

Post-Selection Inference for Models that are Approximations

(Work in Progress)

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joint with the PoSI Group:

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50 Years of Statistics at ETH — 2014/11/25

Problems: Non-Reproducibility in Biomedical Science

Borrowed from: Berger, 2012, "Reproducibility of Science: P-values and Multiplicity"

- Bayer Healthcare: 67 attempts at replicating published research findings
 - ▶ Fewer than 1/4 were viewed as replicated.
 - ▶ Over 2/3 had major inconsistencies leading to project termination.
- Arrowsmith (2011, Nat.Rev.Drug Discovery 10): Drug trial success rates ↓
 - ▶ Phase II: 28% in 2005, 18% in 2010
 - ▶ Phase III: 80% in 2000, 50% in 2010
 - ▶ Phase III cancer drugs: 30%
- The NIH funded randomized clinical trials to follow up exciting results from 20 observational studies: Only one was replicated.
- Ioannidis (JAMA-2005, 218-28):
 - ▶ 5 of 6 highly cited nonrandomized studies were contradicted or had found stronger effects than were established by later studies.

Most Empirical Findings Are False

Bombshell in Biomedical Science:

- **“Why Most Published Research Findings Are False”**

by Ioannidis (2005, PLOS Medicine)

- Demonstrates the combined influences of: Pre-study (true/false) odds R , Type I error α , power β , bias u (!), # independent similar studies n .

- Famous corollaries:

- ▶ the smaller the study sizes,
- ▶ the smaller the effect sizes,
- ▶ the greater the number of tested relationships,
- ▶ the greater the flexibility in design, definitions, outcomes, techniques,
- ▶ the greater the financial and professional interests,
- ▶ the hotter the field,

the less likely the research findings are to be true.

- Note: **“bias”** due to “manipulation in the analysis”, “selective reporting”

Problems: “False-Positive” Social Sciences

Bombshell in psychological research:

- **“False Positive Psychology: Undisclosed Flexibility in Data Collection and Analysis allows Presenting Anything as Significant”**
by Simmons, Nelson, Simonsohn (2011, Psychological Science)
- New concept: **“Researcher Degrees of Freedom”**
 - ▶ “In the course of collecting and analyzing data, researchers have many decisions to make: Should more data be collected? Should some observations be excluded? Which conditions should be combined and which ones compared? Which control variables should be considered? Should specific measures be combined or transformed or both?”
 - ▶ Elaboration of what Ioannidis could have meant with “bias”.
- Soul-searching in social science journals:
 - ▶ disclosure requirements, emphasis on replication, ...

Problem: “False-Positive” Social Sciences (contd.)

- From Simmons, Nelson, Simonsohn (2011):

Table 1. Likelihood of Obtaining a False-Positive Result

Researcher degrees of freedom	Significance level		
	$p < .1$	$p < .05$	$p < .01$
Situation A: two dependent variables ($r = .50$)	17.8%	9.5%	2.2%
Situation B: addition of 10 more observations per cell	14.5%	7.7%	1.6%
Situation C: controlling for gender or interaction of gender with treatment	21.6%	11.7%	2.7%
Situation D: dropping (or not dropping) one of three conditions	23.2%	12.6%	2.8%
Combine Situations A and B	26.0%	14.4%	3.3%
Combine Situations A, B, and C	50.9%	30.9%	8.4%
Combine Situations A, B, C, and D	81.5%	60.7%	21.5%

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 - ▶ All three modes of model selection may be used in much empirical research.
 - ▶ Ironically, the most thorough and competent data analysts may also be the ones who produce the most spurious findings.
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a priori to one formal selection method and nothing else.

Linear Model Inference and Variable Selection

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\epsilon}$$

- \mathbf{X} = fixed design matrix, $N \times p$, $N > p$, full rank.
- $\boldsymbol{\epsilon} \sim \mathcal{N}_N(\mathbf{0}, \sigma^2 \mathbf{I}_N)$

In textbooks:

- 1 Variables selected
- 2 Data seen
- 3 Inference produced

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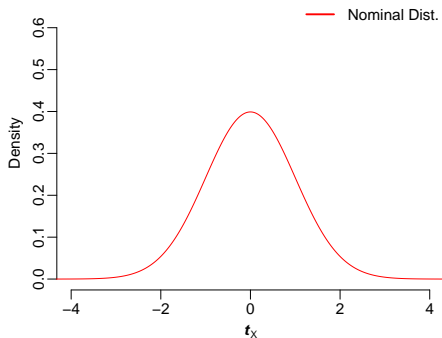
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Is this inference valid?

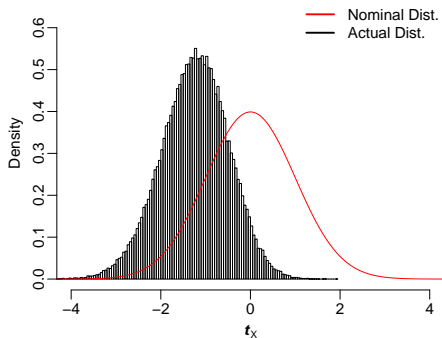
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Marginal Distribution of Post-Selection t -statistics:



- The overall coverage probability of the conventional post-selection CI is **83.5% < 95%**.
- For $p = 30$, the coverage probability can be as low as **39%**.

The PoSI Procedure — Rough Outline

- We propose to construct **Post Selection Inference** (PoSI) with guarantees for the coverage of CIs and Type I errors of tests.
- We **widen** CIs and retention intervals to achieve correct/conservative post-selection coverage probabilities. This is the **price** we have to pay.
- The approach is a reduction of PoSI to **simultaneous inference**.
- Simultaneity is across **all submodels** and **all slopes** in them.
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- But first we need make sense of

Targets of Inference in Approximate Models

Incorrect Submodels — What Is Being Estimated?

- Denote a submodel by integers $M = \{j_1, j_2, \dots, j_m\}$:

$$\mathbf{X}_M = (\mathbf{X}_{j_1}, \mathbf{X}_{j_2}, \dots, \mathbf{X}_{j_m}) \in \mathbb{R}^{N \times m}.$$

- LS coefficient estimates in the submodel M:

$$\hat{\beta}_M = (\mathbf{X}_M^T \mathbf{X}_M)^{-1} \mathbf{X}_M^T \mathbf{Y} \in \mathbb{R}^m$$

- Q: What does $\hat{\beta}_M$ estimate, **not** assuming the truth of M?

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A: Its expectation!

$$\boldsymbol{\mu} := \mathbf{E}[\mathbf{Y}] \in \mathbb{R}^N \quad \text{arbitrary!!}$$

$$\beta_M := \mathbf{E}[\hat{\beta}_M] = (\mathbf{X}_M^T \mathbf{X}_M)^{-1} \mathbf{X}_M^T \boldsymbol{\mu}$$

We do **not** assume that the submodel is correct: $\boldsymbol{\mu} \neq \mathbf{X}_M \beta_M$ allowed!

But $\mathbf{X}_M \beta_M$ is the best approximation to $\boldsymbol{\mu}$.

Adjustment, Estimates, Parameters, t -Statistics

Notation and facts for the components of $\hat{\beta}_M$ and β_M , assuming $j \in M$:

- Let $\mathbf{X}_{j \cdot M}$ be the predictor \mathbf{X}_j adjusted for the other predictors in M :

$$\mathbf{X}_{j \cdot M} := (\mathbf{I} - \mathbf{H}_{M \setminus \{j\}}) \mathbf{X}_j \perp \mathbf{X}_k \quad \forall k \in M \setminus \{j\}.$$

- Let $\hat{\beta}_{j \cdot M}$ be the slope estimate and $\beta_{j \cdot M}$ be the parameter for \mathbf{X}_j in M :

$$\hat{\beta}_{j \cdot M} := \frac{\langle \mathbf{X}_{j \cdot M}, \mathbf{Y} \rangle}{\|\mathbf{X}_{j \cdot M}\|^2}, \quad \beta_{j \cdot M} := \frac{\langle \mathbf{X}_{j \cdot M}, \mathbf{E}[\mathbf{Y}] \rangle}{\|\mathbf{X}_{j \cdot M}\|^2}.$$

- Let $t_{j \cdot M}$ be the t -statistic for $\hat{\beta}_{j \cdot M}$ and $\beta_{j \cdot M}$:

$$t_{j \cdot M} := \frac{\hat{\beta}_{j \cdot M} - \beta_{j \cdot M}}{\hat{\sigma} / \|\mathbf{X}_{j \cdot M}\|} = \frac{1}{\hat{\sigma}} \left\langle \frac{\mathbf{X}_{j \cdot M}^T}{\|\mathbf{X}_{j \cdot M}\|}, \mathbf{Y} - \mathbf{E}[\mathbf{Y}] \right\rangle.$$

Parameters One More Time

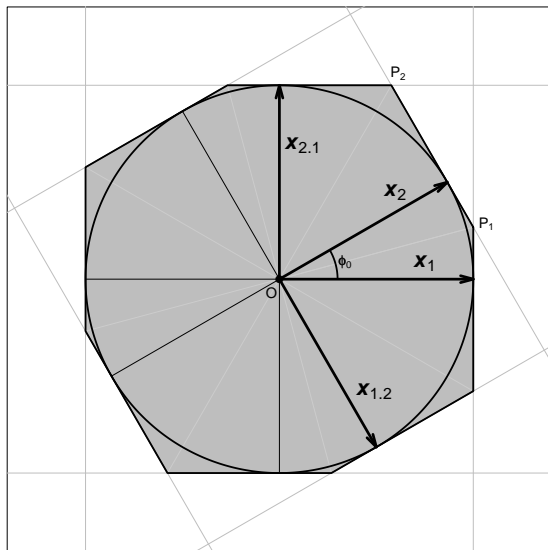
- Important: If the predictors are partly collinear (non-orthogonal) then

$$M \neq M', j \in M \cap M' \Rightarrow \beta_{j \cdot M} \neq \beta_{j \cdot M'}$$

in value and in meaning!

- Rule: A difference in adjustment implies a difference in parameters.
- Number of parameters $\beta_{j \cdot M}$: $p2^{p-1}$

Geometry of Adjustment



Column space
of \mathbf{X} for $p=2$
predictors,
partly collinear

Error Estimates $\hat{\sigma}$: One for All Submodels

- Critical Point: To enable simultaneous inference for all $t_{j \bullet M}$, use **one error estimate $\hat{\sigma}$** for all submodels.
 - ▶ Do **not** use ~~$\hat{\sigma}_M$~~ !
 - ▶ Use $\hat{\sigma} = \hat{\sigma}_{Full}$ instead for all submodels M .
 - ▶ $t_{j \bullet M}$ will have a t -distribution with the same dfs $\forall M, \forall j \in M$.

- Q: What if even the full model is 1st order wrong?

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- Q: What if even the full model is 1st order wrong?
A: $\hat{\sigma}_{Full}$ will be inflated and inference will be conservative.
- A better $\hat{\sigma}$ is available if ...
 - ▶ exact replicates exist: use $\hat{\sigma}$ from the 1-way ANOVA of replicates;
 - ▶ a larger than the full model can be assumed 1st order correct: use $\hat{\sigma}_{Large}$;
 - ▶ a previous dataset provided a valid estimate: use $\hat{\sigma}_{previous}$;
 - ▶ nonparametric estimates are available: use $\hat{\sigma}_{nonpar}$ (Hall and Carroll 1989).

Statistical Inference under First Order Incorrectness

- Same correct inference across all submodels M and all $\beta_{j \bullet M}$:
 - ▶ If $r = \text{dfs}$ in $\hat{\sigma}$ and $K = t_{1-\alpha/2, r}$, then the “almost usual” interval

$$CI_{j \bullet M}(K) := [\hat{\beta}_{j \bullet M} \pm K \hat{\sigma} / \|\mathbf{X}_{j \bullet M}\|]$$

satisfies: $\mathbf{P}[\beta_{j \bullet M} \in CI_{j \bullet M}(K)] = 1 - \alpha \quad \forall M, \forall j \in M$

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- Correct inference in a mean-misspecified homoskedastic model:

$$\mathbf{Y} = \boldsymbol{\mu} + \boldsymbol{\epsilon}, \quad \boldsymbol{\epsilon} \sim \mathcal{N}_N(\mathbf{0}, \sigma^2 \mathbf{I})$$

- ▶ Permitted: $\boldsymbol{\mu} \neq \mathbf{X}\boldsymbol{\beta}$, $\mathbf{X}_M \boldsymbol{\beta}_M \quad \forall M$
- ▶ A single valid $\hat{\sigma}$ with known dfs across all submodels enables **simultaneous inference** across submodels.

Variable Selection

- What is a variable selection procedure?

A map $\mathbf{Y} \mapsto \hat{\mathbf{M}} = \hat{\mathbf{M}}(\mathbf{Y}), \mathbb{R}^N \rightarrow \mathcal{P}(\{1, \dots, p\})$

- ▶ $\hat{\mathbf{M}}$ divides the response space \mathbb{R}^N into up to 2^p subsets.
 - ▶ In a fixed-predictor framework, selection purely based on \mathbf{X} does not invalidate inference (example: deselect predictors based on VIF, \mathbf{H} , ...).
- Candidate for meaningful coverage probabilities:

$$\mathbf{P}[\beta_{j \cdot \hat{\mathbf{M}}} \in \text{CI}_{j \cdot \hat{\mathbf{M}}}(K)]$$

- Problem: No such coverage probabilities are known or can be estimated for most selection procedures $\hat{\mathbf{M}}$.
- Solution: Ask for more! It is possible to construct **universal Post-Selection Inference for all selection procedures.**

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Reduction to Simultaneous Inference

Lemma

For any variable selection procedure $\hat{M} = \hat{M}(\mathbf{Y})$, we have the following “significant triviality bound”:

$$\max_{j \in \hat{M}} |t_{j \cdot \hat{M}}| \leq \max_M \max_{j \in M} |t_{j \cdot M}| \quad \forall \mathbf{Y}, \boldsymbol{\mu} \in \mathbb{R}^N.$$

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Theorem

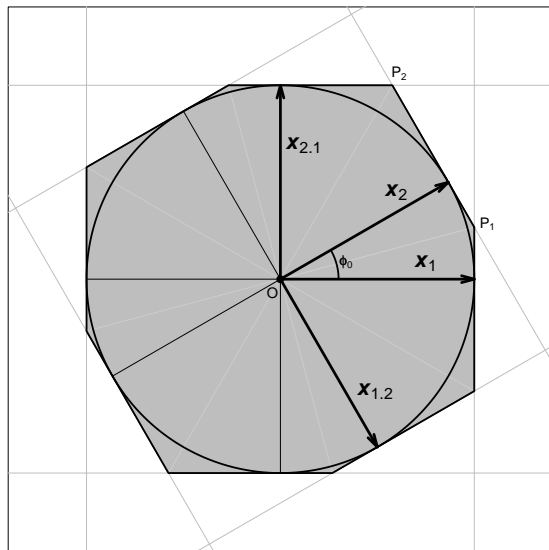
Let K be the $1 - \alpha$ quantile of the “**max-max-|t|**” statistic of the lemma:

$$\mathbf{P} \left[\max_M \max_{j \in M} |t_{j \cdot M}| \leq K \right] \stackrel{(\geq)}{=} 1 - \alpha.$$

Then we have the following universal PoSI guarantee:

$$\mathbf{P} \left[\beta_{j \cdot \hat{M}} \in CI_{j \cdot \hat{M}}(K) \quad \forall j \in \hat{M} \right] \geq 1 - \alpha \quad \forall \hat{M}.$$

PoSI Geometry — Simultaneity



PoSI polytope
= intersection
of all t -bands.

Computing PoSI

- The simultaneity challenge: $\#\{ |t_{j \cdot M}| \} = p 2^{p-1}$

p	3	4	5	6	7	8	9	10	11
$\# t $	12	32	80	192	448	1,024	2,304	5,120	11,264
p	12	13	14	15	16	17	18	19	20
$\# t $	24,576	53,248	114,688	245,760	524,288	1,114,112	2,359,296	4,980,736	10,485,760

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- **Computations:** (for R Code, search “Buja Wharton”)

- ▶ Computational cost is linear in N , exponential in p .
- ▶ Off-the-shelf R software works up to $p \approx 7$.
- ▶ Custom semi-MC-approximation in R works up to $p \approx 20$.
- ▶ **Sparse PoSI:** Limit search to models of size $\leq m$; permit $N < p, m \leq N$.
Example: PoSI for $p = 50$ and $m = 5$ requires $\#\{|t_{j \cdot M}|\} = 11,576,300$.

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- **Large- p Asymptotics:** based on sequences of structured designs \mathbf{X}

- ▶ Worst-case: $K(p) \in \sqrt{p} \cdot [0.78, 0.866\dots]$
- ▶ Best-case: $K(p) \sim \sqrt{2 \log(p)}$

PoSI Benefits

PoSI protection may seem conservative, **but**

PoSI inference will be valid even if one...

- ... tries several formal selection methods and picks the “best”;
- ... uses informal model diagnostics to reject models;
- ... performs “significance hunting”, i.e., selects the model with the most significant effects on preferred predictors;
- ... steps forward/backward till all selected predictors are “significant”;
- ... analyzes clinical trial data in post-hoc “data mining”.

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Cons:

- Artificial randomness from a single split.
- Reduced effective sample size.
- More model selection uncertainty.
- More estimation uncertainty.
- Loss of conditionality on \mathbf{X} .

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- Consequence: Ancillarity of X is invalid if the model is an approximation.

Inference for Random X

- Fact: Econometricians do not condition on \mathbf{X} .

They use an alternative form of inference based on the

Sandwich Estimate of Standard Error.

Eicker-**Huber**-White

PJH, "THE BEHAVIOR OF MAXIMUM LIKELIHOOD ESTIMATES
UNDER NONSTANDARD CONDITIONS", Berkeley Symp. 1967

Inference for Random \mathbf{X}

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to be distinguished from the Residual Bootstrap (which is fixed- \mathbf{X}).
- Fact: The Sandwich estimate of Standard Error is the limit of the
 M -of- N bootstrap as $M \rightarrow \infty$.

The Pairs Bootstrap for Regression

- Assumptions: $(\mathbf{x}_i, y_i) \sim P(d\mathbf{x}, dy)$ i.i.d.,

$P(d\mathbf{x})$ non-degenerate: $\mathbf{E}[\mathbf{x}\mathbf{x}'] > \mathbf{0}$, + technicalities for CLTs of estimates.

- There is no regression model, but we apply regression anyway, LS, say:

$$\hat{\beta} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{y}$$

- The nonparametric pairs bootstrap applies:

$$\text{Resample } (\mathbf{x}_i, y_i) \text{ pairs} \rightarrow (\mathbf{x}_i^*, y_i^*) \rightarrow \hat{\beta}^*.$$

Note: Militant conditionalists would reject this; they would bootstrap residuals.

- Estimate $SE(\hat{\beta}_j)$ by $\hat{SE}_{\text{boot}}(\hat{\beta}_j) = SD^*(\beta_j^*)$.

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Question: Letting $\hat{SE}_{\text{lin}}(\hat{\beta}_j) = \frac{\hat{\sigma}}{\|\mathbf{x}_{j\bullet}\|}$, is the following always true?

$$\hat{SE}_{\text{boot}}(\hat{\beta}_j) \stackrel{?}{\approx} \hat{SE}_{\text{lin}}(\hat{\beta}_j)$$

Conventional vs Bootstrap Std Errors: Can they differ?

Compare conventional and bootstrap standard errors:

- Boston Housing Data (no groans, please! Caveat...)
- Response: MEDV of single residences in a census tract, $N = 506$
- $R^2 \approx 0.74$, residual dfs = 487

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	$\hat{\beta}_j$	SE_{lin}	SE_{boot}	SE_{boot}/SE_{lin}	t_{lin}
CRIM	-0.099	0.031	0.033	1.074	-3.261
ZN	0.121	0.035	0.035	1.004	3.508
INDUS	0.017	0.046	0.038	0.843	0.382
CHAS	0.074	0.024	0.036	1.503	3.152
NOX	-0.224	0.048	0.048	1.003	-4.687
RM	0.290	0.032	0.065	2.049	9.149
AGE	0.002	0.040	0.050	1.236	0.044
DIS	-0.344	0.045	0.048	1.068	-7.598
RAD	0.288	0.062	0.060	0.958	4.620
TAX	-0.233	0.068	0.051	0.740	-3.409
PTRATIO	-0.218	0.031	0.026	0.865	-7.126
B	0.092	0.026	0.027	1.036	3.467
LSTAT	-0.413	0.039	0.078	1.995	-10.558

Conventional vs Bootstrap Std Errors (contd.)

Compare conventional and bootstrap standard errors:

- LA Homeless Data (Richard Berk, UPenn)
- Response: `StreetTotal` of homeless in a census tract, $N = 505$
- $R^2 \approx 0.13$, residual `dfs` = 498

Conventional vs Bootstrap Std Errors (contd.)

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	$\hat{\beta}_j$	SE _{lin}	SE _{boot}	SE _{boot} /SE _{lin}	t_{in}
MedianInc	-4.241	4.342	2.651	0.611	-0.977
PropVacant	18.476	3.595	5.553	1.545	5.140
PropMinority	2.759	3.935	3.750	0.953	0.701
PerResidential	-1.249	4.275	2.776	0.649	-0.292
PerCommercial	10.603	3.927	5.702	1.452	2.700
PerIndustrial	11.663	4.139	7.550	1.824	2.818

Conventional vs Bootstrap Std Errors (contd.)

Compare conventional and bootstrap standard errors:

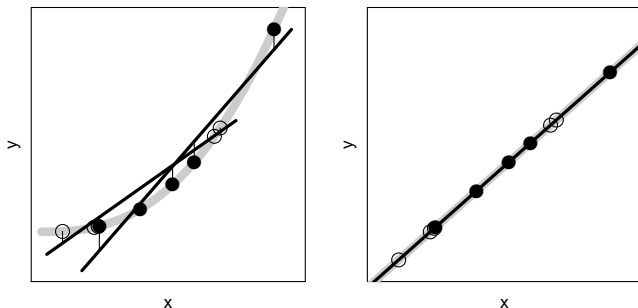
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- Which standard errors are we to believe?
- What is the reason for the discrepancy?
- Is the pairs bootstrap a failure?

First Reason for $SE_{boot} \neq SE_{lin}$: Nonlinearity

Recall the demo: A noise-free nonlinearity $y_i = \mu(\mathbf{x}_i) \sim x_i^2$, x_i i.i.d. fitted by a straight line.

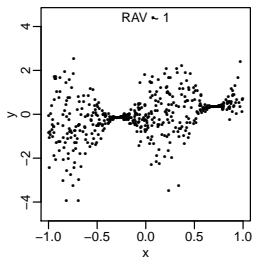
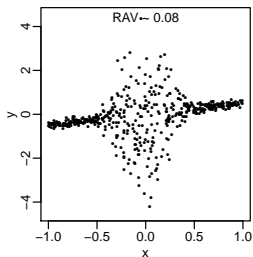
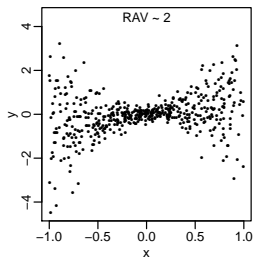


Nonlinearity + randomness of X = sampling variability.

- Hal White^{†2012} (1980), "Using Least Squares to Approximate Unknown Regression Functions," International Economic Review

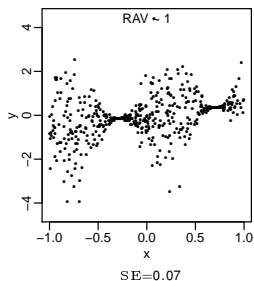
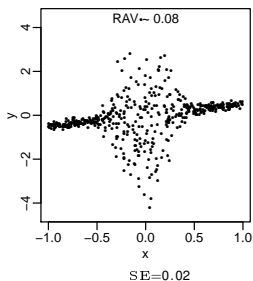
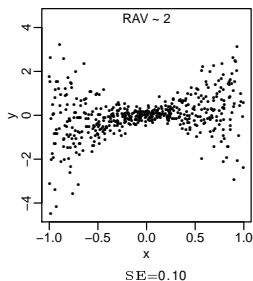
Second Reason for $SE_{boot} \neq SE_{lin}$: Heteroskedasticity

Which has the smallest/largest true $SE(\hat{\beta})$? ($\sum \sigma_i^2$ are the same.)



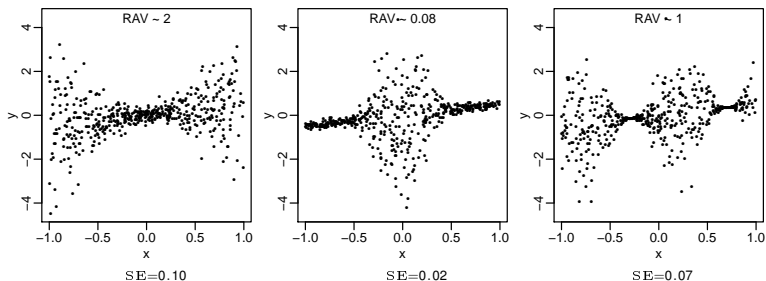
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Heteroskedasticity can invalidate Linear Model SEs.

- Hinkley (1977) "Jackknifing in Unbalanced Situations," Technometrics
- Wu (1986) "Jackknife, Bootstrap and Other Resampling Methods in Regression Analysis," AoS
- Hal White^{†2012} (1980), "A Heteroskedasticity-Consistent Covariance Matrix Estimator and a Direct Test for Heteroskedasticity," Econometrica (1980)

But Why Would Anyone Use an “Incorrect” Model?

- Often we **don't know** that the model is violated by the data.
⇒ An argument in favor of diligent model diagnostics...
- The problem persists even if we use basis expansion
but **miss the nature of the nonlinearity**: curves, jaggies, jumps, ...
- Linear models provide **low-df approximations** which may be all that is feasible when p is large compared to n .
- Even when the model is only an approximation, the slopes contain information about the **direction of the association**.
- \exists interpretations of slopes w/o assuming a correct model:

weighted averages of “case slopes”

$$\hat{\beta} = \sum_{i=1 \dots n} w_i \hat{\beta}_i, \quad \hat{\beta}_i = \frac{y_i - \bar{y}}{x_i - \bar{x}}, \quad w_i = \frac{(x_i - \bar{x})^2}{\sum_{k=1 \dots n} (x_k - \bar{x})^2}.$$

Redefining the Population and the Parameters

- Joint distribution, i.i.d. sampling: $(\mathbf{x}_i, y_i) \sim P(d\mathbf{x}, dy)$

Assume properties sufficient to grant CLTs for estimates of interest.

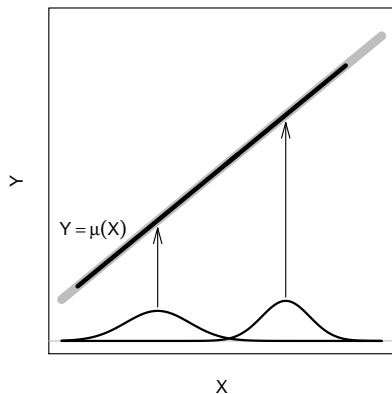
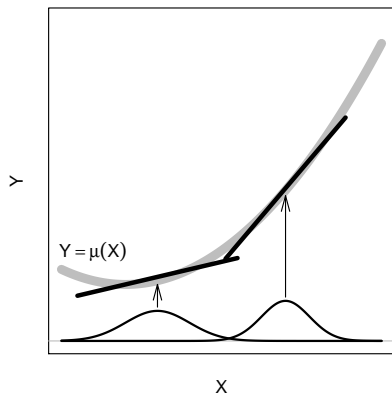
- No assumptions on $\mu(\mathbf{x}) = \mathbf{E}[y | \mathbf{x}]$, $\sigma^2(\mathbf{x}) = \mathbf{V}[y | \mathbf{x}]$.
- Define a population LS parameter:

$$\beta := \operatorname{argmin}_{\tilde{\beta}} \mathbf{E} \left[\left(y - \tilde{\beta}' \mathbf{x} \right)^2 \right] = \mathbf{E}[\mathbf{x} \mathbf{x}']^{-1} \mathbf{E}[\mathbf{x} y]$$

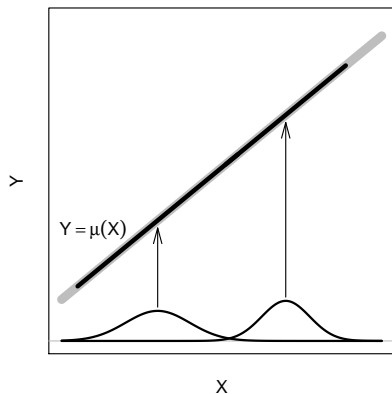
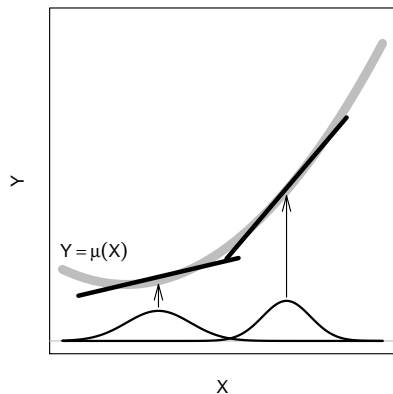
- This is the target of inference: $\beta = \beta(P)$
Thus β is a statistical functional, not a generative parameter.

\implies **“Semi-parametric LS framework”**
(“Random \mathbf{X} Theory”)

The LS Population Parameter



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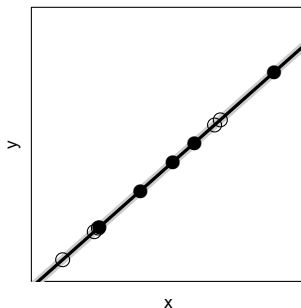
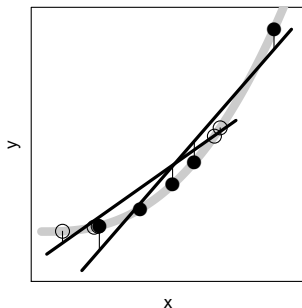
If $\mu(x)$ is nonlinear, $\beta(P)$ depends on the x -distribution $P(dx)$!

The LS Estimator and its Target

- Data: $\mathbf{X} = (\mathbf{x}_1, \dots, \mathbf{x}_N)'$, $\mathbf{y} = (y_1, \dots, y_N)'$,
- Target of estimation and inference in linear models theory:

$$\beta(\mathbf{X}) = \mathbf{E}[\hat{\beta}|\mathbf{X}] = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{E}[y|\mathbf{X}]$$

- When $\mu(\mathbf{x}) = \mathbf{E}[y|\mathbf{x}]$ is nonlinear, then $\beta(\mathbf{X})$ is a random vector.



Linear Models Theory versus Econometrics

- Consider the simplest case of a single predictor, no intercept, and define the conditional MSE by $m^2(x) := \mathbf{E}[(Y - \beta'x)^2|x]$
- The **correct** asymptotic variance of $\hat{\beta}$ is

$$AV_{sand} = \frac{\mathbf{E}[m^2(x)x^2]}{\mathbf{E}[x^2]^2}.$$

- If we were to use standard errors from linear models theory, the following **incorrect** asymptotic variance is implied:

$$AV_{lin} = \frac{\mathbf{E}[m^2(\mathbf{x})]}{\mathbf{E}[x^2]}$$

- Define the “**Ratio of Asymptotic Variances**” or **RAV**:

$$RAV := \frac{AV_{sand}}{AV_{lin}} = \frac{\mathbf{E}[m^2(x)x^2]}{\mathbf{E}[m^2(\mathbf{x})] \mathbf{E}[x^2]}$$

Linear Models Theory versus Econometrics (contd.)

$$\mathbf{RAV} = \frac{\mathbf{AV}_{sand}}{\mathbf{AV}_{lin}} = \frac{\mathbf{E}[m^2(\mathbf{x})x^2]}{\mathbf{E}[m^2(x)]\mathbf{E}[x^2]}$$

Linear Models Theory versus Econometrics (contd.)

$$\mathbf{RAV} = \frac{\mathbf{AV}_{sand}}{\mathbf{AV}_{lin}} = \frac{\mathbf{E}[m^2(\mathbf{x})x^2]}{\mathbf{E}[m^2(x)]\mathbf{E}[x^2]}$$

- **Fact:**

$$\max_m \mathbf{RAV} = \infty, \quad \min_m \mathbf{RAV} = 0$$

- Conclusion: Asymptotically the discrepancy between SE_{sand} and SE_{lin} can be arbitrarily large in either direction.
- In practice, $\mathbf{RAV} > 1$ is more frequent **and** more dangerous because it invalidates conventional linear models inference.

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⇒ SE_{sand} is even less robust than SE_{lin} .
 - ▶ The robustness problem is equally present in SE_{sand} and SE_{boot} .
- A new PoSI technology can be based on asymptotic normality and estimates of **AV**:
 - ▶ Sandwich/bootstrap PoSI computations become slightly more expensive: Initial reduction is to $(p+1)p/2$ rather than p dimensions.
 - ▶ Sandwich/bootstrap PoSI allows us to protect against selection of a finite dictionary of transformations in addition to selection of predictors.
 $(g(Y), f_1(X_1), \dots, f_p(X_p))$ is no different than (Y, X_1, \dots, X_p) .

Some Take-Home Points about Approximate Models

- Robustness should include not just misspecification of error distributions but of 1st and 2nd order misspecifications as well.
⇒ Sandwich or pairs-bootstrap estimates of standard error
- Beware of the ancillarity fallacy: Ancillarity arguments are invalidated by 1st order model misspecifications.
- Fixed- \mathbf{X} standard errors SE_{lin} can be substantial underestimates of true sampling variation; the opposite can occur, too, but rarely.
- In any regression, not all predictors are equally affected by standard error discrepancies.

Back to the Big Picture: Reproducibility

- Contributing factor to non-reproducibility:

Unaccounted data-analytic activities such as

- ▶ selection of predictor variables*
- ▶ selection of outcome variables*
- ▶ selection of data transformations**
- ▶ informal EDA before formal model selection*
- ▶ informal diagnostics after formal model selection*
- ▶ meta-selection of selection methods*

* solved by fixed- \mathbf{X} PoSI under 1st order misspecific. & homoskedasticity.

- From a fixed- \mathbf{X} to a random- \mathbf{X} framework:

- ▶ Correct inference under minimal assumptions: $(y_i, \mathbf{x}_i) \sim \text{iid}$
- ▶ Accounts for nonlinearity and heteroskedasticity.
- ▶ Permits PoSI for selection of transformations; solves **.

THANKS AND
CHEERS TO SfS!