Package 'CausalR'

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Type Package

Title Causal network analysis methods

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

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VignetteBuilder knitr

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`CausalR-package` *The CausalR package*

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 statisitical 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
- "Assessing statistical significance in causal graphs", Chindelevitch *et al.*, BMC Bioinformatics **13** 35 (2012). doi: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 *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
ccg = CreateCCG(network)
```

CreateCG *create a Computational Graph (CG)*

Description

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

Usage

```
CreateCG(sifFile)
```

Arguments

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

Value

a CG network

Examples

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

CreateNetworkFromTable *create network from table*

Description

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

Usage

```
CreateNetworkFromTable(dataTable)
```

Arguments

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

Value

an igraph network

`DetermineInteractionTypeOfPath`
determine interaction type of path

Description

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

Usage

```
DetermineInteractionTypeOfPath(network, nodesInPath)
```

Arguments

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

Value

a signed integer representing the paths sign

`FindApproximateValuesThatWillMaximiseDValue`
find approximate values that will maximise D value

Description

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

Usage

```
FindApproximateValuesThatWillMaximiseDValue(predictionListStats,
  experimentalDataStats)
```

Arguments

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

Value

a 2x2 contingency table which approximately maximises D

References

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

`FindIdsOfConnectedNodesInSubgraph` *find Ids of connected nodes in subgraph*

Description

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

Usage

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

Arguments

`idsOfConnectedNodes`
: a list of connected nodes in the full graph

`subgraphOfConnectedNodes`
: a subgraph

Value

a list of connected nodes in the subgraph

`FindMaximumDValue` *find maximum D value*

Description

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

Usage

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

Arguments

`predictionListStats`
: a vector containing the predicted values q+, q- and q0: numbers of positive, negative and non-significant/contradictory predictions

`experimentalDataStats`
: A vector containing the observed values n+, n- and n0: numbers of positive, negative and non-significant/contradictory observations

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

`returnlog`
: should the result be returned as a log; default FALSE

Value

the maximum possible D value

`GetAllPossibleRoundingCombinations` *get score for numbers of correct and incorrect predictions*

Description

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

Usage

```
GetAllPossibleRoundingCombinations(twoByTwoContingencyTable)
```

Arguments

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

Value

a matrix of rounding combinations

GetApproximateMaximumDValueFromThreeByTwoContingencyTable

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

Description

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

Usage

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

Arguments

threeByTwoContingencyTable	approximate values of n++, n+-, n-+, n–, n0+ and n0-, these values are calculated to optimise the D-value (see page 6 of Assessing statistical significance of causal graphs)
predictionListStats	a vector containing the values q+, q- and q0 (the number of positive/negative/non-significant (or contradictory) predictions)
logOfFactorialOfPredictionListStats	a vector containing the log of the factorial value for each entry in predictionListStats
returnlog	return the result as a log, default is FALSE

Value

an approximate maximum D value or weight

GetApproximateMaximumDValueFromTwoByTwoContingencyTable

computes an approximate maximum D value or weight

Description

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

Usage

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

Arguments

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

Value

the maximum D value or weight

GetCombinationsOfCorrectandIncorrectPredictions

returns table of correct and incorrect predictions

Description

Returns the numbers of correct and incorrect positive and negative predictions

Usage

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

Arguments

predictionDataStats	prediction data statistics table
experimentalDataStats	Experimental data statistics table

Value

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

`GetExplainedNodesOfCCG` *Get explained nodes of CCG*

Description

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

Usage

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

Arguments

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

Value

vector of explained nodes

`GetInteractionInformation` *returns interaction information from input data*

Description

Gets the interaction information from the input data

Usage

```
GetInteractionInformation(dataTable)
```

Arguments

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

Value

a vector of interaction information

`GetMatrixOfCausalRelationships` *compute causal relationships matrix*

Description

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

Usage

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

Arguments

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

Value

causal relationships matrix

`GetMaxDValueForAFamily` *get maximun 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 Signifcance 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 Signifcance 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 predictionListStats 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 he 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 *get CCG node ID*

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')
ccg = CreateCCG(network)
nodeID <- 10
GetNodeName(ccg, nodeID)
```

GetNumberOfPositiveAndNegativeEntries

counts the number of positive and negative entries

Description

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

Usage

```
GetNumberOfPositiveAndNegativeEntries(dataList)
```

Arguments

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

Value

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

Examples

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

GetPathsInSifFormat *Get paths in Sif format*

Description

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

Usage

```
GetPathsInSifFormat(arrayOfPaths)
```

Arguments

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

Value

network visualisation

`GetRegulatedNodes` *get regulated nodes*

Description

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

Usage

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

Arguments

`PPInet`	a protein-protein interaction network
`Expressiondata`	a table of observed gene expression data
`delta`	the number of edges to follow along the network. This should typically be between 1 and 5 dependent on network size/topology
`hypothesisGene`	the name of the hypothesis gene
`signOfHypothesis`	the sign of action expected from the hypothesis, +1 for up regulation, -1 for down
`outputfile`	the file to which the results should be written

Value

Nodes regulated by hypothesis gene

`GetRowAndColumnSumValues`
get row and column sum values

Description

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

Usage

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

Arguments

`predictionListStats`
: a vector containing the number of postive, negative, or non-signficant/contradictory predictions (q+, q- and q0)

`experimentalResultStats`
: a vector containing the number of postive, negative, or non-signficant/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 af a matrix of correct and incorrect prediction scores

Value

the corresponding score for the given row

GetScoresForSingleNode *Get scores for single node*

Description

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

Usage

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

Arguments

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

`experimentalDataStats`
: Stats from the experimental data

`quiet`
: a flag to supress progress output

Value

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

`GetScoresWeightsMatrix` *get scores weight matrix*

Description

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

Usage

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

Arguments

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

`predictionDataStats`
: a table of predicions

`experimentalDataStats`
: a table of observed experimental data

`logOfFactorialOfPredictionListStats`
: a vector containing the log of the factorial value for each entry in 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 differientially 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')
ccg = CreateCCG(network)
hypothesisnode = 1
targetnode = 10
GetShortestPathsFromCCG (ccg, 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

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')
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 Chindelevich 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 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. 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 experimetal data
experimentalData <- ReadExperimentalData(experimentalDataFile, network)
#run in single threaded mode
RankTheHypotheses(network, experimentalData, 2)
#run in parallel mode
RankTheHypotheses(network, experimentalData, 2, doParallel=TRUE, numCores=2)
```

ReadExperimentalData *read experimental data*

Description

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

Usage

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

Arguments

fileName	a file containing the experimental data (text file format)
network	a (Computational) Causal Graph, as an igraph.
removeDuplicates	Optional, defaults to true. Remove duplicated nodes the experimental file (i.e. where the result for a node is repeated, use the first value given only; the alternative is to return a result which contains multiple rows for this node).

Value

(n 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. Dedepending on network size/topology, this value typically ranges between 1 and 5
correctPredictionsThreshold	Minimal score for p-values calculation. Hypotheses with scores below this value will get NAs for p-value and enrichment p-value. The usual default is -inf within the RankTheHypotheses function, where it is employed.

Value

rankedHypothesis table of results produced by the algorithm

runSCANR *run ScanR*

Description

This function will return nodes regulated by the given hypothesisGene

Usage

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

Arguments

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

Value

returns list of genes from each delta scan run

Examples

```
numberOfDeltaToScan <- 2
topNumGenes <- 4
#get path to example network file
networkFile <- system.file(package = 'CausalR', 'extdata', 'testNetwork.sif')
#create ccg
network <-  CreateCCG(networkFile)
#get path to example experimental data
experimentalDataFile <- system.file(package = 'CausalR', 'extdata', 'testData.txt')
#read in 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 ambigous 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 exepects 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 satisfed.

`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(), outputFilesName = "",
  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
outputFilesName	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,
                             outputFilesName=NA)
```

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