Package ‘vissE’

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Title Visualising Set Enrichment Analysis Results

Version 1.10.0

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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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 intermediate 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.
bhuvad_theme

Author(s)

Maintainer: Dharmesh D. Bhuva <bhuva.d@wehi.edu.au> (ORCID)

See Also

Useful links:

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

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

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

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>gs</code></td>
<td>a GeneSet object, representing the list of genes that need to be characterised.</td>
</tr>
<tr>
<td><code>thresh</code></td>
<td>a numeric, specifying the threshold to discard pairs of gene sets.</td>
</tr>
<tr>
<td><code>measure</code></td>
<td>a character, specifying the similarity measure to use: \texttt{ari} for the Adjusted Rand Index, \texttt{jaccard} for the Jaccard Index and \texttt{ovlapcoef} for the Overlap Coefficient.</td>
</tr>
<tr>
<td><code>gscolcs</code></td>
<td>a character, listing the MSigDB collections to use as a background (defaults to h, c2, and c5). Collection types can be retrieved using \texttt{msigdb::listCollections()}.</td>
</tr>
<tr>
<td><code>org</code></td>
<td>a character, specifying the organism to use. This can either be \texttt{&quot;auto&quot;} (default), \texttt{&quot;hs&quot;} or \texttt{&quot;mm&quot;}.</td>
</tr>
</tbody>
</table>

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

```r
library(GSEABase)
data(hgsc)

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

#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

calculateMsigNetwork(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)
overlap <- computeMsigOverlap(hgsc)
ig <- computeMsigNetwork(overlap, 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**

```r
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**

```r
data(hgsc)
overlap <- computeMsigOverlap(hgsc)
```
computeMsigWordFreq  

*Compute word frequencies for a single MSigDB collection*

**Description**

Compute word frequencies for a single MSigDB collection

**Usage**

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

**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 a blacklist of words to discard from the analysis.

**Value**

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

**Examples**

```r
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

```r
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.
getMsigBlacklist

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)

Description

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

Usage

getMsigBlacklist(custom = c())

Arguments

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

Value

a character vector, containing list of blacklist works

Examples

getMsigBlacklist('blacklist')
**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**


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**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-change or p-value).
plotGeneStats

Usage

plotGeneStats(
  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 = "Gene-level statistic",  # a character, specifying the name of the statistic.
  topN = 5  # a numeric, specifying the number of genes to label. The top genes are those with the largest count and statistic.
)

Arguments

geneStat
msigGsc
groups
statName
topN

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

```r
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 singlescore-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

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

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

```r
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 msiGsc.
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 frequency 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-change 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**

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

**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 a blacklist 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.

**Value**

- a ggplot object.
Examples

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