

# Package ‘timeOmics’

March 30, 2021

**Title** Time-Course Multi-Omics data integration

**Version** 1.2.0

**Description** timeOmics is a generic data-driven framework to integrate multi-Omics longitudinal data measured on the same biological samples and select key temporal features with strong associations within the same sample group.

The main steps of timeOmics are:

1. Platform and time-specific normalization and filtering steps;
2. Modelling each biological into one time expression profile;
3. Clustering features with the same expression profile over time;
4. Post-hoc validation step.

**License** GPL-3

**Encoding** UTF-8

**LazyData** true

**Imports** dplyr, tidyr, tibble, purrr, magrittr, ggplot2, stringr, ggrepel, propr, lmtest

**biocViews** Clustering, FeatureExtraction, TimeCourse, DimensionReduction, Software, Sequencing, Microarray, Metabolomics, Metagenomics, Proteomics, Classification, Regression, ImmunoOncology, GenePrediction, MultipleComparison

**Depends** mixOmics, R (>= 4.0)

**RoxygenNote** 7.1.1

**VignetteBuilder** knitr

**Suggests** BiocStyle, knitr, rmarkdown, testthat, snow, tidyverse, igraph, gplots

**Remotes** cran/lmms

**BugReports** <https://github.com/abodein/timeOmics/issues>

**git\_url** <https://git.bioconductor.org/packages/timeOmics>

**git\_branch** RELEASE\_3\_12

**git\_last\_commit** 9fff87c

**git\_last\_commit\_date** 2020-10-27

**Date/Publication** 2021-03-29

**Author** Antoine Bodein [aut, cre],  
Olivier Chapleur [aut],  
Kim-Anh Le Cao [aut],  
Arnaud Droit [aut]

**Maintainer** Antoine Bodein <antoine.bodein.1@ulaval.ca>

## R topics documented:

<code>dmatrix.spearman.dissimilarity</code> . . . . .	2
<code>getCluster</code> . . . . .	3
<code>getNcomp</code> . . . . .	3
<code>getSilhouette</code> . . . . .	5
<code>get_demo_cluster</code> . . . . .	5
<code>get_demo_silhouette</code> . . . . .	6
<code>lmms.filter.lines</code> . . . . .	7
<code>plotLong</code> . . . . .	8
<code>proportionality</code> . . . . .	10
<code>timeOmics.simdata</code> . . . . .	11
<code>tuneCluster.block.spls</code> . . . . .	11
<code>tuneCluster.spca</code> . . . . .	13
<code>tuneCluster.spls</code> . . . . .	14
<code>unscale</code> . . . . .	15
<b>Index</b>	<b>17</b>

---

`dmatrix.spearman.dissimilarity`  
*dmatrix.spearman.dissimilarity*

---

### Description

Compute the spearman dissimilarity distance.

### Usage

```
dmatrix.spearman.dissimilarity(X)
```

### Arguments

`X` A numeric matrix with feature in colnames

### Value

Return a dissimilarity matrix of size  $P \times P$ .

---

`getCluster`*Get variable cluster from (s)PCA, (s)PLS or block.(s)PLS*

---

**Description**

This function returns the cluster associated to each feature from a mixOmics object.

**Usage**

```
getCluster(X)
```

**Arguments**

`X` an object of the class: `pca`, `spca`, `pls`, `sppls`, `block.pls` or `block.sppls`

**Details**

For each feature, the cluster is assigned according to the maximum contribution on a component and the sign of that contribution.

**Value**

A data.frame containing the name of feature, its assigned cluster and other information such as selected component, contribution, sign, ...

**See Also**

[selectVar](#)

**Examples**

```
demo <- suppressWarnings(get_demo_cluster())
pca.cluster <- getCluster(demo$pca)
spca.cluster <- getCluster(demo$spca)
pls.cluster <- getCluster(demo$pls)
sppls.cluster <- getCluster(demo$sppls)
block.pls.cluster <- getCluster(demo$block.pls)
block.sppls.cluster <- getCluster(demo$block.sppls)
```

---

`getNcomp`*Get optimal number of components*

---

**Description**

Compute the average silhouette coefficient for a given set of components on a mixOmics result. For each given `ncomp`, the mixOmics method is performed with the same arguments and the given `'ncomp'`. Longitudinal clustering is performed and average silhouette coefficient is computed.

**Usage**

```
getNcomp(object, max.ncomp = NULL, X, Y = NULL, indY = NULL, ...)
```

**Arguments**

object	A mixOmics object of the class 'pca', 'spca', 'mixo_pls', 'mixo_spls', 'block.pls', 'block.spls'
max.ncomp	integer, maximum number of component to include. If no argument is given, 'max.ncomp=object\$ncomp'
X	a numeric matrix/data.frame or a list of data.frame for block.pls
Y	(only for pls, optional for block.spls) a numeric matrix, with the same nrow as X
indY	(optional and only for block.pls, if Y is not provided), an integer which indicates the position of the matrix response in the list X
...	Other arguments to be passed to methods (pca, pls, block.pls)

**Value**

getNcomp returns a list with class "ncomp.tune.silhouette" containing the following components:

ncomp	a vector containing the tested ncomp
silhouette	a vector containing the average silhouette coefficient by ncomp
dmatrix	the distance matrix used to compute silhouette coefficient

**See Also**

[getCluster](#), [silhouette](#), [pca](#), [pls](#), [block.pls](#)

**Examples**

```
# random input data
demo <- suppressWarnings(get_demo_cluster())

# pca
pca.res <- mixOmics::pca(X=demo$X, ncomp = 5)
res.ncomp <- getNcomp(pca.res, max.ncomp = 4, X = demo$X)
plot(res.ncomp)

# pls
pls.res <- mixOmics::pls(X=demo$X, Y=demo$Y)
res.ncomp <- getNcomp(pls.res, max.ncomp = 4, X = demo$X, Y=demo$Y)
plot(res.ncomp)

# block.pls
block.pls.res <- suppressWarnings(mixOmics::block.pls(X=list(X=demo$X, Z=demo$Z), Y=demo$Y))
res.ncomp <- suppressWarnings(getNcomp(block.pls.res, max.ncomp = 4,
                                     X=list(X=demo$X, Z=demo$Z), Y=demo$Y))
plot(res.ncomp)
```

---

getSilhouette	<i>Get Silhouette Coefficient from (s)PCA, (s)PLS or block.(s)PLS clusters</i>
---------------	--

---

**Description**

getSilhouette is a generic function that compute silhouette coefficient for an object of the type pca, spca, pls, spls, block.pls, block.spls.

**Usage**

```
getSilhouette(object)
```

**Arguments**

object            a mixOmics object of the class pca, spca, pls, spls, block.pls, block.spls

**Details**

This method extract the componant contribution depending on the object, perform the clustering step, and compute the silhouette coefficient.

**Value**

silhouette coefficient

**Examples**

```
demo <- suppressWarnings(get_demo_cluster())
getSilhouette(object = demo$pca)
getSilhouette(object = demo$spca)
getSilhouette(object = demo$pls)
getSilhouette(object = demo$sppls)
getSilhouette(object = demo$block.pls)
getSilhouette(object = demo$block.spls)
```

---

get_demo_cluster	<i>get_demo_cluster</i>
------------------	-------------------------

---

**Description**

Generates random data to be used in examples.

**Usage**

```
get_demo_cluster()
```

**Value**

a list containing:

X	data.frame
Y	data.frame
Z	data.frame
pca	a mixOmics pca result
spca	a mixOmics spca result
pls	a mixOmics pls result
spls	a mixOmics spls result
block.pls	a mixOmics block.pls result
block.spls	a mixOmics block.spls result

**Examples**

```
# Random data could lead to "The SGCCA algorithm did not converge" warning which is not important for a demo
demo <- suppressWarnings(get_demo_cluster())
```

---

get\_demo\_silhouette    *Get data for silhouette demo*

---

**Description**

Get data for silhouette demo

**Usage**

```
get_demo_silhouette()
```

**Value**

A matrix of expression profile, sample in rows, time in columns.

**Examples**

```
data <- get_demo_silhouette()
```

---

lmms.filter.lines      *Filter Linear Profiles from Linear Mixed Model output*

---

## Description

This function filters linear models with highly heterogeneous variability within residues. From an "lmms" output, 2 parameters are tested:

## Usage

```
lmms.filter.lines(  
  data,  
  lmms.obj,  
  time,  
  homoskedasticity = TRUE,  
  MSE.filter = TRUE,  
  homoskedasticity.cutoff = 0.05  
)
```

## Arguments

data	a data.frame used in the <code>lmms::lmmSpline</code> command
lmms.obj	a <code>lmmSpline</code> object
time	a numeric vector containing the sample time point information.
homoskedasticity	a logical whether or not to test for homoscedasticity with the Breusch-Pagan test.
MSE.filter	whether or not to test for low dispersion with a cutoff on the MSE.
homoskedasticity.cutoff	a numeric scalar between 0 and 1, p-value threshold for B-P test.

## Details

\* homo-sedasticity of the residues with a Breusch-Pagan test \* low dispersion with a cutoff on the MSE (mean squared error)

## Value

a list containing the following items

filtering.summary	a data.frame with the different tests per features (passed = TRUE, failed = FALSE)
to.keep	features which passed all the tests
filtered	the filtered data.frame

## See Also

[bptest](#)

**Examples**

```
# data and lmms output
data(timeOmics.simdata)
data <- timeOmics.simdata$sim
lmms.output <- timeOmics.simdata$lmms.output
time <- timeOmics.simdata$time

# filter
filter.res <- lmms.filter.lines(data = data, lmms.obj = lmms.output, time = time)
```

---

plotLong

*Plot Longitudinal Profiles by Cluster*


---

**Description**

This function provides a expression profile representation over time and by cluster.

**Usage**

```
plotLong(
  object,
  time = NULL,
  plot = TRUE,
  center = TRUE,
  scale = TRUE,
  title = "Time-course Expression",
  X.label = NULL,
  Y.label = NULL,
  legend = FALSE,
  legend.title = NULL,
  legend.block.name = NULL
)
```

**Arguments**

object	a mixOmics result of class (s)pca, (s)pls, block.(s)pls.
time	(optional) a numeric vector, the same size as ncol(X), to change the time scale.
plot	a logical, if TRUE then a plot is produced. Otherwise, the data.frame on which the plot is based on is returned.
center	a logical value indicating whether the variables should be shifted to be zero centered.
scale	a logical value indicating whether the variables should be scaled to have unit variance before the analysis takes place.
title	character indicating the title plot.
X.label	x axis titles.
Y.label	y axis titles.
legend	a logical, to display or not the legend.



legend.title if legend is provided, title of the legend.  
legend.block.name a character vector corresponding to the size of the number of blocks in the mixOmics object.

### Value

a data.frame (gathered form) containing the following columns:

time	x axis values
molecule	names of features
value	y axis values
cluster	assigned clusters
block	name of 'blocks'

### See Also

[getCluster](#)

### Examples

```
demo <- suppressWarnings(get_demo_cluster())
X <- demo$X
Y <- demo$Y
Z <- demo$Z

# (s)pca
pca.res <- mixOmics::pca(X, ncomp = 3)
plotLong(pca.res)
spca.res <- mixOmics::spca(X, ncomp =2, keepX = c(15, 10))
plotLong(spca.res)

# (s)pls
pls.res <- mixOmics::pls(X,Y)
plotLong(pls.res)
spls.res <- mixOmics::spls(X,Y, keepX = c(15,10), keepY=c(5,6))
plotLong(spls.res)

# (s)block.spls
block.pls.res <- mixOmics::block.pls(X=list(X=X,Z=Z), Y=Y)
plotLong(block.pls.res)
block.spls.res <- mixOmics::block.spls(X=list(X=X,Z=Z), Y=Y,
                                     keepX = list(X = c(15,10), Z = c(5,6)),
                                     keepY = c(3,6))
plotLong(block.spls.res)
```

---

proportionality	<i>Proportionality Distance</i>
-----------------	---------------------------------

---

### Description

proportionality is a wrapper that compute proportionality distance for a clustering result (pca, spca, pls, spls, block.pls, block.spls). and it performs a u-test to compare the median within a cluster to the median of the entire background set.

### Usage

```
proportionality(X)
```

### Arguments

X an object of the class: pca, spca, pls, spls, block.pls or block.spls

### Value

Return a list containing the following components:

propr.distance	Square matrix with proportionality distance between pairs of features
propr.distance.w.cluster	distance between pairs with cluster label
pvalue	Wilcoxon U-test p-value comparing the medians within clusters and with the entire background set

### References

Lovell, D., Pawlowsky-Glahn, V., Egozcue, J. J., Marguerat, S., Bähler, J. (2015). Proportionality: a valid alternative to correlation for relative data. PLoS Comput. Biol. 11, e1004075. doi: 10.1371/journal.pcbi.1004075

Quinn, T. P., Richardson, M. F., Lovell, D., Crowley, T. M. (2017). propr: an r-package for identifying proportionally abundant features using compositional data analysis. Sci. Rep. 7, 16252. doi: 10.1038/s41598-017-16520-0

### See Also

[propr](#)

### Examples

```
demo <- suppressWarnings(get_demo_cluster())

# pca
X <- demo$pca
propr.res <- proportionality(X)
plot(propr.res)

# pls
X <- demo$spls
propr.res <- proportionality(X)
```

```

plot(propr.res)

# block.pls
X <- demo$block.pls
propr.res <- proportionality(X)
plot(propr.res)

```

---

timeOmics.simdata      *Time-Course Simulated data*

---

### Description

A list of dataset containing simulated data to be used in the vignette, generated as follow. Twenty reference time profiles were generated on nine equally spaced time points and assigned to four clusters (five profiles each). These ground truth profiles were then used to simulate new profiles (5 each). Finally, we modelled expression of new sampled profiles as a function of time.

### Usage

```
timeOmics.simdata
```

### Format

a list of data.frame

**rawdata** data.frame, reference profiles

**sim** data.frame, sampled profiles from reference data

**modelled** data.frame, modelled data

**lmms.output** full lmms object output

**time** numerci vector, time for each sample of rawdata

**Y** another modelled data.frame for multiblock integration

**Z** another modelled data.frame for multiblock integration

---

```
tuneCluster.block.pls
```

*Feature Selection Optimization for block (s)PLS method*

---

### Description

This function identify the number of feautres to keep per component and thus by cluster in `mixOmics::block.pls` by optimizing the silhouette coefficient, which assesses the quality of clustering.

**Usage**

```
tuneCluster.block.spls(
  X,
  Y = NULL,
  indY = NULL,
  ncomp = 2,
  test.list.keepX = NULL,
  test.keepY = NULL,
  ...
)
```

**Arguments**

X	list of numeric matrix (or data.frame) with features in columns and samples in rows (with samples order matching in all data sets).
Y	(optional) numeric matrix (or data.frame) with features in columns and samples in rows (same rows as X).
indY	integer, to supply if Y is missing, indicates the position of the matrix response in the list X.
ncomp	integer, number of component to include in the model
test.list.keepX	list of integers with the same size as X. Each entry corresponds to the different keepX value to test for each block of X.
test.keepY	only if Y is provided. Vector of integer containing the different value of keepY to test for block Y.
...	other parameters to be included in the spls model (see <code>mixOmics::block.spls</code> )

**Details**

For each component and for each keepX/keepY value, a spls is done from these parameters. Then the clustering is performed and the silhouette coefficient is calculated for this clustering.

We then calculate "slopes" where keepX/keepY are the coordinates and the silhouette is the intensity. A z-score is assigned to each slope. We then identify the most significant slope which indicates a drop in the silhouette coefficient and thus a deterioration of the clustering.

**Value**

silhouette	silhouette coef. computed for every combination of keepX/keepY
ncomp	number of component included in the model
test.keepX	list of tested keepX
test.keepY	list of tested keepY
block	names of blocks
slopes	"slopes" computed from the silhouette coef. for each keepX and keepY, used to determine the best keepX and keepY
choice.keepX	best keepX for each component
choice.keepY	best keepY for each component

**See Also**

[block.spls](#), [getCluster](#), [plotLong](#)

**Examples**

```
demo <- suppressWarnings(get_demo_cluster())
X <- list(X = demo$X, Z = demo$Z)
Y <- demo$Y
test.list.keepX <- list("X" = c(5,10,15,20), "Z" = c(2,4,6,8))
test.keepY <- c(2:5)

# tuning
tune.block.spls <- tuneCluster.block.spls(X= X, Y= Y,
                                         test.list.keepX= test.list.keepX,
                                         test.keepY= test.keepY,
                                         mode= "canonical")

keepX <- tune.block.spls$choice.keepX
keepY <- tune.block.spls$choice.keepY

# final model
block.spls.res <- mixOmics::block.spls(X= X, Y= Y, keepX = keepX,
                                       keepY = keepY, ncomp = 2, mode = "canonical")
# get clusters and plot longitudinal profile by cluster
block.spls.cluster <- getCluster(block.spls.res)
```

---

tuneCluster.sPCA

*Feature Selection Optimization for sPCA method*


---

**Description**

This function identify the number of features to keep per component and thus by cluster in `mixOmics::sPCA` by optimizing the silhouette coefficient, which assesses the quality of clustering.

**Usage**

```
tuneCluster.sPCA(X, ncomp = 2, test.keepX = rep(ncol(X), ncomp), ...)
```

**Arguments**

<code>X</code>	numeric matrix (or data.frame) with features in columns and samples in rows
<code>ncomp</code>	integer, number of component to include in the model
<code>test.keepX</code>	vector of integer containing the different value of keepX to test for block X.
<code>...</code>	other parameters to be included in the spls model (see <code>mixOmics::sPCA</code> )

**Details**

For each component and for each keepX value, a spls is done from these parameters. Then the clustering is performed and the silhouette coefficient is calculated for this clustering.

We then calculate "slopes" where keepX are the coordinates and the silhouette is the intensity. A z-score is assigned to each slope. We then identify the most significant slope which indicates a drop in the silhouette coefficient and thus a deterioration of the clustering.

**Value**

silhouette	silhouette coef. computed for every combination of keepX/keepY
ncomp	number of component included in the model
test.keepX	list of tested keepX
block	names of blocks
slopes	"slopes" computed from the silhouette coef. for each keepX and keepY, used to determine the best keepX and keepY
choice.keepX	best keepX for each component

**Examples**

```
demo <- suppressWarnings(get_demo_cluster())
X <- demo$X

# tuning
tune.spca.res <- tuneCluster.spca(X = X, ncomp = 2, test.keepX = c(2:10))
keepX <- tune.spca.res$choice.keepX
plot(tune.spca.res)

# final model
spca.res <- mixOmics::spca(X=X, ncomp = 2, keepX = keepX)
plotLong(spca.res)
```

tuneCluster.spls

*Feature Selection Optimization for sPLS method***Description**

This function identify the number of features to keep per component and thus by cluster in `mixOmics::spls` by optimizing the silhouette coefficient, which assesses the quality of clustering.

**Usage**

```
tuneCluster.spls(
  X,
  Y,
  ncomp = 2,
  test.keepX = rep(ncol(X), ncomp),
  test.keepY = rep(ncol(Y), ncomp),
  ...
)
```

**Arguments**

X	numeric matrix (or data.frame) with features in columns and samples in rows
Y	numeric matrix (or data.frame) with features in columns and samples in rows (same rows as X)
ncomp	integer, number of component to include in the model
test.keepX	vector of integer containing the different value of keepX to test for block X.
test.keepY	vector of integer containing the different value of keepY to test for block Y.
...	other parameters to be included in the spls model (see <code>mixOmics::spls</code> )

**Details**

For each component and for each keepX/keepY value, a spls is done from these parameters. Then the clustering is performed and the silhouette coefficient is calculated for this clustering.

We then calculate "slopes" where keepX/keepY are the coordinates and the silhouette is the intensity. A z-score is assigned to each slope. We then identify the most significant slope which indicates a drop in the silhouette coefficient and thus a deterioration of the clustering.

**Value**

silhouette	silhouette coef. computed for every combination of keepX/keepY
ncomp	number of component included in the model
test.keepX	list of tested keepX
test.keepY	list of tested keepY
block	names of blocks
slopes	"slopes" computed from the silhouette coef. for each keepX and keepY, used to determine the best keepX and keepY
choice.keepX	best keepX for each component
choice.keepY	best keepY for each component

**See Also**

[spls](#), [getCluster](#), [plotLong](#)

**Examples**

```
demo <- suppressWarnings(get_demo_cluster())
X <- demo$X
Y <- demo$Y

# tuning
tune.spls <- tuneCluster.spls(X, Y, ncomp= 2, test.keepX= c(5,10,15,20), test.keepY= c(2,4,6))
keepX <- tune.spls$choice.keepX
keepY <- tune.spls$choice.keepY

# final model
spls.res <- mixOmics::spls(X, Y, ncomp= 2, keepX= keepX, keepY= keepY)

# get clusters and plot longitudinal profile by cluster
spls.cluster <- getCluster(spls.res)
plotLong(spls.res)
```

---

 unscale

*Unscals a scaled data.frame*


---

**Description**

unscale is a generic function that unscale and/or uncenter the columns of a matrix generated by the scale base function

**Usage**

```
unscale(x)
```

**Arguments**

x                    A numeric matrix.

**Details**

unscale uses attributes added by the scale function "scaled:scale" and "scaled:center" and use these scaling factor to retrieve the initial matrix. It first unscales and then uncenters.

**Value**

Return a matrix, uncenterd and unscaled. Attributes "scaled:center" and "scaled:scale" are removed.

**See Also**

[scale](#)

**Examples**

```
X <- matrix(1:9, ncol = 3)
X.scale <- scale(X, center = TRUE, scale = TRUE)
X.unscale <- unscale(X.scale)
all(X == X.unscale)
```



# Index

## \* datasets

timeOmics.simdata, 11

block.pls, 4

block.spls, 13

bptest, 7

dmatrix.spearman.dissimilarity, 2

get\_demo\_cluster, 5

get\_demo\_silhouette, 6

getCluster, 3, 4, 9, 13, 15

getNcomp, 3

getSilhouette, 5

lmms.filter.lines, 7

pca, 4

plotLong, 8, 13, 15

pls, 4

proportionality, 10

propr, 10

scale, 16

selectVar, 3

silhouette, 4

spls, 15

timeOmics.simdata, 11

tuneCluster.block.spls, 11

tuneCluster.spca, 13

tuneCluster.spls, 14

unscale, 15