Package 'MOMA'

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Title Multi Omic Master Regulator Analysis

Version 1.23.0

Description This package implements the inference of candidate master regulator proteins from multi-omics' data (MOMA) algorithm, as well as ancillary analysis and visualization functions.

Depends R (>= 4.0)

License GPL-3

Encoding UTF-8

LazyData true

BugReports https://github.com/califano-lab/MOMA/issues

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Imports circlize, cluster, ComplexHeatmap, dplyr, ggplot2, graphics, grid, grDevices, magrittr, methods, MKmisc, MultiAssayExperiment, parallel, qvalue, RColorBrewer, readr, reshape2, rlang, stats, stringr, tibble, tidyr, utils

Suggests BiocStyle, knitr, rmarkdown, testthat, viper

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Contents

`areaEnrich` *aREA.enrich Compute aREA enrichment between all pairwise combinations of VIPER proteins and gene-level events*

Description

aREA.enrich Compute aREA enrichment between all pairwise combinations of VIPER proteins and gene-level events

Usage

```
areaEnrich(events.mat, vipermat, event.type, verbose)
```

Arguments

`events.mat`	A Binary 0/1 matrix with columns as samples, and rows as proteins
`vipermat`	A VIPER network of inferred activity scores with columns as samples, and rows as proteins
`event.type`	Name of the event type for printing purposes
`verbose`	whether to print extra progress statements

Value

A matrix of enrichment scores with rows as event/gene names and columns as VIPER protein names

---

`associateEvents` *Use 'aREA' to calculate the enrichment between each genomic event - VIPER inferred protein pair.*

Description

Requires pre-computed VIPER scores and a binary events matrix. Will use only samples in both event and VIPER matrices.

Usage

```
associateEvents(
  vipermat,
  events.mat,
  min.events = NA,
  whitelist = NA,
  event.type = c("Amplifications", "Deletions", "Mutations", "Fusions", NA),
  verbose
)
```

Arguments

vipermat	Pre-computed VIPER scores with samples as columns and proteins as rows
events.mat	Binary 0/1 events matrix with samples as columns and genes or events as rows
min.events	Only compute enrichment if the number of samples with these events is GTE to this
whitelist	Only compute associations for events in this list
event.type	Name of the event type being analyzed
verbose	whether to print extra progress statements

Value

A matrix of aREA scores, dimensions are nrow(events.mat) x nrow(vipermat)

---

checkGeneMap *Check Gene Map*

Description

Check Gene Map

Usage

```
checkGeneMap(gene.loc.mapping)
```

Arguments

gene.loc.mapping	dataframe with gene names, entrez ids and cytoband locations

Value

nothing

checkList *Check List of Assays*

Description

Check List of Assays

Usage

```
checkList(assaylist)
```

Arguments

assaylist	list of assays (viper, cnv, mut and fusion)

Value

updated/filter assaylist obj

checkMAE *Check MultiAssayExperiment*

Description

Check MultiAssayExperiment

Usage

```
checkMAE(mae)
```

Arguments

mae	MultiAssayExperiment object

Value

updated/filtered MAE

checkPathways *Check Pathways*

Description

Check Pathways

Usage

```
checkPathways(pathways, x, type)
```

Arguments

pathways	A named list of lists. Each named list represents interactions between proteins (keys) and their associated partners
x	the MAE or Assaylist
type	whether x is MAE or Assaylist

Value

nothing

clusterRange *Cluster Range*

Description

This function generate an cluster structure with 'k' groups and computes the cluster reliability score where 'k' is a range of values

Usage

```
clusterRange(
  dis,
  range = c(2, 100),
  step = 1,
  cores = 1,
  method = c("pam", "kmeans"),
  data = NULL
)
```

Arguments

dis	Distance object
range	vector with start and end 'k'
step	Integer indicating the incremental number of clusters to add in each iteration
cores	Maximum number of CPU cores to use
method	Either 'pam' k-mediods or kmeans. Must supply the original data matrix if using kmeans
data	Original data matrix

Value

list of cluster reliability scores by 'k', 'clustering' (the vector solution) and 'reliability' as well as 'medoids' labels

---

clusterReliability *Cluster membership reliability estimated by enrichment analysis*

Description

This function estimates the cluster membership reliability using aREA

Usage

```
clusterReliability(
  cluster,
  similarity,
  xlim = NULL,
  method = c("element", "cluster", "global")
)
```

Arguments

cluster	Vector of cluster memberships or list of cluster memberships
similarity	Similarity matrix
xlim	Optional vector of 2 components indicating the limits for computing AUC
method	Character string indicating the mthod to compute reliability, either by element, by cluster or global

Value

Reliability score for each element

cnvScoreStouffer *Integrate CNV scores*

Description

Integrate CNV scores

Usage

```
cnvScoreStouffer(
  mapping,
  diggit.interactions,
  cytoband = TRUE,
  from.p = FALSE,
  pos.nes.only = TRUE
)
```

Arguments

mapping	a named vector of genomic locations/cytoband IDs. names are the gene names for each–i.e. a many to one mapping from HUGO or entrez IDs to cytoband location
diggit.interactions	list indexed by MR/TF name in Entrez Space each points to a named vector of NES / z-scores associated with entrez IDs for each interacting event.
cytoband	Boolean to use cytoband locations for computing final integrated score
from.p	Boolean, set TRUE if diggit.interaction values are p-values instead of z-scores
pos.nes.only	Boolean, only consider positive DIGGIT association scores when ranking candidate MRs (default=TRUE)

Value

A vector of z-scores, named by the Master Regulators in 'diggit.interactions'

conditionalModel *Implements the conditional Bayes model to combine VIPER scores with diggit and pathway scores*

Description

Implements the conditional Bayes model to combine VIPER scores with diggit and pathway scores

Usage

```
conditionalModel(viper.scores, diggit.scores, pathway.scores)
```

Arguments

viper.scores	numeric Vector
diggit.scores	List indexed by type char, with numeric score vectors in [0,R+] for each
pathway.scores	List , double indexed by each pathway dataset, then with type char. Each points to a numeric score vectors in [0,R+] for each

Value

a named vector of empirical p-values for each protein/candidate Master Regulator

---

conditionalP *Get the conditional p-value of a gene*

Description

Get the conditional p-value of a gene

Usage

```
conditionalP(gene.name, condition.on, x)
```

Arguments

gene.name	Character
condition.on	named Vector of scores for the distribution we are conditioning ON
x	named Vector of scores for the dependent distribution

Value

a numeric p-value between 0 and 1

---

empiricalP *Get the empirical p-value from a distribution (vector)*

Description

Get the empirical p-value from a distribution (vector)

Usage

```
empiricalP(gene.name, x)
```

Arguments

gene.name	Character
x	named Vector of scores for the distribution

Value

a numeric p-value between 0 and 1

---

example.gbm.mae *Glioblastoma (GBM) Example Dataset*

Description

MultiAssayExperiment Object containing all the genomic assays needed to run the example code for MOMA

Usage

```
example.gbm.mae
```

Format

An MultiAssayExperiment object with 4 different sets of GBM assays

viper matrix of viper scores with samples in columns and regulators across the rows

mut matrix of samples and genes with potential mutations. 0 for no mutation, 1 for presence of some non-silent mutation

cnv matrix of samples and genes with copy number variant scores

---

fitCurvePercent *Fit based on fractional overall coverage of genomic events*

Description

Fit based on fractional overall coverage of genomic events

Usage

```
fitCurvePercent(sweep, frac = 0.85)
```

Arguments

sweep	Numeric vector of genomic coverage values, named by -k- threshold
frac	Fraction of coverage to use as a threshold (default .85 = 85 percent)

Value

The -k- integer where coverage is acheived

gbm.pathways *Glioblastoma (GBM) Pathways*

Description

Object containing information about the biological pathways that will be used in the analysis

Usage

```
gbm.pathways
```

Format

A list of lists named "cindy" and "preppi" respectively

cindy list of regulators, each with a set of modulators and p values representing their CINDY inferred association

preppi list of regulators, each with a set of potential binding partners and PREPPi inferred p values for probability of binding

gene.map *Gene Location Mapping*

Description

Table used for converting between different forms of gene information. Downloaded from HGNC's custom download portal using the "Approved Symbol", "NCBI Gene ID", "Chromosome" and "Ensembl Gene ID" curated data options and only those with "Approved" status. Updated December 2019.

Usage

```
gene.map
```

Format

A Data frame with 4 columns

Gene.Symbol Approved Symbol gene name

Entrez.IDs NCBI Gene ID

Cytoband Chromosome location

Ensembl Ensembl gene ID

@source https://www.genenames.org/download/custom/

genomicPlotSmall *Make small genomic plot*

Description

Make small genomic plot

Usage

```
genomicPlotSmall(input.df, fraction = 0.85, tissue.cluster = NULL)
```

Arguments

input.df	: tissue.coverage.df with mean, k, fraction and unique events.
fraction	: what fraction coverage to use for genomic curve threshold
tissue.cluster	: which cluster subsample to look at

Value

output .png

---

getCoverage *Get coverage of interactions*

Description

Get coverage of interactions

Usage

```
getCoverage(
  MomaObject,
  cMR.ranking,
  viper.samples,
  topN = 100,
  mutation.filter = NULL,
  verbose = FALSE
)
```

Arguments

MomaObject	A numeric vector with cluster membership, names are samples
cMR.ranking	A vector entrez IDs, in order
viper.samples	Calculate the genomic coverage only for these sample
topN	Compute coverage for only the top -N- Master Regulators
mutation.filter	Retain only mutation events in this (positive) list

Value

A list of lists, indexed by sample name, with coverage statistics for each sample

---

`getDataFrame` *Helper function to get data frame for bar plot plot.events function*

Description

Helper function to get data frame for bar plot plot.events function

Usage

```
getDataFrame(
  data,
  highlight.genes,
  genomeBand_2_gene,
  max.muts = 10,
  max.cnv = 5
)
```

Arguments

`data`	data.frame with $type, $id, $Freq per event
`highlight.genes`	genes to look for in mutations/cnv lists (if looking for specific genes because of prior knowledge)
`genomeBand_2_gene`	mapping of genomic location IDs to gene name: vector of HUGO gene ids, named by genomic loci
`max.muts`	maximum number of mutations to get per sample, default is 10
`max.cnv`	maximum number of cnvs to per sample, default is 5

Value

ordered data frame with each genomic event and it's frequency

getDiggitEmpiricalQvalues

Compute the empirical q-values of each genomic-event/VIPER gene pair

Description

Use against the background distribution of associations with a given set of 'null' VIPER genes (i.e. low activity TFs)

Usage

```
getDiggitEmpiricalQvalues(vipermat, nes, null.TFs, alternative = "both")
```

Arguments

vipermat	viper inferences matrix, samples are columns, rows are TF entrez gene IDs
nes	scores for each mutation (rows) against each TF (columns)
null.TFs	low-importance TFs used to calculate null distributions
alternative	Alternative defaults to 'both' : significant p-values can come from both sides of the null distribution

Value

A named list of qvalues for each TF/cMR protein. Each entry contains a vector of q-values for all associated events; names are gene ids

getEmpiricalQvals *Get empirical qvals*

Description

Get empirical qvals

Usage

```
getEmpiricalQvals(test.statistics, null.statistics, alternative = "both")
```

Arguments

test.statistics	P-values generated from the test comparisons
null.statistics	P-values generated under the null (permutation) model
alternative	Optional : 1 or 2 tails used to generate the p-value

Value

A list with both the qvalues and empirical p-values from the supplied test and null stats

---

`getPvalsMatrix` *Utility function*

Description

Utility function

Usage

```
getPvalsMatrix(corrected.scores)
```

Arguments

`corrected.scores`
- corrected p-values processed by 'qvals' package

Value

A matrix of p-values for scores between genes/events (rows) and TFs (columns)

`getSubtypeEventTables` *Helper function to get subtype specific events*

Description

Helper function to get subtype specific events

Usage

```
getSubtypeEventTables(saturation.data, sample.clustering, checkpoints)
```

Arguments

`saturation.data`
: genomic saturation object from MOMA. List indexed by cluster then sample then regulator with the number of events associated with each additional regulator

`sample.clustering`
: clustering vector with sample names and cluster designations

`checkpoints` : from momaObj

Value

a table that has counts of how many times a particular event happens in a cluster

integrateFunction *Numerical integration of functions*

Description

Integrates numerically a function over a range using the trapezoid method

Usage

```
integrateFunction(f, xmin, xmax, steps = 100, ...)
```

Arguments

f	Function of 1 variable (first argument)
xmin	Number indicating the min x value
xmax	Number indicating the max x value
steps	Integer indicating the number of steps to evaluate
...	Additional arguments for f

Value

Number

integrateTZ *Integration with trapezoid method*

Description

This function integrate over a numerical range using the trapezoid method

Usage

```
integrateTZ(x, y)
```

Arguments

x	Numeric vector of x values
y	Numeric vector of y values

Value

Number

makeCoverageDf *Helper function for making the coverage dataframe*

Description

Helper function for making the coverage dataframe

Usage

```
makeCoverageDf(coverage.list, cutoff)
```

Arguments

coverage.list	: List indexed by sample name, contains mut/fus/amp/del interactions
cutoff	: number of regulators to include

Value

dataframe with each sample and which events are captured by the checkpoint mrs

makeSaturationPlots *Main function to generate the summary plots of the analysis*

Description

Main function to generate the summary plots of the analysis

Usage

```
makeSaturationPlots(
  momaObj,
  clustering.solution = NULL,
  important.genes = NULL,
  fCNV = NULL,
  max.events = 30
)
```

Arguments

momaObj	: momaObj that has already run the saturationCalculation function
clustering.solution	: clustering vector with sample names and cluster designations
important.genes	: vector of gene names to prioritize when plotting. Can be general genes of interest, oncogenes, tumor supressors etc

fCNV	: vector of confirmed functional CNVs if calculated. Will filter for only those CNVs
max.events	: maximum number of events to plot for the oncoplots

Value

object with both types of summary plot for each subtype

Examples

```
## Not run:
makeSaturationPlots(momaObj, max.events = 20)

## End(Not run)
```

---

mapEntrez *Convert from entrez ids to hugo gene names*

Description

Convert from entrez ids to hugo gene names

Usage

```
mapEntrez(entrez.ids)
```

Arguments

entrez.ids	: vector of entrez ids requires hugo2entrez to be loaded

Value

: vector of hugo gene names

See Also

mapHugo

Examples

```
mapEntrez(c("29974", "5728"))
```

mapHugo *Convert from hugo gene names to entrez ids*

Description

Convert from hugo gene names to entrez ids

Usage

```
mapHugo(hugo.ids)
```

Arguments

hugo.ids	: vector of hugo gene names, requires hugo2entrez to be loaded

Value

: vector of entrez ids

See Also

mapEntrez

Examples

```
mapHugo(c("A1CF","PTEN"))
```

mapScoresCnvBand *Map scores to cytoband location*

Description

Map scores to cytoband location

Usage

```
mapScoresCnvBand(
  mapping,
  diggit.interactions,
  from.p = FALSE,
  pos.nes.only = TRUE
)
```

Arguments

mapping	a named vector of genomic locations/cytoband IDs. names are the gene names for each–i.e. a many to one mapping from HUGO or entrez IDs to cytoband location
diggit.interactions	list indexed by MR/TF name in Entrez Space
from.p	DIGGIT interactions are in p-value format instead of z-score (default=FALSE)
pos.nes.only	Only consider positive associations with NES scores (default=TRUE) each points to a named vector of NES / z-scores associated with entrez IDs for each interacting event.

Value

A list of input scores, now named by cytoband location

---

mergeData *Helper function for mergeDataBySubtype*

Description

Helper function for mergeDataBySubtype

Usage

```
mergeData(coverage.range, topN)
```

Arguments

coverage.range	: genomic saturation for a particular subtype
topN	: max number of top regulators to search through

Value

dataframe with coverage data for genomic events

`mergeDataBySubtype` *Create data frame from coverage data, including number of total events 'covered' and unique events*

Description

Create data frame from coverage data, including number of total events 'covered' and unique events

Usage

```
mergeDataBySubtype(genomic.saturation, sample.clustering, topN = 100)
```

Arguments

`genomic.saturation`	: data from genomic saturation function
`sample.clustering`	: clustering vector with sample names and cluster designations
`topN`	: number of regulators to look through. default is 100

Value

dataframe with coverage data for genomic events

`mergeGenomicSaturation` *mergeGenomicSaturation Create data frame from coverage data, including number of total events 'covered' and unique events*

Description

mergeGenomicSaturation Create data frame from coverage data, including number of total events 'covered' and unique events

Usage

```
mergeGenomicSaturation(coverage.range, topN)
```

Arguments

`coverage.range`	List indexed by sample, then sub-indexed by # of master regulators, then by event type (mut/amp/del/fus). Holds all events by sample
`topN`	Maximum number of master regulators to compute coverage

Value

A data frame with summary statistics for genomic saturation at each k

mergeLists *Helper function*

Description

Helper function

Usage

```
mergeLists(l1, l2)
```

Arguments

l1	list 1
l2	list 2

Value

single merged list

Moma-class *MOMA Object*

Description

Main class encapsulating the input data and logic of the MOMA algorithm

Fields

`viper` matrix of inferred activity score inferred by viper

`mut` binary mutation matrix 1 for presence of mutation, 0 for not, NA if not determined

`cnv` matrix of cnv values. Can be binary or a range.

`fusions` binary matrix of fusion events if appliable

`pathways` list of pathways/connections to consider as extra evidence in the analysis

`gene.blacklist` character vector of genes to not include because of high mutation frequency

`output.folder` character vector of location to save files if desired

`gene.loc.mapping` data frame of gene names, entrez ids and cytoband locations

`nes` field for saving Normalized Enrichment Matrices from the associate events step

`interactions` field for saving the MR-interactions list

`clustering.results` results from clustering are saved here

`ranks` results field for ranking of MRs based on event association analysis

`hypotheses` results field for saving events that have enough occurences to be considered

`genomic.saturation` results field for genomic saturation analysis

`coverage.summaryStats` results field for genomic saturation analysis

`checkpoints` results field with the MRs determined to be the checkpoint for each cluster

`sample.clustering` field to save sample clustering vector. Numbers are cluster assignments, names are sample ids

Methods

`Cluster( clus.eval = c("reliability", "silhouette"), use.parallel = FALSE, cores = 1 )` Cluster the samples after applying the MOMA weights to the VIPER scores

`makeInteractions( genomic.event.types = c("amp", "del", "mut", "fus"), cindy.only = FALSE )` Make interaction web for significant MRs based on their associated events

`Rank( use.cindy = TRUE, genomic.event.types = c("amp", "del", "mut", "fus"), use.parallel = FALSE, cores =` Rank MRs based on DIGGIT scores and number of associated events

`runDIGGIT(fCNV = NULL, cnvthr = 0.5, min.events = 4, verbose = FALSE)` Run DIGGIT association function to get associations for driver genomic events

`saturationCalculation( clustering.solution = NULL, cov.fraction = 0.85, topN = 100, verbose = FALSE )` Calculate the number of MRs it takes to represent the desired coverage fraction of events

---

`MomaConstructor` *MOMA Constructor Function*

Description

Create MOMA Object from either a MultiAssayExperiment object or a list of assays. See vignette for more information on how to set up and run the MOMA object

Usage

```
MomaConstructor(
  x,
  pathways,
  gene.blacklist = NA_character_,
  output.folder = NA_character_,
  gene.loc.mapping = gene.map,
  viperAssay = "viper",
  mutMat = "mut",
  cnvMat = "cnv",
  fusionMat = "fusion"
)
```

Arguments

x	A MultiAssayExerperiment object or list object with the following assays: (note: by default assays must have these exact names. Otherwise they can be changed using the viperAssay, mutMat, cnvMat and fusionMat parameters.) **viper** VIPER protein activity matrix with samples as columns and rows as protein IDs **mut** An indicator matrix (0/1) of mutation events with samples as columns and genes as rows **cnv** A matrix of CNV scores (typically SNP6 array scores from TCGA) with samples as columns and genes as rows **fusion** An indicator matrix (0/1) of fusion events with samples as columns and genes as rows
pathways	A named list of lists. Each named list represents interactions between proteins (keys) and their associated partners
gene.blacklist	A vector of genes to exclude from the analysis
output.folder	Location to store output and intermediate results
gene.loc.mapping	A data.frame of band locations and Entrez IDs
viperAssay	name associated with the viper assay in the assay object
mutMat	name associated with the mutation matrix in the assay object
cnvMat	name associated with the cnv matrix in the assay object
fusionMat	name associated with the fusion matrix in the assay object

Value

an instance of class Moma

Examples

```
momaObj <- MomaConstructor(example.gbm.mae, gbm.pathways)
```

---

mutSig *MutSig Blacklisted genes*

Description

List of genes to not include in the DIGGIT mutation inference because they have been found to be mutated more often than expected by chance given background mutation processes.

Usage

```
mutSig
```

Format

A character vector of Entrez Gene IDs

Source

https://software.broadinstitute.org/cancer/cga/mutsig

`oncoprintPlot` *Function to plot genomic events in the style of oncoPrint/cBioPortal*

Description

Function to plot genomic events in the style of oncoPrint/cBioPortal

Usage

```
oncoprintPlot(
  summary.vec,
  snpmat.thisClus,
  amps.thisClus,
  dels.thisClus,
  fusions.thisClus,
  important.genes,
  band2gene,
  max.events,
  k
)
```

Arguments

`summary.vec`	: named vector of the counts, named 'Event name':'Type' where type is 'mut', 'amp', 'del', 'fus'. Mutations are in Entrez ID Amp/Deletion CNV events are in genomic band location
`snpmat.thisClus`	: SNP matrix subset to samples in current cluster
`amps.thisClus`	: CNV matrix subset to samples in current cluster (just amplifications)
`dels.thisClus`	: CNV matrix subset to samples in current cluster (just deletions)
`fusions.thisClus`	: Fusion matrix subset to samples in current cluster
`important.genes`	: well known genes to highlight in the analysis
`band2gene`	: mapping of genomic location IDs to gene name: vector of HUGO gene ids, named by genomic location
`max.events`	: maximum number of events to plot for the oncoplots
`k`	: current cluster number

Value

oncoprint event plot

`pathwayDiggitIntersect` *Combine DIGGIT inferences with pathway knowledge*

Description

Combine DIGGIT inferences with pathway knowledge

Usage

```
pathwayDiggitIntersect(diggit.int, pathway, pos.nes.only = TRUE, cores = 1)
```

Arguments

`diggit.int`	List of interactions between MRs - Genomic events, inferred by DIGGIT
`pathway`	- a list indexed by TF/MR entrez ID, contains the named vector of p-values for interactions
`pos.nes.only`	Only use positive associations between MR activity and presence of events (default = True)
`cores`	Number of cores to use if parallel is selected

Value

numeric vector, zscores for each TF/MR

`plotEvents` *Plot barchart of genomic events*

Description

Plot barchart of genomic events

Usage

```
plotEvents(
  summary.vec,
  highlight.genes = NULL,
  genomeBand_2_gene = NULL,
  samples.total,
  max.muts = 10,
  max.cnv = 5
)
```

Arguments

summary.vec	: named vector of the counts, named 'Event name':'Type' where type is 'mut', 'amp', 'del', 'fus'. Mutations are in Entrez ID Amp/Deletion CNV events are in genomic band location
highlight.genes	: well known genes to highlight in the analysis in
genomeBand_2_gene	: mapping of genomic location IDs to gene name: vector of HUGO gene ids, named by genomic loci
samples.total	: number of samples in the subtype, used to calculate percentages
max.muts	: maximum number of mutations to get per sample, default is 10
max.cnv	: maximum number of cnvs to per sample, default is 5

Value

plot object

---

rea *This function calculates an Enrichment Score of Association based on how the features rank on the samples sorted by a specific gene*

Description

This function calculates an Enrichment Score of Association based on how the features rank on the samples sorted by a specific gene

Usage

```
rea(eset, regulon, minsize = 1, maxsize = Inf, event.type = NA, verbose)
```

Arguments

eset	Numerical matrix
regulon	A list with genomic features as its names and samples as its entries, indicating presence of event
minsize	The minimum number of events to use when calculating enrichment
maxsize	The maximum number of events to use when calculating enrichment
event.type	Type of event being analyzed
verbose	whether to print extra progress statements

Value

A list containing two elements:

groups Regulon-specific NULL model containing the enrichment scores

ss Direction of the regulon-specific NULL model

`reaNULL` *This function generates the NULL model function, which computes the normalized enrichment score and associated p-value*

Description

This function generates the NULL model function, which computes the normalized enrichment score and associated p-value

Usage

```
reaNULL(regulon, minsize = 1, maxsize = Inf)
```

Arguments

`regulon`	A list with genomic features as its names and samples as its entries
`minsize`	Minimum number of event (or size of regulon)
`maxsize`	Maximum number of event (or size of regulon)

Value

A list of functions to compute NES and p-value

`sampleNameFilter` *Retain TCGA sample ids without the final letter designation ('A/B/C')*

Description

Retain TCGA sample ids without the final letter designation ('A/B/C')

Usage

```
sampleNameFilter(input, desired.len = 15)
```

Arguments

`input`	Matrix of expression or protein activity scores. Columns are sample names, rows are genes. Input can also just be an input vector of sample names.
`desired.len`	length to reduce strings to. Default is 15 because of TCGA naming conventions

Value

An identical matrix with new (shorter) column names, or a vector with the shortened names.

Examples

```
sample.names <- c("TCGA-14-1825-01A", "TCGA-76-4931-01B", "TCGA-06-5418-01A")
sampleNameFilter(sample.names)
```

`sampleOverlap` *The core function to compute which sample-specific alterations overlap with genomic events that are explained via DIGGIT.*

Description

The core function to compute which sample-specific alterations overlap with genomic events that are explained via DIGGIT.

Usage

```
sampleOverlap(
  MomaObject,
  viper.samples,
  selected.tfs,
  interaction.map,
  cnv.threshold = 0.5,
  mutation.filter = NULL,
  idx.range = NULL,
  verbose = FALSE
)
```

Arguments

`MomaObject`	Object reference of momaRunner class
`viper.samples`	Sample vector to restrict sample-specific analysis to
`selected.tfs`	Transcription factors being analyzed
`interaction.map`	List object of events 'covered' by the supplied interactions of type mut/amp/del/fus
`cnv.threshold`	Numeric absolute value to threshold SNP6 and/or GISTIC or other CNV scores. Above that absolute value is considered a positive event.
`mutation.filter`	A vector of whitelisted mutation events, in entrez gene IDs
`idx.range`	Number of tfs to check for genomic saturation calculation, default is 1253
`verbose`	Output status during the run (default=FALSE)

Value

A list of lists, indexed by sample name, with coverage statistics/data for each sample

`sigInteractorsDIGGIT` *Filter interactions from NES (DIGGIT) scores and corresponding background-corrected scores.*

Description

Use this version in the Bayes model to rank TFs

Usage

```
sigInteractorsDIGGIT(
  corrected.scores,
  nes.scores,
  cindy,
  p.thresh = 0.05,
  cindy.only = TRUE
)
```

Arguments

`corrected.scores`	A list indexed by the genomic event/gene with corresponding pvals and qvals for each TF
`nes.scores`	Matrix with tfs as columns, rows are genomic events
`cindy`	CINDy algorithm output matrix
`p.thresh`	P-value threshold (default=0.05)
`cindy.only`	Consider only CINDy validated interactions (default=TRUE)

Value

a list (indexed by VIPER protein) of significant genomic interactions and associated pvals over the background (null TF) model, and NES scores

`sREA` *Simple one-tail rank based enrichment analysis sREA (for cluster analysis)*

Description

This function performs simple 1-tail rank based enrichment analysis

Usage

```
sREA(signatures, groups)
```

Arguments

signatures	Numeric matrix of signatures
groups	List containing the groups as vectors of sample names

Value

Matrix of Normalized Enrichment Zcores

---

stoufferIntegrate *dispatch method for either CNV location corrected or SNV*

Description

dispatch method for either CNV location corrected or SNV

Usage

```
stoufferIntegrate(interactions, cytoband.map = NULL)
```

Arguments

interactions	List of MR - Genomic Event interactions, inferred by DIGGIT
cytoband.map	Data.frame mapping Entrez.IDs to cytoband locations

Value

Z-scores for each MR

---

stoufferIntegrateDiggit *Use Stouffer's method to combine z-scores of DIGGIT interactions for each cMR protein.*

Description

This function combines only positively associated DIGGIT scores by default to create a culmulative DIGGIT score for each cMR.

Usage

```
stoufferIntegrateDiggit(interactions, from.p = FALSE, pos.nes.only = TRUE)
```

Arguments

interactions	A list indexed by TF, includes z-scores or p-values for each interacting event
from.p	Integrate p-values or z-scores (default z-scores; from.p = FALSE)
pos.nes.only	Use only positive NES scores to rank proteins (default TRUE)

Value

A list indexed by TF, a stouffer integrated z-score

---

subsetListInteractions

Helper function: subset a list to the set of keys supplied return the names of interactions with positive values, in a list structure

---

Description

Helper function: subset a list to the set of keys supplied return the names of interactions with positive values, in a list structure

Usage

```
subsetListInteractions(int.l, keys)
```

Arguments

int.l	List of interactions, at each index this is a numeric named vector
keys	Keys used to reduce interactions

Value

Returns a filtered list of interactions in the same format as the input

---

validDiggitInteractions

Return a set of events 'covered' by specified cMR-event interactions

---

Description

Return a set of events 'covered' by specified cMR-event interactions

Usage

```
validDiggitInteractions(interactions, gene.loc.mapping, selected.tfs)
```

Arguments

`interactions`	List indexed by amp/mut/del/fus from cMRs to interacting events
`gene.loc.mapping`	Data.frame mapping entrezIDs to cytoband locations
`selected.tfs`	For each event type list, search within only these cMRS

Value

a list of events 'covered' by the supplied interactions of type mut/amp/del/fus

---

`viperGetSigTFS` *Calculate p-values from pseudo zscores / VIPER aREA scores, threshold*

Description

Calculate p-values from pseudo zscores / VIPER aREA scores, threshold

Usage

```
viperGetSigTFS(zscores, fdr.thresh = 0.05)
```

Arguments

`zscores`	Vector of normally distributed z-scores representing protein activities.
`fdr.thresh`	Threshold for false discovery rate, default is 0.05

Value

Get the names of proteins with significant z-scores, after multi-hypothesis correction

---

`viperGetTFScores` *Function to normalize TF scores*

Description

Function to normalize TF scores

Usage

```
viperGetTFScores(vipermat, fdr.thresh = 0.05)
```

Arguments

`vipermat`	- matrix of VIPER scores with columns as samples, rows as protein names
`fdr.thresh`	- BH-FDR threshold (default 0.05 FDR rate)

Value

A vector of normalized z-scores, named by TF id

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