Correlated Feature Selection with Extended Exclusive Group Lasso

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Abstract
In many high dimensional classification or regression problems set in a biological context, the complete identification of the set of informative features is often as important as predictive accuracy, since this can provide mechanistic insight and conceptual understanding. Lasso and related algorithms have been widely used since their sparse solutions naturally identify a set of informative features. However, Lasso performs erratically when features are correlated. This limits the use of such algorithms in biological problems, where features such as genes often work together in pathways, leading to sets of highly correlated features. In this paper, we examine the performance of a Lasso derivative, the exclusive group Lasso, in this setting. We propose fast algorithms to solve the exclusive group Lasso, and introduce a solution to the case when the underlying group structure is unknown. The solution combines stability selection with random group allocation and introduction of artificial features. Experiments with both synthetic and real-world data highlight the advantages of this proposed methodology over Lasso in comprehensive selection of informative features.

1. Introduction
New technologies, especially the introduction of massively parallel Next Generation Sequencing of DNA have generated an explosion of very high dimensional biological and biomedical data sets. Intensively studied examples include global transcriptomics, typically involving the simultaneous measurement of 20–100 thousand RNA transcripts, and adaptive immune repertoires, typically involving millions of different RNA or DNA sequences per sample. Generally, these data sets are very sparse, in the sense that only a small proportion of the measurements (features) are relevant to the biological process being investigated, while the rest contribute only noise. Furthermore, features often show high levels of correlation, since they represent the activity of biological components acting together in groups to perform a task. Neither the correlation structure, nor the classification of features as informative or not, is usually known a priori.

In this context, identifying the complete set of informative features connected to a particular biological process or outcome is an important task in itself, since it can provide fundamental mechanistic insights into how the process works, and is regulated, or misregulated in disease. Lasso (Tibshirani, 1996) offers a promising approach since the sparse solution given by the $\ell_1$-norm regularization corresponds naturally to the set of informative features. However, Lasso has some limitations in optimal feature selection. First, Lasso finds at most $m$ features when sample size $m$ is much smaller than feature size $n$. This is often the case in many real-world problems. Secondly, choosing the regularization parameter is non-trivial, and optimizing classification does not always give the optimal solution in terms of accurate feature selection (Leng et al., 2006; Zhang et al., 2008). Thirdly, Lasso performs erratically when features are correlated, selecting only a few features from each group of correlated features (Zou & Hastie, 2005). Theoretical analysis shows that for Lasso to select correct features, informative features (features with nonzero weights) cannot be overly correlated with irrelevant features (features with zero weights), or other informative features (Zhao & Yu, 2006; Wainwright, 2009; Raskutti et al., 2011). Therefore, Lasso will not discover all informative features when there is a strong correlation structure in the data.

A number of Lasso-type algorithms have therefore been developed (Figure 1), which introduce a group structure into the global feature set. Group Lasso (Yuan & Lin, 2006) forces inter-group sparsity through an $\ell_2,1$-norm regularization so that features from the same group, such as genes in the same biological pathways, are either selected or deselected simultaneously. However, group Lasso requires the group structure to be predefined through prior knowledge, while in many biological problems, such group structure is unknown. In contrast, the exclusive group Lasso (Kong et al., 2014) adopts a complementary approach, introducing an $\ell_{1,2}$-norm regularization term, which forces intra-group...
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sparsity but relaxes inter-group sparsity. Thus only a few features within each group are selected. If co-correlated informative features are allocated to different groups, the exclusive group Lasso offers a potential solution to the problem of selecting correlated features.

![Diagram of Lasso, GL, and EGL](image)

Figure 1. A comparison of the regularization terms of Lasso, group Lasso (GL), and exclusive group Lasso (EGL).

Although the properties of exclusive group Lasso have been investigated in several studies, these have focused either on examples where group structure was known, or where the informative features were uncorrelated, or where an proper group number was required (Kong et al., 2014; Huai et al., 2018; Manabe et al., 2018; Huang & Liu, 2018; Ming et al., 2019; Zhao et al., 2019). In this paper we examine the performance of exclusive group Lasso in the accurate selection of synthetic and real-world correlated features, and introduce new methods for relaxing its limitations.

In Section 2, we examine the limitations of Lasso on synthetic data and real-world immunological problems, which motivates the evolution of exclusive group Lasso in Section 3 to select biologically meaningful features. In this section, we develop efficient algorithms for solving the exclusive group Lasso. Lasso can be solved by efficient coordinate descent algorithms (Wu & Lange, 2008; Friedman et al., 2007; 2010). In an analogous manner, group Lasso can be solved by fast implementation of block coordinate descent (Qin et al., 2013). Other strategies such as active set have also been used in Lasso (Friedman et al., 2010) and group Lasso (Meier et al., 2008; Vogt & Roth, 2012). In this paper we extend the algorithm proposed in (Kong et al., 2014) in a different re-weighting approach and develop it to carry out coordinate descent with active set to achieve a fast solution for exclusive group Lasso. Section 4 proposes random group allocation with stability selection (Meinshausen & Bühlmann, 2010) and artificial features for solving the problem of unknown group structure. Synthetic experiments that compare Lasso and our methodology are also included in Section 4. Performance of the proposed methodology on real-world problems is validated in Section 5. We summarize our main findings and contributions in Section 6.

### Notation

Throughout this paper, we represent matrices as upper case, non-bold letters. Vectors are represented by lower-case, bold letters. We denote by $y \in \mathbb{R}^m$ the input labels and by $w \in \mathbb{R}^n$ the weight vector. We let $X$ represent an $m \times n$ matrix of input data, $X_j$ denote the $j$-th feature, and $x_{i}^{(j)}$ denote the $i$-th sample. The term “relevant features” or “informative features” represents features with nonzero weights such that $\{X_j : w_j = 0\}$, and “irrelevant features” represents features with zero weights where $\{X_j : w_j = 0\}$. We assume the $X$ are standardized by default.

### 2. Lasso and correlation

In Section 1, we have reviewed that Lasso does not perform well on correlated features. Let us consider a simple experiment to verify this. We generate a dataset such that

$$y = Xw + \epsilon$$

where $\epsilon_i \sim \mathcal{N}(0, \sigma^2), i = 1, \cdots, m$, is Gaussian noise, informative features $X_S \sim \mathcal{N}(0, \Sigma)$, and irrelevant features $X_{-S} \sim \mathcal{N}(0, 1)$. We split the first $n_S = 50$ features into two groups of 25. Features in the same group are pairwise correlated with correlation $\rho \in \{0.1, 0.2, \cdots, 0.9, 0.99\}$. We set the weight vector $w = [s_1w_S, s_2w_S, \cdots, s_{n_S}w_S, 0, \cdots, 0], s_i \in \{-1, +1\}$, where the first 50 entries equal to $w_S = 0.2$ with random signs. Therefore, the first 50 features are relevant and informative, while the remaining features are irrelevant. Figure 2 shows the false discovery rate (FDR) of Lasso with the largest possible $\lambda$ so that all informative features become discovered based on 200 random datasets. As $\rho$ increases, Lasso can only select all informative features at the cost of including irrelevant features.

![False discovery rate vs Correlation](image)

Figure 2. FDR in a feature selection task as a function of the strength of the correlation among the informative features. Selection threshold was set such that all informative features become chosen. Selection method: Lasso, on 200 random datasets.

To study the performance of Lasso on real-world biological problems, we consider a large dataset (Emerson et al.,

...
We used Cohort 1 for training, and Cohorts 2 and 3 for A fundamental dogma of the current model of adaptive immunologically meaningful features, nor achieved high accuracy Clearly, the ℓ CMV . found to be over-represented in individuals infected with ℓ selected by the results are shown in Table 2. Among the 1950 TCRs se- ℓ included the two additional measurements without affecting ℓ the number of unique TCRs to 241,008. We applied a 10- ℓ test. To improve the efficiency, we preselected TCRs that ℓ 2019). Table 1 summarizes the three cohorts. 3) that was collected by Belgium researchers (Neuter et al., ℓ also use another geographically independent dataset (Cohort ℓ 2, for training and test. To further test the performance, we ℓ to predict which individuals were carrying the virus. The ℓ group (reflecting exposure to the virus) and could be used ℓ of TCRs which would be over-represented in the infected ℓ the study therefore addressed was to identify a small set ℓ that CMV-related TCRs are therefore more likely to be de- ℓ (Burnet, 1957), which proposes that T cells recognizing a virus proliferate, and that CMV-related TCRs are therefore more likely to be de- ℓ in individuals infected with CMV. The task which the study therefore addressed was to identify a small set of TCRs which would be over-represented in the infected group (reflecting exposure to the virus) and could be used to predict which individuals were carrying the virus. The dataset contained two independent US cohorts, Cohort 1 and 2, for training and test. To further test the performance, we also use another geographically independent dataset (Cohort 3) that was collected by Belgium researchers (Neuter et al., 2019). Table 1 summarizes the three cohorts.

We used Cohort 1 for training, and Cohorts 2 and 3 for test. To improve the efficiency, we preselected TCRs that occurred in at least 10 samples in Cohort 1. This reduced the number of unique TCRs to 241,008. We applied a 10- fold cross-validation for parameter tuning. As 35 samples were published for 33 patients in Cohort 3, we also in- ℓ included the two additional measurements without affecting ℓ the training model. We implemented a two stage strategy, identifying informative TCRs using ℓ1-regularized SVM (the classification version of Lasso) followed by RBF or linear ℓ2-regularized SVM for classification. Classification results are shown in Table 2. Among the 1950 TCRs selected by the ℓ1-SVM as informative features, only 44 were found to be over-represented in individuals infected with CMV.

Table 1. Description of the CMV dataset.

| Cohort 1 | Cohort 2 | Cohort 3 |
|----------|----------|----------|
| #CMV+    | 289      | 51       | 9        |
| #CMV-    | 352      | 69       | 24       |
| #TCR     | 89,840,865 | 20,829,966 | 2,204,828 |

Clearly, the ℓ1-regularized algorithm neither selected the bi- logically meaningful features, nor achieved high accuracy with the selected features. In the meantime, it is not possible to apply group Lasso to this problem as underlying group structure is unknown. This motivates us to apply and adjust exclusive group Lasso to select correlated CMV-related TCRs without knowing the explicit group structure.

3. From Lasso to exclusive group Lasso

The exclusive group Lasso (Kong et al., 2014) is defined as

$$\min_w f(w) + \lambda \sum_{g \in G} ||w_g||_1$$

where $f(w)$ is a convex loss function, $G$ represents group allocation and $g$ represents indices of group $g \in G$. Kong et al. (2014) presented an iterative algorithm to solve the optimization problem. Let us denote by $I_g \in \{0, 1\}$ a binary group indicator of the $i$-th feature. The algorithm proceeds by alternating the following steps.

Solve: $\nabla_w f(w) + 2\lambda F w = 0$ \hspace{1cm} (3)

Compute $F$: $F_{ii} = \left( \sum_{g \in G} I_g ||w_g||_1 / ||w_i|| \right), F_{ij} = 0, i \neq j$ \hspace{1cm} (4)

3.1. A re-weighting scheme

In this section, we provide an alternative solution to the exclusive group Lasso particularly by solving $w$ in (3) via a re-weighting approach. For convenience we rewrite (2) as

$$\min_w f(Xw, y) + \lambda \sum_g ||w_g||_1$$

which can be further rewritten as

$$\min_w f(Xw, y) + \lambda w^T F w.$$ \hspace{1cm} (6)

Let $w = \sqrt{F} w$ and substitute $w$ with $\sqrt{F}^{-1} w$; the loss function then becomes $f(X \sqrt{F}^{-1} w, y)$. By denoting $X \sqrt{F}^{-1}$ with $\tilde{X}$, (6) can be rewritten as

$$\min_w f(\tilde{X} w, y) + \lambda w^T \tilde{w}.$$ \hspace{1cm} (7)

Therefore, the exclusive group Lasso converts into an optimization problem with re-weighted features $\tilde{X}$ and weights $\tilde{w}$, which can make use of the widely-studied ℓ2-regularized optimization techniques. An additional benefit of the re-weighting step is that it allows us to introduce additional constraints on the values of the weights. For example, bio- logical knowledge would suggest that CMV infection would lead to over-representation of some TCRs, but not necessarily to under-representation of TCRs in the infected group. To capture this biological prior knowledge, we imposed the constraint that weights should be all be of the same sign. We summarize the re-weighting approach with adjustments in Algorithm 1.
3.2. An iterative approach

Exclusive group Lasso with square loss is given by

\[
\min_w ||y - Xw||^2 + \lambda \sum_{g \in G} ||w_g||^2_2 \tag{8}
\]

Luo & Tseng (1992); Tseng (2001) proved that coordinate descent algorithms converge for the problem

\[
\min_x g(x) + \sum_i h_i(x_i) \tag{9}
\]

under these conditions: 1) \(g(x)\) is convex and differentiable; 2) each \(h_i(x_i)\) is convex; and 3) when \(x_i\) is a vector, it cannot overlap with other vectors. Let \(g\) represent the complement of \(g\) in the set of features. Then (8) can be solved by iteratively solving subproblems of individual blocks,

\[
\min_{w_g} ||y_g - X_g w_g||^2 + \lambda ||w_g||_2^2, \tag{10}
\]

where

\[
y_g = y - X_{-g} w_{-g}. \tag{11}
\]

Solving problem (10) is equivalent to solving

\[
\min_{w_g} ||y_g - X_g w_g||^2 + \lambda z ||w_g||_1 \tag{12}
\]

\[s.t. \quad z = ||w_g||_1\]

which can be further rewritten as

\[
\min_{w_g} ||y_g - X_g w_g||^2 + \lambda' ||w_g||_1. \tag{13}
\]

Now (10) has become converted to Lasso with a new regularization parameter \(\lambda' = \lambda z\). Theoretically we can solve (13) with every possible \(\lambda'\) using Lasso, and the optimal solution is recovered when the solution of (13) satisfies

|Algorithm 1| Exclusive group Lasso with re-weighting |
|---|---|
|**Input:** feature space \(X\), labels \(y\), regularization parameter \(\lambda\), group indicator matrix \(I\), groups \(G\), indicator of constraints for biologically meaningful features \(r \in \{0, 1\}\), constrained class \(c \in \{-1, +1\}\)| |
|\(w \leftarrow \frac{1}{n}\)| |
|**while** not converged do |
|\(w_i \leftarrow \text{sign}(w_i) = c \leftarrow \epsilon\), where \(\epsilon\) is a very small number |
|**end if** |
|\(F_{i1} \leftarrow \frac{1}{|g|} \sum_{g \in G} I_g ||w_g||_1 \)| |
|\(\bar{X} \leftarrow X \sqrt{F^{-1}} \)| |
|\(\bar{w} \leftarrow \arg\min_w f(\bar{X} \bar{w}, y) + \lambda \bar{w}^T \bar{w}\) |
|\(w \leftarrow \sqrt{F^{-1}} \bar{w}\) |
|**end while** |
|return \(w\) |

3.3. A faster solution with the active set of features

For large-scale datasets coordinate descent in \(\ell_1\)-regularized methods such as Lasso is often faster than with \(\ell_2\)-regularized methods like ridge regression. We can therefore reduce the computational time of Algorithm 1 by taking advantage of the sparsity of \(\ell_1\)-regularized algorithms such as Algorithm 3. We first run a single iteration over all groups in Algorithm 3, then apply Algorithm 1 with a reduced feature space of features receiving nonzero weights from the other algorithm until convergence. We usually need another cycle of Algorithm 3 on the complete feature space or to check KKT conditions to ensure convergence—if not converged, we simply run Algorithm 1 again on nonzero features. The double-iteration procedure is repeated until convergence. We summarize the combined algorithm in Algorithm 4.

|Algorithm 2| Bisection algorithm to solve \(w_g\) |
|---|---|
|**Input:** features of current group \(X_g\), labels \(y_g\), regularization parameter \(\lambda\), lower bound \(\lambda_1\), upper bound \(\lambda_2\), \(\lambda' \leftarrow \frac{\lambda_1 + \lambda_2}{2}\) |
|\(w_g \leftarrow \text{Lasso}(X_g, y_g, \lambda')\) |
|**if** converged **then** |
|**return** \(w_g, \lambda'\) |
|**else** **if** \(\lambda' < \lambda ||w_g||_1\) **then** |
|**return** Bisection\((X_g, y_g, \lambda, \lambda_1, \lambda_2)\) |
|**else** |
|**return** Bisection\((X_g, y_g, \lambda, \lambda', \lambda_2)\) |
|**end if** |

|Algorithm 3| Iterative exclusive group Lasso |
|---|---|
|**Input:** feature space \(X\), labels \(y\), regularization parameter \(\lambda\), lower bound \(\lambda_1\), upper bound \(\lambda_2\), groups \(G\) |
|\(w \leftarrow 0\) |
|**while** not converged do |
|**for all** \(g \in G\) do |
|\(y_g \leftarrow y - X_{-g} w_{-g}\) |
|\(w_g \leftarrow \text{Bisection}(X_g, y_g, \lambda, \lambda_1, \lambda_2)\) |
|**end for** |
|**end while** |
|**return** \(w\) |

\(|w_g^*||_1 = \frac{\lambda'}{\lambda}\), under the current choice of \(\lambda\). In practice, solving the problem is fairly fast with bisection approaches, given the piecewise linear property of Lasso (Osborne et al., 2000).

Algorithm 2 shows a bisection algorithm to find the optimal solution to (12) and Algorithm 3 shows solution to (8) with block coordinate descent. It is possible to extend Algorithm 3 to other types of loss functions, as long as the loss function is convex and differentiable and the corresponding \(\ell_1\)-norm solver is piecewise linear.
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Algorithm 4 Exclusive group Lasso with active set

Input: feature space $X$, labels $y$, regularization parameter $\lambda$, lower bound $\lambda_1$, upper bound $\lambda_2$, group indicator matrix $I$, groups $G$

$w \leftarrow 0$

while not converged overall do

Run a single iteration over all groups of Algorithm 3

Run Algorithm 1 on features with nonzero weights

until Algorithm 1 converges

end while

return $w$

Table 3. Computational time (s) of exclusive group Lasso.

| $m$  | $n$  | $n_S$ | EGL-AS  | EGL-RW  |
|------|------|-------|---------|---------|
| 1000 | 5000 | 100   | 44.64   | 187.00  |
| 1000 | 5000 | 500   | 224.99  | 167.10  |
| 1000 | 5000 | 1000  | 511.57  | 190.25  |
| 1000 | 10000| 100   | 53.08   | 564.58  |
| 1000 | 10000| 500   | 244.06  | 574.34  |
| 1000 | 10000| 1000  | 579.52  | 600.42  |
| 1000 | 20000| 100   | 82.13   | 2000.66 |
| 1000 | 50000| 100   | 980.87  | 14206.60|
| 10000| 20000| 100   | 1429.97 | 31332.65|
| 10000| 50000| 100   | 3974.49 | 173769.50|

Optimization in (Kong et al., 2014; Ming et al., 2019) computed $w = (XX^T + \lambda F)^{-1}Xy$ for (3), which resulted in 10,221s even when $m = 1000$, $n = 5000$, $n_S = 100$. Therefore we compared the computational time of exclusive group lasso with active set (EGL-AS) and re-weighting scheme (EGL-RW). We randomly generated 1,000 or 10,000 samples with various numbers of features ($n$) and pairwise correlated informative features ($n_S$) at $\rho = 0.9$. We set $|w_S| = 0.3$ with random signs. Exclusive group Lasso was run with fixed groups on 10 $\lambda$s using Scikit-learn (Pedregosa et al., 2011) in Python 2.7. The computational times are reported in Table 3. There is a pronounced speed-up in convergence time once $n$ exceeds 5000.

4. Random group allocation and beyond

4.1. Fixed and random group allocation

As group Lasso, exclusive group Lasso also requires reliable group allocation. Figure 3 shows the empirical probabilities that a feature is selected when other informative or irrelevant features coexist in the same group. The probabilities were averaged over 100 random datasets, each containing 50 relevant features and 150 irrelevant features. As expected, informative features are more likely to be discovered when no other informative features coexist in the same group, while the probability of selecting an irrelevant feature is lower if a group contains at least one informative feature. The ideal group allocation is therefore to allocate each informative (and correlated) feature into a separate group, and set the number of groups to the number of informative features. We refer to this ideal group allocation as “fixed groups”. In most real-world cases informative features are unknown, so groups are allocated randomly (“random groups”).

We compared the performance of Lasso and exclusive group Lasso with fixed and random groups on synthetic datasets that were generated such that $x_i \sim \mathcal{N}(0, \Sigma), \epsilon_i \sim \mathcal{N}(0, \sigma^2), i = 1, \ldots, m$, with $\Sigma$ being the covariance matrix. We inherit the weight vector in Section 2 with the first $n_S$ entries being some scalar $w_S$ with random signs, and the last $n - n_S$ entries being 0. Noise followed a Gaussian distribution $\epsilon_i \sim \mathcal{N}(0, \sigma^2)$. We computed $y = Xw + \epsilon$. To validate the performance on different covariances, four types of $\Sigma$ were considered.

1. Example 1 (pairwise correlation): relevant features are pairwise correlated at correlation $\rho$. This simulates the case when active biological patterns such as genes and TCRs are correlated because of functional similarity.

2. Example 2 (random pairwise correlation): relevant features are pairwise correlated at $\rho$, while some irrelevant features are correlated with randomly selected relevant features at correlation $\rho^2$. Similar real-world examples...
We therefore introduce stability selection to improve the performance of exclusive group Lasso with fixed and random groups. With fixed groups, the stability of feature selection with random group allocation is usually not possible in real-world scenarios. Stability selection combines subsampling with high-dimensional selection algorithms. Meinshausen & Bühlmann (2010) showed that stability selection performs well even when Lasso fails to select correct features. We adapt stability selection with random group allocation in exclusive group Lasso in Algorithm 5. In practice, a threshold for selection probability is required to distinguish informative and irrelevant features. This can be done with cross-validation with an extra parameter to tune. In our experiments, we rely on $k$-means to partition probabilities for informative and irrelevant features. We applied stability selection with 50 iterations to the same datasets used in Table 4 and compared Lasso and exclusive group Lasso with fixed and random groups in Table 5. The introduction of stability selection provided moderate improvement of exclusive group Lasso with random groups in almost all cases. So far, we have tested the performance when $m = n$ under various correlation types in the above experiments. We further examine the results when $m < n$. The table shows the average F measure using stability selection. Exclusive group Lasso with random groups substantially outperformed Lasso in almost all types of data under these high-dimensional conditions.

### Algorithm 5 Stability selection

**Input:** input data $X$, labels $y$, regularization parameter $\lambda$, number of iterations $N$, group $G$

**for** $i = 1 : N$ do

Subsample from $X$ without replacement to generate subsets $X_{I_i}, y_{I_i}$, where $I_i \subseteq \{1, \ldots, m\}$, $|I_i| = \frac{m}{2}$

Run exclusive group Lasso with $X_{I_i}, y_{I_i}$ to select features $\hat{S}^\lambda_i = \{j \mid w^*_j \neq 0\}$

Shuffle $G$ if using random group allocation

**end for**

$\hat{\Pi}_i^\lambda \leftarrow \frac{1}{N} \sum_{i=1}^{N} I\{j \in \hat{S}^\lambda_i\}$

$S^\text{stable} \leftarrow \{j : \hat{\Pi}_j^\lambda \geq \pi\}$

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**Table 4.** F measure of Lasso, exclusive group Lasso with fixed groups (EGL-F) and random groups (EGL-R). EGL outperformed Lasso in almost all experiments.

| Example | $w_S$ | LASSO | EGL-F | EGL-R |
|---------|-------|-------|-------|-------|
| 1       | 0.1   | 0.44  | 0.88  | 0.88  |
|         | 0.3   | 0.54  | 0.97  | 0.94  |
|         | 0.5   | 0.60  | 0.96  | 0.99  |
| 2       | 0.1   | 0.41  | 0.86  | 0.70  |
|         | 0.3   | 0.51  | 0.98  | 0.93  |
|         | 0.5   | 0.56  | 0.97  | 0.91  |
| 3       | 0.1   | 0.44  | 0.58  | 0.48  |
|         | 0.3   | 0.54  | 0.73  | 0.55  |
|         | 0.5   | 0.62  | 0.76  | 0.65  |
| 4       | 0.1   | 0.47  | 0.44  | 0.46  |
|         | 0.3   | 0.52  | 0.58  | 0.53  |
|         | 0.5   | 0.56  | 0.61  | 0.54  |

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**4.2. Stability selection on random groups**

Stability selection combines subsampling with high-dimensional selection algorithms. Meinshausen & Bühlmann (2010) showed that stability selection performs...
The procedure for classification is slightly different since the labels need to remain unchanged. We let the artificial features corresponding to each class follow different distributions, so the first step of the above method becomes

1. Randomly generate $X' \in R^{m \times n_S}$, where rows of positive samples $X'_{i}^+ \sim N(\mu_1, \Sigma_1)$, and rows of negative samples $X'_{i}^- \sim N(\mu_2, \Sigma_2)$. $\Sigma_1, \Sigma_2$ are diagonal covariance matrices.

In practice, we find Gaussian distributed $X'$ and $w'$, such as $X'_{ij} \sim N(\mu_1, \sigma_1^2)$, $w'_j \sim N(\mu_2, \sigma_2^2)$, generally achieve good performance. $w'$ of fixed values also works well in some experiments.

To evaluate the performance of artificial features, we focused on Examples 3 and 4, where Lasso performed similarly or better, with a slightly more challenging task. We set $m = 1000$, $n = 350$, $n_S = 50$ and $\sigma^2 = 0.1$. We increased the correlation level $\rho$ for Example 3 to 0.99, which is very challenging to Lasso, and $\rho = 0.25$ for Example 4 to ensure positive definite covariance. We set $w_S = 0.2$ and furthermore, we restricted the number of positive and negative weights for informative features to be equal (25 positively weighted and 25 negatively weighted informative features). This is challenging for Lasso since the condition for discovering correct features, the irrepresentable condition (Zhao & Yu, 2006), is easily violated. For Example 3, we used 10 blocks of 5 features. The connection probability in Example 4 was set to $\frac{1}{25}$ to simulate the connection in Example 3. We used 70 groups in random group allocation. Artificial features and weights were generated such that $X'_{ij} \sim N(0, 1)$, $w'_j \sim N(0, 0.05)$ (Example 3) or $w'_j \sim N(0, 0.1)$ (Example 4). All experiments were performed with stability selection of 50 iterations on 100 randomly generated datasets. Apart from F measure, we also report the average selection probabilities for informative and irrelevant features in Table 7. Selection probabilities are shown in Figure 4. Lasso performed well on Example 4, perhaps because of the low correlation ($\rho = 0.25$). However, Lasso failed to select a large proportion of informative features in Example 3. Exclusive group Lasso performed well on both examples. The introduction of artificial features led to lower selection probabilities (more “compressed” points as shown in Figure 4) for irrelevant features but higher probabilities for informative features. Therefore, EGL-R(SA) is promising in more difficult cases.

### 4.3. Artificial features

Recalling Figure 3, it is clear that when a group contains only irrelevant features, some irrelevant features from this group are selected. However, to ensure that two informative features are rarely found in the same group, especially taking into consideration that the real number of informative features is usually unknown, the number of groups will be chosen as larger than the estimated number of informative features. A significant proportion of the groups may therefore contain no informative feature. Hence, we propose a novel method to further reduce the risk of including too many irrelevant features by inserting some artificially generated informative features into feature groups.

For a regression problem, this approach involves:

1. Randomly generate $X' \in R^{m \times n_S}$, $w' \in R^{n_S}$ and new labels $y' = y + X'w'$;
2. Insert a feature from $X'$ into each group;
3. Find solution with $[X, X']$ and $y'$;
4. Remove selected artificial features after convergence.

The procedure for classification is slightly different since

| $w_S$ | LASSO(S) | EGL-F(S) | EGL-R(S) |
|-------|----------|----------|----------|
| EXAMPLE 1 | 0.1 | 0.47 | 0.90 | 0.84 |
|         | 0.3 | 0.56 | 0.97 | 0.95 |
|         | 0.5 | 0.61 | 0.96 | 0.94 |
| EXAMPLE 2 | 0.1 | 0.47 | 0.88 | 0.82 |
|         | 0.3 | 0.54 | 0.99 | 0.97 |
|         | 0.5 | 0.58 | 0.97 | 0.95 |
| EXAMPLE 3 | 0.1 | 0.47 | 0.58 | 0.54 |
|         | 0.3 | 0.56 | 0.77 | 0.68 |
|         | 0.5 | 0.56 | 0.77 | 0.68 |
| EXAMPLE 4 | 0.1 | 0.48 | 0.51 | 0.49 |
|         | 0.3 | 0.66 | 0.68 | 0.62 |
|         | 0.5 | 0.77 | 0.74 | 0.64 |

Table 5. F measure of Lasso, EGL-F, and EGL-R with stability selection (S). (S) showed improvements and EGL-R(S) performed better than EGL-R particularly when EGL did not perform well.

Table 6. F measure for $n = 1500$, $w_S = 0.5$. Compared to $n = 100$, Lasso performed worse while EGL had similar F measure.

|        | LASSO(S) | EGL-F(S) | EGL-R(S) |
|--------|----------|----------|----------|
| EXAMPLE 1 | 0.23 | 0.99 | 0.98 |
| EXAMPLE 2 | 0.24 | 0.96 | 0.95 |
| EXAMPLE 3 | 0.28 | 0.69 | 0.64 |
| EXAMPLE 4 | 0.42 | 0.72 | 0.59 |

## 5. Real-world application

For real-world application, let us consider the datasets introduced in Section 2. We generated artificial features for CMV+ and CMV- samples separately such that $x_{(+) \sim N(0, 1), 0.5}$, $x_{(-) \sim N(0, 1)}$, where $x_{(+)}$ and $x_{(-)}$ denote the artificial features of CMV+ and CMV- samples, respec-
Table 7. F measure (F) and mean selection probabilities of informative (I) and irrelevant (IR) features using Lasso, EGL-F(S), EGL-R(S), EGL-R(SA) (random groups with stability selection and artificial features).

|          | Example 3 | Example 4 |
|----------|-----------|-----------|
|          | F         | I         | IR        | F         | I         | IR        |
| LASSO(S) | 0.79      | 0.61      | 0.01      | 0.99      | 1.00      | 0.13      |
| EGL-F(S) | 1.00      | 1.00      | 0.01      | 1.00      | 1.00      | 0.03      |
| EGL-R(S) | 0.99      | 0.81      | 0.12      | 0.93      | 1.00      | 0.53      |
| EGL-R(SA)| 1.00      | 0.82      | 0.10      | 0.94      | 1.00      | 0.46      |

Figure 4. “Stacked” selection probabilities from 100 random datasets. EGL clearly distinguished informative and irrelevant features in both examples while Lasso failed Example 3. Probabilities using EGL-R(SA) were lower for irrelevant features, but higher for informative features than EGL-R(S).

Table 8. Feature selection and classification accuracy on CMV data. #TCR: number of selected TCRs, #CMV+TCR: number of selected TCRs that are over-represented in CMV-infected samples.

|    | $\ell_1$-SVM(S) | EGL-R(SA) |
|----|-----------------|-----------|
| COHORT 2 | LINEAR SVM: 0.65 | 0.88 |
|       | RBF SVM: 0.65   | 0.88    |
| COHORT 3 | LINEAR SVM: 0.51 | 0.89 |
|       | RBF SVM: 0.63   | 0.89    |

class. Again, exclusive group Lasso was only used for TCR selection, while the classification task was performed by SVM. Stability selection with 30 iterations was also applied to feature selection. Similar to Section 2, the proposed method was applied to Cohort 1 for training and Cohort 2 and 3 for test. Parameters were selected by a 10-fold cross-validation. Feature selection results and classification accuracy are reported in Table 8. For feature selection, EGL-R(SA) selects 47 TCRs, all of which are over-represented in CMV+ samples. Compared to $\ell_1$-regularized SVM, EGL-R(SA) achieved much higher accuracy with a sparse set of biologically meaningful features. The finding that EGL-R(SA) can select a very small set of features (47 from > 200,000) which predict CMV status accurately in two independently-generated validation sets suggests the algorithm finds a stable set of informative features. Further biological experiments will be required to validate that these TCRs are indeed specific for CMV.

6. Conclusion

In this paper, we developed fast algorithms to solve exclusive group Lasso, which also allows the possibility to introduce a priori constraints on the values of the weights which may be derived from prior knowledge. Motivated by the challenges of high-dimensional biological datasets, we addressed the problems that informative features are often highly correlated, and neither the number of informative features, nor the underlying correlation structure (i.e. group structure) is usually known. We proposed solutions with stability selection and artificial features for unknown underlying group structure. The exclusive group Lasso, incorporating random group allocation, with stability selection and artificial features, outperformed Lasso and achieved high performance and robust feature selection in a wide range of challenging problems. Future work will be required to further improve model selection and parameter tuning. However, we believe these new feature selection algorithms will prove useful in extracting mechanistic and conceptual understanding from the increasingly complex “omic” datasets being generated across the biomedical domain.
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