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COMPARISON STUDY OF VARIABLE SELECTION PROCEDURES IN HIGH-DIMENSIONAL GAUSSIAN LINEAR REGRESSION

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ABSTRACT

The size of the data sets is increasing, providing a large number of variables to describe a phenomenon. Assuming that the relationship between the active variables and the response variable is linear, the high-dimensional Gaussian linear regression provides a relevant framework to identify active variables related to the response variable. Many methods exist, and in this article, we focus on methods based on regularization paths. We perform a comparison study by considering different simulation settings and evaluate the performance of the methods. Our results show that the ability to discriminate between active and inactive variables is important and difficult when the data are not normally distributed and there is a dependency structure between variables. We observe that LARS combined with Elastic-net often gives the best performances. Finally, even if no method is optimal, it was possible to group the methods into groups according to their performance and the characteristics of the dataset.

Keywords V

variable selection; Gaussian linear regression; High-dimensional; Regularization path; Comparison study

1 Introduction

Recent scientific advances allow us to have access to large-scale data: the size of the data sets is exploding, as well as the complexity of each of them. In a statistical point of view, the number of parameters to estimate explodes and reduction of dimension is required to select only relevant variables and summarize the redundant information for a given model. In this review, we focus on the variable selection procedures in high-dimensional linear Gaussian regression models. The considered dataset with a number of variables p close to or slightly higher than the number of observations n is a real challenge since it hampers the use of the traditional estimation methods. A regularization of the cost function is required so that only a subset of variables is selected to explain the response variable.

In most reviews on variable selection in high-dimensional Gaussian linear regression, a focus is done on the construction of the regularization path. It is based on the minimization of a cost function penalized by a regularization function and provides an order on variables. [1] provides a meticulous theoretical analysis of the ℓ_1 regularization function. In particular, for a given number of active variables, the author discusses the choice of the number of observations to ensure asymptotic properties to recover these active variables. [2] compared several regularization functions in a simulation study by using semi-real datasets. In their simulation design, they considered several numbers of observations, numbers of variables and numbers of active variables. They also modified the signal-to-noise ratio and considered two scenarios of variable correlations. The results of the different regularization functions are inspected with ROC curves and partial ROC curves when $0.5n$ and $0.9n$ variables are selected. [3] compared a large set of regularization functions with a simulation design similar to [2]. They evaluated both prediction and variable identification but the main difference with our investigations is that the only considered model selection procedure applied from the regularization path is the cross-validation one. Finally some reviews considered different contexts. [4] were interested in robust variable selection strategies when heavy-tailed errors and outliers in response variables exist. They discussed the different steps from the modification of the least squares function to the choice of the parameters for the model selection through a presentation of algorithms accounting for outliers. [5] considered a variety of models from survival models to generalized linear models, frequently used in biomedical research. [6] considered a wide range of model structures (linear, grouped, additive, partially linear and non-parametric) and discussed three main categories of algorithms for the variable selection.

Our review distinguishes itself from the previous ones since we propose an evaluation of both construction of regularization paths and choice of the final selected variables. This leads to 33 combinations. Moreover, for model selection procedure, we add in this review non-asymptotic methods which are generally not considered. To construct the regularization path, we test two regularization functions (Lasso [7] and Elastic-Net [8]) combined with two algorithms (LARS [9] and gradient descent algorithm [10]). Each regularization path provides a collection of variable subsets. To choose one of them, we compare model selection and variable identification approaches. On the one hand, the model selection uses penalization criteria of the least squares (eBIC [11], data-driven calibration strategies [12, 13, 14, 15] and LinSelect [16, 17]). On the other hand, the variable identification methods (ESCV [18], Bolasso [19], Stability Selection [20], Tigress [21] and the knockoffs method [22]) use sampling strategies to stabilize the selected variable subset while limiting the selection of non-active variables. Methods based on multiple testing procedures [23] and Bayesian approaches are not included in this review. We refer the readers to [24] for an empirical comparison of frequentist and Bayesian points of view. Lastly, we assume no prior knowledge between interactions, spatial localization and chronological information and refer to [25, 26] for such approaches.

After a description of the methods and some of their theoretical properties, we compare them in a simulation study by considering three settings. In the first one, the variables are independent and drawn from a Gaussian distribution. It allows a method comparison in the theoretical framework used to develop them. In the second setting, two structures of the correlation between variables are considered to evaluate how dependencies usually observed affect the methods. Observations are generated according to a Gaussian linear model, the most favorable case where assumptions broadly hold. Finally, the third setting mimics the biological complexity of transcription factor regulations. Observations are generated using the *FRANK* algorithm [27].

In these three settings, performances of the method are evaluated for their prediction performance and for their ability to identify the active variables. To discriminate active variables to the others, we use the pROC-AUC metric. We evaluate the performance of prediction by using the mean squared errors (MSE) and characterize the quality of the selected subset of variables through the recall, the specificity, and the false discovery rate (FDR). Our results show that the ability to discriminate between active and inactive variables is important and difficult when the data are not normally distributed and there is a dependency structure between variables. We observe that LARS combined with Elastic-net often gives the best performances. Finally, as [2, 3], we notice that no method is optimal, but it was possible to group the methods into groups according to their performance and the characteristics of the dataset.

2 Methods

2.1 Statistical framework

For the sequel, the norms $|\cdot|_0$, $|\cdot|_1$ and $\|\cdot\|$ on \mathbb{R}^q are defined for a vector $\beta \in \mathbb{R}^q$ by

$$|\beta|_0 = \sum_{j=1}^q \mathbb{1}_{\{\beta_j \neq 0\}}; \quad |\beta|_1 = \sum_{j=1}^q |\beta_j|; \quad \|\beta\| = \sqrt{\sum_{j=1}^q \beta_j^2}.$$

We consider a Gaussian linear regression model where the response variable Y is explained by a linear combination of p variables $X = (X_1, \dots, X_p)$:

$$Y = X\beta^* + \varepsilon.$$

The parameter vector β^* belongs to \mathbb{R}^p and ε follows a centered Gaussian distribution with an unknown variance denoted σ^2 . To estimate them, independent observations are available for $i \in \{1, \dots, n\}$, $y_i \in \mathbb{R}$ and $(x_{i1}, \dots, x_{ip}) \in \mathbb{R}^p$.

We consider the high-dimensional framework with $p \sim n$ or $p \gg n$, preventing the traditional least squares estimation. In this context, we assume that only a small number of the variables explains the response variable. These variables are associated to a non-zero coefficient in β^* and are named active variables. Under this sparsity assumption, the estimation criterion becomes for $t > 0$:

$$\min_{\beta \in \mathbb{R}^p: |\beta|_0 \leq t} \|Y - X\beta\|^2,$$

and its associated Lagrangian form is for $\lambda > 0$:

$$\min_{\beta \in \mathbb{R}^p} \{ \|Y - X\beta\|^2 + \lambda |\beta|_0 \}. \quad (1)$$

The proof of the equivalence and the link between t and λ are provided in [7]. Determining the hyperparameter λ is one of the major issues and the challenge lies in its calibration to adjust a trade-off between sparsity and good adjustment. A large value of λ provides a small subset of variables, but it may correspond to a fit far from the response variable. A small value of λ corresponds to a fit close to the response variable, but it may provide a large subset of variables. Moreover, the criterion being non-convex, the existence and the uniqueness of the solution are not guaranteed. So, as presented in [5], Equation (1) is replaced with the optimization problem:

$$\min_{\beta \in \mathbb{R}^p} \{ \|Y - X\beta\|^2 + \lambda F(\beta) \}, \quad (2)$$

where F is a continuous and convex function satisfying the existence of a minimum for any λ .

2.2 Regularization functions

Here we present the most commonly used regularization functions. The first one is the ℓ_1 regularization, named Lasso [7] with

$$F(\beta) = |\beta|_1.$$

If λ is well chosen, it provides a consistent estimator of β^* . This procedure achieves the best trade-off between regularity (convexity, reasonable computational solution) and sparsity for independent variables. However, when some variables are correlated, Lasso tends to select randomly only one of them rather than selecting none or all of them. A solution to this problem is the Adaptive Lasso procedure where each variable is weighted with respect to an initial estimator [28].

Another well-known regularization function is the Ridge regularization [29] where $F(\beta) = \|\beta\|^2$. In addition to taking variable dependencies into account, Ridge provides a strictly convex and derivable optimization problem with an explicit estimator of β^* . However, this estimator is not sparse. To combine sparsity and correlated variables, [8] proposed the Elastic-Net regularization, where α controls the trade-off

$$F(\beta) = (1 - \alpha)|\beta|_1 + \alpha\|\beta\|^2.$$

When prior knowledge on variable dependencies is available, there exist other regularization functions, not considered here: the Group Lasso [30], Overlap Group Lasso [31], Hierarchical Group Lasso [32], double sparse Lasso [33] and fused Lasso [34].

2.3 Regularization path construction

The optimization problem (2) has generally no explicit solution and requires a computational approach. A first algorithm is LARS [9] where one variable is added at each step and each step corresponds to a value of λ . Briefly speaking, the first subset contains the variable X_j which has the largest absolute correlation with Y . The second subset contains exactly two variables: X_j and the variable which is the most correlated with the residuals of the regression of Y on X_j . LARS provides an exact solution of the optimization problem with nested subsets, an important property for theoretical considerations.

A second algorithm is based on the gradient descent method [10]. This algorithm constructs a regular grid Λ of a given size by starting with the largest λ corresponding to the first nonempty variable subset. Then, a variable subset is obtained for each λ of this grid by solving (2) with the cyclic coordinate descent method. In contrast to LARS, the

gradient descent method provides a proxy of the optimization problem with independent solutions along the grid and possibly several models of the same dimension.

From the regularization function and the algorithm, we obtain a collection of subsets $(m_\lambda)_{\lambda \in \Lambda}$. Each m_λ is associated with an estimator of β^* , however this estimator being known to be biased [35], it is commonly replaced with the least-squares estimator calculated on the subset m_λ and is denoted $\hat{\beta}_\lambda$ [36]. The number of non-zero coefficients of $\hat{\beta}_\lambda$ or in an equivalent manner, the number of variables in m_λ is denoted D_λ .

2.4 Subset selection

To select the best subset $m_{\hat{\lambda}}$, model selection approaches consist of minimizing a penalized loss function in $\lambda \in \Lambda$:

$$\gamma(m_\lambda) + \text{pen}(n, p, D_\lambda). \quad (3)$$

The loss function $\gamma(m_\lambda)$, quantifying the quality of the model fit, is either the least-squares function $\|Y - X\hat{\beta}_\lambda\|^2$ or the deviance $-2 \log(L(Y, X; \hat{\beta}_\lambda, \hat{\sigma}_\lambda^2))$, where L is the likelihood function calculated with $\hat{\beta}_\lambda$ and $\hat{\sigma}_\lambda^2$, the empirical estimators associated to m_λ . The penalty function $\text{pen}(n, p, D_\lambda)$ accounts for the model complexity and the characteristics of the sample.

Asymptotic criteria The first criteria are asymptotic: their properties are verified when the sample size n tends to infinity. In this review, we focus on the more recent asymptotic criterion, called eBIC [11]. Let δ is a value in $[0, 1]$, it is used to get a consistent estimator by penalizing the deviance by:

$$\text{pen}_{\text{eBIC}}(n, p, D_\lambda) = D_\lambda \log(n) + 2\delta \log\left(\binom{p}{D_\lambda}\right), \quad (4)$$

Non-asymptotic criteria In a practical consideration, having guarantees for n going to infinity has no sense and applying criteria with properties confirmed for any fixed sample size n is more relevant [17]. Introduced by [37], the goal of non-asymptotic criteria is to achieve the risk oracle:

$$\inf_{\lambda \in \Lambda} \mathbb{E}[\|X\beta^* - X\hat{\beta}_\lambda\|^2],$$

and instead of getting asymptotic equality of the kind

$$\mathbb{P}\left(\lim_{n \rightarrow +\infty} \frac{\mathbb{E}[\|X\beta^* - X\hat{\beta}_{\hat{\lambda}}\|^2]}{\inf_{\lambda \in \Lambda} \mathbb{E}[\|X\beta^* - X\hat{\beta}_\lambda\|^2]} = 1\right) = 1,$$

they get an inequality holding for any value of n :

$$\mathbb{E}[\|X\beta^* - X\hat{\beta}_{\hat{\lambda}}\|^2] \leq C_n \inf_{\lambda \in \Lambda} \{\mathbb{E}[\|X\beta^* - X\hat{\beta}_\lambda\|^2]\} + R_n, \quad (5)$$

where $C_n \approx 1$ at least for n large and R_n is small comparable to the risk oracle. The selected model is the minimizer of Equation (3) where $\gamma(m_\lambda)$ is the least-squares function and two penalty functions, which do not require the knowledge of the variance, are available. The first penalty is a data-driven penalty [12]:

$$\text{pen}_{\text{Data-driven}}(n, p, D_\lambda) = 2\kappa D_\lambda \left(2.5 + \log\left(\frac{p}{D_\lambda}\right)\right), \quad (6)$$

where the constant 2.5 has been proposed in a context of changepoint detection in a signal [13]. The constant κ is calibrated from the sample. For that, two strategies are proposed. The first one is the slope heuristics: assuming that the least-squares function is linear in $D_\lambda \left(2.5 + \log\left(\frac{p}{D_\lambda}\right)\right)$ as soon as D_λ is large enough (see Figure 2 of [14]), the constant κ is then equal to the estimated slope. The second strategy is the dimension jump: assuming the existence of κ^* such that for all the values smaller than κ^* , the associated model has a very high dimension, whereas for all the values greater than κ^* , the associated model has a reasonable dimension (see Figure 1 of [14]), the constant κ is then equal to the estimated κ^* . For more practical and theoretical details, we refer the reader to [14, 15].

The second penalty function is LinSelect proposed in [16] and generalized for a high dimensional context in [17]. It is built from the empirical estimator of the variance onto each m_λ :

$$\text{pen}_{\text{LinSelect}}(n, p, D_\lambda) = 1.1 \times \frac{n - D_\lambda}{n - D_\lambda - 1} \Psi(D_\lambda + 1, n - D_\lambda - 1, e^{-L_\lambda}), \quad (7)$$

where the L_λ are weights satisfying some properties and the function $\Psi[D, N, q]$ is the unique solution of the equation:

$$\phi[D, N, \Psi(D, N, q)] = q,$$

where $\phi[D, N, x]$ is defined for $x \geq 0$:

$$\phi[D, N, x] = \frac{1}{D} \mathbb{E} \left[\max \left(0, \chi_D^2 - x \frac{\chi_N^2}{N} \right) \right],$$

for χ_D^2 and χ_N^2 two independent χ^2 random variables with degrees of freedom D and N respectively.

2.5 Variable identification

In the high-dimensional framework, addition, suppression, or modification of some observations could radically change the variable subset selected. For prediction, different sets of variables can give the same prediction performances. However, when the objective is the identification of the active variables, this instability is a drawback.

To circumvent this problem, the idea is to work with perturbed datasets generated from the original sample. Cross-validation [38, 39] is commonly proposed. It consists in splitting K times the original sample into a training set and a test set. The training set is used to compute an estimator $\hat{\beta}_\lambda^k$ and the test set is used to evaluate the mean squared error. The selected model minimizes the mean squared error in λ . But applying cross-validation in a high-dimensional context is computationally expensive and known to be unstable. An alternative is ESCV [18] which estimates the instability along the regularization path with the K perturbed datasets and selects the variable subset which minimizes in λ :

$$\frac{\frac{1}{K} \sum_{k=1}^K \|X \hat{\beta}_\lambda^k - \frac{1}{K} \sum_{\ell=1}^K X \hat{\beta}_\lambda^\ell\|^2}{\|\frac{1}{K} \sum_{\ell=1}^K X \hat{\beta}_\lambda^\ell\|^2}.$$

Sampling strategy is also a solution. Two widely used approaches are Bolasso [19] and Stability Selection [20]. They mainly differ in their sampling strategy: Bolasso generates datasets of n data uniformly chosen with replacement among the original sample, whereas Stability Selection generates datasets of $\lfloor \frac{n}{2} \rfloor$ distinct data randomly chosen and includes also the complement of each generated dataset in the sampling strategy to limit the subsampling effects. In Stability Selection, they also propose a random perturbation in the ℓ_1 regularization:

$$F(\beta) = \sum_{j=1}^p \frac{|\beta_j|}{w_j},$$

where $w_j \sim \mathcal{U}([\theta, 1])$ with $\theta > 0$. Both sampling strategies provide a frequency of occurrence for each variable, and those with the highest frequency of occurrence are retained to form the final variable subset. Tigress method [21] modifies the calculation of the frequency of occurrence by averaging over the grid.

The last type of variable identification method is the knockoffs method [22], which controls the False Discovery Rate (FDR). This method starts with the construction of a matrix \tilde{X} such that \tilde{X} and X have the same covariance structure with \tilde{X}_j the least correlated to X_j . It is done through linear algebra tools [22, 40]. Then, a regularization path is constructed on the augmented matrix $X\tilde{X}$ of size $n \times 2p$ where the active variables are expected to be selected very earlier than their copy. Let denote

$$W_j = \max \left(Z_j, \tilde{Z}_j \right) \times \text{sign} \left(Z_j - \tilde{Z}_j \right), \quad (8)$$

where Z_j and \tilde{Z}_j correspond to the largest λ for which X_j and \tilde{X}_j are selected respectively. A positive value of W_j states that X_j is selected before its copy \tilde{X}_j and a large positive value indicates that X_j is selected rapidly. Let q be the target FDR, the final variable subset is composed by the X_j such that $W_j \geq T$ with:

$$T = \min \left\{ t \in \{|W_j|, j = 1, \dots, p\} \setminus \{0\}, \frac{1 + \#\{j : W_j \leq -t\}}{\min(1, \#\{j : W_j \geq t\})} \leq q \right\}.$$

3 Comparison study

3.1 Three simulation settings

The design of the simulation study is thought to study the behavior of the methods with respect to the dependency structures between the variables.

Simulation under independent design This is the simplest setting where the high-dimensional framework is the single handicap [41, 3]. The matrix X is simulated by concatenation of p independent standard Gaussian vectors of size n . The number of non-zero coefficients of the vector β^* is generated from a uniform variable on integers between 10 and 15. Their values are generated from $\mathcal{U}([0.5, 2])$ and the response variable Y is defined by $Y = X\beta^* + \varepsilon$, where $\varepsilon \sim \mathcal{N}(0, I_n)$.

Simulation under a Gaussian graphical model We use the equivalence between the network inference by Gaussian Graphical model and support estimation in Gaussian linear regressions [42]. An edge between the nodes i and j in the network means either X_j is an active variable when X_i is the response variable; or X_i is an active variable when X_j is the response variable. We generate a dataset of size n from a $(p + 1)$ multivariate centered Gaussian distribution with covariance matrix Σ , where the dependency structure is encoded in the precision matrix Σ^{-1} [43, 44]. The response variable Y is chosen as a column of the $(p + 1)$ multivariate centered Gaussian and the remaining columns constitute the matrix X of size $n \times p$. It differs from [45, 46, 47, 3], where the response variable is simulated once the matrix X is fixed. This choice has been motivated by applications such that regulatory network inference where transcription factors can be response variables and also active variables. We consider two graph patterns:

- *Cluster*: the precision matrix is simulated as a block diagonal matrix with B blocks of equal size. The response variable Y is defined as the first variable.
- *Scale-free*: a few variables have many neighbors while all the other have few neighbors in the network. We consider two response variables corresponding to the variables having the highest and the smallest number of neighbors. These simulation designs are called *scale-free-max* and *scale-free-min* respectively.

Simulation under a dynamical process It is based on the algorithm *FRANK* [27] which simulates large networks with characteristics of gene regulatory networks. In this algorithm, variables are categorized into a set of transcription factors that activate or inhibit a set of target genes and the *FRANK* data are generated from a dynamic process and deviate from the statistical model assumptions, especially the Gaussian distribution. We use *FRANK* with only transcription factor variables in order to compare the results with those from the other settings. We consider as response variables the variables having the highest and the smallest number of neighbors. These simulation designs are called *FRANK-max* and *FRANK-min* respectively.

For all the settings except *FRANK*, we set $n = \{150, 300, 600, 1200\}$, $p = 199$ and 100 samples of size $2n$ are generated to create a training set of size n for the estimation and a test set of size n to evaluate the methods. The observations generated for $n = 150$ are included in the datasets of size $n = \{300, 600, 1200\}$. For each sample, before being used, the variables are centered and scaled. To generate data from Gaussian graphical model, we use the function *huge.generator* from the R package *huge* (version 1.3.4.1). For the cluster design, the block number B equals 5 and the probability of connection within a component is set to the default value 0.3. For the *FRANK* algorithm, we use p transcription factors and $2n$ observations with $n = 150$. The number of eigenvalues of the matrix on the unit circle is fixed to 2 and the minimum and maximum of sparsity are set to 1 and 50. Other parameters are set to default values and 40 samples are generated.

3.2 Investigated methods and their parameters

A total of 16 methods of model selection are defined by the combination of a regularization function (Lasso or Elastic-net) with an algorithm (LARS or the gradient descent method) and a penalty function (eBIC, LinSelect or the 2 data-driven penalties). A total of 17 methods of variable identification are defined: when the sampling strategy is performed before the definition of the grids, 8 methods are defined by the combination of the sampling strategy (Bolasso or Stability Selection) with a regularization function (Lasso or Elastic-net) and an algorithm (LARS or the gradient descent method). When the grid Λ is fixed, the sampling strategy is performed for each λ of the grid, which implies using the gradient descent algorithm, hence 4 methods are defined. Furthermore, we include Tigress, the knockoffs method and ESCV. For the last two, a gradient descent algorithm is used with either Lasso or Elastic-net.

For the LARS algorithm, we use the function *enet* of the R package *elasticnet* (version 1.1.1). The maximal number of steps to define the grid size is the default value $50 \times \min(p, n - 1)$. For the gradient descent method, we use the function *glmnet* of the R package *glmnet* (version 3.0) and set the grid size at 1000. The functions *enet* and *glmnet* propose the Lasso and elastic-net regularization functions. We set $\alpha = 0.5$ for Elastic-Net.

To perform model selection, eBIC is implemented with $\delta = 1$. LinSelect is implemented in the function *tuneLasso* of the R package *LINselect* (version 1.1.3). The data-driven penalties are calculated by using the function *capushe* of the

R package *capushe* (version 1.1.1). The parameters are set to the default values except for the minimum percentage of points for the plateau selection set to 0.1.

To perform variable identification, the function *escv.glmnet* of the R package *HDCI* (version 1.0.2) is used for the ESCV strategy, with a number of groups $K = 10$. Bolasso and Stability Selection are implemented with 100 samples. We do not investigate the impact of the presence of a random perturbation in Lasso for Stability Selection. A variable is selected when its occurrence frequency is higher than 0.8. For Tigress, we use the function *tigress* of the R package *tigress* (version 0.1.0) with 50 steps for LARS. For the knockoffs method, we use the function *knockoff.filter* with option *create.second_order* of the R package *knockoff* (version 0.3.2), we calculate the W_j with the function *stat.lasso_lambdasmx* and set the FDR to 0.1.

3.3 Evaluation metrics

We use the partial area under the receiver operating characteristic curve (pROC-AUC) where the x-axis is the proportion of selected non-active variables among the non-active variables and the y-axis is the proportion of selected active variables among the active variables. Since the length of the regularization paths may differ according to the choice of both regularization function and algorithm, the pROC-AUC are calculated by truncating the values of the x-axis at the largest value common to all the regularization paths and normalized to be compared. A value of 1 indicates that the active variables are distinguished from the others.

Second, we evaluate the prediction performance of the methods by calculating the mean squared errors (MSE) on each test set $(\mathcal{Y}, \mathcal{X})$:

$$\frac{1}{n} \sum_{i=1}^n \left(\mathcal{Y}_i - (\mathcal{X} \hat{\beta}_{\hat{\lambda}})_i \right)^2, \quad (9)$$

where $\hat{\beta}_{\hat{\lambda}}$ is the estimator of β^* calculated on the associated training set. As data are centered and scaled, a MSE value lower than 1 means that the selected variables predict Y better than the empty set.

Finally, we calculate the recall (the proportion of the selected active variables among the active variables), the specificity (the proportion of the non-active variables not selected among the non-active variables) and the false discovery rate which is the average of the proportion of selected non-active variables among the selected variables across the samples for which at least one variable was selected. Since the objective is to limit the selection of non-active variables while selecting as many active variables as possible, recall and specificity are expected to be close to 1 while the FDR is expected to be low.

4 Results

The first part is dedicated to the results obtained when samples of $n = 150$ observations described by $p = 199$ variables are generated from Gaussian distributions. We consider the independent setting as benchmark since $n < p$ and the number of active variables verified the sparsity hypothesis (12.59 in average with a standard deviation of 1.76). The cluster setting evaluates the impact of the dependency structure when the number of active variables is similar to those in the independent setting (11.63 in average with a standard deviation of 2.75). With the scale-free design, we investigate the method behavior with respect to the number of active variables: In scale-free-min, the support size always equals 1. In scale-free-max, the support size is 31.41 in average with a high standard deviation (9.70). In the second part we discuss how the sample size n impacts the method performances. In the third part, we investigate the impact of the non-Gaussian assumption through the FRANK datasets.

4.1 Method performances in a high dimensional context

For the sequel, the notations *GD* and *E-Net* denote respectively the gradient descent algorithm and the Elastic-Net regularization function. Finally, *grid* and *sub* denote the strategies when the grids are first generated and the samples are first generated, respectively.

4.1.1 Discrimination of the active variables from the others

Figure 1 summarizes the pROC-AUC values of the different regularization paths for the four settings. We observe that LARS combined with E-Net is the best combination to discriminate between the active and non-active variables. Its value is around 0.99 for the independent setting, whereas the use of Lasso with LARS provides a median value around 0.73. In a general way, The GD algorithm discriminates less well the active and non active variables.

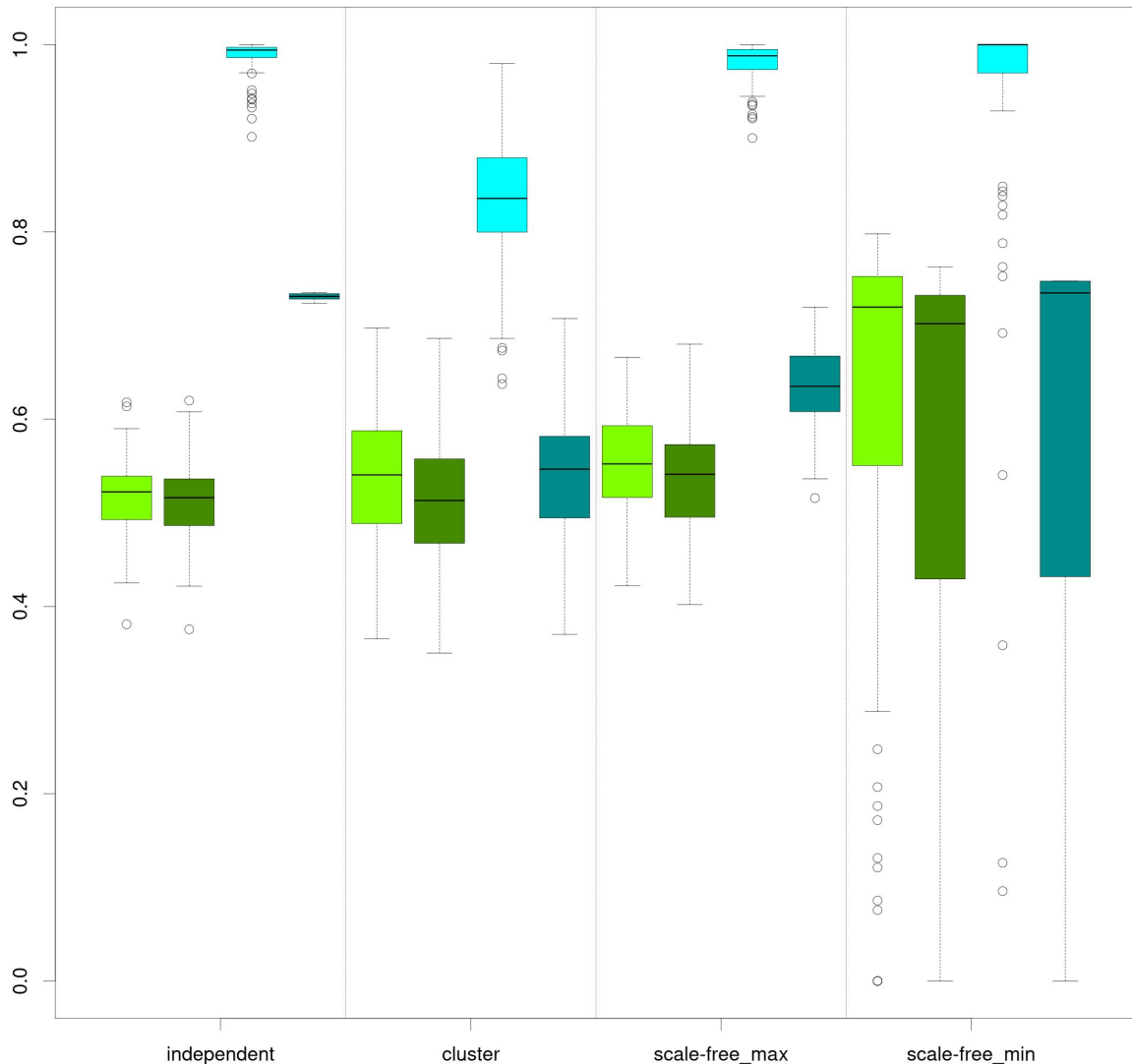


Figure 1: Boxplots of the pROC-AUC values calculated on 100 samples of size $n = 150$. The gradient descent algorithm combined with E-Net is colored light green, the gradient descent algorithm combined with ℓ_1 regularization is colored dark green, LARS combined with E-Net is colored cyan and LARS combined with ℓ_1 regularization function is colored dark cyan.

For the three settings, where a dependency structure exists, the highest median values are always obtained with LARS combined with the E-Net regularization: 0.84 and 0.98 for cluster and scale-free-max designs respectively and 1 for scale-free-min design. LARS combined with Lasso does not differ from the GD algorithm.

4.1.2 Size of the selected subsets

Figure 2A summarizes the size of the estimated support for the four settings. The number of methods compared in this study being large, we represent on this figure the best combination, LARS with E-Net regularization, for the model selection methods, as well as for Bolasso and Stability Selection when samples are first generated (*sub*). For ESCV and the knockoff method which are based on the gradient descent algorithm, we show the MSE obtained with E-Net

since this regularization method seems to be slightly better than with Lasso. For Tigriss, no choice is required since the method is only implemented with LARS and Lasso. The size of the support estimated by the methods with all the possible combinations in the four settings are represented in Figures A1 and A2.

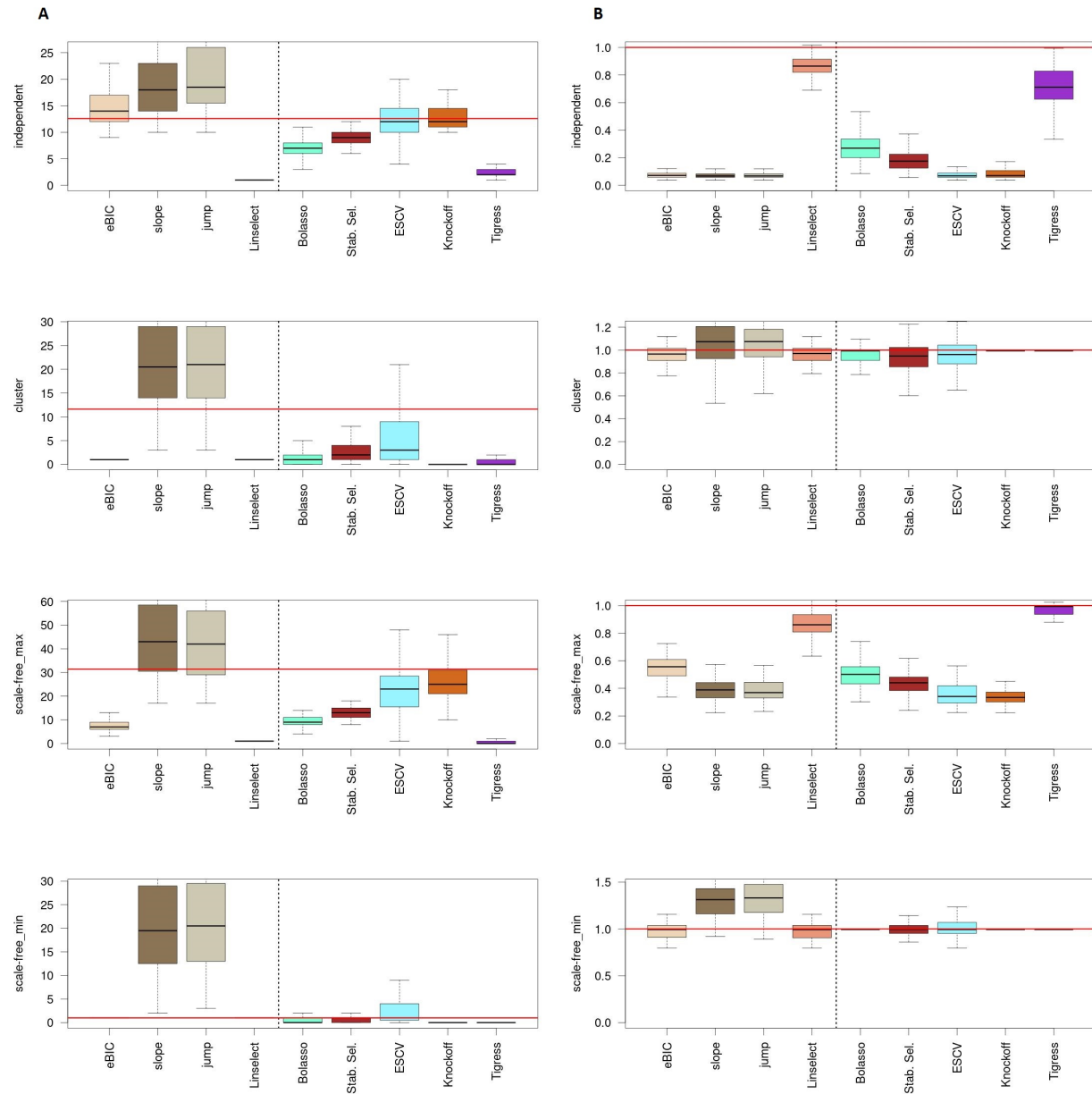


Figure 2: Column A: Boxplots of the size of the support calculated on 100 samples of size $n = 150$ in the four settings. The red line indicates the number of active variables. Column B: Boxplots of the MSE calculated on 100 samples of size $n = 150$ in the four settings. The red line indicates 1, the value below which the methods have a prediction ability. Results are presented with LARS combined with E-Net for the model selection methods, Bolasso and Stability Selection. For ESCV and the knockoff method which are based on the gradient descent algorithm, the MSE is showed with E-Net. Tigriss is implemented with LARS and Lasso. .

In the independent setting, among the model selection methods, eBIC provides the closest number to the size of the support. Linselct generally selects 1 variable, the maximum being 3. Concerning the data-driven penalties, the number of selected variables is always significantly higher than expected. Among the variable identification methods, ESCV and the knockoffs method provide a number of selected variable very close to the number of active variables, whereas all the other methods select less variables than expected. Tigriss is very conservative.

When a dependency structure is introduced, for the model selection methods, eBIC becomes as conservative as Linselect. The data-driven penalties are preferable. All the variable identification methods show difficulties to manage the dependency between the variables. They select very small subsets of variables in the cluster design and favor the empty subset for the scale-free-min. For the scale-free-max design, ESCV and the knockoff method outperform.

4.1.3 Prediction performances

We measure the performance of prediction by the MSE shown in Figure 2B. The MSE values of the methods with all the possible combinations in the four settings are represented in Figure A3 and A4.

For the independent setting, all the methods have a MSE lower than 1 but differences can be observed: For the model selection strategies, the median value is around 0.07 for eBIC and the data-driven penalties and rising to 0.96 for LinSelect. For the variable identification methods, the smallest median values are around 0.07 for ESCV and the knockoffs method. In contrast, Tigress has a median value ten times higher. Concerning the Bolasso and Stability Selection, the MSE median values are 0.27 and 0.17 respectively.

When a dependency structure exists, the results of the model selection methods deteriorate. For the cluster, the median value of eBIC and LinSelect is higher than 0.92, the data-driven penalties are not predictive. For the scale-free-min design, methods are not predictive. For the scale-free-max, the data-driven penalties have a median value at 0.37. The penalty eBIC and Linselect achieve 0.56 and 0.87 respectively. The variable identification methods are not better, the median values are very close to 1 for the cluster and scale-free-min designs. For the scale-free-max design, the median value is around 0.35 for ESCV and the knockoffs method. The values of Bolasso and Stability Selection are 0.5 and 0.44 respectively. Tigress is not predictive.

In summary, when the variables are independent, the best methods are eBIC, the data-driven penalties, ESCV and the knockoffs method. When a dependency structure exists, the predictive performances are deteriorated. For the cluster and scale-free-min designs, the methods are not really predictive. For scale-free-max design, the best methods are ESCV, the knockoffs method followed by the two data-driven penalties.

4.1.4 Recall and specificity

We measure the ability to select the active variables through the recall. Results are shown in Figure 3A.

For the independent setting, all the model selection methods except LinSelect select all the active variables. Among the variable identification methods, ESCV and the knockoffs method select also all the active variables. Bolasso and Stability Selection have median values of 0.57 and 0.71 respectively and finally Tigress is very far with a median value around 0.18. Based on Figures A5 and A6, we observe that the choice of the regularization function for Bolasso and Stability Selection is very important since with Lasso, the recall equals 0, meaning that no active variables are selected.

When a dependency structure exists, among the model selection methods, the data-driven penalties have a better recall better than eBIC and Linselect for the three settings. However, on Figures A5 we observe that their results vary between the settings and depend on the combination of the algorithm and the regularization function. Among the variable identification methods, the results are highly dependent on the setting. For the cluster design, the best median value is obtained by ESCV and Stability Selection. However, the median value remains low, around 0.2 and there is a large variability among the 100 samples. For the scale-free-max design, the knockoffs method and ESCV provide the best results (0.75). The other methods are clearly worst. For the scale-free-min design, only ESCV selects the active variable.

Concerning the ability to not select the non-active variables, it is measured by the specificity, shown in Figure 3B. For the independent setting, only the data-driven penalties show a specificity different from 1 meaning that some non-active variables are selected and it might be explained by the size of the estimated support which is larger than the number of the active variables. All the variable identification methods have a specificity very close to 1. When a dependency structure exists, the conclusions are exactly the same.

In summary, when variables are independent, eBIC, the data-driven penalties, ESCV and the knockoffs method recover the active variables. When a dependency structure exists, the results of the data-driven penalties are the best for the three settings, but at the risk to select some non-active variables. ESCV is the best variable identification method but its performance depend on the design and ESCV recall is always lower than that of the data-driven penalties but its specificity equals 1, meaning that it does not select non-active variables.

4.1.5 False discovery proportion and FDR

For many domain of applications, it is very important to limit the selection of non active variables. To evaluate this ability, we calculate the false discovery proportion and estimate the FDR. Figure 4 shows the results for the four settings.

Variable selection in high-dimensional regression

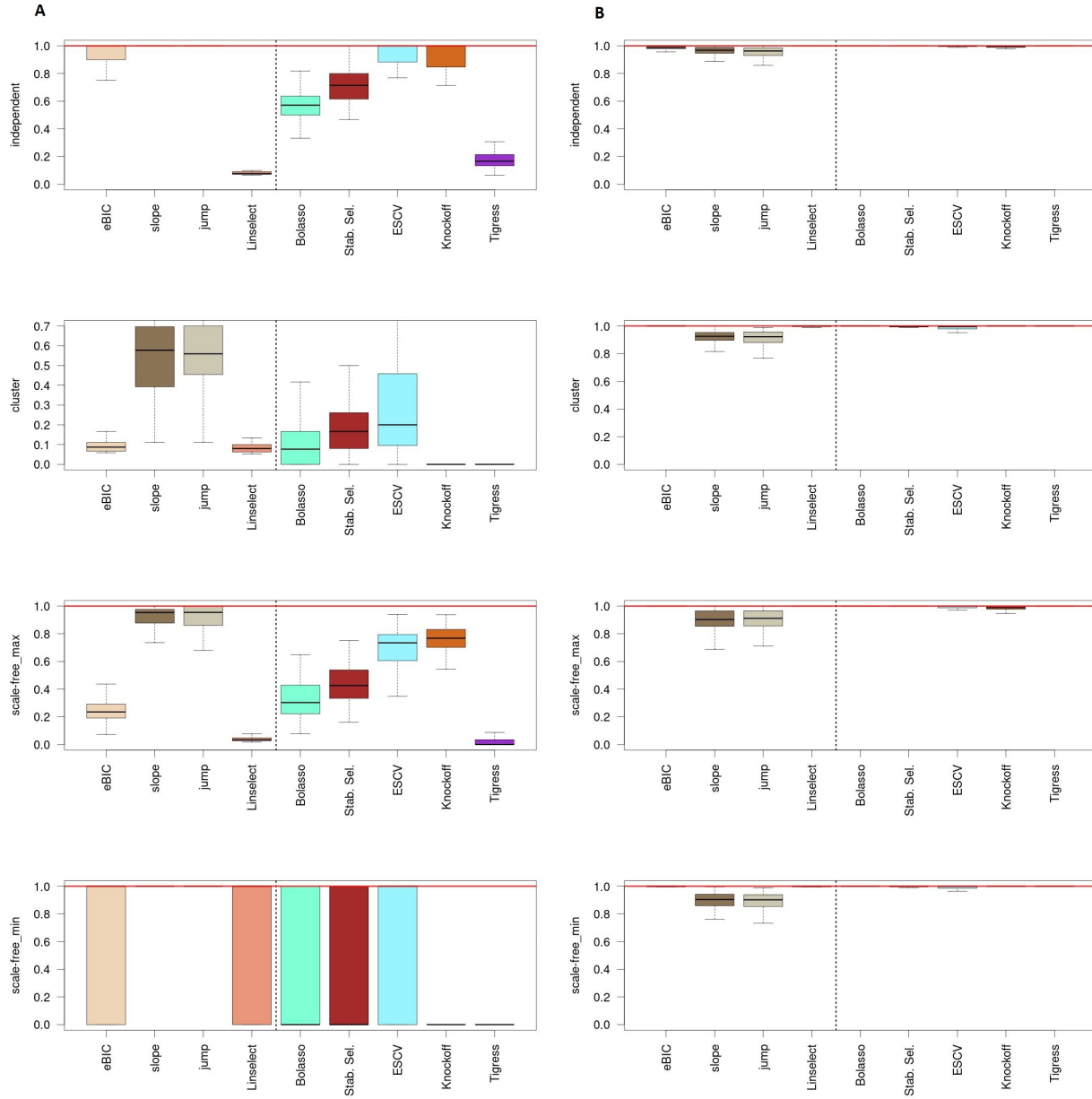


Figure 3: Column A: Boxplots of the recall calculated on 100 samples of size $n = 150$ in the four settings. The red line at 1 indicates the ability to recover all the active variables. Column B: Boxplots of the specificity calculated on the same 100 samples of size $n = 150$ in the four settings. The red line at 1 indicates the ability to not select all the non-active variables. Results are presented with LARS with E-Net regularization for the model selection methods, Bolasso and Stability Selection. For these latter, the sampling strategy is *sub*. For ESCV and the knockoff method which are based on the gradient descent algorithm, the recall is showed with E-Net. Tigress is implemented with LARS and Lasso.

For the independent setting, among the model selection methods, eBIC and the data-driven penalties have an estimated FDR higher than 0.1. For the data-driven penalties, it is a consequence of selecting too many variables. Linselect has an estimated FDR equal to 0 and as we saw that Linselect selects very few variables, it means that it selects variables that are always active. For the variable identification methods, the estimated FDR is very often lower than 0.05 except for the knockoffs method with an estimated FDR of 0.08 for an expected control of 0.1.

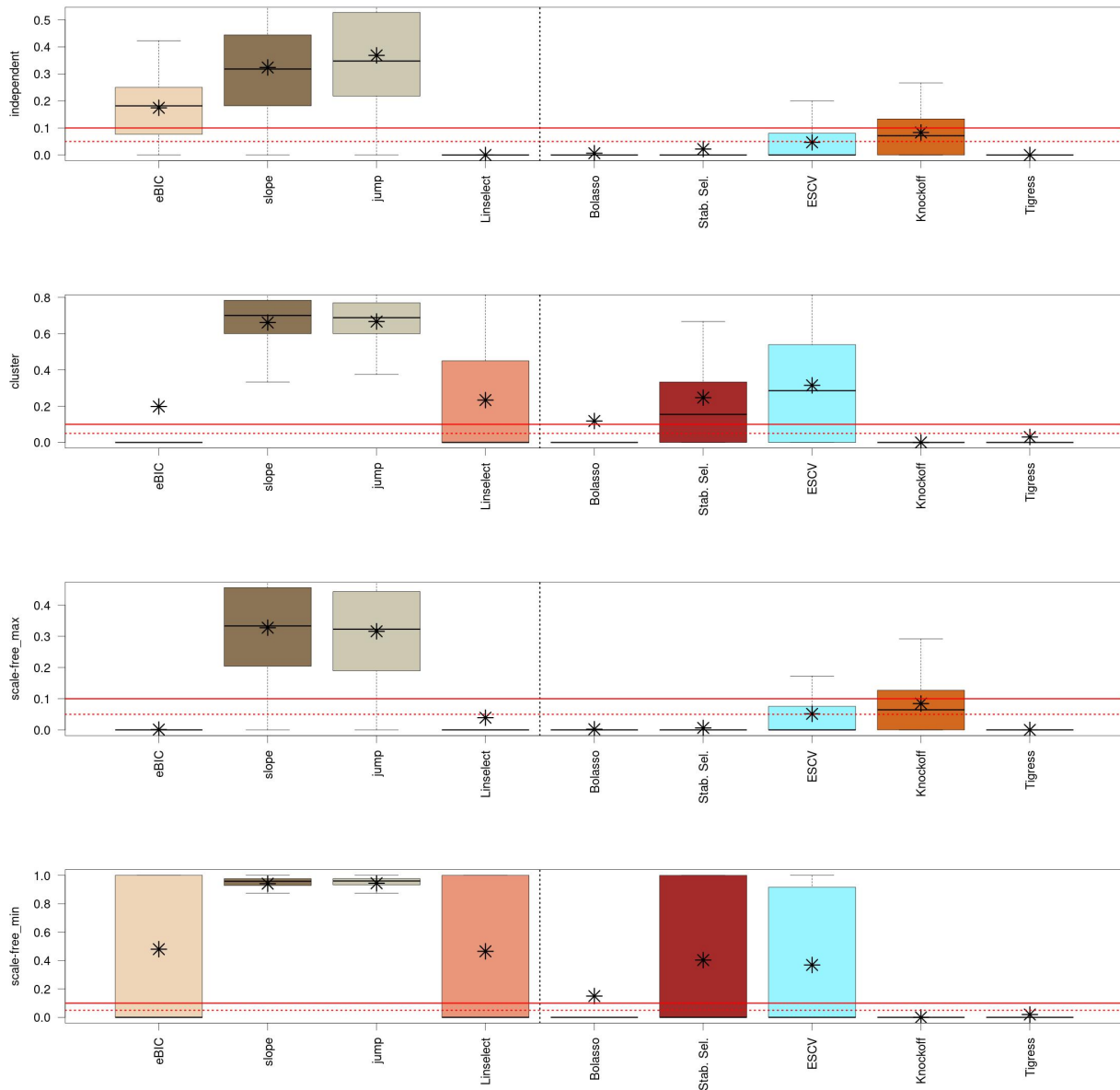


Figure 4: Boxplots of the FDP calculated on 100 samples of size $n = 150$ in the four settings. The star indicates the estimated FDR. Results are presented with LARS with E-Net regularization for the model selection methods, Bolasso and Stability Selection. For these latter, the sampling strategy is *sub*. For ESCV and the knockoff method which are based on the gradient descent algorithm, the FDP is showed with E-Net. Tigress is implemented with LARS and Lasso. The red line indicates 0.1, the threshold for the knockoff method. The dashed red line indicates 0.05.

With the presence of a dependency structure, eBIC and Linsselect have an estimated FDR lower than 0.05 for the scale-free-max setting and about 0.2 for the cluster setting, whereas it increases and is higher than 0.4 for the scale-free-min setting. The estimated FDR of the data-driven penalties is always too high. Among the variable identification methods, for the scale-free-max setting, the estimated FDR is always lower than 0.1. For the other two settings, the knockoff method and Tigress still have an estimated FDR below 0.1. The other methods have an increase of their estimated FDR. In summary, the variable identification methods have a lower estimated FDR than the model selection methods. The knockoffs method gets an estimated FDR close to the threshold given as input to the method. For eBIC, we observe on

Figure A7, that LARS combined with Lasso gives an estimated FDR lower than 0.1 with similar results for MSE and recall.

4.2 Impact of the sample size on the method performances

We evaluate how the number of observations n affects the performance of the method, bearing in mind that if the metric improves as the sample size increases, then the behaviour observed in the previous section is actually due to the high dimension.

4.2.1 Discrimination of the active variables from the others

For the high-dimensional context, we have seen that the ability to discriminate between active and non-active variables is very important. The behavior of each combination with respect to n cannot be commented on, since the length of the regularization path for each sample size can be different. However, with a fixed sample size, we can compare the four combinations. On Figure 5, we observe that LARS combined with E-Net remains the best in all the settings, although the differences between the four combinations decrease as n increases.

4.2.2 Size of the selected variable subset

The evolution of the estimated support is shown in Figure 6A. In the independent setting, eBIC and the data-driven penalties behave well with an estimated support close to the number of active variables as soon as $n = 300$. For the three combinations of algorithm and regularization function, we observe the same results for eBIC and an overestimation of the support size for the data-driven penalties. For Linselect, the size of the support increases sharply as $n = 600$. For the variable identification methods, the behavior of ESCV is constant with n and the estimated support is close to the number of active variables. For Bolasso and Stability Selection, the estimated support increases gradually until the number of active variables. However we observe an instable behavior of the *grid* sampling strategy. For Tigress, the estimated support increases gradually but remains far from the number of active variables. For the knockoff method, a sample size of $n = 300$ seems to put it in difficulty but as soon as $n = 600$, the estimated support is close to the number of active variables.

When a dependency structure exists, for the cluster and scale-free-max settings, the size of the estimated support increases gradually with n , except Linselect that increases sharply in the scale-free-max setting as $n = 600$. For eBIC, the support size is close to the number of active variable when $n = 1200$. For the two data-driven penalties, the estimated supports are always greater than the number of active variables. For Linselect in the cluster setting, the support size is underestimated. For the variable identification methods, the behavior of ESCV is always constant with n but the estimated support is now lower than the number of active variable. For Tigress, the estimated support increases gradually but is still far from the number of active variables. The structure of dependency put in difficulty the knockoff method and the increase of the sample size does not improve its behavior. The estimated support is usually lower than the number of active variables. For Bolasso and Stability, the estimated support increases with n for all the combinations of algorithm and regularization function and for the two sampling strategies. It remains lower than the number of active variables. Finally, for the scale-free-min setting, when only one variable is active, the median value of the estimated support is 1 for eBIC and Linselect, greater than 1 for the data-driven penalties. All the variable identification methods, which favor an empty set at $n = 150$, start to select some variables when n increases.

To summarize, when the variable are independent, as soon as the number of observations equals 300, all the methods except Linselect and the knockoff method behave as expected. We note that Tigress remains conservative even with a sample size increasing. When a dependency structure exists, all the methods have more difficulties to retrieve a number of selected variables close to the number of active variables. The most impacted methods are the data-driven penalties and the knockoff method. The *grid* sampling strategy, which has an instable behavior when the variables are independent, behaves correctly when a dependency structure exists.

4.2.3 Prediction performance

The evolution of the MSE is shown in Figure 6B. For the independent design, the MSE of eBIC and the data-driven penalties is very low whatever n and decreases with n until 0.05. The MSE of Linselect also decreases with n and reaches 0.07 with LARS as soon as $n = 600$. For the variable identification methods, the MSE of Bolasso and Stability Selection decrease with n , except when the *grid* sampling strategy is used. LARS combined with E-Net remains the best combination. For ESCV and Tigress, the MSE also decrease gradually with n but the results are different since ESCV always has a median MSE lower than 0.2, while Tigress has a median MSE always higher than 0.6. The knockoff method is the only method with an unexpected behavior, since the MSE is close to 1 for $n = 300$ and drops to 0.1 as $n = 600$.

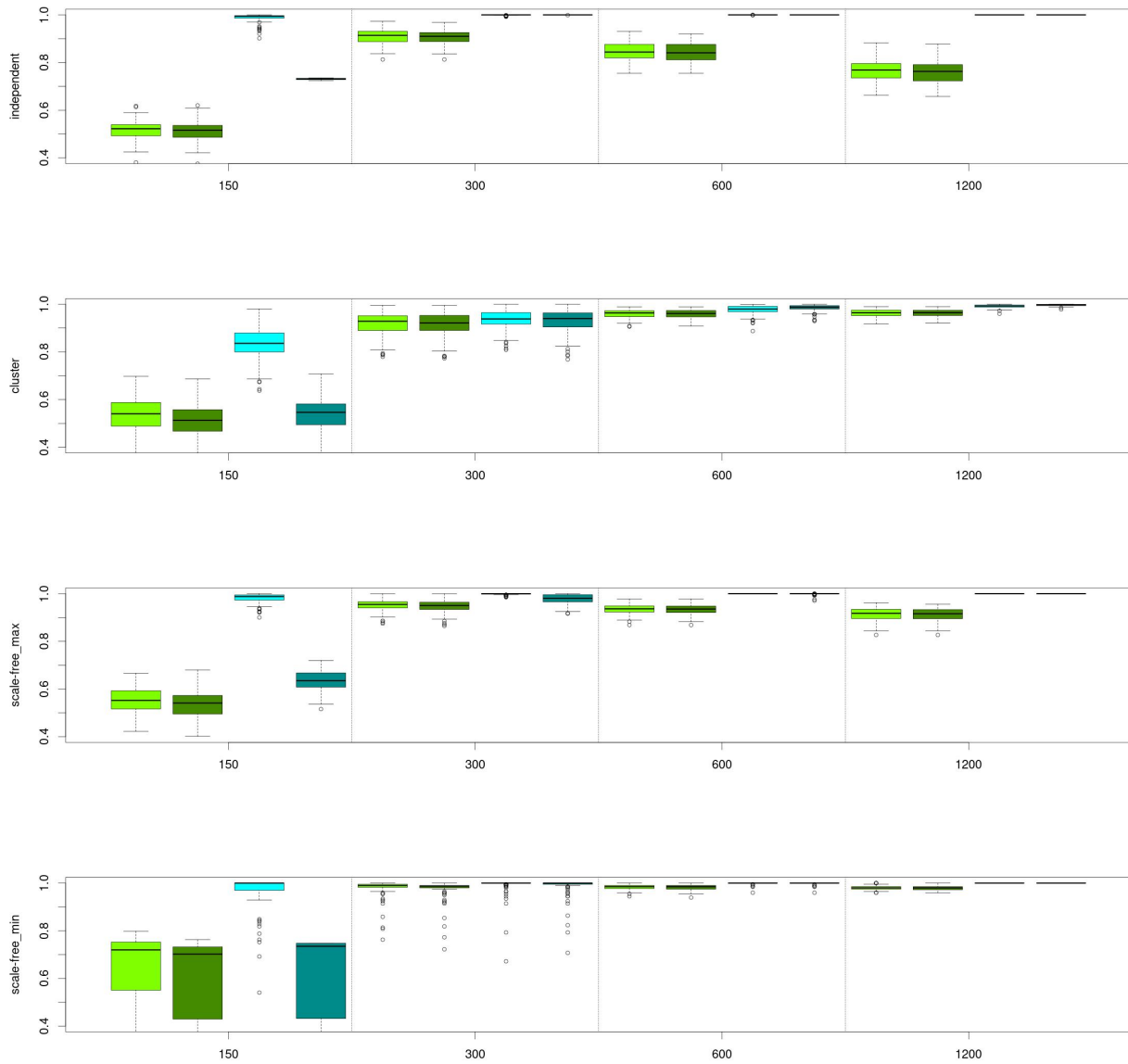


Figure 5: Boxplots of the pROC-AUC values calculated on 100 samples of size $n = \{150, 300, 600, 1200\}$. The gradient descent algorithm combined with E-Net is colored light green, the gradient descent algorithm combined with Lasso is colored dark green, LARS combined with E-Net is colored cyan and LARS combined with Lasso is colored dark cyan.

When there is a dependency, we observe that all the model selection methods have a MSE decreasing with n but the methods are not predictive (median value higher than 0.5). For the variable identification methods, Bolasso and Stability Selection combined with LARS and E-Net are to be preferred with a median MSE around 0.2 to Tigress whose MSE is between 1 and 0.8. ESCV has an averaged MSE that increases slightly from 0.36 to 0.52 between $n = 300$ and $n = 1200$ with an important increase in the inter-sample variability, which makes an observable difference in the median value between the two regularization functions. The knockoff method has an MSE comparable when $n = 1200$ to that when $n = 150$ but between these two sample sizes, the MSE increases to reach 0.85 or more.

To summarize, the MSE of the methods decreases when the number of observations increases. The dependency structure complicates the prediction task.

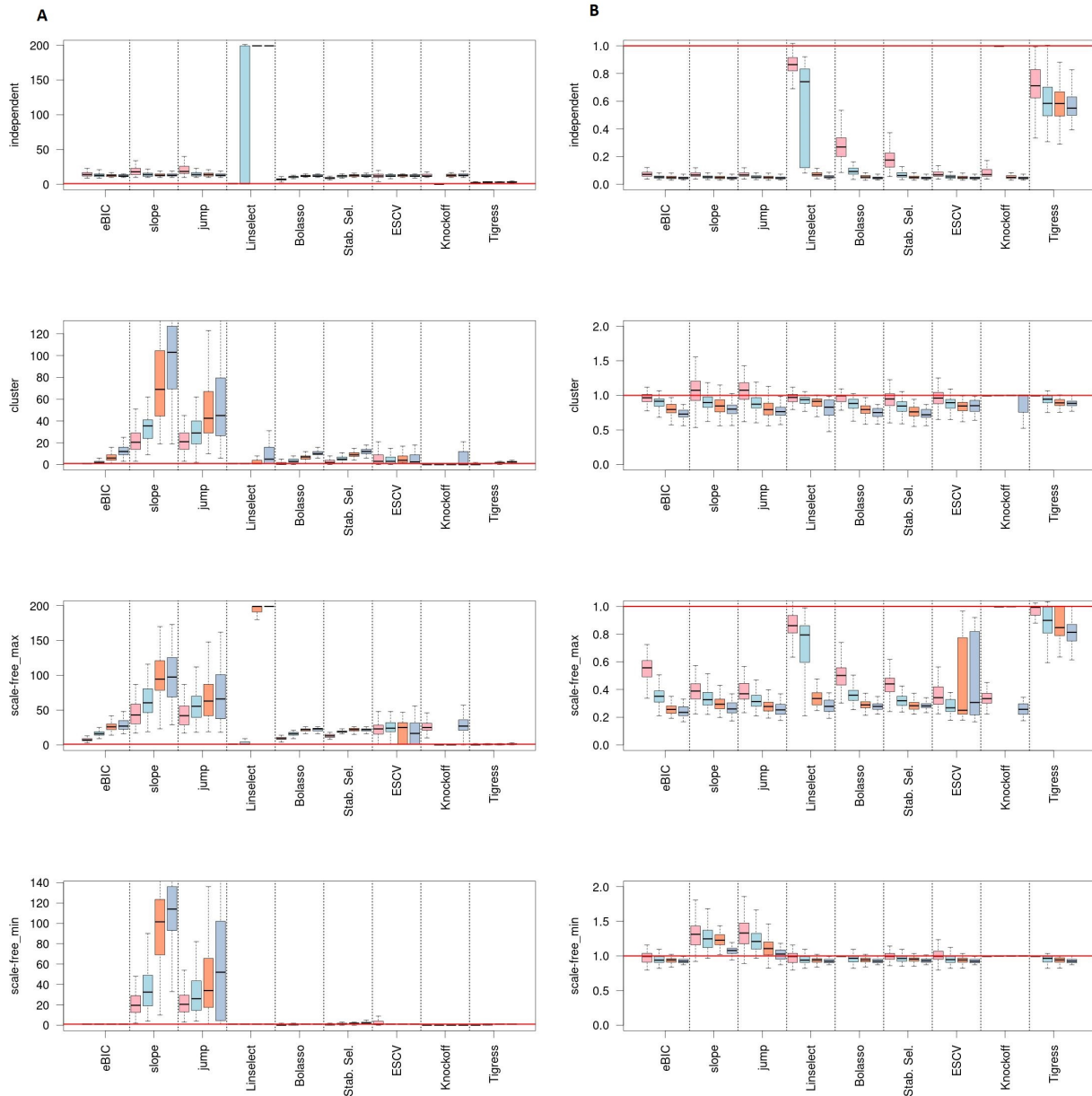


Figure 6: Column A: Boxplots of the estimated support calculated on 100 samples in the four settings. The red line indicates the number of active variables. Column B: Boxplots of the MSE calculated on 100 samples in the four settings. The red line indicates 1, the value below which the methods have a prediction ability. A sample size of $n = 150$ is colored in light pink, $n = 300$ in light blue, $n = 600$ in light salmon and $n = 1200$ in light steel blue. Results are presented with LARS with E-Net regularization for the model selection methods, Bolasso and Stability Selection. For these latter, the sampling strategy is *sub*. For ESCV and the knockoff method which are based on the gradient descent algorithm, the recall is showed with E-Net. Tigress is implemented with LARS and Lasso.

4.2.4 Recall and specificity

The evolution of the ability to recover of the active variables is shown in Figure 7A. For the independent design, among the model selection methods, only Linselect does not have a recall equal to 1 for $n = 150$ but as soon as $n = 600$, Linselect does. For the variable identification methods, the recall of Bolasso and Stability Selection increases with n , except when the *grid* strategy is used. LARS combined with E-Net remains the best combination. The recall of ESCV is equal to 1 as $n = 150$ or more. The recall of Tigress increases gradually with n , but it remains low with a

median value of 0.25. The knockoff method again shows an unexpected behavior when $n = 300$, the averaged recall drops to 0.2 to is back to 1 as $n = 600$.

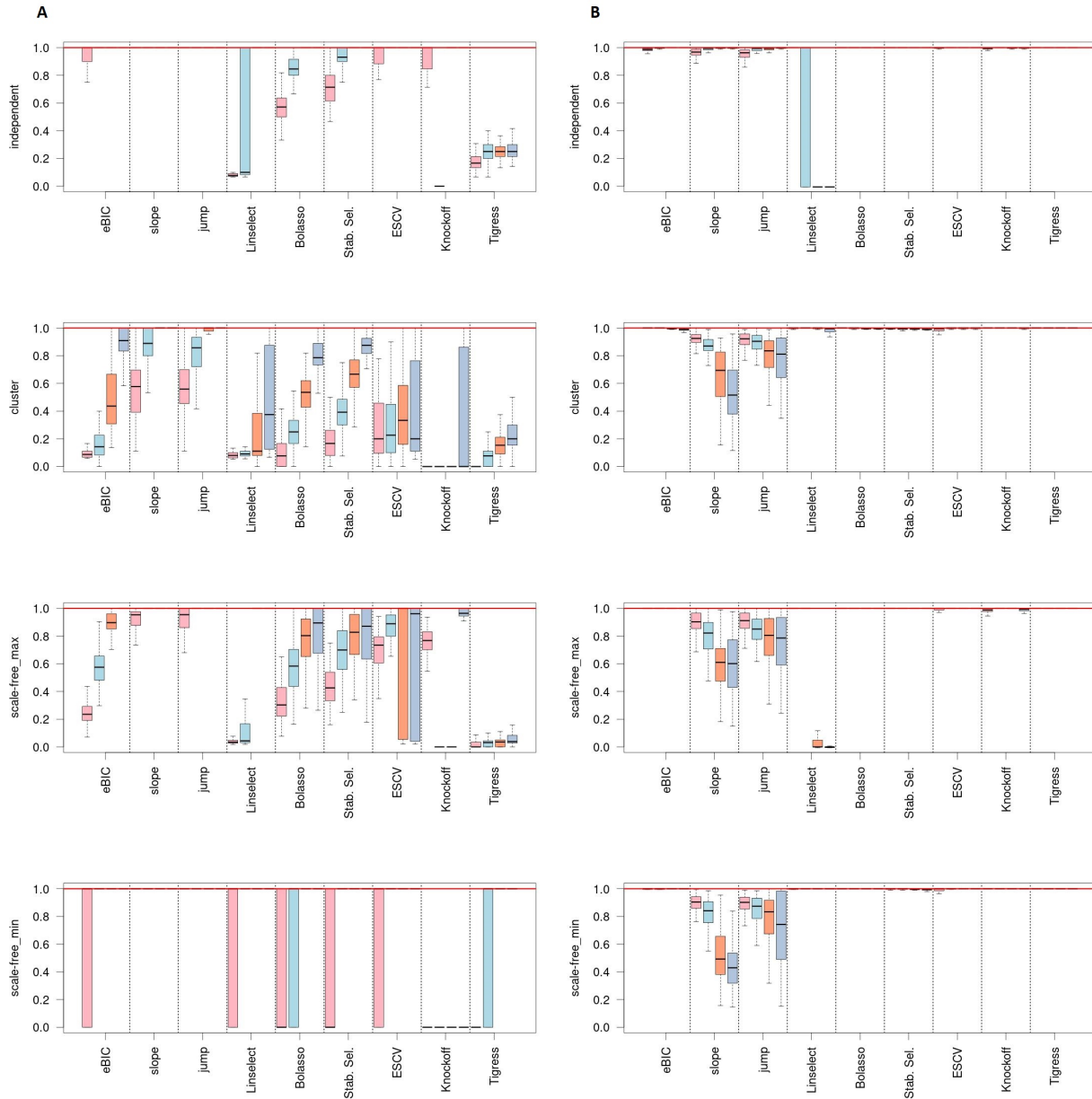


Figure 7: Column A: Boxplots of the recall calculated on 100 samples in the four settings. The red line at 1 indicates the ability to recover all the active variables. Column B: Boxplots of the specificity calculated on 100 samples in the four settings. The red line at 1 indicates the ability to not select all the non-active variables. A sample size of $n = 150$ is colored in light pink, $n = 300$ in light blue, $n = 600$ in light salmon and $n = 1200$ in light steel blue. Results are presented with LARS with E-Net regularization for the model selection methods, Bolasso and Stability Selection. For these latter, the sampling strategy is *sub*. For ESCV and the knockoff method which are based on the gradient descent algorithm, the recall is showed with E-Net. Tigress is implemented with LARS and Lasso.

For the three dependency structures, all the model selection methods have a recall increasing with n . The recall reaches 1 for all the methods as soon as $n = 300$ in the scale-free-min setting. In the scale-free-max and cluster settings, the recall is maximum as soon as $n = 600$. Only Linselect seems to be sensitive to the dependency structure since its recall is below 0.5 in the cluster setting, whereas it reaches 1 in the scale-free-max setting. For the variable identification methods, the results vary between the three dependency structures. In the scale-free-min setting, all the methods retrieve

the active variable as soon as $n = 300$, except the knockoff method that selects the empty set whatever the value of n . For Bolasso and Stability Selection, as usually, the combination LARS and E-Net is to be preferred. When many variables are active, Bolasso and Stability Selection have a recall increasing with n and Stability Selection seems to be slightly better. Tigress has also an increasing recall but the values remain low and differs between the cluster setting and the scale-free-max setting. ESCV has an averaged recall increasing slightly until 0.5 but the inter-sample variability is large leading to a median value lower for $n = 1200$ than for $n = 600$ for the cluster setting. For the scale-free-max setting, ESCV behaves as expected, the recall increases with n and reaches 1 for $n = 1200$ when E-Net is used. The behavior of knockoff method varies with the dependency structure. In the cluster setting, the knockoff method usually selects no variables, while in the scale-free-max setting, its recall reaches 0.86 when $n = 1200$, so better than 0.75 as $n = 150$. However between these two sample sizes, the recall decreases to 0 and 0.2 for $n = 300$ and $n = 600$, respectively.

The evolution of the ability to not select the non-active variables is shown in Figure 7B. For the independent design, among the model selection methods, we observe that only the data-driven penalties do not have a specificity equal to 1 for $n = 150$ but as soon as $n = 300$, they do. When the sample size increases, LinSelect selects non-active variables. It is clearly related to its difficulty to select a relevant number of variables as soon as $n = 600$. For the variable identification methods, the specificity equals 1 for all the sample sizes.

To summarize, all the methods, except Tigress, retrieve the active variables. The model selection methods seem to require less observations than the variable identification methods to have a recall equal to 1. The knockoff method is the only method that gives different results depending on the dependency structure.

4.2.5 False Discovery proportion and FDR

For the independent setting, on Figure 8, we observe that eBIC and the data-driven penalties manage to get an estimated FDR lower than 0.1 as soon as $n = 300$. The estimated FDR of Linselect increases with n but is always higher than 0.1. For all the variable identification methods, the estimated FDR is lower than 0.1.

A dependency structure dramatically increases the estimated FDR of the data-driven penalties for all the sample sizes. The estimated FDR of eBIC varies between the settings. For scale-free-max, it is always below 0.01. For the cluster and scale-free-min settings, it decreases with n and achieves 0.1 as $n = 600$. For Linselect, the behavior of the estimated FDR varies with the dependency structure. In the cluster and scale-free-min settings, the estimated FDR decreases with n and is lower than 0.1 as $n = 300$ and $n = 600$, respectively. For the scale-free-max, it is lower than 0.1 when $n = 300$ and then sharply increases up to 0.7. For all the variable identification methods, the estimated FDR in the scale-free-max setting is lower than 0.1. For the cluster setting, the estimated FDR of Bolasso and Stability Selection decrease with n and is lower than 0.1 for almost all the combinations of algorithm, regularization function and sampling strategy. ESCV has a decreasing estimated FDR with n . With Lasso, the estimated FDR of ESCV achieves to be lower than 0.1. Tigress has an estimated FDR very low due to the very small number of selected variables. The knockoff method has an estimated value always lower than 0.1. For the scale-free-min setting, the estimated FDR of Bolasso and Stability Selection decrease with n and is lower than 0.1 for some combinations of algorithm, regularization function and sampling strategy, but it is difficult to identify the best combination. ESCV maintains an estimated FDR close to 0.1 with Lasso. Tigress has an estimated FDR very low due to the very small number of selected variables. The knockoff method has an estimated value always lower than 0.1.

To summarize, when the variable are independent, and when the sample size increases, all the methods have an estimated FDR lower than 0.1. When the dependency structure exists, the data-driven penalties select many non-active variables, whereas eBIC and Linselect select few non-active variables as soon as n is large enough. The variable identification methods always have a lower estimated FDR than the model selection methods, although the estimated FDR varies with the dependency structure.

4.3 Behavior of the methods in a non-Gaussian framework

Understanding gene regulation is a real challenge in molecular biology and the emergence of high-throughput technologies, such as microarrays and RNA sequencing, has made feasible to measure the activities of thousands of genes simultaneously and to perform genome-scale inference of transcriptional gene regulation. Several studies have already shown that inferring gene network is a difficult task and no single inference method performs optimally [48]. The regression methods are usually included in such studies but always with Lasso. In this section, we would like to investigate whether the regularization function and the algorithm affect the performances of the methods when the distribution of the observation is far from the Gaussian distribution. We also study the nonparanormal transformation *shrinkage* of the R package *huge* known to help relax the assumption of normality.

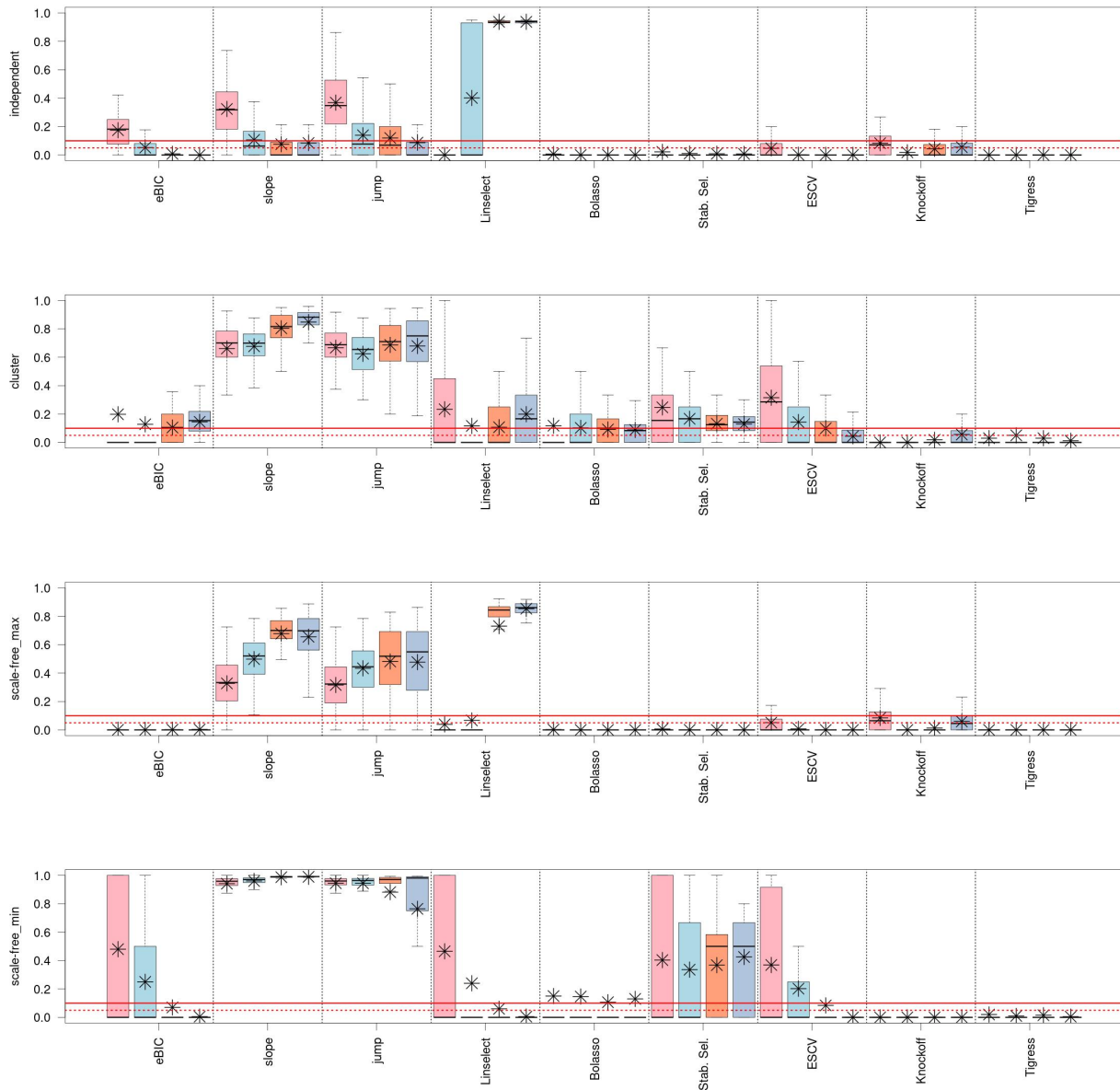


Figure 8: Boxplots of the FDP calculated on 100 samples in the four settings. A sample size of $n = 150$ is colored in light pink, $n = 300$ in light blue, $n = 600$ in light salmon and $n = 1200$ in light steel blue. The star indicates the estimated FDR. Results are presented with LARS algorithm with E-Net regularization for the model selection methods, Bolasso and Stability Selection. For these latter, the sampling strategy is *sub*. For ESCV and the knockoff method which are based on the gradient descent algorithm, the FDP is showed with E-Net. Tigress is implemented with LARS and the ℓ_1 regularization. The red line indicates 0.1, the threshold for the knockoff method. The dashed red line indicates 0.05.

Similarly with scenarios from independent and Gaussian models, the combination of the E-Net regularization with the LARS achieves the highest value of pROC-AUC. However, this value equals 0.5 for FRANK-max and 0.57 for FRANK-min. All other combinations have values smaller than 0.3. We do not observe improvement by using the nonparanormal transformation of the data. Hence, the quality of the regularization paths has clearly deteriorated on FRANK data. No combination between an algorithm and a regularization function achieves to clearly discriminate the active and non-active variables.

Concerning the MSE, for FRANK-max and FRANK-min, all the methods lead to a MSE value very close to 1. The recall is also deteriorated. The median value of the recall is often 0, except for ESCV and the data-driven penalties for FRANK-max design. But their values remain low around 0.05. We do not observe any improvement by using the nonparanormal transformation of the data. Hence, all the methods fail to select the active variables and when the methods sometimes select variables, these variables are non-active variables, since the estimated FDR is high. The exception is Tigress and the knockoff method, which are very conservative, but they seem to be able to select active variable when the subset is not empty.

5 Discussion

High-dimensional regression is commonly used to model real dependent data when the number of variables is close to or larger than the number of observations. This framework raises many methodological questions and this review aims at highlighting the method performances according to different metrics. For each method, the first step is the minimization of least-squares penalized by a regularization function to construct a collection of possible subsets and the second step is the selection of the best subset. We simulated different settings, each one having its own characteristics: The independent setting is the framework used to establish the properties of the estimators. The settings based on the Gaussian graphical model generate correlated variables but observations have still a Gaussian distribution. The FRANK setting completely deviates from the statistical model assumptions. In these different settings, we evaluated the methods with different point of views: the ability to discriminate the active variables from the others, to predict the variable response, to recover the active variables and, to limit the number of selected variables which are non active. We also considered datasets with a number of observations larger than the number of variables to study their behavior with respect to n .

In our simulation study, we investigated how the choice of the regularization function to penalize the estimation criterion and of the algorithm to optimize the penalized criterion numerically affects the results. We conclude that LARS combined with E-Net is the best combination to discriminate the active and non-active variables in all the settings. Moreover, we observed that the differences between the combinations tend to disappear when the number of observation increases. When data distribution is far from a Gaussian distribution and a dependency structure exists, as we simulated with the FRANK setting, the user should be aware that it becomes difficult to discriminate between active and non-active variables even with LARS and E-Net and it affects the performances of the methods, as already pointed by [49].

The ability to discriminate between active and inactive variables is important but does not necessarily predict the performance of the methods in terms of MSE, recall, specificity and FDR. Indeed we observe that there is no effect of the algorithm and the regularization function on ESCV and the knockoffs method, while LARS combined with E-Net should be favoured for Bolasso, Stability Selection, LinSelect and the data-driven penalties. For eBIC, the MSE and the recall are similar when LARS is combined with E-Net or Lasso whereas the estimated FDR is higher than 0.1 with E-Net and lower than 0.1 with Lasso.

The different settings allow us to discuss the results with respect to the proportion of active variables. When this proportion is about 6% and all the variables are independent, we identified three groups of methods at $n=150$. The first group gathers eBIC, ESCV, the knockoffs method which are predictive, sensitive (a mean recall greater than 0.85) and select very few non-active variables (estimated FDR between 0.05 and 0.08). A second group gathers Linselect and Tigress which are very conservative, but when they select variables, these latter are active variables. In between, we find Bolasso and Stability Selection based on LARS, E-Net and the *sub* strategy which are less predictive and less sensitive than the methods of the first group but their advantage is that they select very rarely non-active variables. The data-driven penalties are as predictive and sensitive as the first group, but at the cost of selecting many non-active variables. When the proportion of active variables is up to 6% and a structure of dependency exists as in the cluster and scale-free-min settings, all the methods, except the data-driven penalties, behave similarly by selecting very few variables or none at all. Moreover, when some variables are selected, there is no guarantee that they are active variables, as almost one out of every two selected variables is non active. With the data-driven penalties, more active variables are recovered more often but at the cost of selecting many non-active variables. When the number of active variables is about 15%, as in the scale-free-max setting, the first group now consists of ESCV and the knockoffs method. Their mean MSE is about 0.35, their mean recall of 0.65 and 0.75 respectively and the estimated FDR remains controlled (estimated FDR of 0.05 and 0.08 respectively). The data-driven penalties constitute a second group close to the first one. Their mean MSE is about 0.40, their recall is better with a mean value of 0.90 but their estimated FDR is about 0.34. The eBIC method joins the group consisting of Bolasso and Stability Selection. Their mean MSE is about 0.45, their recall is between 0.26 and 0.43 but their estimated FDR is about 0.1. Finally Linselect and Tigress constitute the fourth group. these two methods are the most impacted by the dependency structure and their metrics are unsatisfying. In practice, these results suggest that ESCV and the knockoffs method could be a good choice. The knockoff method could select very few variables but since the FDR is controlled, the selected variables seem to be more often active than

inactive variables. ESCV selects more variables but the risk of getting more inactive variables is higher. The results of our simulation study show also that the difficulty of retrieving the active variable depends on their number.

When the sample size increases, all the methods have the expected behavior except Linselect and the knockoff method. Tigress remains a very conservative method but when Tigress selects a variable, there is a high probability that it is an active variable. For the knockoff method, it seems that the construction of the matrix \tilde{X} is impacted by the sample size. Finally the data-driven do not manage the dependency structure, they select a very large number of non active variables without selecting all the active variables.

In this simulation study, we decided to include model selection methods with non-asymptotic properties as LinSelect and the data-driven penalties because there are rarely compare to the others. The performances of LinSelect depends on the number of active variables and are impacted by the dependency structure. Concerning the data-driven penalties, the recall is high but so is the estimated FDR. The data-driven penalties performances seem less impacted by the simulation setting. One reason about the differences between LinSelect and the data-driven penalties may be that data-driven methods are based on a heuristic whereas LinSelect was constructed from an oracle inequality. Moreover, the data-driven penalties require a calibration of the shape penalty and the multiplicative constant 2.5 in (6) has been fixed in a context of detection of changepoints in a signal [13]. This value may be not fitted in a high-dimensional Gaussian linear regression. It may be interesting to investigate this in the future.

The last part of our work is dedicated to datasets that do not verify the assumptions usually made in a high-dimensional Gaussian regression. We observe a deterioration of all the metrics, which means that the Gaussian distribution seems to be an important assumption. Even when we include a data transformation, we do not observe a clear improvement in the metrics. These results corroborate previous studies on the difficulties of using high-dimensional Gaussian regression on transcriptomic data [27, 48], but we show that the difficulties arise first from the ranking of the variables. It may be interesting to investigate this in the future.

6 Additional information

The scripts as well as supplementary figures are available on https://forgemia.inra.fr/GNet/high-dimensional_regression_comparison.

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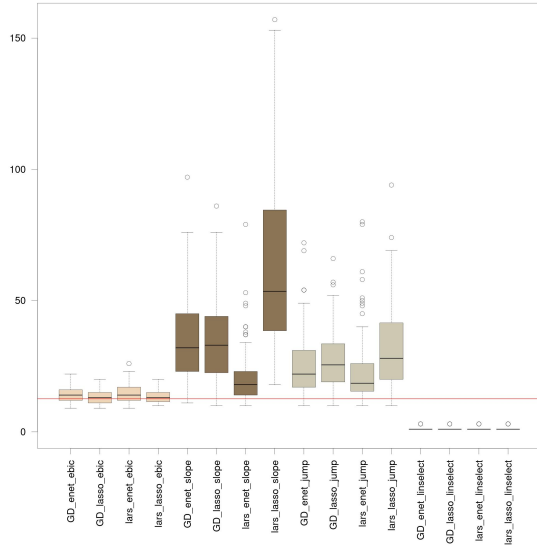
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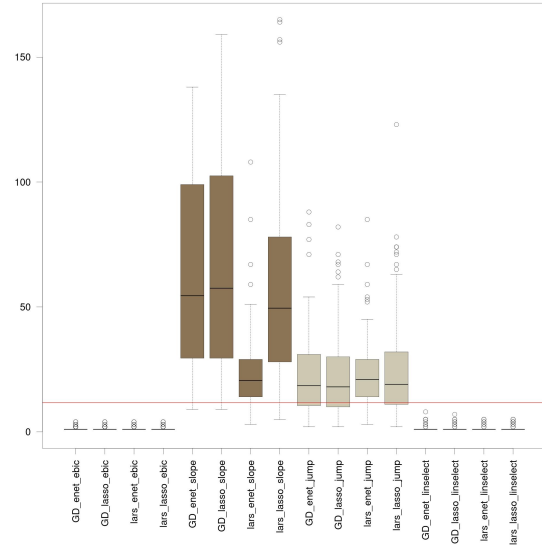
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Appendixes

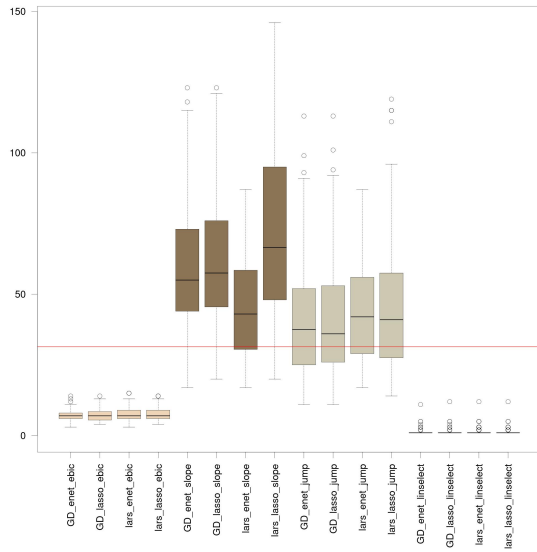
Variable selection in high-dimensional regression



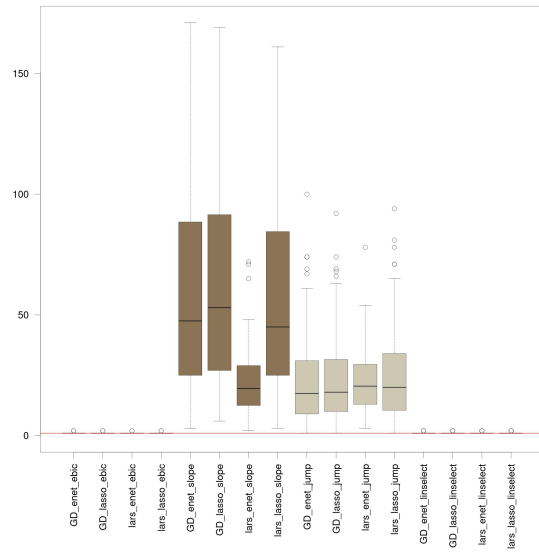
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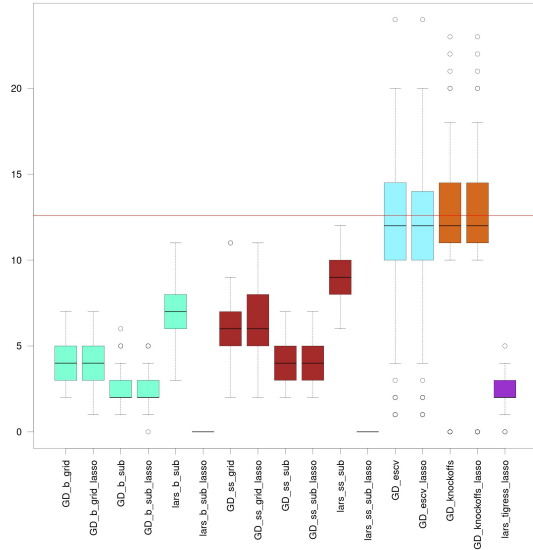
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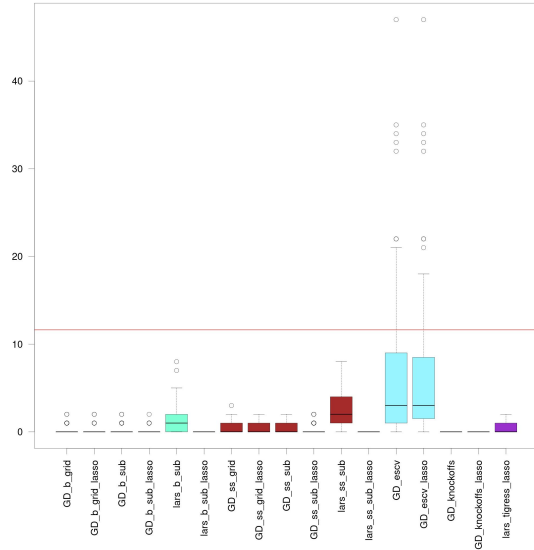
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Figure A1: Boxplots of the size of the support estimated by the model selection procedures from dataset of size $n = 150$ in the four different settings.

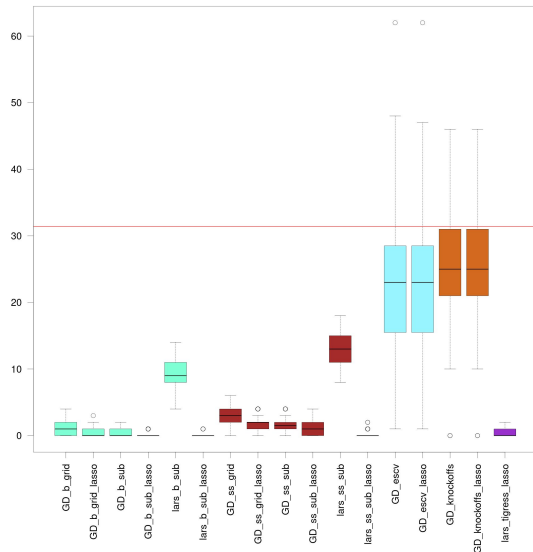
Variable selection in high-dimensional regression



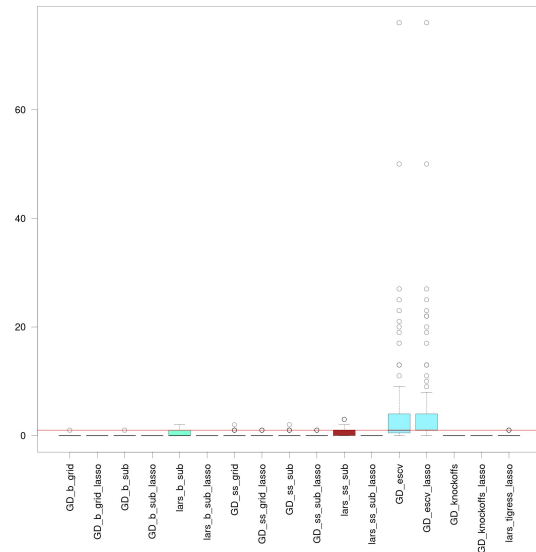
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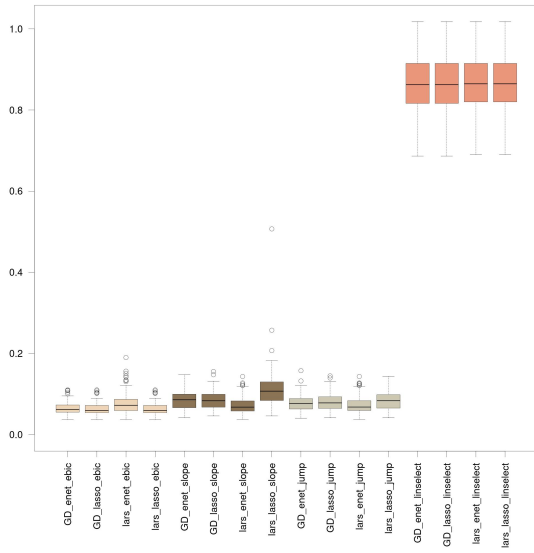
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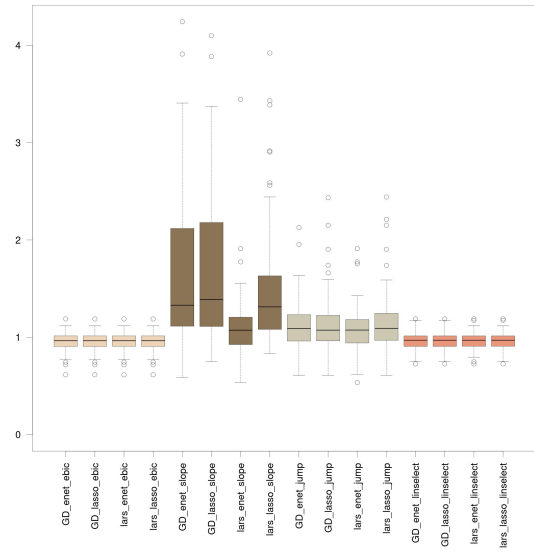
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Figure A2: Boxplots of the size of the support estimated by the variable identification procedures from dataset of size $n = 150$ in the four different settings.

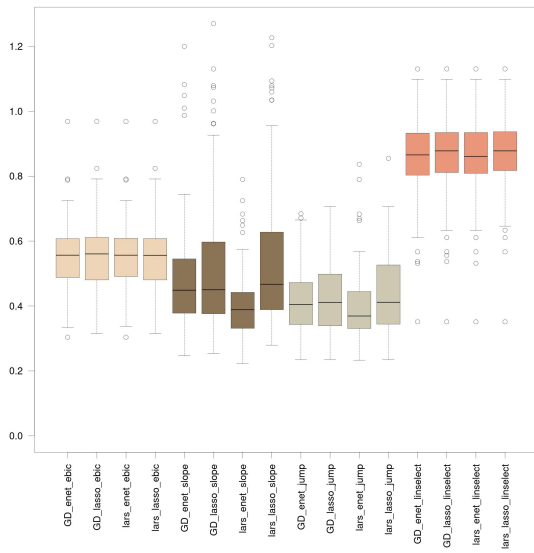
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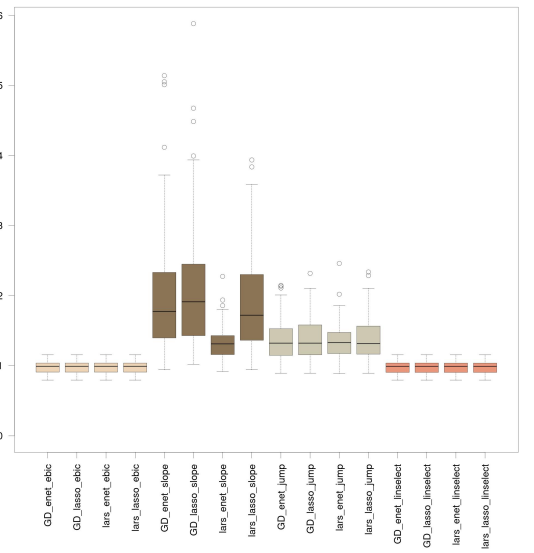
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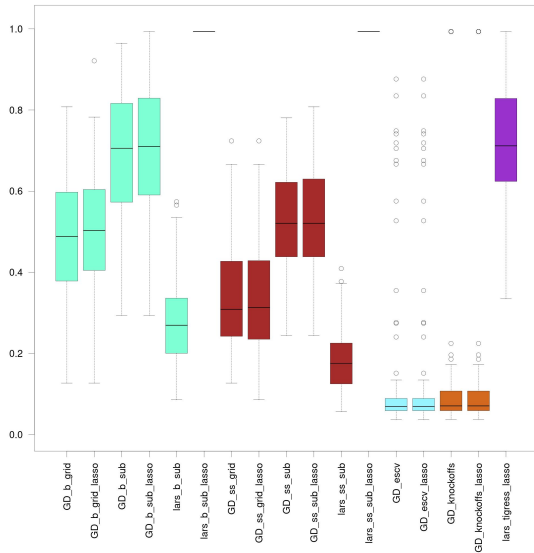
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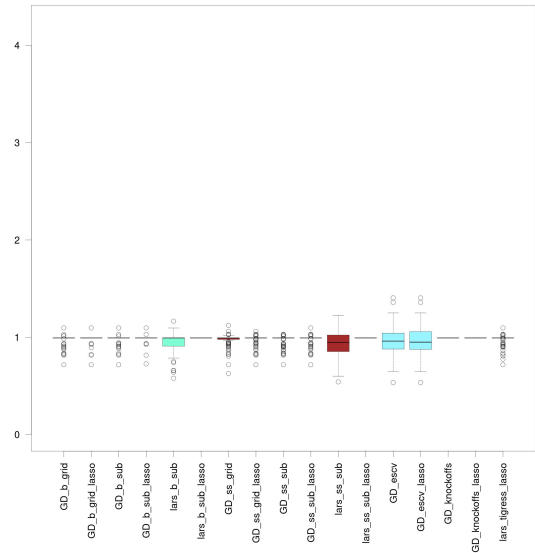
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Figure A3: Boxplots of the MSE values for model selection procedures and for $n = 150$.

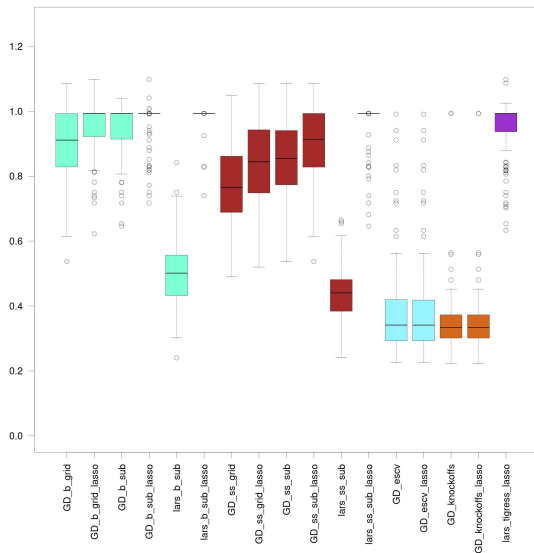
Variable selection in high-dimensional regression



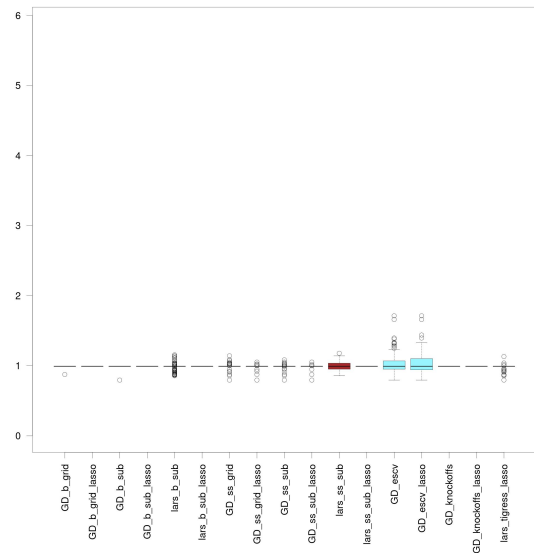
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cluster



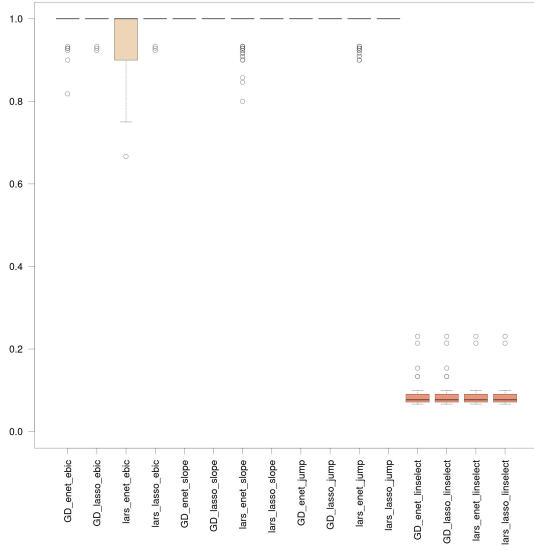
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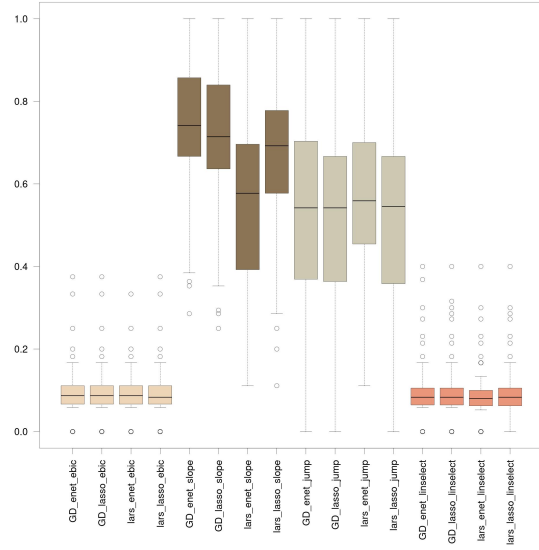
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Figure A4: Boxplots of the MSE values for variable identification procedures and for $n = 150$.

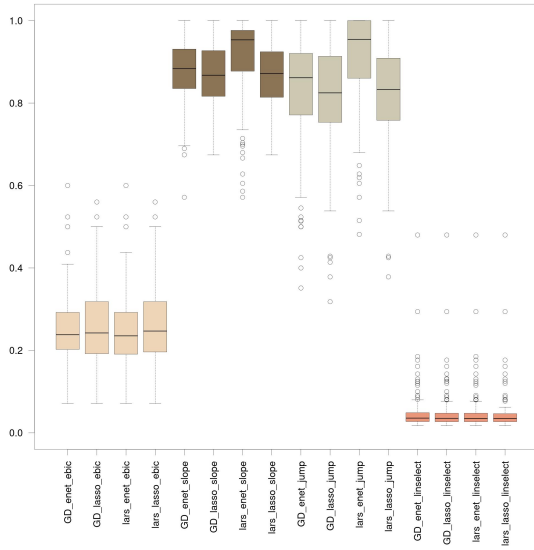
Variable selection in high-dimensional regression



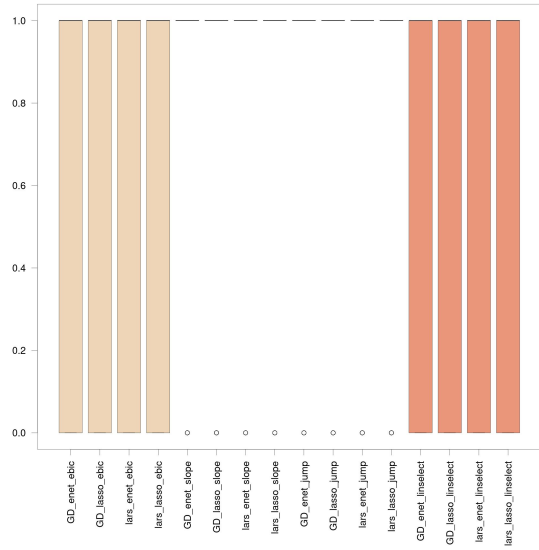
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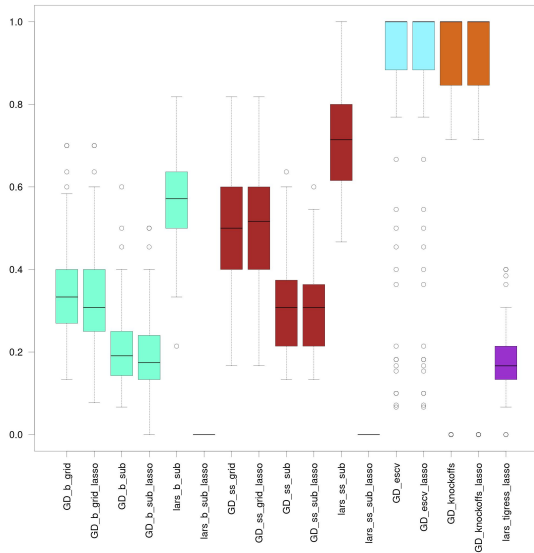
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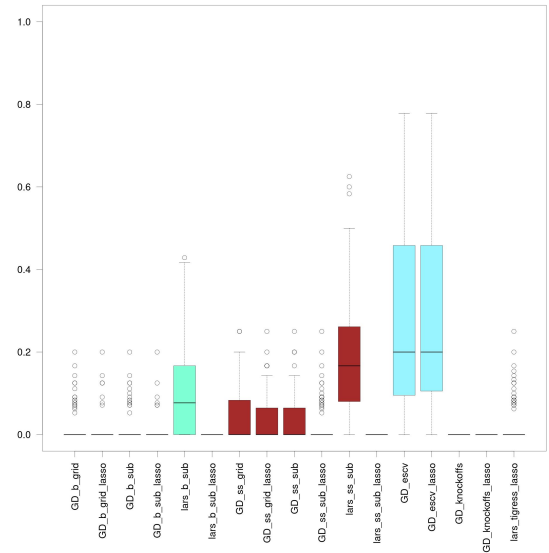
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Figure A5: Boxplots of the recall values for model selection procedures and for $n = 150$.

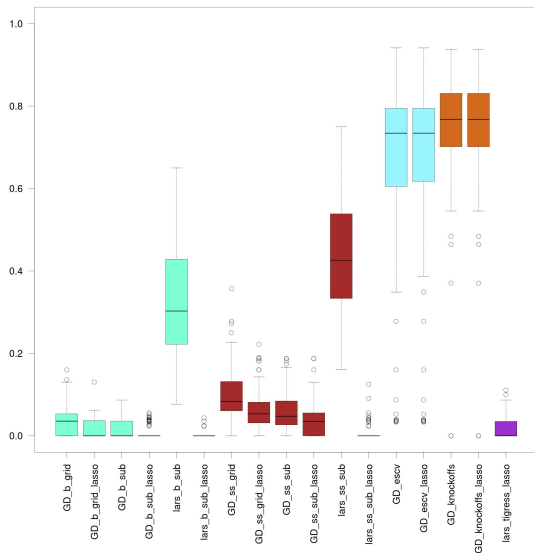
Variable selection in high-dimensional regression



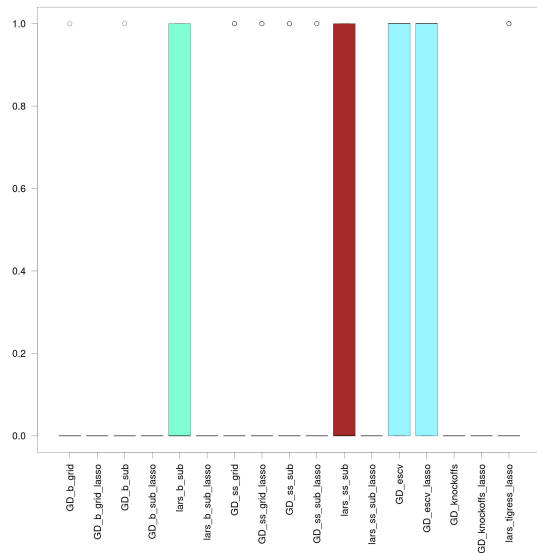
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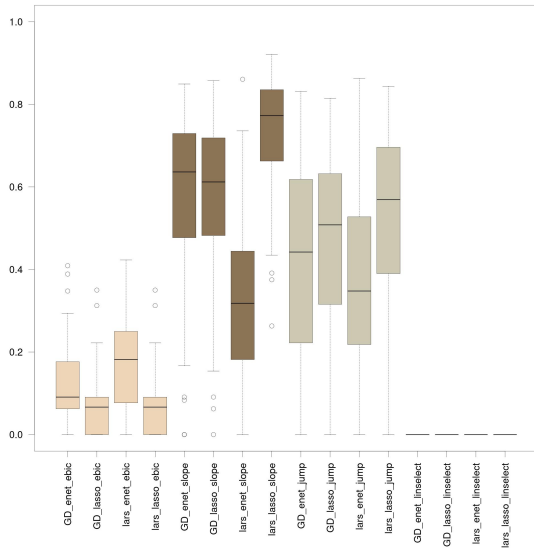
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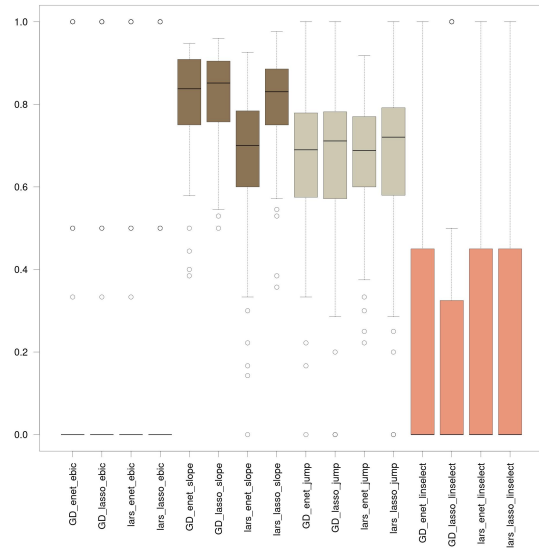
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Figure A6: Boxplots of the recall values for variable identification procedures and for $n = 150$.

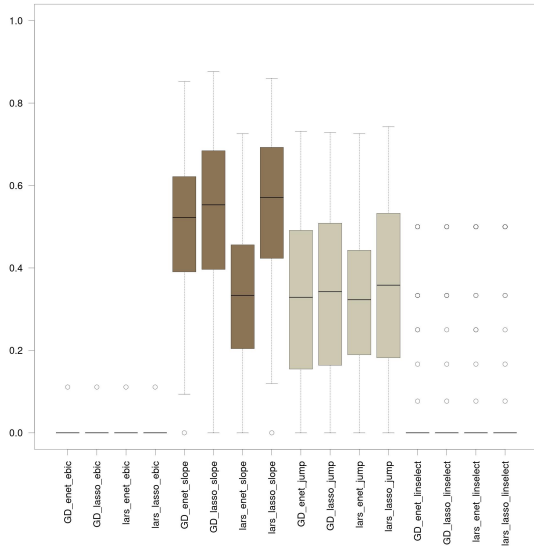
Variable selection in high-dimensional regression



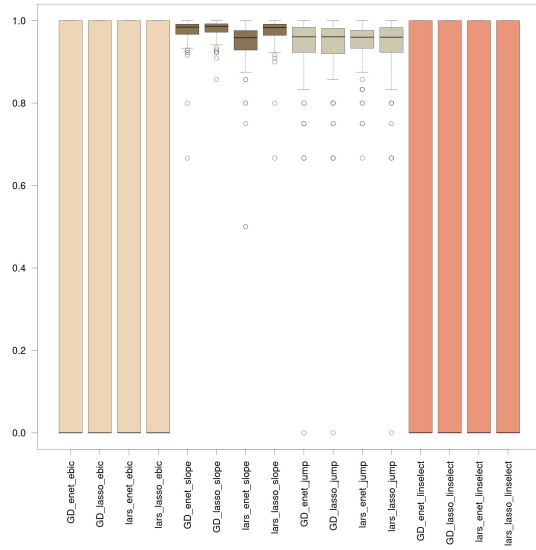
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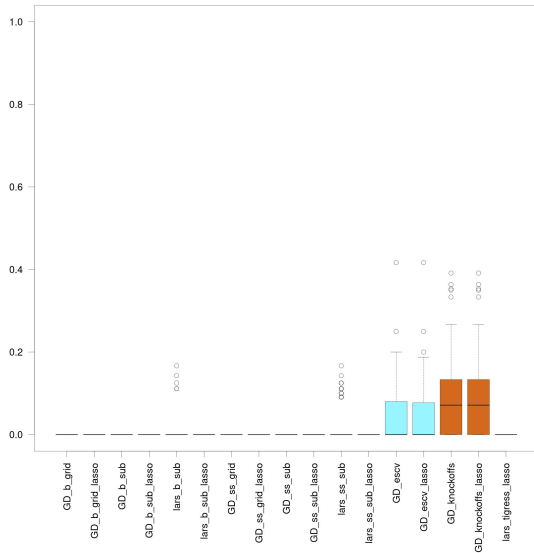
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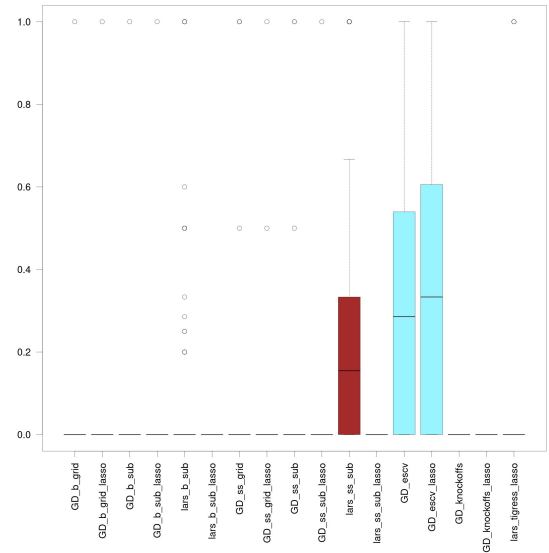
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Figure A7: Estimated FDR for model selection methods and for $n = 150$.

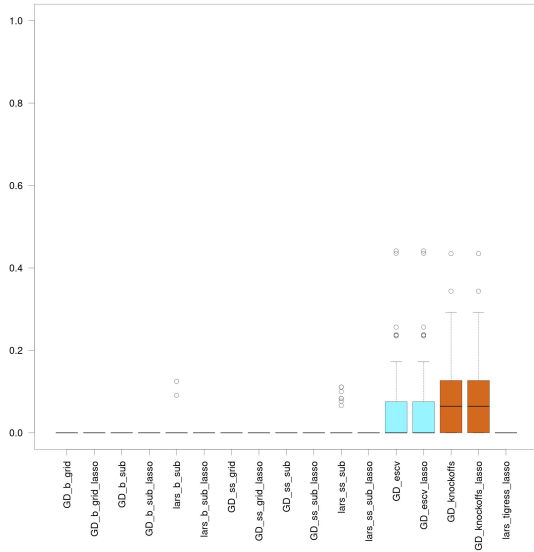
Variable selection in high-dimensional regression



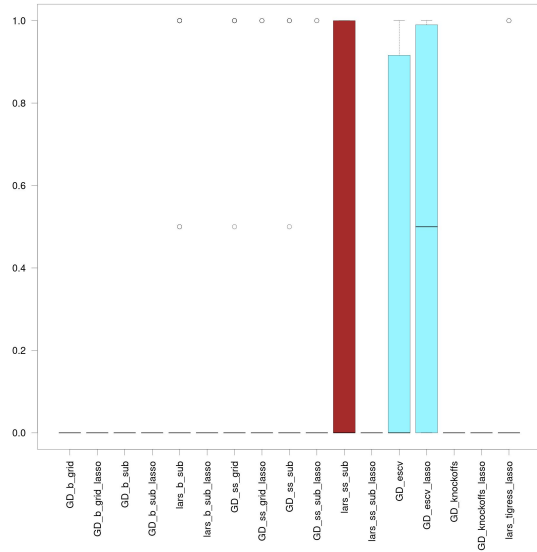
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cluster



scale-free-max



scale-free-min

Figure A8: Estimated FDR for variable identification methods and for $n = 150$.