

Package ‘CausalR’

May 1, 2026

Type Package

Title Causal network analysis methods

Version 1.45.0

Date 2016-11-14

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Description Causal network analysis methods for regulator prediction and network reconstruction from genome scale data.

Depends R (>= 3.2.0)

Imports igraph

Suggests knitr, RUnit, BiocGenerics

VignetteBuilder knitr

biocViews ImmunoOncology, SystemsBiology, Network, GraphAndNetwork, Network Inference, Transcriptomics, Proteomics, DifferentialExpression, RNASeq, Microarray

License GPL (>= 2)

NeedsCompilation no

RoxygenNote 5.0.1

git_url <https://git.bioconductor.org/packages/CausalR>

git_branch devel

git_last_commit 41ac129

git_last_commit_date 2026-04-28

Repository Bioconductor 3.24

Date/Publication 2026-05-01

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| CausalR-package | <i>The CausalR package</i> |
|-----------------|----------------------------|

Description

Causal network analysis methods for regulator prediction and network reconstruction from genome scale data.

Details

The most important functions are:

- `CreateCCG`: read a computational causal graph from a .sif file
- `ReadExperimentalData`: read a experimental data from a .txt file
- `MakePredictions`: make causal reasoning predictions from a CCG
- `ScoreHypothesis`: score causal reasoning predictions
- `CalculateSignificance`: calculate statistical significance of a result
- `RankTheHypotheses`: compare different possible regulatory hypotheses on a single CCG
- `runSCANR`: reduce false positives by selecting common hypotheses across pathlengths
- `WriteExplainedNodesToSifFile`: reconstruct hypothesis specific regulatory network

Author(s)

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References

- "CausalR - extracting mechanistic sense from genome scale data", Bradley, G. and Barrett, S.J., Application note, Bioinformatics (*submitted*)
- "Causal reasoning on biological networks: interpreting transcriptional changes", Chindelevitch *et al.*, Bioinformatics **28** 1114 (2012). doi:[10.1093/bioinformatics/bts090](https://doi.org/10.1093/bioinformatics/bts090)
- "Assessing statistical significance in causal graphs", Chindelevitch *et al.*, BMC Bioinformatics **13** 35 (2012). doi:[10.1186/1471-2105-13-35](https://doi.org/10.1186/1471-2105-13-35)

AddIDsToVertices *add IDs to vertices*

Description

Adds the IDs as a vertex property to the vertices in the network. Used when creating sub-networks where the new nodes will retain the IDs from their original network

Usage

AddIDsToVertices(network)

Arguments

network the network to which the IDs are to be added

Value

network with IDs added

AddWeightsToEdges *add weights to edges*

Description

Adds weight information to the edges of given network (1 for activation and -1 for inhibition)

Usage

AddWeightsToEdges(network, tableOfInteractions)

Arguments

network an igraph constructed from the original .sif file
 tableOfInteractions a column of the corresponding .sif file indicating the direction of activation/interaction

Value

an augmented network

AnalyseExperimentalData
analyse experimental data

Description

Returns the number of up- and down-regulated genes in the experimental data

Usage

```
AnalyseExperimentalData(experimentalData)
```

Arguments

experimentalData
a dataframe containing a list of genes with corresponding direction of change (1 or -1)

Value

up and down regulation statistics for the experimental data

AnalysePredictionsList
analyse predictions list

Description

Taking the list of predictions from a particular hypothesis, counts the number of positive and negative predictions in the list and the number of 0's (from numPredictions).

Usage

```
AnalysePredictionsList(predictionsList, numPredictions)
```

Arguments

predictionsList
list of predictions
numPredictions number of predictions

Value

prediction statistics

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')  
cgg <- CreateCCG(network)  
predictions <- MakePredictions('NodeA', +1, cgg, 2)  
AnalysePredictionsList(predictions,8)
```

CalculateEnrichmentPValue

calculates an enrichment p-value

Description

Calculate an enrichment p-value for a given hypothesis by comparing the corresponding predicted and observed gene changes

Usage

```
CalculateEnrichmentPValue(predictions, results)
```

Arguments

| | |
|-------------|-----------------------------------------------------------------|
| predictions | predictions of changes from the CCG for a particular hypothesis |
| results | gene changes observed in the experimental data |

Value

an enrichment p-value

Examples

```
predictions <- matrix(c(1,2,3,1,1,-1), ncol = 2)
results <- matrix(c(1,2,3,4,1,1,-1,1), ncol = 2)
CalculateEnrichmentPValue(predictions, results)
```

CalculateSignificance *calculate overall significance p-value*

Description

Calculates the p-value of a score given the hypothesis score and the distribution table, using either the quartic or the (faster) cubic algorithm

Usage

```
CalculateSignificance(hypothesisScore, predictionListStats,
  experimentalResultStats, epsilon = 1e-05, useCubicAlgorithm = TRUE,
  use1bAlgorithm = TRUE)
```

Arguments

| | |
|-------------------------|------------------------------------------------------------------------------------------------------------------|
| hypothesisScore | score for a particular hypothesis |
| predictionListStats | numbers of predicted up-regulated, predicted down-regulated and ambiguous predictions predicted by the algorithm |
| experimentalResultStats | numbers of up-regulated, down-regulated and not significantly changed transcripts in the experimental data |
| epsilon | threshold that is used when calculating the p-value using the cubic algorithm |
| useCubicAlgorithm | use the cubic algorithm, defaults to TRUE |
| use1bAlgorithm | use the 1b version of the algorithm, defaults to TRUE used to calculate the p-value |

Value

the resulting p-value

Examples

```
CalculateSignificance(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=TRUE)
CalculateSignificanceUsingQuarticAlgorithm(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=FALSE)
CalculateSignificance(5, c(7,4,19), c(6,6,18), 1e-5)
CalculateSignificance(5, c(7,4,19), c(6,6,18), epsilon=1e-5, useCubicAlgorithm=TRUE)
CalculateSignificanceUsingCubicAlgorithm(5, c(7,4,19), c(6,6,18), 1e-5)
```

CalculateSignificanceUsingCubicAlgorithm

calculate significance using the cubic algorithm

Description

Calculates the p-value of a score given the hypothesis score and the distribution table (calculated using the cubic algorithm)

Usage

```
CalculateSignificanceUsingCubicAlgorithm(hypothesisScore, predictionListStats,
experimentalDataStats, epsilon)
```

Arguments

| | |
|---------------------|----------------------------------------------------------------------------------------|
| hypothesisScore | the score whose p-value we want to find. |
| predictionListStats | numbers of predicted up-regulated, predicted down-regulated and ambiguous predictions. |

experimentalDataStats
 numbers of up-regulated, down-regulated and not significantly changed transcripts in the experimental data.

epsilon
 an epsilon threshold that is used when calculating the p-value using the cubic algorithm. Defaults to 1e-5.

Value

p-value

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. BMC Bioinformatics, 13(35), 2012.

Examples

```
CalculateSignificance(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=TRUE)
CalculateSignificanceUsingQuarticAlgorithm(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=FALSE)
CalculateSignificance(5, c(7,4,19), c(6,6,18), 1e-5)
CalculateSignificance(5, c(7,4,19), c(6,6,18), epsilon=1e-5, useCubicAlgorithm=TRUE)
CalculateSignificanceUsingCubicAlgorithm(5, c(7,4,19), c(6,6,18), 1e-5)
```

CalculateSignificanceUsingCubicAlgorithm1b

Calculate Significance Using Cubic Algorithm

Description

Calculate the p-value of a score given the hypothesis score and the distribution table (calculated using the cubic algorithm 1b in Assessing statistical significance in causal graphs - Chindelevitch et al)

Usage

```
CalculateSignificanceUsingCubicAlgorithm1b(hypothesisScore, predictionListStats,
  experimentalDataStats, epsilon)
```

Arguments

hypothesisScore
 The score whose p-value we want to find.

predictionListStats
 Number of predicted up-regulated, predicted down-regulated and ambiguous predictions.

experimentalDataStats
 Number of up-regulated, down-regulated and not significantly changed transcripts in the experimental data.

epsilon
 The threshold that is used when calculating the p-value using the cubic algorithm. (Defaults to 1e-5, only used for the cubic algorithm, ignored if useCubicAlgorithm is FALSE.)

Value

p value

Examples

```
CalculateSignificance(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=TRUE)
CalculateSignificanceUsingQuarticAlgorithm(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=FALSE)
CalculateSignificance(5, c(7,4,19), c(6,6,18), 1e-5)
CalculateSignificance(5, c(7,4,19), c(6,6,18), epsilon=1e-5, useCubicAlgorithm=TRUE)
CalculateSignificanceUsingCubicAlgorithm1b(5, c(7,4,19), c(6,6,18), 1e-5)
```

CalculateSignificanceUsingQuarticAlgorithm

calculate significance using the quartic algorithm

Description

Computes the significance of a given hypothesis. For a detailed description of the algorithm see Causal reasoning on biological networks: interpreting transcriptional changes - Chindelevitch et al., section 2. from which the methods and notation is taken.

Usage

```
CalculateSignificanceUsingQuarticAlgorithm(hypothesisScore, predictionListStats,
experimentalDataStats)
```

Arguments

hypothesisScore

the score for which a p-value is required

predictionListStats

a vector containing the values q+, q- and q0 (the number of positive/negative/non-significant or contradictory) predictions)

experimentalDataStats

a vector containing the values n+, n- and n0 (the number of positive/negative/non-significant (or contradictory) transcripts in the results) (or contradictory) transcripts in the results)

Value

the corresponding p-value

References

L.Chindelevitch et al. Causal reasoning on biological networks: Interpreting transcriptional changes. Bioinformatics, 28(8):1114-21, 2012.

Examples

```

CalculateSignificance(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=TRUE)
CalculateSignificanceUsingQuarticAlgorithm(5, c(7,4,19), c(6,6,18))
CalculateSignificance(5, c(7,4,19), c(6,6,18), useCubicAlgorithm=FALSE)
CalculateSignificance(5, c(7,4,19), c(6,6,18), 1e-5)
CalculateSignificance(5, c(7,4,19), c(6,6,18), epsilon=1e-5, useCubicAlgorithm=TRUE)
CalculateSignificanceUsingCubicAlgorithm(5, c(7,4,19), c(6,6,18), 1e-5)

```

CalculateTotalWeightForAllContingencyTables

calculate total weight for all contingency tables

Description

Calculates the total weights or D-values for all possible contingency tables. This value can be used to calculate the p-value

Usage

```

CalculateTotalWeightForAllContingencyTables(experimentalDataStats,
      returnlog = FALSE)

```

Arguments

experimentalDataStats
 a vector containing the values n+, n- and n0, the number of positive/negative/non-significant (or contradictory) transcripts in the results

returnlog
 whether the result should be returned as a log. Default is FALSE.

Value

a D-value or weight

CalculateWeightGivenValuesInThreeByThreeContingencyTable

calculate weight given values in three-by-three contingency table

Description

Given the values in the three by three contingency table and the values of the number of positive/negative/non-significant predictions (q+, q-, q0) this function calculates the D-value (or weight).

Usage

```

CalculateWeightGivenValuesInThreeByThreeContingencyTable(threeByThreeContingencyTable,
      logOfFactorialOfPredictionListStats, returnlog = FALSE)

```


Arguments

`rowAndColumnSumValues`
a 4x1 vector containing the row and column sum values (r+, r-, c+, c-) for a 2x2 contingency table

`predictionListStats`
a vector containing the values q+, q- and q0

`experimentalResultStats`
A vector containing the values n+, n- and n0

Value

TRUE if the table is valid; otherwise FALSE

CompareHypothesis *compare hypothesis*

Description

Compare the predictions from a hypothesis with the experimental data returning an matrix with columns for node ID, predictions, experimental results and the corresponding scores.

Usage

```
CompareHypothesis(matrixOfPredictions, matrixOfExperimentalData, ccg = NULL,
  sourceNode = NULL)
```

Arguments

`matrixOfPredictions`
a matrix of predictions

`matrixOfExperimentalData`
a matrix of experimental data

`ccg`
a CCG network (default=NULL)

`sourceNode`
A starting node (default=NULL)

Value

a matrix containing predictions, observations and scores.

Examples

```
predictions <- matrix(c(1,2,3,+1,0,-1),ncol=2)
experimentalData <- matrix(c(1,2,4,+1,+1,-1),ncol=2)
ScoreHypothesis(predictions,experimentalData)
CompareHypothesis(predictions,experimentalData)
```

ComputeFinalDistribution
compute final distribution

Description

Computes a final reference distribution of the score used to compute the final p-value.

Usage

```
ComputeFinalDistribution(resultsMatrix)
```

Arguments

resultsMatrix a matrix containing the scores and weights from which the distribution is to be calculated

Value

distributionMatrix a matrix containing the reference distribution for the score

ComputePValueFromDistributionTable
compute a p-value from the distribution table

Description

Computes the p-value of the score of an hypothesis, based on a distribution table

Usage

```
ComputePValueFromDistributionTable(scoreOfHypothesis, distributionMatrix,  
totalWeights)
```

Arguments

scoreOfHypothesis
a score of hypothesis

distributionMatrix
a distribution table presented as a matrix

totalWeights a matrix of total weights

Value

a p-value

CreateCCG

create a Computational Causal Graph (CCG)

Description

Creates a computational causal graph from a network file.

Usage

```
CreateCCG(filename, nodeInclusionFile = NULL, excludeNodesInFile = TRUE)
```

Arguments

`filename` file name of the network file (in .sif file format)

`nodeInclusionFile` optional path to a text file listing nodes to exclude in the CCG (or include - see argument `excludeNodesInFile`).

`excludeNodesInFile` flag to determine if nodes in inclusion file should be taken as nodes to include or nodes to exclude. Default is TRUE to exclude.

Value

an igraph object containing the CCG.

Note

CreateCG and CreateCCG create causal and computational causal graphs respectively.

References

L Chindelevitch et al. Causal reasoning on biological networks: Interpreting transcriptional changes. *Bioinformatics*, 28(8):1114-21, 2012.

Examples

```
# get path to example .sif file
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
#create ccg
cgg = CreateCCG(network)
```

CreateCG *create a Computational Graph (CG)*

Description

Creates a CG network from a .sif file. Takes in a .sif file output from Cytoscape, and creates an 'igraph' representing the network. The edges will be annotated with the type of interaction and a weight (1 for activation and -1 for inhibition)

Usage

```
CreateCG(sifFile)
```

Arguments

sifFile the path of the .sif file that contains all the information about the network Load in .sif file

Value

a CG network

Examples

```
# get path to example .sif file
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
#create cg
cg = CreateCG(network)
```

CreateNetworkFromTable

create network from table

Description

Creates a network from an internal data table created from a .sif file: this function converts the data read in from the .sif file into an igraph in R.

Usage

```
CreateNetworkFromTable(dataTable)
```

Arguments

dataTable the data table containing the information read in from the .sif file representing the network.

Value

an igraph network

DetermineInteractionTypeOfPath

determine interaction type of path

Description

Determines the sign of a given path. Given a path and through the network, this function will determine if the path results in activation or inhibition. Activation is indicated by 1, inhibition by -1

Usage

DetermineInteractionTypeOfPath(network, nodesInPath)

Arguments

| | |
|-------------|----------------------------------------------------------------------------------------------------------------------------------|
| network | an igraph representing the network |
| nodesInPath | an ordered list of the nodes visited on the path - note that these contain numbers which use R's internal reference to the edges |

Value

a signed integer representing the paths sign

FindApproximateValuesThatWillMaximiseDValue

find approximate values that will maximise D value

Description

Finds an approximate table values to maximise D. Given the values of q+, q-, q0, n+, n- and n0 this function will produce the approximate values of n++, n+-, n-+ and n-- that will maximise the D value. See Assessing statistical significance of casual graphs, page 6. The values are approximate since they need to be rounded, although the direction of rounding is not clear at this stage.

Usage

FindApproximateValuesThatWillMaximiseDValue(predictionListStats,
experimentalDataStats)

Arguments

| | |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------|
| predictionListStats | a vector containing the values q+, q- and q0: numbers of positive, negative and non-significant/contradictory predictions |
| experimentalDataStats | a vector containing the values n+, n- and n0: numbers of positive, negative and non-significant/contradictory predictions |

Value

a 2x2 contingency table which approximately maximises D

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. BMC Bioinformatics, 13(35), 2012.

FindIdsOfConnectedNodesInSubgraph
find Ids of connected nodes in subgraph

Description

Adds the IDs of the connected nodes in a subgraph to an existing list. Given the IDs of connected nodes in the full network, this function will find the corresponding IDs in the subgraph

Usage

```
FindIdsOfConnectedNodesInSubgraph(idsOfConnectedNodes, subgraphOfConnectedNodes)
```

Arguments

idsOfConnectedNodes
 a list of connected nodes in the full graph

subgraphOfConnectedNodes
 a subgraph

Value

a list of connected nodes in the subgraph

FindMaximumDValue *find maximum D value*

Description

computes the maximum possible D-value for given values $q+$, $q-$, $q0$ and $n+$, $n-$, $n0$.

Usage

```
FindMaximumDValue(predictionListStats, experimentalDataStats,  

  logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

| | |
|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| predictionListStats | a vector containing the predicted values q+, q- and q0: numbers of positive, negative and non-significant/contradictory predictions |
| experimentalDataStats | A vector containing the observed values n+, n- and n0: numbers of positive, negative and non-significant/contradictory observations |
| logOfFactorialOfPredictionListStats | a vector containing the log of the factorial value for each entry in predictionListStats |
| returnlog | should the result be returned as a log; default FALSE |

Value

the maximum possible D value

GetAllPossibleRoundingCombinations

get score for numbers of correct and incorrect predictions

Description

Returns all possible rounding combinations of a 2x2 table. Given the values of n++, n+-, n-+ and n- (stored in twoByTwoContingencyTable) this function will compute all possibilities of rounding each value up or down.

Usage

```
GetAllPossibleRoundingCombinations(twoByTwoContingencyTable)
```

Arguments

| | |
|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| twoByTwoContingencyTable | Approximate values of n++, n+-, n-+ and n-, these values are calculated to optimise the D-value (see page 6 of Assessing statistical significance of causal graphs) |
|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Value

a matrix of rounding combinations

GetApproximateMaximumDValueFromThreeByTwoContingencyTable
returns approximate maximum D value or weight for a 3x2 superfamily

Description

Computes an approximate maximum D value (or weight) for a superfamily (3x2 table). The result is only approximate as only the first valid D value that is return. This has been done to speed up the overall algorithm.

Usage

```
GetApproximateMaximumDValueFromThreeByTwoContingencyTable(threeByTwoContingencyTable,
predictionListStats, logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

threeByTwoContingencyTable
 approximate values of n++, n+-, n-, n0+ and n0-, these values are calculated to optimise the D-value (see page 6 of Assessing statistical significance of causal graphs)

predictionListStats
 a vector containing the values q+, q- and q0 (the number of positive/negative/non-significant (or contradictory) predictions)

logOfFactorialOfPredictionListStats
 a vector containing the log of the factorial value for each entry in predictionListStats

returnlog
 return the result as a log, default is FALSE

Value

an approximate maximum D value or weight

GetApproximateMaximumDValueFromTwoByTwoContingencyTable
computes an approximate maximum D value or weight

Description

Computes an approximate maximum D value (or weight). The calculation is approximate since only the first valid D value that is round. This has been done to speed up the overall algorithm - to get the exact answer use GetMaximumDValueFromTwoByTwoContingencyTable.

Usage

```
GetApproximateMaximumDValueFromTwoByTwoContingencyTable(n_pp, n_pm, n_mp, n_mm,
predictionListStats, experimentalDataStats,
logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

| | |
|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| n_pp | the count n++ from the prediction-observation contingency matrix |
| n_pm | the count n+- from the prediction-observation contingency matrix |
| n_mp | the count n-+ from the prediction-observation contingency matrix |
| n_mm | the count n- from the prediction-observation contingency matrix |
| predictionListStats | a vector containing the values q+, q- and q0: the number of positive, negative, non-significant/contradictory predictions |
| experimentalDataStats | a vector containing the values n+, n- and n0: the number of positive, negative, non-significant/contradictory observations |
| logOfFactorialOfPredictionListStats | a vector containing the log of the factorial value for each entry in predictionListStats |
| returnlog | return the result as a log, default is FALSE |

Value

the maximum D value or weight

GetCombinationsOfCorrectandIncorrectPredictions

returns table of correct and incorrect predictions

Description

Returns the numbers of correct and incorrect positive and negative predictions

Usage

```
GetCombinationsOfCorrectandIncorrectPredictions(predictionDataStats,
  experimentalDataStats)
```

Arguments

| | |
|-----------------------|------------------------------------|
| predictionDataStats | prediction data statistics table |
| experimentalDataStats | Experimental data statistics table |

Value

a matrix the numbers of correct and incorrect positive and negative prediction

 GetExplainedNodesOfCCG

Get explained nodes of CCG

Description

Returns a table of node names and values for explained nodes, I.e. nodes that appear in both network and data with the same sign. The table contain the name in column 1 and the value (1 or -1) in column 2

Usage

```
GetExplainedNodesOfCCG(hypothesisnode, signOfHypothesis, network,
  experimentalData, delta)
```

Arguments

| | |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| hypothesisnode | a hypothesis node |
| signOfHypothesis | the direction of change of hypothesis node |
| network | a computational causal graph |
| experimentalData | The experimental data read in using ReadExperimentalData . The results is an n x 2 matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. The name of the first column is the filename the data was read from. |
| delta | the number of edges across which the hypothesis should be followed |

Value

vector of explained nodes

GetInteractionInformation

returns interaction information from input data

Description

Gets the interaction information from the input data

Usage

```
GetInteractionInformation(dataTable)
```

Arguments

| | |
|-----------|----------------------------------------------------------------------------------------------|
| dataTable | a data table containing the information read in from the .sif file representing the network. |
|-----------|----------------------------------------------------------------------------------------------|

Value

a vector of interaction information

GetMatrixOfCausalRelationships

compute causal relationships matrix

Description

Get a matrix of causal relationships from the network and the IDs of connected nodes

Usage

```
GetMatrixOfCausalRelationships(hypothesis, network,
  idsOfConnectedNodesFromSubgraph)
```

Arguments

| | |
|---------------------------------|-------------------------------------------------------|
| hypothesis | a hypothesis node |
| network | a CCG network |
| idsOfConnectedNodesFromSubgraph | a list of connected nodes in the subgraph of interest |

Value

causal relationships matrix

GetMaxDValueForAFamily

get maximum D value for a family

Description

Computes the maximum D value for a particular family - denoted as D_{fam} on page 6 of Assessing Statistical Significance of Causal Graphs

Usage

```
GetMaxDValueForAFamily(r_p, r_m, c_p, predictionListStats,
  experimentalDataStats, logOfFactorialOfPredictionListStats,
  returnlog = FALSE)
```

Arguments

| | |
|-------------------------------------|------------------------------------------------------------------------------------------------------------------------|
| r_p | row sum r+ |
| r_m | row sum r- |
| c_p | column sum c+ |
| predictionListStats | approximate values of n++, n+-, n-+ and n-- |
| experimentalDataStats | a vector containing the values q+, q- and q0: number of positive, negative, non-significant/contradictory predictions |
| logOfFactorialOfPredictionListStats | a vector containing the values n+, n- and n0: number of positive, negative, non-significant/contradictory observations |
| returnlog | return result as log, default value is FALSE |

Value

the maximum DFam Value

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. *BMC Bioinformatics*, 13(35), 2012.

GetMaxDValueForAThreeByTwoFamily

get maximum D value for three-by-two a family

Description

Returns the maximum D value for a particular family as described as D_fam on pages 6 and 7 of *Assessing Statistical Significance of Causal Graphs in Assessing Statistical Significance of Causal Graphs*

Usage

```
GetMaxDValueForAThreeByTwoFamily(r_p, r_m, r_z, n_p, n_m, predictionListStats,
  logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

| | |
|---------------------|----------------------------------------------------------------------------------------------------------------|
| r_p | a r+ row sum from the prediction-observation matrix |
| r_m | a r- row sum from the prediction-observation matrix |
| r_z | a r0 row sum from the prediction-observation matrix |
| n_p | a number of predicted increases from the prediction-observation matrix |
| n_m | a number of predicted decreases from the prediction-observation matrix |
| predictionListStats | a vector contain the number of postive, negative and non-significant/contradictory predictions: q+, q- and q0. |

logOfFactorialOfPredictionListStats
 a vector containing the log of the factorial for each element in the prediction-ListStats object

returnlog
 whether or not the maximum D value should be returned as a log (TRUE). Otherwise a non-logged value is returned.

Value

Maximum D_{fam} Value

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. BMC Bioinformatics, 13(35), 2012.

GetMaximumDValueFromTwoByTwoContingencyTable
get maximum D value from two-by-two contingency table

Description

Computes the maximum D value (or weight) given approximate values of n₊₊, n₊₋, n₋₊ and n₋₋. These values are approximate and in general are non-integer values; they are found by using an approximation detailed in the paper Assessing statistical significance in causal graphs on page 6 i.e. n_{ab} is approximately equal to $q_a * n_b / t$ where a and b are either +, - or 0. The value is an approximation since the direction in which the number should be rounded is not clear and hence this function runs through all possible combinations of rounding before concluding the maximum D-value.

Usage

```
GetMaximumDValueFromTwoByTwoContingencyTable(twoByTwoContingencyTable,
  predictionListStats, experimentalDataStats,
  logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

twoByTwoContingencyTable
 approximate values of n₊₊, n₊₋, n₋₊ and n₋₋, these values are calculated to optimise the D-value

predictionListStats
 a vector containing the values q₊, q₋ and q₀ the number of positive/negative/non-significant (or contradictory) predictions)

experimentalDataStats
 a vector containing the values n₊, n₋ and n₀ (the number of positive/negative/non-significant (or contradictory) transcripts in the results)

logOfFactorialOfPredictionListStats
 a vector containing the log of the factorial value for each entry in predictionListStats

returnlog
 whether or not the value should be returned as a log (TRUE) or not (FALSE)

Value

the maximal D-value

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. *BMC Bioinformatics*, 13(35), 2012.

| | |
|-----------|------------------------|
| GetNodeID | <i>get CCG node ID</i> |
|-----------|------------------------|

Description

Returns the CCG node ID from a node name or a vector of node names and a given direction of regulation.

Usage

```
GetNodeID(network, nodename, direction = 1)
```

Arguments

| | |
|-----------|--------------------------------------------------------------------------------------|
| network | a CCG object |
| nodename | the node name, or names, for which the ID is required |
| direction | the direction of regulation of the required node or nodes. Maybe +1 (default) or -1. |

Value

a scalar or vector containing the node ID or IDs requested

| | |
|-------------|----------------------|
| GetNodeName | <i>get node name</i> |
|-------------|----------------------|

Description

Returns the node name from one or more node IDs, or substitute node names for node IDs, given in first column of a matrix typically of predictions or experimental data

Usage

```
GetNodeName(network, nodeID, signed = FALSE)
```

Arguments

| | |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| network | Built from igraph |
| nodeID | a node ID or a matrix containing node IDs in its first column |
| signed | whether or not the node name should be signed. Setting this value to TRUE gives a signed name indicating whether the gene is up or down regulated in the network |

Value

a node name or a vector of node names depending if the input is an matrix.

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
ccg = CreateCCG(network)
nodeID <- 10
getNodeName(ccg, nodeID)
```

GetNumberOfPositiveAndNegativeEntries

counts the number of positive and negative entries

Description

Counts the number of entries in the in the second column of an input table that are +1 or -1.

Usage

```
GetNumberOfPositiveAndNegativeEntries(dataList)
```

Arguments

`dataList` an array or dataframe in which the second column is numeric

Value

a vector of two components, the first of which giving the number of +1 entries, the second the number of -1's.

Examples

```
expData<-read.table(system.file(package='CausalR', 'extdata', 'testData.txt'))
GetNumberOfPositiveAndNegativeEntries(expData)
```

GetPathsInSifFormat *Get paths in Sif format*

Description

Converts network paths into Simple interaction file (.sif) format for importing into Cytoscape

Usage

```
GetPathsInSifFormat(arrayOfPaths)
```

Arguments

`arrayOfPaths` an array of paths (in the format outputted by `GetShortestPathsFromCCG`) to be converted to .sif format

Value

network visualisation

GetRegulatedNodes *get regulated nodes*

Description

This function will compute the nodes regulated by the given hypothesis gene and write the results to a file

Usage

```
GetRegulatedNodes(PPInet, Expressiondata, delta, hypothesisGene = "",
  signOfHypothesis = 1, outputfile = "")
```

Arguments

PPInet a protein-protein interaction network

Expressiondata a table of observed gene expression data

delta the number of edges to follow along the network. This should typically be between 1 and 5 dependent on network size/topology

hypothesisGene the name of the hypothesis gene

signOfHypothesis the sign of action expected from the hypothesis, +1 for up regulation, -1 for down

outputfile the file to which the results should be written

Value

Nodes regulated by hypothesis gene

GetRowAndColumnSumValues
get row and column sum values

Description

Returns the possible values of r+, r-, c+ and c- (the column and row sum values) following page 6 of Assessing statistical significance in causal graphs (Chindelevitch et. al)

Usage

```
GetRowAndColumnSumValues(predictionListStats, experimentalResultStats)
```

Arguments

predictionListStats

a vector containing the number of positive, negative, or non-significant/contradictory predictions (q+, q- and q0)

experimentalResultStats

a vector containing the number of positive, negative, or non-significant/contradictory observations (n+, n- and n0)

Value

a matrix of row and sum values r+, r-, c+ and c-

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. BMC Bioinformatics, 13(35), 2012.

GetScoreForNumbersOfCorrectandIncorrectPredictions

returns the score for a given number of correct and incorrect predictions

Description

Returns the score based on the values of n++, n+-, n-+ and n--

Usage

```
GetScoreForNumbersOfCorrectandIncorrectPredictions(matrixRow)
```

Arguments

matrixRow a row of a matrix of correct and incorrect prediction scores

Value

the corresponding score for the given row

 GetScoresForSingleNode

Get scores for single node

Description

A helper function for RankTheHypotheses to calculate a line of the scoresMatrix table

Usage

```
GetScoresForSingleNode(iNode, timeToRunSoFar, nodesToBeTested, network, delta,
  processedExperimentalData, numPredictions, epsilon, useCubicAlgorithm,
  use1bAlgorithm, symmetricCCG, correctPredictionsThreshold,
  experimentalDataStats, quiet)
```

Arguments

| | |
|-----------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| iNode | this node |
| timeToRunSoFar | the time to run so far |
| nodesToBeTested | List of all nodes to be tested |
| network | Computational Causal Graph, as an igraph. |
| delta | Distance to search within the causal graph. |
| processedExperimentalData | The processed experimental data |
| numPredictions | The number of predictions |
| epsilon | The threshold that is used when calculating the p-value using the cubic algorithm (see 'Assessing statistical significance in causal graphs'). |
| useCubicAlgorithm | An indicator specifying which algorithm will be used to calculate the p-value. The default is set as useCubicAlgorithm = TRUE which uses the cubic algorithm. If this value is set as FALSE, the algorithm will use the much slower quartic algorithm which does compute the exact answer, as opposed to using approximations like the cubic algorithm. |
| use1bAlgorithm | An indicator specifying whether the 1a or 1b (default, faster) variant of the cubic algorithm described in Chindelevitch's paper will be used to calculate the p-value. |
| symmetricCCG | This flag specifies whether the CCG is assumed to be symmetric. The value is set as TRUE as a default. If this is the case the running time of the algorithm is reduced since the negative node values can be calculated using symmetry and the results of calculations performed for the positive node |
| correctPredictionsThreshold | A threshold on the number of correct predictions for a given hypothesis. If a hypothesis produces fewer correct predictions than predictionsThreshold then the algorithm will not calculate the two p-values. Instead 'NA' will be displayed in the final two columns of the corresponding row of the results table. As a default correctPredictionsThreshold is set as -Inf, so that the p-values are calculated for all specified hypotheses. Note: Set to Inf to turn off p-value calculations entirely. |

experimentalDataStats
Stats from the experimental data

quiet
a flag to supress progress output

Value

If symmetricCCG is false, this returns a single line of the scoreMatrix for the 'iNode'th node in nodesToBeTested. If symmetricCCG is true this returns two lines. The first of which corresponds to the positive node and the second the negative node.

GetScoresWeightsMatrix
get scores weight matrix

Description

Computes the score and weight for a network/set of experimental data based on the table containing possible values of n++, n+-, n-+ and n--.

Usage

```
GetScoresWeightsMatrix(matrixOfPossibleValues, predictionDataStats,
    experimentalDataStats, logOfFactorialOfPredictionListStats)
```

Arguments

matrixOfPossibleValues
values of n++, n+-, n-+ and n-- that need to be assessed

predictionDataStats
a table of predicions

experimentalDataStats
a table of observed experimental data

logOfFactorialOfPredictionListStats
a vector containing the log of the factorial value for each entry in predictionList-Stats

Value

a matrix containing scores and logs of the weights

`GetScoresWeightsMatrixByCubicAlg`*get scores weights matrix by the cubic algorithm*

Description

Implements the cubic algorithm as described on pages 6 and 7 of Assessing statistical significance in causal graphs, Chindelevitch et al. 2012

Usage

```
GetScoresWeightsMatrixByCubicAlg(predictionListStats, experimentalDataStats,  
epsilon)
```

Arguments

`predictionListStats`

a vector containing the values $q+$, $q-$ and $q0$

`experimentalDataStats`

a vector containing the values $n+$, $n-$ and $n0$

`epsilon`

the algorithms tolerance epsilon

Value

a matrix containing the ternary dot product distribution

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. BMC Bioinformatics, 13(35), 2012.

`GetSetOfDifferentiallyExpressedGenes`*get set of differentially expressed genes*

Description

Gets the set of differentially expressed genes in the results, $G+$ as defined by in Causal reasoning on biological networks: Interpreting transcriptional changes, L Chindelevitch et al.

Usage

```
GetSetOfDifferentiallyExpressedGenes(results)
```

Arguments

`results`

a table of results

Value

a matrix of differentially expressed genes

References

L Chindelevitch et al. Causal reasoning on biological networks: Interpreting transcriptional changes. *Bioinformatics*, 28(8):1114-21, 2012.

GetSetOfSignificantPredictions

get set of significant predictions

Description

Gets the set of positive and negative predictions, the combination of the sets Sh+ and Sh- in Causal reasoning on biological networks: Interpreting transcriptional changes, L Chindelevitch et al.

Usage

GetSetOfSignificantPredictions(predictions)

Arguments

predictions a table of predictions

Value

a matrix of positive and negative predictions

References

L Chindelevitch et al. Causal reasoning on biological networks: Interpreting transcriptional changes. *Bioinformatics*, 28(8):1114-21, 2012.

GetShortestPathsFromCCG

get shortest paths from CCG

Description

Gets the node names in the shortest path from one node in a CCG to another

Usage

GetShortestPathsFromCCG(network, hypothesisnode, targetnode,
showbothdirs = FALSE, quiet = FALSE)

Arguments

| | |
|----------------|-----------------------------------------------------------------------------------------------------------------------|
| network | built from iGraph |
| hypothesisnode | hypothesis node ID |
| targetnode | target node ID |
| showbothdirs | where multiple paths from a positive and negative node, FALSE returns only the shortest. Otherwise both are returned. |
| quiet | a flag to suppress output to console. FALSE by default. |

Value

a list of vectors containing the nodes of individual paths

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
cgg = CreateCCG(network)
hypothesisnode = 1
targetnode = 10
GetShortestPathsFromCCG (cgg, hypothesisnode, targetnode)
```

GetWeightForNumbersOfCorrectandIncorrectPredictions

get weight for numbers of correct and incorrect predictions

Description

Gets the weight based on the values of n_{++} , n_{+-} , n_{-+} and n_{--} .

Usage

```
GetWeightForNumbersOfCorrectandIncorrectPredictions(n_pp, n_pm, n_mp, n_mm,
  predictionDataStats, experimentalDataStats,
  logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

| | |
|-------------------------------------|------------------------------------------------|
| n_pp | the contingency table entry n_{++} |
| n_pm | the contingency table entry n_{+-} |
| n_mp | the contingency table entry n_{-+} |
| n_mm | the contingency table entry n_{--} |
| predictionDataStats | prediction data statistics |
| experimentalDataStats | experimental data statistics |
| logOfFactorialOfPredictionListStats | log of factorial of prediction list stats |
| returnlog | true if the result should be returned as a log |

Value

none

GetWeightsAboveHypothesisScoreAndTotalWeights

get weights above hypothesis score and total weights

Description

Gets the score based on the values of n++, n+-, n-+ and n-. Used as part of a p-value calculation.

Usage

```
GetWeightsAboveHypothesisScoreAndTotalWeights(r_p, r_m, c_p,
  predictionListStats, experimentalDataStats,
  logOfFactorialOfPredictionListStats, hypothesisScore, logepsDMax, logDMax)
```

Arguments

| | |
|-------------------------------------|-------------------------------------------|
| r_p | the row sum r+ |
| r_m | the row sum r- |
| c_p | the column sum c+ |
| predictionListStats | statistics for the prediction list |
| experimentalDataStats | statistics for the experimental data |
| logOfFactorialOfPredictionListStats | log of factorial of prediction list stats |
| hypothesisScore | the hypothesis score to be considered |
| logepsDMax | Exponential of logD Maximum value |
| logDMax | A logD Maximum value |

Value

score data

GetWeightsAboveHypothesisScoreForAThreeByTwoTable

updates weights for contingency table and produce values for p-value calculation

Description

Finds the D-Values (weights) from any 3x2 contingency tables that have a score above and including the hypothesis score. It also calculates the total weight, and returns a 2x1 vector of the two values. The ratio of these values is the p-value.

Usage

```
GetWeightsAboveHypothesisScoreForAThreeByTwoTable(weights, r_p, r_m, r_z, n_p,
  n_m, predictionListStats, experimentalDataStats,
  logOfFactorialOfPredictionListStats, hypothesisScore, logepsDMax, logDMax)
```

Arguments

| | |
|-------------------------------------|------------------------------------------|
| weights | Weights |
| r_p | the row sum r+ |
| r_m | the row sum r- |
| r_z | the row sum r0 |
| n_p | the column sum n+ |
| n_m | the column sum n- |
| predictionListStats | a list of prediction statistics |
| experimentalDataStats | the observed experimental data |
| logOfFactorialOfPredictionListStats | log factorial's of prediction list stats |
| hypothesisScore | the hypothesis score to be considered |
| logepsDMax | log of epsilon logD Maximum value |
| logDMax | a logD Maximum value |

Value

a vector containing the hypothesis score and the total weight

```
GetWeightsFromInteractionInformation
  get weights from interaction information
```

Description

Returns a matrix of weights (-1,0,+1) indicating the direction of regulation from the interaction information.

Usage

```
GetWeightsFromInteractionInformation(interactionInfo)
```

Arguments

| | |
|-----------------|------------------------------------------------------------------------|
| interactionInfo | a central column of the .sif file, giving the type of edge interaction |
|-----------------|------------------------------------------------------------------------|

Value

a matrix of weights corresponding the the direction of regulation

MakePredictions *make predictions*

Description

Creates a matrix of predictions for a particular hypothesis. The output is an array containing the relationship between each node and the hypothesis. The hypothesis provided will be the vertex id of one of the nodes in the network (as an integer node ID or name, including + or - for up/down regulation in the case of a CCG). The `signOfHypothesis` variable should be a 1 or -1, indicating up/down regulation.

Usage

```
MakePredictions(hypothesisnode, signOfHypothesis, network, delta,
  nodesInExperimentalData = NULL)
```

Arguments

`hypothesisnode` the node in the causal graph from which predictions should be made. Can be either a (numerical) node ID or a (string) node name.

`signOfHypothesis` whether the hypothesis node is up- or down-regulated. Should be +1 or -1.

`network` a (Computational) Causal Graph, as an `igraph`.

`delta` the distance to search within the causal graph.

`nodesInExperimentalData` optional. Nodes to include in the output. Should be a list of node IDs.

Value

a matrix of predictions for the given particular hypothesis

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
cgg <- CreateCCG(network)
predictions <- MakePredictions('NodeA', +1, cgg, 2)
```

MakePredictionsFromCCG
make predictions from CCG

Description

Create a matrix of predictions for a particular hypothesis starting from a network with separate nodes for up- and down-regulation (+ve and -ve). The output is an array containing the relationship between each node and the hypothesis. The hypothesis provided will be the vertex id of one of the nodes in the network (as an integer or name including + or - for up/down regulation). The `signOfHypothesis` variable should be a 1 or -1, indicating up/down regulation. (It generally shouldn't be necessary to reverse the sign of a node when working from a CCG, but this facility is included for consistency with `MakePredictionsFromCG`)

Usage

```
MakePredictionsFromCCG(hypothesisnode, signOfHypothesis, network, delta,
  nodesInExperimentalData = NULL)
```

Arguments

```
hypothesisnode  a hypothesis node
signOfHypothesis
                 the direction of change of hypothesis node
network         a computational causal graph
delta          the number of edges across which the hypothesis should be followed
nodesInExperimentalData
                 the number of nodes in experimental data
```

Value

an matrix containing the relationship between each node and the hypothesis

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
cgg <- CreateCCG(network)
MakePredictionsFromCCG('NodeA', +1, cgg, 2)
```

MakePredictionsFromCG *make predictions from CG*

Description

Create a matrix of predictions for a particular hypothesis - the output is a matrix containing the relationship between each node and the hypothesis. The hypothesis provided will be the vertex id of one of the nodes in the network (as an integer). The signOfHypothesis variable should be a 1 or -1, indicating up/down regulation

Usage

```
MakePredictionsFromCG(hypothesisnode, signOfHypothesis, network, delta,
  nodesInExperimentalData = NULL)
```

Arguments

```
hypothesisnode  a hypothesis node
signOfHypothesis
                 the direction of change of hypothesis node
network         a computational causal graph
delta          the number of edges across which the hypothesis should be followed
nodesInExperimentalData
                 the number of nodes in experimental data
```

Value

an matrix containing the relationship between each node and the hypothesis

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
cg <- CreateCG(network)
MakePredictionsFromCG('NodeA', +1, cg, 2)
```

| | |
|-----------------|-------------------------|
| OrderHypotheses | <i>order hypotheses</i> |
|-----------------|-------------------------|

Description

Ranks the hypotheses. Takes a matrix containing the scores for each node of the network, and ranks them placing the hypothesis with the most correct predictions is at the top

Usage

```
OrderHypotheses(scoresMatrix)
```

Arguments

`scoresMatrix` a matrix containing the scores for each node of the network

Value

a ranked table of hypotheses

| | |
|------------------------|-----------------------------------|
| PlotGraphWithNodeNames | <i>plot graph with node names</i> |
|------------------------|-----------------------------------|

Description

Plots an igraph with the node names. Plots a igraph to the screen displaying the names of the nodes input rather than R's internal numbering.

Usage

```
PlotGraphWithNodeNames(igraph)
```

Arguments

`igraph` internal an igraph representation of an interaction network

Value

network visualisation

Examples

```
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
ccg <- CreateCCG(network)
PlotGraphWithNodeNames(ccg)
```

PopulateTheThreeByThreeContingencyTable

populate the three-by-three contingency table

Description

Populates 3x3 signed contingency table of expected versus observed changes. Given the values of n++, n+-, n-+ and n--, calculates n0+, n0-, n+0, n-0 and n00. Notation from Chindelevitch et al. Causal reasoning on biological networks Bioinformatics (2012) paper.

Usage

```
PopulateTheThreeByThreeContingencyTable(n_pp, n_pm, n_mp, n_mm,
  predictionDataStats, experimentalDataStats)
```

Arguments

| | |
|-----------------------|-----------------------------|
| n_pp | n++ contingency table entry |
| n_pm | n+- contingency table entry |
| n_mp | n-+ contingency table entry |
| n_mm | n-- contingency table entry |
| predictionDataStats | a prediction data table. |
| experimentalDataStats | an experimental data table |

Value

Vector of calculated values for n0+, n0-, n+0, n-0 and n00 - See: Chindelevitch et al. Bioinformatics (2012).

PopulateTwoByTwoContingencyTable

Populate Two by Two Contingency Table

Description

Calculates a 2x2 contingency table. Given the value of n++ and the row and column sums (r+, r-, c+, c-), Calculates the remaining values in the 2x2 contingency table i.e. n+-, n-+, and n--. See Chindelevitch et al. BMC Bioinformatics (2012) paper 'Assessing Statistical significance of causal graphs' for clarification on notation.

Usage

```
PopulateTwoByTwoContingencyTable(rowAndColumnSumValues, n_pp)
```

Arguments

| | |
|-----------------------|-------------------------------------------|
| rowAndColumnSumValues | the row and column sums (r+, r-, c+, c-). |
| n_pp | the value of n++. |

Value

the completed 2x2 contingency table: n++, n+-, n-+, n-

References

L Chindelevitch et al. Causal reasoning on biological networks: Interpreting transcriptional changes. *Bioinformatics*, 28(8):1114-21, 2012.

ProcessExperimentalData

process experimental data

Description

Processes experimental data to get it into the correct form for scoring. The node names that are read in as strings acquire an internal id when the network is created. This function will replace the node name with its id.

Usage

```
ProcessExperimentalData(experimentalData, network)
```

Arguments

| | |
|------------------|-------------------------------|
| experimentalData | input experimental data. |
| network | an input interaction network. |

Value

processed experimental data formatted ready for scoring

RankTheHypotheses *rank the hypotheses*

Description

Rank the hypotheses in the causal network. This function can be run with parallelisation using the `doParallel` flag.

Usage

```
RankTheHypotheses(network, experimentalData, delta, epsilon = 1e-05,
  useCubicAlgorithm = TRUE, use1bAlgorithm = TRUE, symmetricCCG = TRUE,
  listOfNodes = NULL, correctPredictionsThreshold = -Inf, quiet = FALSE,
  doParallel = FALSE, numCores = NULL, writeFile = TRUE,
  outputDir = getwd())
```

Arguments

| | |
|------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>network</code> | Computational Causal Graph, as an <code>igraph</code> . |
| <code>experimentalData</code> | The experimental data read in using ReadExperimentalData . The results is an $n \times 2$ matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. The name of the first column is the filename the data was read from. |
| <code>delta</code> | Distance to search within the causal graph. |
| <code>epsilon</code> | The threshold that is used when calculating the p-value using the cubic algorithm (see 'Assessing statistical significance in causal graphs'). |
| <code>useCubicAlgorithm</code> | An indicator specifying which algorithm will be used to calculate the p-value. The default is set as <code>useCubicAlgorithm = TRUE</code> which uses the cubic algorithm. If this value is set as <code>FALSE</code> , the algorithm will use the much slower quartic algorithm which does compute the exact answer, as opposed to using approximations like the cubic algorithm. |
| <code>use1bAlgorithm</code> | An indicator specifying whether the 1a or 1b (default, faster) variant of the cubic algorithm described in Chindelevitch's paper will be used to calculate the p-value. |
| <code>symmetricCCG</code> | This flag specifies whether the CCG is assumed to be symmetric. The value is set as <code>TRUE</code> as a default. If this is the case the running time of the algorithm is reduced since the bottom half of the table can be filled in using the results of calculations performed earlier. |
| <code>listOfNodes</code> | A list of nodes specified by the user. The algorithm will only calculate and store the results for the nodes in the specified list. The default value is <code>NULL</code> ; here the algorithm will calculate and store results for all the nodes in the network. |
| <code>correctPredictionsThreshold</code> | A threshold on the number of correct predictions for a given hypothesis. If a hypothesis produces fewer correct predictions than <code>correctPredictionsThreshold</code> then the algorithm will not calculate the two p-values. Instead 'NA' will be displayed in |

| | |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | the final two columns of the corresponding row of the results table. As a default correctPredictionsThreshold is set as -Inf, so that the p-values are calculated for all specified hypotheses. |
| quiet | a flag to suppress output to console. FALSE by default. |
| doParallel | A flag for running RankTheHypothesis in parallel mode. |
| numCores | Number of cores to use if using parallel mode. If the default value of NULL is used, it will attempt to detect the number of cores available and use all of them bar one. |
| writeFile | A flag for determining if the output should be written to a file in the working directory. Default is TRUE. |
| outputDir | the directory to output the files to. Default is the working directory |

Value

A data frame containing the results of the algorithm.

References

L Chindelevitch et al. Assessing statistical significance in causal graphs. BMC Bioinformatics, 13(35), 2012.

Examples

```
#get path to example network file
networkFile <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
#create ccg
network <- CreateCCG(networkFile)
#get path to example experimental data
experimentalDataFile <- system.file(package='CausalR', 'extdata', 'testData.txt')
#read in experimental data
experimentalData <- ReadExperimentalData(experimentalDataFile, network)
#run in single threaded mode
RankTheHypotheses(network, experimentalData, 2)
#run in parallel mode
RankTheHypotheses(network, experimentalData, 2, doParallel=TRUE, numCores=2)
```

ReadExperimentalData *read experimental data*

Description

Reads experimental data for the causal reasoning algorithm from a text file.

Usage

```
ReadExperimentalData(fileName, network, removeDuplicates)
```

Arguments

`fileName` a file containing the experimental data (text file format)

`network` a (Computational) Causal Graph, as an `igraph`.

`removeDuplicates` Optional, defaults to `true`. Remove duplicated nodes the experimental file (i.e. where the result for a node is repeated, use the first value given only; the alternative is to return a result which contains multiple rows for this node).

Value

($n \times 2$) matrix of nodes and direction of regulation. The first column of the matrix contains the node IDs from the network, and the second contains the experimental values.

Examples

```
#get path to example network file
network <- system.file(package='CausalR', 'extdata', 'testNetwork.sif')
##create ccg
ccg <- CreateCCG(network)
#get path to example experimental data
fileName<- system.file(package='CausalR', 'extdata', 'testData.txt')
ReadExperimentalData(fileName, ccg)
```

ReadSifFileToTable *read .sif to Table*

Description

Reads a `.sif` file into a table in R

Usage

```
ReadSifFileToTable(sifFile)
```

Arguments

`sifFile` the `sifFile` to be read in

Value

a R table containing the data from the `.sif` file

RemoveIDsNotInExperimentalData
remove IDs not in experimental data

Description

Takes in a list of connected nodes and removes those not in the experimental data.

Usage

RemoveIDsNotInExperimentalData(connectedNodes, nodesInExperimentalData)

Arguments

connectedNodes a list of connected nodes
 nodesInExperimentalData
 a list of nodes in the experimental data

Value

connectedNodesInExperimentalData a list of connected nodes with the redundant nodes removed

runRankHypothesis *run rank the hypothesis*

Description

A top level function that used to run CausalR

Usage

runRankHypothesis(PPIInet, Expressiondata, delta, correctPredictionsThreshold)

Arguments

PPIInet PPIInet is the PPI interaction file
 Expressiondata observed gene expression data
 delta the number of links to follow from any hypothesis no. Depending on network size/topology, this value typically ranges between 1 and 5
 correctPredictionsThreshold
 Minimal score for p-values calculation. Hypotheses with scores below this value will get NAs for p-value and enrichment p-value. The usual default is -inf within the RankTheHypotheses function, where it is employed.

Value

rankedHypothesis table of results produced by the algorithm

runSCANR

*run ScanR***Description**

This function will return nodes regulated by the given hypothesisGene

Usage

```
runSCANR(network, experimentalData, numberOfDeltaToScan = 5,
  topNumGenes = 150, correctPredictionsThreshold = Inf,
  writeResultFiles = TRUE, writeNetworkFiles = "all", doParallel = FALSE,
  numCores = NULL, quiet = FALSE, outputDir = getwd())
```

Arguments

| | |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| network | Computational Causal Graph, as an igraph. |
| experimentalData | The experimental data read in using ReadExperimentalData . The results is an n x 2 matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. |
| numberOfDeltaToScan | Iteratively scan for 1 to numberOfDeltaToScan delta values |
| topNumGenes | A value to select top genes to report (typically top 100 genes) |
| correctPredictionsThreshold | Minimal score for p-values calculation. Value is passed to RankTheHypothesis - scores below this value will get NAs for p-value and enrichment p-value. The default is Inf, so that no p-values are calculated. |
| writeResultFiles | If set to TRUE the results of the scan will be written to two text files in the working directory. Default is TRUE. |
| writeNetworkFiles | If set to "all" .sif files and corresponding _anno.txt files will be generated for the top correctly explained, incorrectly explained and ambiguously explained nodes. If set to "correct" they will only be calculated for correctly explained nodes. If set to "none", no networks will be generated. Default is "all". |
| doParallel | A flag for running RankTheHypothesis in parallel mode. Default is FALSE. |
| numCores | Number of cores to use if using parallel mode. If the default value of NULL is used, it will attempt to detect the number of cores available and use all of them bar one. |
| quiet | a flag to suppress output to console. FALSE by default. |
| outputDir | the directory to output the files to. Default is the working directory |

Value

returns list of genes from each delta scan run

Examples

```

numberOfDeltaToScan <- 2
topNumGenes <- 4
#get path to example network file
networkFile <- system.file(package = 'CausalR', 'extdata', 'testNetwork.sif')
#create ccg
network <- CreateCCG(networkFile)
#get path to example experimental data
experimentalDataFile <- system.file(package = 'CausalR', 'extdata', 'testData.txt')
#read in experimental data
experimentalData <- ReadExperimentalData(experimentalDataFile, network)
#run in single threaded mode
runSCANR(network, experimentalData, numberOfDeltaToScan, topNumGenes)
#run in parallel mode
runSCANR(network, experimentalData, numberOfDeltaToScan, topNumGenes,
          doParallel = TRUE, numCores = 2)

```

ScoreHypothesis

score hypothesis

Description

Score a single hypothesis, using the predictions from the network and the experimental data returning a vector of scoring statistics

Usage

```
ScoreHypothesis(matrixOfPredictions, matrixOfExperimentalData)
```

Arguments

```

matrixOfPredictions
    a matrix of predictions
matrixOfExperimentalData
    a matrix of experimentaldata

```

Value

scoreBreakdown a vector giving, in order, the overall score, and the numbers of correct, incorrect and ambiguous predictions

Examples

```

predictions <- matrix(c(1,2,3,+1,0,-1),ncol=2)
experimentalData <- matrix(c(1,2,4,+1,+1,-1),ncol=2)
ScoreHypothesis(predictions,experimentalData)
CompareHypothesis(predictions,experimentalData)

```

`ValidateFormatOfDataTable`*validate format of the experimental data table*

Description

Checks the format of the experimental data. This is expected to be two columns, the first containing the gene name and the second the direction of regulation, -1, 0 or 1. The function checks the number of columns and the values of the second column,

Usage`ValidateFormatOfDataTable(dataTable)`**Arguments**`dataTable` the data table to be tested**Value**

true if the data table is valid

`ValidateFormatOfTable` *validate format of table*

Description

Checks the format of the loaded in data. In particular expects a table with threecolumns (in order) a initiating gene, an interaction ('Activates','Inhibits') and a responding gene and checks the number of rows and the values of the middle column.

Usage`ValidateFormatOfTable(dataTable)`**Arguments**`dataTable` the table to be tested**Value**

true if the test is satisfied.

WriteAllExplainedNodesToSifFile

Write all explained nodes to Sif file

Description

Outputs networks of all explained nodes in .sif file format, named by node name with sign of regulation, each with a corresponding annotation file for producing visualisations using Cytoscape.

Usage

```
WriteAllExplainedNodesToSifFile(scanResults, network, experimentalData, delta,
  correctlyExplainedOnly = TRUE, quiet = TRUE)
```

Arguments

| | |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| scanResults | a results object produced by ScanR |
| network | a computational causal graph |
| experimentalData | The experimental data read in using ReadExperimentalData . |
| delta | the number of edges across which the hypothesis should be followed, the setting should be that used to generate the input ScanR object. |
| correctlyExplainedOnly | if TRUE network files will only be produced for correctly explained nodes. If FALSE network files will be produced for each of correctly explained, incorrectly explained and ambiguously explained nodes. |
| quiet | a flag to suppress output to console. FALSE by default. |

Value

files containing paths from hypothesis node to explained nodes in sif format and corresponding annotation (_anno.txt) files

Examples

```
networkFile <- system.file(package='CausalR', 'extdata', 'testNetwork1.sif')
network <- CreateCCG(networkFile)
experimentalDataFile <- system.file(package='CausalR', 'extdata', 'testData1.txt')
experimentalData <- ReadExperimentalData(experimentalDataFile, network)
delta <- 2
scanResults <- runSCANR(network, experimentalData, numberOfDeltaToScan = delta,
  topNumGenes = 2, writeResultFiles = FALSE, writeNetworkFiles = "none",
  quiet = FALSE, doParallel = TRUE, numCores = 2)
WriteAllExplainedNodesToSifFile(scanResults, network, experimentalData, delta,
  correctlyExplainedOnly = TRUE, quiet = TRUE)
```

 WriteExplainedNodesToSifFile

Write explained nodes to Sif file

Description

Outputs networks of explained nodes in .sif file format for producing visualisations using Cytoscape. Output will be to a directory beginning with a timestamp,

Usage

```
WriteExplainedNodesToSifFile(hypothesisnode, signOfHypothesis, network,
  experimentalData, delta, outputDir = getwd(), outputFileName = "",
  correctlyExplainedOnly = FALSE, quiet = FALSE)
```

Arguments

`hypothesisnode` a hypothesis node

`signOfHypothesis`
the direction of change of hypothesis node

`network` a computational causal graph

`experimentalData`
The experimental data read in using [ReadExperimentalData](#). The results is an n x 2 matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. The name of the first column is the filename the data was read from.

`delta` the number of edges across which the hypothesis should be followed

`outputDir` the directory to output the files to. Default is the working directory

`outputFileName`
a character string to use for the name of the output files. Default value is "", which results in files using the default naming convention of "network file name-data file name-delta value-node name". Set to NA if not writing to file.

`correctlyExplainedOnly`
if TRUE network files will only be produced for correctly explained nodes. If FALSE network files will be produced for each of correctly explained, incorrectly explained and ambiguously explained nodes.

`quiet` a flag to suppress output to console. FALSE by default.

Value

files containing paths from hypothesis node to explained nodes in sif format and corresponding annotation (`_anno.txt`) files

Examples

```
hypothesisnode <- "Node0"  
signOfHypothesis <- +1  
networkFile <- system.file(package='CausalR', 'extdata', 'testNetwork1.sif')  
network <- CreateCCG(networkFile)  
experimentalDataFile <- system.file(package='CausalR', 'extdata', 'testData1.txt')  
experimentalData <- ReadExperimentalData(experimentalDataFile, network)  
delta <- 2  
WriteExplainedNodesToSifFile(hypothesisnode, signOfHypothesis, network, experimentalData, delta,  
                             outputFileName=NA)
```

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