

Package ‘MetNet’

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Description MetNet contains functionality to infer metabolic network topologies from quantitative data and high-resolution mass/charge information. Using statistical models (including correlation, mutual information, regression and Bayes statistics) and quantitative data (intensity values of features) adjacency matrices are inferred that can be combined to a consensus matrix. Mass differences calculated between mass/charge values of features will be matched against a data frame of supplied mass/charge differences referring to transformations of enzymatic activities. In a third step, the two levels of information are combined to form a adjacency matrix inferred from both quantitative and structure information.

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MetNet-package	<i>Inferring metabolic networks from untargeted high-resolution mass spectrometry data</i>
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Description

Inferring metabolic networks from untargeted high-resolution mass spectrometry data.

Details

The package infers network topologies from quantitative data (intensity values) and structural data (m/z values of mass features). MetNet combines these two data sources to a consensus matrix.

Author(s)

Author: NA Maintainer: NA

References

Breitling, R. et al. Ab initio prediction of metabolic networks using Fourier transform mass spectrometry data. 2006. *Metabolomics* 2: 155–164. 10.1007/s11306-006-0029-z

Examples

```
data("x_test", package = "MetNet")
x_test <- as.matrix(x_test)
functional_groups <- rbind(
  c("Hydroxylation (-H)", "O", "15.9949146221"),
  c("Malonyl group (-H2O)", "C3H2O3", "86.0003939305"),
  c("C6H10O6", "C6H10O6", "178.0477380536"),
  c("D-ribose (-H2O) (ribosylation)", "C5H8O4", "132.0422587452"),
  c("Disaccharide (-H2O)", "C12H20O11", "340.1005614851"),
  c("Glucuronic acid (-H2O)", "C6H8O6", "176.0320879894"),
  c("Monosaccharide (-H2O)", "C6H10O5", "162.0528234315"),
  c("Trisaccharide (-H2O)", "C18H30O15", "486.1584702945"))
functional_groups <- data.frame(group = functional_groups[,1],
  formula = functional_groups[,2],
  mass = as.numeric(functional_groups[,3]))
struct_adj <- structural(x_test, functional_groups, ppm = 5)

stat_adj_l <- statistical(x_test,
  model = c("pearson", "spearman", "bayes"))
args_top1 <- list(n = 10)
stat_adj <- threshold(stat_adj_l, type = "top2", args = args_top1)
cons_adj <- combine(struct_adj, stat_adj)
```

`.AdjacencyMatrix` *Create S4 class AdjacencyMatrix*

Description

The class ‘AdjacencyMatrix’ extends the ‘SummarizedExperiment’ class. It will add the slots ‘type’, ‘directed’, and ‘thresholded’.

Details

The slot ‘type’ is of type “character”, storing the type of the “AdjacencyMatrix”, i.e. “structural”, “statistical”, or “combined”. The slot ‘directed’ is of type “logical”, storing if the adjacency matrix is directed or not. The slot ‘thresholded’ is of type “logical”, storing if the adjacency matrix was thresholded, e.g. if the functions ‘rtCorrection’ or ‘threshold’ were applied on the ‘structural’ or ‘statistical’ ‘AdjacencyMatrix’ objects.

If any of the ‘AdjacencyMatrix’ objects passed to the ‘combine’ function was ‘directed = TRUE’ or ‘thresholded = TRUEs’ the ‘combine’ ‘AdjacencyMatrix’ object will be ‘directed = TRUE’ or ‘thresholded = TRUE’.

Value

class generator function for class ‘AdjacencyMatrix’

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

`.assays_have_identical_colnames_rownames`
Check if all the assays in the ‘AdjacencyMatrix’ object have identical colnames and rownames

Description

The function will check if all the assays in the ‘AdjacencyMatrix’ object have identical colnames and rownames.

Usage

```
.assays_have_identical_colnames_rownames(object)
```

Arguments

object ‘AdjacencyMatrix’ object

Details

Helper function for validity check of 'AdjacencyMatrix' objects.

Value

'logical' of length 1

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

`.assays_have_identical_dimnames`

Check if the assays in the 'AdjacencyMatrix' object have identical dimnames

Description

The function will check if the assays in the 'AdjacencyMatrix' object have identical dimnames.

Usage

```
.assays_have_identical_dimnames(object)
```

Arguments

object 'AdjacencyMatrix' object

Details

Helper function for validity check of 'AdjacencyMatrix' objects.

Value

'logical' of length 1

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

addToList	<i>Add adjacency matrix to list</i>
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Description

This helper function used in the function ‘statistical’ adds an adjacency matrix to a ‘list’ of adjacency matrices.

Usage

```
addToList(l, name, object)
```

Arguments

l	‘list’ of adjacency matrices
name	‘character’, name of added entry
object	‘matrix’ that will be added

Details

The function ‘addToList’ is a helper function used internally in ‘statistical’.

Value

‘list’ containing the existing matrices and the added matrix

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
cor_pearson <- correlation(x, type = "pearson")
cor_spearman <- correlation(x, type = "spearman")
l <- list(pearson = cor_pearson)
MetNet::addToList(l, "spearman_coef", cor_spearman$r)
```

AdjacencyMatrix	<i>Wrapper to create an instance of S4 class AdjacencyMatrix</i>
-----------------	--

Description

The function ‘AdjacencyMatrix’ will create an object of type ‘AdjacencyMatrix’.

Usage

```
AdjacencyMatrix(  
  adj_l,  
  rowData,  
  type = c("structural", "statistical", "combine"),  
  directed = c(TRUE, FALSE),  
  thresholded = c(TRUE, FALSE)  
)
```

Arguments

adj_l	‘list’ of adjacency matrices
rowData	‘data.frame’, containing information on the features
type	‘character’, either “structural”, “statistical”, or “combine”
directed	‘logical’, if the adjacency matrix underlying the graph is directed or undirected
thresholded	‘logical’, if the functions ‘rtCorrection’ or ‘threshold’ were applied on the ‘structural’ or ‘statistical’ ‘AdjacencyMatrix’ objects

Details

‘adj_l’ is a list of adjacency matrices. The adjacency matrices have identical dimensions and ‘dimnames’ and each adjacency matrix has the same number of columns and rows and identical ‘rownames’ and ‘colnames’. ‘rowData’ will be also used for the ‘colData’ slot (since the ‘rownames’ and ‘colnames’ are identical).

Value

object of S4 class ‘AdjacencyMatrix’

Accessors

- The ‘AdjacencyMatrix’ class extends the [SummarizedExperiment::SummarizedExperiment] class and inherits all its accessors and replacement methods.
- The ‘type’ accessor returns the ‘type’ (“structural”, “statistical”, “combine”) slot.
- The ‘directed’ accessor returns the ‘directed’ (‘logical’ of length 1) slot.
- The ‘thresholded’ accessor returns the ‘thresholded’ (‘logical’ of length 1) slot.

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
binary <- matrix(0, ncol = 10, nrow = 10)
transformation <- matrix("", ncol = 10, nrow = 10)
mass_difference <- matrix("", ncol = 10, nrow = 10)

rownames(binary) <- rownames(transformation) <- rownames(mass_difference) <- paste("feature", 1:10)
colnames(binary) <- rownames(transformation) <- rownames(mass_difference) <- paste("feature", 1:10)

binary[5, 4] <- 1
transformation[5, 4] <- "glucose addition"
mass_difference[5, 4] <- "162"

## create adj_l and rowData
adj_l <- list(binary = binary, transformation = transformation,
             mass_difference = mass_difference)
rowData <- DataFrame(features = rownames(binary),
                   row.names = rownames(binary))

AdjacencyMatrix(adj_l = adj_l, rowData = rowData, type = "structural",
                directed = TRUE, thresholded = FALSE)
```

AdjacencyMatrix-class *Methods for 'AdjacencyMatrix' objects*

Description

'length' returns the length of an 'AdjacencyMatrix' object (number of rows of an assay). 'length' returns a 'numeric' of length 1.

'dim' returns the length of an 'AdjacencyMatrix' object (number of rows of an assay, number of cols of an assay). 'dim' returns a 'numeric' of length 2.

'type' will return the type of an 'AdjacencyMatrix' ('statistical', 'structural' or 'combine'). 'type' returns a 'character' of length 1

'directed' returns the information on directed of an 'AdjacencyMatrix', i.e. if the underlying graph is directed or undirected. 'directed' returns 'logical' of length 1.

'thresholded' returns the information if the adjacency matrix is thresholded, i.e. if the function 'rtCorrection' or 'threshold' was applied to the 'AdjacencyMatrix' object. 'thresholded' returns a 'logical' of length 1.

'show' prints summary information on an object of class 'AdjacencyMatrix'.

'as.data.frame' returns the adjacency matrices (stored in the 'assays' slot) and returns information on the nodes and the associated information on edges as a data frame. 'as.data.frame' returns a 'data.frame'.

Usage

```
## S4 method for signature 'AdjacencyMatrix'  
length(x)  
  
## S4 method for signature 'AdjacencyMatrix'  
dim(x)  
  
## S4 method for signature 'AdjacencyMatrix'  
type(x)  
  
## S4 method for signature 'AdjacencyMatrix'  
directed(object)  
  
## S4 method for signature 'AdjacencyMatrix'  
thresholded(object)  
  
## S4 method for signature 'AdjacencyMatrix'  
show(object)  
  
## S4 method for signature 'AdjacencyMatrix'  
as.data.frame(x)
```

Arguments

x	instance of class 'AdjacencyMatrix'
object	instance of class 'AdjacencyMatrix'

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

AllGenerics

Placeholder for generics functions documentation

Description

Placeholder for generics functions documentation

aracne	<i>Create an adjacency matrix based on algorithm for the reconstruction of accurate cellular networks</i>
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Description

'aracne' infers an adjacency matrix using the algorithm for the reconstruction of accurate cellular networks using the 'aracne.a' function from the 'parmigene' package. The function 'aracne' will return the weighted adjacency matrix of the inferred network after applying 'aracne.a'.

Usage

```
aracne(mi, eps = 0.05)
```

Arguments

mi	matrix, where columns and the rows are features (metabolites), cell entries are mutual information values between the features. As input, the mutual information (e.g. raw MI estimates or Jackknife bias corrected MI estimates) from the 'cmi' function of the 'mpmi' package can be used.
eps	numeric, used to remove the weakest edge of each triple of nodes

Details

For more details on the 'aracne.a' function, refer to '?parmigene::aracne.a'. 'aracne.a' considers each triple of edges independently and removes the weakest one if $MI(i, j) < MI(j, k) - eps$ and $MI(i, j) < MI(i, k) - eps$. See Margolin et al. (2006) for further information.

Value

matrix, matrix with edges inferred from Reconstruction of accurate cellular networks algorithm 'aracne.a'

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

References

Margolin et al. (2006): ARACNE : An algorithm for the reconstruction of gene regulatory networks in a mammalian cellular context. BMC Bioinformatics, S7, doi: [10.1186/1471-2105-7-S1-S7](https://doi.org/10.1186/1471-2105-7-S1-S7)

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
x_z <- t(apply(x, 1, function(y) (y - mean(y)) / sd(y)))
mi_x_z <- mpmi::cmi(x_z)$bcmi
aracne(mi_x_z, eps = 0.05)
```

bayes	<i>Create an adjacency matrix based on score-based structure learning algorithm</i>
-------	---

Description

‘bayes’ infers an adjacency matrix using score-based structure learning algorithm ‘boot.strength’ from the ‘bnlearn’ package. ‘bayes’ extracts then the reported connections from running the ‘boot.strength’ function and assigns the strengths of the arcs of the Bayesian connections to an adjacency matrix. ‘bayes’ returns this weighted adjacency matrix.

Usage

```
bayes(x, algorithm = "tabu", R = 100, ...)
```

Arguments

x	‘matrix’ where columns are the samples and the rows are features (metabolites), cell entries are intensity values
algorithm	‘character’, structure learning to be applied to the bootstrap replicates (default is “tabu”)
R	‘numeric’, number of bootstrap replicates
...	parameters passed to ‘boot.strength’

Details

‘boot.strength’ measures the strength of the probabilistic relationships by the arcs of a Bayesian network, as learned from bootstrapped data. By default ‘bayes’ uses the Tabu greedy search.

For use of the parameters used in the ‘boot.strength’ function, refer to ‘?bnlearn::boot.strength’. For further information see also Friedman et al. (1999) and Scutari and Nagarajan (2001).

Value

‘matrix’ with edges inferred from score-based structure learning algorithm ‘boot.strength’

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

References

Friedman et al. (1999): Data Analysis with Bayesian Networks: A Bootstrap Approach. Proceedings of the 15th Annual Conference on Uncertainty in Artificial Intelligence, 196-201.

Scutari and Nagarajan (2011): On Identifying Significant Edges in Graphical Models. Proceedings of the Workshop Probabilistic Problem Solving in Biomedicine of the 13th Artificial Intelligence in Medicine Conference, 15-27.

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
bayes(x, algorithm = "tabu", R = 100)
```

clr	<i>Create an adjacency matrix based on context likelihood or relatedness network</i>
-----	--

Description

‘clr’ infers an adjacency matrix using context likelihood/relatedness network using the ‘clr’ function from the ‘pirmigene’ package. ‘clr’ will return the adjacency matrix containing the Context Likelihood of Relatedness Network-adjusted scores of Mutual Information values.

Usage

```
clr(mi)
```

Arguments

mi	matrix, where columns and the rows are features (metabolites), cell entries are mutual information values between the features. As input, the mutual information (e.g. raw MI estimates or Jackknife bias corrected MI estimates) from the ‘cmi’ function of the ‘mpmi’ package can be used.
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Details

For more details on the ‘clr’ function, refer to ‘?pirmigene::clr’. CLR computes the score $\sqrt{z_i^2 + z_j^2}$ for each pair of variables i, j , where $z_i = \max(0, (I(X_i, X_j) - \text{mean}(X_i)) / \text{sd}(X_i))$. $\text{mean}(X_i)$ and $\text{sd}(X_i)$ are the mean and standard deviation of the mutual information values $I(X_i, X_k)$ for all $k = 1, \dots, n$. For more information on the CLR algorithm see Faith et al. (2007).

Value

matrix, matrix with edges inferred from Context Likelihood of Relatedness Network algorithm ‘clr’

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

References

Faith et al. (2007): Large-Scale Mapping and Validation of Escherichia coli Transcriptional Regulation from a Compendium of Expression Profiles. PLoS Biology, e8, doi: [10.1371/journal.pbio.0050008](https://doi.org/10.1371/journal.pbio.0050008)

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
x_z <- t(apply(x, 1, function(y) (y - mean(y)) / sd(y)))
mi_x_z <- mpmi::cmi(x_z)$bcmi
clr(mi_x_z)
```

combine

Combine structural and statistical 'AdjacencyMatrix' objects

Description

The function 'combine' takes as input the structural and statistical 'AdjacencyMatrix' objects, created in former steps. It will access the assays 'binary' and 'consensus', adds them together and will report a connection between metabolites if the edge is present in both matrices.

'combine' returns an 'AdjacencyMatrix' containing this consensus matrix supported by the structural and statistical adjacency matrices (assays 'combine_binary', 'combine_transformation', and 'combine_mass_difference').

Usage

```
combine(am_structural, am_statistical)
```

Arguments

am_structural 'AdjacencyMatrix' containing 'numeric' structural adjacency matrices (assays 'binary', 'transformation', and 'mass_difference').

am_statistical 'AdjacencyMatrix' containing the assay 'consensus'

Details

The matrices from the assays 'binary' and 'consensus' will be added and an unweighted connection will be reported when the edges are respectively present in both 'binary' and 'consensus'.

Value

'AdjacencyMatrix' object containing the assays 'combine_binary' ('numeric' adjacency matrix), 'combine_transformation' ('character' adjacency matrix), and 'combine_mass_difference' ('character' adjacency matrix).

The 'AdjacencyMatrix' object will also contain all other assays contained in 'am_structural' and 'am_statistical'.

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
data("x_test", package = "MetNet")
x_test <- as.matrix(x_test)
transformation <- rbind(
  c("Monosaccharide (-H2O)", "C6H10O5", "162.0528234315"),
  c("Disaccharide (-H2O)", "C12H20O11", "340.1005614851"),
  c("Trisaccharide (-H2O)", "C18H30O15", "486.1584702945"))
transformation <- data.frame(group = transformation[, 1],
  formula = transformation[, 2],
  mass = as.numeric(transformation[, 3]))

am_struct <- structural(x_test, transformation, ppm = 5)
x_test_cut <- as.matrix(x_test[, -c(1:2)])
am_stat <- statistical(x_test_cut, model = c("pearson", "spearman"),
  correlation_adjust = "bonferroni")
am_stat <- threshold(am_stat, type = "top2", args = list(n = 10))

## combine
combine(am_structural = am_struct, am_statistical = am_stat)
```

correlation

Create an adjacency matrix based on correlation

Description

'correlation' infers an adjacency matrix using correlation using the 'cor' function (from the 'stats' package), 'pcor' (from 'ppcor') or 'spcor' (from 'ppcor'). 'correlation' extracts the reported pairwise correlation coefficients from the function 'corAndPvalue', 'pcor' or 'spcor' and will return the weighted adjacency matrix of the absolute correlation values.

Usage

```
correlation(x, type = "pearson", p.adjust = "none")
```

Arguments

x	matrix, where columns are the samples and the rows are features (metabolites), cell entries are intensity values
type	'character', either "pearson", "spearman", "pearson_partial", "spearman_partial", "pearson_semipartial" or "spearman_semipartial".
p.adjust	'character', method of p-value adjustment passed to 'p.adjust'

Details

If "pearson" or "spearman" is used as a 'method', the function 'corAndPvalue' from 'stats' will be employed.

If "pearson_partial" or "spearman_partial" is used as a 'method' the function 'pcor' from 'spcor' will be employed.

If "pearson_semipartial" or "spearman_semipartial" is used as a 'method' the function 'spcor' from 'spcor' will be employed.

'type' will be passed to argument 'method' in 'cor' (in the case of "pearson" or "spearman") or to 'method' in 'pcor' ("pearson" and "spearman" for "pearson_partial" and "spearman_partial", respectively) or to 'method' in 'spcor' ("pearson" or "spearman" for "pearson_semipartial" and "spearman_semipartial", respectively).

Value

matrix, matrix with edges inferred from correlation algorithm 'corAndPvalue', 'pcor' or 'spcor' (depending on the chosen 'method')

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
correlation(x, type = "pearson")
```

getLinks

Write an adjacency matrix to a 'data.frame'

Description

'getLinks' vectorizes a numerical square 'matrix' and writes the values and their corresponding ranks to a 'data.frame'.

Usage

```
getLinks(mat, exclude = "== 1")
```

Arguments

mat	matrix containing the values of confidence for a link
exclude	'character', logical statement as 'character' to set 'TRUE' values to NaN in 'mat', will be omitted if 'exclude = NULL'

Details

'getLinks' is a helper function used in the function 'threshold'.

Value

'data.frame' with entries 'row', 'col', 'confidence' and 'rank'

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
mat <- matrix(0:8, ncol = 3, nrow = 3)
MetNet:::getLinks(mat, exclude = "== 0")
```

lasso

Create an adjacency matrix based on LASSO

Description

'lasso' infers a adjacency matrix using LASSO using the 'stabsel.matrix' function from the 'stabs' package. 'lasso' extracts the predictors from the function 'stabsel.matrix' and writes the coefficients to an adjacency matrix.

Usage

```
lasso(x, parallel = FALSE, ...)
```

Arguments

x	matrix, where columns are the samples and the rows are features (metabolites), cell entries are intensity values
parallel	logical, should computation be parallelized? If 'parallel = TRUE' the 'bplapply' will be applied if 'parallel = FALSE' the 'lapply' function will be applied.
...	parameters passed to 'stabsel.matrix'

Details

For use of the parameters used in the 'stabsel.matrix' function, refer to '?stabs::stabsel.matrix'.

Value

matrix, matrix with edges inferred from LASSO algorithm 'stabsel.matrix'

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
x_z <- t(apply(x, 1, function(y) (y - mean(y)) / sd(y)))
## Not run: lasso(x_z, PFER = 0.95, cutoff = 0.95)
```

mat_test

Example data for MetNet: unit tests

Description

mat_test contains 7 toy features that were derived from rnorm. It will be used as an example data set in unit tests.

Format

matrix

Value

matrix

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

Source

```
set.seed(1) random_numbers <- rnorm(140, mean = 10, sd = 2) mat_test <- matrix(random_numbers,
nrow = 7) mat_test[1:3, ] <- t(apply(mat_test[1:3, ], 1, sort)) mat_test[5:7, ] <- t(apply(mat_test[5:7,
], 1, sort, decreasing = TRUE)) rownames(mat_test) <- paste("x", 1:7, sep = "")
```

`mat_test_z`*Example data for MetNet: unit tests*

Description

`mat_test_z` contains 7 toy features that were derived from `rnorm`. It will be used as an example data set in unit tests.

Format`matrix`**Value**`matrix`**Author(s)**

Thomas Naake, <thomasnaake@googlemail.com>

Source

```
set.seed(1) random_numbers <- rnorm(140, mean = 10, sd = 2) mat_test <- matrix(random_numbers,
nrow = 7) mat_test[1:3, ] <- t(apply(mat_test[1:3, ], 1, sort)) mat_test[5:7, ] <- t(apply(mat_test[5:7,
], 1, sort, decreasing = TRUE)) rownames(mat_test) <- paste("x", 1:7, sep = "") mat_test_z <- ap-
ply(mat_test, 1, function(x) (x - mean(x, na.rm = TRUE))/sd(x, na.rm = TRUE))
```

`mz_summary`*Create a summary from adjacency list containing mass differences*

Description

The function `mz_summary` creates a summary from the `AdjacencyMatrix`, containing mass differences. Individual mass differences are counted over all features. The input may be an `AdjacencyMatrix` object originating from the function `structural`, or `combine`. The parameter `filter` will define if data will be filtered above a certain threshold or not.

Usage

```
mz_summary(am, filter = 0)
```

Arguments

am	'AdjacencyMatrix', a formal class of 'AdjacencyMatrix' containing the mass differences, that have previously been generated by the function 'structural' or 'combine'
filter	'numeric', leave empty or set to '0' if unfiltered data are required. Select a 'numeric' as a threshold on counts of mz differences. May be useful to visualize big data.

Details

Summarizes the adjacency matrices containing mass difference values, i.e. either adjacency list from 'structural' or 'combine' may be used. The default is filter = F, so the unfiltered summary will be returned. If filter is set to a 'number', e.g. 1000 only mz differences above this threshold will be displayed. The function can be applied for adjacency lists from 'structural' and 'combine'

Value

'data.frame' containing the numbers of present mz differences and corresponding name.

Author(s)

Liesa Salzer, <liesa.salzer@helmholtz-muenchen.de>

Examples

```
data("x_test", package = "MetNet")
transformation <- rbind(
  c("Monosaccharide (-H2O)", "C6H10O5", "162.0528234315"),
  c("Disaccharide (-H2O)", "C12H20O11", "340.1005614851"),
  c("Trisaccharide (-H2O)", "C18H30O15", "486.1584702945"))
transformation <- data.frame(group = transformation[, 1],
                             formula = transformation[, 2],
                             mass = as.numeric(transformation[, 3]))
am_struct <- structural(x_test, transformation, ppm = 5, directed = TRUE)
# unfiltered mz difference counts
mz_summary(am_struct)
# filtered mz difference counts
mz_summary(am_struct, filter = 2)
```

mz_vis

Visualize mass difference distribution

Description

The function 'mz_vis' visualizes the mass difference distribution, which has been summarized by 'mz_summary'.

Usage

```
mz_vis(df)
```

Arguments

`df` 'data.frame', previously generated by 'mz_summary'. Needs to contain the columns "transformation", "mass_difference" and "counts".

Details

Plots the mass difference distribution, summarized by 'mz_summary'. Visualization is performed using ggplot2

Value

'ggplot' object and corresponding barplot for visualizations

Author(s)

Liesa Salzer, <liesa.salzer@helmholtz-muenchen.de>

Examples

```
data("x_test", package = "MetNet")
transformation <- rbind(
  c("Monosaccharide (-H2O)", "C6H10O5", "162.0528234315"),
  c("Disaccharide (-H2O)", "C12H20O11", "340.1005614851"),
  c("Trisaccharide (-H2O)", "C18H30O15", "486.1584702945"))
transformation <- data.frame(group = transformation[, 1],
                             formula = transformation[, 2],
                             mass = as.numeric(transformation[, 3]))
am_struct <- structural(x_test, transformation, ppm = 5, directed = TRUE)
mz_sum <- mz_summary(am_struct)
mz_vis(mz_sum)
```

peaklist

Example data for MetNet: data input

Description

The object peaklist is a data.frame, where rows are features and the columns are samples (starting with X001-180).

Format

data.frame

Value

data.frame

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

Source

Internal peaklist from metabolite profiling of Nicotiana species after W+OS and MeJA treatment. The data was processed by xcms and CAMERA scripts. All unnecessary information is removed, keeping only the columns "mz", "rt" and the respective columns containing the intensity values. All row entries with retention time < 103 s and > 440 s were removed. Entries with m/z values < 250 and > 1200 were removed as well as entries with m/z values between 510 and 600 to reduce the file size.

randomForest

Create an adjacency matrix based on random forest

Description

'randomForest' infers an adjacency matrix using random forest using the 'GENIE3' function from the 'GENIE3' package. 'randomForest' returns the importance of the link between features in the form of an adjacency matrix.

Usage

```
randomForest(x, ...)
```

Arguments

x	matrix, where columns are the samples and the rows are features (metabolites), cell entries are intensity values
...	parameters passed to 'GENIE3'

Details

For use of the parameters used in the 'GENIE3' function, refer to '?GENIE3::GENIE3'. The arguments 'regulators' and 'targets' are set to 'NULL'. Element $w_{i,j}$ (row i, column j) gives the importance of the link from i to j.

Value

matrix, matrix with the importance of the links inferred from random forest algorithm implemented by 'GENIE3'

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
randomForest(x)
```

rtCorrection	<i>Correct connections in the structural adjacency matrices by retention time</i>
--------------	---

Description

The function ‘rtCorrection’ corrects the adjacency matrix inferred from structural data based on shifts in the retention time. For known chemical modifications (e.g. addition of glycosyl groups) molecules with the moiety should elute at a different time (in the case of glycosyl groups the metabolite should elute earlier in a reverse-phase liquid chromatography system). If the connection for the metabolite does not fit the expected behaviour, the connection will be removed (otherwise sustained).

Usage

```
rtCorrection(am, x, transformation)
```

Arguments

am	‘AdjacencyMatrix’ object returned by the function ‘structural’. The object contains the assays “binary”, “transformation”, and “mass_difference”. The assay “binary” stores the ‘numeric’ matrix with edges inferred by mass differences. The assay “transformation” stores the ‘character’ matrix with the type (corresponding to the “group” column in ‘transformation’). The assay “mass_difference” stores the ‘character’ matrix with the type (corresponding to the “mass” column in ‘transformation’).
x	‘matrix’, where columns are the samples and the rows are features (metabolites), cell entries are intensity values, ‘x’ contains the column “rt” that has the rt information (numerical values) for the correction of retention time shifts between features that have a putative connection assigned based on m/z value difference
transformation	‘data.frame’, containing the columns “group”, and “rt” that will be used for correction of transformation of (functional) groups based on retention time shifts derived from ‘x’

Details

‘rtCorrection’ is used to correct the (unweighted) adjacency matrices returned by ‘structural’ when information is available about the retention time and shifts when certain transformation occur (it is meant to filter out connections that were created by m/z differences that have by chance the same m/z difference but different/unexpected retention time behaviour).

'rtCorrection' accesses the assay 'transformation' of 'am' and matches the elements in the "group" column against the character matrix. In case of matches, 'rtCorrection' accesses the "rt" column of 'x' and calculates the retention time difference between the features. 'rtCorrection' then checks if the observed retention time difference matches the expected behaviour (indicated by "+" for a higher retention time of the feature with the putative group, "-" for a lower retention time of the feature with the putative group or "?" when there is no information available or features with that group should not be checked). In case several transformation were assigned to a feature/feature pair connections will always be removed if there is an inconsistency with any of the given transformation.

Value

'AdjacencyMatrix' containing the slots 'binary', 'transformation', and 'mass_difference'. The slot 'directed' is inherited from 'am'

. The first entry stores the 'numeric' 'matrix' with edges inferred mass differences corrected by retention time shifts. The second entry stores the 'character' matrix with the type (corresponding to the "group" column in 'transformation') is stored.

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
data("x_test", package = "MetNet")
transformation <- rbind(
  c("Monosaccharide (-H2O)", "C6H10O5", "162.0528234315", "-"),
  c("Disaccharide (-H2O)", "C12H20O11", "340.1005614851", "-"),
  c("Trisaccharide (-H2O)", "C18H30O15", "486.1584702945", "-"))
transformation <- data.frame(group = transformation[, 1],
  formula = transformation[, 2],
  mass = as.numeric(transformation[, 3]),
  rt = transformation[, 4])
am_struct <- structural(x = x_test, transformation = transformation, ppm = 5)
am_struct_rt <- rtCorrection(am = am_struct, x = x_test,
  transformation = transformation)
```

statistical

Create an 'AdjacencyMatrix' object containing assays of adjacency matrices from statistical methods

Description

The function 'statistical' infers adjacency matrix topologies from statistical methods and returns matrices of these networks in an 'AdjacencyMatrix' object. The function includes functionality to calculate adjacency matrices based on LASSO (L1 norm)-regression, random forests, context likelihood of relatedness (CLR), the algorithm for the reconstruction of accurate cellular networks

(ARACNE), Pearson correlation (also partial and semipartial), Spearman correlation (also partial and semipartial) and score-based structure learning (Bayes). The function returns an ‘Adjacency-Matrix’ object of adjacency matrices that are defined by ‘model’.

Usage

```
statistical(x, model, ...)
```

Arguments

x	‘matrix’ that contains intensity values of features/metabolites (rows) per sample (columns).
model	‘character’ vector containing the methods that will be used (“lasso”, “randomForest”, “clr”, “aracne”, “pearson”, “pearson_partial”, “pearson_semipartial”, “spearman”, “spearman_partial”, “spearman_semipartial”, “bayes”)
...	parameters passed to the functions ‘lasso’, ‘randomForest’, ‘clr’, ‘aracne’, ‘correlation’ and/or ‘bayes’

Details

The function ‘statistical’ includes functionality to calculate adjacency matrices based on LASSO (L1 norm)-regression, random forests, context likelihood of relatedness (CLR), the algorithm for the reconstruction of accurate cellular networks (ARACNE), Pearson correlation (also partial and semipartial), Spearman correlation (also partial and semipartial) and Constraint-based structure learning (Bayes).

‘statistical’ calls the function ‘lasso’, ‘randomForest’, ‘clr’, ‘aracne’, ‘correlation’ (for “pearson”, “pearson_partial”, “pearson_semipartial”, “spearman”, “spearman_partial”, “spearman_semipartial”) and/or ‘bayes’ as specified by ‘model’. It will create adjacency matrices using the specified methods and will return an ‘AdjacencyMatrix’ containing the weighted adjacency matrices in the ‘assays’ slot.

Internally ‘x’ will be z-scaled and the z-scaled object will be used in ‘lasso’, ‘clr’ and/or ‘aracne’.

The slot ‘type’ is set to ‘statistical’. The slot ‘directed’ is set to ‘TRUE’ if the methods “lasso”, “randomForest”, or “bayes” were used, otherwise ‘directed’ is set to ‘FALSE’. The slot ‘threshold’ is set to ‘FALSE’.

Value

‘AdjacencyMatrix’ containing the respective adjacency matrices in the ‘assay’ slot as specified by ‘model’

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```
data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
statistical(x = x, model = c("pearson", "spearman"))
statistical(x = x, model = c("pearson", "spearman"), p.adjust = "BH")
```

structural

Create adjacency matrix based on m/z (molecular weight) difference

Description

The function 'structural' infers an unweighted adjacency matrix using differences in m/z values that are matched against a 'data.frame' of calculated theoretical differences of loss/addition of functional groups. 'structural' returns an 'AdjacencyMatrix' object containing the unweighted 'numeric' 'matrix' (assay 'binary'), together with a 'character' 'matrix' with the type of loss/addition (assay 'transformation'), and the 'character' 'matrix' with the mass differences (assay 'mass_difference').

Usage

```
structural(x, transformation, ppm = 5, directed = FALSE)
```

Arguments

x	'matrix', where columns are the samples and the rows are features (metabolites), cell entries are intensity values. 'x' contains the column "mz" that has the m/z information (numerical values) for the calculation of mass differences between features
transformation	'data.frame', containing the columns "group", and "mass" that will be used for detection of transformation of (functional) groups
ppm	'numeric', mass accuracy of m/z features in parts per million (ppm)
directed	'logical', if 'TRUE', absolute values of m/z differences will be taken to query against 'transformation' (irrespective the sign of 'mass') and undirected adjacency matrices will be returned as the respective assays. This means, if there is a negative mass in 'transformation[, "mass"]', this negative mass will not be reported. If 'FALSE', directed adjacency matrices will be returned with links reported that match the transformations defined in 'transformation' (respecting the sign of 'mass'). The 'directed' slot of the returned 'AdjacencyMatrix' object will contain the information on 'directed'.

Details

'structural' accesses the column "mz" of 'x' to infer structural topologies based on the functional groups defined by 'transformation'. To account for the mass accuracy of the dataset 'x', the user can specify the accuracy of m/z features in parts per million (ppm) by the 'ppm' argument. The

m/z values in the "mz" column of 'x' will be converted to m/z ranges according to the 'ppm' argument (default 'ppm = 5').

The returned 'AdjacencyMatrix' object contains the assays 'binary', 'transformation', and 'mass_difference'. The 'type' slot is set to 'structural'. The 'directed' slot is set accordingly to the 'directed' argument of the function 'structural'. The 'thresholded' slot is set to 'FALSE'.

Value

'AdjacencyMatrix' object. The object will store the adjacency matrices in the assay slots. The first entry stores the 'numeric' 'matrix' with binary edges inferred from mass differences. The second entry stores the 'character' 'matrix' with the type (corresponding to the "group" column in 'transformation') is stored. The third entry stores the 'character' 'matrix' with the 'mass_difference' information (corresponding to the "mass" column in 'transformation').

Author(s)

Thomas Naake, <thomasnaake@googlemail.com> and Liesa Salzer <liesa.salzer@helmholtz-muenchen.de>

Examples

```
data("x_test", package = "MetNet")
transformation <- rbind(
  c("Monosaccharide (-H2O)", "C6H10O5", "162.0528234315"),
  c("Disaccharide (-H2O)", "C12H20O11", "340.1005614851"),
  c("Trisaccharide (-H2O)", "C18H30O15", "486.1584702945"))
transformation <- data.frame(group = transformation[, 1],
                             formula = transformation[, 2],
                             mass = as.numeric(transformation[, 3]))
am_struct <- structural(x_test, transformation, ppm = 5, directed = TRUE)
```

threeDotsCall	<i>Check if passed arguments match the function's formal arguments and call the function with the checked arguments</i>
---------------	---

Description

The function 'threeDotsCall' gets the formal arguments of a function 'fun' and checks if the passed arguments '...' matches the formal arguments. 'threeDotsCall' will call the function 'fun' with the filtered arguments and will return the result of the function call and the given arguments.

Usage

```
threeDotsCall(fun, ...)
```

Arguments

fun	'function' to check for arguments and to call
...	arguments to be tested to be passed to 'fun'

Details

Used internally in ‘lasso’, ‘randomForest’, ‘bayes’, ‘statistical’ and ‘threshold’.
 ‘threeDotsCall’ will not remove duplicated arguments and throw an error.

Value

Returned object given the function call with passed arguments

Author(s)

Thomas Naake, <thomasnaake@gmail.com>

Examples

```
MetNet::threeDotsCall(stats::sd, x = 1:10, y = 1:10)
## in contrast to the above example, the following example will result in an
## error
## Not run: stats::sd(x = 1:10, y = 1:10)
```

 threshold

Threshold the statistical adjacency matrices

Description

The function ‘threshold’ takes as input an ‘AdjacencyMatrix’ object containing adjacency matrices as returned from the function ‘statistical’. Depending on the ‘type’ argument, ‘threshold’ will identify the strongest link that are lower or higher a certain threshold (‘type = “threshold”’) or identify the top ‘n’ links (‘type’ either “top1”, “top2” or “mean”). It will return this kind of information as a binary matrix in the form of an ‘AdjacencyMatrix’ object.

Usage

```
threshold(
  am,
  type = c("threshold", "top1", "top2", "mean"),
  args,
  values = c("all", "min", "max")
)
```

Arguments

am ‘AdjacencyMatrix’ object of ‘type’ “statistical” as created from the function ‘statistical’. The object will contain the adjacency matrices in the ‘assay’ slot.

type ‘character’, either “threshold”, “top1”, “top2” or “mean”

args	<p>'list'. Depending on the 'type' arguments the list element will be different.</p> <p>In the case of 'type == "threshold"', 'args' has the entry 'filter' ('character' of length 1). The character vector will specify the kind of filtering applied to the adjacency matrices. Elements in 'filter' will refer to the 'assayNames', e.g. 'list(filter = "pearson_coef > 0.8")' will retain all edges with Pearson correlation coefficients > 0.8. 'list(filter = "pearson_coef > 0.8 & spearman_coef > 0.5")' will retain all edges with Pearson correlation coefficients > 0.8 AND Spearman correlation coefficients > 0.5. 'list(filter = "abs(pearson_coef) > 0.8 & spearman_coef > 0.5")' will retain all edges with Pearson correlation coefficients > 0.8 and < -0.8.</p> <p>In the case of 'type == "top1"', 'type == "top2"', or 'type == "mean"', 'args' has the entry 'n' ('numeric' of length 1), that denotes the number of top ranks written to the consensus matrix.</p>
values	<p>'character', take from the adjacency matrix all values ("all"), the minimum of the pairs ("min") or the maximum ("max") $a^{*_ij} = \min(a_{ij}, a_{ji})$ $a^{*_ij} = \max(a_{ij}, a_{ji})$</p>

Details

'values' has to be set carefully depending on if the 'AdjacencyMatrix' object 'am' is 'directed' or not.

In the case of 'type == "threshold"', 'args' has the entry 'filter' ('character' of length 1). The character vector will specify the kind of filtering applied to the adjacency matrices. Elements in 'filter' will refer to the 'assayNames', e.g. 'list(filter = "pearson_coef > 0.8")' will retain all edges with Pearson correlation coefficients > 0.8. 'list(filter = "pearson_coef > 0.8 & spearman_coef > 0.5")' will retain all edges with Pearson correlation coefficients > 0.8 AND Spearman correlation coefficients > 0.5. 'list(filter = "abs(pearson_coef) > 0.8 & spearman_coef > 0.5")' will retain all edges with Pearson correlation coefficients > 0.8 and < -0.8.

If 'type' is equal to "'top1'", "'top2'" or "'mean'", then 'args' has to contain a numeric vector of length 1 that gives the number of top ranks included in the returned adjacency matrix. In this case values that are 0 for the models 'lasso', 'randomForest' and 'bayes' are set to 'NaN'; values from correlation (Pearson and Spearman, including for partial and semipartial correlation) and 'aracne' are taken as they are.

For 'type = "top1"', the best (i.e. lowest) rank in 'am' is taken. For 'type = "top2"', the second best (i.e. second lowest) rank in 'am' is taken. For 'type = "mean"', the average rank in 'am' is taken. Subsequently the first 'n' unique ranks are returned.

Value

'AdjacencyMatrix' object containing a binary adjacency matrix given the links supported by the 'type' and the 'args' (in the slot "'consensus'"). The object will furthermore contain the supplied data input, i.e. all assays from 'am'. The slot 'threshold' is set to 'TRUE'.

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Examples

```

data("x_test", package = "MetNet")
x <- x_test[1:10, 3:ncol(x_test)]
x <- as.matrix(x)
model <- c("pearson", "spearman")
args <- list()
am_stat <- statistical(x, model = model)

## type = "threshold"
args <- list(filter = "pearson_coef > 0.95 & spearman_coef > 0.95")
threshold(am = am_stat, type = "threshold", args = args)

## type = "top1"
args <- list(n = 10)
threshold(am = am_stat, type = "top1", args = args)

## type = "top2"
threshold(am = am_stat, type = "top2", args = args)

## type = "mean"
threshold(am = am_stat, type = "mean", args = args)

```

topKnet

Return consensus ranks from a matrix containing ranks

Description

‘topKnet’ returns consensus ranks depending on the ‘type’ argument from ‘ranks’, a matrix containing the ranks per statistical ‘model’.

Usage

```
topKnet(ranks, type)
```

Arguments

ranks	‘matrix’ containing the ranks per statistical model (in columns) and per feature pair (in rows)
type	‘character’, either “top1”, “top2” or “mean”

Details

See Hase et al. (2014) for further details.

Value

‘numeric’ ‘vector’ with consensus ranks

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

References

Hase et al. (2014): Harnessing Diversity towards the Reconstructing of Large Scale Gene Regulatory Networks. PLoS Computational Biology, 2013, e1003361, doi: [10.1371/journal.pcbi.1003361](https://journals.plos.org)

Examples

```
ranks <- matrix(c(c(1, 2, 3), c(2, 1, 3)), ncol = 2)

## type = "top1"
MetNet::topKnet(ranks = ranks, type = "top1")

## type = "top2"
MetNet::topKnet(ranks = ranks, type = "top2")

## type = "mean"
MetNet::topKnet(ranks = ranks, type = "mean")
```

x_annotation

Example annotation for MetNet: data input

Description

x_annotation contains one selected putative annotation of x_test. Missing annotations are filled with 'NA's. It will be used as an example annotation in the vignette to show the functionality of the packages.

Format

matrix

Value

matrix

Author(s)

Liesa Salzer, <liesa.salzer@helmholtz-muenchen.de>

Source

```

data("x_test", package = "MetNet")
x_annotation <- x_test[,1:2]
x_annotation <- cbind(x_annotation,"database_mz" = NA, "database_identifier" = NA, "chemical_formula" = NA, "smiles" = NA, "inchi" = NA, "inchikey" = NA, "metabolite_identification" = NA, "fragmentations" = NA, "modifications" = NA, "charge" = NA, "database" = NA)
x1856 <- cbind(x_annotation["x1856", "mz"], x_annotation["x1856", "rt"], "database_mz" = 308.2, "database_identifier" = "N-caffeoylspermidine", "chemical_formula" = "C16H25N3O3", "smiles" = "C=1(C=C(C(=CC1)O)O)/C=C/C(NCCCNCCCCN)=O", "inchi" = "InChI=1S/C16H25N3O3/c17-8-1-2-9-18-10-3-11-19-16(22)7-5-13-4-6-14(20)15(21)12-13/h4-7,12,18,20-21H,1-3,8-11,17H2,(H,19,22)/b7-5+", "inchikey" = "AZSUJBAOTYNFDE-FNORWQNLSA-N", "metabolite_identification" = NA, "fragmentations" = NA, "modifications" = NA, "charge" = 1, "database" = NA)
x_annotation[rownames(x_annotation) == "x1856",] <- x1856 x_annotation <- x_annotation[,-c(1:2)]

```

x_test

*Example data for MetNet: data input***Description**

x_test contains 36 selected metabolic features of peaklist. It will be used as an example data set in the vignette to show the functionality of the packages.

Format

matrix

Value

matrix

Author(s)

Thomas Naake, <thomasnaake@googlemail.com>

Source

```

data("peaklist_example", package = "MetNet") peaklist[, 3:dim(peaklist)[2]] <- apply(peaklist[, 3:dim(peaklist)[2]], 2, function(x) x / quantile(x, 0.75)) peaklist[, 3:dim(peaklist)[2]] <- log2(peaklist[, 3:dim(peaklist)[2]] + 1)
## function to add specific features of x (defined by m/z and retention ## time) to x_test addTo_x_test <- function(x_test, x, mz, rt) mzX <- x[, "mz"] rtX <- x[, "rt"] new <- x[mzX>(mz-0.01) & mzX<(mz+0.01) & rtX>(rt-0.01) & rtX<(rt+0.01), ] x_test <- rbind(x_test, new) return(x_test)
## Nicotianoside IX M+Na+ 739.3515 rt 426.1241 x_test <- peaklist[peaklist[, "mz"] > 739.35 & peaklist[, "mz"] < 739.36 & peaklist[, "rt"] > 426.18 & peaklist[, "rt"] < 426.2, ] ## Lyciumoside

```

```
I M+Na+ 653.3497 x_test <- addTo_x_test(x_test, peaklist, mz = 653.3497, rt = 417.46) ## LyciumosideII M+Na+ 815.4043 x_test <- addTo_x_test(x_test, peaklist, mz = 815.40, rt = 383.60)
## Nicotianoside X M+Na+ 825.3503 x_test <- addTo_x_test(x_test, peaklist, mz = 825.35, rt = 434.38) ## Nicotianoside XI M+Na+ 901.39913 x_test <- addTo_x_test(x_test, peaklist, mz = 901.40, rt = 391.15) ## NicotianosideXII M+Na+ 987.4037 x_test <- addTo_x_test(x_test, peaklist, mz = 987.40, rt = 398.46) ## NicotianosideXIII M+Na+ 1074.4042 x_test <- addTo_x_test(x_test, peaklist, mz = 1074.40, rt = 404.92) ## Lyciumoside IV M+Na+ 799.4091 x_test <- addTo_x_test(x_test, peaklist, mz = 799.40, rt = 411.23) ## Nicotianoside I M+Na+ 885.4084 x_test <- addTo_x_test(x_test, peaklist, mz = 885.41, rt = 420.12) ## Nicotianoside II M+Na+ 971.4074 x_test <- addTo_x_test(x_test, peaklist, mz = 971.41, rt = 428.81) ## Nicotianoside III M+Na+ 945.4653 x_test <- addTo_x_test(x_test, peaklist, mz = 945.46, rt = 402.75) ## Nicotianoside IV M+Na+ 1031.4645 x_test <- addTo_x_test(x_test, peaklist, mz = 1031.46, rt = 412.40) ## Nicotianoside V M+Na+ 1117.4681 x_test <- addTo_x_test(x_test, peaklist, mz = 1117.46, rt = 422.19) ## Attenoside (or DTG956) M+Na+ 961.4601 x_test <- addTo_x_test(x_test, peaklist, mz = 961.46, rt = 380.46) ## DTG1042/Nicotianoside VI M+Na+ 1047.4525 x_test <- addTo_x_test(x_test, peaklist, mz = 1047.46, rt = 387.28) ## Nicotianoside-VII M+Na+ 1133.4624 x_test <- addTo_x_test(x_test, peaklist, mz = 1133.46, rt = 394.70) ## NicotianosideVIII M+Na+ 1219.4619 x_test <- addTo_x_test(x_test, peaklist, mz = 1219.46, rt = 400.99) ## N-coumaroylputrescine [M+H+] 235.143 x_test <- addTo_x_test(x_test, peaklist, mz = 235.14, rt = 193.85) ## N',N''-coumaroyl,caffeoylspermidine [M+H+] 454.23 x_test <- addTo_x_test(x_test, peaklist, mz = 454.23, rt = 264.43) ## N-caffeoylputrescine isomer 1 [M+H+] 251.14 x_test <- addTo_x_test(x_test, peaklist, mz = 251.14, rt = 108.34) ## N-caffeoylputrescine isomer 2 [M+H+] 251.14 x_test <- addTo_x_test(x_test, peaklist, mz = 251.14, rt = 143.11) ## N-caffeoylspermidine [M+H+] 308.2 x_test <- addTo_x_test(x_test, peaklist, mz = 308.2, rt = 246.71) ## N-feruloylputrescine [M+H+] 265.153 x_test <- addTo_x_test(x_test, peaklist, mz = 265.15, rt = 191.55) ## N-feruloyl-spermidine iso1 [M+H+] 322.212 x_test <- addTo_x_test(x_test, peaklist, mz = 322.21, rt = 104.13) ## N-feruloyl-spermidine iso2 [M+H+] 322.212 x_test <- addTo_x_test(x_test, peaklist, mz = 322.21, rt = 147.98) ## N'-N''-dicaffeoyl -spermidine [M+H+] 470.23 x_test <- addTo_x_test(x_test, peaklist, mz = 470.23, rt = 247.15) ## N'-N''-diferuloyl-spermidine/ ##N#,N$-Coumaroyl,sinapoyl spermidine isomer [M+H+] 498.260/498.261 x_test <- addTo_x_test(x_test, peaklist, mz = 498.26, rt = 289.05) ## N'-N''-dihydrated-diferuloyl-spermidine [M+H+] 502.25 x_test <- addTo_x_test(x_test, peaklist, mz = 502.25, rt = 242.55) ## unknown conjugate [M+H+] 411.2012 x_test <- addTo_x_test(x_test, peaklist, mz = 411.20, rt = 211.67) ## N'-N''-caffeoyl,feruloyl spermidine iso1 [M+H+] 484.245 x_test <- addTo_x_test(x_test, peaklist, mz = 484.24, rt = 264.44) ## N'-N''-caffeoyl,feruloyl spermidine iso2 [M+H+] 484.245 x_test <- addTo_x_test(x_test, peaklist, mz = 484.24, rt = 270.65) ## O -Coumaroylquinic acid isomer 1 [M+H+] 339.109 x_test <- addTo_x_test(x_test, peaklist, mz = 339.11, rt = 248.79) ## O -Coumaroylquinic acid isomer 1 [M+H+] 339.109 x_test <- addTo_x_test(x_test, peaklist, mz = 339.11, rt = 268.97) ## O-caffeoylquinic acid isomer 1 [M+H+] 355.1014 x_test <- addTo_x_test(x_test, peaklist, mz = 355.10, rt = 175.75) ## O-caffeoylquinic acid isomer 2 [M+H+] 355.1014 x_test <- addTo_x_test(x_test, peaklist, mz = 355.10, rt = 215.85) ## O-caffeoylquinic acid isomer 3 [M+H+] 355.1014 x_test <- addTo_x_test(x_test, peaklist, mz = 355.10, rt = 241.04)

## change rownames (that it is accepted by formulas) rownames(x_test) <- paste0("x", rownames(x_test))
```


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