Package ‘MOMA’

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Title Multi Omic Master Regulator Analysis
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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.
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areaEnrich

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

Description

areaEnrich 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.
### checkGeneMap

#### 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  

**Description**

Check Pathways

**Usage**

```r
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  

**Description**

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

**Usage**

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

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

A 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 method 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)
```
conditionalP

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

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

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 Dataset**

Glioblastoma (GBM) Example Dataset

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

---

**Fit Curve Percent**

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 achieved
### 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**
```r
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**
```r
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
**getDataFrame**

**Value**

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

---

**Description**

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

**Usage**

```r
data.getFrame(
  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**

```r
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**

```r
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
**getPvalsMatrix**

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

**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 integrates 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
)
mergeData

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**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>l1</td>
<td>list 1</td>
</tr>
<tr>
<td>l2</td>
<td>list 2</td>
</tr>
</tbody>
</table>

**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 applicable
- `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 occurrences to be considered
MomaConstructor

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

**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**

```r
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 MultiAssayExperiment 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 pro-
tein 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
oncoprintPlot

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

```r
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**

```r
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**

```r
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

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

```r
testerull(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

```r
testNameFilter(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

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

def 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
```r
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 tfas 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
```r
sREA(signatures, groups)
```
**stoufferIntegrate**

**Arguments**

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

**Value**

Matrix of Normalized Enrichment Zscores

---

**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 cumulative DIGGIT score for each cMR.

**Usage**

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

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)
viperGetSigTFS

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)
viperGetTFScores

Value

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