonstration

Other Statistical Scenarios

Once you calculate a contrast, are you done?

Consider this: My brother and I both play basketball.
If I tell you that I am slightly better than he is, does that mean:

We are both really good, but I'm just a little better?

I'm a little above average, and he's a little below average?

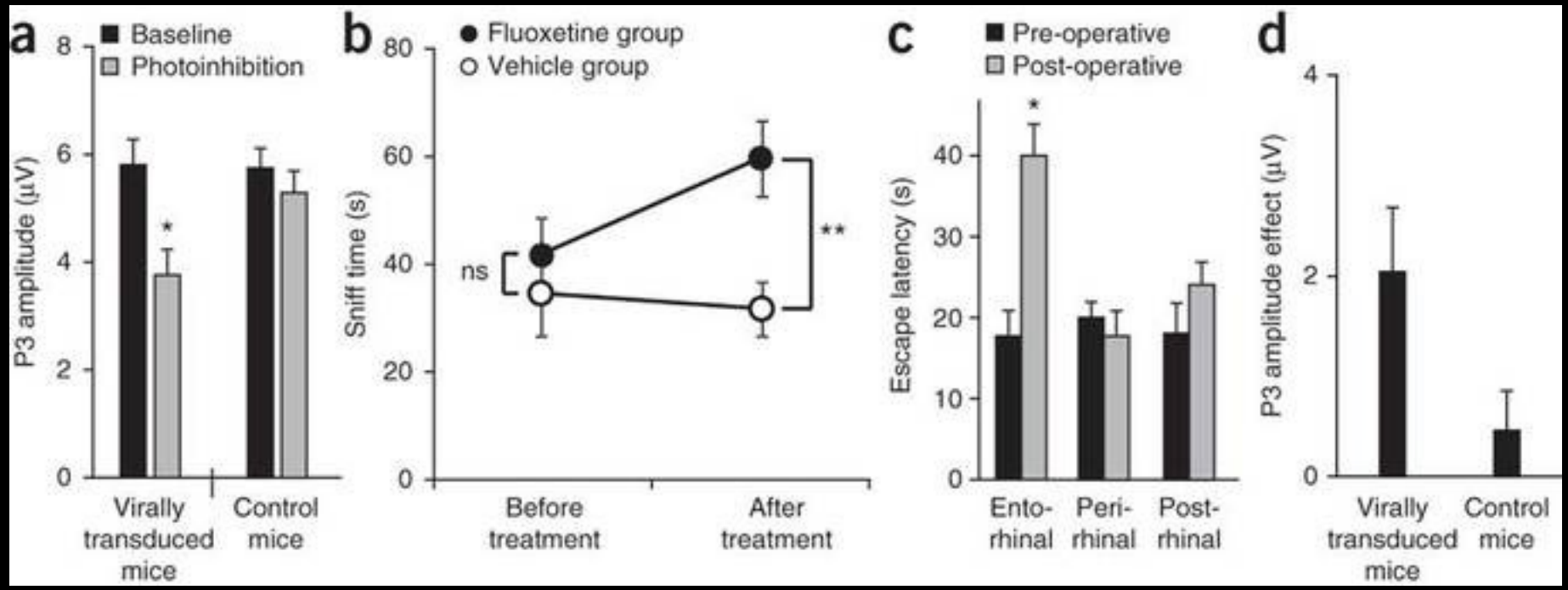
Maybe we're both terrible, and I'm just a little better than he is

Double Dissociations

Condition A is significant in region A but not region B, and condition B is significant is region B but not region A

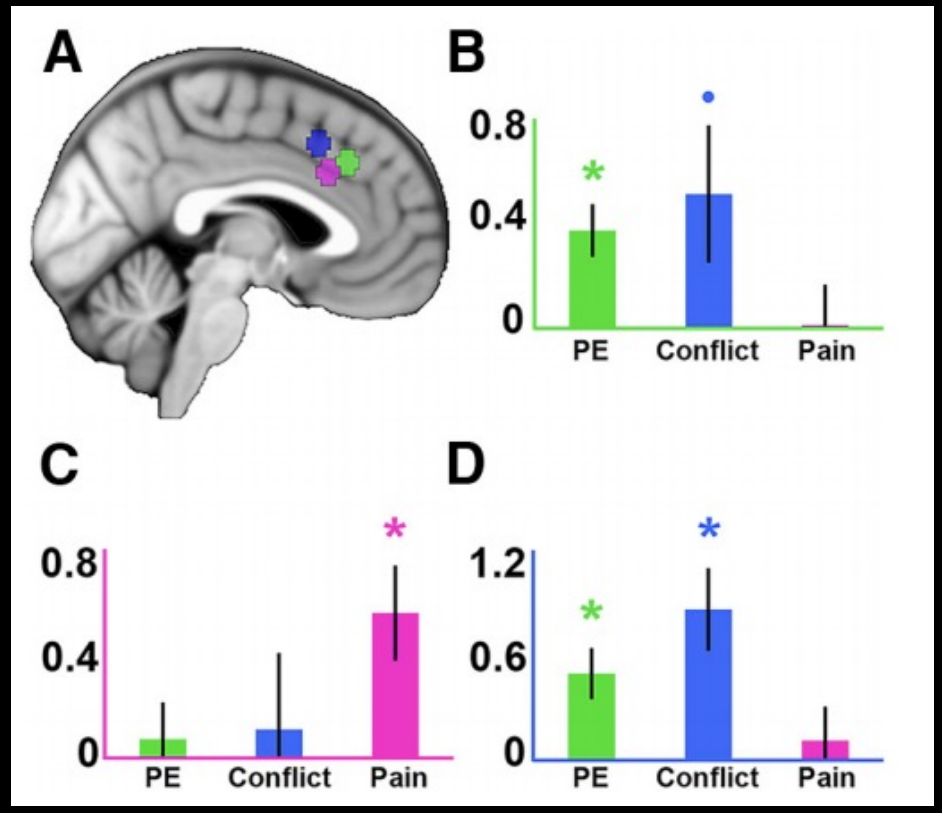
Remember to run a paired t-test within each region, and also a Region x Condition interaction

Double Dissociations



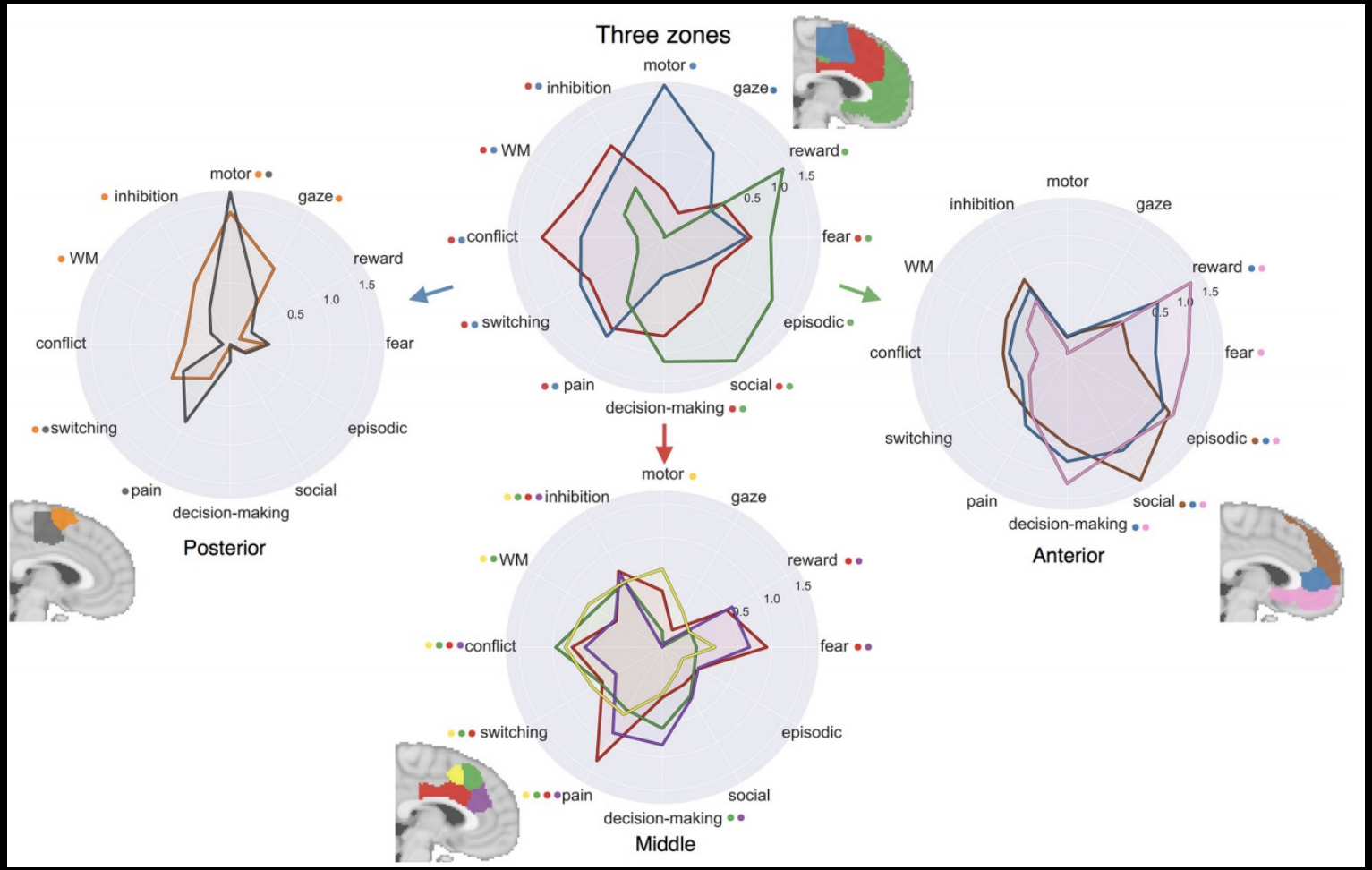
Nieuwenhuis et al., 2011

Double Dissociations



Jahn et al., 2016

Triple Dissociations (!)



De la Vega et al., 2016

Preview: ROI Analysis

In the examples just shown, the data was extracted from Regions of Interest (ROIs)

That is, subsets of voxels that we are interested in

WFU PickAtlas Tool

HUMAN ATLAS->TD brodmann areas+

..
brodmann area 1
brodmann area 2
brodmann area 3
brodmann area 4
brodmann area 5
brodmann area 6
brodmann area 7
brodmann area 8
brodmann area 9
brodmann area 10
brodmann area 11
brodmann area 12
brodmann area 13
brodmann area 14
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brodmann area 38
brodmann area 39
brodmann area 40
brodmann area 41
brodmann area 42
brodmann area 43
brodmann area 44
brodmann area 45
brodmann area 46
brodmann area 47
Amygdala
Anterior Commissure
Caudate Body
Caudate Head

Atlas Information

BASIC | ADVANCED

ADD ->

MOVE ALL ->>

<- REMOVE SELECTED

<<- REMOVE ALL

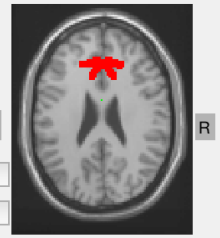
2D | 3D

DILATE: 1

Flip Lock | L/R | U/D

Left | Left + Right | Right

Display: Neurologic 49



ANALYSIS | RESULTS

Write Independent Regions

SAVE MASK

DONE | CANCEL

WORKING REGION1

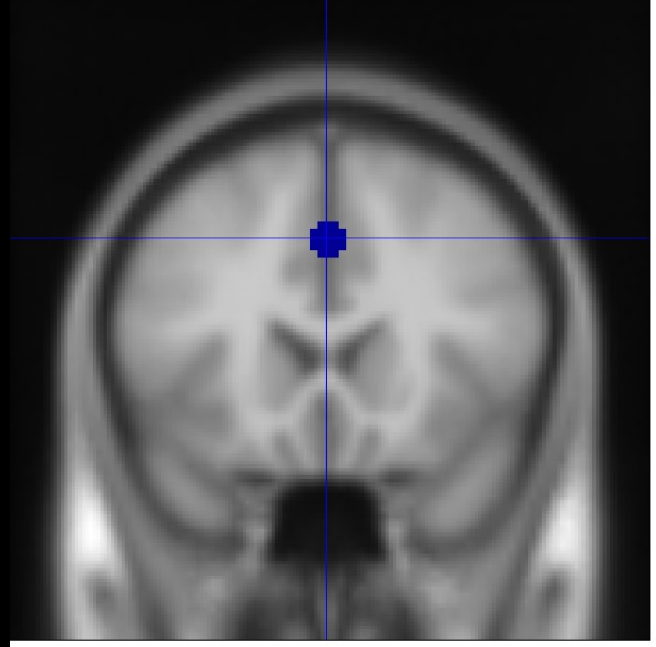
brodmann area 32

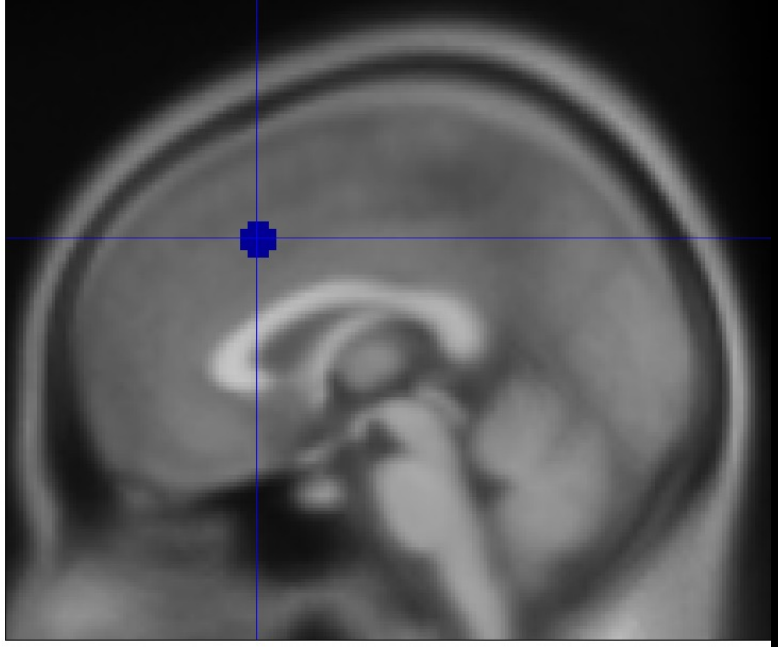
					ATLAS	SUBREGION	VALUE
CUBE	46	64	37	GO			
MNI	0	0	0	GO	TD brodmann areas+	NA	1000
Tal	0	0	0	GO	TD Lobes	NA	1500

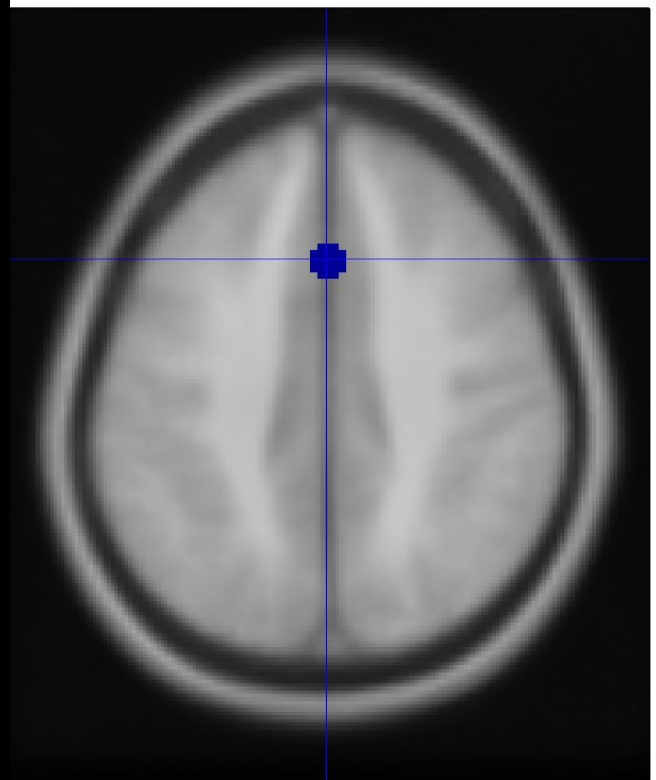
Interrogate Talairach Daemon

Generate Table

Search Range 0







1: dACC_Sphere

Label: **dACC_Sphere**

Centre of mass: **0 20 40**

Volume (mm): **648.00**

Max/min X(mm): **-4 4**

Max/min Y(mm): **16 24**

Max/min Z(mm): **36 44**

Questions?

Lab Preview

Create an ideal experimental design, *before* collecting data

For AFNI users: Similar to using the –nodata option in 3dDeconvolve, calculating correlations

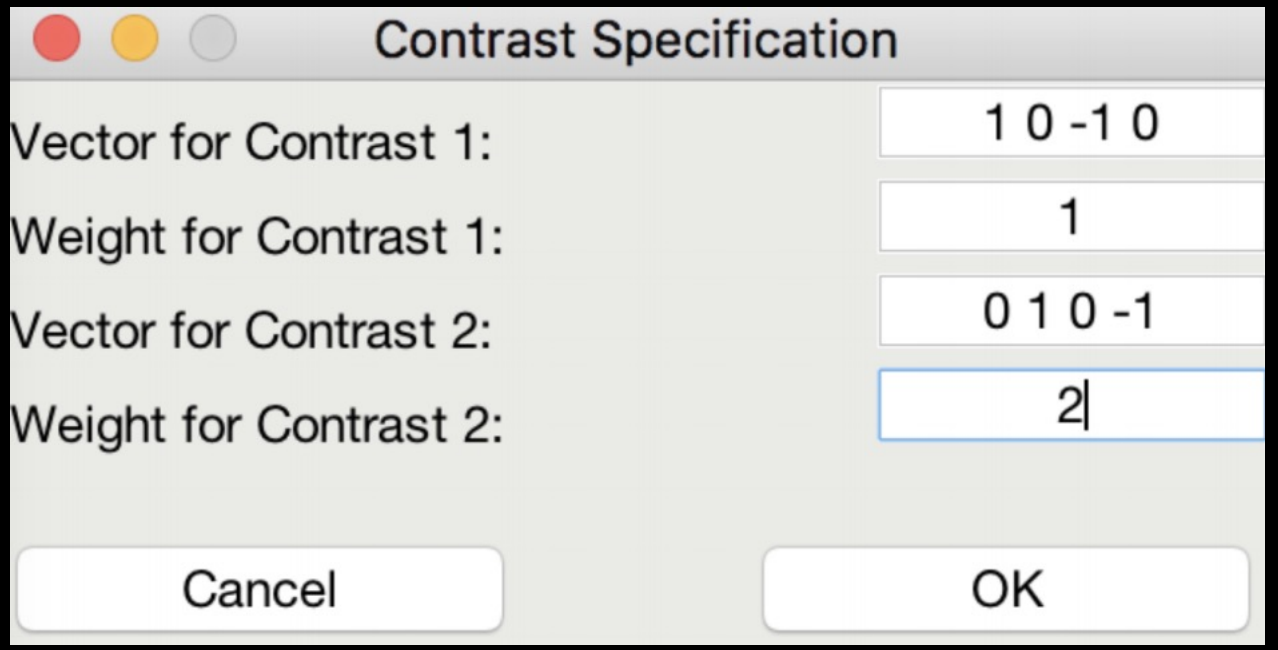
Parameters to change: ISI, number of trials, and contrasts

Lab Preview

```
ts  = output.X0;          % get the raw timeseries from 'output'
tr  = output.TR;          % do the same for the TR
irf = spm_hrf(tr);        % create the impulse response function
cts = conv(ts, irf);      % convolve the timeseries with the IRF
cts = cts(1:length(ts)); % ensure that the long tail of the hemodynamic response hasn't
lengthened our image timeseries
```

Lab Preview

Using OptimizeX to specify which contrasts you are interested in



Lab Preview

Create several design matrices, calculate VIF

We will provide the code for this

Lab Preview

Exploring the SPM.mat file

details on experiment:

SPM.xY.RT - TR length (RT ="repeat time")
SPM.xY.P - matrix of file names
SPM.xY.VY - # of runs x 1 struct array of mapped image volumes (.img file info)
SPM.modality - the data you're using (PET, FMRI, EEG)
SPM.stats.[modality].UFp - critical F-threshold for selecting voxels over which the non-sphericity is estimated (if required) [default: 0.001]
SPM. stats.maxres - maximum number of residual images for smoothness estimation
SPM. stats.maxmem - maximum amount of data processed at a time (in bytes)
SPM.SPMid - version of SPM used
SPM.swd - directory for SPM.mat and img files. default is pwd

basis function:

SPM.xBF.name - name of basis function
SPM.xBF.length - length in seconds of basis
SPM.xBF.order - order of basis set
SPM.xBF.T - number of subdivisions of TR
SPM.xBF.T0 - first time bin (see slice timing)
SPM.xBF.UNITS - options: 'scans'|'secs' for onsets
SPM.xBF.Volterra - order of convolution
SPM.xBF.dt - length of time bin in seconds
SPM.xBF.bf - basis set matrix