

Model-Free Knockoffs: High-Dimensional Variable Selection that Controls the False Discovery Rate

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Controlled Variable Selection

Given:

- Y an outcome of interest (AKA response or dependent variable),
- X_1, \dots, X_p a set of p potential explanatory variables (AKA covariates, features, or independent variables),

How can we select important explanatory variables with few mistakes?

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Problem Statement

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To make sure we do not make too many mistakes, we seek to select a set \hat{S} to control the **false discovery rate (FDR)**:

$$\text{FDR}(\hat{S}) = \mathbb{E} \left(\frac{\#\{j \text{ in } \hat{S} : X_j \text{ unimportant}\}}{\#\{j \text{ in } \hat{S}\}} \right) \leq q \text{ (e.g. 10\%)}$$

“Here is a set of variables \hat{S} , 90% of which I expect to be important”

Model-free knockoffs solves the controlled variable selection problem

- Any model for Y and X_1, \dots, X_p
- Any dimension (including $p > n$)
- Finite-sample control (non-asymptotic) of FDR
- Practical performance on real problems

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Model-free knockoffs used the same FDR of 10% and made **18 discoveries**, with many of the new discoveries confirmed by a larger meta-analysis

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What is required for valid inference?

	Low dimensions	Model for Y	Asymptotic regime	Sparsity	Random design
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The generic knockoffs procedure for controlling the FDR at level q :

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Coin-flipping property: The key to the knockoffs procedure is that steps (1) and (2) are done specifically to ensure that, conditional on $|W_1|, \dots, |W_p|$, the signs of the *unimportant/null* W_j are independently ± 1 with probability $1/2$

The Model-Free Knockoffs Procedure

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(1) **Construct knockoffs**: Exchangeability

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(2) **Compute knockoff statistics:**

- Variable importance measure Z
- Antisymmetric function $f_j : \mathbb{R}^2 \rightarrow \mathbb{R}$, i.e.,

$$f_j(z_1, z_2) = -f_j(z_2, z_1)$$

- $W_j = f_j(Z_j, \tilde{Z}_j)$, where Z_j and \tilde{Z}_j are the variable importances of \mathbf{X}_j and $\tilde{\mathbf{X}}_j$, respectively

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(3) **Find the knockoff threshold:** just requires coin-flipping property

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1. Subjects sampled from a population (oversampling cases still valid)
 - 2a. Strong spatial structure: linkage disequilibrium models, e.g., Markov chains, are well-studied and work well
 - 2b. Other studies have collected same or similar SNP arrays on different subjects

Knockoff Construction

Valid model-free knockoff variables can always be generated:

Algorithm 1 Sequential Conditional Independent Pairs

for $j = \{1, \dots, p\}$ **do**

 | Sample \tilde{X}_j from $\mathcal{L}(X_j \mid X_{-j}, \tilde{X}_{1:j-1})$

end

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If (X_1, \dots, X_p) multivariate Gaussian, exchangeability reduces to matching first and second moments when X_j, \tilde{X}_j swapped

For $\text{Cov}(X_1, \dots, X_p) = \Sigma$:

$$\text{Cov}(X_1, \dots, X_p, \tilde{X}_1, \dots, \tilde{X}_p) = \begin{bmatrix} \Sigma & \Sigma - \text{diag}\{\mathbf{s}\} \\ \Sigma - \text{diag}\{\mathbf{s}\} & \Sigma \end{bmatrix}$$

In non-Gaussian case, can be thought of as second-order-correct model-free knockoffs

Exchangeability Endows Coin-Flipping

Recall [exchangeability](#) property:

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Prior information

- **Bayesian approach:** choose prior and model, and Z_j could be the posterior probability that X_j contributes to the model

Adaptivity and Prior Information in W_j

Lasso Coefficient Difference (LCD): ℓ_1 -penalized regression of \mathbf{y} on $[\mathbf{X} \tilde{\mathbf{X}}]$

$$W_j = |\beta_j| - |\tilde{\beta}_j|$$

Adaptivity

- Cross-validation (on $[\mathbf{X} \tilde{\mathbf{X}}]$) to choose the penalty parameter in the lasso
- Higher-level adaptivity: CV to choose best-fitting model for inference
- Fit random forest and ℓ_1 -penalized regression; derive feature importance from whichever has lower CV error—**still strict FDR control**

Prior information

- **Bayesian approach:** choose prior and model, and Z_j could be the posterior probability that X_j contributes to the model
- Still strict FDR control, **even if wrong prior or MCMC has not converged**

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Thank you!

Appendix

References

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Original Knockoffs (Barber and Candès, 2015)

\mathbf{y} and \mathbf{X}_j are $n \times 1$ column vectors of data: n draws from the random variables Y and X_j , respectively; design matrix $\mathbf{X} := [\mathbf{X}_1 \cdots \mathbf{X}_p]$

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Comments:

- Finite-sample **FDR control** (non-asymptotic)
- Sparsity-based W_j for **greater power than OLS+BHq**
- Requires data follow **Gaussian linear model**
- Can only be run in **low dimensions** ($n \geq p$)
- Sufficiency requirement **restricts choice of W_j** , limiting power/adaptivity

Robustness Simulations

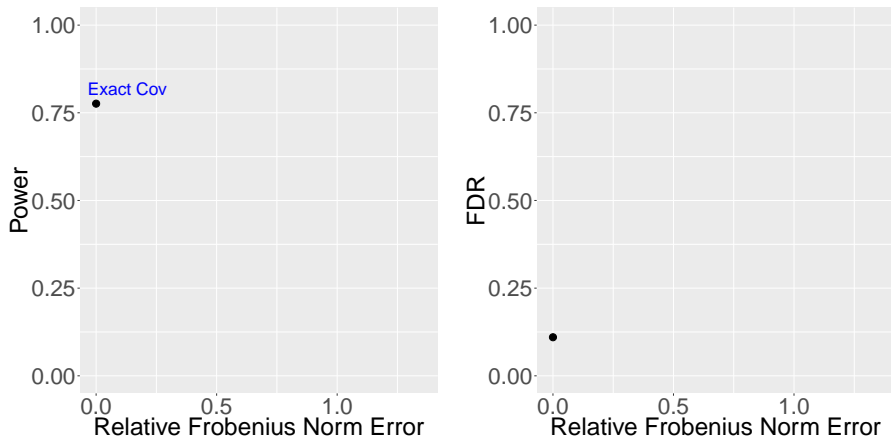


Figure: Covariates are **AR(1)** with autocorrelation coefficient **0.3**. $n = 800$, $p = 1500$, and target FDR is 10%. Y comes from a binomial linear model with logit link function with 50 nonzero entries.

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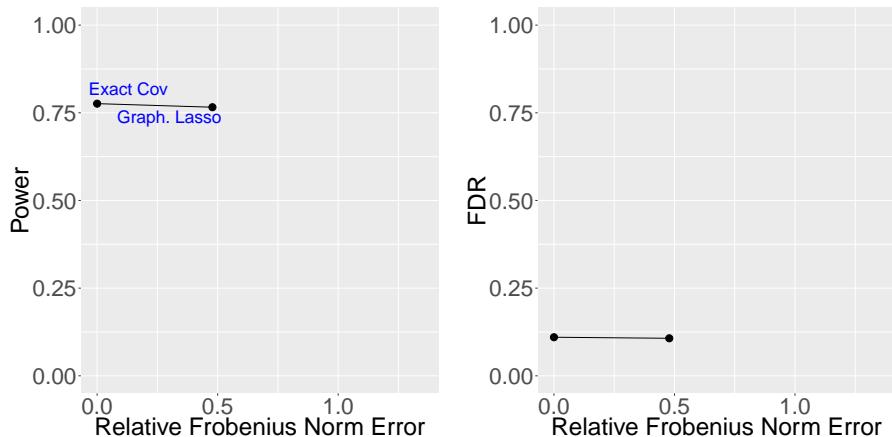


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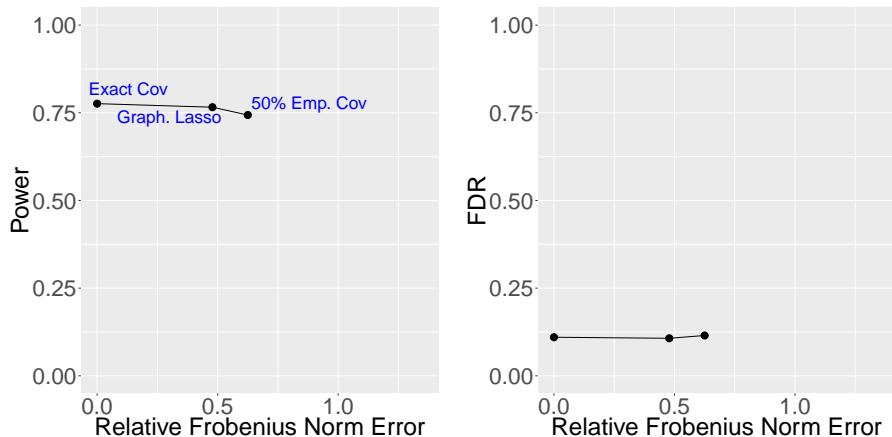


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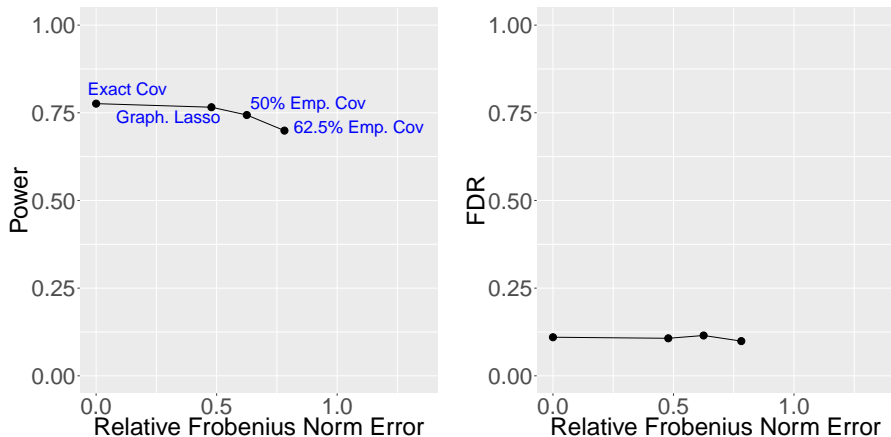


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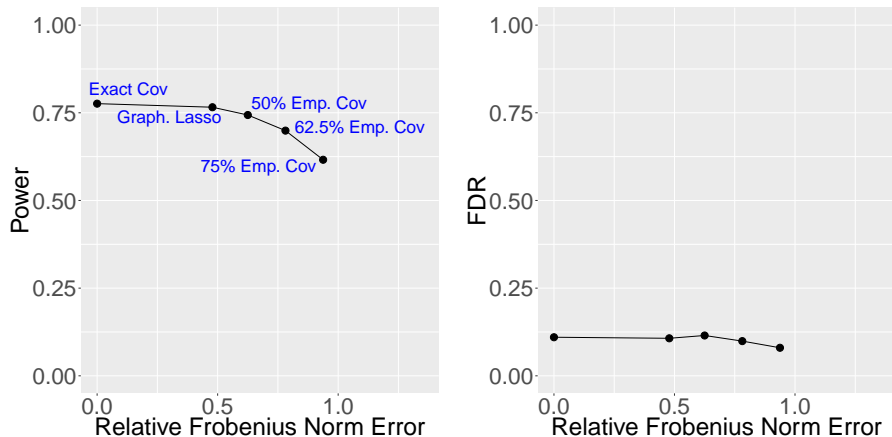


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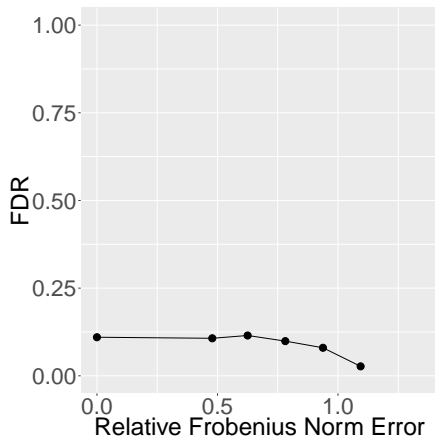
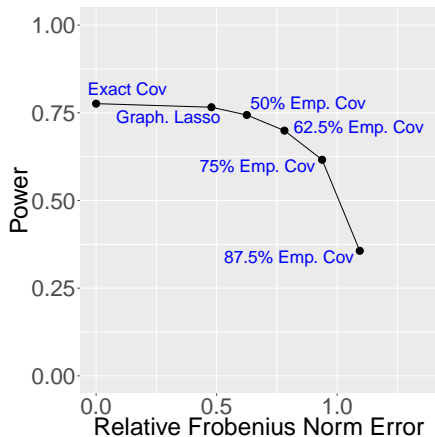


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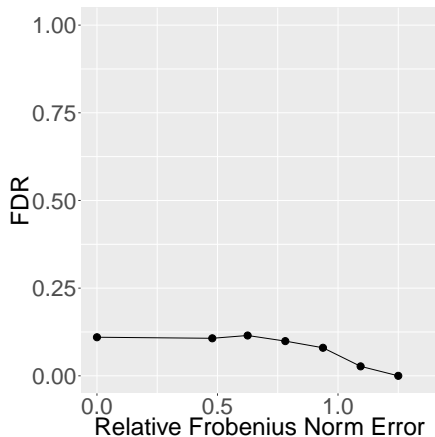
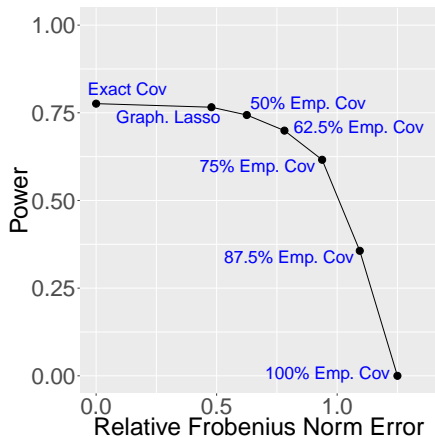


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Robustness on Real Data

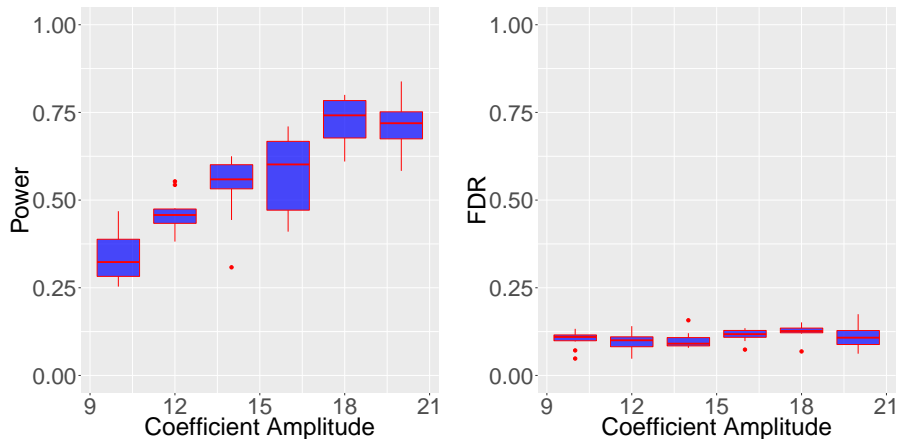


Figure: Power and FDR (target is 10%) for model-free knockoffs applied to subsamples of a real genetic design matrix. $n \approx 1,400$, $p \approx 70,000$, and each boxplot represents 10 different logistic regression models with 60 nonzero coefficients, while each sample in each boxplot is an average over 10 design matrices drawn from actual SNP data.

Genetic Analysis of Crohn's Disease

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 - Some corroborated by work on nearby genes: promising candidates

Simulations in Low-Dimensional Linear Model

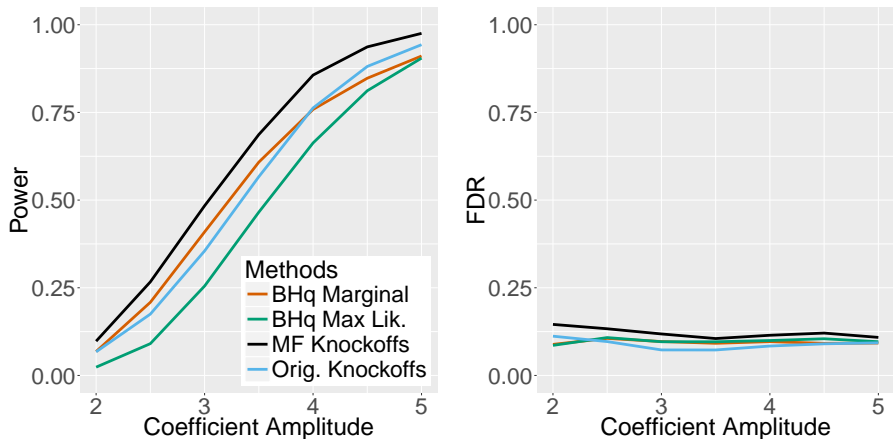


Figure: Power and FDR (target is 10%) for MF knockoffs and alternative procedures. The design matrix is i.i.d. $\mathcal{N}(0, 1/n)$, $n = 3000$, $p = 1000$, and y comes from a Gaussian linear model with 60 nonzero regression coefficients having equal magnitudes and random signs. The noise variance is 1.

Simulations in Low-Dimensional Nonlinear Model

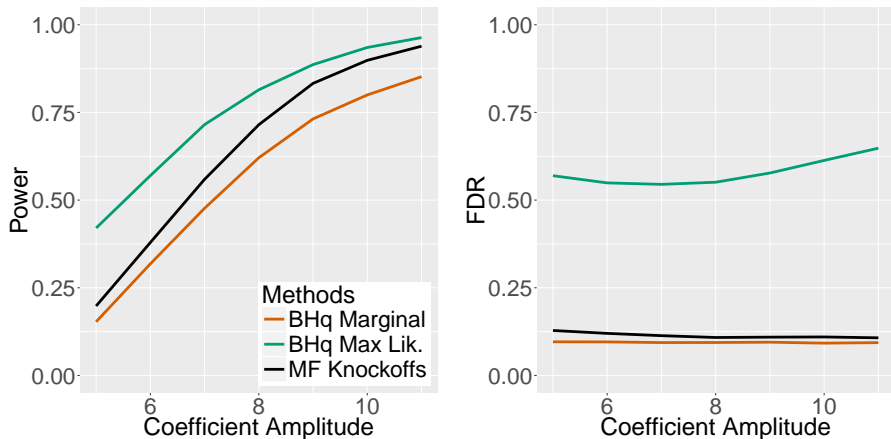


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Simulations in High Dimensions

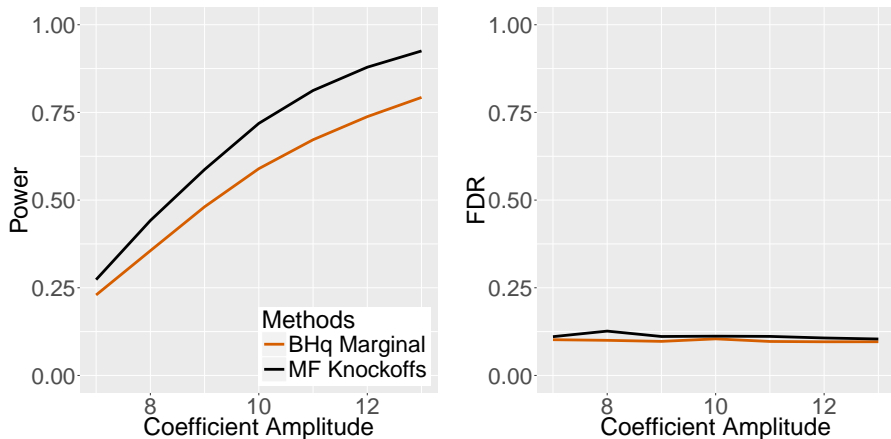


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Simulations in High Dimensions with Dependence

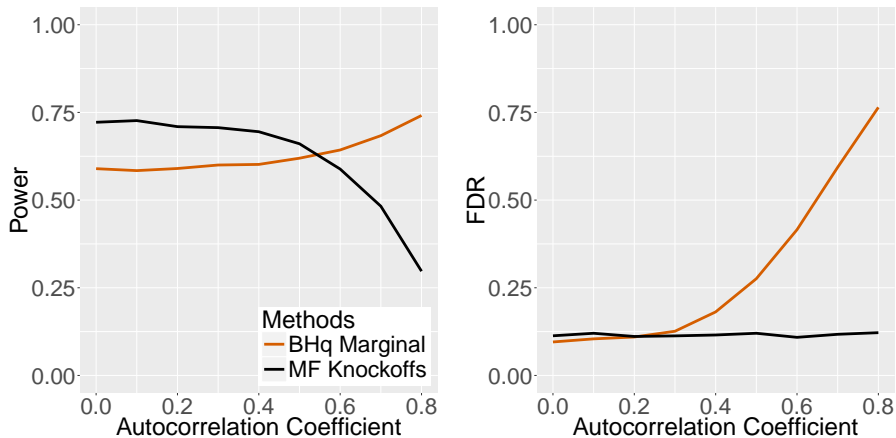


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