

Package ‘CausalR’

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Author Glyn Bradley, Steven Barrett, David Wiley, Bhushan Bonde, Peter Woollard, Chirag Mistry, David Riley, Mark Pipe

Maintainer Glyn Bradley <glyn.x.bradley@gsk.com>, Steven Barrett <steven.j.barrett@gsk.com>, Bhushan Bonde <bkbonde@gmail.com>

Description Causal reasoning methods for biological networks, to enable regulator prediction and reconstruction of regulatory networks from high dimensional data.

Depends R (>= 3.2)

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VignetteBuilder knitr

biocViews GraphAndNetwork, Network

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

Causal Reasoning algorithms for biological networks, including predictions, scoring, p-value calculation and ranking.

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 hypotheses on a single CCG

Author(s)

David Riley <david.riley@tessella.com>, Chirag Mistry, Mark Pipe

References

- "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 *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	<i>create a Computational Causal Graph (CCG)</i>
-----------	--

Description

Creates a computational causal graph from a network file.

Usage

```
CreateCCG(filename)
```

Arguments

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

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_- , q_0 , n_+ , n_- and n_0 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, data, delta)
```

Arguments

hypothesisnode a hypothesis node

signOfHypothesis
the direction of change of hypothesis node

network a computational causal graph

data a data file

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

<code>r_p</code>	row sum r+
<code>r_m</code>	row sum r-
<code>c_p</code>	column sum c+
<code>predictionListStats</code>	approximate values of n_{++} , n_{+-} , n_{-+} and n_{--}
<code>experimentalDataStats</code>	a vector containing the values q_+ , q_- and q_0 : number of positive, negative, non-significant/contradictory predictions
<code>logOfFactorialOfPredictionListStats</code>	a vector containing the values n_+ , n_- and n_0 : number of positive, negative, non-significant/contradictory observations
<code>returnlog</code>	return result as log, default value is FALSE

Value

the maximum D_{fam} 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 positive, 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 q_0 the number of positive/negative/non-significant (or contradictory) predictions)

`experimentalDataStats`
 a vector containing the values n_+ , n_- and n_0 (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')
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 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.

<code>symmetricCCG</code>	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
<code>correctPredictionsThreshold</code>	A threshold on the number of correct predictions for a given hypothesis. If a hypothesis produces fewer correct predictions than <code>predictionsThreshold</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 <code>correctPredictionsThreshold</code> is set as -Inf, so that the p-values are calculated for all specified hypotheses.
<code>experimentalDataStats</code>	Stats from the experimental data
<code>quiet</code>	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

<code>matrixOfPossibleValues</code>	values of <code>n++</code> , <code>n+-</code> , <code>n-+</code> and <code>n--</code> that need to be assessed
<code>predictionDataStats</code>	a table of predictions
<code>experimentalDataStats</code>	a table of observed experimental data
<code>logOfFactorialOfPredictionListStats</code>	a vector containing the log of the factorial value for each entry in <code>predictionListStats</code>

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, display = TRUE)
```

Arguments

<code>network</code>	built from iGraph
<code>hypothesisnode</code>	hypothesis node ID
<code>targetnode</code>	target node ID
<code>showbothdirs</code>	where multiple paths from a positive and negative node, FALSE returns only the shortest. Otherwise both are returned.
<code>display</code>	if true, echo the resulting paths to the screen

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')
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

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)
```

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.
<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.

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 progress output. 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.

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
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')
#read in experimental data
expData<- ReadExperimentalData(fileName, ccg)
#run in single threaded mode
RankTheHypotheses(ccg, expData, 2)
#run in parallel mode
RankTheHypotheses(ccg, expData, 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
cgg <- CreateCCG(network)
#get path to example experimental data
fileName<- system.file(package='CausalR', 'extdata', 'testData.txt')
ReadExperimentalData(fileName, cgg)
```

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 = 1, doParallel = FALSE,
  numCores = NULL)
```

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. 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.
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.

Value

returns list of genes from each delta scan run

Examples

```
NumberOfDeltaToScan <- 2
topNumGenes <- 4
#get path to example network file
network <- system.file(package = 'CausalR', 'extdata', 'testNetwork.sif')
#create ccg
cgg <- CreateCCG(network)
```



```
#get path to example experimental data
fileName<- system.file(package = 'CausalR', 'extdata', 'testData.txt')
#read in experimental data
expData <- ReadExperimentalData(fileName, ccg)
#run in single threaded mode
runSCANR(ccg, expData, NumberOfDeltaToScan, topNumGenes)
#run in parallel mode
runSCANR(ccg, expData, NumberOfDeltaToScan, topNumGenes,
          doParallel = TRUE, numCores = 2)
```

ScoreHypothesis	<i>score hypothesis</i>
-----------------	-------------------------

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.

`WriteExplainedNodesToSifFile`*Write explained nodes to Sif file*

Description

Outputs a network of explained nodes in .sif file format for producing visualisations using Cytoscape

Usage

```
WriteExplainedNodesToSifFile(hypothesisnode, signOfHypothesis, network, data,
  delta, file, display = TRUE)
```

Arguments

<code>hypothesisnode</code>	a hypothesis node
<code>signOfHypothesis</code>	the direction of change of hypothesis node
<code>network</code>	a computational causal graph
<code>data</code>	a data file
<code>delta</code>	the number of edges across which the hypothesis should be followed
<code>file</code>	a character string (without extension) that determines the names of the files created. Extension is added automatically. Set to NA if not writing to file.
<code>display</code>	determines if the output written to file is also displayed

Value

two files containing paths from hypothesis node to explained nodes in sif format

Examples

```
hypothesisnode <- "Node0"  
signOfHypothesis <- +1  
network <- system.file(package='CausalR', 'extdata', 'testNetwork1.sif')  
cgg <- CreateCCG(network)  
data <- system.file(package='CausalR', 'extdata', 'testData1.txt')  
delta <- 2  
WriteExplainedNodesToSifFile(hypothesisnode, signOfHypothesis, cgg, data, delta,  
  file=NA, display=TRUE)
```

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