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IMPROVEMENT OF VARIABLES INTERPRETABILITY IN KERNEL PCA

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ABSTRACT

Kernel methods have been proven to be a powerful tool for the integration and analysis of high-throughput technologies generated data. Kernels offer a nonlinear version of any linear algorithm solely based on dot products. The kernelized version of *Principal Component Analysis* is a valid nonlinear alternative to tackle the nonlinearity of biological sample spaces. This paper proposes a novel methodology to obtain a data-driven feature importance based on the *KPCA* representation of the data. The proposed method, kernel PCA Interpretable Gradient (KPCA-IG), provides a data-driven feature importance that is computationally fast and based solely on linear algebra calculations. It has been compared with existing methods on three benchmark datasets. The accuracy obtained using KPCA-IG selected features is equal to or greater than the other methods' average. Also, the computational complexity required demonstrates the high efficiency of the method. An exhaustive literature search has been conducted on the selected genes from a publicly available Hepatocellular carcinoma dataset to validate the retained features from a biological point of view. The results once again remark on the appropriateness of the computed ranking. The black-box nature of kernel PCA needs new methods to interpret the original features. Our proposed methodology KPCA-IG proved to be a valid alternative to select influential variables in high-dimensional high-throughput datasets, potentially unravelling new biological and medical biomarkers.

Keywords Kernel PCA · Relevant variables · Unsupervised learning · Kernel methods

1 Introduction

The recent advancement in high-throughput biotechnologies is making large multi-omics datasets easily available. Bioinformatics has recently entered the *Big Data* era, offering researchers new perspectives to analyse biological systems to discover new genotype-phenotype interactions.

Consequently, new ad-hoc methods to optimise post-genomic data analysis are needed, considering the high complexity and heterogeneity involved. For instance, multi-omics datasets pose the additional difficulty of dealing with a multilayered framework making data integration extremely challenging.

In this context, kernel methods offer a natural theoretical framework for the high dimensionality and heterogeneous nature of omics data, addressing their peculiar convoluted nature (Schölkopf et al., 2003). These methods facilitate

the analysis and the integration of various types of omics data, such as vectors, sequences, networks, phylogenetic trees, and images, through a relevant kernel function. Using kernels enables the representation of the datasets in terms of pairwise similarities between sample points, which is helpful for handling high-dimensional sample spaces more efficiently than using Euclidean distance alone. Euclidean distance can be inadequate in complex scenarios, as stated in Duda et al. (2000), but kernels can help overcome this limitation. Moreover, kernel methods have the advantage of providing a nonlinear version of any linear algorithm which relies solely on dot products. For instance, Kernel Principal Component Analysis, (Schölkopf et al., 1997), Kernel Canonical Correlation Analysis (Bach and Jordan, 2003), Kernel Discriminant Analysis (Roth and Steinhage, 1999) and Kernel Clustering (Girolami, 2002) are all examples of nonlinear algorithms enabled by kernel transformations.

This work will focus on the kernelised version of Principal Component Analysis, KPCA, that provides a nonlinear alternative to the standard PCA to reduce the sample space dimensions.

However, one of the drawbacks of KPCA and kernel methods, in general, is that they pose new challenges in interpretability. The so-called *pre-image* problem arises since data points are only addressed through the kernel function, causing the original features to be lost during the data embedding process. The initial information contained in the original variables is summarised in the pairwise kernel similarity scores among data sample points. Thus, retrieving the original input dimensions is highly challenging when it comes to identifying the most prominent features. Even if it is possible for certain specific kernels to solve the pre-image problem through a fixed-point iteration method, the provided solution is typically numerically unstable since it involves a non-convex optimisation problem (Schölkopf et al., 1998). Moreover, in most cases, the exact pre-image does not even exist (Mika et al., 1998).

However, it is possible to find works that aim at finding the pre-image problem solution, like the pre-image based on distance constraints in the feature space in Kwok and Tsang (2004) or local isomorphism as in Huang et al. (2011).

Instead, this article concentrates on unsupervised feature selection based on kernel PCA. More specifically, we propose a method to identify the most influential variables for the kernel principal components that account for the majority of the variability of the data. This procedure provides a computationally fast and stable feature ranking to identify the most prominent original variables. Unimportant descriptors can be thus ignored, refining the kernel procedure whose similarity measure can be influenced by irrelevant dimensions (Brouard et al., 2022).

1.1 Existing approaches to facilitate feature interpretability in the unsupervised setting

The literature on unsupervised feature selection is generally less extensive than its supervised learning counterpart. One of the main reasons for this disparity is that the selection is made without a specific prediction goal, making it difficult to evaluate the quality of a particular solution. In the same way, the unsupervised feature selection field that takes advantage of the kernel framework has been found to be less explored than kernel applications with classification purposes. As mentioned earlier, interpreting kernel PCA requires additional attention as the kernel principal component axes themselves are only defined by the similarity scores of the sample points. However, the literature has limited attempts to explain how to interpret these axes after the kernel transformation. Therefore, feature selection methods based on KPCA are rare.

Among others, Reverter et al. (2014) proposed a method to visualize the original variables into the 2D kernel PCs plot. For every sample point projected in the KPCA axes, they propose to display the original variables as arrows representing the vector field of the direction of maximum growth for each input variable or combination of them. This algorithm does not provide variable importance ranking, requiring previous knowledge about which variables to display.

On the contrary, Mariette and Villa-Vialaneix (2017) proposed a variable importance selection method to identify the most influential variables for every principal component based on random permutation. The procedure is performed for all variables, selecting the ones that result in the largest Crone-Crosby (Crone and Crosby, 1995) distance between kernel matrices, i.e. the variables whose permutations of the observations lead to a significant change in the kernel Gram matrix values. However, the method does not come with a variable representation and can be computationally expensive. This method will be denoted as **KPCA-permute** in the rest of the article.

Another method that takes advantage of the kernel framework is the unsupervised method **UKFS** with its extension **UKFS-KPCA** in Brouard et al. (2022) where the authors propose to select important features through a non-convex optimization problem with a ℓ_1 penalty for a Frobenius norm distortion measure.

As exhaustively described in the overview presented in Li et al. (2017), there are different approaches to assess variable importance in an unsupervised setting not based on the kernel framework. Among others, we can mention two methodologies that are based on the computation of a score, the Laplacian Score **lapl** in He et al. (2005) and its extension Spectral Feature Selection **SPEC** in Zhao and Liu (2007). Other alternatives are the Multi-Cluster Feature Selection **MCFS** in Cai et al. (2010), the Nonnegative Discriminative Feature Selection **NDFS** in Li et al. (2021), and the Unsupervised Discriminative Feature Selection **UDFS** in Yang et al. (2011). These methods aim to select features by keeping only the ones that best represent the implicit nature of the clustered data. Then, Convex Principal Feature

Selection **CPFS** Masaeli et al. (2010) adopts a distinct approach to feature selection, focusing on selecting a subset of features that can best reconstruct the projection of the data on the initial axes of the Principal Component Analysis. As mentioned, the present study introduces a novel contribution to the interpretability of variables in kernel PCA, assuming that the first kernel PC axes contain the most relevant information about the data. The newly proposed method follows and extends the idea proposed by Reverter et al. (2014), with the fundamental difference that it gives a data-driven features importance ranking. Moreover, contrarily **KPCA-permute** in Mariette and Villa-Vialaneix (2017), it does not have a random nature while being considerably faster. From now on, it will be referred to as **KPCA-IG**, which stands for KPCA Interpretable Gradient.

2 Methods

This section presents the formulation behind our proposed method **KPCA-IG**, starting with describing the kernel framework.

2.1 Kernel PCA

Given a dataset of n observations $\mathbf{x}_1, \dots, \mathbf{x}_n$ with $\mathbf{x}_i \in \mathcal{X}$, a function k defined as $k: \mathcal{X} \times \mathcal{X} \rightarrow \mathbb{R}$ is a valid kernel if it is symmetric and positive semi-definite i.e. $k(\mathbf{x}_i, \mathbf{x}_j) = k(\mathbf{x}_j, \mathbf{x}_i)$ and $\mathbf{c}'\mathbf{K}\mathbf{c} \geq 0, \forall \mathbf{c} \in \mathbb{R}$, where \mathbf{K} is the $n \times n$ kernel matrix containing all the data pairwise similarities $\mathbf{K} = k(\mathbf{x}_i, \mathbf{x}_j)$. The input set \mathcal{X} does not require any assumption. In this work we consider it to be $\mathcal{X} = \mathbb{R}^d$.

Every kernel function is associated with an implicit function $\phi: \mathcal{X} \rightarrow \mathcal{H}$ which maps the input points into a generic feature space \mathcal{H} , with possibly an infinite dimensionality, with the expression $k(\mathbf{x}_i, \mathbf{x}_j) = \langle \phi(\mathbf{x}_i), \phi(\mathbf{x}_j) \rangle$. This relation allows to compute the dot products in the feature space, implicitly applying the kernel function to the input objects, without explicitly computing the mapping function ϕ .

Principal Component Analysis is a well-established linear algorithm to extract the data structure in an unsupervised setting (Hastie et al., 2009). However, it is commonly accepted that in specific fields, such as bioinformatics, assuming a linear sample space may not help to capture the data manifold adequately (Reverter et al., 2014). In other words, the relationships between the variables may be nonlinear, making linear methods unsuitable. Hence, with high-dimensional data such as genomic data, where the number of features is usually much larger than the number of samples, nonlinear methods like kernel methods can provide a valid alternative for data analysis.

A compelling approach to overcome this challenge is through kernel PCA, which was introduced in Schölkopf et al. (1997). Kernel PCA applies PCA in the feature space generated by the kernel, and as PCA relies on solving an eigenvalue problem, its kernelized version operates under the same principle. The algorithm requires the data to be centered in the feature space, and the diagonalization of the centered covariance matrix in the feature space \mathcal{H} is equivalent to the eigendecomposition of the kernel matrix \mathbf{K} . The data coordinates in the feature space are unknown as ϕ is not explicitly computed. Consequently, the required centering of variables in the feature space cannot be done explicitly. However, it is possible to compute the centered Gram matrix $\tilde{\mathbf{K}}$ as $\tilde{\mathbf{K}} = (\mathbf{K} - \mathbf{1}_n \mathbf{K} - \mathbf{K} \mathbf{1}_n + \mathbf{1}'_n \mathbf{K} \mathbf{1}_n)$ with $\mathbf{1}_n$ a vector with length n and 1 for all entries. If we express the eigenvalues of $\tilde{\mathbf{K}}$ with $\lambda_1 \geq \lambda_2 \geq \dots \geq \lambda_n$ and the corresponding set of eigenvectors $\mathbf{a}^1, \dots, \mathbf{a}^n$, the principal component axes can be expressed as $\mathbf{v}^k = \sum_{i=1}^n a_i^k \phi(\mathbf{x}_i)$ with \mathbf{v}^k and \mathbf{a}^k orthonormal in \mathcal{H} with $k = 1, \dots, n$. Thus solving $n\lambda\mathbf{a} = \tilde{\mathbf{K}}\mathbf{a}$, it is possible to compute the projection of the points into the subspace of the feature space spanned by the eigenvectors. The projection of a test point \mathbf{x} into the k -th eigenvector becomes then $\rho_k := \langle \mathbf{v}_k, \phi(\mathbf{x}) \rangle = \sum_{i=1}^n a_i^k k(\mathbf{x}, \mathbf{x}_i)$. Likewise, utilizing the concise, explicit form of the centered gram matrix $\tilde{\mathbf{K}}$, it is possible to express the projection of an arbitrary point \mathbf{x} onto the k -th kernel principal component as follows:

$$\rho_k = \left(k(\mathbf{x}, \mathbf{x}_i)^T - \frac{1}{n} \mathbf{1}_n^T \mathbf{K} \right) \left(\mathbf{I}_n - \frac{1}{n} \mathbf{1}_n \mathbf{1}_n^T \right) \tilde{\mathbf{v}} \quad (1)$$

As we observe, the kernel PCA algorithm can be mathematically represented using only the entries of the kernel matrix. This means that the algorithm operates entirely on the original input data without requiring the computation of new data coordinates in the feature space. This technique effectively resolves the issue of potentially high computational complexity by allowing the input points to be implicitly mapped into the feature space. However, it also introduces new challenges in terms of interpretation. Determining which input variables have the most significant impact on the kernel principal components can be highly challenging, making it difficult to interpret them in terms of the original features. In other words, since the kernel function maps the data to a higher-dimensional feature space, it can be hard to

understand how the original features contribute to the newly obtained kernel principal components. In the previous section, we have mentioned the few techniques available in the literature that can be used to gain insight into the original input variables that had the most influence on the KPCA solution. The following section presents our contribution to providing practitioners with a data-driven and faster variable ranking methodology.

2.2 Improvement of variable interpretability in KPCA

It is known that gradient descent is one of the most common algorithms for the training phase of most neural networks (Ruder, 2016). In this framework, the norm of the cost function gradient plays a crucial role as it determines the step size of the update at each iteration. Together with the direction, its magnitude is a measure of the steepness of the cost function at a particular point in the parameter space. If the gradient magnitude is high, the cost function changes rapidly; thus, the parameters must be updated with a larger step size. Conversely, if the gradient magnitude is low, it indicates that the cost function is changing slowly, and therefore, the parameters need to be adjusted with a smaller step size. In the same way, we propose to compute at each sample point the norm of the partial derivative of every feature curve projected into the eigenspace of the Gram matrix. When the norm of the partial derivative of a variable is high, it means that the variable substantially affects the position of the sample points in the kernel PC axes. Conversely, when the norm of the partial derivative of a variable is small, the variable can be deemed negligible for the kernel principal axes. Thus, the main idea is to compute the lengths of the gradient vectors for every variable at each sample point as they represent how steep the direction given by the partial derivative of the induced curve is. Some works in the neuroimaging and earth system sciences domain have also shown that kernel derivatives may indicate the influence carried by the original variables as in Rasmussen et al. (2011) and Johnson et al. (2020). Followingly in this work, we apply this intuition to the KPCA framework.

Analytically, Reverter et al. (2014) and Sanz et al. (2018) showed how every variable $j = 1, \dots, p$ can be represented in the input space with a real-valued function $\mathbf{f}^j(\mathbf{x})$ representing the position of the every sample point \mathbf{x} in the input space $\mathcal{X} = \mathbb{R}^d$. This function will be simply addressed as \mathbf{f}^j for the rest of the work.

We are interested in the projection of these j functions onto the linear subspace of the feature space induced by the kernel. First, we can express the projection of \mathbf{f}^j in the feature space through the implicit map ϕ as \mathbf{h}^j .

In the previous section, we showed how to represent the projection of every mapped sample point $\phi(\mathbf{x})$ into the subspace spanned by the eigenvectors of $\tilde{\mathbf{K}}$ in Equation (1).

Similarly, every function \mathbf{h}^j can be further projected from the feature space into the subspace of the kernel PCA.

$$\varphi_{1 \times q}^j = \left(k(\mathbf{h}^j, \mathbf{x}_i)^T - \frac{1}{n} \mathbf{1}_n^T \mathbf{K} \right) \left(\mathbf{I}_n - \frac{1}{n} \mathbf{1}_n \mathbf{1}_n^T \right) \tilde{\mathbf{v}} \quad (2)$$

with q the number of kernel PCs. In order to assess the influence of the j -th variable on the coordinates of the data points into the kernel principal axes, we first compute the derivative of \mathbf{h}^j with respect to the j -th variable at each sample point.

Formally, the partial derivative of the projected curves of \mathbf{h}^j computed at the generic point \mathbf{x} can be defined as follows:

$$\begin{aligned} w^j &= \frac{\partial \varphi^j}{\partial x^j} = \frac{\partial k(\mathbf{x}, \mathbf{x}_i)}{\partial x^j} \left(\mathbf{I}_n - \frac{1}{n} \mathbf{1}_n \mathbf{1}_n^T \right) \tilde{\mathbf{v}} \\ &= \left[\frac{\partial k(\mathbf{x}, \mathbf{x}_1)}{\partial x^j}, \dots, \frac{\partial k(\mathbf{x}, \mathbf{x}_n)}{\partial x^j} \right]^T \left(\mathbf{I}_n - \frac{1}{n} \mathbf{1}_n \mathbf{1}_n^T \right) \tilde{\mathbf{v}} \end{aligned} \quad (3)$$

As said, the direction of maximal variation associated with the variable j is given by this partial derivative of the projected curve as exploited in (Reverter et al., 2014).

If φ^j represents the input variable j locally in the kernel PC axes, w^j is the $n \times q$ matrix giving the direction and length of the gradient associated with the j -th variable for each input point. The mean value of the norm of this partial derivative computed for all the sample points suggests this variable's influence. Analytically:

$$r^j = \frac{1}{n} \sqrt{\sum_{i=1}^n \left(\frac{\partial \varphi^j}{\partial x_i^j} \right)^2} = \frac{1}{n} \sum_{i=1}^n \sqrt{\sum_{t=1}^q (w_{it}^j)^2} \quad (4)$$

Thus, r^j is the mean of the norm vectors of the partial derivative of φ^j among all the n sample points, giving an indication of the overall influence of the j -th variable on the points.

Finally, we can group all the j means in a sorted vector representing the ranking of the original features proposed by the method, i.e. $\mathbf{r} = (r^1, \dots, r^p)$. Every entry of \mathbf{r} is a score that indicates the impact of every variable on the kernel PCA representation of the data, from the most influential to the least important.

The method is non-iterative, and it only requires linear algebra. Thus, it is not susceptible to numerical instability or local minimum problems. It is computationally very fast, and it can be applied to any kernel function that admits a first-order derivative. The described procedure has been implemented on R, and the code can be available upon request to the authors.

3 Results

We conducted experiments on three benchmark datasets from the biological domain to assess the accuracy of the proposed unsupervised approach for feature selection. These datasets include two microarray datasets, named *Carcinom* and *Glioma*, which are available in the Python package scikit-feature Li et al. (2017) and the gene expression data from normal and prostate tumour tissues Chandran et al. (2007), *GPL93* from the GEO, a public functional genomics data repository. *Glioma* contains the gene expression of 4434 for 50 patients, while *Carcinom* 9182 for 174 individuals. Both datasets have already been used as a benchmark in numerous studies including several methods comparisons, such as Li et al. (2017) and Brouard et al. (2022). Then, the dataset *GPL93* contains the expression of 12626 genes for 165 patients, and it has been chosen for its complexity and higher dimensionality.

The idea is to compare the proposed methodology **KPCA-IG** with existing unsupervised feature selection methods from diverse frameworks, as conducted in Li et al. (2017) and Brouard et al. (2022):

- From He et al. (2005), **lapl** to include one method that relies on the computation of a score
- **NDFS** Li et al. (2021), to add one of the methods primarily designed for clustering. It is based on the implicit assumption that samples are structured into subgroups and demands the a priori definition of the number of clusters.
- **KPCA-permute** in Mariette and Villa-Vialaneix (2017) available in the **mixKernel** R package to include another methodology from the context of kernel PCA.

To evaluate the selected features provided by the four methods, we measured the overall accuracy (ACC) and normalized mutual information (NMI) (Danon et al., 2005) based on k-means cluster performance. For each method, the k-means clustering ACC and NMI have been obtained using several subsets with a different number d of selected features, with $d \in \{10, 20, \dots, 290, 300\}$. Thus, the relevance of the selected values has been estimated according to their ability to reconstruct the clustered nature of the data. More specifically, the three datasets *Glioma*, *Carcinom* and *GPL93* are characterized by 4, 11 and 4 groups respectively. Thus, the k-means clustering was computed using the correct number of clusters in the datasets to obtain a metric for the capability of the selected features to keep this nature. Note that only the **NDFS** method is implemented to explicitly obtain an optimum solution in terms of clustering, also requiring in advance the number of groups in the data. For each method, the k-means clustering was run 20 times to obtain a mean of the overall accuracy and normalized mutual information for each of the 30 subsets of selected features. Both our novel method **KPCA-IG** and **KPCA-permute** have been employed with a Gaussian kernel with a sigma value depending on the dataset. The selected features are, in both cases, based on the first 3, 5 and 3 kernel PC axes for *Glioma*, *Carcinom* and *GPL93*, respectively. The CPU time in seconds required to obtain the feature ranking for all the methods has also been observed. The experiment was conducted on a standard laptop Intel Core *i5* with 16GB RAM.

3.1 Evaluation on benchmarks datasets

In Table 1, we can see the results in terms of mean Accuracy and NMI over 20 runs for different numbers of retained features d . For the first dataset *Glioma* **lapl** seems to show the best performance in terms of NMI and AUC, except when $d = 300$ where the Accuracy obtained with **KPCA-IG** is the highest, even if all the methods seem to behave very

Table 1: Comparison of the different methods in terms of mean ACC and NMI over 20 runs of a k-means clustering for several subsets with a different number d of selected features. CPU represents the computational time in seconds required by the four methods only to find the most influential features.

	lapl	NDFS	KPCA-permute	KPCA-IG
<i>Glioma</i> ($n = 50, p = 4434$)				
ACC(10)	0.50 (0.02)	0.37 (0.04)	0.48 (0.03)	0.42 (0.01)
NMI(10)	0.34 (0.02)	0.13 (0.03)	0.31 (0.02)	0.21 (0.01)
ACC(150)	0.56 (0.03)	0.53 (0.04)	0.54 (0.04)	0.56 (0.05)
NMI(150)	0.50 (0.02)	0.41 (0.03)	0.48 (0.02)	0.36 (0.05)
ACC(300)	0.54 (0.04)	0.55 (0.04)	0.52 (0.03)	0.57 (0.05)
NMI(300)	0.48 (0.03)	0.41 (0.03)	0.45 (0.02)	0.35 (0.05)
CPU time	0.4	84.6	620.9	2.9
<i>Carcinom</i> ($n = 174, p = 9182$)				
ACC(10)	0.27 (0.02)	0.47 (0.04)	0.48 (0.02)	0.51 (0.01)
NMI(10)	0.23 (0.01)	0.48 (0.03)	0.43 (0.01)	0.49 (0.02)
ACC(150)	0.61 (0.03)	0.68 (0.04)	0.67 (0.03)	0.70 (0.03)
NMI(150)	0.62 (0.03)	0.72 (0.03)	0.69 (0.03)	0.70 (0.03)
ACC(300)	0.69 (0.04)	0.69 (0.04)	0.70 (0.048)	0.69 (0.03)
NMI(300)	0.73 (0.03)	0.73 (0.03)	0.71 (0.03)	0.70 (0.02)
CPU time	1.4	391.8	7937.6	30.5
<i>GPL93</i> ($n = 165, p = 12626$)				
ACC(10)	0.38 (0.01)	0.41 (0.01)	0.42 (0.01)	0.40 (0.01)
NMI(10)	0.08 (0.01)	0.109 (0.07)	0.11 (0.01)	0.15 (0.01)
ACC(150)	0.38 (0.01)	0.45 (0.01)	0.60 (0.02)	0.58 (0.01)
NMI(150)	0.07 (0.01)	0.18 (0.02)	0.39 (0.01)	0.29 (0.01)
ACC(300)	0.37 (0.01)	0.49 (0.03)	0.56 (0.05)	0.56 (0.01)
NMI(300)	0.07 (0.01)	0.22 (0.02)	0.22 (0.01)	0.31 (0.01)
CPU time	2.1	1277.4	17691.4	39.8

similarly in terms of ACC. Analyzing the results for the other two datasets *Carcinom* and *GPL93* that are considerably bigger and possibly more complex in terms of sample space manifold, the two methods based on the kernel framework exhibit to surpass the **lapl** and **NDFS** approaches, especially in the *GPL93* datasets. The comparison of the different approaches in terms of NMI and ACC of these two datasets can also be observed in Figure 1 and Figure 2.

Moreover, as shown in Brouard et al. (2022) **NDFS** and the other cluster-based methods like **MCFS** and **UDFS** suffer if the user selects an incorrect decision for the a priori number of clusters. In our case, we show that the proposed methodology behaves similarly or even better to a method like **NDFS** that is specifically optimized for this cluster setting.

The two kernel-based approaches, namely **KPCA-permute** and our novel method **KPCA-IG**, reveal an excellent performance in this setting, once again displaying the appropriateness of the kernel framework in the context of complex biological datasets. However, **KPCA-IG** can provide these above-average performances with a considerably lower CPU time.

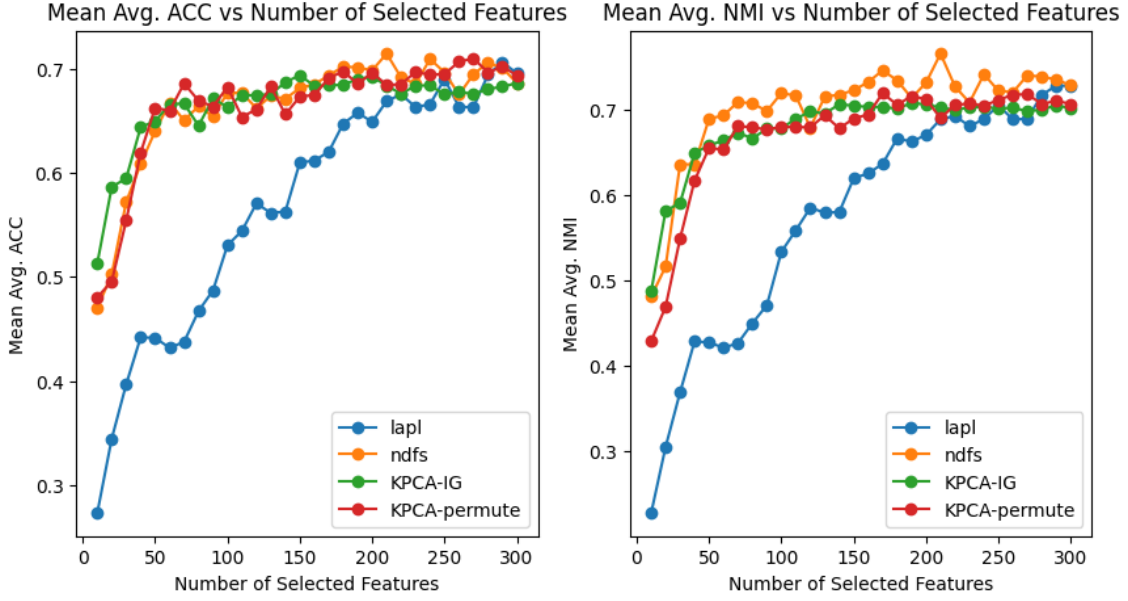


Figure 1: *Carcinom* ACC and NMI: Comparison of the performance of the four methods on the *Carcinom* dataset in terms of Accuracy (left) and Normalized Mutual Information (right) as a function of the number of selected features d . ACC and NMI are computed for the k-means results using only the d selected features.

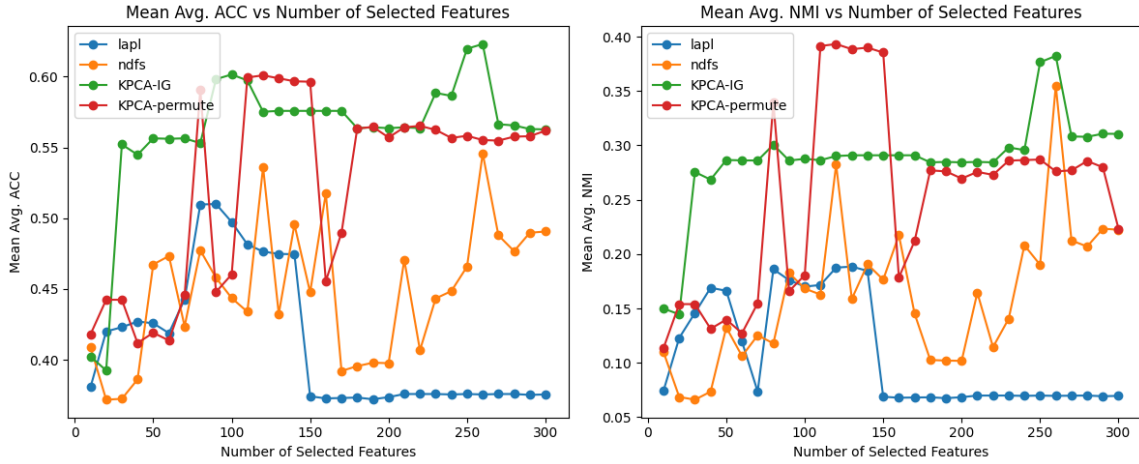


Figure 2: *GPL93* ACC and NMI: Comparison of the performance of the four methods on the *GPL93* dataset in terms of Accuracy (left) and Normalized Mutual Information (right) as a function of the number of selected features d . ACC and NMI are computed for the k-means results using only the d selected features.

Only **lapl** seems as fast as **KPCA-IG** while showing poorer results in the more complex scenario represented in this case by the *GPL93* dataset. Other methods, such as the concrete autoencoder in Abid et al. (2019), have proven successful in this context. The results obtained with the concrete autoencoder, as demonstrated in Brouard et al. (2022), were comparable or even inferior in terms of accuracy and NMI. Furthermore, the computational time required to achieve these results was on the order of days. As a result, we opted not to include it in our simulations.

4 Application on Hepatocellular carcinoma dataset

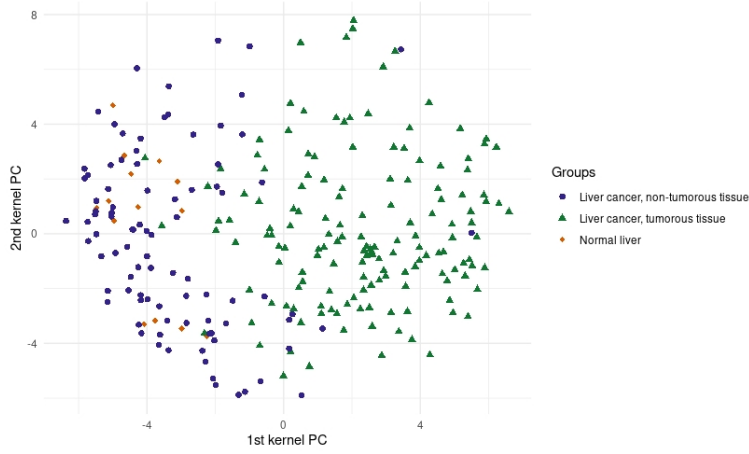


Figure 3: Kernel PCA on HCC (GSE102079) Dataset

Liver cancer is a global health challenge, and it is estimated that there will be over 1 million cases by 2025. Hepatocellular carcinoma (HCC) is the most common type of liver cancer, accounting for around 90% of cases (Llovet et al., 2021). The most significant risk factors associated with HCC are, among others, chronic hepatitis B and C infections, nonalcoholic fatty disease, and chronic alcohol abuse (Morse et al., 2019). To analyse the use of the **KPCA-IG** method, we used the expression profiling by array of an HCC dataset from the Gene expression Omnibus (series GSE102079).

It contains the gene expression microarray profiles of 3 groups of patients. First, 152 patients with HCC who were treated with hepatic resection between 2006 and 2011 at Tokyo Medical and Dental University Hospital. Then, the gene expression of normal liver tissues of 14 patients as control (Chiyonobu et al., 2018). The third group contains the gene expression of 91 patients with liver cancer but of non-tumorous liver tissue. The total expression matrix for the 257 patients contains the expression of 54613 genes, and the data has been normalised by robust multichip analysis (RMA) as in Gautier et al. (2004) and scaled and centered before applying KPCA. To show the potentiality of KPCA-IG, we first perform kernel PCA with radial basis kernel with $\sigma = 0.00001$, which was set heuristically to maximize the explained variance and obtain a clear two dimension data representation.

In Figure 3, it is possible to see the application of kernel Principal Component on the HCC dataset. Even if detecting groups is not the optimization criterion of kernel PCA, it is possible to see that the algorithm catches the dataset's clustered structure. For this reason, applying a method like the proposed KPCA-IG can enlighten the kernel component axes, possibly giving an interpretation of the genes' influence on the sample points representation. The KPCA-IG provides a feature ranking based on the KPCA solution, in this case, based on the first 2 kernel Principal Components. As mentioned before, one of the main advantages of the proposed method is the fast computational time required, as

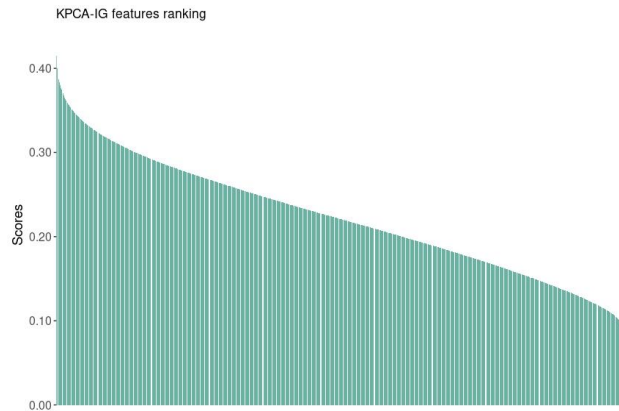


Figure 4: Distribution of the scores for the ordered 54613 genes, from a maximum of 0.428 to a minimum of 0.05×10^3

with this high-dimensional dataset, the CPU time was 654.1 seconds. Table 2 presents the first 25 genes and Figure 4 the distribution of the 54613 variables scores.

One possible way to assess the relevance of the obtained ranking is first to visualize the genes with the method proposed by Reverter et al. (2014) to see if the bio-medical community has already found the retained genes. For instance, Figure 5 displays the representation of the variable 237350_at (TTC36), the second gene in the ranking provided by KPCA-IG. The direction of the arrows suggests an upper expression of the gene towards the cluster of patients that do not have liver cancer or patients whose liver tissue is not tumorous.

Genes	Score	Symbol
1555797_a_at	0.427972	ARPC5
237350_at	0.426140	TTC36
1559573_at	0.424048	LINC01093
230478_at	0.420690	OIT3
203213_at	0.417682	CDK1
205019_s_at	0.417597	VIPR1
1559065_a_at	0.417234	CLEC4G
205984_at	0.417234	CRHBP
220114_s_at	0.416410	STAB2
202604_x_at	0.416228	ADAM10
220496_at	0.415608	CLEC1B
205866_at	0.414893	FCN3
214895_s_at	0.414887	ADAM10
240963_x_at	0.413698	PLXDC1
234304_s_at	0.413574	IPO11
222077_s_at	0.412939	RACGAP1
223341_s_at	0.411044	SCOC
214710_s_at	0.410616	CCNB1
218009_s_at	0.410610	PRC1
219918_s_at	0.410460	ASPM
226524_at	0.410119	C3orf38
201890_at	0.410097	RRM2
207804_s_at	0.409962	FCN2
210481_s_at	0.409839	CLEC4M
209470_s_at	0.409759	GPM6A
...
229461_x_at	0.0520878	NEGR1
230538_at	0.0520119	SHC4
206145_at	0.0507935	RHAG

Table 2: The 25 most relevant genes and the last 3 out of the total number of 54613 according to the proposed KPCA-IG method. The original scores have been multiplied by 10^3 for a better visualization

To validate the procedure, we selected relevant literature about the gene TTC36. This gene, also known as HBP21, is a protein encoder gene. It has been shown that this gene's encoded protein may function as a tumour suppressor in hepatocellular carcinoma (HCC) since it promotes apoptosis while it has been proven to be downregulated in HCC cases (Jiang et al., 2015).

Another gene that shows differential expression in the two groups is 203213_at (CDK1). In this case, Figure 6 suggests that this gene seems to be upregulated in the presence of cancer tissue. The indication found in multiple studies is that the increased expression of this gene is indeed linked with a poorer prognosis or outcome, such as high tumour grade, invasion of lymphovascular or muscularis propria, and the presence of distant metastasis Heo et al. (2022), Li et al. (2020), Sofi et al. (2022), Li et al. (2020), Liu et al. (2022). In the same way, another of the most critical genes, according to KPCA-IG, that seems to be prominent in the case of an HCC patient reflecting the same indication in the medical literature, is 202604_x_at (ADAM10), known to be involved in the RIPing and shedding of numerous substrates leading to cancer progression and inflammatory disease Krzystanek et al. (2016), and indicated as a target for cancer therapy Moss et al. (2008), Crawford et al. (2009), while being upregulated in metastasis cancers Lee et al.

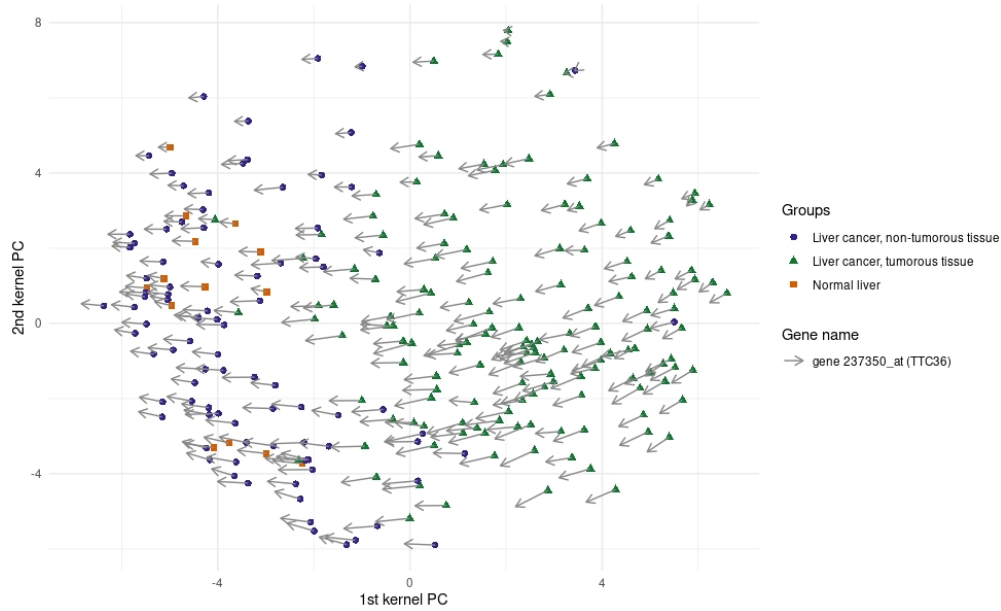


Figure 5: Gene 237350_at (TTC36): Gene visualization obtained using the procedure described in Reverter et al. (2014)

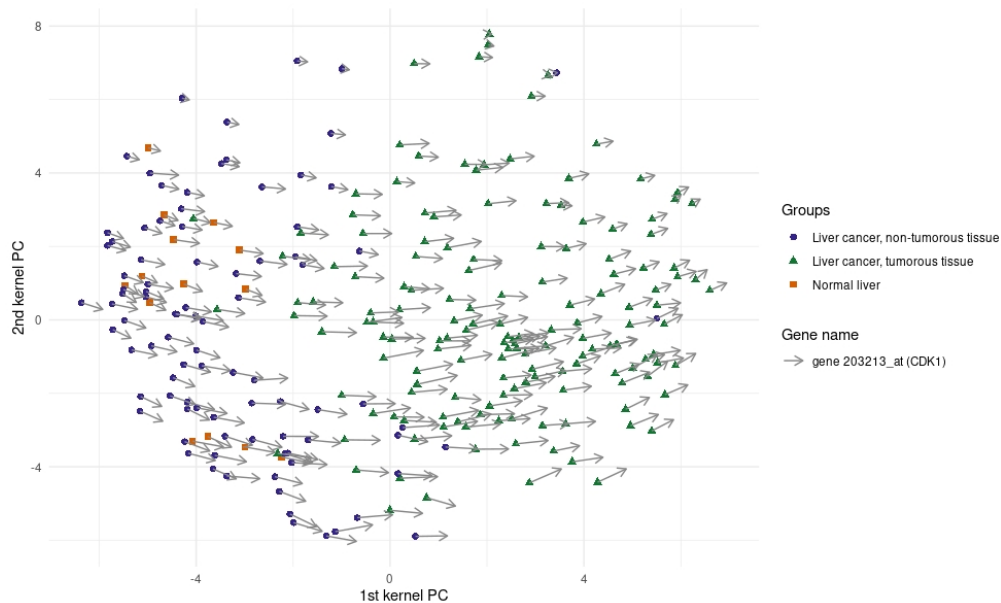


Figure 6: Gene 203213_at (CDK1): Gene visualization obtained using the procedure described in Reverter et al. (2014)

(2010), Gavert et al. (2007). Rac GTPase activating protein 1 gene RACGAP1 (222077_s_at) selected by KPCA-IG shares a similar behaviour with ADAM10 and CDK1. The literature concerning this gene is also broad, where it has been marked as a potential prognostic and immunological biomarker in different types of cancer, such as gastric cancer Saigusa et al. (2014), uterine carcinosarcoma Mi et al. (2016), breast cancer Pliarchopoulou et al. (2012) or colorectal cancer Imaoka et al. (2015) among many others. CCNB1 (202604_x_at) has also been indicated to be an oncogenic factor in the proliferation of HCC cells Chai et al. (2018), showing a significant impact on the patient's survival time Ding et al. (2014), Zhuang et al. (2018) and thus has been targeted for cancer treatments Fang et al. (2014). PRC1 has revealed upper expression in other cancer tissues such as, among others, invasive cervical carcinomas Santin et al. (2005), papillary renal cell carcinoma Yang et al. (2005), pediatric adrenocortical tumour West et al. (2007), while yet not being studied in depth as compared to CCNB1, ADAM10 or RACGAP1.

ASPM (219918_s_at) was known initially as a gene involved in the control of the human brain development and in the cerebral cortical size Zhang (2003), Bond et al. (2002) whose mutations may lead to primary autosomal recessive microcephaly Kouprina et al. (2005), more recently its overexpression has also been linked with tumour progression as in Wang et al. (2013), Xu et al. (2018).

Lastly, for the group of upregulated genes in HCC, RRM2 (201890_at) has also been linked with low overall survival Chen et al. (2019), Jin et al. (2020), leading to exhaustive cancer research suggesting targeting its inhibition for different types of tumour treatments Rahman et al. (2012), Wang et al. (2014), Osako et al. (2019), Ohmura et al. (2021).

On the other hand, the selected genes that manifest down-regulation in cancerous HCC tissues are LINC01093, OIT3, VIPR1, CLEC4G, CRHBP, STAB2, CLEC1B, FCN3, FCN2 and CLEC4M. The literature regarding these genes indicates that they work as suppressors in different cancerous situations, once again endorsing the selection provided by KPCA-IG for the upregulated genes.

The few genes in the first 25 selected by KPCA-IG that do not exhibit differential expression using Reverter et al. (2014) method (ARPC5, IPO11, C3orf38, SCOC) are potential genes that explain much variability in the data or that share a possibly nonlinear interaction with the differential expressed genes. Since the ultimate goal of KPCA is not to discriminate groups, it is expected that some of the variables found by the novel method are not linked with a classification benefit. However, further follow-up on the function of these genes may be done in cooperation with an expert in the field.

5 Conclusion

We have seen how the unsupervised feature selection literature is narrower than its supervised counterpart. Moreover, algorithms that use the kernel Principal Component Analysis for feature selection are reduced to a few works. In the present work, we have introduced a novel method to enhance variables' interpretability in kernel PCA. Using benchmark datasets, we have proven the comparability in terms of accuracy with already existing and recognized methods, where the efficiency of KPCA-IG has proven to be competitive. The application on the real-life Hepatocellular carcinoma dataset and the validation obtained from the comparison of the selected variables by the method with the bio-medical literature have confirmed the effectiveness and strengths of the proposed methodology.

In future works, further in-depth analysis will be realized to assess the impact of the choice of the kernel function on the feature ranking obtained by KPCA-IG. Moreover, the method will be adapted to other linear algorithms that are solely based on dot-products hence supporting a kernelized version, such as kernel Discriminant Analysis or kernel Partial Least-Squares Discriminant Analysis.

Abbreviations KPCA: Kernel principal component analysis; KPCA-IG: Kernel principal component analysis Interpretable Gradient; HCC: Hepatocellular carcinoma; SPEC: Spectral Feature Selection; MCFS: Multi-Cluster Feature Selection; NDFS: Nonnegative Discriminative Feature Selection; UDFS: Unsupervised Discriminative Feature Selection; CPFS: Convex Principal Feature Selection; lapl: Laplacian score

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Availability of data and materials Glioma and Carcinoma datasets are freely available at <https://github.com/jundongl/scikit-feature/tree/master/skfeature/data>, GPL93 is freely available at <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL93> HCC dataset is freely available at <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE102079>

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