

Package ‘HiResTEC’

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Type Package

Title Non-Targeted Fluxomics on High-Resolution Mass-Spectrometry Data

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Description Identifying labeled compounds in a ^{13}C -tracer experiment in non-targeted fashion is a cumbersome process. This package facilitates such type of analyses by providing high level quality control plots, deconvoluting and evaluating spectra and performing a multitude of tests in an automatic fashion.

The main idea is to use changing intensity ratios of ion pairs from peak list generated with 'xcms' as candidates and evaluate those against base peak chromatograms and spectra information within the raw measurement data automatically.

The functionality is described in Hoffmann et al. (2018) <doi:10.1021/acs.analchem.8b00356>.

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URL <https://pubs.acs.org/doi/10.1021/acs.analchem.8b00356>

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CalcMID

CalcMID.

Description

CalcMID will compute a MID (Mass Isotopomer Distribution) based on measured ion intensities in GC-APCI-MS.

Usage

```
CalcMID(int = NULL, fml = "", ratio = NULL, nmz = NULL,
        nbio = NULL)
```

Arguments

int	Vector of measured ion intensities of a fragment.
fml	Chemical formula of fragment.
ratio	If NULL M+H/M+ ratio will be determined from the data if necessary. Can be specified explicitly here.
nmz	Attached as attr to fml for CalcTheoreticalMDV .
nbio	Attached as attr to fml for CalcTheoreticalMDV .

Details

Let's assume we measured the ion intensities of all 3 isotopes of an individual compound containing 2 carbons and observe a vector of 978,22,0. We may calculate the enrichment (E) out of this data, i.e. the relative proportion of ^{13}C vs total carbon which will amount to about 1.1 The equivalent MID vector would be 1,0,0, indicating that the non-labeled isotopologue (where non-labeled means non-labeled above the natural 1.1 During a labelling experiment we may change the measurement values in different ways (either labelling only one carbon or both), which potentially can translate into similar values for E being larger 1.1 The MIDs will provide additional information about the isotopologue fraction which gave rise to the observed E's (cf. examples).

Value

Percent representation of each isotopologue measured (=MIDs).

Examples

#tbd

CalcTheoreticalMDV *CalcTheoreticalMDV.*

Description

CalcTheoreticalMDV will compute the Mass Distribution Vectors of isotopologues as it is used for correction matrix in [CalcMID](#) computations.

Usage

```
CalcTheoreticalMDV(fml = NULL)
```

Arguments

fml The chemical formula of the compound.

Details

CalcTheoreticalMDV basically is a convenience function using `Rdisop` to generate the isotopologue distribution at natural abundance of ^{13}C for a given formula. It will break this down into a matrix where the components of the MID constitute the rows and the expected relative ion intensities are within the columns. The number of exported ion intensities and MID components can be limited if numeric values for "nmz" and/or "nbio" provided as attributes with the formula.

Value

A matrix with dimensions according to the attributes of fml or the number of carbons respectively.

Examples

```
# standard distribution matrix
fml <- "C5H6Si1"
CalcTheoreticalMDV(fml=fml)
attr(fml,"nmz") <- 4
CalcTheoreticalMDV(fml=fml)
attr(fml,"nbio") <- 2
CalcTheoreticalMDV(fml=fml)
```

DeconvoluteSpectrum *DeconvoluteSpectrum.*

Description

DeconvoluteSpectrum will evaluate a list of xcmsRaw objects at a given time (rt) and potential mass (mz1). The main purpose is to deconvolute the mass spectrum at rt including mz1.

Usage

```
DeconvoluteSpectrum(dat = NULL, rt = NULL, rt_dev = 3, mz1 = NULL,
  mz_dev = 0.003, use.mz.adjust = FALSE, ionization = c("APCI",
  "ESI")[1], smooth = 0)
```

Arguments

dat	A list of xcmsRaws or an xcmsSet object.
rt	Retention time to search for maxima.
rt_dev	Allowed retention time window.
mz1	If specified, ensure that this mass is included in the spectrum (assumed base peak). NULL otherwise.
mz_dev	Allowed mz deviation [Da].
use.mz.adjust	Will adjust mz on an experiment wide basis.
ionization	Either APCI or ESI. Choice will modify some internal parameters and checks performed.
smooth	Smoothing parameter passed on to getMultipleBPC .

Details

Will test all mz at spectrum of base peak within range for co-apex, rt diff and ratio consistency/correlation over a set of samples.

Value

A pseudo spectrum at rt (containing mz1 if specified). Effectively a 2-column matrix (mz, int) with rt as attribute

Examples

```
# Please use examples from previous versions as xcms (and xcms objects)
# are no longer supported during CRAN checks leading to package rejection
# if included (and I do not know a work around). :(
```

```
EvaluateCandidateListAgainstRawData
  EvaluateCandidateListAgainstRawData.
```

Description

EvaluateCandidateListAgainstRawData will analyze an xcmsSet result for mass pairs (mz1, mz2) with changes due to ¹³C incorporation.

Usage

```
EvaluateCandidateListAgainstRawData(x = NULL, tp = NULL, gr = NULL,
  dat = NULL, dmz = 0.025, drt = 1, dEcut = 1, Pcut = 0.01,
  Icut = 1000, method = c("APCI", "ESI")[1], rolp = c("non", "pos",
  "neg", "all")[2], smooth = 0)
```

Arguments

x	Dataframe of results (output of EvaluatePairsFromXCMSet).
tp	Timepoint.
gr	group, e.g. different genotypes or concentrations.
dat	list of xcmsRaw's for deconvolution and plotting.
dmz	Allowed mass deviation in Da (for BPC extraction).
drt	Allowed rt deviation in seconds (for get extraction).
dEcut	Minimum required change in enrichment before a candidate ID is assigned.
Pcut	Maximum allowed P value before a candidate ID is assigned.
Icut	Minimum required median peak intensity before a candidate ID is assigned.
method	Either APCI or ESI. Choice will modify some internal parameters and checks performed.
rolp	RemoveOverlappingPeaks paramter.
smooth	Smoothing parameter passed to getMultipleBPC .

Details

This function will evaluate candidate mz pairs found within an `xcmsSet` object by [EvaluatePairsFromXCMSSet](#) against the raw measurement data. A special parameter is `'rolp'` which can be set to `'non'`, `'pos'`, `'neg'` or `'all'`. It will influence the time performance of the function by determining how many peaks are effectively tested. If `'rolp'` is set to `'non'`, no overlapping peaks will be skipped, every individual mz-pair will be sequentially evaluated (slow but most informative). If it is set to `'pos'` or `'neg'`, overlapping peaks (determined by experiment wide deconvolution) will not be tested additionally for positive or negative hits (`'neg'` is standard). If set to `'all'` overlapping peaks will always be removed from the list of mz-pairs to be tested (fast).

Value

A list of evaluation results.

Examples

```
# Please use examples from previous versions as xcms (and xcms objects)
# are no longer supported during CRAN checks leading to package rejection
# if included (and I do not know a work around). :(
```

EvaluatePairsFromXCMSSet

EvaluatePairsFromXCMSSet.

Description

`EvaluatePairsFromXCMSSet` will analyze an `xcmsSet` result for mass pairs (`mz1`, `mz2`) with changes due to any ¹³C incorporation.

Usage

```
EvaluatePairsFromXCMSSet(xg = NULL, tp = NULL, gr = NULL, drt = 1,
  dmz = 0.025, mz_iso = 1.00335, n = 6, method = c("APCI",
  "ESI")[1], specific_row = NULL, testing = FALSE, silent = FALSE)
```

Arguments

<code>xg</code>	<code>xcmsSet</code> object with group information.
<code>tp</code>	Timepoint information for all samples (obviously required, internally converted to factor).
<code>gr</code>	Group information for all samples, e.g. different genotypes or concentrations (optional, factor).
<code>drt</code>	Allowed rt deviation in time units of <code>xcmsSet</code> (usually seconds) to test for candidates.
<code>dmz</code>	Allowed mass deviation in Da.

mz_iso	Mass defect of the isotope under investigation.
n	Number of maximal incorporated carbons to test.
method	Currently APCI or ESI. If APCI, dmz will be modified depending on n (see details).
specific_row	A single row from groupval(xg) to process.
testing	Stop in function using browser() if specific_row is specified; can be a isotope number, i.e. 3 will stop at third isotope.
silent	Suppress warnings and console output if TRUE.

Details

Using 'APCI' as method assumes that (i) you analyze TMS-derivatized compounds and (ii) your MS resolution does not allow to separate Si and C isotopes but reports an intermediate mass as m/z. In this case you will find carbon isotopes below their expected masses, i.e. M+1 would be 1.001mDa apart from M+0 instead of 1.003. The effect is increased with isotope number, i.e. M+6 will be ~20mDa below the expected value. Hence, selecting method 'APCI' will combine your selected dmz with a allowed deviation due to Si-isotope caused mass shifts. Use 'ESI' if you are not sure if this effect takes place in your settings.

Value

A dataframe with all observable pairs within the provided xcmsSet peak list including mean group intensities and P values.

GenerateCandXLSX	<i>GenerateCandXLSX.</i>
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Description

GenerateCandXLSX will produce a XLSX of a list containing test results objects.

Usage

```
GenerateCandXLSX(res_list = NULL, xlsx_file = NULL, rejected = FALSE)
```

Arguments

res_list	A list of result objects (each testing an individual mz pair).
xlsx_file	File name.
rejected	Logical. Return rejected if TRUE.

Details

Not yet.

Value

Candidate table as data.frame.

Examples

```
#load evaluation result of example data
data(res_list)
#generate table within R (use xlsx_file to write to file)
str(GenerateCandXLSX(res_list))
GenerateCandXLSX(res_list)[,1:5]
```

GenerateQCPlots

GenerateQCPlots.

Description

GenerateQCPlots will produce QC plots for a list containing test results objects.

Usage

```
GenerateQCPlots(res_list = NULL, pdf_file = NULL, mfrow = NULL,
  skip_plots = NULL)
```

Arguments

res_list	A list of result objects (each testing an individual mz pair).
pdf_file	Either APCI or ESI. Choice will modify some internal parameters and checks performed.
mfrow	If NULL automatically determined, otherwise useful to specify a layout.
skip_plots	NULL or numeric vector in which case plots with numbers in skip_plots will be empty.

Details

For individual candidates screen output is reasonable, otherwise a target PDF file should be specified.

Value

NULL.

Examples

```
#load evaluation result of example data
data(res_list)
#generate Figures on screen (use PDF output for mass evaluation)
GenerateQCPlots(res_list[1])
```

getMultipleBPC	<i>getMultipleBPC.</i>
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Description

getMultipleBPC will extract multiple BPCs from an xcmsRaw object for a vector of mz within the limits given by rt, rt_dev and mz_dev.

Usage

```
getMultipleBPC(x, mz = NULL, mz_dev = 0.005, rt = NULL, rt_dev = 2,  
  zeroVal = NA, smooth = 0, returnEIC = FALSE)
```

Arguments

x	xcmsRaw object.
mz	mass vector.
mz_dev	allowed deviations (can be a single numeric, a vector, a matrix with one row (lower bound, upper bound) or a matrix with length(mz) rows giving lower and upper bound for each mz).
rt	target timepoint.
rt_dev	allowed window.
zeroVal	Set values <=0 to NA or keep as is with NULL.
smooth	Window size for moving average smoother, 0 = no smoothing.
returnEIC	Return EIC instead of BPC?

Details

While there are other functions to extract BPC information from raw data, this one is particularly useful to get all traces belonging to a isotopologue group. It will attach several derived values to the results object, i.e. describing the observed mass shift (deviation from expected value) which is helpful in QC for non-targeted tracer analyses.

Value

A matrix with scan wise (rows) intensities for all requested masses (columns) as either EIC or BPC.

References

Uses C code modified from XCMS (see citation("xcms")).

Examples

```
# see \link{plotMID} for an example
```

mz_shift_corrector	<i>Predefined mass search windows to be used internally.</i>
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Description

This is a list defining windows for high res APCI or ESI instrumentation..

Author(s)

Jan Lisec <jan.lisec@bam.de>

plotBPC	<i>plotBPC.</i>
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Description

plotBPC will plot for each item of a list of result-objects from [getMultipleBPC](#) the BPC traces and the spectrum at the scan where the summed intensity of all ions is max.

Usage

```
plotBPC(bpc = NULL, mfrow = NULL, skip_plots = NULL, ylim = NULL,
        col = NULL, ids = NULL, type = "both")
```

Arguments

bpc	A bpc object (list of intensity matrixes, rt x mz, including several attributes as attached by getMultipleBPC).
mfrow	Specify mfrow explicitly (is optimized internally if NULL to cover n=length(bpc)).
skip_plots	Allows to block certain subplots in the mfrow matrix to better align replicates.
ylim	Can be specified specifically, will be adjusted to overall min/max otherwise.
col	Specific color vector for masses may be provided.
ids	Specific plot ids may be explicitly provided.
type	Switch between co-plot of BPC and Spectrum ("both") or BPC alone ("bpc").

Details

not yet

Value

A plot to the graphics device and NULL as invisible.

Examples

```
#load example raw data
data(res_list)
plotBPC(bpc = res_list[[1]][["bpc"]][c(1:2,13:14)])
```

plotMID

plotMID.

Description

plotMID will plot a Mass Isotopomer Distribution (MID) as calculated by CalcMID.

Usage

```
plotMID(mid = NULL, gr = NULL, name = "unknown", contr = NULL,
        stackedbars = FALSE, subplot_yylim = 100, ...)
```

Arguments

mid	Matrix of measured ion intensities corrected using CalcMID.
gr	Groups, a factor.
name	Name of metabolite.
contr	Contrasts. Not yet clear if useful.
stackedbars	Alternative plotting layout using stacked bar plot.
subplot_yylim	Calculate ylim individually per subplot if 0, show full range in all subplots if 100 and limit to the minimal specified number otherwise.
...	Further arguments to 'boxplot'.

Details

Not yet.

Value

NULL.

Examples

```
mid <- matrix(c(seq(0,0.3,0.1), seq(1,0.7,-0.1)), byrow=TRUE, nrow=2)
gr <- gl(2,2,labels=letters[1:2])
plotMID(mid=mid, gr=gr, name="Metabolite X")
plotMID(mid=mid, gr=gr, stackedbars=TRUE, las=1, col=2:3, xlab="MID")
```

res_list	<i>The main results object of a non-targeted search for tracer incorporation.</i>
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Description

This is a list containing the evaluations results established based on processing example data with [EvaluateCandidateListAgainstRawData](#).

Author(s)

Jan Lisec <jan.lisec@bam.de>

sam	<i>Sample table</i>
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Description

This data frame contains the sample definition of 18 samples from a larger experiment.

Author(s)

Jan Lisec <jan.lisec@bam.de>

xcms_cand	<i>Dataframe with putative candidates</i>
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Description

This data frame contains the analysis result of an xcmsSet which can not be provided via CRAN anymore using [EvaluatePairsFromXCMSSet](#) with respect to interesting m/z-pairs.

Author(s)

Jan Lisec <jan.lisec@bam.de>

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