A unified approach to nonparametric variable importance assessment

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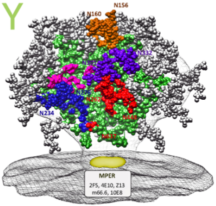
Motivation

AMP
ANTIBODY · MEDIATED · PREVENTION
STUDY

W CARDIOLOGY
UNIVERSITY OF WASHINGTON



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Goal: describe the predictiveness of our estimator

Goal: compare predictiveness of multiple estimators

Linear regression variable importance

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1. estimate the conditional mean
2. estimate the importance of X_s, $s \subseteq \{1, \ldots, p\}$

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Many ways to compare fitted values, including:

- ANOVA decomposition
- Difference in R^2

Linear regression variable importance

Difference in R^2:

$$\left[1 - \frac{MSE(\hat{\mu})}{n^{-1}\sum_{i=1}^{n}\{Y_i - \overline{Y}_n\}^2}\right] - \left[1 - \frac{MSE(\hat{\mu}_s)}{n^{-1}\sum_{i=1}^{n}\{Y_i - \overline{Y}_n\}^2}\right]$$

Mean squared error (MSE) of linear regression function f:

$$MSE(f) = \frac{1}{n}\sum_{i=1}^{n}\{Y_i - f(X_i)\}^2$$

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- how do I define importance?

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Oracle prediction functions:

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Define population importance in terms of $\mu_0, \mu_{0,s}$!

Population variable importance

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\begin{aligned}
DR^2_s(P_0) &:= R^2(\mu_0, P_0) - R^2(\mu_{0,s}, P_0) \\
R^2(\mu, P_0) &:= 1 - \frac{MSE(\mu, P_0)}{var_{P_0}(Y)} \\
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Variable importance: comparing population predictiveness!

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In general: consider function classes $\mathcal{F}_s \subseteq \mathcal{F} \subseteq L_2(P_0)$

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- $V(f, P)$: predictiveness of $f \in \mathcal{F}$ under distribution P

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Variable importance: $\Psi_s(P_0) := V(f_{P_0}^*, P_0) - V(f_{P_0,s}^*, P_0)$

Plug-in estimators of variable importance

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Questions:

- when is $\hat{\psi}_{n,s}$ regular and asymptotically linear?
- can we test $H_0 : \psi_{0,s} = 0$?

U parameters

Specify

$$V(f, P) = E_P G\{O_1, \ldots, O_m, f(O_1), \ldots, f(O_m)\} \equiv E_P G\{O, f(O)\}$$

Examples:

U parameters

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U parameter: $V(f_P^*, P)$

U estimator: $V(\hat{f}_n, \mathbb{P}_n)$, plug-in estimator of a U parameter

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- linear term; (1st order)
- empirical process term; (2nd order)
- remainder term; (2nd order)
- problem term! (1/2-ish order, usually)

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Under optimization* and convergence rate† conditions,

- $\hat{\psi}_{n,s}$ asymptotically linear with influence function D^*
- $\hat{\psi}_{n,s}$ regular
- If $\sigma^2_{0,s} := E_{P_0}\{D^*(P_0)(O)^2\} > 0$, then

$$\sqrt{n}(\hat{\psi}_{n,s} - \psi_{0,s}) \rightarrow_d Z \sim N(0, \sigma^2_{0,s})$$

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*: derivative of V at $f^*_{P_0}$ is 0

†: $E_{P_0}\{\hat{f}_n(O) - f^*_{P_0}(O)\}^2 = o_P(n^{-1/2})$

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4. If CIs do not overlap, reject H_0

Experiment: binary outcome, bivariate feature vector

$Y \sim Bern(0.6)$; $X_1 \mid Y \sim N(\mu_1, \Sigma)$

Under H_0, $X_2 \mid Y \sim N(0, \Sigma)$

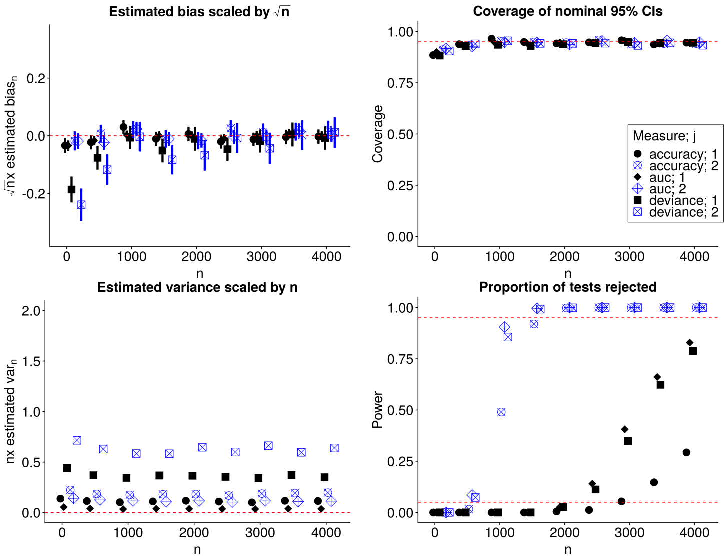
Under H_1, $X_2 \mid Y \sim N(\mu_2, \Sigma)$

Investigate:

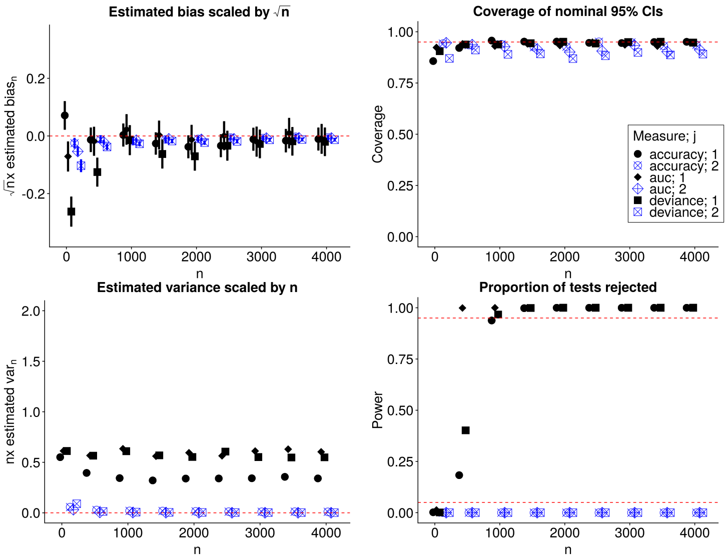
- scaled bias
- coverage of nominal 95% CIs
- type I error (or power)

Estimate using cross-validation and regression stacking

Experiment: results under the alternative



Experiment: results under the null



Studying an antibody against HIV-1 infection

- 611 HIV-1 pseudoviruses, split into two datasets
- Outcome: neutralization sensitivity to antibody
- 493 individual features, 12 groups of interest
- Estimate using cross-validation and regression stacking

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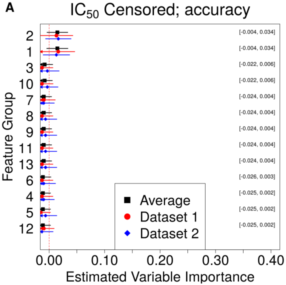

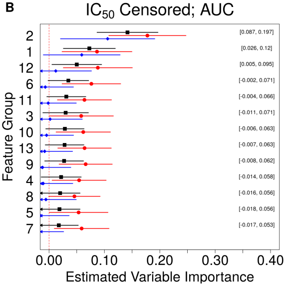

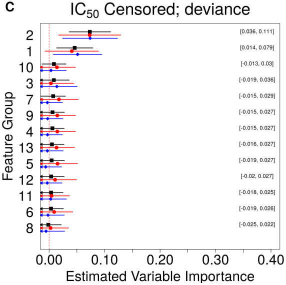

D Feature group definitions

1	VRC01 binding footprint
2	CD4 binding sites
3	Sites with sufficient exposed surface area
4	Sites identified as important for glycosylation
5	Sites with residues that covary with the VRC01 binding footprint
6	Sites associated with VRC01-specific potential N-linked glycosylation (PNGS) effects
7	gp41 sites important for VRC01 binding
8	Sites for indicating N-linked glycosylation
9	Majority virus subtypes
10	Region-specific counts of PNGS
11	Viral geometry
12	Cysteine counts
13	Steric bulk at critical locations

Conclusions

Variable importance: comparing population predictiveness

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Plug-in estimators of R^2, AUC, accuracy, . . . efficient

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`github.com/bdwilliamson/vimp`

Appendix: Asymptotic distribution of U estimators

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$V(f, P)$ is **linear** with EIF

$$D(f, P)(o) := G\{o, f(o)\} - E_P G\{O, f(O)\}$$

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$$\mathbb{P}_n D^*(P_n) = \frac{1}{n}\sum_{i=1}^n \left[G\{O_i, \hat{f}_n(O_i)\} - \frac{1}{n}\sum_{i=1}^n G\{O_i, \hat{f}_n(O_i)\} \right] = 0$$