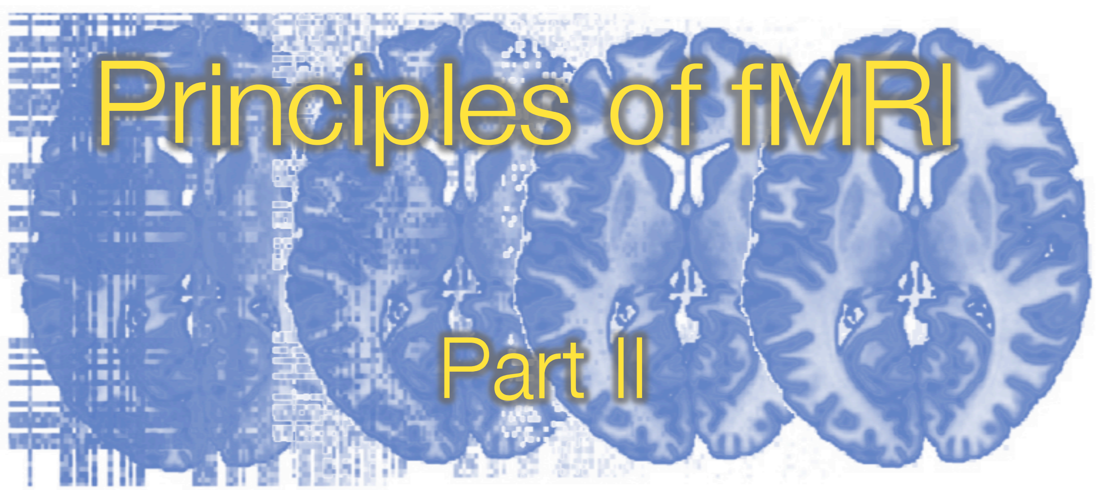
# Principles of fMRI

## Part II

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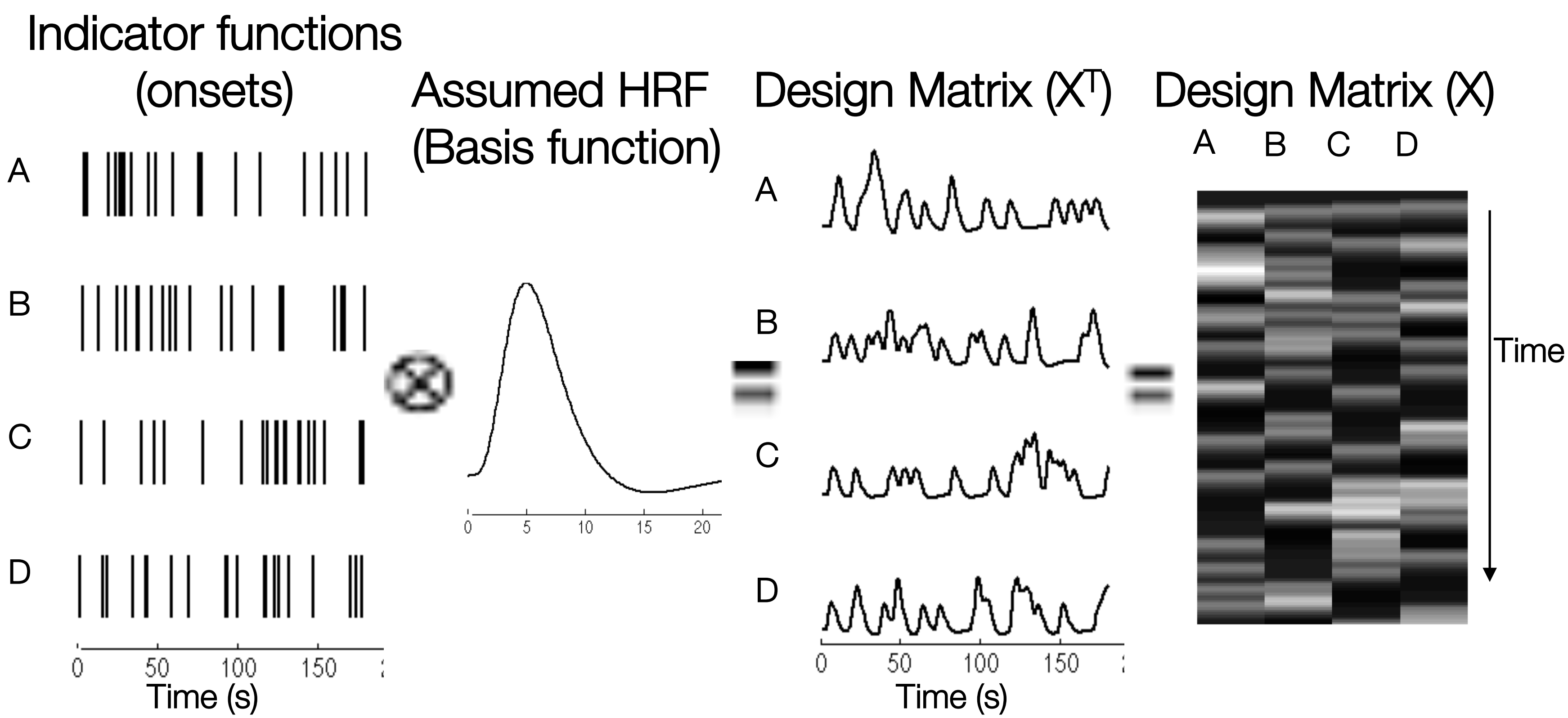
@fMRIstats

# Parametric modulation designs for enhanced psychological specificity

# Convolution for multiple predictors: Discrete event types




## Assumptions!

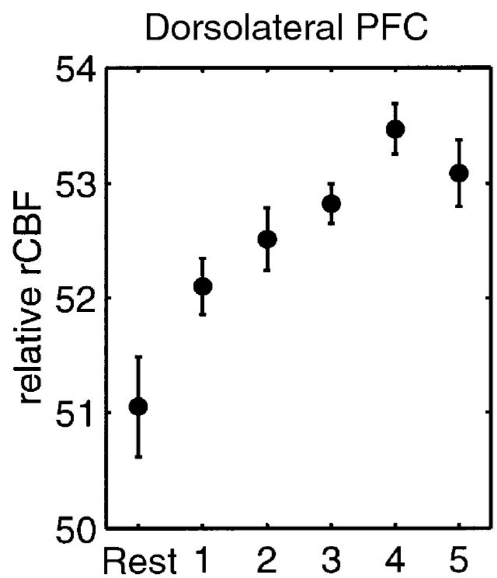
Assume neural activity function is correct

Assume HRF is correct

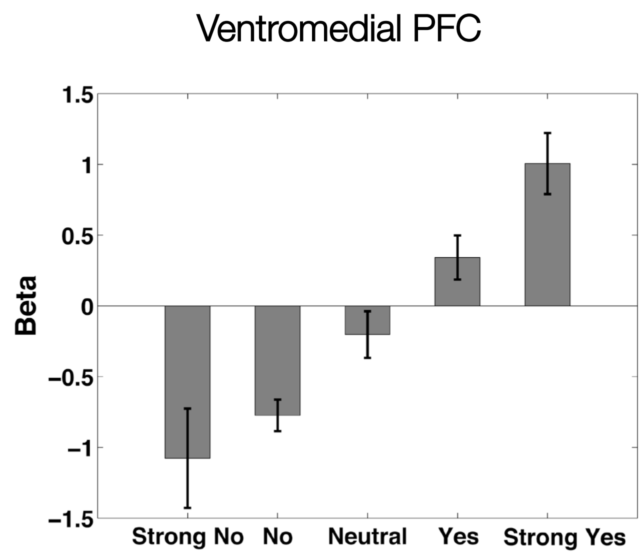
Assume LTI system

# Parametric modulation

- Test for a linear relationship between brain activity and performance/behavioral/psychological variable
- Modeling how brain activity varies across multiple levels can provide stronger evidence than contrasts for brain-performance relationships.



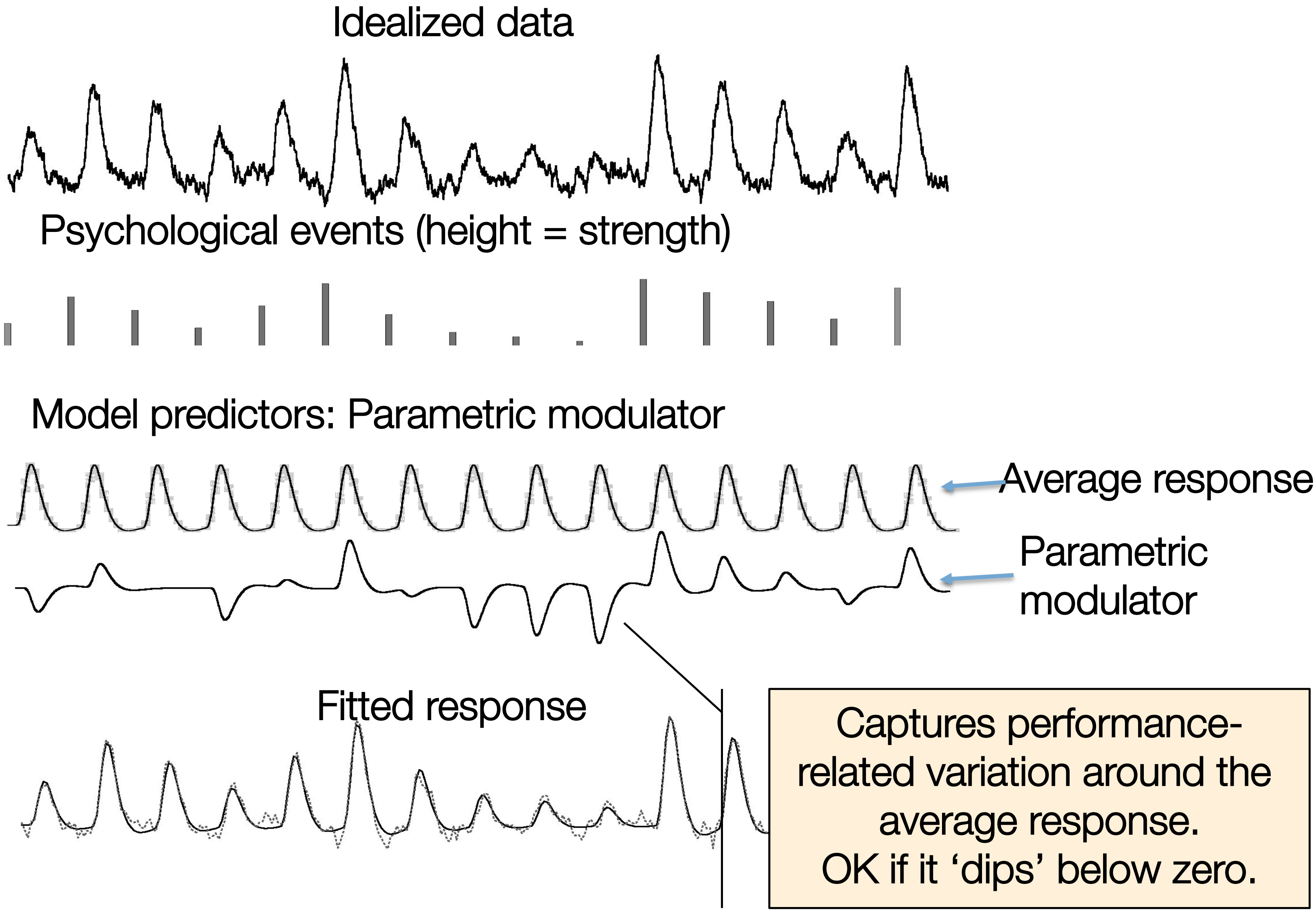

Tower of London task complexity




Goal (purchase) value of an item

Dagher et al. 1999; Hare et al., 2009; Grinband et al., 2006; Wood et al., 2008

# Parametric modulation



# Key properties

- “Standard regressor” captures average event-related response

- Parametric modulator is orthogonal to the “standard regressor,” and so captures modulator variable-related activity above and beyond the average response

- Extendable:

    - Add linear modulators for time (e.g., linear change across trials), very useful for assessing habituation/fatigue and practice effects

    - Add other basis functions to capture some nonlinear effects across performance or time (e.g., quadratic or exponential terms)

- Implementation: All done by adding regressors to the GLM design matrix

# Cautions

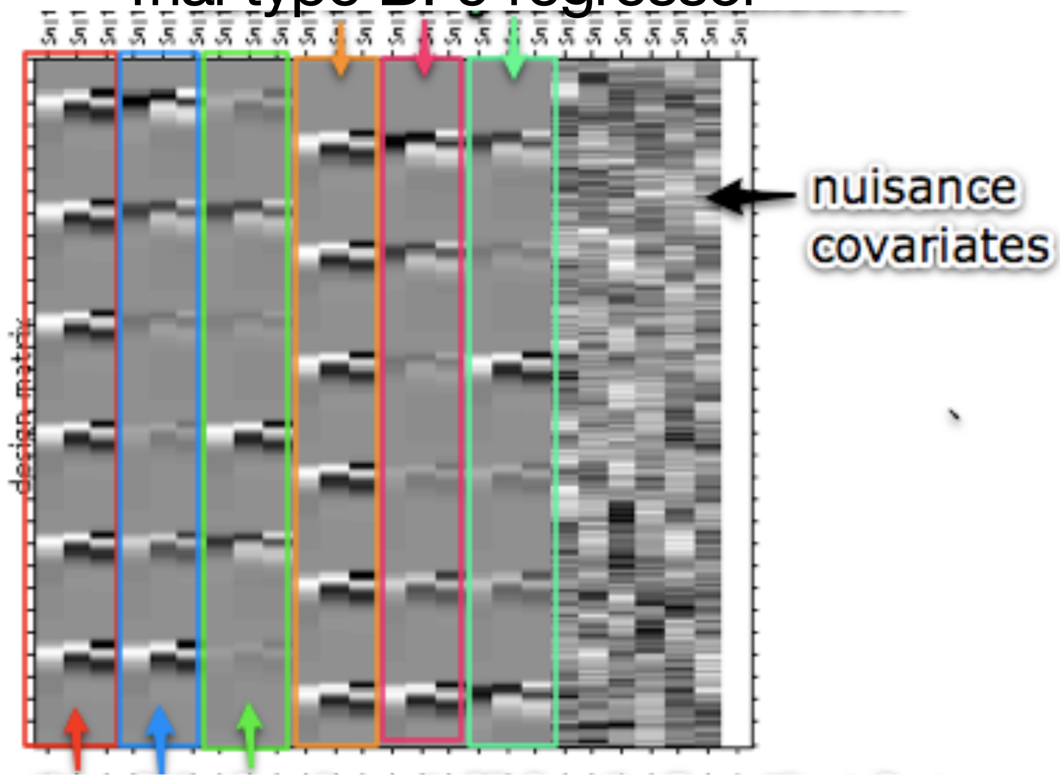
Principles of fMRI

- Standard approach is to modulate only the amplitude of a brief event ('stick function') or epoch
  - Ok for many purposes, but may not be accurate model
  - It is also possible to modulate the duration of an epoch with some tricks
- As with other regressors, may not be straightforward to do a t-test that captures the parametric modulation effect if you have multiple basis functions.
- If you enter multiple modulators: Caution
  - In some software (e.g., SPM), subsequent modulators orthogonalized with respect to earlier ones, so that they are only allowed to explain variance not explained by other modulators.
  - This is not a standard multiple regression, but can be changed by modifying the code.

# Parametric modulation

- Image of design matrix:

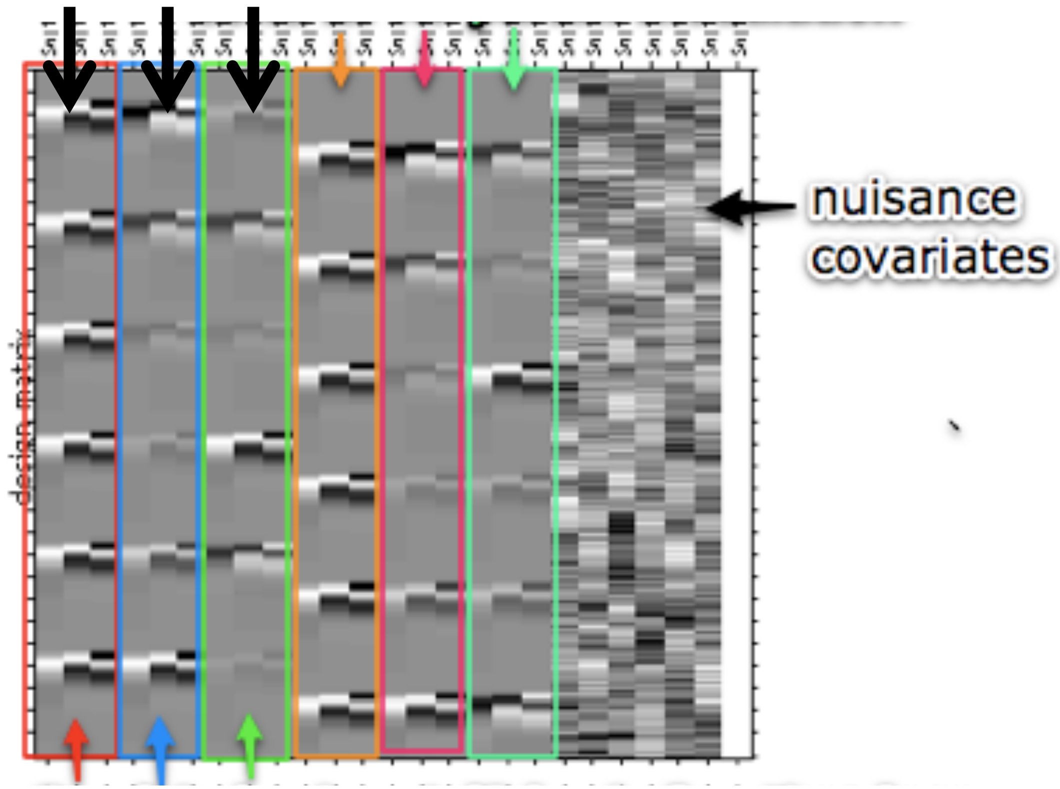
Trial type B: 9 regressor




Trial type A: 9 regressor

# Parametric modulation

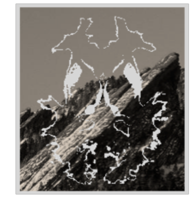
- Image of design matrix:




Trial type A: 9 regressor

End of this section.

# Key properties



- "Standard regressor" captures average event-related response

- Parametric modulator is orthogonal to the "standard regressor," and so captures modulator variable-related activity above and beyond the average response

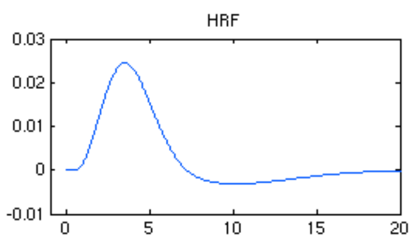
- Assumptions:
  - Linear brain responses based on input variables; sensitive to interval scaling properties of input variables
  - Only stick function amplitude is modulated; may not capture changes in shape/duration

- Subsequent modulators orthogonalized wrt earlier ones, so that they are only allowed to explain variance not explained by other modulators
  - This is done by a call to spm_orth.m and can be changed by modifying the code)

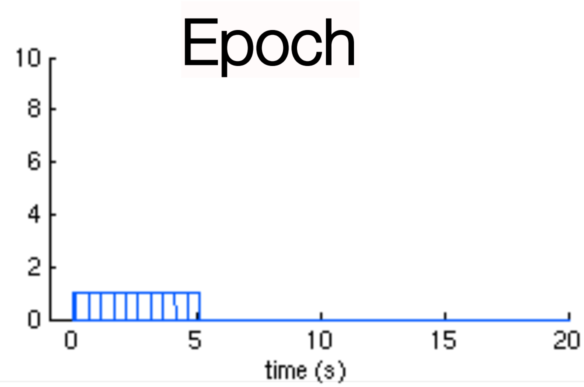
# Parametric modulation of duration vs. amplitude

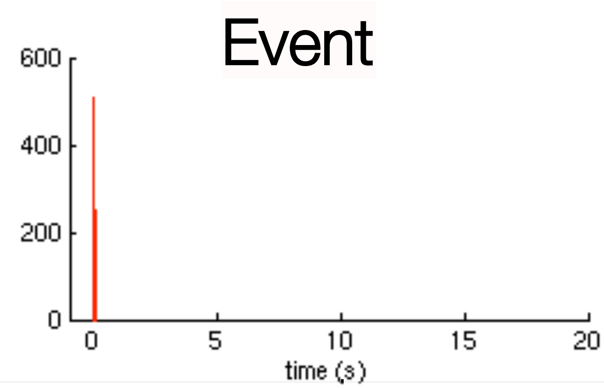
# Choosing a stimulus model: Events vs. epochs

HRF



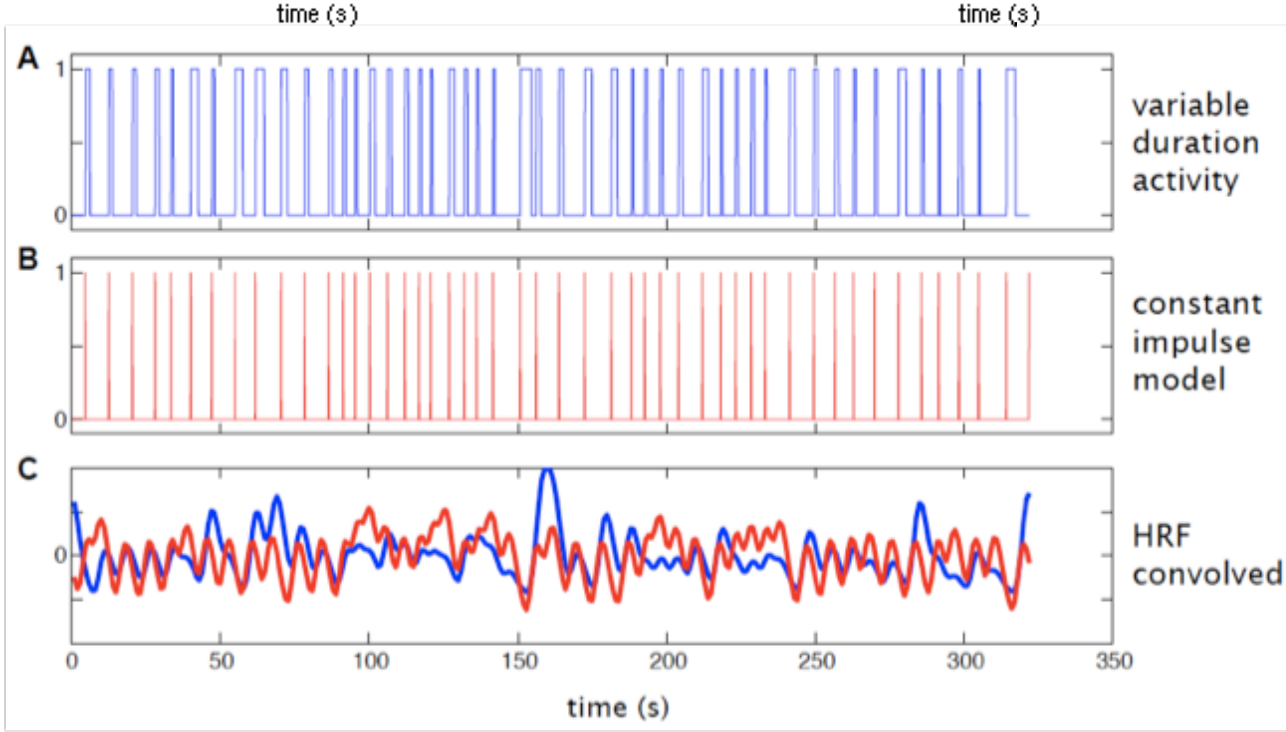

Stimulus Function



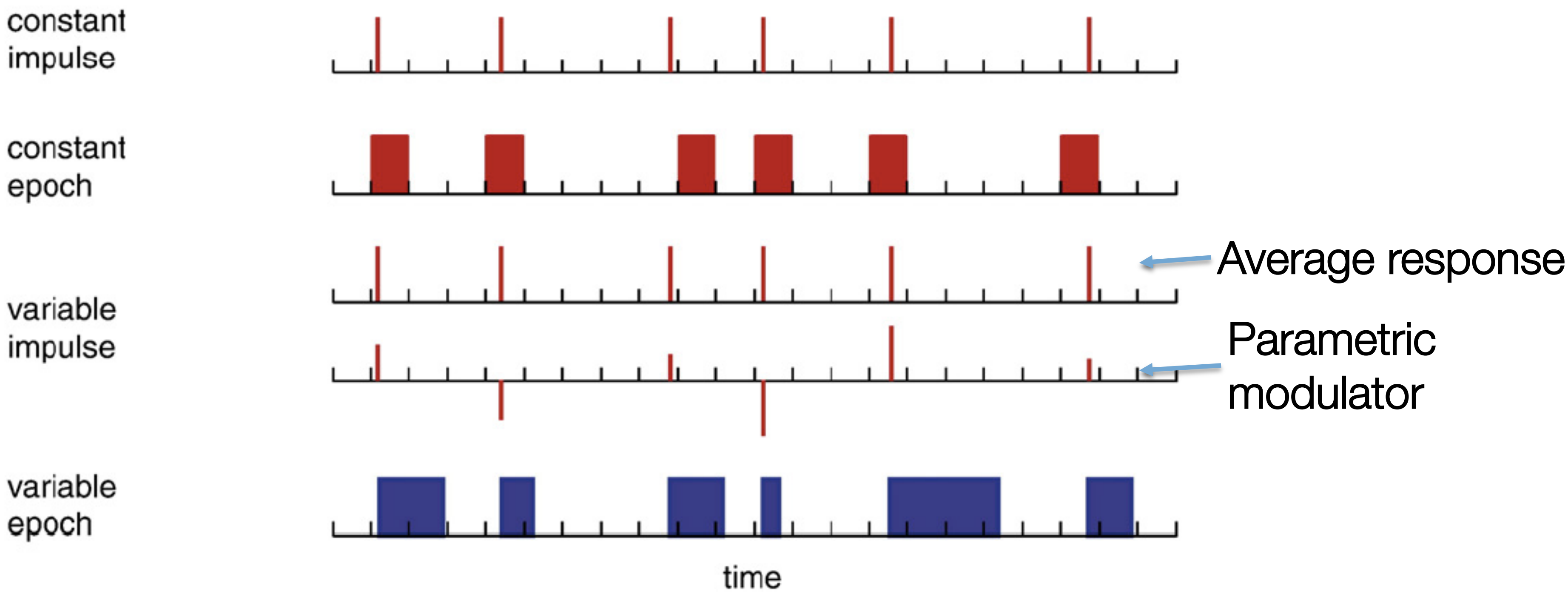




Does it matter for event-related fMRI?
* answer: More than you might think!

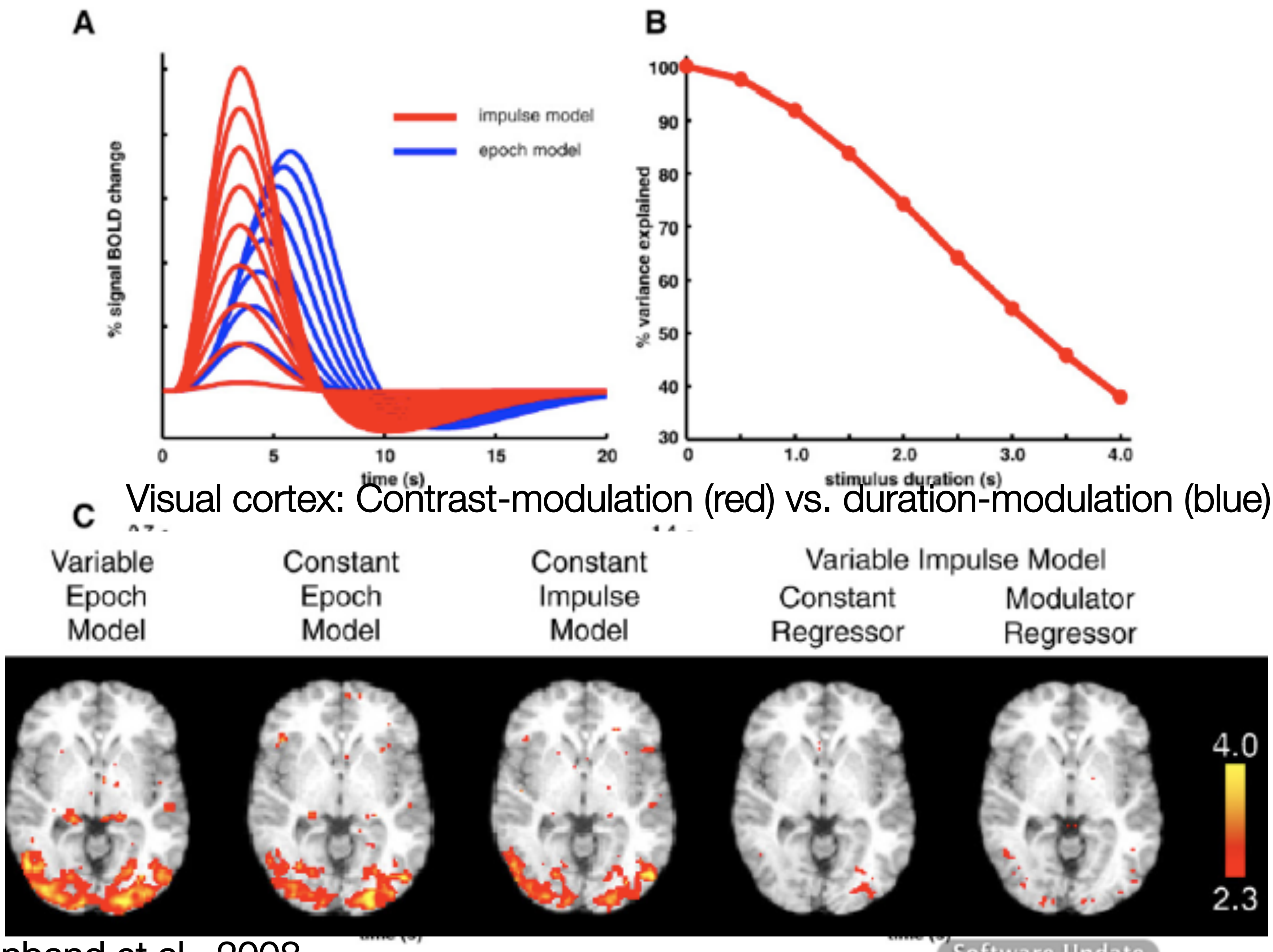
Grinband et al., 2008



# What to modulate: amplitude or duration?



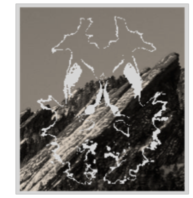

Grinband et al., 2008




Visual cortex: Contrast-modulation (red) vs. duration-modulation (blue)

Grinband et al., 2008

# Key issue



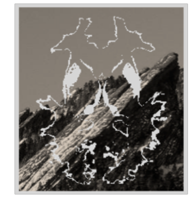
- “Variable epoch” model is not orthogonalized with respect to the average trial response (i.e., there is no “standard regressor”

- How do you test whether a behavioral modulator has an effect “above and beyond” the effect of the average trial response?

- Need to create both “standard regressors” and “variable epoch” regressors, and orthogonalize the 2nd wrt the 1st.

- You can do this using getPredictors (in the CANlab toolset / OptimizeDesign toolbox) and spm_orth (in SPM).

- For example code see: http://www.scan.psych.columbia.edu:16080/pubwiki/doku.php/help/fmri_help/fmri_statistical_models/

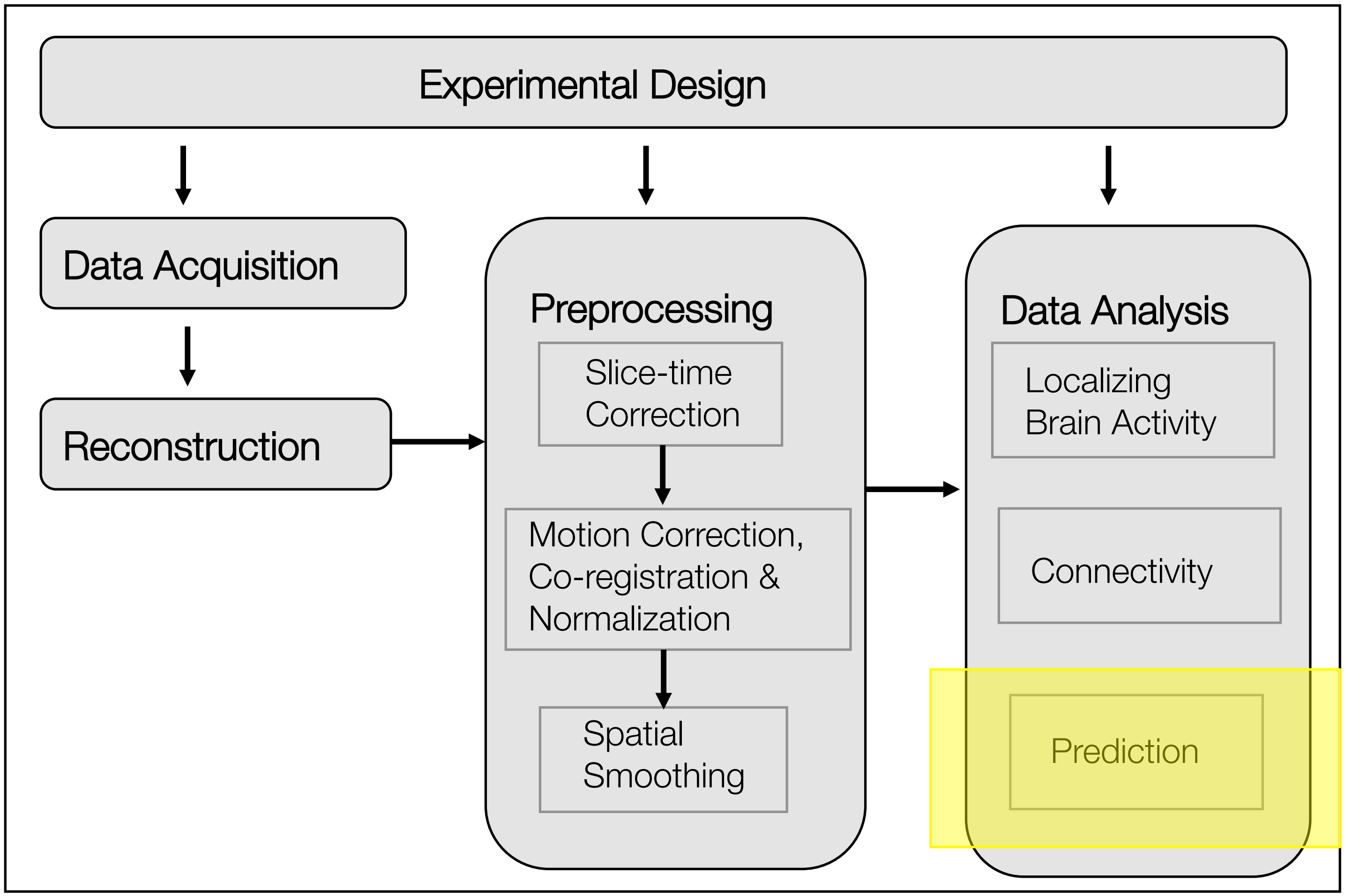


# Example code

```
% This code will turn a series of onset times and durations (e.g., RT)
% into a duration-modulated parametric modulator
% (See Grinband et al., 2008)
% You would add the two variables in X to the SPM design matrix, and repeat
% for each event type.
%
% Needed: SCN_Core_Support (onsets2fmridesign)

% The onsets and modulator are stored in SPM already, assuming:
% You have set up both time and parametric modulation, so that parametric
% modulation is the 2nd modulator (SPM.Sess.U(*).P(2).P)
% AND assuming you have entered things in units of seconds.
% First load SPM.mat.  Then:
onsets_in_sec = SPM.Sess.U(1).ons;  % for the first trial type
durations = SPM.Sess.U(1).P(2).P;   % e.g., reaction time; the modulator

Xavg = onsets2fmridesign(onsets_in_sec, SPM.xY.RT, SPM.nscan, 'hrf');
Xdur = onsets2fmridesign([onsets_in_sec durations], SPM.xY.RT, SPM.nscan, 'hrf');
X = [Xavg(:, 1) Xdur(:, 1)];
figure; subplot(1, 2, 1); plot_matrix_cols(X);
title('Original (non-orthogonalized)')

% We must orthogonalize the modulator with respect to the average response,
% so that significant effects for the modulator regressor are interpretable
% as duration-modulated effects above and beyond the average response to
% the events.

X = spm_orth(X); % orthogonalize
subplot(1, 2, 2); plot_matrix_cols(X)
title('Orthogonalized (add to SPM as regressors)')
```

# Multi-voxel Pattern Analysis

# Data Processing Pipeline



# Classification and Prediction

- There is a growing interest in using fMRI data for classification of mental disorders and predicting the early onset of disease.

- In addition, there is interest in developing methods for predicting stimuli directly from functional data.

- This opens the possibility of inferring information about subjective human experience directly from brain activation patterns.

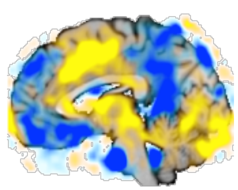
# Machine Learning

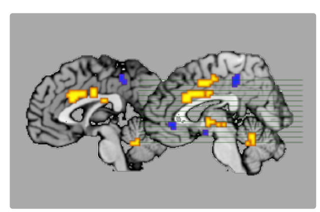
- Predicting brain states is challenging and requires the application of novel statistical and machine learning techniques.

- Various techniques have successfully been applied to fMRI data in which a classifier is trained to discriminate between different brain states and then used to predict the brain states in a new set of fMRI data.

# Machine Learning

- When applied to fMRI data the result is often a pattern of weights across brain regions that can be applied prospectively to new brain activation maps to quantify the degree to which the pattern responds to a particular type of event.





$\underline{w}^T \underline{x} > 0$ Group A

$\underline{w}^T \underline{x} < 0$ Group B

$\underline{x} = (x_1, \ldots . x_V)$ $\underline{w} = (w_1, \ldots . w_V)$

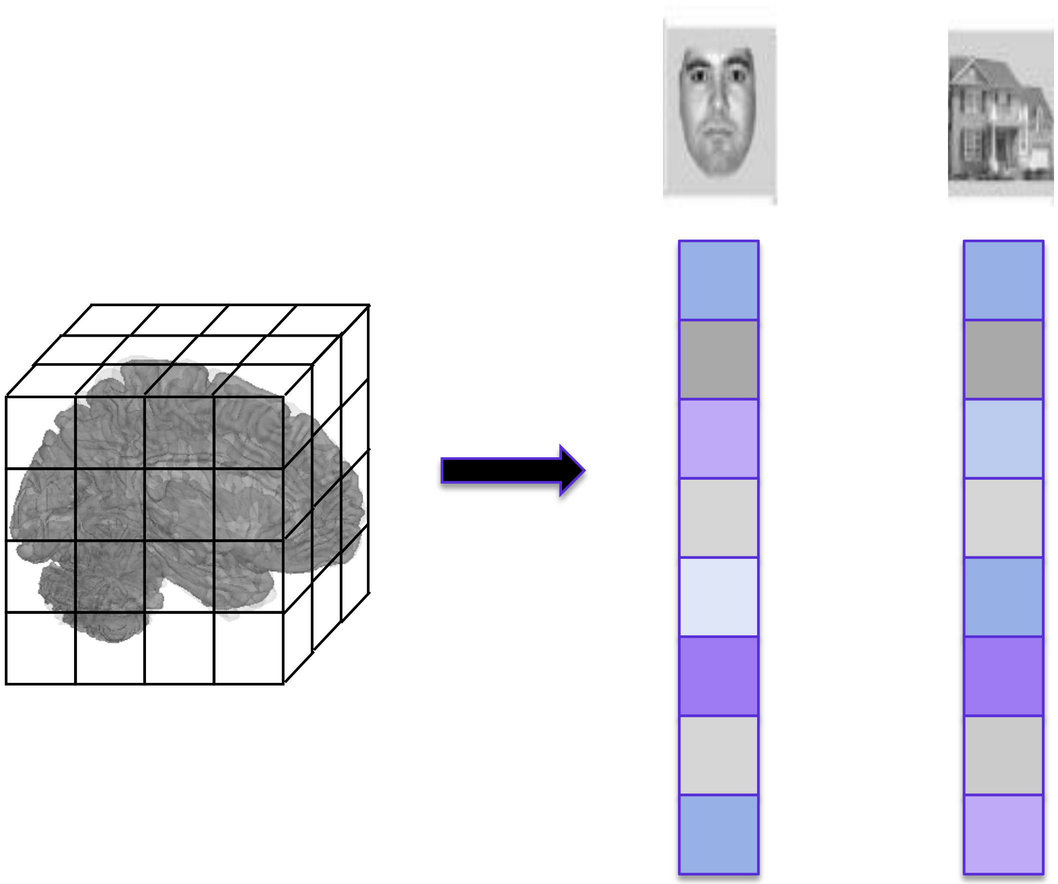
# MVPA



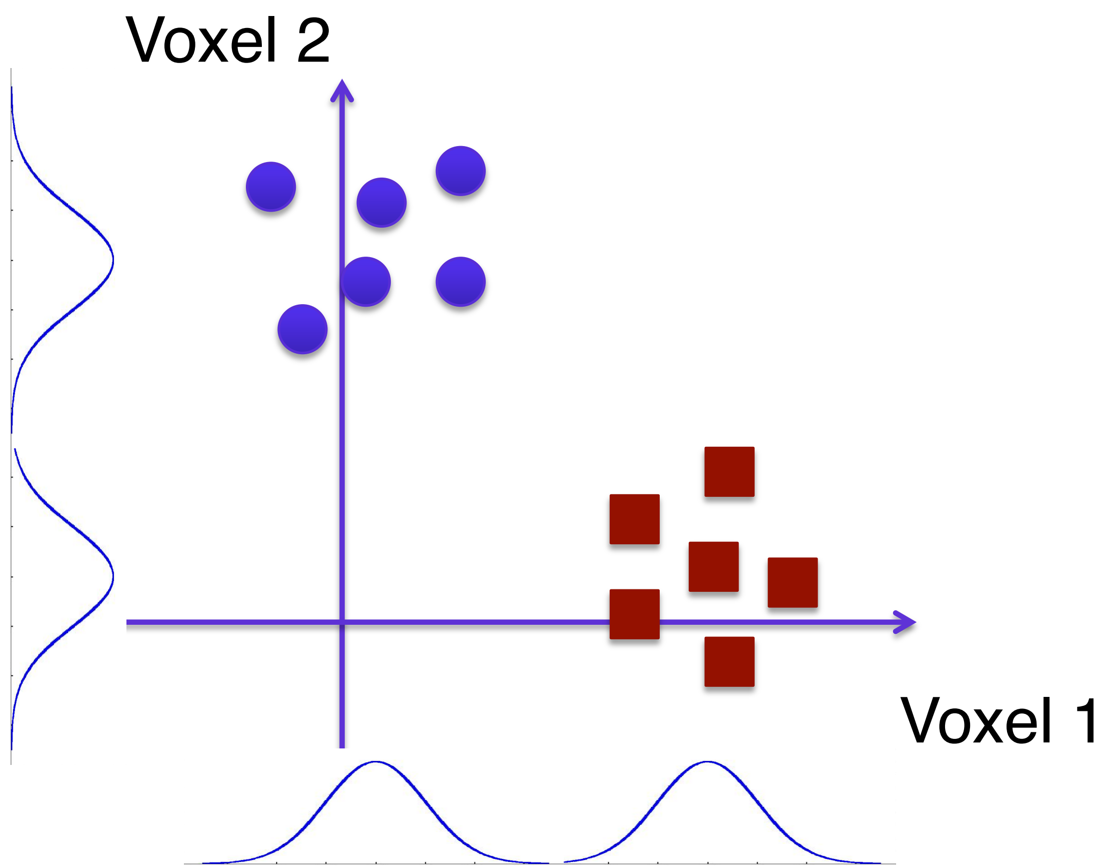
- The application of machine learning methods to fMRI data is often referred to as multi-voxel pattern analysis (MVPA)

- Instead of focusing on single voxels, MVPA uses pattern-classification algorithms applied to multiple voxels to decode the patterns of activity.

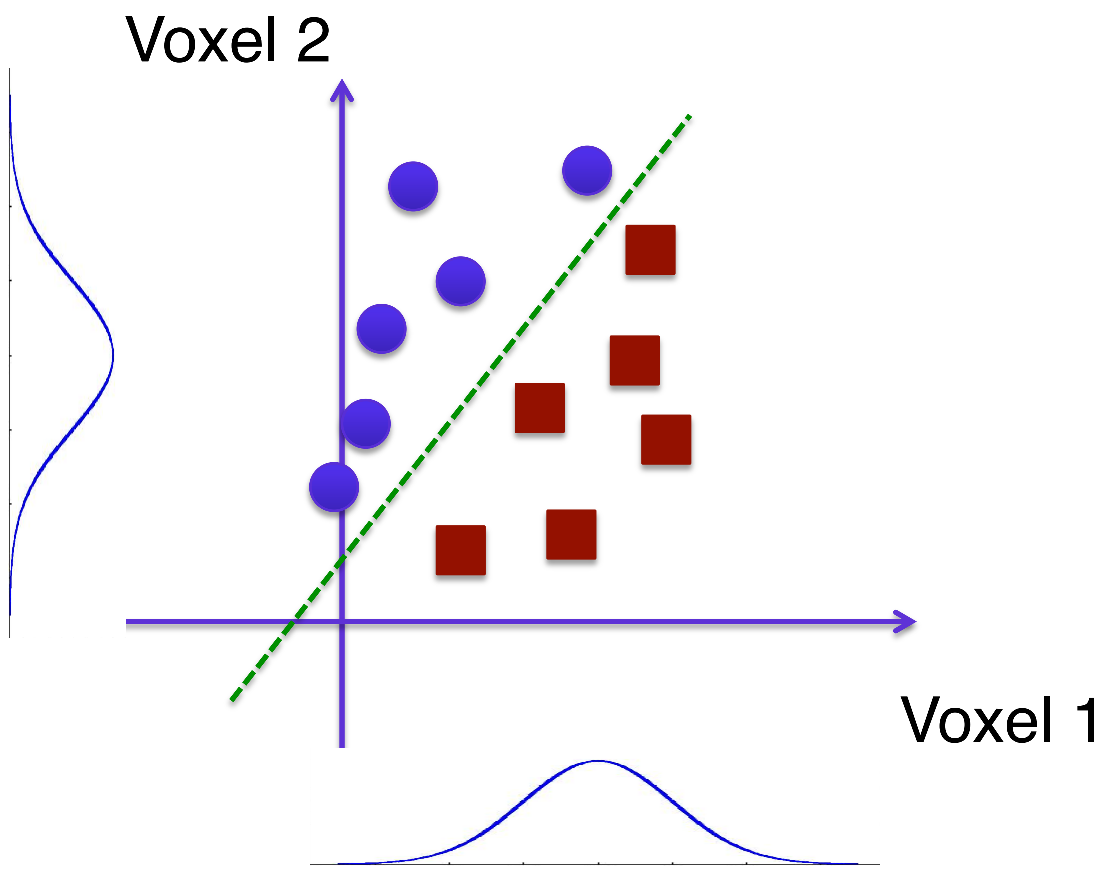
# Multivariate Analysis



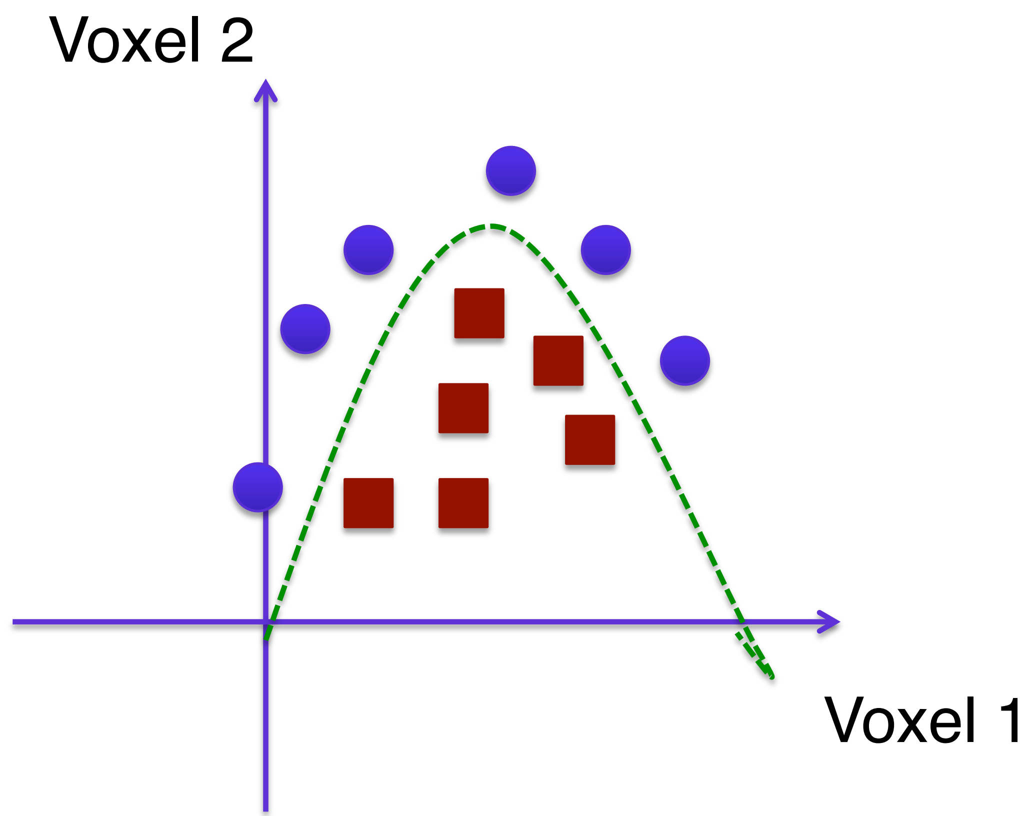
# Multivariate Analysis



# Multivariate Analysis



# Multivariate Analysis



# MVPA vs GLM



- In MVPA the goal is to determine the model parameters that allow for the most accurate prediction of new observations.
  - Seek to create rules that can be used to categorize new observations.

- In contrast, the GLM seeks to determine the model parameters that best fit the data at hand.

# Classifiers

- A classifier is a function f(.) that takes the values of observed features (e.g., voxels) and predicts to which class the observation belongs (e.g., disease state).

- Let us denote the set of features $\underline{x}=(x_1,\ldots x_V)$ and the class label y.

- Predicted class: $\hat{y} = f(\underline{x})$

# Training Data



- A classifier has a number of parameters $\underline{w}$ that needed to be estimated, or learned.

- The learning is typically performed on a subset of the observations called the training data.

- The learned classifier models the relationship between the features and class labels in the training data set.

# Test Data

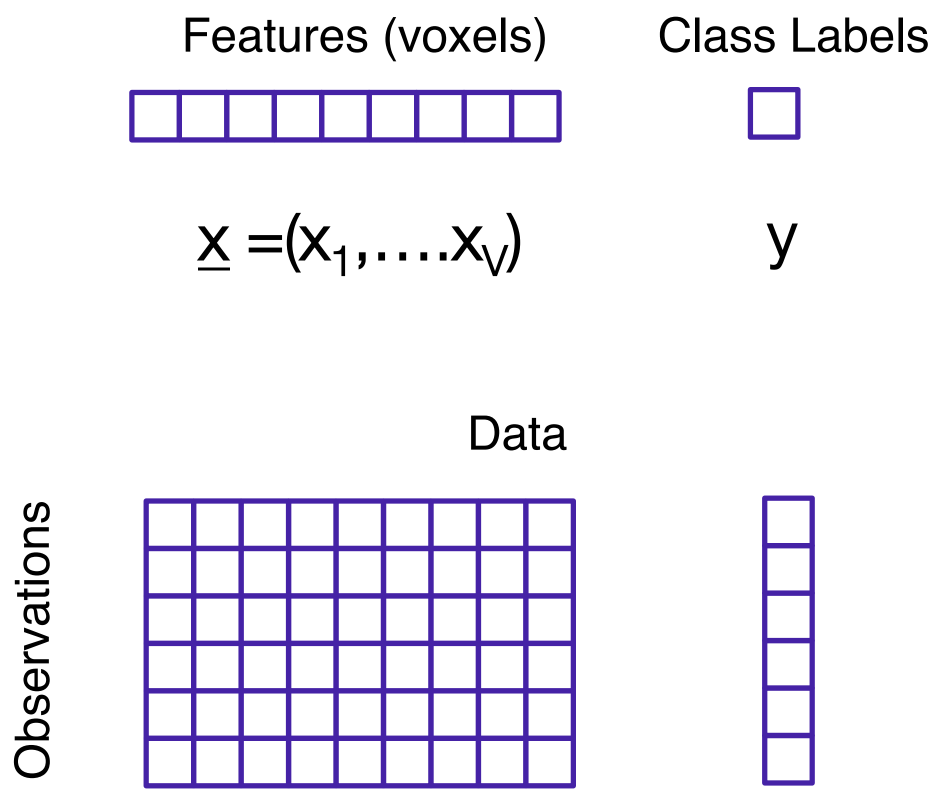
- Once trained, the classifier is evaluated using an independent set of observations called the test data.

- If the classifier truly captures the relationship between features and classes, it should be able to predict the class label for data it hasn't seen before.

- The accuracy of the classifier measures the fraction of observations in the test data for which the correct label was predicted.

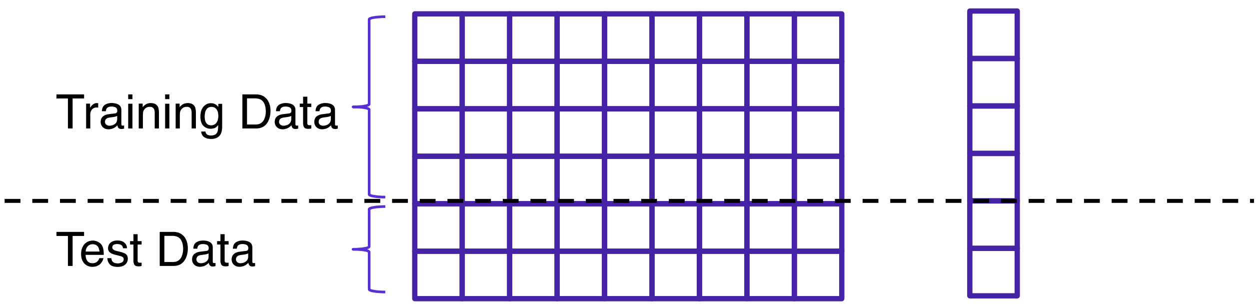
# Illustration





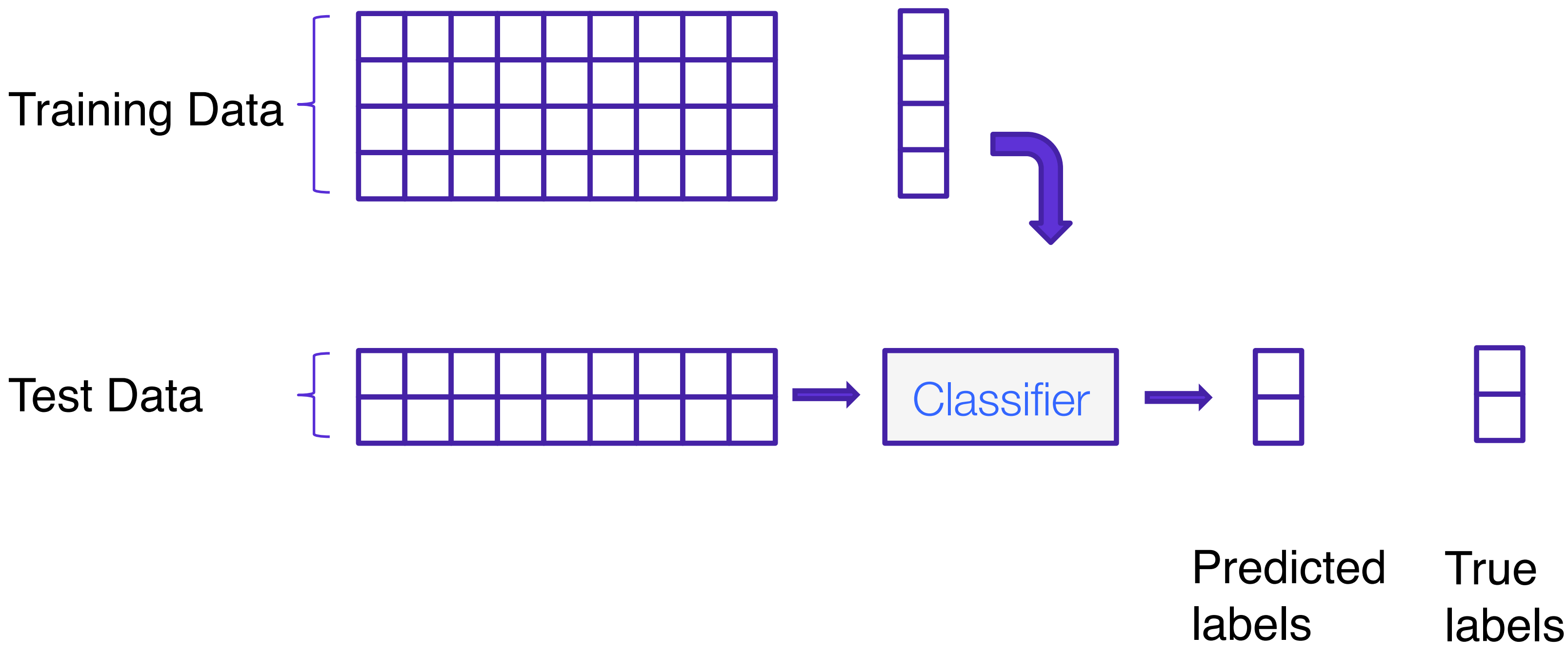
# Illustration

The full data set is split into two parts: training and test data



# Illustration





# End of Module

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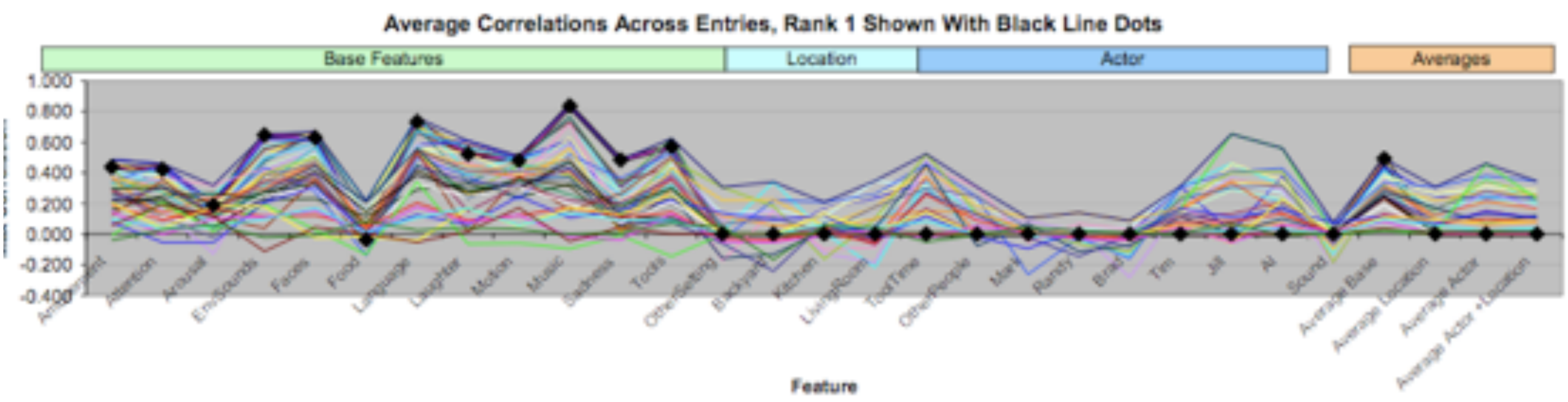
# Criteria for a good prediction algorithm

- Accuracy: How accurate are predictions, and are they good enough to be useful?
- Specificity: How well can a pattern of brain activity discriminate among alternative outcomes or processes?
- Generalizability: Does a pattern predict other, dissimilar variants of the outcome of interest?
- Interpretability: Are the brain maps neuroscientifically interpretable?
- Transparency: Can scientists understand the algorithm and its results, and thus know why it might succeed or fail?

# Interpretability: Example

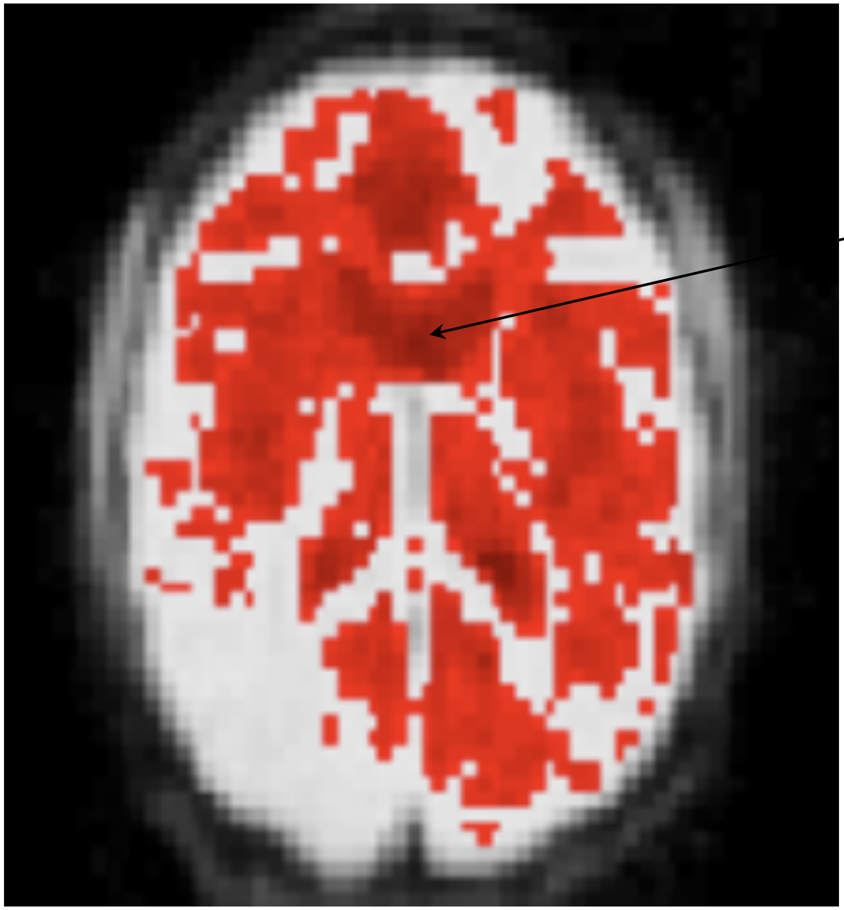
Olivetti et al., 2006
Winner: Pittsburgh Brain Activity Interpretation Competition

# Interpretability: Example




Olivetti et al., 2006

# Interpretability: Example



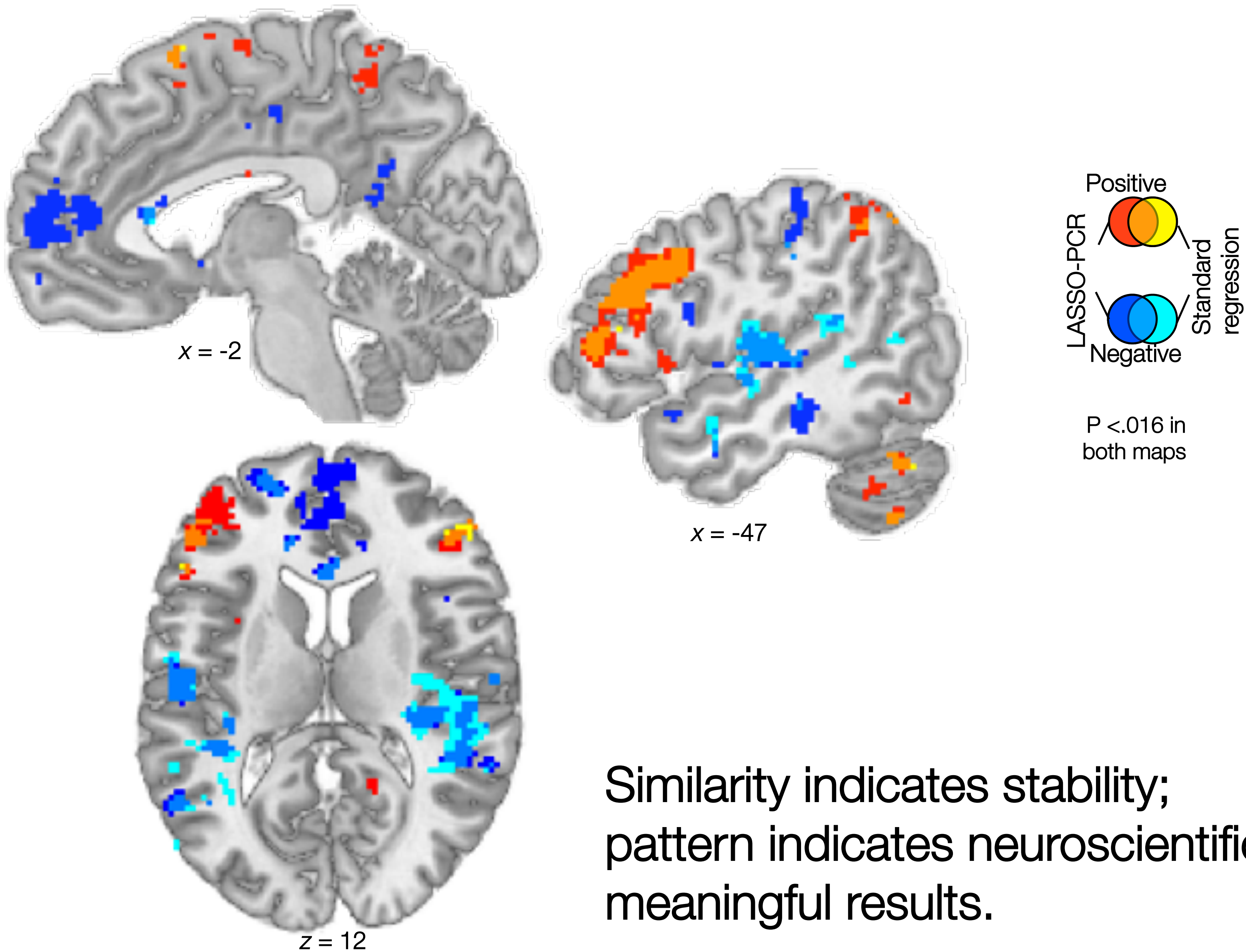
Ventricles

...

???

Language, Subject 2

# Interpretability: Comparison between LASSO-PCR and standard regression weights




Similarity indicates stability; pattern indicates neuroscientifically meaningful results.

Comparison between LASSO-PCR and standard regression weights