Package ‘FELLA’

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Type Package
Title Interpretation and enrichment for metabolomics data
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Maintainer Sergio Picart-Armada <sergi.picart@upc.edu>
Description Enrichment of metabolomics data using KEGG entries.
   Given a set of affected compounds, FELLA suggests affected
   reactions, enzymes, modules and pathways using label propagation
   in a knowledge model network. The resulting subnetwork
   can be visualised and exported.
License GPL-3
LazyLoad yes
Imports methods, igraph, Matrix, KEGGREST, plyr, stats, graphics,
   utils
Depends R (>= 3.5.0)
Suggests shiny, DT, magrittr, visNetwork, knitr, BiocStyle, rmarkdown,
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VignetteBuilder knitr
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biocViews Software, Metabolomics, GraphAndNetwork, KEGG, GO, Pathways,
   Network, NetworkEnrichment
Collate 'AllArguments.R' 'AllClasses.R' 'AllMethods.R'
   'generateResultsTable.R' 'generateEnzymesTable.R'
   'generateResultsGraph.R' 'exportResults.R' 'addGOToGraph.R'
   'buildGraphFromKEGGREST.R' 'buildDataFromGraph.R'
   'defineCompounds.R' 'doc-data.R' 'doc-package.R'
   'runHypergeom.R' 'runDiffusion.R' 'runPagerank.R' 'enrich.R'
   'get.-R' 'is.-R' 'launchApp.R' 'list.-R' 'loadKEGGdata.R'
   'plotBipartite.R' 'plotGraph.R' 'plotLegend.R'
Contents

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Description

This function eases parameter inheritance to centralise the documentation

Usage

.params()

Arguments

databaseDir Path for the KEGG RData files
internalDir Logical, is the directory located in the package directory?
o b ject FELLA.USER object
data FELLA.DATA object
type Character vector, containing entries in "hypergeom", "diffusion" or "pagerank"
level Desired level, can be coded as a number or a character: 1 or "pathway"; 2 or "module"; 3 or "enzyme"; 4 or "reaction"; 5 or "compound".
method Character, exactly one of: "hypergeom", "diffusion", "pagerank"
methods Character vector, containing some of: "hypergeom", "diffusion", "pagerank"
approx Character: "simulation" for Monte Carlo, "normality", "gamma" or "t" for parametric approaches
loadMatrix Character vector to choose if heavy matrices should be loaded. Can contain: "diffusion", "pagerank"
threshold Numeric value between 0 and 1. p.score threshold applied when filtering KEGG nodes. Lower thresholds are more stringent.
thresholdConnectedComponent Numeric value between 0 and 1. Connected components that are below the threshold are kept, while the ones exceeding it (because they are too small) are discarded.
plimit  Pathway limit, must be a numeric value between 1 and 50. Limits the amount of pathways in method = "hypergeom"

nlimit  Node limit, must be a numeric value between 1 and 1000. Limits the order of the solution sub-graph when in method = "diffusion" and method = "pagerank"

niter  Number of iterations (permutations) for Monte Carlo ("simulation"), must be a numeric value between 1e2 and 1e5

layout  Logical, should the plot be returned as a layout?

graph  An igraph object, typically a small one, coming from an enrichment through "diffusion" or "pagerank".

GOterm  Character, GO entry to draw semantic similarity in the solution graph. If NULL, the GO labels will be appended without similarities.

GONamesAsLabels  Logical, should GO names be displayed as labels instead of GO identifiers?

LabelLengthAtPlot  Numeric value between 10 and 50. Maximum length that a label can reach when plotting the graph. The remaining characters will be truncated using "...

godata.options  List, options for the database creator godata

mart.options  List, options for the biomaRt function getBM. Importantly, this defines the organism, see listDatasets for possibilities. If calling generateEnzymesTable, the user can set mart.options = NULL to avoid adding GO labels to enzymes.

p.adjust  Character passed to the p.adjust method

dampingFactor  Numeric value between 0 and 1 (none inclusive), damping factor d for PageRank (page.rank)

t.df  Numeric value; number of degrees of freedom of the t distribution if the approximation approx = "t" is used

compounds  Character vector containing the KEGG IDs of the compounds considered as affected

compoundsBackground  Character vector containing the KEGG IDs of the compounds that belong to the background. Can be NULL for the default background (all compounds)

NamesAsLabels  Logical, should KEGG names be displayed as labels instead of KEGG identifiers?

capPscores  Numeric value, minimum p-score admitted for the readable formatting. Smaller p-scores will be displayed as < capPscores

Value

NULL
**checkArguments**

*Internal function to check arguments and give personalised errors*

**Description**

This function checks if the arguments are of the desired type, length and range. If it fails, it gives an error explaining why the argument is invalid.

**Usage**

```r
checkArguments(databaseDir = "myDatabase", internalDir = TRUE,
                method = "diffusion", methods = "diffusion", approx = "normality",
                loadMatrix = NULL, threshold = 0.05, plimit = 15, nlimit = 250,
                niter = 1000, t.df = 10, dampingFactor = 0.85, layout = FALSE,
                thresholdConnectedComponent = 0.05, GOterm = NULL,
                GONamesAsLabels = TRUE, LabelLengthAtPlot = 22,
                object = new("FELLA.USER"), data = new("FELLA.DATA"), ...)
```

**Arguments**

- `databaseDir` Path for the KEGG RData files
- `internalDir` Logical, is the directory located in the package directory?
- `method` Character, exactly one of: "hypergeom", "diffusion", "pagerank"
- `methods` Character vector, containing some of: "hypergeom", "diffusion", "pagerank"
- `approx` Character: "simulation" for Monte Carlo, "normality", "gamma" or "t" for parametric approaches
- `loadMatrix` Character vector to choose if heavy matrices should be loaded. Can contain: "diffusion", "pagerank"
- `threshold` Numeric value between 0 and 1. p.score threshold applied when filtering KEGG nodes. Lower thresholds are more stringent.
- `plimit` Pathway limit, must be a numeric value between 1 and 50. Limits the amount of pathways in method = "hypergeom"
- `nlimit` Node limit, must be a numeric value between 1 and 1000. Limits the order of the solution sub-graph when in method = "diffusion" and method = "pagerank"
- `niter` Number of iterations (permutations) for Monte Carlo ("simulation"), must be a numeric value between 1e2 and 1e5
- `t.df` Numeric value; number of degrees of freedom of the t distribution if the approximation approx = "t" is used
- `dampingFactor` Numeric value between 0 and 1 (none inclusive), damping factor d for PageRank (page.rank)
- `layout` Logical, should the plot be returned as a layout?
thresholdConnectedComponent
  Numeric value between 0 and 1. Connected components that are below the threshold are kept, while the ones exceeding it (because they are too small) are discarded.

GOterm
  Character, GO entry to draw semantic similarity in the solution graph. If NULL, the GO labels will be appended without similarities.

GONamesAsLabels
  Logical, should GO names be displayed as labels instead of GO identifiers?

LabelLengthAtPlot
  Numeric value between 10 and 50. Maximum length that a label can reach when plotting the graph. The remaining characters will be truncated using "...

object
  FELLA.USER object

data
  FELLA.DATA object

... ignored arguments

Value
  A list with values. Currently only a logical value named valid if the process runs smoothly. If the checking fails, it also returns an object called ans, which depends on the situation (can be the original object, NULL, et cetera).

Examples
  ## This function is internal
  arg1 <- FELLA:::checkArguments(method = "hello")
  arg1$valid
  arg2 <- FELLA:::checkArguments(method = "diffusion")
  arg2$valid

D.diffusion-class
  An internal S4 class for the diffusion data

Description
  An internal S4 class for the diffusion data

Slots
  matrix Numeric (dense) matrix [optional]
  rowSums Numeric named vector with rowSums internal data
  squaredRowSums Numeric named vector with squaredRowSums internal data
D.hypergeom-class

An internal S4 class for the binary matrix (hypergeometric test)

Description

An internal S4 class for the binary matrix (hypergeometric test)

Slots

matrix  Binary sparse matrix

D.keggdata-class

An internal S4 class to represent the KEGG graph and related files

Description

An internal S4 class to represent the KEGG graph and related files

Slots

graph  KEGG graph
id2name  Mapping list: KEGG ID to KEGG name (can contain multiple hits)
pvalues.size  Numeric matrix for the evaluation of CC through their size
id  List with character vectors for KEGG categories
status  Character that specifies the current status of this S4 class

D.pagerank-class

An internal S4 class for the PageRank data

Description

An internal S4 class for the PageRank data

Slots

matrix  Numeric (dense) matrix [optional]
rowSums  Numeric named vector with rowSums internal data
squaredRowSums  Numeric named vector with squaredRowSums internal data
Parse, build and load the KEGG knowledge model

Description

Function `buildGraphFromKEGGREST` makes use of the KEGG REST API (requires internet connection) to build and return the curated KEGG graph.
Function `buildDataFromGraph` takes as input the KEGG graph generated by `buildGraphFromKEGGREST` and writes the KEGG knowledge model in the desired permanent directory.
Function `loadKEGGdata` loads the internal files containing the KEGG knowledge model into a `FELLA.DATA` object.

In general, `generateGraphFromKEGGREST` and `generateDataFromGraph` are one-time executions for a given organism and knowledge model, in this precise order. On the other hand, the user needs to run `loadKEGGdata` in every new R session to load such model into a `FELLA.DATA` object.

Usage

```r
buildGraphFromKEGGREST(organism = "hsa", filter.path = NULL)

buildDataFromGraph(keggdata.graph = NULL, databaseDir = NULL,
                   internalDir = TRUE, matrices = c("hypergeom", "diffusion",
                                                 "pagerank"),
                   normality = c("diffusion", "pagerank"),
                   dampingFactor = 0.85, niter = 100)

loadKEGGdata(databaseDir = tail(listInternalDatabases(), 1),
              internalDir = TRUE, loadMatrix = NULL)
```

Arguments

- **organism** Character, KEGG code for the organism of interest
- **filter.path** Character vector, pathways to filter. This is a pattern matched using regexp. E.g: "01100" to filter the overview metabolic pathway in any species
- **keggdata.graph** An `igraph` object generated by the function `buildGraphFromKEGGREST`
- **databaseDir** Character containing the directory to save KEGG files. It is a relative directory inside the library location if `internalDir = TRUE`. If left to `NULL`, an automatic name containing the date, organism and the KEGG release is generated.
- **internalDir** Logical, should the directory be internal in the package directory?
- **matrices** A character vector, containing any of these: "hypergeom", "diffusion", "pagerank"
- **normality** A character vector, containing any of these: "diffusion", "pagerank"
- **dampingFactor** Numeric value between 0 and 1 (none inclusive), damping factor $d$ for PageRank (page.rank)
- **niter** Numeric value, number of iterations to estimate the p-values for the CC size. Between 10 and 1e3.
- **loadMatrix** Character vector to choose if heavy matrices should be loaded. Can contain: "diffusion", "pagerank"
Details
In function buildGraphFromKEGGREST, The user specifies (i) an organism, and (ii) patterns matching pathways that should not be included as nodes. A graph object, as described in [Picart-Armada, 2017], is built from the comprehensive KEGG database [Kanehisa, 2017]. As described in the main vignette, accessible through browseVignettes("FELLA"), this graph has five levels that represent categories of KEGG nodes. From top to bottom: pathways, modules, enzymes, reactions and compounds. This knowledge representation is resemblant to the one formerly used by MetScape [Karnovsky, 2011], in which enzymes connect to genes instead of modules and pathways. The necessary KEGG annotations are retrieved through KEGGREST R package [Tenenbaum, 2013]. Connections between pathways/modules and enzymes are inferred through organism-specific genes, i.e. an edge is added if a gene connects both entries. However, in order to enrich metabolomics data, the user has to pass the graph object to buildDataFromGraph to obtain the FELLA.USER object. All the networks are handled with the igraph R package [Csardi, 2006].

Using buildDataFromGraph is the second step to use the FELLA package. The knowledge graph is used to compute other internal variables that are required to run any enrichment. The main point behind the enrichment is to provide a small part of the knowledge graph relevant to the supplied metabolites. This is accomplished through diffusion processes and random walks, followed by a statistical normalisation, as described in [Picart-Armada, 2017]. When building the internal files, the user can choose whether to store (i) matrices for each provided method, and (ii) vectors derived from such matrices to use the parametric approaches. These are optional but enable (i) faster permutations and custom metabolite backgrounds, and (ii) parametric approaches. WARNING: diffusion and PageRank matrices in (i) can allocate up to 250MB each. On the other hand, the niter parameter controls the amount of trials to approximate the distribution of the connected component size under uniform node sampling. For further info, see the option thresholdConnectedComponent in the details from ?generateResultsGraph. Regarding the destination, the user can specify the name of the directory. Otherwise a name containing the creation date, the organism and the KEGG release will be used. The database can be stored within the library path or in a custom location.

Function loadKEGGdata returns a FELLA.DATA object from any of the databases generated by FELLA.DATA. This object is the starting point of any enrichment using FELLA. In case the user built the matrices for “diffusion” and “pagerank”, he or she can choose to load them. Further detail on the methods can be found in [Picart-Armada, 2017]. The matrices allow a faster computation and the definition of a custom background, but use up to 250MB of memory each.

Value

buildGraphFromKEGGREST returns the curated KEGG graph (class igraph)
buildDataFromGraph returns invisible(TRUE) if successful. As a side effect, the directory outdir is created, containing the internal data.
loadKEGGdata returns the FELLA.DATA object that contains the KEGG knowledge representation.

References

See Also
class FELLA.DATA

Examples

## Toy example
## In this case, the graph is not built from current KEGG.
## It is loaded from sample data in FELLA
data("FELLA.sample")
## Graph to build the database (this example is a bit hacky)
g.sample <- FELLA:::getGraph(FELLA.sample)
dir.tmp <- paste0(tempdir(), "/", paste(sample(letters), collapse = ""))
## Build internal files in a temporary directory
buildDataFromGraph(  keggdata.graph = g.sample,
                      databaseDir = dir.tmp,
                      internalDir = FALSE,
                      matrices = NULL,
                      normality = NULL,
                      dampingFactor = 0.85,
                      niter = 10)
## Load database
myFELLA.DATA <- loadKEGGdata(  dir.tmp,
                      internalDir = FALSE)
myFELLA.DATA

# Not run:
# Full example

## First step: graph for Mus musculus discarding the mmu01100 pathway
## (an analog example can be built from human using organism = "hsa")
g.mmu <- buildGraphFromKEGGREST(  organism = "mmu",
                      filter.path = "mmu01100")
summary(g.mmu)
cat(comment(g.mmu))

## Second step: build internal files for this graph
## (consumes some time and memory, especially if we compute
## "diffusion" and "pagerank" matrices)
buildDataFromGraph(
Enrich-funs

Enrich-Funs is a set of functions designed to map and enrich a list of metabolites. The functions include:

- **defineCompounds**: Creates a FELLA.USER object from a list of compounds and a FELLA.DATA object.
- **runHypergeom**, **runDiffusion**, and **runPagerank**: Perform enrichment on a FELLA.USER object with the mapped input metabolites (through defineCompounds) and a FELLA.DATA object. They are based on the hypergeometric test, the heat diffusion model, and the PageRank algorithm, respectively.
- **enrich**: A wrapper function with the following order: loadKEGGdata (optional), defineCompounds, and one or more in runHypergeom, runDiffusion, and runPagerank.

### Usage

- **defineCompounds**: `defineCompounds(compounds = NULL, compoundsBackground = NULL, data = NULL)`
- **runHypergeom**: `runHypergeom(object = NULL, data = NULL, p.adjust = "fdr")`
- **runDiffusion**: `runDiffusion(object = NULL, data = NULL, approx = "normality", t.df = 10, niter = 1000)`
- **runPagerank**: `runPagerank(object = NULL, data = NULL, approx = "normality", dampingFactor = 0.85, t.df = 10, niter = 1000)`
- **enrich**: `enrich(compounds = NULL, compoundsBackground = NULL, methods = listMethods(), loadMatrix = "none", approx = "normality", t.df = 10, niter = 1000, databaseDir = NULL, internalDir = TRUE, data = NULL, ...)`

### Description

Function defineCompounds creates a FELLA.USER object from a list of compounds and a FELLA.DATA object.

Functions runHypergeom, runDiffusion, and runPagerank perform an enrichment on a FELLA.USER object with the mapped input metabolites (through defineCompounds) and a FELLA.DATA object. They are based on the hypergeometric test, the heat diffusion model, and the PageRank algorithm, respectively.

Function enrich is a wrapper with the following order: loadKEGGdata (optional), defineCompounds, and one or more in runHypergeom, runDiffusion, and runPagerank.
Arguments

compounds Character vector containing the KEGG IDs of the compounds considered as affected
compoundsBackground Character vector containing the KEGG IDs of the compounds that belong to the background. Can be NULL for the default background (all compounds)
data FELLA.DATA object
object FELLA.USER object
p.adjust Character passed to the p.adjust method
approx Character: "simulation" for Monte Carlo, "normality", "gamma" or "t" for parametric approaches
t.df Numeric value; number of degrees of freedom of the t distribution if the approximation approx = "t" is used
niter Number of iterations (permutations) for Monte Carlo ("simulation"), must be a numeric value between 1e2 and 1e5
dampingFactor Numeric value between 0 and 1 (non-inclusive), damping factor d for PageRank
methods Character vector, containing some of: "hypergeom", "diffusion", "pagerank"
loadMatrix Character vector to choose if heavy matrices should be loaded. Can contain: "diffusion", "pagerank"
databaseDir Character, path to load the FELLA.DATA object if it is not already passed through the argument data
internalDir Logical, is the directory located in the package directory?
... Further arguments for the enrichment function(s) runDiffusion, runPagerank

Details

Function defineCompounds maps the specified list of KEGG compounds [Kanehisa, 2017], usually from an experimental metabolomics study, to the graph contained in the FELLA.DATA object. Importantly, the names must be KEGG ids, so other formats (common names, HMDB ids, etc) must be mapped to KEGG first. For example, through the "Compound ID Conversion" tool in MetaboAnalyst [Xia, 2015]. The user can also define a personalised background as a list of KEGG compound ids, which should be more extensive than the list of input metabolites. Once the compounds are mapped, the enrichment can be performed through runHypergeom, runDiffusion and runPagerank.

Function runHypergeom performs an over representation analysis through the hypergeometric test [Fisher, 1935] on a FELLA.USER object with mapped metabolites and a FELLA.DATA object. If a custom background was specified, it will be used. This approach is included for completeness and it is not the main purpose behind the FELLA package. Importantly, runHypergeom is not a hypergeometric test using the original KEGG pathways. Instead, a compound "belongs" to a "pathway" if it can reach the original pathway in the upwards-directed KEGG graph. This is a way to evaluate enrichment including indirect connections to a pathway, e.g. through an enzymatic family. New "pathways" are expected to be larger than the original pathways in this analysis and therefore the results can differ from the standard over representation.
Function `runDiffusion` performs the diffusion-based enrichment on a `FELLA.USER` object with mapped metabolites and a `FELLA.DATA` object [Picart-Armada, 2017]. If a custom background was specified, it will be used. The idea behind the heat diffusion is the usage of the finite difference formulation of the heat equation to propagate labels from the metabolites to the rest of the graph. Following the notation in [Picart-Armada, 2017], the temperatures (diffusion scores) are computed as:

\[ T = -K I^{-1} \cdot G \]

\( G \) is an indicator vector of the input metabolites (1 if input metabolite, 0 otherwise). \( KI \) is the matrix \(-KI = L + B\), being \( L \) the unnormalised graph Laplacian and \( B \) the diagonal matrix with \( B[i,i] = 1 \) if node \( i \) is a pathway and \( B[i,i] = 0 \) otherwise.

Equivalently, with the notation in the HotNet approach [Vandin, 2011], the stationary temperature is named \( f^s \):

\[ f^s = L^{-1} \gamma b^s \]

\( b^s \) is the indicator vector \( G \) from above. \( L\gamma \), on the other hand, is found as \( L\gamma = L + \gamma I \), where \( L \) is the unnormalised graph Laplacian, \( \gamma \) is the first order leaking rate and \( I \) is the identity matrix. In our formulation, only the pathway nodes are allowed to leak, therefore \( I \) is switched to \( B \). The parameter \( \gamma \) is set to \( \gamma = 1 \).

The input metabolites are forced to stay warm, propagating flow to all the nodes in the network. However, only pathway nodes are allowed to evacuate this flow, so that its directionality is bottom-up. Further details on the setup of the diffusion process can be found in the supplementary file S2 from [Picart-Armada, 2017].

Finally, the warmest nodes in the graph are reported as the relevant sub-network. This will probably include some input metabolites and also reactions, enzymes, modules and pathways. Other metabolites can be suggested as well.

Function `runPagerank` performs the random walk based enrichment on a `FELLA.USER` object with mapped metabolites and a `FELLA.DATA` object. If a custom background was specified, it will be used. PageRank was originally conceived as a scoring system for websites [Page, 1999]. Intuitively, PageRank favours nodes that (1) have a large amount of nodes pointing at them, and (2) whose pointing nodes also have high scores. Classical PageRank is formulated in terms of a random walker - the PageRank of a given node is the stationary probability of the walker visiting it.

The walker chooses, in each step, whether to continue the random walk with probability \( d \) or to restart it with probability \( 1 - d \). In the original publication, \( d = 0.85 \), which is the value used in FELLA by default. If he or she continues, an edge is picked from the outgoing edges in the current node with a probability proportional to its weight. If he or she restarts it, a node is uniformly picked from the whole graph. The "personalised PageRank" variant allows a user-defined distribution as the source of new random walks. The R package `igraph` contains such variant in its `page.rank` function [Csardi, 2006].

As described in the supplement S3 from [Picart-Armada, 2017], the PageRank \( PR \) can be computed as a column vector by imposing a stationary state in the probability. With a damping factor \( d \) and the user-defined distribution \( p \) as a column vector:

\[ PR = d \cdot M \cdot PR + (1 - d) \cdot p \]
enrich-funs

\( M \) is the matrix whose element \( M[i,j] \) is the probability of transitioning from \( j \) to \( i \). If node \( j \) has outgoing edges, their probability is proportional to their weight - all weights must be positive. If node \( j \) has no outgoing edges, the probability is uniform over all the nodes, i.e. \( M[i,j] = 1/nrow(M) \) for every \( i \). Note that all the columns from \( M \) sum up exactly 1. This leads to an expression to compute PageRank:

\[
PR = (1 - d)p \cdot (I - dM)^{-1}
\]

The idea behind the method "pagerank" is closely related to "diffusion". Relevant metabolites are the sources of new random walks and nodes are scored through their PageRank. Specifically, \( p \) is set to a uniform probability on the input metabolites. More details on the setup can be found in the supplementary file S3 from [Picart-Armada, 2017].

There is an important detail for "diffusion" and "pagerank": the scores are statistically normalised. Omitting this normalisation leads to a systematic bias, especially in pathway nodes, as described in [Picart-Armada, 2017].

Therefore, in both cases, scores undergo a normalisation through permutation analysis. The score of a node \( i \) is compared to its null distribution under input permutation, leading to their p-scores. As described in [Picart-Armada, 2017], two alternatives are offered: a parametric and deterministic approach and a non-parametric, stochastic one.

Stochastic Monte Carlo trials ("simulation") imply randomly permuting the input \( niter \) times and counting, for each node \( i \), how many trials led to an equally or more extreme value than the original score. An empirical p-value is returned [North, 2002].

On the other hand, the parametric scores (approx = "normality") give a z-score for such permutation analysis. The expected value and variance of such null distributions are known quantities, see supplementary file S4 from [Picart-Armada, 2017]. To work in the same range \([0,1]\), z-scores are transformed using the routine \( \text{pnorm} \). The user can also choose the Student’s t using approx = "t" and choosing a number of degrees of freedom through t.df. This uses the function \( \text{pt} \) instead.

Alternatively, a gamma distribution can be used by setting approx = "gamma". The theoretical mean \( \mu \) and variance \( \sigma^2 \) are used to define the shape \( \mu^2/\sigma^2 \) and scale \( \sigma/\mu \) of the gamma distribution, and \( \text{pgamma} \) to map to \([0,1]\).

Any sub-network prioritised by "diffusion" and "pagerank" is selected by applying a threshold on the p-scores.

Finally, the function enrich is a wrapper to perform the enrichment analysis. If no \text{FELLA.DATA} object is supplied, it loads it, maps the affected compounds and performs the desired enrichment(s) with a single call. Returned is a list with the loaded \text{FELLA.DATA} object and the results in a \text{FELLA.USER} object. Conversely, the user can supply the \text{FELLA.DATA} object and the wrapper will map the metabolites and run the desired enrichment method(s). In this case, only the \text{FELLA.USER} will be returned.

Value

\text{defineCompounds} \ returns the \text{FELLA.USER} object with the mapped metabolites, ready to be enriched.

\text{runHypergeom} \ returns a \text{FELLA.USER} object updated with the hypergeometric test results

\text{runDiffusion} \ returns a \text{FELLA.USER} object updated with the diffusion enrichment results

\text{runPagerank} \ returns a \text{FELLA.USER} object updated with the PageRank enrichment results
enrich returns a FELLA.USER object updated with the desired enrichment results if the FELLA.DATA was supplied. Otherwise, a list with the freshly loaded FELLA.DATA object and the corresponding enrichment in the FELLA.USER object.

References


Examples

```r
## Load the internal database.
## This one is a toy example!
## Do not use as a regular database
data(FELLA.sample)
data(input.sample)

## Load a list of compounds to enrich
data(input.sample)

# Example, step by step

## First, map the compounds
obj <- defineCompounds(  
  compounds = c(input.sample, "I_dont_map", "me_neither"),  
  data = FELLA.sample)

## See the mapped and unmapped compounds
getInput(obj)
getExcluded(obj)

## Compounds are already mapped
## We can enrich using any method now

## If no compounds are mapped an error is thrown. Example:
## Not run:
```
data(FELLA.sample)
obj <- defineCompounds(
  compounds = c("C00049", "C00050"),
  data = FELLA.sample)
## End(Not run)

## Enrich using hypergeometric test
obj <- runHypergeom(
  object = obj,
  data = FELLA.sample)
obj

## Enrich using diffusion
## Note how the results are added;
## the hypergeometric results are not overwritten
obj <- runDiffusion(
  object = obj,
  approx = "normality",
  data = FELLA.sample)
obj

## Enrich using PageRank
## Again, this does not overwrite other methods
obj <- runPagerank(
  object = obj,
  approx = "simulation",
  data = FELLA.sample)
obj

######################
## Example using the "enrich" wrapper

## Only diffusion
obj.wrap <- enrich(
  compounds = input.sample,
  method = "diffusion",
  data = FELLA.sample)
obj.wrap

## All the methods
obj.wrap <- enrich(
  compounds = input.sample,
  methods = FELLA::listMethods(),
  data = FELLA.sample)
obj.wrap
Description

In general, `generateResultsTable`, `generateEnzymesTable` and `generateResultsGraph` provide the results of an enrichment in several formats.

Function `generateResultsTable` returns a table that contains the best hits from a `FELLA.USER` object with a successful enrichment analysis. Similarly, `generateEnzymesTable` returns a data frame with the best scoring enzyme families and their annotated genes.

Function `generateResultsGraph` gives a sub-network, plottable through `plotGraph`, with the nodes with the lowest p.score from an enrichment analysis. Function `addGOToGraph` can be applied to such sub-networks to overlay GO labels and similarity to a user-defined GO term.

Function `exportResults` is a wrapper around `generateResultsTable`, `generateEnzymesTable` and `generateResultsGraph` to write the results to files.

Usage

```r
generateResultsTable(method = "diffusion", threshold = 0.05,
                      plimit = 15, nlimit = 250, LabelLengthAtPlot = 45,
                      capPscores = 1e-06, object = NULL, data = NULL, ...)

generateEnzymesTable(method = "diffusion", threshold = 0.05,
                       nlimit = 250, LabelLengthAtPlot = 45, capPscores = 1e-06,
                       mart.options = list(biomart = "ensembl", dataset =
                     "hsapiens_gene_ensembl"), object = NULL, data = NULL, ...)

generateResultsGraph(method = "diffusion", threshold = 0.05,
                      plimit = 15, nlimit = 250, thresholdConnectedComponent = 0.05,
                      LabelLengthAtPlot = 22, object = NULL, data = NULL, ...)

exportResults(format = "csv", file = "myOutput",
               method = "diffusion", object = NULL, data = NULL, ...)

addGOToGraph(graph = NULL, GOterm = NULL, godata.options = list(OrgDb
                  = "org.Hs.eg.db", ont = "CC"), mart.options = list(biomart = "ensembl",
                                 dataset = "hsapiens_gene_ensembl"))

plotGraph(graph = NULL, layout = FALSE, graph.layout = NULL,
          plotLegend = TRUE, plot.fun = "plot.igraph", NamesAsLabels = TRUE,
          ...)
```

Arguments

- **method**: one in "diffusion", "pagerank"
- **threshold**: Numeric value between 0 and 1. p.score threshold applied when filtering KEGG nodes. Lower thresholds are more stringent.
- **plimit**: Pathway limit, must be a numeric value between 1 and 50. Limits the amount of pathways in method = "hypergeom"
- **nlimit**: Node limit, must be a numeric value between 1 and 1000. Limits the order of the solution sub-graph when in method = "diffusion" and method = "pagerank"
Export Functions

LabelsLengthAtPlot

- Numeric value between 10 and 50. Maximum length that a label can reach when plotting the graph. The remaining characters will be truncated using "...

capScores

- Numeric value, minimum p-score admitted for the readable formatting. Smaller p-scores will be displayed as < capScores

object

- FELLA.USER object

data

- FELLA.DATA object

...  

- Optional arguments for the plotting function in plotGraph. Arguments passed to the exporting function in exportResults. Ignored otherwise.

mart.options

- List, options for the biomaRt function getBM. Importantly, this defines the organism, see listDatasets for possibilities. If calling generateEnzymesTable, the user can set mart.options = NULL to avoid adding GO labels to enzymes.

thresholdConnectedComponent

- Numeric value between 0 and 1. Connected components that are below the threshold are kept, while the ones exceeding it (because they are too small) are discarded.

format

- Character, one of: "csv" for regular results table, "enzyme" for table with enzyme data, "igraph" for igraph format. Alternatively, any format supported by igraph, see write_graph

file

- Character specifying the output file name

graph

- An igraph object, typically a small one, coming from an enrichment through "diffusion" or "pagerank".

GOterm

- Character, GO entry to draw semantic similarity in the solution graph. If NULL, the GO labels will be appended without similarities.

godata.options

- List, options for the database creator godata

layout

- Logical, should the plot be returned as a layout?

graph.layout

- Two-column numeric matrix, if this argument is not null then it is used as graph layout

plotLegend

- Logical, should the legend be plotted as well?

plot.fun

- Character, can be either plot.igraph or tkplot

NamesAsLabels

- Logical, should KEGG names be displayed as labels instead of KEGG identifiers?

Details

Functions generateResultsTable and generateEnzymesTable need a FELLA.DATA object and a FELLA.USER object with a successful enrichment. generateResultsTable provides the entries whose p-score is below the chosen threshold in a tabular format. generateEnzymesTable returns a table that contains (1) the enzymes that are below the user-defined p-score threshold, along with (2) the genes that belong to the enzymatic families in the organism defined in the database, and (3) GO labels of such enzymes, if mart.options is not NULL and points to the right database.

Function generateResultsGraph returns an igraph object with a relevant sub-network for manual examination. A FELLA.USER object with a successful enrichment analysis and the corresponding
**FELLA.DATA** must be supplied. Graph nodes are prioritised by p.score and selected through the most stringent between (1) p.score threshold and (2) maximum number of nodes nlimit.

There is an additional filtering feature for tiny connected components, controllable through thresholdConnectedComponent (smaller is stricter). The user can choose to turn off this filter by setting thresholdConnectedComponent = 1. The idea is to discard connected components so small that are likely to arise from random selection of nodes. Let k be the order of the current sub-network. A connected component of order r will be kept only if the probability that a random subgraph from the whole KEGG knowledge model of order k contains a connected component of order at least r is smaller than thresholdConnectedComponent. Such probabilities are estimated during buildDataFromGraph; the amount of random trials can be controlled by its niter argument.

Function exportResults writes the enrichment results as the specified filetype. Options are: a csv table ("csv"), an enzyme csv table ("enzyme") an igraph object as an RData file, or any format supported by igraph's write_graph.

Function addGOToGraph takes and returns a graph object with class igraph adding the following attributes: GO labels in V(graph)$GO, and semantic similarities in V(graph)$GO.simil if GOterm != NULL.

The GO database describes genes in terms of three ontologies: molecular function (MF), biological process (BP) and cellular component (CC) [Gene Ontology Consortium, 2015]. The user can be interested in finding which enzymatic families reported with a low p.score are closest to a particular GO term. To assess similarity between GO labels, FELLA uses the semantic similarity defined in [Yu, 2010] and their implementation in the GOSemSim R package. The user will obtain, for each enzymatic family, the closest GO term to his or her GO query and the semantic similarity between them. Exact matches have a similarity of 1. Function plotGraph detects the presence of the GO similarity option and plots its magnitude.

Function plotGraph plots a solution graph from the diffusion and pagerank analysis. For plotting hypergeom results, please use plot instead. Specific colors and shapes for each KEGG category are used: pathways are maroon, modules are violet, enzymes are orange, reactions are blue and compounds are green. If the graph contains the similarity to a GO term, enzymes will be displayed as triangles whose color depicts the strength of such measure (yellow: weak, purple: strong). At the moment, plotGraph allows plotting through the static plot.igraph and the interactive tkplot.

**Value**

generateResultsTable returns a data.frame that contains the nodes below the p.score threshold from an enrichment analysis.

generateEnzymesTable returns a data.frame that contains the enzymes below the p.score threshold, along with their genes and GO labels.

generateResultsGraph returns an igraph object: a sub-network from the whole KEGG knowledge model under the specified thresholds (threshold and thresholdConnectedComponent).

exportResults returns invisible(), but as a side effect the specified file is created.

addGOToGraph returns an igraph object, which is the input graph with extra attributes: GO labels in V(graph)$GO, and semantic similarities in V(graph)$GO.simil if GOterm != NULL.

plotGraph returns invisible() if layout = F and the plotting layout as a data.frame otherwise.
References


Examples

```r
## First generate a toy enrichment
library(igraph)
data(FELLA.sample)
data(input.sample)
## Enrich input
obj <- enrich(
  compounds = input.sample,
  data = FELLA.sample)

# Results table
tab.res <- generateResultsTable(
  method = "hypergeom",
  threshold = 0.1,
  object = obj,
  data = FELLA.sample)
head(tab.res)

# Use wrapper to write the table to a file
out.file <- tempfile()
exportResults(
  format = "csv",
  threshold = 0.1,
  file = out.file,
  object = obj,
  data = FELLA.sample)

# Enzymes table
tab.ec <- generateEnzymesTable(
  threshold = 0.1,
  object = obj,
  data = FELLA.sample)
```
The FELLA package

Description

FELLA is a metabolomics data enrichment tool that contextualises a list of metabolites using KEGG reactions, enzymes, modules and pathways [Picart-Armada, 2017].

Details

FELLA can build knowledge models for the desired organism from the KEGG database [Kanehisa, 2017]. Once a model is ready, the input for the enrichment is introduced as a list of affected metabolites (as KEGG IDs). The output contains a comprehensive biological network layout that relates relevant pathways to the affected metabolites. Results are available in network and tabular format.
FELLA is equipped with a simple graphical interface for the lay user, deployed through launchApp. FELLA relies mainly on the following packages: KEGGREST for the queries to the KEGG server [Tenenbaum, 2013], igraph for the network support [Csardi, 2006] and shiny for the graphical user interface [Chang, 2017].

References

Methodology:

Database:

Main dependencies:

Examples

## Walkthrough
browseVignettes("FELLA")
## I: create database
?buildGraphFromKEGGREST
## II: enrich data
?enrich
## III: export results
?exportResults

---

**FELLA.DATA-class**

An S4 class to represent all the necessary KEGG data

Description

An S4 class to represent all the necessary KEGG data

"show" is an S4 method to show a FELLA.DATA object

Usage

```r
## S4 method for signature 'FELLA.DATA'
show(object)
```
Arguments

object       A FELLA.DATA object

Value

show returns invisible()

Slots

keggdata    A D.keggdata S4 object
hypergeom    A D.hypergeom S4 object
diffusion    A D.diffusion S4 object
pagerank     A D.pagerank S4 object

Description

This FELLA.DATA object is a small KEGG graph object. Despite being a small database that only contains the two metabolic pathways hsa00010 - Glycolysis / Gluconeogenesis, and hsa00640 - Propanoate metabolism, it is useful to play around with FELLA’s functions. It is also used for internal testing of this package.

Usage

data(FELLA.sample)

Format

An object of class FELLA.DATA of length 1.

Value

A FELLA.DATA object

Source

Generated from a mid-2017 KEGG release (http://www.genome.jp/kegg/)

Examples

data(FELLA.sample)
An S4 class to save all the user analysis data

Description

Assigning the value of show to a variable will provide small data frames with the best scoring pathways (hypergeom) and the best nodes in the KEGG network (diffusion and pagerank).

Usage

## S4 method for signature 'FELLA.USER'
show(object)

## S4 method for signature 'FELLA.USER,missing'
plot(x = new("FELLA.USER"),
     method = "hypergeom", threshold = 0.05, plimit = 15,
     nlimit = 250, layout = FALSE, thresholdConnectedComponent = 0.05,
     LabelLengthAtPlot = 22, data = NULL, ...)

Arguments

- **object**: A `FELLA.USER` object
- **x**: A `FELLA.USER` object
- **method**: Character, exactly one of: "hypergeom", "diffusion", "pagerank"
- **threshold**: Numeric value between 0 and 1. p.score threshold applied when filtering KEGG nodes. Lower thresholds are more stringent.
- **plimit**: Pathway limit, must be a numeric value between 1 and 50. Limits the amount of pathways in method = "hypergeom"
- **nlimit**: Node limit, must be a numeric value between 1 and 1000. Limits the order of the solution sub-graph when in method = "diffusion" and method = "pagerank"
- **layout**: Logical, should the plot be returned as a layout?
- **thresholdConnectedComponent**: Numeric value between 0 and 1. Connected components that are below the threshold are kept, while the ones exceeding it (because they are too small) are discarded.
- **LabelLengthAtPlot**: Numeric value between 10 and 50. Maximum length that a label can reach when plotting the graph. The remaining characters will be truncated using "...
- **data**: FELLA.DATA object
- **...**: Additional arguments passed to plotting functions

Value

- show invisibly returns a list of data frames with the best hits for each applied method
- plot returns a layout if layout = T, otherwise invisible()
getBackground

Slots

userinput  A U.userinput S4 object
hypergeom  A U.hypergeom S4 object
diffusion  A U.diffusion S4 object
pagerank  A U.pagerank S4 object

getBackground  Get compounds in the defined background

Description

Extractor function for the compounds defined as background

Usage

getBackground(object)

Arguments

object  FELLA.USER object

Value

Vector of compounds in the background. If this vector is empty, all the compounds are used as background by default.

Examples

data(FELLA.sample)
data(input.sample)
input <- head(input.sample, 12)

## If the background is default, we see an empty vector
## Note that the number of iterations is really small in the example
obj <- enrich(
  compounds = input,
  method = "diffusion",
  approx = "simulation",
  niter = 100,
  data = FELLA.sample)

getBackground(obj)

## Otherwise we see the background compounds that mapped to the graph
obj <- enrich(
  compounds = input,
  compoundsBackground = input.sample,
  method = "diffusion",

getCom

Get community

Description
Extractor function for all the nodes from a level/community of KEGG graph

Usage
getCom(data, level, format = "name")

Arguments

- **data**: FELLA.DATA object
- **level**: Desired level, can be coded as a number or a character: 1 or "pathway"; 2 or "module"; 3 or "enzyme"; 4 or "reaction"; 5 or "compound".
- **format**: Format of the output, "name" returns KEGG IDs whereas "id" returns vertices IDs

Value
Vector of the names/ids of the desired KEGG graph community

Examples

data(FELLA.sample)
## Pathways
getc(FELLA.sample, 1, format = "name")
getc(FELLA.sample, 1, format = "id")
## Modules
getc(FELLA.sample, 2)
## Enzymes
head(getc(FELLA.sample, 3))
## Reactions
head(getc(FELLA.sample, 4))
## Compounds
head(getc(FELLA.sample, 5))
getExcluded  
*Get excluded compounds*

**Description**

Extractor function for the compounds in the input that were not mapped to the KEGG graph

**Usage**

```r
getExcluded(object)
```

**Arguments**

- `object`: FELLA.USER object

**Value**

Vector of the excluded compounds

**Examples**

```r
data(FELLA.sample)
data(input.sample)

## No excluded compounds
obj <- defineCompounds(
  compounds = input.sample,
  data = FELLA.sample)
getExcluded(obj)

## One compound does not map
## The user gets a warning as well
obj <- defineCompounds(
  compounds = c(input.sample, "intruder"),
  data = FELLA.sample)
getExcluded(obj)
```

getGraph  
*Get KEGG graph*

**Description**

Extractor function for the KEGG graph from the FELLA.DATA object

**Usage**

```r
getGraph(data)
```
**getInfo**

**Arguments**

- `data`  
  FELLA.DATA object

**Value**

KEGG graph as an `igraph` object

**Examples**

```r
data(FELLA.sample)
g <- getGraph(FELLA.sample)
class(g)
```

---

**getInfo**  
*Get KEGG version info*

**Description**

Extractor function for the info about the KEGG version used to build the FELLA.DATA object

**Usage**

```r
getInfo(data)
```

**Arguments**

- `data`  
  FELLA.DATA object

**Value**

Character containing the KEGG release details

**Examples**

```r
data(FELLA.sample)
getInfo(FELLA.sample)
```
**getInput**

*Get metabolites in the input*

Description

Extractor function for the metabolites specified by the user in the input

Usage

```
getInput(object)
```

Arguments

- **object**
  - FELLA.USER object

Value

Vector of metabolites in the input

Examples

```r
data(FELLA.sample)
data(input.sample)

## No excluded compounds: the input is recovered as is
obj <- defineCompounds(
  compounds = input.sample,
  data = FELLA.sample)
i1 <- getInput(obj)

## One compound does not map: the input contains only the mapped entities
obj <- defineCompounds(
  compounds = c(input.sample, "intruder"),
  data = FELLA.sample)
i2 <- getInput(obj)

identical(sort(i1), sort(i2))
```

---

**getMatrix**

*Get matrix for the desired methodology*

Description

Extractor function for the matrices of hypergeometric, diffusion and PageRank methodologies

Usage

```
getMatrix(data, method)
```
getName

Arguments

- **data** FELLA.DATA object
- **method** Character, exactly one of: "hypergeom", "diffusion", "pagerank"

Value

Matrix for the desired methodology (internal usage)

Examples

```r
## This function is internal
attach(environment(FELLA:::getMatrix))
data(FELLA.sample)
# When a matrix is loaded:
x <- getMatrix(FELLA.sample, "hypergeom")
dim(x)
# When it is not:
y <- getMatrix(FELLA.sample, "diffusion")
dim(y)
y
```

getName

*Map KEGG identifiers to KEGG names*

Description

Map KEGG identifiers to KEGG names, multiple names for an ID are reported if annotated. The KEGG identifiers may have mixed levels.

Usage

`getName(data, id)`

Arguments

- **data** FELLA.DATA object
- **id** KEGG IDs whose name is desired

Value

List whose names are KEGG IDs and whose entries are the vectors of matches

Examples

```r
data(FELLA.sample)
getName(FELLA.sample, c("C00002", "C00040"))
```
**getPscores**  
*Get p-scores from the desired methodology*

**Description**  
Extractor function for the p-scores using the desired methodology

**Usage**  
```r  
getPscores(object, method)  
```

**Arguments**  
- **object**  
  FELLA.USER object  
- **method**  
  Character, exactly one of: "hypergeom", "diffusion", "pagerank"

**Value**  
Named vector of p-scores

**Examples**  
```r  
data(FELLA.sample)  
data(input.sample)  
obj <- enrich(  
  compounds = input.sample,  
  data = FELLA.sample)  
p <- getPscores(obj, "diffusion")  
sum(p < 0.1)  
```

---

**getPvaluesSize**  
*Get matrix for the p-value regarding CC size*

**Description**  
Extractor function for the matrix containing p-value by CC size that compares to a random selection of nodes in the KEGG graph

**Usage**  
```r  
getPvaluesSize(data)  
```

**Arguments**  
- **data**  
  FELLA.DATA object
getStatus

Value
Matrix with p-values for CC size (internal usage)

Examples
## This function is internal
attach(environment(FELLA:::getPvaluesSize))
data(FELLA.sample)
M <- getPvaluesSize(FELLA.sample)
dim(M)
summary(as.vector(M))

getStatus
Get the slot "status"

Description
Extractor function for the slot "status" for the KEGG data

Usage
getStatus(data)

Arguments
data FELLA.DATA object

Value
Slot "status" (internal usage)

Examples
## This function is internal
data(FELLA.sample)

## Is the object loade?
FELLA:::getStatus(FELLA.sample)
FELLA:::getStatus(new("FELLA.DATA"))
getSums

Get rowSums/squaredRowSums

Description
Extractor function for rowSums/squaredRowSums

Usage
getSums(data, method, squared)

Arguments
- data: FELLA.DATA object
- method: Character, exactly one of: "hypergeom", "diffusion", "pagerank"
- squared: Logical, whether to return rowSums (F) or squaredRowSums (T)

Value
Named vector with rowSums/squaredRowSums (internal usage)

Examples
## This function is internal
attach(environment(FELLA:::getSums))
data(FELLA.sample)
rowsums <- getSums(FELLA.sample, "diffusion", squared = FALSE)
hist(rowsums)

getValid

Get the slot "valid"

Description
Extractor function for the slot "valid"

Usage
getValid(object, method)

Arguments
- object: FELLA.USER object
- method: Character, exactly one of: "hypergeom", "diffusion", "pagerank"
Value

Slot "valid" (internal usage)

Examples

```r
## This function is internal

data(FELLA.sample)
data(input.sample)

obj <- enrich(
  compounds = input.sample,
  method = "diffusion",
  data = FELLA.sample)

## If the analysis is valid
FELLA:::getValid(obj, "diffusion")

## Otherwise
FELLA:::getValid(new("FELLA.USER"), "diffusion")
FELLA:::getValid(obj, "pagerank")
```

---

**infere.con2ec**

*Infer connections to EC*

Description

Function `infere.con2ec` infers network connections to KEGG EC families by passing through genes. This assumes that the category being mapped to enzymes is above them.

Usage

```r
infere.con2ec(ids, ent, ent2gene, gene2enzyme)
```

Arguments

- `ids` Character vector of identifiers to map. For example, all the KEGG pathways
- `ent` Character, entity that we are mapping (one of "pathway" and one of "module")
- `ent2gene` Named character vector, names are the entity `ent` and values are genes
- `gene2enzyme` Named character vector, names are genes and values are EC enzyme families

Value

Two-column data frame. Column "from" contains the KEGG enzyme families whereas "to" contains the entity `ent`. 

```
Examples

```r
ids <- "hsa00010"
ent <- "pathway"
ent2gene <- c("hsa00010" = "hsa:10", "hsa00010" = "hsa:120")
gene2enzyme <- c("hsa:10" = "1.1.1.1", "hsa:120" = "1.2.3.4")
FELLA:::infere.con2ec(ids, ent, ent2gene, gene2enzyme)
```

Description

This character vector object has been generated using the sample data in the object FELLA.sample. The KEGG compounds have been chosen with preference for the hsa00640 pathway, so that the enrichment results choose pathway hsa00640 over hsa00010.

Usage

```r
data(input.sample)
```

Format

An object of class character of length 30.

Value

A character vector containing 30 KEGG IDs

Source

Generated from a mid-2017 KEGG release (http://www.genome.jp/kegg/)

Examples

```r
data(input.sample)
```
is.FELLA.DATA Check FELLA.DATA class

**Description**

Is x a FELLA.DATA object?

**Usage**

```r
is.FELLA.DATA(x = NULL)
```

**Arguments**

- `x` Object to check

**Value**

Logical value stating if x is a FELLA.DATA object

**Examples**

```r
data(FELLA.sample)
is.FELLA.DATA(FELLA.sample)
is.FELLA.DATA(42)
```

is.FELLA.USER Check FELLA.USER class

**Description**

Is x a FELLA.USER object?

**Usage**

```r
is.FELLA.USER(x = NULL)
```

**Arguments**

- `x` Object to check

**Value**

Logical value stating if x is a FELLA.USER object
**Examples**

```r
is.FELLA.USER(new("FELLA.USER"))
is.FELLA.USER(42)

data(FELLA.sample)
data(input.sample)
obj <- enrich(
    compounds = input.sample,
    method = "diffusion",
    data = FELLA.sample)
is.FELLA.USER(obj)
```

## Description

Function `largestcc` extracts the largest connected component of an igraph object.

## Usage

```r
largestcc(graph)
```

## Arguments

- `graph` Igraph object

## Value

Connected igraph object

## Examples

```r
library(igraph)
g <- barabasi.game(10) + graph.empty(10)
FELLA:::largestcc(g)
```
launchApp  

*Launch a shiny app with FELLA*

**Description**

`launchApp` deploys a shiny application to perform the metabolomics data enrichment. Although this app does not provide all the options available in *FELLA*, it is easily accessible for the lay user.

**Usage**

`launchApp(...)`

**Arguments**

... Parameters passed to `runApp`

**Details**

The graphical interface allows to: (1) upload the data and check if the KEGG ids have successfully mapped, (2) select database, set analysis and graphical parameters, (3) interactively browse the resulting sub-network as a graph or as a table, and (4) export such results as a table or a network. At least one database is needed before deploying the app. See `?buildDataFromGraph` for further details.

**Value**

`invisible()`, but as a side effect the app will be launched

**Examples**

```r
## Not run:
r <- try(launchApp())

## End(Not run)
```

listApprox  

*List of approximations*

**Description**

Available approximations for the analysis

**Usage**

`listApprox()`
**listCategories**  
*List of node categories*

**Value**
Character vector

**Examples**
```r
listCategories()
```

**Description**
Node categories used in the internal representations

**Usage**
```r
listCategories()
```

**Value**
Character vector

**Examples**
```r
listCategories()
```

---

**listInternalDatabases**  
*List internal databases*

**Description**
This function lists the directories in the local database path

**Usage**
```r
listInternalDatabases(full.names = FALSE)
```

**Arguments**
- `full.names` Logical, should full paths be returned?

**Value**
Vector with database directories
Examples

listInternalDatabases()

---

listMethods: List of methods

Description

Methods available for the analysis

Usage

listMethods()

Value

Character vector

Examples

listMethods()

---

mytriangle: Add triangular shape to igraph plot

Description

This function enables the usage of triangles as shape in the function `plot.igraph`.

Usage

mytriangle(coords, v = NULL, params)

Arguments

coords, v, params

clipping arguments, see `shapes`

Value

Plot symbols
Examples

## This function is internal
library(igraph)

add.vertex.shape(
  "triangle", clip = shapes("circle")$clip,
  plot = FELLA:::mytriangle)

g <- barabasi.game(10)
plot(
  g, vertex.shape = "triangle",
  vertex.color = rainbow(vcount(g)),
  vertex.size = seq(10, 20, length = vcount(g)))

plotBipartite

Internal function to plot a bipartite graph

Description

This function plots a bipartite graph, tailored for the hypergeometric over representation analysis. As the nodes can only be compounds and pathways, the layout is simple and bipartite.

Usage

plotBipartite(graph = NULL, layout = FALSE, ...)

Arguments

graph       Graph result that must come from the hypergeometric test analysis
layout      Logical, should the plot be returned as a layout?
...          Additional parameters passed to plot.igraph

Value

If layout = FALSE then the value returned is invisible(). Otherwise, the layout is returned, also in an invisible fashion.

Examples

## This function is internal
data(FELLA.sample)
data(input.sample)
## Enrich input
obj <- enrich(
  compounds = input.sample,
  data = FELLA.sample,
  method = "hypergeom")
## Generate the bipartite graph (only in the hypergeometric test)

```r

## Plot it
FELLA:::plotBipartite(g)
```

---

### plotLegend

**Description**

This function adds a legend to a solution plot. It can include the CC similarity.

**Usage**

```r
plotLegend(GO.annot = FALSE, cex = 0.75)
```

**Arguments**

- `GO.annot` Logical, should GO annotations be included?
- `cex` Numeric value, cex parameter for the function `legend`

**Value**

This function is only used for its effect, so it returns `invisible()`.

**Examples**

```r

## This function is internal

library(igraph)
g <- barabasi.game(20)
plot(g)
FELLA:::plotLegend()
plot(g)
FELLA:::plotLegend(GO.annot = TRUE)
```
sanitise

ID sanitiser function

Description
Sanitise KEGG identifiers

Usage
sanitise(x, category, organism)

Arguments
x Character vector, IDs to sanitise
category Character, one of: "pathway", "module", "enzyme", "ncbi", "reaction", "compound"

Value
Character vector, sanitised x

Examples
FELLA:::sanitise(c("path:hsa00010", "path:hsa00020"), "pathway", "hsa")

U.diffusion-class
An internal S4 class for the user data of the diffusion enrichment analysis

Description
An internal S4 class for the user data of the diffusion enrichment analysis

Slots
valid Logical value; is the analysis valid?
pscores Named numeric vector with p-scores
approx Character; which approximation was used? Can be "simulation" for Monte Carlo; "normality", "gamma" or "t" for parametric approaches
niter Numeric value, number of iterations for the simulated approach
U.hypergeom-class  
An internal S4 class for the user data of the hypergeometric over representation analysis

Description

An internal S4 class for the user data of the hypergeometric over representation analysis

Slots

valid  Logical value; is the analysis valid?
pvalues  Named numeric vector with p-values
pathhits  Numeric named vector with the quantities "sample_success" for the hypergeometric distribution (#affected in path)
pathbackground  Numeric named vector with the quantities "total_success" for the hypergeometric distribution (total in path)
nbackground  Numeric value, number of compounds in the background. Equivalently, number of rows for the hypergeometric binary matrix
ninput  Numeric value, number of affected compounds matched to the rownames

U.pagerank-class  
An internal S4 class for the user data of the PageRank enrichment analysis

Description

An internal S4 class for the user data of the PageRank enrichment analysis

Slots

valid  Logical value; is the analysis valid?
pscores  Named numeric vector with p-scores
approx  Character; which approximation was used? Can be "simulation" for Monte Carlo; "normality", "gamma" or "t" for parametric approaches
niter  Numeric value, number of iterations for the simulated approach
An internal S4 class for the user input data

Description

An internal S4 class for the user input data

Slots

- `metabolites` Character vector containing the affected compounds
- `metabolitesbackground` Character vector containing the compounds for the personalised background. Optionally, can be NULL for default background
- `excluded` Character vector containing the compounds that have been excluded because they cannot be mapped to KEGG graph compounds
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