Introduction to Knock-off Filters

"Controlling False Discovery Rates via Knock-offs "
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Introduction

"All models are wrong, but some models are useful" – George Box

- Consider the simple linear regession model:

$$y = X\beta + \varepsilon; \qquad y \in \mathbb{R}^n, \quad X \in \mathbb{R}^{n \times p}, \quad \varepsilon \sim N(0, \sigma^2)$$

$$\Rightarrow \hat{\beta}_{ols} = \underset{\beta}{\operatorname{argmin}} \, (y - X\beta)' \, (y - X\beta)$$

  - Large number of X: low bias but larger variance
  - Small number of X: higher bias but small variance
  - Ideal: Small set of X truly associated with y

- Motivating example from genetics:
  - y: phenotype (observable traits eg: eye color, height)
  - X: genes

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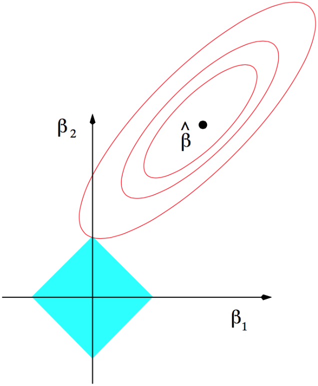
Preliminary Concept 1: Variable Selection Techniques

"Selecting a Small Subset of Variables"

- Forward Stepwise Regression
- Backward Stepwise Regression
- ⇒**LASSO**
  - $\hat{\beta}_\lambda = \underset{\beta}{\operatorname{argmin}} (y - X\beta)' (y - X\beta) + \lambda \sum_{j=1}^{p} |\beta_j|$



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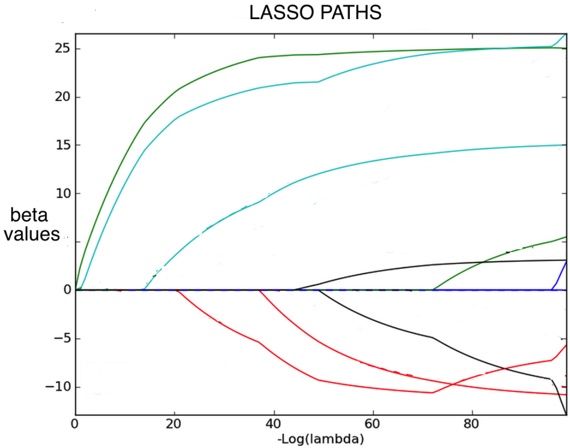
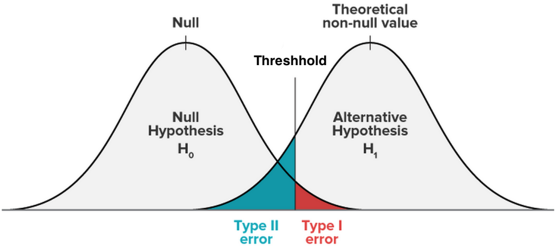


Preliminary Concept 2: False Discovery Rate

"Selecting Variables **truly associated** with y. "

- Null hypothesis $\mathcal{H}_0 : \beta_j = 0$
- Set of selected covariates: $\mathcal{S}$
- 

- Want to control the proportion of Type I error

$$\underset{\substack{\uparrow \\ \text{False discovery rate}}}{\text{FDR}} = \mathbb{E}\underbrace{\left[\frac{\#\text{ false positives}}{\text{total }\#\text{ of features selected}}\right]}_{\text{False discovery proportion}} = \mathbb{E}\left[\frac{|S \cap \mathcal{H}_0|}{|S|}\right].$$

- Work by Benjamini-Hochberg (1995, 2000)

Knock-off Filters: Algorithm

- Step 1: Construct Knock-offs $\tilde{X}$ such that
  - Correlation Structure: $\tilde{X}'\tilde{X} = X'X = \Sigma$
  - Correlation Structure: $X'\tilde{X} = \Sigma - diag(s)$
  - How? $\tilde{X} = X(I - \Sigma^{-1} diag(s)) + \tilde{U}C$
  - Augmented Matrix: $[X \quad \tilde{X}]$
- Step 2: Compute Lasso with Augmented Matrix

$$\beta_\lambda = \underset{\beta \in \mathbb{R}^{2p}}{\arg\min} \left\{ \frac{1}{2} \left\| y - \left[X \ \widetilde{X}\right] \cdot \beta \right\|_2^2 + \lambda \left\| \beta \right\|_1 \right\}$$

- Step 3: For each pair of knock-off and original variables, calculate

$$\lambda_j = \sup \left\{ \lambda \ : \ \beta_j^\lambda \neq 0 \right\} = \text{ first time } X_j \text{ enters Lasso path}$$

$$\widetilde{\lambda}_j = \sup \left\{ \lambda \ : \ \widetilde{\beta}_j^\lambda \neq 0 \right\} = \text{ first time } \widetilde{X}_j \text{ enters Lasso path}$$

-

$$W_j = \max\{\lambda_j, \widetilde{\lambda}_j\} \cdot \text{sign}(\lambda_j - \widetilde{\lambda}_j)$$

Knock-off Filters: Algorithm

- Step 4: For each λ value calculate
- $$\begin{array}{l} S_\lambda = \{j : W_j \geq +\lambda\} \\ \widetilde{S}_\lambda = \{j : W_j \leq -\lambda\} \end{array} \quad \rightsquigarrow \quad \widehat{\mathsf{FDP}}(S_\lambda) := \frac{|\widetilde{S}_\lambda|}{|S_\lambda|}$$
- Step 5: Choose threshold level q
- Step 6: Select the variables based on
- $$\Lambda = min\{\lambda : \widehat{FDP}(S_\lambda) \leq q\}$$
  $$S_\Lambda = \{j : W_j \geq \Lambda\}$$
- Knock-off+ filter:
  $$\widehat{\mathsf{FDP}}_{+}(S_\lambda) := \frac{|\widetilde{S}_\lambda| + 1}{|S_\lambda|}$$
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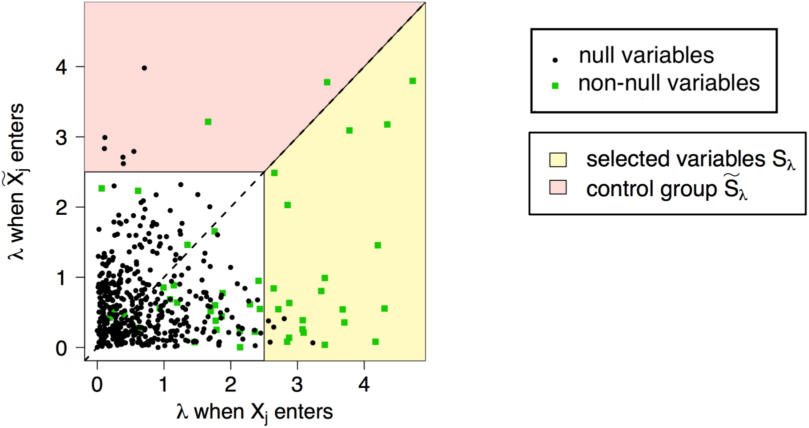
Knock-off Filters: Intuition



Rest of the paper

- Theoretical Guarantees
  - Theorem 1: $\mathbb{E}[mFDP(S_\Lambda)] \leq q; \quad mFDP(S) = \frac{|S \cap \mathcal{H}_0|}{|S| + q^{-1}}$
  - Theorem 2: $\mathbb{E}[FDP(S_{\Lambda_+})] \leq q$
- Simulation Results
  - Compare knock-off, knock-off+ & Benjamini-Hochberg
  - All three techniques lead to FDR below threshold q
  - knock-off, knock-off+ perform better in terms of power
  - Power: $1 - Pr(\text{Type II Error})$
- Empirical Application
  - model drug resistance of HIV-1 (y) on genetic mutations (X)

Going Further: Issues and Possible Applications

- Paper makes very few assumptions:
  - Don't need to know σ^2
  - Don't need any information on β
- But those that it makes may be critical:
  - Full rank $X'X = \Sigma$
  - $n > p$
  - Most practical applications of LASSO not suitable
  - Ongoing work on these aspects
- General issue with LASSO: Confidence interval estimation

- Possible Applications:
  - Useful when we don't have any model of the response.
  - Worthwhile to think about $2 - step$ methods (?)
  - Effect of a particular covariate on response but not sure about others covariates (?)

Thanks!