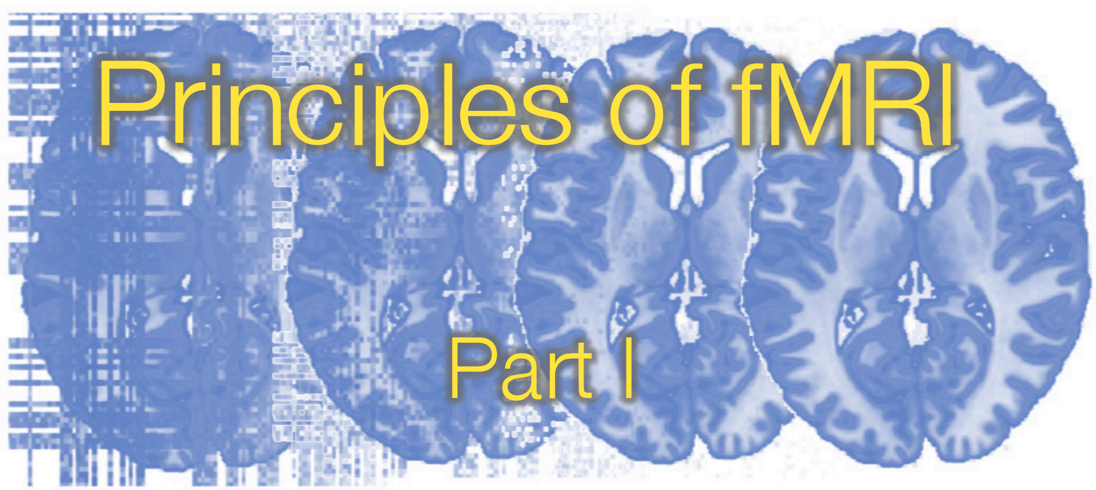
Principles of fMRI

Part I



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The General Linear Model Applied to fMRI

REVIEW: KEY CONCEPTS

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Lindquist & Wager

General Linear Model

- The general linear model (GLM) approach treats the data as a linear combination of model functions (predictors) plus noise (error).

- The model functions are assumed to have known shapes (e.g., straight line, or known curve), but their amplitudes are unknown and need to be estimated.

- The GLM framework encompasses many of the commonly used techniques in fMRI data analysis (and data analysis more generally).

The GLM Family

Dependent Variable	Predictors	Analysis
One continuous	Continuous 1+	Multiple Regression
	Categorical 1+	ANOVA
	Categorical Continuous	ANCOVA
2 repeated measures	0 between 1 within	Paired t-test
k repeated measures	0 between k – 1 categorical within	One-way RM-ANOVA, MANOVA
4+ repeated measures	0 between 2+ *categorical* within	Factorial RM-ANOVA
4+ repeated measures	1+ between 2+ *categorical* within	“GLM”

General Linear Model

Generalized least squares (iterative): correlated errors (e.g., timeseries)

Correlated errors across repeated measures

The structural model for the GLM

Simple or multiple regression, t-tests, ANOVA, ANCOVA

$$\mathbf{Y} = \mathbf{X}\beta + \varepsilon$$

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} & \cdots & X_{1p} \\ 1 & X_{21} & \cdots & X_{2p} \\ \vdots & \vdots & & \vdots \\ 1 & X_{np} & \cdots & X_{np} \end{bmatrix} \times \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_p \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

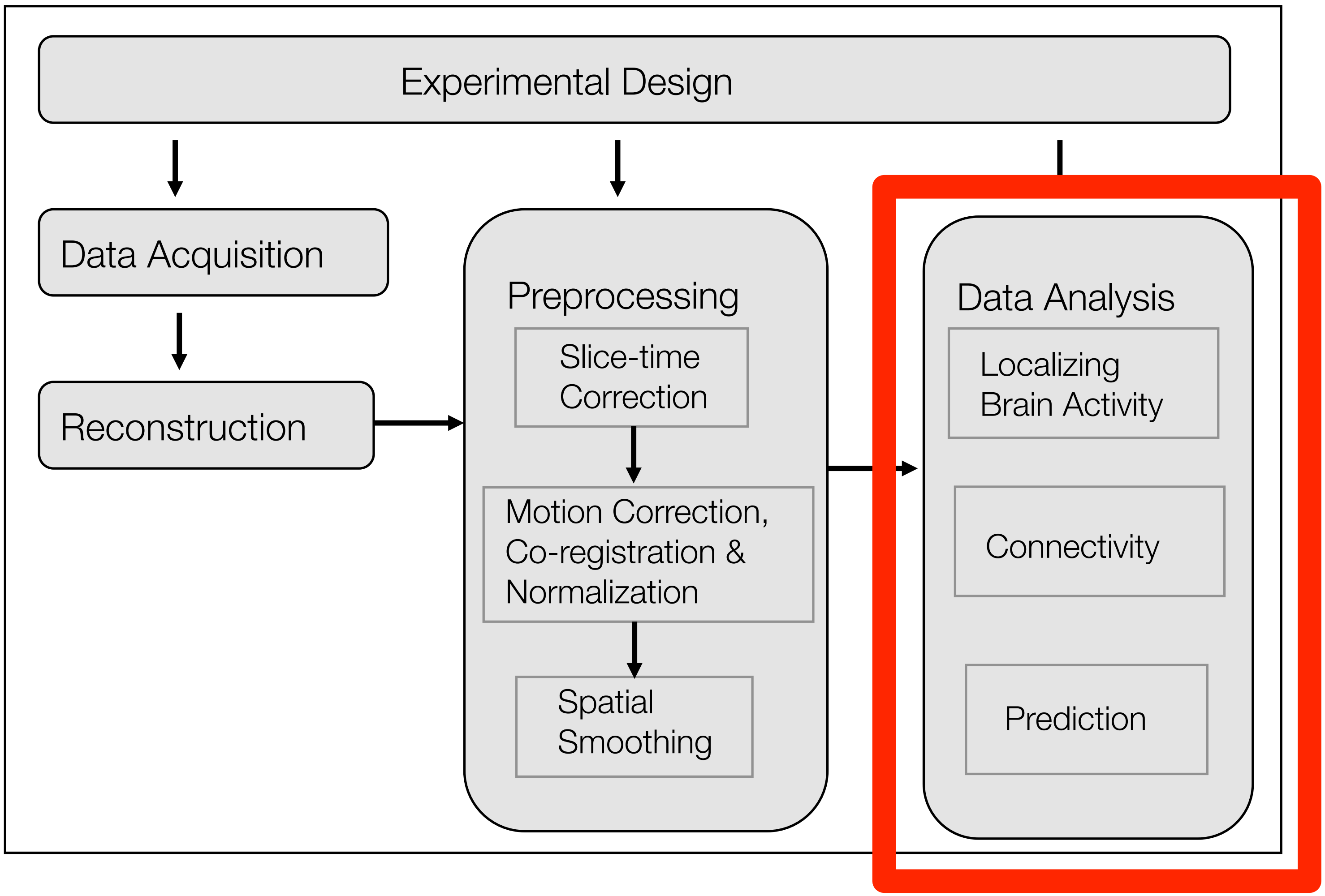
Observed Data

Design matrix

Model parameters

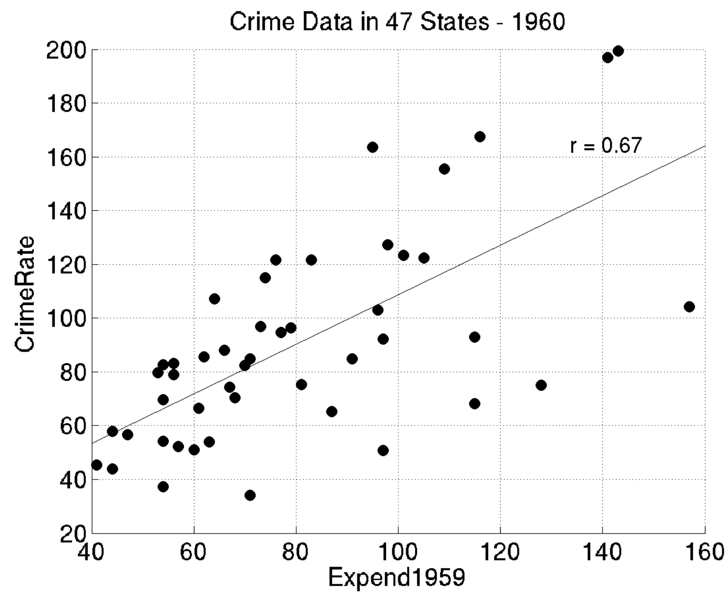
Residuals

Data Processing Pipeline



Principles of fMRI Part I

Simple regression: A simple linear model with one predictor



Specify model → Estimate → Statistical inference → Scientific interpretation

Simplification: “linear relationship”

Find slope, intercept

Test slope: P-value

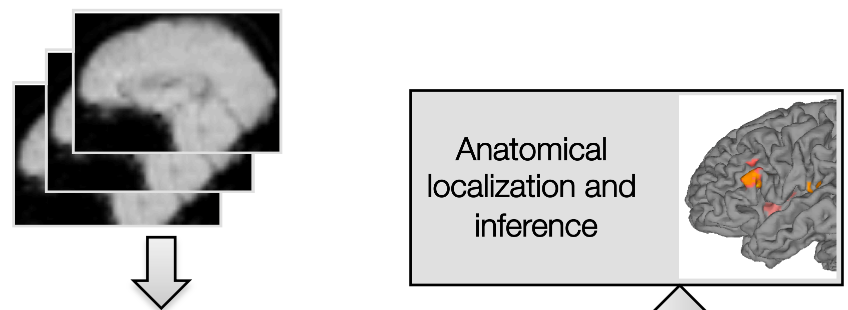
Meaning of relationship?

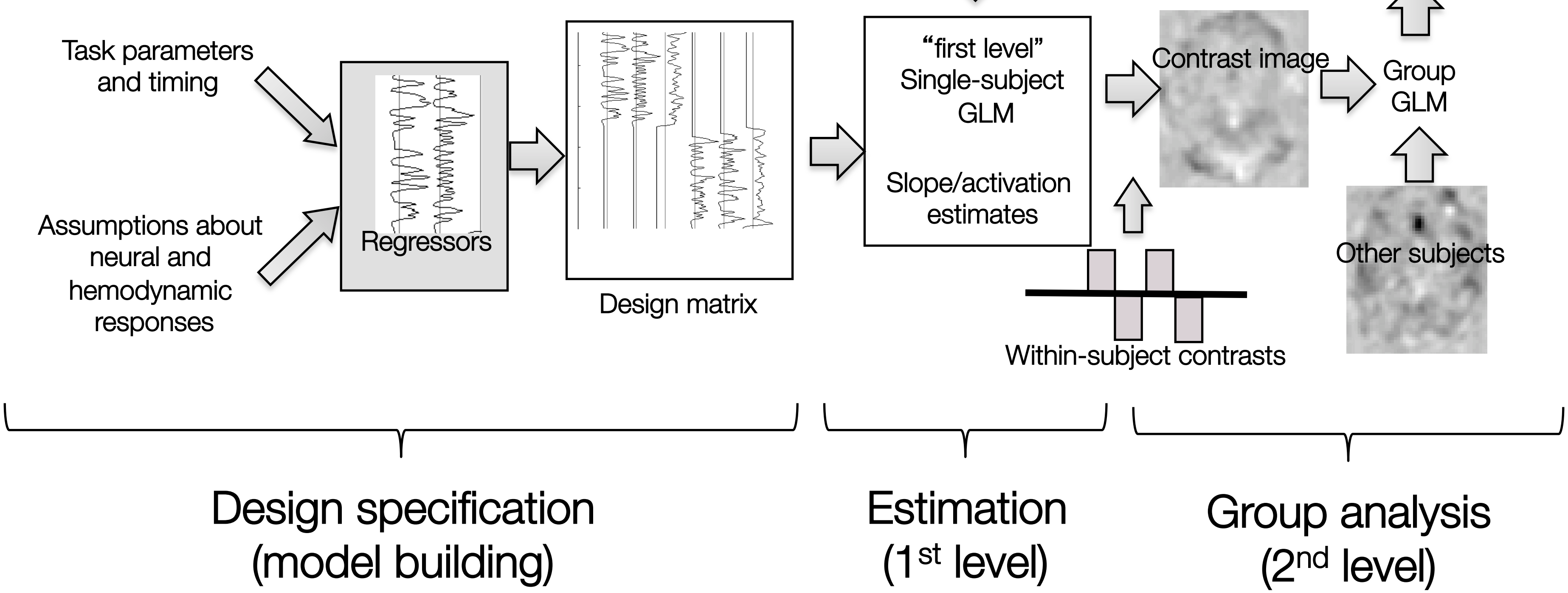
Overview of the GLM analysis process

Typically a two-level hierarchical analysis

1. Within-subject (individual)
2. Across-subject (group)

- Can be done in stages (1^{st}, 2^{nd} level)
- Hierarchical models combine stages into one model





REGRESSION IN FMRI

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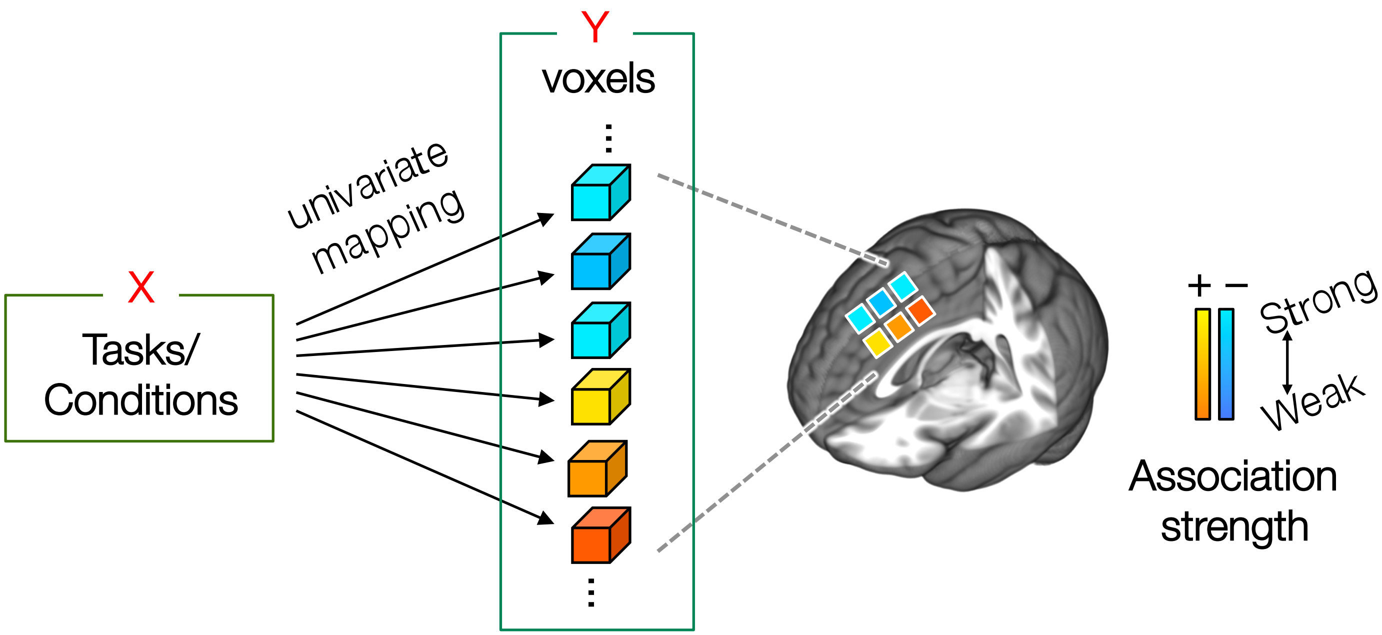
Lindquist & Wager

Mass Univariate Approach

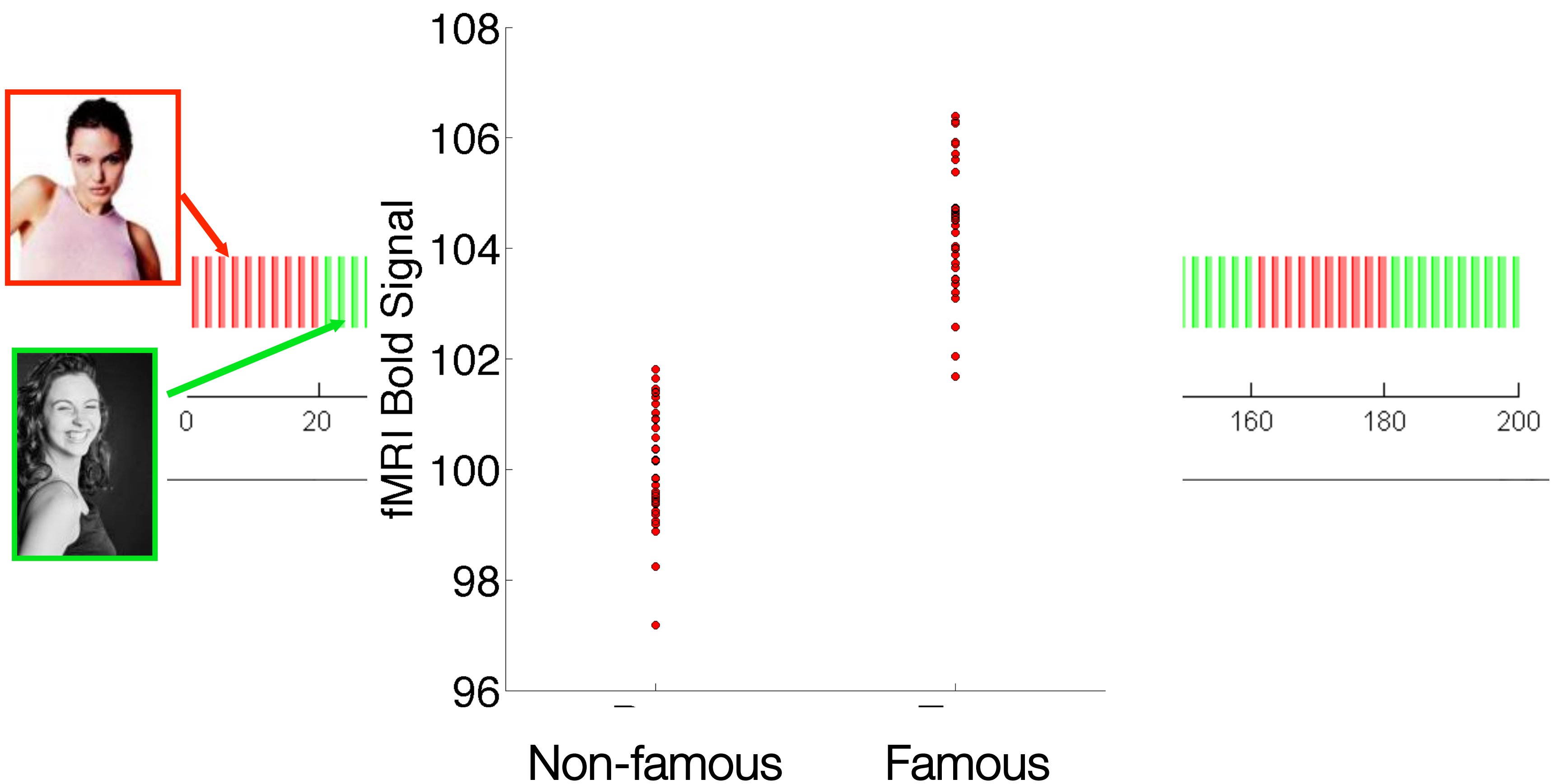
- Typically analysis is performed by constructing a separate model for each voxel
  - Brain activity in one voxel is the outcome (Y)
  - Stimulus, task, and/or behavioral variables are the predictors (X)
  - 'Mass univariate approach': Assumes voxels are independent, each its own separate test



Woo & Wager 2015; Image credit: Wani Woo

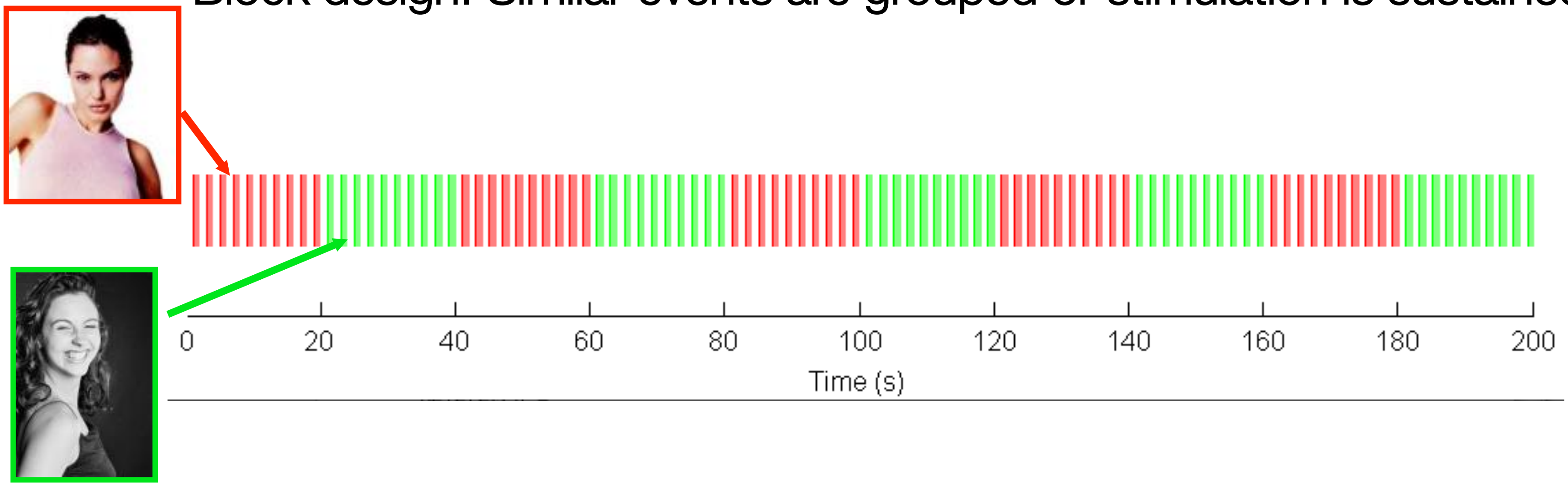
First-level GLM:
Single-voxel, single-subject

- Consider an experiment of alternating blocks of viewing famous and non-famous faces

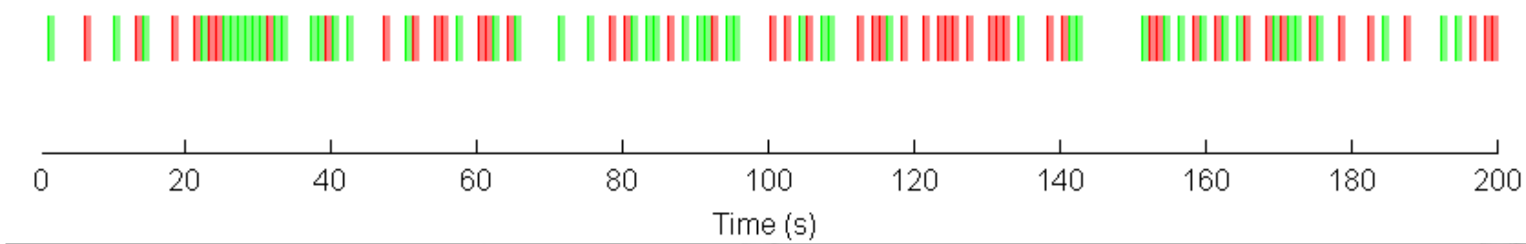


First-level GLM:
Blocked and event-related designs

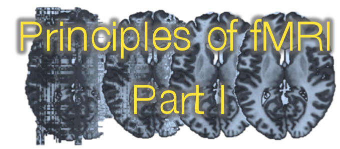
- Block design: Similar events are grouped or stimulation is sustained



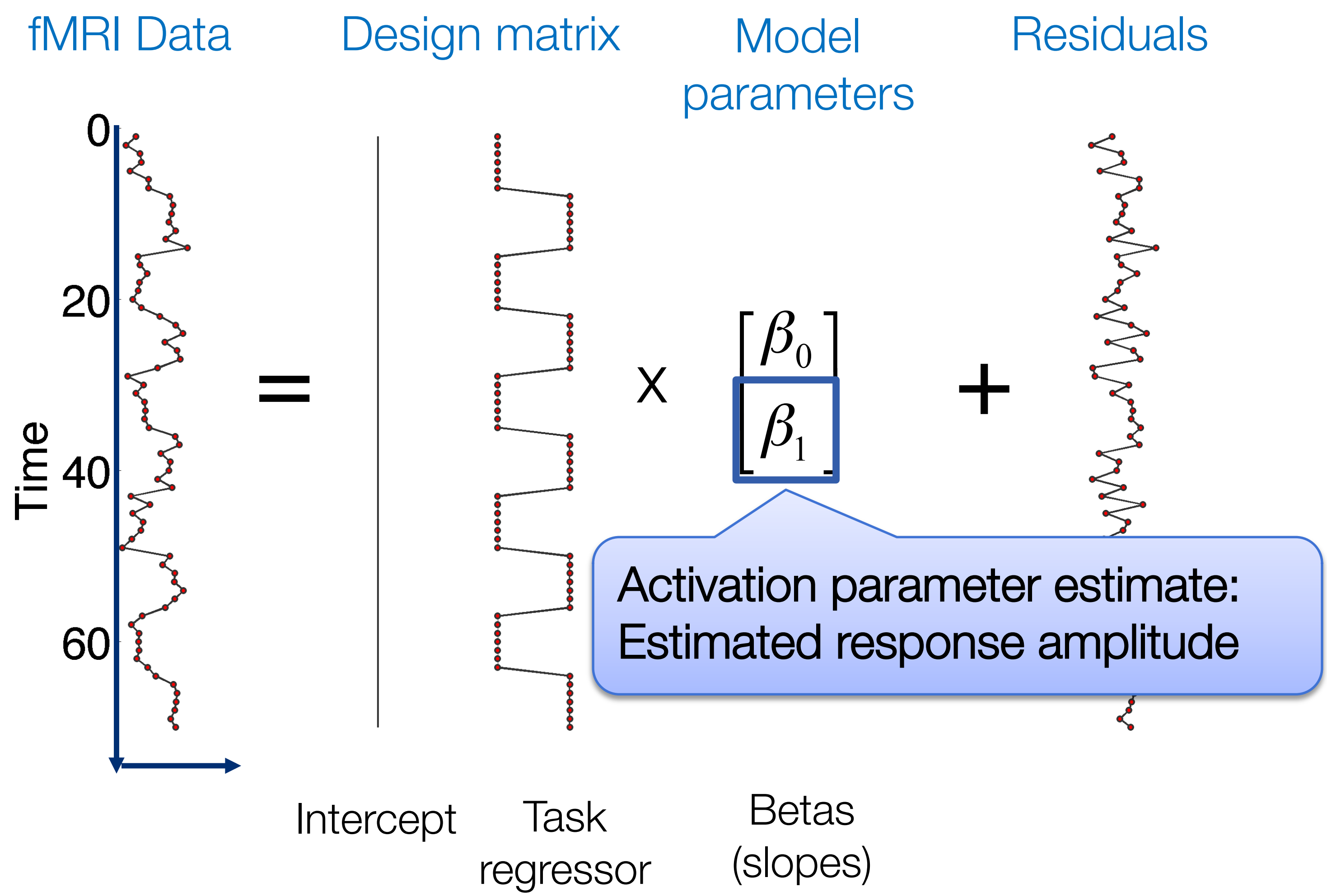
Event-related design: Brief events of different types are intermixed



First-level GLM: Single-voxel, single-subject

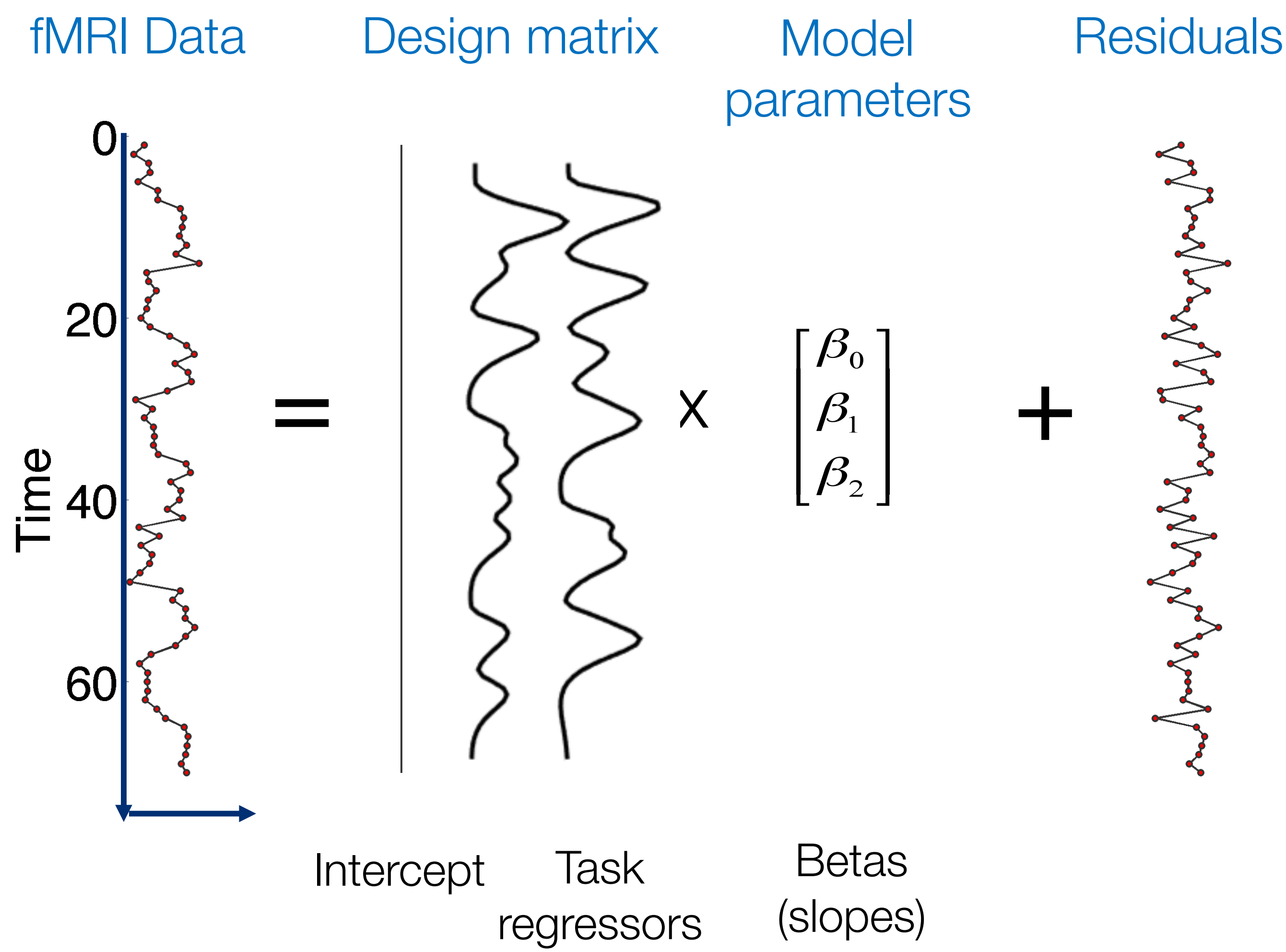


- A basic design matrix with one predictor (regressor) of interest (e.g., Task – Control, Famous vs. Non-famous) :



First-level GLM: Single-voxel, single-subject

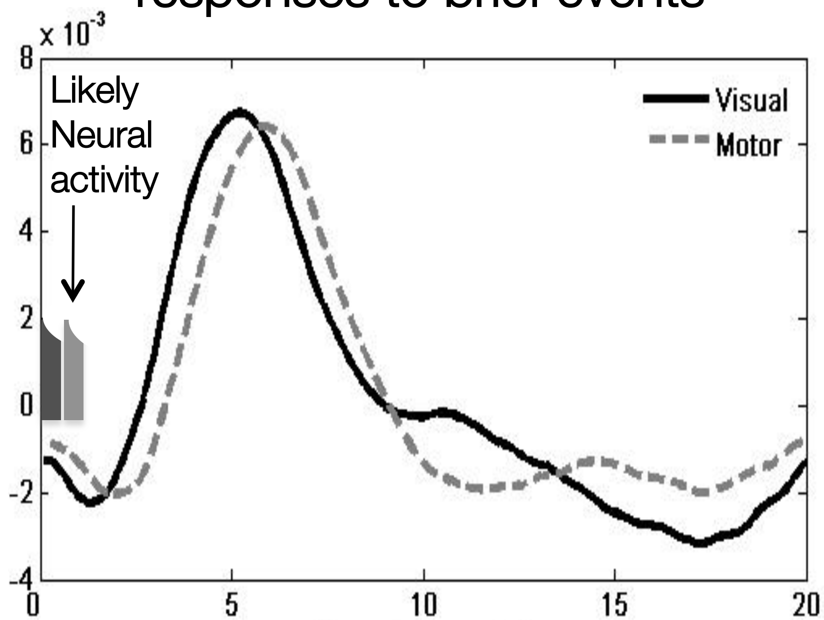
- A basic design matrix with two predictors (e.g., Famous and Non-famous) :



Accounting for hemodyamic delay

- BOLD responses are delayed and dispersed relative to neural activity

Empirical hemodynamic
responses to brief events



- Function of blood oxygenation, flow, volume (Buxton et al, 1998)

- Peaks at 4-6s poststimulus; baseline after 20-30s

- Initial undershoot (Malonek & Grinvald, 1996)

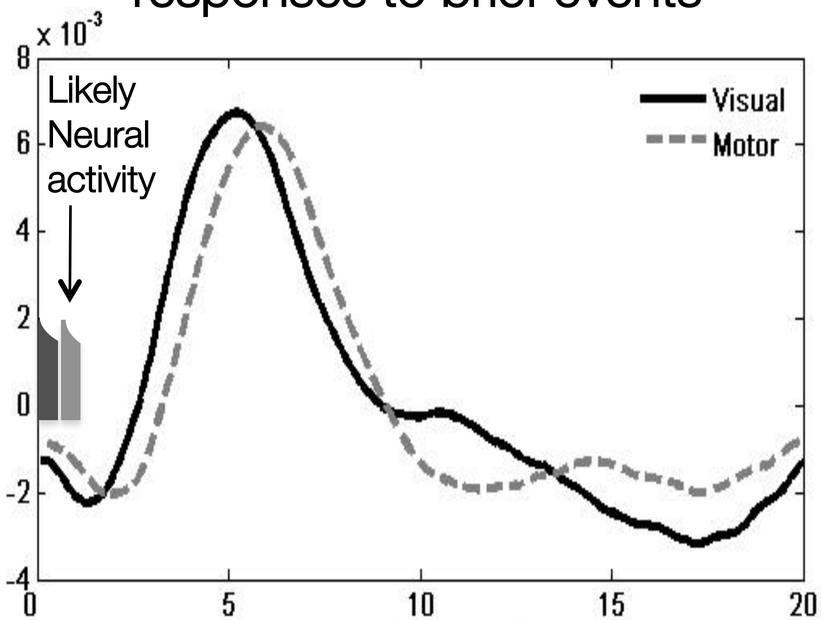
- Similar across brain regions, but not always!

Lindquist et al., 2008

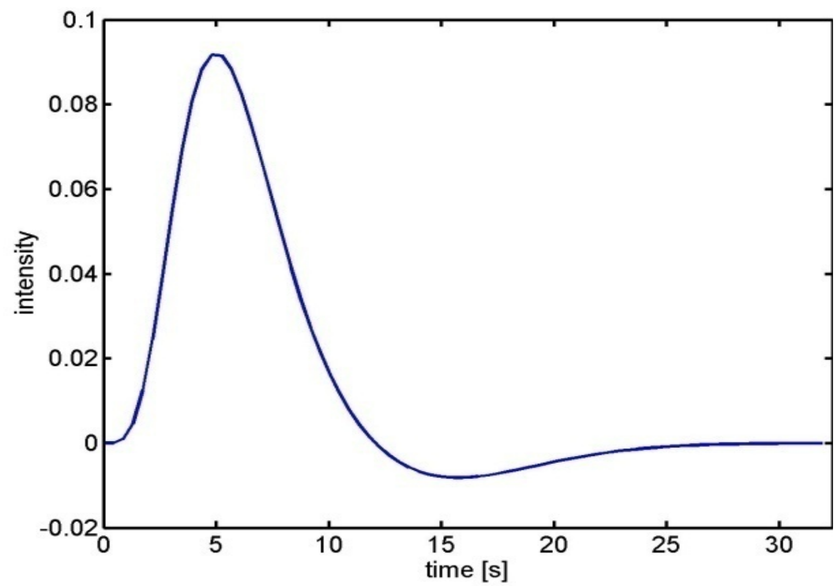
Accounting for hemodyamic delay

- BOLD responses are delayed and dispersed relative to neural activity

Empirical hemodynamic responses to brief events



Assumed 'impulse response' in model

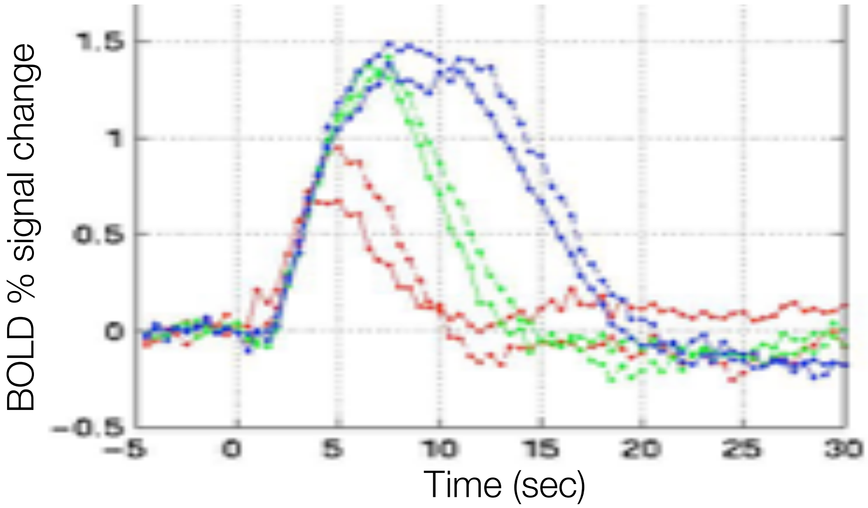


Common model: Fixed linear combination of 2 gamma functions

Lindquist et al., 2008

Building GLM Predictors: LTI system

How to turn assumed neural responses into a predictor in a GLM model?



- Solution: Assume a linear time invariant (LTI) system.
  - Here the neuronal activity acts as the input or impulse and the HRF acts as the impulse response function.
  - Single solution for brief neural events or sustained epochs.

- The fMRI signal at time *t*, *x(t)*, is modeled as the convolution of a stimulus function *v(t)* and the hemodynamic response *h(t)*, that is,

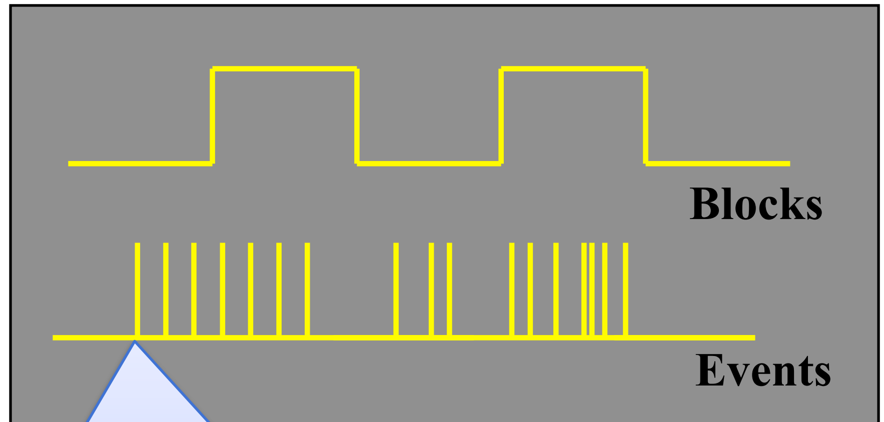
$$x(t) = (v * h)(t)$$

Building GLM Predictors: LTI system

Linear Time-Invariant system

LTI specified solely by

- Stimulus function of experiment

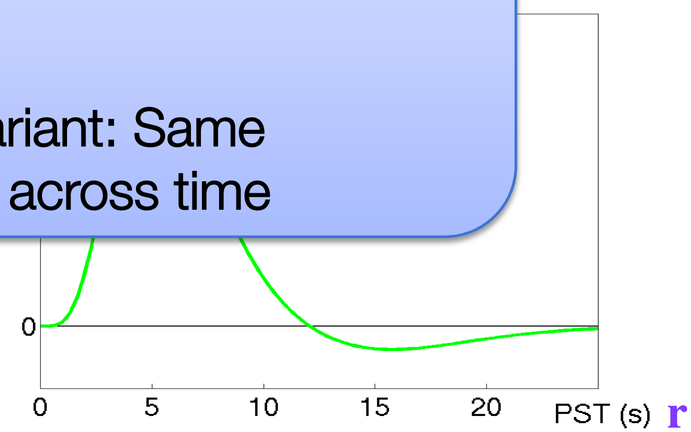


...Convolved with

- Hemodynamic Response Function (HRF), assumes instantaneous impulse

Linear: Same HRF for each event no matter what came before

Time-invariant: Same response across time



Building GLM Predictors: Convolution

Event-Related Design | Block or epoch Design

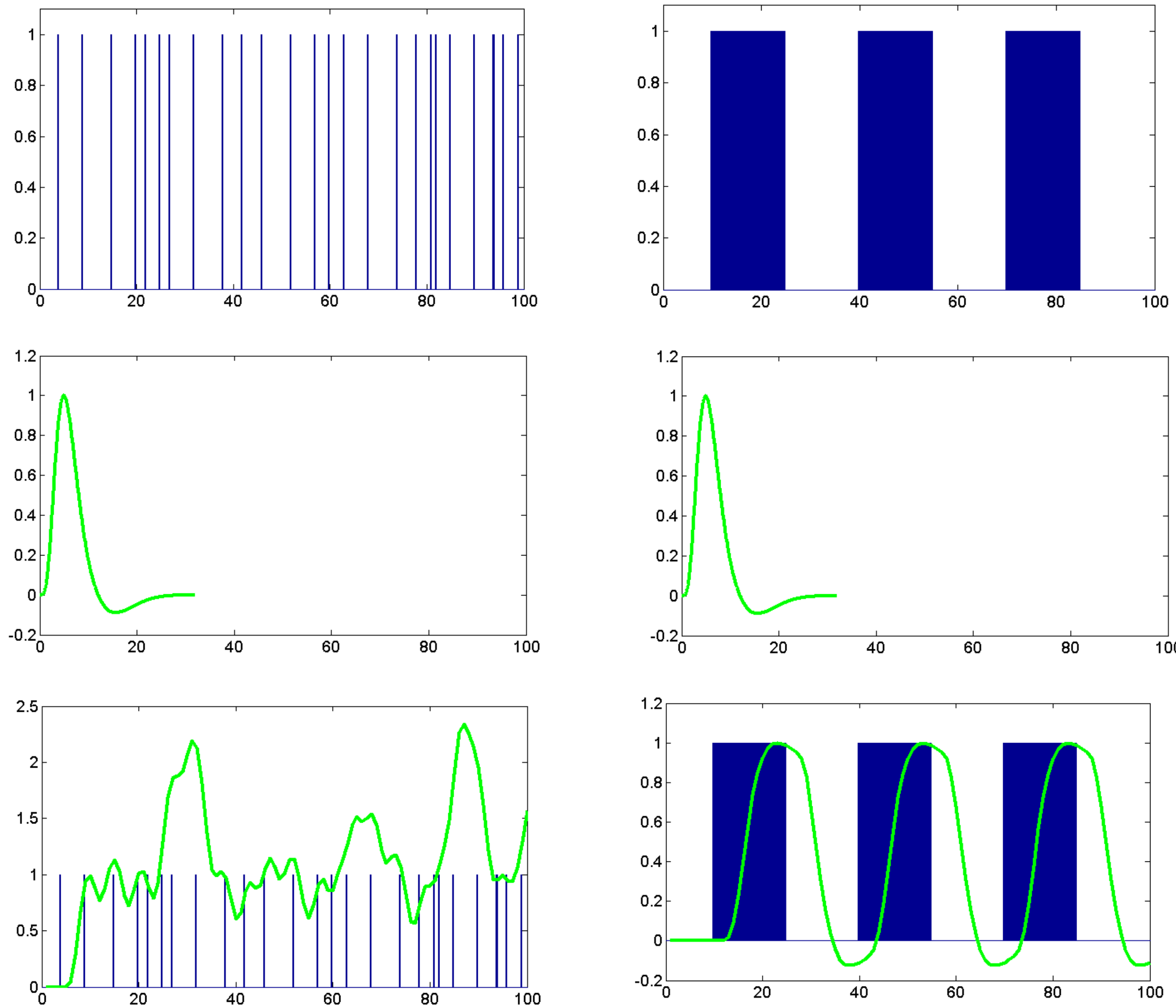
Neural response Function

(assumed)

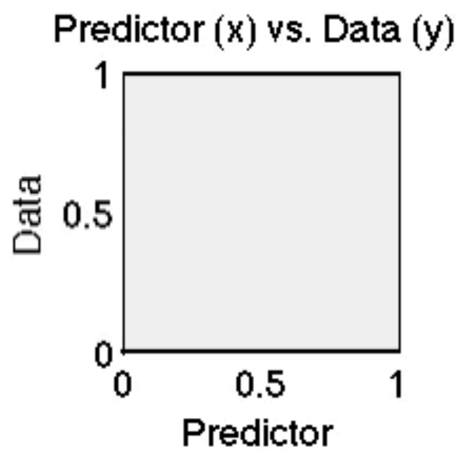
Hemodynamic Response Function

Predicted Response after convolution:

Predictor in GLM



Regression in fMRI: One predictor



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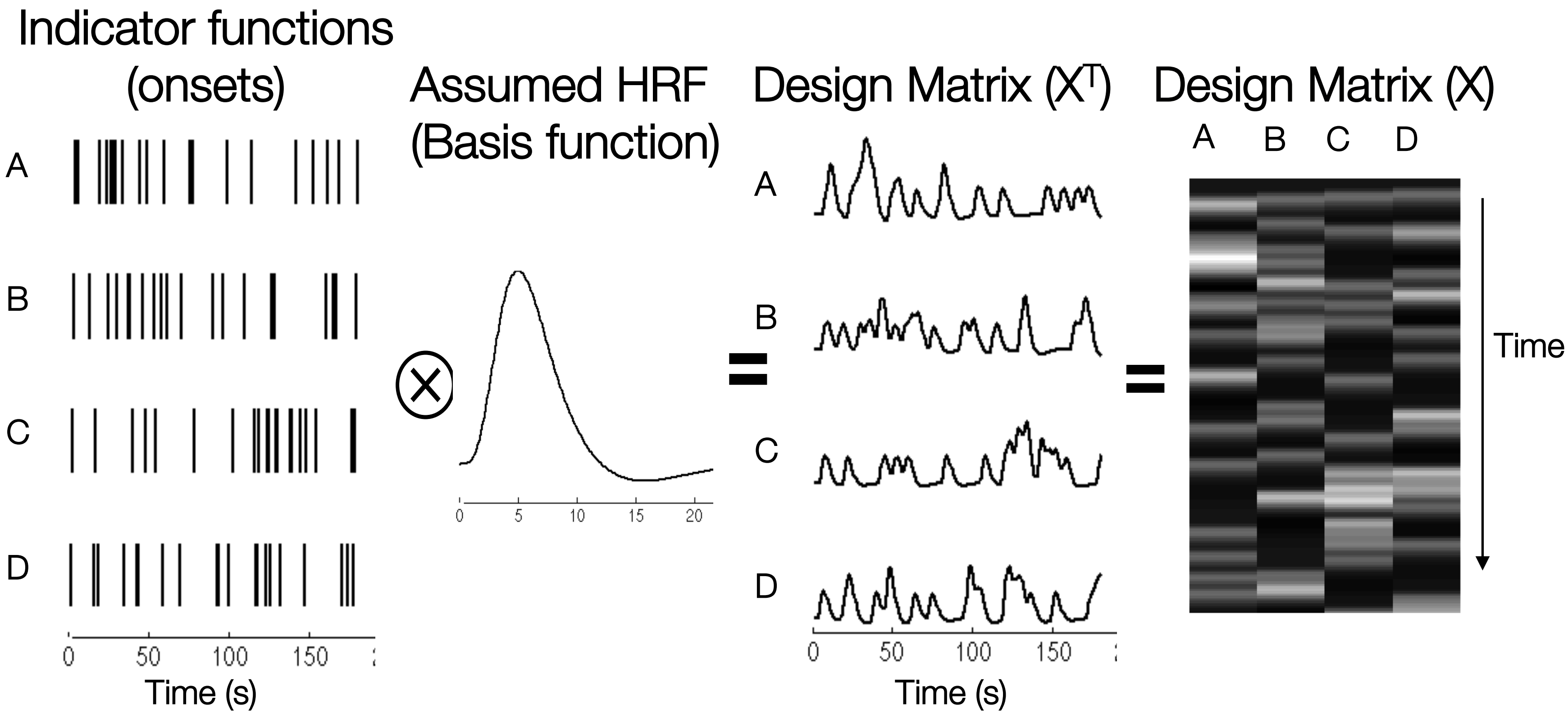
http://psych.colorado.edu/~tor

Model building for multiple predictors: Single-subject, single voxel



End of Module

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