## How good is the de-biased Lasso?

asymptotic efficiency:
for the de-biased Lasso to "work" we require

- sparsity: $s_{0}=o(\sqrt{n} / \log (p))$
this cannot be beaten in a minimax sense
- compatibility condition for $X$
for optimality in terms of the lowest possible asymptotic variance achieving the "Cramer-Rao" lower bound:
- require in addition that $X^{(j)}$ versus $X^{(-j)}$ is sparse: $s_{j} \ll n / \log (p)$
then... skipping details, the de-biased Lasso achieves (see Theorem 10.2):

$$
\sqrt{n}\left(\hat{b}_{j}-\beta_{j}^{0}\right) \Longrightarrow \mathcal{N}(0,
$$

$$
\underbrace{\sigma^{2} \Theta_{j j}}
$$

Cramer-Rao lower bound
$\Theta=\Sigma_{X}^{-1}=\operatorname{Cov}(X)^{-1} \leadsto$ as for OLS in low dimensions!

## Empirical results

R-software hdi

> de-sparsified Lasso

black: confidence interval covered the true coefficient red: confidence interval failed to cover

## Stability Selection (Ch. 10 in Bühlmann and van de Geer (2011))



Stability selection

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[Read before The Royal Statistical Society at a meeting organized by the Research Section on Wednesday, February 3rd, 2010, Professor D. M. Titterington in the Chair]
has been developed before one knew about the de-biased/de-sparsified Lasso
even with new tools such as the de-biased/de-sparsified Lasso: estimation of discrete structures ("relevant" variables in a generalized linear model; edges in a graphical model) is notoriously difficult e.g. choice of tuning parameters...?

## The generic setup

i.i.d. data $Z_{1}, \ldots, Z_{n}$
main example: $Z_{i}=\left(X_{i}, Y_{i}\right)$ from regression or classification
$\hat{S}_{\lambda}$ is a "feature selection" method/algorithm among $\{1, \ldots, p\}$ features
can we assign "relevance" to the selected features in $\hat{S}_{\lambda}$ ?
a "natural" approach: resampling!
here: use subsampling:

- ${ }^{*}$ random sub-sample of size $\lfloor n / 2\rfloor$ of $\{1, \ldots, n\}$
- compute $\hat{S}_{\lambda}\left(I^{*}\right)$
- repeat $B$ times to obtain $\hat{S}_{\lambda}\left(I^{* 1}\right), \ldots, \hat{S}_{\lambda}\left(I^{* B}\right)$
- consider the "overlap" among $\hat{S}_{\lambda}\left(I^{* 1}\right), \ldots, \hat{S}_{\lambda}\left(I^{* B}\right)$
regarding the latter, for example:

$$
\begin{array}{ll} 
& \hat{\Pi}_{K}(\lambda)=\mathbb{P}^{*}\left[K \subseteq \hat{S}_{\lambda}\left(I^{*}\right)\right] \approx B^{-1} \sum_{b=1}^{B} I\left(K \subseteq \hat{S}_{\lambda}\left(I^{* b}\right)\right) \\
\text { e.g. } & \hat{\Pi}_{j}(\lambda)(j \in\{1, \ldots, p\})
\end{array}
$$

the probability $\mathbb{P}^{*}$ is with respect to subsampling: a sum over $\binom{n}{m}$ terms, $m=\lfloor n / 2\rfloor$, i.e., all possible subsampling combinations
$\sim$ it is approximated by $B(\approx 100)$ times random subsampling

## The stability regularization path

Riboflavin data: $n=115, p=4088$
$Y$ : log-production rat of riboflavin by bacillus subtilis
$X$ : gene expressions of bacillus subtilis
all $X$-variables permuted except 6 "a-priori relevant" genes

left: Lasso regularization path (red: the 6 non-permuted "relevant" genes) right: Stability path with $\hat{\Pi}_{j}$ on y-axis (red: the 6 non-permuted "relevant" variables stick out much more clearly from the noise covariates)

## What is a good truncation value (for $\hat{\Pi}$ )?

aim: choose $\pi_{\text {thr }}$ such that

$$
\hat{S}_{\text {stable }}=\left\{j ; \max _{\lambda \in \Lambda} \hat{\Pi}_{j}(\lambda) \geq \pi_{\text {thr }}\right\}
$$

has not too many false positives
$\Lambda$ can be a singleton or a range of values
as a measure for type I error control (against false positives):

$$
V=\text { number of false positives }=\left|\hat{S}_{\text {stable }} \cap S_{0}^{C}\right|
$$

where $S_{0}$ is the set of the true relevant features, e.g.:

- active variables in regression
- true edges in a graphical model
"the miracle":
a simple formula connecting $\pi_{\text {thr }}$ with $\mathbb{E}[V]$
consider a setting with $p$ possible features
$\hat{S}(\lambda)$ is a feature selection algorithm
$\hat{S}_{\Lambda}=\cup_{\lambda \in \Lambda} \hat{S}(\lambda)$
$q_{\Lambda}=\mathbb{E}[|\hat{S}_{\Lambda}(\underbrace{I}_{\text {random subsample }})|]$

Theorem 10.1

## Assume:

- exchangeability condition:

$$
\left.\{1(j \in \hat{S}(\lambda)\}), j \in S_{0}^{c}\right\} \text { is exchangeable for all } \lambda \in \Lambda
$$

- $\hat{S}$ is not worse than random guessing

$$
\frac{\left.\mathbb{E}\left|S_{0} \cap \hat{S}_{\Lambda}\right|\right)}{\mathbb{E}\left(\left|S_{0}^{c} \cap \hat{S}_{\Lambda}\right|\right)} \geq \frac{\left|S_{0}\right|}{\left|S_{0}^{c}\right|}
$$

Then, for $\pi_{\text {thr }} \in(1 / 2,1)$ :

$$
\mathbb{E}[V] \leq \frac{1}{2 \pi_{\mathrm{thr}}-1} \frac{q_{\Lambda}^{2}}{p}
$$

suppose we know $q_{\wedge}$ (see later) strategy: specify $\mathbb{E}[V]=v_{0} \quad($ e.g. $=5)$
$\leadsto$ for $\pi_{\mathrm{thr}}:=\frac{1}{2}+\frac{q_{1}^{2}}{2 p v_{0}}: \mathbb{E}[V] \leq v_{0}$
example: regression model with $p=1000$ variables
$\hat{S}_{\lambda}=$ the top 10 variables from Lasso (e.g. the different $\lambda$ from Lasso by CV and choose the top 10 variables with the largest absolute values of the corresponding estimated coefficients; if less than 10 variables are selected, take the selected variables) the value $\lambda$ corresponds to the "top 10 "; $\Lambda$ is a singleton
we then know that $q_{\Lambda}=\mathbb{E}\left[\left|\hat{S}_{\lambda}(I)\right|\right] \leq 10$
For $\mathbb{E}[V]=v_{0}:=5$ we then obtain

$$
\pi_{\mathrm{thr}}=\frac{1}{2}+\frac{q_{\Lambda}^{2}}{2 p v_{0}}=0.5+\frac{10^{2}}{2 * 1000 * 5}=0.51
$$

there is room to play around recommendation: take $|\hat{S}(\lambda)|$ rather large and stability selection will reduce again to reasonable size
when taking the "top 30", the threshold becomes

$$
\pi_{\mathrm{thr}}=\frac{1}{2}+\frac{q_{\Lambda}^{2}}{2 p v_{0}}=0.5+\frac{30^{2}}{2 * 1000 * 5}=0.59
$$

adding noise...
can always add (e.g. independent $\mathcal{N}(0,1))$ noise covariates enlarged dimension $p_{\text {enlarged }}$
error control becomes better (for the same threshold)

$$
\mathbb{E}[V] \leq \frac{1}{2 \pi_{\mathrm{thr}}-1} \frac{q_{\Lambda}^{2}}{p_{\text {enlarged }}}
$$

this sometimes helps indeed in practice - at the cost of loss in power

## The assumptions for mathematical guarantees

not worse than random guessing

$$
\frac{\left.\mathbb{E}\left|S_{0} \cap \hat{S}_{\Lambda}\right|\right)}{\mathbb{E}\left(\left|S_{0}^{c} \cap \hat{S}_{\Lambda}\right|\right)} \geq \frac{\left|S_{0}\right|}{\left|S_{0}^{c}\right|}
$$

perhaps hard to check but very reasonable...
for Lasso in linear models it holds assuming the variable screening property asymptotically: if beta-min and compatibility condition hold
exchangeability condition $\left.\{1(j \in \hat{S}(\lambda)\}), j \in S_{0}^{c}\right\}$ is exchangeable for all $\lambda \in \Lambda$
a restrictive assumption but the theorem is very general, for any algorithm $\hat{S}$
a very special case where exchangeability condition holds: random equi-correlation design linear model

$$
Y=X \beta^{0}+\varepsilon, \operatorname{Cov}(X)_{i, j} \equiv \rho(i \neq j), \operatorname{Var}\left(X_{j}\right) \equiv 1 \forall j
$$

distributions of ( $\left.Y, X^{\left(S_{0}\right)},\left\{X^{(j)} ; j \in S_{0}^{C}\right\}\right)$ and of
$\left(Y, X^{\left(S_{0}\right)},\left\{X^{(\pi(j))} ; j \in S_{0}^{c}\right\}\right)$ are the same for any permutation
$\pi: S_{0}^{C} \rightarrow S_{0}^{C}$

- distribution of $X^{\left(S_{0}\right)},\left\{X^{(\pi(j))} ; j \in S_{0}^{c}\right\}$ is the same for all $\pi$ (because of equi-correlation)
- distribution of $Y \mid X^{\left(S_{0}\right)},\left\{X^{(\pi(j))} ; j \in S_{0}^{c}\right\}$ is the same for all $\pi$ (because it depends only on $X^{\left(S_{0}\right)}$ )
- therefore: distribution of $Y, X^{\left(S_{0}\right)},\left\{X^{(\pi(j))} ; j \in S_{0}^{c}\right\}$ is the same for all $\pi$ and hence exchangeability condition holds for any (measurable) function $\hat{S}(\lambda)$

An illustration for graphical modeling
$p=160$ gene expressions, $n=115$
GLasso estimator, selecting among the $\binom{p}{2}=12^{\prime} 720$ features stability selection with $\mathbb{E}[V] \leq v_{0}=30$

with permutation (empty graph is correct)


Stability Selection is extremely easy to use and super-generic
the sufficient assumptions (far from necessary) for mathematical guarantees are restrictive but the method seems to work very well in practice

## P-values based on multi sample splitting

(Ch. 11 in Bühlmann and van de Geer (2011))

Stability Selection

- uses subsampling many times - a good thing!
- provides control of the expected number of false positives rather than e.g. the familywise error rate $\leadsto$ we will "address" this with
multi sample splitting and aggregation of P -values
familywise error rate (FWER):
FWER $=\mathbb{P}[V>0], V$ number of false positives


## Fixed design linear model

$$
Y=X \beta^{0}+\varepsilon
$$

instead of de-biased/de-sparsified method, consider the "older" technique (which is not statistically optimal but more generic and more in the spirit of stability selection)
split the sample into two parts $I_{1}$ and $I_{2}$ of equal size $\lfloor n / 2\rfloor$

- use (e.g.) Lasso to select variables based on $I_{1}: \hat{S}\left(I_{1}\right)$
- perform low-dimensional statistical inference on $I_{2}$ based on data $\left(x_{l_{2}}^{\left(\hat{S}\left(l_{1}\right)\right)}, Y_{l_{2}}\right)$; for example using the $t$-test for single coefficients $\beta_{j}^{0}$ (if $j \notin \hat{S}\left(I_{1}\right)$, assign the p -value 1 to the hypothesis $H_{0, j}: \beta_{j}^{0}=0$ (,
due to independence of $I_{1}$ and $I_{2}$, this is a "valid" strategy (see later)
validity of the (single) data splitting procedure consider testing $H_{0, j}: \beta_{j}^{0}=0$ versus $H_{A, j}: \beta_{j}^{0} \neq 0$ assume Gaussian errors for the fixed design linear model : thus, use the $t$-test on the second half of the sample $I_{2}$ to get a $p$-value

$$
\text { Praw,j from } t \text {-test based on } X_{I_{2}, \hat{S}\left(I_{1}\right)}, Y_{l_{2}}
$$

$P_{\text {raw }, j}$ is a valid p -value (controlling type I error) for testing $H_{0, j}$ if $\hat{S}\left(I_{1}\right) \supseteq S_{0}$ (i.e., the screening property holds)
if the screening property does not hold: $P_{\text {raw }, j}$ is still valid for $H_{0, j}(M): \beta_{j}(M)=0$ where $M=\hat{S}\left(I_{1}\right)$ is a selected sub-model and $\beta(M)=\left(X_{M}^{T} X_{M}\right)^{-1} X_{M}^{T} \mathbb{E}[Y]$
a p-value lottery depending on the random split of the data motif regression $n=287, p=195$

$\leadsto$ should aggregate/average over multiple splits!

## Multiple testing and aggregation of $p$-values

the issue of multiple testing:

$$
\tilde{P}_{j}= \begin{cases}P_{\text {raw }, j} \text { based on } \mathbf{Y}_{l_{2}}, \mathbf{X}_{l_{2}, \hat{S}\left(l_{1}\right)} & , \text { if } j \in \hat{S}\left(I_{1}\right), \\ 1 & \text {, if } j \notin \hat{S}\left(l_{1}\right)\end{cases}
$$

thus, we can have at most $\left|\hat{S}\left(I_{1}\right)\right|$ false positives $\leadsto$ can correct with Bonferroni with factor $\left|\hat{S}\left(I_{1}\right)\right|$ (instead of factor $p$ ) to control the familywise error rate

$$
\tilde{P}_{\text {corr }, j}=\min \left(\tilde{P}_{j} \cdot\left|\hat{S}\left(I_{1}\right)\right|, 1\right)(j=1, \ldots, p)
$$

decision rule: reject $H_{0, j}$ if and only if $\tilde{P}_{\text {corr }, j} \leq \alpha$
$\leadsto \mathrm{FWER} \leq \alpha$
the issue with P -value aggregation:
if we run sample splitting $B$ times, we obtain P -values

$$
\tilde{P}_{\mathrm{corr}, j}^{[1]}, \ldots, \tilde{P}_{\mathrm{corr}, j}^{[B]}
$$

how to aggregate these dependent $p$-values to a single one?
for $\gamma \in(0,1)$ define

$$
Q_{j}(\gamma)=\min \left\{q_{\gamma}\left(\left\{\tilde{P}_{\mathrm{corr}, j}^{[b]} / \gamma ; b=1, \ldots, B\right\}\right), 1\right\}
$$

where $q_{\gamma}(\cdot)$ is the (empirical) $\gamma$-quantile function

Proposition 11.1 (Bühlmann and van de Geer, 2011)
For any $\gamma \in(0,1), Q_{j}(\gamma)$ are P-values which control the FWER
example: $\gamma=1 / 2$
aggregate the p -values with the sample median and multiply by the factor 2
avoid choosing $\gamma$ :
$P_{j}=\min \{\underbrace{\left(1-\log \gamma_{\text {min }}\right)}_{\text {price to optimize over } \gamma} \inf _{\gamma \in\left(\gamma_{\text {min }}, 1\right)} Q_{j}(\gamma), 1\}(j=1, \ldots, p)$.

Theorem 11.1 (Bühlmann and van de Geer (2011))
For any $\gamma_{\min } \in(0,1), P_{j}$ are P-values which control the FWER
the entire framework for p -value aggregation holds whenever the single p -values are valid $\left(\mathbb{P}\left[P_{\text {raw }, j} \leq \alpha\right] \leq \alpha\right.$ under $\left.H_{0, j}\right)$ has nothing to do with high-dimensional regression and sample splitting

$$
n=100, p=100
$$





## $n=100, p=1000$




one can also adapt the method to control the False Discovery Rate (FDR)
multi sample splitting and $p$-value construction:

- is very generic, also for "any other" model class
- is powerful in terms of multiple testing correction: we only correct for multiplicity from $\left|\hat{S}\left(I_{1}\right)\right|$ variables
- it relies in theory on the screening property of the selector in practice: it is a quite competitive method!
- Schultheiss et al. (2021): can improve multi sample splitting by multi carve methods, based on "technology" from selected inference

