

Variable Importance in High-Dimensional Settings Requires Grouping

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Abstract

Explaining the decision process of machine learning algorithms is nowadays crucial for both a model’s performance enhancement and human comprehension. This can be achieved by assessing the variable importance of single variables, even for high-capacity non-linear methods, e.g. Deep Neural Networks (DNNs). While only removal-based approaches, such as Permutation Importance (*PI*), can bring statistical validity, they return misleading results when variables are correlated. Conditional Permutation Importance (*CPI*) bypasses *PI*’s limitations in such cases. However, in high-dimensional settings, where high correlations between the variables cancel their conditional importance, the use of *CPI* as well as other methods leads to unreliable results, besides prohibitive computation costs. Grouping variables statistically via clustering or some prior knowledge gains some power back and leads to better interpretations. In this work, we introduce *BCPI* (Block-Based Conditional Permutation Importance), a new generic framework for variable importance computation with statistical guarantees handling both single and group cases. Furthermore, as handling groups with high cardinality (such as a set of observations of a given modality) are both time-consuming and resource-intensive, we also introduce a new stacking approach extending the DNN architecture with sub-linear layers adapted to the group structure. We show that the ensuing approach extended with stacking controls the type-I error even with highly-correlated groups and shows top accuracy across benchmarks. Furthermore, we perform a real-world data analysis in a large-scale medical dataset where we aim to show the consistency between our results and the literature for a biomarker prediction.

1 Introduction

Machine Learning (ML) algorithms are extensively used in many fields of science, such as biomedical application (Strzelecki and Badura 2022; Alber et al. 2019), neuroscience (Kora et al. 2021; Knutson and Pan 2020), and social sciences (Lundberg, Brand, and Jeon 2022; Chen et al. 2021). The increasing importance of ML in society raises issues of accountability, hence, stimulating research on interpretable ML. Reaching a comprehensive understanding of

the decision process is crucial for providing statistical and, ideally, scientific insights to the practitioner (Gao et al. 2022; Molnar et al. 2021a; Fleming 2020; Hooker et al. 2019).

To gauge the impact of variables on model prediction, aka *variable importance*, several model-agnostic attempts have emerged (Molnar 2022; Ribeiro, Singh, and Guestrin 2016). Examples include *Permutation Feature Importance (PFI)* (Breiman 2001), *Conditional Randomization Test* (Candes et al. 2017) and *Leave-One-Covariate-Out (LOCO)* (Lei et al. 2018). All these instances constitute removal-based approaches (Covert, Lundberg, and Lee 2020), and are so far, the only ones known to provide statistically grounded measures of significance. Importantly, removal-based approaches require retraining the model after removing the variable of interest and are, therefore, time-consuming. Moreover, the common Permutation Importance (*PI*, Breiman 2001) risks mistaking insignificant variables for significant ones when variables are correlated (Hooker, Mentch, and Zhou 2021). Conditional Permutation Importance *CPI* can overcome these limitations (Blesch, Watson, and Wright 2023; Watson and Wright 2021; Debeer and Strobl 2020; Fisher, Rudin, and Dominici 2019; Chamma, Engemann, and Thirion 2023). However, in high-dimensional settings, single variable importance computation suffers from very high correlation between the variables (Chevalier et al. 2021). More precisely, this makes conditional importance estimation less informative, as it remains unclear how much information each variable adds. In the extreme case where variables are duplicated, conditional importance can no longer be defined. More generally, correlations larger than .8 are known to present a hard challenge, at least for linear learners (Chevalier et al. 2021). Importance analysis then typically yields spuriously significant variables, which ruins its ability to statistically control the false positive rate (Strobl et al. 2008). Besides, examining the importance of each of the hundreds or thousands variables separately will result in prohibitive computation costs (Covert, Lundberg, and Lee 2020) —removal procedures typically have quadratic complexity— and defy model interpretability.

Group-based analysis can offer a remedy as it regularizes power estimates and leads to reduced computation time (Molnar et al. 2021b; Bühlmann 2013). This can improve inference as it helps handle the curse of correlated vari-

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ables in high-dimensional settings. So far, common group-based methods neglected investigating statistical guarantees, in particular, type-I error control, i.e. the percentage of irrelevant variables identified as relevant (false positives). Statistical error control for groups obviously requires information on variable grouping available through two strategies: *Knowledge-driven* grouping, where the variables are grouped based on their domain-specific information rather than their shared statistical properties and *Data-driven* grouping, where clustering approaches are used such as hierarchical or divisive clustering.

Grouping has also been successfully performed for multimodal applications (Albu, Bocicor, and Czibula 2023; Engemann et al. 2020; Rahim et al. 2015) via model stacking (Wolpert 1992) which is typically based on pipelines of disconnected models.

Contributions We propose *Block-Based Conditional Permutation Importance (BCPI)*, a new framework for variable importance computation (single and group levels) with explicit statistical guarantees (p-values).

- Following our review of the literature (section 2), we provide theoretical results on group-based conditional permutation importance (section 3.2).
- We propose a novel *internal stacking* approach by extending the architecture of our default Deep Neural Network (DNN) model with the use of a linear projection of the groups, which can significantly reduce computation time (section 3.3).
- We conduct extensive benchmarks on synthetic and real world data (section 4) which demonstrate the capacity of the proposed method to combine high prediction performance with theoretically grounded identification of predictively important groups of variables.
- We provide publicly available code (compatible with the Scikit-learn API) on GitHub (https://github.com/achamma723/Group_Variable_Importance).

2 Related Work

Group-based variable importance has been introduced for Random Forests by (Wehenkel et al. 2018), extending the seminal work of Louppe et al. (2013) on *Mean Decrease Impurity (MDI)*. Once all the variables have their corresponding impurity function scores, the importance score of the group of interest are (1) the sum, (2) the average or (3) the maximum of the impurity scores among the participating variables. Despite that, (1) the sum displays bias in favor of larger-sized groups, (2) the average diminishes a group’s significance when only a small fraction of its features hold importance and (3) the maximum suggests that the sole most important feature reflects the collective importance of the group.

Williamson et al. (2021) proposed a model-agnostic approach based on refitting the learner after the removal of a variable of interest also called *LOCO (Leave-One-Covariate-Out)* by Lei et al. (2018). This work has then been adapted to the group-level by considering the removal of all

the variables of the group of interest jointly, as in *Leave-One-Group-Out (LOGO)* presented in (Au et al. 2021). In lieu of removing the group of interest, Au et al. (2021) established *Leave-One-Group-In (LOGI)* that assesses the impact of the group of interest on the prediction compared to the null model - the prediction is the average of the outcome. However, this approach becomes intractable easily due to the necessity of refitting the learner for each group, particularly in the case of low cardinality groups.

Mi et al. (2021) proposed an efficient model-agnostic procedure for black-box models’ interpretation. It uses the *permutation approach* (Breiman 2001; Fisher, Rudin, and Dominici 2019) with the importance score computed as the reduction in a model’s performance when randomly shuffling the variable of interest. To account for group-level structure, (Gregorutti, Michel, and Saint-Pierre 2015) suggested taking into account all the variables of the group of interest in the permutation scheme jointly, known as *Group Permutation Feature Importance (GPF)*. Au et al. (2021) proposed *Group Only Permutation Feature Importance (GOPFI)* which examines the level of the group’s individual contribution to the model’s performance. The random joint shuffling is performed for all the variables of the different groups except the ones of the group of interest. However, according to Strobl et al. (2008), simple permutation approaches yield poor accuracy and specificity in high correlation settings. Lee, Sood, and Craven (2018) applied perturbations to the variables and groups of interest while providing p-values. Nevertheless, they did not focus on the degree of correlation between the variables (and the groups) which increases the difficulty of the problem.

A different angle can be motivated by a recent line of work that developed model-stacking techniques (Wolpert 1992) which combine different input domains and groups of variables rather than aggregating different estimators on the input data. This approach has been used in various applications ranging from video analysis (Zhou et al. 2021) over protein-protein interactions (Albu, Bocicor, and Czibula 2023) to neuroscience applications (Rahim et al. 2015). A key benefit of multimodal or group stacking is that it allows for modality-specific encoding strategies and while approaching inference at the simplified level of the 2nd level model combining the modality-wise predictions or activations. This strategy has been used to explore importance of distinct types of brain activity at different frequencies for age prediction (Sabbagh et al. 2023; Engemann et al. 2020). While stacking is easy to implement with standard software e.g. scikit-learn (Pedregosa et al. 2011), inference with stacking has not been formalized yet. Moreover, it requires fitting multiple disconnected estimators which may limit the capacity of the model.

3 BCPI and Internal Stacking Approach

3.1 Preliminaries

Notations We denote by matrices, vectors, scalar variables and sets by bold uppercase letters, bold lowercase letters, script lowercase letters, and calligraphic letters, respectively (e.g. \mathbf{X} , \mathbf{x} , x , \mathcal{X}). Designating by μ the function

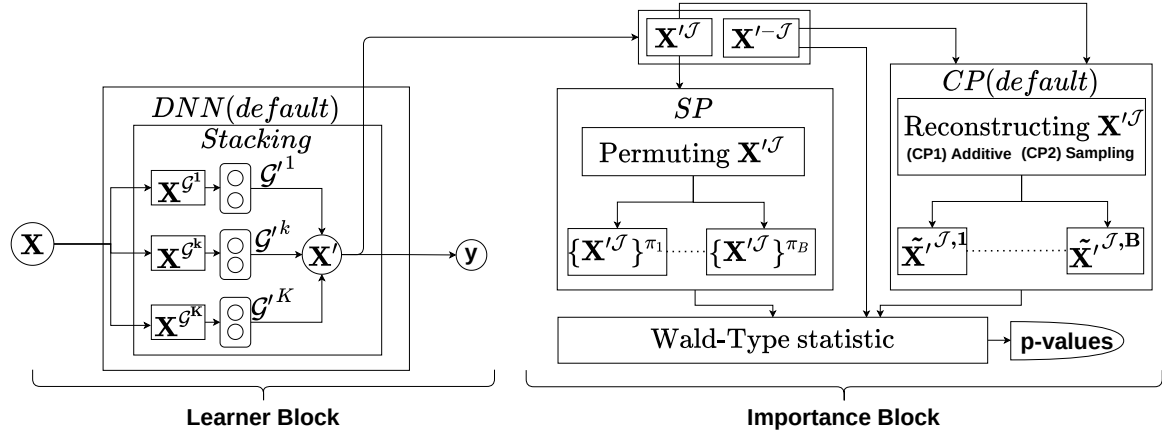


Figure 1: Block-Based Conditional Permutation Importance: Framework for single/group variable importance computation with statistical guarantees. (Learner Block) The learner used to predict the outcome y from the design matrix X . *Internal stacking* linearly projects each group by the mean of an extra linear sub-layer. (Importance Block): Reconstruction of the group of interest $X^{\mathcal{J}}$ is accomplished via *CP (Conditional Permutation)* block with (CP1) the additive or (CP2) the sampling constructions as stated in section 3.2. The permutation scheme can be changed to standard permutation (SP).

that maps the sample space $\mathcal{X} \subset \mathbb{R}^p$ to the outcome space $\mathcal{Y} \subset \mathbb{R}$ and $\hat{\mu}$ is an estimate of μ within a certain class \mathcal{F} of estimators. We express by $\llbracket n \rrbracket$ the set $\{1, \dots, n\}$, by $\langle \cdot, \cdot \rangle$ the standard dot product and by (π) the shuffling process.

Let $\mathcal{S} = \{\mathcal{G}^k, k \in \llbracket K \rrbracket\}$ and $\mathcal{S}' = \{\mathcal{G}^{k'}, k \in \llbracket K \rrbracket\}$ be the set of K pre-defined subset of variables in the data and the set of K new subset of variables following linear projections with a set \mathcal{P} of projection matrices, respectively. Projection matrices are meant to produce a group summary of the information. Let $\mathcal{P} = \{\mathbf{U}_k, k \in \llbracket K \rrbracket\}$ be the set of projection matrices $\mathbf{U}_k \in \mathbb{R}^{|\mathcal{G}^k| \times |\mathcal{G}'^k|}$. Let $\mathcal{J} = \{j_1, \dots, j_r\} \in (\mathcal{S} \cup \mathcal{S}')$ be a subset of r variables with consecutive indices in $\llbracket p \rrbracket$, $r \leq p$. Let $\mathbf{X} \in \mathbb{R}^{n \times p}$ be a design matrix where i^{th} row, j^{th} column and \mathcal{J}^{th} subset of columns are indicated by \mathbf{x}_i , \mathbf{x}^j and $\mathbf{X}^{\mathcal{J}}$ respectively. Let $\mathbf{X}^{-\mathcal{J}} = (\mathbf{x}^1, \dots, \mathbf{x}^{j_1-1}, \mathbf{x}^{j_1+1}, \dots, \mathbf{x}^p)$ be the design matrix with the \mathcal{J}^{th} subset of variables is removed. Let $\mathbf{X}^{(\mathcal{J})} = (\mathbf{x}^1, \dots, \mathbf{x}^{j_1-1}, \{\mathbf{x}^{j_1}\}^\pi, \dots, \{\mathbf{x}^{j_r}\}^\pi, \dots, \mathbf{x}^p)$ be the design matrix with the \mathcal{J}^{th} subset of variables is shuffled. The rows of $\mathbf{X}^{-\mathcal{J}}$ and $\mathbf{X}^{(\mathcal{J})}$ are denoted $\mathbf{x}_i^{-\mathcal{J}}$ and $\mathbf{x}_i^{(\mathcal{J})}$ respectively, for $i \in \llbracket n \rrbracket$. Let \mathbf{X}' be the linearly projected version of \mathbf{X} via \mathcal{P} where $p' = \sum_{k=1}^K |\mathcal{G}'^k|$.

Problem Setting We consider the regression or the classification problem where the response vector $\mathbf{y} \in \mathbb{R}^n$ or $\in \{0, 1\}^n$ respectively and the design matrix $\mathbf{X} \in \mathbb{R}^{n \times p}$ (encompasses n observations of p variables), along with \mathcal{S} (i.e. K pre-defined groups). Across the paper, we rely on an i.i.d. sampling train/validation/test partition scheme where the n samples are divided into n_{train} training and n_{test} test samples. The train samples were used to train $\hat{\mu}$ with empirical risk minimization. This function is utilized for appraising the importance of variables on a novel dataset (test set).

3.2 Group Conditional Variable Importance

We define the joint permutation of group $\mathbf{x}^{\mathcal{J}}$ conditional to $\mathbf{x}^{-\mathcal{J}}$, as a group $\tilde{\mathbf{x}}^{\mathcal{J}}$ that preserves the joint dependency of $\mathbf{x}^{\mathcal{J}}$ with respect to the other variables in $\mathbf{x}^{-\mathcal{J}}$, although the independent part is shuffled. The reconstruction of $\tilde{\mathbf{x}}^{\mathcal{J}}$ is done via two approaches, both, based on fast approximation with a lean model: (1) Additive construction combines the prediction of a Random Forest using the remaining groups and a shuffled version of the residuals i.e. $\tilde{\mathbf{x}}^{\mathcal{J}} = \mathbb{E}(\mathbf{x}^{\mathcal{J}} | \mathbf{x}^{-\mathcal{J}}) + (\mathbf{x}^{\mathcal{J}} - \mathbb{E}(\mathbf{x}^{\mathcal{J}} | \mathbf{x}^{-\mathcal{J}}))^\pi$ where the residuals of the regression of $\mathbf{x}^{\mathcal{J}}$ on $\mathbf{x}^{-\mathcal{J}}$ are shuffled. (2) Sampling construction uses a Random Forest model to fit $\mathbf{x}^{\mathcal{J}}$ from $\mathbf{x}^{-\mathcal{J}}$, followed by sampling the prediction from within its leaves. When dealing with regression, this results in the following importance estimator:

$$\hat{m}_{CPI}^{\mathcal{J}} = \frac{1}{n_{\text{test}}} \sum_{i=1}^{n_{\text{test}}} \left((y_i - \hat{\mu}(\tilde{\mathbf{x}}_i^{(\mathcal{J})}))^2 - (y_i - \hat{\mu}(\mathbf{x}_i)) \right)^2, \quad (1)$$

where $\tilde{\mathbf{X}}^{(\mathcal{J})} = (\mathbf{x}^1, \dots, \mathbf{x}^{j_1-1}, \tilde{\mathbf{x}}^{j_1}, \dots, \tilde{\mathbf{x}}^{j_r}, \dots, \mathbf{x}^p) \in \mathbb{R}^{n_{\text{test}} \times p}$ be the new design matrix including the remodeled version of the group of interest $\mathbf{X}^{\mathcal{J}}$.

In Fig. 1, we introduce *BCPI* a novel general framework for variable importance, at both single and group levels, yielding statistically valid p-values. It consists of two blocks: a *Learner Block* defined by the prediction model of interest *Importance Block* reconstructing the variable (or group) of interest via conditional permutation (CP) – $\hat{m}_{CPI}^{\mathcal{J}}$. The implementation provided with this work supports estimators compatible with the scikit-learn API for both blocks. Yet, our default method *BCPI-DNN* is adapted with: (1) a DNN as a base learner for its high predictive capacity inspired from (Mi et al. 2021) and (2) a Random Forest, a less powerful, but much simpler, yet, still generic model as a conditional probability learner. For study purposes, the frame-

work is also adapted with the standard permutation scheme through the (SP) block (labeled *BPI*). The theoretical results, conditions underlying this proposition as well as limitations of (*PI*) were developed in (Chamma, Engemann, and Thirion 2023) and adapted to the group setting (supplementary materials¹).

Proposition. *Assuming that the estimator $\hat{\mu}$ is obtained from a class of functions \mathcal{F} with sufficient regularity, i.e. that it meets conditions of A1: optimality, A2: differentiability, A3: continuity of optimization, A4: Continuity of derivative, B1: Minimum rate of convergence and B2: Limited complexity, the importance score $\hat{m}_{CPI}^{\mathcal{J}}$ defined in (1) cancels when $n_{train} \rightarrow \infty$ and $n_{test} \rightarrow \infty$ under the null hypothesis, i.e. the \mathcal{J}^{th} group is not significant for the prediction. Moreover, the Wald statistic $z^{\mathcal{J}} = \frac{\text{mean}(\hat{m}_{CPI}^{\mathcal{J}})}{\text{std}(\hat{m}_{CPI}^{\mathcal{J}})}$ obtained by dividing the mean of the importance score by its standard deviation asymptotically follows a standard normal distribution.*

This implies that in the large sample limit, the p-value associated with $z^{\mathcal{J}}$ controls the type-I error rate for all optimal estimators in \mathcal{F} . It entails making sure that the importance score defined in (1) is 0 for the class of learners that meet specific convergence guarantees and are immutable to arbitrary change in their \mathcal{J}^{th} arguments, conditional on the others. We also state the precise technical conditions under which $\hat{m}_{CPI}^{\mathcal{J}}$ used is (asymptotically) valid, i.e. leads to a Wald-type statistic that behaves as a standard normal under the null hypothesis. As a result, all terms in Eq. 1 vanish with speed $\frac{1}{\sqrt{n_{test}}}$ from the *Berry-Essen* theorem, under the assumption that the test samples are i.i.d.

3.3 Internal Stacking

The vector $\mathbf{x} \in \mathcal{X}$ is composed of K groups in \mathcal{S} , each considered as an independent input modality. Performing column slicing on \mathbf{x} , according to \mathcal{S} , yields the set $\{\mathbf{x}^{G^k}, k \in \llbracket K \rrbracket\}$. A linear transformation to a lower space is applied on each input modality \mathbf{x}^{G^k} through the set of projection matrices \mathcal{P} producing a linear variant denoted \mathbf{x}'^k as:

$$\mathbf{x}'^k = \langle \mathbf{x}^{G^k}, \mathbf{U}_k \rangle,$$

where $k \in \llbracket K \rrbracket$.

Concatenating the set of linear variants $\{\mathbf{x}'^k, k \in \llbracket K \rrbracket\}$ provides the linear version of \mathbf{x} i.e. the vector \mathbf{x}' . If the new space is a unidimensional Euclidean space i.e. $\mathbf{x}' \in \mathbb{R}^K$, a group summary of the information within all groups is returned, and the problem is reduced to the single-level case. However, if the new space is not unidimensional, we then have a dimension reduction, where the group summary of information is exclusive per group (multioutputs per group). In this case, the new groups contained in \mathbf{x} are denoted \mathcal{G}'^k with the corresponding linear variant $\mathbf{x}'^{\mathcal{G}'^k}$ as seen in Fig. 1. Instead of performing stacking in a separate estimation step under a different learner, we have incorporated it to the inference process, thus learning a consistent new presentation

of the groups. This is simply implemented as an initial linear sub-layer without activation in the $\hat{\mu}$ network. Therefore, \mathbf{x}'^k can be seen analogous to the predictions from the input models in a classical stacking pipeline that are forwarded to the meta learner, hence, \mathbf{x}'^k can be treated like a regular data column by permutation algorithms.

4 Experiments

To ensure a fair comparison across experiments, we use all methods with their original implementation. As for *BCPI-DNN*, *BCPI-RF* and *BPI-DNN* particularly, the default behavior consists of a 2-fold internal cross validation where the importance inference is performed on an unseen test set. The scores from different splits are thus concatenated to compute the final variable importance. All experiments are performed with 100 runs.

4.1 Experiment 1: Benchmark of Grouping Methods

We include *BCPI-DNN* in a benchmark with other state-of-the-art methods for group-based variable importance. The data $\{\mathbf{x}_i\}_{i=1}^n$ follow a Gaussian distribution with a predefined covariance structure Σ i.e. $\mathbf{x}_i \sim \mathcal{N}(0, \Sigma) \forall i \in \llbracket n \rrbracket$. We consider a block-designed covariance matrix Σ of 10 blocks with an intra-block correlation coefficient $\rho_{intra} = 0.8$ among the variables of each block and an inter-block correlation coefficient $\rho_{inter} \in \{0, 0.2, 0.5, 0.8\}$ between the variables of the different blocks. Each block is considered as a separate group. In this experiment, $n = 1000$ and $p = 50$ i.e. we have 5 variables per block/group. We defined an important group as a group having at least one variable that took part in simulating the outcome y . Thus, to predict y , we rely on a linear model where the first variable of each of the first 5 groups is used in the following model:

$$y_i = \mathbf{x}_i \boldsymbol{\beta} + \sigma \epsilon_i, \forall i \in \llbracket n \rrbracket \quad (2)$$

where $\boldsymbol{\beta}$ is a vector of regression coefficients having only 5 non-zero coefficients (the true model), $\epsilon \in \mathcal{N}(0, \mathbf{I})$ is the Gaussian additive noise with magnitude $\sigma = \frac{\|\mathbf{X}\boldsymbol{\beta}\|_2}{SNR/\sqrt{n}}$. We used the same setting from (Janitza, Celik, and Boulesteix 2018) where the $\boldsymbol{\beta}$ values are drawn i.i.d. from the set $\mathcal{B} = \{\pm 3, \pm 2, \pm 1, \pm 0.5\}$. We consider the following state-of-the-art baselines:

- **Marginal Effects:** A multivariate linear model is applied to each group separately. Importance scores correspond to ensuing p-values.
- **Leave-One-Group-In (LOGI)** (Au et al. 2021): Similar to *Marginal Effects* using a Random Forest. Provides no p-values.
- **Leave-One-Group-Out (LOGO)** (Williamson et al. 2021): Refitting of the model is performed after removing the group of interest.
- **Group Only Permutation Feature Importance (GOPFI)** (Au et al. 2021): Joint permutation of all variables except for those of the group of interest.

¹<https://arxiv.org/abs/2312.10858>

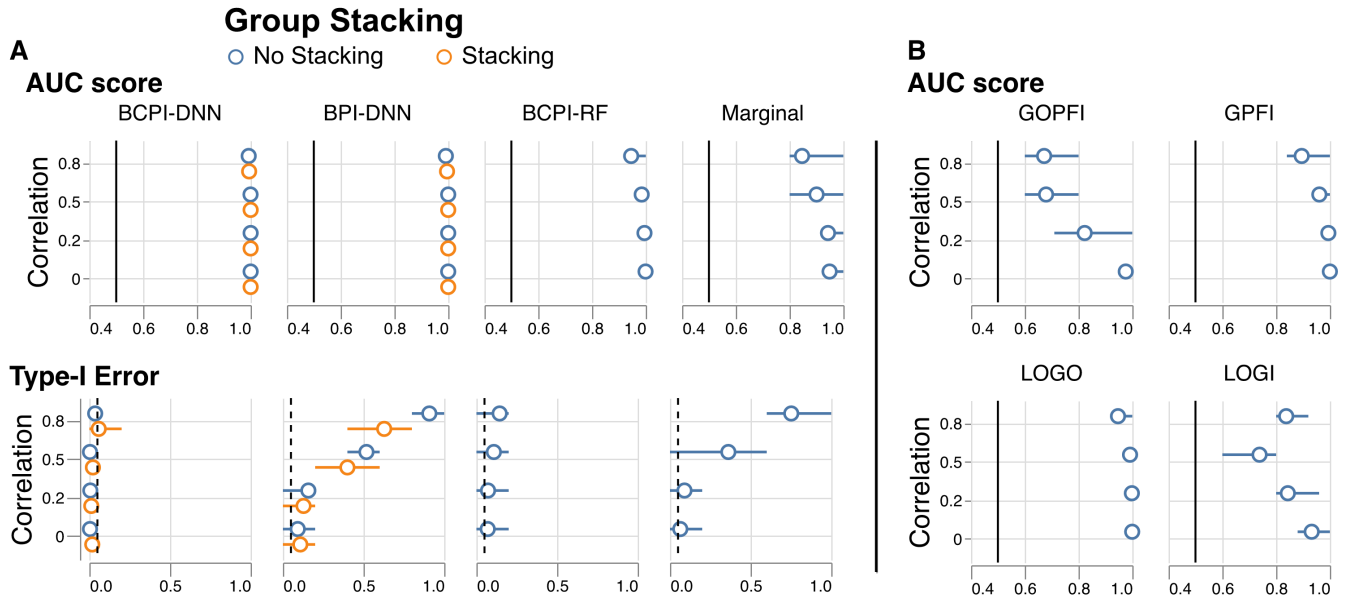


Figure 2: Benchmarking grouping methods: *BCPI-DNN* is compared to baseline models and competing approaches for group variable importance. (A) AUC score (correct ranking of variables) and Type-I error ($p\text{-val} < 0.05$) for methods providing p-values. (B) AUC scores for methods not providing p-values. Prediction tasks were simulated with $n = 1000$ and $p = 50$. Dashed line: targeted type-I error rate at 5%. Solid line: chance level.

- Group Permutation Feature Importance (*GPFI*) (Gregorutti, Michel, and Saint-Pierre 2015; Valentin, Harkotte, and Popov 2020): Joint permutation of all variables of the group of interest.

In addition, we benchmarked the three variants of our proposed method:

- BPI-DNN: Similar to *GPFI* based on a DNN estimator. It is also enhanced by the new *internal stacking* approach.
- BCPI-RF: BCPI where $\hat{\mu}$ is obtained from a Random Forest.
- BCPI-DNN: BCPI where $\hat{\mu}$ is a DNN. It is also enhanced by the new *internal stacking* approach.

4.2 Experiment 2: Impact of Stacking

To assess the impact of performing stacking regarding accuracy in inference and computation time, we conducted a comparison restricted to *BCPI-DNN*. We relied on the same covariance structure setting as in Experiment 1 with an intra-block correlation coefficient $\rho_{intra} = 0.8$ and an inter-block correlation coefficient $\rho_{inter} = 0.8$. The number of samples n and the number of variables p were both set to 1000 i.e. the number of variables per block/group increased to 100 in order to build groups with high cardinality. The outcome y was simulated using the same model as in Eq. 2 where a group is predefined as important having at least 10% of its variables taking part in computing the outcome.

4.3 Experiment 3: Age Prediction with UKBB

We conducted an empirical benchmark of the performance of *BCPI-DNN* combined with *internal stacking* in a real-world biomedical dataset. The UK Biobank project (UKBB)

encompasses imaging and socio-demographic derived phenotypes from a prospective cohort of participants drawn from the population of the UK (Constantinescu et al. 2022; Littlejohns et al. 2020). In the past years, the UKBB dataset has enabled large-scale studies investigating associations between various phenotypes (physiological, cognitive) and environmental or life-style factor. This has given rise to successful analysis of factors associated to personal well-being and health (Newby et al. 2021; Mutz and Lewis 2021) at an epidemiological scale. In the context of machine learning with brain data, age-prediction is an actively studied task which can provide a normative score when applying a reference model on clinical cohorts (Cole and Franke 2017). State-of-the-art models were based on convolutional neural networks and report mean absolute errors between 2-3 years (Roibu et al. 2023; Jonsson et al. 2019). Recent extensions have focused on MRI-contrast and region-specific insights, often based on informal inference (Roibu et al. 2023; Popescu et al. 2021). Another line of work (Dadi et al. 2021; Anatürk et al. 2021) has focused on other sources of normative ageing information, highlighting cognitive social and lifestyle factors. In this context, the analysis of importance of multimodal inputs has so far been hampered by the lack of formal inference procedures and the high-dimensional setting with highly correlated variables.

We approached this open task using the proposed method, reusing the pre-defined groups in the work by (Dadi et al. 2021). We focused on data from participants who attended the imaging visit ($n = 8357$) to study the group-level importance rankings provided by *BCPI-DNN*. We defined important groups by p-value threshold of $< 10^{-3}$. While

Group Stacking



Figure 3: Impact of Stacking: Performance at detecting important groups on simulated data with $n = 1000$ and $p = 1000$ with 10 blocks/groups, each group having a cardinality of 10. AUC scores and Type-1 error as in Fig. 2. (Power) quantifies the average proportion of detected informative variables (p -value < 0.05). Panel (Time) displays computation time in seconds with \log_{10} scale per core on 100 cores. Dashed line: targeted type-I error rate. Solid line: chance level.

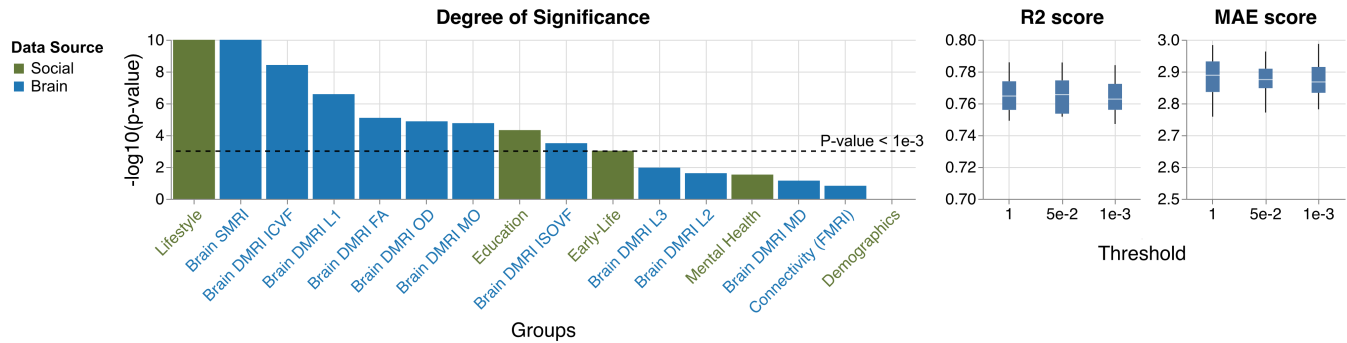


Figure 4: Brain Age prediction in UKBB: Prediction of brain age from various socio-demographic and brain-imaging groups of phenotypes in a sample of $n = 8357$ volunteers from the UK BioBank. (Degree of significance) plots the level of significance for the different brain (in blue) and social (in red) groups in terms of $-\log_{10}$ of the derived p -values. Dashed line: targeted type-I error rate at $p = 0.001$. (R2 score & MAE score) checks the performance of the trained learner when retaining all the groups vs removing non-significant groups.

this setting lacks an explicit ground truth for the important groups, we explored the appropriate group selection through model performance in terms of (R^2 & MAE scores, 10-fold cross-validation) after removing the non-significant groups. We accessed the UKBB data through its controlled access scheme in accordance with its institutional ethics boards (Bycroft et al. 2018; Sudlow et al. 2015).

5 Results

We benchmarked state-of-the-art baselines and the proposed methods across data-generating scenarios under increasing inter-block correlation strength $\{0, 0.2, 0.5, 0.8\}$ (Fig. 2). *BCPI-DNN* and *BPI-DNN* were implemented in two variants: with or without the novel *internal stacking*. For the AUC score, we observed that (*BCPI-DNN* & *BPI-DNN* - based on the DNN) and (*BCPI-RF*, *GPFI* & *LOGO* - based on Random Forests) showed the highest performance across the different scenarios, hence, accurately ordering the variables according to their significance. As expected, the *Marginal* baseline performed lowest as it could not access any conditional information. *GOPFI* and *LOGI* both suffered when the correlation between the groups increased,

which is not surprising. Considering false positive rate, *BCPI-DNN* controlled the type-I error at the targeted rate (5 %) while *BPI-DNN*— based on the standard permutation of the group of interest— failed to do so in the setting of high correlations between the groups, and thus provided spurious results. Interestingly, for *BPI-DNN*, *internal stacking* slightly increased its capacity to control the type-I error. *BCPI-RF*— based on the conditional importance with Random Forests— better controlled the type-I error compared to *BPI-DNN*. Nevertheless, in the presence of strong correlations, it did not fully reach the target rate. Additional analyses suggested that the *marginal* approach failed in the current setting, whereas on average, the DNN had higher scores ($R^2 \sim 0.95$) than the Random Forest ($R^2 \sim 0.8$). Additional analyses of performance in terms of power and computation time of showed that *BCPI-DNN*, *BPI-DNN*, *BCPI-RF* and *Marginal* showed favorable results compared to other baselines and competing methods.

The AUC score, type-I error, power and computation time for Experiment 4.2 are presented in Fig. 3. *BCPI-DNN* with *internal stacking* performed similarly as the same approach without stacking. Thus, both approaches showed

comparable inferential behavior in identifying the significant groups. Nevertheless, in terms of computation time, the dimension reduction brought by stacking added significant benefits (around a factor of 2). In fact, in the *importance block* without stacking, all the variables of the remaining groups are used to predict those of the group of interest. Groups with high cardinality (of variables) are challenging in terms of memory resources and required computation, suggesting that *internal stacking* can help to reduce computational burden. Real-world empirical application of *BCPI-DNN* with *internal stacking* for age-prediction from brain imaging and socio-demographic information are summarized in Fig. 4. Results in (**Degree of Significance**) ranked the groups according to their corresponding level of significance. We choose a conservative significance level of $p = 0.001$ (Dashed line at $\log_{10}(0.0001) = 3$). Using the stacking approach, we scored the heterogeneous *brain* and *social* input variables regarding their predictive importance. As expected, we found that the brain groups - excluding *Brain DMRI MD* - were highly important for age prediction. Interestingly, *Lifestyle* and *Education* were among the top predictive variables, conditional on the brain groups, suggesting the presence of complementary information. To challenge the plausibility of the selected groups, we investigated prediction performance after excluding non-significant groups. We used 10-fold cross validation with significance estimation and refitting the reduced model using the training set while scoring with the reduced model on the testing set. The reduced model did not perform visibly worse than the full model ($R^2 = 0.8$, $MAE = 2.9$), suggesting that our procedure effectively selects predictive groups. Of note the performance is in line with state-of-the-art benchmarks on the UKBB based on convolutional neural networks ($MAE \sim 2$ -3 years, e.g., Roibu et al. 2023; Jonsson et al. 2019). Consequently, results suggest that the proposed approach combined good prediction performance with effective identification of relevant groups of variables. For additional supporting results, see supplementary materials².

6 Discussion

In this work, we proposed *BCPI*, a novel and usable framework for computing single- and group-level variable importance. Our work provides statistical guarantees based on results from *Conditional Permutation Importance (CPI)*, whereas our implementation supports arbitrary regression and classification models consistent with the scikit-learn API. We developed our approach beginning from the observation that standard *Permutation Importance PI*, represented by the *BPI-DNN* approach, lacks the ability to control type-I error (Williamson et al. 2021) with high correlated settings in Fig. 2, despite the high AUC score (Mi et al. 2021). We extended these results, theoretically and empirically, to the group setting by proposing *BCPI-DNN*, which is built on top of an expressive DNN model as a base learner. This recipe led to high AUC scores while maintaining the control of type-I error across different correlation scenarios (Fig. 2).

²<https://arxiv.org/abs/2312.10858>

Inspired by recent applications of model stacking for handling multiple groups or input domains (Albu, Bocicor, and Czibula 2023; Zhou et al. 2021; Engemann et al. 2020), we proposed *internal stacking* which implements stacking inside the DNN model, hence, avoids separate optimization problems common for stacking pipelines. This was achieved through extra sub-linear layers building linear summaries for each group of variables. Our benchmarks suggested that stacking maintained inferential performance of the full model while bringing time benefits (at least up to a factor of 2), especially for groups with high cardinality of variables (Fig. 3). Moreover, additional analyses of calibration of *BCPI-DNN* versus *BPI-DNN* suggested that the p-values for *BCPI-DNN* showed a slightly conservative profile for *BCPI-DNN*. Instead, *BPI-DNN* showed poor calibration, once more underlining the relevance of conditional permutations.

Our empirical investigation of age prediction using the UKBB dataset suggests that the proposed framework facilitates constructing strong predictions models alongside trustworthy insights on the important predictive inputs. While prediction performance of our model was in line with state-of-the-art results for the UKBB (Roibu et al. (2023); Jonsson et al. (2019)), here, we provided a statistically grounded confirmation for the conclusions drawn in Dadi et al. 2021 who used a less formal approach consistent with the *LOGI* approach.

Several limitations apply to our work. *BCPI-DNN* utilizes a DNN model as the base estimator for its high predictive accuracy. However, when the amount of training data is limited, the network can potentially memorize the training examples instead of learning generalizable patterns and a simpler base learner might be preferable, e.g. a Random Forest. Additional analyses of computation time for *BCPI-DNN* in situations of low (5) versus high (100) cardinality showed that the benefit of *internal stacking* became more pronounced with larger groups of variables. This is due to the extra training of the added sub-linear layers. Our work made use of predefined groups, which may not always be available. Instead, statistically defined groups could be used e.g. obtained from clustering. A possible issue might then be that the groups mix heterogeneous variables, which makes their interpretation challenging. Furthermore, it is important to apply one-hot encoding of categorical variables after clustering. On the flip side, reliance on predefined groups may lead to poor inference if the group structure does not track variable importance, e.g. if important variables are distributed in all groups. This topic deserves careful investigation in the future. Moreover, here we only performed *internal stacking* by applying linear projection on the input data. It will be interesting to better understand the potential of non-linear projections.

Finally, additional possible future directions include studying the impact of missing and low values on the accuracy, also across different group definitions.

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