

Inference for Linear Functionals in High-dimensional Linear Models

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Tianxi Cai

High-dimensional linear regression

$$y_{n \times 1} = X_{n \times p} \beta_{p \times 1} + \epsilon_{n \times 1}.$$

- ▶ Number of covariates $p \gg$ sample size n .
- ▶ When $p > n$, $\|\beta\|_0 \leq k$.

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Estimation of β : Basis Pursuit (Chen & Donoho, '94); Lasso (Tibshirani, '96); SCAD (Fan & Li, '01); LARS (Efron, Hastie, Johnstone & Tibshirani, '04) Elastic Net (Zou & Hastie, '05); Adaptive Lasso (Zou, '05); Dantzig Selector (Candès & Tao, '07); Lasso and Dantzig (Bickel, Ritov & Tsybakov, '09); MCP (Zhang '10); scaled Lasso (Sun & Zhang, '10); square-root Lasso (Belloni, Chernozhukov & Wang, '11); ...

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- ▶ $x_{\text{new}}^\top \beta$

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- ▶ $\|\beta\|_2^2$
- ▶ $\beta^\top \Sigma \beta = \text{Var}(\mathbf{X}_i^\top \beta)$
- ▶ $\beta_G^\top \Sigma_{G,G} \beta_G = \text{Var}(\mathbf{X}_{i,G}^\top \beta_G)$

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3. ℓ_q Accuracy Functionals

- ▶ $\|\hat{\beta} - \beta\|_2^2$ (Accuracy assessment of $\hat{\beta}$)
- ▶ $\|\hat{\beta} - \beta\|_q^q$ for $1 \leq q < 2$.

Overview of talk

- 1 Inference for β_j : Review of De-biasing
- 2 Minimality and Adaptivity
- 3 Uniform Procedure for All loadings
- 4 Further Discussion on Optimality

- ▶ **Statistics:** Zhang & Zhang '14; van de Geer, Bühlmann, Ritov & Dezeure '14; Javanmard & Montanari '14;
- ▶ **Econometrics:** Chernozhukov, Belloni & Hansen '13; Chernozhukov, Hansen & Spindler '15;

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- ▶ **Econometrics:** Chernozhukov, Belloni & Hansen '13; Chernozhukov, Hansen & Spindler '15;
- ▶ Main idea: **Bias correction.**

$$\hat{\beta} = \arg \min_{\beta \in \mathbb{R}^p} \frac{1}{2n} \|y - X\beta\|_2^2 + \lambda \|\beta\|_1, \text{ with } \lambda \asymp \sqrt{\log p/n\sigma}$$

- ▶ De-biased Estimator:

$$\tilde{\beta}_i = \hat{\beta}_i + \underbrace{\hat{u}^\top \frac{1}{n} X^\top (y - X\hat{\beta})}_{\text{Correction term}} \text{ with } \left(\frac{1}{n} X^\top X \right) \hat{u} \approx e_i.$$

Construction of Projection Direction

Estimation error of $\hat{\beta}_i$: $\hat{\beta}_i - \beta_i = \mathbf{e}_i^\top (\hat{\beta} - \beta)$

$$\hat{\mathbf{u}}^\top \frac{1}{n} \mathbf{X}^\top (\mathbf{Y} - \mathbf{X} \hat{\beta}) = \hat{\mathbf{u}}^\top \hat{\Sigma} (\beta - \hat{\beta}) + \hat{\mathbf{u}}^\top \frac{1}{n} \mathbf{X}^\top \epsilon$$

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De-biased estimator

$$\tilde{\beta}_i = \mathbf{e}_i^\top \hat{\beta} + \hat{\mathbf{u}}^\top \frac{1}{n} \mathbf{X}^\top (\mathbf{Y} - \mathbf{X}\hat{\beta}).$$

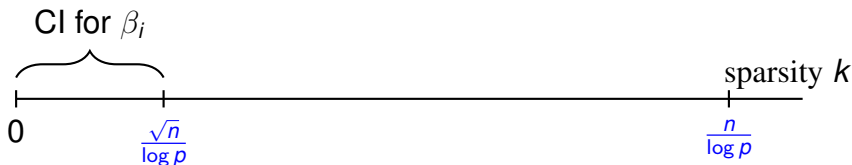
$$\hat{\mathbf{u}} = \arg \min_{\mathbf{u} \in \mathbb{R}^p} \left\{ \underbrace{\mathbf{u}^\top \hat{\Sigma} \mathbf{u}}_{\text{Variance}} : \underbrace{\left\| \hat{\Sigma} \mathbf{u} - \mathbf{e}_i \right\|_\infty}_{\text{Constrained Bias}} \leq \|\mathbf{e}_i\|_2 \lambda_1 \right\}$$

Construction of CI for β_1

$$\tilde{\beta}_i - \beta_i = \underbrace{(\hat{\mathbf{u}}^\top \hat{\Sigma} - \mathbf{e}_i^\top)(\beta - \hat{\beta})}_{\text{Remaining Bias}} + \underbrace{\hat{\mathbf{u}}^\top \frac{1}{n} \mathbf{X}^\top \epsilon}_{\text{Variance}}$$

1. Variance $\sqrt{n} \hat{\mathbf{u}}^\top \frac{1}{n} \mathbf{X}^\top \epsilon \mid \mathbf{X} \sim N(0, \hat{\mathbf{u}}^\top \hat{\Sigma} \hat{\mathbf{u}})$
2. $\sqrt{n} \left| (\hat{\mathbf{u}}^\top \hat{\Sigma} - \mathbf{e}_i^\top)(\beta - \hat{\beta}) \right| \leq \sqrt{n} \|\hat{\Sigma} \hat{\mathbf{u}} - \mathbf{e}_i\|_\infty \|\beta - \hat{\beta}\|_1 \lesssim \frac{k \log p}{\sqrt{n}}$

Ultra-sparse case $k \ll \frac{\sqrt{n}}{\log p} \Rightarrow$ Variance dominates.



CI over $k \lesssim \frac{n}{\log p}$

$$\text{CI}_{\beta_1}(k) = \left[\tilde{\beta}_1 - \rho(k), \quad \tilde{\beta}_1 + \rho(k) \right],$$

$$\text{with } \rho(k) = \frac{c_\alpha}{\sqrt{n}} \hat{\sigma} + \underbrace{ck \frac{\log p}{n} \hat{\sigma}}_{\text{Account for remaining bias}}.$$

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Minimaxity and Adaptivity (Cai and G., '16)



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For $k \lesssim \frac{n}{\log p}$,

1. **Minimax** expected length of CI for β_i .
2. Possible regime to construct **adaptive** CI for β_i .

Minimaxity and Adaptivity (Cai and G., '16)



For $k \lesssim \frac{n}{\log p}$,

1. **Minimax** expected length of CI for β_i .
2. Possible regime to construct **adaptive** CI for β_i .

Adaptivity: without knowing the true sparsity k , construct CI as well as we know k .

Optimal expected length

- ▶ **Coverage**: Guaranteed coverage probability.
- ▶ **Precision**: As short as possible.

$$\Theta(k) = \left\{ \theta = (\beta, \Sigma, \sigma) : \|\beta\|_0 \leq k, \frac{1}{M_1} \leq \lambda_{\min}(\Sigma) \leq \lambda_{\max}(\Sigma) \leq M_1, 0 < \sigma \leq M_2 \right\}$$

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- ▶ For $0 < \alpha < 1$, CI has coverage for β_1 over $\Theta(k)$ if

$$\inf_{\theta \in \Theta(k)} \mathbf{P}_{\theta}(\beta_1 \in \text{CI}) \geq 1 - \alpha.$$

- ▶ For given k , the optimal length over $\Theta(k)$,

$$\mathcal{L}_{\alpha}^*(\Theta(k)) = \underbrace{\inf_{\substack{\text{CI having coverage} \\ \text{for } \beta_1 \text{ over } \Theta(k)}}}_{\text{Precision}} \sup_{\theta \in \Theta(k)} \mathbf{E}_{\theta} \mathbf{L}(\text{CI}).$$

Optimal expected length

Theorem 1 (Cai and G., '16)

For $k \leq c \min\{p^\gamma, \frac{n}{\log p}\}$ with $0 \leq \gamma < \frac{1}{2}$,

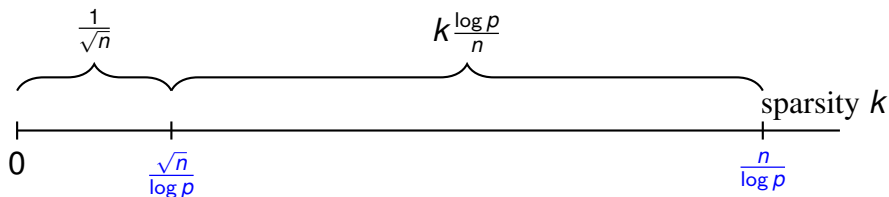
$$L_\alpha^*(\Theta(k)) \asymp \frac{1}{\sqrt{n}} + k \frac{\log p}{n}.$$

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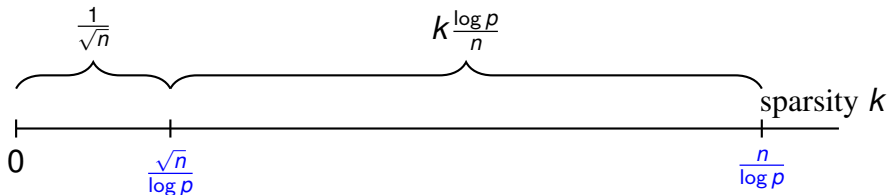


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CIs of length $\frac{1}{\sqrt{n}}$: **NO** coverage for $\frac{\sqrt{n}}{\log p} \ll k \lesssim \frac{n}{\log p}$.

Adaptive Procedures?

$$\text{Length of CI: } \rho(k) = \frac{c_\alpha}{\sqrt{n}} \hat{\sigma} + Ck \frac{\log p}{n} \hat{\sigma}.$$

Adaptivity \implies

Without knowing k , possible to construct CIs as well as known k ?

Adaptive procedures?

k (unknown true sparsity) $\leq k_u$ (known upper bound), $\Theta(k) \subset \Theta(k_u)$

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Is it possible to construct CIs for β_1

1. coverage over $\Theta(k_u)$

Adaptive procedures?

k (unknown true sparsity) $\leq k_u$ (known upper bound), $\Theta(k) \subset \Theta(k_u)$

Is it possible to construct CIs for β_1

1. coverage over $\Theta(k_u)$
2. for any $\theta \in \Theta(k)$,

$$\mathbf{E}_\theta \mathbf{L}(\text{CI}) \lesssim \frac{1}{\sqrt{n}} + k \frac{\log p}{n}?$$

Lack of adaptivity

Theorem 2(Cai and G., '16)

For any $\theta = (\beta, I, \sigma) \in \Theta(k)$ and $k \leq k_u \leq \sqrt{p}$,

$$\inf_{\substack{\text{CI having coverage} \\ \text{for } \beta_1 \text{ over } \Theta(k_u)}} \mathbb{E}_\theta L(\text{CI}) \geq c \left(\frac{1}{\sqrt{n}} + k_u \frac{\log p}{n} \right) \sigma.$$

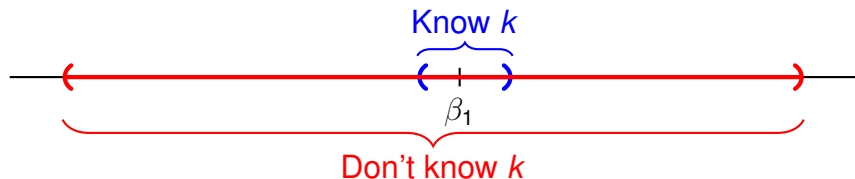
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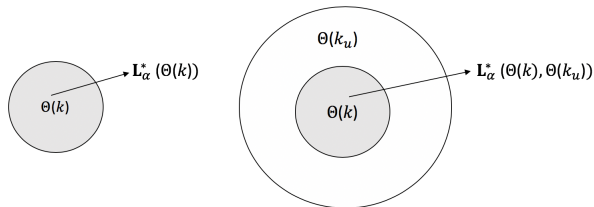
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For $\frac{\sqrt{n}}{\log p} \lesssim k_u \lesssim \frac{n}{\log p}$,

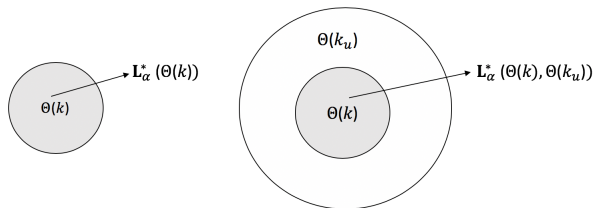


General Adaptation Benchmark



$$L_\alpha^*(\Theta(k), \Theta(k_u)) = \inf_{\text{CI having coverage for } \beta_1 \text{ over } \Theta(k_u)} \sup_{\theta \in \Theta(k)} \mathbb{E}_\theta L(\text{CI})$$

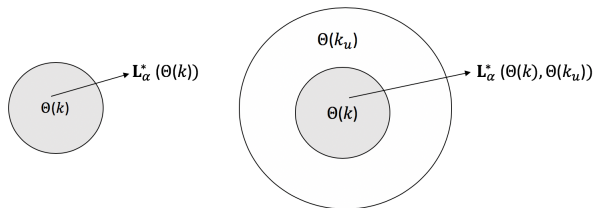
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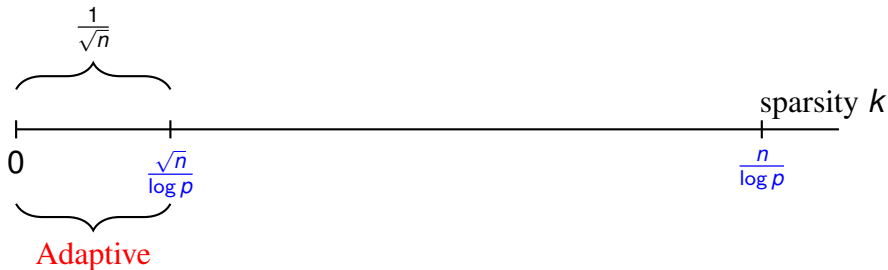
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$$L_\alpha^*(\theta(k), \Theta(k_u)) \gg L_\alpha^*(\theta(k)) \implies \text{Impossible adaptive CI.}$$

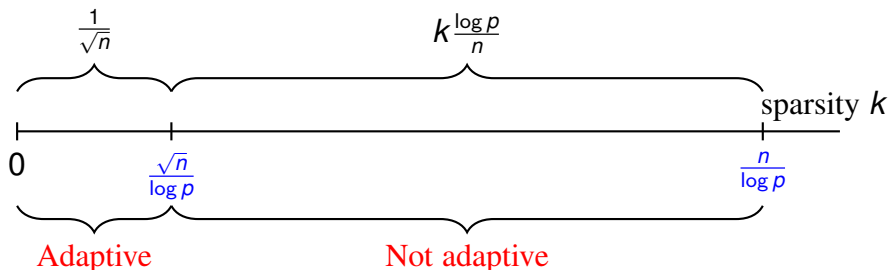
Summary of CI for β_1

- ▶ First constructed CI for β_1 over $k \lesssim \frac{n}{\log p}$.

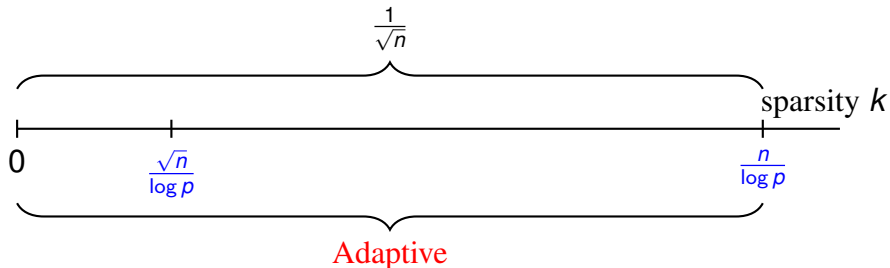


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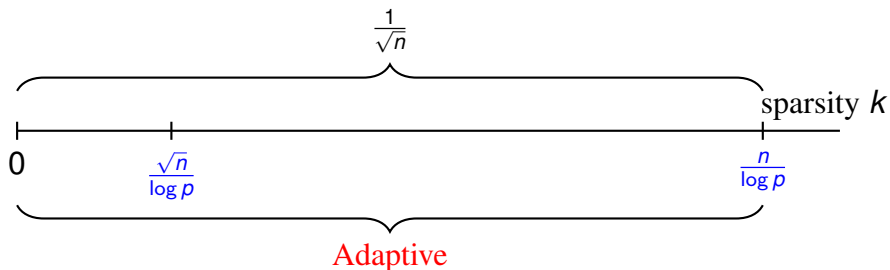


Comparison with known Σ



- ▶ CI for β_1 was constructed in Javanmard & Montanari '15.

Comparison with known Σ



- ▶ CI for β_1 was constructed in Javanmard & Montanari '15.
- ▶ Technical difference: **unknown** covariance structure between X_{i1} and X_{i2}, \dots, X_{ip} .

Four scenarios

Table: Confidence Intervals for $\eta^T \beta$

	Known Σ	Unknown Σ
Sparse Loading η (e.g., β_1)	✓	✓
Dense Loading η (e.g., $\sum_{i=1}^p \beta_i$)	?	?

Exact Loading: Sparse and Dense

We calibrate the sparsity levels as

$$k = p^\gamma, \quad k_u = p^{\gamma_u} \quad \text{for} \quad 0 \leq \gamma < \gamma_u \leq \frac{1}{2},$$

We consider exact loadings.

$$\max_{\{i:\eta_i \neq 0\}} |\eta_i| / \min_{\{i:\eta_i \neq 0\}} |\eta_i| \leq C_0,$$

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(E1) x_{new} is called *exact sparse* if $\gamma_\eta \leq \gamma$;

(E2) x_{new} is called *exact dense* if $\gamma_\eta > 2\gamma$;

CI for $\sum_{i=1}^p \beta_i$ (Cai and G., '16)

1. Centering at Lasso estimator

$$\text{CI}_{\sum \beta_i}(k) = \left[\sum_{i=1}^p \hat{\beta}_i - Ck \sqrt{\frac{\log p}{n}} \hat{\sigma}, \quad \sum_{i=1}^p \hat{\beta}_i + Ck \sqrt{\frac{\log p}{n}} \hat{\sigma} \right],$$

- ▶ **NOT** using de-biased estimator: **Inflation of variance!**

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2. $\text{CI}_{\sum \beta_i}(k)$ achieves optimal expected length $k \sqrt{\frac{\log p}{n}}$.

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▶ Without knowing k , CI must be longer than $k \sqrt{\frac{\log p}{n}}$.

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4. The information Σ is **NOT** useful.

Confidence intervals for $\eta^\top \beta$

	Known Σ	Unknown Σ
Sparse Loading η	$\frac{\ \eta\ _2}{\sqrt{n}}$	$\ \eta\ _2 \left(\frac{1}{\sqrt{n}} + \frac{k \log p}{n} \right)$
Dense Loading η	$\ \eta\ _\infty k \sqrt{\frac{\log p}{n}}$	

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Dense Loading η	$\ \eta\ _\infty k \sqrt{\frac{\log p}{n}}$	
	Known Σ	Unknown Σ
Sparse Loading η	$k \lesssim \frac{n}{\log p}$	$k \ll \frac{\sqrt{n}}{\log p}$
Dense Loading η	Impossible	

Tony Cai and Zijian Guo. *Confidence intervals for high-dimensional linear regression: Minimax rates and adaptivity*. AOS, 2017.

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The minimax results for **dense** η are pessimistic.

Let's put the minimality aside first.

A practical question: Inference procedure for $\eta^\top \beta$?

1. Works for all η .
2. Requires no knowledge of sparsity.

Cai and Guo (2017)	η is sparse
Athey, Imbens, Wager (2018)	$\ \eta\ _2$ is bounded
Zhu and Bradic (2018)	Certain sparse η

Susan Athey, Guido W Imbens, and Stefan Wager. *Approximate residual balancing: debiased inference of average treatment effects in high dimensions*. JRSSB, 2018.

Yinchu Zhu and Jelena Bradic. *Linear hypothesis testing in dense high-dimensional linear models*. JASA, 2018.

A uniform procedure for all $x_{\text{new}} \in \mathbb{R}^p$

$$\begin{aligned}\hat{u}^T \frac{1}{n} X^T (Y - X\hat{\beta}) &= \hat{u}^T \hat{\Sigma}(\beta - \hat{\beta}) + \hat{u}^T \frac{1}{n} X^T \epsilon \\ &= -\mathbf{e}_j^T (\hat{\beta} - \beta) + (\hat{\Sigma} \hat{u} - \mathbf{e}_j)^T (\beta - \hat{\beta}) + \hat{u}^T \frac{1}{n} X^T \epsilon\end{aligned}$$

Bias-corrected estimator

$$\tilde{\beta}_{1,j} = \mathbf{e}_j^T \hat{\beta} + \hat{u}^T \frac{1}{n} X^T (Y - X\hat{\beta}).$$

$$\hat{u} = \arg \min_{u \in \mathbb{R}^p} \left\{ \underbrace{u^T \hat{\Sigma} u}_{\text{Variance}} : \underbrace{\|\hat{\Sigma} u - \mathbf{e}_j\|_{\infty}}_{\text{Constrained Bias}} \leq \|\mathbf{e}_j\|_2 \lambda_1 \right\}$$

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Bias-corrected estimator

$$\widetilde{x}_{\text{new}}^\top \beta = \eta^\top \widehat{\beta} + \widehat{u}^\top \frac{1}{n} X^\top (Y - X\widehat{\beta}).$$

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Challenges for Dense Loadings

Dense η :

$$\text{Feasible Set: } \left\| \widehat{\Sigma} \mathbf{u} - \boldsymbol{\eta} \right\|_{\infty} \leq \|\boldsymbol{\eta}\|_2 \lambda_1$$

$$\|\boldsymbol{\eta}\|_2 \lambda_1 \geq \|\boldsymbol{\eta}\|_{\infty} \Rightarrow \widehat{\mathbf{u}} = \mathbf{0}!$$

Example: If $\boldsymbol{\eta}$ is decaying as $\eta_j \asymp j^{-\delta}$, then $\|\boldsymbol{\eta}\|_2 \asymp p^{\frac{1}{2}-\delta}$.

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$$\text{Feasible Set: } \left\| \widehat{\Sigma} u - \eta \right\|_{\infty} \leq \|\eta\|_2 \lambda_1$$

$$\|\eta\|_2 \lambda_1 \geq \|\eta\|_{\infty} \Rightarrow \widehat{u} = \mathbf{0}!$$

Example: If η is decaying as $\eta_j \asymp j^{-\delta}$, then $\|\eta\|_2 \asymp p^{\frac{1}{2}-\delta}$.

Bias-corrected estimator=plug-in estimator,

$$\widetilde{\eta}^{\top} \beta = \eta^{\top} \widehat{\beta} + \widehat{u}^{\top} \frac{1}{n} X^{\top} (Y - X \widehat{\beta}) = \eta^{\top} \widehat{\beta}.$$

Curse of dimensionality from dense η .

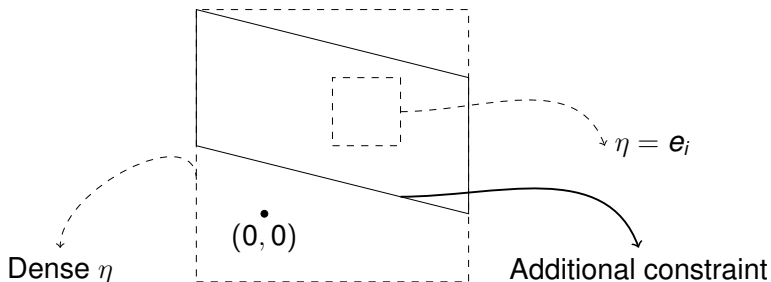
New Projection Direction

$$\begin{aligned} \hat{u} &= \arg \min_{u \in \mathbb{R}^p} u^\top \hat{\Sigma} u \\ \text{subject to } & \left\| \hat{\Sigma} u - \eta \right\|_\infty \leq \|\eta\|_2 \lambda_1 \\ & \left| \eta^\top \hat{\Sigma} u - \|\eta\|_2^2 \right| \leq \|\eta\|_2^2 \lambda_1 \end{aligned}$$

The proposed estimator for $\eta^\top \beta$ is

$$\widehat{\eta^\top \beta} = \eta^\top \hat{\beta} + \hat{u}^\top \frac{1}{n} X^\top (Y - X \hat{\beta}) \quad (1)$$

Additional Constraint and Feasible Set



- ▶ Small dashed: $\eta = e_i$.
- ▶ Large dashed: dense η **without** additional constraint.
- ▶ Solid parallelogram: dense η **with** additional constraint.

$$\left| \eta^\top \widehat{\Sigma} u - \|\eta\|_2^2 \right| \leq \|\eta\|_2^2 \lambda_1$$

Bias-Variance Tradeoff

Bias and Variance Tradeoff.

- ▶ Minimizing variance with **bias** constrained.

$$\left| (\widehat{\Sigma}\widehat{u} - \eta)^\top (\beta - \widehat{\beta}) \right| \leq \|\widehat{\Sigma}\widehat{u} - \eta\|_\infty \|\beta - \widehat{\beta}\|_1$$

- ▶ Minimizing variance with **bias** and **variance** constrained.

$$\begin{aligned} \widehat{u} &= \arg \min_{u \in \mathbb{R}^p} u^\top \widehat{\Sigma} u \\ \text{subject to } & \left\| \widehat{\Sigma} u - \eta \right\|_\infty \leq \|\eta\|_2 \lambda_1 \\ & \left| \eta^\top \widehat{\Sigma} u - \|\eta\|_2^2 \right| \leq \|\eta\|_2^2 \lambda_1 \end{aligned}$$

Enhancing Variance Lemma

Lemma 1 (Cai, Cai, G. (2018)).

Under regularity conditions, we have

$$c_0 \frac{\|\eta\|_2}{\sqrt{n}} \leq \sqrt{\frac{1}{n} \hat{u}^\top \hat{\Sigma} \hat{u}} \leq C_0 \frac{\|\eta\|_2}{\sqrt{n}}$$

- ▶ Lower bound does not hold without the additional constraint
- ▶ Additional constraint leads to a dominating variance

Theorem 2 (Cai, Cai, G. (2018)).

Under regularity conditions and $\|\beta\|_0 \leq c\sqrt{n}/\log p$, then

$$\frac{1}{\sqrt{V}} \left(\widehat{\eta^\top \beta} - \eta^\top \beta \right) \xrightarrow{d} N(0, 1) \quad (2)$$

Theorem 2 (Cai, Cai, G. (2018)).

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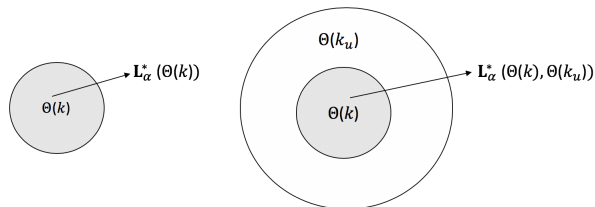
$V \asymp \frac{\|\eta\|_2^2}{\sqrt{n}}$ depends on η .

Works if $\|\beta\|_0 \leq c\sqrt{n}/\log p$.

Overview of talk

- 1 Inference for β_j : Review of De-biasing
- 2 Minimaxity and Adaptivity
- 3 Uniform Procedure for All loadings
- 4 Further Discussion on Optimality

Adaptive Optimal



$$L_\alpha^*(\theta(k), \theta(k_u)) = \inf_{\text{CI having coverage for } \beta_1 \text{ over } \theta(k_u)} \sup_{\theta \in \theta(k)} \mathbb{E}_\theta L(\text{CI})$$

Adaptive optimal: a procedure achieving $L_\alpha^*(\theta(k), \theta(k_u))$.

Review of Exact Loading

We calibrate the sparsity levels as

$$k = p^\gamma, \quad k_u = p^{\gamma_u} \quad \text{for} \quad 0 \leq \gamma < \gamma_u \leq \mathbf{1},$$

$$C_0 \leq \max_{\{i:\eta_i \neq 0\}} |\eta_i| / \min_{\{i:\eta_i \neq 0\}} |\eta_i| \leq C_0,$$

$$\|\eta\|_0 = p^{\gamma_\eta} \quad \text{for} \quad 0 \leq \gamma_\eta \leq \mathbf{1}.$$

(E1) x_{new} is called *exact sparse* if $\gamma_\eta \leq \mathbf{2}\gamma$;

(E2) x_{new} is called *exact dense* if $\gamma_\eta > \mathbf{2}\gamma$;

Possibility of Adaptive Testing

Suppose that $k \leq k_u \lesssim \frac{\sqrt{n}}{\log p}$,

	$\gamma, \gamma_u, \gamma_\eta$	$L_\alpha^*(\Theta(k))$	Rel	$L_\alpha^*(\Theta(k), \Theta(k_u))$	Adpt
(E1)	$\gamma_\eta \leq 2\gamma$	$\frac{\ \eta\ _2}{\sqrt{n}}$	\asymp	$\frac{\ \eta\ _2}{\sqrt{n}}$	Yes
(E2-a)	$\gamma < \gamma_u < \frac{1}{2}\gamma_\eta$	$\ \eta\ _\infty k \sqrt{\frac{\log p}{n}}$	\ll	$\ \eta\ _\infty k_u \sqrt{\frac{\log p}{n}}$	No
(E2-b)	$\gamma < \frac{1}{2}\gamma_\eta \leq \gamma_u$	$\ \eta\ _\infty k \sqrt{\frac{\log p}{n}}$	\ll	$\frac{\ \eta\ _2}{\sqrt{n}}$	No

- Cut-off for “dense” and “sparse” occurs at $\gamma_\eta = 2\gamma$.

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(E2-b)	$\gamma < \frac{1}{2}\gamma_\eta \leq \gamma_u$	$\ \eta\ _\infty k \sqrt{\frac{\log p}{n}}$	\ll	$\frac{\ \eta\ _2}{\sqrt{n}}$	No

- ▶ Cut-off for “dense” and “sparse” occurs at $\gamma_\eta = 2\gamma$.
- ▶ If $\gamma_u \geq \frac{1}{2}\gamma_\eta$, then the optimal test is of order $\frac{\|\eta\|_2}{\sqrt{n}}$
- ▶ In absence of accurate sparsity information, the proposed inference procedure $\eta^\top \beta$ is **adaptive optimal** for **all** exact loadings η .

Take Home Message

- ▶ The best we can aim for: $L_{\alpha}^*(\Theta(k), \Theta(k_U))$
- ▶ Dense linear functionals are harder than sparse ones.
- ▶ Uniform Procedure over all loadings.

Reference and Acknowledgement

Tony Cai and Zijian Guo. *Confidence intervals for high-dimensional linear regression: Minimax rates and adaptivity*. AOS, 2017.

Cai, T., Cai, T.T., Guo, Z. (2018). Individualized Treatment Selection: An Optimal Hypothesis Testing Approach In High-dimensional Models. Submitted.

Acknowledgement to NSF and NIH for fundings.

Thank you!

CI for $\eta^\top \beta$ (Cai and G., '16)

Fundamental difference in terms of minimaxity and adaptivity,

1. Sparse loading $\eta : \beta_i$
2. Dense loading $\eta : \sum_{i=1}^p \beta_i$

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Plug-in Lasso Estimators

$$\beta_1 : \hat{\beta}_1 - \beta_1 = \langle \mathbf{e}_1, \hat{\beta} - \beta \rangle$$

$$\eta^\top \beta : \eta^\top \hat{\beta} - \eta^\top \beta = \langle \eta, \hat{\beta} - \beta \rangle$$

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Fundamental difference in terms of minimaxity and adaptivity,

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Plug-in Lasso Estimators

$$\beta_1 : \hat{\beta}_1 - \beta_1 = \langle \mathbf{e}_1, \hat{\beta} - \beta \rangle$$

$$\eta^\top \beta : \eta^\top \hat{\beta} - \eta^\top \beta = \langle \eta, \hat{\beta} - \beta \rangle$$

- ▶ **Sparse η** : Correct the bias \Rightarrow Similar to β_1 .
- ▶ **Dense η** : NOT correct the bias \Rightarrow Inflated variance.

Balance bias and variance.

Simulation Setting

Simulation Setting with $\eta^\top \beta = 1.08$

- ▶ $p = 501, n = n_2 = n$
- ▶ $\beta_{1,0} = -0.1, \beta_{1,j} = 0.4(j - 1)$ for $1 \leq j \leq 10$
- ▶ $\beta_{2,0} = -0.5, \beta_{2,j} = 0.2(j - 1)$ for $1 \leq j \leq 5$
- ▶ $x_{new,j} \sim N(0, 1)$ for $1 \leq i \leq 10$ and
 $x_{new,j} \sim 0.2 * N(0, 1)$ for $i \geq 11$

- ▶ **Adaptive optimality**: If the sparsity is unknown, what is the optimal length of CI?

The parameter space

$$\Theta(\mathbf{s}) = \left\{ \boldsymbol{\theta} = \begin{pmatrix} \boldsymbol{\beta}, \boldsymbol{\Sigma}_1, \sigma_1 \\ \boldsymbol{\beta}_2, \boldsymbol{\Sigma}_2, \sigma_2 \end{pmatrix} : \|\boldsymbol{\beta}\|_0 \leq \mathbf{s}, 0 < \sigma_k \leq M_0, \lambda_{\min}(\boldsymbol{\Sigma}_k) \geq c_0, \text{ for } k = 1, 2 \right\},$$

For a test ϕ , its size is

$$\alpha(\mathbf{s}, \phi) = \sup_{\boldsymbol{\theta} \in \mathcal{H}_0(\mathbf{s})} \mathbb{E}_{\boldsymbol{\theta}} \phi. \quad (3)$$

with

$$\mathcal{H}_0(\mathbf{s}) = \{ \boldsymbol{\theta} \in \Theta(\mathbf{s}) : \boldsymbol{\eta}^\top (\boldsymbol{\beta} - \boldsymbol{\beta}_2) \leq 0 \}$$

The local alternative parameter space

$$\mathcal{H}_1(\mathbf{s}, \tau) = \{\boldsymbol{\theta} \in \Theta(\mathbf{s}) : \mathbf{x}_{\text{new}}^\top (\boldsymbol{\beta} - \boldsymbol{\beta}_2) = \tau > 0\}.$$

The power of ϕ over $\mathcal{H}_1(\mathbf{s}, \tau)$ is defined as

$$\omega(\mathbf{s}, \tau, \phi) = \inf_{\boldsymbol{\theta} \in \mathcal{H}_1(\mathbf{s}, \tau)} \mathbb{E}_{\boldsymbol{\theta}} \phi. \quad (4)$$

Optimality: identify the **smallest** τ

- ▶ The size is controlled over $\mathcal{H}_0(\mathbf{s})$;
- ▶ The corresponding power over $\mathcal{H}_1(\mathbf{s}, \tau)$ is large

Minimax Detection Boundary

Minimax detection boundary is defined as

$$\tau_{\text{mini}}(k, \mathbf{x}_{\text{new}}) = \arg \min_{\tau} \left\{ \tau : \sup_{\phi: \alpha(\mathbf{s}, \phi) \leq \alpha} \omega(\mathbf{s}, \tau, \phi) \geq 1 - \eta \right\}.$$

A test ϕ is minimax optimal if

$$\alpha(\mathbf{s}, \phi) \leq \alpha \quad \text{and} \quad \omega(\mathbf{s}, \phi, \tau) \geq 1 - \eta \quad \text{for} \quad \tau \asymp \tau_{\text{mini}}(k, \mathbf{x}_{\text{new}})$$

Minimax assumes \mathbf{s} is known.

Capture the optimality for unknown sparsity level?

We consider two sparsity levels, $k \leq k_u$.

- ▶ k denotes the true sparsity level;
- ▶ k_u denotes an upper bound for the sparsity level.

The size is uniformly controlled over $\mathcal{H}_0(k_u)$,

$$\alpha(k_u, \phi) = \sup_{\theta \in \mathcal{H}_0(k_u)} \mathbb{E}_\theta \phi \leq \alpha. \quad (5)$$

Adaptive Detection Boundary

The adaptive detection boundary $\tau_{\text{adap}}(k_U, k, x_{\text{new}})$

$$\tau_{\text{adap}}(k_U, k, x_{\text{new}}) = \arg \min_{\tau} \left\{ \tau : \sup_{\phi: \alpha(k_U, \phi) \leq \alpha} \omega(k, \tau, \phi) \geq 1 - \eta \right\}.$$

A test ϕ is adaptive optimal if

$$\alpha(k_U, \phi) \leq \alpha \quad \text{and} \quad \omega(k, \tau, \phi) \geq 1 - \eta \quad \text{for} \quad \tau \asymp \tau_{\text{adap}}(k_U, k, x_{\text{new}})$$

An adaptive optimal test would be the best that we can aim for if there is lack of accurate information on sparsity.

Adaptive Hypothesis Testing

- ▶ If $\tau_{\text{mini}}(k, x_{\text{new}}) \asymp \tau_{\text{adap}}(k_U, k, x_{\text{new}})$, the testing problem is adaptive.
- ▶ If $\tau_{\text{mini}}(k, x_{\text{new}}) \ll \tau_{\text{adap}}(k_U, k, x_{\text{new}})$, the testing problem is NOT adaptive.

Other methods

1. HITS
2. Plug-in scaled Lasso: $\mathbf{x}_{\text{new}}^T (\hat{\beta} - \hat{\beta}_2)$
3. Plug-in debiased Lasso: $\mathbf{x}_{\text{new}}^T (\tilde{\beta} - \tilde{\beta}_2)$

Numerical Comparison

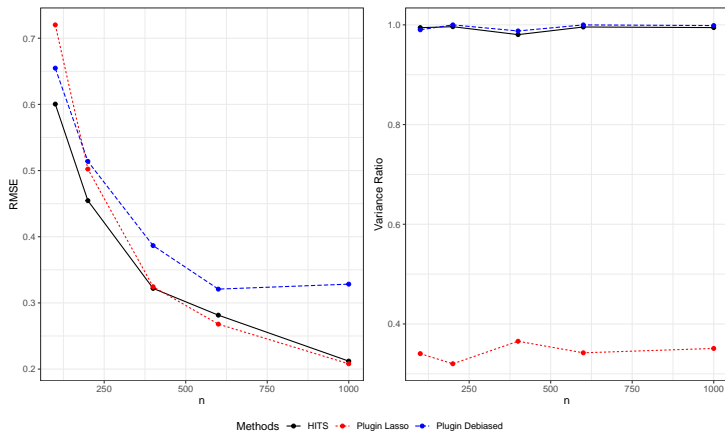
Other methods

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Computation comparison

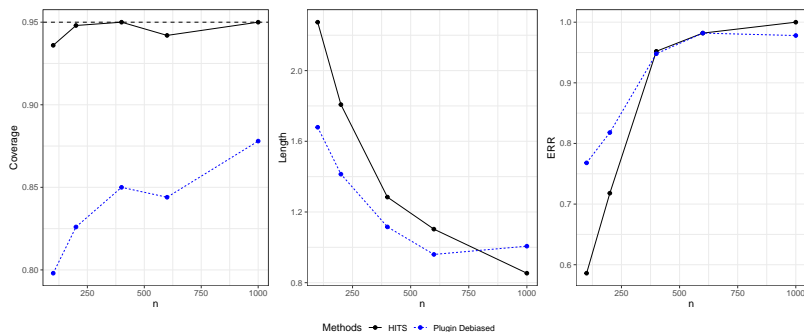
1. HITS: 4 Lasso
2. Plug-in scaled Lasso: 2 Lasso
3. Plug-in debiased Lasso: 1,004 Lasso ($2p + 2$)

RMSE



- ▶ Plug-in Lasso: hard to do inference
- ▶ HITS has smaller RMSE than Plug-in Debiased

ITE and CI

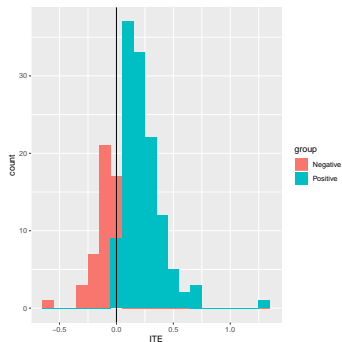


- ▶ Better coverage
- ▶ Computationally more efficient
- ▶ Comparable length and ERR

Rheumatoid Arthritis (RA)

- ▶ Treatment 1: methotraxate+ anti-TNF (92 patients)
- ▶ Treatment 2: methotraxate (91 patients)
- ▶ Outcome – $\log(\text{CRP})$
Higher value of $Y \rightarrow$ Better treatment response.
- ▶ 171 Predictors, including Clinical measurement, EHR and SNP

Real Data Analysis

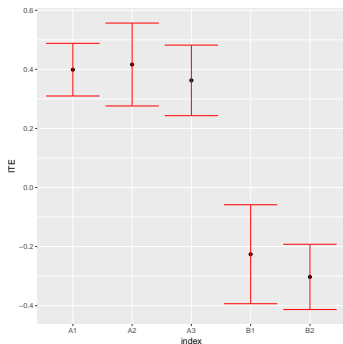


- ▶ About 72% benefit from the combination therapy.

Real Data Analysis

Patients	rs12506688	SLE mention	rs2843401	rs8043085	...
A	=0	≥ 1	= 0	> 0	...
B	>0	No	>0	=0	...

(SLE= Systemic Lupus Erythematosus)



The treatment effect is **heterogeneous** across patients.