

# Package ‘dSimer’

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**Type** Package

**Title** Integration of Disease Similarity Methods

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**Description** dSimer is an R package which provides computation of nine methods for measuring disease-disease similarity, including a standard cosine similarity measure and eight function-based methods. The disease similarity matrix obtained from these nine methods can be visualized through heatmap and network. Biological data widely used in disease-disease associations study are also provided by dSimer.

**Depends** R (>= 3.3.0), igraph (>= 1.0.1)

**Imports** stats, Rcpp (>= 0.11.3), ggplot2, reshape2, GO.db,  
org.Hs.eg.db, AnnotationDbi, graphics

**Suggests** knitr, rmarkdown, BiocStyle

**LinkingTo** Rcpp

**License** GPL (>= 2)

**biocViews** Software, Visualization, Network

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dSimer-package

*Integration of Disease Similarity Methods*


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## Description

dSimer is an R package which provides computation of nine methods for measuring disease-disease similarity, including a standard cosine similarity measure and eight function-based methods. The disease similarity matrix obtained from these nine methods can be visualized through heatmap and network. Biological data widely used in disease-disease associations study are also provided by dSimer.

**Details**

Package: dSimer  
Type: Package  
Version: 1.1.0  
Date: 12-10-2015  
biocViews: Software, Visualization, Network  
Depends: R (>= 3.3.0), igraph (>= 1.0.1)  
Imports: stats, Rcpp (>= 0.11.3), ggplot2, reshape2, GO.db, AnnotationDbi, org.Hs.eg.db, graphics  
Suggests: knitr, rmarkdown, BiocStyle  
LinkingTo: Rcpp  
License: GPL (>= 2)

**Author(s)**

Min Li, Peng Ni

---

BOG

*calculate disease similarity by BOG*

---

**Description**

given two vectors of diseases and a list of disease-gene associations, this function will calculate disease similarity by method BOG.

**Usage**

BOG(D1, D2, d2g)

**Arguments**

D1 a vector consists disease ids  
D2 another vector consists disease ids  
d2g a list of disease-gene associations

**Value**

a matrix of disease disease simialrity which rownames is D1 and colnames is D2

**Author(s)**

Peng Ni, Min Li

**References**

Mathur S, Dinakarbandian D. Automated ontological gene annotation for computing disease similarity[J]. AMIA Summits on Translational Science Proceedings, 2010, 2010: 12

**See Also**[Normalize](#)**Examples**

```
data(d2g_separation) #get disease-gene associations
ds<-sample(names(d2g_separation),5)
sim<-BOG(ds,ds,d2g_separation)
Normalize(sim) #normalize BOG sim scores
```

CosineDFV

*calculate disease similarity by using feature vectors***Description**

given two (lists of) disease names, this function will calculate cosine similarity between these diseases' feature vectors.

**Usage**

```
CosineDFV(D1, D2, d2f, dcol = 2, fcol = 1, ccol = 3)
```

**Arguments**

D1	a vector consists of disease ids/names
D2	another vector consists of disease ids/names
d2f	data.frame, contains term co-occurrences between features and diseases
dcol	integer, disease column number in d2f
fcol	integer, feature column number in d2f
ccol	integer, co-occurrences column number in d2f

**Value**

a matrix of disease disease similarity which rownames and colnames are the disease names

**Author(s)**

Zhihui Fei, Peng Ni, Min Li

**References**

Zhou X Z, Menche J, Barabasi A L, et al. Human symptoms-disease network[J]. Nature communications, 2014, 5.

Van Driel M A, Bruggeman J, Vriend G, et al. A text-mining analysis of the human phenome[J]. European journal of human genetics, 2006, 14(5): 535-542.

**Examples**

```
### this is a disease-symptom-cooccurrence sample, if you want to use
### the complete data, please use "data(d2s_hsdn)" command
data(d2s_hsdn_sample)
ds <- sample(unique(d2s_hsdn_sample[,2]), 10)
simmat <- CosineDFV(ds, ds, d2s_hsdn_sample)
```

---

d2go_sample	<i>d2go_sample</i>
-------------	--------------------

---

**Description**

a sample list of disease-GO term associations.

**Value**

d2go\_sample is a named list of length 3. The names are the DOIDs (DOIDs are ids of terms in Disease Ontology, e.g. "DOID:4" ) and list elements are vectors of GO term ids. The entire data of disease-GO term associations can be obtained by function `HypergeometricTest`.

**See Also**

[HypergeometricTest](#)

**Examples**

```
data(d2go_sample)
```

---

d2g_fundo_entrezid	<i>d2g_fundo_entrezid</i>
--------------------	---------------------------

---

**Description**

a list of disease-gene associations from FunDO.

**Value**

d2g\_fundo\_entrezid is a named list of length 1855 which stored disease-gene associations from FunDO. The names are the DOIDs (DOIDs are ids of terms in Disease Ontology, e.g. "DOID:4" ) and list elements are vectors of Entrez gene IDs.

**References**

Osborne J D, Flatow J, Holko M, et al. Annotating the human genome with Disease Ontology[J]. BMC genomics, 2009, 10(Suppl 1): S6.

**Examples**

```
data(d2g_fundo_entrezid)
```

---

d2g_fundo_symbol	<i>d2g_fundo_symbol</i>
------------------	-------------------------

---

**Description**

a list of disease-gene associations from FunDO.

**Value**

d2g\_fundo\_symbol is a named list of length 1855 which stored disease-gene associations from FunDO. The names are the DOIDs (DOIDs are ids of terms in Disease Ontology, e.g. "DOID:4") and list elements are vectors of gene symbols.

**References**

Osborne J D, Flatow J, Holko M, et al. Annotating the human genome with Disease Ontology[J]. BMC genomics, 2009, 10(Suppl 1): S6.

**Examples**

```
data(d2g_fundo_symbol)
```

---

d2g_separation	<i>d2g_separation</i>
----------------	-----------------------

---

**Description**

a list of disease-gene associations from the reference paper (see below).

**Value**

d2g\_separation is a named list of length 299 which stored disease-gene associations from the reference paper (see below). The names are diseases and list elements are vectors of gene entrez ids.

**References**

Menche J, Sharma A, Kitsak M, et al. Uncovering disease-disease relationships through the incomplete interactome[J]. Science, 2015, 347(6224): 1257601.

**Examples**

```
data(d2g_separation)
```

---

`d2s_hsdn`*d2s\_hsdn*

---

**Description**

diseases, symptoms and their co-occurrences in PubMed

**Value**

`d2s_hsdn` is a `data.frame` of 73726 rows and 3 columns, contains PubMed co-occurrences of diseases and symptoms, will be used in method `CosineDFV`.

**References**

Zhou X Z, Menche J, Barabasi A L, et al. Human symptoms-disease network[J]. Nature communications, 2014, 5.

**See Also**

[CosineDFV](#)

**Examples**

```
data(d2s_hsdn)
```

---

`d2s_hsdn_sample`*d2s\_hsdn\_sample*

---

**Description**

a sample of `d2s_hsdn`

**Value**

`d2s_hsdn__sample` is a `data.frame` of 1480 rows and 3 columns, contains PubMed co- occurrences of diseases and symptoms. It is a sample of `d2s_hsdn`.

**References**

Zhou X Z, Menche J, Barabasi A L, et al. Human symptoms-disease network[J]. Nature communications, 2014, 5.

**See Also**

[d2s\\_hsdn](#), [CosineDFV](#)

**Examples**

```
data(d2s_hsdn_sample)
```

---

FunSim *calculate disease similarity by FunSim*

---

### Description

given two vectors of diseases, a list of disease-gene associations, and a list of gene-gene log-likelihood score from HumanNet, this function will calculate disease similarity by method FunSim

### Usage

```
FunSim(D1, D2, d2g, LLSnList)
```

### Arguments

D1	a vector consists disease ids
D2	another vector consists disease ids
d2g	a list of disease-gene associations, while gene ids should be entrez id.
LLSnList	a list of gene-gene log-likelihood score from HumanNet

### Value

a matrix of disease disease simialrity which rownames is D1 and colnames is D2

### Author(s)

Peng Ni, Min Li

### References

Cheng L, Li J, Ju P, et al. SemFunSim: a new method for measuring disease similarity by integrating semantic and gene functional association[J]. PloS one, 2014, 9(6): e99415.

### See Also

[LLSn2List](#)

### Examples

```
## in this method, we must use disease-gene associations
## which genes are represented by entrez ids because of
## HumanNet
data(d2g_fundo_entrezid)
data(HumanNet_sample)
## we specified 5 DOIDs to match Human_sample
ds<-c("DOID:8176", "DOID:2394", "DOID:3744", "DOID:8466", "DOID:5679")
llsnlist<-LLSn2List(HumanNet_sample)
FunSim(ds,ds,d2g_fundo_entrezid,llsnlist)
```



---

get\_GOterm2GeneAssos *get GO-gene associations*

---

### Description

get GO-gene associations from GO.db and org.Hs.eg.db

### Usage

```
get_GOterm2GeneAssos(GOONTOLOGY = c("BP", "MF", "CC"),
  geneid = c("ENTREZID", "SYMBOL", "OMIM"), rm.IEAs = TRUE,
  rm.termlessthan3genes = TRUE)
```

### Arguments

GOONTOLOGY	"BP" or "MF" or "CC"
geneid	gene id type, "ENTREZID" or "SYMBOL"
rm.IEAs	logical value, remove GO terms with evidence "IEA" or not
rm.termlessthan3genes	logical value, remove terms whose number of annotated genes are less than 3 or not

### Value

a list which names are GO term IDs and elements are gene ids or symbols annotated with GO terms

### Author(s)

Peng Ni, Min Li

### References

Mathur S, Dinakarandian D. Finding disease similarity based on implicit semantic similarity[J]. Journal of biomedical informatics, 2012, 45(2): 363-371.

### See Also

[PSB, Sun\\_function](#)

### Examples

```
go2g<-get_GOterm2GeneAssos(GOONTOLOGY="BP", geneid="SYMBOL")
go2g
```

go2g\_sample                      *go2g\_sample*

---

**Description**

a sample list of GO term-gene associations.

**Value**

go2g\_sample is a named list of length 465. The names are GO term ids (GOIDs) and list elements are vectors of gene symbols. The entire data of GO term-gene assos can be obtained by function `get_GOterm2GeneAssos`.

**See Also**

[get\\_GOterm2GeneAssos](#)

**Examples**

```
data(go2g_sample)
```

---

graphlet\_sig\_hprd                *graphlet\_sig\_hprd*

---

**Description**

graphlet signature of nodes in HPRD PPI network.

**Value**

#' graphlet\_sig\_hprd is a matrix of 9270 rows and 73 rows. The rownames of graphlet\_sig\_hprd are gene symbols of nodes from HPRD. Each row indicates a graphlet signature of one node. Graphlet signatures of nodes in HPRD PPI network were calculated by ORCA tool, will be used in method `Sun_topology`.

**References**

Hocevar T, Demsar J. A combinatorial approach to graphlet counting[J]. *Bioinformatics*, 2014, 30(4): 559-565.

**See Also**

[Sun\\_topology](#)

**Examples**

```
data(graphlet_sig_hprd)
```

---

HumanNet_sample	<i>HumanNet_sample</i>
-----------------	------------------------

---

**Description**

a sample of HumanNet likelihood score data which will be used in method FunSim.

**Value**

HumanNet\_sample is a data.frame has 22708 rows and 3 columns. Each row indicates a pair of genes and their normalized likelihood score in HumanNet. HumanNet\_sample will be used in method FunSim after being converted to list by method LLSn2List. The entire data of HumanNet can be downloaded from the website <http://www.functionalnet.org/humannet/>.

**References**

Cheng L, Li J, Ju P, et al. SemFunSim: a new method for measuring disease similarity by integrating semantic and gene functional association[J]. PloS one, 2014, 9(6): e99415.

**See Also**

[FunSim](#), [LLSn2List](#)

**Examples**

```
data(HumanNet_sample)
```

---

HypergeometricTest	<i>Hypergeometric test and multiple testing</i>
--------------------	---

---

**Description**

given disease-gene associations and go-gene associations, return disease-go associations by using hypergeometric test and fdr multiple testing

**Usage**

```
HypergeometricTest(d2g, go2g, method = "BH", cutoff = 0.05)
```

**Arguments**

d2g	a list of disease-gene associations
go2g	a list of GObase-gene associations
method	multiple testing method, the same as parameter in method p.adjust
cutoff	multiple testing cut off value

**Value**

a list of disease-GO term associations

**Author(s)**

Peng Ni, Min Li

**See Also**

[PSB](#), [Sun\\_function](#), [get\\_G0term2GeneAssos](#)

**Examples**

```
## see more examples in function PSB or Sun_function
data(d2go_sample)
data(go2g_sample)
data(d2g_fundo_symbol)
HypergeometricTest(d2g_fundo_symbol[names(d2go_sample)],go2g_sample)
```

---

ICod

*calculate disease similarity by ICod*

---

**Description**

given two vectors of diseases, a list of disease-gene associations and a PPI network, this function will calculate disease similarity by method ICod

**Usage**

```
ICod(D1, D2, d2g, graph, A = 0.9, b = 1, C = 0)
```

**Arguments**

D1	a vector consists disease ids
D2	another vector consists disease ids
d2g	a list of disease-gene associations
graph	an igraph graph object of PPI network
A	a parameter used in ICod to calculate transformed distance of node pair, default 0.9
b	a parameter used in ICod to calculate transformed distance of node pair, default 1
C	a parameter used in ICod to calculate disease similarity, default 0

**Value**

a matrix of disease disease simialrity which rownames is D1 and colnames is D2

**Author(s)**

Peng Ni, Min Li

## References

Paik H, Heo HS, Ban H, et al. Unraveling human protein interaction networks underlying co-occurrences of diseases and pathological conditions[J]. Journal of translational medicine, 2014, 12(1): 99.

## Examples

```
data(d2g_fundo_symbol)
data(PPI_HPRD)
```

```
graph_hprd<-graph.data.frame(PPI_HPRD,directed=FALSE) #get a igraph object based on HPRD data
ds<-sample(names(d2g_fundo_symbol),5)
ICod(ds,ds,d2g_fundo_symbol,graph_hprd)
```

---

InformationContent     *calculating information content*

---

## Description

calculate information content of all term ids in a term list

## Usage

```
InformationContent(T2G)
```

## Arguments

T2G                    a list of Term-Gene associations which names are term ids

## Value

a list of IC values of inputted term ids

## Author(s)

Peng Ni, Min Li

## Examples

```
data(d2g_fundo_symbol)
InformationContent(d2g_fundo_symbol[1:5])
```

---

interactome	<i>interactome</i>
-------------	--------------------

---

**Description**

interactome data

**Value**

interactome is a data.frame of 141296 rows and 2 columns. Each row indicates an interaction of two gene entrez ids. It was obtained from the reference below.

**References**

Menche J, Sharma A, Kitsak M, et al. Uncovering disease-disease relationships through the incomplete interactome[J]. Science, 2015, 347(6224): 1257601.

**Examples**

```
data(interactome)
```

---

jaccardindex	<i>calculating Jaccard Index</i>
--------------	----------------------------------

---

**Description**

calculate Jaccard Index of two terms by using their annotated genes

**Usage**

```
jaccardindex(x1, x2, x2y)
```

**Arguments**

x1	a disease id
x2	another disease id
x2y	a list of disease-gene associations which consists x1 and x2

**Value**

numeric value of a jaccard index of x1 and x2

**Author(s)**

Peng Ni, Min Li

**Examples**

```
## this function is not just for disease-gene associations
data(d2go_sample)
d1<-names(d2go_sample)[1]
d2<-names(d2go_sample)[2]
jaccardindex(d1,d2,d2go_sample)
```

---

LLSn2List	<i>convert data.frame of HumanNet log-likelihood Score to list</i>
-----------	--

---

**Description**

convert HumanNet normalized log-likelihood score from data.frame to list, which will be used in FunSim method

**Usage**

```
LLSn2List(LLSn)
```

**Arguments**

LLSn                    data.frame of gene-gene normalized log-likelihood score in HumanNet

**Value**

a list of normalized log-likelihood score

**Author(s)**

Peng Ni, Min Li

**References**

Cheng L, Li J, Ju P, et al. SemFunSim: a new method for measuring disease similarity by integrating semantic and gene functional association[J]. PloS one, 2014, 9(6): e99415.

**See Also**

[FunSim](#)

**Examples**

```
## see examples in function FunSim
data(HumanNet_sample)
llsnlist<-LLSn2List(HumanNet_sample[1:100,])
llsnlist
```

Normalize

*normalize data*

---

**Description**

normalize a vector or a matrix based on the formula from SemFunSim

**Usage**

```
Normalize(data)
```

**Arguments**

data                    a numeric/integer vector or matrix

**Value**

normalized vector or matrix

**Author(s)**

Peng Ni, Min Li

**References**

Cheng L, Li J, Ju P, et al. SemFunSim: a new method for measuring disease similarity by integrating semantic and gene functional association[J]. PloS one, 2014, 9(6): e99415.

**Examples**

```
sim<-matrix(1:9,3,3)
Normalize(sim)
```

---

orbit\_dependency\_count*orbit\_dependency\_count*

---

**Description**

orbit dependency count

**Value**

orbit\_dependency\_count is a 73-dim vector, indicating 73 orbits' dependency count in graphlet theory, used to calculate weight factor in method setWeight.

**References**

Milenkovic T, Przulj N. Uncovering biological network function via graphlet degree signatures[J]. Cancer informatics, 2008, 6: 257.



**See Also**[setWeight](#)**Examples**

```
data(orbit_dependency_count)
```

---

plot_bipartite	<i>plot disease-gene (or GO term etc.) associations as a bipartite graph</i>
----------------	--

---

**Description**

plot a bipartite graph which visualizes associations between diseases and genes (or GO terms etc.)

**Usage**

```
plot_bipartite(xylist, vertex.size = 12, vertex.shape1 = "circle",
  vertex.shape2 = "square", vertex.color1 = "darkseagreen",
  vertex.color2 = "turquoise1", vertex.label.font = 2,
  vertex.label.dist = 0, vertex.label.color = "black",
  vertex.label.cex = 0.8, edge.color = "black",
  layout = layout.kamada.kawai)
```

**Arguments**

xylist	a named list object which names are diseases and each element of the list is a gene set with respect to each disease.
vertex.size	vertex size
vertex.shape1	shape for one kind of vertex
vertex.shape2	shape for another kind of vertex
vertex.color1	color for one kind of vertex
vertex.color2	color for another kind of vertex
vertex.label.font	label text font
vertex.label.dist	label text dist
vertex.label.color	label text color
vertex.label.cex	label text cex
edge.color	edge color
layout	layout

**Value**

an igraph plot object

**Author(s)**

Peng Ni, Min Li

## Examples

```
data(d2g_fundo_symbol)
d2g_sample<-sample(d2g_fundo_symbol, 3)
plot_bipartite(d2g_sample)
```

---

plot_heatmap	<i>similarity matrix heatmap plotting</i>
--------------	---

---

## Description

plot heatmap of a disease similarity matrix

## Usage

```
plot_heatmap(simmat, xlab = "", ylab = "", color.low = "white",
             color.high = "red", labs = TRUE, digits = 2, labs.size = 3,
             font.size = 14)
```

## Arguments

simmat	a similarity matrix
xlab	xlab
ylab	ylab
color.low	color of low value
color.high	color of high value
labs	logical, add text label or not
digits	round digit numbers
labs.size	lable size
font.size	font size

## Value

a ggplot object

## Author(s)

Peng Ni, Min Li

## References

Yu G, Wang L G, Yan G R, et al. DOSE: an R/Bioconductor package for disease ontology semantic and enrichment analysis[J]. Bioinformatics, 2015, 31(4): 608-609.

**Examples**

```

data(d2g_separation)
data(interactome)

graph_interactome<-graph.data.frame(interactome,directed=FALSE)
ds<-c("myocardial ischemia","myocardial infarction","coronary artery disease",
      "cerebrovascular disorders","arthritis, rheumatoid","diabetes mellitus, type 1",
      "autoimmune diseases of the nervous system","demyelinating autoimmune diseases, cns",
      "respiratory hypersensitivity","asthma","retinitis pigmentosa",
      "retinal degeneration","macular degeneration")

sep<-Separation(ds,ds,d2g_separation,graph_interactome)
sim<-Separation2Similarity(sep)
plot_heatmap(sim)

```

---

plot\_net

*plot a network based on a symmetric disease similarity matrix*


---

**Description**

plot a network/graph of a symmetric disease similarity matrix, note that a unsymmetric matrix can't be visualized into a network by this method.

**Usage**

```

plot_net(simmat, cutoff = 1, vertex.label.font = 2,
         vertex.label.dist = 0.5, vertex.label.color = "black",
         vertex.label.cex = 0.8, vertex.shape = "circle",
         vertex.color = "paleturquoise", vertex.size = 20, edge.color = "red",
         layout = layout.fruchterman.reingold)

```

**Arguments**

simmat	a symmetric similarity matrix
cutoff	a cutoff value, only disease pairs have similarity scores no less than cutoff will be visualized in the network
vertex.label.font	label text font
vertex.label.dist	label text dist
vertex.label.color	label text color
vertex.label.cex	label text cex
vertex.shape	vertex shape
vertex.color	vertex color
vertex.size	vertex size
edge.color	edge color
layout	layout

**Value**

an igraph plot object

**Author(s)**

Peng Ni, Min Li

**Examples**

```
data(d2g_separation)
data(interactome)

graph_interactome<-graph.data.frame(interactome,directed=FALSE)
ds<-c("myocardial ischemia","myocardial infarction","coronary artery disease",
      "cerebrovascular disorders","arthritis, rheumatoid","diabetes mellitus, type 1",
      "autoimmune diseases of the nervous system","demyelinating autoimmune diseases, cns",
      "respiratory hypersensitivity","asthma","retinitis pigmentosa",
      "retinal degeneration","macular degeneration")

sep<-Separation(ds,ds,d2g_separation,graph_interactome)
sim<-Separation2Similarity(sep)
plot_net(sim,cutoff=0.2)
```

---

plot\_topo

*plot topological relationship of two gene sets*

---

**Description**

plot topological relationship of two gene sets (which are associated with two diseases respectively).

**Usage**

```
plot_topo(geneset1, geneset2, graph, vertexcolor = c("tomato", "orange",
  "lightsteelblue"), vertex.shape = "circle", vertex.size = 14,
  vertex.label.font = 1, vertex.label.dist = 0,
  vertex.label.color = "black", vertex.label.cex = 0.5,
  edge.color = "black", layout = layout.auto)
```

**Arguments**

geneset1	a character vector contains gene ids
geneset2	another character vector contains gene ids
graph	an igraph graph object which represents a gene network
vertexcolor	a character vector contains 3 colors for vertices
vertex.shape	vertex shape
vertex.size	vertex size
vertex.label.font	label text font
vertex.label.dist	label text dist

```
vertex.label.color      label text color
vertex.label.cex        label text cex
edge.color              edge color
layout                  layout
```

**Value**

an igraph plot object

**Author(s)**

Peng Ni, Min Li

**Examples**

```
data("PPI_HPRD")
g<-graph.data.frame(PPI_HPRD,directed = FALSE) #get an igraph graph

data(d2g_fundo_symbol)
a<-d2g_fundo_symbol[["D0ID:8242"]] # get gene set a
b<-d2g_fundo_symbol[["D0ID:4914"]] # get gene set b

plot_topo(a,b,g)
```

---

PPI\_HPRD

*PPI\_HPRD*

---

**Description**

PPI data from HPRD

**Value**

PPI\_HPRD is a data.frame of 36867 rows and 2 columns. Each rows indicates an interaction of two gene symbols. It was fetched from HPRD.

**References**

Prasad T S K, Goel R, Kandasamy K, et al. Human protein reference database-2009 update[J]. Nucleic acids research, 2009, 37(suppl 1): D767-D772.

**Examples**

```
data(PPI_HPRD)
```

---

PSB *calculate disease similarity by PSB*

---

### Description

given two vectors of diseases, a list of disease-GO term associations and a list of GO term-gene associations, this function will calculate disease similarity by method PSB

### Usage

```
PSB(D1, D2, d2go, go2g)
```

### Arguments

D1	a vector consists disease ids
D2	another vector consists disease ids
d2go	a list of disease-go associations
go2g	a list of go-gene associations

### Value

a matrix of disease disease simialrity which rownames is D1 and colnames is D2

### Author(s)

Peng Ni, Min Li

### References

Mathur S, Dinakarpanian D. Finding disease similarity based on implicit semantic similarity[J]. Journal of biomedical informatics, 2012, 45(2): 363-371.

### See Also

[get\\_GOterm2GeneAssos](#), [HypergeometricTest](#), [Normalize](#)

### Examples

```
## these are samples of GO-gene associations and disease-GO associations
data(go2g_sample)
data(d2go_sample)

##### the entire associations can be obtained by follows:
## go2g<-get_GOterm2GeneAssos(GOONTOLOGY = "BP", geneid="SYMBOL") #get go-gene associations
## data(d2g_fundo_symbol)
## d2go<-HypergeometricTest(d2g = d2g_fundo_symbol,go2g = go2g)
##### #####

ds<-names(d2go_sample)
sim<-PSB(ds,ds,d2go_sample,go2g_sample)
Normalize(sim)
```

---

Separation

*calculating network-based separation of disease pairs*

---

### Description

given two vectors of diseases, a list of disease-gene associations and a PPI network, this function will calculate network-based separation by method Separation.

### Usage

```
Separation(D1, D2, d2g, graph)
```

### Arguments

D1	a vector consists disease ids
D2	another vector consists disease ids
d2g	a list of disease-gene associations
graph	an igraph graph object of PPI network

### Value

a matrix of disease disease network-based separation which rownames is D1 and colnames is D2

### Author(s)

Peng Ni, Min Li

### References

Menche J, Sharma A, Kitsak M, et al. Uncovering disease-disease relationships through the incomplete interactome[J]. Science, 2015, 347(6224): 1257601.

### See Also

[Separation2Similarity](#)

### Examples

```
data(d2g_separation)
data(interactome)

graph_interactome<-graph.data.frame(interactome,directed=FALSE)
ds<-sample(names(d2g_separation),5)
sep<-Separation(ds,ds,d2g_separation,graph_interactome)
sim<-Separation2Similarity(sep)
sim
```

---

Separation2Similarity *a method which convert separation to similarity*

---

**Description**

convert a separation matrix to a similarity matrix

**Usage**

```
Separation2Similarity(data)
```

**Arguments**

data                    a numeric/integer matrix calculated by method Separation

**Value**

a similarity matrix

**Author(s)**

Peng Ni

**See Also**

[Separation](#)

**Examples**

```
a<-matrix(c(-4:4),3,3)
Separation2Similarity(a)
```

---

setWeight                    *set weight factor*

---

**Description**

set weight factor of 73-orbits in graphlet theory

**Usage**

```
setWeight(orbit_dependency_count)
```

**Arguments**

orbit\_dependency\_count  
                          a vector which each element are the dependency count of each orbit

**Value**

a vector which contains weight factors to each orbit



**Author(s)**

Peng Ni

**References**

Milenkovic T, Przulj N. Uncovering biological network function via graphlet degree signatures[J]. Cancer informatics, 2008, 6: 257.

**Examples**

```
data(orbit_dependency_count)
setWeight(orbit_dependency_count)
```

---

Sun\_annotation

*Sun's annotation measure of disease similarity calculating*

---

**Description**

given two vectors of diseases and a list of disease-gene associations, this function will calculate disease similarity by method Sun\_annotation

**Usage**

```
Sun_annotation(D1, D2, d2g)
```

**Arguments**

D1	a vector consists disease ids
D2	another vector consists disease ids
d2g	a list of disease-gene associations

**Value**

a matrix of disease disease simialrity which rownames is D1 and colnames is D2

**Author(s)**

Peng Ni, Min Li

**References**

Sun K, Goncalves JP, Larminie C. Predicting disease associations via biological network analysis[J]. BMC bioinformatics, 2014, 15(1): 304.

**Examples**

```
data(d2g_separation)
ds<-sample(names(d2g_separation),5)
Sun_annotation(ds,ds,d2g_separation)
```

---

 Sun\_function

*Sun's function measure of disease similarity calculating*


---

### Description

given two vectors of diseases and a list of disease-go term associations, this function will calculate disease similarity by method Sun\_function

### Usage

```
Sun_function(D1, D2, d2go)
```

### Arguments

D1	a vector consists disease ids
D2	another vector consists disease ids
d2go	a list of disease-go term associations

### Value

a matrix of disease disease simialrity which rownames is D1 and colnames is D2

### Author(s)

Peng Ni, Min Li

### References

Sun K, Goncalves JP, Larminie C. Predicting disease associations via biological network analysis[J]. BMC bioinformatics, 2014, 15(1): 304.

### See Also

[get\\_G0term2GeneAssos](#), [HypergeometricTest](#)

### Examples

```
## get a sample of disease-GO associations
data(d2go_sample)

##### the entire disease-GO associations can be obtained by follows:
## go2g<-get_G0term2GeneAssos(GOONTOLOGY = "BP", geneid="SYMBOL") #get go-gene associations
## data(d2g_fundo_symbol)
## d2go<-HypergeometricTest(d2g = d2g_fundo_symbol,go2g = go2g)
##### #####

ds<-names(d2go_sample)
Sun_function(ds,ds,d2go_sample)
```

---

`Sun_topology`*Sun's topology measure of disease similarity calculating*

---

**Description**

given two vectors of diseases, a list of disease-gene associations, a matrix of genes' graphlet signature in a PPI network and a weight vector of 73 orbits in graphlet theory, this function will calculate disease similarity by method `Sun_function`

**Usage**

```
Sun_topology(D1, D2, d2g, graphlet_sig_mat, weight)
```

**Arguments**

<code>D1</code>	a vector consists disease ids
<code>D2</code>	another vector consists disease ids
<code>d2g</code>	a list of disease-gene associations
<code>graphlet_sig_mat</code>	matrix of graphlet signature of nodes in a ppi network calculated by orca, see examples below.
<code>weight</code>	a vector which elements are weight factors to each orbit in graphlet theory

**Value**

a disease disease similarity matrix

**Author(s)**

Peng Ni, Min Li

**References**

Sun K, Goncalves JP, Larminie C. Predicting disease associations via biological network analysis[J]. BMC bioinformatics, 2014, 15(1): 304.

**Examples**

```
data(d2g_fundo_symbol)
data(graphlet_sig_hprd) #get graphlet signatures of genes in HPRD PPI network
data(weight)
ds<-sample(names(d2g_fundo_symbol),5)
Sun_topology(ds,ds,d2g_fundo_symbol,graphlet_sig_hprd,weight)
```

---

weight	<i>weight</i>
--------	---------------

---

**Description**

weight factor

**Value**

weight is a 73-dim vector, indicating 73 orbits' weight factor, will be used in method Sun\_topology.

**References**

Sun K, Goncalves JP, Larminie C. Predicting disease associations via biological network analysis[J]. BMC bioinformatics, 2014, 15(1): 304.

**See Also**

[setWeight](#), [Sun\\_topology](#)

**Examples**

```
data(weight)
```

---

x2y_conv2_y2x	<i>convert x2ylist to y2ylist</i>
---------------	-----------------------------------

---

**Description**

convert list of x-y associations to list of y-x associations

**Usage**

```
x2y_conv2_y2x(x2ylist)
```

**Arguments**

x2ylist            a list which the names are xs and the elements are ys of each x

**Value**

a list of y2x

**Author(s)**

Peng Ni, Min Li

**Examples**

```
data(go2g_sample)
g2go_sample<-x2y_conv2_y2x(go2g_sample[1:100])
```

---

x2y_df2list	<i>convert x-y associations</i>
-------------	---------------------------------

---

**Description**

convert x-y associations (e.g. disease-gene associations) from data.frame to list

**Usage**

```
x2y_df2list(x2ydf, xcol = 1, ycol = 2)
```

**Arguments**

x2ydf	data.frame of x-y associations
xcol	col of x in x2ydf
ycol	col of y in x2ydf

**Value**

a list of x-y associations

**Author(s)**

Peng Ni, Min Li

**Examples**

```
options(stringsAsFactors = FALSE)

d2g_fundo_sample<-read.table(text = "DOID:5218      IL6
DOID:8649  EGFR
DOID:8649  PTGS2
DOID:8649  VHL
DOID:8649  ERBB2
DOID:8649  PDCD1
DOID:8649  KLRC1
DOID:5214  MPZ
DOID:5214  EGR2
DOID:5210  AMH")

d2g_fundo_list<-x2y_df2list(d2g_fundo_sample)
```

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