# Package 'MineICA'

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Type Package

Title Analysis of an ICA decomposition obtained on genomics data

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Description The goal of MineICA is to perform Independent Component Analysis (ICA) on multiple transcriptome datasets, integrating additional data (e.g molecular, clinical and pathological).

This Integrative ICA helps the biological interpretation of the components by studying their association with variables (e.g sample annotations) and gene sets, and enables the comparison of components from different datasets using correlation-based graph.

License GPL-2

LazyLoad yes

**Depends** R (>= 2.10), methods, BiocGenerics (>= 0.13.8), Biobase, plyr, ggplot2, scales, foreach, xtable, biomaRt, gtools, GOstats, cluster, marray, mclust, RColorBrewer, colorspace, igraph, Rgraphviz, graph, annotate, Hmisc, fastICA, JADE

Imports AnnotationDbi, lumi, fpc, lumiHumanAll.db

**Suggests** biomaRt, GOstats, cluster, hgu133a.db, mclust, igraph, breastCancerMAINZ, breastCancerTRANSBIG, breastCancerUPP, breastCancerVDX

Enhances doMC

Collate 'AllClasses.R' 'AllGeneric.R' 'methods-IcaSet.R' 'methods-MineICAParams.R' 'compareAnalysis.R' 'functions\_comp2annot.R' 'functions\_comp2annottests.R' 'functions\_enrich.R' 'functions.R' 'heatmap.plus.R' 'heatmapsOnSel.R' 'runAn.R' 'compareGenes.R'

biocViews Visualization, MultipleComparison

NeedsCompilation no

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Α

Retrieve and set Source S and Mixing matrix A from IcaSet

# Description

These generic functions access and set the attributes S, SByGene and A stored in an object of class IcaSet.

# Usage

```
S(object)
S(object) <- value
SByGene(object)
SByGene(object) <- value
A(object)
A(object) <- value
nbComp(object)</pre>
```

# **Arguments**

object of class IcaSet

value Data.frame with rows representing: features (for S), genes (for SByGene), or

samples (for A) and columns representing components.

# Value

S returns a data.frame containing feature projection values; SByGene returns a data.frame containing gene projection values; A returns a data.frame containing sample contribution values. nbComp returns the number of components, i.e the number of columns of A.

# Author(s)

Anne Biton

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Alist

Retrieve sample contributions stored in an IcaSet object as a list.

### **Description**

This generic function retrieves, from an IcaSet object, the sample contributions contained in the attribute A as a list where sample IDs are preserved.

# Usage

```
Alist(object)
```

# **Arguments**

object

Object of class IcaSet.

# Value

Alist returns a list whose length equals the number of components contained in the IcaSet object. Each element of this list contains a vector of sample contributions indexed by the sample IDs.

### Author(s)

Anne Biton

### See Also

IcaSet-class

annot2Color

Association of a colour with each annotation level

# **Description**

Given a data.frame consisting of sample annotations, this function returns a vector which gives a colour per annotation level.

### Usage

```
annot2Color(annot)
```

### **Arguments**

annot

a data.frame containing the sample annotations (of dimension 'samples x annotations').

# **Details**

Arbitrary colours are attributed to some specific annotations met by the author, and for the remaining annotation levels, the colours are attributed using packages RColorBrewer and rcolorspace.

annotCarbayo 5

### Value

A vector of colours indexed by the annotation levels.

### Author(s)

Anne Biton

annotCarbayo

Carbayo annotation data

### **Description**

Contains annotations for 93 samples of Carbayo data.

### Author(s)

Anne Biton

#### References

http://jco.ascopubs.org/content/24/5/778/suppl/DC1

annotFeatures

Annotation of features using an annotation package

### **Description**

This function annotates a set of features

# Usage

```
annotFeatures(features, type, annotation)
```

# **Arguments**

features Feature IDs to be annotated

type The object from the package used to annotate the features, must be available in

ls("package:package\_name")

annotation An annotation package

# Value

A vector of gene/object IDs indexed by the feature IDs.

# Author(s)

Anne Biton

```
library (hgu133a.db) \\ annotFeatures (features = c("1007\_s\_at", "1053\_at", "117\_at", "121\_at", "1255\_g\_at"), \\ type="SYMBOL", annotation="hgu133a.db")
```

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sComp Features annotation
---------------------------

### **Description**

##' This function annotates the features of an object of class IcaSet, and fills its attributes SByGene and datByGene.

### Usage

```
annotFeaturesComp(icaSet, params,
  type = toupper(typeID(icaSet)["geneID_annotation"]),
  featureId = typeID(icaSet)["featureID_biomart"],
  geneId = typeID(icaSet)["geneID_biomart"])
```

### **Arguments**

icaSet	An object of class IcaSet whose features have to be annotated. The attribute annotation of this object contains the annotation package to be used.
params	An object of class MineICAParams containing the parameters of the analysis.
type	The ID of the object of the annotation package to be used for the annotation, must be available in ls("package:package_name")
featureId	The type of the feature IDs, in the biomaRt way (type listFilters(mart) to choose one). Used when annotation(icaSet) is of length 0.
geneId	The type of the gene IDs, in the biomaRt way (type listAttributes(mart) to choose one). Used when annotation(icaSet) is of length 0.

#### **Details**

This function is called by function annotInGene which will check the validity of the attributes annotation, typeID, chipManu and eventually chipVersion of icaSet. If available, the attribute annotation of argument icaSet must be an annotation package and will be used to annotate the featureNames of icaSet. If attribute annotation of argument icaSet is not available (of length 0), biomaRt is used to annotate the features.

This function fills the attributes SByGene and datByGene of the argument icaSet. When several feature IDs are available for a same gene ID, the median value of the corresponding features IDs is attributed to the gene (the median of projection values is used for attribute SByGene, and the median of expression values is used for attribute datByGene).

When attribute chipManu of the argument icaSet is "illumina", the features are first converted into nuID using the package 'lumi\*Mapping' and then annotated into genes. In that case, features can only be annotated in ENTREZID or SYMBOL. It means that typeID(icaSet)['geneID\_annotation'] must be either 'ENTREZID' or 'SYMBOL'. You will need to annotate yourself the IcaSet object if you want to use different IDs.

# Value

This function returns the argument icaSet with attributes SByGene and datByGene filled.

#### Author(s)

Anne Biton

#### See Also

annotFeatures, annotFeaturesWithBiomaRt, annotInGene

# **Examples**

```
## load an example of IcaSet
 data(icaSetCarbayo)
 params <- buildMineICAParams()</pre>
 require(hgu133a.db)
 ## Use of annotation package contained in annotation(icaSet)
 ## annotation in SYMBOL
 icaSetCarbayo_annot <- annotFeaturesComp(icaSet=icaSetCarbayo, params=params, type="SYMBOL")</pre>
 # arg 'type' is optional since the function uses contents of typeID(icaSet) as the defaults,
 # it is specified in these examples for pedagogy views
 ## annotation in Entrez Gene
 icaSetCarbayo_annot <- annotFeaturesComp(icaSet=icaSetCarbayo, params=params, type="ENTREZID")</pre>
 ## Not run:
 ## Use of biomaRt, when annotation(icaSet) is of length 0
 ## empty attribute 'annotation' of the IcaSet object
 # when this attribute is not specified, biomaRt is used for annotation
 annotation(icaSetCarbayo) <- character()</pre>
 # make sure the mart attribute is correctly defined
 mart(icaSetCarbayo) <- useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl")</pre>
 ## make sure elements "featureID_biomaRt" and "geneID_biomaRt" of typeID(icaSet) are correctly filled
 # they will be used by function 'annotFeaturesComp' through biomaRt to query the database
 typeID(icaSetCarbayo)
 ## run annotation of HG-U133A probe set IDs into Gene Symbols using biomaRt
 icaSetCarbayo_annot <- annotFeaturesComp(icaSet=icaSetCarbayo, params=params)</pre>
 ## End(Not run)
annotFeaturesWithBiomaRt
```

Annotation of features using biomaRt

# **Description**

This function annotates a set of features using biomaRt

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#### Usage

```
annotFeaturesWithBiomaRt(features, featureId, geneId,
  mart = useMart(biomart = "ensembl", dataset = "hsapiens_gene_ensembl"))
```

### **Arguments**

features Feature IDs to be annotated

featureId The type of the feature IDs, in the biomaRt way (type listFilters(mart) to

choose one)

geneId The type of the gene IDs, in the biomaRt way (type listAttributes(mart) to

choose one)

mart The mart object (database and dataset) used for annotation, see function useMart

of package biomaRt

### Value

A vector of gene IDs indexed by the feature IDs.

#### Author(s)

Anne Biton

# **Examples**

annotInGene

Features annotation of an object of class IcaSet.

# **Description**

This function annotates the features of an IcaSet object and fills its attributes SByGene and datByGene.

# Usage

```
annotInGene(icaSet, params, annot = TRUE)
```

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#### **Arguments**

icaSet An object of class IcaSet to be annotated, must contain a valid annotation

attribute.

params An object of class MineICAParams containing the parameters of the analysis.

annot TRUE (default) if the IcaSet object must indeed be annotated

#### **Details**

When attribute annotation of icaSet is not specified (of length 0), biomaRt is used to annotate the features through function annotFeaturesWithBiomaRt.

When specified, attribute annotation of argument icaSet must be an annotation package and will be used to annotate the featureNames of icaSet. In addition, the attribute typeID (a vector) of argument icaSet must contain a valid element geneID\_annotation that determines the object of the package to be used for the annotation, see IcaSet.

When argument annot is TRUE, this function fills the attributes SByGene and datByGene of icaSet. When several feature IDs are available for a same gene ID, the median value of the corresponding features IDs is attributed to the gene (the median of the projection values is used for attribute SByGene, and the median of the expression values is used for attribute datByGene).

When attribute chipManu of the argument icaSet is "illumina", the features are first converted into nuID using the package 'lumi\*Mapping' and then annotated into genes. In that case, features can only be annotated in ENTREZID or SYMBOL. It means that typeID(icaSet)['geneID\_annotation'] must be either 'ENTREZID' or 'SYMBOL'. You will need to annotate yourself the IcaSet object if you want to use different IDs.

#### Value

The modified argument icaSet, with filled attributes SByGene and datByGene.

resJade <- runICA(X=exprs(mainz), nbComp=5, method = "JADE", maxit=10000)</pre>

#### Author(s)

Anne Biton

data(mainz)
#run ICA

### See Also

annotFeaturesComp

```
#load data
data(icaSetCarbayo)
require(hgu133a.db)

# run annotation of the features into gene Symbols as specified in 'typeID(icaSetCarbayo)["geneID_annotation"
# using package hgu133a.db as defined in 'annotation(icaSetMainz)'
icaSetCarbayo <- annotInGene(icaSet=icaSetCarbayo, params=buildMineICAParams())

## Not run:
#load data
library(breastCancerMAINZ)</pre>
```

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```
#build params
params <- buildMineICAParams(resPath="mainz/")</pre>
#build a new IcaSet object, omitting annotation of the features (runAnnot=FALSE)
#but specifying the element "geneID_annotation" of argument 'typeID'
icaSetMainz <- buildIcaSet(params=params, A=data.frame(resJade$A), S=data.frame(resJade$S),</pre>
                              dat=exprs(mainz), pData=pData(mainz),
                         annotation="hgu133a.db", typeID= c(geneID_annotation = "SYMBOL",
                        geneID_biomart = "hgnc_symbol", featureID_biomart = "affy_hg_u133a"),
                              chipManu = "affymetrix", runAnnot=FALSE,
                        mart=useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl"))
#Attributes SByGene is empty and attribute datByGene refers to assayData
SByGene(icaSetMainz)
head(datByGene(icaSetMainz))
# run annotation of the features into gene Symbols as specified in 'typeID(icaSetMainz)["geneID_annotation"]'
# using package hgu133a.db as defined in 'annotation(icaSetMainz)'
icaSetMainz <- annotInGene(icaSet=icaSetMainz, params=params)</pre>
## End(Not run)
```

# Description

annotReciprocal

This function notes edges of a graph as reciprocal or not.

annotReciprocal

#### Usage

```
annotReciprocal(dataGraph, file,
  keepOnlyReciprocal = FALSE)
```

### **Arguments**

data.frame which contains the graph description, must have two columns n1 and

n2 filled with node IDs, each row denoting there is an edge from n1 to n2.

file file where the graph description is written

keepOnlyReciprocal

if TRUE dataGraph is restricted to reciprocal edges, else all edges are kept (default).

### Value

This function returns the argument dataGraph with an additional column named 'reciprocal' which contains TRUE if the edge described by the row is reciprocal, and FALSE if it is not reciprocal.

### Author(s)

Anne Biton

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### **Examples**

```
 dg \leftarrow data.frame(n1=c("A","B","B","C","C","D","E","F"),n2=c("B","G","A","B","D","C","F","E")) \\ annotReciprocal(dataGraph=dg)
```

buildIcaSet

This function builds an object of class IcaSet.

# **Description**

This function builds an object of class IcaSet.

# Usage

```
buildIcaSet(params, A, S, dat, pData = new("data.frame"),
  fData = new("data.frame"), witGenes = new("character"),
  compNames = new("character"),
  refSamples = new("character"),
  annotation = new("character"),
  chipManu = new("character"),
  chipVersion = new("character"), alreadyAnnot = FALSE,
  typeID = c(geneID_annotation = "SYMBOL", geneID_biomart = "hgnc_symbol", featureID_biomart = "runAnnot = TRUE, organism = "Human",
  mart = new("Mart"))
```

# **Arguments**

params	An object of class MineICAParams containing the parameters of the analysis
A	The mixing matrix of the ICA decomposition (of dimension samples x components).
S	The source matrix of the ICA decomposition (of dimension features x components).
dat	The data matrix the ICA was applied to (of dimension features x samples).
pData	Phenotype data, a data.frame which contains the sample informations of dimension samples x annotations.
fData	Feature data, a data frame which contrains the feature descriptions of dimensions features x annotations.
witGenes	A vector of witness genes. They are representative of the expression behavior of the contributing genes of each component. If missing or NULL, they will be automatically attributed using function selectWitnessGenes.
compNames	A vector of component labels.
refSamples	A vector of reference sample IDs (e.g the "normal" samples).
annotation	An annotation package (e.g a ".db" package specific to the microarray used to generate dat)
chipManu	If microarray data, the manufacturer: either 'affymetrix' or 'illumina'.
chipVersion	For illumina microarrays: the version of the microarray.
alreadyAnnot	TRUE if the feature IDs contained in the row names of dat and S already correspond to the final level of annotation (e.g if they are already gene IDs). In that case, no annotation is performed.

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typeID

A character vector specifying the annotation IDs, it includes three elements:

geneID\_annotation the IDs from the package to be used to annotate the features into genes. It will be used to fill the attributes datByGene and SByGene of the icaSet. It must match one of the objects the corresponding package supports (you can access the list of objects by typing ls("package:packagename")). If no annotation package is provided, this element is not useful.

geneID\_biomart the type of gene IDs, as available in listFilters(mart);
 where mart is specified as described in useMart. If you have directly
 built the IcaSet at the gene level (i.e if no annotation package is used),
 featureID\_biomart and geneID\_biomart will be identical.

**featureID\_biomart** the type of feature IDs, as available in listFilters(mart); where mart is specified as described in function useMart. Not useful if you work at the gene level.

runAnnot If TRUE, icaSet is annotated with function annotInGene.

organism The organism the data correspond to.

mart The mart object (database and dataset) used for annotation, see function useMart

of package biomaRt

#### Value

An object of class IcaSet

# Author(s)

Anne Biton

### See Also

selectWitnessGenes, annotInGene

```
dat <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat) <- paste("g", 1:1000, sep="")</pre>
colnames(dat) <- paste("s", 1:10, sep="")</pre>
## build a data.frame containing sample annotations
annot <- data.frame(type=c(rep("a",5),rep("b",5)))</pre>
rownames(annot) <- colnames(dat)</pre>
resJade <- runICA(X=dat, nbComp=3, method = "JADE")</pre>
## build params
params <- buildMineICAParams(resPath="toy/")</pre>
## build IcaSet object
icaSettoy <- buildIcaSet(params=params, A=data.frame(resJade$A), S=data.frame(resJade$S),</pre>
                           dat=dat, pData=annot, alreadyAnnot=TRUE)
params <- icaSettoy$params</pre>
icaSettoy <- icaSettoy$icaSet</pre>
## Not run:
## load data
```

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```
library(breastCancerMAINZ)
 data(mainz)
 ## run ICA
 resJade <- runICA(X=dataMainz, nbComp=10, method = "JADE", maxit=10000)
 ## build params
 params <- buildMineICAParams(resPath="mainz/")</pre>
 ## build IcaSet object
 # fill typeID, Mainz data originate from affymetrix HG-U133a microarray and are indexed by probe sets
 # we want to annotate the probe sets into Gene Symbols
 typeIDmainz <- c(geneID_annotation="SYMBOL", geneID_biomart="hgnc_symbol", featureID_biomart="affy_hg_u133
 icaSetMainz <- buildIcaSet(params=params, A=data.frame(resJade$A), S=data.frame(resJade$S),</pre>
                                 dat=exprs(mainz), pData=pData(mainz),
                            annotation="hgu133a.db", typeID= c(geneID_annotation = "SYMBOL",
                           geneID_biomart = "hgnc_symbol", featureID_biomart = "affy_hg_u133a"),
                          chipManu = "affymetrix", runAnnot=TRUE,
mart=useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl"))
 ## End(Not run)
buildMineICAParams
                           Creates an object of class MineICAParams
```

# Description

This function builds an object of class MineICAParams. It contains the parameters that will be used by function runAn to analyze the ICA decomposition contained in an object of class IcaSet.

# Usage

```
buildMineICAParams(Sfile = new("character"),
   Afile = new("character"), datfile = new("character"),
   annotfile = new("character"), resPath = "", genesPath,
   annot2col = new("character"), pvalCutoff = 0.05,
   selCutoff = 3)
```

#### **Arguments**

Sfile	A txt file containing the Source matrix S.
Afile	A txt file containing the Mixing matrix A.
datfile	A txt file containing the data (e.g expression data) on which the decomposition was calculated.
annotfile	Either a "rda" or "txt" file containing the annotation data for the samples (must be of dimensions samples x annotations).
resPath	The path where the outputs of the analysis will be written, default is the current directory.
genesPath	The path _within_ the resPath where the gene projections will be written. If missing, will be automatically attributed as resPath/ProjByComp/.

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annot2col A vector of colors indexed by annotation levels. If missing, will be automatically

attributed using function annot2Color.

pvalCutoff The cutoff used to consider a p-value significant, default is 0.05.

selCutoff The cutoff applied to the absolute feature/gene projection values to consider

them as contributors, default is 3. Must be either of length 1 and the same treshold is applied to all components, or of length equal to the number of components

in order to a specific threshold is for each component.

# Value

An object of class MineICAParams

### Author(s)

Anne Biton

#### See Also

MineICAParams, runAn

### **Examples**

```
## define default parameters and fill resPath
params <- buildMineICAParams(resPath="resMineICACarbayo/")

## change the default cutoff for selection of contribugint genes/features
params <- buildMineICAParams(resPath="resMineICACarbayo/", selCutoff=4)</pre>
```

clusterFastICARuns

Run of fastICA and JADE algorithms

# Description

This function runs the fastICA algorithm several times with random initializations. The obtained components are clustered and the medoids of these clusters are used as the final estimates. The returned estimates are ordered by decreasing Iq values which measure the compactness of the clusters (see details).

# Usage

```
clusterFastICARuns(X, nbComp, nbIt = 100,
   alg.type = c("deflation", "parallel"),
   fun = c("logcosh", "exp"), maxit = 500, tol = 10^-6,
   funClus = c("hclust", "agnes", "pam", "kmeans"),
   row.norm = FALSE, bootstrap = FALSE, ...)
```

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#### **Arguments**

X	A data matrix with n rows representing observations (e.g genes) and p columns representing variables (e.g samples).
nbComp	The number of components to be extracted.
nbIt	The number of iterations of FastICA
alg.type	If alg. type="parallel" the components are extracted simultaneously (the default), if alg. type="deflation" the components are extracted one at a time, see fastICA.
fun	The functional form of the G function used in the approximation to neg-entropy (see 'details' of the help of function fastICA).
row.norm	a logical value indicating whether rows of the data matrix $X$ should be standardized beforehand (see help of function fastICA)
maxit	The maximum number of iterations to perform.
tol	A positive scalar giving the tolerance at which the un-mixing matrix is considered to have converged.
funClus	The clustering function to be used to cluster the estimates
bootstrap	if TRUE the data is bootstraped before each fastICA iteration, else (default) only random initializations are done
	Additional parameters for codefunClus

### **Details**

This function implements in R fastICA iterations followed by a clustering step, as defined in the matlab package 'icasso'. Among the indices computed by icasso, only the Iq index is currently computed. As defined in 'icasso', the Iq index measures the difference between the intra-cluster similarity and the extra-cluster similarity. No visualization of the clusters is yet available.

If bootstrap=TRUE a bootstrap (applied to the observations) is used to perturb the data before each iteration, then function fastICA is applied with random initializations.

By default, in 'icasso', agglomerative hierarchical clustering with average linkage is performed. To use the same clustering, please use funClus="hclust" and method="average". But this function also allows you to apply the clustering of your choice among kmeans, pam, hclust, agnes by specifying funClus and adding the adequat additional parameters.

See details of the functions fastICA.

# Value

A list consisting of:

A the estimated mixing matrix

**S** the estimated source matrix, itemWthe estimated unmixing matrix,

Iq Iq indices.

# Author(s)

Anne Biton

#### **Examples**

clusterSamplesByComp Cluster samples from an IcaSet

An IcaSet object

# **Description**

This function allows to cluster samples according to the results of an ICA decomposition. One clustering is run independently for each component.

# Usage

```
clusterSamplesByComp(icaSet, params,
  funClus = c("Mclust", "kmeans", "pam", "pamk", "hclust", "agnes"),
  filename, clusterOn = c("A", "S"),
  level = c("genes", "features"), nbClus,
  metric = "euclidean", method = "ward", ...)
```

if funClus is one of c("Mclust", "pamk"))

### **Arguments**

icaSet

nbClus

params	A MineICAParams object
funClus	The function to be used for clustering, must be one of c("Mclust", "kmeans", "pam", "pamk", "hclu
filename	A file name to write the results of the clustering in
clusterOn	Specifies the matrix used to apply clustering:
	"A": the clustering is performed in one dimension, on the vector of sample contributions,
	"S": the clustering is performed on the original data restricted to the contributing individuals.
level	The level of projections to be used when clusterOn="S", either "features" or "genes".

The number of clusters to be computed, either a single number or a numeric vector whose length equals the number of components. If missing (only allowed

metric	Metric used in pam and hclust, default is "euclidean"
method	Method of hierarchical clustering, used in hclust and agnes
•••	Additional parameters required by the clustering function funClus.res <- clusterSamplesByComp(icaSet=icaSetCarbayo, params=params, funClus="kmeans",

#### Value

A list consisting of three elements

clus: a list specifying the sample clustering for each component,

**resClus:** the complete output of the clustering function, **funClus:** the function used to perform the clustering.

. When clusterOn="S", if some components were not used because no contributing elements is selected using the cutoff, the icaSet with the corresponding component deleted is also returned.

### Author(s)

Anne Biton

### See Also

Mclust, kmeans, pam, pamk, hclust, agnes, cutree

# **Examples**

clusterSamplesByComp\_multiple

Cluster samples from an IcaSet

### **Description**

This function allows to cluster samples according to the results of an ICA decomposition. Several clustering functions and several levels of data for clustering can be performed by the function.

# Usage

```
clusterSamplesByComp_multiple(icaSet, params,
  funClus = c("Mclust", "kmeans", "pam", "pamk", "hclust", "agnes"),
  filename, clusterOn = c("A", "S"),
  level = c("genes", "features"), nbClus,
  metric = "euclidean", method = "ward", ...)
```

### **Arguments**

icaSet An IcaSet object A MineICAParams object params funClus The function to be used for clustering, must be several of c("Mclust", "kmeans", "pam", "pamk", "he filename A file name to write the results of the clustering in clusterOn Specifies the matrix used to apply clustering, can be several of: "A": the clustering is performed in one dimension, on the vector of sample contributions, "S": the clustering is performed on the original data restricted to the contributing individuals. leve1 The level of projections to be used when clusterOn="S", either "features" or "genes". nbClus The number of clusters to be computed, either a single number or a numeric vector whose length equals the number of components. If missing (only allowed if funClus is one of c("Mclust", "pamk")) Metric used in pam and hclust, default is "euclidean" metric Method of hierarchical clustering, used in hclust and agnes method Additional parameters required by the clustering function funClus. . . .

#### **Details**

One clustering is run independently for each component.

#### Value

A list consisting of three elements

**clus:** a data.frame specifying the sample clustering for each component using the different ways of clustering,

**resClus:** the complete output of the clustering function(s),

**comparClus:** the adjusted Rand indices, used to compare the clusterings obtained for a same component.

#### Author(s)

Anne

# See Also

Mclust, adjustedRandIndex, kmeans, pam, pamk, hclust, agnes, cutree

clus Var Analysis 19

clusVarAnalysis	Tests association between clusters of samples and variables	
clusVarAnalysis	Tests association between clusters of samples and variables	

# Description

From a clustering of samples performed according to their contribution to each component, this function computes the chi-squared test of association between each variable level and the cluster, and summarizes the results in an HTML file.

# Usage

```
clusVarAnalysis(icaSet, params, resClus, keepVar,
  keepComp, funClus = "",
  adjustBy = c("none", "component", "variable"),
  method = "BH", doPlot = FALSE,
  cutoff = params["pvalCutoff"],
  path = paste(resPath(params), "clus2var/", sep = ""),
  onlySign = TRUE, typeImage = "png",
  testBy = c("variable", "level"), filename)
```

# **Arguments**

icaSet	An object of class IcaSet
params	An object of class MineICAParams providing the parameters of the analysis
resClus	A list of numeric vectors indexed by sample IDs, which specifies the sample clusters. There must be one clustering by component of icaSet. The names of the list must correspond to the component indices.
keepVar	The variable labels to be considered, i.e a subset of the variables of icaSet available in varLabels(icaSet).
keepComp	A subset of components available in indComp(icaSet) to be considered, if missing all components are used.
funClus	The name of the function used to perform the clustering (just for text in written files).
adjustBy	The way the p-values of the Wilcoxon and Kruskal-Wallis tests should be corrected for multiple testing: "none" if no p-value correction has to be done, "component" if the p-values have to be corrected by component, "variable" if the p-values have to be corrected by variable.
testBy	Chi-square tests of association can be performed either by "variable" (one test by variable, default) or by variable "level" (as many tests as there are annotation levels).
method	The correction method, see p.adjust for details, default if "BH" for Benjamini & Hochberg.
doPlot	If TRUE, the barplots showing the distribution of the annotation levels among the clusters are plotted and the results are provided in an HTML file 'cluster2annot.htm', else no plot is created.
cutoff	The threshold for statistical significance.
filename	File name for test results, if doPlot=TRUE will be an HTML file else will be a 'txt' file. If missing when doPlot=TRUE, will be "clusVar".

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path A directory \_within resPath(params)\_ where the outputs are saved if doPlot=TRUE,

default is 'cluster2annot/'.

onlySign If TRUE (default), only the significant results are plotted.

typeImage The type of image file where each plot is saved.

#### **Details**

When doPlot=TRUE, this function writes an HTML file containing the results of the tests as a table of dimension 'variable levels x components' which contains the p-values of the tests. When a p-value is considered as significant according to the threshold cutoff, it is written in bold and filled with a link pointing to the corresponding barplot displaying the distribution of the clusters across the levels of the variables.

One image is created by plot and located into the sub-directory "plots/" of path. Each image is named by index-of-component\_var.png

#### Value

This function returns a list whose each element gives, for each component, the results of the association chi-squared tests between the clusters and the annotation levels.

### Author(s)

Anne Biton

#### See Also

clusterSamplesByComp

# Examples

```
## load an example of IcaSet
data(icaSetCarbayo)
## build object of class MineICAParams
params <- buildMineICAParams(resPath="carbayo/")</pre>
## cluster samples according to the columns of the mixing matrix A with kmeans in 2 groups
resClus <- clusterSamplesByComp(icaSet=icaSetCarbayo, params=params, funClus="kmeans",
                               clusterOn="A", nbClus=2)$clus
## specify directory for the function outputs (here same directory as the default one)
## this directory will be created by the function in resPath(params)
dir <- "clus2var/"
## compute chi-square tests of association, p-value are not adjusted (adjustBy="none"),
# test results are written in txt format (doPlot=FALSE and filename not missing)
resChi <- clusVarAnalysis(icaSet=icaSetCarbayo, params=params, resClus=resClus, funClus="kmeans",
                       adjustBy="none", doPlot=FALSE, path=dir, filename="clusVarTests")
## Not run:
## compute chi-square tests of association, p-value are not adjusted (adjustBy="none"),
# write results and plots in HTML files (doPlot=TRUE)
resChi <- clusVarAnalysis(icaSet=icaSetCarbayo, params=params, resClus=resClus, funClus="kmeans",
                        path=dir, adjustBy="none", doPlot=TRUE, filename="clusVarTests")
```

## compute chi-square tests of association by only considering a subset of components and variables,

compareAn 21

compareAn

Comparison of IcaSet objects using correlation

### **Description**

Compare IcaSet objects by computing the correlation between either projection values of common features or genes, or contributions of common samples.

### Usage

```
compareAn(icaSets, labAn,
  type.corr = c("pearson", "spearman"), cutoff_zval = 0,
  level = c("samples", "features", "genes"))
```

### **Arguments**

icaSets list of IcaSet objects, e.g results of ICA decompositions obtained on several

datasets.

labAn vector of names for each icaSet, e.g the the names of the datasets on which were

calculated the decompositions.

type.corr Type of correlation to compute, either 'pearson' or 'spearman'.

cutoff\_zval either NULL or 0 (default) if all genes are used to compute the correlation be-

tween the components, or a threshold to compute the correlation on the genes that have at least a scaled projection higher than cutoff\_zval. Will be used only

when correlations are calculated on S or SByGene.

level Data level of the IcaSet objects on which is applied the correlation. It must

correspond to a feature shared by the IcaSet objects: 'samples' if they were applied to common samples (correlations are computed between matrix A), 'features' if they were applied to common features (correlations are computed between matrix S), 'genes' if they share gene IDs after annotation into genes (correlations).

tions are computed between matrix SByGene).

### **Details**

The user must carefully choose the object on which the correlation will be computed. If level='samples', the correlations are based on the mixing matrices of the ICA decompositions (of dimension samples x components). 'A' will be typically chosen when the ICA decompositions were computed on the same dataset, or on datasets that include the same samples. If level='features' is chosen, the correlation is calculated between the source matrices (of dimension features x components) of the ICA decompositions. 'S' will be typically used when the ICA decompositions share common features (e.g same microarrays). If level='genes', the correlations are calculated on the attributes

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'SByGene' which store the projections of the annotated features. 'SByGene' will be typically chosen when ICA were computed on datasets from different technologies, for which comparison is possible only after annotation into a common ID, like genes.

cutoff\_zval is only used when level is one of c('genes', 'features'), in order to restrict the correlation to the contributing features or genes.

When cutoff\_zval is specified, for each pair of components, genes or features that are included in the circle of center 0 and radius cutoff\_zval are excluded from the computation of the correlation.

It must be taken into account by the user that if cutoff\_zval is different from NULL or 0, the computation will be much slowler since each pair of component is treated individually.

#### Value

A list whose length equals the number of pairs of IcaSet and whose elements are outputs of function cor2An.

### Author(s)

Anne Biton

### See Also

cor2An

```
dat1 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat1) <- paste("g", 1:1000, sep="")</pre>
colnames(dat1) <- paste("s", 1:10, sep="")</pre>
dat2 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat2) <- paste("g", 1:1000, sep="")</pre>
colnames(dat2) <- paste("s", 1:10, sep="")</pre>
## run ICA
resJade1 <- runICA(X=dat1, nbComp=3, method = "JADE")</pre>
resJade2 <- runICA(X=dat2, nbComp=3, method = "JADE")</pre>
## build params
params <- buildMineICAParams(resPath="toy/")</pre>
## build IcaSet object
icaSettoy1 <- buildIcaSet(params=params, A=data.frame(resJade1$A), S=data.frame(resJade1$S),</pre>
                            dat=dat1, alreadyAnnot=TRUE)$icaSet
icaSettoy2 <- buildIcaSet(params=params, A=data.frame(resJade2$A), S=data.frame(resJade2$S),</pre>
                            dat=dat2, alreadyAnnot=TRUE)$icaSet
listPairCor <- compareAn(icaSets=list(icaSettoy1,icaSettoy2), labAn=c("toy1","toy2"),</pre>
                           type.corr="pearson", level="genes", cutoff_zval=0)
## Not run:
#### Comparison of 2 ICA decompositions obtained on 2 different gene expression datasets.
## load the two datasets
library(breastCancerMAINZ)
library(breastCancerVDX)
data(mainz)
```

compareAn2graphfile 23

```
data(vdx)
## Define a function used to build two examples of IcaSet objects
treat <- function(es, annot="hgu133a.db") {</pre>
   es <- selectFeatures_IQR(es,10000)
   exprs(es) <- t(apply(exprs(es),1,scale,scale=FALSE))</pre>
   colnames(exprs(es)) <- sampleNames(es)</pre>
   resJade <- runICA(X=exprs(es), nbComp=10, method = "JADE", maxit=10000)</pre>
  resBuild <- buildIcaSet(params=buildMineICAParams(), A=data.frame(resJade$A), S=data.frame(resJade$S),</pre>
                         dat=exprs(es), pData=pData(es), refSamples=character(0),
                         annotation=annot, typeID= typeIDmainz,
                         chipManu = "affymetrix", mart=mart)
   icaSet <- resBuild$icaSet</pre>
## Build the two IcaSet objects
icaSetMainz <- treat(mainz)</pre>
icaSetVdx <- treat(vdx)</pre>
## The pearson correlation is used as a measure of association between the gene projections
# on the different components (type.corr="pearson").
listPairCor <- compareAn(icaSets=list(icaSetMainz,icaSetVdx),</pre>
labAn=c("Mainz","Vdx"), type.corr="pearson", level="genes", cutoff_zval=0)
## Same thing but adding a selection of genes on which the correlation between two components is computed:
# when considering pairs of components, only projections whose scaled values are not located within
# the circle of radius 1 are used to compute the correlation (cutoff_zval=1).
listPairCor <- compareAn(icaSets=list(icaSetMainz,icaSetVdx),</pre>
labAn=c("Mainz","Vdx"), type.corr="pearson", cutoff_zval=1, level="genes")
## End(Not run)
```

# Description

compareAn2graphfile

This function builds a correlation graph from the outputs of function compareAn.

### Usage

```
compareAn2graphfile(listPairCor, useMax = TRUE,
  cutoff = NULL, useVal = c("cor", "pval"), file = NULL)
```

compareAn2graphfile

### **Arguments**

listPairCor	The output of the function compareAn, containing the correlation between several pairs of objects of class IcaSet.
useMax	If TRUE, the graph is restricted to edges that correspond to maximum score, see details
cutoff	Cutoff used to select pairs that will be included in the graph.
useVal	The value on which is based the graph, either "cor" for correlation or "pval" for p-values of correlation tests.
file	File name.

#### **Details**

When correlations are considered (useVal="cor"), absolute values are used since the components have no direction.

If useMax is TRUE each component is linked to the most correlated component of each different IcaSet.

If cutoff is specified, only correlations exceeding this value are taken into account during the graph construction. For example, if cutoff is 1, only relationships between components that correspond to a correlation value larger than 1 will be included.

When useVal="pval" and useMax=TRUE, the minimum value is taken instead of the maximum.

#### Value

A data frame with the graph description, has two columns n1 and n2 filled with node IDs, each row denotes that there is an edge from n1 to n2. Additional columns quantify the strength of association: correlation (cor), p-value (pval), (1-abs(cor)) (distcor), log10-pvalue (logpval).

#### Author(s)

Anne Biton

#### See Also

compareAn, cor2An

```
dat1 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat1) <- paste("g", 1:1000, sep="")
colnames(dat1) <- paste("s", 1:10, sep="")</pre>
dat2 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat2) <- paste("g", 1:1000, sep="")</pre>
colnames(dat2) <- paste("s", 1:10, sep="")</pre>
## run ICA
resJade1 <- runICA(X=dat1, nbComp=3, method = "JADE")</pre>
resJade2 <- runICA(X=dat2, nbComp=3, method = "JADE")</pre>
## build params
params <- buildMineICAParams(resPath="toy/")</pre>
## build IcaSet object
icaSettoy1 <- buildIcaSet(params=params, A=data.frame(resJade1$A), S=data.frame(resJade1$S),</pre>
                            dat=dat1, alreadyAnnot=TRUE)$icaSet
icaSettoy2 <- buildIcaSet(params=params, A=data.frame(resJade2$A), S=data.frame(resJade2$S),</pre>
                            dat=dat2, alreadyAnnot=TRUE)$icaSet
resCompareAn <- compareAn(icaSets=list(icaSettoy1,icaSettoy2), labAn=c("toy1","toy2"),</pre>
                           type.corr="pearson", level="genes", cutoff_zval=0)
## Build a graph where edges correspond to maximal correlation value (useVal="cor"),
compareAn2graphfile(listPairCor=resCompareAn, useMax=TRUE, useVal="cor", file="myGraph.txt")
## Not run:
```

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```
#### Comparison of 2 ICA decompositions obtained on 2 different gene expression datasets.
## load the two datasets
library(breastCancerMAINZ)
library(breastCancerVDX)
data(mainz)
data(vdx)
## Define a function used to build two examples of IcaSet objects
treat <- function(es, annot="hgu133a.db") {</pre>
   es <- selectFeatures_IOR(es,10000)
   exprs(es) <- t(apply(exprs(es),1,scale,scale=FALSE))</pre>
   colnames(exprs(es)) <- sampleNames(es)</pre>
   resJade <- runICA(X=exprs(es), nbComp=10, method = "JADE", maxit=10000)</pre>
  resBuild <- buildIcaSet(params=buildMineICAParams(), A=data.frame(resJade$A), S=data.frame(resJade$S),
                         dat=exprs(es), pData=pData(es), refSamples=character(0),
                         annotation=annot, typeID= typeIDmainz,
                         chipManu = "affymetrix", mart=mart)
   icaSet <- resBuild$icaSet</pre>
}
## Build the two IcaSet objects
icaSetMainz <- treat(mainz)</pre>
icaSetVdx <- treat(vdx)</pre>
## Compute correlation between every pair of IcaSet objects.
resCompareAn <- compareAn(icaSets=list(icaSetMainz,icaSetVdx),</pre>
labAn=c("Mainz","Vdx"), type.corr="pearson", level="genes", cutoff_zval=0)
## Same thing but adding a selection of genes on which the correlation between two components is computed:
# when considering pairs of components, only projections whose scaled values are not located within
# the circle of radius 1 are used to compute the correlation (cutoff_zval=1).
resCompareAn <- compareAn(icaSets=list(icaSetMainz,icaSetVdx),</pre>
labAn=c("Mainz","Vdx"), type.corr="pearson", cutoff_zval=1, level="genes")
## Build a graph where edges correspond to maximal correlation value (useVal="cor"),
## i.e, component A of analysis i is linked to component B of analysis j,
## only if component B is the most correlated component to A amongst all component of analysis j.
compareAn2graphfile(listPairCor=resCompareAn, useMax=TRUE, useVal="cor", file="myGraph.txt")
## Restrict the graph to correlation values exceeding 0.4
compareAn2graphfile(listPairCor=resCompareAn, useMax=FALSE, cutoff=0.4, useVal="cor", file="myGraph.txt")
## End(Not run)
```

compareGenes

Union and intersection of contributing genes

# Description

Compute and annotate the intersection or union between contributiong genes of components originating from different IcaSet objects.

### Usage

```
compareGenes(keepCompByIcaSet, icaSets, lab, cutoff = 0,
```

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```
type = c("union", "intersection"), annotate = TRUE,
file,
mart = useMart("ensembl", "hsapiens_gene_ensembl"))
```

#### **Arguments**

icaSets List of IcaSet objects, the geneNames of the IcaSet objects must be from the

same type (e.g, gene Symbols).

keepCompByIcaSet

Indices of the components to be considered in each IcaSet.

The names of the icaSets (e.g the names of the datasets they originate from).

cutoff The cutoff (on the absolute centered and scaled projections) above which the

genes have to be considered.

type "intersection" to restrict the list of genes to the ones that are common be-

tween all datasets, or "union" to consider all the union of genes available across

the datasets.

annotate If TRUE (default) the genes are annotated using function writeGenes.

file The HTML file name where the genes and their annotations are written, de-

fault is typeGenes\_lab1-i\_lab2-j\_... where i and j are the component indices

contained in keepCompByIcaSet.

mart The mart object (database and dataset) used for annotation, see function useMart

of package biomaRt.

#### Value

A data.frame containing

```
typeID(icaSets[[1]])['geneID_biomart']: the gene IDs,
```

median\_rank the median of the ranks of each gene across the IcaSet objects,

analyses the labels of the IcaSet objects in which each gene is above the given cutoff

min\_rank the minimum of the ranks of each gene across the IcaSet objects,

ranks the ranks of each gene in each IcaSet where it is available,

scaled\_proj the centered and reduced projection of each gene in each IcaSet where it is available.

# Author(s)

Anne Biton

# See Also

writeGenes

```
## Not run:
data(icaSetCarbayo)
mart <- useMart("ensembl", "hsapiens_gene_ensembl")

## comparison of two components
## here the components come from the same IcaSet for convenience
## but they must come from different IcaSet in practice.</pre>
```

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cor2An

Correlation between two matrices

# Description

This function measures the correlation between two matrices containing the results of two decompositions.

### Usage

```
cor2An(mat1, mat2, lab,
  type.corr = c("pearson", "spearman"), cutoff_zval = 0)
```

### **Arguments**

mat1	matrix of dimension features/genes x number of components, e.g the results of an ICA decomposition
mat2	matrix of dimension features/genes x number of components, e.g the results of an ICA decomposition
lab	The vector of labels for mat1 and mat2, e.g the the names of the two datasets on which were calculated the two decompositions
type.corr	Type of correlation, either 'pearson' or 'spearman'
cutoff_zval	cutoff_zval: 0 (default) if all genes are used to compute the correlation between the components, or a threshold to compute the correlation on the genes that have at least a scaled projection higher than cutoff_zval.

### **Details**

Before computing the correlations, the components are scaled and restricted to common row names. It must be taken into account by the user that if cutoff\_zval is different from NULL or zero, the computation will be slowler since each pair of component is treated individually.

When cutoff\_zval is specified, for each pair of components, genes that are included in the circle of center 0 and radius cutoff\_zval are excluded from the computation of the correlation between the gene projection of the two components.

### Value

This function returns a list consisting of:

cor	a matrix of dimensions '(nbcomp1+nbcomp2) x (nbcomp1*nbcomp2)', containing the correlation values between each pair of components,
pval	a matrix of dimension '(nbcomp1+nbcomp2) $x$ (nbcomp1*nbcomp2)', containing the p-value of the correlation tests for each pair of components,
inter	the intersection between the features/genes of mat1 and mat2,
labAn	the labels of the compared matrices.

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# Author(s)

Anne Biton

#### See Also

```
rcorr, cor.test, compareAn
```

### **Examples**

correl2Comp

correl2Comp

# **Description**

This function computes the correlation between two components.

# Usage

```
correl2Comp(comp1, comp2, type.corr = "pearson", plot = FALSE,
    cutoff_zval = 0, test = FALSE, alreadyTreat = FALSE)
```

# **Arguments**

comp1	The first component, a vector of projections or contributions indexed by labels
comp2	The second component, a vector of projections or contributions indexed by labels
type.corr	Type of correlation to be computed, either 'pearson' or 'spearman'
plot	if TRUE, plot comp1 vs comp2
cutoff_zval	either NULL or 0 (default) if all genes are used to compute the correlation between the components, or a threshold to compute the correlation on the genes that have at least a scaled projection higher than cutoff_zval.
test	if TRUE the correlation test p-value is returned instead of the correlation value
alreadyTreat	if TRUE comp1 and comp2 are considered as being already treated (i.e scaled and restricted to common elements)

### **Details**

Before computing the correlation, the components are scaled and restricted to common labels. When  $cutoff\_zval$  is different from 0, the elements that are included in the circle of center 0 and radius  $cutoff\_zval$  are not taken into account during the computation of the correlation.

# Value

This function returns either the correlation value or the p-value of the correlation test.

# Author(s)

Anne Biton

dat 29

dat

Retrieve and set data from IcaSet

# **Description**

These generic functions access and set the attributes dat stored in an object of class IcaSet.

# Usage

```
dat(object)
dat(object) <- value
datByGene(object)
datByGene(object) <- value
geneNames(object)</pre>
```

# **Arguments**

object of class IcaSet

value Matrix with rows representing features or genes and columns samples.

#### Value

dat and datByGene return a matrix containing measured values (e.g expression data) indexed by features and genes, respectively. geneNames returns the names of the genes, i.e the row names of datByGene.

# Author(s)

Anne

dataCarbayo

Carbayo expression data

# Description

Contains bladder cancer expression data based on on HG-U133A Affymetrix microarrays. The data include 93 samples, were normalized with MAS5 by the authors of the paper using Quantile normalization and log2-transformation. They are restricted to the 10000 most variable probe sets.

# Author(s)

Anne Biton

# References

http://jco.ascopubs.org/content/24/5/778/suppl/DC1

30 getProj

getComp	Retrieve feature and sample values on a component stored in an IcaSet object.

# Description

This generic function retrieves, from an IcaSet object, the feature projections (contained in attribute S) and sample contributions (contained in attribute A) corresponding to a specific component.

# Usage

```
getComp(object, level, ind)
```

# Arguments

object Object of class IcaSet.

level Either "features" to retrieve projections contained in S, or "genes" to retrieve

projections contained in SByGene.

ind The index of the component to be retrieved.

### Value

getComp returns a list containing two elements:

**proj:** the feature or gene projections on the given component,

**contrib:** the sample contributions on the given component.

# Author(s)

Anne Biton

### See Also

IcaSet-class

getProj Extract projection values
-----------------------------------

# **Description**

Extract projection values of a given set of IDs on a subset of components.

# Usage

```
getProj(icaSet, ids, keepComp,
  level = c("features", "genes"))
```

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# **Arguments**

icaSet An object of class IcaSet

ids feature or gene IDs

keepComp Index of the components to be conserved, must be in indComp(icaSet)

level The level of projections to be extracted, either "features" or "genes"

### Value

A vector or a list of projection values

# Author(s)

Anne Biton

# **Examples**

```
## load an example of IcaSet
data(icaSetCarbayo)

##get the projection of your favorite proliferation genes
#on all components
getProj(icaSetCarbayo, ids=c("TOP2A","CDK1","CDC20"), level="genes")

#on some components
getProj(icaSetCarbayo, ids=c("TOP2A","CDK1","CDC20"),
keepComp=c(1,6,9,12),level="genes")

##get the gene projection values on the sixth component
getProj(icaSetCarbayo, keepComp=6,level="genes")
```

hgOver Output of hyperGtest

# Description

Example of output of function hyperGtest.

# Author(s)

Anne Biton

32 hypergeoAn

hypergeoAn	Runs an enrichment analysis per component using package GOstats.

# Description

Runs an enrichment analysis of the contributing genes associated with each component, using the function hyperGTest of package GOstats. The easiest way to run enrichment analysis is to use function runEnrich.

### Usage

```
hypergeoAn(icaSet, params,
  path = paste(resPath(params), "GOstatsEnrichAnalysis/", sep = "/"),
  SlistSel, hgCutoff = 0.01, db = "go", onto = "BP",
  cond = TRUE, universe, entrez2symbol)
```

# **Arguments**

È	guments		
	icaSet	An object of class IcaSet	
	params	An object of class MineICAParams containing the parameters of the analysis	
	path	The path where results will be saved	
	SlistSel	A list of contributing gene projection values per component. Each element of the list corresponds to a component and is restricted to the features or genes exceeding a given threshold. If missing, is computed by the function.	
	hgCutoff	The p-value threshold	
	db	The database to be used ("GO" or "KEGG")	
	onto	A character specifying the GO ontology to use. Must be one of "BP", "CC", or "MF", see GOHyperGParams. Only used when argument db is "GO".	
	cond	A logical indicating whether the calculation should conditioned on the GO structure, see ${\sf GOHyperGParams}$ .	
	universe	The universe for the hypergeometric tests, see GOHyperGParams.	
	entrez2symbol	A vector of all gene Symbols involved in the analysis indexed by their Entrez Gene IDs. It is only used when annotation(params) is empty, and allows to associate gene sets to Symbols.	

# **Details**

An annotation package must be available in annotation(icaSet) to provide the contents of the gene sets. If none corresponds to the technology you deal with, please choose the org.\*.eg.db package according to the organism (for example org.Hs.eg.db for Homo sapiens). Save results of the enrichment tests in a '.rda' file located in path/db/onto/zvalCutoff(params).

### Author(s)

Anne Biton

### See Also

runEnrich, xtable, useMart, hyperGTest, GOHyperGParams, mergeGostatsResults

#### **Examples**

```
## Not run:
## load an example of IcaSet
data(icaSetCarbayo)
## define params
# Use threshold 3 to select contributing genes.
# Results of enrichment analysis will be written in path 'resPath(params)/GOstatsEnrichAnalysis'
params <- buildMineICAParams(resPath="~/resMineICACarbayo/", selCutoff=3)</pre>
## Annotation package for IcaSetCarbayo is hgu133a.db.
# check annotation package
annotation(icaSetCarbayo)
## Define universe, i.e the set of EntrezGene IDs mapping to the feature IDs of the IcaSet object.
universe <- as.character(na.omit(unique(unlist(AnnotationDbi::mget(featureNames(icaSetCarbayo),</pre>
                         hgu133aENTREZID, ifnotfound = NA)))))
## Apply enrichement analysis (of the contributing genes) to the first components using gene sets from KEGG.
# Since an annotation package is available, we don't need to fill arg 'entrez2symbol'.
# run the actual enrichment analysis
hypergeoAn(icaSet=icaSetCarbayo[,,1], params=params, db="G0",onto="BP", universe=universe)
## End(Not run)
```

IcaSet

Class to Contain and Describe an ICA decomposition of High-Throughput Data.

# Description

Container for high-throughput data and results of ICA decomposition obtained on these data. IcaSet class is derived from eSet, and requires a matrix named dat as assayData member.

### **Extends**

Directly extends class eSet.

# **Creating Objects**

new("IcaSet",

```
new("IcaSet")
new("IcaSet", annotation = character(0), experimentData = new("MIAME"), featureData = new("
This creates an IcaSet with assayData implicitly created to contain dat.
```

assayData = assayDataNew(dat=new("matrix")),

expe

This creates an IcaSet with assayData provided explicitly.

annotation = character(0),

IcaSet instances are usually created through new("IcaSet", ...). Usually the arguments to new include dat ('features x samples', e.g a matrix of expression data), phenoData ('samples x annotations', a matrix of sample annotations), S the Source matrix of the ICA decomposition ('features

x comp'), A the Mixing matrix of the ICA decomposition ('samples x comp'), annotation the annotation package, typeID the description of the feature and gene IDs.

The other attributes can be missing, in which case they are assigned default values.

The function buildIcaSet is a more convenient way to create IcaSet instances, and allows to automatically annotate the features.

#### **Slots**

```
Inherited from eSet:
annotation: See eSet
assayData: Contains matrices with equal dimensions, and with column number equal to nrow(phenoData).
```

assayData: Contains matrices with equal differsions, and with column number equal to in ow(phenobata) assayData must contain a matrix dat with rows representing features (e.g., reporters) and columns representing samples. Class:AssayData-class

```
experimentData: See eSet
featureData: See eSet
phenoData: See eSet
protocolData: See eSet
Specific slot:
```

organism: Contains the name of the species. Currently only Human ("Human" or "Homo sapiens") and Mouse ("Mouse" or "Mus musculus") are supported. Only used when chipManu="illumina"

mart: An output of useMart of package biomaRt. Only useful if no annotation package is available for argument icaSet.

- datByGene: Data.frame containing the data dat where features have been replaced by their annotations (e.g, gene IDs). Rows represent annotations of the features (e.g., gene IDs) and columns represent samples.
- A: The mixing matrix of the ICA decomposition, contained in a data.frame whose column number equals the number of components and row number equals nrow(phenoData) (dimension: 'samples x comp').
- S: The source matrix of the ICA decomposition, contained in a data.frame whose column number equals the number of components and row number equals nrow(assayData) (dimension: 'features x comp').

SByGene: The matrix Source of the ICA decomposition, contained in a data.frame whose column number equals the number of components and row number equals nrow(datByGene) (dimension: 'annotatedFeatures x comp').

compNames: A vector of component labels with length equal to the number of component.

indComp: A vector of component indices with length equal to the number of component.

witGenes: A vector of gene IDs with length equal to the number of component.

chipManu: The manufacturer of the technology the data originates from. Useful for the annotation of the features when data originates from an \_illumina\_ microarray.

chipVersion: The version of the chip, only useful for when chipManu="illumina"

refSamples: A vector of sample IDs including the reference samples, e.g the "normal" samples. Must be included in sampleNames(object), i.e in colnames(dat).

typeID: A vector of characters providing the annotation IDs. It includes three elements:

**geneID\_annotation** the IDs from the package to be used to annotate the features into genes. It will be used to fill the attributes datByGene and SByGene of the icaSet. It must match one of the objects the corresponding package supports (you can access the list of objects by typing ls("package:packagename")). If no annotation package is provided, this element is not useful.

**geneID\_biomart** the type of gene IDs, as available in listFilters(mart); where mart is specified as described in useMart. If you have directly built the IcaSet at the gene level (i.e if no annotation package is used), featureID\_biomart and geneID\_biomart will be identical.

**featureID\_biomart** the type of feature IDs, as available in listFilters(mart); where mart is specified as described in function useMart. Not useful if you work at the gene level.

### Methods

Class-specific methods.

getComp(IcaSet, ind, level=c("features", "genes")) Given a component index, extract the corresponding sample contribution values from A, and the feature (level="features") or gene (level="genes") projections from S. Returns a list with two elements: contrib the sample contributions and proj the feature or gene projections.

Access and set any slot specific to IcaSet:

slotName(IcaSet), and slotName(IcaSet)<-: Accessing and setting any slot of name slotName
contained in an IcaSet object.</pre>

IcaSet["slotName"], and IcaSet["slotName"]<-: Accessing and setting any slot of name slotName
 contained in an IcaSet object.</pre>

Most used accessors and settors:

A(IcaSet), and A(IcaSet)<-: Accessing and setting Mixing matrix A.

S(IcaSet), and S(IcaSet)<-: Accessing and setting the data.frame Source S.

 ${\tt Slist(IcaSet):}$  Accessing the data.frame Source as a list where names are preserved.

SByGene(IcaSet), and SByGene(IcaSet)<-: Accessing and setting the \_annotated\_ data.frame Source SByGene.

SlistByGene(IcaSet): Accessing the \_annotated\_ Source matrix as a list where names are preserved.

organism(IcaSet), organism(IcaSet, characte) <- Access and set value in the organism slot.

#### Derived from eSet:

```
pData(IcaSet), pData(IcaSet, value)<-: See eSet
assayData(IcaSet): See eSet
sampleNames(IcaSet) and sampleNames(IcaSet)<-: See eSet
featureNames(IcaSet), featureNames(IcaSet, value)<-: See eSet
dims(IcaSet): See eSet
phenoData(IcaSet), phenoData(IcaSet, value)<-: See eSet
varLabels(IcaSet), varLabels(IcaSet, value)<-: See eSet
varMetadata(IcaSet), varMetadata(IcaSet, value)<-: See eSet
varMetadata(IcaSet), varMetadata(IcaSet, value)<-: See eSet</pre>
```

```
experimentData(IcaSet),experimentData(IcaSet,value)<-: See eSet</pre>
    pubMedIds(IcaSet), pubMedIds(IcaSet, value) See eSet
    abstract(IcaSet): See eSet
    annotation(IcaSet), annotation(IcaSet, value) <- See eSet</pre>
    protocolData(IcaSet), protocolData(IcaSet, value) <- See eSet</pre>
    combine(IcaSet,IcaSet): See eSet
    storageMode(IcaSet), storageMode(IcaSet, character)<-: See eSet</pre>
    Standard generic methods:
    initialize(IcaSet): Object instantiation, used by new; not to be called directly by the user.
    validObject(IcaSet): Validity-checking method, ensuring that dat is a member of assayData,
         and that the number of features, genes, samples, and components are consistent across all the
         attributes of the IcaSet object. checkValidity(IcaSet) imposes this validity check, and the
         validity checks of eSet.
    IcaSet[slotName], IcaSet[slotName]<-: Accessing and setting any slot of name slotName con-</pre>
         tained in an IcaSet object.
    IcaSet[i, j, k]: Extract object of class "IcaSet" for features or genes with names i, samples
         with names or indices j, and components with names or indices k.
    makeDataPackage(object, author, email, packageName, packageVersion, license, biocViews, filePath
         Create a data package based on an IcaSet object. See makeDataPackage.
    show(IcaSet): See eSet
    dim(IcaSet), ncol: See eSet
    IcaSet[(index)]: See eSet
    IcaSet$, IcaSet$<-: See eSet</pre>
    IcaSet[[i]], IcaSet[[i]]<-: See eSet</pre>
Author(s)
    Anne Biton
See Also
    eSet-class, buildIcaSet, IcaSet-class, MineICAParams-class.
```

```
# create an instance of IcaSet
new("IcaSet")
dat <- matrix(runif(100000), nrow=1000, ncol=100)</pre>
rownames(dat) <- 1:nrow(dat)</pre>
new("IcaSet",
    dat=dat,
    A=as.data.frame(matrix(runif(1000), nrow=100, ncol=10)),
    S=as.data.frame(matrix(runif(10000), nrow=1000, ncol=10), row.names = 1:nrow(dat)))
```

icaSetCarbayo 37

icaSetCarbayo	IcaSet-object containing a FastICA decomposition of gene expression
•	microarrray-based data of bladder cancer samples.

# **Description**

Object of class IcaSet containing an ICA decomposition calculated by the FastICA algorithm (through matlab function "icasso") on bladder cancer expression data measured on HG-U133A Affymetrix microarrays. The original expression data were normalized with MAS5 by the authors of the paper followed by log2-transformation. ICA was run on the dataset restricted to the 10000 most variable probe sets (based on IQR values). 10 components were computed. Only probe sets/genes having an absolute projection higher than 3 are stored in this object.

# Author(s)

Anne Biton

#### References

http://jco.ascopubs.org/content/24/5/778/suppl/DC1

icaSetKim	IcaSet-object containing a FastICA decomposition of gene expression
	microarrray-based data of bladder cancer samples.

# **Description**

Object of class IcaSet containing an ICA decomposition calculated by the FastICA algorithm (through matlab function "icasso") on bladder cancer expression data measured on illumina Human-6 BeadChip, version 2. It contains 20 independent components. The original expression data contain 165 tumor samples, were normalized by the authors of the paper with Illumina BeadStudio software using Quantile normalization and log2 transformation, and are restricted to the 10000 most variable probe sets.

# Author(s)

Anne

## References

http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13507

38 icaSetStransky

icaSetRiester	IcaSet-object containing a FastICA decomposition of gene expression microarrray-based data of bladder cancer samples.
	The state of the s

# **Description**

Object of class IcaSet containing an ICA decomposition calculated by the FastICA algorithm (through matlab function "icasso") on gene expression data of urothelial tumors. measured on a HG-U133-plus2 Affymetrix microarrays. It contains 20 independent components. The original expression data contain 93 tumor samples, were normalized with GCRMA with log2-transformation, and are restricted to the 10000 most variable probe sets.

## Author(s)

Anne Biton

## References

http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE31684

icaSetStransky	IcaSet-object containing a FastICA decomposition of gene expression microarrray-based data of bladder cancer samples.
	microurray bused data of budger cancer samples.

# **Description**

Object of class IcaSet containing an ICA decomposition calculated by the FastICA algorithm (through matlab function "icasso") on bladder cancer expression data measured on HG-U133-95a and HG-U133-95av2 Affymetrix microarrays. It contains 20 independent components. The original expression data contain 63 tumor samples and were normalized by RMA with log2-transformation.

# Author(s)

Anne Biton

# References

http://microarrays.curie.fr/publications/oncologie\_moleculaire/bladder\_TCM/

indComp 39

indComp	Retrieve and set component labels, IcaSet	indices, and witness genes from

# **Description**

These generic functions access and set the attributes compNames, indComp and witGenes stored in an object of class IcaSet.

# Usage

```
indComp(object)
indComp(object) <- value
compNames(object)
compNames(object) <- value
witGenes(object)
witGenes(object) <- value</pre>
```

# Arguments

object of class IcaSet

value Numeric vector for indComp, character vector for compNames and witGenes,

with length equal to ncol(A(object)) and containing: component indices (for

indComp), labels (for compNames), or gene witness IDs (for witGenes).

# Value

indComp returns a numeric vector containing component indices; compNames returns a character vector containing component labels; witGenes returns a character vector containing witness genes IDs.

# Author(s)

Anne Biton

MineICAParams

Class to contain parameters for the analysis of an ICA decomposition.

# Description

Container for parameters used during the analysis of an ICA decomposition obtained on genomics data.

# **Creating Objects**

```
new("MineICAParams")
new("MineICAParams", resPath="", genesPath="ProjByComp", pvalCutoff=0.05, selCutoff=3)
```

40 MineICAParams

#### **Slots**

Sfile A txt file containing the Source matrix S.

Afile A txt file containing the Mixing matrix A.

datfile A txt file containing the data (typically expression data) on which the decomposition was calculated.

annotfile Either a RData or txt file containing the annotation data for the samples (must be of dimensions samples\*annotations).

resPath The path where the outputs of the analysis will be written.

genesPath The path \_within\_ the resPath where the gene projections will be written. If missing, will be automatically attributed as resPath/gene2components/.

annot2col A vector of colors indexed by annotation levels. If missing, will be automatically attributed using function annot2Color.

pvalCutoff The cutoff used to consider a p-value significant, default is 0.05.

selCutoff The cutoff applied on the absolute feature/gene projection values to consider gene as contributing to a component, default is 3. Must be either of length 1 and the same treshold is applied to all components, or of length equal to the number of components in order to use a specific threshold for each component.

#### Methods

For any slot:

Accessing and setting any slot of name slotName contained in an MineICAParams object.

slotName(MineICAParams) and slotName(MineICAParams)MineICAParams["slotName"] and MineICAParams["slotName"] and Southame (MineICAParams) and Southame (MineICAParams) and Southame (MineICAParams) and Southame (MineICAParams) and MineICAParams) and Southame (MineICAParams) and So

# Author(s)

Anne Biton

## See Also

MineICAParams-class, runAn.

# **Examples**

# create an instance of LocSet
new("MineICAParams")

nbOccByGeneInComp	nbOccByGeneInComp
-------------------	-------------------

# **Description**

For each feature/gene, this function returns the indices of the components they contribute to.

# Usage

```
nbOccByGeneInComp(Slist, cutoff, sel)
```

# **Arguments**

Slist	A list whose each eleme	nt contains projection va	values of features/genes on a
-------	-------------------------	---------------------------	-------------------------------

component.

cutoff A threshold to be used to define a gene as contributor

sel A list whose each element contains projection values of contributing features/genes

on a component (the difference with arg Slist is that sel is already restricted

to the contributing genes).

# Value

This function returns a list which gives for each feature/gene the indices of the components it contributes to.

## Author(s)

Anne Biton

# **Examples**

```
c1 <- rnorm(100); names(c1) <- paste("g",100:199,sep="")
c2 <- rnorm(100); names(c2) <- paste("g",1:99,sep="")
MineICA:::nbOccByGeneInComp(Slist=list(c1,c2), cutoff= 0.5)</pre>
```

nb0ccInComp

Select components the features contribute to

# Description

For each feature/gene, this function returns the components they contribute to and their projection values across all the components.

# Usage

```
nbOccInComp(icaSet, params, selectionByComp = NULL,
  level = c("features", "genes"), file = NULL)
```

42 nodeAttrs

# **Arguments**

icaSet An object of class IcaSet

params An object of class MineICAParams containing the parameters of the analysis,

the attribute cutoffSel is used as a threshold on the absolute projections to

determine which genes contribute to the components.

selectionByComp

The list of components already restricted to the contributing genes

level The attribute of icaSet to be used, are reported the occurences of either the

"features" or the "genes".

file The file where the output data.frame and plots are written.

# **Details**

A feature/gene is considered as a contributor when its scaled projection value exceeds the threshold selCutoff(icaSet).

This function plots the number of times the feature/gene is a contributor as a function of the standard deviation of its expression profile.

The created files are located in genePath(params). An extensiom '.htm' and '.pdf' is respectively added to the file name for the data.frame and the plot outputs.

#### Value

Returns a data.frame whose columns are: 'gene' the feature or gene ID, 'nbOcc' the number of components on which the gene contributes according to the threshold, 'components' the indices of these components, and then the component indices which contain its projection values.

# Author(s)

Anne Biton

# **Examples**

```
data(icaSetCarbayo)
params <- buildMineICAParams(resPath="carbayo/")
nbOcc <- nbOccInComp(icaSet=icaSetCarbayo, params=params, level="genes", file="gene2MixingMatrix")</pre>
```

nodeAttrs

Generate node attributes

# Description

This function builds a data.frame describing for each node of the graph its ID and which analysis/data it comes from.

# Usage

```
nodeAttrs(nbAn, nbComp, labAn, labComp, file)
```

plotAllMix 43

# **Arguments**

nbAn Number of analyses being considered, i.e number of IcaSet objects
--

nbComp Number of components by analysis, if of length 1 then it is assumed that each

analysis has the same number of components.

labAn Labels of the analysis, if missing it will be generated as an1, an2, ...

labComp List containing the component labels indexed by analysis, if missing will be

generated as comp1, comp2, ...

file File where the description of the node attributes will be written

# **Details**

The created file is used in Cytoscape.

#### Value

A data.frame describing each node/component

# Author(s)

Anne Biton

# **Examples**

```
## 4 datasets, 20 components calculated in each dataset, labAn
nodeAttrs(nbAn=4, nbComp=20, labAn=c("tutu","titi","toto","tata"))
```

plotAllMix

Plots the Gaussian fitted by Mclust on several numeric vectors

# Description

Given a result of function Mclust applied on several numeric vectors, this function plots the fitted Gaussian on their histograms.

# Usage

```
plotAllMix(mc, A, nbMix = NULL, pdf, nbBreaks = 20,
    xlim = NULL)
```

# **Arguments**

mc A list consisting of outputs of function Mclust applied to each column of A, if

this argument is missing Mclust is applied by the function.

A A data.frame of dimensions 'samples x components'.

nbMix The number of Gaussian to be fitted.

nbBreaks The number of breaks for the histogram.

x1im x-axis limits to be used in the plot.

pdf A pdf file.

44 plotCorGraph

#### **Details**

This function can only deal with at the most three Gaussian

#### Value

A list of Mclust results.

## Author(s)

Anne Biton

#### See Also

```
plotMix, hist, Mclust
```

# **Examples**

 ${\tt plotCorGraph}$ 

Plots graph using

## **Description**

This function plots the correlation graph in an interactive device using function tkplot.

# Usage

```
plotCorGraph(dataGraph, edgeWeight = "cor", nodeAttrs,
  nodeShape, nodeCol = "labAn", nodeName = "indComp",
  col, shape, title = "", reciproCol = "reciprocal",
  tkplot = FALSE, ...)
```

# Arguments

dataGraph A data.frame containing the graph description. It must have two columns n1

and n2, each row denoting that there is an edge from n1 to n2. Node labels in columns n1 and n2 of dataGraph must correspond to node IDs in column id of

nodeAttrs.

edgeWeight The column of dataGraph used to weight edges.

nodeAttrs A data.frame with node description, see function nodeAttrs.

plotCorGraph 45

nodeShape Denotes the column of nodeAttrs used to attribute the node shapes. nodeCol Denotes the column of nodeAttrs used to color the nodes in the graph. nodeName Denotes the column of nodeAttrs used as labels for the nodes in the graph. col A vector of colors, for the nodes, indexed by the unique elements of nodeCol column from nodeAttrs. If missing, colors will be automatically attributed. shape A vector of shapes indexed by the unique elements of column nodeShape from nodeAttrs. If missing, shapes will be automatically attributed. title Title for the plot reciproCol Denotes the column of dataGraph containing TRUE if the row defines a reciprocal node, else FALSE. See annotReciprocal. tkplot If TRUE, performs interactive plot with function tkplot, else uses plot. igraph. Additional parameters as required by tkplot.

#### **Details**

You have to slighly move the nodes to see cliques because strongly related nodes are often superimposed. The edgeWeight column is used to weight the edges within the fruchterman.reingold layout available in the package igraph.

The argument nodeCol typically denotes the column containing the names of the datasets. Colors are automatically attributed to the nodes using palette Set3 of package RColorBrewer. The corresponding colors can be directly specified in the 'col' argument. In that case, 'col' must be a vector of colors indexed by the unique elements contained in nodeCol column (e.g dataset ids).

As for colors, one can define the column of nodeAttrs that is used to define the node shapes. The corresponding shapes can be directly specified in the shape argument. In that case, shape must be one of c("circle", "square", "vcsquare", "rectangle", "crectangle", "vrectangle") and must be indexed by the unique elements of nodeShape column.

Unfortunately, shapes can't be taken into account when tkplot is TRUE (interactive plot).

If reciproCol is not missing, it is used to color the edges, either in grey if the edge is not reciprocal or in black if the edge is reciprocal.

## Value

A list consisting of

dataGraph a data.frame defining the correlation graph nodeAttrs a data.frame describing the node of the graph graph the graph as an object of class igraph graphid the id of the graph plotted using tkplot

# Author(s)

Anne Biton

# See Also

compareAn, nodeAttrs, compareAn2graphfile, runCompareIcaSets

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```
dat1 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat1) <- paste("g", 1:1000, sep="")
colnames(dat1) <- paste("s", 1:10, sep="")</pre>
dat2 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat2) <- paste("g", 1:1000, sep="")
colnames(dat2) <- paste("s", 1:10, sep="")</pre>
## run ICA
resJade1 <- runICA(X=dat1, nbComp=3, method = "JADE")</pre>
resJade2 <- runICA(X=dat2, nbComp=3, method = "JADE")</pre>
## build params
params <- buildMineICAParams(resPath="toy/")</pre>
## build IcaSet object
icaSettoy1 <- buildIcaSet(params=params, A=data.frame(resJade1$A), S=data.frame(resJade1$S),</pre>
                                                   dat=dat1, alreadyAnnot=TRUE)$icaSet
icaSettoy2 <- buildIcaSet(params=params, A=data.frame(resJade2$A), S=data.frame(resJade2$S),</pre>
                                                   dat=dat2, alreadyAnnot=TRUE)$icaSet
icaSets <- list(icaSettoy1, icaSettoy2)</pre>
resCompareAn <- compareAn(icaSets=list(icaSettoy1,icaSettoy2), labAn=c("toy1","toy2"),</pre>
                                                 type.corr="pearson", level="genes", cutoff_zval=0)
## Build a graph where edges correspond to maximal correlation value (useVal="cor"),
dataGraph <- compareAn2graphfile(listPairCor=resCompareAn, useMax=TRUE, useVal="cor", file="myGraph.txt")</pre>
## construction of the data.frame with the node description
nbComp <- rep(3,2) #each IcaSet contains 3 components</pre>
nbAn <- 2 # we are comparing 2 IcaSets
# labels of components created as comp*i*
labComp <- foreach(icaSet=icaSets, nb=nbComp, an=1:nbAn) %do% {</pre>
                                   paste(rep("comp",sum(nb)),1:nbComp(icaSet),sep = "")}
# creation of the data.frame with the node description
nodeDescr <- nodeAttrs(nbAn = nbAn, nbComp = nbComp, labComp = labComp,</pre>
                                             labAn = c("toy1","toy2"), file = "nodeInfo.txt")
## Plot correlation graph, slightly move the attached nodes to make the cliques visible
## use tkplot=TRUE to have an interactive graph
\verb|res <- plotCorGraph| (title = "Compare toy 1 and 2", dataGraph = dataGraph, nodeName = "indComp", tkplot = FALSE | Algebra | Table | Table
                          nodeAttrs = nodeDescr, edgeWeight = "cor", nodeShape = "labAn", reciproCol = "reciprocal")
## Not run:
## load two microarray datasets
library(breastCancerMAINZ)
library(breastCancerVDX)
data(mainz)
data(vdx)
## Define a function used to build two examples of IcaSet objects
treat <- function(es, annot="hgu133a.db") {</pre>
      es <- selectFeatures_IQR(es,10000)</pre>
      exprs(es) <- t(apply(exprs(es),1,scale,scale=FALSE))</pre>
```

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```
colnames(exprs(es)) <- sampleNames(es)</pre>
   resJade <- runICA(X=exprs(es), nbComp=10, method = "JADE", maxit=10000)
  resBuild <- buildIcaSet(params=buildMineICAParams(), A=data.frame(resJade$A), S=data.frame(resJade$S),
                         dat=exprs(es), pData=pData(es), refSamples=character(0),
                         annotation=annot, typeID= typeIDmainz,
                         chipManu = "affymetrix", mart=mart)
  icaSet <- resBuild$icaSet</pre>
}
## Build the two IcaSet objects
icaSetMainz <- treat(mainz)</pre>
icaSetVdx <- treat(vdx)</pre>
icaSets <- list(icaSetMainz, icaSetVdx)</pre>
labAn <- c("Mainz", "Vdx")</pre>
## correlations between gene projections of each pair of IcaSet
resCompareAn <- compareAn(icaSets = icaSets, level = "genes", type.corr= "pearson",
                           labAn = labAn, cutoff_zval=0)
## construction of the correlation graph using previous output
dataGraph <- compareAn2graphfile(listPairCor=resCompareAn, useMax=TRUE, file="corGraph.txt")</pre>
## construction of the data.frame with the node description
nbComp <- rep(10,2) #each IcaSet contains 10 components</pre>
nbAn <- 2 # we are comparing 2 IcaSets
# labels of components created as comp*i*
labComp <- foreach(icaSet=icaSets, nb=nbComp, an=1:nbAn) %do% {</pre>
                  paste(rep("comp",sum(nb)),1:nbComp(icaSet),sep = "")}
# creation of the data.frame with the node description
nodeDescr <- nodeAttrs(nbAn = nbAn, nbComp = nbComp, labComp = labComp,</pre>
    labAn = labAn, file = "nodeInfo.txt")
## Plot correlation graph, slightly move the attached nodes to make the cliques visible
res <- plotCorGraph(title = "Compare two ICA decomsitions obtained on \n two
              microarray-based data of breast tumors", dataGraph = dataGraph, nodeName = "indComp",
              nodeAttrs = nodeDescr, edgeWeight = "cor", nodeShape = "labAn", reciproCol = "reciprocal")
## End(Not run)
```

plotMix

Plots an histogram and Gaussian fitted by Mclust

# **Description**

Given a result of function Mclust applied to a numeric vector, this function draws the fitted Gaussian on the histogram of the data values.

# Usage

```
plotMix(mc, data, nbBreaks, traceDensity = TRUE,
    title = "", xlim, ylim, ...)
```

## **Arguments**

mc The result of Mclust function applied to argument data

data A vector of numeric values

nbBreaks The number of breaks for the histogram

traceDensity If TRUE (default) density are displayed on the y-axis, else if FALSE counts are

displayed on the y-acis

title A title for the plot

xlim x-axis limits to be used in the plot ylim y-axis limits to be used in the plot ... additional arguments for hist

# **Details**

A shapiro test p-value is added to the plot title. This function can only deal with at the most three Gaussian.

# Value

NULL

# Author(s)

Anne Biton

# See Also

hist, Mclust

# **Examples**

```
## create a mix of two Gaussian
v <-c(rnorm(80,mean=-0.5,sd=1),rnorm(80,mean=1,sd=0.2))
## apply Mclust
mc <- Mclust(v)
## plot fitted Gaussian on histogram of v
plotMix(mc=mc,data=v,nbBreaks=30)</pre>
```

plotPosAnnotInComp

Histograms of sample contributions for each annotation level

# **Description**

This function plots the positions of groups of samples formed by the variables (i.e the sample annotations) across all the components of an object of class icaSet. For each variable level (e.g for each tumor stage) this function plots the positions of the corresponding samples (e.g the subset of samples having this tumor stage) within the histogram of the global sample contributions. The plots are saved in pdf file, one file is created per variable. The pdf files are names 'variable.pdf' and save either in pathPlot if specified or the current directory.

plotPosAnnotInComp 49

## Usage

```
plotPosAnnotInComp(icaSet, params,
  keepVar = varLabels(icaSet),
  keepComp = indComp(icaSet),
  keepSamples = sampleNames(icaSet), pathPlot = NULL,
  breaks = 20, colAll = "grey74", colSel, resClus,
  funClus = c("Mclust", "kmeans"), nbClus = 2,
  by = c("annot", "component"),
  typeImage = c("pdf", "png", "none"), ...)
```

# **Arguments**

icaSet An object of class IcaSet
params A MineICAParams object
keepVar The variable labels to be

keepVar The variable labels to be considered, i.e a subset of the column labels of the

pheno data of icaSet available in (varLabels(icaSet))

keepComp A subset of components available in indComp(icaSet); by default, all compo-

nents are used

keepSamples A subset of samples, must be available in sampleNames(icaSet); by default,

all samples are used

pathPlot A character specifying the path where the plots will be saved

breaks The number of breaks to be used in the histograms

colSel The colour of the histogram of the group of interest, default is "red"

colAll The colour of the global histogram, default is "grey74"

resClus A list containing the outputs of function clusterSamplesByComp, which con-

sists of sample clustering applied to matrix A of argument icaSet. If missing,

the clustering is performed by the function.

funClus The clustering method to be used, either "Mclust" or "kmeans". If resClus is

not missing, equals resClus\$funClus.

nbClus If resClus is missing, it provides the number of clusters to be computed by

funClus, default is 2

by Either "annot" to plot the histograms of each variable across all components, or

"component" to plot the histograms for each component across variables. When by="annot" one pdf file is created by variable name, while when annot="component",

one pdf file is created by component.

typeImage The type of image to be created, either "pdf" (default) or "png". "png" is not

recommended, unless there are at the most 4 histograms to be plotted, because

it does not allow to deal with multiple pages of plots.

... Additional parameters for function hist

# **Details**

The plotted values are the sample contributions across the components, i.e across the columns of A(icaSet).

If argument resClus is missing, the function computes the clustering of the samples on each component (i.e on each column of A(icaSet)) using funClus and nbClus.

The association between the clusters and the considered sample group is tested using a chi-square test. The p-values of these tests are available in the title of each plot.

50 plot\_heatmapsOnSel

When by="annot" this function plots the histograms of each variable across all components, to plot the histograms for each component across variables, please use by="component".

# Value

**NULL** 

#### Author(s)

Anne Biton

#### See Also

```
plotPosSamplesInComp, chisq.test
```

# **Examples**

```
## Not run:
## load an example of IcaSet
data(icaSetCarbayo)

## Use icaSetCarbayo, look at the available annotations
varLabels(icaSetCarbayo)

## Plot positions of samples in components according to annotations 'SEX' and 'STAGE'
# plots are saved in files SEX.pdf and STAGE.pdf created in the current directory
plotPosAnnotInComp(icaSet=icaSetCarbayo, keepVar=c("SEX","STAGE"), keepComp=1:2, funClus="Mclust")
# specifiy arg 'pathPlot' to save the pdf in another directory, but make sure it exists before
# specifiy arg 'by="comp"' to create one pdf file per component

## End(Not run)
```

plot\_heatmapsOnSel

Plot heatmap associated with each component

# **Description**

This function plots the heatmaps representing the measured values of the contributing features/genes on each component. It also plots the sample annotations above each heatmap using colours.

# Usage

```
plot_heatmapsOnSel(icaSet, selCutoff = 4,
  level = c("features", "genes"), samplesOrder,
  featuresOrder, selectionByComp, keepVar,
  keepComp = indComp(icaSet), doSamplesDendro = TRUE,
  doGenesDendro = TRUE,
  heatmapCol = maPalette(low = "blue", high = "red", mid = "yellow", k = 44),
  file = "", path = "", annot2col, ...)
```

plot\_heatmapsOnSel 51

# **Arguments**

icaSet The IcaSet object

selCutoff A numeric threshold used to select the contributing genes based on their projec-

tion values. Must be either of length 1 and the same treshold is applied to all components, or of length equal to the number of components and one specific

threshold is used for each component.

samplesOrder A list providing the order of the samples, per component, to be used in the

heatmaps. If missing, the contribution values of the samples are used to rank the

columns of the heatmaps.

featuresOrder A list providing the order of the genes, per component, to be used in the heatmaps.

If missing, the projection values of the genes are used to rank the rows of the

heatmaps.

selectionByComp

A list of gene projections per component already restricted to the contributing

genes, if missing is computed by the function.

level A character indicating which data level is used to plot the heatmaps: either

 $\hbox{'features' to represent the data at the feature levels (e.g expression profiles of probe sets), or \\\hbox{'genes' to represent the data at the annotated-features level (e.g.)}$ 

gene expression profiles).

keepVar The variable labels to be considered, i.e a subset of the column labels of the

pheno data of icaSet available in (varLabels(icaSet))

keepComp A subset of components, must be included in indComp(icaSet). By default, all

components are used.

doSamplesDendro

A logical indicating whether a hierarchical clustering has to be performed on

the data matrix restricted to the contributing features/genes, and whether the

corresponding dendrogram has to be plotted, default is TRUE.

doGenesDendro A logical indicating if the dendrogram of features/genes has to be plotted, de-

fault is FALSE.

heatmapCol A list of colors used to for heatmap coloring (see argument col of the function

image).

file A character to add to each pdf file name. This function creates one file by

component named "index-of-component\_file.pdf" .

path A directory for the output pdf files, must end with "/". Default is current direc-

tory.

annot2col A vector of colours indexed by the levels of the variables of icaSet (i.e all

the annotation values available in pData(icaSet)). If missing the colours are

generated automatically using the function annot2Color

... Additional parameters for function heatmap.plus

# Details

This function restricts the data matrix of an IcaSet object to the contributing genes/features, and order features/genes and samples either as asked by the user or according to their values in the ICA decomposition.

The heatmap is plotted using a slightly modified version of the function heatmap.plus from the package of the same name. By default in this function, the hierarchical clustering is calculated using the function agnes with euclidean metric and Ward's method.

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#### Value

A list with one element per component, each of them being a list consisting of three elements:

```
x the matrix represented by the heatmap,breaks the breaks used for the colours of the heatmap,dendro the dendrogram.
```

#### Author(s)

Anne Biton

#### See Also

heatmap.plus, image, annot2Color, build\_sortHeatmap

## **Examples**

```
## Not run:
## load an example of IcaSet object
data(icaSetCarbayo)
## check which variables you would like to use in the heatmap
varLabels(icaSetCarbayo)
keepVar <- c("STAGE","SEX")</pre>
## Use only component 1
keepComp <- 1
## For each component, select contributing *genes* using a threshold of 2 on the absolute projection values,
## and plot heatmaps of these contributing genes by ordering genes and samples according to their contribution
plot_heatmapsOnSel(icaSet = icaSetCarbayo, selCutoff = 2, level = "genes", keepVar = keepVar,
                   keepComp=1, doSamplesDendro = TRUE, doGenesDendro = TRUE,
                 heatmapCol = maPalette(low = "blue", high = "red", mid = "yellow", k=44),
                   file = "heatmapWithoutDendro_zval3.pdf")
## For each considered component, select contributing *features* using a threshold of 2 on the absolute project
## and plot heatmaps of these contributing genes with dendrograms
plot_heatmapsOnSel(icaSet = icaSetCarbayo, selCutoff = 2, level = "features", keepVar = keepVar,
                   keepComp=1, doSamplesDendro = TRUE, doGenesDendro = TRUE,
                 heatmapCol = maPalette(low = "blue",high = "red", mid = "yellow", k=44),
                   file = "heatmapWithDendro_zval3.pdf")
## End(Not run)
```

# Description

qualVarAnalysis

This function tests if the groups of samples formed by the variables are differently distributed on the components, in terms of contribution value (i.e of values in matrix A(icaSet)). The distribution of the samples on the components are represented using either density plots of boxplots. It is possible to restrict the tests and the plots to a subset of samples and/or components.

Tests association between qualitative variables and components.

qualVarAnalysis 53

## Usage

```
qualVarAnalysis(params, icaSet, keepVar,
  keepComp = indComp(icaSet),
  keepSamples = sampleNames(icaSet),
  adjustBy = c("none", "component", "variable"),
  method = "BH", doPlot = TRUE, typePlot = "density",
  addPoints = FALSE, onlySign = TRUE,
  cutoff = params["pvalCutoff"],
  colours = annot2col(params), path = "qualVarAnalysis/",
  filename = "qualVar", typeImage = "png")
```

# Arguments

params An object of class MineICAParams providing the parameters of the analysis.

icaSet An object of class IcaSet.

keepVar The variable labels to be considered, must be a subset of varLabels(icaSet).

keepComp A subset of components, must be included in indComp(icaSet). By default, all

components are used.

keepSamples A subset of samples, must be included in sampleNames(icaSet). By default,

all samples are used.

adjustBy The way the p-values of the Wilcoxon and Kruskal-Wallis tests should be cor-

rected for multiple testing: "none" if no p-value correction has to be done, "component" if the p-values have to be corrected by component, "variable" if

the p-values have to be corrected by variable

method The correction method, see p. adjust for details, default is "BH" for Benjamini

& Hochberg.

doPlot If TRUE (default), the plots are done, else only tests are performed.

addPoints If TRUE, points are superimposed on the boxplot. typePlot The type of plot, either "density" or "boxplot".

onlySign If TRUE (default), only the significant results are plotted.

cutoff A threshold p-value for statistical significance.

colours A vector of colours indexed by the variable levels, if missing the colours are

automatically generated using annot2Color.

path A directory \_within resPath(params)\_ where the files containing the plots and

the p-value results will be located. Default is "qualVarAnalysis/".

typeImage The type of image file to be used.

filename The name of the HTML file containing the p-values of the tests, if NULL no file

is created.

## **Details**

This function writes an HTML file containing the results of the tests as a an array of dimensions 'variables \* components' containing the p-values of the tests. When a p-value is considered as significant according to the threshold cutoff, it is written in bold and filled with a link pointing to the corresponding plot. One image is created by plot and located into the sub-directory "plots/" of path. Each image is named by index-of-component\_var.png. Wilcoxon or Kruskal-Wallis tests are performed depending on the number of groups of interest in the considered variable (argument keepLev).

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#### Value

Returns A data.frame of dimensions 'components x variables' containing the p-values of the non-parametric tests (Wilcoxon or Kruskal-Wallis tests) wich test if the samples groups defined by each variable are differently distributed on the components.

# Author(s)

Anne Biton

#### See Also

```
, \verb"qualVarAnalysis", \verb"p.adjust", \verb"link" \{ \verb"writeHtmlResTestsByAnnot"\}, \verb"wilcox.test", \verb"kruskal.test" \}, \verb"wilcox.test", \verb"wilcox.test", \verb"kruskal.test" ], \verb"wilcox.test", \verb"kruskal.test" ], \verb"wilcox.test", \verb"wilcox.test", \verb"kruskal.test", \verb"wilcox.test", "wilcox.test", "wilcox.test",
```

# **Examples**

quantVarAnalysis

Correlation between variables and components.

# **Description**

This function tests if numeric variables are correlated with components.

# Usage

```
quantVarAnalysis(params, icaSet, keepVar,
  keepComp = indComp(icaSet),
  keepSamples = sampleNames(icaSet),
  adjustBy = c("none", "component", "variable"),
  method = "BH", typeCor = "pearson", doPlot = TRUE,
  onlySign = TRUE, cutoff = 0.4,
  cutoffOn = c("cor", "pval"), colours,
  path = "quantVarAnalysis/", filename = "quantVar",
  typeImage = "png")
```

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# **Arguments**

params	An object of class MineICAParams providing the parameters of the analysis.
icaSet	An object of class IcaSet.
keepVar	The variable labels to be considered, must be a subset of varLabels(icaSet).
keepComp	A subset of components, must be included in indComp(icaSet). By default, all components are used.
keepSamples	A subset of samples, must be included in sampleNames(icaSet). By default, all samples are used.
adjustBy	The way the p-values of the Wilcoxon and Kruskal-Wallis tests should be corrected for multiple testing: "none" if no p-value correction has to be done, "component" if the p-values have to be corrected by component, "variable" if the p-values have to be corrected by variable
method	The correction method, see p.adjust for details, default is "BH" for Benjamini & Hochberg.
doPlot	If TRUE (default), the plots are done, else only tests are performed.
onlySign	If TRUE (default), only the significant results are plotted.
cutoff	A threshold p-value for statistical significance.
cutoffOn	The value the cutoff is applied to, either "cor" for correlation or "pval" for p-value
typeCor	the type of correlation to be used, one of $c("pearson", "spearman", "kendall")$ .
colours	A vector of colours indexed by the variable levels, if missing the colours are automatically generated using annot2Color.
path	A directory _within resPath(params)_ where the files containing the plots and the p-value results will be located. Default is "quantVarAnalysis/".
typeImage	The type of image file to be used.
filename	The name of the HTML file containing the p-values of the tests, if NULL no file

# **Details**

This function writes an HTML file containing the correlation values and test p-values as a an array of dimensions 'variables \* components' containing the p-values of the tests. When a p-value is considered as significant according to the threshold cutoff, it is written in bold and filled with a link pointing to the corresponding plot. One image is created by plot and located into the subdirectory "plots/" of path. Each image is named by index-of-component\_var.png.

# Value

Returns A data.frame of dimensions 'components x variables' containing the p-values of the non-parametric tests (Wilcoxon or Kruskal-Wallis tests) wich test if the samples groups defined by each variable are differently distributed on the components.

# Author(s)

Anne Biton

# See Also

qualVarAnalysis, p.adjust, link{writeHtmlResTestsByAnnot}, code

is created.

56 relativePath

## **Examples**

```
## load an example of IcaSet
data(icaSetCarbayo)
# build MineICAParams object
params <- buildMineICAParams(resPath="carbayo/")</pre>
# Define the directory containing the results
dir <- paste(resPath(params), "comp2annottest/", sep="")</pre>
# pData(icaSetCarbayo)
## Perform pearson correlation tests and plots association corresponding
# to correlation values larger than 0.2
quantVarAnalysis(params=params, icaSet=icaSetCarbayo, keepVar="AGE", keepComp=1:2,
                                              adjustBy="none", path=dir, cutoff=0.2, cutoffOn="cor")
## Not run:
## Perform Spearman correlation tests and do scatter plots for all pairs
quant Var Analysis (params=params, ica Set=ica Set Carbayo, keep Var="AGE", adjust By="none", path=dir, adjust B
                                              cutoff=0.1, cutoffOn="cor", typeCor="spearman", onlySign=FALSE)
## Perform pearson correlation tests and plots association corresponding
# to p-values lower than 0.05 when 'doPlot=TRUE'
quantVarAnalysis(params=params, icaSet=icaSetCarbayo, keepVar="AGE", adjustBy="none", path=dir,
                                              cutoff=0.05, cutoffOn="pval", doPlot=FALSE)
## End(Not run)
```

relativePath

Relative path

# **Description**

Computes the relative path between two imbricated paths

# Usage

```
relativePath(path1, path2)
```

# Arguments

path1 The first path
path2 The second path

# **Details**

path1 and path2 must be imbricated.

# Value

The relative path between path1 and path2

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#### Author(s)

Anne Biton

### **Examples**

```
path1 <- "home/lulu/res/gene2comp/"
path2 <- "home/lulu/res/comp2annot/invasive/"
relativePath(path1,path2)</pre>
```

runAn

Run analysis of an IcaSet object

# **Description**

This function runs the analysis of an ICA decomposition contained in an IcaSet object, according to the parameters entered by the user and contained in a MineICAParams.

# Usage

```
runAn(params, icaSet, keepVar,
  heatmapCutoff = params["selCutoff"],
  funClus = c("Mclust", "kmeans"), nbClus,
  clusterOn = "A", keepComp, keepSamples,
  adjustBy = c("none", "component", "variable"),
  typePlot = c("boxplot", "density"),
  mart = useMart(biomart = "ensembl", dataset = "hsapiens_gene_ensembl"),
  dbGOstats = c("KEGG", "GO"), ontoGOstats = "BP",
  condGOstats = TRUE,
  cutoffGOstats = params["pvalCutoff"],
  writeGenesByComp = TRUE, writeFeaturesByComp = FALSE,
  selCutoffWrite = 2.5, runVarAnalysis = TRUE,
  onlySign = T, runClustering = FALSE, runGOstats = TRUE,
  plotHist = TRUE, plotHeatmap = TRUE)
```

# **Arguments**

funClus

params An object of class MineICAParams containing the parameters of the analysis.

icaSet An object of class IcaSet.

keepVar The variable labels to be considered, i.e a subset of the annotation variables

available in (varLabels(icaSet)).

keepSamples The samples to be considered, i.e a subset of (sampleNames(icaSet)).

heatmapCutoff The cutoff (applied to the scaled feature/gene projections contained in S/SByGene)

used to select the contributing features/genes.

Default is "Mclust".

The function to be used to cluster the samples, must be one of c("Mclust", "kmeans", "pam", "pamk"

nbClus The number of clusters to be computed when applying funClus. Can be missing

(default) if funClus="Mclust" or funClus="pamk".

keepComp The indices of the components to be analyzed, must be included in indComp(icaSet).

If missing, all components are treated.

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adjustBy The way the p-values of the Wilcoxon and Kruskal-Wallis tests should be corrected for multiple testing: "none" if no p-value correction has to be done, "component" if the p-values have to be corrected by component, "annotation"

if the p-values have to be corrected by variable

typePlot The type of plot used to show distribution of sample-groups contributions, either

"density" or "boxplot"

mart A mart object used for annotation, see function useMart

dbGOstats The used database to use ('GO' and/or 'KEGG'), default is both.

ontoGOstats A string specifying the GO ontology to use. Must be one of 'BP', 'CC', or 'MF',

see GOHyperGParams. Only used when argument dbGOstats is 'GO'.

condGOstats A logical indicating whether the calculation should conditioned on the GO struc-

ture, see GOHyperGParams.

cutoffGOstats The p-value threshold used for selecting enriched gene sets, default is params["pvalCutoff"]

writeGenesByComp

If TRUE (default) the gene projections (SByGene(icaSet)) are written in an

html file and annotated using biomaRt for each component.

writeFeaturesByComp

If TRUE (default) the feature projections (S(icaSet)) are written in an html file

and annotated using biomaRt for each component.

runGOstats If TRUE the enrichment analysis of the contributing genes is run for each com-

ponent using package GOstats (default is TRUE).

plotHist If TRUE the position of the sample annotations within the histograms of the

sample contributions are plotted.

plotHeatmap If TRUE the heatmap of the contributing features/genes are plotted for each

component.

runClustering If TRUE the potential associations between a clustering of the samples (per-

formed according to the components), and the sample annotations, are tested

using chi-squared tests.

runVarAnalysis If TRUE the potential associations between sample contributions (contained in

A(icaSet)) are tested using Wilcoxon or Kruskal-Wallis tests.

onlySign If TRUE (default), only the significant results are plotted in functions qualVarAnalysis, quantVar

else all plots are done.

selCutoffWrite The cutoff applied to the absolute feature/gene projection values to select the

features/genes that will be annotated using package biomaRt, default is 2.5.

clusterOn Specifies the matrix used to apply clustering if runClustering=TRUE:

"A": the clustering is performed in one dimension, on the vector of sample con-

tributions,

"S": the clustering is performed on the original data restricted to the contribut-

ing individuals,

"AS": the clustering is performed on the matrix formed by the product of the

column of A and the row of S.

# **Details**

This function calls functions of the MineICA package depending on the arguments:

writeProjByComp (if writeGenesByComp=TRUE or writeFeaturesByComp) which writes in html files the description of the features/genes contributing to each component, and their projection values on all the components.

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plot\_heatmapsOnSel (**if** plotHeatmap=TRUE) which plots heatmaps of the data restricted to the contributing features/genes of each component.

- plotPosAnnotInComp (if plotHist=TRUE) which plots, within the histogram of the sample contribution values of every component, the position of groups of samples formed according to the sample annotations contained in pData(icaSet).
- clusterSamplesByComp (if runClustering=TRUE) which clusters the samples according to each
   component.
- clusVarAnalysis (if runClustering=TRUE) which computes the chi-squared test of association between a given clustering of the samples and each annotation level contained in pData(icaSet), and summarizes the results in an HTML file.
- runEnrich (if runGOstats=TRUE) which perforns enrichment analysis of the contributing genes of the components using package GOstats.
- qualVarAnalysis **and** quantVarAnalysis (**if** varAnalysis=TRUE) which tests if the groups of samples formed according to sample annotations contained in pData(icaSet) are differently distributed on the components, in terms of contribution value.

Several directories containing the results of each analysis are created by the function:

**ProjByComp:** contains the annotations of the features or genes, one file per component;

**varAnalysisOnA:** contains two directories: 'qual/' and 'quant/' which respectively contain the results of the association between components qualitative and quantitative variables;

**Heatmaps:** contains the heatmaps (one pdf file per component) of contributing genes by component;

**varOnSampleHist:** contains athe histograms of sample contributions superimposed with the histograms of the samples grouped by variable;

**cluster2var:** contains the association between a clustering of the samples performed on the mixing matrix A and the variables.

# Value

**NULL** 

# Author(s)

Anne Biton

# See Also

writeProjByComp,

```
## Not run:

## load an example of IcaSet
data(icaSetCarbayo)

## make sure the 'mart' attribute is correctly defined
mart(icaSetCarbayo) <- useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl")

## creation of an object of class MineICAParams
## here we use a low threshold because 'icaSetCarbayo' is already
# restricted to the contributing features/genes</pre>
```

60 runCompareIcaSets

```
params <- buildMineICAParams(resPath="~/resMineICACarbayotestRunAn/", selCutoff=2, pvalCutoff=0.05)
require(hgu133a.db)
runAn(params=params, icaSet=icaSetCarbayo)
## End(Not run)</pre>
```

runCompareIcaSets

runCompareIcaSets

# Description

This function encompasses the comparison of several IcaSet objects using correlations and the plot of the corresponding correlation graph. The IcaSet objects are compared by calculating the correlation between either projection values of common features or genes, or contributions of common samples.

# Usage

```
runCompareIcaSets(icaSets, labAn,
  type.corr = c("pearson", "spearman"), cutoff_zval = 0,
  level = c("genes", "features", "samples"),
  fileNodeDescr = NULL, fileDataGraph = NULL,
  plot = TRUE, title = "", col, cutoff_graph = NULL,
  useMax = TRUE, tkplot = FALSE)
```

# **Arguments**

	T. 0			
icaSets	List of IcaSet objects,	e a recults of ICA	decompositions	obtained on several
ICascis	List of Icaset objects,	c.g results of rem	uccompositions	obtained on several

datasets.

labAn Vector of names for each icaSet, e.g the the names of the datasets on which were

calculated the decompositions.

type.corr Type of correlation to compute, either 'pearson' or 'spearman'.

cutoff\_zval Either NULL or 0 (default) if all genes are used to compute the correlation

between the components, or a threshold to compute the correlation using the genes that have at least a scaled projection higher than cutoff\_zval. Will be used

only when level is one of c("features", "genes").

level Data level of the IcaSet objects on which is applied the correlation. It must

correspond to a data level shared by the IcaSet objects: 'samples' if they were applied to common samples (correlations are computed between matrix A), 'features' if they were applied to common features (correlations are computed between matrix S), 'genes' if they share gene IDs after annotation into

genes (correlations are computed between matrix SByGene).

fileNodeDescr File where node descriptions are saved (useful when the user wants to visualize

the graph using Cytoscape).

fileDataGraph File where graph description is saved (useful when the user wants to visualize

the graph using Cytoscape).

plot if TRUE (default) plot the correlation graph

title title of the graph

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col vector of colors indexed by elements of labAn; if missing, colors will be auto-

matically attributed

cutoff\_graph the cutoff used to select pairs that will be included in the graph

useMax if TRUE, the graph is restricted to edges that correspond to maximum correlation

between components, see details

tkplot If TRUE, performs interactive plot with function tkplot, else uses plot.igraph

#### **Details**

This function calls four functions: compareAn which computes the correlations, compareAn2graphfile which builds the graph, nodeAttrs which builds the node description data, and plotCorGraph which uses tkplot to plot the graph in an interactive device.

If the user wants to see the correlation graph in Cytoscape, he must fill the arguments fileDataGraph and fileNodeDescr, in order to import the graph and its node descriptions as a .txt file in Cytoscape.

When labAn is missing, each element i of icaSets is labeled as 'Ani'.

The user must carefully choose the data level used in the comparison: If level='samples', the correlations are based on the mixing matrices of the ICA decompositions (of dimension samples x components). 'A' will be typically chosen when the ICA decompositions were computed on the same dataset, or on datasets that include the same samples. If level='features' is chosen, the correlation is calculated between the source matrices (of dimension features x components) of the ICA decompositions. 'S' will be typically used when the ICA decompositions share common features (e.g same microarrays). If level='genes', the correlations are calculated on the attributes 'SByGene' which store the projections of the annotated features. 'SByGene' will be typically chosen when ICA were computed on datasets from different technologies, for which comparison is possible only after annotation into a common ID, like genes.

cutoff\_zval is only used when level is one of c('features', 'genes'), in order to restrict the correlation to the contributing features or genes.

When cutoff\_zval is specified, for each pair of components, genes or features that are included in the circle of center 0 and radius cutoff\_zval are excluded from the computation of the correlation.

It must be taken into account by the user that if cutoff\_zval is different from NULL or zero, the computation will be much slowler since each pair of component is treated individually.

Edges of the graph are built based on the correlation values between the components. Absolute values of correlations are used since components have no direction.

If useMax is TRUE each component will be linked to only one component of each other IcaSet that corresponds to the most correlated component among all components of the same IcaSet. If cutoff\_graph is specified, only correlations exceeding this value are taken into account to build the graph. For example, if cutoff is 1, only relationships between components that correspond to a correlation value higher than 1 will be included. Absolute correlation values are used since the components have no direction.

The contents of the returned list are

dataGraph: dataGraph data.frame that describes the correlation graph,

nodeAttrs: nodeAttrs data.frame that describes the node of the graph

graph graph the graph as an igraph-object,

graphid: graphid the id of the graph plotted using tkplot.

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#### Value

A list consisting of

dataGraph: a data.frame defining the correlation graph nodeAttrs: a data.frame describing the node of the graph, graph: the graph as an object of class igraph, graphid the id of the graph plotted with tkplot.

## Author(s)

Anne Biton

#### See Also

compareAn2graphfile, compareAn, cor2An, plotCorGraph

```
dat1 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat1) <- paste("g", 1:1000, sep="")
colnames(dat1) <- paste("s", 1:10, sep="")</pre>
dat2 <- data.frame(matrix(rnorm(10000),ncol=10,nrow=1000))</pre>
rownames(dat2) <- paste("g", 1:1000, sep="")
colnames(dat2) <- paste("s", 1:10, sep="")</pre>
## run ICA
resJade1 <- runICA(X=dat1, nbComp=3, method = "JADE")</pre>
resJade2 <- runICA(X=dat2, nbComp=3, method = "JADE")</pre>
## build params
params <- buildMineICAParams(resPath="toy/")</pre>
## build IcaSet objects
icaSettoy1 <- buildIcaSet(params=params, A=data.frame(resJade1$A), S=data.frame(resJade1$S),</pre>
                             dat=dat1, alreadyAnnot=TRUE)$icaSet
icaSettoy2 <- buildIcaSet(params=params, A=data.frame(resJade2$A), S=data.frame(resJade2$S),</pre>
                             dat=dat2, alreadyAnnot=TRUE)$icaSet
## compare IcaSet objects
## use tkplot=TRUE to get an interactive graph
rescomp <- runCompareIcaSets(icaSets=list(icaSettoy1, icaSettoy2), labAn=c("toy1", "toy2"),</pre>
                                 type.corr="pearson", level="genes", tkplot=FALSE)
## Not run:
## load the microarray-based gene expression datasets
## of breast tumors
library(breastCancerMAINZ)
library(breastCancerVDX)
data(mainz)
data(vdx)
## Define a function used to build two examples of IcaSet objects
## and annotate the probe sets into gene Symbols
treat <- function(es, annot="hgu133a.db") {</pre>
```

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```
es <- selectFeatures_IQR(es,10000)
   exprs(es) <- t(apply(exprs(es),1,scale,scale=FALSE))</pre>
   colnames(exprs(es)) <- sampleNames(es)</pre>
   resJade <- runICA(X=exprs(es), nbComp=10, method = "JADE", maxit=10000)</pre>
  resBuild <- buildIcaSet(params=buildMineICAParams(), A=data.frame(resJade$A), S=data.frame(resJade$S),</pre>
                         dat=exprs(es), pData=pData(es), refSamples=character(0),
                         annotation=annot, typeID= typeIDmainz,
                         chipManu = "affymetrix", mart=mart)
   icaSet <- resBuild$icaSet
}
## Build the two IcaSet objects
icaSetMainz <- treat(mainz)</pre>
icaSetVdx <- treat(vdx)</pre>
## compare the IcaSets
runCompareIcaSets(icaSets=list(icaSetMainz, icaSetVdx), labAn=c("Mainz","Vdx"), type.corr="pearson", level=
## End(Not run)
```

runEnrich

Enrichment analysis through GOstats

# **Description**

This function tests the enrichment of the components of an IcaSet object using package GOstats through function hyperGTest.

# Usage

```
runEnrich(icaSet, params, dbs = c("KEGG", "GO"),
  ontos = c("BP", "CC", "MF"), cond = TRUE,
  hgCutoff = params["pvalCutoff"])
```

# **Arguments**

an object of class IcaSet

An object of class MineICAParams providing the parameters of the analysis

The database to use, default is c("GO", "KEGG")

A string specifying the GO ontology to use. Must be one of "BP", "CC", or "MF", see GOHyperGParams-class. Only used when argument dbs includes "GO".

A logical indicating whether the calculation should condition on the GO structure, see GOHyperGParams-class. Only used when argument dbs includes "GO".

The threshold p-value for statistical significance, default is pvalCutoff(params)

# **Details**

An annotation package should be available in annotation(icaSet) to provide the contents of the gene sets. If none corresponds to the technology you deal with, please choose the org.\*.eg.db package according to the organism (for example org.Hs.eg.db for Homo sapiens). By default, if annotation(icaSet) is empty and organism is one of c("Human", "HomoSapiens", "Mouse", "Mus Musculus"), then either org.Hs.eg.db or org.Mm.eg.db is used.

64 runEnrich

Use of GOstats requires the input IDs to be Entrez Gene, this function will therefore annotate either the feature names or the gene names into Entrez Gene ID using either the annotation package (annotation(icaSet)) or biomaRt.

Three types of enrichment tests are computed for each component: the threshold is first used to select gene based on their absolute projections, then positive and negative projections are treated individually.

For each database db (each ontology if db is "GO"), this function writes an HTML file containing the outputs of the enrichment tests computed through the function hyperGTest. The corresponding files are located in resPath(icaSet)/GOstatsEnrichAnalysis/byDb/. The results obtained for each database/ontology are then merged into an array for each component, this array is written as an HTML file in the directory resPath(icaSet)/GOstatsEnrichmentAnalysis/ (this directory is first deleted if it already exists). This file is the one the user should look at.

The outputs of hyperGTest that are given in each table are:

**DB**, **ID**, **Term:** the database, the gene set ID, and the gene Set name

**P-value:** probability of observing the number of genes annotated for the gene set among the selected gene list, knowing the total number of annotated genes among the universe,

**Expected counts:** expected number of genes in the selected gene list to be found at each tested category term/gene set,

**Odds ratio:** odds ratio for each category term tested which is an indicator of the level of enrichment of genes within the list as against the universe,

**Counts:** number of genes in the selected gene list that are annotated for the gene set,

Size: number of genes from the universe annotated for the gene set.

# Value

NULL

# Author(s)

Anne Biton

### See Also

buildIcaSet, useMart, hyperGTest, GOHyperGParams, hypergeoAn, mergeGostatsResults

```
## Not run:
# Load examples of IcaSet object
data(icaSetCarbayo)

## Define parameters
# Use threshold 3 to select contributing genes on which enrichment analysis will be applied
# Results of enrichment analysis will be written in path 'resPath(params)/GOstatsEnrichAnalysis'
params <- buildMineICAParams(resPath="carbayo/", selCutoff=3)

## Run enrichment analysis on the first two components contained in the icaSet object 'icaSetCarbayo'
runEnrich(params=params,icaSet=icaSetCarbayo[,,1:2],dbs="GO", ontos="BP")

## End(Not run)</pre>
```

runICA 65

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Run of fastICA and JADE algorithms

# **Description**

This function performs ICA decomposition of a matrix using functions fastICA and JADE.

# Usage

```
runICA(method = c("fastICA", "JADE"), X, nbComp,
  alg.type = c("deflation", "parallel"),
  fun = c("logcosh", "exp"), maxit = 500, tol = 10^-6,
   ...)
```

# **Arguments**

method	The ICA method to use, either "JADE" (the default) or "fastICA".
Χ	A data matrix with n rows representing observations (e.g genes) and p columns representing variables (e.g samples).
nbComp	The number of components to be extracted.
alg.type	If alg.type="parallel" the components are extracted simultaneously (the default), if alg.type="deflation" the components are extracted one at a time, see fastICA.
fun	The functional form of the G function used in the approximation to neg-entropy (see 'details' of the help of function fastICA).
maxit	The maximum number of iterations to perform.
tol	A positive scalar giving the tolerance at which the un-mixing matrix is considered to have converged.
	Additional parameters for fastICA and JADE

# **Details**

See details of the functions fastICA and JADE.

# Value

A list, see outputs of fastICA and JADE. This list includes at least three elements:

**A** the estimated mixing matrix

 ${\bf S}$  the estimated source matrix, itemWthe estimated unmixing matrix

# Author(s)

Anne Biton

```
set.seed(2004);
M <- matrix(rnorm(5000*6,sd=0.3),ncol=10)
M[1:10,1:3] <- M[1:10,1:3] + 2
M[1:100,1:3] <- M[1:100,1:3] +1
resJade <- runICA(X=M, nbComp=2, method = "JADE", maxit=10000)</pre>
```

66 selectContrib

# **Description**

This function selects elements whose absolute scaled values exceed a given threshold.

# Usage

```
selectContrib(object, cutoff, level, ...)
```

# **Arguments**

object	Either an IcaSet object, or a list of projection vectors, e.g the list of feature or gene projections on each component.
cutoff	The threshold according to which the elements will be selected. Must be either of length 1 and the same treshold is applied to all components, or of length equal to the number of components in order to use a specific threshold for each component.
level	The level of the selection: either "genes" to select contributing genes using SByGene(icaSet), or "features" to select contributing features using S(icaSet).

# **Details**

Each vector is first scaled and then only elements with an absolute scaled value higher than cutoff are kept.

# Value

A list of projections restricted to the elements that are higher than cutoff.

# Author(s)

Anne Biton

```
## Not run:
## load an example of icaSet
data(icaSetCarbayo)

##### ========
#### When arg 'object' is an IcaSet object
##### ========

## select contributing genes
selectContrib(object=icaSetCarbayo, cutoff=3, level="genes")

## select contributing features
selectContrib(object=icaSetCarbayo, cutoff=3, level="features")
```

selectFeatures\_IQR 67

selectFeatures\_IQR

Selection of features based on their IQR

# **Description**

This function selects the features having the largest Inter Quartile Range (IQR).

# Usage

```
selectFeatures_IQR(data, nb)
```

# **Arguments**

data Measured data of dimension features x samples (e.g, gene expression data)

nb The number of features to be selected

# Value

A subset of data restricted to the features having the nb highest IQR value

# Author(s)

Pierre Gestraud

```
dat <- matrix(rnorm(10000),ncol=10,nrow=1000)
rownames(dat) <- 1:1000
selectFeatures_IQR(data=dat, nb=500)</pre>
```

68 selectWitnessGenes

selectWitnessGenes	selectWitnessGenes

# **Description**

This function selects a gene per component.

# Usage

```
selectWitnessGenes(icaSet, params,
  level = c("genes", "features"), maxNbOcc = 1,
  selectionByComp = NULL)
```

# **Arguments**

icaSet An object of class IcaSet

params An object of class MineICAParams containing the parameters of the analysis,

the attribute cutoffSel is used as the threshold.

level The attribute of icaSet to be used, the witness elements will be either selected

within the "features" or the "genes"

maxNb0cc The maximum number of components where the genes can have an absolute

projection value higher than cutoffSel(params) in order to be selected.

selectionByComp

The list of components already restricted to the contributing genes

# **Details**

Selects as feature/gene witness, for each component, the first gene whose absolute projection is greater than a given threshold in at the most maxNbOcc components. These witnesses can then be used as representatives of the expression behavior of the contributing genes of the components.

When a feature/gene respecting the given constraints is not found, maxNbOcc is incremented of one until a gene is found.

# Value

This function returns a vector of IDs.

## Author(s)

Anne Biton

```
## load an example of IcaSet
data(icaSetCarbayo)

## define parameters: features or genes are considered to be contributor
# when their absolute projection value exceeds a threshold of 4.
params <- buildMineICAParams(resPath="carbayo/", selCutoff=4)

## selection, as gene witnesses, of the genes whose absolute projection is greater than 4</pre>
```

Slist 69

```
# in at the most one component. I.e, a gene is selected as a gene witness of a component
# if he has a large projection on this component only.
selectWitnessGenes(icaSet=icaSetCarbayo, params=params, level="genes", maxNbOcc=1)

## selection, as gene witnesses, of the genes whose absolute projection is greater than 4
# in at the most two components.
# I.e, a gene is selected as a gene witness of a given component if he has a large projection
# in this component and at the most another.
selectWitnessGenes(icaSet=icaSetCarbayo, params=params, level="genes", maxNbOcc=2)
```

Slist

Retrieve feature/gene projections stored in an IcaSet object as a list.

# **Description**

These generic functions retrieve, from an IcaSet object, the feature and gene projections contained in the attribute S and SByGene as a list where feature and gene IDs are preserved.

# Usage

```
Slist(object)
SlistByGene(object)
```

# **Arguments**

object

Object of class IcaSet.

# Value

Slist and SlistByGene return a list whose length equals the number of components contained in the IcaSet object. Each element of this list contains a vector of feature or gene projections indexed by the feature or gene IDs.

# Author(s)

Anne Biton

# See Also

IcaSet-class

70 writeGenes

writeGenes	Description of features using package biomaRt.	
	1 01	

# **Description**

This function annotates IDs (typically gene IDs) provided by the user and returns an html file with their description.

# Usage

```
writeGenes(data, filename = NULL,
  mart = useMart(biomart = "ensembl", dataset = "hsapiens_gene_ensembl"),
  typeId = "hgnc_symbol", typeRetrieved = NULL,
  sortBy = NULL, sortAbs = TRUE, colAnnot = NULL,
  decreasing = TRUE, highlight = NULL, caption = "")
```

# **Arguments**

data	Either a data.frame whose rownames or one of its columns contain the IDs to be annotated, or a vector of IDs.
filename	The name of the HTML file where gene annotations are written.
mart	Output of function useMart from package biomaRt.
typeId	The type of IDs available in data, in the biomaRt way (type listFilters(mart) to choose one).
typeRetrieved	The descriptors uses to annotate the features of data (type listAttributes(mart) to choose one or several).
sortBy	Name of a column of data used to order the output.
sortAbs	If TRUE absolute value of column sortBy is used to order the output.
colAnnot	The column containing the IDs to be annotated, if NULL or missing and argument data is a data.frame, then rownames of data must contain the IDs.
decreasing	If TRUE, the output is sorted by decreasing values of the sortBy column
highlight	IDs to be displayed in colour red in the returned table

# **Details**

caption

"hgnc\_symbol", "ensembl\_gene\_id", "description", "chromosome\_name", "start\_position", "end\_position" and "strand", are automatically added to the list of fields available in argument typeRetrieved queried on biomaRt. The web-links to www.genecards.org and www.proteinatlas.org are automatically added in the columns of the output respectively corresponding to hgnc\_symbol and ensembl\_gene\_id.

# Value

This function returns a data.frame which contains annotations of the input data.

A title for the HTML table

# Author(s)

Anne Biton

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## See Also

```
getBM, listFilters, listAttributes, useMart
```

# **Examples**

```
if (interactive()) {
## define the database to be used
mart <- useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl")</pre>
### Describe:
## a set of hgnc symbols with default descriptions (typeRetrieved=NULL)
genes <- c("TOP2A","E2F3","E2F1","CDK1","CDC20","MKI67")</pre>
writeGenes(data=genes, filename="foo", mart=mart, typeId = "hgnc_symbol")
## a data.frame indexed by hngc symbols, sort output according to column "values", add a title to the HTML out
datagenes <- data.frame(values=rnorm(6),row.names = genes)</pre>
writeGenes(data=datagenes, filename="foo", sortBy = "values", caption = "Description of some proliferation ge
## a set of Entrez Gene IDs with default descriptions
genes <- c("7153","1871","1869","983","991","4288")
writeGenes(data=genes, filename="foo", mart=mart, typeId = "entrezgene")
## Not run:
## add the GO category the genes belong to
## search in listAttributes(mart)[,1] which filter correspond to the Gene Ontology -> "go_id"
writeGenes(data=genes, filename="foo", mart=mart, typeId = "entrezgene", typeRetrieved = "go_id")
## End(Not run)
```

writeProjByComp

writeProjByComp

# **Description**

This function writes in an html file the description of the features, or genes, that contribute to each component. It also writes an html file containing, for each feature or gene, its projection value on every component.

## Usage

```
writeProjByComp(icaSet, params, mart = useMart(biomart = "ensembl",
    dataset = "hsapiens_gene_ensembl"), typeRetrieved = NULL, addNbOcc =
    TRUE, selectionByComp = NULL, level = c("features", "genes"), typeId, selCutoffWrite=2.5)
```

# Arguments

icaSet An object of class IcaSet

params An object of class MineICAParams containing the parameters of the analysis.

The files are written in the path genesPath(params). selCutoff(params) is

used to select the features or genes by component.

mart An output of function useMart containing the database used for annotation.

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typeRetrieved The annotations biomaRt is queried about. They describe the feature or gene

IDs of the argument icaSet, see listFilters.

addNbOcc If TRUE, the number of components the features/genes contribute to is added to

the output. A gene/feature is considered as a contributor of a component if its

absolute scaled projection value is higher than selCutoff(icaSet).

selectionByComp

A list containing the feature/gene projections on each component, already re-

stricted to the ones considered as contributors.

level The data level of icaSet that will be annotated: either the feature projections

("features"), or the gene projections ("genes").

typeId The type of ID the features or the genes of icaSet correspond to. By de-

fault typeID(icaSet) is used. It must be provided in the biomaRt way (type

listFilters(mart) to choose the appropriate value).

selCutoffWrite The cutoff applied to the absolute projection values to select the features/genes

that will be annotated using package biomaRt, default is 2.5.

#### **Details**

One file is created by component, each file is named by the index of the components (indComp(icaSet)) and located in the path genePath(params).

In case you are interested in writing the description of features and their annotations, please remember to modify codegenesPath(params), or the previous files will be overwritten.

The genes are ranked according to their absolute projection values.

This function also writes an html file named "genes2comp" providing, for each feature or gene, the number of components it contributes to (according to the threshold cutoffSel(params)), and its projection value on all the components. The projection values are scaled.

See function writeGenes for details.

## Value

This function returns a list of two elements:

listAnnotComp: a list with the output of writeGenes for each component

**nbOccInComp:** a data.frame storing the projection values of each feature/gene (row) across all the components (columns).

## Author(s)

Anne Biton

# See Also

```
writeGenes, getBM, listFilters, listAttributes, useMart, selectContrib, nbOccInComp
```

```
## Not run:
## load IcaSet object
## We will use 'icaSetCarbayo', whose features are hgu133a probe sets
## and feature annotations are Gene Symbols.
data(icaSetCarbayo)
```

writeRnkFiles 73

```
## define database to be used by biomaRt
mart <- useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl")</pre>
## define the parameters of the analysis
params <- buildMineICAParams(resPath="~/resMineICACarbayo/", selCutoff=0)</pre>
## Make sure the elements "_biomaRt" of attribute 'typeID' are defined
typeID(icaSetCarbayo)
### Query biomaRt and write gene descriptions in HTML files
### The files will be located in the directory 'genesPath(params)'
## 1. Write description of genes
res <- writeProjByComp(icaSet=icaSetCarbayo, params=params, mart=mart,</pre>
           level="genes") #, typeId="hgnc_symbol")
## 2. Write description of features
# change attribute 'genesPath' of params to preserve the gene descriptions
genesPath(params) <- paste(resPath(params), "comp2features/", sep="")</pre>
res <- writeProjByComp(icaSet=icaSetCarbayo, params=params, mart=mart,</pre>
           level="features") #, typeId="affy_hg_u133a")
## End(Not run)
```

writeRnkFiles

Write rnk files containing gene projections

# **Description**

Writes the gene projection values of each component in a '.rnk' file for GSEA.

# Usage

```
writeRnkFiles(icaSet, abs = TRUE, path)
```

# **Arguments**

icaSet An object of class IcaSet

abs If TRUE (default) the absolute projection values are used.

path The path that will contain the rnk files.

# **Details**

The .rnk format requires two columns, the first containing the gene IDs, the second containing the projection values. The genes are ordered by projection values. The files are named "index-of-component\_abs.rnk" if abs=TRUE, or "index-of-component.rnk" if abs=FALSE.

# Value

NULL

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# Author(s)

Anne

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