Package 'vissE'

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Title Visualising Set Enrichment Analysis Results

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Description This package enables the interpretation and analysis of results from a gene set enrichment analysis using network-based and text-mining approaches. Most enrichment analyses result in large lists of significant gene sets that are difficult to interpret. Tools in this package help build a similarity-based network of significant gene sets from a gene set enrichment analysis that can then be investigated for their biological function using text-mining approaches.

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Contents

`vissE-package` *vissE: Visualising Set Enrichment Analysis Results*

Description

This package enables the interpretation and analysis of results from a gene set enrichment analysis using network-based and text-mining approaches. Most enrichment analyses result in large lists of significant gene sets that are difficult to interpret. Tools in this package help build a similarity-based network of significant gene sets from a gene set enrichment analysis that can then be investigated for their biological function using text-mining approaches.

Details

This package supports four workflows to enhance gene set enrichment analysis:

1. Clustering results from a gene set enrichment analysis (e.g. using limma::fry, singscore or GSEA). The functions required for this analysis are `computeMsigOverlap`, `computeMsigNetwork` and `plotMsigNetwork`.
2. Interpreting gene set clusters (identified in the first analysis) by performing text-mining of gene set names and descriptions. The main function required to perform text-mining of gene sets is `plotMsigWordcloud`. Other functions can be used to access intermmediate results.
3. Visualise gene-level statistics for gene set clusters identified in the first analysis to link back gene set clusters to the genes of interest. This can be done using the `plotGeneStats` function.
4. Identifying gene sets similar to a list of genes identified from a DE analysis using set overlap measures. This can be done using the `characteriseGeneset` function.

Author(s)

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See Also

Useful links:

- https://davislaboratory.github.io/vissE
- Report bugs at https://github.com/DavisLaboratory/vissE/issues

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`bhuvad_theme` *Custom theme*

Description

Custom theme

Usage

```
bhuvad_theme(rl = 1.1)
```

Arguments

`rl`	a numeric, scaling factor to apply to text sizes

Value

a ggplot2 theme

Examples

```
p1 = ggplot2::ggplot()
p1 + bhuvad_theme()
```

`characteriseGeneset` *Functionally characterise a list of genes*

Description

This function can be used to perform a network-based enrichment analysis of a list of genes. The list of genes are characterised based on their similarity with gene sets from the MSigDB. A network of similar gene sets is retrieved using this function.

Usage

```
characteriseGeneset(
  gs,
  thresh = 0.2,
  measure = c("ovlapcoef", "jaccard"),
  gscolcs = c("h", "c2", "c5"),
  org = c("auto", "hs", "mm")
)
```

Arguments

`gs`	a GeneSet object, representing the list of genes that need to be characterised.
`thresh`	a numeric, specifying the threshold to discard pairs of gene sets.
`measure`	a character, specifying the similarity measure to use: `ari` for the Adjusted Rand Index, `jaccard` for the Jaccard Index and `ovlapcoef` for the Overlap Coefficient.
`gscolcs`	a character, listing the MSigDB collections to use as a background (defaults to h, c2, and c5). Collection types can be retrieved using `msigdb::listCollections()`.
`org`	a character, specifying the organism to use. This can either be "auto" (default), "hs" or "mm".

Value

an igraph object, containing gene sets that are similar to the query set. The network contains relationships between results of the query too.

Examples

```
library(GSEABase)
data(hgsc)

#create a geneset using one of the Hallmark gene sets
mySet <- GeneSet(
  geneIds(hgsc[[2]]),
  setName = 'MySet',
  geneIdType = SymbolIdentifier()
)
```

```
#characterise the custom gene set
ig <- characteriseGeneset(mySet)
plotMsigNetwork(ig)
```

---

computeMsigNetwork *Compute a network using computed gene set overlap*

Description

Computes an igraph object using information on gene sets and gene sets computed using the computeMsigOverlap() function.

Usage

```
computeMsigNetwork(genesetOverlap, msigGsc)
```

Arguments

genesetOverlap	a data.frame, containing results of an overlap analysis computed using the computeMsigOverlap() function.
msigGsc	a GeneSetCollection object, containing gene sets used to compute overlap.

Value

an igraph object

Examples

```
data(hgsc)
ovlap <- computeMsigOverlap(hgsc)
ig <- computeMsigNetwork(ovlap, hgsc)
```

`computeMsigOverlap` *Compute gene set overlap*

Description

Compute overlap between gene sets from a GeneSetCollection using the Jaccard index or the overlap coefficient. These values can then be used to compute a network of gene set overlaps.

Usage

```
computeMsigOverlap(
  msigGsc1,
  msigGsc2 = NULL,
  thresh = 0.25,
  measure = c("ari", "jaccard", "ovlapcoef")
)
```

Arguments

`msigGsc1`	a GeneSetCollection object.
`msigGsc2`	a GeneSetCollection object or NULL if pairwise overlaps are to be computed.
`thresh`	a numeric, specifying the threshold to discard pairs of gene sets.
`measure`	a character, specifying the similarity measure to use: `ari` for the Adjusted Rand Index, `jaccard` for the Jaccard Index and `ovlapcoef` for the Overlap Coefficient.

Value

a data.frame, containing the overlap structure of gene sets represented as a network in the simple interaction format (SIF).

Examples

```
data(hgsc)
ovlap <- computeMsigOverlap(hgsc)
```

`computeMsigWordFreq` *Compute word frequencies for a single MSigDB collection*

Description

Compute word frequencies for a single MSigDB collection

Usage

```
computeMsigWordFreq(
  msigGsc,
  weight = NULL,
  measure = c("tfidf", "tf"),
  version = msigdb::getMsigdbVersions(),
  org = c("auto", "hs", "mm"),
  rmwords = getMsigExclusionList(),
  idf = NULL
)
```

Arguments

`msigGsc`	a GeneSetCollection object, containing gene sets from the MSigDB. The `GSEABase::getBroadSets()` function can be used to parse XML files downloaded from MSigDB.
`weight`	a named numeric vector, containing weights to apply to each gene-set. This can be -log10(FDR), -log10(p-value) or an enrichment score (ideally unsigned).
`measure`	a character, specifying how frequencies should be computed. "tf" uses term frequencies and "tfidf" (default) applies inverse document frequency weights to term frequencies.
`version`	a character, specifying the version of msigdb to use (see `msigdb::getMsigdbVersions()`).
`org`	a character, specifying the organism to use. This can either be "auto" (default), "hs" or "mm".
`rmwords`	a character vector, containing an exclusion list of words to discard from the analysis.
`idf`	a list of named numeric vectors, specifying inverse document frequencies to use to penalise terms from gene-set names and short descriptions. This should be a vector of length 2 with names "Name" and "Short". Numeric vectors should contain weights and names should represent the term. Precomputed versions can be retrieved using the `msigdb::getMsigdbIDF()`.

Value

a list, containing two data.frames summarising the results of the frequency analysis on gene set names and short descriptions.

Examples

```
data(hgsc)
freq <- computeMsigWordFreq(hgsc, measure = 'tfidf')
```

`findMsigClusters` *Identify gene-set clusters from a gene-set overlap network*

Description

This function identifies gene-set clusters from a gene-set overlap network produced using vissE. Various graph clustering algorithms from the `igraph` package can be used for clustering. Gene-set clusters identified are then sorted based on their size and a given statistic of interest (absolute of the statistic is maximised per cluster).

Usage

```
findMsigClusters(
  ig,
  genesetStat = NULL,
  minSize = 2,
  alg = igraph::cluster_walktrap,
  algparams = list()
)
```

Arguments

`ig`	an igraph object, containing a network of gene set overlaps computed using `computeMsigNetwork()`.
`genesetStat`	a named numeric, containing statistics for each gene-set that are to be used in cluster prioritisation. If NULL, clusters are prioritised based on their size (number of gene-sets in them).
`minSize`	a numeric, stating the minimum size a cluster can be (default is 2).
`alg`	a function, from the `igraph` package that should be used to perform graph-clustering (default is `igraph::cluster_walktrap`). The function should produce a `communities` object.
`algparams`	a list, specifying additional parameters that are to be passed to the graph clustering algorithm.

Details

Gene-sets clusters are identified using graph clustering and are prioritised based on a combination of cluster size and optionally, a statistic of interest (e.g., enrichment scores). A product-of-ranks approach is used to prioritise clusters when gene-set statistics are available. In this approach, clusters are ranked based on their cluster size (largest to smallest) and on the median absolute statistic

of gene-sets within it (largest to smallest). The product of these ranks is computed and clusters are ranked based on these product-of-rank statistic (smallest to largest).

When prioritising using cluster size and gene-set statistics, if statistics for some gene-sets in the network are missing, only the size is used in cluster prioritisation.

Value

a list, containing gene-sets that belong to each cluster. Items in the list are organised based on prioritisation.

Examples

```
data(hgsc)
ovlap <- computeMsigOverlap(hgsc, thresh = 0.25)
ig <- computeMsigNetwork(ovlap, hgsc)
findMsigClusters(ig)
```

---

getMsigExclusionList *Exclusion list of words for MSigDB gene set text mining*

Description

List of words to discard when performing text mining MSigDB gene set names and short descriptions.

Usage

```
getMsigExclusionList(custom = c())
```

Arguments

custom	a character vector, containing list of words to add onto existing exclusion list.

Value

a character vector, containing words to be excluded from the text mining analysis.

Examples

```
getMsigExclusionList('remove')
```

hgsc *The Hallmark collection from the MSigDB*

Description

The molecular signatures database (MSigDB) is a collection of over 25000 gene expression signatures. Signatures in v7.2 are divided into 9 categories. The Hallmarks collection contains gene expression signatures representing molecular processes that are hallmarks in cancer development and progression.

Usage

```
hgsc
```

Format

A GeneSetCollection object with 50 GeneSet objects representing the 50 Hallmark gene expression signatures.

References

Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., ... & Mesirov, J. P. (2005). Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. Proceedings of the National Academy of Sciences, 102(43), 15545-15550.

Liberzon, A., Subramanian, A., Pinchback, R., Thorvaldsdóttir, H., Tamayo, P., & Mesirov, J. P. (2011). Molecular signatures database (MSigDB) 3.0. Bioinformatics, 27(12), 1739-1740.

Liberzon, A., Birger, C., Thorvaldsdóttir, H., Ghandi, M., Mesirov, J. P., & Tamayo, P. (2015). The molecular signatures database hallmark gene set collection. Cell systems, 1(6), 417-425.

plotGeneStats *Plot gene statistics for clusters of gene sets*

Description

This function plots gene statistics against gene frequencies for any given cluster of gene sets. The plot can be used to identify genes that are over-represented in a cluster of gene-sets (identified based on gene-set overlaps) and have a strong statistic (e.g. log fold-chage or p-value).

Usage

```
plotGeneStats(
  geneStat,
  msigGsc,
  groups,
  statName = "Gene-level statistic",
  topN = 5
)
```

Arguments

geneStat	a named numeric, containing the statistic to be displayed. The vector must be named with either gene Symbols or Entrez IDs depending on annotations in msigGsc.
msigGsc	a GeneSetCollection object, containing gene sets from the MSigDB. The GSEABase::getBroadSets() function can be used to parse XML files downloaded from MSigDB.
groups	a named list, of character vectors or numeric indices specifying node groupings. Each element of the list represent a group and contains a character vector with node names.
statName	a character, specifying the name of the statistic.
topN	a numeric, specifying the number of genes to label. The top genes are those with the largest count and statistic.

Value

a ggplot object, plotting the gene-level statistic against gene frequencies in the cluster of gene sets.

Examples

```
library(GSEABase)

data(hgsc)
groups <- list('g1' = names(hgsc)[1:25], 'g2' = names(hgsc)[26:50])

#create statistics
allgenes = unique(unlist(geneIds(hgsc)))
gstats = rnorm(length(allgenes))
names(gstats) = allgenes

#plot
plotGeneStats(gstats, hgsc, groups)
```

`plotMsigNetwork` *Plot a gene set overlap network*

Description

Plots a network of gene set overlap with overlap computed using the `computeMsigOverlap()` and a graph created using `computeMsigNetwork()`.

Usage

```
plotMsigNetwork(
  ig,
  markGroups = NULL,
  genesetStat = NULL,
  nodeSF = 1,
  edgeSF = 1,
  lytFunc = "graphopt",
  lytParams = list(),
  rmUnmarkedGroups = FALSE,
  maxGrp = 12
)
```

Arguments

`ig`	an igraph object, containing a network of gene set overlaps computed using `computeMsigNetwork()`.
`markGroups`	a named list, of character vectors. Each element of the list represent a group and contains a character vector with node names. Up to 12 groups can be visualised in the plot.
`genesetStat`	a named numeric, statistic to project onto the nodes. These could be p-values, log fold-changes or gene set score from a singscore-based analysis.
`nodeSF`	a numeric, indicating the scaling factor to apply to node sizes.
`edgeSF`	a numeric, indicating the scaling factor to apply to edge widths.
`lytFunc`	a character, specifying the layout to use (see `ggraph::create_layout()`).
`lytParams`	a named list, containing additional parameters needed for the layout (see `ggraph::create_layout()`).
`rmUnmarkedGroups`	a logical, indicating whether unmarked groups should be removed from the network (TRUE) or retained (FALSE - default).
`maxGrp`	a numeric, specifying the maximum number of groups to plot.

Value

a ggplot2 object

Examples

```
data(hgsc)
ovlap <- computeMsigOverlap(hgsc, thresh = 0.15)
ig <- computeMsigNetwork(ovlap, hgsc)
groups <- list(
  'g1' = c("HALLMARK_HYPOXIA", "HALLMARK_GLYCOLYSIS"),
  'g2' = c("HALLMARK_INTERFERON_GAMMA_RESPONSE")
)

plotMsigNetwork(ig, markGroups = groups)
```

`plotMsigPPI` *Plot PPI network for gene-set clusters identified using vissE*

Description

This function plots the protein-protein interaction (PPI) network for a gene-set cluster identified using vissE. The international molecular exchange (IMEx) PPI is used to obtain PPIs for genes present in a gene-set cluster.

Usage

```
plotMsigPPI(
  ppidf,
  msigGsc,
  groups,
  geneStat = NULL,
  statName = "Gene-level statistic",
  threshConfidence = 0,
  threshFrequency = 0.25,
  threshStatistic = 0,
  threshUseAbsolute = TRUE,
  topN = 5,
  nodeSF = 1,
  edgeSF = 1,
  lytFunc = "graphopt",
  lytParams = list()
)
```

Arguments

ppidf	a data.frame, containing a protein-protein interaction from the IMEx database. This can be retrieved from the `msigdb::getIMEX()` function.
msigGsc	a GeneSetCollection object, containing gene sets from the MSigDB. The `GSEABase::getBroadSets()` function can be used to parse XML files downloaded from MSigDB.

`groups` a named list, of character vectors or numeric indices specifying node groupings. Each element of the list represent a group and contains a character vector with node names.

`geneStat` a named numeric, containing the statistic to be displayed. The vector must be named with either gene Symbols or Entrez IDs depending on annotations in msigGsc.

`statName` a character, specifying the name of the statistic.

`threshConfidence`
a numeric, specifying the confidence threshold to apply to determine high confidence interactions. This should be a value between 0 and 1 (default is 0).

`threshFrequency`
a numeric, specifying the frequency threshold to apply to determine more frequent genes in the gene-set cluster. The frequecy of a gene is computed as the proportion of gene-sets to which the gene belongs. This should be a value between 0 and 1 (default is 0.25).

`threshStatistic`
a numeric, specifying the threshold to apply to gene-level statistics (e.g. a log fold-change). This should be a value between 0 and 1 (default is 0).

`threshUseAbsolute`
a logical, indicating whether the `threshStatistic` threshold should be applied to absolute values (default TRUE). This can be used to threshold on statistics such as the log fold-chage from a differential expression analysis.

`topN` a numeric, specifying the number of genes to label. The top genes are those with the largest count and statistic.

`nodeSF` a numeric, indicating the scaling factor to apply to node sizes.

`edgeSF` a numeric, indicating the scaling factor to apply to edge widths.

`lytFunc` a character, specifying the layout to use (see `ggraph::create_layout()`).

`lytParams` a named list, containing additional parameters needed for the layout (see `ggraph::create_layout()`).

Value

a ggplot object with the protein-protein interaction networks plot for each gene-set cluster.

Examples

```
data(hgsc)
grps = list('early' = 'HALLMARK_ESTROGEN_RESPONSE_EARLY', 'late' = 'HALLMARK_ESTROGEN_RESPONSE_LATE')
ppi = msigdb::getIMEX(org = 'hs', inferred = TRUE)
plotMsigPPI(ppi, hgsc, grps)
```

`plotMsigWordcloud` *Compute and plot word frequencies for multiple MSigDB collections*

Description

Given a gene set collection, this function computes the word frequency of gene set names from the Molecular Signatures Database (MSigDB) collection (split by _). Word frequencies are also computed using short descriptions attached with each gene set object.

Usage

```
plotMsigWordcloud(
  msigGsc,
  groups,
  weight = NULL,
  measure = c("tfidf", "tf"),
  version = msigdb::getMsigdbVersions(),
  org = c("auto", "hs", "mm"),
  rmwords = getMsigExclusionList(),
  type = c("Name", "Short"),
  idf = NULL
)
```

Arguments

`msigGsc`	a GeneSetCollection object, containing gene sets from the MSigDB. The `GSEABase::getBroadSets()` function can be used to parse XML files downloaded from MSigDB.
`groups`	a named list, of character vectors or numeric indices specifying node groupings. Each element of the list represent a group and contains a character vector with node names.
`weight`	a named numeric vector, containing weights to apply to each gene-set. This can be -log10(FDR), -log10(p-value) or an enrichment score (ideally unsigned).
`measure`	a character, specifying how frequencies should be computed. "tf" uses term frequencies and "tfidf" (default) applies inverse document frequency weights to term frequencies.
`version`	a character, specifying the version of msigdb to use (see `msigdb::getMsigdbVersions()`).
`org`	a character, specifying the organism to use. This can either be "auto" (default), "hs" or "mm".
`rmwords`	a character vector, containing an exclusion list of words to discard from the analysis.
`type`	a character, specifying the source of text mining. Either gene set names (`Name`) or descriptions (`Short`) can be used.

idf — a list of named numeric vectors, specifying inverse document frequencies to use to penalise terms from gene-set names and short descriptions. This should be a vector of length 2 with names "Name" and "Short". Numeric vectors should contain weights and names should represent the term. Precomputed versions can be retrieved using the `msigdb::getMsigdbIDF()`.

Value

a ggplot object.

Examples

```
data("hgsc")
groups <- list('g1' = names(hgsc)[1:25], 'g2' = names(hgsc)[26:50])
plotMsigWordcloud(hgsc, groups, rmwords = getMsigExclusionList())
```

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