Package 'MOSClip'

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Title Multi Omics Survival Clip

Version 1.2.2

Depends R (>= 4.4.0)

Description Topological pathway analysis tool able to integrate multi-omics data. It finds survival-associated modules or significant modules for two-class analysis. This tool have two main methods: pathway tests and module tests. The latter method allows the user to dig inside the pathways itself.

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Imports MultiAssayExperiment, methods, survminer, graph, graphite, AnnotationDbi, checkmate, ggplot2, gridExtra, igraph, pheatmap, survival, RColorBrewer, SuperExactTest, reshape, NbClust, S4Vectors, grDevices, graphics, stats, utils, ComplexHeatmap, FactoMineR, circlize, corpcor, coxrobust, elasticnet, gRbase, ggplotify, qpgraph, org.Hs.eg.db, Matrix

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Contents

`annotePathwayToFather` *Find Pathway Fathers*

Description

Given the hierarchy of the pathways, this formula finds the fathers of the respective pathway (e.g. pathway: 'PI3K Cascade'; father: 'Signaling Pathways'). This function is necessary for calculating the contribution of different omics to survival prediction in different biological processes, grouping the pathways by hierarchy.

Usage

```
annotePathwayToFather(pathways, graphiteDB, hierarchy)
```

Arguments

pathways	vector of pathway names
graphiteDB	graphite DB object (e.g. an object containing all reactome pathways)
hierarchy	a graph object with the pathway hierarchy

Value

a vector of the pathway fathers' names

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_list <- lapply(reactSmall[1:2], function(g) {
    fcl <- multiOmicsSurvivalModuleTest(multiOmics, g,
        survFormula = "Surv(days, status) ~",
        autoCompleteFormula = TRUE,
        useTheseGenes = genesToUse
    )
    fcl
})

moduleSummary <- multiPathwayModuleReport(MOM_list)

pathHierarchy <- downloadPathwayRelationFromReactome()
pathHierarchyGraph <- igraph::graph.data.frame(
    d = pathHierarchy,
    directed = TRUE
)

omicsClasses2pathways <- computeOmicsIntersections(
    moduleSummary,
    pvalueThr = 1, zscoreThr = 1,
    excludeColumns = c("pathway", "module")
)

omicsClasses2pathways <- lapply(
```

```
    omicsClasses2pathways,
    stripModulesFromPathways
)

# This step requires to download the whole reactome graph, which usually
# takes a lot of time.
# reactome <- graphite::pathways('hsapiens', 'reactome')
# reactome <- graphite::convertIdentifiers(reactome, 'entrez')
# omicsClasses2fathers <- lapply(omicsClasses2pathways,
#                                annotePathwayToFather,
#                                graphiteDB = reactome,
#                                hierarchy = pathHierarchyGraph)
```

`availableOmicMethods` *Get available Omics Summarizing Methods*

Description

Gives a vector of the available methods to summarize omics.

Usage

```
availableOmicMethods()
```

Value

character vector with the implemented methods.

Examples

```
availableOmicMethods()
```

`checkOrder` *Check if all the list object have the same order of pathway module*

Description

For internal use only

For internal use only

For internal use only

For internal use only

For internal use only

Prepare subset of patients for permutations

Usage

```
checkOrder(li)

resolveAndOrder(li)

mergeCol(li, col = "PC1", resolve = FALSE)

filterExpr(exp, samples)

filterMultiOmicsForSamples(MO, samples)

preparePerms(fullMultiOmics, nperm = 100, nPatients = 3)
```

Arguments

li	a list of summaries
col	the column to merge
resolve	weather to resolve the issues
exp	a matrix
samples	the vector of samples to select
MO	a multiOmic object
fullMultiOmics	a multiOmic object
nperm	number of permutations
nPatients	number of patients to remove for resampling

Value

a matrix

a filtered matrix

a filtered MultiOmics objects

list of sampled patients for each permutation

---

compPCs *Regular PCA*

Description

Regular PCA

Usage

```
compPCs(exp, shrink, k)
```

Arguments

exp	a matrix
shrink	logical, whether to shrink or not.
k	the number of components to use

Value

a list with the following elements:

x	the computed PCs
sdev	the standard deviation captured by the PCs
loadings	the loadings

---

computeFreqs *Compute Frequencies in a Named List*

Description

Compute frequencies in a named list. This function is necessary for plotFrequencies, in which it will calculate the frequency of each pathway father for every omics intersection.

Usage

```
computeFreqs(elementsIntersections)
```

Arguments

elementsIntersections	a named list

Value

a data.frame of the frequencies

Examples

```
omicsIntersection <- list(
    "exp;met" = c("PathwayA", "PathwayB", "PathwayC"),
    "exp;mut" = c("PathwayA", "PathwayC"),
    "cnv;mut" = c("PathwayB")
)
freqDf <- computeFreqs(omicsIntersection)
```

computeOmicsIntersections *Compute Omics Intersections*

Description

Finds the modules that have any intersection among the available omics

Usage

```
computeOmicsIntersections(
  multiPathwayReportData,
  pvalueThr = 0.05,
  zscoreThr = 0.05,
  resampligThr = NULL,
  excludeColumns = NULL
)
```

Arguments

multiPathwayReportData	data.frame, the output of the multiPathwayReport or multiPathwayModuleReport functions.
pvalueThr	numeric value. Overall pvalue cut-off to be used
zscoreThr	numeric value. Covariates coefficient cut-off to be used.
resampligThr	numeric value. Filters the modules according to the number of success in the resampling procedure, takes only the modules above this threshold.
excludeColumns	a vector of characters listing the columns of multiPathwayReportData object to be excluded by the analysis. In the case multiPathwayReportData derives from multiPathwayModuleReport you should set excludeColumns = c('pathway','module').

Value

a list of pathway modules present for every intersection of omics present

Examples

```
df <- data.frame(
    pvalue = c(0.06, 0.04, 0.04, 0.03, 0.02),
    cnv = c(0.07, 0.03, 0.02, 0.04, 0.01),
    mut = c(0.08, 0.02, 0.01, 0.04, 0.04),
    row.names = c(
        "PathwayA", "PathwayB", "PathwayC",
        "PathwayD", "PathwayE"
    )
)
```

```
omicsClasses2Pathways <- computeOmicsIntersections(df,
    pvalueThr = 0.1,
    zscoreThr = 0.1
)
```

`computePCs` *compute PCs.*

Description

For internal use only. Performs Principal Componenent analysis.

Usage

```
computePCs(
  exp,
  shrink = FALSE,
  method = c("regular", "topological", "sparse"),
  cliques = NULL,
  maxPCs = 3
)
```

Arguments

`exp`	a matrix
`shrink`	logical, whether to shrink or not.
`method`	one of 'regular', 'topological' and 'sparse'
`cliques`	the pathway topology summarized in a list of cliques
`maxPCs`	the maximum number of PCs to consider

Details

Three methods are implemented:

- regular: a regular PCA ('prcomp')
- topological: PCA using a pathway topology.
- sparse: sparse PCA analysis implemented by 'elasticnet'

Value

a list with the following elements:

`x`	the computed PCs
`sdev`	the standard deviation captured by the PCs
`loadings`	the loadings

convertPathway *A generic function to convert pathway*

Description

A generic function to convert pathway

Usage

```
convertPathway(graph, useTheseGenes)
```

Arguments

graph	a graphNEL object
useTheseGenes	list of genes to be used

Value

NULL. No value is returned

createCoxObj *Create Cox Object*

Description

Create the coxObj from the covariates used in the test

Usage

```
createCoxObj(colData, moView)
```

Arguments

colData	colData from multiOmic object
moView	modulesView or pathView from multiOmicsModules or multiOmicsPathway object

Value

data.frame, samples in the rows, covariates in the columns

createDataModule *Create Data Module*

Description

Extract sub-matrix for the genes of a module or pathway from data matrix of a specific omic

Usage

```
createDataModule(omic, multiOmicObj)
```

Arguments

omic	modulesView or pathView object
multiOmicObj	object of class 'Omics'

Value

matrix, genes in the rows, samples in the columns

createMOMView *Create the list of covariates that are going to be tested*

Description

Create the list of covariates that are going to be tested

Usage

```
createMOMView(omicsObj, genes)
```

Arguments

omicsObj	Omics class object
genes	genes of the clique

Value

list with 1 reduced representation of the omics 2 sdev 3 loadings or eigenvector 4 usedGenes 5 method 6 namesCov 7 omicName

downloadPathwayRelationFromReactome *Download Reactome Pathway Relations*

Description

Download Pathway Relations from Reactome. The file is retrieved from the url

Usage

```
downloadPathwayRelationFromReactome(url = NULL, speciesAbbr = "HSA")
```

Arguments

url	the location of the file. Can be local. If NULL pick the package reactome file.
speciesAbbr	species acronim

Value

A data frame with 2 columns:

parent	The Reactome pathway ID of the parent pathway.
child	The Reactome pathway ID of the child pathway.

Examples

```
downloadPathwayRelationFromReactome()
```

estimateExprCov *Estimate Single Covariance Matrix*

Description

For internal use only. Estimate Covariance from one matrix

Usage

```
estimateExprCov(expr, shrink)
```

Arguments

expr	a numeric matrix
shrink	logical wheter to shrink the matrix

Value

a covariance matrix

extractCliquesFromDag *Extract the maximal cliques*

Description

For internal use only. Extract the cliques.

For internal use only. Force Moralization

Usage

```
extractCliquesFromDag(dag, root = NULL)

mmmoralize(graph)
```

Arguments

dag	a Directed Aciclic Graph
root	a node to use as root
graph	a graphNEL object

Value

list of nodes cliques

extractSummaryFromBinary *Extract Summary Binary from MultiOmics Objects*

Description

Given an omic summarized by 'summarizeToBinaryEvents' extract the most important features.

Usage

```
extractSummaryFromBinary(omic, multiOmicObj, n = 3)
```

Arguments

omic	a summarized omic
multiOmicObj	Omics object
n	maximum number of features to retrieve

Value

Meant for internal use only. The summary for omic summarized using binary events.

sigModule	the original data for significant features
discrete	the discrete version of the significant covariates converted (when needed) into the discrete version
subset	data.frame(row.names=names(topGenes), cov=sum binary events)
covsConsidered	the name of the considered omic

`extractSummaryFromCluster` *Extract Summary Cluster from MultiOmics Objects*

Description

Given an omic summarized by 'summarizeInCluster' extract the most important features.

Usage

```
extractSummaryFromCluster(omic, multiOmicObj, n = 3)
```

Arguments

omic	a summarized omic
multiOmicObj	Omics object
n	maximum number of features to retrieve

Value

summary for omic summarized using clusters

sigModule	the original data for significant features
discrete	the discrete version of the significant covariates converted (when needed) into the discrete version
subset	data.frame(row.names=names(topGenes), metClust=topGenes)
pvalues	Kruskal Wallis pvalues of the selected features
covsConsidered	the name of the considered omic

`extractSummaryFromNumberOfEvents` *Extract Summary Binary from MultiOmics Objects*

Description

Given an omic summarized by 'summarizeToNumberOfEvents' extract the most important features.

Usage

```
extractSummaryFromNumberOfEvents(
  omic,
  multiOmicObj,
  moduleCox,
  analysis,
  n = 3,
  minprop = 0.1,
  labels = c("few", "many")
)
```

Arguments

`omic`	a summarized omic
`multiOmicObj`	`Omics` object
`moduleCox`	the coxObj of the interesting module
`analysis`	two-class or survival type
`n`	maximum number of features to retrieve
`minprop`	the minimal proportion of cutp
`labels`	the category labels

Value

Meant for internal use only. The summary for omic summarized using counting of events.

`sigModule`	the original data for significant features
`discrete`	the discrete version of the significant covariates converted (when needed) into the discrete version
`subset`	data.frame(row.names=names(topGenes), covariates=covariate)
`covsConsidered`	the name of the considered omic

`extractSummaryFromPCA` *Extract Summary PCA from MultiOmics Objects*

Description

Given an omic summarized by 'summarizeWithPca' extract the most important features.

Usage

```
extractSummaryFromPCA(
  omic,
  multiOmicObj,
  moduleCox,
  analysis,
  loadThr = 0.6,
  atleast = 1,
  minprop = 0.1
)
```

Arguments

`omic`	a summarized omic
`multiOmicObj`	`Omics` object
`moduleCox`	the coxObj of the interesting module
`analysis`	two-class or survival type
`loadThr`	the thr value to select the most influent features according to the loading
`atleast`	the minimum number of gene to retrieve
`minprop`	the minimal proportion of cutp

Value

summary for omic summarized using pca

`sigModule`	the original data for significant features
`discrete`	the discrete version of the significant covariates converted (when needed) into the discrete version
`subset`	data.frame(row.names=names(topGenes), covariate)
`covsConsidered`	the name of the considered omic

getPathFathers *Retrieves pathways relatives*

Description

For internal use only. Retrieves relatives given a pathway id.

Usage

```
getPathFathers(pathway, hierarchyGraph, ord = 3, plot = FALSE)
```

Arguments

pathway	a pathway id
hierarchyGraph	a igraph with pathway hierarchy
ord	how far you need to go backward
plot	plot relatives. For checking purpose

Details

Pathway Hierarchy is needed as igraph object.

Value

a character vector with the relatives

glmTest *Two-classes glm test.*

Description

Two-classes glm test.

Usage

```
glmTest(data, fullModelFormula, nullModelFormula)
```

Arguments

data	data
fullModelFormula	complete model
nullModelFormula	null model formula

Value

Two-classes glm test results

`guessInvolvement` *Guess the most influent features from MultiOmics Survival or Two-class results.*

Description

Given a pathway analyzed by `multiOmicsModuleSurvivalTest` or `multiOmicsTwoClassModuleTest`, it retrieves for each omic the most influent features.

Usage

```
guessInvolvement(
  pathway,
  moduleNumber,
  loadThr = 0.6,
  n = 3,
  atleast = 1,
  min_prop_pca = 0.1,
  min_prop_events = 0.1,
  ...
)
```

Arguments

`pathway`	`MultiOmicsModules` object from a pathway
`moduleNumber`	the module number
`loadThr`	the loading threshold to select genes (PCA only)
`n`	the maximum number of genes to retrieve (cluster and binary only)
`atleast`	the minimum number of features to select (PCA only)
`min_prop_pca`	the minimal proportion to compute the PCA classes
`min_prop_events`	the minimal proportion to compute the event classes
`...`	additional arguments passed to `get` function

Value

a list. Each item of the list corresponds to an omic that is summarized with the specific 'extractSummary' functions. Each item is the summary for an omic summarized using the setted method: pvalues are present only for cluster method.

guessInvolvementPathway *Guess the most influent features from MultiOmics Survival or Two-class results.*

Description

Given a pathway analyzed by `multiOmicsSurvivalPathwayTest` or `multiOmicsTwoClassPathwayTest`, it retrieves for each omic the most influent features.

Usage

```
guessInvolvementPathway(
  pathway,
  loadThr = 0.6,
  n = 3,
  atleast = 1,
  min_prop_pca = 0.1,
  min_prop_events = 0.1,
  ...
)
```

Arguments

`pathway`	`MultiOmicsModules` object from a pathway
`loadThr`	the loading threshold to select genes (PCA only)
`n`	the maximum number of genes to retrieve (cluster and binary only)
`atleast`	the minimum number of features to select (PCA only)
`min_prop_pca`	the minimal proportion to compute the PCA classes
`min_prop_events`	the minimal proportion to compute the event classes
`...`	additional arguments passed to `get` function

Value

a list. Each item of the list corresponds to an omic that is summarized with the specific 'extractSummary' functions. Each item is the summary for an omic summarized using the setted method: pvalues are present only for cluster method.

id2name *Convert id to pathway name*

Description

For internal use only. Retrieves name from pathway id.

Usage

```
id2name(idList, namedVect)
```

Arguments

idList	a list of pathway id
namedVect	a named vector

Details

You must provide a namedVect to be used as translator.

Value

a character vector with the names

makeOmics *Omics class initializer function*

Description

makeOmics creates the Omics object necessary to perform most of the analyses of this package. It contains all the omics data in the format of a ExperimentList, the clinical data, and all the information necessary for the dimensionality reduction step.

Usage

```
makeOmics(
  experiments = ExperimentList(),
  colData = S4Vectors::DataFrame(),
  sampleMap = S4Vectors::DataFrame(assay = factor(), primary = character(), colname =
    character()),
  metadata = list(),
  drops = list(),
  modelInfo = character(),
  specificArgs = list()
)
```

Arguments

experiments	A list or ExperimentList of all combined experiments
colData	A DataFrame or data.frame of characteristics for all biological units
sampleMap	A DataFrame or data.frame of assay names, sample identifiers, and colname samples
metadata	An optional argument of 'ANY' class (usually list) for content describing the experiments
drops	A list of unmatched information (included after subsetting)
modelInfo	A list with length equal to length(data) that are modelInfo to process each dataset
specificArgs	a list with length equal to length(data) to set additional parameters specific of the modelInfo

Value

an Omics class object

Examples

```
data(ovarianDataset)

myColData <- data.frame(
    status = sample(c(0, 1), 50, replace = TRUE),
    days = sample(c(0, 500), 50, replace = TRUE),
    row.names = colnames(ovarianDataset$exp)
)

myOmicsObj <- makeOmics(
    experiments = ovarianDataset,
    colData = myColData,
    modelInfo = c(
        "summarizeWithPca",
        "summarizeInCluster",
        "summarizeToNumberOfEvents",
        "summarizeToNumberOfDirectionalEvents"
    ),
    specificArgs = list(
        pcaArgs = list(
            name = "exp", shrink = "FALSE",
            method = "sparse", maxPCs = 3
        ),
        clusterArgs = list(
            name = "met",
            max_cluster_number = 3
        ),
        countEvent = list(name = "mut", min_prop = 0.05),
        cnvAgv = list(name = "cnv", min_prop = 0.05)
    )
)
```

makePositiveDefinite *Make positive and definite covariance matrix*

Description

Make positive and definite covariance matrix

Usage

```
makePositiveDefinite(m1, m2 = NULL, m3 = NULL, threshold = 0.1)
```

Arguments

m1	matrix 1
m2	matrix 2
m3	matrix 3
threshold	threshold of difference

Value

list with

m1	the matrix m1 positive and definite
m2	the matrix m2 positive and definite
m3	the matrix m3 positive and definite
correction	the magneturde of the correction
value	the value

mapPathwaysIDfromGraphite *Map Pathways ID from Graphite*

Description

For internal use only. Retrieve pathway id and names from Pathways object.

Usage

```
mapPathwaysIDfromGraphite(pathways, pathwayNames = NULL)
```

Arguments

pathways	a PathwayList object
pathwayNames	in not NULL, a subset of pathway to extract

Value

a data frame, id and pathway name

`minOrNA` *Minimum or NA*

Description

For internal use only. Get back minimum or NA.

Usage

```
minOrNA(x)
```

Arguments

`x`	a numeric

Value

a numeric. The minimum or NA

Examples

```
# minOrNA(c(1,5,0.1,NA))
# minOrNA(c(NA,NA,NA))
```

`MOSClip` *MOSClip: Multi-Omics Survival Clip*

Description

`MOSClip` R package implements a statistical approach able to integrate multi-omic data and look for survival associated gene modules. It integrates multiple omics - trascriptomics, methylomics, genomic mutations, and genomic copy number variations - using various data dimensionality reduction strategies and multivariate models. Exploiting graph theory, pathways can be decomposed into their connected components, that we call modules. The analysis can then be performed at the level of entire pathways or pathway modules. `MOSClip` pathway analysis serves two primary purposes: testing the survival association of pathways or modules using the Cox proportional hazard model, and conducting a two-class analysis with a generalized linear model. Additionally, the package offers valuable graphical tools to visualize and interpret the results.

Details

To conduct a multi-omic survival analysis on pathways or modules use:

- multiOmicsSurvivalPathwayTest
- multiOmicsSurvivalModuleTest

To perform a two-class comparison enrichment analysis on pathways or modules use:

- multiOmicsTwoClassPathwayTest
- multiOmicsTwoClassModuleTest

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References

Paolo Martini, Monica Chiogna, Enrica Calura, and Chiara Romualdi. 2019. "MOSClip: Multi-Omic and Survival Pathway Analysis for the Identification of Survival Associated Gene and Modules." Nucleic Acids Research 47 (14): e80. https://doi.org/10.1093/nar/gkz324

See Also

Useful links:

- https://github.com/CaluraLab/MOSClip/
- Report bugs at https://github.com/CaluraLab/MOSClip/issues

multiOmics *Omics class object with TCGA ovarian data*

Description

An Omics class object containing data from TCGA ovarian cancer. The TCGA data was manually selected and preprocessed. It contains 4 omics: expression, methylation, mutation, and copy number variation. Additionally, it contains specific arguments to perform the dimensionality reduction. The datasets were downloaded from TCGA using TCGABiolink R package, selecting only patients with primary solid tumors. Expression matrix was processed first, converting gene identifiers into Entrez IDs. The profiles of genes present more than once were averaged. Genes with at least 100 counts in at least one patients were selected, to avoid data sparsity. Mutation matrix was filtered, keeping only genes with expression data available. We chose to consider only missense and nonsense mutations and mutation impact was also considered following Mutect2 pipeline. CNV values were transformed into numeric values. Methylation data were processed with Methyl Mix R package. Patients that had both normal and primary tumors samples were selected. With the help of a dictionary array probes were connected to CpG clusters, and finally CpG clusters were mapped to genes (Entrez ID). Survival annotation curated by Liu et al. (2018) was used to extract PFS information. Only patients with matched data across the four omics were considered. After the selection of patients and genes, we performed expression normalization and log2 of the counts+1 transformation. This will ensure us to work with expression data approximately close to a normal distribution, the most suitable distribution for the subsequent MOSClip tests. Genes and samples were manually selected to create this small example dataset for demonstration purposes.

Usage

```
data('multiOmics')
```

Format

multiOmics**:**

An Omics with 4 omics:

exp Matrix with 151 rows and 50 columns of RNA expression values

met A matrix with 178 rows and 50 columns of methylation data with probes clustered

mut A matrix with 107 rows and 50 columns of mutation counts

cnv A matrix with matrix with 145 rows and 50 columns of copy number ...

MultiOmicsModules-class *Multi Omics Modules.*

Description

This class organizes the results of the Multi Omics Module Test analysis, in which corresponds to one pathway decomposed into modules.

Usage

```
## S4 method for signature 'MultiOmicsModules'
showModule(object)
```

Arguments

object	an object of class MultiOmicsModules

Methods (by generic)

- showModule(MultiOmicsModules): shows module info

Slots

alphas a numeric vector of the pvalues of all the modules.

zlists a list of numeric vectors with the zs of the covariates for each module.

modulesView a list of module information: for each omic, the name of the omic, the genes used, the method, the name of the covariates analyzed and other specific information based on the omic.

modules a list with the genes that belong to the module.

title the name of the pathway.

analysis the type of analysis done: survival or two-class.

MultiOmicsPathway-class

Multi Omics Pathway.

Description

This class organize the results of the Multi-Omics Pathway Survival Test analysis.

Usage

```
## S4 method for signature 'MultiOmicsPathway'
showPathway(object)
```

Arguments

object	an object of class MultiOmicsPathway

Methods (by generic)

- showPathway(MultiOmicsPathway): shows module info

Slots

`pvalue` a numeric vector of the pvalues of the pathways.

`zlist` a numeric vector with the zs of all the covariates.

`pathView` a list of pathway information: for each omic, the name of the omic, the genes used, the method, the name of the covariates analyzed and other specific information based on the omic.

`title` the name of the pathway.

`analysis` the type of analysis done: survival or two-class.

`multiOmicsSurvivalModuleTest`
Compute Multi Omics Survival in Pathway Modules

Description

Performs survival analysis using an `Omics` object. The pathway (graph) used is decomposed in modules (cliques) using graph theory.

Usage

```
multiOmicsSurvivalModuleTest(
  omicsObj,
  graph,
  survFormula = "Surv(days, status) ~",
  autoCompleteFormula = TRUE,
  useTheseGenes = NULL,
  pathName = NULL,
  robust = FALSE,
  include_from_annot = FALSE
)
```

Arguments

`omicsObj`	Object of class `Omics`
`graph`	a pathway in `graphNEL`, `Pathway` or geneset format
`survFormula`	a character with the formula to compute survival
`autoCompleteFormula`	logical. If TRUE autocomplete the `survFormula` using all the available covariates
`useTheseGenes`	vector of genes used to filter pathways
`pathName`	title of the pathway. If NULL and graph is `Pathway`, `graph@title` is used as title
`robust`	logical, whether the robust mode should be used for cox model analysis
`include_from_annot`	logical. If TRUE compute cox model analysis using additional covariates from `colData`

Value

MultiOmicsModules object

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_survival <- multiOmicsSurvivalModuleTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)
```

---

multiOmicsSurvivalPathwayTest

Compute Multi Omics Survival in Pathways

Description

Performs topological survival analysis using an Omics object.

Usage

```
multiOmicsSurvivalPathwayTest(
  omicsObj,
  graph,
  survFormula = "Surv(days, status) ~",
  autoCompleteFormula = TRUE,
  useTheseGenes = NULL,
  pathName = NULL,
  robust = FALSE,
  include_from_annot = FALSE
)
```

Arguments

omicsObj	Object of class Omics
graph	a pathway in graphNEL, Pathway or geneset format
survFormula	a character with the formula to compute survival
autoCompleteFormula	logical. If TRUE autocomplete the survFormula using all the available covariates
useTheseGenes	vector of genes used to filter pathways

pathName	title of the pathway. If NULL and graph is Pathway, graph@title is used as title
robust	logical, whether the robust mode should be used for cox model analysis
include_from_annot	logical. If TRUE compute cox model analysis using additional covariates from colData

Value

MultiOmicsPathway object

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOP_survival <- multiOmicsSurvivalPathwayTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)
```

---

multiOmicsTopo *Omics class object with TCGA ovarian data for topological analysis*

Description

An Omics class object containing data from TCGA ovarian cancer. The data are the same as in multiOmics object. Arguments in specificArgs slot have been set to efficiently run a topological pathway analysis, i.e., the topological method is used for PCA and shrink parameter is set to TRUE. This method can't be used for analyses on modules.

Usage

```
data('multiOmicsTopo')
```

Format

multiOmicsTopo:

An Omics with 4 omics:

exp Matrix with 151 rows and 50 columns of RNA expression values

met A matrix with 178 rows and 50 columns of methylation data with probes clustered

mut A matrix with 107 rows and 50 columns of mutation counts

cnv A matrix with matrix with 145 rows and 50 columns of copy number ...

multiOmicsTwoClassModuleTest *Computes Multi Omics Two-Class in Pathway Modules*

Description

Performs topological two-class analysis using an Omics object. It decomposes graphs (pathways) into modules.

Usage

```
multiOmicsTwoClassModuleTest(
  omicsObj,
  graph,
  classAnnot,
  baseFormula = "classes ~",
  autoCompleteFormula = TRUE,
  useTheseGenes = NULL,
  nullModel = "classes ~ 1",
  pathName = NULL
)
```

Arguments

omicsObj	object of class Omics
graph	a pathway as a graphNEL object.
classAnnot	a data.frame with the class annotation. It is necessary at least a column with the classes labels, and the row.names as the samples labels
baseFormula	model formula to be used for the test. It should be written as 'classes ~ ', while 'classes' being the column name for the class labels
autoCompleteFormula	a logical value. If TRUE. It autocompletes the formula used to fit generalized lienar models function using all the available covariates (omics)
useTheseGenes	(optional) vector of specific genes to be used
nullModel	the null model formula. It should be written the same as the baseFormula, followed by ' 1'. (e.g. 'classes ~ 1')
pathName	(optional) title of the pathway. If NULL, graph@title is used as title

Value

MultiOmicsModule object

Examples

```
data("multiOmics")
data("reactSmall")

genesToUse <- row.names(multiOmics[[1]])

classAnnot <- data.frame(
    "treatment" = c(rep("A", 25), rep("B", 25)),
    row.names = colnames(multiOmics[[1]])
)

MOM_twoclasses <- multiOmicsTwoClassModuleTest(
    multiOmics, reactSmall[[1]], classAnnot,
    baseFormula = "treatment ~ ", nullModel = "treatment ~ 1",
    useTheseGenes = genesToUse
)
```

---

multiOmicsTwoClassPathwayTest

Compute Multi Omics Two-Class in Pathways

Description

Performs topological two-class analysis using an `Omics` object.

Usage

```
multiOmicsTwoClassPathwayTest(
  omicsObj,
  graph,
  classAnnot,
  baseFormula = "classes ~ ",
  autoCompleteFormula = TRUE,
  useTheseGenes = NULL,
  nullModel = "classes ~ 1",
  pathName = NULL
)
```

Arguments

`omicsObj`	object of class `Omics`
`graph`	a pathway as a `graphNEL` object.
`classAnnot`	a `data.frame` with the class annotation. It is necessary at least a column with the classes labels, and the row.names as the samples labels
`baseFormula`	model formula to be used for the test. It should be written as 'classes ~ ', while 'classes' being the column name for the class labels

autoCompleteFormula
: a logical value. If TRUE. It autocompletes the formula used to fit generalized lienar models function using all the available covariates (omics)

useTheseGenes
: (optional) vector of specific genes to be used

nullModel
: the null model formula. It should be written the same as the baseFormula, followed by ' 1'. (e.g. 'classes ~ 1')

pathName
: (optional) title of the pathway. If NULL, `graph@title` is used as title

Value

`MultiOmicsPathway` object

Examples

```
data("multiOmics")
data("reactSmall")

genesToUse <- row.names(multiOmics[[1]])

classAnnot <- data.frame(
    "treatment" = c(rep("A", 25), rep("B", 25)),
    row.names = colnames(multiOmics[[1]])
)

MOP_twoClasses <- multiOmicsTwoClassPathwayTest(
    multiOmics, reactSmall[[1]], classAnnot,
    baseFormula = "treatment ~ ", nullModel = "treatment ~ 1",
    useTheseGenes = genesToUse
)
```

---

multiPathwayModuleReport

Provides a Table of the Modules Test Results

Description

Summarizes the results of a multi omics module test given a list of MultiOmicsModules objects

Usage

```
multiPathwayModuleReport(multiPathwayModuleList, priority_to = NULL)
```

Arguments

multiPathwayModuleList
: a list of `MultiOmicsModules` objects resulting from a multi-omics module test.

priority_to
: a vector with the covariates (the omics names) that should appear first in the dataframe columns

Value

a data.frame class object. Rows correspond to the modules, and the columns to the overall and covariates pvalues of the test.

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_list <- lapply(reactSmall[1:2], function(g) {
    fcl <- multiOmicsSurvivalModuleTest(multiOmics, g,
        survFormula = "Surv(days, status) ~",
        autoCompleteFormula = TRUE,
        useTheseGenes = genesToUse
    )
    fcl
})

moduleSummary <- multiPathwayModuleReport(MOM_list)
```

`multiPathwayReport` *Summarize pathways' info from a list of MultiOmicsPathway objects (MOP)*

Description

Given the list of MOPs, it creates the table.

Usage

```
multiPathwayReport(multiPathwayList, priority_to = NULL)
```

Arguments

`multiPathwayList`	a list of `MultiOmicsPathway` objects resulting from a multi-omics pathway test.
`priority_to`	a vector with the covariates (omic name) that should go first.

Value

a data.frame, pathways in rows, overall pvalue of the coxph, followed by covariates pvalues, in columns.

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOP_list <- lapply(reactSmall, function(g) {
    fcl <- multiOmicsSurvivalPathwayTest(multiOmics, g,
        survFormula = "Surv(days, status) ~",
        autoCompleteFormula = TRUE,
        useTheseGenes = genesToUse
    )
    fcl
})

pathwaysSummary <- multiPathwayReport(MOP_list)
```

Omics-class *Omics.*

Description

This class is the storage for the different omic datasets that we need to analyze. It is based on `MultiAssayExperiment`.

Usage

```
## S4 method for signature 'Omics'
showOmics(object)
```

Arguments

`object`	an object of class `Omics`

Methods (by generic)

- `showOmics(Omics)`: shows model parameters

Slots

`modelInfo` a list with length equal to length(data) that are modelInfo to process each dataset.

`specificArgs` a list with length equal to length(data) to set additional parameters specific of the modelInfo.

ovarianDataset *ExperimentList class object with TCGA ovarian data*

Description

An ExperimentList class object containing data from TCGA ovarian cancer. The TCGA data was manually selected and preprocessed. It contains 4 omics: expression, methylation, mutation, and copy number variation.

Usage

```
data('ovarianDataset')
```

Format

`ExperimentList`:

An ExperimentList with 4 omics:

exp Matrix with 101 rows and 50 columns of RNA expression values

met A matrix with 97 rows and 50 columnsof methylation data with probes clustered

mut A matrix with 55 rows and 50 columns of mutation counts

cnv A matrix with matrix with 101 rows and 50 columns of copy number ...

plotFrequencies *Plot Frequencies of Pathway Fathers for Omics intersection*

Description

Plots the frequencies of the pathway fathers by every omics intersection from a data.frame of the frequencies returned with the function `computeFreqs`.

Usage

```
plotFrequencies(
  frequencies,
  manualColors = NULL,
  minSize = 4,
  maxSize = 20,
  width = 20,
  relMagnificationOfLegend = 0.5,
  lineSize = 1
)
```

Arguments

frequencies	a data.frame created from 'computeFreqs'
manualColors	optional vector of colors to be used
minSize	the minimal font size. Maximal frequencies will be added for each class
maxSize	the maximal font size dimension, all values above are clipped
width	the number of character to wrap the labels
relMagnificationOfLegend	the relative magnification of the text of the legend
lineSize	the thickness of the lines

Value

a circular plot of the frequencies of pathway fathers

Examples

```
df <- data.frame(
    category = c("PathwayA", "PathwayB", "PathwayC", "PathwayD"),
    frequencies = c(1, 2, 1, 3),
    class = rep("Mut", 4), stringsAsFactors = FALSE
)
plotFrequencies(df)
```

---

plotModuleHeat *Plot a Heatmap of a Module by Omics*

Description

It creates a heatmap of the most involved genes of each omic of a specific module from a `MultiOmicsModule` object.

Usage

```
plotModuleHeat(
  moduleobj,
  moduleNumber,
  sortBy = NULL,
  paletteNames = NULL,
  additionalAnnotations = NULL,
  additionalPaletteNames = NULL,
  withSampleNames = TRUE,
  fontsize_row = 10,
  fontsize_col = 1,
  nrowsHeatmaps = 3,
  orgDbi = "org.Hs.eg.db",
```

```
  discr_prop_pca = 0.15,
  discr_prop_events = 0.05,
  ...
)
```

Arguments

moduleobj	MultiOmicsModule class object
moduleNumber	module number of interest
sortBy	a covariate (omic) to sort by
paletteNames	a palette containing three colors
additionalAnnotations	optional additional sample annotations
additionalPaletteNames	optional additional colors for annotations
withSampleNames	show sample names
fontsize_row	font size for row labels
fontsize_col	font size for column labels
nrowsHeatmaps	magnification respect to annotation of sample (annotations take 1 row)
orgDbi	a Dbi organism to be used. Default is org.Hs.eg.db
discr_prop_pca	the minimal proportion to compute the PCA classes
discr_prop_events	the minimal proportion to compute the event classes
...	additional arguments passed to guessInvolvement function

Value

A heatmap of a pathway module (results of the module test)

Examples

```
data(multiOmics)
data(reactSmall)

survAnnot <- data.frame(
    status = multiOmics$status,
    days = multiOmics$days,
    row.names = colnames(multiOmics[[1]])
)

genesToUse <- row.names(multiOmics[[1]])

MOM_survival <- multiOmicsSurvivalModuleTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)
```

```
plotModuleHeat(MOM_survival, 1,
    sortBy = c("mut", "expPC1", "status", "days"),
    additionalAnnotations = survAnnot,
    additionalPaletteNames = list(status = "teal", days = "violet"),
    withSampleNames = F
)
```

`plotModuleInGraph` *Plot a Directed Graph of the MultiOmicsModules Object*

Description

From a `MultiOmicsModules` object, it plots the position of a given module in the pathway. The omics are also represented in the graph.

Usage

```
plotModuleInGraph(
  modulesobj,
  pathList,
  moduleNumber,
  orgDbi = "org.Hs.eg.db",
  paletteNames = NULL,
  legendLabels = NULL,
  fileName = NULL,
  discr_prop_pca = 0.15,
  discr_prop_events = 0.05,
  pathTitle = NULL,
  ...
)
```

Arguments

`modulesobj`	a `MultiOmicsModule` class object
`pathList`	a `PathwayList` from `graphite` package that contains the pathways to be used
`moduleNumber`	a module number
`orgDbi`	if needed, indicates an organism Dbi to translate the vectors
`paletteNames`	named vector of MOSpalettes, names replace makeLegend arguments
`legendLabels`	set up your favourite names for the omics
`fileName`	optional filenames to save the plot
`discr_prop_pca`	the minimal proportion to compute the PCA classes
`discr_prop_events`	the minimal proportion to compute the event classes
`pathTitle`	title of the graph, to be searched in `pathList`
`...`	additional arguments passed to `guessInvolvement` function

Value

a MOSClip plot in form of a list class object

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_survival <- multiOmicsSurvivalModuleTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)

plotModuleInGraph(MOM_survival, reactSmall,
    moduleNumber = 1,
    paletteNames = c(exp = "red", met = "green",
                     mut = "blue", cnv = "yellow")
)
```

---

plotModuleKM *Plot Kaplan-Meier survival curves of a specific module*

Description

Given a `MultiOmicsModule` class object and a specific module number, it plots Kaplan-Meier curves, in which the strata corresponds to the omics

Usage

```
plotModuleKM(
  MOM,
  moduleNumber,
  formula = "Surv(days, status) ~ PC1",
  fileName = NULL,
  paletteNames = NULL,
  h = 9,
  w = 7,
  risk.table = TRUE,
  pval = TRUE,
  size = 1,
  inYears = FALSE,
  discr_prop_pca = 0.15,
  discr_prop_events = 0.05,
  additional_discrete = NULL,
  additional_continuous = NULL,
```

```
  ...
)
```

Arguments

MOM	a MultiOmicsModule class object
moduleNumber	numeric value. The module number of interest
formula	a formula for the survival analysis. It should be written as 'Surv(days, status) ~ omic'. To plot more than one omic, write them separated by a '+' character after the separator (~)
fileName	optional filenames to save the plot
paletteNames	a palette name to be used
h	the height of the plot
w	the width of the plot
risk.table	logical value. If TRUE, shows the risk.table. Default is TRUE.
pval	logical value. If TRUE, shows the p-value of the curves. Default is TRUE.
size	line width of the KM curves
inYears	set time in years
discr_prop_pca	the minimal proportion to compute the PCA classes
discr_prop_events	the minimal proportion to compute the event classes
additional_discrete	names of the additional discrete variables to include
additional_continuous	names of the additional continous variables to include
...	additional arguments passed to guessInvolvement and get function

Value

a ggsurvplot class object

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_survival <- multiOmicsSurvivalModuleTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)

plotModuleKM(MOM_survival, 1,
    formula = "Surv(days, status) ~ mut + expPC2",
    paletteNames = "Paired", inYears = TRUE
)
```

plotModuleReport *Plot a table of a* MultiOmicsModules *(MOM) object*

Description

Given a MultiOmicsModules object, it plots its results in a tabular fashion

Usage

```
plotModuleReport(
  modulesObj,
  MOcolors = NULL,
  priority_to = NULL,
  fontsize = 12,
  ...
)
```

Arguments

modulesObj	MultiOmicsModules class object
MOcolors	character vector with the omic colors. The colors should be among the colors in showMOSpalette
priority_to	a vector with the covariates (omic names) that should go first
fontsize	Size of the font to be used in the plot
...	additional argument to be passed to pheatmap

Value

a Heatmap list object from ComplexHeatmap package of the results contained in the MultiOmicsModules object provided

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_survival <- multiOmicsSurvivalModuleTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)

plotModuleReport(MOM_survival,
    MOcolors = c(
        exp = "red", met = "green", mut = "blue",
        cnv = "yellow"
```

```
    )
)
```

`plotMultiPathwayReport` *Summarize and plot pathways' info from a list of* `MultiOmicsPathway` *(MOP)*

Description

Given the list of MOPs, it plots a table of its results.

Usage

```
plotMultiPathwayReport(
  multiPathwayList,
  top = 25,
  MOcolors = NULL,
  priority_to = NULL,
  fontsize = 6,
  ...
)
```

Arguments

`multiPathwayList`	a `list` of `MultiOmicsPathway` class objects
`top`	numeric value. Plot only the top number of pathways
`MOcolors`	character vector with the omic colors. The colors should be among the colors in `showMOSpalette`
`priority_to`	a vector with the covariates (omic names) that should go first
`fontsize`	the font size to be used. Default is 12.
`...`	additional argument to be passed to pheatmap

Value

a Heatmap list object from ComplexHeatmap package of the results contained in the `MultiOmicsPathway` object provided

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOP_list <- lapply(reactSmall, function(g) {
    fcl <- multiOmicsSurvivalPathwayTest(multiOmics, g,
        survFormula = "Surv(days, status) ~",
        autoCompleteFormula = TRUE,
        useTheseGenes = genesToUse
    )
    fcl
})

plotMultiPathwayReport(MOP_list,
    MOcolors = c(
        exp = "red", met = "green", mut = "blue",
        cnv = "yellow"
    ),
    fontsize = 12
)
```

`plotPathwayHeat` *Plot heatmaps of the pathway by omics*

Description

Given the pathway, it creates the heatmaps of the mostly involved genes for each omic.

Usage

```
plotPathwayHeat(
  pathway,
  sortBy = NULL,
  paletteNames = NULL,
  additionalAnnotations = NULL,
  additionalPaletteNames = NULL,
  discr_prop_pca = 0.15,
  discr_prop_events = 0.05,
  withSampleNames = TRUE,
  nrowsHeatmaps = 3,
  orgDbi = "org.Hs.eg.db",
  ...
)
```

Arguments

pathway	MultiOmicsPathway class object
sortBy	one or more covariates to sort the samples
paletteNames	name of the colors for each omic
additionalAnnotations	optional additional sample annotations (e.g. survival annotation)
additionalPaletteNames	colors for additional annotations. The colors available are the ones in showMOSpalette
discr_prop_pca	the minimal proportion to compute the PCA classes
discr_prop_events	the minimal proportion to compute the event classes
withSampleNames	show the sample names in the plot
nrowsHeatmaps	magnification respect to annotation of sample (annotations take 1 row)
orgDbi	a Dbi organism to be used. Default is org.Hs.eg.db
...	additional arguments passed to guessInvolvementPathway function (internal use)

Value

An object of class ggplot plotted with ComplexHeatMap package.

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

survAnnot <- data.frame(
    status = multiOmics$status,
    days = multiOmics$days,
    row.names = colnames(multiOmics[[1]])
)

# Creating the MultiOmicsPathway object
MOP_survival <- multiOmicsSurvivalPathwayTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)

# Plotting
plotPathwayHeat(MOP_survival,
    sortBy = c("expPC2", "mut", "status", "days"),
    paletteNames = c(exp = "red", met = "green",
                     mut = "blue", cnv = "yellow"),
    additionalAnnotations = survAnnot,
    additionalPaletteNames = list(status = "teal", days = "violet"),
```

```
    nrowsHeatmaps = 2, withSampleNames = F
)
```

`plotPathwayKM` *Plot Kaplan-Meier survival curves of a specific pathway*

Description

Given a `MultiOmicsPathway` class object, it plots Kaplan-Meier curves, in which the strata corresponds to the chosen omics

Usage

```
plotPathwayKM(
  pathway,
  formula = "Surv(days, status) ~ PC1",
  fileName = NULL,
  paletteNames = NULL,
  h = 9,
  w = 7,
  risk.table = TRUE,
  pval = TRUE,
  size = 1,
  inYears = FALSE,
  discr_prop_pca = 0.15,
  discr_prop_events = 0.05,
  additional_discrete = NULL,
  additional_continuous = NULL,
  ...
)
```

Arguments

`pathway`	`MultiOmicsPathway` class object
`formula`	a formula to compute the plot
`fileName`	optional filenames to save the plot
`paletteNames`	a palette containing three colors
`h`	the height of the plot
`w`	the width of the plot
`risk.table`	logical value. If TRUE, shows the `risk.table`. Default is TRUE.
`pval`	logical value. Shows p-value of the curves
`size`	line width of the KM curves
`inYears`	logical value. If TRUE, converts days to years

discr_prop_pca the minimal proportion to compute the PCA classes

discr_prop_events
: the minimal proportion to compute the event classes

additional_discrete
: names of the additional discrete variables to include

additional_continuous
: names of the additional continuous variables to include

... additional arguments passed to guessInvolvementPathway and get function (internal use)

Value

a ggsurvplot class object

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

# Creating the MultiOmicsPathway object
MOP_survival <- multiOmicsSurvivalPathwayTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)

plotPathwayKM(MOP_survival,
    formula = "Surv(days, status) ~ mut + expPC2",
    paletteNames = "Paired", inYears = TRUE
)
```

---

pvalueSummary *Compute pvalue Summary*

Description

Compute pvalue Summary

Usage

```
pvalueSummary(multiPathwayReportData, excludeColumns = NULL, as.list = FALSE)
```

Arguments

multiPathwayReportData	data.frame, the output of the multiPathwayReport or multiPathwayModuleReport functions.
excludeColumns	a vector of characters listing the columns of multiPathwayReportData object to be excluded by the analysis. In the case multiPathwayReportData derives from multiPathwayModuleReport you should set excludeColumns = c('pathway','module').
as.list	return a list rather than a data.frame

Value

a list

---

reactSmall *PathwayList of pathways from Reactome*

Description

A PathwayList with three pathways necessary for the analysis: 'Activation of Matrix Metalloproteinases', 'FGFR1 mutant receptor activation', and 'VEGFA-VEGFR2 Pathway'. Pathways were downloaded using graphite package and the names of the nodes were converted into Entrez IDs.

Usage

```
data('reactSmall')
```

Format

reactSmall:

A PathwayList with Reactome pathways for hsapiens

entries Three Reactome pathways with their nodes

---

removeSelfLoops *Remove self loops from a graphNEL*

Description

Remove the self loops that a present in the graph graphNEL object

Usage

```
removeSelfLoops(graph)
```

Arguments

graph	a graphNEL object

Value

a graphNEL object

#' @rdname graph-processing

`resamplingModulesSurvival` *Resampling function for survival analysis on modules*

Description

Resampling function for survival analysis on modules

Resampling function for pathways (survival analysis)

Usage

```
resamplingModulesSurvival(
  fullMultiOmics,
  pathdb,
  nperm = 100,
  pathwaySubset = NULL,
  nPatients = 3,
  genesToConsider = NULL
)

resamplingPathwaySurvival(
  fullMultiOmics,
  pathdb,
  nperm = 100,
  pathwaySubset = NULL,
  nPatients = 3,
  genesToConsider = NULL
)
```

Arguments

fullMultiOmics	a multiOmic object
pathdb	pathway database
nperm	number of permutations
pathwaySubset	a list of pathways to resample
nPatients	number of patients to remove for resampling
genesToConsider	vector of genes used to filter pathways; if NULL, genes found in the first experiment of the multiOmic object are used

Value

list of the resampling tables of results

list of the resampling tables of results

Examples

```
data(multiOmics)
data(reactSmall)

perms <- resamplingModulesSurvival(
    fullMultiOmics = multiOmics, reactSmall,
    nperm = 10,
    pathwaySubset =
        "FGFR1 mutant receptor activation"
)
```

---

resamplingModulesTwoClass

Resampling function for two-class analysis on modules

Description

Resampling function for two-class analysis on modules

Resampling function for pathways (two-class analysis)

Usage

```
resamplingModulesTwoClass(
  fullMultiOmics,
  classAnnot,
  pathdb,
  nperm = 100,
  pathwaySubset = NULL,
  nPatients = 3,
  genesToConsider = NULL
)

resamplingPathwayTwoClass(
  fullMultiOmics,
  classAnnot,
  pathdb,
  nperm = 100,
  pathwaySubset = NULL,
  nPatients = 3,
  genesToConsider = NULL
)
```

Arguments

fullMultiOmics	a multiOmic object
classAnnot	patients class annotations
pathdb	pathway database
nperm	number of permutations
pathwaySubset	a list of pathways to resample
nPatients	number of patients to remove for resampling
genesToConsider	vector of genes used to filter pathways; if NULL, genes found in the first experiment of the multiOmic object are used

Value

list of the resampling tables of results

list of the resampling tables of results

Examples

```
data(multiOmics)
data(reactSmall)

classAnnot <- data.frame(
    "treatment" = c(rep("A", 25), rep("B", 25)),
    row.names = colnames(multiOmics[[1]])
)

perms <- resamplingModulesTwoClass(
    fullMultiOmics = multiOmics,
    classAnnot, reactSmall,
    nperm = 10,
    pathwaySubset =
        "FGFR1 mutant receptor activation"
)
```

---

runSupertest *Performs a Exact test - analysis of omics intersection*

Description

This function performs a exact test implementing a theorical framework using the SuperExactTest package. It calculates the statistical distributions of multi omics set intersections. It can be used with both a MultiOmicsModules or MultiOmicsPathway class objects.

Usage

```
runSupertest(
  multiPathwayReportData,
  pvalueThr = 0.05,
  zscoreThr = 0.05,
  resampligThr = NULL,
  plot = c("circular", "landscape", "noplot"),
  sort.by = c("set", "size", "degree", "p-value"),
  excludeColumns = NULL,
  color.on = "#f6bb42",
  color.off = "#D3D3D3"
)
```

Arguments

multiPathwayReportData	data.frame, the output of the multiPathwayReport or multiPathwayModuleReport functions.
pvalueThr	numeric value. Overall pvalue cut-off to be used
zscoreThr	numeric value. Covariates coefficient cut-off to be used.
resampligThr	numeric value. Filters the modules according to the number of success in the resampling procedure, takes only the modules above this threshold.
plot	character indicating the layout for plotting. It is one of circular, landscape or noplot. By default, plot='circular', if plot='noplot' no plot will be provided.
sort.by	character indicating how to sort the intersections in the plot. It is one of 'set' (by omics), 'size' (by intersection size), 'degree' (by number of intersected omics), and 'p-value'.
excludeColumns	a vector of characters listing the columns of multiPathwayReportData object to be excluded by the analysis. In the case multiPathwayReportData derives from multiPathwayModuleReport you should set excludeColumns = c('pathway','module').
color.on	color that represent the active omics in the sector
color.off	color that represent the omics mnot considered in the sector

Details

This function calculates intersection sizes between multiple set of pathways or modules and performs statistical test of the intersections using the total amout of analyzed pathways or modules as background. The super exact test of this function was described in Wang et al 2015.

Value

a data.frame containing all the numeric information of the plot included the pathways shared by different omics.

References

Minghui Wang, Yongzhong Zhao, and Bin Zhang (2015). Efficient Test and Visualization of Multi-Set Intersections. Scientific Reports 5: 16923.

Examples

```
df <- data.frame(
    pvalue = c(0.06, 0.04, 0.04, 0.03, 0.02),
    cnv = c(0.07, 0.03, 0.02, 0.04, 0.01),
    mut = c(0.08, 0.02, 0.01, 0.04, 0.04),
    row.names = c(
        "PathwayA", "PathwayB", "PathwayC",
        "PathwayD", "PathwayE"
    )
)

runSupertest(df, pvalueThr = 0.05, zscoreThr = 0.05)
```

---

selectStablePathwaysModules

Select stable pathway modules

Description

Select stable pathway modules

Count the resampling success

Add resampling counts to module summary

Usage

```
selectStablePathwaysModules(perms, moduleSummary, success = 90, col = "pvalue")

getPathwaysModulesSuccess(perms, moduleSummary, col = "pvalue", thr = 0.05)

addResamplingCounts(moduleSummary, resamplingCounts)
```

Arguments

perms	a list. Result of resampling function
moduleSummary	summary of modules or pathways obtained from multiPathwayModuleReport or multiPathwayReport
success	number of success to consider the pathway or module stable
col	the name of the column in the summary to be used to evaluate resampling success
thr	the threshold for significance
resamplingCounts	the counts of success obtained with getPathwaysModulesSuccess

Value

the subset of stable modules

the counts of success for each pathway or module

a module or pathway summary with resampling counts column appended

Examples

```
data("multiOmics")
data("reactSmall")

perms <- resamplingPathwaySurvival(multiOmics, reactSmall, nperm = 5)
res <- lapply(reactSmall, function(g) {
    multiOmicsSurvivalPathwayTest(multiOmics, g,
        useTheseGenes = row.names(multiOmics[[1]])
    )
})
pathSummary <- multiPathwayReport(res)
getPathwaysModulesSuccess(perms, pathSummary)
```

---

showModule *A generic function showing pathway's module info*

Description

A generic function showing pathway's module info

Usage

```
showModule(object)
```

Arguments

object	an object of class MultiOmicsModules

Value

NULL. No value is returned

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOM_survival <- multiOmicsSurvivalModuleTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
```

```
    useTheseGenes = genesToUse
)

showModule(MOM_survival)
```

---

showMOSpalette *Shows the MOSClip palette.*

Description

This function shows the MOSClip palette. Each omic should be coupled to a color panel, this match will be preserved in plots.

Usage

```
showMOSpalette()
```

Value

NULL. No value is returned

Examples

```
showMOSpalette()
```

---

showOmics *A generic functions showing parameter associated with each omics*

Description

A generic functions showing parameter associated with each omics

Usage

```
showOmics(object)
```

Arguments

object	an object of class Omics

Value

NULL. No value is returned

Examples

```
data(multiOmics)

showOmics(multiOmics)
```

---

showPathway *A generic function showing pathway info*

Description

A generic function showing pathway info

Usage

```
showPathway(object)
```

Arguments

object	an object of class MultiOmicsPathway

Value

NULL. No value is returned

Examples

```
data(multiOmics)
data(reactSmall)

genesToUse <- row.names(multiOmics[[1]])

MOP_survival <- multiOmicsSurvivalPathwayTest(multiOmics, reactSmall[[1]],
    survFormula = "Surv(days, status) ~", autoCompleteFormula = TRUE,
    useTheseGenes = genesToUse
)

showPathway(MOP_survival)
```

sparseCompPCs *Sparse PCA*

Description

Sparse PCA

Usage

```
sparseCompPCs(exp, shrink, k)
```

Arguments

exp	a matrix
shrink	logical, whether to shrink or not.
k	the number of components to use

Value

a list with the following elements:

x	the computed PCs
sdev	the standard deviation captured by the PCs
loadings	the loadings

stripModulesFromPathways *Remove Module Number From Pathway Name*

Description

Function to remove the suffix corresponding to the module number of the pathway name. Necessary step for annotePathwayToFather and plotFrequencies

Usage

```
stripModulesFromPathways(pathways)
```

Arguments

pathways	vector of pathway names

Value

list of pathway names without the module number

Examples

```
pathwaysModules <- list(
    "Intrinsic Pathway for Apoptosis.1",
    "Intrinsic Pathway for Apoptosis.2",
    "Opioid Signalling.1", "Opioid Signalling.2"
)

resPathwayNames <- stripModulesFromPathways(pathwaysModules)
```

---

summarizeInCluster *Summarize Using Cluster Analysis*

Description

Given a matrix it summarize in classes

Usage

```
summarizeInCluster(
  data,
  features,
  name = "clu",
  dictionary = NULL,
  max_cluster_number = 3,
  cliques = NULL
)
```

Arguments

data	a data matrix
features	a vector with the features to analyze
name	prefix of the covariates
dictionary	translate features (genes) into sets (row.names of the data)
max_cluster_number	the maximum number of cluster to evaluate
cliques	the features organized in cliques. Only use for topology

Details

The user can define a maximum of classes. The function guess the optimal number of clusters using NbClust methods.

Value

a list with summary of the omic:

x	summary of the omic for each sample
usedGenes	genes list of genes used to calculate the summary
namesCov	names of the covariates
cls	the genes in clusters
method	method used for the analysis
omicName	name of the omic

---

summarizeOmicsResByMinPvalue

Summarize Omics Covaraites By Min Pvalue

Description

For internal use only. for each line extrac 'col' and get the minimum.

Usage

```
summarizeOmicsResByMinPvalue(col, mat)
```

Arguments

col	columns to extract from the line
mat	the matrix to be summarized (were to extract lines and 'col')

Value

a summarized version of the matrix.

Examples

```
# summarizeOmicsResByMinPvalue(2:3, mat=matrix(c(1,2,4,1,2,5), nrow=2))
```

summarizeToBinaryDirectionalEvents
Summarize To Binary Directional Events

Description

Given a matrix it summarize the positive and negative to 0 or 1 in two vectors

Usage

```
summarizeToBinaryDirectionalEvents(
  data,
  features,
  name = "dirBin",
  binaryClassMin = 10,
  eventThr = 2,
  cliques = NULL
)
```

Arguments

data	a data matrix
features	a vector with the features to analyze
name	prefix of the covariates
binaryClassMin	the minimum number of event to include the covariate
eventThr	the absolute value to threshold an event
cliques	the features organized in cliques. Only use for topology

Value

a list with summary of the omic:

x	summary of the omic for each sample
usedGenes	genes list of genes used to calculate the summary
namesCov	names of the covariates
method	method used for the analysis
omicName	name of the omic
evenThr	threshold fot event counting

summarizeToBinaryEvents *Summarize To Binary Events*

Description

Given a matrix it summarize to a 0 or 1

Usage

```
summarizeToBinaryEvents(
  data,
  features,
  name = "bin",
  binaryClassMin = 10,
  cliques = NULL
)
```

Arguments

data	a data matrix
features	a vector with the features to analyze
name	prefix of the covariates
binaryClassMin	the minimum number of event to include the covariate
cliques	the features organized in cliques. Only use for topology

Value

a list with summary of the omic:

x	summary of the omic for each sample
usedGenes	genes list of genes used to calculate the summary
namesCov	names of the covariates
method	method used for the analysis
omicName	name of the omic
evenThr	threshold fot event counting

`summarizeToNumberOfDirectionalEvents` *Summarize With Directed Sum*

Description

Given a matrix it summarize the positive and negative in two vectors, with counts of the events

Usage

```
summarizeToNumberOfDirectionalEvents(
  data,
  features,
  name = "dCount",
  eventThr = 2,
  min_prop = 0.1,
  cliques = NULL
)
```

Arguments

`data`	a data matrix
`features`	a vector with the features to analyze
`name`	prefix of the covariates
`eventThr`	the absolute value to threshold an event
`min_prop`	minimal proportion in classes
`cliques`	the features organized in cliques. Only use for topology

Value

a list with summary of the omic:

`x`	summary of the omic for each sample
`usedGenes`	genes list of genes used to calculate the summary
`namesCov`	names of the covariates
`method`	method used for the analysis
`omicName`	name of the omic
`evenThr`	threshold fot event counting
`min_prop`	minimum proportion of samples to exclude to check the variability of values

`summarizeToNumberOfEvents` *Summarize To Number of Binary Events*

Description

Given a matrix it summarize to a 0 or 1

Usage

```
summarizeToNumberOfEvents(
  data,
  features,
  name = "event",
  min_prop = 0.1,
  cliques = NULL
)
```

Arguments

`data`	a data matrix
`features`	a vector with the features to analyze
`name`	prefix of the covariates
`min_prop`	minimal proportion in classes
`cliques`	the features organized in cliques. Only use for topology

Value

a list with summary of the omic:

`x`	summary of the omic for each sample
`usedGenes`	genes list of genes used to calculate the summary
`namesCov`	names of the covariates
`method`	method used for the analysis
`omicName`	name of the omic
`evenThr`	threshold fot event counting
`min_prop`	minimum proportion of samples to exclude to check the variability of values

summarizeWithPca *Summarize Using PCA*

Description

Given a matrix it summarize to principal components. The user can specify the number of principal components. Default 3.

Usage

```
summarizeWithPca(
  data,
  features,
  name = "pca",
  shrink = FALSE,
  method = "regular",
  cliques = NULL,
  maxPCs = 3,
  loadThr = 0.6
)
```

Arguments

data	a data matrix
features	a vector with the features to analyze
name	prefix of the covariates
shrink	shirnk or not the covariance matrix.
method	either 'regular', 'sparse' or 'topological'
cliques	the features organized in cliques. Only use for topology.
maxPCs	maximum number of pcs to consider
loadThr	loading threshold

Value

a list with summary of the omic:

x	summary of the omic for each sample (principal components)
sdev	standard deviation of the principal components
loadings	loadings of PCA
usedGenes	genes list of genes used to calculate the summary
namesCov	names of the covariates
method	method used for the analysis
omicName	name of the omic

survivalcox *Cox Model Analysis*

Description

Cox Analysis

Usage

```
survivalcox(coxObj, formula)
```

Arguments

coxObj	data.frame: patients x covariates
formula	formula to use

Details

For internal use only

Value

A list with

pvalue	pvalue of the model
zlist	pvalues of single covariates
coxObj	the original coxObj passed to the function

survivalcoxr *Cox Robust Model Analysis*

Description

Cox Robust Analysis

Usage

```
survivalcoxr(coxObj, formula)

coxrsummary(x)
```

Arguments

coxObj	data.frame: patients x covariates
formula	formula to use
x	a coxr.obj

Details

For internal use only

Value

A list with

pvalue	pvalue of the model
zlist	pvalues of single covariates
coxObj	the original coxObj passed to the function

a list with wald test and robust and partial coefficients

---

topoCompPCs *Topological PCA*

Description

Topological PCA

Usage

```
topoCompPCs(exp, shrink, cliques, k)
```

Arguments

exp	a matrix
shrink	logical, whether to shrink or not.
cliques	the pathway topology summarized in a list of cliques
k	the number of components to use

Value

a list with the following elements:

x	the computed PCs
sdev	the standard deviation captured by the PCs
loadings	the loadings

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