

# Package ‘CausalR’

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

**Maintainer**

Glyn Bradley <glyn.x.bradley@gsk.com>, Steven Barrett <steven.j.barrett@gsk.com>

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

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

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## 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 statististical 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)

Glyn Bradley, Steven J. Barrett, Chirag Mistry, Mark Pipe, David Riley, David Wille, Bhushan Bonde, Peter Woollard

## References

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

---

|                  |                            |
|------------------|----------------------------|
| AddIDsToVertices | <i>add IDs to vertices</i> |
|------------------|----------------------------|

---

### 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 | <i>add weights to edges</i> |
|-------------------|-----------------------------|

---

### 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

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

## Usage

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

**Arguments**

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

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

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

**Value**

TRUE if the table is valid; otherwise FALSE

---

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

---

**Description**

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

**Usage**

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

**Arguments**

`matrixOfPredictions`  
a matrix of predictions

`matrixOfExperimentalData`  
a matrix of experimental data

`ccg`  
a CCG network (default=NULL)

`sourceNode`  
A starting node (default=NULL)

**Value**

a matrix containing predictions, observations and scores.

**Examples**

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

---

ComputeFinalDistribution  
*compute final distribution*

---

**Description**

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

**Usage**

ComputeFinalDistribution(resultsMatrix)

**Arguments**

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

**Value**

distributionMatrix a matrix containing the reference distribution for the score

---

ComputePValueFromDistributionTable  
*compute a p-value from the distribution table*

---

**Description**

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

**Usage**

ComputePValueFromDistributionTable(scoreOfHypothesis, distributionMatrix,  
totalWeights)

**Arguments**

scoreOfHypothesis  
                    a score of hypothesis  
distributionMatrix  
                    a distribution table presented as a matrix  
totalWeights    a matrix of total weights

**Value**

a p-value

CreateCCG

*create a Computational Causal Graph (CCG)***Description**

Creates a computational causal graph from a network file.

**Usage**

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

**Arguments**

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

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

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

**Value**

an igraph object containing the CCG.

**Note**

CreateCG and CreateCCG create causal and computational causal graphs respectively.

**References**

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

**Examples**

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

---

**CreateCG***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 <a href="#">ReadExperimentalData</a> . The results is an n x 2 matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. The name of the first column is the filename the data was read from. |
| delta            | the number of edges across which the hypothesis should be followed                                                                                                                                                                                                                                                                                                                                                                                    |

### Value

vector of explained nodes

---

GetInteractionInformation

*returns interaction information from input data*


---

### Description

Gets the interaction information from the input data

### Usage

```
GetInteractionInformation(dataTable)
```

### Arguments

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

**Value**

a vector of interaction information

---

GetMatrixOfCausalRelationships

*compute causal relationships matrix*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

causal relationships matrix

---

GetMaxDValueForAFamily

*get maximum D value for a family*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

the maximum DFam Value

**References**

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

---

GetMaxDValueForAThreeByTwoFamily

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

---

**Description**

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

**Usage**

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

**Arguments**

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

|                                     |                                                                                                                  |
|-------------------------------------|------------------------------------------------------------------------------------------------------------------|
| logOfFactorialOfPredictionListStats | a vector containing the log of the factorial for each element in the prediction-ListStats object                 |
| returnlog                           | whether or not the maximum D value should be returned as a log (TRUE). Otherwise a non-logged value is returned. |

**Value**

Maximum D<sub>fam</sub> 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<sub>++</sub>, n<sub>+-</sub>, n<sub>-+</sub> and n<sub>--</sub>. 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<sub>ab</sub> is approximately equal to  $q_a \cdot n_b / t$  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 <sub>++</sub> , n <sub>+-</sub> , n <sub>-+</sub> and n <sub>--</sub> , these values are calculated to optimise the D-value                               |
| predictionListStats                 | a vector containing the values q <sub>+</sub> , q <sub>-</sub> and q <sub>0</sub> the number of positive/negative/non-significant (or contradictory) predictions)                 |
| experimentalDataStats               | a vector containing the values n <sub>+</sub> , n <sub>-</sub> and n <sub>0</sub> (the number of positive/negative/non-significant (or contradictory) transcripts in the results) |
| logOfFactorialOfPredictionListStats | a vector containing the log of the factorial value for each entry in predictionListStats                                                                                          |
| returnlog                           | whether or not the value should be returned as a log (TRUE) or not (FALSE)                                                                                                        |

**Value**

the maximal D-value

**References**

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

---

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

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

a scalar or vector containing the node ID or IDs requested

---

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

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

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

**Examples**

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

---

GetNumberOfPositiveAndNegativeEntries

*counts the number of positive and negative entries*

---

**Description**

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

**Usage**

```
GetNumberOfPositiveAndNegativeEntries(dataList)
```

**Arguments**

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

**Value**

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

**Examples**

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

---

GetPathsInSifFormat

*Get paths in Sif format*

---

**Description**

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

**Usage**

```
GetPathsInSifFormat(arrayOfPaths)
```

**Arguments**

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

**Value**

network visualisation

---

|                   |                            |
|-------------------|----------------------------|
| GetRegulatedNodes | <i>get regulated nodes</i> |
|-------------------|----------------------------|

---

**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 | <i>get row and column sum values</i> |
|--------------------------|--------------------------------------|

---

**Description**

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

**Usage**

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

**Arguments**

predictionListStats

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

experimentalResultStats

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

**Value**

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

**References**

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

---

GetScoreForNumbersOfCorrectandIncorrectPredictions

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

---

**Description**

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

**Usage**

```
GetScoreForNumbersOfCorrectandIncorrectPredictions(matrixRow)
```

**Arguments**

matrixRow

a row of a matrix of correct and incorrect prediction scores

**Value**

the corresponding score for the given row

---

GetScoresForSingleNode

*Get scores for single node*


---

## Description

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

## Usage

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

## Arguments

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

experimentalDataStats  
Stats from the experimental data

quiet  
a flag to supress progress output

### Value

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

---

GetScoresWeightsMatrix  
*get scores weight matrix*

---

### Description

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

### Usage

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

### Arguments

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

predictionDataStats  
a table of predicions

experimentalDataStats  
a table of observed experimental data

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

### Value

a matrix containing scores and logs of the weights

---

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

---

**Description**

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

**Usage**

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

**Arguments**

`predictionListStats`

a vector containing the values  $q_+$ ,  $q_-$  and  $q_0$

`experimentalDataStats`

a vector containing the values  $n_+$ ,  $n_-$  and  $n_0$

`epsilon`

the algorithms tolerance epsilon

**Value**

a matrix containing the ternary dot product distribution

**References**

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

---

`GetSetOfDifferentiallyExpressedGenes`*get set of differentially expressed genes*

---

**Description**

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

**Usage**

```
GetSetOfDifferentiallyExpressedGenes(results)
```

**Arguments**

`results`

a table of results

**Value**

a matrix of differentially expressed genes

**References**

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

---

GetSetOfSignificantPredictions

*get set of significant predictions*

---

**Description**

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

**Usage**

GetSetOfSignificantPredictions(predictions)

**Arguments**

predictions      a table of predictions

**Value**

a matrix of positive and negative predictions

**References**

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

---

GetShortestPathsFromCCG

*get shortest paths from CCG*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

a list of vectors containing the nodes of individual paths

**Examples**

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

---

GetWeightForNumbersOfCorrectandIncorrectPredictions

*get weight for numbers of correct and incorrect predictions*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

none

---

GetWeightsAboveHypothesisScoreAndTotalWeights  
*get weights above hypothesis score and total weights*

---

**Description**

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

**Usage**

GetWeightsAboveHypothesisScoreAndTotalWeights(r\_p, r\_m, c\_p,  
predictionListStats, experimentalDataStats,  
logOfFactorialOfPredictionListStats, hypothesisScore, logepsDMax, logDMax)

**Arguments**

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

**Value**

score data

---

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

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

a vector containing the hypothesis score and the total weight

---

```
GetWeightsFromInteractionInformation
```

*get weights from interaction information*

---

**Description**

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

**Usage**

```
GetWeightsFromInteractionInformation(interactionInfo)
```

**Arguments**

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

**Value**

a matrix of weights corresponding the the direction of regulation

---

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

---

### Description

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

### Usage

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

### Arguments

|                         |                                                                                                                                  |
|-------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| hypothesisnode          | the node in the causal graph from which predictions should be made. Can be either a (numerical) node ID or a (string) node name. |
| signOfHypothesis        | whether the hypothesis node is up- or down-regulated. Should be +1 or -1.                                                        |
| network                 | a (Computational) Causal Graph, as an igraph.                                                                                    |
| delta                   | the distance to search within the causal graph.                                                                                  |
| nodesInExperimentalData | optional. Nodes to include in the output. Should be a list of node IDs.                                                          |

### Value

a matrix of predictions for the given particular hypothesis

### Examples

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

---

|                        |                                  |
|------------------------|----------------------------------|
| MakePredictionsFromCCG | <i>make predictions from CCG</i> |
|------------------------|----------------------------------|

---

### Description

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

**Usage**

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

**Arguments**

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

**Value**

an matrix containing the relationship between each node and the hypothesis

**Examples**

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

---

MakePredictionsFromCG *make predictions from CG*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

an matrix containing the relationship between each node and the hypothesis

**Examples**

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

---

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

---

**Description**

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

**Usage**

```
OrderHypotheses(scoresMatrix)
```

**Arguments**

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

**Value**

a ranked table of hypotheses

---

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

---

**Description**

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

**Usage**

```
PlotGraphWithNodeNames(igraph)
```

**Arguments**

`igraph` internal an igraph representation of an interaction network

**Value**

network visualisation

**Examples**

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

---

PopulateTheThreeByThreeContingencyTable

*populate the three-by-three contingency table*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

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

---

PopulateTwoByTwoContingencyTable

*Populate Two by Two Contingency Table*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

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

**References**

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

---

ProcessExperimentalData

*process experimental data*

---

**Description**

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

**Usage**

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

**Arguments**

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

**Value**

processed experimental data formatted ready for scoring

---

|                   |                            |
|-------------------|----------------------------|
| RankTheHypotheses | <i>rank the hypotheses</i> |
|-------------------|----------------------------|

---

## Description

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

## Usage

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

## Arguments

|                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>network</code>                     | Computational Causal Graph, as an <code>igraph</code> .                                                                                                                                                                                                                                                                                                                                                                                                            |
| <code>experimentalData</code>            | The experimental data read in using <a href="#">ReadExperimentalData</a> . The results is an <code>n x 2</code> matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. The name of the first column is the filename the data was read from. |
| <code>delta</code>                       | Distance to search within the causal graph.                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <code>epsilon</code>                     | The threshold that is used when calculating the p-value using the cubic algorithm (see 'Assessing statistical significance in causal graphs').                                                                                                                                                                                                                                                                                                                     |
| <code>useCubicAlgorithm</code>           | An indicator specifying which algorithm will be used to calculate the p-value. The default is set as <code>useCubicAlgorithm = TRUE</code> which uses the cubic algorithm. If this value is set as <code>FALSE</code> , the algorithm will use the much slower quartic algorithm which does compute the exact answer, as opposed to using approximations like the cubic algorithm.                                                                                 |
| <code>use1bAlgorithm</code>              | An indicator specifying whether the 1a or 1b (default, faster) variant of the cubic algorithm described in Chindelevitch's paper will be used to calculate the p-value.                                                                                                                                                                                                                                                                                            |
| <code>symmetricCCG</code>                | This flag specifies whether the CCG is assumed to be symmetric. The value is set as <code>TRUE</code> as a default. If this is the case the running time of the algorithm is reduced since the bottom half of the table can be filled in using the results of calculations performed earlier.                                                                                                                                                                      |
| <code>listOfNodes</code>                 | A list of nodes specified by the user. The algorithm will only calculate and store the results for the nodes in the specified list. The default value is <code>NULL</code> ; here the algorithm will calculate and store results for all the nodes in the network.                                                                                                                                                                                                 |
| <code>correctPredictionsThreshold</code> | A threshold on the number of correct predictions for a given hypothesis. If a hypothesis produces fewer correct predictions than <code>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 correctPredictionsThreshold is set as -Inf, so that the p-values are calculated for all specified hypotheses. |
| quiet      | a flag to suppress output to console. FALSE by default.                                                                                                                                         |
| doParallel | A flag for running RankTheHypothesis in parallel mode.                                                                                                                                          |
| numCores   | Number of cores to use if using parallel mode. If the default value of NULL is used, it will attempt to detect the number of cores available and use all of them bar one.                       |
| writeFile  | A flag for determining if the output should be written to a file in the working directory. Default is TRUE.                                                                                     |
| outputDir  | the directory to output the files to. Default is the working directory                                                                                                                          |

### Value

A data frame containing the results of the algorithm.

### References

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

### Examples

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

---

ReadExperimentalData    *read experimental data*

---

### Description

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

### Usage

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

**Arguments**

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

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

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

**Value**

(n 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 | <i>read .sif to Table</i> |
|--------------------|---------------------------|

---

**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 | <i>run ScanR</i> |
|----------|------------------|

---

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

## Value

returns list of genes from each delta scan run

**Examples**

```

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

```

---

ScoreHypothesis

*score hypothesis*


---

**Description**

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

**Usage**

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

**Arguments**

```

matrixOfPredictions
    a matrix of predictions
matrixOfExperimentalData
    a matrix of experimentaldata

```

**Value**

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

**Examples**

```

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

```

---

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

---

**Description**

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

**Usage**

```
ValidateFormatOfDataTable(dataTable)
```

**Arguments**

`dataTable`          the data table to be tested

**Value**

true if the data table is valid

---

`ValidateFormatOfTable`    *validate format of table*

---

**Description**

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

**Usage**

```
ValidateFormatOfTable(dataTable)
```

**Arguments**

`dataTable`          the table to be tested

**Value**

true if the test is satisfied.

---

WriteAllExplainedNodesToSifFile

*Write all explained nodes to Sif file*


---

## Description

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

## Usage

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

## Arguments

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

## Value

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

## Examples

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

---

WriteExplainedNodesToSifFile

*Write explained nodes to Sif file*


---

## Description

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

## Usage

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

## Arguments

|                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| hypothesisnode         | a hypothesis node                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| signOfHypothesis       | the direction of change of hypothesis node                                                                                                                                                                                                                                                                                                                                                                                                            |
| network                | a computational causal graph                                                                                                                                                                                                                                                                                                                                                                                                                          |
| experimentalData       | The experimental data read in using <a href="#">ReadExperimentalData</a> . The results is an n x 2 matrix; where the first column contains the node ids of the nodes in the network that the results refer to. The second column contains values indicating the direction of regulation in the results - (+)1 for up, -1 for down and 0 for insignificant amounts of regulation. The name of the first column is the filename the data was read from. |
| delta                  | the number of edges across which the hypothesis should be followed                                                                                                                                                                                                                                                                                                                                                                                    |
| outputDir              | the directory to output the files to. Default is the working directory                                                                                                                                                                                                                                                                                                                                                                                |
| outputFileName         | a character string to use for the name of the output files. Default value is "", which results in files using the default naming convention of "network file name-data file name-delta value-node name". Set to NA if not writing to file.                                                                                                                                                                                                            |
| correctlyExplainedOnly | if TRUE network files will only be produced for correctly explained nodes. If FALSE network files will be produced for each of correctly explained, incorrectly explained and ambiguously explained nodes.                                                                                                                                                                                                                                            |
| quiet                  | a flag to suppress output to console. FALSE by default.                                                                                                                                                                                                                                                                                                                                                                                               |

## Value

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

**Examples**

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

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