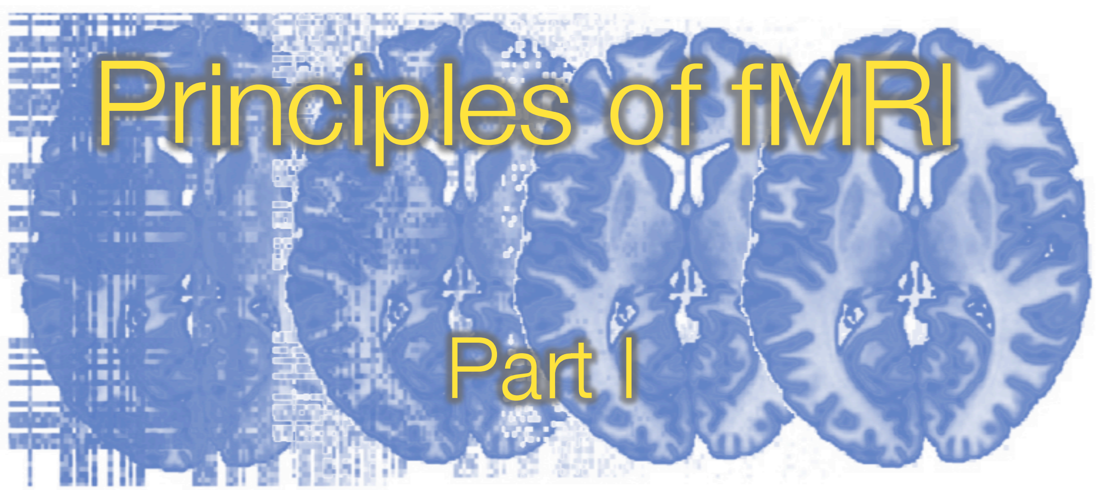
JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

University of Colorado **Boulder**

CANlab

SMART JHSPH Biostatistics



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@fMRIstats

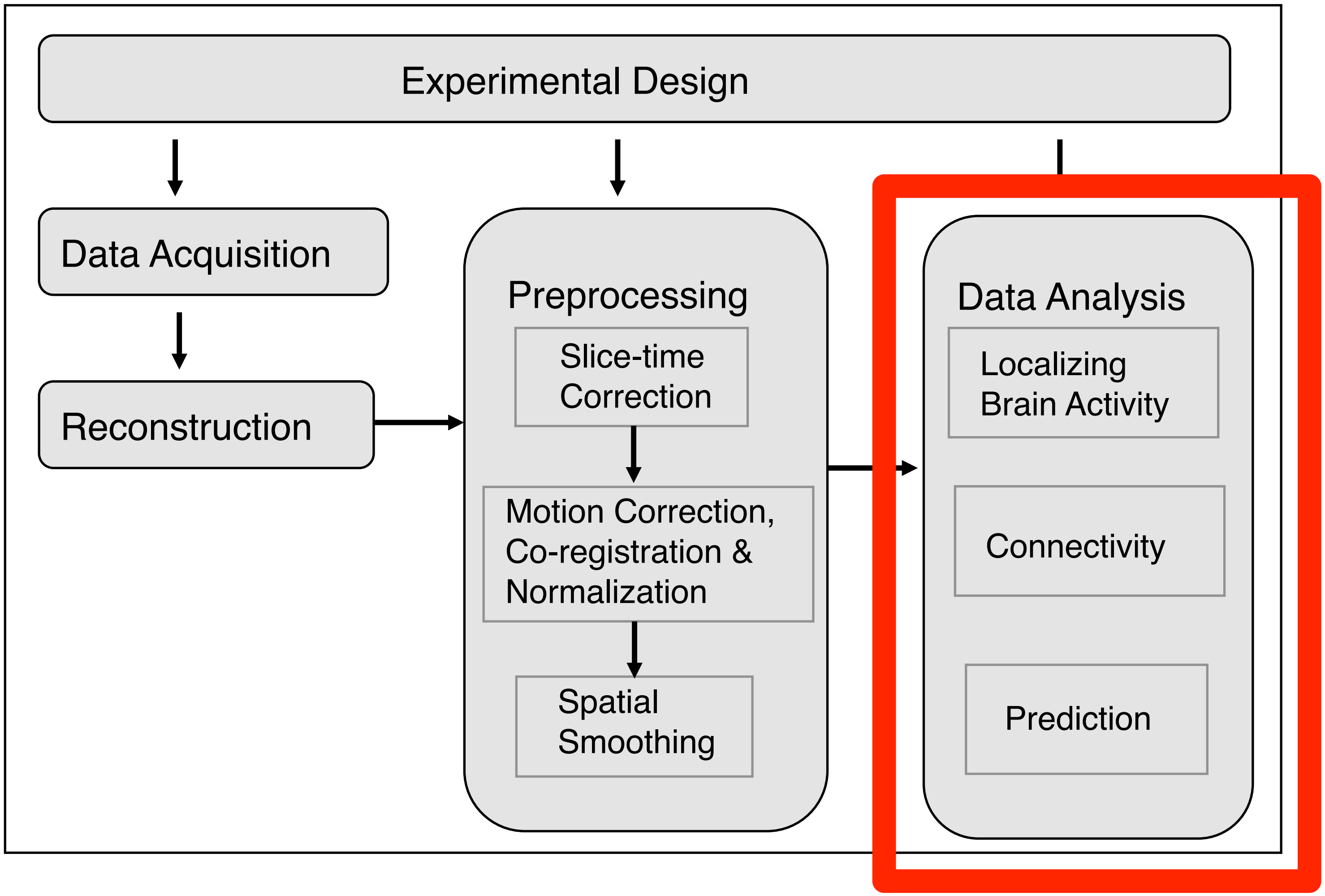
The General Linear Model: Introduction

Statistical Analysis

- There are multiple goals in the statistical analysis of fMRI data.

- They include:
  - localizing brain areas activated by the task;
  - determining networks corresponding to brain function; and
  - making predictions about psychological or disease states.

Data Processing Pipeline

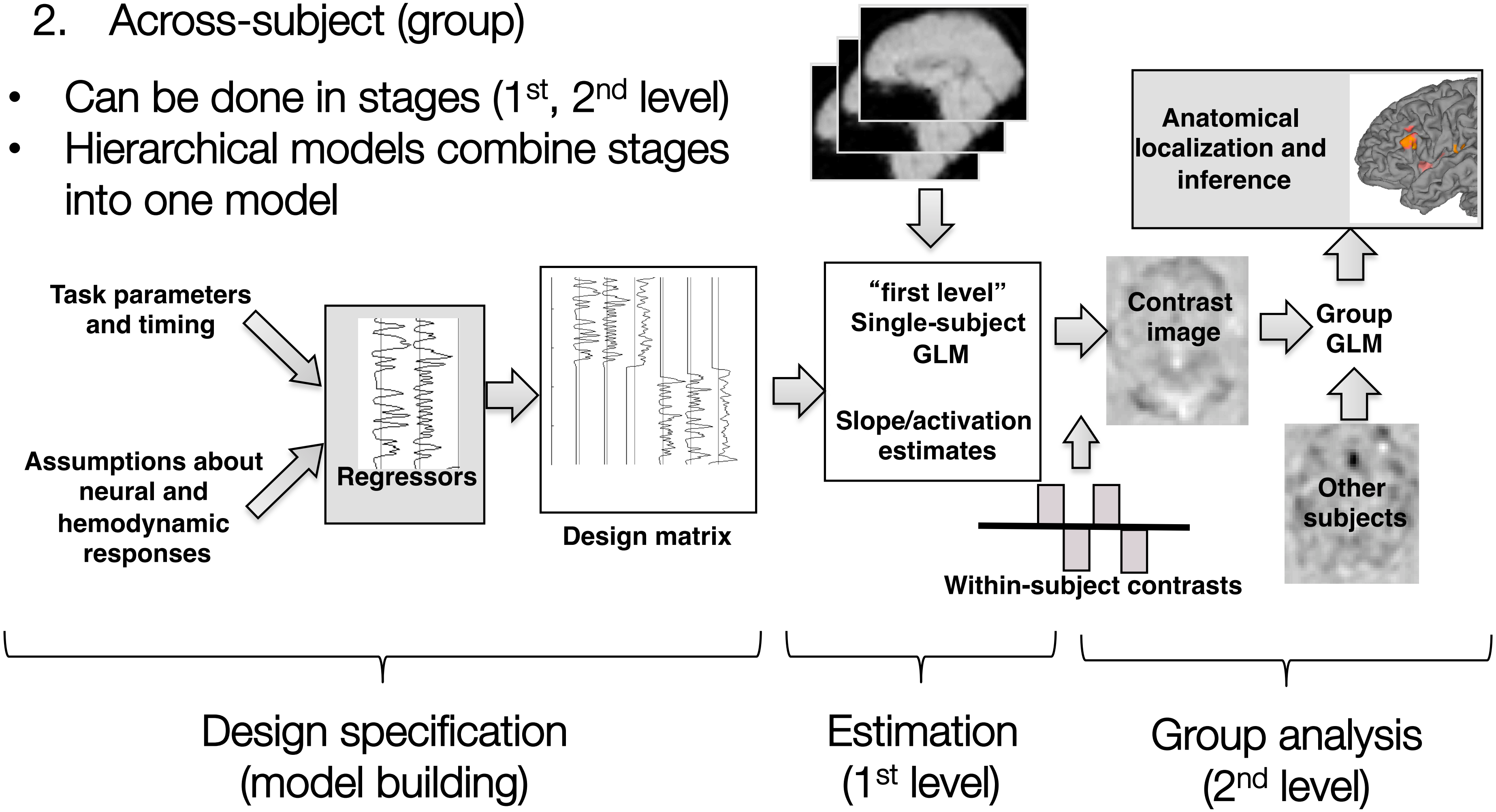


Overview of the GLM analysis process

Typically a two-level hierarchical analysis

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

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



INTRODUCING THE GLM FAMILY

@fMRIstats

Lindquist & Wager

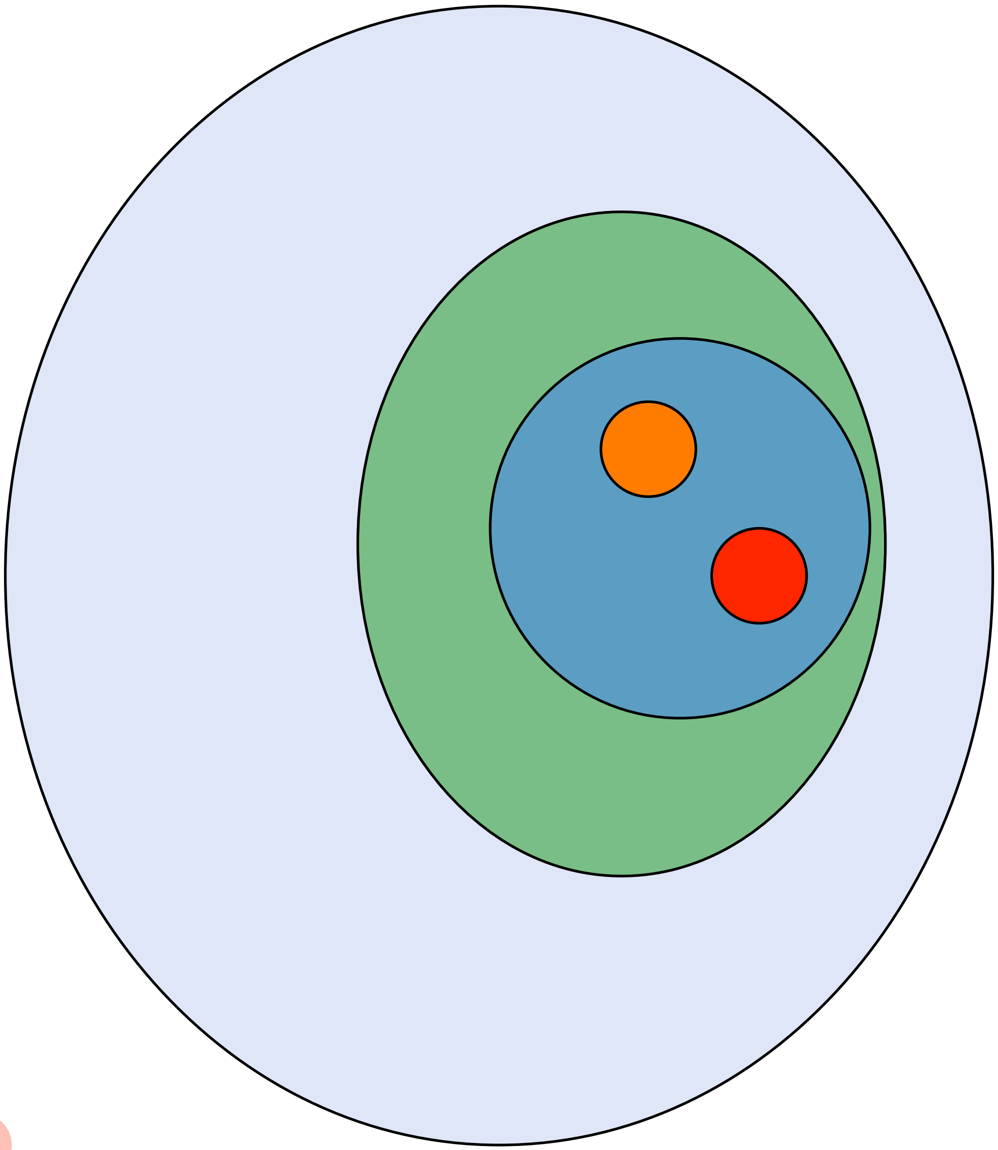
General Linear Model

- 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 (i.e., straight line, or known curve), but their amplitudes (i.e., slopes) 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



Simple regression

ANOVA

Multiple regression

General linear model

- Mixed effects/hierarchical
- Timeseries models (e.g., autoregressive)
- Robust, penalized regression (LASSO, Ridge)

Generalized linear models

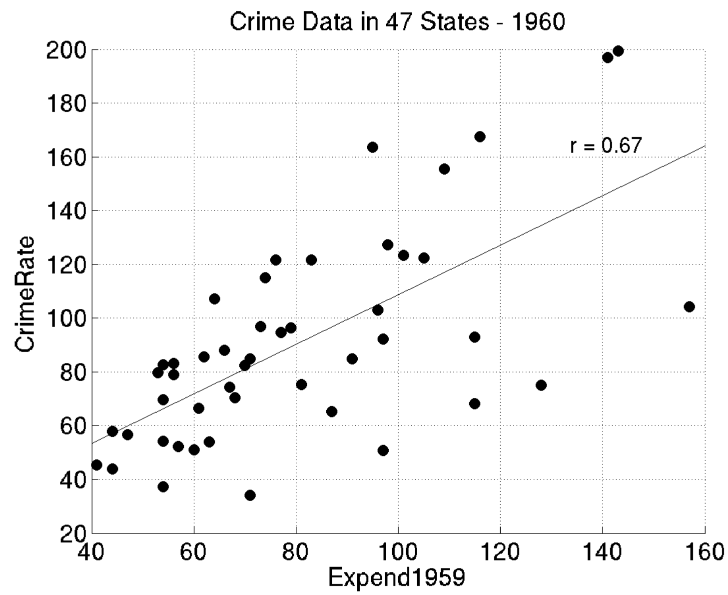
- Non-normal errors
- Binary/categorical outcomes (logistic regression)

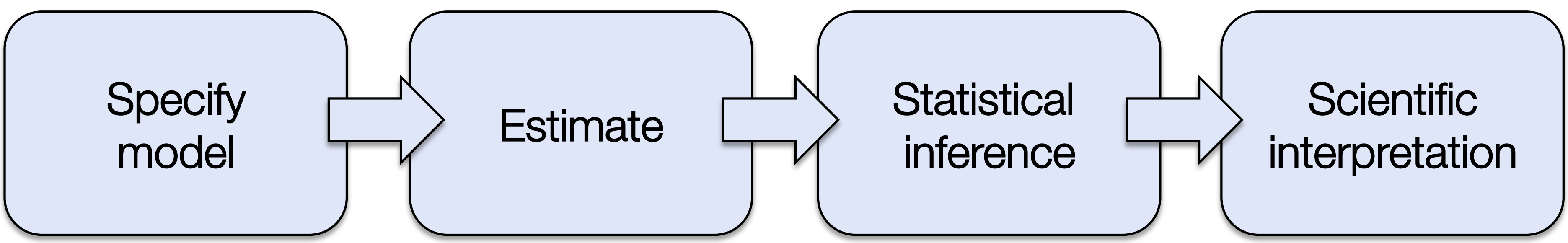
Closed form solution

Iterative solutions

Simple regression:
A simple linear model with one predictor

Principles of fMRI
Part I





Simplification: "linear relationship"

Find slope, intercept

Test slope: P-value

Meaning of relationship?

The GLM Family

Dependent Variable	Predictors	Analysis
One continuous	Continuous One predictor	Regression
	Continuous Two+ preds	Multiple Regression
	Categorical 1 pred., 2 levels	2-sample t-test
	Categorical 1 p., 3+ levels	One-way ANOVA
	Categorical 2+ predictors	Factorial ANOVA

General Linear Model

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 multiple regression model
basic model for the GLM

- Structural model for regression

Variables: DV, Pred1, Pred2, Pred*k*

$$\overset{\text{DV}}{y_i} = \underset{\text{intercept}}{\beta_0} + \underset{\text{Slope 1}}{\beta_1} \overset{\text{Pred1}}{x_{i1}} + \underset{\text{Slope 2}}{\beta_2} \overset{\text{Pred2}}{x_{i2}} + \cdots + \underset{\text{Slope k}}{\beta_k} \overset{\text{Pred}k}{x_{ik}} + \underset{\text{Error}}{\varepsilon_i}$$

Parameters: intercept, Slope 1, Slope 2, Slope k, Error

- solve for beta vector
- minimize sum of squared residuals

Matrix notation

$$y = X\beta + \varepsilon$$

Matrix Notation

- Alternatively, we can write

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

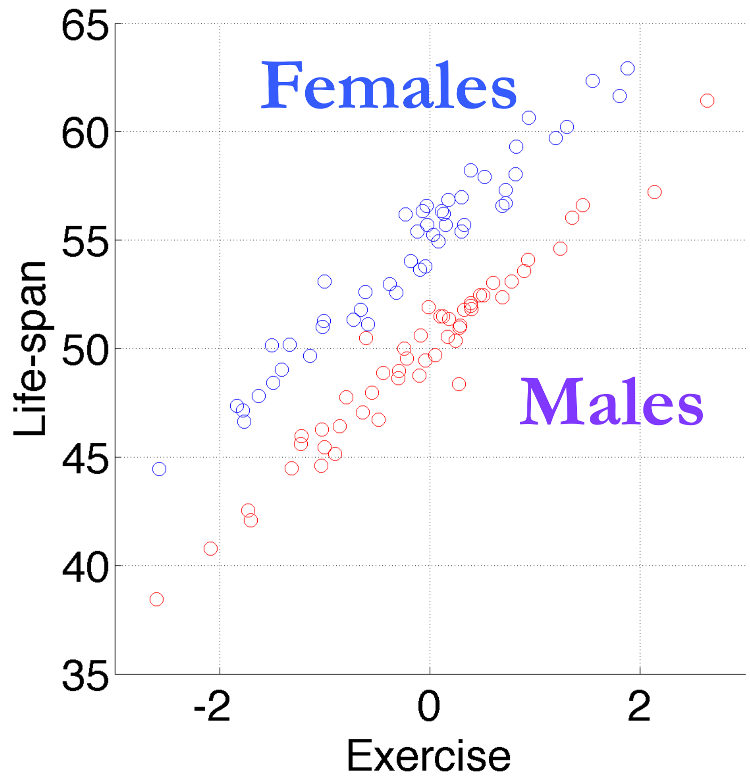
as

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

Observed Data **Design matrix** **Model parameters** **Residuals**

A non-fMRI example

- Does exercise predict life-span?
- Made-up (not real data)
- Control for other variables that might be important, i.e., gender (M/F)

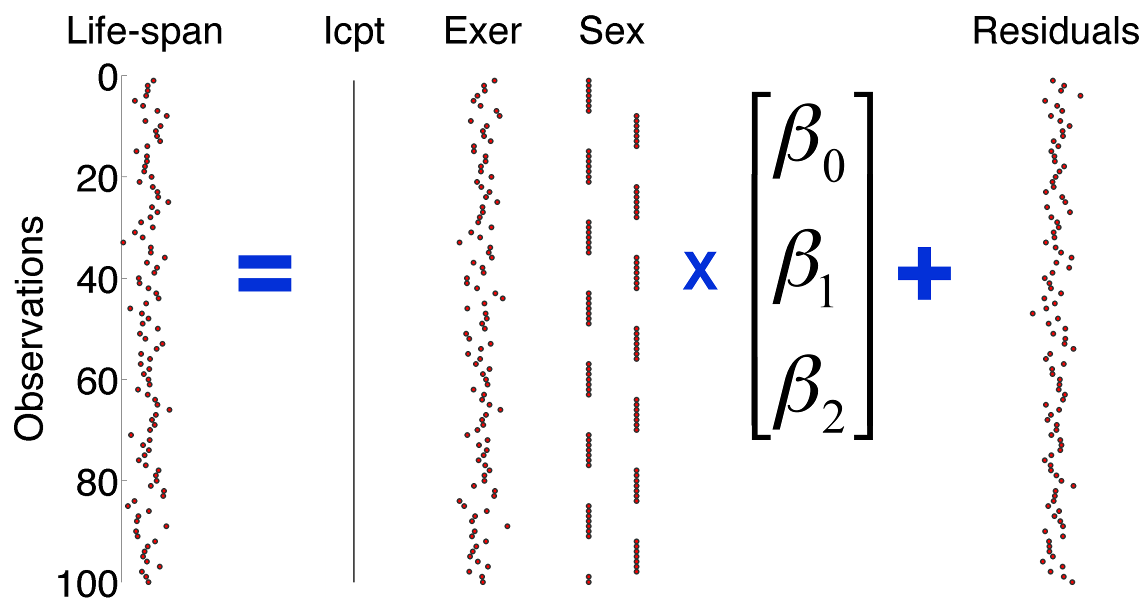


A non-fMRI example

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

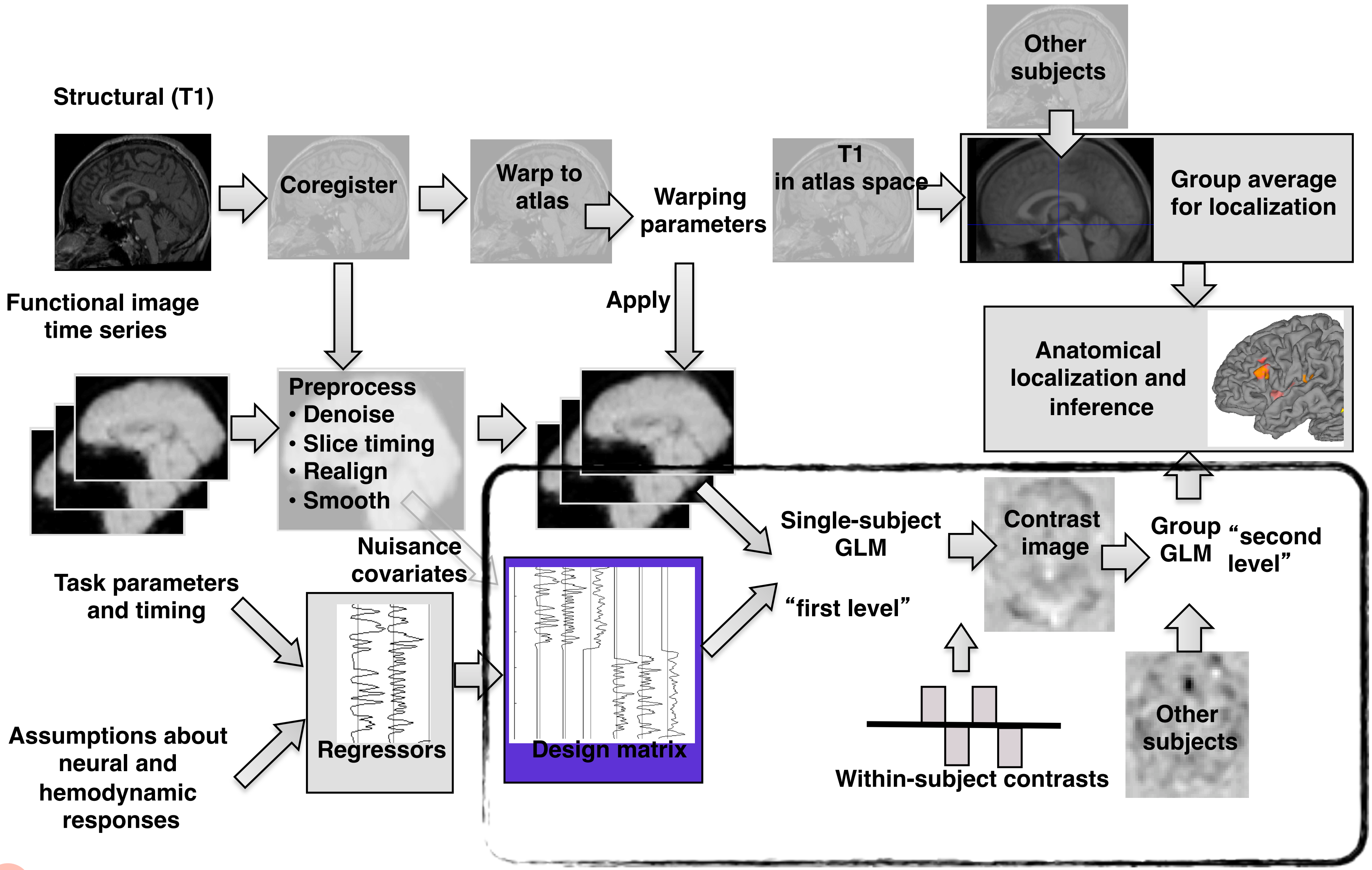
$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} & \cdots & X_{1p} \\ 1 & X_{21} & \cdots & X_{2p} \\ \vdots & \vdots & & \vdots \\ 1 & X_{np} & \cdots & X_{np} \end{bmatrix} \times \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_p \end{bmatrix} + \begin{bmatrix}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

Outcome Data **Design matrix** **Model parameters** **Residuals**



End of Module

A standard processing pipeline



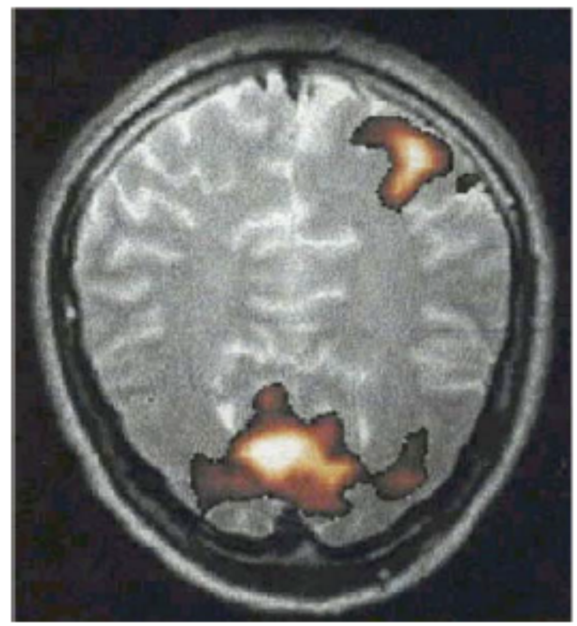
General Linear Model

- General model
  - Categorical or continuous predictor
- Linear model
  - Parameters that are
    - not multiplied by other parameters, e.g., not $Y = abX$
    - only first-power, e.g., NOT $Y = b^2X$
    - not exponents, e.g., NOT $Y = X^b$
  - Variables do not need to satisfy the above criteria
    - transformation workaround, e.g., $Y = bX^2$ can be rewritten as $Y = bZ$
  - Not necessary straight-line relationship

Human Brain Mapping

- The most common use of fMRI to date has been to localize areas of the brain that activate in response to a certain task.

- These types of human brain mapping studies are necessary for the development of biomarkers and increasing our understanding of brain function.



The regression model

- Vector notation: y, x, and e are vectors of N values corresponding to N observations

$$y = b + mx + e$$

Outcome (DV)

Intercept (constant)

slope

Predictor value

Error (residual)

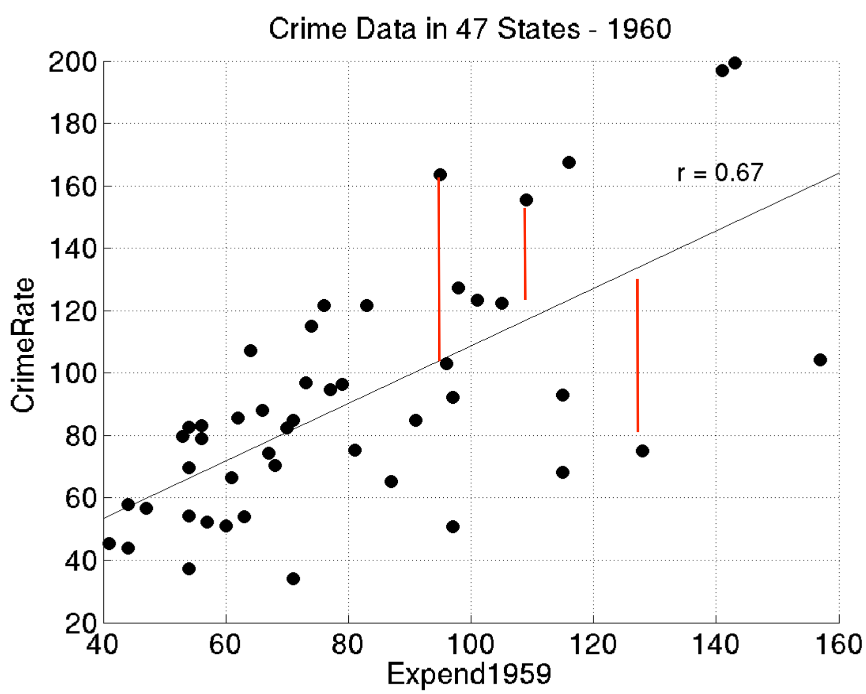
For point i: $$y_i = b + mx_i + e_i$$

Fitting and residual variance

- Minimize squares of vertical distance to lines.

  Minimize: $\sum e_i^2 = \sum (y_i - \hat{y}_i)^2$

  – The line is being pulled by vertical rubber bands attached to each point. Vector of red lines is *e*



Matrix Notation

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

Observed Data **Design matrix** **Model parameters** **Residuals**

Is the same as

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

Design matrix

- In fMRI the design matrix specifies how the factors of the model change over time.

- The design matrix is an $n \times p$ matrix where n is the number of observations over time and p is the number of model parameters

$$\mathbf{X} = \begin{bmatrix} 1 & X_{11} & \cdots & X_{1p} \\ 1 & X_{21} & \cdots & X_{2p} \\ \vdots & \vdots & & \vdots \\ 1 & X_{np} & \cdots & X_{np} \end{bmatrix}$$