Package 'GOstats'

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Collate zzz.R AllClasses.R AllGenerics.R hyperGTest-methods.R GOHyperGResult-accessors.R GOgraph.R GOhyptest.R hyperGtable.R shortestPath.R triad.R									
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R topics documented:									
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Description

A set of tools for interacting with GO and microarray data. A variety of basic manipulation tools for graphs, hypothesis testing and other simple calculations.

Details

Package: GOstats Version: 1.7.4 Date: 23-08-2006

biocViews: Statistics, Annotation, GO, MultipleComparisons

Depends: graph (>= 1.9.25), GO, annotate, RBGL, xtable, Biobase, genefilter, multtest, Category (>= 1.3.7), methods

Imports: methods, Category
Suggests: hgu95av2.db (>= 1.6.0)

License: Artistic

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Further information is available in the following vignettes:

GOstats Using GOstats (source, pdf)
GOusage Basic GO Usage (source, pdf)

GOvis Visualizing Data Using GOstats (source, pdf)

Author(s)

R. Gentleman with contributions from S. Falcon

Maintainer: R. Gentleman <rgentlem@fhcrc.org>

compCorrGraph A function to compute a correlation based graph from Gene Expression Data

Description

Given a set of gene expression data (an instance of the ExpressionSet class) this function computes a graph based on correlations between the probes.

Usage

```
compCorrGraph(eSet, k = 1, tau = 0.6)
```

Arguments

eSet An instance of the ExpressionSet class.

k The power to raise the correlations to.

tau The lower cutoff for absolute correlations.

Details

Zhou et al. describe a method of computing a graph between probes (genes) based on estimated correlations between probes. This function implements some of their methods.

Pearson correlations between probes are computed and then these are raised to the power k. Any of the resulting estimates that are less than tau in absolute value are set to zero.

Value

An instance of the graph class. With edges and edge weights determined by applying the algorithm described previously.

Author(s)

R. Gentleman

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References

Zhou et al., Transitive functional annotation by shortest-path analysis of gene expression data.

See Also

```
compGdist
```

Examples

```
## Create an ExpressionSet to work with
set.seed(123)
exprMat <- matrix(runif(50 * 5), nrow=50)
genData <- new("ExpressionSet", exprs=exprMat)
corrG = compCorrGraph(genData)</pre>
```

compGdist

A function to compute the distance between pairs of nodes in a graph.

Description

Given a graph, g, and a set of nodes in the graph, whNodes, Dijkstra's shortest path algorithm is used to compute the distance between all pairs of nodes in whNodes.

Usage

```
compGdist(g, whNodes, verbose = FALSE)
```

Arguments

g An instance of the graph class.

whNodes A vector of lables of the nodes in g for which distances are to be computed.

verbose If TRUE then output reporting the progress will be reported.

Details

This function can be quite slow, computation of the pairwise distances is not especially fast and if whNodes is long then there are many of them to compute.

Value

A matrix containing the pairwise distances. It might be worth making this an instance of the dist class at some point.

Author(s)

R. Gentleman

See Also

```
compCorrGraph
```

Examples

```
example(compCorrGraph)
compGdist(corrG, nodes(corrG)[1:5])
```

GOHyperGResult-class Class "GOHyperGResult"

Description

This class represents the results of a test for overrepresentation of GO categories among genes in a selected gene set based upon the Hypergeometric distribution.

For details on extracting information from this object, be sure to read the accessor documentation in the Category package: HyperGResult-accessors.

Objects from the Class

Objects can be created by calls of the form new("GOHyperGResult", ...).

Slots

goDag: Object of class "graph" representing the DAG of GO terms tested.

pvalue.order: Object of class "integer". The sort order of the computed p-values.

annotation: Object of class "character". The name of the annotation data package used in the analysis.

geneIds: Object of class "ANY". The intersection of the gene identifiers given as input and the computed gene universe.

testName: Object of class "character". Identifies the testing method used to produce this result instance.

pvalueCutoff: Object of class "numeric". The cutoff for significance used for some testing methods. Also used for pretty display in the show method.

conditional: A logical indicating whether the calculation should condition on the GO structure.

testDirection: A string which can be either "over" or "under". This determines whether the test performed detects over or under represented GO terms.

Extends

Class "HyperGResultBase", directly.

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Methods

goDag signature(r = "GOHyperGResult"): return the graph instance representing the DAG of the GO terms that were tested.

summary signature(r = "GOHyperGResult"): Returns a data.frame summarizing the test result. Optional arguments pvalue and categorySize allow specification of maximum pvalue and minimum categorySize, respectively. Optional argument htmlLinks is a logical value indicating whether to add HTML links (useful in conjunction with xtables print method with type set to "html").

htmlReport signature(r = "GOHyperGResult"): Write an HTML version of the table produced by the summary method. The path of a file to write the report to can be specified using the file argument. The default is file="" which will cause the report to be printed to the screen. If you wish to create a single report comprising multiple results you can set append=TRUE. The default is FALSE (overwrite preexisting report file). You can specify a string to use as an identifier for each table by providing a value for the label argument. Additional named arguments will be passed to the summary method.

description signature(object = "GOHyperGResult"): Return a string giving a one-line description of the result.

Author(s)

Seth Falcon

See Also

HyperGResult-accessors

GOstats-defunct

Defunct Functions in GOstats Package

Description

The functions or variables listed here are no longer part of GOstats as they are not needed (any more).

Usage

combGOGraph()
hyperGtable()
hyperG2Affy()
selectedGenes()
GOHyperG()
GOKEGGHyperG()
getGoGraph()

Details

combGOGraph was replaced by join. hyperGtable was replaced by summary. hyperG2Affy was replaced by probeSetSummary. GOLeaves was replaced by graph::leaves. selectedGenes was replaced by geneIdsByCategory. GOHyperG was replaced by hyperGTest. GOKEGGHyperG was replaced by hyperGTest. getGoGraph was replaced by GOGraph.

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hyperGTest

Hypergeometric Tests for GO term association

Description

Given a GOHyperGParams instance containing a set of unique Entrez Gene Identifiers, a microarray annotation data package name, and the GO ontology of interest, this function will compute Hypergeomtric p-values for over or under-representation of each GO term in the specified ontology among the GO annotations for the interesting genes. The computations can be done conditionally based on the structure of the GO graph.

Arguments

р

A GOHyperGParams instance

Details

When conditional(p) == TRUE, the hyperGTest function uses the structure of the GO graph to estimate for each term whether or not there is evidence beyond that which is provided by the term's children to call the term in question statistically overrepresented.

The algorithm conditions on all child terms that are themselves significant at the specified p-value cutoff. Given a subgraph of one of the three GO ontologies, the terms with no child categories are tested first. Next the nodes whose children have already been tested are tested. If any of a given node's children tested significant, the appropriate conditioning is performed.

Value

A GOHyperGResult instance.

Author(s)

Seth Falcon

References

FIXME

See Also

```
GOHyperGResult-class,
geneGoHyperGeoTest, geneKeggHyperGeoTest
```

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idx2dimnames

Index to Dimnames

Description

A function to map from integer offsets in an array to the corresponding values of the row and column names. There is probably a better way but I didn't find it.

Usage

```
idx2dimnames(x, idx)
```

Arguments

x a matrix or data.frame.

idx An integer vector of offsets into the matrix (values between 1 and the length of

the matrix.

Value

A list with two components. If it is a LIST, use

rowNames The row names corresponding to the integer index.

colNames The column names corresponding to the integer index.

Author(s)

R. Gentleman

See Also

dimnames

Examples

```
data(Ndists)
ltInf = is.finite(Ndists)
xx = idx2dimnames(Ndists, ltInf)
```

makeGOGraph

Construct a GO Graph

Description

The directed acyclic graph (DAG) based on finding the most specific terms for the supplied Entrez Gene IDs is constructed and returned. The constructuion is per GO ontology (there are three, MF, BP and CC) and once the most specific terms have been identified then all less specific terms are found (these are the parents of the terms) and then their parents and so on, until the root is encountered.

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Usage

Arguments

x A vector of Entrez Gene IDs.

Ontology Which GO ontology to use (CC, BP, or MF).

removeRoot A logical value indicating whether the GO root node should be removed or not.

mapfun A function taking a character vector of Entrez Gene IDs as its only argument

and returning a list of "GO lists" matching the structure of the lists in the GO maps of annotation data packages. The function should behave similarly to mget(x, eg2gomap, ifnotfound=NA), that is, NA should be returned if a specified Entrez ID has no GO mapping. See details for the interaction of mapfun

and chip.

chip The name of a DB-based annotation data package (the name will end in ".db").

This package will be used to generate an Entrez ID to GO ID mapping instead

of mapfun.

Details

For each supplied Entrez Gene identifier all the GO annotations (in the specified ontology) are found. The mapping is achieved in one of three ways:

- 1. If mapfun is provided, it will be used to perform the needed lookups. In this case, chip will be ignored.
- 2. If chip is provided and mapfun=NULL, then the needed lookups will be done based on the Entrez to GO mappings encapsulated in the specified annotation data package. This is the recommended usage.
- 3. If mapfun and chip are NULL or missing, then the function will attempt to load the GO package (the environment-based package, distinct from GO.db). This package contains a legacy environment mapping Entrez IDs to GO IDs. If the GO package is not available, an error will be raised. Omitting both mapfun and chip is not recommended as it is not compatible with the DB-based annotation data packages.

The mappings are different for the different ontologies. Typically a GO indentifier is used only in one specific ontology.

The resulting structure is stored in a graph using the graph package, again from Bioconductor.

Value

An object that inherits from the graph class. The particular implementation is not specified.

Author(s)

R. Gentleman

References

The Gene Ontology Consortium

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See Also

```
oneGOGraph
```

Examples

```
library("hgu95av2.db")
set.seed(321)
gN <- unique(sample(keys(hgu95av2.db, 'ENTREZID'), 4))
gg1 <- makeGOGraph(gN, "BP", chip="hgu95av2.db")</pre>
```

Ndists

Distance matrices for the BCR/ABL and NEG subgroups.

Description

These are precomputed distance matrices between all transcription factors selected. In the future they will be computed on the fly but currently that takes about 3 hours and so precomputed versions are supplied.

Usage

```
data(Ndists)
  data(Bdists)
```

Format

These are both distance matrices.

Source

They are based on the ALL data, ALL.

Examples

```
data(Ndists)
data(Bdists)
```

notConn

Find genes that are not connected to the others.

Description

A function that takes as input a distance matrix and finds those entries that are not connected to any others (ie. those with distance Inf.

Usage

```
notConn(dists)
```

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Arguments

dists

A distance matrix.

Details

It is a very naive implementation. It presumes that not connected entries are not connected to any other entries, and this might not be true. Using the connComp function from the graph package or the RBGL package might be a better approach.

Value

A vector of the names of the items that are not connected.

Author(s)

R. Gentleman

See Also

connComp

Examples

data(Ndists)
notConn(Ndists)

oneGOGraph

Construct the GO graph given a set of leaves.

Description

Given one or more GO identifiers (which indicate the leaves in the graph) and a set of mappings to the less specific sets of nodes this function will construct the graph that includes that node and all children down to the root node for the ontology.

Usage

```
oneGOGraph(x, dataenv)
GOGraph(x, dataenv)
```

Arguments

x A character vector of GO identifiers.

dataenv An environment for finding the parents of that term.

Details

For any set of GO identifiers (from a common ontology) we define the induced GO graph to be that graph, based on the DAG structure (child - parent) of the GO ontology of terms, which takes the most specific set of GO terms that apply (for that ontology) and then joins these to all less specific terms. These functions help construct such graphs.

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Value

The induced GO graph (or NULL) for the given GO identifier.

Author(s)

R. Gentleman

See Also

makeGOGraph

Examples

```
library("GO.db")
g1 <- oneGOGraph("GO:0003680", GOMFPARENTS)
g2 <- oneGOGraph("GO:0003701", GOMFPARENTS)
g3 <- join(g1, g2)

g4 <- GOGraph(c("GO:0003680", "GO:0003701"), GOMFPARENTS)
if( require("Rgraphviz") && interactive() )
plot(g3)</pre>
```

probeSetSummary

Summarize Probe Sets Associated with a hyperGTest Result

Description

Given the result of a hyperGTest run (an instance of GOHyperGResult), this function lists all Probe Set IDs associated with the selected Entrez IDs annotated at each significant GO term in the test result.

Usage

```
probeSetSummary(result, pvalue, categorySize, sigProbesets, ids = "ENTREZID")
```

Arguments

result	A GOHyperGResult instance. This is the output of the hyperGTest function when testing the GO category.
pvalue	Optional p-value cutoff. Only results for GO terms with a p-value less than the specified value will be returned. If omitted, pvalueCutoff(result) is used.
categorySize	Optional minimum size (number of annotations) for the GO terms. Only results for GO terms with categorySize or more annotations will be returned. If omitted, no category size criteria will be used.
sigProbesets	Optional vector of probeset IDs. See details for more information.
ids	Character. The type of IDs used in creating the GOHyperGResult object. Usually 'ENTREZID', but may be e.g., 'ACCNUM' if using A. thaliana chip.

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Details

Usually the goal of doing a Fisher's exact test on a set of significant probesets is to find pathways or cellular activities that are being perturbed in an experiment. After doing the test, one usually gets a list of significant GO terms, and the next logical step might be to determine which probesets contributed to the significance of a certain term.

Because the input for the Fisher's exact test consists of a vector of unique Entrez Gene IDs, and there may be multiple probesets that interrogate a particular transcript, the ouput for this function lists all of the probesets that map to each Entrez Gene ID, along with an indicator that shows which of the probesets were used as input.

The rationale for this is that one might not be able to assume a given probeset actually interrogates the intended transcript, so it might be useful to be able to check to see what other similar probesets are doing.

Because one of the first steps before running hyperGTest is to subset the input vectors of geneIds and universeGeneIds, any information about probeset IDs that interrogate the same gene transcript is lost. In order to recover this information, one can pass a vector of probeset IDs that were considered significant. This vector will then be used to indicate which of the probesets that map to a given GO term were significant in the original analysis.

Value

A list of data.frame. Each element of the list corresponds to one of the GO terms (the term is provides as the name of the element). Each data.frame has three columns: the Entrez Gene ID (EntrezID), the probe set ID (ProbeSetID), and a 0/1 indicator of whether the probe set ID was provided as part of the initial input (selected)

Note that this 0/1 indicator will only be correct if the 'geneId' vector used to construct the GOHyperGParams object was a named vector (where the names are probeset IDs), or if a vector of 'sigProbesets' was passed to this function.

Author(s)

S. Falcon and J. MacDonald

Examples

```
## Fake up some data
library("hgu95av2.db")
library("annotate")
prbs <- ls(hgu95av2G0)[1:300]</pre>
## Only those with GO ids
hasG0 <- sapply(mget(prbs, hgu95av2G0), function(ids)</pre>
if(!is.na(ids) && length(ids) > 1) TRUE else FALSE)
prbs <- prbs[hasG0]</pre>
prbs <- getEG(prbs, "hgu95av2")</pre>
## remove duplicates, but keep named vector
prbs <- prbs[!duplicated(prbs)]</pre>
## do the same for universe
univ <- ls(hgu95av2G0)[1:5000]
hasUnivGO <- sapply(mget(univ, hgu95av2GO), function(ids)</pre>
if(!is.na(ids) && length(ids) > 1) TRUE else FALSE)
univ <- univ[hasUnivG0]</pre>
univ <- unique(getEG(univ, "hgu95av2"))</pre>
p <- new("GOHyperGParams", geneIds=prbs, universeGeneIds=univ,</pre>
```

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```
ontology="BP", annotation="hgu95av2", conditional=TRUE)
## this part takes time...
if(interactive()){
  hyp <- hyperGTest(p)
  ps <- probeSetSummary(hyp, 0.05, 10)
}</pre>
```

shortestPath

Shortest Path Analysis

Description

The shortest path analysis was proposed by Zhou et. al. The basic computation is to find the shortest path in a supplied graph between two Entrez Gene IDs. Zhou et al claim that other genes annotated along that path are likely to have the same GO annotation as the two end points.

Usage

```
shortestPath(g, GOnode, mapfun=NULL, chip=NULL)
```

Arguments

g An instance of the graph class.

GOnode A length one character vector specifying the GO node of interest.

mapfun A function taking a character vector of GO IDs as its only argument and return-

ing a list of character vectors of Enterz Gene IDs annotated at each correspond-

ing GO ID. The function should behave similarly to mget(x, go2egmap, ifnotfound=NA),

that is, NA should be returned if a specified GO ID has no Entrez ID mappings.

See details for the interaction of mapfun and chip.

chip The name of a DB-based annotation data package (the name will end in ".db").

This package will be used to generate an Entrez ID to GO ID mapping instead

of mapfun.

Details

The algorithm implemented here is quite simple. All Entrez Gene identifiers that are annotated at the GO node of interest are obtained. Those that are found as nodes in the graph are retained and used for the computation. For every pair of nodes at the GO term the shortest path between them is computed using sp.between from the RBGL package.

There is a presumption that the graph is undirected. This restriction could probably be lifted if there was some reason for it - a patch would be gratefully accepted.

The mapping of GO node to Entrez ID is achieved in one of three ways:

- 1. If mapfun is provided, it will be used to perform the needed lookups. In this case, chip will be ignored.
- 2. If chip is provided and mapfun=NULL, then the needed lookups will be done based on the GO to Entrez mappings encapsulated in the specified annotation data package. This is the recommended usage.

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3. If mapfun and chip are NULL or missing, then the function will attempt to load the GO package (the environment-based package, distinct from GO.db). This package contains a legacy environment mapping GO IDs to Entrez IDs. If the GO package is not available, an error will be raised. Omitting both mapfun and chip is not recommended as it is not compatible with the DB-based annotation data packages.

Value

The return values is a list with the following components:

shortestpaths A list of the ouput from sp.between. The names are the names of the nodes

used as the two endpoints

nodesUsed A vector of the Entrez Gene IDs that were both found at the GO term of inter-

est and were nodes in the supplied graph, g. These were used to compute the

shortest paths.

nodesNotUsed A vector of Entrez Gene IDs that were annotated at the GO term, but were not

found in the graph g.

Author(s)

R. Gentleman

References

Transitive functional annotation by shortest-path analysis of gene expression data, by X. Zhou and M-C J. Kao and W. H. Wong, PNAS, 2002

See Also

```
sp.between
```

Examples

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simLL	Functions to compute similarities between GO graphs and also be-
SIIILL	Functions to compute similarities between GO graphs and also be-
	tween Entrez Gene IDs based on their induced GO graphs.

Description

Both simUI and simLP compute a similarity measure between two GO graphs. For simLL, first the induced GO graph for each of its arguments is found and then these are passed to one of simUI or simLP.

Usage

```
simLL(ll1, ll2, Ontology = "MF", measure = "LP", dropCodes = NULL,
    mapfun = NULL, chip = NULL)
simUI(g1, g2)
simLP(g1, g2)
```

Arguments

111	A Entrez Gene ID as a character vector.
112	A Entrez Gene ID as a character vector.
Ontology	Which ontology to use ("MF", "BP", "CC").
measure	Which measure to use ("LP", "UI").
dropCodes	A set of evidence codes to be ignored in constructing the induced GO graphs.
mapfun	A function taking a character vector of Entrez Gene IDs as its only argument and returning a list of "GO lists" matching the structure of the lists in the GO maps of annotation data packages. The function should behave similarly to mget(x, eg2gomap, ifnotfound=NA), that is, NA should be returned if a specified Entrez ID has no GO mapping. See details for the interaction of mapfun and chip.
chip	The name of a DB-based annotation data package (the name will end in ".db"). This package will be used to generate an Entrez ID to GO ID mapping instead of mapfun.
g1	An instance of the graph class.
g2	An instance of the graph class.

Details

For each of 111 and 112 the set of most specific GO terms within the ontology specified (Ontology) that are not based on any excluded evidence code (dropCodes) are found. The mapping is achieved in one of three ways:

- 1. If mapfun is provided, it will be used to perform the needed lookups. In this case, chip will be ignored.
- 2. If chip is provided and mapfun=NULL, then the needed lookups will be done based on the Entrez to GO mappings encapsulated in the specified annotation data package. This is the recommended usage.

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3. If mapfun and chip are NULL or missing, then the function will attempt to load the GO package (the environment-based package, distinct from GO.db). This package contains a legacy environment mapping Entrez IDs to GO IDs. If the GO package is not available, an error will be raised. Omitting both mapfun and chip is not recommended as it is not compatible with the DB-based annotation data packages.

Next, the induced GO graphs are computed.

Finally these graphs are passed to one of simUI, (union intersection), or simLP (longest path). For simUI the distance is the size of the intersection of the node sets divided by the size of the union of the node sets. Large values indicate more similarity. These similarities are between 0 and 1.

For simLP the length of the longest path in the intersection graph of the two supplied graph. Again, large values indicate more similarity. Similarities are between 0 and the maximum leaf depth of the graph for the specified ontology.

Value

A list with:

sim The numeric similarity measure.

measure Which measure was used.
g1 The graph induced by 111.
g2 The graph induced by 112.

If one of the supplied Gene IDs does not have any GO terms associated with it, in the selected ontology and with the selected evidence codes then NA is returned.

Author(s)

R. Gentleman

See Also

makeGOGraph

Examples

```
library("hgu95av2.db")
eg1 = c("9184", "3547")

bb = simLL(eg1[1], eg1[2], "BP", chip="hgu95av2.db")
```

termGraphs

Extraction and Plotting of GO Terms from a GOHyperGResult Object

Description

These functions extract and plot graph instances representing the relationships among GO terms tested using hyperGTest.

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Usage

Arguments

r	A GOHyperGResult object as returned by hyperGTest when given a GOHyperGParams object as input.
id	A character vector of category IDs that specifies which terms should be included in the graph.
pvalue	Numeric p-value cutoff to use for selecting category terms to include. Will be ignored if id is present.
use.terms	Logical value indicating whether a "term" node attribute should be added to the returned graph providing the more descriptive, but possibly much longer, GO Terms.
children	A logical value indicating whether to include direct child terms of the terms specified by id.
parents	A logical value indicating whether to include direct parent terms of the terms specified by id.
g	A graph object as returned by inducedTermGraph or termGraphs.
add.counts	A logical value indicating whether category size counts should be added to the node labels when plotting.
max.nchar	The maximum character length for node labels in the plot.
node.colors	A named character vector of length two with compoents sig and not, giving color names for the significant and non-significant nodes, respectively.
node.shape	This argument controls the shape of the plotted nodes and must take on a value allowed by Rgraphviz.
	For plotGOTermGraph, extra arguments are passed to the plot function.

Details

termGraphs returns a list of graph objects each representing one of the connected components of the subgraph of the GO ontology induced by selecting the specified GO IDs (if id is present) or by selecting the GO IDs that have a p-value less that pvalue. If use.terms is TRUE the GO IDs will be translated into GO Term names and attached to the nodes as node attributes (see nodeData). Edges in the graphs go from child (more specific) to parent (less specific).

inducedTermGraph returns a graph object representing the GO graph induced by the terms specified by id. The children and parent arguments control whether direct children and/or direct parents of the terms specified by id are added to the graph (at least one of the two must be TRUE).

plotGOTermGraph Create a plot using Rgraphviz of a graph object as returned by either termGraphs or inducedTermGraph. If a GOHyperGResult object is provided, then the nodes will be colored according to significance (based on the result object's pvalueCutoff) and counts will be added to show the size of the categories.

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Author(s)

Seth Falcon

|--|

Description

These functions provide some tools for finding triads in an undirected graph. A triad is a clique of size 3. The function triadCensus returns a list of all triads.

Usage

```
triadCensus(graph)
isTriad(x, y, z, elz, ely)
reduce2Degreek(graph, k)
enumPairs(iVec)
```

Arguments

graph	An instance of the graph class.
k	An integer indicating the minimum degree wanted.
х	A node
у	A node
z	A node
elz	The edgelist for z
ely	The edgelist for y
iVec	A vector of unique values

Details

enumPairs takes a vector as input and returns a list of length choose(length(iVec),2)/2 containing all unordered pairs of elements.

isTriad takes three nodes as arguments. It is already known that x has edges to both y and z and we want to determine whether these are reciprocated. This is determined by examining elz for both x and y and then examining ely for both x and z.

reduce2Degreek is a function that takes an undirected graph as input and removes all nodes of degree less than k. This process is iterated until there are no nodes left (an error is thrown) or all nodes remaining have degree at least k. The resultant subgraph is returned. It is used here because to be in a triad all nodes must have degree 2 or more.

triadCensus makes use of the helper functions described above and finds all triads in the graph.

Value

A list where each element is a triple indicating the members of the triad. Order is not important and all triads are reported in alphabetic order.

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Note

See the graph package, RBGL and Rgraphviz for more details and alternatives.

Author(s)

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Examples

```
##---- Should be DIRECTLY executable !! ----
##-- ==> Define data, use random,
```

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