

Package ‘CausalR’

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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')  
ccg <- CreateCCG(network)  
predictions <- MakePredictions('NodeA', +1, ccg, 2)  
AnalysePredictionsList(predictions,8)
```

CalculateEnrichmentPValue

calculates an enrichment p-value

Description

Calculate a 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

threeByThreeContingencyTable
a 3x3 contingency table

logOfFactorialOfPredictionListStats
log of Factorial of prediction statistics

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

Value

a D-value (or weight)

CheckPossibleValuesAreValid
check possible values are valid

Description

Checks if the a given set of possible values for n++, n+-, n-+ and n- are agree with the predicted and experimental data

Usage

```
CheckPossibleValuesAreValid(predictionDataStats, experimentalDataStats,
    possibleValues)
```

Arguments

predictionDataStats
a vector of predicted results

experimentalDataStats
a vector of observed experimental results

possibleValues a vector of possible values n++, n+-, n-+ and n-

Value

TRUE if and only if the given vector of possible values is valid

CheckRowAndColumnSumValuesAreValid
check row and column sum values are valid

Description

Checkes to see if the values of r+, r-, c+ and c- which are stored in rowAndColumnSumValues define a valid contingency table

Usage

```
CheckRowAndColumnSumValuesAreValid(rowAndColumnSumValues, predictionListStats,
    experimentalResultStats)
```

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 | <i>compare hypothesis</i> |
|-------------------|---------------------------|

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 | <i>create a Computational Graph (CG)</i> |
|----------|--|

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 | <i>create network from table</i> |
|------------------------|----------------------------------|

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_- , q_0 and n_+ , n_- , n_0 .

Usage

```
FindMaximumDValue(predictionListStats, experimentalDataStats,
  logOfFactorialOfPredictionListStats, returnlog = FALSE)
```

Arguments

`predictionListStats`
a vector containing the predicted values q_+ , q_- and q_0 : numbers of positive, negative and non-significant/contradictory predictions

`experimentalDataStats`
A vector containing the observed values n_+ , n_- and n_0 : 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_{-+} , n_{--} , n_{0+} and n_{0-} , 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 q_0 (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 $n \times 2$ 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. |
| 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 arecalculated 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 *get node name*

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')
cgg = CreateCCG(network)
nodeID <- 10
GetNodeName(cgg, 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(PPIInet, Expressiondata, delta, hypothesisGene = "",
  signOfHypothesis = 1, outputfile = "")
```

Arguments

| | |
|------------------|--|
| PPIInet | 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 postive, negative, or non-significant/contradictory predictions (q+, q- and q0) |
| experimentalResultStats | a vector containing the number of postive, 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 suppress 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 predictionListStats

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 | <i>make predictions</i> |
|-----------------|-------------------------|

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')  
ccg <- CreateCCG(network)  
predictions <- MakePredictions('NodeA', +1, ccg, 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')  
ccg <- CreateCCG(network)  
MakePredictionsFromCCG('NodeA', +1, ccg, 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 *order hypotheses*

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

plot graph with node names

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')
cgg <- CreateCCG(network)
PlotGraphWithNodeNames(cgg)
```

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

| | |
|-----------------------------|--|
| network | Computational Causal Graph, as an igrph. |
| experimentalData | 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. |
| delta | Distance to search within the causal graph. |
| 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 bottom half of the table can be filled in using the results of calculations performed earlier. |
| listOfNodes | 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 NULL; here the algorithm will calculate and store results for all the nodes in the network. |
| 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. |
| 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, removeDuplicataes)
```

Arguments

| | |
|-------------------|---|
| fileName | a file containing the experimental data (text file format) |
| network | a (Computational) Causal Graph, as an igrph. |
| removeDuplicataes | 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 x 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(PPInet, Expressiondata, delta, correctPredictionsThreshold)
```

Arguments

| | |
|-----------------------------|---|
| PPInet | PPInet 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 igrph. |
| 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 experimetal 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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