Package 'MOSS'

July 16, 2021

Title Multi-Omic Integration via Sparse Singular Value Decomposition

Version 0.2.0

Description High dimensionality, noise and heterogeneity among
samples and features challenge the omic integration task. Here we
present an omic integration method based on sparse singular value
decomposition (SVD) to deal with these limitations, by: a. obtaining
the main axes of variation of the combined omics, b. imposing sparsity
constraints at both subjects (rows) and features (columns) levels
using Elastic Net type of shrinkage, and c. allowing both linear and
non-linear projections (via t-Stochastic Neighbor Embedding) of the
omic data to detect clusters in very convoluted data
(Gonzalez-Reymundez & Vazquez, 2020) <doi:10.1038/s41598-020-65119-5>.

License GPL-2

URL https://github.com/agugonrey/MOSS

BugReports https://github.com/agugonrey/MOSS/issues

Imports cluster, dbscan, Rtsne, stats

Suggests annotate, bigparallelr, bigstatsr, future.apply, scatterpie,
clValid, ComplexHeatmap, fpc, ggplot2, ggpmisc, ggthemes,
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R **topics documented:**

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aest.f *Assign point color and shape aesthetics.*

Description

This function is called by moss whenever a plot is produced. It simply assigns colors and shape to points based on input labels.

Usage

```
aest.f(x, n.cat = 2, option = "D")
```

Arguments

x	Character vector with labels, or a numerical vector to be discretized in 'n.cat' categories.
n.cat	Number of categories to split vector 'x'. Numeric. Ignored if 'x' is a character vector.
option	Controls color palette. One of the possible 'option' arguments for the 'viridis' function.

Value

A data.frame with labels as rownames and two columns representing point colors and shape, respectively.

---

cov_adj *Adjust omic blocks for covariates effects.*

Description

This function is called by moss to adjust a series of omic blocks for covariates effects.

Usage

```
cov_adj(data.blocks, covs, n, dim.names = NULL)
```

Arguments

data.blocks	List containing omic blocks of class 'matrix' or 'FBM'. In each block, rows represent subjects and columns features.
covs	Covariates which effect we wish to adjust for. Accepts objects of class matrix, data.frame, numeric, or character vectors.
n	Number of subjects. Numeric.
dim.names	list of vectors with samples names, and features names by omic block. If NULL, a list of artificial names is created. Defaults to NULL.

Value

Returns the covariates-adjusted elements in data.blocks.

Examples

```
library("MOSS")
sim_data <- simulate_data()
set.seed(43)

# Extracting simulated omic blocks.
sim_blocks <- sim_data$sim_blocks[-4]

# Using fourth block as covariates.
covs <- sim_data$sim_blocks[[4]]

# Adjust omic blocks for covariates effects.
sim_blocks_adj <- cov_adj(sim_blocks,covs,nrow(covs))
```

---

metdat   *Extracts (and merges) chunks of characters.*

Description

Extracts (and merges) chunks of characters.

Usage

```
metdat(x, i, sep = "-", collapse = sep)
```

Arguments

x	A character vector.
i	Index specifying which chunks of characters will be extracted (and merged).
sep	Chunks separator character. Defaults to "-".
collapse	New chunks separator character. Default to 'sep'.

Value

A character vector with the extracted (and merged) chunks of characters.

Examples

```
x <- "this is one chunk of characters & this is another one"
metdat(x, 1, " & ")
metdat(x, 2, " & ")
metdat(x, c(1, 2), " & ")
metdat(x, c(1, 2), " & ", " and ")
```

---

moss   *Multi-Omic integration via Sparse Singular value decomposition.*

Description

This function integrates omic blocks to perform sparse singular value decomposition (SVD), non-linear embedding, and/or cluster analysis. Both supervised and unsupervised methods are supported. In both cases, if multiple omic blocks are used as predictors, they are concatenated and normalized to form an 'extended' omic matrix 'X' (Gonzalez-Reymundez and Vazquez, 2020). Supervised analysis can be obtained by indicating which omic block defines a multivariate response 'Y'. Each method within MOSS returns a matrix 'B', which form depends on the technique used (e.g. $B = X$ in pca; $B = X'Y$, for pls; $B = (X'X)^-X'Y$, for lrr). A sparse SVD of matrix B is then obtained to summarize the variability among samples and features in terms of latent factors.

Usage

```
moss(
  data.blocks,
  scale.arg = TRUE,
  norm.arg = TRUE,
  method = "pca",
  resp.block = NULL,
  covs = NULL,
  K.X = 5,
  K.Y = K.X,
  verbose = TRUE,
  nu.parallel = FALSE,
  nu.u = NULL,
  nu.v = NULL,
  alpha.u = 1,
  alpha.v = 1,
  plot = FALSE,
  cluster = FALSE,
  clus.lab = NULL,
  tSNE = FALSE,
  axes.pos = seq_len(K.Y),
  approx.arg = FALSE,
  exact.dg = FALSE,
  use.fbm = FALSE,
  lib.thresh = TRUE
)
```

Arguments

`data.blocks`	List containing omic blocks of class 'matrix' or 'FBM'. In each block, rows represent subjects and columns features.
`scale.arg`	Should the omic blocks be centered and scaled? Logical. Defaults to TRUE.
`norm.arg`	Should omic blocks be normalized? Logical. Defaults to TRUE.
`method`	Multivariate method. Character. Defaults to 'pca'. Possible options are pca, mbpca, pca-lda, mbpca-lda, pls, mbpls, pls-lda, mbpls-lda, lrr, mblrr, lrr-lda, mblrr-lda.
`resp.block`	What block should be used as response? Integer. Only used when the specified method is supervised.
`covs`	Covariates which effect we wish to adjust for. Accepts matrix, data.frame, numeric, or character vectors.
`K.X`	Number of principal components for predictors. Integer. Defaults to 5.
`K.Y`	Number of responses PC index when method is supervised. Defaults to K.X.
`verbose`	Should we print messages? Logical. Defaults to TRUE.
`nu.parallel`	Tuning degrees of sparsity in parallel. Defaults to FALSE.
`nu.u`	A grid with increasing integers representing degrees of sparsity for left Eigenvectors. Defaults to NULL.

nu.v	Same but for right Eigenvectors. Defaults to NULL.
alpha.u	Elastic Net parameter for left Eigenvectors. Numeric between 0 and 1. Defaults to 1.
alpha.v	Elastic Net parameter for right Eigenvectors. Numeric between 0 and 1. Defaults to 1.
plot	Should results be plotted? Logical. Defaults to FALSE.
cluster	Arguments passed to the function tsne2clus as a list. Defaults to FALSE. If cluster=TRUE, default parameters are used (eps_range=c(0,4), eps_res=100).
clus.lab	A vector of same length than number of subjects with labels used to visualize clusters. Factor. Defaults to NULL. When sparsity is imposed on the left Eigenvectors, the association between non-zero loadings and labels' groups is shown by a Chi-2 statistics for each pc. When sparsity is not imposed, the association between labels and PC is addressed by a Kruskal-Wallis statistics.
tSNE	Arguments passed to the function pca2tsne as a list. Defaults to FALSE. If tSNE=T, default parameters are used (perp=50,n.samples=1,n.iter=1e3).
axes.pos	PC index used for tSNE. Defaults to 1 : K.Y. Used only when tSNE is different than NULL.
approx.arg	Should we use standard SVD or random approximations? Defaults to FALSE. If TRUE and at least one block is of class 'matrix', irlba is called. If TRUE & is(O,'FBM')==TRUE, big_randomSVD is called.
exact.dg	Should we compute exact degrees of sparsity? Logical. Defaults to FALSE. Only relevant When alpha.s or alpha.f are in the (0,1) interval and exact.dg = TRUE.
use.fbm	Should we treat omic blocks as Filed Backed Matrix (FBM)? Logical. Defaults to FALSE.
lib.thresh	Should we use a liberal or conservative threshold to tune degrees of sparsity? Logical. Defaults to TRUE.

Details

Once 'dense' solutions are found (the result of SVD on a matrix B), the function ssvdEN_sol_path is called to perform sparse SVD (sSVD) on a grid of possible degrees of sparsity (nu), for a possible value of the elastic net parameter (alpha). The sSVD is performed using the algorithm of Shen and Huang (2008), extended to include Elastic Net type of regularization. For one latent factor (rank 1 case), the algorithm finds vectors u and v' and scalar d that minimize:

$$\|B\text{-}d* uv'\|^2 + lambda(nu\_v)(alpha\_v\|v'\|\_1 + (1\text{-}alpha\_v)\|v'\|^2) + lambda(nu\_u)(alpha\_u\|u\|\_1 + (1\text{-}alpha\_u)\|u\|^2)$$

such that $\|u\| = 1$. The right Eigenvector is obtained from v / $\|v\|$ and the corresponding d from u'Bv. The element lambda(nu_.) is a monotonically decreasing function of nu_. (the number of desired element different from zero) onto positive real numbers, and alpha_. is any number between zero and one balancing shrinking and variable selection. Selecting degree of sparsity: The function allows to tune the degree of sparsity using an ad-hoc method based on the one presented in Shen & Huang (2008, see reference) and generalized for tuning both nu_v and nu_u. This is done by exploring the proportion of explained variance (PEV) on a grid of possible values. Drastic and/or

steep changes in the PEV trajectory across degrees of sparsity are used for automatic selection (see help for the function ssvdEN_sol_path). By imposing the additional assumption of omic blocks being conditionally independent, each multivariate technique can be extended using a 'multi-block' approach, where the contribution of each omic block to the total (co)variance is addressed. When response Y is a character column matrix, with classes or categories by subject, each multivariate technique can be extended to perform linear discriminant analysis.

Value

Returns a list with the results of the sparse SVD. If *plot*=TRUE, a series of plots is generated as well.

- **B:** The object of the (sparse) SVD. Depending of the method used, B can be a extended matrix of normalized omic blocks, a variance-covariance matrix, or a matrix of regression coefficients. If at least one of the blocks in 'data.blocks' is of class FBM, is(B,'FBM') is TRUE. Otherwise, is(B,'matrix') is TRUE.
- **Q:** Matrix with the SVD projections at the level of subjects.
- **selected_items:** List containing the position, name, and loadings of selected features and subjects by latent dimension. if 'plot=TRUE', a scatterplot is displayed, where the x-axis represents the latent dimensions, the y-axis the total number of features selected in log scale, and each point is a pie chart showing the relative contribution of each omic to the number of features selected. The radio of the pie-chart represents the coefficient of variation among squared loadings (mean squared loadings divided by their standard deviation)
- **dense:** A list containing the results of the dense SVD.
  - **u:** Matrix with left Eigenvectors.
  - **v:** Matrix with right Eigenvectors.
  - **d:** Matrix with singular values.
- **sparse:** A list containing the results of the sparse SVD.
  - **u:** Matrix with left Eigenvectors.
  - **v:** Matrix with right Eigenvectors.
  - **d:** Matrix with singular values.
  - **opt_dg_v** Selected degrees of sparsity for right Eigenvectors.
  - **opt_dg_u:** Selected degrees of sparsity for left Eigenvectors.
- Graphical displays: Depending on the values in 'plot', 'tSNE','cluster', and 'clus.lab' arguments, the following ggplot objects can be obtained. They contain:
  - **scree_plot:** Plots of Eigenvalues and their first and second order empirical derivatives along PC indexes.
  - **tun_dgSpar_plot:** Plots with the PEV trajectory, as well as its first and second empirical derivatives along the degrees of sparsity path.
  - **PC_plot:** Plot of the first principal components according to axes.pos. By default the first two are plotted.
  - **tSNE_plot:** Plot with the tSNE mapping onto two dimensions.
  - **clus_plot:** The output of function tsne2clus.
  - **subLabels_vs_PCs:** Plot of the Kruskal-Wallis (or Chi-square) statistics of the association test between PC (or selected subjects) and pre-established subjects groups.
  - **clusters_vs_PCs:** Plot of the Kruskal-Wallis (or Chi-square) statistics of the association test between PC (or selected subjects) and detected clusters.

Note

1. The function does not return PEV for EN parameter (alpha_v and/or alpha_u), the user needs to provide a single value for each.

2. When number of PC index > 1, columns of T might not be orthogonal.

3. Although the user is encouraged to perform data projection and cluster separately, MOSS allows to do this automatically. However, both tasks might require further tuning than the provided by default, and computations could become cumbersome.

4. Tuning of degrees of sparsity is done heuristically on training set. In our experience, this results in high specificity, but rather low sensitivity. (i.e. too liberal cutoffs, as compared with extensive cross-validation on testing set).

5. When 'method' is an unsupervised technique, 'K.X' is the number of latent factors returned and used in further analysis. When 'method' is a supervised technique, 'K.X' is used to perform a SVD to facilitate the product of large matrices and inverses.

6. If 'K.X' (or 'K.Y') equal 1, no plots are returned.

7. Although the degree of sparsity maps onto number of features/subjects for Lasso, the user needs to be aware that this conceptual correspondence is lost for full EN (alpha belonging to (0, 1); e.g. the number of features selected with alpha < 1 will be eventually larger than the optimal degree of sparsity). This allows to rapidly increase the number of non-zero elements when tuning the degrees of sparsity. In order to get exact values for the degrees of sparsity at subjects or features levels, the user needs to set the value of 'exact.dg' parameter from 'FALSE' (the default) to 'TRUE'.

References

- Gonzalez-Reymundez, and Vazquez. 2020. Multi-omic Signatures identify pan-cancer classes of tumors beyond tissue of origin. Scientific Reports 10 (1):8341

- Shen, Haipeng, and Jianhua Z. Huang. 2008. Sparse Principal Component Analysis via Regularized Low Rank Matrix approximation. Journal of Multivariate Analysis 99 (6). Academic Press: 1015_34.

- Baglama, Jim, Lothar Reichel, and B W Lewis. 2018. Irlba: Fast Truncated Singular Value Decomposition and Principal Components Analysis for Large Dense and Sparse Matrices.

- Taskesen, Erdogan, Sjoerd M. H. Huisman, Ahmed Mahfouz, Jesse H. Krijthe, Jeroen de Ridder, Anja van de Stolpe, Erik van den Akker, Wim Verheagh, and Marcel J. T. Reinders. 2016. Pan-Cancer Subtyping in a 2D-Map Shows Substructures That Are Driven by Specific Combinations of Molecular Characteristics. Scientific Reports 6 (1):24949.

- van der Maaten L, Hinton G. Visualizing Data using t-SNE. J Mach Learn Res. 2008;9: 2579–2605

Examples

```
# Example1: sparse PCA of a list of omic blocks.
library("MOSS")
sim_data <- simulate_data()
set.seed(43)


# Extracting simulated omic blocks.
```

```
sim_blocks <- sim_data$sim_blocks

# Extracting subjects and features labels.
lab.sub <- sim_data$labels$lab.sub
lab.feat <- sim_data$labels$lab.feat
out <- moss(sim_blocks[-4],
  method = "pca",
  nu.v = seq(1, 200, by = 100),
  nu.u = seq(1, 100, by = 50),
  alpha.v = 0.5,
  alpha.u = 1
)

library(ggplot2)
library(ggthemes)
library(viridis)
library(cluster)
library(fpc)

set.seed(43)

# Example2: sparse PCA with t-SNE, clustering, and association with
# predefined groups of subjects.
out <- moss(sim_blocks[-4],axes.pos=c(1:5),
  method = "pca",
  nu.v = seq(1, 200, by = 10),
  nu.u = seq(1, 100, by = 2),
  alpha.v = 0.5,
  alpha.u = 1,
  tSNE = TRUE,
  cluster = TRUE,
  clus.lab = lab.sub,
  plot = TRUE
)

# This shows clusters obtained with labels from pre-defined groups
# of subjects.
out$clus_plot

# This shows the statistical overlap between PCs and the pre-defined
# groups of subjects.
out$subLabels_vs_PCs

# This shows the contribution of each omic to the features
# selected by PC index.
out$selected_items

# This shows features forming signatures across clusters.
out$feat_signatures

# Example3: Multi-block PCA with sparsity.
out <- moss(sim_blocks[-4],axes.pos=1:5,
  method = "mbpca",
```

```
  nu.v = seq(1, 200, by = 10),
  nu.u = seq(1, 100, by = 2),
  alpha.v = 0.5,
  alpha.u = 1,
  tSNE = TRUE,
  cluster = TRUE,
  clus.lab = lab.sub,
  plot = TRUE
)
out$clus_plot

# This shows the 'weight' each omic block has on the variability
# explained by each PC. Weights in each PC add up to one.
out$block_weights

# Example4: Partial least squares with sparsity (PLS).
out <- moss(sim_blocks[-4],axes.pos=1:5,
  K.X = 500,
  K.Y = 5,
  method = "pls",
  nu.v = seq(1, 100, by = 2),
  nu.u = seq(1, 100, by = 2),
  alpha.v = 1,
  alpha.u = 1,
  tSNE = TRUE,
  cluster = TRUE,
  clus.lab = lab.sub,
  resp.block = 3,
  plot = TRUE
)
out$clus_plot

# Get some measurement of accuracy at detecting features with signal
# versus background noise.
table(out$sparse$u[, 1] != 0, lab.feat[1:2000])
table(out$sparse$v[, 1] != 0, lab.feat[2001:3000])

# Example5: PCA-LDA
out <- moss(sim_blocks,
  method = "pca-lda",
  cluster = TRUE,
  resp.block = 4,
  clus.lab = lab.sub,
  plot = TRUE
)
out$clus_plot
```

---

moss_heatmap   *Creates a heatmap from the output of MOSS.*

Description

Creates a heatmap from the output of MOSS.

Usage

```
moss_heatmap(B, SVD, right.lab, left.lab, axes.pos = NULL, verbose = TRUE)
```

Arguments

B	An bject of class 'matrix' or 'FBM'.
SVD	List with the results of a sparse or dense SVD.
right.lab	Columns title. Character.
left.lab	Rows title. Character.
axes.pos	What SVD dimensions should be used to plot the heatmap? If NULL, all the SVD dimensions are use. Defaults to NULL.
verbose	Should we print messages? Logical. Defaults to TRUE.

Value

Returns a 'ComplexHeatmap' plot representing the cross-product between left and right Eigenvectors.

---

moss_select *Returns features and subject selected by latent dimension.*

Description

This function is meant to used after moss. Its main purpose is to extract the features and subjects by latent dimension. The selection depends on loadings at each dimension being different from zero.

Usage

```
moss_select(data.blocks, SVD, resp.block = NULL, K = NULL, plot = FALSE)
```

Arguments

data.blocks	a list of omic blocks as provided to moss.
SVD	a list with SVD results. The function is meant to work with the results from sparse SVD. However, 'dense' solutions are also accepted.
resp.block	Which omic block was used as response in moss? Integer. Defaults to NULL.
K	How many dimensions should be displayed? Vector. Defaults to the 1 : ncol(SVD$v).
plot	Should the results be plotted? Logical. Defaults to FALSE

Value

Returns a list containing the position, name, and loadings of selected features and subjects by latent dimension. if 'plot=TRUE', a scatterplot is displayed, where the x-axis represents the latent dimensions, the y-axis the total number of features selected in log scale, and each point is a pie chart showing the relative contribution of each omic to the number of features selected. The radio of the pie chart represents the coefficient of variation among squared loadings (mean squared loadings divided by their standard deviation).

---

moss_signatures   *Returns signatures of features by groups of subjects*

Description

This function is meant to used after moss_select. Its main purpose is to visualize how each selected feature (non-zero loading feature) contributes to each group of subjects by latent dimension.

Usage

```
moss_signatures(
  data.blocks,
  moss_select.out,
  clus_lab = NULL,
  plot = FALSE,
  feature.labels = NULL,
  th = 1,
  only.candidates = FALSE
)
```

Arguments

data.blocks   A list of omic blocks as provided to moss.

moss_select.out
                 The output of moss_select.

clus_lab   A vector of same length than number of subjects with labels used to visualize
                 clusters. Defaults to NULL.

plot   Should the results be plotted? Logical. Defaults to FALSE

feature.labels   List with with features names for each omic. Defaults to NULL.

th   Show the th Default to th=1 (all the features). Numeric.

only.candidates
                 Should we plot only candidate features? Logical.

Value

Returns a list with 'signatures', and if plot=TRUE, a ggplot object named 'sig_plot'. The element 'signatures' is a data frame with columns corresponding to 'Cluster' (groups of subjects), 'Omic', 'Dim' (PC index or latent dimension), 'Feature_name', 'Feature_pos' (column index of the selected feature within the corresponding omic), 'Loadings' (non-zero loadings from moss), 'Means', 'L1' and 'L2' (mean +/- standard error of the selected feature values within an omic).

Examples

```
library("MOSS")
# Extracting simulated omic blocks.
sim_data <- simulate_data()
sim_blocks <- sim_data$sim_blocks

# Extracting subjects and features labels.
lab.sub <- sim_data$labels$lab.sub

out <- moss(sim_blocks[-4],
  method = "pca",
  nu.v = 10,
  exact.dg = TRUE,
  plot = TRUE,
  alpha.v = 0.5
)
out2 <- moss_select(data.blocks = sim_blocks[-4],
                    SVD = out$sparse,
                    plot = TRUE)

# Display signature plots.
out3 <- moss_signatures(data.blocks = sim_blocks[-4],
                        clus_lab=lab.sub,
                        moss_select.out = out2,
                        plot = TRUE)
out3$sig_plot
```

---

pca2tsne   *Mapping principal components onto a 2D map via tSNE.*

Description

This function is called by moss whenever 'moss(tSNE=TRUE)' to project latent factors onto two dimensions via t-stochastic neighbor embedding (tSNE) However, it can be used on any generic data matrix. The function uses the Barnes-Hut tSNE algorithm from Rtsne package, and uses an iterative procedure to select a tSNE map minimizing the projection cost across several random initial conditions. The function is inspired by the iterative procedure discussed in Taskesen et al. 2016 and code originally provided with the publication.

Usage

```
pca2tsne(Z, perp = 50, n.samples = 1, n.iter = 1000, parallel = FALSE)
```

Arguments

Z	A matrix with axes of variation (typically PCs) as columns and subjects as rows.
perp	Perplexity value. Defaults to 50.
n.samples	Number of times the algorithm starts from different random initial conditions. Defaults to 1.
n.iter	Number of iterations for each run of the algorithm.
parallel	Should random starts be done in parallel? Logical. Default to FALSE. Defaults to 1000.

Value

Returns output of function 'Rtsne::Rtsne' from the random initial condition with the smallest 're-construction error'.

References

- van der Maaten L, Hinton G. Visualizing Data using t-SNE. J Mach Learn Res. 2008;9: 2579–2605

- Krijthe JH. Rtsne: T-Distributed Stochastic Neighbor Embedding using a Barnes-Hut Implementation. 2015

- Taskesen, Erdogan, Sjoerd M. H. Huisman, Ahmed Mahfouz, Jesse H. Krijthe, Jeroen de Ridder, Anja van de Stolpe, Erik van den Akker, Wim Verheagh, and Marcel J. T. Reinders. 2016. Pan-Cancer Subtyping in a 2D-Map Shows Substructures That Are Driven by Specific Combinations of Molecular Characteristics. Scientific Reports 6 (1):24949.

Examples

```
library("MOSS")
sim_blocks <- simulate_data()$sim_blocks

# Example of pca2tsne usage.
Z <- pca2tsne(sim_blocks$`Block 3`,
              perp = 50,
              n.samples = 1,
              n.iter = 1e3)$Y
plot(Z, xlab = "x_tSNE(X)", ylab = "y_tSNE(X)")

# Example of usage within moss.
set.seed(34)
moss(sim_blocks[-4],
  tSNE = list(
    perp = 50,
    n.samples = 1,
```

```
    n.iter = 1e3
  ),
  plot = TRUE
)$tSNE_plot
```

---

prepro_na	*Missing values imputation by the mean of each column.*

Description

This function is called by moss to count the impute missing values by the mean of each column within omic blocks.

Usage

```
prepro_na(X)
```

Arguments

X   An object of class 'matrix', 'FBM', or 'array'.

Details

Meant for objects of class 'matrix', 'FBM', or 'array'.

Value

Returns input with imputed missing values.

---

prepro_sub	*Scale and normalize columns of a matrix.*

Description

This function is called by moss to scale and normalize (extended) matrices.

Usage

```
prepro_sub(X, scale.arg, norm.arg)
```

Arguments

X	An object of class 'matrix', 'FBM', or 'array'.
scale.arg	Should we scale columns? Logical.
norm.arg	Should we normalize columns? Logical.

Details

Ment for objects of class 'matrix', 'FBM', or 'array'.

Value

A matrix with scaled and/or normalized columns.

---

simulate_data   *Simple simulation of regulatory modules.*

Description

This a simple simulation to use in MOSS' examples. The specifics of the simulation are shown in the "Examples" section.

Usage

```
simulate_data(moss_seed = 42)
```

Arguments

moss_seed   The seed for random number generator. Numeric. Defaults to 42.

Value

A list of two elements 'sim_blocks' and 'labels'. First element 'sim_blocks' is a list of three numeric matrices, and one character matrix. Second element 'labels' has two character vectors. The first element 'lab.sub' identifies the groups of 'signal' subjects. The second element 'lab.feat' identifies the groups 'signal' features from background 'noise'.

Examples

```
sim_data <- simulate_data()

# Extracting simulated omic blocks.
sim_blocks <- sim_data$sim_blocks

# Extracting subjects and features labels.
lab.sub <- sim_data$labels$lab.sub
lab.feat <- sim_data$labels$lab.feat

# Check dimensions and objects class.
lapply(sim_blocks, dim)
lapply(sim_blocks, function(x) class(x[, 1]))

# Showing how the data was generated.
set.seed(42)
O1 <- matrix(data = 0, nrow = 5e2, ncol = 1e3)
O2 <- O1
```

```
O1[1:20, 1:150] <- 1
O1 <- O1 + rnorm(5e5, mean = 0, sd = 0.5)
O2[71:90, 71:200] <- 1
O2 <- O2 + rnorm(5e5, mean = 0, sd = 0.5)
# Simulating a continous response blocks.
O3 <- 3 * O1 - 5 * O2 + rnorm(5e5, mean = 0, sd = 0.5)

# Creating a vector labeling clusters of subjects.
aux <- rep("Background", 500)
aux[1:20] <- "Group 1"
aux[71:90] <- "Group 2"
all.equal(aux, lab.sub)

# Generating a classification response.
O4 <- as.matrix(aux)

# Storing all blocks within a list.
all.equal(sim_blocks, list(
  "Block 1" = O1,
  "Block 2" = O2,
  "Block 3" = O3,
  "Block 4" = O4
))

# Creating a vector labeling signal and background features.
aux <- rep("Background features", 3000)
aux[c(1:150, 1072:1200, 2001:2200)] <- "Signal features"
all.equal(aux, lab.feat)
```

---

ssvdEN	*Sparse Singular Value Decomposition via Elastic Net.*

Description

This function performs sparse singular value decomposition (SVD) on a matrix 'x' via Elastic Net types of penalties. For one PC (rank 1 case), the algorithm finds left and right Eigenvectors (u and w, respectively), that minimize: $\|x - u\ w'\|\_F^2 + \lambda_w (\alpha_w\|w\|\_1 + (1 - \alpha_w)\|w\|\_F^2) + \lambda_u (\alpha\|u\|\_1 + (1 - \alpha_u)\|u\|\_F^2)$ such that $\|u\| = 1$. The right Eigen vector is obtained from $v = w / \|w\|$ and the corresponding Eigen value $= u^T x v$. The penalties λ_u and λ_w are mapped from specified desired degree of sparsity (dg.spar.features & dg.spar.subjects).

Usage

```
ssvdEN(
  O,
  n.PC = 1,
  dg.spar.features = NULL,
  dg.spar.subjects = NULL,
```

```
    maxit = 500,
    tol = 0.001,
    scale.arg = TRUE,
    center.arg = TRUE,
    approx.arg = FALSE,
    alpha.f = 1,
    alpha.s = 1,
    svd.0 = NULL,
    s.values = TRUE,
    ncores = 1,
    exact.dg = FALSE
)
```

Arguments

O	Numeric matrix of n subjects (rows) and p features (columns). It can be a File-backed Big Matrix.
n.PC	Number of desired principal axes. Numeric. Defaults to 1.
dg.spar.features	
	Degree of sparsity at the features level. Numeric. Defaults to NULL.
dg.spar.subjects	
	Degree of sparsity at the subjects level. Numeric. Defaults to NULL.
maxit	Maximum number of iterations for the sparse SVD algorithm. Numeric. Defaults to 500.
tol	Convergence tolerance for the sparse SVD algorithm. Numeric. Defaults to 0.001.
scale.arg	Should O be scaled? Logical. Defaults to TRUE.
center.arg	Should O be centered? Logical. Defaults to TRUE.
approx.arg	Should we use standard SVD or random approximations? Defaults to FALSE. If TRUE & is(O,'matrix') == TRUE, irlba is called. If TRUE & is(O, "FBM") == TRUE, big_randomSVD is called.
alpha.f	Elastic net mixture parameter at the features level. Measures the compromise between lasso (alpha = 1) and ridge (alpha = 0) types of sparsity. Numeric. Defaults to 1.
alpha.s	Elastic net mixture parameter at the subjects level. Defaults to alpha.s = 1.
svd.0	List containing an initial SVD. Defaults to NULL.
s.values	Should the singular values be calculated? Logical. Defaults to TRUE.
ncores	Number of cores used by big_randomSVD. Default does not use parallelism. Ignored when class(O)!=FBM.
exact.dg	Should we compute exact degrees of sparsity? Logical. Defaults to FALSE. Only relevant When alpha.s or alpha.f are in the (0,1) interval and exact.dg = TRUE.

Details

The function allows the use of the base svd function for relatively small problems. For larger problems, functions for fast-partial SVD (irlba and big_randomSVD, from irlba and bigstatsr packages) are used.

Value

A list with the results of the (sparse) SVD, containing:

- u: Matrix with left eigenvectors.
- v: Matrix with right eigenvectors.
- d: Matrix with singular values.

Note

When elastic net is used ('alpha.s' or 'alpha.f' in the (0,1) interval), the resulting number of non-zero subjects or features is larger than the 'dg.spar.subjects' or 'dg.spar.features' values. This allows to rapidly increase the number of non-zero elements when tuning the degrees of sparsity with function ssvdEN_sol_path. In order to get exact values for the degrees of sparsity at subjects or features levels, the user needs to set the value of 'exact.dg' parameter from 'FALSE' (the default) to 'TRUE'.

References

- Shen, Haipeng, and Jianhua Z. Huang. 2008. Sparse Principal Component Analysis via Regularized Low Rank Matrix Approximation. Journal of Multivariate Analysis 99 (6). Academic Press:1015_34.
- Baglama, Jim, Lothar Reichel, and B W Lewis. 2018. Irlba: Fast Truncated Singular Value Decomposition and Principal Components Analysis for Large Dense and Sparse Matrices.

Examples

```
library("MOSS")

# Extracting simulated omic blocks.
sim_blocks <- simulate_data()$sim_blocks

X <- sim_blocks$`Block 3`

# Equal to svd solution: exact singular vectors and values.
out <- ssvdEN(X, approx.arg = FALSE)

# Uses irlba to get approximated singular vectors and values.
library(irlba)
out <- ssvdEN(X, approx.arg = TRUE)
# Uses bigstatsr to get approximated singular vectors and values
# of a Filebacked Big Matrix.
library(bigstatsr)
out <- ssvdEN(as_FBM(X), approx.arg = TRUE)

# Sampling a number of subjects and features for a fix sparsity degree.
```

```
s.u <- sample(1:nrow(X), 1)
s.v <- sample(1:ncol(X), 1)

# Lasso penalties.
all.equal(sum(ssvdEN(X, dg.spar.features = s.v)$v != 0), s.v)
all.equal(
  unique(colSums(ssvdEN(X, dg.spar.features = s.v, n.PC = 5)$v
  != 0)),
  s.v
)

all.equal(sum(ssvdEN(X, dg.spar.subjects = s.u)$u != 0), s.u)
all.equal(
  unique(colSums(ssvdEN(X, dg.spar.subjects = s.u, n.PC = 5)$u
  != 0)),
  s.u
)

out <- ssvdEN(X, dg.spar.features = s.v, dg.spar.subjects = s.u)
all.equal(sum(out$u != 0), s.u)
all.equal(sum(out$v != 0), s.v)

out <- ssvdEN(X,
  dg.spar.features = s.v, dg.spar.subjects = s.u,
  n.PC = 10
)
all.equal(unique(colSums(out$u != 0)), s.u)
all.equal(unique(colSums(out$v != 0)), s.v)

# Ridge penalties.
all.equal(
  sum(ssvdEN(X, dg.spar.features = s.v, alpha.f = 0)$v != 0),
  ncol(X)
)
all.equal(
  unique(colSums(ssvdEN(X,
    dg.spar.features = s.v, n.PC = 5,
    alpha.f = 0
  )$v != 0)),
  ncol(X)
)

all.equal(
  sum(ssvdEN(X, dg.spar.subjects = s.u, alpha.s = 0)$u != 0),
  nrow(X)
)
all.equal(
  unique(colSums(ssvdEN(X,
    dg.spar.subjects = s.u, n.PC = 5,
    alpha.s = 0
  )$u != 0)),
  nrow(X)
)
```

```
out <- ssvdEN(X,
  dg.spar.features = s.v, dg.spar.subjects = s.u,
  alpha.f = 0, alpha.s = 0
)
all.equal(sum(out$u != 0), nrow(X))
all.equal(sum(out$v != 0), ncol(X))

out <- ssvdEN(X,
  dg.spar.features = s.v, dg.spar.subjects = s.u,
  n.PC = 10, alpha.f = 0,
  alpha.s = 0
)
all.equal(unique(colSums(out$u != 0)), nrow(X))
all.equal(unique(colSums(out$v != 0)), ncol(X))

# Elastic Net penalties.
sum(ssvdEN(X, dg.spar.features = s.v, alpha.f = 0.5)$v != 0) >= s.v
all(unique(colSums(ssvdEN(X,
  dg.spar.features = s.v, n.PC = 5,
  alpha.f = 0.5
)$v != 0)) >= s.v)

sum(ssvdEN(X, dg.spar.subjects = s.u, alpha.s = 0.5)$u != 0) >= s.u
all(unique(colSums(ssvdEN(X,
  dg.spar.subjects = s.u, n.PC = 5,
  alpha.s = 0.5
)$u != 0)) >= s.u)

# Elastic Net penalties with exact degrees of sparsity.
sum(ssvdEN(X,
  dg.spar.features = s.v, alpha.f = 0.5,
  exact.dg = TRUE
)$v != 0) == s.v
all(unique(colSums(ssvdEN(X,
  dg.spar.features = s.v, n.PC = 5,
  alpha.f = 0.5, exact.dg = TRUE
)$v != 0)) == s.v)

sum(ssvdEN(X,
  dg.spar.subjects = s.u, alpha.s = 0.5,
  exact.dg = TRUE
)$u != 0) == s.u
all(unique(colSums(ssvdEN(X,
  dg.spar.subjects = s.u, n.PC = 5,
  alpha.s = 0.5, exact.dg = TRUE
)$u != 0)) == s.u)
```

---

ssvdEN_sol_path   *'Solution path' for sparse Singular Value Decomposition via Elastic Net.*

Description

This function allows to explore values on the solution path of the sparse singular value decomposition (SVD) problem. The goal of this is to tune the degree of sparsity of subjects, features, or both subjects/features. The function performs a penalized SVD that imposes sparsity/smoothing in both left and right singular vectors. The penalties at both levels are Elastic Net-like, and the trade-off between ridge and Lasso like penalties is controlled by two 'alpha' parameters. The proportion of variance explained is the criteria used to choose the optimal degrees of sparsity.

Usage

```
ssvdEN_sol_path(
  O,
  center = TRUE,
  scale = TRUE,
  dg.grid.right = seq_len(ncol(O)) - 1,
  dg.grid.left = NULL,
  n.PC = 1,
  svd.0 = NULL,
  alpha.f = 1,
  alpha.s = 1,
  maxit = 500,
  tol = 0.001,
  approx = FALSE,
  plot = FALSE,
  ncores = 1,
  verbose = TRUE,
  lib.thresh = TRUE,
  left.lab = "Subjects",
  right.lab = "Features",
  exact.dg = FALSE
)
```

Arguments

O	Numeric matrix of n subjects (rows) and p features (columns). Only objects supported are 'matrix' and 'FBM'.
center	Should we center? Logical. Defaults to TRUE.
scale	Should we scale? Logical. Defaults to TRUE.
dg.grid.right	Grid with degrees of sparsity at the features level. Numeric. Default is the entire solution path for features (i.e. 1 : (ncol(O) - 1)).
dg.grid.left	Grid with degrees of sparsity at the subjects level. Numeric. Defaults to dg.grid.left = nrow(O).
n.PC	Number of desired principal axes. Numeric. Defaults to 1.
svd.0	Initial SVD (i.e. least squares solution). Defaults to NULL.
alpha.f	Elastic net mixture parameter at the features level. Measures the compromise between lasso (alpha = 1) and ridge (alpha = 0) types of sparsity. Numeric. Defaults to 1.

alpha.s	Elastic net mixture parameter at the subjects level. Defaults to alpha.s = 1.
maxit	Maximum number of iterations. Defaults to 500.
tol	Convergence is determined when ‖U_j - U_j-1‖_F < tol, where U_j is the matrix of estimated left regularized singular vectors at iteration j.
approx	Should we use standard SVD or random approximations? Defaults to FALSE. If TRUE & is(O,'matrix') == TRUE, irlba is called. If TRUE & is(O, "FBM") == TRUE, big_randomSVD is called.
plot	Should we plot the solution path? Logical. Defaults to FALSE
ncores	Number of cores used by big_randomSVD. Default does not use parallelism. Ignored when is(O, "FBM") == TRUE.
verbose	Should we print messages?. Logical. Defaults to TRUE.
lib.thresh	Should we use a liberal or conservative threshold to tune degrees of sparsity? Logical. Defaults to TRUE.
left.lab	Label for the subjects level. Character. Defaults to 'subjects'.
right.lab	Label for the features level. Character. Defaults to 'features'.
exact.dg	Should we compute exact degrees of sparsity? Logical. Defaults to FALSE. Only relevant When alpha.s or alpha.f are in the (0,1) interval and exact.dg = TRUE.

Details

The function returns the degree of sparsity for which the change in PEV is the steepest ('liberal' option), or for which the change in PEV stabilizes ('conservative' option). This heuristics relax the need of tuning parameters on a testing set.

For one PC (rank 1 case), the algorithm finds vectors u, w that minimize: $\|x - u\ w'\|\_F^2 + \lambda_w\ (alpha_w\|w\|\_1 + (1 - alpha_w)\|w\|\_F^2) + \lambda_u\ (alpha\|u\|\_1 + (1 - alpha_u)\|u\|\_F^2)$ such that $\|u\| = 1$. The right Eigen vector is obtained from $v = w\ /\ \|w\|$ and the corresponding Eigen value $= u^T\ x\ v$. The penalties lambda_u and lambda_w are mapped from specified desired degrees of sparsity (dg.spar.features & dg.spar.subjects).

Value

A list with the results of the (sparse) SVD and (if argument 'plot'=TRUE) the corresponding graphical displays.

SVD: a list with the results of the (sparse) SVD, containing:

- u: Matrix with left eigenvectors.
- v: Matrix with right eigenvectors.
- d: Matrix with singular values.
- opt.dg.right: Selected degrees of sparsity for right eigenvectors.
- opt.dg.left: Selected degrees of sparsity for left eigenvectors.

- plot: A ggplot object.

Note

Although the degree of sparsity maps onto number of features/subjects for Lasso, the user needs to be aware that this conceptual correspondence is lost for full EN (alpha belonging to (0, 1); e.g. the number of features selected with alpha < 1 will be eventually larger than the optimal degree of sparsity). This allows to rapidly increase the number of non-zero elements when tuning the degrees of sparsity. In order to get exact values for the degrees of sparsity at subjects or features levels, the user needs to set the value of 'exact.dg' parameter from 'FALSE' (the default) to 'TRUE'.

References

- Shen, Haipeng, and Jianhua Z. Huang. 2008. Sparse Principal Component Analysis via Regularized Low Rank Matrix Approximation. Journal of Multivariate Analysis 99 (6).

- Baglama, Jim, Lothar Reichel, and B W Lewis. 2018. Irlba: Fast Truncated Singular Value Decomposition and Principal Components Analysis for Large Dense and Sparse Matrices.

Examples

```
library("MOSS")

# Extracting simulated omic blocks.
sim_blocks <- simulate_data()$sim_blocks
X <- sim_blocks$`Block 3`

# Tuning sparsity degree for features (increments of 20 units).
out <- ssvdEN_sol_path(X, dg.grid.right = seq(1, 1000, by = 20))
```

---

ssvdEN_sol_path_par   *'Solution path' for sparse Singular Value Decomposition via Elastic Net using parallel computing.*

Description

This function is a copy of 'ssvdEN_sol_path' meant to be used in combination with the future.apply package to allow for parallel computing of the optimal degrees of sparsity by subjects and/or features.

Usage

```
ssvdEN_sol_path_par(
  O,
  center = TRUE,
  scale = TRUE,
  dg.grid.right = seq_len(ncol(O)) - 1,
  dg.grid.left = NULL,
  n.PC = 1,
  svd.0 = NULL,
  alpha.f = 1,
```

```
    alpha.s = 1,
    maxit = 500,
    tol = 0.001,
    approx = FALSE,
    plot = FALSE,
    ncores = 1,
    verbose = TRUE,
    lib.thresh = TRUE,
    left.lab = "Subjects",
    right.lab = "Features",
    exact.dg = FALSE
)
```

Arguments

O	Numeric matrix of n subjects (rows) and p features (columns). Only objects supported are 'matrix' and 'FBM'.
center	Should we center? Logical. Defaults to TRUE.
scale	Should we scale? Logical. Defaults to TRUE.
dg.grid.right	Grid with degrees of sparsity at the features level. Numeric. Default is the entire solution path for features (i.e. 1 : (ncol(O) - 1)).
dg.grid.left	Grid with degrees of sparsity at the subjects level. Numeric. Defaults to dg.grid.left = nrow(O).
n.PC	Number of desired principal axes. Numeric. Defaults to 1.
svd.0	Initial SVD (i.e. least squares solution). Defaults to NULL.
alpha.f	Elastic net mixture parameter at the features level. Measures the compromise between lasso (alpha = 1) and ridge (alpha = 0) types of sparsity. Numeric. Defaults to 1.
alpha.s	Elastic net mixture parameter at the subjects level. Defaults to alpha.s = 1.
maxit	Maximum number of iterations. Defaults to 500.
tol	Convergence is determined when $\|U\_j - U\_j\text{-}1\|\_F < tol$, where U_j is the matrix of estimated left regularized singular vectors at iteration j.
approx	Should we use standard SVD or random approximations? Defaults to FALSE. If TRUE & is(O,'matrix') == TRUE, irlba is called. If TRUE & is(O, "FBM") == TRUE, big_randomSVD is called.
plot	Should we plot the solution path? Logical. Defaults to FALSE
ncores	Number of cores used by big_randomSVD. Default does not use parallelism. Ignored when is(O, "FBM") == TRUE.
verbose	Should we print messages?. Logical. Defaults to TRUE.
lib.thresh	Should we use a liberal or conservative threshold to tune degrees of sparsity? Logical. Defaults to TRUE.
left.lab	Label for the subjects level. Character. Defaults to 'subjects'.
right.lab	Label for the features level. Character. Defaults to 'features'.
exact.dg	Should we compute exact degrees of sparsity? Logical. Defaults to FALSE. Only relevant When alpha.s or alpha.f are in the (0,1) interval and exact.dg = TRUE.

Note

Although the degree of sparsity maps onto number of features/subjects for Lasso, the user needs to be aware that this conceptual correspondence is lost for full EN (alpha belonging to (0, 1); e.g. the number of features selected with alpha < 1 will be eventually larger than the optimal degree of sparsity). This allows to rapidly increase the number of non-zero elements when tuning the degrees of sparsity. In order to get exact values for the degrees of sparsity at subjects or features levels, the user needs to set the value of 'exact.dg' parameter from 'FALSE' (the default) to 'TRUE'.

Examples

```
library("MOSS")

# Extracting simulated omic blocks.
sim_blocks <- simulate_data()$sim_blocks
X <- sim_blocks$`Block 3`

# Comparing ssvdEN_sol_path_par and ssvdEN_sol_path.
t1 <- proc.time()
out1 <- ssvdEN_sol_path(X, dg.grid.right = 1:1000, dg.grid.left = 1:500)
t1 <- proc.time() - t1

t2 <- proc.time()
out2 <- ssvdEN_sol_path_par(X, dg.grid.right = 1:1000, dg.grid.left = 1:500)
t2 <- proc.time() - t2
```

---

  tsne2clus   *t-Stochastic Neighbor Embedding to Clusters*

Description

Finds clusters on a 2 dimensional map using Density-based spatial clustering of applications with noise (DBSCAN; Esther et al. 1996).

Usage

```
tsne2clus(
  S.tsne,
  ann = NULL,
  labels,
  aest = NULL,
  eps_res = 100,
  eps_range = c(0, 4),
  min.clus.size = 10,
  group.names = "Groups",
  xlab = "x: tSNE(X)",
  ylab = "y: tSNE(X)",
```

```
    clus = TRUE
)
```

Arguments

S.tsne	Outcome of function "pca2tsne"
ann	Subjects' annotation data. An incidence matrix assigning subjects to classes of biological relevance. Meant to tune cluster assignation via Biological Homogeneity Index (BHI). If ann=NULL, the number of clusters is tuned with the Silhouette index instead of BHI. Defaults to NULL.
labels	Character vector with labels describing subjects. Meant to assign aesthetics to the visual display of clusters.
aest	Data frame containing points shape and color. Defaults to NULL.
eps_res	How many eps values should be explored between the specified range?
eps_range	Vector containing the minimum and maximum eps values to be explored. Defaults to c(0, 4).
min.clus.size	Minimum size for a cluster to appear in the visual display. Defaults to 10
group.names	The title for the legend's key if 'aest' is specified.
xlab	Name of the 'xlab'. Defaults to "x: tSNE(X)"
ylab	Name of the 'ylab'. Defaults to "y: tSNE(X)"
clus	Should we do clustering? Defaults to TRUE. If false, only point aesthetics are applied.

Details

The function takes the outcome of pca2tsne (or a list containing any two-columns matrix) and finds clusters via DBSCAN. It extends code from the MEREDITH (Taskesen et al. 2016) and clValid (Datta & Datta, 2018) R packages to tune DBSCAN parameters with Silhouette or Biological Homogeneity indexes.

Value

A list with the results of the DBSCAN clustering and (if argument 'plot'=TRUE) the corresponding graphical displays.

dbscan.res: a list with the results of the (sparse) SVD, containing:

- cluster: Cluster partition.
- eps: Optimal eps according to the Silhouette or Biological Homogeneity indexes criteria.
- SIL: Maximum peak in the trajectory of the Silhouette index.
- BHI: Maximum peak in the trajectory of the Biological Homogeneity index.

- clusters.plot: A ggplot object with the clusters' graphical display.

References

- Ester, Martin, Martin Ester, Hans-Peter Kriegel, Jorg Sander, and Xiaowei Xu. 1996. "A Density-Based Algorithm for Discovering Clusters in Large Spatial Databases with Noise," 226_231.

- Hahsler, Michael, and Matthew Piekenbrock. 2017. "Dbscan: Density Based Clustering of Applications with Noise (DBSCAN) and Related Algorithms." https://cran.r-project.org/package=dbscan.

- Datta, Susmita, and Somnath Datta. 2006. Methods for Evaluating Clustering Algorithms for Gene Expression Data Using a Reference Set of Functional Classes. BMC Bioinformatics 7 (1). BioMed Central:397.

- Taskesen, Erdogan, Sjoerd M. H. Huisman, Ahmed Mahfouz, Jesse H. Krijthe, Jeroen de Ridder, Anja van de Stolpe, Erik van den Akker, Wim Verheagh, and Marcel J. T. Reinders. 2016. Pan-Cancer Subtyping in a 2D-Map Shows Substructures That Are Driven by Specific Combinations of Molecular Characteristics. Scientific Reports 6 (1):24949.

Examples

```
library(MOSS)
library(viridis)
library(cluster)
library(annotate)

# Using the 'iris' data tow show cluster definition via BHI criterion.
set.seed(42)
data(iris)
# Scaling columns.
X <- scale(iris[, -5])
# Calling pca2tsne to map the three variables onto a 2-D map.
Z <- pca2tsne(X, perp = 30, n.samples = 1, n.iter = 1000)
# Using 'species' as previous knoledge to identify clusters.
ann <- model.matrix(~ -1 + iris[, 5])
# Getting clusters.
tsne2clus(Z,
  ann = ann,
  labels = iris[, 5],
  aest = aest.f(iris[, 5]),
  group.names = "Species",
  eps_range = c(0, 3)
)

# Example of usage within moss.
set.seed(43)
sim_blocks <- simulate_data()$sim_blocks
out <- moss(sim_blocks[-4],
  tSNE = TRUE,
  cluster = list(eps_range = c(0, 4), eps_res = 100, min_clus_size = 1),
  plot = TRUE
)
out$clus_plot
out$clusters_vs_PCs
```

Index