Stacked Penalized Logistic Regression for Selecting Views in Multi-View Learning

Wouter van Loon[1], Marjolein Fokkema[1], Botond Szabo[2], and Mark de Rooij[1]

[1]Department of Methodology and Statistics, Leiden University
[2]Mathematical Institute, Leiden University

November 7, 2018

Abstract

In multi-view learning, features are organized into multiple sets called views. Multi-view stacking (MVS) is an ensemble learning framework which learns a prediction function from each view separately, and then learns a meta-function which optimally combines the view-specific predictions. In case studies, MVS has been shown to increase prediction accuracy. However, the framework can also be used for selecting a subset of important views.

We propose a method for selecting views based on MVS, which we call stacked penalized logistic regression (StaPLR). Compared to existing view-selection methods like the group lasso, StaPLR can make use of faster optimization algorithms and is easily parallelized. We show that nonnegativity constraints on the parameters of the function which combines the views are important for preventing unimportant views from entering the model.

We investigate the view selection and classification performance of StaPLR and the group lasso through simulations, and consider two real data examples. We observe that StaPLR is less likely to select irrelevant views, leading to models that are sparser at the view level, but which have comparable or increased predictive performance.

1 Introduction

Integrating information from different feature sets describing the same set of objects is known as *multi-view learning* [1, 2, 3]. Such different feature sets (*views*) occur naturally in biomedical research as different types of omics data (e.g. genomics, transcriptomics, proteomics, metabolomics) [3], but also as the same profiling data summarized at different levels [4], or as different gene sets or genetic pathways [5]. In neuroimaging, views may present themselves as different MRI modalities, such as functional MRI and diffusion-weighted MRI [6], but also as different feature sets computed from the same structural image [7]. As there is a growing interest in integrating multi-omics and imaging data with other sources of information – electronic health records, patient databases, and even social media, wearables and games – the abundance of multi-view data is only expected to increase [8, 9].

One common problem in biomedical research is a high-dimensional joint classification and feature selection problem, where – given different classes of objects – the goal is to identify the features most important for accurate classification [3]. When integrating data from multiple views, a typical approach to this problem is *feature concatenation*: simply aggregating the features from all views into one large feature set and fitting a single model on the complete data [3]. This is also known as *early integration* as the views are combined before any further processing [10]. Commonly used models for feature selection are generalized linear models (GLMs) with an L_1 penalty on the coefficients [*lasso*; 11], or a mixture of L_1 and L_2 penalties [*elastic net*; 12]. Although these methods can obtain sparse solutions by setting some of the coefficients to zero, they do so without regard for the multi-view structure of the data. This structure is important as data from a single view is often collected together so that the largest potential savings in time and costs are made by selecting or discarding entire views, rather than individual features. Or, for example, when views correspond to genetic pathways, the most associated gene in a pathway may not necessarily be the best candidate for therapeutic intervention [5], and selection of complete pathways may be preferable to selecting individual genes.

The *group lasso* [13] is an extension of the lasso which places a penalty on the sum of L_2 norms of predefined groups of features, leading to a lasso fit at the view level (i.e. view selection), and a ridge fit (shrinkage) within views. The group lasso has a single tuning parameter which is typically optimized through cross-validation. It is known, however, that the lasso with prediction-optimal penalty parameter selects too many irrelevant features [14, 15]. Likewise, it can be observed in the simulation study of Yuan and Lin [13] that the group lasso tends to select too many groups. Fitting the group lasso can be slow compared to the regular lasso, as parameter updates are performed block-wise rather than coordinate-wise [16, 17]. Furthermore, if sparsity within views is desired, an additional mixing parameter needs to be optimized [18].

We propose an alternative approach to the view selection problem based on a framework called *multi-view stacking* (MVS) [19, 20]. MVS is a generalization of *stacking* [21] to multi-view data. In stacking, a pool of learning algorithms (the *base-learners*) are fitted on the complete data, and their outputs are combined by another algorithm (the

meta-learner) to obtain a final prediction. The parameterization of the meta-learner is obtained through training on the cross-validated predictions of the base-learners. Since its inception, stacking has been further studied and expanded upon [22, 23, 24]; a more extensive discussion of stacking is provided by Sesmero et al. [25].

In MVS, a base-learner (or pool of base-learners) is trained on each view separately, and a meta-learner is used to combine the predictions of the view-specific models. MVS is thus a *late integration* approach to multi-view learning. Several biomedical studies have applied methods which can be considered a form of MVS, showing improved prediction accuracy compared to single-view models and feature concatenation [7, 19, 26, 27]. Nevertheless, there is no established standard for choosing the base- and meta-learners. Learners which perform well in terms of prediction accuracy often do so at the expense of interpretability (e.g. random forests). Furthermore, applications of MVS have so far focused solely on improving prediction accuracy, ignoring its potential for feature selection. No unified theoretical underpinning is available regarding the performance of MVS in terms of either prediction accuracy or feature selection.

To better understand this popular approach we introduce *stacked penalized logistic regression* (StaPLR): a special case of MVS where penalized logistic regression is used for both the base-learners and the meta-learner. StaPLR has several advantages over other combinations of base- and meta-learners: logistic regression models are easy to interpret; with appropriately chosen penalties it can be used to perform view selection and/or feature selection within views; and for L_1 and L_2 penalties the regularization path is fast to compute even for a very large number of features [28]. To perform view selection, StaPLR can be applied with, for example, an L_2-penalty at the base level and an L_1-penalty at the meta-level, forming a late integration alternative to the group lasso.

Of primary interest is whether StaPLR selects the correct views, that is, whether it can separate the views containing signal from those containing only noise. Additionally, it is of interest how the classifiers produced by StaPLR perform in terms of predictive accuracy. The derived results can be used as an indicator of the view selection potential of the general MVS approach.

The rest of this article is structured as follows. In Section 2.1 we discuss the multi-view stacking algorithm. In Section 2.2 we verify the importance of nonnegativity constraints on the parameters of the meta-learner for preventing degenerate behavior in MVS with a broad class of base-learners, including penalized GLMs. In Section 3 we introduce StaPLR as a special case of MVS. In Section 4 we compare, on simulated data, the view selection and classification performance of StaPLR with that of the group lasso, and in Section 5 we apply both methods to two gene expression data sets. In Section 6 we present our conclusions and relate our results on the performance of StaPLR to the general MVS framework. Theoretical proofs are given in the Appendix.

2 Multi-View Stacking (MVS)

2.1 The MVS Algorithm

Let us denote by $\boldsymbol{X}^{(1)}, ..., \boldsymbol{X}^{(V)}$ a multi-view data set, with $\boldsymbol{X}^{(v)}$ the $n \times m_v$ matrix of features in view v. Note that the views are not required to be disjoint. Let us denote by $\boldsymbol{y} = (y_1, ..., y_n)$ the vector of corresponding outcomes. We define a (supervised) learning algorithm or *learner* A as a function that takes as input a labeled data set and produces as output a learned function $\hat{f}$ mapping input vectors to outcomes.

We define the MVS procedure with two levels as in Algorithm 1. This definition is more general than those given by Li et al. [19] and Garcia-Ceja et al. [20], allowing for general base- and meta-learners, and for multiple learners per view. We denote by $A_{v,b}$ the bth base-learner for view v, with B_v the total number of base-learners for that view. In MVS with two levels we use a single meta-learner A_{meta}, but in general one can use multiple meta-learners and combine their predictions at even higher levels if desired.

The two key components of training any stacked model are (1) training the base-learners, and (2) training the meta-learner. These can be performed in any order, but in Algorithm 1 we first show the training of the base-learners: for each view $\boldsymbol{X}^{(v)}$, $v = 1, ..., V$, we apply the base-learners $A_{v,1}, ..., A_{v,B_v}$ to all n observations of that view to obtain a set of learned functions $\hat{f}_{v,1}, ..., \hat{f}_{v,B_v}$.

To train the meta-learner, we need to obtain a set of cross-validated predictions for each learned function $\hat{f}_{v,b}$. Therefore, we partition the data into K groups, and denote by $S_1, S_2, ..., S_K$ the K-partitioning of the index set $\{1, 2, ..., n\}$. For each fold $k = 1, ..., K$, we apply the learner $A_{v,b}$ to the observations which are not in S_k, which we denote by $\boldsymbol{X}^{(v)}_{i \notin S_k}$, $\boldsymbol{y}_{i \notin S_k}$. We then apply the learned function $\hat{f}_{v,b,k}$ to the observations in S_k to obtain the corresponding cross-validated predictions. Thus we obtain an n-vector of cross-validated predictions for each view and corresponding base-learner, which we denote by $\boldsymbol{z}^{(v,b)}$. We collect these vectors in an $n \times B$ matrix $\boldsymbol{Z}$, where $B = \sum_v B_v$. These cross-validated predictions are then used as the input features for the meta-learner to obtain $\hat{f}_{\text{meta}}$. The final stacked prediction function is then $\hat{f}_{\text{meta}}\big(\hat{f}_{1,1}(\boldsymbol{X}^{(1)}), ..., \hat{f}_{V,B_V}(\boldsymbol{X}^{(V)})\big)$.

It is clear that if the meta-learner is chosen such that it returns sparse models, MVS can be used for view selection. If we choose a single base-learner for each view, the view selection problem is just a feature selection problem involving V features. Compared to feature concatenation, where one has to solve a group-wise feature selection problem involving $\sum_v m_v$ features, this is an easier task. Furthermore, all computations performed on lines 3 and 9 of Algorithm 1 are independent across views, base-learners, and cross-validation folds, and can thus be parallelized to improve the scalability of MVS.

2.2 Nonnegativity Constraints

In the context of stacked regression, Breiman [22] suggested to constrain the parameters of the meta-learner to be nonnegative and sum to one, in order to create a so-called interpolating predictor, i.e. to ensure that the predictions of the meta-learner stay within the

Algorithm 1: Multi-View Stacking (2 levels)

Data: Views $\boldsymbol{X}^{(1)}, \ldots, \boldsymbol{X}^{(V)}$ and outcomes $\boldsymbol{y} = (y_1, \ldots, y_n)$.

for $v = 1$ to V **do**
  for $b = 1$ to B_v **do**
    $\hat{f}_{v,b} = A_{v,b}(\boldsymbol{X}^{(v)}, \boldsymbol{y})$
  end
end
for $v = 1$ to V **do**
  for $b = 1$ to B_v **do**
    for $k = 1$ to K **do**
      $\hat{f}_{v,b,k} = A_{v,b}(\boldsymbol{X}^{(v)}_{i \notin S_k}, \boldsymbol{y}_{i \notin S_k})$
      $\boldsymbol{z}^{(v,b)}_{i \in S_k} = \hat{f}_{v,b,k}(\boldsymbol{X}^{(v)}_{i \in S_k})$
    end
  end
end
$\boldsymbol{Z} = (\boldsymbol{z}^{(1,1)}, \boldsymbol{z}^{(1,2)}, \ldots, \boldsymbol{z}^{(1,B_1)}, \boldsymbol{z}^{(2,1)}, \ldots, \boldsymbol{z}^{(V,B_V)})$
$\hat{f}_{\text{meta}} = A_{\text{meta}}(\boldsymbol{Z}, \boldsymbol{y})$
$\hat{\boldsymbol{y}} = \hat{f}_{\text{meta}}\big(\hat{f}_{1,1}(\boldsymbol{X}^{(1)}), \ldots, \hat{f}_{1,B_1}(\boldsymbol{X}^{(1)}), \hat{f}_{2,1}(\boldsymbol{X}^{(2)}), \ldots, \hat{f}_{V,B_V}(\boldsymbol{X}^{(V)})\big)$

range $[\min_b f_b(\boldsymbol{x}), \max_b f_b(\boldsymbol{x})]$. The sum-to-one constraint proved to be generally unnecessary, but the nonnegativity constraints were crucial in finding the most accurate model combinations [22], a finding corroborated by LeBlanc and Tibshirani [29]. However, in a classification context Ting and Witten [30] found that nonnegativity constraints did not substantially affect classification accuracy.

Here we provide an additional argument in favor of nonnegativity constraints from a view-selection perspective. Consider MVS with a base-learner for which one of the possible learned functions returns a constant prediction, such as the intercept-only model. Such base-learners include L_1- and L_2-penalized GLMs. For penalized base-learners, the tuning parameter is often chosen through cross-validation. If we apply a penalized base-learner to some view which contains only noise (i.e., for each feature in this view the true regression coefficient is zero), then it is not unlikely that the model with the lowest cross-validation error is the intercept-only model.

Now let us partition a view into K groups, and again denote by $S_1, S_2, ..., S_K$ the K-partitioning of the index set $\{1, 2, ..., n\}$. Assuming that for each partitioning the fitted model is the linear intercept-only model, the K-fold cross-validated predictor $\boldsymbol{z} = (z_1, ..., z_n)$ is given by

$$z_i = \frac{1}{n - |S_k|} \sum_{j \notin S_k} y_j \qquad \text{for all } i \in S_k,\ k = 1, ..., K. \tag{1}$$

Given the intercept-only model, the cross-validated predictor is not a function of the

features in the corresponding view. Therefore, this view should ideally obtain a weight of zero in the meta-learner. However, the cross-validated predictor is not independent of the outcome: in view of Lemma 1 the correlation between the cross-validated predictor $\boldsymbol{z}$ and the outcome $\boldsymbol{y}$ is always negative, with the strength of the correlation increasing with the number of folds.

Lemma 1 *Let $\boldsymbol{y} = (y_1, ..., y_n)$ be the outcome variable, and let $\boldsymbol{z}$ be the cross-validated predictor as defined in* (1)*. Let $\sigma^2(\boldsymbol{y})$ and $\sigma^2(\boldsymbol{z})$ be the empirical variance of the vector $\boldsymbol{y}$ (i.e. $\sigma^2(\boldsymbol{y}) = (n-1)^{-1}\sum_{j=1}^{n}(y_j - \bar{y})^2$, with $\bar{y} = n^{-1}\sum_{j=1}^{n} y_j$) and the empirical variance of $\boldsymbol{z}$ (i.e. $\sigma^2(\boldsymbol{z}) = (n-1)^{-1}\sum_{j=1}^{n}(z_j - \bar{z})^2$, with $\bar{z} = n^{-1}\sum_{j=1}^{n} z_j$), respectively. Then the Pearson correlation between $\boldsymbol{y}$ and $\boldsymbol{z}$ is equal to*

$$\rho(\boldsymbol{y}, \boldsymbol{z}) = -\frac{\sum_{k=1}^{K}\Big(\sum_{j \in S_k}(y_j - \bar{y})\Big)^2/(n - |S_k|)}{(n-1)\sigma(\boldsymbol{y})\sigma(\boldsymbol{z})}.$$

Corollary 1.1 *In the special case when all folds are of the same size, i.e. $|S_k| = n/K$,*

$$\rho(\boldsymbol{y}, \boldsymbol{z}) = -\frac{(K-1)\sigma(\boldsymbol{z})}{\sigma(\boldsymbol{y})}.$$

Corollary 1.2 *In the special case of leave-one-out cross-validation, i.e. $K = n$,*

$$\rho(\boldsymbol{y}, \boldsymbol{z}) = -1.$$

This negative correlation is an artifact of the cross-validation procedure and can produce misleading results in the meta-learner. Consider MVS with two views, $\boldsymbol{X}^{(1)}$ and $\boldsymbol{X}^{(2)}$, where all features are standard normal, and again a single base-learner for which one of the possible fitted models is the intercept-only model. Assume that the true relationship between the features and the response is $\boldsymbol{y} = \beta_0 + \boldsymbol{\beta}\boldsymbol{X}^{(2)} + \boldsymbol{\epsilon}$. Then Lemma 2 shows that it can happen that MVS with a linear meta-learner will select the wrong view.

Lemma 2 *Let $\hat{f}_1$ be the linear intercept-only model, with leave-one-out cross-validated predictor $\boldsymbol{z}^{(1)}$. Let $\hat{f}_2$ be a linear model fitted on $\boldsymbol{X}^{(2)}$, with cross-validated predictor $\boldsymbol{z}^{(2)}$, so that $0 < \rho(\boldsymbol{y}, \boldsymbol{z}^{(2)}) < 1$. Then for the linear meta-learner $\beta_0 + \beta_1\hat{f}_1(\boldsymbol{X}^{(1)}) + \beta_2\hat{f}_2(\boldsymbol{X}^{(2)})$, the least-squares parameter estimates are*

$$\hat{\beta}_1 = 1 - n,$$

$$\hat{\beta}_2 = 0.$$

In Lemma 2 a negative weight is given to $\hat{f}_1$ (the intercept-only model), while $\hat{f}_2$ (the model containing signal) is excluded from the meta-learner. The selected view is $\boldsymbol{X}^{(1)}$, which contains only noise. Estimating the coefficients using L_1- or L_2-penalized estimation with tuning parameter selected through cross-validation does not help since the estimated prediction function described in Lemma 2 has zero cross-validation error.

Cross-validation will therefore always select the least-penalized model under consideration, thus providing no meaningful shrinkage of β_1. However, nonnegativity constraints can prevent such degenerate behavior by forcing β_1 to be zero, allowing a nonzero estimate of β_2.

Leave-one-out cross-validation is an extreme case, as for smaller values of K such negative correlations will be lower in magnitude. Nevertheless, the introduced correlations can cause the meta-learner to include superfluous views in the model. This does not need to have large consequences for prediction accuracy, as they simply provide additional intercept terms. However, from a view-selection perspective this is clearly undesirable.

3 Stacked Penalized Logistic Regression (StaPLR)

We define StaPLR as a special case of MVS where we use penalized logistic regression for both the base-learners and the meta-learner. For binary $\boldsymbol{y}$, the logistic regression model is given by

$$\Pr(y_i = 1|\boldsymbol{x}_i) = \frac{1}{1 + \exp(-\beta_0 - \boldsymbol{\beta}^T \boldsymbol{x}_i)}, \tag{2}$$

where $\boldsymbol{x}_i$ is the feature vector corresponding to observation i. Parameter estimates are typically obtained through maximum likelihood estimation. In penalized estimation, a penalty term on $\boldsymbol{\beta}$ is added to the optimization problem. We write the intercept β_0 separately, as it is usually not penalized.

In StaPLR, the parameters for a base-learner b trained on view v are estimated as

$$\hat{\beta}_0^{(v,b)}, \hat{\boldsymbol{\beta}}^{(v,b)} = \underset{\beta_0, \boldsymbol{\beta}}{\arg\max} \left\{ \sum_{i=1}^{n} \left[y_i(\beta_0 + \boldsymbol{\beta}^T \boldsymbol{x}_i^{(v)}) - \log(1 + \exp(\beta_0 + \boldsymbol{\beta}^T \boldsymbol{x}_i^{(v)})) \right] - P_b(\boldsymbol{\beta}, \boldsymbol{\lambda}) \right\}, \tag{3}$$

with $\boldsymbol{\beta} \in \mathbb{R}^{m_v}$, and where $P_b(\boldsymbol{\beta}, \boldsymbol{\lambda})$ is the penalty function, and $\boldsymbol{\lambda}$ the tuning parameter(s). Analogously, the parameters of the meta-learner are estimated as

$$\hat{\beta}_0^{\text{meta}}, \hat{\boldsymbol{\beta}}^{\text{meta}} = \underset{\beta_0, \boldsymbol{\beta}}{\arg\max} \left\{ \sum_{i=1}^{n} \left[y_i(\beta_0 + \boldsymbol{\beta}^T \boldsymbol{z}_i) - \log(1 + \exp(\beta_0 + \boldsymbol{\beta}^T \boldsymbol{z}_i)) \right] - P_{\text{meta}}(\boldsymbol{\beta}, \boldsymbol{\lambda}) \right\}, \tag{4}$$

with $\boldsymbol{\beta} \in \mathbb{R}^B$. In this article we use a single base-learner which we apply to every view, and for which we choose $P(\boldsymbol{\beta}, \boldsymbol{\lambda}) = \lambda_v \|\boldsymbol{\beta}\|_2^2$. For the meta-learner we choose $P_{\text{meta}}(\boldsymbol{\beta}, \boldsymbol{\lambda}) = \lambda_{\text{meta}} \|\boldsymbol{\beta}\|_1$. This way we induce sparsity at the view level and shrinkage within each view, thus providing the configuration most similar to the group lasso model. We use probabilities rather than hard classifications as input for the meta-learner as these values contain information about the uncertainty of the predictions and were previously found to work better in stacked generalization than hard class labels [30]. In order to preserve this information, and because the predictions of the base-learners are already on a common scale, we do not standardize the inputs to the meta-learner. Parameters are estimated using coordinate descent [28]. To select the tuning parameter for each learner,

100 different values of λ are evaluated, and the value with lowest 10-fold cross-validation error is selected.

We demonstrate in our simulations that the addition of nonnegativity constraints on the parameters of the meta-learner improves the view selection performance of StaPLR. When differentiating between StaPLR with and without nonnegativity constraints we use the notation StaPLR$^+$ and StaPLR$^-$, respectively. In coordinate descent, nonnegativity constraints are easily implemented by simply setting coefficients to zero if they become negative during the update cycle [16, 28].

4 Simulations

In this section we compare, on simulated data, the performance of StaPLR with that of the group lasso. In Subsection 4.1 we investigate the view selection performance of both methods under a number of experimental conditions, and in Subsection 4.2 we evaluate the obtained classifiers in terms of area under the receiver operating characteristic curve (AUC). In Subsection 4.3 we investigate the view selection performance of both methods for larger sample sizes, and in Subsection 4.4 we explore how the number of features in a view affects the view selection performance if the amount of signal strength is kept constant.

All simulations are performed in R (version 3.4.0) [31]. Penalized logistic regression models are fitted using the package `glmnet` 1.9-8 [28]. The (logistic) group lasso is fitted using the package `gglasso` 1.3 [17]. All tuning parameters are chosen through 10-fold cross-validation such that the binomial deviance with respect to the left out data is minimized.

4.1 View Selection Performance

We investigate the ability of StaPLR and the group lasso to select the correct views. We use two different sample sizes (n = 200 or 2000) and two different view sizes (m_v = 250 or 2500). We use block correlation structures defined by two parameters, namely the population correlation between features in the same view ρ_w, and the population correlation between features in different views ρ_b. We use three different parameterizations: ($\rho_w = 0.1, \rho_b = 0$), ($\rho_w = 0.4, \rho_b = 0$), and ($\rho_w = 0.4, \rho_b = 0.2$), for a total of $2 \times 2 \times 3 = 12$ experimental conditions.

We generate 30 disjoint views of equal size $\boldsymbol{X}^{(v)}$, $v = 1 \ldots 30$, each consisting of normally distributed features scaled to zero mean and unit variance. Within each view, we randomly determine which features are signal (i.e. have a true relation with the response) and which are noise, using a pre-defined signal probability (π_{sig}) for each view. For example, within a view with signal probability 0.5, each feature has probability 0.5 of having a true relation with the response. We take 5 views with signal probability 1, 5 views with signal probability 0.5, and 20 views with signal probability 0. For each feature we then determine a regression weight β. For the signal features, we take β = 0.04 or -0.04, each with probability 0.5. This effect size was chosen such that with

$n = 200$, $m_v = 250$, and $(\rho_w = 0.4, \rho_b = 0)$, the simulated class probability distribution is approximately uniform. For the noise features, we take $\beta = 0$. We then determine class probabilities $p_i = 1/(1 + \exp(-\beta_0 - \boldsymbol{\beta}^T \boldsymbol{x}_i))$, and class labels $y_i \sim \text{Bernoulli}(p_i)$.

The aim of applying each method is to select the views which contain signal, and discard the others. For each value of π_{sig}, we calculate the observed probability of a view being included in the final model. We perform 100 replications per condition. Box plots over all replications are shown in Figure 1. It can be observed that StaPLR with nonnegativity constraints (StaPLR$^+$) maintains a lower false positive rate than the group lasso regardless of sample size, number of features or correlation structure, with the largest differences seen in the $n = 2000$ case (Figure 1b). It is, however, also more conservative, selecting fewer views in general, including views containing signal. Without the nonnegativity constraints, StaPLR$^-$ sometimes has higher false positive rates than the group lasso, particularly when n is small (Figure 1a).

4.2 Classification Performance

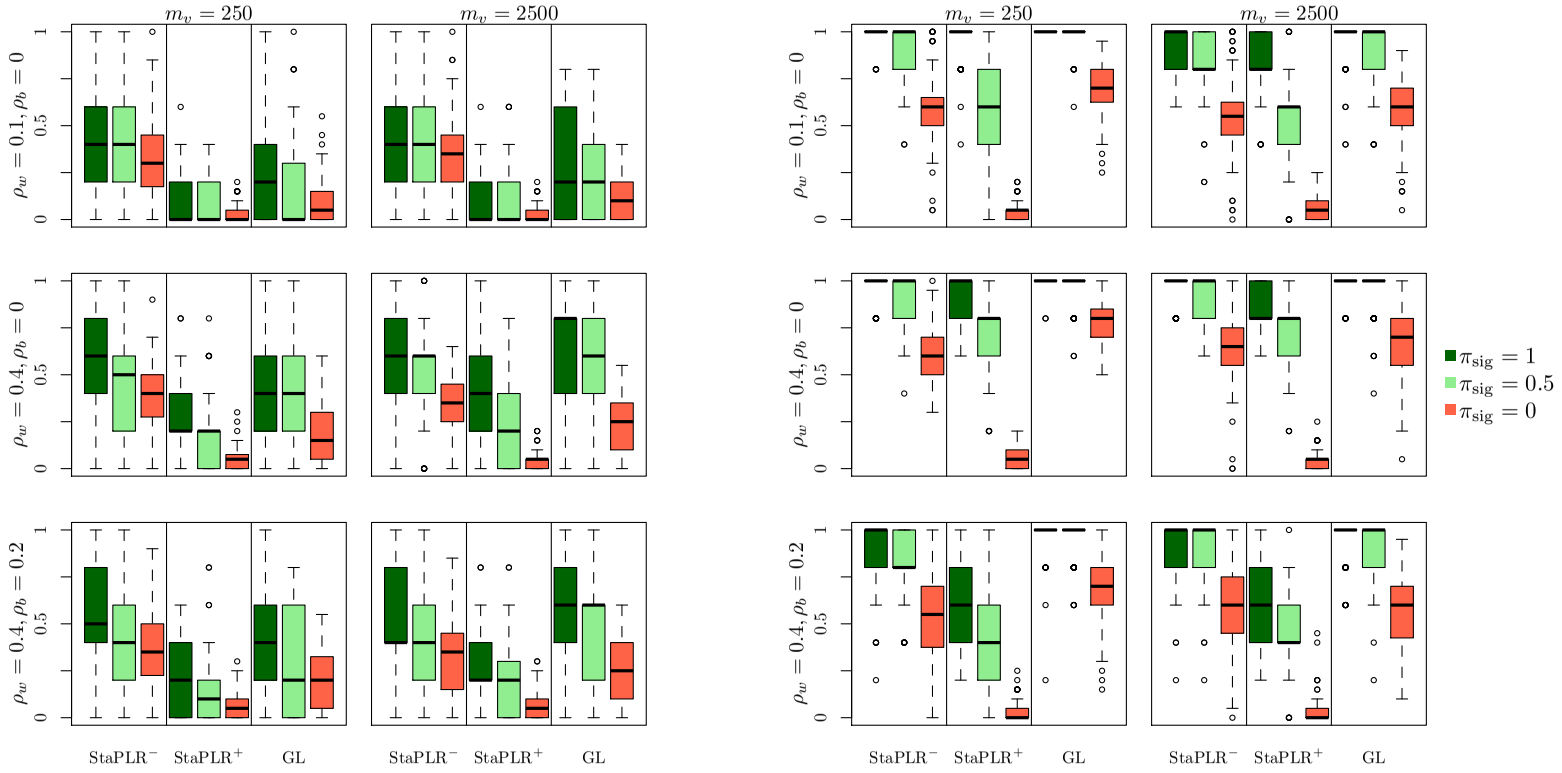
For each replication of each condition from the previous experiment, we generate a test set of size $n = 1000$ and calculate the AUC for each of the three methods. It can be observed in Figure 2 that the different methods have a comparable performance with only minor differences between the AUC distributions.

4.3 Larger Sample Sizes

In this experiment we investigate the view selection behavior of StaPLR and the group lasso for larger sample sizes n. We again use 30 views, but now with 25 features per view, and regression weights $\beta = 0.12$ or -0.12 to create a smaller problem which is more easily upscaled to larger sample sizes. We consider ten different sample sizes ranging between 50 and 10000, and calculate the average inclusion probabilities for each value of π_{sig}. It can be observed in Figure 3 that as n increases, StaPLR$^+$ has an increased probability of selecting views containing signal, while the probability of selecting views containing only noise remains low and even decreases slightly. In contrast, the group lasso and StaPLR$^-$ have an increased probability of selecting both signal and noise views as n increases. Only in some cases for very high values of n is a decrease in the false positive rate observed. StaPLR with nonnegativity constraints consistently has the lowest false positive rate, and at high values of n often perfectly distinguishes signal and noise.

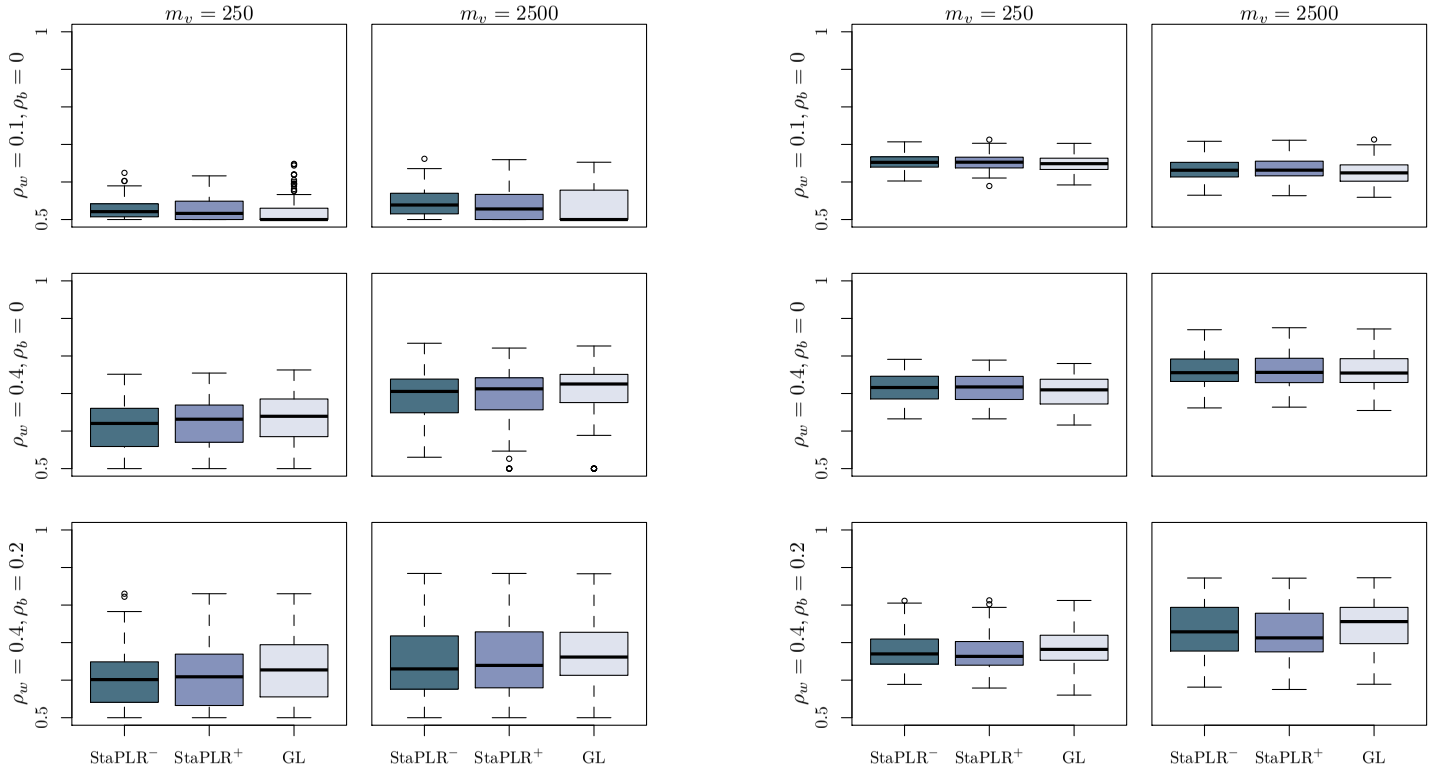
4.4 Different View Sizes

In this experiment we investigate the view selection behavior of StaPLR and the group lasso when views of different sizes are considered at the same time. We consider five different view sizes: 10, 50, 250, 750 and 2500 features. For each view size, we generate one view with signal proportion 1, one view with signal proportion 0.5, and 4 views with signal proportion 0, for a total of 21,360 features across 30 views. We use sample size $n = 2000$, and effect size $|\beta| = 1/\sqrt{m_v}$, where m_v is the number of features in view v.



(a) $n = 200$ **(b)** $n = 2000$

Figure 1: Box plots of the observed inclusion probabilities for views with different values of π_{sig}. The within-view correlation is denoted by ρ_w, the between-view correlation by ρ_b, and the number of features per view by m_d.



(a) $n = 200$ **(b)** $n = 2000$

Figure 2: Box plots of the AUC values for 100 test sets per condition. The within-view correlation is denoted by ρ_w, the between-view correlation by ρ_b, and the number of features per view by m_d.

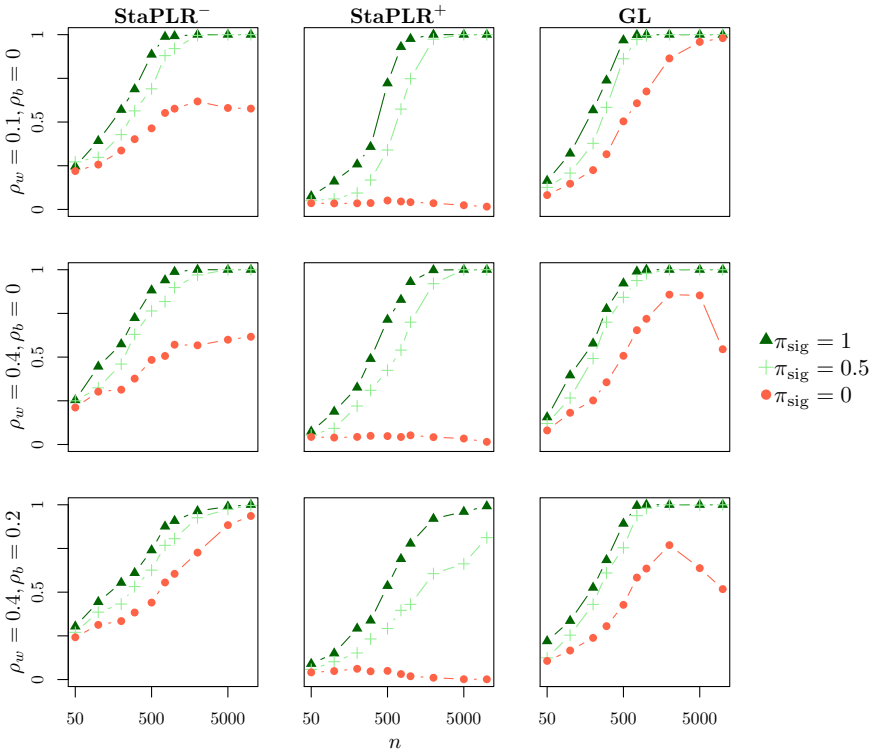


Figure 3: Average inclusion probabilities for different values of π_{sig}, separated by method and correlation structure, across a range of sample sizes. The different sampling points are $n = 50$, 100, 200, 300, 500, 750, 1000, 2000, 5000 and 10000. Note that the distances along the x-axis are on a $\log_{10}$ scale.

The results can be observed in Figure 4. Again, StaPLR$^+$ has the lowest false positive rate, and the inclusion probability of a view containing only noise does not appear to depend on its size. In contrast, the group lasso is more likely to select a view containing only noise if it consists of more features. For views containing signal, it can be observed that larger views are less likely to be included by StaPLR$^+$. This indicates that for views with the same amount of signal strength in an L_2 sense, StaPLR$^+$ favors views containing less features.

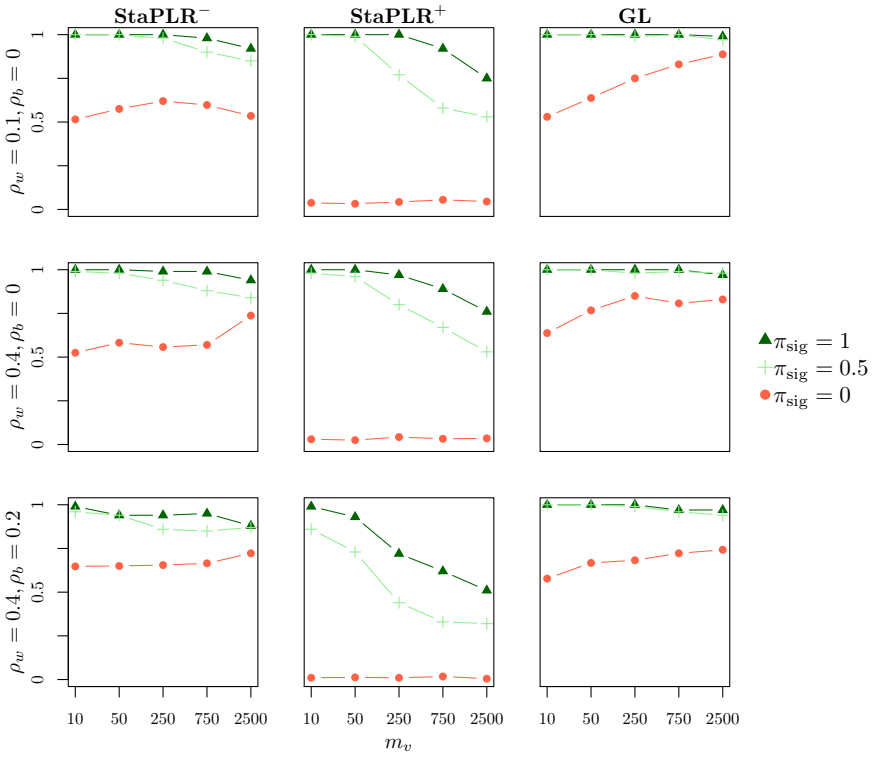


Figure 4: Average inclusion probabilities for different values of π_{sig}, separated by method and correlation structure, as a function of view size.

5 Application to Gene Expression Data

One type of multi-view data occurs in gene expression profiling where genes can be divided into gene sets based on, for example, signaling pathway involvement or cytogenetic position [32]. We base our experiments on the real data examples of Simon et al. [18] by applying StaPLR and the group lasso to two gene expression data sets: the colitis data of Burczynski et al. [33], and the breast cancer data of Ma et al. [34].

The colitis data consists of 127 patients: 85 colitis cases (ulcerative colitis or Crohn's disease) and 42 healthy controls. For each patient, gene expression data was collected using an Affymetrix HG-U133A microarray, containing 22,283 probe sets. We matched this data to the C1 cytogenic gene sets as available from MSigDB 6.1 [32]. We removed any duplicate probes, any genes not included in the C1 gene sets, and any gene sets for which only a single gene was found in the colitis data. Our final feature matrix consisted of 11,761 genes divided across 356 gene sets, with an average of 33 genes per set. All expression levels were $\log_2$-transformed, then standardized to zero mean and unit variance. In Simon et al. [18], the data was randomly split into a training and test set. We apply a similar strategy, randomly splitting the data into two parts of roughly equal size, then using a model fitted on one part to predict the other (i.e. 2-fold cross-

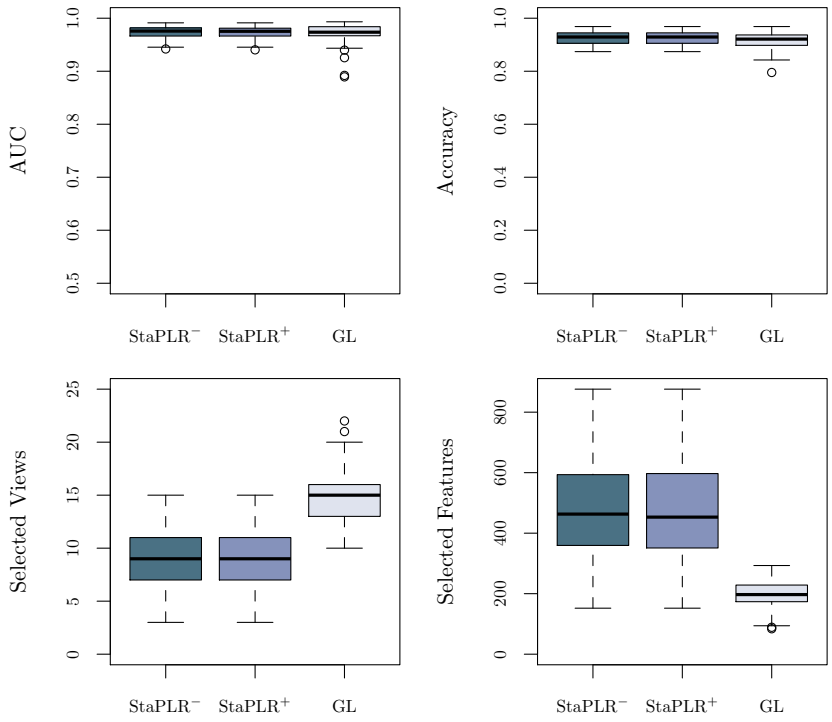


Figure 5: Results of applying StaPLR and group lasso to the colitis gene expression data, in terms of AUC, accuracy, number of selected views and number of selected features.

validation). Additionally, we repeat this process 50 times to account for variability due to the random partitioning. We thus obtain 50 sets of predictions for each of the three methods: StaPLR$^-$, StaPLR$^+$, and the group lasso. We calculate both classification accuracy (using a cut-off of .5) and AUC. Additionally, for each of the 50×2 fitted models, we record the number of selected views (gene sets) and features (genes). The results can be observed in Figure 5. All methods have comparable performance in terms of AUC and accuracy. However, StaPLR selects fewer views but more features, whereas the group lasso selects more views but fewer features. The differences between StaPLR$^+$ and StaPLR$^-$ appear negligible.

The breast cancer data consists of 60 tumor samples of patients diagnosed with estrogen positive breast cancer treated with tamoxifen for 5 years, and are labeled according to whether the patients were disease free (32 cases) or cancer recurred (28 cases). For each sample, gene expression data was collected using an Arcturus 22k microarray. We applied the same procedure of matching the gene expression data to the C1 gene sets, obtaining a feature matrix of 12,722 genes divided across 354 sets, with an average of 36 genes per set. As the data was already $\log_2$-tranformed, we only standardized each feature to zero mean and unit variance. The results can be observed in Figure 6. StaPLR, both with and without nonnegativity constraints, outperforms the group lasso in

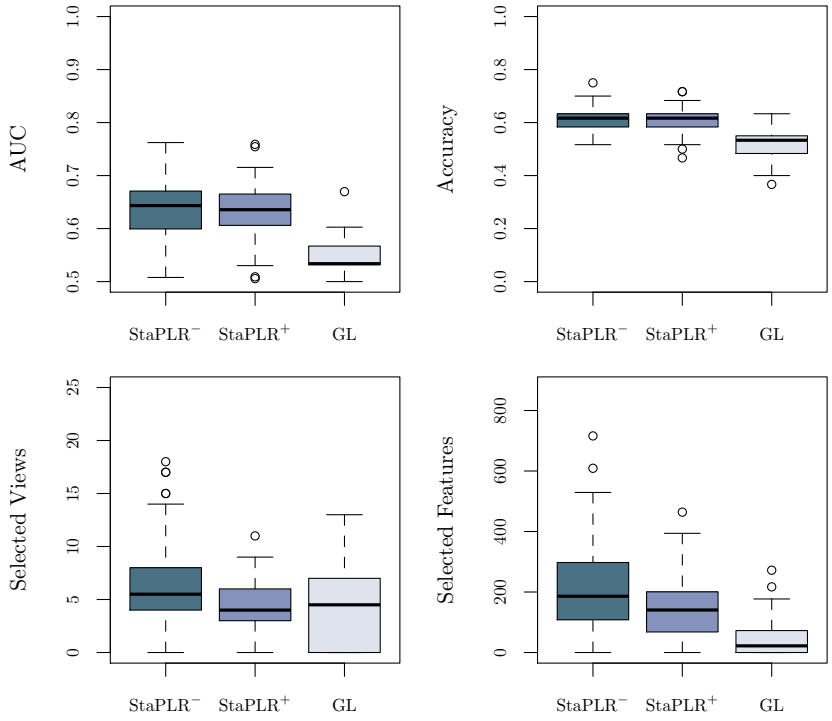


Figure 6: Results of applying StaPLR and group lasso to the breast cancer gene expression data, in terms of AUC, accuracy, number of selected views and number of selected features.

terms of AUC and accuracy. The differences between StaPLR$^+$ and StaPLR$^-$ in terms of AUC and accuracy are negligible, but the addition of nonnegativity constraints leads to fewer views and fewer features selected on average. Compared to the group lasso, StaPLR$^+$ selects on average a similar number of views, but a larger number of features. However, this is in part caused by the fact that the group lasso selects no views at all in 27% of the produced models, whereas StaPLR$^+$ selects no views in only 4% of the models.

6 Conclusion

We have introduced stacked penalized logistic regression (StaPLR) as a late integration view selection method based on multi-view stacking. We have further motivated the use of nonnegativity constraints on the parameters of the meta-learner in MVS with a broad class of base-learners, and shown that such constraints improve the view selection performance of StaPLR. Compared to the group lasso, our simulations have shown that StaPLR with nonnegativity constraints has a much lower false positive rate in terms of the selected views, producing sparser models with a comparable classification performance. In our real data examples StaPLR$^+$ provided similar or better classification

accuracy than the group lasso, while selecting a similar or lower number of views.

Although the models produced by StaPLR in the colitis data were sparser at the view level than those produced by the group lasso, they were not sparser at the feature level: StaPLR$^+$ tended to select a smaller number of views with a larger number of features, while the group lasso tended to select a larger number of views with a smaller number of features. In our simulation experiments on different view sizes (Section 4.4) we observed that StaPLR favored views containing fewer features, under the condition that the views contained the same amount of signal strength in an L_2-sense. Although this condition allowed us to investigate the effect of the number of features in isolation from the effect of signal strength, it is unlikely for such a condition to be satisfied in real data. In its presented form, StaPLR does not explicitly favor smaller views, but if such behavior is desired a scaling factor depending on the number of features can easily be added.

In our simulations, fitting models using StaPLR was considerably faster than the group lasso although in practice this will depend on the number of views, view size, and available computational resources. Nevertheless, our experience suggests that in the event of a small number of views compared to the number of features per view, a large speed-up can be gained even without any parallelization, by using coordinate-wise rather than block-wise updating. Parallelization can increase this computational speed advantage even further.

The parameter space of StaPLR is very restricted compared to applications of MVS with multiple or more complex base-learners. More complex base-learners may be able to capture non-linear relationships, possibly increasing performance further. Changing the meta-learner could have a large effect on the view selection performance of MVS. Nevertheless, the lasso with tuning parameter selected through cross-validation may not necessarily be the best possible meta-learner, and other meta-learners such as stagewise methods or different lasso variants can be considered. However, many other popular meta-learners will not be able to perform automatic view selection (e.g. random forests), and have limited use for a reduction in data collection time and costs.

In this article we compared a specific parameterization of StaPLR with the group lasso, and found that StaPLR provides a fast and accurate alternative. Our aim was to select or discard entire views. If sparsity within views is desired, this could be achieved by simply choosing an L_1 penalty for the base-learner. This indicates that StaPLR may also form an alternative to other complex penalties such as the sparse group lasso [18].

A Proof of Lemma 1, Corollary 1.1 and 1.2

The Pearson correlation between the cross-validated predictor $\boldsymbol{z}$ and the outcome $\boldsymbol{y}$ is defined as

$$\rho(\boldsymbol{y}, \boldsymbol{z}) = \frac{\sum_{j=1}^{n}(y_j - \bar{y})(z_j - \bar{z})}{(n-1)\sigma(\boldsymbol{y})\sigma(\boldsymbol{z})}.$$

To show that this correlation is always negative we introduce a change of variables. Let $a_j = y_j - \bar{y}$, $j = 1, ..., n$, and $\boldsymbol{b} = (b_1, b_2, ..., b_n)$ be the corresponding K-fold cross-validated predictor. Let us denote by b_k^* the value of the predictor in group S_k, $k = 1, ..., K$. Note that $b_j = z_j - \bar{y}$ and that $\sigma(\boldsymbol{z}) = \sigma(\boldsymbol{b})$, $\sigma(\boldsymbol{y}) = \sigma(\boldsymbol{a})$. Then

$$\rho(\boldsymbol{y}, \boldsymbol{z}) = \rho(\boldsymbol{a}, \boldsymbol{b}) = \frac{\sum_{j=1}^{n} a_j (b_j - \bar{b})}{(n-1)\sigma(\boldsymbol{a})\sigma(\boldsymbol{b})} = \frac{\sum_{k=1}^{K} (b_k^* - \bar{b}) \sum_{j \in S_k} a_j}{(n-1)\sigma(\boldsymbol{a})\sigma(\boldsymbol{b})}.$$

By noting that $\sum_{k=1}^{K} \sum_{j \in S_k} a_j = \sum_{j=1}^{n} a_j = \sum_{j=1}^{n} y_j - n\bar{y} = 0$ and $\sum_{j \in S_k} a_j = -\sum_{j \notin S_k} a_j$ we get that the numerator on the right hand side of the preceding display is further equal to

$$\begin{aligned}
\sum_{k=1}^{K} (b_k^* - \bar{b}) \sum_{j \in S_k} a_j &= \sum_{k=1}^{K} \Big(b_k^* \sum_{j \in S_k} a_j \Big) \\
&= \sum_{k=1}^{K} \Big(\frac{\sum_{j \notin S_k} a_j}{n - |S_k|} \sum_{j \in S_k} a_j \Big) \\
&= -\sum_{k=1}^{K} \frac{(\sum_{j \in S_k} a_j)^2}{n - |S_k|},
\end{aligned}$$

where the term on the right hand side is smaller than or equal to zero and it is exactly zero if in all folds S_k, $k = 1, ..., K$ the sum of a_j is zero (i.e. $\sum_{j \in S_k} a_j = 0$). This means that in all folds the average of the observations has to be the same as the total average $\bar{y}$, otherwise the correlation between the vectors will be negative. The final formula for the correlation is then given by

$$\rho(\boldsymbol{y}, \boldsymbol{z}) = -\frac{\sum_{k=1}^{K} \Big(\sum_{j \in S_k} (y_j - \bar{y}) \Big)^2 / (n - |S_k|)}{(n-1)\sigma(\boldsymbol{y})\sigma(\boldsymbol{z})}.$$

Next we consider the special case when all folds are of the same size (i.e. $|S_k| = n/K$, for all $k = 1, ..., K$). Note that in this case $\bar{z} = \bar{y}$, and the formula simplifies to

$$\begin{aligned}
\rho(\boldsymbol{y}, \boldsymbol{z}) &= -\frac{\sum_{k=1}^{K} \Big(n\bar{y} - \sum_{j \notin S_k} y_j - |S_k|\bar{y} \Big)^2 / (n - |S_k|)}{(n-1)\sigma(\boldsymbol{y})\sigma(\boldsymbol{z})} \\
&= -\frac{\sum_{k=1}^{K} (n - |S_k|) \Big(\bar{z} - z_k^* \Big)^2}{(n-1)\sigma(\boldsymbol{y})\sigma(\boldsymbol{z})} \\
&= -\frac{(K-1) \sum_{k=1}^{K} |S_k| \Big(\bar{z} - z_k^* \Big)^2}{(n-1)\sigma(\boldsymbol{y})\sigma(\boldsymbol{z})} \\
&= -\frac{(K-1)\sigma(\boldsymbol{z})}{\sigma(\boldsymbol{y})}.
\end{aligned}$$

In the special case of leave-one-out cross-validation $K = n$. To show that in this case $\rho(\boldsymbol{y}, \boldsymbol{z}) = -1$ it suffices, by the preceding display, to show that $\sigma(\boldsymbol{z}) = \sigma(\boldsymbol{y})/(n-1)$:

$$\begin{aligned}
\sigma^2(\boldsymbol{z}) &= \frac{1}{n-1}\sum_{j=1}^{n}\Big(z_j - \bar{z}\Big)^2 \\
&= \frac{1}{n-1}\sum_{j=1}^{n}\Big(\bar{y}_{(-j)} - \bar{y}\Big)^2 \\
&= \frac{1}{n-1}\sum_{j=1}^{n}\Big(\frac{n\bar{y}}{n-1} - \frac{y_j}{n-1} - \bar{y}\Big)^2 \\
&= \frac{1}{(n-1)^3}\sum_{j=1}^{n}\Big(\bar{y} - y_j\Big)^2 \\
&= \frac{\sigma^2(\boldsymbol{y})}{(n-1)^2}.
\end{aligned}$$

B Proof of Lemma 2

Let $\hat{f}_1$ be the linear intercept-only model, with leave-one-out cross-validated predictor $\boldsymbol{z}^{(1)}$. Let $\hat{f}_2$ be a second model, with leave-one-out cross-validated predictor $\boldsymbol{z}^{(2)}$, where $0 < \rho(\boldsymbol{y}, \boldsymbol{z}^{(2)}) < 1$. Since $\rho(\boldsymbol{y}, \boldsymbol{z}^{(1)}) = -1$, it follows that $\rho(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)}) = -\rho(\boldsymbol{y}, \boldsymbol{z}^{(2)})$.

For the linear meta-learner $\beta_0 + \beta_1\hat{f}_1(\boldsymbol{X}^{(1)}) + \beta_2\hat{f}_2(\boldsymbol{X}^{(2)})$, the least-squares parameter estimate of β_1 is given by [35]

$$\hat{\beta}_1 = \frac{1}{\gamma}\Big(\sigma^2(\boldsymbol{z}^{(2)})\mathrm{cov}(\boldsymbol{y}, \boldsymbol{z}^{(1)}) - \mathrm{cov}(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)})\mathrm{cov}(\boldsymbol{y}, \boldsymbol{z}^{(2)})\Big),$$

where $\sigma^2(\cdot)$ denotes the empirical variance, $\mathrm{cov}(\cdot, \cdot)$ denotes the empirical covariance, and $\gamma = (1 - \rho^2(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)}))\sigma^2(\boldsymbol{z}^{(1)})\sigma^2(\boldsymbol{z}^{(2)})$. We can rewrite this in terms of correlations as

$$\begin{aligned}
\hat{\beta}_1 &= \frac{1}{\gamma}\Big(\rho(\boldsymbol{y}, \boldsymbol{z}^{(1)}) - \rho(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)})\rho(\boldsymbol{y}, \boldsymbol{z}^{(2)})\Big)\sigma^2(\boldsymbol{z}^{(2)})\sigma(\boldsymbol{z}^{(1)})\sigma(\boldsymbol{y}) \\
&= \frac{(\rho^2(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)}) - 1)\sigma^2(\boldsymbol{z}^{(2)})\sigma(\boldsymbol{z}^{(1)})\sigma(\boldsymbol{y})}{(1 - \rho^2(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)}))\sigma^2(\boldsymbol{z}^{(2)})\sigma^2(\boldsymbol{z}^{(1)})} \\
&= -\frac{\sigma(\boldsymbol{y})}{\sigma(\boldsymbol{z}^{(1)})} \\
&= -\frac{\sigma(\boldsymbol{y})}{\sigma(\boldsymbol{y})/(n-1)} \\
&= 1 - n.
\end{aligned}$$

Analogously, we can obtain the least-squares estimate of β_2:

$$\begin{aligned}\hat{\beta}_2 &= \frac{1}{\gamma}\Big(\rho(\boldsymbol{y}, \boldsymbol{z}^{(2)}) - \rho(\boldsymbol{z}^{(1)}, \boldsymbol{z}^{(2)})\rho(\boldsymbol{y}, \boldsymbol{z}^{(1)})\Big)\sigma^2(\boldsymbol{z}^{(1)})\sigma(\boldsymbol{z}^{(2)})\sigma(\boldsymbol{y}) \\ &= \frac{1}{\gamma}\Big(\rho(\boldsymbol{y}, \boldsymbol{z}^{(2)}) - \rho(\boldsymbol{y}, \boldsymbol{z}^{(2)})\Big)\sigma^2(\boldsymbol{z}^{(1)})\sigma(\boldsymbol{z}^{(2)})\sigma(\boldsymbol{y}) \\ &= 0.\end{aligned}$$

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