Package ‘wTO’

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Type Package

Title Computing Weighted Topological Overlaps (wTO) & Consensus wTO Network

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Description Computes the Weighted Topological Overlap with positive and negative signs (wTO) networks given a data frame containing the mRNA count/ expression/ abundance per sample, and a vector containing the interested nodes of interaction (a subset of the elements of the full data frame). It also computes the cut-off threshold or p-value based on the individuals bootstrap or the values reshuffle per individual. It also allows the construction of a consensus network, based on multiple wTO networks. The package includes a visualization tool for the networks. More about the methodology can be found at <arXiv:1711.04702>.

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LazyData TRUE

Imports data.table, igraph, magrittr, plyr, parallel, som, visNetwork, reshape2, shiny

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Suggests knitr, rmarkdown

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Description

This function computes the correlation between Nodes and the Overlapping Nodes of interest.

Usage

CorrelationOverlap(Data, Overlap, method)

Arguments

- **Data**: data.frame containing the expression data. Nodes on the Rows, Individuals on the Columns. Don't forget to give the names to the Nodes and to the Individuals. Nodes must have the row.names() with the Node Name.
- **Overlap**: A vector containing the names of the Nodes of interest.
- **method**: Spearman ("s", "spearman") or Pearson ("p", "pearson") correlation

Author(s)

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ExampleGRF

Description

ExampleGRF data.frame containing names of GRFs.

Usage

data(ExampleGRF)

Format

data.frame 184 lines, 1 column.
**Description**

Metagenomics abundance

**Usage**

```r
data('metagenomics_abundance')
```

**Format**

data.frame from The USC Microbial Observatory. The data is public available at <https://www.ebi.ac.uk/metagenomics/project/ERP013549>

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**Microarray_Expression1**

**Description**

Microarray_Expression1 data.frame containing expression data for 1000 genes and 18 individuals.

**Usage**

```r
Microarray_Expression1
```

**Format**

data.frame 1000 lines, 18 columns.

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**Microarray_Expression2**

**Description**

ExampleExpression data.frame containing expression data for 1000 genes and 18 individuals.

**Usage**

```r
ExampleExpression
```

**Format**

data.frame 1000 lines, 18 columns.
**NetVis**

**Description**

Given a set of Nodes and the weight of the edges, a cutoff for the edges, it draws the networks. Returns a list with the nodes and edges attributes. And plots the network.

**Usage**

```r
NetVis(Node.1, Node.2, wTO, pval = NULL, MakeGroups = FALSE,
padj = NULL, cutoff = list(kind = "Threshold", value = 0.5),
layout = NULL, smooth.edges = T, path = NULL, Cluster = F,
legend = T, shape = list(shape = "triangle", names = NULL),
manipulation = F)
```

**Arguments**

- **Node.1**: Names of the Nodes.1 that are connected to the Nodes.2. It’s the output from wTO.Complete or Consensus.
- **Node.2**: Names of the Nodes.2 that are connected to the Nodes.1. It’s the output from wTO.Complete or Consensus.
- **wTO**: weight of the links, the wTO output from wTO.Complete or wTO.Consensus.
- **pval**: p-values for the wTO value. By default it is NULL.
- **MakeGroups**: algorithm to find clusters. One of the followings: walktrap, optimal, spinglass, edge.betweenness, fast_greedy, infomap, louvain, label_prop, leading_eigen. Default to FALSE.
- **padj**: Adjusted p-values for the wTO value. By default it is NULL.
- **cutoff**: It’s a list containing the kind of cutoff to be used (pval, Threshold or pval.adj) and it’s value. Example: cutoff= list(kind = "Threshold", value = 0.5)
- **layout**: a layout from the igraph package.
- **smooth.edges**: If the edges should be smoothed or not.
- **path**: If the graph should be saved specify the name of the file.
- **Cluster**: TRUE or FALSE if the nodes should be clustered (double click to uncluster).
- **legend**: TRUE or FALSE if the legend should appear.
- **shape**: a list shape=list(shape = "triangle", names = NULL), with the shape and the IDs that should have a different shape, shape can be: diamond, star, triangle, triangleDown or square.
- **manipulation**: TRUE or FALSE if the graph should be editable.

**Author(s)**

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**Examples**

```r
X = wTO.Complete( k = 1, n = 5, Data = Microarray_Expression, 
Overlap = ExampleGRF$x, method = "p", plot = FALSE)

# Plot with the default arguments.
NetVis(Node.1 = X$wTO$Node.1, Node.2 = X$wTO$Node.2, 
wTO = X$wTO$wTO_sign, cutoff = list(kind = 
"Threshold", value = 0.50))

## Not run:
# Plotting just the edges with p-value < 0.05, with straight edges, nodes clustered, 
# no legend and manipulation of the graph enabled.
NetVis(Node.1 = X$wTO$Node.1, Node.2 = X$wTO$Node.2, 
wTO = X$wTO$wTO_sign, pval = X$wTO$pval_sign, 
adj = X$wTO$adj_sign, 
cutoff = list(kind = "pval", value = 0.05), 
smooth.edges = FALSE, 
Cluster = TRUE, legend = FALSE, manipulation = TRUE)

## Not run:
# Plotting just the edges with wTO > 0.50, no legend and the nodes:
# "ZNF738", "ZNF677" with triangle shape, 
# no legend and manipulation of the graph enabled.
NetVis(Node.1 = X$wTO$Node.1, Node.2 = X$wTO$Node.2, 
wTO = X$wTO$wTO_sign, pval = X$wTO$pval_sign, 
adj = X$wTO$adj_sign, cutoff = list(kind = "Threshold", value = 0.5), legend = FALSE, 
shape = list(shape = "triangle", names = c("ZNF738", "ZNF677")))

## End(Not run)
```

---

**Description**

Calculates the weighted topological overlap (wTO) between a set of Nodes and the Overlapping nodes. This function implements the method from Nowick (2009).

**Usage**

```r
wTO(A, sign = c("abs", "sign"))
```

**Arguments**

- `A` Is the weighted adjacency matrix (correlation matrix).
- `sign` ("abs", "sign") if the user wants to use the absolute correlation or the signed correlation.

**Value**

A matrix containing the wTO values.
**Author(s)**

Deisy Morselli Gysi <deisy at bioinf.uni-leipzig.de>

**References**


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**Description**

Compute the wTO and also the bootstraps. Proposed at: arXiv:1711.04702

**Usage**

```r
wTO.Complete(k = 1, n = 100, Data, Overlap = row.names(Data),
method = "p", method_resampling = "Bootstrap", pvalmethod = "BH",
savecor = F, expected.diff = 0.2, lag = NULL, ID = NULL,
normalize = F, plot = T)
```

**Arguments**

- **k**
  - Number of threads to be used for computing the weight Topological Overlap. Default is set to 1.

- **n**
  - Number of resamplings, used to compute the empirical distributions of the links. Default is set to 100.

- **Data**
  - data.frame containing the count / expression data for the correlation.

- **Overlap**
  - Set of nodes of interest, where the Overlapping weights will be computed.

- **method**
  - Type of the correlation that should be used. "s" / "spearman" will compute the rank spearman correlation, "p" / "pearson" will compute the linear correlation. If no value is given, the default is to use "p".

- **method_resampling**
  - method of the resampling. Bootstrap, BlockBootstrap or Reshuffle. Bootstrap null hypothesis is that the wTO is random, and Reshuffle tests if the wTO is equal to zero.

- **pvalmethod**
  - method to compute the multiple test correction for the pvalue. for more information check the function `p.adjust`.

- **savecor**
  - T/F if need to save the correlation.

- **expected.diff**
  - Difference expected between the real wTO and resampled wTO. By default, it is set to 0.2.

- **lag**
  - time dependency, lag, if you are using the BlockedBootstrap.

- **ID**
  - ID of the samples for the blocked bootstrap (for repeated measures).

- **normalize**
  - T/F Should the data be normalized?

- **plot**
  - T/F Should the diagnosis plot be plotted?
Value

a list with results.

- wTO is a data.frame containing the Nodes, the wTO computed using the signed correlations, the pvalue and the adj.pvalue.
- abs.wTO is a data.frame containing the Nodes, the wTO computed using the absolute correlations, the pvalue and the adj.pvalue.
- Correlation is a data.frame containing the correlation between all the nodes.
- Empirical.Quantile quantile values for the empirical distribution.
- Quantile quantile values for the sample distribution.

Author(s)

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Examples

```r
## Not run:
# Using spearman rank correlation and bonferroni correction for the pvalues.
wTO.Complete( k = 8, n = 1000, Data = Microarray_Expression[,1],
  Overlap = ExampleGRF$x, method = "s", pvalmethod = "bonferroni")
# Changing the resampling method to Reshuffle.
wTO.Complete( k = 1, n = 1000, Data = Microarray_Expression[,1],
  Overlap = ExampleGRF$x, method_resampling = "Reshuffle")
# Changing the resampling method to BlockBootstrap, with a lag of 2.
  row.names(metagenomics_abundance) = metagenomics_abundance$OTU
  metagenomics_abundance = metagenomics_abundance[,,-1]
  wTO.Complete( k = 1, n = 1000, Data = metagenomics_abundance, method = "s",
    Overlap = row.names(metagenomics_abundance), method_resampling = "BlockBootstrap", lag = 2)
  wTO.Complete( k = 2, n = 1000, Data = Microarray_Expression[,1], method = "s",
    Overlap = ExampleGRF$x, method_resampling = "BlockBootstrap", ID = rep(1:9,each = 2))
  X = wTO.Complete( k = 1, n = 1000, Data = Microarray_Expression[,1],
    Overlap = ExampleGRF$x, method = "p", plot = FALSE)

## End(Not run)
```

---

Description

Consensus requires a list of data.frame containing the pair of nodes, and the wTO values for all networks that need to be joined. Reference: arXiv:1711.04702

Usage

```r
wTO.Consensus(data)
```
Arguments

data list of data.frame containing the "Node.1", "Node.2" and "wTO".

Author(s)

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Examples

```r
## Not run:
EXAMPLE = wTO.Complete( k =1, n = 200, Data = Microarray_Expression1,
                         Overlap = ExampleGRF$x, method = "p")

# Constructing the consensus network
data = list(data.frame(Node.1 = EXAMPLE$wTO$Node.1,
                      Node.2 = EXAMPLE$wTO$Node.2,
                      wto_s = EXAMPLE$wTO$wTO_sign,
                      pvalsig = EXAMPLE$wTO$pval_s,
                      data.frame(Node.1 = EXAMPLE$wTO$Node.1,
                      Node.2 = EXAMPLE$wTO$Node.2,
                      wtoabs = EXAMPLE$wTO$wTO_abs,
                      pvalsabs = EXAMPLE$wTO$pval_abs))
CONS = wTO.Consensus(data)

## End(Not run)
```

Description

Exports the significative interactions, the wTO weight and pvalues into a .txt file, tab separated.
This file can be imported in other visualization tools (Cytoscape for example).

Usage

```r
wTO.export(DATA, path, sign = TRUE, pvalue = 0.05, padj = 0.05,
prop.NA = 0.5)
```

Arguments

- **DATA**: Output from the function wTO.Complete or wTO.Consensus.
- **path**: Path and file name where the .txt file should be saved.
- **sign**: Should the network contain the results for the signed network or unsigned? Only for data coming from wTO.Complete.
- **pvalue**: cutoff p-value for the network. Only for data coming from wTO.Complete.
- **padj**: cutoff adjusted p-value for the network. Only for data coming from wTO.Complete.
- **prop.NA**: cutoff proportion of NAs for the network. Only for data coming from wTO.Consensus.
Examples

## Not run:

```r
EXAMPLE = wTO.Complete( k =1, n = 200, Data = ExamplefExpression,
    Overlap = ExampleGRF$x, method = "p")
wTO.export(EXAMPLE , './EXAMPLE.txt')

#Selection of only the significative ones for the Consensus
Ex_k1_cor_p_boot_p005_sig = subset(EXAMPLE$wTO,
    EXAMPLE$wTO$pval_sig < 0.05,
    select = c("Node.1", "Node.2", "wTO_sign"))
Ex_k1_cor_p_boot_p005_abs = subset(EXAMPLE$wTO,
    EXAMPLE$wTO$pval_abs < 0.05,
    select = c("Node.1", "Node.2", "wTO_abs"))

# Constructing the consensus network
CN = wTO.Consensus(data = list(Ex_k1_cor_p_boot_p005_sig,
    Ex_k1_cor_p_boot_p005_abs))
wTO.export(CN, './CN.txt')

# You can store the result on the workspace.
y = wTO.export(CN, './CN.txt')
head(y)

## End(Not run)
```

---

Description

Compute the wTO and also the bootstraps. Proposed at arXiv:1711.04702. This is a quicker version of the wTO.Complete. It doesn’t contain diagnose plots nor a parallel version.

Usage

```r
wTO.fast(Data, Overlap = row.names(Data), method = "p",
    sign = "sign", delta = 0.2, n = 10,
    method_resampling = "Bootstrap", lag = NULL, ID = NULL)
```

Arguments

- **Data**: data.frame containing the count / expression data for the correlation.
- **Overlap**: Set of nodes of interest, where the Overlapping weights will be computed.
- **method**: Type of the correlation that should be used. "s" / "spearman" will compute the rank spearman correlation, "p" / "pearson" will compute the linear correlation. If no value is given, the default is to use "p".
- **sign**: Should the wTO be signed?
delta  expected difference between the real wTO and the bootstrap.

n  Number of resamplings, used to compute the empirical distributions of the links. Default is set to 100.

method_resampling  method of the resampling. Bootstrap or BlockBootstrap. If the second is used, please give the lag (time dependency among the data).

lag  Time dependency for the blocked bootstrap (for time series).

ID  ID of the samples for the blocked bootstrap (for repeated measures).

Author(s)

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Examples

wTO.fast(Data = Microarray_Expression1,
Overlap = ExampleGRF$x,
method = "p")

# For a time series with lag = 4
wTO.fast(Data = Microarray_Expression1,
Overlap = ExampleGRF$x,
method = "p",
method_resampling = 'BlockBootstrap',
lag = 4)
# For a study where the individuals were measured multiple times.
wTO.fast(Data = Microarray_Expression1,
Overlap = ExampleGRF$x,
method = "p",
method_resampling = 'BlockBootstrap',
ID = rep(1:9, each = 2))

wTO.in.line  wTO.in.line
**Description**

Compute the wTO for a repeated measures experiment and also the bootstraps. Proposed at arXiv:1711.04702. This is a quicker version of the wTO.Complete. It doesn’t contain diagnose plots nor a parallel version.

**Usage**

```r
wTO.rep_measure(Data, Overlap = row.names(Data), ID, sign = "sign",
                 delta = 0.2, n = 10)
```

**Arguments**

- `Data`: data.frame containing the count / expression data for the correlation.
- `Overlap`: Set of nodes of interest, where the Overlapping weights will be computed.
- `ID`: a vector with the individuals identification
- `sign`: Should the wTO be signed?
- `delta`: expected difference between the real wTO and the bootstrapped.
- `n`: Number of resamplings, used to compute the empirical distributions of the links. Default is set to 100.

**Author(s)**

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**Examples**

```r
# wTO.rep_measure(Data = Microarray_Expression1, ID = rep(c(1:9),2),
# Overlap = ExampleGRF$x)
```
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