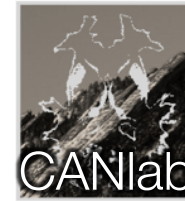




JOHNS HOPKINS
BLOOMBERG
SCHOOL of PUBLIC HEALTH



University of Colorado **Boulder**



Principles of fMRI

Part II

Martin Lindquist

Department of Biostatistics
Johns Hopkins
Bloomberg School of Public Health

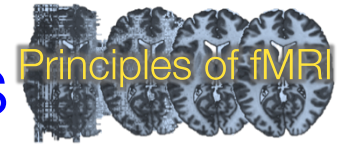
Tor Wager

Department of Psychology and
Neuroscience and the
Institute for Cognitive Science
University of Colorado, Boulder

 @fMRIstats

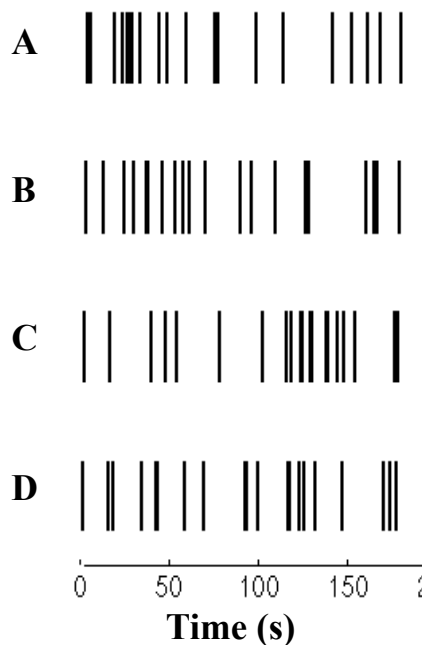
The General Linear Model: Assumptions and Multicollinearity

Model Building for Multiple Predictors

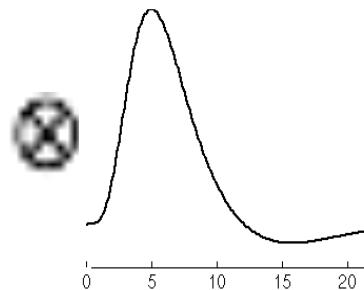


Indicator functions

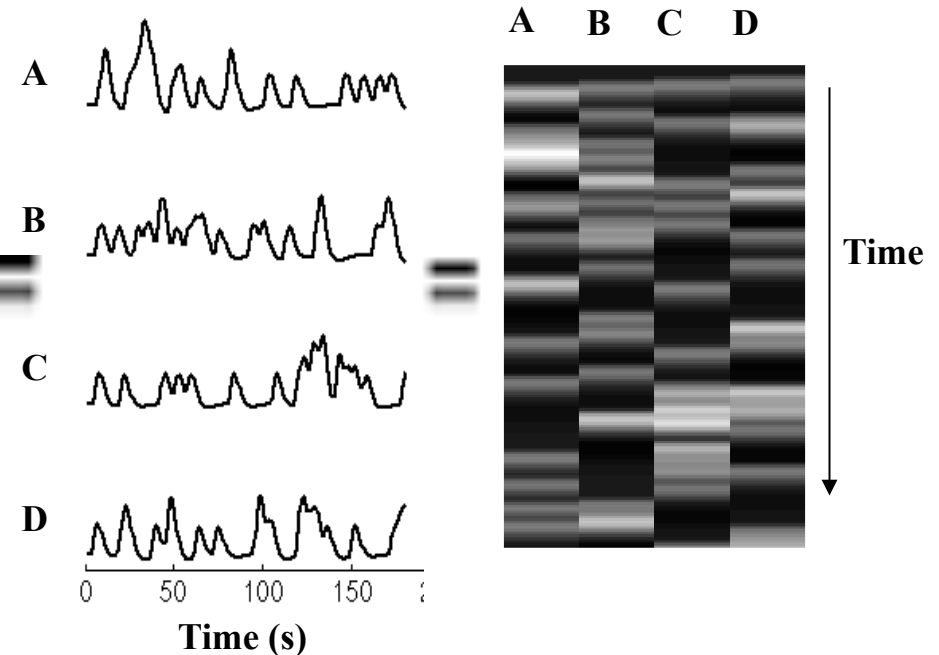
(onsets)



Assumed HRF
(Basis function)



Design Matrix (X^T) Design Matrix (X)



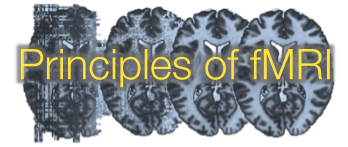
Assumptions!

Assume neural
activity function
is correct

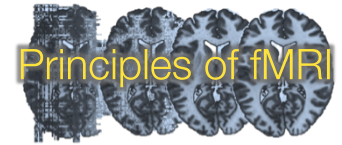
Assume HRF
is correct

Assume LTI
system

Assumptions Required for Valid p-values



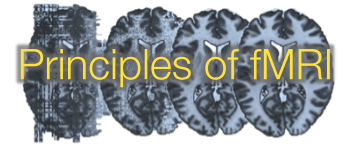
What to do?



- Check assumptions
 - Look for outliers, skewed variables
 - Pay particular attention to behavioral predictors in brain-behavioral correlations
- Fixes: Variable transformation
 - e.g., log transform behavioral data for positive skew
- Fixes: Nonparametric and robust statistics
 - SnPM, Statistical nonParametric Mapping (Nichols & Holmes, 2001)
 - Rank statistics (e.g., Spearman's rho)
 - Robust statistics (e.g., IRLS, Wager et al., 2005)



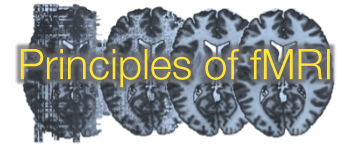
A Note on Multicollinearity



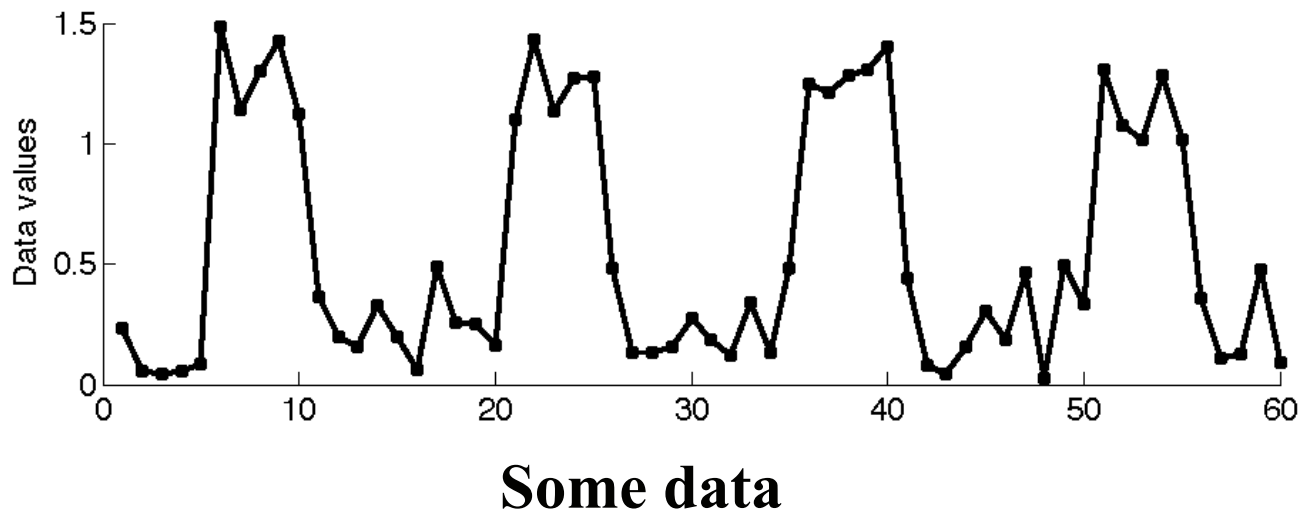
- Correlated predictors increase the variance (uncertainty) in parameter estimates
- Because of fundamental uncertainty in which predictor should be “assigned credit” for variation in the data.



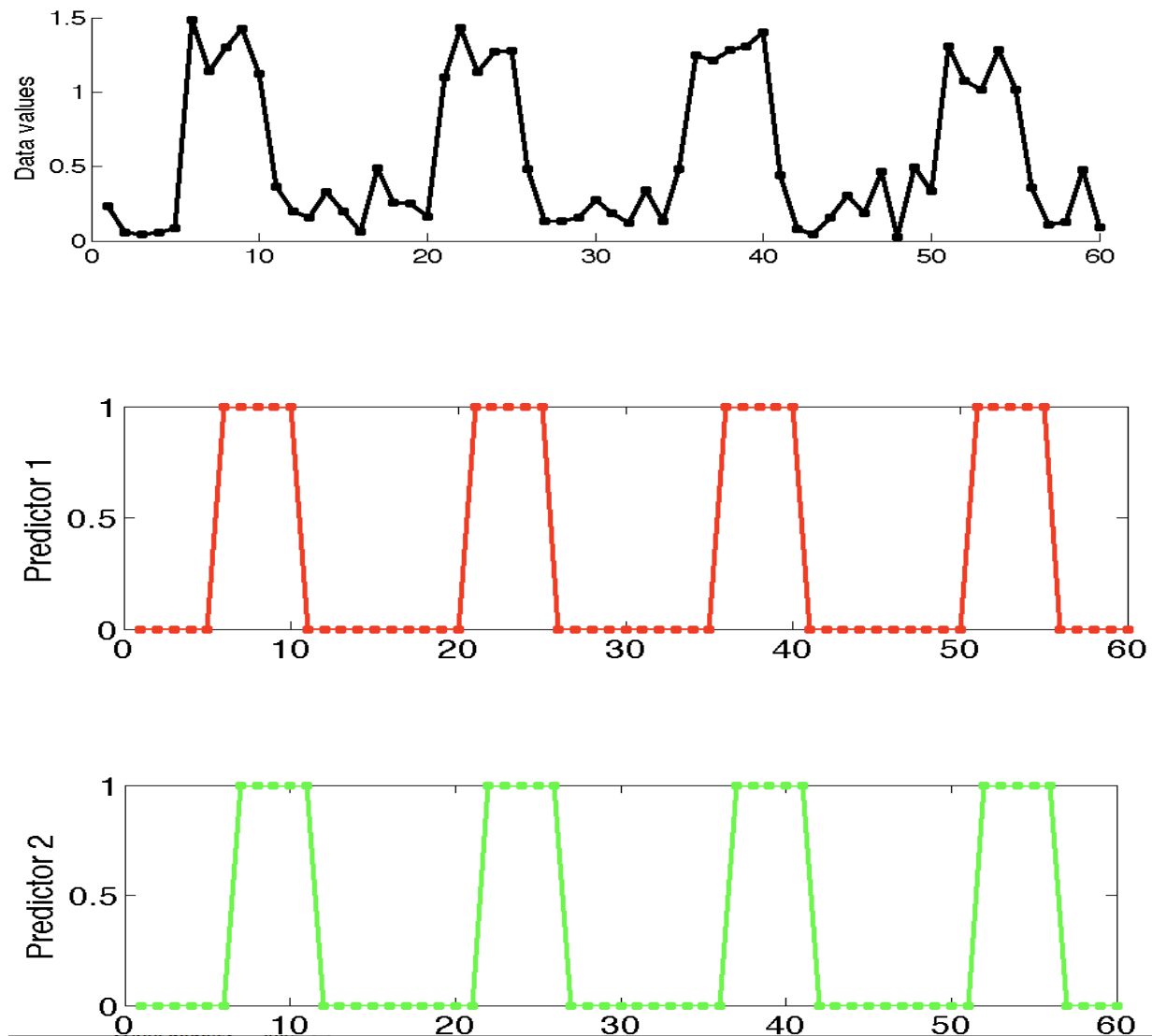
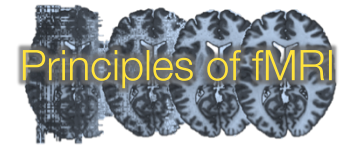
A Note on Multicollinearity



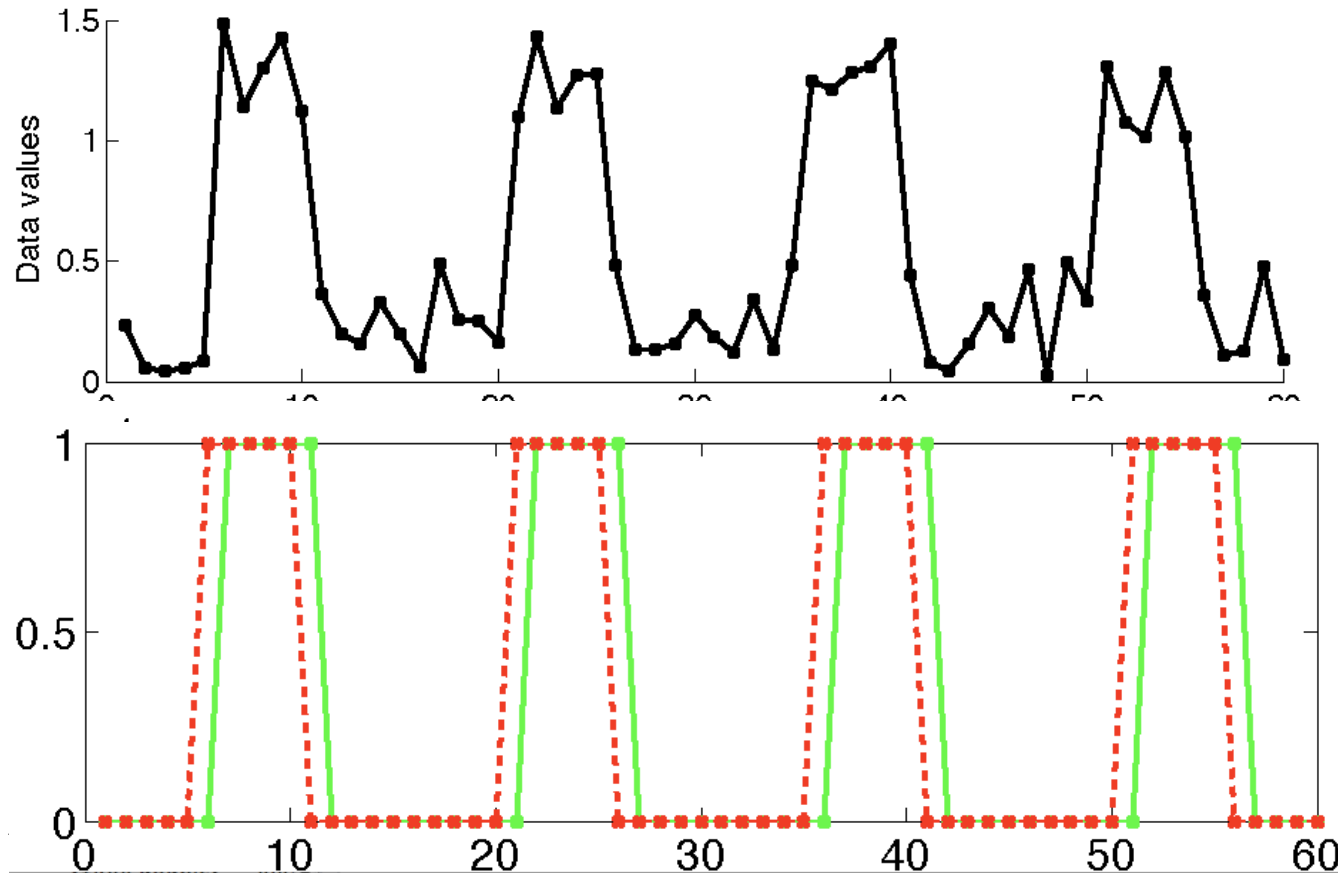
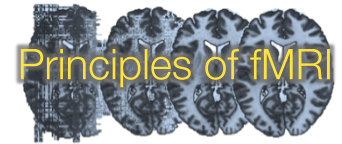
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A Note on Multicollinearity



A Note on Multicollinearity

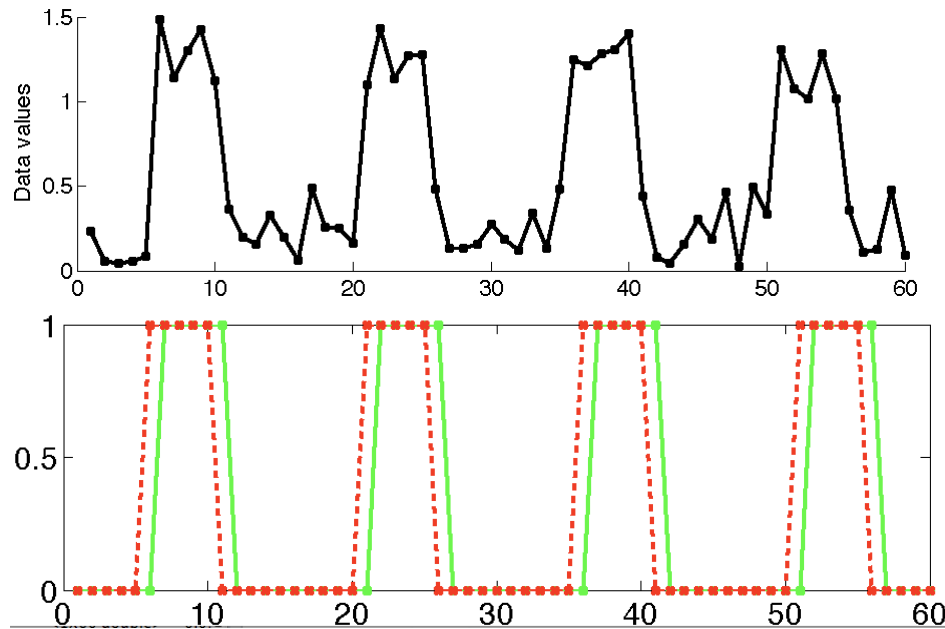
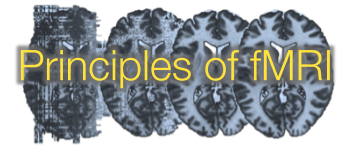


Where are the predictor values different?

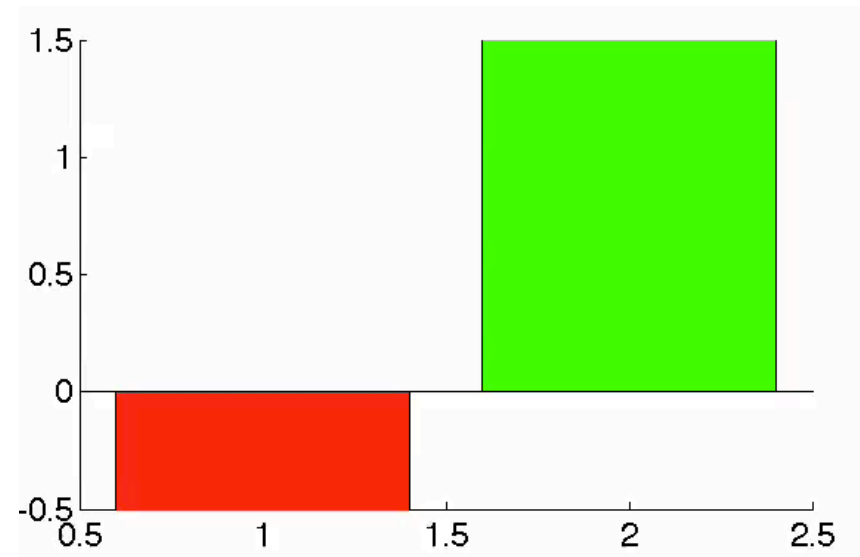
Which predictor fits best depends only the data at these points!



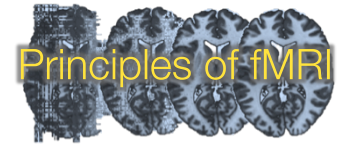
A Note on Multicollinearity



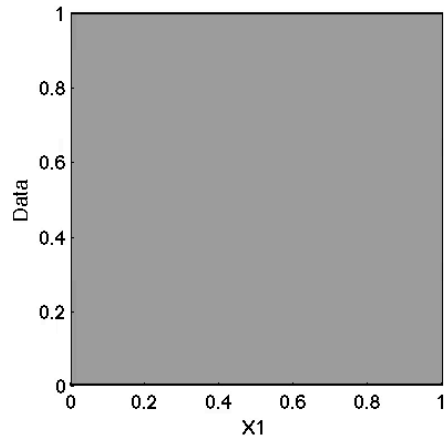
Amplitudes (betas)



Regression with Two Predictors

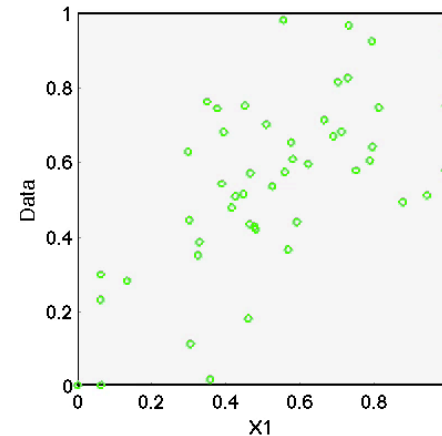


No multicollinearity



Tor Wager, C2008

Multicollinearity



Tor Wager, C2008

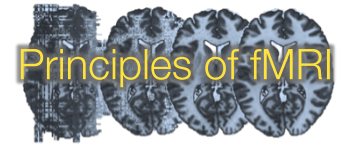
- With multicollinearity, P-values can be misleading:
Easy to 'flip-flop' from significant positive to negative

Ground truth in simulations is the same:

- Strong, positive effects of both predictors X_1 and X_2
- Same noise variance

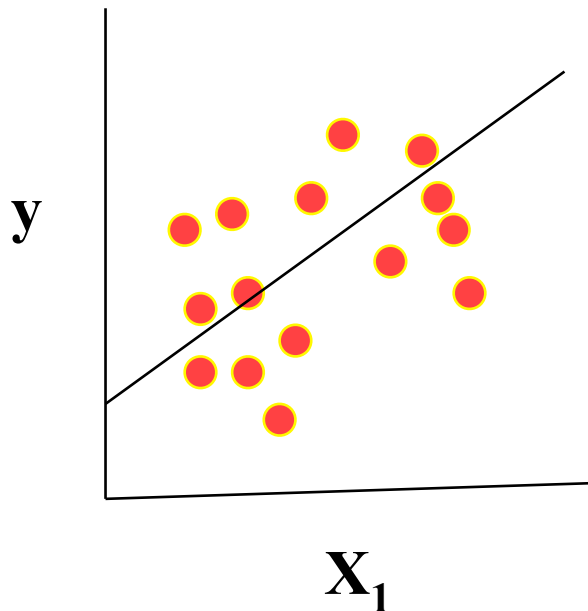


Multiple Regression is Tricky Business!

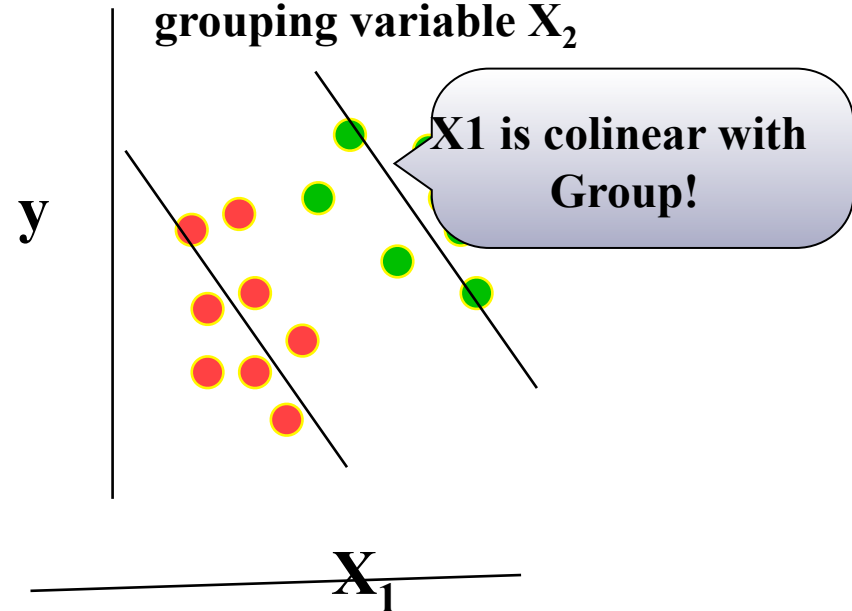


- Inferences on parameters (betas) depend on getting the model for *other* parameters right
- Including parameters you didn't know should be included in the model!
- Interpretation of parameters is model-dependent

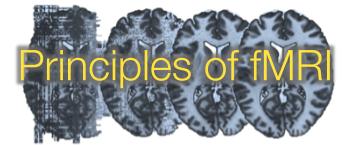
Positive beta for X_1



Negative beta for X_1
Same data, control for omitted
grouping variable X_2

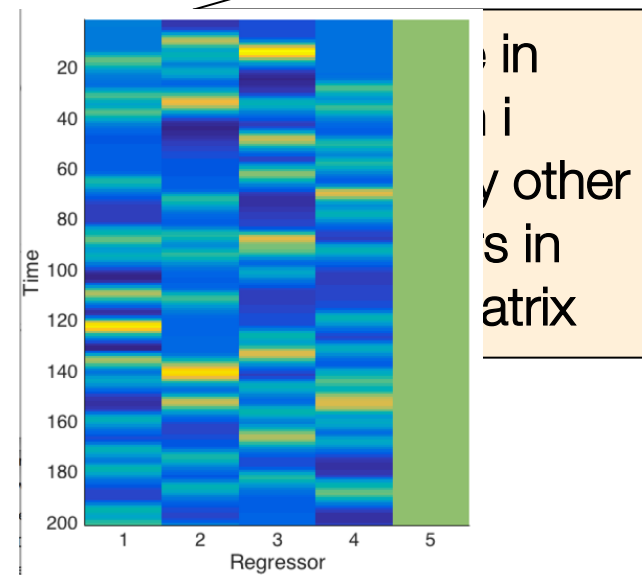
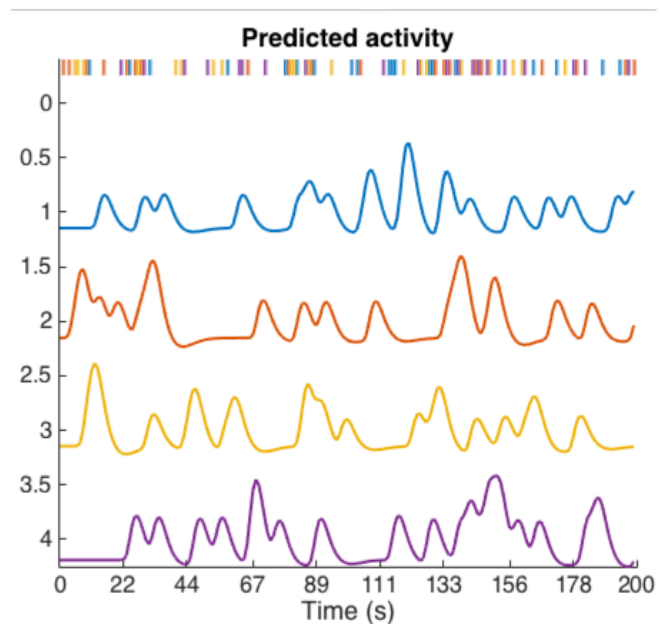


Diagnosis: Variance inflation factors



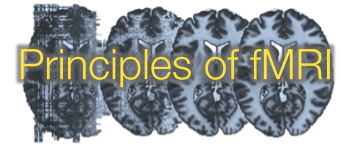
- Variance Inflation Factors (VIFs) of each regressor in your design matrix
- Increase in error variance due to design multicollinearity.
 - e.g., VIF = 2 means your error variance will be *doubled*.
- For a design matrix X with columns $i = 1 \dots I$

$$vif_i = \frac{1}{1 - R_i^2}$$



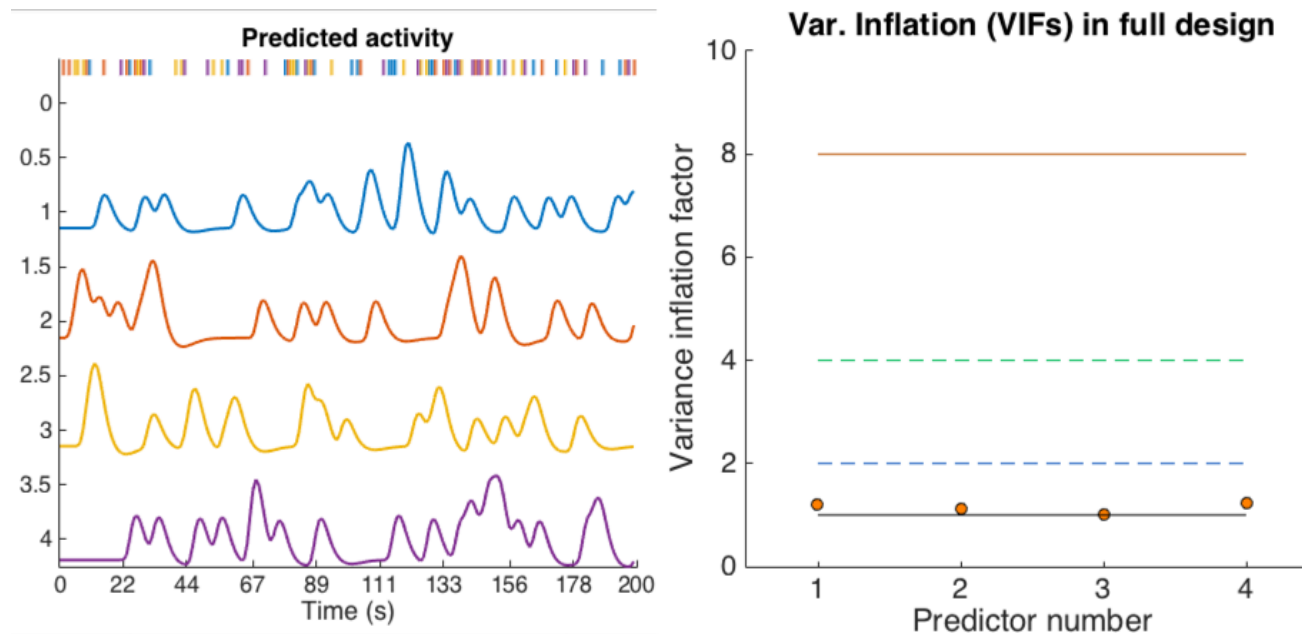
e.g., Kutner et al. 2004

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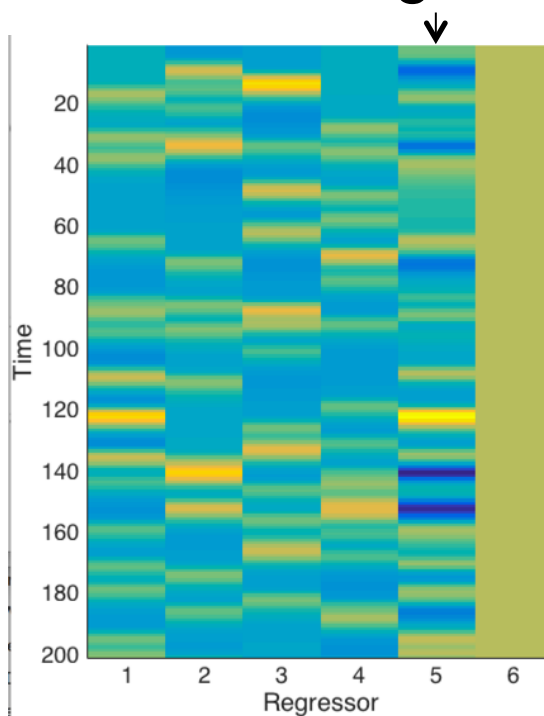


● e.g., Kutner et al. 2004

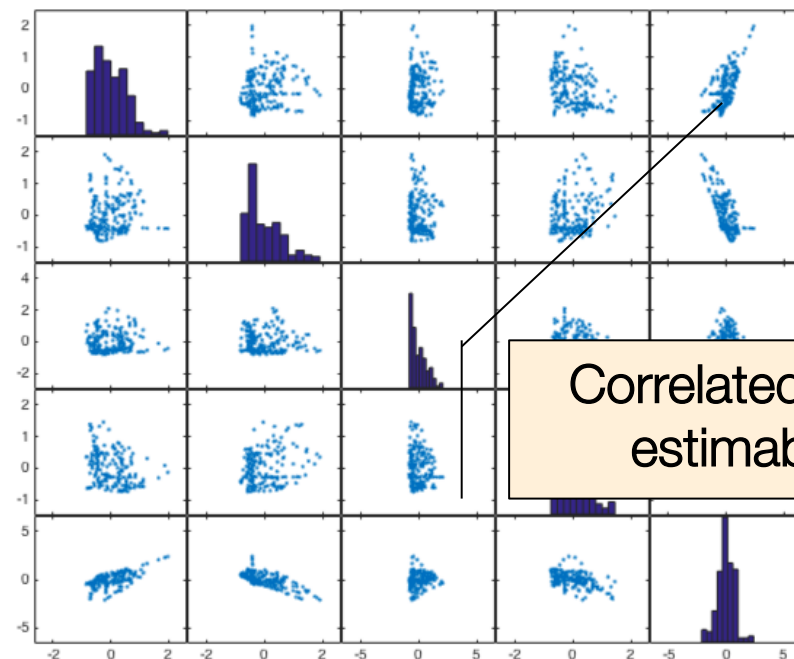
Properties of VIFs

- Estimated for each column in design matrix; some may have high VIFs, others low VIFs
- Adding nuisance regressors may increase VIFs for some regressors more than others
- Pairwise correlations are not enough to assess multicollinearity

New regressor



Pairwise correlations

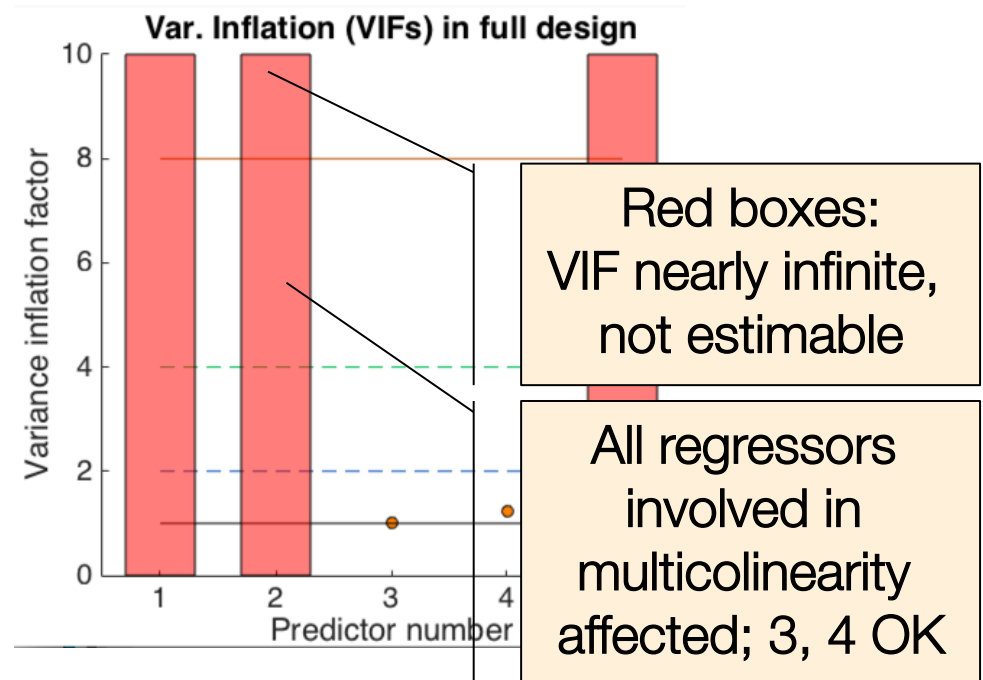
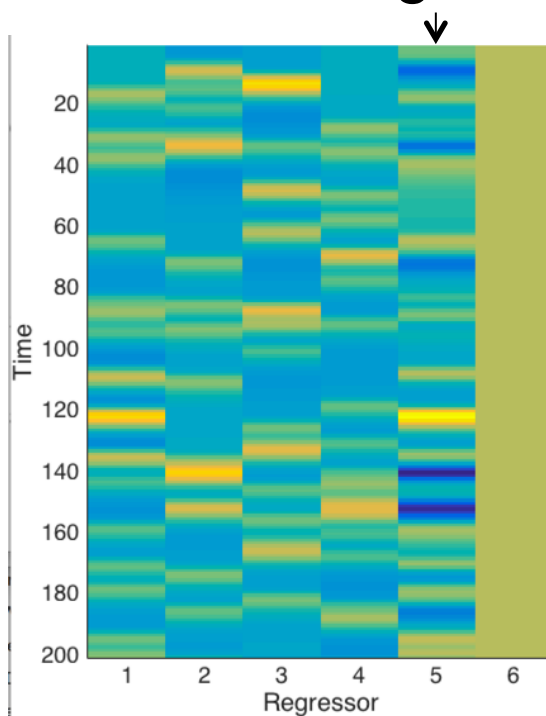


Correlated but
estimable

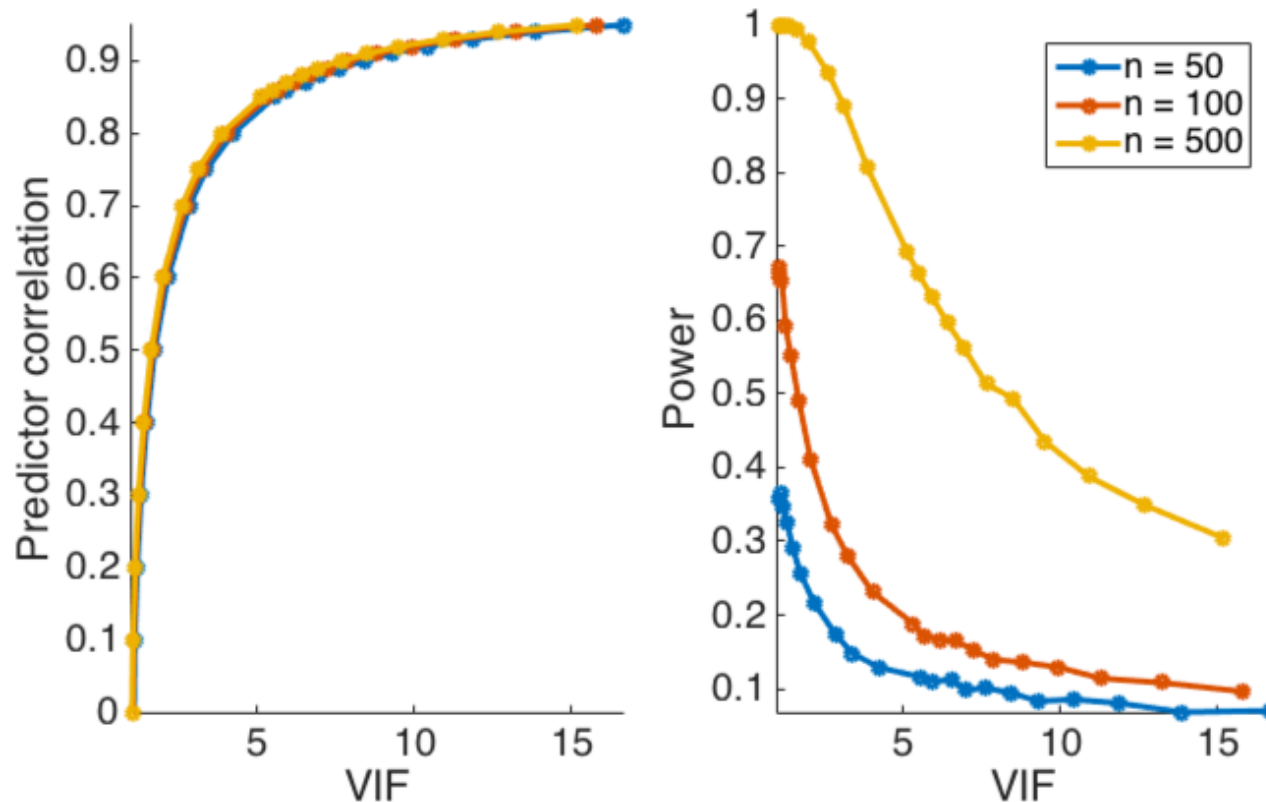
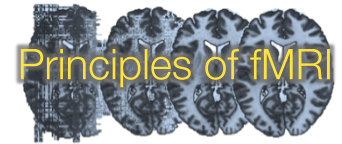
Properties of VIFs

- Looks ok?
- BUT: New regressor is **perfect linear combination** of original regressors: $X_1 - X_2$!
- Which VIFs will be affected, and which model parameters not uniquely estimable?

New regressor

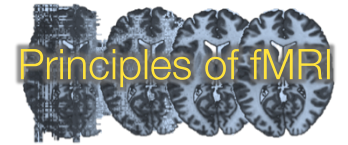


How are VIFs related to correlations and power?



- VIFs above 5 signal strong multicollinearity ($r = 0.8$)
- Power depends on sample size too
- No hard and fast rule for “too high”
- P-values can be misleading: Can ‘flip-flop’ from significant positive to negative effects

Take-home: Regression



- Take-home: Multicollinearity
 - It is important to check for multicollinearity
 - Look at your design matrix visually
 - Pairwise correlations are not enough
 - Variance inflation factors are a good way to check
- Take-home: Interpretation
 - P-values, t-values, Z-values are only valid if the GLM assumptions hold
 - A predictor with a significant fit does not mean that the predictor is the “right” model
 - Variables that you have not modeled may actually be causing effects in your data

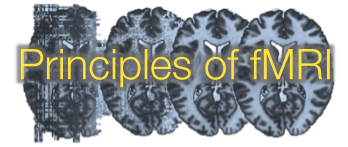


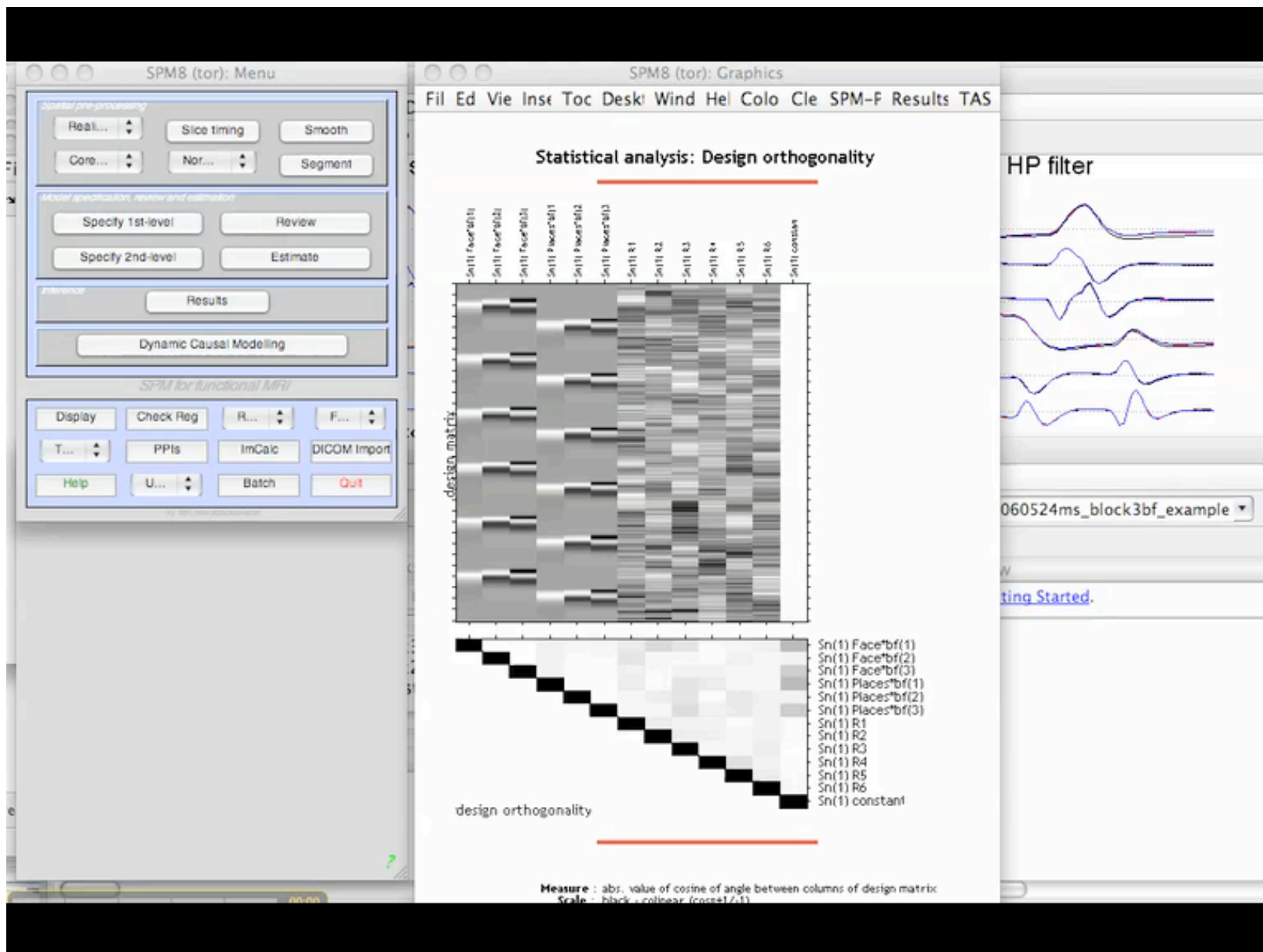
End of Module



@fMRIstats

Practical: Checking an SPM design





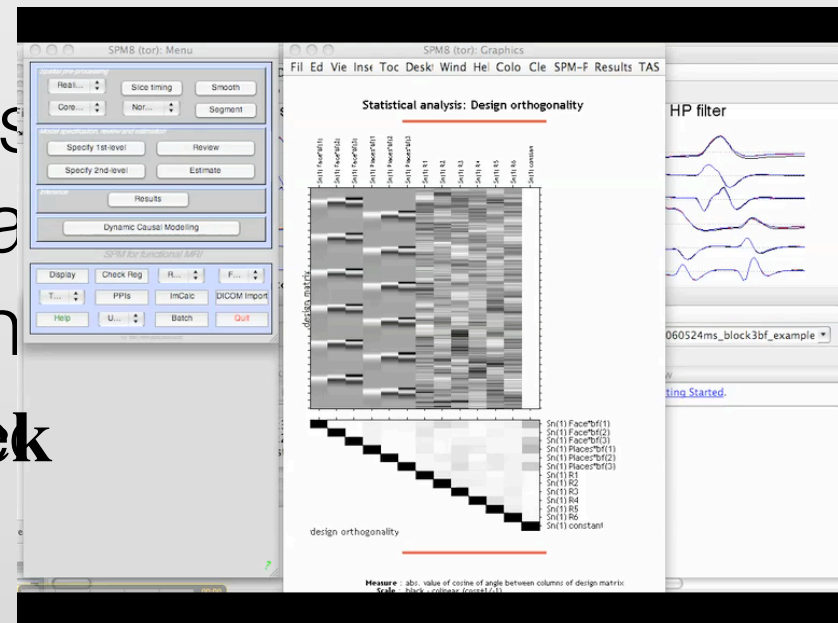
Contrasts, filtering, and estimability

Having regressors that satisfy the above does not imply that contrasts do.

...run `scn_spm_design_check` after specifying contrasts.

Contrasts are uniquely estimable

Contrast values are estimated with



Condition number and Variance Inflation Factor

MATLAB 7.5.0 (R2007b)

File Edit Debug Desktop Window Help

/Applications/MATLAB_R2007b

Shortcuts How to Add What's New

Current Directory Workspace

Name	Value	Min
X	<100x4 double>	-2..
a	<1x60 double>	0
ans	1.2113e+16	1.2..
b	<1x60 double>	0
betas	[1.1443;-0.868...	-0..
data	<60x1 double>	-5..
hh	1.2870e+03	1.2..
hh2	1.2900e+03	1.2..
i	20	20
sig	<1x15 double>	0
vifs	[1.8931,2.5352...	0
wh	[6,11,21,26,36,...	6

Command Window

New to MATLAB? Watch this [Video](#), see [Demos](#), or read [Getting Started](#).

```

1.0e+15 *
-0.9007    1.8014    0.0000    0.0000    0

>> vifs = getvif(X, 1)
Warning: Rank deficient, rank = 3,   tol =   2.3190e-13.
> In getvif at 20
Warning: Rank deficient, rank = 3,   tol =   2.3312e-13.
> In getvif at 20

vifs =

1.0e+15 *
0.0000    1.8014    0.0000    2.2518    0

>> X = mvnrnd([0 0 0], [1 .6 .6; .6 1 .6; .6 .6 1], 100);
>> X(:, end+1) = 1;
>> vifs = getvif(X, 1);
>> vifs

vifs =

1.8931    2.5352    2.0439    0

>>

```

Command History

```

create_figure('X'); imagesc(X); co
corrcoef(X)
cond(X)
close all
create_figure('X'); imagesc(X); co
create_figure('Design Matrix'); i
create_figure('Scatterplot'); plo
X = mvnrnd([0 0 0], [1 .6 .6; .6
% 3 correlated variables
X = mvnrnd([0 0 0], [1 .6 .6; .6
% The fourth is an exact linear co
X(:, end+1) = .5 * X(:, 1) - X(:,
% Let's look at the correlation m

```

Start 00:00

Name	Value	Min
SPM	<1x1 struct>	
X	<100x4 double>	-2..
a	<1x60 double>	0
ans	3	3
b	<1x60 double>	0
betas	[1.1443;-0.868...	-0..
data	<60x1 double>	-5..
hh	1.2870e+03	1.2
hh2	1.2900e+03	1.2
i	20	20
sig	<1x15 double>	0
vifs	[1.4541,1.1486...	0

```

vifs = getvif(X, 1); vifs
% really high!!
vifs(1)
vifs(3)
% VIF for predictor 3 is OK, because
% of other predictors!
load('/Users/tor/Documents/Tor_Doc
SPM.xX.X
create_figure('Design Matrix'); im
vifs = getvif(X, 1); vifs
vifs = getvif(SPM.xX.X, 1); vifs
create_figure('Scatterplot'); plo

```

New to MATLAB? Watch this [Video](#), see [Demos](#), or read [Getting Started](#).

1.0000

```

>> create_figure('Design Matrix'); imagesc(SPM.xX.X); colormap gray;
>> vifs = getvif(X, 1); vifs
Warning: Rank deficient, rank = 2, tol = 2.1962e-13.
> In getvif at 20

```

vifs =

1.0e+15 *

0.0000 -2.2518 0.0000 -4.5036

```

>> vifs = getvif(SPM.xX.X, 1); vifs

```

vifs =

Columns 1 through 6

1.4541 1.1486 1.3086 1.3617 1.3399 1.0750

Column 7

0

```

>> create_figure('Scatterplot'); plotmatrix(SPM.xX.X); axis tight
>>

```