

# Package ‘BioNAR’

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**Title** Biological Network Analysis in R

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**Description** the R package BioNAR, developed to step by step analysis of PPI network. The aim is to quantify and rank each protein’s simultaneous impact into multiple complexes based on network topology and clustering. Package also enables estimating of co-occurrence of diseases across the network and specific clusters pointing towards shared/common mechanisms.

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---

addEdgeAtts                      *Copy edge attributes from one graph to another*

---

### Description

Copy edge attributes from one graph to another

### Usage

```
addEdgeAtts(GG, gg)
```

### Arguments

GG	igraph object, source of attributes
gg	igraph object, attributes recipient

### Value

annotated version of gg igraph object

### Examples

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
GG <- igraph::read_graph(file, format="gml")
gg<-findLCC(GG)
gg <- addEdgeAtts(GG, gg)
edge_attr_names(gg)
```

---

annotateGeneNames              *Annotate Human Gene Names*

---

### Description

For the protein-protein interaction (PPI) or disease gene interaction (DGN) graphs that have EntrezID as a vertex name this function extract standard name from [org.Hs.eg.db](http://org.Hs.eg.db) and annotate vertices.

### Usage

```
annotateGeneNames(gg, orgDB = org.Hs.eg.db, keytype = "ENTREZID")
```

### Arguments

gg	igraph object to annotate
orgDB	ordDB object, by default human is assumed from <a href="http://org.Hs.eg.db">org.Hs.eg.db</a>
keytype	type of IDs stored in the name vertex attribute, by default ENTREZID is assumed.

**Details**

If vertex name attribute stores not EntrezID or network is build not from human genes, other `OrgDb-class` object could be provided in `orgDB` and one of `keytypes` from that object that correspond to the nature of the vertex name attribute could be provided in the `keytype` attribute.

If for some vertices name attribute does not match `keys` with particular `keytypes` in the `orgDB` object, empty string is added as `GeneName`.

**Value**

igraph object with new vertex attribute `GeneName`

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
agg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(agg)$name == '80273')
paste(V(agg)$GeneName[idx], 'GRPEL1')
```

---

annotateGoBP

*Add GO BP annotation to the graph vertices*

---

**Description**

The function loads an annotation data matrix called `annoF`, which contains three columns; the first containing gene Entrez IDs, the second gene GO BP ID terms, the third gene GO BP description terms. The function then performs a many-to-one mapping of each matrix row to a network vertex using matching Entrez IDs, filling the vertices attributes `GO_BP_ID` and `GO_BP`.

**Usage**

```
annotateGoBP(gg, annoF, idatt = "name")
```

**Arguments**

<code>gg</code>	graph to update
<code>annoF</code>	annotation matrix in Pair form
<code>idatt</code>	optional name of the vertex attribute to map to the annotation data.frame first column

**Value**

annotated igraph object

**See Also**

`getAnnotationVertexList`

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
sfile<-system.file("extdata", "flatfile.go.BP.csv", package = "BioNAR")
goBP <- read.table(sfile, sep="\t", skip=1, header=FALSE,
strip.white=TRUE, quote="")
sgg <- annotateGoBP(gg, goBP)
```

---

 annotateGoCC

*Add GO CC annotation to the graph vertices*


---

**Description**

The function loads an annotation data matrix called annoF, which contains three columns; the first containing gene Entrez IDs, the second gene GO ID terms, the third gene GO CC description terms. The function then performs a many-to-one mapping of each matrix row to a network vertex using matching Entrez IDs, filling the vertices attributes GO\_CC\_ID and GO\_CC.

**Usage**

```
annotateGoCC(gg, annoF, idatt = "name")
```

**Arguments**

gg	graph to update
annoF	annotation matrix in Pair form
idatt	optional name of the vertex attribute to map to the annotation data.frame first column

**Value**

annotated igraph object

**See Also**

getAnnotationVertexList

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
sfile<-system.file("extdata", "flatfile.go.CC.csv", package = "BioNAR")
goCC <- read.table(sfile, sep="\t", skip=1, header=FALSE,
strip.white=TRUE, quote="")
sgg <- annotateGoCC(gg, goCC)
```

annotateGoMF *Add GO MF annotation to the graph vertices*

**Description**

The function loads an annotation data matrix called annoF, which contains three columns; the first containing gene Entrez IDs, the second gene GO MF ID terms, the third gene GO MF description terms. The function then performs a many-to-one mapping of each matrix row to a network vertex using matching Entrez IDs, filling the vertices attributes GO\_MF\_ID and GO\_MF.

**Usage**

```
annotateGoMF(gg, annoF, idatt = "name")
```

**Arguments**

gg	graph to update
annoF	annotation matrix in Pair form
idatt	optional name of the vertex attribute to map to the annotation data.frame first column

**Value**

annotated igraph object

**See Also**

getAnnotationVertexList

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
sfile<-system.file("extdata", "flatfile.go.MF.csv", package = "BioNAR")
goMF <- read.table(sfile, sep="\t", skip=1, header=FALSE,
strip.white=TRUE, quote="")
sgg <- annotateGoMF(gg, goMF)
```

annotateGOont *Annotate nodes with GO terms*

**Description**

For the protein-protein interaction (PPI) or disease gene interaction (DGN) graphs that have EntrezID as a vertex name this function extract GeneOntolgy annotation from orgDB, which should be [OrgDb-class](#), split them into three ontology group (MF,BP,CC) and annotate vertices with .

**Usage**

```
annotateGOont(gg, orgDB = org.Hs.eg.db, keytype = "ENTREZID", idatt = "name")
```

**Arguments**

gg	igraph object to annotate
orgDB	ordDB object, by default human is assumed from <a href="#">org.Hs.eg.db</a>
keytype	type of IDs stored in the name vertex attribute, by default ENTREZID is assumed.
idatt	optional name of the vertex attributes that contains IDs matching the keytype

**Details**

If vertex name attribute stores not EntrezID or network is build not from human genes, other [OrgDb-class](#) object could be provided in orgDB and one of [keytypes](#) from that object that correspond to the nature of the vertex name attribute could be provided in the keytype attribute.

If for some vertices name attribute does not match [keys](#) with particular [keytypes](#) in the orgDB object, empty string is added as GeneName.

**Value**

igraph object with new vertex attribute GeneName

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
ggGO <- annotateGOont(gg)
```

---

annotateInterpro      *Add InterPro Family and Domain annotation to the graph vertices*

---

**Description**

Function takes data from annoF matrix and add them to attributes InterPro\_Family for term and InterPro\_Family\_ID for IDs.

**Usage**

```
annotateInterpro(gg, annoF, annoD, idatt = "name")
```

**Arguments**

gg	graph to update
annoF	family annotation matrix in Pair form
annoD	domain annotation matrix in Pair form
idatt	optional name of the vertex attributes that contains Entrez IDs

**Details**

Function takes data from annoD matrix and add them to attributes InterPro\_Domain for term and InterPro\_Domain\_ID for IDs.

**Value**

annotated igraph object

**See Also**

getAnnotationVertexList

annotatePresynaptic *Add presynaptic functional groups*

**Description**

Function takes from anno matrix manually curated presynaptic genes functional annotation derived from Boyken at al. (2013) [doi:10.1016/j.neuron.2013.02.027](https://doi.org/10.1016/j.neuron.2013.02.027) and add them to attributes PRESYNAPTIC.

**Usage**

```
annotatePresynaptic(gg, anno, idatt = "name")
```

**Arguments**

gg	graph to update
anno	annotation matrix in Pair form
idatt	optional name of the vertex attributes that contains Entrez IDs

**Value**

annotated igraph object

**See Also**

getAnnotationVertexList

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
sfile<-system.file("extdata", "PresynAn.csv", package = "BioNAR")
pres <- read.csv(sfile,skip=1,header=FALSE,strip.white=TRUE,quote="")
gg <- annotatePresynaptic(gg, pres)
```

---

annotateSCHanno      *Add SCHanno synaptic functional groups*

---

## Description

The function loads an annotation data matrix of functional groups for schizophrenia risk genes (1) called anno, which contains three columns; the first containing gene Entrez IDs, the second gene functional group ID terms, the third gene functional group description terms. The function then performs a many-to-one mapping of each matrix row to a network vertex using matching Entrez IDs, filling the SCHanno vertices attribute.

## Usage

```
annotateSCHanno(gg, anno, idatt = "name")
```

## Arguments

gg	igraph object to annotate
anno	annotation matrix in Pairs form
idatt	optional name of the vertex attributes that contains Entrez IDs

## Details

References:

1. Lips E, Cornelisse L, Toonen R, Min J, Hultman C, the International Schizophrenia Consortium, Holmans P, Donovan M, Purcell S, Smit A, Verhage M, Sullivan P, Visscher P, D P: Functional gene group analysis identifies synaptic gene groups as risk factor for schizophrenia. *Molecular Psychiatry* 2012,17:996–1006.

## Value

annotated igraph object

## See Also

getAnnotationVertexList

## Examples

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
afile <- system.file("extdata", "SCH_flatfile.csv", package = "BioNAR")
dis <- read.table(afile, sep="\t", skip=1, header=FALSE,
strip.white=TRUE, quote="")
agg <- annotateSCHanno(gg, dis)
```

---

annotateTopOntoOVG     *Annotate graph with disease terms*

---

## Description

The function loads a human disease annotation matrix called `dis`, which contains three columns; the first containing gene Entrez IDs, the second gene Human Disease Ontology (HDO) ID terms, the third gene HDO description terms. For human protein-protein interaction (PPI) or disease-gene networks (DGN) that have human Entrez IDs for the `igraph` vertex name attribute. The function then performs a many-to-one mapping of each matrix row to a network vertex using matching Entrez IDs, filling the vertices attributes `TopOnto_OVG_HDO_ID` and `TopOnto_OVG`.

## Usage

```
annotateTopOntoOVG(gg, dis, idatt = "name")
```

## Arguments

<code>gg</code>	<code>igraph</code> object to annotate
<code>dis</code>	annotation matrix in Pairs form
<code>idatt</code>	optional name of the vertex attributes that contains Entrez IDs

## Value

annotated `igraph` object

## See Also

`getAnnotationVertexList`

## Examples

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
# read HDO data extracted from hxin/topOnto.HDO.db for synaptic network
afile<-system.file("extdata", "flatfile_human_gene2HDO.csv",
package = "BioNAR")
dis <- read.table(afile, sep="\t", skip=1, header=FALSE,
strip.white=TRUE, quote="")
agg<-annotateTopOntoOVG(gg, dis)
```

annotateVertex      *Generic annotation function*

---

### Description

Function to build and fill a vertex attribute given an igraph object. Where parameter 'name' is the new vertex attribute name and values are filled from a two column data.frame supplied to 'value' attribute. The first containing vertex name IDs, and the second the vertex annotation value.

### Usage

```
annotateVertex(gg, name, values, idatt = "name")
```

### Arguments

gg	igraph object to annotate
name	name of the attribute
values	annotation data.frame
idatt	optional name of the vertex attribute to map to the annotation data.frame first column

### Details

As a first step all attributes with provided names will be removed.

### Value

igraph object where vertex attribute name contains annotation terms separated by semicolon.

### See Also

getAnnotationVertexList

### Examples

```
g1 <- make_star(10, mode="undirected")
V(g1)$name <- letters[1:10]
m<-rbind(data.frame(ID=letters[1:10], terms=letters[1:10]),
data.frame(ID=letters[1:10], terms=LETTERS[1:10]))
g2<-annotateVertex(g1, name='cap', values=m)
V(g2)$cap
```

---

aplpMatrixToGraph     *Add attributes to the vertex.*

---

### Description

This function suits more for updating calculated vertex properties rather than node annotation. For the later case use [annotateVertex](#).

### Usage

```
aplpMatrixToGraph(gg, m)
```

### Arguments

<code>gg</code>	igraph object
<code>m</code>	matrix of values to be applied as vertex attributes. matrix should contains column "ID" to map value to the vertex.

### Details

Unlike [annotateVertex](#), which is able to collapse multiple annotation terms, this function assume that vertex ID values are unique in the `m` matrix and corresponds to the name vertex attribute. If graph has no name vertex attribute error will be raised.

### Value

modified igraph object

### See Also

[annotateVertex](#)

### Examples

```
g1 <- make_star(10, mode="undirected")
V(g1)$name <- letters[1:10]
m<-cbind(ID=letters[1:10],capital=LETTERS[1:10])
g1<-BioNAR::aplpMatrixToGraph(g1,m)
V(g1)$capital
```

### Description

The R package BioNAR, developed to step by step analysis of PPI network. The aim is to quantify and rank each protein's simultaneous impact into multiple complexes based on network topology and clustering. Package also enables estimating of co-occurrence of diseases across the network and specific clusters pointing towards shared/common mechanisms.

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**See Also**

Useful links:

- Report bugs at <https://github.com/lptolik/BioNAR/issues/>

---

buildConsensusMatrix *Build a consensus matrix from list of resampled clustering matrices outputted from the function [sampleGraphClust](#)*

---

**Description**

Build a consensus matrix from list of resampled clustering matrices outputted from the function [sampleGraphClust](#)

**Usage**

```
buildConsensusMatrix(lcc)
```

**Arguments**

lcc                    list of membership matrices obtained from the [sampleGraphClust](#)

**Details**

Function build a consensus matrix from list of membership matrices, which are a three column matrix: the first column contains the vertex IDs of input network; the second column the vertex IDs of the subsampled network, or -1 if the vertex has been masked; the third column the cluster membership of subsampled network, or -1 if vertex has been masked. The randomised resampled membership matrices could be obtained from the function [sampleGraphClust](#).

**Value**

consensus matrix of Nvert X Nvert

---

buildNetwork	<i>Build network from data.table</i>
--------------	--------------------------------------

---

### Description

Wrapper for [graph\\_from\\_data\\_frame](#) function which will always return the largest connect component for a given network `ff`. The function will also annotated the edges in `ff` with PubMed data from `kw` if provided.

### Usage

```
buildNetwork(ff, kw = NA, LCC = TRUE, simplify = TRUE)
```

### Arguments

<code>ff</code>	network structure data.frame with first two columns defining the network edge nodes
<code>kw</code>	pmid keyword annotation data.frame. If NA no annotation will be added
<code>LCC</code>	if TRUE only largest connected component is returned
<code>simplify</code>	if TRUE loops and multiple edges will be removed

### Value

igraph object of the largest connected component

### Examples

```
f<-data.frame(A=c('A', 'A', 'B', 'D'), B=c('B', 'C', 'C', 'E'))
gg<-buildNetwork(f)
V(gg)$name
```

---

calcAllClustering	<i>Calculate memberships for all clustering algorithms and store them on the graph vertices.</i>
-------------------	--

---

### Description

This function will call [calcClustering](#) for each clustering algorithm given in our predefined list. In the event no clustering could be performed, warnings will be issued and no new vertex attribute added to the graph.

### Usage

```
calcAllClustering(gg, weights = NULL)
```

**Arguments**

gg	graph for analysis
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

**Value**

new graph object with all membership results stored as a vertex attribute.

**See Also**

calcClustering

**Examples**

```
g1 <- make_star(10, mode="undirected")
V(g1)$name <- letters[1:10]
g1 <- calcAllClustering(g1)
clusteringSummary(g1)
```

---

calcBridgeness	<i>Helper function that uses <a href="#">getBridgeness</a> to calculate graph node bridgeness values for selected algorithm and consensus matrix and save them as a graph attribute BRIDGENESS.&lt;alg&gt; with &lt;alg&gt; replaced by the selected algorithm name.</i>
----------------	--

---

**Description**

Helper function that uses [getBridgeness](#) to calculate graph node bridgeness values for selected algorithm and consensus matrix and save them as a graph attribute BRIDGENESS.<alg> with <alg> replaced by the selected algorithm name.

**Usage**

```
calcBridgeness(gg, alg, conmat)
```

**Arguments**

gg	igraph object
alg	clustering algorithm
conmat	consensus matrix calculated with that algorithm

**Value**

graph with additional attributes to store Bridgeness value

**See Also**

`getBridgeness`

**Examples**

```
library(BioNAR)
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
set.seed(100)
gg <- calcClustering(karate, 'louvain')
cnmat <- makeConsensusMatrix(gg, N=10, alg = 'louvain', type = 2, mask = 10)
gg<-calcBridgeness(gg, alg = 'louvain', cnmat)
hist(V(gg)$BRIDGENESS.louvain)
```

---

calcCentrality

*Calculate the vertex centrality measures*

---

**Description**

Calculate the vertex centrality measures (degree, betweenness, closeness, semi-local, etc....) for each graph vertex and store each result as new vertex attribute in the graph.

**Usage**

```
calcCentrality(gg, weights = NULL)
```

**Arguments**

<code>gg</code>	igraph object
<code>weights</code>	Possibly a numeric vector giving edge weights. If this is NULL and the graph has a weight edge attribute, then the attribute is used. If this is NA then no weights are used (even if the graph has a weight attribute).

**Details**

A wrapper function that first calls [getCentralityMatrix](#), to calculate all vertex centrality measures, and then [applMatrixToGraph](#) to store each centrality result as a new vertex attribute in the graph. The use of weights explained in details in [getCentralityMatrix](#).

**Value**

modified igraph object

**See Also**

[getCentralityMatrix\(\)](#)

**Examples**

```
data(karate,package='igraphdata')
ggm<-calcCentrality(karate)
V(ggm)$DEG
```

calcCentralityExternalDistances

*Function to calculate a distance matrix between a list of permuted vertex centrality matrices and a unperturbed reference matrix.*

---

### Description

Function to calculate a distance matrix between a list of permuted vertex centrality matrices and a unperturbed reference matrix.

### Usage

```
calcCentralityExternalDistances(m, l, keepOrder = FALSE, dist = "euclidean")
```

### Arguments

m	reference matrix, for example centrality obtained by invocation <a href="#">getCentralityMatrix</a>
l	list of permuted matrix, for example centrality obtained by invocation <a href="#">getRandomGraphCentrality</a>
keepOrder	if FALSE values will be sorted
dist	methods available from dist function

### Value

matrix with seven columns containing distances between each element of l and reference matrix m

### See Also

[getRandomGraphCentrality](#)  
[getCentralityMatrix](#)  
[calcCentralityInternalDistances](#)

### Examples

```
data(karate, package='igraphdata')
m<-getCentralityMatrix(karate)
gnp<-list()
for(i in 1:10){
  gnp[[i]]<-getRandomGraphCentrality(karate, type = 'gnp')
}
gnpEDist<-calcCentralityExternalDistances(m,gnp)
summary(gnpEDist)
```

---

`calcCentralityInternalDistances`

*Function calculates a set of distance metrics between each vertex pair given a list of vertex centrality matrices*

---

### Description

Function calculates a set of distance metrics between each vertex pair given a list of vertex centrality matrices

### Usage

```
calcCentralityInternalDistances(l, keepOrder = FALSE, dist = "euclidean")
```

### Arguments

<code>l</code>	list of matrices, for example centrality obtained by invocation <a href="#">getRandomGraphCentrality</a>
<code>keepOrder</code>	if FALSE values will be sorted before distance calculations
<code>dist</code>	methods available from <a href="#">dist</a> function

### Value

matrix with seven columns containing distances between all pairs of `l` elements.

### See Also

[getRandomGraphCentrality](#)  
[getCentralityMatrix](#)  
[calcCentralityExternalDistances](#)

### Examples

```
data(karate, package='igraphdata')
m<-getCentralityMatrix(karate)
gnp<-list()
for(i in 1:10){
  gnp[[i]]<-getRandomGraphCentrality(karate,type = 'gnp')
}
gnpIDist<-calcCentralityInternalDistances(gnp)
summary(gnpIDist)
```

---

calcClustering	<i>Calculate community membership for given clustering algorithm and store the results as new vertex attributes in the graph..</i>
----------------	--

---

### Description

When applying resampling the clustering results of a clustering algorithm applied to a graph can differ due to the stochastic nature of the resampling algorithm. To allow reproducible downstream analysis clustering results are stored as vertex attributes in the graph. This function call `getClustering` and stores community membership as new vertex attribute in the graph, and Modularity as a new graph attribute prefix with the alg name.

### Usage

```
calcClustering(gg, alg, weights = NULL)
```

### Arguments

<code>gg</code>	igraph object to cluster
<code>alg</code>	algorithm to apply
<code>weights</code>	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

### Details

NOTE: `getClustering` verifies algorithm names with `match.arg` so correct membership will be calculated, but name of the attribute is taken from `alg` argument, so it is possible that vertex attribute name won't exactly match name of the algorithm from `link{getClustering}`.

### Value

modified igraph object with calculated membership stored as a vertex attribute and modularity as a graph attribute

### See Also

`getClustering`

### Examples

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
g<-calcClustering(karate, 'louvain')
vertex_attr_names(g)
graph_attr(g, 'louvain')
```

---

calcDiseasePairs	<i>Calculate each disease-disease pair overlap given a list of disease terms.</i>
------------------	---

---

### Description

Calculate each disease-disease pair overlap (or separation) on a given PPI network model, based on analysis described in Menche et al. 2015

### Usage

```
calcDiseasePairs(  
  gg,  
  name,  
  diseases = NULL,  
  permute = c("none", "random", "binned")  
)
```

### Arguments

gg	interactome network as igraph object
name	name of the attribute that stores disease annotation
diseases	list of diseases to match
permute	type of permutations. none – no permutation is applied, random – annotation is randomly shuffled, binned – annotation is shuffled in a way to preserve node degree-annotation relationship by <a href="#">degreeBinnedGDAs</a> .

### Value

list with three matrices:

- disease\_separation – N<sub>disease</sub> X N<sub>disease</sub> matrix of separations
- gene\_disease\_separation – N<sub>genes</sub> X N<sub>disease+2</sub> matrix of gene-disease separation
- disease\_localisation – matrix with diseases in rows and number of genes (N), average and standard deviation of gene-disease separation in columns

### References

Menche, J. et al. Uncovering disease-disease relationships through the incomplete interactome. *Science*, 347, (6224):1257601 (2015).

### See Also

[degreeBinnedGDAs](#)  
[sampleDegBinnedGDA](#)

**Examples**

```

file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
agg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(agg)$name == '80273')
paste(V(agg)$GeneName[idx], 'GRPEL1')
p <- calcDiseasePairs(
  agg,
  name = "TopOntoOVGHDOID",
  diseases = c("DOID:10652", "DOID:3312", "DOID:12849"),
  permute = "n"
)
p$disease_separation

```

---

calcEntropy	<i>Calculate the graph entropy for each perturbed vertex, and save the results as new vertex attributes in the graph.</i>
-------------	---

---

**Description**

This function calculate the graph entropy for each perturbed vertex by calling [getEntropy](#), and save the results as new vertex attributes SR\_UP and SR\_DOWN in the graph.

**Usage**

```
calcEntropy(gg, maxSr = NULL, exVal = NULL)
```

**Arguments**

gg	igraph object
maxSr	the maximum entropy rate <i>maxSR</i> , if NULL <a href="#">getEntropyRate</a> will be called.
exVal	expression values boundaries. Two columns are expected: xx and lambda. If NULL default values c(2, 14) and c(-14, 14) will be used for xx and lambda respectively.

**Details**

According to Teschendorf et al., 2010, network entropy measure quantifies the degree of randomness in the local pattern information flux around single genes. For instance, in metastatic cancer this measure was found significantly higher than in non-metastatic and helped to identify genes and entire pathways involved on metastasis. However, for the assessment of scale-free structure we do not actually require gene expression data as it based solely on the network topology.

**Value**

graph with SR\_UP and SR\_DOWN vertex attributes storing the graph entropy values with over- or under-expressing each vertex.

**See Also**

[getEntropy\(\)](#)

Other Entropy Functions: [getEntropy\(\)](#), [getEntropyRate\(\)](#), [plotEntropy\(\)](#)

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
gg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(gg)$name == '80273')
paste(V(gg)$GeneName[idx], 'GRPEL1')
gg<- calcEntropy(gg)
```

calcMembership

*Calculate cluster memberships for the graph.***Description**

Calculates the clustering membership for one of the 10 clustering algorithms defined in function [getClustering](#)

**Usage**

```
calcMembership(
  gg,
  alg = c("lec", "wt", "fc", "infomap", "louvain", "sgG1", "sgG2", "sgG5", "spectral"),
  weights = NULL
)
```

**Arguments**

gg	igraph object to cluster
alg	algorithm name
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If it is NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph has a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

**Value**

data.frame with columns names and membership

**See Also**

[getClustering](#)

**Examples**

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
m<-calcMembership(karate, 'lec')
head(m)
```

---

calcReclusterMatrix    *Hierarchical graph clustering*

---

### Description

This function takes in a `gg` and initial vertex community membership values `mem` as returned by `calcMembership`, and then performs a reclustering of the graph given the clustering algorithm `alg` to those clusters of size greater than `CnMAX`

### Usage

```
calcReclusterMatrix(
  gg,
  mem,
  alg,
  CnMAX = 10,
  weights = NULL,
  keepSplit = FALSE
)
```

### Arguments

<code>gg</code>	graph to cluster
<code>mem</code>	data.frame with previous level clustering results
<code>alg</code>	algorithm to apply
<code>CnMAX</code>	maximum size of the cluster in <code>mem</code> that will not be processed
<code>weights</code>	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.
<code>keepSplit</code>	logical, whether to keep previous membership in the output matrix

### Value

membership matrix, that contains vertex ID membership and result of reclustering

### Examples

```
data(karate, package='igraphdata')
alg<-'louvain'
mem<-calcMembership(karate, alg = alg)
remem<-calcReclusterMatrix(karate, mem, alg, 10)
```

---

calcSparsness	<i>Calculate sparsness of the graph.</i>
---------------	--

---

### Description

For a simple unweighted, undirected graph  $G(N,E)$ . Network sparseness is defined as the ratio of the actual number of graph edges ( $E$ ) to the maximum number of edges possible in a graph with same number of vertices ( $N$ ):  $E/\text{binom}(N,2)$

### Usage

```
calcSparsness(gg)
```

### Arguments

gg                      graph to evaluate

### Value

sparsness value

### Examples

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
calcSparsness(gg)
```

---

clusteringSummary	<i>Matrix of cluster characteristics</i>
-------------------	--

---

### Description

Function to calculate basic summary statistics after apply clustering algorithm:

- N – number of vertices in the graph `vcount`
- mod – clustering modularity `modularity`, the ratio of edges found within communities to the number of edges found between communities, relative to a randomised model
- C – number of clusters
- Cn1 – number of singletons (clusters of size 1)
- Cn100 – number of clusters containing more than 100 nodes
- mu – the ratio of edges found within communities to the number of edges found between communities
- Min. C – minimum of the cluster size
- 1st Qu. C – first quartile of the cluster size
- Median C – median of the cluster size
- Mean C – average cluster size
- 3rd Qu. C – third quartile of the cluster size
- Max. C – maximum of the cluster size

**Usage**

```
clusteringSummary(
  gg,
  att = c("lec", "wt", "fc", "infomap", "louvain", "sgG1", "sgG2", "sgG5", "spectral")
)
```

**Arguments**

gg	graph to analyse
att	vector of attribute names that contains membership data

**Value**

matrix of clustering characteristics

**Examples**

```
data(karate, package='igraphdata')
g<-calcAllClustering(karate)
clusteringSummary(g)
```

---

clusterORA

*Calculate annotation enrichment for clusters in the graph*

---

**Description**

Calculate the cluster enrichment of a graph given a clustering algorithm `alg` and vertex annotation attribute `name`. Function generates an enrichment table, one row for each cluster, containing: size of the cluster ( $C_n$ ), number of annotated vertices in the graph  $F_n$  ( $F_n$ ), number of annotated vertices in the cluster  $\mu$  ( $\mu$ ), odds ratio (OR) and its 95% Confidence interval [ $CI_l$ ,  $CI_u$ ] ( $CI_l$  and  $CI_u$ ), two fold enrichment values  $F_e$  ( $F_e$ ) and  $F_c$  ( $F_c$ ). We also provide the list of vertices from the cluster that contribute to the annotation term, p.value of enrichment (`pval`) and depletion (`palt`) using the Hypergeometric test, adjusted p.values using Benjamini and Yekutieli correction (BY).

**Usage**

```
clusterORA(g, alg, name, vid = "name", alpha = 1, col = COLLAPSE)
```

**Arguments**

g	graph to get annotation from
alg	cluster algorithm and membership attribute name
name	annotation attribute name
vid	attribute to be used as a vertex ID
alpha	probability threshold
col	list separation character in attribute, by default is ;

## Details

Given the enrichment results, we can calculate the log of the Odds Ratio (OR) as:

$$\ln(OR) = \ln\left(\frac{\mu(N - F_n + \mu - C_n)}{(C_n - \mu)(F_n - \mu)}\right)$$

and it's upper and lower 95% Confidence Interval:

$$CI(\ln(OR)) = \ln(OR) \pm 1.96\sqrt{\frac{1}{\mu} + \frac{1}{C_n - \mu} + \frac{1}{F_n - \mu} + \frac{1}{N - F_n + \mu - C_n}}$$

Using the odds ratio allows us to distinguish functionally enriched communities relative to functionally depleted communities.

Two types of fold enrichment values calculated as follow:

$$F_e = \frac{\left(\frac{\mu}{F_n}\right)}{\left(\frac{C_n}{N}\right)}$$

$$F_c = \frac{\left(\frac{\mu}{C_n}\right)}{\left(\frac{C_n}{N}\right)}$$

## Value

A table with overrepresentation results. Each row corresponds to a tested annotation in particular cluster. The columns are the following:

- alg – name of the clustering algorithm;
- cl – cluster ID;
- FL – name of the enriched term;
- N – number vertices in the network;
- Fn – number of vertices in the graph annotated by term Fl ( $F_n$ );
- Cn – size of the cluster;
- Mu – number of vertices in the cluster annotated by term Fl ( $\mu$ );
- OR – odds ratio ;
- CII – odds ratio 95% confidence interval lower bound ( $CI_l$ );
- CIu – odds ratio 95% confidence interval upper bound( $CI_u$ );
- Fe – fold enrichment  $F_e$ ;
- Fc – fold enrichment  $F_c$ ;
- pval – an enrichment p-value from hypergeometric test;
- padj – a BY-adjusted p-value;
- palt – an depletion p-value from hypergeometric test;
- paltadj – a BY-adjusted depletion p-value;
- overlapGenes – vector with overlapping genes.

**Examples**

```
options("show.error.messages"=TRUE)
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
g <- igraph::read_graph(file, format="gml")
anL<-getAnnotationVertexList(g, 'TopOntoOVGHDOI')
res<-clusterORA(g, alg='louvain', name='TopOntoOVGHDOI', vid='name')
andf<-unique(data.frame(ID=vertex_attr(g, 'TopOntoOVGHDOI'),
Term=vertex_attr(g, 'TopOntoOVG')))
rr<-merge(andf, res, by.y='FL', by.x='ID')
rr[order(rr$c1), ]
```

---

compMembership

*Calculate cluster memberships for one of the graph component.*


---

**Description**

Calculates the clustering membership for one of the 10 clustering algorithms defined in function [getClustering](#) for selected graph component

**Usage**

```
compMembership(
  gg,
  alg = c("lec", "wt", "fc", "infomap", "louvain", "sgG1", "sgG2", "sgG5", "spectral"),
  compnum = 0,
  weights = NULL
)
```

**Arguments**

gg	igraph object to cluster
alg	algorithm name
compnum	number of the componet to cluster
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If it is NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph has a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

**Value**

data.frame with columns names and membership

**See Also**

[getClustering](#)

---

degreeBinnedGDAs	<i>Prepare mapping for degree-aware annotation shuffling.</i>
------------------	---

---

## Description

Function to randomly shuffle vertex annotation terms, whilst preserving the vertex degree originally found with that annotation term.

## Usage

```
degreeBinnedGDAs(gg, GDA, dtype)
```

## Arguments

gg	graph to analyse
GDA	vertex annotations returned by <a href="#">prepareGDA</a>
dtype	list of unique annotation terms to analyze

## Value

mapping matrix between vertices, vertex-degree groups and annotation terms.

## See Also

[prepareGDA](#)  
[getAnnotationList](#)  
[sampleDegBinnedGDA](#)

## Examples

```
options("show.error.messages"=TRUE)
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
agg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(agg)$name == '80273')
paste(V(agg)$GeneName[idx], 'GRPEL1')
gda<-prepareGDA(agg, 'TopOntoOVGHDOI')
m<-degreeBinnedGDAs(agg, gda, getAnnotationList(gda))
c(dim(m), vcount(agg), length(getAnnotationList(gda)))
head(m)
```

---

diseasome

*Barabasi's Diseasome Network*


---

### Description

In the paper Goh.t al. (2007) doi:10.1073/pnas.0701361104 Barabasi with colleagues published Diseasome: a network of disorders and disease genes linked by known disorder–gene associations. We extract definition of the genes, disorders and interactions from papers supplementary materials and store it as `graph` object.

### Usage

```
diseasome
```

### Format

A bipartite graph as `graph` object.

Vertex attributes: 'name' for the node ID, 'Name' for the human readable node name, 'Disorder.class', 'Type' for the human readable node type, 'label' and 'shape' for plotting the graph, 'type' the node type for bipartite `graph` representation.

### Details

Diseasome is a bipartite graph that have nodes of two types gene and disease and links are allowed only between nodes of different types. It could be projected to Human Disease Network (HDN) and Disease Gene Network (DGN).

### Source

Goh, K.-I. et al. The human disease network. Proc. Natl. Acad. Sci. U.S.A. 104, 8685–8690 (2007). <https://pnas.org/doi/full/10.1073/pnas.0701361104>

---

escapeAnnotation

*Escapes elements of list in annotation.*


---

### Description

In situations when a given list of annotation ID terms may not be well formatted, and therefore not be interoperated as unique. For example, given a list of HDO IDs: HDO:14, HDO:143, HDO:1433, and HDO:14330, a grep for the term HDO:14 could return: HDO:143, HDO:1433, HDO:14330. To avoid this all terms should be enclosed in escape characters, which unlikely to find within annotation itself.

### Usage

```
escapeAnnotation(annVec, col = COLLAPSE, esc = ESC)
```

**Arguments**

annVec	vector of annotation strings
col	term list separator character
esc	escape character

**Details**

NOTE: spaces are treated as regular characters, no trimming is applied before or after escaping.

**Value**

vector of annotation strings with elements escaped

**See Also**

unescapeAnnotation

**Examples**

```
annVec<-apply(matrix(letters, ncol=13), 2, paste, collapse=';')
cbind(annVec, escapeAnnotation(annVec, ';', '|'))
```

---

evalCentralitySignificance

*Compare distance distributions of internal and external distances*

---

**Description**

Function to compare two distance distributions using the Kolmogorov-Smirnov test. Where the first distance distribution is generated internally and calculates the distance between random graph centralities. The second distance distribution is generated externally, and measures the distance between random and the original graph centralities.

**Usage**

```
evalCentralitySignificance(dmi, dme)
```

**Arguments**

dmi	distribution of internal distances between random graph centralities
dme	distribution of external distances between random and original graph centralities

**Value**

list of lists for each centrality value in the input matrix three element list is created where ks contains Kolmogorov-Smirnov test result from class ks.test; pval contains Kolmogorov-Smirnov test pvalue; and dt contains input distribution.

**See Also**

ks.test

**Examples**

```

data(karate, package='igraphdata')
m<-getCentralityMatrix(karate)
gnp<-list()
for(i in 1:10){
  gnp[[i]]<-getRandomGraphCentrality(karate, type = 'gnp')
}
gnpIDist<-calcCentralityInternalDistances(gnp)
gnpEDist<-calcCentralityExternalDistances(m,gnp)

simSig<-evalCentralitySignificance(gnpIDist,gnpEDist)
sapply(simSig,function(.x).x$ks$p.value)

```

---

findLCC

*Find Largest Connected Component of the graph*


---

**Description**

Find Largest Connected Component of the graph

**Usage**

```
findLCC(GG)
```

**Arguments**

GG                   igraph object to analyze

**Value**

igraph representation LCC

**Examples**

```

g1 <- make_star(10, mode="undirected") %du% make_ring(7) %du% make_ring(5)
lcc<-findLCC(g1)
summary(lcc)

```

---

fitDegree

*Fit Power Law to degree distribution.*


---

**Description**

Fit a Powerlaw distribution to graph's degree distribution using the R "PowerLaw" package (version 0.50.0) (Gillespie, 2015)

**Usage**

```
fitDegree(
  DEG,
  Nsim = 100,
  plot = FALSE,
  DATAleg = "Fit power-law",
  threads = 4,
  WIDTH = 480,
  HEIGHT = 480,
  legpos = "bottomleft",
  showErr = TRUE
)
```

**Arguments**

DEG	degree distribution
Nsim	number of bootstrap iterations
plot	logical, do you want plot to be drawn
DATAleg	legend string for degree data
threads	number of parallel computational threads
WIDTH	width of the plot in ptx
HEIGHT	height of the plot in ptx
legpos	position of the legend @seealso <a href="#">legend()</a>
showErr	logical, do you want error on the plot legend

**Value**

an object of class [law-class](#) with results of fitting

**Examples**

```
##No: of bootstrap iterations use nsim > 100 for reliable result
nsim <- 10

##Legend Titles
Legend <- "Presynaptic PPI"

file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
pFit <- fitDegree( as.vector(igraph::degree(graph=gg)),
  DATAleg=Legend, threads=1, Nsim=nsim)
```

---

fitSigmoid

*Fit Fold-enrichment distribution to sigmoid function*


---

**Description**

This function calculates fit of the Fold-Enrichment distribution to the sigmoid function with the levels of noise specified in SDV for all clustering algorithms, which have non-zero SUM3\$`Psi&ORsig` in the enrichment table summary results. The function returns the list in which each element contains result for one of the noise level.

## Usage

```
fitSigmoid(stat, SDv = c(0, 0.05, 0.1, 0.5))
```

## Arguments

stat	enrichment results obtained from <a href="#">summaryStats</a>
SDv	vector of noise SD values

## Details

Results are represented as a list with five elements:

- gridplot that allow comparison of fitting for different clustering algorithms;
- plots the list of individual plots from gridplot;
- fitInfo the data.frame that contains results of fitting, such as message, number of iterations and exit code;
- parInfo values and standard deviations for all sigmoid parameters;
- ks table of Kolmogorov-Smirnov test p-values.

Grid plot is designed in a way to be viewed in the device at least 12 inches in width and 12 inches in height.

## Value

list of fitted functions tables and plots

## See Also

[summaryStats\(\)](#)

---

flatfile.go.BP.csv      *Annotation from Gene Ontology Biological Process (GO\_BP)*

---

## Description

Annotation, downloaded from Gene Ontology for Biological Process domain. The table has columns: the first containing gene gene functional group ID terms, the second gene functional group description terms, the third - Human gene Entrez IDs; in csv format

## See Also

[annotateGoBP](#)

---

flatfile.go.CC.csv      *Annotation from Gene Ontology Cellular Compartment (GO\_CC)*

---

**Description**

Annotation, downloaded from Gene Ontology for Cellular Compartment domain. The table has columns: the first containing gene functional group ID terms, the second gene functional group description terms, the third - Human gene Entrez IDs; in csv format

**See Also**

[annotateGoCC](#)

---

flatfile.go.MF.csv      *Annotation from Gene Ontology Molecular Function (GO\_MF)*

---

**Description**

Annotation, downloaded from Gene Ontology for Molecular Function domain. The table has columns: the first containing gene functional group ID terms, the second gene functional group description terms, the third - Human gene Entrez IDs; in csv format

**See Also**

[annotateGoMF](#)

---

flatfile\_human\_gene2HDO.csv  
*Human Gene Disease Associations (GDA)*

---

**Description**

Annotation derived from Human Disease Ontology database (HDO). The table contains three columns; the first containing gene Entrez IDs, the second gene Human Disease Ontology (HDO) ID terms, the third gene HDO description terms; in csv format

**See Also**

[annotateTopOntoOVG](#)

---

getAnnotationList      *Extract unique values from annotations.*

---

### Description

It is not uncommon to find both duplicated vertex annotation terms, and vertices annotated with multiple terms, in a given annotation list. This function creates a vector of unique annotation terms for each vertex given an input annotation list.

### Usage

```
getAnnotationList(
  annVec,
  col = COLLAPSE,
  sort = c("none", "string", "frequency")
)
```

### Arguments

annVec	vector of annotation strings
col	list separator character
sort	how to sort the result list

### Value

vector of unique annotation terms

### See Also

getAnnotationVertexList

### Examples

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
annVec<-V(gg)$TopOntoOVG
al<-getAnnotationList(annVec)
al
```

---

getAnnotationVertexList  
*Return vertex list for each term in annotation attribute*

---

### Description

For different purposes annotation of graph vertices could be represented in three forms:

**Pairs** dataframe with vertex ID and annotation terms

**Vertex Annotation** list named with vertex ID and containing terms annotating each vertex

**Annotation Vertices** list named with term and containing vertex IDs

**Usage**

```
getAnnotationVertexList(g, name, vid = "name", col = COLLAPSE)
```

**Arguments**

<code>g</code>	graph to get annotation from
<code>name</code>	annotation attribute name
<code>vid</code>	attribute to be used as a vertex ID
<code>col</code>	list separation character in attribute, by default is ;

**Details**

This function takes Vertex Annotation from vertex attribute and convert it to Annotation Vertices form.

**Value**

named list with annotation in Annotation Vertices form

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
avl<-getAnnotationVertexList(gg, 'TopOntoOVGHDOID')
head(avl)
```

---

getBridgeness

*Calculate bridginess from consensus matrix*

---

**Description**

Bridginess takes into account a vertices shared community membership together with its local neighbourhood. It was proposed in Nepusz et al., 2008 [doi:10.1103/PhysRevE.77.016107](https://doi.org/10.1103/PhysRevE.77.016107).

**Usage**

```
getBridgeness(gg, alg, conmat)
```

**Arguments**

<code>gg</code>	igraph object
<code>alg</code>	clustering algorithm
<code>conmat</code>	consensus matrix calculated with that algorithm

**Details**

Function assumes clustering already been performed by the clustering algorithm, and its membership values stored in vertex attributes. If clustering algorithm vertex `alg` attribute is not found an error will be issued.

**Value**

data.frame with first column contains vertex ID, if GeneName attribute assigned to the vertices its value will be stored as a second column, the last column contains bridginess values for the

**Examples**

```
library(BioNAR)
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
gg <- calcClustering(karate, 'louvain')
cnmat <- makeConsensusMatrix(gg, N=10, alg = 'louvain', type = 2, mask = 10)
br<-getBridginess(gg, alg = 'louvain', cnmat)
```

---

getCentralityMatrix     *Calculate centrality measures for graph nodes.*

---

**Description**

Calculate centrality measures for graph nodes.

**Usage**

```
getCentralityMatrix(gg, weights = NULL)
```

**Arguments**

gg	igraph object
weights	Possibly a numeric vector giving edge weights. If this is NULL and the graph has a weight edge attribute, then the attribute is used. If this is NA then no weights are used (even if the graph has a weight attribute).

**Details**

The edge attribute weights treated differently by different functions calculating centrality measures. For example, [betweenness](#) use weights as an edge length, while in [page\\_rank](#) "an edge with a larger weight is more likely to be selected by the surfer", which infer the opposite meaning. Taking into account that all methods in [getClustering](#) treat edge weights in the same way as [page\\_rank](#), we calculate the distance=1/weights as edge weights for BET, dBET, mnSP, and sdSP values. So we treat weights in the package consistently as the strength and closeness of vertices, rather the distance between them.

**Value**

data.frame with following columns:

- ID - vertex ID
- DEG - degree
- iDEG - in-degree (directed graph only)
- oDEG - out-degree (directed graph only)
- BET - betweenness for undirected graph

- dBET - betweenness when directionality is taken into account (directed graph only)
- CC - clustering coefficient
- SL - semilocal centrality
- mnSP - mean shortest path
- PR - page rank for undirected graph
- dPR - page rank when directionality is taken into account (directed graph only)
- sdSP - standard deviation of the shortest path

### Examples

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
m<-getCentralityMatrix(gg)
```

---

getClustering	<i>Get clustering results for the graph.</i>
---------------	--

---

### Description

Wrapper function for calculation of clustering for predefined set of ten algorithms:

- lec – leading eigenvector community (version of [cluster\\_leading\\_eigen](#)), directed graph will be converted to undirected by [as\\_undirected](#) with mode collapse;
- wt – walktrap community [cluster\\_walktrap](#);
- fc – fastgreedy community [cluster\\_fast\\_greedy](#), directed graph will be converted to undirected by [as\\_undirected](#) with mode collapse;
- infomap – infomap community [cluster\\_infomap](#);
- louvain – cluster\_louvain [cluster\\_louvain](#), directed graph will be converted to undirected by [as\\_undirected](#) with mode collapse;
- sgG1 – spin-glass model and simulated annealing clustering (version of [cluster\\_spinglass](#) with spins=500 and gamma=1);
- sgG2 – spin-glass model and simulated annealing clustering (version of [cluster\\_spinglass](#) with spins=500 and gamma=2);
- sgG5 – spin-glass model and simulated annealing clustering (version of [cluster\\_spinglass](#) with spins=500 and gamma=7);
- spectral – spectral modularity clustering [spectral\\_igraph\\_communities](#);

### Usage

```
getClustering(
  gg,
  alg = c("lec", "wt", "fc", "infomap", "louvain", "sgG1", "sgG2", "sgG5", "spectral"),
  weights = NULL
)
```

**Arguments**

gg	igraph object to cluster
alg	clustering algorithm name
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

**Details**

graph suppose to be undirected. If algorithm failed warning will be issued and function returned NULL.

Algorithm names are verified with [match.arg](#).

**Value**

`communities` object or NULL if algorithm failed.

**Examples**

```
data(karate, package='igraphdata')
c<-getClustering(karate, 'lec')
c$modularity
```

---

getClusterSubgraphByID

*Return induced subgraph for cluster*

---

**Description**

Function reads in a graph gg, vertex cluster membership vector mem, and returns an induced sub-graph given a cluster membership number 'clID'.

**Usage**

```
getClusterSubgraphByID(clID, gg, mem)
```

**Arguments**

clID	cluster ID to extracte
gg	graph to analyze
mem	membership vector

**Value**

induced subgraph as igraph object

**Examples**

```
data(karate, package='igraphdata')
alg<- 'louvain'
c<-getClustering(karate, alg = alg)
gc3<-getClusterSubgraphByID(3, karate, membership(c))
#plot(gc3, vertex.label=V(gc3)$name)
```

---

getCommunityGraph	<i>Create new graph with communities as a nodes.</i>
-------------------	--

---

**Description**

The idea based upon [this StackOverflow answer](#)

**Usage**

```
getCommunityGraph(gg, membership)
```

**Arguments**

gg	graph to convert
membership	participation list for new graph

**Value**

community graph

**Examples**

```
data(karate, package='igraphdata')
alg<- 'louvain'
mem<-calcMembership(karate, alg = alg)
cg<-getCommunityGraph(karate, mem$membership)
```

---

getDiseases	<i>Get HDO disease IDs</i>
-------------	----------------------------

---

**Description**

Return vector of HDO disease IDs for synaptic PPI analysis.

**Usage**

```
getDiseases()
```

**Value**

vector of disease IDs of interest

**See Also**

getDType

**Examples**

```
getDiseases()
```

---

getDType	<i>Get DiseaseTypes</i>
----------	-------------------------

---

**Description**

Return vector of disease abbreviations for synaptic PPI analysis.

**Usage**

```
getDType()
```

**Value**

vector of disease abbreviations for synaptic PPI analysis.

**See Also**

getDiseases

**Examples**

```
getDType()
```

---

getDYNAMO	<i>Calculate DYNAMO sensitivity matrix.</i>
-----------	---

---

**Description**

This function calculates sensitivity matrix that represents perturbation patterns defined by topology and edge weights of the network. If weights are signed value sensitivity matrix is able to reproduce not only activation but inhibition relationships in the network.

**Usage**

```
getDYNAMO(g, attr = NULL, vid = "name", alpha = 0.9)
```

**Arguments**

g	igraph object
attr	NULL or the name of edge attribute containing numerical weight values
vid	name of the vertex attribute to be used as row and column names
alpha	parameter characterizing the propagation strength, default value 0.9 taken from Santolini paper.

**Details**

Algorithm proposed in:

Santolini, M. and Barabasi, A.-L. (2018) Predicting perturbation patterns from the topology of biological networks. Proc Natl Acad Sci USA, 169, 201720589.

**Value**

sparse sensitivity matrix defined by the network topology and edge values

**Examples**

```
data(karate, package='igraphdata')
upgrade_graph(karate)
d<-getDYNAMO(karate, attr='weight')
df<-metlMatrix(d)
head(df)
```

---

getEntropy

*Calculates vertex perturbation graph entropy.*

---

**Description**

According to Teschendorf et al., 2010, network entropy measure quantifies the degree of randomness in the local pattern information flux around single genes. For instance, in metastatic cancer this measure was found significantly higher than in non-metastatic and helped to identify genes and entire pathways involved on metastasis. However, for the assessment of scale-free structure we do not actually require gene expression data as it based solely on the network topology.

**Usage**

```
getEntropy(gg, maxSr = NULL, exVal = NULL)
```

**Arguments**

gg	igraph object
maxSr	the maximum entropy rate <i>maxSR</i> , if NULL <i>getEntropyRate</i> will be called.
exVal	expression values boundaries. Two columns are expected: <i>xx</i> and <i>lambda</i> . If NULL default values <i>c(2, 14)</i> and <i>c(-14, 14)</i> will be used for <i>xx</i> and <i>lambda</i> respectively.

**Details**

In this function, following procedure described in (Teschendorff et al., 2015), all vertexes are artificially assigned a uniform weight then sequentially perturbed with the global entropy rate (SR) after each protein's perturbation being calculated and plotted against the log of the protein's degree. In case of scale-free or approximate scale-free topologies, we see a clear bi-modal response between over-weighted vertices and their degree and an opposing bi-phasic response in under-weighted vertices and their degrees.

**Value**

matrix containing for each Gene:

- Entrez ID,
- Name,
- Degree,
- UP – Graph Entropy values when gene is expressed up,
- DOWN – Graph Entropy values when gene is expressed down.

**Note**

Entropy is calculated with respect to GeneName property, if there is no such vertex attribute in the graph vertex name will be copied to the GeneName attribute. If any NA is found in GeneNames error will be thrown.

**See Also**

Other Entropy Functions: [calcEntropy\(\)](#), [getEntropyRate\(\)](#), [plotEntropy\(\)](#)

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
gg<-annotateGeneNames(gg)
any(is.na(V(gg)$GeneName))
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(gg)$name == '80273')
paste(V(gg)$GeneName[idx], 'GRPEL1')
e<- getEntropy(gg)
```

---

getEntropyRate

*Calculate the maximum entropy rate and initial entropy rate .*

---

**Description**

This function calculates the maximum entropy rate  $maxSR$  (maxSr) and initial entropy rate  $SR_0$  (SRo) given a connected network.

**Usage**

```
getEntropyRate(gg)
```

**Arguments**

gg                   igraph object

**Details**

The maximum entropy rate being calculated from the network's adjacency matrix:

$$\text{maxSR} = \sum_{i,j} p_{ij} = \frac{A_{ij}\nu_j}{\lambda\nu_i}$$

where  $\nu$  and  $\lambda$  are the leading eigenvector and eigenvalue of the network adjacency matrix  $A$  respectively.

The initial configuration occurs when the entropy for each node is maximal. This can be calculated by setting the expression value for each gene/node in the network to be the same, and thus the maximal node entropy is dependent only on the node's degree  $k$ :

$$SR_0 = \frac{1}{N\bar{k}} \sum_j k_j \log k_i$$

where  $N$  here is the number of nodes and  $\bar{k}$  the average node degree found in the network.

**Value**

list with values of maxSr and SRo

**See Also**

Other Entropy Functions: [calcEntropy\(\)](#), [getEntropy\(\)](#), [plotEntropy\(\)](#)

**Examples**

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
ent <- getEntropyRate(karate)
```

---

getGNP

*Generate random graph from reference*

---

**Description**

Function generates random  $G(n,p)$  Erdos-Renyi graph ([sample\\_gnp](#)) with the same number of vertices and edges as in in the reference graph  $gg$ .

**Usage**

```
getGNP(gg, ...)
```

**Arguments**

`gg` reference graph  
`...` additional arguments to be passed to [sample\\_gnp](#)

**Value**

new instance of the random graph.

**Examples**

```
data(karate, package='igraphdata')
vcount(karate)
ecount(karate)
rg<- getGNP(karate)
vcount(rg)
ecount(rg)
```

---

getGraphCentralityECDF

*Convert centrality matrix into ECDF*

---

**Description**

Convert centrality matrix into ECDF

**Usage**

```
getGraphCentralityECDF(m)
```

**Arguments**

**m** centrality matrix from [getCentralityMatrix](#) invocation.

**Value**

list of several ecdf objects, corresponding to values in centrality matrix from [getCentralityMatrix](#) invocation.

**See Also**

[getCentralityMatrix](#)

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
m<-getCentralityMatrix(gg)
ecdfL<-getGraphCentralityECDF(m)
```

---

getIDs	<i>Utility function to get vertex ids from vertex attributes The function obtain attribute values and check duplicates in it. It fails if any duplicate found.</i>
--------	--

---

### Description

Utility function to get vertex ids from vertex attributes The function obtain attribute values and check duplicates in it. It fails if any duplicate found.

### Usage

```
getIDs(gg, idatt)
```

### Arguments

gg	graph
idatt	attribute name

### Value

idatt attribute values

---

getPA	<i>Generate random graph from reference</i>
-------	---

---

### Description

The function generates random Barabasi-Albert graph ([sample\\_pa](#)) with the same vertex number as in the reference graph gg and the power specified by parameter pwr. If pwr is missing, we are trying to estimate pwr from the reference graph gg.

### Usage

```
getPA(gg, pwr, ...)
```

### Arguments

gg	reference graph
pwr	the power parameter for the <a href="#">sample_pa</a>
...	additional parameters to be passed to the <a href="#">sample_pa</a>

### Value

new instance of the random graph.

**Examples**

```
data(karate, package='igraphdata')
vcount(karate)
ecount(karate)
rg<- getPA(karate, pwr=1.25)
vcount(rg)
ecount(rg)
```

---

```
getRandomGraphCentrality
```

*Centrality measures for random graphs induced by input one*

---

**Description**

Generate a random graph that mimics the properties of the input graph and calls [getCentralityMatrix](#) to calculate all available vertex centrality measures. There are four different types of random graph to generate

**Usage**

```
getRandomGraphCentrality(
  gg,
  type = c("gnp", "pa", "cgnp", "rw"),
  power = NULL,
  weights = NULL,
  ...
)
```

**Arguments**

<code>gg</code>	template graph to mimic
<code>type</code>	type of random graph to generate: <ul style="list-style-type: none"> <li>• <code>gnp</code> – G(n,p) Erdos-Renyi model (<a href="#">sample_gnp</a>)</li> <li>• <code>pa</code> – Barabasi-Albert model (<a href="#">sample_pa</a>)</li> <li>• <code>cgnp</code> – new random graph from a given graph by randomly adding/removing edges (<a href="#">sample_correlated_gnp</a>)</li> <li>• <code>rw</code> – new random graph from a given graph by rewiring 25% of edges preserving the degree distribution <a href="#">sample_gnp</a>, <a href="#">sample_correlated_gnp</a>, and <a href="#">sample_pa</a></li> </ul>
<code>power</code>	optional argument of the power of the preferential attachment to be passed to <a href="#">sample_pa</a> . If power is NULL the power of the preferential attachment will be estimated from <a href="#">fitDegree</a> function.
<code>weights</code>	Possibly a numeric vector giving edge weights. If this is NULL and the graph has a weight edge attribute, then the attribute is used. If this is NA then no weights are used (even if the graph has a weight attribute).
<code>...</code>	other parameters passed to random graph generation functions

**Value**

matrix of random graph vertices centrality measure.

**See Also**

[getCentralityMatrix\(\)](#) for explanation of the use of weights.

**Examples**

```
data(karate,package='igraphdata')
m<-getRandomGraphCentrality(karate,'pa',threads=1)
# to avoid repetitive costly computation of PowerLaw fit
# power parameter could be send explicitly:
pFit <- fitDegree( as.vector(igraph::degree(graph=karate)),
  Nsim=10, plot=FALSE,threads=1)
pwr <- slot(pFit,'alpha')
m<-getRandomGraphCentrality(karate,'pa',power=pwr)
lpa<-lapply(1:5,getRandomGraphCentrality,gg=karate,type='pa',
  power=pwr,weights = NULL)
```

---

getRobustness

---

*Calculate cluster robustness from consensus matrix*


---

**Description**

This function takes as argument a network (gg), the name of a clustering algorithm (alg) which can be found in the network, and a consensus matrix (conmat) generated from the clustering network. The function uses the consensus matrix to generate a measure of cluster robustness  $C_{rob}$  (Crob) for each cluster (C) using the R function [clrob](#). Briefly, this is done by summing elements of the consensus matrix that are found in the same cluster, and dividing this by the total number of entries in the matrix:

$$C_{rob} = \frac{2}{C_n(C_n - 1)} \sum_{\substack{i,j \in I_C \\ i \leq j}} conmat_{i,j}$$

where  $I_C$  – indices of vertices of the cluster  $C$ ,  $C_n$  is the number of nodes found inside the cluster  $C$ .

**Usage**

```
getRobustness(gg, alg, conmat)
```

**Arguments**

gg	igraph object
alg	clustering algorithm
conmat	consensus matrix

**Value**

data.frame that for each cluster C shows

- its size  $C_n$  (Cn),
- robustness  $C_{rob}$  (Crob) and
- robustness scaled to range between 0 and 1 (CrobScaled).

**See Also**

Other Robustness Functions: [makeConsensusMatrix\(\)](#)

**Examples**

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
alg<-'louvain'
gg<-calcClustering(karate, alg = alg)
conmat<-makeConsensusMatrix(gg, N=100, mask = 10, alg = alg, type = 2)
clrob<-getRobustness(gg, alg = alg, conmat)
clrob
```

---

gofs	<i>Goodnes of fit KS test</i>
------	-------------------------------

---

**Description**

This is internal function and do not suppose to be called by user.

**Usage**

```
gofs(x, rate, model, sigma2 = NULL, countDATA = TRUE)
```

**Arguments**

x	steps along the Fe
rate	parameters of the sigmoid
model	fitted model
sigma2	noise strength
countDATA	should points to be counted

**Value**

list of [ks.test](#) values for each value in rate

---

law-class	<i>Result of PowerLaw fit</i>
-----------	-------------------------------

---

**Description**

Result of PowerLaw fit

**Slots**

fit [displ-class](#) result of power law fit.  
p numeric.  
alpha numeric degree of power-law.  
SDxmin numeric bootstrap sd of Xmin.  
SDalpha numeric bootstrap sd of alpha.

---

layoutByCluster	<i>Calculate layout based upon membership</i>
-----------------	---

---

**Description**

Function to split graph into clusters and layout each cluster independently..

**Usage**

```
layoutByCluster(gg, mem, layout = layout_with_kk)
```

**Arguments**

gg	graph to layout
mem	membership data.frame from <a href="#">calcMembership</a>
layout	algorithm to use for layout

**Value**

Layout in a form of 2D matrix.

**See Also**

[igraph::layout\\_](#)

**Examples**

```
data(karate, package='igraphdata')
alg<-'louvain'
mem<-calcMembership(karate,alg = alg)
lay<-layoutByCluster(karate,mem)
#plot(karate,layout=lay)
```

---

layoutByRecluster	<i>Calculate two-level layout from recluster matrix</i>
-------------------	---

---

**Description**

Takes results of recluster and apply layoutByCluster to each

**Usage**

```
layoutByRecluster(gg, remem, layout = layout_with_kk)
```

**Arguments**

gg	graph to layout
remem	recluster result obtained by <a href="#">calcReclusterMatrix</a> invocation
layout	one of the layout algorithms from <a href="#">layout_</a>

**Value**

Layout in a form of 2D matrix.

**Examples**

```
data(karate, package='igraphdata')
alg<- 'louvain'
mem<-calcMembership(karate, alg = alg)
remem<-calcReclusterMatrix(karate, mem, alg, 10)
lay<-layoutByRecluster(karate, remem)
#plot(karate, layout=lay)
```

---

makeConsensusMatrix     *Function to make random resampling consensus matrix in memory*

---

**Description**

Function to make random resampling consensus matrix in memory

**Usage**

```
makeConsensusMatrix(
  gg,
  N = 500,
  mask = 20,
  alg,
  type,
  weights = NULL,
  reclust = FALSE,
  Cnmax = 10
)
```

**Arguments**

gg	graph to perturb
N	number of perturbation steps
mask	percentage of elements to perturb
alg	clustering alg.
type	edges (1) or nodes (2) to mask
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.
reclust	logical to decide whether to invoke reclustering via <a href="#">recluster</a>
Cnmax	maximum size of the cluster in mem that will not be processed if reclustering is invoked

**Details**

Function to assess the robustness of network clustering. A randomisation study is performed apply the same clustering algorithm to N perturbed networks, and which returns the consensus matrix where each vertex pair is assigned the probability of belong to the same cluster. The inputted network is perturbed by randomly removing a mask percentage of edges (type=1) or vertices (type=2) from the network before clustering.

**Value**

consensus matrix of Nvert X Nvert

**See Also**

Other Robustness Functions: [getRobustness\(\)](#)

**Examples**

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
alg<-'louvain'
gg<-calcClustering(karate, alg = alg)
conmat<-makeConsensusMatrix(gg, N=100, mask = 10, alg = alg, type = 2)
dim(conmat)
```

---

makeMembership

*Create membership data.frame from graph for arbitrary annotation*

---

**Description**

Create membership data.frame from graph vertex attribute or vector of cluster names, IDs or indices. This function is similar to [calcMembership](#) but do not linked to clustering algorithm.

**Usage**

```
makeMembership(gg, membership)
```

**Arguments**

gg	igraph object to assign membership
membership	either name of the vertex attribute or vector of membership

**Details**

Any annotation coercible to factor could be converted to the membership data.frame. This function is useful, for example, to make layout with [layoutByCluster](#).

**Value**

data.frame with two columns names and membership

**Examples**

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
m<-makeMembership(karate,rep(c(1,2),length.out=vcount(karate)))
head(m)
```

markBowTie

*Calculates bow-tie decomposition and marks vertices with one of the following in the BowTie attribute:*

- *SCC – maximal strong connected component;*
- *IN – vertices not in SCC, but SCC is reachable from them;*
- *OUT – vertices not in SCC, but reachable from SCC;*
- *TU – vertices not in all three above, but reachable from IN and OUT is reachable from them (TUBES);*
- *IDR – vertices not in SCC, but they are reachable from IN and OUT is NOT reachable from them (INTENDRILS);*
- *ODR – vertices not in SCC, but they are NOT reachable from IN and OUT is reachable from them (OUTTENDRILS);*
- *OTR – all other vertices.*

**Description**

Algorithm proposed in:

**Usage**

```
markBowTie(g)
```

**Arguments**

**g** graph to analyse

**Details**

"Bow-tie Decomposition in Directed Graphs" - Yang et al. IEEE (2011)

**Value**

graph with BowTie vertex attribute

---

metlMatrix	<i>Convert sparse matrix into triplet data.frame.</i>
------------	---

---

### Description

For very large graphs handling adjacency-like matrices is difficult due to its sparse nature. This function convert sparse matrix into triplet data.frame with row and column indices and names, and cell value.

### Usage

```
metlMatrix(sparceM)
```

### Arguments

sparceM            sparce matrix to convert into triplet data.frame

### Value

data.frame with three colums:

- i – row index;
- j – column index;
- x – cell value;
- Rname – i-th row name;
- Cname – j-th column name.

### Examples

```
data(karate, package='igraphdata')
upgrade_graph(karate)
Ws <- as_adjacency_matrix(karate,type='both',attr='weight',sparse = TRUE)
mdf<-metlMatrix(Ws)
head(mdf)
```

---

normModularity	<i>Calculates the normalised network modularity value.</i>
----------------	--

---

### Description

Function to compare network Modularity of input network with networks of different size and connectivity.

### Usage

```
normModularity(
  gg,
  alg = c("lec", "wt", "fc", "infomap", "louvain", "sgG1", "sgG2", "sgG5"),
  Nint = 1000,
  weights = NULL
)
```

**Arguments**

gg	graph object to analyze
alg	clustering algorithm
Nint	number of iterations
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

**Details**

Used the normalised network modularity value  $Q_m$  based on the previous studies by Parter et al., 2007, Takemoto, 2012, Takemoto, 2013, Takemoto and Borjigin, 2011, which was defined as:

$$Q_m = \frac{Q_{real} - Q_{rand}}{Q_{max} - Q_{rand}}$$

Where  $Q_{real}$  is the network modularity of a real-world signalling network and,  $Q_{rand}$  is the average network modularity value obtained from 10,000 randomised networks constructed from its real-world network.  $Q_{max}$  was estimated as:  $1 - 1/M$ , where  $M$  is the number of modules in the real network.

Randomised networks were generated from a real-world network using the edge-rewiring algorithm (Maslov and Sneppen, 2002).

**Value**

normalized modularity value

**References**

Takemoto, K. & Kihara, K. Modular organization of cancer signaling networks is associated with patient survivability. *Biosystems* 113, 149–154 (2013).

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)

nm<-normModularity(gg, alg='louvain',Nint=10)
```

---

permutate	<i>Randomly shuffle annotations</i>
-----------	-------------------------------------

---

### Description

This function is a convenience wrapper to [sample](#) with `replace= FALSE`

### Usage

```
permutate(GNS, N)
```

### Arguments

GNS	annotation list to take data from
N	size of the sample

### Value

random list of GNS values

### Examples

```
permutate(LETTERS, 15)
```

---

plotBridgeness	<i>Plot Bridgeness values</i>
----------------	-------------------------------

---

### Description

Semi-local centrality measure (Chen et al., 2011) lies between 0 and 1 indicating whether protein is important globally or locally. By plotting Bridgeness against semi-local centrality we can categorise the influence each protein found in our network has on the overall network structure:

- Region 1, proteins having a 'global' rather than 'local' influence in the network (also been called bottle-neck bridges, connector or kinless hubs ( $0 < SI < 0.5$ ;  $0.5 < Br < 1$ )).
- Region 2, proteins having 'global' and 'local' influence ( $0.5 < SI < 1$ ,  $0.5 < Br < 1$ ).
- Region 3, proteins centred within the community they belong to, but also communicating with a few other specific communities ( $0 < SI < 0.5$ ;  $0.1 < Br < 0.5$ ).
- Region 4, proteins with 'local' impact, primarily within one or two communities (local or party hubs,  $0.5 < SI < 1$ ,  $0 < Br < 0.5$ ).

**Usage**

```
plotBridgeness(
  gg,
  alg,
  VIPs,
  Xatt = "SL",
  Xlab = "Semilocal Centrality (SL)",
  Ylab = "Bridgeness (B)",
  bsize = 3,
  spsize = 7,
  MainDivSize = 0.8,
  xmin = 0,
  xmax = 1,
  ymin = 0,
  ymax = 1,
  baseColor = "royalblue2",
  SPColor = "royalblue2"
)
```

**Arguments**

gg	igraph object with bridgeness values stored as attributes, after call to <a href="#">calcBridgeness</a>
alg	clustering algorithm that was used to calculate bridgeness values
VIPs	list of 'special' genes to be marked on the plot
Xatt	name of the attribute that stores values to be used as X-axis values. By default SL for semi-local centrality
Xlab	label for the X-axis
Ylab	label for the Y-axis
bsize	point size for genes
spsize	point size for 'special' genes
MainDivSize	size of the line for the region separation lines
xmin	low limit for X-axis
xmax	upper limit for X-axis
ymin	low limit for Y-axis
ymax	upper limit for Y-axis
baseColor	basic color for genes
SPColor	colour highlighting any 'special' genes

**Value**

[ggplot](#) object with plot

**Examples**

```
karate <- make_graph("Zachary")
# We need vertex ID in the 'name' attribute of the vertex
V(karate)$name<-c(LETTERS,letters)[1:vcount(karate)]
set.seed(100)
gg <- calcClustering(karate, 'louvain')
```

```
gg <- calcCentrality(gg)
cnmat <- makeConsensusMatrix(gg, N=10, alg = 'louvain', type = 2, mask = 10)
gg<-calcBridgeness(gg, alg = 'louvain', cnmat)
plotBridgeness(gg,alg = 'louvain',VIPs=c("Mr Hi","John A"))
```

---

plotEntropy	<i>Plot graph entropy values versus vertex degree for each perturbed vertex value.</i>
-------------	--

---

### Description

Following procedure described in (Teschendorff et al., 2015), all vertexes are artificially assigned a uniform weight then sequentially perturbed with the global entropy rate (SRprime) after each protein's perturbation being calculated by [getEntropy](#) function.

### Usage

```
plotEntropy(SRprime, subTIT = "Entropy", SRo = NULL, maxSr = NULL)
```

### Arguments

SRprime	results of <a href="#">getEntropy</a> invocation
subTIT	entropy axis label
SRo	initial entropy rate $SR_0$ , results of <a href="#">getEntropyRate</a> invocation
maxSr	the maximum entropy rate $maxSR$ , results of <a href="#">getEntropyRate</a> invocation

### Details

This function plot SRprime against the log of the protein's degree. In case of scale-free or approximate scale-free topologies, we see a clear bi-modal response between over-weighted vertices and their degree and an opposing bi-phasic response in under-weighted vertices and their degrees.

If maxSr or SRo is set to their default value NULL [getEntropyRate](#) will be called and returned values will be used in the following calculations. As maxSr is required for SRprime calculation by [getEntropy](#) using explicit values could save some time in the case of large network.

### Value

ggplot2 object with diagram

### See Also

[getEntropy\(\)](#)

Other Entropy Functions: [calcEntropy\(\)](#), [getEntropy\(\)](#), [getEntropyRate\(\)](#)

**Examples**

```

file <- system.file("extdata", "PPI_Presynaptic.csv", package = "BioNAR")
tbl <- read.csv(file, sep="\t")
gg <- buildNetwork(tbl)
gg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(gg)$name == '80273')
paste(V(gg)$GeneName[idx], 'GRPEL1')
ent <- getEntropyRate(gg)
SRprime <- getEntropy(gg, maxSr = NULL)
plotEntropy(SRprime, subTIT = "Entropy", SRo = ent$SRo, maxSr = ent$maxSr)

```

---

plotRatio

*Plot fraction of enriched communities*


---

**Description**

Plot fraction of enriched communities

**Usage**

```

plotRatio(
  x,
  desc = "",
  anno = "",
  LEGtextSize = 1.5,
  LEGlineSize = 4,
  type = NULL
)

```

**Arguments**

x	enrichment statistics
desc	plot subtitle
anno	name of annotation used
LEGtextSize	size of the text
LEGlineSize	width of the line
type	type of the plot

**Value**

ggplot object

---

plotSigmoid *Plot results of the sigmoid fit*

---

### Description

Plot results of the sigmoid fit

### Usage

```
plotSigmoid(x, rates, model, alg = "", pv = 0)
```

### Arguments

x	steps along the Fe
rates	parameters of the sigmoid
model	fitted model
alg	name of the clustering algorithm
pv	Kolmogorov-Smirnov test's p-value

### Value

[ggplot](#) object with sigmoid fit plot

---

PPI\_Presynaptic.csv *Table of protein protein interactions for presynaptic compartment*

---

### Description

Protein-protein interactions (PPIS) for presynaptic compartment, extracted from Synaptome.db, in a csv form. Columns A and B correspond to Entrez IDs for interacting proteins A and B (node names); column We contains the edge weights, if available.

### See Also

[buildNetwork](#)

---

PPI\_Presynaptic.gml *PPI graph for presynaptic compartment*

---

### Description

Protein-protein interactions (PPIS) for presynaptic compartment, extracted from Synaptome.db, and saved in a graph format. Graph contains node attributes, such as names (Entrez IDs), Gene Names, disease association (TopOntoOVG, TopOntoOVGHDOID), annotation with schizophrenia-related genes (Schanno (v/c), function annotation from GO (GOBPID, GOBP, GOMFID, GOMF, GOC-CID, GOCC), centrality measures (DEG - degree, BET - betweenness, CC - clustering coefficient, SL - semilocal centrality, mnSP - mean shortest path, PR - page rank, sdSP - standard deviation of the shortest path), and clustering memberships for 8 clustering algorithms (lec, wt, fc, infomap, louvain, sgG1, sgG2, sgG5)

---

prepareGDA	<i>Function to return vertex annotation from a graph in the Vertex Annotation form and format it for further analysis.</i>
------------	--

---

**Description**

Function to return vertex annotation from a graph in the Vertex Annotation form and format it for further analysis.

**Usage**

```
prepareGDA(gg, name)
```

**Arguments**

gg	igraph object to take annotation from
name	name of the vertex attribute that contains annotation. If graph has no such vertex attribute an error is thrown..

**Value**

escaped annotation in Vertex Annotation form

**See Also**

getAnnotationVertexList  
escapeAnnotation

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
agg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(agg)$name == '80273')
paste(V(agg)$GeneName[idx], 'GRPEL1')
gda<-prepareGDA(agg, 'TopOntoOVGHDOID')
gda<-prepareGDA(agg, 'TopOntoOVGHDOID')
head(gda)
```

---

PresynAn.csv	<i>Presynaptic genes specific functional annotation</i>
--------------	---

---

**Description**

Presynaptic genes functional annotation derived from Boyken et al. (2013) [doi:10.1016/j.neuron.2013.02.027](https://doi.org/10.1016/j.neuron.2013.02.027). The table has columns: the first containing functional group ID terms, the second - gene functional group description terms, third - gene Human Entrez Ids; in csv format

**See Also**

[annotatePresynaptic](#)

---

recluster	<i>Hierarchical graph clustering</i>
-----------	--------------------------------------

---

### Description

Function reads in a graph GG with cluster membership stored in vertex attribute ALGN, and reapplies the clustering algorithm ALGN to all clusters larger than CnMAX

### Usage

```
recluster(GG, ALGN, CnMAX, weights = NULL)
```

### Arguments

GG	graph to cluster
ALGN	algorithm to apply
CnMAX	maximum size of the cluster in mem that will not be processed
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.

### Value

membership matrix, that contains vertex ID membership and result of reclustering

### Examples

```
data(karate, package='igraphdata')
alg<-'louvain'
mem<-calcMembership(karate, alg = alg)
remem<-calcReclusterMatrix(karate, mem, alg, 10)
```

---

removeVertexTerm	<i>Remove vertex property.</i>
------------------	--------------------------------

---

### Description

Remove vertex property.

### Usage

```
removeVertexTerm(GG, NAME)
```

**Arguments**

GG	igraph object
NAME	name of the vertex property to remove

**Value**

igraph object with attribute removed

**Examples**

```
data(karate, package='igraphdata')
upgrade_graph(karate)
vertex_attr_names(karate)
m<-removeVertexTerm(karate, 'color')
vertex_attr_names(m)
```

---

runPermDisease	<i>Calculate disease-disease pair overlaps on permuted network to estimate its statistical significance</i>
----------------	---

---

**Description**

Function to calculate the disease-pair overlap characteristics of an inputted network, before applying  $N_{perm}$  permutations on the disease annotations of # type "random" or "binned" permute. From the permuted networks the function estimates the significance of disease overlap: p-value, Bonferoni-adjusted p-value, and q-value in the `Disease_overlap_sig`. The function also compares the average disease separation between inputted and permuted networks, and calculates its significance using the Wilcox test and store. Significance of disease-pair overlap and disease separation results are stored in the matrix `Disease_location_sig`.

**Usage**

```
runPermDisease(
  gg,
  name,
  diseases = NULL,
  Nperm = 100,
  permute = c("random", "binned"),
  alpha = c(0.05, 0.01, 0.001)
)
```

**Arguments**

gg	interactome network as igraph object
name	name of the attribute that stores disease annotation
diseases	list of diseases to match
Nperm	number of permutations to apply
permute	type of permutations. random – annotation is randomly shuffled, binned – annotation is shuffled in a way to preserve node degree-annotation relationship by <a href="#">degreeBinnedGDAs</a> .
alpha	statistical significance levels

**Details**

Run with care, as large number of permutations could require a lot of memory and be timeconsuming.

**Value**

list of two matrices: `Disease_overlap_sig` gives statistics for each pair of disease, and `Disease_location_sig` gives intra-disease statistics

**Examples**

```
file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
agg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(agg)$name == '80273')
paste(V(agg)$GeneName[idx], 'GRPEL1')
r <- runPermDisease(
  agg,
  name = "TopOntoOVGHDOID",
  diseases = c("DOID:10652", "DOID:3312", "DOID:12849", "DOID:1826"),
  Nperm = 10,
  alpha = c(0.05, 0.01, 0.001))
r$Disease_location_sig
```

---

sampleDegBinnedGDA	<i>Function to randomly shuffle vertex annotation terms, whilst preserving the vertex degree originally found with that annotation term..</i>
--------------------	---

---

**Description**

Function to randomly shuffle vertex annotation terms, whilst preserving the vertex degree originally found with that annotation term..

**Usage**

```
sampleDegBinnedGDA(org.map, term)
```

**Arguments**

org.map	degree-annotation mapping returned by <a href="#">degreeBinnedGDAs</a>
term	annotation term to shuffle

**Value**

vertex IDs to assign term in shuffled annotation

**See Also**

[degreeBinnedGDAs](#)

**Examples**

```

file <- system.file("extdata", "PPI_Presynaptic.gml", package = "BioNAR")
gg <- igraph::read_graph(file, format="gml")
agg<-annotateGeneNames(gg)
# due to error in org.Hs.eg.db we have to manually check annotation of one node
idx <- which(V(agg)$name == '80273')
paste(V(agg)$GeneName[idx], 'GRPEL1')
gda<-prepareGDA(agg, 'TopOntoOVGHDOID')
diseases<-getAnnotationList(gda)
m<-degreeBinnedGDAs(agg, gda, diseases)
sampleDegBinnedGDA(m, diseases[1])

```

sampleGraphClust

*Perturbe graph and calculate its clustering***Description**

Function will mask a percentage of edges (type=1) or vertices (type=2) from the network, find the largest connected component of the masked network and cluster it. The clustering results are stored in a three column matrix: the first column contains the vertex IDs of input network; the second column the vertex IDs of the subsampled network, or -1 if the vertex has been masked; the third column the cluster membership of subsampled network, or -1 if vertex has been masked.

**Usage**

```

sampleGraphClust(
  gg,
  mask = 20,
  alg,
  type,
  weights = NULL,
  reclust = FALSE,
  Cnmax = 10
)

```

**Arguments**

gg	graph
mask	percentage of elements to perturb
alg	clustering alg.
type	edges=>1 or nodes=>2 to mask
weights	The weights of the edges. It must be a positive numeric vector, NULL or NA. If it is NULL and the input graph has a 'weight' edge attribute, then that attribute will be used. If NULL and no such attribute is present, then the edges will have equal weights. Set this to NA if the graph was a 'weight' edge attribute, but you don't want to use it for community detection. A larger edge weight means a stronger connection for this function. The weights value is ignored for the spectral clustering.
reclust	logical to decide whether to invoke reclustering via <a href="#">recluster</a>
Cnmax	maximum size of the cluster in mem that will not be processed if reclustering is invoked

**Details**

This is internal function and not supposed to be called by end user.

**Value**

list of Nx3 matrices

**Examples**

```
data(karate,package='igraphdata')
alg<-'louvain'
mem<-calcMembership(karate,alg = alg)
smp1<-BioNAR:::sampleGraphClust(karate,mask=10,alg,type=2)
```

---

SCH_flatfile.csv	<i>Schizophrenia related synaptic gene functional annotation.</i>
------------------	---

---

**Description**

Annotation, manually curated from an external file: Lips et al., (2012) doi:10.1038/mp.2011.117. The table has columns: the first containing gene Human Entrez IDs, the second gene functional group ID terms, the third gene functional group description terms; in csv format

**See Also**

[annotateSCHanno](#)

---

summaryStats	<i>Calculate summary statistics from enrichment table</i>
--------------	---

---

**Description**

Calculate summary statistics from enrichment table

**Usage**

```
summaryStats(RES, ALPHA, usePadj = FALSE, FeMAX = 0, FcMAX = 0)
```

**Arguments**

RES	enrichment results data.frame
ALPHA	p-value cut-off
usePadj	logical, whether to use plain or adjusted p-value
FeMAX	max of the FE
FcMAX	max of the FC

**Value**

list of data.frame

---

unescapeAnnotation      *Unescape annotation strings*

---

### Description

Function to remove all escape characters from annotation strings (opposite to escapeAnnotation).

### Usage

```
unescapeAnnotation(annVec, col = COLLAPSE, esc = ESC)
```

### Arguments

annVec	vector of annotation strings
col	list separator character within annotation string
esc	escape character

### Details

NOTE: spaces are treated as regular characters, no trimming is applied before or after escaping.

### Value

vector of annotation strings with removed escape characters

### See Also

escapeAnnotation

### Examples

```
annVec<-apply(matrix(letters, ncol=13), 2, paste, collapse=';')
escVec<-escapeAnnotation(annVec, ';', '|')
cbind(annVec, escVec, unescapeAnnotation(escVec, ';', '|'))
```

---

zeroNA      *Auxiliary function to replace NAs with zeros.*

---

### Description

Auxiliary function to replace NAs with zeros.

### Usage

```
zeroNA(x)
```

### Arguments

x	matrix or vector to process
---	-----------------------------

**Value**

matrix or vector with NAs replaced by zero.

**Examples**

```
x<-matrix(NA,nrow = 3,ncol = 3)
zeroNA(x)
```

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